2016

# ME/CFS Research Funding

## AN OVERVIEW OF ACTIVITY BY MAJOR INSTUTIONAL FUNDERS INCLUDED ON THE DIMENSIONS DATABASE

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# Acknowledgements


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## Executive Summary

It is widely acknowledged that ME/CFS has faced significant under-investment in biomedical research over many years, both in the UK and overseas. In the past decade, there have been efforts by charities and researchers in the UK to redress this imbalance, and these efforts culminated in the award by the Medical Research Council (MRC) of five discrete grant awards under its "Understanding the Mechanisms" call in 2012, at a cost of approximately £1.65 million.

Today, ME/CFS research remains a highlighted area and a high priority for the MRC, yet research activity remains chronically low. There also remains a pressing need to raise the profile of the illness among active researchers and research-funding bodies and to obtain targeted investment.

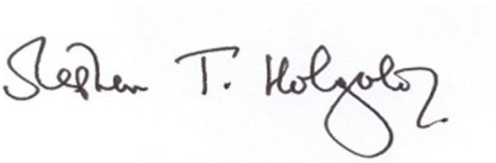
Surprisingly, there has never been a comprehensive analysis of research funding into ME/CFS, so we still do not have a clear picture of the levels of funding provided and how these have changed over time. Also, little is known about how funding for ME/CFS compares with funding for other illnesses, including chronic conditions with which ME/CFS is directly comparable.

The UK CFS/ME Research Collaborative commissioned ÜberResearch to interrogate its Dimensions database for relevant funding information. The resulting report presents hard evidence of the chronic lack of research funding for ME/CFS from major funding agencies. I hope that it will prove to be a foundation for larger mainstream funders to reassess their attitudes towards ME/CFS and review their funding policies towards the illness.

**Key Message 1: The scale and impact of ME/CFS on individuals and society is significant.** Around 250,000[1] people in the UK have ME/CFS which is at least as disabling as multiple sclerosis and congestive heart failure.[2] Many more people – carers, children and family members – are directly affected by the illness each year. The economic cost of ME/CFS was estimated at £6.4 billion[3] per year in the UK in 2006, and this figure will certainly have increased since.

**Key Message 2: Research funding has been low-level and patchy**, and investment needs to be increased, particularly for high-quality studies of biological mechanisms and treatments.

**Key Message 3: The skills, expertise and insight of researchers outside the field** are required to tackle the gaps in knowledge and understanding about ME/CFS.



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# 1. Introduction

## 1.1 Background

The aim of this report is to provide a comprehensive overview of funding provided for research into myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) at an international level since 2006. It examines the funders and funding recipients identified from the Dimensions database owned by ÜberResearch (www.uberresearch.com), and its conclusions are based on 'active' research awards that were current from 1 January 2006 to 31 December 2015.

It is important to note the limitations of the data: the list of funders is not exhaustive and does not include all the funding awarded for research into the illness; the funding provided by ME/CFS research charities is not included in the database, and there are some gaps where funders have not provided key data.

Also, in relation to the UK, the Dimensions database does not include the additional 'add-on' amounts given by Class one funders to cover institutional costs (circa £2 million and £1 million for the MRC-funded PACE and FINE trials, respectively). Appendix I provides a summary of the methodology used.

While this report may be the most comprehensive overview to date, it can only provide a snapshot of research funding over the last 10 years, and it highlights ongoing gaps in our knowledge base. Furthermore, it is important to note that the gaps in information held within the database appear to be more pronounced for ME/CFS than in other illnesses.

## 1.2 The Scale and Impact of ME/CFS

ME/CFS is a chronic illness that causes fluctuating symptoms affecting many body systems, most commonly the nervous and immune systems. People with ME/CFS experience severe mental and physical fatigue associated with chronic pain and post-exertional symptoms (the inability of the body to recover and/or a flare-up of symptoms after expending even small amounts of energy on simple physical or mental activity; sometimes also called 'payback'). However, ME/CFS is also characterised by a diverse range of additional symptoms which fluctuate and vary considerably in severity.

Listed by the World Health Organisation as a disorder of the nervous system,[4] ME/CFS affects an estimated 250,000[5] people in the UK, and at least 17million people across the world.[6] Prevalence estimates can vary widely due to the definitions used and the methods of diagnosis.

ME/CFS is at least as disabling as multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, congestive heart failure and other chronic conditions[7] and people with ME/CFS experience high levels of functional impairment across physical and mental domains, scoring lower overall on health-related quality of life tests than most other chronic conditions,[8] including lung disease, depression, heart disease and diabetes.[9]

Although the aetiology of ME/CFS is unknown, evidence suggests that there are likely to be a number of factors involved in triggering the onset of illness, the most common being viral infection. It is widely accepted that there are probably a number of clinical sub-groups or sub-types within the illness. For this reason, the UK CFS/ME Research Collaborative (CMRC) facilitated the Grand Challenge Workshop which resulted in the ME/CFS Epidemiology and Genomics Alliance (MEGA) being established to seek funding for a 'big data' study to better understand the underlying pathophysiology of the illness.

