A PERSONALIZED APPROACH IN CLINICAL PRACTICE TO IDENTIFY GOALS AND PRIORITIES OF EACH INDIVIDUAL PATIENT: THE PERSONALLY MEANINGFUL OUTCOMES–ASSESSMENT PROCESS (PMO-AP)

by

Venkata Narendra Sravan Jaggumantri

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The following individuals certify that they have read, and recommend to the Faculty of Graduate and Postdoctoral Studies for acceptance, the dissertation entitled:

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submitted by Venkata Narendra Sravan Jaggumantri in partial fulfillment of the requirements for

the degree of Doctor of Philosophy

in Experimental Medicine

Examining Committee:

Dr. Jean Paul Collet, Clinical Professor, Department of Pediatrics, UBC
Supervisor

Dr. William McKellin, Professor, Department of Anthropology, UBC
Co-Supervisor

Dr. Richard Sawatzky, Professor, School of Nursing, Trinity Western University
Supervisory Committee Member

Dr. Skye Barbic, Associate Professor, Department of Occupational Science and Occupational Therapy, UBC
University Examiner

Dr. Jan Friedman, Professor, Department of Medical Genetics, UBC
University Examiner

Abstract

Determining tangible outcomes that reflect the personal goals and priorities of individual patients regarding their treatment's effects are currently not part of the treatment evaluation in clinical practice. My doctoral research addressed one overarching question: how can clinicians provide an effective person-centered approach to clinical care that identifies what matters most to the individual patient and the expected level of change that is considered meaningful? In this dissertation, I present a new strategy to evaluate treatment effectiveness at a personal level: the Personally Meaningful Outcomes – Assessment Process (PMO-AP). PMO-AP is administered in four successive stages using an interview-based format, which includes generation of personally meaningful outcomes (PMOs) with clear indicators and a modified goal attainment scaling corresponding to the different levels of meaningful changes in PMOs expected by each individual patient described a-priori in collaboration with the clinician using a modified goal attainment scaling process. At each stage of PMO-AP from identification of PMOs to why a particular score is selected for a PMO at a follow-up visit, there is a dialogue between the clinician and the patient, which provides context and rationale for the information collected.

I conducted a study with 50 participants to evaluate the test-retest reliability, validity, and ability of PMO-AP to generate information in the context of personalized medicine. The results showed that the PMO-AP is a reliable process that generates valid PMOs and meets the characteristics of a truly personalized assessment. I evaluated the feasibility of using PMO-AP in clinical practice through focus groups with staff from three separate clinics serving diverse types of patients. All participants found the PMO-AP compatible with their current clinical practice and indicated their willingness to use it in clinical practice with certain clinic-specific modifications after training. PMO-AP has the potential to be relevant for all chronic conditions

as a patient-centered system that promotes trust and partnership between the patient and clinician.

Lay Summary

How do we know that a treatment is useful for the patient? This dissertation's overarching goal is to develop a strategy that can be used in the clinic to identify tangible personally meaningful outcomes (PMO) and describe the expected levels of change that reflect the goals and priorities of the individual patient. For my thesis, I developed a process to identify PMO—the PMO Assessment process (PMO-AP)—and conducted a study to evaluate its reliability, validity, and contribution to personalized medicine and the feasibility of using the PMO-AP in clinical practice. I found that PMO-AP can identify outcomes that matter most to patients at an individual level. It consistently generated valid and reliable information. In the clinic, it requires a minimal amount of additional time and effort from the clinician to work with the patient to complete this assessment. PMO-AP allows the clinical team to acknowledge and embrace the individual patient's perspective.

Preface

This dissertation is an original, unpublished work by Venkata Narendra Sravan Jaggumantri, who was responsible for study proposal, conceptual framework, protocol development, data collection, and analysis of results. Dr. Jean Paul Collet guided and supported the whole process. Dr. William McKellin, Dr. Richard Sawatzky, Dr. Sylvia Stockler, and Dr. Clara van Karnebeek offered significant assistance in understanding the important theoretical concepts, evaluating clinical assessment, developing the study methodology, and data analyses. This study was approved by the Children's and Women's Research Ethics Board of the University of British Columbia (UBC C&W REB; Certificate number: H14-03281). Dr. Timothy Oberlander and his team from the Complex Pain Service, Dr. David Cabral and his team from the Pediatric Rheumatology Division and Dr. Kevan Jacobson from the Gastroenterology Division provided support on study recruitment and follow up.

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List of Abbreviations

ACE	Angiotensin-Converting-enzyme
BCCH	BC Children's Hospital
CD	Crohn's Disease
CHAQ	Childhood Health Activity Questionnaire
COSMIN	Consensus-based Standards for the Selection of Measurement Instruments
CPS	Complex Pain Service
DMD	Duchenne Muscular Dystrophy
EMA	European Medicines Agency
EMPRO	Evaluating Measures of Patient Reported Outcomes
EuroQoL	European Quality of Life
FDI	Functional Disability Index
GAS	Gaol Attainment Scaling
HCP	Health Care Professional
IBD	Inflammatory Bowel Disease
ISPOR	International Society of Pharmacoeconomics and Outcomes Research
JA	Judgment Analysis
JLA	Juvenile Idiopathic Arthritis
MDU	Medical Day Unit
MYMOP	Measure Yourself Medical Outcome Profile
PCM	Patient-Centered Medicine
PedSQL	Pediatric Quality of Life 4.0 Generic Core Scale
PGI	Patient Generated Index

PMO	Personally Meaningful Outcomes
PMO-MI	Personally Meaningful Outcomes – Measurement Instrument
PM	Precision Medicine
PPQ	Pediatric Pain Questionnaire
PRO	Patient Reported Outcome
PROMS	Patient Reported Outcome Measures
PROMIS®	Patient Reported Outcomes Measurement Information
QoL	Quality of Life
RALES	Randomized Aldactone Evaluation Study
RCT	Randomized Controlled Trials
SEIQOL	Schedule for the Evaluation of Individual Quality of Life
SMART	Specific, Measurable, Attainable, Realistic, and Timely
US-FDA	United States – Food and Drug Administration
VAS	Visual Analogue Scale

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- Dr. Timothy Oberlander and his team from the Complex Pain Service, Dr. David Cabral and his team from the Pediatric Rheumatology Division, and Dr. Kevan Jacobson from the Gastroenterology Division for collaborating with me and helping with the study recruitment and follow up.
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Dedication

This work is also dedicated to all rare disease patients and their caregivers.

Chapter 1: Introduction

My doctoral research addressed one basic question: how can clinicians provide an effective person-centered approach to clinical care that identifies what matters most to each individual patient and engages them in co-developing a treatment plan? Put another way, the aim of this thesis was to understand how to identify and evaluate the tangible personally meaningful outcomes of patients that reflect their personal goals and priorities for treatment. This research question stemmed from the research conducted as part of the Treatable Intellectual Disabilities Endeavour – British Columbia (TIDE-BC) project and the British Columbia Children's Hospital's Biochemical Diseases Clinic with the objective of generating better evidence for treatments (TIDE-BC, n.d.). TIDE-BC leverages diverse experiences of a clinical research team and extensive patient involvement to help shape the need for the research to improve clinical outcomes and experiences.

This dissertation focused on an assessment strategy to identify and monitor treatment outcomes that matter most to the individual patient. My goal was to create a knowledge product that can help improve the clinical interactions between the patient and service provider, while prioritizing what is important to the patient. Additionally, the dissertation includes a description of approaches to identify and track the most important outcomes to each individual, thereby informing a highly specialized person-centered course of treatment, and way to document the treatment effectiveness in clinical practice. This new type of evidence complements conventional biological markers and standardized measures by providing important information about the individual patient's experience, priorities, and expectations of the effects of treatment during their daily lives in the community. This approach also facilitates the clinical process of shared

decision-making between clinicians and patients. The use of this personally meaningful outcomes assessment process for decision-making will be assessed in future research.

As noted previously, the research presented in this doctoral dissertation leveraged data and results from the TIDE-BC project, a program composed of clinicians and researchers from various disciplines in numerous subprojects (TIDE-BC, n.d.). I was involved in the subgroup that evaluated the benefits of new treatments. Part of this program entailed conducting several n-of-1 studies to generate evidence regarding the treatments of inborn errors of metabolism (IEM).

IEM are monogenic conditions caused by defective enzymes or cofactors impeding conversion of lipids, proteins, and carbohydrates into energy, often accompanied by the build-up of toxins in the body. The clinical course is often progressive with damage to the central nervous system and other organs unless timely treatment is initiated. IEM constitute the largest group of monogenic diseases amenable to treatments that either directly target the underlying pathophysiology (often with improvement of symptoms) or have the potential to halt disease progression and prevent/minimize further damage (van Karnebeek & Stockler, 2012). In studies of each treatment, the goal was to measure changes using surrogate endpoints, such as biochemical markers, but they were limited in the ability to measure changes in outcomes related to intellectual disability, behavior, and executive function, assessed using standardized scales. For example, in an n-of-1 study evaluating a lysine restricted diet as treatment for pyridoxine dependent epilepsy, testing showed a reduction in biochemical marker levels, but developmental outcomes using standardized scales were inconclusive (van Karnebeek et al., 2012). Parents/caregivers reported seeing changes in outcomes that were important for them but not being evaluated as part of the standardized assessments.

The limitations of the current assessment tools and scales in evaluating outcomes that matter to each individual in IEM became evident during discussions involving clinicians, caregivers, and patients. These stakeholders reported perceiving changes in outcomes, both positive and negative, in response to treatments that were significant to the individual patient. These changes were, however, not adequately captured by the assessments and measures used in clinical encounters.

Clinicians expressed frustration with only using standardized scales and recognized the importance of identifying and precisely assessing specific outcomes that could measure the treatment effects at the individual patient level. The inadequacy of the existing scales in accurately assessing outcomes in IEM patients primarily stemmed from their standardized nature. Such tools are often designed to detect changes within a group or population (such as a homogenous research cohort), rather than in an individual. Consequently, they may fail to identify outcomes that are personally important to the individual or lack the sensitivity needed to detect subtle changes in an individual's condition over time. This limitation can result in an inability to capture meaningful improvements or deteriorations in an individual patient's health.

In the context of IEM, which are all rare diseases characterized by significant heterogeneity, the phenotypic manifestation of the disease in each patient, its impact on their life, and the outcomes that matter most to them can vary widely, even among patients with the same condition (Cossu et al., 2023; Murray et al., 2023). This variation underscores the critical need to identify personalized outcomes that are relevant from the individual patient's perspective and to establish an appropriate method to identify the outcomes that matter most and the corresponding approach to capture change over time.

The TIDE-BC experience also showed that most clinical encounters are informal, unstructured, and lack a rigorous approach to assess each patient and caregiver's expectations, as well as their responses to treatments and outcomes (Caeiro et al., 2022). In clinical practice, a significant deficit exists in structured procedures to systematically document the individual patient's specific health care needs and desired health outcomes, which should be one of the main determinants that support health care decisions. The clinicians involved in TIDE-BC highlighted the need for tools and assessment methods that would help identify whether the prescribed treatments were perceived as beneficial by patients or, in the case of TIDE-BC, their care givers, and met their important personal outcomes and expectations. Together, recognition included the need to identify the outcomes that matter most for each individual patient and to determine the desired changes in the patient's condition that would ensure the patient's satisfaction with the treatment's effectiveness.

The concept of nomothetic and idiographic knowledge, introduced by the neo-Kantian philosopher Wilhelm Windelband in the late nineteenth century, helped distinguish between two forms of knowledge: (a) knowledge that pertains to general principles and (b) knowledge that pertains to specific particulars (Thornton, 2010). In the realm of outcome measures, traditional nomothetic assessments seek to establish universal principles, laws, or rules that apply broadly to a population or group. These standardized outcome measures consist of validated and reliable items, resulting in measurement scores that are assumed to represent the population. They are designed with a uniform set of questions, items, or assessments that remain consistent for all participants, ensuring data collection consistency and facilitating meaningful comparisons within a given population.

In contrast, idiographic assessments take an individualized approach, with the primary focus being understanding and assessing specific individual cases in depth, rather than aiming for generalized or standardized data applicable to a larger group (Haynes et al., 2009). Idiographic assessments prioritize the unique characteristics and experiences of each individual studied. These assessments aim to reveal the individual's distinct experience and interpretation of their personal situation or condition (Cox & Klinger, 2023). Idiographic assessments are particularly valuable when standardized or nomothetic approaches may not sufficiently address the unique circumstances of an individual or when gaining an in-depth understanding of an individual's experiences is crucial for clinical or research purposes. Idiographic assessments complement nomothetic approaches and contribute to a more comprehensive understanding of individual human experiences and outcomes (Ashworth et al., 2019).

One type of tool, known as patient-reported outcome measures (PROMs), is intended to gather assessments directly from patients, capturing their perspectives on various issues, including the severity of symptoms, functional abilities, psychological well-being, treatment satisfaction, and health-related quality of life (HRQoL). Most widely used PROMs are (a) standardized instruments developed with reference to a group or population and (b) nomothetic in nature. PROMs include standardized items that can be employed in comparisons across patients but not ideal in the context of individualized assessment (Cohen et al., 2012).

The use of disease specific PROMs that are not generic but developed for a specific condition or indication if available also fall short of measuring the outcomes that matter most for the patient at an individual level (McKenna, 2011). This situation highlights the major constraint with any standardized nomothetic assessments. They are developed at a population level and consequently do not always translate into appropriate assessments of outcomes that reflect

individual patients' goals and priorities. This contrast between population-level and individual-level perspectives is not limited to IEM or rare diseases, which have an inherent problem of heterogeneity and lack of adequate outcomes measures. It is also applicable to patients with more frequent conditions in the context of clinical practice as the objective is always to prescribe the right treatment and the correct extent of the treatment for the patient seeking clinician's care. Application of nomothetic measures to individual clinical practice is not ideal.

For PROMs to be effective at an individual patient level in clinical practice, they need to take an idiographic approach that captures the disease characteristics that matter to a distinct, singular patient (Godlee, 2012). Several individualized PROMs were developed to capture the specific needs, preferences, and concerns of each patient on an individual level. However, they are not truly idiographic in their method of implementation. The information collected through their use is individualized and helps identify outcomes that matter to the individual patient. Unfortunately, they do not fully uncover the individual's unique history, context, and subjective experiences, which would require discussion and collaboration with the clinician, which is against the principle of PROMs.

The aim of this doctoral dissertation was to address these limitations of PROMs by presenting an assessment process that is systematic and translates the conventional informal discussions between the clinician or health care provider (HCP) and the patient to capture the individual's preferred outcomes and expectations of the treatment's effects. This assessment approach to personally meaningful outcomes (PMOs) includes a specific step-by-step approach designed to be used in the context of clinical practice to identify and track outcomes that matter most to each individual patient's condition. Besides identifying the PMOs, the new assessment approach also captures the patient's personal expectations of meaningful changes; both the

choice of PMO and expectation of levels of meaningful changes are discussed with the clinician to ensure relevance with the patient's illness. These choices reflect the patient's social context and cultural background, as well as personal values and preferences related to their unique personal experiences. This systematic assessment approach, once validated, could be used in routine clinical practice to measure effectiveness of the treatment plan as perceived at a personal level.

This dissertation includes the presentation of the development of a systematic assessment process to be used during the clinical encounter, the evaluation of the reliability and validity of the information obtained using this assessment process, and an examination of its feasibility in clinical practice. Chapter 2 contextualizes the research hypothesis in relationship to existing individualized PROMs. This chapter also includes a description of important concepts related to person-centered medicine and the importance of looking beyond the symptoms when considering a patient's preferences and personal experiences in treatment evaluation. Additionally, Chapter 2 contains an overview of PROMs and their use in clinical practice. Included is an examination of their limitations in addressing the issue of population- or group-based versus individual level assessments. Included in Section 2.4 is an overview of the evolution of the field of individualized PROMs intended to measure an individual's quality of life (QoL), looking specifically at several individualized PROMs currently available. This section focuses on PROMs' limited ability to identify outcomes meaningful to the individual patient and to measure their expectations of changes in a clinical context. The discussion also includes another significant limitation of personalized PROMs—the lack of a partnership between the patient and the clinician while determining the desired course of treatment.

In Chapter 3, the rationale and research objectives for developing an assessment approach that can help identify and track an individual patient's outcomes over time are presented. Also included are explanations of how patient expectations can be measured in collaboration with the clinician as part of routine clinical practice. Chapter 4 illustrates the development of the assessment process to identify (PMOs) and systematically track them against expected changes from the patient's perspective as expressed during a clinical encounter. Chapter 5 includes descriptions of the study conducted to evaluate the reliability and validity of the information collected using the personally meaningful outcome - assessment process (PMO-AP) developed to respond to the limitations of existing individualized PROMs. This chapter includes the study design, the population, recruitment, the outcomes and assessment, follow-up, and the study results. Finally, Chapter 6 includes the feasibility of using PMO-AP in clinical practice, along with the recommendations made by clinicians in several focus groups based on their experience with the PMO-AP.

Chapter 2: Background

Determining tangible outcomes that reflect the personal goals and priorities of individual patients regarding the treatment's effects are currently not part of the treatment evaluation in clinical practice (Krumholz, 2011). Clinicians do not have the time, expertise, or tools to identify and interpret an individual patient's desired personalized outcomes related to their illness and track meaningful changes over time (Hofgastein, 2010).

2.1 TIDE-BC Experience

The experience on the TIDE-BC project highlighted the need to include the PMOs of the individual patient in their assessment to conduct a comprehensive treatment evaluation in clinical practice. The BC Children's Hospital Foundation funded TIDE-BC to develop and promote new best care practices for children with difficult-to-diagnose rare, but potentially treatable, IEM disorders, which, if left untreated, cause intellectual disabilities (ID). A systematic literature review revealed 81 treatable IEM with ID as a distinguishing feature (van Karnebeek & Stockler, 2012). TIDE-BC developed a two-tiered protocol to place screening for treatable IEMs at the forefront of the diagnostic evaluation process for children with unexplained ID (TIDE-BC, n.d.). The TIDE protocol was the standard of care in the Metabolic Diseases Clinic for diagnosis and treatment of IEM patients with ID. I was a member of the research team that focused on conducting n-of-1 studies to evaluate the therapies used to treat children diagnosed using the TIDE protocol.

In the n-of-1 studies, the decision to initiate treatment was multifactorial—based on patients' characteristics, physician's opinions, the availability of treatments, and potential side effects. Evaluation of treatments involved measuring improvement in neurocognitive outcomes, such as psychomotor/cognitive development and biomarkers. Behavior measurement used

standardized psychometric scales, and measurement of metabolic changes was by using biochemical markers. The assessment of neurological and systemic manifestations was by clinical examinations. The assessment tools were part of the standard of care at BC Children's Hospital. Assessments were conducted systematically at defined intervals as part of the n-of-1 study.

For example, in the TIDE-BC n-of-1 study, to determine the effect of lysine restricted diet on Pyridoxine dependent epilepsy, the following outcomes were used: (a) neurological exam by the clinician; (b) parents' reports of the frequency of seizures; (c) biomarker levels for α-aminoadipic semialdehyde (AASA), Δ-1-piperideine-6-carboxylate (P6C), and pipecolic acid. Neurodevelopmental outcomes included assessments using age-appropriate standardized scales including the Bayley's scale for infants and toddlers to determine cognitive development, and the Vineland Adaptive Behavior Scales to assess changes in behavior (van Karnebeek et al., 2012).

Some assessments were of significance for both the patient and the clinician, whereas others were only significant to the clinician. For example, although seizure frequency is an important clinical outcome meaningful for both the clinician and patient, biomarker levels are surrogate outcomes because of their reasonable likelihood of measuring the impact of the treatment on the underlying disease pathophysiology, but they are only useful to the clinician. In general, biomarkers, though meaningful to clinicians, are of little meaning or concern to the caregivers or parents. Similarly, the assessment of neurodevelopmental outcomes was based on performance on standardized scales. The information obtained from these scales is useful in clinical practice to give an indication of how far the individual patient is from the *normal* population. This information is, however, abstract for the caregivers because it does not translate directly to the functioning or deficits that are the primary concern of the individual patient or

caregivers. The patient or caregiver is more interested in understanding the effects of the treatment that will affect the child's functioning in daily life or improve specific tasks affected by the disease. For instance, a low score on a behavior scale is less important than being able to sit through a class without being distracted or the ability to complete homework because of increased attention.

During the n-of-1 trials, patients and caregivers provided invaluable insights that eluded standard-of-care assessments. These insights often revolved around a frequently overlooked aspect of their treatment: the personalized treatment and outcome goals and priorities of each individual patient. This persistent observation was a common thread in all n-of-1 studies. Each patient's life experience is inherently unique, even when they share the same medical condition. This uniqueness translates into distinct objectives and priorities concerning treatment outcomes and expected effects.

Furthermore, it is crucial to recognize that patient heterogeneity extends beyond mere variations in observable traits. It encompasses the profound variability in how the disease impacts their daily lives in specific environmental, familial, and cultural contexts. Consequently, a significant divergence exists in the outcomes that patients aspire to achieve through their specific treatments. Therefore, when evaluating the impact of a particular treatment, it is imperative to refrain from predominantly relying only on biomarkers and standardized outcomes or assessments that are generic and only applicable at a population level.

In contrast, the approach developed in this study pivots towards the inclusion of personalized and patient-centric evaluation methods that genuinely capture the individual's unique needs and goals. This shift in perspective bridges the gap between the expectations and experiences of patients and caregivers, ensuring that the assessment of treatment effectiveness

aligns authentically with the dynamic and distinctive nature of each patient's journey. Notably, the challenge of heterogeneity is not limited to rare diseases but is also highly relevant to any patient, especially those with a chronic conditions and medical complexity. Therefore, adopting a person-centered, patient-centric approach in various health care contexts is important to ensure that treatment outcomes align with the diverse and dynamic experiences of patients, regardless of the rarity or commonality of their conditions.

In Section 2.2, I outline why a person-centered medicine approach in clinical practice is needed to identify the PMOs based on individual preference in collaboration with the clinician's expertise. This approach allows the clinician to engage with the patient and incorporate the various dimensions of well-being for each individual patient, including a person's social context and individual experience in treatment evaluation. This section also includes descriptions of the PROMs initially developed as a step toward measuring what matters from the patient's perspective (Brook et al., 1983; Revicki et al., 2007). Section 2.3 includes a description of how existing PROMs capture the information from the patients' perspectives in research and clinical practice. Standardized PROMs are inadequate to address individual patient's priorities when attempting to identify, monitor, and track their PMOs as they are nomothetic in nature (Wiering et al., 2017). Section 2.4 focuses on how individualized PROMs can address the challenge of identifying PMOs, including a summary of existing individualized PROMs and their limitations. Finally, Section 2.5 highlights the gap and the need for a more effective personalized assessment that overcomes these limitations to address the issue identified through TIDE-BC.

2.2 Personalized Clinical Evaluation Approach

The TIDE-experience showcased the need for a clinical assessment approach personalized to the individual patient. The objective was to develop a holistic method that

enables a clinician and a patient to systematically identify PMOs of the individual regarding the treatment's physiological effects and obtain and incorporate the patient's perception of the effectiveness of the treatment in meeting their own desired outcomes. This concept of personalization is an extension to the notion of personalized medicine (PM) that goes beyond its biomedical framework and combines with a person-centered care (PCC) model (Berman et al., 2016).

