Abbott

SCIENCE BACKED NUTRITION THAT SUPPORTS MUSCLE HEALTH

HMB: β-hydroxy-β-methylbutyrate

IE-ENSPA-2500014- October 2025

PROTEIN ALONE IS NOT ENOUGH.
HMB IS CLINICALLY PROVEN TO SLOW MUSCLE LOSS AND PRESERVE MUSCLE PROTEIN SYNTHESIS[1-3]

Increase muscle protein synthesis two-fold*[1]

x10

Results in 10x more muscle maintenance with the same protein intake†[2]

Reduce muscle protein breakdown by half*^[1]

HMB: β-hydroxy-β-methylbutyrate. *Compared to baseline at the post absorptive state in healthy adults. ^In healthy adults who were not involved in formal training program. †In a RCT including 19 healthy adults aged ≥ 65 years confined to bed rest for 10 days. Calcium β-hydroxy-β-methylbutyrate (3g/day) prevented the decline in total Lean Body Mass over bed rest (-0.17 ± 0.19 kg; *p*=0.23) in treated group versus control group (-2.05 ± 0.66 kg; *p*=0.02).

References: 1. Wilkinson DJ et al. J Physiol 2013;591(11):2911-2293. **2.** Deutz NEP et al. Clin Nutr 2013;32(5):704-712. **3.** Engelen MPKJ & Deutz NEP. Curr Opin Clin Nutr Metab Care 2018;21(3):207-213.

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THE MODE OF ACTION OF HMB

Reduction in protein degradation
inhibits ubiquitin-proteasome system[1,2]

Enhanced Protein Synthesis
activating mTOR pathway[1,2] & improved collagen production[1]

Increase tissue repair
increased cholesterol synthesis, increase proliferation of satellite cells & inhibit autophagy–caspase system[2]

Increase growth hormone
& IGF-1[1,2]

Anti-inflammatory effects
reducing pro-inflammatory cytokines[1,2]

Enhances muscle contraction
calcium release from SR[2]

Improves cellular energy
mitochondrial biogenesis[1]

Support immune system
support macrophage & lymphocytes[1]

HMB: β-hydroxy-β-methylbutyrate. mTOR: Mammalian target of rapamycin. SR: sarcoplasmic reticulum. IGF-1: insulin growth factor 1.

References: 1. Rathmatcher JA et al. J Int Soc Sports Nutr. 2024;22. **2.** Holecek M. J Cachexia Sarcopenia Muscle. 2017;8(4):529-541.

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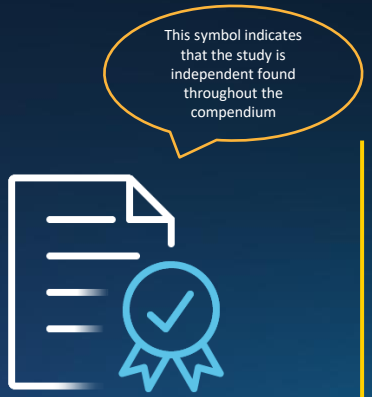
EVIDENCE FOR ONS WITH HMB

VALIDATED IN > 30 TRIALS/STUDIES*

RESULTS IN > 11,000 PARTICIPANTS^



BACKED BY INDEPENDENT RESEARCH

ENDORSED BY ESPEN GUIDELINES[1,2]

ESPEN: The European Society for Clinical Nutrition and Metabolism. *30 studies included in this compendium. Various other publications are available which include ONS with HMB. ^Within this compendium ~n=5358 participants consumed ONS with 1.5kcal/mL with HMB various studies the remainder acted as controls.

References: 1. Wunderle C et al. Clin Nutr 2023;42:545-1568. **2.** Gomes F et al. Clin Nutr 2018 Feb;37(1):336-353.

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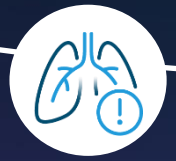
EVIDENCE FOR ONS WITH HMB

CARDIOVASCULAR

Luu et al. 2025
Baggs et al. 2023
Loman et al. 2019
Deutz et al. 2016
Matheson et al. 2021

RESPIRATORY



Deutz et al. 2016
Olveira et al. 2020
Olveira et al. 2016
Matheson et al. 2021
Deutz et al. 2021
Loman et al. 2019
Baggs et al. 2023
Deutz et al. 2021

ONCOLOGY

Triguero-Canovas et al. 2023
Cornejo-Pareja et al. 2021
Lopez-Rodriguez et al. 2021
Ritch et al. 2019
Cornejo-Pareja et al. 2023
Cornejo-Pareja et al. 2025
Fiorindi et al. 2025

POLYMORBID MALNUTRITION

Vegas-Aguilar I et al. 2025
De Luis et al. 2018
Chew et al. 2021
Cornejo-Pareja et al. 2021
Doyev et al. 2024
Pereira et al. 2022
Muangpaisan et al. 2024
De Luis et al. 2025
Tey et al. 2024
Cornejo-Pareja et al. 2025

HIP FRACTURES

Malafarina et al. 2016
Ekinci et al. 2016
Pareja-Sierra et al. 2024

WOUNDS

Ekinci et al. 2016
Malafarina et al. 2016
Zana et al. 2021

LIVER

Espina et al. 2021

SARCOPENIA

Pereira et al. 2022
Cramer et al. 2016
Zana et al. 2021
De Luis et al. 2025

SURGERY

Triguero-Canovas et al. 2023
López-Rodríguez et al. 2021

PRE-FRAIL/FRAIL

Peng et al. 2021
Matheson et al. 2021

HMB: β-hydroxy-β-methylbutyrate. ONS: Oral Nutritional Supplement.

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EVIDENCE FOR ONS WITH HMB

COMMUNITY

Berton et al. 2015
De Luis et al. 2015
Chew et al. 2021
De Luis et al. 2018
Peng et al. 2021
López-Rodríguez et al. 2021
Cramer et al. 2016
Cornejo-Pareja et al. 2023
Olveira et al. 2020
Pereira et al. 2022
Muangpaisan et al. 2024
De Luis et al. 2025
Triguero-Canovas et al. 2023
Cornejo-Pareja et al. 2021
Tey et al. 2024
Cornejo-Pareja et al. 2025

HOSPITAL

Pareja-Sierra et al. 2024
Deutz et al. 2016
Deutz et al. 2021
Matheson et al. 2021
Loman et al. 2019
Doyev et al. 2024
Ekinci et al. 2016
Luu TN et al. 2025
Espina et al. 2021

NURSING HOME

Malafarina et al. 2016
Pareja-Sierra et al. 2024
Zana et al. 2021
De Luis et al. 2018

REHABILITATION

Malafarina et al. 2016
Pareja-Sierra et al. 2024
Zana et al. 2021
Deutz et al. 2016
Ritch et al. 2019
Olveira et al. 2016
Ekinci et al. 2016
Loman et al. 2019
Deutz et al. 2021
Olveira et al. 2020
Muangpaisan et al. 2024
Baggs et al. 2023

HMB: β-hydroxy-β-methylbutyrate. ONS: Oral Nutritional Supplement.

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EVIDENCE FOR ONS WITH HMB

~1 BOTTLE PER DAY

Berton L et al. 2015
Chew et al. 2016
Olveira C et al. 2020
Olveira G et al. 2016
Zana S et al. 2021
Doyev et al. 2024
Luu TN et al. 2025
Triguero-Canovas et al. 2023

VS STANDARD/ HIGH-PROTEIN ONS

Cramer et al. 2016
Cornejo-Pareja et al. 2021
Espina et al. 2021
Pereira et al. 2022
Cornejo-Pareja et al. 2023
Doyev et al. 2024
Cornejo-Pareja et al. 2025

WITHOUT EXERCISE INTERVENTION

Pareja-Sierra et al. 2024
Chew et al. 2021
Deutz et al. 2016
Deutz et al. 2021
Ritch et al. 2016
Ekinci et al. 2016
Cramer et al. 2016
De Luis et al. 2015
Peng et al. 2021

WITH EXERCISE INTERVENTION

Berton et al. 2015
Malafarina et al. 2016
Zana et al. 2021
Olveira et al. 2016
Cornejo et al. 2021
Lopez-Rodriguez et al. 2021

2024/2025 RESEARCH

Doyev et al. 2024
Pareja-Sierra et al. 2024
De Luis et al. 2025
Vegas-Aguilar et al. 2025
Tey et al. 2024
Luu TN et al. 2025
Muangpaisan et al. 2024
Cornejo-Pareja et al. 2025

HMB: β-hydroxy-β-methylbutyrate. ONS: Oral Nutritional Supplement.

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Berton L, et al. *PloS One*. 2015;10(11):e0141757.

EFFECT OF ORAL BETA-HYDROXY-BETA-METHYLBUTYRATE (HMB) SUPPLEMENTATION ON PHYSICAL PERFORMANCE IN HEALTHY OLD WOMEN OVER 65 YEARS: AN OPEN LABEL RANDOMISED CONTROLLED TRIAL

Study: Parallel-group, randomised, controlled, open-label trial.

Aim: To evaluate if ONS with HMB could improve physical performance and muscle strength parameters in a group of community-dwelling healthy older women (n=80).

Intervention: A mild fitness program, twice weekly, for both the intervention and control groups. The intervention group received 1 bottle of ONS with HMB a day for 8 weeks, taken at breakfast; the control group received no ONS.

