

Triangulation approach to develop a conceptual framework for the patient-reported outcome measures across the life cycle: a case of patients with x-linked hypophosphatemia

Hyun Jin Han^{1,2} and Hae Sun Suh^{1,2,3} *

1 Department of Regulatory Science, Graduate School, Kyung Hee University, Seoul, Republic of Korea
2 Institute of Regulatory Innovation through Science (IRIS), Kyung Hee University, Seoul, Republic of Korea
3 College of Pharmacy, Kyung Hee University, Seoul, Republic of Korea

*Corresponding author

Pharmaceutical Economics
Big Data Analysis and Policy Lab

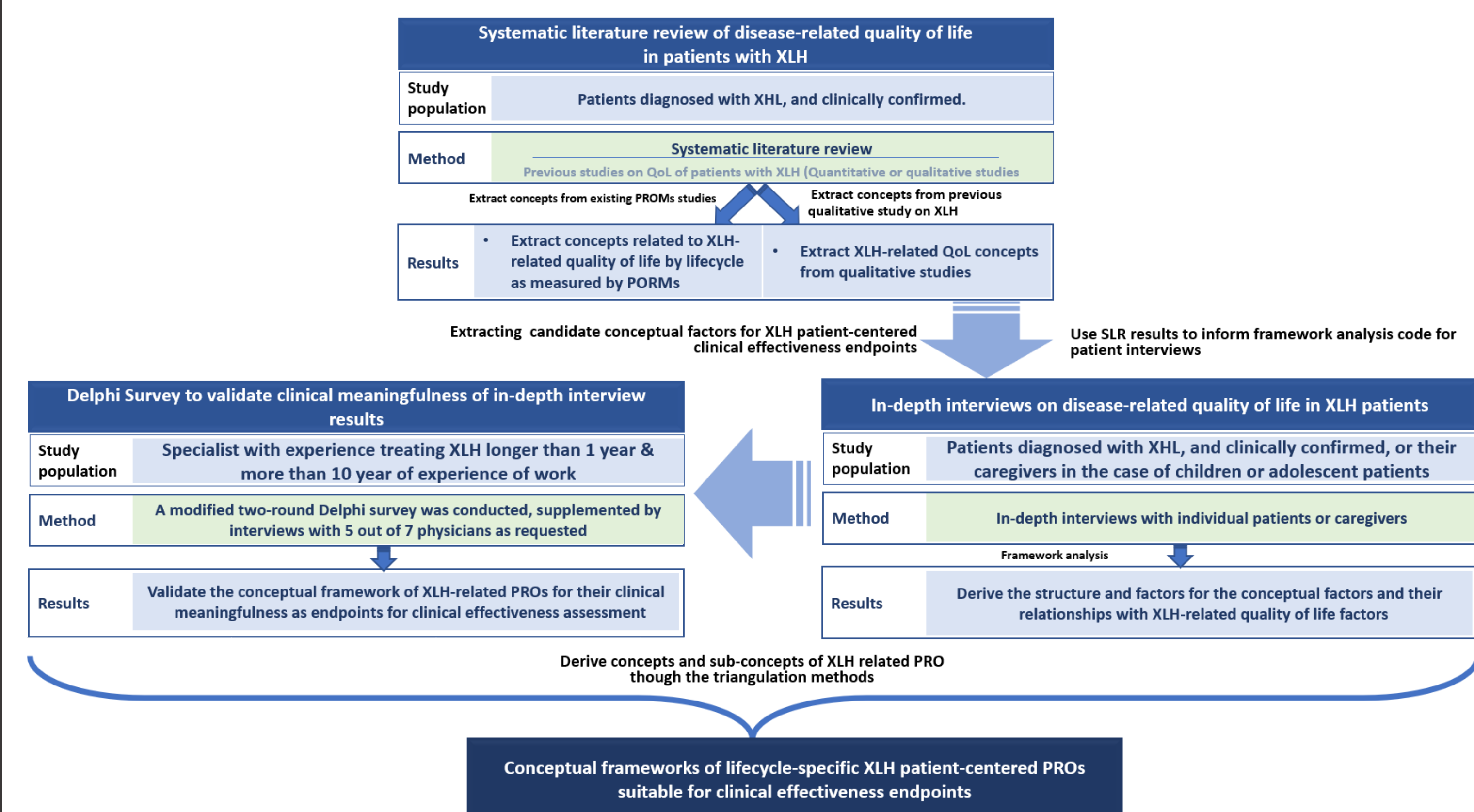
hyunjin.han@gmail.com

Background

- X-linked hypophosphatemia (XLH) is a rare genetic disorder causing phosphorus wasting and leads to poor bone mineralization, resulting rickets and skeletal, muscular, and dental manifestation throughout the life^{1,2,3}.
- In the process of developing a conceptual framework for patient-reported outcomes (PROs), it is recommended to apply various literature, expert, and patient perspectives to derive a more appropriate conceptual model, but patient participation in research is very limited^{4,5,6}.
- **Objective:** This study aims to develop a comprehensive and clinically meaningful conceptual framework for patient-reported outcome measures (PROMs) in X-linked hypophosphatemia (XLH) through triangulation method.

Methods

Study design



Qualitative analysis

