Congenital Hyperinsulinism International Research Priorities: The HI Global Registry and the Collaborative Research Network

Julie Raskin

Congenital Hyperinsulinism Family Conference

September 17, 2022

NH Villa Carpegna, Rome, Italy

CHI supports HI research for better treatments and cures, raises awareness of HI to reduce brain damage and death, improves access to care and treatment for those with HI, while providing a community for HI families.

CHI Congenital Hyperinsulinism International

Congenital Hyperinsulinism International
When too little sugar hurts, we help.™

CHI AT A GLANCE

9 MDBR Grants Totaling
$700,000+ Funded

444 HIGR Participants
51 Countries
3rd Report Published

6 Biotechs in pre-clinical or clinical development for new HI treatments

6 Centers of Excellence Designations

58 Experts and Patient Leaders
19 Countries
7 Workstreams

CHI Family Support Forum
2,073 Members
79 Countries

25 International Family Conferences

3 articles published in peer-reviewed journals

8 Sugar Soirées
35 Awards Given

13 Listening Sessions

HI Genetic Testing
685 Children
59 Countries

CHI Website
17,423 Visitors
155 Countries

37 virtual HI convenings including conferences, meetings and HI community events

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?

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

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Surveys

Submit once

- Pregnancy
- Birth

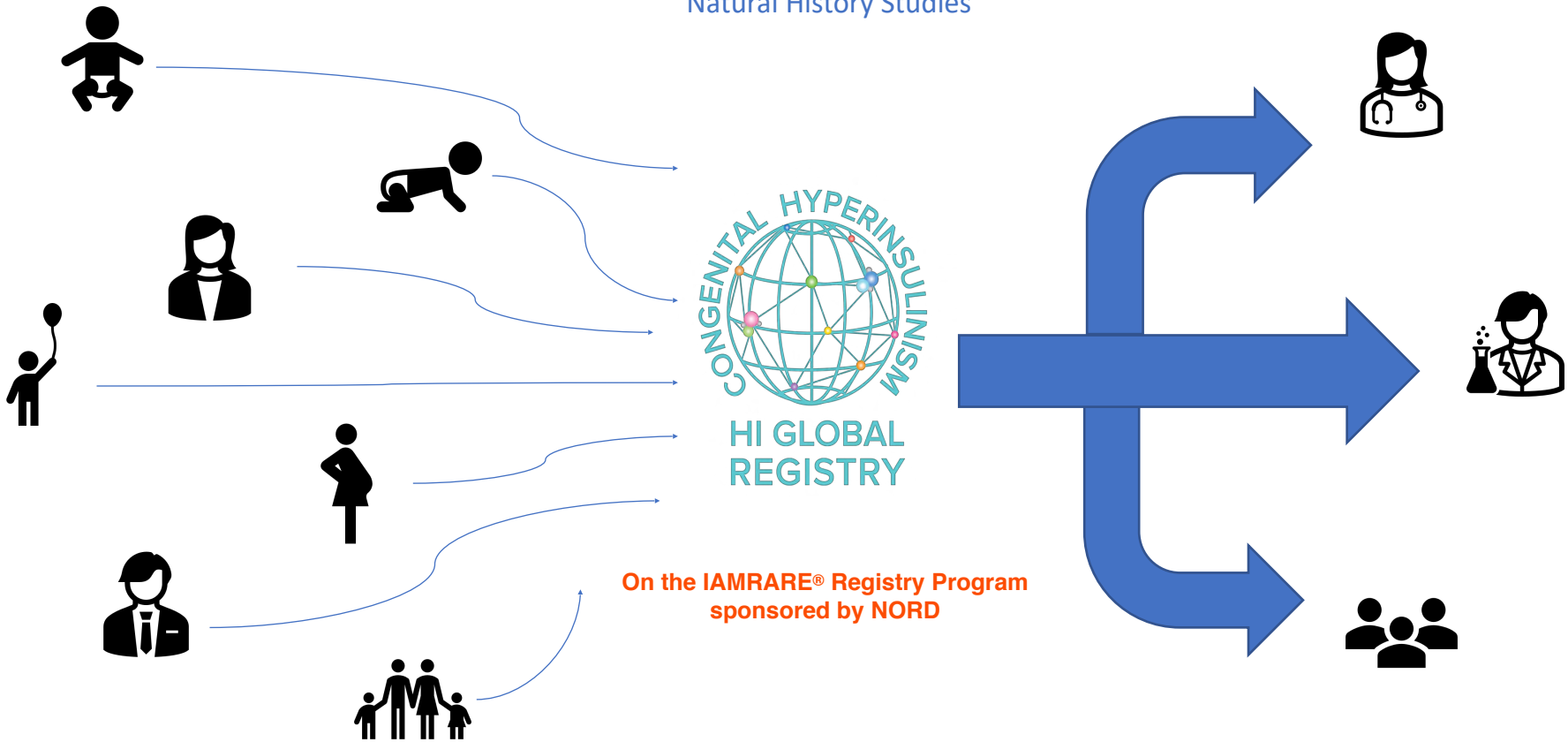
Longitudinal

- 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

Natural History Studies



On the IAMRARE® Registry Program sponsored by NORD

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When too little sugar hurts, we help.™

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 hosted by NORD
- 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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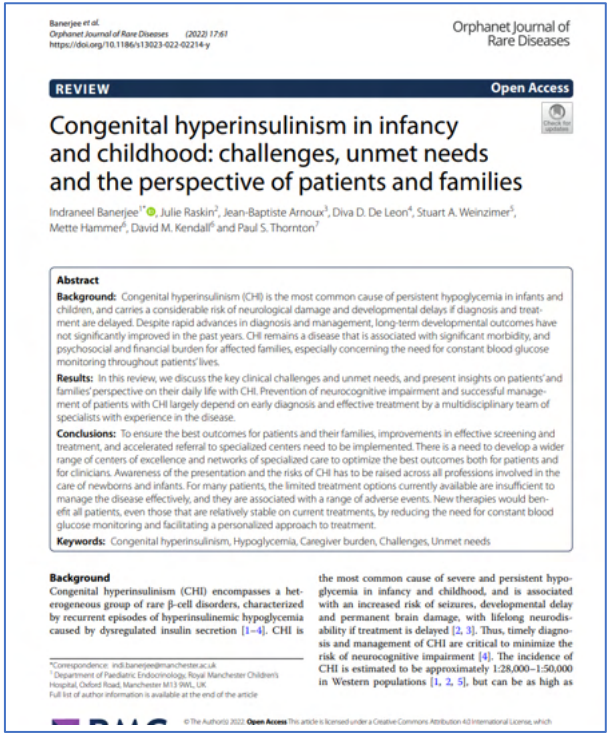
Peer-Reviewed Publications Using Registry Data



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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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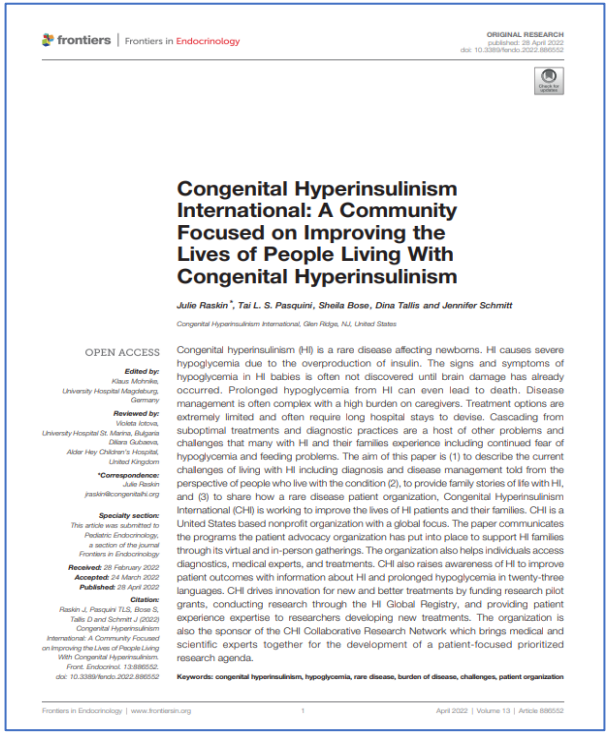

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Congenital Hyperinsulinism International: A Community Focused on Improving the Lives of People Living With Congenital Hyperinsulinism

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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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Global Registries in Congenital Hyperinsulinism

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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

