An Ounce of Prevention Is Equivalent to How Much Decolonization Exactly?

TO THE EDITOR—We read with interest the recent Brief Report by Ghani et al entitled “Disease Prevention Not Decolonization: A Model for Fecal Microbiota Transplantation in Patients Colonized with Multidrug-resistant Organisms.” As infectious disease physicians who conduct translational microbiome therapeutic clinical trials of fecal microbiome transplantation (FMT; <https://clinicaltrials.gov/ct2/show/NCT02922816>), and a senior administrator in a large academic medical center, we recognize that reduced antimicrobial administration, length of stay, and bloodstream infections may be important benefits of FMT in the increasingly complex landscape of potential risks [1]. We thank the authors for their work toward advancing understanding of the application of FMT to address threats of antimicrobial resistance.

After reviewing the manuscript and supplemental materials, we were disappointed to find that the authors did not report the absolute multidrug-resistant organism (MDRO) decolonization frequencies or proportions in their study. There are multiple important challenges in attempting to define or detect intestinal colonization with MDROs, much less response to a treatment [2]. However, a major limitation in trying to advance the study of FMT and other microbiome therapeutics is publication bias both in terms of omission of key data and the less frequent publication of studies with negative results. We encourage the authors to make these data available, both to advance understanding and to potentially inform future meta-analyses of data from similar clinical trials.

The authors also do not report the number of FMTs that these patients received. This is a key factor in reproducibility of this work and has been a critical component of understanding the success rates of approximately 90% that have been reported for FMT treatment of recurrent *Clostridioides difficile* infection (RCDI) [3–6]. The dosing strategies of FMT for RCDI, inflammatory bowel diseases, and other applications also vary widely. Dose-response data in FMT as well as timing of FMT relative to antibiotic administration or microbiome conditioning are not well established, largely because of the high observed effectiveness for RCDI but also because of the lack of understanding of mechanisms and hierarchical complexity of metabolite, microbiologic, and clinical data. We encourage the authors to report their FMT treatment data in more direct terms for reproducibility purposes, as well as to contextualize the reportedly lower decolonization rates that the authors observed but did not report in this study.

We agree that there are likely important healthcare utilization, public health, and preventive benefits of FMT that are not fully appreciated. As multiple microbiome pharmaceutical companies are making advances in completion and reporting of phase 3 studies, we expect that expanded access to approved therapeutics will translate to improved care and decreased cost and utilization. We believe that this clinical translation will be best accelerated by publication of absolute effects and detailed description of study interventions and respectfully request that the authors consider a postpublication release of these data.

Notes

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References

- DeFilipp Z, Bloom PP, Torres Soto M, et al. Drug-resistant *E. coli* bacteremia transmitted by fecal microbiota transplant. *N Engl J Med* 2019; 381:2043–50.
- Woodworth MH, Hayden MK, Young VB, Kwon JH. The role of fecal microbiota transplantation in reducing intestinal colonization with antibiotic-resistant organisms: the current landscape and future directions. *Open Forum Infect Dis* 2019; 6:1–9.
- Kelly CR, Khoruts A, Staley C, et al. Effect of fecal microbiota transplantation on recurrence in multiply recurrent *Clostridium difficile* infection: a randomized trial. *Ann Intern Med* 2016; 165:609–16.
- Cammarota G, Masucci L, Ianiro G, et al. Randomised clinical trial: faecal microbiota transplantation by colonoscopy vs. vancomycin for the treatment of recurrent *Clostridium difficile* infection. *Aliment Pharmacol Ther* 2015; 41:835–43.
- Kao D, Roach B, Silva M, et al. Effect of oral capsule- vs colonoscopy-delivered fecal microbiota transplantation on recurrent *Clostridium difficile* infection: a randomized clinical trial. *JAMA* 2017; 318:1985–93.
- Youngster I, Russell GH, Pindar C, Ziv-Baran T, Sauk J, Hohmann EL. Oral, capsulized, frozen fecal microbiota transplantation for relapsing *Clostridium difficile* infection. *JAMA* 2014; 312:1772–8.

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