NOURISH THE MUSCLE
Nutritional Supplementation in Sarcopenia
GENERAL DISCUSSION

Maintaining functional capacity, mobility and ultimately independence, are cornerstones for older adults to actively participate in society. Preserving muscle mass, strength and physical function are, as such, critical prerequisites for performing daily activities and living independently. If these muscle measures are below a critical threshold, it is called sarcopenia (1). Sarcopenia is a strong driver of physical frailty phenotype, and both conditions are affected by dietary intake throughout the lifespan. In part I of this thesis (chapter 2-4) we assessed the nutritional status, physical and clinical characteristics of primarily community-dwelling older adults with sarcopenia and physical frailty. Part II (chapter 5-7) presents the effects of specific nutritional interventions on nutritional status and muscle measures in older adults with sarcopenia and/or obesity.

Part I
Nutritional assessment and malnutrition in sarcopenic and frail older adults

In principle, malnutrition is an umbrella term. It encompasses undernutrition (quantitative malnutrition or in the past often called protein-energy malnutrition), as well as ‘poor’ nutrition in the broad sense of inadequate nutritional status (thus selective or qualitative malnutrition), and even overnutrition. In our meta-analysis (chapter 2) we found that only approximately 8% of physically frail community-dwelling older adults with a mean age of 75-80 years were identified as malnourished by the Mini-Nutritional Assessment (MNA). The majority of the frail older adults are thus not assessed as malnourished, but as at risk of malnutrition (43%) or with normal nutritional status (49%). The majority of older adults at risk for malnutrition have a normal BMI, often with a mean BMI around 26 kg/m² (2, 3) and are probably not protein-energy malnourished. Both the at risk group and the older adults with a normal nutritional status, however, may have an increased risk of qualitative or selective malnutrition, due to suboptimal intake of single nutrients, such as protein and vitamins (4). These suboptimal diets lead to inadequate nutritional status and may contribute to the development of sarcopenia and frailty (5, 6). Improving the nutritional status may help to slow down the decline of muscle mass, strength and function, which also provides a physiological buffer to cope with negative health events. Especially during periods of muscle disuse and immobilisation due to trauma, acute illness and hospitalisation, older adults often lose substantial muscle mass and functional capacity that hampers recovery to their normal active daily life. Moreover, the decline of their physiological reserve makes them more vulnerable for subsequent incidents or crisis periods and thus increases the risk for frailty (7-10). The goal is to maintain and build physiological buffer in anticipation for such crises, which will eventually facilitate recovery and allow older adults to maintain independent. For example, we have shown in the EMPOWER study (chapter 3) that muscle measures, greater muscle mass, more muscle strength measured by handgrip strength, self-reported ability to walk, and absence of malnutrition at hospital admission are positively associated with survival and independent living of older patients. These relevant findings are in line with other studies that described associations between sarcopenia and malnutrition with negative clinical outcomes and increased risk of mortality in older hospitalized patients (11-15), although these studies all used different definitions to describe sarcopenia and malnutrition. Because of these negative associations, it should be recommended to assess sarcopenia and nutritional
status in hospitalized older population as part of routine care. Moreover, prevention of sarcopenia and inadequate nutritional status in community-dwelling older adults may be more effective. In two recent systematic reviews, Ter Borg et al. found suboptimal energy intakes and macronutrient distributions, with a high fat (especially saturated) intake among community-dwelling older adults (16, 17). The mean protein intake was 1.0 and 1.1 g/kg body weight/day (+/- SD 0.2) for older men and women respectively and 10–12% of older adults did not meet the estimated average requirement (EAR) cut point of 0.66 g protein/kg body weight/day. Furthermore, there was a high prevalence of inadequate micronutrient intakes, especially the mean intakes of vitamin D (approximately 5 µg/d), thiamin, riboflavin, calcium, magnesium and selenium were below adequate. In chapter 4, we compared the nutritional intake and status of non-malnourished sarcopenic older adults with age and sex matched non-sarcopenic controls in the UK. The energy intake was similar, but the sarcopenic group consumed less protein and had (even) lower intake of several micronutrients, such as vitamin D (2.6 vs. 4.0 µg/d), vitamin B-12, magnesium, selenium, and phosphorus compared to the non-sarcopenic controls. Furthermore, these non-protein-energy malnourished older adults with sarcopenia reported lower quality of life and physical activity levels. The differences in nutrient concentrations and dietary intakes might be related to the differences in muscle mass, strength and physical function between the two groups. However, since this was a cross-sectional study (chapter 4), it is not possible to comment on the direction of the relationship, whether sarcopenia leads to lower intakes of micronutrients or vice versa. This study did, however, serve to illustrate that there is indeed a discrepancy in the diets of adults with sarcopenia, compared with their non-sarcopenic counterparts. In another cross-sectional study with older adults with and without sarcopenia (Maastricht Sarcopenia Study), we also looked at other nutritional markers and found lower omega-3 fatty acid intake and higher homocysteine levels, potentially explaining the observed lower vitamin B intake in the sarcopenic group (18).

