# TIMOTHY SYNDROME ALLIANCE (TSA)

England & Wales · Charity number 1185523

## Details

| | |
|---|---|
| **Other names** | TIMOTHY SYNDROME ALLIANCE, TSA |
| **Status** | Registered |
| **Legal form** | CIO |
| **Registered** | 2019-09-27 |
| **Register** | View on the Charity Commission register |

## Contact

| | |
|---|---|
| **Address** | 8 Butt Street<br>Minchinhampton<br>Stroud<br>GL6 9JP |
| **Phone** | 07941881340 |
| **Email** | sophie@timothysyndrome.org |
| **Website** | www.timothysyndrome.org |

## Activities

**Objects:** THE OBJECTS OF THE CIO ARE TO RELIEVE THE NEEDS OF THOSE AFFECTED BY DELETERIOUS CACNA1C GENE CHANGES RESULTING IN CACNA1C-RELATED DISORDERS INCLUDING TIMOTHY SYNDROME AND LONG QT8, THEIR FAMILIES AND CARERS WORLDWIDE IN PARTICULAR BUT NOT EXCLUSIVELY BY:- (1) PROMOTING GREATER UNDERSTANDING OF THE CAUSES, SYMPTOMS AND TREATMENT OF CACNA1C-RELATED DISORDERS INCLUDING TIMOTHY SYNDROME AND LONG QT8, BY THE PROMOTION OF RESEARCH AND SHARING AND DISSEMINATING OF THE RESULTS OF SUCH RESEARCH FOR THE BENEFIT OF THE GENERAL PUBLIC; (2) RAISING PUBLIC AWARENESS OF THE SYMPTOMS, NEEDS AND RELATED MEDICAL CONDITIONS OF THOSE LIVING WITH CACNA1C-RELATED DISORDERS INCLUDING TIMOTHY SYNDROME AND LONG QT8.

**Activities:** Timothy Syndrome Alliance (TSA) supports individuals with CACNA1C-Related Disorders, including Timothy Syndrome and Long QT8, and their families/carers. From the UK, we provide guidance, information, and advocacy to families worldwide, raise awareness, and promote research and clinical development to improve understanding, care, and treatment.

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## Classification

- **How:** Provides Services, Provides Advocacy/advice/information, Sponsors Or Undertakes Research
- **What:** The Advancement Of Health Or Saving Of Lives, Disability
- **Who:** Children/young People, People With Disabilities

## Geography

- Throughout England

## Finances

| Period end | Income | Expenditure | Assets | Employees |
|---|---|---|---|---|
| 2025-11-30 | £205,304 | £128,996 | - | - |
| 2024-11-30 | £93,687 | £19,756 | - | - |
| 2023-11-30 | £21,405 | £12,305 | - | - |
| 2022-11-30 | £10,005 | £4,706 | - | - |
| 2021-11-30 | £6,084 | £3,226 | - | - |

## Trustees

| Name | Role | Appointed |
|---|---|---|
| **SOPHIE MUIR** | Chair | 2019-09-27 |
| Achsah James | | 2024-11-06 |
| Dr Christine Ziegler | | 2025-09-10 |
| Galina Gardiner | | 2019-09-27 |
| Gemma Duncan | | 2024-03-11 |
| Glenn Miller | | 2025-09-10 |
| Meg McLaughlin | | 2019-09-27 |
| Nicholas Muir | | 2019-09-27 |
| Susan Bresnahan | | 2024-06-11 |

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**TIMOTHY SYNDROME ALLIANCE (TSA)**

England & Wales - Charity number 1185523

# Accounts

TIMOTHY SYNDROME ALLIANCE (TSA)

# ANNUAL REPORT 2025

For financial period

**1 DECEMBER 2024 TO 30 NOVEMBER 2025**

tsa
Timothy Syndrome Alliance
CACNA1C

Charity Registration Number: 1185523

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# Message from the Chair

2025 has been a year of consolidation, growth and increasing responsibility for Timothy Syndrome Alliance (TSA). Behind every statistic in this report is a family searching for answers. As understanding of CACNA1C-Related Disorders continue to evolve, so too does the complexity of the environment in which we operate. What was once viewed as a narrowly defined condition is now recognised as a broader group of related disorders. This brings new opportunities for research and care, but also a responsibility to ensure that information, support, and clinical guidance evolve alongside the science.

TSA delivers its work through six strategic priorities, as outlined in our strategic framework and previous annual reporting. During 2025 we strengthened communications reach, expanded community infrastructure, deepened clinical and research collaboration, and continued to build the systems required to support responsible long-term progress.
Our global registry grew, our community support network expanded, and we secured significant pro bono scientific collaboration to strengthen the evidence base. We continued to prioritise trusted information and careful language, recognising that clarity reduces harm in rare and poorly understood conditions.

Importantly, we have done this as a predominantly volunteer-led organisation. Trustees and volunteers contribute substantial time and expertise, and I remain deeply grateful for their professionalism and commitment. Alongside this, we reached an important milestone in our organisational development. With grant support from the Chan Zuckerberg Initiative, we began to invest in core capacity, enabling us to appoint our first paid staff roles. We are deeply grateful for this support, which strengthens the infrastructure required to deliver our work responsibly and sustainably.

The past year has also reinforced important lessons. Families often reach us at moments of uncertainty and vulnerability. Clinical pathways remain variable. Research interest is increasing, but must be grounded in ethical engagement and lived experience. Infrastructure, though less visible than programmes, remains the foundation upon which progress depends.

Financially, the charity remains stable, with income of £205,304. We continue to rely primarily on restricted funding and recognise the importance of increasing unrestricted income to strengthen resilience. Trustees monitor risk carefully and remain committed to proportionate, sustainable growth.

None of this work is undertaken in isolation. We are grateful to our Scientific Advisory Board, Patient Advisory Board, Research and Public Engagement Officer, Mission Support Officer, funders, research partners, and the global community of families who place their trust in us. Their willingness to collaborate makes responsible progress possible.

Looking ahead to 2026, our priorities are clear: dissemination of emerging consensus guidance, analysis and publication of registry data, continued strengthening of community support, and preparation for our international in-person conference. We remain focused on building understanding, improving care, and enabling research that is rigorous, ethical and community-informed.

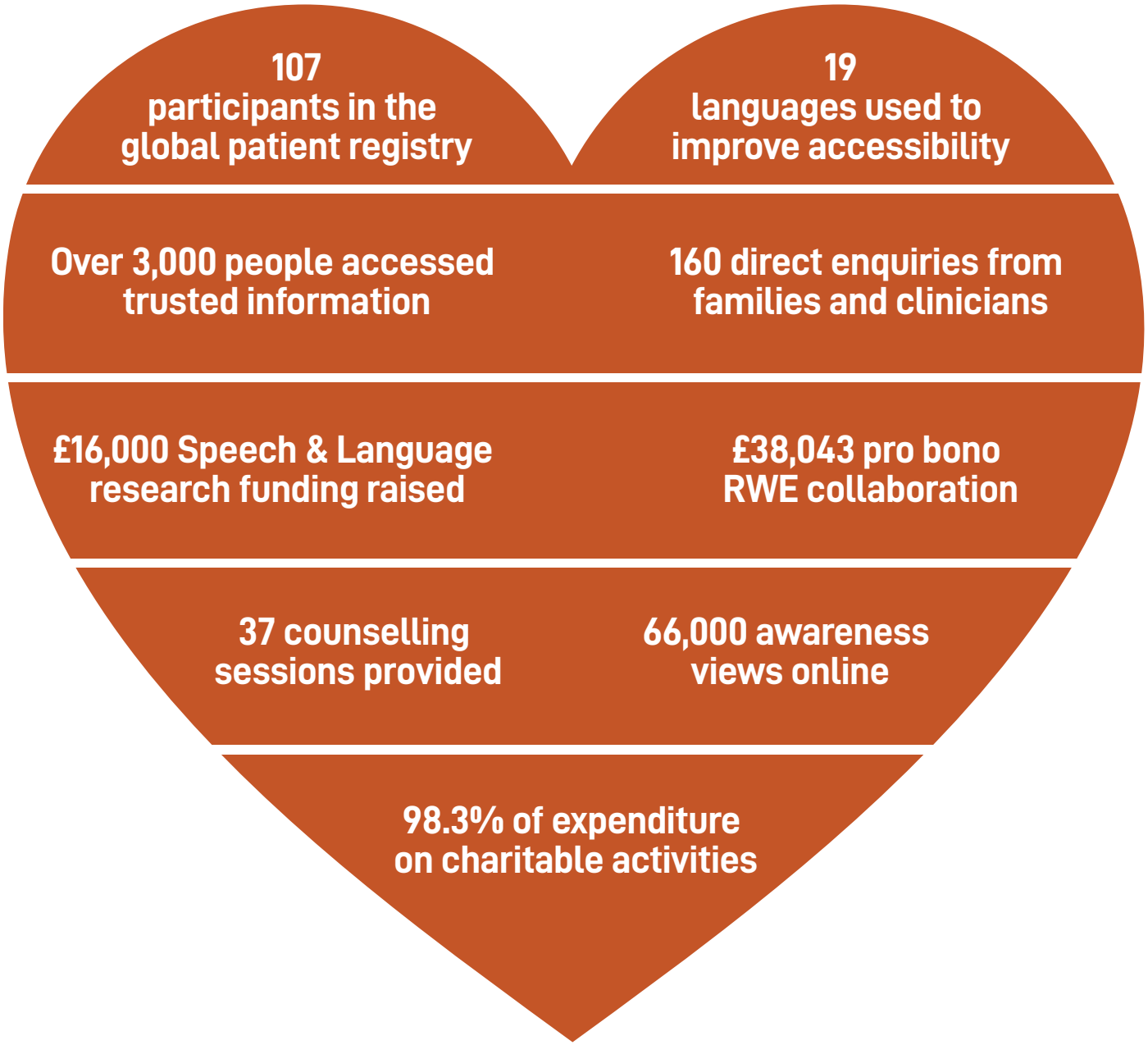
TSA was established in response to uncertainty and isolation. Six years on, we are seeing the foundations of a more coordinated and informed field emerging. While significant challenges remain, there is growing evidence that shared understanding can reduce harm and accelerate progress.

On behalf of the Trustees, thank you to everyone who contributes to this work.
Sophie (& mum to Calvin)
Chair of the Board of Trustees

# IMPACT AT A GLANCE

**250+ families supported worldwide**

**39 countries represented**




**First international consensus guidance submitted**

# INTRODUCTION AND OVERVIEW

The Trustees are pleased to present the Annual Report and Financial Statements of Timothy Syndrome Alliance (TSA) for the year ended 30 November 2025.

During 2025, TSA continued to operate as a small, volunteer-led international charity with a singular focus on improving understanding, care, and research for individuals impacted by CACNA1C-Related Disorders, including Timothy Syndrome and Long QT type 8. Despite limited capacity and modest financial resources, TSA delivered significant progress during the year. The charity strengthened its role as a trusted source of information and connection for families, clinicians, and researchers worldwide.

With input from our 227-member Patient Advisory Board, we updated our logo this year to better reflect who we are and the families we support. As a charity that advocates for everyone affected by CACNA1C-Related Disorders, not just Timothy Syndrome, we felt it was important that our new look truly represents our whole community.

This new design was created as a pro bono project.

# WHO WE ARE AND WHY WE EXIST

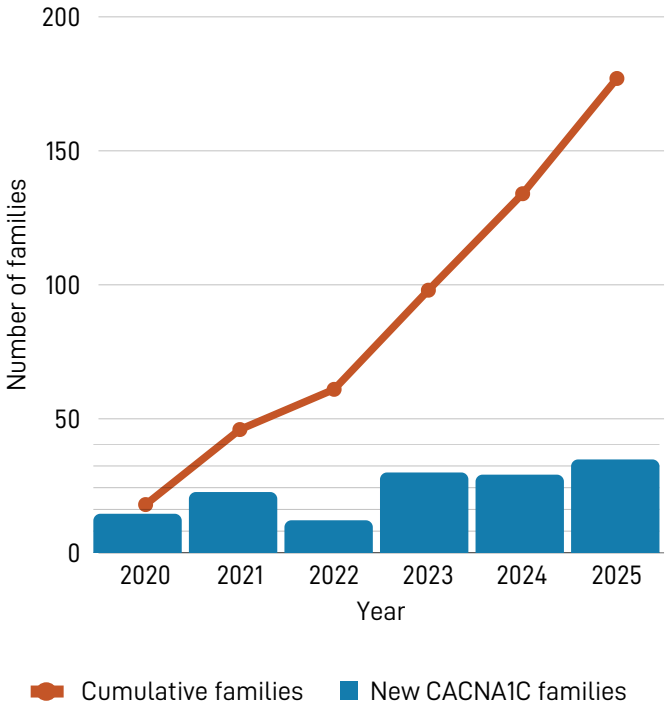
## Our Cause

Timothy Syndrome Alliance exists to support individuals and families impacted by CACNA1C-Related Disorders, which include Timothy Syndrome and Long QT type 8, a group of life-altering and life-shortening ultra-rare genetic conditions associated with complex, multi-system impacts including cardiac, neurological, developmental and psychiatric features.

In 2025, TSA continued to provide global support to a growing and geographically dispersed community. The charity's patient registry increased to 107 participants during the year, and the wider community now includes over 250 families worldwide. Trustees note that this growth reflects increased visibility, trust, and unmet need rather than increased prevalence.

Families consistently describe the period after diagnosis as overwhelming. Many immediately begin searching for information, often finding little reliable guidance and feeling deeply isolated.

**CACNA1C Community Growth (2020-2025)**




The graph shows the annual number of newly connected CACNA1C families and individuals to TSA, with each family counted once, regardless of affected members. It doesn't reflect diagnostic incidence or the overall count of individuals with CACNA1C gene changes.

One parent described the experience starkly:

"When you type in CACNA1C you immediately see Timothy Syndrome and a life expectancy under the age my child was."

For many families, the difference between distress and stability is not simply receiving a diagnosis, but finding accurate information, informed community, and credible guidance. Trustees consider this point of connection to be a core public benefit delivered by the charity.

Beyond providing support, the charity exists to help change the future of these conditions. TSA combines the power of lived experience with scientific expertise. Led by impacted families and guided by world-class researchers, the organisation focuses on what matters most: earlier diagnosis, meaningful real-world data, and collaborative research that reflects the priorities of those living with CACNA1C-Related Disorders. Through its patient registry, international research collaborations, and growing global community, the charity is helping to build the knowledge base needed to improve understanding, influence care, and accelerate progress toward effective treatments. Trustees believe that when families, clinicians and researchers work together in this way, rare conditions that were once poorly understood can become the focus of meaningful scientific progress.

**250+ families worldwide**

**39 countries**

**107 patient registry participants**

# FAMILY STORIES

Families describe the moment of diagnosis as one of the most difficult periods they face. The reflections below illustrate the importance of connection and shared understanding.

"After our diagnosis, we felt overwhelmed at first," one mother recalls. "It took about three months to find our new family, and we are so grateful — not feeling alone on this journey means everything." She adds that "having that connection to knowledge is priceless," and remembers how "Sophie's words of encouragement... truly helped me in my darkest moments."

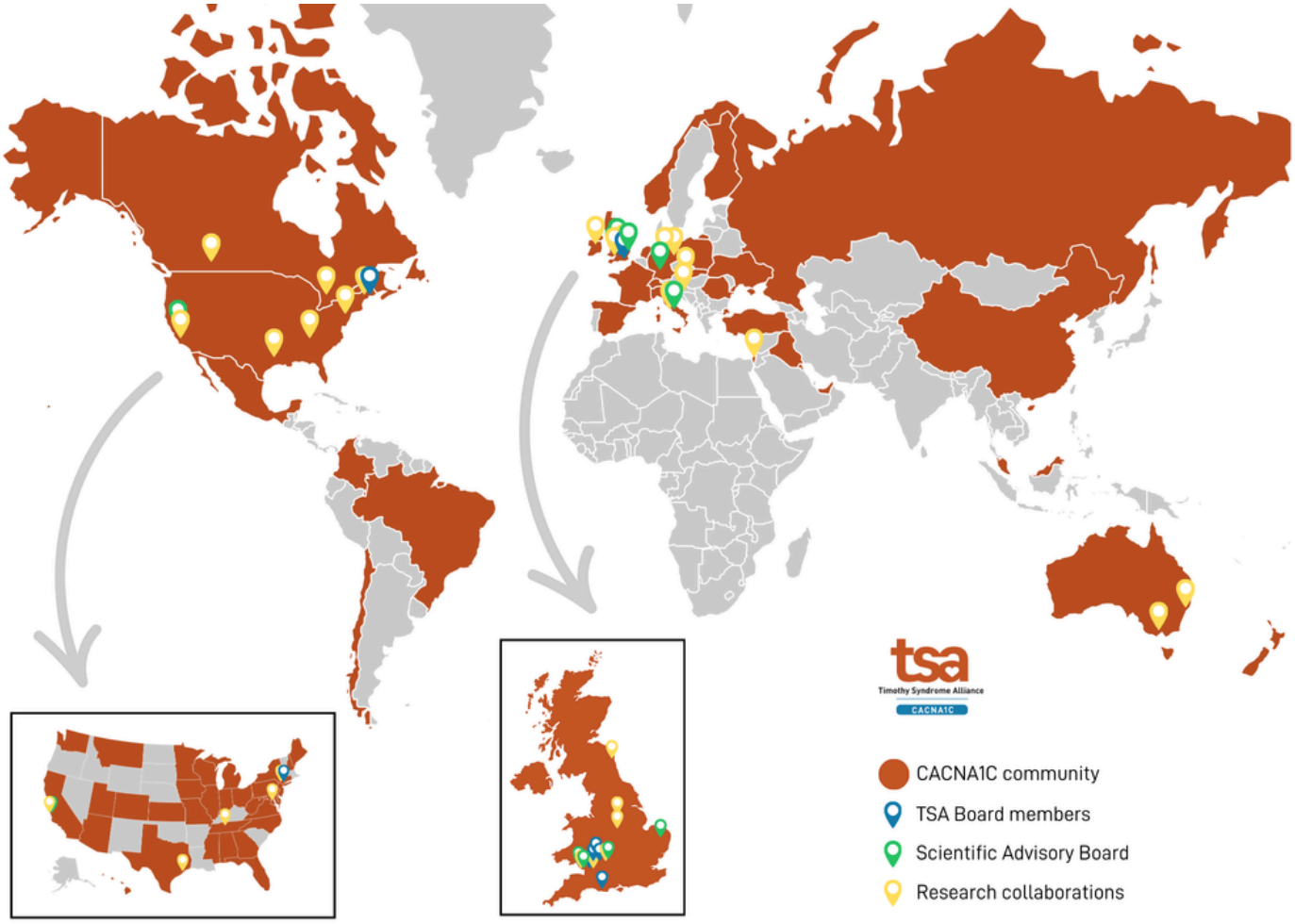
"I remember feeling very lost and alone, wondering if anyone else was going through this," one parent says. "Then I found this community and it was a shock — there were so many others sharing our story. This community has given our family hope, showing that despite the challenges of Timothy Syndrome, our child can still live a meaningful life."

"It took me about six months to find the community, and I was relieved to see that there were other children like mine," one mother recalls (translated from French). Thanks to a tip from her son's physiotherapist, she discovered the group online. "Understanding the condition a little better through the community helps me," she adds, especially since her son is the first known case in her country.

"Within 15 minutes of getting off the phone with genetics, I found the TSA Facebook group," recalls a mother. "Finding this has been amazing for our family. We are so thankful for the connections we've made, the wisdom we've learned, and for not feeling like we're alone as we figure this all out."

"We couldn't believe it — after 23 years we found an entire group within a day of our diagnosis," one family says. "It was incredible to discover other families experiencing the same thing. Now there is always someone to share a question with. It's invaluable to know that a dedicated team is moving this cause forward for a better future for our children," they add.

"About three months after my daughter's diagnosis, I learned about the Alliance," says a mother (translated from Italian). "I had felt so afraid and lost. Finding the community was like breathing again — it gave us answers, hope, and reassurance."




# Why This Matters

## And why it should matter to You

The CACNA1C gene plays a key role in how our brains and hearts function.

Although rare changes in the CACNA1C gene cause severe, life-limiting disorders, the gene itself also plays an important role in common mental health conditions like depression, bipolar disorder and schizophrenia.

> **Depression** affects over **300 million** people worldwide.
> **Bipolar disorder** impacts **1–2 in every 100** people.
> **Schizophrenia** touches **24 million** lives.
>
> **These are not rare experiences.**

By understanding these rare, high-impact cases, we gain crucial insight into the biology behind more common conditions. This work doesn't just help a small community - it could open the door to breakthroughs in mental health and precision medicine that would benefit millions.

# VISION, MISSION AND VALUES

## VISION

Our vision is a world where shared knowledge and understanding lead to a cure for everyone with a CACNA1C rare variant.

## MISSION

Our mission is to improve diagnosis, treatment and care of individuals worldwide with CACNA1C-Related Disorders including Timothy Syndrome, and to support the families and carers of those diagnosed.

Our core values and beliefs shape how we deliver our mission in practice. In 2025, these values were expressed through the following commitments:

## DETERMINED

## EMPOWERING

## SUPPORTIVE

## COMMUNITY-LED

Trustees review these statements regularly to ensure they remain aligned with the evolving evidence base, the needs of our global community, and the charity's objects.

# Values in Practice

In 2025, TSA's values were demonstrated through operational and strategic decision-making rather than aspirational language. Trustees undertook a detailed review of the international consensus preprint to ensure terminology reflected both clinical accuracy and lived experience, recognising that language can directly influence care, expectations and psychological wellbeing.

The registry continued to be refined with family-informed input to ensure ethical participation and meaningful engagement. Peer support spaces were actively moderated to maintain psychological safety, and the charity continued to avoid sensationalised awareness activity in favour of proportionate, evidence-based communication.

As one community member reflected:

*"Knowing this is not my fault. I did the very best I could with what I had available."*

Trustees regard this reframing from blame to understanding as a significant outcome of values-led practice and a clear example of public benefit.

# OUR STRATEGIC MODEL
## The Problem We Are Solving

Rare diseases affect over 300 million people worldwide, yet each condition often impacts only a small number of individuals. CACNA1C-Related Disorders, including Timothy Syndrome, are ultra-rare.

Because these conditions are so rare, many healthcare professionals are unfamiliar with them. As a result, people are often treated only for individual symptoms rather than receiving coordinated care based on an accurate diagnosis.

Rarity makes diagnosis more challenging. Typically it takes around 4 to 5 years for a rare disease to be diagnosed, though it can often take much longer; 40% of rare disease patients are initially misdiagnosed.

**9.7 years on average to receive a CACNA1C diagnosis**

Rarity means that we are among the 95% of rare diseases without an approved treatment or cure. Research knowledge is often fragmented with information scattered across different disciplines meaning rare diseases remain poorly characterised at the genetic or molecular level. Drug companies may not see a profitable market, leading to less investment in developing treatments.

Raising awareness to gain widespread attention and support is challenging due to limited patient populations, lack of steady funding, low recognition within the medical community, being overshadowed by more prevalent conditions, the complexity of the disease, and a general lack of urgency.

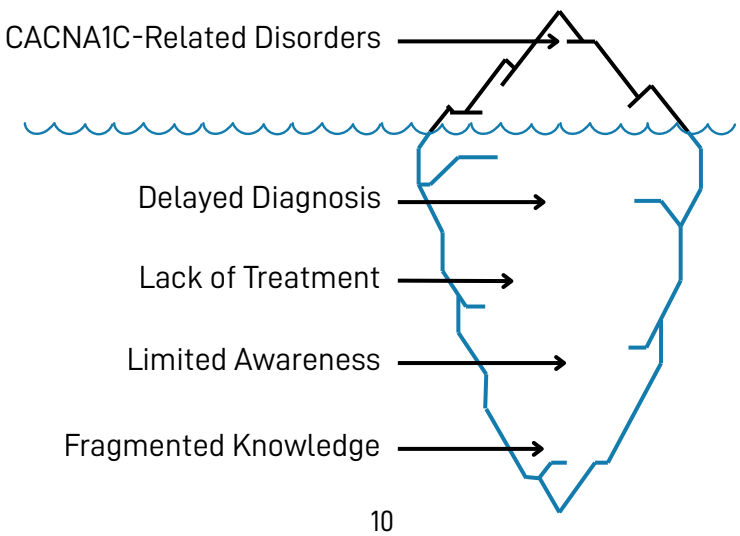
Evidence gathered during 2025 reinforced a consistent pattern across families globally. The period following diagnosis is frequently characterised by fear, shock, anxiety, and confusion. Interviews conducted through collaborative projects, including the Illumina Variant of Uncertain Significance work, highlighted the difficulty families face when clinical teams cannot yet provide holistic advice and when publicly available information is sparse or misleading.

Families reported:

"Google did not hold that much info, neither did the doctors."

"I spent a whole day after the diagnosis crying."

Trustees recognise that these experiences are not isolated but systemic within ultra-rare disease contexts, where clinical pathways, research evidence and support infrastructure are still emerging.



# Our Solution

Families impacted by CACNA1C-Related Disorders consistently describe the period following diagnosis as one of profound uncertainty. TSA's Theory of Change is designed to address this directly.

Because CACNA1C-Related Disorders are rare, poorly understood, and often met with delay, misinformation and isolation, we work globally to help affected individuals and families, clinicians and researchers build understanding, improve care and generate evidence, so that people receive the right support at the point of diagnosis and throughout life, and research and clinical progress can advance responsibly when it matters most.

This model recognises that meaningful research participation depends on informed and supported families, and that improvements in care require shared language, lived experience and credible data.

Current clinical care is hindered by a lack of standardised protocols, insufficient research, and limited access to comprehensive genetic data. This unmet need provides a unique opportunity to create a knowledge base that consolidates data and drives innovation in the diagnosis and treatment of CACNA1C-Related Disorders.

By building strong data foundations, fostering collaborative research, engaging our activated patient community, and leveraging regulatory incentives to reduce development risk, we position CACNA1C as a strategically aligned and investment-ready target.

**Theory of Change**

# How we will do it

Expand communications to raise awareness and reach new audiences

Build clinical and research networks to improve diagnosis, treatment, and care

Strengthen community support through global connection and shared resources

Provide trusted information that empowers families and professionals

Advance research by supporting funding, collaboration, and participation

Influence policy to improve systems and outcomes for our community

# 2025 IN REVIEW - STRATEGIC DELIVERY

In 2025, TSA continued to deliver its charitable objectives through its established strategic priorities. Trustees consider this structure essential for transparency, proportional reporting, and alignment with both current Charities SORP and anticipated SORP 2026 expectations regarding outcomes, public benefit, and organisational learning.

Our activities are reported below against each priority, reflecting how change occurs in practice within an ultra-rare, globally dispersed community.

## Expand communications to raise awareness and reach new audiences

The short film *Connections* produced with Cardiff University, received the People's Choice Award at the *Smiley Charity Film Awards 2025* and was selected for international screening at *Rare by Design's The Film Festival!*, increasing awareness while preserving dignity and authenticity in representation.

During the year, communications remained carefully managed and proportionate, delivered in-house without a dedicated marketing team and alongside programme, governance, and research activities. The focus remained on accuracy, safeguarding, and trusted visibility rather than scale.

Between 1 December 2024 and 30 November 2025:

- Social media channels Facebook and Instagram were viewed over 66,000 times
- With engagement exceeding 1,500 meaningful interactions
- Profiles were visited over 4,300 times
- And organic following grew to just over 1,500.
- Over 3,000 individuals accessed trusted information via the TSA website
- Resulting in more than 160 direct enquiries received through the website from families and professionals across multiple countries.
- On YouTube, our films and conference recordings (excluding shorts) received 1,928 views
- Averaging an audience of 93 viewers per month
- And a watch time of 96.4 hours.
- All our conference and Mind the Gap webinars are available in a minimum of 17 human-checked language transcripts.

These figures show that families and professionals are actively seeking reliable information in a field where accurate resources remain scarce.

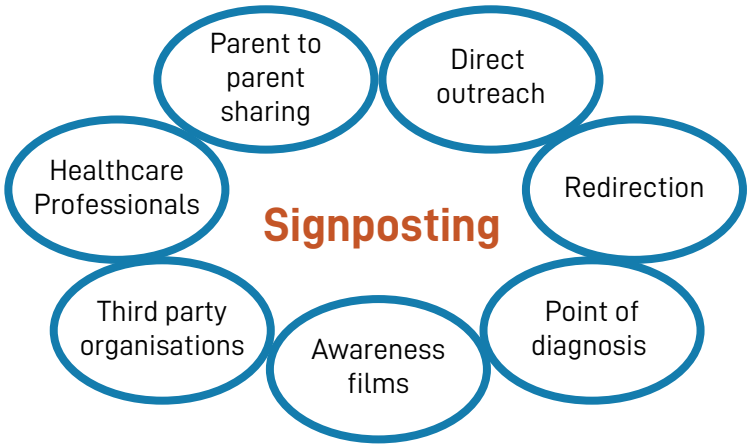
**YouTube Audience by watch behaviour**

**Monthly audience**

- **New viewers** 77.4%
- **Casual viewers** 19.4%
- **Regular viewers** 3.2%

Expanding communications to raise awareness and reach new audiences also balances the need for us to be signposting to new and existing families not yet aware of, or in contact with, TSA. Signposting pathways are wide-ranging.

**Signposting pathways**




Community feedback indicates that families most commonly find TSA through Facebook searches, Google searches, clinician recommendation, peer referral, and rare disease media content. This reinforces the importance of maintaining accurate and moderated digital visibility.

One parent reflected:

"The community found me."

Trustees consider this a priority to deliver clear public benefit by reducing isolation, improving access to accurate information, and enabling earlier connection to appropriate support.

**Common online search pathways**

**"A film called Rare Strikes Back helped us find the community."**
**I saw it on TikTok, then searched for the group on Facebook - and realised we weren't alone.**

# Build clinical and research networks to improve diagnosis, treatment, and care

Strengthening clinical and research networks remained a major focus in 2025, particularly in light of evolving understanding of CACNA1C-Related Disorders as a broader and more heterogeneous spectrum than previously described.

Trustees and advisors supported the completion and submission of the *Timothy Syndrome and CACNA1C-Related Disorder: First International Language and Management Guidelines Consensus Statement*, currently under review with the European Journal of Human Genetics. This work is expected to improve consistency of language, clinical understanding, and care approaches internationally.

Every month we joined fellow Rare As One Network members for dedicated channelopathy, science and network calls to connect, collaborate, share research priorities, discuss common challenges, and explore opportunities to accelerate progress.

Additional activities included:

- Conference presentations, including the Royal College of Psychiatrists Congress and World Orphan Drug Congress (thanks to the Sciensus team for their support in enabling this)
- Ongoing engagement with clinicians across cardiology, neurology, psychiatry and genetics
- Collaboration with research partners in the UK, Europe, the United States and Australia
- Scientific engagement through advisory discussions and knowledge exchange
- Wikipedia training in preparation for evidence-aligned public information updates

**World Orphan Drug Congress (Europe) Preconference Workshop – October 27, 2025.** Photo credit: Sciensus.

Our Chan Zuckerberg Initiative (CZI) Rare As One Network multi-year funding enabled the appointment of Dr Amy Houseman, our Research and Public Engagement Officer, who holds a PhD in Rare Disease Genetics from Cardiff University.
Amy coordinates global research efforts, facilitates knowledge sharing, promotes collaboration, and accelerates research that prioritises our CACNA1C patient needs. This is a key role in developing and managing our communications and engagement with UK and international stakeholders, which include researchers, clinicians, healthcare professionals, our CACNA1C community, and the general public.

Amy Houseman
Research and Public Engagement Officer

Families consistently report that clinical teams often have limited access to condition-specific guidance at the point of diagnosis. TSA will continue to strengthen professional networks and contribute to evidence-informed language, helping to reduce harm caused by outdated or overly narrow clinical narratives.
This knowledge can be incredibly powerful, as one parent noted:

"It helped me advocate for my daughter when I know how others are affected."

# Strengthen community support through global connection and shared resources

TSA continued to provide structured, moderated, and globally accessible community support to a dispersed ultra-rare population exceeding 250 individuals worldwide.

Evidence gathered through direct engagement and registry insights confirms that the period following diagnosis is characterised by fear, confusion, and profound isolation, often compounded by limited reliable information and misrecognition of the condition.

Key support activities in 2025 included:

- Continued free at point of access 'Mind the Gap' counselling provision through Rareminds
- Private (secure sharing with community) CACNA1C 'Mind the Gap' Support webinars 'Dealing with Diagnosis', 'Managing Uncertainty' and 'You and your Mental Wellbeing' have received in excess of 250 views.
- Ongoing moderation of peer support spaces to ensure psychological safety

- Expansion of multilingual accessibility, including conference recordings via website and YouTube with transcripts in 19+ languages
- Development of bereavement resources (in progress)

Community testimonies demonstrate consistent psychosocial impact:

"My anxiety minimised when I joined the group."

"Seeing older children gave me hope."

"The feeling of not being alone is a relief."

Trustees note that demand for support frequently begins immediately after diagnosis and often precedes research engagement or formal clinical pathway stabilisation.

**37**

**'Mind the Gap' counselling sessions**

**provided**

**250+**

**support webinar**

**views**

**'Dealing with Diagnosis'**
**'Managing Uncertainty'**
**'You and your Mental Wellbeing'**

# Provide trusted information that empowers families and professionals

Providing accurate, accessible, and evidence-based information remained a core charitable activity and a key area of public benefit in 2025.

Website and digital engagement data indicate that users most frequently accessed:

- Condition-specific information pages
- Research updates
- Conference materials
- Support and connection resources, including our newsletters

Our 'Parent as Partner' approach ensures information is shared proactively rather than reactively. Our information is offered in multiple formats (written, video, verbal) and in preferred languages to accommodate diverse needs. As a community, we now span a total of 39 countries and speak 21 languages.

During 2025 eight global mailings to subscribed families, researchers and healthcare professionals achieved an average 41% open rate, demonstrating engagement levels well above typical nonprofit sector benchmarks, which generally average around 25-30% open rates. The total audience subscribed to our newsletters has also doubled in size over the 12 months.

Direct emails and messages are commonplace. When personalised and translated into the recipient's native language, this supports faster comprehension and relatability, alongside improved accessibility and inclusivity.

Engagement was reflected through attendance at the online CACNA1C conference, with 70+ attendees, both families and healthcare professionals, from 19 countries. The conference was delivered with real-time translation,

enabling attendees from multiple countries to listen and read in their preferred language. This significantly improved accessibility and equitable knowledge dissemination in a rare disease context.

Families repeatedly report limited reliable online information about CACNA1C-Related Disorders, reinforcing the importance of a trusted, moderated information source.

As one parent stated:

"Google did not hold that much info, neither did the doctors."

Trustees consider the provision of trusted information to be a core safeguarding function as well as an educational activity.

# Advance research by supporting funding, collaboration, and participation

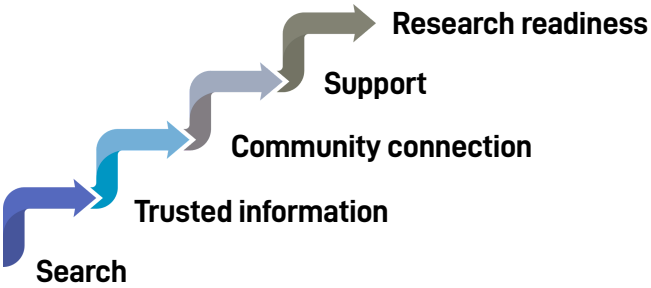
In 2025, research progress focused on building the foundations needed for future breakthroughs: strong data infrastructure, global collaboration and ethical research readiness.

Importantly, qualitative evidence shows that informed and supported families are more confident engaging with research opportunities, reinforcing TSA's model that support enables ethical participation.

One parent shared:

"Having that connection to knowledge is priceless."

**Identified steps to research readiness**




Key developments included:

- Submission of the *Timothy Syndrome and CACNA1C-Related Disorder: First International Language and Management Guidelines Consensus Statement* to the European Journal of Human Genetics.

