ANNUAL REPORT & ACCOUNTS 2021/2022

Scottish Charitable Incorporated Organisation Registered Charity No. – SC036942

ME Research UK

Contents

ME Research UK

Reference and Administrative Details

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Charity registration number	SC036942
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ME Research UK

Trustees' Report

Introduction by the Chair

It gives me great pleasure to present our latest Annual Report and Accounts, which reflect the continuing delivery of our strategy and a year of significant change in the ME landscape.

Despite the challenges we have all faced over the last twelve months, we are both humbled and extremely grateful to all of our supporters for the faith they place in us and in the work we do. With over £700,000 of donations and legacies received during the year, our ability to inform, influence and ultimately invest in biomedical research continues to grow and ME Research UK remains committed to putting every penny to the best possible use. Thank you for your invaluable support - we could not exist without you.

To this end, we have awarded a further £490,000 in new research grants this year, including three new PhD-level research projects. We are delivering on our commitment to supporting and encouraging both young and established researchers into the field of ME research and continue to strive to increase the pace and value of funding we provide to rigorous biomedical research.

Our cumulative research funding now stands at over £3m and we enter the new financial year with a healthy balance sheet and substantial pipeline of research grant applications under review. I am confident that the coming year will see us approve further significant grant funding.

We have no doubt that more research still needs to be done and beyond our own funding activities we are actively involved in the major research initiative led by the Department for Health and Social Care, working collaboratively with funders, researchers and the patient community. Despite ministerial changes, we remain hopeful that this initiative will result in further positive change over the coming years.

A final word of thanks to our dedicated staff team without whom none of what we do would be possible. On behalf of the Board, I thank them for their commitment and the value they bring.

Our determination to make a positive difference remains undimmed and we will continue to work towards our vision to bring to an end the suffering caused by ME.

Jonathan Davies

Chair of Board of Charity Trustees

ME Research UK

Trustees' Report

The Trustees present their report along with the financial statements of the charity for the period 1st November 2021 to 31st October 2022 - see Note 1 to the accounts. The financial statements have been prepared in accordance with the accounting policies set out in Note 2 to the accounts and comply with the charity's Constitution dated 3rd June 2019; the Charities and Trustee Investment (Scotland) Act 2005 and the Charities Accounts (Scotland) Regulations 2006 (as amended); and the requirements of the Office of the Scottish Charity Regulator (OSCR).

The Illness

Myalgic encephalomyelitis (ME) is characterised by a range of neurological symptoms and signs, muscle pain with intense physical or mental exhaustion, relapses, and specific cognitive disabilities. Both the World Health Organisation's 'International Classification of Disease' (ICD10 (G93.3) under 'Post-Viral Fatigue Syndrome') and the Systematized Nomenclature of Medicine (SNOMED CT) list ME as a disorder of the nervous system.

During the 1990s, the term Chronic Fatigue Syndrome (CFS) came into use. As there was (and presently remains) no specific diagnostic test for ME, and, as post-exercise 'fatigue' was one of its prominent symptoms, people with ME began to be diagnosed with CFS. In recent years, however, there has been a growing recognition that the diagnosis 'CFS'– based on a list of vague non-specific symptoms shared with other illnesses is so broad that it can encompass a range of diverse patient groups. The National Institute for Health and Care Excellence (NICE) in their 2021 'Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management' guideline (NG206) recognises that "Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgmental." It is to be welcomed that the 2021 NICE guideline refers to the illness as ME/CFS rather than the 2007 guideline label of CFS/ME. This change formed part of ME Research UK's submission to NICE during the consultation process and, increasingly, the media now use ME/CFS or even just ME when describing the illness.

Of course, none of the issues surrounding the name alter the reality of the illness for thousands of people, and the lay term 'ME' is still used by patients, patient groups and charities (including ME Research UK) to describe the illness affecting people diagnosed with ME/CFS, including that subgroup of CFS patients with an organic illness, characterised by neurological signs and symptoms.

NICE records that recent data from the UK ME/CFS Biobank suggests that there are over 250,000 people in England and Wales with ME/CFS, with about 2.4 times as many women affected as men. ME/CFS can affect people of all ages. It is a complex, multi-system, chronic medical condition that has considerable personal, social and economic consequences and a significant impact on a person's quality of life, including their psychological, emotional and social wellbeing.

Everyday life for people with ME/CFS, their family and carers is disrupted and unpredictable. Many people with the condition are unemployed, and less than a fifth work full-time. Approximately 25% have severe disease and are housebound or bedbound. The quality of life of people with ME/CFS is lower than that of many people with other severe chronic conditions, including multiple sclerosis and some forms of cancer.

It is not clear what causes ME/CFS. In many cases, symptoms are thought to have been triggered by an infection but the exact cause of the illness remains unknown. Over the years there have been a number of attempts to devise a more sensitive way of diagnosing patients but none have yet been successful. Indeed, NICE identifies clinical and cost effective diagnostic tests as a key area where they recommended further research be undertaken.

What is certain is that ME/CFS is not a simple post-illness fatigue. It lasts longer and even minimal mental or physical activity can make symptoms worse. NICE records neither a cure nor a treatment for ME/CFS.

There is no diagnostic test or universally accepted research or diagnostic definition for ME/CFS. People with the condition report delays in diagnosis, and many healthcare professionals lack the confidence and knowledge to recognise, diagnose and manage it. Fatigue associated with another chronic disease may be confused with ME/CFS and some practitioners are reluctant to positively diagnose ME/CFS when no other causes are found.

Many people with ME/CFS report a lack of belief and acknowledgement from health and social care professionals about their condition and related problems, which may lead them to be dissatisfied with care and to disengage from services. This lack of belief by healthcare professionals and even family members is also recognised by NICE in the 2021 guideline. There are added issues for children and young people if illness makes school attendance difficult, bringing families to the attention of educational and social care services.

One welcome aspect of the 2021 NICE clinical guideline is the weight given to post exertional malaise after activity and this was one of a set of four diagnostic criteria which were established through the guideline development process. This accords with the realities of those with the illness and will aid delineation from other conditions. The four key diagnostic criteria in the guideline are -

(1) Debilitating fatigue that is worsened by activity, is not caused by excessive cognitive, physical, emotional or social exertion, and is not significantly relieved by rest.

(2) Post-exertional malaise after activity in which the worsening of symptoms:

- is often delayed in onset by hours or days;
- is disproportionate to the activity;
- has a prolonged recovery time that may last hours, days, weeks.

(3) Unrefreshing sleep or sleep disturbance (or both), which may include:

- feeling exhausted, feeling flu-like and stiff on waking;
- broken or shallow sleep, altered sleep pattern or hypersomnia.

(4) Cognitive difficulties (sometimes described as 'brain fog'), which may include problems finding words or numbers, difficulty in speaking, slowed responsiveness, short-term memory problems, and difficulty concentrating or multitasking, along with debilitating fatigue worsened by activity, unrefreshing sleep and/or sleep disturbance, and cognitive difficulties.

Given the illnesses' prevalence and impact, it is widely acknowledged that ME/CFS has faced significant under-investment in biomedical research over many years, both in the UK and overseas. Within the UK specifically, for example, ME/CFS receives comparatively little funding compared to other neurological disorders. MS affects about 100,000 people compared to the 240,000 estimated to have ME/CFS but has received 20 times the funding.

ME Research UK

Trustees' Report

ME Research UK exists solely to fund biomedical research and, to date, we have invested c£3 million in biomedical research world-wide on 60 distinct projects and funded 3 PhD-level researcher studies. There is more to do and we are determined to do more. In fact, ME Research UK has funded more specific biomedical research ME/CFS projects than any other charitable organisation in the world outside North America. However, it is vital that more high-quality research is carried out into both the cause(s) of the illness and its effects with the ultimate aim to discover a treatment or a cure for this most disabling of illnesses. ME Research UK's Constitution specifically charges the charity "To advance scientific knowledge by commissioning or funding research into the causes, consequences and treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS)".

ME Research UK is dedicated to ensuring that research into ME/CFS reflects the prevalence and seriousness of the illness and to funding the highest quality of biomedical research possible.

Objectives

Our vision is to end the suffering caused by ME/CFS by investing in high quality, scientific (biomedical) research into the causes, consequences and treatment(s) of the illness. Only through biomedical research, will the illness be understood, accepted and real change to the lived experience of those with the illness become a reality.

In particular, we:

- invest in high quality biomedical research into ME/CFS globally which we believe has the potential to further the understanding of the illness;
- inform the science community, civic society and those affected by the illness by taking a leading role in interpreting, analysing and commenting on published biomedical research into ME/CFS; and
- influence the biomedical research and funding agenda by working proactively and collaboratively with other organisations.

ME Research UK - Year in Review

The impact of Covid-19 on the operational aspects of the charity lessened during the reporting year as working restrictions eased. Researchers likewise returned to their institutions and significant progress has been made in completing research which bodes well for publication of results next year. However, the impact of the pandemic and that of the current economic situation in the UK is a source of concern for future fundraising activities. The Charities Aid Foundation (CAF) 'UK Giving Report 2021' shows that the number of people donating remains below average, even as the economy reopened post COVID and that donation levels continued to be lower than average in 2021. It is likely that the current 'cost of living crisis' will force many to re-examine non-essential expenditure and this will inevitably include charitable giving. This may impact regular donations as well as donations to fundraisers.

Trustees extend their gratitude to supporters who, despite the current period of economic uncertainty, continued to support our work financially. ME Research UK is fortunate to have been chosen as a supported charity of both Walk for ME and Celtic Wiseman Perpetual as they continue to raise much appreciated funds. These initiatives both inspire and involve our supporter-base. Fortunately, activity-based fundraising remains only one part of ME Research UK's fundraising mix but the Trustees recognise the need to build and widen our relationship with our supporter base and wider public profile to ensure that funds are available to fulfil the charity's mission to invest, inform and influence ME globally.

In consequence, this year has seen the beginning of the considered expansion of our staff base, with a full time post for a science writer being filled and the process to recruit for part time communications and donor relations roles underway.

Thanks to supporter donations and the funds provided by legacies, ME Research UK has been able to expand its research commitment and add substantially to the number of research projects curated.

Currently, ME Research UK operates 2 pillars of support for researchers.

Firstly, research funding, where ME Research UK made two awards achieved through the results of a global call for research applications in Spring 2021.

ME Research UK's decision to publicise the availability of research funding to active ME research groups worldwide evidenced its commitment to support the ME research base at a point where other sources of finance were unclear. By proactively allowing a 12-month no-cost extension to project award holders the charity aided stability and offered hope to researchers. The delays have, however, impacted the schedules of work and that is reflected in the lower than normal conclusion of research projects.

Secondly, being pledged to encourage researchers with fresh, novel ideas to become active in ME/CFS research and provide them with the resources to undertake their work, ME Research UK embarked on a PhD-level research initiative. The unmet need to encourage more researchers to make a career in ME/CFS research has long been recognised in ME research. ME Research UK Trustees determined to help close this lacuna. A call was made for applications and a PhD-level research funding programme was launched. During the reporting year, three awards have been made. The first to Edinburgh University for a project which dovetails with the DecodeME study, the second in a collaborative venture with Action for ME, at Kings University, London, and the third with Dr Annesley in Australia looking at mitochondrial abnormalities.

