

IPA Response to Washington Post article, "Probiotic supplements may do the opposite of boosting your gut health"

"Probiotics" according to the WHO/FAO definition are, "Live microorganisms that, when administered in adequate amounts, confer a health benefit on the host. "Thus if the microbes themselves do not provide a benefit, they cannot be considered "probiotic", but potentially even pathogens if they cause harm. The Washington Post article makes some very strong conclusions about probiotics offering little benefit using what appears to be 'social media' instead of scientific evidence.

The 'Hype' of Probiotics is Real

Underpinning this multibillion-dollar industry are over 1600 registered probiotic clinical studiesⁱⁱⁱ, over 700 indications for probiotic supplements^{iv}, and millions of probiotic doses taken daily around the world by a variety of individuals, with no reported deaths in healthy people due to probiotic supplementation to date. Probiotics foods and dietary supplements are regulated around the world with a variety of safe lists, and a number of quality and manufacturing procedures. This is not hype, this is a science-backed, established industry^v.

Probiotics do not Damage the Microbiome

The article states, "Studies show that taking probiotic supplements — for overall health or to counter the effects of antibiotics — can alter the composition of your microbiome and reduce the levels of microbial diversity in your gut, which is linked to a number of health problems." This is a false equivalency and is not at all supported by scientific evidence. Microbiome profiling is often performed in probiotic studies, but is not a clinically-accepted biomarker, and varies greatly in how it is performed, analyzed, and interpreted. Also, a recent scientific review paper on safety of probiotics discourages relying on microbiome profiling as a safety assessment^{vi}. Thus, while lower diversity in the gut microbiota is generally linked to several health problems, no evidence has been provided by the author to demonstrate that probiotics can lower the diversity and thus cause health problems.

The Suez et al paper form 2018 has already been dismantled by scientific experts^{vii} but suffice to say that the paper is misquoted and the data has unfortunately been taken out of context yet again. The design of the study was such that all groups experienced significant damage to their microbiota by antibiotic administration and then the treatments - including a probiotic - were applied. The reality is that most doctors recommend a probiotic at the latest during antibiotic treatment if not before to help mitigate the damage of antibiotics. It is antibiotics that cause damage to the microbiota, not probiotics.

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Divorcing the Biotic Family?

Comparing or contrasting benefits of a fermented food, a prebiotic, a postbiotic, a probiotic, or any other biotic can be useful, but ultimately each has its own place in supporting and maintaining health. Unfortunately, the Washington Post falls prey to the misconception that fermented foods contain probiotics the microbial components have demonstrated a health benefit in a good quality clinical trial at the strain level, the microbes in fermented foods should be considered beneficial dietary microbes, not probiotics. Fermented foods by default also do not necessarily contain prebiotics or postbiotics, as they do not typically list specific microbial components, nor their live microbial content through to end of shelf life. It is also noteworthy that not all fermented foods contain live microbes if they have been heat treated or pasteurized. Furthermore, fermented foods may contain an uncharacterized synbiotic culture of bacteria and yeast, so inconsistencies may occur between batches depending on the manufacturing process.

Moreover, from a purely conceptual point of view, a fermented food is more complex and unknown in its composition than a probiotic product, thus to infer that probiotics could be more detrimental than fermented foods are is a paradox. There is not one best diet or food, as such there is not one best product nor ingredient for supporting gut health. As we move to personalization and personalized health, all biotics need to be considered for their specific and unique benefits. It is irresponsible for a public media outlet to make such bold inaccurate contrasts without doing appropriate scientific due diligence to back up their statements.

The Effects of Concentrated Doses of Microbes

Taking a probiotic supplement is indeed a concentrated dose of microbes, typically in the range of a couple of billion live microbes. However, when comparing that dose to the amount of microbes that reside in the innate gut microbiota (trillions to quadrillions, depending on the location in the gastrointestinal tract), it is like a drop in the ocean. It is well accepted within the scientific community that probiotics do not colonize and are not detectable after 7-14 days of cessation of administration; they also do not have the capacity to eliminate species already entrenched in the gut microbiota^{xi}. A vast majority of individuals cannot achieve adequate levels of proper nutrition via diet alone, hence the need for supplementation; this is due to a variety of reasons acknowledged at a global level^{xii}. A similar hypothesis exists in the scientific community regarding exposure to and ingestion of beneficial microbes, of which probiotic supplementation is considered to be a component of.

