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

Alex Vasquez DO ND DC FACN

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 potently 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:
2. Vasquez A. Nutritional and Botanical Treatments against “Silent Infections” and Gastrointestinal Dysbiosis. Nutritional Perspectives 2006 Jan;29(1):5-21
International Journal of Human Nutrition and Functional Medicine is a peer-reviewed evidence-based clinically-oriented publication produced quarterly with periodic special releases in print and/or digital formats (per author request/permission and Editor judgment), available as pay-per-issue, free/open access, or as a membership benefit (included or discounted), in English and/or other languages. As the title of the journal indicates, the focus of the journal is human nutrition (i.e., we publish only human-referent information, not animal studies; however, we will publish translational summaries of new animal research) and functional medicine, a broad clinical and conceptual discipline that seeks to protect, restore, and optimize human health by appreciating human physiology’s systems biology construct and thus the necessity of addressing the totality of factors that influence health and disease outcomes in the psyche and soma of individual patients as well as the social corpus of local and international groups of persons. The journal is dynamic and adaptive; updated information about the journal is available on-line at the website www.IntJHumNutrFunctMed.org. Statement of Social Responsibility: Due to the recent mis-use of science and the misuse of prominent positions to mis-direct public opinion away from science and logic, ICHNFM has found necessity in forming a statement of social responsibility. ICHNFM requires—starting in 2015—that educational materials be socially contextualized with a humanistic emphasis; humanism is a philosophical and ethical stance that emphasizes the value and agency of human beings, individually and collectively, and requires critical thinking and evidence (rationalism, empiricism). In direct opposition to any notion that science and intellectual work are and should be separate from the goal of benefiting human life (ie, financial profiteering, or political misuse of science), we affirm that work in the sciences, healthcare, and medicine should hold preeminent the goal of providing benefit to humanity at large and not private or political interests, in particular what we have defined as the goals of healthcare: physical health and psychosocial freedom, both of which are required for the optimization of human potential and human culture. Likewise, faculty members and teaching staff are required to model beneficence, nonmaleficence, ethics, and justice; repeated violations of these ethical considerations will result first in conversation and if not resolved will result in termination of any working relationship because ICHNFM will maintain its ethics and integrity and will not be tainted by affiliation with faculty or presenters who are socially reckless or maleficent, regardless of the scale or medium (ie, including private emails and public/social conversations and comments). ICHNFM will maintain the highest standards of science, clinical applicability, ethics, and social effect/influence/beneficence.

Upcoming CE/CME Events: Delivered to your home or office

What makes this system great:

- **Your convenience**: Learn at your leisure, at your own pace, in the comfort of your own space. Access the materials anytime, even after completion of the program.
- **Your preference**: Order the monograph in full-color or black-and-white to be delivered to your home or office—see descriptive videos: #1: https://vimeo.com/128642618, #2: https://vimeo.com/129841003
- **Discounts**: Discount code for printed monograph provided on website.
- **Applicability**: Strong foundation in molecular biology, translated for immediate clinical use.
- **Discussions, perspectives, experiences**: Online forums and live discussions available.
- **Time-efficiency**: Save money, time, energy and *the massive carbon footprint* from the hassle of travel (taxis, airport security and waiting, flying, hotels...) just for a conference; use your travel time for your own real/vacation—not for work, just to sit in a conference.

Important clinical topics:

1. Dysbiosis and the Microbiome
2. Mitochondrial Medicine and Mitochondrial Nutrition in Primary and Specialty Care
3. Nutritional Immunomodulation for the Treatment of Allergy and Autoimmunity
4. Implications of Xenobiotic/POP (Persistent Organic Pollutant) Accumulation in the Pathogenesis of Clinical Disease: Evidence-Based Practical Detoxification Interventions

ICHNFM provides R.E.A.L. continuing education

- **Rigorous**: Experience the difference with *expert-level* CE/CME.
- **Engaging**: Attendees access the material via several different media—text, graphics, audio-video, interactive sessions, and the final exam.
- **Accountable**: Each program requires a “final exam” to demonstrate competency (not simply “attendance”) and awards a Certificate of Achievement with the CE/CME hourly credits.
- **Life-changing**: At every step of the way in the preparation of these educational materials, the primary goals are to improve clinician intellectual understanding and clinical skills, ultimately culminating in improved healthcare delivery and clinical practice success.
"Throughout the centuries there were men who took first steps down new roads armed with nothing but their own vision. .... The great creators—the thinkers, the artists, the scientists, the inventors—stood alone against the men of their time. Every great new thought was opposed. Every great new invention was denounced. .... But the men of unborrowed vision went ahead. They fought, they suffered and they paid. But they won."

Chapter XVIII; testimony of Howard Roark in _The Fountainhead_ by Ayn Rand
Note: The Editors at PLOS ONE published my correspondence on their website after it had been publicized on the ICHNFM website, social media, PubMed Commons, and in IJHNFM.

Microbiome restoration diet improves digestion, cognition and physical and emotional wellbeing

Kate Lawrence , Jeannette Hyde

Published: June 14, 2017 • https://doi.org/10.1371/journal.pone.0179017

Reader Comments

Post a new comment on this article

Reader Comment on “Microbiome restoration diet improves digestion, cognition and physical and emotional wellbeing”

Posted by PLOS ONE Group on 11 Sep 2017 at 15:30 GMT

The following comment is posted on behalf of Alex Vasquez. The views expressed are those of the reader Alex Vasquez and do not necessarily represent those of PLOS ONE.

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

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; their response that “We encourage you to contact the corresponding authors of the article directly” is absurd as it will not address either 1) lack of editorial quality, 2) the defects in the review process, or 3) the [in my opinion] erroneous publication of this article.

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.”

Therefore 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 suggest that the intervention may change 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. 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

8. 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.”

9. 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 thirty veiled infomercials 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 potently 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 16S rRNA, 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.

Alex Vasquez DO ND DC FACN
Barcelona, Spain: International College of Human Nutrition and Functional Medicine
orcid.org/0000-0002-9347-4832

2. Vasquez A. Nutritional and Botanical Treatments against “Silent Infections” and Gastrointestinal Dysbiosis, Nutritional Perspectives 2006 Jan;29(1):5-21 academie.edu/3862817
3. Vasquez A. Human Microbiome and Dysbiosis in Clinical Disease, Volume 1, Barcelona: International College of Human Nutrition and Functional Medicine; 2015

Competing interests declared: Competing Interests: Alex Vasquez is founder and Program Director of the International College of Human Nutrition and Functional Medicine, a limited liability company (LLC) in the US and registered business entity in Spain, which sells books and course materials. He is author of a number of books, including “Inflammation Mastery”, which includes the topics of nutrition and the microbiome. Additionally, he provides personal and professional consultations on a fee-for-service basis.