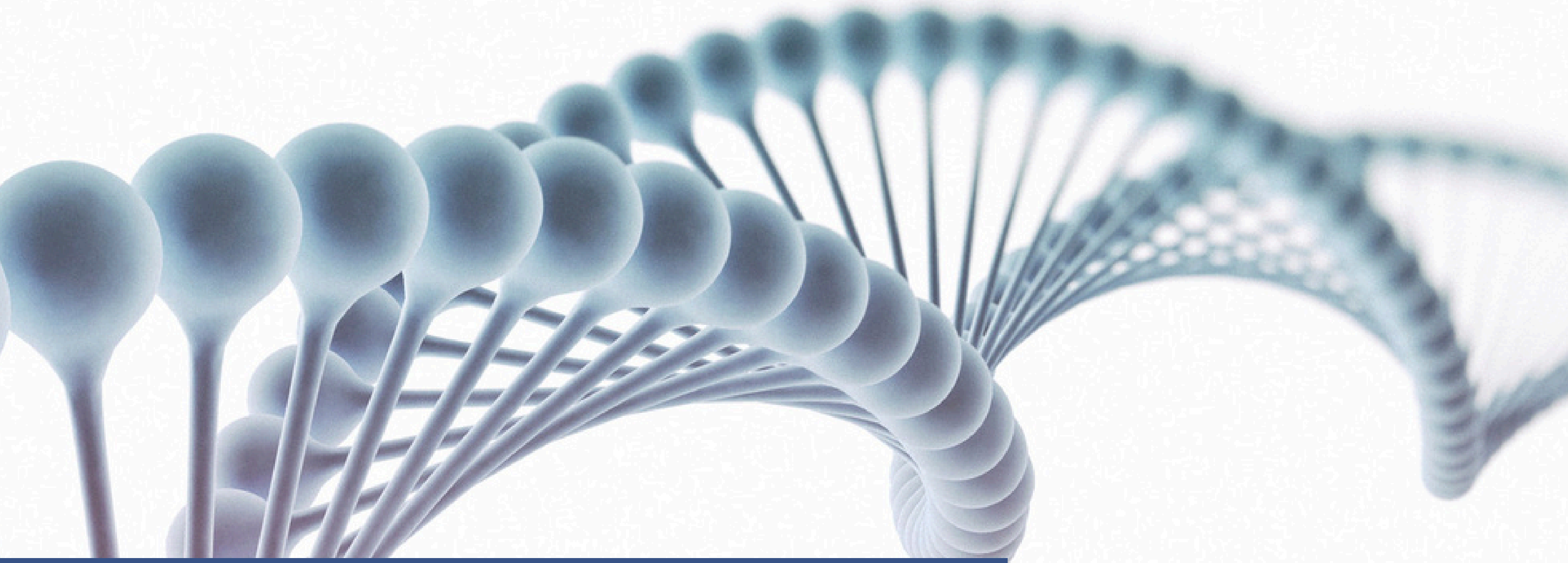
CASK RESEARCH FOUNDATION



End of year trustees report

2024-2025

Table of Contents

Section 1

What is CASK?

CASK is the name of a gene essential for healthy development of the brain. Mutations in this gene cause a range of inherited disorders that all affect brain function, including 'MICPCH' and 'X-linked intellectual disability with or without nystagmus'. To simplify things, we often use the term 'CASK' to describe all disorders.

CASK gene mutations are ultra rare. The brain doesn't grow as it should, giving the child microcephaly (literally meaning 'small head'). Several children show abnormal brain morphology, such as a small cerebellum and pons. Children with a CASK disorder can have a multitude of problems, including intractable epilepsy, inability to feed or drink, inability to walk, low tone, poor balance, global developmental delay, vision and/or hearing loss.

Some affected males have mutations resulting in intellectual disability whilst those males with severe mutations often pass away in infancy. Females with CASK have an unknown prognosis but some are classed as having a life-limiting condition and rely on hospice care.

Most children with CASK cannot communicate other than by crying, smiling or laughing. Caring for a child with CASK is exhausting since many suffer from sleep disturbances. Often, children with CASK cannot play independently due to the inability to control their limbs effectively. The children who are less medically complex can display challenging behaviours due to their low cognitive function.

Who are CASK Research Foundation?

CASK Research Foundation (or CRF) is a UK-wide Charitable Incorporated Organisation (CIO) registered with the Charity Commission in England and Wales.

It was founded in 2022 by Laura Hattersley, BSc, MSc, who is the mother to a child with MICPCH. CRF commenced work as an organisation in March 2022, setting about to create an informative network, connect with researchers and clinicians, create annual family meet ups and fundraise in order to fund scientific research to accelerate the path to treatments. CASK Research Foundation is also known informally as CASK Research UK.

