CO130

Health-related Quality of Life (HRQoL) Impacts in Individuals With Hypophosphatasia (HPP): A Systematic Literature Review (SLR)

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Background

- Hypophosphatasia (HPP) is an inborn error of metabolism characterized by various clinical manifestations, including skeletal abnormalities, muscle weakness, pain, and renal manifestations.[1-3]
- With limited treatment options, the unmet needs and burden remain high for adults with HPP.[4]
- Characterizing the health-related quality of life (HRQoL) impacts for adults with HPP would be valuable to better understand the benefits of novel treatments for these patients.

Objectives

To characterize HRQoL in adults with HPP, and highlight evidence gaps that remain in the literature.

Methods

- A systematic literature review was conducted to identify studies reporting HRQoL in HPP (**Figure 1**).

Figure 1 *Systematic literature review approach*

1. Literature search
- Databases: MEDLINE, Embase, and Northern Light

2. Study selection
- Abstract and full-text review were conducted by two reviewers against eligibility criteria.

3. Data synthesis
- Data were tabulated and narratively synthesized

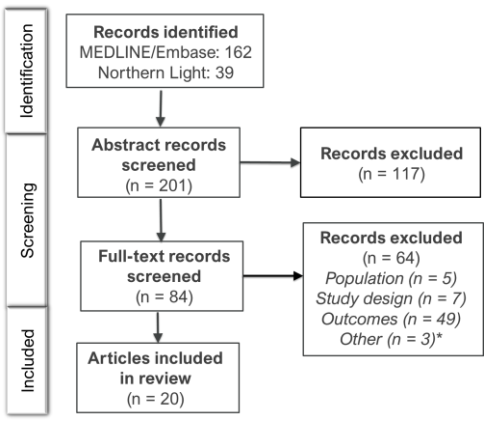
Eligibility criteria
- **Population:** adults with HPP (≥18 years)
- **Outcomes:** HRQoL, pain, fatigue, mental health
- **Study design:** clinical trials; observational studies
- **Other:** published from 2010 to present

Abbreviations: HPP, hypophosphatasia; yrs, years; HRQoL, health-related quality of life.

Results

- 21 articles were included (**Figure 2**), which described HRQoL using standardized instruments.
- None of the instruments were specific to HPP.
- Assessments of HRQoL covered a variety of components (**Table 1**).
- Scores using the Short Form Surveys (SF-36 and 12) were below population norms across Physical Component Summary (PCS) scores (**Figure 3**).

Figure 2 *PRISMA flow diagram*



Abbreviations: PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses
*Unable to access full text for 3 conference posters