- Informed framework analysis was performed based on the systematic literature review using MAXQDA Analytics Pro 2022 (BERBI GmbH Berlin) and Microsoft Excel (Microsoft Corporation).

Results

- Based on the SR results, we extract 22 main themes and 127 sub-themes. These themes were compared with previously developed .
- A total of 11 participants, XLH patients (n=4) and caregivers of pediatric patients (n=7) were interviewed.
- 5 Out of 7 specialists with experience of treatment of XLH patients were participated 2 round modified Delphi survey.
- We identified the differentiated HRQoL conceptual frameworks for adult and children: 6 main and 19 sub domains for adult, and 11 main and 32 sub domains for children (Figure 2).

Table 1. Baseline characteristics of participants of in-depth interview

No	Participants	Sex	Age	Age at diagnosis (year)	Procedure /surgery experience
P-1	Patient	Female	38	4	
P-2	Patient	Female	46	6	○
P-3	Patient	Female	32	2	○
P-4	Patient	Female	26	1.5	○
P-5	Caregiver	Male	5	1.6	○
P-6	Caregiver	Male	9	0.9	○
P-7	Caregiver	Female	9	3	
P-8	Caregiver	Male	8	1.7	
P-9	Caregiver	Female	7	1.5	
P-10	Caregiver	Male	14	5	○
P-11	Caregiver	Female	3	1.7	



The triangulation approach enabled us to develop a conceptual framework of HRQoL in XLH, despite the limited literature and patient numbers, and it uncovered the differences in the factors that constitute the conceptual framework of patient-reported quality of life outcomes between adults and children/adolescent.

Results (continued)

