



CASK
RESEARCH FOUNDATION

End of year report

2022-2023



Table of Contents

01

What is CASK
What is CASK
Research
Foundation

02

This annual
report – general

03

Meeting our legal
requirements

04

Structure,
governance and
management

05

Objectives and
activities

06

Achievements
and performance

07

Financial review

08

Public benefit
statement

09

Plans for future
periods

10

Signed stateent

11

Your section
titles go here

12

Your section
titles go here

Section 1

What is CASK?

CASK is the name of a gene essential for healthy development of the brain. Mutations in this gene cause two disorders: 'MICPCH' and 'XL-ID with or without nystagmus'. To simplify things, we often use the term 'CASK' to describe either disorder.

CASK gene mutations are ultra rare. The brain doesn't grow as it should, giving the child microcephaly (literally meaning 'small head'). Children with CASK can suffer from 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.

Male infants with CASK generally pass away within the first few years of life. Females with CASK have an unknown prognosis but many 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 most suffer from sleep disturbances.

Many 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.

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

Because our income lies between £25,000 and £250,000, we have prepared our accounts on a "Receipts and Payments" basis. 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 year.

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

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

Secretary
Nicole Poole, 47 Elm Drive, Hove, BN3 7JA

Emily Richards, 16 Magdalen Drive,
Evesham, 26/6/84

4.4 Cont.

Grants advisor
Rachel Manktelow, 71 New Wokingham
Road, RG45 XXXXXX

Sarah Sanders, Cross at hand farm
Cottage, Maidstone Rd, TN12 ORJ

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 The Main Activities Undertaken

Since our establishment, we have:

- Created a Scientific Advisory Board of experts in the field of neurodevelopmental disorders
- Created a Research Review Committee
- Established CASK Coalition in partnership with Angelina CASK Neurological Research Foundation and Association Enfant CASK France
- Established the CASK Rare-X Data Collection Programme. This is an initiative delivered by Global Genes. We currently have over eighty patients registered internationally.
- Joined UK Rare Epilepsies Together (UKRET) network and attended a conference as a member of this network
- Liased with the charity Unique to enable the first ever disorder guide to be written for families.

6.2 Continued

- Developed patient leaflets to raise awareness of CASK
- Created a website
- Raised over £25,000 in fundraising;
- Joined a charity mentoring programme led by Beacon;
- Facilitated a research study into a patient with a CASK gene mutation
- Held several webinars for the international community
- Assisted in the creation and promotion of CASK coalition's first annual fundraiser – CASK Race for Research
- Held a CASK family meet up
- Committed to the CURE CASK campaign
- Got the CASK gene included in the BINGO project

6.2.1 Created an SAB

Our Scientific Advisory Board currently consists of:

- Dr Sam Amin – consultant paediatric neurologist
- Professor Kerstin Kutsche – Geneticist
- Dr Catherine Tuffrey – paediatrician

We are hoping to continue to expand this board.

6.2.2 Research Review Committee

Our Research Review Committee advises us on funding proposals along with any member of the SAB who wishes to.

- Dr Lucy Robinson PhD – founder of Insight Editing (handed notice in January 2023)
- Dr Jessica Tamamini (handed notice in January 2023)
- Dr Isabel Zwart – Director Regulatory CMC at AstraZeneca
- Magda Ellis ???

6.2.3 Founded CASK Coalition

The CASK coalition was established in June 2023 in order to formalise the partnerships between three CASK research charities: CRF, Angelina CASK Neurological Research Foundation (Australia and USA) and Association Enfants CASK France. We hold shared aims and objectives and share workload and skills in order to improve efficiency.

6.2.4 RARE-X DCP

The CASK RARE-X Data Collection Programme – a patient owned, free, secure, streamlined, international registry. We now have over eighty patients registered from 21 countries. See section 7.4 for more detailed information.

