

Enaika Kishnani; Emily Reinhardt; Heidi Wallis
 Association for Creatine Deficiencies, Carlsbad, CA, USA

Background

- Cerebral creatine deficiency syndromes (CCDS) are a group of inborn errors of creatine metabolism that affect the biosynthesis and transport of creatine within the body.¹
- The three types of CCDS are creatine transporter deficiency (CTD), guanidinoacetate methyltransferase (GAMT) deficiency, and arginine:glycine amidinotransferase (AGAT) deficiency.
- Research has found that many patients with CTD may be at risk of developing a cardiovascular condition called prolonged QTc, which is an irregular heart rhythm.²
- It is currently unknown if AGAT and/or GAMT deficiency patients are also at risk of developing prolonged QTc.

Objective

- The goal was to better understand the relationship between all three CCDS and cardiovascular health using patient- and caregiver-reported data.

Methods

- CCDS patients and caregivers completed a short cardiovascular health survey in ACD's online CreatineInfo Patient Registry and Natural History Study.
- We collaborated with NIH-cardiologist Mark Levin, MD, ACD's Family Advisory Board (FAB), and ACD's Registry Advisory Board (RAB) to develop the survey for the CCDS community.
- The survey included questions about cardiovascular history, cardiovascular intervention history, cardiovascular medications, and family cardiovascular history.
- The survey was promoted on all of ACD's social media platforms, email list, and website to maximize the number of responses. The survey and all recruitment materials were IRB-approved.