PM is defined as using an individual's specific biological characteristics to tailor therapies to that person (Di Paolo et al., 2017; Huang & Hood, 2019). PCC is defined with respect to the patient as a person, and the individual's right to self-determination and mutual respect, with an understanding of the importance of personhood (Berman et al., 2016; Byrne et al., 2020). PCC is holistic, flexible, creative, and personal, and recognizes the uniqueness of each individual (McCance et al., 2011). The concept of personalization being referred to in this section unites PM and PCC and moves toward individually tailored strategies for both the treatment prescription and assessment of its effectiveness. This holistic approach encompasses both the biological and phenomenological aspects when assessing the treatment's response (Horwitz et al., 2017; Rogowski et al., 2015).

Current approaches in clinical practice may create a distorted picture of the treatment response with possible discordance between the clinicians' satisfaction and the patients' perceptions of treatment effectiveness or impact in their daily lives because clinicians lack a means of determining patients' desired personal outcomes that reflect their goals and priorities. This discordance is clear when the improvement in treatment effects is based only on biological markers and is not reflected in the patient's perception of change. The discordance still exists when using standard clinical assessments and not just biological markers.

For example, in patients with Duchenne Muscular Dystrophy (DMD), the standard 6-minute Walk Test is routinely used in clinical practice as an assessment for endurance. Capturing this information from the Walk Test may be a useful performance-based measure for endurance, but from a patient or caregiver perspective, it is an inadequate substitute for of the outcomes that matter most for a patient with DMD. It does not capture changes such as the ability to decrease or eliminate spontaneous falls and the ability to maintain or increase their participation in daily life social activities. This explains the discordance between the absence of an improved 6-minute Walk Test in a clinical trial and parents' reports of meaningful improvements in everyday activities among clinical trial participants (Condin, 2010; Sheridan, 2013). In the Ataluren trial, parents reported that their children could stay at school for the full day, but that was not considered as part of the efficacy evaluation or in any of standardized scales used in the study. Parents are interested in endurance—in completion of idiographic social activities as opposed to endurance as assessed by the standardized performance measure, the 6-minute Walk Test.

The patient-centered outcomes report developed by the Jett Foundation (2015) also highlighted this gap between outcomes that are routinely used to evaluate treatments for DMD both in research and practice and outcomes that matter most to the DMD patients. This gap can be reduced by incorporating the holistic personalization concept when measuring treatment outcomes. Focusing on the outcomes that are important to the individual patient as opposed to only using concerns that are relevant at a group or population level is important especially when considering equity-denied groups or individuals who may not represent current "norms" in research or clinical practice. In practice, it is difficult for clinicians to implement the personalized approach proposed above and incorporate the individual's perspective into the clinical assessment of treatment response, because the frequently used standard of care

assessments of treatment effects is inadequate to identify, interpret, monitor, and track the PMOs of individual patients.

2.3 Past Attempts at Measuring the Patient Outcomes and Experiences Using PROMs

In last 30 years, the need to capture the patient's perspective about their own illness and about the intervention showed rapid development. Any report of the status of a patient's health condition that comes directly from the patient without interpretation of the patient's response by a clinician, or anyone else, is referred to as a patient reported outcome (PRO) (Gill & Feinstein, 1994; Weldring & Smith, 2013). The tools or instruments used to measure PROs include as a reference PROMs (Powers et al., 2017; Speight & Barendse, 2010).

PROMs measure different concepts ranging from the signs and symptoms of the disease to the overall state of a health condition and other aspects of life affected by a health condition important to a person's overall QoL (Chang et al., 2011; Chen et al., 2013; Fayers & Machin, 2007). Several measurement scales or instruments have been developed and standardized to capture PROs. Access to the patient perspective using PROMs can cover a wide range of aspects related to the delivery of effective health care including, identifying issues faced by patients living with an illness and their families and how this knowledge might impact treatment decisions and adherence, and provide a better understanding of how clinicians can improve outcomes.

Though PROMs are designed with the intention to report information about patients, the majority are standardized assessments. The process of development, validation, and standardization results in a PROM that identifies outcomes that matter most to the hypothetical average patient (Alrubaiy et al., 2014; Meadows, 2011). Consequently, most PROMs are

inadequate in identifying, assessing, and interpreting the outcomes that are meaningful and important from an individual patient perspective (Cohen et al., 2012).

Greenhalgh (2009) proposed a taxonomy for the different PROMs in clinical practice. PROMs are categorized into generic, disease specific, and individualized PROMs. Most of the generic and disease specific measures are nomothetic in nature, where the measures are standardized and constructed to represent what one population or a group of individuals with the same disease think/feel/express regarding specific their areas of concern such as QoL, dyspnea, behavior, function, and mood. Therefore, the standardized PROMs may well represent the group's values, but they are only a surrogate representation of each individual's experience. These PROMs do not produce meaningful and accurate information regarding the outcomes at an individual level (Cohen et al., 2012). Additionally, implementing PROMs in routine clinical practice to aid individual patient management involves several methodological and practical decisions. To help clinicians interested in implementing PROMs, the International Society for Quality-of-Life Research developed a User's Guide for Implementing Patient-Reported Outcomes Assessment in Clinical Practice (Snyder et al., 2012).

Even with this strong push and advocacy for PROMs in clinical practice, the guide acknowledges that researchers are much more interested in using PROs than practicing clinicians (Litchfield et al., 2021; Snyder et al., 2012). Clinician's skepticism about the clinical meaning of the information from nomothetic standardized PROMs also inhibits their use in practice (Greenhalgh, 2009; Greenhalgh et al., 2018). A key practical issue is that in clinical practice, each individual patient may have a different condition, and the clinicians will not have the time to research and select a valid PROM that can be used for each patient. Even if the clinician could select the appropriate PROM, their selection may be copyrighted and may require purchasing a

license. Quantitative systematic reviews of PROMs used in the care of individual patients have not yielded definitive conclusions about their impact (Gibbons et al., 2021). In these reviews, the researchers questioned whether the content and structure of standardized PROMs adequately capture and reflect individual patient's view (Carfora et al., 2022).

The current study addressed this gap in knowledge. This thesis focused on developing an assessment approach that can be used with an individual patient in clinical practice to implement the personalized approach. Therefore, to better reflect the individual perspective, individualized PROMs were developed.

2.4 Can Individualized PROMs Address the Problem?

As outlined in the preceding sections, it is crucial, at a personal level, to ascertain the extent to which an assessment captures outcomes that are significant to the individual patient. This assessment includes understanding their perception of meaningful change in these outcomes and evaluating whether such changes have a tangible impact on their life. The central questions here are as follows: Is the assessment person-centered? and can the assessments inform person-centered care that is meaningful?

For an assessment to be deemed person-centered, it must align with the aims, values, and goals of the individual patient. Furthermore, it should mirror the patient's priorities when evaluating the impact of treatment on these specific outcomes (Carr & Higginson, 2001). Traditional nomothetic standardized PROMs often fall short in addressing this challenge because their focus is at a population level. Consequently, individualized PROMs have been developed to overcome these limitations.

Individualized PROMs fall under the idiographic category wherein the individual completing the assessment generates the items and/or domains. These PROMs help identify the

concerns of the individual patient rather than imposing an external standard that may be less relevant for the individual (Blair et al., 2010; Bugatti & Boswell, 2022; Sales & Alves, 2016). They empower each patient to contribute their unique voice when measuring outcomes in contrast to the collective patient voice of the population (Paterson, 2004). The Schedule for Evaluation of Individualized Quality of Life (SEIQOL), Patient General Index (PGI), Measure Your Medical Outcome (MYMOP), and Canadian Occupational Performance Measure (COPM) are the four commonly used individualized PROMS. In the following sections, a thorough analysis of each of these scales and their capacity to discern outcomes that are significant to each individual is provided. The examination also includes an analysis of their ability to facilitate an understanding of meaningful changes resulting from the treatment based on individual preferences.

2.4.1 SEIQOL

In the contemporary measures of QoL, SEIQOL was developed first (Joyce et al., 2003). Therefore, the measure significantly shaped the formation of the other individualized PROMS. The development of SEIQoL was based on the following definition: "quality of life is what the individual determines it to be". From this perspective, the overarching argument is that SEIQoL has high face and content validity. SEIQOL is designed to measure three elements of QoL:

- Those aspects of life considered by the individual to be crucial to their QoL. They are elicited through a structured interview.
- Current functioning/satisfaction with each aspect as rated by the individual.
- The relative importance of each aspect of QoL as measured by deriving the weight the individual assigns to each in judging overall QoL.

Researchers have administered SEIQoL in the form of a semistructured interview. The interviewer first asks the participant to nominate five domains (cues) they currently consider as most important in their life. If someone finds difficulty to nominate five domains, a standard list of prompts is used. Second, the person rates how they are doing in each of these domains on a 0–100 visual analogue scale, with 0 = *worst possible* and 100 = *best possible*. In the third stage, the person rates the relative importance of each area by a weighting procedure.

The two instruments, the original SEIQoL and its abbreviated version, differ in the way in which the weighting is performed. Weighting in the original SEIQoL includes the foundation on judgment analysis (JA). JA, also known as policy capturing, is a research method widely used in studies of judgment and decision-making. JA externalizes the way a person makes a judgment or decision. SEIQoL-DW uses a direct and simpler technique for weighting the importance of the nominated domains. Participants are then asked to quantify the relative importance of each area, represented by five differently colored areas in a pie chart, by adjusting the sizes of the identified life areas. All areas add up to 100, and the area perceived to be of greatest importance should be assigned the largest pie area. Both versions produce an overall QoL index score calculated by multiplying the rating of each domain with the same domain's weight, and then summing the values for each of the five domains. This result can range from 0 = *lowest QoL* to 100 = *highest QoL*.

The advantage of SEIQoL is that the individual identifies the domains as opposed to selecting them from predetermined domains. The disadvantage is in the time-consuming constraints in which to administer because of the interview format and ranking process. Additionally, SEIQoL only elicits responses to a domain level and does not go into the details or specific aspects in that domain. The calculation of the QoL index score allows the clinician to

see whether there is an improvement or decrease in QoL, but the score does not provide information about how significant the change was for the individual (Felgoise et al., 2009).

2.4.2 PGI

PGI is a self-administered individualized PROM developed by Ruta et al. (1994) using Calman's (1984) definition of QoL as the conceptual framework. Calman defined QoL as "the extent to which our hopes and ambitions are matched by experience," and suggested that a key aim of medical care should be to "narrow the gap between a patient's hopes and expectations and what actually happens" (Fernandes et al., 2012). This approach is patient-centered and seeks to understand how patients perceive their status and how they expect to live. Fernandes et al. (2012) combined two existing techniques from unrelated fields to produce PGI. The first technique is a questionnaire developed by Guyatt et al. (1987) to measure QoL in patients with chronic lung disease and the second technique is the priority evaluator method developed by Hoinville (1977) to aid town planning.

According to Ruta et al. (1994), three major stages are involved in the use of the PGI. The first step involves asking the patient to identify the five most important activities or areas in their life significantly influenced by their condition (Ruta et al., 1994). In the second step, the patient rates how they are affected in each area identified in step one. In this stage, the patient provides a rating of how poorly they perceive the effects in each of the identified areas. The scale used ranges from 0 to 100 with 0 = *the worst that the patient can imagine about the area* and 100 = *how exactly they would prefer to be*. In this stage, the clinician asks a sixth box to the five questions to allow the patient to rate any area in their life affected by their health condition not mentioned in the previous five questions (Tang et al., 2014).Additionally, the box gives patients

a chance to mention areas of their life that might be unrelated to their condition or even to their health.

The third step involves the identification of the relative potential for patients to improve in different areas (Lien et al., 2011). In this case, the patients imagine it is possible for them to improve in all or some of the areas identified in Step 2. Sixty points are provided to each patient to be distributed on different areas. The points allocated to each field show the significance of the desire to improve in the identified area.

After the third step, it is possible to generate an index that ranges from 0 to 100. To obtain this index, each of the six ratings identified in the first and second steps is multiplied by the proportion of the points allocated to the area. Later, the sums for each zone are obtained to generate a score from 0 to 100. The final score obtained will be used to identify the level at which reality differs from the patient's expectations in the areas of life with strong desire for improvement. The major advantage of PGI is that it is self-administered. Additionally, the PGI allows the patient to identify activities in addition to areas of life affected due to the medical condition. The PGI generates a summary score at the end and supports tracking of the change in each individual area or activity and to see whether the overall change in summary score is meaningful for the individual.

2.4.3 MYMOP

MYMOP PROM uses an individualized questionnaire that focuses on the general well-being of the respondent (Chung et al., 2010). Paterson (1996) developed the original version of MYMOP in 1996, and the second validation of this PROM occurred in 2000 (Paterson & Britten, 2000). Translations include different languages and dialects without losing its validity (Chung et al., 2010). Various clinical settings include applications to evaluate expectations in patients

receiving massage or acupuncture (Hull et al., 2006), as well as treatment for acute bronchitis and patellar tendinopathy (Jarosz, 2010; Paterson et al., 2000).

When first used with a patient, the MYMOP is completed during the clinical encounter. The patient chooses one or two symptoms and one activity of daily living, which they seek to improve and consider to be the most important in affecting their lives. The items must all relate to the same problem, in the patient's opinion. The patient writes these choices down in their own words and then scores them for severity over the past week on a 7-point scale. The patient also answers a general well-being question. In the follow-up questionnaires, the wording of the previously chosen items remains unchanged, but an optional fifth item is added for a new symptom. The second symptom and the activity are optional.

Used in this way, the MYMOP produces a problem-specific profile of four scores: (a) one for each of the two symptoms, (b) one for the activity, and (c) one for well-being. The mean of these scores, the MYMOP profile score, can also be computed. Although such a single score remains attractive to policymakers looking for simplicity, a loss of information results for clinical use.

The MYMOP is suitable for use in any symptomatic condition and, because of the ability to be problem-specific but flexible, it is useful when the study population has a variety of problems. Similar to PGI, the self-administered approach for MYMOP increases the ease to administer it. Using a 5-point Likert-type scale for each symptom and activity, as opposed to an overall summary score to track change in each problem area, adds value but does not inform whether the change is meaningful from the patient perspective. Last, flexibility does not exist to measure more than one activity from the individual’s daily living.

2.4.4 COPM

COPM is an individualized PROM designed to detect changes in a client's self-reported performance over time (Law et al., 1990). COPM is designed to be used by occupational therapists to set up intervention goals. Since 1991, the COPM includes translation into more than 36 languages in over 40 countries. Furthermore, the COPM prompts a discussion between patients and therapists about different areas of activity, concerns, and problems to be resolved.

COPM is a criterion-referenced measured administered in five steps. Step 1 is defining the problem. Using a semistructured interview, the therapist engages the client in identifying whether the patient has any problems performing occupations of importance that they want to do, need to do, or are expected to do, but are unable to accomplish. Areas of everyday living explored during the interview include self-care, productivity, or leisure. Once the therapist is confident that the client has identified the occupational performance problems experienced in everyday living, they move to Step 2 of problem weighting.

In Step 2, the client rates the importance of each of the occupations to their life using a 10-point rating scale. In Step 3, the client chooses up to five of the most important problems identified in Step 2 to address in the intervention. The therapist enters the chosen problems and their importance ratings in the scoring section. This process serves as the basis for identifying intervention goals. In Step 4, the client rates their own level of performance and satisfaction with the performance for each of the five identified problems. They rate their performance and satisfaction on a 10-point scale with a score range 1 = *not able to do it/not satisfied at all* to 10 = *able to do it extremely well/extremely satisfied*.

The therapist calculates an average COPM performance score and satisfaction score. After an appropriate period or a predetermined time of intervention, the therapist moves to the final Step 5 of reassessment by asking the client to rate their performance and satisfaction for the

five problem activities chosen in Step 3. The change in the occupational performance reported is calculated by subtracting the ratings given at the start of the intervention from the ratings determined at reassessment for satisfaction with a score of 10 indicating very good performance and high satisfaction (Carswell et al., 2019).

The COPM is the most used outcome measure in occupational therapy. The semistructured interview format allows the client to identify issues of importance in all areas of their life. The COPM is not suitable for use with stroke patients who exhibit cognitive deficits, as they may not be able to set achievable goals during a COPM interview (Caire et al., 2022; Yang et al., 2017). Using summary scores for performance and satisfaction to measure change due to the intervention is not sensitive enough to show the specific change in each individual problem. Also, the COPM is not designed to determine whether a change in the summary scores is meaningful to the patient.

2.5 Summary

A personalized assessment approach that captures the information generated from the individual patient's voice is needed, which can used in conjunction with the standardized assessments and biomarker data. PROMs provide an opportunity to capture the patient voice and include a recommendation to be used alongside standard clinical assessments by clinicians to guide real-time, individual patient care. Both generic and disease-specific PROMs are, however, typically nomothetic. These standardized questionnaires measure patients' self-reported experiences on a predetermined set of items or domains, supporting population-level comparisons. They, however, lack suitability for the personalized approach as described in Section 2.2.

Individualized PROMs could be a potential solution as they focus on the uniqueness of each patient's condition. Among the most prominent individualized PROMs is the SEIQOL (Browne et al., 1994; Joyce, 1994), which was the first individualized PROM that allowed the individual patient to nominate five areas most important to their QoL. The PGI (Ruta et al., 1994) was later developed with a greater focus on the medical condition of the individual. Individuals completing the PGI identify five most important activities or areas in their life significantly influenced by their condition. The MYMOP (Paterson & Britten, 2000) builds on the strengths of PGI and documents both symptoms and activities which the individual patient seeks to improve. Last, COPM is an individualized PROM successfully used in occupational therapy, offering the flexibility to the patient to identify the problems in their life due to their condition with a primary focus on occupational measures of daily living. Appendix A includes summary of the strengths and limitations of individualized PROMs.

These individualized PROMs are based on the recognition that each patient has a unique clinical condition, with a set of problems and presentations specific to their person and their circumstances. Individualized PROMs inform clinicians about idiosyncratic problems that cannot be captured in preset standardized PROMs. Patients are empowered to tailor measurement and play an active role in the care process and its evaluation. Ultimately individualized PROMs *see the person in the patient*. These more individualized measures indicate an important direction in the development of patient-reported outcomes.

Also, an inherent requirement for PROMs is its need to come directly from the patient without any interpretation of the patient's response by a clinician or anyone else (Coons et al., 2011; Snyder et al., 2012; U.S. Department of Health and Human Services FDA Center for Drug Evaluation Research et al., 2006). Although this approach may be considered a valuable strategy

for obtaining the report of the status of a patient's health condition directly from them and identifying the areas of concern for them, the requirement not to interact with the clinician in terms of interpretation of the outcomes is also a potential weakness when it is applied in the context of the implementing the holistic personalized assessment in the clinic, as described in Section 2.2.

Even in interview-based individualized PROMS such as SEIQoL and COPM, the direction of questioning is one way and the wording of the outcomes generated by the patient should not be altered, otherwise the validity of the PROM, as underpinned by psychometric testing, is threatened. To be truly idiographic and realistic about the medical condition, collaboration between the patient and the HCP is necessary to identify the personalized outcomes (Berman et al., 2016; Coaccioli, 2011; Morel & Cano, 2017). Therefore, a much better solution is a dialogue-based individualized assessment that not only mimics the more open structure clinicians use in their interactions with patients but also allows patients to present their illness narratives (Kleinman, 1988; Mattingly, 1994; Mattingly & Garro, 2001a) to *tell their story* in their own words. This interaction between patient and clinician provides opportunities to check interpretations of events and the personal significance of experiences.

In conclusion, a more effective personalized assessment approach is needed that overcomes the limitations of existing individualized tools to identify tangible outcomes that reflect the goals and priorities related to the illness from the individual patient's perspective. Such an approach should build on the strengths of the individualized PROMs. This new approach should employ the strategy of PCC by providing an opportunity for patients to identify goals and priorities for the treatment through collaboration with their clinician. The approach should also allow the individual to define the expected change in the mutually shared set of

preferred treatment outcomes based on their patient's individual goals and priorities. The innovation I developed in this thesis is to involve the patient in choosing meaningful outcomes and create the PMO-AP.

Chapter 3: Rationale and Objectives

A more effective personalized assessment process is needed to better incorporate the patient's voice in a systematic way during the clinical encounter. The process should reflect the patients' perceptions of their health, enabling the patients and clinicians to identify and capture the outcomes that matter most in the patients' lives. Additionally, the process should allow the patient to outline their expectation about the magnitude of improvement/change from the treatment for those outcomes. Finally, the important outcomes and the expectations of changes selected by the patient need to be discussed with the clinician to ensure that they are pertinent to their specific condition.

Findings from the n-of-1 studies conducted as part of TIDE-BC indicated that caregivers identified changes in outcomes not always captured by the existing standardized nomothetic tools. Findings also suggested how important and meaningful these changes were to patients. This trend identified through TIDE-BC led to the question regarding how this missing information specific to the patient could be identified during a clinic visit, including the expected changes post treatment, to ensure the patient is satisfied. How should the communication between the clinician and patient be structured to capture this missing information and systematically track it during follow up? Existing individualized PROMs do not address this issue and are not ideal for implementing the holistic personalized approach in clinical practice as discussed in Chapter 2.

A personalized patient-centric approach for gathering a patient's input and performing a holistic evaluation of treatment effect in clinical practice should build on the strengths of existing individualized PROMs. This approach should also improve communication between the clinician and the patient by facilitating a partnership that would lead to a more complete and

comprehensive understanding of the patients' experience, goals, and expectations shared between the patient and the clinician. Existing PROMs including individualized PROMs, however, do not allow for this systematic dialogue between the clinician and the patient, as the information collected using PROMs should directly come from the patient without amendment or interpretation by a clinician or anyone else (Greenhalgh et al., 2018). Clinicians using PROMs also found incorporating completion and review PROMs into the natural flow of consultations difficult (Leydon et al., 2011; Mitchell et al., 2011).

Across all care contexts, clinicians and patients felt that having a trusting relationship was necessary to support the sharing of concerns and problems. Clinicians placed significant emphasis on developing rapport and a trusting relationship with patients through verbal interactions and preferred to let patients tell their story in their own words (Greenhalgh et al., 2018). Therefore, instead of developing a new measurement instrument or modifying an existing individualized PROM, the goal of this research was to develop an assessment process that can be implemented during the clinical encounter to facilitate a structured dialogue between the clinician and the patient. Such an assessment should lead to the identification of PMOs that reflect the goals and priorities of the individual patient for their treatment, as well as a systematic means to track the patient's satisfaction and determine whether the treatment meets their expectations.

In developing a genuinely personalized assessment, I established the following criteria. These criteria were informed by a review of individualized PROMs, with particular attention to the attributes delineated by Ruta et al. (1994) during the development of the PGI. Additionally, I garnered input through extensive discussions with various clinicians at BC Children's Hospital,

insights from members of my committee, and valuable perspectives from patients and caregivers as follows:

- For personalized assessment of most important outcomes and expectation of changes to be satisfied, the process should allow for a true partnership—a shared understanding between individual patient and their clinician—one where the individual's needs and aspirations drive both health care decisions, the selection of outcomes, indicators, and expectation of effects for obtaining satisfying results.
- Similar to the PGI, the personalized assessment approach should help describe the effect of the illness on those aspects of the patient's life that they consider most important.
- The personalized assessment should identify the specific symptoms, tasks, activities, and/or concerns specific to that individual and give the patient the flexibility to choose which ones are most important to them. The outcome should not be restrict the patient to only focusing on QoL-related activities or only one symptom of concern.
- The personal assessment should allow the patient to define a-priori, the extent of change/improvement in the selected outcomes, expected from treatment that would be considered satisfactory from the patient's point of view.
- Given that the assessment targets the measurement of treatment impact on personalized outcomes chosen by the individual patient, it is essential to incorporate a dialogue between the patient and clinician. This discussion aims to ensure that the selected outcomes are pertinent to the specific condition for which the treatment is being administered.

