New Product Planning Network Group

How to Grow Patient-Centricity in Pipeline Decisions

October 25, 2023

2023 NPP Network Schedule of Forums

Bi-monthly event extended to 90 minutes

Feb-28 — Value and Access for NPP Professionals

Apr-12 — Impact of the Inflation Reduction Act on Pipeline Development

Jun-14 — NPP Structures and Models from Emerging Biotech to Large Pharma

Sep 6 — Digital Innovation (AI) and Advanced Analytics for NPP Professionals

Oct 25 — How to Grow Patients Centricity in Pipeline Decisions?

Dec-08 — Planning Drug-Device Value Creation

Events led by the NPP Network Steering Committee Members

How to Grow Patient Centricity in Pipeline Decisions

October 25th, 10-11:30 EST

Julia Carpenter-Conlin
Alkeus Pharma

Stefan Cano
Modus Outcomes

Patrick Marquis
Modus Outcomes

Panelists

What is Patient Centricity for New Product Planning and why is it important?

"Although all biopharma companies claim to be patient-centric, some walk the talk more than others…"

Who is the primary “customer” of a new drug?

There are multiple potential stakeholders who influence approval and use of medical products

- ***Patients***
- ***General Practitioners/Primary Care Physicians***
- ***Specialist Physicians***
- ***Key Opinion Leaders***
- ***Caregivers***
- ***Pharmacists***
- ***Payers***
- ***Legislators***

Regulatory endpoints are just the ticket to enter a market

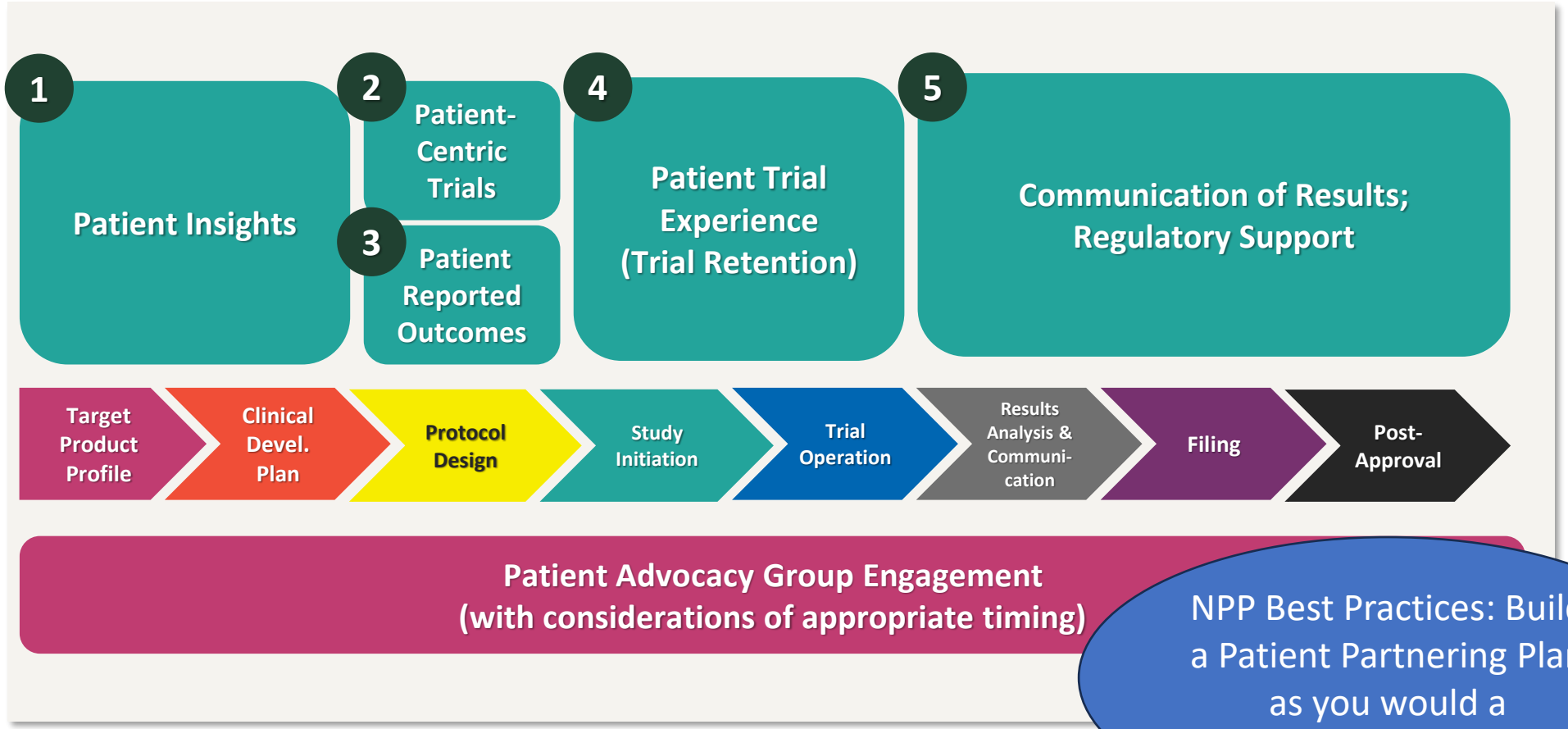
What value does our drug deliver across key stakeholders? (Value Propositions)

- To be successful, new products need to provide value to patients and other stakeholders with diverse perspectives

Why do most biopharma organizations focus on interactions and insights from physicians?

Like other key stakeholders, engagement with patients is needed to optimize our programs

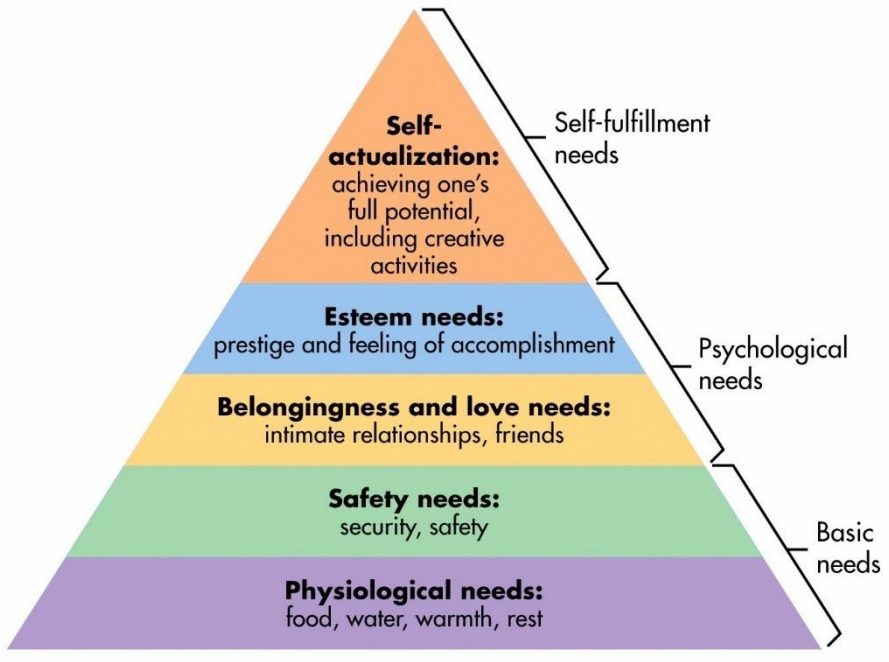
Potential areas on the development path where patient engagement could provide value to program



NPP Best Practices: Build a Patient Partnering Plan as you would a Publication Plan

