Congenital Hyperinsulinism International

Compiling shared experiences to better diagnose and treat HI:

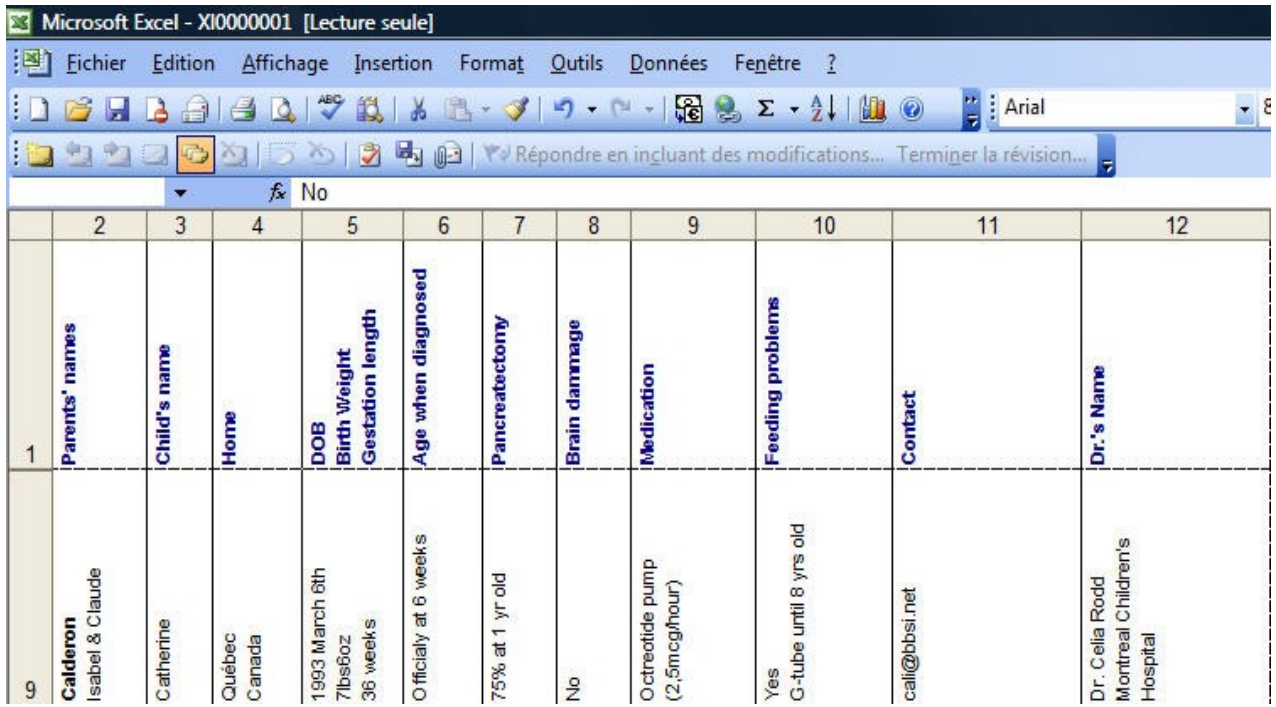
The HI Global Registry

Tai Pasquini, PhD, Mahi Mesfin

CONGENITAL HYPERINSULINISM HI GLOBAL REGISTRY

The Origins of HIGR

- First HI patient-reported data collection began in 1999
- An outgrowth of the email support group
- Parents in the group wanted to be able to better remember who was who, initially, it was for the members of the group.



	2	3	4	5	6	7	8	9	10	11	12
1	Parents' names	Child's name	Home	DOB Birth Weight Gestation length	Age when diagnosed	Pancreatectomy	Brain dammage	Medication	Feeding problems	Contact	Dr.'s Name
9	Calderon Isabel & Claude	Catherine	Québec Canada	1993 March 6th 7lbs6oz 36 weeks	Officialy at 6 weeks	75% at 1 yr old	No	Octreotide pump (2,5mcg/hour)	Yes G-tube until 8 yrs old	cali@bbsi.net	Dr. Celia Rodd Montreal Children's Hospital

CHI Congenital Hyperinsulinism International

The HI Global Registry

- Launched in 2018, the HI Global Registry (HIGR) is a patient powered registry that can be used to generate natural history data
- Provides a baseline or an overall understanding of the reality of the day-to-day experience of living with HI
- Helps identify the most pressing issues and on-going challenges

Why are patient registries for rare diseases such important tools?

- Rare diseases affect very few people spread across the world
- Rare disease registries invite people worldwide to participate, increasing the pool of knowledge about the condition
- Patient-reported registries collect information directly from the patient or caregiver who has the most knowledge of day-to-day life with a disease
- Patient-reported registries collect information from the people who live with a disease over the course of their life, so we can understand every phase of life with a condition

Have you ever asked?

Is use of emergency/rescue glucagon routine in the HI Community?

At what age are babies typically diagnosed with HI?

How often do babies with HI need to feed?

HI Parents - how often are your child's blood sugar levels checked?

How many HI Global Registry families have more than one affected member?

For those who have had subtotal pancreatectomies for diffuse HI, how many go on to become diabetic?

Are seizures common with HI?

Do kids with HI usually have g-tubes?

Who can join the HI Global Registry?

