BBSRC Research in Food, Nutrition and Health

Strategic Framework: 2015 – 2020

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BBSRC Research in Food, Nutrition and Health – *Strategic Framework: 2015 – 2020*

Food, Nutrition and Health is a complex and interdisciplinary research area with key public health and economic relevance. This document aims to provide the academic and wider stakeholder communities with a clear roadmap for BBSRC's strategic support for the area over the next five years, complementing the joint vision of BBSRC, MRC and ESRC for integrative research across Council remits. It focuses on those aspects which form part of BBSRC's Strategic Research Priority in ***Bioscience for Health***, but clearly recognises and seeks to foster synergies with the *Agriculture and Food Security* priority in supporting research to inform the sustainable provision of safe and nutritious food.

BBSRC's Vision for research in Food, Nutrition and Health

It is only by fully understanding the interactions between food, nutrition and physiological systems that they can be preserved or enhanced to promote long-term health. BBSRC's vision is therefore to support world-class research which will make use of emerging techniques and technologies to advance understanding of how foods, nutrients and whole diets influence cellular processes, how these influences affect overall health outcomes, and how these responses vary between population groups, individuals and across the lifecourse.

By harnessing expertise across the BBSRC research space from crop and livestock science to food science and human physiology, BBSRC aims to foster multidisciplinary and integrative research which will address complex questions around the production, processing and consumption of healthy foods. This research will underpin a stronger and more coherent evidence base to inform nutritional policy decisions and develop new or reformulated foods which will enhance health. The knowledge gained will be crucial to addressing the growing social and economic challenges posed by modern lifestyles and dietary habits, and driving innovation in a key manufacturing sector for the UK economy.

Key goals

- To foster a more co-ordinated approach to research in food, nutrition and health through better integration of nutrition science, production and food processing research - including fundamental plant and animal studies
- To understand diet-mediated physiological changes on the transition between healthy and unhealthy or dysregulated states
- To understand how relationships between food and health change over the lifecourse, and how these changes may be influenced by genotype, epi-genotype and microbiome
- To advance understanding of the mechanistic basis of a healthy gut, its relationship with wider physiological function and potential for manipulation to positively influence health
- To understand the health implications of modern lifestyles and food processing techniques
- To understand the biological and behavioural determinants of food intake, including sensory qualities and satiety
- To actively collaborate with the food industry to drive innovation in healthy food products
- To generate a robust evidence base which will underpin policy to influence food behaviour

The strategic importance of research and innovation in Food, Nutrition and Health

Changing diets and dietary habits are placing an unsustainable burden on healthcare systems, individuals, families and societies

Adequate nutritional status and appropriate energy balance are fundamental requirements for continued health, yet more than half of the UK population are obese or overweight[1], consumption of fruit and vegetables is falling[2] and the calorie density of the average shopping basket is increasing[3]. Around three million people in the UK are malnourished, including 25 % of those in hospital 42 % in long-term care[4]. Consequences of malnourishment include impaired growth and development and compromised immune function, making improved nutritional care one of the largest potential cost-savings for the NHS[5].

Poor or inappropriate nutrition is also associated with increased cardiovascular risk, cancer and serious chronic conditions such as Type 2 diabetes and hypertension, placing a large proportion of individuals at increased disease risk. The widespread tendency towards consumption of excess energy and consequent rise in obesity-related disease is therefore a pressing challenge for the developed and, increasingly, the developing world[6]. High body mass index is one of the leading risk factors for chronic disease in the UK, accounting for 8.6 % of the burden of all disease[7] and 9 % (£5.1bn per annum) of NHS spend[8]. The cost to the wider economy is vast at around £16bn per annum, rising to £50bn by 2050 if new strategies to address the consequences of modern lifestyles are not developed[9].

As costs escalate, the need for products and interventions to prevent or manage the wide range of chronic diseases with strong dietary influences is becoming ever more pressing. The potential benefits are significant: reducing cardiovascular events by just 1 % would result in savings to the National Health Service of at least £30M per year[10].

Many of the mechanisms underpinning the effects of food and nutrition on long-term health are under-investigated

Despite the clear influence of diet on health, many of the fundamental mechanisms which link nutritional intake to physiological consequences remain undetermined. Epidemiological analysis is valuable in identifying correlations between foods or diets and health outcomes, but without a firm mechanistic basis such evidence can be uninformative or misleading (see case study Dietary cholesterol and cardiovascular disease risk below). The robust and authoritative evidence base which can only be delivered through basic research is crucial to development of healthier food products, optimisation of nutritional guidelines and determination of effective intervention strategies.

CASE STUDY: *Dietary cholesterol and cardiovascular disease risk: the public health and economic consequences of (mis)understanding correlations*

Reducing the burden of cardiovascular disease, which claims over two million life-years annually in the UK[11], is a major aim of public health policy. Whilst the link between increased plasma cholesterol and cardiovascular disease is well established, heart-health policy to limit consumption of cholesterol-rich foods was based on the unfounded assumption that dietary cholesterol is a key determinant of plasma cholesterol[12]. Subsequent basic research and epidemiological studies have clearly demonstrated that there is, in fact, no direct relationship between dietary and plasma cholesterol[13].

By dispelling a misguided assumption, this advance in understanding of the relationship between nutritional intake and physiological outcome has driven revision of dietary policy in Europe and beyond, leading to the removal of restrictions on cholesterol-containing foods, including eggs, in 2006[14]. Its impacts have gone beyond nutritional guidelines to influence public perception, with a significant shift in public perception of the risks and benefits associated with egg consumption[15] following a media campaign. Consumer egg sales, having been previously stagnant, increased by 6.1 % year-on-year between 2009 and 2011[16], providing an important source of nutrients (including vitamin D, vitamin K and selenium)[17] and generating additional revenue for poultry farmers.

There is therefore an urgent need to answer fundamental questions about the ways in which nutrients, foods and whole diets interact with biological and behavioural systems to influence health. For example, the gut is the primary point of interaction between foods and the body, yet understanding of its healthy function, including relationships to immunity, allergy and intolerance, is far from complete. More widely, determining the precise effects of nutrients and bioactive compounds on cell function will be key to understanding how whole diets influence physiological processes such as resilience, metabolic stress and ageing. Research to uncover the influences of genotype and microbiota will aid understanding of individual differences in dietary responses, whilst elucidation of the behavioural determinants of food intake will be crucial to understanding consumer responses to new products or guidelines.