Hierarchy of Patient Needs & Evidence Generation

Maslow's Hierarchy of Human Needs



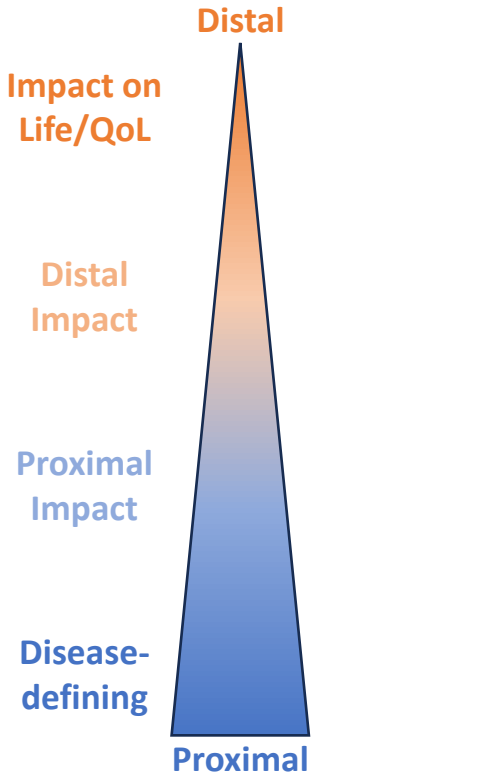
"Kuyler's" Hierarchy of Patient Needs

Self-Fulfillment Needs/Life-Changing
- Ability to work to full capacity
- Ability to interact socially and engage in normal relationships
- Increased independence with limited caregiver burden
- Ability to live a "normal" life

Psychological and Emotional Needs
- Reduced fear and uncertainty related to symptoms, acute episodes, or overall condition and future
- Avoidance of stigma associated with condition
- Reduced fatigue and apathy, with increased energy and feeling of renewal

Basic and Functional Needs
- Increased symptom control
- Ability to perform activities of daily living
- Reduced medication burden and side effects
- Improved financial burden of disease or treatments
- Avoidance of hospitalization

Evidence of Treatment Benefit



Collaborating with Patient Advocacy in Early-Stage Drug Development

NPP Patient Centricity Panel

October 2023

Julia Carpenter-Conlin

Sr. Director, Patient Advocacy

Alkeus Pharma

What is Patient Advocacy in Pharma

Patient Advocacy sit at the disease state level to champion the patient perspective and work cross-functionally to support corporate and therapeutic area goals

Your Patient Advocacy team should:

- ❑ Be empathetic, collaborative, and creative
- ❑ Understand where the patients and caregivers are coming from and how to incorporate patient insights/learnings
- ❑ Help manage expectations with patient organizations around the drug development process and about where the company is at any one point in time
- ❑ Appropriately and collaboratively message key learnings back to company
- ❑ Understand role and compliance – org. relationships are not in place to promote products

Julia Carpenter-Conlin, Sr. Director, Patient Advocacy

Why Patient Advocacy in Pharma

- ❑ Organizational Reputation and Trust
- ❑ Amplify Disease Knowledge and Education
- ❑ Clinical Trials Informed by Patients
- ❑ Patients Gain Access Sooner
- ❑ Services and Solutions that Patients Need and Actually Use
- ❑ Talent Acquisition and Retention

Why Collaborate with Patients/Patient Groups

- Patients are experts in their conditions—engagement will lead to deep understanding of therapeutic community (as people vs only as patients)
- Partnerships facilitate listening, learning, collaborating, ultimately addressing areas of unmet need
- Shared research and collaborations are mutually beneficial; credible and a respected source of data
- Patient Advocacy groups have direct access to pt. community, thus able to recruit appropriately; MR vendors often leverage Patient Advocacy groups for recruiting but typically not preferred by many groups, why not work with them directly? Collaborations can lead to more precise recruitment, especially in rare disease/hard-to-reach patient populations
- Opportunity to build deeper knowledge through in depth interactions
- Allows data gathering that may have strong credibility with Regulators (or HTAs) vs. data collected through market research
- The two approaches are not mutually exclusive! You can do traditional MR to reach a broader group of patients but ALSO work with PA groups. Work with your PA team at your company to identify the best approach to meet your patient insight needs while also supporting your therapeutic area patient communities

Some key principles on Patient Advocacy engagement

- ❑ The independence of Patient Organizations is paramount
- ❑ Build trust by listening and understanding
- ❑ Create partnerships that are transparent, respectful and mutually beneficial
- ❑ Aim for partnerships that are long-term commitments vs. one-time interactions/transactional
  - ❑ Be thoughtful about best time to engage
  - ❑ Manage expectations appropriately
- ❑ Work cross-functionally to involve patients across the product lifecycle
- ❑ Feedback loops – share your research with the people and organizations that helped you
- ❑ Don't use Patient Organizations as a way to promote your products

Types of Strategic Patient Engagement

- Patient Advisory Boards
  - Patients, Caregivers, Patient Advocates and Opinion Leaders, etc.
- Patient Advisory Panels
  - Standing groups of Patient/Caregivers/Advocates in your therapeutic area to advise, challenge, and co-create
- Partnering with Patient Advocacy Groups on Qualitative and Quantitative Research
  - Burden of Illness Studies
  - Sub-studies on patient registry data
- Co-creation with Patients
  - Patient Journey Co-Creation
  - Disease state education (e.g. patient-facing websites/materials)
  - Product Value Stories
  - Patient Services and Solutions
  - Patient recruitment / retention materials

Methods and best practices for running a patient ad board

- ❑ Work with Patient Advocacy team to identify the most appropriate patient organization and patients for your objectives
- ❑ Engage patient organization to assist in identifying appropriate patient advisors (what is the feedback goal for meeting?)
- ❑ Engage advisors and contract as appropriate
- ❑ FMV honorarium provided
- ❑ Make it easy for advisors to participate (ensure accessibility; zoom vs. in-person; meeting length/time of day; breaks)
- ❑ Set expectations with advisors – explain meeting goals, can you share questions in advance to ensure appropriate preparation?
- ❑ Work with compliance team – compliance team as partners

Types of Patient Focused Drug Development

- Development Informed by Patients
  - Clinical trials
  - Target Product Profile (TPP)
  - Evidence Generation (RWE, Natural History studies, Registries)
  - Lay summary development of data results

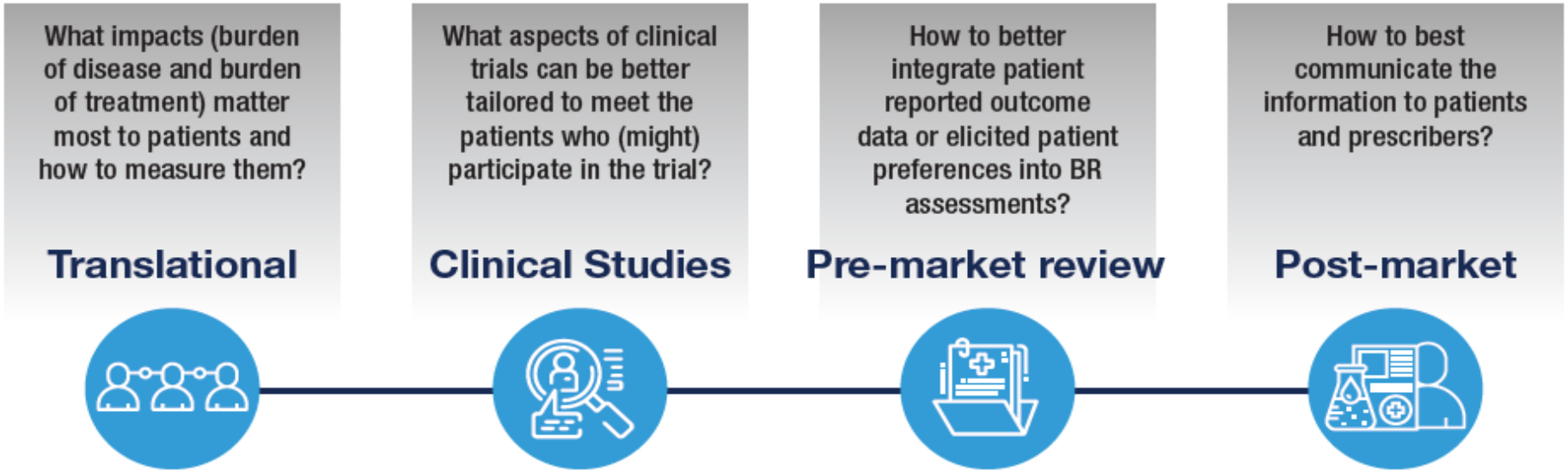
FDA's Key Milestones for Patient Engagement

- ❑ 1988 – Office of AIDS Coordination established
- ❑ 1992 – PDUFA Established
- ❑ 1993 -- First FDA Patient Representative served on an advisory committee
- ❑ 1996 -- FDA Patient Reps receive voting rights on advisory committees
- ❑ 2012 – A section of the FDA website is created specifically For Patients & Patient-Focused Drug Development Initiative launched
- ❑ 2016/17 – 21st Century Cures Act, 4-Part PFDD Guidance Docs
- ❑ To present --

- FDA meetings with patient communities (60+)
- Voice of the Patient reports
- PFDD guidances created
- FDA PFDD website with LOTS of great info

U.S. FOOD & DRUG ADMINISTRATION

Opportunities to Conduct Patient-Focused Drug Development Across the Lifecycle



How do we ensure that we get input representative of the whole disease population?

