Collective Voices in Gut1 Deficiency Project Survey – Report

The Glut1 Deficiency Collective Voices Project was designed to have a better understanding of the patient and family experience across a broad range of areas. The goals for the survey were to better define the range of symptoms, identify gaps in treatment and patient care, identify the gaps in knowledge and understanding of this disease, better understand disease burdens, identify the most important components of a future natural history study, develop and prioritize a patient-led strategic research plan, and to develop better and more effective clinical trials for potential future treatments.

The report will be presented in sections, and the first section reported is **Diagnosis**.

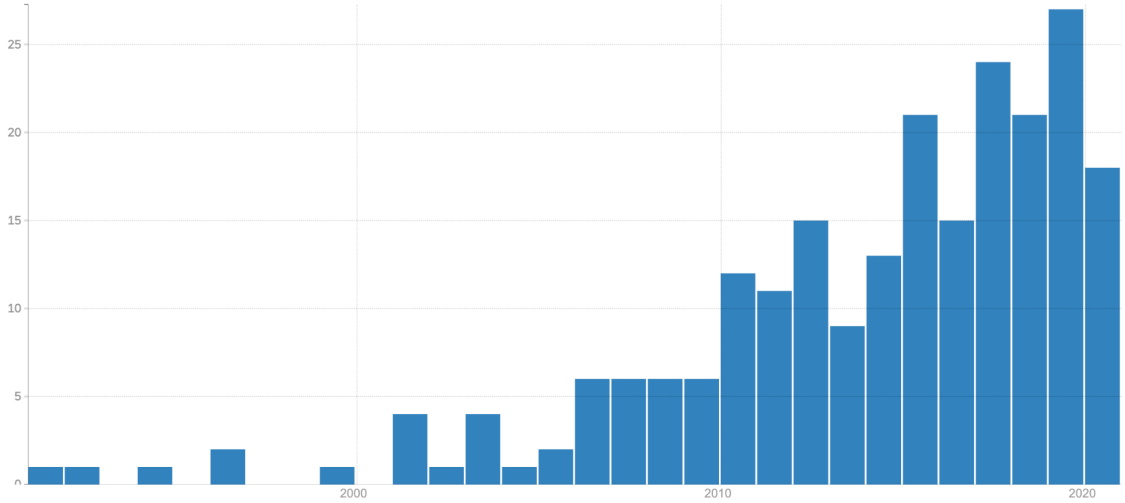
Questions:

1. **How old were you when you were diagnosed with Glut1 Deficiency?**

The average age of diagnosis was 6 years old. Over time, the average age of diagnosis has decreased.

2. **What year were you diagnosed with Glut1 Deficiency?**

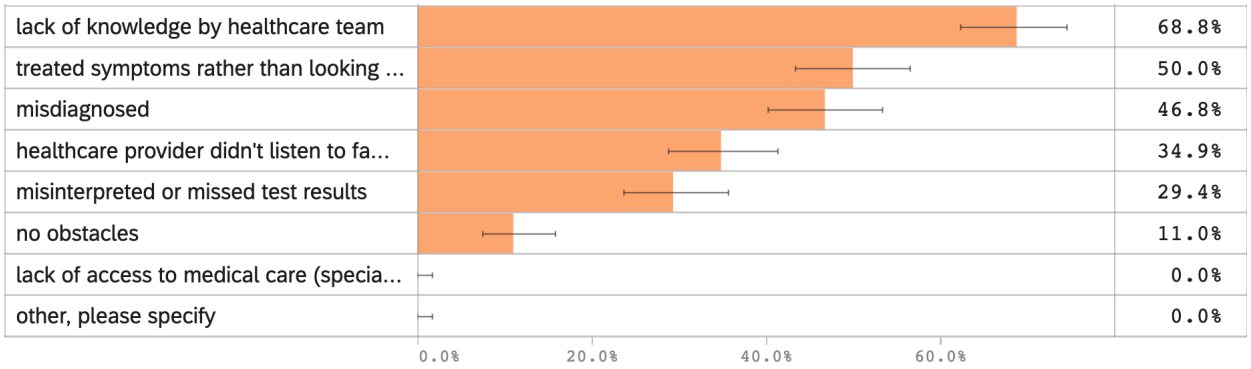
As time passes, the number of diagnoses per year continues to increase. 10 years ago, in 2010, 12 diagnoses were reported and in recent years, that number has jumped to over 20.



3. **How much time passed from first symptom to diagnosis?**

The average time from first symptom to diagnosis is 2.8 years.