Effective nutritional advice requires accurate definition of nutritional needs between individuals, population groups and across the lifecourse

Appropriate nutritional advice and effective public health messaging depend upon reliable evidence to determine diets which will benefit health. Whilst there is much advice and policy based on valid existing knowledge, in many cases the lack of robust underpinning evidence base leaves key questions unanswered and recommendations uncertain. Incomplete understanding of the basic relationships between food and health means that advice around what constitutes a "healthy diet" is subject to revision and reassessment (see case study *Fat, fat, fat or sugar* above), leading to confusion and often cynicism towards dietary advice[18].

Provision of effective nutritional advice is further complicated by largely unexplored differences in requirements between individuals, population groups and across the lifecourse. Understanding the interactions between food and physiology at critical stages of the lifecourse, including pregnancy and early life, in the context of differing genetic profiles and amongst those with food hypersensitivities will underpin development of stratified public health advice and improved health outcomes. For example, a full understanding of the consequences of diet for processes such as cognitive decline could make a major contribution to extending health and independence in line with increasing life expectancies.

CASE STUDY: *Fat, fat, fat or sugar? A key outstanding question*

Largely on the basis of epidemiological evidence linking total cholesterol levels to cardiovascular disease (CVD) and cancer risk, dietary guidelines over the past decade have consistently recommended reducing total, and particularly saturated, fat intake. As a consequence, many products have been reformulated to substitute carbohydrate for fat, or unsaturated for saturated fats. However, evidence is emerging that the relationships between fats (saturated, monounsaturated and polyunsaturated), carbohydrates and disease risk is complex and, in the absence of a full understanding, policy and reformulation may be doing harm as well as good.

Some evidence suggests that substituting carbohydrates for fat can have adverse health consequences by raising triglyceride levels and reducing beneficial HDL cholesterol[19], with associated increases in Type 2 diabetes and CVD risk[20]. In contrast, substituting unsaturated for saturated fat may be actively beneficial for CVD risk, possibly by reducing levels of damaging LDL cholesterol without affecting HDL cholesterol[21]. The evidence for dairy products - a major source of saturated fatty acids in UK diets – is complex, with recent large-scale analyses suggesting that milk consumption is associated with a reduction in CVD disease risk[22]. The picture is complicated further by evidence from animal studies that high levels of some polyunsaturated fats, including omega-6, may promote tumour growth[23] and inflammation.

It is not clear whether these effects are present in humans and at what levels they may become apparent. What is clear is that our understanding of what constitutes a "healthy diet" is far from complete, and policy decisions made on the basis of incomplete evidence may have unintended consequences for public health. Fundamental research into these relationships is urgently needed in order to inform the guidelines, reformulation and consumer information which will be most beneficial to public.

Innovation in the food industry depends upon underpinning research

Food and drink industries are of critical importance to the UK economy. They constitute the largest manufacturing sector, contributing £24.7bn per annum to the UK economy and employing 16% of the manufacturing work force[24]. They are also key players in addressing the challenges posed by modern diets. Food innovation is crucial to developing the healthier products which will widen consumer choice, and to achieving effective reformulation to improve the health properties of existing products. Recent reductions in the salt, trans- and saturated-fat content of foods available to the UK consumer, and consequent reduction in consumption amongst the UK population[25], is testament to the potential for industrial innovation to improve diets independent of behaviour change (see case study *Salt reduction in UK diets* below).

CASE STUDY: *Salt reduction in UK diets: the benefits of establishing a robust causal association between intake and disease*

The link between increased sodium consumption - through dietary salt - and raised blood pressure, with consequent effects on cardiovascular disease risk, is now well known and an important determinant of dietary policy across the world. However, it has not always been apparent. The association was established through a robust combination of mechanistic studies and epidemiological analysis, identifying the adverse effects of sodium on fluid homeostasis[26] and demonstrating an association between salt intake and hypertension[27].

The consequences of confidently establishing this link have been significant. Following recommendations made by the Scientific Advisory Committee on Nutrition in 2003[28], the Department of Health and Food Standards Agency set a target to reduce average adult salt consumption to 6g per day. Their policy approaches have been varied, encompassing public awareness campaigns, clear front-of-pack labelling and, crucially, collaboration with the food industry to reformulate the processed foods which contribute 75-80% salt in UK diets[29].

Between 2003 and 2011, average UK adult salt intake has fallen by 15% (from 9.5 to 8.1g per day)[30] – a reduction which has removed more than 11 million kg salt from UK plates and is estimated to have prevented at least 9,000 deaths from stroke and heart attack[31]. Targets set in 2006 and 2010 have been largely met by UK retailers, achieving a 30% reduction in the salt content of pre-packaged bread and 49% in branded breakfast cereals[32]. A new set of targets was agreed in March 2014, aiming for further significant reductions by 2017.

There is clearly progress still to be made in reducing salt intake, and doing so will require careful consideration of the technical and antimicrobial properties of salt in food production, as well as consumer palates. However, significant improvements over the past ten years de demonstrate the substantial policy and industry impact of collaboration on the basis of a robust underpinning evidence base – a model which is now being replicated worldwide[33].

