# Transforming Nutrition Science for Better Health

A joint Wellcome and WHO consultation





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## **Executive Summary**

Every country in the world has a malnutrition problem, yet nutrition science has an image problem and is not 'keeping up' with the evolving global patterns of malnutrition that herald major health and economic consequences for generations to come.

#### **Box 1: Challenges for Nutrition Science**

- 1. Be more objective
- 2. Move away from purely descriptive research
- 3. Ensure that research is impact focused
- 4. Be more rigorous
- 5. Capitalise on the latest discoveries e.g. adopting "big science" approaches
- 6. Embrace team science and other disciplines into the field
- Look at old problems differently e.g. muscle as an endocrine organ, systems biology approach to nutrition research
- 8. Do as much science in country as possible

In response to this Wellcome and WHO hosted a workshop to broker dialogue with the nutrition science community. The primary aim was to stimulate new collaborative research that embraced cutting edge thinking, techniques and technologies, and could impact human health in the future.

#### **Box 2: Actions for Funders**

- 1. Support team science and incentivise different disciplines to work together
- 2. Support methodological advancement and standards
- 3. Work together on strategic priorities to achieve more
- 4. Encourage diversity and inclusion look beyond the usual suspect research groups
- 5. Encourage the next generation of nutrition researchers
- 6. Ensure the importance of nutrition is recognised more broadly
- 7. Coordinate global nutrition agenda reduce papers and increase action
- 8. Involve industry and policy makers in discussions
- 9. Be open to risk

Researchers from a range of disciplines brainstormed emerging nutrition research priorities and made new collaborative connections. Over 2.5 days of intense discussion and facilitated group work, research priorities were captured, distilled and potential solutions identified. On the final day, newly formed groups pitched their research concept to an expert panel. Four groups received pump priming funds to develop their ideas and collaboration over the next year.

During the meeting, several barriers to nutrition science were identified that the global community need to tackle in partnership (Box 1, 2 and 3). By sharing these findings with the wider research and funding communities, we hope to catalyse further dialogue on the identified research priorities. Nutrition science needs new approaches and voices to initiate change and to have a positive impact on human health. Wellcome has demonstrated its interest in nutrition science and will continue global conversations to tackle some of the more intractable problems facing nutrition science.

#### Box 3: Six themes for the future Defining health: How do we define nutritional health? Study design: How can innovative trial design be used in nutrition research? Measurement: With new technology can we rethink how we measure nutrition? Data: How can big data, machine learning and artificial intelligence be harnessed to address nutritional research questions? Implementation: How do we best implement strategies to improve nutrition? Social context: To what extent does our social setting, education and advertising influence the nutritional value of our diets?

## **Transforming Nutrition Science for Better Health**

#### Background

Malnutrition is a problem for every country in the world. Almost 90% are facing a double burden of undernutrition and over-weight/obesity1 - with an estimated annual cost of \$3.5 trillion US dollars<sup>2,3</sup>. The fundamental importance of nutrition to health and sustainable development is well documented<sup>4</sup> however, the world remains woefully off track to meet global targets<sup>5</sup>.

Though the burden of malnutrition remains unacceptably high, there is a window of opportunity to provide renewed impetus both at a policy and research level through the UN Decade of Action on Nutrition 2016–2025<sup>6</sup> and the Sustainable Development Goals (SDGs)7. Both highlight the urgent need for progress. In the UK, the 2017 Review of Nutrition and Human Health Research<sup>8</sup> highlighted the unfulfilled potential of nutrition research and the need for funders and the wider research community to work together to address existing barriers.

Despite the large global burden of malnutrition and importance of nutrition to health and wellbeing, nutrition science has a problem. It is perceived by some as being too siloed (not considering malnutrition in all its forms), lacking deep biological understanding and being less rigorous than other scientific fields. Cutting-edge techniques are not being applied to nutrition problems. There is concern that research is not keeping up with the evolving global patterns of malnutrition, heralding major health and economic consequences for generations to come.

In response to these observations, Wellcome and WHO joined forces to co-host a workshop to start a global conversation about nutrition research and invigorate the field.

#### The Workshop

Transforming Nutrition Science for Better Health brought together 70 multisectoral stakeholders, including

<sup>1</sup> Global Nutrition Report 2017: Nourishing the SDGs.