- People with HI or their parent can share their experiences with the disease by answering 13 surveys through an online platform
- All information collected is kept on a secure system
- Questions were developed by HI patients, clinicians, and researchers

Parent of a child living with HI

Respondent

Participant

Adult living with HI

Participant and respondent

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Experiences of Interest

- ALL!
  - positive/negative genetics,
  - diffuse/focal,
  - on treatment/ no longer on treatment,
  - surgery/no surgery,
  - daily lows/ no longer experiencing lows, etc.
- EVERY story is an important piece of the constellation!





Benefits of Participating

- Research increases our knowledge of HI and potentially leads to:
  - More timely diagnosis
  - New and better treatments
  - Fewer undesirable effects
- Receive information about medical advances and other news
- Personal satisfaction of being part of scientific innovation as a member of the research team and process

Risks of Participating (Minimal)

- We follow the best practices of data privacy, security, and all applicable laws (HIPPA, GDPR)
- Questions can be sensitive, and you may feel uncomfortable
  - You do not have to share information that you do not want to
- Risk that the participant's information could be misused, but the chance of this happening is very small
  - We have protections in place to lower this risk!
- Respondents may withdraw consent at any time

Surveys

Submit once

- Pregnancy
- Birth

Longitudinal

- Glucose monitoring - 6 months
- Quality of life (Parent/ LAR) - Annual
- Quality of life (Participant) - Annual

Updatable

- Contact information
- Demographics
- Diagnosis
- Medication management
- Diet & feeding management
- Surgical management
- Other diagnosis
- Developmental

Longitudinal and Updateable Surveys

- Longitudinal data
  - Data tracked over time on a set schedule
  - Provides the basis of natural history
  - Helps us understand changes across time
- Updateable data
  - To capture updates as they occur
  - Not tied to a particular timeframe
  - Important to capture new diagnoses, track developmental delays, report on changes in feeding, update medications, etc.

Importance of completing all surveys

- Complete data!
- Even if an experience doesn't apply, we can't make assumptions





Case Studies

Example: Other Diagnoses Survey (n=179)

Does the participant have any other medical diagnoses or chronic symptoms (check all that apply)?

- (n=160)
- 56.3% responded “Does Not Have Other Diagnoses”
- 43.6% had one or more of the following
- Asthma, Blood-related condition, Cancer, GE Reflux, GI Motility Disorder, Dumping Syndrome, Inflammatory Bowel Disease, Heart-related Condition, Kidney-Related Condition, Lung-Related Condition, Menstrual-related Condition, Reproductive Condition, Scoliosis, Skin Condition

Example: Other Diagnoses Survey (n=179)

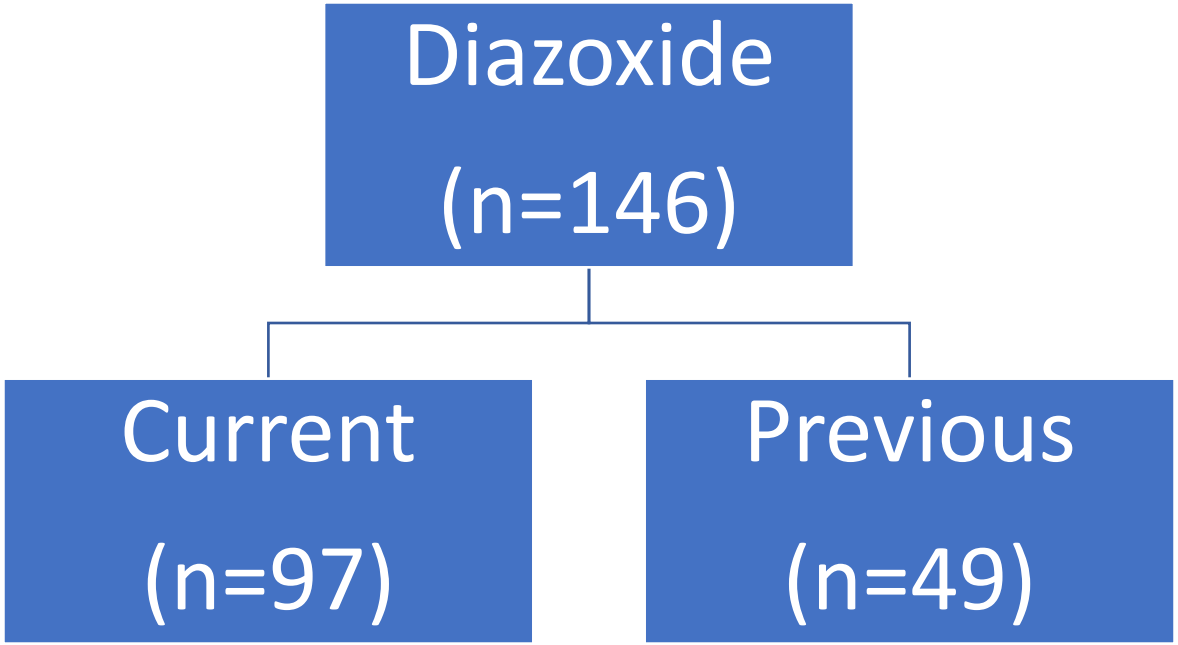
- What about the 19 people who completed this survey, but did not answer this question?
- Why did they not answer?
  - Didn't want to
  - Didn't know
  - Didn't see the question
  - Are waiting to find out if their child gets a diagnosis
  - Their child showed up at the door and they had to go, and they couldn't get back to it
  - It was dinnertime
  - We simply don't know! And can't guess!