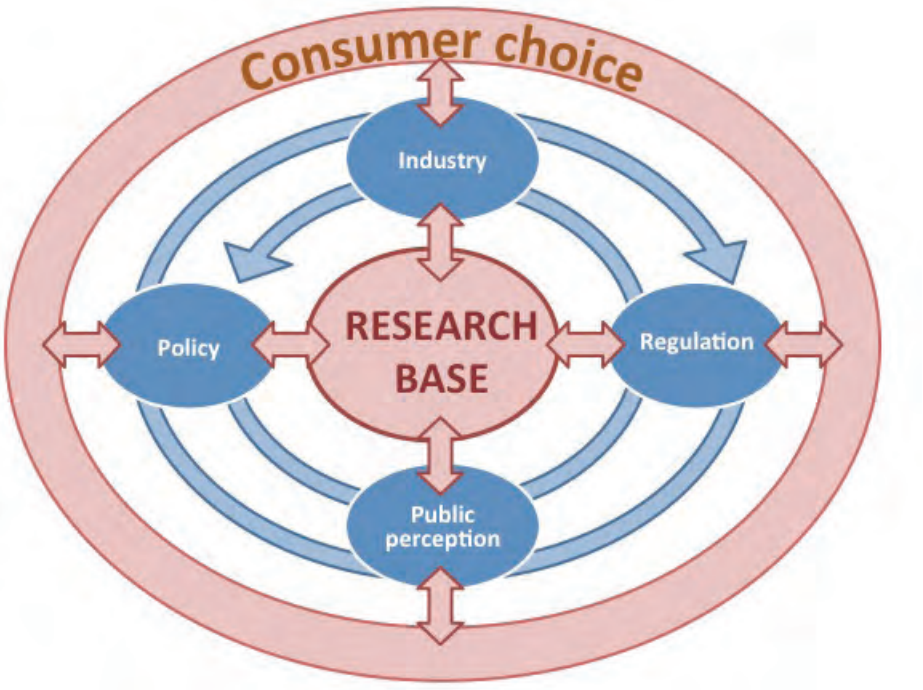


Figure 1: the crucial position of the fundamental research base relative to policy, industry, regulation and public perception. Robust research will underpin more effective food policy and regulation, industrial innovation and public health messaging

Policy and consumer pressure to develop healthier products is increasing, presenting significant opportunities for businesses able to produce innovative health-promoting products, including probiotics and nutraceuticals, or to reform existing products with improved health benefits and unimpaired palatability. However, the significant gaps in understanding of the mechanisms which link food components to health benefits make it difficult to substantiate health claims to the approval of regulatory bodies, stifling innovation and inhibiting informed consumer choice.

Fully exploiting these opportunities will require innovation underpinned by a strong body of research evidence, together with effective harnessing of industry expertise to inform academic research. A full understanding of the relationships between processing methods and nutritional value, and between the structures of foods and neurobiological responses will be critical, both to drive innovation and to ensure that developments in production and manufacturing effectively benefit health outcomes.

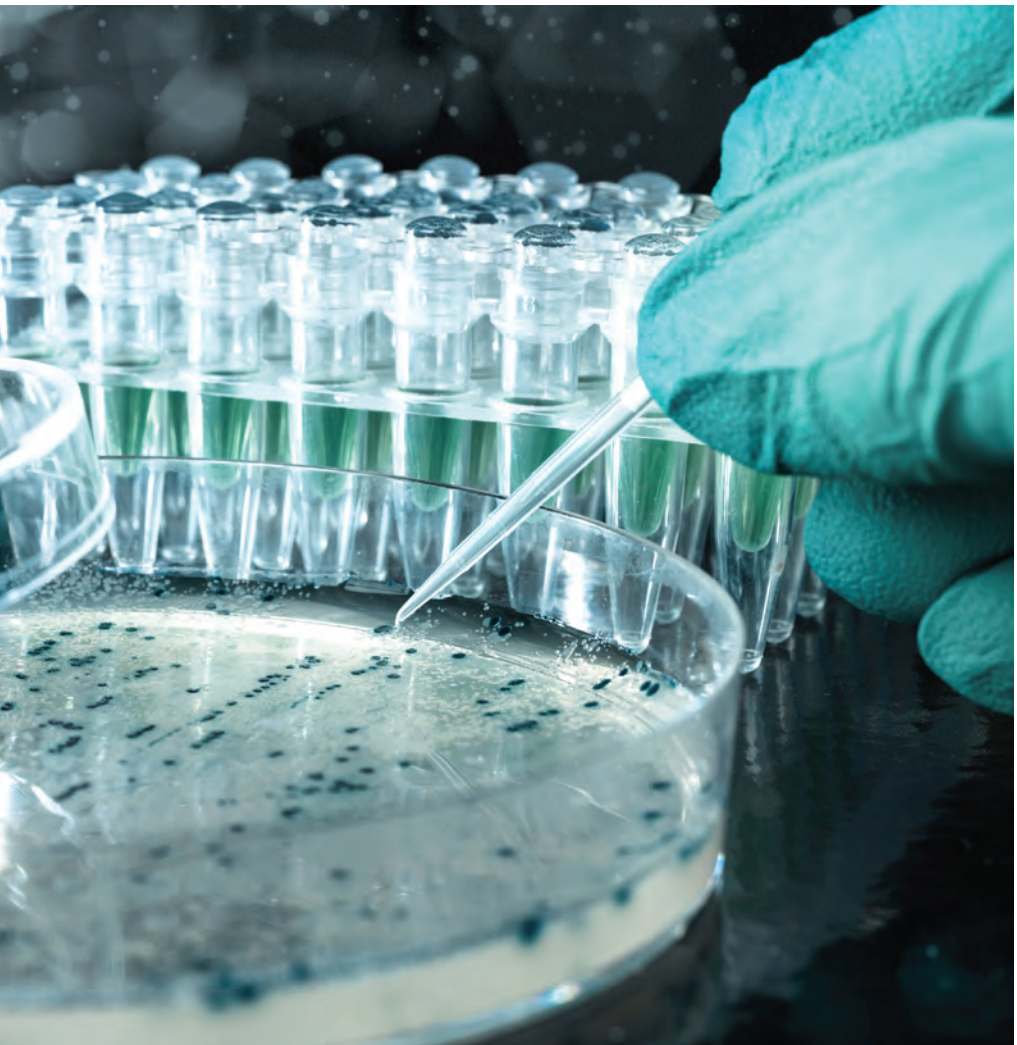
New opportunities for research in Food, Nutrition and Health

Advances in basic science are generating new approaches and techniques to address key questions in food, nutrition and health

New techniques and technologies are already generating fresh insight into how nutrition operates at a molecular and cellular level, and have the potential to radically advance understanding. New model systems, including the self-organising mini-guts derived from BBSRC investment in stem-cell research, will allow researchers to study the gut as an organ, rather than a collection of individual cells. Developing in-vivo imaging capability is providing new possibilities to study processes such as bacterial colonisation of the gut in real-time and in complex biological settings.

