2025

Patient-Centered Value Research Checklist for Rare Disease

CENTER FOR INNOVATION & VALUE RESEARCH

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Center for Innovation & Value Research

Introduction

Our Mission

The Center for Innovation & Value Research (Center) is an independent nonprofit research organization working to make sure that all patients have access to the right care at the right time. Our mission is to advance the science, practice, and use of patient-centered health technology assessment (HTA) to support decisions that make healthcare more meaningful and equitable.

The Checklist

This checklist is mainly designed for value researchers to complete to ensure they are using a comprehensive and patient-centered approach to rare disease value research. It aims to guide researchers in integrating patient engagement into the processes, data, and methods of patient-centered value research.

To further support researchers, the checklist is supplemented with a list of resources, including relevant frameworks, checklists, tools, and similar initiatives. For example, NHC's Patient Compensation Tools are linked within the checklist and in the Supplementary Resources to aid patient engagement research planning.

Key Audience

Value researchers, the individuals who will be using the checklist to guide their research process.

Scope and Focus

HTA includes and builds upon comparative clinical effectiveness research (CER) by incorporating additional dimensions such as cost-effectiveness, budget impact, and societal considerations. However, without robust CER, HTA would lack the necessary clinical evidence to make comprehensive value assessments.[1, 2] Therefore, this checklist addresses both CER and HTA as interconnected and complementary approaches to evaluating treatments and interventions.

1. **Comparative Clinical Effectiveness Research (CER):** Focuses on comparing two or more medical treatments, services, or health practices to help patients and others make better-informed decisions.
2. **Health Technology Assessment (HTA):** Encompasses broader considerations, including cost-effectiveness, societal impact, and resource allocation for evaluating the value, effectiveness, and impact of health technologies.

To aid users, HTA-specific items are highlighted in blue within the checklist contents.

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[1] https://onlinelibrary.wiley.com/doi/10.1111/j.1468-0009.2010.00598.x
[2] https://www.dovepress.com/implementation-of-comparative-effectiveness-research-in-personalized-m-peer-reviewed-fulltext-article-CER

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Checklist Development Process

In the realm of rare diseases, conducting patient-centered outcomes research (PCOR), CER, and HTA presents significant challenges. As advancement in identifying, diagnosing, and treating rare diseases accelerates, the demand for innovative approaches in CER and tools for HTA also rises.

The Center's rare-disease project aims to address challenges in conducting comprehensive CER and HTA that incorporates the full spectrum of outcomes crucial to patients with rare diseases.

In 2023, the Center for Innovation & Value Research partnered with the EveryLife Foundation for Rare Diseases to convene experts and explore common patient-centered outcomes across rare diseases. The project focused on identifying evidence gaps and reaching a consensus on addressing unique research challenges. This effort resulted in a report with prioritized recommendations for identifying patient-centered outcomes in rare diseases.

In 2024, building on these findings, the Center established an advisory board of 19 stakeholders, including individuals with lived experience with and advocates dedicated to rare diseases. Guided by the board, the Center developed a patient-centered framework and checklist aimed at ensuring a patient-centered approach to and meaningful patient engagement in rare-disease value research.

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Rare-Disease Patient-Centered Value Research Checklist

This checklist is organized into **four sections**: **Initiation & Planning, Execution, Monitoring, Dissemination & Assessment**. Each section includes key considerations and guiding questions to guide patient-centered rare disease value research.

Initiation & Planning

1) Early and continuous patient engagement

Objective: Ensure early and continuous patient engagement and that patient and caregiver experiences are integrated and captured throughout the value research process. Engagement should be designed to meaningfully integrate patient and caregiver experiences into all stages of research. The goal is to ensure that patient perspectives shape not only study design and implementation, but also decision-making, such as regulatory approvals, reimbursement, and health technology assessments.

- Have partnerships with patient groups/communities been established during the planning phase?
  (Options: Yes, Partially, No)
  Example: Establish partnerships with patient groups/communities during the planning phase and schedule regular check-ins throughout the study to gather their input and adjust approaches as needed.
- Are key outcomes selected for the research process supported by a rationale derived from data on patient and caregiver experiences?
  (Options: Not at all, Somewhat, Moderately, Substantially, Fully)
  Example: This applies both at the initial selection of outcomes of interest (i.e., patient-relevant factors identified at the start of the research), or later when considering model-derived drivers (i.e., factors identified by the model as influencing outcomes).