These findings are in line with other studies that describe that many sarcopenic older adults, community-dwelling and institutionalized, have an inadequate intake and status of several nutrients including protein, leucine, unsaturated fatty acids, vitamin D, anti-oxidants, B vitamins, which may negatively affect the progression of sarcopenia (19-22) and (directly or indirectly) physical frailty (5, 23, 24). In addition to addressing dietary insufficiencies and deficiencies, these sarcopenic older adults may even have higher nutritional needs in order to enhance muscle mass, strength and function. Improving their dietary intake, potentially supported by supplementation with specific nutritional formulas, may contribute to successful prevention and management of sarcopenia.

**Part II**

*Effects of nutritional supplementation on nutritional status and muscle measures in older adults with sarcopenia and/or obesity*

In Part II of the thesis, we studied the effects of a targeted nutritional intervention on the nutritional status and muscle measures in non-malnourished sarcopenic or obese older adults. We designed a nutritional formula specifically targeting muscle mass, strength and function in sarcopenic and physically frail older adults. The target group was predominantly older adults with a stable body weight, not particularly those who are
characterized as ‘malnourished’ (i.e. undernourished and/or protein-energy malnourished) according to screening tools such as MNA and SNAQ. The 150 kcal nutritional supplement contained 21 g high quality protein, i.e. the fast digestible whey protein, enriched with the free amino acid leucine (in total 3 g) per serving. In addition it contained 9 g carbohydrates, 3 g fat, and 1.3 g fiber, which resulted in a relatively low caloric beverage with a glycaemic index of 23. Furthermore, 800IU vitamin D was added as essential ingredient of a vitamin-mineral blend enriched with the micronutrients that may be inadequately consumed by sarcopenic and frail older adults, such as vitamin D, B12, E and folate (5, 18, 19).

Effects of supplementation with specific nutritional formula on nutritional status

The intervention with one or two servings per day of this nutritional formula was meant to supplement the habitual dietary intake, improve the nutritional status and to stimulate muscle protein synthesis in older adults with sarcopenia. The nutritional supplements were well tolerated, did not give any indication for safety concern, and compliance was high (>90%) during the intervention studies. In the PROVIDE trial (chapter 5), we observed a lower intake of habitual diet of the primarily community-dwelling older adults with sarcopenia. Supplementation with two servings (i.e. 300 kcal) led to a significant increase in total energy intake in the active as well as the control group by 165 kcal per day (25). In another study with healthy older men, supplementation with one serving per day (i.e. 150 kcal) led to a decrease of 158 kcal in total energy intake per day (26). These study results suggest that part of the additional calories provided to non-protein-energy malnourished older adults is compensated by a modification of the normal diet during the study periods. The relatively small changes in energy intake may have a cumulative effect over time, and can eventually impact the body composition. Therefore, it is crucial to follow up patients’ body composition when supplementing the diet.

Supplementation with the high protein nutritional formula increased the total daily protein intake in the PROVIDE study (chapter 5) to the recommended range of 1.2-1.5 g/kg/d for geriatric patients. This increase in protein intake did not lead to a clinically relevant alteration of the renal status of this group of sarcopenic older adults. The PROVIDE study population had a median (Q1-Q3) baseline eGFR of 77 (63-87) mL/min/1.73m², considered as a normal value for this specific age group around 75-80 years old. The 13 weeks supplementation led to a small improvement in eGFR of the test group (1.0 (-2.8-4.2) mL/min/1.73m²; versus no change in the control group) and no change in eGFR was shown during the 13 week study extension. Thus, the protein supplementation did not give any indication of adverse effects of the high protein test product on the participants’ renal function (27).