Case Study: How do we use HIGR to answer research questions?

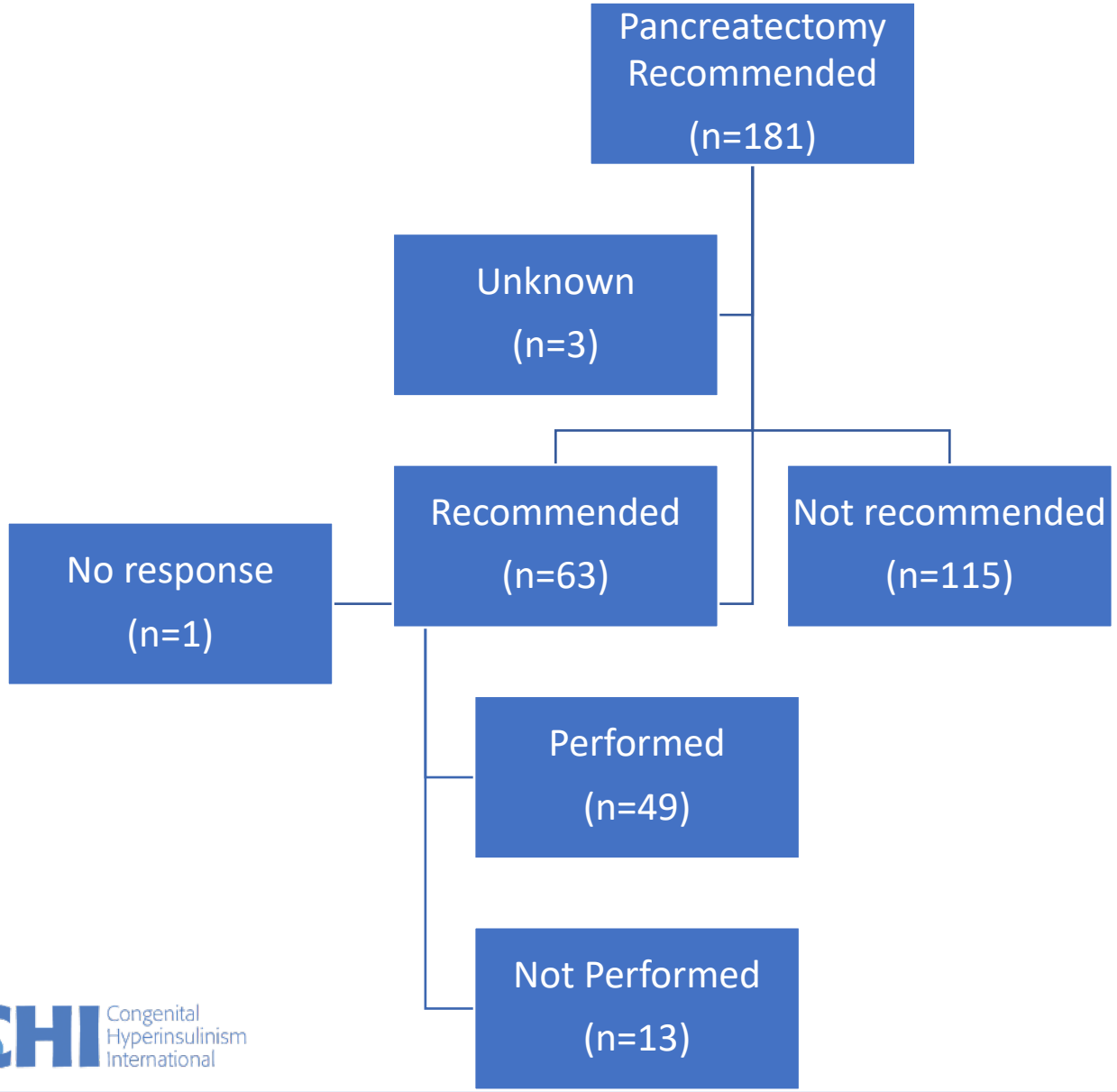
How many people have had a pancreatectomy and previously or currently take diazoxide?

Step 1: Diazoxide (Medication Survey) (n=180)

- Question 1: What medications has the participant taken to treat hyperinsulinism (check all that apply)?
- Question 2: Is the participant currently taking diazoxide (Proglycem, Eudamine)?