Apparently, the author not only disagrees with the FAO/WHO on the probiotic definition, but also agrees with Professor Cohen's statement that concentrated doses of microbes are dangerous, which is contrary to the opinion of the FDA, who recently approved the first fecal microbiota product for use in the United States^{xiii}. This live biotherapeutic product also delivers concentrated doses of microbes (at similar or higher

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doses) for targeted medical reasons for specific medical populations. The FDA surely would have not approved this product for specific patient groups, nor allowed for probiotic as dietary supplements for healthy persons to exist on the US market if there were intrinsic safety concerns with administering a bolus of otherwise-determined-to-be-safe microbes for either group of individuals.

The Wastyk Trial

Sadly, the results of the Wastyk trial have been also taken out of context. The observed differences between groups can be explained by differences in the diet; the study was not able to clearly isolate the diet/probiotic effect. The effect of diet interaction is often observed with drug intake. For example, patients on certain medications (Tetracyclines, Fluoroquinolones, Bisphosphonates, Iron, etc) are told to avoid milk or consume it within a certain window before, during, or after medication intake. The study probiotics were designed for metabolic outcomes: "These strains were chosen due to reports of beneficial effects on features of metabolic syndrome..." thus the lack of anti-inflammatory effect is not surprising. When examining the study, one can see that the probiotic group blood sugar and insulin levels actually went down, making it appear that the placebo increased.

Professor E. Sonnenburg is correct that "probiotic supplements can have very different effects in different people", which is an accurate conclusion from her research study and also supports the scientific opinion of the IPA regarding strain specificity. This only serves to underscore the need for science-backed products according to the globally accepted probiotic definition^{xv}. Clinical data on specific strains is critical, in the appraisal of effects and studies conclusions. However, her comment, "...but it also seems that for some individuals [probiotics] can make things worse.", is not only in direct disagreement with the entire scientific probiotic community — probiotic foods and dietary supplements are designed, manufactured, and administered to healthy individuals — but also to some of her previous statements regarding beneficial microbes present in fermented foods^{xvi}. This is no different from drugs and their side affects and the period of dose-finding in certain patients. Many food components can also cause harm to certain individuals: lactose from dairy products, fructose from fruit, high amounts of fiber, certain natural polyols and so on.

Furthermore, the difference in effects can also be attributed to responders and non-responders within a clinical trial. Research should be tailored to separate out responders and non-responders from the screening process, during the baseline measurements, and throughout the study duration. A number of new developments in clinical trials are showing promise to support this, including biosensors, patient staging, etc.

Closing Comments

Probiotics have documented health benefits for healthy individuals in America and across the world. Within the probiotic industry there is generally a lack of longitudinal studies on safety, efficacy, and 'nutri-

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vigilance', and this is typically due to the high cost and low return on investment for low margin products in the food and dietary supplement categories. That being said, the probiotic industry is moving towards interconnected standards and best practice guidelines not only for manufacturing and production, but also for scientific and technical aspects. As health issues worsen within the US and globally, the negative focus on "beneficial biotic" ingredients should instead give rise to the benefits of probiotics, fermented foods and all other biotics. The Washington Post should focus their efforts to highlight positive research regarding immunity, gastrointestinal, and overall health instead of relying on social media evidence to fear monger amongst consumers who seek to derive benefit for their gut and overall health.

The International Probiotics Association (IPA) is a global non-profit organization bringing together through its membership, the probiotic sector's stakeholders including but not limited to academia, scientists, health care professionals, consumers, industry and regulators. The IPA's mission is promoting the safe and efficacious use of probiotics throughout the world. Holding NGO status before *Codex Alimentarius*, the IPA is also recognized as the unified "Global Voice of Probiotics®" around the world.

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iv https://pubmed.ncbi.nlm.nih.gov/32715136/

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xv https://www.frontiersin.org/articles/10.3389/fmicb.2020.01662/full

xvi https://www.nature.com/articles/s41579-019-0191-8