Section 2

This annual report

This Annual Report explains our aims and how we have gone about achieving them.
It has been prepared in accordance with the applicable legal requirements. It gives a balanced view of the charity's structure, aims, objectives, activities and performance. Importantly, it describes our primary sources of funding, and describes how the money was spent.
It highlights the main activities we have undertaken.

.

Section 3

Meeting our legal requirements

We have still prepared our accounts on a "Receipts and Payments" basis as per our obligation. This means that our accounts contain a statement summarising all money received and paid out in the financial year, and a statement of our assets and liabilities at the end of the period.

The detailed legal requirements for this report are set out in The Charities (Accounts and Reports) Regulations 2008 which provide a legal underpinning for many of the recommendations made in the applicable Charities SORP.

The headings used in our report follow this guidance, as follows:

- Reference and administrative details;
- Structure, governance and management;
- Objectives and activities;
- Achievements and performance;
- A financial review;
- Funds held as custodian trustee on behalf of others;
- Public benefit statement.

Section 4

Reference & administrative details

4.1. The Charity's Name

The Charity's name is CASK Research Foundation (informally CASK Research)

4.2. The Charity's Registration Number

The Charity's number is 1197434

4.3. The Address of the Principal Office

The Charity does not own any premises, but operates via a network from their own homes. The Charity's formal legal contact is through the Chief Executive Director, whose name and address are as follows:

Laura Hattersley

33 Finchdean Road, Rowlands Castle,
Hampshire. PO9 6DA

4.4 Names of Trustees

Chief Executive Director
Laura Hattersley, 33 Finchdean Road,
PO9 6DA

Treasurer
Elizabeth Cook, 11 Reedsmere Walk,
Comberbach, CW9 6BZ

Sarah Sanders, 2 Newtown Cottages,
George Street, Staplehurst, TN12 0RA

Andrea Leforte, 12 Pitfold Avenue,
Haslemere, Surrey, GU27 1PN

Section 5

Structure, governance & management

5.1 Particulars of the Governing Document

The Charity has a formal Constitution, which was approved by the Charity Commission in January 2022. The Charity is run by the Trustees, as a management committee. Any new Trustees will be appointed at the Charity's Annual General Meeting,

The Charity operates by means of committee meetings, held on a video-conference basis. The minutes of the meeting are formally recorded by the Secretary.

Section 6

Objectives & activities

6.1 The Purposes of the Charity

CRF was formed in order to primarily accelerate research into CASK gene mutations and the associated conditions.

It is our mission to enable medical advances to improve the lives of people with CASK gene disorders

Our Vision: A world where people with a CASK gene mutation have treatments and ultimately a cure.

6.2 Activities Undertaken 1 April 2024- 31st March 2025

1. CASK RARE-X Data Collection Programme.
2. European expansion
3. Family support
4. Gift of £40,000
5. Completion of research projects
6. Conferences and events
7. Awareness
8. Mental health support
9. Won £21,000 worth of pro-bono work from Costello Medical
10. Creation of the Kicking CASK podcast
11. Assisting in drug discovery for cerebellar degeneration
12. Created Kicking CASK shop – raise awareness and raise funds

6.2.1 RARE-X DCP

The CASK RARE-X Data Collection Programme - a patient owned, free, secure, streamlined, international registry. This is an initiative delivered by Global Genes. We now have over 140 patients registered from 21 countries (up from 120 last reporting year). See section 7.4 for more detailed information.

6.2.2 Expanded into Europe

We currently have two Polish volunteers and 1 volunteer resident in Ireland. We have our CASK Fast Facts leaflets translated into German and Polish.

6.2.3 Family Support

We continue to offer monthly virtual socials, regular newsletters and an annual family meet up in the UK. In July 2024 we organised the first ever International CASK Family meeting where expert clinicians gave talks and answered parents' questions. This was attended by over fifty families.

6.2.4 £40,000 gift

We gifted £40,000 to University of Bristol to enable Professor Hodge's work on creating a translational platform for CASK disorders to continue. The team continue to apply for grants to help fund this. The gift has also enabled the creation of the CASK clinical registry, sponsored by University of Bristol. This will enable patient data to be collected and analysed by NHS clinician Dr Amin for at least the next three years.

6.2.5 Completion of Research

- Cambridge University completed their study on 'The neurodevelopmental spectrum of CASK-related disorder' which was instigated and recruited for by CRF. 31 patients took part. It is currently waiting publication in a peer-reviewed journal.
- Bristol University GenROC study to improve understanding of how rare genetic syndromes affect the way children grow, their physical health and their development. 11 CASK patients took part in this study.

6.2.6 Conferences and events

- ·Founder Laura Hattersley attended GW4 meetings on epilepsy and neurodevelopmental disorders, and presented at them.
- Founder Laura attended the CLCN4 conference in order to network and learn more about the conference process.