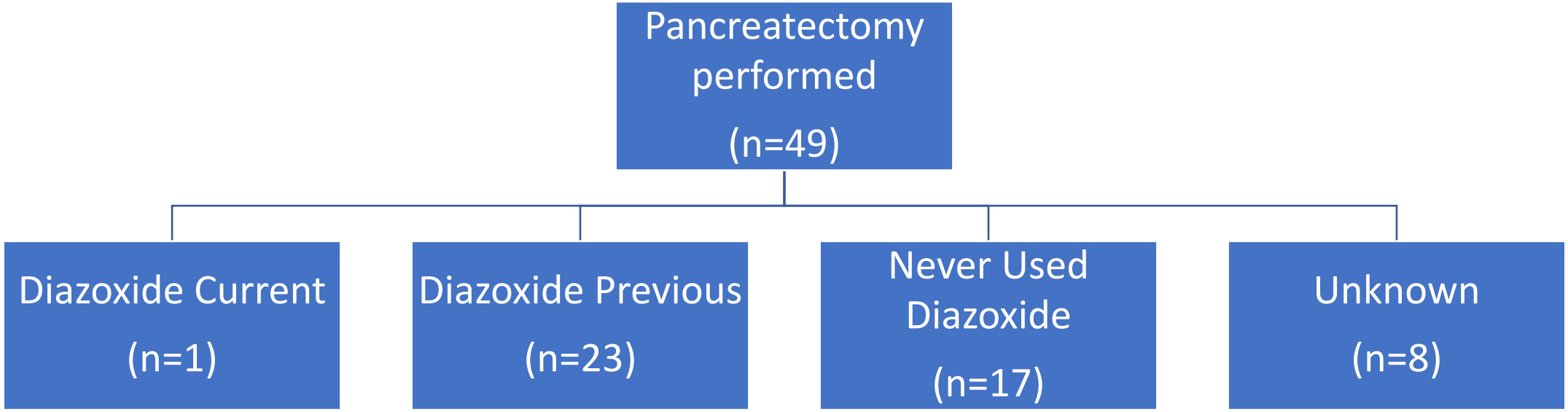


Step 2: Surgery



- Question 1: Was a pancreatectomy recommended to treat hyperinsulinism?
- Question 2: Was a pancreatectomy performed to treat hyperinsulinism?

Step 3: Surgery and Diazoxide



Case Study: Increasing Accuracy

Has the participant experienced any feeding issues on a regular basis (check all that apply)?

	Feeding Issues	No Feeding Issues
Responses	0 (0%)	2 (100%)

#1: No feeding issues

#2: No feeding issues

Case Study: Feeding Issues

	Feeding Issues	No Feeding Issues
Responses	2 (40%)	3 (60%)