2) **Budgeting for patient engagement activities**

Objective: Ensure resources are allocated to support patient engagement, including fair compensation, expense coverage, and training.

- Is there a budget to support engagement that includes compensating patients/patient representatives for their time based on *NHC's Patient Compensation Tools* and to cover their travel and other expenses and efforts?
  (Options: Not at all, Somewhat, Moderately, Substantially, Fully)
  Examples: reimbursement for expenses, non-monetary incentives, or other appropriate forms of compensation that comply with IRS and income-based program regulations.
- Is there a budget allocated to provide needed training for patient/patient representatives based on a needs assessment?
  (Options: Not at all, Somewhat, Moderately, Substantially, Fully)

3) Partner capacity-building

Objective: Ensure patients, researchers, and others involved have the skills and knowledge for effective and meaningful engagement in the value research process.

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(Example resource: Free training courses from CIHR[3]). Capacity building should be tailored to support practical application, ensuring that training is not just theoretical but equips participants with the tools to contribute meaningfully to patient engagement activities across all phases of research.

- Is training available to value researchers to help them understand how to effectively engage with patients?
  (Options: Not at all, Somewhat, Moderately, Substantially, Fully)
- Have you used training programs designed to help rare disease patients understand and engage in the value research process?
  (Options: Not at all, Somewhat, Moderately, Substantially, Fully)

Execution

1) **Representative input and diversity in patient engagement**
   Objective: Ensure diverse representation in patient engagement to capture a comprehensive understanding of their needs. Engagement should be inclusive of individuals across socioeconomic, cultural and literacy backgrounds, using plain-language communication accessible to adults with lower reading levels. Caregiver perspectives should also be incorporated to reflect a full range of patient and family experiences.
   - Considering the target population demographic distribution (e.g., socioeconomic status, racial/ethnic, sex/gender, cultural factors, geographic diversity, age-related factors, disability, accessibility, etc.), has a diverse group of patients been included to ensure input is representative of the target population's experiences and needs? (Example resource: PFDD Guidance 1[4])

     (Options: Not at all, Somewhat (Representation on 1 dimension but not others), Moderately (Representation on 2-3 dimensions but not all), Substantially (Representation on >3 dimensions but not all), Reasonably representative)

   - Are caregivers or proxies engaged for patients who cannot themselves be engaged (e.g., too young, severely cognitively impaired, other health reasons)?
     (Options: Yes, Partially, No, Not applicable)

2) **Accessible communication**
   Objective: Ensure clear communication channels for all stakeholders, especially patients and caregivers from diverse backgrounds, so they are easily able to contribute to the value research process.

[3] https://cihr-irsc.gc.ca/e/27297.html
[4] https://www.fda.gov/drugs/development-approval-process-drugs/fda-patient-focused-drug-development-guidance-series-enhancing-incorporation-patients-voice-medical

(Example resource: NHC Patient Engagement Best Practices[5] provide tools including a project coordinator guide, interview guide template, and health literacy toolkit, to support better communication)

- Have communication methods been designed using plain language and/or translation options to be easily understandable and accessible to individuals with varying levels of health literacy or for language preferences?
  (Options: Not at all, Somewhat, Moderately, Substantially, Fully)
- Have communication methods been adapted to engage geographically or culturally diverse populations, or those with accessibility barriers, ensuring equitable representation in the value research process?
  (Options: Not at all, Somewhat, Moderately, Substantially, Fully)
- Have patients/patient representatives been engaged in the design and deployment of communications to ensure acceptability of the content, design, and methods?
  (Options: Not at all, Somewhat, Moderately, Substantially, Fully)
- Have researchers clearly communicated research purposes and potential outcomes to patients?
  (Options: Not at all, Somewhat, Moderately, Substantially, Fully)

3) Co-creation through bi-directional communication

Objective: Ensure co-creation and bi-directional communication between patients and researchers.

