Goals

- better understand the patient and family experience
- better define the range of symptoms
- identify gaps in treatment and patient care
- identify gaps in knowledge and understanding of this disease
- better understand the burdens of this disease on the patient and the family
- identify the most important components of a future natural history study
- develop and prioritize future service programs
- create and prioritize a patient-led strategic research plan
- develop better and more effective clinical trials for potential future treatments

**method**
anonymous survey, Qualtrics, Castle IRB
Demographics

31 countries

United States 44%
UK 8%
Italy 6%
GER 5%
CAN 4%
ARG 3.3%
NL, ES, RO, PL 3%

28 states

all others 2% or less

COLLECTIVE VOICES PROJECT
**Demographics**

- **Female**: 57% (n=242)
- **Male**: 43% (n=240)

- **Caregiver or Parent**: 95% (n=250)
- **Patient**: 5% (n=250)

**Age and Distribution**

- **Youngest Infant**: n=242
- **Average 22 Years**: n=250
- **Oldest 53 Years**: n=238

<table>
<thead>
<tr>
<th>Age Group</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth to 6 yr</td>
<td>23%</td>
</tr>
<tr>
<td>7-12 years</td>
<td>37%</td>
</tr>
<tr>
<td>13-17 years</td>
<td>17%</td>
</tr>
<tr>
<td>18-53 years</td>
<td>23%</td>
</tr>
</tbody>
</table>

**Identity Groups**

- **White NH**: 79% (n=242)
- **Hispanic**: 10% (n=242)
- **Other**: 2% (n=250)
- **Multi**: 4% (n=250)
- **Asian/PI**: 3% (n=250)
- **Black**: 1% (n=250)

**Location**

- **Urban**: 40.4% (n=242)
- **Suburban**: 34.3% (n=250)
- **Rural**: 25.3% (n=250)

**Additional Information**

- Female: 57%
- Male: 43%
- Caregiver or parent: 95%
- Patient: 5%
- Average age: 22 years
- Oldest: 53 years
- Youngest: Infant (birth to 6 yr)
- Distribution: White NH - 79%, Hispanic - 10%, Other - 2%, Multi - 4%, Asian/PI - 3%, Black - 1%
- Location: Urban - 40.4%, Suburban - 34.3%, Rural - 25.3%
**Diagnosis**

**additional family members** 10%  
\( n=230 \)

**first symptom to diagnosis**
- shortest 1.5 weeks
- longest 34 years
- average 2.8 years

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>0 to 11 months</td>
<td>18%</td>
</tr>
<tr>
<td>1-4 years</td>
<td>44%</td>
</tr>
<tr>
<td>5-9 years</td>
<td>22%</td>
</tr>
<tr>
<td>10-14 years</td>
<td>9%</td>
</tr>
<tr>
<td>15-35 years</td>
<td>7%</td>
</tr>
</tbody>
</table>

\( n=203 \)

**age at diagnosis**
- youngest 12 days
- oldest 39 years
- average 6 years

**year of diagnosis**

- 1997: 23 cases
- 1998: 24 cases
- 1999: 25 cases
- 2000: 26 cases
- 2001: 27 cases
- 2002: 28 cases
- 2003: 29 cases
- 2004: 30 cases
- 2005: 31 cases
- 2006: 32 cases
- 2007: 33 cases
- 2008: 34 cases
- 2009: 35 cases
- 2010: 36 cases
- 2011: 37 cases
- 2012: 38 cases
- 2013: 39 cases
- 2014: 40 cases
- 2015: 41 cases
- 2016: 42 cases
- 2017: 43 cases
- 2018: 44 cases
- 2019: 45 cases
- 2020: 46 cases
- 2021: 47 cases

\( n=227 \)

**COLLECTIVE VOICES PROJECT**
Diagnosis

biggest obstacles to diagnosis

- lack of knowledge by healthcare team
- treated symptoms rather than looking for cause
- misdiagnosed
- didn't listen to family concerns
- misinterpreted or missed test results
- other
- lack of access to specialty care/testing
- no obstacles

n=260
Genetics

had genetic testing
- yes 92%
- no 6%
- unsure 2%
- n=230

variant found
- yes 82%
- no 8%
- unsure 10%
- n=209

additional genes
- yes 16%
- no 53%
- unsure 31%
- n=192

Type of testing
- unsure 30%
- single gene 20%
- epilepsy panel 16%
- WES 12%
- WGS 10%
- movement panel 6%
- other 6%