Results: After 8 weeks, there were:

- Sig. improvements in **leg strength** in the intervention group vs control through PT isokinetic flexion (delta = 1.56±1.56 Nm; p=0.03), extension (delta = 3.32±2.61 Nm; p=0.03) & isometric strength (delta = 9.74 ±3.90 Nm; p=0.02)
- Sig. improvements in **physical performance** (6 Minute Walk Test) in intervention group vs control (delta=7.67±8.29m; p=0.04)
- Sig. improvements in **handgrip endurance** in intervention group vs control (delta = 21.41±16.28 s; p=0.02)
- Sig. greater **muscle density** in intervention vs control (tibia: delta = 0.56±0.62 mg/cm3; p=0.03)
- No significant differences between the groups' SPPB, hand grip strength or DXA parameters
- The proportion of ONS with HMB consumed by the treatment group was 96%

Conclusion: Eight weeks of supplementation with an ONS with HMB in healthy elderly women had no significant effects on SPPB, but did significantly improve several muscle strength and physical performance parameters.

SPPB: Short Physical Performance Battery; DXA: Dual-energy X-ray Absorptiometry; PT: Peak Torque; ONS: Oral Nutritional Supplement; ; HMB: β-hydroxy-β-methylbutyrate. *Abbott provided the oral nutritional supplements free of charge. No other conflicts of interest.

Chew S, et al. *Clin Nutr.* 2021;40:1879-1892.

IMPACT OF SPECIALISED ORAL NUTRITIONAL SUPPLEMENT ON CLINICAL, NUTRITIONAL, AND FUNCTIONAL OUTCOMES: A RANDOMISED, PLACEBO-CONTROLLED TRIAL IN COMMUNITY-DWELLING OLDER ADULTS AT RISK OF MALNUTRITION

Study: SHIELD study randomised, placebo-controlled, double-blind, parallel design, multicentre study.

Aim: To assess the impact of ONS with HMB combined with dietary counselling on survival without hospital readmission and achieving at least 5% weight gain over 180 days, compared to a control group receiving a placebo supplement and dietary counselling.

Intervention: n=811 >65-year-old community ambulant adults with medium to high risk of malnutrition and stable chronic illnesses, were randomly assigned to either the intervention (n=405; dietary counselling and 1 bottle ONS with HMB, split in 2 doses x 180 days) or control group (n=406; dietary counselling and placebo supplement).

Results:

- A significantly higher percentage of those taking ONS with HMB had 5% weight gain compared to placebo (36.2% vs. 9.4%; p <0.001)
- Weight, **BMI**, and **MUAC** were significantly greater in those taking ONS with HMB at days 30, 90 and 180
- Those taking ONS with HMB had sig. higher **25-hydroxyvitamin D** levels vs placebo (31.86 ± 0.42 mg/L vs. 27.30 ± 0.43 mg/L; p <0.001)
- At day 90, **leg strength** was sig. higher in those receiving ONS with HMB than placebo (12.85 ± 0.22 kg vs. 12.17 ± 0.22 kg; p=0.030)
- **Leg muscle mass** was sig. higher in those receiving ONS with HMB than placebo (13.40 ± 0.83 kg vs. 11.88 ± 0.56 kg; p=0.031)
- **Handgrip strength** was sig. higher in those who received ONS with HMB than placebo (14.18 ± 0.17 kg vs.13.70 ± 0.17 kg; p=0.048)
- The odds of better nutritional status at day 30, 90 and 180 was higher in those taking ONS with HMB (OR 2.29, 3.35, and 2.50; all p < 0.001).

Conclusion: For community-dwelling older adults at risk of malnutrition, daily consumption of ONS with HMB for six months, along with dietary counselling, significantly improved nutritional and functional outcomes compared to placebo supplement with dietary counselling.

SHIELD: Strengthening Health In ELDerly through nutrition; BMI: Body Mass Index. MUAC: Mid Upper Arm Circumference.; MUST: Malnutrition Universal Screening Tool; ONS: Oral Nutritional Supplement; HMB: β-hydroxy-β-methylbutyrate.

Deutz NE, et al. *Clin Nutr.* 2016;35(1):18–26.

READMISSION AND MORTALITY IN MALNOURISHED, OLDER, HOSPITALISED ADULTS TREATED WITH A SPECIALISED ORAL NUTRITIONAL SUPPLEMENT: A RANDOMISED CLINICAL TRIAL

Study: NOURISH study, multicentre, prospective, randomised, double-blind, placebo-controlled, parallel group study.

Aim: To evaluate the effect of ONS with HMB on post-discharge outcomes, non-elective readmissions and mortality in malnourished (SGA class B or C), older adults (≥ 65 years), hospitalised for congestive heart failure, acute myocardial infarction, pneumonia, or COPD.

Intervention: Standard nutritional care and ONS with HMB or placebo supplement, 2 servings/day.

Results: Compared to placebo, participants consuming ONS with HMB had significantly:

- Lower 90-day **mortality** rate (4.8% vs 9.7%; RR=0.49, 95% CI: 0.27-0.90, p=0.018)
- The **number-needed-to-treat** to prevent 1 death was 20.3 (95% CI: 10.9, 121.4)
- Improved odds of better nutritional **status** at day 90 (OR=2.04, 95% CI: 1.28-3.25, p=0.009)
- Higher levels of **serum 25-hydroxyvitamin D** at day 30 and 60 (p=0.035 and p=0.008, respectively)

Conclusion: Compared to the placebo, ONS with HMB decreased mortality and improved indices of nutritional status during the 90-day observation period.

NOURISH: Nutrition Effect On Unplanned Readmissions and Survival in Hospitalised patients; SGA: Subjective Global Assessment; COPD: Chronic Obstructive Pulmonary Disease; RR: Relative Risk; CI: Confidence Interval; OR: Odds Ratio. ONS: Oral Nutritional Supplement; HMB; β-hydroxy-β-methylbutyrate.

Pareja Sierra TP, et al. *Nutrients.* 2024;16(8):1223.

A PROSPECTIVE, OBSERVATIONAL STUDY OF THE EFFECT OF A HIGH-CALORIE, HIGH-PROTEIN ORAL NUTRITIONAL SUPPLEMENT WITH HMB IN AN OLD AND MALNOURISHED OR AT-RISK-OF-MALNUTRITION POPULATION WITH HIP FRACTURES: A FRACNUT STUDY

Study: An observational, prospective, national, multicentre study (17 hospitals).

Aim: To observe the effect of ONS with HMB on nutritional status, recovery, activities of daily living, quality of life, and length of hospital stay in older people with malnutrition or at risk of malnutrition after hip fracture surgery.

Intervention: n=270 older adults (≥75 years), living either at home or in nursing homes, who were malnourished or at risk of malnutrition following hip fracture surgery, received ONS with HMB twice daily for 12 weeks.

Results:

- Mean **MNA** total score showed a significant increase in nutritional status compared to baseline ($p < 0.001$)
- By week 12, 62.4% gained or maintained weight (+0.3 kg), 29.2% achieved normal nutritional status (mean MNA score +2.8), and46.8% improved nutritional status
- Participants remained in the same level of dependence score (Barthel**ADL Index**) from baseline to follow-up
- Mean **serum 25-hydroxyvitamin D** levels increased ($p <0.001$)
- 87.1% of the healthcare professionals considered the ONS with HMB to be well **tolerated**

Conclusion: ONS with HMB markedly enhanced nutritional status and biochemical parameters in older hip-fracture patients, with high compliance and tolerability. Both patients and healthcare professionals expressed satisfaction with ONS with HMB.

ONS: Oral Nutritional Supplement; ; HMB: β-hydroxy-β-methylbutyrate; BMI Body Mass Index; MNA: Mini Nutritional Assessment; ADL: Activities of Daily Living.

Deutz NE et al. *Clin Nutr.* 2021;40(3):1388–1395.

REDUCED MORTALITY RISK IN MALNOURISHED HOSPITALISED OLDER ADULT PATIENTS WITH COPD TREATED WITH A SPECIALISED ORAL NUTRITIONAL SUPPLEMENT: SUB-GROUP ANALYSIS OF THE NOURISH STUDY

Study: Post-hoc sub-group analysis from the NOURISH study - a multicentre, randomised, placebo-controlled, double-blind trial.

Aim: To examine the effect of ONS with HMB in malnourished, hospitalised, older adults with COPD and to identify predictors of outcomes.

Intervention: Patients with an admission diagnosis of COPD (n=214) received either standard-of-care plus ONS with HMB or placebo supplement, 2 servings/day from within 3 days of admission to hospital and up to 90 days after discharge.

Results: Compared to placebo, participants consuming ONS with HMB had significantly:

- Lower 30, 60, and 90-day **mortality** risk (1.83%, 2.75%, 2.75% vs. 6.67%, 9.52% and 10.48%, p=0.036, 0.019, 0.011, respectively)
- Increased **handgrip strength** from discharge to day 30 (+1.56kg ±0.67kg vs -0.34kg ±0.63kg, p=0.0413)
- Improved **body weight** from baseline to discharge (+0.61kg ±0.26kg vs -0.09kg ±0.29kg, p=0.0472)
- Improved nutritional biomarkers, including **haemoglobin** (p=0.0284) and serum **25-hydroxyvitamin D** (p< 0.0001)

Conclusion: Among malnourished, hospitalised patients aged ≥65 years with COPD, supplementation with ONS with HMB was associated with a 71% decreased mortality risk, improved handgrip strength, body weight, and nutritional biomarkers within a 90-day period after hospital discharge.