- Is there Is there an established process where patients and researchers work together, with ongoing feedback?
  (Options: Yes, No, Planned)
- Are all materials co-created with patient partners?
  (Options: Not at all, Somewhat, Moderately, Substantially, Fully)

4) Data collection and utilization

Objective: Ensure transparency in data usage and ensure data used meaningfully benefits the rare disease patient community

- Are flexible methods being used to identify and utilize patient experienced data at different stages of the research process (e.g., pre-, during, and post- treatment)?
  (Options: Not at all, Somewhat, Moderately, Substantially, Fully)
  Example: These may include real-time data collection, use of digital tools, or methods that adjust based on emerging insights or patient feedback.
- To what extent are rare disease patients and caregivers informed how their experience data are being used in the value research?
  (Options: Not at all, Somewhat, Moderately, Substantially, Fully)
- Are patient preference-based data sourced from established datasets, surveys, etc. integrated into the value research process?
  (Options: Not at all, Somewhat, Moderately, Substantially, Fully)

[5] https://nationalhealthcouncil.org/issue/patient-engagement/

- Are data related to patient economic burdens (e.g., cost, access, and utilization) sourced from established datasets and integrated into economic evaluations to reflect patient-centered outcomes?
  (Options: Not at all, Somewhat, Moderately, Substantially, Fully)
- Are longitudinal data sourced from established datasets or other reliable resources, incorporated into the economic modeling process to track patient outcomes over time?
  (Options: Not at all, Somewhat, Moderately, Substantially, Fully)
- Have researchers engaged patients, caregivers, or other experts to help identify appropriate data sources and ensure that the data were patient-focused and representative?
  (Options: Yes, Partially, No, Not applicable)

5) **Patient experience data integration into economic modeling**
   Objective: Ensure patient experience data are integrated and meaningfully inform the value assessment process.
   - Where disease-specific outcomes or data are missing, did researchers explore using common outcomes across rare diseases, with disease-specific customization where needed, in the context of economic evaluation?
     (Options: Not at all, Somewhat, Moderately, Substantially, Fully, Not applicable)
   - Are robust methodologies such as mixed methods (e.g., qualitative interviews and quantitative surveys), patient-reported outcome measures (PROMs), or discrete choice experiments (DCEs) being utilized and appropriately incorporated into the HTA process to reflect outcomes and preferences that matter most to patients?
     (Options: Not at all, Somewhat, Moderately, Substantially, Fully)
   - Have the outcomes of focus in the HTA been demonstrated to be important to the rare disease target population?
     (Options: Not at all, Somewhat, Moderately, Substantially, Fully)
   - Are patient preferences consistently integrated into the economic evaluation framework, ensuring alignment with what matters most to patients?
     (Options: Not at all, Somewhat, Moderately, Substantially, Fully)

Monitoring

1) Patient partnership
Objective: Document meaningful patient partnership in value research and adherence to guidelines.

- Have you documented what you did/did not do (with a rationale) regarding patient engagement activities?
  (Options: Yes, Partially, No)
- In addition to this checklist, are there specific guidelines (e.g., NHC rubric, START checklist) you have used to ensure meaningful patient engagement in value research?
  (Options: Yes, No)

2) Incorporation of patient data

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Objective: Ensure that patient experience data is effectively integrated into value research and regularly updated as new data become available. Acknowledge that ongoing updates may be limited by resource or funding constraints and encourage proactive planning for data sustainability where possible.

- To what extent is evidence derived from patient experience data being incorporated into value research?
  (Options: Not at all, Somewhat, Moderately, Substantially, Fully)
- Is there a plan to review and update the assessment as new patient experience data becomes available?
  (Options: Yes, Partially, No, Not applicable)

3) **Acknowledgement of challenges**

Objective: Acknowledge the unique challenges throughout rare diseases value research and take specific actions to address these challenges. These challenges may include limited sample sizes, gaps in patient experience data, and difficulties in achieving demographic diversity, particularly in ultra-rare disease populations.

- Are the unique challenges in rare diseases value research clearly acknowledged in reports/manuscripts/publications? (e.g., challenges in integrating PED, challenges related to patient engagement in value assessment process for rare diseases.)
  (Options: Not at all, Somewhat, Moderately, Substantially, Fully)
- Have specific actions been taken to alleviate these challenges?
  (Options: Yes, Partially, No, Not applicable)

Dissemination & Assessment

1) **Accessible results sharing**

Objective: Ensure that research results are shared in an accessible, understandable, and culturally appropriate way for patients and caregivers.