There is no specific, universally agreed single test to diagnose ME/CFS, though potential biomarkers are being investigated. Diagnosis is currently made after other causes for symptoms for disabling chronic fatigue have been excluded, and a diagnosis of ME/CFS requires many other symptoms in addition to fatigue. At present, there are many sets of diagnostic criteria for a diagnosis of ME/CFS; this creates challenges when comparing research studies and clinical trials, and the lack of standardisation of diagnosis and assessment complicates biomedical research.

There is presently no specific pharmaceutical treatment for ME/CFS. Currently, a symptom management approach is used by most clinicians, involving a combination of pharmacological treatments, symptom management, cognitive behavioural and graded exercise therapies, and management or coping strategies.[10]

## 1.3 Terminology

Within the NHS in the UK, healthcare professionals usually make a diagnosis of chronic fatigue syndrome (CFS) or CFS/ME. A variety of other terms can be used to describe the illness, including systemic exertion intolerance disease (SEID)[11], post-viral fatigue syndrome (PVFS) and chronic fatigue immune dysfunction syndrome (CFIDS).

The term Myalgic Encephalomyelitis or ME was first used in 1956 to describe a potentially chronic illness often associated with 'outbreaks,' of which one at the Royal Free Hospital in London is the most widely known. During the 1980s and 1990s, the term Chronic Fatigue Syndrome (CFS) came into use.

As there was (and presently remains) no specific diagnostic test for ME/CFS and, because 'fatigue' after exertion was one of its prominent symptoms, people with M.E. began to be diagnosed with CFS.

At present, the combination term ME/CFS is used by many people with the illness, clinicians and researchers to describe the illness. It is also the term now preferred by the National Institutes of Health (NIH) in the USA.

Currently, healthcare professionals in the UK tend to use the terms CFS, ME and ME/CFS interchangeably. However, as new evidence emerges it may become possible to define different illnesses presently included under the wide-ranging and commonly used term ME/CFS. Additionally, many research papers use the case definition based on the Fukuda *et al*[12] criteria, which requires presence of ongoing and significant fatigue in addition to four of eight core symptoms.

Another case definition for ME/CFS was suggested by Carruthers *et al*[13] which specified other core symptoms. More recently, Carruthers *et al* have developed, from the ME/CFS literature, another consensus-based case definition (ME-ICC) which specifies eight symptoms within four domains.[14]

None of the issues surrounding the name and diagnostic criteria alter the reality of the illness for thousands of people in the UK and millions across the world.

For the purposes of this report, the term ME/CFS will be used.

# 2. Overview of Data

## 2.1 ÜberResearch – Dimensions Database

ÜberResearch is a solutions and services company focused on the specific needs of science funders. For the last 10 years the ÜberResearch team has provided funders with information derived from tools based on natural language processing and search technologies. ÜberResearch was commissioned by the CMRC to provide data and commentary to inform this report.

ÜberResearch's online tool Dimensions contains a database of more than 200 funders across the world that allows for interrogation by subject area, and the information on ME/CFS research funding activity in this report was extracted from this source.

The Dimensions database includes details of most of the medical research funding in the UK, and has details of funding provided by 34 major grant funders, including all of the larger organisations, such as Research Councils UK, the Wellcome Trust, the British Heart Foundation, and Cancer Research UK.

It also holds information provided by major funding organisations outside the UK which fund UK institutions, such as the European Commission and the European Research Council, and on funders in the USA, Canada and Australia. However, coverage of research funding elsewhere in the world is less comprehensive.

