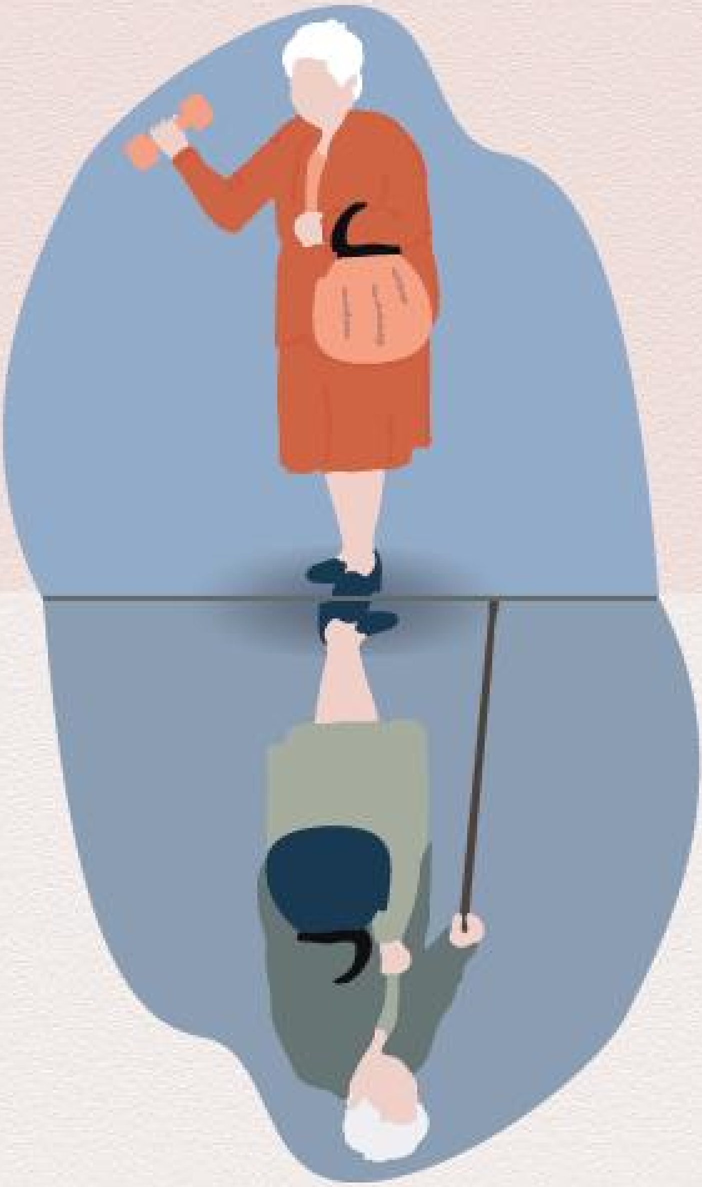
Improving muscle health later in life
The wider benefits of adapting lifestyle interventions



Berber Dorhout

Propositions

1. Heterogeneity in the ageing population should be considered in the development and implementation of lifestyle interventions.
   (this thesis)

2. Specific - rather than generic - quality of life questionnaires should be considered when conducting an economic evaluation in the field of public health.
   (this thesis)

3. A national database listing best practice interventions, such as loketgezondleven.nl, ensures high-quality interventions but is of little use without sustainable resources for implementation and upscaling.

4. The old saying 'An innovation either finds a champion or dies[1]' needs to be revived.

5. Movement must be prescribed as easily as medicine.

6. Scientists should be equally valued for their societal impact as for their scientific merit.

7. Older adults and adults suffering from chronic diseases should not be labelled as 'Dor Hout' in the battle against Covid-19.[2]

Propositions belonging to the thesis, entitled

Improving muscle health later in life - the wider benefits of adapting lifestyle interventions.

Berber Dorhout
Wageningen, 21 January 2022

References

1. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: A consolidated framework for advancing implementation science. *Implement Sci*. 2009;4(1):1-15. doi:10.1186/1748-5908-4-50
2. Zwagerman M. M. De Volkskrant. Published 2020. Accessed September 28, 2021. https://www.volkskrant.nl/mensen/marianne-zwagerman-mijn-column-over-dor-hout-heeft-enorme-impact-gehad~bd61c7d1/

Improving muscle health later in life

The wider benefits of adapting lifestyle interventions

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Improving muscle health later in life

The wider benefits of adapting lifestyle interventions

Berber G. Dorhout

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General introduction

REACHING ADVANCED AGE

It is no longer an exception to survive into old age. Global life expectancy at birth is 73 years, and in the Netherlands the life expectancy even reaches 81.8 years.[1] More and more people are reaching advanced ages and the prospects are that the ageing population will further grow in the coming decades. In 2019, 1 billion people were aged 60 years and over. In the coming 30 years, this number is expected to double.[2] Major improvements in public health and technological progressions in the biomedical sciences have contributed to the increased lifespan.[3] A longer life can provide opportunities to enjoy old age, such as contributing to one's family or community, spending time on new hobbies or sports, or helping by engaging in voluntary work. However, a crucial aspect that influences the possibilities to fully enjoy these opportunities, is health.[2]

Throughout life, everyone has to deal with aging and morbidity, but the process and consequences are different for each individual.[3,4] Regarding disease, the age of onset, rate of development and response to treatment are different from person to person, which is due to biological, behavioral, social and environmental factors.[3,5,6] This contributes to interindividual variation regarding health status, creating a heterogeneous older population.[3,6–8]

CONSEQUENCES OF AGEING

A major consequence of ageing is a decline in functional capabilities. One-third up to half of adults aged 65 years and over have difficulties walking or climbing stairs.[9] During ageing, the process of muscle regeneration, stimulated by muscle protein synthesis, becomes less active. In addition, the response of muscles to anabolic stimuli, such as physical activity and food intake, is blunted in older adults.[10] This leads to a loss of lean body mass (0.5-1.0% per year) and muscle strength (2.5-4.0% per year), contributing to sarcopenia.[11–13] Sarcopenia can be defined as a muscle disorder characterized by a decreased muscle strength, muscle mass and physical functioning.[13] Estimates of the sarcopenia prevalence in community-dwelling older adults range from 9.9 to 40.4%, dependent on the definition used.[14] The disorder is related with poor health outcomes, such as physical disability, increased risk of falls, loss of independence, increased hospitalization rates and even death.[10,13,14] Additionally, age-related consequences such as sarcopenia are associated with increased healthcare costs.[13,15] In the Netherlands, healthcare costs in elderly care are expected to increase from 17 billion in 2015 to 43 billion in 2040 (+153%).[16] As the proportion of older adults is growing rapidly, it is a public health priority to delay or rather prevent the onset of age-related impairments such as sarcopenia and to contribute to independence of older adults.[17] Postponing the onset of chronic disease and decreasing lifetime disability is also referred to as the Compression of Morbidity. This can eventually lead to an extended number of healthy life years.[18,19]

COUNTERACTING SARCOPENIA

Although sarcopenia is a multicausal condition,[20] two major factors that contribute to its development are inactivity and an inadequate protein intake. Therefore, the cornerstones in combatting sarcopenia are resistance exercise (RE) and dietary protein intake.[10] Multiple meta-analyses summarized the effects of randomized controlled trials including RE and protein intake, showing improvements on muscle strength, muscle mass and physical functioning in older adults.[21–24]

VARIATION IN RESPONSIVENESS – THE INFLUENCE OF CONTEXT

1

ProMuscle in Practice, combining RE and dietary protein intake, was found to be effective in improving muscle strength, muscle mass and physical functioning (Box 1).[28] However, heterogeneity in responsiveness to exercise and nutrition interventions is common.[21–23,30,31] To start with, heterogeneity in the intervention itself can lead to varying effects. Aspects that contribute to variation in effect sizes are type, intensity, and duration of training sessions, part of the body that is trained during RE, and type, dose, and timing of protein supplementation (PS).[21–23,30,31]

Not only aspects related to the content of the intervention, but also contextual factors influence the effect size of an intervention.[32,33] Context can be defined as "Any feature of the circumstances in which an intervention is implemented that may interact with the intervention to produce variation in outcomes."[34] Contextual factors include, but are not limited to, the target population, professionals involved, organisations, and the sociocultural and political environment.[35] These factors can be roughly subdivided into three levels: micro, meso and macro (figure 1).[32] The categorization include the contextual factors and is based on a simplified form of Dahlgren and Whitehead's model of the main influences on health.[36]

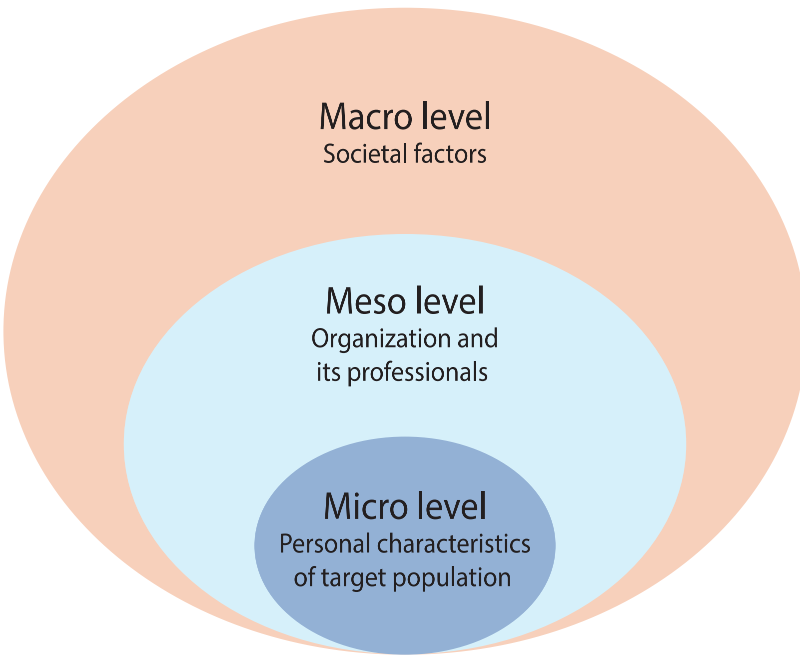

Figure 1. *Factors related to health interventions divided in three levels: micro, meso and macro*

The micro level includes factors on the individual level, such as characteristics of the individuals that are participating.[32,37] The meso level includes factors related to the organisation, that is, the organisation and its professionals conducting the intervention.[38] The macro level includes factors related to societal aspects and public policy, comprising both local and national policies related to health promotion and prevention.[32] In addition to factors within levels, interactions between levels are present.[39] For example, the implementation of an intervention is influenced by interactions between the professionals of an organisation and the target population. The organisation that implements the intervention is additionally influenced by local policies. So, aspects within and across levels affect the intervention, eventually leading to heterogeneity in effect sizes. It is crucial to understand how interventions and contextual factors are related. This will gain insights into success and failure of implementation, the way interventions lead to effects, why the effects vary across settings, and whether interventions can be translated to and implemented in other settings.[34]

Box 1. Timeline of ProMuscle: more than a decade of research

The ProMuscle program studied the importance of protein supplementation in addition to resistance exercise in counteracting sarcopenia. The intervention took place at the human level in a controlled setting and was implemented by researchers. Findings of the ProMuscle program showed that frail older adults improved in muscle strength and physical functioning in response to resistance exercise, however, protein supplementation was required on top of resistance exercise to gain muscle mass.[25]

Before implementing the ProMuscle intervention in the practice setting, the program was adapted to fit the real-life setting. However, the effective core elements, resistance exercise and an increased protein intake, were retained. Main adaptations to the original intervention included the design of the training for healthcare professionals and the integration of an extended nutrition program. After the translation process, the intervention was tested in a pilot study, leading to improvements on muscle strength and physical functioning.[26]

Following the promising findings of the pilot study, the intervention was tested for effectiveness in a large multicentre randomized controlled trial: the ProMuscle in Practice intervention.[27] The intervention was conducted in five Dutch municipalities and was implemented by physiotherapists and dieticians according to guidelines. Results showed that the intervention was effective on improving muscle strength, lean body mass, and physical functioning in community-dwelling older adults.[28] The process evaluation showed that essential elements for successful implementation included tailored interventions, extensive supervision by skilled professionals, social aspects, fidelity and fit within real-world settings. These aspects were found to be important for optimization of the intervention.[29]

Pilot studies were conducted to study further implementation in the practice setting. The pilot studies took place in local practices and were implemented by physiotherapists and dietitians. The core elements, resistance exercise and an increased protein intake, remained central. However, professionals were free to adjust the intervention to their setting, resources, and to participants' capabilities. Figure 1 shows the timeline of the ProMuscle interventions over the last decade.

Figure 2. *Timeline of ProMuscle interventions*

MICRO LEVEL

The micro level includes individual factors, which can be translated into personal characteristics. Personal characteristics that might lead to heterogeneity in responsiveness include the distribution of age, sex, disease, and ethnicity in the target population.

First of all, age is expected to influence the response of individuals to an exercise and nutrition intervention. The muscular response to anabolic stimuli is possibly blunted in older adults.[10] For this reason, the responsiveness of older adults to exercise and nutrition interventions is expected to be lower compared with younger people.[40] Although limited studies have investigated the variation in responsiveness among subgroups of older adults (>65 years), several studies are available in which the effectiveness of RE and protein interventions is compared between younger and older adults. Findings show either no differences in fat free mass change between age groups (≤65 vs. >65 y[41]; ≤49 vs. >49 y[21]) or a higher fat free mass increase in younger compared to older adults (≤45 vs. >45 y).[31] No differences in leg strength were found for subgroups based on age.[21,31] Although the combination of RE and an increased protein intake leads to positive effects on muscle-related outcomes in young as well as older adults[21–24,31], older adults display anabolic resistance to protein intake and RE.[42–44] As a consequence, older adults might need a higher protein intake or a greater RE stimulus (i.e. increased number of working sets) to stimulate muscle protein synthesis and achieve effects comparable to those in younger adults.[44,45]

Secondly, sex differences in responsiveness to diet and exercise interventions were found for older adults, although findings remain inconsistent. One meta-analysis found greater changes in lean body mass and leg strength in men compared to women.[23] Two other meta-analyses reported no sex-based differences on changes in fat free mass or leg strength.[31,41] However, limited studies investigated the effects of RE and protein interventions in women, complicating adequate comparison.[23,31,41]

A third personal characteristic that could influence the older adults' response to an exercise and nutrition intervention is disease or health status.[34,46] Interindividual variability regarding health characteristics such as functional status and mobility increases over the life course, contributing to a heterogeneous older population in terms of health status.[3,4,6–8] Presence of diseases can influence the responsiveness to an intervention. A disease that is common with ageing is sarcopenia, defined as the loss of muscle strength, muscle mass and physical functioning.[13] Many exercise and nutrition interventions are targeted at the prevention of sarcopenia but less studies have investigated the effect of such interventions in sarcopenic older adults.[21–23,30,47] However, some studies are available. Meta-analyses or reviews including interventions combining RE and PS showed improvements on lower body muscle strength, but less clearly on walking speed and grip strength[48], improvements on muscle mass and muscle strength, but less clear results on physical functioning[49], or greater effects on fat free mass change in older adults with an age-related disease (frailty, mobility limitations, or sarcopenia) compared with relatively healthy participants.[41] For older adults who are frail, results are more straightforward. Several studies showed that interventions including RE and PS lead to improvements on leg strength, muscle mass and physical functioning in frail older adults.[25,50,51] On the contrary, studies on the effects of RE and PS in older adults suffering from osteoarthritis are still limited. Most available interventions are postoperative and consist of a short timeframe (2 weeks). However, a meta-analysis including these studies reported that exercise training and PS improved muscle mass, muscle strength, and functional outcomes in older adults with lower limb osteoarthritis.[52] Although several studies indicate that older adults suffering from mobility-impairing diseases benefit from RE and PS interventions in terms of muscle mass, muscle strength, and physical functioning, overall, results remain inconsistent and unclear.

A fourth personal characteristic that might lead to differences in responsiveness to exercise and nutrition interventions is ethnicity. To date, interventions including RE and protein intake were frequently aimed at the majority population, instead of tailoring ethnic minorities. Therefore, the responsiveness of ethnic minorities to this type of interventions is still unknown. Nevertheless, it is known that ethnic minorities are more likely to have an unfavorable health status compared to the majority population.[53–56] Specifically, prevalence of diseases, such as obesity, type 2 diabetes, hypertension and cardiovascular disease are higher among ethnic minorities compared to the Dutch majority population.[53,57,58] An age-related condition that is associated with chronic diseases is sarcopenia.[13,59,60] To date, the exact prevalence of sarcopenia among ethnic minorities in the Netherlands is still unknown. However, the prevalence of sarcopenia is expected to be higher in ethnic minorities compared to the majority population, as differences in muscle mass and muscle strength between ethnic minorities have been reported worldwide.[61–64]

Besides, dietary health behaviours are expected to differ among ethnic minorities.[65] This is because health behaviours are affected by social and cultural factors, and these factors are known to differ between ethnic groups.[66] To date, the role of culture in dietary habits was described in several studies, indicating behavioural factors that determine food patterns in general.[67–69] However, it is still unknown which factors affect or explain the intake of protein in particular. Therefore, it is necessary to gain insights in the sarcopenia prevalence and dietary protein intake of older ethnic minorities. Besides, personal and environmental behavioural determinants underlying protein intake in older adults from ethnic minority groups should be explored. These insights can be used to tailor interventions to the specific needs of ethnic minority populations.

MESO LEVEL

Heterogeneous effects of interventions can also be related to the meso level. The meso level, also referred to as the 'inner setting', reflects the organisation in which the intervention is being conducted.[32,70] Individuals are embedded in the organisation, which in turn affects their behaviour, attitudes, and beliefs.[32] Implementing the intervention in different organisations by different individuals is therefore likely to result in different effects.[33] Factors within the meso level determine for a certain part the outcomes of an intervention in a specific setting.[32,70] Factors related to the inner setting include the characteristics of the organisation (e.g. age, size), but also networks, communications and culture (e.g. norms, values, assumptions) within an organisation. The implementation climate is also part of the inner setting, and includes the openness of the individuals to an intervention, capacity for change, and how use of the intervention will be assessed and supported within the organisation.[34] Lastly, readiness for implementation belongs to the inner setting, which includes the organisation's commitment, involvement and available resources to implement the intervention.[70] Besides, the individuals who conduct the intervention are of major importance. Characteristics of the individuals, such as attitude, knowledge, beliefs, motivation, competence, values and self-efficacy towards the intervention influence the conduction and implementation of the intervention.[70] For example, involvement of individuals who are motivated, skilled, and committed to conduct the intervention, will probably positively affect the intervention's implementation and eventually its effects.[34,71]

Not only aspects within the organisation, but also aspects directly outside the organisation affect the implementation and outcomes of an intervention. This can also be referred to as the 'outer setting'.[70] An important aspect of the outer setting is cosmopolitanism, which includes the connections of the organisation to external organisations.[70] For example, connections with local sports organisations, the general practitioner, the municipality, and the municipal health centre might contribute to successful implementation of a diet and exercise intervention. These parties can for example raise awareness of the intervention or contribute to recruitment of participants.

MACRO LEVEL

The macro level is related to the external setting on the societal level, including for example financial, policy, and political features.[70] Financial factors, such as sources and funding, often influence implementation. Besides, the wider framework of policies can either enhance or limit the intervention's implementation and its effects.[34] The implementation of an intervention is for a certain part dependent on the political climate related to health promotion. Political support on a local as well as national level, referring to the backing from public officials or special interest groups, can either facilitate or impede implementation of an intervention.[35] An example on the macro level is the 'Pact for Elderly Care', which was launched in 2018 by the Dutch government, municipalities and societal organisations.[72] One of its main themes is 'Longer at Home', which aims to ensure that older adults are able to age independently in their own familiar environment, with a good quality of life. External parties, such as municipalities, health insurance companies, industry, and providers of homecare, were appointed to translate the Pact from paper to actual projects that contribute to quality of life of older adults. The involvement of and cooperation between organisations from various levels can facilitate implementation of an intervention, which might in turn positively affect the intervention's outcome.[73]

Cost-effectiveness

Since the proportion of older adults is growing rapidly, preventing age-related consequences such as sarcopenia and maintaining independence of the older population is essential.[17] A relevant question that is often raised includes the financial aspect of strategies to counteract sarcopenia. What are the costs of a diet and exercise intervention targeted at the older population? And do the benefits of such an intervention outweigh the costs? It is essential to answer these questions because the economic burden of the ageing population is expected to increase.[16] Public health policy makers need information to make proper decisions on health-related investments.[15] Although many studies assessed the effects of diet and exercise interventions to counteract sarcopenia, less studies performed an economic evaluation of such interventions.[21–23,31,74] However, economic evaluations of comparable interventions in older adults aiming to prevent falls are available.[75–77] These studies showed variable results regarding cost-effectiveness. Although positive effects on falls prevention were found, the effects on quality of life were absent or minimal when generic questionnaires such as EQ-5D-5L or SF-36 were used. These results lead to doubts on using such generic questionnaires in preventive interventions and create room for investigating alternatives. Therefore, it is necessary to assess the cost-effectiveness of diet and exercise interventions and gain insights into benefits regarding health-related quality of life.

One step further, it is also necessary to assess costs when systematically and sustainably implementing a diet and exercise intervention. The costs of the intervention are expected to be different between the research setting and the implementation setting. For example, participants do not receive protein-rich products when the intervention is being implemented. Besides, fitness machines were purchased for the ProMuscle in Practice research, but when the intervention is implemented in physiotherapist practices, fitness equipment is already available. When sustainably implementing the intervention in a municipality, local parties should collaboratively arrange the financial aspect. Involved parties include physiotherapists, dietitians, older adults, municipality, municipal health service and healthcare insurances. Opportunities such as subsidies, reimbursements, and policies must be considered to locally arrange the financial aspect.