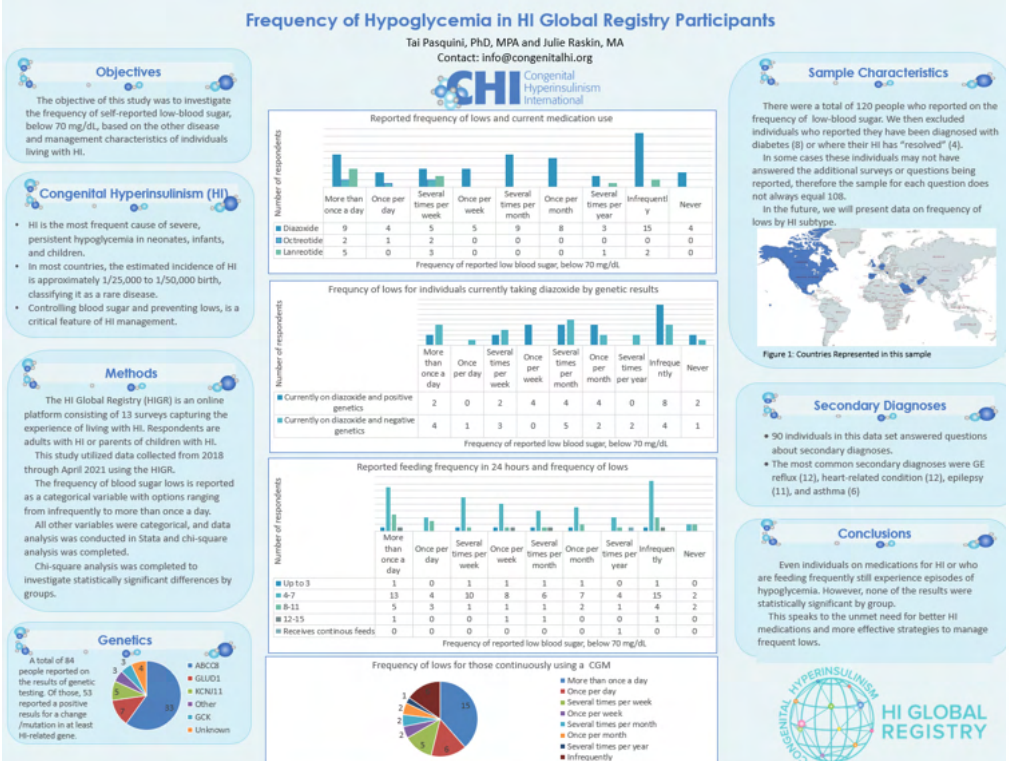
Conference Posters or Submissions

2021

Pediatric Endocrine Society (PES) 2021 Virtual Annual Meeting, *Hypoglycemia experience for patients with congenital hyperinsulinism as reported in the HI Global Registry*

2022

European Society for Paediatric Endocrinology (ESPE) 2022, *Utilizing PES hypoglycemia guidelines to evaluate presence of known risk factors in HI Global Registry participants*



HIGR Partnerships: MaxHIGR

- Map information between patient-populated HIGR and clinician-derived information
- Clinically validate the Quality-of-Life Questionnaires
- Synchronize patient and clinician populated information to develop a model prototype for an integrated database
- Investigate and utilize data for future research into natural history of the disease
- Define outcome parameters
- Accelerate the development of novel therapies

HIGR Partnerships: HI/HA Natural History Study

Create a comprehensive characterization of the natural history of the hyperinsulinism hyperammonemia (HI/HA) syndrome through the combination of clinical data from HI Centers of Excellence, phone interviews, and HIGR data.

- Aim to develop a deeper understand of the natural history of the HI/HA syndrome that will lead to improved outcomes and quality of life
- Findings will be used to explore the adaptability of this approach beyond the HI/HA syndrome to examine the natural history of different HI subtypes

CHI CRN Mission and Cornerstones

Create a congenital hyperinsulinism (HI) collaborative research network (CRN) that puts patients at the center of a strategy that leads to faster and more accurate diagnosis, drives new evidence-based treatments and cures, standardizes clinical guidelines, and facilitates increased and improved access.

(58 members including physicians, scientists, and patient experts from 18 countries and 5 continents)

The HI CRN has a commitment to:

- supporting **collaboration** across the globe;
- elevating the **patient voice** and ensuring the patient perspective is central to our work;
- guaranteeing **access** to information, medical specialists, and treatments regardless of income and geography;
- engaging **new researchers and ideas** to find innovative concepts and foster additional leaders in the HI network; and
- **addressing diversity, equity, and inclusion** in our work and our community.