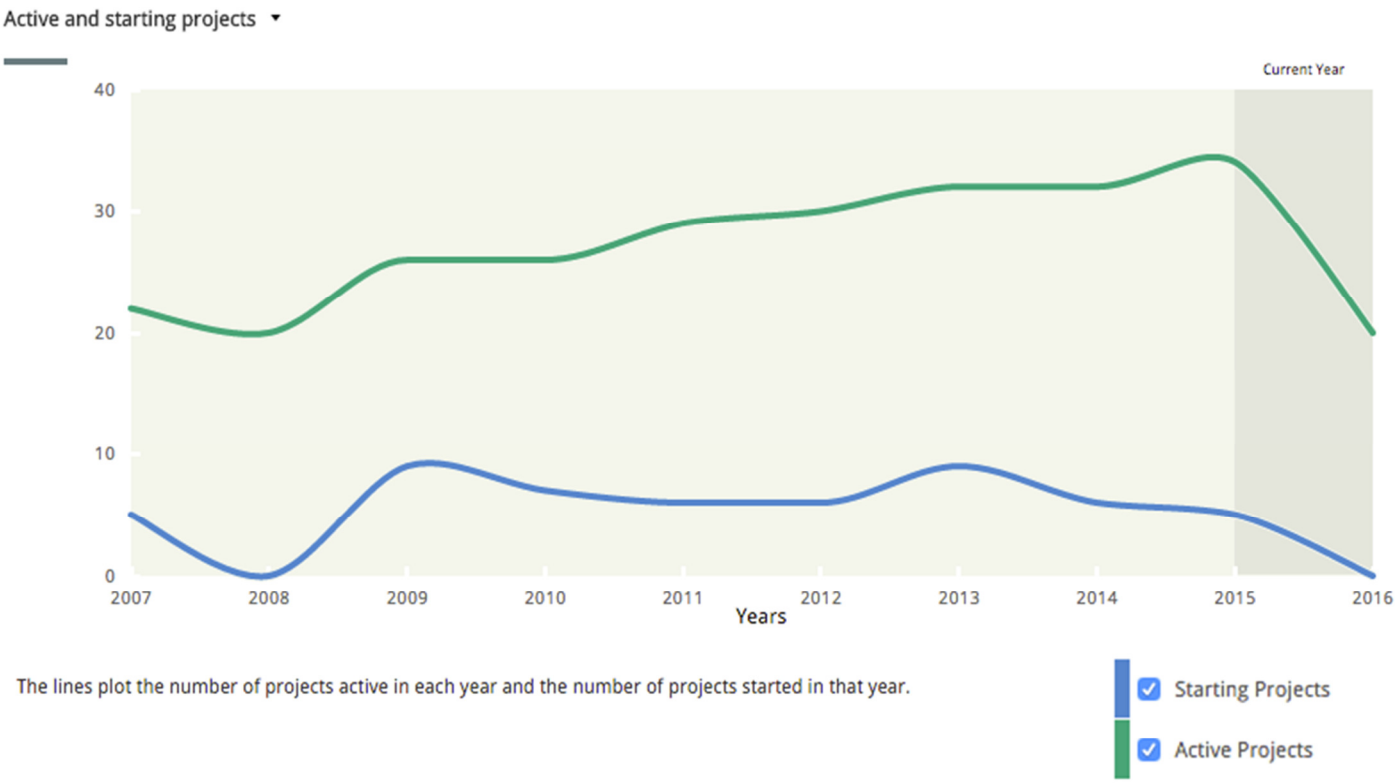
## 2.2 Research Funding by Country and Funders/Organisations

For the period reviewed (1 January 2006 to 31 December 2015) 99 grants amounting to £49 million had been awarded for ME/CFS research. However, 13 of these grants had missing details concerning the value of the award and so the total research spend on ME/CFS will have exceeded £49 million over the 10-year period.

The break-down of grants by country was as follows:

- 63 in the USA
- 20 in the UK
- 12 in Europe (excluding UK)
- 4 in Canada.

## Figure 1 - Global ME/CFS Grants (excluding the UK) since 2007




As Figure 1 above indicates, funding varies from year to year, but funding is provided for around six new projects each year on average in countries outside the UK. The figure is low, however, compared with the level of global funding for other comparable illnesses.

Most of the awards have come from the NIH in the USA through its different panels or boards:

- 20 grants from the National Institute of Allergy and Infectious Diseases
- 12 from the National Institute of Neurological Disorders and Stroke
- 5 from the National Institute of Nursing Research
- 3 from the National Institute of Arthritis and Musculoskeletal and Skin Diseases
- 2 from the National Heart, Blood and Lung Institute.

In 2015, the NIH announced a more robust approach to funding ME/CFS, following a report from the Institute of Medicine[15] which received wide publicity, together with its own commissioned report, Pathways to Prevention.[16]

## Table 1 - Non-UK organisations receiving most funding from grant-awarding bodies

| Organisation | Country | No. Grants | Value £ms | Recipient 1 | Recipient 2 |
|---|---|---|---|---|---|
| University of Miami | USA | 4 | 3.7 | Michael Howard Antoni | Mary A Fletcher |
| Cornell University | USA | 6 | 3 | Maureen Hanson | Dikuma Shungu |
| Ohio State University | USA | 1 | 2.5 | Marshall Vance williams | |
| Beth Israel Deaconess Medical Center | USA | 1 | 2.4 | Roy Freeman | |
| DePaul University | USA | 2 | 2.2 | Leonard A Jason | |
| Tufts University | USA | 3 | 2 | Theoharis Theoharides | Brigette Huber |
| University of Illinois at Chicago | USA | 1 | 1.4 | Renne Taylor | |
| Rutgers University | USA | 2 | 1.4 | Benjamin Natelson | Steven Schutzer |
| Nova Southeastern University | USA | 4 | 1.3 | Mary A Fletcher | Lubov Nathanson |
| Whittemore Peterson Institute | USA | 2 | 1.2 | Vincent Lombardi | |

Table 1 above provides a breakdown of the institutions receiving most funding from grant-awarding bodies (excluding UK) over the 10-year period.

Clearly, the University of Miami and Cornell University have received most funding, but the pattern overall is of a small number of grants distributed over a small number of institutions.

It is important to note that the amounts of money awarded (£1–4 million) are relatively small in a biomedical research context; and that grant-holders may move between academic institutions.

