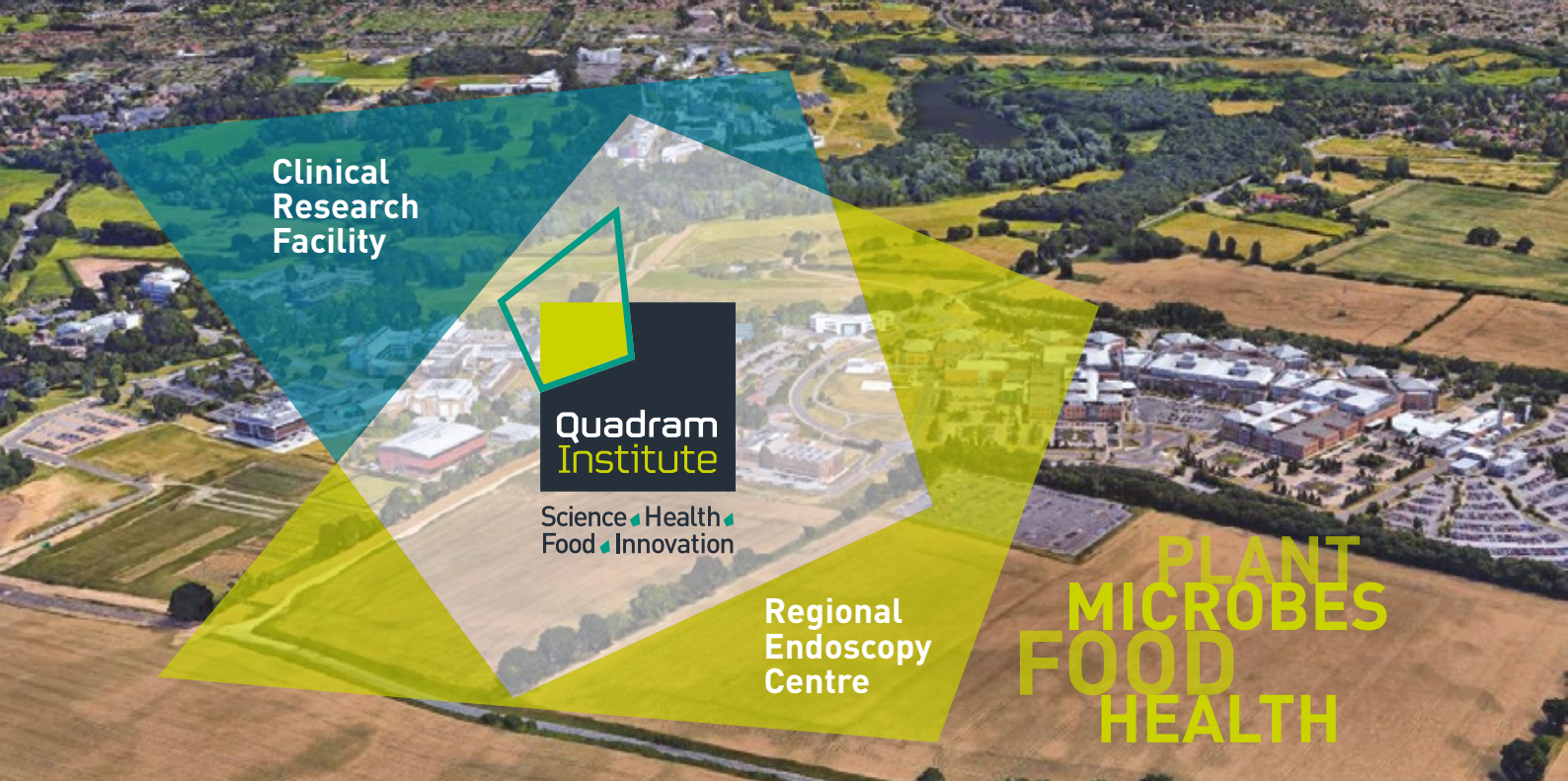




**Quadram  
Institute**

Science • Health •  
Food • Innovation

**SCIENCE  
STRATEGY**



**Food is central to human existence but the world is facing an epidemic of food-related health conditions that have a huge impact on society and the economy. While lifespan is increasing, healthspan is not and we need to address the burden of non-communicable diet-associated diseases, the impact of pathogens in the food chain and malnutrition.**

The **Quadram Institute** seeks to address these major challenges by conducting world-class research into the impact of food on health. The **Quadram Institute** will deliver interdisciplinary excellence across the areas of clinical practice, clinical research and food and health science. It is the first international centre of research and clinical excellence of its kind working in the area of food and health.