- Are results shared back with patient and caregiver partners in a meaningful and understandable way? (e.g., using plain language, providing multiple formats such as infographics, charts, or short videos, offering translation options, and acknowledging patient and caregiver contributions in reports or presentations)
  (Options: Not at all, Somewhat, Moderately, Substantially, Fully)
- Are final materials prepared in plain language, addressing health literacy, numeracy, and cultural appropriateness(e.g., using plain language, visual aids, or videos)?
  (Options: Not at all, Somewhat, Moderately, Substantially, Fully)
- Are results shared through methods recommended/most preferred by patient partners (e.g., open access, posting on websites)?
  (Options: Not at all, Somewhat, Moderately, Substantially, Fully)
- Are patient partners appropriately recognized and acknowledged as authors, in acknowledgements, as presenters, and through other methods?
  (Options: Not at all, Somewhat, Moderately, Substantially, Fully)
- Do dissemination efforts include culturally grounded storytelling, relatable communication from researchers, and multiple ways for patients to engage with the findings (e.g., through stories, videos, group discussions, or written summaries?

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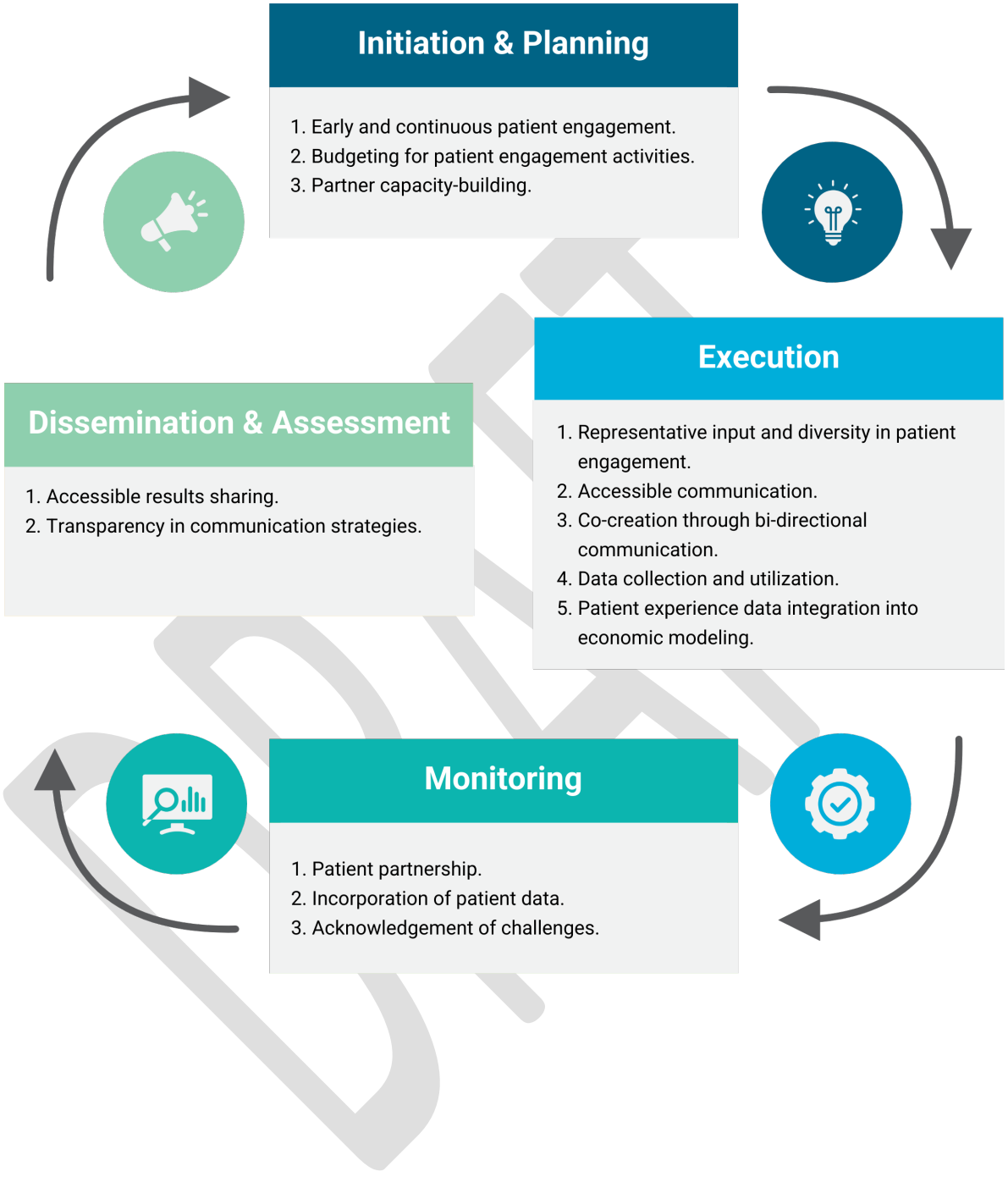
2) Transparency in communication strategies

Objective: Ensure clear and open communication of research goals, methods, and the role of patient involvement to all stakeholders.