It is at this leading edge that ME Research UK sees its role: to give financial aid and other assistance to biomedical scientists for novel but scientifically sound research projects which would otherwise not be funded. We will continue to support research groups to the stage where they can apply, based on their ME Research UK funded work, to major funding agencies for support but we will also stimulate the research field by facilitating the entrance of new researchers into the field.

Whilst October 2021 saw the delayed publication of publication of NICE's 2021 guideline on ME/CFS, the year since has been marked by implementational issues in all 4 nations of the UK. Individual English NHS trusts have been forced to reconsider their treatments and guidance especially in light of the withdrawal of Graded Exercise Therapy and the repositioning of Cognitive Behavioural Therapy as a support strategy and not a treatment. Scotland, in turn, works to weave together NICE's recommendations with commitments given as part of the Scottish Parliament Petition Committee process and the current stance taken in the Scottish Good Practice Statement.

The single most important intervention during the reporting year came from a statement by the Rt Hon Sajid Javid (then Secretary of State for Health and Social Care) on International ME Awareness Day 2022 (12th May). Research was a central theme. The Secretary of State not only committed to develop a cross-Government delivery plan on ME/CFS for England, but in partnership with devolved nation undertook to explore areas of potential shared interest and learning, especially in terms of research into ME/CFS.

Further, he announced his intention to co-chair a roundtable with the Department's Chief Scientific Adviser, to bring together experts on ME/CFS, including people with lived experience to discuss what needs to happen next. The Chief Scientific Adviser, in turn, caused the UK Clinical Research Collaboration to convene a subgroup on ME/CFS to work with funders, researchers, charities, and people with ME/CFS. The aim being to drive high-quality applications for research into ME/CFS and support the research community to build capacity and capability in this field.

ME Research UK welcomed this initiative and has been recognised as a funder of research alongside such major bodies such as the NIHR and Wellcome Trust and allocated a position in the ME/CFS Research Working Group. ME Research UK is fully involved with the process and contributes to both the research Working Group and a dedicated funder-led sub-committee.

The charity is uniquely placed to influence the outcome given its unique position as a major funder of research built up over decades and with its unparalleled contacts within the ME research community.

Achievements and Performance

A. Investing in Research

The most significant aspect of our charity and the core of our charitable purposes and aims is the provision of funding for research.

Through the provision of funds, we aim to -

- Be an accessible source of finance for scientifically sound research from researchers (normally) at the beginning of their careers;
- Fund projects, the results of which produce findings to enrich the research-world's understanding of ME/CFS;
- Generate data for larger studies or to build upon for applications to central funding bodies e.g. United Kingdom Research and Innovation/Medical Research Council;
- Encourage new researchers into ME/CFS research.

ME Research UK's charitable activities in the current period resulted in a further investment of £286,224 (2020/21: £577,746) in two ME research projects in two countries. In addition, three PhD-level research grants at a total commitment of £203,624, (2020/21: £0) in three countries. This level of commitment is consistent with the charity's objectives and is judged to be manageable within the charity's overall financial position. The policy to never agree to fund projects unless funds are available engenders trust between the researchers and the charity and has proven to be a sound financial principle in the most trying of circumstances.

A further 15 (2020/21: 16) research applications were received in the year, of which two were not progressed to the full application stage. Of the remaining 13 full applications, all are currently progressing through the external peer review process, after which they will be considered by the Science Committee. The size and complexity of the applications means additional scrutiny is required in order to ensure charity resources are expended wisely and that the tangible benefits to the research field and to people with ME are capable of being ascertained and quantified.

There were two PhD-level research applications, one of which is currently being assessed by the Science Committee, while a full application has yet to be received for the other proposal. The open call for PhD-level applications was paused, for the time being, in July 2022.

ME Research UK wishes to thank the members of the Science Committee (including volunteer peer reviewers) for their dedication throughout the year. Due to the additional resources available (for example from The Gordon Parish Charitable Trust and The Fred and Joan Davies Bequest), the charity has attracted an increased number of high quality applications from notable sources globally and for sums which demand additional scrutiny. Also, the increased knowledge-base of the illness and tools/methods available to researchers mean a high degree of skill and knowledge is required by Science Committee members and peer reviewers. Administrative steps have been taken to streamline the review progress, but the charity acknowledges that additional capacity within the science Committee and peer reviewers will be required to ensure the level of scrutiny which the charity prides itself upon.

The number of applications bodes well for progress in research in 2022/23 and for the reputation and future evolution of the charity beyond the current year. The applications currently before us, if funded, would cost £2,249,897- an increase on last year's total applications (£1,009,711) - which illustrates the value of a research-centred charity devoted to biomedical research into ME/CFS but also the needs of the research base for increased funding.

ME Research UK is heartened by the geographic spread of applications for funding received within the year, the diverse range of research topics and the number of applications themselves.

In summary, ME Research UK has 12 ongoing studies, including two newly funded projects and three PhD-level research projects, and these represent more than £1.3 million currently invested in ME/CFS research globally. The research for which we have recently awarded funding covers a number of areas of interest, including two studies investigating genetic causes of ME/CFS, one looking at mitochondrial abnormalities, and two investigating potential viral involvement in the disease.

New Research Projects in 2021/22

MERUK22059

Amy Proal, PolyBio Research Foundation, Medford, MA, USA

Use of advanced metagenomic technologies for the identification of viruses in ICC-diagnosed ME/CFS patient tissue and nerve biopsy samples

£162,350 – Subject to concluded contract.

It is possible that polio-type and related viruses connected to ME/CFS do not "clear" from patients after acute infection, but remain in a persistent state. If that is the case, it is important to search for such viruses in samples beyond just the blood. That is because the viruses most connected to ME/CFS – especially the polio-type enteroviruses and herpesviruses – can infect nerves and "hide" in tissue.

New computer-based technologies have been developed to identify viruses in human samples, including novel viruses that earlier techniques might have missed. The goal of this project is to use these technologies to search for viruses in two types of samples collected from ME/CFS patients: 1) Tissue/nerve samples obtained from the ankle via punch biopsy, which contain tissue and pain-associated nerves called C fibres; and 2) Stomach tissue/nerve samples obtained via endoscopy. The investigators will compare any viruses identified in the ME/CFS samples to those in similar samples obtained from healthy people.

MERUK22060

Simon Carding, Quadram Institute, Norwich, UK

Gut eukaryotic viruses as a player in ME/CFS

£123,874

Disturbances of the gut microbiome are seen in numerous human diseases including ME/CFS, where many patients also suffer from gut disorders. To date, most gut microbiome studies, including those on ME/CFS, focused on bacteria, ignoring or excluding viruses (the virome). However, viruses living or gaining access to the body via the gut have long been associated with ME/CFS. Gut virome studies have identified striking alterations in virus type and/or numbers in patients with colon cancer, inflammatory bowel disease, diabetes and Parkinson's disease, with evidence suggesting this may also be true for ME/CFS. These studies in ME/CFS have focused on specific virus families, but excluded others with more pathogenic potential. The investigators plan a comprehensive analysis of the intestinal virome of ME/CFS patients enrolled in a clinical trial microbiota transplantation therapy (MRT). The study aims to: 1) Define the virome of ME/CFS patients and identify "signature viruses" which can be distinguished as a new biomarker of disease; and 2) Establish the impact of MRT in those patients who respond positively to such treatment, by looking at any loss of identified "signature viruses", as well as evidence of reactivation of latent viruses.

Projects completed in 2021/22

a. Reported, grant liability ended, publications awaited

MERUK14037

Faisel Khan, The Institute of Cardiovascular Research, University of Dundee, Dundee, UK

A study examining Nrf2 antioxidant gene expression and its role in combatting oxidative stress

£72,448.12

If low Nrf2 levels are found to play a central role in the increased oxidative stress found in ME/CFS patients, stimulation of Nrf2 could become an important treatment strategy, as there are currently no specifically effective treatments for the illness. The findings may also have broader implications for studies of Nrf2-targetted treatments in other conditions characterised by elevated oxidative stress, such as cancer, diabetes and liver disease.

MERUK19049

Sanjay Kumar, Oxford Brookes University, Oxford, UK

Investigating sensory processing and cognitive function in people with ME: a pilot study

£29,641

Although hypersensitivity is not considered a primary factor in the diagnosis of ME/CFS, it is a common finding in people with the condition. The brain has to work hard to process sensory-inputs and filter out what is irrelevant so we can concentrate on what is important at any given moment. The resulting physical and mental overload can lead to poor coordination, dizziness, clumsiness, numbness, tingling and nausea, and may affect individuals' ability to take in information and make decisions. Researchers at Oxford Brookes University wish to understand the nature and impact of the sensory problems experienced by people with ME/CFS, and to determine whether they are associated with any functional or electrical changes in the brain. The investigators' hope is that the results of this preliminary work will help in our understanding of the brain mechanisms that underlie the abnormal sensory experiences of people with ME/CFS, and also lead to the development of interventions to help manage these problems.

b. Complete, report received and grant funds still to be paid

MERUK20053

Carmen Scheibenbogen, Charité University Medicine Berlin; and Nuno Sepúlveda, London School of Hygiene & Tropical Medicine, London, UK,

Analysing antibody responses against EBV-derived antigens as putative biomarkers and candidates for molecular mimicry in ME/CFS

£51,096.17 over 1 year including additional funding for staff and publications.

Epstein-Barr virus (EBV) is one of the strongest candidates as an infectious trigger of ME/CFS across different populations. This is based on the fact that almost all adults are silent carriers of the virus, and the virus can produce proteins similar to the ones found in the body. To understand the role of EBV on disease pathogenesis, the investigators have previously evaluated the antibody responses against more than 3,000 EBV-derived proteins, and identified up to twenty candidate antigens whose antibody responses were either increased or decreased in patients compared with healthy controls. They attempted to replicate these findings in samples from the UK ME/CFS Biobank, but found no differences in antibody responses between blood samples from 92 ME/CFS patients and 50 healthy control subjects. However, when analysing only patients with a reported infectious onset of disease, antibody responses against two EBV-related antigens were stronger in the patient group. The researchers plan to confirm these findings in other cohorts of patients from the UK ME/CFS Biobank. They also suggest that the specific EBV-derived antigens identified may provide some evidence of how the reactivation of EBV plays a role in the development of ME/CFS.

Ongoing projects

Initiated in previous financial years, and payable (subject to progress) in 2021/2022 – Sums due represent total funding commitment.

Research studies

MERUK18047

Jarred Younger, University of Alabama at Birmingham, USA

Tracking peripheral immune cell infiltration of the brain in ME

$134,516.70 (£113,900.68 at date of conversion to US$)

The central hypothesis behind Prof. Younger's project is that activated immune cells infiltrate the brain of ME/CFS patients causing neuroinflammation and symptoms such as fatigue, pain sensitivity, cognitive problems and sleep disturbances. The team plans to track radio-labelled peripheral immune cells using positron emission scanning to see whether they do indeed break the blood-brain barrier and infiltrate the brain. The project will be carried out in 15 women with ME/CFS and 10 age-matched healthy control women, who will be scanned at 24 hours and then 96 hours following injection of the labelled cells. As well as advancing our understanding of the pathogenesis of ME/CFS and the role of the immune system, the results of this study may indicate whether neuroinflammation is a worthwhile target for treatment of the illness, and even help in establishing a diagnostic test that can distinguish between patients and healthy control subjects.