6.2.7 Awareness

- Improved awareness of CASK gene disorders by speaking at conferences, networking, maintaining and updating website and creating summaries of scientific papers, making complex research accessible to parents, carers and supporters.
- Our CASK Gene Awareness Day (July 15th) campaign was well supported and followed.
- We also took part in Rare Disease Day 2025 and designed conversation starting T shirts for the global community.

6.2.8 Mental Health support

·We have partnered with the charity Rare Minds to offer our community mental health support specifically designed for people living with a rare disease. With the assistance of Rare Minds we created a survey for UK families, to assess the mental health impact of caring for someone with a CASK-related disorder.

6.2.9 Costello Medical

·We won a contract to receive £21,000 of pro-bono work from the health company Costello Medical. They are creating an infographic for the community to share insights from the RARE-X data collection platform. The aim of this project is to feedback information to caregivers in visually appealing ways as well as improve uptake of the RARE-X DCP. The results will be shared with the community on July 15th,

6.2.10 Podcast creation

Laura started a podcast called the Kicking CASK Podcast as a way to easily share updates with the global community, build community and bring about more support. It is aired on YouTube and Spotify.

6.2.11 Supporting Dr Tabuchi

A Japanese scientist, Dr Tabuchi, has found out more about the cerebellar cell death (in animal models) and has found a mechanism to prevent it. We have been helping him find a way to develop this discovery into a viable therapeutic.

6.2.12 The Kicking CASK Shop

·CASK Research partnered with TeeMill, a sustainable online retailer, to deliver CASK and general additional needs merchandise to the community. Profit margins are minimal however it is bringing a regular trickle of revenue.

6.3 Statement of compliance

The Trustees are in agreement that the CIO is a public benefit entity, complying with the definition in FRS 102.

Section 7

Achievements and performance

7.1 Our main missions and aims

It is our mission to advance the education on the CASK gene and its disorders. We achieved this aim by assisting with the Cambridge university research study as well facilitating the growth of the RARE-X DCP and sharing findings with the community by our partnership with Costello Medical.

Another aim is to promote and protect the physical and mental health of UK sufferers. Partnering with Rare Minds and having monthly virtual socials enables us to provide some mental health support to families.

7.2 Our mission to support and provide advice

We have achieved this by:
- Improving our informative website.
- Holding a family meet up day in September 2024.
- Creating and facilitating the creation of information guides.
- Holding the family conference in July 2024. This helped educate and inform parents and provide answers.
- A bi-monthly newsletter.
- Holding a UK registry purely for collecting contact details and a patient count.

7.3 Mailchimp

The Mailchimp account was created in June 2022. We now have 198 subscribers. We send out a monthly newsletter. This has an average opening rate of 56% based on information from Mailmodo (https://www.mailmodo.com/guides/mailchimp-open-rate/), 21% classed as a 'good' opening rate for a newsletter.

222

mailchimp subscribers. 12% increase in 12 months

56%

Average opening rate for monthly newsletter

38

No. of UK patients officially registered in the UK registry

144

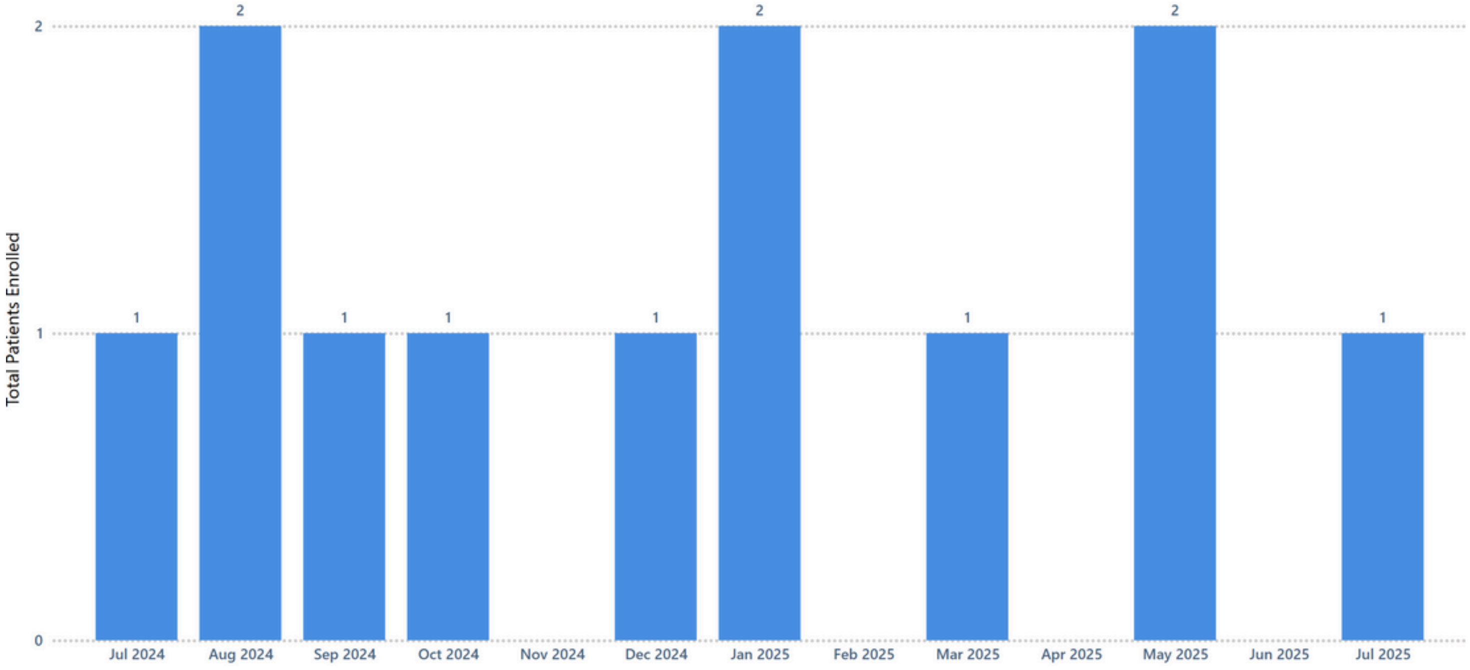
international members of the Global CASK Registry RARE-X