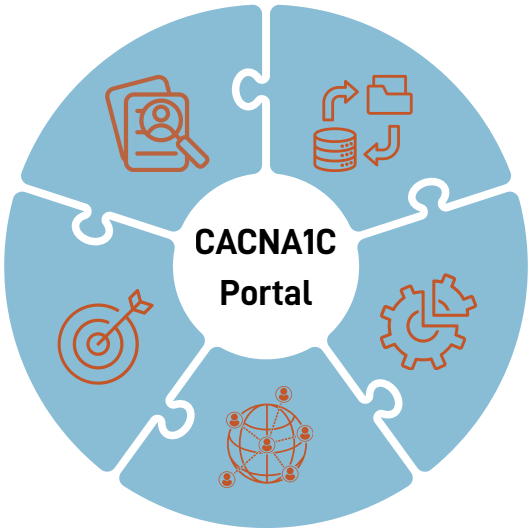
  Following our 2023 conference, key gaps in terminology and clinical guidance for CACNA1C were identified, highlighting the need for a dedicated international consensus paper.
  In response, this led to a Delphi-style consensus process meaning clinicians, scientists and researchers from institutions across the USA, UK and Europe worked together with the CACNA1C community to develop agreed terminology and minimum standards for diagnosis and care.
  Community engagement through TSA networks reached more than 200 families, ensuring the final recommendations reflected both clinical expertise and lived experience.

- CACNA1C Community Registry growth to 107 participants.

  The CACNA1C Community Registry is a patient registry for all CACNA1C-Related Disorders, managed by Timothy Syndrome Alliance (TSA) and powered by Pulse Infoframe. The purpose of the CACNA1C Community Registry is to obtain insights to better characterise CACNA1C-Related Disorders, including Timothy Syndrome and LongQT8, and their presentation, management and treatment. The registry was launched in June 2022 and is available for worldwide participation. This decentralised

**The CACNA1C Portal**

**Community-specific Customisation**
Tailors the portal to meet community needs




**Centralised Data Repository**
A comprehensive resource for CACNA1C data

**Supporting Precision Medicine**
Provides tools for personalised treatment strategies

**Data Integration and Analysis**
Enables sophisticated analyses of CACNA1C data

**Global Collaboration**
Facilitates worldwide collaboration among researchers

registry is not tied to a site and enables anyone, anywhere in the world with a CACNA1C-related disorder to sign up for the registry and participate from their home.
The first registry data pull is scheduled for the end of the year. The aim is to run preliminary data analysis and share our findings at the in-person conference this summer 2026.

- Building of a CACNA1C Portal.

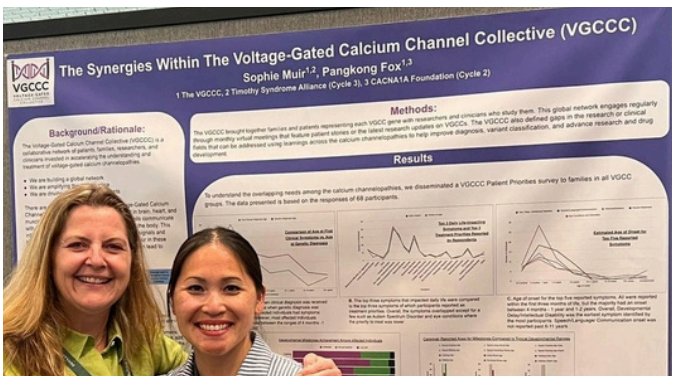
  The CACNA1C Portal is a centralised, globally accessible platform that integrates clinical, genetic and molecular data to enable deeper genotype–phenotype understanding, support precision diagnosis and care, and accelerate research and therapeutic development for CACNA1C-Related Disorders.

- Research focusing on understanding the speech and language abilities of children with CACNA1C-Related Disorders.

  The study will deliver inclusive, globally accessible gene-specific speech and language research. It will support parents, carers and clinicians through improved understanding of diagnosis, prognosis and treatment planning, addressing the significant impacts these difficulties can have on learning, education, social interaction, self-esteem, mental health and daily living. Findings will also inform speech and language outcome measures for future clinical trials and will be widely shared to maximise clinical impact worldwide.

  The research is led by Professor Angela Morgan within the Speech and Language Group at the Murdoch Children's Research Institute (MCRI). With funding now secured, the study is expected to begin in the first quarter of 2026.

- CACNA1C Biobanking viability investigations
- Illumina Variant of Uncertain Significance qualitative work
- Ongoing research engagement in genetics, functional assays, sex differences in the causes and symptoms of psychiatric illness, calcium influx - see articles on the TSA website
- Ongoing epilepsy research as part of South West and Wales Epilepsy Research Network and GW4 epilepsy group
- Early exploration of antisense oligonucleotide (ASO) research pathways
- Continued collaboration as part of The Voltage-Gated




**CACNA1C and CACNA1A representing the VGCCC**

Calcium Channel Collective (VGCCC) who are dedicated to raising awareness and promoting collaboration across the calcium channelopathies. This group is composed of caregivers and individuals impacted by the channelopathies, alongside researchers and clinicians focused on the 10 calcium genes.

As members of the CZI RareAsOne Network we met everyone in person at the Science in Society meeting in Las Vegas. Both Sophie and Rebecca Levy from our Scientific Advisory Board represented TSA, and felt truly welcomed as Cycle 3 grantees. Over three days, we dived deeper into cross-disease collaborations, explored new ways to move science forward together and shared capacity-building strategies to strengthen the rare disease patient group ecosystem as a whole. The Chan Zuckerberg Initiative created a powerful space for connection, collaboration and hope.

The value of collaboration in working towards shared goals and achieving real impacts is something TSA have been advocates of from the get-go. We were therefore delighted to see Dr Jack Underwood, Chair of our Scientific Advisory Board, receive Highly Commended in the Rare Disease Research UK Early Career Researcher PPIE Awards for his work with our community. These awards highlight the real partnership between researchers, scientists, and people and families living with rare conditions. Rare Disease Research UK, working in partnership with Genetic Alliance UK, seeks to encourage Patient and Public Involvement and Engagement (PPIE), with the aim of involving people with relevant lived experience as partners and advisors in research, and engaging wider audiences with scientific progress.
Read Jack and Sophie's blog.

Jack is also the recipient of a Best Public Engagement Award from Cardiff University School of Medicine for his work with TSA.

## Scientific Advisory Board

Dr. Jack Underwood (Chair)
WCAT Clinical Lecturer in Forensic Psychiatry, NMHII, Cardiff University

Dr. Rebecca Levy
Clinical Scholar, Neurology & Neurological Sciences.
Stanford Medicine

Dr. Gemma Wilkinson
Research Associate, NMHII, Cardiff University

Dr. Nicola Hall
Postdoctoral Researcher, University of Oxford

Dr. Anwar Baban
Bambino Gesù Children Hospital and Research Institute, IRCCS, Rome

Dr. Wilfried Haerty
Group Leader of Evolutionary Genomics, Earlham Institute

Prof Liz Tunbridge
Director of Translational Neuroscience, Boehringer Ingelheim

# Influence policy to improve systems and outcomes for our community

Participation in influencing policy during 2025 was primarily achieved through evidence contribution, language standardisation, and responsible knowledge dissemination rather than formal lobbying, reflecting the charity's size and governance model.

Key contributions included:

- Input into international consensus language and management guidance
- Dissemination of evolving evidence across clinical and research audiences
- Preparation for updates to public knowledge platforms aligned with peer-reviewed evidence
- Representation at international conferences and rare disease forums

By improving shared language and understanding of CACNA1C-Related Disorders as a spectrum condition, TSA is contributing to longer-term system improvements in diagnosis, care coordination, and research design.

During 2025, TSA participated in a pro bono Real-World Evidence (RWE) project led by Costello Medical, valued at £38,043 in specialist consultancy support. The project brought together leading RWE, regulatory, and genomic experts to explore how real-world data could be used to advance understanding of CACNA1C-related disorders. Through a facilitated roundtable and follow-up work, the project provided the charity with access to expertise that would otherwise be far beyond the reach of a small rare disease organisation.

Discussions focused on the barriers that currently limit evidence generation in rare diseases and how better use of real-world data could support improved diagnosis, clinical awareness, and policy engagement.

For TSA, the discussions centred on a key research question: whether barriers to reporting genetic findings may be masking cases of CACNA1C-Related Disorders in the UK.

Experts provided strategic guidance on challenges such as limited coordination between stakeholders, the lack of standardised approaches for recontacting patients with variants of uncertain significance, and the need to present emerging evidence in ways that can engage policymakers and clinical leaders.

The insights and recommendations generated through this collaboration will help inform the charity's future research and advocacy work, and the meetings themselves would not have taken place without Costello Medical's generous support.

## Data Standardisation

The **lack of standardised data** across patient registries for rare disease populations, and varying disease classification, **hinders collaborative RWE research**

(Troster et al., 2023)

**Ensure data utility and access by:**

- Using Findable, Accessible, Interoperable and Reusable (FAIR) data principles
- Sharing data via global platforms like the Genome-Phenome Analysis Platform (GPAP) (Licata et al., 2023)

## Resource Limitations

Rare disease charities representing small patient populations have **limited funding and capacity** to engage in RWE activities **requiring technical and scientific expertise**

**Help rare disease charities generate robust RWE by:**

- Facilitating partnerships with research groups and industry
- Advising on impactful data communication, to support with funding applications
- Organising workshops to train charity staff in RWE activities
- Encouraging collaborative grant applications; for example, working with partners outside of academia to secure funding

## Genomic Reporting

Some genomic variants associated with rare diseases are missing from open access registries, resulting in **incomplete datasets** that **delay diagnosis** and treatment development

(Lyons et al., 2023)

**Report genomic variants to central databases:**

In the UK, it is **mandatory** for NHS laboratories to report genomic variants to ClinVar – a public database of genetic variants and phenotypes

(ClinVar UK Practice Guidelines, 2024)

## RWE Collection

Clinical trials are sometimes unfeasible for **small patient populations**, so rare disease charities often rely on RWE for regulatory applications. However, collecting real-world data (RWD) **robust enough** to meet regulatory standards remains challenging

(Vaghela et al., 2024)

**Help rare disease charities collect robust RWD by:**

- Connecting them with regulatory experts
- Advising on study design and data collection methods
- Identifying ways to recruit more people to rare disease studies

**Key Policy Contributions in 2025**

1. International Clinical Guidance
   Contributed to the first international consensus language and management guidance for CACNA1C-Related Disorders.
2. Improving Public Medical Information
   Prepared evidence-aligned updates to widely used medical information platforms, including Wikipedia.
3. Advancing Real-World Evidence for Rare Disease
   Contributed to expert discussions on how genomic real-world data can improve diagnosis and reporting of CACNA1C-Related Disorders.

# Capacity builds capacity

Despite operating with a turnover of £205,304 and a predominantly volunteer leadership model, TSA continued to strengthen organisational infrastructure in 2025 to support sustainable and accountable growth.

Productivity and programme delivery have been greatly accelerated thanks to support from CZI Rare As One.

Amanda Sanders
Mission Support Officer

Governance remained robust throughout the year, led by a voluntary Board of nine Trustees, including four parents of children with CACNA1C-related disorders, and supported by an international Scientific Advisory Board and a global Patient Advisory Board.
During 2025, the Board was strengthened through the appointment of two additional Trustees. Three Trustees are now based in the United States, reflecting the international composition of the community we serve and strengthening the charity's ability to engage effectively with partners, researchers and supporters across multiple regions.

Operational developments included:

- Implementation of Beacon CRM
- Embedding of Xero accounting systems
- Mailchimp automation improvements
- Increase in external communications, newsletters, programmes,
- Establishment of US fiscal sponsorship via Rare Village Foundation
- Significant unpaid clinical and strategic contribution from expert collaborators
- Operational support

Trustees recognise that infrastructure investment directly underpins programme delivery, research readiness, and safeguarding, and that capacity funding remains one of the most critical yet challenging areas to secure.

**Trustee Board**

Sophie Muir (Chair)
Mum to Calvin with a CACNA1C-Related Disorder

Gemma Duncan
Mum to Noah with Timothy Syndrome

Galina Gardiner (Treasurer)

Susan Bresnahan
Mum to Patrick with a CACNA1C-Related Disorder

Meg McLaughlin

Achsah James

Nick Muir
Dad to Calvin with a CACNA1C-Related Disorder

Glenn Miller

Christine Ziegler

# MEASURING IMPACT (QUANTITATIVE AND QUALITATIVE)

Trustees recognise that meaningful impact measurement in an ultra-rare disease context must combine quantitative indicators with qualitative evidence of lived experience change. Because the CACNA1C community is small and research is still emerging, impact cannot be measured by scale alone.

**Community Reach and Connection**
These indicators reflect the charity's ability to reach and connect individuals and families affected by CACNA1C-Related Disorders worldwide.

- **250+ individuals connected** through community support spaces
- **39 countries represented** within the community
- **Over 160 direct enquiries** from families and professionals via the website alone
- **107 individuals participating** in the CACNA1C Community Registry

**Information Access and Engagement**
These metrics show how families, clinicians and researchers access and engage with trusted information.

- **Over 3,000 people accessed trusted information** via the TSA website
- **66,000 social media content views** across digital platforms
- **Approximately 1,500 meaningful digital interactions**
- **More than 4,300 profile visits** across TSA Facebook and Instagram platforms
- **19 language transcripts produced** to support accessible conference content

**Research Progress and Infrastructure**
These indicators demonstrate progress in building the research foundations needed to improve understanding and care.

- **107 participants enrolled in the CACNA1C Community Registry**
- **£16,000 raised to support speech and language research**
- **Pro bono real-world evidence collaboration secured,** valued at approximately **£38,043**

**Qualitative outcomes**
Feedback gathered through direct engagement, counselling provision, webinars, and collaborative projects indicates important changes in experience and understanding.

Families report:

- Reduced anxiety following connection to the community
- Increased understanding of condition complexity
- Greater confidence in interactions with healthcare professionals
- Reduction in parental self-blame
- Earlier access to peer support following diagnosis
- Increased confidence to engage in research participation

One family reflected:

> "Finding this community didn't just help us cope. It helped us breathe."

Trustees acknowledge that further development of structured outcome measurement tools would strengthen longitudinal reporting, and this will be explored in future years subject to capacity and funding.

# LEARNING, CHALLENGES AND RISK

In line with SORP 2026 emphasis on transparency and adaptive governance, Trustees have reflected carefully on key learning during 2025.

**Key Learning**

- The period immediately following diagnosis is the most destabilising and highest risk for psychological harm.
- Families frequently access community before structured clinical pathways are in place.
- Language used in clinical and public contexts significantly affects wellbeing and understanding.
- Ethical research participation is only possible when families feel informed and supported.
- Infrastructure investment can enable disproportionate impact in small organisations.

**Key Challenges**

- Infrastructure funding remains harder to secure than programme funding.
- Staff and volunteer capacity limits the pace of strategic development.
- Managing global engagement requires careful safeguarding and moderation.
- Evolving clinical understanding requires continual updating of materials.
- Despite delivering 37 'Mind the Gap' counselling sessions and clear evidence of impact in reducing isolation and strengthening coping strategies, the programme was placed on hold in September due to a lack of available funds. Securing funding for psychosocial support remains a persistent challenge.

**Principal Risks**

Trustees maintain a risk register which is reviewed regularly. Key risks identified include:

- Concentration of restricted income
- Limited unrestricted reserves
- Dependence on a small leadership team
- Data governance responsibilities associated with registry growth
- International regulatory and coordination complexity

Mitigation strategies include:

- Diversification of funding sources, including US fiscal sponsorship
- Strengthening operational systems including CRM and accounting platforms
- Structured input from Scientific and Patient Advisory Boards
- Formal data transfer agreements and governance review
- Phased capacity growth aligned with available resources

Trustees consider risk management to be proportionate and appropriate to the size and scope of the charity.

# LOOKING AHEAD TO 2026

Trustees have identified the following strategic priorities for 2026:

- Publication and dissemination of the international consensus statement
- Registry data analysis and preparation for publication
- Completion of speech and language research project
- Delivery of the in-person international conference planned for July 2026
- Completed production of bereavement resources
- Continued Scientific Advisory Board engagement
- Expansion of fundraising capacity and diversification of income

The charity will continue to prioritise accuracy, safeguarding, collaboration and long-term impact over rapid expansion.

# FINANCIAL REVIEW

For the year ended 30 November 2025, the charity reported turnover of £205,304.

The majority of income remained restricted to specific programme areas, particularly research and community support activities. Trustees recognise the continued importance of increasing unrestricted income to strengthen operational resilience.

The charity benefited from significant pro bono support during the year, including a £38,043 real-world evidence project delivered in partnership with Costello Medical. Trustees note that such in-kind contributions substantially enhance impact relative to expenditure and represent strong value for money.

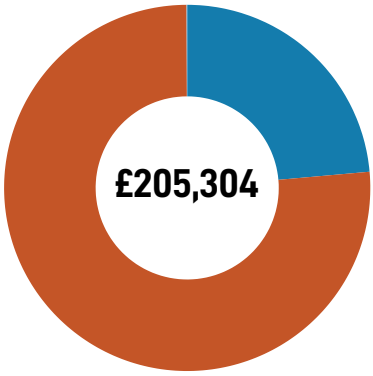
Expenditure remained aligned with charitable objectives, prioritising community support, research infrastructure, communications, and operational systems.

TSA continues to operate as a predominantly volunteer-led organisation, with Trustees contributing substantial unpaid time equivalent to senior executive leadership roles.

Reserves are monitored carefully to ensure financial prudence while enabling delivery of core charitable activities.

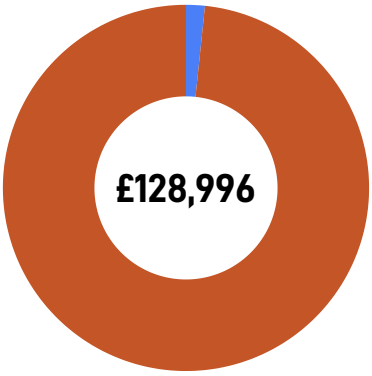
### Income

- **Donations and legacies** 23.6%
- **Charitable activities** 76.4%
- **Investments** 0.05%



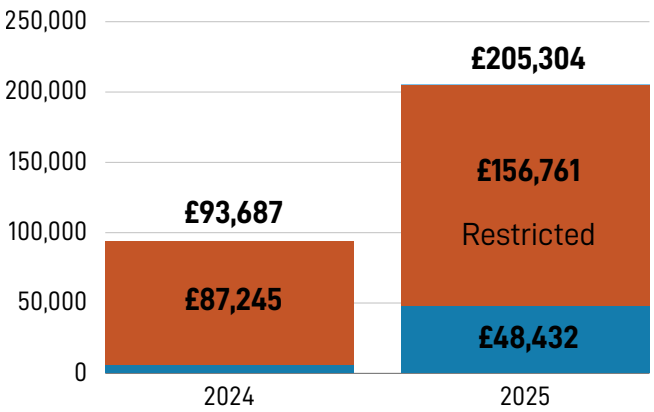

### Expenditure

- **Raising funds** 1.7%
- **Charitable activities** 98.3%

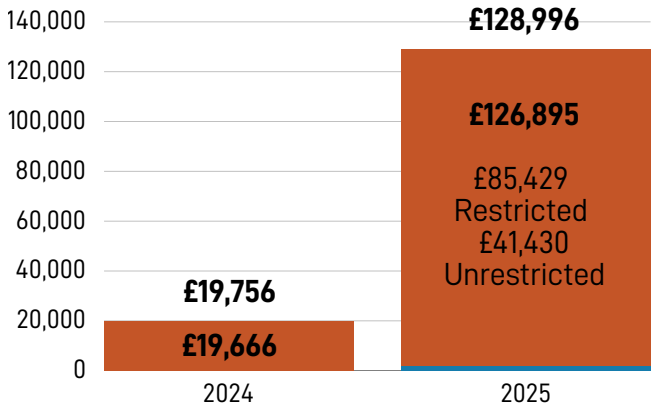



### Comparing 2024 and 2025

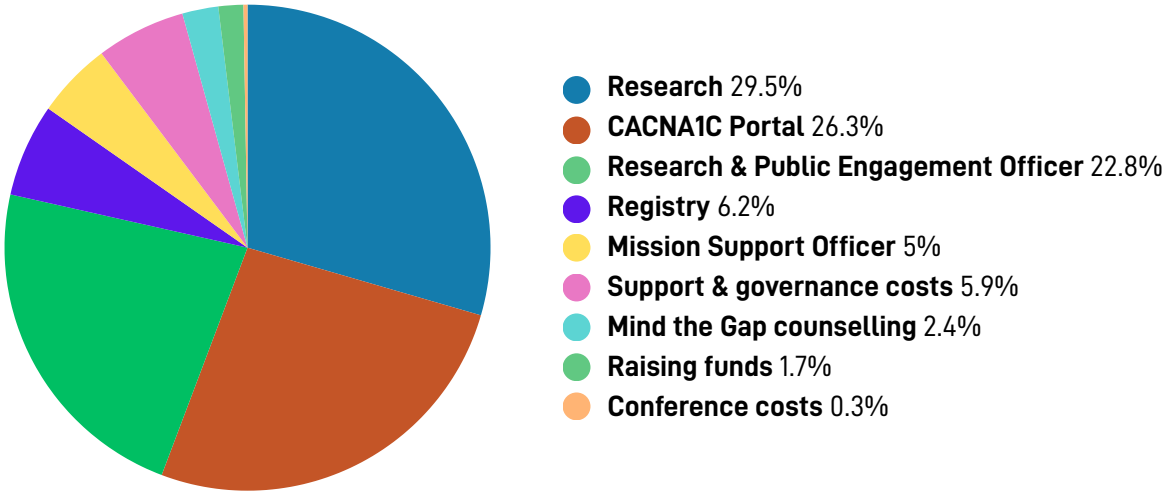
#### Income breakdown



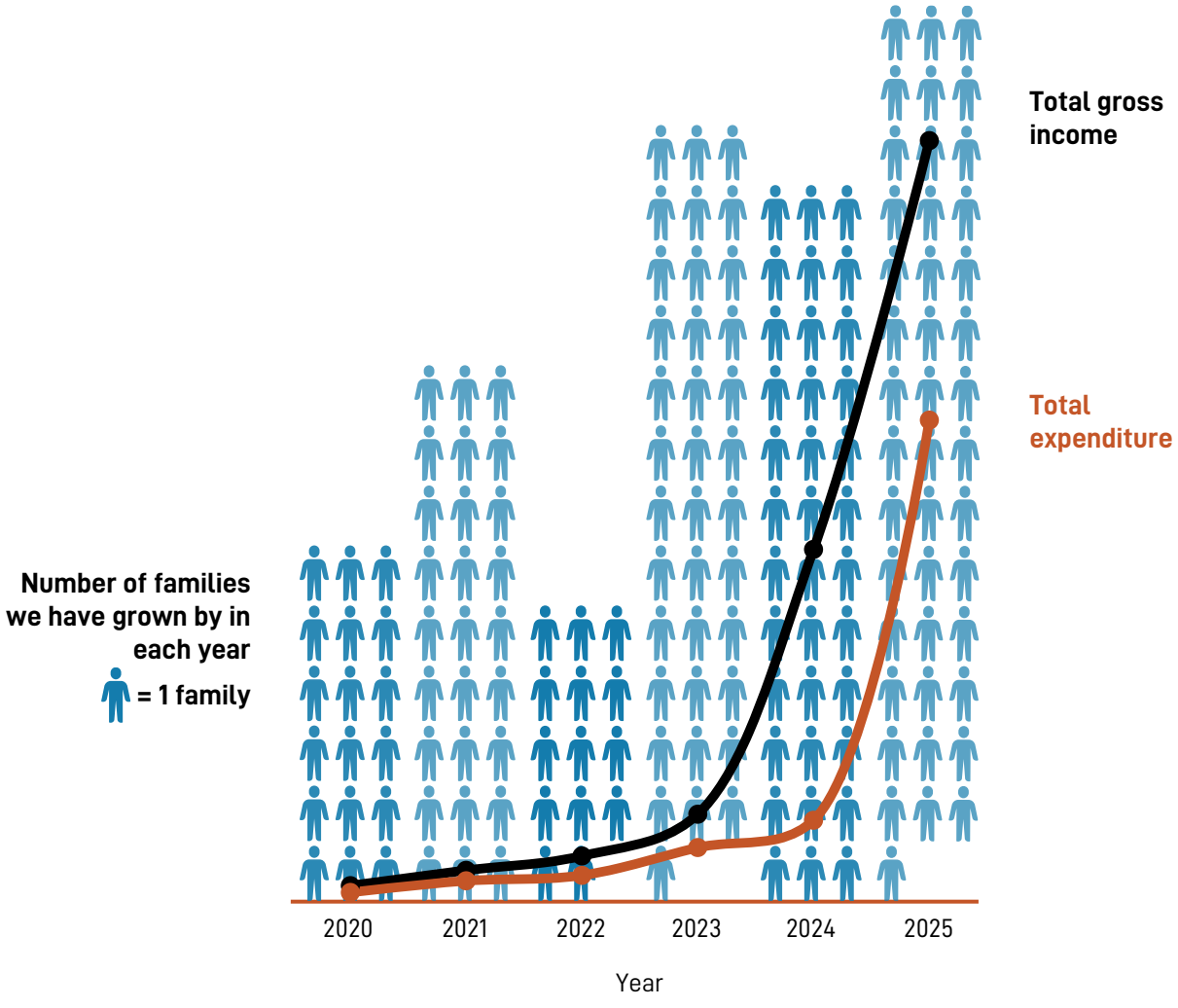

#### Expenditure breakdown



## Expenditure categories




## Sustainable Growth: Expanding our community and financial stability



# FUNDRAISING AND PARTNERSHIPS

TSA operates within a highly specialised ultra-rare disease field where patient numbers are small and traditional mass fundraising models are neither proportionate nor appropriate. The charity therefore adopts a targeted, relationship-based fundraising approach aligned with its strategic priorities and values.

**Income Profile**
During 2025, total income was £205,304. The majority of funding remained restricted to specific programme areas, particularly research and community support. Trustees recognise that increasing unrestricted income remains critical to long-term sustainability and operational resilience.

Income was derived from a combination of:

- Strategic grant funding, including support through the CZI Rare As One Network
- Trust and foundation grants
- Corporate and research partnerships
- Community-led fundraising and individual giving
- Platform-based giving through platforms such as GlobalGiving, JustGiving and Benevity
- US-based donations facilitated through Rare Village Foundation fiscal sponsorship

No single income source fully underwrites the charity's core costs. Trustees monitor funding concentration risk carefully and seek to diversify income streams across UK, US and international sources.

**Supporting the Vision**

**Partnership Approach and Ethical Safeguards**
Given the increasing interest in CACNA1C-Related Disorders from research and industry stakeholders, Trustees are committed to maintaining independence, transparency and clear governance safeguards in all collaborations.

Partnerships are evaluated against:

- Alignment with charitable objects
- Scientific integrity
- Community safeguarding
- Conflict of interest management
- Long-term public benefit

Trustees retain full oversight of decision-making and ensure that engagement with industry or research partners does not compromise independence or community trust.

**Stewardship and Leverage**
During the year, TSA secured a £38,043 pro bono real-world evidence collaboration through Costello Medical. Trustees note that such in-kind support significantly amplifies delivery capacity relative to cash expenditure and represents strong stewardship of relationships and resources.

As a predominantly volunteer-led organisation, including significant unpaid executive-level contribution, the charity continues to deliver impact that exceeds what would typically be expected at this level of turnover.

**Sustainability and Future Funding Priorities**
Trustees recognise that infrastructure funding remains the most challenging yet strategically important funding category. Investment in systems, governance, registry infrastructure and coordination capacity directly underpins programme delivery and research readiness. Priorities for 2026 include:

- Increasing unrestricted income
- Expanding trust and foundation relationships
- Strengthening US-based fundraising capacity
- Developing longer-term funding partnerships aligned with research and registry development

Trustees remain committed to careful growth that prioritises integrity, sustainability and long-term impact over rapid expansion.

# TRUSTEES' RESPONSIBILITIES, POLICIES AND FINANCIAL STEWARDSHIP

This report sets out how TSA delivered public benefit during the year, the outcomes achieved, the learning gained, and the challenges faced, in line with current Charities SORP requirements and the anticipated changes under SORP 2026. Trustees have sought to ensure that reporting is transparent, proportionate and grounded in evidence, recognising the particular responsibilities of operating within a rare disease context where misinformation and uncertainty can directly affect wellbeing and care.

**Fundraising Policy:** We are committed to upholding the highest standards in fundraising, ensuring that all our supporters feel safe, respected, and valued. As a UK-registered charity, we adhere to the standards set by the Fundraising Regulator and follow guidance from other relevant professional fundraising bodies. We never buy or sell personal data, and we take great care to honour individuals' preferences about how and when they wish to hear from us. The principles of the UK General Data Protection Regulation (UK GDPR) are fully embedded in the way we work. We do not use cold calling or cold mailing, and we do not employ third-party fundraising agencies. All of our fundraising is conducted with integrity, transparency, and respect for our community.

**Reserves Policy:** The charity receives funding for specific purposes which are restricted funds – these are not available for expenditure on other purposes. The general reserves are the unspent unrestricted funds of the charity. The charity currently owns no fixed assets, so the general reserve is held in cash. The general reserve is therefore the free reserves of the charity plus any designated funds, also termed 'unrestricted funds' in the charity's balance sheet.
The purpose of the general reserve is to:
a) fund shortfalls when income does not reach expected levels.
b) fund unexpected expenditures, for example, when projects overrun or unplanned events occur.
c) ensure that the Charity is not unnecessarily holding back on spending in favour of using the resources it has to meet its charitable objectives.
We aim to hold a general reserve, estimated to be in the range £9,000 - £10,000, to cover operating costs for a 3 to 6 month period. At 30 November 2025 total free reserves were £8,150. We are able to operate on a low-funds base as we have kept overheads to a minimum and are not committed to fixed-term costs such as rent or other long-term contracts. This enables us to make sure the majority of income is directed to charitable activities. Our reserves policy is reviewed annually and updated as necessary.

**Going Concern:** The trustees have reviewed the circumstances of the Charity and consider that adequate resources continue to be available to fund its activities for the foreseeable future. The trustees are of the view that the Charity is a going concern.

# ACKNOWLEDGEMENTS AND THANK YOU

Trustees extend sincere thanks to the families who share their experiences, to clinicians and researchers who collaborate generously, to funders and partners who provide financial and pro bono support, and to volunteers who contribute time and expertise.

We also acknowledge the dedication of trustees, advisors, and collaborators whose commitment guides and strengthens the charity's work.

The charity's progress depends on this collective effort and on the willingness of individuals and organisations to support greater understanding. The work continues because of shared commitment, lived experience, and a belief that understanding reduces harm and enables progress.

This Annual Report was created with care in-house at no cost to TSA.

www.timothysyndrome.org

# STRUCTURE, GOVERNANCE, AND MANAGEMENT

For the year ended
30 November 2025.

Registered Charity Number: 1185523

Trustees: Sophie Muir – Chair
Nick Muir
Galina Gardiner
Meg Mcloughlin
Gemma Duncan
Susan Bresnahan
Achsah James
Christine Zeigler (appointed 10 September 2025)
Glenn Miller (appointed 10 September 2025)

Registered Office: 8 Butt Street, Minchinhampton, Gloucestershire GL6 9JP

**Objectives**: To relieve the needs of those affected by deleterious CACNA1C gene changes resulting in CACNA1C-Related Disorders including Timothy Syndrome and Long QT8, their families and carers worldwide in particular but not exclusively by:- (1) Promoting greater understanding of the causes, symptoms and treatment of CACNA1C-Related Disorders including Timothy Syndrome and Long QT8, by the promotion of research and sharing and disseminating of the results of such research for the benefit of the general public; (2) Raising public awareness of the symptoms, needs and related medical conditions of those living with CACNA1C-Related Disorders including Timothy Syndrome and Long QT8.

**Structure, governance, and management**: Timothy Syndrome Alliance (TSA) is a registered charity number 1185523, governed by the Charities Act 2006. The charity is a Charitable Incorporated Organisation registered on 27 September 2019 under the Foundation Governing Document. The Trustees delegate the charity's day-to-day management to Sophie Muir. Trustees met four times during the year and corresponded regularly via email and other digital means, particularly to keep financial performance under review. New trustees are appointed by the serving trustees, considering the skills required by the board. Trustee induction includes online training (NCVO) to give an overview and understanding of charity governance, regulation and best practice alongside Essential Information for Trustees from the Charities Commission.

**Public Benefit**: The Trustees confirm that they referred to the Charity Commission's general guidance on public benefit when reviewing the Charity's aims and objectives for the year. Public benefit has been achieved through the activities outlined in the Achievements and Performance section of this report.

**Statement of responsibilities of the trustees**
The trustees are responsible for preparing the trustees' report and the financial statements in accordance with applicable law and United Kingdom Accounting Standards, including Financial Reporting Standard 102: The Financial Reporting Standard applicable in the UK and Republic of Ireland (United Kingdom Generally Accepted Accounting Practice).

The law applicable to charities in England and Wales requires the trustees to prepare financial statements for each financial year, which give a true and fair view of the state of affairs of the charity and the incoming resources and application of resources, including the net income or expenditure, of the charity for the year. In preparing those financial statements the trustees are required to:

- select suitable accounting policies and then apply them consistently;
- observe the methods and principles in the Charities SORP;
- make judgements and accounting estimates that are reasonable and prudent;
- state whether applicable accounting standards and statements of recommended practice have been followed, subject to any material departures disclosed and explained in the financial statements; and
- prepare the financial statements on the going concern basis unless it is inappropriate to presume that the charity will continue in operation.

The trustees are responsible for keeping proper accounting records which disclose with reasonable accuracy at any time the financial position of the charity and which enable them to ensure that the financial statements comply with the Charities Act 2011, the Charity (Accounts and Reports) Regulations 2008 and the provisions of the constitution. The trustees are also responsible for safeguarding the assets of the charity and hence for taking reasonable steps for the prevention and detection of fraud and other irregularities.

The trustees are responsible for the maintenance and integrity of the corporate and financial information included on the charity's website. Legislation in the United Kingdom governing the preparation and dissemination of financial statements may differ from legislation in other jurisdictions.

Members of the charity have no liability to contribute to the assets of the charity in the event of winding up. The trustees are members of the charity but this entitles them only to voting rights. The trustees have no beneficial interest in the charity.

**Auditors / Independent examiners**
Godfrey Wilson Limited were appointed independent examiners to the charity during the year and have expressed their willingness to continue in that capacity.

Approved by the trustees on 30 March 2026 and signed on their behalf by

Sophie Muir

Sophie Muir - Chair of the trustees

**Independent examiner's report**

**To the trustees of**

**Timothy Syndrome Alliance (TSA)**

I report to the trustees on my examination of the accounts of Timothy Syndrome Alliance (TSA) (the CIO) for the year ended 30 November 2025, which are set out on pages 33 to 43.

**Responsibilities and basis of report**
As the charity trustees of the CIO you are responsible for the preparation of the accounts in accordance with the requirements of the Charities Act 2011 ('the Act').

I report in respect of my examination of the CIO's accounts carried out under section 145 of the 2011 Act and in carrying out my examination I have followed all the applicable Directions given by the Charity Commission under section 145(5)(b) of the Act.

**Independent examiner's statement**
I have completed my examination. I confirm that no material matters have come to my attention in connection with the examination giving me cause to believe that in any material respect:

(1) accounting records were not kept in respect of the CIO as required by section 130 of the Act; or
(2) the accounts do not accord with those records; or
(3) the accounts do not comply with the applicable requirements concerning the form and content of accounts set out in the Charities (Accounts and Reports) Regulations 2008 other than any requirement that the accounts give a 'true and fair view' which is not a matter considered as part of an independent examination.

I have no concerns and have come across no other matters in connection with the examination to which attention should be drawn in this report in order to enable a proper understanding of the accounts to be reached.

