Advancing the science of human nutrition

Held on 4 December 2023

Conference report

Part of the conference series
Transforming our future
Introduction

On 4 December 2023 the Royal Society hosted a hybrid conference on Advancing the science of human nutrition. This meeting forms part of the Royal Society’s Transforming our future series.

The Transforming our future conferences are unique, high-level meetings featuring cutting-edge science. They bring together experts from industry, academia, funding bodies, the wider scientific community and government to explore and address key scientific and technical challenges of the coming decade. These conferences are organised with the support of the Royal Society’s Science, Industry and Translation committee.

“At the end of the day, we all want to improve the health of the population. To do this, we need to use all the tools we have, including pharmacological solutions, personalised nutritional and lifestyle guidance, and numerous other approaches.”

Dr Sarah Berry, King’s College London and Zoe Ltd

The conference series forms part of the Royal Society’s Science and Industry programme which demonstrates the Society’s commitment to integrating science and industry across its activities, promoting science and its value, building relationships, and fostering translation.

The programme for this meeting focused on nutrition was organised by Dr Sarah Berry (King’s College London and Zoe Ltd), Professor Richard Flavell CBE FRS (International Wheat Yield Partnership), Professor Cathie Martin FRS (John Innes Centre and University of East Anglia), and Dr Andrew Morgan (Royal Society Entrepreneur in Residence, University of Exeter).
An opening keynote from Professor Julie Lovegrove (University of Reading) set the scene for the day by discussing how nutritional research can inform government policy to facilitate healthy outcomes, using recent work on saturated fat as a case study. Three sessions of talks focused on: (i) nutrition-associated determinants of health; (ii) bioactives and biofortification; and (iii) nutritional, behavioural and pharmacological interventions. A panel discussion explored several themes including how to create a sustainable food system, rethinking science for the sake of science, collaboration between academia and industry to inform policy, and the importance of education. The event finished with a closing keynote from Henry Dimbleby MBE (LEON and the Sustainable Restaurant Association) which explored the future paths the UK may take in its efforts to tackle the challenges associated with diet-related ill health.

This report is not a verbatim record, but a summary of the discussions that took place during the day and the key points raised. Comments and recommendations reflect the views and opinions of the speakers and not necessarily those of the Royal Society.

“The Royal Society is dedicated to promoting excellence in science for the benefit of humanity. Exploring the future of human nutrition science is closely aligned to this aim.”

Professor Richard Flavell CBE FRS, International Wheat Yield Partnership
Executive summary

Nutrition plays an important role in health and wellbeing. Poor nutrition is a leading cause of chronic disease, including type 2 diabetes, non-alcoholic fatty liver disease, cardiovascular disease, and various forms of cancer. With an increasingly overweight and ageing UK population, the incidence of such diseases and the associated healthcare costs continue to rise.

The Advancing the science of human nutrition conference brought together speakers from industry and academia to discuss how scientific breakthroughs can be translated into effective strategies for improved health, including the prevention and management of chronic disease. Topics covered during the meeting included:

Evidence-based policy for prevention
- Encouraging dietary change via nutritional guidelines can be challenging. A case study showed how provision of tailored foods (e.g., substituting saturated with unsaturated fat in dairy products) can contribute to compliance with current saturated fat recommendations.
- Although pharmaceutical approaches may help tackle some issues associated with diet-related ill health, it is important to consider the role of prevention and the need for large-scale changes to our food system.

“Diets that tell you what not to eat are of little interest. People want to know what foods are good for them and how they can improve their health.”

Professor Cathie Martin FRS, John Innes Centre and University of East Anglia

Nutrition-associated determinants of health
- Novel technologies and community science approaches are now being used in combination with clinical, in vivo and in vitro studies to offer new insights into nutritional science.
- A person’s genetics can influence their appetite, and understanding this link can inform personalised treatment for obesity as well as public health policy.
Interactions between diet and the human microbiome can shape health outcomes, which can be particularly important for infants in terms of immune function and disease susceptibility.

Bioactives and biofortification
- Machine learning approaches and multivariate analysis of metabolomes and metagenomes can provide insight into the chemicals produced by gut microbiota that impact human health.
- Understanding how dietary bioactives impact the function of gut microbiota will be key to future efforts to improve health through new food products or food-based dietary guidelines.
- Biofortification increases the nutritional value of food pre-harvest and can be a useful tool for addressing micronutrient deficiencies, particularly for populations with limited access to a diversified diet.

Nutritional, behavioural and pharmacological interventions
- Interventions to encourage dietary change should be tailored to target groups, taking socioeconomic status, current diet and food insecurity into account.
- Interventions can be delivered cost-effectively and at scale, as demonstrated by two studies that showed the benefits of weight management therapies delivered in a primary care setting and personalised nutritional advice delivered over the internet, respectively.
- Analogues of the intestinal satiety hormone GLP-1 are proving effective as a therapeutic option for weight loss in obesity.
- Supermarkets can incentivise healthier and more sustainable choices through data-driven approaches to managing price, promotions, range, marketing and merchandising.

“The UK has an impressive range of capabilities in the multidisciplinary science of human nutrition. We must continue to build on this foundation to urgently find practical solutions to the ever-growing problem of diet-related chronic disease and ill-health.”

Dr Andrew Morgan, Royal Society Entrepreneur in Residence, University of Exeter
Policy to plate – The case of translating dietary saturated fat guidance into practice

Professor Julie Lovegrove, University of Reading, explored the evidence for saturated fat recommendations and discussed how food policy can be translated into practical dietary change.

Cardiovascular diseases (CVD) are a major cause of death globally. There is inequality in their prevalence in the UK, as it is almost four times more likely to occur in low-income groups. This is partially due to dietary differences between income groups.

Metabolic syndrome is a collection of conditions that signify a person is at risk from type 2 diabetes and CVD. These conditions include obesity, insulin resistance, high blood pressure, high blood triacylglycerols levels and low concentrations of high-density lipoprotein (HDL) cholesterol.

