Overview of Rare Disease Patient-centered Studies Methodologies and Recommendations to Overcome Challenges

RWD218

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Introduction and study objectives

Background: Over 300 million people worldwide live with a rare disease, yet capturing their perspectives in research remains challenging due to extremely **small** and **heterogeneous** patient populations[1]. Patient-centered studies (PCS) help ensure that patient voices are heard in rare disease research[2].

Objective: Identify and recommend **optimal PCS methodologies** for rare diseases that overcome these challenges, thereby improving how patient insights inform rare disease outcomes research.

Methods

Literature search and data synthesis

- A targeted literature search was conducted on PubMed using generative artificial intelligence to identify studies from 2020 to 2025 in Asia Pacific (APAC) regions, based on predefined search terms and eligibility criteria (Table 1).
- Predefined prompts and Qwen2 model[3], a series of large language models, were applied to generate structured outputs, which can be used as filters in Microsoft Excel to exclude reviews, meta-analyses, and case reports.
- Study objectives, populations, methodologies, and limitations were extracted and analyzed using narrative synthesis[4-5].

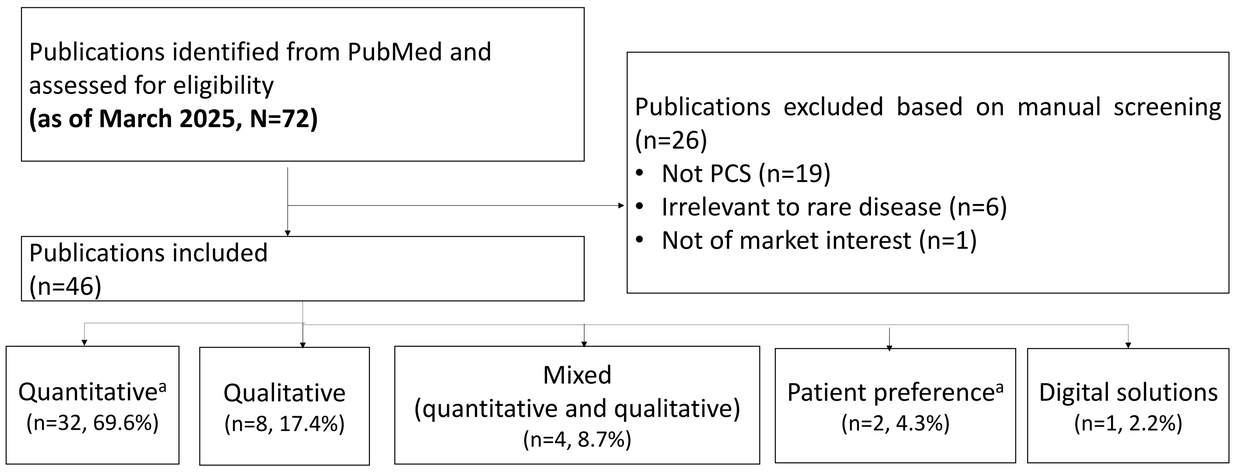
Table 1. Search strategy and eligibility criteria for literature search

Items	Definitions	Items	Definitions
Data sources	• PubMed	**Search terms**	#1 AND #2 AND #3
Publication period	2020 – March 2025	#1	"rare disease" OR "rare disorder"
Inclusion criteria	• Patient-centered studies • Studies related to rare disease	#2	"quality of life" OR "survey" OR "questionnaire" OR "Delphi" OR "DCE" OR "discrete choice experiment" OR "patient centered" OR "patient-centric" OR "patient centric" OR "patient-centered" OR "patient preference"
Exclusion criteria	• Studies published in non-English language • Review articles, systematic review and meta-analyses, RCTs, case studies, cost analysis, protocols • Non-human studies	#3	"Australia" OR "China" OR "Hong Kong" OR "Korea" OR "Japan" OR "Singapore" OR "Taiwan"

Results

- Among 72 identified publications, 46 were included for analysis. Quantitative methods (69.6%) predominated, followed by qualitative (17.4%), mixed methods (8.7%), preference studies (4.3%), and digital solutions (2.2%) (Figure 1).
- Nearly half of PCS were found to understand knowledge, attitude, and practice (KAP) (46.8%), followed by disease burden (29.9%), financial burden (11.7%), and therapeutic options (10.4%) (Table 2).
- When stratified by research theme, multiple approaches can be considered to understand KAP, disease burden and therapeutic options, whereas quantitative approach may be primarily considered to understand financial burden (Figure 2).
- Common limitation across methodologies included limited sample size, selection bias, and high heterogeneity. Various solutions applied in the identified publications can be implemented, which are synthesized in Table 3.