Rob Wilson

Date: 30 March 2026
**Robert Wilson FCA**
**Member of the ICAEW**
For and on behalf of:
**Godfrey Wilson Limited**
Chartered accountants and statutory auditors
5th Floor Mariner House
62 Prince Street
Bristol
BS1 4QD

**Timothy Syndrome Alliance (TSA)**

**Statement of financial activities**

**For the year ended 30 November 2025**

| | Note | Restricted £ | Unrestricted £ | **2025 Total £** | 2024 Total £ |
|---|---|---|---|---|---|
| **Income *(and endowments)* from:** | | | | | |
| Donations and legacies | 3 | 73 | 48,359 | **48,432** | 6,442 |
| Charitable activities | 4 | 156,761 | - | **156,761** | 87,245 |
| Investments | | - | 111 | **111** | - |
| **Total income *(and endowments)*** | | 156,834 | 48,470 | **205,304** | 93,687 |
| **Expenditure on:** | | | | | |
| Raising funds | | - | 2,137 | **2,137** | 90 |
| Charitable activities | | 85,429 | 41,430 | **126,859** | 19,666 |
| **Total expenditure** | 6 | 85,429 | 43,567 | **128,996** | 19,756 |
| Net gains / (losses) on investments | | - | - | **-** | - |
| **Net income / (expenditure)** | | 71,405 | 4,903 | **76,308** | 73,931 |
| Transfers between funds | | - | - | **-** | - |
| **Net movement in funds** | 7 | 71,405 | 4,903 | **76,308** | 73,931 |
| **Reconciliation of funds:** | | | | | |
| Total funds brought forward | | 79,941 | 13,086 | **93,027** | 19,096 |
| **Total funds carried forward** | | 151,346 | 17,989 | **169,335** | 93,027 |

All of the above results are derived from continuing activities. There were no other recognised gains or losses other than those stated above. Movements in funds are disclosed in note 11 to the accounts.

**Timothy Syndrome Alliance (TSA)**

**Balance sheet**

**As at 30 November 2025**

| | Note | **2025** **£** | 2024 £ |
|---|---|---|---|
| **Current assets** | | | |
| Cash at bank and in hand | | **171,155** | 94,287 |
| **Liabilities** | | | |
| Creditors: amounts falling due within 1 year | 9 | **(1,820)** | (1,260) |
| **Net assets / (liabilities)** | 10 | **169,335** | 93,027 |
| **Funds** | 11 | | |
| Restricted funds | | **151,346** | 79,941 |
| Unrestricted funds | | | |
| Designated funds | | **9,839** | 6,000 |
| General funds | | **8,150** | 7,086 |
| **Total charity funds** | | **169,335** | 93,027 |

Approved by the trustees on 30 March 2026 and signed on their behalf by

Sophie Muir

Sophie Muir - Chair of the trustees

**Timothy Syndrome Alliance (TSA)**

**Notes to the financial statements**

**For the year ended 30 November 2025**

## 1. Accounting policies

### a) General information and basis of preparation

Timothy Syndrome Alliance (TSA) is an unincorporated charity registered in England and Wales. The registered office address is 8 Butt Street, Minchinhampton, Gloucestershire, GL6 9JP.

The financial statements have been prepared in accordance with Accounting and Reporting by Charities: Statement of Recommended Practice applicable to charities preparing their accounts in accordance with the Financial Reporting Standard applicable in the UK and Republic of Ireland (FRS 102) (effective 1 January 2019) - (Charities SORP (FRS 102)), the Financial Reporting Standard applicable in the UK and Republic of Ireland (FRS 102).

Timothy Syndrome Alliance (TSA) meets the definition of a public benefit entity under FRS 102. Assets and liabilities are initially recognised at historical cost or transaction value unless otherwise stated in the relevant accounting policy note.

### b) Going concern basis of accounting

The accounts have been prepared on the assumption that the charity is able to continue as a going concern, which the trustees consider appropriate having regard to the current level of unrestricted reserves. There are no material uncertainties about the charity's ability to continue as a going concern.

### c) Income

Income is recognised when the charity has entitlement to the funds, any performance conditions attached to the item of income have been met, it is probable that the income will be received and the amount can be measured reliably.

Income from the government and other grants, whether 'capital' grants or 'revenue' grants, is recognised when the charity has entitlement to the funds, any performance conditions attached to the grants have been met, it is probable that the income will be received and the amount can be measured reliably and is not deferred.

For legacies, entitlement is taken as the earlier of the date on which either: the charity is aware that probate has been granted, the estate has been finalised and notification has been made by the executor(s) to the Trust that a distribution will be made, or when a distribution is received from the estate. Receipt of a legacy, in whole or in part, is only considered probable when the amount can be measured reliably and the charity has been notified of the executor's intention to make a distribution. Where legacies have been notified to the charity, or the charity is aware of the granting of probate, and the criteria for income recognition have not been met, then the legacy is treated as a contingent asset and disclosed if material.

Income received in advance of provision of a service is deferred until criteria for income recognition are met.

### d) Donated services and facilities

Donated professional services and donated facilities are recognised as income when the charity has control over the item, any conditions associated with the donated item have been met, the receipt of economic benefit from the use by the charity of the item, is probable and the economic benefit can be measured reliably. In accordance with the Charities SORP (FRS 102), general volunteer time is not recognised.

On receipt, donated professional services and donated facilities are recognised on the basis of the value of the gift to the charity which is the amount the charity would have been willing to pay to obtain services or facilities of equivalent economic benefit on the open market; a corresponding amount is then recognised in expenditure in the period of receipt.

**e) Interest receivable**

Interest on funds held on deposit is included when receivable and the amount can be measured reliably by the charity: this is normally upon notification of the interest paid or payable by the bank.

**f) Funds accounting**

Unrestricted funds are available to spend on activities that further any of the purposes of the charity. Designated funds are unrestricted funds of the charity which the trustees have decided at their discretion to set aside to use for a specific purpose. Restricted funds are donations which the donor has specified are to be solely used for particular areas of the charity's work or for specific projects being undertaken by the charity.

**g) Expenditure and irrecoverable VAT**

Expenditure is recognised once there is a legal or constructive obligation to make a payment to a third party, it is probable that settlement will be required and the amount of the obligation can be measured reliably.

Irrecoverable VAT is charged as a cost against the activity for which the expenditure was incurred.

**h) Allocation of support and governance costs**

Support costs are those functions that assist the work of the charity but do not directly undertake charitable activities. Governance costs are the costs associated with the governance arrangements of the charity, including the costs of complying with constitutional and statutory requirements and any costs associated with the strategic management of the charity's activities. These costs have been allocated between cost of raising funds and expenditure on charitable activities based as follows:

| | **2025** | 2024 |
|---|---|---|
| Raising funds | **1.8%** | 0.0% |
| Charitable activities | **98.2%** | 100.0% |

**i) Debtors**

Trade and other debtors are recognised at the settlement amount due after any trade discount offered. Prepayments are valued at the amount prepaid net of any trade discounts due.

**j) Cash at bank and in hand**

Cash at bank and cash in hand includes cash and short term highly liquid investments with a short maturity of three months or less from the date of acquisition or opening of the deposit or similar account.

**k) Creditors**

Creditors and provisions are recognised where the charity has a present obligation resulting from a past event that will probably result in the transfer of funds to a third party and the amount due to settle the obligation can be measured or estimated reliably. Creditors and provisions are normally recognised at their settlement amount after allowing for any trade discounts due.

**l) Financial instruments**

The trust only has financial assets and financial liabilities of a kind that qualify as basic financial instruments. Basic financial instruments are initially recognised at transaction value and subsequently measured at their settlement value with the exception of bank loans which are subsequently recognised at amortised cost using the effective interest method.

**m) Foreign currency transactions**

Transactions in foreign currencies are translated at rates prevailing at the date of the transaction. Balances denominated in foreign currencies are translated at the rate of exchange prevailing at the year end.

**n) Accounting estimates and key judgements**

In the application of the charity's accounting policies, the trustees are required to make judgements, estimates and assumptions about the carrying values of assets and liabilities that are not readily apparent from other sources. The estimates and underlying assumptions are based on historical experience and other factors that are considered to be relevant. Actual results may differ from these estimates.

The estimates and underlying assumptions are reviewed on an ongoing basis. Revisions to accounting estimates are recognised in the period in which the estimate is revised if the revision affects only that period, or in the period of the revision and future periods if the revision affects both current and future periods.

## 2. Prior period comparatives: statement of financial activities

| | Restricted £ | Unrestricted £ | 2024 Total £ |
|---|---|---|---|
| **Income from:** | | | |
| Donations and legacies | - | 6,442 | 6,442 |
| Charitable activities | 87,245 | - | 87,245 |
| **Total income** | 87,245 | 6,442 | 93,687 |
| **Expenditure on:** | | | |
| Raising funds | - | 90 | 90 |
| Charitable activities | 18,286 | 1,380 | 19,666 |
| **Total expenditure** | 18,286 | 1,470 | 19,756 |
| **Net income / (expenditure)** | 68,959 | 4,972 | 73,931 |

## 3. Income from donations and legacies

| | Restricted £ | Unrestricted £ | **2025 Total £** |
|---|---|---|---|
| Donations | 73 | 10,316 | **10,389** |
| Gifts in kind | - | 38,043 | **38,043** |
| **Total income from donations and legacies** | 73 | 48,359 | **48,432** |

Gifts in kind comprise of donated services from Costello Medical for a research project carried out for the charity.

**Prior period comparative:**

| | Restricted £ | Unrestricted £ | 2024 Total £ |
|---|---|---|---|
| Donations | - | 5,692 | 5,692 |
| Grants | - | 750 | 750 |
| **Total income from donations and legacies** | - | 6,442 | 6,442 |

## 4. Income from charitable activities

| | Restricted £ | Unrestricted £ | **2025 Total £** |
|---|---|---|---|
| Grants | 156,761 | - | **156,761** |
| **Total income from charitable activities** | 156,761 | - | **156,761** |

**Prior period comparative:**

| | Restricted £ | Unrestricted £ | 2024 Total £ |
|---|---|---|---|
| Grants | 87,245 | - | 87,245 |
| **Total income from charitable activities** | 87,245 | - | 87,245 |

## 5. Government grants

The charity received no government grants in the period.

## 6. Total expenditure

| | Raising funds £ | Charitable activities £ | Support and governance costs £ | **2025 Total £** | Raising funds £ | Charitable activities £ | Support and governance costs £ | 2024 Total £ |
|---|---|---|---|---|---|---|---|---|
| Research | - | 38,043 | - | **38,043** | - | 7,871 | - | 7,871 |
| App development costs CACNA1C portal | - | 33,869 | - | **33,869** | - | 623 | - | 623 |
| Research and public engagement officer | - | 29,375 | - | **29,375** | - | - | - | - |
| Registry | - | 7,976 | - | **7,976** | - | - | - | - |
| Virtual assistant mission support officer | - | 6,500 | - | **6,500** | - | - | - | - |
| IT software & consumables | - | - | 5,194 | **5,194** | - | - | 4 | 4 |
| Mind the Gap counselling | - | 3,095 | - | **3,095** | - | 7,654 | - | 7,654 |
| Trusts fundraiser | 2,000 | - | - | **2,000** | - | - | - | - |
| Accountancy | - | - | 1,320 | **1,320** | - | - | 1,260 | 1,260 |
| Training | - | - | 427 | **427** | - | - | - | - |
| Subscriptions | - | - | 411 | **411** | - | - | 131 | 131 |
| Conference costs | - | 344 | - | **344** | - | - | - | - |
| Travel | - | - | 214 | **214** | - | - | 1,709 | 1,709 |
| Online donation platform fees | 137 | - | - | **137** | 90 | - | - | 90 |
| Printing, postage & stationery | - | - | 36 | **36** | - | - | 80 | 80 |
| Legal fees | - | - | 35 | **35** | - | - | 35 | 35 |
| Insurance | - | - | 20 | **20** | - | - | 299 | 299 |
| **Sub-total** | 2,137 | 119,202 | 7,657 | **128,996** | 90 | 16,148 | 3,518 | 19,756 |
| Allocation of support and governance costs | - | 7,657 | (7,657) | - | - | 3,518 | (3,518) | - |
| **Total expenditure** | **2,137** | **126,859** | **-** | **128,996** | **90** | **19,666** | **-** | 19,756 |

Total governance costs were £1,320 (2024: £1,260)

## 7. Net movement in funds

This is stated after charging:

| | **2025** | 2024 |
|---|---|---|
| | **£** | £ |
| Trustees' remuneration | **Nil** | Nil |
| Trustees' reimbursed expenses | **214** | 1,655 |
| Independent examiner's remuneration: | | |
| ▪ Independent examiner's fee | **1,320** | 1,260 |

Two trustees (2024: one trustee) were reimbursed for travel expenses.

## 8. Taxation

The charity is exempt from corporation tax as all its income is charitable and is applied for charitable purposes.

## 9. Creditors: amounts falling due within 1 year

| | **2025** | 2024 |
|---|---|---|
| | **£** | £ |
| Trade creditors | **500** | - |
| Accruals | **1,320** | 1,260 |
| | **1,820** | 1,260 |

## 10. Analysis of net assets between funds

| | Restricted funds | Designated funds | General funds | **Total funds** |
|---|---|---|---|---|
| | £ | £ | £ | **£** |
| Current assets | 151,346 | 9,839 | 9,970 | **171,155** |
| Current liabilities | - | - | (1,820) | **(1,820)** |
| **Net assets at 30 November 2025** | **151,346** | **9,839** | **8,150** | **169,335** |

| **Prior year comparative** | Restricted funds | Designated funds | General funds | Total funds |
|---|---|---|---|---|
| | £ | £ | £ | £ |
| Current assets | 79,941 | 6,000 | 8,346 | 94,287 |
| Current liabilities | - | - | (1,260) | (1,260) |
| **Net assets at 30 November 2024** | 79,941 | 6,000 | 7,086 | 93,027 |

## 11. Movements in funds

| | At 1 December 2024 £ | Income £ | Expenditure £ | Transfers between funds £ | **At 30 November 2025 £** |
|---|---|---|---|---|---|
| **Restricted funds** | | | | | |
| Chan Zuckerberg Initiative DAF | 75,540 | 148,821 | (78,015) | - | **146,346** |
| GlobalGiving | 1,901 | 73 | (1,974) | - | **-** |
| The Renishaw Charities Committee | 500 | - | - | - | **500** |
| Souter Charitable Trust | 2,000 | - | - | - | **2,000** |
| St. James's Place | - | 2,140 | (2,140) | - | **-** |
| The Stanley Grundy Foundation | - | 2,500 | - | - | **2,500** |
| The Waterloo Foundation | - | 3,300 | (3,300) | - | **-** |
| **Total restricted funds** | 79,941 | 156,834 | (85,429) | - | **151,346** |
| **Unrestricted funds** | | | | | |
| *Designated funds:* | | | | | |
| Registry project | 4,000 | 5,043 | (2,000) | - | **7,043** |
| Speech and language project | 2,000 | 796 | - | - | **2,796** |
| *Total designated funds* | 6,000 | 5,839 | (2,000) | - | **9,839** |
| General funds | 7,086 | 42,631 | (41,567) | - | **8,150** |
| **Total unrestricted funds** | 13,086 | 48,470 | (43,567) | - | **17,989** |
| **Total funds** | 93,027 | 205,304 | (128,996) | - | **169,335** |

**Purposes of restricted funds**

| | |
|---|---|
| Chan Zuckerberg Initiative DAF | An advised fund of Silicon Valley Community Foundation, over a five-year period, is supporting capacity building of our patient-led rare disease organisation, the development of a prioritised research agenda, convening our community, and accelerating collaborative research in our area of scientific focus. |
| GlobalGiving | Donors giving via our GlobalGiving (a US 501(c)(3) intermediary organisation that facilitates tax-effective donations from U.S. donors to U.K. charities) project page, specifically supported the running of our worldwide CACNA1C patient registry designed to obtain insights to better characterise CACNA1C, its presentation, management and treatment. |
| The Renishaw Charities Committee | Contributed towards a funding goal to support breakthrough speech and language research for young people affected by CACNA1C-related disorders. |

**11. Movements in funds (continued)**

| | |
|---|---|
| Souter Charitable Trust | Contributed towards a funding goal to support breakthrough speech and language research for young people affected by CACNA1C-related disorders. |
| St. James's Place | Contributed towards the continued provision of our 'Mind theGap' Counselling Service, delivering specialist mental health support to individuals, couples and families impacted by CACNA1C. |
| The Stanley Grundy Foundation | Contributed towards a funding goal to support breakthrough speech and language research for young people affected by CACNA1C-related disorders. |
| The Waterloo Foundation | Concluded its three year support of the CACNA1C Community Registry, enabling meaningful change for our existing and future CACNA1C community. |

**Purposes of designated funds**

| | |
|---|---|
| Registry project | The CACNA1C Community Registry (CCR) enables meaningful change for our existing and future CACNA1C community - the registry collects real-world data to obtain insights to better characterise CACNA1C, its presentation, management and treatment. Funds paid were for the annual platform fee. |
| Speech and language project | The Speech and Language Research Project delivers inclusive, globally accessible research to support families and clinicians, inform clinical trials, and advocate widespread sharing to improve diagnosis, treatment, and outcomes for individuals with CACNA1C rare variants. |

## 11. Movements in funds (continued)

| **Prior year comparative** | At 2 December 2023 £ | Income £ | Expenditure £ | Transfers between funds £ | At 30 November 2024 £ |
|---|---|---|---|---|---|
| **Restricted funds** | | | | | |
| Chan Zuckerberg Initiative DAF | - | 77,423 | (1,883) | - | 75,540 |
| GlobalGiving | 1,886 | 3,322 | (3,307) | - | 1,901 |
| Postcode Local Trust | 8,531 | - | (8,531) | - | - |
| The Renishaw Charities Committee | - | 500 | - | - | 500 |
| Souter Charitable Trust | - | 2,000 | - | - | 2,000 |
| The Waterloo Foundation | 565 | 4,000 | (4,565) | - | - |
| **Total restricted funds** | 10,982 | 87,245 | (18,286) | - | 79,941 |
| **Unrestricted funds** | | | | | |
| *Designated funds:* | | | | | |
| Registry project | - | - | - | 4,000 | 4,000 |
| Speech and language project | - | - | - | 2,000 | 2,000 |
| *Total designated funds* | - | - | - | 6,000 | 6,000 |
| General funds | 8,114 | 6,442 | (1,470) | (6,000) | 7,086 |
| **Total unrestricted funds** | 8,114 | 6,442 | (1,470) | - | 13,086 |
| **Total funds** | 19,096 | 93,687 | (19,756) | - | 93,027 |

## 12. Related party transactions

There were no related party transactions in the current or prior period.

**TIMOTHY SYNDROME ALLIANCE (TSA)**

England & Wales - Charity number 1185523

# Accounts

Timothy Syndrome Alliance (TSA)

# ANNUAL REPORT 2024

For financial period

**1 DECEMBER 2023 TO 30 NOVEMBER 2024**

www.timothysyndrome.org

Charity Registration Number: 1185523

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# What we do

Our charity was formed in 2019 to improve knowledge and understanding of our ultra-rare genetic disease while also providing support to those impacted by it.

We are run by parents of children and young adults from our community, along with volunteers.

We are led by the needs of our community and by working together and collaborating globally, we can harness greater strength. By empowering and nurturing a thriving global community through sustainable growth strategies, we create a lasting positive impact.

We focus on five interdependent areas of activity – raising awareness, improving diagnosis treatment and care, supporting the global community, providing information and advice, and driving research and clinical development.

CACNA1C-related disorders including Timothy Syndrome and LongQT8 are rare and their prevalence is unknown. Raising awareness is challenging due to our limited patient population, lack of steady funding, low recognition within the medical community, being overshadowed by more prevalent conditions, the complexity of our disease, and a general lack of urgency, all of which make it difficult to gain widespread attention and support.

The complexity of our disease is reflected in its wide range of symptoms, which include abnormal heart function, irregular heartbeat, and abnormal heart structure, as well as developmental delays, incoordination, hypotonia, and features of autism spectrum disorder. Additional symptoms include seizures, attention-deficit/hyperactivity disorder, low blood sugar (hypoglycaemia), immunodeficiencies, endocrinological dysfunction, gastrointestinal issues, hypothermia, facial anomalies, syndactyly (joined fingers or toes), and mild dental, skin, eye, and hair anomalies. In addition, conditions like Long QT and Short QT affect the electrical activity of the heart, causing it to take longer or shorter than normal to recharge between beats, potentially leading to irregular heartbeats that can result in fainting, seizures, or even sudden death.

## Vision

Our vision is a world where shared knowledge and understanding lead to a cure for everyone with a CACNA1C rare variant.

## Mission

Our mission is to improve the diagnosis, treatment and care of individuals worldwide with CACNA1C-related disorders including Timothy Syndrome and LongQT8, and to support the families and carers of those diagnosed.

## Values

Our core values and beliefs combine to form a solid foundation for the way we approach everything we do. We are determined, supportive, empowering and we are a community.

# Our strategic purposes and priorities

## Our strategic purposes

- Raising awareness.
- Improving diagnosis, treatment and care.
- Supporting the global community.
- Providing information and advice.
- Driving research and clinical development.

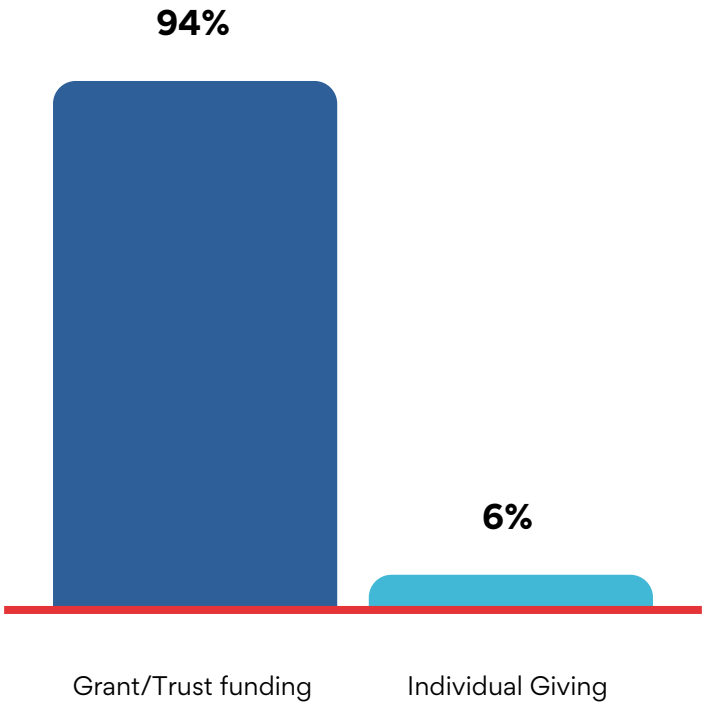
## Our priorities to enable our strategy

### Uniting families, advancing science, and driving change to transform lives and accelerate progress toward cures.

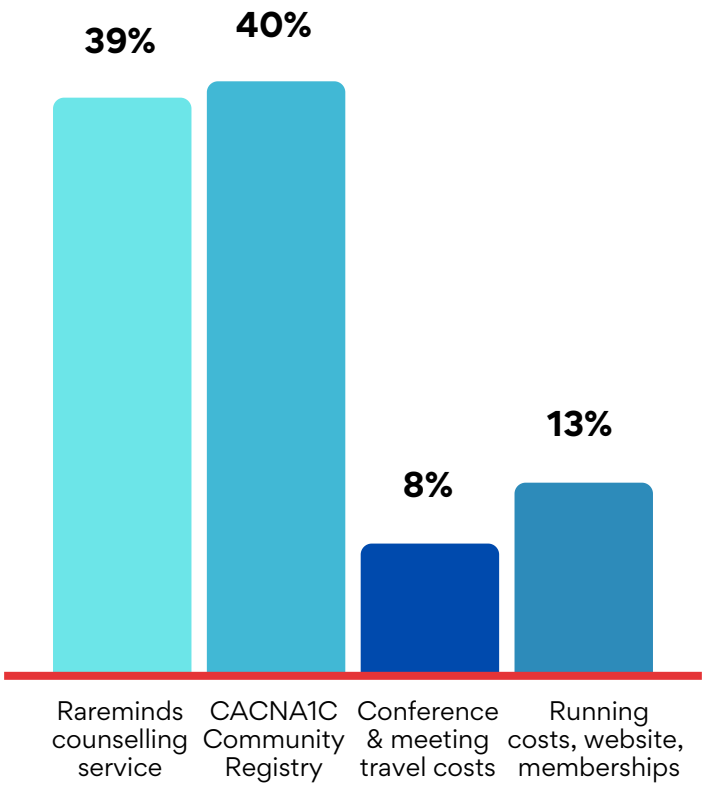
- Expand communications to raise awareness and reach new audiences.
- Build clinical and research networks to improve diagnosis, treatment, and care.
- Strengthen community support through global connection and shared resources.
- Provide trusted information that empowers families and professionals.
- Advance research by supporting funding, collaboration, and participation.
- Influence policy to improve systems and outcomes for our community.

# Our finances 2024: Summary

## Source of Income




## Summary of Expenditure



# Our year in review

## Delivery against 2024 priorities

**Raising Awareness** - We have to build awareness of what CACNA1C-related disorders actually are. The typical diagnostic odyssey for people with a rare disease is around 4 to 5 years, though it can often take much longer, and 40% of rare disease patients are initially misdiagnosed. Data from participants in our CACNA1C Community Registry indicate the mean age of diagnosis for individuals with CACNA1C findings is 9.7 years. We're determined to change that, because we want patients/families/professionals to have improved access to the facts they need especially on receipt of diagnosis. Receiving an accurate diagnosis for a rare condition is crucial for appropriate management and support. And we want them to find us, so we can offer support and a community of people who understand, and to help connect them to what could be a life-saving piece of information, or the chance to engage with research that they might not otherwise hear about.

- TSA was named **Charity of the Year 2024** by Healx and through this partnership we gained increased visibility, benefited from fundraising efforts, and engaged in meaningful collaborations to advance the understanding of CACNA1C-related disorders. Sophie and Dr Jack Underwood (TSA Scientific Advisory Board Chair) attended the Healx Team Day in Cambridge presenting in-depth on the challenges of CACNA1C. Healx is a pioneering AI-driven biotech company focused on accelerating the discovery and development of treatments for rare diseases. Their support amplified our reach and provided valuable exposure including a collaborative post on Rare Disease Day.

- The **2024 Smiley Charity Film Awards** received over 500 entries, and our film **"The Diagnosis Challenge"** released on Rare Disease Day 2023, was a finalist. Trustees Sophie and Galina along with our film-maker Rob Bradshaw attended the awards ceremony – we didn't win this time however we continue to punch above our weight.
  The Smiley Charity Film Awards celebrate the power of film in raising awareness for important causes. As the world's largest campaign of its kind, the awards recognise outstanding storytelling from charities, amplifying their messages and inspiring action. They are the world's largest cause-based film campaign, recognised by BFI and IMDb.
  Our short film highlights the lengthy and frustrating journey from first noticing that something isn't right and going to the doctor to actually receiving a diagnosis. This period of time even has a name, the 'Diagnostic Odyssey'. It's a process that can take many years, with seemingly endless tests along the way. The film is a montage list of healthcare professionals seen by just four of our families during their diagnostic odysseys.

- The production of what we were calling the Rare Disease Research Journey has been completed, and the film aptly named **"Connections"**. It was launched on our 5th birthday of becoming a registered charity. This film, a collaboration between TSA and Cardiff University, explores the importance of connections between individuals and families with lived experience of CACNA1C-related disorders (CRDs) and Timothy Syndrome (TS), academics, clinical teams and researchers. The more links we make, the stronger our network becomes and the faster we grow our understanding of our rare disease. Without connections, we can't grow or learn.

- We again entered the **Student Voice Prize**, an annual international essay competition that gives students the opportunity to engage with the rare disease community. Run by Medics4RareDiseases and Beacon for Rare Diseases, the competition encourages future healthcare professionals to explore the challenges faced by rare disease patients and advocate for improved diagnosis, research, and care. Whilst our 3rd-year medical student Diana did not win the competition, her essay summary below sums up how powerful campaigns such as this can be and the impact on the students taking part.
"The paradox of the low statistical prevalence of a rare disease coupled with its high potential to cause adverse health outcomes and emotional turbulence was called to my attention when I had the privilege of speaking to S about her diagnostic journey with CACNA1C-related disorders. The unpredictability that such a minute gene change can have on a person's life and those that surround them encourages me to be on high alert as a future doctor, especially with the scarcity of information and awareness that coexist with these conditions. Whilst researching and writing this essay, I indubitably knew that change must be made within my practice as well as the medical system itself."

- Being part of an alliance strengthens collaboration, amplifies advocacy efforts, and provides access to shared resources, expertise, and a wider support network. We are delighted to have joined the following alliances:
**ePAG ERN-ITHACA**, the European Reference Network for Rare Malformation Syndromes, Intellectual and Other Neurodevelopmental Disorders.
**AGENDA** (Alliance for the Genetic Etiologies of Neurodevelopmental Disorders and Autism), led by the Autism Science Foundation. At one meeting we were joined by one of our SAB members, Dr Rebecca Levy from Stanford University, to talk about the importance of the recent findings of using organoids to understand the role of gene therapies using Timothy Syndrome as an example.
**CombinedBRAIN** (The Consortium for Outcome Measures and Biomarkers for Neurodevelopmental Disorders). This followed a project we undertook with Terry Jo Bichell and one of her students Lipika who focused on CACNA1C as part of her Translational Neuroscience pre-medical undergraduate course at Vanderbilt University.
**CZI Rare As One Network** whose vision is to create, nurture, and support an engaged community of collaborative interdisciplinary research teams who will enable scientific breakthroughs that grow from combined expertise.

- Our digital presence plays a crucial role in raising awareness and engaging the community, and this year, our social media platforms and website have proven their impact. Compared to the previous year, we have seen growth in reach, engagement, and website visits, demonstrating that our message is resonating with a wider audience. By sharing research updates, personal stories, and advocacy efforts, we have strengthened our network and inspired more people to take an interest in CACNA1C and the work of TSA. This momentum highlights the power of clear, consistent communication in driving awareness and support.

  A great example of the butterfly effect from social media is the increase in the growth of our CACNA1C community in the months following an intensive campaign. The “For The Love Of CACNA1C” campaign ran every day for the month of February on our social media channels. We expanded this campaign during April with a focus on our families in Brazil ensuring posts were created in both Brazilian Portuguese and English languages. In March and May, each campaign saw community growth double compared to the previous month, including in May a new family from Brazil.

- We continue to be active with existing alliances ePAG ERN GUARD-Heart, UK Rare Epilepsies Together (UKRET), The Neurological Alliance, Genetic Alliance UK, Rare Diseases International, EURORDIS, Global Genes Global Advocacy Alliance, Global Heart Hub and The Voltage-Gated Calcium Channel Collective (VGCCC). Alongside this TSA benefits from services provided by Beacon for Rare Diseases, Costello Medical and CamRARE including mentoring, training, and networking opportunities.

  We were delighted to share how we are involved and engaged in the ePAG ERN GUARD-Heart (European Reference Network for Rare and Low Prevalence Complex Diseases of the Heart) as part of their **podcast** series in June and featured in the April **Newsletter** with a focus on CACNA1C.

  We have also participated in the **Talking Charities podcast** series hosted by St. James’s Place, a previous funder of our work. This series explores key topics in the charity sector and features expert insights on fundraising, governance, and impact. This was a wonderful opportunity to share the impact of our work, including the Mind the Gap counselling, and raise awareness. Discussions took place over two episodes (1 and 2).

Our Scientific Advisory Board Chair Jack was one of the scientists who took part in **ART-TRAnslations: Translating Science Through Art**. Paired with talented artist Naomi Tomkys OBE this is a creative initiative that uses visual storytelling to communicate complex scientific concepts related to rare diseases. This project was sponsored by LifeArc and supported by CamRARE. It was featured at RAREfest24, an event dedicated to rare diseases. By bridging the gap between research and public understanding, ART-TRAnslations makes science more accessible, engaging, and inclusive for diverse audiences.

The plaque reads:
'Ivory Tower
The origin came from Dr Jack Underwood as we discussed scientists being seen as living in Ivory towers, the reality of this is wonderfully different. I've used symbolism as a shorthand to the nature of Jack's work. A bee (dummy) - hard work; a boat (child's plate) - journey; a bear - strength, courage. I've also played with iconography giving Jack's daughter a halo of socks lit up with a computer screen rather than gold leaf.

I've included some of Jack's personal items including a slightly broken old globe. It reflects the way the world thinks about these genetic diseases, often out of date, like the old map of the world.
The drawings highlight that when you look at graphs and academic papers, there are children and families struggling behind every data point. These portraits are named after 4 children with CACNA1C variants that recently passed away. In memory of Halle; Xavier; Theodora; and Griffin.'

**Improving diagnosis treatment and care** - CACNA1C-related disorders have no geographic boundaries. They impact individuals worldwide regardless of location, ethnicity, or socioeconomic status. Gaps in healthcare systems and workforces vary from region to region and the need for global collaboration in diagnosis, treatment and care couldn't be greater. The more we identify and tackle these gaps in the early detection, diagnosis, monitoring or treatment of CACNA1C, the better the diagnostic and post-diagnostic journey will be for individuals who receive a positive CACNA1C finding.

TSA noted a significant lack of individuals in the UK joining the global CACNA1C community. To investigate this, we set up a project in 2023 to identify if there were any barriers to reporting our rare disease. We began mapping real-world data from Freedom of Information requests in England and found that over 100 individuals with CACNA1C rare variants had been classified as having Variants of Uncertain Significance (VUS).

VUS are a common challenge for ultra-rare diseases like ours. Because awareness is low and symptoms can vary widely, it is difficult to link specific genetic changes to predictable health outcomes. There are no large-scale studies of CACNA1C-related disorders, so genetic test results often do not guide medical care. Many results are classified as VUS, meaning their impact on health is unclear and the result is not reported to the individual.

In August, as one of three rare disease charities we were awarded £38,000 worth of pro bono support from Costello Medical to assist with our **real-world evidence (RWE) generation and communication**. Costello Medical provides scientific support to the healthcare industry.

**Our challenge**: CACNA1C-related disorders, including Timothy Syndrome and LongQT8, are multisystemic and individuals found to have a CACNA1C rare variant should receive cardiac, developmental, psychiatric, endocrine (particularly diabetic) and neurological (epilepsy) screening [1, 2, 3, 4]. This is currently not understood nor advocated for by key bodies including the National Health Service (NHS) and Genomics England.

**Our primary objective**: Efficiently disseminate impactful information on the recommended approach in response to a CACNA1C rare variant finding, ideally utilising the NHS and Genomics England data obtained via Freedom of Information Act requests, to increase the screening of individuals with CACNA1C findings in the UK (including those with VUS), to educate healthcare professionals and help patients make informed decisions about their care and to guide future advocacy initiatives.

We are incredibly grateful and excited to be working with Costello Medical on this huge impactful project and look forward to sharing the outcomes in 2025.

References:

1. Levy RJ, Timothy KW, Underwood JFG, Hall Jeremy, Bernstein JA, Pașca SP. A cross-sectional study of the neuropsychiatric phenotype of CACNA1C-related disorder. Pediatr Neurol. 2022;102542. doi:10.1016/j.pediatrneurol.2022.10.013

2. Bauer R, Timothy KW, Golden A. Update on the Molecular Genetics of Timothy Syndrome. Front Pediatr. 2021;9(May). doi: 10.3389/fped.2021.668546

3. Cipriano L, Piscopo R, Aiello C, Novelli A, Iolascon A, Piscopo C. Expanding the Phenotype of the CACNA1C-Associated Neurological Disorders in Children: Systematic Literature Review and Description of a Novel Mutation. Children. 2024 May;11(5):541. doi: 10.3390/children11050541

4. Timothy KW, Bauer R, Larkin KA, Walsh EP, Abrams DJ, Gonzalez Corcia C, et al. A Natural History Study of Timothy Syndrome. Orphanet J Rare Dis. 2024 Nov 23;19(1):433. doi: 10.1186/s13023-024-03445-x

We are also working on a project with Illumina, exploring the various paths families take to obtain a diagnosis. We are focusing particularly on the reasons why families often receive a Variant of Unknown Significance (VUS) as a result of genetic testing. We're aware that a VUS is both a specific yet also an unspecific result. In order to understand what happens when families receive a VUS as a result of testing, we are hearing about experiences and thoughts from within our community on this topic. Through their experiences we want to develop some themes that might be useful to create change in how people receive results and what information families would find helpful.