The **Quadram Institute** brings together fundamental and translational science with a clinical research facility for human trials and one of the largest gastrointestinal endoscopy units in Europe. The unique co-location of these three elements in the same building will

synergise interactions between basic and clinical research to deliver a step-change in the understanding of the role of food in health and microbiology in food safety.

Situated on the Norwich Research Park, the **Quadram Institute** will be at the centre of a cluster of academic resources including:

- ✔ the John Innes Centre (JIC) and The Sainsbury Laboratory (TSL)
- ✔ the Earlham Institute (EI)
- ✔ the University of East Anglia (UEA)
- ✔ the Norfolk and Norwich University Hospital (NNUH)

The partnerships and interaction arising from this co-location will generate a powerhouse for research and innovation across the plant-microbe-food-health spectrum delivering both fundamental and translational science in collaboration with food, pharmaceutical and related industries.

## Our Vision

The **Quadram Institute** will create new interfaces between food science, gut biology, human health and disease, capitalising on the world-class bioscience cluster based at the Norwich Research Park.

Scientists working with clinicians will work closely with major national and international funding bodies and charities, collaborators and investors to ensure translation of our fundamental science to benefit patients, consumers and wider society.

The mission of the **Quadram Institute** is to understand how food and the gut microbiota are linked to the promotion of health and the prevention of disease, with an emphasis on diet- and age-associated diseases.

We will use this knowledge to develop evidence-based strategies to maximise positive impacts of food on health, from early life to the extension of a healthy lifespan in old age, and reduce the economic and societal costs of chronic diseases.



### The Quadram Institute

– an interdisciplinary institute to maximise the unique cluster of academic excellence and clinical expertise at the Norwich Research Park, working alongside the food and pharmaceutical industries

# HEALTHY GUT SAFE FOOD HEALTHY AGEING FOOD HEALTH IMPROVED NUTRITION

## The challenges we're tackling

The world is facing an epidemic of food-related health conditions. We need to address non-communicable diet-associated diseases and malnutrition. Foodborne pathogens are responsible for much disease in humans and animals and increase the spread of antimicrobial resistance.

- ✔ Collectively, food-related illnesses are a worldwide problem, causing over 350 million deaths each year
- ✔ Chronic, diet-related disease costs the UK £5.1 billion per annum in direct health costs and is estimated to cost the wider economy around £16 billion every year
- ✔ The economic impact is predicted to rise to £50 billion by 2050 if no action is taken

✔ Tackling the problem of antimicrobial resistance will help save one life every 3 seconds by 2050

