Adaptation and Validation of an Individualised Paediatric Health-Related Quality of Life Measure (Paediatric Measure Yourself Medical Outcome Profile) and its Evaluation in a Clinical Setting

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THESIS ABSTRACT

There is evidence that the measurement of patient-reported outcomes (PROs) during or before clinical encounters can improve patient outcomes. Individualised PRO measures (PROMs) are known to empower patients by incorporating their values, goals and preferences in clinical encounters. There is no validated, individualised, generic, PRO assessment tool for paediatric populations available. The objectives of the PhD were to 1) assess evidence on the effectiveness of the use of PROMs in clinical practice; 2) adapt and validate an adult individualised health-related quality of life (HRQOL) measure, Measure Yourself Medical Outcome Profile (MYMOP), for clinical use for children 7-11 years old; and 3) conduct a pilot study to evaluate the administration methods and feasibility of application of the new tool in a clinical setting.

A systematic search was performed using a controlled vocabulary relating to the terms, clinical care setting, and patient-reported outcomes. An English-language study was included if it was a randomised controlled trial (RCT) with a PROM as an intervention in a patient population. Included studies were synthesised and their methodologic quality appraised using the Cochrane Risk of Bias tool. Twenty-two RCTs reporting on 25 comparisons of efficacy were included in the systematic review. Overall, positive findings in favour of the PROM intervention were reported on 21 occasions, but these effects were robust in only five cases, (i.e. were statistically significant and adequately powered). While combined evidence supports the use of PROMS in clinical practice, standards of reporting remain inadequate, with many published RCTs failing to pre-specify primary and secondary outcomes or adequately power their comparisons for clinically meaningful differences.

Adaptation of the MYMOP was achieved via the following four iterative steps: 1. an online survey of local paediatricians and paediatric trainees; 2. a focus group discussion with paediatricians; 3. an online survey with paediatric research experts and paediatricians across Australia; and 4. interviews with child-parent pairs in a clinical setting. Four paediatricians completed the first survey, five paediatricians participated in the focus group, and four paediatric HRQOL research experts completed the second survey. Twenty-five children (17 from general medicine, and eight from a diabetes/endocrine clinic) aged 7-11 years completed the draft paediatric MYMOP (P-MYMOP) with parental help in a few cases and were interviewed afterwards. Analysis of the interview data were performed according to Braun and Clarke's (2006) guidelines on thematic analysis. An inductive, interpretative approach with realist epistemology was used. Data from the completed P-MYMOP and interviews demonstrated that the majority of participating children were able to identify their own problems and activity limitations, and all children in the study understood the 7-point faces-scale. Most parents and children perceived that the P-MYMOP would be useful to complete before clinic appointments and enthusiastically welcomed the opportunity for their children to have a voice in a setting where they are often passive recipients of care.

Finally, a feasibility pilot study was performed in the Department of General Medicine Outpatient clinic, Women's and Children's Hospital in Adelaide. The participants of this study were clinic nurses and doctors working in the Department of General Medicine. The study ran for 19 days with 11 doctors and eight clinic nurses taking part. The newly content-validated Paediatric MYMOP (P-MYMOP) was distributed to children 7-11 years old, who were invited to take their completed form to their doctors to discuss it. Both the participating nurses and doctors found the P-MYMOP to be feasible to use in the clinic and distribution of the tool and its integration into the clinical consultation did not appear to compromise nurses'

or doctors' time management. In addition, interviews with clinicians suggest this tool would be a welcome addition to care of their paediatric patients.

The P-MYMOP is the first content-validated generic individualised HRQOL measure for children. The wording, layout, and scale of the P-MYMOP have been successfully adapted for children 7-11 years old. Given validation is an iterative process, further research to assess its reliability and construct validity is needed but results thus far suggest that this tool would be welcomed by children, carers and healthcare practitioners.

DECLARATION

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint award of this degree.

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To my husband, thank you Aamir for being a support and understanding why I was not home most of the weekends.

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List of Abbreviations

MYMOP	Measure Yourself Medical Outcome Profile
P-MYMOP	Paediatric Measure Yourself Medical Outcome Profile
PRO	patient-reported outcome
PROM	patient-reported outcome measure
HRQOL	health-related quality of life
RCT	randomised controlled trials

PUBLICATIONS CONTRIBUTING TO THIS THESIS

1. S. Ishaque, Prof. J. Karnon, Dr G. Chen, Dr R. Nair, Dr A.B. Salter

   A Systematic Review of Randomised Controlled Trials Evaluating the Use of Patient-reported Outcome Measures (PROMs)

   Accepted for publication by the *Quality of Life Research*

2. S. Ishaque, Associate Prof. R. Roberts, Prof. J. Karnon, Dr D. Thomas, Dr A.B. Salter

   Adaptation/Content Validation of Measure Yourself Medical Outcomes Profile (MYMOP) Questionnaire for 7-11 year-old Children

   To be submitted to a peer-reviewed journal

3. S. Ishaque, Associate Prof. R. Roberts, Prof. J. Karnon, Dr D. Thomas, Dr A.B. Salter

   Feasibility of using the Paediatric Measure Yourself Medical Outcome Profile (P-MYMOP) at a Paediatric Outpatient clinic

   To be submitted to a peer reviewed journal

CONFERENCE PRESENTATIONS ARISING FROM THIS THESIS

1. Randomized Controlled Clinical Trials Evaluating the Use of Patient-reported Outcome Measures: A Systematic Review.

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2. Adaptation/Content Validation of Measure Yourself Medical Outcomes Profile (MYMOP) Questionnaire for 7-11 year old Children.

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3. A Systematic Review of Randomized Controlled Trials Evaluating the Use of Patient-reported Outcome Measures (PROMs).

   Accepted for oral presentation at ISOQOL 25th Annual Conference, 24-27 October 2018, Dublin Ireland

CHAPTER 1 THESIS INTRODUCTION

1.1 Project Title

Adaptation and Validation of an Individualised Paediatric Health-Related Quality of Life Measure (Paediatric Measure Yourself Medical Outcome Profile) and its Evaluation in a Clinical Setting

1.2 Background

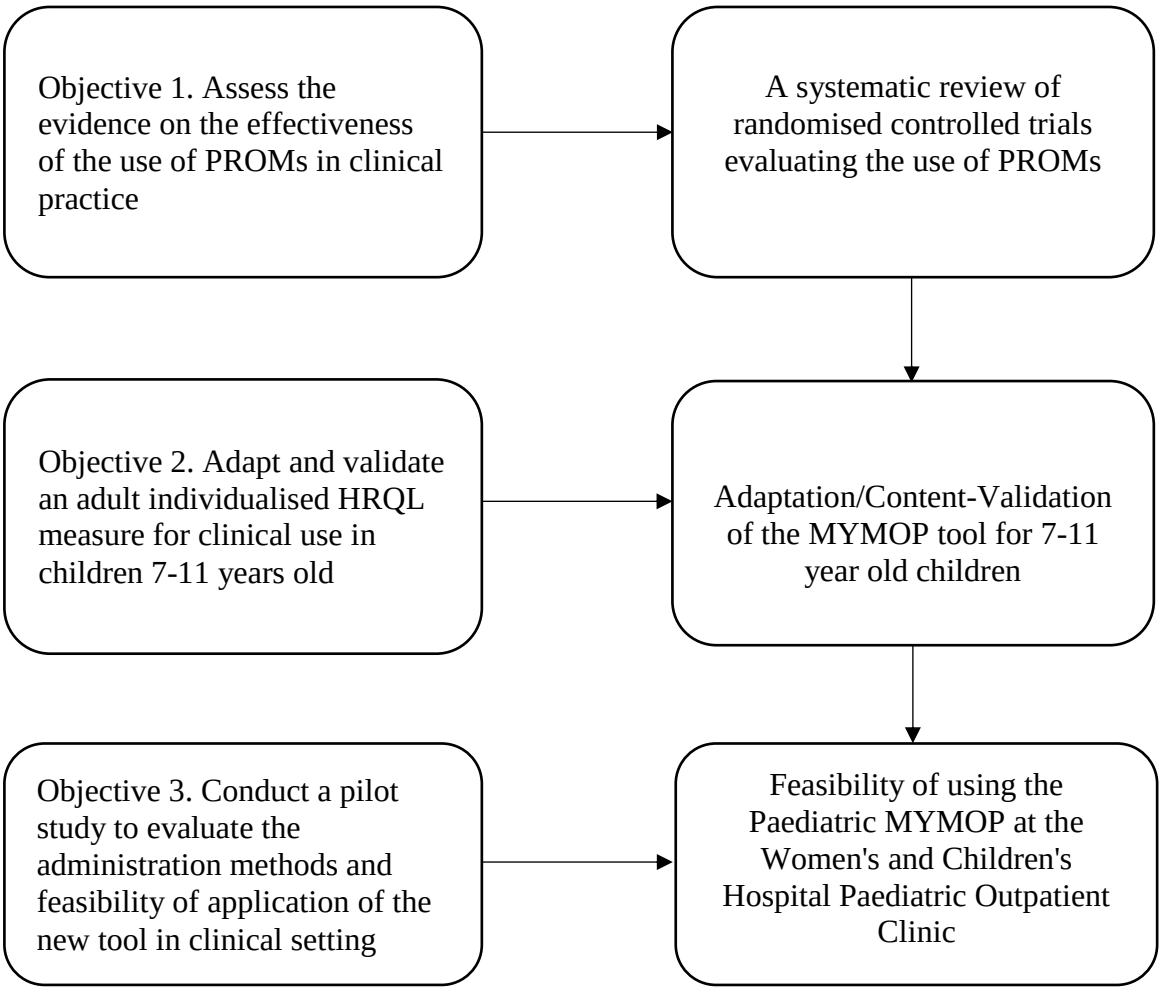
Routine assessment of patient-reported outcomes (PROs) is likely to improve patient outcomes [1]. Individualised patient-reported outcome measures are known to empower patients by including their values, goals and preferences in clinical encounters [2]. However, there is no validated individualised generic paediatric health-related quality of life (HRQOL) tool available [3-7].

1.3 Objectives

The objectives of the PhD project were to: 1) assess the evidence on the effectiveness of the use of patient-reported outcome measure (PROMs) in clinical practice; 2) initiate adaptation and validation of an adult individualised HRQOL measure for clinical use for children 7-11 years old; and 3) conduct a pilot study to evaluate the administration methods and feasibility of application of the new tool in a clinical setting (Figure 1). These objectives were achieved by performing a systematic review of all publications of randomised controlled trials (RCTs) examining the use of PROMs as an intervention to improve patient outcomes, undertaking several iterations to adapt the contents of Measure Yourself Medical Outcome Profile (MYMOP) to make it suitable for children 7-11 years old, and performing a pilot feasibility

study to test the application of Paediatric MYMOP (P-MYMOP) in a general medicine outpatient clinic at a tertiary-care hospital. Figure 1 shows the methods with which each objective of the thesis was achieved.

Figure 1.1 Thesis Objectives



1.4 Thesis Structure

Chapter 2 provides necessary background to the research, considering patient-reported outcomes and the methods with which they are typically assessed. Chapter 2 also describes different types of measurement tools, measurement properties, and paediatric PROMs, and finally, focuses on individualised PROMs, identifying the absence of a validated generic individualised PROM for children.

Chapter 3 is a summary of a preliminary literature search on the evidence of effectiveness of routine measurement of patient-reported outcomes. Based on this search, a systematic review protocol was prepared on the topic.

Chapter 4 is a systematic review of RCTs on the effectiveness of PROM use in routine clinical care. The systematic review has been accepted for publication by the *Quality of Life Research Journal*. Chapter 4 also has a subsection (4.9) that elaborates on the methodological issues identified in the included RCTs. This subsection was not submitted for publication due to word count limitation.

Chapter 5 is a primary study on the adaptation/validation of an adult individualised PROM, MYMOP, for children 7-11 years old.

Chapter 6 presents the rationale for the feasibility study.

Chapter 7 presents results of a feasibility study on the use of the new content-validated individualised measure in a busy outpatient clinic of a tertiary-care hospital.

Chapter 8 provides a discussion of the thesis as a whole.

This thesis is presented in the form of ‘Thesis by publication.’ Chapters 4, 5, and 7 are written as manuscripts for peer reviewed journals. References and Appendices are provided at the end of each Chapter.

1.5 References

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CHAPTER 2. THESIS BACKGROUND

2.1 Patient-Reported Outcomes

The process of healthcare delivery involves the collection of much data, but only a small subset of this is reported by individual patients. Collected data, therefore, can be divided into two broad categories: a) data on objective measures and b) data on patient-reported outcomes (PROs). Examples of objective measures include mortality rates, lab reports, x-rays, and results from other imaging techniques etc. Alternatively, PROs are the direct reports of things such as patients' feelings, satisfaction with care, or quality of life (QOL), independent of input from healthcare providers and/or anyone else [1-3].

Objective measures have been the primary focus in healthcare for decades, but with the paradigm shift of the provision of healthcare towards patient-centred care, PROs are promoted to provide additional experiential understanding and insight into patients' health. It has become clear that while clinical indicators provide only a partial view of the effect of an intervention on patients' health, PROs typically matter most to patients with regard to their health and well-being [4-7]. Common aspects of PROs include: patient symptoms, health status, some aspects of functional status, quality of life, and health-related quality of life (HRQOL).

The inclusion of PROs in research and clinical consultations is encouraged globally by health-governing authorities such as the National Health Services in the UK [8], the Food and Drug Administration in the United States [1,9], the Canadian Institute of Health Information in Canada [10], and in Australia by the Australian Pharmaceutical Advisory Committee of Australia [11]. The National Health Service, which provides healthcare to UK citizens, officially supports the use of PRO assessment, particularly for hip and knee replacements,

hernia and varicose vein surgeries [8]. The Food and Drug Administration has made it obligatory to collect data on PROs for all RCTs on drug labelling claims [1]. The Australian Pharmaceutical Benefits Advisory Committee recognises the assessment of QOL as essential in circumstances where improvement in QOL is the main aim of treatment or where a proposed medicine might cause deterioration to patients' health [11].

2.1.1 Health-related Quality of Life (HRQOL), an example of Patient-Reported Outcomes

In the current era of evidence-based patient-centred medicine, there is increasing advocacy for assessing HRQOL in clinical trials, physician offices, and for resource allocation (where HRQOL is often thought to reflect patients'/clients' satisfaction with a healthcare intervention) [12-14]. HRQOL is a multidimensional, subjective patient-reported outcome, capturing an individual's perception of personal well-being [15].

It is important to define HRQOL comprehensively and to distinguish between QOL and HRQOL. The former is a broad term, defined by the World Health Organisation as

> individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the persons' physical health, psychological state, level of independence, social relationships and their relationship to salient features of their environment' [16, p. 263s].

HRQOL is a comparatively narrower concept and it includes QOL directly associated only with health-related issues. There are numerous comprehensive definitions of HRQOL in the literature. Leidy et al. [17, p. 114] stated that HRQOL is 'an individual's subjective perception of the impact of their health status, including disease and treatment, on

physiological, psychological, and social functioning.' This definition is based on the World Health Organization's definition of health (WHO constitution of 1948) as 'a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity.' Spilker defined the concept as 'the functional effect of an illness and its consequent therapy upon a patient, as perceived by the patient [18, pp. 11-35]. This definition is clearly based on the underlying idea that HRQOL is a subjective construct.

A definition reported for QOL that can be modified for HRQOL is 'the extent to which our hopes and ambitions are matched by experience [19].' For HRQOL this definition could be altered to state 'the extent to which our hopes and ambitions regarding health-related issues are matched by experience.' Currently, there is no consensus on the definition/dimensions of HRQOL. Given the variation in the field, it is important that the developers of HRQOL measures precisely define what they mean by HRQOL so that its implications in a clinical setting can be understood. As a recent attempt to promote standardisation within the field, *The Dictionary of Quality of Life and Health Outcomes Measurement* has defined HRQOL as 'a measure of the value assigned to duration of life as modified by impairments, functional states, perceptions and opportunities, as influenced by disease, injury, treatment, and policy [2, pp. 1325-1326],' and this is the definition adopted within this thesis.

2.1.2 The value of measuring Patient-Reported Outcomes (specifically with HRQOL)

The continued advancements in healthcare has seen populations living longer and an increase in the prevalence of chronic diseases [20-21]. Clinical objective outcomes are often not sufficient for patient management of chronic conditions, in part as a condition of the same severity may affect individuals differently. For example, the same (clinically defined) degree of diabetes might affect two patients differently with one remaining active in many areas of

life and the other experiencing depression and withdrawal from many daily activities. Hence HRQOL measurement is important in order to assess the impact of chronic diseases in populations [14,20,21] and thus help to target appropriate help where it is needed most.

HRQOL measurement is also crucially important in patients receiving end-of-life care, as, in the absence of a complete cure, the only available option is supportive treatment with the hope of betterment in patients' HRQOL. It is particularly beneficial to provide symptomatic treatment to terminally ill patients, as symptom relief is usually associated with better physical, mental and psychological functioning [22-25]. Additionally, in situations where alternative interventions are comparably effective, their effect on patients' HRQOL and hence patients' satisfaction and preferences, might help to differentiate the most appropriate patient-specific choice of treatment.

Beside the above-mentioned clinical uses, HRQOL measurement is also needed for resource allocation and policy making [26,27]. With a limited healthcare budget, different areas of healthcare compete for allocation of resources and decision-makers need some comparable index, which is commonly provided by degrees of change in HRQOL in the form of Quality Adjusted Life Years (QALYs). A QALY is a single index number that is derived by combining quantity and QOL.

2.2 The assessment of Patient-Reported Outcomes

The purpose of PROs is to elicit a patient's voice and involve them in clinical decisions pertaining to their care. The PROs are assessed by questionnaires that are specifically developed for this purpose. Ideally a PRO measurement tool should be patient-centred and

meet the basic requirement of PRO measurement, that is, providing a voice for individual patients.

PRO measurement tools or PROMs can be classified in a number of ways. One classification is based on the type of issues assessed in questionnaire: disease-specific and generic measures [27,28]. Disease-specific PROMs are designed for use by people with a particular health issue whereas generic PROMs are appropriate for anyone to report their health issues. Disease-specific measures focus on a particular disease or disorder and address the most relevant issues for a target population. Thus, these measures are specific and potentially more sensitive in identifying small differences for that population [25]. Generic measures, on the other hand, capture aspects that are broader and applicable to all types of individuals regardless of their illness or disorder. These measures are therefore useful for comparisons between healthy and diseased populations.

PROMs can also be divided into standardised and individualised questionnaires [25]. Standardised questionnaires have a predetermined set of questions (e.g. Short Fort 36 [29]) that are applied across population groups [29,30], whereas individualised questionnaires do not have predetermined domains [28,31]. Instead, individualised measures examine patients' own definitions of HRQOL and challenge the prevailing approach of pre-defined PROs. Both standardised and individualised questionnaires can be disease-specific or generic.

Each approach to PRO measurement has strengths and weaknesses. While standardised measures of PRO are suitable for comparisons between different populations and are useful for economic evaluation, these tools have been criticised for their lack of patient centeredness and the extent to which they truly represent patient values [28,31-36]. For instance, standardised measures may not represent all health domains valued by each individual patient

[31-36]. By asking the same questions for each individual, the standardised tools limit the assessment of personal health and treatment experiences of individual patients [37] to their predetermined fixed questions. In fact, several studies have found predetermined sets of questions on standardised measures to be irrelevant to particular patients [28,31-37].

Individualised PROMs (also known as patient-generated measures) also have some weaknesses. These tools cannot be used to compare different groups or for economic evaluations [28,31,33]. However, individualised PROMs are of particular importance to patients as they reflect their personal values that may not be measured by standardised tools. These instruments are designed to capture the true meaning of PROs by essentially measuring what an individual patient determines to be important about their health and well-being. Individualised measures are superior in picking up individual patient needs, values, and goals, and are reported in the literature to identify issues missed by standardised tools [37]. A recently published primary study by Mayo et al. compared the use of the Patient Generated Index, an individualised measure, to fully standardised generic and disease-specific measures across four populations with disease [38]. The participating populations identified a number of health-related issues that were not presented in the standardised tools [38].

The decision to focus on the use of individualised PROMs to support the provision of patient-centred care for children is based on the following lines of reasoning:

- There is evidence that PROMs support the provision of patient-centred care.
- The cited comparative research indicates that individualised measures may provide advantages over standardised measures when used in clinical practice.
- Individualised measures have been comparatively under-researched compared to standardised tools, especially in children.

2.3 Validation of PROMs

Regardless of the type of PROM used for the assessment of PROs, accurate and consistent measurement of PROs result only from PROMs that are developed systematically and possess sound psychometric properties. Without the required measurement properties, an instrument might not measure what it is supposed to measure, not do so consistently under various circumstances, or might not capture changes in patients' health when they occur.

Important measurement properties identified in the literature include: content validity, construct validity, criterion validity, reliability, and responsiveness [39,40]. International consensus via a Delphi study has been achieved on the definitions of these measurement properties and are thus adopted in this thesis [40]. According to this Delphi study 'content validity is the degree to which contents of a health-related PRO instrument is an adequate reflection of the construct to be measured,' 'construct validity is the degree to which scores of a health-related PRO instrument are consistent with hypotheses based on the assumption that the PRO instrument validly measures the construct to be measured,' and 'criterion validity is the degree to which the scores of a health-related PRO instrument are an adequate reflection of a 'gold standard [40].'' Reliability is defined as 'the degree to which the measurement is free from measurement error,' and 'responsiveness is the ability of a health-related PRO instrument to detect change over time [40]'.

Key measurement properties for any measurement instrument depend upon the purpose of the instrument [39-42]. PRO measures are usually constructed for three purposes: evaluation, discrimination, or prediction. The evaluative instruments are those applied to patients to assess their health in a longitudinal fashion. As a result, while content validity and construct validity are crucial, instruments must also have evidence of responsiveness and test/retest

reliability [22]. Discriminative instruments are applied, for example, to differentiate healthy patients from those with a disease [22,42]. These measurements are conducted at a single point in time. Important psychometric properties for discriminative tools include content validity, cross-sectional construct validity and internal consistency reliability [42,43]. Predictive measures are used for prediction of future health, survival [44,45], resource allocation, and health policy [46], and need to have content and construct validity as a minimum [44-46].

2.4 Paediatric Patient-Reported Outcomes and Patient-Reported Outcome Measures

Further to the psychometric properties discussed above, there are additional requirements for the valid self-assessment of paediatric PROs. These include requirements specific to children and the general characteristics of measurement tools [47]. Some of the challenges identified in the literature include: accounting for the variable cognitive maturity of children, and availability of a valid and reliable questionnaire designed with consideration of the developmental stage and cognitive skills of the target population [47-49].

The challenge of the assessment of PROs in children is implicit in their very definition, in that reports of outcomes/symptoms must come directly from patients without any input from family or healthcare providers [1]. For outcomes to be consistent with this definition, they must be self-reported by patients, which is not possible for children lacking necessary verbal capacity (e.g. infants, young children, and/or children with developmental delays). Accordingly, proxy assessment is the only option for these children, though patient self-reporting is encouraged whenever possible among children with verbal capacity. Nevertheless, in today's paediatric PRO assessment, proxy measurement is considered as an

evaluation of direct patient outcomes and is often discussed alongside PRO measurement for children [50,51]. Alongside discussion on other challenges in the measurement of paediatric PROs, the following paragraphs outline why proxy measurement is not synonymous with the self-assessment of paediatric PROs.

There are other reasons why the application of PROMs to children in the context of clinical care and research is unsatisfactory [48]. Often, adult PROMs are applied to children without consideration of their suitability to this population [48,51-53]. In the healthcare system there can be a tendency to see children simply as small human beings who are only different in terms of their size, with no unique or special needs. The reality, however, is that children are a special population group, with unique needs and must be treated as such.

Furthermore, existing adult PROMs may not be appropriate for use in a paediatric population, as they may not have content validity. In a 2011 systematic review (unpublished—part of an MSc thesis, University of Alberta, S. Ishaque) of individualised HRQOL measures used in children (0-18 years), six major databases were searched from inception to mid-2011; it included clinical trials and observational studies if they assessed HRQOL as their primary or secondary outcome with individualised tools. Sixty-eight studies were included. The review identified five disease-specific and three generic individualised HRQOL measures used to assess the HRQOL of children. With the exception of the Paediatric Asthma Quality of Life Questionnaire (PAQLQ), none of the disease-specific or generic individualised tools were validated for children.

There are other limitations in this approach. For example, in situations when child-specific PROMs are utilised and/or developed, the self-reporting ability of children is often underestimated [52,53] and parents/caregivers/healthcare providers are assumed to be able to

provide an assessment of children's outcomes [52,53]. Compounding this, the opinions of adults are given more weight, and parents/caregivers are often asked to choose and name what may be important to their child. Contrary to the widespread belief that adults are more reliable in completing questionnaires, there is evidence that parents'/caregivers' completed PROMs do not match with their child's perception of their well-being [54-46]. Considerable discordance between parent-proxy-completed to child-completed questionnaires is reported in the literature [50,51,54-58]. This discordance of proxy versus child-completed questionnaires is most profound in the domain of emotional well-being [16,47,54-56], and social interactions [54,55]. Despite this, a high correlation on parent-to-child rating of externally observable measures has been reported [54,55]. Based on this, some argue that the use of parent-proxy for the measurement of externally observable factors is appropriate [56]. However, it is important to remember that the proxy assessment of PROs is still inconsistent with the definition of the concept. Though it may be theoretically sound to assess a child's QOL from a 'parental perspective,' it does not equate to the self-reporting of a QOL. Questions have also been raised about which parent (mother, father or other carer) to use as a proxy if the need arises [16,51,56]. This is because there is evidence that mother's ratings of children's PRO is different from that of their father's [16]. Given this finding, one solution recommended in the literature to avoid systematic error with parent proxy assessment in longitudinal trials is to use the same parent throughout the study [57]. Another important consideration in parent-proxy assessment of children's PROs is the impact of the child's disease and the increased responsibility as a carer on parental well-being which, in turn might affect how parent rate their child's health. Given all the issues with parental-proxy assessment, and most importantly to attain the subjective perspective of children, self-reporting and self-completed PROMs must be applied, unless this is not possible due to a child's inability or unwillingness to do so.

As argued above, self-completion/self-reporting is clearly a necessity for the assessment of PROs for children. Besides the requirement of cognitive maturity of a certain level, another challenge in the assessment of paediatric PROs is the ongoing and sometimes rapid change in developmental stages and needs. Furthermore, all verbal children who are able to complete PRO questionnaires cannot be considered as one homogenous group. For example, the term *child* is loosely applied to individuals 5-16 (or 5-18 years old in some countries) and within this age group children differ considerably according to their developmental stage. A child beyond the age of 7 (or in some cases 5) is considered to be able to reliably complete a self-report PROMs [59]. However, it is not likely that a questionnaire appropriate for a 7 year-old would be suitable for a 14 year-old child. For example, a domain related to sexuality would be important on a questionnaire for teenagers but may be less relevant and possibly inappropriate for young children. Therefore, the consideration of the age-appropriateness of measurement tools is critical for a paediatric population. While developing a PROM for a paediatric population it is critical that the children in the age bracket for which the tool is being created are at a relatively similar developmental stage and are reasonably homogenous in their cognitive abilities [47,60-62].

As mentioned above, to promote self-reporting of PROs for children, there are certain requirements specific to the measurement tools. For example, even for children who have achieved a reasonable cognitive ability and are developmentally mature enough to understand their issues and disease processes, instruments should be simple so that the child can complete them with minimal to no help from their parents/caregivers. Thus, the development of self-reporting paediatric PROMs requires consideration of domains and content suitable for children. This can only occur when the primary respondents, that is, the children, are consulted in the development of a PROM.

Consulting a primary population is also a pre-requisite for achieving content validation of a PROM [47]. Adopting an appropriate reporting or recall period has been identified as one of the potential difficulties with children's self-completion of PROMs. Young children may have difficulties in recalling information and/or in understanding questions asking about what happened over time, for example, 1 week, 2 weeks, or a month ago [50,54,55,]. Therefore, testing what recall periods the target population can comprehend is vital. For the assessment of PROs, after the selection of a domain, the respondent is asked to measure it on a scale. Selection of a scale for a measurement tool can affect the ease with which a child can complete it and thus affect the self-reporting property of a measurement tool. There are different types of scales used in PROMs, such as the Visual Analogue Scale (VAS), Likert Scale, and faces scales [63]. Although several types of scales have been used for children, face-based tools have been found to increase self-reporting among paediatric populations; children as young as three, and as old as seven years have validly used them for pain [64,65] and nausea [66] measurement. Examples of face-based tools include: Faces Pain Scale-Revised [65], Wong-Baker faces pain scale [67] and the Baxter Retching Faces Scale (measuring nausea) [66].

2.4.1 Evidence regarding a Valid Paediatric Generic Individualised Tool

The search for a validated, generic, individualised, paediatric PROM began during my research project within the Master of Clinical Epidemiology at the School of Public Health, University of Alberta in 2011. This unpublished systematic review aimed to specifically identify any generic individualised paediatric HRQOL tool used in children. The review retrieved 68 studies and identified five disease-specific and three generic individualised HRQOL measures used to assess paediatric HRQOL or QOL. The disease-specific tools identified were: PAQLQ [68], Asthma Quality of Life Questionnaire (AQLQ) [69], Patient

Specific Index (PASI-pg) [70], Rhiniconjunctivitis Quality of Life Questionnaire (RQLQ) [69], and Global Quality of Life-8 (GLQ-8) [71]. The generic HRQOL measures identified were: Measure Yourself Medical Outcomes Profile (MYMOP) [72], Patient Generated Index [55, 73], and Schedule for the Evaluation of Individual Quality of Life – Direct Weighting (SEIQOL-DW) [74].

This review was wide in its scope and included all clinical trials and observational studies that assessed paediatric HRQOL by an individualised HRQOL measure. The included studies were therefore not necessarily about the evaluation of psychometric properties of the eight identified tools. It was hypothesised that if a measurement tool was applied to a paediatric population, it would have evidence of validity and reliability for such use. To confirm this hypothesis a further search was performed that targeted paediatric and mixed population studies on the psychometric properties of these tools. The initial search began with the view of identifying a paediatric validated generic individualised HRQOL measure. A second study within that Masters dissertation (unpublished – review of psychometric properties of generic individualised paediatric HRQOL measures) focused on the identification of psychometric studies of the three generic tools used to assess paediatric HRQOL. This search identified six studies [75-80]. The Terwee criteria was used to assess the quality of psychometric properties reported in the studies [81] and the Consensus-based Standards for the Selection of Health Measurement Instruments (COSMIN) were used to evaluate the risk of bias among the included studies [82, 83]. This review of the measurement properties established the lack of sound psychometric properties of the identified tools and a lack of a paediatric, validated, generic, individualised HRQOL measure for their use in a paediatric population [75-80]. The results of these literature reviews served to develop research questions for the present PhD research.

The database searches for both of the above described literature reviews were conducted in 2011, and thus an update was required to ascertain the development of any new paediatric generic individualised tool between 2011 to August 2018. This update was performed by: 1) retrieving and the reviewing literature reviews on generic paediatric measures, and 2) a search update of the unpublished literature reviews in the Masters dissertation summarised above.

2.4.2 Published literature reviews on Paediatric Generic PROMs

In this section, I examine the available generic paediatric PROMs by in published literature reviews on the topic. A Scopus search was conducted to identify literature reviews evaluating the psychometric properties of generic paediatric PROMs. Two recent systematic reviews of generic multidimensional PROMs for children [52,53] provided specific citations, followed by examination of the reference lists within these. A number of literature reviews of paediatric generic PROMs, HRQOL measures, and QOL measures have been published in the literature [50-58,84-90]. Of the 16 identified reviews, four were systematic reviews [52,53,58,87]. Seven of the identified reviews (including one systematic review) discussed methodological considerations for the use of PROMs in children [50,51,54-56,86,87]. The remaining reviews appraised the currently available generic and disease-specific paediatric PROMs. My focus was on the identification of a valid, generic, individualised measure for children, and the following sections will examine the relevant available references.

Janssens et al. [52] published a series of systematic reviews in 2015. In the first, the authors aimed to identify all generic, multidimensional patient-reported outcomes for children from birth to 18 years old, and map the construct that the PROMs claimed to measure; the authors included 35 PROMs meeting their inclusion criteria. [52]. In the second systematic review

psychometric properties of the identified PROMs were evaluated within 35 identified PROM. [53]. Only five PROMs had six or more psychometric properties evaluated, and positive findings for some of these properties were reported for four PROMs. None of the included measures in both reviews were partly or completely individualised.

A systematic review by Solans identified 30 generic and 64 disease-specific HRQOL measures for children of 0-18 years old [87]. This review included all the identified HRQOL measures from the previous three literature reviews [85,88,89] reporting on the literature from 1980 to 2000. The Solans systematic review also included an original search for any additional paediatric HRQOL measures published between 2000 to 2006. Again, no individualised paediatric PROM was included.

Two further literature reviews by Rajmil et al. [89.90] identified paediatric HRQOL measures for Spanish-speaking countries. A narrative review by Schmidt [86] identified 16 generic multidimensional instruments that claimed to measure paediatric HRQOL. Of these, four questionnaires were to be completed by parents. None of the included measures were individualised.

The reviews described above were not designed specifically to identity paediatric generic individualised PROMs, and therefore their search strategy could not retrieve any of these tools. In contrast, the unpublished literatures reviews described in section 2.4.1 as part of my Master of Science in Clinical Epidemiology at University of Alberta were more focused and were specifically performed to identify a validated paediatric generic individualised HRQOL tool. However, the search performed in 2011 was seven years old by the end of my PhD in 2018 and therefore needed to be updated. In the below section (2.4.3) I have reported on this search update.

2.4.3 Updated search to identify Validation of Generic Individualized Paediatric Measures published since 2011

To update the reviews performed as part of the MSc Clinical Epidemiology Thesis, summarised in the Section 2.4.1, a search in the PubMed database was conducted with the search strategy shown in Figure 2.1. To avoid missed studies, I also performed a SCOPUS search with the names of the generic individualised tools identified in my MSc systematic review, that is, PGI, SEIQOL-DW, SEIQOL, and MYMOP. Finally, I searched the six studies [81-83,87-89] included in the review of psychometric of the generic individualised tools, and relevant studies citing these since 2011 until August 2018.

The purpose of these searches was to identify and review any psychometric or validation studies on: a) a new generic individualised HRQOL measure for children, or b) studies that may have validated the previously identified generic individualised tools used for children. Therefore, only studies of psychometric analysis conducted on a paediatric population were included. Inclusion and exclusion criteria are provided in Figure 2.2.

