MRC Medical Research Council

MRC STRATEGIC REVIEW OF NUTRITION AND ENERGY BALANCE

Report of the Strategic Review Meeting, 16-18 April 2008

MRC Strategic Review of Nutrition and Energy Balance

1. EXECUTIVE SUMMARY

The purpose of this review is to advise the MRC's Council, through Strategy Board, of the current state of research in this area and opportunities for future development.

Research into nutrition and energy balance is central to addressing major public health challenges of the 21st century, including obesity and the health of an ageing nation.

UK strengths, needs and opportunities

Bibliometric analysis indicates that the UK is an international leader in the field and the impact of UK research is high relative to the level of investment. Particular UK strengths include the study of early life nutrition and its impact on later health outcomes, epidemiology, genetics, molecular biology, biochemistry and micronutrients.

The investment into fundamental 'classical' nutrition research has been declining. New developments and innovation are needed in core disciplines of nutrition research, **integrating nutrition and modern biological approaches**, and developing novel tools and technologies for robust and sensitive measurements of nutritional exposure and energy expenditure.

The UK has a shortage of well-trained innovative nutrition researchers and there is a **major need for training** of, in particular, clinically-qualified researchers and basic and clinical scientists between post-doctoral and first substantive academic post. Strong leadership is required, and a recognisable centre of excellence that is competitive on the world stage and acts as a magnet for the training of the next generation of integrative[1] nutrition researchers.

Research relevant to nutrition and energy balance is supported by the UK research councils, government departments and agencies, charitable organisations and industry. There is a need and opportunity for the development of a **national strategy** for the entire nutrition field, connecting with the National Institute for Health Research (NIHR) strategic lead on obesity, and for the coordination of activities between funders; there is also potential to influence public health agendas through developing better **models of engagement with the food industry**, including food manufacturers, suppliers and retailers, as is currently being pursued in other fields with the pharmaceutical and biotechnology industries.

The MRC portfolio in Cambridge

The critical mass of outstanding expertise across a range of disciplines relevant to nutrition and energy balance in Cambridge provides a real opportunity for the creation of an **identifiable centre of excellence for integrative nutrition research** under the umbrella of the MRC. This would not necessarily require a new physical entity; rather, it would facilitate collaboration between existing groups and allow recognition of the expertise present in nutrition. This should have an externally communicated, overarching scientific strategy and could form

[1] combining classical nutrition research with cutting-edge approaches in other areas

the hub of a wider UK network linking in other MRC and non-MRC centres of excellence in nutrition research.

Mitochondrial dysfunction is linked to multiple complex diseases, including obesity, diabetes, cardiovascular disease, cancer, muscle disorders and age-related neurodegenerative disease. Furthermore, even in healthy agers the numbers of mitochondria, as well as their efficiency, decline in muscle and other cells. MRC research has broadened from mitochondrial energy conversion into more general but no less important research into mitochondrial biology. This has opened multiple avenues for research and translation relating to complex diseases both within and outwith the field of nutrition and energy balance. There is an unrivalled opportunity for the MRC to provide leadership in the increasingly important and cross-cutting area of mitochondrial biology.

2. INTRODUCTION

2.1 Scope of the review

This review covers the current state of research in nutrition and energy balance, current needs and opportunities for future development. It provides advice to the MRC's Council through Strategy Board.

Nutrition can be described as the study of the interaction between one component of the environment - food[2] - and an organism at the individual (molecular to whole-body) or population level. For the purposes of this review, research relevant to nutrition and energy balance includes: research on the impact of diet or food components on normal biological function, health status or behaviour; the effect of maternal diet/birth weight on life course events; gut function and nutrition-related diseases; food safety; food production and supply where directly relevant to nutrition; consumer choice and food availability; energy balance at the cellular and physiological level; and appetite control and factors influencing malnutrition and obesity. Within these areas, the review group's discussion was mainly focused on those aspects relevant to the remit of the MRC.

2.2 Background to the MRC's strategic review

The MRC funds medical research through its four research boards. Research on nutrition and energy balance is mainly supported through the Population and Systems Medicine Board (PSMB) and is a major component in PSMB's portfolio.

The review was undertaken by an international review group, chaired by Professor Stephen Holgate (Southampton, Chair of PSMB) with the aim of formulating advice to PSMB and the MRC's Council on the MRC's medium to long-term strategy for supporting research in nutrition and energy balance. It comprised two elements:

- A field review to advise on UK strengths, gaps, needs and opportunities and within that broader remit to focus on MRC's strengths, the opportunities to add value to MRC's investments and the potential for partnerships.
- A review of mitochondrial energy conversion research to advise on the current contribution and future opportunities of this research in nutrition as well as its relevance to other areas.

The terms of reference and membership of the review panel are at Annex 1.

The review took into account submissions from a wide range of experts and stakeholders in the nutrition and energy balance field, including UK universities, research funders and policy-makers, major MRC intramural and extramural investments, and industry. Organisations that have provided comments are listed at Annex 2. Additional comments were received from UK and international experts in a personal capacity. The review group was impressed by the quality of the submissions received. All comments were considered at a preliminary meeting to determine the key issues and areas for discussion with MRC unit and centre directors at the main meeting. The preliminary meetings also involved the BBSRC[3], the Food Standards Agency and the Department of Health as a first step towards the identification of emerging opportunities for partnerships.

[2] including nutrients, non-nutrient components and beverages
[3] Biotechnolology and Biological Sciences Research Council

3. CURRENT RESEARCH FUNDING IN NUTRITION AND ENERGY BALANCE

3.1 The UK landscape

Research relevant to nutrition and energy balance is supported by the UK Research Councils (MRC, BBSRC, and ESRC[4]), government departments and agencies (Department of Health/NIHR[5], Food Standards Agency, Scottish Executive), charitable organisations (The Wellcome Trust, Cancer Research UK, British Heart Foundation) and industry. The annual spend across the public and not for profit sector (including charities) is currently in excess of £70m[6]. Joint funding initiatives include the National Prevention Research Initiative (NPRI); the UKCRC[7] initiative for Public Health Centres of Excellence; the joint research council initiative on Lifelong Health and Wellbeing; and the BBSRC-led Diet and Health Research Industry Club (DRINC). An analysis of the UK funding is at Annex 3.

3.2 The MRC's portfolio

In 2006/07, the MRC spent £38m on research relevant to nutrition and energy balance. Approximately three-quarters of this investment supported research and training in the MRC's own units and institutes. The remainder was spent in UK universities supporting research grants, fellowships and centres of excellence. An analysis of the MRC's portfolio and list of major intra- and extra-mural investments is at Annex 4.

3.3 European Union funding

Framework Programme 7 (FP7) supports collaborative research relevant to nutrition and energy balance undertaken by European consortia through two broad research themes:

- The Food, Agriculture and Biotechnology Theme supports research on nutrition, food processing, food quality and safety, and environmental impacts and the total food chain.
- The Health Theme funds research on immunotherapy for food allergies and nutritional signals for the development of new obesity therapeutic agents.

3.4 US funding

In the US, federal support for nutrition research is mainly provided by the NIH[8] ($1b pa) and at a lower level by the USDA[9] ($97m a year). The percentage of NIH spend on nutrition research relative to the total budget is similar to that of BBSRC and the MRC (3-8 per cent). NIH funding is dispersed across the US and there is no dedicated NIH nutrition institute. The USDA supports nutrition research through the Agricultural Research Service National Research Programme on Nutrition Research at several locations in the US. A major focus for nutrition research in the US is the Pennington Research Institute in Louisiana, with an annual budget of $61m. Although multidisciplinary and multifaceted in approach, the current focus at this institute is the prevention of obesity and obesity-related diseases.

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[4] Economic and Social Research Council
[5] National Institute for Health Research
[6] Based on the consultation inputs into the review (Annex 2)
[7] UK Clinical Research Collaboration
[8] National Institutes of Health
[9] United States Department of Agriculture

3.5 Global impact of UK nutrition research

To evaluate the impact of UK nutrition research, Evidence Ltd was commissioned to undertake a bibliometric analysis. The limitations of the analysis, which was mainly based on publications in nutrition and dietetics journals meant that only very general conclusions could be drawn:

- The publication volume in nutrition and dietetics has increased globally over the last 10 years.
- The impact of UK nutrition and dietetics research has consistently improved over this time period, while the rest of the world has shown little change.
- The impact of publications from MRC units relevant to nutrition and energy balance across the full range of their core disciplines is above the world benchmark and UK baseline in these disciplines.