Type of variant
- unsure 49%
- other 13%
- missense 13%
- whole deletion 9%
- small deletion 8%
- splice site 4%
- nonsense 4%
- duplication 1%

NF1, MBDS, TUBA1A, HCN4, SCN4A, SHH, CHD2 - CHRNA2, GPR98, TANGO2, USP7, IFIH1, PIGG, EPM2A, MTOR, SCN1A, BRAT1, BRCA1, CENPJ

Collective Voices Project
Medical Care

- Setting for highest level of care for Glut1 Deficiency (top 3):
  - Neurologist within hospital clinic: 40%
  - Epilepsy clinic within hospital: 23%
  - Metabolic clinic within hospital: 14%

- Quality of care rating average (0-10): 7

- Worked with a dietitian: 90%

- Quality of care rating average (0-10): 7

- Roughly 1/2 eligible to transition to adult care have done so.

- Roughly 1/3 have traveled out of state or country for medical care.

*30% have experienced transition difficulties, mostly around specialty care.

n=209
are your medical professionals proactive in learning about Glut1 Deficiency

- Unsure: 28%
- Yes: 55%
- No: 17%

68% report their healthcare providers have other Glut1 patients

71% of those feel it results in better care

n=209
Symptoms

**first symptom**

- unusual eye/head movements: 34%
- seizures: 27%
- missing milestones: 12%
- unusual body movements: 10%
- floppiness/tone issues: 8%
- other: 9%

*n=203*

**"classical" symptoms**

- seizures
- cognitive
- developmental delays
- speech/language issues
- floppiness/tone
- eye/head movements
- unusual body movements

COLLECTIVE VOICES PROJECT
Symptoms

n=260

- Stamina/endurance: 45%
- Low energy: 44%
- ADD/focus: 34%
- Memory problems: 31%
- Sleep disturbances: 32%
- Temperature regulation: 26%
- Mood disturbances: 24%
- Anxiety: 23%
- Migraines: 22%
- Swallowing/chewing issues: 21%
- Retina/vision issues: 21%
- OCD: 19%
- Episodic confusion: 19%
- Behavior disturbances: 19%
- Gastro issues: 18%
- Autism spectrum: 19%
- Cyclic vomiting: 14%
- Teeth/nail issues: 12%
- Chronic pain: 13%
- MRI issues: 8%
- Kidney issues: 9%
- Heart issues: 6%
- Other: 2%
- Leg pain: 10%
Seizures

- **Absence**: 47%
- **Atypical absence**: 29%
- **Tonic-clonic**: 27%
- **Myoclonic**: 26%
- **Atonic**: 20%
- **Tonic**: 17%
- **Automatisms**: 9%
- **Sensations/Emotions**: 6%

84% experienced seizures. 2/3 no longer have seizures - diet? 36% report difficulty distinguishing between seizure & movement episode.
Movements

77% of participants reported muscle or movement issues

2/3 report certain body parts affected most and both sides of body affected equally

legs, eyes, arms, fingers, mouth

- Ataxia: 71%
- Dysarthria: 48%
- Dyspraxia: 45%
- Hypotonia: 44%
- Dystonia: 43%
- Spasticity: 34%
- PED: 28%
- Tremor: 26%
- Athetosis: 25%
- Ballismus: 19%
- Hemiplegia: 16%
- Chorea: 15%
- Other: 14%
- Total: 5%

n=202

COLLECTIVE VOICES PROJECT
Symptom Triggers

- Fatigue: 37%
- Heat: 31%
- Hunger: 28%
- Prolonged exercise: 28%
- Illness: 25%
- Dehydration: 21%
- Excitement: 21%
- Strong emotions: 20%
- Anxiety: 17%
- Hormones: 16%
- Weather/barometric changes: 10%
- Other: 6%
- Altitude changes: 5%

Symptom triggers? Yes 61%, No 14%, Not sure 25%

n=203
Other Symptoms & Behaviors

- high pain threshold: 44%
- sensory seeking: 27%
- sensory avoidance: 19%
- self-stimulatory: 25%
  - occasionally 66%
  - frequently 33%

Vascular Issues
- port wine stain birthmark
- unusual brain vascular findings (MRI)
- hemangioma/strawberry mark
- stork bite birthmark
- none

Self-reported disease severity rating (0-10)
- 6 avg.
  - n=211
  - avg.