ONS: Oral Nutritional Supplement; HMB: β-hydroxy-β-methylbutyrate; NOURISH: Nutrition Effect On Unplanned Readmissions and Survival in Hospitalised patients; COPD: Chronic Obstructive Pulmonary Disease.

Ritch CR, et al. *J Urol.* 2019;201(3):470–477.

PERIOPERATIVE ORAL NUTRITION SUPPLEMENTATION REDUCES PREVALENCE OF SARCOPENIA FOLLOWING RADICAL CYSTECTOMY: RESULTS OF A PROSPECTIVE RANDOMISED CONTROLLED TRIAL

Study: Prospective randomised, controlled pilot trial.

Aim: To investigate the effects of ONS with HMB on body composition and clinical outcomes following radical cystectomy.

Intervention: 61 participants were randomised to receive either ONS with HMB or a multivitamin mineral supplement, twice daily for 8 weeks peri-operatively.

Results: Compared to the multivitamin supplement group, participants consuming ONS with HMB had significantly:

- Reduced **weight** loss (average weight loss of 5kg vs 6.5kg, p=0.04)
- Less **muscle** mass loss (-5cm^2/m^2 vs -3.2cm^2/m^2, p=0.01)
- Lower rates of developing **sarcopenia** post-operatively (no change vs 20% increase in control group, p=0.01)
- Decreased rate of **sarcopenic** obesity (33.3% reduction vs 16.6% increase in control group, p=0.01)
- Reduced total **complication** rate (48% vs 67%, p=0.16)

Conclusion: Patients who undergo radical cystectomy after consuming ONS with HMB perioperatively have a reduced prevalence of sarcopenia and may also experience fewer and less severe complications and readmissions.

ONS: Oral Nutritional Supplement; HMB: β-hydroxy-β-methylbutyrate.

Malafarina V et al. *Maturitas*. 2017;101:42–50.

EFFECTIVENESS OF NUTRITIONAL SUPPLEMENTATION ON SARCOPENIA AND RECOVERY IN HIP FRACTURE PATIENTS: A MULTI-CENTRE RANDOMISED TRIAL

Study: Multi-centre, randomised open label study.

Aim: To assess whether ONS with HMB improves muscle mass and nutritional markers in elderly patients with a hip fracture.

Participants: 92 older patients (≥65 years) with hip fractures admitted to rehabilitation facilities.

Intervention: The patients were randomly assigned to receive a standard diet of 1500kcal/day* with no ONS (n = 43) or with ONS with HMB (n = 49) x2/day.

Results:

- More **weight** loss was observed in the control group than in the ONS with HMB group ($p < 0.001$)
- Appendicular **lean mass** reduced in the control group but stayed the same in the ONS with HMB group. The difference between values upon discharge, corrected for baseline values, was statistically significant ($p=0.020$)
- The recovery of **activities of daily living** was more common in ONS with HMB group (68 %) than in the control group (59 %)
- Total protein values, transthyretin and **25-hydroxyvitamin D** upon discharge were significantly higher in ONS with HMB group than in the control group ($p = 0.007$, $p = 0.037$ and $p < 0.001$, respectively)

Conclusion: A diet enriched in HMB improves muscle mass, prevents the onset of sarcopenia and is associated with functional improvement in elderly patients with hip fractures. ONS with HMB can help to prevent the onset of sarcopenic obesity.

*Standard diet = 23 .3 % protein, 35 .5 % fat and 41 .2 % carbohydrates. ONS: Oral Nutritional Supplement; HMB: β-hydroxy-β-methylbutyrate.

Olveira G et al. *Clin Nutr.* 2016;35(5):1015–1022.

ORAL SUPPLEMENT ENRICHED IN HMB COMBINED WITH PULMONARY REHABILITATION IMPROVES BODY COMPOSITION AND HEALTH RELATED QUALITY OF LIFE IN PATIENTS WITH BRONCHIECTASIS (PROSPECTIVE, RANDOMISED STUDY)

Study: Single-centre randomised controlled trial, parallel treatment design.

Aim: To assess the effect of pulmonary rehabilitation (PR) with ONS with HMB for 12 weeks on body composition, muscle strength, quality of life and serum biomarkers, in patients with bronchiectasis who were adequately nourished.

Intervention: n= 30 randomised to receive PR ± ONS for 12 weeks. PR included supervised twice weekly 60-minute exercise session and one unsupervised session with 1 bottle of ONS with HMB for 12 weeks. Control received no ONS.

Results: From baseline to 12 and 24 weeks, participants who received PR with ONS with HMB had significantly improved:

- Bone mineral density ($p<0.01$)
- Mean and maximum handgrip dynamometry (both $p<0.01$)
- Mid-arm muscle circumference, quality of life ($p<0.05$)
- Prealbumin ($p<0.01$)

Those in the control group only had sig. increases in mean handgrip dynamometry and prealbumin.

Conclusion: The addition of ONS with HMB to pulmonary rehabilitation could improve body composition, bone mineral density, muscle strength and health-related quality of life in bronchiectasis patients.

HMB: β-hydroxy-β-methylbutyrate; ONS: Oral Nutritional Supplement.

Ekinci O et al. *Nutr Clin Pract.* 2016;31(6):829–835.

EFFECT OF CALCIUM β-HYDROXY-β-METHYLBUTYRATE (CaHMB), VITAMIN D, AND PROTEIN SUPPLEMENTATION ON POSTOPERATIVE IMMOBILISATION IN MALNOURISHED OLDER ADULT PATIENTS WITH HIP FRACTURE: A RANDOMISED CONTROLLED STUDY

Study: Randomised controlled study.

Aim: To investigate the effects of ONS with HMB on wound healing, mobilisation time and muscle strength in older female patients following surgery for a hip fracture.

Intervention: n=62 older female patients (≥ 65 years) with hip fractures admitted to orthopaedic clinics. Participants randomly assigned to standard postoperative nutrition* alone (n = 30) or post operative nutrition with ONS with HMB (n = 32) x2 bottles/day for 30 days.

Results:

- **Wound** healing period was significantly shorter in the group receiving ONS with HMB ($p<0.05$)
- 81.3% of patients in the ONS with HMB group were **mobile** at day 15 and 30 vs. 26.7% in control group ($p=0.001$)
- **Muscle strength** was sig. higher in the ONS with HMB group vs the control group at day 30 ($p=0.026$) and **muscle strength** was sig. greater in the ONS with HMB group at day 30 than at day 1 ($p=0.015$), but no sig. differences were observed in the control group
- **Arm circumference** and **Tricep Skinfold Thickness** sig. improved in the ONS with HMB group at day 30 vs day 1 ($p=0.001$, $p < 0.001$) but there was no difference in the control group.
- **Calf circumference** sig. improved from day 15 to day 30 in the ONS with HMB group ($p=0.023$), no sig. difference in the control group.

Conclusion: Nutrition with ONS with HMB in elderly patients led to acceleration of wound healing, shortening of immobilisation period, and increased muscle strength without changing BMI. It also reduced dependence to bed and related complications.

HMB: β-hydroxy-β–methylbutyrate; ONS: Oral Nutritional Supplement; BMI: Body Mass Index. *Post-operative nutrition plan was 1900kcal/day through 3 main courses.

Cramer JT et al. *J Am Med Dir Assoc.* 2016;17(11):1044–1055.

IMPACT OF HIGH-PROTEIN ORAL NUTRITIONAL SUPPLEMENTS AMONG MALNOURISHED MEN AND WOMEN WITH SARCOPENIA: A MULTICENTER, RANDOMISED, DOUBLE-BLINDED, CONTROLLED TRIAL

Study: A multicentre, randomised, double-blinded, controlled clinical trial.

Aim: To evaluate the effects of ONS with HMB (experimental ONS) vs Ensure® Plus (control ONS).

Intervention: For 24 weeks, n=165 were provided ONS with HMB x2/day & n=165 in the control group were provided Ensure® Plus x2/day. Isokinetic peak torque (PT, Nm) leg strength, grip strength, and gait speed were assessed at baseline, 12 & 24 weeks.

Results:

- Both ONS groups improved PT, MQ, grip strength, and gait speed from baseline
- In those with severe sarcopenia - there was an improvement from baseline in PT at 24 weeks with ONS with HMB
- In those with mild/moderate sarcopenia & normal grip strength – those with ONS with HMB showed greater improvements in PT and MQ than those in the Ensure® Plus group at 12 weeks (p=0.032)
- In those with mild/moderate sarcopenia receiving ONS with HMB, BMI and body weight significantly improved at 12 weeks (p=0.42 and p=0.32, respectively) compared to those receiving Ensure® Plus
- In those with sarcopenia & normal grip strength – improvements in MQ were grater in those in the ONS with HMB group than Ensure® Plus group (p=0.027). Improvements in MQ were sustained in the ONS with HMB group, those in the Ensure® Plus group showed an attenuated ability to maintain the changes in MQ

Conclusion: ONS improved strength outcomes in malnourished older adults with sarcopenia. In those with mild to moderate sarcopenia, but not severe sarcopenia, consumption of ONS with HMB improved leg muscle strength and quality compared with Ensure® Plus.

HMB: β-hydroxy-β–methylbutyrate; ONS: Oral nutritional supplement; PT: Peak Torque; Nm: Neuromuscular Myopathy; MQ: Muscle Quality.

De Luis DA et al. *Nutr Hosp.* 2015;32(1):202–207.