Furthermore, 25-hydroxyvitamin D serum concentrations increased as a result of the supplementation in the PROVIDE study (chapter 5). The majority of the 380 sarcopenic older adults reached the desirable range for 25-hydroxyvitamin D serum concentrations between 50-100 nmol/L. Vitamin D insufficiency (<50 nmol/L) in the intervention group was reduced from 53% of participants at baseline to 8% at week 13 with the two servings per day each containing 800 IU vitamin D. Three percent of the intervention group had serum 25(OH)D concentrations ≥125nmol/L at week 13. After the extended exposure of 13 weeks, vitamin D serum concentrations were similar and appeared to have reached a plateau. Supplementation
up to 6 months with a vitamin D and calcium enriched medical nutrition drink improved vitamin D status without any sign of disturbed calcium homeostasis or hypercalcaemia (28). Furthermore, we examined the concentrations of several other micronutrients such as vitamin B12, vitamin E and folate in the PROVIDE study before and after supplementation. All of the serum micronutrient concentrations that were monitored increased significantly and led to a meaningful decrease in the number of participants with vitamin D, vitamin B12 and folate deficiency (29).

In summary, supplementation with this specific nutritional formula led to improved nutritional status in healthy older adults and older adults with sarcopenia or obesity. The nutritional interventions increased the total daily protein intake to the recommended levels. Specifically targeting breakfast (when protein intakes are commonly lowest) and the periods around exercise may provide more evenly distributed and effective boluses of protein during the day. The total energy intake was only minimally impacted and mainly compensated by the habitual diet. The serum concentration of vitamin D and some other relevant micronutrients increased to desirable levels and led to a meaningful decrease in deficiencies. The vitamin D and leucine-enriched whey protein nutritional supplements were well tolerated and did not give any safety concern regarding renal function or any other adverse effects.

Effects of supplementation with specific nutritional formula on muscle measures

Although nutritional intervention is considered a potentially effective intervention in sarcopenia, much of the evidence is based on short-term protein synthesis studies. Large well-controlled, high quality clinical trials of the mid and long term effects of adequate nutritional Supplementation are still lacking (30). The composition of the daily diet as well as of supplements, the quantity and quality of protein intake, intake of other macro- (energy, carbohydrates, fatty acids) and micronutrients (e.g. vitamin D), the timing and distribution of meals and supplementation, associated physical activity and exercise programs, target groups (healthy, compromised, obese, acute or chronic patients) and outcome measures (muscle mass, strength, functional) are all variables that determine the success of a nutritional intervention in the field of sarcopenia.

The composition of the nutritional formulas and timing of supplementation in combination with the appropriate exercise programs are important determinants of optimizing the benefits of targeted interventions in older adults with sarcopenia. It has been shown that co-ingestion of leucine may improve muscle protein synthesis in response to suboptimal protein meals in older adults (31, 32). This leucine-enriched whey protein mixture has been tested in several mechanistic studies and showed that it led to a rapid and high postprandial increase in essential amino acids including leucine to sufficient levels to overcome the anabolic threshold in older adults (33). Furthermore, this protein mixture appeared to effectively stimulate muscle protein synthesis in healthy and sarcopenic older adults (26, 34-36). A recent meta-analysis concluded that leucine-rich protein supplements may enhance body weight and lean body mass, but not muscle strength, in those older adults already prone to sarcopenia (37). Supplementing breakfast (and during lunch in the PROVIDE trial) aimed to increase the protein intake during these specific meals to overcome the higher anabolic resistance in older adults and to achieve an even distribu-
tion of protein intake boluses during the day (Figure 1) (26, 38, 39). Moreover, an additional post-exercise serving may further enhance the anabolic effect of the resistance training (38). This adjusted timing of protein intakes can lead to additional triggers of muscle protein synthesis stimulation over the course of the day. Such additional triggers of muscle protein synthesis may have resulted in net muscle protein accretion in the healthy (26), obese (38), and sarcopenic older adults (39).

We have consistently reported positive effects on skeletal muscle mass with the vitamin D (800IU) and leucine-enriched whey protein (21 g protein, 3 g total leucine) nutritional supplement in intervention studies with different study populations. In healthy older adults, we observed a 0.37 kg gain in appendicular muscle mass after six weeks of supplementing the breakfast (26). In line with this study, protein supplementation at breakfast and lunch for 24 weeks resulted in a 0.45 kg gain in lean body mass in a RCT with 60 healthy older adults (41). In contrast to the study of Norton et al., we did not find a significant change in body weight in the healthy older men, which may be explained by the low-caloric content of the test product and a non-caloric placebo that minimally affected the total energy intake. supplementation with higher energy products may lead to undesirable gain in fat mass.