The relationship between cholesterol and CVD is complex. High levels of HDL cholesterol are associated with a reduced risk of CVD. Conversely, high levels of low-density lipoprotein (LDL) cholesterol, particularly small dense LDL-cholesterol, increase the risk of CVD because LDL-cholesterol is intimately linked to atherosclerosis, accumulating in plaques in blood vessels, causing them to narrow.

Dietary intervention research

There is compelling evidence that replacement of dietary saturated fatty acids (SFAs) can reduce the risk of CVD. The degree of reduction depends on numerous factors including the type of replacement.

A meta-analysis of published randomised control trials showed that replacing SFAs with poly-unsaturated fatty acids (PUFAs) was linked to a 27% reduction in CVD events. However, replacement of SFAs with proteins or carbohydrates showed no significant reduction in CVD events.

A study of 543 men and women at risk of metabolic syndrome examined how replacing dietary SFAs with either mono-unsaturated fatty acids (MUFAs) or carbohydrates impacted insulin resistance and other CVD risk factors. Replacement of SFAs with either MUFAs or carbohydrates had the beneficial effect of reducing LDL-cholesterol levels, although only MUFA replacement had a beneficial impact on the clinically relevant total cholesterol:HDL-cholesterol ratio. A different study followed 183 people at risk of CVD and found that replacing SFAs with either PUFAs or MUFAs had beneficial impacts on both LDL-cholesterol and total cholesterol:HDL-cholesterol ratio levels.

Current UK dietary guidance states SFAs should contribute no more than 10% of total dietary energy and be replaced with unsaturated fat. However, most people in the UK population exceed this recommendation. Replacing regular dairy with SFA-reduced alternatives is one strategy for reducing overall SFA intake (see case study).

“Provision of healthful foods with more balanced composition that are acceptable to the consumer is key to facilitating beneficial change from policy to plate.”

Professor Julie Lovegrove, University of Reading

CASE STUDY

Low-SFA dairy

Dairy foods are nutritionally complex: they contain high levels of protein, bioactive peptides, minerals, and some fermented dairy foods contain probiotics. These foods are nutrient dense, particularly in terms of calcium, phosphorus, iodine, riboflavin and Vitamin B12. Although dairy foods are the greatest contributor to SFA in the average UK diet, studies have shown that consumption of dairy foods is not associated with significant detriment in terms of CVD risk, and consumption of fermented dairy is associated with a significant reduction in CVD risk. This apparent anomaly could be due to other beneficial components of dairy foods, such as bioactive peptides and minerals.

Supplementing the diet of dairy cows with 1 kg per cow per day of high-oleic sunflower oil resulted in modified milk enriched in MUFAs and reduced in SFAs. When hard cheese and butter made from this milk was consumed by men and women at risk from CVD for 12 weeks, it prevented the increase in LDL-cholesterol observed after conventional dairy consumption and improved blood vessel health. In trials, consumers preferred the modified butter, due to it being spreadable from the fridge, but not the modified cheese compared with commercial alternatives due in part to textural properties. Future work on optimising texture and flavour properties of SFA-reduced food products could further improve their appeal to consumers.
The future of diet-related disease prevention: novel technologies and community science?

Dr Sarah Berry, King’s College London and Zoe Ltd, discussed how remotely delivered health interventions and large-scale remote app-based data collection can be undertaken at scale and with the precision and breadth required to advance the science of human nutrition.

Personalised nutrition tailors recommendations on what, when and how much to eat to optimise the health of an individual. Research in this area and its widespread application requires large volumes of high-precision dietary, lifestyle, physiological and multi-omic data. This has been difficult to achieve in the past, as most data collection has been either high precision but small in scale/breadth (e.g. randomised controlled trials) or large in scale/breadth but low precision (e.g. epidemiological studies).

However, we are living in an exciting era of biological research. New ways of acquiring data using digital tools (e.g. using wearable technologies or mobile phones) and remote clinical testing are enabling a shift in how human health research is conducted. It is often no longer necessary to choose between high resolution and large-scale data collection.

Studies conducted by Zoe Ltd in collaboration with King’s College London, outlined below, demonstrate how innovative methodologies and digital tools can be used to advance human health, and especially nutritional science, research.

**COVID Symptom Study**

This health research project used a mobile app that was created in response to the COVID-19 pandemic in 2020 by Zoe Ltd, King’s College London, Guy’s and St Thomas’ Hospitals. The app tracks users’ COVID-19 symptoms as well as diet and lifestyle data. Within a week of launching, the app had one million users, and by four weeks this had grown to four million users. Information from the app changed the World Health Organisation’s definition of COVID-19 symptoms.
Zoe Health Study
Following the Covid Symptom Study, learnings about home-based, app-enabled data collection were leveraged to research other health and lifestyle issues as part of the Zoe Health Study. This platform has been used to conduct several large-scale studies, including the Big IF Study. This experiment examined whether intermittent fasting makes an impact on human health. For a week, users logged the start and end times of their meals, their mood, and energy and hunger levels. They next started an intermittent fasting regime for a minimum of two weeks. Those who adhered to the programme (approximately 37,500 people) recorded improvements in mood, energy, hunger and weight, and a dose response was observed: those who had longer fast periods or who followed the intermittent fasting regime for a longer duration recorded greater weight loss. Adherence was greater in older, physically active users. A caveat to this study is that it was not a randomised trial, as people self-enrolled in the programme. However, it was the first study of its kind to explore the impact of a nutrition intervention in a real-life free-living environment at this scale and is reflective of the current transition to app-based wellness approaches.