Figure 2.1 PubMed database search strategy

(((health-related quality of life OR hrql OR hrqol OR qol OR quality of life OR health status OR functional status OR activities of daily living OR patient reported outcomes OR patient reported outcome OR patient reported outcome measures OR patient reported outcome instruments OR patient reported outcome instrument OR outcome assessment OR outcome measure OR outcome measures OR patient centered OR patient centred OR patient reported OR patient-reported OR patient oriented OR patient-oriented))

AND (psychometrics OR psychometric OR measurement properties OR clinimetric OR validation study OR validation studies OR valid OR validity OR reliable OR reliability OR responsiveness OR cross cultural validity OR content validity OR content-validity OR face validity OR criterion Validity OR construct validity))

AND (patient generated OR patient generated outcomes OR consumer generated OR patient perspective OR individualized OR individualised OR individualized patient reported outcome measures OR individualized patient-reported outcome measures OR individualised patient reported outcome measures OR individualised patient-reported outcome measures OR individualized patient reported outcomes OR individualised patient reported outcomes OR personalized OR personalised)

Filters: Publication date from 2011/01/01 to 2018/12/31; Humans; English; Child: birth-18 years

Figure 2.2 Inclusion and Exclusion Criteria

Inclusion Criteria

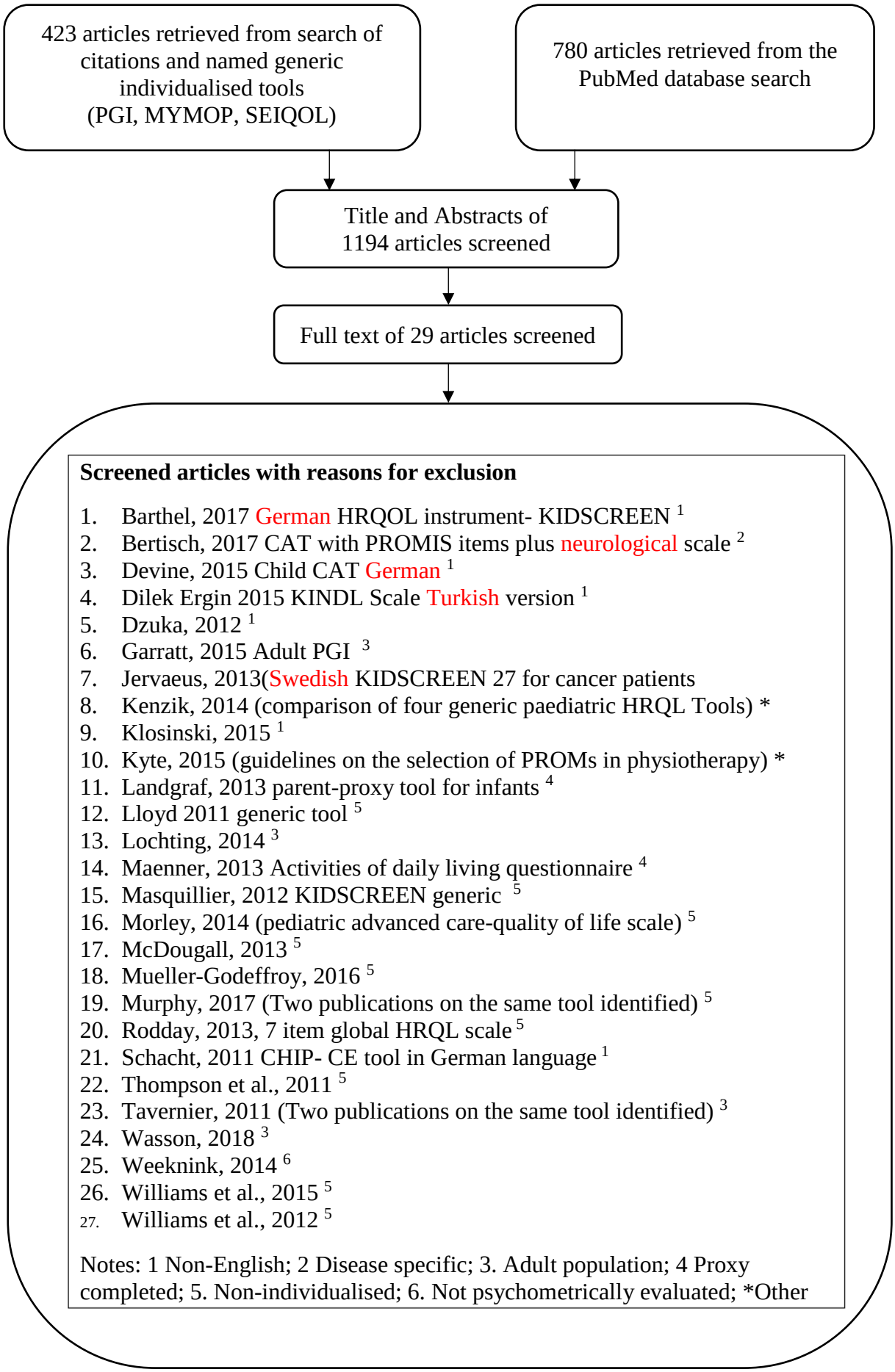
1. Validation studies on generic individualized measures
2. Paediatric population (0-18 years) studies

Exclusion Criteria

1. Disease-specific PROMs
2. Paediatric proxy completed PROMs
3. Studies reporting on the psychometric properties of non-English PROM
4. Studies on preference-based measures
5. Literature reviews

The search yielded 1203 articles, which was reduced to 1194 after removal of duplicates. The titles and abstracts of these 1194 articles were screened to identify relevant studies. The full text of 29 articles was retrieved and screened to find studies reporting on evidence of psychometric analysis of a new or previously identified generic individualised HRQOL measure for their use in children (PGI, SEIQOL-DW, SEIQOL, MYMOP) [91-120]. Two articles reported their results at two different occasions from the validation of the same tools [109,110,114,115]. Conclusions from the full text screen were that none of the 29 identified studies reported a psychometric analysis or the development of any paediatric generic individualised HRQOL measure (see Figure 2.3).

Figure 2.3 Search yield (2011 – 2018)



2.5 Psychometric evidence on the individualised generic HRQOL tools previously used in paediatric populations

Due to the absence of any validated paediatric generic PROMs it was decided to analyse the available psychometric evidence on the three generic individualised tools from psychometric studies conducted in adult populations. Instead of searching for primary studies on psychometric analysis of the identified tool, it was decided to focus on reviews summarising those studies. The reviews of outcome measurement instruments are important tools as they can provide a comprehensive overview of the quality of instruments and thereby can support evidence-based selection of the most suitable instrument for a population [83].

A number of literature reviews on the measurement properties of these adult, individualised HRQOL and QOL measurement tools (PGI, MYMOP, SEIQOL-DW, SEIQOL) have been published [38, 121-124]. A review by Aburub evaluated the feasibility and psychometric properties of two individualised HRQOL tools, namely, the Patient Generated Index and the Schedule for the Evaluation of Individual Quality of Life (SEIQOL) and its short Form (the direct weighting SEIQOL-DW) in adult cancer patients [121]. This review reported that the tools were acceptable, feasible, and responsive to change; furthermore, that both the PGI and SEIQOL were able to identify QOL concerns not represented in other generic standardised HRQOL measures [121]. A systematic review by Wettergren evaluated the feasibility and psychometric properties of SEIQOL-DW [122]. The review included 39 studies that reported on psychometric properties of the tool and the use of the tool in research and clinical settings. It concluded that SEIWOL-DW was feasible and valid in a variety of populations including healthy and ill adults. An older review by Martin published in 2007 evaluated the feasibility and psychometric properties of the PGI [123]. Eighteen studies were included in the review,

and the PGI was found to be valid, with the evidence for reliability being stronger for the versions with a shorter Likert scale. There was no review on the quality of psychometric properties of the MYMOP. Given this, primary studies reporting on the psychometric properties of the MYMOP were retrieved from the literature and are summarised below.

Four primary studies on the measurement properties of MYMOP use in adults were identified [76,77, 124,125]. Two studies reported on the content validity of the tool. The first study (all patients of complementary medicine) compared qualitative interviews of 20 patients with their scores on the MYMOP forms [76]. Revision of the MYMOP was performed, based on participants' feedback [76]. The new MYMOP was named MYMOP2 and is the current version. The MYMOP2 was then applied to acupuncture patients (26-83 years) and in-depth interviews and focus groups were conducted to evaluate content validity [124]. No further revisions were made after the second study.

Studies on construct validation of MYMOP2 reported on correlation of MYMOP score with 'self-perceived change in condition' [77,125] and clinical outcomes measured by physicians [125]. It was hypothesised *post hoc* that MYMOP scores would have a significantly larger correlation with improvement (measured by patient self-perceived change in health condition) for acutely ill patients compared to chronically ill patients [77]. The expected correlation of the MYMOP scores of patients with their corresponding SF36 scores was also studied [77]. While evidence supporting these hypotheses was found in these studies [77, 125], the fact that they were not postulated a priori is a limitation.

Responsiveness was assessed by gradient change in the MYMOP scores on multiple applications across the spectrum of clinical change by physicians [125] and patients [77]. The

change in the MYMOP score of patients who described themselves as ‘a little better’ was compared with the change in scores of patients that reported being ‘about the same,’ by t-test [77]. However, this assessment of responsiveness was not in accordance with current guidelines/standards for evaluation of this measurement property [81, 77, 125] as the groups were intimately related to the outcome of interest.

Proper scaling of responses is crucial for validity and clinical applicability of any HRQL measure. The MYMOP2 has a seven-point rating scale. This was found difficult to comprehend by older people, people with low literacy, and those with little confidence in completing forms [126,127]. Therefore, a faces scale was then introduced, which included faces alongside each number [126,127]. The row of faces represented a continuum of emotion of happiness at one end and worry at the other end. The measure has reported evidence of content validity, construct validity, and responsiveness for adults (see Table 2.1 for a summary of evidence on psychometric properties of the MYMOP).

In summary, none of the included generic individualised measures used to assess paediatric PROs were thoroughly validated for children. Both the PGI and SEIQOL-DW were complicated in their layout. Studies on the PGI have shown that the questionnaire was found to have poor validity in populations with a low education level [128-131], older ages [128,131-135], and for individuals who had physical or mental limitations [131,132,135]. SEIQOL-DW had negative results on content validation for children with diabetes under 12 years of age, partly as children below 12 years could not understand the standard instructions to complete SEIQOL, and about 1/3rd had difficulty in completing the tool [80].

Overall, the MYMOP was the simplest generic individualised tool identified, and thus was chosen for adaptation for a paediatric population. Beside its simplicity, the other reason for

selecting the MYMOP was based on the experience at a paediatric clinical and research group, *CARE Program for Integrative Health & Healing*, Department of Pediatrics, University of Alberta's complementary and alternative paediatric clinic. The MYMOP was used successfully in the complementary and alternative paediatric clinic of the *CARE Program*, with children, possibly as the tool was simple and avoided non-applicable questions to non-verbal and developmentally delayed children.

Table 2.1 Validation of MYMOP

Measurement Property	Methods	Weaknesses/limitations
Content Validity		
	1. Qualitative interviews of 20 patients and comparison of this qualitative data to corresponding MYMOP scores (the current version MYMOP2 was developed as a result) [76]. 2. Twenty-three patients of eight acupuncturists underwent: focus groups, in-depth interview/cognitive interviews [124]. Issues identified were: - floor effect	No revision of the tool was made after the 2004 study [124] which identified that MYMOP had a floor effect (i.e. more than 15% of patients reported the lowest possible score and if they got worse, no further change in their condition could be recorded); periodic conditions such as headache could not be measured.

	- inability to score episodic conditions - inaccurate measurement of medication change	
Construct Validity	1. Correlation between 'perceived change in condition' and MYMOP score was assessed [77,125] 2. Correlation between MYMOP and physician-assessed clinical outcome [125] 3. Known group comparison: MYMOP score in patients with acute conditions (< 4 weeks) was compared to patients with chronic conditions. It was hypothesised that MYMOP score would have a significantly larger correlation with improvement for	No *a priori* hypotheses were defined.

	acutely ill patients compared to chronically ill patients [77]. 4. Correlation of MYMOP to SF-36 scores [77].	
Responsiveness [77,125]	1. Gradient change in MYMOP scores at repeat applications across perceived changes by clinicians and patients 2. Standardised response mean 3. Index of responsiveness 4. t-test conducted to compare the MYMOP scores of patients who reported being a 'little better' to those who were 'about the same.'	Statistics reported were not in accordance with the current guideline [81]

2.6 Characteristics of the MYMOP

The Measure Your Self Medical Outcome Profile (MYMOP) is an individualised tool for adults, which is publicly available for clinical use [72]. It was specifically designed and evaluated for use in primary care. Most of the validation work was conducted in general practitioners' offices.

The current version of the MYMOP has two forms: the initial form, and a follow-up form. The initial form can be filled in by a patient with or without help; it addresses two symptoms, one activity affected by the named symptoms, overall well-being, and medication use. The follow-up form consists of scoring of the originally identified symptoms and activity limitation at the time of follow-up, with a third optional symptom. Each question, except for the medication questions, is scored on a seven-point scale (0-6). High scores indicate worse outcomes. A profile score can be calculated, being a mean of all nominated scaled scores [72].

Within this thesis, the aim of adapting the MYMOP for children was to assess the suitability of MYMOP to supplement clinical encounters through the use of an individualised patient-centred tool in a paediatric setting.

2.7 References

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CHAPTER 3. PATIENT-REPORTED OUTCOME MEASURES (PROMS) IN CLINICAL CARE

3.1 PROMs: their utility in practice

To introduce a new practice in the world of evidence-based medicine, a question that requires a satisfactory answer is: 'how effective is a new practice, relative to standard care?' Evidence-based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients [1]. Hence for PROMs to become an integral part of routine clinical care, PRO assessment is required to empower patients and produce a positive impact on future patient outcomes and/or the process of future healthcare delivery.

3.2 Existing evidence on the use of PROMs in clinical care

To examine the present-day use of PROMs in clinical care, a search was performed in the PubMed database to identify literature reviews evaluating the use of PROMs as an intervention to improve patient outcomes. The search terms used were: reviews, systematic reviews, meta-analysis, patient-reported outcomes, patient-reported outcome measures, and clinical care. The relevant systematic and narrative literature reviews were selected, their reference list was scanned, and relevant cross-references were reviewed. Only literature reviews (systematic and narrative) were included at this stage.

The search identified 21 literature reviews [2-22] on the use of PROMs in adult populations published between1999-2016, of which 13 were systematic reviews [2-5,8-12,14,16,17,22].

The systematic review by Alsaleh [2], Boyce [4], and Chen [8] investigated PROM use in adult oncology patients in various settings. The Alsaleh review focused on the effectiveness of the use of QOL measures, in an oncology outpatient clinic, on patient management by examining published RCTs between January 1990 to December 2012. The review by Boyce investigated the use of PROM feedback for both patient and group level outcomes. The review by Chen investigated the impact of PROM collection among oncology patients on provider behaviour and organisational change. Five of the identified reviews [6, 12, 15, 16, 18] were focused on the use of PROMs in mental health and two focused on palliative care [3,11]. The review by Carlier was reported in Dutch [7] and the review by Mitchell [20] was on screening for distress in cancer patients. The systematic review by Duncan and Murray was on routine outcomes assessment by allied health professionals [9]. A further review by Boyce included qualitative studies, only with no RCTs included [5]. The literature search did not identify any systematic or narrative reviews of paediatric studies on the use of PROs in a clinical setting.

Of 21 identified reviews, seven literature reviews specifically focused on the effect of the presentation of patients' PROM results to their healthcare providers [10,12,13,16,18,19,22]. These reviews are summarised in Table 3.1. All of the reviews identified differed in their aims, scope, and methodological quality; however all of them concluded that the current evidence on the use of PROMs in clinical care is equivocal. Therefore the evidence on the effectiveness of PROMs use in routine clinical care remains inconclusive.

Table 3.1 Literature reviews evaluating the impact of presentation of results of PROMs to physicians

Review	Type of review (no. of studies)	Population	Intervention	Outcomes	Design of included studies	Comprehensive-ness	Quality appraisal	Data pooling	Conclusions and recommend-dations
Espallargues 2000 [10]	System-atic review (n = 21)	Patients, physicians, hospitals / clinics	Impact of presentation of results of patient completed PROMs to physicians	Process of care, diagnosis, use of health services, treatment, health status, patient satisfaction with care	RCTs	MEDLINE (1982-1997), manual searches of the reference lists, contact with authors	Criteria proposed by Guyatt et al. and Sackett et al.	Meta-analysis of trials that included feedback of information about mental health status (diagnosis, notation or recognition, and prescribed medications or treatments)	Some impact on process of care, increased diagnosis and health services utilisation, but no impact on health status
Gilbody 2002 [12]	System-atic review (n = 9)	Patient from psychiatric and non-psychiatric settings	Impact of presentation of results of patient completed	Detection of depression or anxiety, initiation of treatment or	RCTs and qualitative studies	MEDLINE (1966-2000), CINAHL (1982-2000), EMBASE (1981-2000),	Jadad Scale	No meta-analysis was performed. Specific design and features of	Routine HRQOL measurement is costly and there is no evidence

HRQOL instruments to physicians	referral for psychiatric disorders Impact on HRQOL, consulting behaviour, and service use Hospital discharge, re-admission or length of stay Patient satisfaction, physician-patient. communication and cost Acceptability	PsycLIT (to 2000), Cochrane Controlled Trials Register (to 2000), Cochrane schizophrenia and depression, anxiety and neurosis group specialist registers (to 2001)	included studies were reported according to the NHS Centre for Reviews and Dissemination guidline	of its benefit in improving psychological outcomes of patients managed in non-psychiatric settings

Greenhalgh 1999 [13]	Narrative review (n = 13)	Patients and physicians	Impact of presentation of results of patient completed PROMs to physicians	Process of care, patient functioning, patient satisfaction, feasibility, acceptability	RCTs	Database searching 1987-1997 (OVID, MEDLINE, CINAHL (Ovid), Psych-Lit); CRD's strategy, the UK Clearing House on Health Outcomes	CRD Guideliness 1996	No	Weak evidence to suggest use of PROMs can substantially change patient management or patient outcomes. Theory building work to specify what realistic benefits are likely to be gained from PROMs' use are likely to be gained
Kotronoulas 2014 [16]	System-atic review (n = 26)	Adult oncology patients irrespec-tive of the	Impact of presentation of results of patient completed	Process of care outcomes, patient health outcomes,	Random-ised and non-randomised	MEDLINE, EMBASE, CINAHL, PsycINFO, PBCS	Cochrane Risk of Bias Tool	No	There is mixed evidence of the effectiveness of PROMs use in routine care on

		disease stage and their healthcare providers: nurses and/or physicians	PROMs to physicians		controlled trials	(inception – 2012) Reference list of previous reviews and relevant articles were hand searched Study authors were contacted for clarification when needed			patient symptoms, supportive care measures, and patient satisfaction. More research is required on PROM cost-benefit, patient safety, and feasibility
Luckett 2009 [18]	Narrative review (n = 6)	Oncology patients and their healthcare providers	Impact of presentation of results of patient completed PROMs to physicians	Patient satisfaction, health status and resource use	RCTs	MEDLINE, PsycINFO	No	No	Limited evidence for the impact of the presentation of PROM results to their healthcare providers. Information on PROMs was not

									used by physicians,
Marshal 2006 [19]	Narrative review (n = 38)	Physicians and patients	Impact of presentation of results of patient completed PROMs to physicians	Process (communi-cation, patient-doctor agreement about problems and solutions, provider behaviours, patient behaviours; Patient satisfaction with consultation, treatment, or care overall; health status, resource use	Random-ised and non-randomised Controlled trials	MEDLINE (1976 – 2004), reference lists of relevant articles were hand searched	No	No	Acknowledges the lack of clarity in the field in terms of appropriate goals and methods with which they can be achieved. Future studies should evaluate the use of PROMs that capture issues of importance to patients and to measure impacts relating to the patient-provider relationship and

										patient contributions to their well-being. Evaluate the use of PROMs as a means to facilitate patient-centred care, or their full potential in clinical practice will remain unknown.
Valders 2008 [22]	System-atic review (n = 34)	Individual physicians, group of physicians (hospitals, practices), patients	Impact of presentation of results of patient completed PROMs to physicians	Process of care outcomes, satisfaction with care outcomes and patients' health outcomes	RCTs	MEDLINE (until Sep 2007), Cochrane Library Hand searches of the reference list of previous literature reviews Study authors were contacted to help identify additional	Jaded scale	No		Some evidence of improvement in the diagnosis and recognition of problems and patient-physician communi-cation, more work needed before routine

	published / unpublished work	use can be recommended

Centre for Reviews and Dissemination (CRD), Randomised Controlled Trials (RCTs)

Regardless of the evidence of effectiveness on patient outcomes, the evaluation of PROs is in line with provision of patient-centred healthcare, as the assessment of PROs allows patients to present and thereby integrate their values, opinions and wishes into their clinical care [23,24]. Patients are the experts on their own health and well-being. Only they have the internal knowledge of their health problems, and they are the ones who, based on their social and cultural values, can decide what treatment options and lifestyle changes might work best for them. Without respecting and integrating patients' values and desires, the healthcare provided to them will not be patient-centred, and therapies that may have been proved 'effective' on average in a clinical trial setting may not work for an individual patient.

Besides the indefinite conclusion of the identified adult literature reviews and absence of any literature reviews of paediatric studies on the use of PROs in clinical care, it was surprising that none of identified literature reviews evaluated the effectiveness of the use of PROMs as an intervention intended to support the representation of patient values and preferences in clinical encounters. Since systematic reviews of randomised controlled trials are considered to produce the highest level of evidence for the effectiveness of any intervention, it was therefore decided to perform a systematic review of randomised controlled trials with this aim, and to consider the evidence in a subset of paediatric studies. The review protocol was developed and registered with PROSPERO (registration number: CRD42016034182) [25]. The systematic review was performed as part of this PhD thesis and the Manuscript, as presented in Chapter 4 has been submitted to the *Quality of Life Research Journal*.

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CHAPTER 4. A SYSTEMATIC REVIEW OF RANDOMISED CONTROLLED TRIALS EVALUATING THE USE OF PATIENT-REPORTED OUTCOME MEASURES (PROMS)

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Chapter 4 A Systematic Review of Randomised Controlled Trials Evaluating the Use of Patient-reported Outcome Measures (PROMs)

Statement of Authorship

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Name of Principal Author (Candidate)	Sana Ishaque
Contribution to the Paper	Developed the review protocol, conducted database search, screened retrieved articles, extracted data, analysed data, performed methodological quality appraisal of the included articles, conceptualised the manuscript structure, wrote the manuscript. Revised the manuscript based on reviewer's comments and suggestions. Re-submitted for publication.
Overall percentage (%)	75 %
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.
Signature	**Date** 27/09/2018

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);
ii. permission is granted for the candidate in include the publication in the thesis; and
iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

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4.1 Abstract

Background

Patient-reported outcome measures (PROMs) could play an important role in identifying patients' needs and goals in clinical encounters, improving communication and decision-making with clinicians, while making care more patient-centred. Comprehensive evidence that PROMS are an effective intervention is lacking in single randomised controlled trials (RCTs).

Methods

A systematic search was performed using controlled vocabulary related to the terms: *clinical care setting* and *patient-reported outcome*. English language studies were included if they were a RCT with a PROM as an intervention in a patient population. Included studies were analysed and their methodologic quality was appraised using the Cochrane Risk of Bias tool. The protocol was registered with PROSPERO (CRD42016034182).

Results

Of 4,302 articles initially identified, 115 underwent full text review resulting in 22 studies reporting on 25 comparisons. The majority of included studies were conducted in USA (11), among cancer patients (11), with adult participants only (20). Statistically significant and robust improvements were reported in the pre-specified outcomes of the process of care (2), and healthcare (3). Additionally; five, eight, and three statistically significant but possibly non-robust findings were reported in the process of care, health, and patient satisfaction outcomes respectively.

Conclusions

Overall, studies that compared PROM to standard care either reported a positive effect or were not powered to find pre-specified differences. There is justification for the use of a PROM as part of standard care, but further adequately powered studies on their use in different contexts are necessary for a more comprehensive evidence base.

Keywords: patient-reported outcome measures; PROMs; health-related quality of life; HRQOL; HRQOL; quality of life; QOL; patient outcomes; patient-reported outcomes; clinical care.

4.2 Abbreviations/Acronyms

± PROM studies: studies that compared patient completion of a PROM with standard care in the control group

PROM ± summary studies: studies in which all patients completed a PROM and compared the presentation of PROM summary scores to clinicians vs. no presentation of summary scores

FDA: Food and Drug Administration

HRQOL: health-related quality of life

PRO: patient-reported outcomes

PROM: patient-reported outcome measure

QOL: quality of life

RCT: randomised controlled trial

SR: systematic review

4.3 Background

According to the ISOQOL *Dictionary of Quality of Life and Health Outcomes Measurement*, a patient-reported outcome (PRO) is 'a measurement of any aspect of a patient's health that comes directly from the patient, without interpretation of the patient's response by a physician or anyone else' [1]. Patients' experiential knowledge of the effects of any intervention is essential for the delivery of high quality clinical care. All patients in clinical care are unique and therefore may experience different benefits or side effects from the same treatment [2], which cannot be captured by the mere assessment of traditional physiological outcomes. It is therefore important to ask patients about their preferences and values to set self-directed health goals and promote compliance with treatment.

The assessment of PRO requires instruments that are valid and reliable. These instruments are often termed PRO measures (PROMs). It is suggested that regular use of PRO instruments to collect patients' health-related outcomes can affect the health and well-being of patients by improving patient-physician interaction, focusing the clinical encounter on patient-directed concerns, and by promoting shared clinical decision-making [3]. PROMs are commonly used in comparative effectiveness research, comparative safety analysis and economic evaluations to inform resource allocation [4,5], with contexts including the ongoing monitoring of PROs for patients with chronic diseases or in palliative care [6].

The existing evidence on the effectiveness of regular assessment of PROs comes from a variety of sources including observational studies and individual randomised controlled trials (utilising qualitative, quantitative and mixed methods) and gold standard literature reviews of RCTs [7]. The effectiveness of PROMs has been explored in a number of literature reviews [6, 8-25]. Despite having different aims, these synopses [6,8-25] highlight that the evidence is

equivocal. There are several potential reasons for this ambiguity in the field, such as the attempt to aggregate heterogeneous tools under the umbrella term of PROM (which inappropriately considers them equivalent) [26], assessment of different RCT outcomes by various different methods and at different times, as well as a lack of standardised procedures for the provision of PROM results to healthcare providers and methodological issues with primary studies [27].

The aim of this systematic review was to assess the evidence on the effectiveness of the use of PROMs as an intervention intended to support the representation of patient values and preferences in clinical encounters. This review of RCTs is not limited by disease, age of patient population, nor year of publication. In addition, this is the first systematic review to consider the statistical robustness of results reported, and differentiate between the use of PROMs with and without the formal presentation of completed PROMs to treating clinicians.

4.4 Methods

A detailed systematic review protocol outlining the search strategy; methods for relevance and full text screening; data extraction form; quality assessment method; plan for data analysis, synthesis, and statistical issues; sensitivity and subgroup analysis; publication bias, and any conflicts of interest was developed and registered with PROSPERO; registration number: CRD42016034182 [28].

4.4.1 Search strategy

With the help of a health research librarian, a systematic search strategy was developed to search three major databases (PubMed, EMBASE, and PsycINFO) from inception to February 2017.

The search was conducted using controlled vocabulary and keywords related to the terms: *clinical care setting* and *patient-reported outcomes* [28]. The search strategy for the Medline database is included in the Supplementary 1 and was modified to adapt to variations in indexing among the databases. Reference lists of relevant literature reviews [8-13, 21] were also screened to identify additional articles. Citation searches were performed in *Scopus*.

4.4.2 Eligibility criteria

A publication of a study was eligible for inclusion if it reported on a RCT that applied a PROM to patients with or without providing the patients' PROM score (summary/profile/dimension) to healthcare providers as an intervention. The review was restricted to studies that were published and reported in English. There were no restrictions on types of PROM, the form in which the PROM was used as an intervention, the health condition being studied, the country or setting in which the study was conducted.

Trials were excluded if they applied PROMs only for screening of psychological disorders such as depression and anxiety, were in the palliative care setting, compared one type of PROM to another type of PROM, compared only paper application to computer application of the same or different PROMs applied PROMs assessing specific constructs such as pain.

4.4.3 Relevance and full text screening

First: a title, abstract, and keyword screening of initially identified articles was performed. In order to pilot the inclusion criteria, (see review protocol [28]), two authors (SI and RN) initially screened a random 10% of the search results. Discrepancies were discussed and inclusion criteria were modified accordingly. Full text articles identified from this search were retrieved and discussed. Once agreement on the inclusion criteria was achieved, the primary author (SI) completed the relevance-screening with the remaining studies. Next, the

same authors (SI, RN) independently applied the inclusion criteria to full texts of potentially relevant studies (n = 115) to identify studies for final inclusion. Any discrepancies were resolved through discussion. While it was initially planned to contact authors of studies where there was doubt concerning eligibility, this was not necessary as all doubts were resolved by discussion. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines were followed to ensure transparent and comprehensive reporting [29].

4.4.4 Data extraction, analysis, synthesis, and statistical issues

The primary author extracted data from all studies including characteristics of the study design, the nature of the PROM, method of intervention and study outcomes.

Consistent with previous systematic reviews in this setting [9,11,12], study outcomes were classified into three categories: process of healthcare, health outcomes and satisfaction with healthcare. Outcomes relating to how the care was delivered (e.g. consultation time, discussion of quality of life (QOL)/health-related quality of life (HRQOL), return visit referral to other health practitioners, etc.) were classified as ‘process of care’; monitoring of changes in a patient’s QOL/HRQOL or in any symptoms were classified as ‘health outcomes;’ and finally outcomes relating to patients’ satisfaction with healthcare or feasibility were classified as ‘satisfaction with healthcare.’ Given the heterogeneous nature of the data (both for PROMs used and patient populations studied) it was not considered meaningful to perform a meta-analysis.

Positive results (i.e. in favour of the PROM intervention) were considered ‘robust’ when statistically significant differences in a pre-specified outcome were reported for a study which was adequately powered to determine them. Positive non-significant or significant results for

an outcome that was not pre-specified and/or for which the study was not powered to determine were considered ‘non-robust’.

4.4.5 Quality assessment

Three authors (SI, RN/AS) performed methodological quality assessments of seven included studies independently using Cochrane’s Risk of bias tool [30]; any discrepancies were resolved by discussion. Thereafter, the primary author (SI) performed the quality assessment and discussed it with another team member (AS), both carefully considering the reasons for specified rankings.

4.5 Results

After removal of duplicates, 4,302 articles were identified from database searches of which, 77 were found eligible for full text screening. An additional 36 articles (of which 4 were included) were identified from previous literature reviews, and two articles were identified from other sources. After full text screening of 116 articles, 22 RCTs met the inclusion criteria and were consequently included in this systematic review (Figure 4.1) [31-52].

Table 4.1 summarises characteristics of included studies and Table 4.2 presents additional summary details of the RCTs, including the PROMs assessed, the intervention process, and whether training was provided for health providers and/or patients. Based on the nature of the intervention evaluated, articles are grouped into two panels in Table 4.2: 18 studies in which all patients completed a PROM and compared the presentation of the PROM summary scores to clinicians vs. no presentation of summary scores (labelled ‘PROM ± summary’ studies) [31-38,40,41,45-52]; 7 studies that compared patient completion of a PROM with standard care in the control group (i.e. no use of a PROM) (labelled ‘± PROM’ studies) [39,42-44,49].

Studies by Velikova [49] and Rosenbloom [44] compared more than two treatment arms and their data is thus represented in both tables and panels by specific comparisons. For example, the Velikova study (2004) RCT [49] compared PROM with presentation of results to healthcare providers vs. standard care, and PROM without presentation of results to healthcare providers vs. standard care.

Publication dates ranged from 1989 to 2016. Most of the studies took place in the USA [31,32,34,35,38,40,44-46,48,51,52], followed by the UK [43,49,50], Netherlands [36,37,39], Australia [33,41], Ireland [42] and Norway [47]. More than half of the studies (55%) included cancer patients [31-33,35,37,39,41,42,44,47,49,52] and were performed in tertiary hospitals. Four studies [34,40,48,50] were performed in tertiary-care hospitals in sub-specialties other than cancer, and the remaining studies took place in GP/internal medicine/family physician offices [36,38,43,45,46,51]. Six studies reported enrolling only new patients, five studies enrolled only patients who were previously known to clinicians, and the remaining 11 studies did not specify. Sample size calculations to detect a specified effect size for named primary outcomes were reported in 11 studies [31,32,35-37,40-44,49]; three studies reported sample size calculations but their named primary outcome had multiple sub-components with no subsequent P value adjustments for multiple comparisons [39,46,47]; and one performed only a post-hoc power calculation [40].

A total of 23 PROMs were used in these 22 studies (Table 4.2). Reference to previous validation work for all PROMs was provided in the RCTs for each PROM in use. However, an evaluation of whether the PROM was a valid choice for the target population of the RCT in which it was in use was not reported. Cancer-specific (9) or generic tools (8) were most commonly applied; four studies used more than one PROM as an intervention [33,36,41,49] (depression-specific and cancer-specific tools (2), generic and cancer-specific tools (1), and

generic and diabetes-specific tools (1)); and one applied two arthritis-specific tools [40]. The most commonly utilised tool was the European Organization for Research and Treatment of Cancer, Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) (reported in three studies). The Beth Israel/UCLA Functional Status Assessment Questionnaire, the Hospital Anxiety and Depression Scale (HADS), the SF 36 and PedsQL-generic were used in two studies each. The remaining PROM interventions were applied in one study only (Table 4.2).

In 18 studies [31-33,36-47,49-51], PROMs were self-administered by patients on paper (15) or via a computer touch screen (3); in three studies [34,35,48] PROMs were completed via telephone with assistance, and one study[52] (on paediatric patients) varied the administration method according to the child's age. In this latter trial; children younger than 7 years were allowed a parent proxy PROM completion, children aged 7 to 13 years had combined child and parent proxy PROM completion and children >13 years self-administered the PROM.

PROMs were mostly completed in waiting rooms/clinics [32,33,37,38,40,41,44,47,49-51], followed by home/place of convenience [36,39,42,45,46], over the telephone [34,48], first in clinic then subsequently over the telephone [35], a mixture of clinic and telephone interview [52], computer/paper-based completion according to patients' preferences [31], or unspecified [43].

Of the 18 studies that compared presentation of PROM ± summary studies (completion of a PROM with presentation of results to clinicians vs. completion of a PROM alone), [34,36-38,45-52] provided training to clinicians/patients about interpretation of PROM scores. One [42] of the five studies that compared completion of a PROM with no PROM provided training to physicians about the layout of the PROM. The content of the training/education

sessions provided to physicians and patients concerning the interpretation of the PROM varied substantially between studies (Table 4.2).

Table 4.3 summarises outcomes reported in the included studies classified into the three categories: process of care, health, and satisfaction with healthcare. Pre-specified primary outcomes of studies are italicised.

In PROM ± summary studies: a *process of care* outcome was reported in nine studies [31,32,37-40,45-47,51], of which two were primary outcomes [32,37]. In both studies that specified a *process of care* primary outcome intervention, patients reported a significant increase in the discussion of HRQOL issues with their clinician [32,37]. Four studies [31,38,47,51] either did not report if their *process of care* outcomes were of primary or secondary interest, or claimed to power their study around a primary outcome that consisted of multiple sub-components. While these studies reported statistically significant results, their findings are considered non-robust due to the lack of adjustment for multiple comparisons.

Health outcomes were reported in 13 PROM ± summary studies [31,33-37,40,41,45-47,49,52], of which four were primary outcomes [31,36,41,49]. A significant improvement in HRQOL and psychosocial health was reported in the Basch [31] and De Wit [36] studies respectively, whereas Velikova et al. [49] reported no significant difference in self-reported HRQOL, and McLachlan et al. [41] reported that the intervention did not significantly reduce the need for patient information regarding psychological and other health conditions. McLachlan et al. [41] reported a significant decrease in the spiritual needs of intervention patients, but without power for this comparison it was thus considered non-robust (Table 4.4). Cleeland [35] and Ruland [47] reported on studies whose outcomes had multiple sub-components; of which some showed significant improvement in intervention patients (Table

4.3). These effects were similarly considered non-robust given no p-value adjustments for multiple comparisons (of sub-components) were made. Another seven studies [33,34,37,40,45,46,52] reported *health outcomes* without adequate power calculations for these comparisons, of which four reported significant non-robust results. In total, seven significant results for health outcomes were considered non-robust.