#1: No feeding issues

#2: No feeding issues

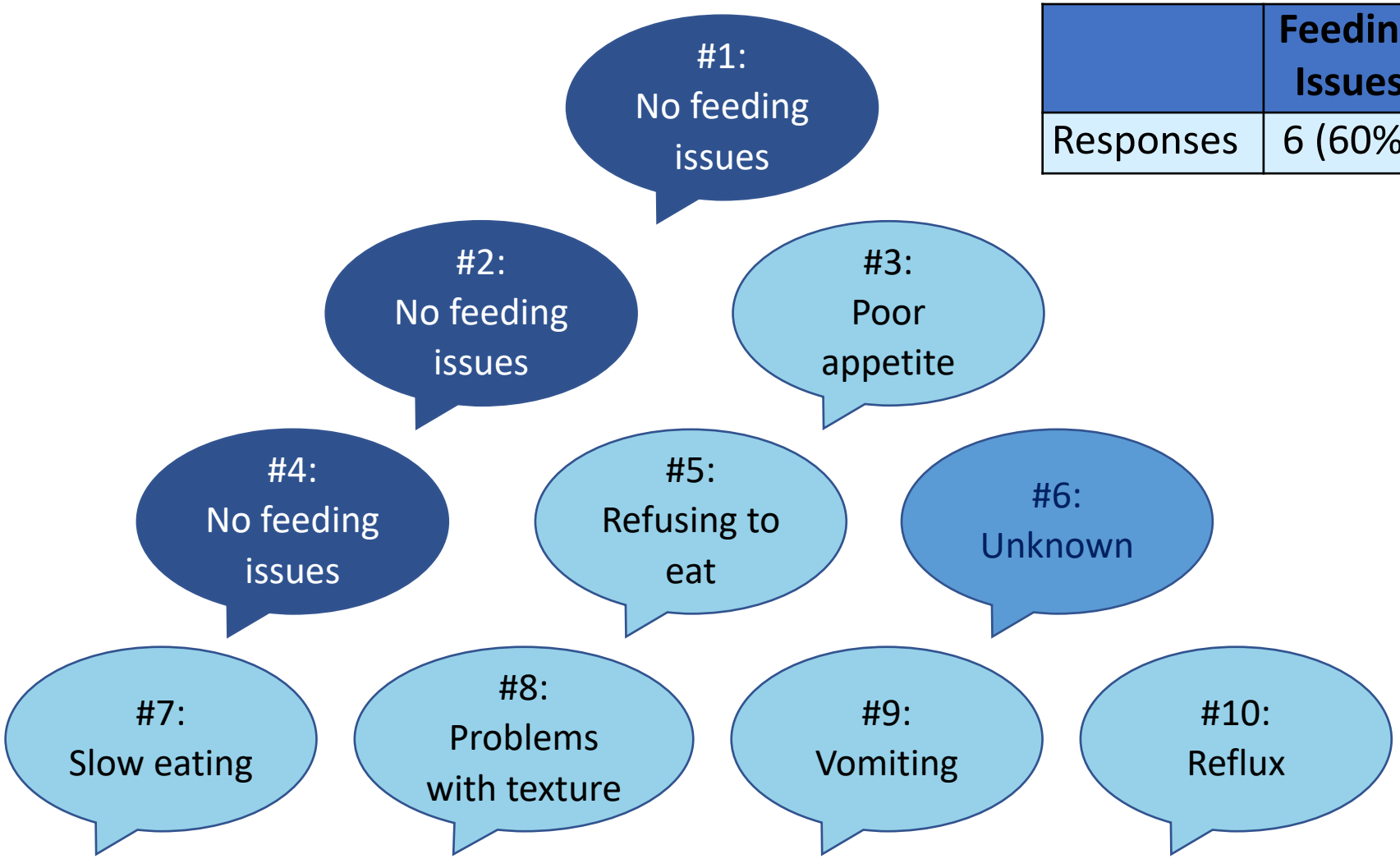
#3: Poor appetite

#4: No feeding issues

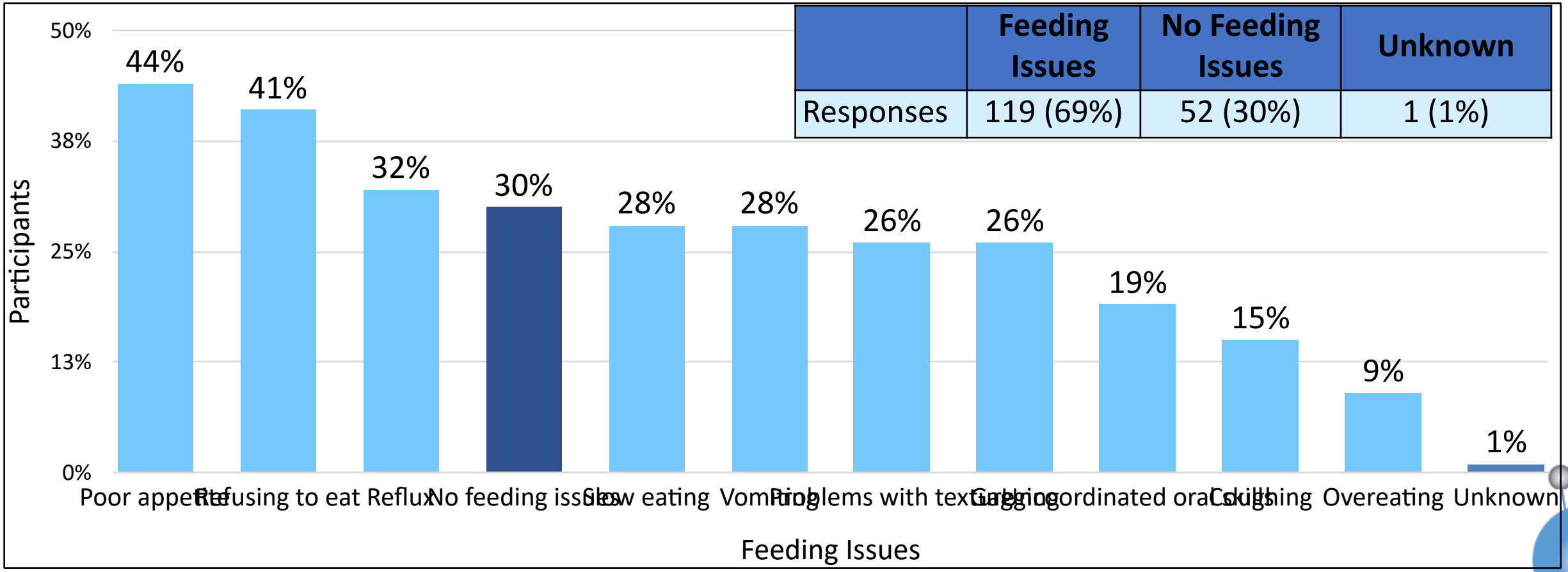
#5: Refusing to eat

Case Study: Feeding Issues

	Feeding Issues	No Feeding Issues	Unknown
Responses	6 (60%)	3 (30%)	1 (10%)



Feeding Issues (n=172)



	Feeding Issues	No Feeding Issues	Unknown
Responses	119 (69%)	52 (30%)	1 (1%)

Case Study: Caregiver Worry

Do you worry because of the Participant's HI or HI-related condition?

	Always or Often Worry	Seldom or Never Worry
Responses	1 (50%)	1 (50%)