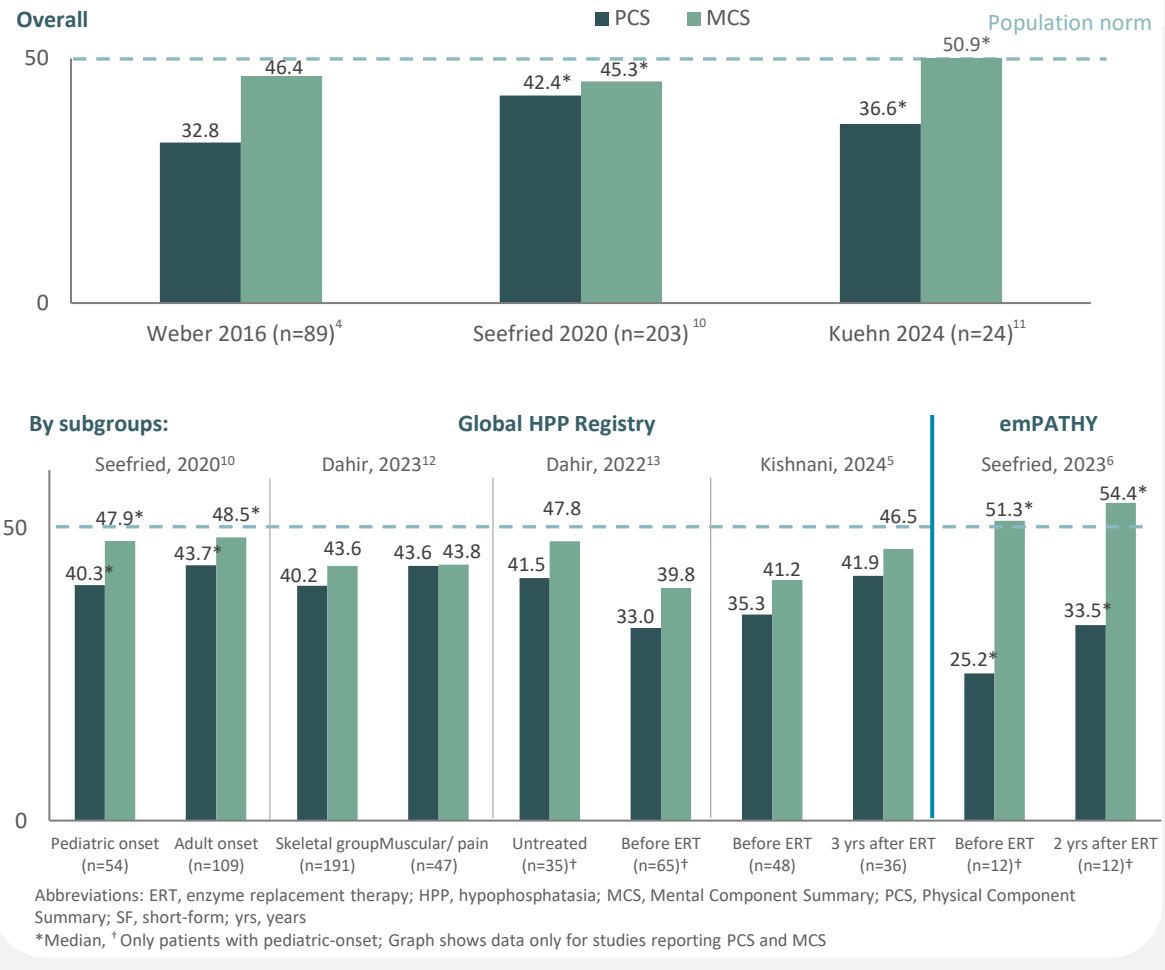
- In two cohorts, a statistically significant improvement in PCS scores was reported during the first year of enzyme replacement therapy (ERT),[5,6] though one study found no changes afterward.[5] Further, no statistically significant improvements were reported in disability scores (one study),[5] or Mental Component Summary (MCS; two studies) scores after ERT.[5,6]
- Work productivity improved within one year of ERT, though gains reversed or plateaued thereafter.[7]
- Two cross-sectional studies reported statistically significantly higher fatigue in adults with HPP versus the general population; [8,9] levels of anxiety, depression and stress were also higher.[8]

Table 1 *Overview of HRQoL instruments used to evaluate adults with HPP*

HRQoL instrument	Number of publications (sample sizes)	Age at diagnosis range (in years)
Generic HRQoL		
SF-36 / SF-12	9 (N = 12 – 203)	37.1 – 51.5
HAQ-DI	4 (N = 38 – 212)	37.1 – 43.2
PROMIS-29	2 (N = 12 – 50)	-
Pain		
BPI	4 (N = 10 – 203)	27.0 – 40.9
VAS	2 (N = 25 – 40)	51.5
PDI	1 (N = 26)	51.5
Fatigue		
FSS	2 (N = 14 – 17)	-
FAS	1 (N = 26)	51.5
Mental health		
PHQ	2 (N = 12 – 50)	-
DASS	1 (N = 14)	-
Symptom-specific		
RAPID-3*	2 (N = 12 – 50)	-
Work impact		
WPAI	2 (N = 12 – 33)	-

Abbreviations: BPI, Brief Pain Inventory; DASS, Depression, Anxiety, and Stress; FAS, Fatigue Assessment Scale; FSS, Fatigue Severity Scale; HAQ-DI, Health Assessment Questionnaire-Disability Index; HPP, hypophosphatasia; HRQoL, health-related quality of life; PDI, Pain Disability Index; PHQ, patient health questionnaire; PROMIS, Patient-Reported Outcomes Measurement Information System; RAPID-3, routine assessment of patient index data 3; SF, Short Form; VAS, Visual Analog Scale; WPAI, Work Productivity and Impairment Questionnaire
*Measures rheumatoid arthritis disease activity