An analysis performed by the review group demonstrated that relative to funding the impact of UK-based nutrition research was higher than that in the US.

4. STATE OF SCIENCE AND FUTURE DIRECTIONS

The review group selected a number of key themes that formed a focus for detailed discussion at the review meeting. These were identified based on a preliminary consideration of the consultation inputs (Annex 2). The section below summarises the debate focusing in particular on the needs an opportunities in the field.

4.1 Obesity

The rapid rise in obesity is a major challenge. The incidence of obesity in the UK has grown three-fold since the 1980s and an estimated 70 per cent of adults are overweight/obese (BMI >25) and ~25 per cent are clinically obese (BMI >30). Obesity is associated with an increased incidence of several major diseases, including diabetes, coronary heart disease, and breast and colon cancer. The economic cost of obesity is substantial and is projected to rise to £45 billion a year by 2050[10] in the UK.

<u>Research needs and opportunities</u>

Obesity is heterogeneous in nature. Although obesity is a clear risk factor for poor health, its relationship to associated diseases is not clear and there is significant individual variation in what constitutes optimal weight. A better understanding is needed of fundamental **adipose biology** and how excess adipose tissue relates to disease. Although the study of adipose cells themselves is important, an equally important and neglected aspect is the investigation of fat and energy metabolism in non adipose tissue such as muscle. Proposed research includes better characterisation of the obesity phenotype and understanding of the relationship between obesity and health consequences in different phases of the life-course and in different ethnic groups. There is an opportunity to harness new technologies, including genetics and metabolomics, and improved mechanistic understanding for the development of biomarkers to predict health endpoints.

Many genes associated with obesity are related to the neuro-endocrine system and understanding the fundamental biology of **appetite regulation** in humans and model systems is an important priority for the future. This includes

[10] Foresight, Tackling Obesities: Future Choices – Project Report (2007)

integration of neurosciences and the investigation of neuro-endocrine networks and peripheral signals, including social and cultural influences on dietary choice and habits, and their amenability to change. Better tools are needed to analyse the neuro-endocrine control of tissues (fat, muscle, bone), as well as measures of appetite for population studies.

An important area is the impact of **physical activity** on obesity. There is a need for medium-sized and sustainable cohorts with detailed information on diet, behaviour and phenotype, requiring robust tools for the measurement of dietary exposure, the characterisation of physical activity and behaviour, and 'deep-phenotyping'. Long-term studies are also required to understand the determinants of physical behaviour at the population level, including the investigation of natural experiments on how the environment impacts on physical activity and health. Although not specifically covered as part of this review, the science of physical activity and metabolism is very important to the understanding of energy balance. The levels of investment in this science area are disproportionately low relative to its importance to public health.

Public health strategies are needed for the **prevention** of obesity. There is a requirement for the development of complex behavioural interventions relating to food choice and physical activity throughout the life-course, and the development of tools for the evaluation of interventions at the population level.

4.2 Nutrition for optimal health throughout the life-course

On average, longevity in developed countries has increased by the equivalent of six hours a day since 1830 (~2.5 years a decade). For the first time in UK history, there are now more people above the age of 60 years than below the age of 16 years. However, the length of healthy lives has not increased at the same rate. Lifestyle factors, including the quality of diet and level of physical activity, and metabolic health are key determinants for a long and healthy lifespan.

Research needs and opportunities

There is a dearth of information about nutritional needs at different stages of the lifespan, in particular in early and late life. More research is needed on the impact of nutrition on the maintenance of well-being, the prevention and management of disease and the amelioration of the effects of ageing. This requires a better **characterisation of the healthy phenotype** at different stages of the life-course, including knowledge of what to measure (cognitive health, muscle function and quality of life), functional intermediary measures for disease risk and ageing (damage repair, inflammation, metabolic or oxidative stress), as well as the development of nutritional challenge tests. An important area of research is the optimal intake of **micronutrients** at different stages of the life-course.

We need a better understanding of the **long-term effects of nutrition on the phenotype**, including what nutritional challenges under which circumstances are enduring, how these are 'memorised' and revealed, and the basic epigenetic mechanisms contributing to this process.

Most nutritional challenges are addressed by homeostatic mechanisms. A better understanding is needed of what determines our **changing ability to meet challenges with appropriate responses** during the life-course, the switches between healthy growing, ageing and disease development, and how they vary across cultures.

Mitochondrial defects are associated with many age-related diseases but little is known about the underlying mechanisms. Even in healthy agers, mitochondrial numbers are significantly reduced and mitochondrial efficiency is attenuated. Hence, an important area of research is the **role of mitochondria in the ageing process**. For instance, the relationship between physical activity and mitochondrial numbers in muscle cells, how mitochondrial DNA mutations affect ageing and the capability for energy conversion, and the contribution of mitochondria generated reactive oxygen species. A better understanding is needed of cellular senescence and the relationship between metabolic phenotype and ageing in animal models to inform human studies.

Research on healthy ageing needs an **integrated approach** involving mechanistic studies, epidemiology, the relationship between the physiology and psychology of health, interventions and socio-economic studies. The evidence for the major influence of diet and activity on a long and healthy life stems mostly from observational studies with a high risk of confounding and there has been little investment in large intervention studies to clinical endpoints. There is an opportunity to build on the UK strength in life-course research and use the available mechanistic knowledge for **behavioural intervention studies**.

Other important areas of nutrition research include the **impact of nutrition on infectious disease, the immune system, recovery from illness and gastrointestinal function**, including food allergies.

A critical area of research is **nutrition in developing countries**, including malnutrition and vitamin and other micronutrient deficiencies and their relationship to disease. This area was not discussed extensively, but will be covered by other mechanisms as appropriate.

4.3 Nutritional genomics

The response to dietary intervention varies between individuals and ethnic groups. Major progress has recently been made with the identification of genetic variants associated with obesity and metabolic disease in whole genome association studies. Although care needs to be taken to justify these studies on the basis of personalised prevention, these studies provide powerful discovery tools. There is a need and opportunity to **link the observed effects to gene function** in order to verify outcomes and to advance mechanistic understanding of pathways that are amenable for nutritional or other modulation.

The immense scale required for gene nutrient interactions to achieve sufficient power necessitates studies at European level and the analysis of the effects of multiple genetic and nutritional factors needs new **sophisticated mathematical approaches**, and data mining tools as well as suitable measures for diet and physical activity. While significant progress has been made on the development of the “omics” technologies for the definition of phenotypes, substantial work is needed on the identification and measurement of **dietary intake patterns,** as well as defining the **bioactive components of food**.

4.4 Cohorts

The UK has a key **strength in cohort studies** with relevance to nutrition research and a competitive advantage based on good systems for follow-up, NHS data bases, and the integration into cutting edge Biomedical Science Departments. Cohorts that have made significant contributions to the nutrition

field include for instance ALSPAC[11], EPIC[12] and NSHD[13], and there are opportunities to maximise the potential of major new cohorts, including UK Biobank. Different approaches and scales are needed to address the range of research questions, weighing up precision of measurements against frequency of outcomes, and for many applications smaller studies with detailed characterisation of exposures and phenotypes will be valuable. Risk factors and public health impacts are changing over time, which will require the updating of existing cohorts and establishment of new ones. Although there are obvious benefits in opening up cohorts to external collaborators in terms of maximising the output from investments in those cohorts, the intellectual input to keep high-quality and informative cohorts together and the non-insignificant long-term resourcing commitment of funders needs to be recognised.

4.5 Mitochondrial energy conversion

Mitochondria are involved in many physiological processes and mitochondrial dysfunction is linked to multiple complex diseases, including diabetes, cardiovascular disease, cancer and age-related neurodegenerative disease. It is estimated that one in five to ten thousand people in the UK will suffer from a disease resulting from a mutation in mitochondrial DNA at some point in their lives.

The importance of mitochondrial biology is recognised in the US through dedicated mitochondrial research and disease societies and substantial NIH involvement, including a roadmap initiative and symposia. There are major gaps in our knowledge of basic mitochondrial function, including enzyme mechanisms at the molecular level, mitochondrial metabolism, chemistry/human pharmacology and quantitative experimental biochemistry. In particular, there is a major gap between the physiological and clinical aspects of mitochondrial research and the basic biochemistry and molecular interactions of critical molecules in the energy conversion cascade. There is also a lack of understanding and training of clinicians in the basic biochemistry underlying mitochondrial function and energy metabolism more broadly.