6.2.5 Joined UK RET

UK Rare Epilepsies Together (UK RET) brings together like-minded charities and support groups in the UK to see how we might work more collaboratively to support rare and complex epilepsy communities on a national scale. CRF founder Laura attended the Rare Epilepsies Conference in March 2023.

6.2.6 Unique pamphlet

The charity Unique provides specialist information on rare chromosome and gene disorders. Following contact from our Director Unique created a pamphlet that parents can be directed to following diagnosis.

6.2.7 Family leaflets

CRF's family leaflets on CASK have proven extremely popular (over twenty personalised pamphlets created) within the CASK community. We identified a need for some literature to educate their friends and families on their child's rare disease. We offer to personalise the leaflets with a photo of their child. We created these also for our CASK Coalition partners.

Flyers have also been created to go alongside fundraising pots as well as detailed fundraising booklets. All materials are created free of charge by our director using the CANVA professional software which is free for registered charities.

6.2.8 Created website

The CRF website www.caskresearch.org delivers information to families and researchers. It was created by Laura Hattersley, CRF's director, in combination with a generous donation that allowed funding of a web developer to professionalise it.

6.2.9 Raised £xxxxx

CRF have been fortunate to have been the recipients of many fundraising activities during 2022–2023. We have worked hard on fundraising campaigns and our social media presence.

6.2.10 Beacon mentoring programme

Our Director Laura is currently on the Beacon mentoring scheme and is being mentored by a business manager of the charity LifeArc.

6.2.11 Facilitated a research study

We were contacted by a foreign parent whose child has unusual and alarming symptoms. We share their story with Professor Kerstin Kutsche who was keen to study the case. The research is ongoing.

6.2.12 Webinars

We have so far held three webinars for the international community: RARE-X and how this programme can benefit our community; UC Davis and X reactivation of X-linked genes; Kerstin Kutsche and the genetics of CASK including a Q&A.

6.2.13 Race for Research

As members of the CASK Coalition, we helped create a fundraising platform for an international fundraiser..

6.2.14 Family meet up

We held a family meet up at Worcester Snoozelen in 2022 and in 2023 we have Camp Mohawk booked for September 9th.

6.2.15 CURE CASK

Shortly after our creation we were contacted by ACNRF about a proposal from UC Davis. Their research aims to reactivate the CASK gene on the silenced X chromosome. The proposal was peer reviewed by four scientists with an understanding of either the CASK gene and/or the epigenetic technique/theory. These peer reviews were then read by our Research Review Committee who suggested to our Board that it was a project worth funding. This information was fed back to our partner organisations AECF and ACNRF. This culminated in the

6.2.15 CURE CASK cont.

This culminated in the creation of a memorandum of understanding stating that CRF will raise awareness of this project and attempt to raise funds for it. The success of the fundraising project named CURE CASK will be re-evaluated on April 2024. We created a separate fundraising platform to identify funds a donor specifically wants to go towards this campaign.

6.2.16 BINGO project

The BINGO project is run by the University of Cambridge. It brings together developments in genetics, psychology, and brain sciences. The researchers want to understand the range of problems that affect individuals with neurodevelopmental disorders, after a rare genetic cause has been found. They also want to understand how genetic differences affect brain function. In future, the information they gather might make it easier to support people with neurodevelopmental conditions, because they will have a better understanding of which patterns of difficulty are associated with each cause, and why these patterns of difficulty occur.

6.3 Statement of compliance

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

Section 7

Achievements and performance

7.1 Our main mission and aim

It is our mission to enable medical advances to improve the lives of people with CASK gene disorders. This is a long term goal and will take some time to accomplish. Whilst we have not achieved this mission at this early stage we are making good headway towards raising awareness within the scientific community and facilitating research.