**39**

**CACNA1C**

**families/ individuals**

**+55**

**individuals**

**in our Facebook community**

**212**

**members**

**Patient Advisory Board**

**Supporting our global community** - Every person found to have a CACNA1C rare variant has a unique experience and healthcare journey. We make sure we're there, to offer support, reassurance and information - this includes our Scientific Advisory Board as a point of contact for healthcare professionals and our community when it's needed too. A key bit of knowledge of CACNA1C and shared lived experience can significantly impact your next medical appointment and the care you should expect or request. The right support can be life-changing, even life-saving.

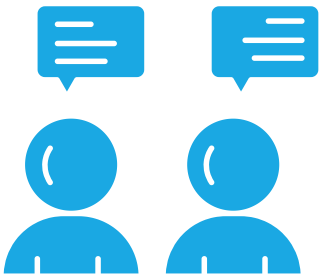
TSA administrates an online private **Facebook Support Group** for individuals and families of CACNA1C-related disorders including Timothy Syndrome and LongQT8, offering 24/7 access to emotional and practical support and information via our community.

The benefits of this are huge. It enables:

- meeting and befriending other people with the same rare disorder and similar experiences from across the world
- learning about CACNA1C
- giving and receiving emotional support
- having a place to speak openly about the impact of CACNA1C and one's thoughts and feelings
- learning coping skills
- feeling empowered and hopeful
- advocating to improve healthcare

As well as welcoming 39 individuals/families impacted by CACNA1C over the year, we saw a 22% increase in our community support group membership as a result of a spouse/partner also joining.

Each request to join our rare disease support group is carefully triaged to ensure it is the right fit, helping us maintain a safe, trusted space for our community. While this process takes time and care, it is an essential part of offering meaningful, immediate support, and ensuring no one feels alone.



**49**
**counselling sessions**
**provided**

**106**
**Dealing with Diagnosis**
**webinar views**

We have been providing our **'Mind the Gap' counselling service** to our community since 2022 when we piloted the service, from which feedback found 100% of participants feeling more positive, resilient, and less isolated. We work with Rareminds, qualified and experienced counsellors and psychotherapists with additional training in addressing psychosocial, physical, and mental health challenges faced by those diagnosed with a rare disease, to address significant psychological strain (including bereavement, anxiety, stress, low mood, emotional exhaustion and bearing uncertainty).
Demand for this confidential service continues to increase and this year we have provided 49 counselling sessions for individuals and couples in our community. This support helps participants cope with the challenges of having or supporting someone with our rare disease through tailored counselling which helps foster a sense of belonging, reducing isolation and providing long-term support for personal growth and coping strategies.

## “My counsellor has been my lifeline... Thank you to TSA for allowing us to use this service."

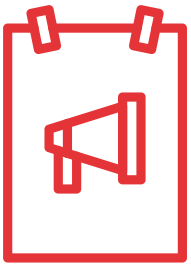
We have additionally created three recorded webinars with Rareminds with open access for our community to enable them to work around caring commitments and time zones; **Dealing with Diagnosis** (received 106 views in the 4 months since production), Looking after Mental Health & Wellbeing, and Managing Uncertainty (will be released 2025). Multiple language transcripts are underway for Dealing with Diagnosis to ensure this is accessible for all our community. A bereavement resource is also under production. When you lose someone you care about as a result of a rare condition, the feelings involved can be challenging and complex.

**Providing Information and advice** - A variety of new developments this year were shared through our online private Patient Advisory Board, which has 212 members. This hub allows TSA to provide updates and collaborate with our global community on advocacy efforts, ongoing research, partnerships, and campaigns.

- We've also added content to our website, notably our **Glossary** which explains genetic and medical terms in plain English. This original template was created by Genetic Alliance UK and adapted by our TSA Scientific Advisory Board. Plans are underway for our new quarterly newsletter to keep everyone abreast of the very latest happenings, with the first mailing anticipated in February 2025.

- We are delighted to see how much our Wikipedia CACNA1C-related disorders page has grown in views over this last year (92% increase on its first year) and plan to make time in 2025 to contribute further and expand on the content.

- Production of our pathway-focused Educational CACNA1C Interactive Guide for Healthcare Professionals will resume following confirmation of CACNA1C nomenclature expected during 2025. We remain steadfast in our commitment to accuracy and this delay will ensure alignment of the guide with outcomes not yet published.



## 2 x Scientific poster conference presentations

**The impact of CACNA1C real-world data: CACNA1C Community Registry (CCR) design**

**Driving research and clinical development** - This year has been about building on our existing research achievements and partnerships to inform clinical developments and we're proud of all this work. More awareness of CACNA1C-related disorders means more attention, more research and bigger steps towards our vision where shared knowledge and understanding lead to a cure for everyone with a CACNA1C rare variant.

- **CACNA1C Language Consensus** - 20 years ago Timothy Syndrome was first described and named. As the number of people identified with CACNA1C gene variants grows, how do we describe those who don't neatly fit Timothy Syndrome? This is the project we've set out to answer.
  Earlier this year our SAB Chair Jack began convening a panel of international experts with the aim of coming up with clear, well-defined language around Timothy Syndrome and CACNA1C. There are lots of terms being used beyond the original Timothy Syndromes Type 1 and 2, Atypical Timothy Syndrome, Timothy Syndrome Type 3, Timothy Syndrome Variants, Long QT 8, Short QT, CACNA1C variants, CACNA1C-Related Disorders. There isn't a consensus or agreement on what these mean. This isn't helpful for the individuals, their families, their doctors, or researchers.
  Our CACNA1C community has been consulted in this process. The outcome is currently being prepared to be shared with the community and published.

Our Scientific Advisory Board (SAB) has expanded with the addition of Professor Liz Tunbridge, Director of Translational Neuroscience, Boehringer Ingelheim. Liz has a long-standing interest in understanding how the diversity of CACNA1C channels affects different tissues, and therefore symptoms. We are immensely grateful for all the time, effort and enthusiasm our SAB continues to give to our community. It is this teamwork that helps drive us forward.

## Scientific Advisory Board

Dr. Jack Underwood (Chair)
Wellcome Trust GW4-CAT Clinical Research Fellow, NMHII, Cardiff University

Dr. Nicola Hall
Postdoctoral Researcher, University of Oxford

Dr. Rebecca Levy
Clinical Scholar, Neurology & Neurological Sciences. Postdoctoral Scholar, Neurology & Neurological Sciences, Stanford Medicine

Dr. Anwar Baban
Bambino Gesù Children Hospital and Research Institute, IRCCS, Rome

Dr. Gemma Wilkinson
Research Associate, NMHII, Cardiff University

Dr. Wilfried Haerty
Group Leader of Evolutionary Genomics, Earlham Institute

Prof Liz Tunbridge
Director of Translational Neuroscience, Boehringer Ingelheim

Following the success of our **Connect CACNA1C Global Network Conference** last year all six presentation recordings are now available with transcripts in 14 languages. Initially accessible via a private link, as much of the work presented had yet to be published, the presentations with transcripts will transfer to a public viewing link at the end of the year to continue to educate and inform both families and healthcare professionals.

October brought Dan Haynes, a new PhD student at NMHII, Cardiff University funded by the Hodge Foundation. His project, which focuses on the role that the CACNA1C gene plays in psychiatric illness onset, will be partly supervised by Dr Jack Underwood. We are the external partner, meaning Dan will support Jack and Sophie by communicating with families, completing administrative duties and helping to organise conferences.

# 87%

**of children face challenges with**

# speech, language & communication

87% of children with our rare disease face challenges with speech, language and communication.
Some individuals do not develop enough verbal speech to rely on it for their daily communication needs. On top of this, parents and carers are commonly also managing cardiac concerns, developmental delay, incoordination, hypotonia, autism spectrum disorder, seizures, and attention-deficit/hyperactivity disorder.
Early intervention and the correct support can help reduce these impacts and improve communication skills and overall quality of life. No studies have thoroughly looked at speech and language problems using consistent methods or formal tests to clearly distinguish between different speech and language issues. Right now, we don't clearly understand the difference between speech problems caused by issues with the muscles used for speaking (like speech apraxia) and those caused by problems with thinking and language skills. These distinctions are crucial, as without accurate diagnoses, parents and clinicians remain unsure about what therapies to implement.

We have launched a **fundraising campaign** to

- DELIVER inclusive and representative gene-specific speech and language research which will be accessible to our globally marginalised community.

- SUPPORT parents, carers and clinicians with clearer diagnosis, prognosis and treatment planning to alleviate the substantial impact on learning, education, social interaction, self-esteem, mental health, and daily living.

- INFORM speech and language outcome measures for future clinical trials through clearly explained data.

- ADVOCATE the widespread sharing of the research upon conclusion to maximise clinical impact worldwide to transform diagnosis and prognosis and enable precision therapies.

The **CACNA1C Community Registry** has continued to grow and at the end of this year had 90 participants enrolled. The registry collects real-world data to obtain insights to better characterise CACNA1C, its presentation, management and treatment. We are working with our SAB to analyse the Registry data and see how this can be published as research and used to inform clinical and medical treatment.

We created a **scientific poster** using registry data presented at our Connect CACNA1C Global Network Conference. Sophie presented this poster at the British Paediatric Neurology Association (BPNA) Conference in January and again at the Genomics England Research Summit Conference in July.

We are members of the **Bristol University Neurodevelopment Hub** which launched in July and brings together a diverse group of researchers and clinicians interested in mechanisms and consequences of brain development and function to better understand, improve diagnosis of, and identify new therapeutic targets for neurodevelopmental, neurological, and psychiatric conditions. Our strong links with the multi-disciplinary cross-GW4 community researching, modelling, diagnosing, monitoring and treating epilepsy has resulted in a GW4 Building Communities Development Award. The project aims to develop the community to better address the lack of fundamental understanding of epilepsies, improve (epi)/genotypic diagnosis, animal, cell and computational epilepsy models facilitating testing of better targets, screen for novel genetic and drug therapies plus develop better devices for diagnosis, monitoring and treatment.

(The GW4 Alliance (also known as GW4) is a consortium of four research intensive universities in South West England and Wales.)

We were selected to attend the Aspire Biosciences **Rare Neurology/CNS Partnering Event** at the Royal Society of Medicine in London. Both Sophie and SAB member Nicola Hall attended the "speed-date" style networking event designed to build collaborations between patient groups, and pharmaceutical and biotech companies interested in finding treatments for rare diseases that affect the brain and nervous system. The day was a whirlwind—exciting, intense, and full-on. So many great conversations took place, and there are plenty of follow-ups to keep the momentum going.

We are also now members of the **BHF Clinical Research Collaborative**, a large national cardiovascular clinical research network that is funded by the British Heart Foundation but is supported by all of the national specialist societies. They aim to link clinicians and researchers more with patients to ensure great collaboration in research.

- Since October 2023 Sophie has been part of the **Rare Diseases Research Network (RDRN)** working group, a partnership project between CamRARE and Patient Led Research Hub, funded by the National Institute for Health and Social Care Research (NIHR) and sponsored by Cambridge University Hospitals NHS Foundation Trust, building an online platform to facilitate rare disease research. This platform was successfully launched in November.

- The **Voltage-Gated Calcium Channel Collective (VGCCC)** unites patients, families, researchers, and clinicians in a collaborative, patient-centred community. We formulated last year and believe we can drive breakthroughs in understanding and treating voltage-gated calcium channelopathies, ultimately improving the lives of those impacted by these conditions. We meet monthly to share updates, discuss challenges, and strategise on our collective efforts. These meetings provide a vital platform for collaboration, ensuring that all voices are heard and that we remain aligned in our mission. On Rare Disease Day we launched our Facebook, Instagram and Bluesky VGCCC accounts and are now underway with the building of our website.

- In June Sophie attended the **EURORDIS Open Academy School on Scientific Innovation and Translational Research** which consisted of one week of intensive in-person training in Barcelona, and followed the e-learning modules and pre-training webinars. The training, delivered by over 20 rare disease expert specialists from across Europe, aims to deepen patient representatives' understanding of how pre-clinical research translates into real benefits for rare disease patients. The training equips participants with knowledge and skills to empower them to effectively participate in discussions with researchers, policymakers, and companies active in rare disease research.

- To complete another incredible year it was confirmed in October that we were one of the first international patient organisations to join the **Chan Zuckerberg Initiative Rare As One Network (Cycle 3)** to help drive forward research (but not fund it directly).
  The Chan Zuckerberg Initiative invites applications for five-year projects from patient-led rare disease advocacy organisations to join the Rare As One Network. Grantee organisations will accelerate research within individual disease areas and work across specified areas of scientific focus (channelopathies; ciliopathies; or inborn errors of metabolism) to develop shared research priorities and proposals.
  For the 2024 award cycle, Timothy Syndrome Alliance (TSA) is one of 30 patient organisations around the world to receive a funding grant and has been awarded $800,000 over five years.
  Further information is available at: Rare As One Project – Chan Zuckerberg Initiative and Rare As One Network RFA – Chan Zuckerberg Initiative
  We look forward to sharing our ambitious and well-informed strategy as a result of this support in the coming year, and believe this will transform the progress for CACNA1C-related disorders.

RARE AS ONE

# Fundraising

TSA operates day-to-day with just one core team member and limited internal capacity. While rare diseases are collectively common, our specific condition remains under-recognised, making it harder to attract attention and funding. There is often a perception that rare disease needs will be met by national healthcare systems or government services, but many in our community tell us they have found support nowhere else. Unlike more widely known conditions, we face significant barriers to public fundraising, despite the urgent and unmet needs we address. In an increasingly competitive funding landscape, we are often applying alongside larger organisations with established teams and broader visibility — yet our work delivers targeted impact where few others can reach.

**Grants** - Our primary source of income comes from charitable trusts and foundations. Over the past year, we have successfully secured support from several of these organisations.
We would like to extend our heartfelt thanks to the following trusts and foundations for their generous support this year:

The Renishaw Charities Committee
The Waterloo Foundation
Souter Charitable Trust
Jeans For Genes
Chan Zuckerberg Initiative DAF, an advised fund of Silicon Valley Community Foundation

**Donations** - With rising living costs continuing to strain household budgets in 2024, individual giving became harder for many. Even so, the kindness and commitment of our community shone through, helping us grow despite the odds.
We are so grateful to everyone who found a way to support us this year.
Thank you to those who contributed to the JustGiving Healx appeal (£1,301) and Ethan's incredible Sahara Desert Trek fundraiser (£1,195).
Heartfelt thanks also to Susan, MaryAnn, and Jill for choosing us for their Facebook birthday fundraisers, and to the Minchinhampton Community Choir and the Crown Public House for hosting a fantastic quiz night.
We're equally grateful to those who gave through platforms like Benevity and GlobalGiving, to our generous one-off donors, and to our wonderful regular donors who support us through standing orders.
Your generosity continues to sustain our work and bring hope to families who need it most.

We are eager to achieve the Speech & Language Research campaign target (detailed on page 16). £4,238 of the £5,693 raised by you has been allocated towards this ambitious £16,000 target total. In October we were delighted to learn that the Trustees of the Speech, Language and Hearing Foundation agreed to make a commitment of £4,000 towards the project dependent on us being able to secure the outstanding amount required to launch this project.
Fundraising continues into 2025.

**Fundraising events** - A ball you say? What a great idea.

A group of amazing friends, that trustees Sophie and Nick met at their local nursery and mother/baby groups with their middle son Calvin, organised a ball for the last evening of TSA's financial year. They'd been witness to Calvin growing up. Their kids had even learnt Makaton sign language to communicate with Calvin as he didn't talk for his first 7 years. Alongside this, they had seen the battles and struggles of hospital and therapy visits, educational support, the near 10-year diagnostic odyssey of not knowing the reason why he was presenting with so many challenges, genetic testing and then the post-genetic odyssey search for information and other children just like him.

They have seen us put our heart and soul into growing Timothy Syndrome Alliance (TSA) as a charity over the last 5 years. Organising a ball was such a kind and thoughtful display of support. Huge thank you to The Hunter Moon Ball team for such an amazing event (which included a viewing of the film Connections), to the sponsors and donors of silent auction prizes and of course to those who came to support in their black tie glamour for live music and dancing. What a ball!

Spoiler alert for the 2025 Annual Report: the event raised an amazing £3,005.

'Twas the night of the Hunter Moon Ball, what a sight,
When you gathered together to make the night bright.
For TSA's cause, you gave up your eve,
Your kindness and giving, hard to believe!

You bought raffle tickets, you bid with great flair,
Your generosity truly filled up the air.
With dancing and laughter, old friends and new,
We hope that the evening brought joy to you too.

To those who donated, both funds and fine wares,
Your gifts have brought hope beyond all compares.
And to our sponsors, who helped pave the way,
Your support made the night a resounding hooray.

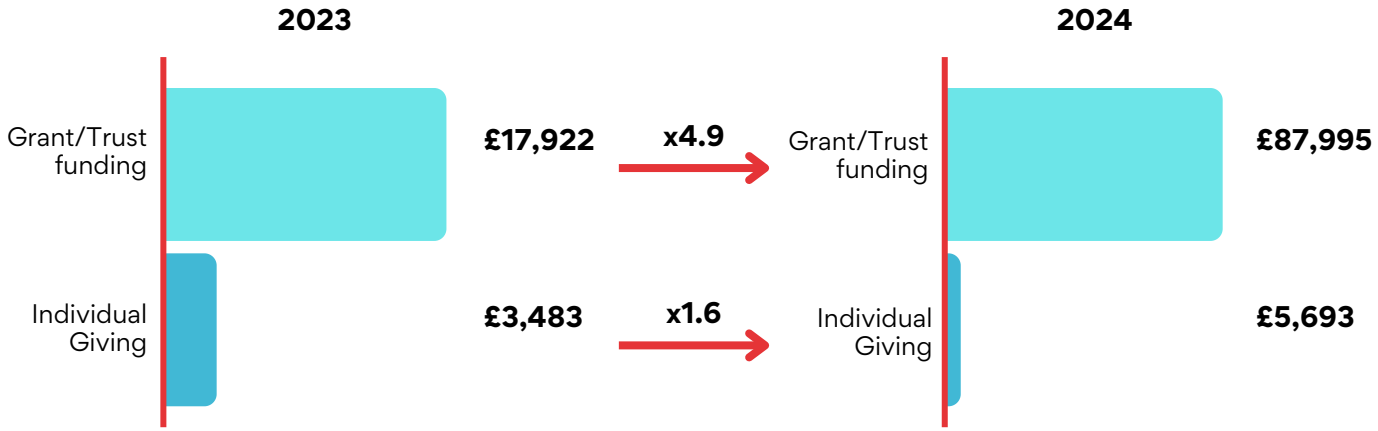
The team worked so hard, their passion so clear,
To bring us together and spread festive cheer.
Their efforts were shining, the event a success,
To them and to you, our heartfelt address.

So thank you for coming, for showing you care,
For helping rare lives with the love that you share.
We wish you a season that's merry and bright,
And thank you again for such a magical night.

'The Hunter Moon Ball team, headed by Rosie, were Charlotte, Kathryn, Annie, Hannah, Sophie B, Cathy and Sue.

# Financial review

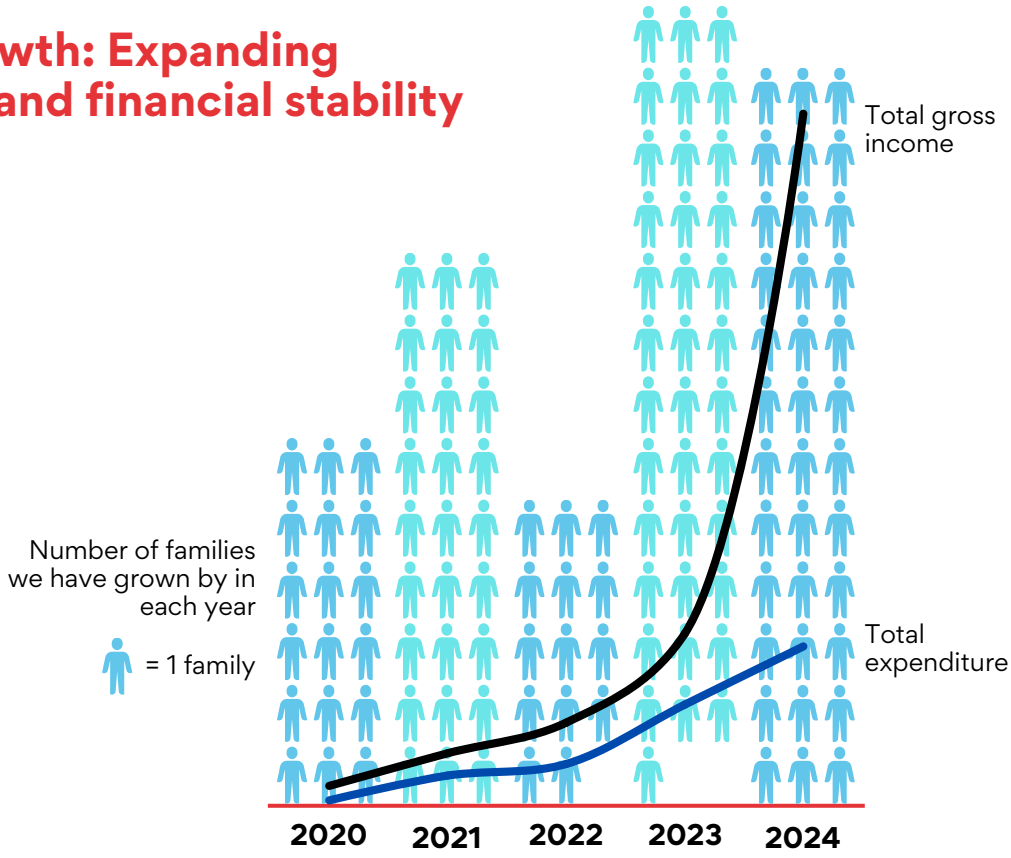
## Income by source




Our determination and drive have fuelled significant growth this year, including a notable increase in our community size.

- Our income from trusts and foundations has increased nearly five times and individual giving (including gift aid) has increased by 60%. Thank you to all of our supporters this year for their generous contributions.
- This has powered an expenditure increase of 60% on last year, ensuring we are meeting our aims by uniting families, advancing science, and driving change to transform lives and accelerate progress toward cures.

## Sustainable Growth: Expanding our community and financial stability



- **Fundraising Policy:** We are committed to upholding the highest standards in fundraising, ensuring that all our supporters feel safe, respected, and valued. As a UK-registered charity, we adhere to the standards set by the Fundraising Regulator and follow guidance from other relevant professional fundraising bodies.
  We never buy or sell personal data, and we take great care to honour individuals' preferences about how and when they wish to hear from us. The principles of the UK General Data Protection Regulation (UK GDPR) are fully embedded in the way we work.
  We do not use cold calling or cold mailing, and we do not employ third-party fundraising agencies. All of our fundraising is conducted with integrity, transparency, and respect for our community.

- **Reserves Policy:** The charity receives funding for specific purposes which are restricted funds – these are not available for expenditure on other purposes. The general reserves are the unspent unrestricted funds of the charity. The charity currently owns no fixed assets, so the general reserve is held in cash. The general reserve is therefore the free reserves of the charity plus any designated funds, also termed 'unrestricted funds' in the charity's balance sheet.
  The purpose of the general reserve is to:
  a) fund shortfalls when income does not reach expected levels.
  b) fund unexpected expenditures, for example when projects overrun or unplanned events occur.
  c) ensure that the Charity is not unnecessarily holding back on spending in favour of using the resources it has to meet its charitable objectives.
  We aim to hold a general reserve, estimated to be in the range £9,000 - £10,000, to cover operating costs for a 3 to 6 month period. At 30 November 2024 total free reserves were £7,086. We are able to operate on a low funds base as we have kept overheads to a minimum and are not committed to fixed term costs such as rent or other long-term contracts. This enables us to make sure the majority of income is directed to charitable activities. Our reserves policy is reviewed annually and updated as necessary.

- **Going Concern:** The trustees have reviewed the circumstances of the Charity and consider that adequate resources continue to be available to fund its activities for the foreseeable future. The trustees are of the view that the Charity is a going concern.

# Looking forward to 2025

We are focused on the same strategic priorities as last year, but have added a fifth as we want to become better equipped *to do more, reach more people, and achieve greater impact*.
We will be having an **online conference** with an **in-person conference** the following year.
We will also aggregate and harmonise clinical, genetic, and molecular data, and develop **a global CACNA1C Portal** to provide a unified resource for characterising the clinical spectrum of CACNA1C-related disorders, linking specific genetic variants with their phenotypic manifestations.
The portal will support clinical variant interpretation, enhance patient care management, and identify biomarkers for clinical trials.

- Expand communications to raise awareness and reach new audiences.
- Build clinical and research networks to improve diagnosis, treatment, and care.
- Strengthen community support through global connection and shared resources.
- Provide trusted information that empowers families and professionals.
- Advance research by supporting funding, collaboration, and participation.
- Influence policy to improve systems and outcomes for our community.
- Capacity builds capacity.
  Building capacity creates the conditions for further growth and effectiveness.
  We will hire a **Mission Support Officer** — a vital role that will helps us grow our capacity and focus on what matters most. By having dedicated support behind the scenes, we can work more efficiently, respond faster, and take on more without burning out.
  Making sure research stays grounded in the real lives and voices of the people it aims to help we will welcome a **Research and Public Engagement Officer** to the team — a role designed to strengthen the bridge between science and our community. They'll play a key role in making complex research easier to understand. By sharing updates in clear, accessible language, they'll help, families stay informed and involved, while keeping researchers connected and aware of community needs.
  We will support our core operations with a **CRM and accounting software**, helping us stay organised, accountable, and ready to grow. Our CRM, which stands for Customer Relationship Management, will help us stay connected with our community, thank people properly, and make sure no one falls through the cracks. Our accounting software will help us manage our finances clearly and accurately — tracking income, expenses, and budgets so we can report transparently and meet all our financial obligations. It means we will spend less time on admin and more time delivering impact.

# Thank you

None of this impact would be possible without the incredible people and organisations who stand beside us — funding our work, offering pro bono support, and generously sharing their time, expertise, and energy. Huge thanks to Dmitry for continued voluntary commitment to our TSA website and as well as the build of the website for The VGCCC, to our conference language transcript volunteers Hugo, Therese and Tricia for their human attention to detail and to Rob at Limestone Media for going above and beyond with our filming. We're deeply grateful to our Scientific Advisory Board members for their unwavering dedication to advancing understanding of CACNA1C and guiding our research efforts.

As Chair, I would also like to personally thank my fellow trustees for their continued guidance, expertise, and commitment throughout the year. It is a privilege to serve alongside such a dedicated team. An extra thank you to Costello Medical for their pro bono support with our trustee recruitment project, through which we came up trumps with Achsah, and the amazing resources we now have for future recruitment rounds

Our voice wouldn't be as strong without the support and engagement of our CACNA1C community. Besides sharing stories and photos which greatly helps signpost new families, encouraging and supporting each other, attending our conferences, supporting our social media channels, joining the registry, and contributing to research, they make the impossible possible. Thank you. We are Stronger Together.

## How to connect and support

We have been certified as the equivalent of a U.S. public charity, allowing U.S. donors to give with confidence via your Donor Advised Fund (DAF).
Ensure you select the correct organisation using our Registered Charity number: 1185523.

NGOsource
Equivalency Determination on File

Help us make a difference

GlobalGiving tax-deductible in the US

Create online fundraising page

Benevity Workplace Giving

Take on a challenge in support of TSA

Raise awareness on social media

Be the difference. Volunteer

This Annual Report was designed and created with love at no cost to TSA

## TIMOTHY SYNDROME ALLIANCE (TSA) TRUSTEES' REPORT General Information

For the year ended
30 November 2024.

Registered Charity Number: 1185523

Trustees: Sophie Muir – Chair
Nick Muir
Galina Gardiner
Meg Mcloughlin
Gemma Duncan (appointed 11 March 2024)
Susan Bresnahan Appointed 11 June 2024)
Achsah James (appointed 6 November 2024)
Katherine W Timothy (resigned 24 November)

Registered Office: 8 Butt Street, Minchinhampton, Gloucestershire GL6 9JP

**Objectives**: To relieve the needs of those affected by deleterious CACNA1C gene changes resulting in CACNA1C-related disorders including Timothy Syndrome and Long QT8, their families and carers worldwide in particular but not exclusively by:- (1) Promoting greater understanding of the causes, symptoms and treatment of CACNA1C-related disorders including Timothy Syndrome and Long QT8, by the promotion of research and sharing and disseminating of the results of such research for the benefit of the general public; (2) Raising public awareness of the symptoms, needs and related medical conditions of those living with CACNA1C-related disorders including Timothy Syndrome and Long QT8.

**Structure, governance, and management**: Timothy Syndrome Alliance (TSA) is a registered charity number 1185523, governed by the Charities Act 2006. The charity is a Charitable Incorporated Organisation registered on 27 September 2019 under the Foundation Governing Document. The Trustees delegate the charity's day-to-day management to Sophie Muir. Trustees met four times during the year and corresponded regularly via email and other digital means, particularly to keep financial performance under review. New trustees are appointed by the serving trustees, considering the skills required by the board. Trustee induction includes online training (NCVO) to give an overview and understanding of charity governance, regulation and best practice alongside Essential Information for Trustees from the Charities Commission.

**Public Benefit**: The Trustees confirm that they referred to the Charity Commission's general guidance on public benefit when reviewing the Charity's aims and objectives for the year. Public benefit has been achieved through the activities outlined in the Achievements and Performance section of this report.

**Statement of responsibilities of the trustees**
The trustees are responsible for preparing the trustees' report and the financial statements in accordance with applicable law and United Kingdom Accounting Standards, including Financial Reporting Standard 102: The Financial Reporting Standard applicable in the UK and Republic of Ireland (United Kingdom Generally Accepted Accounting Practice).

The law applicable to charities in England and Wales requires the trustees to prepare financial statements for each financial year, which give a true and fair view of the state of affairs of the charity and the incoming resources and application of resources, including the net income or expenditure, of the charity for the year. In preparing those financial statements the trustees are required to:

- select suitable accounting policies and then apply them consistently;
- observe the methods and principles in the Charities SORP;
- make judgements and accounting estimates that are reasonable and prudent;
- state whether applicable accounting standards and statements of recommended practice have been followed, subject to any material departures disclosed and explained in the financial statements; and
- prepare the financial statements on the going concern basis unless it is inappropriate to presume that the charity will continue in operation.

The trustees are responsible for keeping proper accounting records which disclose with reasonable accuracy at any time the financial position of the charity and which enable them to ensure that the financial statements comply with the Charities Act 2011, the Charity (Accounts and Reports) Regulations 2008 and the provisions of the constitution. The trustees are also responsible for safeguarding the assets of the charity and hence for taking reasonable steps for the prevention and detection of fraud and other irregularities.

The trustees are responsible for the maintenance and integrity of the corporate and financial information included on the charity's website. Legislation in the United Kingdom governing the preparation and dissemination of financial statements may differ from legislation in other jurisdictions.

Members of the charity have no liability to contribute to the assets of the charity in the event of winding up. The trustees are members of the charity but this entitles them only to voting rights. The trustees have no beneficial interest in the charity.

**Auditors / Independent examiners**
Godfrey Wilson Limited were appointed independent examiners to the charity during the year and have expressed their willingness to continue in that capacity.

Approved by the trustees on 6 May 2025 and signed on their behalf by

Sophie Muir

Sophie Muir - Chair of the trustees

**Independent examiner's report**

**To the trustees of**

**Timothy Syndrome Alliance (TSA)**

I report to the trustees on my examination of the accounts of Timothy Syndrome Alliance (TSA) (the CIO) for the year ended 30 November 2024, which are set out on pages 28 to 38.

**Responsibilities and basis of report**
As the charity trustees of the CIO you are responsible for the preparation of the accounts in accordance with the requirements of the Charities Act 2011 ('the Act').

I report in respect of my examination of the CIO's accounts carried out under section 145 of the 2011 Act and in carrying out my examination I have followed all the applicable Directions given by the Charity Commission under section 145(5)(b) of the Act.

**Independent examiner's statement**
I have completed my examination. I confirm that no material matters have come to my attention in connection with the examination giving me cause to believe that in any material respect:

(1) accounting records were not kept in respect of the CIO as required by section 130 of the Act; or
(2) the accounts do not accord with those records; or
(3) the accounts do not comply with the applicable requirements concerning the form and content of accounts set out in the Charities (Accounts and Reports) Regulations 2008 other than any requirement that the accounts give a 'true and fair view' which is not a matter considered as part of an independent examination.

I have no concerns and have come across no other matters in connection with the examination to which attention should be drawn in this report in order to enable a proper understanding of the accounts to be reached.

Rob Wilson

Date: 6 May 2025
**Robert Wilson FCA**
**Member of the ICAEW**
For and on behalf of:
**Godfrey Wilson Limited**
Chartered accountants and statutory auditors
5th Floor Mariner House
62 Prince Street
Bristol
BS1 4QD

**Timothy Syndrome Alliance (TSA)**

**Statement of financial activities**

**For the year ended 30 November 2024**

| | Note | Restricted £ | Unrestricted £ | **2024 Total £** | 2023 Total £ |
|---|---|---|---|---|---|
| **Income *(and endowments)* from:** | | | | | |
| Donations and legacies | 3 | - | 6,442 | **6,442** | 3,483 |
| Charitable activities | 4 | 87,245 | - | **87,245** | 17,922 |
| **Total income *(and endowments)*** | | 87,245 | 6,442 | **93,687** | 21,405 |
| **Expenditure on:** | | | | | |
| Raising funds | | - | 90 | **90** | - |
| Charitable activities | | 18,286 | 1,380 | **19,666** | 12,305 |
| **Total expenditure** | 6 | 18,286 | 1,470 | **19,756** | 12,305 |
| Net gains / (losses) on investments | | - | - | **-** | - |
| **Net income / (expenditure)** | | 68,959 | 4,972 | **73,931** | 9,100 |
| Transfers between funds | | - | - | **-** | - |
| **Net movement in funds** | 7 | 68,959 | 4,972 | **73,931** | 9,100 |
| **Reconciliation of funds:** | | | | | |
| Total funds brought forward | | 10,982 | 8,114 | **19,096** | - |
| **Total funds carried forward** | | 79,941 | 13,086 | **93,027** | 9,100 |

All of the above results are derived from continuing activities. There were no other recognised gains or losses other than those stated above. Movements in funds are disclosed in note 11 to the accounts.

**Timothy Syndrome Alliance (TSA)**

**Balance sheet**

**As at 30 November 2024**

| | Note | **2024** **£** | 2023 £ |
|---|---|---|---|
| **Current assets** | | | |
| Cash at bank and in hand | | **94,287** | 19,096 |
| **Liabilities** | | | |
| Creditors: amounts falling due within 1 year | 9 | **(1,260)** | - |
| **Net assets / (liabilities)** | 10 | **93,027** | 19,096 |
| **Funds** | 11 | | |
| Restricted funds | | **79,941** | 10,982 |
| Unrestricted funds | | | |
| Designated funds | | **6,000** | - |
| General funds | | **7,086** | 8,114 |
| **Total charity funds** | | **93,027** | 19,096 |

Approved by the trustees on 6 May 2025 and signed on their behalf by

Sophie Muir

Sophie Muir - Chair of the trustees

**Timothy Syndrome Alliance (TSA)**

**Notes to the financial statements**

**For the year ended 30 November 2024**

## 1. Accounting policies

### a) General information and basis of preparation

Timothy Syndrome Alliance (TSA) is an unincorporated charity registered in England and Wales. The registered office address is 8 Butt Street, Minchinhampton, Gloucestershire, GL6 9JP.

The financial statements have been prepared in accordance with Accounting and Reporting by Charities: Statement of Recommended Practice applicable to charities preparing their accounts in accordance with the Financial Reporting Standard applicable in the UK and Republic of Ireland (FRS 102) (effective 1 January 2019) - (Charities SORP (FRS 102)), the Financial Reporting Standard applicable in the UK and Republic of Ireland (FRS 102).

Timothy Syndrome Alliance (TSA) meets the definition of a public benefit entity under FRS 102. Assets and liabilities are initially recognised at historical cost or transaction value unless otherwise stated in the relevant accounting policy note.

### b) Going concern basis of accounting

The accounts have been prepared on the assumption that the charity is able to continue as a going concern, which the trustees consider appropriate having regard to the current level of unrestricted reserves. There are no material uncertainties about the charity's ability to continue as a going concern.

### c) Income

Income is recognised when the charity has entitlement to the funds, any performance conditions attached to the item of income have been met, it is probable that the income will be received and the amount can be measured reliably.