**SAVE  
1 LIFE  
EVERY  
3 SECONDS  
BY 2050**



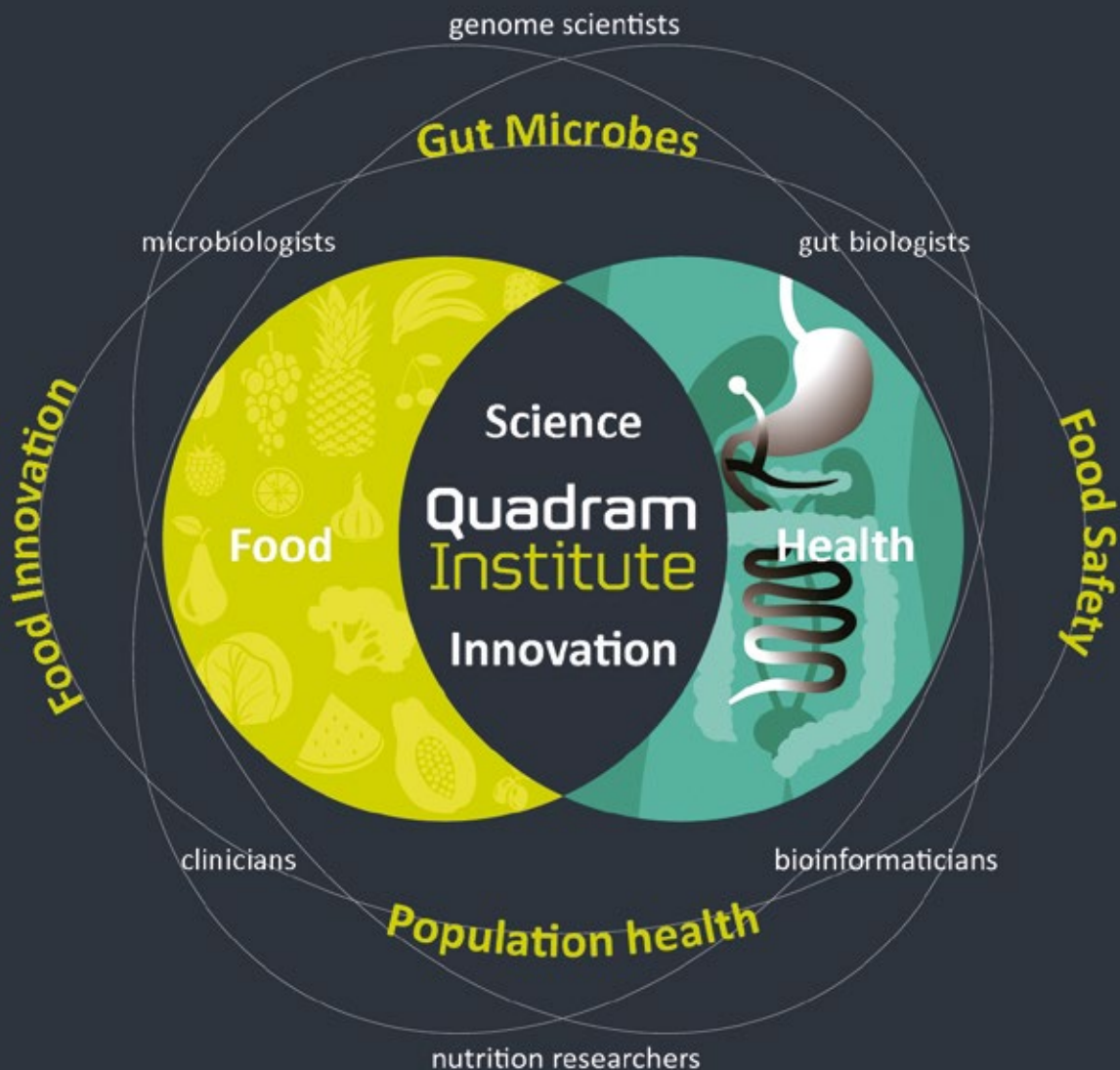
**FOODBORNE DISEASE  
AFFECTS  
600 MILLION PEOPLE.  
REDUCING ITS IMPACT WILL  
SAVE UP TO  
400,000  
LIVES**

Gut microbes are becoming a significant area of medicine and health, although their full role is not yet understood. The microbes that colonise our digestive systems create an ecosystem that helps to promote healthy functioning of the whole body, and when this ecosystem is disrupted, the resulting "dysbiosis" may initiate and accelerate disease. We do not yet understand the full extent of the connections between gut health and a host of diseases that are linked to ageing, including cancer, cardiovascular disease, arthritis and dementia. We are living longer in developed countries but the majority do not live longer well, which will – left unchecked – put huge pressure on our healthcare systems.

**There is an urgent need to understand the connections between food, gut microbiota and the health of populations.**

# FOOD INNOVATION GUT MICROBES FOOD SAFETY POPULATION HEALTH

Four interconnected research areas will be developed in the Quadram Institute





Theme 1

# Food Innovation and Health

## CASE STUDY

A \$1million Challenge Award from the Prostate Cancer Foundation has allowed us to study the protective effects of consuming glucosinolate-containing vegetables against prostate cancer, in collaboration with the University of East Anglia and the Norfolk and Norwich University Hospital. This builds upon many years of research on the biological activity of naturally occurring sulphur-containing compounds found in vegetables, leading to the development of innovative new products.

# Food Innovation and Health

## *How can we enhance the quality of food to promote lifelong health?*

The theme brings together a multidisciplinary team of scientists and clinicians that collectively seek to understand the mechanistic basis of how food can modulate digestive and metabolic processes to maintain and promote health and healthy ageing. An important part of this research theme is undertaking human intervention studies and clinical trials to exploit advances in human genomics to understand how individuals respond to specific foods and diets. Our focus is on promoting health and preventing and ameliorating the effects of age- and diet-related chronic disease, including gut inflammatory syndromes, cardiovascular disease, cancer and cognitive decline. New knowledge will be gained that will enable the design and development of innovative foods and products to promote health.

### Research priorities

#### **Harnessing the advances in plant and crop genomics to develop new crop cultivars with enhanced quality traits for human nutrition.**

We seek to work with UK and international partners to exploit the major advances in crop genomics to develop novel cultivars with enhanced nutritional qualities for human health. A major interest is to understand how to manipulate carbohydrate quality in wheat and other major crops and develop new cultivars with high levels of resistant starch. A further emphasis is the development of new genotypes of fruits and vegetables that have modified levels of bioactive compounds that may underpin the health promoting effects of these dietary components.