EFFECT ON QUALITY OF LIFE AND HANDGRIP STRENGTH BY DYNAMOMETRY OF AN ENTERAL SPECIFIC SUPPLEMENT WITH BETAHYDROXY-BETA-METHYLBUTYRATE AND VITAMIN D IN ELDERLY PATIENTS

Study: Open label study.

Aim: To investigate the effect on strength and quality of life of ONS with HMB in elderly patients.

Intervention: All participants were provided 2 bottles a day of ONS with HMB for 12 weeks for patients with recent weight loss (>5% in the past 3 months). Participants kept food diaries at baseline and at week 12 to control for diet. For the results, participants were divided into 2 groups by median percentage weight improvement (group 1: <3.4% weight improvement; group 2: >3.4% weight improvement)

Results:

- All participants showed sig. improvements ($p<0.05$) in BMI (0.97+/-1.0 kg/m^2), weight (2.5+/-2.2 kg), FFM (-7.2+/-4.4 cm), prealbumin (1.5+/-4.1 mg/dl) and vitamin D levels (11.9+/-10.1 ug/dl) after 3 months of ONS with HMB x2/day
- All participants showed sig. improvements in role physical domain of SF36 (0.76+/1.7 points), general health domain of SF36 (1.4+/-1.9 points), right (3.7+/-9.1 kg/cm^2) and left (3.1+/-9.8 kg/cm^2) handgrip strength
- In group 2: BMI (1.1+/-1.4 kg/m^2), weight (4.9+/-2.8 kg), fat free mass (2.2+/-4.4 kg), prealbumin (1.9+/-3.1 mg/dl) and vitamin D levels (14.8+/-11.1 ug/dl) improved with significance. In group 1: vitamin D levels (-13.1+/-10.8 ug/dl) improved with significance.
    - Group 2 had higher consumption rates of ONS with HMB and thus HMB than group 1 (1.25 + 0.78 units/day [1.81 +/-0.9 g per day of HMB] vs. 1.86 + 0.82 units/day [2.79 +/-1.1 g per day of HMB]).

Conclusion: Elderly patients with a previous weight loss and with a high consumption ONS with HMB had a significant improvement in anthropometric, biochemical parameters, handgrip strength and quality of life.

BMI: Body Mass Index; FFM: Fat Free Mass; SF36: Short-Form 36; HMB: β-hydroxy- β-methylbutyrate; ONS: Oral Nutritional Supplement.

De Luis DA et al. *Eur Geriatr Med.* 2018;9(6):809–817.

ADNUT STUDY: EFFECTIVENESS OF A HIGH CALORIE AND PROTEIN ORAL NUTRITIONAL SUPPLEMENT WITH β-HYDROXY-β-METHYLBUTYRATE IN AN OLDER MALNOURISHED POPULATION IN USUAL CLINICAL PRACTICE

Study: Observational, prospective, open label, multicentre study.

Aim: To evaluate the effectiveness of ONS with HMB, on nutritional status, activities of daily living and QoL in malnourished subjects.

Intervention: n=235 participants aged >65 with malnutrition (NRS >3), under HCP care and prescribed ONS with HMB 7 days before enrolment, received 2 bottles daily plus standard care for 12 weeks.

Results: Participants who consumed ONS with HMB x2/day for 12 weeks, compared to baseline, had significant improvements in:

- Mean weight increased by 2.1 ± 3.8 kg ($p<0.001$)
- Mean BMI increased by 0.8 ± 1.5 kg/m^2 ($p<0.001$)
- NRS Tool 2002 decreased by 0.9 ± 1.2 ($p=0.002$)
- Mean EuroQol-5D score (measure of QoL) increased by 0.5 ± 1.9 points ($p < 0.001$)
- Mean Katz Index of Independence in Activities of Daily Living score increased by 0.3 ± 1.4 points ($p < 0.001$)

Conclusion: The results suggest that administration of a ONS with HMB improves the nutritional status and may led to a significant improvement in patients' activities of daily living and QoL, independent of baseline BMI.

QoL: Quality of life; BMI: Body Mass Index; NRS: Nutritional Risk Score; HCP: Healthcare Professional; ONS: Oral Nutritional Supplement; HMB: β-hydroxy-β–methylbutyrate.

Matheson EM et al. *Clin Nutr.* 2021;40(3):844-849.

SPECIALISED ORAL NUTRITIONAL SUPPLEMENT (ONS) IMPROVES HANDGRIP STRENGTH IN HOSPITALISED, MALNOURISHED OLDER PATIENTS WITH CARDIOVASCULAR AND PULMONARY DISEASE: A RANDOMISED CLINICAL TRIAL

Study: Randomised clinical trial.

Aim: To examine the effect of ONS with HMB on hand grip strength (HGS) and its relationship to nutritional status in hospitalised, older adults with malnutrition who were participants in the NOURISH trial.

Intervention: Standard of care with 2 servings of ONS with HMB in n = 328 or placebo supplement in n = 324

Results:

- Compared to those who consumed the placebo supplement, those who consumed ONS with HMB showed sig. improvements in handgrip strength (Least Squares Means ± Standard Error: (23.25 ± 0.25 in intervention vs. 22.63 ± 0.25 in placebo, p=0.043)).
- Those taking ONS with HMB had higher changes in HGS compared to placebo at day 30, day 60 and 90-days post-discharge (p=0.006, [Placebo - S-ONS: 0.62±0.22])
- In those taking ONS with HMB there was a sig. association between HGS and improvements in nutritional status (p<0.003).

Conclusion: ONS with HMB provided during hospitalisation and up to 90 days post-discharge improves HGS in malnourished older adults following cardiovascular and pulmonary events and may contribute to improvements in patients' overall recovery.

NOURISH: Nutrition effect On Unplanned Readmissions and Survival in Hospitalised patients. HMB: β-hydroxy-β–methylbutyrate; ONS: Oral Nutritional Supplement. *Abbott provided the oral nutritional supplements, no other conflicts of interest.

Peng LN et al. *J Nutr Health Aging*.2021;25(6):767–773.

ORAL NUTRITIONAL SUPPLEMENT WITH β-HYDROXY-β-METHYLBUTYRATE (HMB) IMPROVES NUTRITION, PHYSICAL PERFORMANCE AND AMELIORATES INTRAMUSCULAR ADIPOSITY IN PRE-FRAIL OLDER ADULTS: A RANDOMISED CONTROLLED TRIAL

Study: Open-label, parallel group, randomised control trial.

Aim: To evaluate the changes of muscle mass, muscle strength, physical performance and intramuscular adiposity among community-dwelling pre-frail older persons supplemented with ONS with HMB.

Intervention: n= 29 participants were provided ONS with HMB x2/day for 12 weeks and n = 33 were provided dietary counselling to meet their daily protein requirements.

Results:

- Significant improvements in CSA of mid-thigh muscle in the ONS with HMB vs. control (149.1±272.3 vs -22.9±309.1 mm^2 p=0.045)
- Serum vitamin D levels were significantly increased in the ONS with HMB group vs. control (3.83±8.18 ng/mL vs. -1.30±4.81 ng/mL, p=0.002)
- Body weight and BMI were significantly increased in the ONS with HMB group versus control (1.10±1.18 vs. 0.24±1.13 kg/m^2, p=0.005; 0.56±0.68 vs. 0.22±0.47 kg/m^2, p=0.019)
- IMAT-to-CSA ratio was significantly reduced in the ONS with HMB group (-0.38±1.21 vs. -0.02±2.56 %, p=0.06)
- SPPB score in chair rise test was significantly improved in the ONS with HMB group (β=0.71, 95% C.I. 0.09-1.33, p=0.026)

Conclusion: The 12-week supplementation with ONS with HMB significantly increased muscle mass, as well as nutritional status and physical performance, and ameliorated the intramuscular adiposity of prefrail older persons.

CSA: Cross-Sectional Area; BMI: Body Mass Index; IMAT: Intermuscular Adipose Tissue; SPPB: Short physical performance battery; ONS: Oral Nutritional Supplement; HMB: β-hydroxy-β–methylbutyrate.

Loman BR et al. *J Parenter Enteral Nutr.* 2019;43(6):794–802.

SPECIALISED HIGH-PROTEIN ORAL NUTRITION SUPPLEMENT IMPROVES HOME NUTRIENT INTAKE OF MALNOURISHED OLDER ADULTS WITHOUT DECREASING USUAL FOOD INTAKE

Study: A subset analysis of the NOURISH trial- a prospective, randomised, double-blind controlled trial.

Aim: To examine the impact of ONS with HMB on nutrient intake post discharge.

Intervention: Standard of care plus ONS with HMB or placebo supplement, 2 servings/day, for 90 days.

Results:

- Patients receiving ONS with HMB and the placebo consumed similar amounts of nutrients from food alone.
- At 90 days, dietary intake of the micronutrients iron, magnesium, phosphorus, zinc, copper, manganese, selenium, vitamin A, vitamin B12, and choline were higher in the ONS with HMB group compared with placebo controls (all <0.05)
- Including nutrient intake from both food and ONS with HMB within the intervention group, numerically more patients met energy (50%) and protein (71%) goals compared with controls (29% and 36%, respectively)
- Higher consumption of ONS with HMB was associated with a higher number of DRIs met (regression coefficient, $\beta = 4.46$, $p=0.0002$), whereas there was no significant relationship observed for the placebo group ($\beta=1.21$, $p=0.41$)

Conclusion: Three months of ONS with HMB consumption increases intake of numerous nutrients without decreasing nutrient intake from food in older malnourished adults post discharge.