AIM AND OUTLINE OF THIS THESIS

Health promotion interventions, and in particular those including diet and exercise, are often targeted at the general population. However, it is important to additionally investigate the effects of such interventions in specific groups, based on age, sex, ethnicity, or health status. Especially in the ageing population, there is a large heterogeneity regarding health status, and individuals respond differently to treatments or health interventions. Therefore, it is important to study interindividual variation in responsiveness to diet and exercise interventions. Besides, the outcomes of an intervention are expected to be dependent on the setting in which the intervention is being conducted. Contextual factors might help to explain the intervention's effectiveness in a specific setting. Regarding practical implications of implementing an intervention, costs are often of major importance to the stakeholders involved.

Therefore, this thesis aimed to study 1) The sarcopenia prevalence, dietary protein intake, and underlying behavioural and environmental factors affecting protein intake in ethnic minorities in the Netherlands, 2) Personal, organisational, and other contextual factors affecting responsiveness to a diet and exercise intervention, and 3) The cost-effectiveness of ProMuscle in Practice. The studies included in chapter 2 and 3 were both part of the Healthy Life in an Urban Setting (HELIUS) study. **Chapter 2** describes the sarcopenia prevalence and its relation to protein intake in ethnic minorities in the Netherlands. The focus of **chapter 3** is on the dietary protein intake and underlying behavioural and environmental factors affecting protein intake in ethnic minorities. Chapters 4-6 are focused on the ProMuscle interventions. An in-depth analysis to answer the question 'who benefits most from the ProMuscle in Practice intervention?' is provided in **chapter 4**. The three successive ProMuscle interventions, that were conducted in different settings, are aligned in **chapter 5**. This mixed-methods study provides insights into the effects and contextual factors of the three ProMuscle interventions. In **chapter 6**, we assess the cost-effectiveness of ProMuscle in Practice and provide insights into the benefits regarding health-related quality of life. In **chapter 7**, the main findings are presented and discussed in order to place the results into a broader perspective. Besides, implications for further research, implementation and dissemination are provided.

2

Sarcopenia and its relation to protein intake across older ethnic populations in the Netherlands: the HELIUS study

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ABSTRACT

Objective: To examine the prevalence of sarcopenia and its association with protein intake in men and women in a multi-ethnic population.

Design: We used cross-sectional data from the HELIUS (Healthy Life in an Urban Setting) study, which includes nearly 25,000 participants (aged 18-70 years) of Dutch, South-Asian Surinamese, African Surinamese, Turkish, Moroccan, and Ghanaian ethnic origin. For the current study, we included 5161 individuals aged 55 years and older. Sarcopenia was defined according to the EWGSOP2. In a subsample (n=1371), protein intake was measured using ethnic-specific Food Frequency Questionnaires. Descriptive analyses were performed to study sarcopenia prevalence across ethnic groups in men and women, and logistic regression analysis were used to study associations between protein intake and sarcopenia.

Results: Sarcopenia prevalence was found to be sex- and ethnic-specific, varying from 29.8% in Turkish to 61.3% in South-Asian Surinamese men and ranging from 2.4% in Turkish up to 30.5% in South-Asian Surinamese women. Higher protein intake was associated with a 4% lower odds of sarcopenia in the subsample (OR= 0.96, 95% CI 0.92-0.99) and across ethnic groups, being only significant in the South-Asian Surinamese group.

Conclusions: Ethnic differences in the prevalence of sarcopenia and its association with protein intake suggest the need to target specific ethnic groups for prevention or treatment of sarcopenia.

INTRODUCTION

It is expected that in 2060 almost 25% of the Dutch population will consist of adults aged 65 years and over, of which almost 28% is expected to be from an ethnic minority group.[78] These demographic changes will influence society's health status as a whole. In particular, older ethnic minorities are more likely to have an unfavorable health status compared to the majority population.[53–55]

A consequence of the ageing population is the increasing number of older adults with physical limitations. Part of these limitations are caused by decreased muscle mass and strength, also called sarcopenia.[10] Treatment and preferably prevention of sarcopenia is necessary, since sarcopenia may lead to reduced quality of life, disability, hospitalization, loss of independence and increased risk of falls[13] In addition, sarcopenia is associated with e.g. cardiac and respiratory diseases, and all-cause mortality.[13,59,60]

The prevalence of sarcopenia may differ between subgroups of the population, e.g. between men and women and between ethnic groups.[54,55,79] Variations in the prevalence of sarcopenia have been documented for limited ethnic groups, namely Hispanic, Non-Hispanic white and Non-Hispanic Black populations in the US.[80] In several parts of the world, differences in muscle mass and muscle strength have been described between ethnic minority groups, which may contribute to differences in the prevalence of sarcopenia.[61–63] Ethnic minorities in the Netherlands were reported to have a lower handgrip strength than the Dutch majority population have.[64] Further investigation seems imperative to target preventive interventions to specific ethnic groups at high risk of sarcopenia within the population.

Sarcopenia is a multifactorial condition, with physical inactivity and insufficient protein intake contributing predominantly to its development.[13,59,80–83] In recent years, several interventions aimed at preventing sarcopenia have been developed. They are often based on (a combination of) protein intake and physical activity.[23,84] However, those interventions are frequently tailored to the majority population, whereas the ethnic minorities are overlooked. Lifestyle factors, such as dietary intake and physical activity are expected to differ between ethnic minorities.[65] Limited data on protein intake across ethnic minorities in the Netherlands is available. One study reported the protein energy% of Moroccan women (~14.4%) and Surinam men (~16.5%) in the Netherlands. However, study populations were rather small (n=36 and n=42, respectively).[85] Therefore, we reported protein intake, and studied the prevalence of sarcopenia and its association with protein intake, taking into account age, sex and physical activity, in older participants of the HELIUS study, comprising the largest ethnic populations living in Amsterdam, the Netherlands.

METHODS

Baseline data from the HELIUS (Healthy Life in an Urban Setting) study were used. Detailed information about the study design, aim and measurements can be found elsewhere.[86,87] In short, HELIUS is a large cohort study, including the largest ethnic groups living in Amsterdam: Dutch, South-Asian Surinamese, African Surinamese, Turkish, Moroccan, and Ghanaian origin groups. The main aim of the HELIUS study is to elucidate the causes and consequences of the unequal burden of disease across these ethnic groups. Baseline data of the HELIUS study were collected between 2011 and 2015 among nearly 25,000 participants. People aged 18-70 years were randomly recruited, stratified by ethnic origin, through the municipality register of Amsterdam. Data were collected using a questionnaire, either self-administered or by interview performed by an ethnically matched, trained interviewer. Additionally, a physical examination, including anthropometry, bioelectrical impedance analysis (BIA) and handgrip strength measurements, was performed by a trained research assistant according to standardized protocols.[87] The HELIUS study has been approved by the Ethical Review Board of the Academic Medical Center Amsterdam. All participants provided written informed consent.

Study population

Among 22,165 HELIUS participants, both questionnaire and physical examination data were available. The current study is based on a subsample of participants aged 55 years and older (n=5523). We excluded those of Javanese Surinamese (n=63), unknown/other Surinamese (n=104), or other/unknown ethnic origin (n=19), because of small numbers in these groups. In addition, participants without the descriptive data of sarcopenia (handgrip strength and/or bioelectrical impedance resistance analysis) were excluded (n=176). Therefore, sarcopenia prevalence was assessed in a study population including 5161 participants (1495 Dutch, 846 South-Asian Surinamese, 1386 African Surinamese, 398 Turkish, 601 Moroccan and 435 Ghanaian participants).

A subsample of the HELIUS study (approximately 5000 participants) was asked to complete an additional Food Frequency Questionnaire (FFQ) to measure dietary intake.[88] So, for the second research question on protein intake, we included older participants who also filled in an FFQ (n=1430). Ghanaian participants were not included in this dietary intake study. Participants with extreme values for total energy intake (for men <800 kcal or >4000 kcal per day; for women <500 kcal or >3500 kcal per day) were excluded (n=58).[89] Finally, one participant without data for physical activity (PA) (n=1) was excluded, which resulted in a subsample of 1371 individuals (550 Dutch, 311 South-Asian Surinamese, 355 African Surinamese, 57 Turkish and 98 Moroccan origin participants) for associating protein intake and sarcopenia.

Measures and definitions

Ethnicity

Country of birth of participants and their parents were used to determine ethnicity[90].[90] If one of the following criteria was met, a person was defined as of non-Dutch ethnic origin: 1) the participant was born outside the Netherlands and has at least one parent born outside the Netherlands (first generation), or 2) the participant was born in the

Netherlands and both parents were born outside the Netherlands (second generation). After data collection, participants of Surinamese origin were further classified according to self-reported ethnic origin (by questionnaire) into 'South-Asian', 'African', 'Javanese' or 'other/unknown' For the Dutch sample, people who were born in the Netherlands and whose parents were born in the Netherlands were invited.[87]

Sarcopenia

In this study, the revised sarcopenia definition of the European Working Group on Sarcopenia in Older People (EWGSOP2) was used. Low muscle strength (criterion 1) indicates probable sarcopenia. As a next step, low muscle quantity or quality (criterion 2) confirms the diagnosis. If low physical performance is present on top of low muscle mass and strength (criterion 3), severe sarcopenia is detected.[13] In this study, the focus is on indicating probable sarcopenia and sarcopenia diagnosis and therefore criterion 1 and 2 are taken into account.

Muscle strength – criterion 1

Muscle strength was assessed in Newton via maximal handgrip strength using a Citec handheld dynamometer (CIT Technics, Haren, the Netherlands). Participants were sitting up in a chair without armrests, hanging their arms loosely at their sides. They were asked to squeeze the handle of the handheld dynamometer as hard as possible. Each participant performed two measurements of both hands. The highest of these four measurements of strength (in Newton) was used in the analysis. The data were converted from Newton to kg by dividing by 9.81. The cut-points used for defining sarcopenia are <27 kg for men and <16 kg for women.[13]

Muscle quantity – criterion 2

Arm-to-leg bioelectrical impedance analysis (BIA) measured impedance, resistance, and reactance in Ohm at 50 Hz using a Bodystat 1500 analyzer (Bodystat Ltd, Isle of Man, UK). Participants were not allowed to consume any food or drink (also no water) from 10 pm the evening before the testing. Muscle mass was calculated using the formula by Janssen et al:[91] Skeletal muscle mass (kg) = $[(\text{height}^2/\text{resistance} * 0.401) + (\text{sex} * 3.825) + (\text{age} * -0.071)] + 5.102$. Height was measured in cm, BIA resistance in ohms, men=1 and women=0 for sex, and age was measured in years. Skeletal muscle mass was normalized for height (muscle mass (kg)/height (m^2)), which resulted in the Skeletal Muscle Index (SMI).[92]

The cut-points defined by EWGSOP2 for muscle mass are based on DXA data. The cut-points from EWGSOP definition (2010) were recently revised for the EWGSOP2 definition (2018) (M: <7.23 to <7.0 kg/m^2, F: <5.67 to <5.5 kg/m^2, respectively). Because the HELIUS study includes fat free mass measures based on BIA data, we used cut-points based on BIA data (M: <10.75 kg/m^2, F: <6.75 kg/m^2) and applied the same conversion factor to them.[92] The altered cut-points based on SMI used for defining moderate to high sarcopenia are <10.41 kg/m^2 for men and <6.55 kg/m^2 for women.

Anthropometric measures and educational level

Body weight, height and calf circumference were measured in duplicate. The mean was used for analysis. A third measure was performed if the two measurements differed more than 0.5 kg (weight), 0.5 cm (height) or 1.0 cm (circumference). In that case, the two measurements closest together were averaged. Body Mass Index (BMI) was calculated as weight (kg)/height $(m)^2$.

Educational level was assessed as highest educational degree obtained in the Netherlands or in the country of origin. It was classified as 'Lower education' (never attended school, elementary schooling only, lower vocational schooling or lower secondary schooling), 'Intermediate education' (intermediate vocational schooling or intermediate/higher secondary schooling) or 'Higher education' (higher vocational schooling or university).

Lifestyle factors

Dietary intake was measured using ethnic specific semi-quantitative Food Frequency Questionnaires (FFQs), specifically designed for the HELIUS study.[88] Data from the Food Composition Table 2011 were used to construct a nutrient database for each FFQ.[93] For ethnic specific foods the database was expanded with international data and new chemical analyses. The FFQs were used to collect information on portion size and frequency of approximately 220 food items eaten in the previous 4 weeks.

In HELIUS, data on physical activity were collected by the SQUASH questionnaire.[94] *Dutch Physical Activity norm (Dutch PA norm)* was used to assess physical activity (categorical variable: yes/no for meeting the norm). The Dutch PA norm was set at 30 minutes of moderate to high intensity exercise for at least 5 days per week.[95]

Statistical analyses

Characteristics of the study population were presented as means and standard deviations for continuous variables and percentages for categorical variables per ethnic group. Additionally, descriptives of sarcopenia were reported for men, women, and ethnic groups separately. Characteristics as well as sarcopenia descriptives of the subsample are presented in supplementary table 1.

Protein intake was adjusted for energy intake *(Protein Energy %)*.[96] Logistic regression analysis was used to generate Odds Ratios (ORs) for the association between protein energy% (per 1 en% higher protein intake) and sarcopenia in the study subsample and in separate strata for sex, ethnicity, PA norm and BMI. Sensitivity analyses included estimating Prevalence Ratios (PRs) from Cox regression. ORs were replaced by PRs from Cox regression, in case of ORs overestimating PRs. Follow-up time was set to one for all participants.[97] We adjusted for age, sex, PA, and ethnicity. All analyses were performed with SPSS version 23. A p-value <0.05 was considered statistically significant.

RESULTS

Characteristics

The characteristics of the study population are presented per ethnic group in table 1. The total study population consisted for 45% of men. Almost half of Dutch participants reported a high education (48.4%), whereas most of Moroccan participants reported a low education (85.0%). Mean BMI ranged from 26.2 kg/m^2 in Dutch up to 31.5 kg/m^2 in Turkish participants. The characteristics of the subsample and the study population are comparable, except for the Turkish participants, due to small numbers in this group (n=57) (supplementary table 1). Among those who filled out the FFQ, mean protein intake also varied among ethnic groups. The lowest mean protein intake (g/kg BW/day) was reported by African Surinamese (1.03 ± 0.44), whereas Turkish participants reported the highest (1.28 ± 0.44).

Descriptives of sarcopenia and associated measures are presented by ethnicity for men and women separately (table 2). Mean maximum handgrip strength varied among ethnic groups and was found to be lower in women compared to men in all ethnic groups. For both sexes, the highest handgrip strength was found in the Dutch and African Surinamese groups. Mean Skeletal Muscle Index (SMI) was highest in Turkish women (8.5 ± 1.2) and men (10.8 ± 1.2) compared to other ethnic groups. Probable sarcopenia rates were comparable between men and women in the same ethnic group but differed between ethnic groups (lowest rates in Dutch, highest in South-Asian Surinamese group). Sarcopenia prevalence (diagnosis) was found to be lower in women (ranging from 2.4% in Turkish up to 30.5% in South-Asian Surinamese) compared to men (ranging from 29.8% in Turkish up to 61.3% in South-Asian Surinamese). Descriptives of sarcopenia and associated measures are reported for the subsample separately (supplementary table 2). Results are comparable to the total study population, except for Turkish participants, likely due to a low number of participants in this subsample.

Table 1. *Characteristics of the study population (n=5161) per ethnic group and food-related data in subsample (n=1371) per ethnic group.*

	Dutch	**South-Asian Surinamese**	**African Surinamese**	**Turkish**	**Moroccan**	**Ghanaian**
	mean±SD, n (%)	**mean±SD, n (%)**	**mean±SD n (%)**	**mean±SD, n (%)**	**mean±SD, n (%)**	**mean±SD, n (%)**
n = 5161	*1495 (29.0%)*	*846 (16.4%)*	*1386 (26.9%)*	*398 (7.7%)*	*601 (11.6%)*	*435 (8.4%)*
Mean age (years)	61.8 ± 4.3	60.7 ± 4.3	60.5 ± 4.1	59.6 ± 4.1	60.3 ± 4.2	58.2 ± 3.1
Sex (men)	724 (48.4%)	364 (43.0%)	568 (41.0%)	191 (48.0%)	266 (44.3%)	239 (54.9%)
Education						
Lower	468 (31.3%)	584 (69.0%)	762 (55.0%)	322 (80.9%)	511 (85.0%)	302 (69.4%)
Intermediate	287 (19.2%)	124 (14.7%)	339 (24.5%)	41 (10.3%)	68 (11.3%)	106 (24.4%)
Higher	724 (48.4%)	131 (15.5%)	271 (19.6%)	29 (7.3%)	17 (2.8%)	17 (3.9%)
Mean BMI (kg/m²)	26.2 ± 4.4	27.4 ± 4.5	28.6 ± 5.6	31.5 ± 5.8	30.1 ± 5.2	29.2 ± 5.0
Mean height (cm)	173 ± 10	162 ± 9	167 ± 9	161 ± 9	164 ± 9	166 ± 8
Mean weight (kg)	78.7 ± 15.0	71.5 ± 12.8	80.0 ± 15.8	81.4 ± 14.2	80.6 ± 13.7	80.0 ± 13.5
Current smoking	315 (21.1%)	206 (24.3%)	394 (28.4%)	85 (21.4%)	49 (8.2%)	32 (7.4%)
Dutch PA norm§	1232 (82.4%)	574 (67.8%)	1004 (72.4%)	238 (59.8%)	397 (66.1%)	30 (70.8%)
Mean energy intake (kcal/day)	2110 ± 585	1913 ± 671	1932 ± 707	2258 ± 677	2020 ± 783	n.a.†
Mean protein intake (g/kg BW/d)	1.05 ± 0.32	1.15 ± 0.49	1.03 ± 0.44	1.28 ± 0.44	1.12 ± 0.53	n.a.†
Mean proteinEN%	15.4 ± 2.6	16.7 ± 3.4	16.7 ± 3.6	17.7 ± 3.6	17.3 ± 3.0	n.a.†
Mean animal proteinEN%	9.2 ± 2.9	9.5 ± 4.0	10.1 ± 4.0	10.6 ± 4.1	9.5 ± 3.6	n.a.†
Mean plant proteinEN%	6.3 ± 1.4	7.2 ± 1.6	6.6 ± 1.7	7.0 ±1.7	7.8 ± 1.8	n.a.†

BMI=Body Mass Index.

** Education: Highest obtained educational degree: 'Lower' (never been to school or elementary schooling only, lower vocational schooling or lower secondary schooling), 'Intermediate' (intermediate vocational schooling or intermediate/higher secondary schooling) or 'Higher' (higher vocational schooling or university). Education unknown: n=58 (data not shown).*

§ Dutch PA norm: performing moderate or high intensity activities lasting at least 30 minutes, for a minimum of 5 days a week.

† FFQ data were not available for Ghanaian participants.

Table 2. *Descriptives of sarcopenia and associated measures per ethnic group for men and women in the study population (n=5161).*

	Dutch	South-Asian Surinamese	African Surinamese	Turkish	Moroccan	Ghanaian
	mean±SD, n (%)	**mean±SD, n (%)**	**mean±SD, n (%)**	**mean±SD, n (%)**	**mean±SD, n (%)**	**mean±SD, n (%)**
Men						
n = 2353	*724 (30.8%)*	*364 (15.5%)*	*568 (24.1%)*	*191 (8.1%)*	*266 (11.3%)*	*239 (10.2%)*
Mean HGS (kg)	28.2 ± 6.8	22.5 ± 5.8	26.8 ± 7.1	24.3 ± 6.0	25.2 ± 7.0	23.1 ± 6.2
Sarcopenia (probable)*	331 (45.7%)	289 (79.4%)	314 (55.3%)	172 (72.0%)	133 (69.6%)	161 (60.5%)
Mean SMI (kg/m²)	10.1 ± 1.3	9.7 ± 1.3	10.2 ± 2.2	10.8 ± 1.2	10.3 ± 1.1	10.2 ± 2.2
Sarcopenia (diagnosis)§	228 (31.5%)	223 (61.3%)	218 (38.4%)	57 (29.8%)	101 (38.0%)	103 (43.1%)
Women						
n = 2810	*771 (27.4%)*	*482 (17.2%)*	*818 (29.1%)*	*207 (7.4%)*	*335 (11.9%)*	*196 (7.0%)*
Mean HGS (kg)	16.6 ± 4.4	12.9 ± 3.5	16.0 ± 4.7	13.3 ± 4.4	13.8 ± 4.2	14.2 ± 4.2
Sarcopenia (probable)†	360 (46.7%)	396 (82.2%)	418 (51.1%)	136 (69.4%)	151 (72.9%)	234 (69.9%)
Mean SMI (kg/m²)	7.5 ± 0.9	7.1 ± 1.5	7.8 ± 1.3	8.5 ± 1.1	8.1 ± 1.1	7.9 ± 1.0
Sarcopenia (diagnosis)‡	59 (7.7%)	147 (30.5%)	56 (6.8%)	5 (2.4%)	19 (5.7%)	8 (4.1%)

HGS=maximal handgrip strength in kg, SMI=Skeletal Muscle Index (skeletal muscle mass divided by height²).

** Sarcopenia probable men, based on following criterion: HGS<27 kg.*

§ Sarcopenia diagnosis men, based on following criteria: HGS<27 kg and SMI<10.41 kg/m².

† Sarcopenia probable women, based on following criterion: HGS<16 kg.

‡ Sarcopenia diagnosis women, based on following criteria: HGS<16 kg and SMI<6.55 kg/m².

Association between protein intake and sarcopenia

The first model shows that a higher protein energy% was non-significantly associated with a 0.98 (95%-CI: 0.94-1.02) lower odds of sarcopenia in the subsample population, adjusted for age and sex (table 3, model 1). Further adjustment for ethnicity and PA norm emphasized this statistically significant association: OR: 0.96 (95%-CI: 0.92-0.99) (model 2 and 3).