## Figure 2 – Grants for ME/CFS research from funding agencies in the UK since 2007

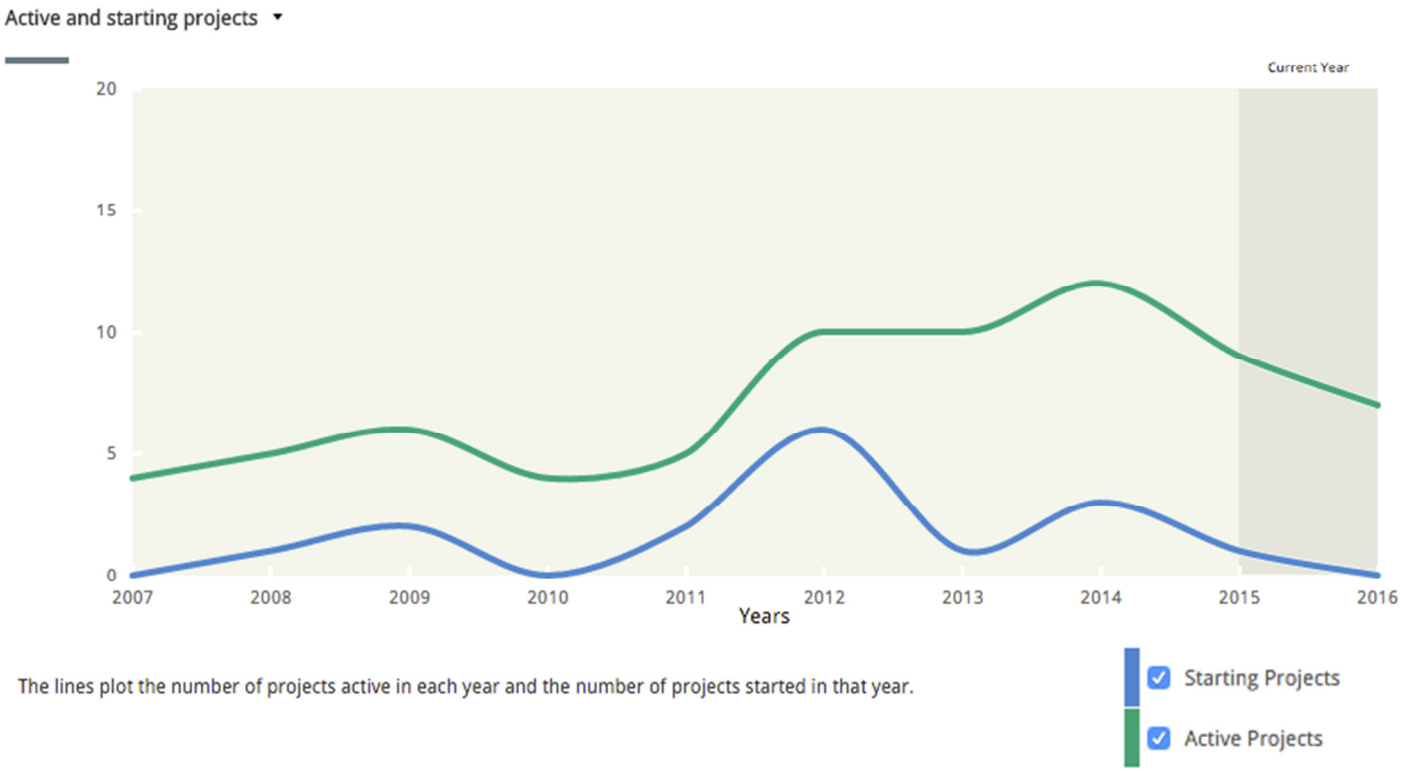



Figure 2 below above shows the active projects and the number of projects begun between 2007 and 2015 in the UK (snapshot taken in January 2016).

Grants awarded were few, around two per year on average, making it difficult to draw conclusions. The number varies from year to year, with the largest number awarded in 2012 when the Medical Research Council (MRC) announced funding for five projects following a previous highlight notice.

Of the 20 grants funded in the UK in the 10-year period, the breakdown by funder was:

- 12 from the MRC
- six from the National Institute of Health Research
- 1 from the Chief Scientist Office in Scotland
- 1 from the Wellcome Trust.

