

# WHITEBOOK

4th Annual Forum

## Better Foods for Better Health CHALLENGES & SOLUTIONS

SEPTEMBER 18th to 20th 2013

Fondation Mérieux Conference Centre 'Les Pensières'  
Veyrier-du-Lac - France

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# WHITEBOOK

## PREFACE

Improving nutrition for the burgeoning global population is one of today's the major public challenges. Over the past four years, 'Better Foods for Better Health,' our international symposium dedicated to pursuing advances in nutrition, has brought together leading scientists, NGOs, policy stakeholders and key opinion leaders to exchange ideas and drive progress for this global cause.

Fondation Mérieux, the inaugurator of the Symposium, with the support of Mérieux NutriSciences, has sought new views on the fundamental link between health and nutrition from scientific, business and regulatory perspectives.

With health matters occupying a pressing dimension in a global agenda, the Symposium is dedicated to sharing the latest scientific developments in nutrition in both developed and developing countries. Valuable insight from industry is provided by esteemed moderators, placing the consumer at the centre of the dialogue between scientific evidence and public policy makers.

This year's symposium, '**Health Economic & Prevention for Advanced Nutrition**', addressed the importance of moving forward with new solutions and nutritional strategies for prevention and economic impact in developed and developing communities. Designed to support the need for a broader regulatory framework at both a global and regional level, the mission of the Symposium is to both foster and anticipate innovation for responsible and effective nutrition.



Our increased understanding of obesogenic factors, whether genetic, lifestyle, environment, socioeconomic status or education has empowered our ability to influence individuals, communities, food producers, regulators and policy-makers.

Increasing dialogue between the scientific community, regulatory, nutrition and industry stakeholders is a top priority. This White Book provides a summary and recommendations of the stellar cast of participants who took part in the Symposium, confirming their commitment to promoting 'Better Foods for Better Health.' We are proud to be a part of to all-important discussion.

Alexandre Mérieux  
Vice President  
Fondation Mérieux

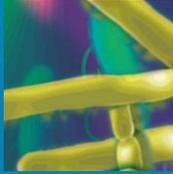
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# EXECUTIVESUMMARY

4th Annual Forum



## Better Foods for Better Health

CHALLENGES & SOLUTIONS

SEPTEMBER 18th to 20th 2013



Experts from academia, international organizations, NGOs, regulatory authorities and industry gathered at Les Pensières, the Fondation Mérieux Conference Centre, for the fourth annual 'Better Foods for Better Health' Symposium. Organized by the Fondation with the support of Mérieux NutriSciences, the annual meeting was held September 18-20th, 2013.

The prevailing theme of the meeting '**Health economic & Prevention for Advanced Nutrition**' discussed how the latest developments in nutrition science could be translated into recommendations to address:

- Effective prevention *versus* intervention;
- Education centered around nutritional labelling;
- Healthy behaviour and health economic impact in developed and developing communities.
- Due to an ongoing obesity epidemic, rethinking how we approach this issue is long overdue. Almost collectively, experts agree that a shift from intervention to health promotion and disease prevention is the desired course. Understanding the science behind obesity is essential, requiring both research and concrete actions, such as changes in physical environments, communication strategies, and regulation and management of at-risk populations, to develop meaningful approaches. The most promising approaches for obesity prevention are population-based and multilevel, dependent largely on environmental and policy changes, necessitating participation from actors in multiple sectors.

Continued research covering biomarkers, probiotics, and the intestinal microbiome are must items on our agenda, as well as the development of communication technologies which directly affect consumer behaviour. These elements are essential in how we regulate these new technologies and provide advice to policy-makers.

The over arching goal is to move away from individual elements and focus on how they interact with each other. Currently available technologies are useful in predicting a predisposition to certain illnesses. Treating all patients using their own personal "omic" profiling should be a scientific aim within the next decade. Extending this technique to millions and billions of individuals, however, would certainly require broad stakeholder involvement.

# EXECUTIVE SUMMARY

The fourth 'Better Foods for Better Health' Symposium produced a number of messages and key action items:

- The first, and perhaps most pressing, is to shift the balance of treatment and prevention in health care. Our understanding of obesogenic factors, whether genetic, lifestyle, environment, socioeconomic status or education, has improved significantly. This can be used to influence individuals, communities, food producers, regulators and policy-makers.
- A multi-stakeholder investment is essential. Through community-based projects or broader investments in public-private partnerships, it is clear that a complex multifactorial problem such as obesity and its associated co-morbidities require a large investment in funds and energy.
- With increased availability of innovative technologies and treatments, regulatory agencies will need to adapt in order to accommodate them. Whether it be in terms of treatment with the use of faecal microbiome transplantation (FMT), biomarkers (to determine the impact of food, FMT, probiotics or antibiotics), techniques for evaluating food safety, or mobile health apps. Regulators are now facing a different realm to the traditional one of medicines or food regulation.
- Advances in nutrition and product development are blurring the line between foods and medicines. Nutraceuticals, functional foods and other health food categories, are defined as a food or part of a food that provides medical or health benefits. This includes the prevention and/or treatment of disease, falling at the very intersection of the food and medicine spectra.
- The emergence of the intestinal microbiome as an organ with an enormous potential to exploit via novel technologies, such as high throughput sequencing, has allowed old concepts to be revisited and better understood. More than ever before, methods and technological approaches need to be standardised to better deal with population-based studies *versus* individual studies.
- Personalised solutions founded on an understanding of the individual's microbiome will require further dialogue to examine how this fits into the concepts of nutrition, exercise and regulation.

- The importance of involving of the most important stakeholders, the individual concerned by the effects on their health and environment, along with the fundamental role of empowerment, involvement and education in longer term changes cannot be overstated.

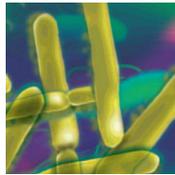


Going forward, all of these concepts are ideally suited to public-private partnerships, which can assist when recruiting large cohorts of normal individuals or patients. Additionally, it will aid in the important and often limiting issue of obtaining funding for such research. It could be envisaged that the extensive group of stakeholders involved in these meetings could put together a proposal for a European or IMI funded project.

With the shifting landscape, future Better Food for Better Health symposia are likely to need greater contributions from regulatory agencies, other institutions and organisations with a view to discussing and directly impacting decision-making processes.

# WHITTEBOOK

4th Annual Forum



## Better Foods for Better Health

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How do we define health if not by disease? Is it not only by the loss or lack of a healthy state that we understand and appreciate what it is? How can individuals measure when they are in good health and how can a government measure when its citizens are practicing healthy behaviour?

With an undeniable obesity epidemic, it is evident that the time has come to rethink the way we approach this problem as well as who is responsible for addressing the issues and when. It is clear that an interdisciplinary approach is crucial, involving all stakeholders from the individual, families, educators, employers, scientists, the food industry, regulators through to policy-makers.