A similar association between protein energy% and sarcopenia was found for men and women, adjusted for age, ethnicity and PA norm (men: OR: 0.95, 95%-CI: 0.90-1.01; women: OR: 0.96, 95%-CI:0.90-1.04). We found comparable associations across ethnic groups, albeit only statistically significant in the South-Asian Surinamese group (model 5, OR: 0.92, 95%-CI: 0.85-0.99), and a minor deviating result in the Turkish participants. Sensitivity analyses showed that ORs from logistic regression were comparable to PRs from Cox, suggesting that ORs did not overestimate the PRs. Chronic disease (self-reported history (or presence) of diabetes, myocardial infarction, or stroke) did not affect the association under study.

Stratification by reaching the PA norm showed that a higher protein energy% was associated with a 13% lower odds of sarcopenia for participants who did not reach the PA norm, compared to a 2% lower odds for those who did reach the PA norm (OR: 0.87, 95%-CI: 0.79-0.96, OR: 0.98, 95%-CI 0.93-1.03, respectively). No such difference was found for BMI strata (data not shown).

Table 3. *Association between protein energy% and sarcopenia in the subsample and within ethnic groups.*

Population	N	Model	Odds Ratio	95% CI
Total subsample	1371	**Model 1:** protein energy %, age, sex	0.98	0.94-1.02
	1371	**Model 2:** model 1+ ethnicity	0.96	0.92-0.99
	1371	**Model 3:** model 2+ PA norm§	0.96	0.92-0.99
	550	**Model 4:** model 3 in Dutch	0.94	0.87-1.03
By ethnic group	311	**Model 5:** model 3 in South-Asian Surinamese	0.92	0.85-0.99
	355	**Model 6:** model 3 in African Surinamese	1.00	0.92-1.09
	57	**Model 7:** model 3 in Turkish	1.06	0.87-1.29
	98	**Model 8:** model 3 in Moroccan	0.96	0.82-1.12

CI=Confidence Interval

Sarcopenia based on following criteria; for men: HGS<27 kg and SMI<10.41 kg/m^2; for women: HGS<16 kg and SMI<6.55 kg/m^2.

§ Dutch PA norm: performing moderate or high intensity activities lasting at least 30 minutes, for a minimum of 5 days a week.

DISCUSSION

To our knowledge, this is the first study on sarcopenia prevalence and its association with protein intake in different ethnic groups of older age in the Netherlands. Prevalence rates were highest for South-Asian Surinamese men, and lowest for Turkish women. In the total subsample, a higher protein energy% was significantly associated with a 4% lower odds of sarcopenia. A comparable association was found when studying separate strata for sex and ethnicity.

Data from the HELIUS study were used for this study. The overall response rate was relatively low (28%), which could have led to selection bias. However, Snijder and colleagues (2017) compared participants and non-participants of the HELIUS study.[87] Women were slightly more likely to participate than men, and those who participated were slightly older than those who refused to participate. Finally, socio-economic indicators were slightly more favorable among participants as compared with non-participants. However, these differences were relatively small, particularly when compared to differences across the ethnic groups. Furthermore, large numbers of each ethnic group in which all social-economic levels are represented were included, which suggests that selection bias is probably limited.[87]

In this study, the EWGSOP2 definition of sarcopenia was used, which consists of three criteria. The first step is measuring handgrip strength to assess muscle strength.[13] EWGSOP2's cut-points for grip strength are based on a reference population from the UK.[98] Grip strength measures in our study population were slightly lower compared to the reference population from the same age group, which might reflect true differences or differences in dynamometers used (respectively Citec vs Jamar, Smedley, Nottingham, Takei).[99] Though this might affect prevalence rates, it does not affect the comparison of handgrip strength across the ethnic groups in our study population.

The second step is assessing skeletal muscle mass using BIA. The skeletal muscle mass related cut-points used in our study were defined by Janssen and colleagues[92] and were adjusted according to the latest cut-points defined by EWGSOP2. The adjusted cut-points resulted in a 4.5% lower sarcopenia prevalence in the total population as compared to using the original cut-points formulated by Janssen et al. Furthermore, several factors related to BIA could have influenced muscle mass estimates. First of all, the BIA device used in this study was not similar to the device used by Janssen and colleagues to derive the BIA equation.[91] Since technical aspects of the two devices were comparable, only small fluctuations in measurements due to different brands of BIA device were expected.[100–102] Secondly, different BIA equations can result in dissimilar muscle mass estimates. For this reason we compared the equation of Janssen et al. to a commonly used BIA equation of Kyle et al.[103] The BIA equations of Janssen et al. and Kyle et al. resulted in comparable SMM (mean ± SD: 24.8 ± 6.5, 25.0 ± 4.7 respectively) and therefore the type of equation might result in only small differences in sarcopenia prevalence. Thirdly, BIA equations are particularly valid for the populations in which they have been derived.[13,104] The BIA equation we used[91] was cross-validated in a heterogeneous population (multi-ethnic, age 18-86 years, BMI 16-48 kg/m^2) and found to be suitable for Hispanics and African-Americans, but underestimated skeletal muscle mass in Asians.[91] This may partly explain the high number of sarcopenia cases in the South-Asian Surinamese population in our study.

We found a higher prevalence of sarcopenia in men as compared to women. A recent meta-analysis reported comparable results, in both European and non-European populations.[14] In our study, also variations in sarcopenia prevalence between ethnic groups were apparent. This may be related to differences in body composition, which is known to differ between ethnic groups.[62,105] More specifically, black adults were found to have a relatively higher muscle mass (leading to a lower sarcopenia prevalence) compared to whites and Asians. In our study, black participants (African Surinamese and Ghanaian) had lower sarcopenia prevalence compared to Asian participants as well, but not compared to the other ethnic groups.[62,105–108]

In most ethnic groups, sarcopenia prevalence was between 2.4% and 7.7% in women and between 29.8% and 43.1% in men, comparable to literature.[79,109] Notably higher prevalence rates were found for the South-Asian Surinamese group (30.5% in women; 61.3% in men). First of all, this might be related to the aforementioned underestimation of skeletal muscle mass in this group. Secondly, it might be due to high prevalence of diseases in South-Asians (i.e. type 2 diabetes 19%, hypertension 42%), which is known to affect muscle mass.[80,87,110] Thirdly, the high sarcopenia prevalence in this group might be related to sarcopenia cut- points. The Asian Working Group for Sarcopenia (AWGS) described cut-points for the Asian population, because their body size, lifestyle and cultural background differ from that of the Caucasian population.[111] Sarcopenia prevalence rates in Asian populations were found to be higher when using EWGSOP2 compared to AWGS criteria (men: 13.8% vs. 6.4%, women: 12.4% vs. 11.5%, respectively).[112] However, currently available Asian studies on sarcopenia prevalence were mainly performed in Eastern Asia and therefore more studies on this topic should be performed in other parts of Asia. In addition, due to the wide variety of ethnicities in Asia, ethnic-specific sarcopenia cut-points might be needed.[111] Altogether, the underestimated skeletal muscle mass, high prevalence of diseases and use of EWGSOP2 sarcopenia cut-points might contribute to the high sarcopenia prevalence in our South-Asian participants.

Furthermore, lifestyle behaviors such as dietary protein and physical activity may contribute to the variation in sarcopenia, since these are evident causes underlying sarcopenia.[13,59,80–83] Associations between protein energy% and sarcopenia were found in the total subsample (OR: 0.96, 95% CI: 0.92;0.99), indicating that a higher protein energy% was associated with a 4% lower odds of sarcopenia. Observational studies have shown similar positive associations of dietary protein intake with muscle mass and strength.[113–118] Studying the ethnic groups separately resulted in comparable, relatively small, associations between protein intake and sarcopenia, most obvious in South-Asian Surinamese participants. A recent review showed that protein intake is rather low in older Asian populations,[119] emphasizing the importance of increasing their protein intake in order to contribute to counteracting sarcopenia.

In conclusion, the prevalence of sarcopenia varied in older adults across ethnic groups, with the lowest prevalence in the Turkish group and the highest prevalence in South-Asian Surinamese, in both men and women. Besides, the association between protein intake and sarcopenia was mostly comparable across ethnic minorities and consistent with the literature. Therefore, the varying levels of sarcopenia prevalence calls for a targeted approach for specific ethnic groups in case of sarcopenia-related prevention or treatment strategies. Ethnic-specific interventions could be aimed at increased protein intake. In order to be effective, ethnic-specific interventions should be implemented in conversation with the target group, family values should be incorporated, the adaptations should imply a high intensity of the intervention, and adaptations should be implemented as a package of adaptations.[68,120] More research is needed to study the protein intake in relation to physical activity and sarcopenia in ethnic minorities.

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CHAPTER 2 - SUPPLEMENTARY MATERIAL

Supplementary table 1. *Characteristics of the subsample per ethnic group (n=1371).*

	Dutch	South-Asian Surinamese	African Suri-namese	Turkish	Moroccan
	mean±SD N (%)	mean±SD, N (%)	mean±SD N (%)	mean±SD, N (%)	mean±SD, N (%)
N = 1371	*550 (40.1%)*	*311 (22.7%)*	*355 (25.9%)*	*57 (4.2%)*	*98 (7.1%)*
Mean age (years)	61.6 ± 4.1	60.4 ± 4.1	60.1 ± 3.9	58.8 ± 3.4	60.0 ± 4.3
Sex (men)	268 (48.7%)	135 (43.4%)	135 (38.0%)	30 (52.6%)	50 (51.0%)
Education					
Lower	156 (28.4%)	197 (63.3%)	163 (45.9%)	36 (63.2%)	69 (70.4%)
Intermediate	119 (21.6%)	53 (17.0%)	89 (25.1%)	12 (21.1%)	22 (22.4%)
Higher	272 (49.5%)	58 (18.6%)	102 (28.7%)	8 (14.0%)	7 (7.1%)
Mean BMI (kg/m²)	26.1 ± 4.2	27.2 ± 4.3	28.8 ± 5.6	29.9 ± 5.1	29.6 ± 4.9
Mean height (cm)	173 ± 10	162 ± 9	167 ± 9	163 ± 8	164 ± 9
Mean weight (kg)	78.3 ± 14.7	71.3 ± 12.4	80.0 ± 15.5	78.5 ± 11.2	79.8 ± 14.5
Current smoking	111 (20.2%)	61 (19.6%)	72 (20.3%)	11 (19.3%)	9 (9.2%)
Dutch PA norm§	456 (82.9%)	216 (69.5%)	266 (74.9%)	35 (61.4%)	69 (70.4%)
Mean energy intake (kcal/day)	2110 ± 585	1913 ± 671	1932 ± 707	2258 ± 677	2020 ± 783
Mean protein intake (g/kg BW/d)	1.05 ± 0.32	1.15 ± 0.49	1.03 ± 0.44	1.28 ± 0.44	1.12 ± 0.53
Mean proteinEN%	15.4 ± 2.6	16.7 ± 3.4	16.7 ± 3.6	17.7 ± 3.6	17.3 ± 3.0
Mean animalprotein-EN%	9.2 ± 2.9	9.5 ± 4.0	10.1 ± 4.0	10.6 ± 4.1	9.5 ± 3.6
Mean plant protein-EN%	6.3 ± 1.4	7.2 ± 1.6	6.6 ± 1.7	7.0 ±1.7	7.8 ± 1.8

BMI=Body Mass Index.

** Education: Highest obtained educational degree: 'Lower' (never been to school or elementary schooling only, lower vocational schooling or lower secondary schooling), 'Intermediate' (intermediate vocational schooling or intermediate/higher secondary schooling) or 'Higher' (higher vocational schooling or university). Education unknown: n=8 (data not shown).*

§ Dutch PA norm: performing moderate or high intensity activities lasting at least 30 minutes, for a minimum of 5 days a week.

Supplementary table 2. *Descriptives of sarcopenia and associated measures per ethnic group for men and women in subsample (n=1371).*

	Dutch	South-Asian Surinamese	African Surinamese	Turkish	Moroccan
	mean±SD, n (%)	**mean±SD, n (%)**	**mean±SD, n (%)**	**mean±SD, n (%)**	**mean±SD, n (%)**
Men					
n = 618	*268 (43.4%)*	*135 (21.8%)*	*135 (21.8%)*	*30 (4.9%)*	*50 (8.1%)*
Mean HGS (kg)	27.2 ± 6.1	22.5 ± 6.1	26.1 ± 6.2	22.7 ± 6.4	24.9 ± 5.6
Sarcopenia (probable)*	139 (51.9%)	103 (76.3%)	78 (57.8%)	24 (80.0%)	31 (62.0%)
Mean SMI (kg/m2)	10.0 ± 1.1	9.7 ± 1.0	10.7 ± 4.0	10.4 ± 1.0	10.3 ± 1.0
Sarcopenia (diagnosis)§	92 (34.3%)	84 (62.2%)	55 (40.7%)	14 (46.7%)	19 (38.0%)
Women					
n = 753	*282 (37.5%)*	*176 (23.4%)*	*220 (29.2%)*	*27 (3.6%)*	*48 (6.4%)*
Mean HGS (kg)	15.9 ± 4.0	12.8 ± 3.3	15.7 ± 4.0	13.8 ± 3.5	14.1 ± 3.6
Sarcopenia (probable)†	153 (54.3%)	146 (83.0%)	118 (53.6%)	21 (77.8%)	33 (68.8%)
Mean SMI (kg/m2)	7.4 ± 0.8	7.0 ± 0.9	7.9 ± 1.4	8.2 ± 1.0	8.0 ± 1.1
Sarcopenia (diagnosis)‡	28 (9.9%)	49 (27.8%)	14 (6.4%)	0 (0.0%)	4 (8.3%)

HGS=maximal handgrip strength in kg, SMI=Skeletal Muscle Index (skeletal muscle mass divided by height).

** Sarcopenia probable men, based on following criterion: HGS<27 kg.*

§ Sarcopenia diagnosis men, based on following criteria: HGS<27 kg and SMI<10.41 kg/m^2.

† Sarcopenia probable women, based on following criterion: HGS<16 kg.

‡ Sarcopenia diagnosis women, based on following criteria: HGS<16 kg and SMI<6.55 kg/m^2.

3

Dietary protein intake in older adults from ethnic minorities in the Netherlands, a mixed methods approach

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ABSTRACT

Optimizing protein intake is a novel strategy to prevent age associated loss of muscle mass and strength in older adults. Such a strategy is still missing for older adults from ethnic minority populations. Protein intake in these populations is expected to be different in comparison to the majority of the population due to several socio-cultural factors. Therefore, the present study examined the dietary protein intake and underlying behavioral and environmental factors affecting protein intake among older adults from ethnic minorities in the Netherlands. We analyzed frequency questionnaire (FFQ) data from the Healthy Life in an Urban Setting (HELIUS) cohort using ANCOVA to describe dietary protein intake in older adults from ethnic minorities in the Netherlands (N = 1415, aged >55 years, African Surinamese, South Asian Surinamese, Moroccan, and Turkish). Additionally, we performed focus groups among older adults from the same ethnic minority populations (N = 69) to discover behavioral and environmental factors affecting protein intake; 40–60% of the subjects did not reach minimal dietary protein recommendations needed to maintain muscle mass (1.0 g/kg bodyweight per day (BW/day)), except for Turkish men (where it was 91%). The major sources of protein originated from animal products and were ethnic specific. Participants in the focus groups showed little knowledge and awareness about protein and its role in aging. The amount of dietary protein and irregular eating patterns seemed to be the major concern in these populations. Optimizing protein intake in these groups requires a culturally sensitive approach, which accounts for specific protein product types and sociocultural factors.

INTRODUCTION

In the Netherlands, the number of non-western older adults is rising rapidly, and is expected to grow even further, from 70,000 in 2010 to more than 500,000 in 2050.[121] In many high-income countries, ethnic minority groups show a worse disease risk profile from a younger age and have lower life expectancies compared to the majority population.[122] For instance, in the Netherlands, chronic diseases and physical limitations appear, on average, ten years earlier compared to the Dutch majority population.[56–58,123,124] A major risk factor for developing chronic diseases and physical limitations, is sarcopenia; the age-associated loss of skeletal muscle mass, muscle strength, and physical performance.[13] A recent paper described higher probable sarcopenia rates among older ethnic minority groups in the Netherlands (OR: 0.96, 95% CI: 0.92–0.99) indicating a higher risk of developing chronic diseases compared to the Dutch majority population.[125]

The progression of sarcopenia is caused by multiple lifestyle factors, including inadequate dietary protein intake.[113] To minimize the risk of developing sarcopenia, nutritional strategies are needed to help preserve or improve skeletal muscle mass, strength and function in older adults from ethnic minority populations.[13,81] It is yet unknown at which aspects of protein intake interventions should focus in older adults from ethnic minority populations. Several Randomized Controlled Trials (RCTs) show the beneficial effects of protein and amino acid supplementation on muscle mass, muscle strength, and/or physical functioning.[25,28,126–128] Based on these, recommendations on protein intake for older adults have been formulated. For instance, the European Society for Clinical Nutrition and Metabolism (ESPEN) expert groups recommend that healthy older adults consume at least 1.0–1.2 g of protein per kilogram bodyweight per day (g/kg BW/d) to maintain muscle mass,[126,129] which is in contrast to the lower recommended dietary allowance of 0.8 g/kg BW/d for healthy adults.[130] In addition to the total amount of protein intake, the source and timing of protein is of importance to optimize the effect of the daily protein intake on prevention of sarcopenia in older populations. Animal proteins, especially those from dairy, are higher quality proteins and seem to better support muscle protein synthesis than plant proteins.[131] Furthermore, protein distribution or timing may impact muscle protein synthesis and muscle mass gain. Increasing the protein intake at breakfast, lunch, and prior to sleep represent effective strategies to stimulate muscle protein synthesis and muscle mass growth.[132,133]

Besides, information to determine how interventions may be improved to account for the specific needs of minority populations is scarce. Social and cultural factors differ between ethnic groups and affect daily health behaviors of individuals.[66] Previous studies have highlighted the role of culture in dietary habits.[67–69] These studies describe behavioral factors that determine food patterns in general, but more insight is needed in factors that affect, or may explain, dietary protein intake. We expect that older adults from ethnic minorities lack awareness and knowledge about the importance of dietary protein intake while aging due to their generally lower educational and health literacy levels.[134] We also expect that the choice for specific protein sources strongly depend on sociocultural determinants within the different older ethnic groups. Clear insights in these factors in older adults from ethnic minorities are still lacking.

We carried out a mixed methods study to examine quantitatively the dietary protein intake, including protein sources, and explore qualitatively its underlying personal and environmental behavioral determinants among older adults from ethnic minority groups in the Netherlands. The insights from our results provide a window of opportunity to develop an intervention aimed at optimizing protein intake in older ethnic minority populations in a real-life setting.

MATERIALS AND METHODS

Quantitative Research

For the cross-sectional analysis, baseline data were used from the Healthy Life in an Urban Setting (HELIUS) study; a cohort study that aims to gain insight in the causes of the unequal burden of disease across ethnic groups.[87] The baseline data were collected between 2011 and 2015, among nearly 25,000 participants aged 18–70, recruited by the municipality of Amsterdam, the Netherlands.

Study Population

A subsample of the HELIUS study population completed ethnic-specific food frequency questionnaires (FFQs; N = 5276).[88] We selected participants older than age 55 in the current study (N = 1430). Subsequently, participants who missed values for dietary intake or showed extreme values for total energy intake (for men <800 kcal per day or >4000 kcal per day; for women <500 kcal per day or >3500 kcal per day) were excluded. This resulted in a subsample of 1415 subjects who were included for further analyses. The population characteristics are described in the results section and can be found in Table 1.

Measures

Country of birth of participants and their parents were used to determine ethnicity for the HELIUS study.[90] The definitions of each ethnic group and criteria for inclusion to one of the ethnic groups was described elsewhere.[87]

Body weight and height were measured in duplicate based on standardized protocols. The mean was used for analysis. A third measure was performed if the two measurements differed more than 0.5 kg (weight) or 0.5 cm (height). In that case, the two measurements closest together were averaged. Body mass index (BMI) was calculated as weight (kg)/height $(m)^2$.

Dietary intake was measured using ethnic specific semi-quantitative FFQs, specifically designed for the HELIUS study.[88] Data from the Food Composition Table 2011 were used to construct a nutrient database for each FFQ (Dutch Food Composition Table 2011). For ethnic specific foods, the database was expanded with international data and new chemical analyses. Participants reported the frequency and portion size of 238 food items eaten in the previous four weeks. From the FFQ total energy intake, total dietary protein intake and animal and plant derived protein intake were determined. Energy intake is formulated in kcal/day. Protein intake is presented as g/day and g/kg BW/day as well as a percentage of total energy intake (EN%). Moreover, the protein intake on product level was assessed.

Statistical Analyses

Characteristics were stratified by sex and ethnic background. Age, BMI, total dietary protein intake, and animal and plant derived protein intake are presented as means +/− standard deviations of the mean. To compare the protein intake between ethnic minority groups and the Dutch, which was considered as the reference population, an ANCOVA analysis was performed, controlling for age, chronic diseases, physical activity, smoking, alcohol use, and energy intake.

Proportions of the ethnic populations reaching the recommended daily allowance (RDA) (0.8 g protein/kg BW/day) and the recommended 1.0–1.2 g protein/kg BW/day stated by the ESPEN discussion group[129] were presented and compared for the different ethnic minority populations.

To gain insight in the food sources that contribute most to daily protein intake among the different ethnic groups, we summed the absolute protein intake per product in gram/day for the whole group.

A p-value <0.05 was considered statistically significant. The quantitative analyses were performed using SPSS Statistics (version 24, IBM, Armonk, NY, USA).

Qualitative Research

Recruitment, Study Population and Moderation of Focus Groups

To gain in-depth insights into behavioral factors affecting protein intake, we conducted focus group discussions. Older adults with Surinamese African, Surinamese South Asian, Turkish, and Moroccan origin were consulted in separate focus group discussions. These ethnic minority groups are the largest non-western minority groups living in the Netherlands. Subjects were recruited at community centers in Amsterdam and the region of Apeldoorn. After written informed consent, participants were assigned to one of the focus groups. The focus group discussions with both Surinamese groups were conducted in Dutch and discussions with Turkish and Moroccan older adults were guided by trained native Turkish and native Moroccan moderators. This enabled the focus group participants to speak in their native language.