What symptom or functions matter most to people with this disease?

How to best measure? (endpoints, frequency, mode of reporting, etc.)

Do endpoints planned for the trial include the ones that matter most to patients?

Does the protocol facilitate (or discourage) enrollment or continued participation?

Do informed consent and other processes within the trial reflect the needs and preferences of people with that disease?

How to utilize elicited patient preference studies?

How to factor in key uncertainties?

How could individual differences in patient experience (or preference) of benefit versus harm be considered?

How to convey info that helps facilitate patients' and clinicians' informed decision making?

How to convey uncertainty to inform and support clinical decision-making?

Framework for the Use of Patient Experience Data Throughout the Product Lifecycle

Biotechnology Innovation Organization

Clinical Development

Current Meeting Opportunities	Critical Path Innovation Meetings	Pre-IND Meetings Other Type A , B, or C Meetings Critical Path Innovation Meetings INTERACT Meetings (CBER)	EoP1 Meetings Other Type A, B, or C Meetings	EoP2 Meetings Other Type A, B, or C Meetings	Pre-NDA/BLA Meetings Other Type A, B or C Meetings	Mid-cycle Communication Late Cycle Meetings Advisory Committee Meetings	Other Type B or C Meetings
Product Stage	**Research & Discovery**	**Preclinical Development**	**Phase I**	**Phase 2**	**Phase 3**	**Health Authority Review and Marketing Authorization**	**Postmarketing**
Examples of Patient Experience Data Applicable to the Product Lifecycle	• Experience on current treatments • Unmet medical need • Disease familiarization	• Treatment burden • Patient input on protocol designs • Clinical trial burden • Disease burden • Natural history study • Identification of clinical outcome assessments	• Patient preference for treatment • Patient benefit-risk acceptability • Treatment burden • Patient input on protocol designs • Clinical trial burden • Disease burden • Natural history study • Validating clinical outcome assessments • Patient reported outcomes • Quality of life			• Patient risk tolerance • Clinical outcome assessments	• Patient outcome in clinical practice • Clinical outcome assessments • Development of patient support applications
Relevant Decisions made During this Phase of the Product Lifecycle	• Product design adaptation	• Product design (i.e., type of device, how to take the medicine, etc.) • Protocol design (i.e. meaningful endpoints) • Clinical trial participation • Understanding the feasibility of trial participation	• Treatment arm selection • Subpopulation identification • Risk mitigation • Benefit-risk assessment • Clinical outcome Assessment Identification • Clinical trial design • Personalized medicine/biomarker • To inform the development of drug development tools • Eligibility for expedited programs			• Structured benefit-risk assessment • Subpopulation identification • Labeling optimization • Discussion at Advisory Committee meetings • Labeling	• Label/indication expansion • Shared decision making • Personalized medicine/ biomarkers • Quality of care/adherence (i.e., label clarification, physician counseling) • Risk management • Value frameworks

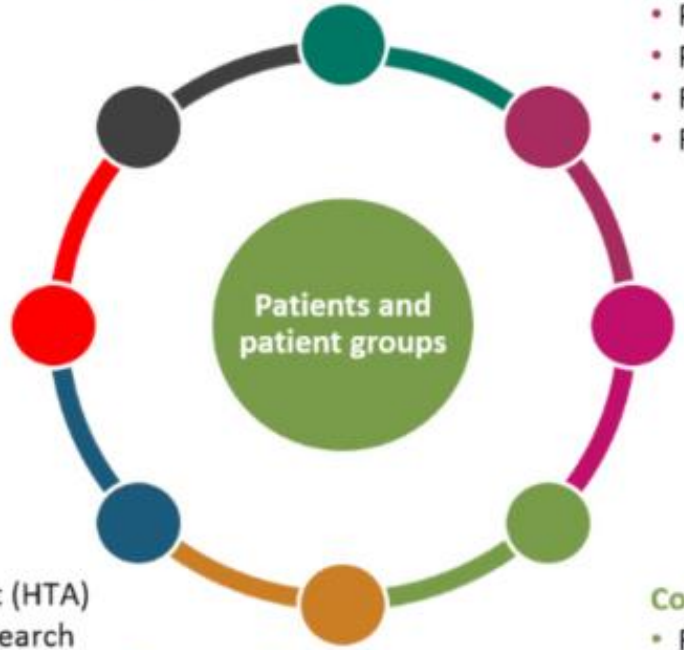
Julia Carpenter-Conlin, Sr. Director, Patient Advocacy

Patient involvement across functions

Drug Discovery
- Target selection
- Disease strategy
- Patient experience mapping
- Environmental factors

Chemistry, Manufacturing, and Controls
- Acceptability of options for clinical trial formulations
- Final dose and route of administration
- Packaging

Clinical Development
- Research questions
- Target patient profile
- Trial protocols and end points
- Proof of value studies
- Patient reported outcomes
- Registries
- Recruitment and retention



Regulatory Affairs
- Health Technology Assessment (HTA) strategy and interactions
- Patient input at regulatory meetings

Global Outcomes Research
- Real-world evidence to quantify return on investment and unmet needs
- Clinical Outcomes Assessment (COA)/Patient-related outcomes (PRO) strategy and execution
- Disease modeling and comparative effectiveness research
- Value evidence for regulators, HTAs, HCPs

Market Access
- Value propositions
- Health Technology Assessment (HTA)
- Comparative Effectiveness Research (CER)
- Reimbursement
- Coverage policies
- Policy

Corporate Compliance
- Financial and in-kind support
- Guidelines

Commercial
- Global marketing strategy
- Patient education materials
- Medication adherence

Integrating the patient voice can have value across the organization.