MERUK20051

Jo Nijs, Vrije Universiteit Brussel; and Lode Godderis, Katholieke Universiteit Leuven, Belgium

Unravelling the role of epigenetic modification on the brain derived neurotrophic factor gene and histone de-acetylases for pain and post-exertional malaise in people with myalgic encephalomyelitis / chronic fatigue syndrome

£91,499 over 2 years

Epigenetics looks at genetic changes that can be passed from one generation to the next, not as a result of alterations in the DNA sequence, but instead caused by changes in gene activity and expression (how information from the gene is used to make proteins). There is evidence that epigenetic changes may play a role in the pathophysiology of ME/CFS, including the post-exertional malaise experienced by many people. The investigators' previous research has uncovered the role of central sensitisation in the chronic pain experienced by many people with ME/CFS at rest and/or after exercise. In this new study, they will be investigating further the role of brain-derived neurotrophic factor (BDNF) and histone de-acetylases (HDACs) in the central sensitisation and post-exertional malaise experienced by people with ME/ CFS, and particularly the epigenetic changes occurring in the *BDNF* gene and in the genes regulating HDAC expression

MERUK20054

Elisa Oltra, Catholic University of Valencia, Valencia, Spain

Metabolic impact of activated HERVs and associated innate immune response in severe ME: towards disease modelling

£76,000 over 30 months

Human endogenous retroviruses (HERVs) are a family of viruses contained within the human genome and inherited by successive generations. They have been proposed as potential triggers of ME, and the applicants plan to identify HERVs that are overexpressed in a group of 12 women with severe ME compared with a matched group of women with fibromyalgia. These HERV 'fingerprints' could be used for diagnosis or patient subtyping. They also plan to look at the effects of activation of these ME-associated HERVs on nerve and muscle cells in laboratory conditions, to understand their potential impact on the symptoms of the illness. In an addition, the identified HERVs will be validated in an extended cohort of 50 ME patients, 25 fibromyalgia patients and 25 healthy control subjects.

MERUK21055

James Allison, Newcastle University, UK

EluCidATe: Exploring pain and autonomic dysfunction in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis and Temporomandibular disorders

£13,576

Widespread pain is a problem for people with ME/CFS and impacts on everyday activities. In particular, a group of musculoskeletal conditions affecting the muscles that move the jaw, temporomandibular disorders (TMD), are more common in ME/CFS and cause pain in the face and jaws. The grant holder's research suggests that one reason for the link between ME/CFS and TMD may be that they have a similar underlying problem affecting the autonomic nervous system (ANS), which controls many unconscious activities such as breathing and circulation. The ANS is known to work less well in ME/CFS and this is worse still when TMD is also present. To investigate the contribution of the ANS to painful symptoms, the researchers will examine brain responses to, and subjective experience of experimentally induced pain in four groups of people: 1) ME/CFS only; 2) ME/CFS who also have TMD; 3) TMD only; and 4) Healthy participants with no ME/CFS and no TMD. To examine brain responses, the researchers will use electroencephalography which measures electrical activity from the scalp. Examining the brain's response to painful pressure applied to different body regions (finger and jaw) in each of these groups will help understand how pain differs in ME/CFS to in other people, and where in the brain these differences are located. They will also investigate whether they can "calm" the ANS using non-invasive stimulation of the vagus nerve (part of the ANS) and measure the effect this has on both brain activity and levels of pain. The study will inform future treatments for ME/CFS by identifying where in the brain differences in response to pain occur, what part the ANS plays, and by understanding why some people might differ in their response to treatment.

MERUK21056

Bhupesh Prusty, Julius-Maximilians-Universität Würzburg, Germany

Understanding potential infectious triggers behind mitochondrial dysfunction in ME/CFS

£207,100

ME/CFS is a complex disease with many potential unknown triggers. Recently it has been observed that a large subset of patients who had recovered from SARS-CoV-2 infection are developing ME/CFS-like symptoms and are continuing to have ME/CFS-like clinical conditions even after several months post infection. This has strengthened the idea of infectious origin behind ME/CFS. However, there are no strong experimental evidences to support this. Mounting epidemiological evidences implicate Human herpesvirus 6 (HHV-6), HHV-7 and Epstein-Barr virus (EBV) as three highly probable infectious triggers for ME/CFS. The researchers have recently observed several cellular changes in cells carrying functionally active HHV-6 virus, which overlaps with clinical abnormalities frequently observed in ME/CFS patients. The most convincing changes included dysfunctional mitochondria, and altered mitochondrial glucose metabolism. The researchers' results supported the previously documented notion that mitochondrial dysfunction and changed mitochondrial metabolic signatures might be induced by a soluble factor that can be transferred from cell to cell through serum. Their preliminary studies have detected several possible serum-transferable factors in ME/CFS patients that can originate after an infectious trigger. Preliminary infection experiments with SARS-CoV-2 supports the idea that it may not be the SARS-CoV-2 that directly causes ME/CFS like symptoms. Rather regaining of functional activity by herpesvirus genome, which often remains inactive in a healthy cell, might be a key factor for ME/CFS development. The researchers aim to identify and characterise some of these serum-transferrable factors using innovative, inter-disciplinary methodologies and ME/CFS patient samples, which will allow them to understand molecular mechanism(s) behind mitochondrial dysfunction in ME/CFS and hopefully help to develop different strategies for therapeutic interventions.

MERUK21057

Leighton Barnden, Griffith University, Australia

Investigation of brain stem dysfunction using 7 Tesla MRI in ME/CFS

£151,000

Impaired concentration and memory, visual and auditory changes, headache and autonomic manifestations, predominate the signs and symptoms of ME/CFS and indicate primary brain involvement. Over 15 years, the Griffith University team has applied Magnetic Resonance Imaging (MRI) to study the brain in ME/CFS. Initially, they used unorthodox spin-echo MRI sequences which deliver the sensitivity and stability critical for group comparisons with healthy controls. They also performed correlations of MRI levels with severity and autonomic measures (heart rate and blood pressure) and discovered that ME/CFS severity was associated with upregulated white matter myelin independent of anxiety and depression. They also detected abnormal MRI correlations with autonomic measures within the brainstem reticular activation system (RAS), a diffuse network of small interconnected nuclei with important regulatory functions. Both findings implied impaired nerve conduction within the brainstem. In 2019, they used functional MRI to directly confirm deficits in connectivity between RAS nuclei. The RAS regulates the sleep-wake cycle and brain arousal levels, which affect attention, sensory perception, cognitive performance and memory, which are all deficient in ME/CFS and constitute its major symptoms. The RAS is the primary target of this proposal.

Their RAS results, although unique, were limited by conventional 3T MRI imaging. This new ME Research UK-funded study will investigate the brainstem RAS with a higher powered research 7T MRI scanner, repeating the key MRI measurements of the earlier work with increased sensitivity and spatial resolution, but also adding recently developed MRI measurements to identify and characterise new aspects of RAS pathophysiology. Although targeting the brainstem RAS, they will again test for differences throughout the brain in ME/CFS. To confirm and expand the understanding of RAS dysfunction in ME/CFS the researchers will also test associations of RAS connectivity with extended clinical parameters. Advanced MRI imaging may yield valuable RAS biomarkers of ME/CFS.

MERUK21058

Sarah Annesley, La Trobe University, Australia

Cell type specificity, molecular scope and epigenetic basis for mitochondrial and cellular dysfunction in ME/CFS cells

£198,076

Previously, the researchers identified a clear and specific defect in immortalised white blood cells (lymphoblasts) from ME/CFS patient namely an inefficient function of the last enzyme involved in production of energy by mitochondria (Complex V). The mitochondria are tiny compartments in cells which are responsible for generating most of the cell's energy. The inefficiency in mitochondrial energy production is accompanied by compensatory increases in the activity of a key regulator (TOR Complex I) of the production of mitochondrial proteins and in the levels and activities of mitochondrial energy-producing proteins. The increased levels of mitochondrial proteins has since been confirmed by another research group in white blood cells. Importantly, the researchers also showed that these abnormalities correlated with clinical markers of symptom severity and are highly specific and sensitive biomarkers of the disease. Whilst identification of changes in blood cells is beneficial due to their accessibility and involvement in immune responses, it is also important to determine if these changes occur in other cells and systems of the body. The next most accessible tissue is the skin. In this project the researchers will determine if the abnormalities in mitochondrial energy production and compensatory upregulation are present in cells from a different tissue, the skin, and if these alterations correlate with clinical measures of the disease. They will also determine if this is associated with alterations in other pathways and proteins and how this regulation is likely to occur through changes at the DNA, RNA and protein level. The results of this research will expand our knowledge of the underlying defect in energy production in ME/CFS and could lead to the identification of proteins and pathways for the development of therapeutic treatments and the identification of biomarkers of the disease for future development of a specific and sensitive diagnostic test.

PhD-level research projects

MEPHD21001

Alfredo Iacoangeli, King's College London, UK

Identification of new classes of genetic susceptibility to ME

£46,493.50 (co-funded with Action for ME)

The biological abnormalities leading to the development of ME/CFS are not well understood, but genetics are thought to play an important part. This new project will look at a specific type of genetic variation called an RIP (retrotransposon insertion polymorphism). Retrotransposons are pieces of DNA often referred to as jumping genes because they can move around within the genome of a cell, potentially causing mutations (RIPs) that can change the function of that cell. RIPs have been implicated in the development and progression of disorders such as motor neurone disease and Parkinson's disease, and this project aims to use genetic-sequencing data from the UK Biobank to determine whether a specific RIP or set of RIPs is also involved in ME/CFS. As well as contributing to a better understanding of ME/CFS, this research may help identify new directions for treating the disease.

MEPHD22002

Chris Ponting, University of Edinburgh, UK

Experimental investigation of genetic risk factors for ME/CFS revealed by the DecodeME project

£92,193.68

DecodeME is a genome-wide association study (GWAS) which aims to look for locations on the genome with DNA changes that are significantly different between ME/CFS patients and healthy control subjects, and which may therefore be associated with an increased ME/CFS risk. The aim of this PhD project will be to identify which specific genes are involved, what types of cell are affected by those genes, and how those changes may lead to alterations in cellular function in people with ME/CFS. Firstly, the researchers will identify which dysfunctional genes highlighted by the GWAS are most likely to contribute to the risk of ME/CFS. Then they will investigate the impact of these genetic changes in more detail by looking at their effects on the function of the cells involved.

MEPHD22003

Sarah Annesley, La Trobe University, Australia

Cause-effect relationships in the mitochondrial energy inefficiency in ME/CFS

£64,937

The investigators have previously identified key changes in the way that ME/CFS cells make energy, specifically a decrease in energy production efficiency and activation of a major stress-sensing protein (TORC1). This combination of changes can accurately distinguish ME/CFS patients from healthy controls. The aim of this new study is to look at the interaction between these changes, and determine which event comes first and potentially causes the other defects. This will identify which proteins or processes could potentially be targeted for treatment, while understanding this cause-and-effect relationship may also help in predicting the effects of these treatments.