7.4 RARE-X DCP

The CASK RARE-X Data Collection Programme was officially launched in early September 2022 by CRF. We now have over 140 participants signed up and answering surveys.

The registry is international and RARE-X are rolling out more languages every year.

There are now four CASK non-profits working with the CASK RARE-X data collection programme: Association Enfants CASK France; Angelina CASK Neurological Research Foundations, Project CASK and CASK Research Foundation.



7.4.1 Quality of data

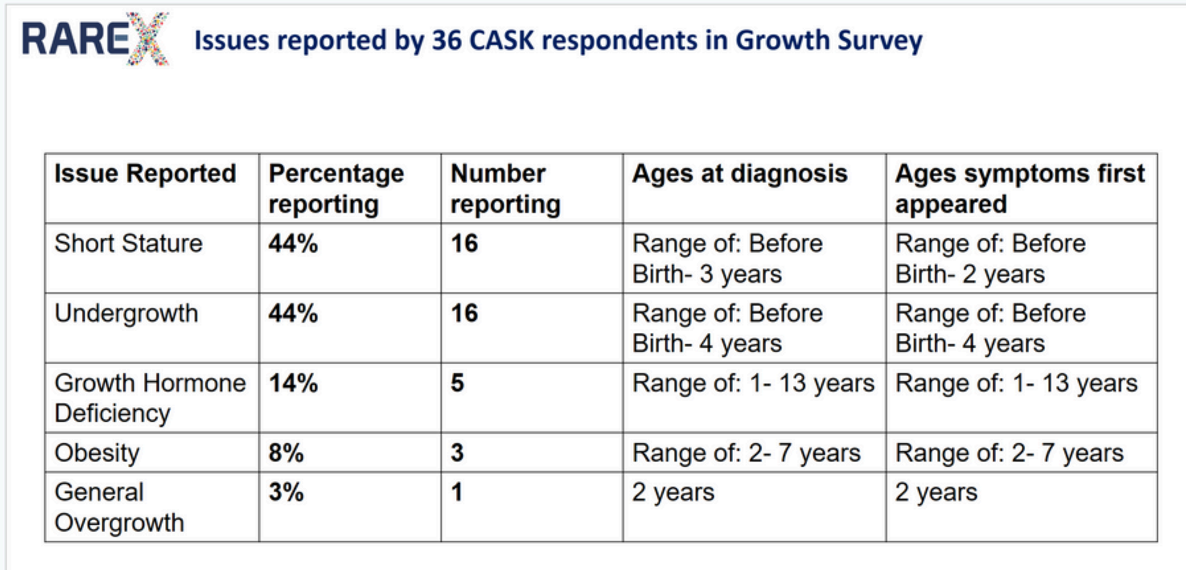
We now have a substantial registry however the completion or initiation of surveys can be very low. This is why we asked Costello Medical to look into this and create an infographic to help parents see the value in the data.

7.4.2 Data obtained

Only verified researchers and clinicians are able to gain access to the entire data sets. As a PAG leader and having completed the CITI compliance training our Director Laura has access to basic data sets that are sporadically delivered out by RARE-X. Even this simple data provides the opportunity to help improve patient care, educate and facilitate advocacy on behalf of ones child.

Example 1: Question from a parent on a Facebook group

"We had an appointment yesterday with XXs genetic doctor and he’s asked me if all/most of our kids have Microcephaly and are below the average weight Centile for their age. Are any of our CASK kids on any kind of steroids for their growth hormones as he is really wanting XX to start them but I am still in two minds..."