Improvements in the sensitivity and resolution of 'omics technologies, coupled with increased data-handling capacity, are facilitating comprehensive characterisation of biological systems. They offer new opportunities to determine how foods and nutrients interact with genes, proteins and metabolites to influence health, and particularly to characterise and analyse the gut microbiome. 'Omics technologies are likely to play an important role in identifying and validating biomarkers for health and nutritional status, and, in the longer term, may provide the basis for stratified nutritional recommendations for optimal health specific population groups.

The UK and BBSRC have world-class science basis upon which to build. Strength in molecular biology, biochemistry, genetics and epigenetics means that we are well placed to take advantage of the latest opportunities to drive forward increased understanding of the mechanisms by which food and nutrition are linked to biological outcomes. The UK is also world-leading in its breadth and depth of cohort studies, many including nutritional intake, physiological and genetic data collected over many years, providing a key epidemiological resource from which hypotheses can be formed and mechanistic analyses developed.



Computational innovation is making complex problems more tractable

The relationships between food, nutrition and health are complex, requiring both detailed physiological studies and high-throughput multi-scale approaches to unpick them. However, this complexity is being rendered increasingly tractable by advances in analytical capabilities and the increasing acceptance of data sharing.

Systems-based approaches, made possible by improvements in computational power and data-handling capacity, will provide new opportunities for researchers to tackle the multiple levels of interaction between food, nutrition and health. Where research has often been reductive in assessing the effect of one nutrient on one phenotypic outcome, systems analysis will facilitate consideration of whole diets and complete physiological systems.

BBSRC's *Exploiting New Ways of Working* research priority offers strong support for the development of innovative bioinformatics tools, technologies and approaches. Researchers in food, nutrition and health will be supported in making full use of these opportunities to ensure that the potential offered by new technologies and modes of working is fully realised.

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Multidisciplinary and integrative research provides new opportunities to understand the relationships between food, nutrition and health

Unpicking what is truly meant by healthy nutrition, and how we can best deliver it, is a multidisciplinary challenge. Insight will come from disciplines across crop science, food science, basic biology, health and clinical science, epidemiology, behavioural, social and political science – but the complex nature of key research questions means that they are not well served by interrogation from individual perspectives alone. The strong impetus for research funders to work in effective partnerships, taking advantage of differing areas of expertise, will foster new approaches to complex challenges. It will also address research gaps, avoid overlaps, tackle interface issues and make more efficient use of overall resources.

Particular opportunities for BBSRC exist in integrative research between

- nutrition and fundamental bioscience; to understand the mechanisms which underpin relationships between food, nutrition and health
- human, plant and animal (livestock) biosciences; to understand the relationships between nutrient (macro and micro) and bioactive content (including bioavailability and bioaccessibility) and health implications, informing agricultural research aims
- human and food microbiology; to understand interactions in the GI tract in relation to health and disease

The importance of integrative research across Research Council remits is reflected in a new joint vision for food, nutrition and health research between BBSRC, MRC and ESRC. By approaching the challenges of food, nutrition and health research from a joint perspective, the Councils will support their respective communities in identifying and exploiting areas in which integrative research bringing together basic bioscience, health, medical and social science can address problems more effectively than individual disciplines.

The multifactorial nature of challenges in food, nutrition and health mean that partnerships must go beyond academic research funders to stakeholders in the policy and industrial communities (see below). In supporting research, academic funders must draw on their understanding and consider their needs as end-users who will be instrumental in deriving economic and social impact from fundamental research. Through leadership of the *Diet and Health Research Industry Club* (DRINC; see case study below), schemes such as *LINK* and *Industrial Partnership Awards* and collaborative funding with Innovate UK as part of the *Nutrition for Life programme*, BBSRC investments are already demonstrating the benefits of cross-sector partnerships. BBSRC is committed to working in partnership with other funders and stakeholders, and will maintain a prominent role in joint activities to maximise the impact of knowledge gained from fundamental research.

DRINC as a mechanism for fostering integrative research

BBSRC, in partnership with MRC and EPSRC, established the Diet and Health Research Industry Club[34] in 2007. The club involves 15 company members, who contribute to research funds and form part of the grant awarding panel. Through 25 projects at 26 research centres, over £15M has been provided to support high quality pre-competitive research into diet and health within UK universities and research institutes, helping the food and drink industry to develop and deliver new foods of benefit to the consumer (see case study *Vitamin D or Vitamin D?* for an example of research funded through DRINC).

DRINC has brought together over 200 academic and 100 industrial researchers through regular dissemination events and workshops, forming a community which has secured an additional £25M of funding. Following an independent evaluation in 2011[35], DRINC is building on its success with a second phase of research projects worth approximately £10M.

BBSRC's role in the Food, Nutrition and Health research landscape

Research across the food system

BBSRC has responsibilities for bioscience research from basic plant, microbial and animal science to food science, food safety and human nutrition – placing it in a unique position of responsibility for research across the food system. Addressing the nutritional challenges facing the UK and the world will require solutions which encompass the whole food chain, and BBSRC is well-placed to integrate human physiological research with the plant, microbial, animal and food science within its remit.

Whilst the research challenges in food, nutrition and health outlined in this document sit primarily within BBSRC's *Bioscience for Health strategic priority*, there are strong links to the *Agriculture and Food Security priority* – and to the cross-Council *Global Food Security* programme. For example, BBSRC is in a strong position to bring together the crop science community with nutritional and food scientists for integrative research which considers crop characteristics and how they relate to health through processing. Plant and crop science can supply fully characterised food materials – such as alternative types of fibre in an identical grain matrix – which will enhance the ability of nutritional studies to determine physiological effects of specific food components. This information, together with consideration of processing and other factors, can in turn inform the development of crops which will produce healthier foods. BBSRC will make full use of its range of interests in bioscience to foster this type of integrative research across its portfolio.

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Mechanistic research in food & nutrition

The research landscape in food, nutrition and health is complex, with many national and international funders across the spectrum from agricultural research to food behaviour. BBSRC has a crucial role in supporting the fundamental bioscience research which will provide robust, authoritative evidence on which nutritional policy can be based and healthier products developed. BBSRC's responsibility in this area has been heightened by the changing roles of the Food Standards Agency and Department of Health, which has left a critical gap in public funding for nutrition and health research.