- The personalized assessment process should capture any possible changes in the nature of outcomes identified or changes in the expectation of effects over time to reflect the real-life situations where context and priorities may change over time, which may affect the choice of preferred outcomes.
- The assessment process should also be able to detect and record unexpected changes that may be beneficial or detrimental to the patient's QoL.
- Similar to the PGI, the assessment process should be reproducible.

In this doctoral research, I developed an idiographic process that meets these criteria by systematically identifying the PMOs and the expected treatment effects determined by patients in collaboration with the clinicians. This process transforms the informal subjective discussion between the HCP and the patient during the clinical interaction into a systematic dialogue that captures the patient's voice. The process allows for a comprehensive evaluation of the treatment effects in clinical practice. Chapter 4 includes an outline of the development of the PMO-AP.

3.1 Research Objective 1

The first research objective was to develop an approach that can serve as an effective strategy to support personalized medicine in clinical practice: a patient-centric individualized assessment method that reflects the patient's perceptions of their health, allowing outcomes that matter most in the context of their lives to be captured. This new systematic assessment approach could be used in routine clinical practice to measure the effectiveness of the treatment plan as perceived by the individual patient.

3.2 Research Objective 2

The second research objective was to evaluate if the new assessment process can serve as an effective strategy to support a holistic personalized medicine approach in clinical practice as follows:

- Determine the reliability of the information generated using the PMO-AP;
- Review the validity evidence from the PMO-AP information and its use in clinical practice;
- Assess the capacity of the PMO-AP to generate useful data when implementing a truly personalized assessment; and
- Document the feasibility of using the new assessment process in clinical practice.

Chapter 4: Developing the Personally Meaningful Outcomes—Assessment Process

The primary objective of this doctoral research was to develop a patient-centric personalized assessment process that enables the doctor and patient to identify outcomes that reflect the patient's perceptions of their health. The process should capture the outcomes that matter most for the patient in their everyday lives, and the expected changes in these outcomes that would satisfy the patient. A new systematic assessment process could be used in routine clinical practice to assess the effectiveness of the patient-centered treatment plans.

4.1 Development of a New Process to Assess PMO

Before deciding to develop a new assessment, I reviewed the prominent individualized PROMs and assessed whether they can be modified to implement the holistic PM concept in the clinic. I compared each individualized PROM against the characteristics outlined in Chapter 3. First, all existing individualized PROMs do not allow any discussion between the clinician and the patient when completing them. SEIQoL or COPM, which are interview-based measures, only permit the administrator to provide cues to the patient to help think but not to engage in a dialogue. Second, even though these measures allow each patient to generate their own outcomes, they are not flexible and specific to the selected outcomes and have internal restrictions. For example, the SEIQoL focuses on broad domain-level concepts and the MYMOP restricts the choice of outcomes to one or two symptoms and one activity of daily living. Third, the monitoring or tracking of the status of the outcomes is done using a Likert-type scale. Consequently, when a change in score is reported at follow up, it is not clear what it means to the patient, as there is no opportunity for the clinician to confirm their interpretation of the patients'

responses. Therefore, I determined that it was not possible to simply modify existing individualized PROMs, as the interaction between the clinician and the individual patient is critical to the implementation of the holistic PCM approach. I then reviewed the properties of the individualized PROMs to determine whether I could employ some characteristics in the new assessment process that meets the criteria I established for a person-centered, holistic, personalized assessment process.

Based on review of individualized PROMs, the feedback from the clinicians at BC Children's Hospital, caregivers of the parents who were part of the TIDE-BC project, from other clinicians at BC Children's Hospital as part of the Research Rounds and the recommendation from my committee, I set my goal to develop an assessment process that could be adapted during a clinical encounter to identify the patient's PMOs. I named this process the "Personally Meaningful Outcomes – Assessment Process" (PMO-AP), which meets all the characteristics outlined in Chapter 3. The PMO-AP is not a PROM but an idiographic assessment process. The feedback obtained from the stakeholders guided the development of steps involved in administration of the PMO-AP.

4.1.1 Characteristic #1

The process should allow for a true partnership, a shared understanding between individual patient and their HCP. In this relationship, individual's needs and aspirations drive both health care decisions, the selection of outcomes, indicators, and expectation of effects for satisfying results. The PMO-AP should prompt the patient to reflect on their health and in doing so, develop a deeper understanding of how their condition affects them. The content generated through the PMO-AP will be done using an interview-based format that can be integrated into

the clinical consultation. The clinician will play an active role in the interview process to establish a partnership with the patient to develop a shared understanding of the selected PMOs.

Illness narratives provided by the patient will facilitate this shared understanding. Illness narratives are significantly different from the medical history taken by the clinician (Garro, 2011; Kleinman, 1988; Mattingly & Garro, 2001a). The primary function of an illness narrative is to enable the patient to express their experience of illness in their own words. It is often part of a patient-centered, holistic approach to care. It takes the form of a personal story or narrative, where the patient shares their thoughts, feelings, and experiences related to their illness.

An illness narrative may include cultural, emotional, and psychosocial dimensions of the illness experience. The act of telling the story is often therapeutic in nature. It helps patients explain their illness to others and themselves, gain insights, and provide a therapeutic plot of how they would like a treatment to help them. By contrast, a clinician's medical history assessment is structured to gather specific medical and clinical information relevant to diagnose the patient's disease and assess their perceived state of health. The assessment forms the basis for the logic underlying diagnosis, treatment planning, and medical decision-making. Therefore, guided interview prompts will be needed in the PMO-AP for the clinician to facilitate a dialogue with the patient, gain shared understanding, and create the illness narrative with the patient and/or caregiver.

4.1.2 Characteristic #2

The personalized assessment approach should help describe the effects of the illness on those aspects of the patient's life that they consider most important. This characteristic is similar to the PGI. In the context of the PMO-AP, this characteristic entails employing a process to learn

about the activities that the patient values and incorporating this knowledge into the therapeutic and assessment processes.

From a theoretical point of view, the PMO-AP uses an idiographic approach that draws upon medical anthropology and psychology and is strongly influenced by phenomenology (Bouwens et al., 2008). To allow the patient to describe their illness, the PMO-AP uses the concept of therapeutic emplotment (Mattingly, 1994; Mattingly & Fleming, 1994). Mattingly (1991, 1994, 1998), building on research on patients' illness narratives, developed this concept.

Mattingly's (1994) concept of therapeutic emplotment includes the assumption that individuals create illness narratives to make sense of their condition to themselves and express to others the aspects of their condition important to themselves, and relevant in their social and cultural context. By telling these narratives, patients make their experience both socially and personally meaningful (Garro, 2011; Kleinman, 1988; Mattingly & Garro, 2001b). Mattingly found, through studies of occupational therapists' work in rehabilitation, that a therapist and patient could transform ordinary actions in their encounters into meaningful steps in a new unfolding story of the patient's life. Visions for a plot grew out of the therapists' questioning about what similar stories they had been involved in and to find endings to stories or outcomes, which were acceptable to the patient (Mattingly, 1998, p. 72). The main reason for making therapeutic plots was to build a desire to move the therapeutic process together in the same direction over time (Mattingly, 1998). These clinical plots, which were not generally explicitly expressed or clearly articulated in the minds of either the therapist or patient, could be read from observing the entirety of their clinical interaction (Mattingly, 1994; Tropea, 2012).

Thus, in the process of therapeutic emplotment, the patient and their clinician come to a shared understanding and collaboratively identify the narrative's underlying plot or conceptual scenarios and cultural schemas, and the inferences that help make the narrative coherent with the values and assumptions that they employ in everyday life. The shared understanding between patient and clinician developed in the process create a framework to identify a medically appropriate course of action. Based on medical information and the patient's illness narrative of the situation, and the assumptions and values that they discover together, the patient and clinician can identify the outcomes that matter most to the patient to create a therapeutic scenario. In this way, therapeutic emplotment moves from the illness account of the patient to a shared, jointly constructed prospective treatment scenario (Mattingly, 2014; Strauss, 1992). This process allows the patient to frame their health issues in contexts personally coherent and socially relevant to them and their HCP (Ipsiroglu et al., 2013).

4.1.3 Characteristic #3

The personalized assessment approach should help identify the specific symptoms, tasks, activities, or concerns that are specific to that individual and allow the patient to choose which one is important to them. The approach should not be restrict the patient to only focusing on QoL-related activities such as SEIQoL or only one symptom of concern and an activity of daily living such as MYMOP.

The PMO-AP should provide a comprehensive assessment of any type of outcome generated by the patient. Thus, a PMO can be related to a patient's QoL, activities, or symptoms. The PMO-AP overcomes the limitations of individualized PROMs such as SEIQoL that limits the patient to select an outcome related to QoL domains without specifying the important tasks

or activities in the domain. This process should also allow the PMO to be anything that the individual chooses, rather than being limited to only two symptoms, activities, or occupational tasks related to daily life function. The semistructured interview format of the PMO-AP using the concept of therapeutic emplotment enables the physician to probe and lead the patient to identify specific symptoms, tasks, or activities of concern. Identifying the specific activities/symptoms/tasks that can be used as an indicator to measure the PMO generated by the patient is a critical step in the PMO-AP.

4.1.4 Characteristic #4

The personalized assessment approach should allow the patient to define the extent of change or improvement expected from treatment that would be considered meaningful from the patient's point of view. All individualized PROMs ask the patient to rate the status of the outcomes selected on a 5- or 10-point Likert-type scoring system. This process does not inform whether the patient was satisfied with the change in the scores at follow up and whether the process was meaningful from their perspective. COPM is the only individualized PROM that captures satisfaction along with status related to the outcomes. The COPM, however, includes a 10-point Likert scoring system to measure the level of satisfaction, and it is unclear whether the satisfaction related to the change in the outcome is meaningful only if the score is 10 or if there is a cut off. Therefore, a-priori defining in detail the extent of the changes or improvement expected is another important characteristic of the PMO-AP. The patient should be able to determine and describe a-priori the extent of change that they consider meaningful for the PMOs. Using a standard 5-point Likert-type scale similar to other individualized PROMS to rate the status of the PMOs at follow up does not indicate whether the patient is satisfied with the change

or whether it is meaningful. Therefore, adaptations include the goal attainment scaling (GAS) approach, which enables the patient and clinician to discuss and document a detailed description of the different levels of change that is considered meaningful the instead of just using the standard 5-point Likert-type scoring system.

GAS is a measurement method first introduced by Kiresuk and Sherman (1968) for program evaluation in mental health centers as a measure of treatment induced change. The GAS process involves identifying a goal that is realistic to achieve in a given time period, precisely described, and measurable. The PMO-AP adapts the GAS approach to a-priori define and precisely describe the expected change considered meaningful, and includes discussions of the magnitude of change in the PMOs with the clinician. This process allows both individualization of PMOs according to the needs of each individual and offers an assessment that is truly patient-centered (Becker et al., 2000; Kiresuk et al., 1994/2014).

The visible scaling provides the patient and clinician with a shared, tangible representation of the PMO. The scaling serves as a boundary or mediating object (Leigh Star, 2010; Star & Griesemer, 1989) or a material anchor (Hutchins, 2005)—a shared focal point between the patient and the clinician's perspectives, rather than presenting information dominated by one participant's perspective. Boundary objects provide loosely structured schematic representation of information that enables several parties to bring together their different perspectives to the interpretation of the object and employ it as the anchor for discussion (Leigh Star, 2010). The schematic structure of the boundary object reduces the potential power imbalance between the patient and clinician and enables them to develop their shared understanding of the treatment scenario. For each PMO identified, the patient will a-priori

determine and precisely describe the specific indicators that correspond to the PMO and the magnitude of change for each GAS rating through a dialogue with the clinician using the modified GAS approach. The discussion that follows becomes the collaborative strategy for therapeutic emplotment of the treatment, shaped by the patient's PMO.

The feedback from the clinicians involved in developing the PMO-AP included a recommendation to modify the GAS rating system to increase its receptivity by patients. In the standard GAS rating system, the patient would select a rating of "0" when they reach the a-priori described expected meaningful change, a positive rating of "+1" or "+2" if the change exceeds the expected level of meaningful change, and a negative rating of "-1" or "-2" even if the change in the outcome is in the desired direction but not to the extent that patient considers meaningful (Kiresuk et al., 1994/2014). This rating system also does not capture the baseline status of the patient that can be used as an anchor to track the change in the PMOs. Thus, modifications in the rating system included to capture the baseline status of the PMOs and the status at each desired levels of change in the PMOs. PMOs will be rated on a scale of 0–5 with a detailed description of each level of rating. The rating of "0" will be used to describe the baseline status of the PMO and will be used as the corresponding rating if the PMO did not change from baseline or worsened from baseline during follow up. The choice to not discriminate between no change and negative change at follow up was made based on the feedback from the clinicians as they considered it not ideal to ask the patient to a-priori discuss and describe the various levels of negative change in the PMO that is not acceptable. A rating of "1" corresponds to the description that an observed positive change in the PMO that is much less than the expected change that is considered meaningful. A rating of "2" corresponds to the description that an observed change in

the PMO is less than the expected change considered meaningful. A rating of "3" corresponds to an observed change in the PMO considered meaningful (i.e., the expected change). A rating of "4" corresponds to an observed change in the PMO greater than the expected change that is considered meaningful. A rating of "5" corresponds to an observed change in the PMO that is much greater than the expected change that is considered meaningful.

PMO-AP is an idiographic qualitative assessment. The modified GAS rating of "0" to "5" is a classification that corresponds to the description of the different levels of the expect changes for easy reference and not a not a numerical scoring to be used in a quantitative way over time. The modified GAS rating is used only as an anchor or symbol for point of reference, and it is not be used to calculate any cumulative scores of all the PMOs. The status of each individual PMOs will be individually monitored and tracked at follow up to see whether the change observed corresponds to the a-priori description of expected levels of change. The important aspect of using GAS is to allow the patient to explain in their own words their baseline status, which is anchored to a rating of "0" and different levels of expected change "1–5". If the patient at follow up attains what was a-priori defined as a meaningful change anchored to a rating of "3," that rating would be selected. The intervals between the ratings are assumed to be non-equidistant, which can be confirmed by reviewing the extent of change in the description corresponding to each rating. When verbal descriptions where used at all points to test the equidistance assumption in Likert-type scales, a larger perceived distance between points in the middle of the scale (middle-of-scale effect) was obtained (Lantz., 2013).

Table 1

PMO-AP—Rating of PMOs Using Modified GAS

Standard GAS Rating	Modified GAS Rating	Predicted Attainment for the PMO
N/A	0	Baseline or less than baseline
-2	1	Much less than the expected outcome considered meaningful by the patient
-1	2	Less than the expected outcome considered meaningful by the patient
0	3	Expected outcome (target) considered meaningful by the patient
+1	4	Greater than the expected outcome considered meaningful by the patient
+2	5	Must greater than the expected outcome considered meaningful by the patient

4.1.5 Characteristic #5

Given that the assessment is being designed to gauge the treatment impact on PMOs chosen by individual patients, it is imperative to foster a dialogue between the patient and clinician. Following the generation of the illness narrative by the patient, the clinician and patient, in the process of selecting PMOs and detailing the anticipated degree of changes using the modified GAS rating, should engage in a collaborative discussion. The aim of this discussion should be to ensure that the chosen outcomes and the predefined criteria for meaningful change are both realistic and pertinent to the specific condition being treated.

Although patient perspectives and individually identified outcomes using individualized PROMs may encompass a broad spectrum of health-related concerns, not all of them may be

directly attributable to the illness requiring treatment. This thesis focused on evaluating the treatment impact on outcomes specifically linked to the illness. Therefore, it is crucial that, in addition to outcomes generated directly by the patient through their illness narrative, a collaborative discussion occurs during the selection and scaling of expected changes to guarantee relevance to the targeted disease.

4.1.6 Characteristic #6

The personalized assessment process should capture any possible changes in the nature of outcomes identified or changes in the expectation of effects over time. This PMO-AP requirement indicates that the approach should respond to the reality of a patient's life by adapting to possible changes of interest in outcomes over time or possible modifications in desired changes. During the follow-up visit, a PMO-AP should allow the clinician to further probe the rating selected by the patient, continue the dialogue with the patient, and further develop their shared understanding of the treatment effect. This process is different from PROMs where the patient does not have to explain why they selected a particular score for an outcome. This process is an improvement over individualized PROMs that do not give clear guidance whether an outcome generated initially by the patient can be changed at follow up or not. With the PMO-AP, some PMOs may be removed (because they have been met or are no longer relevant), and other PMOs may be added including the changes to the details of the GAS of the PMO if there is a change in the context during follow up.

4.1.7 Characteristic #7

The individual measurement process should be able to detect and record unexpected changes that may be beneficial or detrimental to the patient's QoL. The PMO-AP should be able

to detect unexpected changes related to the disease during the course of the treatment. Having this information allows the clinician to do a better follow up. All individualized PROMs focus only on the outcomes generated by the patient but do not probe or ask regarding any unexpected events or changes that the patient observed separate from the outcomes in the context of treatment. The process offers no means of measuring any other changes (positive or negative) that occurred that were important to the patient. In the PMO-AP, a clinician would check whether the patient noticed any unexpected events or changes related to the disease since starting the treatment at follow up.

I presented the entire concept of the PMO-AP and the process of identifying, finalizing, and scaling of the outcomes to the PhD supervisory committee and developed the final assessment based on their recommendations and changes suggested. The final PMO-AP used in the clinics is presented in Section 4.2. Testing included the PMO-AP approach with a patient with creatine transporter deficiency initiating a treatment in the Biochemical Diseases clinic under the innovative intervention protocol approved by the scientific committee at BC Children's Hospital. The effectiveness of the treatment was assessed using standardized clinical outcomes and the PMOs using the PMO-AP. The case report was published in JIMD (Jaggumantri et al., 2015).

4.2 Results: Description of the PMO-Assessment Process

The PMO-AP is a criterion-referenced assessment and includes the administration in four successive stages aimed at identifying and assessing the PMOs using an interview-based format. The first three stages are completed at the initial visit before treatment initiation, resulting in a set of PMOs with clear indicators and the precisely described expected magnitude of change

defined a-priori by the patient in collaboration with the clinician. The last stage (Stage 4) includes description of how the follow up and evaluation of PMOs is conducted during follow-up clinic visits.

4.2.1 Stage 1 – PMO Identification

The first step in administering a PMO-AP is identifying a list of PMOs most relevant to the patient's personal needs and perception of wellness. The process entails first obtaining a patient's narrative account of their condition, a process similar to the medical histories commonly recorded by clinicians. Using a set of guided prompts, the clinician starts the interview to let the patient tell their story in their own words. From this point, the patient, along with the clinician, identify several PMOs coherent with the patient's understanding of their condition. This partnership also anticipates how the patient would like their treatment to affect their daily life.

The PMO identification interview prompts listed below are open-ended questions that can be used to initiate the discussion and elicit the patient's illness narrative.

- How does the condition affect your everyday life?
- How would you envision a good day for you?
- What kinds of changes would you like the treatment to have in your daily life?
- Do you have any concerns due to your illness? Additional possible probing questions could of focus on concerns regarding the below domains:
  - Physical functioning? (Walking, running, daily activities, energy level, etc.)
  - Emotional functioning? (Behavior, mood, and sleep)
  - Social functioning? (Getting along with other children, friends, playtime, etc.)

- School functioning? (Memory, attention, grades etc.)
- Any other areas of concerns?

The prompts provide general guidance. Clinicians are advised to not restrict themselves to the prompts but personalize them based on the patient's concerns, the social and psychological context, and the style of the clinicians' practice. These questions may be included as an initial part of a clinical consultation, obtaining the patient's illness narrative before the more structured medical history. The clinician documents all of the PMOs identified in the PMO Identification Form (see Appendix B). The form allows documentation of five PMOs; however, there are no strict rules on the final number of PMOs to be selected at the end of Stage 1. It is recommended that at least five PMOs are identified but less or more PMOs are also acceptable.

As the example below illustrates, the study included the use of the PMO-AP to identify outcomes that mattered most from the perspective of Participant 01, Jane, a caregiver of an 8-year-old boy diagnosed with creatine transporter deficiency. I did not interview the patient as he had an ID. I interviewed Participant 01 using the PMO-AP identification interview prompts as a reference to get the illness narrative and identify the PMOs. Going over the illness narrative with me, Participant 01 identified the following PMOs, describing them in her own words:

- **PMO#1 – communication:**

  Yes, whole sentences and that he can reply and interact and communicate back and forth like, 'How was your day?' or 'Do you want to go and play?'' that type of thing, you know. 'Come and play with me at my house,' 'Let's have a play date,' just the basic requirements.

- **PMO#2 – decision-making:**

  What he wants, yes, his own choice individually—no influence from me or anybody else. I want him to make his own choices because at the moment, I mean he does make his own choice but then he's not quite sure. You know what I mean?

- **PMO#3 – social life:**

  So, although he is social, he knows how to socialize, but he doesn't know how to interact with that socializing. I want him to have two hours a day at school or more, if possible, to go into the normal grade one class and associate and socialize with [others].

4.2.2 Stage 2 – PMO Finalization and Measurement

At this stage, the PMOs identified are finalized through a discussion and the creation of a therapeutic emplotment scenario agreed upon between the clinician and the patient to ensure their relevance and realism (i.e., that the selected PMOs fit in the range of medically reasonable options). The clinician and patient will then collaborate to determine how the PMO will be monitored using a specific indicator that they jointly identify. For example, Jane identified "Reduction in Impulsive Behavior" as a final PMO and its measurement might include by checking the "Ability to sit still without getting distracted; listening to instructions given by the parents, etc." The whole process of selecting a PMO and deciding how they are measured is a collaboration between the patient and clinician to ensure both meaningfulness and relevancy of the PMO to the condition.

The patient then provides a weight for each selected PMO to reflect their respective importance. The clinician asks the patient or caregiver to provide a weight or rank for each PMO on a scale of 1–10, which sum to 10. This process is completed using the PMO-AP Finalization

Form (see Appendix C). It is recommended that at least three PMOs are finalized along with their indicators. Like in Stage 1, there are no strict rules on the final number of the PMOs. PMO-AP is a flexible assessment with the main objective to generate PMOs and how they can be tracked at the follow up. An example of the output from Stage 2 is as follows: In collaboration with Jane, we agreed to focus on three PMOs:

- **PMO#1 – communication:** The measurement includes being able to communicate in complete sentences and the ability to reply without being prompted.
- **PMO#2 – decision-making:** The measurement includes a clear decision and the ability to choose what a patient wants without influence.
- **PMO#3 – social life:** The measurement includes the ability to play with normal grade children apart from skills program at school for 2 hours.

Ranking was also determined, which included the physician asking the patient or caregiver to provide a weight or rank for each PMO on a scale of 1–10 which summed to 10 (i.e., PMO#1 = 5, PMO#2 = 3, and PMO#3 = 2; thus 5 + 3 + 2 = 10).