Satisfaction with healthcare was reported in seven [34,36,37,40,41,50,51] PROM ± summary studies as one of the outcomes of interest, with none of these studies explicitly specifying it as their primary or secondary outcome. Significantly more intervention patients were reported to be satisfied with their emotional support [37], overall care [36], and management of pain [51] (male patients only); with results categorised as non-robust. Three studies [34,40,41] reported no significant difference between the groups, and one [50] reported a greater (but non-significant) satisfaction with care in the control group.

In ± PROM studies (PROM completion with or without presentation of scores to clinicians vs. Standard Care): four studies [42,44,49] reported on *process of care* variables as one of their non-primary outcomes of interest. Of those, only Velikova [49] reported significantly (but non-robust) greater discussion of intervention patients' HRQOL issues.

Health outcomes were reported in five ± PROM studies [42-44,49] as primary outcomes. Significant improvement in HRQOL of intervention patients was reported by Velikova [49]. Four studies did not report any significant differences in health outcomes [42-44]. *Health outcome* variables were reported as secondary outcomes in Mills [42] and Velikova [49]. Mills [42] reported non-significant (and non-clinically meaningful) poorer lung cancer-specific QOL in the intervention group, whereas Velikova [49] reported non-robust significantly higher physical, emotional, functional well-being, and HRQOL of participants

in the intervention group. The study by Hoekstra [39] reported on change in the prevalence and severity of several symptoms, some of which were reduced significantly, but the lack of adjustment for multiple comparisons rendered them non-robust.

Comparisons on *satisfaction with care* for ± PROM studies were reported in three publications of RCTs [42,44], none of which were positive or statistically significant, thus there was no significant evidence that intervention patients were more satisfied than their comparator group regarding the healthcare that they received.

Feasibility data (including physician satisfaction) on acceptance and the perceived usefulness of the PROM intervention tools were collected in nine studies [32-34,37,40,45,49,50,52] with largely positive results (Table 4.3).

Methodological quality was evaluated using the Cochrane Collaboration's Risk of Bias tool [30], with detailed assessment reported in Supplementary 2. The potential for bias was assessed in the domains of random sequence generation, allocation concealment, detection (blinding of outcome assessment), attrition (incomplete outcome data), and reporting (selective outcome reporting). The risk of introducing systematic error was found to be high in two studies on random sequence generation [46,48], two studies on allocation concealment [46,48], none on detection bias, two on attrition bias [40,46], and six on reporting bias [34,40,46-48,50]. Some studies had missing information, noted by the categorisation of domains as uncertain. Information regarding the likelihood of detection bias (blinding of outcome assessors/data analyst) and allocation concealment was missing in a large number of studies; 13 [32-36,39-41,43-45,48,50] and 10 [34,37-40,43-45,50,51] respectively.

We considered the potential for performance bias (blinding of participants and personnel) difficult to avoid due to the nature of the PROM interventions. However, in one study authors acknowledged that they were able to blind patients and staff to the study hypothesis [44], but not to the interventions, and as such were considered to have low risk of performance bias.

Apart from performance bias, reporting bias was the most common domain, being present in six studies [34,40,46-48,50]. Of those two were conducted in the internal medicine units, one in each of an arthritis, obstetrics and gynaecology, and neurology clinic, and one in a tertiary-care cancer hospital.

4.6 Discussion

This systematic review of results from RCTs evaluating the use of PROMs in clinical practice categorised the reported comparisons into two groups. While in the first group of 18 studies [31-38,40,41,45-52], the intervention participants completed the PROM and had their PROM results presented to the clinicians providing their clinical care (PROM+/- summary), in the remaining seven studies [39,42-44,49] participants in the intervention group were simply asked to complete the PROM (+/- PROM). Reported results were grouped in one of three outcome categories: process of care, health, and satisfaction with care (Table 4.4). Analysis of tabulated results led to the following findings: more positive results were reported for health outcomes, compared to those for the process of care or satisfaction with care; PROM interventions worked better when PROM results were provided to clinicians; and the inclusion of PROM training to clinicians prior to a trial commencement appeared to result in no obvious differences in positive results.

Reviewed studies focused predominantly on statistically significant results, without typically mentioning whether they were clinically meaningful. If the results were positive but non-significant, there was no consideration in the publication of whether this may have been the result of a smaller than necessary sample size. Equally, when results were positive and significant, there was no discussion of whether this was possibly due to an inflated Type I error resulting from multiple comparisons. This concurs with results from the methodological quality assessment, indicating that the most common form of bias was that of reporting bias, regardless of the study context. Indeed, when considering characteristics of studies that may have been more prone to bias in any one (or more) domains, no one type of study appeared more prone.

All positive results were reported in this systematic review, regardless of significance, with Table 4.4 presenting a summary of the results differentiated by robustness, which includes studies reporting no evidence of a difference in treatment groups.

For the 18 studies classified as PROM+/- summary, six [31,32,36,37,41,49] were powered to detect an effect for their pre-specified primary outcome (two *process of care* [32,37] and four *health outcome* variables [31,36,41,49]), with the remaining studies either not pre-specifying a primary outcome, not reporting on power calculations for pre-specified outcomes, or reporting that power calculations were performed for outcomes with multiple sub-components without evidence of this. Of the four studies with *health outcomes* as their primary focus, two reported significant results in favor of the intervention group [31,36]. Non-significant improvement was reported in one study for the intervention group [41] and for the control group in another study [49]. Comparing the characteristics of studies reporting significant versus non-significant effects, there were no identifiable differences in sample size, disease area, clinician training, mean age of participants or risk of bias.

Among seven studies [39,42,44,49] in the group classified as +/-PROM, none reported a *process of care* primary outcome. Five studies [42-44,49] reported a *health outcome* of primary interest with only one [49] reporting results in favor of the intervention, three reporting no significant evidence of a difference [43,44] and one reporting a non-significant poorer effect in the intervention patients [42]. Studies that failed to show any significant difference or reported poorer effects in intervention patients either stated that they did not achieve their desired sample size [42,44] or did not state this but appeared to have a relatively small sample size [43].

A total of 15 comparisons (in all identified studies) were on HRQOL/health status/PROM score outcomes [31,33,34,36,37,42-46,49,52]. One key observation noted in over half of these studies was the lack of discussion on what constitutes a clinically important difference. A predefined 'clinically important' and statistically significant difference in HRQOL was reported in only three comparisons [31,49]. The Mills study [42] reported non-significant non-clinically important poorer HRQOL in intervention patients, but while the Detmar study [37] found no significant difference in health status measured by SF-36; a significantly larger percentage of people in the intervention group had clinically meaningful improved SF-36 scores [53]. The Velikova et al. PROM +/- summary comparison did not find any significant and clinically important HRQOL differences [49]. The remaining studies (8/15) [33,34,36,43-46,52], simply referred to P values to oppose or support the PROM intervention without reference to whether differences were considered to be clinically meaningful. While P values can provide important evidence of a difference in average outcome scores, they indicate only the probability that study findings such as those reported (or more extreme) could have occurred due to chance alone if there really was no difference in the two groups in the underlying population [54,55]. As such, they lack the ability to inform clinicians of whether

(in general) the difference really matters to their patients, that is, if it was clinically meaningful [54,55].

There are a large number of validated PROMs available for use (generic and disease-specific) and their selection for a particular clinical population can be challenging [56]. The fact that different PROMs are often designed for and used in different populations means that the recommendation of one particular PROM over another in any given scenario is generally not possible. Given that studies in this review reported some positive and robust effects of PROM interventions, there is likely to be value in the use of PROMs in clinical care.

Thirteen studies provided training sessions to clinicians (and patients/families in some cases) on the interpretation and understanding of the PROM [34,36-38,42,45-52]. Contrary to our expectation that clinicians would be more engaged in the use of the PROMs if training was provided [57-59], there appeared to be no obvious difference in positive outcomes when this took place. Some studies assessed the feasibility of PROM use, but none evaluated changes in clinicians' perceptions before and after the intervention and thus the role of the clinician in the use of PROMs may require further study to be understood.

Compared to the previous literature [6,8-25], this systematic review provides more contemporary evidence on the use of PROMs in RCTs and additional information about the use of PROMs in children, by including two RCTs with patients under 18 years old. The fact that only two paediatric studies [36,52] met the inclusion criteria and were included in this review highlights the fact that little has been done to understand the value of PROMs in this context. It is well documented that children often struggle to communicate their health issues with parents and clinicians, and so a rationale for the use of PROMs to provide a voice for children is strong. Wolfe et al. [52] reported improvements in children's and parents'

perceptions of talking to doctors, and in parents' understanding of their child's feelings. Clinicians also found PROM reports by children provided useful and new information in many cases [52]. While the study by Wolfe [52] did not report significant effects on primary health outcomes from the PROM intervention, a post hoc analysis of survivors beyond 20 weeks showed significant improvement in the emotional subscale of the PROM and in overall sickness scores. These findings were even stronger in children aged 8 years and older who were more likely to have completed the PROM without a proxy. Hemmingsson [60] recommended the use of self-reporting paediatric PROMs whenever possible, or observable components of HRQOL when parent-proxy assessment is unavoidable, e.g. for young children. The De Wit [36] study on diabetic adolescents also reported a positive effect of PROMs on patients' HRQOL and patient satisfaction with healthcare. Also, provided that haemoglobin A1C levels were kept under control, a positive effect of PROMs on psychological outcomes was reported [36].

Methodological quality was evaluated using the Risk of Bias tool [30]. Detection bias occurs when outcome assessors are not blinded to the group allocation and study hypothesis. Although the studies in this review are considered pragmatic trials, blinding of the data analyst could have been achieved relatively easily.

This review has several methodological strengths. To minimise bias and to ensure that the systematic review was conducted in a transparent manner, a review protocol was submitted to PROSPERO. There are several benefits of developing a review protocol *a priori* as outlined in the PRISMA statement on reporting items for systematic review and meta-analysis protocols [61], and they include assurance that methods are replicable and in line with current recommendations. A comprehensive systematic search of three major databases was

performed to reduce the possibility of missing relevant studies. An especially wide time frame, age range of target population, and disease type was considered.

We acknowledge that there are some limitations of this review. Firstly, the inclusion criteria were restricted to studies published in the English language only. While this means we may have missed some important studies, it is unlikely that our conclusions would change given that previously documented systematic reviews included articles in multiple languages (in French, German, Italian, Russian, or Spanish) and yielded similar results [9,10]. Secondly, the relevance-screening was performed by a single author, and data were extracted by the same author, but the title, abstract, and keywords of a random 10% of the search were independently screened and inclusion criteria was modified after discussion with a second author (RN) and a more cautious (inclusive) approach was taken when screening. We acknowledge that single data extraction could result in missed items, and thus could affect the conclusions of a review. However, in an effort to minimise issues with interpretation, double extraction for the quality assessment and risk of bias analysis was performed. Thirdly, unlike previous systematic reviews, we excluded trials that claimed to use PROMs for screening of psychological conditions. Studies on psychological and mental health conditions were excluded from our systematic review. Patient-reported outcomes in these contexts are typically used for the purpose of diagnosing psychological or mental health conditions. Given that our focus was on the use of PROMs to effectively incorporate patient values and preferences in clinical encounters, these studies did not meet with the aim of our systematic review. Therefore, despite a much larger time frame for inclusion, there were fewer studies in this review compared to previous systematic reviews [6,9-22]. Our justification for this decision was our interest in the use of PROMs as a behavioural intervention and not as a screening tool. Given that the results of screening tools are typically reviewed by clinicians as

part of a process to identify a disease at an earlier stage for secondary prevention, and thus identify patients who require follow-up, their use in this context is not optional. Hence, the use of PROMs as part of diagnostic tools for mental health disorders is different from proposing their use to inform patient-centred decision-making related to the choice of approach to care or treatment, and thus does not add to our evidence base.

4.7 Conclusions

Overall, positive findings in favor of the PROM intervention were reported on 21 occasions but the reported effects were robust in only five cases, i.e. statistically significant and adequately powered. Despite explicit CONSORT guidelines [27], many trials on PROM interventions failed to pre-specify their primary and secondary outcomes and/or adequately power their comparisons for clinically meaningful differences. Despite this, the combined evidence appears to support the use of PROMs to improve communication and decision-making in clinical practice. It is vital that future trials on PROM interventions follow CONSORT guidelines and continue to contribute robust evidence on the use of PROMs in clinical practice.

4.8 Compliance with Ethical Standards

Funding: no external funding was sought to perform this review.

Conflict of Interest: The authors declare that they have no conflict of interest.

Ethical Approval: This review does not contain any studies with human participants performed by any of the authors.

Informed Consent was not applicable to this review as no primary data were collected.

4.9 Addendum: Elaboration of methodological issues identified in the included RCTs not included in the systematic review manuscript accepted for publication

A sample size calculation for a predefined primary outcome was reported in only half of the included RCTs in the systematic review. Explicit reporting of sample size calculations and power calculations (and their underlying assumptions) is required by the CONSORT statement [27] and provide basic requirements to authentically accept or reject a hypothesis on the effectiveness of an intervention. In the included RCTs, results were highlighted if they were statistically significant and positive. The reported statistically significant and non-significant positive results were not examined for their clinical significance in the majority of the included RCTs. Consideration of clinical significance was even more relevant to 15 comparisons (in 12 RCTs) that reported comparisons on HRQOL/health status/PROM score outcomes [31,33,34,36,37,42-46,49,52], more than half of which did not report on what constituted a clinically important difference in their PROM outcome scores.

The achievement of statistically significant differences in HRQOL/health status/QOL scores might look impressive for publication purposes (leading to publication bias—the most common type of bias found in the RCTs included in the systematic review), but if changes reported are not clinically meaningful, they are unlikely to provide enough evidence to bring change in clinical practice. A change in average PROM scores that is considered important by clinicians in consultation with experts on PROMs (i.e. considered clinically significant) is often needed to convince the healthcare industry for formulary and reimbursement decisions, clinicians to include PROM results in clinical consultations, patients to complete PROMs and use the information to make healthcare decisions, and healthcare policy-makers regarding

resource allocation to support the regular use of PROMs in healthcare. Given that only 50% of the included 22 RCTs were adequately powered to find a pre-specified difference in a primary outcome, it is possible that studies reporting positive non-significant results were not achieve statistical significance because of their inadequate sample size. In addition, the reported positive significant results may have been achieved due to a lack of appropriate adjustment for the multiple comparisons that were made. These findings of the lack of specified clinically meaningful differences that were adequately powered and selective reporting of significant findings when multiple comparisons were made were not context specific as they appeared unrelated to study characteristics.

Randomised controlled trials when performed rigorously can provide gold standard evidence on the effectiveness of an intervention. However, the absence of reporting of a sample size in RCTs affects the quality of the trial and makes its results less reliable. The importance of explicit reporting of sample size calculations and how its absence can affect conclusions of an RCT were highlighted first in 1994 by Moher et al. The authors concluded that the appraised RCTs not in favour of the intervention results did not have a sufficient sample size in 25% to 50% of the cases [62]. Future RCTs performed on the effectiveness of PROMs or using PROMs as a primary outcome should include explicit sample size calculations for the main outcomes and the assumptions behind these which include statement of a difference that is considered clinically significant/meaningful.

Since the use of PROMs in randomised controlled trials conducted for medical products development and labelling has been encouraged by the Food and Drug Administration (FDA) [63], a >500% increase in the use of PROMs in pre-market submissions to the Centre for Devices and Radiological Health over a period of six-years (2009-2015) has been observed [64]. Given the lack of explicit reporting of sample size calculations and statement of what

difference would be considered clinically significant for a PROM as an intervention in the majority of RCTs considered in the Chapter 4 systematic review report it would be interesting to audit these pre-marketing submissions to analyse if their use of PROMs in the clinical trials follows recommended best practice.

Table 4.1. Characteristics of studies

Publication ID	Setting (e.g. primary care, emergency room, hospital) country	Clinicians (e.g. residents, surgeon, etc.) sample size of healthcare providers	Patient Population (sample size, age (years), condition/disease) Sample size calculation reported or not	Patient provider relationship (new, known, not reported)
PROM completed and presented to clinicians vs. PROM completed without presentation to clinicians				
Basch 2016 [31]	Tertiary-care cancer hospital USA	Nurse practitioners and treating oncologists Sample size of healthcare providers was not reported	Cancer patients n = 766 (C 42.42%) C mean age (range) 62 (26-88), I mean age (range) 61 (30-91) Sample size calculation was reported	Not reported

Berry 2011[32]	Tertiary-care cancer hospital USA	Members of clinical team at the hospital n = 262 (C 53.2%)	Cancer patients n = 660 (C 49.54%) C mean age (range) 54 (18-86), I mean age (range) 54 (18-89) Sample size calculation was reported	New patients
Boyes 2006 [33]	Medical oncology outpatient clinic at a tertiary-care hospital Australia	Oncologists n = 4	Oncology outpatients n = 80 (C 47.5%) Sample size calculation was NOT reported	New patients
Calkins 1994 [34]	Tertiary-care hospital internal medicine unit USA	Four teams of internal medicine physicians n = 60 (C 47%)	Patients with functional disability n = 497 mean age of all participants at baseline 59 Sample size calculation was NOT reported	Known patients

Cleeland 2011 [35]	Tertiary-care cancer clinic at University of Texas Huston USA	Surgical team's advance practice nurse Sample size of healthcare providers was not reported	Patients with primary lung cancer or lung metastasis n = 100 (C 52%) C mean age (SD) 60.9 (11.8), I mean age 59.2 (13.6) Sample size calculation was reported but there were multiple outcomes and P-values were not adjusted for the comparisons	Not reported
De Wit et al. 2008 [36]	Four paediatric diabetes outpatient clinics Netherlands	Paediatricians n = 13 (C 46%)	Patients with diabetes n = 80 (C 49%) C mean age (SD) 14.9 (1), I mean age (SD) 14.8 (1.1) Sample size calculation was reported	Not reported
Detmar 2002 [37]	Tertiary-care oncology inpatients	Oncologists n = 10	Outpatient palliative chemotherapy patients	Not reported

	Netherlands		n = 214 (C 47%) C men age (range) 55(24-81), I mean age (range) 58 (25-84) Sample size calculation was reported	
Goldsmith 1989 [38]	Family medicine training clinic of Texas Medical Branch USA	General Practitioners n = 27 (C 48%)	Patient with at least one diagnosed chronic disease n = 62 C mean age (SD) 66.9 (9.2), I mean age (SD) 70.3 (8.7) Sample size calculation was NOT reported	Not reported
Kazis 1990 [40]	Two independent arthritis centers at tertiary-care hospitals USA	Rheumatologists	Arthritis patients Centre 1:356 I, 176 attention-placebo, and 175C	Not reported

			Centre 2: 614 I, 306 attention-placebo, and 290 C. Average age (centre 1=56, centre 2= 57) Post hoc power calculation	
McLachlan 2001 [41]	Ambulatory clinics at Peter MacCallum Cancer Institute tertiary-care hospital Australia	Oncologists and coordination nurse	Cancer patients n = 450 Median age of all participants (range) 61 (18-92) Sample size calculation was reported	Known patients
Rubenstein 1989 [45]	Community internal medicine practices, Greater Los Angeles Area USA	Internists in community office practices. n = 76 (C 49%)	N = 649 (C 50%) Sample size calculation was NOT reported	Known patients

Rubenstein 1995 [46]	University Primary Care Clinic Community internal medicine practices, Greater Los Angeles Area USA	Internal medicine house officers n = 73 (C 45%)	Primary care patients n = 557 (C 45%) Sample size calculation was NOT reported	New patients
Ruland 2010 [47]	Outpatient and inpatient clinics of a Tertiary-care hospital Norway	Physicians and nurses treating leukemia patients Sample size of healthcare providers was not reported	Patients starting leukemia or lymphoma treatment n = 145 (C 48%) Sample size calculation was reported but there were multiple outcomes and P-values were not adjusted for the comparisons	New patients
Street 1994 [48]	Department of Obstetrics and Gynecology at Scott and White clinic Texas USA	Resident physicians n = 7	Prenatal patients n = 58 visits (C 47%) Mean age of all participants (range) 21.9 (17-37)	New patients

			Sample size calculation was NOT reported	
Velikova 2004 [49] (comparison 1)	Tertiary-care oncology hospital UK	Oncologists n = 28	Cancer patients n = 214 (C 33%) Mean age of all participants 54.9 SD (12.52) Sample size calculation was reported	New patients
Wagner 1997 [50]	Outpatient epilepsy clinic of a tertiary-care hospital UK	Neurologists n = 2	Epilepsy patients n = 163 patients (C 23%) 210 clinical encounters (C 21%) C mean age (SD) 45(16), I mean age (SD) 43(13) Sample size calculation was NOT reported	Known patients

Wasson 1992 [51]	Three large urban health maintenance organizations internal medicine clinical sites USA	Internists (n = 41) and nurse practitioners (n = =15) n = 56 (C 48%)	Internal medicine patients n = 1522 Sample size calculation was NOT reported	Known patients
Wolfe 2014 [52]	Three large tertiary-care paediatric cancer centers USA	Oncologists and nurses n = 69	Progressive, recurrent, or nonresponsive cancer patients were included n = 104 (control 49%) Sample size calculation was not feasible	Not reported
PROM completed vs. PROM not completed				
Hoekstra 2006 [39]	Two hospitals in the Amsterdam region and general practitioners in the catchment area caring for cancer	General practitioners n = 89	Non-curable cancer with life expectancy of 1-12 months as judged by their physician n = 159 (C 53%)	Not reported

	patients in their palliative phase Netherlands		C mean age 64.6, I mean age 64.1 Sample size calculation was reported but there were multiple outcomes and P-values were not adjusted for the comparisons	
Mills 2009 [42]	Three tertiary-care cancer hospitals Northern Ireland	Not reported	Inoperable lung cancer patients n = 115 (C 50%) I age strata (n): <60 (21), 61-70 (18), 70+ (18) C age strata (n): <60 (20), 61-70 (18), 70+ (20) Sample size calculation was reported	Not reported
Qureshi 2001 [43]	Single primary care clinic with mix catchment area in UK	General practitioners Sample size of healthcare	Participants in the general practitioners' list for 2 years n = 100 (C 50%)	Known patients

		providers was not reported	C mean age (range, median) 43.14(30.75-53.5, 45.5) I mean age (range, median) 44.96 (36-53,48) Sample size calculation was reported	
Rosenbloom 2007 [44] (comparison 1)	Cancer tertiary-care Chicago USA	Nurse practitioners Sample size of healthcare providers was not reported	Advance lung, breast, or colorectal cancer n = 144 (C 49.3%) C mean age 60.4, I mean age 60.2 Sample size calculation was reported	Not reported
Rosenbloom 2007 [44] (comparison 2)	Cancer tertiary-care Chicago USA	Nurse practitioners Sample size of healthcare	Advance lung, breast, or colorectal cancer n = 140 (C 51%) Mean age of all participants 59 Sample size calculation was reported	Not reported

		providers was not reported		
Velikova 2004 [49] (comparison 2)	Tertiary-care oncology hospital UK	Oncologists n = 28	Cancer patients n = 142 (C 50%) Mean age of all participants 54.8 SD (12.52) Sample size was not powered to detect this change	New patients
Velikova 2004 [49] (comparison 3)	Tertiary-care oncology hospital UK	Oncologists n = 28	Cancer patients n = 216 (C 33%) Mean age 54.9 SD (12.52) Sample size calculation was reported	New patients

Notes: C: control group, I: intervention group, SD: Standard Deviation

Table 4.2. PROM used and the process of intervention

Publication ID	Intervention PROM	Type of PROM (generic, disease specific,	Process of intervention	Method of administration of PROM	Department of physician training
PROM completed and presented to clinicians vs. PROM completed without presentation to clinicians					
Basch [31]	STAR	Cancer specific	Patients were randomised to control and intervention arms with stratification by 'computer experienced,' (CE) vs 'computer inexperienced' (CIE) groups.	Self-administered	No training was provided
Berry [32]	ESRA-C	Cancer specific	Patients were randomised to control and intervention groups after second application of PROM. Clinicians of intervention group patients received a summary of participants' self-reported SQLIs	Self-administered	No training was provided
Boyes [33]	Touch screen surveys:	Disease and cancer specific	Each time an intervention group patient completed the survey a	Self-administered	No training was provided

	HADS, SCNS		summary graphical representation of anxiety and depression scores, list of debilitating physical symptoms in the past week, and supportive care needs plus management strategies was generated. Summary scores were added to patient charts		
Calkins [34]	FSQ	Generic	FSQ was applied to all patients. Summary report was only provided to intervention group physicians	Phone	A two-hour seminar with I group physicians regarding PROM report's interpretation, and management of functional disability
Cleeland [35]	MDASI	Cancer specific	On the occurrence of one or more symptom threshold in intervention group email with PROM response was sent to the surgical team's advanced practice nurse	Phone	No training was provided

De Wit et al. [36]	PedsQL generic, PedsQL Diabetes specific	Disease-specific	HRQOL was monitored with PedsQL generic and PedsQL diabetes specific completed before 3month appointment AND HRQOL scores were discussed with patient during the appointment; Control group completed a lifestyle questionnaire instead	Self-administered	Training to interpret and discuss HRQOL scores
Detmar [37]	EORTC QLQ-C30 (Version 3.0)	Cancer specific	Intervention patients' responses to QLQ-C30 were scored and printed as a graphical summary and were given to physicians and patients immediately before consultation; and were added to patient charts	Self-administered	Intervention group physicians had 30 min educational session on interpretation of QLQ-30 summary score. Patients in the intervention group received a similar explanation via mailed pamphlet. If desired a research assistant provided further

					explanation of the summary. No specific guidelines were provided for the use of summary during the medical consultations
Goldsmith [38]	SIP	Generic	SIP scores were provided to the intervention group family physicians immediately before patient consultation;	Self-administered	The intervention group (n = 14) physicians received a one-hour introduction and written instructions on using SIP in clinical setting
Kazis [40]	AIMS, MHAQ	Disease-specific	Intervention consisted of application of PROMs followed by sending health status summary to clinicians on a quarterly basis over a 1-year period;	Self-administered	No training was provided
McLachlan [41]	CNQ, EORTC	CNQ, and EORTC QLQ-	A self-reported questionnaire was completed and summary reports	Self-administered	No training was provided

	QLQ-C30, BDI short form	C30 are cancer specific; BDI Short Form depression specific	were available immediately for consideration during clinical consult. Study coordination nurse discussed the summary with patient and physicians during consultation		
Rubenstein 1989 [45]	The Beth Israel/UCLA Functional Status Assess-ment Questionnaire	Generic	Questionnaire was applied to all patients; a 1-page summary report resembling laboratory test result was provided only to physicians of intervention group patients	Self-administered	I group physicians attended a single two-hour educational and structured discussion program.
Rubenstein 1995 [46]	Beth Israel-UCLA Function-al Status Questionnaire	Generic	Both the experimental and control groups completed the questionnaire. The experimental group physicians were given functional status summary reports and management guidelines regarding patient deficit attached to the front of each new patient's medical record	Self-administered	The I group physicians attended an initial and booster (at three months) half-hour educational session.

Ruland [47]	ITPAs	Cancer specific	All patients completed baseline questionnaire and a choice Interactive Tailored Patient Assessment (ITPA). Summary of intervention group patients added to patients' charts for physicians and nurses	Self-administered	Training provided, but details were not reported
Street [48]	SF-36	Generic	All patients completed SF36 over phone 1-2 days before the consultation. Experimental group's information was included to in their medical record	Phone	I physicians were educated about the PROM report structure and told that it would be included in patient charts.
Velikova [49] (comparison 1)	EORTC-QLQ-C30 and HADS	Cancer specific	Both groups completed PROM questionnaires on a touch screen computer program and the graphic printouts of results were provided to intervention physicians	Self-administered	Physicians were individually trained about interpretations of PROM scores, and to review examples of HRQOL and clinical details of real patients.

					They were asked to review and use the HRQOL results, unless totally inappropriate. Posters with interpretative information were displayed in clinics. No recommendations for specific responses were made.
Wagner [50]	SF-36	Generic	Baseline SF36 was completed by all patients (no feedback was provided at that time), At 6 months f/u the health status profiles of intervention group were printed and handed to the neurologist and added to the patient charts	Self-administered	Two 1-hour training sessions were conducted by principal investigator and a nephrologist with previous experience of using health status instruments in clinical care.

					Another session to discuss the experiences of physicians was conducted three months after the start of I arm.
Wasson [51]	COOP charts	Generic	COOP charts were applied to intervention group patients, who were instructed to hand the results to their clinicians	Self-administered	I group clinicians were educated about the use of PROM in a 10 minutes face to face session.
Wolfe [52]	PediQUEST system included three tools: PQ-MSAS, PedsQL4.0, and an overall sickness question	PedsQL4.0 is generic, PQ-MSAS is cancer specific	Summary report was provided to families immediately after completion, and to clinicians before the clinic visit; email alerts were sent to oncologist, nurse, and psychosocial clinician, the palliative care service, and when pain was reported to pain service.	Varied as per child's age	Training on interpretation of PROM report was provided to families at enrolment and annually to healthcare providers. No training was provided to healthcare

					providers about how to respond to email alerts.
PROM completed vs PROM not completed					
Hoekstra [39]	The Symptom Monitor	Cancer specific	The Symptom Monitor was completed by intervention group only and patients were encouraged to take the questionnaire to the clinical consultation with their general practitioners;	Self-administered	Not applicable
Mills [42]	Diary completed at home /week that included: EORTC-C30 plus related lung cancer module LC13	Cancer specific	EORTC-C30 plus related lung cancer module LC13; patients could share their diary information to physicians if they wished	Self-administered	Basic training on layout of diary was provided
Qureshi [43]	Family history questionnaire	Generic	Family history questionnaire was applied to the intervention group patients. They were told that the questionnaire would be reviewed by	Self-administered	Not applicable

			general practitioner and clinical geneticist.		
Rosenbloom [44] (comparison 1)	FACT-G, including cancer specific 9-item subscales	Cancer specific	Intervention patients completed PROM at baseline and 1, 2, 3 and 6 months and their PROM scores were shared with treating nurses before consultation with patients.	Self-administered	No training was provided
Rosenbloom [44] (comparison 2)	FACT-G, including cancer specific 9-item subscales	Cancer specific	Intervention patients completed PROM at baseline and 1, 2, 3 and 6 months; PROM scores were shared with treating nurses, and a structured interview (by a trained interviewer) about the patients' responses was conducted at baseline, 1, and 2 months.	Self-administered	No training was provided
Velikova [49] (Comparison 2)	EORTC-QLQ-C30 and HADS	Cancer specific	Intervention group completed PROM questionnaires on a touch screen computer program	Self-administered	Not applicable

Table 4.3 Outcomes reported

Study identifier	Outcomes assessed		
	Process of healthcare	**Health outcomes**	**Satisfaction with healthcare**
PROM completed and presented to clinicians vs. PROM completed without presentation to clinicians			
Basch [31]	Intervention patients had significantly fewer emergency visits at 1 year (p = 0.02). Intervention patients received significantly longer duration of palliative chemotherapy (p = 0.002) There was moderate evidence of a smaller proportion of intervention patients hospitalised at 1 year (45% vs. 49%; p = 0.08)	Clinically meaningful HRQOL (evaluated by EQ-5D) improved in the I Vs. C 21% Vs. 11% (p = 0.0059) At 1 year, quality adjusted survival was significantly different between I vs. C (mean of 8.7 vs. 8.0 months) p = 0.004	73% of I participants completed the PROM at any given clinic visit

	No significant difference in the number of nursing calls to patients during participation		
Berry [32]	Intervention patients had increased likelihood of SQLI, that were reported problematic at first, being discussed ($p = 0.032$). No significant difference in the average length of clinic visit.	Not reported	Of enrolled clinicians, 43.1% completed questionnaire on PROM usability. Clinicians found PROM useful in: identifying appropriate areas of SQLI (67.8%), guiding the interview (64.3%), promoting communication (50%), identifying appropriate areas for referral (53.6%).
Boyes* [33]	Not reported	Intervention patients reporting debilitating symptoms at visit 2 were significantly less likely to report debilitating symptom at visit 3 ($P = 0.04$), and reported significantly lower mean depression scores ($p = 0.02$).	Patients found PROM easy to complete, a good way for doctors to get patients' well-being information and were willing to complete the PROM at each visit. Oncologists felt that the feedback was useful, helped to provide good patient care, and promoted communication.

		Intervention patients reported non-significant reduction in mean anxiety scores, in number of patients classified as clinically anxious or clinically depressed or with moderate or high psychological needs .	Half (n = 2) of the oncologists felt that the discussion of feedback report with their patients increased the consultation time by 3-5 minutes.
Calkins* [34]	Not reported	FSQ subscales: Intervention patients had significantly fewer bed days ($p < 0.05$). Intervention patients had non-significant improvement in restricted activity days, basic activities of daily living, intermediate activities of daily living, mental health,	Intervention patients were non-significantly more satisfied with their health status.

		and quality of interaction; and work performance. Intervention patients had non-significant decline in social activities.	
Cleeland [35]	Not reported	Intervention patients had significant reduction in the number of symptom threshold events (pain, distress, sleep, shortness of breath, constipation) p = 0.003.	Intervention patients were significantly more comfortable with the PROM reporting system (p = 0.03) and rated the system easy to use (p = 0.01).
De Wit et al. [36]	Not reported	Significant improvement in HRQOL at follow- up compared to baseline in I patients CHQ-CH87 (p = 0.006), vs C I vs C no significant difference on physical health (CHQ-CH87), family conflict	At 1 year f/u: I vs C significantly more satisfied with their care (p = 0.009).

		(DFCS), or depression (CES-D) I vs C no significant difference in Hb A1C level Note: baseline A1C level had confounding effect on psychosocial summary scale. For lower A1C level patients, psychological outcome significantly improved in the intervention group and remained stable for controls. Whereas, at highest A1C level >9.5 there was no difference in the baseline and f/u scores of I &C.	
Detmar [37]	HRQOL issues were discussed more frequently in intervention group. Significant differences in discussion of fatigue ($p = 0.02$),	No significant difference in any of the SF-36 scales.	Intervention patients had significantly greater satisfaction with the degree of emotional support received ($p < 0.05$).

	dyspnea (p = 0.02), and social functioning (p = 0.05) Intervention patients received more counseling on managing their health problems (p < 0.05); No significant differences in medication prescription, ordering of tests, referral to other providers and mean duration of visits	Larger percentage of I vs C showed improvement of 0.5 SD* or more in mean health (43% vs. 30% p =0.04) and role function (22% vs. 11% p = 0.05) *a change of 0.5 SD is considered a clinically important difference.	No significant difference in physician satisfaction.
Goldsmith* [38]	No significant difference in return visits to the family physician; referrals to other physicians or allied health professionals or to social or community services.	Not reported	Not reported
Kazis** [40]	AIMS study group (one of the centres): Intervention patients had non-significant decrease in	Intervention patients in the MHAQ group had non-	No significant differences in patient satisfaction with care

	the number of visits to doctors in the previous three months. Intervention patients had non-significant increase in the drug category change over one year, and more referrals to other arthritis health professionals over one year. MHAQ group: Intervention patients had non-significant reduction in the number of visits to doctors in previous three months, and referrals to other arthritis health professionals over one year. Intervention patients had a non-significant increase in drug category change over one year	significant increase in compliance Control group had non-significantly better compliance in AIMS group.	Physicians found PROM report helped in patient management (79%), had moderate to substantial value (55%), contributed to doctor-patient relationship (no percentage reported) 2/3rd physicians always examined the report and filed them in on patient chart, 50% discussed it with patients most of the time, 38% never discussed it.