Impact and Scientific Publications

A widely accepted means by which the work of the charity can be assessed is to gauge the number of scientific publications emanating from specific projects. Since 2000, ME Research UK has awarded or agreed to award 63 specific grants totalling c£3 million, to research institutions in the UK, Austria, Australia, Belgium, Canada, Germany, Spain, Sweden and the USA. The results of our studies are published as research papers in peer-reviewed scientific journals worldwide and are available to researchers globally.

Three papers were published in the charity year 2021/22 (2020/21: five) acknowledging the support of ME Research UK.

1. Bertinat R, Villalobos-Labra R, Hofmann L, Blauensteiner J, Sepúlveda N, Westermeier F

Decreased NO production in endothelial cells exposed to plasma from ME/CFS patients

Vascular Pharmacology, 2022, Apr; 143:106953

Nitric oxide (NO) production was reduced in endothelial cells exposed to blood plasma from people with ME/CFS. Inadequate NO release is an important cause of the endothelial dysfunction which has been reported in a subgroup of patients. These findings therefore show the mechanisms potentially involved in the endothelial dysfunction that affects some people with ME/CFS.

2. Sepúlveda N, Malato J, Sotzny F, Grabowska AD, Fonseca A, Cordeiro C, Graça L, Biecek P, Behrends U, Mautner J, Westermeier F, Lacerda EM, Scheibenbogen C

Revisiting IgG antibody reactivity to Epstein-Barr virus in myalgic encephalomyelitis/chronic fatigue syndrome and its potential application to disease diagnosis

Frontiers in Medicine, 2022 Jun 24; 9:921101

Epstein-Barr virus (EBV) infection is commonly reported at the onset of ME/CFS, but could antibodies against EBV serve as biomarkers of the disease? No differences in antibody responses were found between blood samples from 92 ME/CFS patients and 50 healthy control subjects. However, when analysing only patients with a reported infectious onset of disease, antibody responses against two EBV-related antigens were stronger in the patient group; these results need confirmation.

3. Polli A, Hendrix J, Ickmans K, Bakusic J, Ghosh M, Monteyne D, Velkeniers B, Bekaert B, Nijs J, Godderis L

Genetic and epigenetic regulation of Catechol-O-methyltransferase in relation to inflammation in chronic fatigue syndrome and Fibromyalgia

Journal of Translational Medicine, 2022 Oct 25; 20(1):487

The aim of this study was to investigate a number of genetic and epigenetic alterations to the *COMT* gene in patients with ME/CFS and fibromyalgia, and whether they were associated with markers of inflammation or clinical symptoms. The COMT protein is known to have effects on pain and inflammation, both of which are key features in these diseases. Polymorphisms in the *COMT* gene were found in patients with ME/CFS and fibromyalgia, and also in healthy control subjects. However, the patient group had around twice the level of DNA methylation (an epigenetic alteration) compared with controls. The researchers believe their findings may point to DNA methylation of the *COMT* gene as being an important factor in the development of ME/CFS and fibromyalgia.

Key Findings of Our Research:

- Exposing endothelial cells to blood from ME/CFS patients reduced their production of nitric oxide. This may underlie the endothelial dysfunction that affects some people with the disease.
- Antibody responses to two Epstein-Barr virus-related antigens were higher than normal in ME/CFS patients who reported an infectious onset to their illness.
- Epigenetic alterations to the COMT gene were found more frequently in patients with ME/CFS and fibromyalgia than in healthy controls, suggesting this may be an important factor in the development of these illnesses.

B. **Informing**

During 2021/22, the charity continued its role as an independent, science-centred provider of high-quality information and education for key decision-makers, healthcare professionals and those affected directly or indirectly by ME/CFS. In addition to the capacity to provide speakers for external events - to discuss ME Research UK's role, its achievements and to provide insight into current research and the research landscape for ME/CFS, ME Research UK also produces printed literature (leaflets and Breakthrough magazine) and embraces the opportunities afforded by new means of communication to remain relevant and at the forefront of research funding.

Our 'Breakthrough' magazine is provided free of charge to all who request it and is normally dispatched on a biannual basis. in both hard and electronic form. The magazine not only informs the reader of the charity's newly funded research but also describes and interprets the results of ME Research UK projects. Breakthrough also reports non-ME Research UK published studies that are presented in a form, which aims to ensure that readers have a holistic perspective of worldwide research and of findings which may be relevant to them. The magazine is also available on-line ensuring as wide a readership as possible without any barriers to access. It is often cited as being especially useful to people with ME/CFS when speaking to GPs, nurses and other healthcare professionals about their symptoms. To expand its breadth and bring a new voice to our communications, the Trustees contracted with Cort Johnston, the highly regarded writer and creator of the influential Health Rising blog, to contribute articles to Breakthrough and the charity's website. The international view and research sectoral review adds significantly to the scope of ME Research UK's output.

Our Facebook page (MEResearchUK) strives to balance postings relating to fundraising activities of our active supporters with a more scientific focus with summaries of the most important worldwide research into ME/CFS and news of ME Research UK funded projects. In this way, those affected by ME/CFS can be kept abreast of recent developments. This, it is believed, results in a lively but informative realm that is both engaging and educational. Where possible, postings link back to the charity's main website thus driving traffic to one of our central resources and providing a route by which the casual visitor could become more engaged with our work and our cause. Since its launch in July 2012, our Facebook page has amassed 11,317 (10,201 in previous period) 'likes' - an increase of 10.9% over the charity year (2020/21 increase over 2019/2020 being - 6%) - and is viewed regularly worldwide. It has steadily increased the audience for postings, created a community of regular commentators and provided a new platform from which we can connect to supporters both old and new. ME Research UK's active Twitter account further drives the successful dissemination of our research news and it will act as a further avenue to engage more fully with potential donors and create a new community of supporters. With 3336 followers (2020/21 - 2630), representing an increase of 26.8%, the facility has proved to be a useful, addition avenue for engagement with the ME community.

As part of the evolution of the charity, ME Research UK continues its brand review to ensure maximum impact of its news and output to ensure supporters and the wider public are aware, trust and engage with the charity. The Board's decision to appoint a Communications Officer will enable the charity to implement its Communications Strategy. The purpose of the strategy is to concentrate on the charity's social media output making it more connected, focused and appropriate to identify target audiences. The employment of a Science Writer allows a positive impact on the written output of the charity and the communications role will build upon this.

C. **Influencing**

Highlights of the charity year included ME Research UK being:

- invited to and attended a roundtable event to discuss research priorities for ME. The meeting was jointly chaired by the Secretary of State for Health and Social Care, the Right Honorable Sajid Javid MP, and the Department of Health and Social Care's Chief Scientific Adviser, Professor Lucy Chappell.
- invited to and attended UK Clinical Research Collaboration's ME/CFS Research Subgroup. This structure being part of the Secretary of State's initiative and reports directly to the Chair of the UKCRC, and to the ME/CFS Delivery Plan Task and Finish Group. ME Research UK is also a participant in the funder-led sub-group 'Building capacity and capability in the research community'.
- invited to and attended meetings of the ME/CFS Stakeholder Group meetings under the auspices of the Clinical Priorities Unit, Scottish Government's Healthcare and Quality Improvement Directorate discussing NICE 2021 implementation in Scotland as well as undertakings given by Scottish Government during the Scottish Parliament's Petitions Process to transform ME treatment, education, and research in Scotland - e.g. medical school education, prevalence data, diagnosis and care infrastructure for Scotland.

- attending and contributed to the Forward-ME Group meetings. Forward-ME members work collaboratively to improve recognition and understanding of ME/CFS. The focus of the Group is the urgent need for biomedical research; effective diagnosis and appropriate symptom management; and appropriate care and support services for ME/CFS. ME Research UK's Chair sits on the Steering Group.

  Through membership, ME Research UK influences the grouping's contributions to other areas of the Secretary of State for Health and Social Care's initiative - namely the overarching ME/CFS Delivery Plan Task and Finish Group and the Working Group sub-committees on attitudes and Education, and Living with ME/CFS.

  Forward-ME is also a partner in DecodeME the world's largest ME/CFS study which seeks, through the recruitment of 25,000 people with ME, to see whether the disease is partly genetic and, if so, help pinpoint what its causes are. The study should help researchers understand the disease and ultimately find treatments.
- attending and played active part in Steering Group meetings of the UK ME/CFS Biobank hosted by the London School of Hygiene and Tropical Medicine. ME Research UK was a financial supporter of the biobank in its formative stages (Projects 29 & 32 - combined investment £76,542). The charity notes that samples for the biobank have been utilised by Prof Khan (Project 37) and Dr Westermeier (Project 50) as part of their ME Research UK funded projects.
- been in contact with ME Research UK grant holders and potential funders to raise the profile of the charity.
- collaborating with Action for ME to co-fund a PhD-level research project at King's College, London.
- through the efforts of the Chair, discussed with other organisations the research landscape and scope for collaborative working and a more pro-active approach to research project funding.
- attending the International Association for Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (IACFS/ME) Conference, Edinburgh University's ME Genetics Symposium, a 4 day conference hosted by leading ME/CFS researcher Prof Ron Davies, and a symposium on genetic research organised by the University of Edinburgh.
- Vice Chair and staff invited to and attended a meeting to discuss advancing genetic research and how best to leverage support from the Medical Research Council.

Overall, 2022 has seen the charity deliver and become more focused on informing, influencing and investing in ME research.

Structure, Governance and Procedures

Governance and Management

At quarterly Trustees' meetings, the Trustees agree the broad strategy and areas of activity for the charity, including consideration of grant making, investment, reserves, risk management policies and performance. The day-to-day administration of grants and the processing and handling of applications, prior to consideration by the Trustees, is delegated to the Research & Communications Director.

The Board of Charity Trustees exercise operational planning responsibilities.

ME Research UK

Trustees' Report

Recruitment and Appointment of New Trustees

In terms of the Constitution, new Trustees are appointed by the Board of Charity Trustees acting by a majority decision. Application for appointment as a Charity Trustee is open to any individual aged 16 and over, whose skills, experience and qualifications are in accord with the charity's purposes. Prospective Trustees are required to complete and to sign a written application in such form as the Board of Charity Trustees may decide; completed applications are considered at the next scheduled Board meeting after receipt of the form.

No person, whether natural or legal, has the power to appoint a Trustee to the Board of ME Research UK.

The Board of Charity Trustees welcomes new applications but is acutely aware that applicants must contribute towards the good management of the charity and ought to enhance the capabilities of the Board. The Board of Charity Trustees therefore considers applications against the skill-set required for the proper functioning and evolution of the charity.

Grant Making Policy and Procedures

ME Research UK has established its grant making policy to achieve its objectives for the public benefit. Any private benefit received by researchers, and research institutions and other bodies is purely incidental to the objects of our work. Policies and procedures are reviewed regularly and aim to ensure that research grants are awarded to projects which are scientifically sound, fall within the charity's purposes and have justifiable costings.

The charity actively encourages applications for pilot studies and seed-corn projects concerned with novel aspects of research into ME/CFS.