Zoe PREDICT studies
The Zoe PREDICT programme aims to unravel the complexity in individual responses to food and predict how dietary changes may affect an individual’s metabolic responses. It is underpinned by a two-week test phase utilising wearable technologies, app-based data collection and remote clinical testing. Participants use an app to monitor everything they eat and drink as well as their mood, energy and hunger. Stools are collected for microbiome profiling, blood is collected for lipids analysis and continuous glucose monitors are worn to measure glucose levels. Collected data is used to examine the variability between people and within individuals, what might explain these differences, and whether machine learning can be used to predict individual responses to a change in diet or an individual food. The PREDICT programme is ongoing in hundreds of thousands of individuals to further explore how personalised dietary and lifestyle advice impacts health outcomes, including the causal relationship between diet-microbiome-health interactions.

“There is no point in doing science for the sake of science. We need to think about how we go about effecting change.”
Dr Sarah Berry, King’s College London and Zoe Ltd

Looking ahead
Novel data collection tools and methodologies must be combined with traditional scientific approaches to expand or expedite aims; they are not replacements. It is also critical to think about how these large volumes of data can be used to generate advice and effect change at a population level.

7. Berry, S.E. et al. 2020. The current stage of the PREDICT programme aims to predict how individuals’ microbiomes may be shifted by a change in diet. Nature Medicine, 26, 964-973. https://doi.org/10.1038/s41591-020-0934-0
Is obesity a choice?

Professor Giles Yeo MBE, University of Cambridge, explored the relationship between genetics and body weight. He discussed how this knowledge can be used to improve personalised treatment for obesity and inform public health policy.

People gain weight by eating more calories than they burn. This is a well-understood function of physics. However, it is less clear what drives some people to eat more than others. Although discussions of obesity often focus on willpower and lifestyle decisions, obesity is not a choice. Genetic differences mean that some people are slightly hungrier all the time and therefore eat more than others. People who are obese may be fighting their biology.

The genetics of body weight is a study of how the brain influences feeding behaviour. The brain controls food intake in response to signals about long-term energy stores (eg volumes of fat in the body) and short-term energy reserves (eg levels of glucose in the gastrointestinal tract).

Leptin is a protein hormone that regulates long-term energy balance in the body. It circulates in the blood in proportion to the amount of fat in an organism (ie more fat, more leptin). Leptin molecules act on pro-opiomelanocortin (POMC) neurons in a brain region called the hypothalamus, which in turn signal to receptors to influence appetite. Genetic disruption at any level of this pathway may result in obesity.

Leptin deficiency
If an individual is unable to produce leptin, they are likely to be severely obese. The brain interprets the absence of leptin as an absence of fat stores, thus enacts signals to increase food intake. The use of leptin-replacement therapy can counteract this disruption and is associated with reduced likelihood of obesity. However, leptin is not a panacea. In an individual with a functional leptin pathway, the presence of additional leptin does not cause reduced food intake or weight loss.

POMC deletion
A disruption of the POMC gene can have a similar impact on weight and appetite. A study of Labrador retriever dogs found that a deletion of 14 base pairs in the POMC gene is associated with increased body weight and greater food motivation.

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Melanocortin 4 receptor (MC4R)

Mutations in the MC4R gene can also influence food intake and body weight. A recent study explored whether MC4R deficient individuals had altered preferences for fat and sucrose compared to obese and lean controls. In the fat test, participants were fed chicken korma with varying levels of fat mixed in. MC4R deficient individuals consumed a larger volume of the highest fat option compared to both lean and obese controls. In the sucrose test, participants were fed Eton Mess with varying levels of sugar. Individuals deficient in MC4R demonstrated a reduced preference for the high sugar variant compared to obese and lean controls, suggesting that this mutation is associated with a preference for fat over sugar.

Summary

For most people, weight is not significantly impacted by a single gene. Genetics brackets a set of possibilities for an individual, but luck and lifestyle decisions can result in different outcomes within these brackets.

“When I say I study the genetics of bodyweight, I become ‘the bad person’ because I am perceived as giving obese people an excuse. If I were studying the genetics of dementia, this wouldn’t be the case.”

Professor Giles Yeo MBE, University of Cambridge

Early life nutrition and the microbiome

Professor Lindsay Hall, University of Birmingham and Quadram Institute, explained the relationship between early life microbiome and health, and offered considerations for establishing causal contributions of the gut microbiota on health.

Each person harbours their own unique microbiota. The composition of the microbiota evolves throughout life - from birth to old age - and is the result of different external influences. Gut microbial communities play a critical role in human health. They regulate immune system development, infection resistance and food digestion, including the generation of energy and beneficial compounds, the extraction of nutrients, and the bioconversion of metabolites.

**The early-life developmental window**

The first 1000 days of life (conception to age two) represents a critical developmental window. It is defined by rapid maturation of metabolic, endocrine, neural and immune pathways, which strongly influence infant development. The gut microbiome develops concurrently with these pathways. In full-term newborn infants, gut microbial communities closely match the maternal skin, stool and/or vaginal microbiota, depending on delivery mode.

**Milk and microbes**

Breast milk contains human milk oligosaccharides which, counterintuitively, are not metabolism by the infant. Instead, they pass undigested into the colon where they are broken down by *Bifidobacterium*. Babies on a diet of human milk have higher concentrations of these bacteria in their gut microbiomes than formula-fed infants, which impacts their immune systems. Low levels of *Bifidobacterium* are associated with a higher risk of infection.

Recent work has explored whether supplementing the pre-term infant gut microbiota can be used to increase the abundance of *Bifidobacterium*. Analysis showed that the supplemented infants had a lower abundance of potential pathobionts and were able to metabolise human milk oligosaccharides.

**Microbiota-directed foods**

Microbiota-directed foods (MDFs) are a potential way to modulate the gut microbiome. They promote the growth of microbiota associated with positive gut health. In the context of early life nutrition, a recent study showed that delivering an MDF dietary supplement to undernourished children in Bangladesh changed the microbiota of the children and boosted their overall weight gain.
The future of early life microbiota and nutrition

Emerging areas of interest in the field of childhood nutrition include:

- **Precision nutrition for infants**: investigating how tailored dietary interventions during early life can optimise microbial colonisation, immune development, and long-term health outcomes.