Adiposity increases the risk for several chronic diseases such as diabetes type II and cardiovascular disease. Furthermore, the muscle quality in older adults is reduced due to increased intramuscular adipose tissue (42), which may contribute to muscle weakness and the development of sarcopenia and frailty (43).

The PROVIDE study examining the effect of this supplement among 380 non-protein-energy malnourished older adults with sarcopenia demonstrated 0.17 kg increase in appendicular muscle mass after the 13-weeks intervention (chapter 5) (39). The subgroup of PROVIDE participants who had sufficient protein intake (≥1.0 g/kg/d) and serum 25-hydroxyvitamin D (≥50 nmol/L) at baseline, showed an even higher gain in appendicular muscle mass, i.e. 0.59 kg, without any support of an exercise program (chapter 6) (44). Furthermore, the nutritional intervention alone led to an additional improvement in chair-stand test as measure for lower-extremity function in these mainly community-dwelling, sarcopenic older adults.

**Figure 1:** Adequate daily protein intake distribution for maximal muscle protein synthesis. Adapted from Paddon-Jones et al., 2009 (40)
adults in the PROVIDE study. In a large, well-controlled study in 277 older adults who were suffering from both sarcopenia and malnutrition, a 24-week intervention with two different energy-rich oral nutritional supplements improved strength outcomes, increased body weight and fat mass in both groups, but had no effect on muscle mass and did not show a difference between the groups (35). Accomplishing a sufficient nutritional status may be the first prerequisite in order to stimulate muscle accretion in malnourished people. Another high-quality study by Tieland et al. (45) without an associated exercise program in a (pre-)frail, community-dwelling population showed that supplementation with 15 g milk protein twice daily alone improved physical performance compared to placebo, but no increases in muscle mass, fiber size, or muscle strength. However, they did find substantial improvements in lean body mass (1.3 kg) after supplementation with the 30 g of high-quality protein compared with placebo if combined with a resistance exercise program, while both the study groups improved their strength and physical performance. When no additional protein was provided, the (pre-)frail older adults did not have measurable increases in skeletal muscle (46). Recently, in a comparable study with 130 older adults with sarcopenia examining the combined effect of a controlled physical activity program with nutritional interventions, the supplementation with whey protein (22 g) and vitamin D (2.5 mg (100 IU)) increased fat-free mass (1.7 kg), handgrip strength, the MNA score and some biomarkers compared with an isocaloric control (47). In contrast, after a 6 month intervention including progressive resistance exercise and 40g/d of whey protein, Chalé et al. (48) observed greater improvement in knee extensor peak power in older men and women with mobility limitations. There were, however, no additional exercise-induced improvements in muscle size, strength, or physical function versus the isocaloric control.