HMB: β-hydroxy-β–methylbutyrate; ONS: Oral Nutritional Supplement; NOURISH: Nutrition effect On Unplanned Readmissions and Survival in Hospitalised patients. DRI: Dietary Reference Intake.

Olveira C et al. *Nutr Hosp.*2020;37(1):6–13.

OXIDATIVE AND INFLAMMATORY EFFECTS OF PULMONARY REHABILITATION IN PATIENTS WITH BRONCHIECTASIS: A PROSPECTIVE, RANDOMISED STUDY

Study: A prospective, randomised control trial.

Aim: To investigate the effect of PR in non-cystic-fibrosis bronchiectasis (NCFB) patients, and to compare it with the effect of PR plus ONS with HMB on serum inflammatory and oxidative biomarkers.

Intervention: Thirty participants (< 65 years of age with BMI >18.5kg/m^2 or > 65 years of age with BMI >20kg/m^2) were recruited and randomly assigned to receive PR (60-minute exercise bi-weekly at hospital and 1 unsupervised session with breath training exercises) and Mediterranean diet advice or PR, Mediterranean diet advice and ONS with HMB x1 bottle/day.

Results:

- The intervention group with ONS with HMB showed significantly lower neutrophil levels at 6 months than at baseline (neutrophIs at baseline (x 10^9/L): 4.24 ± 1.55 vs. neutrophils at 6 months (x 10^9/L): 3.62 ± 1.09, p=0.01).
- In the intervention group, oxidative biomarkers 8-ISOP, TAC, TBARS, SOD and anti-inflammatory markers TNFα, IL6CRP, and adiponectin remained stable throughout.

Conclusion: A PR program induced a pro-oxidative effect accompanied by changes in circulating inflammatory cytokine levels in NCFB patients. The results would also suggest a possible beneficial effect of ONS with HMB on neutrophil level regulation in these patients and pointing to a balancing effect of HMB on the inflammatory changes caused by exercise in untrained NFCB patients. The information provided in this study could be useful for choosing the right therapeutic approach in the management of bronchiectasis.

PR: Pulmonary rehabilitation; NCFB: Non-cystic-fibrosis bronchiectasis; HMB: β-hydroxy-β–methylbutyrate; ONS: Oral Nutritional Supplement. 8-ISOP: 8-isoprostane; TAC: total antioxidant capacity; TBARS: thiobarbituric acid reactive substances; SOD: superoxide dismutase; TNFα: tumor necrosis factor alfa; IL-6: interleukin 6; CRP: C-reactive protein.

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Zana S et al. *J Am Med Dir Assoc.*2021;22(7):1358–1360.

MULTICOMPONENT REHABILITATION AFTER COVID-19 FOR NURSING HOME RESIDENTS

Study: Exploratory study.

Aim: Report experience in nursing home residents previously affected by COVID-19 using a nutritional supplementation program together with rehabilitative indications.

Participants: n=28 older adults (mean age 87.8 years) who had a negative nasopharyngeal swab three days prior to the start of the study. Patients were bedridden and at high risk of pressure ulcers.

Intervention: Physical rehabilitation program x3 times/week and ONS with HMB once/day for 30 days.

Results:

- The mean Barthel Index, for **ADLs** significantly improved from baseline to 30 days ($p<0.001$)
- The risk of **pressure sores** significantly reduced ($p<0.001$)
- The **Exton-Smith Scale** for general condition, activity and mobility all significantly improved ($p<0.001$, $p<0.001$, $p<0.001$)
- The compliance was high at 85% taking ONS with HMB each day.

Conclusion: ONS with HMB and physical rehabilitation were able to significantly improve disability and reducing the risk of pressure sores in very old nursing home residents previously affected by COVID-19, indicating the need for early intervention in these patients to reduce the risk of negative consequences of sarcopenia.

ADLs: Activities of Daily Living; HMB: β-hydroxy-β–methylbutyrate; ONS: Oral Nutritional Supplement.

Standley RA, et al. *J Gerontol A Biol Sci Med Sci.* 2020;75(9):1744–1753.

SKELETAL MUSCLE ENERGETICS AND MITOCHONDRIAL FUNCTION ARE IMPAIRED FOLLOWING 10 DAYS OF BED REST IN OLDER ADULTS

Study: Prospective, randomised, double-blinded, placebo-controlled trial.

Aim: To explore the impact of bed rest (BR) on mitochondrial energetics in the muscle of older adults and the effect of ONS with HMB on mitochondrial energetics.

Intervention: 20 adults (67 years old, BMI 26.4kg/m^2). Provided ONS with HMB or control (CON) (CON = same calories and protein, no HMB) 5 days before and during 10 days of BR. All participants on a controlled diet* of 0.8g/kg/day from diet. Percutaneous biopsies of the vastus lateralis to measure mitochondrial respiration were conducted.

Results:

- After 10 days BR, there was reductions in type IIa skeletal muscle fibre CSA and elevations in skeletal muscle markers of atrophy
- RNA sequencing showed less protein synthesis and more muscle scarring and stiffening in the CON vs ONS with HMB
- During BR mitochondrial function dropped, ONS with HMB markedly blunted this drop with the number of affected genes and the size of the changes being less severe in the ONS with HMB group than CON
- After 10 days BR, mitochondrial energy production dropped, oxidative stress increased, key mitochondrial proteins and lipids reduced – all impairing energy production. ONS with HMB helped to protect against this loss compared to CON

Conclusion: 10 days BR in older adults causes a sig. deterioration in mitochondrial energetics, some of these negative effects may be attenuated by ONS with HMB.

*Energy requirements were using Harris Benedict equation with PAL of 1.375 pre–BR and 1.1 during BR; BMI: Body Mass Index; CSA: Cross Sectional Area; RNA: Ribonucleic Acid; ONS: Oral Nutritional Supplement; HMB: β-hydroxy-β–methylbutyrate.

Pereira SL, et al. *Nutrients.*2022;14(6):1196.

BIOMARKER CHANGES IN RESPONSE TO A 12-WEEK SUPPLEMENTATION OF AN ORAL NUTRITIONAL SUPPLEMENT ENRICHED WITH PROTEIN, VITAMIN D AND HMB IN MALNOURISHED COMMUNITY DWELLING OLDER ADULTS WITH SARCOPENIA

Study: Prospective, randomised, double-blinded, controlled study.

Aim: To determine if ONS with HMB would modulate additional biomarkers beyond those modulated by Ensure® Plus in malnourished sarcopenic older adults at the end of a 12-week intervention period.

Intervention: n = 193 were provided 2 servings of ONS with HMB along with continued normal diet, aiming for 0.8g protein/kg/day. Fasted bloods were checked at baseline and 12 weeks post-intervention. There was no sig. differences between groups at baseline.

Results:

- Both groups showed sig. changes in prealbumin, transferrin, vitamin B_{12}, blood urea nitrogen, Apo C-III, Lpa, IGF-1 and leptin. Showing that these biomarkers are responsive to nutritional interventions in general.
- Significant changes were observed in the ONS with HMB group, but not in the Ensure® Plus group in the following
  - Reducing osteopenia & ferritin (showing an anti-inflammatory effect from ONS with HMB)
  - Increasing IL-6 receptors, TNF-α receptors 1 & 2 (to reduce inflammatory effects of IL-6 and TNF-α)
  - Increasing immunity related markers (IgA & IgM)
  - Increasing total protein, myoglobin (for oxygen delivery to muscle), magnesium & vitamin E (associated with skeletal muscle health)

Conclusion: Incremental biomarker changes were observed in response to ONS with HMB and not standard ONS that could link to improvements in skeletal muscle health.

HMB: β-hydroxy-β-methylbutyrate; ONS: Oral Nutritional Supplement; Apo C-III: Apolipoprotein C-III; Lpa: Lipoprotein (a); IGF-1: Insulin Growth Factor 1; TNF-α: Tumour Necrosing Factor alpha; IL-6: Interleukin – 6. IgA: Immunoglobulin A; IgM: Immunoglobulin M.

Luu TN et al. *Medicine*.2025;13:104(24):pe42941,.

EFFECTIVENESS OF HIGH-ENERGY, HIGH-PROTEIN NUTRITIONAL SUPPLEMENTATION ON PATIENTS WITH CHRONIC HEART FAILURE AND MALNUTRITION

Study: A randomised, open-label, controlled clinical study.

Aim: To evaluate the effects of high-energy, high-protein nutritional supplementation on hospitalised patients with chronic heart failure combined with malnutrition.

Intervention: 40 patients diagnosed with chronic heart failure were randomly selected for intervention (diet + ONS with HMB o.d.-b.d.) or control (hospital dietary guidelines for heart failure). Intakes of energy and protein throughout the trial were not statistically significant (1560kcal vs 1428kcal and 68.02g vs 67.51g) to control for the impact of HMB.

Results:

- The prevalence of malnutrition at admission was 65% based on BMI and 80% based on the subjective global assessment.
- The ONS with HMB group had sig. improved weight, BMI, phase angle, hang grip strength and prealbumin level ($p<0.05$)
- The control group has reduced BMI, weight loss, reduced pre-albumin and showed no improvements in phase angle.
- None of the patients in either group developed symptoms of gastrointestinal intolerance.

Conclusion: ONS with HMB helps improve nutritional status for patients hospitalised with chronic heart failure, as shown by changes in body weight, BMI, phase angle, handgrip strength, and serum prealbumin

HMB: β-hydroxy-β-methylbutyrate; ONS: Oral Nutritional Supplement; BMI: Body Mass Index; o.d.: Once a day; b.d.: Twice a day.

