

# Strategic Framework and Prioritized Recommendations for Patient-Centered Outcomes Research in Rare Diseases

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## OBJECTIVE

The aim is to establish a consensus on recommendations for enhancing patient-centered outcomes research for rare diseases and comprehending the attributes and outcomes significant to patients grappling with rare diseases.

## STUDY DESIGN

A steering committee of 15 members was convened in 2023 to guide this research. Eight multi-stakeholder engagement discussions, including patients, caregivers, payers, manufacturers, employers, regulators, and researchers within the rare disease domain (N=46), were conducted to develop approaches to comparative effectiveness research and value assessment in the context of understanding outcomes important to rare disease patients (Figure 1).

Discussions identified several themes important to consider when identifying patient-centered rare disease outcomes. Multiple recommendations per theme were ranked through a survey to derive a list of prioritized recommendations within each domain based on urgency and feasibility. A targeted literature review of PubMed and gray literature enhanced the understanding of outcomes for 11 specific rare diseases, including Duchenne muscular dystrophy, spinal muscular atrophy, myasthenia gravis, amyotrophic lateral sclerosis, sickle cell disease, amyloidosis, cystic fibrosis, beta thalassemia, hemophilia, Sanfilippo syndrome, and Huntington's disease.

## RESULTS

A total of 999 articles were retrieved using both general and specific rare disease search terms. During the abstract review, an additional 15 articles were incorporated. A review of gray literature through rare disease organization websites and reports (N=30) complemented the findings. After screening, 122 articles were identified as closely addressing patient-centered outcomes (Figure 2).

Seven key themes and several recommendations per theme emerged on what matters most to patients, caregivers, and other stakeholders in developing approaches to identifying rare disease outcomes for comparative effectiveness research and value assessment (Figure 3). Prioritized recommendations include earlier engagement and collaboration with patients/caregivers throughout the drug development timeline, continuous advocacy for research on outcomes significant to patients, and consistent data collection on these outcomes over time.

Through literature review and discussions with stakeholders, patient-centered outcomes common to more than 5 out of the 11 specific rare diseases were identified. These encompass physical functioning (motor, respiratory, and speech), fatigue, sleep, social relationships, pain, mental deterioration, mental health, employment/work impacts, and economic impacts.