BBSRC's investment in strategically focussed food, nutrition and health research is built on a large foundation of underpinning world-class bioscience, which supports fundamental understanding of healthy systems. BBSRC is therefore in an excellent position to build capacity for mechanistic research by linking nutrition with underpinning work in cell biology, immunology, gut physiology and others. It is only through embedding nutrition research in leading-edge basic biology that fundamental questions around precisely how food and nutrients influence health can be addressed.

In line with its research funding, BBSRC has a leadership role in advocating the importance of fundamental research in food, nutrition and health. It is crucial that other funders and stakeholders recognise the importance of developing a mechanistic understanding of healthy systems, and appreciate the contribution that bioscience research will make to development of new products and a strong evidence base for policy and regulatory decisions.

Food processing and links to the food industry

Unlike many funders in the food, nutrition and health research landscape, BBSRC's remit includes the basic food science which will inform optimal processing and manufacture. Without careful consideration of the consequences of processing, the health benefits of "improved" plant materials may be lost, or resultant products may be unpalatable. Food science and processing research will also enable reformulation of existing products with enhanced health benefits.

Food processing and manufacture is of crucial importance to the food industry, who stand to gain from innovative products with enhanced health benefits. BBSRC has developed strong links to the food industry, ensuring that research is informed by industrial needs and effectively translated where appropriate (see case study *Vitamin D or Vitamin D?* right). These links will be developed to ensure that, where processing research is directly related to enhanced health properties, BBSRC continues to be an effective link between underpinning research and industrial relevance.

BBSRC's existing investments in food, nutrition and health research

BBSRC currently invests £10-15M per annum on (post farm-gate) research related to food, nutrition and health – built on a larger foundation of underpinning world-class bioscience.

Around half of this investment is made through Institute Strategic Programme Grants, which play a key role in providing sustained and coordinated support for research not conducted in HEIs. The Institute of Food Research (IFR) is a particular focus for both fundamental and translational research, hosting the *Food and Health* and *Gut Health* and *Food Safety* Strategic Programme Grants.

A proposed new *Centre for Food and Health* in Norwich aims to build on BBSRC strategic investments in IFR and across the wider Norwich Research Park, in partnership with the University of East Anglia and the North Norfolk University Hospital. Its vision is to uniquely integrate multidisciplinary bioscience and clinical excellence to deliver new understanding of interactions between food and the gastro-intestinal tract and their implications for health, production of safe and nutritionally enhanced crop-based food and accelerated innovation and commercial exploitation by UK industry.

The remaining half of the research portfolio is shared between Responsive Mode and the *Diet and Health Research Industry Club*, reflecting the importance of BBSRC's investment in industrially relevant research. Through implementation of this strategic framework, BBSRC will support researchers in increasing their use of Responsive Mode to complement other funding streams.

CASE STUDY: *Vitamin D or Vitamin D? The science of supplementation*

Vitamin D is crucial for bone and muscle health and there is concern that many people do not get enough of it, either through their diet or exposure to sunlight. As a result, many foods are fortified with vitamin D and it is commonly included in nutritional supplements.

However, vitamin D comes several forms and new research is suggesting that they may not have equal health benefits. Vitamin D_3 (cholecalciferol) is the type found in animal-derived foods and produced in human skin on exposure to sunlight, but most fortification and supplementation is in the form of plant-derived vitamin D_2 (ergocalciferoland).

Research funded by the *Diet and Health Research Industry Club* suggests that vitamin D_3 is more effectively converted than vitamin D_2 to the hormone responsible for human health benefits[36]. This would mean that widely-used vitamin D_2 supplements may be less beneficial to health than equivalent vitamin D_3 supplements, a realisation which could have significant implications for how the food industry can most effectively fortify foods. Further studies to compare supplementation are underway, together with investigation into how gender, ethnicity and genetic make-up play a role in how our bodies use both types of vitamin D.

Key Science Challenges

BBSRC will support underpinning science in food, nutrition and health which addresses the key health, policy and innovation needs outlined above. Strategic research will be framed around the four key research challenges summarised (*figure 2*) and outlined in more detail below, recognising that much research will address cross-cutting questions. Current BBSRC investment encompasses all four of the challenges areas, reflecting the nature of this strategic framework as a clarification and focussing, rather than radical change, of strategic direction.

Key research tools and approaches are outlined alongside the research challenges. These should not be taken to be restrictive, but represent areas which offer potential for significant advances in the current research climate. The cross-cutting issues of research infrastructure and capability, skills, deriving impact and partnership needs are addressed below.

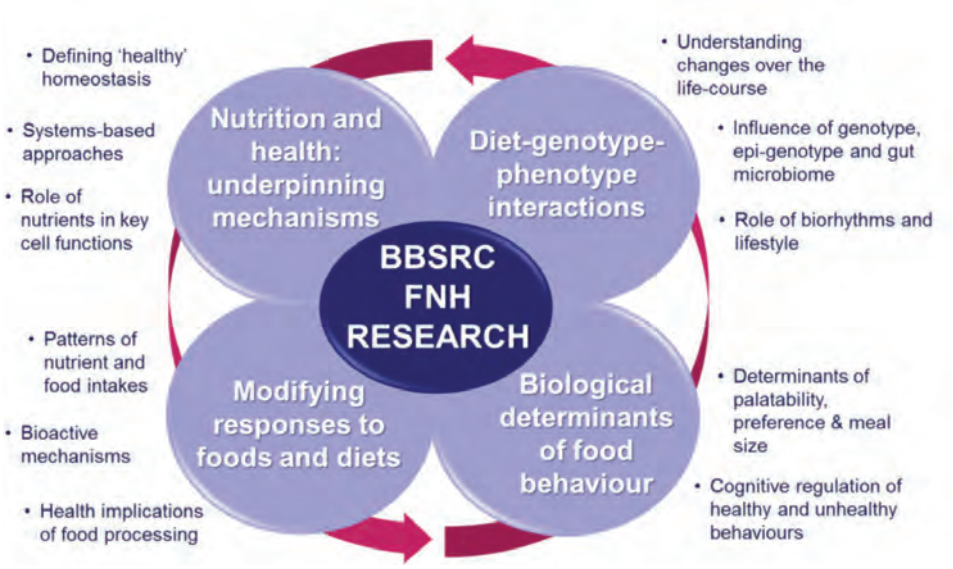

Figure 2: Summary of key research challenges for strategic research in food, nutrition and health. Each challenge is outlined in more detail below