## Table 2 – Research organisations receiving the largest grant awards, with funding recipients since 2006

| Organisation | No. Grants | Value £ms | Recipient |
|---|---|---|---|
| Queen Mary University of London | 4 | 3.5 | Peter Denton White |
| University of Bristol | 4 | 2.3 | Esther Crawly |
| NewCastle University | 2 | 0.9 | Julia Lindsay Newton |
| King's College London | 1 | 0.37 | Carmine M Pariante |
| University of Manchester | 1 | 0.9 | Graham Dunn |
| St George's, University of London | 1 | 0.7 | Mark John James Edwards |
| King's College London | 1 | 0.29 | Kimberley Goldsmith |
| Imperial College London | 2 | 0.27 | David Nutt |
| University of Liverpool | 1 | 0.26 | Anne Mcardle |
| North Bristol NHS Trust | 1 | 0.25 | Hazel O'Dowd |
| King's College London | 1 | 0.24 | Leone Ridsdale |
| University of Aberdeen | 1 | 0.19 | Neil Basu |

Of the 20 grants identified in Table 2 above, Prof Peter White (Queen Mary University of London and Barts Health NHS Trust) has received most funding, more than £3.5 million. Prof White and Dr Crawley each hold four grants as principal applicants, so that eight of the 20 grants awarded were held by two recipients.

This may reflect the current emphasis on funding epidemiological aspects or treatment trials. It may also reflect the enthusiasm of the individual researchers, as grants can only be awarded to those who apply for funding. Additionally, it is important to note that the table refers only to principal applicants and not co-applicants who also 'hold' a grant.

Other major UK/European funders, such as the Biotechnology and Biological Sciences Research Council or the European Research Council (ERC), had given no funding for research into ME/CFS over the relevant period.

## 2.3 Breakdown of Broader Research Areas of the UK Grants

These 20 grants are also coded into Fields of Research[17] and Health Research Classification System Research Activity Codes (HRS RAC).[18] Please note, many grants will fall into multiple categories.

Looking into these areas gives a wider sense of the type of research being undertaken: 'basic' research is given a lower HRCS RAC number, and more 'applied' research is allocated a higher number. Each grant falls into one of eight main categories which have the following subdivisions:

1. Underpinning
2. Aetiology
3. Prevention
4. Detection and Diagnosis
5. Treatment Development
6. Treatment Evaluation
7. Disease Management
8. Health Services.

## Table 3 – Health Research Classification Codes

| Health Research Classification System Research Activity Codes | Count |
|---|---|
| Biological and endogenous factors 2.1 | 8 |
| Individual Care needs 7.1 | 6 |
| Pharmaceuticals 6.1 | 5 |
| Physical 6.7 | 4 |
| Psychological and behavioural 6.6 | 4 |
| Psychological, social and economic factors 2.3 | 4 |
| Management and decision making 7.3 | 3 |
| Surveillance and distribution 2.4 | 3 |
| Discovery and preclinical testing of markers and technology 4.1 | 1 |
| Evaluation of markers and technologies 4.2 | 1 |
| Methodologies and measurements 1.4 | 1 |

The HRS RAC codes shown in Table 3 range from quite basic research (biological and endogenous factors) to very applied (management and decision making).

## Table 4 – Fields of Research Codes

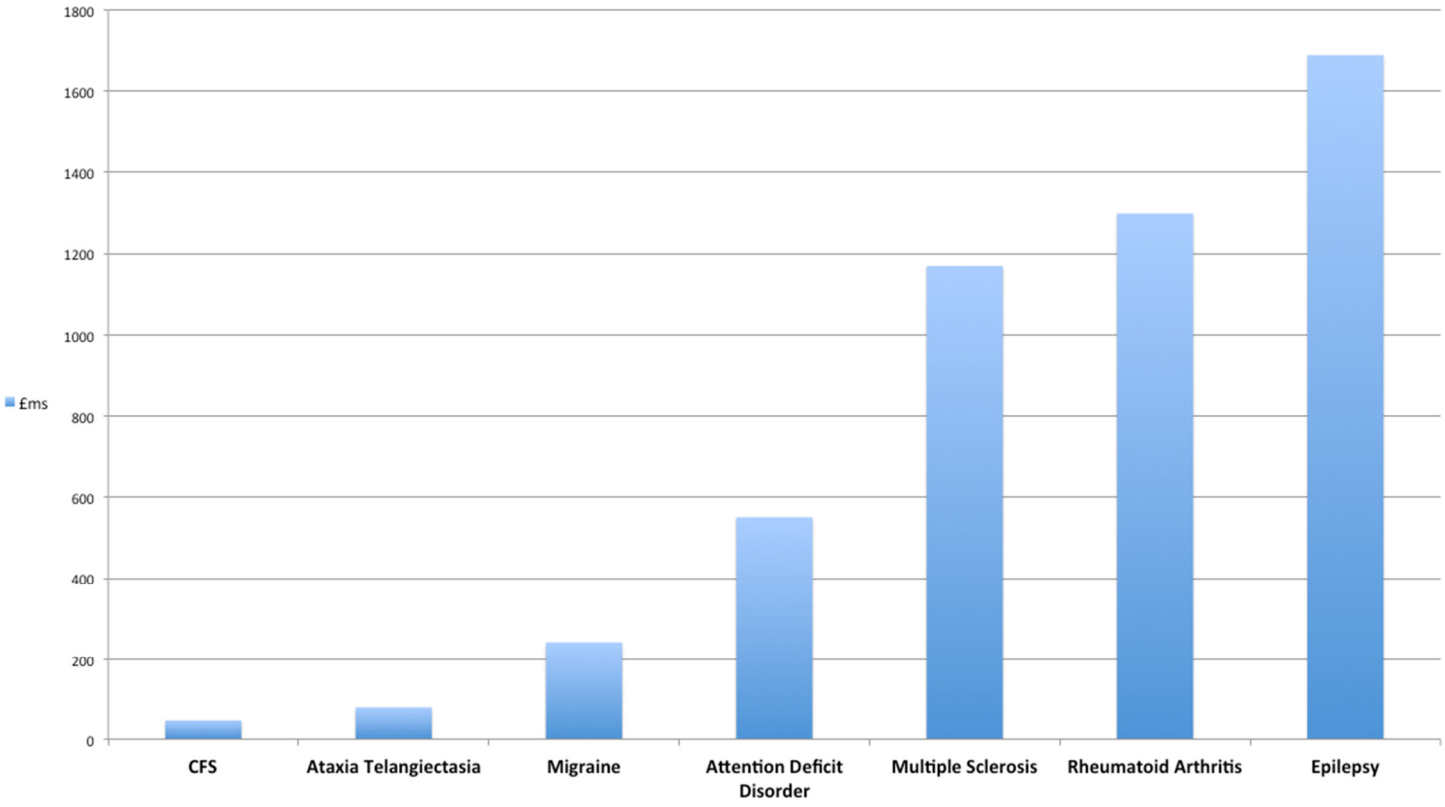
| Fields of Research Codes | Count |
|---|---|
| Public Health and Health Services | 11 |
| Clinical Sciences | 7 |
| Psychology | 4 |
| Neurosciences | 2 |
| Paediatrics and Reproductive Medicine | 1 |
| Immunology | 1 |
| Medical Physiology | 1 |
| Sociology | 1 |