In the fourth edition of the Better Foods for Better Health series, these stakeholders came together to discuss the issues surrounding effective prevention *versus* intervention, education around nutritional labelling and



healthy behaviour. Research was also high on the agenda with biomarkers, probiotics, and the intestinal microbiome being discussed, as well as the development of communication technologies, which directly affect consumer behaviour. These elements all contribute to the overarching issue of how to regulate these new technologies and provide advice to policy-makers.

## **Rethinking old concepts: are BMI and weight loss appropriate health endpoints?**



As research in this domain advances, the picture emerging is one of increasing layers of complexity. Traditional ideas of managing obesity as simply an excess of weight that needs to be lost and the use of an anthropometric index of total adiposity, the body mass index (BMI), as a measure of obesity an associated health risks such as heart disease need to be reconsidered. In the United States, research shows that while BMI has increased for all age groups since 1900 a corresponding increase in calories has not been observed.

Correlating obesity with food intake and managing it via weight loss with its associated significant costs from surgery and lost productivity is clearly no longer adapted to the enormity and reality of this problem. Studies have found that patients considered extremely obese based on the BMI do not always present with major metabolic abnormalities, while there are mildly overweight individuals with a host of diabetogenic and atherogenic metabolic abnormalities. Today, the hip-to-waist ratio as an index of abdominal fat distribution is considered predictive of risk for heart disease and type 2 diabetes. Irrespective of how it is measured, it is clear that obesity and its associated health issues have increased dramatically worldwide.



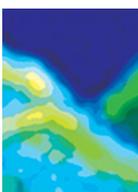
Historically, the scientific community has been slow to accept change in this domain; the first evidence that obesity could be measured in terms of distribution of body fat was reported 30 years before it became accepted theory. Rethinking such approaches is critical to understanding the relationship between food and health and using this to change the current status. If overeating alone cannot account for the increase in obesity; the reasons must be multifactorial, rendering it a 'wicked' problem. Like other wicked problems, it is complex and caused by biological, social, genetic and behavioural and environmental interactions.



## Moving from intervention towards prevention

How can rethinking help? Innovation is needed to help shift the current status quo. Understanding the science behind obesity is essential however prevention extends far beyond scientific studies and requires a multi-faceted, multi-stakeholder approach. Effective prevention requires both research and concrete actions, such as changes in physical environments, communication strategies, regulation and management of at-risk populations. Medical and social evidence is also needed to ensure sustainability.

Today, government health budgets are dedicated almost exclusively to treatment, with an average of only 3% allocated to prevention compared with 90% spent on treatment of non-communicable diseases. This imbalance is currently changing and the prediction is that up to 9% of the budget will be allocated to prevention by 2030.



## Tackling obesity from local to global

Until prevention becomes part of the standard of care in health care, global community-based projects involving private funding are attempting to fill the gaps and unravel some of the underlying issues contributing to obesity. EPODE (Together Let's Prevent Childhood Obesity) is an example of an international programme for the prevention of childhood obesity, initiated in France and currently being rolled out in 22 countries involving more than 4 million people worldwide.

The programme was developed in collaboration with major health actors including the World Health Organisation, and the European Commission (EC), ensuring a sound methodological design. The programme is built on four pillars: i) a strong political commitment at local to national levels, ii) sound evidence-based and continuous evaluation, iii) support services including social marketing, communication, media,



organisation expertise, and an advisory board to build a system network, and iv) resources, notably public-private partnership (PPP) schemes.

Underlying these pillars, and fundamental to its success, is the implication of important resources such as the end-users. The programme revolves around a steering community, which involves local stakeholders; businesses, media, schools, health and infant professionals, associations, extra-curricular organisations, etc. The steering committee works with local project managers and town mayors, who in turn interact with a centralised EPODE group. An independent scientific committee, institutional support and private partners feed directly into the EPODE organisation.

Back-to-basics approaches such as access to cooking classes, sports, playgrounds, vegetable gardens, nursing home visits, etc. establish solid health habits and skills in a fun environment. Results from two pilot studies showed that EPODE interventions have significantly reduced obesity and overweight.

Continuous evaluation is performed by taskforces using a common framework with emphasis on dissemination of results and feedback. Improvements such as workshops for programme coordinators and exchanges of best practices are implemented. Feedback also raises awareness of the importance of early intervention and multi-stakeholder involvement and is a powerful advocacy tool as regular meetings are held with key stakeholders such as politicians, scientists and policy-makers.

EPODE funding comes in part from industry partners, an aspect open for criticism; however programme coordinators acknowledge that this is also an important feature of the project. All stakeholders need to be involved and take their part of responsibility in community-based programmes, which offer a cost-effective preventative position enabling local political feedback.

## **Early intervention: a bottom-up approach for addressing the 'sedentary' problem**

Mortality statistics show a tip in the balance, with illnesses associated with inactivity now accounting for more deaths than those associated with smoking. The French ICAPS (Intervention Centred on Adolescent Physical Activity and Sedentary behaviour) programme implemented over a 4-year period encourages physical exercise in adolescents. A multi-partnership approach was used, simultaneously implicating the adolescents themselves imparting them with knowledge, motivation and attitude, while concurrently providing social support from parents, teachers and other educators. A reduction in excessive weight gain was reported in participating students relative to controls during the study. Even



more encouraging was that this reduction was maintained more than two years after the programme end. The impact was greater in less wealthy students, suggesting a means of effectively targeting poorer socioeconomic groups. Furthermore, participating students continued to fare better than non-participating control students in terms of maintaining changed habits, spending more time on physical activity in both leisure and daily habits, and less time watching television.

Other programmes are being implemented to reverse the trend towards inactivity, such as the European Joint Programming Initiative (JPI) which aims to improve diet, activity and associated diseases over the next 30 years. The DEDIPAC programme is designed to improve and harmonise behavioural measures, determinants of dietary behaviour, physical activity and sedentary behaviour, and evaluate and benchmark public health and policy interventions.



## **The 1000-day window: confronting obesity early on**

With management strategies for obesity clearly falling short of resolving the problem, tackling this from a different perspective may offer alternative solutions. The importance of a preventative approach is key, but 'how early is early enough'? The ICAPS programme shows that working with teenagers has long-term effects. There is now strong support for the importance of the '1000-day window' (between a woman's pregnancy and her child's 2<sup>nd</sup> birthday); a critical time impacting a child's physical and cognitive growth.

The value of an early intervention was demonstrated by a European birth cohort study reporting that longer duration of breast feeding correlated with higher vegetable intake during early childhood. This demonstrates that early feeding habits may be able to influence future food intake, possibly by a greater plasticity in taste earlier in life encouraging greater acceptance of taste variation.

A poor start to life is associated with an increased risk of cardiovascular disease, obesity, and type 2 diabetes. The DOHaD (Developmental Origin of Health and Disease) principle is that during development (up to and including adolescence), the environment induces developmental changes that have a long-term impact on later health and disease risk. Some of these changes are supported by epigenetic alterations that have a lasting effect and may impact on the risk of the individual to develop disease.

