

INTERNATIONAL JOURNAL OF HUMAN NUTRITION AND FUNCTIONAL MEDICINE

International Journal of Human Nutrition and Functional Medicine® www.IntJHumNutrFunctMed.org
(ISSN 2378-4881) is published and © copyrighted by the
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Photo of town center and Roman aqueduct in Segovia Spain by Dr Vasquez

Critical Review • Research Methodology • Research Analysis Tutorial • Microbiome • Diet

Open Correction to PLOS One and Grave Concern about the Journal's Editorial Quality and Review Process: Comment on "Microbiome restoration diet improves digestion, cognition and physical and emotional wellbeing" PLOS One 2017 Jun

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Background

As a researcher, author, clinician, and recent (2015) reviewer for *PLOS One*, I am writing with great concern about the editorial quality and review process of this previously esteemed journal, particularly with regard to the article discussed below. This Letter was sent to the *PLOS One* Editor by email on 20 July 2017 with receipt acknowledged on 21 July 2017; the response that "We encourage you to contact the corresponding authors of the article directly" is absurd as it will not address either the 1) lack of editorial quality, 2) the defects in the review process, or 3) the [in my opinion] erroneous publication of this article. Oddly, *PLOS One* does not publish letters and therefore provides no means for the archived biomedical record (e.g., in Pubmed, PubMed Central, Europe PMC, etc) to be corrected; the only public-access option provided by *PLOS One* is a comments section on their own website which is virtually invisible and unknown to people accessing the article via indexed databases. Thus, given the aforementioned lackluster response and nearly nonexistent channels to correct and critique this *PLOS One* article, this critique is published online publicly and also noted via Pubmed Commons.

Article Review and Critique

In their 4-week open trial with no control group, no laboratory testing, and which relied on participant-reported "data" for every aspect of treatment compliance and treatment effect, the Lawrence and Hyde [1] (*PLOS One* 2017 Jun; doi.org/10.1371/journal.pone.0179017) prescribed a program of psychosocial support (conference call with in-person/online contact with healthcare

provider and support group) and dietary improvements (including avoidance of sugar, alcohol, grains and refined carbohydrates) and then attributed the purported health benefits (including self-reported weight loss and subjective improvements in digestion, cognition, physical and emotional wellbeing) to changes in the participants' gut microbiome. Further compromising the study design, participants were a self-selected "convenience sample of people seeking the services of a nutritional therapist. The majority of participants' primary goal was therefore weight-loss, with several additionally aiming to improve digestive symptoms (chronic acid reflux, bloating, constipation, loose stools, wind), plus energy, and pain issues." Without providing any data to support their conclusion that the intervention changed a single microbe or metabolite from the gut microbiota, the authors assert that, "This dietary microbiome intervention has the potential to improve physical and emotional wellbeing in the general population but also to be investigated as a treatment option for individuals with conditions as diverse as IBS, anxiety, depression and Alzheimer's disease." Similarly and without evidence showing that the intervention modified any parameter of the gut microbiome, the authors assert, "Taken together with our findings, these results suggest that dietary interventions to optimise gut bacteria may have a role to play both in the treatment of Alzheimer's disease but also in optimising cognitive functioning in non-clinical populations." The most remarkable aspect of this research is the attribution of the mechanism of action of their diet intervention to gut microbial modification without a single original data point of evidence; indeed, the authors acknowledge that

the effect of the “diet on the health and diversity of the microbiome has not been directly tested.” To allegedly monitor changes during the intervention, the authors utilized a participant-completed medical screening questionnaire which they acknowledge “was not selected specifically for the purpose of research, and is lacking in detailed information relating to its reliability and validity compared to scales used more specifically for research.”