4. **What were the biggest obstacles to getting a diagnosis?**



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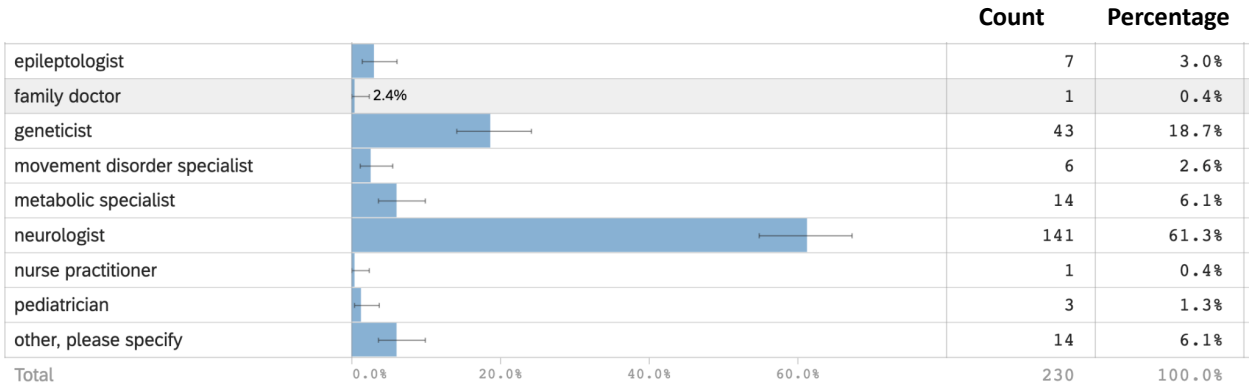
The most commonly reported obstacles to getting a diagnosis were lack of knowledge by the healthcare team, treatment of symptoms rather than looking for the cause, and misdiagnosis. This is suggestive of an underlying lack of awareness or understanding of Glut1 among healthcare professionals.

Correlation between obstacles to getting a diagnosis and time passed from first symptom to diagnosis:

As the number of challenges to receiving a diagnosis increases, so does the average (and median) time from first symptom to diagnosis. Those who reported no challenges waited about a year (median 6 months) between having their first symptom and getting a diagnosis.

For teens and young adults, more severe symptoms were associated with increased time to diagnosis.

5. **What type of medical provider made the diagnosis?**

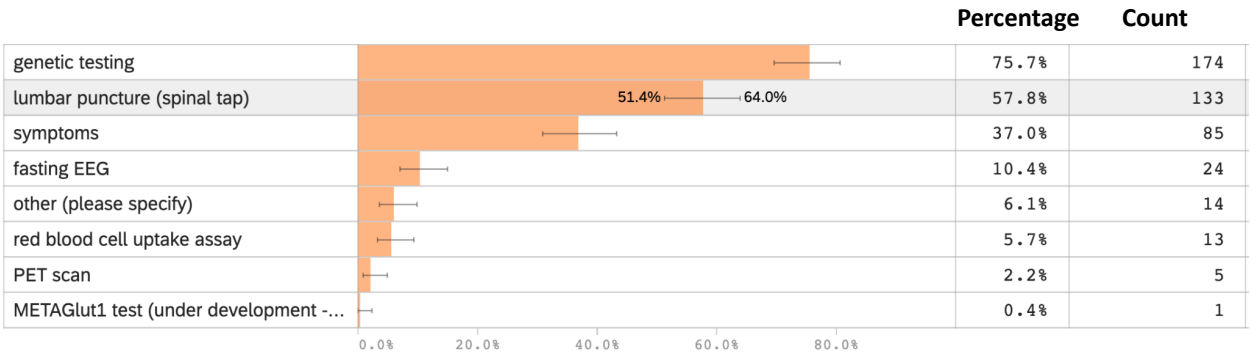


61% of patients surveyed report Neurologists to be the medical providers making Glut1 Deficiency Syndrome diagnosis, while 19% of patients surveyed report geneticists making the

diagnosis. It's important to point out that metabolic specialists, epileptologists and movement disorder specialists are among the medical providers making a diagnosis; this could mean that more medical providers are learning about the condition.

This is what some of the patients chose in ***other*** category as the type of medical provider making diagnosis: Developmental pediatrician, neurometabolic specialist and neuropsychiatrist among others.