Throughout an individual's life, he or she will respond to their changing environment, which will impact by increasing their allostatic load. This is dependent



on the individual's functional capital, and the disease threshold will be reached at different ages depending on the particular experience of the individual. Frequently this is the point where treatment is being applied, which is often too late, as the 'organism' is worn out.

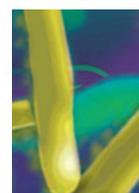
Birth cohorts are an excellent method of evaluating the impact of childhood on adulthood. The ELFE programme (the French Longitudinal Study from Childhood), is part of a research platform using a multidisciplinary approach designed to understand how the early environment affects adult health in terms of family, socioeconomic, geographic, physical and chemical factors. This recent initiative involves a representative sample of children (one in fifty) born in France in 2011. Data collection is both active, via questionnaires and biological sampling, and passive from national databases and health insurance data. Data will be used i) to evaluate infant feeding practices to develop recommendations for breastfeeding, ii) to identify risks associated with exposure of pregnant mothers and the foetus to contaminants and those related to work environmental factors, and iii) to inform professionals and drive policy and research priorities.

The value of birth cohorts lies in the provision of longitudinal data collected from birth allowing us to address health and social sciences issues by evaluating the impact of changes in environment, pollutants etc. These studies provide information on evolving social sciences, country-specific data for policy building, and also enable cross-country comparisons. As studies with large numbers of participants, birth cohorts also offer a data source for rare conditions at a country, regional and international level. Historically, strong contributions have been made by the United Kingdom and Scandinavia, while more recently studies have been initiated in the American continent and Asia.

## **Linking maternal health, epigenetics and childhood outcomes**

Further support emphasising the importance of maternal nutrition during pregnancy comes from two Chinese examples of early intervention to reduce gestational metabolic risks in pregnant women and improve offspring outcomes.

Changing obesity statistics in China are startling, overweight and obesity rates have increased by 31% relative to 1991, while childhood obesity rates in major Chinese cities are now approaching 20%. Obesity-related hypertension, diabetes, stroke and heart disease account for 25% of national medical costs. In addition to the acknowledged long-term health impacts, obesity and hyperglycaemia during pregnancy are associated with increased risk of complications for the health of both



the mother (obstetric) and the baby (macrosomia, 'big baby syndrome') as reported in the HAPO (Hyperglycaemia and Adverse Pregnancy Outcomes) study.

Evidence of these trends is reported in two large city-based cohorts. Analysis of the KunShan cohort of over 25,000 pregnant women included between 2006 and 2010 gave an 18% rate of underweight mothers while nearly 10% were overweight or obese. Gestational diabetes was reported in 18% of the population, including 1.5% with clinical diabetes, and macrosomia in approximately 9%. During pregnancy, nearly 60% of obese and overweight mothers incurred excessive weight gain, compared to less than 30% of underweight women.

In the Shanghai IPMCH welfare Institute cohort, data were collected for over 10,000 pregnant women registered between 2010 and 2012, and a dietary counselling programme based on the individual and on national guidelines was implemented during pregnancy. Gestational diabetes was reported in over 800 (16%) women and macrosomia in 6.2% of neonates. The value of dietary counselling was shown with reductions in macrosomia (by 9%) and gestational hypertension (by 21%) for women attending at least two dietary visits compared to those not attending at all. In addition, underweight women were more likely to gain insufficient weight during pregnancy, while overweight women were more likely to gain too much, suggesting the need to address socioeconomic aspects.

Reductions in obesity rates are not however reflected in corresponding reductions in gestational diabetes. As previously mentioned, control of total food intake alone is inadequate for managing obesity and its consequences. The quality of what is eaten has an important role to play. Studies evaluating epigenetic mechanisms such as that planned in China on the impact of a low glycaemic diet in overweight pregnant women should go some way towards answering this question.



## Evolution and transgenerational effects

Thousands of years ago, ectopic fat was a survival advantage, this positive energy balance functioning as a reserve for future energy needs. Anecdotal evidence from historical data of weight increase in Denmark (between 1920 and 1970) is not explained by traditional thinking. Explanations require thinking outside the box.

While transgenerational effects are recognised as important in under-nutrition, application of this concept to over-nutrition and obesity is often overlooked. The impact of stress (environmental, emotional, nutritional, etc.) during pregnancy or even before conception allows room for great individual variation, between the anticipation of future needs and the limits of capacity for storage, all of which is likely to be influenced by genes and environment.

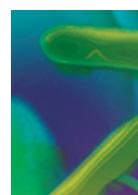


Thus, an obese individual can send a signal to their gametes which is translated epigenetically to indicate that fat should be stored, but when this individual loses weight then the message is one of stress. An obese individual who loses weight is thus a combination of both signals that will be transmitted to subsequent offspring. These epigenetic memories of past parental (mother and father) obesity, weight loss, stress, low social class, adversity or natural disasters are like time bombs, remaining silent for a period of time and being expressed differently depending on environment.

## Factoring genetics into obesity

Genetics undoubtedly plays a role in the susceptibility of an individual to gain weight and even to develop obesity. One such example is GPR120, a lipid receptor in the gut, adipose tissue and lung, playing an important role in various physiological homeostasis mechanisms such as adipogenesis, regulation of appetite and food preferences. A missense mutation in this gene inhibiting signalling is associated with a 60% increased risk of obesity. Mutation studies in a mouse model fed a high-fat diet confirmed this with loss-of-function animals having significantly higher body weight than controls, along with worsening of metabolic syndrome, and increased visceral adiposity and inflammation, while in humans, a particular missense variant is associated with obesity. These studies show that use of dietary fat and the control of the organism's energy balance can be affected by a single gene, and mutations could thus impact the consequences of a high fat diet.

In addition to genetic mutations, recent evidence suggests that gene copy number also influences obesity. A comparison of copy numbers of the salivary amylase gene (AMY1) in siblings discordant for obesity with different copy numbers. Copy number can vary between 2 and 19 in humans; the higher the copy number, the higher the expression and the lower the BMI and adiposity. High AMY1 copy numbers have been observed in populations on high-starch diets compared to those with low-starch intake, while low  $\alpha$ -amylase levels are associated with alterations in the metabolism of lipids, bile acids, phenylalanine, and the TCA cycle. Thus genetically-determined AMY1 levels may provide a biomarker for insulin sensitivity, pre-diabetes and changes in the microbiome that may be associated with obesity and type-2 diabetes.





## Multi-biomarkers: exploiting big data

Technological advances are creating an exponential increase in data generation from multiple sources such as electronic records from general practitioners and clinicians, home-based detectors, smart phone applications as well as the massive data influx generated from the 'omic' technologies. How can these data be exploited in the health domain?