Inutritionreport.ora/the-report

<sup>2</sup> FAO 2013 State of food and agriculture 2013: Food systems for better nutrition http://www.fao.org/3/i3300e/i3300e00.htm <sup>3</sup> Glopan technical brief 2016 "the cost of malnutrition" report

(https://glopan.org/sites/default/files/pictures/CostOfMaln utrition.pdf) https://scalingupnutrition.org/nutrition/nutrition-and-the-sustainable-developmentgoals/

researchers at the cutting edge of both under- and overnutrition; basic science and clinical research, and from across different stages of the life course. The purpose was to create the opportunity for learning, challenge, invention and cross-fertilisation. We wanted to bring new technologies to old problems and foster creative multidisciplinary collaboration breaking down scientific siloes. Attendees were encouraged to be 'disruptive' in their thinking, challenging the old ways of conducting nutrition research and interrogating the perennial questions in new ways.

In addition to the spectrum of researchers, the workshop was attended by a range of other funders and actors in the global nutrition space (see appendix 1).

Over 2.5 days of intense discussion and facilitated group work, research priorities were captured, distilled and potential solutions identified. We adopted a modified "sandpit" approach9. After a series of perspective talks to set the scene, facilitated group discussions challenged attendees to think about the research gaps and opportunities in nutrition science and how these could be addressed. We asked everyone to think about different approaches, the value of multi-disciplinary working, and how to make a step change in nutrition science. Ideas generated by initial brainstorming were further interrogated through three rounds of development; taking the seed of a research idea and thinking through multidisciplinary approaches to the problem (Figure 1). On the final day, groups that had self-selected an idea and team, had the opportunity to pitch their emerging research projects to an expert panel for pump prime funding. Importantly, attendees were not aware of this option at the beginning of the meeting, to help the conversations be as open as possible.

- <sup>6</sup> https://www.un.org/nutrition/ 7 https://sustainabledevelopment.un.org/?menu=1300
- <sup>8</sup> https://mrc.ukri.org/documents/pdf/review-of-nutrition-and-human-health/
- <sup>9</sup> <u>https://epsrc.ukri.org/funding/applicationproc</u> atisasandpit/ s/routes/ne

<sup>&</sup>lt;sup>5</sup> Global Nutrition Report 2018 https://globalnutritionreport.org/reports/globalnutrition-report-2018

Figure 1 The process of a 'sandpit' style meeting



To bring new voices to these discussions we also ran a competition which identified 6 promising early career researchers to join the discussions (*appendix 2*). To engage delegates ahead of the meeting, we used a Facebook group to encourage attendees to connect before the meeting, provide content about the meeting and to stimulate discussion ahead of the meeting (see *appendix 3*). During the workshop we used this group to update the wider research community about discussions taking place.

#### Thinking differently about nutrition

The grand ambition, and primary aim of the workshop was to stimulate new and innovative collaborative research in nutrition science. We could not hope to cover everything in 2.5 days and working with an international group of experts (*appendix 1*), we identified two focal topics to open the dialogue. These were body composition/muscle and the microbiome and how they relate to nutrition; both areas were felt to be ripe for transformative discussion. The conversation, however, was open to all aspects of malnutrition from acute undernutrition to obesity, and our two focal topics were

chosen as a way into discussion not as a limit to the scope.

Professor <u>Andrew Prentice</u> opened proceedings with a personal "Vison for Disruptive Nutrition Research" exhorting the nutrition research community to be more objective and to face our failures. He made 10 recommendations to the nutrition community:

- Be more objective. The recent null results of the large WASH trials<sup>10</sup> are huge disappointments, but we must accept them and move on. We should face our failures and challenge: why aren't we having impact?
- Beware of nutritional epidemiology<sup>11</sup>. We must look for causation not correlation and avoid bias. Too many intervention trials have failed due to a flawed evidence base.
- 3) Beware too many surveys. We know the world is full of malnutrition. Surveys are useful for policy makers and should be supported by government funding rather than research grants.
- 4) Be realistic. There are no silver bullets. We should strengthen the theoretical base; "suck it and see" experiments are not good enough. We need to understand how the human body responds to nutritional inputs before considering diet and disease interactions.
- 5) Challenge the "Omics" field to deliver a realworld difference. There is exciting potential in areas, such as the microbiome, but we need to grapple with the complexity too- it isn't easy.
- 6) Be more rigorous. "Impatient optimism" isn't a way forward. We should learn from the drug discovery and vaccine pathways taking logical steps from discovery science to clinical translation. In nutrition we often miss vital steps and jump ahead to large scale intervention too soon.
- 7) Capitalise on the latest discoveries. For example, increased mechanistic understanding of the causes of anaemia can help stop the indiscriminate use of iron which has previously been shown to be ineffective in some settings<sup>12</sup>.