McLachlan [41]	Not reported	Intervention patients had non-significant reduction in their psychologic and health information needs Intervention patients had significant reduction in spiritual needs at 6 months (P<0.02).	No significant difference found in patient satisfaction.
Rubenstein*** [45]	No significant difference in the number of office visits to physicians; hospitalisations; contacts with nurses, physical therapists, or other health professionals; new medications started; medical equipment purchased; or new diet or exercise regimens	Intervention patients non-significantly improved on three subscales of PROM questionnaire (Intermediate Activities of Daily living, Frequency of social contact, and Sexual satisfaction). Control group non-significantly improved on eight subscales.	Physicians found the PROM accurate and useful (97%), felt that it would improve patient health and physician-patient communication (43%), used the PROM results to change patient therapy (43%).

Rubenstein [46]	Intervention patients were more likely to have a specific treatment plan for their symptoms ($p = 0.05$), had more medical and functional status problems listed in the visit notes ($p < 0.01$), were more likely to be identified as having physical, psychological, social or functional status problems ($p < 0.05$), and had more diagnosis of depression ($p < 0.05$) and anxiety ($p < 0.001$)	Intervention patients had significantly better Mental Health scores ($p < 0.03$), and Social Activities scores for people >70 years ($p = 0.03$). Intervention patients' scores for Basic Activities of Daily Living, Social Activities, and Work Performance improved non-significantly. Control group had non-significant improvement in the Intermediate Activities of Daily Living.	Not reported
Ruland [47]	Significantly increased number of symptoms addressed by physicians and nurses in the inpatient and outpatient records	Intervention patients had significantly reduced symptom distress in pain, eating/drinking, bowel/bladder, energy, sleep/rest,	Not reported

	of intervention patients ($p < 0.05$)	concentration/memory, activities of daily living/self-care, and worries/concern ($P<0.01$); bleeding/infection and sexuality ($P<0.05$). Control patients had significant reduction in symptom distress in worries/concern ($p = 0.03$)	
Street* [48]	Not reported	Not reported	Non-significant increase in intervention patients' perception of physician inquiry about their health status
Velikova [49] (Comparison 1)	Not reported	No significant difference was found in the emotional well-being, physical well-being, functional well-being, and social or family well-being	Not reported

		Control patients had non-significant improvement in HRQOL 40% Intervention patients had clinically meaningful improvement, whereas 32% of controls.	
Wagner [50]	Not reported	Not reported	Physicians reported that availability and discussion of PROM: resulted in change in therapy (12.3%), was at least moderately useful for communication with patients (14.2%), and helped with patient management (8.4%). Physicians indicated the PROM result lengthened 67% of the encounters. Intervention patients' perception that their doctor considered how they felt emotionally and considered their usual daily activities when advising them increased non-significantly.

			Control patients showed non-significant increase in patients' satisfaction with clinical encounter, and the concerns shown by their doctor for their feelings.
Wasson [51]	Female Intervention patients had significant increase in the ordering of tests and procedures ($p<0.001$). Male Intervention patients had non-significantly increased ordering of tests and procedures	Not reported	Male Intervention patients significantly reported receiving greater help with functional problems related to pain ($p = 0.016$ Male Intervention patients were significantly more satisfied with management of pain ($p = 0.02$).
Wolfe* [52]	Not reported	No significant change in average scores of PQ-MSAS, PedsQL4.0, or Sickness scores during 20 weeks f/u Post hoc analysis: survivors beyond 20 weeks I vs. C PedsQL4.0 emotional score	52% children, and 71% parents found reports easy to understand. 28% children and 54% parents thought reports helped them quite a bit/very much to talk to their doctors.

		(by an average of +6 points) and overall sickness scores (average -5.3 points) significantly improved. Post hoc analysis: Children >= 8 years. I vs. C PedsQL4.0 emotional score (by an average of +8.1 points) and overall sickness scores (average -8.2 points) significantly improved.	75% parents agreed that PROM reports helped them understand their child's feelings. 21/34 providers completed satisfaction survey. 50% found reports useful when speaking to their patients and did not cause increase in consultation time. Reports provided new information (61% on psychosocial issues; and 22% physical symptoms). Reports contributed at least sometimes to their decision to initiate a psychosocial (56%), pain (34%), social work (33%), or palliative care (29%) consult and to discuss goals with families (36%).
PROM completed vs. PROM not completed			
Hoekstra [39]	Not reported	Intervention patients had significant reduction in the prevalence of constipation ($p<0.008$) and vomiting.	Not reported

		(p<0.01); and a non-significant reduction in fatigue, pain, lack of appetite, shortness of breath, sleeplessness, nausea, and diarrhea. Intervention patients had non-significant increase in the prevalence of cough. Intervention patients displayed reduced severity of all reported symptoms, except for constipation and vomiting, (p<0.05).	
Mills**** [42]	No significant associations at 2 and 4 months regarding the discussion of patient problems with healthcare professionals	Intervention patients QOL declined non-significantly (and non-clinically meaningful) (p = 0.14);	Control patients were non-significantly more satisfied.

		47% Intervention vs. 32% controls had clinically meaningful declined QOL; this difference was non-significant. 52% Intervention vs. 26% controls had clinically meaningful* decline in lung cancer specific QOL (p = 0.03) *a difference of 6 or more is considered clinically meaningful.	
Qureshi [43]	Not reported	No difference in anxiety scores at three months	The only significant difference in the perception of self-health was found in response to the question ‘what do you think is your risk of developing something wrong in the future?’ 26% of the intervention and 7% of the control group

			patients gave a negative response to this (Fisher's exact test, two-tailed, p = 0.025). There was no significant difference in having concerns about family history.
Rosen-bloom [44] (com-parison 1)	No significant difference in clinical treatment changes between the groups	There was no significant difference in HRQOL across the groups	No significant difference in general satisfaction, and satisfaction with communication.
Rosen-bloom [44] (com-parison 2)	No significant difference in clinical treatment changes between the groups	There was no significant difference in HRQOL across the groups	No significant difference in general satisfaction, and satisfaction with communication
Velikova [49]***** (com-parison 2)	Not reported	Intervention patients had significant improvement in HRQOL (p = 0.01), physical well-being (p = 0.003). No significant difference was found on emotional well-being, functional well-being,	Not reported

		and social or family well-being 32% of Intervention patients and 24% of control patients showed clinically meaningful improvement in HRQOL	
Velikova [49] (comparison 3)	Intervention patients had significantly more HRQOL symptoms mentioned during the clinical encounter (p = 0.03). No significant difference was found in the number of other symptoms discussed, and length of clinical encounter, medical decisions, and non-medical decisions.	Intervention patients had significant improvement in HRQOL (p = 0.006), emotional well-being (p = 0.008), physical well-being (p = 0.006), functional well-being (p = 0.03). No significant difference was found in social or family well-being. 40% of Intervention patients and 24% of control patients	Physicians explicitly mentioned/referred to HRQOL data in 64% of intervention encounters, 43% found HRQOL information clinically very useful, 28% found it somewhat useful, 21% found it a little useful, and 9% found it not useful. Physicians found that HRQOL data provided an overall assessment of patients (69%), additional information (33%), identified problems for discussion (27%), and contributed to patient management (11% encounters). Oncologists did not use the HRQOL information if the ‘data were irrelevant for the purpose of the

	showed clinically meaningful improvement in HRQOL	encounter or irrelevant to patients' major problems.'

Notes: AIMS: Arthritis Impact Measurement Scales, CHQ-CF87: 87-item child report version of the Child Health Questionnaire, CES-D: 20-item Center for Epidemiological Studies scale for Depression, C: Control group, DFCS: Diabetes Specific Family Conflict Scale, HRQOL: health-related quality of life, I: intervention group, MHAQ: Modified Health Assessment Questionnaire, PEQ-D: Patient Evaluation of the Quality of Diabetes Care, PedsQL4.0: Pedatric Quality of Life Inventory, STAI: Spielberger State Trait Anxiety Inventory, PQ-MSAS: PediQUEST Memorial Symptom Assessment Scale, PCQ: Psychological consequences questionnaire, PROM: Patient-reported outcome measure, QOL: Quality of life, SD: Standard deviation, SQLI: Symptoms and quality-of-life issues, FSQ: Functional Status Questionnaire, Hb A1C: Haemoglobin A1C, EQ-5D: EuroQoL 5D, HRQOL: health-related quality of life

Sections are italicised when pre-specified primary outcomes of studies were detailed

*No sample size calculation was reported

**A post-hoc power calculation was performed, no pre-specified primary outcome

***No pre-specified primary outcome

****Sample size was calculated but was not achieved for the comparison

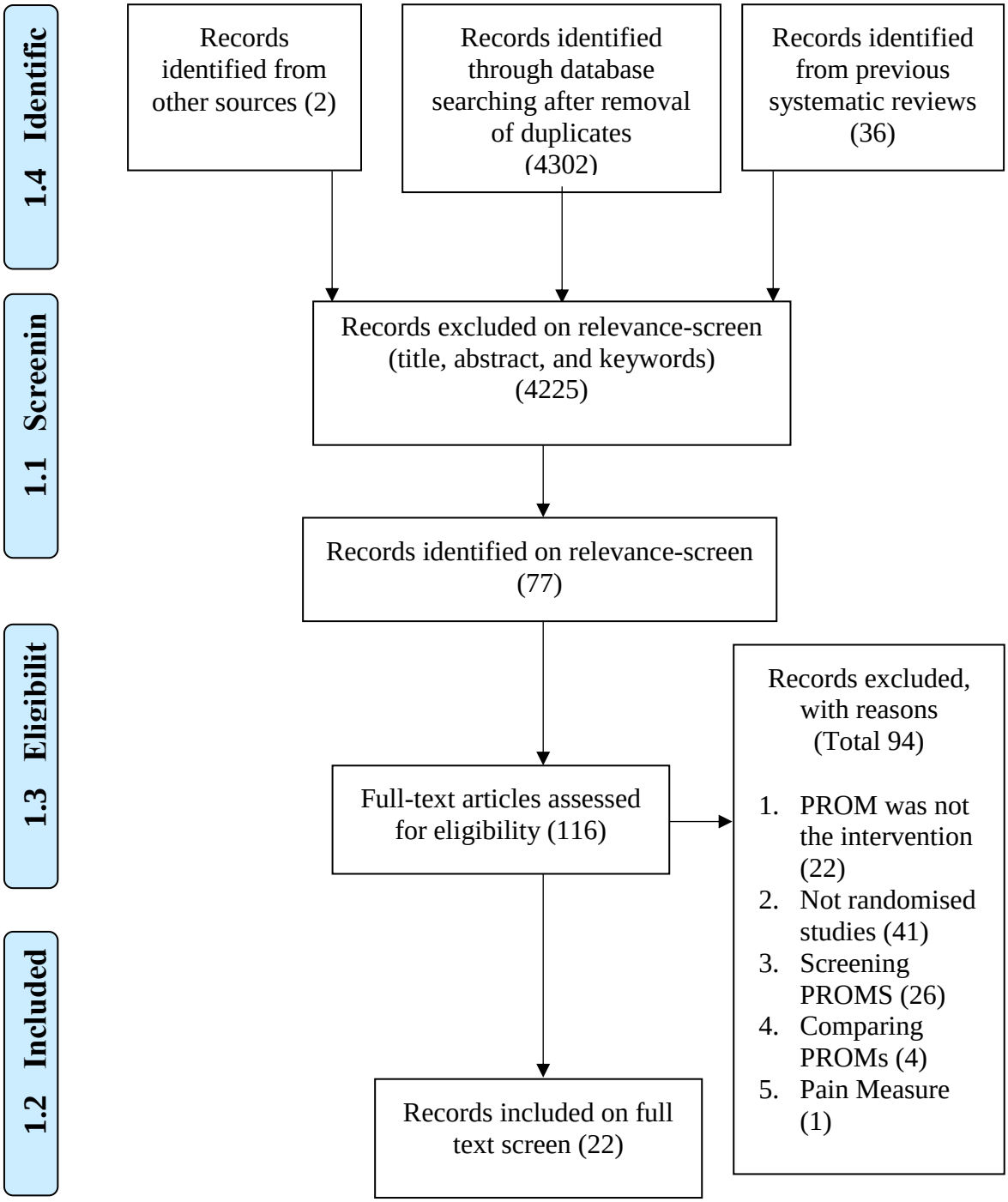
*****Study was not powered to detect differences in these groups

Table 4.4. Summary of reported results for comparisons in both panels

	1. PROM results to clinician vs. no PROM results to clinician (n = 18)			2. PROM vs. Standard care (n = 7)		
	No. studies reporting no evidence of effect	No. studies reporting non-robust effect(s)	No. studies reporting robust effect(s)	No. studies reporting no evidence of effect	No. studies reporting non-robust effect(s)	No. studies reporting robust effect(s)
Processes of care	3	4	2	3	1	0
Health outcomes	4	7	2	4	1	1
Satisfaction	4	3	0	3	0	0

Note: Reported effects were considered ‘robust’ if they were statistically significant and pertained to a single reported comparison or there was evidence that the study was adequately powered for more than one comparison. Other positive effects were classified as ‘non-robust.’

Figure 4.1 PRISMA Flow Diagram



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4.11 Supplementary 1: Search Strategy

Primary care.mp OR General practi*.mp OR Primary health*.mp OR Family practice.sh OR family practice.mp OR Family physicians.sh OR family physician*.mp OR Family practice.mp OR Family medicine.mp OR general medical setting*.mp OR medical inpatients.mp OR (clinical oncology adj2 practice).mp OR (oncology adj2 clinical practice).mp OR routine oncology practice.mp OR outpatient oncology practice*.mp OR outpatient adj2 oncology clinic*.mp OR cancer outpatient clinic*.mp OR cancer center.mp OR cancer centre.mp OR cancer centres.mp OR oncology department.mp OR cancer survivors.mp OR cancer survivor.mp OR (general adj3 medicine clinic).mp OR neurology patient*.mp OR community practice*.mp OR emergency department.mp OR (inpatient OR inpatients).mp OR (palliative phase.mp AND cancer.mp) OR (feedback adj3 oncologist*).mp. OR patient-reported cancer need*.mp

AND

patient-reported outcome*.mp OR treatment intention*.mp OR functional assessment instrument.mp OR functional status questionnaire*.mp OR intention to treat.mp OR (awareness adj3 clinicians).mp OR health personnel attitude.xm OR attitude of health personnel.mp OR patient referral.mp OR physician patient relations.xm OR physician patient relations*.mp OR self report* questionnaire*.mp OR (self administered adj3 questionnaire*).mp OR (self administered adj3 interview).mp OR self report screening.mp OR screening questionnaire*.mp OR self-assessed health status.mp OR self rating scale*.mp OR patient satisfaction.xm OR patient satisfaction.mp OR physician satisfaction.mp OR consumer satisfaction.xm OR consumer satisfaction.mp OR physicians prescription pattern*.mp OR physician attitude.mp OR (recognition adj3 treatment adj3 depression).mp

OR (health status report OR health status reports OR health status questionnaire*).mp OR symptom monitor.mp OR cancer related pain.mp OR (communication adj5 patient problem*).mp. OR attention towards symptom*.mp

limits: human, English, clinical trials all

4.12 Supplementary 2: Risk of bias assessment

Author's name	**Basch [31]**	
Entry	Judgment	Support for judgment (direct quotation from published article)
Random sequence generation	Low	Randomisation was conducted via a computer system using randomly permutated blocks
Allocation concealment	Low	The patients in each subgroup were independently allocated to self-reporting versus usual care
Performance: blinding participants and patients	Not applicable	Non-blinded, randomised, controlled trial of web-based self-reporting of symptoms Pragmatic trial
Detection bias: blinding of outcome assessment	Not applicable	Not applicable
Attrition bias: incomplete outcome data	Low	Sensitivity analyses were performed to justify assumptions about missing data
Reporting bias: selective outcome reporting	Low	Pre-specified outcomes (primary and secondary) were reported
Other sources of bias	Low	Judged based on overall RCT methods
Author's name	**Berry [32]**	
Entry	Judgment	Support for judgment (direct quotation from published article)

Random sequence generation	Low	After second assessment patients were randomly assigned automatically by the ESRA-C application to study groups (1:1)
Allocation concealment	Low	Automated assignment
Performance: blinding participants and patients	Not applicable	Not possible to blind the clinicians (recipient of intervention e.g. summary PROM scores); no report of blinding patients and outcome assessors Pragmatic trial
Detection bias: blinding of outcome assessment	Uncertain	Not reported
Attrition bias: incomplete outcome data	Low	Patients were randomised at second application of PROM and outcomes were assessed by audio recording of the session. No missing data
Reporting bias: selective outcome reporting	Low	One primary and two secondary outcomes were pre-specified and reported
Other sources of bias	Uncertain	Judged based on the overall RCT methods
Author's name	**Boyes [33]**	
Entry	Judgment	Support for judgment (direct quotation from published article)
Random sequence generation	Low	Participants were alternately allocated, by the computer, to either the intervention or the control group

Allocation concealment	Low	Computer assisted allocation to groups
Performance bias: blinding participants and personnel	Not applicable	No description reported; pragmatic trial
Detection bias: blinding of outcome assessment	Uncertain	Not reported
Attrition bias: incomplete outcome data	Low	Similar proportions missing in intervention and control groups.
Reporting bias: selective outcome reporting	Low	Reported both positive and negative results
Other sources of bias	Uncertain	Judged based on overall RCT methods

Author's name	**Calkins [34]**	
Entry	Judgment	Support for judgment (direct quotation from published article)
Random sequence generation	Uncertain	We selected up to eight patients at random from each physician's panel.
Allocation concealment	Uncertain	Same as above
Performance bias: blinding participants and personnel	Not applicable	Not reported if the participants (patients) were blinded. Not possible to blind physicians as only the intervention group physicians were offered training seminar, and the printed summary

		report was handed to and added to the medical record of intervention physicians only. Pragmatic trial
Detection bias: blinding of outcome assessment	Uncertain	Not reported
Attrition bias: incomplete outcome data	Low	Similar proportions missing in intervention and control groups.
Reporting bias: selective outcome reporting	High	Non-significant results were also reported, however no primary or secondary outcomes were pre-specified
Other sources of bias	Uncertain	Judged based on overall RCT methods
Author's name	**Cleeland [35]**	
Entry	Judgment	Support for judgment (direct quotation from published article)
Random sequence generation	Low	Random assignment was completed electronically by M.D Anderson's System Inventory
Allocation concealment	Low	Same as above
Performance bias: blinding participants and personnel	Not applicable	Not reported Pragmatic trial

Detection bias: blinding of outcome assessment	Uncertain	Not reported
Attrition bias: incomplete outcome data	Low	Similar proportions missing in intervention and control groups.
Reporting bias: selective outcome reporting	Low	Pre-specified primary and secondary outcome were reported in results section
Other sources of bias	Uncertain	Judged based on overall RCT methods
Author's name	**Detmar [37]**	
Entry	Judgment	Support for judgment (direct quotation from published article)
Random sequence generation	Low	The physicians were initially assigned, at random, to either the intervention or control condition.
Allocation concealment	Uncertain	Not reported
Performance bias: blinding participants and personnel	Not applicable	Pragmatic trial
Detection bias: blinding of outcome assessment	Low	Coding was performed by 3 trained raters who were blinded to group assignment
Attrition bias: incomplete outcome data	Low	Similar proportions missing in intervention and control groups.
Reporting bias: selective outcome reporting	Low	One primary outcome, and four secondary outcomes were specified a priori
Other sources of bias	Low	The study was a cross over RCT (risk of Carry over effect)

		There was a buffer period of two months before the physicians were switched to the other group
Author's name	**De Wit [36]**	
Entry	Judgment	Support for judgment (direct quotation from published article)
Random sequence generation	low	Cluster randomization of four centers: two intervention and two control
Allocation concealment	Not applicable	Not Applicable
Performance bias: blinding participants and personnel	Uncertain	Not reported
Detection bias: blinding of outcome assessment	Uncertain	Not Reported
Attrition bias: incomplete outcome data	Low	Similar proportions missing in intervention and control groups.
Reporting bias: selective outcome reporting	Low	Outcomes were predefined and all of them were reported in the results section
Other sources of bias	Uncertain	Judged based on overall RCT methods
Author's name	**Qureshi [43]**	
Entry	Judgment	Support for judgment (direct quotation from published article)
Random sequence generation	Low	A block randomization process was used. This involved allocating patients to one of the three strata according to their age. The first 26 males

		and the first 26 females were selected from each stratum. Within each of these six groups, patients were allocated at random to intervention or control group. The allocation occurred prior to recruitment
Allocation concealment	Uncertain	Not reported
Performance bias: blinding participants and personnel	Not applicable	Clinic staff was unaware of the purpose of the study Not possible to blind as only intervention group patients completed the questionnaire Pragmatic trial
Detection bias: blinding of outcome assessment	Uncertain	Not reported
Attrition bias: incomplete outcome data	Low	Similar proportions missing in intervention and control groups.
Reporting bias: selective outcome reporting	Low	One primary and two secondary outcomes were specified in the methods.
Other sources of bias	Uncertain	Judged based on overall RCT methods
Author's name	**Goldsmith [38]**	
Entry	Judgment	Support for judgment (direct quotation from published article)
Random sequence generation	Low	The providers were first stratified into four groups by length of clinical experience, and

		then randomly assigned to experimental and control groups so that each group had approximately equal number of faculty, first, second, and third year residents.
Allocation concealment	Uncertain	Not reported
Performance bias: blinding participants and personnel	Not Applicable	Pragmatic Trial
Detection bias: blinding of outcome assessment	Low	A retrospective chart review of patients participating in the study was conducted by the principal investigator 'blinded' to the patient's group
Attrition bias: incomplete outcome data	Uncertain	Not reported
Reporting bias: selective outcome reporting	Uncertain	Not reported
Other sources of bias	Uncertain	Judged based on overall RCT methods
Author's name	**Hoekstra [39]**	
Entry	Judgment	Support for judgment (direct quotation from published article)
Random sequence generation	Low	All patients who had given informed consent were randomised to either the intervention or the control group. Randomization took place with the GP as a unit, if a GP was in one group

		all patients who were subsequently included by this GP were allocated to the same group
Allocation concealment	Uncertain	Not reported
Performance bias: blinding participants and personnel	Not Applicable	Pragmatic trial
Detection bias: blinding of outcome assessment	Uncertain	Not reported
Attrition bias: incomplete outcome data	Low	Similar proportions missing in intervention and control groups
Reporting bias: selective outcome reporting	Uncertain	No outcome (s) identified as primary
Other sources of bias	Uncertain	Judged based on overall RCT methods
Author's name	**Velikova [49]**	
Entry	Judgment	Support for judgment (direct quotation from published article)
Random sequence generation	Low	The random assignment was unbalanced 2:1:1 in favour of the intervention group and stratified by site of cancer in random permuted blocks (block size was 8). Random assignment was carried out by telephone, by the Administrative Office at Cancer Research UK Centre (Leeds).
Allocation concealment	Low	Same as above

Performance bias: blinding participants and personnel	Not applicable	Pragmatic trial
Detection bias: blinding of outcome assessment	Low	Coding was performed directly from the audio taped by three raters, blinded to patient identity
Attrition bias: incomplete outcome data	Low	Similar proportions missing in intervention and control groups (slightly more in control arms.
Reporting bias: selective outcome reporting	Low	Two primary and five secondary outcomes specified.
Other sources of bias	High	Several outcomes - could lead to cherry picking significant results
Author's name	**Mills [42]**	
Entry	Judgment	Support for judgment (direct quotation from published article)
Random sequence generation	Low	Patients were randomly assigned to intervention or control groups using block randomization with computer generated random numbers
Allocation concealment	Low	Patient were randomised with a computer program
Performance bias: blinding participants and personnel	Not Applicable	Pragmatic trial
Detection bias: blinding of outcome assessment	Not Applicable	Completion of a mailed QOL questionnaire (FACT-L) was considered the primary outcome

		of the trial, and therefore blinding of outcome assessor was not applicable
Attrition bias: incomplete outcome data	Low	Similar proportions missing in intervention and control groups
Reporting bias: selective outcome reporting	Low	One primary outcome identified in the methods and reported in the results section
Other sources of bias	High	Several secondary outcomes
Author's name	**Kazis [40]**	
Entry	Judgment	Support for judgment (direct quotation from published article)
Random sequence generation	Low	In the BU component of the study, 710 RA patients from 12 community practices were randomised into three groups within each practice. The VU component involved 1210 RA patients from 15 practices, also randomised into three groups within each practice.
Allocation concealment	Uncertain	Same as above
Performance bias: blinding participants and personnel	Not Applicable	Pragmatic trial
Detection bias: blinding of outcome assessment	Uncertain	Not reported
Attrition bias: incomplete outcome data	High	Multi-center study: 80% of patients completed study at VU group, and 87% completion at BU

		center. No comparison was made between the completers and non-completers
Reporting bias: selective outcome reporting	High	No primary outcome identified at the start of the study
Other sources of bias	Uncertain	Judged based on overall RCT methods
Author's name	**McLachlan [41]**	
Entry	Judgment	Support for judgment (direct quotation from published article)
Random sequence generation	Low	Computer-generated randomization charts were prepared for each clinic and held in the statistical office
Allocation concealment	Low	Same as above
Performance bias: blinding participants and personnel	Not Applicable	Pragmatic trial
Detection bias: blinding of outcome assessment	Uncertain	Not reported
Attrition bias: incomplete outcome data	Low	Similar proportions missing in intervention and control groups
Reporting bias: selective outcome reporting	Low	Two primary outcome variables were specified a priori.
Other sources of bias	High	Secondary outcomes mentioned but not specified a priori; many secondary outcomes could have led to cherry picking
Author's name	**Rosenbloom [44]**	

Entry	Judgment	Support for judgment (direct quotation from published article)
Random sequence generation	Low	'After signing informed consent, patients were randomly assigned to one the three condition.' Random assignment of participants was stratified by primary cancer diagnosis to ensure balance across treatment arms.
Allocation concealment	Uncertain	Same as above
Performance bias: blinding participants and personnel	Low	The author acknowledges in the discussion that they were able to blind the patients and staff to the study hypothesis but they could not be blinded to group assignment
Detection bias: blinding of outcome assessment	Uncertain	Not reported
Attrition bias: incomplete outcome data	Low	Patient did not complete assessment due to worsening illness (10) or death (46). Logistic regression analysis indicated that type of cancer and baseline quality of life scores were associated with study dropout. Dropout was not random, and therefore analysis was performed to account for the dropouts.
Reporting bias: selective outcome reporting	Low	Primary outcome identified in the methods section.
Other sources of bias	Uncertain	Three additional outcomes reported

Author's name	**Rubenstein [45]**	
Entry	Judgment	Support for judgment (direct quotation from published article)
Random sequence generation	Low	Physicians and their patients were randomised to the experimental or the control group. Physicians in the group practices whose partners were in the study were randomised together.
Allocation concealment	Uncertain	Not reported
Performance bias: blinding participants and personnel	Not Applicable	Pragmatic trial
Detection bias: blinding of outcome assessment	Uncertain	Not reported
Attrition bias: incomplete outcome data	Low	Similar proportions missing in intervention and control groups
Reporting bias: selective outcome reporting	Low	Primary outcome was pre-specified
Other sources of bias	High	Multiple secondary outcomes
Author's name	**Rubenstein [46]**	
Entry	Judgment	Support for judgment (direct quotation from published article)
Random sequence generation	High	(Non-random) allocation was stratified by gender and by medical education program (general internal medicine vs 'straight' internal

		medicine). Patients were alternatively assigned to the modules according to the order in which they called the clinic. The experimental module was determined by coin toss.
Allocation concealment	High	Probably high as the random sequence generation is high
Performance bias: blinding participants and personnel	Not Applicable	Pragmatic trial
Detection bias: blinding of outcome assessment	Low	Medical records were reviewed by a non-physician abstractor, and were over-read by a physician; both were blinded to group allocation
Attrition bias: incomplete outcome data	High	Only 190/309 experimental, and 152/248 control group patients completed the study. The non-completers were significantly younger, more disabled, more socially isolated, and more financially distressed at enrolment that were the completers
Reporting bias: selective outcome reporting	High	Multiple outcomes, primary outcome not specified
Other sources of bias	Uncertain	Judged based on overall RCT methods
Author's name	**Ruland [47]**	
Entry	Judgment	Support for judgment (direct quotation from published article)

Random sequence generation	Low	patients were randomised into the intervention or control group via a computer-generated minimization algorithm that equalized the groups on gender and type of treatment
Allocation concealment	Low	Same as above
Performance bias: blinding participants and personnel	Not Applicable	Pragmatic trial
Detection bias: blinding of outcome assessment	Low	Two raters blinded to patients' study group assignment conducted independent chart audits
Attrition bias: incomplete outcome data	Low	Similar proportions missing in intervention and control groups
Reporting bias: selective outcome reporting	High	Multiple outcomes, no pre-specified primary outcome
Other sources of bias	Uncertain	Judged based on overall RCT methods
Author's name	**Street [48]**	
Entry	Judgment	Support for judgment (direct quotation from published article)
Random sequence generation	High	The study design was implemented by assigning patients and physicians to the control condition for the first 2 weeks of the month and to the experimental group for the remainder of the month.
Allocation concealment	High	Same as above

Performance bias: blinding participants and personnel	Not Applicable	Pragmatic trial
Detection bias: blinding of outcome assessment	Uncertain	Not reported
Attrition bias: incomplete outcome data	Uncertain	Not reported
Reporting bias: selective outcome reporting	High	No primary or secondary outcome pre-specified
Other sources of bias	Uncertain	Judged based on overall RCT methods
Author's name	**Wagner [50]**	
Entry	Judgment	Support for judgment (direct quotation from published article)
Random sequence generation	Low	Patients were randomly assigned to two groups using a random number table
Allocation concealment	Uncertain	Not reported
Performance bias: blinding participants and personnel	Not Applicable	Pragmatic trial
Detection bias: blinding of outcome assessment	Uncertain	Not reported
Attrition bias: incomplete outcome data	Low	Similar proportions missing in intervention and control groups
Reporting bias: selective outcome reporting	High	Primary outcome not specified
Other sources of bias	Uncertain	Judged based on overall RCT methods

Author's name	**Wasson [51]**	
Entry	Judgment	Support for judgment (direct quotation from published article)
Random sequence generation	Low	A sample of participating clinicians were studied prior to start of study. Clinicians were then blocked in the proportion of patients for whom they reported multiple reasons for office visit and were randomly assigned to the experimental conditions within blocks
Allocation concealment	Uncertain	Not reported
Performance bias: blinding participants and personnel	Not Applicable	Pragmatic trial
Detection bias: blinding of outcome assessment	Low	Reasons for visit were coded by one member of the research staff who was blinded to the patient study group using the international classification of primary care
Attrition bias: incomplete outcome data	Uncertain	No mention of missing data
Reporting bias: selective outcome reporting	Uncertain	Primary outcomes not specified
Other sources of bias	Uncertain	Judged based on overall RCT methods
Author's name	**Wolfe [52]**	
Entry	Judgment	Support for judgment (direct quotation from published article)

Random sequence generation	Low	Random sequence assignment was computer generated and integrated into the PediQUEST system
Allocation concealment	Low	The random assignment was concealed to researchers, patients, and provider
Performance bias: blinding participants and personnel	Not Applicable	Author acknowledges that blinding was not feasible. Pragmatic trial
Detection bias: blinding of outcome assessment	Low	Author acknowledges that blinding was not feasible
Attrition bias: incomplete outcome data	Low	Of 51 intervention and 53 control patients 49 from each group completed at least one f/u and were included in the analysis
Reporting bias: selective outcome reporting	Low	Primary outcomes were predefined and were reported in the results section
Other sources of bias	Uncertain	Judged based on overall RCT methods

BU: The Boston University Arthritis Centre, RA: Rheumatoid arthritis, RCT: randomised controlled trial, VU: The Vanderbilt University Division of Rheumatology and Immunology

CHAPTER 5. ADAPTATION AND CONTENT VALIDATION OF MEASURE YOURSELF MEDICAL OUTCOMES PROFILE (MYMOP) FOR 7-11 YEAR-OLD CHILDREN

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Chapter 5: Adaptation and Content Validation of Measure Yourself Medical Outcomes Profile (MYMOP) for 7-11 year-old Children

Statement of Authorship

Title of Paper	Adaptation and Content Validation of Measure Yourself Medical Outcomes Profile (MYMOP) for 7-11 year-old Children
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Principal Author

Name of Principal Author (Candidate)	Sana Ishaque
Contribution to the Paper	Developed the research protocol, submitted and obtained necessary ethics approvals, conducted focus group, interviews, transcribed recorded data, analysed data, conceptualised the manuscript structure, wrote the manuscript. .
Overall percentage (%)	75 %
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.
Signature	**Date** 27/09/2018

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);
ii. permission is granted for the candidate in include the publication in the thesis; and
iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

Name of Co-Author	Rachel Roberts		
Contribution to the Paper	Supervised the development of the research protocol, helped to evaluate and edit the manuscript, provided feedback, comments and suggestions		
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Contribution to the Paper	Supervised the development of the review protocol, helped to evaluate and edit the manuscript, provided feedback, comments and suggestions		
Signature		Date	28/09/2018

5.1 Abbreviations

Patient/client/respondent: used interchangeably

HRQOL: Health-related quality of life

ISOQOL: International Society of Quality of Life Research

MYMOP: Measure Yourself Medical Outcome Profile

MYMOP2: Current adult version of the Measure Yourself Medical Outcome Profile

P-MYMOP: Paediatric MYMOP

Research Team: the PhD student and supervisory panel

WCH: Women's and Children's Hospital

ABSTRACT

Background and Objectives

A systematic review to identify validated paediatric generic individualised HRQOL measures confirmed the absence of any such tools. The Measure Yourself Medical Outcome Profile (MYMOP) was identified as one of the adult individualised tools used for children without any evidence of validation in this setting. Individualised instruments are patient-specific rather than disease-specific and therefore can be applied across various different diseases or health conditions. This study aimed to adapt and subsequently content validate the MYMOP for use in paediatric clinical encounters of children 7-11 years old.

Methods

There were four iterations of the adaptation and validation process: 1) an online survey of local paediatricians and paediatric trainees, 2) a focus group discussion with paediatricians, 3) an online survey with paediatric research experts and paediatricians across Australia, and 4) interviews with child-parent pairs at the General Medicine and Diabetes/Endocrine Outpatient clinic of a local Children's Hospital. Analysis of the interview data was performed according to Braun and Clarke (2006) guidelines on thematic analysis. An inductive, interpretative approach with realist epistemology was used.

Results

Four paediatricians completed the first survey, five paediatricians participated in the focus group, and four paediatric HRQOL research experts completed the second survey. Several changes were recommended to the wording and layout of the MYMOP by the expert groups. Twenty-five children (17 general medicine, and 8 diabetes/endocrine clinic) aged 7-11 years

old completed the draft paediatric MYMOP (P-MYMOP) and were interviewed afterwards. Data from the completed P-MYMOP and interviews demonstrated that the majority of participating children were able to identify their own problems and activity limitations, and all children in the study understood the 7-point faces scale. Most parents and children perceived that the P-MYMOP would be useful to complete before clinic appointments.

