Yakult

Science for Health

YAKULT SCIENCE WEBINAR: THE MICROBIOME, APPETITE & CARDIOMETABOLIC HEALTH

YAKULT SCIENCE WEBINAR
THURSDAY 9TH JUNE 2022

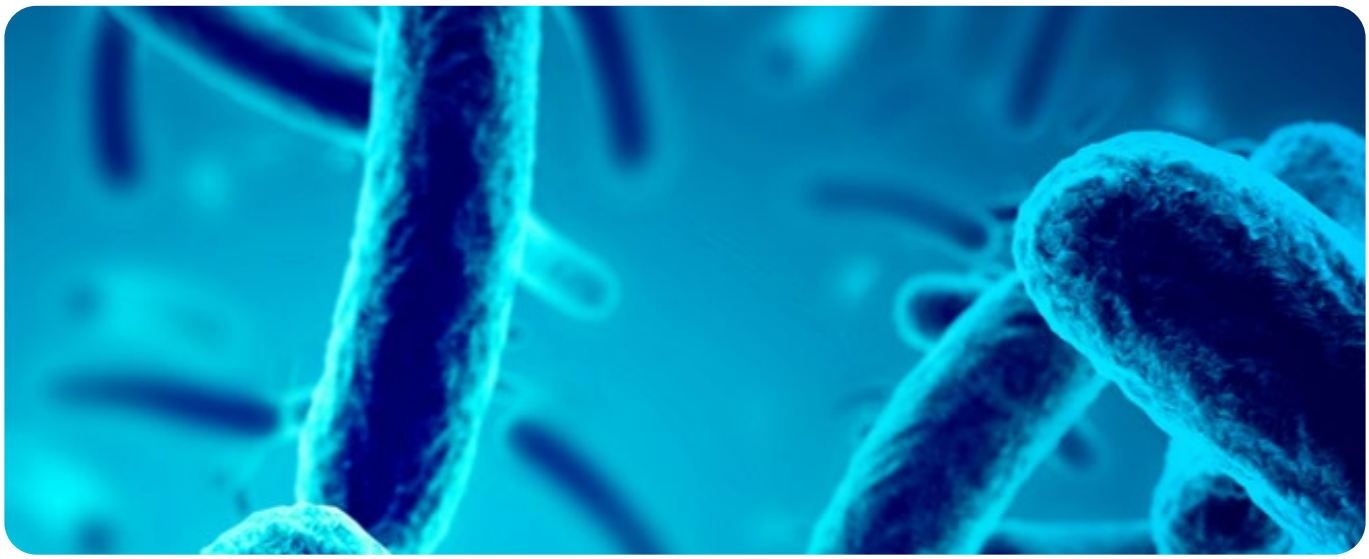
FREE WEBINAR
VIRTUAL EVENT

EXECUTIVE SUMMARY

INTRODUCTION

The gut harbours an enormous diversity of microbes essential for the maintenance of metabolic homeostasis and wellbeing. The importance of the microbiota has been shown in metabolic disorders, including obesity, as well as in affective disorders, such as anxiety and depression, which are often associated with changes in food preference and intake.

Yakult Science presented a webinar to delegates across UK and Ireland on the microbiome, appetite and cardiometabolic health, moderated by Brittany Pearse ANutr, Science Officer, Yakult.



EXPERT PRESENTATIONS

HOW BARIATRIC SURGERY WORKS AND WHY IT DOESN'T – HOW CHANGES IN THE POST-OPERATIVE WEIGHT LOSS MICROBIOME INFLUENCE OBESITY-RELATED CO-MORBIDITIES PRESENTED BY DR JAMES KINROSS

Over 250,000 weight loss surgeries (known as bariatric surgery) are performed in the USA each year, [around **6-7 thousand** performed annually in the UK] and it is increasingly accepted as a highly effective treatment for obesity and its associated metabolic complications. Bariatric surgery induces changes in weight and insulin resistance through a complex series of mechanisms beyond calorific restriction and the microbiome is thought to play an important part in this process. Moreover, the gut microbiome may even be used to predict the effectiveness of specific surgical strategies for weight loss. However, several types of bariatric surgical techniques are used and their influence on the microbiome is variable depending on the approach.