1. To establish how food and nutrition can optimise health and reduce disease risk

- by defining 'healthy[37]' and identifying early indices of 'unhealthy[38]' states that are modifiable by diet
  - o Understanding the molecular and cellular signatures of metabolism and their dynamics, and responses to stress[39] in a healthy state
  - o Using the healthy state as a comparator to identify and characterise early-stage homeostatic disturbance, particularly in the non-fasted (postprandial) state
  - o Understanding maintenance of gut health
  - o Understanding dietary modulation of the healthy mucosal immune system, including its relationship with allergy and intolerance
  - o Determining how nutrition and nutritional status contribute to resilience[40] at cellular, tissue and whole body levels
- by defining and understanding how dietary needs and responses to dietary intake change across the lifecourse
  - o Understanding and quantifying nutritional needs and responses at critical times in the lifecourse and for specific population groups
  - o Understanding how maternal nutrition and nutritional modulation during the neonatal period and other critical developmental stages influence later life health outcomes
  - o Conducting mechanistic analysis to test hypotheses generated by epidemiological, prospective and other cohort studies
- by understanding the biological basis of converging pathways shared between cell metabolism and other systems

2. To understand how diet interacts with external and internal factors to modulate phenotypic responses that influence health

- by understanding how nutrients regulate key cell functions, including proliferation, recognition, apoptosis, DNA repair and cell-to-cell signalling
  - o Understanding nutrient sensing at the cellular level, and its consequences for cellular and organ messaging, and for behavioural decision-making
  - o Understanding the mechanisms through which energy balance, nutrients and bioactive compounds modulate physiological responses
- by understanding the contribution of genotype to individual responses to diet and consequences for health outcomes
- by characterisation and mechanistic analysis of the gut microbiome

o Understanding nutritional modulation of the gut microbiome and its physiological impact on the host

- o Understanding interactions between the host genotype, phenotype and the gut microbiome which are influenced by diet or nutritional status
- o Understanding the role of the gut microbiome in the metabolism and biological activities of food, and on immune interactions and tissue homeostasis

- by understanding the role of biological rhythms and lifestyle in determining responses to diet and subsequent health outcomes
  - o Understanding mechanisms of metabolic "fine-tuning" by dietary means
  - o Understanding the potential for sustained physiological impact of small, repeated changes in behaviour, appetite, circulating metabolic perturbations or energy expenditure mechanisms
  - o Hypothesis-led study of modern lifestyle impacts - including shift-work, sleep deprivation, artificial light exposure, sedentary behaviour, meal patterning and overconsumption[41]

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3. To understand the contribution of dietary patterns, individual nutrients, whole and processed foods[42] and food structures to promoting and maintaining health

- by using systems biology[43], labelling and imaging approaches to study responses to foods and diets
  - o Understanding and characterising food behaviour in the gut
  - o Understanding the uptake, processing and storage of dietary compounds
- by understanding functional characteristics of gut receptors, including interaction with micro and macro nutrients and effects on satiety through gut-brain signalling
- by providing robust evidence of the mechanisms of action for bioactive components within foods[44], which can be translated to human models
- by understanding the effects of processing and modification on health-related food properties
  - o Understanding the relationship between biofortification, food processing and bioavailability, including determining optimal processing methods for maximising nutrient bioavailability
  - o Manipulating the physical and chemical structures of foods and evaluating metabolic and neurobiological responses

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4. To understand the biological determinants of personalised behavioural responses and attitudes toward food, nutrition and health

- by understanding the determinants of palatability and flavour preference
  - o Understanding the processes by which flavour preferences are learned and modified over time
  - o Establishing sensory/textural determinants of food choice with a focus on understanding the acceptability of lower-sodium and less energy-dense foods
- by understanding the formation of unhealthy dietary habits and behaviours
  - o Understanding bidirectional interactions between food and emotion
  - o Evaluating determinants of food motivation and reward and understanding their underlying neurobiology
  - o Understanding how early-life experience influences behavioural responses to foods in adulthood
- by understanding determinants of meal size and overconsumption
  - o Understanding how environmental cues promote overconsumption and how responses can be influenced to promote desired intake patterns
  - o Understanding determinants of portion size and dietary decision making, and sustained effects on meal size, satiety and energy intake
- by understanding "top-down" and/or cognitive controls of dietary behaviour
  - o Understanding barriers to sustained behaviour modification
  - o Understanding the role of memory and attentional processes in appetite control

Key research tools & approaches

Key research approaches

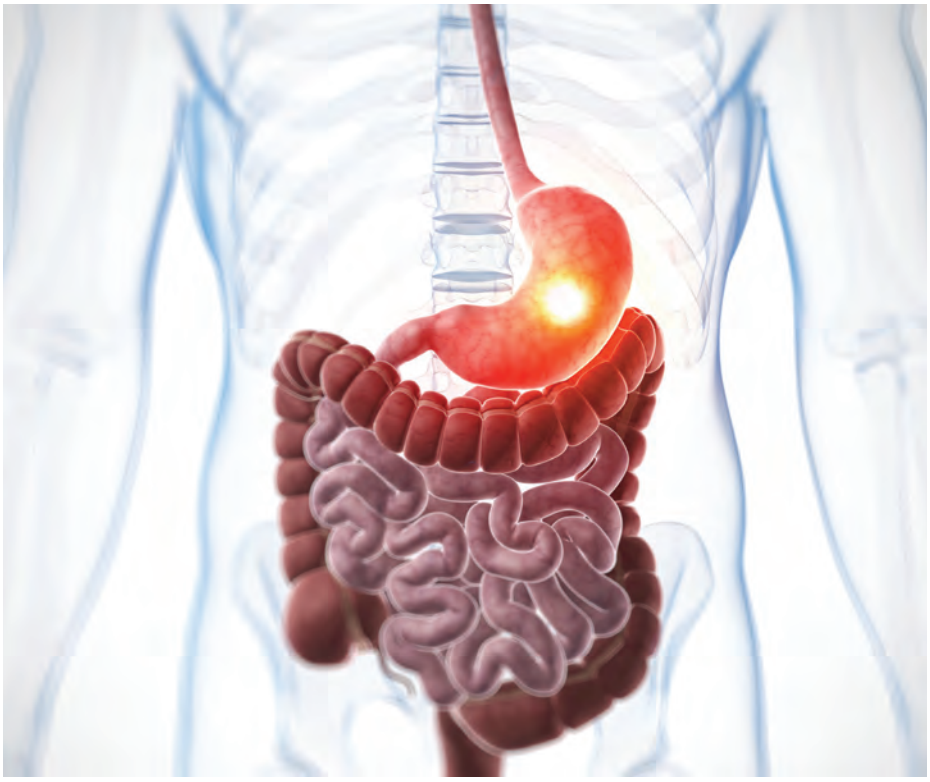
- Systems biology; recognition that mechanistic analysis can go beyond the molecular
- Diet-gene interaction analysis
- Intervention studies[45] to integrate human and molecular analysis
- Human-relevant model systems for comparative biology and life-history analysis
- Co-ordination of high-throughput technologies for effective mechanistic studies
- Human in-vivo physiological studies, including postprandial challenge responses
- Biomarker validation[46]
- Integration of food science and nutrition research
- Collaboration between physiological and behavioural science
- Gut microbiome modulation