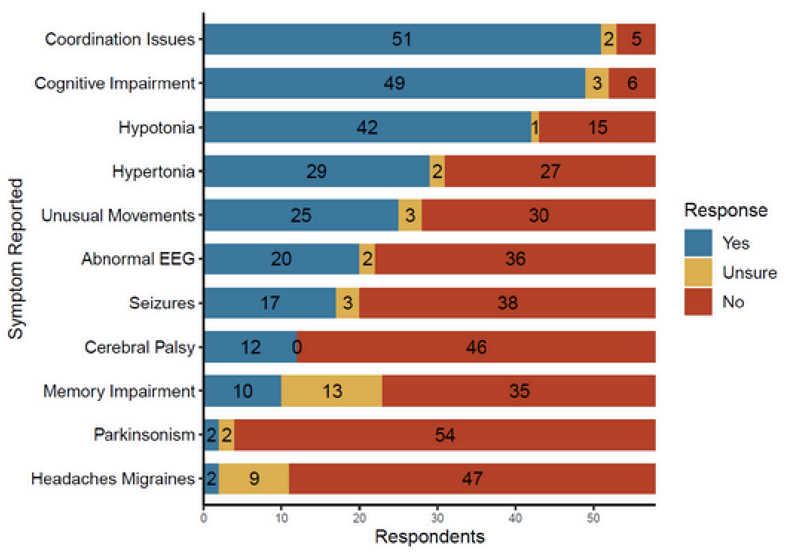
RAREX **Issues reported by 36 CASK respondents in Growth Survey**

Issue Reported	Percentage reporting	Number reporting	Ages at diagnosis	Ages symptoms first appeared
Short Stature	**44%**	**16**	Range of: Before Birth- 3 years	Range of: Before Birth- 2 years
Undergrowth	**44%**	**16**	Range of: Before Birth- 4 years	Range of: Before Birth- 4 years
Growth Hormone Deficiency	**14%**	**5**	Range of: 1- 13 years	Range of: 1- 13 years
Obesity	**8%**	**3**	Range of: 2- 7 years	Range of: 2- 7 years
General Overgrowth	**3%**	**1**	2 years	2 years

Rather than relying on Facebook and reporting unverified information back to a clinician, this parent could now show their geneticist this table of offical results from 36 respondents.