To support its aims, ME Research UK accepts both formal applications and informal funding queries. Once an application is received core members of the Science Committee undertake an initial assessment to ensure alignment with the call for funding and that the research is in conformity with ME Research UK aims. Thereafter applications are subject to peer review (including review by external experts). The peer review reports are collated and considered by the Science Committee which assesses the application, the peer review results (which include a standardised scoring system), and the charity's research objectives. Any queries are referred to the applicants before the Science Committee arrives at a decision of whether or not to recommend funding to the Board of Charity Trustees. The final decision on whether to fund lies with the full Board.

In the current year, a number of grant applications were unsuccessful either that, upon peer review and Science Committee input, they were deemed to fall out-with ME Research UK's charitable objectives or that their research methodology or submitted expenses did not meet the requisite standards. Through careful scrutiny of applications - the scientific basis of the submission, the itemised costs - ME Research UK strives to ensure proper and rigorous safeguards for the stewardship of funds under its control.

The 2020 Science Committee Plan was put into effect aiming to streamline the awards process; capture key data; focus the applicants' proposals; introduce application deadlines and key time indicators. The alterations further professionalise the charity's operations and provide the structure to allow it to operate effectively in best interests of its supporters. Upon reviewing the implementation of the plan, the Science Committee consider the changes to have made a positive impact on their work and also for researchers as they provide certainty as to requirements and timescales. Further improvements are required as the Science Committee workload increases in volume and complexity and additional resources will be required. The additional experience and insight of the science writer will aid greatly the work of the Committee.

ME Research UK

Trustees' Report

ME Research UK's Standard Grant Conditions provide that all payments of research funding are dependent upon satisfactory proof of research progress. Longer term projects i.e. those in excess of 1 year, are subject to regular (normally 6-monthly) progress reports. The charity therefore ensures that grant monies which have been given are utilised in line with the charity's purposes and that progress merits payment of further instalments of financial assistance.

ME Research UK endorses the position of the Association of Medical Research Charities as regards university funding, and ME Research UK-sponsored projects are conducted in accordance with the principles outlined in the Declaration of Helsinki, and approved by local research ethics committees as appropriate.

On PhD level research funding, applications must be made via the Institution concerned to ensure charity funds are protected. The charity funds the research and so the proposal progresses through the normal stages in our review process.

ME Research UK does not agree to fund research without having sufficient funds available to satisfy its liabilities.

Grant Making Objectives

Through funding studies at recognised Institutions worldwide, ME Research UK funded-projects enrich the scientific literature of ME/CFS and have the ultimate aim of helping those affected directly or indirectly by ME/CFS and those who may develop ME/CFS in the future. The research we fund helps lay the foundation for further research in an area that is under-represented in scientific research and where replicated and larger scale studies are rare. ME Research UK believes that, by providing albeit small scale funding to research projects, momentum will build and lead ultimately to large scale research through the involvement of major governmental and private philanthropic bodies. Once the mechanisms of the illness are understood, more effective treatment and ultimately hopefully a cure will follow.

ME Research UK, through its website, publications, attendance at conferences and contacts worldwide, invites applications for research grants. Having the name of the charity noted in the 'Funding Acknowledgment' section of scientific papers is an important way of bringing ME Research UK to the attention of other scientists. In the current year, all the projects accepted for funding were the result of our 'Call for Funding Applications' which went to researchers across the world. Full applications received are peer reviewed by independent researchers with specialist knowledge of the area, subject to the funding requested.

ME Research UK only funds projects at established institutions – such as universities, research centres and NHS hospitals (or equivalent overseas) – to ensure that, in the case of non-compliance with the terms of the research award, charity funds are protected and recoverable. Research grant instalments are normally paid only upon receipt of regular progress reports, which are reviewed against the requirements of the prevailing research award by the Research & Communications Director.

By careful, structured and objective consideration of applications and a prudent approach to payment of research monies, ME Research UK ensures high standards of care of the funds entrusted to it. Details of the application process, together with relevant forms are available on the charity's website - www.meresearch.org.uk.

ME Research UK

Trustees' Report

Monitoring Achievement

Research is assessed by the completion of approved research projects within the planned timescale for the project and of publication of the results in peer-reviewed journals. Longer-term consequences of the research are more difficult to assess but published papers build a critical mass of information in the scientific literature. In addition, our funding lays the foundation for future work by allowing researchers to acquire pilot data on which to base applications to larger, often governmental, funding bodies. ME Research UK strives to repeat the success of Prof. Julia Newton, Dr Wan Ng and colleagues at Newcastle University who, in 2012, were awarded almost £1 million by the UK's Medical Research Council. Their successful application for funding was under a call for 'Understanding the Mechanisms of CFS/ME' and resulted in funding for two biomedical projects. At the time, Prof. Newton acknowledged ME Research UK for providing "the pilot/seed corn funding for four distinct projects from 2006 to 2011, which have allowed us to accumulate the data on which these successful applications to the MRC were based".

The Trustees monitor closely the feedback from Breakthrough and the data on uptake and use of Facebook and Breakthrough. It would appear that there is a strong demand for impartial, informed scientific comment in the sphere of ME/CFS.

Future Plans

Through the momentum built by ME Research UK over the past 22 years, the charity is now in the position where the quality of applications is far higher than previously and the 'ask' from applications at funding Calls is in excess of funds available. The charity will not lower its rigorous standards in reviewing applications but will look to grow the resource availability in order that it can meet the needs of researchers.

In addition, the charity plans to invest in the 'ladder of success' through increased PhD-level research, post-doctoral research support, as well as full grants. It has always been the aim of the charity to nurture and curate research until the researcher is at the stage where central funding, via MRC or NIHR, is appropriate. Creating this stepped approach will enable the charity to remain relevant and broaden its influence in ME research generally.

To achieve this the charity looks to increase the staff pool through targeted hiring in the areas of science writing, communications, and donor relations to ensure that the charity's output improves, brand recognition rises and income is maximised.

Due to the Department of Health and Social Care's Delivery Plan in ME/CFS there will be changes in the research landscape and ME Research UK recoginises that it must be well placed to mold these changes and to facilitate such advantages which may arise.

Accounting Matters

Donated Facilities and Services

It is estimated that approximately 1,286 voluntary hours were donated by members i.e. the Trustees of ME Research UK, and 89 voluntary hours were donated by others (most notably by peer-reviewers and members of our Science Committee to whom ME Research UK owes a great debt for their insightful input).

The charity continued to take advantage of donation facilities from Microsoft, Google Ads, and the SAGE Foundation. The value of these donations in kind was approximately £42,185 and has been recognised in the accounts - the calculated 'cost' of the advertising of $46,473 (£37,384) is included in expenditure on raising funds.

Key Management Personnel Remuneration

The Trustees consider key management to be the Board of Charity Trustees, in terms of setting strategy and policy and in assessing risk and responsibility for these matters rests with the Board.

No Trustee received any remuneration directly from the charity, other than approved expenses. Details of remuneration and expenses are disclosed in note 10 to the financial statements.

Financial Review

The total funds held at the year-end were £1,757,750 (2020/21: £1,616,136,), including £466,296 of restricted funds (2020/21: £754,779). These funds are further explained at note 21.

The charity continues to rely on the generous donations of its supporters - as detailed in Note 3 to the accounts. The amount of charitable activity funded during the period is set out in Note 7 to the accounts, and the charities assets and liabilities are detailed in the Balance Sheet presented in page 33.

Given OSCR's recommendations for limitation of Trustees' liability insurance, our financial policy remains as it has always been, namely that no new projects be initiated until the necessary funds to complete them are secure and in place in the charity's bank accounts. This ensures that, for research project purposes, the charity assets will always be in excess of its liabilities. In this regard, the charity aims to be regarded as a sound partner in any project award and therefore to ensure a high level of trust between funding agencies. For non-restricted funds, the Trustees remain prudent in their outlook.

Risk Management

The Board of Charity Trustees has considered the major risks to which the charity is exposed and has reviewed those risks and established procedures to manage them. At their meeting on 8th Oct 2022, the Trustees adopted an updated Risk Register and the items recorded therein will remain under scrutiny.

The principle risks faced by the charity lie in continued reliance on the generosity of individual donors for income and, in the case of operational risks, from ineffective grant making and the ability of the charity to make grants, which fulfil its objectives.

It is fully anticipated that opportunities for active fundraising activity by supporters will recover in 2022/23; there will be (and is) increased competition between charities for donations and trust funders will see income squeezed due to anticipated challenges cause by the current economic situation. The employment of a Donor Relations Officer will add capacity to the charity to enable it to more effectively deepen and broaden our supporter base and opportunities to maximise the funds available for biomedical research.

The financial risks of increased employee numbers and slow recovery of donation income are containable given the financial strength of the charity both in terms of assets and in terms of relatively low running costs.

As scientific research is largely ineligible for funding support from certain bodies, e.g. the National Lottery, and as other bodies, notably companies, prefer to support 'community based projects', ME Research UK must rely mainly on voluntary donations. The charity strives to encourage active fundraising by facilitating giving through multiple on-line platforms; supporting individual and group projects (such as Walk for ME); and by forging strong links with fundraisers. The Trustees will bolster the current fundraising model by expanding marketing activities to ensure the work of the charity and fundraising opportunities are projected as widely as possible.

The operational risk from ineffective research is managed by retaining staff, peer reviewers and Science Committee members who understand the science and research methodologies behind research. The Trustees are aware that biomedical research is expensive and that the grants provided will be insufficient for large-scale research, which is why pilot studies and seed-corn projects concerned with novel aspects of research into ME/CFS are the focus of our work. ME Research UK is open to working cooperatively with other bodies to promote high quality research into ME/CFS.

Through collaboration and skillful targeting of resources, the Trustees ensure that maximum benefit flows from funds invested and that the aims of the charity are fulfilled.

Charity Test

The Trustees are mindful of the continuing legal duty to fulfil the charity test under the 2005 Act.

It is considered that the charity fulfils the 'public benefit' test both directly, by the provision of research grants to institutions, and also indirectly, through the dissemination of research outcomes, news and analysis to the general public and by the provision of information via our website, Facebook and meetings. Our staff are also available to answer queries from members of the public by both telephone and e-mail. There are no identifiable disbenefits in the acts of the charity or any concerns relating to private benefit.

There are considered to be no restrictive elements in the provision of information in that the Charity's website and Facebook page are freely accessible to the general public without registration and the biannual magazine 'Breakthrough' is provided completely free of charge to any individual or group which requests copies.

Access to grants is via an open grant application system where the merits of the application are judged in a peer-reviewed system based on scientific merit. The results of ME Research UK funded projects are published, enabling the wider scientific community to enjoy the benefits of the results.

Due to the nature of biomedical scientific research, there is necessarily a limited pool of potential recipient institutions; scientific research requires trained staff, appropriate facilities and administrative support. ME Research UK, however, is committed to stimulating new research into ME/CFS; encouraging scientists to enter the field; and increasing the published research base on the illness.

The Trustees keep under review the level of still to be utilised funds, and it ought to be noted that the charity does not undertake to fund research until the funds have been raised and that payment of successful grants is made to the recipient Institution in instalments. In addition, grant requests are impossible to predict, and so funds may accumulate unavoidably until suitable applications come to the charity. The Trustees continue to monitor the situation and have, and will continue to, take all opportunities to source new project opportunities.