4.2.3 Stage 3 – PMO Scaling to Determine Possible Changes over time.

The final PMOs are scaled by employing the modified GAS rating. This process uses the PMO-AP scaling form (see Appendix D). The scaling of the PMO indicators is completed using the specific, measurable, achievable, Realistic, and timely (SMART) approach to improve goal assessment precision and validity in this context. The clinician will record the baseline status and the a-priori defined expected changes for each PMO by the patient on the PMO-AP scaling form. The time for follow up for each PMO will also be agreed between the clinician and the patient or caregiver. This document will serve as a reference and a boundary object for future assessments

and discussions. As explained earlier, the modified GAS rating of 0–5 is only for point of reference or anchoring and not for any quantitative evaluation. Table 2 shows an example of a PMO with the modified GAS rating in the PMO scaling charter, which will be completed for each finalized PMO by the clinician through the shared understanding with the patient:

Table 2

PMO-AP Example—Modified GAS Rating

Rating	Expected Level of Change
	PMO#1 Communication/Conversation
0	Never communicates or replies in full sentences.
1	Unable to communicate and reply in full sentence once per day.
2	Able to communicate and reply in full sentences at least 1–2 times per week.
3	Able to communicate and reply in full sentences 1–2 times per day.
4	Able to communicate and reply in full sentences between 3–5 times per day.
5	Able to communicate and reply in full sentences at least 6–10 times per day.
	PMO#2 Decision-Making
0	Never makes clear decision or choice without input from parents.
1	Unable to make s clear decision and choices without influence once per day.
2	Able to make a clear decision and choice without influence at least 1–2 times per week.
3	Able to make clear decisions and choices without influence 3–5 times per day.
4	Able to make clear decisions and choices without influence 6–10 times per day.
5	Able to make clear decisions and choices without influence at least 11–15 times per day.
	PMO#3: Social Life
0	Never spends time with kids in their class during school play time.
1	Unable to spend time with kids in their class during school play time at least once per week.
2	Unable to spend time with regular education kids during school play time once per week.
3	Spends time with regular education kids during school play time at least once per week.
4	Spends time with regular education kids during school play time 2 times per week.
5	Spends time with regular education kids during school play time at least 3 times per week.

Note. Modified Goal Attainment Scaling (GAS) Rating is based on the PMO achievement level, where 0 = *Baseline*, 1 = *much less than the expected outcome*, 2 = *slightly worse than the expected outcome*, 3 = *expected outcome (target)*, 4 = *slightly better than the expected outcome*, 5 = *much better than the expected outcome*.

4.2.4 Stage 4 – PMO-AP Follow Up

During follow-up visits, the clinician asks the patient to review their PMO scaling

forms and rate their performance on each PMO by selecting the score that reflects their current status. The clinician then asks the patient to explain the response process they went through to select the rating that corresponds to the described expected level of change and their interpretation. By asking the patient to explain why they selected a particular rating at follow up, the clinician can confirm the patient's interpretation of the status of the PMO and whether it is in line with what was defined a-priori and documented in the PMO-AP form. This process is completed by asking the following probing questions:

1. What does the PMO mean to you now?
2. What did you remember when you read this PMO?
3. Describe your experience in relation to the PMO since the last visit?
4. How did you select the present rating?

At each follow-up visit, the clinician also asks the patient about any new events or changes noticed during the interval; these new events are recorded for further investigation in relation to the treatment. After reviewing the PMO rating, the clinician and the patient have a discussion to determine whether they (a) would like to keep the same PMOs, (b) change how to monitor the PMO, (c) change the scaling levels, (d) select a different PMO if there was a change in the relevance or context of an existing PMO, or (e) decide to stop monitoring the PMO if they achieved the expected level of change. All this information includes documentation in the PMO Follow up and Evaluation form (see Appendix E). If they decide to add a new PMO or adjust the scaling of an existing PMO, a new PMO scaling form is completed by going over the process outlined in the Stage 3. This follow-up description shows that the PMO-AP is a continuous

approach for the personalized care of individual patients with chronic conditions.

4.3 Discussion

The PMO-AP can be developed to be a more effective PCM-based idiographic assessment for identifying and measuring tangible outcomes that reflect the goals and priorities of an individual patient in clinical practice. It is a criterion-referenced assessment due to inclusion of the modified GAS where the expected changes are predefined. Most significantly, the process is a vehicle for developing and tracking the shared understanding between a patient and a clinician about a treatment and its possible effectiveness in meeting these goals. The five unique characteristics of the PMO-AP that differentiates it from other existing individualized tools or measures are as follows:

1. The PMO-AP is an idiographic assessment process designed to establish a framework for the generation of outcomes specific to the individual, using their own illness narrative. It does not function as an individualized scale or measurement instrument. When administered to a patient, it aids in identifying outcomes of interest that are unique to that particular individual. Conversely, if administered to a caregiver, it assists in recognizing outcomes that are significant to them based on their individual illness narrative and their interpretation of what is meaningful within the context of the patient's condition.
2. The form necessitates an ongoing dialogue between the clinician and the patient throughout the process, facilitating the development of shared understanding regarding treatment outcomes and scenarios. This collaborative approach helps prevent the selection of PMOs that are irrelevant to the patient's illness. This

collaborative process does not require the clinician to approve each PMO individually, but rather, it encourages both the patient and clinician to reach mutual understanding regarding the selection of PMOs. Respecting the patient's right to self-determination, the clinician's interaction plays a crucial role in identifying PMOs that are most relevant to the specific disease being treated for the individual patient. It is crucial for the clinician to recognize the power imbalance in the clinician-patient relationship. They should actively listen to the patient's illness narrative and therapeutic journey, avoiding any unintentional bias towards solely biomedical outcomes.

3. The adapted GAS can be used to monitor an a-priori determination of the extent of the desired changes that is considered meaningful by the patient. This determination constitutes written documentation that helps in structuring a more informative discussion at follow-up, describing them precisely.
4. The process enables clinicians and patients to modify the selected outcomes during follow up to account for real life events and possible changes in the life of the patient, allowing a continuous dialogue and a personalized follow-up process in clinical practice.
5. The process has the capacity to reveal unexpected events at follow-up visits that the patient and clinician might otherwise ignore with the other personalized PROMs.

The PMO-AP is an idiographic assessment of PMOs that are specific to the individual patient. Each PMO is an individual outcome and treated separately. The PMOs identified through PMO-AP are not like items of PROM measuring a unified construct. The PMO is a

simple description, generated by the patients, and it can measure any construct (symptom, activity of daily living, behavior etc.) that is considered personally meaningful by the patient during the PMO-AP administration. Therefore, there is no underlying measurement model within the conceptual framework. The output of the PMO-AP is individualized. PMO-AP is also different from other individualized PROMs such as the SEIQoL, which are also administered in a semistructured interview format.

In the SEIQoL, the person interviewing the patient does not actively participate with the patient in the selection of the domains of interest. The PMO-AP requires the active participation of the clinician not only during selection and scaling of the PMO but also during the PMO scoring at follow up. This shared understanding of the outcomes between the clinician and the patient is one of the core principles of the PMO-AP to ensure a selection of relevant and realistic outcomes (PMO and expected changes). This process can lead to better communication and a stronger clinician-patient relationship. Establishing effective communication between the clinician and the patient is essential during the administration of PMO-AP. In this process, the patient plays a pivotal role by sharing their illness narrative, which forms the basis for selecting and scaling of the PMOs. The clinician's role is to facilitate this interaction and ensure that PMOs selected are relevant to the patient's disease and that realistic expectations for change within the designated follow-up timeframe are set. For instance, if a patient with Rett syndrome, who is non-ambulant and has severe joint contractures, chooses "walking ability" as a PMO, with a meaningful change defined as "walking up or down 10 stairs independently," the clinician can help by explaining that achieving this independently is not feasible due to the severe contractures and the limitations imposed by the current treatment. Following this discussion, the patient may

choose to adjust the scaling to something more realistic, such as "walking up or down 10 stairs with support." PMO-AP is a flexible assessment and does not mandate a specific number of PMOs to be generated.

Taking the “Top 3 concerns” in visual analogue scale as a reference, at least three PMOs should be generated for Stage 3. The modified scoring system in the GAS step is only for use as point of reference. Each PMO documented in the PMO scaling charter will be evaluated independently and not aggregated to compute a global score.

The PMO-AP meets all the characteristics outlined in Chapter 3: that are needed to implement a personalized approach in clinical practice. The PMO-AP also enables a dynamic follow-up process to systematically track the PMOs and modify them depending on the context or preference of the patient with chronic disease. The PMO-AP strengthens the structure and enlarges the scope of the informal clinical consultation usually focused on the biomedical aspects of the disease. The PMO-AP supports social interaction and leads to an explicit discussion between the clinician and patient about either the patient’s symptoms or their functional status. Using the PMO scaling form at follow up, with a precise description of the expected changes, also minimizes recollection and reporting biases that may occur in routine and less structured clinical consultations. By involving the patient in generating the PMOs and tracking them together at follow up, the patient is likely to develop a sense of ownership. This process could lead to better compliance and adherence to the treatment by the patient.

For example, if there is no improvement or change in the PMOs during follow up, this process may help inform the clinician to explore additional treatments or alternative strategies that can lead to the expected meaningful change in the PMOs as determined by the patient. To

summarize, the PMO-AP was developed to provide a unique personalized assessment process for clinicians and patients to develop shared treatment goals that are important to the individual patient across multiple diseases and different treatments. This method does not change the character of informal patient-physician encounters but rather enables a systematic process around personalized outcome evaluation that takes into consideration the patient's lifestyle, values, preferences, and social environment.

In summary, the PMO-AP will be a new process that facilitates personalized follow-up in clinical practice, based on solid and well-documented discussions that help consolidate trust and partnership. This approach has the potential to be relevant for all chronic conditions, in context of a consolidated patient-centered system. Following initial process development, I conducted testing to evaluate the reproducibility, validity of information collected, and the feasibility of using the PMO-AP in clinical practice, described in Chapter 5:.

Chapter 5: Evaluating the PMO-AP Assessment Properties

Development of the PMO-AP included the intention to enable clinicians to establish shared understanding of what is most important for individual patients as a more effective personalized assessment strategy. The goal of the process is to facilitate a holistic personalized approach in clinical practice across diseases and settings in assessing the treatment's response. PMO-AP is not another scale or a measurement instrument but an idiographic assessment process to identify outcomes and establish a-priori the extent of change that is considered meaningful for the individual patient using the concepts of therapeutic emplotment and goal attainment scaling. PMO-AP provides clinicians an opportunity to collect information at an individual level, which may have been missed by the standardized measures developed at a population level. Chapter 5 includes description of the evaluation of the PMO-AP as a new individualized assessment process and its ability to generate useful data when used in the context of holistic PM.

To determine whether the PMO-AP can serve as an effective idiographic strategy to identify and track outcomes of the individual patient to support a holistic PM approach in clinical practice, I evaluated the following:

- The reliability of the assessment process through the PMO-AP
- The validity of the information collected through the PMO-AP
- The capacity of the PMO-AP to generate data useful for personalized discussions when implementing a truly personalized assessment approach in line with the characteristics outlined in Chapter 3.

5.1 Evaluation Methods

The design of the PMO-AP allows it to be used at the individual level within the context of clinical practice specifically in the management of patients with chronic diseases or medical complexity. The information gathered through the administration of PMO-AP is inherently dependent on the individual being assessed. When PMO-AP is administered to a patient, the resulting information is shaped by the patient's personal illness narrative and what they personally deem meaningful. In contrast, when PMO-AP is administered to a caregiver, the outcomes are influenced by the caregiver's own narrative of the child's illness and their interpretation of what holds significance in the context of the patient's condition.

I conducted a prospective study at BC Children's Hospital (BCCH) to determine whether PMO-AP possesses properties that render it a valuable assessment for clinical use in the field of PM. This study specifically focused on using PMO-AP with individual patients capable of self-reporting, and as such, I did not data from caregivers. It is important to emphasize that the primary objective of this study was not to compare the PMOs generated by individual patients through self-report with those generated by their caregivers through a proxy-report. This aspect is a critical consideration and will be addressed in future research endeavors focused on the ongoing development and refinement of PMO-AP.

5.1.1 Study Design

This prospective, single-center, single-arm, open-label study took place in collaboration with the Complex Pain Service, the Gastroenterology Division, and the Pediatric Rheumatology Division. Patients who consented to participate in the study completed the PMO-AP and a set of standardized PROMs that included the following:

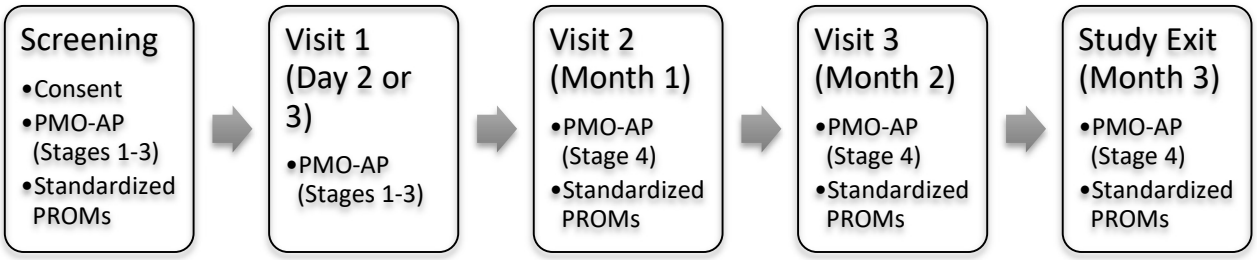
- Pediatric Quality of Life 4.0 Generic Core Scale (PedsQL; Varni et al., 2001)
- Pediatric Pain Questionnaire (PPQ; Varni et al., 1987)
- Functional Disability Index (FDI; Walker & Greene, 1991)
- Childhood Health Activity Questionnaire (CHAQ; Singh et al., 1994), and
- IMPACT-III (Otley, 2008).

The study included these standardized PROMs to compare responses to these PROMs with the PMO-AP for validation purposes.

The study involved a total of five visits—a screening visit and four follow-up visits. The first follow up visit (Visit-1) occurred 2–3 days after screening and the remaining three follow up visits occurred at 1-month intervals. The total study duration for each participant was 3 months. The study design is shown in Figure 1. I chose 2–3-day time interval between screening and follow up Visit-1 to perform a test and retest of the PMO-AP. Timing was closely spaced to ensure that any variation reflected the reliability of the information provided by the patient when the PMO-AP was administered rather than change in the information because of change in the patient's status. The time was also long enough to minimize memory effects. Also, it would be unethical to withhold treatment for a longer duration to allow for test-retest evaluation. The timeframe for the remaining visits was based on the frequency of the patient's visit to the clinic as per standard of care (see Figure 1).

Figure 1

Study Design



5.1.2 Participation Criteria

The aim of participant recruitment was to include patients with a chronic condition that had a significant impact on their daily lives. The inclusion criteria for participation in the study were as follows:

- male and female patients aged 12–18 years,
- patients starting new treatments[1],
- children and teens seen at the Complex Pain Service (CPS) for pain management, or
- patients with Crohn's Disease (CD) initiating Infliximab treatment in the Gastroenterology Division, or
- patients treated for juvenile idiopathic arthritis (JIA) at the outpatient clinic in Pediatric Rheumatology Program.

[1] This was an important criterion as the PMO-AP included development to determine the outcomes or goals and priorities of the individual patient at the beginning of the treatment and track how they changed in response to the treatment.

Likewise, some patients were not good candidates for participation in the study. The exclusion criteria were inability to communicate in English, and inability to independently complete the study assessments. Additionally, based on the treating physician's judgment, also excluded from the study were patients who were in crisis, had an unstable mental state, had a severe illness, or could not provide a valid self-report.

The study was not conducted at the Biochemical Disease Division, where PMO-AP was initially conceptualized and developed as part of the TIDE-BC project. This rationale for this decision is that most indications diagnosed in the clinic did not have a treatment available. Additionally, for patients whose treatments were available, many of them in this clinic were very young or had IDs, which necessitated a proxy report from their caregiver. The current study's criteria required the initiation of treatment and the ability to self-report, which limited the enrollment of participants from the Biochemical Disease Clinic.

5.1.3 Sample Size

PMO-AP is an idiographic assessment designed to facilitate the collection of individual-level outcomes. The information gathered is qualitative and tailored to each individual, without generating standardized numerical data for quantitative analysis. Consequently, conventional statistical sample size estimation methods do not apply to PMO-AP.

In qualitative research, justification of sample size is not required. In addition, the traditional approach of saturation sampling is also not applicable to PMO-AP because PMO-AP focuses on the individual rather than a population-level study where data collection continues with additional participants until no new information or insights can be obtained.

The objective of this study was to assess the various stages of PMO-AP administration

and determine the reproducibility and validity of the information collected for each individual. To achieve this goal, I used a convenience sampling approach and a sample size of 50. I did not perform formal sample size estimation, power analysis, or statistical analysis, as the data analyzed were predominantly descriptive. Data collected from 50 study participants supported a rigorous preliminary evaluation of the PMO-AP's performance while acknowledging its unique qualitative nature and focus on individual-level outcomes.

5.1.4 Study Enrollment

The study participants were enrolled at the Complex Pain Service, the Gastroenterology Division, and the Pediatric Rheumatology Division clinics in BC Children's Hospital.

5.1.4.1 Complex Pain Service

CPS helps children and teens manage pain. The CPS is a multidisciplinary team of health care professionals consisting of a physician, psychologist, nurse clinician, and a physiotherapist. The CPS assesses and treats children and teens with complex chronic pain. The CPS works with the patients, families, and caregivers to better understand the reasons for chronic pain and to develop a plan to manage pain. The goal is to reduce or eliminate pain and to help the child/teen return to a normal life by addressing the physical, psychological, and social needs of the patients. Treatment options may include medication, mind-body techniques for relaxation and pain management, exercises for strengthening, stretching, and general reconditioning, or support to relieve life stressors at school or home that can make pain worse.

I approached eligible patients for recruitment after their consultation with the CPS team during the first visit.

5.1.4.2 Gastroenterology Division

The division of gastroenterology provides care for patients with diseases and conditions of the digestive tract including the stomach and intestines. I approached eligible patients with CD at the outpatient clinic before their initiation of Infliximab treatments. A condition of some of the patients, CD, is an inflammatory bowel disease (IBD). IBD causes inflammation of the digestive tract, which can lead to abdominal pain, severe diarrhea, fatigue, weight loss, and malnutrition. Inflammation caused by CD can involve different areas of the digestive tract in different people. Infliximab, a chimeric monoclonal antibody against tumor necrosis factor-α used to treat CD, was administered intravenously in the Medical Day Unit at BCCH.

5.1.4.3 Pediatric Rheumatology Program

The Pediatric Rheumatology Program diagnoses and treats children and adolescents with rheumatic diseases. The program provides coordinated care and diagnostic consultation services, follow up clinics in an outpatient setting, consultation and treatment by specialized pediatric rheumatology physiotherapists and occupational therapists, weekly procedures clinic for joint injections done under conscious sedation, and supervision of intravenous therapies in the Medical Day Unit. I approached eligible patients with JIA, the most common type of arthritis in children, for recruitment at the outpatient clinic.

5.1.5 Study Variables

In each of the clinics, I collected the information regarding the PMO-AP. I also asked every participant to complete several standardized PROMs.

5.1.5.1 Variables identified with the Personally Meaningful Outcomes – Assessment Process (PMO-AP)

The PMO-AP includes administration in four successive stages aimed at identifying and assessing the PMOs using a semistructured interview-based format (see Chapter 4). The first three stages took place at the screening and follow up Visit-1, before treatment initiation, and resulted in a set of PMOs with the precisely described expected magnitude of change defined a priori by the patient in collaboration with the clinician. The fourth stage corresponded to the follow-up assessment of changes at visits 2, 3, and 4.

- Stage 1 resulted in identification of several PMOs through the illness narrative documented in the PMO Identification form (see Appendix B).
- Stage 2 resulted in selection of PMOs to be tracked, as well as the identification of the indicators to measure them, and the specific weight given to each selected PMO to reflect their respective importance. The output included documentation in the PMO Finalization form (see Appendix C).
- Stage 3 included scaling of the selected PMOs using the modified GAS for the participants to define a-priori the magnitude of changes that were expected for the treatment to be considered useful. The PMO Scaling form included the information for each selected PMO from Stage 2 (see Appendix D).

- Stage 4 included a description of how the follow up assessment of changes were conducted at each follow up visits 2, 3, and 4. At each follow-up visit, the participants reviewed their PMO Scaling forms and rated their performance on each PMO by selecting the rating (modified GAS scale established at baseline) that reflected their

status. The participant elaborated on the response process they went through to select the new rating and their interpretation. I also asked each participant about any new events or changes at each follow up. The PMO Follow up and Evaluation form included all documentation of this information (see Appendix E). If the participant decided to add a new PMO or to change the scaling of an existing PMO, a new PMO scaling form was completed.

5.1.5.2 Pediatric Quality of Life 4.0 Generic Core Scale

Participants recruited from all three clinics completed the PedsQL. This generic quality of life PROM consists of 23 items grouped into physical, emotional, social, and school functioning scales. The design is intended to measure the core dimensions of health as delineated by the World Health Organization, as well as the ability to function in roles such as school student. PedsQL is a flexible scale designed for use in clinical pediatric populations and takes less than 4 minutes to complete. In this study, I administered age-appropriate Child Self-Report versions with an internal consistency reliability score of 0.88 for the child self-report version, distinguishing between healthy children and children with acute and chronic health conditions. The form can also distinguish disease severity within a chronic health condition (Varni et al., 2001).

5.1.5.3 Pediatric Pain Questionnaire

Participants recruited from CPS completed the child or teen version of the PPQ. The PPQ is a generic symptom-specific instrument to measure pain in patients with acute and chronic health conditions. Specifically, this instrument measures pain intensity, location, and the sensory, evaluative, and affective qualities of the pain. It is a well-established questionnaire with test-

retest reliability scores of 0.29–0.41 and a convergent validity score of 0.27–0.68 with disease status (Varni et al., 1987).

5.1.5.4 Functional Disability Index

Participants recruited from the CPS also completed the child report version of FDI. FDI is a measure of the degree to which children experience difficulty in physical and psychosocial functioning due to their physical health status. Participants rated how much physical difficulty was perceived for a variety of everyday activities (Walker & Greene, 1991). The Child Report FDI consists of 15 items concerning perceptions of activity limitations during the past 2 weeks, has a test-retest reliability score of 0.74, and validity supported by significant correlations with measures of school-related disability, pain, and somatic symptoms (Claar & Walker, 2006).

5.1.5.5 Childhood Health Activity Questionnaire

Participants recruited at the outpatient clinic from the Pediatric Rheumatology program with JIA completed the CHAQ. The CHAQ was adapted from the Stanford Health Assessment Questionnaire and evaluates functional capacity and independence in activities of daily living during the last week. The CHAQ included specific construction to evaluate children and adolescents with JIA. This process includes eight domains: (a) dressing, (b) arising, (c) eating, (d) walking, (e) reach, (f) grip, (g) hygiene, and (h) activities. Also included are two visual analogue scales for pain evaluation and overall well-being evaluation (Machado et al., 2001; Ruperto et al., 2001). The CHAQ has test-retest reliability scores of 0.79–0.96, internal consistency of 0.93, and a strong to moderate correlation for validity (van Mater et al., 2012).