Nutrient intake for an individual is dependent upon multiple socio-economic, cultural and biological factors. Metabonomic approaches can be used to measure the metabolic endpoints when assessing nutrient requirement and metabolism. Evidence that metabolic phenotypes differ between healthy and diseased individuals is increasing the feasibility of using biomarkers to signal risk and move these at-risk individuals towards a healthy state with targeted nutrition.

The trend today in nutrition follows the example set in cancer research, with the chase underway to identify multiple marker profiles that can offer increased accuracy and significantly stronger predictive values over single markers, overcoming risks associated with false positive and negatives and inadequate sensitivity. However, the multi-marker approach brings with it a new set of challenges and the 'pharma' model may not be optimally adapted for nutrition. Different interpretations of the same methodology (from sample collection to reagents used) and multiple analysers with different computational methods can give different metabolomic signatures each with equivalent statistical significance. Increasing the number of parameters to analyse runs the risk of overfitting data and hiding the true underlying relationship by the complexity of the model. Looking at relationships between markers will help to weed out those contributing too much 'noise', and select markers and statistical analyses to evaluate them on the basis of biological and clinical relevance.

There are a number of problems with current biochemical methods, including cost and time involved. There is also a lack of standardised protocols and experience in capturing nutrient patterns is limited as there is a tendency to study them in isolation. Technology-driven approaches are needed to build platforms, measure biomarkers, nutrients and metabolic products using new generation analytic methods, and generate multifactorial metabolic profiles. Cross-linking this information with nutritional intake can guide nutritional modifications to achieve the desired metabonomic profile. Templates of complementary technologies are being developed for use in critical medical care situations with a view to future applications in high-throughput diagnostic platforms in hospitals and clinical institutions. Industry is investing in these new techniques that can be applied in molecular nutrition with a key role in disease prevention, particularly in multifactorial diseases.



## The microbiome as a source of nutritional health biomarkers



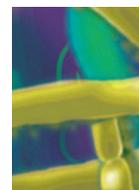
The microbiome is a dynamic organ with 100-fold more genes than the human genome and has huge potential for 'biomarker' exploitation. It varies between body regions (gut versus the vagina, for example), countries, populations, and over time - both from an evolutionary perspective and within an individual. Changes in the microbiome are introduced from many sources, such as alterations to our diet, different methods of food processing, and antibiotic use. Healthy and diseased states are reflected in different microbiome profiles.

A 'healthy' microbiome is established early in life and with the exception of antibiotics, is generally resistant to short-term perturbations. A more enriched gut microbiome is associated with less adiposity, insulin resistance, dyslipidaemia and inflammation. With only a few bacterial species necessary to distinguish between individuals with high and low bacterial richness which in turn correlates with lean and obese individuals respectively as well as the likelihood of gaining weight over time, the microbiome offers an 'obesity' biomarker.

Food can thus be considered as an active partner of the microbiome, a hormone able to influence it via activation of signalling pathway receptors; *Enterobacteriaceae* are known to be enriched in individuals with a high fat/high sugar diet. The challenge will be to establish system networks between the individual and their gut bacteria so as to exert nutritional pressure on the gut ecology. Likewise, the dynamic adaptable nature of this organ can cloud interpretation; food interacts with the gut microbiome and circulating products feedback on the microbiome.

One way of exploiting the gut microbiome is to look for features associated with 'health'. Using the gut microbiome of centenarians as a model for healthy aging reveals that around the age of 80 to 90 years in these individuals, the gut microbiome composition undergoes a change to one reflecting a profile of individuals with metabolic features associated with living longer. Moreover a healthy aging epigenetic effect also seems likely with the gene ELOVL2 encoding omega-3 fatty acid synthesis identified to be associated with long life.

## Altering the microbiome with antibiotics



While the main positive effect of using antibiotics is the elimination of specific pathogens, on the negative side antibiotics have an associated risk of major bacterial imbalance (or dysbiosis), which facilitates colonisation by pathogens such as



*Clostridium difficile* (*C. difficile*), *Salmonella enterica*, and *Shigellae*, activates defence mechanisms and selects for bacterial resistance. However as the gut ecosystem is quite resilient, the microbiome generally returns to a balanced state after the homeostasis of the intestinal ecosystem has been disturbed, although this can take up to a year for normal colonisation to return when drug-resistant strains develop.

Evidence is also accumulating that the influence of antibiotic-induced dysbiosis on the microbiome has a role to play in other disease conditions, such as obesity. In an experiment using mice fed a high-fat diet, when concomitant broad-spectrum antibiotics were administered, mice gained less fat mass, and had less inflammation and glucose intolerance compared to those without antibiotics.

In light of the conundrum that administration of low-dose antibiotics promotes weight gain in farm animals, it is clear that much remains to be understood and caution needs to be exercised, as possible side effects, interactions and consequences are unknown. Modulation of the microbiome to change the balance in obese individuals merits further exploration, along with the reduction of symptoms in other pathologies such as inflammatory bowel disease, autism, etc. by immunomodulation via the microbiome.

A number of options exist for counteracting microbiome changes brought on by antibiotics or for intentionally modulating the microbiome in disease states, the most advanced of which are the use of probiotics and faecal microbiome transplantation (FMT).



## Introducing probiotics to the microbiome

What promise do probiotics offer for modulating the microbiome? Probiotics are live bacteria that confer health benefits. Although frequently used for treating diarrhoea, the lack of good harmonised trial data means that regulation is difficult and physicians rarely prescribe them to their patients.

Scientifically solid evidence on their usefulness in the treatment of various conditions is patchy. The complexity of this situation is increased by the absence of a consensus on the methodology to assess their efficacy and the safety. Testing a probiotic is more difficult than a standard drug as their viability in the gut is independent of their purity. In contrast to chemical agents, a library of probiotics cannot be screened, they are intended to interact with other gut bacteria and the host response is intended to vary according to individual microbiome. Further, probiotic efficacy is enterotype-specific with no consensus on enterotyping methods, the definition of a normal *versus* a pathogenic enterotype, nor on the predictive value of a particular enterotype for probiotic response.



Assimilating and analysing studies using probiotics is challenging due to variations in study quality, diverse exclusion criteria and the generalisation of findings. To generate evidence-based data that would be acceptable to regulators, clinical trials with probiotics should ideally use only one genotyped quantified strain that has a good shelf life, which can be used in developing countries and is antibiotic-sensitive. The target population should be all-inclusive to optimise the chance of applying the outcome to other groups. To date, probiotics have shown minimal to low toxicity and side effects, and efficacy endpoints should be both early and late nutritional endpoints.

There is much which is not yet well understood about the microbiome; what triggers changes in the microbiome, how do they change over time and what pathways are involved? What are the mechanisms, direct and indirect, behind reported effects and how do they differ between body sites and different influences? Immunomodulation clearly plays a role in establishing the microbiome (both vaginal and gut), but other factors, such as competitive exclusion, are implicated. How do stable and unstable microbiomes differ? Functional rather than compositional differences in the microbiome appear important, with different bacterial profiles giving the same functional phenotype. Research is critical to further exploit this system and obtain convincing clinical evidence to implement probiotic use to treat health conditions.