Figure 1. Study flow diagram of literature review



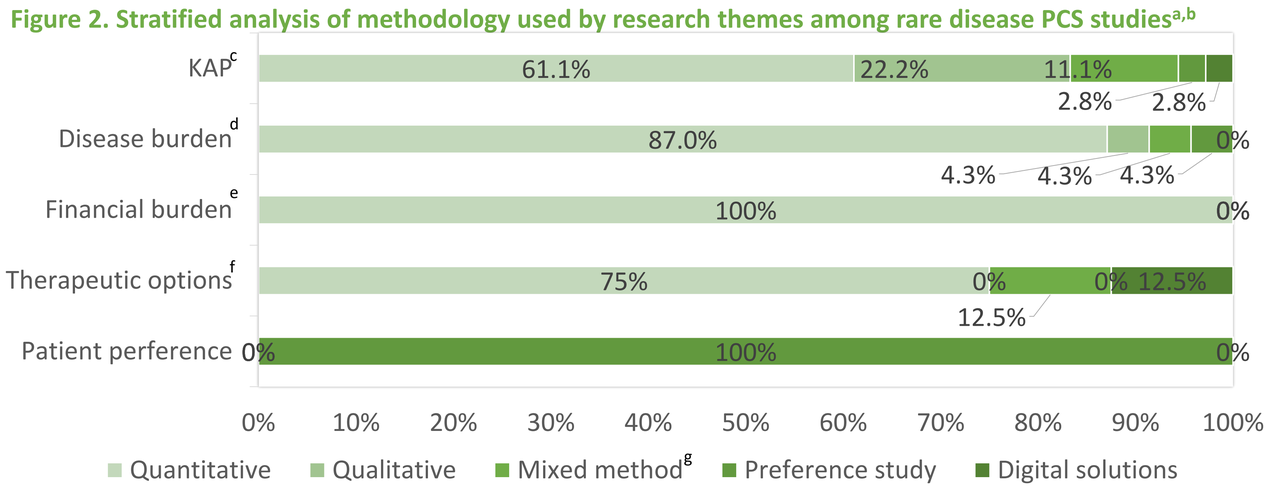
Footnote: [a]one publicaiton was both a quantitative study and a preference study because it measured HRQoL and examined the relationship between respondents' socioeconomic characteristics and preference-based health utility scores
Abbreviation: HRQoL, health-related quality of life

Table 2. Methodology used by research themes among rare disease PCS studies

Research theme[a]	N	%[b]
KAP[c]	36	46.8%
Disease burden[d]	23	29.9%
Financial burden[e]	9	11.7%
Therapeutic options[f]	8	10.4%
Patient preference	1	1.3%

Footnotes: [a]multiple research themes may be addressed within a single publication; [b]the denominator refers to the total number of research themes identified across all publications; [c]included disease awareness, knowledge, and understanding of prior experience or clinical practice; [d]included disease prevalence, quality of life, and utility; [e]included cost and healthcare resource utilization; [f]included treatment patterns

Figure 2. Stratified analysis of methodology used by research themes among rare disease PCS studies[a,b]



Footnotes: [a]multiple research themes may be addressed within a single publication; [b]the denominator refers to the total number of each individual research theme; [e]included disease awareness, knowledge, and understanding of prior experience or clinical practice; [d]included disease prevalence, quality of life, and utility; [e]included cost and healthcare resource utilization; [f]included treatment patterns; [g]mixed methods included quantitative and qualitative approaches

Table 3. Solutions to overcome the challenges of rare disease PCS methodologies

Challenges of rare disease PCS methodologies	Solutions and recommendations
Limited sample size	• Collaboration with patient groups, arranging patient advocacy or leveraging social media could supplement qualitative concept elicitation
	• Combining populations with similar disease presentations could increase the sample size for evaluating quality of life
Selection bias	• Stratified sampling methods could mitigate selection bias
High heterogeneity	• Developing a tailored, multi-attribute questionnaire can enhance applicability of outcomes across heterogeneous RD manifestations
	• Deploying a mixed method could provide an in-depth understanding of humanistic burden of RD

Conclusions

Dominance of quantitative methods among rare disease PCS studies:

- While quantitative approaches predominated, this study indicates that surveys and other quantitative tools have been the go-to choice, but other methodologies (qualitative and mixed-method studies) remain underutilised.
- Leveraging these underused approaches can address additional research questions – for example, exploring patient experiences or preferences that numbers alone might not fully captured.

Fit-for-purpose study designs are recommended to overcome rare disease research challenges

- Researchers should consider strategies like combining multiple methods, adaptive sampling, or collaboration with patient registries to counteract limited sample sizes, mitigate selection bias, and handle high heterogeneity in patient populations.
- Implementing such tailored designs will enhance the robustness and relevance of PCS findings, ensuring that insights are credible and truly reflective of the rare disease community.

Abbreviations: PCS, patient-centered studies; RD, rare diseases; APAC, Asia Pacific; KAP, knowledge, attitude, and practice.

References: 1. Gagnon et al. J Neuromuscul Dis . 2021;8(6):1017-1029; 2. Lanar, S., et al. Orphanet J Rare Dis 15, 134 (2020); 3. Qwen2 Technical Report. Available from: https://arxiv.org/abs/2407.10671. Accessed 17 Aug 2025
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