n=203
Symptoms & Quality of Life

top 3 symptoms negatively impacting quality of life

- cognitive or intellectual difficulties: 44%
- speech/communication issues: 35%
- lack of independence: 24%
- movement issues present all the time: 23%
- seizures: 18%
- fatigue: 15%
- movement episodes: 15%
- ADD/focus: 9%
- other: 9%
- anxiety: 8%
- mood disturbances: 6%
- behavior disorders: 5%

percentages

n=260
Puberty

41% have experienced or are currently in puberty

Did symptoms change in puberty?
- Yes: 56.2% (n=80)
- No: 17.5% (n=80)
- Unsure: 26.3%

How did symptoms change?
- improved
  - none
- stayed same
  - cognitive
  - speech/language
- worsened
  - movements
  - stamina/energy
  - seizures
  - anxiety

Did treatments need to change?
- 45% yes

How did treatment need to change?
- diet changes 49%
- new meds 36%
- new therapies 8%
- other 8%
Puberty

Did you experience new symptoms for the first time in puberty?

- Yes: 37.7%
- No: 44.2%
- Unsure: 18.2%

What new symptoms did you experience for the first time in puberty?

- Seizures first time: 0%
- New seizure types: 10%
- Movements first time: 20%
- New movement types: 30%
- Anxiety: 0%
Adulthood

20% of responses

Did symptoms change in adulthood?
- no 23.7%
- unsure 2.6%
- yes 73.7%

n=38

How did symptoms change?
- improved
  - seizures
  - cognitive
  - speech/language
  - memory
- stayed same
  - movements
  - stamina/energy
- worsened

n=38

quality of life in adulthood
- improved 45%
- same 34%
- worsened 21%

n=38

on KDT
- 57%
  - able to manage diet independently 20%

10% have children of own
- 75% of children also have Glut1 Deficiency
- How do symptoms compare?
  - similar 67%
  - more severe 33%
  - less severe 0%

n=38
Development

Meet developmental milestones on time?

- Physical/motor: 75
- Speech/language: 50
- Cognitive: 25
- Social/emotional: 0

- Yes
- No
- Unsure

n=190

Experience challenges in any of these developmental domains?

- Fine motor: 21.8%
- Gross motor: 21%
- Speech/language: 21.1%
- Cognitive: 20.5%
- Social/emotional: 15.6%

- Most major childhood milestones met but delayed
- Most major adult milestones not met
Development & Mobility

Do you walk independently?

- yes | without support: 71%
- yes | but use support only for longer distances: 14%
- yes | but use support: 8%
- no: 7%

average age for walking: 2 years
   oldest: 9 years
   youngest: 8 months

n=190

COLLECTIVE VOICES PROJECT
Development

early intervention services 73%

- adults able to manage KDT independently
  - yes: 20%
  - no: 80%
  - n=26

- adults able to manage medications independently
  - yes: 45%
  - no: 55%
  - n=38

toileting

- reached on time: 30%
- reached but delayed: 51%
- n=190
Speech & Language

- **able to communicate using own voice**: 84% (n=190)
  - no issues: 22.1%
  - fluency: 30%
  - minor articulation: 20%
  - severe articulation: 10%

- **receptive language better than expressive?**
  - yes: 65.8%
  - both equal: 22.1%
  - unsure: 9.5%
  - no: 2.6%

- **average age to speak well enough to communicate**: 3.5 years

- **n=190**

- half feel speech issues make them appear less capable/intelligent than they are
- 2/3 experience frustrations around communication issues

**COLLECTIVE VOICES PROJECT**
Cognitive

special education services 74% n=145

83% report certain subjects harder
- math 39%
- writing/composition 33%
- reading 15%
- spelling 7%
- science 3%
- social studies 3%

only 56% reported neuropsychological testing

87% reported deficits
- attention/focus
- visuospatial, visual attention
- planning and organization
- reasoning and problem solving
- memory
- language functions

only 25% knew IQ score
- majority reported 60-70 range
- average of all scores reported was 79

COLLECTIVE VOICES PROJECT
Cognitive & School

performing at grade level 33%  n=145

beneficial supports

- IEP 66%
- 1:1 aide 60%
- 504 plan 18%
- special transportation 31%
- shortened school day 20%

all forms of school based therapies were reported as highly beneficial

college/vocational 27%

trouble getting good curriculum fit?