Despite the strong evidence for its health benefits, weight loss surgery also carries some risk, and the unintended consequences of permanent changes in the gut microbiome are not fully known. In his presentation, Dr James Kinross explained how the microbiome is altered after bariatric surgery and defines how this in turn influences both the success of the procedure and its associated increased risks e.g., bowel cancer.

Dr Kinross defined how weight-loss surgeries alter the body's other microbial niches, including the vaginal microbiome and can have an impact across generations. There are metabolic changes across multiple systems in the body post-surgery and the disruption of the microbiome bile acid signalling axis is one example of the influence metabolic surgery has on gut-microbial-host metabolic cross-talk (Li et al., 2011). There is a complex chain of events that occurs as a result of redirecting bile acids post-surgery, causing changes in the gut microbiota and bacteria present, this in turn perturbs the gut-liver and gut-brain axes which are vital for human health. Finally, Dr Kinross demonstrated how the microbiome could be treated with probiotics or engineered to improve the efficacy and safety of these procedures. Probiotic use to improve the outcomes of bariatric surgery still needs more research but it is clear that the microbiome can be targeted to improve the safety and efficacy of bariatric surgery.

QUESTIONS FROM THE AUDIENCE

Q: What would be your recommendations for probiotic post gastric surgery at present given that it sounds like the evidence is not strong based on current studies undertaken to date- what do you do in practice?

A: The diet can have an impact on the gut microbiome but we need more research on probiotic intake in the post-operative phase. It also slightly depends on why you are giving them e.g. to augment the resolution of insulin resistance or to prevent the complications from surgery? General advice would be to go for multistrain and high-dose probiotics.

Q: What are your thoughts on alternatives to the use of bariatric surgery outside of the food you eat?

A: Implement policies that could impact the food environment and consider alternative therapies, including a multidisciplinary approach with a team to support behaviour change.

Q: Do you recommend psychosocial intervention with the surgery?

A: Bariatric surgery is delivered alongside psychosocial intervention in the UK and is part of a tier 4 system.

Q: People who undergo bariatric surgery usually follow various diets to get them to lose weight quickly prior to surgery e.g. the ketogenic diet. How damaging is this for their microbiota and are there any benefits to starting them on probiotics prior to surgery?

A: Bariatric weight-loss diets are designed to improve liver function and make it more amenable to surgery. In these super obese patients, these radical diets are essential. However, they are really poor for gut health in general. High protein and high fat drives inflammation.

Q: Post-surgery, people with a smaller stomach may tend to not eat as many or plenty of vegetables/ fruits due to feeling fuller quickly and therefore missing key nutrients and prebiotics in their diet. Are these populations at higher risk of microbiota dysbiosis and how can this be overcome? Could powdered or freeze-dried vegetables/fruits play a key role in this population?

A: Post operatively, yes, getting fibre in is a challenge, and many patients develop a sort of post-operative IBS. The trick here is a) education b) very gradual and selected increase in fibre content and c) removing animal fat. Yes, you can use fibre supplements as an adjunct (We have a trial on this).

Q: How much of an impact do you think exercise levels have on the microbiota?

A: Different people will have different responses to exercise and their microbiota, Men and women have different responses to exercise and the gut microbiota. Athletes have a different microbiota to the general population The take-away message is that exercise can improve diversity in the microbiota which might have secondary gut-brain axis effects and in some populations like in an IBS population exercise can reduce their mental health burden.

Q: Primary care patients are often confused about doses for probiotics do you have a rough guide?

A: This is a massive problem. I always recommend Kefir as a starting point. It is cheap and easily accessible. Not technically a probiotic, but often works as well. **hcp.yakult.co.uk/resources/341/probiotics-toolkit**

Q: For how long would one have to follow a diet rich in prebiotics/probiotics to notice any changes in mood?