Figure 1. PRISMA

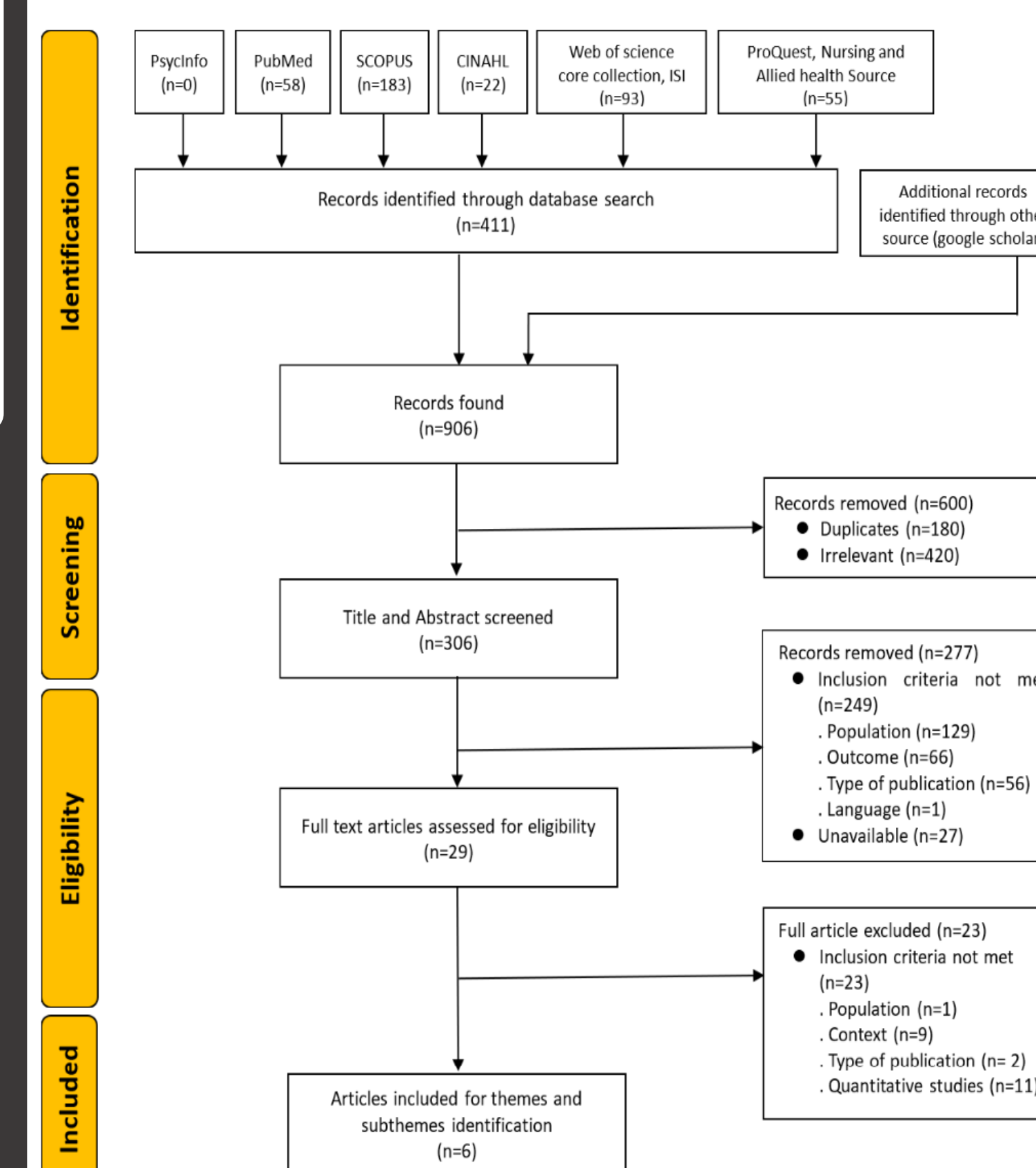


Table 2. Main and sub themes extracted from SR

Main Themes	Sub-themes	Main Themes	Sub-themes
Musculoskeletal	Stiffness/difficulty bending torso or joints	Psychological (cont.)	Shame
	Stiff shoulders		Anxiety (worrying condition)
	Stomach discomfort		Depression
	Joint weakness/Sore bones/Back pain		Stress or run-down/lost sleep
	Chronic fatigue		Resentment
Pain	Chronic/difficult anomalies	Education	Regrets
	Fracture		Reaching in the night due to pain
	General pain		Activities and participants
	Bone pain		Unemployment (Conversations about lessons)
	Tooth pain		Working hours
Sensory	Loss of vision/hearing/loss of touch	Employment	Reluctance to consent
	Tinnitus		Unemployment
	Loss of hearing		Reluctance to consent
	Tinnitus		Overall or societal
	Tinnitus/fatigue		Insurance
Dental	Weakness	Financial Issues	Insurance
	Dental abscesses		Financial issues
	Alcohol abscesses		Attitude to behavior before appearance or treatment
	Tooth loss		Attitude or behavior
	Swelling		Social isolation
Other symptoms	Hyperreflexia	Social relationship or isolation	Social isolation
	Hypertension		Refusing to leave child in care
	Weight management		Giving children
	Weight		Parenting (congregating or play with others)
	Work		Family
Refinement	Housework	Family	Family not understood by society
	Difficulty getting dressed (clothes, shoes)		Adherence
	Shopping		Downing
	Getting in and out of car		Disciplinarian with current
	Getting in and out of car		Surgery/surgery-surgery
Activities of daily living	Showering	Treatment	Prophylactic, rehabilitation
	Showering		Frequency and severity of operations
	Limitation of leisure		Scars
	Disability		Prophylactic, rehabilitation
	Disability		Treatment associated side effects
Physical functioning	Disability	Treatment	Hospital visit
	Disability		Pain control
	Disability		Lack of interest/understanding
	Disability		Lack of education of doctors
	Disability		Lack of expertise
Use of assistive devices	Balance	Diagnosis	Medication improved symptoms
	Medicated home and equipment		Treatment pathway
	Using walking aids		Prosthetic
	Anxiety		Chinese medicine
	Coping with emotional		Assessment
Psychological	Self-esteem/self-conscious	Diagnosis	Difficulties getting children diagnosed
	Lack of motivation		Misdiagnosis
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Psychological	Depression	Diagnosis	Unacknowledged

