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Hypophosphatasia (HPP) patient and caregiver disease burden, quality of life, and treatment experience: a mixed methods study concept

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Background

Hypophosphatasia

- Hypophosphatasia (HPP) is a rare inherited disorder characterized by deficient tissue-nonspecific alkaline phosphatase activity[1-3]
- HPP affects people of all ages and carries a high disease burden, with a substantial negative impact on quality of life (QoL)[3]
  - Patients with HPP can exhibit a broad spectrum of manifestations ranging from respiratory failure in infants with life-threatening disease to chronic debilitating musculoskeletal symptoms in adults[1-3]
  - HPP affects growth and development, with manifestations including dental complications, bone malformations, frequent fractures, and chest deformities that may lead to respiratory complications[1,4]
- HPP is often misdiagnosed, which can worsen the prognosis[1]

Patient burden

- Currently, few fit-for-purpose disease measures are available to accurately describe the disease experience of the patient
  - Generic QoL measures fail to fully and accurately capture the wide range of manifestations and high disease burden in patients with HPP
- Using qualitative methods in which themes important to patients are extracted from interviews – rather than prespecified by researchers – will help further the understanding of the burden of disease and treatment experiences in patients with HPP beyond what can be captured with structured instruments

Caregiver burden

- A fuller understanding of the burden associated with caring for a family member with HPP is needed
  - Caring for others can be associated with adverse effects including anxiety, depression, financial hardship, and even impaired immune function and earlier mortality[5-7]
  - Existing research on caregiver burden is focused almost exclusively on elder care, with less attention on genetic pediatric conditions[8] and no published studies on HPP caregiver burden

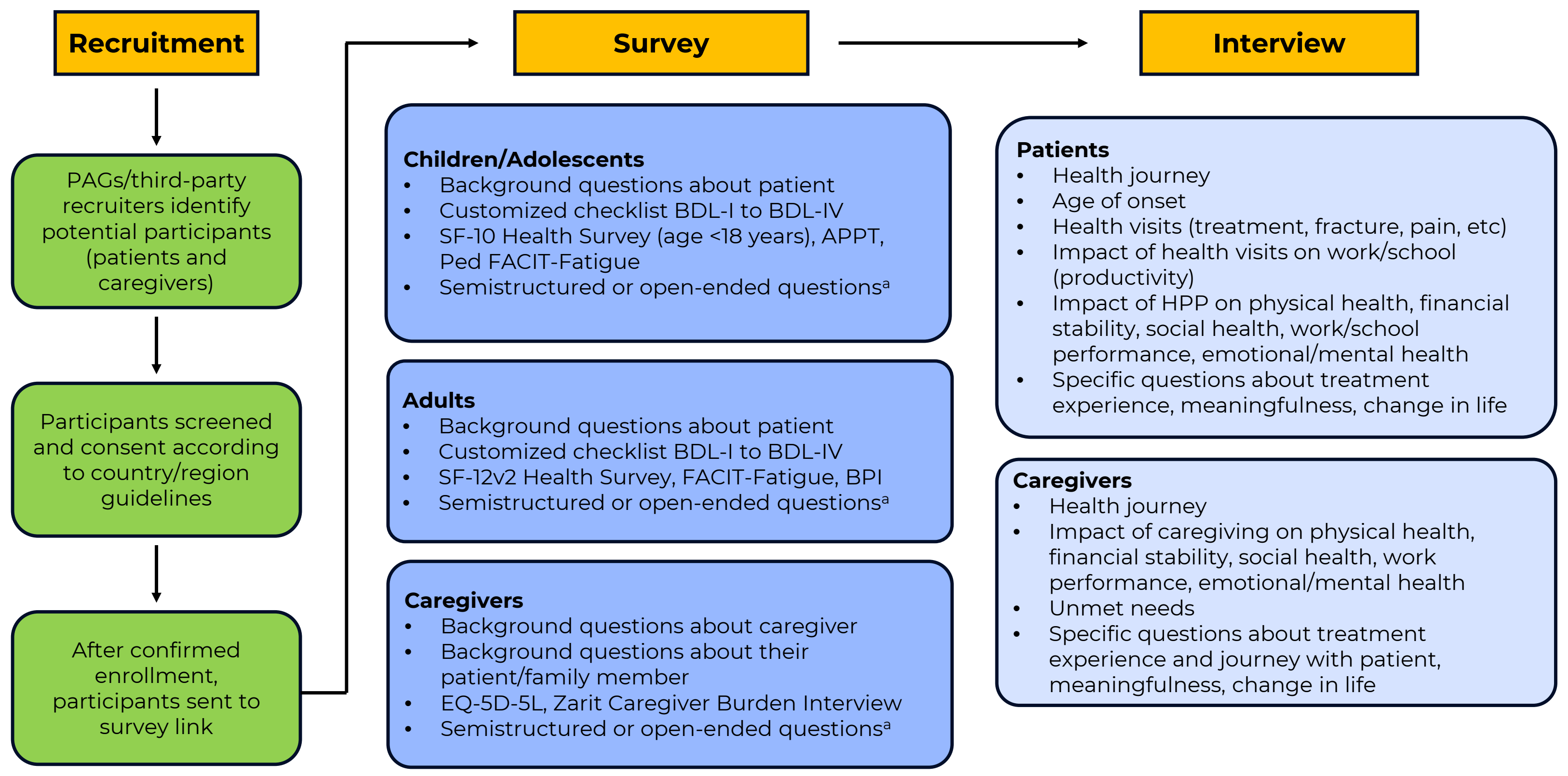
Objectives

- To quantitatively and qualitatively describe disease burden and treatment experience in patients with HPP
- To measure burden and QoL among caregivers of patients with HPP across patients at various ages and burden of disease levels