A: Generally, I recommend 4 weeks for the probiotic to engraft. However, a high-fibre diet can have an impact within two weeks.

Q: Can you please explain the role of faecal transplant (FMT) in improving the microbiota and who is it indicated for??

A: Currently this is only used for C. *difficile* infection but there are a number of trials ongoing to determine the use of FMT for obesity but it only seems to be effective alongside dietary intervention.

THE MICROBIOME, MOOD AND FOOD: NOVEL INSIGHTS IN THE MICROBIOTA-GUT-BRAIN AXIS AT THE INTERFACE OF METABOLISM, THE CENTRAL REGULATION OF FOOD INTAKE AND STRESS PRESENTED BY DR HARRIËT SCHELLEKENS

In the last decade, there has been an enormous expansion in our knowledge of the gut microbiota. Obesity, diet and stress are linked. Poor diet and unhealthy food choices increase stress vulnerability and can lead to low mood. Stress can drive the intake of so-called high-caloric comfort foods. Understanding the mechanisms by which the gut microbiota influences host appetite and eating behaviour, to impact metabolism and mood, will provide a better understanding of conditions wherein appetite is dysregulated. Moreover, the microbiota is emerging as a unique source of metabolites with the potential to modulate targets across the gut-brain axis, which provides a promising opportunity to mine the gut microbiota for novel effective biotherapeutics and microbiota-targeting strategies against obesity and stress-related disorders.

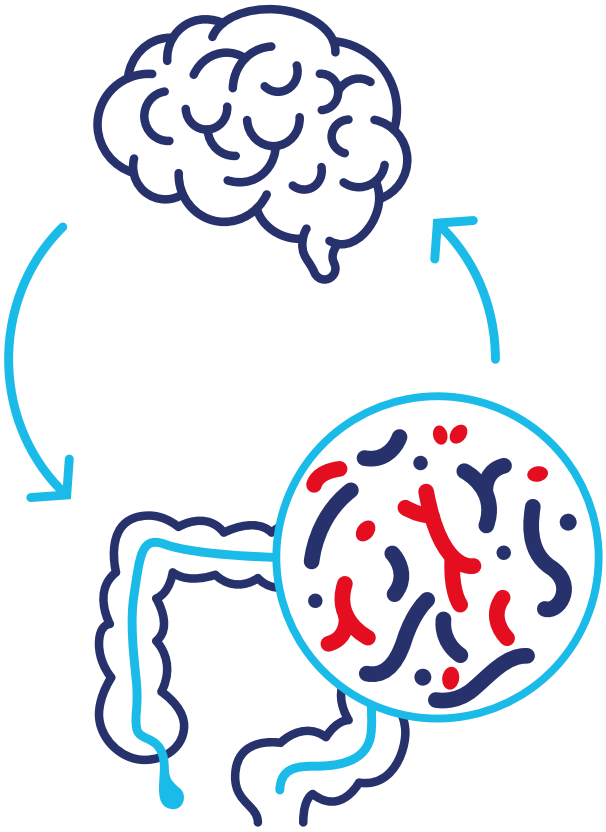
In her presentation, Dr Harriët Schellekens highlighted novel evidence of microbiota-mediated effects on metabolic health and the stress response.

In the postprandial state, anorexigenic hormones glucagon-like peptide-1 (GLP-1) and peptide YY (PYY) are secreted by enteroendocrine cells. Nutrient sensors in the proximal gut stimulate the release of these hormones. However, it appears that in the distal gut, bacterial metabolites (including SCFAs, specifically acetate, and secondary bile acids) may also stimulate the secretion of these hormones. This is notable, given bacteria will continue to ferment nondigested nutrients many hours after consuming a meal. The metabolites can act locally in the gut and mediate enteroendocrine cells and have an impact on the central regulations on metabolism and appetite. The ultimate goal is to identify novel dietary and microbiota-derived strategies to support mental health and metabolic health (Torres-Fuentes et al., 2017).