Income from the government and other grants, whether 'capital' grants or 'revenue' grants, is recognised when the charity has entitlement to the funds, any performance conditions attached to the grants have been met, it is probable that the income will be received and the amount can be measured reliably and is not deferred.

For legacies, entitlement is taken as the earlier of the date on which either: the charity is aware that probate has been granted, the estate has been finalised and notification has been made by the executor(s) to the Trust that a distribution will be made, or when a distribution is received from the estate. Receipt of a legacy, in whole or in part, is only considered probable when the amount can be measured reliably and the charity has been notified of the executor's intention to make a distribution. Where legacies have been notified to the charity, or the charity is aware of the granting of probate, and the criteria for income recognition have not been met, then the legacy is treated as a contingent asset and disclosed if material.

Income received in advance of provision of a service is deferred until criteria for income recognition are met.

### d) Donated services and facilities

Donated professional services and donated facilities are recognised as income when the charity has control over the item, any conditions associated with the donated item have been met, the receipt of economic benefit from the use by the charity of the item, is probable and the economic benefit can be measured reliably. In accordance with the Charities SORP (FRS 102), general volunteer time is not recognised.

On receipt, donated professional services and donated facilities are recognised on the basis of the value of the gift to the charity which is the amount the charity would have been willing to pay to obtain services or facilities of equivalent economic benefit on the open market; a corresponding amount is then recognised in expenditure in the period of receipt.

**e) Interest receivable**

Interest on funds held on deposit is included when receivable and the amount can be measured reliably by the charity: this is normally upon notification of the interest paid or payable by the bank.

**f) Funds accounting**

Unrestricted funds are available to spend on activities that further any of the purposes of the charity. Designated funds are unrestricted funds of the charity which the trustees have decided at their discretion to set aside to use for a specific purpose. Restricted funds are donations which the donor has specified are to be solely used for particular areas of the charity's work or for specific projects being undertaken by the charity.

**g) Expenditure and irrecoverable VAT**

Expenditure is recognised once there is a legal or constructive obligation to make a payment to a third party, it is probable that settlement will be required and the amount of the obligation can be measured reliably.

Irrecoverable VAT is charged as a cost against the activity for which the expenditure was incurred.

**h) Allocation of support and governance costs**

Support costs are those functions that assist the work of the charity but do not directly undertake charitable activities. Governance costs are the costs associated with the governance arrangements of the charity, including the costs of complying with constitutional and statutory requirements and any costs associated with the strategic management of the charity's activities. These costs have been allocated between cost of raising funds and expenditure on charitable activities based as follows:

| | **2024** | 2023 |
|---|---|---|
| Raising funds | **0.0%** | 0.0% |
| Charitable activities | **100.0%** | 100.0% |

**i) Debtors**

Trade and other debtors are recognised at the settlement amount due after any trade discount offered. Prepayments are valued at the amount prepaid net of any trade discounts due.

**j) Cash at bank and in hand**

Cash at bank and cash in hand includes cash and short term highly liquid investments with a short maturity of three months or less from the date of acquisition or opening of the deposit or similar account.

**k) Creditors**

Creditors and provisions are recognised where the charity has a present obligation resulting from a past event that will probably result in the transfer of funds to a third party and the amount due to settle the obligation can be measured or estimated reliably. Creditors and provisions are normally recognised at their settlement amount after allowing for any trade discounts due.

**l) Financial instruments**

The trust only has financial assets and financial liabilities of a kind that qualify as basic financial instruments. Basic financial instruments are initially recognised at transaction value and subsequently measured at their settlement value with the exception of bank loans which are subsequently recognised at amortised cost using the effective interest method.

**m) Foreign currency transactions**

Transactions in foreign currencies are translated at rates prevailing at the date of the transaction. Balances denominated in foreign currencies are translated at the rate of exchange prevailing at the year end.

**n) Accounting estimates and key judgements**

In the application of the charity's accounting policies, the trustees are required to make judgements, estimates and assumptions about the carrying values of assets and liabilities that are not readily apparent from other sources. The estimates and underlying assumptions are based on historical experience and other factors that are considered to be relevant. Actual results may differ from these estimates.

The estimates and underlying assumptions are reviewed on an ongoing basis. Revisions to accounting estimates are recognised in the period in which the estimate is revised if the revision affects only that period, or in the period of the revision and future periods if the revision affects both current and future periods.

## 2. Prior period comparatives: statement of financial activities

| | Restricted £ | Unrestricted £ | 2023 Total £ |
|---|---|---|---|
| **Income from:** | | | |
| Donations and legacies | - | 3,483 | 3,483 |
| Charitable activities | 17,922 | - | 17,922 |
| **Total income** | 17,922 | 3,483 | 21,405 |
| **Expenditure on:** | | | |
| Raising funds | - | - | - |
| Charitable activities | 10,940 | 1,365 | 12,305 |
| **Total expenditure** | 10,940 | 1,365 | 12,305 |
| **Net income / (expenditure)** | 6,982 | 2,118 | 9,100 |

## 3. Income from donations and legacies

| | Restricted £ | Unrestricted £ | **2024 Total £** |
|---|---|---|---|
| Donations | - | 5,692 | **5,692** |
| Grants | - | 750 | **750** |
| **Total income from donations and legacies** | - | 6,442 | **6,442** |

**Prior period comparative:**

| | Restricted £ | Unrestricted £ | 2023 Total £ |
|---|---|---|---|
| Donations | - | 3,483 | 3,483 |
| **Total income from donations and legacies** | - | 3,483 | 3,483 |

## 4. Income from charitable activities

| | Restricted £ | Unrestricted £ | **2024 Total £** |
|---|---|---|---|
| Grants | 87,245 | - | **87,245** |
| **Total income from charitable activities** | 87,245 | - | **87,245** |

**Prior period comparative:**

| | Restricted £ | Unrestricted £ | 2023 Total £ |
|---|---|---|---|
| Grants | 17,922 | - | 17,922 |
| **Total income from charitable activities** | 17,922 | - | 17,922 |

## 5. Government grants

The charity received no government grants in the period.

## 6. Total expenditure

| | Raising funds £ | Charitable activities £ | Support and governance costs £ | **2024 Total £** | Raising funds £ | Charitable activities £ | Support and governance costs £ | 2023 Total £ |
|---|---|---|---|---|---|---|---|---|
| Research | - | 7,871 | - | **7,871** | - | 8,135 | - | 8,135 |
| Counselling | - | 7,654 | - | **7,654** | - | 1,280 | - | 1,280 |
| App development costs | - | 623 | - | **623** | - | - | - | - |
| Translation services | - | - | - | **-** | - | 1,096 | - | 1,096 |
| Consultancy | - | - | - | **-** | - | 176 | - | 176 |
| Accountancy | - | - | 1,260 | **1,260** | - | - | - | - |
| Online donation platform fees | 90 | - | - | **90** | - | - | - | - |
| Insurance | - | - | 299 | **299** | - | - | - | - |
| Legal fees | - | - | 35 | **35** | - | - | 35 | 35 |
| Printing, postage and stationery | - | - | 80 | **80** | - | - | 23 | 23 |
| IT software and consumables | - | - | 4 | **4** | - | - | 98 | 98 |
| Subscriptions | - | - | 131 | **131** | - | - | 136 | 136 |
| Travel | - | - | 1,709 | **1,709** | - | - | 1,326 | 1,326 |
| **Sub-total** | 90 | 16,148 | 3,518 | **19,756** | - | 10,687 | 1,618 | 12,305 |
| Allocation of support and governance costs | - | 3,518 | (3,518) | - | | 1,618 | (1,618) | - |
| **Total expenditure** | **90** | **19,666** | **-** | **19,756** | **-** | **12,305** | **-** | 12,305 |

Total governance costs were £1,260 (2023: £nil)

## 7. Net movement in funds

This is stated after charging:

| | **2024** | 2023 |
|---|---|---|
| | **£** | £ |
| Trustees' remuneration | **Nil** | Nil |
| Trustees' reimbursed expenses | **1,655** | 1,207 |
| Independent examiner's remuneration: | | |
| ▪ Independent examiner's fee | **1,260** | - |

One trustee was (2023: one trustee) was reimbursed for travel expenses.

## 8. Taxation

The charity is exempt from corporation tax as all its income is charitable and is applied for charitable purposes.

## 9. Creditors: amounts falling due within 1 year

| | **2024** | 2023 |
|---|---|---|
| | **£** | £ |
| Accruals | **1,260** | - |
| | **1,260** | - |

## 10. Analysis of net assets between funds

| | Restricted funds | Designated funds | General funds | **Total funds** |
|---|---|---|---|---|
| | £ | £ | £ | **£** |
| Current assets | 79,941 | 6,000 | 8,346 | **94,287** |
| Current liabilities | - | - | (1,260) | **(1,260)** |
| **Net assets at 30 November 2024** | **79,941** | **6,000** | **7,086** | **93,027** |

| **Prior year comparative** | Restricted funds | Designated funds | General funds | Total funds |
|---|---|---|---|---|
| | £ | £ | £ | £ |
| Current assets | 10,982 | - | 8,114 | 19,096 |
| Current liabilities | - | - | - | - |
| **Net assets at 30 November 2023** | 10,982 | **-** | 8,114 | 19,096 |

## 11. Movements in funds

| | At 1 December 2023 £ | Income £ | Expenditure £ | Transfers between £ | **At 30 November 2024 £** |
|---|---|---|---|---|---|
| **Restricted funds** | | | | | |
| Chan Zuckerberg Initiative DAF | - | 77,423 | (1,883) | - | **75,540** |
| GlobalGiving | 1,886 | 3,322 | (3,307) | - | **1,901** |
| Postcode Local Trust | 8,531 | - | (8,531) | - | **-** |
| The Renishaw Charities Committee | - | 500 | - | - | **500** |
| The Stanley Grundy Foundation | - | - | - | - | **-** |
| Souter Charitable Trust | - | 2,000 | - | - | **2,000** |
| The Waterloo Foundation | 565 | 4,000 | (4,565) | - | **-** |
| **Total restricted funds** | 10,982 | 87,245 | (18,286) | - | **79,941** |
| **Unrestricted funds** | | | | | |
| *Designated funds:* | | | | | |
| Registry project | - | - | - | 4,000 | **4,000** |
| Speech and language project | - | - | - | 2,000 | **2,000** |
| *Total designated funds* | - | - | - | 6,000 | **6,000** |
| General funds | 8,114 | 6,442 | (1,470) | (6,000) | **7,086** |
| **Total unrestricted funds** | 8,114 | 6,442 | (1,470) | - | **13,086** |
| **Total funds** | 19,096 | 93,687 | (19,756) | - | **93,027** |

**Purposes of restricted funds**

| | |
|---|---|
| Chan Zuckerberg Initiative DAF | An advised fund of Silicon Valley Community Foundation, over a five-year period, is supporting capacity building of our patient-led rare disease organisation, the development of a prioritised research agenda, convening our community, and accelerating collaborative research in our area of scientific focus. |
| GlobalGiving | Donors giving via our GlobalGiving (a US 501(c)(3) intermediary organisation that facilitates tax-effective donations from U.S. donors to U.K. charities) project page, specifically supported the running of our worldwide CACNA1C patient registry designed to obtain insights to better characterise CACNA1C, its presentation, management and treatment. |
| Postcode Local Trust | A grant-giving charity funded entirely by players of People's Postcode Lottery, supported the continued provision of our 'Mind the Gap' Counselling Service for our CACNA1C community. |

**11. Movements in funds (continued)**

| | |
|---|---|
| The Renishaw Charities Committee | Contributed towards a funding goal to support breakthrough speech and language research for young people affected by CACNA1C-related disorders. |
| The Stanley Grundy Foundation | Enabled our conference to be inclusive, accessible and global through a translation service. |
| Souter Charitable Trust | Contributed towards a funding goal to support breakthrough speech and language research for young people affected by CACNA1C-related disorders. |
| The Waterloo Foundation | Concluded its three year support of the CACNA1C Community Registry, enabling meaningful change for our existing and future CACNA1C community. |

**Purposes of designated funds**

| | |
|---|---|
| Registry project | The CACNA1C Community Registry (CCR) enables meaningful change for our existing and future CACNA1C community - the registry collects real-world data to obtain insights to better characterise CACNA1C, its presentation, management and treatment. Funds paid were for the annual platform fee. |
| Speech and language project | The Speech and Language Research Project delivers inclusive, globally accessible research to support families and clinicians, inform clinical trials, and advocate widespread sharing to improve diagnosis, treatment, and outcomes for individuals with CACNA1C rare variants. |

| **Prior year comparative** | At 1 December 2022 £ | Income £ | Expenditure £ | Transfers between £ | At 30 November 2023 £ |
|---|---|---|---|---|---|
| **Restricted funds** | | | | | |
| GlobalGiving | - | 1,886 | - | - | 1,886 |
| Postcode Local Trust | - | 9,636 | (1,105) | - | 8,531 |
| The Renishaw Charities Committee | - | 500 | (500) | - | - |
| The Stanley Grundy Foundation | - | 1,200 | (1,200) | - | - |
| Souter Charitable Trust | 4,000 | - | (4,000) | - | - |
| The Waterloo Foundation | - | 4,700 | (4,135) | - | 565 |
| **Total restricted funds** | 4,000 | 17,922 | (10,940) | - | 10,982 |
| **Unrestricted funds** | | | | | |
| General funds | 5,996 | 3,483 | (1,365) | - | 8,114 |
| **Total unrestricted funds** | 5,996 | 3,483 | (1,365) | - | 8,114 |
| **Total funds** | 9,996 | 21,405 | (12,305) | - | 19,096 |

**12. Related party transactions**

There were no related party transactions in the current or prior period.

**TIMOTHY SYNDROME ALLIANCE (TSA)**

England & Wales - Charity number 1185523

# Accounts

# TIMOTHY SYNDROME ALLIANCE (TSA)

Timothy Syndrome Alliance

## ANNUAL REPORT

### FOR FINANCIAL PERIOD
### 1 DECEMBER 2022 TO 30 NOVEMBER 2023

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# WELCOME

Timothy Syndrome Alliance (TSA) is a Registered Charity in England (Charity number: 1185523) run entirely by parents and volunteers.

## Our Vision:

Our vision is a world where shared knowledge and understanding lead to a cure for everyone with a CACNA1C genetic variant.

## Our Mission:

Our mission is to improve the diagnosis, treatment and care of individuals worldwide with CACNA1C-related disorders including Timothy Syndrome and LongQT8, and to support the families and carers of those diagnosed.

## How we work

In order to achieve our mission our focus is on five interdependent areas of activity – raising awareness, improving diagnosis treatment and care, supporting the global community, providing information and advice, and driving research and clinical development.

By working together and collaborating globally, we can harness greater strength. Using a method of sustainable growth, our goal is to build and support our global community.

Our core values and beliefs combine to form a solid foundation for the way we approach everything we do. We are determined, supportive, empowering and we are a community.

# CACNA1C

## What is CACNA1C?

CACNA1C is a gene that provides instructions for making a protein that forms part of a calcium channel in cells throughout the body. This protein manages the movement of calcium in and out of the cell (crucial for many cells' functions). Changes to the gene can cause changes to the protein and its ability to manage calcium movement, making it work more, less, or not at all.

## What is a CACNA1C-related disorder (CRD)?

CACNA1C variants have been identified in a broad spectrum of both cardiac and neurodevelopmental disorders including typical and atypical syndromic Timothy Syndrome (TS), structural heart disease with Long QT Syndrome (LQTS), isolated long or short QTS, and isolated neurologic symptoms. This is now referred to as the CACNA1C-related disorder (CRD) spectrum that encompasses a range of clinical features caused by variants predicted to both increase and decrease channel function.

The most common symptoms include abnormal heart function, irregular heartbeat, abnormal heart structure, developmental delay, incoordination, hypotonia, autism spectrum disorder (autistic features), seizures, and attention-deficit/hyperactivity disorder.

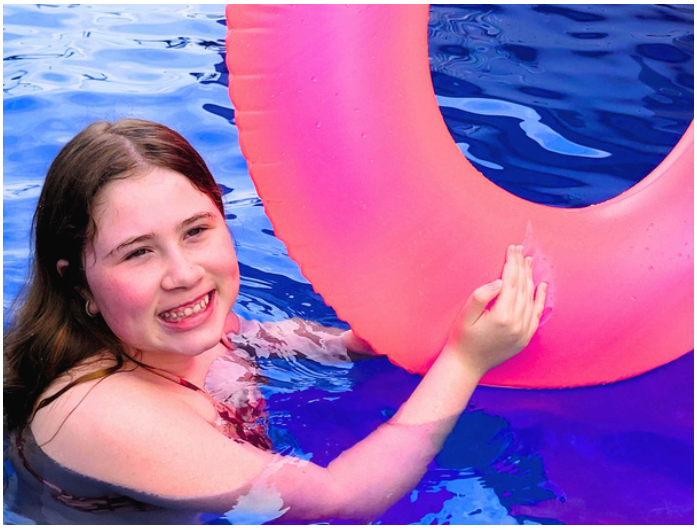
Other symptoms include low blood sugar levels (hypoglycaemia), immunodeficiencies, endocrinological dysfunction, gastrointestinal concerns, an unusually low body temperature (hypothermia), facial anomalies, syndactyly (joined fingers or toes), mild dental, skin, eye, and hair anomalies.

## What is Timothy Syndrome?

Timothy Syndrome (TS) is a sub-diagnosis of just 1 genetic CACNA1C variant with mixed neurologic and cardiac symptoms. There are two types of TS: TS1 (exon 8A) and TS2 (exon 8).

## What is LongQT Syndrome (LQTS) and Short QT Syndrome (SQTS)?

Long QT and Short QT are heart conditions that affect the electrical activity of the heart, causing it to take longer or shorter than normal to recharge between beats. This can lead to irregular heartbeats, which in some cases may cause fainting, seizures, or sudden death. LQTS associated with CACNA1C is known as LQTS 8 or LongQT8.



## How common are CRDs?

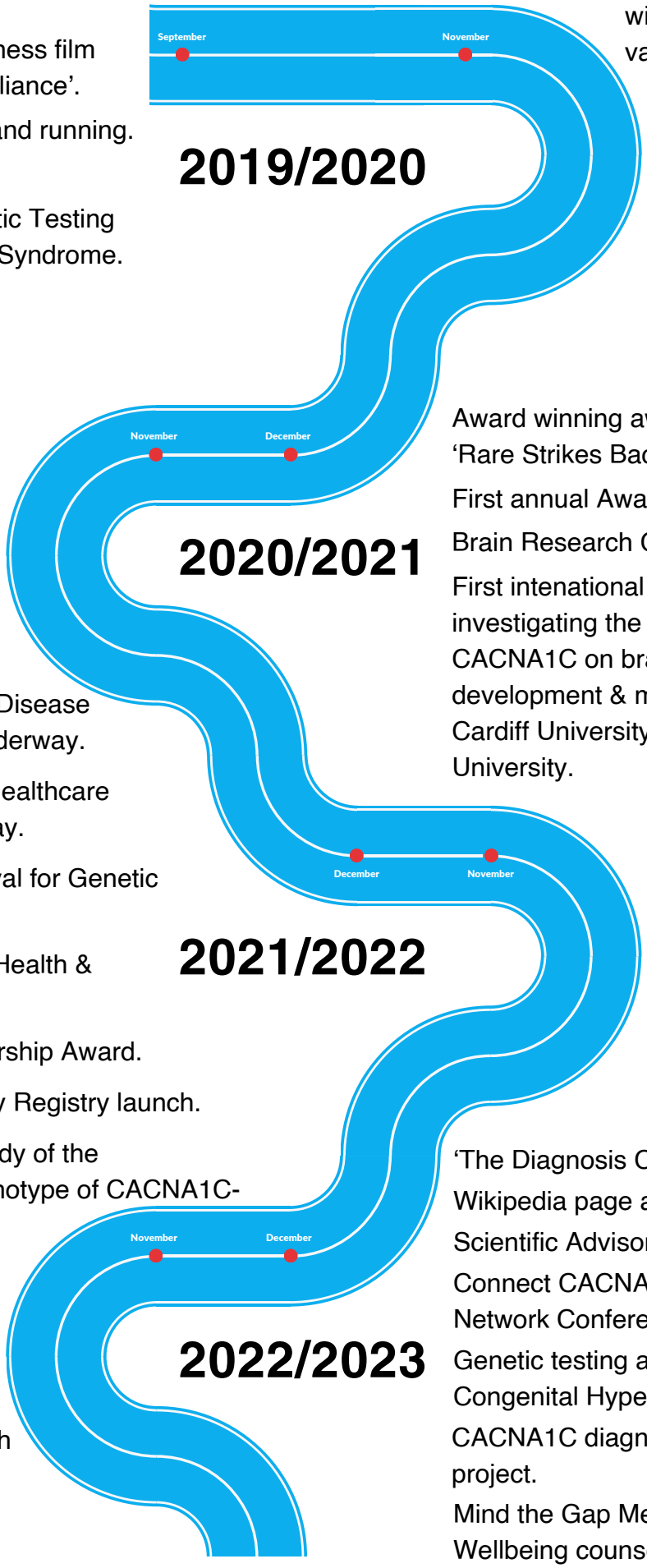
CRDs are rare and their prevalence is unknown.

There are <100 cases of TS diagnosed worldwide.

Prevalence is unknown due to the rarity and recent identification of CRDs.

# IMPACT ROADMAP

43 known (living) individuals with CACNA1C variants in the world.




Award winning awareness film 'Timothy Syndrome Alliance'.

Website built and up and running.

Family Day.

Preimplantation Genetic Testing approved for Timothy Syndrome.

Award winning awareness film 'Rare Strikes Back'.

First annual Awareness Day.

Brain Research Conference.

First intenational study investigating the effects of CACNA1C on brain development & mental health Cardiff University & Stanford University.

Film production 'Rare Disease Research Journey' underway.

Interactive Guide for Healthcare Professionals underway.

Genetic testing approval for Genetic Epilepsy.

Mind the Gap Mental Health & Wellbeing counselling.

Best Research Partnership Award.

CACNA1C Community Registry launch.

A Cross-Sectional Study of the Neuropsychiatric Phenotype of CACNA1C-Related Disorder, Levy et al published.

'The Diagnosis Challenge' film.

Wikipedia page approved.

Scientific Advisory Board formed.

Connect CACNA1C Global Network Conference.

Genetic testing approval for Congenital Hyperinsulinism.

CACNA1C diagnosis in the UK project.

Mind the Gap Mental Health & Wellbeing counselling.

Approx 160 known families/individuals with CACNA1C variants in the global CACNA1C Support Group

# ACHIEVEMENTS AND PERFORMANCE

## Raising Awareness

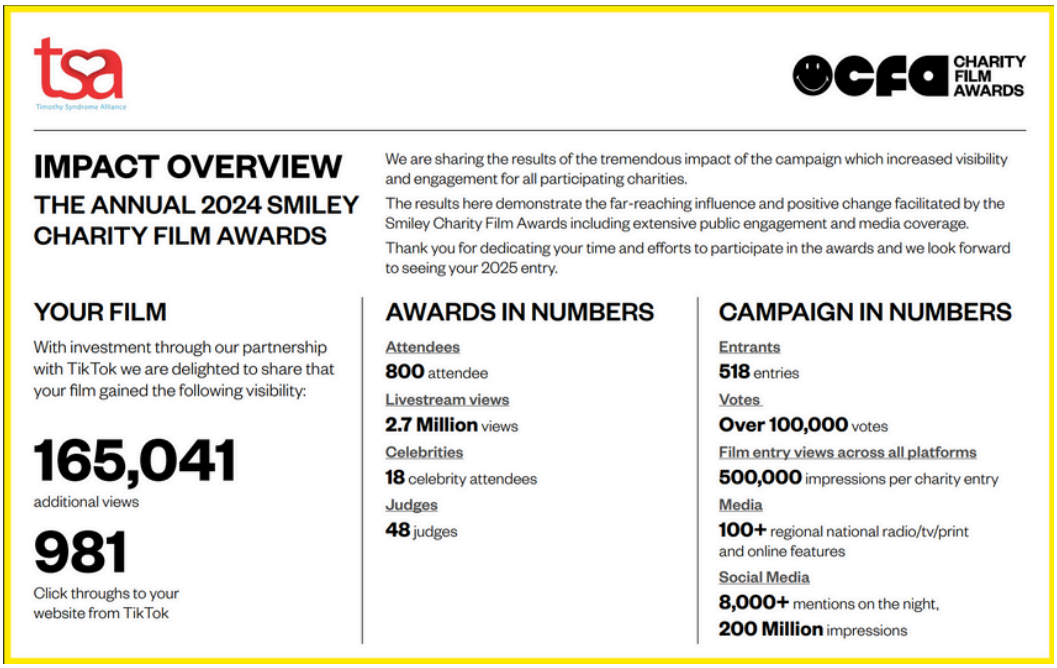
Out of more than 780 entries received, our film Rare Strikes Back earned its place among the 93 films selected for the World Health Organization (WHO) 4th Health for All Film Festival 2023. WHO staff from all over the world participated in this preselection.
Further broadening our reach, Rare Strikes Back made an appearance at the Health in Focus Film Festival, hosted by the School of Public Health at Boston University. This event featured our film and included a virtual Q&A session, providing an opportunity for meaningful dialogue on the issues addressed in the film.

The collaborative effort behind The Rare Disease Research Journey highlights our commitment to advancing understanding and awareness. This film continues to evolve, a product of the ongoing partnership between the Neuroscience and Mental Health Innovation Institute (NMHII) University of Cardiff and TSA. Significant strides have been made with the interviews conducted with families and researchers such that we have been able to share film shorts on our social media platforms to reach diverse audiences, particularly on CACNA1C Awareness Day.

Simultaneously, considerable efforts have been devoted to our pathway-focused Educational CACNA1C Interactive Guide for Healthcare Professionals. We extend our heartfelt appreciation to OPEN Health, a leading global healthcare communications agency with extensive scientific expertise, for their invaluable contribution of 200 hours of support. As filming for case studies nears completion, we remain steadfast in our commitment to accuracy, delaying the guide's launch to ensure alignment with ongoing high-level discussions regarding CACNA1C nomenclature.

For Rare Disease Day on the 28th of February (29th in a leap year), we created a short film titled 'The Diagnosis Challenge'. Using a montage of interview snippets, the film conveys families' frustrating journeys, through the naming of healthcare professionals they've seen from first noticing that something isn't right and going to the doctor to actually receiving a diagnosis.
It is a process that can take many years, with seemingly endless tests along the way, a journey known as the 'Diagnostic Odyssey'. Tackling this challenge is crucial to provide families with the necessary knowledge and resources. It is equally as important to empower primary healthcare professionals to be able to identify and consider rare diseases

# ACHIEVEMENTS AND PERFORMANCE



tsa Timothy Syndrome Alliance

CFA CHARITY FILM AWARDS

## IMPACT OVERVIEW

### THE ANNUAL 2024 SMILEY CHARITY FILM AWARDS

We are sharing the results of the tremendous impact of the campaign which increased visibility and engagement for all participating charities.

The results here demonstrate the far-reaching influence and positive change facilitated by the Smiley Charity Film Awards including extensive public engagement and media coverage.

Thank you for dedicating your time and efforts to participate in the awards and we look forward to seeing your 2025 entry.

### YOUR FILM

With investment through our partnership with TikTok we are delighted to share that your film gained the following visibility:

**165,041**
additional views

**981**
Click throughs to your website from TikTok

### AWARDS IN NUMBERS

Attendees
**800** attendee

Livestream views
**2.7 Million** views

Celebrities
**18** celebrity attendees

Judges
**48** judges

### CAMPAIGN IN NUMBERS

Entrants
**518** entries

Votes
**Over 100,000** votes

Film entry views across all platforms
**500,000** impressions per charity entry

Media
**100+** regional national radio/tv/print and online features

Social Media
**8,000+** mentions on the night,
**200 Million** impressions

when making a diagnosis. The film was entered in the Smiley Charity Film Awards 2024 and widely shared.
In addition to our internal productions, we have participated in two external film projects, further expanding our reach and impact.
Firstly, we had the privilege of collaborating on "CEOs in Unusual Places", a short film produced at the Neuroscience and Mental Health Innovation Institute (NMHII) at Cardiff University by the Smiley Movement team, the same team behind The Charity Film Awards, an accolade we were honoured to receive last year, winning the Gold award. Through this partnership, we continue to leverage the power of storytelling.
Our friends at Media Trust organised a film project to highlight the invaluable contributions of volunteers. Our website volunteer with whom we were matched through Media Trust and who has been with us on this journey since 2020, was featured in the film to accentuate the profound impact of their efforts on micro charities like ours.

Continuing to use our social media platforms to raise awareness, build lasting relationships and inspire support for our mission we joined the TikTok platform as well running some focused campaigns. Notably during the month of February leading up to Rare Disease Day our social media channels underwent an informative and engaging takeover thanks to biology student Gavriella who is based in Atlanta, Georgia, who aims to become a Genetic Counsellor.
Our Awareness Day on 1st October focused on support in its many forms complete with a takeover of Rare Revolution Magazine social media channels in the lead-up to the big day.

# ACHIEVEMENTS AND PERFORMANCE

The best way to raise awareness and gather interest is to spread the word so we are delighted to see that our social media platforms and website are doing just that. Compared to our previous year we can evidence growth in all areas.

Organic traffic (from search engine results) to our website is more likely to be from users who are new to the diagnosis, looking for community or looking to find out more information about CACNA1C. For direct traffic (typing our website's URL directly) these users typically have a specific purpose and prior knowledge of our charity, driving them to access the website directly for support, information, and community resources. Additional signposting to our website has been successful through our collaborations, press and blog articles, plus partnerships with ERN-GUARD Heart, Neurological Alliance, EURORDIS, Rare Diseases International, and Global Genes to name a few.

It is heartening to see that people are leaving their social networks and social media platforms (16.3%) to directly visit our informative website and learn more about CACNA1C. Everything we post uses the same signposts #CACNA1C #TimothySyndrome #LongQT8.

## Organic growth of our social media platforms and website

| | | | |
|---|---|---|---|
| | ↑32.4% Page reach | ↑31.3% Profile visits | ↑43.1% New followers |
| | ↑155.4% Page reach | ↑87.7% Profile visits | ↑28% New followers |
| | | | ↑65.9% New followers |
| | ↑115.2% Users | ↑96.8% Views | ↑114.3% New users |

ALL DATA REPRESENTS DATE RANGE 1ST DECEMBER 2022 TO 30 NOVEMBER 2023

## #CACNA1C Awareness Day

↑2.2K% Page reach

↑2.2K% Page reach

DATA BASED ON TSA SOCIAL MEDIA POSTS MADE ON 1ST OCTOBER 2023

Reach visits continue to increase post event

# ACHIEVEMENTS AND PERFORMANCE

The Student Voice Prize was again on our radar this year. It is an annual international essay competition raising the profile of rare diseases within the medical field, particularly with medical students, nurses and scientists who may not come across rare diseases in their training. Both Beacon for Rare Diseases and Medics4RareDiseases host the competition together and the winner gets published in The Orphanet Journal of Rare Diseases. Our students didn't win but we are thankful to both Hussain and Diana for submitting their essays and for their increased awareness of rare diseases in particular CACNA1C.
Finally, there have also been plenty of in-person and online opportunities to raise awareness and network including the Beacon London Rare Disease Showcase, RAREsummit23, Advanced Therapies Conference, EJPRD Networking Symposium, Gene People Leadership Symposium, Rare Disease Research Network and EURORDIS Alumni training.

## Improving diagnosis, treatment and care

In January 2023 our application was approved for both Timothy Syndrome and CACNA1C-related disorders to be included as a green (diagnostic evidence level) gene on the Congenital hyperinsulinism panel R144 within the NHS National Genomic Test Directory (PanelApp). This sits alongside the Epilepsy syndromes panel we advocated for last year. These additions widen the symptom net for CACNA1C to be identified on an individual's diagnostic pathway.
As PanelApp is an open platform and knowledge base of evidence for gene-disease associations used by the wider global scientific community it is hoped these gene panel additions may influence panels used in other countries.

We continue to be members of ePAG ERN GUARD-Heart, EURORDIS, Neurological Alliance, British Heart Rhythm Society, Rare Diseases International, Genetic Alliance and Gene People, offering us invaluable access to expertise, resources, and networking opportunities, whilst empowering us to advocate effectively at both national and European levels.

# ACHIEVEMENTS AND PERFORMANCE

This year we have worked with two global genetic testing companies, GeneDx and Invitae, to make the post-diagnostic journey easier for individuals who receive a positive CACNA1C result. Collaborating with these companies ensures patients receive trustworthy information and support resources including signposting to TSA, our community and the CACNA1C Community Registry.

Advocacy Project

As a patient advocacy organisation, we have observed a notable lack of growth in the number of individuals identified with a CACNA1C variant in the UK, compared to rapid growth globally. This year we began to question the assumption that it is because we are ultra-rare. We launched a project to investigate if there were any barriers to reporting rare diseases in the UK. Barriers hinder global diagnosis, research, development of treatments and therapeutics, recognition and support mechanisms, particularly concerning ongoing healthcare. Obtaining more information about the prevalence and incidence of CACNA1C in the UK could also help identify gaps in diagnosis and signposting where we need to focus, which in turn would aid our global advocacy efforts.

We know that CACNA1C is currently included in several gene panels used to test various clinical indications. Some are delivered by the centralised Whole Genome Sequencing (WGS) service and others are testing with alternative technologies within the Genomic Laboratory Hubs (GLHs). The data generated from both testing pathways is analysed within the GLHs but the way pathogenic variants detected through that analysis are recorded is slightly different. GLHs will hold locally derived reported variant database but in addition for WGS there is a centralised variant database called the clinical variant ark.

At present, most of this data is not shared outside of the NHS Genomic Medical Service (GMS) nor is anonymous data on variants detected shared with an international open source database called ClinVar which helps support the diagnosis of other individuals with the same genomic variants. We therefore made a significant number of Freedom of Information (FOI) requests to understand the diagnostic pathways of CACNA1C in the UK and to see how this compared with the numbers on ClinVar for the rest of the world alongside those in our global CACNA1C Support Group. Our initial requests were made in England for the years 2021 and 2022, under the Freedom of Information Act 2000, which allows the public to access information held by public authorities.

# ACHIEVEMENTS AND PERFORMANCE

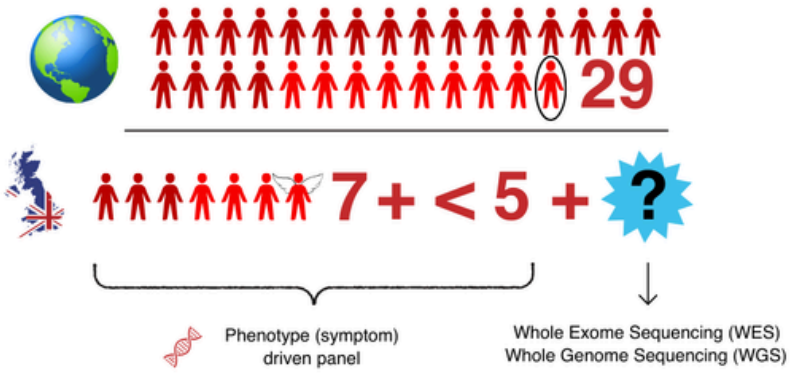
The infographic below summarises our FOI findings. In 2021 and 2022 there were 7 + < 5 individuals in England confirmed to have pathogenic or likely pathogenic (disease causing) CACNA1C variants.
TSA is only aware of two of these individuals; the individual represented with wings and the individual circled with the ring. The individual circled is the son of TSA Chair Sophie. He is the only CACNA1C individual to have been submitted by a GLH in England on ClinVar in 2021 and 2022 following a specific request from the family. The UK did not submit any of the remaining 28 individuals.

In 2023 we were unable to obtain the anonymised data from Genomics England. However, in April 2024 they confirmed there were no patients with pathogenic or likely pathogenic CACNA1C variants identified as a result of whole-genome sequencing across the three years (2021-2023).

## Are barriers to reporting hiding cases of Rare Diseases?

Knowing how many people are currently affected by a rare genetic disease (prevalence) can help us understand how often new cases are emerging (incidence). It also helps in allocating resources for research and developing treatments. Where the number of existing cases is small every new case can significantly impact the overall picture.