Table 3. Final round Delphi results

Main Theme	Subtheme	Descriptive statistics				I-CVI	Consensus	Convergence
		Mean	SD	Q1	Q3			
Symptom	Musculoskeletal symptoms	5.00	0.00	5.00	5.00	1.00	1.00	0.00
	Pain	4.80	0.45	5.00	5.00	1.00	1.00	0.00
	Dental symptoms	4.80	0.45	5.00	5.00	1.00	1.00	0.00
	Fatigue	4.40	0.55	4.00	5.00	1.00	0.75	0.50
	Sensory	4.00	0.71	4.00	4.50	0.60	0.88	0.25
Physical function	Activity of daily living	4.20	0.84	4.00	5.00	0.60	0.75	0.50
	Physical ability	4.40	0.55	4.00	5.00	1.00	0.75	0.50
Social function	Sleep	4.40	0.55	5.00	5.00	1.00	0.75	0.50
	Personal and social relationships	4.40	0.55	4.00	5.00	1.00	0.75	0.50
	Travel/social activities	4.20	0.84	4.00	5.00	0.60	0.75	0.50
	Self-esteem	4.40	0.55	4.00	5.00	1.00	0.75	0.50
	Work/school participation	4.40	0.55	4.00	5.00	1.00	0.75	0.50
Emotional burden	Understanding & communicating	4.20	0.84	4.00	5.00	0.60	0.75	0.50
	Depression	4.20	0.84	4.00	5.00	0.60	0.75	0.50
	Anxiety	4.20	0.84	4.00	5.00	0.60	0.75	0.50
	Fear	4.00	0.71	4.00	4.50	0.60	0.88	0.25
	Stressfulness	4.40	0.55	4.00	5.00	1.00	0.75	0.50
Treatment burden	Frustration	4.40	0.55	4.00	5.00	1.00	0.75	0.50
	Thought of death	3.80	0.45	4.00	4.50	0.60	0.88	0.00
	Financial burden	4.20	0.45	4.00	4.50	1.00	0.88	0.25
	Productivity loss	4.20	0.45	4.00	4.50	1.00	0.88	0.25
	Satisfaction of treatment	4.60	0.55	4.00	5.00	1.00	0.80	0.50
Family burden	At/Complications	4.60	0.55	4.00	5.00	1.00	0.80	0.50
	Care utilization	4.60	0.89	5.00	5.00	1.00	1.00	0.00
	Care experience	4.00	0.71	4.00	4.50	1.00	0.88	0.25
	Pregnancy and childbirth	5.00	0.89	5.00	5.00	0.60	1.00	0.00
	Sorry for the family	5.00	0.89	5.00	5.00	0.60	1.00	0.00
Development	Growth & development	4.80	0.45	5.00	5.00	1.00	1.00	0.00
	Puberty disorder	2.80	1.10	2.00	4.00	-0.20	0.00	1.00
Peer abuse	Limitation/loss of dream/plan	4.00	0.71	4.00	4.50	0.60	0.88	0.25
	Bullied or teased	4.20	0.84	4.00	5.00	0.60	0.75	0.50
Pediatric or adolescent specific treatment burden	Exposure to school violence	4.20	0.45	4.00	4.50	1.00	0.88	0.25
	Adherence to treatment	4.60	0.55	4.00	5.00	1.00	0.80	0.50
	Interruption of education	4.20	0.45	4.00	4.50	1.00	0.88	0.25
	Hardship with surgery	4.40	0.55	4.00	5.00	1.00	0.75	0.50
	Social life disruption	4.40	0.55	4.00	5.00	1.00	0.75	0.50
Care-giver's daily life impact	Care of self	4.20	0.84	4.00	5.00	0.60	0.75	0.50
	Change of plan	4.20	0.84	4.00	5.00	0.60	0.75	0.50
Care-giver's emotional burden	Guilty	4.40	0.89	4.00	5.00	0.60	0.80	0.50
	Frustration	4.20	0.45	4.00	4.50	1.00	0.88	0.25
Care-giver's Conflict with family	Stressfulness	4.00	0.00	4.00	4.00	1.00	1.00	0.00
	Patient parenting	4.00	0.71	4.00	4.50	0.60	0.88	0.25
	Healthy sibling parenting	4.00	0.71	4.00	4.50	0.60	0.88	0.25