- **Microbiome-targeted therapies**: examining novel interventions for infants (e.g., pro-, pre-, and postbiotics) and their potential to prevent or mitigate health issues.

- **Long-term health consequences**: exploring how nutritional choices during infancy may influence microbiome composition and risk of diseases later in life.

- **Ethical and societal implications**: addressing questions related to equitable access, commercial interests and the societal impact of shaping the microbiome in early childhood.

‘Most of our knowledge is based on data from babies from high income countries. What we’re seeing at the moment is only a small piece of the global health puzzle.’

Professor Lindsay Hall, University of Birmingham and Quadram Institute

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**Image:** from left to right, Dr Sarah Berry, Professor Giles Yeo, Professor Lindsay Hall and Professor Susan Lanham-New – Chair of Session 1: Nutrition-associated determinants of health.
Microbiome-derived bioactive metabolites: moving from association to causation in cardiometabolic health

Professor Marc-Emmanuel Dumas, Imperial College London, described how innovative approaches improve understanding of how microorganisms in the human gut can impact health.

The collection of microorganisms found in the human digestive tract, referred to as the gut microbiome, has been intensively studied for decades. Scientists have known for at least 50 years that these microorganisms produce compounds that may have beneficial, harmful or neutral impacts on human health. The gut microbiome is now recognised as a key driver of human metabolic health as it shapes the pathophysiology and common low-grade inflammatory components of obesity, type 2 diabetes and cardiometabolic diseases. However, questions remain about how these interactions work.

Research is now being done to identify the largely unknown chemical signals sent from the gut microbiota to the human host. These signals are often metabolites, which are compounds like amino acids, lipids and sugars that are produced or used when breaking down food, chemicals, or tissues.

**Choline metabolism**

Choline is an essential nutrient required for brain, liver and other bodily functions. Small amounts are produced in the liver, but diet is also an important source. People with low-choline diets are at an increased risk of developing non-alcoholic fatty liver disease, which can result in serious liver damage. However, high intake of choline-rich foods may also have harmful health impacts.

Microbiota in the human gut metabolise choline into trimethylamine (TMA), which can be absorbed by the intestine. In the liver, TMA is further metabolised into trimethylamine N-oxide (TMAO). High levels of TMAO in the blood are associated with increased risk of cardiovascular disease, and while diet may be partially responsible there are several other factors that may be at play.

A recent study examined the impacts of a variety of elements (diet, microbiome composition, age, sex, kidney function and presence of chronic disease) on TMAO concentrations in blood10. Machine learning and multivariate approaches showed that age and kidney function are the key variables impacting TMAO levels, with diet and microbiome composition having minor effects.

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**Hippurate**

Hippurate is an abundant metabolite associated with human-gut microbiota interactions. High levels of hippurate are typically associated with a diverse gut microbiome. Conversely, conditions such as non-alcoholic fatty liver disease and Crohn’s disease that are linked with low gut microbiome diversity are also associated with low levels of hippurate. A recent study investigated the links between hippurate levels, diet, microbiome composition and markers of metabolic health. By integrating metabolomics with metagenomics in a study of 271 middle-aged non-diabetic subjects, hippurate was identified as the metabolite most significantly associated with microbial gene richness, and data showed that hippurate is associated with health benefits in individuals consuming a diet rich in saturated fat.

**Looking ahead**

Further research is needed to better understand the diet-microbiome-metabolite-immune axis. The full breadth of metabolites impacting human health and the mechanisms by which they work are still not well understood. Obesity levels in the UK are rising and are associated with decreased microbiome diversity. This ‘invisible extinction’ of microorganisms could also mean we are losing as yet unknown but incredibly valuable metabolites.

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“There are about 20 thousand genes in the human genome. In comparison, there are about 20 million microbial genes in our gut microbiome. This reservoir of functionality and chemistry is like a mini pharmaceutical plant in our body.”

Professor Marc-Emmanuel Dumas, Imperial College London

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Plant bioactives and health

Dr Maria Traka, Quadram Institute, discussed the scientific importance of bioactives in fruit and vegetables for preventing disease.

Overwhelming epidemiological evidence suggests that increasing the intake of fruit and vegetables decreases our risk of increasing weight and developing cardiovascular disease, cancer and type 2 diabetes. Alarmingly, fewer than one in five children and fewer than one in three adults in the UK eat the recommended five portions of fruit and vegetables per day.

The dark matter of nutrition

While the vitamins and minerals found in fruits and vegetables are well known to be nutritionally important, plants also contain non-essential bioactives (the 'dark matter of nutrition') that impact health. Approximately 5000 bioactives have been identified, although estimates suggest there may be as many as 50,000 of these compounds across the plant kingdom. Only a few hundred have been studied in detail. Plant bioactives can be classed into six groups: alkaloids, terpenoids, carotenoids, phytosterols, sulphur-containing metabolites and polyphenols. There are also a host of subclasses which introduce further complexity.

‘We need to improve nutrition education in our medical curriculum. Our doctors need to understand the complexities of nutrition, and how it can contribute to reducing the disease burden.’

Dr Maria Traka, Quadram Institute

Bioactives have myriad effects on human health. Epigallocatechin gallate (a polyphenol found in green tea) reduces the viability of cancer cells\textsuperscript{12}. Anthocyanins in red wine have been shown to have antioxidant properties. Cocoa polyphenols have been shown to improve cardiovascular health. Additionally, our gut bacteria further transform these food bioactives to more complex compounds which are largely unknown, so it is important to concentrate research on these more biologically relevant forms.