## 2.4 Research Funding Compared to Other Illnesses

In the Dimensions database up to December 2015, there are 34 international active grants for ME/CFS research, at a value of approximately £17 million. To contextualise this, the UK's MRC has funded approximately 2,000 active grants, at a cost of approximately £2.3 billion, and the Wellcome Trust has funded 200 currently active grants costing £1.6 billion. ME/CFS research therefore represents approximately 0.02% of all active awards given by these mainstream agencies.

As the Dimensions database contains data from all large medical funders (including the MRC, the Biotechnology and Biological Sciences Research Council, the Wellcome Trust, the European Commission and European Research Council), the figure of £17 million is probably a reasonable approximation of the true situation.

**Figure 3 - ME/CFS funding compared with other neurological disorders (worldwide funding)**




As figure 3 above shows, ME/CFS receives comparatively little funding compared to other neurological disorders.

Furthermore within the UK specifically, for example, ataxia telangiectasia affects about 1,200 people in the UK[19] compared to the 250,000 estimated to have ME/CFS, yet its research funding is almost twice as large. MS affects about 100,000 people[20] but has received 20 times the funding.

While the prevalence of a disease is only one of the factors determining its level of research funding (7.6% of males and 18.3% of females of all people get migraines, for example[21]), funding for ME/CFS is nevertheless sparse compared with comparable conditions.

This is particularly surprising given research which indicates that people ME/CFS experience high levels of functional impairment across physical and mental domains, scoring lower overall on health-related quality of life tests than most other chronic conditions,[22] including lung disease, depression, heart disease and diabetes.[23] Researchers have concluded that "quality of life is particularly and uniquely disrupted"[24] in ME/CFS and that patients are, on the whole, not able to retain their previous capacity to remain active and perform roles in society.[25]

For example, the Dimensions database shows that of the total spent on research into chronic pain (£3.5 billion based on RCDC Pain Research category), only 1% was awarded for ME/CFS research.

The paucity of research into ME/CFS compared with other chronic conditions is particularly evident in Table 5 below, which shows that the global research spend per patient is far lower for ME/CFS than for rheumatoid arthritis, MS or epilepsy.

### Table 5 - Research spend per patient, by medical condition

| Disease | Research spend per patient from 2006 to 2015 (£) |
|---|---|
| Migraine | 1 |
| ME/CFS | 40 |
| Attention deficit disorder | 60 |
| Epilepsy | 200 |
| Rheumatoid arthritis | 320 |
| MS | 800 |
| Ataxia telangiectasia | 3333 |