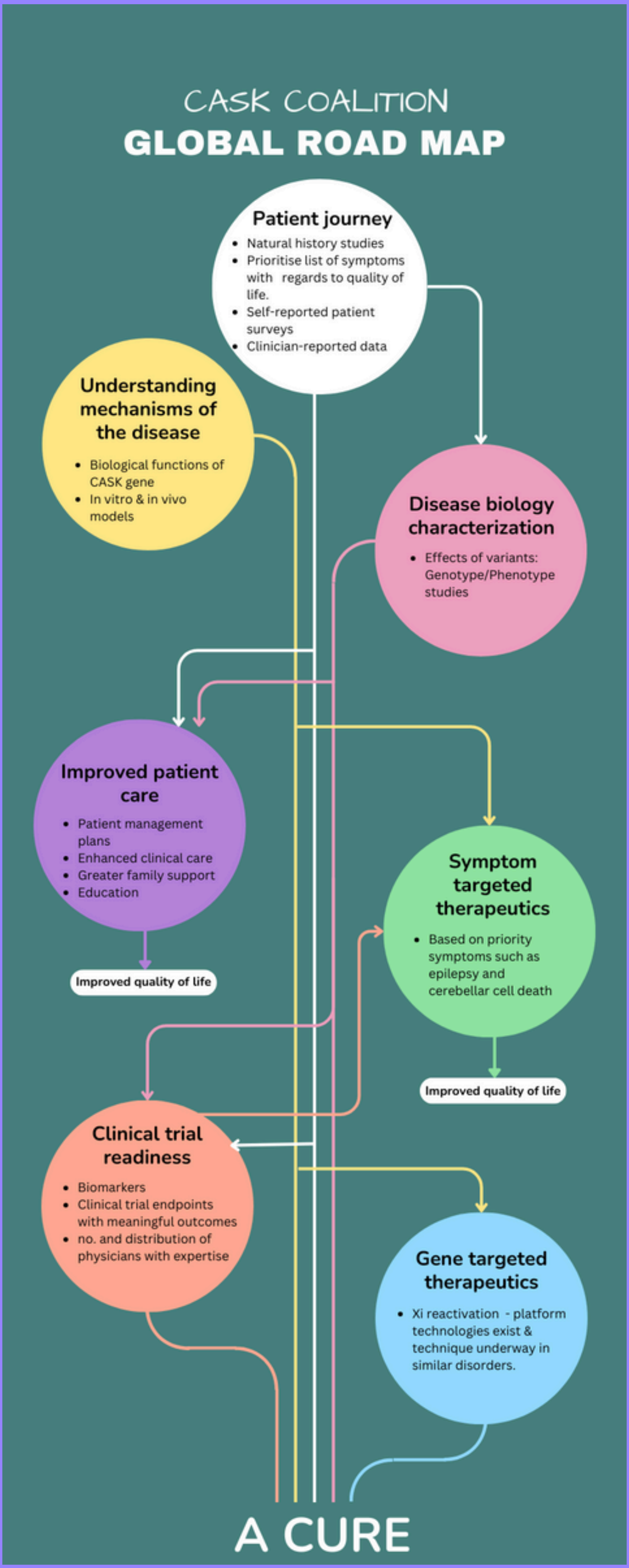
Example 2: Epilepsy incidence

"The published prevalence of epilepsy is as high as 50% (cohort of 34). Our current findings show a lower prevalence (29%). A larger data set, properly analysed, will help us understand occurrance rates better.



Issues reported by 58 CASK Gene Mutations respondents in the Brain and Nervous System Domain

7.5 CASK Coalition Road map



CASK COALITION
GLOBAL ROAD MAP

Patient journey
- Natural history studies
- Prioritise list of symptoms with regards to quality of life.
- Self-reported patient surveys
- Clinician-reported data

Understanding mechanisms of the disease
- Biological functions of CASK gene
- In vitro & in vivo models

Disease biology characterization
- Effects of variants: Genotype/Phenotype studies

Improved patient care
- Patient management plans
- Enhanced clinical care
- Greater family support
- Education

Improved quality of life

Symptom targeted therapeutics
- Based on priority symptoms such as epilepsy and cerebellar cell death

Improved quality of life

Clinical trial readiness
- Biomarkers
- Clinical trial endpoints with meaningful outcomes
- no. and distribution of physicians with expertise

Gene targeted therapeutics
- Xi reactivation - platform technologies exist & technique underway in similar disorders.

A CURE

CASK families
- **RARE-X** Registry
- CASK Coalition patient surveys
- US patients - Citiizen & CRID
- Enrollment in studies

Understanding mechanisms
- UK Pilot grants available
- **CURE CASK campaign** will result in in vivo and in vitro models, available to all

Understanding the genetics
- **RARE-X** collecting Genotype and phenotype data
- Bristol University investigating relationships

Patient care
- **RARE-X** data enabling greater understanding of symptoms and prognosis
- Cambridge BINGO study to enhance understanding of behaviour and emotions

Targeting symptoms
- Ongoing project with the **Mukherjee lab** funded by ACRNF Australia
- UK Pilot grants available

Clinical trials
- Detailed natural history studies using RARE-X data plus, for example, Citiizen
- Physician/expertise list from Coalition countries

Targeting the gene
- UC Davis ready to start Xi reactivation on CASK. The **CURE CASK campaign** is raising money to initiate this.
- UK Pilot grants available.
- Alternative avenues yet to be elucidated due to inadequate knowledge of gene and protein.
- Platform technologies not yet established for CASK e.g. protein replacement, gene replacement, mRNA therapy.

CASK COALITION
United for our CASK warriors

The CASK Coalition prioritises the neglected aspects of the Roadmap. These include the longterm, detailed patient journey, improving quality of life, clinical trial readiness and gene targeted therapeutics. There is global, increasing and diverse research on the CASK gene, its mechanisms and its role in disease. What is lacking is translational research with an end point of a treatment.

The Global Roadmap was created and agreed by all members of the CASK Coalition. In 2023/24 the CASK Coalition acted on all sections of the Roadmap, either by funding projects or by improving the Patient Data Collection Programme uptake. All members are committed to the Roadmap and use it to direct their actions and funding.

Section 8

Financial Review

8.1 The Reporting Period for this Report

The Charity's financial performance reported below is for the period from 1st April 2024 to 31st March 2025.

8.2 Our Accounts and Bankers

The charity operates using only one bank account as follows:
Natwest Bank
Account Name: CASK Research Foundation
Sort Code: 52-41-20
Account Number: 43690068

8.3 Financial Performance: Receipts and Payments, and Assets and Liabilities

We have prepared our accounts on a "Receipts and Payments Accounts" basis, which means that we have recorded cash flows in and out during the accounting period. The data has been transferred from the Charity's internal spreadsheet onto a standard Charity Commission Form CC16a.

8.3 cont.

The Charitable Incorporated Organisations Regulations 2012 do require the following additional information:
a) particulars of any guarantee given by the CIO, where any potential liability under the guarantee is outstanding at the date of the statement of assets and liabilities; and b) particulars of any debt outstanding at the date the statement of assets and liabilities which is owed by the CIO and which is secured by an express charge on any of the assets of the CIO

Section A of the form presents the receipts and payments, disaggregated into the Charity's main areas of activity. A1 shows these receipts; A3 shows these payments.