Caregiver Worry

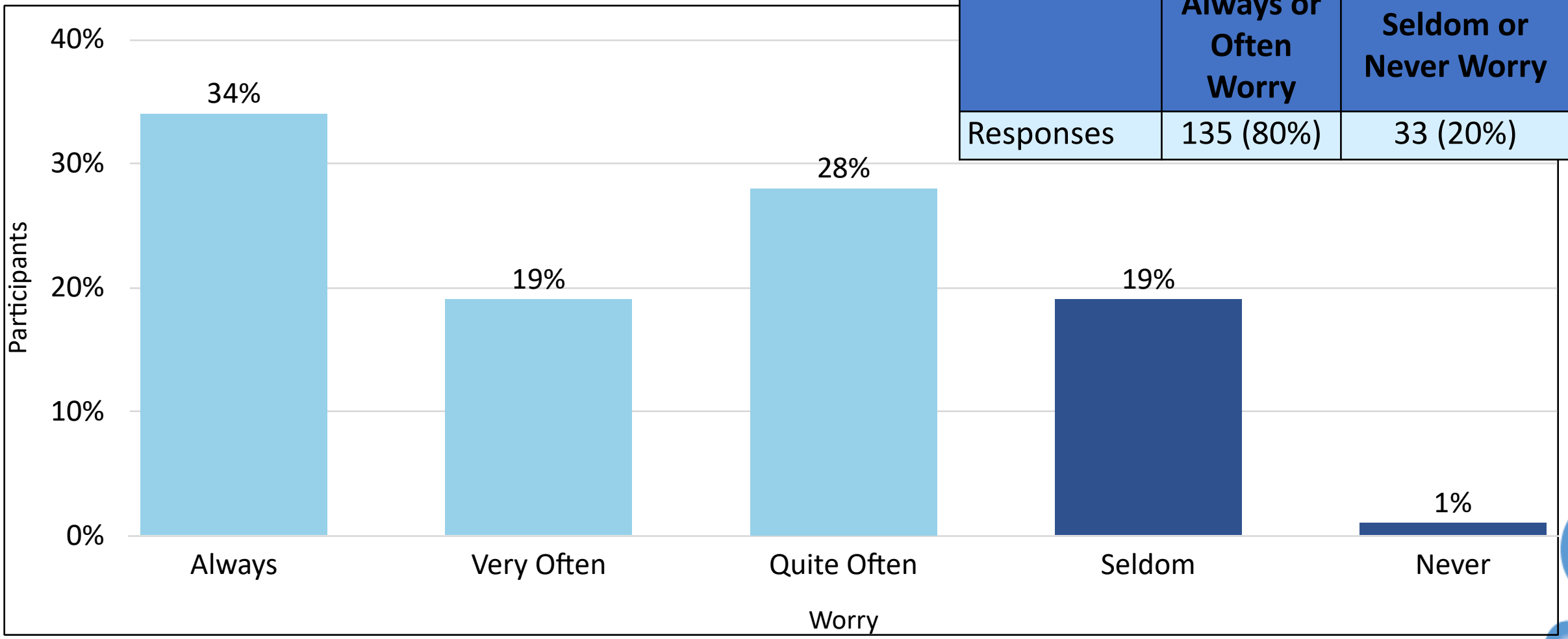
	Always or Often Worry	Seldom or Never Worry
Responses	2 (40%)	3 (60%)

Caregiver Worry

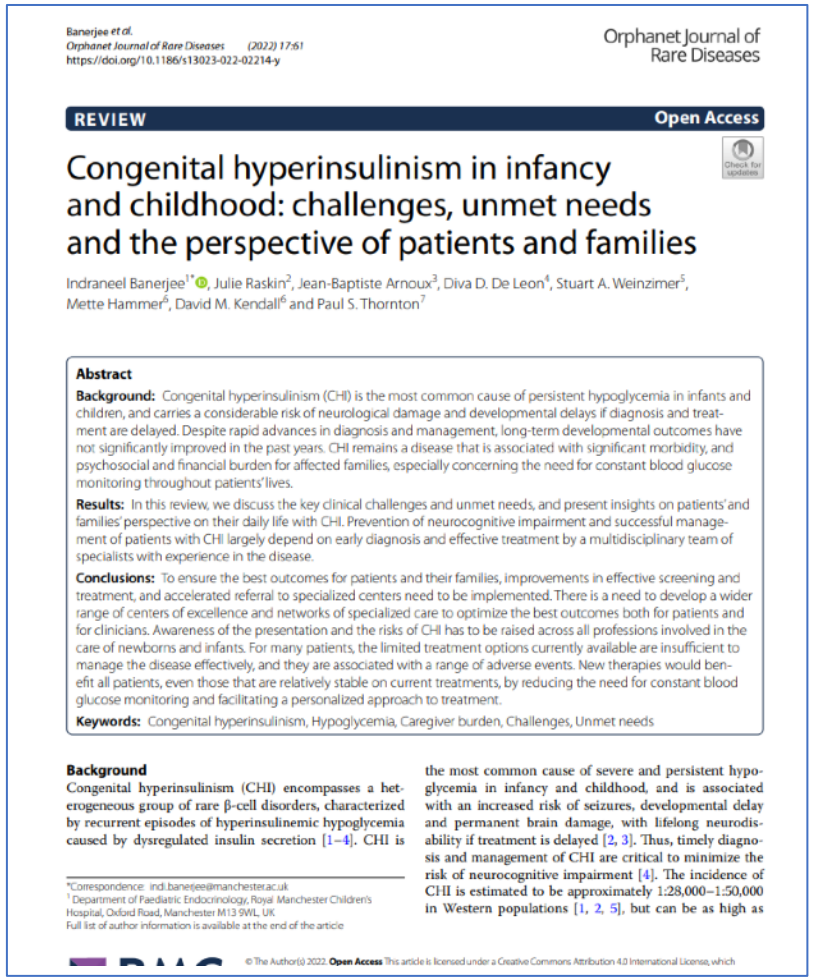
	Always or Often Worry	Seldom or Never Worry
Responses	7 (70%)	3 (30%)

Caregiver Worry (n=168)

	Always or Often Worry	Seldom or Never Worry
Responses	135 (80%)	33 (20%)