Plant science for health
There is evidence that consumption of cruciferous vegetables is associated with a reduced risk of prostate cancer progression. This is largely attributed to the effects of bioactives, such as sulforaphane (derived from glucoraphanin in broccoli). To investigate the effectiveness of dietary interventions to reduce prostate cancer progression, 49 men on active prostate cancer surveillance were recruited to participate in a blinded intervention study for 12 months. Individuals received weekly 300 mL broccoli soup portions with standard or enhanced glucoraphanin levels. RNA sequencing was used to assess gene expression associated with oncogenic pathways in patient tissues obtained before and after the study. Results showed a dose-dependent relationship between consumption of glucoraphanin-rich soup and changes in gene expression consistent with a reduced risk of cancer progression.

Plant bioactives affect gut microbiota
The Dietary Bioactives and Microbiome Diversity (DIME) study is investigating whether levels of dietary bioactives impact gut microbiota diversity. Twenty healthy adults were placed on a high- or low-bioactive diet for two weeks. After a four-week ‘washout’, they were then placed on the alternate bioactive diet for two weeks. Participants used a smartphone app to record their meals. Continuous glucose monitors recorded blood glucose measurements and a wearable device was used to monitor activity and sleep levels. Stool and urine samples were analysed and showed that having diets full of bioactives increases gut bacteria diversity, which is an indication of a healthy gut.

What next?
Developing robust bioactive composition data will be vital for understanding what compounds are being consumed, in what amounts, and whether they act synergistically, additively, or opposingly. Future research must focus on whole foods rather than single compounds.

Deficiencies in micronutrients are associated with a suite of health issues including compromised immunity, anaemia and stunted growth in children. Recent global estimates suggest that over half of pre-school aged children and two thirds of women of reproductive age are deficient in at least one micronutrient\textsuperscript{14}. Increasing micronutrient levels in crops may help address this challenge.

**Biofortified crops**

HarvestPlus specialises in the biofortification of crops pre-harvest, specifically targeting wheat, rice and maize. These staple crops constitute 60% of global calorie consumption. Other biofortified crops developed by HarvestPlus and partners include pearl millet, beans, sweet potato and cassava. Conventional breeding techniques are used to increase the density of commonly deficient nutrients (iron, zinc, vitamin A) in high-yielding crop varieties. Genetic modification approaches are not used due to limited consumer and government acceptance, although regulations in some countries are beginning to change.

Randomised control trials are continuously conducted to determine the efficacy of biofortified crops in improving nutrition. While there is clear evidence that the nutrients in biofortified crops are bioavailable, and are present in quantities sufficient to make a difference and positively influence consumer health symptoms, it is too early to gather large-scale epidemiological evidence for impact assessment.

**Climate impacts**

Environmental factors such as declining soil health and extreme weather events affect crop nutritional value. For example, as global temperatures and CO\(_2\) levels rise, crops reach peak yield faster and the plant is unable to assimilate as much nutrition as it otherwise would. Biofortification may be needed just to maintain micronutrient levels in response to climate change impacts. To further ensure crops are climate-smart, HarvestPlus uses varieties that are bred for tolerance to heat, aridity, and drought.
Scaling up
There are now over 100 million people in farming families eating biofortified food, and an additional 400 million consumers buying it in markets. HarvestPlus aims for one billion to regularly consume biofortified foods by 2030. Enablers for scaling up the use of biofortification include:

- **Policy solutions**, such as setting micronutrient targets in agricultural policy.
- **Procurement and processing solutions**, such as public and private procurers requiring nutrient-enriched raw materials.
- **Consumer solutions**, such as the ability to purchase nutrient enriched foods at the same price.

India serves as an example of how a country can facilitate the scale-up of biofortified foods. They have incorporated nutrition benchmarks into their agricultural policy, and publicly endorse biofortified foods in their nutrition and food policies. Furthermore, by easing their labelling legislation to allow producers of staples to make health claims about lower levels of micronutrients, India is actively encouraging the regular consumption of nutrient-rich foods.

‘We have to biofortify staples just to keep up with climate change.’

Jenny Walton, Head of Commercialization and Scaling at HarvestPlus
Strategies and barriers to improving diet quality across the lifecourse

Professor Louise Dye, University of Leeds and University of Sheffield, highlighted the challenges associated with improving diet quality in low agency groups in the UK and strategies for overcoming these barriers. She also discussed the psychological impacts associated with food insecurity.

For the UK population, diet quality and nutritional intake are intrinsically linked with socioeconomic status. Fibre intake levels clearly reflect socio-economic gradients. Lower socioeconomic status groups have the lowest fibre intake, with consumption increasing as income rises. This is also true for consumption of key micronutrients. Despite public health campaigns and reformulation and innovation in the food industry, fibre consumption amongst UK adults remains well below the current recommendation of 30g per day across all groups.

A key driver of this disparity is the cost, both real and perceived, of healthy diets. Increased costs, longer preparation and cooking time, and a lack of cooking skills contribute to the avoidance or abandonment of high-fibre diets. Additionally, consumer perception is that starchy, high-fibre foods are linked with weight gain and/or digestive discomfort.

Targeted behaviour change interventions
Encouraging behaviour change through targeted policy interventions is often proposed as a means to reduce dietary-related health inequalities. An ‘intervention ladder’ can provide a framework for thinking about how different approaches can be used to encourage behaviour change15. Levels of interventions range from monitoring / doing nothing (bottom of the ladder) to eliminating all choices available to consumers via regulation (top of the ladder). Deciding on a proportionate intervention requires certain questions to be answered, such as whether the likely benefits justify the cost and disruption.

However, behaviour change interventions can have differential effects depending on socioeconomic status\textsuperscript{16}. Some dietary interventions may have smaller effects on low socioeconomic populations and thus may disproportionately benefit higher socioeconomic groups, leading to ‘intervention-generated inequalities’. In addition to limited economic resources, lower socioeconomic groups may have less social support, prioritise convenience over health and/or have limited health literacy. Strategies to improve nutritional intake and reduce health inequalities need to take into account the agency of the target population and the resources required to achieve a healthy diet, which have been significantly reduced by the cost-of-living crisis.