5.1.5.6 IMPACT-III

Participants with CD, recruited from the outpatient clinic of the Gastroenterology Division, completed the IMPACT-III questionnaire. This questionnaire is a disease specific questionnaire with 35 questions encompassing six domains: (a) bowel, (b) body image, (c) functional/social impairment, (d) emotional impairment, (e) tests/treatments, and (f) systemic impairment. IMPACT-III has a reliability score of 0.92 for internal consistency and used as a measure of QoL in pediatric CD. Additionally, this questionnaire is self-administered and used in children aged 10–17 (Otley, 2008; Otley et al., 2006).

5.1.6 Data Collection Process

The standardized PROMs (PedsQL, PPQ, FDI, CHAQ, and IMPACT-III) used in the study are all self-report questionnaires. Participants completed the questionnaire independently in paper format at each study visit. I employed PMO-AP as described in Chapter 4:. I interviewed the participants and completed the three initial PMO-AP forms (PMO Identification Questionnaire, PMO Finalization Form, and PMO Scaling Form) during the screening and the first follow-up visit. I recorded all interactions with the participants and took notes of my interactions with patients and discussions to document the illness narrative they provided.

During the second and third follow-up visits and the study exit visit, the participant independently provided the scoring in the PMO-AP. I took notes of the discussions with the participants, paying specific attention to their explanations and reasons given for selecting a particular rating and interpretation of their PMOs, selecting a different PMO or an indicator at each follow up visit. I then entered all data into the study database for analysis and assessing consistency, in concordance between scores on specific domains of standard scales and the

PMOs identified by patients with the help of the physicians.

5.1.7 Evaluation of the PMO-AP

The study included an assessment of the reliability and validity of the PMO-AP. PMO-AP is an idiographic criterion-referenced assessment administered through an interview process. PMO-AP forms can be used to document the result after each stage of administration and serve as a boundary object during follow up visits. The information obtained in the study was specific for each participant to generate a set of specific items or identify domains of interest. It is not used for any group-level analysis. All the information collected was qualitative and therefore conventional quantitative analysis methodology for assessing reliability and validity were not applicable. Also, as PMO-AP is not another individualized PROM or scale, the standard psychometric methods for assessing reliability and validity were not used in the study. PMO-AP lacks scoring for the PMOs; therefore, methods such as Cronbach alpha for internal consistency and intraclass correlation coefficient for test-retest reliability were not applicable to the information generated using the PMO-AP. Similarly, PMO-AP also lacks predetermined items of domains, which precluded using methods such as factor analysis for construct validity. Additionally, the study also included an evaluation to determine whether the data collected using the PMO-AP met the characteristics of personalized assessment outlined in Chapter 3 and whether it could make it a valuable assessment for use in the context of holistic PM in the clinic.

5.1.7.1 PMO-AP Reliability determination

An essential requirement for all outcome assessments is to be reliable. Reliability includes definition as an index of the extent to which measurements from the same individuals obtained at different times yield similar results when everything else remains the same (Streiner

& Norman, 1990). Reliability of the process administering the PMO-AP and the reproducibility of the information generated after it is administered to the same individual twice was evaluated in this study. Test-retest reliability included measurement of consistency or reproducibility of the PMO-AP in generating the same outputs after Stages 1–3 when administered twice (2–3 days apart), first at screening and again at the first follow-up visit 2–3 days later.

- Consistency of the outputs after Stage 1 (PMOs identification) included evaluation by comparing the list of the PMOs identified in the PMO-AP Identification form after each administration (baseline and visit 1) and calculating the number of instances and percentages in which the PMOs identified remained the same when repeating the administration of PMO-AP.
- Consistency of the output after Stage 2 of the PMO-AP process included evaluation by comparing the baseline assessment of (a) the PMOs selected and listed in the PMO-AP finalization form, (b) the indicators identified to rate them, and (c) the priority weight given by patients to each selected PMO to the data collected when repeating administration of the PMO-AP process 2–3 days later.
- Consistency of the outputs after Stage 3 of the PMO-AP process included evaluation by comparing the PMO-AP scaling forms and calculating the percentage instances in which the a-priori description of the expected changes in PMOs (i.e., PMO scaling scoring) remained the same at the two assessments.

I calculated the percentage of discord at the 95% confidence interval around the estimate of consistency for all three stages described. Finally, because I noted a discrepancy in the content of the forms of the PMO-AP at the first follow-up visit, in comparison to screening, I further

probed the participant to describe the reason for the inconsistency and kept a record of the discussion. This procedure differs from the conventional method of assessing test-retest reliability, which typically involves calculating the correlation between scores obtained during the first and second administrations of a test or questionnaire. In the case of PMO-AP, however, there are no numerical scores involved. Instead, the output after each stage of the PMO-AP process is qualitative in nature. I assessed the degree of consistency in identifying the same PMOs, indicators, ranking, and description corresponding to the modified GAS rating.

For instance, at the end of Stage 1, a list of PMOs is identified. At the conclusion of Stage 2, a final set of PMOs is determined, along with how the individual wishes to measure them and their respective levels of importance or priority. Additionally, Stage 3 involves detailed documentation of baseline status and the levels of expected change that are considered meaningful for each PMO, using the modified GAS within the PMO-AP form.

It is important to note that the numbers within the PMO-AP form are used solely as points of reference and not for calculating any scores or cumulative totals for all the PMOs. As such, there is no scoring of the PMOs at the end of Stage 3 when the PMO-AP form is generated during screening and follow-up visit 1. The test-retest reliability assessment focuses on the reproducibility of the qualitative information contained within the PMO-AP forms after each stage of the assessment process.

5.1.7.2 PMO-AP Validity determination

Kelley (1927) formulated the original concept of validity suggesting that a test is valid if it really measures what it claims to measure. Since this early formulation, researchers have refined the concept of validity from being considered as a statistical property to a process of

generating evidence (Hawkins et al., 2018). In line with the recent advances in validity theory and methodology in education and psychology, included in the study was a more comprehensive and structured approach to testing the validity evidence of the PMO-AP by assessing the meaning of the outputs generated by the PMO-AP (Messick, 1989; Zumbo, 2007, 2009). This approach reflects modern or contemporary views of measurement validation (Chan, 2014; Sawatzky et al., 2017). This perspective includes the concern with the validity of the inferences, claims, or decisions based on the ratings or the output from the assessment. In this approach, validation is the process by which one gathers and evaluates the evidence to support the appropriateness, meaningfulness, and usefulness of the decisions and inferences that can be made from the ratings or outputs from the assessment (Chan, 2014; Sawatzky et al., 2017).

This study included development of a validation plan to evaluate the validity evidence for the PMO-AP based on three sources of information. First, the content generated in the PMO scaling forms (i.e., final output after Stages 1–3) of the PMO-AP provided evidence. This process was similar to measuring content validity in the traditional view of validity. This validity can be determined by performing a thematic discourse analysis (Gee, 2014) of the patient illness narrative (i.e., the content provided by the participant in the interview transcriptions of Stages 1–3) and comparing it with their PMO scaling forms that include the final PMOs (the patient's indicators and scaling).

Second, the response processes of each participant when selecting a rating in the PMO scaling forms (Stage 3) at the second and third follow-up visits provided evidence. The process to generate this evidence of validity is built into the PMO-AP. The PMO-AP requires the administrator to ask each participant why they selected the rating and to explain the reason that

led to this selection. At follow-up visits, to better understand the response process of the study participant, I asked the participants the following probing questions:

1. What does the PMO mean to you?
2. What did you remember when you read this PMO?
3. Describe your experience in relation to the PMO since the last visit, and
4. How did you select the rating?

This discussion was part of Stage 4 of the PMO-AP (follow-up) and differed from the interaction that happens during PMO content generation, based on the illness narrative. I performed a thematic discourse analysis of the content of the narrative data from the discussions and responses provided by the study participants to the above questions during follow up. Results of this analysis included a comparison of the study participants' new ratings with the PMOs at that visit, which provided evidence of validity based on the response process of the participants (the quality of their rationale in relation to their specific disease/life experience) when selecting a rating for the PMOs at follow up.

Last, the relationship between the content of the PMO scaling forms (PMOs and indicators) and some specific corresponding items or domains of the standardized PROMs generated evidence of validity. This correspondence analysis could be assessed at baseline to correspondence between the PMOs identified and relevant items or domains from the PROMs that were used at the same time and in a dynamic way, by assessing the correspondence between the changes from baseline to visit 2 in PMOs scoring and corresponding changes in the relevant PROMs items. As the PMO-AP is individualized and participants generate PMOs covering all areas of concern due to the illness, the correspondence of each PMO includes evaluation against

multiple items from different standardized PROMs. In addition to validity evidence for the respective PMO, the process also confirms that the individual perspective cannot be captured by a single standardized PROM. Multiple PROMS (generic, disease specific etc.) should be administered, which is not ideal in a clinical practice scenario.

5.1.7.3 Ability of the PMO-AP to Generate Information for Personalized Medicine

The information collected using the PMO-AP included additional evaluation to determine whether the evaluation met the important characteristics of a truly personalized assessment as outlined in Chapter 3. Specifically, was the information generated by the PMO-AP useful for supporting personalized discussions? Three characteristics of the PMO-AP were included in the assessment for this purpose.

First, I examined whether the PMO-AP enabled patients to identify outcomes of importance. The PMO-AP should allow identification of symptoms, tasks, activities, or concerns specific to that individual and give the flexibility to choose which ones are most important to the patient. It was necessary to review all the PMOs identified and finalized by the study participants and classify the PMOs into three broad classes: *symptoms*, *QoL*, and *activities related to daily living* to check whether the PMO-AP was flexible and allowed the participants to select PMOs that covered all areas of concern and not just those limited to measuring only one domain. Also, another strategy was comparing the PMOs and responses to the standardized PROMs between individuals with the same disease to determine whether the PMOs were personalized to each individual and whether a corresponding item or domain in the standardized PROMs was also a point of concern.

Next, the PMO-AP included an assessment of whether the process could capture potential changes in outcomes identified or changes in the expectation of effects over time, as well as whether it provided an explanation of the reasons for the change. This approach required the clinician to review the information collected using the PMO-AP from the participants and list the instances in which the study participants made changes to the PMO, the indicator or the scaling at follow-up visits 2 and 3. This method was different from reliability assessment conducted between the information collected at screening and follow-up visit 1. I will collected information regarding the reason for the changes to ascertain the root cause(s), which are important in personalized discussions with patients.

Finally, the PMO-AP included an evaluation of whether the process could detect and record unexpected changes different from the PMOs and treatment-emergent at each follow-up visit and explain the reasons for the change. At each visit, it was necessary to ask the study participants whether they noticed any new events or unexpected changes. I will review the data collected at follow-up visits to check how many participants reported these unexpected events and the nature of the events. This aspect is also important in context of PM.

5.2 Results of Evaluating PMO-AP Properties

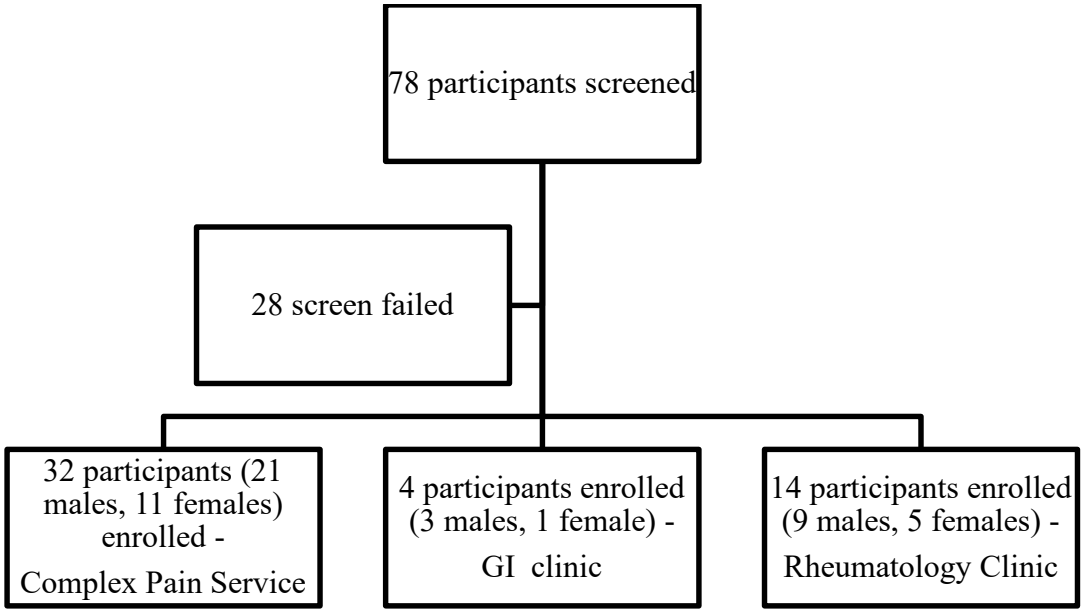
I approached a total of 78 patients who met the basic study criteria (described in Section 5.1.2) during their consultations at the three clinics. I discussed the study with each participant and their parents, or guardian, age-appropriate assent and obtained informed consent before any study-related assessments. Of these 78 patients, I could enroll 50 (64%). Of the individuals approached and assessed for eligibility, 28 (36%) did not enroll due to an inability to speak or read English (n = 5), no new treatment was being initiated (n = 12), or chose not to participate (n

= 11).

The 50 participants successfully contacted and deemed eligible included 32 from Complex Pain Clinic, four from GI Clinic, and 14 from Rheumatology Clinic. The flow of participant recruitment and retention is depicted in Figure 2.

Figure 2

Study Recruitment Flow Chart



The 50 enrolled participants generated and finalized a total of 146 PMOs. I attempted to have each participant finalize at least three PMOs at the end of Stage 3; however, four participants generated only two PMOs each.

5.2.1 Reliability of the PMO-AP

The reliability of the PMO-AP included assessment in terms of the consistency of the information obtained during the PMO-AP process performed at screening and the first follow-up visit (2–3 days later) for all 50 participants. I conducted Stages 1–3 of the PMO-AP at baseline

and repeated at the first follow-up visit. I assessed the reliability of the PMO-AP at Stage 1 in selecting PMOs. The initial list of PMOs identified in the PMO Identification Forms remained the same for all 50 participants at the end of both administrations of the PMO-AP, revealing 100% consistency from screening to the first follow-up visit (95% CI: $0.93 \leq p \leq 1.00$).

Next, I assessed the reliability of the PMO-AP at Stage 2 in selecting indicators of measurement for PMOs. Of the 50 participants, 48 (96%) kept the same PMO tracking indicators as initially selected through the end of both administrations of the PMO-AP, revealing 96% consistency from screening to the first follow-up visit (95% CI: $0.86 \leq p \leq 0.995$). Only two participants selected a different PMO at the first follow-up visit from the PMO initially selected during screening. Table 3 displays details of the PMOs that changed and the reasons.

Table 3

Participants who Changed Their PMOs

Study Participant	PMO		Reason for the Change
	Screening	Visit 1	
013	School	Swimming	Summer break started, so he changed to an activity he preferred during the break.
038	Fatigue	Eat regular meals	This was more important to the participant. She felt she would have more energy if she was able to eat regular food.

Among the 48 participants who kept the same PMO, 44 (92%) also kept the same indicator chosen during screening to measure changes, revealing 92% consistency from screening to the first follow-up visit (95% CI: $0.80 \leq p \leq 0.98$). For the four participants who changed tracking indicators, details and rationale for the changes are provided in Table 4. Further, analysis of the interview transcripts from the screening and first follow-up visit revealed that the

study participants provided sound reasons for their changes that justified their choices.

Table 4

Participants who Changed Their PMO Indicator

Participant	PMO	Indicator		Reason
		Screening	Visit 1	
004	Daily Activity	Help in the kitchen	Perform chores at home	Participant felt the indicator identified during the screening was too specific and wanted to keep it generic.
015	Regulated sleep	Sleep duration (hours)	Awake refreshed	Participant felt it was more important to wake up refreshed and energetic after sleep than to count the hours of sleep.
032	Physical activity	Attend PE class	Ride a bike	Participant liked riding a bike more than PE class and wanted to be able to do something fun if the treatment worked.
037	Energy level	Attend full PE class	Reduce fatigue after school	Participant wanted to choose an indicator that she can measure daily.

Of the 48 participants who kept the same PMOs, 40 (83%) did not change the ranking of the PMO, revealing 83% consistency from screening to the first follow-up visit (95% CI: $0.70 \leq p \leq 0.925$). Furthermore, although the weight given to the outcomes may have changed from screening to the first follow-up visit, the outcome with highest ranking remained the same for all subjects (distributing the sum of 10, over the three outcomes). Table 5 shows an example of the change in weighting for one participant.

Table 5

Participants who Changed the Weight of Their PMO

Participant	PMO	Weight	
		Screening	Visit 1

003	#1 Improved physical activity	3	3
	#2 Improved school attendance	5	4
	#3 Improved sleep	2	3
	Total Weight (1 + 2 + 3)	10	10

Finally, I assessed the reliability of the PMO-AP with respect to the different levels of expected change using modified GAS rating at Stage 3. Of the 44 participants who kept their initial PMOs and indicators of measurement from screening to the first follow-up visit, 39 participants also kept the same scaling measurement, revealing 89% consistency from screening to the first follow-up visit (95% CI: $0.75 \leq p \leq 0.96$). I conducted the scaling of the PMOs using the SMART goal approach to improve precision and validity in this context. Among the five subjects who changed scaling, four changed the time for measuring the PMO. For example, Participant 019 changed the scaling of the number of yoga sessions he could attend from weekly to monthly. The fifth subject (Participant 043) changed his scaling of the PMO to be more realistic in his opinion. His PMO was "not to be handicapped at school due to migraine headaches." His initial indicator was measured by the number of days in a week he did not have to use the spare class at school as a refuge. During the screening, his target indicator for meaningful change was "not needing to use the spare class at all." He changed this during the first follow-up visit to "using the spare class only 2 days in a week," which he believed to be more realistic.

Overall, the process of administering PMO-AP revealed a high percentage of consistency, indicating evidence of test-retest reliability. Furthermore, for any change observed, there was a good rationale for the change of personal preferences or context. This process is

further described in section 5.2.3 because the information generated prompted meaningful personal discussions with the patient.

5.2.2 Evidence of Validity

Evidence of content validity was based on my analysis of the interview transcripts of all 50 participants in Stages 1, 2 and 3 of the PMO-AP assessment and comparison with the PMO finalization and scaling forms of the participants. I transcribed and analyzed participants' interviews at each stage to identify the discourse topics that the participants believed were anaphorically related and thematically relevant to the prompts and provided the basis of discourse coherence through their utterances (Gee, 2014). This analysis built on Mattingly and Garro's (2001a) observation that storytellers select episodic information to contribute to the coherent development of their narrative. Because this was an idiographic study, each individual's statements were intended to represent their own personal experience; therefore, a comparison of themes across participants was irrelevant.

In Stage 1, the study participants provided their illness narratives and identified a list of PMOs. In Stage 2, the study participant finalized the PMOs they would like to be tracked and how to measure them. The interview transcripts from Stages 1 and 2 of the PMO-AP enabled me to confirm that all PMOs finalized by the study participants and the indicators were consistent with the narrative provided by the study participants. This approach provided evidence of content validity for both PMOs, and indicators generated by the PMO-AP. An assumption underlying this approach, in context of PM, is that the patient is the expert to know their most relevant concerns. The PMO-AP, through the interview with the patient, enables the clinician to accurately capture the patient perspective during the development of the PMO.

In Stage 3 (scaling), for each finalized PMO, the study participants mentioned their status of the PMO (i.e., baseline level) and how much they wanted it to change to be meaningful. The qualitative review of the interview transcripts of Stage 3 confirmed the details in the PMO scaling forms for the study participants' baseline status and proactively defining the target expected change for that PMO. I conducted the goal attainment scaling to define what would be more than or less than the expected change (refer to Table 1) later through a dialogue with the study participants using the steps outlined as per the GAS technique.

Interview transcripts and the final output of the PMO-AP of two of the participants provide insight into reasons study participants may have made changes from their choices in the initial screening. In Stage 2, Participant 003 described,

> I am unable to attend school because of my condition. I frequently skip school when the pain is too much. I just stay home and lie down. I want to go to school and be with my friends. I do not like that I miss many classes. I want this treatment to help me manage my pain and not have the severe episodes.

In Stage 3, Participant 003 noted, "Due to my frequent pain episodes, I almost skip half a month of classes. I would like to go to school at least 3 days in a week." Table 6 shows an illustration of the Participant 003's achievement for PMO#2.

Table 6

Participant 003 PMO#2: Improve School Attendance

PMO Achievement	Expected Level of Change in PMO	Rating
Baseline	50% attendance at school in a month	0
Expected Outcome (Target)	60% attendance at school in a month	3

Note. The indicator was measured by the percentage of the number of days the participant attended school.

In Stage 2, Participant 013 shared, *"Yes, I want to do some physical activity. Maybe start with something simple like walking*." In Stage 3, Participant 013 reported as follows (see Table 7):

> Due to pain and stiffness in my legs I cannot walk now and would love to be able to walk. I want to measure my ability to walk. It would be the best if I can walk an hour everyday which is highly unlikely. Maybe let's aim for 40 min in the next couple of months.

Table 7

Participant 013 PMO#1: Improve Physical Activity

PMO Achievement	Expected Level of Change in PMO	Rating
Baseline	Do not go walking at all	0
Expected Outcome (Target)	36–40 min of walking per day	3

Note. The indicator was measured by the duration of walking.

The above examples show evidence of content validity built into the process of the PMO-AP. Each individual study participant constructed their PMOs, indicator, baseline, and expected change. Evidence of validity was also demonstrated by evaluating the underlying response processes of the participant when selecting a rating during follow up visits 2, 3, and study exit. Content analysis of the interview transcripts from the discussions with all study participants during the follow up visits confirmed that the interpretation of changes in the PMO indicators by the study participants matched with the scoring they selected in the PMO Scaling forms as part of Stage 4 of the PMO-AP. Below is narrative data of two study participants who explained why

they selected a particular rating for the PMO at follow up. Participant 008 noted as follows (see Table 8):

> I reached my expected change for this outcome. I feel much better now and able to do more stuff. I did not like that I was not able to hang out with my friends before. Now I go out with them almost every week. I select the rating of 3 as it is in line with the expected level of change column.

Table 8

Participant 008 PMO#1: Increase Social Activity

PMO Achievement	Expected Level of Change in PMO	Rating
Expected Outcome (Target)	Go out with friends 3–4 times in a month.	3

Participant 035 reported as follows (see Table 9):

> I almost do not have any pain in my knees after playing basketball. Before my knees hurt all the time and I couldn't play. I still have pain sometimes. I think I am doing better than what I was expecting. That's why I selected 4. Also, now I play almost every alternated day.

Table 9

Participant 035 Outcome of PMO#1: Reduce Knee Pain

PMO Achievement	Expected Level of Change in PMO	Rating
Slightly better than Expected Outcome	Knee pain 25–50% of the time after basketball game in a week.	4

Note. The indicator was measured by the percent of time the participant experienced no pain after playing basketball.

I measured evidence of convergent validity by examining the correspondence between

the PMOs and their indicators, against some items or domains of the standardized PROMs. All 146 PMOs identified corresponded to either a domain or a specific item in the standardized PROMs. The scoring for the corresponding PROMs' specific item or domain at screening visit was also low, showing that the study participants were performing poorly or not doing well.

Last, the change in PMO rating at study exit visit included additional comparison against the extent/direction of changes in score for the relevant item or domain in the standardized PROM. Change in rating was reported in 70% of PMOs (i.e., participants selected a rating that ranged between 1 = *the change is positive, but much less than expected outcome* to 5 = *the rating is much better than expected outcome*). I also observed that 30% of participants selected a rating of 0 = *the score was identical to baseline or worse than baseline* at follow-up.