Results

Heart Conditions

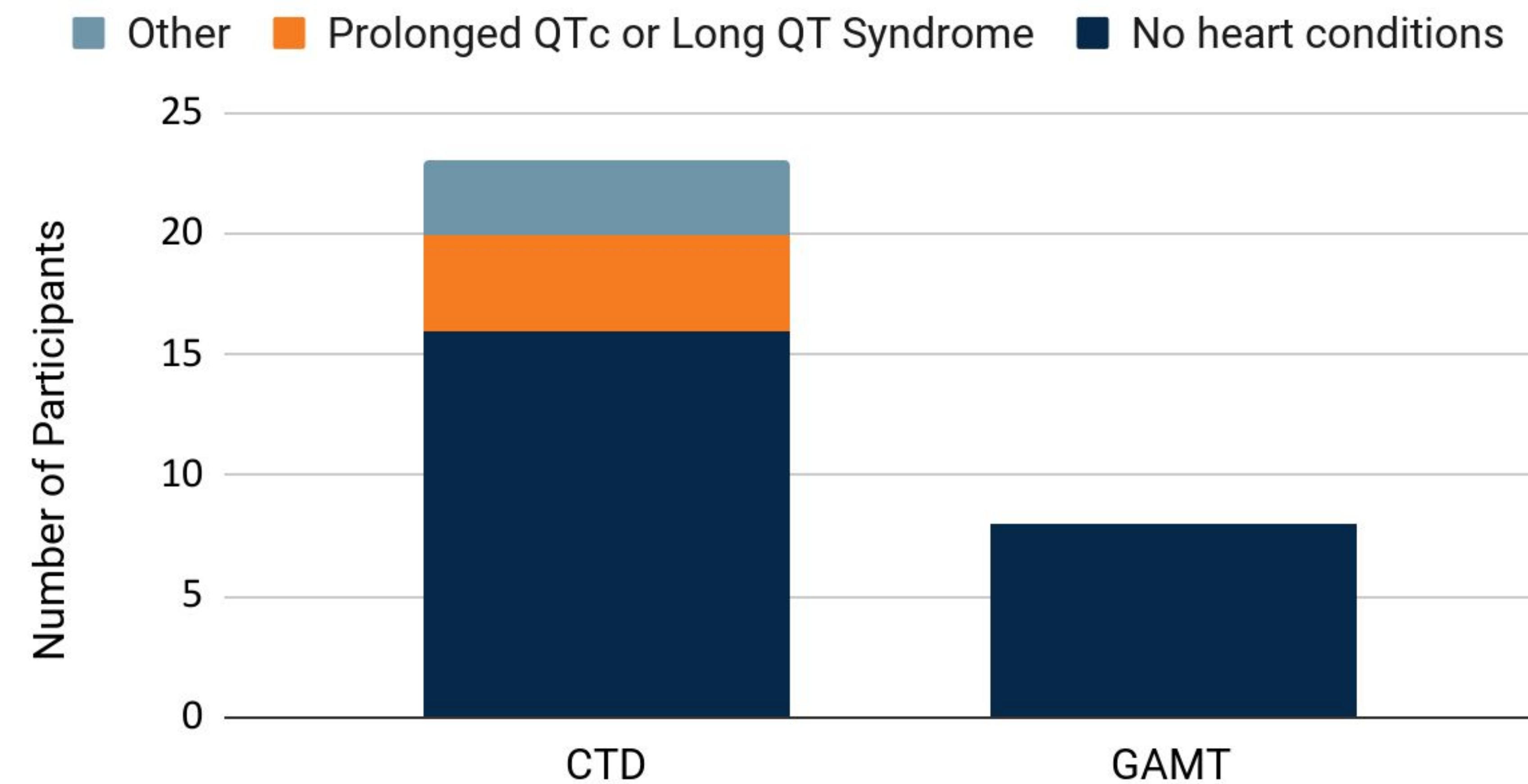


Figure 1: Number of survey participants reporting a heart condition(s) among CTD (n=23) and GAMT (n=8) patients. Only CTD participants reported experiencing "Prolonged QTc or Long QT Syndrome" (n=4) and "Other" (n=3) heart conditions, including heart murmur, subclinical noncompaction left ventricular cardiomyopathy, vasomotor instability, low blood pressure, and orthostatic intolerance.

Types of Physical Activity

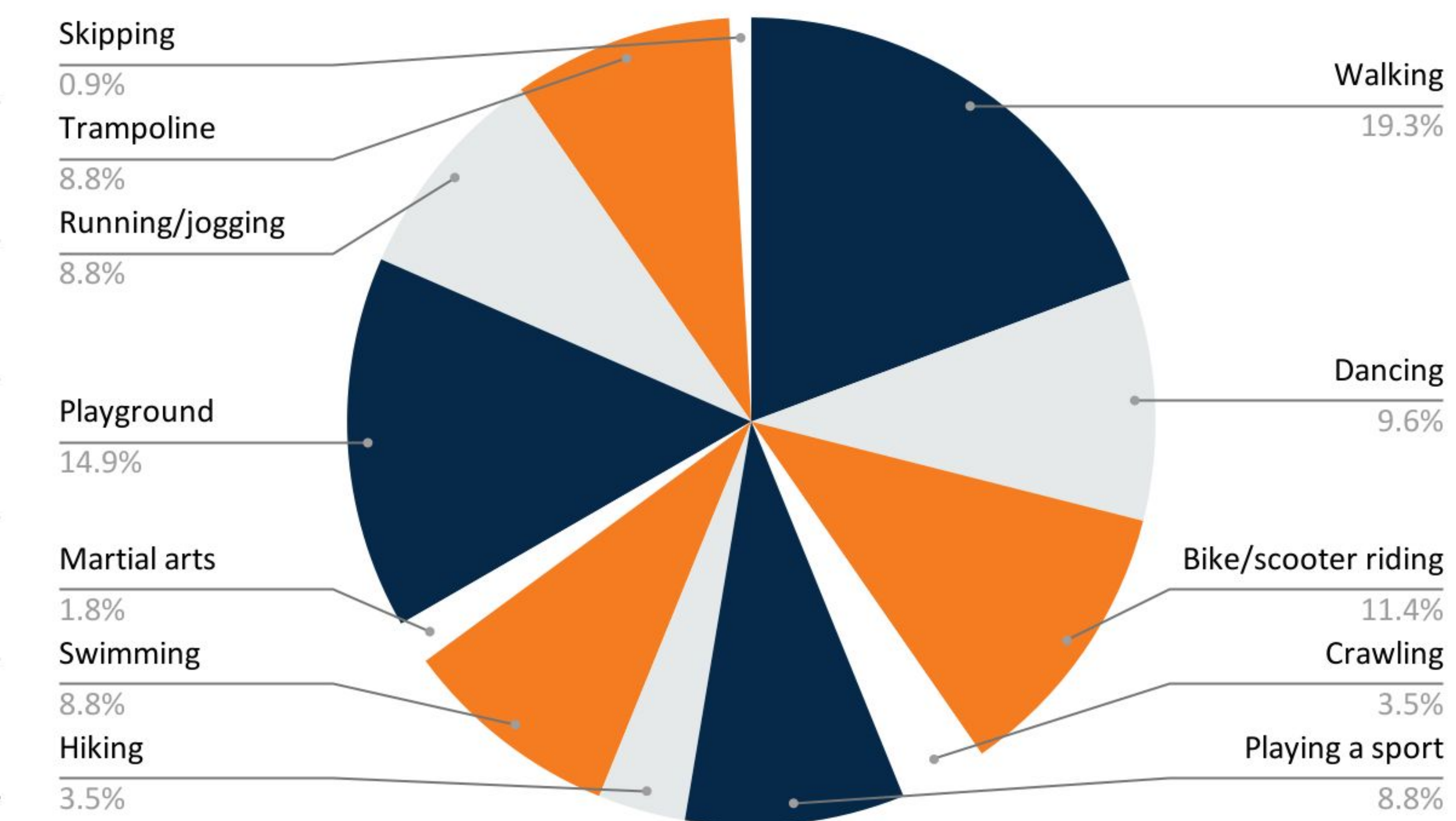


Figure 3: Types of physical activity that CCDS participants (n=33) regularly engage in.