Muangpaisan W et al. *Geriatrics*.2024;9(4):104.

EFFECTS OF SPECIALISED ONS WITH DIETARY COUNSELING ON NUTRITIONAL OUTCOMES IN COMMUNITY-DWELLING OLDER ADULTS AT RISK OF MALNUTRITION

Study: A prospective, multicentre, randomised controlled, open-label, parallel-design study.

Aim: To investigate the effects of ONS with HMB* along with dietary counselling (DC) compared with DC alone on body weight and nutritional outcomes in community-dwelling older adults aged ≥60 years at risk of malnutrition in Thailand.

Intervention: 196 older adults who were at risk of malnutrition, identified MUST were randomly assigned to receive ONS with HMB twice daily with dietary counselling (intervention) or dietary counselling only (control) for 60 days.

Results:

- The change in body weight was sig. greater in the intervention group vs control group at 30 days and 60 days ($p < 0.0001$)
- A significantly larger increase in BMI was found in the intervention group compared to the control group at (0.34 ± 0.08, $p < 0.0001$) and day 60 (0.62 ± 0.09, $p < 0.0001$)
- The odds of achieving better nutritional status were sig. higher in intervention group than the control ($p=0.0001$)
- The average compliance with ONS with HMB* over 60 days was high (92.8%) in the intervention group

Conclusion: The use of ONS with HMB along with DC sig. improved body weight, BMI, and nutritional status among community-dwelling older adults at risk of malnutrition. These findings underscore the importance of early nutritional intervention in this population.

ONS: Oral Nutritional Supplement. HMB; β-hydroxy-β-methylbutyrate. *Supplement was Ensure®, Abbott Nutrition, Zwolle with 270kcal, 11g protein, 9g fat, 34.5g carbohydrate, 0.74g CaHMB (Calcium β-hydroxy-β-methylbutyrate) per 220 mL serving; BMI: Body Mass Index; MUST: Malnutrition Universal Screening Tool.

De Luis et al. *JCSM*.2025;16,13700.

IMPACT OF HYDROXY-METHYL-BUTYRATE SUPPLEMENTATION ON MALNOURISHED PATIENTS ASSESSED USING AI-ENHANCED ULTRASOUND IMAGING

Study: Prospective interventional study.

Aim: To evaluate the effects of ONS with HMB in subjects with disease related malnutrition.

Intervention: For 3 months, patients with a diagnosis of malnutrition received nutritional education and ONS with HMB x2/day. Malnutrition was diagnosed with GLIM and patients received follow-up and compliance calls. Patients were assessed at baseline and follow-up with anthropometry, BIA, muscle ultrasonography and biochemical changes.

Results: 50 patients with a mean age of 57.8 years. Following treatment with ONS with HMB :

- The prevalence of sarcopenia decreased significantly (24% to 18%; p=0.01) and severe malnutrition decreased (14% to 2%; p=0.01)
- The percentage of confirmed sarcopenia (24% to 18% p=0.01) and severe sarcopenia (12% to 6% p=0.01) reduced with significance
- Handgrip strength (0.36 ± 0.21 kg; p=0.009) and Time Up and Go Test (1.16 ± 0.15 s; p=0.02) improved with significance
- Phase angle (0.14 ± 0.02°; p=0.02), phase angle index (0.07 ± 0.01°/$m^{2;}$ p=0.01); fat free mass (1.31 ± 0.12 kg; p=0.006); skeletal muscle mass (0.51 ± 0.11 kg; p=0.01); and skeletal muscle mass index (0.31 ± 0.13 kg/m^2; p=0.01) increased.
- The thickness of vastus intermedius muscle (0.09 ± 0.01 cm; p=0.008) and rectus femoris (1.06 ± 0.4 cm; p=0.07) increased
- Sarcopenia index increased with significance (1.03 ± 0.3 cm; p=0.03)
- Muscle quality, assessed with echogenicity analysis, improved with significance (0.04 ± 0.01; p=0.04)

Conclusion: The use of ONS with HMB in disease-related malnutrition significantly improved nutritional status, muscle mass, and muscle quality as assessed by echogenicity and with AI-based ultrasound imaging.

GLIM: Global Leadership In Malnutrition; BIA: Bioelectrical Impedance Analysis; AI: Artificial Intelligence; ONS: Oral Nutritional Supplement; HMB; β-hydroxy-β-methylbutyrate.

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Triguero-Cánovas D et al. *Support Care Cancer*.2023;6;31(12):673.

HOME-BASED PREHABILIATION IMRPOVES PHYSICAL CONDITIONS MEASURED BY ERGOSPIROMETRY & 6MWT IN COLORECTAL CANCER PATIENTS

Study: A prospective and randomised clinical study.

Aim: To evaluate the impact of outpatient prehabilitation on the physical condition of patients treated surgically for colorectal cancer, measured with the 6MWT and CPET, and to establish a relationship between both tests.

Intervention: Patients were receiving treatment for colorectal cancer and randomised into intervention group (PreH) or control group. Those in the PreH group underwent the prehabilitation program; with x3 weekly sessions of resistance training, dietary recommendations and ONS with HMB to meet 1.2-1.5g protein/kg/day and recommendations for relaxation and breathing techniques. Patients in the control group did not receive any education or recommendation on patterns of physical activity, nutrition, or relaxation.

Results:

- Prehabilitation reduced postoperative complications compared to control (17.4% vs 33.3%, p=0.22)
- Length of stay was lower in the PreH group compared to control (5.74 vs. 6.67 days; p=0.30)
- Sig. improvement in 6MWT 6-weeks after surgery in the PreH group (+68.9m vs. -27.2m, p=0.01)
- Postoperative ileus was more frequent in the control group (14.3% vs. 4.3%; p=0.22)
- Sig. differences in ergospirometry improvements between PreH group and control group (+0.79 METs vs. −0.84 METs, p=0.001)
- Infectious complications were only present in the control group, with 3 surgical wound infections and 1 case of pneumonia.

Conclusion: Home prehabilitation achieved lower overall postoperative complications than standard care, sig. attenuates the loss of functional capacity in patients with colorectal cancer and reached significant improvements in 6MWT.

6MWT: 6-Minute Walk Test; CPET: Cardiopulmonary Exercise Testing; HMB; β-hydroxy-β-methylbutyrate; ONS: Oral Nutritional Supplement.

Cornejo-Pareja I et al. *Nutrients*.2021;13(12):4355.

EFFECT OF AN ORAL NUTRITIONAL SUPPLEMENT (ONS) WITH β-HYDROXY-βMETHYLBUTYRATE AND VITAMIN D ON MORPHOFUNCTIONAL ASPECTS, BODY COMPOSITION, AND PHASE ANGLE IN MALNOURISHED PATIENTS

Study: Retrospective analysis.

Aim: The aim of this study was to observe the effect of ONS with HMB on nutritional status, body weight, and muscle-related outcomes in adult patients with or at risk of malnutrition under standard of care.

Intervention: 283 adult patients (63% with a diagnosis of cancer) with/at risk of malnutrition were enrolled. Intervention included muscle strength training exercises (3 sessions x 30-45 mins/session) and diet enrichment to 30-35kcal/kg/day and 1.2-1.3g protein/kg/day, plus 2 servings of either standard ONS (S-ONS^) or ONS with HMB x2/day for 6 months.

Results:

- PA and BCM increased only in the patients receiving ONS with HMB but not in those receiving S-ONS(0.95(0.13) vs. −0.36(0.4), and 2.98(0.5) vs. −0.6(1.5) kg, mean difference (SE) from baseline for PA and BCM, respectively)
- The estimated increase in hand grip strength was higher in patients receiving ONS with HMB than S-ONS (6.2 vs. 4.7kg)
- Fat-free mass significantly increased from baseline in the ONS with HMB group but not in the ONS group (1.3 vs. 0.9kg)
- In a subgroup analysis of oncology patients with ONS with HMB
  - BMI, arm circumference, bicep skinfold, handgrip strength, fat-free mass, prealbumin, and CRP all improved with significance ($p<0.05$)

Conclusion: This study shows a program with dietary and strength exercise counselling, together with ONS, is beneficial to support nutritional, clinical, and functional outcomes in outpatients with malnutrition. This study also adds more evidence to the use of an ONS with HMB to improve nutritional status and body composition in malnourished patients, especially in cancer patients

*This study was a collaboration between the Institution and Abbott Laboratories. The company covered the publication cost. No other funding was provided. ^S-ONS contained 206–320 kcal, 10.7–20 g protein, 7.8–13 g fat, and 25.5–37.7 g carbohydrates. ONS: Oral Nutritional Supplement; HMB; β-hydroxy-β-methylbutyrate; SE: Standard Error; BMI: Body Mass Index; CRP: C-reactive Protein; PA: Phase Angle.

López-Rodríguez-Arias F, et al. *Support Care Cancer.*2021;29(12):7785–7791.

EFFECT OF HOME-BASED PREHABILITATION IN AN ENHANCED RECOVERY AFTER SURGERY PROGRAM FOR PATIENTS UNDERGOING COLORECTAL CANCER SURGERY DURING THE COVID-19 PANDEMIC

Study: A prospective and randomised clinical study.

Aim: To assess the effect of home prehabilitation on body composition, complications, and hospital stay in 20 patients undergoing oncological colorectal surgery

Intervention: Patients were randomised into 2 study groups – prehabilitation group (PH) vs standard care (SC). The prehabilitation program was trimodal with recommendations on physical exercise (aerobic and resistance training), nutritional counselling including ONS with HMB to meet 1.2-1.3g protein/kg/day, and relaxation techniques. The SC group did not receive any recommendations.