## Table 6 – Funding since 2007 for selected conditions including ME/CFS with estimated number of people with the illnesses

| Disease | Number of patients in UK | UK funding (£) | Number of patients worldwide | Worldwide funding (£) |
|---|---|---|---|---|
| Batten disease | 60 | 1m | 1,500 | 55m |
| Ataxia telangiectasia | 1,200 | 4m | 45,000 | 74m |
| Rett syndrome | 3,000 | 9m | 75,000 | 160m |
| ALS | 5,000 | 49m | 130,000 | 492m |
| Fragile X syndrome | 12,000 | 8m | 300,000 | 233m |
| Charcot-Marie-Tooth disease | 24,000 | 3m | 600,000 | 81m |
| MS | 100,000 | 74m | 2.5m | 1.1bn |
| Aphasia | 200,000 | 18m | 5m | 200m |
| ME/CFS | 250,000 | 10m | 17m | 47m |
| Epilepsy | 600,000 | 117m | 15,000,000 | 1.6bn |
| Rheumatoid arthritis | 700,000 | 223m | 30,000,000 | 1.3bn |
| Neuropathy | 1,200,000 | 100m | 30,000,000 | 1.3bn |
| Fibromyalgia | 2,500,000 | 3m | 63,000,000 | 105m |
| Migraine | 9,000,000 | 17m | 225,000,000 | 216m |
| Attention deficit disorder | 300,000 | 31m | 7,500,000 | 529m |

Table 6 above shows the funding amounts since 2007 for selected comparison diseases, and the estimates of numbers of patients affected in the UK and across the world.

Clearly, ME/CFS receives a disproportionally small amount of UK research funding given the prevalence of the condition. Despite the disease burden, the level of research spend per ME/CFS patient is considerably lower than in other illnesses. MS, for example, receives approximately 20 times more funding worldwide despite being far less prevalent than ME/CFS.

However, complex issues are involved when comparing research funding and disease burden across different illnesses, and simple comparisons can be indicative only. For example, the disease burden involves not only numbers of patients but the severity of illness, quality of life and economic costs.

As previously stated in this report, ME/CFS is at least as disabling as many other chronic illnesses and severely impacts on patients' quality of life. The cost to the economy remains high with costs estimated at £6.4bn in 2006 with the loss in earnings calculated as £101 million in 2011.[26] It is anticipated that these figures have significantly increased in subsequent years.

A 2014 ME/CFS charity survey identified that less than one in 10 people with M.E./CFS were in full-time paid work, education or training and only 14% in part-time paid work, education or training.[27] The pressures on the NHS are significant with 19,985 estimated newly diagnosed cases in the UK each year[28] and a reported reduction in secondary care service provision which is not meeting demand.

For example, 46% of GPs report that ME/CFS is the top illness group for which they have difficulty in making referrals with 30% reporting concern that ME/CFS treatments as the most likely to be excluded from the NHS in the next five years; ME/CFS was at the top of the list with infertility.[29] In the same report by Aviva, 22% of GPs reported an increase in patients reporting ME/CFS in the past year.

While calculating the disease burden is complex, it is nonetheless abundantly clear that ME/CFS receives a disproportionately low level of funding, and this issue needs to be addressed.

# 2. Challenges and Actions

This report has identified the comparative lack of mainstream research funding into ME/CFS in the UK, highlighting a mismatch between the disease burden and the funding invested in research compared with other comparable physical illnesses.

The impact and cost of ME/CFS is high at a personal, economic and societal level, but levels of investment have been completely inadequate to address the fundamental causes of the condition and build the knowledge base required to inform better, more targeted treatments.

This report has identified a number of challenges. The CMRC has identified a number of actions which it will lead to help significantly advance research into ME/CFS.

## Challenge 1: Increase investment in research

This report has presented evidence that ME/CFS has been poorly supported by research funding over the past decade, and that more research is needed. In essence, the data has confirmed what most of us already knew: the illness is an 'orphan' when it comes to research and recognition.

Research is vital if the underlying biology of ME/CFS is to be understood, and if different subsets (phenotypes) of patients, which may be caused by differing underlying mechanisms, are to be identified. This data can then be used to inform the development of new diagnostic tests and treatments targeted to specific phenotypes. It is particularly important that all avenues are explored, including genetics, epigenetics, proteomics and metabolomics.

The CMRC will increase its work with mainstream funders in the UK and will circulate the report to these agencies with a request that they reconsider their current positions *vis a vis* the specific allocation of funds to ME/CFS. These funders should work with the CMRC to identify actions that can be taken to enrich their portfolios of investment in ME/CFS, including the review of current programmes and highlight notices.

While funding investment is critical, it is also essential to stimulate interest from leading researchers and scientists from outside the field to accelerate progress in ME/CFS research. It is widely recognised that inter-disciplinary approaches to tackling diseases are the way forward, particularly to delineate underlying causal pathways and develop treatments, and such collaborative approaches are necessary for ME/CFS.

The CMRC held a Grand Challenge workshop in 2016, leading to the establishment of the ME/CFS Epigenetics and Genomics Alliance (MEGA). MEGA is working to establish a funding application for a big data study, as previously outlined earlier in this report. The success of engaging nine leading researchers from outside the ME/CFS field will form the basis of further progress.

## Challenge 2: Undertake a critical analysis of categories of research funding to identify under-researched areas for future investment

The CMRC will work with mainstream UK funders to undertake a more detailed analysis of the gaps in current funding programmes to inform future funding priorities. Additionally, the CMRC will work with researchers and people affected by ME/CFS to use this analysis to set priorities to shape future funding in the UK.