<sup>&</sup>lt;sup>10</sup> Pickering et al Lancet Glob Health 2019 Aug;7(8):e1139-e1146. doi: 10.1016/S2214-109X(19)30268-2.

<sup>&</sup>lt;sup>11</sup> Ioannidis. JAMA 2018; 320(10):969-970

<sup>&</sup>lt;sup>12</sup> Prentice et al. Sci Adv 2019; 5(3): eaav9020.

- Adopt a "big science" approach. Multi-country collaborative studies, open data and Big Data should be applied to nutrition research.
- 9) Mandate pathway to impact statements. Researchers should be required to tell us how they are going to make a difference. They should be realistic in what they can achieve and there should be an appreciation that time is needed to see real world impact.
- Do as much science in country as possible. Build the science base where the issues are. Most importantly money should follow science and not vice versa.

To encourage delegates to think differently about nutrition research we also heard from <u>Scott Smith</u>, head of the Nutritional Biochemistry Lab at NASA about nutrition research in space and what it can teach us about human health on earth. He gave a truly out of this world perspective showcasing how nutrition can help overcome the effects of space flight and highlighted the rich research environment at the international space station and on the ground. Scott showed how research in this extreme environment is relevant to people on Earth, sometimes in surprising ways<sup>13,14</sup>.

#### Starting the conversation

To begin the conversation with delegates the two focal topics of muscle and the microbiome were used as tools to spark debate.

We know body composition and muscle changes in response to nutritional challenges across the lifespan including childhood undernutrition, obesity and sarcopenia in older age. However, we don't currently understand *why* muscle is sensitive to nutritional changes and so don't know the best way to respond to manage these. A robust discussion around this topic identified 7 take home messages.

### Take home messages about muscle and body composition

- It's time to think differently about muscle. It's not just a structural tissue but also functions as an organ responding to nutritional challenge, changes in energy balance and communicating to other body systems.
- 2. We should move away from descriptive studies to understand the broader functions of muscle and how nutritional status alters these functions e.g. of myokines.
- 3. New technologies could help study muscle and how nutrition influences it e.g. MR spectroscopy and metabolomics.
- 4. Consider how inflammation and the immune system impact nutrition and muscle/body composition.
- 5. A need to understand muscle interactions with body systems so that we can correctly treat patients.
- 6. We need to remember what a poor measure of nutritional status BMI is and consider fat and lean mass indices instead
- 7. The mismatch between evolutionary drivers of metabolic decisions relating to muscle and adipose tissue and the nutritional challenges experienced by todays populations are an important risk factor for metabolic diseases

<sup>13</sup> Smith et al. <u>Curr Opin Clin Nutr Metab Care.</u> 2018
 Nov;21(6):481-488
 <sup>14</sup> <u>https://www.bbc.co.uk/news/health-45735361</u>

Microbiome-nutrition interactions are important across the malnutrition spectrum and could provide insights into metabolic changes associated with obesity and acute undernutrition. There is a growing appreciation of how gut microbes transform dietary ingredients into metabolic products and bioactive molecules that contribute to 'normal' physiologic functions; changing our concept of 'essential nutrients' and altering our definitions of the nutritional value of foods. However, it is not known which of these microbiota-derived products are a common feature of a healthy human being. Such knowledge could enable the design of microbiota-directed foods (MDFs) and provide biomarkers to establish their efficacy. From delegate discussions 8 key messages emerged.

#### Take home messages about microbiome

- Host microbiome interactions need further study to fully understand the impact of the microbiome on nutritional status
- 2. Embrace individual variation to help realise the potential of personalised nutrition
- 3. Capitalise on big data and machine learning
- 4. Move from description and correlation to understanding function and causation
- 5. Harness chemistry to create better tools to study the microbiome function
- 6. Learn from human milk to better understand the role of carbohydrates in our diet
- 7. A need for better analytical techniques
- 8. Sharing data in food encyclopaedias could help move the field forward

#### Emerging nutrition research priorities

Next, we opened the conversation to all areas of nutrition. Facilitated group discussions about nutrition science research priorities initially generated 224 questions across 17 broad themes (Figure 2). The most common themes were around measurement, thinking differently about how we define nutritional status and what we mean by 'good' nutrition. While many themes discussed are topics that are well known to the nutrition community, there were also some 'disruptive ideas' that emerged (appendix 4).



