

## ISAPP 2023: Discussion Group 2

### What is the evidence that a biotic intervention can benefit healthy people?

Chairs: Dan Merenstein and Dan Tancredi

#### Discussion Group Description

**Objective:** To explore available evidence and possible research approaches to establishing that a biotics intervention can maintain health or prevent certain diseases.

**Secondary Aim:** To see if there are sufficient data to propose a review from USPSTF.

**Output:** Peer-reviewed perspective paper or USPSTF proposal.

The FDA generally requires at least two adequate and well-controlled studies to establish effectiveness. However, that level of evidence seldom exists for most interventions – including biotics – **when it comes to keeping healthy people healthy or preventing illness**. If two RCTs are not available, the [Bradford-Hill criteria](#) for evidence of a causal relationship are often suggested to be applicable. Regardless, it is inherently difficult to demonstrate that any intervention can keep healthy people healthy, including diet, exercise, sleep, stress reduction, etc.

The U.S. Preventive Services Task Force (USPSTF) makes evidence-based recommendations for clinical preventive services, including screenings, counseling, and preventive medications. Their approaches are a worth considering, and one can find their recommendations and grades for evidence [here](#).

As an example, it is widely assumed that diet and exercise have a robust evidence base for preventing adverse cardiovascular conditions. However, the USPSTF gives only a C recommendation for behavioral counseling to increase diet and exercise for adults without cardiovascular risk factors. The USPSTF “recommends that clinicians individualize the decision to offer or refer adults without cardiovascular disease risk factors to behavioral counseling interventions to promote a healthy diet and physical activity.” With regard to their assessment of the strength and quality of the evidence, the USPSTF “concludes with moderate certainty that behavioral counseling interventions have a small net benefit on CVD risk in adults without CVD risk factors.”

Is there enough existing data in biotics for any preventive outcome to lead to the same or stronger conclusions as did the USPSTF for behavioral counseling interventions to promote a healthy diet and physical activity?

#### Questions for speakers to consider and try and address for their talks:

Scope: The focus of our discussion will be on endpoints studied in generally healthy populations. We will not discuss use of probiotics for UC, rheumatoid arthritis, at risk of developing NEC, etc.

1. What is the evidence that biotics can prevent disease or help maintain health?

2. Are there data from biotics interventions for one population that are sufficiently robust to enable extrapolation to another population? For example, are there data from a population with a disease that can be extrapolated to a population without that disease? Or are there data that can be extrapolated to a population with substantively different demographics? USPSTF uses an approach that allows a C level recommendation from extrapolated data. EFSA may allow extrapolation of benefits for certain subpopulation and outcomes (weight loss for obese patients) to the general population but not for other subpopulations and outcomes (joint function for patients with arthritis).
3. Are there subpopulations of the generally healthy population for whom biotics may prevent disease or help maintain health? For example, infants born via C-section, travelers at risk of traveler's diarrhea, etc.
4. Are there novel approaches that may provide evidence for keeping healthy people healthy? For example, using [real world data](#), biomarkers of health, homeostasis of microbiota or clinical biomarker readouts, vaginal microbiota composition, etc.
5. Consider how adverse events and cost of intervention weighs on evidence assessment.