Discussion Guide

The qualitative study focused on behavioral determinants affecting protein intake, both personal and environmental. First, we explored personal determinants, such as current knowledge and awareness, about protein and its role in healthy aging. Second, we explored environmental determinants that explained dietary (protein) behavior and habits. Participants were asked to come up with associations and explanations on the topic of protein and aging (i), followed by a short informative presentation by the researchers filling in the knowledge gap on this topic. Second, questions were asked about dietary habits, food patterns, and sociocultural factors affecting dietary (protein) intake (ii).

Qualitative Analyses

The audio recordings of all focus group discussions were transcribed verbatim and translated by bilingual members of the research team into Dutch within the software program MaxQDA Analytics Pro 18 (version 2018). A random sample of the translationswere checked by an independent native speaker. A framework approach based on the discussion guide was used as base for the coding scheme to analyze the transcripts. Two researchers agreed upon a coding scheme and assigned codes independently to the same transcripts. The coding scheme distinguished behavioral determinants affecting dietary protein intake and timing, both related to the person (e.g., knowledge, awareness, attitude), and environment (e.g., social norms and cultural factors). To ensure intercoder reliability, the two researchers discussed coding differences until consensus was reached. Then codes were rearranged and clustered by axial coding according to the research questions to be answered. After restructuring the codes, the results section was formulated by re-reading segments and linking codes and coded segments from the different transcripts through an iterative process.

RESULTS

Quantitative Study

Subject Characteristics

The mean age of all ethnic groups ranged from 58.5 to 61.7 years. In men, the lowest BMI was found in Dutch (26.3 ± 3.7 kg/m^2) and the highest in Moroccan (28.2 ± 4.1 kg/m^2). In women, the lowest BMI was also found in Dutch (25.9 ± 4.5 kg/m^2) and the highest in Turkish (32.9 ± 6.1 kg/m^2). South Asian men and African Surinamese women reported on average the lowest energy intakes (2130 ± 751 kcal/day and 1748 ± 634 kcal/day, respectively). In Turkish participants, both men and women reported, on average, the highest energy intake (2331 ± 648 kcal/day in men and 2122 ± 699 kcal/day in women) (Table 1).

Amount of Protein

Mean relative protein intake ranged from 1.04 ± 0.33 g/kg BW/day in Dutch women to 1.38 ± 0.38 g/kg BW/day in Turkish men, with a significant difference in South Asian Surinamese and Turkish men, in comparison to the Dutch reference population ($p = 0.024$ and $p = 0.001$ respectively; Table 1). Adjusting for chronic disease (self-reported history (or presence) of diabetes, myocardial infarction, or stroke), smoking status, alcohol consumption, or physical activity did not change these results (data not shown). Furthermore, the majority of the study population reached the RDA of 0.8 g with the highest percentage in Turkish men (97%) and the lowest percentage in African Surinamese women (59%). Between 49% and 60% of people in all older populations reached the minimal ESPEN protein recommendation of 1.0 g/kg BW/day, except the Turkish men, of which 91% met this guideline (Table 1).

Protein Source

Next to total protein intake, Table 1 shows the protein intake in g/kg BW/day in the different older ethnic groups by source and stratified by gender. Mean animal derived protein intake was lowest in both Dutch men and women (0.63 ± 0.22 g/kg BW/day and 0.61 ± 0.24 g/kg BW/day, respectively) and the highest in both Turkish men and women (0.86 ± 0.36 g/kg BW/day and 0.68 ± 0.35 g/kg BW/day respectively), with a significant difference in Turkish men compared to Dutch men ($p = 0.001$). Mean plant protein ranged from 0.38 ± 0.18 g/kg BW/day in African Surinamese women up to 0.53 ± 0.28 g/kg BW/day in Moroccan men and differed significantly in South Asian Surinamese men ($p = 0.024$), Turkish men ($p = 0.010$), South Asian Surinamese women ($p = 0.001$), and African Surinamese women ($p = 0.033$) compared to the Dutch reference population. Adjusting for chronic disease (self-reported history (or presence) of diabetes, myocardial infarction, or stroke), smoking status, alcohol consumption of physical activity did not change these results (data not shown).

Protein Product Sources

Ethnic differences were observed concerning the contribution of specific food sources to total daily protein intake and were different from the Dutch majority population, where Dutch cheese and milk contributed most to daily protein intake. In general, the most important sources of protein are ethnic specific. Despite the fact that bread is not considered to be a protein rich source, different types of bread made a large contribution to daily protein intake in all ethnic groups. In both Surinamese groups, chicken and dried fish were typical protein rich products to consume. Turkish older adults derived most of their dietary protein from different types of bread and different types of meat (veal, minced beef, lamb). The most important protein rich products consumed by Moroccan participants were comparable to the Turkish group, except for some animal derived products such as milk, chicken, and crustaceans.

Table 1. *Characteristics of the subsample from participants of Healthy Life in an Urban Setting (HELIUS) (N = 1415).*

	Dutch	South Asian Surinamese		African Surinamese		Turkish		Moroccan	
MEN	**mean ± SD, N (%)**	**mean ± SD, N (%)**		**mean ± SD, N (%)**		**mean ± SD, N (%)**		**mean ± SD, N (%)**	
N = 638	272 (19.2%)	140 (9.9%)		143 (10.1%)		32 (2.2%)		51 (3.6%)	
Age (years)	61.7 ± 4.0	60.7 ± 4.0		60.6 ± 4.2		58.5 ± 3.2		60.5 ± 4.2	
BMI (kg/m2)	26.3 ± 3.7	26.4 ± 3.7		26.6 ± 4.0		27.3 ± 3.0		28.2 ± 4.1	
Energy intake (Kcal/day)	2333 ± 587	2130 ± 751		2250 ± 739		2331 ± 648		2244 ± 843	
Protein intake (g/day)	88.9 ± 22.7	87.8 ± 34.5		89.2 ± 32.3		105.3 ±28.7		95.5 ± 39.2	
Protein intake (g/kg BW/d) *	1.06 ± 0.31	1.20 ± 0.54	p = 0.024	1.13 ± 0.46	p = 0.613	1.38 ± 0.38	p = 0.001	1.18 ± 0.53	p = 0.351
Animal protein intake (g/kg BW/d) *	0.63 ± 0.22	0.70 ± 0.41	p = 0.203	0.67 ± 0.36	p = 0.714	0.86 ± 0.36	p = 0.001	0.65 ± 0.34	p = 0.993
Plant protein intake (g/kg BW/d) *	0.44 ± 0.17	0.50 ± 0.23	p = 0.024	0.46 ± 0.19	p = 0.841	0.52 ± 0.16	p = 0.128	0.53 ± 0.28	p = 0.010
Protein intake (% EN)	15.4 ± 2.6	16.4 ± 3.3		16.1 ± 3.4		18.1 ± 3.6		17.1 ± 3.4	
>0.8 g/kg BW/d (%) $	226 (83.1%)	106 (75.7%)		113 (79.0%)		31 (96.9%)		36 (70.6%)	
>1.0 g/kg BW/d (%) §	154 (56.6%)	78 (55.7%)		87 (60.8%)		29 (90.6%)		28 (54.9%)	

Table 1 *continued.*

	Dutch	South Asian Surinamese		African Surinamese		Turkish		Moroccan	
WOMEN	**mean ± SD, N (%)**	**mean ± SD, N (%)**		**mean ± SD, N (%)**		**mean ± SD, N (%)**		**mean ± SD, N (%)**	
N = 777	290 (20.5%)	179 (12.7%)		230 (16.3%)		29 (2.0%)		49 (3.4%)	
Age (years)	61.6 ± 4.1	60.2 ± 4.1		59.7 ± 3.8		59.3 ± 4.0		59.6 ± 4.4	
BMI (kg/m2)	25.9 ± 4.5	28.0 ± 4.6		30.2 ± 5.9		32.9 ± 6.1		31.0 ± 5.2	
Energy intake (Kcal/day)	1888 ± 493	1752 ± 558		1748 ± 634		2122 ± 699		1783 ± 679	
Protein intake (g/day)	72.4 ± 21.1	74.3 ± 27.8		73.6 ± 28.1		91.3 ± 35.8		77.3 ± 32.0	
Protein intake (g/kg BW/d) *	1.04 ± 0.33	1.11 ± 0.44	p = 0.249	0.96 ± 0.42	p = 0.261	1.16 ± 0.48	p = 0.490	1.05 ± 0.52	p = 0.999
Animal protein intake (g/kg BW/d) *	0.61 ± 0.24	0.62 ± 0.34	p = 0.999	0.59 ± 0.32	p = 0.888	0.68 ± 0.35	p = 0.799	0.56 ± 0.36	p = 0.819
Plant protein intake (g/kg BW/d) *	0.42 ± 0.15	0.50 ± 0.20	p = 0.001	0.38 ± 0.18	p = 0.033	0.49 ± 0.22	p = 0.439	0.49 ± 0.24	p = 0.153
Protein intake (% EN)	15.4 ± 2.7	17.0 ± 4.0		17.1 ± 3.8		17.2 ± 3.3		17.2 ± 2.7	
>0.8 g/kg BW/d (%) $	222 (76.7%)	131 (73.2%)		135 (58.7%)		23 (79.3%)		35 (71.4%)	
>1.0 g/kg BW/d (%) §	143 (49.3%)	103 (57.5%)		96 (41.7%)		17 (58.6%)		24 (49.0%)	

*BMI = body mass index, %EN = percentage of energy intake, g/kg BW/d = grams per kilogram bodyweight per day. * p-values represent comparison to Dutch majority population. $ RDA (recommended daily allowance) of protein set by WHO (World Health Organization). § Minimum protein recommendation set by European Society for Clinical Nutrition and Metabolism (ESPEN) discussion group.*

Qualitative Study

Subject Characteristics

In total, 11 focus group discussions were held among older adults from different ethnic groups (Table 2). Most participants were women, except for the Moroccan group where most participants were men.

Table 2. *Subject characteristics of the focus group participants.*

	South Asian Surinamese	African Surinamese	Turkish	Moroccan
	Mean, N	**Mean, N**	**Mean, N**	**Mean, N**
N (number of focus group discussions)	2	2	5	2
N (number of participants)	14	11	29	15
Sex (men/women)	2/12	0/11	9/20	12/3
Age (years)	74	80	64	-*

** The age of the Moroccan participants is unknown due to unwillingness to provide any personal details.*

Qualitative Exploration of Behavioral Determinants of Protein Intake

Personal determinants affecting protein intake: during the focus group discussions, all ethnic groups seem to lack knowledge and awareness of the role of protein in healthy aging. Participants made only a few associations to the term "protein", when the moderator asked for it; often associations were incorrect and participants were not able to substantiate their answers. This is illustrated by questions asked by participants about the role of protein in a healthy diet and participants showing strong beliefs about the role of protein and other nutrients in losing weight. In other words, protein was mostly related to losing weight rather than maintaining muscle mass and function.

"I don't know why, but I do know that I should eat more protein and avoid carbohydrates".

"Don't you lose weight by eating protein? Please explain to us"!

Indeed, most participants also indicated not knowing which products to choose and what is needed to consume an adequate amount of protein. However, participants were motivated to learn more about the role of protein for healthy aging and daily functioning. This is based on the curiosity participants showed by asking further questions on how to improve their protein intake, especially in Turkish and South Asian Surinamese groups.

"I want to know which products I should take, there are so many, it is confusing"!

"I have a question; I am a vegetarian, what food can I eat to reach a sufficient amount of protein"?

The participants showed their willingness to adopt new dietary habits towards a more protein rich diet, but felt unable to do so. Although participants in each ethnic group showed a positive attitude towards eating an adequate amount of protein, they preferred to receive more information about the role of protein and exact protein sources first. An expected barrier related to optimizing dietary habits, and, thus, improving protein intake, mentioned by participants, is the irregularity of daily meal consumption. Often meals are skipped, postponed, or even combined with other meals. Reasons that were mentioned are a lack of appetite, having an irregular daily schedule, waking up late, suffering from pain or forget to eat.

"I preferably stay in bed, rather than consuming my breakfast. No, I don't eat breakfasts".

Environmental determinants affecting protein intake: although their positive attitudes to optimize protein intake, the respondents showed a lack of confidence in their ability to change dietary habits towards optimizing protein intake due to several environmental factors that affect dietary behaviors in daily living. Food cultures, for example, are deeply rooted in daily living and are characterized by traditional ethnic specific products and dishes.

"We are born with rice, no kidding, we grew up with rice, from the age of 6 months we eat rice".

Several environmental factors were mentioned by individuals from all ethnic groups that might be relevant in optimizing protein intake. For example, factors related to food cultures were mentioned, characterized by the abundance of food during social activities, family visits and special festivities. In particular, Moroccan and Turkish older adults indicated that the social environment influences dietary habits, as they often eat together with their families and show great hospitality to guests.

"When people come to visit, we spend half a day in the kitchen to cook plenty of food for the guests, because we know that they expect that from us".

Participants emphasize that the social cohesion and traditions contribute to strong dietary habits, which lead to the maintenance of their current dietary behaviors. Several Moroccan and Turkish participants reported not feeling comfortable enough to alter their diet in favor of protein without the support of their social environment. Surinamese older adults mainly named social activities and frequent festivities to be most challenging in changing dietary behaviors.

DISCUSSION

To our knowledge this study was the first to examine the dietary protein intake and the behavioral and environmental factors that affect protein intake among older adults from ethnic minorities in the Netherlands, in order to look at how protein intake may be improved.

First, the amount of protein is important to consider in order to maintain muscle mass while aging.[113] Based on the recommended daily allowance of 0.8 g/kg BW/day cut-off, the majority of the ethnic populations from our study consume an adequate amount of protein. Still, 5–25% of the older adults from the different ethnic minorities, with exception of the Turkish, may improve their total daily protein intake to reach the RDA levels. Ethnic minority groups show higher sarcopenia prevalence rates compared to the Dutch majority populations,[125] so they generally have a worse disease risk profile. Indeed chronic diseases and physical limitations appear at a younger age in Dutch ethnic minority group.[56,123,124] Therefore 1.0–1.2 g of protein per kilogram bodyweight per day is suggested to be relevant for these populations to maintain or improve muscle mass.[129,135] Since 40% to 60% of older adults from Dutch ethnic minorities, except for Turkish men, do not reach the ESPEN recommendation, the amount of dietary protein should be improved to at least 1.0 g/kg BW/day.

Our quantitative analyses also pointed out that the largest proportion of the dietary protein intake in all ethnic groups originate from animal sources, and a smaller proportion originate from plant sources. This is comparable to other older populations in the Netherlands.[136] These results are beneficial from a physiological perspective, since animal protein, especially those from dairy, seems to be most beneficial to improve muscle protein synthesis compared to plant protein, and is, therefore, to be favored.[132,133,137] Unfortunately, from this study, it is still unclear what the exact distribution is of protein sources throughout the day in these minority populations. More research is needed in this field.

From our qualitative analyses, we found indications that the timing of protein intake is suboptimal, due to the irregularity of daily schedules, thus, unconcise timing of daily meals. These findings correspond to recent quantitative findings from HELIUS showing that ethnic minority populations skip breakfast more often and eat more erratically.[138] Additionally, in an earlier qualitative study, Turkish and Moroccan participants in the Netherlands experienced a contrast between lifestyles in the Netherlands and lifestyles in their country of origin, inducing unconcise timing of meals.[68] Irregular eating patterns are specifically not favorable for maintaining muscle mass in older adults. Several studies show an importance of dietary protein intake distributed throughout the day to maintain muscle mass.[139,140] An amount of 25–30 g of protein per meal is needed to maximally stimulate skeletal muscle protein synthesis, where 20 g of high quality protein or 10 g of essential amino acids is considered the minimum.[133] Several studies suggest that a protein intake pattern that is evenly distributed throughout the day is most favorable to stimulate muscle protein synthesis in older adult.[141,142] Indeed, RCTs showed the effectiveness of a concise timing of protein throughout the day for muscle mass and physical functioning.[25,28] Therefore, a concise timing of the breakfast and other meals throughout the day should be advised to maintain and/or gain muscle mass in older adults from ethnic minorities.

Our qualitative study also provided information on personal and environmental factors that affect protein intake in these minority populations. The majority of the participants in the focus group discussions lack knowledge and awareness on protein containing food products and its importance for the aging process. They also indicated not to know how to consume adequate protein in daily living. Future interventions to optimize protein intake in these minority populations should include methods that target personal determinants as knowledge, skills, and awareness, to be able to improve dietary protein intake.[143] Additionally, our qualitative study showed that cultural background determines food choices, certain beliefs about health behaviors, and strong eating habits. This is in line with our quantitative analysis that showed that food products that contributed the most to daily protein intake were ethnic specific and varied between ethnic groups. Cultural background also seems to determine the influence of the social environment on dietary intake. These cultural and social influences on food consumption are also comprehensively discussed in earlier qualitative studies in these ethnic groups in the Netherlands.[68,69] The strong social norms, religion and cultural beliefs play a crucial role in dietary behaviors in ethnic minority groups.[67] Such determinants are deeply rooted and challenging to modify, so are expected not to be sustainable in changing behaviors. However, previous studies have shown the importance of cultural adaptations for effective culturally targeted interventions. As such, to account for specific cultural needs, a strategy to optimize protein intake in older ethnic minorities should consider, for example, ethnic specific dietary needs and active involvement of the social environment to increase social support and acceptance.[144]

3

Based on the current study we advise to improve the amount of protein and timing of protein to be the windows of opportunity for optimizing protein intake in older adults from ethnic minorities. Hence, when aiming to improve muscle strength and physical functioning, the effectiveness of an intervention focusing on protein alone may not be enough. Several studies, including a meta-analyses, indicate that a higher amount of protein is not associated with increased muscle mass[145–147] or muscle strength.[148] A more effective strategy to improve muscle mass and physical functioning in these older ethnic minority populations should include a physical exercise component, preferably resistance exercise. Several trials showed the effectiveness of combined exercise and protein interventions in older adults, with protein intake levels well above the RDA.[21,25,149,150] As such, if combined with (resistance) exercise, increasing the amount of dietary protein to a minimum of 1.0–1.2 g/kg BW/day, might be a beneficial strategy to improve muscle mass and functioning in these populations. Based on a recent study among the HELIUS study population, which shows a lower percentage of the older adults from ethnic minorities meet the Dutch physical activity norm compared to the Dutch majority population, (resistance) exercise behavior should also be targeted.[125]

CONCLUSIONS

In conclusion, the amount and timing of protein intake seem to be major concerns in older adults from ethnic minorities in the Netherlands. Optimizing protein intake in these groups requires a culturally sensitive approach, which accounts for ethnic specific protein product types and strong social norms. Future studies should therefore focus on developing and evaluating a culture-sensitive intervention that is community based to increase social support, and includes methods to improve awareness and skills related to protein intake among different ethnic minority populations. An intervention that manages to optimize protein intake may eventually contribute to improved muscle mass, strength, physical functioning, and quality of life in older adults from ethnic minorities in the Netherlands.

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CHAPTER 3 - SUPPLEMENTARY MATERIAL

Supplementary table 1. *Most important protein food sources per ethnic group, based on the contribution to the total daily protein intake.*

	Dutch (n=562)	South Asian Suriname (n=319)	African Surinamese (n=373)	Turkish (n=61)	Moroccan (n=100)
1	Whole wheat bread	Semi skimmed milk	Chicken meat	Lamb, mutton	Moroccan bread
2	Dutch cheese 40+	Whole wheat bread	White rice	Turkish bread	Whole wheat bread
3	Semi skimmed milk	White rice	Dutch cheese 40+	Brown bread	Lamb, mutton
4	Brown bread	Salted and dried cod	Whole wheat bread	Turkish wheat bread	Chicken fillet
5	Dutch cheese 20+	Chicken	Smoked chicken slices	Whole wheat bread	Crustaceans
6	Chicken fillet	Brown bread	Salted and dried cod	Minced beef	Semi skimmed milk
7	Lean beef	Sardines, mackerel, salmon, eel, herring	Brown bread	Veal	Moroccan minced beef
8	Boiled chicken egg	Peanut butter	Nuts, peanuts	Boiled chicken egg	Brown bread
9	Minced beef	Dutch cheese 40+	Dutch cheese 20+	Turkish legumes soup	Boiled chicken egg
10	White pasta	Surinamese legumes	Peanut butter	Legumes	Legumes

4

In-depth analyses of the effects of a diet and resistance exercise intervention in older adults: who benefits most from ProMuscle in Practice?

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ABSTRACT

Background: The ProMuscle in Practice intervention, comprising resistance exercise and an increased protein intake, was effective in improving muscle strength, lean body mass, and physical functioning in older adults aged ≥65 years (n=168). However, a heterogeneous response to such interventions is common. Therefore, we explored the differences in responsiveness to the intervention in subgroups based on demographic characteristics and mobility-impairing disorders.

Methods: Multiple regression analyses were performed to study mean changes between baseline and 12 weeks on the Short Physical Performance Battery, chair rise test, lean body mass, knee extension strength, leg press strength, and leg extension strength. The interaction term treatment x subgroup was included to study differences in effects between subgroups. Subgroups comprised age (≤75 vs. >75 years), sex (men vs. women), presence of frailty, presence of sarcopenia, and presence of osteoarthritis.

Results: A significant interaction effect including age was found on lean body mass (β=-0.8, 95% CI: -1.5; -0.2), favoring participants aged ≤75 years. A significant interaction effect including sex was found on leg press strength (β=15.5, 95% CI: 0.6; 30.3), favoring women. Participants with or without frailty, sarcopenia, or osteoarthritis responded equally to the intervention in terms of absolute effects.

Conclusions: Participants aged ≤75 years and women benefited to a great extent from the intervention, as they improved significantly on nearly every outcome. Effects in participants with and without a mobility-impairing disorder were comparable, indicating that the intervention is suitable for both groups.