The 32 participants who reported a change in rating of PMOs also showed a change in the same direction of the corresponding item(s) or domain in standardized PROMs. Eighteen participants who did not change their PMO rating selected scores that reflected a change in the opposite direction of corresponding items or domains in standardized PROMs, which confirmed worsening or negative outcomes. Two examples of PMOs and corresponding items/domains in standardized PROMS that measure the same construct, as well as their scores, are shown in Tables 10–12. In the example provided in Tables 10–11, the PMO corresponded with items in two standardized PROMs. The scores of the standardized PROMs at screening confirmed that the study participant had problems with sleeping, which he selected as a PMO (see Table 10).

Table 10

Participant 004: PMO#1 Domain Scores at Screening and Exit

PROM	Domain/Item	Score at Screening	Score at Exit
Functional disability inventory	Getting to sleep at night and staying asleep	3–A lot of trouble	2–Some trouble
PedsQoL	I have trouble sleeping	4–Almost always	2–Sometimes

At follow up, the participant selected a rating of 2 for the PMO, confirming that the outcome did not change to his expectations (see Table 11). The participant reported similar scores in the standardized PROMs, indicating the persistence of some sleep problems.

Table 11

Participant 004: Outcome of PMO#1

PMO #1	PMO Achievement	Expected Level of Change	Rating
Better quality of sleep	Slightly worse than expected outcome	Feel fresh only 3–4 days per week	2

Note. The indicator was measured by how fresh (vs. tired and weak) the participant felt after awakening.

In the example provided in Tables 12–13, the PMO corresponded with an item in the Functional Disability Inventory that received a score of 3 (a lot of trouble), confirming it as an area of concern (see Table 12).

Table 12

Participant 009: PMO#1 Domain Score at Screening and Exit

PROM	Domain/Item	Score at Screening	Score at Exit
Functional disability inventory	Eating regular meals	3–A lot of trouble	4=–Impossible

At follow up, the patient gave a rating of 0 for the PMO, indicating there was no positive change (see Table 13). The corresponding score in the FDI was worse than at screening time, which confirmed some deterioration of the clinical situation.

Table 13

Participant 009: Example of PMO With No Change or Worse Than Baseline

PMO #1	PMO Achievement	Expected Level of Change	Rating
Improve appetite	Baseline	I do not eat a normal amount of food and always feel sick after	0

5.2.3 Ability of PMO-AP to Generate Information for Personalized Medicine

The PMO-AP was developed as a patient-centric approach for gathering patient's input, initiating highly relevant discussions, and performing a holistic evaluation of treatment effect in clinical practice. As noted in Chapter 3, the characteristics of PMO-AP are as follows:

- PMO-AP should allow the study participant to select any outcome that they consider as important, relevant, and personalized to their situation.
- PMO-AP should be flexible and allow the participant to change the outcomes as priorities change in relation to external factors at follow up.
- PMO-AP should facilitate the communication between the clinician and the patient by establishing a partnership that leads to setting up a-priori expectation of change and recording the rationale when selecting a rating or making changes to the PMO or expected changes.

The PMOs identified by the study participants were specific for each individual given their social context and illness narrative. Of the 146 PMOs, 15 (10%) were related to disease

symptoms (i.e., pain, diarrhea, etc.), 44 (30%) were related to activities of daily living (sleep, eating, etc.) and 87 (60%) related to QoL. PMOs under QoL could be further classified into the following domains: 30 (20%) were related to physical activity (running, playing sports etc.), 26 (18%) were related to emotion/mood/behavior, 17 (12%) were related to functioning at school, and 14 (10%) were related to social interactions.

When comparing PMOs of participants with the same diseases, the notes indicated that all were unique to each individual participant and very personal. In patients from the Complex Pain Clinic, there was some overlap in the PMOs identified by some participants; however, the indicators chosen by the participant to measure the PMO, and the scaling were unique to each individual with no overlap. Below are some examples of the above analysis.

5.2.3.1 GI Clinic – Participants with IBD

Two examples of the PMOs identified by the participants from the GI clinic are presented in Tables 14 and 15. Results show that both participants suffer from the same illness or condition (i.e., IBD), but the PMOs were unique to each individual. Participant 10 wanted to be physically active (activities of daily living, QoL) and improve his appetite (activities of daily living; see Table 14).

Table 14

PMO for Participant 010

PMO Achievement	Expected Level of Change	Rating
	PMO#1: Be Physically Active	
Baseline	I do not play soccer now.	0
Much less than expected	Play soccer at least once in a week.	1

Slightly worse than expected	Play soccer only 2 times in a week.	2
Expected outcome	Play soccer 3 times in a week.	3
Slightly better than expected	Play soccer 4 times in a week.	4
Much more than expected	Play soccer 5 times in a week.	5
	PMO#2: Improve Appetite	
Baseline	I drink one or two bottles of calorie drink in a day.	0
Much less than expected	Drink three bottles of calorie drink in a day.	1
Slightly worse than expected	Drink four bottles of calorie drink in a day.	2
Expected outcome	Drink five bottles of calorie drink in a day.	3
Slightly better than expected	Drink six bottles of calorie drink in a day.	4
Much more than expected	Drink seven or eight bottles of calorie drink in a day.	5

Participant #17, also a participant from the GI clinic who suffers from the same illness or condition as (i.e., IBD) as Participant 10 selected stomach pain (symptom) as the first PMO. Also important to this participant was not looking skinny (QoL), which was the second PMO he selected (see Table 15).

Table 15

PMO for Participant 017

PMO Achievement	Expected Level of Change	Rating
	PMO#1: Stomach Pain	
Baseline	Stomach pains every day.	0
Much less than expected	1–2 pain-free days per week.	1

Slightly worse than expected	3–4 pain-free days per week.	2
Expected outcome	5 pain-free days per week.	3
Slightly better than expected	6 pain-free days per week.	4
Much more than expected	7 pain-free days per week.	5
	PMO#2: Not Look Skinny (Gain Weight)	
Baseline	Current weight is 29 kilograms.	0
Much less than expected	Gain 1 kilogram per month.	1
Slightly worse than expected	Gain 2 kilograms per month.	2
Expected outcome	Gain 3 kilograms per month.	3
Slightly better than expected	Gain 4 kilograms per month.	4
Much more than expected	Gain 5 kilograms per month.	5

5.2.3.2 Rheumatology Clinic – Participants with JIA:

Two examples of the PMOs identified by participants from the Rheumatology Clinic are displayed in Tables 17 and 18. Both participants suffer with JIA. Both participants generated PMOs that impact their QoL or activities of daily living unique to their context and priorities.

Participant #23 wanted to be more socially active (QoL) and chose this as PMO#1. Additionally, Participant #23 wanted to participate in an outdoor activity (activity of daily living) and chose this as PMO#2. Table 16 displays the measurement criteria for both PMOs.

Table 16

PMO for Participant 023

PMO Achievement	Expected Level of Change	Rating
	PMO#1: Improve Social Activity	
Baseline	Does not hang out with friends.	0
Much less than expected	Hang out with friends 1 day a week.	1
Slightly worse than expected	Hang out with friends 2 days a week.	2

Expected outcome	Hang out with friends 3 days a week.	3
Slightly better than expected	Hang out with friends 4 days a week.	4
Much more than expected	Hang out with friends more than 4 days a week.	5
	PMO#2: Participate in Outdoor Sport	
Baseline	Does not swim due to join pain.	0
Much less than expected	Take one class in a month.	1
Slightly worse than expected	Take two classes in a month.	2
Expected outcome	Take three classes in a month.	3
Slightly better than expected	Take four classes in a month.	4
Much more than expected	Take more than four classes in a month.	5

The PMOs selected by Participant #20, also from the Rheumatology Clinic and suffering with JIA, illustrated different priorities. Specifically, Participant #29 did not want to wake up with stiff muscles that caused delays in getting to school. This participant chose going to school on time (symptom related to activity of daily living) as PMO#1 and walking outdoors (activity of daily living, QoL) as PMO#2 (see Table 17).

Table 17

PMO for Participant 029

PMO Achievement	Expected Level of Change	Rating
	PMO#1: Reduce stiff muscles/Go to school on time	
Baseline	Go to school on time 1–2 days a week.	0
Much less than expected	Go to school on time 3 days a week.	1
Slightly worse than expected	Go to school on time 4 days a week.	2
Expected outcome	Go to school on time 5 days a week.	3
Slightly better than expected	NA	4
Much more than expected	NA	5

	PMO#2: Walk outdoors	
Baseline	Walk once in a month.	0
Much less than expected	Walk two times in a month in a month.	1
Slightly worse than expected	Walk three times in a month in a month.	2
Expected outcome	Walk four times in a month or once every week.	3
Slightly better than expected	Walk five to six times in a month.	4
Much more than expected	Walk twice in a week or eight times in a month	5

5.2.3.3 Complex Pain Clinic:

Below I present two examples of participants from the complex pain clinic. The PMOs identified were related to their QoL and activities of daily living. Specifically, Participant #5 chose three PMOs; the first one was to have a better quality of sleep (QoL). PMO #2 was to be more active (activity of daily living), and PMO#3 was to reduce stress (QoL; see Table 18).

Table 18

PMO for Participant 005

PMO Achievement	Expected Level of Change	Rating
	PMO#1: Improve quality of sleep	
Baseline	Feel refreshed only 1 day in a week.	0
Much less than expected	Feel refreshed 2 days in a week.	1
Slightly worse than expected	Feel refreshed 3–4 days in a week.	2
Expected outcome	Feel refreshed during all weekdays.	3
Slightly better than expected	Feel refreshed 6 days in a week.	4
Much more than expected	Feel refreshed all days in a week.	5
	PMO#2: Be more active	
Baseline	Feel tired/have pain after every game.	0
Much less than expected	Feel tired/have pain 30% of the time monthly after the game.	1

Slightly worse than expected	Feel tired/have pain 31–49% of the time monthly after the game.	2
Expected outcome	Feel tired/have pain 50% of the time monthly after the game.	3
Slightly better than expected	Feel tired/have pain 51–75% of the time monthly after the game.	4
Much more than expected	Feel tired/have pain 76–100% of the time monthly after the game.	5
	PMO#3: Reduce Stress	
Baseline	Finish homework 0 days a week before dinner.	0
Much less than expected	Finish homework 1 day a week before dinner.	1
Slightly worse than expected	Finish homework 2 days a week before dinner.	2
Expected outcome	Finish homework 3 days a week before dinner.	3
Slightly better than expected	Finish homework 4–5 days a week before dinner.	4
Much more than expected	Finish homework every day before dinner.	5

Participant #1 wanted to participate in daily activity (activity of daily living), be socially active (QoL), and improve sleep quality (QoL) during flare-ups. Like Participant #5, sleep was a PMO; however, Participant #1 wanted to improve sleep duration (see Table 19).

Table 19

PMO for Participant 001

PMO Achievement	Expected Level of Change	Rating
	PMO#1: Participate in daily activity during a flare up	
Baseline	Do nothing at all during a flare.	0
Much less than expected	Do household work 1%–30% of the time during a flare.	1
Slightly worse than expected	Do household work 31%–60% of the time during a flare.	2
Expected outcome	Do household work 61%–70% of the time during a flare.	3
Slightly better than expected	Do household work 71%–90% of the time during a flare.	4
Much more than expected	Do household work 91%–100% of the time during a flare.	5

	PMO#2: Be socially active during a flare up	
Baseline	Do not go out of the house at all during a flare.	0
Much less than expected	Go out 1%–30% of the time during a flare.	1
Slightly worse than expected	Go out 31%–60% of the time during a flare.	2
Expected outcome	Go out 61%–70% of the time during a flare.	3
Slightly better than expected	Go out 71%–80% of the time during a flare.	4
Much more than expected	Go out 91%–1000% of the time during a flare.	5
	PMO#3: Improve sleep quality during a flare	
Baseline	Sleep only 1–2 hours a day during a flare.	0
Much less than expected	Sleep 3–4 hours a day during a flare.	1
Slightly worse than expected	Sleep 4–6 hours a day during a flare.	2
Expected outcome	Sleep 6–7 hours a day during a flare.	3
Slightly better than expected	Sleep 7–8 hours a day during a flare.	4
Much more than expected	Sleep more than 8 hours a day during a flare.	5

Of the 50 study participants, four participants decided to select a different PMO at follow-up visit 2, and one study participant decided to select a different PMO at follow-up visit 3 (see Table 20). Two study participants who kept the same PMO decided to use a different indicator to measure their PMO at follow-up visit 2 (see Table 20). Three study participants revised the scaling of the PMOs at follow-up visit 2, and one study participant revised the scaling of the PMOs at follow-up visit 3.

These changes confirm that the PMO-AP is flexible, allowing study participants to modify their PMO, indicators, and/or scaling to suit their personal goals, which may change over time. These changes are different from the results on reliability of the PMO-AP presented in Section 5.2.1, which was conducted by comparing information between the screening and visit 1 within a period of 2–3 days. The time interval between visit 2 and 3 was 30 days.

Table 20

Example of PMO or Indicator Changes from Screening to Follow Up

Participant ID #	PMO		Indicator	
	Screening	Follow Up	Screening	Follow Up
029	Walking outdoors	Climb steps unassisted	Number of days per month	Number of days per week
043	Regulated sleep	Increase social activity	Number of times per month	Number of times per month
015	Physical activity	Physical activity	Days of attending PE per month	Days of riding a bike per week

The PMO-AP also documented that these changes were not made randomly but resulted from specific reasons captured through a methodical dialogical process part of the PMO-AP. Good justifications of the changes provided useful material for developing interesting and personalized discussions. The justifications may also be used to establish the validity of PMO-AP to identify, in a dynamic way, what is most important for the individual.

In the follow-up, Participant 029 explained, "I am not able to walk outdoors as it is raining and want to choose something more appropriate." Participant 015 clarified, "School is closed for summer holidays so no PE class, but I like to ride my bike and not have too much pain." Participant 043 described,

> Sleep is not completely better but I would like my pain meds to allow me to be more socially active like attend friend's birthdays and play with them or go to a park with friends. This is more important to me.

Finally, at each follow up visit, I asked the study participants if they noticed any new events or unexpected changes. Two study participants reported unexpected events at follow up visit recorded in the PMO Follow up form. The identification of unexpected events is another

useful material to initiate personalized discussion with the patient; it is useful for the practice of PM in clinical practice.

5.3 Discussion

My experience on the TIDE-BC project highlighted the major limitation of only using standardized outcome measures in an n-of-1 context. There is a need to include the goals and priorities of the individual patient when conducting a comprehensive assessment of treatment evaluation in clinical practice. Evaluating the treatment effect in chronic conditions solely using a standard set of outcomes when a high variability exists in clinical expression and differing treatment goals among patients is challenging. Therefore, an assessment that can be tailored is needed to measure what an individual patient wants, which would account for the heterogeneity and can be used as a complementary approach to conventional outcomes to assess whether (and to which degree) the treatment may improve specific elements or aspects of the patients' lives—above and beyond the classic standard core set of outcomes.

The thesis project's objective was to develop a holistic individualized idiographic assessment method that facilitates the identification of personally meaningful outcomes and a-priori describe the expectation of change that would be considered meaningful. The PMO-AP extends the concept of PM from a purely biomedical framework by and combining it with personally meaningful outcomes generated by the individual patient, to create a truly patient oriented and personalized assessment.

The concept of PMO-AP originated from n-of-1 studies conducted within a research context. The impetus for its development in clinical practice came from valuable feedback received from clinicians across various clinics at BC Children's Hospital when the results of the

TIDE-BC n-of-1 studies were presented during pediatric research rounds. These clinicians recognized that the challenges addressed by PMO-AP were not unique to biochemical diseases but were applicable to any chronic disease patient characterized by significant heterogeneity in clinical practice. In fact, heterogeneity exists whatever the condition as each patient lives in specific environment with unique culture, values and priorities. The disease does not make the PMO but rather PMOs are generated in the context of disease or treatment and reflect the uniqueness of the patient.

Much like n-of-1 studies, where the primary objective is to assess treatment benefit for an individual patient, clinical practice also aims to provide the right treatment to the patient seeking care during a consultation. PMO-AP emerged as an assessment to support this goal, bridging the gap between research-driven n-of-1 studies and the practical application of PCM within clinical practice.

The PMO-AP included development to be used at an individual level across different chronic diseases and various settings. The PMO-AP's applicability was demonstrated by its use among adolescent patients attending three different clinics at BCCH: 32 (64%) of the enrolled participants were from chronic pain clinic, four (8 %) from the gastroenterology division, and 14 (28%) from the pediatric rheumatology clinic. The participants were required to start a new treatment at screening visit to administer the PMO-AP. Most of the patients seen in the Gastroenterology and Rheumatology clinic were already on treatment during the study enrollment period. The CPS clinic had an intake of 1–2 new cases every week, which is the reason for the high enrollment in this study. Due to the interactive design of the PMO-AP, the study participants needed to be old enough (12–18 year) for reliable self-reporting. Selection

included this age group based on recommendations outlined in the report of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) good research practices for the assessment of children and adolescents task force to obtain valid self-reported data (Matza et al., 2013).

The participants completed all standardized PROMs used in the study via self-report. The PMO-AP administration used an interview format and the person conducting the interview completed the forms. In a clinical setting, the PMO-AP would be conducted by the clinician who could engage in a dialogue directly with the patient or the caregiver. The PMOs generated are reported by the patient or, as proxy-report, by the caregiver; in this study evaluations included only the self-report by the participants.

This exploratory study included an evaluation of the reliability and validity of the PMO-AP, as well as its ability to generate useful information to be used in context of a patient-centered form of PM. Evaluation of the information collected using the PMO-AP confirmed that the assessment met the characteristics of a truly personalized assessment. The study results showed that the PMO-AP enables generating the PMOs, selecting the indicators to measure them, and a-priori determining the expected changes in a reliable way. The results also confirmed that the information generated using the PMO-AP and the process of establishing validity are built into the way the assessment is administered. Furthermore, its key characteristic of requiring a dialogue between the patient and the clinician throughout all stages of the PMO-AP resulted in useful information to understand PMO selection, rating, and any changes made during follow up. Also, this collaborative discussion ensured that the selected outcomes are pertinent to the specific condition for which the treatment is being administered.

Reliability of the PMO-AP included measurement in this study by assessing the reliability in terms of consistency of the PMO-AP's outputs at various stages when administered twice within an interval of 2–3 days. One hundred percent of the PMOs identified by participants in the PMO identification forms remained the same during both screening and follow-up visit 1. Regarding the selection of PMOs, two participants changed their selection at follow-up visit 1. The participants provided a strong rationale for a change made in comparison to screening visit, which confirmed that the changes were not random but reflected a more appropriate choice from the participants' point of view. This change in PMO selection affected the reliability but through the dialogical process built into the PMO-AP, the context and reasoning behind these changes were captured, offering elements of validation for the new response and promoting personalized dialogue. Only the changes of ranking or weighting PMOs could be made because the participants had to distribute the sum of 10 over the selected PMOs. However, even though there was a change in values, the order of PMOs' importance did not change. As shown in Table 5 for Participant #3, improved school attendance was the most important PMO at both visits even though the weight given at screening was 5 and became 4 at follow-up visit 1. The consistency in the information obtained through the test-retest results confirmed that the information obtained using the process outlined for Stages 1–3 of the PMO-AP is reliable.

Reliability is a major concern in the development of an assessment. Test-retest reliability for PGI included measurement using the Pearson correlation coefficient (Klokkerud et al., 2013; Lochting et al., 2014; Tully & Cantrill, 2002). I assessed reliability in patients who reported no change in their health status at second administration. Reliability (test-retest and internal consistency) was not reported for MYMOP (Ruta & Garratt, 1996). Internal consistency and test-

retest reliabilities have been reported using Cronbach's alpha for COPM across several indications, age groups, and formats of administration (Berardi et al., 2019). An important distinction to note between the PMO-AP and all individualized and standardized PROMs is that they employed a questionnaire format where the participant selected a score indicating their personal status relating to the items in the questionnaire.

For example, in MYMOP, the participant selects a score on a scale of 0 to 6 (0 = *as good as it can be*; 6 = *as bad as it can be*). This scoring takes place every time the MYMOP is administered, including the first time when the participant generates the symptom or activity that bothers them the most due to their condition, which provides a baseline status in terms of a score related to the items in the MYMOP. The score obtained at the second administration (re-test) is used to calculate the reliability coefficient.

Conversely, the PMO-AP does not use a questionnaire. For the scoring of each PMO, a modified GAS approach is undertaken. The rating is always 0 at both administrations when testing reliability as the baseline is always rated 0. Therefore, in this study, reliability included evaluation using consistency in the outputs of the three stages of the PMO-AP. Test-retest reliability of the COPM was different from that of other individualized PROMs.

In a study involving stroke patients, COPM interviews were administered twice with a mean interval of 8 days. On both occasions, the patient identified a maximum of five problems in daily activities and gave a scoring for performance and satisfaction rating scales for those problems. The problems identified in both interviews were compared in terms of percentage consistency and correlation coefficient for the scores. Of the 115 problems identified during the first COPM, 64 (56%) were also identified 1 week later. Correlation coefficients for the scores

were 0.89 ($p < 0.001$) for performance and 0.88 ($p < 0.001$) for satisfaction (Cup et al., 2003). When compared to COPM, the PMO-AP has a higher percentage of consistency.

Establishing validity of the PMO-AP was informed by contemporary views of validation instead of traditional statistical techniques. In conceptualizing the validation process, the Standards outlines five sources of validity evidence (American Educational Research Association et al., 2014). In this study, I showed evidence of validity of PMO-AP from three sources: (a) content validity, (b) validity based on underlying response process when selecting a rating and interpretating changes in the PMO at follow up, and (c) convergent-relationship between the content of the PMOs with some items or domains of the standardized PROMs, as per the validation plan. For all individualized and standardized PROMs, I ensured content validity by conducting in-depth interviews with patients who completed the instruments. Additionally, I conducted content analysis of the outcomes generated using PGI, COPM and MYMOP through evaluating the interview transcripts (Chung et al., 2010; Cup et al., 2003; Tavernier et al., 2011).

For the PMO-AP, I ensured content and response validity through the dialogical interaction between the patient, as I served as the substitute clinician for the research project, beginning with the initial phenomenologically oriented semistructured interview at screening visit and including interviews after every follow-up visit. For the qualitative methodology, one must generate and confirm that evidence of validity is already integrated into the way PMOs are identified, constructed, and scaled including the underlying response process of the participant when selecting a rating at follow-up. This qualitative approach allowed me to investigate hypotheses about the PMO-AP that were atypical for a traditional psychometric validity analysis,

but which still reflected the constructs of the outcome measurement method. Reviewing the in-depth interviews done during Stages 1–3 of the PMO-AP to generate the PMO-AP scaling form and its subsequent scoring in Stage 4 during follow up, I gained an increased appreciation of how the PMOs were understood and generated by patients and the response process employed by the participants to interpret the change in the PMO when scoring them at follow-up, which would not have been possible by statistical methods.

The PMO-AP also showed good convergent validity when compared with relevant items or domains of standardized PROMs. All PMOs identified corresponded to an item, or a domain being measured by the standardized PROMs in which the study participants also gave a low score or identified them as an area of concern. In a study of stroke patients evaluating validity of COPM, of the individual problems identified with the COPM, 25% or less were present in the standardized measures. Correlations between the scores on the COPM and the standardized measures were low and nonsignificant (Cup et al., 2003).