#### **Food structure and digestion.**

The chemical composition and physical structures of foods determine the rate of digestion and passage through the digestive tract, and the absorption of nutrients within the small and large intestine. This in turn affects the release of gut-derived signalling compounds that are important in determining satiety. We seek to develop experimental foods to understand the factors that influence digestive processes and gut-brain signalling.

#### **The interplay between food and gut microbiota.**

The role of the gut microbiota in modulating health is increasingly realised, and is a major part of the **Quadram Institute's** science strategy, as further described in Theme 2. We seek to elucidate on the interplay between food and the gut microbiota from two perspectives: firstly, how food can modify the gut microbiota, and, secondly, how the gut microbiota can modify and metabolise foods leading to microbial products that are bioactive either within the gut lumen or following absorption.

#### **Food bioactives as metabolic modulators.**

Many observational studies continue to support the role of small specialised plant metabolites in the maintenance and promotion of health. However, there remains a lack of understanding of the underlying mechanisms of how a relatively low, yet highly variable intake of a range of these metabolites can affect physiological processes. We seek to understand at a biomolecular level how these plant-derived metabolites cell signalling and physiological processes that may impact on health and contribute to the prevention of cardiovascular disease, cancer and other chronic conditions.

### WHAT NEXT

Overconsumption of easily digested carbohydrates is linked to obesity. Using wheat, the most widely grown cereal crop, we will identify the wheat starch genes associated with starch structure and digestibility. We will use this information to design new wheats with resistant and slowly digested starch that can support the development of innovative foods to reduce the impact of obesity-related diseases such as diabetes.



## Theme 2

# Gut Microbes and Health

### CASE STUDY

In a collaboration with the Norfolk and Norwich University Hospital, a success rate of 92% was achieved using Faecal Microbiota Therapy (FMT) as a new treatment for patients with recurrent *Clostridium difficile* infection. FMT uses microbiota from healthy donors to restore a healthy balance of gut bacteria that can inhibit the development of *C. difficile* in affected patients. This offers, for the first time, the potential for a realistic cure for this intractable pathogen with opportunities to extend its use to treatments for ulcerative colitis.

# Gut Microbes and Health

## ***What is a healthy gut, and how is health modulated by our resident gut microbes?***

There is a growing realisation that our resident gut microbial community contributes to our health, but relatively little understanding of how this occurs. We seek to understand the functioning of our intestinal microbiome in order to promote and restore health across the life course. This knowledge will help define a healthy gut and abnormalities from this healthy state, allowing more targeted, timely and effective individual interventions to promote, preserve and restore health. We adopt an interdisciplinary approach, working from the cell up to the whole human body, to define pathways of microbe-host crosstalk and mechanisms of immune-mediated microbial tolerance – across the whole life course.

## **Research priorities**

### **How is host-microbe mutualism established?**

Early in life, the gut becomes colonised with microbes that remain with us for our entire lifespan. The establishment of a gut microbial population in the first months and years of life is critical to lifelong health. In later life the gut microbe ecosystem may break down impacting chronic illness. We aim to define integrated pathways of microbe-host cell crosstalk and mechanisms of microbial tolerance at key stages during the life course, particularly in the young when it is first established, and in the elderly when it may be in functional decline.

### **How the microbiome influences host physiology, systemic health and the Central Nervous System..**

We aim to determine how enteric microbes influence signalling pathways within the enteric endocrine system and the liver to influence metabolic homeostasis, and the conditions under which these interactions result in altered metabolism. These studies are enabled by novel organ-based culture systems in addition to pre-clinical *in vivo* model systems incorporating 'omics technologies and systems biology, and human studies. We seek to elucidate the microbial cues capable of driving hunger and satiety responses that influence metabolic health.

### **How to change gut microbes to improve health.**

While many people establish a gut microbiota early in life that will contribute to lifelong health, our changing lifestyles, environment and ageing may lead to our resident gut microbiota community becoming sub-optimal for good health. Moreover, through reasons we do not understand, major microbial dysbiosis may occur leading to severe chronic illness. We seek to develop biomarkers to identify early signs of a sub-optimal or dysfunctional gut microbiota, and approaches to restore a healthy functioning gut microbiota community. This may be through prebiotic and probiotic food and other therapeutic approaches or, in severe cases of dysbiosis, through entire gut microbiota transplantation. As part of these research activities we seek to explore the gut virome, which may enable new therapeutic interventions for bacterial dysbiosis such as phage therapy.