- yes 42%
- no 42%
- unsure 16%

COLLECTIVE VOICES PROJECT
Social & Emotional

**Impacts on Social Life**
choose top 3

- speech/articulation: 33%
- cognitive or intellectual: 31%
- ketogenic diet challenges: 25%
- lack of independence: 21%
- immaturity: 20%
- movement issues: 17%
- unpredictability of symptoms: 9%
- behavior disturbances: 8%
- seizures: 7%
- other: 7%
- autism spectrum symptoms: 4%

**Frequency of Symptoms**

- 77% describe self as social
- 2/3 report having close friendships
- 27% report mood disturbances
- 20% report behavior disturbances

**Self-reported Happiness Rating (0-10)** 7.6 average

n=260
Social & Emotional

Sibling Impacts

- Close friendship with Glut1 Deficiency sibling
- Missed out on traditions and food celebrations due to KDT
- Taken on caregiving responsibilities
- Missed out on social opportunities
- Significant time at medical appointments, therapies, etc.
- Extreme jealousy or resentment
- Taken on advocacy role
- Other

n=260
Ketogenic Diets

91% have tried ketogenic dietary therapy

shortest: 1 month   longest: 21 years
average: 5 years

has KDT lost effectiveness over time?

7.5% have stopped KDT due to lack of effectiveness

n=260

types used

classical 3:1 or 4:1
modified ketogenic diet
modified Atkins diet
MCT oil version
low glycemic index

65%
41%
32%
16%
5%

91% have tried ketogenic dietary therapy

58%
34%
27%
10%

COLLECTIVE VOICES PROJECT
Ketogenic Diet Benefits

- **seizures**: very effective
- **movement issues**: somewhat effective
- **ADD/focus**: not at all effective
- **energy/stamina**: very effective
- **headaches**: not at all effective
- **behavior**: very effective
- **speech/language**: not at all effective

Overall, n=167
Ketogenic Diet Benefits

by age

- attention/focus
- behavior
- cognition
- energy/stamina
- headaches/migraines
- movement issues
- seizures
- speech/communication

Age Group
- 0-12
- 13 and Over

n=167
Ketogenic Diets

83% measure ketones

- Blood: 78%
- Urine: 21%
- Breath: 1%

Method

- Correlation to symptoms?
  - Yes: 65%
  - No: 11%
  - Unsure: 24%

Ideal ratio: 3:1

"Just right" ketone level: 3-5

53% report using MCT oils

- 65% of those feel MCT oil makes the diet more effective

8% report using feeding tube

n=167

Collective Voices Project
Ketogenic Diets

reasons for not trying KDT

- family wasn’t supportive: 0%
- doctor wasn’t supportive
- foods too expensive
- thought it was too difficult
- thought I was too old
- thought I wouldn’t be able to give up foods I like
- no KDT services available to me
- thought it wouldn’t work for my symptoms

other
- Doctor advised that Triheptanoin was working for me as well or better than I could expect with a ketogenic diet will start soon
- I just got diagnosed and plan to meet with a dietitian soon to start the diet.
- GONG TO BE IN A STUDY THAT REQUIRES NO KETO DIET
- She does not eat enough with a diet will be worst, seizures are under control with medicine kapra
- Thought it might be too challenging since I am 14.
- Didn’t try because it would exclude her from the trial
- I do modified Atkins

percentages
Ketogenic Diet Side Effects

- Constipation: 59%
- Weight gain: 26%
- High cholesterol: 25%
- Gastro issues: 23%
- Slowed physical growth: 23%
- Kidney issues: 21%
- Acidosis: 17%
- Weight loss: 16%
- Bone density issues: 16%
- Other: 10%
- Pancreatitis: 1%

Experienced side effects: 41%

Stopped KDT due to side effects:
- 4% temporarily
- 3% permanently

Factors mentioned:
- Psychological stress, dehydration, hair loss, bad breath, headaches, carnitine & calcium deficiencies, leg cramps

n=167

Collective Voices Project
Ketogenic Diet Challenges

choose top 3

- Social: feeling different, 54%
- Social: impact on family celebrations/holidays, 52%
- Lack of opportunities for spontaneity, 43%
- Time required, 40%
- Costs of food and supplies, 28%
- Cooperation/compliance, 18%
- Managing complexities of diet (calculations, etc.), 17%
- Lack of effectiveness for all symptoms, 11%
- Other, 9%
- Lack of medical support, 7%
- Managing side effects, 6%

n=167

Patient 6.4

Family 6.6

Do benefits outweigh challenges? Yes 83%, No 4%, Unsure 13%

Level of difficulty (0-10)

Collective Voices Project
Ketogenic Diet Challenges

have you had issues getting KDT supplies and services covered by insurance?