Peer-Reviewed Publications Using Registry Data



Banerjee et al.
Orphanet Journal of Rare Diseases (2022) 17:61
https://doi.org/10.1186/s13023-022-02214-y

Orphanet Journal of Rare Diseases

REVIEW Open Access

Congenital hyperinsulinism in infancy and childhood: challenges, unmet needs and the perspective of patients and families

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Abstract

Background: Congenital hyperinsulinism (CHI) is the most common cause of persistent hypoglycemia in infants and children, and carries a considerable risk of neurological damage and developmental delays if diagnosis and treatment are delayed. Despite rapid advances in diagnosis and management, long-term developmental outcomes have not significantly improved in the past years. CHI remains a disease that is associated with significant morbidity, and psychosocial and financial burden for affected families, especially concerning the need for constant blood glucose monitoring throughout patients' lives.

Results: In this review, we discuss the key clinical challenges and unmet needs, and present insights on patients' and families' perspective on their daily life with CHI. Prevention of neurocognitive impairment and successful management of patients with CHI largely depend on early diagnosis and effective treatment by a multidisciplinary team of specialists with experience in the disease.

Conclusions: To ensure the best outcomes for patients and their families, improvements in effective screening and treatment, and accelerated referral to specialized centers need to be implemented. There is a need to develop a wider range of centers of excellence and networks of specialized care to optimize the best outcomes both for patients and for clinicians. Awareness of the presentation and the risks of CHI has to be raised across all professions involved in the care of newborns and infants. For many patients, the limited treatment options currently available are insufficient to manage the disease effectively, and they are associated with a range of adverse events. New therapies would benefit all patients, even those that are relatively stable on current treatments, by reducing the need for constant blood glucose monitoring and facilitating a personalized approach to treatment.

Keywords: Congenital hyperinsulinism, Hypoglycemia, Caregiver burden, Challenges, Unmet needs

Background

Congenital hyperinsulinism (CHI) encompasses a heterogeneous group of rare β-cell disorders, characterized by recurrent episodes of hyperinsulinemic hypoglycemia caused by dysregulated insulin secretion [1–4]. CHI is the most common cause of severe and persistent hypoglycemia in infancy and childhood, and is associated with an increased risk of seizures, developmental delay and permanent brain damage, with lifelong neurodisability if treatment is delayed [2, 3]. Thus, timely diagnosis and management of CHI are critical to minimize the risk of neurocognitive impairment [4]. The incidence of CHI is estimated to be approximately 1:28,000–1:50,000 in Western populations [1, 2, 5], but can be as high as

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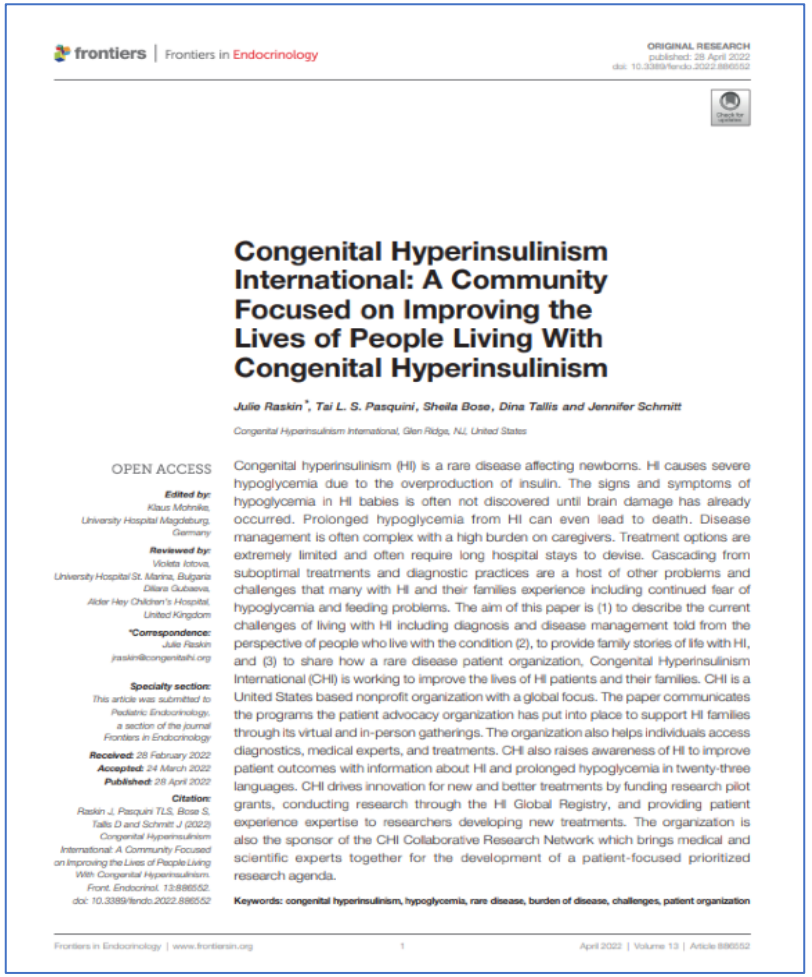

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ORIGINAL RESEARCH
published: 28 April 2022
doi: 10.3389/fendo.2022.886552