In summary, this “research article” has the following attributes:

1. No objective data on health outcomes was collected; the study presents only participant-reported subjective data,
2. No objective data on treatment compliance was collected; we do not know if the participants followed the diet nor to what extent,
3. No objective data on treatment effect/mechanisms: **The authors claim that the intervention changes the gut microbiome but failed to measure even a single parameter, microbe, molecule, or metabolite.**
4. Participants were a positively self-selected “convenience sample” ripe and ready for a placebo response given their demonstrated positive expectations.
5. Impossible attribution, especially to the gut microbiome: With no control group, no-one knows if the supposed “improvements” were due to the psychosocial intervention, the diet, the season, the natural history the non-disease being non-studied, chance; the attribution of supposed benefit to a mechanism involving the gut microbiome is not supported by any data in this publication.
6. Short duration with no durability of effect: No demonstrated durability to the supposed benefits; the study was of notably short duration (4 weeks),
7. Wild attribution without any shred of evidence: The treatment included 1) diet intervention and 2) psychosocial support and **then the authors attributed (without any supporting data whatsoever) the subjective/undocumented/purported benefits to 3) changes in the gut microbial composition.**
8. Unreliable methods: The authors note that their use of the Functional Medicine Medical Symptoms Questionnaire “was not selected specifically for the purpose of research, and is lacking in detailed information relating to its reliability and validity compared to scales used more specifically for research” and that
9. No previous validation, as the diet plan “has not been directly tested” for its effect on the “health and diversity of the microbiome.” If this had been a

follow-up survey or symptom assessment based on previous research, then such a publication might be reasonable; however, the authors acknowledge that the effect of the “diet on the health and diversity of the microbiome has not been directly tested.”

10. The financial and self-promotional conflict of interest and the prominent mention of their proprietary book not fewer than 16 times in the manuscript. Does *PLOS One* now publish thinly veiled infomercials—masquerading as clinical research—for proprietary products?

Given all these confounding variables and lack of objective data including zero data showing changes in the gut microbiome, a reasonable reviewer and reader can ask “What—if any—scientific value does this article provide?”

To be sure, we as researchers and clinicians have increasingly appreciated the role of the body-wide microbiome in health and disease, and we appreciate that diet potentially shapes the gut microbiome [2,3]. However, to ascribe health benefits to changes in the microbiome from uncontrolled positively-selected participant-collected data following diet modification and psychosocial intervention is premature at best, unscientific at worst; the authors failed to collect even a single data point showing change in any microbe, molecule, or metabolite related to the gut microbiome, and yet the published title of the article is “Microbiome restoration diet.” (By analogy, we would not attribute a theoretical mechanism of benefit to a new drug that promises, for example, reduction in hypertension without the corresponding evidence via measurements of blood pressure, and I cannot imagine that a high-quality journal would publish an article promoting a new antihypertensive drug if said drug has zero supporting evidence, not even a single measurement of blood pressure.) Studies attributing therapeutic benefit to microbiome improvements should provide evidence supporting their hypothesis via the quantitative correlation of direct microbial analysis (or at the very least via surrogate markers such as serum endotoxin levels or serum 16SrRNA, both of which are also influenced by other factors such as intestinal permeability) with mostly objective data from biochemical markers and reliable tests of neurocognitive and emotional status. The financial and self-promotional conflict of interest and the **prominent mention of their proprietary book not fewer than 16 times in the manuscript** further calls into question the motive and actual value of this publication in a scientific journal. ❖

References:

1. Lawrence K, Hyde J. Microbiome restoration diet improves digestion, cognition, physical emotional wellbeing. *PLoS One* 2017 Jun:e0179017
2. Vasquez A. Nutritional and Botanical Treatments against “Silent Infections” and Gastrointestinal Dysbiosis. *Nutritional Perspectives* 2006 Jan;29(1):5-21 academia.edu/3862817
3. Vasquez A. *Human Microbiome and Dysbiosis in Clinical Disease, Volume 1*. Barcelona: International College of Human Nutrition and Functional Medicine; 2015



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Journal title, ISSN: *International Journal of Human Nutrition and Functional Medicine*
ISSN: 2378-4881

Abbreviation: *Int J Hum Nutr Funct Med*

Websites: www.IntJHumNutrFunctMed.org and www.ICHNFM.ORG

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Chapter XVIII; testimony of Howard Roark in *The Fountainhead* by Ayn Rand



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