Reserves Policy

Transfers are made from unrestricted funds to ensure that sufficient is held in restricted funds to cover the charity's grant making obligations, and to effect minor adjustments.

The Trustees have also reviewed their Reserves Policy by examining income, expenditure and risk factors prior to implementing the results.

As the Trustees do not commit to funding research projects until the full costs have been raised, the Trustees minimise financial risk. Trustees continue to monitor their Reserves Policy in implementation of OSCR's general advice to Scottish charities. Within Unrestricted Funds, three months' operating expenses (£30,000) are identified as a financial reserve. Surplus funds beyond this level are available for immediate utilisation to fund research.

In recent years, surplus revenues have accumulated as the Trustees seek relevant research projects worldwide and the level of funds held has been augmented by inflow of larger donations from trusts/charities and executry income.

There are no significant doubts as to the charity's ability to continue as a going concern.

Investment Policy

The Trustees adopted an Investment Policy at their meeting in January 2022. This policy is reviewable on an annual basis and this will include a report on investment returns.

Funds arising from investments are insufficient to make a material contribution to charity assets and are incidental to the charity's operation.

ME Research UK is a small charity with limited resources, the majority of which are dedicated to funding research commitments. The timing of payments to settle commitments is outwith the control of the charity.

As the timing of payments to settle research commitments is not within the control of the charity, our policy is to hold the vast majority of charity funds in cash on short-term deposit to be readily available but to seek to maximise the return. Thus, the vast majority of funds held is invested in UK banks and building societies to a) earn a competitive rate of interest on funds until they are required for use and b) to maximise deposit protection under the Financial Services Compensation Scheme.

On cash deposits, interest rates are such that growth in excess of inflation (RPI) is not possible without excessive risk or overly lengthy notice periods. The Trustees aim for a competitive rate given market conditions and need for liquidity.

As charity reserves are held on a longer basis (albeit that the investments can be traded on a daily basis), the Trustees mandated a balanced approach between income and capital growth be adopted. The Trustees wished to maintain the capital value of these Investment Funds at least in line with inflation.

Ideally, the charity's investment objective is for capital growth in excess of inflation (RPI) and a stable, growing income stream. The charity seeks to produce the best financial return within an acceptable level of risk – namely low to medium level of risk. This balances the need to generate income from investments in the short term with the requirement for longer-term growth in the value of the portfolio.

The charity's reserves are held in Charifund and Charibond investments managed actively by M&G.

Disclosure of information to auditor

Each trustee has taken steps that they ought to have taken as a trustee in order to make themselves aware of any relevant audit information and to establish that the charity's auditor is aware of that information. The trustees confirm that there is no relevant information that they know of and of which they know the auditor is unaware.

The annual report was approved by the trustees of the charity on 26 April 2023 and signed on its behalf by:

.....
Jonathan P J Davies
Trustee

ME Research UK

Statement of Trustees' Responsibilities

The Trustees are responsible for preparing the Trustees' Annual Report and the financial statements in accordance with the United Kingdom Accounting Standards (United Kingdom Generally Accepted Accounting Practice) and applicable law and regulations.

The law applicable to charities in Scotland 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 of its incoming resources and application of resources, including its income and expenditure, for that period. In preparing these financial statements, the Trustees are required to:

- select suitable accounting policies and apply them consistently;
- observe the methods and principles in the Charities SORP;
- make judgements and estimates that are reasonable and prudent;
- state whether applicable UK Accounting Standards 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 business.

The Trustees are responsible for keeping adequate accounting records that are sufficient to show and explain the charity's transactions and disclose with reasonable accuracy at any time the financial position of the charity and enable them to ensure that the financial statements comply with the Charities and Trustee Investment (Scotland) Act 2005, regulation 8 of the Charities Accounts (Scotland) Regulations 2006 (as amended) and the provisions of the Constitution. They 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.

ME Research UK

Independent Auditor's Report to the Members of ME Research UK

Opinion

We have audited the financial statements of ME Research UK (the 'charity') for the year ended 31 October 2022, which comprise the Statement of Financial Activities, Balance Sheet, Statement of Cash Flows, and Notes to the Financial Statements, including a summary of significant accounting policies. The financial reporting framework that has been applied in their preparation is United Kingdom Accounting Standards, comprising Charities SORP - FRS 102 'The Financial Reporting Standard applicable in the UK and Republic of Ireland' and applicable law (United Kingdom Generally Accepted Accounting Practice).

In our opinion the financial statements:

- give a true and fair view of the state of the charity's affairs as at 31 October 2022 and of its results for the year then ended;
- have been properly prepared in accordance with United Kingdom Generally Accepted Accounting Practice; and
- have been prepared in accordance with the requirements of the Charities and Trustee Investment (Scotland) Act 2005 and regulation 8 of the Charities Accounts (Scotland) Regulations 2006 (as amended).

Basis for opinion

We conducted our audit in accordance with International Standards on Auditing (UK) (ISAs (UK)) and applicable law. Our responsibilities under those standards are further described in the Auditor's responsibilities for the audit of the financial statements section of our report. We are independent of the charity in accordance with the ethical requirements that are relevant to our audit of the financial statements in the UK, including the FRC's Ethical Standard, and we have fulfilled our other ethical responsibilities in accordance with these requirements. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

Conclusions relating to going concern

In auditing the financial statements, we have concluded that the trustees' use of the going concern basis of accounting in the preparation of the financial statements is appropriate.

Based on the work we have performed, we have not identified any material uncertainties relating to events or conditions that, individually or collectively, may cast significant doubt on the charity's ability to continue as a going concern for a period of at least twelve months from when the financial statements are authorised for issue.

Our responsibilities and the responsibilities of the trustees with respect to going concern are described in the relevant sections of this report.

Independent Auditor's Report to the Members of ME Research UK

Other information

The trustees are responsible for the other information. The other information comprises the information included in the annual report, other than the financial statements and our auditor's report thereon. Our opinion on the financial statements does not cover the other information and, except to the extent otherwise explicitly stated in our report, we do not express any form of assurance conclusion thereon.

In connection with our audit of the financial statements, our responsibility is to read the other information and, in doing so, consider whether the other information is materially inconsistent with the financial statements or our knowledge obtained in the audit or otherwise appears to be materially misstated. If we identify such material inconsistencies or apparent material misstatements, we are required to determine whether there is a material misstatement in the financial statements or a material misstatement of the other information. If, based on the work we have performed, we conclude that there is a material misstatement of this other information, we are required to report that fact.

We have nothing to report in this regard.

Matters on which we are required to report by exception

In the light of our knowledge and understanding of the charity and its environment obtained in the course of the audit, we have not identified material misstatements in the Trustees' Report.

We have nothing to report in respect of the following matters where the Charities Accounts (Scotland) Regulation 2006 (as amended) requires us to report to you if, in our opinion:

- adequate accounting records have not been kept, or returns adequate for our audit have not been received from branches not visited by us; or
- the financial statements are not in agreement with the accounting records and returns; or
- certain disclosures of trustees remuneration specified by law are not made; or
- we have not received all the information and explanations we require for our audit.

Responsibilities of trustees

As explained more fully in the Statement of Trustees' Responsibilities [set out on page 27], the trustees are responsible for the preparation of the financial statements and for being satisfied that they give a true and fair view, and for such internal control as the trustees determine is necessary to enable the preparation of financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the financial statements, the trustees are responsible for assessing the charity's ability to continue as a going concern, disclosing, as applicable, matters related to going concern and using the going concern basis of accounting unless the trustees either intend to liquidate the charity or to cease operations, or have no realistic alternative but to do so.

Auditor's responsibilities for the audit of the financial statements

Our objectives are to obtain reasonable assurance about whether the financial statements as a whole are free from material misstatement, whether due to fraud or error, and to issue an auditor's report that includes our opinion. Reasonable assurance is a high level of assurance, but is not a guarantee that an audit conducted in accordance with ISAs (UK) will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decision of users taken on the basis of these financial statements.

Extent to which the audit was considered capable of detecting irregularities, including fraud

We identify and assess the risks of material misstatement of the financial statements, whether due to fraud or error, and then design and perform audit procedures responsive to those risks, including obtaining audit evidence that is sufficient and appropriate to provide a basis for our opinion.

Identifying and assessing potential risks related to irregularities

Irregularities, including fraud, are instances of non-compliance with laws and regulations. We design procedures in line with our responsibilities, outlined above, to detect material misstatements in respect of irregularities, including fraud. The extent to which our procedures are capable of detecting irregularities, including fraud is detailed below:

- the nature of the regulated sector, control environment and understanding of the entity including, but not restricted to, the understanding that the trustees are not remunerated, and the prevalence of fraud in the sector especially in the current uncertain economic environment;
- results of our enquiries of trustees about their own identification and assessment of the risks of irregularities;
- any matters we identified having obtained and reviewed the Charity's documentation of their policies and procedures relating to:
    - identifying, evaluating and complying with laws and regulations and whether they were aware of any instances of non-compliance;
    - detecting and responding to the risks of fraud and whether they have knowledge of any actual, suspected or alleged fraud;
    - the internal controls established to mitigate risks of fraud or non-compliance with laws and regulations;
- the matters discussed among the audit engagement team regarding how and where fraud might occur in the financial statements and any potential indicators of fraud.

As a result of these procedures, we considered the opportunities that may exist within the organisation for fraud and identified the greatest potential for fraud in relation to revenue recognition. In common with all audits under ISAs (UK), we are also required to perform specific procedures to respond to the risk of management override.

We also obtained an understanding of the legal and regulatory frameworks that the Charity operates in, focusing on provisions of those laws and regulations that had a direct effect on the determination of material amounts and disclosures in the financial statements. The key laws and regulations we considered in this context included the charity's own constitution, and various charity-specific legislation, including The Charities and Trustee Investment (Scotland) Act 2005.

Our procedures to respond to risks identified included the following:

- reviewing the financial statement disclosures and testing to supporting documentation to assess compliance with provisions of relevant laws and regulations described as having a direct effect on the financial statements;
- enquiring of Trustees concerning actual and potential litigation and claims;
- performing analytical procedures to identify any unusual or unexpected relationships that may indicate risks of material misstatement due to fraud;
- reading minutes of meetings of those charged with governance;
- tested a sample of income for understatement and other relevant audit procedures while consideration was given to revenue recognition;
- tested a sample of expenditure for overstatement and other relevant procedures;
- in addressing the risk of fraud through management override of controls, testing the appropriateness of journal entries and other adjustments; assessing whether the judgements made in making accounting estimates are indicative of a potential bias; and evaluating the business rationale of any significant transactions that are unusual or outside the normal course of business.

We also communicated relevant identified laws and regulations and potential fraud risks to all engagement team members and remained alert to any indications of fraud or non-compliance with laws and regulations throughout the audit.

Due to the inherent limitations of an audit, there is an unavoidable risk that we may not have detected some material misstatements in the financial statements, even though we have properly planned and performed our audit in accordance with auditing standards. For example, as with any audit, there remained a higher risk of non-detection of irregularities, as these may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal controls. We are not responsible for preventing fraud or non-compliance with laws and regulations and cannot be expected to detect all fraud and non-compliance with laws and regulations.