**How it works:** Illustrated are the number of people with a rare disease-causing CACNA1C change in their DNA sequence detected by genetic testing in 2021 and 2022. During this time period the global CACNA1C Support Group grew by 42 individuals.*




Likely pathogenic / Pathogenic (disease-causing)

My son. The only submission in ClinVar to have come from England (as result of personal request following reclassification). This is therefore a duplicate.

Child reclassified Likely pathogenic post-mortem from Variant of Uncertain Significance (specific yet uspecific result) known to tsa

FOI responses - Do not hold WES/WGS information.

NHS England, 125 NHS Trusts and Genomics England.

< 5 Less than 5 Freedom of Information Act 2000 anonymisation.

Global accessible genetic record database ClinVar.

* Handful on post-diagnostic odyssey from pre-2021.

# ACHIEVEMENTS AND PERFORMANCE

As part of this project, we are looking at CACNA1C Variants of Uncertain Significance (VUS). Variants of Uncertain Significance are variants detected during genetic sequencing, for which there is no or insufficient evidence either for or against pathogenicity - a VUS is both a specific yet also an unspecific result. Often this is because they have only been identified in a limited number of people (sometimes only one). This is a very common situation for ultra-rare diseases such as ours.
Due to low awareness, phenotypic variability, a lack of genotype-phenotype correlations for atypical variants, and no extant multicentric CACNA1C cohorts, clinical genetic testing results are not influencing clinical management, with many classified as VUS. Our project confirms this.
FOI findings so far confirm more than 96 individuals in England were found to have a CACNA1C variant classified as VUS between 2021 and 2023. It is standard practice in the UK and in many other countries not to inform individuals of VUS findings. These individuals are therefore also unlikely to have received cardiac or neuropsychiatric screening.

According to the ACMG (American College of Medical Genetics and Genomics) Guidelines - who produce internationally accepted guidelines for the interpretation of variants, adopted for UK laboratories by the ACGS (Association for Clinical Genomic Science) - a VUS should not be used in clinical decision-making. If a patient is identified to have a VUS, all clinical decisions should be based on personal and family history and not on the presence of the VUS. Re-analysis in the future may establish that the VUS either is or is not Pathogenic.

TSA advocates that all individuals found to have a CACNA1C gene change, even if classified as VUS, should receive cardiac and neuropsychiatric screening due to the multisystemic effects of CACNA1C. CACNA1C-related disorder is a syndromic cause of cardiac arrhythmia that also impacts neurodevelopment.[1]

It is clear there is much more work to be done to inform clinical and medical treatment. We will continue this project in 2024, incorporating CACNA1C diagnostic findings from Wales and Scotland.

1. Levy, Rebecca J.; Timothy, Katherine W.; Underwood, Jack F.G.; Hall, Jeremy; Bernstein, Jonathan A.; Pașca, Sergiu P. (January 2023). "A Cross-Sectional Study of the Neuropsychiatric Phenotype of CACNA1C-Related Disorder". Pediatric Neurology. 138: 101–106. doi:10.1016/j.pediatrneurol.2022.10.013. PMID 36436328

# ACHIEVEMENTS AND PERFORMANCE

## Supporting our global community

The diagnosis of a rare disease emotionally impacts all areas of life. Living with a rare disease is psychologically and emotionally demanding. Lengthy diagnostic odysseys, uncertain prognoses and treatment pathways, and fears about the future can impact physical and mental health.

The focus of care however is often just managing the physical symptoms. With Rareminds we are helping build the emotional resilience and wellbeing of our CACNA1C community through our 'Mind the Gap' workshops and individual /couples counselling delivered by qualified, specialist therapists and designed to address the key challenges in our rare journey.

raremínds
Mental Health for the Rare Disease Community

**"Connecting with families in the same journey has given us hope; we realise we're not alone."**

TSA also administrates an online private Facebook Support Group for individuals and families of CACNA1C-related disorders including Timothy Syndrome and LongQT8, offering 24/7 access to emotional and practical support and information via our community.
The benefits of this are huge. It enables:

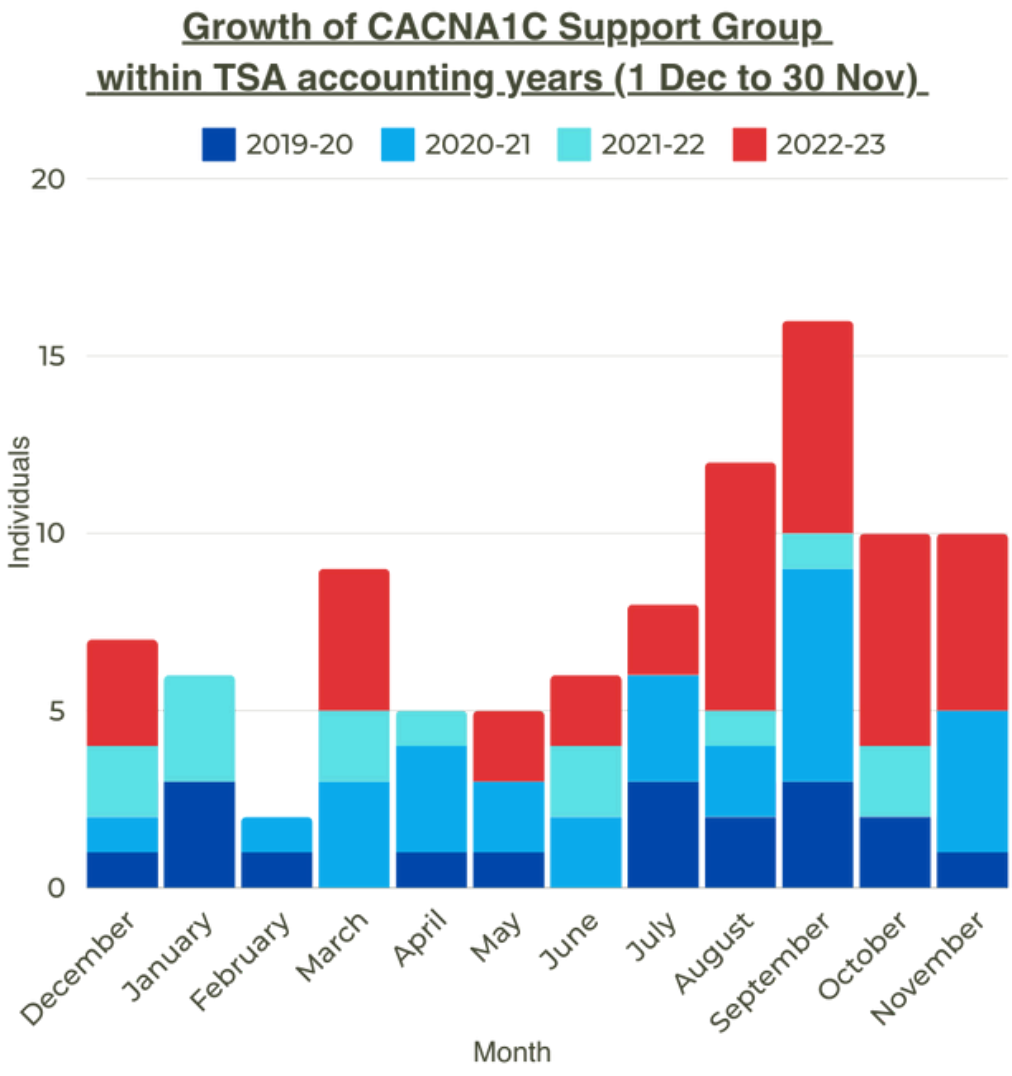
- meeting and befriending other people with the same rare disorder and similar experiences from across the world
- learning about CACNA1C
- giving and receiving emotional support
- having a place to speak openly about the impact of CACNA1C and one's thoughts and feelings
- learning coping skills
- feeling empowered and hopeful
- advocating to improve healthcare

**"Parent and support groups like the TSA are incredible because they give us support. The exchange of experiences between families is very important because even today, 8 years after the diagnosis, almost no doctor in Brazil has been able to help us because they have never heard of the CACNA1C mutation."**

# ACHIEVEMENTS AND PERFORMANCE

Many people find it comforting and helpful to talk to someone who has experienced the same things they are facing when they or their child have a health problem. Having a rare condition can often be extremely isolating due to the lack of people with the same condition. It can be just as challenging to be a parent to someone with a rare disease. Rare disease support groups are an important source of emotional and practical support. 'The use of such advocacy-based coping may help patients to foster a sense of empowerment, efficacy, and hope' (Ayme et al., 2008)

**“I think anyone new to the diagnosis should know there are people who understand a lot as well have their own experiences which gives you comfort and support even if you‘re not quite ready yet.”**




Note, this represents the net number of families/individuals with different CACNA1C variants joining the Support Group and NOT the number of individuals in which CACNA1C gene changes were identified.

# ACHIEVEMENTS AND PERFORMANCE

## Providing information and advice

At the beginning of the year, thanks to support from Healx the first Wikipedia page for CACNA1C-related disorders was approved creating:

- Visibility and Awareness: a dedicated page on Wikipedia increases visibility for our rare disease. It provides a platform where people can learn about CACNA1C, symptoms, research and available resources serving as a central hub where experts, patients, and advocates can contribute accurate and up-to-date details including research, and clinical trials.
- Educational Resource: Medical professionals, students, and caregivers can use the Wikipedia page as a quick reference as it provides concise information, reducing the need to search multiple sources.

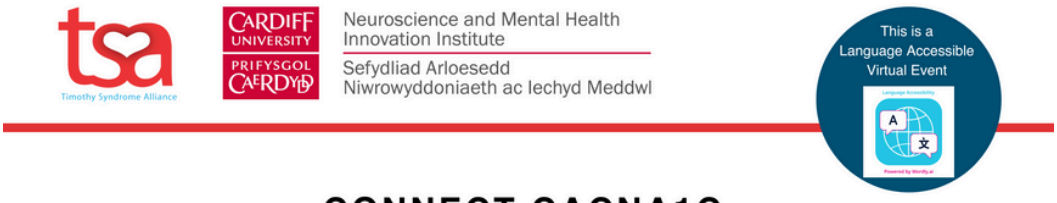
Pageviews since approval:874 Monthly average:73

In addition to the information available on our website and social media channels, TSA administers an online private Patient Advisory Board with 190 members of our global CACNA1C community. It is here TSA updates and works with our community on advocacy, ongoing research, collaborations and campaigns - in fact, anything of interest to our community relating to CACNA1C and our mission. Together we aim to build upon the progress made in previous years and work towards new actions to address the priorities of our community.

# ACHIEVEMENTS AND PERFORMANCE

## Driving research & clinical development

On 23 June 2023, we were thrilled to gather our global CACNA1C individuals, families, caregivers, researchers, scientists, healthcare professionals, advocates, and supporters, for our virtual language-accessible conference. By embracing this digital platform, we ensured that everyone, regardless of their geographic location, had the opportunity to join us.




We collectively shared current knowledge and ongoing studies, exchanged ideas, and fostered collaborations to help shape the future of CACNA1C research, and improve diagnosis and care.

Our programme featured presentations by members of our Scientific Advisory Board and guest speakers, all experts in their respective fields. In addition, we had two breakout discussion rooms and a dedicated Q&A session where speakers were available to address questions. Using the inclusive Translation app, participants engaged in real-time listening or reading along in their preferred language.

With 75 registrants and 48 attendees at any one time we were aware that not everyone could join us for the entire 4.5 hours. In anticipation of time constraints and varying time zones, we recorded the presentations to be available post-event.
All six presentations from the day are available via our website with language transcripts (Arabic, Brazilian Portuguese, Chinese, English, Finnish, French, German, Hindi, Italian, Norwegian, Polish, Russian, Spanish, Turkish and Ukrainian). While we cannot guarantee perfect translation, as that is not possible with AI, our approach in preparing these

# ACHIEVEMENTS AND PERFORMANCE

presentations has eliminated transcription errors that by definition contribute to ultimate translation errors.

We hope the conference for those attending left you feeling inspired and well-informed about the latest advancements in the field of CACNA1C, and will do the same for those yet to see the recordings. This conference was a product of collaboration and passion to understand CACNA1C.
A sincere thank you to all speakers and members of the Scientific Advisory Board who generously shared their latest knowledge and understanding of CACNA1C and to Cardiff University for hosting through their conference Zoom subscription.
To the CACNA1C families and individuals – you are not alone on this journey!

**TSA Scientific Advisory Board**

**Dr. Jack Underwood**
Wellcome Trust GW4-CAT Clinical Research Fellow, NMHII, Cardiff University

**Dr. Rebecca Levy**
Clinical Scholar, Neurology & Neurological Sciences. Postdoctoral Scholar, Neurology & Neurological Sciences, Stanford Medicine

**Dr. Gemma Wilkinson**
Research Associate, NMHII, Cardiff University

**Dr. Nicola Hall**
Postdoctoral Researcher, University of Oxford

**Dr. Anwar Baban**
Bambino Gesù Children Hospital and Research Institute, IRCCS, Rome

**Dr. Wilfried Haerty**
Group Leader of Evolutionary Genomics, Earlham Institute

**Prof Liz Tunbridge**
Director of Translational Neuroscience, Boehringer Ingelheim

The CACNA1C Community Registry (CCR), accessible worldwide, continues to increase in participants and at the end of this year had 59 individuals enrolled. This is a vitally important research tool in which all families and individuals with an identified CACNA1C gene change are encouraged to participate. The CACNA1C Community Registry has been designed with the input of clinical researchers to identify information and issues relevant to families and pertinent to developing translational research. People are unique genetically and even though everyone in our community has the same gene in common, not everyone has the same genetic variant. Genetic variants are not the same - they don't necessarily act in the same way and they might have different mechanisms in terms of how they are treated. As variants in CACNA1C are so rare clinicians may only see one or two individuals in their lifetime, and therefore gathering global data is vital to understanding the natural history and

# ACHIEVEMENTS AND PERFORMANCE

features of the condition. We are working with our SAB to analyse the Registry data and see how this can be published as research and used to inform clinical and medical treatment.

Preliminary findings from those who consented to participate in the CACNA1C Community Registry between June 10, 2022, and May 5, 2023 were presented at the Connect CACNA1C Global Network Conference and have been summarised on the poster (next page).

In November and April, we were successful in being selected, together with members of our SAB, to attend 'Collaborating for Change' Rare Neurology/CNS Partnering Events held at The Royal Society of Medicine, London. The "speed-date" style networking events build collaborations between patient groups, and pharmaceutical and biotech companies interested in finding treatments for rare diseases that affect the brain and nervous system.

As our community grows epilepsy and seizures are seemingly becoming a more common symptom. To understand more we are now part of the GW4 Epilepsy Community, which links researchers and clinicians aiming to improve research models, diagnosis and treatment of epilepsy. They are studying ion channel mutations, like CACNA1C that cause epilepsy using brain tissue from epileptic patients, genomics, electrophysiology, fly and computational modelling. PhD student Sophie, funded by Bristol University, will study the role of CACNA1C voltage-gated calcium channel signalling in epilepsy and Alzheimer's disease using fruit fly models in Dr James Hodge's lab. Epilepsy is the most common primary neurological disorder worldwide and is a co-morbidity of Alzheimer's but what is the connection? They wish to test genes like CACNA1C that might contribute to both.
TSA is now a patient and public involvement and engagement (PPIE) member of Bristol Neuroscience Research Hub in Neurodevelopment (ND). The Network supports strategic planning and networking across the University of Bristol, two Bristol NHS Trusts, GW4 and Industry partners through collaborative research, planning funding bids and events.

Continuing with epilepsy TSA are now part of UK Rare Epilepsies Together (UKRET) a network of patient support groups and charities representing all those impacted by rare and complex epilepsies across the UK.

# The impact of *CACNA1C* real-world data: *CACNA1C* Community Registry (CCR) design

Sophie Muir (1), Joshua Henderson (2)
(1) Timothy Syndrome Alliance (TSA), UK (2) Pulse Infoframe, London, Ontario, Canada

The *CACNA1C* Community Registry is a patient registry for all *CACNA1C* gene related conditions, managed by Timothy Syndrome Alliance (TSA) and powered by Pulse Infoframe. The purpose of the *CACNA1C* Community Registry is to obtain insights to better characterise *CACNA1C*-related disorders, including Timothy Syndrome and LongQT8, and their presentation, management and treatment.
The registry was launched in June 2022 and is available for worldwide participation. This decentralised registry is not tied to a site and enables anyone, anywhere in the world with a *CACNA1C*-related disorder to sign up for the registry and participate from their home.

## REGISTRY AIMS

- Allow researchers to study common aspects among the different conditions caused by variations in *CACNA1C*.
- Increase the visibility of *CACNA1C* so those navigating the many health concerns may be improved through research and clinical trials.
- Document how different variants present with different symptoms and outcomes.
- Assist researchers anywhere in the world interested in studying variations in this gene.

## ESTABLISHING *CACNA1C* COMMUNITY REGISTRY

TSA set out to create a patient registry to help increase the visibility of *CACNA1C*-related disorders and gain insights that will help facilitate research into this group of rare genetic disorders. The Pulse Infoframe platform follows a governance framework that allows data to be collected and housed from multiple different rare disease communities. As a result, researchers are enabled to study multiple conditions. These capabilities made Pulse Infoframe the ideal candidate to build the *CACNA1C* Community Registry. With this partnership, Pulse Infoframe and Timothy Syndrome Alliance hope to facilitate better research for the *CACNA1C* community.
Different variants on this same gene present a variety of outcomes. By collecting data on one platform, TSA and researchers can work with patients anywhere in the world which has proven to be critical when studying diseases with patient populations this small.

## PRELIMINARY FINDINGS

Results are based upon individuals with *CACNA1C*-related disorders (CRD) who consented to participate in the *CACNA1C* Community Registry between June 10, 2022, and May 5, 2023.
Through May 5, 2023, 43 individuals with CRD consented to participate in the registry, of which 32 completed forms that provided information on demographics, clinical characteristics, and symptoms.
Data presented here are based on these 32 participants.
As of June 2024 there are 73 participants in the *CACNA1C* Community Registry.

## CONCLUSION

Families living with a *CACNA1C* variation face many difficulties, including having to educate many healthcare professionals about the condition. They also have limited treatment options. Continued enrollment and participation in the *CACNA1C* registry will help those affected by a variation and researchers in this gene in many ways:

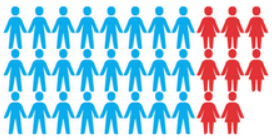
- Increase understanding of all *CACNA1C*-related disorders
- Encourage efficient and timely diagnosis
- Enable progress in research and clinical trials
- Facilitate the development of treatments for *CACNA1C*-related disorders

## Demographics

2 — Youngest participant
14 — Average age of participants
38 — Oldest participant

24 participants under the age of 18
8 participants over the age of 18

## Gender

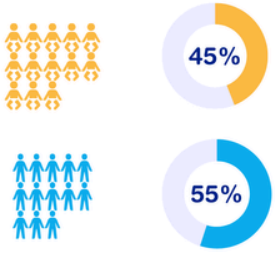


75% male 25% female

## Age at Diagnosis

| | |
|---|---|
| Mean | 9.7 |
| Median | 6.0 |
| IQR | 1.0, 13.0 |
| Min-Max | 0-37.0 |

## Age at First Symptom




## Overview of current symptoms.

| Symptom Categories * | Number of Participants reporting this symptom |
|---|---|
| Bowel problems (Gastrointestinal) | 53.1% |
| Dental | 34.4% |
| Dermatological/skin symptoms and abnormalities | 18.8% |
| ENT (issues of the ears, nose and throat) | 15.6% |
| Eyes (Ophthalmological) | 15.6% |
| Genitourinary | 9.4% |
| Heart symptoms (Cardiac-related symptoms or abnormalities) | 25% |
| Lungs and breathing problems (Laryngeal & Respiratory) | 46.9% |
| Multisystemic symptoms and abnormalities | 12.5% |
| Musculoskeletal (i.e. diseases of the muscles, ligaments, tendons, cartilage and bones) | 18.8% |
| Neurological (neuropsychiatric and neuropsychological) /Developmental, Behavioral or Mental Health | 46.9% |
| Neurological (motor/movement symptoms and abnormalities) | 34.4% |
| Neurological (seizures or epilepsy) | 25% |
| Neurological (sensory deficits/disturbances to sensation) | 28.1% |
| Neurology (diseases of the spinal cord) | 6.2% |
| Bone Skin Muscle (Orthopaedical) | 9.4% |
| Sensory conditions (i.e. diseases of the special senses) | 9.4% |
| Speech and language | 50% |
| Vascular or cardiovascular (together with heart problems) | 9.4% |

*Participants can present with multiple symptoms

sophie@timothyalliance.org

pulse infoframe

CACNA1C Community Registry
https://ccr.healthie.net/register

Registered Charity no: 1185523

SCAN ME

# ACHIEVEMENTS AND PERFORMANCE

We joined UKRET rare epilepsy members with our respective scientific advisors for a first-of-its-kind Patient Advisory Group Roundtable meeting with Genomics England (GEL) to discuss the GEL service offering and potential for data access for research to address the unmet needs of our patient communities.

In January our scientific poster (next page) was accepted at the London's Festival of Genomics & Biodata, the UK's largest annual life sciences event. In October it was part of RAREsummit23, an event that brings all stakeholders in rare diseases together as equals to drive patient group, researcher and industry partnering opportunities and our abstract has been accepted for the British Paediatric Neurology Association (BPNA) Conference in January.

In May we were honoured guests at the University of Cardiff launch of the innovation institute where we presented on our collaboration with the NMHII to date.

Supporting the mission of TSA Sophie (Chair of TSA) is a Working Group Member of the Rare Diseases Research Network (RDRN), a partnership project between CamRARE and Patient Led Research Hub, funded by the National Institute for Health and Social Care Research (NIHR) and sponsored by Cambridge University Hospitals NHS Foundation Trust. The project aims to support the rare disease community in building an online network of partnerships and resources to facilitate new patient-centred research opportunities.
Finally, the Voltage-Gated Calcium Channel Collective (VGCCC) has formed, a collaboration of the ten CACNA1 channel patient advocacy groups dedicated to raising awareness and promoting collaboration across the voltage-gated calcium ion channelopathies.

# "*Clinical importance* of *screening* and therapeutically addressing *neuropsychiatric* symptoms in *all* individuals with *CRD*."[1]

## *CACNA1C*-related disorders (CRD) & Timothy Syndrome Alliance (TSA)

### INTRODUCTION TO TSA

Timothy Syndrome Alliance (TSA) registered as a UK charity in 2019:

- Raises awareness of *CACNA1C*-related disorders including Timothy Syndrome and LongQT8 to improve the diagnosis, treatment and co-ordination of care
- Shares expertise and best practice - Scientific Advisory Board established January 2023
- Maintains a global *CACNA1C* Community Registry to improve the understanding of the epidemiology of *CACNA1C* to accelerate and support clinical and basic research
- Promotes research on treatment options and diagnostics
- Facilitates a global support network for individuals, families and carers of those diagnosed

### INTRODUCTION TO *CACNA1C*

*CACNA1C* is a gene that provides the code for a protein found in the walls of cells throughout the body. This protein manages the movement of calcium in and out of the cell, which is critical for many cells' function. Changes to the gene can affect the protein's structure and its ability to manage calcium movement, making it work more, less, or not at all. Variants in the gene are associated with *CACNA1C*-related disorders including Timothy Syndrome (pathognomonic p.G406R protein change)[2] and LongQT8 (non-syndromic cardiac-only).[3] As we identify more individuals with *CACNA1C* variants there is considerable variability in the phenotype (ranging from severely affected with serious cardiac events to apparently mildly affected with only a few features). These phenotypes are multi-system, but typically individuals present with autism spectrum disorder, developmental delay, prolonged cardiac QT interval, syndactyly/ hip dysplasia, hypotonia, epilepsy and hypoglycaemia.

Due to low awareness, phenotypic variability, a lack of genotype-phenotype correlations for atypical variants, and no extant multicentric *CACNA1C* cohorts, clinical genetic testing results are not influencing clinical management, with many classified as Variants of Uncertain Significance (VUS).

It is now recognised that *CACNA1C* variants result in a spectrum of phenotypes[4], from neurodevelopmental through cardiac and musculoskeletal. *CACNA1C* studies have highlighted substantial advances in our understanding of *CACNA1C*. TSA and the *CACNA1C* community have been collaborating on research with NMHII, Cardiff University, University of Oxford and Stanford University for the past 3 years.

### *CACNA1C* COMMUNITY REGISTRY

This registry went live June 2022 and collects information from *CACNA1C* individuals and caregivers worldwide to serve as a research platform of real-world data.
Comprehensive multisystemic characteristics and symptomology data including variant, age at diagnosis plus full demographics data are collected upon enrollment and yearly thereafter.

## Phenotypes include Epilepsy[5]/ Seizures...

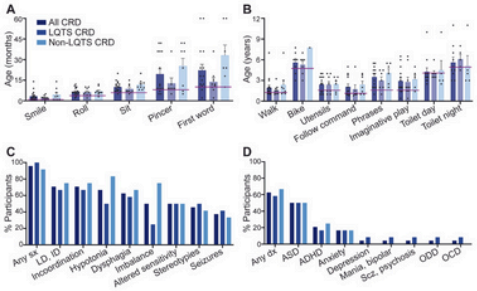
Caregiver-reported survey-based data (TSA Nov 2022) representing n=18; 17 CRD, 1 TS and 1 LQT8 individuals from our *CACNA1C* community (global support network comprising ~120 individuals with identified CRD in which n=19 are known to have presented with seizures/epilepsy - in some cases this may be just one occasion). Final survey awaiting translation.

- Typical absence (very brief lapse in awareness, sometimes with staring)
- Tonic (body, arms, or legs suddenly stiff or tense)
- Automatisms (such as lip smacking, finger rubbing, chewing)
- Clonic (sustained, rhythmic jerking of part or the whole body)
- Myoclonic (brief, shock-like jerks)
- Infantile spasms
- Atypical absence (some/no lapse in awareness, sometimes with staring. Individual may be able to respond a bit)
- Behaviour arrest (movement stops, sometimes called a freeze or pause)
- Eyelid myoclonia (rapid blinking or jerks of one or both eyelids, sometimes with eyeball movements)
- Cognitive (such as impaired language, confusion, feeling of deja vu, illusions, or hallucinations)
- Autonomic (such as increased heart rate or blood pressure, sweating, facial flushing)
- Emotional (such as sudden fear or joy)
- Atonic also known as drop (sudden loss of muscle tone causing body to go limp and fall down)
- Restless leg syndrome (RLS) or the urge to move the legs
- Hyperkinetic (such as thrashing legs, pedaling, or rocking back and forth)
- Sensory (such as tingling or numbness, visual symptoms, smells, sounds)

## ...developmental delay, incoordination, hypotonia, autism spectrum disorder (autistic features) and attention deficit hyperactivity disorder with and without prolonged QT.

### PHENOTYPE

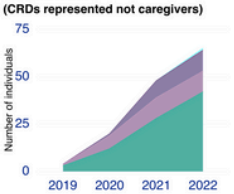
**Developmental, neurologic, and psychiatric symptoms are highly prevalent in CRD but do not differ by history of LQTS. Figure and data from Levy et al 2022.** [1]




(A) Mean age in months or (B) years at which participants achieved developmental milestones. All participants are depicted next to participants with and without LQTS. There were no significant differences between subgroups. Age at achievement in 50% of typical population denoted by purple lines derived from the Denver II Developmental Scale.42 Error bars show standard error of the mean. (C) Percent of participants who reported the most common neurologic symptoms. There were no significant differences between subgroups. (D) Percent of participants who reported the most common psychiatric diagnoses. There were no significant differences between subgroups. Abbreviations: ADHD: attention deficit hyperactivity disorder; ASD: autism spectrum disorder; CRD: *CACNA1C*-related disorder: dx: diagnosis; ID: intellectual disability; LD: learning disability; LQTS: long QT syndrome; OCD: obsessive compulsive disorder; ODD: oppositional defiant disorder; Scz: schizophrenia; sx: symptoms.

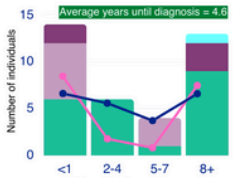
### COMMUNITY

**Cumulative yearly increase of individuals joining our *CACNA1C* Community (global support network) since registration of TSA as CIO on 27 September 2019 (CRDs represented not caregivers)**




### DIAGNOSIS

***CACNA1C* Community survey based data (TSA Aug 2022) indicating time to accurate diagnosis (survey completed by 34 individuals representing a total of 37 CRD individuals)**



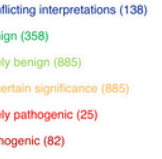

*CACNA1C*-related disorder  Timothy Syndrome  Long QT8  Short QT  Male  Female

Abbreviations: CIO: Charitable Incorporated Organisation.

### Common misdiagnoses reported by *CACNA1C* Community (TSA March 2022)

- Fragile X syndrome
- Angelman syndrome
- DiGeorge syndrome
- Cystic Fibrosis
- Coeliac disease
- Failure to thrive (FTT)
- Prader-Willi syndrome
- Ehlers-Danlos syndrome
- Glycogen storage disease
- Wolff-Parkinson-White syndrome
- Muscular dystrophy
- Down syndrome
- Myotonic dystrophy
- Cardiomyopathy

### *CACNA1C* Clinical significance on ClinVar submitted records (SCV)[6]

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1. Levy RJ, Timothy KW, Underwood JFG, Hall J, Bernstein JA, Paşca SP. A cross-sectional study of the neuropsychiatric phenotype of *CACNA1C*-related disorder. Pediatr Neurol [Internet]. 2022;102542. Available from: https://doi.org/10.1016/j.pediatrneurol.2022.10.013
2. Bauer R, Timothy KW, Golden A. Update on the Molecular Genetics of Timothy Syndrome. Front Pediatr. 2021;9(May).
3. Splawski I, Timothy KW, Sharpe LM, Decher N, Kumar P, Bloise R, et al. CaV1.2 calcium channel dysfunction causes a multisystem disorder including arrhythmia and autism. Cell Cell Press; Oct 1, 2004.
4. Rodan LH, Spillmann RC, Kurata HT, et al. Phenotypic expansion of *CACNA1C*-associated disorders to include isolated neurological manifestations. Genet Med 2021
5. Bozarth X, Dines JN, Cong Q, et al. Expanding clinical phenotype in *CACNA1C* related disorders: From neonatal onset severe epileptic encephalopathy to late-onset epilepsy. Am J Med Genet A 2018;176(12):2733–9.
6. https://www.ncbi.nlm.nih.gov/clinvar/?gr=1&term=cacna1c%5Bgene%5D&redir=gene (Accessed 3 January 2023)



**Author: Sophie Muir, Chair**
**Timothy Syndrome Alliance (TSA)**
**sophie@timothysyndrome.org**


**Registered Charity no: 1185523**

SCAN ME

# ACHIEVEMENTS AND PERFORMANCE

## Funding/Fundraising

Our total income for the year was £21,405, compared to £10,005 in the previous year (2021/22). This represents an overall increase of 114%, however, this was not experienced evenly across all sources of income. Support through voluntary donations continues to be a challenge due to low awareness of ultra-rare diseases compared to more well-known rare diseases hence low audience numbers, and because many of our supporters are families caring for children while also managing the cost of living crisis.

That said, a wonderful selection of Facebook birthday and activity-based fundraisers, one-off and regular gifts raised £3,483 of income to support our community and projects. Unrestricted income such as this allows us to direct funds to those aspects of our work which will have the greatest impact on achieving our global goals. We have been deeply touched by your support. We couldn't do what we do without you. Thank you.

We have the tools to raise funds from an international audience as well as those in the UK. GlobalGiving allows tax-deductible giving for donors who are US taxpayers, and JustGiving accepts donations in five default currencies, which eliminates bank currency conversion fees and makes the donation process more cost-effective. Moving forward, we will increase communication of these options.

Restricted income from grants, as well as a restricted donation, was £17,922 (2021/22: £4,706). We would like to extend a special thank you to the following trusts and foundations who have given grants during this financial year:

The Waterloo Foundation for their committed three year support of the CACNA1C Community Registry enabling meaningful change for our existing and future CACNA1C community.

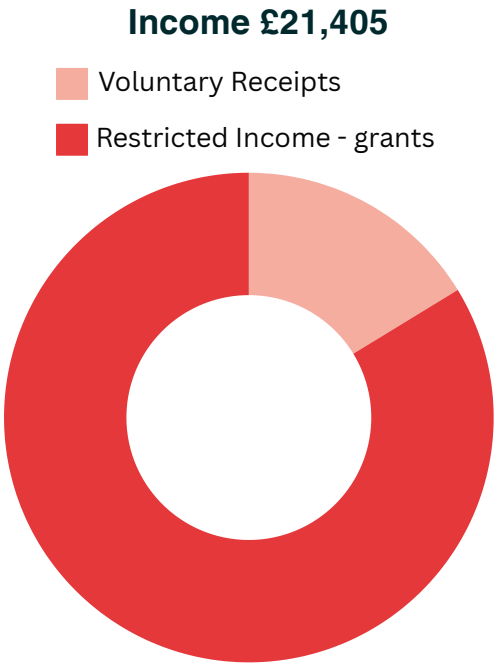
The Stanley Grundy Foundation for funding the translation service. Their generous support enabled our conference to be inclusive, accessible and global.

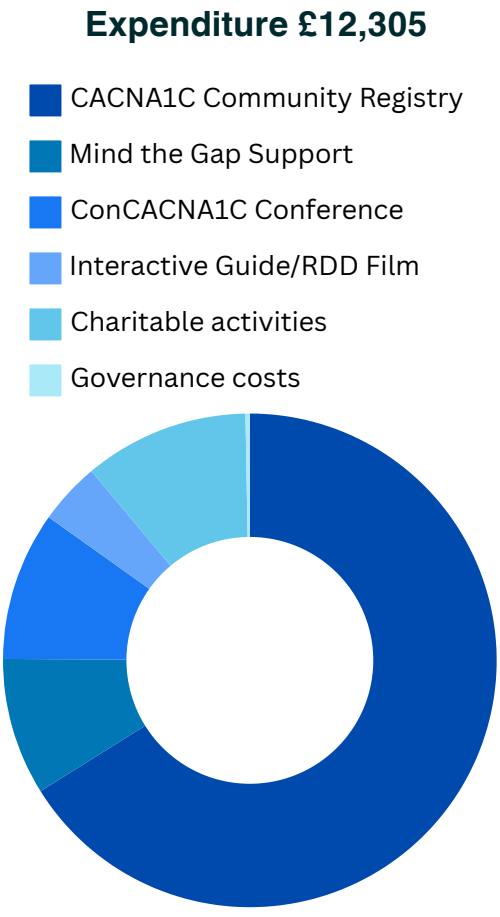
'Mind the Gap' Mental Health & Wellbeing Support. This work has been made possible by an award from Postcode Local Trust, a grant-giving charity funded entirely by players of People's Postcode Lottery.

# ACHIEVEMENTS AND PERFORMANCE

The Renishaw Charities Committee for supporting the Educational CACNA1C Interactive Guide for Healthcare Professionals.

Our total expenditure for the year was £12,305 an increase of 161% on the previous year. The mix of spending included: CACNA1C Community Registry (66.3%), community Mental Health and Wellbeing support (9%), Connect CACNA1C Global Network Conference (9.8%), Interactive Guide/Rare Disease Day film (7.5%) and other charitable activities eg. alliance memberships, website (7.1%).
Restricted funds remaining in the account (£10,982) are for the upcoming annual CACNA1C Community Registry and further 'Mind the Gap' Mental Health & Wellbeing Support with our partners Rareminds.
In the next financial year the current unrestricted funds (£8,114) will assist with the remainder of the annual registry payment alongside an anticipated Speech and Language Research project we are finalising and for which we will need to source additional funding support.



# THANK YOU

We would like to express our gratitude to our anonymous donor for supplying this specialised and adjustable classroom seat designed to promote strength and independence for one of our families. We also want to thank Gardiner Bros & Co (Leathers) Ltd for covering the shipment costs from the UK to the USA.

We sincerely thank our anonymous donor for their generous gift towards our registry payment. Your support is vital to our mission's success. Thank you.

TSA is a small charity punching above its weight and making a significant impact despite limited resources. This is made possible thanks to the people and organisations who help fund our work and provide pro bono support through internal resources and dedication of time and energy. Thank you to all of you, as well as to those we have mentioned throughout this report and our Scientific Advisory Board members, for their dedication to understanding CACNA1C.