In this study, convergence included additional evaluation during the follow up by checking the changes in the PMOs ratings and the scores for the corresponding PROM's items or domains. A worsening of the situation could not be captured for the PMOs due to the modified GAS scoring system, which included a score of "0" for no change and worsening of PMO as follows:

1. The dialogic approach and follow-up requiring the participant to provide context for the ratings provided details and rationale as to why the study participant gave a particular rating for the PMO at follow up.

2. This process also showcases the validity of the information from the PMO-AP regarding changes at follow up.

There is evidence of correspondence, as the standardized PROMs capture the areas of concern for the individual study participant. However, each study participant had to complete multiple standardized PROMs to adequately cover all areas of concern for them. This outcome would be challenging in standard clinical practice because each individual patient is different and the clinician would have to first identify all the right PROMs that would cover all areas of concern, and the budget required to pay for licensing those PROMs. This outcome represents as one clear advantage of using the PMO-AP.

In addition to reliability and validity of the information obtained using the PMO-AP, I checked whether the PMO-AP met the characteristics of a truly personalized assessment to be used in the context of holistic PM. One strength of the PMO-AP is its ability to collect information that is individualized and personalized. Compared to standardized PROs, PMO-AP's unique ability to capture personal information is clear when considering the goals of different study participants with the same illness. Using the PMO-AP, I identified different PMOs even though they could be classified under the same broad diagnosis category.

PMO-AP also gives the flexibility to change the PMOs at follow-up rather than requiring patients to respond to the initial, possibly irrelevant outcome finalized at the screening visit. Most importantly, any change gives the clinician an opportunity to discuss with the study patient the reasons for the changes. The PMO-AP provides the context for more in-depth and relevant discussion regarding what counts most for the individual patient.

Last, the ability to detect any unexpected events not related to the PMOs provides the clinician an opportunity to discuss with the patients any new occurrences and their consequences. The most important aspect of the PMO-AP is the ability to allow for a structured dialogue between the clinician and patient, not only during the initial PMO selection but also during the follow-up that explores the patient's reasons for any changes.

This study has several limitations. The first limitation is that the administration of the PMO-AP was to all participants by me, rather than by a clinician or a nurse who would have administered the PMO-AP in a natural clinical setting. The PMO-AP included development to be used by any clinician to evaluate the treatment effect from the patient visiting the clinic. As a non-clinician, I could not use the participant's information for making treatment decisions, which would have created other bonds between the patient and clinician. Further, I have reported my experience with the PMO-AP and do not know how this would differ from a clinician's experience using the PMO-AP. This outcome will have to be evaluated in future studies.

The PMO-AP should also be evaluated in other settings such as primary care or family practice clinics. Further evaluation should also take place in adults, or in younger patients for whom patients or other caregivers would serve as proxies to report the PMOs. However, the objective of the PMO-AP is to measure outcomes that matter most to the patient, therefore proxy reporting may measure a different construct (i.e., outcomes that matter most in the opinion of the caregiver).

The second use of the PMO-AP to assess reliability took place only 2–3 days after the first assessment, which is on the shorter side of possible time gaps. This short delay included selection because there was a new treatment to start, and it was not acceptable to ask patients

waiting for longer time. This re-test process after a short delay may have increased the reliability results.

Inter-rater reliability should be measured considering that different clinicians may administer the PMO-AP on the same individual patient at different times. I did not measure internal consistency reliability in this study because the PMO-AP does not use multiple items to measure a single construct or domain. Sources of validity evidence using test internal structure were not relevant for the same reason as the PMO-AP is not a multi-item questionnaire measuring a domain of interest.

Complete elimination of selection bias could not be guaranteed primarily because the study criteria necessitated the judgment and approval of the treating physician before approaching potential participants to gauge their interest in participating in the study. In many instances, exclusion from the study was a consequence of the patients' severe illness, rendering them unable to participate effectively. Additionally, language proficiency was a factor leading to exclusion, as some individuals did not speak English fluently. Furthermore, it is worth noting that a majority of the participants in the study were male. In future studies, it is imperative to consider and assess PMO-AP in the context of these scenarios. This approach will help ensure a more comprehensive understanding of PMO-AP's applicability and effectiveness across various patient profiles, including those with severe conditions, language barriers, and diverse demographics.

Finally, the assessment did not include sensitivity to change, as that would have required a different design and populations. The observations, however, were that PMO-related scoring changed in the same direction as the specific items or domains of the standardized PROMs. If

assumptions included that the change of one or a few items in a PROM scale will likely be diluted by the absence of changes in a larger number of other items, one could anticipate that PMO-related changes in scoring, as reported by patient, is likely more sensitive than the changes observed in the score of standardized scale. In the study, the total duration of follow-up for the PMOs was 3 months with a monthly check-in on the status. I selected this period to collect at least three datapoints on the status of each PMO to get a preliminary understanding on the sensitivity of the PMOs to change in response to the treatment. The duration of follow-up was also dependent on the pharmacokinetic and pharmacodynamic profile of the treatment. In practice, the clinician and the individual patient determine the follow-up duration for the PMOs based on their specific treatment. This was another benefit of the discussion required as part of the PMO-AP, especially when describing the expected levels of meaningful change using the SMART approach, which includes specifying the time of follow-up for the PMO. The follow-up was for each specific PMO and not same for all PMOs selected by the patient.

I did not evaluate the evidence of validity of intended and unintended consequences of using PMO-AP in this study, as the PMO-AP was administered by me, and no other clinician made treatment-related decisions based on the information from the PMO scoring at follow-up. Anecdotal evidence from a physician in Biochemical Diseases Division at BC Children's Hospital who used PMO-AP in clinical practice to measure treatment effect in a patient with creatine transporter deficiency, however, confirmed that the PMO-AP was helpful in making better clinical decisions. She reported that the patient appreciated the use of the PMO-AP with the ability to provide a platform to include the patient's voice when measuring treatment response. The intended consequence of using the PMO-AP was to help identify the outcomes

that mattered most to the patient. This outcome is especially important for patients with a rare disease such as creatine transporter deficiency where there are no standard outcomes or assessments except for clinical biomarkers like creatine level. In this specific case, the unintended consequences of the PMO-AP were in improving the patient's treatment compliance and tracking of PMOs

Overall, this study indicated that the PMO-AP is an individualized assessment with good test-retest reliability and strong evidence of validity for the PMOs generated. The discussion with patients regarding the PMOs, indicators, and ratings selected and possible changes over time support a solid rationale for using PMO-AP in practice as a way to develop stronger clinician-patient relationships and meaningful discussions. More robust and larger studies are needed to further validate these findings, especially in different contexts and for longer periods. This is the first version of the PMO-AP aimed at developing a means of determining outcomes meaningful to the patient and assessing the course of the treatment in clinical practice, therefore supporting a more informed PM practice.

Chapter 6: Assessing Feasibility of Using PMO-AP in Clinical Practice

6.1 Introduction

One of the constraints on introducing a new procedure in a clinical setting is feasibility. Feasibility concerns the ease of administration and processing of an PMO-AP in the context of a clinical setting (Aaronson, 1992; Erickson et al., 1995). Because the PMO-AP is an intensive interviewer-based process with the health care professionals playing an active role in its administration, with its use in clinical practice as the ultimate goal, it is critical to determine the feasibility of its clinical use. Therefore, further qualitative research is needed to understand the specific advantages and disadvantages, and challenges of implement and assessing the PMO-AP and determine the feasibility of employing the PMOs in a clinical setting.

6.2 Methods

This qualitative study involved health care professionals working at BC Children's Hospital. I used focus groups, a qualitative research method, to address the research question. The intended aim of using focus groups was not to develop consensus but to produce qualitative data that would provide insight into the attitudes, perceptions, and acceptance of health care professionals on the concept of PMO-AP and its use in the clinic t. I used the COnsolidated criteria for REporting Qualitative research checklist to report the study methods and results (Tong et al., 2007).

6.2.1 ***Research Team and Reflexivity***

I led the focus groups with my PhD supervisor Dr. Jean Paul Collet in the audience. I followed identical standards for rigor and trustworthiness, including the use of reflexive notes and a consideration of my insider perspectives as the developer of PMO-AP along with my

experience of administering it. I knew the participants professionally as I worked in the same hospital. However, I provided them the assurance from the outset that anonymity and impartiality would be respected. Participant information highlighted the purpose of the study for evaluating the feasibility of the PMO-AP.

6.2.2 Theoretical Framework

The methodological orientation of the focus groups was to investigate health care professionals' perspectives on the PMO-AP, feasibility of use in clinical practice, strength, and challenges for implementing it in clinical practice.

6.2.3 Study Setting

To maximize the potential for representative responses, I conducted the focus groups with the three clinics (the Biochemical Diseases Division, the Pediatric Rheumatology Division, and Complex Pain Services) where I had administered PMO-AP as part of its evaluation at BC Children's Hospital.

6.2.4 Study Participants

I used a purposive sampling strategy to recruit participants to ensure an adequate representation from different professional groups and levels of seniority. I sent an open invitation via email to all clinical staff working in the three participating clinics. The message included detailed information about the focus group process and consent forms for those interested. Medical, nursing, allied health professional, and ancillary staff who worked within the three participating clinics were eligible for inclusion.

6.2.5 Data Collection

I facilitated the three focus groups. The participants included doctors, nurses, other allied

health workers, and clerks from the three units. Participants were asked to self-report their staff group, level of experience and professional education level. The prompt questions posed to each focus group directly reflected the questions presented to patients when administering the PMO-AP, whilst also considering the need to obtain professional perspectives. Therefore, I employed a 'question route' (Plumer, 2017) to facilitate the flow of constructive and in-depth conversations using principles of active listening (see Doody et al., 2017). The focus groups were audio recorded and field notes taken to capture nonverbal aspects of communication.

I began by asking participants about their current practices to obtain information about a patient's functioning, well-being, and everyday activities. I also asked them questions about how they obtained information about patient preferences, how that information was integrated into the treatment plans for the patient, and how the effectiveness of these treatments were documented and assessed. Then, I presented an overview of the PMO-AP and asked each group about their understanding of the PMO-AP. I also asked how this process might work in their practice, including both the advantages and disadvantages, if this were to be applied as a means of following a patient's progress and evaluating outcomes.

Initial questions were as follows:

- Describe how you capture information regarding patient functioning and well-being related to activities of daily living.
- Describe how you incorporate a patient's opinion or experience to inform treatment related decision-making.
- Describe the process of determining treatment effectiveness in your practice.
- Presentation of the PMO-AP – Concept, Process, Templates, and Examples.

Follow-up questions were as follows:

- What do you think of this idea? Is it appealing to you?
- Describe the advantages of using the PMO-AP in determining treatment response?
- Describe the disadvantages of using the PMO-AP in determining treatment response?
- Describe the feasibility of implementing the PMO-AP in your practice?
- Describe the constraints for using the PMO-AP in the clinic?
- Describe how you would implement the PMO-AP in your practice?
- Overall describe your opinion on using the PMO-AP to evaluate treatment response?

6.2.6 Data Analysis

I transcribed verbatim the audio-recordings of the focus group discussions and then analyzed the transcriptions using discourse analysis (see Gee, 2014). I identified thematic discourse units of analysis from written transcripts and labeled them for analysis using NVivo Version 12 (QSR International, 2012). The next step was coding the segments of the focus group text closely following the discourse topics and meaning of the segments. Then, I grouped the segments into analytical themes. I analyzed the data to identify the common themes within each clinic and across all three clinics and themes specific to each clinic to understand how the PMO-AP could be adapted to each clinic's pattern of practice. The goal was to identify the aspects considered challenging or, constraining, and beneficial to each clinical setting.

6.3 Results

6.3.1 Description of the Participants

I recruited a total of 20 participants, consisting of eight physicians, three fellows, four nurses, two nurse practitioners, two dietitians, one psychologist, and one physiotherapist. I pre-

assigned the participants to a focus group held within their clinic. Focus group participants were predominately female (17/20; 85%). The length of the discussion ranged from 54 to 78 minutes per focus group, with an average length of 67 minutes. A summary of focus group characteristics is presented in Table 21.

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Focus Group Characteristics

Focus Group #	Clinic	Duration hh:mm	Total n Participants Occupational Group, n	Gender, n	Setting
1	Biochemical Diseases	01:18	Total 9 Clinician, 4 Allied Health, 6	Male, 0 Female, 9	Research Rounds
2	Pediatric Rheumatology	01:09	Total 7 Clinician, 6 Allied Health, 1	Male, 2 Female, 5	Journal Club Meeting
3	Complex Pain Service	00.54	Total 4 Clinician, 1 Allied Health, 3	Male, 1 Female, 3	Monthly team meeting

6.3.2 Themes

I identified themes that were unique at each clinic. In the Biochemical Disease clinic, all participants across all professional groups showed interest in at least one aspect of the PMO-AP. Members of the Complex Pain Clinic stated that they were already implementing most of the concepts of PMO-AP but did not have a structured way to identify patients' PMOs, determine priorities, and assess their ability to meet patients' desired goals. Staff of the Pediatric

Rheumatology doubted that they would be able to implement the PMO-AP and expressed preference for the use of standardized PROMs to collect patient preferences by applying the POMs using more personalized approach. The major themes that emerged during the analysis of the interview across all three clinics were (a) the importance of medical history to get the status of the patient; (b) the current lack of a standard process for treatment evaluation; (c) reliance on biomedical framework over patient preference,; (d) value added by an individualized assessment like the PMO-AP; (e) concern around the time required for using PMO-AP as an assessment at every clinic visit; and (f) the need for training for administering PMO-AP.

6.3.3 Presentation of Findings

6.3.3.1 Biochemical Diseases Division

Most clinicians, in response to the initial questions about their current practice of how information related to functioning or well-being related to activities of daily living is obtained, reported that they normally just ask this question while obtaining the medical history. The way they ask this question, however, varied depending on who was asking the question. Some clinicians said that they may ask the patient directly or use other sources of information if available from previous reports such as a letter from a child development clinic. One clinician described their current practice as follows:

> Like me in particular, the social history is very important. Specifically asking what they do, what they do during the day, what they do after school, and if anything, if there's any limitation to what they'd like to be doing based on either impairment of function or social circumstance.

Though the patient's level of functioning was an important factor for a physician, all participants agreed that they did not have a standard process or an assessment to incorporate the patient's description about their ability to engage in everyday activities, which could inform treatment-related decision-making. During the focus groups, the clinicians stated that they based their assessment of the effectiveness of treatments on objective measures such as blood levels or improvement in symptoms. One clinician noted that their assessment of the effectiveness of treatments can vary depending on whether effectiveness is labeled by chemical markers, symptom management, or family happiness.

The global assessment across all the clinics of the PMO-AP was positive. Clinicians stated that they liked the concept and wanted to understand how either the PMO-AP or its principals could be practically implemented, indicating a potential opportunity to improve patient engagement to give patients a sense of control in their treatment management. As one clinician said,

> It's a really lovely idea to try to capture what the family really identifies, those important targets for them. Especially when you may have very different targets for treatment, right? And if you're not meeting your goals, and I think it's going to help you identify potentially why you're not getting to where you want to get together. I think a rotation probably would be quite difficult, and you'd have to iterate because it probably wouldn't be static. Like their goals would probably not be static, either right?

A nurse mentioned that the PMO-AP will be useful in cases when it is not clear how to measure if a patient has improved. Some considered the process potentially very useful for

teenagers transitioning from pediatric into adult care. The main concern was the length of time it would take to administer and complete the PMO-AP. The nurse explained,

> It's not like formal questionnaire that we do, but if we do it as in everyday clinic, then the number of patients, we can't every patient needs an hour to see and discuss and do the questionnaire and then follow up these things. So, I don't know how it is going to be practical?

Training to use the PMO-AP was brought up by everyone. As one clinician described,

> I think we would need training. Training would be helpful. How can we come to an agreement with the patient in regard to the outcomes, as he said? How can I ask a patient in a way, how can I work with a patient in order to get a meaningful outcome which is also specific for the condition and for the treatment that I'm giving because I could imagine that some of the patients have so many issues and we're treating them only for one particular segment of all those issues and their outcomes might, however, never be achievable with our treatment. So, we must make sure that we work out with the patients, what would be the outcomes that might be influenced by our treatment. I think that's a bit difficult.

Suggestions included tweaking the PMO-AP a bit to save time by only identifying the outcomes and the extent of change that a patient would want to see rather than going through the goal attainment scaling process. Some participants suggested developing an app to avoid paper, which would enable the patient to complete scaling remotely online.

The main advantage everyone saw with PMO-AP was its ability to help identify what is important to the patient sitting in front of them in the clinic, and the PMO-AP's ability to track

patients longitudinally and use this record for discussions with patients. One clinician suggested, "I could see it as being a way to identify patients' values, and identify out what's important to them initially, and then setting goals." The time involved in applying the PMO-AP process was the most significant disadvantage identified for the PMO-AP. Changing goals or outcomes during follow-up, making sure that realistic outcomes are identified, and language barriers were other possible challenges mentioned during the focus group.

6.3.3.2 Pediatric Rheumatology Division

In response to the initial questions about their current practice of obtaining information on functioning or wellbeing during daily activates, all participants stated that medical history is the first information requested, followed by direct questions about problems that the clinician thought might be relevant. One participant said,

> With arthritis patients, their hands, we'll say can you do your hair, or can you open the car door, can you open jars? So, it is very direct and usually related to the patient's disease as for a start. If it's arthritis and limb-based, that's what we do, patient functioning, which is both a mixture of functioning and activities of daily living.

The participants acknowledged that everyone had a different way of asking those questions before the clinic started using standardized instruments such as the CHAQ. One of the clinicians stated,

> Something that I regularly ask from patients with arthritis is whether they can keep up with their peers in school and whether they are doing full physical education or not. And then the questions that they will provoke, which is more focus-dependent on if I know about the history of that patient, if that patient has wrist involvement, then I may ask

about writing or typing. Maybe they don't have less movement this moment, I wouldn't ask that

Clinicians reported that their approach to incorporating a patient's opinion in treatment related decision-making varied from patient to patient. They also noted that when discussing the patient with the social worker and physiotherapist, they also take the patient's lifestyle into account while developing a treatment plan. The patient's previous experience of medical care and the family's belief system were important factors for one clinician:

> [The patient] has severe needle phobia and is unable to take any medication that is administered by injection or get a blood test, then we have to say okay let's have a think about how we're goanna design some treatment plan that's going to be able to be achievable.

When asked how a patient's experience helps with determining treatment effectiveness during follow up, the decisions within the division were based on a comprehensive review of history, physical findings and results from clinical investigations. As one physician expounded, the patient's opinion should not be the only thing to base the decision solely on:

> Patients with lupus, the patient and the parent may say we don't like this prednisone because I gained weight, I look ugly, I have stretch marks, whatever, and I don't feel sick anyway. Your kidney inflammation that you can't see or feel, it's not clear that the patient's opinion in that situation is the best choice for their health. So, in that case, we have to incorporate understanding their opinion whilst educating the parent and the child to say yup I hear you but if you want to have kidneys that are working in five years, let's talk about how we can do that.

The members of the clinic were receptive to the concept of the PMO-AP, but they had concerns regarding its practical application in a clinical setting. One clinician stated,

> I think the idea is interesting and appealing, and I believe it has some value. I think in a busy clinical setting, it would require significant time or commitment by some staff member. When we have a clinic where we have multiple staff members, we have each patient being seen by a learner, attending physician, the nurse, maybe the physio, the OT, social worker, communication amongst all those people at point of care, this information to make it useful is pretty daunting.

One unique aspect about the division is that all their patients are part of several observational and interventional research studies. As participants in these studies, they are asked to complete a set of standard outcome measures, which conflicts with the concept of the PMO-AP. A clinician noted,

> So, it's a respondent burden type of issue, which to say well we'd want to use this thing because it's more relevant to the ongoing patient care, but we're still going to ask people to put 15 minutes into filling out these other questionnaires, it becomes difficult to work out the logistics of how that's going to happen, without pissing parents off, frankly.

The primary concern among participants of the focus groups was that a majority of the rheumatic conditions have a physiological component that patients will not be able to identify as an outcome. Also, patients lack control over the outcomes and even if the treatment is working, they might still have a flare-up of the disease. If the disease flare-up is identified as an outcome, then it is difficult for families or children to distinguish it:

We have patients that come in and the parent will say my child has a flare once a week, and they have joint pain, and his ankle is swollen for an hour, and he has to be carried. But that's actually not even consistent with a flare of arthritis.

Members of the clinic, however, still thought they have patients who would benefit from the PMO-AP. They commented that if the PMOs that are identified are realistic and related to the treatment that the PMO-AP could help with treatment compliance.

And in those patients too, then we go the next step, and we say well your joints are better. But they say no I still can't do exactly what used to, but he's still not going to play soccer every week. But then we say no he hasn't but now he's walking to school, and he didn't. Their aim is for that peak, right? And you say but you have made this small gain. So that's the sort of thing we feed back to them. And so that is sort of like an individualized. It's to try and help people, encourage people to keep with the program.

The clinicians identified the limitations of time and resources as the most significant barriers to implementation in their divisions. One clinician said,

I also think that implementation is always the factor that makes it really difficult to incorporate any kind of new, and those are very basic things, like who's going to administer this thing, how is that information collected on a piece of paper, where's that piece of paper going, is it going in the chart, where is it going? Is it being collected on a device? We don't have electronic medical records. We do not have any way of tracking things, essentially other than on paper. How is that going to be tracked over time? So, Dr. X saw the patient last time, Dr. Y saw them the time before, and I go in the third time, how am I going to access that information in order to, and is that even a valid way of

utilizing this kind of approach, having different providers doing that? So, it is those kinds of small things I think are actually disadvantages of this kind of system, just because, it's not to say it can't be done, but takes a lot more time to organize those things.

When comparing the PMO-AP to standardized questionnaires in which patients are expected to respond to items, which sometimes are not relevant to them, the clinicians appreciated PMO-AP as a method that would allow patients to express problems in their own words. A clinician said,

> I think the most valuable thing about this kind of approach is what I would say is I know from some focus groups we did with youth, with JIA, they clearly stated that the thing they don't like is they don't like the questionnaires that we give with the tick boxes because they feel that it doesn't entirely represent their experience. So, I mean this came up in this focus group that we were doing. And they felt that it was limiting because it just did not have the ability to really describe what was going on, whereas what you're doing really answers that need very well.

6.3.3.3 Complex Pain Service

As part of their existing practice, the CPS sends out a detailed questionnaire to each patient before their initial clinic visit, which includes questions related to activities of daily living. Patients are also asked specific follow-up questions by everyone in the team related to their functioning in everyday activities during the clinic visit. A clinician noted, "Function is at the core of our clinical service, symptom reduction incorporated into function. So, while it is collected systematically in a questionnaire it's also part of every clinic encounter with questions about function."

Patients are also asked to identify specific goals they expect out of their care from CPS that allows the team to incorporate the patient's goals in the treatment plan. One participant observed,

> Well, one of the questions on our questionnaire relates specifically to goals that the patients have for return to function, specifically in the areas of physical activity and school. We ask them directly what it is they want to return to and that's very important and informing our treatment and decision making in terms of knowing what their personal goals are and to learn our approach which is somewhat more generic but tailoring it specifically to what they say they want … A goal is the number one question we ask everybody. So, we design the core clinical cutter around the goals and obviously there are investigations we must do because even when they are, but the return to function is the critical part and so is patient directed goals.