## **WHAT NEXT**

Evidence shows that changes in the microbiome are influential beyond the gastrointestinal tract, impacting other organ systems including the brain. We will unpick the complicated interactions between the microbiome (including the understudied virome) and the cells lining the gut, the immune system, and the host genome to elucidate links between the microbiome and illnesses such as dementia and ME (Chronic Fatigue Syndrome), thus underpinning the development of new therapies.

## Theme 3

# Microbes in the Food Chain: Food Safety

### CASE STUDY

Using whole-genome sequencing we have demonstrated that *Salmonella* evolves much faster than previously anticipated. Adaptations included the acquisition of genes for toxin production and resistance to heavy metals, providing the pathogen with a competitive advantage over other bacteria. Understanding the remarkable evolutionary speed and diversity of adaptations has provided the essential trait-based information necessary to better combat these rapidly adapting strains, and reduce the impact of foodborne illness.



# Microbes in the Food Chain: Food Safety

## ***How can we reduce microbial pathogens in the food chain, and prevent the emergence of antimicrobial resistance?***

Foodborne infection has major impacts on human health and wealth nationally and globally. The ecology of microbes and the lifestyles they adopt are of crucial relevance to animal health and welfare, food production, food safety and the emergence of pathogens with new resistance and virulence phenotypes. In this theme we seek to deliver an enhanced understanding of the ecology, evolution and survival strategies of pathogens in the food chain, including the drivers of antimicrobial resistance, to improve human and animal health and productivity.

### **Research priorities**

#### **To understand the evolution, emergence and spread of foodborne pathogens.**

We will document the national and global genomic epidemiology of key foodborne and animal pathogens, including *Salmonella*; *Escherichia coli*; *Campylobacter*; *Listeria*; *Brachyspira*; and *Clostridium botulinum*. This will incorporate isolates from a range of different contexts, including farm animals, the farm environment and food and water destined for human consumption. This will be contextualised through comparisons with isolates from other settings (e.g. humans, wild animals, plants, rivers, soil). We will also drive forward the development of novel approaches to sequencing to improve the speed, cost and ease of use of microbial genome sequencing. We will explore the genomic epidemiology of antimicrobial resistance in cultured isolates. This will involve investigating patterns of resistance genes to identify selective pressures that drive antimicrobial resistance (AMR) and developing novel methods for linking sequences from resistance elements and mobile genetic elements to the host-cell chromosomes in microbial metagenomes.

#### **To understand the microbial ecology of the human food chain.**

We will investigate the gut microbiomes of food animals and the microbial communities that occur in animal feeds, in farm environments (e.g. slurry) and in food (e.g. in supermarket chickens). This will involve using culture and sequence-based approaches to document taxonomic diversity as well as mathematical and systems-based approaches to modelling microbial functions and interactions.. These efforts will include bioprospecting for potentially useful enzymes, probiotic strains and novel ecological approaches to the control of foodborne pathogens (e.g. bacteriophages, predatory microbes).



### **WHAT NEXT**

The global burden of foodborne illness is massive, causing an estimated 420,000 deaths and 600 million cases of illness each year. We will use state of the art microbial genomics, metagenomics, bioinformatics and synthetic biology to understand how microbes evolve, spread, survive and compete in the food chain and to develop novel interventions that reduce the risk of illness and the spread of antimicrobial resistance.



## Theme 4

# Population Health

### CASE STUDY

The Baby Associated MicroBiota of the Intestine (BAMBI) study is examining the microbiota of preterm infants and characterising how its development is modulated by factors such as antibiotic use and probiotic supplementation. Working with the NNUH, researchers are following babies in their early years to understand the links between microbiota development and future health, which will inform future strategies for optimising the health of preterm infants.

# Population Health

*How do we translate our research on food, gut microbes and human biology to enhance the health of the population and reduce societal health costs, both in the UK and internationally?*

The translation of our research on food, gut microbes and human biology will help enhance the overall health of the population, reducing the burden of healthcare costs in the UK and internationally.

Technological advances have seen the costs and ease of genome sequencing and associated approaches becoming reduced to such an extent that they can be readily applied on a population basis, such as the Genomics England 100,000 Genome Project. In this theme we seek to integrate our experimental research programme with public health, population biology and health economic approaches to understand how the research output of the **Quadram Institute** can have a significant effect on the health of our nation – and that of other nations. Moreover, dietary advice remains largely a 'one size fits all' approach, but as medicine becomes more personalised, with individual therapies tailored to an individual's genotypes, we ask the question as to what extent can we refine dietary advice, for different population groups.