Congenital Hyperinsulinism International: A Community Focused on Improving the Lives of People Living With Congenital Hyperinsulinism

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OPEN ACCESS

Edited by: Klaus Mohnike, University Hospital Magdeburg, Germany

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Specialty section: This article was submitted to Pediatric Endocrinology, a section of the journal Frontiers in Endocrinology

Received: 28 February 2022
Accepted: 24 March 2022
Published: 28 April 2022

Citation: Raskin J, Pasquini TLS, Bose S, Tallis D and Schmitt J (2022) Congenital Hyperinsulinism International: A Community Focused on Improving the Lives of People Living With Congenital Hyperinsulinism. Front. Endocrinol. 13:886552. doi: 10.3389/fendo.2022.886552

Congenital hyperinsulinism (HI) is a rare disease affecting newborns. HI causes severe hypoglycemia due to the overproduction of insulin. The signs and symptoms of hypoglycemia in HI babies is often not discovered until brain damage has already occurred. Prolonged hypoglycemia from HI can even lead to death. Disease management is often complex with a high burden on caregivers. Treatment options are extremely limited and often require long hospital stays to devise. Cascading from suboptimal treatments and diagnostic practices are a host of other problems and challenges that many with HI and their families experience including continued fear of hypoglycemia and feeding problems. The aim of this paper is (1) to describe the current challenges of living with HI including diagnosis and disease management told from the perspective of people who live with the condition (2), to provide family stories of life with HI, and (3) to share how a rare disease patient organization, Congenital Hyperinsulinism International (CHI) is working to improve the lives of HI patients and their families. CHI is a United States based nonprofit organization with a global focus. The paper communicates the programs the patient advocacy organization has put into place to support HI families through its virtual and in-person gatherings. The organization also helps individuals access diagnostics, medical experts, and treatments. CHI also raises awareness of HI to improve patient outcomes with information about HI and prolonged hypoglycemia in twenty-three languages. CHI drives innovation for new and better treatments by funding research pilot grants, conducting research through the HI Global Registry, and providing patient experience expertise to researchers developing new treatments. The organization is also the sponsor of the CHI Collaborative Research Network which brings medical and scientific experts together for the development of a patient-focused prioritized research agenda.

Keywords: congenital hyperinsulinism, hypoglycemia, rare disease, burden of disease, challenges, patient organization

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ORIGINAL RESEARCH
published: 02 June 2022
doi: 10.3389/fendo.2022.876903

Global Registries in Congenital Hyperinsulinism

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OPEN ACCESS

Edited by: Klaus Mohnike, University Hospital Magdeburg, Germany

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Specialty section: This article was submitted to Pediatric Endocrinology, a section of the journal Frontiers in Endocrinology

Received: 16 February 2022
Accepted: 02 May 2022
Published: 02 June 2022

Citation: Pasquini TLS, Mesfin M, Schmitt J and Raskin J (2022) Global Registries in Congenital Hyperinsulinism. Front. Endocrinol. 13:876903. doi: 10.3389/fendo.2022.876903

Congenital hyperinsulinism (HI) is the most frequent cause of severe, persistent hypoglycemia in newborn babies and children. There are many areas of need for HI research. Some of the most critical needs include describing the natural history of the disease, research leading to new and better treatments, and identifying and managing hypoglycemia before it is prolonged and causes brain damage or death. Patient-reported data provides a basis for understanding the day-to-day experience of living with HI. Commonly identified goals of registries include performing natural history studies, establishing a network for future product and treatment studies, and supporting patients and families to offer more successful and coordinated care. Congenital Hyperinsulinism International (CHI) created the HI Global Registry (HIGR) in October 2018 as the first global patient-powered hyperinsulinism registry. The registry consists of thirteen surveys made up of questions about the patient's experience with HI over their lifetime. An international team of HI experts, including family members of children with HI, advocates, clinicians, and researchers, developed the survey questions. HIGR is managed by CHI and advised by internationally recognized HI patient advocates and experts. This paper aims to characterize HI through the experience of individuals who live with it. This paper includes descriptive statistics on the birthing experience, hospitalizations, medication management, feeding challenges, experiences with glucose monitoring devices, and the overall disease burden to provide insights into the current data in HIGR and demonstrate the potential areas of future research. As of January 2022, 344 respondents from 37 countries consented to participate in HIGR. Parents or guardians of individuals living with HI represented 83.9% of the respondents, 15.3% were individuals living with HI. Data from HIGR has already provided insight into access challenges, patients' and caregivers' quality of life, and to inform clinical trial research programs. Data is also available to researchers seeking to study the pathophysiology of HI retrospectively or to design prospective trials related to improving HI patient outcomes. Understanding the natural history of the disease can also guide standards of care. The data generated through HIGR provides an opportunity to improve the lives of all those affected by HI.

Keywords: rare disease, registry, congenital hyperinsulinism, hypoglycemia, patient-reported outcomes

CHI Congenital Hyperinsulinism International

Takeaways

- We are **all** part of this research team
- We have some exciting new features launching this year including:
  - Medication reminders
  - Symptom trackers
  - CGM & glucometer data streams
  - New languages
- We know it can be overwhelming, but the HIGR team in here to help!
- Actions:
  - Enroll
  - Update
  - Stay Engaged