Are research goals, methods, and the role of patient involvement clearly communicated to all stakeholders, both at the start of the project and through timely updates during and after the research process? *(Options: Not at all, Somewhat, Moderately, Substantially, Fully)*

- Are patients given meaningful roles in dissemination activities (e.g., being listed as co-authors, co-presenters, or contributing artists) and is mentorship or support provided to enable their participation?
  (Options: Not at all, Somewhat, Moderately, Substantially, Fully)


Initiation & Planning
1. Early and continuous patient engagement.
2. Budgeting for patient engagement activities.
3. Partner capacity-building.
Execution
1. Representative input and diversity in patient engagement.
2. Accessible communication.
3. Co-creation through bi-directional communication.
4. Data collection and utilization.
5. Patient experience data integration into economic modeling.
Monitoring
1. Patient partnership.
2. Incorporation of patient data.
3. Acknowledgement of challenges.
Dissemination & Assessment
1. Accessible results sharing.
2. Transparency in communication strategies.

Appendices

Glossary

Term	Definition
Value Research (also referred to value assessment research)	Value assessment research seeks to accurately define and quantify the value of health care interventions. However, health care stakeholders — patients, payers, providers — often have different opinions on what "value" means to them. Even patients with the same disease may value a treatment differently because of their genetics, clinical contexts, or individual preferences. To illustrate the comprehensive benefits and potential drawbacks of a health care intervention, value assessment research explores how to incorporate diverse elements of value, such as a treatment's impact on patient and caregiver quality of life and productivity and its ability to reduce health inequities. (PhRMA)
Health Technology Assessment (HTA)	HTA refers to the systematic evaluation of properties, effects, and/or impacts of health technology. It is a multidisciplinary process to evaluate the social, economic, organizational and ethical issues of a health intervention or health technology. The main purpose of conducting an assessment is to inform policy decision making. (WHO)
Comparative Clinical Effectiveness Research (CER)	CER is a type of clinical research that compares two or more medical treatments, services, or health practices to help patients and others make better-informed decisions. (PCORI)
Patient-Centered (also referred to as patient-focused)	Ensuring that patients' experiences, perspectives, needs, and priorities are meaningfully incorporated into decisions and activities related to their health and well-being. (PFDD)
Patient-Reported Outcome (PRO)	Any report of the status of a patient's health condition or health behavior coming directly from the patient, without interpretation of the patient's response by a clinician or anyone else. (CMS)
Discrete Choice Experiment (DCE)	A quantitative method used in healthcare to elicit preferences from participants (patients, payers, commissioners) without directly asking them to state their preferred options. In a DCE, participants are

	typically presented with a series of alternative hypothetical scenarios containing a number of variables or "attributes" (usually ≤5), each of which may have a number of variations or "levels". Participants are asked to state their preferred choice between 2 or 3 competing scenarios, each of which consists of a combination of these attributes/levels. Typically, survey instruments include 5-10 such choices to be completed. Preferences are revealed without participants explicitly being asked to state their preferred level for each individual attribute. (York Health Economics Consortium)
Patient Experience Data	Patient experience data can be interpreted as information that captures patients' experiences, perspectives, needs, and priorities related to (but not limited to): 1) the symptoms of their condition and its natural history; 2) the impact of the conditions on their functioning and quality of life; 3) their experience with treatments; 4) input on which outcomes are important to them; 5) patient preferences for outcomes and treatments; and 6) the relative importance of any issue as defined by patients. (PFDD)
Patient partners	People with lived experience, such as patients, family members, caregivers, community members, and organizations that represent a population of interest. They are engaged in planning, conducting and disseminating the research. Patient partners should not be confused with study participants. (PCORI Foundational Expectations for Partnerships in Research)

Supplementary Resources

Additional patient engagement frameworks, checklists, and tools for improving patient-centered value research.