Figure 2: 17 broad research themes were identified by the group as being priorities in nutrition research. The text size relates to the number of questions generated by the group that related to this topic. The clustered research themes were distilled into questions to begin thinking about research approaches changing the focus of the meeting from finding questions and challenges to identifying potential solutions.

#### Research questions identified from themes

- How do you model interactions and trade-offs for nutrition in complex systems? (physiological to environmental)
- 2. How do you know that microbiome directed interventions really improve health and development?
- 3. How do we promote recovery of muscle? Is this the right outcome?
- 4. How do you recommend the right diet for an individual in different settings?
- 5. Breaking the cycle: inflammation or malnutrition what comes first?
- 6. In what ways might we best measure nutritional phenotypes?
- 7. How might we re-think muscle as a driver of health? Measurements and impact on health
- 8. In what ways might we reverse engineer to characterise responder and non-responders to diet?
- How might we approach influencing/advising/manipulating nutritional behaviours and choice?
- 10. What are the genetic, epigenetic and early life environmental exposures that predict health and impact on human capital? How might we take this forward in a disruptive way?
- 11. How to influence population health by understanding and improving food composition?

From these 11 research questions, 8 were developed more fully into research pitches that were considered for pump priming funding. Each attendee selected which question they worked on and which group they worked with. The teams showcased their preliminary research project in a 10-minute presentation on the final day to a specially convened Nutrition Advisory Panel.

## Research questions developed into project pitches

- 1. How does diet and exercise mediate muscle physiology to influence health: a systems framework
- 2. Determining the optimal staple waning food across global populations ad within individuals
- 3. INFALM consortium: interactions between nutritional status and inflammation
- 4. Enhance the burn: long term nutritional health challenges following childhood disease
- 5. Nu-MET: Nudges to metabolically characterise nutritionally compromised individuals
- 6. DOMINO: diet on microbiome interactions for better immune outcomes
- 7. Individualising diets for life course health
- 8. ROAM refugee camp trial. What is the impact of a radical improvement of social and environmental change on child growth and development?

Four of the groups were shortlisted for pump priming funds to continue development for the next 12 months. The projects will be followed up at 6, 12 and 24 months to review process of the developing research concept, collaborative team and plans for follow on funding.

#### The successful research pitches

- DoMInO: Diet on Microbiome interactions for better Immune Outcomes.
  Applicants: Sophie Moore (Kings), Andrew Prentice (MRC Gambia), Carlito Lebrilla (UC David), Ruairi Robertson (QMUL) and Eran Elinav (Weizmann Institute).
  Summary: A novel project that will use the seasonal variation in vaccine response as an 'experiment of nature' to interrogate how diet-microbiome interactions might influence infant immune development
- 2) Nu-MET: NUDGES to Metabolically Characterise Nutritionally Compromised Individuals. Applicants: Albert Koulman (Cambridge), Jay Berkely (Oxford, KEMRI), Robert Bandsma (Toronto), Jessica Farebrother (Kings), and Lars Dragstead (Copenhagan).

**Summary:** Creating an adaptive mechanistic research platform to investigate how nutritionally compromised individuals (at both ends of the nutrition spectrum) respond to metabolic challenges.

3) Enhance the Burn: Improving metabolic 'burn' to re-establish healthy skeletal and adipose metabolism. Applicants: Steve Wooton (Southampton), Mike Stevens (Bristol), Marlou Dirks (Exeter), Julian Hamilton-Shield (Bristol), Helen Roche (UCDublin), Saaed Shoaie (Kings), Adil Mardinogl (Kings) and Lars Dragstead (Copenhagan).

**Summary:** Generating a deeper understanding of muscle metabolism and nutritional status by investigating survivors of childhood cancer as a model for accelerated aging.

#### 4) Applying food science to inform diet choices and improve health.

Applicants: Luke Bell (Reading), Alan Walker (Rowatt), Emily Balskus (Harvard), Cathrina Edwards (Quadram), Margaret Kosek (John Hopkins) and Lindsay Hall (Quadram).
 Summary: Approaching the concept of the nutritional value of weaning foods across the entire food pathway from crop variation to individual effects on metabolism and the microbiome.

## **Reflections for nutrition science**

Through the planning and delivery of *Transforming Nutrition Science for Better Health* meeting several important themes emerged that may have relevance to the wider nutrition community.