At CPS, the treatment plan developed by the clinicians and given to the patient are designed to help the clinician and patient to reach the patient's goals, which puts the patient experience at the core of any decisions related to changes in the treatment and determining the treatment's effectiveness. A clinician stated, "Yes, because one of our first question to a family is why you are here, what do you hope to get out coming and working with the pain team?"

In the clinic's current procedures, during follow-up the clinician and patient return to the initial questionnaire and clinic notes to review and determine if the patient's goals were met after starting the treatment:

> I think that would help if we knew that there was a tool that we should be using for goal setting and goal evaluation. It is as simple as asking a question and seeing whether it can

be combined with some metric, you know, steps per day or return to classroom or sleep hours, whatever their metric is, if it is as simple as that then it's fine. But if there is a tool that we should be using it would be great to learn about that.

The CPS team very much liked the concept of PMO-AP, as it was in line with their clinic principle of improving function. The team also felt that the PMO-AP identifies something that is personal and meaningful to the patient, as this physician stated,

> I think it's brilliant to include exceed goals, so funny, I just realize how much I think in the box. Have we help them meet their goal and then sometimes in fact they do exceed in some areas though, yeah, it's really cool.

A second clinician said,

> I think it really goes well with how our main outcome is function and not necessarily reduce pain because sometimes the patient will come back and say, like my pain is the same, it hasn't changed but then it's good to have a way to kind of remind them or kind of help them to see that even though the pain hasn't changed but maybe some of these other things have changed. Like their sleep or their physical activity and their function.

A third clinician commented on the ability of the PMO-AP to encourage the patient:

> I think it's really validating and really engenders hope as well. The fact that you know you take the time to ask them what's personally meaningful right there, I think that's actually therapeutic not just assessment. And that's something we got our whole team, you know that' why we take so much time in that first time of meeting with complicated patients and families as we really want them to feel like they've been heard and this tool I

think is one way that we can really do that and then end up with even something quantifiable as well. And so, from that perspective I think it's fantastic.

The CPS team also appreciated the fact that PMO-AP allows the flexibility to change the outcomes depending on the context at the follow up visits. The CPS team also identified time and effort as disadvantages in administering the PMO-AP in a clinical setting and concluded that, for their team, which spends considerable time with every patient, the PMO-AP would actually help to formalize their way of practice, transforming it from using subjective assessments and discussions to objective, measured outcomes. They recognized that training was very critical if PMO-AP had to be implemented. One clinician noted,

> So, you must do a certain amount of training and I am sure that they understand it, practice it, see how it fits in their clinical population and then use it perfectly. So, training in mindset is very, very important.

CPS recommended that the PMO-AP be implemented in an electronic format rather than as a paper-based instrument. This application could be accessed remotely, supporting a conversation between the clinicians, allowing the patients to continue interacting with the clinician even after the clinic visit. This method would enable them to overcome time constraints and allow longitudinal tracking of information in a database both for the patient and for a meta-analysis of therapeutic interventions.

6.4 Discussion

The focus groups yielded valuable feedback that included a discussion of the feasibility of using the PMO-AP in clinical practice. First, as seen in the quotes related to training to use the PMO-AP, the goals of the patient may exceed the disciplinary limitations of the clinic. This

outcome may reflect the complexity of the condition, and the need for a multidisciplinary approach. Because the PMO-AP can serve as the boundary object that does not reflect a disciplinary bias, PMOs can serve as the vehicle for multidisciplinary discussions for the care of complex patients.

Second, the major limitation identified in using the PMO-AP was the time to administer it. I suggest adapting the process outlined for administering the PMO-AP to the individual clinical setting while retaining the core concepts of therapeutic emplotment and goal attainment scaling. For example, Stages 1 and 2 could be integrated into the medical history activity of the clinical encounter if the phenomenological focus of the illness narrative portion of the history is maintained to reflect the events that are relevant to the patient. Time might also be saved if the PMO-AP can be converted, as suggested by one of the clinicians, into an electronic format where the patient is familiarized with the process before the clinic visit and allowed to generate the PMO via the web remotely from home rather than during the clinic visit. A robust training module should also be developed for anyone interested in using the PMO-AP.

All three clinics that were part of the focus group are organized differently and have their own pattern of practice to managing patients. In the Biochemical Disease's clinic, the patient is seen by the same clinician or a fellow, the nurse, and the dietitian at each visit. Patients in the Rheumatology clinic are seen by whoever is available during the visit who could be a different clinician or a fellow or a nurse depending on availability. The PMO-AP can serve as a means for communication and provide consistency across the various HCP in clinics that have complex staffing.

The differences in practice patterns in the Complex Pain Clinic and the Biomedical Disease Unit may explain their differing responses to the PMO-AP. The Complex Pain Clinic uses a multidisciplinary team approach, and the same team meets each patient as a team together during the clinic visit. The Biochemical disease team wanted to have a structure and a process set up to implement the PMO-AP where an individual clinician would partner with the patient to complete Stages 1–4, but the nurses and dietitian would then use the information from the PMO-AP during their interactions with the patient. The Rheumatology clinic was most hesitant to the idea of implementing the PMO-AP in their regular practice, primarily due to their pattern of practice, where the patient could be seen by different clinician each time they are in clinic. The Complex Pain Clinic was the most receptive to the PMO-AP and willing to implement in their practice. This clinic was encouraged by the fact that the PMO-AP brings structure to their evaluation by identifying specific outcomes, as pain assessment is a very subjective.

This study is limited by the characteristics of patients and the three clinics that provided their care. The patients all had complex chronic diseases and the clinics were offered in a tertiary care center. The uniqueness of the patents and the high level of specialization of the clinics raise questions about the applicability and feasibility of using the PMO-AP with patients with less complex conditions and in less specialized clinics. Consequently, assessment of the PMO-AP in other clinics and in different hospital settings, such as primary care clinics, is needed. In addition, because I moderated and conducted the PMO-AP process and the analysis, I may have introduced some unintentional bias towards endorsing a particular view. If an independent person moderates the focus groups in the future, they must have adequate background knowledge of the topic and be intimately familiar with the goals of the study and the question route.

These focus groups revealed some remaining apprehension towards a holistic approach to PM. Clinicians' willingness to accept the concept of PM is based on having an approach that is easier, well standardized, and focused on biological mutations and tailoring treatments based on biomarker response. Including the patient's perspective is, based on comments in the focus group, however, more challenging and would require a shift in the clinician's mindsets and practice. Assessments such as the PMO-AP could foster these changes by providing a systematic process to partner with the patient and include the voice with biological markers and standardized tests in defining and evaluating treatments.

In conclusion, more studies are warranted to assess the use of the PMO-AP in real clinical settings. Further studies could help tailor the process to specific clinical practices. Certainly, future studies should focus on the benefit of using the PMO-AP to improve the quality of patient-physician relationships and personalized care.

Chapter 7: Conclusion

This chapter includes the presentation of a summary of the findings from my dissertation research and discussions of their implications. Also included are discussions of the adequacy of the research methods and the implications for reliability and validity of the PMO-AP. The chapter contains a description of the contribution of this research to the field of individualized outcome evaluation and the limitations of the study. The chapter also includes descriptions of the significance of this research for the practice of PM in the clinic and concludes with some considerations for future research.

7.1 Summary of Findings

This dissertation research set out to develop a method to identify and monitor personally meaningful outcomes at an individual patient level. This project originated in the context of rare conditions characterized by large heterogeneity in phenotype expression, which makes it problematic to use nomothetic standardized assessments to measure outcomes. Therefore, a prerequisite was to tailor the outcome assessment to the needs of individual patients. The process developed allowed the patient to identify and generate outcomes that were meaningful and individualized. This dissertation includes a description of the development of a more effective idiographic personalized approach to identifying and monitoring treatment outcomes in a clinical context, which engage the patient and the doctor in a dialogue, mediated by the PMO-AP, to incorporate the patient's voice in a systematic way during the clinical encounter.

The research started with the narrow focus of developing another individualized PROM. However, during the initial stages of the research, while conducting the n-of-1 studies as part of TIDE-BC, it became apparent that it was important for the patient and clinician to reach a shared

understanding on the areas of concern or outcomes, to identify desired changes in those outcomes, and track them during the process of the treatment. To be truly personalized and to ensure that the outcomes identified by the patient are meaningful in the patient's treatment, it was necessary to establish a dialogue between the patient and the clinician. Therefore, neither conventional nomothetic nor individualized PROMs were appropriate and should be replaced by an idiographic process driven by the dialogue between the patient and clinician that can be used during the clinical encounter. Through this dialog, in which the PMO-AP serves as a boundary object, clinicians can collaborate with the patient to proactively identify tangible outcomes with well-defined indicators that reflect the goals and priorities of the individual patient, and result in a useful treatment. The process should also support monitoring of these outcomes to assess the treatment response.

The PMO-AP was designed to be administered in four successive steps aimed at identifying and assessing the PMOs. The first three steps of the PMO-AP are to be completed before treatment initiation. They involve identifying the PMO, finalizing, and scaling the PMO for expected changes. These processes require the patient and the clinician to develop both the patient's illness narrative (through an interview) and a medical history, which enables them to then collaboratively and explicitly identify, a priori, the desired goals, and then determine the desired magnitude of change. Each of these steps is done through a dialogue between the patient and the clinician, to create a shared understanding.

The last step of the PMO-AP took place during follow-up clinic visits when the clinician and patient review the changes during the interval and the patient selects the rating of the PMOs. A discussion between the patient and the clinician occurs during each follow-up visit to

understand why a particular rating was selected and to assess whether the change was satisfactory.

While developing the PMO-AP, I discovered that some patients changed their choices of PMOs during follow-up visits, and they provided significant justifications for the changes during the review of the scoring. These amendments often resulted from changes in the family, school, and other social contexts that might not have been identified by other assessment approaches. These discussions demonstrated the high degree of personalization and person-centeredness of well-defined PMOs and monitored changes, which were contextualized in the patients' experiences and very personalized. Consequently, I concluded that the PMO-AP is a more appropriate strategy in PM than conventional PROMs.

The reliability and validity of the PMO-AP included evaluation in a prospective longitudinal cohort study of 50 participants from three different clinics. Overall, the process of administering the PMO-AP showed a high percentage of consistency indicating evidence of test-retest reliability in identifying the PMOs and relevant indicators and in describing the expected changes for the adapted GAS ratings that would make the intervention useful. All of the PMOs finalized by the study participants and the indicators they selected remained consistent with the narrative generated directly from the dialogue between the study participants and the researcher. This consistency provided evidence of content validity. Content analysis of the interview transcripts from the discussions with all study participants during the follow-up visits confirmed that the interpretation of changes in the PMO indicators by the study participants matched with the scoring they selected.

The PMO-AP also demonstrated evidence of convergent validity. The PMOs identified corresponded to either a domain or a specific item in the standardized PROMs (collected at the same time), which had a low score, indicative of a level of disease burden or problem. At follow-up, any or no change in PMOs also corresponded to an increase or further decrease in the scores for the corresponding item in the standardized PROMs.

Finally, the changes that some study participants made to their PMOs, and/or the indicators they selected, or the scaling at follow-up visits were not evidence of the inconsistency of the process and a weakness in the validity. To the contrary, whenever there was a change, the study participants were able, during the dialogue, to provide a good rationale for the changes. As noted, before these modifications commonly reflected change in their personal preferences or context. The methodical analysis of the dialogical process that is part of the PMO-AP between the patient and the clinician confirmed that these changes made by the study participants were not random but well reasoned.

In assessing the feasibility of employing the PMO-AP in a clinical setting, I conducted focus groups with clinicians from the three different clinics at the BC Children's Hospital. These groups confirmed the usefulness of the PMO-AP. They also identified the need for training to administer the PMO-AP especially in relation to goal attainment scaling. Discoveries included that the PMO-AP could not be administered in the same way in each clinic but needed to be adapted to their particular patterns of clinical practice for easy adoption. Time constraints were a major concern in the clinics. One interesting value mentioned by each group was the usefulness of the PMO-AP to provide a more systematic and structured dialog to elicit and discuss relevant personal information that leads to improve the patient's personalized care. When comparing the

PMO-AP with their regular practice, the clinical teams recognized that they routinely focused on the disease and symptoms, while paying less attention to the consequences of the condition and treatments in the patient's personal life.

7.2 Adequacy of Research Methods

The evaluation of the reliability and validity of the PMO-AP did not take place using the conventional methods as the information collected using the PMO-AP was qualitative and specific to the individual participant. The PMO-AP used an adapted GAS approach instead of a standard Likert scale. The numerical assignment of 0–5 for each PMO in the PMO-AP form at the end of Stage 3 was only to provide a point of reference and not for calculating any summary scores at the follow-up visits. Additionally, baseline is always 0, which does not allow the calculation of a correlation coefficient for test-retest reliability in comparison to an individualized PROM such as the MYMOP or PGI, which uses a Likert-type scale to mark the level of burden. Test-retest reliability of the PMO-AP included measurement by assessing the consistency of the PMO-AP's outputs at various steps, when administered twice within an interval of 2–3 days. Therefore, the focus of measuring test-retest reliability of the PMO-AP was not the rating of the PMOs at screening and follow-up visit 1 but the description of each PMO, how they were assessed, and the description of each number of the modified GAS, which was evaluated in terms of consistency.

Validity of the PMO-AP included assessment as a unified concept based on the perspective of *validation* as an ongoing process pertaining to the collection and use of the information collected through PMO-AP towards making inferences. I developed an explicit validation plan guided by a conceptual or theoretical orientation for validating inference from

three sources of evidence. These sources include (a) evidence from the content generated after completion of Steps 1–3 of the PMO-AP scaling forms; (b) evidence from the response processes of each participant when selecting a rating for the PMOs at follow up; and (c) evidence of validity generated from the relationship between the content of the PMO-AP and some specific corresponding items or domains of the standardized PROMs.

The feasibility of using the PMO-AP in the clinic included evaluation in a focus group format. Three clinics at BC Children's Hospital were part of the feasibility assessment. Each clinic has a different format of practice and clearly provided input on how the PMO-AP should be adapted to overcome the challenges identified, and additional evidence related to inter-rater reliability is needed when the patient is seen by a different clinician at each visit.

7.3 Contribution

This dissertation makes two significant contributions to research on personalized and person-centered care and clinical practice. A recurring new theme in clinical practice is the need to tailor care and treatment plans to individual patient's needs. The PMO-AP offers an idiographic, patient-specific dialogic response to the limitations of PROMs. The PMO-AP also offers a unique approach to evaluate the effectiveness of these personalized treatments, advocating for a shift in how one thinks of the practice of outcomes assessments—especially, to reflect what matters most to the individual patient.

The PMO-AP offers a process that is distinct from conventional PROMs. PROMs will continue to become a key outcome indicator for bringing the patient perspective forward. A hermeneutical problem, however, relates to how to use information from PROMs. As a principle, the information collected using PROMs should come directly and only from the patient. The

information collected using PROMs is interpreted and used by clinicians without any patient involvement. If there is a change in the rating, it is the clinician's role to determine whether it was significant without any input from the patient and without considering the patient's unique individual circumstances.

In contrast to PROMS, the PMO-AP capitalizes on the interdependency between the individual patient and the clinician toward achieving a shared concept of understanding on tangible outcomes related to the illness and a-priori clearly defining what is a meaningful change. Thus, the main contribution of this dissertation is a process for engaging patients and clinicians in a dialogue to identify patients' preferred outcomes. This dialogue is facilitated by using the PMO-AP as a boundary object mediating the interaction between the individual patient and clinician. This mediated dialogue is a key distinction between the PMOs and PROMs. Even though other individualized PROMs also allow the patient to generate their own outcomes, they do not allow for a dialogue between the patient and the person administering them. Also, the ability of both the patient and the clinician to reflect on the adapted GAS instead of a standard 5-point Likert-type scale makes it possible to determine a-priori the meaningful change in the health condition before starting the treatment and understand the reason for selecting a particular rating, or possible changes in PMOs or indicators at follow-up clinics.

Unlike generic or disease specific PROMs where the outcomes measured are predetermined, the PMO-AP allows for change in the PMO, the indicator for measuring the PMO and the GAS scoring to adapt to changes in the patient's social context. Also, the inbuilt dialogue process allows the clinician to capture the clear rationale for the change at follow-up. Therefore, the PMO-AP approach meets the objective of implementing a patient centered way of

systematic evaluation of outcomes to assess treatments in clinical practice. Clinicians in the focus groups evaluating feasibility of the PMO-AP found the work process to collect information challenging, but they acknowledged the benefit for personalized patient care.

In the era of patient focused drug development, the PMO-AP enables the clinician to include the patient voice in clinical trials. It is a good alternative to the routinely used "Top 3 concerns" outcome used in randomized controlled trials to identify the top three areas of concern to the patient due to the illness. Especially in the scenario of advanced therapies, the PMO-AP can be used as a key exploratory endpoint reflecting the patient voice when developing, for instance, new individualized antisense oligonucleotide therapies that utilizes a n-of-1 study design.

7.4 Limitations

There are two major limitations to the study. The first limitation is the difference between the time available to develop a PMO-AP in a research context, as opposed to the time available in a clinic. During the focus groups, the participants highlighted this aspect of PMO-AP as the primary concern for implementation in the clinic. Also, structuring dialogue is not easy and not every patient may be able to follow the process. The process may then require a specific training, as suggested in one focus group.

The second important limitation was that I was not the medical doctor treating the patients. Therefore, I could not infer from this experience what the reactions of clinicians would be. Additionally, I may have been limited in my ability to fully understand the appropriateness of choosing one outcome or one specific indicator. Finally, my interaction with the patients at

follow-up may have missed some aspects of the disease expression, related to some of the patients' decisions.

Other limitations regarding the selection of an adolescent population, from three different clinics only, and having only one person in charge of recruiting and following all patients have already been discussed in other chapters. Although the high consistency and solid logical reasoning observed is encouraging, it is an initial study, and the results must be replicated by conducting in different settings and used by different clinicians. This process would give the ability to evaluate inter rater reliability.

7.5 Future Research

As developing new treatment and assessment strategies is iterative, the PMO-AP will continue to evolve. Future research should focus on developing a training module for the PMO-AP. Reviewing the feedback from the focus group is important with the objective of reducing the time and effort for administering PMO-AP. Options such as an electronic version of the PMO-AP should also be strongly considered. Test-retest to be revisited using larger sample and different populations. To build on the validation work presented in this thesis and generate evidence of validity from other sources such as value implications of using PMO ratings, intended and unintended personal and societal consequences need to be examined and considered. Lastly, it will be important to conduct additional research to understand the clinical utility of the information obtained through the PMO-AP in treatment-related decision-making.

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Appendices

Appendix A: Strengths and Limitations of Individualized PROMS

Individualized PROMs	Strengths	Limitations
SEIQoL	• First individualized PROM • May nominate five domains (cues) patients currently consider as most important in their life. • Semi-structured interview format uses cues that allow the patient to think about the areas.	• Limited selection of domains/areas of life, which may/may relate to the patient's medical condition. • Presents an administrative burden (e.g., interview format, ranking, pie chart, etc.) • Calculates a summary QoL index score that does not clearly show whether the change is meaningful or only limited to one of the domains. • As it is a PROM, it does not permit collaboration or discussion with the patient about the outcomes selected.
PGI	• Self-administered. • Patients identify the five most important activities or areas in their life that are significantly influenced by their condition.	• Does not measure any symptoms or disease traits. • Generates a summary score at the end. • Does not track the change in each individual area or activity nor whether the change in the summary score is meaningful for the individual.
MYMOP	• Self-administered. • Focuses on symptoms, activities of daily living, and overall well-being.	• Lacks flexibility in outcome identification. Patient can only choose one or two symptoms and one activity of daily living.

Individualized PROMs	Strengths	Limitations
	• Uses a 5-point Likert scale for each symptom and activity, which is valuable for tracking changes in each problem area (vs. an overall summary score).	• Use of a 5-point Likert scale does not reveal whether the change is meaningful from the patient's perspective.
COPM	• Semi-structured interview. • Focuses on areas of everyday living explored during the interview to include self-care, productivity, and leisure. • Measures both performance and satisfaction related to the outcomes selected.	• Intended to be used for occupational therapy. Limited to any problems related to performing occupations of importance vs. symptoms due to the patient's medical condition. • Similar to PGI and SEIQoL, it generates a summary score at the end and does not track the change in individual outcomes or whether such changes were significant. • As it is a PROM, it does not permit collaboration or discussion with the respondent related to the selection of outcomes.

Appendix B: PMO-AP Identification Form

Participant ID: ..... Date: .....

Form Completed by: .....

1. *How does the condition affect your everyday life?*

   Notes: .....

2. *How would you envision a good day for you?*

   Notes: .....

3. *What kind of changes you would like the treatment to have in your daily life?*

   Notes: .....

4. *Do you have any concerns regarding your?*

   - *Physical functioning? (Walking, Running, Daily Activities, energy level etc.)*

     Notes: .....

   - *Emotional functioning? (Behavior, Mood, Sleep)*

     Notes: .....

   - *Social functioning? (Getting along with other children, friends, playtime)*

     Notes: .....

   - *School functioning? (Memory, attention, grades etc.)*

     Notes: .....

(Note to the interviewer: Review the responses given above and identify PMO with the patient)

PMO 1: .....

PMO 2: .....

PMO 3: .....

PMO 4: .....

PMO 5: .....

Comments: .....

Appendix C: PMO-AP Finalization Form

Participant ID: ..... Date: .....

Form Completed by: .....

Example:

PMO #: Reduction in Impulsive Behavior.

How it can be measured? Ability to sit still without getting distracted, listening to instructions given by the parents etc.

PMO#1: .....

How it can be measured?.....

PMO#2: .....

How it can be measured?.....

PMO#3: .....

How it can be measured?.....

Ask the patient /caregiver to provide a weight/ rank the PMO on a scale of 1–10 which sums up to 10?

1 [ ] + 2. [ ] + 3. [ ] = **Total** [10]

Appendix D: PMO-AP Scaling Form

Participant ID: ..... Date: .....

Form Completed by: .....

PMO- #____: _____ Timeline: _____

- **Indicator:** _____ (Egg: Sleep Duration, Seizure frequency)
- **How is it measured:** _____
  (e.g., number of seizure free days in a week, hours of sleep in a day)
- **Scaling for expected change in PMO (Use *SMART* Technique):**

PMO Achievement	***Expected Level Change in PMO***	***Rating***
Baseline		0
Much Less Than Expected Outcome		1
Slightly Worse Than Expected Outcome		2
Expected Outcome (Target)		3
Slightly better Than Expected Outcome		4
Much More Than Expected Outcome		5

Appendix E: Follow Up and Evaluation Form

Evaluation of PMO-AP

Participant ID: ..... Date: .....

Form Completed by: .....

PMO- #____: _____

What is the PMO related performance till date: _____

Contrast with initial prediction - Level of expected change in PMO at Follow up:

Baseline or anything less than that 0 ☐

Above expectation 4 ☐ 5 ☐

Success as expected 3 ☐

Below expectation 1 ☐ 2 ☐

Discussion & Decision for the PMO

……..……...
……..……...

Keep the same PMO: ☐

Revise the PMO Indicator: Yes ☐ Reason: ……
No ☐

Revise the PMO Scaling: Yes ☐ Reason: ……
No ☐

Change the PMO ☐ Reason: .....

Stop the PMO ☐ Reason: .....

Comments: ……..……...