## Using *C. difficile* to fight infection

*C. difficile* infections of the gut mainly result from overuse of antibiotics and cause symptoms ranging from diarrhoea to life-threatening inflammation of the colon. Over the last two decades, the incidence of *C. difficile* infection has quadrupled along with associated morbidity. Mortality due to *C. difficile* in the US is estimated at over 20,000 deaths annually, although in reality this is probably closer to 100,000.

Recurrent *C. difficile* infection syndrome is typically initially triggered by antibiotics which cause dysbiosis of the gut microbiome allowing *C. difficile* to become established. This is in turn treated with antibiotics, generally vancomycin or rifaximin which usually resolves the infection, and the microbiome returns to its normal status. However, recurrent infection is common with this syndrome, with an average of six relapses and morbidity rates are high.

Non-toxigenic strains of *C. difficile*, which lack toxin genes, are being investigated for their potential to reduce recurrent infection. Using a Syrian golden hamster model, non-toxigenic strains were able to protect against further infection by toxigenic strains. Three *C. difficile* strains were found more frequently in hospitals



as colonisers and two typing groups, M and T, were identified for non-toxicogenic strains with the potential for use in protection.

Phase II trials in healthy volunteers showed that high doses of non-toxicogenic *C. difficile* administered for 14 days gave less protection than the same dose administered for 7 days, but both were better than the lower dose. Further trials are planned to determine if treating *C. difficile*-induced diarrhoea by co-administration of antibiotics and non-toxicogenic *C. difficile* will prevent colonisation by toxic *C. difficile*. To date no transfer of the virulence-associated region from the toxic strain to the non-toxic strain has been reported. Should such treatments be considered probiotics? Further research is needed as the mechanism by which the non-toxicogenic strain excludes colonisation by the toxicogenic strain remains unclear.



## Exchanging microbiomes

Faecal enemas were in fact first conducted with some degree of success as long as 50 years ago by Eiseman and colleagues, showing that repopulation of the microbiome with external bacterial sources can be successful. The technique has recently been revived, and is now termed faecal microbiome transplantation involving administration of a microbiome solution derived from a healthy donor stool, and has been successfully used to treat *C. difficile* infections. The treatment is effective with rapid repopulation (within 2 days), and efficacy is reported in patients with very different initial microbiome profiles, despite establishment of unique microbiome populations. Even more encouraging, the effect is long-lasting with the renewed microbiome present at least 6 months later and an absence of further *C. difficile* infections.

Patients typically receiving this treatment are mostly infected with Proteobacteria such as *Pseudomonas*, *E. coli*, *Klebsiellae*, and *Enterobacteriaceae* which expand during *C. difficile* infection. Several criteria must be met in order to be considered a suitable FMT donor, including ensuring no antibiotic use within six months prior to the procedure, an absence of infectious diseases, metabolic syndrome, liver abnormalities or allergies, nor can a donor be suffering from malnutrition.

Despite the relatively basic technology employed and the fact that the injected product cannot be standardised, the success rates are impressive, with a consistent 90% clearance rate without recurrence over 2 months after one application, and a further 90% clearance rate after a second application in the 10% who failed, giving an overall success rate of 99%. It may also be feasible to extend this technique to other applications, such as storage of a patient's microbiome prior to a major operation with the potential to cause dysbiosis, to allow restoration of



one's own microbiome post-operation.

As FMT represents the first instance that a human waste product is being used as treatment for human beings, it is understandable that there is confusion for regulators as to how best to deal with this. The current position of the Food and Drug Administration (FDA) is that a product is considered a drug when it is used to cure, treat, mitigate or prevent a disease. As such, faecal microbiome for transplantation meets this legal definition of a drug and biological product. However in July 2013, the FDA decided to exercise enforcement discretion regarding investigational new drug (IND) requirements for FMT provided that the treating physician obtains adequate informed consent from the patient. Not surprisingly, reimbursement is still under negotiation, but in the meantime, both patients and their clinicians are relieved to have as FMT as an option.

## Uncharted waters: regulating nutraceuticals

Innovative approaches for managing health, such as FMT and more recently nutraceuticals, highlight the need for regulation to keep up with such innovations. Advances in nutrition and product development are blurring the line between foods and medicines. Nutraceuticals, functional foods or foods for health, are defined as a food or part of a food that provides medical or health benefits including the prevention and/or treatment of disease, and fall at the very intersection of the food and medicine spectra.

Food and beverage companies are attracted to nutraceuticals' comparatively high profit margins. The interest for pharmaceutical companies is the need for significantly less research and development compared to prescription and over-the-counter products, along with the consequently lower regulatory burdens. The flip side to this is that the lack of stringent regulation in this area may lead to products of dubious quality and claims of questionable merit, which in turn may create a perception that nutraceuticals are not as 'good' as pharmaceutical products, tainting the medical foods domain, which has a high potential for benefit.

Product positioning for nutraceuticals, striking the right balance between credible scientific evidence, regulation and pharmaceuticals hurdles, is a major challenge. From the payer's point of view on reimbursement, the key questions are the anticipated use of the nutraceuticals, the impact on the healthcare budget, pricing and usage limitations that may be imposed.

From a regulatory standpoint, there is no global uniformity for nutraceuticals with approaches varying from country to country. International harmonisation of the



concept of food for special purposes is needed to avoid products being considered a drug in some countries but not in others. Similarly the perception of value for payers needs to be understood, as well as which comparators can be used for evaluation. Increased regulatory harmonisation already underway between the EU and US for medicines (e.g. orphans and paediatric) is expected to be extended to nutraceuticals.

In Europe two agencies, European Food Safety Authority (EFSA) and the European Medicines Agency (EMA), regulate food and medicines, respectively, in contrast to the situation in the US where the FDA is responsible for both. One of EFSA's roles is to evaluate 'novel foods and food ingredients', providing independent scientific advice and communication on existing and emerging risks associated with the food chain. Harmonisation of EFSA with European Member States is planned via the 'EU Menu' project, which will gather information on food consumption. A European Food Composition database, FoodEx, is a nutrient database that will provide information on risk/benefit of nutrients via the use of national codes.

Health claims are classified as i) nutritional claims (what it contains), ii) functional claims (what it does) and iii) reduction of disease risks and children's development and health. Unfavourable opinions are due primarily to incomplete characterisation, lack of sufficient information on the food, constituent, claimed effect, or even that the effect is not considered to be a beneficial physiological effect. Product safety and health claims on effects of foods on markers are evaluated separately.