[11] Avon Longitudinal Study of Parents and Children
[12] European Prospective Investigation of Cancer
[13] MRC National Survey of Health and Development

5. CONCLUSIONS FROM THE REVIEW GROUP

5.1 UK strengths

The UK has a high-quality research base in many areas relevant to nutrition and energy balance. The investment in Nutrition Departments across UK universities has increased continuously over recent years and there is a **growing strength and multi-disciplinarity in university-based nutrition research**. There is a critical mass of MRC-supported nutrition research in Cambridge, benefiting from the co-location of basic, clinical and population-based research with relevance to obesity and cancer and strong links into neurosciences.

UK scientists are **world leaders in the study of early life nutrition** and its impact on later health outcomes, including the developmental origins of adult disease. Other UK strengths include epidemiology, building on the long-term investment in cohorts, and genetics, molecular biology, biochemistry and micronutrients.

5.2 Needs/opportunities

The absence of a clinical (sub)-speciality in nutrition is a continuing weakness that has so far not been addressed. Although a long-standing problem, there is a real need for recognition of **nutrition as a scientific discipline** in its own right, rather than being merely seen as a tool for other areas, notwithstanding the strong interfaces that also need to be fostered with other disciplines, including epidemiology and public health.

The investment in **high-quality 'classical' nutrition research** has been declining, and there is a need for new developments and innovation in fundamental core disciplines of nutrition research, including the composition and functionality of food at the micro- and macronutrient level, mechanistic studies integrating nutrition and modern biology, and the advancement of novel technologies and tools, such as instruments to measure nutritional intake and composition much more accurately and precisely.

The institutional infrastructure for nutrition research in the UK has changed towards institutes with narrower remits, diluting visibility and momentum. This has been exacerbated by the reduced investment into animal nutrition research. There is a **need for strong leadership,** and a recognisable centre of research excellence with critical mass in nutrition and energy balance that is competitive on the world stage and which would act as a magnet for first-rate scientists and the training of the next generation of integrative nutrition researchers.

The UK has a shortage of well-trained, innovative nutrition researchers with deep knowledge in nutritional core disciplines and in particular of clinical researchers with nutritional expertise. Although capacity and training in university departments have increased in recent years, this is predominantly focused on applied aspects of nutrition (for example, dietetics). There is a major **need for training and career development** of clinical and basic nutrition researchers especially mid-career, between post-doctoral and first substantive academic post in order to maintain a high-quality research base when the current generation of leading nutrition researchers retire.

Nutrition research should continue to **harness modern biology** and **adopt integrated systems approaches** to studying interactions at multiple levels (molecular to physiological) and linking this knowledge to populations, behavioural and social sciences. The centrality of nutrition in many processes

means that an integrated approach to training is particularly important. However, this should not be at the expense of in-depth of knowledge in core disciplines. For instance, nutritional epidemiologists and public health scientists require a strong education and training in epidemiology/public health, integrating modules or additional qualifications in nutrition research.

To move the field forward, reliable and sensitive **measures and biomarkers** are needed for dietary exposure, food and stress challenges, energy expenditure and intermediary outcome measures for disease and ageing as well as a detailed characterisation of phenotypes. There are opportunities to build on mechanistic understanding in model systems, and novel technologies ('omics', imaging) to develop functional biomarkers for improving assessment and phenotyping. Better analytical nutrition biomarkers are needed for high throughput screening in population-based studies.

There is an opportunity to improve the health of the nation through sustained behavioural change integrating nutritional and lifestyle approaches. Building on the UK strength in cohorts and the integration of epidemiology and mechanisms to understand disease aetiology, it will be important to develop complex behavioural interventions and evaluate natural experiments to inform public health strategies for **prevention of disease**.

An important dimension is how the **social environment, family structure and inequalities** influence food choices and physical activity and how interventions can be implemented that lead to sustained behavioural change.

The NIHR/Department of Health-led cross-government obesity R&D strategy "**Healthier Weight, Healthier Lives**", produced in response to the Foresight Obesities report, covers an important part of nutrition research. Despite the substantial overlaps between obesity and nutrition research, however, there are many aspects of nutrition research not directly related to obesity. There is therefore a need and opportunity for the development of a **coordinated national strategy** for research in nutrition and energy balance, involving major UK funders including the BBSRC, the Department of Health/NIHR, the Food Standards Agency, ESRC, the Wellcome Trust and industry. The MRC should build on the outcomes of this strategic review and engage with other funders with the view of coordinating activities and establishing partnerships.

Although models for engagement between academia and the pharmaceutical and biotechnology industries are well understood, there is considerable potential for working towards **better relationships with the food industry**, including food manufacturers, suppliers and retailers. The outreach of the food industry is enormous with a real opportunity to influence public health agendas, and models for engagement with this sector should be developed and explored.

Research into nutrition and energy balance is an important aspect of the MRC's portfolio, given its **centrality in addressing major public health challenges of the 21st century, including obesity and the health of an ageing nation.** There is an opportunity for the MRC to work together with other partners to address the insights gained from the Foresight report[14]; and the potential for nutrition and energy balance research to play a role in the current cross-council Initiative for Lifelong Health and Wellbeing.

The critical mass of outstanding expertise across a range of disciplines relevant to nutrition and energy balance in Cambridge provides a real opportunity for the

[14] Foresight, Tackling Obesities: Future Choices – Project Report (2007)

creation of an **identifiable centre of excellence for integrative nutrition research**. Although envisaged as being flexible in nature, the centre should have visibility as a focus of research excellence to the outside world and provide leadership for the field. It should have an externally communicated, scientific strategy, and might provide funding for cross-unit/centre activities, training or appointments, in particular strengthening the interface between nutrition and other disciplines. It could also form the hub of a wider UK network of excellence. Such a network could be modelled on the MRC Population Health Science Research Network (PHSRN) and reach out to other MRC investments, including the Epidemiology Resource Centre, the Social and Public Health Unit and the International Nutrition Group, as well as non-MRC centres of excellence in nutrition research across the UK. The centre and network should report to PSMB.

MRC research in has broadened from mitochondrial energy conversion into wider aspects of mitochondrial biology and has achieved international recognition across the spectrum of its interests. Multiple new avenues for research and translation have been opened, some of which are not directly related to the nutrition field. Examples include the recently increased recognition of the role of mitochondria in numerous complex diseases and the ageing process. Also, reactive oxygen species and apoptosis have emerged as important themes in inflammation and tissue injury. There are opportunities for the application and exploitation of work within and outwith the nutrition field. The number of dedicated institutes world-wide with expertise in biochemistry and basic mechanisms of energy balance has declined, and there is an opportunity for the MRC to take leadership in the increasingly important and cross-cutting area of mitochondrial biology and the potential for translation in terms of multiple complex diseases.

6. REVIEW GROUP RECOMMENDATIONS

The MRC should:

1. Work, in partnership with other UK funders, to develop a **coordinated national strategy for nutrition research**, feeding into the NIHR-led cross-government R&D strategy in response to the Foresight report; this should include the development of **better models of engagement between academia and the food industry.**

2. Promote **research underpinning the development of public health** strategies that foster nutrition and behaviour for optimal health throughout the life-course and the prevention of obesity.

3. contribute to **addressing the national skill shortage of basic and clinical nutrition researchers**, for instance through the provision of dedicated clinical and non-clinical fellowships in nutrition research or sponsoring a national training programme for integrative nutrition research, which could be modelled on the Integrative Toxicology Training Partnership (ITTP; www.le.ac.uk/mrctox/MRCTox/ittp.htm).

4. Grasp the opportunity to establish an **identifiable centre of excellence for integrative nutrition research** that provides leadership for the field and forms the hub of a wider UK network linking in other MRC and non-MRC centres of excellence in nutrition research.

5. In the light of the growing evidence of the importance of mitochondria in multiple complex diseases and the ageing process, to consider continued support for a **dedicated MRC investment in mitochondrial biology**, exploiting translational links in nutrition and other areas.