INTRODUCTION

Interindividual variability regarding health characteristics, such as functional status, mobility, and weight status, increases over the life course.[4,151] This contributes to a heterogeneous older population, with the rate and consequences of the ageing process being different between individuals.[3,6–8] One of those consequences is an impaired mobility, which is often the beginning of further functional decline.[10,152–154] As the proportion of older adults is growing rapidly, it is important to delay or rather prevent the onset of functional decline.[10,153,155]

An effective strategy in improving older adults' physical functioning and mobility is the combination of resistance exercise (RE) and protein supplementation (PS).[22,23,47] Although a recent study showed that there are no non-responders to RE among older adults,[156] several meta-analyses reported that differential effect sizes and heterogeneity in responsiveness to RE and PS is common.[21–23,30] On the one hand, the varying effects can be explained by heterogeneity in interventions, such as duration of the intervention, type of training sessions, and type, dose, and timing of PS. On the other hand, variation in effect sizes can be due to heterogeneity in study populations, including differences in age, sex, health status and training status of the participants.[21–23,30]

Several studies investigated the role of age and sex in the heterogeneous RE response.[156–158] However, findings remain inconclusive, showing either no differences for age and sex groups,[157] or sex-related differences favoring either men or women depending on the outcome studied.[156,158] Interventions combining RE and PS also show inconsistent results in subgroups based on age or sex. A recent meta-analysis reported a higher increase in fat free mass (FFM) in younger compared to older adults (≤45 vs. >45 y),[31] whereas another meta-analysis found no significant differences among subgroups based on age but reported a higher increase in FFM in the older subgroup (≤65 vs. >65 y).[41] A meta-analysis comparing intervention effects between men and women showed greater changes in lean body mass and leg strength in men compared to women,[23] whereas two other meta-analyses reported no clear sex-based differences.[31,41] However, the number of studies investigating the effects of RE and PS in women is limited, which complicates adequate comparison.[23,31,41]

Varying effects in muscle health in response to RE and PS are also found in older adults suffering from mobility-impairing disorders, such as frailty, sarcopenia, and osteoarthritis. Although numerous interventions combining RE and an increased protein intake have been performed in healthy older adults aiming to prevent sarcopenia,[22,23,47] limited interventions have been conducted specifically in sarcopenic older adults. Nevertheless, available literature showed that effects on muscle health in sarcopenic participants were rather positive.[48] With regards to frail older adults, multiple interventions including RE and PS were conducted, resulting in improvements on lean body mass, leg strength, and physical mobility.[50] To date, the preventive effects of RE and PS interventions have not been studied extensively in older adults suffering from osteoarthritis.[159] However, aerobic, strengthening and flexibility exercises are an important part of its treatment[160] and were found to reduce pain and increase physical functioning in osteoarthritis patients.[161,162]

Thus, there is a discrepancy in literature related to the responsiveness of subgroups to interventions combining RE and PS. In our intervention, ProMuscle in Practice, we expect to find heterogeneous responses as well. Our 12-week intensive support intervention including RE and an increased protein intake was found to be effective in improving muscle strength, lean body mass, and physical functioning in community-dwelling older adults.[28] However, variation was found in the effects, possibly indicating heterogeneous responses between subgroups. Therefore, we aimed to explore the differences in responsiveness to RE and PS between subgroups based on demographic characteristics and mobility-impairing disorders in the ProMuscle in Practice intervention.

METHODS

Study design

The study design, intervention description and main results of ProMuscle in Practice are described in detail elsewhere.[27,28] In short, ProMuscle in Practice is a randomized controlled multicentre intervention, implemented in a phased manner at five Dutch municipalities (Apeldoorn, Epe, Ermelo/Putten, Harderwijk and Ede) between 2016 and 2018.

Study population

Researchers recruited and screened older adults aged 65 years and older, according to the following criteria: master the Dutch language, being pre-frail or frail according to Fried criteria[153] or being non-frail but experiencing difficulties in daily activities and being inactive (i.e. not participate in RE >30 minutes a day on more than 2 days a week). The exclusion criteria (supplementary table 1) were checked by the older adults' general practitioner (GP). In total, 168 older adults were randomized, stratified for sex and frailty state, to the intervention or control group. The study protocol was approved by the Wageningen University Medical Ethics Committee, and all subjects gave their written informed consent before the start of the study. The ProMuscle in Practice study is registered at the Dutch Trial Register (identifier NTR6038).

Description of the intervention

The intervention consisted of a 12-week intensive support program, followed by a 12-week moderate support program. In the current study we focused on the intensive intervention only. The intensive support program included twice weekly progressive RE, primarily focused on the leg muscles. Each session had a duration of 1 hour, was group-based (4-7 participants) and was supervised by physiotherapists according to ProMuscle in Practice manuals. Additionally, a dietitian advised participants to increase their protein intake to 25 grams per main meal, via individual consultations (at baseline, week 1 and week 6) and by providing products, such as dairy foods and protein-rich cakes or desserts. The control group received usual health care and was asked to retain their habits regarding exercise and diet.

MEASURES

Outcome measures

Outcomes were measured at baseline in week 0 (T0) and after the 12-week intensive support intervention (T1). Data were collected by trained researchers and research assistants.

Physical functioning

The Short Physical Performance Battery (SPPB) was used to measure physical functioning (score 0-12, 12 representing best score). The test consists of three components: a standing balance, repeated chair rise and gait speed test.[163] In addition to total SPPB score, chair rise was included in the data analyses, as chair rise is highly correlated with lower body strength; the main training focus of the intervention.[164]

Muscle mass

Lean body mass was measured through dual-energy X-ray absorptiometry (DXA, Lunar Prodigy Advance; GE Health Care, Madison, WI). Scans were performed in the morning. Participants were asked to consume a standardized breakfast and to defecate shortly before the scan. Bioelectrical impedance spectroscopy was used to assess hydration state (SFB7; ImpediMed Limited, Pinkenba, QLD, Australia).

Muscle strength

Lower limb muscle strength was measured through 3-Repetition Maximum (3RM) tests on the leg press and leg extension machines. Before the measurement, a familiarization session was performed. The formula of Brzycki was used to recalculate 3RM to 1RM scores, reported in kg.[165] Knee extension strength was measured using a hand-held dynamometer (MicroFET). Three repeated tests were performed alternating both legs. The highest measurement of the dominant leg was included for analyses, reported in Newton.

Subgroups

Subgroups were created based on demographic variables and mobility-impairing disorders, both assessed at baseline (T0). Demographic variables included age and sex. Age was divided in two groups based on median age (75 years). Mobility-impairing disorders included frailty, sarcopenia, and osteoarthritis and are described in detail below.

Frailty

Frailty was assessed according to the Fried frailty criteria.[153] Participants in the categories pre-frail and frail were combined due to low number of participants being frail (n=7). Non-frail participants were included in the study if they experienced difficulties in daily activities and being inactive (i.e. not participate in RE >30 minutes a day on more than 2 days a week).

Sarcopenia

The revised sarcopenia definition of the European Working Group on Sarcopenia in Older People (EWGSOP2) was used.[13] Low muscle strength (criterion 1) indicating probable sarcopenia was assessed with grip strength (<27 kg for men and <16 kg for women). Low muscle quantity (criterion 2) confirms the sarcopenia diagnosis and was assessed according to low appendicular muscle mass (<20 kg for men and <15 kg for women) on top of having low muscle strength. Severe sarcopenia is detected if low physical performance is present on top of low muscle strength and mass (criterion 3). Low physical performance was assessed according to gait speed (≤0.8 m/s for both men and women). Participants in the category 'probable sarcopenia' were included in the analyses as being sarcopenic and remaining participants were classified as non-sarcopenic. Categories 'sarcopenia diagnosis' and 'severe sarcopenia' were too small to be analysed separately (n=10 and n=6, respectively).

Osteoarthritis

Whether participants had osteoarthritis in the hips or knees was assessed via a questionnaire, including answer options 'no', 'yes, not diagnosed by GP', and 'yes, diagnosed by GP'. The latter two categories were combined in the category indicating osteoarthritis.

Statistical analyses

Baseline characteristics were analysed using independent samples t-tests or Mann Whitney U tests for continuous data, and Pearson's chi-squared test or Fishers exact tests for categorical data. Multiple regression analyses were performed to study the mean changes between T1 and T0 between the intervention and control group, in the total study population as well as in subgroups. Besides, differences in effects between subgroups were studied by including treatment x subgroup as interaction term. Subgroups comprised age, sex, frailty, sarcopenia, and osteoarthritis. Change scores were calculated by subtracting the effects at T0 from the effects at T1. Participants with complete measurements at T0 as well as T1 were included in the analyses, which was assessed per study outcome. Separate models were conducted for each outcome: SPPB total score, chair rise test, lean body mass, knee extension strength, leg press strength, and leg extension strength. We assessed the crude model as well as the adjusted model (adjusted for age, sex, educational level, and municipality). Estimated mean differences and 95% confidence intervals are presented for the total study population, per subgroup and between subgroups (interaction effects). We additionally calculated 'relative effects', defined as changes relative to baseline in %, calculated as follows: (absolute effect T1-T0 / baseline measure) x 100%. Multiple regression analyses were also performed including relative effects as dependent variable. To assess the treatment effect in combinations of subgroups, three-way interactions and related post-hoc analyses were conducted. Three-way interactions were examined for the outcomes chair rise, lean body mass and leg press strength, as chair rise is highly correlated with lower body strength, the main training focus of the intervention,[164] and lean body mass and leg press strength showed significant two-way interactions indicating further exploration of the pattern of treatment effects. Data was analysed using SPSS version 23. Statistical significance was indicated with p-value <0.05.

RESULTS

Baseline characteristics

Table 1 presents the baseline characteristics for the intervention and control group separately. No significant differences between the two groups were observed at baseline. About 21% of the study population could be indicated with sarcopenia diagnosis, 52% as being pre-frail or frail, and almost 48% suffered from osteoarthritis.

Table 1. *Baseline characteristics of participants of the ProMuscle in Practice intervention.*

	Intervention group (n=82)	Control group (n=86)
Age (years)	74.7 ± 5.8	75.9 ± 6.5
Sex (*n* female, %)	51 (62%)	51 (59%)
Bodyweight (kg)	76.3 ± 14.4	75.6 ± 13.6
Height (cm)	167.6 ± 9.0	169.2 ± 9.3
Education level (n, %)[a]		
Low, intermediate	56 (68%)	46 (54%)
High	26 (32%)	40 (47%)
Ethnicity: native Dutch (n, %)	79 (96%)	81 (94%)
Care use (n, %)	11 (13%)	16 (19%)
Frailty status (n, %)		
Non-frail	41 (50%)	39 (45%)
Pre-frail, frail	41 (50%)	47 (55%)
Sarcopenia (n, %)[b]		
Probable	17 (21%)	19 (22%)
Diagnosis	3 (4%)	7 (8%)
Severe	2 (2%)	4 (5%)
Osteoarthritis (n, %)	38 (46%)	42 (49%)
SPPB total score (0-12)[c]	10.1 ± 1.4	10.1 ± 2.0
Standing balance (points)	3.7 ± 0.6	3.6 ± 0.7
4-meter gait speed (sec)	4.2 ± 0.9	4.2 ± 1.2
Repeated chair rise (sec)	13.7 ± 3.4	13.1 ± 3.9
Lean body mass (kg)[d]	47.7 ± 9.1	48.0 ± 9.5
Leg press strength (kg)[e]	129.2 ± 41.1	122.8 ± 36.6
Leg extension strength (kg)[f]	66.8 ± 23.3	67.5 ± 22.9
Knee extension strength (N)[g]	309.9 ± 107.0	302.5 ± 96.1

Note: Data is presented as mean ± SD or n (%). SPPB = Short Physical Performance Battery

[a]Education level, low: primary school or less, intermediate: secondary professional education or vocational school, high: higher vocational education or university. Low and intermediate education level were combined due to low numbers in the low education category (n=6). [b]n=160;[c]n=167; [d]n=163; [e]n=156; [f]n=157;[g]n=166.

Effects in total study population and per subgroup

Table 2 presents the mean changes per study outcome after 12 weeks for the total study population and per subgroup. The model was adjusted for age, sex, educational level, and municipality. Adjustments affected the estimates of the interaction effect by more than 10% compared with the crude model (crude model; supplementary table 2). Further, two-way interactions for treatment x subgroup are presented. In the total study population, significant mean changes were found on every study outcome. Effects in subgroups are described below and represent differences between the intervention and control group between T0 and T1.

Age

A significant positive effect on every study outcome was found for participants aged ≤75 years (mean age: 71±3). Participants aged >75 years (mean age: 81±4) showed a significant increase on knee extension strength, leg press and leg extension strength. The interaction effect treatment x age was found to be significant on lean body mass (β=-0.8, 95% CI: -1.5; -0.2). The increase in lean body mass for participants aged ≤75 years was 0.9 kg (95% CI: 0.5; 1.4) and the increase in participants aged >75 years was 0.1 kg (95% CI: -0.4; 0.6). Relative changes and interaction effects were comparable to absolute changes and interaction effects (supplementary table 3); only the interaction treatment x age was found to be significant on lean body mass (β=-1.98, 95% CI: -3.3; -0.3), showing a higher increase in participants aged ≤75 years compared to those aged >75 (figure 1A). No significant three-way interaction effects including age were found.

Sex

In women, a significant effect in the intervention compared to control group was found on every study outcome except for lean body mass. Men only showed a significant effect on lean body mass and leg extension strength. For leg press strength, the interaction effect treatment x sex was found to be significant (β=15.5, 95% CI: 0.6; 30.3). The increase on leg press strength was 7.4 kg (95% CI: -3.8; 18.6) in men and 22.8 kg (95% CI: 12.9; 32.8) in women. Relative changes and interaction effects were comparable to absolute changes and interaction effects (supplementary table 3). However, when assessing relative changes, the interaction effect treatment x sex was significant for leg press strength (β=13.9%, 95% CI: 3.1; 24.7), and leg extension strength (β=15.2%, 95% CI: 4.0; 26.4), as presented in figure 1, showing a higher relative change in women compared to men on both outcomes. Three-way interactions including sex were not significant. Only treatment x sex x osteoarthritis for leg press strength was nearly significant (F=3.047, p-value=0.051), showing the largest effects on leg press strength in women with osteoarthritis (mean effect: 26.5 kg, 95% CI: 12.8-40.3).

Table 2. *Adjusted mean differences per study outcome (mean Δ Int – Con) and interaction terms treatment x subgroup for each subgroup separately (continued on next page).*

	SPPB (points)			Chair rise (seconds)			Lean body mass (kg)		
	n	**Mean Δ Int – Con (95% CI)**	**Treatment x subgroup β (95% CI)**	**n**	**Mean Δ Int – Con (95% CI)**	**Treatment x subgroup β (95% CI)**	**n**	**Mean Δ Int– Con (95% CI)**	**Treatment x subgroup β (95% CI)**
Total study population	152	0.5 (0.1; 1.0)*		148	-1.6 (-2.6; -0.7)*		150	0.5 (0.2; 0.9)*	
Subgroup									
Age									
Age≤75	84	0.7 (0.1; 1.3)*	-0.3 (-1.3; 0.6)	84	-2.0 (-3.2; -0.7)*	0.8 (-1.2; 2.7)	84	0.9 (0.5; 1.4)*	-0.8 (-1.5;-0.2)‡
Age>75	68	0.3 (-0.4; 1.0)		64	-1.2 (-2.7; 0.3)		66	0.1 (-0.4; 0.6)	
Sex									
Men	63	0.3 (-0.4; 1.0)	0.4 (-0.6; 1.3)	62	-1.0 (-2.5; 0.5)	-1.1 (-3.0; 0.9)	65	0.8 (0.3; 1.3)*	-0.4 (-1.1; 0.3)
Women	89	0.7 (0.1; 1.3)*		86	-2.1 (-3.3; -0.8)*		85	0.4 (-0.1; 0.8)	
Frailty state									
Pre-frail, frail	78	0.4 (-0.2; 1.1)	-0.1 (-1.1; 0.8)	74	-1.9 (-3.2; -0.5)*	-0.6 (-2.5; 1.4)	76	0.5 (0.1; 1.0)*	0.0 (-0.7; 0.7)
Non-frail	74	0.6 (-0.1; 1.3)		74	-1.3 (-2.7; 0.1)		74	0.6 (0.1; 1.1)*	
Sarcopenia									
Sarcopenia	33	0.1 (-0.9; 1.1)	-0.6 (-1.7; 0.6)	31	-0.8 (-2.9; 1.3)	1.1 (-1.2; 3.5)	32	0.3 (-0.5; 1.0)	-0.3 (-1.2; 0.5)
No sarcopenia	114	0.7 (0.1; 1.2)*		112	-1.9 (-3.0; -0.8)*		113	0.6 (0.2; 1.0)*	
Osteoarthritis									
Osteoarthritis	72	0.7 (0.0; 1.4)	0.3 (-0.7;1.2)	69	-1.8 (-3.3; -0.4)*	-0.3 (-2.3; 1.6)	69	0.5 (0.0; 1.0)	-0.1 (-0.8; 0.6)
No osteoarthritis	80	0.4 (-0.3; 1.0)		79	-1.5 (-2.8; -0.2)*		81	0.6 (0.1; 1.1)*	

Table 2 *continued.*

	Knee extension strength (Newton)			Leg press strength (kg)			Leg extension strength (kg)		
	n	**Mean Δ Int– Con (95% CI)**	**Treatment x subgroup β (95% CI)**	**n**	**Mean Δ Int – Con (95% CI)**	**Treatment x subgroup β (95% CI)**	**n**	**Mean Δ Int – Con (95% CI)**	**Treatment x subgroup β (95% CI)**
Total study population	142	36.2 (17.8; 54.7)*		136	16.0 (8.5; 23.6)*		138	11.3 (7.6; 14.9)*	
Subgroup									
Age									
Age≤75	78	41.0 (16.0; 66.0)*	-10.3	79	12.5 (2.6; 22.4)*	8.4	80	10.1 (5.3; 14.9)*	2.7
Age>75	64	30.6 (3.4; 57.8)*	(-47.1; 26.4)	57	20.9 (9.4; 32.5)*	(-6.7; 23.6)	58	12.8 (7.2; 18.4)*	(-4.7; 10.1)
Sex									
Men	61	22.1 (-6.0; 50.2)	24.3	61	7.4 (-3.8; 18.6)	15.5	60	8.0 (2.4; 13.6)*	5.7
Women	81	46.5 (22.5; 70.5)*	(-12.3; 61.0)	75	22.8 (12.9; 32.8)*	(0.6; 30.3)‡	78	13.7 (8.9; 18.5)*	(-1.6; 13.1)
Frailty state									
Pre-frail, frail	72	34.9 (9.1; 60.7)*	-3.2	72	19.5 (9.2; 29.9)*	7.7	72	13.8 (8.8; 18.8)*	4.8
Non-frail	70	38.2 (11.0; 65.3)*	(-40.8; 34.4)	64	11.9 (0.6; 23.1)*	(-7.7; 23.0)	66	9.0 (3.6; 14.4)*	(-2.6; 12.2)
Sarcopenia									
Sarcopenia	30	23.5 (-16.9; 63.9)	-13.7	29	23.0 (6.9; 39.1)*	9.7	29	15.4 (7.7; 23.1)*	6.3
No sarcopenia	108	37.2 (15.8; 58.5)*	(-59.0; 31.6)	103	13.3 (4.7; 22.0)*	(-8.5; 27.8)	104	9.1 (5.0; 13.1)*	(-2.3; 15.0)
Osteoarthritis									
Osteoarthritis	67	45.1 (17.8; 72.4)*	16.1	60	16.7 (4.8; 28.5)*	1.1	63	10.3 (4.7; 15.9)*	-1.8
No osteoarthritis	75	29.0 (3.9; 54.2)*	(-21.1; 53.3)	76	15.6 (5.5; 25.7)*	(-14.6; 16.8)	75	12.0 (7.0; 17.0)*	(-9.3; 5.8)

*Note: Int = Intervention group; Con = Control group. Adjusted estimated mean differences between intervention and control group and 95% CIs are shown per subgroup; β-coefficients and 95% CIs are shown for the treatment x subgroup interaction. Adjusted for: age, sex, educational level, municipality. Treatment: control group is reference. Subgroup: reference groups are respectively men; age ≤75; non-frail; no sarcopenia; no osteoarthritis. *Significant effect between intervention and control group (P < .05). ‡Significant interaction effect: treatment x subgroup (P < .05).*

Frailty

Non-frail participants showed a significant increase on every study outcome, except for SPPB and chair rise. (Pre-)frail participants showed a significant improvement on every study outcome, except for SPPB. No significant two-way or three-way interaction effects were found for frailty. Relative changes and interaction effects were comparable to absolute changes and interaction effects (supplementary table 3).

Sarcopenia

Non-sarcopenic participants showed significant improvements on every study outcome, whereas sarcopenic participants only showed significant effects on leg press and leg extension strength. No significant two-way interaction effects were found. Relative changes and interaction effects were comparable to absolute changes and interaction effects, except for leg extension strength (supplementary table 3). The interaction effect treatment x sarcopenia was found to be significant for relative changes in leg extension strength (β=13.2%, 95% CI: 0.4; 26.1), showing a larger increase in participants with sarcopenia compared to those without sarcopenia, as presented in figure 1. The three-way interaction treatment x osteoarthritis x sarcopenia on leg press strength was found to be significant (F=3.765, p-value=0.026). Exploring this interaction showed that the largest effects were found in sarcopenic participants without osteoarthritis (mean effect: 31.1 kg, 95% CI: 10.3; 52.0).

Osteoarthritis

Participants with osteoarthritis were found to have a significant increase on every study outcome, except for SPPB and lean body mass. Participants without osteoarthritis were found to have a significant increase on every study outcome, except for SPPB. No significant two-way interaction effects were found for osteoarthritis. Relative changes and interaction effects were comparable to absolute changes and interaction effects (supplementary material 3). A nearly significant three-way interaction on leg press strength was found for treatment x sex x osteoarthritis (F=3.047, p-value=0.051), and a significant three-way interaction on leg press strength was found for treatment x osteoarthritis x sarcopenia (F=3.765, p-value=0.026), as described in previous paragraphs.