Julia Carpenter-Conlin, Sr. Director, Patient Advocacy

From DIA's eLearning course, "Introduction to Patient Engagement in Drug Development"

MODUS OUTCOMES
A THREAD Company

Concept-driven measurement leads to patient centric endpoints

25 October 2023

Biopharma New Product Planning Network

Patrick Marquis
MD, MBA

Stefan Cano
PhD, CPsychol, AFBPsS

Patient Centricity in Industry Clinical Studies: Talking Points

1. Raison d’etre: our perspective
2. Alignment: regulatory considerations
3. Navigation: examples and further reading

Raison d’etre

Patient Centered Outcomes

Quantify impact of disease and treatment on health outcomes

How patients "feel or function"

Embraces all clinical outcome assessments:

- patient-reported outcome (PRO)
- clinician-reported (ClinRO)
- observer-reported (ObsRO)
- performance outcome (PerfO)

https://ojrd.biomedcentral.com/track/pdf/10.1186/s13023-017-0718-x?site=ojrd.biomedcentral.com

Enabling Studies to be *more* Patient-Centric

Patient-Centered Outcomes Research

High science expertise to ensure studies are patient-centered, well designed and inclusive

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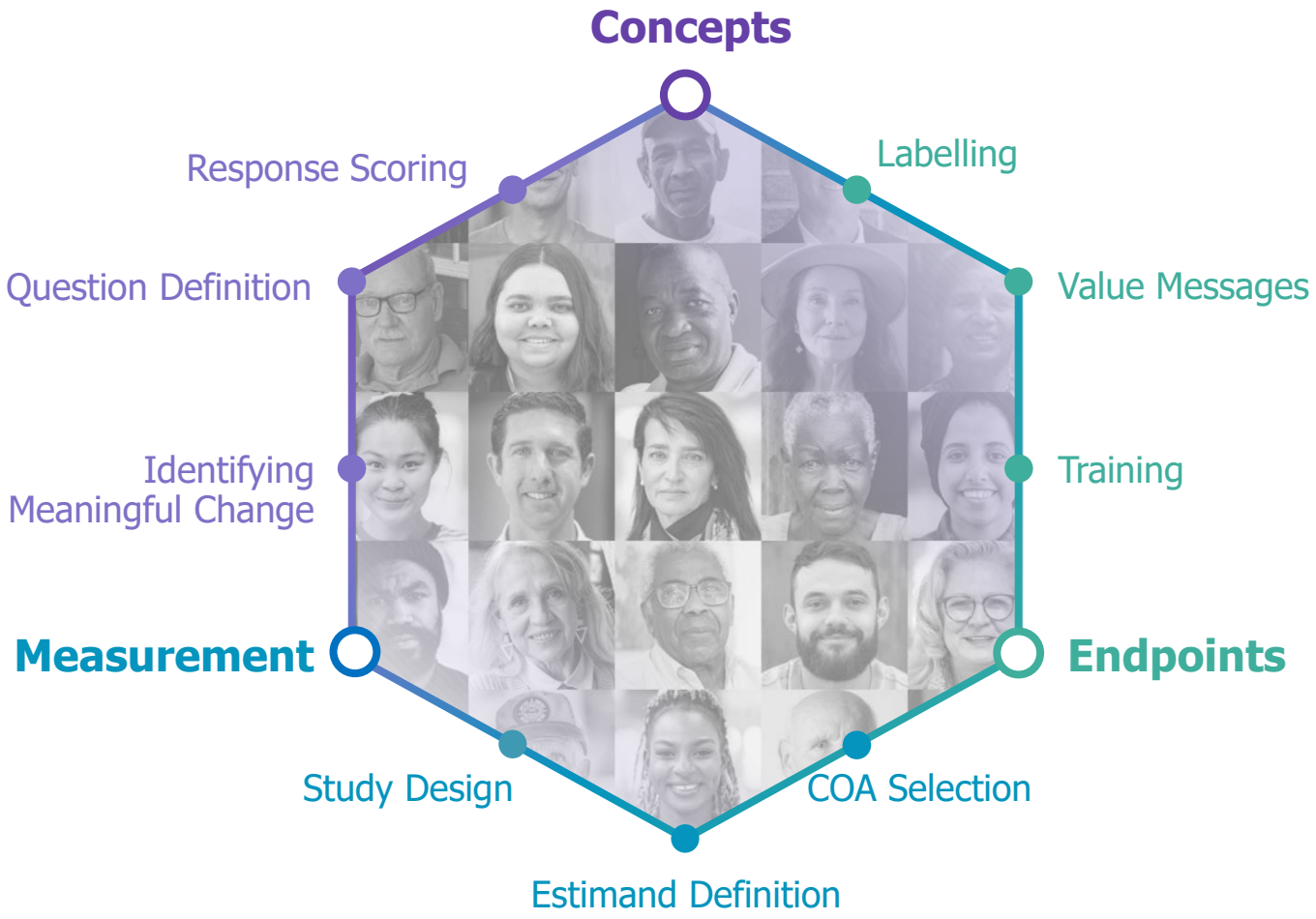
50+
international team members

100+
years of experience

400+
Scientific Articles Published

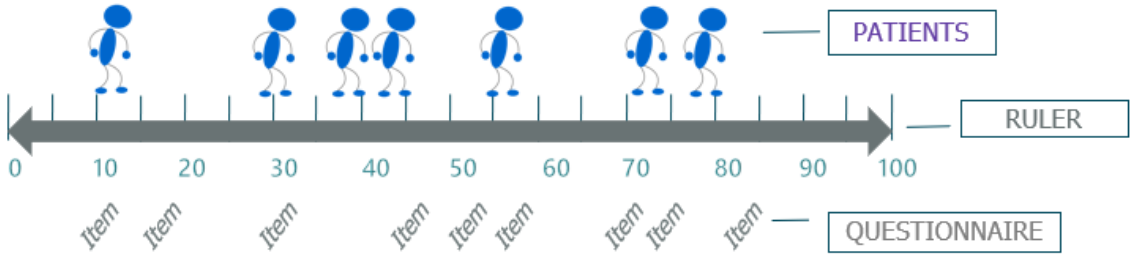
Our background of combined academic excellence (PhDs) with business standards (MBAs) provide capabilities in qualitative research, advanced psychometric analysis, and biostatistics

Enabling Studies to be *more* Patient-Centric



Concept-driven...

Conceptual clarity with hierarchy of unique concepts making clinical sense
Covering the range of patients' experience in context of use



...Measurement

Linear based on a simple stochastic measurement model
Statistical sufficiency, parameter separation - no modelling of data

Enabling Studies to be *more* Patient-Centric

Design/ Planning

- Explore concepts of interest (COI) in context of use (COU)
- Review the scientific literature, media, and qualitative research

Phase 1

- Confirm COI in COU
- Qualitative research
- Select/modify/develop COA instrument(s)
- SAP and endpoint strategy

Phase 2

- Document/confirm psychometric properties
- Develop instrument interpretation guide

Phase 3

- Confirm psychometric properties in trial sample
- Provide further evidence for interpreting meaningful within-patient change

Regulatory

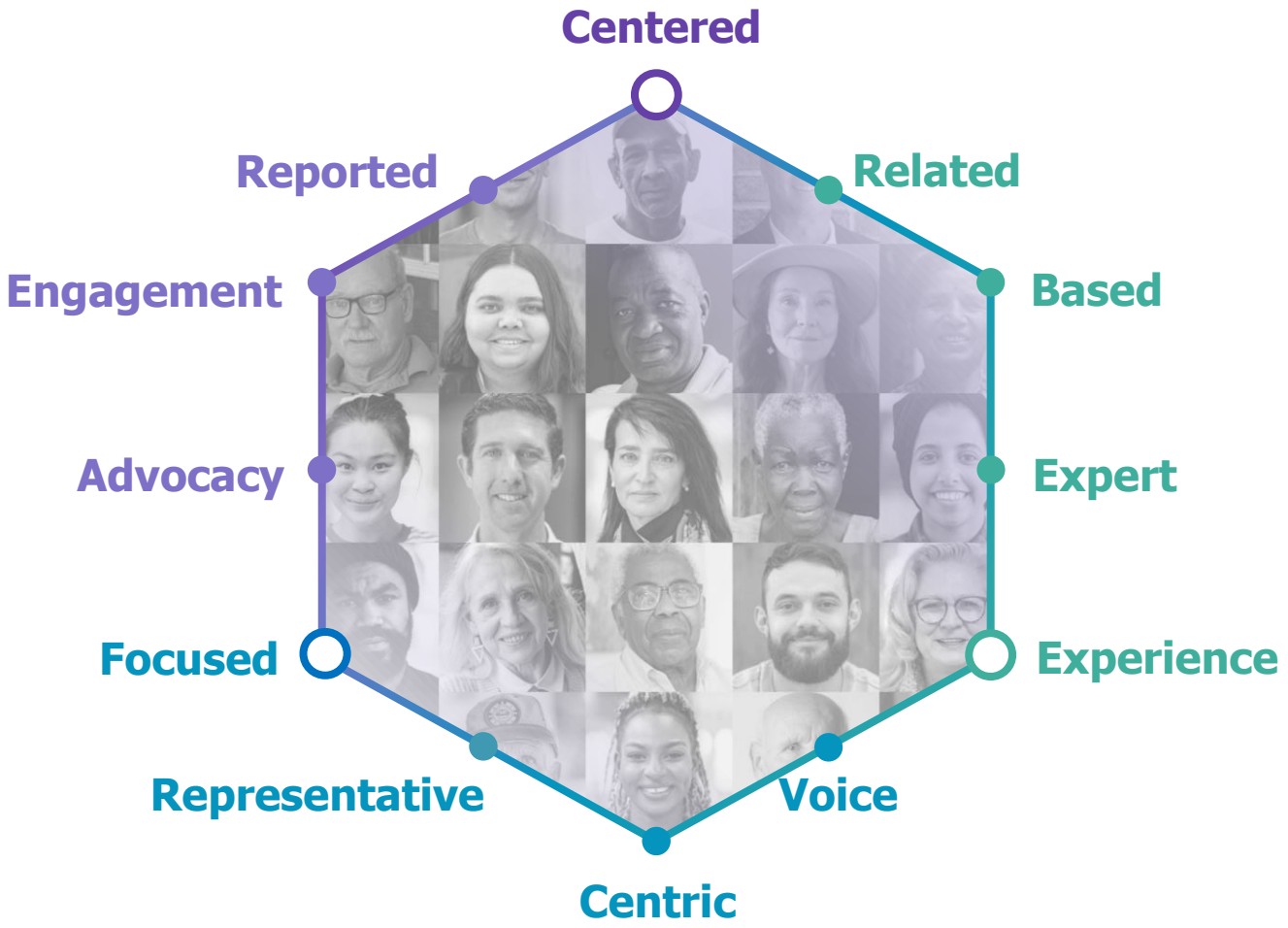
- Develop dossiers around the COA aspect of trials
- Attend regulatory meetings (FDA / EMA)
- Assisting sponsors with comments from regulatory bodies (FDA / EMA)