#### The challenge of being truly disruptive

This meeting sought to spark different and innovative thinking; over two thirds of delegates felt new ideas emerged and praised the format for getting attendees to think differently:

> "I have heard so many different opinions about so many things outside my field, which was really helpful"

#### "made one think 'out of the box'"

At the same time, there was a sense that the truly different ideas did not come forward. The meeting was short and so there was limited time for groups to form and reach the depths required for innovative ideas. The need for different expertise to help address some of the research questions was also identified. Some felt that the successful pitches were not different enough from standard nutritional research highlighting a major lesson learned - that it's hard to think disruptively:

> "I felt the endeavour was great – well intentioned – accurately targeted – good facilitation etc. I think you were let

down by we, the participants. Many seemed to find disruptive thinking just beyond their scope."

The question of succession within the field of nutrition research, particularly in undernutrition, was raised. In addition, delegates highlighted the difficultly of generating truly novel ideas and approaches with so many wellestablished nutrition scientists in attendance. There was a plea for more mid-career participants and fewer very established, senior scientists to ensure truly disruptive ideas.

> "The 'most experienced' of the attendees are like the elders of the tribe – we need them, their experience and their input: they have so much to add. However, they must also realise when to step back and not run the show"

## Reaching other disciplines is challenging

Despite inviting an array of multidisciplinary researchers to discuss nutrition science, a skills matrix revealed that most delegates were involved in human/clinical or population studies partly due to differential dropout rates (Figure 4). Some delegates indicated there was a need for a greater breadth of voices to truly spark new ideas; suggested disciplines included sociology, engineering, physics, geography. Many of the missing areas identified had been on our 'long list' of invitees but they were not able to attend. To foster multidisciplinary team science in nutrition, funders need to consider how to engage disciplines that may not view nutrition as a core interest; a first step is ensuring researchers from a variety of fields can see value in attending a meeting such as this.



Figure 4: The expertise of over 200 potential meeting attendees was mapped according to research area (defined loosely on Wellcome Science Division funding streams).

## We need to bridge gaps between disciplines

The meeting format was successful in supporting networking as 88% of attendees said they had made new collaborative connections with 81% stating that they planned to work with these new contacts in the future. Professional facilitators managed the diverse delegation well, keeping the group work dynamic, and were very effective at getting full engagement from everyone. "great to meet people who I wouldn't otherwise meet and see that there is a lot of common ground"

### "the 'musical chairs' format worked really well"

While there were clear successes, it's important to recognise that cross-disciplinary discussions also brought challenges. Finding a common language and starting point for discussion between more mechanistic researchers and the applied nutrition community was challenging with some groups not fully exploring the potential that more fundamental scientific insights could provide.

#### There are opportunities for

#### invigorating nutrition science

We asked attendees what else could be done to invigorate nutrition science. Some of the common suggestions included:

- 1. More meetings like this!
- 2. Training ensure methodological rigour in all research
- Increased pull-through from research to policy
- Funding Calls for really innovative projects. Grants for bold steps not just incremental studies. Funding for interdisciplinary science collaborations. Greater opportunities and support for early career researchers. ECRs

Specifically, funders were asked to:

- 1. Provide leadership and support for effective partnerships between nutrition science and other disciplines
- 2. Support methodological advancement and standards
- Encourage diversity and inclusion look beyond the same research groups that are always funded
- 4. Force different disciplines to work together
- 5. Ensure the importance of nutrition is realised within broader disciplines
- 6. Involve industry and policy makers in these discussions
- Show coordination on the global nutrition agenda/action plan: reduce papers and increase actions
- 8. Provide a safe space for collaborative discussions for funders
- 9. Work together on shared strategic priorities to achieve more.

## Conclusion and next steps

The Wellcome/WHO meeting *Transforming Nutrition Science for Better Health* was an innovative way of starting a conversation about emerging research priorities in nutrition science. The collaboration with the WHO ensured the identified research questions had a view to global policy requirements. The meeting demonstrated a huge appetite for increased multidisciplinary working in nutrition and for coordinated research across basic biological, clinical and applied population fields and for breaking down the silos that currently exist.

The two focal topics of muscle and the microbiome highlighted the untapped potential of these frontiers in nutrition research. Both require truly multi-disciplinary approaches to advance our understanding and are well placed to benefit from advances in technology including Big Data approaches.