Our voice wouldn't be as strong without the support and engagement of our CACNA1C community. Besides sharing stories and photos which greatly helps signpost new families, encouraging and supporting each other, attending our conferences, supporting our social media channels, joining the registry, and contributing to research, they make the impossible possible. Thank you. We are Stronger Together.

As we enter 2024, we are thrilled to announce that we have been selected as the Healx Charity of the Year. We look forward to making an even greater impact together.

This Annual Report was designed and created with love at no cost to TSA

## Our growth is through strength, our strength is through growth.

# WAYS YOU CAN HELP

Like and share our social media

@timothysyndromealliance

@timothysyndromealliance

@tsa_charity

@timothysyndromealliance

Timothy-Syndrome-Alliance

Donate to support our work

JustGiving

GlobalGiving

Charities Aid Foundation

Join the registry

Start a fundraiser

Volunteer

Feedback on how we can help you

## TIMOTHY SYNDROME ALLIANCE (TSA) TRUSTEES' REPORT General Information

REGISTERED CHARITY NUMBER: 1185523
TRUSTEES:
Sophie Muir – Chair
Nick Muir
Katherine W Timothy
Galina Gardiner
Meg Mcloughlin
REGISTERED OFFICE:
8 Butt Street, Minchinhampton, Gloucestershire GL6 9JP

For the year ended
30 November 2023.

Objectives: To relieve the needs of those affected by deleterious CACNA1C gene changes resulting in CACNA1C-related disorders including Timothy Syndrome and Long QT8, their families and carers worldwide in particular but not exclusively by:- (1) Promoting greater understanding of the causes, symptoms and treatment of CACNA1C-related disorders including Timothy Syndrome and Long QT8, by the promotion of research and sharing and disseminating of the results of such research for the benefit of the general public; (2) Raising public awareness of the symptoms, needs and related medical conditions of those living with CACNA1C-related disorders including Timothy Syndrome and Long QT8.

Structure, governance, and management: Timothy Syndrome Alliance (TSA) is a registered charity number 1185523, governed by the Charities Act 2006. The charity is a Charitable Incorporated Organisation registered on 27 September 2019 under the Foundation Governing Document. The Trustees delegate the charity's day-to-day management to Sophie Muir. Trustees met four times during the year and corresponded regularly via email and other digital means, particularly to keep financial performance under review. New trustees are appointed by the serving trustees, considering the skills required by the board. Trustee induction includes online training (NCVO) to give an overview and understanding of charity governance, regulation and best practice alongside Essential Information for Trustees from the Charities Commission.

Public Benefit: The Trustees confirm that they referred to the Charity Commission's general guidance on public benefit when reviewing the Charity's aims and objectives for the year. Public benefit has been achieved through the activities outlined in the Achievements and Performance section of this report.

Reserves Policy and Going Concern: The charity receives funding for specific purposes which are restricted funds – these are not available for expenditure on other purposes. The general reserves are the unspent unrestricted funds of the charity. The charity currently owns no fixed assets, so the general reserve is held in cash. The general reserve is therefore the free reserves of the charity plus any designated funds, also termed 'unrestricted funds' in the charity's balance sheet.
The purpose of the general reserve is:
a) fund shortfalls when income does not reach expected levels.
b) fund unexpected expenditures, for example when projects overrun or unplanned events

occur.
c) ensure that the Charity is not unnecessarily holding back on spending in favour of using the resources it has to meet its charitable objectives.
We assess the level of general reserve needed by looking forward and considering the risks to our funding balanced against our expenditure commitments. Future plans show levels of committed expenditure for which we are seeking funding, but to ensure we can continue to operate in accordance with our plans, we hold a general reserve in the range £1,500 - £2,000 to cover unfunded committed costs for the next 6 months.
Our general reserves on 30 November 2023 were £8,114 (of which £2,000 will go towards the registry fees and £4,000 towards a Speech and Language Research project), leaving £2,114 of Free Reserves which is slightly over policy. Our reserves policy is reviewed annually and updated as necessary.
The trustees have reviewed the circumstances of the Charity and consider that adequate resources continue to be available to fund its activities for the foreseeable future. The trustees are of the view that the Charity is a going concern.

Trustees' responsibilities statement
The trustees are responsible for preparing the trustees' report and the financial statements in accordance with applicable law and United Kingdom Accounting Standards (United Kingdom Generally Accepted Accounting Practice).
The trustees are required to prepare accounts for each financial year, which reflect the receipts and payments of the charity and the surplus or deficit of income against payments for the year.
The trustees are responsible for:
• keeping proper accounting records which disclose with reasonable accuracy at any time the financial position of the charity and to enable them to ensure that the financial statements comply with the Charities Act 2011, the applicable Charities (Accounts and Reports) Regulations, and the provisions of the Trust deed; and
• safeguarding the assets of the charity and hence taking reasonable steps for prevention and detection of fraud and other irregularities.

Approved by the trustees on .8 July 2024 and signed on their behalf by

Sophie Muir - Trustee (Chair)

CHARITY COMMISSION FOR ENGLAND AND WALES

| Charity Name | No (if any) |
|---|---|
| Timothy Syndrome Alliance (TSA) | 1185523 |

# Receipts and payments accounts

**CC16a**

| For the period from | 01/12/2022 | To | 30/11/2023 |
|---|---|---|---|

## Section A Receipts and payments

| | Unrestricted funds to the nearest £ | Restricted funds to the nearest £ | Endowment funds to the nearest £ | Total funds to the nearest £ | Last year to the nearest £ |
|---|---|---|---|---|---|
| **A1 Receipts** | | | | | |
| Voluntary Receipts | 3,483 | 17,922 | - | 21,405 | 10,005 |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| ***Sub total** (Gross income for AR)* | 3,483 | 17,922 | - | 21,405 | 10,005 |
| **A2 Asset and investment sales, (see table).** | | | | | |
| | - | - | - | - | |
| | - | - | - | - | - |
| ***Sub total*** | - | - | - | - | - |
| ***Total receipts*** | 3,483 | 17,922 | - | 21,405 | 10,005 |
| **A3 Payments** | | | | | |
| Cost of Charitable Activities | 1,330 | 10,940 | - | 12,270 | 4,706 |
| Governance Costs | 35 | - | - | 35 | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| ***Sub total*** | 1,365 | 10,940 | - | 12,305 | 4,706 |
| **A4 Asset and investment purchases, (see table)** | | | | | |
| | - | - | - | - | |
| | - | - | - | - | |
| ***Sub total*** | - | - | - | - | - |
| ***Total payments*** | 1,365 | 10,940 | - | 12,305 | 4,706 |
| ***Net of receipts/(payments)*** | 2,118 | 6,982 | - | 9,100 | 5,299 |
| **A5 Transfers between funds** | - | - | - | - | - |
| **A6 Cash funds last year end** | 5,996 | 4,000 | - | 9,996 | 4,697 |
| ***Cash funds this year end*** | 8,114 | 10,982 | - | 19,096 | 9,996 |

## Section B Statement of assets and liabilities at the end of the period

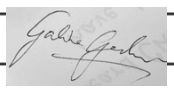
| Categories | Details | Unrestricted funds to nearest £ | Restricted funds to nearest £ | Endowment funds to nearest £ |
|---|---|---|---|---|
| **B1 Cash funds** | | 8,114 | 10,982 | - |
| | | - | - | - |
| | | - | - | - |
| | ***Total cash funds*** | 8,114 | 10,982 | - |
| | (agree balances with receipts and payments account(s)) | OK | OK | OK |

| | Details | Unrestricted funds to nearest £ | Restricted funds to nearest £ | Endowment funds to nearest £ |
|---|---|---|---|---|
| **B2 Other monetary assets** | | - | - | - |
| | | - | - | - |
| | | - | - | - |
| | | - | - | - |
| | | - | - | - |
| | | - | - | - |

| | Details | Fund to which asset belongs | Cost (optional) | Current value (optional) |
|---|---|---|---|---|
| **B3 Investment assets** | | | - | - |
| | | | - | - |
| | | | - | - |
| | | | - | - |
| | | | - | - |

| | Details | Fund to which asset belongs | Cost (optional) | Current value (optional) |
|---|---|---|---|---|
| **B4 Assets retained for the charity's own use** | | | - | - |
| | | | - | - |
| | | | - | - |
| | | | - | - |
| | | | - | - |
| | | | - | - |
| | | | - | - |
| | | | - | - |
| | | | - | - |

| | Details | Fund to which liability relates | Amount due (optional) | When due (optional) |
|---|---|---|---|---|
| **B5 Liabilities** | | | - | |
| | | | - | |
| | | | - | |
| | | | - | |
| | | | - | |

| Signed by one or two trustees on behalf of all the trustees | Signature | Print Name | Date of approval |
|---|---|---|---|
| |  | Galina Gardiner | 8 July 2024 |

**TIMOTHY SYNDROME ALLIANCE (TSA)**

England & Wales - Charity number 1185523

# Accounts

# TIMOTHY SYNDROME ALLIANCE (TSA)

Timothy Syndrome Alliance

## ANNUAL REPORT

### FOR FINANCIAL PERIOD
### 1 DECEMBER 2021 TO 30 NOVEMBER 2022

www.timothysyndrome.org

Charity Registration Number: 1185523

# WELCOME

## Vision:

Our vision is a world where shared knowledge and understanding lead to a cure for everyone with a CACNA1C genetic variant.

## Mission:

Our mission is to improve the diagnosis, treatment and care of individuals with CACNA1C-related disorders including Timothy Syndrome and LongQT8, and to support the families and carers of those diagnosed.

## How we work

In following our mission our focus is on each of these five inter dependable areas of activity – raising awareness, improving diagnosis treatment and care, supporting the global community, providing information and advice, and driving research and clinical development.

Through collaborations globally we are stronger together. We will build our community and support it with sustainable growth.

Our values combine to form a solid foundation for how we do things and what we believe in. We are determined, supportive, empowering, and a community.

# CACNA1C

## What is CACNA1C?

CACNA1C is a gene that provides the code for a protein found in cells throughout the body. This protein manages the movement of calcium in and out of the cell, which is critical for many cells' functions. Changes to the gene can cause changes to the protein and its ability to manage calcium movement, making it work more, less, or not at all.

## What is Timothy Syndrome?

Timothy Syndrome (TS) is caused by specific changes to the CACNA1C gene. There are two types of TS: TS1 and TS2.
The most common symptoms include abnormal heart function, irregular heartbeat, abnormal heart structure, neuronal developmental delays, immunodeficiencies, endocrinological dysfunction, gastrointestinal concerns, effects on smooth muscle, effects on skeletal muscle, facial anomalies, syndactyly (joined fingers or toes), mild dental, skin, eye, and hair anomalies. Some individuals have significant episodes of low blood sugar levels (hypoglycemia), seizures, and/or an unusually low body temperature (hypothermia).

## What is a CACNA1C-related disorder (CRD)?

A novel variant in the CACNA1C gene - individuals have some but not all symptoms typical of Timothy Syndrome. Some affected individuals may present with multisystem health concerns that overlap entirely with Timothy Syndrome.

## What is Non-syndromic LongQT8?

Non-syndromic LongQT8 overlaps with Timothy Syndrome in that the affected individual has LongQT (a prolonged QT interval on an ECG). There are many variants throughout the CACNA1C gene that appear to cause non-syndromic LongQT8.

**Prevalence**
CRDs are rare and their prevalence is unknown.There are <100 cases of TS diagnosed worldwide. Prevalence is unknown due to the rarity and recent identification of CRDs.

# IMPACT IN NUMBERS

**2**
New genomic test analysis panels

**+24**
New members in our Support Group

**2**
New films in production

**50%**
Increase in social media followers

**1**
'Connect CACNA1C Global Network Conference' 2023 in the planning

**1**
Scientific Advisory Board

**1**
New Wikipedia page

**1**
Presentation to leading NHS Hand Surgeons

**~500**
New website visitors per month

**1**
4 hour Brain Research Conference transcribed into Brazilian Portuguese

**130**
Countries visited our website

**1**
CACNA1C Community Registry

**2**
Award-winning films

**1**
Best Research Partnership Award

**+12**
Increase in individuals with CRD / TS / LQT8

**1**
Published study of the Neuropsychiatric Phenotype of CACNA1C-Related Disorder

**1**
'Mind the Gap' Parental Resilience Programme

**1**
Psychosocial impact study

# ACHIEVEMENTS AND PERFORMANCE

## Raising Awareness

We have made two award-winning films to date; 'Timothy Syndrome Alliance' which highlights the challenges faced by families and how peer support and the friendship and information that brings can make a huge difference, and 'Rare Strikes Back' a Rare Disease Day film made with puppets that balances the reality of living with a rare condition with the hope of the Rare Disease Community. Both continue to raise awareness and can be found on our social media channels, website, and The Disorder Channel (available through Roku or Amazon Fire TV). The films have also successfully signposted families to TSA to connect with the CACNA1C Community for knowledge and support.

To widen our audience further we enter film festivals. This year Rare Strikes Back won the Gold award at the Charity Film Awards 2022 (£0 - £100,000 Turnover Category) and we were welcomed for a virtual Q&A session at the Health in Focus Film Festival, School of Public Health, Boston University.

More filming and interviews have been underway for the making of 'The Rare Disease Research Journey', a film demonstrating the importance of public engagement in research. The project is a collaboration between the Neuroscience and Mental Health Innovation Institute (NMHII) University of Cardiff and TSA and is anticipated to be ready for release in early 2023.

# ACHIEVEMENTS AND PERFORMANCE

Rare Disease Day is observed every year on 28 February (or 29 in leap years) – the rarest day of the year. It is a day when we join together and help build awareness for the 7000 rare diseases affecting 300 million individuals worldwide. Rare Disease Day 2022 was very successful for TSA this year with many social media posts being shared globally by our community and supporters. We were part of a Genetic Alliance Twitter takeover and also involved in a recorded interview with Abcam, a manufacturer of protein research tools for life scientists, helping to expand our audience reach.

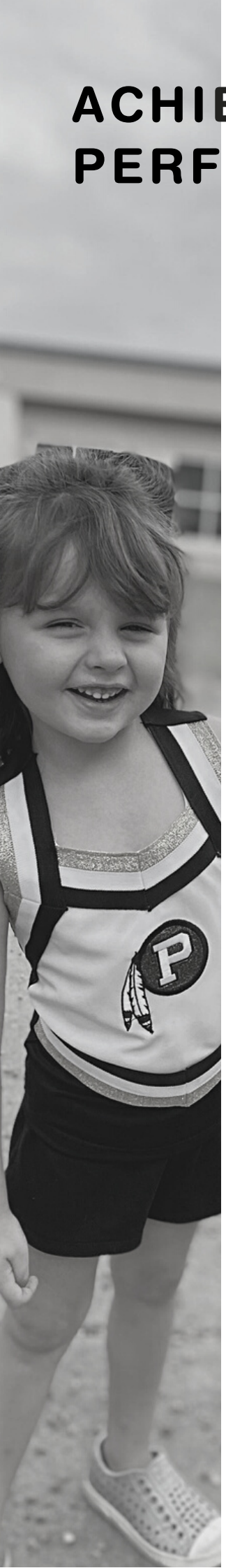
Awareness Day on 1st October also involved much activity on social media including takeovers of both Rare Revolution Magazine and Genetic Alliance UK channels. The day was also marked with the release of a 2-minute trailer for The Rare Disease Research Journey which was well received with regard to views and engagement.

Initial insights from Awareness Day 2022

| | | | |
|---|---|---|---|
| | 4,357 Page reach | 757 Profile visits | +25 New followers |
| | 2,685 Page reach | 159 Profile visits | +23 New followers |
| | 7,862 Page reach | 1,643 Profile visits | +10 New followers |

All data based on TSA social media posts made on 1st October 2022

The TSA website continues to grow in users (on average 500 new visitors per month) as well as updated content. Our website is frequently accessed in the German language via the simple flag click and has received visits from all over the world - in June we posted on social media a collage detailing the flags of the 130 countries that have visited our website since it launched 19 months ago. Additional signposting to our website has been successful through our collaborations, press articles, and partnerships with ERN-GUARD Heart, Neurological Alliance, EURORDIS, Rare Diseases International, and Global Genes to name a few.
Social media performance on all channels has increased over the year with engagement and 'follows' up by 50% on some platforms. Everything we post uses the same core signposts #CACNA1C #TimothySyndrome #LongQT8.



# ACHIEVEMENTS AND PERFORMANCE

## Improving diagnosis, treatment and care

Over this last year, we have been working with OPEN Health (a leading global healthcare communications agency with extensive scientific expertise) and members of our community to co-create a pathway-focused educational interactive guide for healthcare professionals. This resource will ensure different stakeholders understand their roles and responsibilities along the patient journey for an individual identified with a CACNA1C gene change. It is anticipated that this will be ready to launch during 2023.

Our application has been approved for CACNA1C to be included as a gene within the Genetic Epilepsy syndromes genomic test listed in the NHS National Genomic Test Directory (PanelApp). 'CACNA1C-related disorders' has also been added to the phenotype list for all CACNA1C panels – this includes Intellectual disability, Long QT syndrome, Short QT syndrome, Fetal Anomalies, DDG2P (Developmental Disorders Genotype-to-Phenotype), Hypertrophic cardiomyopathy and Paediatric or syndromic cardiomyopathy. This means CACNA1C variants, other than the Timothy Syndrome causing variant (G406R), are analysed as part of the diagnostic pathway. Update: In January 2023 our application for Timothy Syndrome and CACNA1C-related disorders was approved for the Congenital hyperinsulinism panel.
PanelApp is an open platform and as such this knowledgebase of evidence for gene-disease associations is used by the wider global scientific community.

# ACHIEVEMENTS AND PERFORMANCE

Working further afield TSA has been collaborating with several genetic sequencing companies across the world. We are ensuring that resources are available for patients and families when they receive testing through their laboratories and have been identified to have variants in CACNA1C/a diagnosis of Timothy Syndrome. This support and signposting to our community are an important part of the rare disease journey.

In July we were delighted to join ERN GUARD-Heart Patient Advocacy Board (ePAG). European Reference Networks (ERNs) are virtual networks involving healthcare providers across Europe. They aim to tackle complex or rare diseases and conditions that require highly specialised treatment and concentration of knowledge and resources. No country alone has the knowledge and capacity to treat all rare and complex diseases. ERNs offer the potential to give patients and doctors across Europe access to the best expertise and timely exchange of life-saving knowledge without having to travel to another country. There are 24 European Reference Networks that bring together nearly 1,500 Expert centres located in the 27 EU Member States and Norway.
Each Network focuses on a different group of diseases (e.g. Rare heart diseases). The mission of ERN GUARD-Heart is to facilitate access to diagnosis and treatment of rare and complex diseases of the heart in adult and paediatric patients across the European Union.
ERN GUARD-Heart brings together 44 expert healthcare providers from 16 different Member States committed to patient-centred care and efficient practice based on evidence, knowledge, education, and translational research.

September involved in-person discussions and a presentation to leading NHS hand surgeons in Birmingham on the links between syndactyly, Timothy Syndrome Type 1, prolonged QT, and the additional anaesthesia risks to those who may not have been diagnosed pre-corrective surgery. A bonus was the opportunity to present to hand surgeons in Dubai and Amsterdam virtually at the same time.

# ACHIEVEMENTS AND PERFORMANCE

## Supporting our global community

Following a taster session and establishment of need from our community, we launched ‘Mind the Gap’. This Building Parental Resilience Programme with Rareminds, an organisation (CIC) that specialises in providing counselling and emotional wellbeing services for the rare disease community, consisted of 1 x 8-week closed group sessions allowing for a maximum of 10 participants. Held on Zoom the timings made the sessions accessible for as many global time zones as possible.
An anonymous feedback questionnaire at the end of the 8 weeks confirmed the following:

**100%** 100% of participants responded Yes to 'After this group I feel more positive'

**100%** 100% of participants responded Yes to 'After this group I feel more resilient'

**100%** 100% of participants responded Yes to 'After this group I feel less isolated'

**100%** 100% of participants responded Yes when asked 'Would you recommend this group to others?'

**100%** 100% of participants responded Yes when asked 'Would you like to attend further groups of this sort?'
Comments included "Absolutely!" "Yes 100%" "Definitely"

“I didn’t realise that I needed this group but I did, thank you.”

# ACHIEVEMENTS AND PERFORMANCE

TSA administrates an online private Facebook Support Group for individuals and families of CACNA1C-related disorders including Timothy Syndrome and LongQT8, offering 24/7 access to emotional and practical support and information via our families.
The benefits of this are huge. It enables:

- meeting and befriending other people with the same rare disorder and similar experiences from across the world
- learning about CACNA1C
- giving and receiving emotional support
- having a place to speak openly about the impact of CACNA1C and one's thoughts and feelings
- learning coping skills
- feeling empowered and hopeful
- advocating to improve healthcare

"I am actually over here in tears reading your welcome note to the group. I have been so isolated through this whole ordeal"

Many people find it comforting and helpful to talk to someone who has experienced the same things they are facing when they or their child have a health problem. Having a rare condition can often be extremely isolating due to the lack of people with the same condition. It can be just as challenging to be a parent to someone with a rare disease. Rare disease support groups are an important source of emotional and practical support. 'The use of such advocacy-based coping may help patients to foster a sense of empowerment, efficacy, and hope' (Ayme et al., 2008)

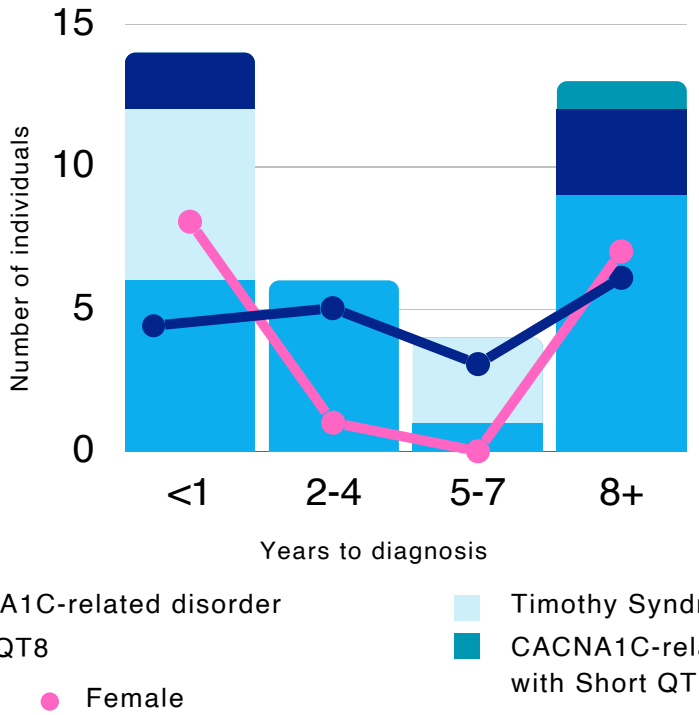
**+ 24** Total increase in support group members joining between 1 December 2021 and 30 November 2022

Representing **12** individuals with CACNA1C-related disorders including Timothy Syndrome and LongQT8

# ACHIEVEMENTS AND PERFORMANCE

As our community continues to grow in size so does the spectrum of affectedness of those living with these conditions. In August TSA ran a survey to find out how long it can take to receive an accurate diagnosis.

Average years until diagnosis = 4.6




Survey completed by 34 individuals representing a total of 37 CACNA1C individuals

The huge project to transcribe and translate our 4-hour Brain Research Conference 2021 to Brazilian Portuguese was completed by volunteers at Charity Translators and shared with our community.

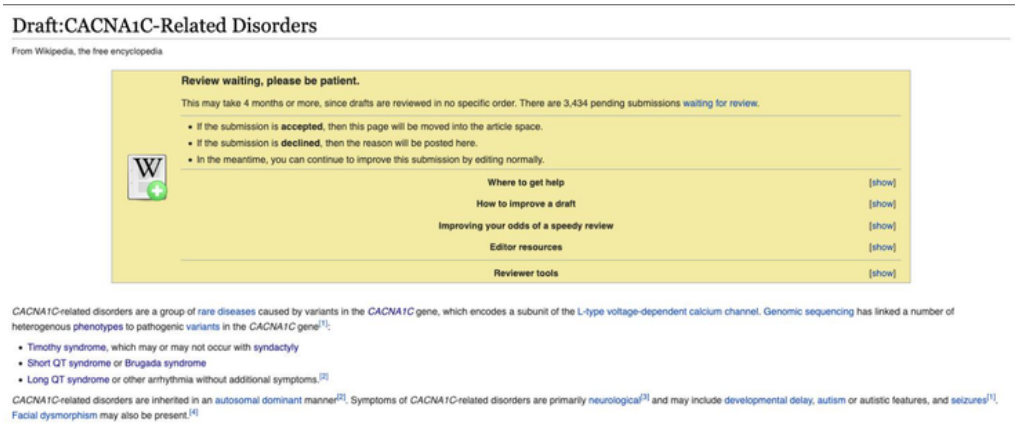
"I loved the initiative, and congratulations to the volunteers, the translation of videos and online dialogues, yes they are important because I don't know how to say almost anything and I don't understand much."

Charity Translators' work with important epilepsy healthcare surveys has also been immensely helpful this year ensuring reliable and accurate recording of specific health concerns.

# ACHIEVEMENTS AND PERFORMANCE

## Providing information and advice

Alongside information provision on our website and social media platforms TSA also administrates an online private Patient Advisory Board for individuals and families of CACNA1C-related disorders including Timothy Syndrome and LongQT8. It is here that TSA updates our community on advocacy, ongoing research, and published papers of interest - in fact, anything that would be of interest to our community relating to CACNA1C and our mission, thus ensuring that the Support Group remains for support only.



Draft:CACNA1C-Related Disorders

From Wikipedia, the free encyclopedia

**Review waiting, please be patient.**

This may take 4 months or more, since drafts are reviewed in no specific order. There are 3,434 pending submissions waiting for review.

- If the submission is **accepted**, then this page will be moved into the article space.
- If the submission is **declined**, then the reason will be posted here.
- In the meantime, you can continue to improve this submission by editing normally.

| | |
|---|---|
| **Where to get help** | [show] |
| **How to improve a draft** | [show] |
| **Improving your odds of a speedy review** | [show] |
| **Editor resources** | [show] |
| **Reviewer tools** | [show] |

*CACNA1C*-related disorders are a group of rare diseases caused by variants in the *CACNA1C* gene, which encodes a subunit of the L-type voltage-dependent calcium channel. Genomic sequencing has linked a number of heterogenous phenotypes to pathogenic variants in the *CACNA1C* gene[1]:

- Timothy syndrome, which may or may not occur with syndactyly
- Short QT syndrome or Brugada syndrome
- Long QT syndrome or other arrhythmia without additional symptoms.[2]

*CACNA1C*-related disorders are inherited in an autosomal dominant manner[2]. Symptoms of *CACNA1C*-related disorders are primarily neurological[3] and may include developmental delay, autism or autistic features, and seizures[1]. Facial dysmorphism may also be present.[4]

Accurate and trusted information elsewhere on the internet is not easy to find. CACNA1C-related disorders is a newly characterised disorder. We are delighted to be working with scientists at Healx who are supporting us with Wikipedia updates on the Timothy Syndrome page and the creation of a brand new CACNA1C-related disorders Wikipedia page. Update: this page has been approved which means the growing CACNA1C community now have an accurate and validated Wikipedia source to learn from and enhance with their own insights and citations.

TSA continues to advocate with authoritative knowledge-based websites and reference portals to ensure CACNA1C information is up-to-date and accurate. This includes OMIM, Orphanet, and ICD-11.

# ACHIEVEMENTS AND PERFORMANCE

## Driving research and clinical development

TSA is integrated and co-producing research at a number of levels with teams at Cardiff University and Stanford University. This includes co-production of research aims and goals, designing of studies, recruitment, and engagement to feedback results. We have further links to Oxford University (transcription and clinical translation) and the Earlham Institute. Research areas include clinical phenotyping and cell lines for lab work, with further grants towards public engagement.

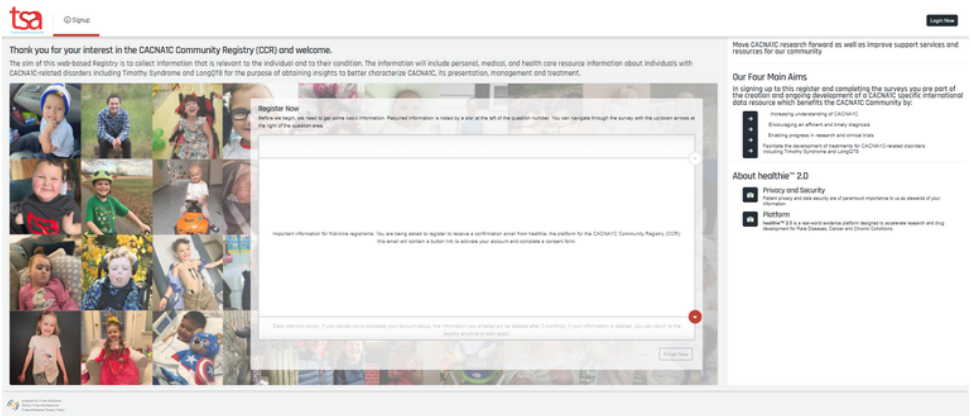
TSA and NMHII were successful in selection to attend 'Collaborating for Change' a Rare Neurology/CNS Partnering Event held at The Royal Society of Medicine, London. The event was focused on building collaborations around rare neurological/ central nervous system disorders between patient groups and companies that have assets, technology, and interest in this space.

In a new awards ceremony focused entirely on genetic conditions TSA and NMHII Cardiff University received the award for Best Research Partnership. Gene People Awards commemorate outstanding individuals and groups who have achieved incredible things in genetic conditions, whether across the genetic community or for a specific condition. These awards focused on achievements from 2020 and 2021, including campaigns that took place during the pandemic.

# ACHIEVEMENTS AND PERFORMANCE

A dissertation study undertaken as part of MSc Genetic & Genomic Counselling at Cardiff University has now been completed with the student, Bhavna Vadukul, receiving a Distinction. ‘Exploring the psychosocial impact of Timothy Syndrome and CACNA1C-related disorders on affected individuals and their families’ was a study undertaken by UK families. To date, no other research has been conducted on the lived experience of affected individuals and their families living with these conditions. Medical professionals require further knowledge about these conditions in order to provide appropriate support to affected individuals and families. There is a general lack of research on the psychosocial impact of rare and ultra-rare conditions such as Timothy Syndrome and CACNA1C-related disorders. A summary of Bhavna's work can be found under the research tab on our website.

People are unique genetically and even though everyone in our community has the same gene in common, not everyone has the same genetic variant, it may be different from someone else in the next state or the next country. Genetic variants are not the same, they don't necessarily act in the same way and they might have different mechanisms in terms of how they are treated.
Our CACNA1C Community Registry, accessible worldwide, launched in June. This is a vitally important research tool in which all families and individuals with an identified CACNA1C gene change (this includes CRD, TS, LQT8, duplications, and deletions) are encouraged to participate. Parents/carers may register on behalf of children and there are appropriate questionnaires to represent those who are sadly no longer with us.



# ACHIEVEMENTS AND PERFORMANCE

The CACNA1C Community Registry has been designed with the input of clinical researchers to identify information and issues relevant to families and pertinent to developing translational research. As variants in CACNA1C are so rare clinicians may only see one or two individuals in their lifetime, and therefore gathering global data is vital to understanding the natural history and features of the condition. The information being collected will be reviewed by the TSA Scientific Advisory Board, and make available high quality clinical data for research.

In the new year, we will have a Scientific Advisory Board to help steer the research efforts of the charity offering expertise on scientific and clinical developments with regard to CACNA1C. We are fortunate to have internationally leading researchers and medics serving on the board chaired by Dr. Jack Underwood, Cardiff University.

Planning has also commenced on the 'Connect CACNA1C Global Network Conference' 2023 an online conference to share with families, healthcare professionals, and researchers the very latest knowledge and understanding of CACNA1C. It is the intention for this to be accessible in several languages with successful funding.

Published paper of note:
Levy, Rebecca J.; Timothy, Katherine W.; Underwood, Jack F.G.; Hall, Jeremy; Bernstein, Jonathan A.; Pașca, Sergiu P. (January 2023). "A Cross-Sectional Study of the Neuropsychiatric Phenotype of CACNA1C-Related Disorder". Pediatric Neurology. 138: 101–106. doi:10.1016/j.pediatrneurol.2022.10.013. PMID 36436328

Understanding what strengths and challenges may happen for a disorder can help families and their medical providers plan, screen, and treat individuals more effectively. TSA collaborated on this study which focuses on experienced issues in development, as well as symptoms involving mood, learning, and the nervous system.
Summary of findings: Many individuals with CACNA1C-

# ACHIEVEMENTS AND PERFORMANCE

related disorders had delays in learning to walk and talk, as well as other developmental milestones. They also commonly reported neuropsychiatric symptoms such as imbalance, incoordination, difficulty with chewing, learning or cognitive disability, seizures, and symptoms associated with autism spectrum disorder.
Whether or not an individual had long QT syndrome did not affect the risk of developmental or neuropsychiatric symptoms, so in CACNA1C-related disorders this risk may be related to brain-specific and not heart-related impacts of the CACNA1C gene.

## Fundraising

Every donation we receive goes to help fund the vital work that we do as a charity.

We are global in our advocacy and support and as such, it is important to ensure that we can be supported globally too.

This year TSA was approved as a partner on a crowdfunding platform called GlobalGiving on which we are raising funds for the CACNA1C Community Registry. All donations are tax-deductible for donors who are US taxpayers, and all projects on GlobalGiving.org have been pre-qualified for 501(c)(3) equivalency status. The GlobalGiving project page has functionality similar to Facebook making it simple to create a personalised fundraising page to raise funds. It can also be used to set up a monthly giving program by using the recurring donations feature.

Our size (day-to-day management of the charity's activities is undertaken by the Chair of Trustees) alongside low awareness of rare diseases continues to make fundraising a challenge. Running a small charity with such great ambition is only possible thanks to the people and organisations who help fund our work and support us through internal resources and team member time commitments as well as our volunteers who dedicate time and energy.

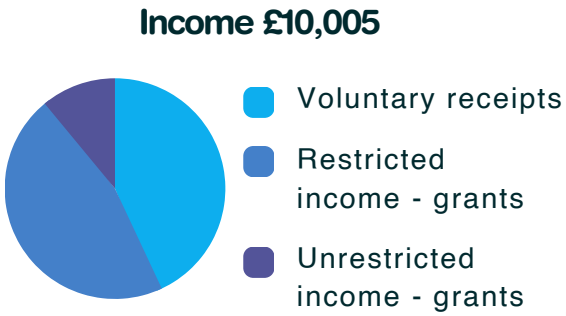
# ACHIEVEMENTS AND PERFORMANCE

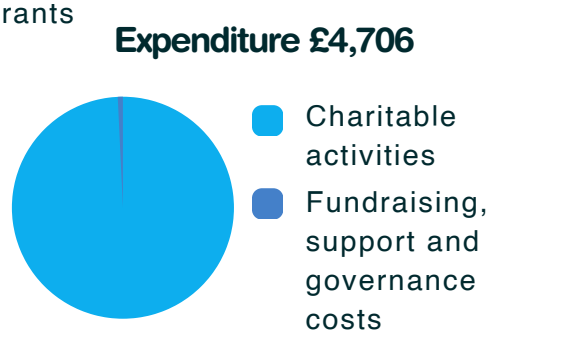
Our total income for the year is £10,005 (2020/21: £6,084) Against a backdrop of economic and pandemic-related uncertainty, we are immensely grateful to everyone who so generously donated to TSA this year through one-off and regular donations as well as creating birthday and activity-based fundraisers to support our community and projects.

Unrestricted income was £5,405 (previous year: £6,084), including unrestricted grants of £1,100. Restricted income from grants was £4,600 of which £4,000 is allocated towards our Registry platform fees which are due in February 2023.

We are encouraged that funders understand and align with our research outlook, focus, and passion for the cause and commitment to improving the information and support for families and individuals with CACNA1C changes.