Methods

- This is an observational, cross-sectional, mixed methods study that is designed to use quantitative measurement and qualitative interviews with patients with HPP and their caregivers
- Study has 2 components:
  - Online survey of approximately 50 patients with HPP and 30 to 50 caregivers using validated measures
  - Qualitative interview of approximately 20 to 30 patients with HPP and 10 caregivers
- Interviews will be conducted by trained interviewers using a semistructured interview guide
  - All interviews will be audio-recorded, transcribed verbatim, and analyzed

Figure 1. Overview of Study Methodology



Recruitment

PAGs/third-party recruiters identify potential participants (patients and caregivers)

Participants screened and consent according to country/region guidelines

After confirmed enrollment, participants sent to survey link

Survey

Children/Adolescents
- Background questions about patient
- Customized checklist BDL-I to BDL-IV
- SF-10 Health Survey (age <18 years), APPT, Ped FACIT-Fatigue
- Semistructured or open-ended questions[a]

Adults
- Background questions about patient
- Customized checklist BDL-I to BDL-IV
- SF-12v2 Health Survey, FACIT-Fatigue, BPI
- Semistructured or open-ended questions[a]

Caregivers
- Background questions about caregiver
- Background questions about their patient/family member
- EQ-5D-5L, Zarit Caregiver Burden Interview
- Semistructured or open-ended questions[a]

Interview

Patients
- Health journey
- Age of onset
- Health visits (treatment, fracture, pain, etc)
- Impact of health visits on work/school (productivity)
- Impact of HPP on physical health, financial stability, social health, work/school performance, emotional/mental health
- Specific questions about treatment experience, meaningfulness, change in life

Caregivers
- Health journey
- Impact of caregiving on physical health, financial stability, social health, work performance, emotional/mental health
- Unmet needs
- Specific questions about treatment experience and journey with patient, meaningfulness, change in life

[a]The final selection of the measures to be used will be based on agreement by members of the steering committee leading the study, composed of clinicians, patient representatives, and Alexion representatives.
APPT, Adolescent Pediatric Pain Tool; BDL-I, burden of disease level I; BDL-IV, burden of disease level IV; BPI, Brief Pain Inventory; EQ-5D-3L, EuroQol's 5-dimension/3-level descriptive system; FACIT-Fatigue, Functional Assessment of Chronic Illness–Fatigue Scale; HPP, hypophosphatasia; PAG, patient advocacy group; Ped FACIT-Fatigue, Pediatric Functional Assessment of Chronic Illness Therapy–Fatigue scale; SF-12v2, 12-Item Short Form Health Survey, version 2; SF-10, 10-Item Short Form Health Survey.

Table. Inclusion/exclusion criteria for the survey and interview

Criteria	Patient	Caregiver
Inclusion		
Able to self-report diagnosis of HPP as confirmed by practicing physician	✓	
Experiencing limitations (signs and/or symptoms) in physical or mental health due to HPP	✓	
Able to converse and read local language	✓	✓
Consents to study	✓	✓
Has access to internet and an electronic device (eg, computer, mobile phone, tablet)	✓	✓
Age ≥18 years		✓
Currently the main caregiver (providing >50% of needed, nonprofessional care) for a patient with HPP for ≥6 months		✓
Exclusion		
Has limitations that may preclude participation in an online study	✓	✓
Experienced perinatal/infantile onset of disease prior to 6 months of age	✓	
Current participation by patient in an interventional study	✓	
Unwilling or unable to comply with study requirements	✓	✓
Employed as a professional caregiver		✓

Survey Measures[a]

Patients:

- Demographics and background health information
- Self-reported burden of HPP
- The 12-Item Short Form Health Survey (children aged ≥18 years) and 10-Item Short Form Health Survey (children aged <18 years) to assess health-related QoL[9]
- Functional Assessment of Chronic Illness Therapy (or Pediatric Functional Assessment of Chronic Illness Therapy for children) to assess the well-being of patients with chronic illness[10,11]
- Brief Pain Inventory and Adolescent Pediatric Pain Tool to assess pain severity and impact on daily functioning[12,13]

Caregivers:

- EuroQol's EQ-5D-5L 5-dimension/5-level descriptive system, a measure of health utility[14]
- Zarit Burden Interview, a self-reported measure of caregiver burden[15,16]

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Figure 2. Geographic Regions of Recruitment

This study is the first:
- **Mixed methods study to determine disease burden and treatment experience in patients with HPP**
- **To measure QoL in caregivers of patients with HPP**

What this study will tell us

- A quantitative analysis of survey data will provide demographic data on patients and caregivers as well as the results of QoL, physical, emotional, and functional measures
- Caregiver surveys will provide data for health utility estimates and other aspects of their burden caring for patients with HPP
- Semistructured qualitative interviews using thematic analysis will improve understanding of disease impacts and treatment experience
- The responses to the surveys and interviews will further the understanding of the impact of HPP beyond the patient
- The results will inform the allocation of resources in the treatment of HPP that will reduce the burden of disease for patients with HPP and their caregivers

Patients

- Patients across a span of ages with a wide range of HPP manifestations, asfotase alfa treatment status, and country income levels (and corresponding healthcare systems) will be included
- Patients will be recruited from Canada, China, Colombia, France, Saudi Arabia, Turkey, and the United Kingdom
- HPP patient advocacy groups in each country will be the primary recruitment resource

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Disclosures:

RH, **PL**, and **DS** are employees of Alexion, AstraZeneca Rare Disease and may have stock ownership and/or stock options or interests in the company. **LS** consults for/has received research funding/honoraria from Alexion, AstraZeneca Rare Disease. **RP** consults for/has received research funding/honoraria from Alexion, AstraZeneca Rare Disease, Ultragenyx-Mereo, and Bridgebio.

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