Annex 1

Strategic Review of Nutrition: membership and terms of reference

Strategic review panel membership

Professor Stephen Holgate (Southampton) * # – chair
Professor John Mathers (Newcastle/PSMB) * # – nutrition
Professor Michael Shipston (Edinburgh/PSMB) *# – signalling
Professor Paul Trayhurn (Liverpool/PSMB)*# - nutrition
Professor Pierluigi Nicotera (MRC Toxicology Unit)* - intramural representative
Dr Jose Ordovas (Tufts) *# International expert - nutrition
Professor Frans van der Ouderaa (Unilever) **#- industry
Professor Valerie Beral (Oxford)# – epidemiology/public health
Dr George Sarna*# - MRC Executive Board
Professor David Barford (Chester Beatty/MCMB) **#– signal transduction/structural biology
Professor Leslie Dutton, FRS (Pennsylvania) **- international expert - energy conversion

*	Core members represented on both reviews
**	Members of the Dunn review panel; observers of the field review, if available
#	Attendees of preliminary meeting

Terms of reference

Field review

- To review the MRC's portfolio in nutrition and energy balance in the light of other UK activities and the needs and opportunities for research and training; and to recommend a medium to long-term (5 to 10 years) strategy for nutrition research to PSMB;
- To advise on the most appropriate structure for future investments (for example, the balance between centres of excellence and other support) to deliver this strategy;
- To consider how the MRC's investments might be best coordinated.

In reaching any recommendations, to consider:

- Existing investment UK-wide (MRC and non-MRC);
- Existing strengths and weaknesses of research in nutrition in the UK and internationally;
- Needs and strategies of other stakeholders, such as Health Departments, government agencies and industry;
- The MRC's position/niche in the funding landscape;
- Is there a need to bolster the area in the UK, and, if so, what aspects, and how to support these?

Review of basic nutrition research / mitochondrial energy conversion

- To advise PSMB on the current role of the Dunn Human Nutrition Unit in supporting nutrition research and on the future needs and opportunities for research in mitochondrial energy conversion.

In reaching any recommendations, to consider:

- the niche of the Dunn Human Nutrition Unit in terms of scientific expertise, infrastructure and training and how this might evolve in the future;
- the fit of the unit in the broader MRC portfolio and in relation to the needs and activities of other stakeholders, such as the Health Departments, government agencies and industry.

Annex 2

Strategic Review of Nutrition and Energy Balance: Organisations that have provided comments

UK academia

Kings College London

University of Southampton

University of Reading

University of Nottingham

Newcastle University

University of Ulster

University of Sheffield

University of Surrey

University of Glasgow

University of Cambridge

Assoc of Prof's of Human Nutrition

The Nutrition Society

British Nutrition Foundation

Industry

Food & Drink Federation

Funders and policy makers

Dept of Health/NIHR

Food Standards Agency

BBSRC

ESRC

Wellcome Trust

Cabinet Office Strategy Unit

CRUK

MRC Technology (MRCT)

MRC units and MRC investments

MRC Dunn Human Nutrition Unit

MRC Collaborative Centre for Human Nutrition Research

MRC Epidemiology Unit

MRC Epidemiology Resource Centre

MRC Centre for Nutritional Epidemiology

MRC Centre for Obesity & Related Metabolic Disease

MRC International Nutrition Group

MRC Social & Public Health Unit

MRC Laboratory of Molecular Biology

MRC Centre for Epidemiology for Child Health (Professor TJ Cole)

MRC Childhood Nutrition Research Centre (Professor A Lucas)

Annex 3

Analysis of national research portfolio in nutrition and energy balance

1 Overview

This Annex provides a brief analysis of national (UK) investment relevant to nutrition and energy balance, based on 2006/07 spend figures[15].

UK investment in nutrition and energy balance research exceeds **£70m**[16], a figure which excludes contribution from the Department of Health (DH) and the National Institute for Health Research (NIHR).

DH and NIHR have been unable to provide quantitative data relating to spend on nutrition and energy balance, and have thus been excluded from quantitative analysis. A list of funded work, however, can be found in **Section 5.1**.

The assumptions made in this process are listed under the relevant funding body in **Section 3**.

2 Spend by research area

The national research portfolio in nutrition and energy balance has been categorised according the following scheme, chosen to allow comparison of MRC activities with those of other funding bodies:

1 - Early origins of disease
Includes research investigating how nutrition, nutritional status, foetal growth, birth weight, and factors contributing to growth and weight gain in early life affect disease or health status (including obesity) in later life.
2 – Obesity-related
Includes research investigating genetic or molecular factors affecting obesity, appetite control, or energy balance; the effect of diet, exercise, life-style or environmental factors on obesity, strategies for prevention or treatment of obesity; and how obesity affects other disease.
3 - Other nutrition
Includes research investigating how diet, food components, or nutrients affect disease or health status; treatment or prevention strategies based on diet or nutrients; and research into eating disorders.
4 - Gastrointestinal disease
Includes research investigating normal gut function; and the molecular basis, detection and diagnosis, and treatment strategies for gastro-intestinal disease.
5 - Mitochondrial energy metabolism
Includes research on components of the mitochondrial respiratory chain, mitochondrial physiology and oxidative stress; and ATP metabolism.

An overview of total UK spend by research area is shown in **Figure 1**. Research relevant to obesity is the major focus of activity in nutrition and energy balance. 'Other nutrition' includes research on diet and ageing, a priority of BBSRC (£1.7m, >10 per cent of total BBSRC investment) and of increasing relevance in the Western world. Early origins of disease is also well-represented, reflecting the current trend towards early intervention. Gastro-intestinal research, including

[15] Estimated from available data from other periods as necessary.
[16] Based on available data from awarding bodies, excluding DH/NIHR investment, for which spend figures were not available.

work on gastro-intestinal microbiology, and mitochondrial energy balance are active research areas.

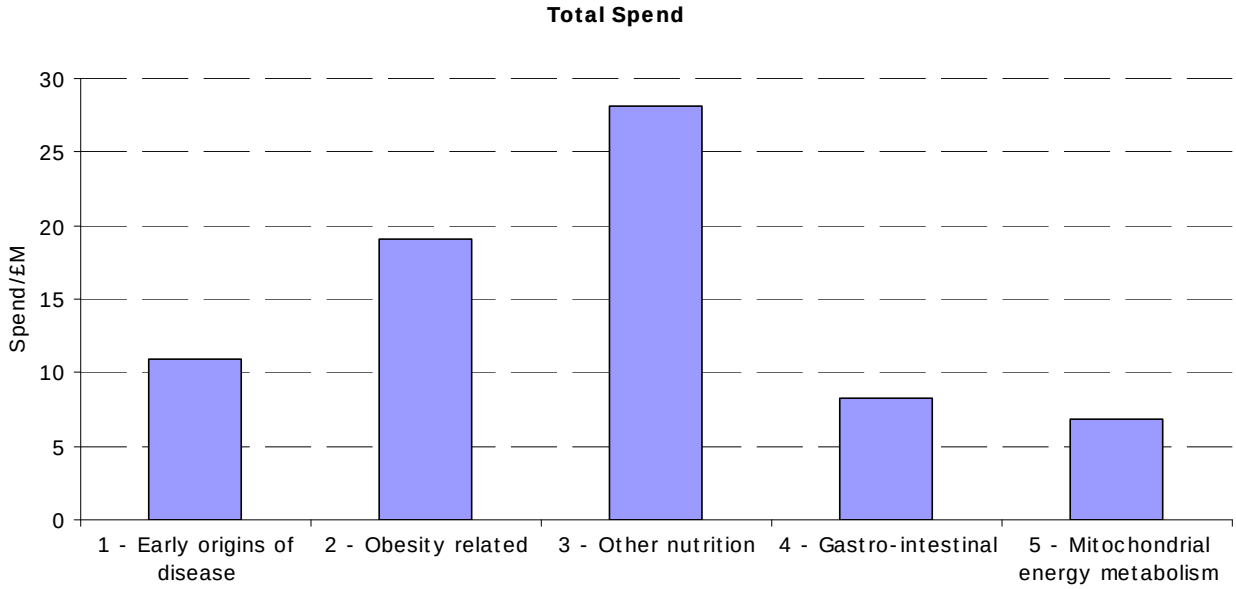


Figure 1 – Total UK Research Spend on Nutrition and Energy Balance (2006/7)

Figure 2 shows the breakdown in spending across research areas by funding body. From this analysis, it is clear that the MRC supports the large majority of research into early origins of disease and mitochondrial energy metabolism, with a major contribution to obesity and gastro-intestinal research. Research on 'other nutrition' and obesity are both well-supported by other funding bodies in addition to MRC investment.