CHI Congenital Hyperinsulinism International

Workstreams

Themes

- What is HI?: Nomenclature and Inclusion
- Medical and surgical treatments
- Care Guidelines/centers of excellence
- Diagnostics
- Glucose monitoring
- Clinical trials/industry engagement
- Genetics

Activities and Deliverables

- Clearly defined workstream topics
- Brainstorm to generate a gap analysis document
- Identify the gaps in:
  - Research gaps or needs
  - Infrastructure/ Pooled Research Resources/ Collaboration
  - Knowledge/ Expertise
  - Dissemination/ Funding
- Describe the elements needed to fill the gaps
- Prioritize the elements and create a workplan

Workflow

Gap analysis and research/ project component identification

Completed by CRN Workstreams

Infrastructure planning

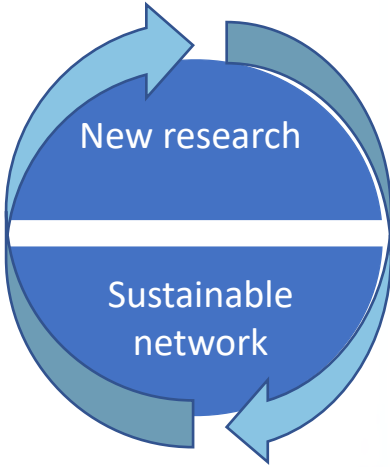
Completed by CRN Core Team

CHI CRN Convening

Prioritized research agenda

Membership structure

CRN research projects and committee work



Sustainable Network

Phase 1: 2020- May 2022

Phase 2: June 2022-

Evolving Structure

Phase 1: 2020-2022

- CRN Core Team (Leadership)
  - CHI Staff, Lead Researcher, Lead Clinician
  - CRN Council Members
  - Academic and industry researchers, clinicians, patient/ caregiver experts, who work on a specific workstream
- Followers
  - Members of the community who receive updates and provide feedback on the process

Phase 2: 2022-beyond

- CHI CRN Core Team (Leadership
- CHI Staff, Lead Researcher, Lead Clinician
- CHI CRN Council Members (Leadership):
  - Medical/Scientific Track
  - Patient/Caregiver Track
  - Industry Track
- CHI CRN Affill

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Top 12 Gaps/Needs Prioritized at Lisbon CRN Convening

Workstream	Gap/Need
All	HI Natural History Study
Diagnostics	Identification and adoption of newborn screening approach
Diagnostics	Glucose as a vital sign
Medical and Surgical Treatments	Knowledge of the cause of neurological damage
Care Guidelines & Centers of Excellence	Continually evolving global care guidelines
Clinical Trials & Industry Engagement	An expert group to develop novel clinical trials and outcome measures for regulatory approval
Genetics	Access to genetic testing
Diagnostics	A biomarker for hyperinsulinism
Clinical Trials & Industry Engagement	Meaningful glycemic endpoints
Glucose Monitoring	Device technology for HI patients
Medical and Surgical Treatments	Implementation of personalized medicine
Clinical Trials & Industry Engagement	Expand access and accelerate enrollment in clinical trials

Concrete Project Actions: Lisbon CHI CRN Convening

All projects will be mapped to the patient journey and will be led by goals and cornerstones

Identification and adoption of newborn screening approach/ Glucose as a vital sign

- Marketing campaign, buy-in and pledge for funding from all 5 companies
- Newborn glucose and ketone pilot studies (Denmark and Brazil)
-
-

Knowledge of the cause of neurological damage

- Multi-center prospective cohort study utilizing CGMs and standardized outcome measures
- Basic science / lab studies for specific gene mutations and understanding mechanisms

Continually evolving global care guidelines

- Caregiver care guidelines
- Guidelines adapted for different languages/ cultures that reflect resource restraints
- Incorporation of the patient voice

An expert group to develop novel clinical trials and outcome measures for regulatory approval

- Assemble outside expertise
- PFDD FDA meeting
- Establish a workgroup and committee

Dare to Dream of a Future without Lows

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Photos From 2013 CHI Family Conference in Milan

CHI Congenital Hyperinsulinism International