Phase 4

- Confirmation in larger populations
- Computerized adaptive testing
- Use in clinical practice
- Real-world evidence studies

Alignment

Patient…



A systematic approach to help ensure that patients' experiences, perspectives, needs, and priorities are captured and meaningfully incorporated into drug development and evaluation

Patient-Focused Drug Development: Collecting Comprehensive and Representative Input
Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders

Patient-Focused Drug Development: Methods to Identify What Is Important to Patients
Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders

Patient-Focused Drug Development: Selecting, Developing, or Modifying Fit-for-Purpose Clinical Outcome Assessments
Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders

Patient-Focused Drug Development: Incorporating Clinical Outcome Assessments Into Endpoints For Regulatory Decision-Making
Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders

- The symptoms of their condition and its natural history
- Impact of the conditions on their functioning and quality of life
- Their experience with treatments
- Input on which outcomes are important to them
- Their preferences for outcomes and treatments
- The relative importance of any issue as defined by patients

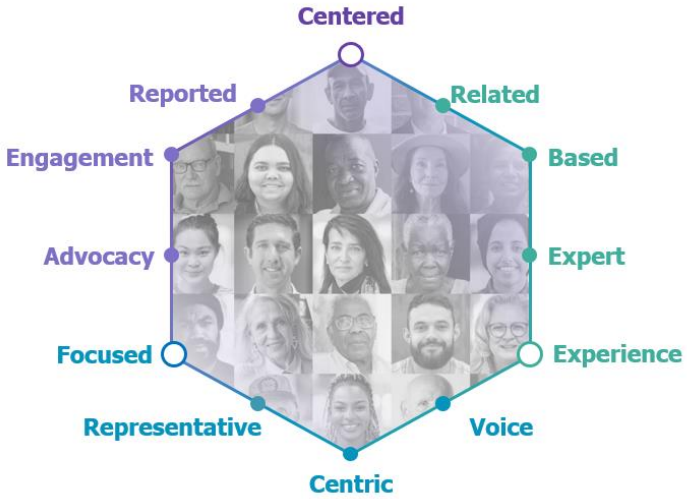
Patient Experience Data is Key

Patient Experience Data

Patient Experience Data Relevant to this Application (check all that apply)

			Section of review where discussed, if applicable
☐	**The patient experience data that were submitted as part of the application include:**		
	☐	Clinical outcome assessment (COA) data, such as	
		☐ Patient reported outcome (PRO)	
		☐ Observer reported outcome (ObsRO)	
		☐ Clinician reported outcome (ClinRO)	
		☐ Performance outcome (PerfO)	
	☐	Qualitative studies (e.g., individual patient/caregiver interviews, focus group interviews, expert interviews, Delphi Panel, etc.)	
	☐	Patient-focused drug development or other stakeholder meeting summary reports	
	☐	Observational survey studies designed to capture patient experience data	
	☐	Natural history studies	
	☐	Patient preference studies (e.g., submitted studies or scientific publications)	
	☐	Other: (Please specify):	
☐	**Patient experience data that were not submitted in the application, but were considered in this review:**		
	☐	Input informed from participation in meetings with patient stakeholders	
	☐	Patient-focused drug development or other stakeholder meeting summary reports	
	☐	Observational survey studies designed to capture patient experience data	
	☐	Other: (Please specify):	
	Patient experience data was not submitted as part of this application.		

- Mitigates risks in drug development (patient-centric endpoints)
- Improves trial design to increase patient engagement
- Ensures what is important to patients is measured
- Helps communicating treatment benefit using data important to patients



Insight on patient experience

- What is it like to live with the condition?
- What is the impact of the disease?
- The experience of treatment?
- What do patients think about their current treatment?
- How do patients experience unmet needs?
- What do patients want in a treatment for the condition?
- How do patients view benefit-risk acceptability?
- What are patients' preferences related to outcomes and treatment of their condition?

Inform patient centric-endpoint development

- Have we identified the most relevant concepts to assess based on patient experience and hypotheses of benefit?
- What is the best way to measure these concepts?
- An existing, modified, or newly developed clinical outcome assessment (COA): ClinRO, PRO, ObsRO, PerfO, digital monitoring
- Are the endpoints relevant for patients and can we interpret the endpoints in a meaningful way?