1. **NHC Patient Engagement Best Practices**: A site of National Health Council provides practical strategies and resources for integrating patient engagement into research processes. Available at: NHC Patient Engagement Best Practices
2. **NHC PC-CIS**: The Patient-Centered Core Impact Set (PC-CIS) provides a standardized approach for capturing and incorporating patient-prioritized impacts into research, healthcare decision-making, and value assessment. Available at: NHC PC-CIS.
3. **NHC Fair-Market Value (FMV) Calculator**: The NHC's FMV Calculator, part of the NHC Patient Compensation Tools, provides guidance on how companies can provide fair compensation and reimbursements to patients, caregivers, and patient representatives who are involved in patient-engagement activities. Available at: NHC's FMV Calculator
4. **NHC Rubric**: A rubric to guide the incorporation of the patient voice into the health ecosystem. Available at: NHC Rubric
5. **NHC Value Assessment Get-Ready Checklist:** A value assessment checklist for patient organizations updated in August 2024. Available at: NHC Value Assessment Get-Ready Checklist
6. **PCORI Partnerships in Research**: Engagement resources developed by the PCORI that outlines best practices for involving patients in research. Available at: PCORI Engagement in Research
7. **FDA Patient Engagement Playbook**: Created by the FDA, this playbook provides a comprehensive overview of methods and tools for engaging patients in drug development and regulatory processes. Available at: FDA Patient Engagement Playbook
8. **NORD IAMRARE® Program:** The IAMRARE® Program is a patient-powered research platform developed by the National Organization for Rare Disorders (NORD) that collects patient natural history data and provides training and education materials to accelerate research and improve outcomes for rare diseases. Available at: NORD IAMRARE®

9. **EURORDIS Survey Design Toolkit:** This e-toolkit is a resource hub developed by EURORDIS-Rare Diseases Europe that provides practical guide on survey design adapted to the rare disease context. Available at: EURORDIS Survey Design Toolkit
10. **PFMD Patient Engagement Management Suite**: A global and collaborative platform developed by Patient Focused Medicine (PFMD) that shares resources, practical tools, and guidance for plan, assess and execute any patient engagement initiative. Available at: PEM Suite
11. **NIH Patient Engagement through Pragmatic Clinical Trials (PCT)**: The National Institutes of Health (NIH) Pragmatic Trials Collaboratory site provides resources for patient engagement throughout the PCT research process. Available at: NIH Pragmatic Trials Collaboratory
12. **CIHR Patient Engagement Framework**: A framework published by Canadian Institutes of Health Research (CIHR) for patient engagement throughout the research process. Available at: CIHR Strategy or Patient-Oriented Research
13. **EveryLife Guide to Patient Involvement in Rare Disease Therapy Development**: A guide from EveryLife Foundation for Rare Diseases that provides action steps to patient involvement in rare disease therapy development. Available at: EveryLife Guide to Patient Involvement in Rare Disease Therapy Development
14. **PARADIGM Patient Engagement Toolbox**: A toolbox from Patients Active in Research and Dialogues for an Improved Generation of Medicines (PARADIGM), providing guidance, templates, and resources for patient engagement across the medical development lifecycle. Available at: PARADIGM Patient Engagement Toolbox
15. **PARADIGM framework with metrics:** A framework offers evaluation metrics for assessing patient engagement in the medicine development process. Available at: https://doi.org/10.1111/hex.13191
16. **Aspire4Rare framework for rare disease policy**: A global guidance framework for rare diseases policy. Available at: Aspire4Rare Global Report
17. **Jonker et al. (2023)**: How to START? Four pillars to optimally begin your orphan drug development. *Orphanet Journal of Rare Diseases*, *18*(1). This article demonstrates a tool

that provides an overview of the key pillars to be considered when starting an orphan drug development: Stakeholder mapping, Available information on the disease, Resources, and Target. Available at: https://doi.org/10.1186/s13023-023-02845-9

18. **Klein et al. (2024)**: Measuring and Demonstrating the Value of Patient Engagement Across the Medicines Lifecycle: A Patient Engagement Impact Measurement Framework. Patient, 2024. A framework provides guidance for measuring the value and impact of patient engagement. Available at: https://doi.org/10.1007/s40271-024-00713-7