Conclusions

The P-MYMOP is the first content-validated generic individualised HRQOL measure for children. The wording, layout, and scale of the P-MYMOP has been successfully adapted for children 7-11 years old. Given that validation is an iterative process, further research to assess its feasibility, reliability, and construct validity is required.

5.2 Introduction

Health-Related Quality of Life (HRQOL) is a multidimensional, subjective, patient-reported outcome defined as ‘a measure of the value assigned to the duration of life as modified by impairments, functional states, perceptions and opportunities – as influenced by disease, injury, treatment and policy [1 pp. 1325-1326].’ HRQOL measurement during or before clinical encounters is reported to improve patient outcomes [2] and has several additional benefits. In the current era of evidence-based, patient-centred medicine, assessing HRQOL is encouraged as essential practice in physicians’ offices, clinical trials, and for resource allocation (where HRQOL is often thought to reflect patients’/clients’ satisfaction with a healthcare intervention).

There are various methods reported in the literature to assess HRQOL. The construct can be assessed by generic or disease-specific questionnaires that can be standardised—consisting of pre-determined domains, or individualised—allowing each individual patient to choose what is important to them. Each approach to HRQOL measurement has strengths and limitations. While standardised measures of HRQOL provide easy comparisons between different populations, these instruments have been criticised for a lack of patient-centredness [3,4]. Studies by Bowling and Clinch [5,6] demonstrated that standardised measures often miss aspects of life that are comparatively more important to patients. Individualised measures on the other hand are superior in picking up individual patient needs, values, and goals. However, they cannot be used for economic evaluations [5,6]. Hence the choice of a measurement method depends on the purpose of the measurement.

A systematic review (2011, unpublished MSc thesis, University of Alberta, S. Ishaque) to identify paediatric individualised HRQOL measures confirmed the absence of any such validated tool for use in children. This search was updated in September 2018 and it was confirmed that to date no generic individualised tool had been validated for paediatric use. The details of the search update are reported in Chapter 2, section 2.5.2. In the systematic review (2011, unpublished MSc thesis, University of Alberta, S. Ishaque), the Measure Yourself Medical Outcome Profile (MYMOP) was identified as one of the adult individualised tools being used for children without any published evidence of validity for this cohort. In addition to the lack of the availability of a validated paediatric tool, the MYMOP was also found suitable for validation in a paediatric population based on the personal experience of a paediatric clinical and research group, *CARE Program for Integrative Health & Healing*, Department of Pediatrics, University of Alberta. The tool was used successfully with children in the *Program*, as it was simple and avoided non-applicable questions to developmentally delayed children.

The current version of the MYMOP available for use in adult populations is called MYMOP2 [7]. It is a simple one-page tool that has three individualised questions for the patient to name two of their most important symptoms, and one activity which is limited to the identified symptoms. After the individualised questions, it enquires about the feeling of overall well-being, and medication usage by the patient. The tool is publicly available free of cost, but the developer has asked to be informed about any usage [7].

This study, therefore, was designed to adapt and validate the MYMOP2 tool for use in a paediatric population of children aged 7-11 years old, by consultation with paediatric health practitioners (first and second iteration), paediatric researchers (third iteration), and child-parent pairs (fourth iteration) at a children's hospital outpatients' clinic. This age group was

selected in view of the anticipated relative ease of most children of this age group in completing such a tool themselves, and the well-established homogeneity in cognitive abilities [8-10] of children in this age bracket. The participant groups to be recruited for consultation were selected as they were considered suitable stakeholders in the application, usage, and integration of a paediatric PROM to a clinical setting.

5.3 The current study

The adaptation of the MYMOP2 was conducted by a research team that consisted of a PhD student (S. Ishaque), and her supervisory panel. This team will subsequently be referred as the 'Research Team'.

The adaptation of the MYMOP2 to make it suitable for children 7-11 years old used a mixed-methods research design combining quantitative and qualitative sub-studies, referred as iterations henceforth. This approach is considered appropriate for instrument adaptation [11]. As per the recommendations of the COSMIN criteria for content validation of measurement tools [12], it was deemed essential to check the relevance of included items to the construct of interest and context of use. The four iterative stages were: 1) an online survey of local paediatricians and paediatric trainees; 2) a focus group discussion with paediatricians; 3) an online survey with paediatric research experts and paediatricians across Australia; and 4) interviews with child-parent or child-guardian pairs at the outpatients department of a local children's hospital (Figure 5.1). After each iteration, Research Team meetings were held to discuss the results of the prior phase and to design and implement the next iterative stage.

5.3.1 Sampling Logic

As the paediatric MYMOP (P-MYMOP) was being adapted for use in a clinical setting, the Research Team, paediatricians, paediatric researchers and stake-holders were consulted to ensure relevancy. First, a local group of paediatricians with whom the researcher had some previous contact was consulted to ensure that the changes suggested by the Research Team to the response options, recall period, wording, and comprehensiveness of the key concepts for inclusion in the P-MYMOP were appropriate. This group was consulted via an online survey followed by a focus group of an available subset of the local group that not only provided more open responses, but also helped clarify some of the responses given in the online survey and resulted in a refined version of the P-MYMOP. In the next iteration the intension was to widen the sample by including Australia-wide paediatricians and paediatric researchers from a quality of life special interest group to comment on the current P-MYMOP and provide comment on any further refinements. The sample for the last phase was drawn to test that the further refined P-MYMOP had appropriate content to use with children and parents in a clinical setting. In this phase it was necessary that participants were key stakeholders in the adaptation process, i.e. child-parent pairs at the Women's and Children's hospital, who were also provided with the opportunity to suggest any changes to the content if needed and this resulted in the near final version of P-MYMOP (seen in Appendix 5.6).

The methods and results of the iterations are separately described below followed by an overall discussion.

5.4 First iteration: Online survey of paediatricians and paediatric trainees

5.4.1 Methods

Ethics approval for the first online survey and the focus group with local paediatricians (Second iteration) was obtained from the Women's and Children's Health Network Human Research Ethics Committee (HREC/16/WCHN/8).

The potential participants were doctors working in the Department of General Medicine at the Women's and Children's Hospital (WCH), Adelaide. The survey was distributed to 10 paediatricians at the WCH through staff email addresses.

To develop the first online survey using SurveyMonkey, several Research Team discussions were held and changes were suggested in the wording and layout of the MYMOP2 to make it suitable for children 7-11 years old. The Research Team also considered the addition of a 'faces scale' to promote and assist self-completion of the paediatric PROM. As a previous version of MYMOP2 had included a faces scale [13,14] for use in older adults (Pictorial version of MYMOP), use of the same faces in the P-MYMOP was considered. However, the methods of content validation of the Pictorial Version of MYMOP were not clearly reported [13,14]. In addition, the number of faces in the Pictorial Version of MYMOP was not consistent with the numerical rating scale of the MYMOP2 and the faces scale had tears shown on it, which are not considered suitable for use in children [15]. The corresponding author of this study [13] was contacted to provide additional details of methods that may not had been published and the developer of MYMOP2 (Dr Charlotte Paterson) was also contacted. No additional details of the methods were provided. Therefore, additional faces

scales were searched for and considered to be included in the P-MYMOP. A relatively simple set of seven faces [15] was selected. The Research Team's suggested changes to the MYMOP2 were incorporated to develop the first online survey (see Appendix 5.1).

5.4.1.1 Statistical analysis

The data were analysed using descriptive statistics using basic counts and qualitative responses of the participants were analysed via a summative approach to qualitative content analysis [16]. As per this approach the principal researcher (SI) started with identifying and quantifying certain words in the participants' text responses to explore usage and interpreted their usage via discussion with the Research Team.

5.4.2 Results

There were four responses (4/10) to the first online survey by paediatric consultants at the WCH. All respondents agreed to the suggestion of changing the word 'symptoms' to 'problems' as it was perceived that the word 'symptoms' may be difficult for children 7-11 years old to understand. After Research Team discussion, the term was refined to 'health problems.' Three respondents did not agree with the replacement of the word 'bother' by 'bug,' therefore the word 'bother' was retained.

There were four different responses to the selection of the most appropriate time interval for the P-MYMOP. One respondent suggested to keep it unchanged, that is, 'over the last week,' another suggested changing it to 'over the past few days,' a third to change it to 'today,' whereas the fourth respondent did not have a preference, but mentioned that the time interval would depend on the acute or chronic nature of the problem identified on the P-MYMOP. After Research Team discussion on these responses, the time interval was changed to 'over

the last few days,' with the decision to test this change in the next stage of the adaptation process by asking respondents if they agreed or disagreed with it, and to give a reason.

There was complete agreement on the deletion of words 'physical, mental, or social' from the activity question in MYMOP2, as well as to substitute the word 'activity' with 'thing,' although this was later changed to 'something' after Research Team discussion. The well-being question was retained after changing the word 'symptom' to 'problem.' There was a 50/50 split among respondents on the use of a 'faces scale' for P-MYMOP, and it was therefore decided by the Research Team to leave the faces scale for discussion for the next stage of the study.

All respondents agreed that the medication questions would be challenging for children to complete, and therefore it was suggested that this section be offered to primary caregivers (i.e. parent/guardian) of the children for completion. The P-MYMOP draft Tool (Appendix 5.2) was prepared based on the first online survey responses.

5.5 Second iteration: Focus group discussion with paediatricians

5.5.1 Methods

Results of the first online survey were used to facilitate a focus group discussion with paediatricians at the Department of General Medicine WCH before a usual weekly staff meeting. Five paediatric consultants from the Department participated in the focus group discussion, which was held for approximately 20 minutes.

The focus group aimed to discuss the results of the first online survey with paediatric consultants, facilitate discussion concerning the use of P-MYMOP in the hospital setting, and help plan the next stages of validation. The P-MYMOP draft Tool (Appendix 5.2) as prepared

based on the first survey responses was presented to the focus group participants for discussion, along with a summary of first online survey responses. Some questions to guide the focus group discussion, as approved by the Ethics Committee are attached as Appendix 5.3. The focus group data were also analysed using the summative approach to qualitative content analysis [16].

5.5.2 Results

Five paediatricians participated in focus group discussion. As a result of the focus group discussion, the well-being question was simplified to 'how you have been feeling?' rather than 'rate your general feeling of well-being.' The medication question was changed from 'are you taking any medication?' to 'are you taking any therapy or treatment?' and the word 'medicine' was preferred over 'medication.' After Research Team discussion on the focus group responses, the medication question was changed to 'do you take any tablets, medicine, or treatment?' and was open to further validation in the next iterative stage.

Use of a large font and more spaces for writing were suggested to make the layout more user-friendly. Participants of both the online survey and the focus group agreed that it would be best for the P-MYMOP to be completed in a waiting room, before a scheduled appointment with a paediatrician.

5.6 Third iteration: Online survey of paediatric research experts and paediatricians across Australia

Ethics approval for this iterative stage was obtained from the University of Adelaide's Human Research Ethics Committee (H-2016-270).

5.6.1 Methods

After further modification of the P-MYMOP informed by the opinions of local paediatricians via the online survey and focus group, a second online survey (Appendix 5.4) was designed to enable consultation with paediatric research experts and paediatricians across Australia.

The survey was circulated to the Australian members of the International Society of Quality of Life Research (ISOQOL)—Child Health Special Interest Group as a representative body of researchers interested in child HRQOL/QOL (n = 22), and to paediatricians via the monthly Newsletter of the Paediatric and Child Health Division of the Royal Australian College of Physicians. One reminder was sent to potential participants. The data were analysed via the same methods reported in section 5.4.

5.6.2 Results

The second online survey was designed to gather opinions of paediatric research experts and paediatricians in Australia. Unfortunately, only four responses were received, with all respondents being paediatric researchers. There were no additional responses to the reminder included in the next Newsletter and it was decided to close the survey.

Of the four respondents, three agreed to asking children to name their ‘health problems’ as the opening question on P-MYMOP, and confirmed that the time interval of ‘over the last few days’ was suitable for children 7-11 years old. In addition, the replacement of the word ‘activity’ with ‘something’ was considered acceptable for the target population.

All respondents confirmed that the ‘faces scale’ would be a beneficial addition to the paediatric tool to help elicit meaningful responses from the children. One of the respondents voiced concern about young children not being able to circle a face. It was suggested that

instead of asking children to circle a face, asking them to cross it out might be simpler. In the Research Team meeting, it was decided to keep the tool as it was, let the children fill it out, and then re-visit this concern based on their observed ease of circling the faces. The Research Team also changed the term ‘health problems’ to ‘problems’ on the P-MYMOP, to be tested with child-parent pairs, because ‘health problems’ was thought to be too narrow to capture issues that may be important for young children.

5.7 Fourth iteration: Child-parent interviews at the Women’s and Children’s Hospital’s Paediatric Outpatients Department

Ethics approval for the child-parent interviews was obtained from the WCH Network Human Research Ethics Committee (HREC/17/WCHN/36).

5.7.1 Methods

Content validation of the P-MYMOP involved interviewing children 7-11 years old and their parent/guardian visiting the Department of General Medicine and Diabetes/Endocrine Outpatient clinic at the WCH Adelaide. A child-parent or child-guardian pair was eligible to participate in the study if: 1) the child was 7-11 years old; 2) the parent/guardian and the child could speak and read English; and 3) child was able to name their own issues. Potential participants (7-11-year-old children and their parent/guardian) were identified by the Paediatric Outpatients Department’s Clinic nurse, or by reception staff, who provided them with a study information leaflet. This leaflet sought permission to be approached later by the principal researcher (SI). Once the parent of an eligible child-parent/child-guardian pair granted permission to be approached by the researcher (SI), a detailed information sheet was handed to the parent/guardian and written informed consent was sought from parent/guardian

for themselves and on behalf of their child. The researcher (SI) then asked the parent/guardian to complete a short demographic information form (Appendix 5.5) followed by both child and parent/guardian together completing the P-MYMOP (Appendix 5.6). After completion of the demographic information form and the P-MYMOP, a semi-structured interview was conducted about the wording, layout, willingness of the pair to complete the P-MYMOP as a routine task before their clinic appointment, and the benefit they perceived of completing the Tool. The interview questions for children 7-11 years old and their parents are attached as Appendix 5.7. Data from this session included: demographic information, the completed P-MYMOP, the interviewer's observations, and the semi-structured interview. The session was audio recorded and later transcribed by the researcher (SI).

This iteration was a mixed-methods study that collected information from multiple sources as described above to adapt the contents of the MYMOP2 for children 7-11 years old. The demographic form and P-MYMOP provided both quantitative and qualitative data, whereas the interviewer's observations and transcribed interviews were the qualitative components of the iteration. These methods were found suitable for content validation of patient-reported outcome measures [12,17-20]. Inclusion of parent's/guardian's and children's views in the adaptation of MYMOP is in line with current recommendations to consult the target population for the development of PROMs. Participants were recruited until saturation was reached [21]. Saturation was defined as the emergence of no new information from three consecutive interviews of child-parent pairs, and this was achieved for both of the clinic sub-groups (i.e. for patients from the Department of General Medicine and Diabetes/Endocrine Outpatient clinics).

Analysis of the interview data were performed according to the Braun and Clarke (2006) guidelines on thematic analysis [22]. An inductive, interpretative approach with realist

epistemology was used. Thematic Analysis is defined as ‘a method for identifying, analysing, and reporting patterns (themes) within data [22].’

5.7.1 Results

This phase of the study ran for 12 weeks (three days/week) in the Department of General Medicine Outpatient clinic and for 4 weeks (2 days/week) in the Diabetes and Endocrine Clinic. A total of 25 child-parent pairs participated. One participant was a non-verbal child whose mother completed the P-MYMOP for him. As the aim of the P-MYMOP is identification of issues by children through self-completion, the data for the non-verbal child was excluded from subsequent analyses. The participating children’s ages were representative of the target population: 7 years (6), 8 years (10), 10 years (6), 11 years (3). Demographic characteristics of these children are presented in Table 5.1. Of the 24 children, 20 were native English speakers. Sixteen children were from the General Medicine Clinic and eight children were from the Diabetes and Endocrine Outpatient clinic.

The completion of the P-MYMOP was followed by the semi-structured Interview. An important aspect of the process of the P-MYMOP completion was to observe if the children appeared to understand the concepts represented on the tool. Six themes were generated from the coded data collected during the interaction of the researcher with child-parent pairs:

1. children’s understanding of the concepts represented on the P-MYMOP (i.e. ‘problems,’ duration of problems, and ‘faces scale’)
2. reading and writing on the P-MYMOP
3. perceived value in using the P-MYMOP
4. approach to the medication questions
5. suggested changes to P-MYMOP, and
6. connecting activity with identified problems.

These themes are reported below and their supporting codes from the data are presented in Table 5.2.

5.7.1.1 Theme 1 Children's understanding of the concepts represented on the P-MYMOP (i.e. 'Problems,' Duration of problems, and 'Faces scale')

Theme 1 had three sub-themes: 1) child named their problem; 2) the child's understanding of the 'faces scale'; and 3) understanding of the duration of the problem. The ability of children to identify their own problems and the time period for which they have these is crucial in the completion of an individualised PROM. In addition, the selection of faces on the 'faces scale' by children, with little or no help from their parent, is crucial for the P-MYMOP to yield meaningful outcomes.

Information about a child being able to name his/her problem and their understanding of the 'problem duration' came from the Interviewer's observation of the completion of the P-MYMOP form by the child-parent pair. Data on understanding of the 'faces scale' was both observational and in response to the direct question asked to the children about their impression of the 'faces scale.'

Twelve children from the General Medicine (12/16) and six children from the Diabetes/Endocrine cohort (6/8) were able to name their problem and then measure the effect of it using the 'faces scale'. Of the participating children, some children were not able to readily identify their own problems, in which case parents/guardians either provided them with some examples or reminded them of recent issues that the child had discussed with them. With this small amount of help, the majority of participating children were able to name their problems.

Of the six children (4 General Medicine, 2 Diabetes/Endocrine) who did not name their problems, four were attending the Clinic for follow-up appointments and had no presenting complaints. In two cases (1 General Medicine, 1 Diabetes/Endocrine), parents chose the problems on their own without confirming with their child; but proceeded to ask the child to score these problems on the 'faces scale'.

The 'faces scale' was unanimously accepted as helpful by all participating children and parents in the study. All of the children appeared to understand the duration of the problem question on the P-MYMOP.

The new paediatric tool, the P-MYMOP, was self-completed by most of the participating children with limited exceptions where the parents took over and named the most important problems for their child. Overall, most of the participating children were able to understand the concepts presented on the P-MYMOP. The data therefore provided positive evidence for the content validation of the tool in our target population.

5.7.1.2 Theme 2 Reading and writing on the P-MYMOP

There were three sub-themes under the main theme of 'reading and writing on the

P-MYMOP': 1) who wrote the individualised items on P-MYMOP; 2) who read the P-MYMOP; and, 3) completion of the 'faces scale' on the paper form.

Most data about the reading and writing of the P-MYMOP was gathered through observation of how the child-parent pair completed the tool. No issues were identified with the reading of the P-MYMOP questions, as it was permissible for either the child or parent to read them. Regardless of who read the tool, the wording appeared to be understood by all participating children. A child from the youngest age group, was a 7 year old who could not read the P-

MYMOP, but was able to understand it when their father read it to them. Direct code from the interview of this child is included in Table 5.2. Similarly, writing individualised problems into the space provided on the P-MYMOP was not an issue. The participating children, in some cases, needed help with spelling which was readily provided by their parents. Overall, children were able to read and complete P-MYMOP with some support from their parent/guardian.

To explore how the faces were selected to score the questions on the P-MYMOP, participants' completed paper forms were examined. Of the 24 participant responses, three children had ticked the faces they wanted to select, one had filled in their selected face with ink, one had marked their selected face with a cross, one underlined their selected face, and another child chose to circle and tick a few of the faces. These responses demonstrated that the children understood the idea of selecting a face by making a mark on them. Therefore, it was decided to keep the instructions about the selection of the faces of the measurement scale as they were, as it appeared to be intuitive for children to do as they felt comfortable.

5.7.1.3 Theme 3 Perceived value in using the P-MYMOP

There were two sub-themes under the main theme of 'value in using the P-MYMOP':
1) interested in completing in future (as routine practice); and, 2) statements on child's voice in consultation.

Of the 24 child-parent pairs who participated, most perceived the use of the P-MYMOP as beneficial for routine clinical practice. It was believed by the parents/guardians that the P-MYMOP would help their child to identify and remember important issues to be discussed with their doctor and provide an opportunity to their child to speak for themself in a setting

where it was often less likely for them to do so. Parents also appeared to show an interest in using the tool during future clinic visits as part of usual clinical practice.

Three parents, two from the Endocrine/Diabetes Clinic and one from the General Medicine Clinic did not see any value in using the P-MYMOP for their children. A common feature of these interviews (1 Endocrine/Diabetes and 1 General Medicine) was that the children involved were visiting the Clinic as a follow-up appointment and had no presenting complaints. The majority of the study participants perceived the completion of the P-MYMOP as valuable, and were willing to complete the tool before their clinic appointments.

5.7.1.4 Theme 4 Approach to the medication questions

The medication questions were completed by the parents of 12/16 General Medicine patients. All parents mentioned that their children were not taking any prescription, although two o stated that their child had been taking some over-the-counter and/or herbal remedies that they did not consider as ‘medication.’ No parents from the General Medicine cohort considered the medication questions as irrelevant (Table 5.2).

In the Diabetes/Endocrine Clinic, one parent did not complete the medication section on the form. Of the five parents who completed the tool, one clearly mentioned that the section was not relevant for patients with diabetes, and the rest of the parents also had concerns, as is evident in the data codes (Table 5.2).

Indeed, examination of the medication questions of the P-MYMOP, as currently written, suggest that these are not relevant for children with diabetes, as these questions ask if patients would like to stop taking their medication—which is not possible for patients with type 1 Diabetes. For patients visiting the General Medicine Clinic, however, these questions can

help with capturing information about any alternative therapies/herbs/over-the-counter medicines that they might be taking.

5.7.1.5 Theme 5 Suggested changes to P-MYMOP

Three parents from the Diabetes/Endocrine Clinic, and one from the General Medicine Clinic suggested some changes to the P-MYMOP form as presented for completion. The children from the Diabetes/Endocrine and General Medicine Clinic whose parents suggested changes, did not have any presenting complaints and therefore left the first two questions about problem-1 and problem-2 on the P-MYMOP blank. The changed suggested were: increased slots for number of problems, change the P-MYMOP to ask more disease-specific questions, and to change the word 'problem' with 'worry' or 'concern.' Specific interview codes in this regard are presented in Table 5.2.

One parent from the Diabetes/Endocrine Clinic, whose child enthusiastically completed the questionnaire, and who mentioned that P-MYMOP would be a good form to complete as it would help with organising thoughts before any clinic consult, suggested that they would like to see more space to describe the problems they had to discuss. They also showed the Interviewer the list of issues that they had prepared before coming to the Clinic for discussion. Another parent from the Diabetes/Endocrine Clinic did not like the P-MYMOP and found it too generic, suggesting alternative questions to be asked and mentioning their own experience on developing questionnaires.

Inspection of the P-MYMOP for eight participants who self-completed the questionnaire during the study, showed that the spaces provided for children to write their own issues were not enough to easily allow for the size of their handwriting. The written responses to problems/activity questions were long and did not fit easily in the space provided on the

current P-MYMOP. Therefore, a decision was made to provide increased space to answer the three individualised questions. Other changes suggested in the Diabetes/Endocrine clinic were parent-centred and therefore were not incorporated into the adaptation of P-MYMOP.

5.7.1.6 Theme 6 Connecting activity limitation with identified problems

The third question on the P-MYMOP asks respondents to identify a relative activity limitation due to their identified problem(s). This theme specifically articulated whether children were able to connect the activity limitation question with their self-identified problems or not.

Of the 24 included children, five did not mention any activity limitation on the questionnaires and that column was subsequently left blank. Two children specifically wrote that there was no activity limitation by writing ‘no,’ and ‘doesn’t stop me.’ Of the 19 children who mentioned some activity limitation, three were unable to understand that the activity limitation had to be connected to the problems that they had identified.

One parent said that the activity question was completed by the child without considering the problems that the child mentioned, and that as a result parent and child response were completely unrelated to each other. Another parent advised a change to the activity question from ‘now look at the faces below and circle the face that shows how hard it has been to do over the last few days’, to ‘now look at the faces below and circle the face that shows how hard it has been for you not to be able to do this.’ Based on this helpful comment, the Research Team decided to change the wording of the activity question accordingly. Overall, children were able to connect the activity question to their identified problems. In cases where the mentioned activity was separated from the identified problems, it was obvious from the written responses and still provided useful information for the clinical consultation.

5.8 Discussion

In this study an adult individualised questionnaire, the MYMOP2 [7], was adapted for children 7-11 years old. The results provide early evidence of content validation of the P-MYMOP in such children in General Medicine and Endocrine/Diabetes Outpatients populations. The content validation was achieved by simplifying the tool's wording, layout, and scaling method by several iterative stages that started with an online survey of local paediatricians; this was followed by a focus group discussion with local paediatricians, a second online survey of paediatric researchers; and finally, through testing the simplified language and layout with child-parent pairs in relevant Outpatient clinics by asking dyads to complete the P-MYMOP. The participating child-parent pairs were also interviewed about their experience of completing the P-MYMOP. In this study, children as young as 7 years old were able to understand and select faces to rate their named symptoms without any help from parents. Most children were also able to name their own problems with some help from parents.

Based on the direct observation of the children's completion of the MYMOP questionnaire and the interview responses of the participating children and parents, it was evident that most children could understand the concept of Problems, the P-MYMOP's recall period, and the faces scale. The medication questions were completed by the participating parents/guardians and they were able to complete it without any difficulty. After the expert feedback from the thesis examiner the medication question was changed to include inquiry on herbals as well as alternative therapies because patient's use of these is important information for their treatment (Appendix 5.8).

HRQOL is a subjective construct, so assessment may vary according to whose perception is sought. Parents/caregivers are often asked to provide an assessment of paediatric health outcomes, including measurement of subjective symptoms such as pain, anxiety, and depression. When children are non-verbal or pre-verbal, parents, caregivers, or healthcare providers may be an acceptable proxy for deriving paediatric outcomes; however, self-assessment of HRQOL should be encouraged whenever possible, given evidence that proxy ratings of childrens' HRQOL by their parents/caregivers are systematically different from the child's self-rated HRQOL [23-26]. Indeed, considerable discordance between children's and parents' ratings of HRQOL, psychological functioning, and physical functioning has been reported in children with chronic diseases [23-26]. The new tool, the P-MYMOP, is simple and is designed to support self-rating of HRQOL in children 7-11 years old.

Valid self-completion of individualised HRQOL instruments requires respondents to identify their own specific issues and then measure them with a scale. For this to occur using the P-MYMOP it was important that children could either read the tool themselves or at the very least understand the questions when read to them by their accompanying adult. With the adapted wording and layout of the P-MYMOP, most participating children in this study were able to name their own problems, with occasional help from parents/guardians. It is of note that some participating children did not have any 'problems' on the appointment day and therefore they left the P-MYMOP 'Problems' column blank. The participating children were asked in the interview if they could understand all the questions on the P-MYMOP and they confirmed it. The adapted paediatric version of MYMOP is shown in Appendix 6.

In addition to the use of simple wording and layout, to promote self-completion of the P-MYMOP by children, a faces scale was incorporated to the P-MYMOP. Comparative use of scaling methods such as the 'visual analogue scale' (VAS), the 'numeric rating scale,' and the

‘faces scale’ have been studied in relation to the measurement of pain in children [26-28]. The reason to include the ‘faces scale’ in the P-MYMOP was ease of its use in children over numeric rating scales [27,28,30]. The use of faces as a measurement scale for children is known to improve self-reporting [28] and has been found to be successfully understood by children as young as 4 years old [28]. The change from numeric rating scale to the ‘faces scale’ was further supported by the data collected during the child-parent interviews, and the observation that children as young as 7 years old were able to understand and appropriately respond to the ‘faces scale’ to rate their named symptoms without any help from parents. When calculating the score for the P-MYMOP, the ‘faces scale’ is intended to convert back to the 0-6 numeric-scale of the MYMOP2. Similar to the MYMOP2, the profile score will be calculated by adding the score from each response and is then interpreted in parallel with the individual item scores (because an increase or decrease in the overall profile score at different clinic visits may occur due to changes in one or more of the patient’s issues).

As has occurred in areas of paediatric research [31], development of a generic individualised HRQOL measure for children has lapsed behind adult measure development. The adult MYMOP, also known as MYMOP2, was developed in 1996 [32] and has been adapted for adult cancer patients [33-37], mental health outcomes [38-42], elderly patients undergoing acupuncture [13,14]; and has been translated into 12 languages [7]. The MYMOP2 offers a simple and patient-centred approach to the measurement of HRQOL. The adaptation of this tool for children may enhance their clinical care using self-assessment of paediatric HRQOL which integrates their values and preferences.

Development of the P-MYMOP is an essential precursor to the first generic individualised assessment of paediatric HRQOL. Validity and reliability (or sound psychometric properties) are relative terms, and an instrument is only valid for a population for which it has been

developed [15,16]. Accordingly, development of tools for disease-specific populations and age-specific groups is a weighty task to undertake. Alternatively, generic individualised questionnaires can provide measurement of patient-specified domains or symptoms and is encouraged by the recent establishment of Patient-reported Outcomes Information System (PROMIS) [42]. As stated by PROMIS researchers, domain-specific measures are the way forward, as the presence of a particular disease alone is not likely to define the experience of fatigue, headache, sleep difficulty, anger, sadness, etc. [43]. In the current study, P-MYMOP was tested for the suitability of its content with children with a variety of health conditions. Despite differences in parent-reported diagnoses, children were able to complete the questionnaire successfully, and to provide positive feedback when interviewed.

As with any measurement approach to HRQOL, there are some limitations to using individualised instruments for this purpose. Scores on individualised measures represent measurement of unique patient issues, and thus these scores cannot be used to discriminate between individual patients or patient groups, or for economic evaluations [4-6, 44-46]. Furthermore, since the patients nominate the individualised domains or symptoms that are important to them, changes in the importance of certain domains or symptoms over time may limit the evaluative properties of these tools in longitudinal fashion [4-6, 44-46]. Some may argue that this would limit measurement properties of individualised instruments [47]. However, there are reasons to consider that this does not affect their validity in the context of their use to inform clinical practice. Change in nominated symptoms for evaluation, for example, can inform clinicians that the patient's experience and priorities have changed over time; and hence clinicians should now focus on other aspects of life that are important to their patient. These limitations, moreover, are shared by all individualised questionnaires and are not unique to the P-MYMOP.

As the P-MYMOP allows child-parent pairs to complete the tool together, another potential limitation of the tool could be that parents select the symptoms/problems without confirming that these are important with their child. In the current study, it was decided that the interviewer would not interfere as the child-parent pair completed the questionnaire. During the study, most children completed the P-MYMOP on their own with some help from parents. Nonetheless, two participating parents were reluctant to let their child name their own issues. Therefore, acknowledging that potential proxy completion is a weakness of the questionnaire and could have contributed to an under-representation of parents who wished to provide parental help when not required, explicit instructions are now included for parents on the P-MYMOP that the questionnaire is for their child to complete with parental help only when necessary.

Similar to any study where consent must be gained, there was potential for selection here which might have resulted in more parents agreeing to participate if they were willing to allow their children to nominate their own problems. We believe that this was however minimal as the first point of contact was made with parents of potential participants by clinic nurses, who asked for parental permission to be approached by the researcher. At the point of first contact, the parents did not know what was involved with regard to children's participation into the study and none of the parents declined to be approached by the researcher. After the parental agreement the researcher handed the study Information Sheet to the caregiver and answered any questions that were asked. At this point, only one parent declined to participate in the study.

It can be argued that the P-MYMOP was developed through a top-down approach where the starting point was an adult questionnaire that underwent several rounds of adaptation through expert consultations and was eventually completed by child-parent pairs instead of starting

from scratch to develop a tool specifically for children [48,49]. There are limitations to this approach especially when this is applied to tools with predetermined dimensions/domains, as the adoption of a top-down method may mean that dimensions pertinent to the target population (children 7-11 years-old in case of the P-MYMOP) are be missed. The P-MYMOP however has no predetermined dimensions/domains. Each respondent (child) is given an opportunity to identify the domains/areas of life that are important to them on the day of P-MYMOP completion and an opportunity to quantify their impact using the faces scale. The participant child-parent/child-guardian pairs were given opportunities to provide feedback on the wording, layout, response options, and recall period of the tool in the fourth iteration of the adaptation study. Moreover, additional interviews and/or focus groups with parents and children could have been undertaken to explore issues further in the feasibility study but while this would be crucial for the effective adaptation of standard PROMs, it is less helpful for individualised PROMs.

A limitation of our approach to validation of P-MYMOP is acknowledged due to no responses being received from paediatricians to the second online survey. Fortunately, however, the opinions of this group of users were collected via the first survey and focus group discussion with the local paediatricians. According to the guidance on validation of PROMs it is not necessary to sample a large group of service providers for validation [12,17].

Assessing HRQOL may improve physician-patient communication and thus help achieve better health outcomes [2]. However, integrating HRQOL assessment into routine clinical care can be challenging. Individualised measures that are short, straightforward and quick to administer may help integrate HRQOL assessment in the time-constrained healthcare system.

P-MYMOP is the first paediatric generic individualised HRQOL measure which offers a set of brief and easy-to-complete questions that can be used to assess variation in patient-concerns, regardless of their diagnosis. The P-MYMOP may also provide a useful source of information to assist in the understanding of inevitable heterogeneity of treatment effects. Given the global initiatives advocating patient-centred research and outcomes [42,52-55], and a better understanding of the limited application of evidence from a group of patients in clinical trials to individual patients [55]; P-MYMOP can also help provide more comprehensive data from paediatric patients' perspective. Individualised outcome assessment tools such as P-MYMOP hold much promise, as personalised medicine approaches to tailor conventional therapies from a patient-perspective gain momentum.

The P-MYMOP is the first generic individualised HRQOL questionnaire adapted for use in a paediatric population [56-61]. Individualised instruments can be beneficial in clinical consultations in primary, secondary, and tertiary-care settings, N-of-1 trials, as well as in randomised controlled trials to better understand heterogeneity of the treatment effect and derive individual level recommendations [62]. Importantly, individualised HRQOL measures can help patient and healthcare provider to tailor healthcare according to the patient's needs, values, and preferences.

5.9 Conclusions

The P-MYMOP is the first generic individualised HRQOL measure created for children. The tool can be a starting point for individualised measurement of paediatric HRQOL. The wording, layout, and scale of the P-MYMOP has been successfully adapted for children 7-11 years old. Preliminary evidence on content validity has been generated, but as validation is an

iterative process, further research to assess its feasibility, reliability, and construct validity is required.