Dr Schellekens highlighted recent findings from her laboratory on the translational effects of a novel identified probiotic *Bifidobacterium longum* in obesity, the central regulation of appetite and stress. They found that *Bifidobacterium longum* attenuated Ghrelin receptor signalling and had anti-obesity effects and was successful in translation to humans. The beneficial effects were seen in relation to glucose homeostasis and reduction in corticosterone in those with the probiotic supplement. The findings reinforced the link between metabolic disease, mental health and the potential amelioration of both via microbiota-targeted interventions (Schellkens et al., 2021).

Microbiota-mediated approaches can impact stress responses and stress eating involved in the neural control of homeostasis of eating and stress reactivity. Prebiotics fructo- and galacto- oligosaccharides (FOS/GOS), have been related to reductions in stress hormones, beneficial anxiolytic effects and antidepressant effects in preclinical models. The changes in behaviour were associated with increases in bifidobacteria (Burokas et al., 2017). The studies on stress with prebiotics and fibre supplements show overlap with the gut-brain axis in obesity and neuro-inflammation. Other dietary fibre interventions have been demonstrated to improve other cognitive parameters, showing the nutritional impact on the gut-brain axis in the context of the psychobiotic diet. There is still incomplete evidence on the mechanisms for mental health and the gut microbiota in the psychobiotic diet (Leyrolle et al., 2021)

Future areas for exploration are treatments targeting microbiota support, investigating the mechanisms of the individual strains of bacteria and determining their specific properties to understand their interaction. Determining the right bacteria, at the right time and for the right person to apply to precision nutrition. Selecting specific strains and discovering their mechanism with the gut-brain axis can support further developments in psychobiotics and precision nutrition for metabolic and mental health.



QUESTIONS FROM THE AUDIENCE

Q: What role do you think that the mechanisms of the microbiota-gut-brain axis have in eating disorders?

A: We know there is an alteration in gut microbiota in eating disorders but we need to be careful with [establishing] causation. We need to determine if there is a modulatory role of the microbiota or does it mediate some of the mechanisms in eating disorders and the interactions with the microbiota and the diet. The microbial composition can change in eating disorders and we need to understand baseline microbial composition. We are not there yet to say that microbial composition is a mechanism in the development of eating disorders.

Q: When it comes to the GOS/FOS ratio, which ratio and dosage do you recommend in adults?

A: 1:1 ratio but our research is in preclinical models. There is a lot of research out there using different dosages. More research is needed to determine the dosage.

Q: If you are born with poor microbiota, can the risk of obesity be overcome with improved microbiota through diet?

A: Eat more foods from all colours of the rainbow and diversity of foods to increase fibre intake. Yes!! You can make massive changes quickly with diet and fibre is key… at least 30f/day more likely 50g/day: **nature.com/articles/ncomms7342**

Q: Is it most beneficial to prioritise pre-biotics and enhance bacteria already present or to add pro-biotics in those with obesity or mental health conditions?

A: Both are valid strategies but it comes down to precision and individuality and what the mechanisms are. We need more research on precision probiotics but to cover all angles, the recommendation currently is to eat a diverse diet.

Q: You mentioned kefir at some point. Do you think that it can benefit stress and cognition?

A: Kefir in animal studies can improve cognition and memory and there are some translational studies that have shown that as well. Introduce fermented foods slowly. We also have to acknowledge that it won't work for everyone and it is not itself a panacea. So, this intervention has to be made as part of a larger behavioural support package.

UNCOVERING NEW INSIGHTS: THE COMPLEXITIES OF DIET-MICROBIOME RELATIONS PRESENTED BY MS EMILY LEEMING

The gut microbiota is a dynamic ecosystem predominantly residing in the lower colon, comprised of bacteria, viruses, fungi, and archaea. There are multiple influences on the gut microbiota, including diet, xenobiotics, the environment, and genetics. Diet is of particular interest as a potential non-invasive modifiable contributor to the microbiome to improve host health. The relationship between the gut microbiota, diet and host health, however, is complex.