A further description of our responsibilities for the audit of the financial statements is located on the Financial Reporting Council's website at www.frc.org.uk/auditorsresponsibilities. This description forms part of our auditor's report.

ME Research UK

Independent Auditor's Report to the Members of ME Research UK

Use of our report

This report is made solely to the charity's trustees, as a body, in accordance with Section 44 (1)(c) of the Charities and Trustee Investment (Scotland) Act 2005 and Regulation 10 of the Charities Accounts (Scotland) Regulations 2006 (as amended). Our audit work has been undertaken so that we might state to the charity's trustees those matters we are required to state to them in an auditor's report and for no other purpose. To the fullest extent permitted by law, we do not accept or assume responsibility to anyone other than the charity and its trustees as a body, for our audit work, for this report, or for the opinions we have formed.

.....
Morris & Young, Statutory Auditor
Eligible to act as an auditor in terms of section 1212 of the Companies Act 2006
Chartered Accountants
6 Atholl Crescent
PERTH
PH1 5JN

Date:.....

ME Research UK

Statement of Financial Activities for the Year Ended 31 October 2022
(Including Income and Expenditure Account and Statement of Total Recognised Gains and Losses)

	Note	Unrestricted funds £	Restricted funds £	Total 2022 £	Unrestricted funds £	Restricted funds £	Total 2021 £
Income and Endowments from:							
Donations and legacies	3	568,628	164,605	733,233	441,472	152,738	594,210
Other trading activities	4	8,079	-	8,079	8,488	-	8,488
Investment income	5	7,384	5,561	12,945	3,625	5,829	9,454
Total Income		584,091	170,166	754,257	453,585	158,567	612,152
Expenditure on:							
Raising funds	6	(63,767)	(305)	(64,072)	(59,099)	(113)	(59,212)
Charitable activities	7	(85,665)	(458,344)	(544,009)	(70,009)	(584,109)	(654,118)
Total Expenditure		(149,432)	(458,649)	(608,081)	(129,108)	(584,222)	(713,330)
Gain/(loss) on investment assets		(4,562)	-	(4,562)	8,305	-	8,305
Net income/(expenditure)		430,097	(288,483)	141,614	332,782	(425,655)	(92,873)
Net movement in funds		430,097	(288,483)	141,614	332,782	(425,655)	(92,873)
Reconciliation of funds							
Total funds brought forward		861,357	754,779	1,616,136	528,575	1,180,434	1,709,009
Total funds carried forward	21	1,291,454	466,296	1,757,750	861,357	754,779	1,616,136

All of the charity's activities derive from continuing operations during the above two periods.

The funds breakdown for 2021 is shown in note 21.

ME Research UK

(Registration number: SC036942)
Balance Sheet as at 31 October 2022

	Note	2022 £	2021 £
Fixed assets			
Tangible assets	13	1,434	2,061
Investments	14	42,604	47,166
		44,038	49,227
Current assets			
Stocks	15	1,609	1,568
Debtors	16	9,953	201,357
Cash at bank and in hand	17	2,694,972	2,267,811
		2,706,534	2,470,736
Creditors: Amounts falling due within one year	18	(512,270)	(564,185)
Net current assets		2,194,264	1,906,551
Total assets less current liabilities		2,238,302	1,955,778
Creditors: Amounts falling due after more than one year	19	(480,552)	(339,642)
Net assets		1,757,750	1,616,136
Funds of the charity:			
Restricted income funds			
Restricted funds	21	466,296	754,779
Unrestricted income funds			
Unrestricted funds		1,291,454	861,357
Total funds	21	1,757,750	1,616,136

The financial statements on pages 33 to 51 were approved by the trustees, and authorised for issue on 26 April 2023 and signed on their behalf by:

.....
Jonathan P J Davies
Chair/Trustee

.....
Mrs Sue Waddle
Vice Chair/Trustee

ME Research UK

Statement of Cash Flows for the Year Ended 31 October 2022

	Note	2022 £	2021 £
Cash flows from operating activities			
Net cash income/(expenditure)		141,614	(92,873)
Adjustments to cash flows from non-cash items			
Depreciation	13	1,246	1,031
Investment income	5	(12,945)	(9,454)
(Gain)/loss on investment assets		4,562	(8,305)
		134,477	(109,601)
Working capital adjustments			
(Increase)/decrease in stocks	15	(41)	257
Decrease in debtors	16	191,404	35,124
Increase in creditors	18	88,995	480,763
Net cash flows from operating activities		414,835	406,543
Cash flows from investing activities			
Interest receivable and similar income	5	11,092	7,802
Purchase of tangible fixed assets	13	(619)	(3,092)
Income from dividends	5	1,853	1,652
Net cash flows from investing activities		12,326	6,362
Net increase in cash and cash equivalents		427,161	412,905
Cash and cash equivalents at 1 November		2,267,811	1,854,906
Cash and cash equivalents at 31 October		2,694,972	2,267,811

All of the cash flows are derived from continuing operations during the above two periods.

1 Charity status

ME Research UK is a Scottish Charitable Incorporated Organisation (SCIO) and is registered with the Office of the Scottish Charity Regulator under Charity Number SC036942.

The address of its registered office is:
The Gateway
North Methven Street
PERTH
PH1 5PP

2 Accounting policies

Summary of significant accounting policies and key accounting estimates

The principal accounting policies applied in the preparation of these financial statements are set out below. These policies have been consistently applied to all the years presented, unless otherwise stated.

The financial statements are presented in Sterling (£). The financial statements are rounded to the nearest £1.

Basis of preparation

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), the Charities and Trustee Investment (Scotland) Act 2005 and the Charities Accounts (Scotland) Regulations 2006 (as amended).

ME Research UK 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 notes.

Going concern

At the time of approving the financial statements, the Trustees have a reasonable expectation that the Charity has adequate resources to continue in operational existence for the next 12 months. Thus the Trustees continue to adopt the going concern basis of accounting in preparing the financial statements.

Income and endowments

All income is recognised once the charity has entitlement to the income, it is probable that the income will be received and the amount of the income receivable can be measured reliably.

Donations and legacies

Donations and legacies are recognised on a receivable basis when receipt is probable and the amount can be reliably measured.

Incoming resources from tax reclaims are included in the statement of financial activities at the same time as the gift to which they relate.

Investment income

Investment income is recognised on a receivable basis.

Other income

The value of any voluntary help received is not included in the financial statements but is described in the Trustees' Report.

Expenditure

All expenditure is recognised once there is a legal or constructive obligation to that expenditure, it is probable settlement is required and the amount can be measured reliably. All costs are allocated to the applicable expenditure heading that aggregate similar costs to that category. Where costs cannot be directly attributed to particular headings they have been allocated on a basis consistent with the use of resources, with central staff costs allocated on the basis of time spent, and depreciation charges allocated on the portion of the asset's use. Other support costs are allocated based on the spread of staff costs.

Raising funds

These are costs incurred in attracting voluntary income, the management of investments and those incurred in trading activities that raise funds.

Charitable activities

Charitable expenditure comprises those costs incurred by the charity in the delivery of its activities and services for its beneficiaries. It includes both costs that can be allocated directly to such activities and those costs of an indirect nature necessary to support them.

Grant expenditure

Grants payable are payments made to third parties in the furtherance of the charitable objectives.

Where the charity gives a grant with conditions for its payment being a specific level of service or output to be provided, the grant has been recognised in the accounts on a prudent basis.

Grants payable without performance conditions are only recognised in the accounts when a commitment has been made and there are no conditions to be met relating to the grant which remain in the control of the charity.

Grant provisions

Provisions for grants are made when the intention to make a grant has been communicated to the recipient but there is uncertainty about either the timing of the grant or the amount of grant payable.

Support costs
Support costs include central functions and have been allocated to activity cost categories on a basis consistent with the use of resources, for example, allocation property costs by floor areas, or per capita, staff costs by the time spent and other costs by their usage.

Governance costs
These include the costs attributable to the charity's compliance with constitutional and statutory requirements, including audit, strategic management and trustees' meetings and reimbursed expenses.

Tangible fixed assets
Individual fixed assets costing £500 or more are initially recorded at cost, less any subsequent accumulated depreciation and subsequent accumulated impairment losses.

Depreciation and amortisation
Depreciation is provided on tangible fixed assets so as to write off the cost or valuation, less any estimated residual value, over their expected useful economic life as follows:

Asset class	Depreciation method and rate
Fixtures and fittings	33% straight line

Fixed asset investments
Fixed asset investments, other than programme related investments, are included at market value at the balance sheet date. Realised gains and losses on investments are calculated as the difference between sales proceeds and their market value at the start of the year, or their subsequent cost, and are charged or credited to the Statement of Financial Activities in the period of disposal.

Unrealised gains and losses represent the movement in market values during the year and are credited or charged to the Statement of Financial Activities based on the market value at the year end.

Stock
Stock is valued at the lower of cost and estimated selling price less costs to complete and sell, after due regard for obsolete and slow moving stocks. Items donated for resale or distribution are not included in the financial statements until they are sold or distributed.

Foreign exchange
Transactions in foreign currencies are recorded at the rate of exchange at the date of the transaction. Monetary assets and liabilities denominated in foreign currencies at the balance sheet date are reported at the rates of exchange prevailing at that date.

Fund structure
Unrestricted income funds are general funds that are available for use at the trustees' discretion in furtherance of the objectives of the charity.

Restricted income funds are those donated for use in a particular area or for specific purposes, the use of which is restricted to that area or purpose.

Financial instruments

The charity only has financial assets and liabilities of a kind that would qualify as basic financial instruments which are recognised at their transaction value and subsequently measured at their settlement value.

3 Income from donations and legacies

	Unrestricted funds £	Restricted funds £	Total 2022 £	Unrestricted funds £	Restricted funds £	Total 2021 £
Donations and legacies;						
Donations from companies, trusts and similar proceeds	564	-	564	1,237	-	1,237
Donations from individuals	92,296	144,731	237,027	132,617	85,777	218,394
Legacies	462,560	13,383	475,943	296,300	60,019	356,319
Gift Aid reclaimed	13,208	6,491	19,699	11,318	6,942	18,260
	568,628	164,605	733,233	441,472	152,738	594,210

4 Income from other trading activities

	Unrestricted funds £	Total 2022 £	Unrestricted funds £	Total 2021 £
Trading income;				
Other trading income	8,079	8,079	8,488	8,488
	8,079	8,079	8,488	8,488

5 Investment income

	Unrestricted funds £	Restricted funds £	Total 2022 £	Unrestricted funds £	Restricted funds £	Total 2021 £
Income from dividends;						
Dividends receivable from other listed investments	1,853	-	1,853	1,652	-	1,652
Interest receivable and similar income;						
Interest receivable on bank deposits	5,531	5,561	11,092	1,973	5,829	7,802
	7,384	5,561	12,945	3,625	5,829	9,454

6 Expenditure on raising funds

	Unrestricted funds £	Restricted funds £	Total 2022 £	Unrestricted funds £	Restricted funds £	Total 2021 £
Staff costs	7,522	-	7,522	6,760	-	6,760
Communication costs	3,062	-	3,062	3,616	-	3,616
Office and accommodation costs	3,392	-	3,392	2,448	-	2,448
Fundraising costs and fees	2,261	51	2,312	3,070	53	3,123
Advertising	37,385	-	37,385	39,856	-	39,856
Costs of goods sold	3,023	-	3,023	3,131	-	3,131
Other	7,122	254	7,376	218	60	278
	63,767	305	64,072	59,099	113	59,212

7 Expenditure on charitable activities

	Unrestricted funds £	Restricted funds £	Total 2022 £	Unrestricted funds £	Restricted funds £	Total 2021 £
Research grant funding	-	478,366	478,366	-	577,746	577,746
Staff costs	66,175	-	66,175	48,358	-	48,358
Accommodation	6,150	-	6,150	5,985	-	5,985
Breakthrough costs	6,771	-	6,771	10,075	-	10,075
Trustee travel and accommodation costs	1,652	-	1,652	217	-	217
Employee travel and accommodation costs	78	-	78	81	-	81
Other	759	(20,022)	(19,263)	600	6,363	6,963
Advertising	-	-	-	1,093	-	1,093
Governance costs	4,080	-	4,080	3,600	-	3,600
	85,665	458,344	544,009	70,009	584,109	654,118

Other costs include a credit of £20,022 (2021: expense of £6,363) relating to a foreign currency exchange difference. The charity agreed to fund two projects in US Dollars during 2019 and purchased the currency when the funding was contractually agreed. The US Dollars balance held at 31 October 2022 were translated into £ Sterling at the balance sheet date.