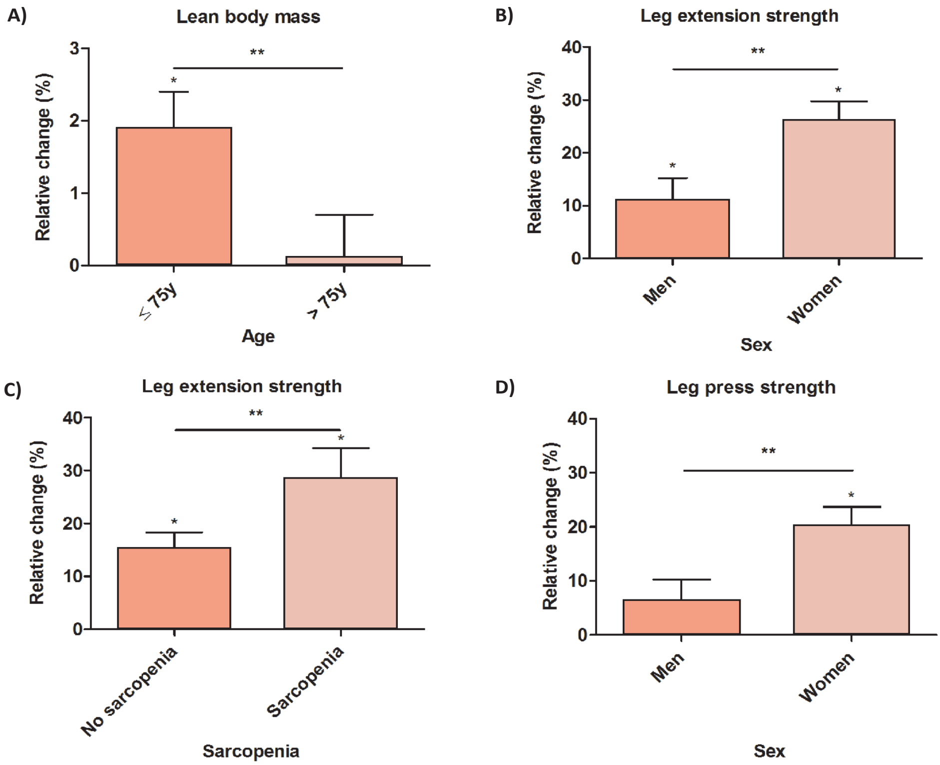

Figure 1. *Significant 2-way interactions for relative changes (compared to baseline, in %) on (A) lean body mass: Treatment × Age, (B) leg extension strength: Treatment × Sex, (C) leg extension strength: Treatment × Sarcopenia, and (D) leg press strength: Treatment × Sex. Relative change is presented as adjusted estimated mean difference between intervention and control group in % and Standard Error. Adjusted for: age, sex, educational level, municipality. *Significant effect in relative change compared to baseline (P < .05). **Significant interaction effect: treatment x subgroup (P < .05).*

DISCUSSION

The question 'Who benefits most from ProMuscle in Practice?' can be answered after performing this in-depth analysis of the effects of the intervention. Participants aged ≤75 years and women benefited to a great extent as they improved significantly on nearly every study outcome. Participants with and without a mobility-impairing disorder benefited equally from the intervention.

The randomized controlled trial was designed to study intervention effects in the total study population. As the current analyses were post-hoc, the sample size was not calculated to detect differences between subgroups. Despite this, we were able to conduct in-depth analyses and report specific intervention effects in subgroups of older adults.

Age

Significant effects were found on every study outcome in participants aged ≤75 years, whereas participants aged >75 years only showed significant effects on strength-related outcomes. Two-way interaction effects (treatment x age) were only significant for lean body mass, favoring participants aged ≤75 years. In general, muscle mass is reported to decrease annually with 1-2% after the age of 50,[109] however, our intervention led to a relative increase in lean body mass, being significantly higher in participants aged ≤75y (+1.9%) compared with participants aged >75y (+0.1%). Two large meta-analyses of randomized controlled trials reported a trend towards higher changes in FFM in younger (±24y) compared to older adults (±65y) in response to RE and PS.[21,31] This might be due to the blunted response of muscle protein synthesis to anabolic stimuli, such as exercise and food intake, that occurs with aging.[166–168] Although other studies compared effects in younger and older adults, we were among the first to compare subgroups of older adults (≥65 years). Available meta-analyses reporting effects in FFM in older groups (>50 years, >65 years, respectively)[21,41] show results that are in line with the increases in lean body mass in our younger group (≤75 years). Hence, it is advised to start early with interventions such as ProMuscle in Practice, to prevent and counteract loss of muscle mass as early as possible.

Sex

In women, significant effects were found on every study outcome except lean body mass. On the contrary, in men, significant effects were only found on lean body mass and leg extension strength. Significant interaction effects including sex were found on leg press strength, favoring women. Additionally, the difference in relative change was found to be significant on leg press as well as leg extension strength, also indicating higher effects in women than in men. The sex-differences cannot be attributed to compliance, as men and women adhered comparably to the intervention. Larger improvements in women might be due to their lower starting point compared with men, indicating more room for improvement. Mechanisms underlying these sex-differences in leg strength changes in older adults are unclear to date and therefore need further investigation.[169] Overall, similar studies show contradictory findings on changes in leg strength when comparing men and women. Retrospective analyses including RE studies in older adults also reported a higher relative change in 1RM in women compared with men,[156] however, no statistically significant interaction with sex was found when assessing absolute effects.[156,157] One meta-analysis reported a significant increase in leg strength in response to RE and PS in older men but not in older women. However, limited studies (n=2) in older women were included.[23] Another meta-analysis reported no sex-differences in leg strength changes in older adults.[49] Differences in results between these meta-analyses and the current study may be attributed to variations in population (older adults living in a nursing home or suffering from diseases vs. community-dwelling older adults), length of the intervention (8 to 36 weeks vs. 12 weeks), type of RE intervention (RE or multi-component exercise training vs. RE), and type and amount of protein intake (supplementation of 3.0 to 40.8 g/day vs. protein intake of 25 g per main meal).[23,49]

Only on lean body mass, significant effects were found in men and not in women. Comparable results were reported in a meta-analysis by Liao et al. (2017).[23] They indicated that sex may influence effects in muscle mass or muscle strength following RE and PS. The smaller changes in lean body mass in women might be due to older women's decreased hypertrophy capacity in response to RE and their impaired ability to increase muscle protein synthesis after protein consumption.[170] However, more research is needed to substantiate this. Conversely, two other meta-analyses found no difference in effects of RE and PS on changes in FFM between sexes.[31,41] Again, the authors point to the fact that far less studies have been conducted in women.[31] Altogether, more research is needed to examine sex-specific effects on lean body mass in response to RE and PS.

Mobility-impairing disorders

Because the study population included older adults with varying health status, tailoring the intervention to the (dis)abilities of the participants was essential.[29] Results demonstrated no significant differences in two-way interactions (regarding absolute effects) between treatment and respectively frailty, sarcopenia, and osteoarthritis. This indicates that both participants with and without mobility-impairing disorders can benefit from the intervention.

Frailty

Participants who were (pre-)frail improved significantly on every study outcome except for SPPB. Other studies also reported that exercise training combined with protein supplementation improved physical functioning, lean body mass, and leg strength in frail older adults.[25,50,51]

Sarcopenia

Our findings indicate that participants with sarcopenia benefit to a great extent from the intervention in terms of leg strength, as they showed a significant increase on leg press and leg extension strength. Additionally, the three-way interaction treatment x osteoarthritis x sarcopenia for the outcome leg press strength was found to be significant, with the largest effects in sarcopenic participants without osteoarthritis. Moreover, when assessing relative changes to baseline, we found a significant difference in effects on leg extension strength between participants with and without sarcopenia. This is in line with results of a recent meta-regression analysis including interventions combining RE and PS, in which significant effects on leg muscle strength were found in older adults at high risk of sarcopenia and frailty.[49] However, opposite to our results, two meta-analyses additionally reported improvements on physical functioning and muscle mass in sarcopenic older adults.[41,49] The fact that we did not find comparable improvements in participants with sarcopenia, may be due to several aspects. First, in this study sarcopenia was defined as probable sarcopenia (based on low handgrip strength), which differed from the definition of sarcopenia in other studies. Second, the small subgroup of participants classified with probable sarcopenia (n=36) likely decreased the power to detect differences between subgroups.

Osteoarthritis

Participants with osteoarthritis improved significantly on chair rise, knee extension, leg press and leg extension strength. To date, few studies have investigated the effect of exercise training and protein supplementation in older adults with osteoarthritis. Nevertheless, a recent meta-analysis reported that exercise training and protein supplementation improved muscle mass, muscle strength, and functional outcomes in older adults with lower-limb osteoarthritis.[52] However, five out of six interventions were post-operative, included participants who underwent total joint replacement, and most interventions consisted of 2 sessions/day for the duration of 2 weeks. Therefore, the populations and interventions included in the meta-analysis are not directly comparable to ProMuscle in Practice. Overall, interventions comprising RE and PS seem promising in improving muscle health in older adults, regardless of the nature of the intervention (preventive or post-operative) but more research is needed in both settings.

Outcome reflections

SPPB score at baseline was relatively high (10.1 out of 12 points). Besides, two thirds of the participants had a SPPB score of 10 points or higher at baseline. This indicates that ceiling effects might have played a role in measuring change in physical performance.[171] Therefore, a mix of outcome measures was included, consisting of chair rise performance, lean body mass and strength-related measures, which were not subject to ceiling effects.

In addition to reporting 'who benefits most' in terms of statistical significance, it is of importance to elaborate on the clinical meaningfulness of the results. Participants aged <75 years and women improved significantly on nearly every outcome, including chair rise performance. Although the definition of a clinically meaningful change for chair rise performance is lacking to date, a definition for SPPB is available.[172,173] Perera et al. (2006) indicated that a 1.0 point change in SPPB could be considered a substantially meaningful change. In their study, a 1.0 point change represented a 12% increase in performance relative to baseline (SPPB: 8.3 ± 2.7).[173] This corresponds with the percentage of change for chair rise performance in participants aged<75 and women in our study (17% and 16% mean change relative to baseline, respectively). Results for strength-related measurements are in line with this. Participants aged <75 years showed mean changes ranging from 11 to 17% relative to baseline. Women showed mean changes ranging from 19 to 26% relative to baseline. Although definitions of clinically meaningful changes remain unclear for many outcomes, based on the aforementioned percentages, our results might be considered clinically meaningful.

CONCLUSION

Specific subgroups benefit to a greater extent from ProMuscle in Practice compared to others. In particular, older adults aged ≤75 years and women exhibited larger increases on various outcomes compared to their counterparts. Additionally, participants with and without mobility-impairing disorders both benefited from ProMuscle in Practice, which suggests that the intervention is suitable for older adults regardless of having a mobility-impairing disorder. More insight is needed in underlying mechanisms to unravel the differences in responsiveness between subgroups.

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CHAPTER 4 - SUPPLEMENTARY MATERIAL

Supplementary table 1. *Exclusion criteria of the ProMuscle in Practice intervention*

Exclusion criteria
Allergy/sensitivity to milk proteins or being lactose intolerant
Diagnosed COPD or cancer
Diagnosed diabetes Type 1 or 2 or hypertension (systolic blood pressure > 160 mmHG) that is unstable or not well regulated with medication
Severe heart failure
Renal insufficiency (eGFR < 30 ml/min)
Physical or cognitive impairment that hinder participation
Receiving terminal care
Not fully recovered from newly fitted artificial hip or knee prosthesis
Recent surgery (<3 months)

Supplementary table 2. *Crude mean differences per study outcome (mean Δ Int – Con) and interaction terms treatment x subgroup for each subgroup separately*

	SPPB (points)			Chair rise (seconds)			Lean body mass (kg)		
	n	**Mean Δ Int – Con (95% CI)**	**Treatment x subgroup β (95% CI)**	**n**	**Mean Δ Int – Con (95% CI)**	**Treatment x sub-group β (95% CI)**	**n**	**Mean Δ Int– Con (95% CI)**	**Treatment x subgroup β (95% CI)**
Total study population	152	0.5 (0.0; 0.9)*		148	-1.6 (-2.6; -0.7)*		150	0.6 (0.2; 0.9)*	
Subgroup									
Age									
Age≤75	84	0.7 (0.0; 1.3)*	-0.4 (-1.4; 0.5)	84	-2.0 (-3.2; -0.7)*	0.8 (-1.2; 2.7)	84	1.0 (0.5; 1.4)*	-0.8 (-1.5; -0.1)‡
Age>75	68	0.3 (-0.5; 1.0)		64	-1.2 (-2.6; 0.3)		66	0.1 (-0.4; 0.6)	
Sex									
Men	63	0.3 (-0.5; 1.0)	0.4 (-0.6; 1.3)	62	-1.0 (-2.5; 0.5)	-1.0 (-3.0; 0.9)	65	0.8 (0.2; 1.3)*	-0.3 (-1.0; 0.4)
Women	89	0.6 (0.0; 1.2)*		86	-2.1 (-3.3; -0.8)*		85	0.5 (0.0; 0.9)	
Frailty state									
Pre-frail, frail	78	0.5 (-0.1; 1.2)	0.1 (-0.8; 1.1)	74	-2.1 (-3.4; -0.7)*	-0.9 (-2.8; 1.0)	74	0.5 (0.1; 1.0)*	-0.1 (-0.8; 0.6)
Non-frail	74	0.4 (-0.3; 1.1)		74	-1.1 (-2.5; 0.2)*		76	0.6 (0.1; 1.1)*	
Sarcopenia									
Sarcopenia	33	0.0 (-1.0; 1.0)	-0.6 (-1.8; 0.5)	31	-0.7 (-2.8; 1.3)	1.2 (-1.1; 3.5)	32	0.4 (-0.3; 1.2)	-0.2 (-1.0; 0.7)
No sarcopenia	114	0.6 (0.1; 1.2)*		112	-1.9 (-3.0; -0.9)*		113	0.6 (0.2; 1.0)*	
Osteoarthritis									
Osteoarthritis	72	0.7 (0.1; 1.4)*	0.5 (-0.5; 1.4)	69	-2.0 (-3.4; -0.6)*	-0.6 (-2.5; 1.3)	69	0.6 (0.0; 1.1)*	-0.1 (-0.8; 0.7)
No osteoarthritis	80	0.3 (-0.4; 0.9)		79	-1.4 (-2.7; -0.2)*		81	0.6 (0.1; 1.1)*	

Supplementary table 2 continued.

	Knee extension strength (Newton)			Leg press strength (kg)			Leg extension strength (kg)		
	n	Mean Δ Int– Con (95% CI)	Treatment x subgroup β (95% CI)	n	Mean Δ Int – Con (95% CI)	Treatment x subgroup β (95% CI)	n	Mean Δ Int – Con (95% CI)	Treatment x subgroup β (95% CI)
Total study population	142	36.6 (18.0; 55.3)*		136	16.5 (9.1; 23.8)*		138	11.5 (7.9; 15.2)*	
Subgroup									
Age									
Age≤75	78	38.6 (13.5; 63.8)*	-6.1 (-43.5; 31.4)	79	12.7 (3.1; 22.3)*	8.5 (-6.4; 23.4)	80	10.1 (5.2; 14.9)*	3.4 (-4.1; 10.9)
Age>75	64	32.6 (4.8; 60.3)*		57	21.2 (9.8; 32.6)*		58	13.5 (7.7; 19.2)*	
Sex									
Men	61	24.9 (-3.8; 53.5)	20.9 (-17.0; 58.8)	61	8.7 (-2.3; 19.6)	14.1 (-0.7; 28.8)	60	7.9 (2.4; 13.5)*	6.2 (-1.2; 13.6)
Women	81	45.8 (21.0; 70.6)*		75	22.7 (12.9; 32.6)*		78	14.1 (9.3; 19.0)*	
Frailty state									
Pre-frail, frail	72	30.0 (3.6; 56.4)*	-12.6 (-50.2; 25.0)	72	19.4 (9.1; 29.6)*	6.4 (-8.5; 21.2)	72	13.2 (8.0; 18.4)*	3.0 (-4.4; 10.5)
Non-frail	70	42.6 (15.8; 69.3)*		64	13.0 (2.2; 23.7)*		66	10.1 (4.8; 15.5)*	
Sarcopenia									
Sarcopenia	30	21.6 (-19.4; 62.6)	-16.7 (-63.0; 29.7)	29	23.6 (7.8; 39.5)*	9.8 (-8.1; 27.8)	29	16.4 (8.4; 24.3)*	6.9 (-2.1; 15.9)
No sarcopenia	108	38.2 (16.7; 59.8)*		103	13.8 (5.4; 22.2)*		104	9.5 (5.3; 13.7)*	
Osteoarthritis									
Osteoarthritis	67	41.6 (14.4; 68.8)*	8.6 (-28.8; 46.0)	60	16.0 (4.8; 27.2)*	-0.7 (-15.7; 14.3)	63	9.9 (4.4; 15.4)*	-3.0 (-10.4; 4.4)
No osteoarthritis	75	33.0 (7.3; 58.6)*		76	16.7 (6.8; 26.7)*		75	12.9 (7.9; 17.9)*	

Supplementary table 3. *Adjusted mean differences of relative changes (compared to baseline, in %) per study outcome (mean Δ Int – Con) and interaction terms treatment x subgroup for each subgroup separately.*

	SPPB (points)			Chair rise (seconds)			Lean body mass (kg)		
	n	Mean Δ Int – Con (95% CI)	Treatment x subgroup β (95% CI)	n	Mean Δ Int – Con (95% CI)	Treatment x sub-group β (95% CI)	n	Mean Δ Int– Con (95% CI)	Treatment x subgroup β (95% CI)
Total study population	152	5.9 (0.5; 11.3)*		148	-12.8 (-20.4; -5.3)*		150	1.1 (0.3; 1.9)*	
Subgroup									
Age									
Age≤75	84	6.5 (-0.8; 13.7)	-1.3 (-12.0; 9.4)	84	-16.5 (-26.4; -6.5)*	8.3 (-6.6; 23.2)	84	1.9 (0.9; 2.9)*	-1.8 (-3.3; -0.3)‡
Age>75	68	5.2 (-2.8; 13.1)		64	-8.2 (-19.4; 3.1)		66	0.1 (-1.0; 1.2)	
Sex									
Men	63	2.7 (-5.7; 11.1)	5.3 (-5.4; 16.1)	62	-9.0 (-20.6; 2.6)	-6.5 (-21.5; 8.5)	65	1.4 (0.2; 2.5)*	-0.5 (-2.0; 1.0)
Women	89	8.0 (1.1; 15.0)*		86	-15.5 (-25.2; 5.8)*		85	0.9 (-0.1; 1.9)	
Frailty state									
Pre-frail, frail	78	5.5 (-1.9; 12.9)	-0.5 (-11.3; 10.4)	74	-15.3 (-25.7; -4.8)*	-5.3 (-20.4; 9.8)	76	1.0 (0.0; 2.1)	-0.1 (-1.6; 1.4)
Non-frail	74	5.9 (-2.0; 13.9)		74	-10.0 (-20.8; 0.9)		74	1.2 (0.1; 2.3)*	
Sarcopenia									
Sarcopenia	33	-0.6 (-12.1; 10.9)	-8.6 (-21.6; 4.4)	31	-7.5 (-23.4; 8.4)	6.7 (-11.2; 24.5)	32	0.6 (-1.0; 2.2)	-0.5 (-2.3; 1.3)
No sarcopenia	114	8.0 (1.8; 14.2)*		112	-14.2 (-22.6; -5.8)*		113	1.1 (0.3; 2.0)*	
Osteoarthritis									
Osteoarthritis	72	8.1 (0.1; 16.2)*	4.1 (-6.8; 15.0)	69	-13.7 (-24.8; -2.6)*	-1.1 (-16.1; 13.8)	69	1.2 (0.0; 2.3)*	0.1 (-1.4; 1.7)
No osteoarthritis	80	4.0 (-3.4; 11.4)		79	-12.6 (-22.6; -2.6)*		81	1.0 (0.0; 2.0)*	

***Supplementary table 3** continued.*

	Knee extension strength (Newton)			Leg press strength (kg)			Leg extension strength (kg)		
	n	Mean Δ Int– Con (95% CI)	Treatment x subgroup β (95% CI)	n	Mean Δ Int – Con (95% CI)	Treatment x subgroup β (95% CI)	n	Mean Δ Int – Con (95% CI)	Treatment x subgroup β (95% CI)
Total study population	142	14.1 (7.2; 21.1)*		136	14.0 (8.5; 19.6)*		138	19.5 (13.8; 25.2)*	
Subgroup									
Age									
Age≤75	78	15.4 (6.0; 24.8)*	-2.8 (-16.7; 11.0)	79	10.6 (3.4; 17.8)*	8.1 (-2.9; 19.1)	80	17.3 (9.8; 24.8)*	5.3 (-6.1; 16.7)
Age>75	64	12.6 (2.4; 22.8)*		57	18.7 (10.3; 27.2)*		58	22.6 (13.9; 31.3)*	
Sex									
Men	61	7.7 (-2.8; 18.2)	11.1 (-2.7; 24.8)	61	6.2 (-1.9; 14.3)	13.9 (3.1; 24.7)‡	60	10.9 (2.4; 19.3)*	15.2 (4.0; 26.4)‡
Women	81	18.8 (9.8; 27.8)*		75	20.1 (12.9; 27.3)*		78	26.0 (18.7; 33.4)*	
Frailty state									
Pre-frail, frail	72	12.5 (2.9; 22.2)*	-3.6 (-17.7; 10.5)	72	18.1 (10.6; 25.7)*	9.0 (-2.2; 20.1)	72	23.8 (16.1; 31.5)*	7.9 (-3.5; 19.3)
Non-frail	70	16.2 (6.0; 26.3)*		64	9.2 (1.0; 17.4)*		66	15.9 (7.6; 24.2)*	
Sarcopenia									
Sarcopenia	30	9.4 (-5.7; 24.4)	-4.9 (-21.8; 12.0)	29	21.8 (10.0; 33.6)*	10.3 (-3.0; 23.7)	29	28.4 (17.0; 39.9)*	13.2 (0.4; 26.1)‡
No sarcopenia	108	14.3 (6.3; 22.3)*		103	11.5 (5.2; 17.8)*		104	15.2 (9.2; 21.2)*	
Osteoarthritis									
Osteoarthritis	67	21.3 (11.3; 31.3)*	13.1 (-0.5; 26.7)	60	15.7 (7.0; 24.3)*	2.9 (-8.6; 14.3)	63	21.2 (12.5; 29.9)*	3.0(-8.7; 14.7)
No osteoarthritis	75	8.2 (-1.0; 17.4)		76	12.8 (5.4; 20.2)*		75	18.2 (10.5; 26.0)*	

*Note: Int = Intervention group; Con = Control group. Adjusted estimated mean differences of relative changes (compared to baseline, in %) between intervention and control group and 95% CIs are shown per subgroup; β-coefficients and 95% CIs are shown for the treatment x subgroup interaction. Adjusted for: age, sex, educational level, municipality. Treatment: control group is reference. Subgroup: reference groups are respectively men; age ≤75; non-frail; no sarcopenia; no osteoarthritis. *Significant effect between intervention and control group ($P < .05$). ‡Significant interaction effect: treatment x subgroup ($P < .05$)*

5

Effects and contextual factors of a diet and resistance exercise intervention vary across settings: an overview of three successive ProMuscle interventions

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ABSTRACT

Background: Although many effective interventions have been developed, limited interventions have successfully been implemented. An intervention that was translated across settings is ProMuscle: a diet and resistance exercise intervention for older adults. However, varying contexts often lead to varying effects. The current study aimed to gain insights into effects and contextual factors of ProMuscle in the controlled setting (ProMuscle: PM), real-life setting (ProMuscle in Practice: PiP), and real-life setting of the implementation pilots (ProMuscle Implementation Pilots: IP).