## Food, Microbes and Public Health

- ▶ Applying our knowledge of food and gut microbiology to enhance the health of the UK population, to reduce hospital admissions and length of stay, and reduce the growing burden of healthcare costs
- ▶ The Norfolk population is relatively settled and ageing. We seek to gain a greater understanding of its demographics, lifestyle variations, genetic diversity, and variation in gut microbial populations. This will be both through integrating existing data held by different organisations and acquiring new data on biological variation
- ▶ Applying our expertise to help tackle the global epidemic of non-communicable disease
- ▶ We live in a global community in which changing lifestyles and increasing economic prosperity are resulting in rapid increases in non-communicable diseases. The research we are undertaking with **Quadram Institute** on food, gut microbes and health has importance and relevance to low and middle income countries, as well as to the UK



## Research priorities

### **Bringing - 'omics and Big Data to population health: the unique advantage of the Norfolk population for longitudinal studies of gut health.**

Never has there been such a unique opportunity to capture Big Data to further inform our understanding and knowledge of both population health and personalised medicine. With the ability to routinely perform whole genome sequencing and transcriptomics on an individual patient's tissues and their gut microbiota, scientists and clinicians are now able to develop a greater understanding of how a person's unique transcriptome, physiology and microbiome can generate or be altered by disease.

In order for this powerful technology to realise its full potential it is vital that this data is joined up with detailed clinical informatics. Detailed health records (concurrent diagnoses; physical characteristics; medication; blood results and medical imaging) will supplement the 'omics approach. These Big Data sets will be fundamental in helping understand population health and disease in the future and delivering a personalised medicine approach.

With a strong partnership between Primary Care, Secondary Care and the Norwich Research Park the potential to configure a unique IT solution for population health will be developed that will align NHS data with 'omics data for population health prediction and monitoring.

East Anglia is ideally positioned to study population health through Big Data with its stable population dynamic and high representation of the diseases that affect population health (cardiovascular disease, stroke, mental health, cancer, metabolic disease and liver disease).

Whilst generating large 'omics datasets for individual and common diseases, this unique scientific study, of which the **Quadram Institute** will be the hub, will go much further. It will inform us how through cloud technology and machine learning we can learn about population health including both predictions and trends. It will link with health planning (e.g, the NHS Sustainability and Transformation Partnerships) to evolve strategies for personalised and population health.

The Big Data collected will be unique and will provide a bi-directional approach. Taking advantage of Norfolk's unique age structure we will be able to capture a large demographic over the age of 70 that have already declared the "lifetime health record." This will allow us to investigate how their genome, microbiome and metabolome relate to the development of disease over the lifetime of an individual.

In addition, we will be able to determine what changes occur in a prospective manner, and how the genome and microbiome can better predict the future health of the individual. This will inform the health economics of the UK and be vital for monitoring trends in health that can drive global social and health policy.

This large scale longitudinal bioinformatics/ patient data study will be a unique scientific resource for the UK and beyond and begin to establish how Big Data can be used and stored by the NHS, academic partners and industry to achieve the essential goal of extended health throughout the life course.

### WHAT NEXT

Unique longitudinal studies will provide the necessary genomic data from both patients and their microbiota, to build an understanding of both individual and population health. Coupled with clinical information and health records we will unlock the secrets of population health and disease over people's lifetimes, enabling personal predictions of future health and delivery of personalised therapies that extend lifelong health nationally and internationally.



## FOOD DATABANKS

The **Quadram Institute** hosts the Food Databanks National Capability. This provides information on food composition from sources across the world and is important in interfacing with the public, the food industry and regulators. Food composition data and the value added by our expertise are essential for high quality academic food and public health research into the links between diet and health, that support the aim to encourage people to eat a healthy, sustainable diet.



08/17

If you are interested in working at the  
**Quadram Institute** please email  
[recruitment@quadram.ac.uk](mailto:recruitment@quadram.ac.uk)

All commercial enquiries should be sent to  
[business@quadram.ac.uk](mailto:business@quadram.ac.uk)

For all other information or queries please  
email [info@quadram.ac.uk](mailto:info@quadram.ac.uk)

[quadram.ac.uk](http://quadram.ac.uk)



Norfolk and Norwich University Hospitals   
NHS Foundation Trust