In terms of fibre consumption, interventions can be modified or tailored to the level of agency of the target group\textsuperscript{17}. A fibre information leaflet might be taken up by high agency groups, but the need to read the information, understand it, buy high-fibre foods, cook them and eat them are all points of attrition particularly for lower agency groups. Low-agency interventions could include incorporating high fibre foods into children’s breakfast clubs and school meals, or adding fibre to popular, low-cost foods.

**Food insecurity and well-being**

In 2022, more than 11 million people in the UK struggled to access diets which deliver adequate nutrition. Of these, 4 million are currently suffering from severe food insecurity. It is these people who are most impacted by shocks to the food system because they lack the financial and psychosocial or cognitive resilience to plan and organise food provision in financially efficient ways.

“We’ve talked about the amazing things we can do with diet - the missing link is getting people to do these things.”

Professor Louise Dye, University of Leeds and University of Sheffield


Diet for disease prevention and remission

Professor John C Mathers, Newcastle University, shared learnings from two innovative studies that could inform the design of more effective dietary interventions that can be delivered cost-effectively, and at scale, to improve health equity.

Improving eating habits is a critically important global public health challenge. In 2017, poor diet was responsible for 11 million deaths and 255 million disability-adjusted life years (a measure of disease burden, representing number of years lost to ill-health)\(^18\).

Despite ongoing efforts to improve diets using nutritional guidelines and generic advice, there has not been a substantial shift in eating habits. The disease burden associated with poor diet continues to grow.

“Even for someone who is 70 years old, life expectancy can be extended through improved diet – it is never too late to eat better”\(^19\).”

Professor John C. Mathers, Newcastle University

Food4Me study

The Food4Me study was designed to test the hypothesis that personalised nutritional advice would improve eating behaviour and health markers to a greater degree than standard dietary recommendations\(^20\). The study was internet-delivered. Participants from seven European countries were randomly assigned to one of four treatment groups:

1. Generic dietary advice that integrated guidelines from several European countries (control).
2. Individual diet based on current diet and lifestyle.
3. Individual diet based on diet, lifestyle and phenotype (anthropometry and blood biomarkers).
4. Individual diet based on diet, lifestyle, phenotype and genotype (five genetic markers).

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After six months, participants receiving personalised nutrition advice (categories ii – iv) consumed less red meat, salt and saturated fat and had bigger improvement in overall diet healthiness than those in the control group. However, the type of personalised advice (ie inclusion of phenotypic and genotypic data) did not matter. This study showed that personalised nutrition works and that internet-based intervention delivery is effective.

**DiRECT study**

An estimated 500 million people have diabetes, and numbers (particularly of type 2 diabetes) are growing. It is associated with significant health consequences and treatment can be very expensive.

The DiRECT study examined whether effective weight management achieved via dietary changes delivered in the primary care setting could produce sustained remission of type 2 diabetes\(^1\). Participants had been diagnosed with type 2 diabetes within the previous six years, had a body-mass index of 27–45 kg/m\(^2\) and were not receiving insulin. They were randomly assigned to either receive best-practice care according to NHS guidelines (control) or take part in a weight management programme (intervention). Those receiving the intervention had their antidiabetic and antihypertensive drugs withdrawn and underwent total diet replacement (liquid diet for 12 weeks) followed by food reintroduction based on the Eatwell Guide (weeks 12–18), then a weight-loss maintenance phase.

After one year, 4% of the control group were in remission compared to 46% of the intervention group. In both groups, likelihood of remission was linked to degree of weight loss. None of the participants who gained weight over the course of the study achieved remission, whereas 86% of participants who lost 15 kg or more were in remission. Type 2 diabetes does not have to be a life sentence. This study showed that sustained dietary change is an effective tool in the treatment of type 2 diabetes.

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Gut hormones as therapeutic targets for appetite suppression

Dr Tony Goldstone, Imperial College London, discussed the burgeoning use of gut hormone-based interventions to address obesity, over-eating and addictive behaviours.

Appetite is regulated by hormones, especially from the gut and fat tissue. These circulating hormones act on the brain to influence when and how much people eat. Hormone levels in the blood change in response to food intake. Appetitive gut hormones that reduce appetite increase in concentration as more calories are consumed. As hormone levels rise, subsequent signalling via the vagus nerve, the hypothalamus and brainstem inhibits further eating (satiety). Only one hormone is known to stimulate appetite: ghrelin levels from the stomach decrease with food consumption. Some of these hormones may also act to change the brain responses to food pictures and can potentially impact the appeal of and craving for food, especially high-energy foods.

Bariatric surgery changes appetitive hormone levels

In recent decades, obesity has been increasingly treated via bariatric surgery, which is generally considered the gold-standard amongst weight loss interventions. Gastric bypass surgery is associated with an average weight loss of 25% and reduces the risk of death, cardiovascular disease and several cancers. Following surgery, food is delivered to the intestine in a largely undigested form. This results in enhanced secretion of gut-based hormones regulating appetite, especially intestinal satiety hormones glucagon-like peptide 1 (GLP-1) and peptide YY (PYY).

Gut hormone analogue therapies

There is growing interest in the use of GLP-1 analogues alone and in combination with other gut hormone-based treatments as therapeutic options for weight loss in obesity. These mimic the functions of the natural hormone(s). Several of these drugs are already licensed for treatment of type 2 diabetes mellitus (T2DM) and obesity. However, more people with T2DM tend to lose less weight when using these drugs than people who do not have T2DM. The reason for this is unclear.
Second generation GLP-1 analogues (eg Liraglutide, requiring daily subcutaneous injections) produce mild to moderate weight loss. The third generation drug Semaglutide is given as weekly subcutaneous injections and achieves greater weight loss (10–17%). It is licensed for obesity and T2DM. If injections are stopped, patients regain weight. Orforglipon is a later generation GLP-1 analogue (currently unlicensed) that can be taken orally every day. It produces ~15% weight loss in people with obesity without T2DM. Notably, as this is a non-peptide drug, it will be cheaper and easier to manufacture.