Figure 1. Study Approach

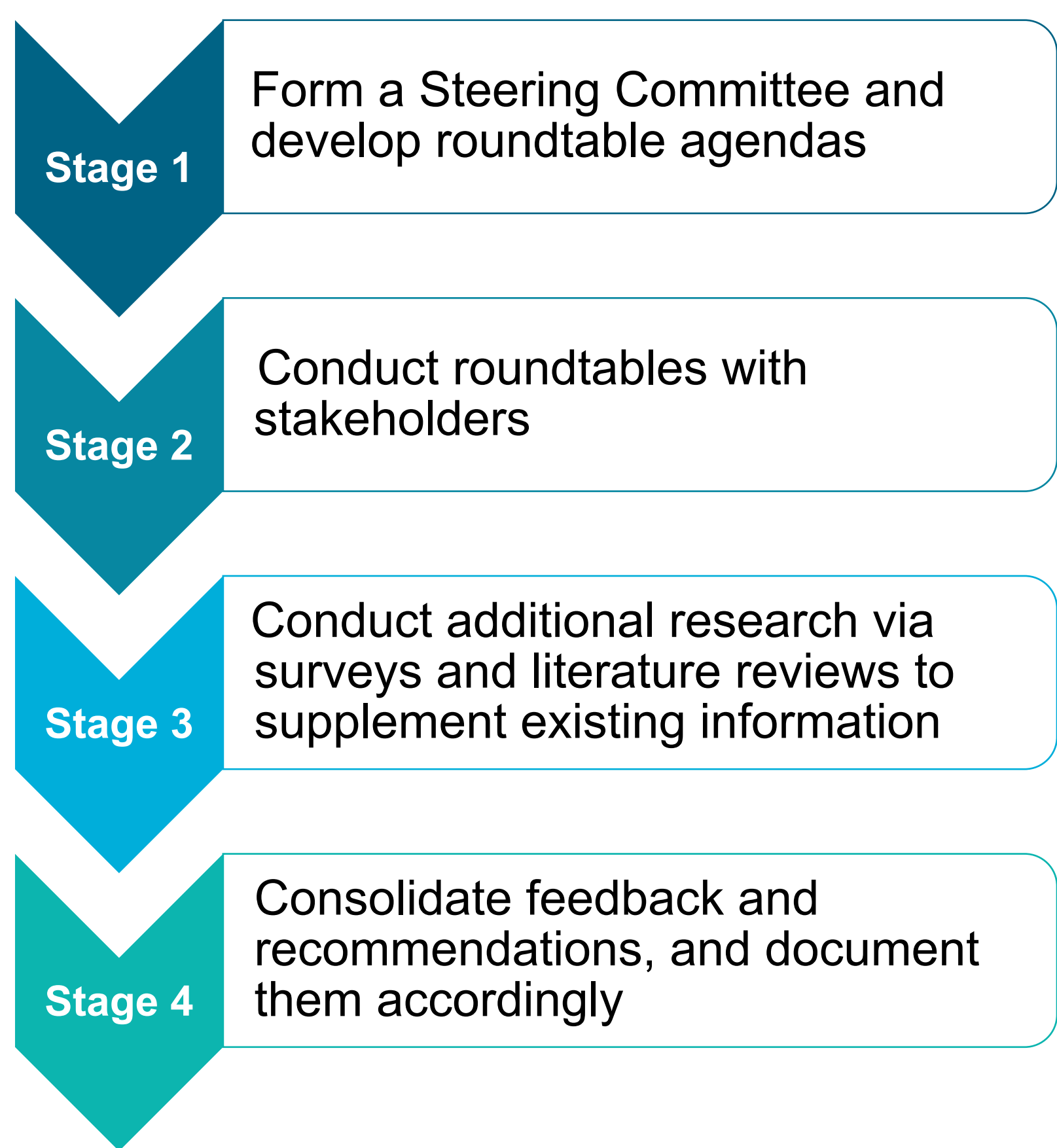
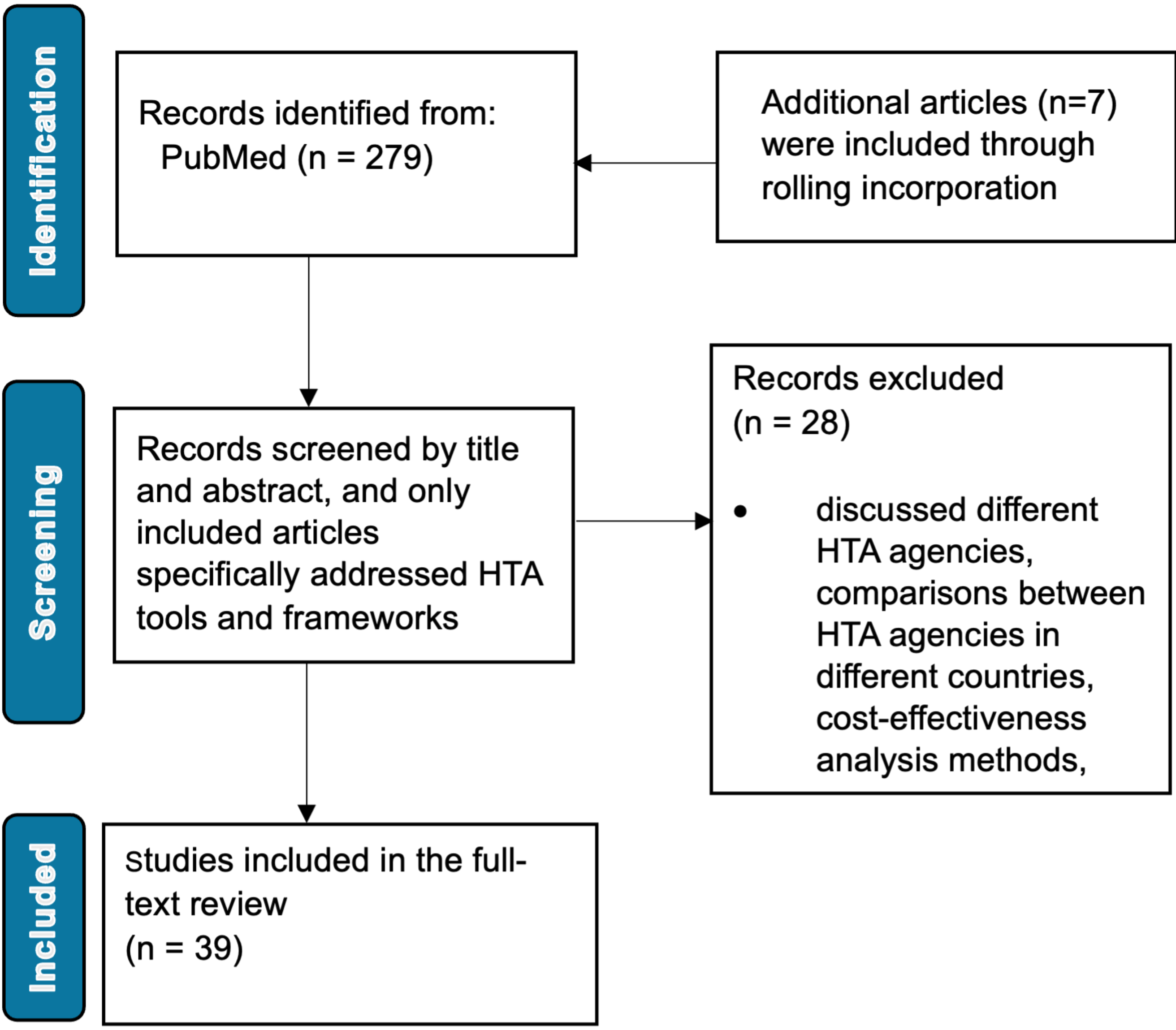


