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MATTERS ARISING

Bridging the gap between microbiome function and clinical benefit in sarcopenia

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Abstract

We read the recent systematic review and meta-analysis on nutrition-based, gut microbiota–targeted interventions for sarcopenia in older adults with great interest. While the evidence suggests that probiotics and fiber-enriched diets may improve surrogate outcomes such as muscle strength and gait speed, we highlight two priorities to strengthen future mechanistic and clinical translation. First, microbiome measurements in existing trials are often limited to genus-level taxonomic shifts, which can be biologically misleading because a single genus may include members with divergent immunomodulatory properties. Even species-level profiling may be insufficient, as strains within the same species can differ markedly in genetic content and metabolic capacity. Moreover, taxonomic composition does not necessarily reflect functional output due to functional redundancy across microbial communities. We therefore recommend transitioning to whole-genome shotgun metagenomics to enable strain-level resolution and functional profiling, allowing investigators to quantify pathways and metabolites relevant to muscle preservation, including short-chain fatty acids and vitamin biosynthesis. Second, we argue that improvements in sarcopenia-defining parameters should be linked to patient-centered clinical benefit. Future randomized controlled trials should be adequately powered to assess hard endpoints, including falls, fractures, hospitalization rates, and functional independence, alongside muscle mass and performance measures, to establish whether microbiota modulation delivers meaningful reductions in healthcare burden.

To the Editor,

We read with great interest the systematic review and meta-analysis by Lapauw et al., which provides a timely and rigorous synthesis of nutrition-based interventions targeting the gut microbiota for sarcopenia in older adults [1]. The authors successfully demonstrated that specific interventions, particularly probiotics and fiber-enriched diets, hold promise for improving muscle strength and gait speed. While the authors correctly identified the scarcity of fecal sampling as a limitation and called for its inclusion in future studies, we would like to offer two additional perspectives on how future microbiome analyses and clinical trials should be designed to maximize their translational value.

Our first observation concerns the methodological resolution required to decipher the true mechanisms of the gut-muscle axis. The data summarized in the article show that the few studies including microbiome analysis largely reported changes at the genus level. However, relying on genus-level associations is biologically insufficient because this taxonomic rank is too broad; a single genus can harbor members with opposing immunomodulatory effects. Furthermore, even resolving microbiota to the species level may not be precise enough, as distinct strains within the same species often possess vastly different genomic repertoires and metabolic phenotypes [2]. Most importantly, taxonomic composition does not necessarily reflect functional state. The gut microbiome exhibits high functional redundancy, meaning that a change in the abundance of specific microbes does not guarantee a corresponding change in metabolic output, such as the biosynthesis of short-chain fatty acids or vitamins essential for muscle preservation [3].

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Since the physiological impact on the host is driven by these functional metabolites rather than the mere presence of bacteria, we strongly suggest that future research must transition to shotgun metagenomics. This approach is the only way to achieve strain-level identification and, crucially, to profile the functional microbiome—revealing what the bacteria are doing rather than just who they are.

Furthermore, there is a critical need to bridge the gap between improving sarcopenia-defining parameters and achieving tangible clinical benefits. The authors comprehensively analyzed surrogate markers such as muscle mass, strength, and physical performance. While a statistically significant improvement in handgrip strength or gait speed is scientifically encouraging, these parameters do not always translate linearly to improved quality of life or a reduced healthcare burden for the patient. Consequently, we propose that future randomized controlled trials should be powered to assess hard clinical endpoints, specifically the incidence of falls, fractures, and hospitalization rates, alongside functional independence. As the authors notably found that probiotics improved gait speed—a strong predictor of fall risk—establishing a direct link between gut microbiota modulation and a reduction in actual fall rates would provide the definitive evidence needed to incorporate these interventions into standard geriatric care guidelines.

We congratulate Lapauw et al. for their valuable contribution, which sets a solid foundation for the field. By embracing higher-resolution omics technologies and focusing on patient-centered clinical outcomes, future research can move closer to developing precise, microbiome-targeted therapies for sarcopenia.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Competing interests The authors declare no competing interests.

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