We are now on the fourth generation of gut hormone interventions which utilise multiple targets in combination. Tirzepatide is a medication licensed to treat T2DM. It is both a GLP-1 analogue and a glucose-dependent insulino-tropic polypeptide (GIP) analogue and achieves an average weight loss of 16–23%. There are also several as yet unlicensed fourth generation drugs undergoing clinical trials, including dual GLP-1/amylan analogues, such as Semaglutide/Cagrilintide, and triple GLP-1/GIP/glucagon analogues, such as Retatudride.

Looking ahead
There is growing evidence that targeting the GLP-1 system may also be of benefit for attenuating addictive behaviours unrelated to food consumption. Studies suggest GLP-1 analogues may have potential as a treatment to encourage cessation of smoking and alcohol22,23,24.

There are also novel potential therapeutic targets. The recently discovered liver-foregut satiety hormone LEAP2 is an endogenous (naturally occurring) antagonist for the appetite stimulating stomach-derived hormone ghrelin25,26. Future research may explore therapies mimicking the action of LEAP2 to suppress food intake in obesity and potentially also treat addiction.

“GLP-1 analogues are a game-changer for patients with obesity.”
Dr Tony Goldstone, Imperial College London

References:
25. Mani B. et al. 2019. LEAP2 changes with body mass and food intake in humans and mice. The Journal of Clinical Investigation, 129(9), 3909-3923. https://doi.org/10.1172/JCI125332
Supporting the nation’s health: a retailer’s perspective

Julie Dean, Asda, described how supermarkets can use price, promotions, product range, marketing and merchandising to incentivise healthier and more sustainable choices. She focused on retailers’ responsibility to support lower socioeconomic communities in accessing healthier options.

Supermarkets are an integral part of the UK food system. Decisions made by food retailers influence the accessibility and affordability of nutritious foods at several levels, from farm to shelf. They can support farmers, food processors and manufacturers to use approaches that optimise nutritional profiles. They can use distribution, pricing and promotion to promote healthy options. Signposting, labelling and product placement can guide customer decision-making, and marketing can be used to educate and incentivise healthy choices.

The supermarket chain Asda has a disproportionate presence in the most deprived communities in the UK compared to other retailers. Many of its customers have a limited understanding of what constitutes a healthy and sustainable diet, thus Asda is undertaking a suite of activities to support healthier choices.

Strategic partnerships

In partnership with Nesta, Asda is undertaking a programme of work to validate, test, trial and evaluate their health strategy. They have conducted large-scale consumer research across the UK to gauge attitudes and barriers to healthy dietary choices. Of the ~4,000 customers surveyed, 95% want to be healthier, citing nutritional, physical, mental and lifestyle goals. Key barriers are motivation, cost and time. Needs, goals and barriers vary significantly according to socioeconomic status. This research led Asda to identify distinctive customer health segments that differ in their willingness and ability to cook from scratch or exercise regularly, amongst other health characteristics. Different interventions to support healthy eating are being designed to target each segment based on their requirements.
Asda is also working with the Leeds Institute for Data Analytics to explore data-driven solutions that support customers in managing budgets while making healthy food choices. They have held an ideathon and a hackathon to begin the process of testing and trialling interventions. One focus area has been on the impact of merchandising on meat-free purchasing in the meat aisle.

**Complexities of retail collaborations**
Partnerships with retailers can be challenging. Issues around data privacy and security, relationships with suppliers, timelines, regulatory considerations, and potential commercial risk complicate the context of the research. These are not necessarily barriers to collaboration, but understanding these complexities is key to success.

Although there are myriad complexities associated with retail collaborations, there are also significant benefits to all parties involved. These may include transfer of knowledge, access to specialised skills and resources, the practical application of academic research and generation of application-derived research questions, increased credibility and the building of extended networks.

“How can we support consumers to not only make healthier choices while shopping, but to prepare and cook it, want to eat it, enjoy it and buy it again?”

Julie Dean, Asda
Improving health through diet

A panel of experts shared their thoughts on how improved nutrition can improve health in the UK and globally. The session was chaired by Sarah Berry, King’s College London and Zoe Ltd.

Collaboration is necessary to achieve meaningful change from nutrition science. Linking efforts across industry, academia and the healthcare system is crucial for driving innovation and realising real-world impact from lab-based research.

A panel of speakers was convened to provide diverse perspectives on the future of human nutrition research. Panellists included Nusrat Kausar, Primary Care Dieticians, NHS and Nutribytes; Professor John O’Brien, Ulster University and Trends in Food Science and Technology; Professor Sumantra (Shumone) Ray, NNEdPro, University of Cambridge, and Ulster University; Professor Tim Spector, King’s College London, and Dr Emma Williams, Nutritionists in Industry.

Some of the key themes highlighted in the wide-ranging panel discussion are summarised below.

Rethinking science for the sake of science

- A huge range of tools are now available for research purposes (eg multi-omics, machine learning) and enormous volumes of data are being gathered. These data must be translated into interventions and tangible advice to improve the health of the UK population.
- Data from nutritional research can be used to inform policy. Policies relating to diet should be evidence-based and developed in consultation with a wide range of stakeholders including industry and academia as well as the populations they are targeting.
- Misinformation about food (eg on social media) is a major barrier to improving healthy diets. The nutritional science community in both industry and academia are the custodians of information reaching the consumer. They have a responsibility to share their knowledge. Science is trusted because it is social and collaborative.

“Children need to be given the skillset to deal with the complex food environment of the future.”

Professor John O’Brien, Ulster University and Trends in Food Science and Technology
Working with industry
- Industry has access to consumers. Working with industry (eg retailers) is an invaluable route to applying scientific research in a real-world environment and achieving meaningful impact.
- For results to be trusted, research collaborations with industry must be conducted transparently.
- There is a role within industry, from an educational perspective, to help consumers make informed decisions. For example, Waitrose has employed Healthy Eating Specialists trained to speak to customers about what constitutes a healthy, balanced diet.