## Challenge 3: Improve the success rate of applications for research funding to mainstream funders

Anecdotal information highlights both the low number of applications submitted to funders for ME/CFS-focused research and the low success rates for those applications actually submitted. The CMRC is seeking to address this through peer review support for research members and with a focused session at the CMRC's forthcoming conference.

Additionally, the CMRC's Board will invite mainstream funders to engage with them to explore what further action can be taken to enhance the quality of applications and increase the overall competitiveness of research applications in this field.

# Appendix I – Methodology

This review of ME/CFS Research was undertaken using the Dimensions tool from ÜberResearch (www.uberresearch.com).

The Dimensions database has collated and disambiguated grants data from more than 140 funders worldwide. The majority of grants given in the UK are included (RCUK, Wellcome Trust, CRUK, British Heart Foundation, etc) as well as American (NIH, NSF, Veterans Affairs, CDC etc), Canadian (NSERC, CIHR etc), Australian (ARC, NHMRC etc) and European funding (EC, ERC) with many others being added all the time.

Action for M.E., in conjunction with the Dimensions staff, created a semantic category to reasonably represent ME/CFS research. The final category did include three false positives (which were removed manually from this report). Even so, this meant that there was a 96% accord, with no false negatives, from the Subject Matter Experts. This makes for a more than acceptable reporting category. This category involves a complex but repeatable query.

There are three elements to a Dimensions category:

- a Boolean expression
- an ability to 'Boost' terms
- an ability to remove the long tail of grants that mention ME/CFS but are not deemed to be of a sufficient degree to make it into the ME/CFS set.

The Boolean expressions are linked to algorithms utilising the Natural Language Processing that underpins Dimensions. Each term expression receives a score based on the following rules.

- More specific terms receive a higher score than more common terms. This is calculated exactly by determining the total number of mentions a term has against the whole of the grants database.
- A term found in the title scores more than the same term found in the abstract.
- The same term found in a short abstract score more than the same term found in a longer abstract.

A Boost term also scores points but does not, in itself, increase the return set. The idea of Boost terms is to find a congregation of terms in 'true' grants to remove the false positive grants.

Each term, whether Boolean or Boost, scores points, and those points are summed per grant. A high score means more terms have been found, whereas a low score means fewer terms found. A threshold can then be applied to remove the tail of false positives.

This process ensures the best compromise between acceptable recall (finding all grants) and Precision (removing false positives).

ÜberResearch believe the category used in this report provides some representation of ME/CFS research, with the following caveats.

- Grant data sources are public, and therefore not perfect. That is, Public Grant databases may not hold all grants awarded; they may not be updated regularly, and may have missing data.
- Where the grants data only have titles, they are likely to show fewer grants, because the scores will necessarily be lower due to the missing abstracts.
- All Subject searches require a degree of subjective decision-making: there is no perfect set.

- It is acknowledged that not all ME/CFS funding has been captured as some funders do not use the Dimensions database; this particularly includes all ME-CFS charities which provide funding for research.
- Overlaps with other illnesses were considered and non-relevant grant funding was removed through a process of assessment of abstracts by three current researchers

The ME/CFS Category has now been saved within the Dimensions application and can therefore be re-used in future years for a repeatable review based on a consistent approach. Therefore by re-using this approach any change to the ME/CFS research activity in future years will be easy to determine.

# Appendix II – Clarifications

This report looks at ME/CFS research over the past decade. If a grant was active at any time during the last 10 years then the whole amount awarded was included in the figures.

## 1) Sterling Values

All figures are shown in £ UK. In Dimensions amounts awarded are held in local currencies, but Dimensions makes an automatic translation to US dollars (other currencies will be available soon) based on the exchange rate for the relevant date. Therefore all figures were original in US dollars. For this paper these were converted to sterling by multiplying by 0.65.

## 2) Funding Data

Some funding data is missing. Dimensions uses publically available data sources (such as Gateway to Research, Euro PubMed Central, eReporter, etc as well as some direct feeds) and these data sources do have some data quality issues. Notably a small percentage of other grants from other funders (about 5%) are submitted without award amounts.

## 3) Data Sources

Dimensions holds the data of more than 200 funders worldwide, but not all of these are biomedical funders and therefore do not contribute to this report.

## 4) Double Counting

The exercise looked at grouping categories together under broad headlines. For each subsection the results are accurate (with the provisos on data given above) but within the broad headlines of 'Molecular and Cellular Medicine' etc. there can be double counting.

## 5) RCDC Category Chronic Fatigue Syndrome (ME/M.E.)

The NIH has a category called "Chronic Fatigue Syndrome M.E./ME" which, upon advice from subject matter experts, we decided not to use. This category, which is emulated in Dimensions, brings back more grants, but many were considered to be 'false positive' returns. This is mainly due to interpretation in a complex area. A number of USA grants in Gulf War Syndrome are classified by the NIH as ME/CFS. However, including these grants artificially increases the amount of research in ME/CFS itself, and therefore we crafted a new Category to better reflect this.

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