Methods: Data from the intervention arms of PM (n=31) and PiP (n=82), and from IP (n=35) were used. Physical functioning (chair-rise test) and leg strength (1-10 repetition maximum) were measured at baseline and after 12-weeks intervention. Paired t-tests and General Linear Models were used to study changes after 12 weeks and differences between interventions. To explore contextual factors, researchers of PM and physiotherapists and dietitians of PiP and IP were interviewed. Factors were categorized according to the five domains and its underlying constructs of the Consolidated Framework for Implementation Research (CFIR).

Results: Improvements on chair-rise performance were found in PM (-2.0 ± 7.0 sec, p=0.186), PiP (-0.8 ± 2.9 sec, p=0.019) and IP (-3.3 ± 4.2 sec, p=0.001). Similar results were found for leg strength in PM (32.6 ± 24.8 kg, p<0.001), PiP (17.0 ± 23.2 kg, p<0.001), and IP (47.8 ± 46.8 kg, p<0.001). Probable explanations of the strongest effects in IP included room for adapting and tailoring the intervention, involvement of experienced professionals, availability of and access to facilities, and participants characteristics.

Conclusions: Effects of the intervention appeared to be strongest in the real-life setting of the implementation pilots. Specific contextual factors contributed to explaining the different findings across settings. Future studies should investigate crucial factors that determine successful implementation of interventions in the real-life setting, to ensure that effective interventions are put into action and reach a broad population.

INTRODUCTION

Although many lifestyle interventions are being developed and achieve promising effects in clinical settings, only few interventions are in the end successfully implemented and disseminated in the real-life setting.[174] In particular, implementing a project that modifies the common way of working in an organization has been estimated to fail about 65% of the times.[70,175] The process of transforming basic research into a widely implemented intervention is often complex, time consuming, and expensive.[71,176]

Besides, it is common to find effects fading away or differing across settings, especially when an intervention is implemented in the real-life setting.[33] The varying effects can be due to the influence of context in the different settings.[32] Context can be defined as "a set of characteristics and circumstances that consist of active and unique factors, within which the implementation is embedded".[32] The Consolidated Framework For Implementation Research (CFIR) can be used to investigate which form of intervention works where and why across various settings.[70] CFIR includes five major domains: intervention characteristics, outer setting, inner setting, characteristics of the individuals involved, and the process of implementation. These domains are subdivided into constructs. For example, the domain 'inner setting', referring to the organisation in which the intervention is being conducted, can be subdivided into the constructs: structural characteristics of the organisation, networks and communications, culture, implementation climate, and readiness for implementation. Different sets of constructs interact with interventions when conducting the program in a controlled setting compared to implementing the program in a practice setting. When taking the inner setting as an example, structural characteristics of an organisation may play a role in the controlled setting, whereas readiness for implementation is expected to be more important in the practice setting. The CFIR domains and their constructs can help unravel which factors play a role in a specific setting and can help explain intervention effects in the different settings.[70]

As a large part of effective treatments and interventions is not yet available to a wide population, it is essential to study implementation of health promotion interventions.[174,177] This is particularly of great importance for older adults, as the ageing population is expected to grow even more in the coming decades.[10,155] Health promotion programs can contribute to the prevention of the negative consequences of ageing, such as development of diseases or decline in functioning.[177] An intervention that aimed to counteract functional decline in older adults is the ProMuscle program, consisting of resistance exercise and protein supplementation.[25] During the past decade, the program has moved through a translation process from basic and efficacy research towards implementation. Starting with testing the efficacy of the combination of nutrition and exercise in improving muscle health (ProMuscle),[25,82] followed by designing and evaluating an intervention in the real-life setting (ProMuscle in Practice),[26–28] and currently exploring the possibilities of implementing the intervention in multiple organisations and populations (ProMuscle Implementation Pilots). The basic elements, progressive resistance exercise and increased protein intake, were retained in every intervention. However, the adaptable content of the intervention, the role of involved professionals, and the influence of other contextual factors impacting the intervention effects are expected to vary across settings.

Therefore, the aim of this study was to explore contextual factors that can help to explain the potential differences in effects of the three successive ProMuscle interventions across settings.

METHODS

This paper includes data from three versions of the ProMuscle intervention: ProMuscle (clinical setting), ProMuscle in Practice (real-life setting), and the ProMuscle Implementation Pilots (real-life setting of the implementation pilots). An extensive description of the study design, study population, and intervention of ProMuscle and ProMuscle in Practice can be found elsewhere.[25,27] In short, methods for each program are described below.

Study design and setting

ProMuscle (PM) was a randomized, double-blind, placebo-controlled trial with 2 arms in parallel. Participants were randomly allocated to the intervention or control group, stratified by sex. Both groups were included in a 24-week resistance exercise program. The intervention group received protein supplementation, whereas the control group received placebo supplementation. The intervention was delivered by researchers at a university in the Netherlands, in a room equipped as gym location.

ProMuscle in Practice (PiP) was a randomized controlled multicentre intervention study, implemented at five Dutch municipalities. Participants were randomly allocated to the intervention or control group, stratified by sex and frailty state. The program focused on resistance exercise and increasing dietary protein intake, implemented by physiotherapists and dietitians. Participants of the intervention group started with an intensive support intervention (week 1-12), followed by a moderate support program (week 13-24). The control group received no intervention.

ProMuscle Implementation Pilots (IP) were two case studies, including only an intervention group (pre-test post-test). The IP were implemented by physiotherapists and dietitians at two separate physiotherapist and dietitian practices in two Dutch municipalities. The 12-week program included progressive resistance exercise and a nutrition program, consisting of individual consultations and group meetings.

In the current paper, we included the intervention groups of the first 12-week intervention period of PM, PiP, and IP.

Study population

ProMuscle – Older adults were recruited from an existing database, via distribution of flyers and by organising local information meetings. PM included older adults (≥65 years) who were prefrail or frail according to the Fried criteria,[153] after checking medical history and exclusion criteria (described in detail elsewhere[25]). The Wageningen University Medical Ethical Committee approved the study and participants gave their written informed consent.

ProMuscle in Practice – Older adults were recruited mainly through local media. PiP included older adults (≥65 years) being prefrail or frail according to the Fried criteria,[153] or being non frail but experiencing difficulties in daily activities and being inactive (defined as not participating in resistance exercise >30 minutes a day on more than 2 days a week). Exclusion criteria were checked by the older adults' general practitioner (GP), including renal functioning (eGFR) (described in detail elsewhere[28]). The study protocol was approved by the Wageningen University Medical Ethics Committee and included participants provided written informed consent before participation.

ProMuscle Implementation Pilots – Older adults were recruited through local media, and word of mouth by the physiotherapist, or were referred by the practice assistant of the GP. The IP included older adults (≥65 years) who were either deemed suitable by the physiotherapist or who were referred by the practice assistant of the GP (with one of the following reasons: improving muscle strength; insight in and improving intake of protein; recovery after inactive period). Medical status and renal functioning (eGFR) were checked in collaboration with the GP, before starting the intervention. No medical ethical approval was needed as this research did not fall within the remit of the Dutch 'Medical Research Involving Human Subjects Act' (in Dutch: WMO). Participants provided informed consent before participation.

Intervention

The content of the PM, PiP and IP interventions is described in table 1, subdivided into the exercise program (table 1A) and the nutrition program (table 1B). In short, the basic elements of the intervention, providing RE training sessions and increasing dietary protein intake, were present in each intervention. Differences across exercise programs are related to location, type of guidance, and structure of the training sessions. Differences across the nutrition programs are related to type and frequency of guidance and protein product.

Table 1A. *Intervention description: Content of exercise program (12 weeks) in the various ProMuscle interventions.*

	ProMuscle	ProMuscle in Practice	ProMuscle Implementation Pilots
Setting	Training at university in room equipped as gym location for the trial.	Training at local care organization in room equipped as gym location for the trial (in neighbourhood of older adults).	Training at training room of the local physiotherapist practice (in neighbourhood of older adults).
Frequency	Two times per week for one hour.	Two times per week for one hour.	Two times per week for one hour.
Intake	No intake consultation. Medical assessment was performed during inclusion.	No intake consultation. Before the start of the program, physiotherapists received participants' medical and baseline strength-related measures from researchers.	Individual intake consultation with physiotherapist, to assess training level, potential injuries, and medical status.
Supervision	Researcher assisted by trained students. One trainer per two participants. 5-6 participants per group.	Physiotherapists and their assistants. Two to three trainers per group. 4-7 participants per group.	Physiotherapists and their assistants. One trainer per group. First 2-3 weeks: two trainers. 5-8 participants per group.
Type of guidance	Researcher organized individual training schedules; individual guidance during exercise performance.	Physiotherapists organized training sessions according to detailed training protocol. Tailored the training intensity when necessary (e.g. in case of an injury).	Physiotherapists used the protocol as a guideline for creating a training schedule and tailored the training intensity to individuals' capabilities and limitations.
Training session structure	Warming-up; progressive resistance exercises on leg press, leg extension, chest press, lat pulldown, pec deck, and vertical row machines; warm-down. Focus on main muscle groups.	Warming-up; progressive resistance exercises on leg press, leg extension, chest press, lat pulldown, and vertical row; warm-down. Focus on main muscle groups.	Dependent on training location, including: Warming-up; progressive resistance exercises on leg press, leg extension, back extension, pull down, cable row, chest press; warm-down. Focus on main muscle groups. Tailored to individual needs: cardio exercises (bike, treadmill, cross trainer), squats with free weights.
Workload	Started at 3-4 sets of 10-15 repetitions (50% of 1-RM) and increased toward 3-4 sets of 8-10 repetitions (75% of 1-RM).	Leg exercises: started with 3-4 sets of 15 repetitions (50% of 1-RM) and increased toward 4 sets of 8 to 12 repetitions (75%-80% of 1-RM). Other exercises: According to insights of physiotherapist. Adjustments made e.g., in case of injury.	Leg exercises: Started with 3-4 sets of 15 repetitions (50% of 1-RM) and increased toward 4 sets of 8 to 12 repetitions (75%-80% of 1-RM) (location 1). Building up intensity according to own insights and based on 3-RM measurement on leg press and leg extension, intensity was on average increased with 5% per weight increase (location 2). Other exercises: According to insights of physiotherapist. Adjustments made e.g., in case of injury.

Table 1B. *Intervention description: Content of nutrition program (12 weeks) in the various ProMuscle interventions.*

	ProMuscle	ProMuscle in Practice	ProMuscle Implementation Pilots
Type and frequency of guidance	Short explanation on protein drinks at start of intervention by research dietitian (no consultation).	Individual consultations with dietitian; before intervention, after 6 weeks, and additional phone consultation when needed.	Individual consultations with dietitian; at the start of the intervention, in week 2 or 3, and at the end of the intervention and additional consultations when needed. One group meeting at the end (location 1). One individual consultation with dietitian at the start, three group meetings (location 2).
Type and frequency of protein product	Provision of 250mL protein supplemented beverage containing 15 g protein. One drink directly after breakfast, one drink directly after lunch.	Provision of range of free protein-rich products, such as dairy drinks, cheese, or yoghurt. Tailored to individual needs and preferences. Protein-rich products were mainly consumed during breakfast and lunch, aimed at reaching consumption of 25g protein per main meal.	No provision of supplements or products. Advise was focused on animal-based as well as protein-based protein. Tailored to individual needs and preferences. Aimed at 20-25g protein per main meal.

Quantitative measures

Baseline characteristics – Questionnaires were used to collect baseline characteristics including age and sex. Body weight was measured to the nearest 0.1 kg using a digital scale, and height was measured to the nearest 0.1 cm using a stadiometer.

For this study, we included measures that were collected in all three intervention groups at baseline and after 12 weeks of intervention: chair-rise test and leg muscle strength.

Chair-rise test - Physical performance was measured by the chair-rise test.[163] The measurement was performed according to a standardized protocol. In PM and PiP, measurements were conducted by trained researchers and their assistants. In IP, measurements were conducted by researcher-instructed physiotherapists.

Leg muscle strength - In PM, researchers performed 1 Repetition Maximum (1-RM) strength tests on leg press machines. In PiP, researchers measured muscle strength through 3-RM tests at leg press machines. In both PM and PiP, measurements were performed according to a standardized protocol. In IP, physiotherapists measured muscle strength through 3-RM at leg press machines according to protocol. In some case in PiP, and more often in IP, more repetitions were used, if necessary (up to 10-RM), to align with older adults' physical capacities. The RM scores were recalculated to 1-RM, based on the formula of Brzycki.[165]

Qualitative measures

Semi-structured interviews were conducted to collect information regarding process indicators and in particular contextual factors that could influence intervention outcomes and intervention implementation. A PhD-level researcher and a MSc-level researcher conducted a face-to-face semi-structured interview with the main researcher and a research-assistant who delivered PM.[26] A MSc-level researcher conducted semi-structured interviews via telephone with 18 physiotherapists and 8 dietitians involved in the first 12 weeks of PiP [29]. Interview questions were based on pretested interview guides.[26] A MSc-level researcher conducted semi-structured interviews via video calling with two physiotherapists and one dietitian involved in IP. Interview questions were based on interview guides from PiP and were supplemented with questions on contextual factors.

Statistical analyses

Baseline data were expressed as means with standard deviations or as percentages. Baseline differences between treatment groups were analysed using one-way ANOVA for continuous data, and Pearson's chi-squared tests for categorical data. Paired samples t-tests were used to analyse changes between the pre-test and post-test measurements (baseline vs. week 12) for each of the interventions separately. Differences in effects between the three interventions were analysed using General Linear Models. Data of complete cases (measurement at baseline and week 12) were included. Data was analysed using SPSS version 23 (IBM Corp., Armonk, NY). Statistical significance was indicated with p-value<0.05.

Qualitative data were analysed in Atlas.ti, version 9. Interviews were taped, transcribed verbatim, and transcripts from the interviews were analysed and coded. Results were classified according to relevant constructs of the five domains of CFIR. Constructs that were highlighted in the interviews were selected and included in the classification.[70]

RESULTS

Baseline characteristics

Table 2 presents the baseline characteristics of participants for each program separately. No baseline differences were found between the three settings, except for sex. PiP and IP comprised more female participants compared to PM.

Table 2. *Baseline characteristics of intervention group participants from ProMuscle (PM), ProMuscle in Practice (PiP), and the ProMuscle Implementation Pilots (IP).*

	ProMuscle	ProMuscle in Practice	ProMuscle Implementation Pilots
	n=31	n=82	n=35
Age (years)	77.7 ± 8.8	74.7 ± 5.8	75.0 ± 6.5
Sex (n female, %)	11 (36%)	51 (62%)	28 (80%)
Bodyweight (kg)	79.5 ± 15.8	76.1 ± 14.4	75.4 ± 12.8*
Height (m)	1.67 ± 0.1*	1.68 ± 0.1	1.67 ± 0.1§
BMI (kg/m2)	28.6 ± 4.6*	27.1 ± 4.8	27.3 ± 3.9§

*Note: Data is presented as means ± SD or n (%). BMI = Body Mass Index. *n=30; §n=22*

Effects in ProMuscle, ProMuscle in Practice, and the ProMuscle Implementation Pilots

The effects on chair-rise test (seconds) and leg press strength (kg) were investigated in the total study population and in the intervention group of each program separately (table 3A and 3B, Figure 1). No baseline differences on chair-rise test and leg press strength were found between the three settings.

Table 3A. *Results of chair-rise test (seconds) after 12 weeks in the intervention group of ProMuscle, ProMuscle in Practice and the ProMuscle Implementation Pilots.*

	Complete cases	Wk 0 Mean ± SD	Wk 12 Mean ± SD	Mean difference ± SD	p-value
Total	n=121	14.5 ± 4.9	13.0 ± 4.4	-1.6 ± 4.3	P<0.001
ProMuscle	n=23	16.2 ± 7.6	14.2 ± 6.3	-2.0 ± 7.0	P=0.186
ProMuscle in Practice	n=73	13.8 ± 3.4	13.0 ± 3.4	-0.8 ± 2.9	P=0.019
ProMuscle Implementation Pilots	n=25	14.8 ± 5.2	11.5 ± 4.9	-3.3 ± 4.2	P=0.001

Chair-rise test

An improvement on chair-rise performance was found in the total study population as well as in each intervention group separately, with the highest increase in IP (-3.3 ± 4.2 seconds, p=0.001). Figure 1A shows that the mean change in IP was significantly higher compared to the mean change in PiP.

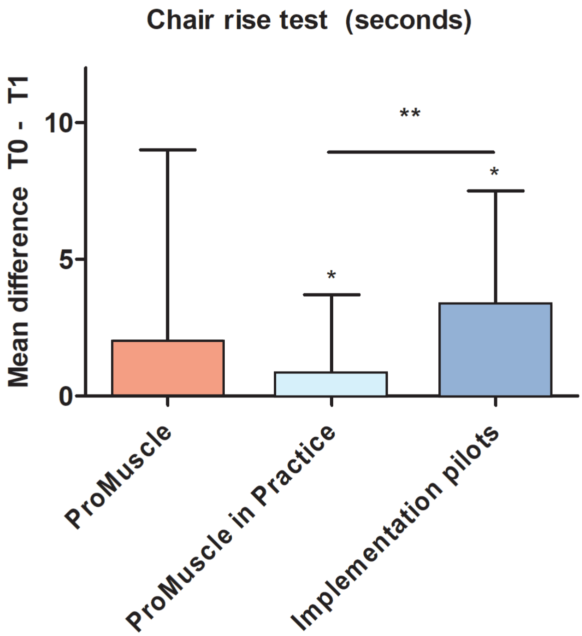
Leg press strength

An improvement on leg press strength was found in the total study population and in each intervention group, with the largest change in IP (47.8 ± 46.8 kg, p<0.001). Figure 1B shows that the mean change in IP was significantly higher compared to the mean change in PiP.

Table 3B. *Results of leg press strength (kg) after 12 weeks in the intervention group of ProMuscle, ProMuscle in Practice and the ProMuscle Implementation Pilots.*

	Complete cases	Wk 0 Mean ± SD	Wk 12 Mean ± SD	Mean difference ± SD	p-value
Total	n=123	129.1 ± 34.7	157.7 ± 45.7	28.6 ± 34.0	P<0.001
ProMuscle	n=26	127.3 ± 29.2	159.9 ± 38.8	32.6 ± 24.8	P<0.001
ProMuscle in Practice	n=64	134.6 ± 38.3	151.6 ± 40.3	17.0 ± 23.2	P<0.001
ProMuscle Implementation Pilots	n=33	119.9 ± 29.5	167.6 ± 58.2	47.8 ± 46.8	P<0.001

A)



B)

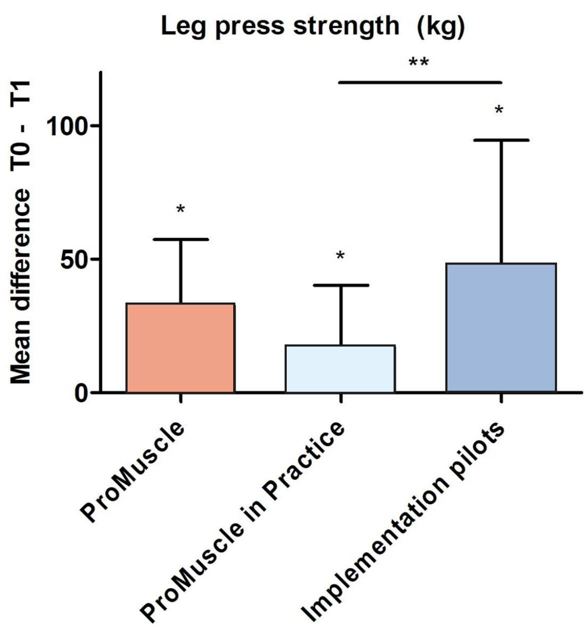


Figure 1. *Effects after 12 weeks in chair-rise performance (A) and leg press strength (B) for each of the interventions separately. *Statistically significant effect after 12 weeks (p<0.05). **Statistically significant difference between two interventions (p<0.05).*

Contextual factors in ProMuscle, ProMuscle in Practice, and the ProMuscle Implementation Pilots

Contextual factors related to the PM, PiP and IP interventions are categorized according to relevant constructs of the CFIR domains: intervention characteristics (Table 4A), inner setting and outer setting (Table 4B), characteristics of individuals (Table 4C) and process (Table 4D). Under each table, similarities and differences between interventions are summarized.