Section B presents the Statement of Assets and Liabilities at the End of the Period. We have no fixed or material assets of any significance. We have no property assets. The financial assets of the Charity are therefore the current funds in our Natwest Account, and that is the only account we hold.

The Examiner has agreed that the Natwest account accurately expresses the assets of the Charity, as the influence of these future sums is minor in respect of the total turnover, and the profitability of the Charity.

CHARITY COMMISSION
FOR ENGLAND AND WALES

Charity Name	No (if any)
Cask Research UK	1197434

Receipts and payments accounts

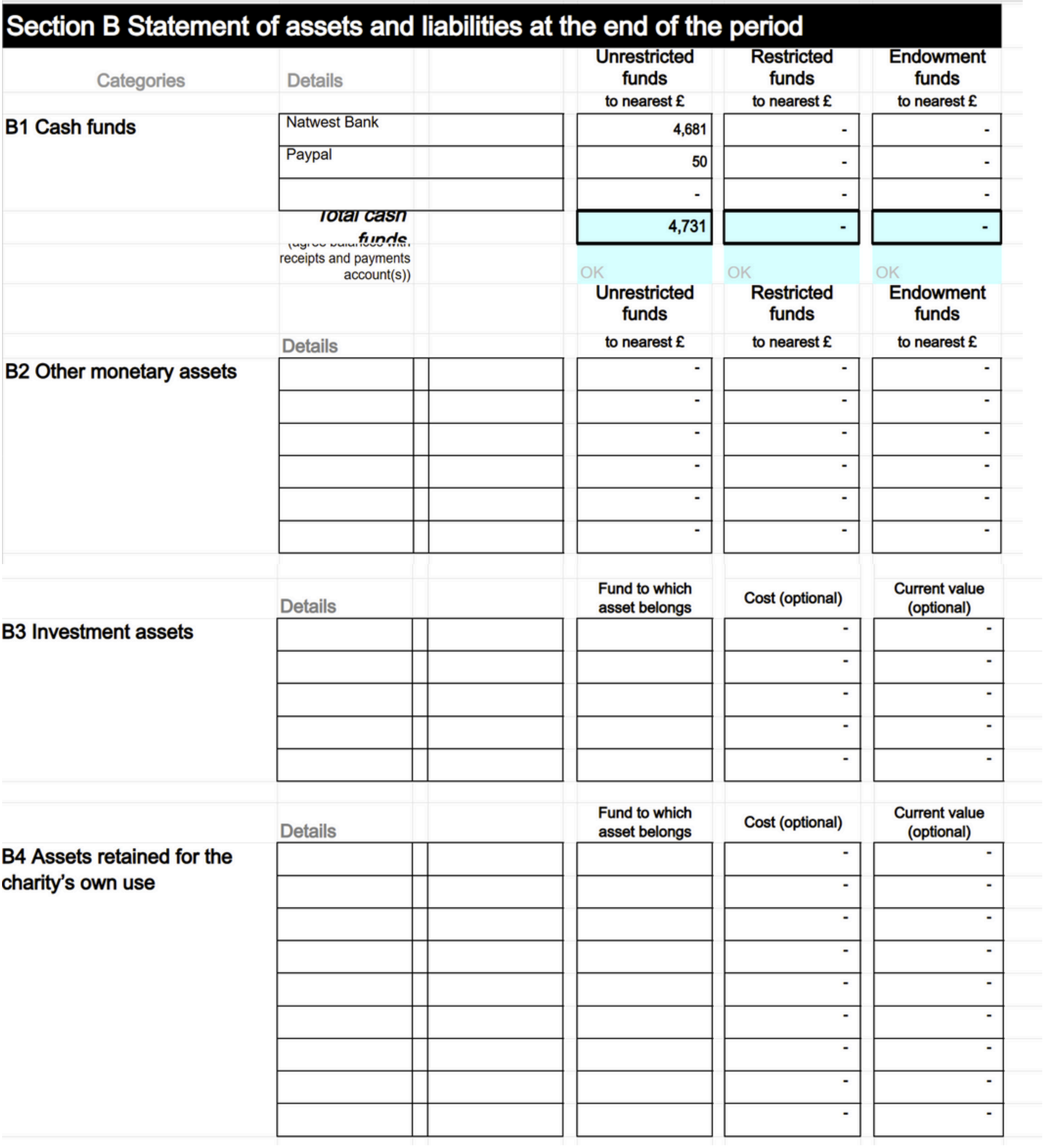
CC16a

For the period from	Period start date	To	Period end date
	4/1/2024		3/31/2025

Section A Receipts and payments

	Unrestricted funds	Restricted funds	Endowment funds	Total funds	Last year
	to the nearest £	to the nearest £	to the nearest £	to the nearest £	to the nearest £
A1 Receipts					
	-	-	-	-	-
Sales	-			-	338
Donations	4,632			4,632	783
Donations - Fayres				-	133
Donations - PayPal	1,302			1,302	3,008
Donations - Facebook				-	2,991
Donations - Amazon				-	88
Donations - Sponsored events	14,356			14,356	9,422
Donations - Bingo	2,199			2,199	1,439
Donations - Coffee Morning	1,241			1,241	
Donations - Advent Trail				-	803
Donations - Raffles				-	721
Donations - CAF	7,507	-	-	7,507	7,499
Donations - Open Gardens	200	-	-	200	10,377
Donations - Easy Fundraising	158	-	-	158	326
Donations - Merchandise	20	-	-	20	221
Donations - Wills	100	-	-	100	6,000
Donations - Art Auction	6,609	-	-	6,609	-
Donations - Golf day	905	-	-	905	-
Sub total *(Gross income for AR)*	39,229	-	-	39,229	44,148
A2 Asset and investment sales, (see table).					
	-	-	-	-	
	-	-	-	-	-
Sub total	-	-	-	-	-
Total receipts	39,229	-	-	39,229	44,148
A3 Payments					
Grants Given - UC Davies Cure Cask	-	-	-	-	23,373
Grants Given - University of Bristol	65,000			65,000	
Cost of Sales	7,517	-	-	7,517	269
Materials				-	180
Subcontractor Costs				-	150
CASK Meet ups				-	-
Documentary Costs				-	1,950
Licenses and Permits	-	-	-	-	20
Advertising and Promotion	379	-	-	379	1,710
Legal and Professional Fees	-	-	-	-	50
Subscriptions	581	-	-	581	604
Bank/Finance Charges	-	-	-	-	28
Insurance	96	-	-	96	96
Miscellaneous	3	-	-	3	1
Sub total	73,576	-	-	73,576	28,429

A4 Asset and investment purchases, (see table)					
	-	-	-	-	
	-	-	-	-	
Sub total	-	-	-	-	-
Total payments	73,576	-	-	73,576	28,429
Net of receipts/(payments)	- 34,347	-	-	- 34,347	15,719
A5 Transfers between funds	-	-	-	-	-
A6 Cash funds last year end	39,077	-	-	39,077	23,358
Cash funds this year end	4,731	-	-	4,731	39,077



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	Natwest Bank	4,681	-	-
	Paypal	50	-	-
		-	-	-
	Total cash funds	**4,731**	**-**	**-**