There is emerging evidence that dietary protein interventions may provide surplus benefits if provided in close temporal proximity to resistance exercise. A thorough meta-analysis by Cermak et al. (49) stated that long-term protein intervention studies have been able to demonstrate further augment to the gains in muscle mass and strength (by often more than 30%) by prolonged progressive resistance-type exercise training in both healthy younger and older adults. Physical activity, including resistance exercises to preserve muscle mass is particularly relevant for older adults with obesity who follow an intentional weight loss program. Sufficient dietary protein intake is recommended for preservation of muscle mass despite the energy restriction (50, 51) and nutritional Supplementation can help to maintain the relatively higher protein intake. During a 13-week weight loss regime including an exercise program, obese older adults in the active group preserved 0.95 kg appendicular muscle mass more than the control group, while muscle strength and function in both groups improved by the exercise program (chapter 7) (38). In a very well-controlled weight loss study as part of the Top Institute Food and Nutrition (TIFN) collaboration, 61 overweight and obese men and women followed 12 weeks of 25% energy intake restriction with either a high protein diet (1.7 g/kg/d) or normal protein diet (0.9 g/kg/d) (52). Although the weight loss regime was successful, both groups lost a similar amount of lean body mass, suggesting that only increasing the protein intake of may be insufficient to preserve lean body mass in these obese older adults. A well-balanced, energy restricted, protein-rich diet in combination with resistance exercise has
shown positive effects on muscle measures in older adults with (sarcopenic) obesity (53). This may potentially be enhanced by a well-timed bolus supplementation with high quality protein and vitamin D. In addition to the positive impact on muscle mass, we also found some indications in the PROVIDE trial that the nutritional supplementation supported bone health in sarcopenic older adults. There was a small significant increase in bone mass density and change in levels of biomarkers for bone metabolism, such as IGF-1, PTH, and CTX. These data are in line with the recommendations of ESCEO that adequate protein, vitamin D and calcium intake, alongside regular physical activity could be helpful for prevention of age-related deterioration of both muscle and bone health (54). In conclusion, the studies show inconsistent, but promising results of nutritional supplementation in sarcopenic and frail older adults. A well-timed supplementation with a sufficient dose of dietary protein that are selected for rapid digestion and absorption kinetics, that are also rich in leucine and/or specifically enriched protein with leucine, appear to be able to compensate for anabolic resistance and stimulate muscle protein synthesis in older adults with sarcopenia. Other nutrients such as vitamin D, anti-oxidants, B vitamins, fiber (and creatine and fish oil-derived fatty acids, which were not in the scope of this thesis) may enhance the beneficial effects. High quality nutritional supplementation, in conjunction with resistance exercise, may be an effective strategy to preserve muscle mass, strength, and function, which may be most valuable in periods of immobilization, hospitalization, disease or other periods of accelerated muscle decline. An expert panel (55) concluded that more well-designed standardized studies on exercise and nutritional intervention in different settings are required before treatment guidelines for sarcopenia can be developed. Nevertheless, it is essential to pilot test specific interventions in general medical practice, which will help to strengthen the evidence contributing to effective guidelines for managing sarcopenia.

**Future perspectives**

Inadequate nutrition clearly contributes to the age-related loss of muscle mass, strength and function. Malnutrition accelerates sarcopenia and is implicated in the development of the physical frailty phenotype (chapter 2) (56). Thus, malnutrition is a relevant contributor of increased vulnerability for developing negative health outcomes, loss of independency and mortality (23). Older adults with undernutrition, i.e. involuntary weight loss and a reduced body or fat-free mass, have to be thoroughly examined and assessed in order to find out the underlying cause of the malnutrition, and to make a nutrition care plan. Irrespective of underlying cause, dietary treatment, often supervised by a professional, need to be started as soon as possible. Dietary treatment may include adequate provision of food items and food fortification where also optimizing stimuli for appetite are vital (4). In addition, support with oral nutritional supplementation is often indicated. Because of the shift in interest in the field of malnutrition towards body weight in combination with lean body mass (57), dietary protein intake gets more attention. To achieve a protein intake of 1.2 to 1.5 g/kg body weight/day in combination with sufficient energy intake is often a challenge to meet for an already undernourished person. Supplementation with medical nutrition drinks may be helpful to improve the nutritional status and to maintain or increase body weight in older patients. However, large studies demonstrating that oral nutritional supplementation increase
lean body mass in malnourished older adults are scarce (58, 59). Older adults with undernutrition and weight loss may be beyond a critical threshold of being able to preserve or even gain muscle mass. The current screening tools for malnutrition, i.e. undernutrition or quantitative malnutrition are likely to be inadequate to detect qualitative or selective malnutrition, insufficiencies in nutrients such as protein, essential amino acids including leucine, unsaturated fatty acids, vitamins and minerals, which might be present in older adults with sarcopenia (chapter 4). Recognition of the relevance of an adequate nutritional status in an early phase, rather than only undernutrition and over-nutrition, followed by implication in clinical practice with adequate screening and assessment tools, are important future aims.

Prevention of poor nutritional status and muscle loss (chapter 5, 6) seems to be a more effective strategy for healthy aging than treatment of malnutrition and its manifest muscle wasting. Physical activity is hereby an inevitable ‘driver’ for both physical (60) and cognitive function (61). An active lifestyle, including a resistance exercise component, in combination with a healthy diet with sufficient vitamin D and dietary protein in close proximity to the exercise may support the preservation of musculoskeletal health and thereby the prevention of sarcopenia, osteoporosis and frailty (47, 49, 54). Prefrail and frail community-dwelling and institutionalized older adults can still benefit from targeted exercise and nutritional support programs, as recent promising initiatives show (45, 46, 62). The social aspects of training together with others as well as enjoying meals are of utmost importance as well.