Figure 5.1 Iterations in the adaptation of the Paediatric MYMOP and their outcomes

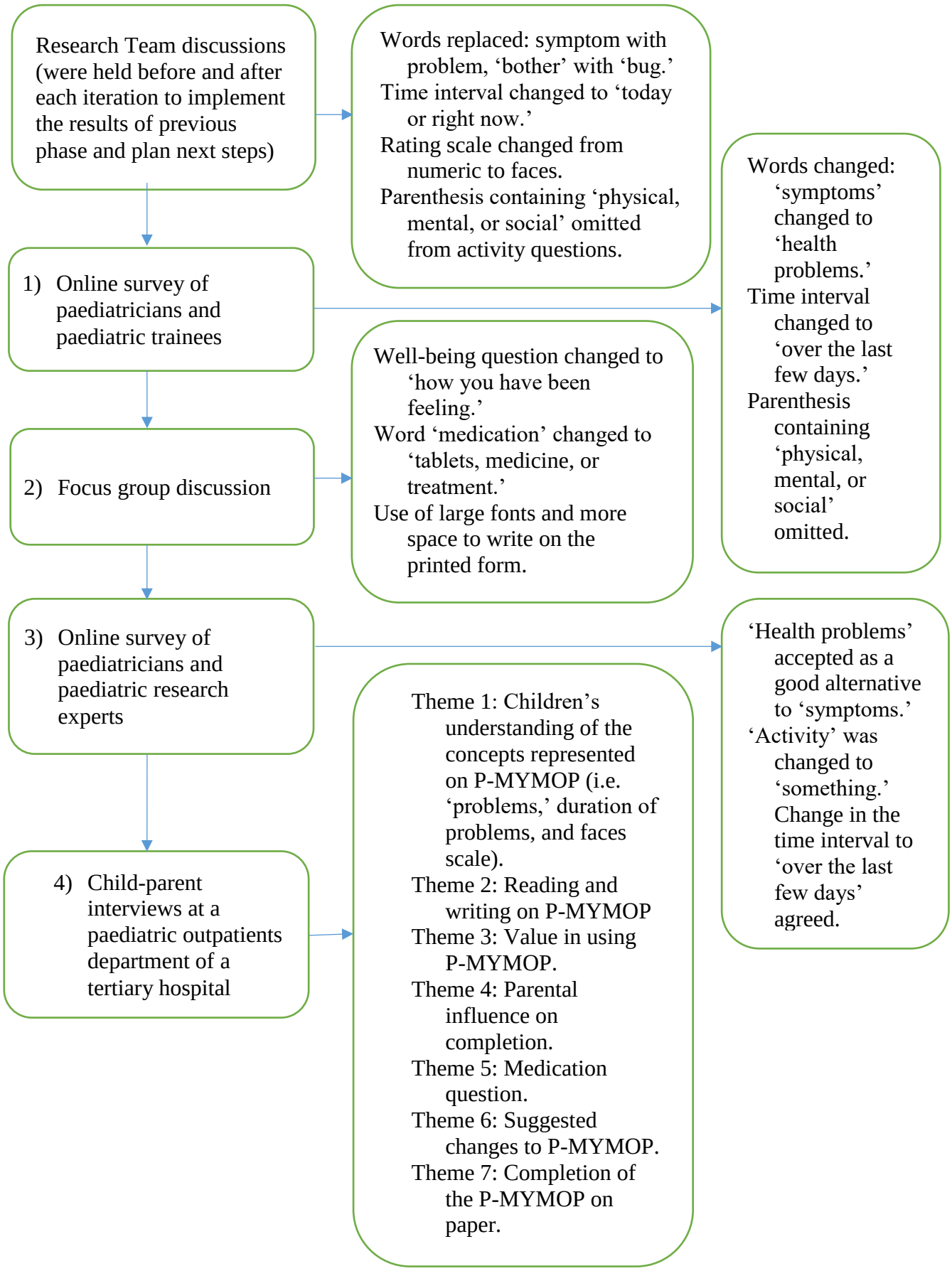

Table 5.1 Demographic Characteristics

No	Age	Child's gender	Mother/ father/ guardian	1st language	Parent's report of presenting complaint/possible diagnosis	Problem 1	Problem 2	Activity
GM1	7	M	Mother	English	Behavioural problems	Happy	Not sure	Left blank
GM2	10.5	M	Mother	English	Sleep apnoea	Not getting work done	People calling me names	Get 200 tasks done
GM3	8	M	Mother	English	Auditory processing disorder & dyslexia	Sore toe	Learning, auditory and sensory processing diagnosed 3 months;1 year ago had for at least 1-5 years	No
GM4	8	M	Mother	English	Obesity & behaviour issues	Being blamed for things he hasn't done	When things are hard to do	Unable to finish school work

GM5	10.5	F	Mother	English	Enlarged liver, raised liver function, increased IgE level	Bullies at school	Bullies get rewarded for bad behaviour	Swimming because of my eczema
GM6	8	F	Mother	English	Follow-up	Not allowed to have too much lollies	When I fall down and scratch myself	I can't play on the monkey bars
GM7	7	M	Mother	English	Asperger's	My sister annoys me	I want to have a normal break at school	Playing on Xbox 360
GM8	8	F	Mother	English	Diagnosis of small height and weight	Noise issues	Left blank	Doesn't stop me
GM9	8	F	Mother	English	Migraines	Left blank	Left blank	Left blank
GM10	10	M	Mother	English	Autism	Getting off the internet	Going to school and doing work	Is to find it easy to learn
GM12*	10	F	Mother	English	Cerebral Palsy	Cutting my hair	Go to sleep	School
GM12a*	11	M	Mother	English	Asthma	Left blank	Left blank	Left blank

GM13	7	M	Mother	English	Left blank	School	Stomach	Football
GM14	8	M	Mother	English	Mozaki Chromosomes	Fight	Mum hard at act	Stop getting angry
GM15	10	F	Mother	English	seizure of unknown cause	My mum getting angry with me	Dying	Feeling happy
GM16	7	F	Mother	Malayalam	Follow up after neurosurgery	Left blank	Left blank	Left blank
Endo1	11	F	Mother	English	Growth delay	Left blank	Left blank	Left blank
Endo2	8	F	Mother	English (non-native)	Left blank	Scared	Left blank	Jumping into the water
DM1	10	M	Mother	Arabic	Type 1 diabetes	Coming here and missing school	Staying away from my family for a long time	Make a new kind of pump
DM2	7	M	Father	Punjabi	Type 1 diabetes	Insulin injections	Reading/studies	Can’t eat sweet stuff like ice cream
DM3	8	F	Foster mother	English	Type 1 diabetes	Food	Mood	Making friends

DM4	8	F	Mother	English	Type 1 diabetes	Getting interrupted in school	Always having to check by readings	Left blank
DM5	7	F	Father	English	Type 1 diabetes	Erin (older sister) has got to eat sweets	Sweets	Eat sweets
DM6	8	F	Mother	English	Type 1 diabetes	About my friends arguing at school	One of my friends does not like to play with my other friends	Make a friendship club
*GM12 and GM12a were siblings								

Table 5.2 Themes and codes

Themes	Themes & subthemes defined	Subthemes	Codes
1) Children's understanding of concepts represented on P-MYMOP (i.e. 'Problems,' 'Duration of problems,' and 'Faces scale')	If children are able to name their problems, they can complete individualised questionnaires. Child's identification of his/her problems tells us that they can understand the P-MYMOP and hence provide positive mark to the content validity of our questionnaire	1. Child named their own problem	C: (thinking…and then wrote down something on the form - observation) is that it?' M: What do you think, what your problem would be? C: Hmmmm you can write… M: You can write it down. Come on (handed the pen to child) Observation: Child is completing questionnaire on her own. Getting help with spelling M: (helping with spelling) u i n g. Example when parent named the problem for child: GM3: Mother: to do you want to fill out this? This is like a visual way for us instead of using words. So, you can write up here. You can say sore toe.

		Mother: No no no, you just write on the smiley faces. You show me, show the lady how good or how bad it is you finding learning, reading, and writing at the moment.
	1. Children's understanding of the faces scale	DM3: M: Now look at the faces below and circle the face that shows how bad that problem has been over the last few days. C: Hmmmm M: So how bad it has been over the last few days. Have you thought about food lots, not a lot, or (pointing to faces) C: Hmmm what do you think? M: No this is your question. C: Hmm I think this one. DM5: F: now, look at the faces below and circle the face that shows how you have been feeling over the last few days.' Observation: child selects a face
	1. Understanding of the duration of problem	DM2 F: How long have you had problem 1. How long this problem (pointing to questionnaire). C: Since a year. F: 3 months to 1 year.

			DM3:C: How long have you had problem 1 either all the time or on and off please circle (reading the duration question) C: I have had it for five years M: How long have you had problem with food? C: Five years M: Over five years C:N, five years'
2) Reading and writing on P-MYMOP	This theme included observational data if the participating children were able to read and write on the P-MYMOP.	1) Who wrote the individualised items on P-MYMOP.	Example of getting help with spelling: GM3: Child: how do I spell sore? Mother: You tell me how you spell sore? Child: s o r? Mother: Hmmm (affirming) and e .hmm DM5: F: You can tell daddy if you want him to write. C: I want to write.
		2) Who read P-MYMOP	DM5: Codes from interview of a 7 year old child from diabetes clinic:

		Interviewer: Could you understand the questions when you were reading them or when your dad was reading? C: Indicated no (observation) I: No? Was it confusing? C: No I just can't read but I know what daddy said.
	3) Circle/cross to Select a face on the paper form	
3) Perceived value in using P-MYMOP	Value in using P-MYMOP	GM15:' Mother: yeah for sure. Yes absolutely which I guess for children often parent is the one who does talking so I guess this is an easy way to get them to be able to comment without having to may be face to face with the doctor. GM3: So this questionnaire, and I really like the visuals (referring to faces scale) because that is something they really can use and often in learning you use visuals in every element of learning for kids, specially kids with developmental and

learning difficulties that you rely on visual stimulus a lot and that's really handy.

It's a great scale and a great questionnaire for GP but for specialists ... a specialist or a paediatricians for longer term care they might not necessarily understand that there may be even an issue and therefore a questionnaire for parent might be a better thing. As I said when we were at (hospital) with his broken arm I loved the fact they talked to him about his body (referring to his son) and as a parent often I find that very refreshing.

And they hate, kids hate being talked about. [Name] coz she really have had a life time of medical appointments about her. She really really hates being talked about in her presence and I often, if I can get to see the therapist by making appointment to see them (Interviewer: Before?) before to meet with them to discuss it so that I don't have to say it in front of her.

GM3: Still a good scale to use, I do love ... I love the use of visuals. Any part of you know teaching kids or communicating with them they work really well.

	GM5: M: Also it is a very good idea, isn't it? (asking child) It's about the emotional side of how they are feeling as well as physical. I: So do you see value in that? M: oH yeah. Yeah I do a lot for sure.
Interested in completing in future	GM14: M: I reckon, it should be done. Because like sometimes you forget what you forget stuff that you wanted to ask and if the kids can it themselves it will make it a lot easier for all of us.
Statements on child's voice in consultation	DM3: M: Well it is (P-MYMOP) beneficial. We actually see someone else outside of here for these problems so for the doctors to know the problems that are going on. ... I think would help.
	M: Do you like this? Being able to give this to Dr (name) or would you rather tell Dr (name)? C: Give it to Dr (name) M: right. Give it ,give something like that to her.

			C: so she knows what I am saying. C: Coz it will be difficult to explain it to her. M: Yeah ... C: …very difficult ‘
4)	Approach to the meditation questions	Completion of medication questions on the paper form and any particular issues raised about the medication questions in the interview	DM1: M: (medication) with this one I believe it wasn’t much relevant to the insulin because they are all type 1(diabetes). In their case it’s all type 1. All attending the hospital are type 1 and they are taking insulin so it was a bit confusing. DM2: ‘: ok this is about the medications if he is taking anything. He is taking insulin obviously but is taking anything else? F: No I: OK then just leave this out. F: It’s not applicable. Dm5: F: Yes unfortunately we cannot cut insulin.

DM6: M: Is avoiding it … It's quite important that she takes it. .... Not important

5) Suggested changes to P-MYMOP

As observed by the researcher from the P-MYMOP forms, the children from the Diabetes/Endocrine and General Medicine Clinic whose parents suggested changes, did not have any presenting complaints.

DM1: M: yeah. If you can please give us more space to write down that we are here to see the educator, the doctor and seek guidance and speak to this and this. Aaah … couple of issues.

DM2: F: I have done this thing in my own masters. I have done an MBA so I have done this research program and sort of thing.

If you … If you make this questionnaire related, more specific towards diabetes. For example, are you ... are you happy? First of all you need to tell this kind of faces, how happy you are with your diabetes ... You will you will understand from kids point of view whether kid is happy with diabetes or not, one thing.

(observation: child pointed to a face)
F: See this is a specific answer. I didn't tell him anything. This is first question. Second question is OK the way you are taking insulin, is that insulin is helping you control your Hbgl levels. So what other help you need in terms of controlling it.

Endo1: M: I guess. With it says 'problem', it's kind of like, I don't know. This doesn't really make sense. Yeah.
I: What would make sense? Can you suggest a different word?
M: I don't know. Any worries or concerns I guess. May be. I don't know.

GM6: M: (reading the activity question to point out the place of confusion for her) Look at the faces below and circle the face that shows how hard it has been to you. I think there is something wrong with the instructions there coz I got confused.
How hard it has been to you. … I think has been for you, for you not to be able to do this for the last few days?

6) Connecting activity with identified problems	The theme is about the completion of the activity question on the P-MYMOP, and any issues raised in the interview about the particular question.	DM 1: M: No, he separated the problems from what he really wants to do. So we believe that this question is separated, totally separated from the second question. When he expressed his feelings here about the problems he didn't believe that this problem would stop him from (I: doing anything) doing anything. DM6: M: OK choose something you really want to do but find it hard because of your problems. I think it's about these problems right. So what did you want to do that is hard? C: Writes down something M: Hmm that is tricky M: But that doesn't make you super sad like your other ones? C: No

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5.11 Appendices

5.11.1 Appendix 5.1 First online survey

What is your current position?

☐ Consultant

☐ Registrar

☐ Fellow

☐ Trainee/medical resident

☐ Other

Please specify_____

We would like to adapt the wording of the current Measure Yourself Medical Outcome Profile (MYMOP), which is an adult questionnaire, for use in paediatric patients.

The first four questions of the adult MYMOP ask for a score on a seven-point scale and the rest ask for qualitative information (i.e. there is no scale).

The adult MYMOP questionnaire starts by asking patients to name two symptoms (symptom 1 & symptom 2). The exact wording of the first two questions on the adult version of MYMOP is as below:

Choose one or two symptoms (physical or mental) which bother you the most. Write them on the lines. Now consider how bad each symptom is, over the last week, and score it by circling

your chosen number.

SYMPTOM 1: 0 1 2 3 4 5 6

As good as it could be — As bad as it could be

SYMPTOM 2: 0 1 2 3 4 5 6

As good as it could be — As bad as it could be

We have drafted some changes to the above statements to make them easier for children (aged 7-11 years) to understand and respond to.

Drafted wording for item 1 on the paediatric MYMOP:

Choose one or two *problems* which ***bug*** you the most. Write them on the line (or ask someone to write them for you). Now look at the faces below and circle the face that shows how bad that problem is today or right now.

1) We have replaced the word ‘symptoms’ (in the adult MYMOP) with ‘problems’. Which of them do you prefer?

☐Symptoms

☐Problems

☐Other (please specify)

2) We have changed the time interval from ‘over the last week’ (in the adult MYMOP) to ‘today or right now.’ Which of the recall intervals do you think is appropriate for 7-11 year old children?

☐ Right now

☐ Today

☐ Today or right now

☐ Over the last week

☐ Other (please specify)_____

3) We have replaced the word ‘bother’ (in the adult MYMOP) with ‘bug.’ Which of them do you prefer?

☐Bother

☐Bug

☐Other (please specify)

4) Please suggest any other changes to this item that might aid in the understanding of a child aged 7-11 years so they can respond in a meaningful way.

The next item on the adult MYMOP is about an activity that the patient/responder identifies as important. The exact wording of the question on the adult version of MYMOP is as below:

Now choose one activity (physical, social or mental) that is important to you, and that your problem makes difficult or prevents you doing. Score how bad it has been in the last week.

ACTIVITY: 0 1 2 3 4 5 6

As good as it could be — As bad as it could be

Draft wording for activity item on the paediatric MYMOP:

Choose one activity that you really want to do but find it hard because of your problem. Write this on the line (or ask someone to write it for you). Now look at the faces below and circle the face that shows how hard it is to do right now or today

ACTIVITY:
.....
.....
.....

5) We have deleted the parenthesis containing (physical, social or mental). Do you agree with this change?

☐ Yes ☐ No ☐ other (please specify)_____

6) Please suggest any other changes to this item that might aid in the understanding of a child aged 7-11 years so they can respond in a meaningful way.

After the responder identifies two symptoms and one activity in the adult MYMOP, they are asked about their overall feeling of well-being. The question on well-being is worded as follows:

Lastly how would you rate your general feeling of well-being during the last week?

0 1 2 3 4 5 6

As good as it could be — As bad as it could be

Draft wording for the well-being item on paediatric MYMOP:

Look at the faces below and circle the face that shows how you are feeling today.

Do you agree with this change?

☐ Yes

☐ No

☐ Other (please specify)_____

No other questions on the adult MYMOP are scored.

After the well-being question, the respondent is asked about the length of time they have been experiencing symptom 1. The exact wording of the question (on the adult MYMOP) is as below:

How long have you had symptom 1, either all the time or on and off? Please circle:

0-4 weeks 4-12 weeks 3 month-1 year 1-5 years over 5 years

Do you think that the above question (with 'problem' rather than 'symptom') would be useful for the paediatric MYMOP?

☐ Yes

☐ No

☐ Other (please specify)_____

7) Would you suggest any more changes to the above question?

The last section on the adult MYMOP is about medication usage for the problem (symptoms) identified. The exact wording of this section (on the adult MYMOP) is worded as below:

Are you taking any medication FOR THIS PROBLEM? Please circle: YES/NO

IF YES:

1. Please write in name of medication, how much a day/week_____

2. Is cutting down this medication: please circle:

Not important a bit important very important not applicable

IF NO:

Is avoiding medication for this problem:

Not important a bit important very important not applicable

8) As it might be difficult for children (aged 7-11 years) to respond about medication use, it has been suggested that the medication questions are answered either by a primary caregiver or by relevant health practitioners. Do you agree?

☐ Yes

☐ No

☐Other (please specify)_____

The adult MYMOP has a seven-point interval scale to score the named symptoms. We would like to retain the seven-point format; however, as seen in the previous questions, we plan to introduce faces along the seven points to improve children's understanding of the scale. The proposed faces are replicated below:

9) Do you think these faces would help to elicit a meaningful response in children aged 7-11?

☐ Yes ☐ No ☐ Other (please specify)

10) Do you think the use of faces is more appropriate than numbers for paediatric patients?

☐ Yes ☐ No ☐ Other (please specify): _____

11) Are there any other changes you believe should be made to the adult version of MYMOP to make the tool more suitable for a paediatric population? _____

☐ Yes ☐ No ☐ Other (please specify):

12) This first administration of MYMOP for adults usually takes place within a medical consultation or in a waiting room. The follow-up questionnaire can be administered by post if needed. Do you think an adapted version of the MYMOP would be a useful tool for paediatric use in a similar context?

☐ Yes ☐ No ☐ Other (please specify):

13) Are there any other comments you would like to make?

Thank you!

Thank you for taking the time to complete this survey, it is greatly appreciated,

If you wish to be informed about the progress of this study, please share your contact information

Name

Email Address

Phone Number_____

5.11.2 Appendix 5.2 Paediatric MYMOP Draft as prepared after the First online survey

Full name _____

Date of birth _____

Address and postcode

Today's date _____

Practitioner seen _____

Choose one or two *problems* which bother you the most. Write them on the line (or ask someone to write them for you). Now look at the faces below and circle the face that shows how bad that problem has been over the last few days.

PROBLEM 1:_____

PROBLEM2: _____

Choose something that you really want to do but find it hard because of your problem. Write this on the line (or ask someone to write it for you). Now look at the faces below and circle the face that shows how hard has been to do over the last few days

Thing that I really want to do: _____

Look at the faces below and circle the face that shows how you have been feeling over the last few days.

How long have you had Problem 1, either all the time or on and off? Please circle:

0 - 4 weeks 4 - 12 weeks 3 months - 1 year 1 - 5 years over 5 years

Following questions may be completed by a primary caregiver or medical practitioner.

Is your child taking any medicine(s) FOR THIS PROBLEM ? Please circle: YES/NO

IF YES:

1. Please write in name of medication, and how much a day/week _____

_____

_____

2. Is cutting down this medication: Please circle:

Not important a bit important very important not applicable

IF NO:

Is avoiding medication for this problem:

Not important a bit important very important not applicable

5.11.3 Appendix 5.3 Focus group preparation and potential questions

1. Take copies for all focus group participants of i) consent form, ii) information sheet, iii) Paediatric MYMOP, and iv) recorder.
2. Start by introducing yourself to new members, present info from the information sheet (highlight potential risks and benefits, and that the discussion will be recorded).
3. Get signatures on consent forms
4. Play the recorder

Potential questions:

- It was mentioned by one team member that some questionnaires are used regularly in Hospital Palliative care unit. Can I please get the names of the questionnaires used in WCH currently?
    - How is your experience with them?
    - What do you like/dislike about them?
- In which patients do you think the MYMOP could be used?
- How do you envisage the MYMOP being used in these patients?
- How might the use of MYMOP change clinical practice and improve patient outcomes in different patient groups?

- *If the child is unable or unwilling to complete the questionnaire, who do you think would be best to complete the questionnaire? Parents? Nurse?
- What do you think about the language/words used in the current version? (Comment made: Language overall needs to be simplified more so for 7 year olds)

- What do you think about the current wording of the question on medication use? (For medication question, it was suggested that the word ‘medication’ is changed to ‘medicine’)
- What are your thoughts about the formatting i.e: text size on paper questionnaire and the space provided to write down the name of problem?
- Discussion about the current 7-11 year cohort at the Hospital was made. There are kids with diabetes (mostly don’t have symptom, their complaints can be around restricted diet and taking medicine), cystic fibrosis, epilepsy, ADHD (not so appropriate cohort), inflammatory bowel disease.

5.11.4 Appendix 5.4 Second online survey

1) Are you a member of

☐ International Society for Quality of Life Research (ISOQOL)

☐ Paediatric & Child Health Division, Royal Australian College of Physicians

☐ Both

☐ Other

Please specify_____

2) What is your current position?

☐ Researcher

☐ Clinician

☐ Consultant

☐ Registrar

☐ Fellow

☐ Trainee/medical resident

☐ Other

Please specify_____

3) If you are a physician, which age of children do you usually treat?

☐ 0-2 years

☐ 2-5 years

☐ 5-7 years

☐ 7-11 years

☐ Not applicable

☐ Other

Please specify_____

We would like to adapt the wording of the current Measure Yourself Medical Outcome Profile (MYMOP), which is an adult questionnaire, for use in paediatric patients.

The first four questions of the adult MYMOP ask for a score on a seven-point scale and the rest ask for qualitative information (i.e. there is no scale).

The adult MYMOP questionnaire starts by asking patients to name two symptoms (symptom 1 & symptom 2). The exact wording of the first two questions on the adult version of MYMOP is as below:

Choose one or two symptoms (physical or mental) which bother you the most. Write them on the lines. Now consider how bad each symptom is, over the last week, and score it by circling your chosen number.

SYMPTOM 1: 0 1 2 3 4 5 6

As good as it could be — As bad as it could be

SYMPTOM 2: 0 1 2 3 4 5 6

As good as it could be — As bad as it could be

We have drafted some changes to the above statements to make them easier for children (aged 7-11 years) to understand and respond to.

Drafted wording for item 1 on the paediatric MYMOP:

Choose one or two *problems* which bother you the most. Write them on the line (or ask someone to write them for you). Now look at the faces below and circle the face that shows how bad that problem *has been over the last few days.*

PROBLEM 1:_____

4) We have replaced the word ‘symptoms’ (in the adult MYMOP) with ‘health problems’. Which of them do you prefer?

☐ Symptoms

☐ Health problems

☐ Problems

☐ Other

Please specify_____

5) We have changed the time interval from ‘over the last week’ (in the adult MYMOP) to ‘over the last few days.’ Which of the recall intervals do you think is appropriate for 7-11 year old children?

☐ Over the last few days

☐ Over the past few days

☐ Over the last week

☐ Today

☐ Other

Please specify_____

6) Please suggest any other changes to this item that might aid in the understanding of a child aged 7-11 years so they can respond in a meaningful way.

The next item on the adult MYMOP is about an activity that the patient/responder identifies as important. The exact wording of the question on the adult version of MYMOP is as below:

Now choose one activity (physical, social or mental) that is important to you, and that your problem makes difficult or prevents you doing. Score how bad it has been in the last week.

ACTIVITY: 0 1 2 3 4 5 6

As good as it could be

As bad as it could be

Draft wording for activity item on the paediatric MYMOP:

Choose *something* that you *like doing* but find it hard because of your health problem. Write this on the line (or ask someone to write it for you). Now look at the faces below and circle the face that shows how hard it has been to do over the last few days

The thing that I really like doing: _____

7) We have replaced the word ‘activity’ (in the adult MYMOP) with ‘something.’ Which of these options do you prefer?

☐Activity

☐Something

☐ Other

(Please specify)_____

8) Please suggest any other changes to this item that might aid in the understanding of a child 7-11 years so they can respond in a meaningful way.

After the responder identifies two symptoms and one activity in the adult MYMOP, they are asked about their overall feeling of well-being. The exact wording of the question (in the adult MYMOP) is as below:

Lastly how would you rate your general feeling of well-being during the last week?

0	1	2	3	4	5	6
As good as it could be						As bad as it could be

Draft wording for the well-being item on paediatric MYMOP:

Look at the faces below and circle the face that shows how you have been feeling over the last few days.

9) Do you agree with this change?

☐ Yes

☐ No

(Please explain)_____

No other questions on the adult MYMOP are scored.

After the well-being question, the respondent is asked about the length of time they have been experiencing symptom 1. The exact wording of the question (on the adult MYMOP) is as below:

How long have you had symptom 1, either all the time or on and off? Please circle:

0-4 weeks 4-12 weeks 3 month-1 year 1-5 years over 5 years

10) Do you think that the above question (with 'health problem' rather than 'symptom') would be useful for the paediatric MYMOP?

☐ Yes

☐ No

(Please explain)_____

11) We would like to know your opinion on deletion of 'either all the time or on and off,' from the above wording of the adult MYMOP. Do you agree with the change?

☐ Yes

☐ No

(Please explain)_____

12) Would you suggest any more changes to the above question?

The last section on the adult MYMOP is about medication usage for the health problem (symptoms) identified. The exact wording of this section (on the adult MYMOP) is as below:

Are you taking any medication FOR THIS PROBLEM? Please circle: YES/NO

IF YES:

Please write in name of medication, how much a day/week_____

Is cutting down this medication: please circle:

Not important a bit important very important not applicable

IF NO:

Is avoiding medication for this problem:

Not important a bit important very important not applicable

Drafted Wording for the medication question on paediatric MYMOP:

Are you taking any therapy or treatment for your health problem? Please Circle: YES/NO

IF YES

Please write in the name of the therapy/treatment _____

Is reducing this therapy: please circle:

Not important a bit important very important not applicable

IF NO

Is avoiding therapy for this problem:

Not important a bit important very important not applicable

13) Do you agree with the above change?

☐ Yes

☐ No

(Please explain)_____

The adult MYMOP has a seven-point interval scale to score the named symptoms. We would like to retain the seven-point format; however, as seen in the previous questions, we plan to introduce faces along the seven points to improve children's understanding of the scale. The proposed faces are replicated below:

14) Do you think these faces would help to elicit a meaningful response in children aged 7-11?

☐ Yes

☐ No

(Please explain)_____

15) Do you think the use of faces is more appropriate than numbers for paediatric patients?

☐ Yes

☐ No

(Please explain)_____

16) Are there any other changes you believe should be made to the adult version of MYMOP to make the tool more suitable for a paediatric population? _____

☐ Yes

☐ No

(Please explain)_____

17) This first administration of MYMOP for adults usually takes place within a medical consultation or in a waiting room. The follow up Questionnaire can be administered by post if needed. Do you think an adapted version of the MYMOP would be a useful tool for paediatric use in a similar context?

☐ Yes

☐ No

(Please explain)_____

18) Which 7-11 years disease group do you think the paediatric MYMOP would be most applicable (select all that apply)?

☐ Children with diabetes

☐ Asthma

☐ Attention deficit hyperactivity disorder (ADHD)

☐ Cystic fibrosis

☐ Autism

☐ Other (please specify)_____

19) Are there any other comments you would like to make?

Thank you!

Thank you for taking the time to complete this survey, it is greatly appreciated,

If you wish to be informed about the progress of this study, please share your contact information below.

Email Address

5.11.5 Appendix 5.5 Demographic information used in the fourth iteration

Child's age _____

Parent/Guardian's highest level of education (please tick one)

☐ High school diploma or equivalent

☐ Some college degree

☐ Trade/technical/vocational training

☐ Bachelor's degree

☐ Master's degree

☐ Doctorate degree

Your relationship with the child _____

Language spoken at home _____

Home postcode _____

Name of physician seen today _____

Primary/main diagnosis (if any) _____

Presenting complaint (problem for which you saw doctor today)

5.11.6 Appendix 5.6 P-MYMOP (as it was presented to the child-parent/child-guardian pairs in the fourth iteration of the adaptation study)

Choose one or two *problems* which bother you the most. Write them on the line (or ask someone to write them for you). Now look at the faces below and circle the face that shows how bad that problem has been over the last few days.

PROBLEM 1:_____

PROBLEM2: _____

Choose something that you really want to do but find it hard because of your problem (s). Write this on the line (or ask someone to write it for you).

Thing that I really want to do: _____

Now look at the faces below and circle the face that shows how hard has been to do over the last few days

Look at the faces below and circle the face that shows how you have been feeling over the last few days.

How long have you had Problem 1, either all the time or on and off? Please circle:

0-4 weeks 4-12 weeks 3 months-1 year 1-5 years over 5 years

The following questions may be completed by a primary caregiver

1. *Do you take any tablets, medicine, or treatment? Please circle: YES/NO*

IF YES:

a. Please write in name of medication, and how much a day/week _____

_____

_____

b. Is cutting down this medication: Please circle:

Not important a bit important very important not applicable

IF NO:

c. Is avoiding medication for this problem:

Not important a bit important very important not applicable

5.11.7 Appendix 5.7 Interview questions

Interview questions to child-parent/child-guardian pair after the parent had completed the demographic information form and the child had completed the P-MYMOP

I am going to ask you to complete a form with the help of your parent. After you are done, I would like to know what you think about the questions on the form.

Parent/guardian and child's Interview Schedule:

Note: Now I have a few questions. There is no right or wrong answer- I just want to know what you think because you are the expert on you, not me. Listen carefully to each question and if you have any problem understanding, let me know and I'll try to ask them in a different way. Do you have any questions before we start?

Interview questions for child:

1. How easy were the questions on the form to understand?
2. How easy were the faces on the form to understand?
3. When you were selecting faces, the questionnaire asked to circle a face. Was it easy to circle a face or would you rather prefer crossing a face?
4. Do you have any ideas about how to make the form better for children?

We hope to use a form like this so that doctors know more about how children think about their problems – and so that it can help them make children feel better.

5. Do you think this form would help your doctor to know more about your problems?
6. Would you like to fill in a form like this every time you see the doctor?

Interview questions for parent:

Thank you for completing this process with your child. I have a few questions for you before we finish this session.

7. Do you have any additional thoughts about the form that you completed with your child?
8. Do you have any suggestions to make it more child friendly?

As explained previously, the purpose of this form is to assess the health-related quality of life of your child and to help your doctor to know more about your child from their own perspective. It also provides you and your child with an opportunity to highlight important health issues.

9. With this is mind, would you find it helpful to complete this form each time you see a doctor for your child?

10. Are there times where it might be unhelpful?

5.11.8 Appendix 5.8 P-MYMOP (as it was presented to the child-parent/child-guardian pairs in the fourth iteration of the adaptation study)

Choose one or two *problems* which bother you the most. Write them on the line (or ask someone to write them for you). Now look at the faces below and circle the face that shows how bad that problem has been over the last few days.

PROBLEM 1:_____

PROBLEM2: _____

Choose something that you really want to do but find it hard because of your problem (s). Write this on the line (or ask someone to write it for you).

Thing that I really want to do: _____

Now look at the faces below and circle the face that shows how hard has been to do over the last few days

Look at the faces below and circle the face that shows how you have been feeling over the last few days.

How long have you had Problem 1, either all the time or on and off? Please circle:

0-4 weeks 4-12 weeks 3 months-1 year 1-5 years over 5 years

The following questions may be completed by a primary caregiver

2. *Do you take any tablets, medicines, or treatments including any over-the-counter, herbal, or alternative therapies? Please circle: YES/NO*

IF YES:

a. Please write in name of medication, and how much a day/week _____

_____

_____

b. Is cutting down this medication: Please circle:

Not important a bit important very important not applicable

IF NO:

c. Is avoiding medication for this problem:

Not important a bit important very important not applicable

CHAPTER 6. LINKING CHAPTER BEFORE FEASIBILITY STUDY

Integration of patient-reported outcome measures (PROMs) into routine clinical practice has the potential to enhance patient-centred care, which may lead to better health outcomes [1,2]. Clinical indicators such as lab reports and radiographic imaging might not have much relevance to the day-to-day functioning of patients with chronic diseases. Often the most important patient-centred assessment of the effectiveness of any treatment or intervention for patients with chronic conditions is change in health-related quality of life, symptom severity, or physical and mental functioning. Data from PROMs can be used along with other clinical indicators (e.g. lab reports, imaging studies, and clinical history) for optimal patient management. Routine collection of patient-reported outcomes (PROs) can help monitor treatment effect on health-related quality of life (HRQOL)/quality of life (QOL)/health status [3,4], and detect previously unrecognized problems [5,6]. In particular, alongside clinical indicators, the detection of increased or reduced QOL or HRQOL with a validated PROM can provide clinicians with a holistic picture which will allow clinical decision making to be more patient-centred [3-6].

Validation of a PROM is a prerequisite to their use in research and clinical settings [7-11]. However, sound psychometric properties such as validity and reliability of a PROM are not sufficient to ensure its successful integration into busy clinical routine practice [12,13]. There are a number of practical and methodological challenges identified in the literature that must be managed as best as possible to enable the successful implementation of PROMs in clinical care [14-17]. Some of the identified barriers are: cost and limited resources, lack of agreed upon methods among healthcare management for integration of PROMs into routine clinical practice, difficulties in the selection of a suitable PROM for a particular clinical setting, low

priority given to PROMs in busy clinic environments, a lack of requisite technology (to enable electronically completed PROMs), and knowledge of how to interpret PROM data clinicians [14-17]. Similarly, knowledge of facilitators in the literature is essential for successful implementation. Some of the facilitators as identified in the literature are: firm but sensitive leadership that encourages the use of PROMs while managing any fear-related beliefs of healthcare providers being judged about quality of care provided based on patients' PROM results, continuous involvement of and feedback to clinicians and clinic staff on the use of a selected PROM, ongoing organisational and technical support, education of clinicians around evidence of the use of PROMs in clinical practice, and selection of a suitable PROM as per the needs of a clinical practice [14, 17-20]. The barriers and facilitators identified in the literature are context-specific and therefore it is likely that previously unidentified barriers and facilitators are discovered when a PROM is applied in a new setting [21,22]. While the process of identifying these barriers and facilitators is often iterative and takes time and patience, this ultimately leads to better integration of the PROM in practice and an enhancement of the patient experience as well as to the literature in this field.