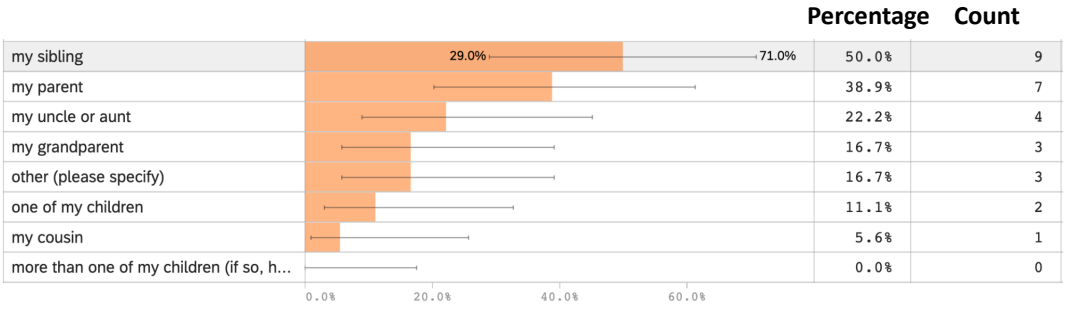
6. **<u>How was the diagnosis made?</u>**



For this question, patients could select all the options that applied.
Patients selected genetic testing as the technique most frequently used (76%) to make a Glut1 Deficiency Syndrome diagnosis. Lumbar puncture came in second place (58%) as the method used to make a diagnosis.

Some of the answers in ***other*** category are: MRI and skin biopsy.

7. **<u>Are there any additional members of your family diagnosed with Glut1 Deficiency? Who?</u>**
   10% of patients surveyed report having additional members diagnosed with Glut1 Deficiency.



Within this population of patients, most (50%) report having a *sibling* with Glut1 Deficiency, followed by a *parent* (39%), *uncle or aunt* (22%) and *grandparent* (17%).

8. **Do you have any other conditions or diseases diagnosed in addition to Glut1 Deficiency?**

30 % of surveyed patients report being diagnosed with other conditions in addition to Glut1 Deficiency.

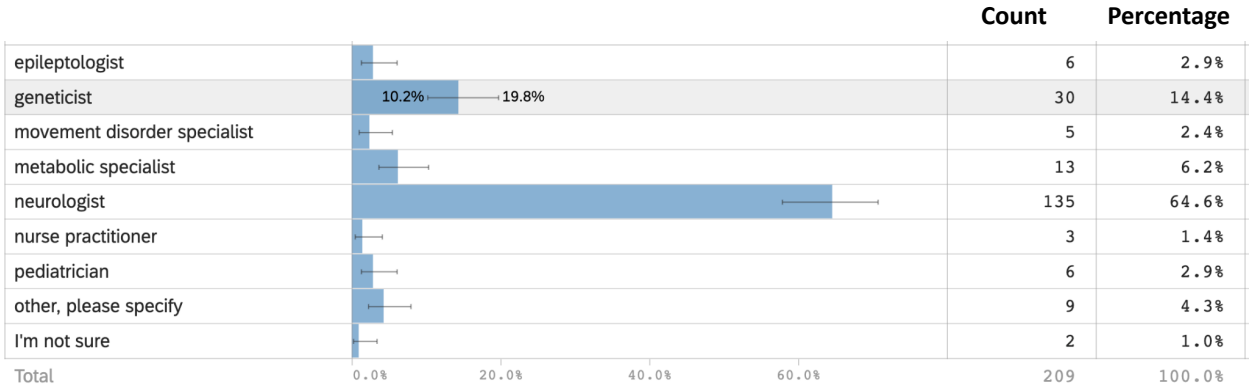
Which other conditions?

Out of all surveyed patients, 67 answered this question. Out of these patients, 24% of them reported Epilepsy as an additional diagnosis, 13% reported autism, 10% reported developmental delay and 9% reported ADHD.
Among some of the other conditions patients reported are: Cerebral palsy (6%), cognitive disability (4%), celiac disease (3%) and strabismus (3%).

9. **Have you had genetic testing done?**

91% of patients surveyed report they had genetic testing done, 6% did not have genetic testing and about 3 % are not sure if they had genetic testing done.

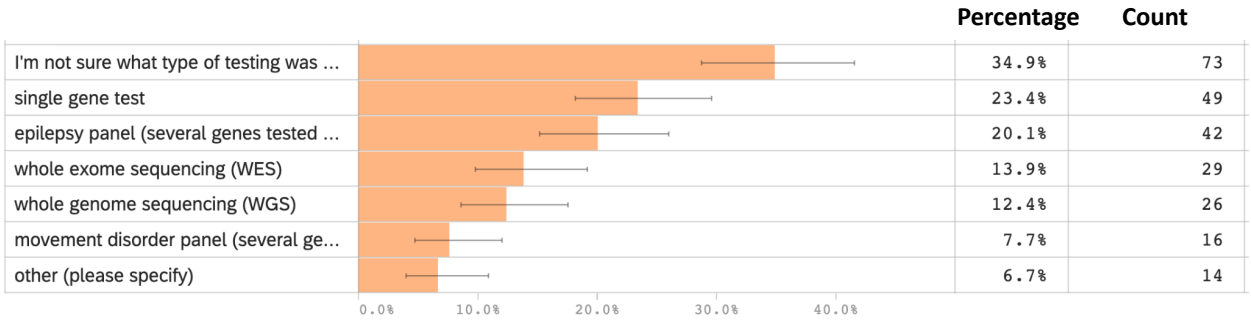
Who ordered the genetic testing?