Inform on study design

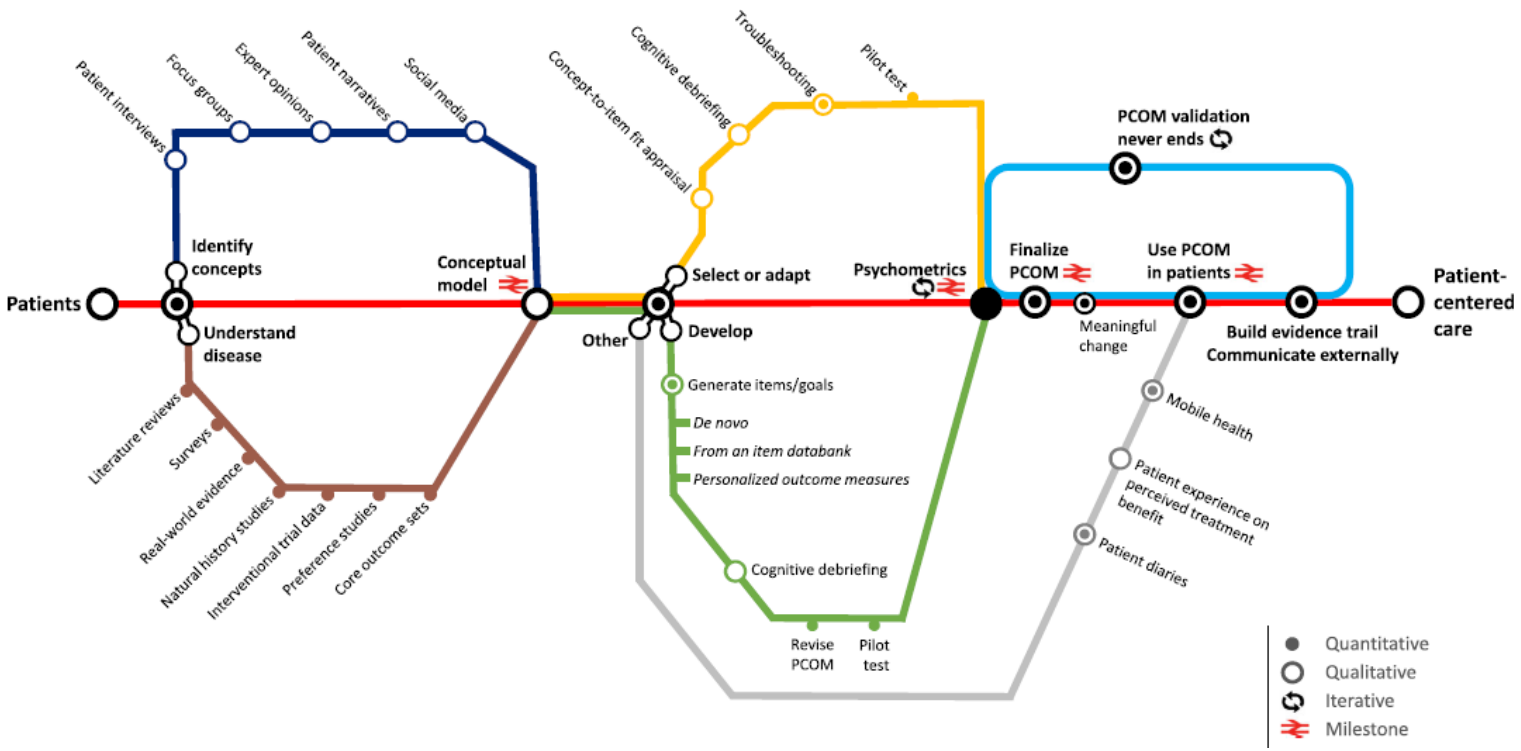
- How can we design clinical trials that work better for patients?
- How can we ensure patient engagement while trials are underway?

Patient Insight & Engagement in HTA Decision Making

PATIENT INSIGHT (Patient-Based Evidence)	PATIENT ENGAGEMENT
• Qualitative evidence synthesis	• Informal discussions with patient organizations on an ad-hoc basis
• Qualitative patient interviews and focus groups	• Open Public Consultation where patients, physicians, and members of the public can comment
• Case studies, patient-reported outcomes studies, and surveys	• Formal processes for submission of written information from patient groups and inclusion as part of the considered evidence
• Qualitative interviews within clinical trials to collect patient experience and understand treatment benefit from a patient perspective	• Involvement during early HTA scientific advice to provide input on the design of clinical trials and ensure evidence generated in clinical trials reflects outcomes of importance to patients
• Social media research	• Representation at committee meetings as patient experts to give testimony and answer questions
• Patient preference studies	• Voting rights in appraisal committees

Enhancing Patient Centricity in HTA: Opportunities in Europe. Fall 2019. The Evidence Forum White Paper. www.evidera.com

Navigation



Roadmap towards greater PCOM use in rare diseases

Patient-centered outcome measures (PCOMs) are core to 'patient-based evidence' [61] and to the realisation of 'patient-centered care' in rare diseases. They highlight the need to systematically include patients in the process of identifying meaningful treatment outcomes that resonate with their experience, preferences, expectations and values [27]. We believe that research and use of PCOMs in the future should be guided by the five principles of: Collaboration, Alignment, Integration, Innovation and Communication.

Morel and Cano *Orphanet Journal of Rare Diseases* (2017) 12:171
DOI 10.1186/s13023-017-0718-x

Orphanet Journal of Rare Diseases

POSITION STATEMENT Open Access

Measuring what matters to rare disease patients – reflections on the work by the IRDiRC taskforce on patient-centered outcome measures

Thomas Morel[1*] and Stefan J. Cano[2]

Abstract

Our ability to evaluate outcomes which genuinely reflect patients' unmet needs, hopes and concerns is of pivotal importance. However, much current clinical research and practice falls short of this objective by selecting outcome measures which do not capture patient value to the fullest. In this Opinion, we discuss Patient-Centered Outcomes Measures (PCOMs), which have the potential to systematically incorporate patient perspectives to measure those outcomes that matter most to patients. We argue for greater multi-stakeholder collaboration to develop PCOMs, with rare disease patients and families at the center. Beyond advancing the science of patient input, PCOMs are powerful tools to translate care or observed treatment benefit into an 'interpretable' measure of patient benefit, and thereby help demonstrate clinical effectiveness. We propose mixed methods psychometric research as the best route to deliver fit-for-purpose PCOMs in rare diseases, as this methodology brings together qualitative and quantitative research methods in tandem with the explicit aim to efficiently utilise data from small samples. And, whether one opts to develop a brand-new PCOM or to select or adapt an existing outcome measure for use in a rare disease, the anchors remain the same: patients, their daily experience of the rare disease, their preferences, core concepts and values. Ultimately, existing value frameworks, registries, and outcomes-based contracts largely fall short of consistently measuring the full range of outcomes that matter to patients. We argue that greater use of PCOMs in rare diseases would enable a fast track to Patient-Centered Care.

Keywords: Patient-centered outcome measures, Rare diseases, Patient-focused drug development (PFDD), Clinical outcome assessments, Patient-reported outcomes, Patient-relevant outcomes, Mixed methods research, Patient centricity, Rasch measurement theory

Background

Rare disease patients are increasingly confronted with a multi-faceted paradox.

First, despite growing acceptance that patients have the clearest view of the health outcomes that matter, the success (or failure) of the majority of rare disease drug development programmes rests on surrogate outcomes (e.g. laboratory measures, organ size) that may not reflect treatment benefits that patients value [1]. Has the rare disease voice been lost in translation?

Second, whilst patients' plea for new treatments was duly heard and resulted in worldwide efforts to accelerate and intensify rare disease research (as attested by the increase in orphan designations granted by regulatory agencies [2–4]), the regulatory approval and the critically important reimbursement of new treatments for rare diseases are increasingly difficult to obtain. This is due, in part, to the lack of demonstration of improvement in meaningful health outcomes for patients.

The difficult choice of which outcomes to measure, the acceptance of surrogate endpoints, and the question of what represents a meaningful treatment benefit for patients have led to heated debates among regulatory agencies. Drug reviews of new orphan drugs aimed at