Our aim is to accelerate research into CASK gene mutations and the associated conditions. We have achieved this aim this year (see 6.2.1; 6.2.11; 6.2.16) and have a number of potential or upcoming projects to build on this including:

- an upcoming meeting with Dr Kate Baker, Cambridge University, on a CASK specific study
- meetings with Harvard/Boston's Childrens Hospital regarding our collaboration
- Meeting with Andrea Cerase on X-reactivation
- Increasing our registration numbers with RARE-X
- Building our own UK contact registry
- Potential PhD (funded by the Bristol University) into CASK gene disorders

7.2 Our mission to support and provide advice

We have achieved this by:

- creating our informative website and keeping it updated
- Held a Family meet up day in 2022 with another planned in Sept 2023
- Created and facilitated the creation of information guides (see 6.2.6 & 6.2.7)
- Held webinars (6.2.12) to help educate and inform parents and provide answers
- Created a map of UK families to reduce feeling of isolation and facilitate socialising.

7.3 Engaged Members

Currently CRF does not have a formal 'membership' structure for the charity and uses polls on the UK Facebook support group to communicate

In the next 12 months we want to create a formal 'free' membership system with can act as a simple registry in order to collect more accurate and trusted data on UK disease prevalence as well as creating an additional mailing list to our Mailchimp newsletter.

7.3.1 Mailchimp

The Mailchimp account was created in June 2022. We now have 153 subscribers. We send out a monthly newsletter. This has an average opening rate of 70.1%. Based on information from Mailmodo (<https://www.mailmodo.com/guides/mailchimp-open-rate/>), 21% is a good opening rate for a newsletter.

153

mailchimp subscribers

70%

Average opening rate
for monthly newsletter

33

No. of UK patients,
based on Facebook
poll by CRF

82

international members
of the DCP

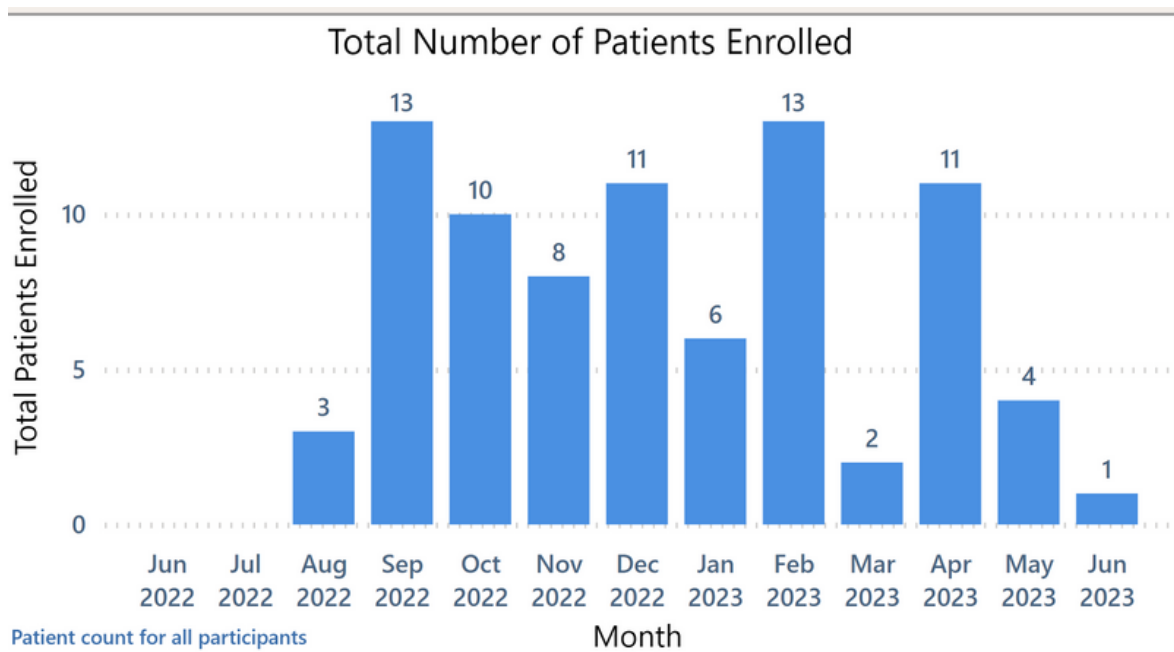


7.4 RARE-X DCP

Readers appreciate accurate information

The CASK RARE-X Data Collection Programme was officially launched in early September 2022. We now have over 80 participants signed up and answering surveys.