The previous Chapter described how an adult generic individualized tool was adapted and content-validated for use in a paediatric population. The next Chapter reports on a pilot feasibility study of the integration of the newly content-validated paediatric tool (Paediatric Measure Yourself Medical Outcome Profile—P-MYMOP) into the same setting whereon it was content-validated. The methods of the Feasibility Pilot Study were informed by the results of Chapter 4 (Systematic Review). For instance, given that PROM interventions had more positive results in RCTs in which PROM scores were presented to clinicians, this pilot feasibility study planned to ensure this took place. Similarly, given that the systematic review revealed that there was only weak (non-significant) evidence that clinician training was

associated with more positive results, it was planned that the participants (nurses and doctors) of the feasibility study would be advised to discuss the completed PROM with their patient, but no special training on the integration of PROM scores into clinical consultation would be provided.

In the context of this pilot feasibility study, it was also important to be mindful that the P-MYMOP was only content-validated and that further validation of the tool requiring recruitment of a large sample of child-parent pairs is necessary. Once the feasibility of the tool in a clinical context is studied and there is evidence that it can be adopted in this setting, this will strengthen the ethical argument (thus facilitating obtaining ethical approval) for the necessary recruitment of a larger sample of child-parent pairs to assess the construct validation and responsiveness of the P-MYMOP. This later stage was considered beyond the scope of the research required for this PhD but provides motivation for the pilot feasibility study that was undertaken. The feasibility pilot study was conducted to: a) understand the barriers and facilitators to the routine use of the P-MYMOP in a tertiary-care outpatients setting, and b) to plan the next phases of the validation of the P-MYMOP.

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CHAPTER 7. FEASIBILITY OF USING THE PAEDIATRIC MEASURE YOURSELF MEDICAL OUTCOME PROFILE (P-MYMOP) AT A PAEDIATRIC OUTPATIENT CLINIC

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Chapter 7 Feasibility of using the Paediatric Measure Yourself Medical Outcome Profile (P-MYMOP) at a Paediatric Outpatients Clinic

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Overall percentage (%)	75 %
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.
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By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);
ii. permission is granted for the candidate in include the publication in the thesis; and
iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

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7.1 Abstract

Introduction: The measurement of patient-reported outcomes (PROs) is a means of including opinions and values of patients, who are the key stakeholders of the healthcare system, in the process of clinical decision making regarding their care. This study was designed to identify the barriers and facilitators to the routine use of the Paediatric Measure Yourself Medical Outcome Profile (P-MYMOP) in a tertiary hospital outpatient clinic, and to inform further validation processes.

Methods: The study required participating clinic nurses to introduce the P-MYMOP to eligible child-parent pairs attending their clinic and recommend that they take the completed tool to their clinic consultation. Participating doctors at the clinic were asked to discuss the completed P-MYMOP form with child-parent pair if the patient wished. Nineteen nurses and 11 doctors consented to participate in the study. Six participants, (three nurses and three doctors) were subsequently interviewed about their experience of the process. The resulting data was analysed qualitatively using deductive content analysis.

Results: The study ran for 19 afternoons in the Department of General Medicine Outpatient Clinic. Over the study period, 129 children of 7-11 years old were booked to attend the clinic and 77 of these presented on the day. Forty-two forms were distributed and approximately 70% patients (n = 29) who received the P-MYMOP completed it. Participating nurses were able to distribute the forms to relevant children and stated that they would be willing to do so in future. Clinic doctors found the P-MYMOP simple and straightforward, also stating that they would be willing to use it in future. The barriers identified to the implementation of the P-MYMOP were: misunderstanding of patients and clinic nurses about necessary processes involved in the use of the P-MYMOP which led to a number of patients leaving their

completed forms at reception, parent proxy completion of the P-MYMOP, impact of the busy clinic workload on nurses' ability of distribute the P-MYMOP, and that children 7-11 years old constituted only a small fraction of the total clinic population with some potentially eligible children overlooked by nursing staff. Some facilitators identified were: identification of a clinic leader to the successful implementation of the P-MYMOP, marking of the potentially eligible patients on the appointment lists by clinic nurses, and printed copies available for distribution. During the study a decision was made to recruit all outpatient clinic doctors on duty in the study on a particular day.

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Conclusions: This feasibility study collected evidence on the barriers and facilitators of implementing the P-MYMOP in a clinical practice. Both participating nurses and doctors were able to implement the tool within their routine clinical consultations with relative ease. Ensuring opportunities for meaningful engagement with doctors and clinic staff prior to study start is a potential facilitator identified in this study and this information will be invaluable in future application of the P-MYMOP.

7.2 Abbreviations/Acronyms

Clinicians:	This term includes both nurses and doctors
Doctors:	Specifically used only for physicians
HRQOL:	Health-related quality of life
MYMOP:	Measure Yourself Medical Outcome Profile
PRO:	Patient-reported outcomes
PROM:	Patient-reported outcome measures
P-MYMOP:	Paediatric Measure Yourself Medical Outcome Profile

7.3 Introduction

The measurement of patient-reported outcomes (PROs) provides an opportunity of including opinions and values of patients in process of clinical decision making regarding their care. PROs allow patients to share their views and priorities about what is important for them in accordance with their lifestyle and social system. Doctors as the 'experts' of treatment options may have more knowledge about the biological state of a patient's body and how it might physically respond to a treatment, but it is the patient who is the expert in what healthcare choices they can practically implement in their life in accordance with their priorities [1,2]. As patients are living and experiencing their disease and wellness within the socio-cultural system they are part of, it is therefore invaluable to include them in the preparation of a healthcare plan that incorporates their lived experiences.

The Paediatric Measure Yourself Medical Outcome Profile (P-MYMOP) is a generic individualised tool that has been adapted and content-validated for use in children 7-11 years old. The adult MYMOP questionnaire [3] has been adapted and content-validated for use in a paediatric population [see Chapter 5] in consultation with paediatric health practitioners, paediatric researchers, and volunteer child-parent/child-guardian pairs at the Department of General Medicine Outpatient clinic Women's and Children's Hospital (WCH), Adelaide. The current version of the P-MYMOP is considered to have appropriate content for children 7-11 years old. [The details of the adaptation process are reported in Chapter 5 of this thesis.]

According to current recommendations for construct validation of PROs [4-7], the P-MYMOP needs to be applied to a sample of 50-100 children along with the application of an external tool for comparison purposes (another questionnaire or clinical consultation record). Before conducting validation work with a large sample of children, it was considered to be

ethically and methodologically appropriate to check the feasibility and acceptability of incorporating the P-MYMOP into clinical care, with staff including clinic clerks, nurses, and practicing doctors at a paediatric outpatients department of a tertiary-care hospital.

While the use of PROMs in routine clinical care has been shown to benefit patients in some contexts [8], the focus to date has been primarily on adults, overlooking individuals ordinarily less able to communicate their health priorities, such as children, with rare exceptions [9,10]. Besides having sound psychometric properties, PRO tools intended for use in paediatric populations need to be easy to understand and supportive of self-completion [11-14]. Given the context in which they are likely to be implemented, paediatric PRO tools also need to be short and succinct for their swift inclusion into routine clinical care, not least as their inclusion may mean more work for nurses, unit clerks, and paediatricians [15,16]. Furthermore, successful implementation of PROMs in clinical care can only occur when clinicians involved in PROM distribution, interpretation, and implementation perceive PROM use as an important and useful adjunct to their clinical practice [17-19]. This may require some training of clinic staff prior to using PROMs to collect patients' health-related quality of life (HRQOL), but current evidence on the value of this is weak. Thus, clinicians' views on their experience of implementing a PROM in their clinical practice may provide evidence on the value of PROMs in clinical practice and inform improvements to the implementation of PROMs in clinical practice.

The process of integrating PROMs into clinical practice is complex as it includes several interacting components such as: distribution of a PROM by clinic staff to patients with some introduction, completion of the PROM by the child with or without help from their parent, presentation of PROM results to doctors, discussion of PROM results between patient and doctor, use of PROM results in clinical decisions made, and inclusion of PROM results in

patients' health records [20]. In addition, [as noted in Chapter 6], there are common issues reported with the literature, including cost and limited resources, lack of consensus among healthcare management regarding methods for integration of PROMs into routine practice, difficulties in the selection of a suitable PROM for a particular clinical setting, continuous involvement of and feedback to clinicians and clinic staff on the use of a selected PROM, and ongoing organisational and technical support [15,17-19,21-25]. Barriers and facilitators for these interacting components will vary across clinical settings. Therefore, a thorough understanding of the factors associated with the implementation of the P-MYMOP is needed to inform the integration of the P-MYMOP with clinical practice.

This feasibility study was designed to: a) understand the barriers and facilitators to the routine use of the P-MYMOP by testing the implementation process of introducing the P-MYMOP to child-parent pairs in an outpatient clinic waiting room, documenting any perceived changes in the workload of unit clerks nurses and paediatricians and length of time needed for consultation; and b) help in the planning of the further validation work on the P-MYMOP.

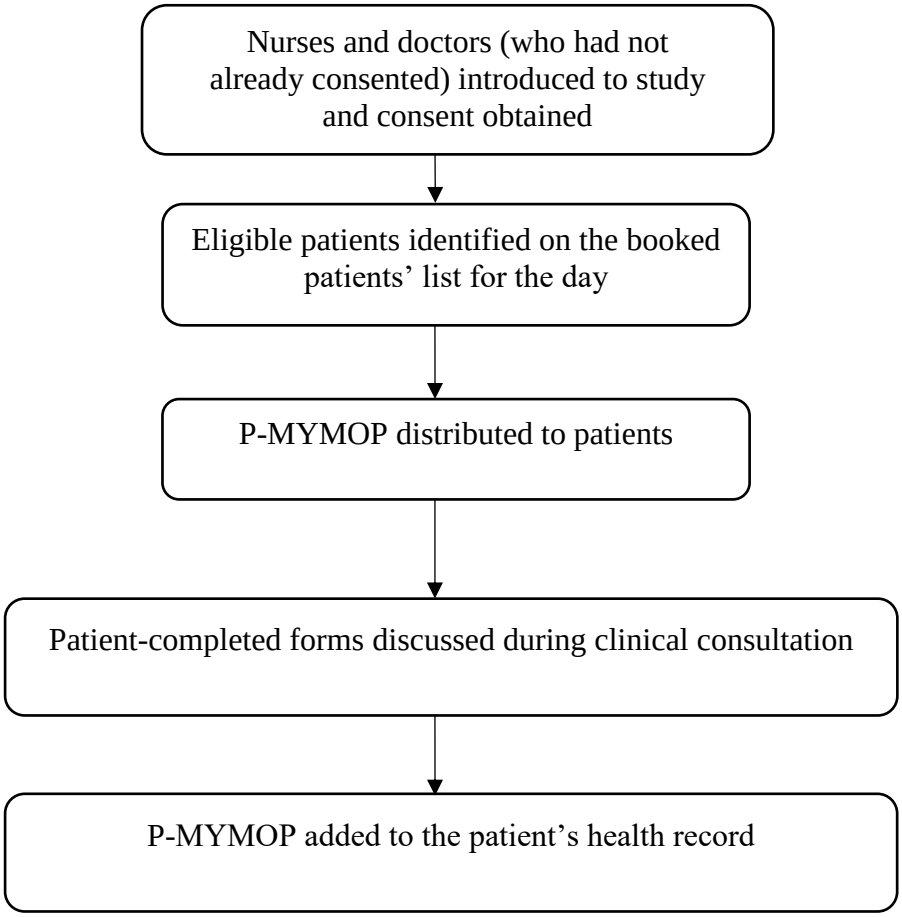
This study will also explore the impact of the P-MYMOP on clinical consultations in terms of healthcare decisions made, and report additional observations that will support or hinder the integration of the P-MYMOP in clinical settings such as an outpatient clinic.

7.4 Methods

The process for this study was as follows: a 7-11 year old child (with parent/s) arrived at the Outpatient clinic for their appointment; the clinic nurse introduced the P-MYMOP (Appendix 7.5) to child-parent pairs, asking them to complete the tool and take it to their doctor if they wished. Based on the judgement of the clinic nurse, the P-MYMOP was only given to

children who were considered able to name their own concerns. However, child-parent pairs were not the participants for this study and their completed P-MYMOP Forms were not reviewed by the researcher (SI). Completed P-MYMOPs were intended to be taken to the child's clinical consultation, and after the consultation to be added to their patient health record. The intended flow of the activities is shown in Figure 7.1.

Figure 7.1 Intended flow of activities in clinic



7.4.1 Participants

Potential participants of this study were unit clerks, clinic nurses, and doctors working in the Department of General Medicine Outpatient clinic at the WCH, Adelaide.

The primary plan was to recruit both clinic nurses and clerks for distribution of the P-MYMOP to patients, however, it was not possible to meet clerks in the nursing staff meeting because they did not attend the meeting. As a result, only clinic nurses were recruited for handing the P-MYMOP to eligible patients. Other target participants of this study were doctors working in the Department of General Medicine Outpatient clinic. The study was introduced to this group of potential participants during their weekly staff meeting by the Researcher (SI).

7.4.2 Procedure

This pilot feasibility study was approved by the WCH Network Human Research Ethics Committee (HREC/17/WCH/186). Consenting participants were informed that they were free to withdraw at any time.

7.4.2.1 Recruitment of nurses and doctors

Nurses were introduced to the study during regular biweekly meetings. The researcher (SI) provided a brief introduction to the study and an Information Sheet (Appendix 7.1) to nurses and answered any questions. Signatures on the Consent Form (Appendix 7.2) were sought from the nurses who agreed to participate in the study on the day of their shift at the Department of General Medicine Outpatient clinic. All nurses approached in the Outpatient's Clinic agreed to participate so selection bias was not a concern. Doctors working in the Department of General Medicine were introduced to the study during their weekly staff

meeting, provided with an Information Sheet (Appendix 7.1) to read, and the researcher (SI) answered any questions they had. Signatures on the Consent Form (Appendix 7.2) were sought from interested doctors at that time.

Although ethical approval for the study was obtained to recruit all doctors from the Department of General Medicine, the Departmental Head (and author 4) noted that registrars and residents (trainees at the Department) were unlikely to be interested in being recruited to the study due to workload. Therefore, six consultant paediatricians and one senior registrar (six years training) were recruited. However, as the clinic is generally staffed by two consultant paediatricians and four paediatric trainees, some patients who received and completed the P-MYMOP were scheduled to see a doctor who had not consented to participate in the Study. This would mean that the opportunity to observe the role of P-MYMOP in the clinical consultation was missed and patient issues mentioned on the P-MYMOP may have remained unaddressed. To avoid this where possible, it was decided that all doctors staffing an Outpatient clinic on a particular day would be asked for their consent to participate in the study on that day, and if this was not provided, their patients would not be handed the P-MYMOP Form. However, when approached, no doctors declined to participate.

The Department of General Medicine Outpatient clinic runs for 3.5 hours per day, three days per week. On average, each week 140 patients are booked for consultation with approximately 20% of these patients between the ages of 7-11 years, the age group of focus for this study. Consultations in the clinic are provided by approximately 14 different doctors every week.

Participating nurses and doctors were informed that they could be interviewed about their experience at a later date. At the time of consent, all participants were given the opportunity to provide contact details, only used to schedule this interview.

Participating nurses completed an Impression Form for Nurses (Appendix 7.3) after their clinic shift and were interviewed later about their experience. Consenting doctors were asked to discuss the P-MYMOP with patient if their patient wished and then to complete an Impression Form for Doctors (Appendix 7.4) after consultation with patients who had filled in the P-MYMOP (Appendix 7.5).

7.4.2.2 Analysis

Data for the study came from the nurses' and doctors' completed Impression Forms and subsequent interviews. Interviews were audio recorded and summarised directly following the interview session. Interview recordings were not transcribed verbatim, but direct quotes were extracted where necessary. Data were analysed using a qualitative content analysis that involved a directed deductive approach [26,27]. Recruitment continued until saturation of data were achieved [28], with saturation defined as the 'emergence of no new information from participants' completed Impression Forms and interviews. This occurred after interviewing three nurses and three doctors working in the Department of General Medicine Outpatient clinic.

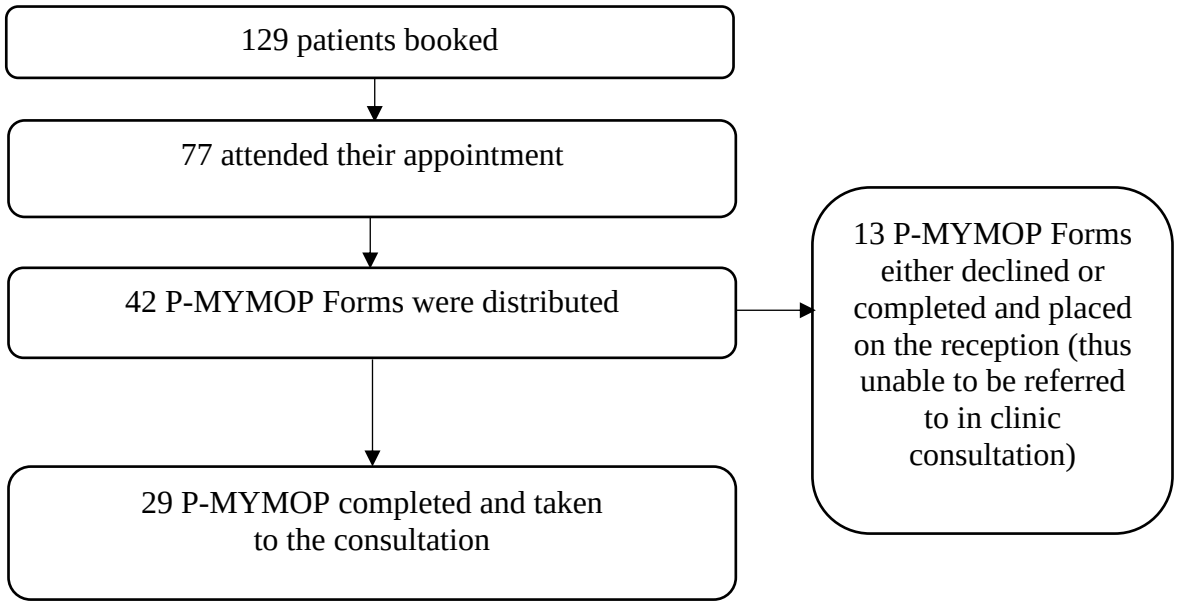
7.5 Results

The study ran for 19 afternoons in the Department of General Medicine Outpatient's Clinic, with 129 children of 7-11 years old were booked to attend during this time. On average, 40% of booked patients in the target age group missed their appointment each day, resulting in a

total of 77 patients of this target age group attending. Of the 77 children 7-11 years old, who attended their appointments about 45% received a P-MYMOP form from a clinic nurse (n = 42). Approximately 70% patients (n = 29) who received the P-MYMOP completed it, with the remaining either declining to complete the P-MYMOP or returning the P-MYMOP to the reception desk rather than to their doctor. The flow of patients during the study period is presented in Figure 7.2.

Nineteen nurses and 11 doctors working in the Department of General Medicine Outpatient clinic consented to participate in the study. Six of the participating nurses completed the Impression Form (Appendix 7.3), and three of them were subsequently interviewed. Of the 11 consenting doctors, four provided a completed Impression Form (Appendix 7.4) and three of them were interviewed about their experience.

Figure 7.2 Patient flow during the Study



7.5.1 Opinions of Nurses about the study and the P-MYMOP

From the Impression Forms completed by the six participating nurses and subsequent interviews of three of those nurses, there was agreement that the training and information provided to the nurses about the distribution and use of the P-MYMOP was sufficient and the nurses felt comfortable introducing the P-MYMOP to child-parent pairs. Two direct quotes from the Impression Forms in this regard were 'Yes I felt comfortable and confident while introducing the questionnaire to patients after reading the information pamphlet,' and 'I had not engaged with many patients previously, but all were happy with the explanation of the study.' One nurse who confirmed that she was comfortable while introducing the P-MYMOP to patients wrote on the Impression Form that '[the P-MYMOP] feels broad to me, I would like to see the questions more focused, e.g. 'do you like coming to the appointment,' 'what you do or don't like about it.' This comment demonstrated that further clarification about the aim of the P-MYMOP implementation in the Clinic would have been helpful for this nurse. The remaining five nurses did not provide comments indicating a lack of understanding of the study.

Two reasons for not distributing the P-MYMOP to eligible patients as mentioned on the Impression Form were: being busy (n = 2) and patients not attending their appointments (n = 4). When explored further during the interviews, nurses indicated that if the printed P-MYMOP Forms were added to the start of the patient file where weight and height measurement forms are kept, it would be a useful cue to distribute the P-MYMOP and would have been a useful reminder ahead of children's presentation to the clinic. Another nurse mentioned that if the P-MYMOP is introduced as an ongoing process it will require ongoing involvement of staff, further noting in interview that 'I would have liked to distribute more forms,' and that if 'a permanent folder with the printed copies of the questionnaire is present

at the reception, it would help as a reminder.' A barrier identified by one participant on the Impression Form was 'language barrier.' As some patients coming to the Outpatient clinic needed an interpreter, they could not complete the P-MYMOP on their own. However, this nurse was not available for an interview and further exploration of this issue was not possible.

When asked about how the distribution and introduction of the P-MYMOP affected time management along with the other tasks of the day, five nurses noted on the Impression Form that they did not find the task noticeably affecting their time management. Interview quotes in this regard were: 'just took a few extra minutes with each patient to explain questionnaire,' 'not really, generally steady flow of patients today.' In contrast, however, one nurse noted that the distribution of the P-MYMOP was time consuming and said 'it made the interaction with parents longer as the questionnaire requires an explanation.'

When asked about the distribution rate and on average what proportion of booked eligible patients it was feasible to hand the P-MYMOP to on a given day, five nurses noted on the Impression Form that they could achieve an 80% or above distribution rate, though one noted that the distribution rate was only 20%, due to the Clinic being very busy (15 patients of 7-11 years were booked that day). Being busy with other clinic tasks was provided as one of the reasons for missing patients by the nurse who estimated distributing 80% of the Forms, 'I got a little busy at one stage and that is when I missed a patient.'

When asked about their impression of child-parent pairs' acceptance of the P-MYMOP, all felt that there were no negative comments about having to complete the P-MYMOP from parents. One nurse did mention on the Impression Form that 'parents question motives of the questionnaire. I think a short letter explaining what the questionnaire is for and how the information will be used would help.' Other quotes in this regard were: 'No I did not receive

any feedback from the children or parents about the P-MYMOP,' 'there were no negative comments but no real feedback either.'

Overall, the participating nurses helped identify some barriers to the implementation of the P-MYMOP (i.e. busy clinic schedule and need of reminders for nurses). It was perceived that the tool distribution had a negligible impact on their time management, and one nurse showed interest in seeing the results of the study. However, one of the five nurses was not clear about the purpose of the P-MYMOP, indicating that training about the role of the P-MYMOP in clinical consultations and ongoing involvement in the implementation process may be an important facilitator.

7.5.2 Opinions of doctors about the study and the P-MYMOP

Four doctors completed the Impression Forms after clinical consultation with patients who had completed the P-MYMOP; three were subsequently interviewed. In interviews with doctors 2 and 3, no additional major themes were raised and therefore the recruitment stopped. Of the four, two had seen one patient each with a completed P-MYMOP, one had consulted two patients with a completed P-MYMOP, and one had consulted about four or five patients (they were unable to confirm the exact number) with a completed P-MYMOP.

All four doctors mentioned on the Impression Form (three subsequently confirming in interview) that the information provided in the Study Information Sheet (Appendix 7.1) was enough for them to understand the purpose of the P-MYMOP and its application in a clinical consultation, and they believed the use of the P-MYMOP should not require them to have any additional training. When asked in the interview if they would like to receive training on the use of the P-MYMOP, one participant said

> no, not really. I think it was quite a self-explanatory thing. You don't want to make it too much of a burden and it is quite easy too for them to fill out so I don't think we need any further training. Having that quite simple, it would allow conversation to flow. I just didn't have much opportunity to do that much.

Another doctor wrote in the Impression Form, 'questionnaire is self-explanatory and easy to understand. The faces make it more interesting.' When this comment was explored further during an interview, they said 'no. I don't think any additional training is needed. After reading the Information Sheet I was clear on the purpose of the questionnaire and didn't need more information.' When asked if the participating doctors had previously used any PRO questionnaire, all three interviewed doctors stated that they had never used any PROM in their practice, one saying 'no, I have not used anything similar. I like the idea.' One doctor mentioned that they had seen PROMs used during their practice in the Palliative Care Unit at the WCH, although the only trainee doctor interviewed as part of the study noted that they had never heard about PROMs and was never trained on their use. One doctor who consulted with approximately five patients with a completed P-MYMOP noted on the Impression Form (see Appendix 7.4) that 'no negative comments from parents or children about the P-MYMOP were raised,' and 'the questionnaire was helpful and the children felt involved in their consult.' The same doctor also noted that inclusion of the P-MYMOP affected their time management as 'yes, took time for patients to complete. I had to wait for them.' When explored further in the interview, however, they stated that 'it didn't impact the overall time management. I was able to finish the Clinic at the usual time.' The other two doctors did not find that the P-MYMOP negatively impacted their time management.

Three out of four doctors completing the Impression Form mentioned their concern that there was a possibility that the parent might have completed the Form despite the clear instructions

(in red, at the top of the form) that it was to be completed by the child. The same concern was mentioned during interviews by two (out of three) doctors, one stating that ‘the questionnaire opened the conversation with the child. The child seemed interested in discussing the mentioned issue, but I am not sure if the form was completed by the child or the parent.’ Another mentioned

> The one experience I had with it was a boy who I think was seven who has intellectual disability and developmental delay. And I got the impression when he came in that his parents, his mother and grandmother, had filled that out and they gave it to me quite proudly and it had written on it that biggest problem was bullying at school. When I tried to explore that with the patient, he didn’t have much idea.

The third doctor similarly state that ‘the child was involved in the discussion of the issues mentioned on the questionnaire’, but was unsure if the form was completed by the child or the parent. Interestingly, the doctor who did not share this concern either on the Impression Form or during the Interview was one who had seen about 4 or 5 patients with the completed P-MYMOP; the others had consulted with only one (n = 2 doctors) or two patients (n = 1 doctor) with the completed P-MYMOP.

When asked about the willingness to include the P-MYMOP in their future clinical consultations, the doctors wrote on the Impression Forms that ‘it could be of value if [the] child completes it,’ that the ‘overall impression of the questionnaire is very good. I am happy to use it,’ and that it ‘could be helpful in some situations.’ These views were echoed in the Interviews as the doctors said ‘I think for the right patient it would work,’ and ‘Yes, especially its useful to know that they are coming to the doctor and hoping to get some help

with bullying for example, I am not sure a doctor can help much with that, but if that is their preoccupation, it is important to know that.'

The reason why the doctors who had provided the completed Impression Form and were then interviewed had consulted with only a few patients with completed P-MYMOP was explored in the interview with one doctor, who stated that 'In my patient group I did not have that many patients between 7-11. In general paediatrics, I see a lot of babies so they are preschool age group and the ones I see over seven often they have severe autism or intellectual disabilities, so it is difficult to get them to fill that out.'

Overall, participating doctors believed that: they did not need extra training to understand the purpose of the P-MYMOP in clinical consultation; time management for the overall shift was not an issue; they did not receive any negative comments about the tool; and, appeared to be positive about its use in the future if requested/needed. There were, however, some concerned that parents, rather than the intended children, might complete the P-MYMOP in clinic.

7.6 Discussion

This study examined the practical aspects of the implementation of the recently content-validated P-MYMOP in a tertiary-care hospitals outpatient clinic. Clinical staff (i.e., nurses and doctors) working in the Department of General Medicine Outpatient clinic at WCH Adelaide were the participants of this study. All participating nurses were able to include distribution of the P-MYMOP into their daily clinic tasks, and most found this additional task easy. Similarly, participating doctors were willing to include the P-MYMOP in the clinical consultation with, albeit with a few expressing concerns on whether the P-MYMOP was actually including the children's voice in the clinical consultation or not. It was however,

interesting that the doctor who consulted with the largest number of patients with completed P-MYMOP did not have this concern. This possibility of parent proxy completion of the P-MYMOP, however, cannot be ignored and in future, it might be strategic for the distributor of the P-MYMOP to include a reminder that the child, rather than another (e.g. a parent) should complete the form. It may also be helpful for the consulting doctor to ask the child-parent pair to indicate who had completed the P-MYMOP, in order to consider this when interpreting the outcomes.

The acceptance of the P-MYMOP by all participant (nurses and doctors) in this study is similar to what has been observed in other PROM implementation studies [29-32]. For example, there are some reports that the routine assessment of HRQOL is considered to be important among paediatricians [32] and urologists [31]; in a survey of 362 members of Dutch Paediatric Association, over 80% thought routine assessment of quality of life was especially necessary for children with chronic diseases [32]. However, only 17% of paediatricians included QOL assessment to their clinical practice at the time of the survey [32].

The issue regarding recruitment noted at the beginning of the study was also instructive. Specifically, whilst it was thought that registrars and residents would be unwilling to participate due to already heavy workload, the impossibility of ensuring that forms were only handed to patients consulting with participating doctors meant a change in the recruitment process. The method of recruiting all doctors consulting on the targeted clinic day proved successful, as all attending agreed to participate. This suggests that further studies to determine the feasibility of implementing the P-MYMOP through longitudinal studies would involve necessary recruitment of a whole practice (or clinic) with provision of information

about the P-MYMOP for all practising doctors, with an opt-out option for doctors who may not wish to be involved.

As per the ethical requirement to not add any distress to children/parents, the P-MYMOP was distributed to the scheduled, eligible children based on the judgement of the distributing nurse. While this could be considered gate-keeping, the selection of eligible children was made on ethical and feasible grounds based on the diagnosis (that the nurses either knew or could read from patients' clinical records) and hence judge their ability to participate in the study. Children with severe intellectual disability for example were not offered the P-MYMOP because presumably they would not be able to complete the P-MYMOP on their own as ideally required and parents/children may find the invitation distressing.

Only certain information could be gathered in this feasibility study as the researcher was intentionally not present in the Clinic when the distribution of the P-MYMOP to patients occurred. This was to study the real life implementation and usage of the P-MYMOP in clinical setting where a researcher would not be present.

Another observation was that, although 42 P-MYMOP Forms were distributed to eligible patients with 29 completed and taken into the consultation rooms, only four doctors completed the Impression Forms with only three of them interviewed after consultation with (a combined) seven patients who had completed a P-MYMOP Form. One partial explanation for this low proportion (7/29) was that some patients did not take their completed P-MYMOP with them to the consultation room, but rather they left the forms at the reception desk. In future, this issue can be resolved by clear instructions to both the clinic nurse and clerk to direct patients to take the completed P-MYMOP with them in the clinic consultation room.

This may be expedited through the use of posters within the clinic stating, for example, ‘Please take your completed P-MYMOP Form with you in the consultation room to discuss with your doctor.’ There is also potential for electronic data capture and sharing in future applications, which would streamline the implementation of PROMs. If IT infrastructure and electronic platforms are intended to be implemented, this would need to involve considerations of cost versus effectiveness.

There were some misunderstandings of patients and clinic nurses about necessary processes involved in the use of the P-MYMOP which created barriers to its use. Several patients left their completed P-MYMOP Form at the reception desk rather than taking it to their doctor in the consultation room. Unfortunately, the number of such forms was not tracked as the researcher (SI) did not stay in the clinic once the process was explained and the printed P-MYMOP Forms were handed over. A possible strategy to deal with this issue, to some extent, would be to provide ongoing support, reminders, and training to reception staff about the use of the P-MYMOP and to inform all the reception staff of a clinic that the completed P-MYMOP should be taken by the patient to their clinic consultation room. The need for ongoing support to clinic staff, nurses, and practicing doctors has been previously noted as a facilitator to implementation of PROMs in the past [17,18,25], and confirmed in this study.

In this study, the education to the clinicians on the use of P-MYMOP was provided via the Information sheet and the initial introduction provided by the researcher. The results of education/information provided to nurses and doctors about the use of P-MYMOP was captured by their completed impression forms and interviews. Of all participating clinicians, one nurse provided answers on the impression form demonstrating that her understanding about the P-MYMOP was not as expected/needed. I believe that this particular nurse represented clinicians that require ongoing support, by a specialist on the implementation of

PRO measures. It is expected that PROM implementation into clinical care requires continuous support and adaptation of the process until assimilation into a health care facility is complete.

Another potential barrier identified in this study to the implementation of the P-MYMOP was that parents might have completed the P-MYMOP as a proxy for their child. This concern was voiced by three doctors, two of whom believed that the parent had completed the form. This would defeat the purpose of the P-MYMOP tool, designed to encourage self-assessment of child's HRQOL, as if the tool is not completed by the child it would merely represent parental views. Although parent-proxy-completed PROMs might be needed in some situations (as discussed in Chapter 1, Section 2.4), this was not the focus of the P-MYMOP. In future, a strategy to circumvent this issue could be for the clinic staff to provide clearer instructions when handing the P-MYMOP to child-parent/child-guardian pair, namely, that the tool is to be completed by the child. In addition, parents could be instructed to let their doctor know who completed the form.

There were other barriers affecting the feasibility of distributing and/or implementing the P-MYMOP in a busy outpatient clinic. One of these was the impact of a busy clinic on nurses' ability to hand out forms. Although five out of six nurses noted that they were able to achieve 80% distribution rates, on one particularly busy day, the attending nurse could only distribute the P-MYMOP to 20% of eligible patients. A further barrier was the language spoken by child-parent pairs, potentially affecting both the evaluation of the feasibility of the P-MYMOP and its implementation in outpatient clinics. As it is routine practice to offer patients who cannot speak English a foreign language interpreter who accompanies them during their clinic appointment. According to international standards, a questionnaire needs to be translated and tested for cultural suitability if it is intended to be used with participants

with other first languages [33]. While I believe the simplicity of the P-MYMOP means that assessing suitability should be a simple process, it is one we should remain mindful of.

While much was learned about the feasibility of integrating the P-MYMOP with clinical practice, this study has some limitations. The sample of doctors who completed the Impression Forms and were subsequently interviewed treated only a handful of patients with a completed P-MYMOP. Therefore, the results of this feasibility study in terms of understanding doctor's opinions are limited. However, study results also provide a complementary understanding of nurses' behaviours and opinions, contributing to an overall understanding of how the distribution of the P-MYMOPs to patients and its integration to clinical consultation (including inclusion in patient records) might occur in a busy tertiary-care outpatient clinic. Although only few doctors were interviewed, all appeared happy and willing to use the P-MYMOP in their clinics, considering that the P-MYMOP, if completed by children, was a valuable addition to clinical consults. As already mentioned, the purpose of the feasibility study was to analyse the process of the clinical application of the P-MYMOP and while taking part in the feasibility study required consent from doctors and nurses, none declined when asked so the selection bias was considered to be minimal in the recruitment process. I acknowledge that there is potential for selection bias in the responses gathered from nurses and doctors as although all of the participating clinicians (nurses and doctors) completed the impression forms, not all were available for an interview. However, their unavailability for interview is not obviously associated with their experience of the implementation of P-MYMOP.

Only certain information could be gathered in this feasibility study and unfortunately I was unable to gather denominator necessary for participation rates. I acknowledge that the low

numbers may have meant that I only spoke to people more likely to be positive about the experience.

As this study did not include patients as participants, another limitation of this study was the researcher's (SI) inability to observe the patients while they completed the P-MYMOP. This limitation made it impossible to know if the children who completed the P-MYMOP did so independently, or if their parents completed the form for them. However, in order to determine how the P-MYMOP would work in practice with minimal to no interference by a researcher, it was decided not to observe patient-parents when working with the P-MYMOP.