The meeting met its main objective to develop new research collaborations and projects in nutrition science. Time will tell if these fledgling research concepts develop into larger scale projects. We hope that sharing meeting information with the wider research community will highlight the topics identified that were not addressed in this meeting and that they will be picked up by others in the field. More broadly, we hope that the nutrition community will consider Wellcome as a potential funder of nutrition science (see *appendix 5*).

Over the course of the meeting several themes emerged that have wider implications for the nutrition community:

- Defining health: How do we define nutritional health? This seemingly simple question was discussed at length. With many asking if we can truly define nutritional health or realise the promise of personalised nutrition without this information. With new technology do we need to rethink what this is and how we measure it?
- 2) Study design: Limitations of animal models highlighted the importance of innovative human trials. A discussion on dietary assessment showcased its major role in nutritional research but there is a need to find more accurate and objective ways to measure dietary intake. A need to incorporate mechanistic understanding into studies was identified.

- Measurement/Phenotype: Calls for a consortium to 3) develop human nutritional metabotype classification and tools to stratify populations to ensure consistent approaches to functional biomarkers, for example. Other questions included: What do we base the right diet on? What is the right marker for health? Is it alucose metabolism, bone health. muscle metabolism? There is also a need to understand variation: why do different people respond differently to different food environments, diets and to interventions? How could we use this information to target nutritional advice? Can we develop noninvasive clinical measures of muscle health and performance?
- 4) Data/Al/Machine learning: This topic was raised several times during the meeting, including by the research pitches that are planning to use Big Data to help address their research questions. Standard data collection, harmonisation of smaller data sets that can be combined, and long-term data collection across the life course need further consideration. What about real-world health data? How can social media be used to study the behavioural and social aspects of nutrition?
- 5) Implementation: How do we best implement strategies to improve nutrition, and what can we achieve before 2030 (urbanisation tipping point)?
- 6) Social context: To what extent does our social setting influence the nutritional value of our diets? What is the effect of advertising and food education? How do we protect the public from inappropriate or overinflated claims? Furthering understanding from how to eat a healthy plant-based diet to help the environment as well as nutrition to understanding the impact of processing, cooking and preparation on the nutritional status of the food we eat. There were calls for a food encyclopaedia to capture this information in a useable format.

A final question from the meeting was 'how do we put the good back into food and find the pleasure in change?!'

This meeting provided a useful opportunity to reflect on some of the barriers and opportunities that exist in nutrition science globally and to consider how the field could develop to make a greater impact on health. Collated responses revealed some commonly perceived barriers to be overcome:

- i) Compartmentalised and fragmented research community
- Narrow focus of research projects often a one-dimensional perspective focusing on a single nutrient rather than a holistic approach to health. Often the socio-political drivers are ignored in favour of a biomedical focus.
- iii) Lack of mechanistic understanding need for innovative approaches
- iv) Need to bring up the next generation nutrition needs to recruit the brightest
- v) Funding opportunities felt not to encourage the risky and multi-disciplinary research projects needed to move the field forward
- vi) Lack of respect for the field lack of scientific rigour

While some of these were discussed at the meeting, many were not fully explored, and most are not amenable to investigator-led research project funding. We will continue conversations with funders and others about how we can tackle the more intractable problems facing nutrition science globally.

To overcome these barriers, we need a shift in the international field and a system change to how nutrition research is carried out, that requires coordinated action on a global scale. Nutrition is fundamental to the health of individuals and societies. Researchers, funders and policymakers need to come together to embrace new opportunities to transform the field of nutrition science that has the potential to improve health for all.

# Appendix 1: Details of organisational attendees and organising committee

#### **Funders and Actors**

World Health Organisation

International Atomic Energy Agency

Bill and Melinda Gates Foundation

UK Department for International Development

South African Medical Research Council

Canadian Institute for Health Research

UK Medical Research Council

Cancer Research UK

UK National Institute of Health Research

UK Biotechnology and Biological Sciences Research Council

#### **Expert Advisory Group**

Professor Alan Jackson, Southampton University, UK

Professor Sadaf Farooqi, Cambridge University, UK

Professor <u>Jeff Gordon</u>, Washington University, St Louis, USA

Dr Jonathan Wells, University College London, UK

Dr Robert Bandsma, University of Toronto, Canada

Professor John Draper, Aberystwyth University, UK

Dr Eran Elinav, Weissman Institute, Israel

Dr Jay Berkley, University of Oxford, UK

Dr Lindsay Hall, Quadram Institute Bioscience, UK

## Appendix 2: Capacity building case study

Several reviews have raised concerns about the lack of capacity in the nutrition research field. The broad scope of nutrition research, which touches everything from metabolism to food policy, often mean that the topic falls between areas and can be an orphan science. This coupled with the reputation of being less of a rigorous science than other disciplines, results in fewer well-trained nutrition researchers ready to carry the baton for the next generation of nutrition leaders.