Creating a sustainable food system
- Consumer demand for sustainable food products is growing, although an understanding of what makes a food item sustainable is limited.
- Efforts to enhance the sustainability of the food system must try to ensure there are no unintended consequences. For example, switching to more sustainable food production methods has the potential to drive up price or reduce supply, which could restrict access to a healthy diet for those in lower socioeconomic groups.
- Incentivising the consumption of plant-based and minimally processed foods, or possibly taxing environmentally damaging or unhealthy ultra-processed foods, could support both a more sustainable food system and improved health.

Education is key
- Education about healthy eating is particularly effective when it is tailored to the person. However, personalised nutrition advice is not just about a person’s biology. It also involves looking at their family, the generation to which they belong, their resources, and their community.
- It is important to educate consumers of all ages as well as the businesses within the food supply chain on what constitutes a healthy and sustainable food product and how nutrition can be optimised.
- Formal education at a range of levels (in schools, in universities) should include a focus on both emerging areas of nutritional research (eg microbiome science) and technical skills including food preparation.
- The discussion around ultra-processed foods currently lacks precision and clarity in terms of categorisation. Better classification systems are needed for food in general, not just for ultra-processed foods.

“In healthcare settings, personalised nutritional advice should look at the whole person – their cultural heritage, family history and socioeconomic circumstances. A holistic approach that accounts for these contextual factors is essential.”
Nusrat Kausar, Primary Care Dieticians, NHS and Nutribytes

“I think the future is going to be in personalised nutrition and making microbiome science into a mainstream study. It needs to be seen as a core part of nutrition science.”
Professor Tim Spector, King’s College London

“Nutrition science is a very lateral discipline, going from molecules to mankind. Additionally, the global challenges that we face in food security need concerted efforts without borders to enable nutrition science to better serve society”
Professor Sumantra (Shumone) Ray, NNEdPro Global Institute; Fitzwilliam College at the University of Cambridge; Ulster University

“It’s time to liberate science from the lab and ignite real-world impact. This entails a dynamic conversation with all players, including the food industry, to turn theory into powerful, practical solutions.”
Dr Emma Williams, Nutritionists in Industry.
At a crossroads: Hacking the food system or hacking our bodies?

Henry Dimbleby MBE, LEON and the Sustainable Restaurant Association, argued that the UK is at a crossroads in the future of our health, and advocated for better cooking education and more government regulation of unhealthy food. Key themes from his talk have been summarised below.

Predictions made by scientists in the mid-20th century regarding the future of the planet painted a bleak picture. For thousands of years, it was standard practice to use more land as more food was needed. However, in 1945 the world’s human population was projected to rise from 2.8 billion to 8 billion over the next 50 years, and viable agricultural land was becoming increasingly scarce. As a result, it was estimated that the next century would be rife with wars over resources, starvation and mass migration.

‘Passing a law is often necessary, but it is not sufficient to create change. We need people to come in behind those laws who care, to implement change at a local level.’

Henry Dimbleby MBE, LEON and the Sustainable Restaurant Association

The Green Revolution, pioneered by the agronomist Norman Borlaug, transformed the relationship between food production and land use. By developing crops with desirable qualities (eg high yield, disease-resistance, structural strength) and increasing the use of chemical fertilisers, pesticides and irrigation, the rate of food production for the same area of land increased dramatically. However, the increased intensity of global agriculture is driving a wide range of other issues including biodiversity collapse, freshwater pollution, water shortages, soil degradation, and deforestation.

The food system and health

In addition to its environmental impacts, the food system also influences human health. The world now produces double the number of calories per person compared to 1945. Correspondingly, the number of people in the UK who are overweight or obese has risen dramatically. Over-consumption of food is now the greatest cause of avoidable ill health, outweighing smoking (Figure 1). The risk of diet-related ill-health increases in poorer areas.
To solve this system-wide problem, the National Food Strategy: Part one (2020) highlighted the need to examine feedback loops and understand what is malfunctioning within the food system. One of these feedback loops is the junk food cycle.

Humans have an evolutionarily developed appetite for calorie-dense foods. Modern calorie-dense foods are highly processed, high in fat, salt and sugar (HFSS) and often suppress satiety responses. As such, consumption of such foods is higher than that of non-processed foods. Increased demand leads to higher investment of time and money within food companies in the development and production of processed foods. This in turn increases consumption in a vicious cycle.

FIGURE 1
Proportion of years lost to avoidable ill-health and death by cause.


At a crossroads
There are two potential futures ahead. One involves continuing down the current path and exacerbating the junk food cycle. In this future, it is possible that more than 40% of the UK population will be using weight loss drugs permanently. Such drugs are extremely useful to some patients, but do not address the root of the food problem.

The other future involves changing the food landscape and escaping the cycle. Often-cited solutions for this are exercise and education on what is good to eat. However, while exercise is excellent for health and wellbeing, it may not obviously or quickly result in weight-loss. Many people who exercise in an effort to reduce their weight become discouraged. Data shows that around 90% of the UK population know what a healthy and balanced diet looks like and know they should be eating less processed food. Education on what to eat is not the problem.

There are three solutions that can potentially mitigate the problems the current food system has propagated:

1. **Cooking skills:** Improving the provision of food technology education in schools is vital. Efforts to enable school kitchen teams to prepare delicious and nutritious food for children, as well as help them learn how to cook for themselves, must be supported.

2. **Government intervention:** Mandatory taxation encourages food companies to reformulate their products and reduces the consumption of such products. For example, three years after the Soft Drinks Industry Levy was introduced, the average sugar content of soft drinks had decreased by 29%.

3. **Local initiatives:** Individuals have the power to change the food culture within their communities and social groups. Engaging communities in the conversation can help us escape the junk food cycle.

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