The registry is international and, although currently in English, RARE-X are rolling out more languages. This will enable us to focus on countries where data is lacking such as Germany and Spain.



7.4.1 Patient enrollment increases when we do a big social media drive or directly contact parents.

RARE-X held the Open Science Data Challenge which launched in May 2023. Initially there was a deadline of December to register onto the DCP. We promoted this deadline and successfully got 11 more patients enrolled. An extended deadline was then given for February 28th, which we again promoted on social media, leading to 13 more enrollments. In April we contacted a large number of families and asked them to register – this led to 11 more families.

We will be holding a webinar in September 2023 on our findings from the DCP and will use this as our next big deadline to try and reach 100 families. UK families currently stand at 17, which is 50% of known families. We have found that by having a successful registry we are garnering interest from researchers.

Country	Patient Count	Percent of Global Patients
Albania	1	1.2%
Argentina	1	1.2%
Australia	4	4.9%
Brazil	1	1.2%
Canada	3	3.7%
Chile	1	1.2%
France	8	9.8%
Germany	4	4.9%
Greece	1	1.2%
Italy	1	1.2%
Lebanon	1	1.2%
Luxembourg	1	1.2%
Malta	1	1.2%
Netherlands	1	1.2%
Poland	2	2.4%
Romania	1	1.2%
Slovenia	1	1.2%
Sweden	1	1.2%
Ukraine	1	1.2%
United Kingdom	17	20.7%
United States	30	36.6%
Total	82	100.0%

Our social media campaigns have had international reach with patients from 21 countries enrolled

7.4.2 Data obtained

Only verified researchers and clinicians are able to gain access to the entire set 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 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."



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 official results from 36 respondents.

Example 2: Epilepsy incidence

"The published prevalence of epilepsy is as high as 50% (cohort of 34)*1. Our current findings show a lower prevalence. A larger data set, properly analysed, will help us understand occurrence rates better.



Issues reported by 34 CASK respondents in Brain and Nervous System Survey

Issue Reported	Percentage reporting	Number reporting	Ages at diagnosis	Ages symptoms first appeared
Cognitive impairment	88%	30	Range of: 0-3 months- 8 years	Range of: 0-3 months- 7 years
Coordination	88%	30	Range of: 0-3 months- 8 years	Range of: 0-3 months- 7 years
Hypotonia	71%	24	Range of: 0-3 months- 8 years	Range of: 0-3 months- 7 years
Hypertonia	56%	19	Range of: 0-3 months- 10 years	Range of: 0-3 months- 9 years
Unusual movements	42%	14	Range of: 0-3 months- 8 years	Range of: 0-3 months- 7 years
Memory impairment	38%	13	Range of: 4-7 months- 8 years	Range of: 4-7 months- 7 years
Abnormal EEG	38%	13	Range of: 0-3 months- 7 years	Range of: 0-3 months- 13 years
Seizures	29%	10	Range of: 0-3 months- 6 years	Range of: 0-3 months- 6 years
Cerebral Palsy	18%	6	Range of: 0-3 months- 4 years	Range of: 0-3 months- 1 year
Headaches and Migraines	6%	2	6 years old	6 years old

Section 8

Financial Review

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

Although only larger charities subject to statutory audit are required to provide details of plans for future periods, we have nevertheless set out that we wish to undertake the following activities in the financial year 2023/24:

- Create a UK contact and demographic registry
- Create a global roadmap in collaboration with the other members of the CASK Coalition
- Fund a UK research project
- Continue to raise funds;
- Apply to the Charities Commission to enable the charity to act as advocates between families and medical professionals;
- Develop a fundraising and awareness video for the website and use on social media;
- Continue to create contacts with researchers within the UK and Europe
- Have the RARE-X data analysed and published

References

1.