To ensure that early career researchers (ECRs) were represented at our meeting we ran an open competition where applicants were asked to submit a blog or vlog outlining an area of health where they felt nutrition science could be transformative. We received 67 applications from 16 different countries and selected six researchers to attend the meeting (see below).



Most of the ECRs said that they felt fully included in the meeting and felt that their voice was heard though, some found it difficult to discuss ideas across disciplines at the start of the meeting. Only 2 ECRs felt that they had met new mentors at the meeting, but all reported that they would pursue a career in nutrition science.

## Appendix 3: Broadening our reach

We wanted these nutrition science conversations to be open to the wider community outside of the London meeting. The purpose of these activities was to 'mobilise, inspire and engage' (see below). A Facebook group was set up especially for this meeting which had over 200 members. This was a forum for both meeting attendees and other interested parties who were unable to attending the meeting itself. Group members were encouraged to introduce themselves on the forum and content was posted to stimulate discussion. Ahead of the meeting we shared expert videos with perspectives on the need for this meeting and live streamed some of the talks. The aim was to facilitate discussion within this larger Facebook group that could feed into the discussions in the room at Wellcome HQ.



## Appendix 4: Summary of research themes

Broad theme	Definition	Topics	Example of disruptive thinking
Consequences	What are the consequences of poor nutrition?	Neurocognitive effects of poor nutrition, predictors on outcome, prevention, variation in response.	Is widespread human malnutrition a unique scenario in nature? And if so why?
Defining health	How do we define health to ensure that we know the outcome that optimal nutrition will achieve (defining what is normal)?	How do we define health, how do we measure health in a standard way, what is the effect of different environments and on different populations?	What functional characteristics are important to understand effects of food and health?
Measurement	How do we measure nutrition?	Move away from using weight as a proxy marker of nutrition, functional biomarkers, best measurements for trials, methods for dietary assessment, standard reporting frameworks for basic science, what are the best measures of health outcome, using technology to improvement measurement of nutrition	Solid phase contrast for measuring metabolism in real time Mismatch between the huge potential of modern measurement science and our ability to use it
Phenotype	How do we define nutritional phenotype of an individual?	Basic nutritional and metabolic phenotyping to redefine malnutrition (metabotype classification system), link genotype and environment to this to understand huge individual variation, dissect risk of heterogeneity to better understand disease risk	Use of Bioprinting and microfluidics
Study design	What is the best way to design a nutritional study?	Innovative trial design, outcome measures (need to be functional), breadth of data collection to allow mechanistic	How can we design interventional studies if we don't know the physiological response to a single meal?

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		analysis, how to control for individual variation, long term outcomes of interventions, big data, combining existing data sets	
Personalised nutrition	Embracing the individual variation in response to nutrition to provide tailored nutritional advice.	How do we understand personal nutrition requirement? What is causing the individual differences? What is the best outcome measure to study personalised nutrition?	ready for prime time?
Implementation	How to take nutritional knowledge and use it effectively at scale to improve people lives?	How do we determine cost effective strategies to tackle under and over nutrition? What can be done pre-2030?	What can be done pre-2030 when urbanisation tipping point is -trade/industry
Life course	Studying nutrition at all ages	What to eat to ensure lifelong health? Diet and aging, how does environment impact on aging, infant feeding and lifelong health, how does the mother's microbiome influence fertility/birth outcomes?	We all age! What diet enables us to age well?
Data / Al	How can data and artificial intelligence help in nutrition?	Need for infrastructure to analyse big data, more knowledge needed of AI and machine learning in the field to understand what the best team is composed of, combine existing data sets, use of social media data	AI, machine learning: what is the ideal makeup of the team? How do we direct the questions?
Diet and food	What do we need to know about diet and food to better understand nutrition?	Functional foods, plant derived foods/plant-based diets, characterising local food staples, how do we reliably measure what food goes in, weaning foods, protecting the public from inappropriate or overinflated	Can we develop a food map? What data are important? Modern food-what does it contain? How it impacts on health? Going beyond micro/macronutrients