- yes 44%
- no 56%

n=167

prescribed medical foods
prescribed supplements
ketone testing supplies
medications
dietitian services

COLLECTIVE VOICES PROJECT
Therapies & Assistive Devices

most common therapies

speech
occupational
physical

85% have tried and found beneficial

1/3 report that moderate physical exercise is beneficial for symptom management

assistive devices used most

orthotics, eyeglasses, wheel and stroller chairs, walkers, adaptive clothing
Other Treatments

Have you tried other treatments that help?

- **seizures 35%**
  - keppra/levetiracetam - 22% or 14 total
  - sodium valproate/depakote - 11% or 7 total
  - acetazolamide/diamox - 8% or 5 total
  - ethosuximide - 8% or 5 total
  - lamotrigine/lamictal - 6% or 4 total

- **ADD/focus 16%**
  - vyvanse
  - methylphenidate/ritalin

- **movements 17%**
  - baclofen
  - acetazolamide/diamox

- **anxiety 10%**
  - CBD oil
  - sertraline
  - paroxetine

- **migraines 10%**
  - acetaminophen/paracetamol

28% have used rescue meds for seizures
- diazepam/diastat/stesolid
- midazolam

16% have used rescue meds for movement episodes
- diazepam/diastat/stesolid
- lorazepam
- clobazam
- CBD oil

n=184
Other Treatments

**ketone supplements**
- 20% have tried
- 60% found it effective

**CBD Oil**
- 9% have tried
- 53% found it effective
  *movement, anxiety*

**VNS**
- 5% have tried
- 12.5% found it effective

**corn starch**
- 6% have tried
- 40% found it effective

**C7 oil/triheptanoin**
- 14% have tried
- How effective?

**Use both together**
- KDT 50%
- C7 oil 16.7%
- Equal effectiveness 16.7%

**Which is most effective?**
- 48% of those have tried both KDT and C7

<table>
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<tr>
<th>Condition</th>
<th>Very Effective</th>
<th>Somewhat Effective</th>
<th>Not at All</th>
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</thead>
<tbody>
<tr>
<td>Energy/stamina</td>
<td>0</td>
<td>25</td>
<td>50</td>
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<tr>
<td>Cognition</td>
<td>75</td>
<td>100</td>
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<tr>
<td>Attention</td>
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<tr>
<td>Behavior</td>
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<tr>
<td>Headaches</td>
<td>0</td>
<td>25</td>
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</tbody>
</table>

n=184
Patient & Family Research Priorities

choose top 3

- new and better treatments: 46%
- basic science for better understanding disease: 27%
- changes in adulthood: 22.3%
- long term KDT effects: 21.8%
- changes in puberty: 21.4%
- potential impact on other body systems: 19.3%
- different ketogenic diets/which best?: 14%
- newborn screening development: 12%
- better understand genetic mutations: 10%
- improved diagnostic testing: 3.4%
- role of inflammation: 2.9%
- unusual eye/head movements: 2.5%
- other: 2.5%

n=260
Priority Outcomes for New Treatments
choose top 3

- able to eat a normal diet: 35%
- improved cognition: 27%
- better speech/communication: 25%
- eat an easier or less restrictive keto diet: 23%
- greater independence: 23%
- more typical development: 16%
- fewer movement issues: 14%
- improved coordination/balance: 12%
- fewer seizures: 10%
- improved fine motor skills: 9%
- better sleep: 5%
- improved gross motor skills: 4%

n=260
Types of New Treatments Willing to Try

- Pill or tablet: 65%
- Oil or liquid: 58%
- Dietary therapy: 56%
- IV or injection into skin/muscle: 42%
- Infusion pump: 25%
- IV or injection into spinal fluid: 23%
- IV or injection into brain: 17%

Willing to do clinical trials?

- Yes: 60.4%
- Maybe: 34.7%
- No: 5%

n=260
Family Burdens

choose top 3

**financial burden**
- cost of ketogenic diet: 32%
- gave up career for caregiving: 27%
- out of pocket therapies: 23%
- out of pocket medical costs: 20%
- travel costs for medical care: 15%
- more expensive insurance plans: 9%

**overall burden**
- overall family life: 43%
- social life: 42%
- emotional/mental: 40%
- finances: 32%
- sibling life: 30%
- career: 24%
- relationship spouse/partner: 24%
- other: 4%

- significant sibling impact
- long term care & financial planning often needed

n=260

**COLLECTIVE VOICES PROJECT**
Please join the Natural History Study to help tell the full story of Glut1 Deficiency across the lifespan.

Thank you!