Weekly Activity Levels

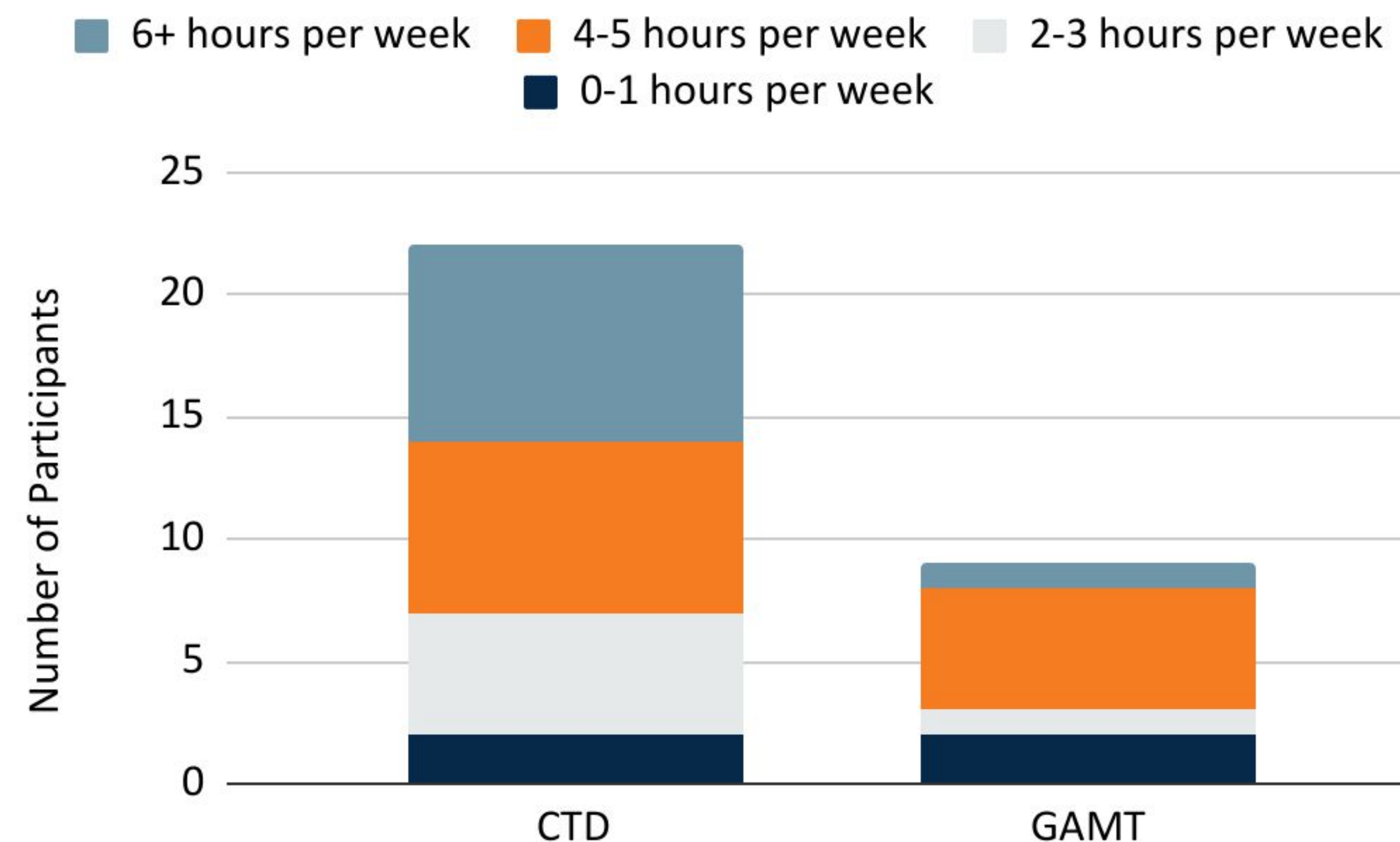


Figure 2: Number of survey participants reporting weekly activity levels among CTD (n=22) and GAMT (n=9) patients.

Conclusions

- This survey was the first to capture cardiovascular health data within our CreatineInfo Patient Registry and Natural History Study.
- Our preliminary findings show that CTD patients report experiencing cardiovascular conditions, unlike GAMT deficiency patients.
- These data support previous research showing that patients with CTD are at risk of developing cardiovascular conditions, including prolonged QTc.
- More research is needed to determine the risks of AGAT and GAMT deficiency patients of developing cardiovascular issues, including prolonged QTc.

References

1. Stockler-Ipsiroglu S, van Karnebeek CD. Cerebral creatine deficiencies: a group of treatable intellectual developmental disorders [published correction appears in Semin Neurol. 2014 Sep;34(4):479]. Semin Neurol. 2014;34(3):350-356. doi:10.1055/s-0034-1386772
2. Levin, M. D., Bianconi, S., Smith, A., Cawley, N. X., Do, A. D., Hammond, D., ... & Hannah-Shmouni, F. (2021). X-linked creatine transporter deficiency results in prolonged QTc and increased sudden death risk in humans and disease model. Genetics in Medicine, 23(10), 1864-1872.