Data / Al	How can data and artificial	claims, role of diet diversity, interaction between host and diet, effect of food processing on nutrients, variation in crops	Al machine learning: what is the ideal makeup of
	intelligence help in nutrition?	analyse big data, more knowledge needed of AI and machine learning in the field to understand what the best team is composed of, combine existing data sets, use of social media data	the team? How do we direct the questions?
Diet and food	What do we need to know about diet and food to better understand nutrition?	Functional foods, plant derived foods/plant-based diets, characterising local food staples, how do we reliably measure what food goes in, weaning foods, protecting the public from inappropriate or overinflated claims, role of diet diversity, interaction between host and diet, effect of food processing on nutrients, variation in crops	Can we develop a food map? What data are important? Modern food-what does it contain? How it impacts on health? Going beyond micro/macronutrients
Inflammation	How does inflammation affect nutrition and vice versa?	Immune system nutritional requirements, what is the role of inflammation in poor nutrition, is inflammation a driver of poor nutrition, what drives inflammation, how can we break the cycle of chronic inflammation in under nutrition	In children which comes first: 1) innate immune dysfunction, 2) inflammation, 3) malnutrition or the reverse?
Microbiome	The gut microbiome and nutrition	effect of the microbiome on host metabolism, how does the microbiome interact with food, how does the microbiome impact inflammation in poor nutrition, scalability and generalisability of microbiome interventions,	How do we know what trajectory to put the microbiome on to affect health? How much does the microbiome contribute to a phenotype and the host?

Metabolism	How does nutrition influence metabolism	functional outcomes after microbiome interventions, standardisation of approach to studying the microbiome, how resilient is the microbiome Metabolomics in poor nutrition, whole body metabolism at	How far does early weaning/programming predict/influence/determine metabolic and
		systems level, outcome measures to determine physiologically relevant impact of nutritional interventions.	immune health?
Muscle	Interactions between nutrition and muscle	How best to measure muscle? (mass, function, body composition), muscle as an endocrine organ, myokine profiles to characterise status before and after recovery.	What interventions could act on the microbiome to promote muscle health?
Conceptual thinking	Ideas that did not fit in well with other categories – often about the approach that should be taken	Funder collaboration, diets that are good for people and the planet, sustainability agenda impact on food and nutrition, understand the complexity of food to make it easier to alter/manipulate, innovative metrics to link food security, nutritional status, health outcomes; public awareness of nutrition	Could we just survive on bowl of leaves? Like gorillas or cows?

These themes emerged from group discussions aimed at identifying transformative nutrition research ideas. Themes were then grouped into common areas as clusters for further group discussions.

## Appendix 5: Current funding sources at Wellcome

Wellcome supports research across a broad range of subjects with the overarching aim of improving health by helping great ideas to thrive. Our funding schemes offer grants across biomedical science, population health, medical innovation, humanities and social science and public engagement. The majority of Wellcome funding schemes are 'open-mode' where there is no specific theme or targeted population. For most schemes the principal applicant needs to be based either in the UK, Republic of Ireland or a Low or Middle-Income Country. More information on our funding schemes can be found on our <u>website</u>.

Some key schemes of interest to the nutrition community:

<u>Collaborative Awards in Science</u> promote the development of new ideas and speed the pace of discovery. We fund teams of researchers, consisting of independent research groups, to work together on the most important scientific problems that can only be solved through collaborative efforts. Awards are available for up to £4 million and up to 5 years.

<u>Collaborative Awards in Humanities and Social Science</u> funds teams who are tackling major health-related questions in the humanities and social sciences that require a collaborative approach. Awards are available for up to £1.5 million for 3-5 years.

<u>Investigator Awards in Science</u> enable independent researchers with a compelling research vision to tackle the most important questions in science. Awards are available for up to £3 million and up to 7 years.

<u>Investigator Awards in Humanities and Social Science</u> enable humanities and social science researchers with a compelling research vision to tackle the most significant questions in human health. Awards are available for up to £1 million for 3- 5 years.

<u>Innovator Awards</u> supporting researchers transform great ideas into healthcare innovations that could have a significant impact on human health. Awards available for up to £500k over 2 years or up to £750k over 3 years for multidisciplinary projects.

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Wellcome exists to improve health for everyone by helping great ideas to thrive. We're a global charitable foundation, both politically and financially independent. We support scientists and researchers, take on big problems, fuel imaginations and spark debate.

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