In her presentation, Emily Leeming discussed this complexity, and how we might further unravel our understanding of these relations. The talk gives a brief overview of new potential ways to model dietary data, considerations for covariates such as transit time, and introduces the metabolome.

The PREDICT programme is an ongoing research programme to measure postprandial responses to food. It uniquely combines traditional academia with a tech company of data scientists and machine learning experts to achieve precise, high-quality output at scale. Under this programme, a 2021 study used microbiome features to predict each dietary variable from Food Frequency Questionaires (FFQs). Researchers found tight correlations between microbial composition, and dietary patterns, such as healthful and unhealthful plant-based dietary intakes, and specific foods, such as coffee. Healthy plant food intake was associated with beneficial microbial species (including butyrate-producing bacteria) and cardiometabolic health indicators (e.g., blood glucose, blood lipids, body fat and CVD and T2DM risk).

Emily Leeming discussed that we need to consider not only how we model dietary data but also the covariates we should adjust for. For example, one of the most commonly shared statements in gut health is that consuming 30 or more plant-based foods a week is associated with increased microbiota diversity from the American Gut Project. The dietary data was based on a self-reported survey question which was less granular than a FFQ, while the '30 plants' was due to the analytical approach of investigating tertiles rather than specifically 30. Likewise other metrics in the study, e.g. snack intake and fruit intake were more strongly associated with microbial composition than plant diversity, though these were not adjusted for confounding factors (McDonald et al., 2018). Emily Leeming suggested that this is an example (despite being a positive message for health), where we need to improve the quality of dietary data collected and the analytical approach so we can fully understand what specifically impacts the microbiota for dietary therapeutic interventions.

There are other questions to be answered concerning the gut microbiota and diet. We need to determine what the microbes are doing and the impact the chemicals they produce, such as, short-chain fatty acids (SCFAs), have on health. Menni et al. (2019) found that bacterial metabolites are more strongly associated with health traits than markers of bacterial diversity. There are large differences in the metabolomes of those eating a vegan diet compare to omnivores yet there were not significant differences in microbial composition (Wu et al., 2014). This highlights that perhaps we need further focus on the function of the gut microbiota vs. the composition.

In conclusion, increased emphasis is required on the precision, depth and breadth of dietary data and dietary analytical methods in diet-microbial research.

QUESTIONS FROM THE AUDIENCE

Q: When looking at the effect of diet on the [gut] microbiome, would looking at healthy diet diversity be better than looking at dietary patterns such as the Mediterranean diet or plant bioactive molecules like polyphenols?

A: In the past, we have looked at a priori dietary patterns but we should move away from this to look at specific dietary patterns in a person's diet and how similar that is to another person. The polyphenol databases are not always comprehensive.

Q (continued): Also, is there a way to more accurately capture habitual diet than using FFQs?

A (continued): A common approach is using weighted food diaries over 3 days or more to capture cultural foods, how foods are cooked and more specific quantities. Using technology can make more precise collections of dietary data and make it more accessible.

Q: What are your thoughts on antibiotic consumption impacting e gut microbiome stability over the life course?

A: If antibiotics are prescribed by a healthcare professional, they should always be taken. There are certain periods throughout the life course that they can have more of an impact like in the first few years of life which has been associated with increased risk of autoimmune diseases and obesity in later life.

Q: Have there been any foods that you have found to be particularly detrimental to the health of microbiota that you would find in the typical western diet?

A: It's important to focus more on having enough whole foods in the diet that fuel gut bacteria to give the microbes what they need rather than zooming in on 'bad' foods. However, not enough fibre, typical in a Western diet, is detrimental to health of microbiota.

Q: What is your opinion on the influence of timing of food intake on the microbiome and its function (for example in the framework of intermittent fasting)?

A: Time-restricted eating is about having an eating window where eating begins at a certain time and eating then stops at the close of that window. This gives the microbes time to stop and rest and clear everything out. Currently it seems that an eating window of 8-10 hours likely helps to support your metabolic health as well as your gut microbes.

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