Most of the genetic tests were ordered by neurologists (65%) followed by geneticists (14%). In addition, other medical providers such as metabolic specialists, epileptologists, pediatricians, and movement disorder specialists are among the medical providers ordering genetic tests.

Some of the medical providers reported in the *other* category are: Dietitian, neuropsychiatrist, and developmental pediatrician.

What type of testing was done?



The graph above shows that most of the patients surveyed who had genetic testing do not know what type of testing was done. This could indicate a lack of communication between medical providers and patients/families, or maybe lack of curiosity from patients/families.

Most of the patients with knowledge about the type of genetic testing performed reported having a single gene test (23%). This test is performed when the medical provider ordering the test believes the patient has the symptoms of a specific condition or syndrome (CDC).

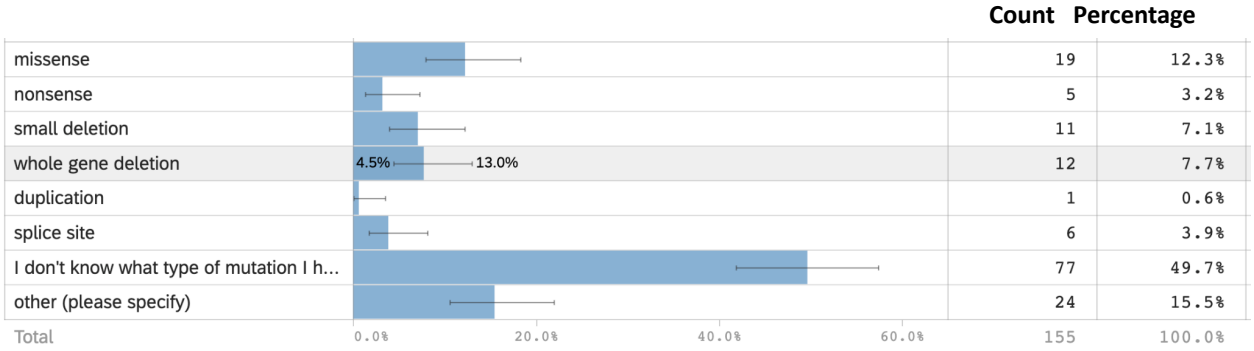
Among other genetic tests ordered by medical providers are: Epilepsy panel (20%), Whole exome sequencing (14%), whole genome sequencing (12%) and movement disorder panel (8%).

Some of the tests reported in the *other* category are: Comparative genomic hybridization, next generation sequencing, multiplex ligation-dependent probe amplification (MLPA), fluorescence in situ hybridization (FISH).

10. **Was a mutation or variant found in the SLC2A1 gene in the testing results?**

82% of patients surveyed report that genetic tests found a variant in the SLC2A1 gene or the gene for the Glut1 protein, while 8 % report not finding a variant. Interestingly, 10% of surveyed patients are not sure if the tests found a variant. This is important to point out because it could indicate that there is a need for more education for families to understand the importance of the information provided by medical providers, as well as the importance of communication between medical providers and patients/families.

What type of mutation do you have?



50 % of surveyed patients who have a variant in the SLC2A1 gene don't know the type of mutation they have. It's key to emphasize the importance of knowing this information because it allows one to have a better understanding of the condition. In addition, it is important to have this type of information if one participates in a patient registry or natural history study.

Most of the patients who reported having a variant on the SLC2A1 gene (12 %), report having a missense mutation, 8% report a whole gene deletion, 7% report a small deletion. The *other* category accounts for 15% of the responses; among some of the mutations reported are frameshift mutation and substitution.

11. **Were mutations found in any genes besides SLC2A1 gene?**

16% of patients reported having mutations in other genes besides SLC2A1, while 53% report not having mutations in other genes. Additionally, 32% report not being sure if they have mutations in other genes.

Some of the **additional** genes patients reported having mutations are: NF1, MBD5, TUBA1A, HCN4, SCN4A, SHH, CHD2 -CHRNA2, GPR98, TANGO2, USP7, IFIH1, PIGG, EPM2A, MTOR, SCN1A, BRAT1, BRCA1 and CENPJ.