## Pushing health policy revisions

Development of policies for novel products also needs to be complemented with revisions of existing health policies. It is predicted that by 2030, non-communicable diseases will account for more than 50% of diseases in low income countries and 75% in middle income countries. In economic terms, 169 billion are spent annually in the EU for cardiovascular diseases (62% of costs) and 1.3% of the GDP on obesity-related illnesses, while 6.5% of all healthcare budgets are spent on cancer.

At a political level, the current approach to developing policy for healthy eating is directed towards individual-focused nutritional education and food labelling. Policy needs to be developed at international, regional, state/member state, and local levels and must involve all stakeholders. Collaborative efforts are needed for policies to be successfully implemented. The increasing complexity of the issues being faced exceeds the capabilities of any single sector to solve them. Areas to address include consumer education and information (in particular labelling), promoting healthy lifestyle, marketing, food content and availability.



Current dietary guidelines and reference values may also no longer be adapted and may need to be adjusted to take into account changes in food patterns, epigenetics, interplay between food and the influence on the microbiome, concomitant drug intake and lifestyle.

Policy makers are facing many challenges, notably the absence of robust methodology in many current and past studies, making it difficult to assess the impact and relevance of past actions, and establishing the optimal balance between soft measures (e.g. education) and hard measures (enforcement of regulations). Further complicating the issue, interested parties are faced with a cacophony of nutritional messages – science has a responsibility to be involved but must also offer simpler messages. Policy needs to be sustainable, with long-term studies providing evidence. Deciding who drives policy and balancing implementation of changes at individual *versus* population level are delicate and debatable matters. The concept of using behavioural evaluations to testing policies prior to their implementation such as with controlled trials has also recently been raised.

## Managing health inequalities

In times of austerity, the healthcare budget is often the first to be scrutinised, leading to increased health inequalities. Current figures estimate that 25% of EU citizens (116 million people) are at risk of social exclusion or poverty, with increasing numbers of households nourished from food banks and greater use of 'cheap' foods with low nutritional quality.

Health inequalities are seen between countries and socio-economic groups, with disadvantaged populations more likely to have unhealthy diets and be physically inactive. Data from the Organisation for Economic Co-operation and Development (OECD) shows that over the last decade in Western Europe, there is a clear socioeconomic gradient in the prevalence of obesity, and particularly so in women.

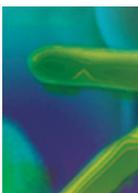
Women are more often victim to social inequalities and are the most underutilised economic asset in the world economy. If women in the United States, Japan, and Egypt were employed at the same rates as men, the GDPs of these countries would be higher by 5%, 9%, and 34% respectively. This inequality is reflected in higher obesity rates, most likely driven by poorer income and education, along with pregnancy and child-rearing responsibilities. A domino effect is seen, with women in poorer socioeconomic groups more likely to have overweight or obese children and less likely to follow breast-feeding guidelines, as reported in studies in China. In France, one in four women of childbearing age is overweight while in the US, it is two in four women. These women have a high risk of developing



gestational diabetes, which in turn increases the risk of obesity in offspring.

Given as women will often forego certain behaviours for the benefit of their unborn child, pregnancy is underutilised in the study of health preventative measures. The right nutrition during the 1000-day window has been shown to save lives, reduce the human and economic burden of diseases, both communicable (e.g. tuberculosis, malaria and HIV/AIDS) and non-communicable (e.g. diabetes), as well as increase a country's GDP. This has also been described in the Foresight obesity map, which takes populations, education, physical and environmental aspects into consideration to improve conditions for foetal and early childhood development and to reduce poverty.

While the importance of women has not received enough attention in health and economic studies, it is important not to let the pendulum swing too far the other way and forget the impact of nutrition in boys.



## **Malnutrition: the other end of the nutritional health scale**

While progress has been made to alleviate malnutrition in developing countries, a significant burden still remains. Undernutrition is responsible for 45% of child deaths annually with an estimated impact of 2% to 3% on GDP, although these figures may be as high as 10% to 11%. Part of the United Nation's Millennium project's development goals is to halve hunger; currently 30 countries are on track - but 37 still need to move forward with their objectives. The prevalence of stunting has declined to 26% (165 million children), however stunting rates are not declining as fast as poverty rates, implying that increased income does not necessarily translate into better nutritional outcomes.

The Global Alliance for Improving Nutrition (GAIN) has three key features: i) food-based solutions (not medical), ii) multi-sector partnerships, and iii) implementation of large-scale programmes with an overall goal of reaching 1.5 billion of the 2 billion individuals worldwide who are currently micronutrient deficient. In the first 10 years, the programme has achieved over 50% of this goal.

Haiti, one of the world's most extreme cases of poverty, is an example of how projects address malnutrition. The prevalence of malnutrition is dramatically higher than in other low income countries, with at least one in four Haitians experiencing food insecurity. Several large-scale paediatric programmes targeting malnutrition prevention and treatment (including severe malnutrition) have been implemented in the community and in HIV and TB populations treated in specialist centres.



The approach is simple; children receive daily rations of locally-produced, fortified, energy-dense, ready-to-use food, are monitored monthly for growth, while local community caregiver support groups offer counselling to mothers, encouraging 6-months of breast-feeding, infant feeding and hygiene, and prevention and treatment of diarrhoea, and other illnesses, including HIV. Programs are adapted for cases of severe malnutrition, while microcredit programmes encourage sustainability in the home.

The success of these programmes can be measured in a marked improvement in malnutrition and childhood survival rates. Programme completion rates are high, with increases in stunting and wasting with age in community-populations seen before the programme, were inversed by more than two-fold within 6 months, while severe malnutrition was absent in the 3000 children treated. Similar successes were seen in HIV populations, while goal weights have been reached by 75% of children suffering from severe malnutrition, and in total less than 5% did not reach their goal weight or died.

Active and wide-reaching community-based and acute-care programmes such as those in Haiti allow large-scale and accurate evaluation of the impact of early simple nutritional prevention and malnutrition rehabilitation strategies for mothers and their children. Continued primary healthcare services, local community clubs to reinforce positive messages, education, job opportunities, and economic empowerment are all critical in the continued fight against malnutrition. Close and continuous monitoring and simple measurements ensure accurate real-life results with rapid visibility of outcomes. The success of the simplicity of the Haitian programme is reflected in the rapid and effective scale-up in response to the devastating earthquake in 2010. Programmes educating people on the importance of water hygiene and the development of simple methods for testing water security are also critical to ensure health.

The importance of disseminating successful project outcomes not only locally but also to governments and policy-makers cannot be underemphasised. Policies specifically addressing lower socioeconomic groups are rare and there are large gaps in global investment in malnutrition. The World Bank estimates that an investment of approximately US\$12 billion annually is needed to scale up direct nutrition intervention in 68 countries with significant malnutrition burden. The countries concerned by these problems are also investing in their own solutions, which lie in part in strengthening links with agriculture, to ensure optimum nutritional value of what is produced and marketed.





