

Summary of a scientific publication: β -hydroxy- β -methyl butyrate (HMB) supplementation in ageing and clinical practice: an umbrella review

Phillips S.M. et al. An umbrella review of systematic reviews of β -hydroxy- β -methyl butyrate supplementation in ageing and clinical practice. J. Cachexia Sarcopenia Muscle. 2022.
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Introduction

Muscle mass and function decline with age and can negatively impact the quality of life of older adults. Research has investigated various nutritional interventions to help mitigate muscle loss. The compound β -hydroxy- β -methyl butyrate (HMB) is a metabolite of the amino acid leucine formed in vivo through a series of enzyme-catalyzed reactions. In humans, the biosynthesis of HMB is rate limited, such that only an estimated 5% of leucine is converted to HMB. There are some systematic reviews of HMB to examine HMB as a compound alone or combined with macronutrients and micronutrients, to stimulate gains or mitigate losses in muscle mass. A review published in 2021 suggested the need for high-quality studies investigating the effectiveness of HMB to improve outcomes related to muscle strength in older persons, both hospitalized and living in the community¹. This article is a **review of systematic reviews** of the **effect of HMB alone or combined with macro and micronutrients** (usually as part of an ONS available from one medical nutrition company) **and other amino acids on muscle mass and function in adults aged ≥ 50 years and clinical populations**.

Objectives & Materials and Methods

Determine the role of HMB in improving muscle mass or function, manifesting as improved mobility or physical function outcomes and mitigating sarcopenia.

Methodological quality of the reviews was assessed using A Measurement Tool to Assess Systematic Reviews (AMSTAR)

- Score: 1 (very low quality) to 4 (very high quality).

Search strategy: Embase, PubMed, and the Web of Science core collection were searched. The search was restricted to English-language systematic reviews of HMB supplementation and was confined to humans. We included studies per the PICO statement:

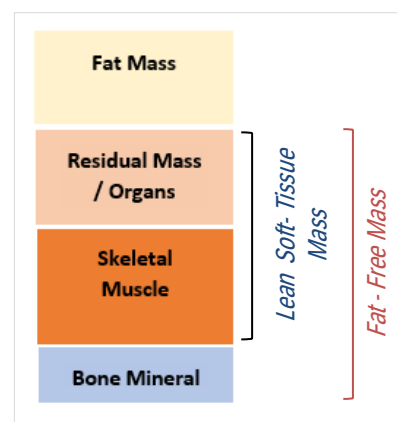
- Adults aged ≥ 50 years: healthy or clinical populations (**P**)
- Efficacy of HMB supplementation (**I**)
- Compared with placebo or any other intervention (**C**)
- Affecting muscle mass (lean soft-tissue mass) or muscle function (**O**)

Results

A total of **230 papers were identified** (Embase, PubMed, and the Web of Science) using the search strategy. **15 systematic reviews were included in the analysis.**

A) Impact of the interventions on **BODY COMPOSITION**:

- Most reviews (10 out of 15) found no effect or inconclusive evidence for the effectiveness of HMB supplementation in increasing **lean soft-tissue mass (LSTM) levels** [quality of evidence ranged from High (1 out of 10 reviews) to Very Low (2 out of 10 reviews)]
- **No effect** of HMB supplementation on **fat-free mass** across the systematic reviews has been found



Results

B) Impact of the intervention on MUSCLE STRENGTH and PHYSICAL FUNCTION:

- ✓ Most systematic reviews (8 out of 12) concluded that HMB supplementation showed no positive effect or insufficient data to conclude a positive effect on muscle strength [quality of evidence ranged from QoE-Moderate (1 out of 8 reviews) to QoE-Very Low (1 out of 18 reviews)].
- ✓ Only 4 out of 12 reviews showed positive effects on the gain in strength [quality of evidence ranged from QoE-High (1 out of 4 reviews) to QoE-Very Low (2 out of 4 reviews)] .
- ✓ The authors didn't find evidence to support HMB supplementation for augmenting physical function [quality of evidence ranged from high (1 out of 10 reviews) to Very Low (2 out of 10 reviews)] .

Relevance of results in clinical practice:

Impact of the HMB as part of an Oral Nutritional Supplement or as a stand-alone supplement in ELDERLY PEOPLE or in PEOPLE WITH SARCOPENIA

- ✓ This review of systematic reviews concluded that the recommendation that **HMB effectively mitigates any aspect of sarcopenia** is **not aligned with the results of this research** that demonstrated inconsistent results and relatively small effect sizes reported for augmentation of gains or mitigation of loss of LSTM and fat-free mass across the systematic reviews and more evidence is needed.

Impact of the interventions in CLINICAL SETTINGS

- ✓ The review notes that in older people hospitalized with malnutrition/sarcopenia and those undergoing orthopedic intervention, the effects of HMB were low to moderate for changes in LSTM and **no significant effects of HMB on strength or physical function were observed**.
- ✓ There is **little evidence to support the role of HMB supplementation** in the treatment of older hospitalized patients due to the heterogeneity of the populations studied and interventions, the small effects, and the lack of translation of changes in LSTM to strength, functional outcomes, or mobility.
- ✓ **Leucine**, which is a **potent stimulator of skeletal muscle protein synthesis (MPS)** and **suppressor of muscle protein breakdown (MPB)** is **more rapidly absorbed** and **has a greater concentration maximum than the CaHMB** resulting in almost identical rises in MPS. The amino acid leucine and HMB (as a free acid or calcium form) are mechanistically redundant.



This Review of Systematic Reviews concludes that HMB supplementation as part of an oral nutritional supplement or as a stand-alone supplement (or combined with other amino acids):

- ✓ **Does not improve physical function** in older adults or clinical populations
- ✓ **The published data are limited, inconsistent, or insufficient to recommend HMB to mitigate or promote retention of muscle mass (or proxies thereof) or improve muscle strength** in adults aged ≥ 50 y and/or clinical populations.