	(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				-	-
				-	-
				-	-
				-	-
				-	-
				-	-
				-	-
				-	-
				-	-

B5 Liabilities

Details		Fund to which liability relates	Amount due (optional)	When due (optional)
			-	
			-	
			-	
			-	
			-	

Signed by one or two trustees on behalf of all the trustees	Signature	Print Name	Date of approval
		Laura Hattersley	24/07/2025
		Liz Cook	24/07/2025

8.3 Cont.

The accounts have been scrutinised by an independent accountant holding ACCA status. The Examiner concludes that there are no material matters of concern, and that the accounts were prepared in accordance with section 130 of the relevant Act.

8.4 Policies on Reserves

Our current position is that we seek to hold a minimum bank balance of £1500. We have minimal overheads and so this provides a more than sufficient buffer to allow us to undertake our activities, and to pay our suppliers and fees promptly. It is the Charity's view that such a minimum balance would have been more than sufficient to meet our obligations. This value has been based on analysis of the previous years incomings. This is highlighted in our Finance Policy.

8.5 Funds in Deficit

We do not have any funds in deficit. Our only funds are, as has been described, held in the Natwest account. This is in healthy surplus, as the charity is currently saving these funds in order to pay for the projects and future plans as outlined in section 11.

Section 9

Funds held as custodian trustee on behalf of others

CRF does not hold any assets in respect of other charities.

Section 10

Public benefit statement

We believe we have complied with the duty to have due regard to the guidance on public benefit published by the commission in exercising their powers or duties.

Section 11

Plans for the future period

Below we set out that we wish to undertake the following activities in the financial year 2025/2026:

- Continue to raise funds and create a 2nd research grant of £40,000.
- Apply to the Charities Commission to enable the charity to act as advocates between families and medical professionals.
- Assist with the creation of the UK clinical database in association with University of Bristol and the NHS
- Coordinate collaboration between European clinicians setting up their own patient databases, to ensure uniformity.
- Roll out the Global CASK Census, in collaboration with partner PAGs.
- Provide mental health support to the UK community
- Hold the annual CASK family meet up

Section 12

Signed statement

I, Laura Hattersley, hereby sign this Annual Report as a true record of the activities of the Charity for the year from 6th April 2024 - 5th April 2025

Signed: ....

Name: Laura Hattersley
Position: Chief Executive Director, CASK Research Foundation

Date: 16/7/2025.....
Having been duly authorised to do so by the Trustees of the Charity.