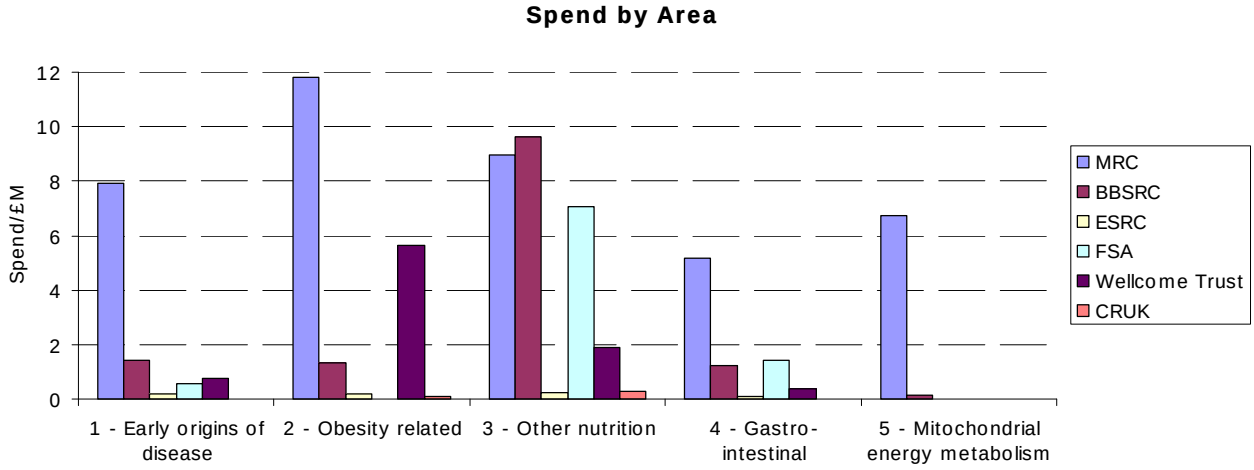


Figure 2 – UK Research Spend on Nutrition and Energy Balance by Research Area and Funding Body (2006/07)

3 Spend by funding body

From **Figure 3**, below, the extent of the MRC's contribution to research into nutrition and energy balance is clear. The MRC is estimated to fund around 50 per cent of research in this area. A detailed description of the MRC's investments can be found in **Annex 4**.

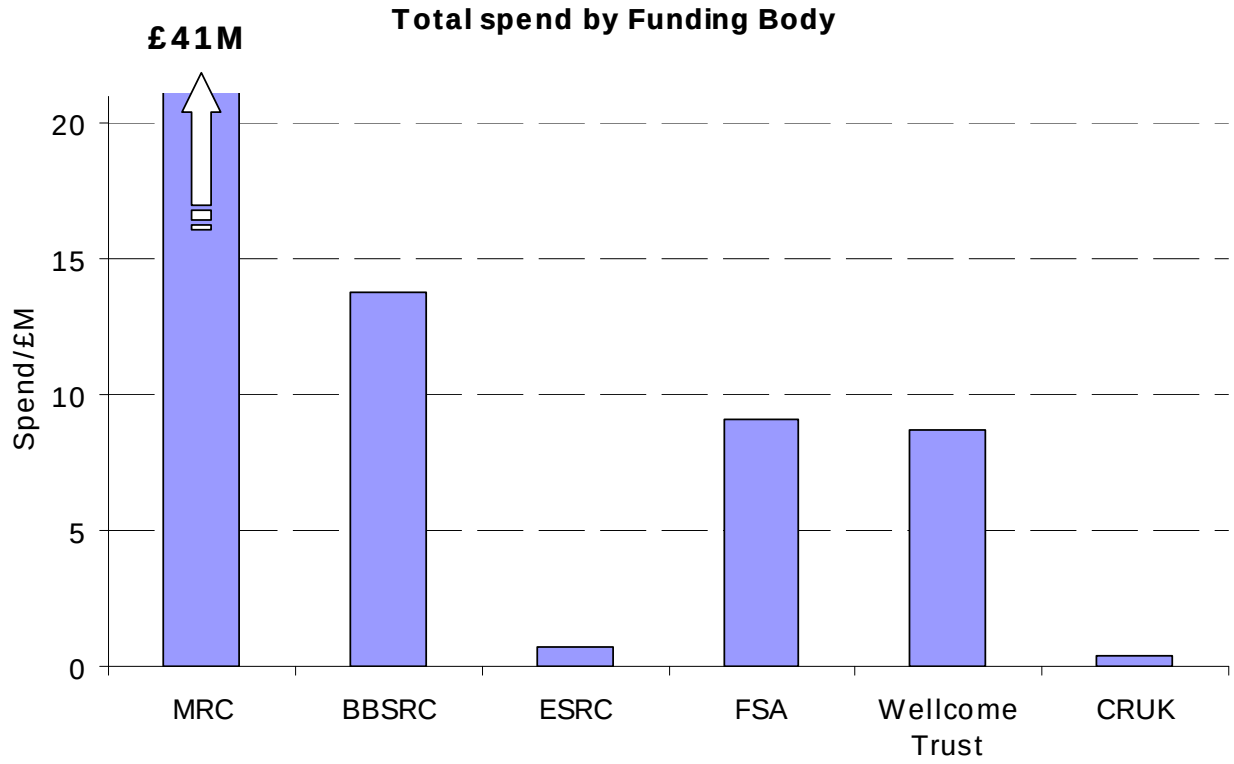


Figure 3 – UK Research Spend on Nutrition and Energy Balance by Funding Body (2006/7)

Figure 4 shows a breakdown of spend by funding bodies by research area. 'Other nutrition' features strongly in the portfolios of BBSRC and the FSA, and the Wellcome Trust make a substantial contribution to research relevant to obesity. As can also be seen in **Figure 2**, research into mitochondrial energy metabolism is funded almost entirely by the MRC.

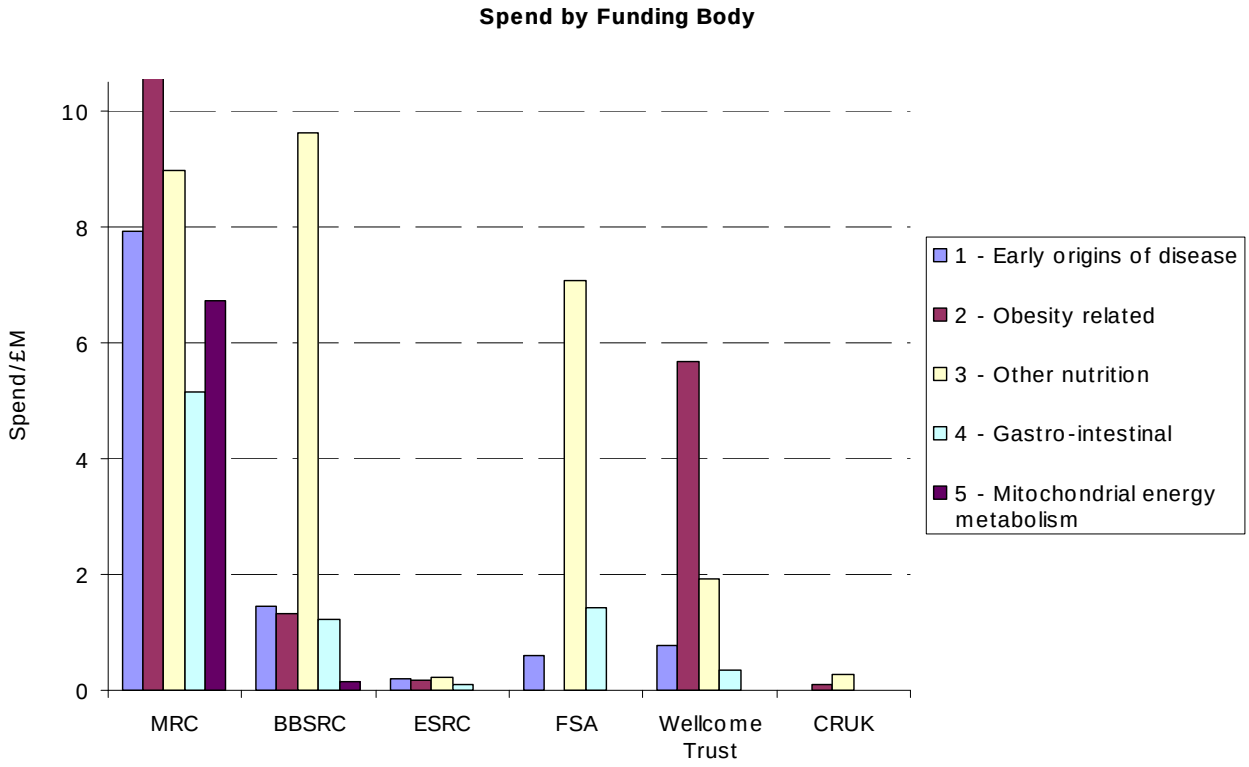


Figure 4 - UK Research Spend on Nutrition and Energy Balance by Funding Body and Research Area (2006/07)