General tools (which, where appropriate, should be applied primarily in hypothesis-driven research)

- Metabolomics
- Transcriptomics
- Proteomics
- Genomics
- Cell biology
- Cellular and whole-body imaging; including liver, pancreas, gut and brain
- Epigenetic analysis
- In-vivo trace-labelling
- Microbiology
- Animal models including gnotobiotic (germ-free) animals
- Trace element and micronutrient measurement
- Mathematical modelling

Research capacity and skills

The UK has world-class facilities, resources and people which underpin its research excellence. Capitalising on this excellent research base will require continued support for essential infrastructure, and the development of young scientists in the food, nutrition and health area.



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BBSRC will build and broaden the fundamental research base in food, nutrition and health through mechanisms such as responsive mode prioritisation and Strategic Longer Larger Grants focus areas. Sustainable research capacity will be safeguarded by supporting researchers in applying to and winning funding from responsive mode, in part by developing Committee expertise and ensuring that interdisciplinary applications, including those which cut across Council remits, are assessed in the most appropriate manner. Through its *Exploiting New Ways of Working* enabling theme, BBSRC will ensure that food, nutrition and health research benefits fully from the opportunities offered by new capacities in systems biology and e-science. BBSRC supports and will continue to support national capacity, particularly through the longer term funding available to BBSRC's institutes.

The focus on fundamental understanding of gut health and its interactions with food and nutrients outlined in this strategic framework will be attractive to early-career scientists interested in mechanistic studies of health. Furthermore, emerging interest in diverse areas - including the gut microbiome and gut immunology – will encourage world-class basic scientists from a range of backgrounds to apply their expertise to food, nutrition and health challenges. BBSRC will encourage early-career researchers in food, nutrition and health to take full advantage of the range of career support mechanisms available, including *David Phillips Fellowships* and *Doctoral Training Partnership* schemes, and support more established researchers in applying their skills to emerging challenges.

BBSRC will also facilitate networking and collaboration between researchers across disciplines. Fostering scientific literacy across the plant and food science, human physiology and human behaviour communities will be key to enabling effective interdisciplinary research. BBSRC will ensure that the mechanisms available to support interdisciplinary expertise and approaches, including *Strategic Longer Larger Awards* and interchange schemes, are fully exploited by the full breadth of the food, nutrition and health community.

Deriving impact from basic research in Food, Nutrition and Health

An increased understanding of the basic mechanisms underpinning relationships between food, nutrition and health can generate significant benefits for society and the economy, and it is imperative that this potential is realised wherever possible. The fundamental research supported by BBSRC forms an essential part of the pipeline from research to impact, but other stakeholders are critical to effective translation.

We will continue to engage with industry and policy stakeholders to ensure effective exchange of knowledge between the research community and end-users, ultimately deriving maximum impact from research investment.

Impact through Industrial application

Food, nutrition and health research has relevance to a wide industrial base, including farming and food manufacture, representing key components of the UK economy. The research challenges facing the sector are extensive, with stringent safety and health claims frameworks at national and European levels. However, industrial research and development investment is relatively low, reflecting the limited margins of food products and the scale of challenges to be addressed.

The food industry is therefore in an excellent position to exploit the basic science that BBSRC funds, and the skilled biologists which it trains. Fundamental research elucidating the mechanisms which link food components to physiological changes will underpin evidence for human health effects, crucial for the health claim approvals which will drive innovation. The integration of bioscience and food science will facilitate formulation of healthier and more palatable foods, stimulating development of new products.

Building on successful models of collaboration, BBSRC will facilitate engagement between the research base, food companies and other key stakeholders. Effective partnerships with translational funders such as *Innovate UK* and industry groups such as *Campden BRI* and *Leatherhead Food Research* (see *Partnerships* below) will ensure that industrial needs are communicated to researchers and support effective translation of research outputs to application.

Impact through evidence-based policy and practice

Food and nutrition are major determinants of health, and an improved understanding of the nature of their influence can directly inform health strategies and consumer advice. Fundamental research in food, nutrition and health can therefore contribute significantly to evidence-based policy making, delivering the social and economic benefits that result from implementation of more effective policies.

A more complete understanding of the physiological effects of foods and nutrients is likely to have implications for optimal nutritional care and disease prevention or management through diet. In some cases, impact will therefore be most effectively derived by connecting fundamental research to more clinically-focused studies. BBSRC will engage with translational research funders such as the *National Institute for Health Research* and relevant policy bodies (including the *Department of Health*) to support translation into clinical practice where appropriate.

A mechanistic understanding of the relationships between food and health will also underpin evidence for robust nutritional guidelines across the lifecourse, particularly during critical phases of development and for vulnerable groups. In the longer term, understanding the variability in individual responses to foods will facilitate more personalised nutritional advice. Government bodies involved in food and nutrition policy, such as the *Food Standards Agency*, *Public Health England* and the *Department of Health* form a crucial interface between basic research and translation into public health practice with whom BBSRC will engage.

Communication and Partnerships

The issues surrounding food, nutrition and health are complex and multidisciplinary, extending across organisational responsibilities. However, there remain disconnections at many levels: between funders, between research and policy, between disparate research disciplines, between underpinning science and translational research, between funders and research communities and between research outputs and the public.