## Public-private partnerships

Nutritional health is well beyond being a public health problem and cannot be solved with public systems alone. It is not only developing countries that need to look beyond the public sector for solutions. The nutrition/public health interface includes food science and agriculture, and technology innovations are needed so that all consumers across all socioeconomic groups can meet the recommendations being made.

Moving towards individual responsibility in obtaining and maintaining a healthy lifestyle requires a shift in focus from public policy and the health sector. Non-governmental organisations (NGOs), the food industry, educators, caterers, food retailers, advertising companies and scientists all have a role to play. PPPs are paving the way, allowing multiple partners to share the responsibility. PPPs encourage businesses and the health care sector to be implicated in issues in the broader community which can affect them, governments to improve efficiency, transparency and cost-effectiveness, and NGOs to be answerable for results and use of resources.

Successful policy changes need a co-ordinated approach, but multi-stakeholder programmes are complex. Challenges facing PPPs to be taken into account include lengthy processes in obtaining funds, bureaucracy, finding adapted evaluation guidelines and tools, potential conflicts of interest, possible scientific scepticism levelled at private groups, and finding a balance between the need for long-term evidence to motivate actions and the need to implement changes now.

Multi-stakeholder approaches along with integrative system biology approaches, which combine high-dimensional functional genomic data with biological, clinical, environmental and lifestyle assessments through iterative statistical analyses, computational modelling and experimental validation are powerful tools in addressing complex medical issues such as obesity, severe asthma and other chronic diseases.

The P4 systems (predictive, preventive, personalised and participatory) require harmonisation of experimental and computational methods for data, information and knowledge collection, storage and sharing. The inclusion of researchers, industry, academia, regulatory and funding bodies, individuals as well as patient organisations in the process, addresses the many ethical, legal and social issues, which are sometimes relegated as less important.

The European Institute for Systems Biology and Medicine (EISBM) is implicated in several projects designed to improve understanding of infectious, non-communicable and chronic diseases through these cross-disciplinary projects funded by the EC.

The idea is to move away from individual elements and look more at how they interact with each other. The technologies available currently can be, and have been, used to



predict a predisposition to certain illnesses. Projecting 10 years ahead to 2023, the aim would be to treat all patients using their own personal “omic” profiling, however extending this technique to millions and billions of individuals would certainly require broad stakeholder involvement.

## Measures for prevention

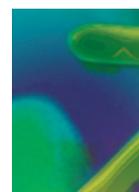
The need to shift from intervention towards health promotion and disease prevention is irrefutable; “The most promising approaches for obesity prevention are population-based and multilevel, focus on environmental and policy changes, and require participation from actors in multiple sectors”. However, the first question that needs to be addressed is whether the right regulatory, policy, and educational framework in place to support this move.

Education, responsibility and technology are fundamental elements in the move towards prevention. Numbers of health-conscious consumers are growing. There is increased attention to and education in nutrition coupled with increasing wellness initiatives. Part of the answer lies in changing the customer’s default choice, however food manufacturers also have a responsibility to change the default options provided. Research into change in group or societal behaviour and analysis of what is initiating these drivers is essential, along with understanding how behaviours spread and how individual choices are influenced.

## Understanding consumer attitude: better food and health via better education

Changing consumer’s behaviour toward healthier food and more exercise requires research into how people think as well as how to make the healthy options more attractive. Humans have a dual thinking/decision-making process, the first part being a fast/automatic process which is spontaneous and emotional, while the second is more controlled, deliberate, slow and rational.

Our behaviour when we buy, cook and eat food plays an important role in the decisions we make. The time an individual takes to make the decision and the time frame concerning the decision impact behaviour. There is a clear preference for decision making for the present rather than the future, as the future is a value that is not in our thoughts when making quick decisions. When thinking quickly, there is a distinct bias in choices, and these preferences are socially determined.



Behavioural research was conducted using a mini e-shop to compare shopping behaviour in a lab with real life. The stated healthy choices were reflected more closely in the e-shop shopping cart than in real-life decisions. Reasons for this are likely to be linked to the fact that choices in the supermarket are made quickly, circumstances in which most individuals stick to ritual habits. The effect was more obvious in individuals of low socioeconomic groups where resistance to change was higher, whereas individuals with higher revenues responded more positively to nutritional policies. Psychological studies have demonstrated that individuals from a low income bracket facing a financially restrictive situation remain more in the present and do not tend to make decisions for the coming decade. With this in mind, nutrition policies should be presented with an emphasis on the short-term positive benefits of remaining healthy such as being in better shape and a better position to find work.

Economists have evaluated individual choices, and found that they result from trade-offs between costs and benefits. Food demand is determined by 'preferences' including habit, education, culture, health, genetics, addiction and peers, but also environment (supply of goods), prices, budget, and complementary goods. These choices are considered fixed in the short-term but may change in the long-term. While it is evident that cost will play an important role in decision-making, consumers also requested a nutritional labelling system which is easy to understand, and considered that information technologies and 'smart' tools can facilitate decision-making.

Differences in food purchasing based on price, types of products, culture, eating habits and preferences were evaluated in a study of approximately 25 000 households in France, the UK and the US over a 2-year period. When different scenarios were simulated by changing prices, quantities, attributes of the food or tastes, choice patterns across the three regions also changed; for example, when US citizens were confronted with French prices for products, then their choices in terms of carbohydrates, proteins or fats resembled those of a typical French consumer. It is the interaction of preferences, prices and attributes that explains cross-country differences. Consumer behaviour can change and in the long run, preferences will adapt.



## Employer responsibility: behavioural changes with the right environment



Primordial prevention requires targeting behaviour in order to impact the development of diseases. Simple metrics have been developed to define ideal cardiovascular health, and studies show clearly that meeting all criteria equates with absence of cardiovascular disease. It is undeniable that the risk of heart disease is reduced by stopping smoking as does having access to the powerful pharmacological arsenal against elevated cholesterol and blood pressure. Reports in the literature are also clear that the risk of coronary disease is greatly increased in inactive individuals. Inactivity is often associated with poor nutritional habits and is responsible for more deaths worldwide than smoking. On the other hand, evidence from real-life interventions targeting inactivity is lacking.

In Canada, a community-based programme targeting blue collar workers was introduced focusing on improving nutritional quality and exercise habits by modifying diets of individuals with excess visceral fat combined with 160 minutes exercise weekly. A mobile metabolic unit was equipped for measuring weight, body composition, blood pressure, blood samples, and cardiovascular fitness, and also provided treadmills. The programme worked with representatives of the company's unions and upper management, using a team competition-based approach with a point system rewarding 'healthy' behaviours. After 3 months, there was an average 4 cm reduction in waist circumference, physical activity increased by 10% and participants had a reduced risk of pre-diabetes.

More employers need to provide these types of initiatives to employees with sedentary jobs, while also building participation in such schemes into their job structure. Similarly, some insurance companies in the US are providing reimbursement for attendance to fitness clubs, coverage for obesity medication and surgery and nutrition education, which are all good incentives for individuals to take control of their health.