The EMPOWER study findings (chapter 3) confirm that a preventative approach is valuable for older adults. Preservation of muscle mass, strength and function and prevention of malnutrition can help older patients to better manage a ‘crisis’ such as hospitalisation. Whereas sarcopenia increases risk of morbidity and hospitalization, hospitalisation itself may significantly accelerate the decline in muscle mass, strength and functional capacity and to poorer clinical outcomes (11), limited recovery (63, 64), and even a higher risk of mortality (12). The acute inactivity due to bed rest, often in combination with a pro-inflammatory condition, leads to a reduction in muscle protein synthesis and increase of muscle protein breakdown and the negative metabolic and morphologic consequences of bed rest are compounded by pre-existing sarcopenia (65). Such an episode of accelerated loss of muscle and functional capacity during a “catabolic crisis”, in addition to the insidious sarcopenic process, has strong negative effects on the recovery of the physical function, mobility and thus quality of life of older patients (7). Some recent reports on the dietary intake in hospitals show that protein and specifically leucine intake of patients do not meet the RDA and certainly not the recent recommendations for older and geriatric patients (66, 67) and will thus be inadequate to stimulate muscle protein synthesis maximally. To limit the accelerated loss of muscle mass and function in older patients during hospitalization, a pro-active preventative approach is recommended during hospital stay (7, 68, 69). Reduction of catabolic inflammation, often triggered by the disease or trauma, is a major goal of hospital treatment. In addition, bed rest should be limited and patients should be, as much as possible, mobilized and physically active. Targeted resistance exercise guided by designated physiotherapists and preferably in close proximity to protein-containing meals should be encouraged as part of regular hospital routine. The diet in hospital should
include at least three meals with a sufficient amount (25-30 g) of high quality protein including (3 g) leucine. Nutritional supplementation, including adequate levels of vitamin D, may support this approach, and caregivers are encouraged to advocate for an earlier start, rather than at the point when a patient becomes malnourished. After hospital discharge and during rehabilitation treatment plans need to include exercise and possibly in combination with nutritional supplements.

Another potential target for prevention of accelerated muscle loss is during intentional weight loss programs. Muscle preservation during weight loss is highly relevant for older adults, for both physical functioning and mobility and for various metabolic functions like blood glucose handling. The exploratory MPS study (chapter 7) in overweight and obese older adults is currently followed up by the same intervention in overweight and obese type II diabetes patients. The first results are expected in 2017 and may include an improvement of glucose-insulin metabolism and decreased reliance on medications. Resistance training should be an integral part of a weight loss program in overweight, obese older adults, with special attention to the timing of intake of sufficient high quality protein and vitamin D in the energy-restricted diet.

In chronic diseases such as cancer, chronic obstructive pulmonary disease (COPD), chronic heart failure (CHF), and rheumatoid arthritis, evidence is emerging about the importance of preservation of muscle mass. Sarcopenia can dramatically increase morbidity and mortality of illnesses in aged patients. Sarcopenia is, for example, associated with toxicity during chemotherapy and survival rates in cancer patients (70, 71). In advanced stages of CHF, patients often experience an enhanced fatigue due to the loss of muscle mass and strength. Structured physical exercise supported by protein and vitamin D supplementation should probably be a part of the therapy that may reduce the progression of muscle wasting (72). The INTERCOM study in muscle-wasting COPD patients with moderate airflow obstruction is a striking example of a multi-modal rehabilitation program that shows a prolonged positive and cost-effective response to integrated nutritional support (73). Although often overlooked and difficult to address, muscle preservation by integration of physical exercise and nutritional support in disease management seems a promising strategy.

In conclusion, malnutrition including suboptimal intake of nutrients such as protein and micronutrients may contribute to the development of sarcopenia and physical frailty. An active lifestyle and adequate dietary intake are essential for healthy aging and may prevent or postpone negative health events. Specific nutritional supplementation, preferably in close temporal proximity to resistance exercise, can help older adults to preserve muscle mass, strength, and physical function. Targeted nutritional supplementation, especially during vulnerable periods, can be of added value to cope with catabolic stress and diseases, enhance recovery and maintain a mobile and active life.