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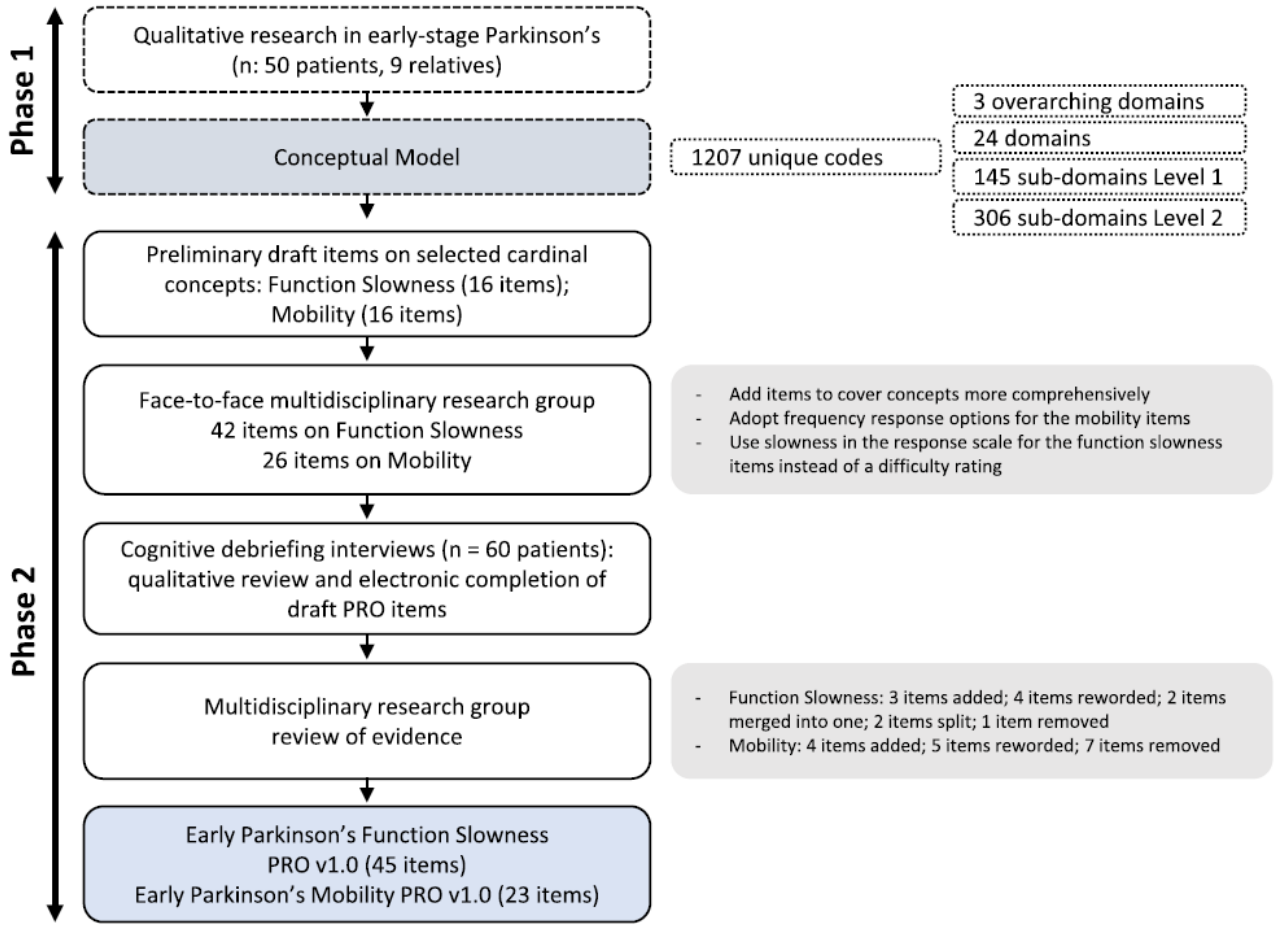

Fig. 1 An overview of the research and development process across phases 1 [17, 19] and 2. PRO, patient-reported outcome

Morel *et al.*
Journal of Patient-Reported Outcomes (2023) 7:40
https://doi.org/10.1186/s41687-023-00577-9

Journal of Patient-Reported Outcomes

RESEARCH Open Access

Development and early qualitative evidence of two novel patient-reported outcome instruments to assess daily functioning in people with early-stage Parkinson's

Thomas Morel[1*], Sophie Cleanthous[2], John Andrejack[3†], Roger A. Barker[4], Milton Biagioni[1], Geraldine Blavat[3†], Bastiaan R. Bloem[5], Babak Boroojerdi[6], William Brooks[3†], Paul Burns[7†], Stefan Cano[2], Casey Gallagher[3], Lesley Gosden[7†], Carroll Siu[7†], Ashley F. Slagle[8], Natasha Ratcliffe[7] and Karlin Schroeder[3]

Abstract

Background Previous research on concepts that are important to people living with early-stage Parkinson's indicated that '*functional* slowness, fine motor skills, and subtle gait abnormalities are cardinal concepts that are not comprehensively captured by existing patient-reported outcome (PRO) instruments that are used in clinical practice and research to assess symptoms and daily functioning within this patient population. We sought to develop novel PRO instruments to address this unmet need.

Methods PRO instrument development was led by a multidisciplinary research group, including people living with Parkinson's (termed 'patient experts'), as well as patient engagement and involvement, regulatory science, clinical, and outcome measurement experts. A first set of PRO instruments, termed Early Parkinson's Function Slowness (42 items) and Early Parkinson's Mobility (26 items), were drafted to capture '*functional* slowness, fine motor skills, and subtle gait abnormalities. These PRO instruments were used in cognitive debriefing interviews with people living with early-stage Parkinson's (who were not involved with the multidisciplinary research group) to identify issues with relevance, clarity, ease of completion, conceptual overlap, or missing concepts.

Results Sixty people living with early-stage Parkinson's were interviewed, which led to refining the items to 45 for the Early Parkinson's Functional Slowness and 23 for the Early Parkinson's Mobility PRO instruments. Refinement included rewording items to address clarity issues, merging or splitting items to address overlap issues, and adding new items to address missing concepts. The Early Parkinson's Function Slowness PRO instrument resulted in a multidimensional instrument covering upper limb, complex/whole body, general activity, and cognitive functional slowness. The Early Parkinson's Mobility PRO instrument resulted in comprehensive coverage of everyday mobility tasks, with a focus on gait concepts, plus complex/whole body, balance, and lower limb mobility.

Conclusions The Early Parkinson's Function Slowness and Early Parkinson's Mobility PRO instruments aim to address gaps in existing PRO instruments to measure meaningful symptoms and daily functioning in people living with

[†]John Andrejack, Geraldine Blavat, William Brooks, Paul Burns, Lesley Gosden and Carroll Siu: Patient expert

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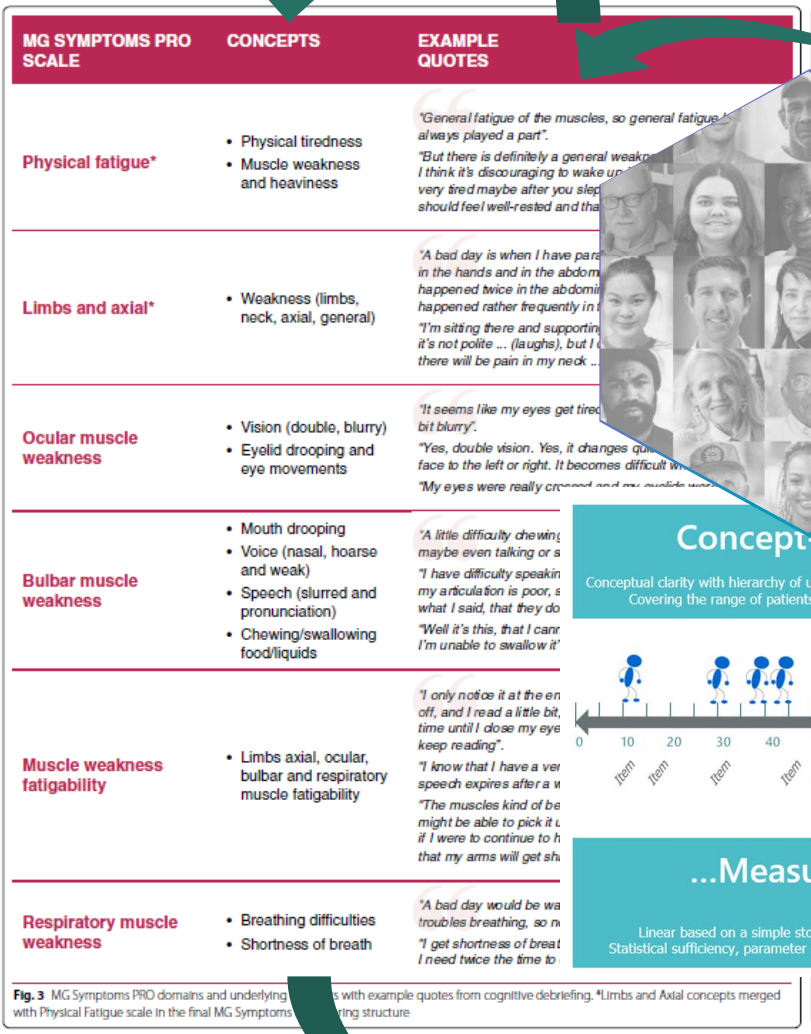