4 Limitations of analysis

Assumptions made when calculating contribution of each research body are detailed below:

MRC: See separate annex detailing MRC spend.
BBSRC: Data provided by BBSRC – assumes classification parameters used match those of the MRC.
ESRC: Figures include response mode grants only, estimated from data for 2008/09. ERSC also has many centres and institutes which include nutrition research within their remit (**Section 5.2**).
FSA: Allergy research categorised as gastro-intestinal. Other funding categorised based on title of research programme.
Wellcome Trust: Research categorised from abstracts. Spend for 2006/07 estimated by dividing value by duration.
CRUK: Values estimated from data provided in period '3.2'. Categorised from research programme title.
Department of Health/National Institute for Health Research: Values not included in analysis.

5 Qualitative summaries for DH/NIHR and ESRC (non-response mode)

5.1 Department of Health/National Institute for Health Research Projects Relevant to Nutrition and Energy Balance

Below is a current title list of projects supported by DH and NIHR, showing the main areas of commissioning. This is not a comprehensive list, and does not include completed projects.

- Supporting the self management of obesity: the role of information and communication technologies
- Evaluation of healthy start – scoping study
- Do young people engage with food branding?
- Buywell: Evaluation of a targeted marketing intervention to influence food purchasing behaviour by low income consumers
- Optimisation of the National School Fruit and Vegetable Scheme
- Web-based weight loss interventions for African-Caribbean women
- Breastfeeding promotion in special care and neonatal intensive care units; an evidence synthesis
- Feasibility study to develop and test the potential effectiveness of a peer-led intervention to increase physical activity and healthy eating in adolescence
- Preventing disease through opportunistic, rapid engagement by primary care teams using behaviour change counselling
- Preventing obesity in the UK, with a focus on South Asian children
- Descriptive map of large-scale and locally-based schemes to promote healthy weight amongst obese and overweight children in England
- Exploring the ability of lay workers to support health-related behaviour change in deprived communities
- Healthforce – development and feasibility of a peer-led, bodyweight and lifestyle management programme
- EMPOWER – Empowering mothers to prevent obesity at weaning. RCPCH pilot and feasibility study
- The changing social patterning of obesity: an analysis to inform practice and policy development
- A systematic review of the routine monitoring of growth in children of primary school age to identify growth related conditions
- Early origins of obesity: early strategies for intervention
- Social ecological mapping of physical activity behaviours and health outcomes in deprived inner-city communities
- Profiles of physical activity in older adults
- Environmental and social influences on physical activity
- Early emergence of ethnic differences in chronic disease risk: the contribution of diet and exercise
- Environmental determinants of physical activity and obesity in adolescents
- An economic evaluation of obesity prevention for UK adults

5.2 ESRC centres and contributions relevant to nutrition and energy balance

- Centre for the Microeconomic Analysis of Public Policy (CPP)
- Egenis – ESRC Centre for Genomics in Society
- Cesagen – ESRC Centre for Economic and Social Aspects of Genomics
- The Genomics Forum
- The ESRC Centre for the Analysis of Risk and Regulation
- Social Contexts of Pathways into Crime

- CLS – The Centre for Longitudinal Studies
- ULSC – The UK Longitudinal Studies Centre
- MISOC – The ESRC Centre on Micro-Social Change
- Understanding Population Trends And Processes: A 2° Data Analysis Initiative
- National Prevention Research Initiative (NPRI) (ESRC has contributed £1.25m to the NPRI initiative for Phases 1 and 2)

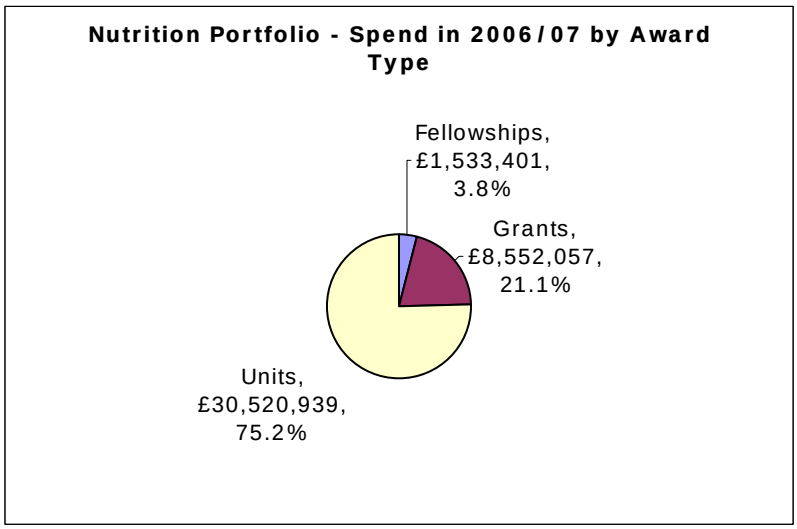
Annex 4

Analysis of the MRC's research portfolio in nutrition and energy balance

This Annex provides a general analysis of MRC's investment relevant to nutrition and energy balance, which totals approximately £40.5m a year. Analysis is based on 06/07 spend figures.

Major MRC investments

The MRC supports nutrition research through intramural support at MRC units and institutes and through research grants and training awards to Universities. Nearly three-quarters of MRC's nutrition portfolio (~£30.5m) is supported in MRC Units, followed by grants (~£8.5m) and fellowships (~£1.5m). Figure 1



MRC units

The major MRC units conducting research relevant to nutrition and energy balance and their annual spend in these areas is listed below:

- The **Dunn Human Nutrition Unit** (Professor Sir John Walker, Cambridge; £6.6m a year, including Diet and Health programme £450k a year) – investigates fundamental mechanisms underlying nutrition, and the influence of nutrients on health and longevity http://www.mrc-dunn.cam.ac.uk/

- **Human Nutrition Research** (Professor Ann Prentice, Cambridge; £5.7m a year) - carries out scientific research into relationships between nutrition and health, of national and international priority, through partnerships with other academic groups, governments, industry and others http://www.mrc-hnr.cam.ac.uk/

- The **MRC Epidemiology Unit** (Director: Professor Nick Wareham, Cambridge; £5.6m a year) - investigates the causes and prevention of diabetes and obesity http://www.mrc-epid.cam.ac.uk/

- The **MRC Epidemiology Resource Centre** (Professor Cyrus Cooper, Southampton; £1.5m a year) - provides an international centre of excellence in epidemiological research, which maintains and develops the long-term cohort studies assembled in Southampton as national resources to explore the developmental origins of adult disease http://www.mrc.soton.ac.uk/

- The **MRC Social and Public Health Unit** (Professor Sally Macintyre, Glasgow; £2m a year) - promotes human health via the study of social and environmental influences on health www.sphsu.**mrc**.ac.uk/

In addition, the MRC funds a directly-supported group:

- The **MRC International Nutrition Group** (Professor Andrew Prentice, LSTMH; £1.8m a year) - undertakes research focused on understanding the role of nutrient-gene interactions in the occurrence and severity of infectious disease. http://www.lshtm.ac.uk/nphiru/research/nutrition.html

Grants

The MRC's Council has recently established two MRC/university centres relevant to nutrition and energy balance:

- The **MRC Centre for Obesity and Related Metabolic Disease** (Professor Steve O'Rahilly, Cambridge; £1.9m/five years) – investigates the fundamental causes of obesity and how it is related to insulin resistance, diabetes and cardiovascular disease http://www.mrl.ims.cam.ac.uk/

- The **MRC Centre for Nutritional Epidemiology in Cancer Prevention and Survival** (Professor Sheila Bingham, Cambridge; £2.5m/five years) – researches the epidemiology and molecular origins of the dietary causes of cancer http://www.srl.cam.ac.uk/cnc/

The MRC also supports two members of External Scientific Staff (ESS) with nutrition programmes:

- Professor Alan Lucas (Childhood Nutrition Research Centre; University College London) Nutritional interventions in childhood and cardiovascular disease risk (PA:Dr Atul Singhal; £1.3m/5yrs); Early growth and later bone health (PA:Dr Mary Fewtrell; 300k/three years)

- Professor Tim Cole (University College London) Mathematical methods in the assessment of human growth (£350k/three years)

Examples of other major awards include support for EPIC- Diet, lifestyle and biological determinants of health and chronic diseases (Professor K-T Khaw, Cambridge £2.2m), the Million Women Study (Professor V Beral, Oxford £4.2m), programmes on the genetics and molecular mechanisms of obesity (Professor P Froguel, Imperial College, £1.25m; Professor S O'Rahilly, Cambridge, £1.5m) and clinical trials on parenteral nutrition for critically ill patients (Professor P Andrews, Edinburgh, £1m) and Crohn's disease (Professor J Satsangi, Edinburgh, £1.5m).