There are guidelines available to design pilot and feasibility studies [20,34,35]. However, their main focus is on process of pilot studies before undertaking a full randomised controlled trial; as a consequence, there is little on assessing the process of implementing PROMs in a clinical setting. Some feasibility studies on the use of PROMs have been reported in the literature in the context of hip arthroplasty [36], rheumatology [29], neurology [37], and palliative care [38]. However, whilst these studies have included patients as participants, the current feasibility study aimed to understand the process of the implementation of the P-MYMOP in a busy paediatric outpatient clinic, and assess the acceptability of the tool among the clinic staff and doctors. Furthermore, the opinions of children 7-11 years old and their parents/guardians were collected earlier during the content validation of the P-MYMOP as reported in Chapter 5 of this thesis.

Another study limitation was the large number of missed appointments in the outpatient clinic; this occurred as the study took considerably longer than initially anticipated and estimated in the ethics protocol. Approximately 40% of booked patients aged 7-11 years old did not attend their appointments during the study period, something beyond the control of

the researcher (SI), clinic nurses, and doctors. At present the WCH has a Fail to Attend (FTA) policy in place that helps the administration staff decide about further action required for a child who fails to attend an appointment. The policy takes account of the fact that children are dependent on their parents to attend appointments, that some children might be more vulnerable than others, and thus not rescheduling their appointment them might place the child at risk. Therefore, despite failure to attend their appointments without any notice, children are rebooked for the next available date. In the meantime, attempts to contact parents are made and only after all attempts at contact are unsuccessful is a child not rebooked, and is taken off the system. This FTA policy might account for why a large number of patients miss their appointment each day in the Outpatient Clinic—knowing that re-booking will be possible.

The relatively small percentage of patients within the eligible age group for this study (i.e. 7-11 years old), and thus consulting with participating doctors over time of the study (i.e. 19 days), was also a limitation to a timely evaluation of feasibility of the P-MYMOP in the Outpatient clinic. Eleven doctors initially consented, but as four did not provide contact details requested on their consent form, only seven were approached for an interview. Of these seven approached, three doctors declined as they had not consulted with any patient who had a completed P-MYMOP during the study period; one doctor had completed an Impression Form but was not available for interview.

Ideally, for implementation of the P-MYMOP as a part of routine practice, all children attending an outpatient clinic should be offered the tool. At present, however, the P-MYMOP is content-validated only for children 7-11 years old. This suggests the need for content validation of a self-report version for children 11-18 years old and possibly for children 5-6 years old. As children younger than 5 years are not generally considered capable to self-

report [39,40] a parent proxy version of the P-MYMOP for young children might also be content-validated. Once completed, this would see the provision of similar care for all patients coming to the clinic and the issue of age-based eligibility would be resolved.

Advocacy on the use of PROMs in research and clinical practice is widespread and has led to many global initiatives [41-45]. As the current paradigm of patient-centredness recognises patients as the key stakeholders in a healthcare system, development and use of PROMs for research and clinical purposes has grown rapidly [46]. However, mere development of a PROM for clinical (or research) use does not mean this tool would be useful and feasible in practice, as it may encounter barriers prohibiting its inclusion in routine practice by clinical managers and clinicians. As with other innovations/interventions, there is a wide gap between what researchers advocate and what is possible or probable in real life clinical settings [47-51]. Integration of PROMs in a clinical setting can be much more complicated than, for example, the introduction of a new medical intervention prescribed by a doctor. Integration of PROMs involves multiple steps such as: selection of a suitable PROM for a population, distribution of PROM to eligible patients, addition of PROM data to patient records, discussion of PROM results between patients and their doctor, and finally clinical decision(s) made based on PROM results. Integrating these multiple steps into a clinical practice requires a change at system level. This study was planned to consider these multiple steps. The qualitative work included in this study provides an understanding of the perspectives of the Department of General Medicine Outpatient clinic staff regarding the use of the P-MYMOP in the clinic. More specifically, this study meets recommendations to perform feasibility investigations before the full implementation of a complex intervention [20].

7.7 Conclusions

A vital way to improve healthcare and make it patient-centred is to ask patients what is important to them, perhaps by using PROMs. This, however, requires that a PROM is feasible and acceptable to healthcare providers involved. This study collected evidence on the barriers and facilitators of implementing the P-MYMOP in a clinical practice. Both the participating nurses and doctors were able to implement the tool into their routine clinical consultations. The study provides an understanding of barriers and facilitators that can inform improvements in future application of the P-MYMOP. Further research on the tool to evaluate its feasibility and acceptability in longitudinal study design is needed before introducing it as routine practice.

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7.9 Appendices

7.9.1 Appendix 7.1 Study Information Sheet

Title: Feasibility of using the Paediatric Measure Yourself Medical Outcome Profile (P-MYMOP) at the Women's and Children's Hospital Paediatric Outpatient Clinic

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What is the project about?

Quality of life is important for everyone, it is a broad concept that covers self-perception of mental, physical, and social wellbeing. Health-related quality of life (HRQOL) is concerned with components of quality of life that are directly related to health.

In order to provide better healthcare to children, it is important to ask them about their perceptions of their own health and related issues. The formal assessment of HRQOL using a validated instrument may assist the patient clinician relationship and better inform ongoing treatment decisions.

Paediatric Measure Yourself Medical Outcome Profile (P-MYMOP) is a brief 1-page individualized tool designed to quickly and validly assess HRQOL of children during a clinical encounter.

This project involves completion of P-MYMOP by 7-11 year old children visiting Women's and Children's Hospital's general medicine clinic for a consultation; this would be followed by interviews with paediatric outpatient clinic clerks, nurses, and paediatricians about their experience of the process.

Why am I being invited to participate?

You are invited to participate in the project because you work as a unit clerk, nurse, or paediatrician, registrar, or a paediatric resident at the general medicine outpatient clinic at the Women's and Children's Hospital, Adelaide.

What will I be asked to do?

If you are a nurse or a unit clerk, you will be asked to hand the P-MYMOP form to parents of 7-11 year old children booked for the consultation on that day. You will be trained on introducing the form to families. After you have completed at least a couple of shifts at the general medicine outpatient clinic, you will be interviewed about the experience. The short interview will be performed at the Women's and Children's Hospital at a time convenient to you.

If you are a paediatrician, registrar, or a paediatric resident and you agree to participate in the study; you will be asked to incorporate the P-MYMOP form into the consultation of 7-11 year old children, provided that they have completed the form. After at least three such consultations you will be interviewed by the researcher, Sana Ishaque, at a time of your convenience about the experience of including P-MYMOP in the clinical encounter. The

interview will take a maximum 10-15 minutes of your time, there will not be any monetary compensation for participation in the project.

What are the benefits of the project?

There may be no direct benefits to participants. By participating in this study, you will help ensure that the health-related quality of life tool is administered in a practical and feasible manner which may assist the patient clinician relationship and better inform ongoing treatment decisions.

Can I withdraw from the project?

Participation in this study is completely voluntary, you are not obligated to take part. During the interview you can choose not to answer a question or to end the interview at any time. Following the interview, you can choose to withdraw your information from the study at any point before data analysis begins (approximately one week after the interview). If you wish to withdraw you can do so by contacting the Researcher (Sana Ishaque, phone: 08 8313 0603, email: sana.ishaque@adelaide.edu.au).

What will happen to my information?

With your permission, interviews will be audio recorded. This allows the interviewer to focus on the flow of discussion, rather than on taking notes. The interviewer or a paid transcriber who has signed a confidentiality agreement will transcribe the recordings. Any identifying information will be removed from the transcriptions.

Transcriptions will be kept confidential and stored securely by the researchers. They will not be shared with anyone outside of the research team.

The results of this study will be presented in a PhD thesis, and may be published in academic journals and presented at conferences. You will not be identified in any report or publications. If interview extracts are quoted, they will be anonymous with any identifying data omitted.

Who will know that I participated?

Any report published as a result of this study will not identify you by name. All information will be stored in a password protected computer in a locked office at the University of Adelaide. The information will be kept for a minimum of fifteen years after the study is completed and will be destroyed after 15 years.

Who do I contact if I have questions about the project?

If you have any questions or would like additional information, contact Sana Ishaque (PhD student) by phone on 08 83130603 or by email at sana.ishaque@adelaide.edu.au

What if I have a complaint or any concerns?

The study was approved by Women's and Children's Health Network Human Research Ethics Committee (Approval number: HREC/17/WCHN/186). If you have any concerns or complaints about the study you may wish to contact the Women's and Children's Health Network Human Research Ethics Committee's Research Information Officer Mr Luke Fraser by phone 08 8161 6521 or by email at luke.fraser2@health.sa.gov.au.

If I want to participate, what do I do?

If you agree to participate please sign the Consent Form provided.

7.9.2 Appendix 7.2 Consent Form

1. I have read the attached Information Sheet and agree to take part in the following research project:

Title:	Feasibility of Using the Paediatric Measure Yourself Medical Outcome Profile (P-MYMOP) at the Women's and Children's Paediatric Outpatient Clinic
Ethics Approval Number:	HREC/17/WCHN/186

2. I have had the project, so far as it affects me, fully explained to my satisfaction by the research worker. My consent is given freely.
3. Although I understand the purpose of the research project it has also been explained that involvement may not be of any benefit to me personally.
4. I have been informed that, while information gained during the study may be published, I will not be identified and my personal results will not be divulged.
5. I understand that I am free to withdraw from the project up to a week after participating.
6. I agree to the interview being audio recorded. Yes ☐ No ☐

I am aware that I should keep a copy of this Consent Form, when completed, and the attached Information Sheet.

Participant to complete:

Name:_____

Signature:_____

Date:_____

Email (optional) _____

Researcher/Witness to complete:

I have described the nature of the research to

,

and in my opinion she/he understood the explanation.

Signature: Date:

7.9.3 Appendix 7.3 Impression Form for clinic nurses

Date:

This handout covers the questions Sana Ishaque will be asking you at the end of the trial of the P-MYMOP. Feel free to use this to capture your impressions of the measure. You are welcome to share this with Sana in the interview if you wish, but this is not required.

1. Did you feel that the introduction/training on the P-MYMOP that was provided on the Handout was appropriate and adequate?

☐ Yes

☐ No

☐ Other; please explain

2. Did you feel comfortable/confident while introducing the questionnaire to patients?

3. On average, what proportion of booked children in the 7-11 age group was it feasible to distribute the P-MYMOP to?

4. What were the reasons for not distributing the P-MYMOP to children in the 7-11 age group?

5. Did introducing P-MYMOP and handing the form to parents affect your time management while attending patients? If yes, please explain

☐ Yes

☐ No

6. What was your overall impression of the P-MYMOP?

7. How do you think the P-MYMOP was received by children and parents? Did you get any feedback from them about the MYMOP?

Thank you for your participation in the study

7.9.4 Appendix 7.4 Impression Form for doctors

Date:

1. Did you feel that the introduction/training on the P-MYMOP that was provided (during the DGM meeting) was appropriate and adequate?

☐ Yes

☐ No

☐ Other, Please explain

2. What aspects of P-MYMOP were raised during the clinic consultation?

3. Do you think the P-MYMOP improved the consultation?

☐ Yes

☐ No

If yes, how did it improve the consultation?

If no, why not?

4. How do you think the P-MYMOP was received by children and parents? Did you get any feedback from them about the MYMOP?

5. Did the introduction of P-MYMOP affect your time management during or after consultation? If yes, please explain.

6. What was your overall impression of the P-MYMOP?

Thank you for participating in this study.

7.9.5 Appendix 7.5 Final Content-validated P-MYMOP

Instructions for parent/guardians: the questionnaire below is designed for your child to select their own problems, with your help only when necessary.

Choose one or two *problems* which bother you the most. Write them on the line (or ask someone to write them for you). Now look at the faces below and circle the face that shows how bad that problem has been over the last few days.

PROBLEM 1:_____

PROBLEM2: _____

Choose something that you really want to do but find it hard because of your problem (s). Write this on the line (or ask someone to write it for you).

Thing that I really want to do: _____

Now look at the faces below and circle the face that shows how hard has been to do over the last few days

Look at the faces below and circle the face that shows how you have been feeling over the last few days.

How long have you had Problem 1, either all the time or on and off? Please circle:

0-4 weeks 4-12 weeks 3 months-1 year 1-5 years over 5 years

The following questions may be completed by a primary caregiver

3. Do you take any tablets, medicine, or treatment? Please circle: YES/NO

IF YES:

a. Please write in name of medication, and how much a day/week _____

_____

_____

b. Is cutting down this medication: Please circle:

Not important a bit important very important not applicable

IF NO:

c. Is avoiding medication for this problem:

Not important a bit important very important not applicable

8. CHAPTER 8 THESIS DISCUSSION

This chapter summarizes the major findings of the thesis and provides recommendations for future research and practice. There were three objectives of this thesis. The first was to assess the evidence on the effectiveness of the use of PROMs as an intervention intended to support the representation of patient values and preferences in clinical encounters by examining published randomised controlled trials (RCTs) using patient-reported outcome measures (PROMs) as an intervention; the second objective was to adapt and assess the content validity of an adult generic individualised health-related quality of life (HRQOL) tool for use in a paediatric population; and the third objective was to test the feasibility of the adapted HRQOL tool (Paediatric Measure Yourself Medical Outcome Profile: P-MYMOP) in a tertiary-care hospital paediatric outpatients department.

Results of the systematic review (Objective 1) and the content-validated P-MYMOP (Objective 2) were utilized to plan the feasibility study (Objective 3). The feasibility study collected evidence on practical issues of implementation and helped to establish the usability of the P-MYMOP in a tertiary-care outpatient clinic. The overall aim of this research was to review how the routine use of PROMs can help represent patient values and preference in their clinical care and to develop a self-report individualised paediatric PROM suitable for routine implementation in a time-constrained busy clinical practice.

The combined results of this thesis provide guidelines for the implementation of the P-MYMOP in a tertiary-care hospital outpatient clinic and can inform future studies to further test the psychometric properties of the P-MYMOP, as well as to implement an RCT on the effectiveness of routine clinical use of the P-MYMOP.

8.1.Summary of the thesis research

An initial impression of the lack of attention paid to the value of PROM use in paediatric research and clinical care, as discussed in Chapter 2, remained unchanged after the completion of the systematic review (Chapter 4). Of the 22 included studies, only two reported on the inclusion of a PROM in RCTs performed in paediatric populations [1,2]. In addition to the lack of attention to PROM research in children, there was a lack of consideration given to the value of individualised PROMs overall. A total of 23 PROMs were used as an intervention in the 22 RCTs included in the systematic review and none of these was a generic individualised tool. The two paediatric RCTs included used the PediQuest Memorial Symptom Assessment Scale (PQ-MSAS), the Pediatric Quality of Life Inventory 4.0 Generic Core Scales (PedsQL4.0), the Pediatric Quality of Life Inventory (PedsQOL) Diabetic-specific, and an overall sickness question [1,2]. Again, none of these were individualised and generic. Nonetheless, the importance of a validated, individualised and generic HRQOL tool for children cannot be ignored. Globally, there is emphasis on the use of person-centred measures that can evaluate patient concerns regardless of their underlying diagnosis [3]. A key example of this international interest in PROMS is the Patient-Reported Outcomes Measurement Information System (PROMIS) initiated in the USA' this organisation supports and promotes the valid measurement of life domains by instruments that are applicable to a wide variety of populations [3].

As the experience of mental, physical, and social health issues are not influenced solely by the presence or absence of a particular health condition, a validated paediatric generic individualised tool such as the P-MYMOP can validly assess children's perceptions of their health issues and is applicable to children with a variety of health conditions. Although the

current P-MYMOP has been content-validated with children 7-11 years old, the individualised selection of domains by the responding child in the P-MYMOP lends itself well to use in a broader age group of potential responders. The proposal that the P-MYMOP might be applicable to a wider age group of children should consider, however, that older children might not find the smiley faces appropriate, whilst younger children might need proxy completion of the P-MYMOP as their cognitive and language development might not allow for self-report. Therefore, the proposal needs to be examined in future research on the tool.

The lack of validated paediatric PROMs for several populations with specific health issues has resulted in the use of adult tools in RCTs on paediatric populations [4-9]. The use of these tools in this context has been criticised [10] and a call for further research into the development of validated paediatric PROMS has been made in a number of disease-specific populations [10]. The adaptation of the MYMOP to a validated paediatric generic individualised tool is one important response to that call. The P-MYMOP is the first content-validated generic individualised HRQOL tool for children. Prior to the adaptation of the P-MYMOP a partly individualised disease-specific paediatric questionnaire (Pediatric Asthma Quality of Life Questionnaire—PAQLQ) was validated for use in children [11]. As the name indicates the PAQLQ is not generic and is therefore only applicable to children who have asthma. In comparison, the P-MYMOP has much wider potential for application. The children who participated in the adaptation process on the P-MYMOP were recruited from the Department of General Medicine Outpatient Clinic at Women’s and Children’s Hospital Adelaide and included children experiencing variety of health conditions.

As indicated in the systematic review (Chapter 4), routine collection of PROs in clinical settings along with the presentation of their results to treating doctors has demonstrated benefits to patient outcomes in some contexts. The ultimate goal for the adaptation of the P-MYMOP is to integrate it successfully into paediatric clinical practice. The fulfilment of this aim, however, requires further validation of the P-MYMOP and evaluation of the effectiveness of the new tool, which was beyond the scope of this thesis. In preparation for these further research projects, studies conducted as part of this thesis investigated the acceptability and potential value of the tool from the patient and health professionals' perspectives.

The adaptation and content validation of the P-MYMOP involved interviews of 24 children 7-11 years old and their parents/guardians. Children as young as seven years old were able to complete the tool. Most participating parent/guardians perceived the P-MYMOP to be a useful adjunct to the healthcare of their child and were interested to use the tool during future clinic visits.

Feasibility studies are considered necessary in the planning of RCTs and large-scale observational studies [12-16]. The feasibility study performed as part of this thesis examined the process of the P-MYMOP implementation in the Department of General Medicine Outpatient clinic at the Women's and Children's Hospital. The study collected the views of nurses and doctors working in the Clinic to identify barriers and facilitators to the implementation of the P-MYMOP from the health professionals' perspective. The feasibility study results were promising in that the nurses and doctors were able to introduce the P-MYMOP into their usual practice without much of a perceived burden to their allotted time with each patient.

8.2.Key Findings of the Thesis

This section discusses the key finding of the Thesis. The section has five subheadings, each heading summarises one main finding of the thesis and where possible connects the learning points from the three studies conducted.

8.2.1. Utility of PROMs in routine clinical care

As reported in Chapter 4, the systematic review performed as part of this thesis included 22 RCTs. There were two different kinds of RCTs addressing PROM interventions: a) RCTs comparing the presentation of PROM summary scores to clinicians vs. no presentation of summary scores (labelled 'PROM ± summary' studies) and b) those that compared patient completion of a PROM with standard care in the control group (i.e. no use of a PROM) (labelled '± PROM' studies). The outcomes reported in the 22 included RCTs were divided into three categories: process of care outcomes, health outcomes, and satisfaction with healthcare. Reported effects were considered 'robust' if they were statistically significant and pertained to a single reported comparison or there was evidence that the study was adequately powered for more than one comparison. Other positive effects were considered as 'non-robust.'

As reported in Chapter 4, analysis of tabulated results led to the following findings: more positive results were reported for health outcomes (n = 11 studies, three considered 'robust'), compared to those for the process of care or satisfaction with care; PROM interventions worked better when PROM results were provided to clinicians; and, the inclusion of PROM training to clinicians prior to a trial commencement appeared to result in no obvious differences in positive results. This analysis of results was combined with the learning from the multi-iterative adaptation of the P-MYMOP to develop the feasibility study, the last and

final study of this thesis. As reported in the Chapter 6 linking piece before the feasibility study, the results of systematic review (Chapter 4) informed the methods of the feasibility study performed as part of this thesis. For example, given that PROM interventions had more positive results in RCTs in which PROM scores were presented to clinicians, this pilot feasibility study planned to ensure this took place. Similarly, given that the systematic review revealed that clinician training did not appear to be significantly associated with more positive results, it was planned that the participants (nurses and doctors) of the feasibility study would be advised to discuss the completed PROM with their patient, but, other than basic introduction to study as required under the ethics protocol as outlined in the Participant Information Sheet used to commence the feasibility study reported in Chapter 7 (Appendix 7.1), no special training on the integration of PROM scores into clinical consultation would be provided.

8.2.2. Methodological issues identified in the systematic review (Chapter 4) and recommendations for future RCTs

There were a number of methodological concerns identified in the RCTs included in the systematic review (Chapter 4). These concerns limit the ability of many included RCTs to provide definitive conclusions about the effectiveness of PROM interventions. These methodological issues are discussed in detail in Chapter 4, but issues that are specific to the evaluation of PROMs are briefly discussed below.

As a rationale for the use of a selected PROM, all RCTs included in the systematic review (Chapter 4) cited previous psychometric evaluation of their chosen PROM. However, none of these RCTs that used PROMs as their primary or secondary outcome reported on whether the context and demographic characteristics of the population in which the psychometric evaluation was performed was similar to those in the target population of the RCT. Given that

psychometric properties of a PROM are not inherent properties and that a PROM is only valid and reliable for a population in which the primary validation study was performed, it was not possible to ascertain if the PROMs identified in the included RCTs were valid for the context in which they were being used. Developing a new PROM before each RCT is extremely challenging and would result in multiple PRO tools, thus rendering comparison of RCTs impossible. Nonetheless, at the minimum researchers performing a RCT should match the baseline characteristics of the population in which the PROM was validated with the baseline characteristics of their target population. The provision of citations to previous validation work as well as reporting a rationale for the selection of a particular PROM in RCTs is recommended by the CONSORT PRO extension developed in 2013 [17]. However, the recommendation of provision of 'a rationale' by RCTs is broad and consequently open to interpretation and does not clearly identify the need to match demographic characteristics and context of the PROM psychometric study with the intended RCT population; this requires further clarification in the guideline document [17]. As included RCTs in Chapter 4 were published between 1989 to 2016 and the CONSORT PRO Extension was published in 2013, the trials previous to this date cannot be criticised for not reporting their rationale for the selection of the PRO tool used. In addition, the uncertainty that this issue created regarding the conclusions of RCTs included in Chapter 4 could be addressed with a retrospective analysis of the populations from which psychometric properties of PROMs were evaluated, their suitability for the RCT population and for use within clinical studies where outcomes are aggregated over individuals. An examination of their suitability in all contexts would be informative.

A PROM that is selected for evaluation of its effectiveness in a population must be acceptable to that population and feasible within the clinical context that it is to be used.

When choosing a PROM to assess pre-defined primary or secondary outcomes in future RCTs, a clear rationale behind the selection process should be stated. If the rationale cannot be reported in the publication of the RCT due to space limitations it should be noted in the RCT protocol required to register the RCT prior to commencement.

8.2.3. Perspectives of child-parent/guardian pairs about the P-MYMOP

The P-MYMOP is the first self-report, content-validated, generic, individualised tool for children 7-11 years old. As reported in Chapter 5, the adaptation and content validation study utilised multi-iterative mixed methods. The multiple iterations in the study ensured that all relevant stakeholders contributed their knowledge of the field to the process.

Typically, PROMs are initially developed for research purposes and then introduced into clinical use. Implementation of such PROMs to a clinical setting may be limited due to their pragmatic characteristics [18]. Pragmatic characteristics of PROMs—such as appropriateness for relevant clinical setting, self-administration, response options, and scoring—are considered important factors affecting their acceptance and feasibility of implementation in a clinical setting [18]. Lengthy, complicated PROMs are often not readily adopted in clinical settings due to the training, knowledge, time and resources required for their implication in already busy clinics. In this study, the wording, layout and length of the P-MYMOP was kept simple and succinct for ease of successful implementation in paediatric clinical settings.

The final phase of the content validation of the P-MYMOP included children 7-11 years old from the Department of General Medicine and Diabetes/Endocrine Outpatient clinics at the Women's and Children's Hospital, Adelaide. Twenty-four children participated in the study along with their accompanying parents/guardians. The purpose of the study was to test the children's understanding of and responses to the wording, layout, and newly-added faces

scale of the P-MYMOP. In addition, the opinions of children and their parents/guardians were sought about the usefulness and acceptability of the P-MYMOP in their clinical care in the outpatient clinics. Details of the adaptation process are reported in Chapter 5. The P-MYMOP was developed to encourage self-reporting, and it was confirmed in the adaptation study that most participating children were able to complete the P-MYMOP on their own, with only a few exceptions where parents completed the form for the child or helped with the process. Children as young as 7 years old were able to understand the tool and to report their main problems. All participating children and their parents/guardians considered the use of a faces scale on the tool as a positive addition. The participating parents/guardians perceived the P-MYMOP as a valuable addition to the healthcare of their child and that it would provide an opportunity for children to speak about concerns they felt were important to them. As asserted in section 5.10, the P-MYMOP is the first paediatric generic individualised tool content-validated for children 7-11 years old. In summary, the wording, layout, and scale of the P-MYMOP has been successfully adapted for children 7-11 years old, and children and their parents/guardians have found the tool acceptable.

8.2.4. Perspectives of nurses and doctors about the implementation of the P-MYMOP to clinical care

The feasibility study was performed to examine the implementation of the P-MYMOP in the Department of General Medicine outpatient clinic at the Women's and Children's Hospital. Nurses and doctors working in the outpatient clinic were study participants. As reported in Chapter 7 in the feasibility study results, the overall impression of the participating nurses about the P-MYMOP was positive, as they perceived that the tool distribution had a negligible impact on their time management. Nonetheless, the need to train nurses about the role of the P-MYMOP in clinical consultations was identified. In contrast, participating

doctors did not think that they needed training to understand the purpose of the P-MYMOP in clinical consultation, stating that time management for the overall shift did not appear to be compromised, and, as they did not receive any negative comments about the tool from families, they were happy to use it in the future if requested/needed.

8.2.5 Involving clinical staff in the integration of PROMs into routine clinical practice

Involving clinical staff in the integration of PROMs in a clinical setting is essential. Any clinic operates with a number of staff, such as unit clerks/receptionists, nurses, doctors, dietitians, physiotherapists, and others. Generally, clinic reception staff as well as clinicians in general are not trained on the use and utility of PROMs. Therefore, the introduction of a new PRO tool might cause confusion and raise questions about its utility for clinical purposes.

In addition, because clinic staff are required to facilitate distribution to eligible patients, the format of a PROM (e.g. in hardcopy, as is currently the case for the P-MYMOP, or as an electronic version) will affect its use in routine clinical care. At the time of distribution patients or their parents/guardians may have queries about the purpose of completing this tool and its role in their clinical care. Therefore, successful integration of a PROM may require distributing staff to have some understanding of its purpose and role in clinical consultation. As the results of the systematic review (Chapter 4) demonstrated that PROMs are more likely to have a positive impact on patient outcomes if their results are presented to clinicians, during integration of the P-MYMOP it is recommended that the results of completed forms are presented to doctors (or caring clinicians) for discussion during clinical consultation, and that staff are aware of likely benefits for patients. Furthermore, doctors presented with PROM results will need to know how to incorporate these results in the provision of clinical care.

Whilst the systematic review of RCTs (Chapter 4) demonstrated that clinician-training regarding the interpretation of PROM results was not significantly associated with the effectiveness of the PROM interventions, the present feasibility study results (Chapter 7) suggested otherwise. Although participating doctors did not feel it was necessary for additional training, they did need to understand what the purpose of the P-MYMOP, how they could interpret the results, and how it might be integrated into routine clinical care of their patients. This brief training was provided by the researcher (SI) at the time of their recruitment to the feasibility study. It is possible that additional training was not needed by participating doctors because some had been involved in the adaptation and content validation phase of the P-MYMOP (Chapter 5).

Engaging healthcare providers into the integration process of PROMs is also likely to create a collective responsibility among stakeholders involved [19-22]. With increased advocacy on the use of PROMs in clinical care [19-22], educational programs on what PRO and PROMs are, what constructs they might incorporate, as well as the value of PROs for patients with chronic health conditions may prove useful for clinicians. Given the rapid emergence of and uptake of PROMs, such educational programs could be targeted at undergraduate nursing and medical education programs, as well as constituting part of continuing professional development education for practising doctors.

8.3.Future research implications

8.3.1. Further validation of the P-MYMOP for children 7-11 years old

At the time of writing, the P-MYMOP is only content-validated for children 7-11 years old. The measurement properties for a particular application/use of a PRO tool depend upon the purpose for which the tool is being used [23-25]. Before the clinical (and/or research) use of

the P-MYMOP, it is critical to undertake further validation processes. This should include assessment of construct validity, responsiveness, and internal consistency for children 7-11 years old. The evaluation of construct validity and internal consistency requires single use of a PROM by patients [24,25], but evaluation of responsiveness requires a longitudinal study involving application of a tool on more than one occasion with the same patients [24]. During the present study, it was noted that the time interval between clinic appointments of visiting patients can be anywhere between two and twelve months. Responsiveness evaluation requires a much shorter time interval between two consecutive administrations of a tool [24,26], in part because a longer time interval between two applications of the tool might see changes in multiple aspects of the patient, such that a different score on the tool might not represent change on the domains originally measured. This is particularly salient given the rapid developmental changes likely to be present in children within a targeted age range. Therefore, the evaluation of responsiveness of the P-MYMOP might require a different setting, such as recruitment of children from a school. Guidelines available for the evaluation of measurement properties can be referred to in designing these future research studies [23-26].

8.3.2. Adaptation and content validation of the P-MYMOP for children below 7 years old and above 11 years old

At the commencement of this thesis the decision was made to focus the development of the P-MMOP only on children 7-11 years old. This age group was chosen based on the cognitive homogeneity of age bracket [27-29]. The successful adaptation, content validation, and feasibility evaluation of the P-MYMOP for children 7-11 years old in an outpatient clinic has provided sufficient evidence to support continuing this work for children of other ages. Indeed, since routine measurement of PROs may improve patient outcomes, it would be ideal

to offer a PROM to children of all ages. To promote successful implementation of the P-MYMOP in a clinical setting, the tool should therefore be validated for children below 7 and above 11 years of age. The P-MYMOP was adapted and content-validated to promote self-assessment of individualised HRQOL among children, but self-report may not be possible for children below 5 years old and a parent proxy version of the tool might be needed [30,31]. Nonetheless, future versions of the P-MYMOP should continue to promote self-report of paediatric HRQOL whenever possible.

8.3.3. Longitudinal testing of the implementation of the P-MYMOP

The feasibility study performed as part of this thesis evaluated a cross-sectional use of the P-MYMOP. It would, however, be important to evaluate how the tool performs when used in a longitudinal fashion, that is, to evaluate patients on their repeat visits for the issues that they had mentioned on their P-MYMOP forms previously. In practice, the use of the P-MYMOP is likely to occur longitudinally as patients visit a clinic on multiple occasions. Therefore, it would be important to gather the opinions of patients, reception clinic staff, nurses, and doctors in a longitudinal feasibility evaluation of the tool [32].

8.3.4. Implementation of the P-MYMOP in a clinical setting

As the first generic, individualised, paediatric HRQOL tool, the P-MYMOP was developed for routine use in paediatric clinical practice. Once additional measurement properties of the P-MYMOP are evaluated, the tool may be implemented in paediatric clinical setting. The hypothesis behind the proposed implementation of the P-MYMOP is that the tool will help identify and monitor patient symptoms and treatment planning by providing a voice to children and helping them play an active participatory role in their clinical care. Due to its self-selected domains (individualised), the P-MYMOP is highly patient-centred and therefore

it provides a unique opportunity for responding children to inform clinicians about important areas of their life for which they would like help. The current version of the P-MYMOP is available in a paper format. It is a one-page tool that is two-sided as a large font size was required for readability purposes. There are specific instructions for parents/guardians at the top of the tool printed in red requesting that the tool is for their child to select and rate their own problems, with parental help only when necessary. As reported in the feasibility study (Chapter 7), clinic nurses responsible for the distribution of the tool were likely to feel better supported for integration if a printed blank copy of the tool was added to the health records of eligible patients. Besides this, no other additional resources or requirements are needed to implement the current paper version of the P-MYMOP. If implementation of the tool is done in a clinic where electronic health records are already in place, development of an electronic format of the tool and process of integration with electronic health records would be required.

As the P-MYMOP is a self-completed tool, staff distributing it should be asked to make a judgement as to which children in the eligible age group would not be able to complete the tool on their own. This necessary element of judgement mirrors the content adaptation process when the researcher (SI) was only allowed to approach patients once they had agreed to be approached after the initial contact by clinic nurses; similarly, in the feasibility study, clinic nurses were able to make this judgement, informing the researcher at the end of the clinic day as to why they would not distribute the tool to a particular children. Based on this learning, clearer guidance on criteria for distribution could be added to an information pamphlet handed to reception staff and clinic nurses. Further general directions to the implementation of the P-MYMOP in a clinical setting can be obtained from published guidelines on the implementation of PROMs in clinical settings [33,34].

8.4. Thesis strengths and limitations

The systematic review performed as part of this thesis is the first systematic review in which all statistically significant and non-significant results of the included RCTs were taken into account. This foundation lay the groundwork for the first research (to my knowledge) to develop a paediatric individualised generic HRQOL measure. Given the value that generic individualised tools offer by their applicability to populations with different health conditions, this new tool is likely to benefit clinical research and practicing clinicians. The tool is also short and succinct, and was developed to promote self-completion by children. The adaptation/content validation involved multiple stakeholders of the paediatric healthcare system and most importantly the opinions of the primary stakeholders, namely, children, were also sought. The involvement of paediatric researchers helped confirm that the content of the tool was suitable according to their experience in the field of paediatric PROMs. The involvement and collaboration with paediatricians helped in designing the P-MYMOP to be a clinically relevant and practically implementable tool. The feasibility study confirmed that it was feasible to implement the P-MYMOP in a clinical setting; results will also help with the planning of the next validation study of the P-MYMOP and the integration of the tool into routine clinical care.

There are certain limitations of this thesis. The adaptation of the P-MYMOP was planned to include opinions of a large group of paediatricians via an online survey. However, participation was limited and paediatricians from only one tertiary-care hospital could be recruited. In addition, the feasibility study was conducted in the same department, with participating child-parent/child-guardian pairs also recruited from the same outpatient clinic. This may limit the extent to which the sample of participants may represent all tertiary-care

hospitals across Australia. Finally, the study only tested cross-sectional use of the P-MYMOP and further research on doctors' ability and understanding of the longitudinal use of the P-MYMOP (including information concerning their interpretation of the qualitative information reported in the P-MYMOP and P-MYMOP scores (P-MYMOP data)) may be required.

8.5.Concluding remarks

It may be argued that the use of PROMs in routine clinical care is simply an adjunct (or alternative) to clinical history-taking. However, there are reports in the literature that healthcare providers underestimate the level of patients' functioning and under-report symptoms that patients find worrying [35-42]. This suggests that medical history-taking alone is likely to miss important patient-centred values. Though the need for systematic use of PROMs is increasingly recognised, actual integration of these tools in routine clinical care remains challenging. Despite evidence on effectiveness, the implementation of a new practice requires that the end users perceive it to be useful and in line with their needs and values.

The P-MYMOP is a succinct self-report generic individualised tool that was found acceptable by children and parents/guardians and feasible by nurses and doctors during its implementation in an outpatient clinic and provided a voice for children to play an active participatory role during their clinical encounter. As such it is my hope that, pending additional validation and longitudinal feasibility work, this tool will empower children with the knowledge that their views and opinions (always) matter and that they can play an active role in decision-making regarding their health.

8.6 References

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