We thank you for your ongoing support of our programme

Ref 1 <https://pubmed.ncbi.nlm.nih.gov/33640666/>

Acknowledgements

Many thanks to the following people who made this report possible and who have assisted the projects mentioned.

Our **SAB**, for guidance and support and exploring/creating research avenues

Our **Research Review Committee**, past and present, for ensuring we only support the most suitable and scientifically thorough projects

Liz Cook for writing the Financial Report and doing the accounts

The **Trustees** for being a sounding board, providing momentum, advice and guidance

Renee Roquet for helping to promote our projects, in particular the RARE-X DCP

Our **colleagues** from AECF and ACNRF

Your **contributors**

CASK Research Foundation
33 Finchdean Road
Rowlands Castle
PO9 6DA
www.caskresearch.org
info@caskresearch.org



CHARITY COMMISSION
FOR ENGLAND AND WALES

Charity Name
CASK Research Foundation

No (if any)
1197434

Receipts and payments accounts

CC16a

For the period
from

Period start date
1/11/2022

To

Period end date
3/31/2023

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					
Donations	639	-	-	639	-
Donations - Fayres	2,590	-	-	2,590	-
Donations - PayPal	10,938	-	-	10,938	-
Donations - Facebook	2,176	-	-	2,176	-
Donations - Amazon	117	-	-	117	-
Donations - Sponsored events	1,904	-	-	1,904	-
Donations - Bingo	1,624	-	-	1,624	-
Donations - Coffee morning	728	-	-	728	-
Donations - Advent Trail	1,498	-	-	1,498	-
Donations - CAF	1,269	-	-	1,269	-
Donations - Open Gardens	850	-	-	850	-
	-	-	-	-	-
Sub total (Gross income for AR)	24,333	-	-	24,333	-
A2 Asset and investment sales, (see table).					
	-	-	-	-	-
	-	-	-	-	-
Sub total	-	-	-	-	-
Total receipts	24,333	-	-	24,333	-
A3 Payments					
Cost of Sales	324	-	-	324	-
CASK Meet ups	-	-	-	-	-
Licenses and Permits	40	-	-	40	-
Miscellaneous	4	-	-	4	-
Advertising and Promotion	186	-	-	186	-
Legal and Professional Fees	220	-	-	220	-
Subscriptions	82	-	-	82	-
Bank/Finance Charges	23	-	-	23	-
Insurance	96	-	-	96	-
Sub total	975	-	-	975	-
A4 Asset and investment purchases, (see table)					
	-	-	-	-	-
	-	-	-	-	-
Sub total	-	-	-	-	-
Total payments	975	-	-	975	-
Net of receipts/(payments)	23,358	-	-	23,358	-
A5 Transfers between funds	-	-	-	-	-
A6 Cash funds last year end	-	-	-	-	-
Cash funds this year end	23,358	-	-	23,358	-

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	23,176	-	-
	Paypal	182	-	-
		-	-	-
	Total cash funds	23,358	-	-
	(agree balances with receipts and payments account(s))	OK	OK	OK
		Unrestricted funds to nearest £	Restricted funds to nearest £	Endowment funds to nearest £
B2 Other monetary assets	Details			
		-	-	-
		-	-	-
		-	-	-
		-	-	-
		-	-	-
		-	-	-
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 asset belongs	Cost (optional)	Current value (optional)
			-	-
			-	-
			-	-
			-	-
			-	-
			-	-
			-	-
			-	-
			-	-
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	
		Elizabeth Anne Cook	6/10/2023	
		Laura Elizabeth Hattersley		