Fellows

The MRC supports a broad portfolio of fellowships; the majority of these are obesity-related.

Breakdown of portfolio

Research areas

The MRC's portfolio can broadly be divided into the following areas:

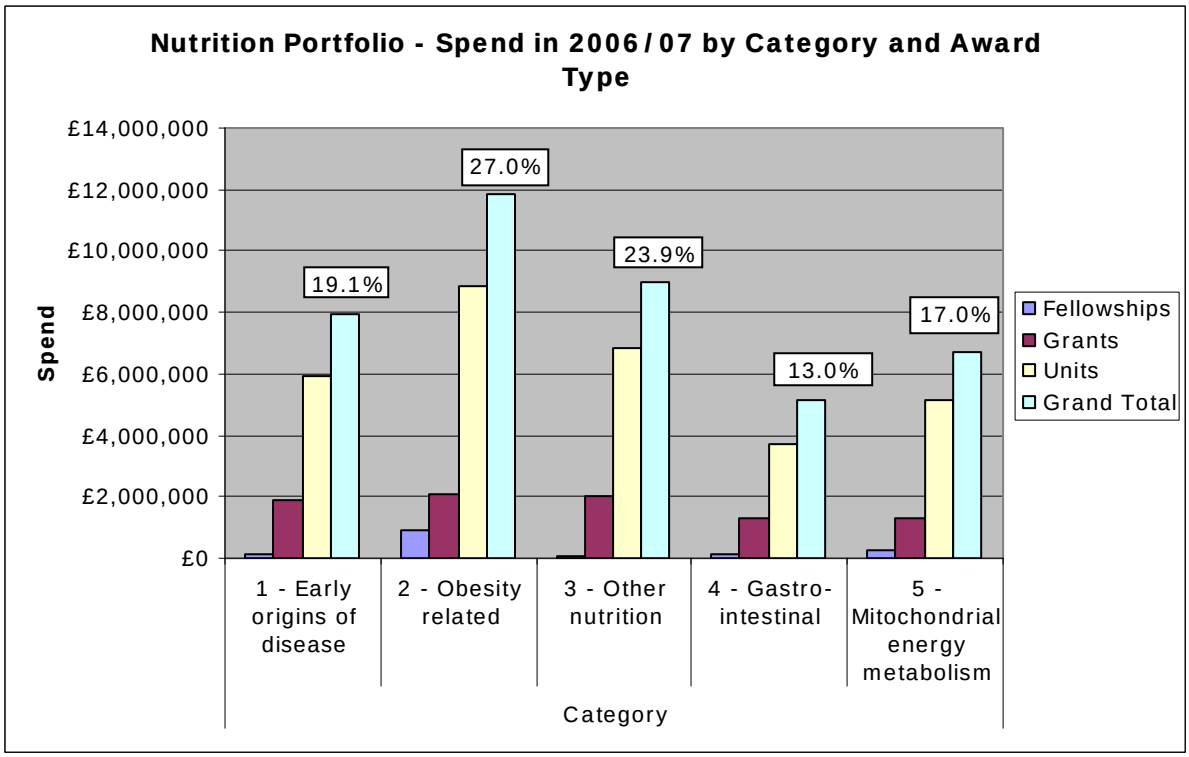
1. Early origins of disease - £7.9m a year
Includes research investigating how nutrition, nutritional status, fetal growth, birth weight, and factors contributing to growth and weight gain in early life affect disease or health status (including obesity) in later life.

2. Obesity-related - £11.8m a year
Includes research investigating genetic or molecular factors affecting obesity, appetite control, or energy balance; the effect of diet, exercise, life style or environmental factors on obesity, strategies for prevention or treatment of obesity; and how obesity affects other disease.

3. Other nutrition - £9.0m a year
Includes research investigating how diet, food components, or nutrients affect disease or health status; treatment or prevention strategies based on diet or nutrients; and research into eating disorders.

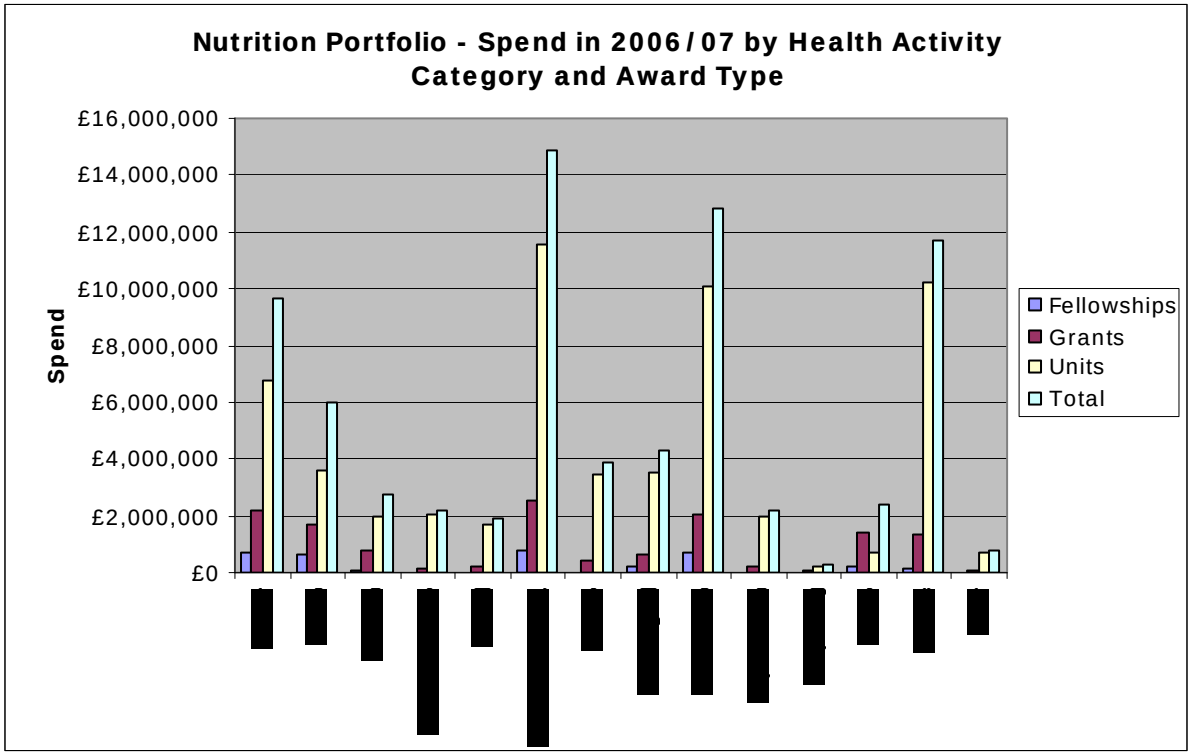
4. Gastrointestinal disease - £5.1m a year
Includes research investigating normal gut function; and the molecular basis, detection and diagnosis, and treatment strategies for gastro-intestinal disease.

5. Mitochondrial energy metabolism - £6.7m a year
Includes research on components of the mitochondrial respiratory chain, mitochondrial physiology and oxidative stress; and ATP metabolism.