Figure 2. PRISMA Diagram of Literature Review



## CONCLUSION

The key themes identified here offer a strategic framework for addressing research challenges in rare disease therapy evaluation.

Utilizing mixed-methods approaches ensures rare disease outcomes research is more patient-centered.

Understanding common patient-centered outcomes across various rare diseases not only addresses uncertainties in the evidence base but can also alleviate the burden on researchers tasked with defining outcome measures for each individual disease.

Implementing this framework into actual practice would represent a pivotal step towards advancing patient-centered outcomes research for rare diseases.

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Figure 3. Seven Key Themes

- Patient Journey and Time**
  - The patient journey and time, which include the disease's natural history and its evolving impact on patients, is important to consider when identifying and prioritizing outcomes important to rare disease patients.
- Caregiver Journey**
  - Throughout a patient's health journey, caregivers provide vital support, assistance, and advocacy for their loved ones. It is essential to understand the health and other impacts on caregivers.
- Early and Continuing Engagement and Communication**
  - Initiating and continuing patient/caregiver engagement with other stakeholders is critically essential to conducting fully patient-centered research and decision-making.
- Data and Methods**
  - Comprehensive, representative data plays an important role in value assessment and patient-centered outcomes research, especially when dealing with rare diseases. Collaboration should be encouraged to enhance data collection; and mixed (quantitative and qualitative) methods should also be promoted to incorporate lived experiences as meaningful input.
- Economic Impacts**
  - Understanding the economic impacts on patients and caregivers can help payers and other decision-makers to better design plans and strategies to ultimately improve patients' experiences and outcomes.
- Scientific Spillovers**
  - Innovative treatments developed for one rare disease may be re-purposed or modified to treat additional rare diseases. Given the limited resources and data available for study of rare disease treatments, this value could be especially beneficial.
- Identifying Common Patient-Centered Outcomes for Economic Modeling**
  - Identifying common patient-centered outcomes across rare diseases can help accelerate cross-cutting research, enhancing our understanding of diseases themselves, and potentially streamline comparative effectiveness research and value assessments.