These initiatives together with those evidenced in community projects such as ICAPS and EPODE demonstrate unequivocally that involving and empowering the individual at the heart of the matter results in higher compliance and adherence as well as higher and longer term success rates.



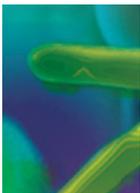


## Technology platforms in health and nutrition

Technology analysis platforms are proof of the effectiveness of PPPs. Nano- and micro-technologies are a burgeoning area offering novel and innovative options for food and drug development, screening and safety. The nano/micro aspect offers the advantage of facilitating high throughput with minimal space requirements. Techniques include detecting small organic molecules and gases which can be used to evaluate food integrity and offer 'smart' packaging, micro-organisms analyses for microbiome monitoring, 'organs on a chip' offer *in vitro* models for testing food and drugs, nano-encapsulation of flavours can be used as a means of preserving food, and food sensors can be used to follow nutrients once inside the human body.

Analytic platforms provide a technical tool for interpreting the effects of products on the microflora, intervening from preclinical studies through to international clinical trials. Such platforms create the infrastructure for analysing scenarios such as when dysbiosis occurs, offering a structured and efficient means of evaluating product effects. Experienced specialists optimise analyses with well-designed approaches developed using the literature and scientific advice, and adapted sampling protocols. A choice of genomics, proteomics and metabolomics are used to identify bacterial strains.

This technology is also useful in evaluating the potential benefit of the microbiome in the context of cancer. Tumour sample analysis to identify biomarkers is run in parallel with gut microbiome sequencing. These data can then be used to identify microbiome profiles associated with tumour types, progression and sensitivity to different chemotherapies. Personalised nutritional intake can be proposed depending on type of cancers and treatments.



## Smart moves for better health

Modern technologies offer an ideal framework for changing behaviour and cultivating health optimism, and creating the potential for enormous savings in healthcare costs. While investment in traditional healthcare is in decline, the digital market (applications, gaming, social networks, biosensors, etc.) is exploding, with estimates that the mobile health industry will be worth US\$50 billion by 2020. Current estimates put the number of mobile phones at 2.7 billion worldwide, 50% of which is accounted for by smartphones, with this share growing rapidly.

Smart mobile devices and applications provide an easy, fast, accessible, wide-reaching, and inexpensive means of accessing a huge number of people in both developed and developing countries. Currently there are an estimated 1.5 billion



app users, 200 million of whom are already using smart phone/technology to self-quantify. Apps offer a secure, mobile and integrated platform for individuals to track and benchmark their health and well-being in real-time, with personalised solutions feeding into a network system of cloud computing, social networking and big data analysis.

The human body generates 3500 measurable biosignals per minute, representing a rich resource to tap into. Biosensors can be used to record data and take photographs which are sent to a mobile device and can be integrated with other data, while the API (application programming interface) coordinates software interaction and accesses databases. A wide variety of biosensors is already available, such as ingestible sensors, including one recently approved by the FDA, others are inserted into a major artery, or behind the jaw where chewing pressure can track what is eaten. Or they can simply be worn on the wrist or slipped into a pocket. Biosensors can coordinate with associated skin patches which collect and transmit data on the body's physiological reactions and behaviour.

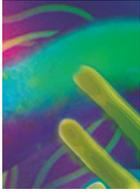
Thanks to these biosensors, apps can track and evaluate food intake, physical activity, health, habits, medication intake, sleep, and psychosocial factors such as stress and moods - continuously, automatically and in real-time. Input can be automated using biosensors, product scanning or image recognition for price and nutritional value and quality, or manual and vocal input may be used. Once processed, these data can then be used to feed back personalised advice to the user on what to buy and eat, what to eat more or less of, and to determine energy input and output to guide activity. Possibilities are unlimited.

Keys to the success of health apps include that they are cheap, fun, and are easy to adapt culturally. They also offer convenient, virtual, and continuous social support to maintain motivation and accountability. Social networks and mobile apps are an excellent opportunity to create a new concept of local and global 'real-life communities'. Motivation is boosted when an interactive approach with personalised advice is used, along with follow-up, creation of goals and recognition of achievements.

With apps generating a phenomenal amount of data, discussion between app developers and the food industry, regulators and health and nutrition experts is needed to consider whether data can be regrouped and if it should be made available to third-parties. This opens up the debate of maintaining privacy *versus* potential benefits which can be derived from the wealth of data. Regulation will also come into question with the need for user guidance to ensure the most adapted and reliable apps are used. In a recent decision by the FDA, it was announced that some of the health apps on the market will be regulated. The intention of the



Agency is to “encourage these exciting innovations” while setting “risk-based priorities” for applications where safety and effectiveness are critical. Clinical trials are already anticipated to evaluate the effect of apps on behaviour outcomes.



## Moving towards the future

Several clear messages have emerged from this fourth BFBH symposium, the first and perhaps most pressing, being the need to shift the balance of treatment and prevention in health care. Our understanding of obesogenic factors, whether genetic, lifestyle, environment, socioeconomic status or education, has improved significantly and can be used to attempt to influence individuals, communities, food producers, regulators and policy-makers.

A multi-stakeholder investment is essential. Through community-based projects or broader investments in PPPs, it is clear that a complex multifactorial problem such as obesity and its associated co-morbidities is much more than a simple public health issue, and requires an equally large investment of funds and energy.

With increased availability of innovative technologies and treatments, regulatory agencies will need to adapt in order to accommodate them, whether it be in terms of treatment with the use of FMT, biomarkers (to determine the impact of food, FMT, probiotics or antibiotics), techniques for evaluating food safety, or mobile health apps. Regulators are now facing a different realm to the traditional one of medicines or food regulation.

The emergence of the intestinal microbiome as an organ with an enormous potential to exploit via novel technologies such as high throughput sequencing, has allowed old concepts to be revisited and better understood. Methods and technological approaches need to be standardised to better deal with population-based studies *versus* individual studies.

Personalised solutions founded on an understanding of the individual's microbiome will also require further dialogue to examine how this fits into the concepts of nutrition, exercise and regulation.

Notably, we have observed the importance of involving of the most important stakeholder, the individual concerned by the effects on their health and environment, along with the fundamental role of empowerment, involvement and education in longer term changes.

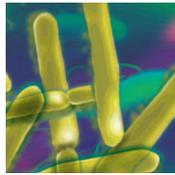
The way forward for all of these concepts is ideally suited to PPPs, which can assist when recruiting large cohorts of normal individuals or patients and will also aid in



the important and often limiting issue of obtaining funding for such research. It could be envisaged that the extensive group of stakeholders involved in these meetings could put together a proposal for a European or IMI funded project.

With the landscape changing in this way, future Better Food for Better Health symposia are likely to need greater contributions from regulatory agencies, other institutions and organisations with a view to discussing and directly impacting decision-making processes.





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