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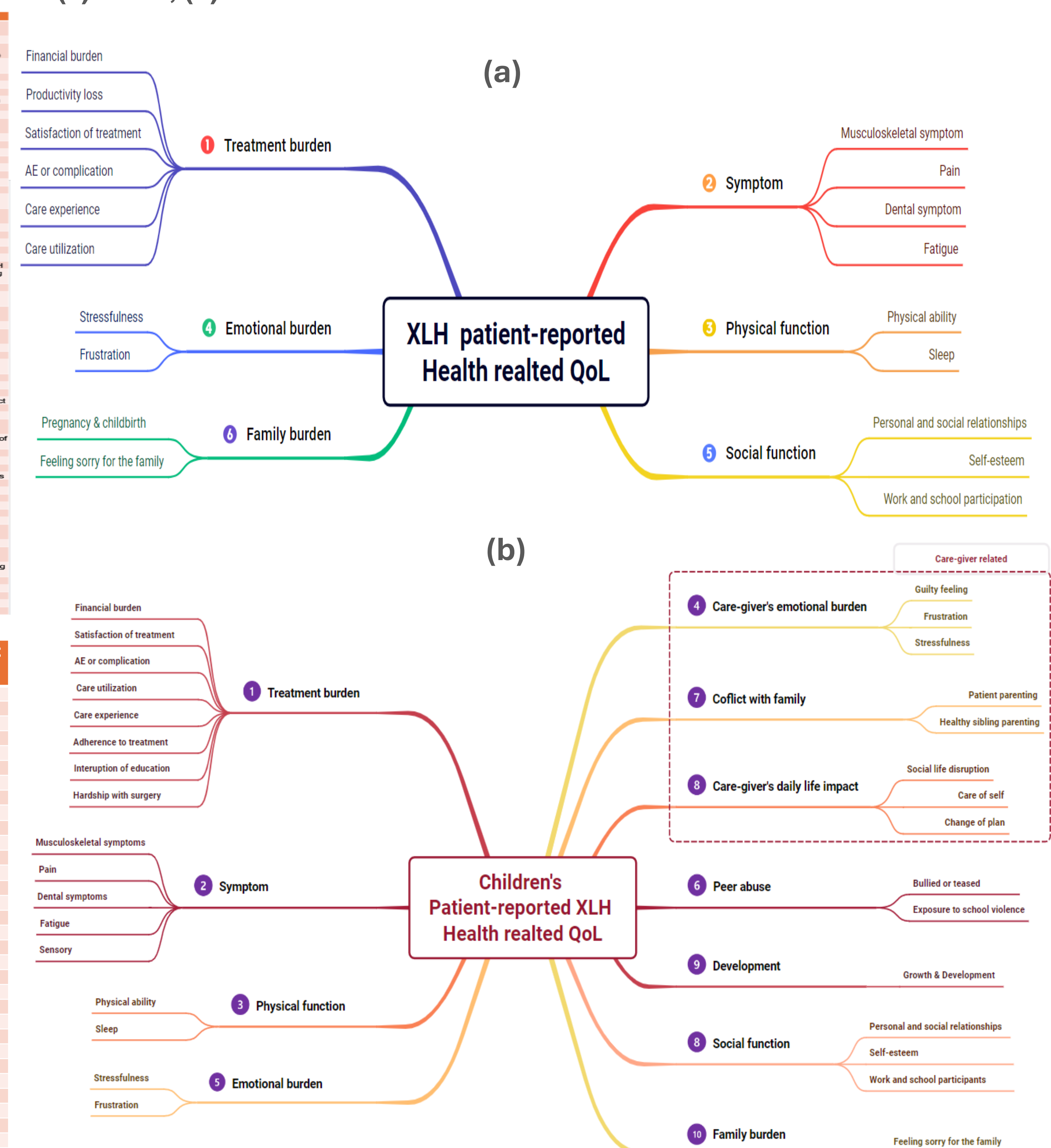
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Figure 2. Conceptual framework for a HRQoL PROM for patient with XLH: (a) Adult, (b) Children and Adolescent



Limitation

- Due to the rare nature of the condition, our study had a limited number of patients, particularly adolescents and male.

Conclusions

- The study shed light on understanding conceptual framework of PRO and disease burden of XLH and highlights the importance of lifecycle considerations in assessing their quality of life.
- These findings have potential implications for other lifelong inherited diseases and chronic conditions, underscoring the need for tailored approaches in patient-centered healthcare assessment and management.