# Advancing Patient-Centered Outcomes Research for Rare Diseases: A Mixed-Methods Approach

Michelle Y. Cheng, MHS[1], Richard H. Chapman, PhD[1], Annie Kennedy[2]
[1]Innovation and Value Initiative, Alexandria, VA, USA, [2]EveryLife Foundation For Rare Diseases, Washington, DC, USA

PCR199

## BACKGROUND

Rare diseases collectively impact over 30 million people in the United States and impose a significant economic burden estimated to be $997 billion per year. However, due to the limited number of patients affected by any individual rare disease, conventional research methods face challenges in effectively studying them. Therefore, novel approaches to measuring outcomes and conducting research are needed. The goal is to comprehend attributes and outcomes that hold significance for patients grappling with rare diseases.

## METHODS

A targeted literature review was conducted in PubMed to retrieve English language articles through March 31, 2023. Search strings included terms related to "rare disease," "health technology assessment," and "economic evaluation" in either the title/abstract or MeSH terms. Search terms were refined through discussions with a Steering Committee and revised multiple times to ensure comprehensive coverage.

Titles and abstracts were screened and categorized into 13 different categories by topic within HTA (including framework, methods for economic evaluation, reimbursement and pricing, methods for comparative effectiveness research/patient-centered outcomes research, tools, policy, data, engagement process, patient engagement procedure specifically, budget impact, diagnosis issue, and others), and classified into either "rare disease in general" or "specific rare disease(s)." Articles were excluded if they reported on HTA processes that did not deal with treatments of rare diseases.

To enhance our understanding of outcomes for 11 specific rare diseases, we conducted targeted literature reviews on 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. A review of gray literature was also conducted to supplement the findings. **(Figure 1).**

## RESULTS

A total of 279 articles were retrieved for title and abstract screening. Of these, 51 were excluded for not meeting the inclusion criteria. Among the remaining 228 articles, more focused on HTA frameworks and methods, with fewer discussing patient engagement processes specifically **(Table 1)**. Additionally, there was a greater emphasis on "rare disease in general" rather than specific rare diseases.

A secondary search was conducted on 11 specific rare diseases, which yielded 999 articles from PubMed. Subsequently, an additional 15 articles were included during the abstract review, resulting in a total of 1014 articles for title and abstract screening. Gray literature from rare disease organization websites and reports (N=30) complemented these findings. After screening, 122 articles were identified as closely addressing patient-centered outcomes **(Figure 1).**

Targeted literature reviews and discussions with stakeholders were used to identify patient-centered outcomes common to more than 5 out of the 11 specific rare diseases listed above. These were: physical functioning (motor, respiratory, and speech), fatigue, social relationships, pain, mental deterioration, mental health, employment/work, economic impacts, and sleep **(Figure 2).**

**Figure 1. PRISMA Diagram of Literature Search**

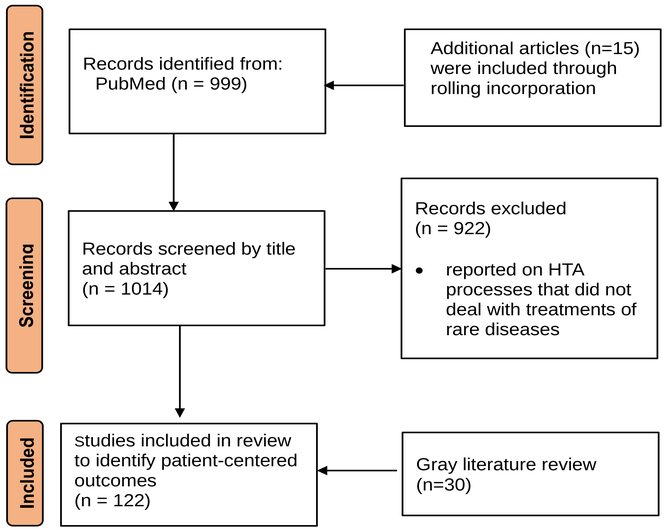
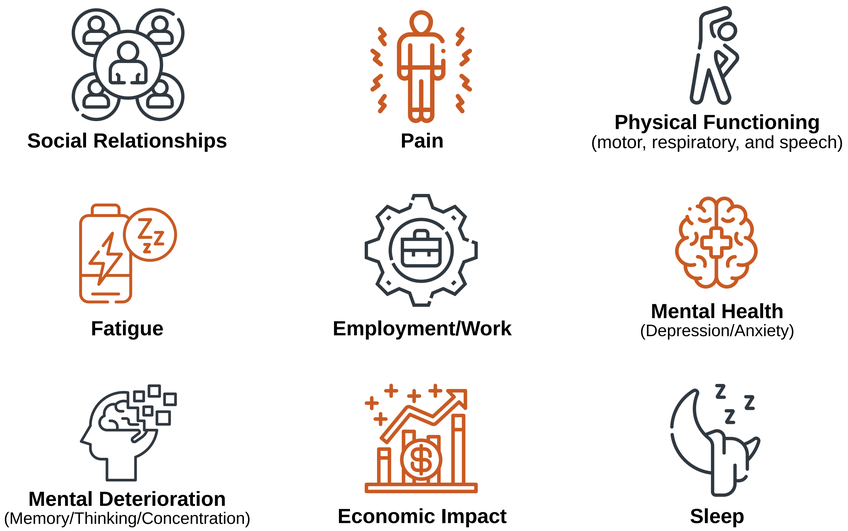



**Table 1. Results of Literature Review by Article Topic**

| Category | Rare disease in general | Specific RD(s) | Grand Total (N) | Grand Total (%) |
|---|---|---|---|---|
| HTA - framework (e.g., conceptual resources, frameworks, key definitions, principles, guidance and recommendation) | 37 | 5 | 42 | 18.42% |
| HTA - method for economic evaluation e.g, CEA, cost of illness) | 23 | 18 | 41 | 17.98% |
| HTA - reimbursement and pricing | 31 | 6 | 37 | 16.23% |
| HTA - method for CER/ PCOR e.g., PRO, patient centered outcome) | 15 | 18 | 33 | 14.47% |
| HTA - tools (e.g., evaluation criteria, checklist) | 16 | 2 | 18 | 7.89% |
| Policy | 13 | 4 | 17 | 7.46% |
| HTA - data | 6 | 5 | 11 | 4.82% |
| HTA - patient engagement procedure specifically | 6 | 4 | 10 | 4.39% |
| Budget impact | 4 | 2 | 6 | 2.63% |
| Diagnosis issue | 2 | 3 | 5 | 2.19% |
| HTA - engagement process | 2 | 2 | 4 | 1.75% |
| Other | 3 | 1 | 4 | 1.75% |
| Total | 158 | 70 | 228 | 100.00% |

**Figure 2. Common Outcomes Across ≥Five of Eleven Rare Diseases**




## CONCLUSIONS

**A focus on patient engagement has been relatively rare in the published literature on HTA and rare diseases.**

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

**Moreover, this approach has the potential to expedite cross-cutting research, offering deeper insights into patient preferences and enhancing the timeliness of value assessments of emerging technologies for rare diseases.**

## CONTACT

> Email: michelle.cheng@thevalueinitiative.org
> Website: https://thevalueinitiative.org/rare-disease-initiative/