8 Analysis of governance and support costs

Governance costs

	Unrestricted funds				
	General £	Total 2022 £	General £	Total 2021 £	
Audit fee	4,080	4,080	3,600	3,600	
	4,080	4,080	3,600	3,600	

9 Grant-making

Grants payable at 1 November 2021	897,087
Grants paid	(395,053)
New grants committed	489,848
Commitments withdrawn	(11,482)
Grants payable at 31 October 2022	980,400

Institution		Title of Project	Grants paid 2022	Grants committed/ (withdrawn) 2022	Payable 2022	Payable 2021
University of Dundee	37	Insights into Pathophysiology of CFS/ME	12,473	-	-	12,473
University of Alabama at Birmingham	47	Tracking peripheral immune cell infiltration of the brain in ME	-	-	113,901	113,901
University of Vermont College of Medicine	48	Exploring an anti-citrullinated antibody signature in ME/CFS	3,386	(11,482)	-	14,868
Oxford Brookes University	49	Investigating sensory processing and cognitive function in people with ME: a pilot study	9,881	-	-	9,881
University of Applied Sciences, Graz, Austria	50	Role of Sirt1/NOS axis in vascular and immune homeostasis: A missing piece in the ME/CFS puzzle?	22,558	-	-	22,558
Universiteit Brussel	51a	Unravelling the role of epigenetic modification on the brain derived neurotrophic factor gene and histone de-acetylases for pain and post-exertional malaise in people with myalgic encephalomyelitis / chronic fatigue syndrome	26,329	-	13,165	39,494
Carried forward to page 42			74,627	(11,482)	127,066	213,175

Institution		Title of Project	Grants paid 2022	Grants commited/ (withdrawn) 2022	Payable 2022	Payable 2021
Continued from page 41			74,627	(11,482)	127,066	213,175
Universiteit Leuven	51b	Unravelling the role of epigenetic modification on the brain derived neurotrophic factor gene and histone de-acetylases for pain and post-exertional malaise in people with myalgic encephalomyelitis / chronic fatigue syndrome	17,335	-	17,335	34,670
Charité University, Berlin	53	The role of autoantibodies in ME/CFS	22,276	-	4,014	26,290
University of Valencia	54	Metabolic impact of activated HERVs and associated innate immune response in severe ME: towards disease modelling	26,600	-	26,600	53,200
University of Newcastle	55	ELUCIDATE: Exploring pain and autonomic dysfunction in ME/CFS and temporomandibular disorders	4,525	-	9,051	13,576
Universitait Wurzburg	56	Infectious triggers and mitochondrial dysfunction in ME/CFS	69,000	-	138,100	207,100
Griffith University	57	Investigating brain-stem dysfunction in ME/CFS using 7-Tesla MRI	100,000	-	51,000	151,000
La Trobe University	58	Cell-type specificity, molecular scope and epigenetic basis for mitochondrial and cellular dysfunction in ME/CFS	66,025	-	132,051	198,076
PolyBio Research Foundation	59	Use of advanced metagenomic technologies for the identification of viruses in ICC-diagnosed ME/CFS patient tissue and nerve biopsy samples	-	162,350	162,350	-
Quadram Institute	60	Gut eukaryotic viruses as a player in ME/CFS	-	123,874	123,874	-
Kings College, London	PhD1	Understanding potential infectious triggers behind mitochondrial dysfunction in ME/CFS	14,665	46,493	31,828	-
Carried forward to page 43			395,053	321,235	823,269	897,087

Institution	Title of Project	Grants paid 2022	Grants commited/ (withdrawn) 2022	Payable 2022	2021
Continued from page 42		395,053	321,235	823,269	897,087
Edinburgh University	PhD2 Experimental investigation of genetic risk factors for ME/CFS revealed by the DecodeME project	-	92,194	92,194	-
La Trobe University	PhD3 Cause-effect relationships in the mitochondrial energy inefficiency in ME/CFS	-	64,937	64,937	-
		395,053	478,366	980,400	897,087

As stated in the Trustees' Report, each of these projects relate to research which advances the objectives of the charity.

10 Trustees remuneration and expenses

Two Trustees were reimbursed for travelling and meeting expenses totalling £1,652.09 during the year (2021: one Trustee was reimbursed £217.17). No Trustees, nor any persons connected with them, have received any remuneration from the charity during the year.

11 Staff costs

The aggregate payroll costs were as follows:

	2022	2021
	£	£
Staff costs during the year were:		
Wages and salaries	70,846	50,779
Social security costs	-	2,134
Pension costs	2,851	2,205
	73,697	55,118

The average number of employees (full time equivalent) during the year was:

	2022	2021
	£	£
Charitable activities	1.1	0.9
Fundraising	0.2	0.2
Governance	0.7	0.7
	2.0	1.8

No employee received emoluments of more than £60,000 during the year.

The Trustees consider key management to be the Board of Charity Trustees. No Trustee received any remuneration, other than approved expenses, from the charity.

12 Taxation

No corporation tax was charged during the year (2021: £nil). ME Research UK is a registered charity and has been accepted as a charity for tax purposes.

13 Tangible fixed assets

	Furniture and equipment £	Total £
Cost		
At 1 November 2021	7,892	7,892
Additions	619	619
Disposals	(340)	(340)
At 31 October 2022	8,171	8,171
Depreciation		
At 1 November 2021	5,831	5,831
Charge for the year	1,246	1,246
Eliminated on disposals	(340)	(340)
At 31 October 2022	6,737	6,737
Net book value		
At 31 October 2022	1,434	1,434
At 31 October 2021	2,061	2,061

14 Fixed asset investments

Other investments

	Listed investments £	Total £
Cost or Valuation		
At 1 November 2021	47,166	47,166
Revaluation	(4,562)	(4,562)
At 31 October 2022	42,604	42,604
Net book value		
At 31 October 2022	42,604	42,604
At 31 October 2021	47,166	47,166

The market value of the listed investments at 31 October 2022 was £42,604 (2021 - £47,166).

All investment assets were held in the UK.

15 Stock

	2022 £	2021 £
Stock	1,609	1,568

16 Debtors

	2022 £	2021 £
Other debtors	9,953	201,357

17 Cash and cash equivalents

	2022 £	2021 £
Cash at bank	2,694,972	2,267,811

18 Creditors: amounts falling due within one year

	2022	2021
	£	£
Other creditors	499,848	557,443
Accruals	12,422	6,742
	512,270	564,185

19 Creditors: amounts falling due after one year

	2022	2021
	£	£
Other creditors	480,552	339,642

20 Obligations under leases and hire purchase contracts

The total value of future minimum lease payments was as follows:

	2022	2021
	£	£
Within one year	2,318	2,318

21 Funds

	Balance at 1 November 2021 £	Incoming resources £	Resources expended £	Other recognised gains/(losses) £	Balance at 31 October 2022 £
Unrestricted funds					
General					
Unrestricted funds	861,357	584,091	(149,432)	(4,562)	1,291,454
Restricted funds					
Restricted funds	754,779	170,166	(458,649)	-	466,296
Total funds	1,616,136	754,257	(608,081)	(4,562)	1,757,750

	Balance at 1 November 2020 £	Incoming resources £	Resources expended £	Other recognised gains/(losses) £	Balance at 31 October 2021 £
Unrestricted funds					
General					
Unrestricted funds	528,575	453,585	(129,108)	8,305	861,357
Restricted funds					
Restricted funds	1,180,434	158,567	(584,222)	-	754,779
Total funds	1,709,009	612,152	(713,330)	8,305	1,616,136

The specific purposes for which the funds are to be applied are as follows:

Restricted Funds are for the purpose of grant-making for research projects.

22 Analysis of net assets between funds

	Unrestricted Funds £	Restricted funds £	Total funds 2021 £
Tangible fixed assets	1,434	-	1,434
Fixed asset investments	42,604	-	42,604
Current assets	1,259,838	1,446,696	2,706,534
Current liabilities	(12,422)	(499,848)	(512,270)
Creditors over 1 year	-	(480,552)	(480,552)
Total net assets	1,291,454	466,296	1,757,750

	Unrestricted funds £	Restricted funds £	Total funds 2020 £
Tangible fixed assets	2,061	-	2,061
Fixed asset investments	47,166	-	47,166
Current assets	818,818	1,651,918	2,470,736
Current liabilities	(6,688)	(557,497)	(564,185)
Creditors over 1 year	-	(339,642)	(339,642)
Total net assets	861,357	754,779	1,616,136

23 Analysis of net funds

	At 1 November 2021 £	Financing cash flows £	At 31 October 2022 £
Cash at bank and in hand	2,267,811	427,161	2,694,972
Net debt	2,267,811	427,161	2,694,972

	At 1 November 2020 £	Financing cash flows £	At 31 October 2021 £
Cash at bank and in hand	1,854,906	412,905	2,267,811
Net debt	1,854,906	412,905	2,267,811

24 Related party transactions

Controlling entity
The charity is controlled by the Trustees of the charity.

Related party transactions

Prof Faisel Khan (Trustee)

Insights into Pathophysiology of CFS/ME

The above Project was paid funding of £12,473 during the year (2021 - £7,846). £nil remains payable at 31 October 2022 (2021 - £12,473). Prof Khan joined the Board after the decision was made to award this Project a grant and was not involved in the decision to award additional funding.

Dr Eleanor Roberts (Trustee)

Beeline Science Communications Ltd, a business owned by Dr Eleanor Roberts, was contracted to provide additional writing capacity aligned to a specific agreed schedule of work to the charity following the departure of ME Research UK's Science & Engagement Director. Amounts paid during the year were £1,690 (2021 - £5,070). At the balance sheet date the amount due to Beeline Science Communications Ltd was £nil (2021: £nil). Dr Roberts was not involved in any decisions regarding the awarding of the contract.