Fig. 3 MG Symptoms PRO domains and underlying ... with example quotes from cognitive debriefing. *Limbs and Axial concepts merged with Physical Fatigue scale in the final MG Symptoms ... ring structure

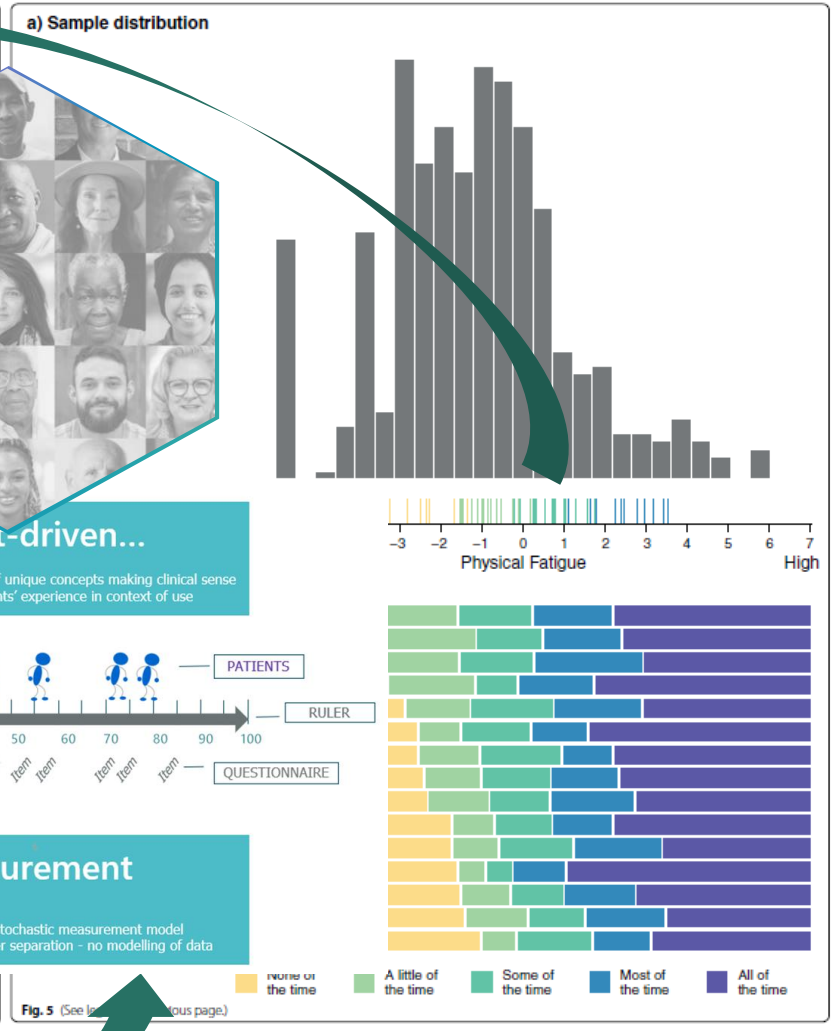

Fig. 5 (See l... ...ous page.)

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Development of the Myasthenia Gravis (MG) Symptoms PRO: a case study of a patient-centred outcome measure in rare disease

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Abstract

Background: Myasthenia gravis (MG) is a chronic autoimmune neuromuscular disease, characterised by fluctuating muscle weakness which makes it challenging to assess symptom severity. Mixed methods psychometrics (MMP), which combines evidence from qualitative research and modern psychometrics, is a versatile approach to the development of patient-centred outcome measures (PCOM) in the context of rare disease. Our objective was to develop the MG Symptom patient-reported outcome (PRO) to assess key aspects of MG severity from the patient perspective.

Methods: We used MMP to develop a novel PRO instrument in a multi-step process. An initial conceptual model for MG patient experience was developed and expanded based on preliminary literature review and two waves of concept elicitation interviews with people with MG (Step 1). Based on this, the novel PRO instrument, the MG Symptoms PRO, was drafted. The draft instrument was refined by combining qualitative and quantitative data collected in a Phase 2 clinical study (Step 2).

Results: Findings from the literature review and concept elicitation interviews (n = 96) indicated that patient experience in MG includes proximal muscle weakness symptoms related to several body parts, along with muscle weakness fatigability and general fatigue. Then, a set of 42 items across five scales (ocular-, bulbar-, and respiratory muscle weakness, physical fatigue, and muscle weakness fatigability) was developed. Qualitative evidence endorsed its relevance, clarity, and ease of completion; quantitative analysis with Rasch measurement theory methods demonstrated strong measurement properties, including good targeting and high reliability. Classical test theory analyses showed adequate reliability of the instrument and mild to moderate correlations with other widely used MG-specific outcome measures.

Conclusions: The MG Symptoms PRO has potential to be used both to measure treatment benefit in clinical trials and monitor symptom severity in clinical practice. Its component scales were purposefully designed to stand alone, enhancing interpretability of scores given the heterogeneity of MG, and enabling modular use. Compared with existing MG PROs, it contains more detailed assessments of muscle weakness and muscle weakness fatigability symptoms, which are of key importance to people with MG. The MMP approach used may serve as a case study for developing PCOMs across rare disease indications.

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Concept-driven measurement leads to patient centric endpoints

25 October 2023

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Questions & Answers

1. What about post-marketing patient experience? (beyond the label "promise")? **Seizure is a great example; we have a lot of drugs which are efficient (prevent seizures) to some extent. But what about the side effect profiles (e.g., change your personality or the way you think) that could affect adherence. With poor adherence due to the side effect profile not being well understood from the patient perspective. Another good example is where hard endpoints are used to evaluate the benefit of the treatment (e.g., hospitalization). But when you talk to patients, they may want symptoms to go away and wouldn't go to the hospital for a variety of reasons (bad experiences, insurance problems, etc..) So, using hospitalizations as a hard endpoint could be misleading as it masks the treatment benefit from a patient perspective.**
2. Can you comment on compliance considerations in engaging patient advocacy groups for a pre-commercial org. vs one that has commercial products on the market? **We worked with patient groups at both stages but much closer to the compliance team post-launch (my experience is that I worked closely with compliance at all stages). An example of what might come up after an approval is when a patient advocacy group has not listed all approved therapies, it is helpful to approach them to add the missing therapy in order to serve their patient community, noting this can take a lot of time (and back and forth) to get updated and you want to be clear that your goal is to ensure that the patient community has all current information in order to make informed decisions about their care.**

Questions & Answers

3. How does the research differ by stage of development? Do you ever do early (Ph1/2)? Would there ever be a need to repeat later on (P3) prior to file/launch? **Since this is building blocks through research, starting early is super important, noting this is very much at the exploratory stage. As time goes on you can confirm your hypothesis and continue to get patient feedback on trial design, patient facing materials, etc. And continue to engage with the patient community as your program advances to get feedback. Then you have needed data and can interpret the benefit with patients/patient community.**
4. When creating a new endpoint, do you involve "KOL" physicians? There are frequently egos associated with creation of endpoints and preference of which scales to use, so curious if important to pull them in (or work independently)? **Yes, the clinical perspective is key, comes down to the personality of the KOL, some are very friendly and understand the patient perspective and others aren't as helpful. My advice is when selecting a KOL, try to understand their background, where they come from and learn about previous interactions with them.**

Questions & Answers, cont'd

4. Have there been any examples of high-quality PROs/Pex data on a product label that have shown to be responsible for some form of competitive advantage? **Yes, one example is related to differentiating on side effects (e.g., less GI side effects, constipation, and nausea) and these eventually were added to the label and were a differentiator.**
5. How do you work with a patient advocacy group /organization that is working with all your competitors as well? I am thinking for example, of some orphan diseases with a lot of pipeline molecules being developed. **You do just that -- work with the patient community, regardless of whether other companies are also working with them. Ensure you have a CDA in place and do your patient-focused drug development work. Ultimately, our collective goal is to ensure the patient community has access to better care and therapies.**