Disease areas *(based on UKCRC disease classifications)*

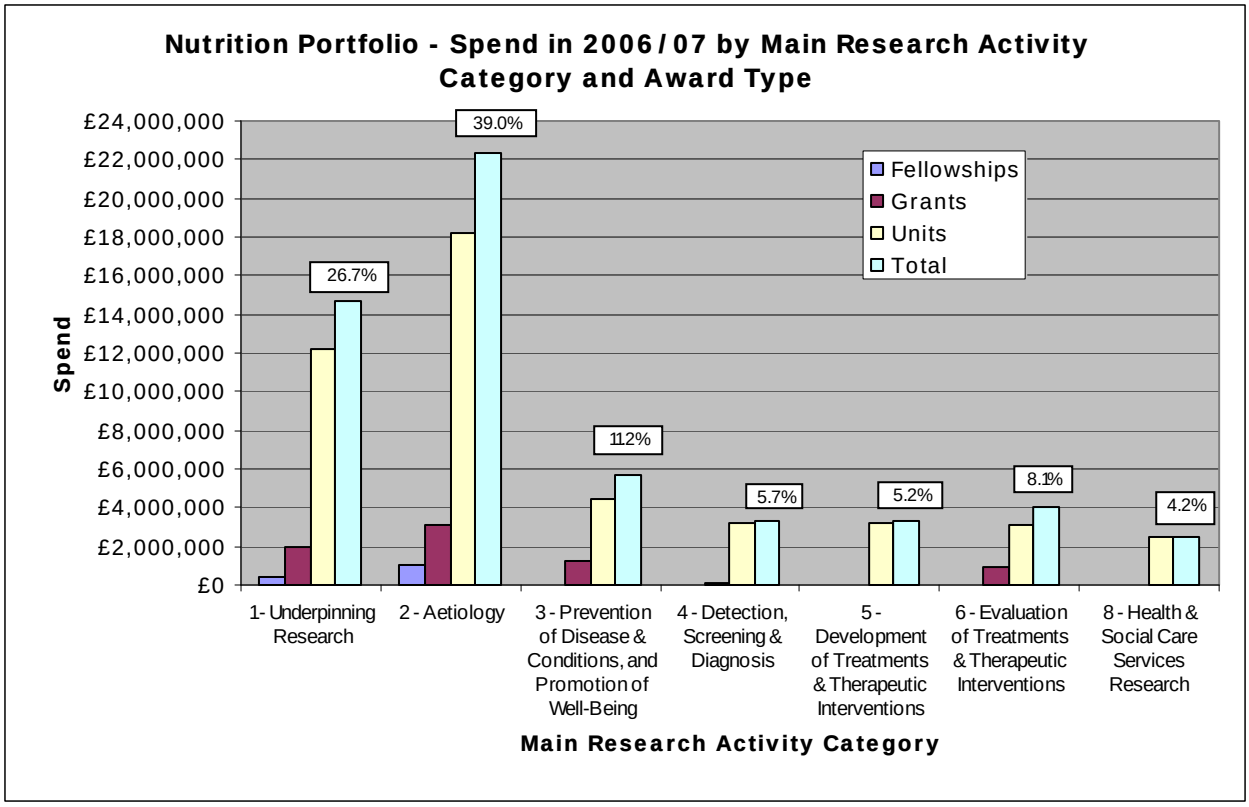
The majority of the MRC's portfolio in nutrition and energy balance falls into the categories of metabolic and endocrine disease, oral and gastrointestinal disease or generic health relevance; this is followed by cancer, cardiovascular disease, musculoskeletal and neurological disease.



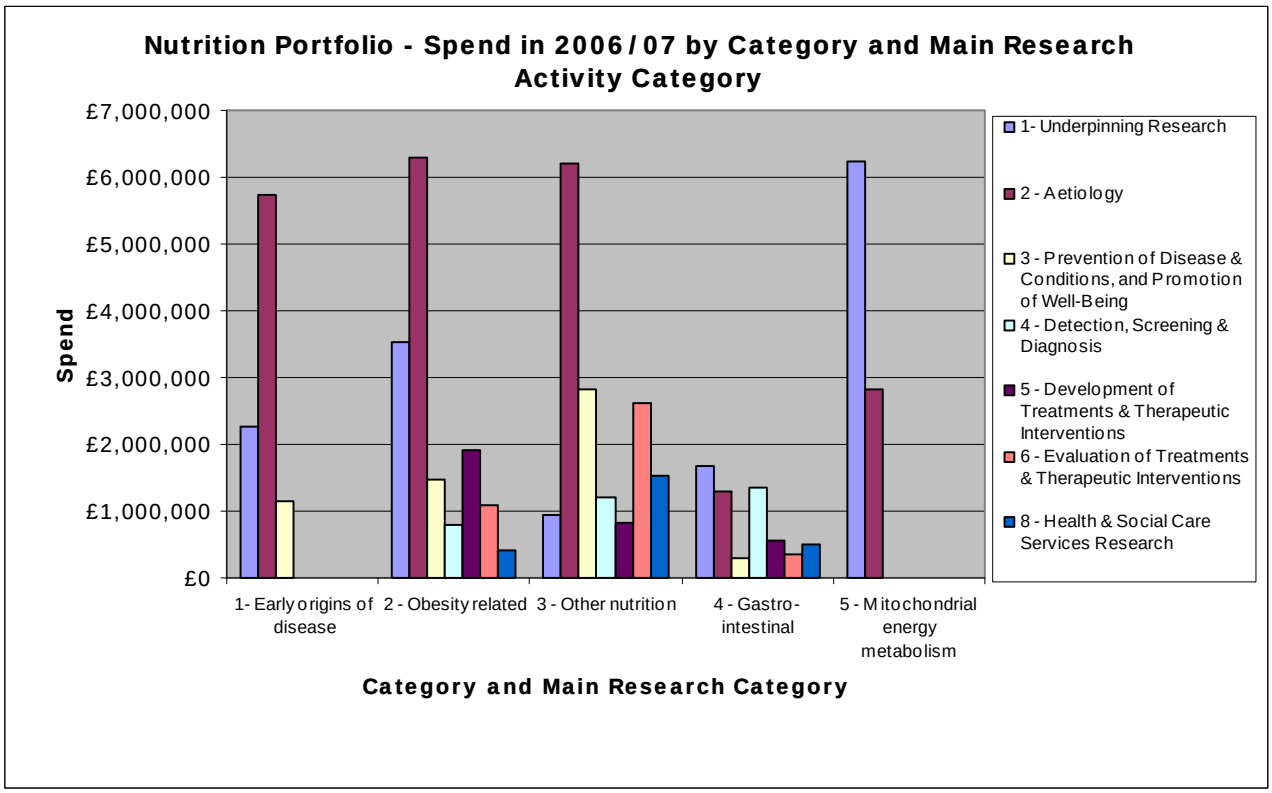
Research activities *(based on UKCRC classifications)*

Approximately 40 per cent (£22m a year) of the MRC's research portfolio in nutrition and energy balance involves aetiological research (research on determinants involved in the cause, risk, or development of disease or ill health) followed by 26 per cent (£15m a year) of underpinning research (research underpinning investigations into cause, development, detection, treatment or management of disease). Approximately £6m a year is spent on prevention research, followed by the evaluation of treatments or interventions (£4m a year); and detection, screening or diagnosis; development of treatments or interventions; and health and social care services research at approx. £2-3m a year each.

The annual spend on epidemiology, including nutritional epidemiology and studies relating to fetal growth and obesity, is approximately £14m a year.



A breakdown of the research activities in different research areas is below:



Partnerships

National Prevention Research Initiative (NPRI)

MRC manages the National Prevention Research Initiative a national initiative including government departments, research councils and major medical charities that are working together to encourage and support research into chronic disease prevention. The first round or awards made in 2005 included 13 awards relevant to nutrition and energy balance.

Lifelong Health and Wellbeing

MRC works together with BBSRC, ESRC and EPSRC on the joint Research Council Initiative on Lifelong Health and Wellbeing. The MRC managed call for proposals for Centres in Lifelong Health and Wellbeing focuses on strengthening multidisciplinary and collaborative research in this area. An award has recently been made to Newcastle University for a Centre for Brain Ageing and Vitality, which includes programmes on the impact of nutritional factors on musculoskeletal and brain ageing.

Food Allergy

The MRC co-funds in partnership with the Food Standard Agency a clinical trial on the early introduction of allergenic foods to introduce tolerance in infancy (Professor Gideon Lack, King's College London)

Foresight Tackling Obesities Project

Dr Susan Jebb (MRC Collaborative Centre for Human Nutrition Research) was a key scientific expert for the Foresight project and other MRC researchers and Officers have contributed to the project.