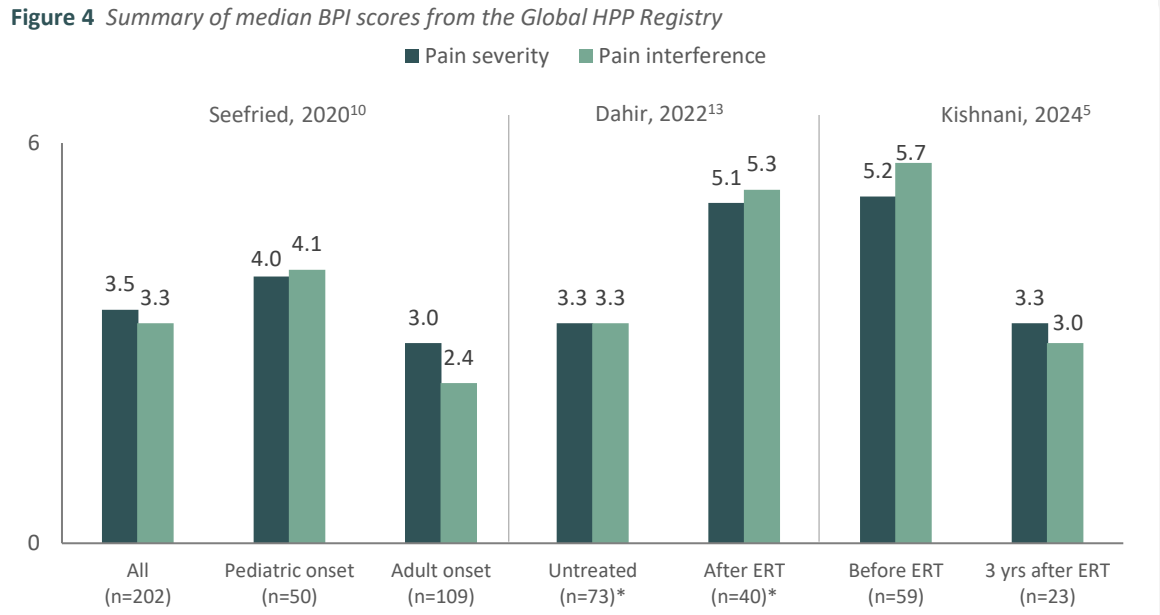
Figure 3 *Summary of mean/median SF scores*



Abbreviations: ERT, enzyme replacement therapy; HPP, hypophosphatasia; MCS, Mental Component Summary; PCS, Physical Component Summary; SF, short-form; yrs, years
*Median, † Only patients with pediatric-onset; Graph shows data only for studies reporting PCS and MCS

- Pain severity and interference were notable across Global HPP Registry populations. Though reduction in pain was observed following ERT, pain still impacted patients (**Figure 4**).

Figure 4 *Summary of median BPI scores from the Global HPP Registry*



Abbreviations: BPI, Brief Pain Inventory; ERT, enzyme replacement therapy; HPP, hypophosphatasia; yrs, years
*Only patients with pediatric-onset; Graph shows data only for studies reporting BPI scores on pain severity and pain interference

Data summary

- Available evidence suggests that adults with HPP experience substantial impacts in physical functioning, fatigue, and disability, although findings vary by study design and size.
- Though currently available therapies provided benefits, improvements in individual components of HRQoL, including pain, mental well-being, and disability, were unclear.

Evidence gaps

- As HRQoL was evaluated using instruments that were not specifically designed to capture the symptoms and impacts of HPP, findings may not adequately represent the burden for those with HPP.
- For example, while evidence on mental health was available, the specific impact of cognitive dysfunction that individuals with HPP experience remains unclear. The underpinnings of the neurological/cognitive effects of HPP are poorly understood, and sensitive tools to quantify either the deficits or improvements are lacking.[9]
- Evidence on impacts of HPP on daily living were also sparse, with limited data available on work impacts. Such data would be especially valuable to understand the burden for an adult population, and how novel treatments could address this burden.

Conclusion

Adults with HPP have considerable HRQoL burden, including those receiving existing therapies. These findings highlight the need for new interventions that deliver sustained improvements. Additionally, the findings highlight a gap in existing measures, which may not fully capture the nuances of HPP or the potential value of emerging therapies through meaningful outcomes assessments.

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