Effective communication and partnership is therefore essential to draw on the breadth of knowledge and capability in multiple disciplines, organisations and sectors. BBSRC is committed to working with others to maximise the outputs of basic research, and to ensure an effective pipeline from fundamental research to translation and impact.

Joint working with other Research Councils

Alongside this document, BBSRC, MRC and ESRC have developed a *Joint Vision for Food, Nutrition and Health* which recognises the importance of integrative research and will form the basis for future cross-Council working.

BBSRC is also effectively engaged with other Councils in relevant areas through the *Global Food Security* (GFS) and cross-Council coordinated ageing research (e.g. *Life and Lifelong Health & Wellbeing* (LLHW) Programme) Nutrition, consumer behaviour and food choice are key priorities for the Global Food Security programme[47], and early scoping work around the broader topic of sustainable nutrition has reinforced the need for a coordinated and multidisciplinary approach. BBSRC, GFS and LLHW will work closely together to ensure our research programmes are complementary in these and other areas.

Partnership with other research funders and key stakeholders

The research challenges in food, nutrition and health are too great to be tackled by one funder or the UK Research Councils alone. Other national and international funders have significant existing and developing interests in relevant areas, with which BBSRC will engage to prevent duplication and maximise collaboration. For example, *Diet and Health* forms one of seven themes of the Scottish Government's Rural and Environmental Science and Analytical Services (RESAS) Division's research agenda, whilst the EU Joint programming Initiative *A healthy diet for a Healthy Life* and other *Horizon 2020* programmes represent significant European investment in relevant research. Partnership with translational funders in industry-focused, clinical-focused and policy-focused research (including *Innovate UK*, *National Institute for Health Research* and *Public Health England* respectively) will be particularly crucial in ensuing that the pipeline from basic research to impact is effective.

The food industry and associated bodies represent key partners in, and users of, food, nutrition and health research. As well as building relationships with individual companies, BBSRC will engage with organisations such as the *Food and Drink Federation* and *Institute of Grocery Distribution* to improve awareness of the support provided by the UK research base to business, and to encourage academic participation in the research challenges facing industry. As membership-based food and drink research organisations, *Campden BRI* and *Leatherhead Food Research* represent a significant UK capability for translation of fundamental research into industrial application with whom BBSRC will continue to work. Their extensive membership provides an effective route to communicate the excellence of the UK research base to business, whilst offering insight into the industrial research challenges which may be solved through fundamental research.

Communication with the food, nutrition and health research community

This document underlines BBSRC's commitment to food, nutrition and health research and aims to clarify emerging strategic interests. Alongside the new responsive mode priority in Food, Nutrition and Health[48], it serves to demonstrate BBSRC's intention to support word-class research in this area.

BBSRC will proactively engage with the research community to develop and raise awareness of its strategic interests and relevant funding mechanisms – for example, the research challenges outlined in this document were informed by an open consultation with the research and wider stakeholder communities[49]. We will ensure that applications in food, nutrition and health areas – particularly multidisciplinary proposals - are reviewed appropriately, both at peer review and committee stages, and that researchers are confident in review procedures. BBSRC will also foster the development of multidisciplinary collaborations through workshops and networking events, both within BBSRC's remit (for example connecting plant scientists with human nutrition researchers) and across Research Councils.

Public Engagement

The relationships between food, nutrition and health arouse significant public interest. This represents both an opportunity for productive engagement, and a risk that scepticism may be aroused by poor or misrepresented research. BBSRC must ensure a continued license to operate by developing an understanding of areas of public interest and concern, and taking steps to maintain public confidence in the quality and utility of basic nutrition research.

In March 2014, BBSRC held a public dialogue around research in food, nutrition and health, with the aim of engaging in a meaningful conversation about the key research challenges on which BBSRC should be focussing[50]. The dialogue clearly demonstrated that people have a strong desire to understand how foods and diets affect individuals, their families and future generations - and consequently saw food, nutrition and health as an important area of public research. The outputs of the event have fed into the research challenges outlined in this document, and particularly highlighted the relationships between food and mental health as a key area for joint working between BBSRC and MRC.

The dialogue also highlighted that participants felt they did not have sufficient accurate, clear and objective information to enable them to make informed dietary choices. BBSRC will continue to work hard to ensure that the results of the work we fund are effectively and straightforwardly publicised. Routes for communication will include our own channels (such as Twitter, YouTube and the BBSRC website), traditional media and increased collaboration with organisations – such as the *British Nutrition Foundation* – which specialise in interpreting and communicating research.

BBSRC will continue to actively look for opportunities where public engagement can be used to inform our strategies and we will carry on encouraging the researchers we fund to do likewise.

Footnotes

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[37] 'healthy' should be interpreted as a state of metabolic homeostasis

[38] 'unhealthy' should be interpreted as a state of metabolic dysregulation

[39] 'stress' includes both endogenous (e.g. metabolic responses) and exogenous (e.g. chemical stimuli)

[40] 'resilience' refers to homeostatic flexibility to adapt to endogenous and exogenous stress (including ageing), conferring disease resistance

[41] It should be recognised that overconsumption (of energy) and undernutrition (of other essential food components) are not mutually exclusive

[42] Analysis should focus on widely-consumed foods rather than niche products

[43] Emphasis should be placed on systems-based approaches to move away from reductionist analysis towards interrogation of complex interactions

[44] Bioactive components should be taken to include nutrients, phytochemicals and other physiologically relevant compounds found in food

[45] Human intervention studies using a supplementation approach should maintain levels of intake realistically achievable through normal food consumption

[46] Biomarkers identified in the course of wider research should be effectively validated

[47] BBSRC, ESRC and MRC are all partners in the Global Food Security programme, which brings together the major UK public sector funder of food-related research: **www.foodsecurity.ac.uk/programme/index.html.**

[48] **http://www.bbsrc.ac.uk/funding/priorities/food-nutrition-and-health.aspx** this responsive mode priority incorporates research areas captured in this document with relevant interdisciplinary themes, including food safety and nutritional enhancement

[49] **http://www.bbsrc.ac.uk/organisation/policies/reviews/consultations/1308-role-in-food-nutrition-health-research.aspx**

[50] **http://www.bbsrc.ac.uk/society/dialogue/activities/food-nutrition-health.aspx**

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