Results:

- PH patients had a shorter hospital stay compared to SC (4.8 vs 7.2 days, p=0.052)
- Postoperative complications were also lower in PH patients compared to SC (20% vs 50%, p=0.16)
- PH patients' loss of lean mass was 1.7% compared to 7.1% loss of lean mass in SC (p=0.17)
- Loss of lean mass was attenuated at 90 days; SC increased fat mass considerably compared to PH group (+ 8.72% vs − 8.16%)

Conclusion: Home prehabilitation, including ONS with HMB, has proven its effectiveness, achieving an attenuation of lean mass loss in the early postoperative period and a lower gain in fat mass in the late postoperative period. In addition, it has managed to reduce hospital stays and postoperative complications.

HMB; β-hydroxy-β-methylbutyrate; ONS: Oral Nutritional Supplement.

Doyev R et al. *Clin Nutr ESPEN*.2024;24-LB-2661.

NUTRITION CARE WITH HIGH PROTEIN AND β-HYDROXY-β-METHYLBUTYRATE IS ASSOCIATED WITH 6-MONTH READMISSION REDUCTION AMONG MALNOURISHED PATIENTS

Study: Retrospective review of electronic medical records from 2 inpatient hospitals from 2015 to 2021.

Aim: To assess if ONS with HMB is effective at alleviating the clinical and economic burden of malnutrition and healthcare costs.

Intervention: Records of 16,175 patients were reviewed with the inclusion criteria of MST score >2, 18+ years old, treated with ONS during hospitalisation, and BMI < 20kg/m^2. Readmission rates at 1-, 3-, and 6- months were compared between those on high-protein or standard ONS versus ONS with HMB. There was a 1:1 ratio of n=720 receiving ONS with HMB and n=720 receiving other ONS. Propensity Score Matching (PSM) controlled for department/medical unit, age, ONS volume, and length of stay.

Results:

- 16,175 were at-risk/malnourished patients with a mean age 72±2 years, 50% were female, median BMI was 24.5 kg/m^2, median hospitalisation of 8 days, mainly with oncology, cardiovascular/cardiopulmonary, and gastrointestinal diagnoses
- 97% of patients received ONS, and 49% were readmitted within 6 months
- ONS with HMB during hospitalisation was associated with significantly reduced readmission rates at 1 month (OR 0.698 95%CI (0.548-0.888), p= 0.0034); 3 months (OR 0.772 95%CI (0.623-0.958), p = 0.0187); and 6 months (0.780 95%CI (0.633-0.961, p= 0.0195) compared to high-protein or standard ONS

Conclusion: The use of ONS with HMB has a significantly greater impact on reducing 6-month readmission rates than standard ONS.

MST: Malnutrition screening tool; ONS: Oral Nutritional Supplement; BMI: Body Mass Index; HMB; β-hydroxy-β-methylbutyrate.

Baggs GE et al. *Clin Nutr.*2023;42(11)2116-2123.

IMPACT OF A SPECIALISED ORAL NUTRITIONAL SUPPLEMENT ON QUALITY OF LIFE IN OLDER ADULTS FOLLOWING HOSPITALISATION: POST-HOC ANALYSIS OF THE NOURISH TRIAL

Study: The NOURISH trial was a multicentre, prospective, randomised, double-blind, placebo-controlled, parallel-group study.

Aim: This post-hoc focused on determined whether ONS with HMB benefits were further associated with measurable improvements in Quality of Life (QoL) during the post-hospitalisation period.

Intervention: In the NOURISH study, 622 patients with a diagnosis of CHF, AMI, pneumonia or COPD were included. Patients were provided ONS with HMB x2/day or placebo during hospital stay and for 90 days post-discharge.

Results:

- Patients consuming placebo had lower QoL than those consuming ONS with HMB
- Those taking ONS with HMB had sig. improvements in health at discharge (p=0.019), mental component summary score (p=0.019), mental health (p=0.007), vitality (p=0.049), social functioning (p=0.023) and general health (p=0.005)
- Those taking ONS with HMB showed trends towards significant QoL differences for physical component, physical functioning, bodily pain and emotion (p=0.061, p=0.052, p=0.055, p=0.084)

Conclusion: Among malnourished, hospitalised patients (aged 65 years), supplementation with ONS with HMB during hospitalisation and 90-days post discharge resulted in improvements in QoL. These benefits complement survival benefits previously shown in the NOURISH trial analyses.

NOURISH: Nutrition Effect On Unplanned Readmissions and Survival in Hospitalised patients; CHF: Chronic Heart Failure; AMI: Acute Myocardial Infarction; COPD: Chronic Obstructive Pulmonary Disease; ONS: Oral Nutritional Supplement; HMB; β-hydroxy-β-methylbutyrate.

Espina S et al. *Nutrients.* 2021;13:3764.

AMINO ACID PROFILE IN MALNOURISHED PATIENTS WITH LIVER CIRRHOSIS AND ITS MODIFICATION WITH ORAL NUTRITIONAL SUPPLEMENTS: IMPLICATIONS ON MINIMAL HEPATIC ENCEPHALOPATHY

Study: Post-hoc study of a double-blind parallel-group randomised control trial.

Aim: To investigate the effect of ONS with HMB in the clinical setting of liver cirrhosis and malnutrition and identify the metabolic signature of minimal hepatic encephalopathy (MHE) and evaluate its modification with ONS with HMB.

Intervention: 43 individuals with cirrhosis and malnutrition were randomised into groups to receive ONS with HMB or Ensure® Plus HP x2/day for 12 weeks.

Results:

- There was no significant difference between the 2 groups at baseline; 72% of the patients were evaluated as moderately malnourished, and the other 28% as severely malnourished.
- ONS with HMB allowed a larger increase in Valine, Leucine, Phenylalanine, Tryptophan and Branched-Chain Amino Acids fasting plasma levels compared to Ensure® Plus HP
- ONS with HMB treatment reduced the MHE prevalence from 38% to 21%, with no reduction in the Ensure® Plus HP group

Conclusion: ONS with HMB increased Fischer´s ratio without varying glycine or ammonia plasma levels in liver cirrhosis and malnutrition, a protective amino acid profile that can help prevent MHE.

ONS: Oral Nutritional Supplement; HMB; β-hydroxy-β-methylbutyrate.

Vegas-Aguilar I et al. *Nutrients*.2025;7,17(9):1601.

ADHERENCE TO β-HYDROXY-β-METHYLBUTYRATE-ENRICHED ONS ENHANCES SURVIVAL AND NUTRITIONAL RECOVERY IN MALNOURISHED OUTPATIETNS: PROGNOSTIC INSIGHTS

Study: Retrospective observational study.

Aim: To evaluate the effects of a six-month nutritional recovery program combining ONS with HMB, dietary recommendations, and exercise on survival, morpho functional markers, and adherence in malnourished outpatients.

Intervention: n=135 (mean age 61.3 years and BMI 22.0kg/m^2) were diagnosed with DRM based on the GLIM criteria. Morpho functional assessment included Phase Angle measured through BIA, Muscle CSA with ultrasound, handgrip strength (HGS) and Timed Up and Go test (TUG). Recommended intakes of 30-35kcal/kg and 1.2-1.3g protein/kg/day in addition to ONS with HMB x2/day.

Results: After 6 months

- There was significant improvements in Phase Angle (+0.47°, p=0.010), Muscle CSA (+0.90 cm^2, p=0.0001), HGS (+4.1 kg, p=0.001) and TUG (-0.93 s, p=0.001) from baseline to 6 months follow-up
- Fat Free Mass and Fat Free Mass Index significantly improved (p=0.009, p=0.013) from baseline to 6-month follow-up
- Changes in muscle mass quality seen through improved CSA (m^2) and HGS (kg) demonstrated superior muscle mass recovery and functional improvement in those more adherent to ONS with HMB at 6-month follow-up
- Those with better ONS with HMB compliance also had reduced mortality risk (HR 0.42, p<0.05)
- Changes in PA and HGS were strongly associated with survival (ΔPA = HR of 0.27 (95% CI: 0.15-0.50, p<0.001) and ΔHGS = HR of 0.82 (95% CI: 0.75-0.89, p<0.001)).

Conclusion: A nutritional recovery program with ONS with HMB significantly improves survival and morpho functional markers in malnourished patients. These improvements included enhanced cellular integrity, superior muscle mass recovery and functional improvement.

BMI: Body Mass Index; DRM: Disease related malnutrition; GLIM: Global Leadership Initiative on Malnutrition; BIA: Bioelectrical Impedance Analysis; CSA: Cross-Sectional Area; ONS: Oral Nutritional Supplement; HMB; β-hydroxy-β-methylbutyrate.

Koh et al. *Nutrients*.2024;16(24),4351.

EVALUATING THE IMPACT OF MULTIMODAL PREHABILITATION WITH HIGH PROTEIN ORAL NUTRITIONAL SUPPLEMENTATION WITH β-HYDROXY-β-METHYLBUTYRATE (HMB) ON SARCOPENIC SURGICAL PATIENTS—INTERIM ANALYSIS OF THE HEROS STUDY

Study: Prospective non-randomised interventional pilot cohort study

Aim: To evaluate the effect of a multimodal prehabilitation program using ONS with HMB and resistance exercise on muscle quality and functional outcomes in sarcopenic patients undergoing gastrointestinal surgery.