Our total expenditure for the year is £4,706 (2020/21: £3,226)




We would like to thank the following Trusts and Foundations for their support during this financial year:
Arnold Clark Community Fund
Blakemore Foundation
St. James's Place Charitable Foundation
The Souter Charitable Trust

# THANK YOU

Thank you, to those we have mentioned throughout this report, plus volunteers Dmitry Kran for website building, Zoe Shaked for German translations, Peter Gardiner for database diving, Rob Bradshaw for adding the extra spark to our films and so many others.

We would also like to say a heartfelt thank you to our CACNA1C families and individuals who allow us to share their photos and stories on our website and social media. This makes a huge difference in letting our supporters know how their donation has helped whilst also helping us reach new families and individuals who need support and community.

https://www.facebook.com/timothysyndromealliance

https://www.instagram.com/timothysyndromealliance

https://twitter.com/tsa_charity

https://www.tiktok.com/@timothysyndromealliance

https://www.linkedin.com/company/timothy-syndrome-alliance

https://www.justgiving.com/campaign/timothysyndromealliance

This Annual Report was designed and created in house at no cost to TSA

The trustees present their report for the period 1 December 2021 to 30 November 2022.

TIMOTHY SYNDROME ALLIANCE (TSA)
TRUSTEES' REPORT General Information

REGISTERED CHARITY NUMBER: 1185523

TRUSTEES:
Sophie Muir – Chair
Katherine W Timothy
Andy Golden (Until March 2022)
Sally Johns (Until June 2022)
Galina Gardiner
Meg Mcloughlin
Nick Muir

REGISTERED OFFICE:
8 Butt Street, Minchinhampton, Gloucestershire GL6 9JP

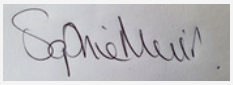
Objectives: To relieve the needs of those affected by CACNA1C-related disorders including Timothy Syndrome and LQT8, their families, friends, and carers. Promote a greater understanding of the causes, symptoms, and treatment. Raise public awareness of the symptoms, needs, and related medical conditions.

Structure, governance, and management: Timothy Syndrome Alliance (TSA) is a registered charity number 1185523, governed by the Charities Act 2006. The charity is a Charitable Incorporated Organisation registered on 27 September 2019 under the Foundation Governing Document. New trustees are appointed by the serving trustees, considering the skills required by the board.

Public Benefit: The Trustees confirm that they referred to the Charity Commission's general guidance on public benefit when reviewing the Charity's aims and objectives for the year. Public benefit has been achieved as per the activities outlined in the Achievements and Performance section of this report.

Reserves Policy and Going Concern: The trustees regularly monitor income and re-plan expenditures. To ensure a sound infrastructure and financial base trustees will identify our level of reserves as we begin to develop long-term commitments. The trustees have reviewed the circumstances of the Charity and consider that adequate resources continue to be available to fund its activities for the foreseeable future. The trustees are of the view that the Charity is a going concern.

Trustees' responsibilities statement
The trustees are responsible for preparing the trustees' report and the financial statements in accordance with applicable law and United Kingdom Accounting Standards (United Kingdom Generally Accepted Accounting Practice).
The trustees are required to prepare accounts for each financial year, which reflect the receipts and payments of the charity and the surplus or deficit of income against payments for the year.
The trustees are responsible for:
• keeping proper accounting records which disclose with reasonable accuracy at any time the financial position of the charity; and
• safeguarding the assets of the charity and hence taking reasonable steps for prevention and detection of fraud and other irregularities.
The trustee's annual report was approved on ……26 April 2023… and signed on behalf of the board of trustees by



Sophie Muir  Chair of Trustees

CHARITY COMMISSION FOR ENGLAND AND WALES

| Charity Name | No (if any) |
|---|---|
| Timothy Syndrome Alliance (TSA) | 1185523 |

# Receipts and payments accounts

**CC16a**

| For the period from | Period start date | To | Period end date |
|---|---|---|---|
| | 01/12/2021 | | 30/11/2022 |

## Section A Receipts and payments

| | Unrestricted funds to the nearest £ | Restricted funds to the nearest £ | Endowment funds to the nearest £ | Total funds to the nearest £ | Last year to the nearest £ |
|---|---|---|---|---|---|
| **A1 Receipts** | | | | | |
| Voluntary receipts | 5,405 | 4,600 | - | 10,005 | 6,084 |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| ***Sub total** (Gross income for AR)* | 5,405 | 4,600 | - | 10,005 | 6,084 |
| **A2 Asset and investment sales, (see table).** | | | | | |
| | - | - | - | - | |
| | - | - | - | - | - |
| ***Sub total*** | - | - | - | - | - |
| ***Total receipts*** | 5,405 | 4,600 | - | 10,005 | 6,084 |
| **A3 Payments** | | | | | |
| Cost of Charitable Activities | 4,106 | 600 | - | 4,706 | 3,226 |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| ***Sub total*** | 4,106 | 600 | - | 4,706 | 3,226 |
| **A4 Asset and investment purchases, (see table)** | | | | | |
| | - | - | - | - | |
| | - | - | - | - | |
| ***Sub total*** | - | - | - | - | - |
| ***Total payments*** | 4,106 | 600 | - | 4,706 | 3,226 |
| ***Net of receipts/(payments)*** | 1,299 | 4,000 | - | 5,299 | 2,858 |
| **A5 Transfers between funds** | - | - | - | - | - |
| **A6 Cash funds last year end** | - | - | - | - | - |
| ***Cash funds this year end*** | 1,299 | 4,000 | - | 5,299 | 2,858 |

## Section B Statement of assets and liabilities at the end of the period

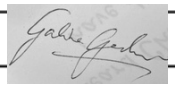
| Categories | Details | Unrestricted funds to nearest £ | Restricted funds to nearest £ | Endowment funds to nearest £ |
|---|---|---|---|---|
| **B1 Cash funds** | Bank Balance | 1,299 | 4,000 | - |
| | | - | - | - |
| | | - | - | - |
| | ***Total cash funds*** | 1,299 | 4,000 | - |
| | (agree balances with receipts and payments account(s)) | OK | OK | OK |

| | Details | Unrestricted funds to nearest £ | Restricted funds to nearest £ | Endowment funds to nearest £ |
|---|---|---|---|---|
| **B2 Other monetary assets** | | - | - | - |
| | | - | - | - |
| | | - | - | - |
| | | - | - | - |
| | | - | - | - |
| | | - | - | - |

| | Details | Fund to which asset belongs | Cost (optional) | Current value (optional) |
|---|---|---|---|---|
| **B3 Investment assets** | | | - | - |
| | | | - | - |
| | | | - | - |
| | | | - | - |
| | | | - | - |

| | Details | Fund to which asset belongs | Cost (optional) | Current value (optional) |
|---|---|---|---|---|
| **B4 Assets retained for the charity's own use** | | | - | - |
| | | | - | - |
| | | | - | - |
| | | | - | - |
| | | | - | - |
| | | | - | - |
| | | | - | - |
| | | | - | - |
| | | | - | - |

| | Details | Fund to which liability relates | Amount due (optional) | When due (optional) |
|---|---|---|---|---|
| **B5 Liabilities** | | | - | |
| | | | - | |
| | | | - | |
| | | | - | |
| | | | - | |

| Signed by one or two trustees on behalf of all the trustees | Signature | Print Name | Date of approval |
|---|---|---|---|
| |  | Galina Gardiner | 26 April 2023 |
| | | | |

**TIMOTHY SYNDROME ALLIANCE (TSA)**

England & Wales - Charity number 1185523

# Accounts

# TIMOTHY SYNDROME ALLIANCE (TSA)

Timothy Syndrome Alliance

## ANNUAL REPORT

### FOR FINANCIAL PERIOD
### 1 DECEMBER 2020 TO 30 NOVEMBER 2021

www.timothysyndrome.org

Charity Registration Number: 1185523

# WELCOME

## Vision:

Our vision is a world where shared knowledge and understanding lead to a cure for everyone with a *CACNA1C* genetic variant.

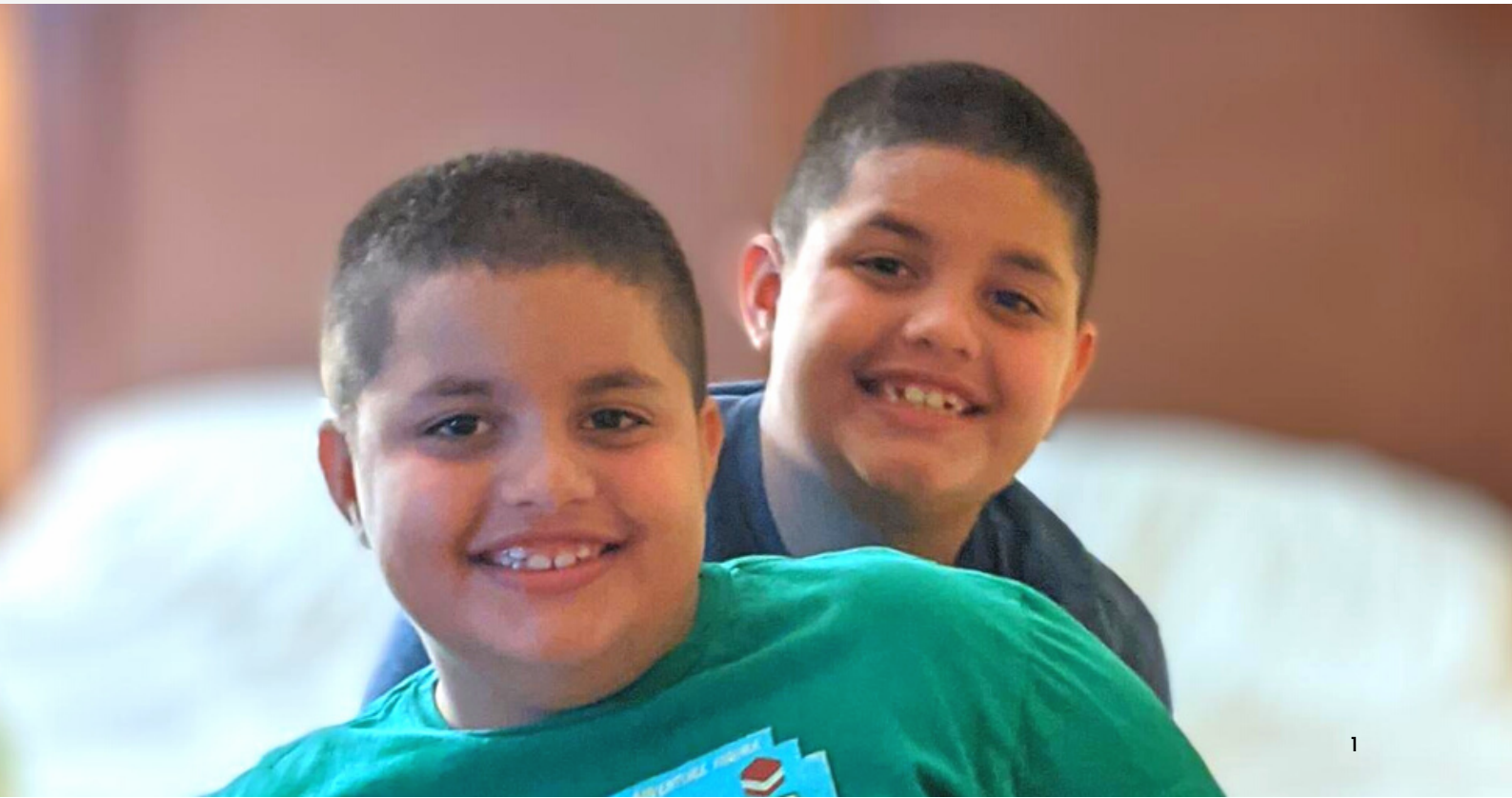
## Mission:

Our mission is to improve the diagnosis, treatment and care of individuals with *CACNA1C*-related disorders, including Timothy Syndrome and LongQT8, and to support the families and carers of those diagnosed.

## Our values:

Our values combine to form a solid foundation for the way in which we do things and what we believe in. We are **determined**, **supportive, empowering** and **a community.**

*CACNA1C*-related disorders, including Timothy Syndrome and LongQT8, do not have geographic boundaries. TSA has no boundaries. We support families wherever they are in the world. Why? Because we are #**strongertogether**



# CACNA1C

## What is *CACNA1C*?

*CACNA1C* is a gene that provides the code for a protein found in cells throughout the body. This protein manages the movement of calcium in and out of the cell, which is critical for many cells' function. Changes to the gene can cause changes to the protein and its ability to manage calcium movement, making it work more, less, or not at all.

## What is Timothy Syndrome?

Timothy Syndrome (TS) is caused by specific changes to the *CACNA1C* gene. There are two types of TS: TS1 and TS2.

Most common symptoms include: abnormal heart function, irregular heart beat, abnormal heart structure, neuronal developmental delays, immunodeficiencies, endocrinological dysfunction, gastrointestinal concerns, effects on smooth muscle, effects on skeletal muscle, facial anomalies, syndactyly (joined fingers or toes), mild dental, skin, eye and hair anomalies.

Some individuals have: significant episodes of low blood sugar levels (hypoglycemia), seizures, an unusually low body temperature (hypothermia).

## What is a CACNA1C-related disorder?

A novel variant in the *CACNA1C* gene - individuals have some but not all symptoms typical of Timothy Syndrome. Some affected individuals may present with multisystem health concerns that overlap entirely with Timothy Syndrome.

## What is Non-syndromic LongQT8?

Non-syndromic LongQT8 overlaps with Timothy Syndrome in that the affected individual has LongQT (a prolonged QT interval on an ECG). There are many variants throughout the *CACNA1C* gene that appear to cause non-syndromic LongQT8.

**Increase in Support Group members between**
**1 December 2020 and 30 November 2021**
**+44**

# ACHIEVEMENTS AND PERFORMANCE

## Raising Awareness

Our first **film** from 2019 continues to raise awareness and to signpost families to TSA to connect with the *CACNA1C* Community for knowledge and support. Film festivals widen our audience; this year we were a finalist at the International Rare Disease Festival (Berlin) and Uno Sguardo Raro Festival – The Rare Disease International Film Festival (Rome). The film took Silver in the Best Creative Campaign category at the PM Society Awards 2021 (UK), whose audience is the pharmaceutical and healthcare industry.

To coincide with Rare Disease Day on the 28th February we made a film called 'Rare Strikes Back' with aligned aims of improving knowledge amongst the general public of rare diseases whilst encouraging researchers and decision makers to address the needs of those living with rare disease. It signposts to both the TSA and the Rare Disease Day websites.

The film was launched on all our social media channels and has been viewed over 11,000 times on Twitter alone. 'Rare Strikes Back' went on to win Best Storytelling by a Voluntary Group at the Rare Reach Festival - Rare Disease UK 2021 and Gold at the Charity Film Awards (UK) £0 - £100,000 Turnover Category. It won Bronze at the PM Society Digital Awards - Effectiveness Category, was a finalist at Uno Sguardo Raro

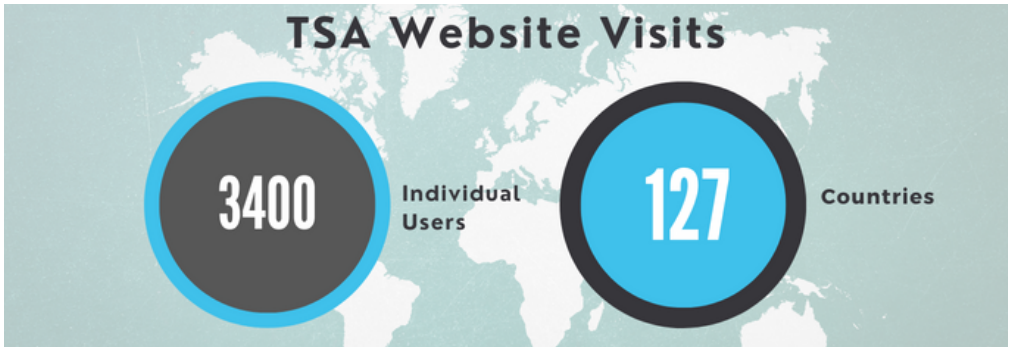
# ACHIEVEMENTS AND PERFORMANCE

Festival - The Rare Disease International Film Festival, QIFF: Quarantine International Film Festival (India)) and PM Society Digital Awards 2021 - Craft category. The film is also available on The Disorder Channel streaming through Amazon Fire and Roku.

Our next film will be a deeper dive into *CACNA1C* aimed at healthcare professionals.

**'OPEN Health is a leading Global healthcare communications agency with extensive scientific expertise. It's a pleasure to work with the team at TSA following their deserved award at the 2021 Rare Reach festival. It's always wonderful working with a talented team that are collectively dedicated to better patient outcomes where there is such unmet need. OPEN Health are committed to providing expert pro bono resources to play a part in making this important and much needed film a success. Our role is to identify and validate the key clinical messages that the film needs to convey and create a script that makes both impact and mobilises healthcare professional into positive change. To enable this we have assembled a team of both scientific experts and project managers to ensure the film is scientifically robust, has the necessary impact and that we deliver on our promise.' Gavin Jones | Global Advisor | Rare Diseases**

The TSA **website** continues to grow and is now available in the German language via a simple flag click. Our presence on **social media** forums such as Facebook, Instagram, Twitter and LinkedIn also show steady growth in supporters. With repeated use of hashtags we were delighted when a new family found us having seen **#CACNA1C** on Rare Disease Day. #TSAwareness21, our first **awareness day** was successfully celebrated on 1st October with many posts shared globally as well as awareness support from Congenica, Rare Revolution and Genetic Alliance UK.



# ACHIEVEMENTS AND PERFORMANCE

## Community

Timothy Syndrome Alliance (TSA) and the Neuroscience and Mental Health Research Institute (NMHRI) hosted online the Brain Research **Conference** online on 25th June 2021. The conference gave over 70 registered attendees 4 hours of the latest insight into *CACNA1C* research delivered by seven leading figures in this field.
A worldwide attendance saw families with TS or *CACNA1C* gene variants and researchers drawn in from as far east as Malaysia to as far west as California.

**"It's a great privilege to be able to host the TSA annual meeting again. These events offer an opportunity for families with this rare disorder to come together from around the globe, make connections and hear about the latest advances in understanding it."**
**Dr Jack Underwood**
**Wellcome Trust GW4-CAT Clinical Research Fellow, NMHRI**

The conference began with a talk from Gemma Wilkinson, who discussed using patient-derived calls to investigate *CACNA1C*. Talks throughout the conference focused on research within *CACNA1C*, including a session from Dr. Underwood, before a concluding discussion from Dr Rebecca Levy. Questions from attendees were taken in between talks, sparking in-depth conversation and constructive interaction between speakers and guests.

**"The Brain and TSA research conference was wonderful, with four hours of the newest research information on CACNA1C and Timothy Syndrome shared. I've waited for years for researchers to study neuronal issues observed in TS in-depth and I'm very pleased with the collaborative efforts now being undertaken with Dr. Jeremy Hall and his associates, Dr. Liz Turnbridge and the Stanford University group."**
**Katherine Timothy**

Dr. Underwood highlighted, "Meeting the families and hearing their thoughts and hopes provides meaning to our research, and is leading to discussions, partnerships and international collaborations among researchers investigating TS and CACNA1C-related disorders."

# ACHIEVEMENTS AND PERFORMANCE

Every session of this conference was **transcribed and translated** into Brazilian Portuguese to ensure the information was accessible to our families.

## Early and accurate diagnosis

TSA has submitted an application via NHS England and NHS Improvement to update the 2021/22 National Genomic Test Directory. The application is to update the nomenclature to include '*CACNA1C*-related disorders' on existing panels and to include *CACNA1C* on a new panel 'Early onset or syndromic epilepsy'.
The Genomics England PanelApp, a publicly-available knowledgebase used by experts throughout the worldwide scientific community relates to genomic tests listed in the NHS National Genomic Test Directory. Clinicians and other healthcare professionals use PanelApp to view and interpret a panel that has been applied to their patient and to look at the evidence for the inclusion of a gene(s) in their patient report during a Multidisciplinary Team (MDT). If successful these changes will make a difference to improving early and accurate diagnosis.

## Research and education

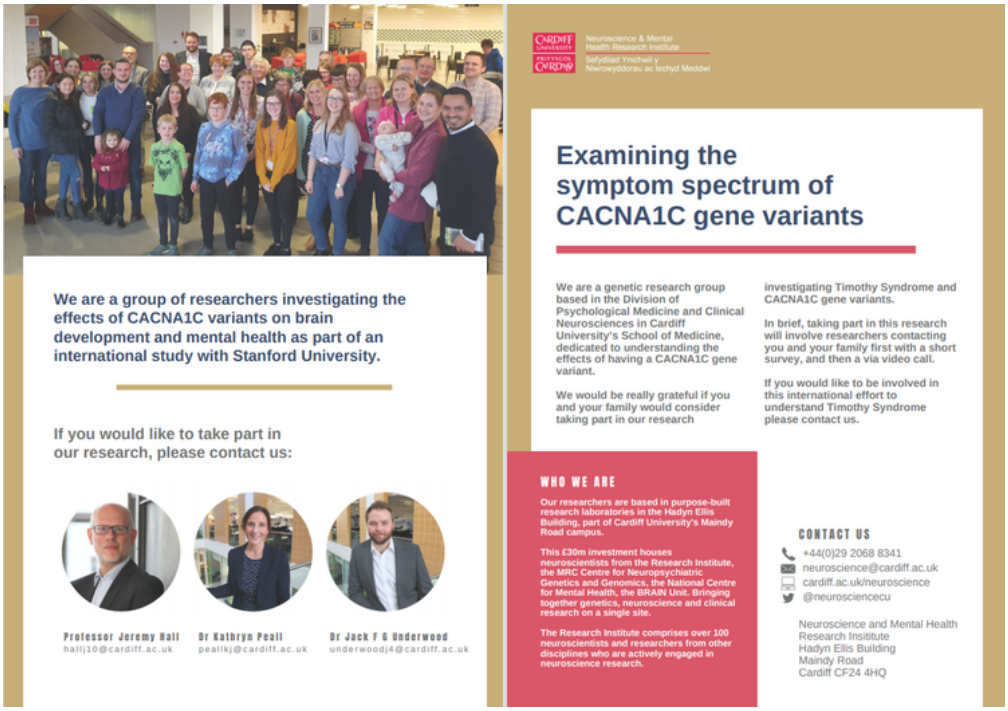
In October 2020 TSA entered The Student Voice Prize, an annual international essay competition that raises the profile of rare disease within the medical field, particularly with medical students, nurses and scientists who may have never come across rare diseases in their training. We worked with our amazing student Zoe who has been a TSA advocate ever since and even translated our website into German. Our German based families have also now worked with Zoe participating in a rare disease neonatology and paediatrics university scheme.
TSA were delighted to be invited by Cambridge Rare Disease Network (CRDN) to take part in the inaugural Patient Group and Industry Partnering event. This event brought together 10-12 rare disease patient groups alongside a similar number of companies working in the orphan drug space with the

# ACHIEVEMENTS AND PERFORMANCE

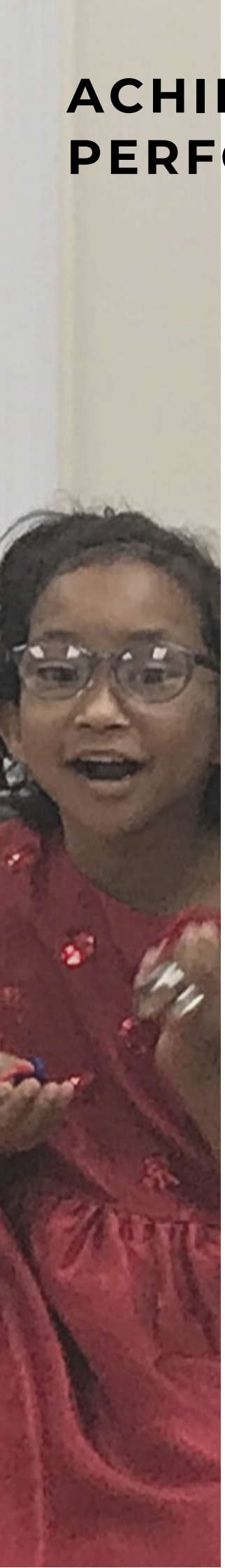
goal of finding new avenues for collaboration between individual companies and patient groups towards the development of new treatments.

A dissertation study looking at the psychosocial impact of living with *CACNA1C*/TS/LongQT8 diagnosis has begun for a MSc Genetic & Genomic Counselling student we are working with at Cardiff University.

Recruitment of *CACNA1C* families has begun for the first international study investigating the effects of *CACNA1C* variants on brain development and mental health (Cardiff University and Stanford University). We look forward to better understanding *CACNA1C* as a result of this collaboration.

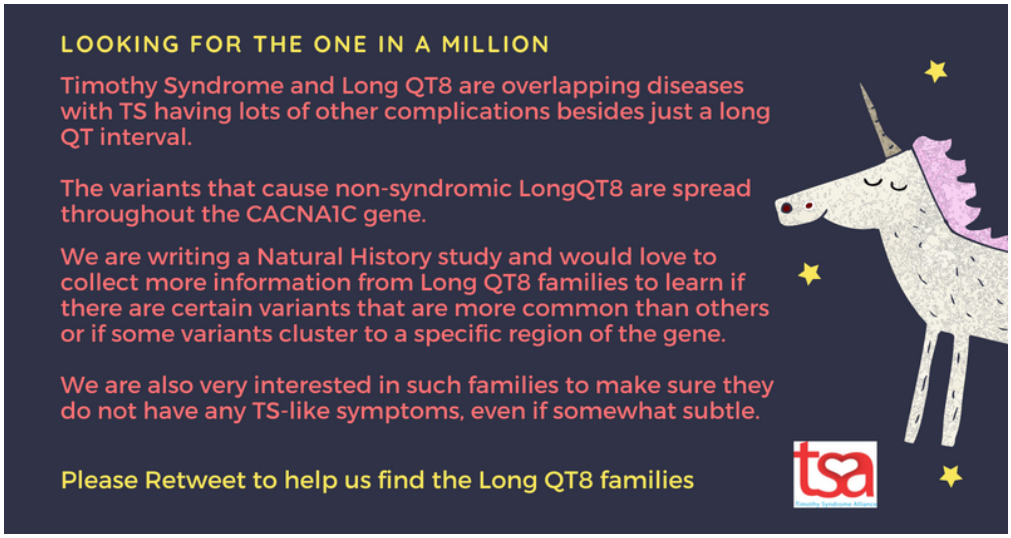



We are working with Cardiff University on The Rare Disease Research Journey project which aims to create a short film with global reach showcasing the importance of public engagement in research, and the research journey from an individual's involvement through clinical research to changes in practice and understanding. The project is a collaboration between the Neuroscience and Mental Health Research Institute (NMHRI) and TSA, with combined academic, charity and public involvement in production.



# ACHIEVEMENTS AND PERFORMANCE

In September we ran a campaign on our social media channels which was successful in signposting new LongQT8 families to our support group.




Published papers of note:

- Bauer, R., Timothy, K. and Golden, A. (2021). Update on the Molecular Genetics of Timothy Syndrome. Frontiers in Pediatrics, 9. https://doi.org/10.3389/fped.2021.668546
- Rodan, L. H., Spillmann, R. C., Kurata, H. T., Lamothe, S. M., Maghera, J., Jamra, R. A., Alkelai, A., Antonarakis, S. E., Atallah, I., Bar-Yosef, O., Bilan, F., Bjorgo, K., Blanc, X., Van Bogaert, P., Bolkier, Y., Burrage, L. C., Christ, B. U., Granadillo, J. L., Dickson, P., … Shashi, V. (2021). Phenotypic expansion of CACNA1C-associated disorders to include isolated neurological manifestations. Genetics in Medicine, 1–11. https://doi.org/10.1038/s41436-021-01232-8

## Support

**'having the TSA Facebook group has helped massively in understanding that we aren't alone in this, and that we all can support each other even at a distance.'**

TSA administrates an online Facebook Support Group for individuals and families of *CACNA1C*-related disorders including Timothy Syndrome and LongQT8, offering 24/7 access to emotional and practical support and information via our families. The benefits of this are huge, enabling:

- meeting and befriending other people with the same rare disease and similar experiences from across the world

# ACHIEVEMENTS AND PERFORMANCE

- learning about the disease
- giving and receiving emotional support
- having a place to speak openly about the disease and one's feelings
- learning coping skills
- feeling empowered and hopeful
- advocating to improve healthcare.

**'like minded people who don't judge and are always there if you have a lot of questions'**

The support group is growing in size as is the spectrum of affectedness as we find more families. Identified previously as a need, TSA began Support Each Other 'drop in' Zooms which were well attended. This support has now progressed to working with Rareminds which is an organisation that specializes in providing counselling and emotional wellbeing services for the rare disease community.

**'Not being alone is a tremendous help.'**

Sometimes other forms of support can help our community. Donations have enabled cardiac equipment – a defibrillator – to be donated to a family and, sadly, contributions have also helped another family towards unexpected funeral expenses for their child.

**'Just beyond wonderful to be connected with other families.'**

## Fundraising

**'I feel seen (you see us as others cannot)'**

Every donation we receive goes to help fund the vital work that we do as a charity.
We:

- support and connect the *CACNA1C* community
- improve *CACNA1C* diagnosis, outcomes and quality of life
- support *CACNA1C* research initiatives

The impact of the pandemic accompanied by low awareness of rare diseases and TSA makes fundraising a challenge however by widening our digital reach and using creative ways to engage audiences we are continuing to connect and

# ACHIEVEMENTS AND PERFORMANCE

actively grow our support base.
We have only one volunteer managing TSA full time which means the amount of time available to specifically fundraise is limited due to the other mission based activities. The generosity of your support has been amazing. Whether it be regular monthly donations, a one off gift, creating a birthday fundraiser on Facebook or sponsorship from running a marathon our heartfelt thanks goes to each and every one of you.

**'TSA is the conduit of all the advances in medical research, care, and quality of life support.'**

Voluntary Receipts 100%

Total income £6084

Charitable Activities 97%

Charity costs 3%

Total expenditure £3226

Special thanks to the following for your support and projects: Limestone Media, the teams at the NMHRI Cardiff University, Department of Psychiatry, Oxford University and Stanford University, OPEN Health and Charity Translators. Dmitry Kran, Zoe Shaked, Bhavna Vadukul and our students Tali Feen, Laurel Mangelsdorf and Raivat Shah from Muhlenberg College.

**The trustees present their report for the period 1 December 2020 to 30 November 2021.**

## TIMOTHY SYNDROME ALLIANCE (TSA)
## TRUSTEES' REPORT General Information

## REGISTERED CHARITY NUMBER: 1185523

TRUSTEES:
Sophie Muir – Chairperson
Galina Gardiner – Treasurer
Meg McLoughlin - Secretary
Nick Muir
Katherine W Timothy (Appointed 14 December 2020)
Andy Golden (Appointed 14 December 2020)
Sally Johns (Appointed 8 September 2021)

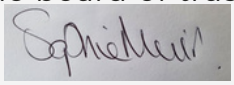
REGISTERED OFFICE:
8 Butt Street, Minchinhampton, Gloucestershire GL6 9JP

**Objectives:** To relieve the needs of those affected by *CACNA1C*-related disorders including Timothy Syndrome and LQT8, their families, friends and carers. Promote greater understanding of the causes, symptoms and treatment. Raise public awareness of the symptoms, needs and related medical conditions.

**Structure, governance and management:** Timothy Syndrome Alliance (TSA) is a registered charity number 1185523, governed by the Charities Act 2006. The charity is a Charitable Incorporated Organisation registered on 27 September 2019 under the Foundation Governing Document. New trustees are appointed by the serving trustees, considering the skills required by the board.

**Public Benefit:** The Trustees confirm that they referred to the Charity Commission's general guidance on public benefit when reviewing the Charity's aims and objectives for the year. Public benefit has been achieved as per the activities outlined in the Achievements and Performance section of this report.
Trustees' responsibilities statement
The trustees are responsible for preparing the trustees' report and the financial statements in accordance with applicable law and United Kingdom Accounting Standards (United Kingdom Generally Accepted Accounting Practice).
The trustees are required to prepare accounts for each financial year, which reflect the receipts and payments of the charity and of the surplus or deficit of income against payments for the year.

**The trustees are responsible for:**
· keeping proper accounting records which disclose with reasonable accuracy at any time the financial position of the charity; and
· safeguarding the assets of the charity and hence for taking reasonable steps for prevention and detection of fraud and other irregularities.
The trustees annual report was approved on 13 July 2022 and signed on behalf of the board of trustees by



Sophie Muir Chair of Trustees

CHARITY COMMISSION FOR ENGLAND AND WALES

| Timothy Syndrome Alliance | 1185523 | CC16a |
|---|---|---|

# Receipts and payments accounts

| For the period from | 01/12/2020 | To | 30/11/2021 |
|---|---|---|---|

## Section A Receipts and payments

| | Unrestricted funds to the nearest £ | Restricted funds to the nearest £ | Endowment funds to the nearest £ | Total funds to the nearest £ | Last year to the nearest £ |
|---|---|---|---|---|---|
| **A1 Receipts** | | | | | |
| Voluntary Receipts | 6084.2 | - | - | 6,084 | - |
| | | - | - | - | - |
| | | - | - | - | - |
| | | - | - | - | - |
| | | - | - | - | - |
| | | - | - | - | - |
| | | - | - | - | - |
| | | - | - | - | - |
| | - | - | - | - | - |
| ***Sub total** (Gross income for AR)* | 6,084 | - | - | 6,084 | - |
| **A2 Asset and investment sales, (see table).** | | | | | |
| | - | - | - | - | |
| | - | - | - | - | - |
| ***Sub total*** | - | - | - | - | - |
| ***Total receipts*** | 6,084 | - | - | 6,084 | - |
| **A3 Payments** | | | | | |
| Cost of Charitable Activities | 3127.8 | - | - | 3,128 | - |
| Governence Costs | 98.6 | - | - | 99 | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| | - | - | - | - | - |
| ***Sub total*** | 3,226 | - | - | 3,226 | - |
| **A4 Asset and investment purchases. (see table)** | | | | | |
| | - | - | - | - | |
| | - | - | - | - | |
| ***Sub total*** | - | - | - | - | - |
| ***Total payments*** | 3,226 | - | - | 3,226 | - |
| ***Net of receipts/(payments)*** | 2,858 | - | - | 2,858 | - |
| **A5 Transfers between funds** | - | - | - | - | - |
| **A6 Cash funds last year end** | - | - | - | - | - |
| ***Cash funds this year end*** | 2,858 | - | - | 2,858 | - |

## Section B Statement of assets and liabilities at the end of the period

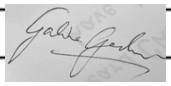
| Categories | Details | Unrestricted funds to nearest £ | Restricted funds to nearest £ | Endowment funds to nearest £ |
|---|---|---|---|---|
| **B1 Cash funds** | Bank balance | 2,843 | - | - |
| | | - | - | - |
| | | - | - | - |
| | ***Total cash funds*** (agree balances with receipts and payments account(s)) | 2,843 | - | - |
| | | Agreement Error | OK | OK |

| | Details | Unrestricted funds to nearest £ | Restricted funds to nearest £ | Endowment funds to nearest £ |
|---|---|---|---|---|
| **B2 Other monetary assets** | | - | - | - |
| | | - | - | - |
| | | - | - | - |
| | | - | - | - |
| | | - | - | - |
| | | - | - | - |

| | Details | Fund to which asset belongs | Cost (optional) | Current value (optional) |
|---|---|---|---|---|
| **B3 Investment assets** | | | - | - |
| | | | - | - |
| | | | - | - |
| | | | - | - |
| | | | - | - |

| | Details | Fund to which asset belongs | Cost (optional) | Current value (optional) |
|---|---|---|---|---|
| **B4 Assets retained for the charity's own use** | | | - | - |
| | | | - | - |
| | | | - | - |
| | | | - | - |
| | | | - | - |
| | | | - | - |
| | | | - | - |
| | | | - | - |
| | | | - | - |

| | Details | Fund to which liability relates | Amount due (optional) | When due (optional) |
|---|---|---|---|---|
| **B5 Liabilities** | | | - | |
| | | | - | |
| | | | - | |
| | | | - | |
| | | | - | |

| Signed by one or two trustees on behalf of all the trustees | Signature | Print Name | Date of approval |
|---|---|---|---|
| |  | Galina Gardiner | 17 March 2022 |