

Establishing causality in probiotic and prebiotic intervention trials

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To date, nearly all published microbiome intervention studies have assessed changes in the microbiota in response to a specific intervention and then correlated those changes, positively or negatively, to whatever health outcome had been measured. Such studies can show associations but not causality. Demonstrating a causal relationship between the treatment and outcome, is required, however, to establish a mechanistic involvement of microbiome modulation for a given health benefit. Indeed, the establishment of a causative contribution of the microbiome in the health effects of probiotics and prebiotics, in particular, may be required for regulatory recognition. However, it is extremely difficult to establish cause and effect relationships in microbiome studies, and in biomedical sciences, in general.

In this session, the panel will discuss philosophical and experimental aspects for establishing causality and apply these aspects to microbiome interventions. The discussion will focus specifically on the limitations (and potential strengths) of associative or correlations studies, inferring causation versus proving causation, how mechanistic studies can inform causality, and the role of biostatistics in causation studies. We will further try to formulate recommendations on the level of evidence necessary for applied studies to make claims for causality.