Intervention: 40 participants enrolled in a 2–4-week program pre-surgery with resistance exercise, ONS with HMB x3/day and meeting 120% energy and protein requirements, vitamin D supplementation (50,000 IU/week) and a dose of 1g IV ferric derisomaltose. Muscle quality was measured with MuscleSound®, Ultrasound. Other functional parameters measured included; handgrip strength, 30-sec chair rise, functional reach test, 6MWT and gait speed and anthropometry

Results: 36 patients with median age 71.5 years and BMI 21.6kg/m^2, 66% had severe sarcopenia and 33.3% had sarcopenia

- Sig increase in IMAT index after 2 weeks prehabilitation and to 1-month post-surgery
- Sig. improvements in 6MWT and gait speed after 2-week prehabilitation
- There was improvements in HGS, 30 second chair rise, 6MWT and gait speed from week 0 of prehabilitation to 1-month post-op
- Average length of stay was 7 days, lower that average length of stay

Conclusion: There was an increase in the IMAT index in sarcopenic patients after prehabilitation including ONS with HMB which may be a result of altered muscle metabolism in elderly skeletal muscle. Functional outcomes were all at least maintained at baseline, with improvements seen in gait speed and the 6MWT.

IV: Intravenous; 6MWT: 6-minute Walk Test; BMI: Body Mass Index; IMAT: Intramuscular Adipose Tissue; HGS: Handgrip Strength; ONS: Oral Nutritional Supplement; HMB; β-hydroxy-β-methylbutyrate.

Cornejo-Pareja et al. *Nutrients* 2025,17,2854.

INTERVENTION WITH ORAL NUTRITION SUPPLEMENTS WITH B-HYDROXY-B-METHYLBUTYRATE AND VITAMIN D IN MALNOURISHED ONCOLOGY OUTPATIENTS ASSOCIATED WITH REDUCED HEALTHCARE RESOURCE UTILISATION AND COSTS

Aim: To analyse healthcare resource use and cost data from a retrospective study in malnourished oncology patients that previously reported benefits of an ONS with HMB[1].

Intervention: For this single-arm study, data on number and cost of hospital admissions, emergency department (ED) visits, general practitioner (GP) and specialist physician visits for one year before and after ONS with HMB were collected for 179 patients. Comparisons of health care visits over 3, 6 and 12 months before and after ONS with HMB use by the same patients were made using univariate Poisson regression. Total costs before and after intervention were compared using t-tests. The impact of ONS with HMB was examined using a difference-in-differences (DID) model of healthcare resource use or costs regressed on patient demographics and ONS use.

Results:

- Patients had average age of 62.3 ± 12.0 years; 86.6% received ONS with HMB . Hospital admissions, ED visits, GP visits, and specialist visits per patient declined over all time periods.
- Costs were lower by €8,899, €12,165, and €15,631 (all $p<0.01$) over 3, 6, and 12 months, respectively.
- DID modelling showed patients receiving ONS with HMB had fewer hospital admissions over 12 months (β = -1.08), ED visits over 12 months (β = -0.768), GP visits over 12 months (β = -0.447), and specialist visits 12 months (β = -0.199) (all $p<0.05$).

Conclusion: This study demonstrates that the clinical and functional improvements previously observed in oncology patients using ONS with HMB were associated with significant reductions in healthcare resource utilisation and costs.

ONS: Oral Nutritional Supplement; HMB; β-hydroxy-β-methylbutyrate. 1. Cornejo-Pareja I, et al. *Nutrients* 2021;13(12):4355

Tey et al. *Nutrients.*2024;16(15),2495.

EFFECTS OF ORAL NUTRITIONAL SUPPLEMENT WITH β-HYDROXY-β-METHYLBUTYRATE (HMB) ON BIOCHEMICAL AND HEMATOLOGICAL INDICES IN COMMUNITY-DWELLING OLDER ADULTS AT RISK OF MALNUTRITION: FINDINGS FROM THE SHIELD STUDY

Study: Randomised, double-blind, placebo-controlled, multi-centre study.

Aim: To investigate the effects of a 6-month nutritional intervention ONS with HMB on a wide range of biochemical and haematological indices in community-dwelling older adults at risk of malnutrition.

Intervention: n= 811 older adults aged 65 years were randomly allocated to either ONS with HMB and dietary counselling (intervention group) or a placebo and dietary counselling (placebo group). Both groups consumed study products twice a day for 180 days. Data were collected at baseline, day 90, and day 180.

Results:

- Compared with placebo, ONS with HMB group showed significantly greater increases in weight, BMI and fat mass ($p<0.001$)
- Compared to placebo at 180 days follow-up, ONS with HMB group had significantly greater urea (6.0 mmol/L vs. 5.4 mmol/L, $p<0.001$), urea to creatinine ratio (4.39 vs. 4.26, $p<0.001$), prealbumin (24.9 mg/dL vs. 24.0 mg/dL, $p<0.001$), vitamin B12 (480.0 pmol/L vs. 420.1 pmol/L, $p < 0.001$), and globulin levels (26.8 g/L vs. 26.5 g/L, $p=0.032$).
- Compared to placebo, ONS with HMB group had a significantly higher absolute reticulocyte count (62.0 × 103/μL vs. 58.2 × 103/μL, overall $p<0.001$), mean platelet volume (10.0 fL vs. 9.9 fL, overall $p=0.003$) and in absolute monocyte count at day 90 (0.50 × 103/μL vs. 0.47 × 103/μL, $p=0.009$) in the intervention group.

Conclusion: Daily consumption of ONS with HMB for six months led to significant improvements in biochemical and haematological indices in community-dwelling older adults at risk of malnutrition.

BMI: Body Mass Index; ONS: Oral Nutritional Supplement; HMB; β-hydroxy-β-methylbutyrate.

Cornejo-Pareja et al. *Nutrients*.2025;17(17),2854.

HEALTHCARE RESOURCE UTILISATION DURING A MULTIMODAL NUTRITIONAL PROGRAM WITH ORAL NUTRITIONAL SUPPLEMENTS IN MALNOURISHED OUTPATIENTS

Study: Retrospective analysis.

Aim: To determine whether a nutritional intervention including consumption on standard ONS or ONS with HMB as part of a multimodal program, was associated with reduced use of healthcare resources and lowered costs.

Intervention: n=283 patients received nutritional counselling with a trained dietitians and advised to have standard ONS or ONS with HMB x2 servings/day for 3-6 months along with strong exercise recommendations from the hospital's rehabilitation unit.

Results:

- Overall, ONS use was associated with reduced patient healthcare costs by half (€27,024.80 to €13,349.60, $p < 0.001$).
- Patients receiving ONS with HMB (−0.583) had a greater reduction in healthcare associated costs than patients receiving standard ONS in the 12 months after nutritional intervention.
- Patients who received ONS with HMB had eight times lower odds of reduction in dose or suspension of oncological treatment versus standard ONS over 12 months (−2.144; OR = 0.117).
- Oncology patients receiving ONS with HMB had 1.14 fewer hospital readmissions (−1.08, mfx = −1.14), 1.98 fewer ED visits (−0.768, mfx = −1.98), 2.29 fewer GP visits (−0.447, mfx = −2.29) and 2.21 fewer specialist visits (−0.20; mfx = −2.21) than standard ONS.

Conclusion: The use of ONS with HMB provided advantages over standard ONS, both in health outcomes and cost-of-care reductions including lower healthcare resource use, and, for patients being treated for cancer, a reduced likelihood of treatment failure.

HMB: β-hydroxy-β-methylbutyrate; ONS: Oral Nutritional Supplement.

Fiorindi et al. *ESPEN*.2025;ABS-2318.

EFFECTS OF PREOPERATIVE BETA-HYDROXY-BETA-METHYLBUTYRATE SUPPLEMENTATION ON PREOPERATIVE NUTRITIONAL AND FUNCTIONAL STATUS DURING MULTIMODAL PREHABILITATION FOR PATIENTS UNDERGOING NEOADJUVANT CANCER THERAPY

Study: Retrospective analysis.

Aim: To explore the effects of HMB supplementation during a multimodal prehabilitation (MPreHab) program on nutritional status and physical function in patients receiving neoadjuvant therapy (NAT).

Intervention: Consecutive patients with oesophageal, gastric or colorectal cancer referred to the Careggi MPreHab centre were included. All were treated with a personalised MPreHab, including medical optimisation, aerobic and resistance exercise, nutritional and psychological support during NAT. Malnourished patients and/or those with reduced muscle mass received at least 1.5 g of HMB/day, if tolerated. Outcome measures were measured at baseline and before surgery. 78 patients (mean age 67.1 ± 10.6 years) were analysed.

Results:

- Patients who received HMB group (n=39) demonstrated a statistically significant improvement in the 30CST from baseline (0.68 ± 2.59 vs. -0.51 ± 3.54; p=0.035)
- Prealbumin, CRP, 6MWD and HGS also improved in patients receiving HMB, but these changes were not significant
- FFMI and ASMI increased, independently from receiving HMB.

Conclusion: HMB supplementation during MPrehab in cancer patients undergoing NAT resulted in a better improvement of lower extremity strength. Overall, physical function, strength and muscle mass were maintained with PreHab during NAT.

HMB: β-hydroxy-β-methylbutyrate; CST: Chair Stand Test; CRP: C- Reactive Protein; 6MWD: 6-min walking distance; HGS: Handgrip Strength; FFMI: Fat Free Mass Index; ASMI: Appendicular Muscle Mass Index.