Intervention characteristics

An extensive description of the exercise and nutrition program for each intervention separately can be found in Table 1A and B.

Similarities

Exercise program – All interventions conducted RE training based on a training protocol two times per week, used training machines, and focused on the main muscle groups.

Nutrition program – All interventions focused on increasing protein intake during the main meals.

Differences

Exercise program – Physiotherapists in IP included individual intake consultations, whereas the other two interventions did not.

Nutrition program – During PM, protein supplemented beverages were provided for free. During PiP, a range of protein-rich products were provided for free. During IP, no food products were provided.

Adaptability – Training sessions in the PM program were conducted according to strict guidelines, whereas the training intensity was adjusted when necessary in PiP and IP. The latter program also offered additional exercises based on capabilities of participants. PM included no nutritional consultations. PiP included two individual consultations with a dietitian and offered optional additional phone contact. IP included a combination of group-based meetings and individual consultations with a dietitian and offered optional additional individual consultations.

Complexity – During PM, researchers conducted the intervention in a controlled setting and were not dependent on collaborations with external parties. In PiP, professionals were dependent on external parties for receiving materials and baseline data, causing delays in the training schedule of some participants. In IP, professionals are project leader of the intervention implementation, and therefore less dependent on others.

Cost – In PM and PiP, older adults could participate for free, whereas in IP, participants had to pay a monthly fee. In PM and IP professionals could conduct the program within their regular working hours, whereas some professionals in PiP could not (also due to the temporary character of the project).

Table 4A. *Intervention characteristics of the three interventions: ProMuscle, ProMuscle in Practice and the ProMuscle Implementation Pilots.*

Intervention characteristics

An extensive description of the PM, PiP, and IP interventions was provided in Table 1A (exercise program) and Table 1B (nutrition program). Under this table, similarities and differences between the interventions were indicated separately for the exercise and the nutrition program.

	ProMuscle	ProMuscle in Practice	ProMuscle Implementation Pilots
Adaptability	*Exercise* Strict guidelines implemented by researchers. Participants conducted training sessions according to protocol. *Nutrition* Participants received standard product for protein supplementation.	*Exercise* Most physiotherapists adhered to the training protocol, adjusting when necessary (intensity too high/too low). Participants and professionals indicated they would have liked more variation in type of exercises. Older adults could indicate their preference for a timeslot of the training sessions. *Nutrition* Number of consultations with dietitian was set. Dietitian provided individual advice, based on three-day food diary and preferences of participants, primarily including protein-rich products that were distributed for free. Participants mentioned they would like more variation in products, and that advice was hard to adhere to (25g per main meal). Consultations were scheduled together with participant.	*Exercise* Physiotherapists personalized the training intensity, based on the training protocol and adjusting when necessary (intensity too high/too low). Additional exercises were added based on capabilities of participants. Training sessions were scheduled considering daily activities of older adults. *Nutrition* Number of consultations with dietitian was personalized (minimum of three, more if needed). Dietitians provided individual advice, based on 24hr recall and preferences of participants, also included plant-based protein. Dietary protein intake around training sessions was emphasized in advice. Dietitian realized 25g protein per main meal might be hard to achieve and maintain on the long term, therefore she focused on 20-25g protein per main meal. Consultations were scheduled together with participant. Group-based meetings were scheduled prior to training sessions, to facilitate participation.

Table 4A *continued.*

Intervention characteristics

An extensive description of the PM, PiP, and IP interventions was provided in Table 1A (exercise program) and Table 1B (nutrition program). Under this table, similarities and differences between the interventions were indicated separately for the exercise and the nutrition program.

	ProMuscle	ProMuscle in Practice	ProMuscle Implementation Pilots
Complexity	Duration of total intervention was 6 months. In this study, focus is on first 3 months. No implementation of intervention.	Duration of total intervention was 6 months. In this study, focus is on first 3 months. Logistics at the start and during the program were sometimes constraining. Professionals were dependent on others for: receiving/repairing fitness machines and weights, receiving information on medical background and baseline food intake of participants, and provision of protein rich products. This led to delays, and some participants trained on a lowered intensity because of this.	Duration of total intervention was 3 months; dietitian indicated this as a manageable period for participants. Professionals are project leader of their own intervention implementation, and therefore less dependent on others.
Cost	Research was subsidized. Older adults could participate in the program for free. Researchers could conduct the program within their regular working hours.	Research was subsidized. Older adults could participate in the program for free (first 12 weeks). Most professionals could conduct the program within their regular working hours.	Research was not subsidized. Older adults could participate in the program for 70 euros per month (for training sessions with physiotherapist). Professionals indicated that this might lead to a selected group of participants, who can afford it. Consultations with the dietitian were reimbursed from the basic health insurance. Professionals could conduct the program within their regular working hours, and could cover the costs of the program using the participation contribution (physiotherapists) or the reimbursement from the health insurance (dietitians).

Outer and inner setting

Similarities

Inner setting: Readiness for implementation – Professionals who conducted the intervention had access to materials such as guidelines and training protocols.

Differences

Outer setting: External collaborations and policies – There were no external collaborations during PM. During PiP, researchers collaborated with the municipal health service, sport facilities, care facilities and health care professionals. During IP, professionals collaborated with the GP and medical practice assistant of GP, municipalities, the municipal health service, and professionals of other physiotherapist practices.

Inner setting: Structural characteristics of organization – PM was conducted in the university, PiP in a care institution, and IP in physiotherapist and dietitian practices.

Inner setting: Networks & communications – There were no relevant communications during the PM program. During PiP, communications between physiotherapists and dietitians could have been improved in some cases. During IP, communications between physiotherapists and dietitians went well.

Inner setting: Implementation climate – Implementation was not a goal of PM. During the PiP program, some dietitians experienced too little time to conduct the program. During IP, conducting the program fell within regular working hours of professionals.

Inner setting: Readiness for implementation – During the PiP program, some training rooms were not suitable (noisy, not clean, or small) and issues with training machines occurred. During IP, a spacious and safe training room with training machines was available. During the PiP program, some professionals received participant's baseline and medical data too late, causing delays or restrictions in the intervention. During IP, professionals conducted baseline measurements themselves and received medical data directly from the GP or the participants.

Table 4B. *The outer and inner setting of the three interventions: ProMuscle, ProMuscle in Practice and the ProMuscle Implementation Pilots.*

	Outer setting		
	ProMuscle	**ProMuscle in Practice**	**ProMuscle Implementation Pilots**
External collaborations (cosmopolitanism) and policies	No collaboration with external parties.	Collaboration with care facilities led to involvement of professionals and availability of local facilities (i.e., training rooms). Health care professionals in the intensive support intervention were not always aware of the content of the moderate support program, limiting the transition.	Collaboration with GP and medical practice assistant of GP facilitated recruitment and screening of participants. Collaboration with municipality facilitated subsidy for one group of participants. Collaboration with municipal health service led to the establishment of an implementation network overarching both municipalities.
	Inner setting		
	ProMuscle	**ProMuscle in Practice**	**ProMuscle Implementation Pilots**
Structural characteristics of organization	Intervention was conducted in the university (controlled setting).	Intervention was conducted in care institution, within the municipality where participants live (real-life setting).	Intervention was conducted in physiotherapist practices and dietitian practices within the municipality where participants live (real-life setting of the implementation pilots).
Networks & communications	Researchers conducted the intervention completely; no further relevant communications in the inner setting.	Overall, communication among physiotherapists or among dietitians went well. Communication between physiotherapists and dietitians could be improved in some cases.	Communication among physiotherapists or among dietitians went well. Communications between physiotherapists and dietitians went well. Communication between physiotherapists and dietitians of different practices was facilitated during project meetings and included sharing experiences and best practices.

***Table 4B** continued.*

	Outer setting		
	ProMuscle	**ProMuscle in Practice**	**ProMuscle Implementation Pilots**
Implementation climate	The study was performed to investigate efficacy of the intervention, and implementation was not part of the study aims.	Most of the professionals chose to be involved in the intervention and enjoyed facilitating it. Most of the professionals received enough working hours to conduct the intervention, although some dietitians experienced too little time to conduct the program.	Professionals chose to be involved in the intervention and enjoyed facilitating it. Conducting the program fell within their regular working hours.
Readiness for implementation	The study was performed to investigate efficacy of the intervention, and implementation was not part of the study aims.	Conducting the program fitted regular working procedures of professionals. However, the intervention was implemented in secondary care, while it would fit better within primary care or public health, based on the target population and professionals involved. In some cases, the training room was not suitable (noisy, not clean, small), and issues with training machines occurred (delay in delivery and repairments). Professionals could use materials such as guidelines, training protocols, calendars (protein intake) and registration lists. Professionals indicated they received participants' baseline data and medical information too late from researchers, preventing them from tailoring the training intensity at the start of the program or causing a delay in providing the dietary advice.	Conducting the program fitted regular working procedures of professionals. Available facilities included a spacious, safe environment for training sessions with training machines, and a room for consultations with the dietitian. Professionals could use materials such as information brochures, recruitment flyers, guidelines, training protocols, registration lists, and workshop materials for the nutrition course. In one of the municipalities a network with the medical practice assistant of GP was created to facilitate continuous recruitment of participants.

Characteristics of individuals

Similarities

Professionals – Researchers or professionals involved were skilled and motivated to conduct the intervention.

Participants – Participants joined the program voluntarily and were motivated.

Differences

Professionals – Researchers or professionals involved in PM and PiP, conducted the intervention for the first time. Most of the professionals involved in IP were experienced in conducting the intervention, as they already conducted the program several times.

Participants – Professionals of PM, PiP and especially of IP indicated that the social aspect of the training sessions was very important to participants.

Table 4C. *Characteristics of individuals of the three interventions: ProMuscle, ProMuscle in Practice and the ProMuscle Implementation Pilots.*

Characteristics of individuals	ProMuscle	ProMuscle in Practice	ProMuscle Implementation Pilots
Professionals	Researchers were skilled, committed, and motivated to conduct the intervention. Professionals conducted the program for the first time.	Professionals had knowledge on the main components of the program, were experienced in working with the target group, and were motivated to conduct the program. Professionals conducted the program for the first time.	Professionals were familiar with the content of the program, were experienced in working with the target group, and were motivated to conduct the program. Most of the professionals had already conducted the program several times and believed in the working mechanism of the program.
Participants	Participants joined the program voluntarily and were motivated to participate in the program. The social aspect of the program was important to participants.	Participants joined voluntarily and were motivated to participate in the program. The social aspect of the program was important to participants, and in some cases, participants continued the training sessions after the intervention (with the same group of participants).	Participants joined voluntarily and were motivated to participate in the program. Professionals indicated that some participants lacked knowledge regarding the goal of the program. Social interactions among older adults highly stimulated participants to adhere to the program and in some cases to continue the training sessions after 12 weeks (with the same group of participants).

Process

Similarities

Planning and executing – There was a protocol available for conducting the intervention.

Table 4D. *Process of the three interventions: ProMuscle, ProMuscle in Practice and the ProMuscle Implementation Pilots.*

Process			
	ProMuscle	**ProMuscle in Practice**	**ProMuscle Implementation Pilots**
Planning and executing	Researchers created a protocol and conducted the intervention according to it.	Researchers created a protocol for conducting the intervention, based on the protocol of ProMuscle. Researchers trained professionals to conduct the intervention. Professionals adhered to the guidelines and adjusted the training intensity when necessary (too high/too low).	Professionals could use the protocol of ProMuscle in Practice as an inspiration for conducting the intervention. Researchers trained professionals to conduct the intervention. Researchers discussed the protocol for implementing the intervention with professionals and discussed how this could be applied and adjusted to their specific setting. Basic elements of the intervention remained central, but there was room for own insights and adjustments according to available facilities/ resources and capabilities of individuals.
Engaging	Researchers conducted the intervention themselves (i.e., providing training sessions).	Managers of care organizations chose to be involved in the project and looked for physiotherapists and dietitians within their organization who were willing to practically conduct the intervention.	Physiotherapists chose to be involved in the project and conducted the intervention themselves or instructed a colleague who was willing to be involved. Physiotherapists recruited dietitians to conduct the nutrition program of the intervention. A medical practice assistant of GP was involved to facilitate recruitment of participants.

Differences

Planning and executing – During PM, researchers conducted the intervention strictly according to the protocol. During PiP, professionals adhered to the protocol and adjusted the training intensity when necessary. During IP, basic elements of the protocol remained central, but professionals adjusted the intervention according to their facilities and to the capabilities of individuals.

Engaging – During PM, researchers conducted the intervention themselves. During PiP, managers of care organizations chose to be involved in the project and looked for physiotherapists and dietitians within their organization to conduct the intervention. During IP, physiotherapists chose to be involved in the project and conducted the intervention themselves or instructed a colleague who was willing to be involved. Physiotherapists involved a dietitian to conduct the nutrition program.

DISCUSSION

Effects on chair-rise test and leg press strength were not only found in the controlled setting but remained present in the real-life setting and were found to be even more pronounced in the real-life setting of the implementation pilots. The fact that effects vary across settings can be explained by several aspects, including the room for adapting and tailoring the intervention (*Intervention characteristics - adaptability*), the availability of and access to facilities (*Inner setting - readiness for implementation*), the involvement of experienced and independent professionals (*Characteristics of individuals - professionals*), and specific characteristics of the participants (*Characteristics of Individuals - participants*).

First of all, the experiences from a decade of working on the ProMuscle interventions were used to continuously develop and refine the intervention. It should be noted that the interventions we included in the current study are three successive rather than three separate interventions. The original study was developed to investigate the efficacy of PM in the controlled setting.[25,82] To work from the controlled to the practice setting, we conducted two translation steps. The first step included a translation from the effective PM program to the PiP program, in which the basic elements of the intervention were maintained and the intervention was tailored to the real-life setting.[26] PiP aimed to investigate the effectiveness and feasibility of PM in the real-life setting. Research played a major role in PiP, as professionals conducted the intervention according to guidelines and researchers were responsible for recruiting participants and conducting measurements. The second step included a translation from the effective PiP program to the IP program. The IP aimed to investigate how the program could fit the real-life setting best and focused mainly on the experiences and insights of professionals. Professionals played a major role, as they adapted the program according to their own insights and were responsible for recruiting older adults and performing measurements in participants. Continuous evaluation, in cooperation with professionals and participants involved, facilitated ongoing development of the intervention.[26,29] Although effects often fade away when implementing an intervention in the real-life setting,[33,178] effects of the ProMuscle interventions remained present after both translation steps. This indicates that the development and translation process of ProMuscle was successful.

An essential step in transferring a health intervention from the controlled setting to the practice setting is adaptation.[73,179] Adaptation includes adapting the intervention to fit a specific population or setting, and adapting intervention delivery while retaining the basic components of the intervention.[180] Ideally, adaptation proceeds via co-creation, meaning that researchers collaborate with local stakeholders and use their input to adapt the intervention.[73,180] Quantitative as well as qualitative studies reported improved program outcomes and better implementation if intervention providers made small adaptations to the program.[73] This is in line with our results, which show increased effects when the intervention was adapted by professionals to the real-life setting of the implementation pilots. This is due to the fact that providers such as health care professionals are familiar with their community and are therefore able to fit the intervention to the needs and preferences of the local community, also called tailoring.[73] *Adaptability* was present in PiP but more pronounced in IP, which may have contributed to the difference in effects between the interventions. In IP, individual intakes facilitated tailoring of the intervention to the needs and capabilities of participants. A variety of exercises was offered, and dietary advice included a broad range of protein-rich food products, which made the program appropriate for a diverse group of participants. Besides, participants' daily activities were considered when scheduling the intervention activities. Systematic reviews also highlight the importance of personalized modification. Tailoring the intervention to the needs and capabilities of participants appeared to be a key element for success in physical activity as well as dietary interventions.[46,181–183] Besides, convenient scheduling was indicated as an enabling factor for participating in an intervention.[46] The results are in line with the process evaluation of PiP, in which tailoring and more variety in the intervention were highlighted as important elements.[29]

An important aspect regarding *characteristics of individuals (professionals)* is the involvement of experienced professionals in delivering the intervention. The two physiotherapists and dietitians that conducted IP were already involved in the PiP study and could be indicated as 'first users' or champions. Champions are individuals that are dedicated to support the implementation and are characterised by their perseverance and strong believe in the intervention.[70,184,185] The involvement of champions, who are committed to and experienced with the intervention is associated with the intervention's success.[70,186] An important aspect related to the *Inner setting* is *readiness for implementation*. A relevant part of this aspect is the availability of and access to resources.[70,178] Whereas during PiP physical space was sometimes suboptimal and training machines and data of baseline measurements were delivered too late, professionals of IP had direct access to their own facilities, including a spacious and safe environment with their own training machines, and data of baseline measurements. As baseline measurements were used as a starting point for the training program, receiving the data too late caused some delays in the PiP program. Other studies also indicate factors such as the availability of facilities, a safe, accessible, and convenient physical environment, and the access to documentation as enabling factors for intervention implementation.[46,70] The fact that experienced professionals conducted IP independently, using their own facilities, without large delays or constraints, contributed to the intervention success and may partly explain the larger effects in IP compared with PiP.

In addition, baseline *characteristics of individuals (participants)* played a role in explaining intervention effects. Whereas the PM study included a relatively low number of female participants (36%), this number was relatively higher in the PiP study (62%) and IP (80%). As was reported in the in-depth analyses of the PiP study, women benefited to a greater extent from the intervention than men did.[187] The higher effects in IP could partly be explained by its high number of female participants, compared with the other two interventions. When adjusting our model (GLM) for sex, the significant effect of intervention setting remained present for leg press effects but disappeared for chair-rise effects. This implies that sex can partly explain the differences in effects on chair-rise performance between the settings. Besides, chair rise performance and leg strength measurements of participants of PiP were already better at baseline, compared with the other two interventions (although differences between interventions were not statistically significant), leaving less room for improvement.

Although many studies have been tested for efficacy in a controlled setting, few have been implemented in practice or were scaled-up.[179,180] This can be described as the know-do gap, which reflects the gap between what is known in research and what gets done in practice.[179,188] It indicates the need for studying intervention implementation. Up till now, the intervention was picked up by innovators and early adopters, according to the diffusion of innovations model.[189] Since IP showed positive results, it is time to additionally reach the early and late majority. An important point of attention of implementation, which was also highlighted in IP, are the costs related to the intervention, since financial aspects are often a barrier in implementation.[71] To gain insight in such barriers, but also enablers of implementation, and investigate how to systematically implement and consequently scale-up the ProMuscle intervention in the real-life setting, we recently started with the ProMuscle Implementation study (PUMP-fit).

Several strengths and limitations should be pointed out. A major strength of the intervention is its social aspect. Although the ProMuscle interventions are aimed at improving older adults' muscle health and physical functioning, a positive side-effect is the emergent of strong social connections, a feeling of togetherness, new friendships, and even new relationships. Besides, the social aspect of the group training sessions highly motivated participants to adhere to the intervention in all three interventions, but especially during IP. Another major strength is the gradual development of the ProMuscle program. Continuous evaluation and development led to an effective intervention which can be implemented by professionals in the real-life setting. Only intervention groups were included in this study. Normally, it would not be suitable to highlight the intervention arms of these three studies to compare its effects, since the studies were not designed to be compared to each other. However, because the basic elements of the interventions are similar and the interventions expanded on the previous version, it provided us the unique opportunity to conduct the current study. A limitation that should be indicated is the low number of interviews with professionals involved in PM and IP. Consequently, the aspects highlighted from the interviews might not be generalizable to other professionals. To cover the opinion of a broader group on aspects related to implementation, focus group discussions and interviews are currently being conducted with professionals.

Although we expected effects to fade away when implementing the intervention in the practice setting, the opposite appeared to be true. Specific contextual factors contributed to explaining the different findings across settings. For an intervention to remain successful in a new setting, it is essential to continuously reassess, renew, and refine, while remaining the intervention's basic elements. To make sure health promotion programs reach a wide population, future studies should focus on systematic and sustainable implementation of effective interventions in the real-life setting.

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6

Cost-effectiveness of a diet and resistance exercise intervention in community-dwelling older adults: ProMuscle in Practice

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ABSTRACT

Objectives: Ageing is associated with a decline in functioning and a loss of independence, which will lead to increased healthcare costs in the future. The ProMuscle in Practice intervention was found to be effective in improving muscle strength, muscle mass, and functioning of older adults. The current study assesses the cost-effectiveness and perceived benefits of the intervention.

Design: Trial-based cost-effectiveness analysis complemented by interviews.

Setting and participants: 168 community-dwelling older adults were included. Intervention participants started with a 12-week intensive support program, comprising resistance exercise guided by physiotherapists and consultations with a dietician to increase protein intake. To maintain the adapted lifestyle pattern, they continued with a 12-week moderate support intervention. The control group received usual care.

Methods: Costs and outcomes were measured at baseline, after 12 and 24 weeks. Costs were assessed from a societal perspective. Healthcare use, out-of-pocket costs and productivity losses were measured using questionnaires. Intervention costs were quantified according to bottom-up micro-costing. Outcomes included quality of life (EQ-5D-5L) and physical functioning (Short Physical Performance Battery; SPPB). Bootstrap analyses were used to generate cost-effectiveness planes and acceptability curves. Interviews with participants and professionals were conducted after 24 weeks to measure perceived benefits.

Results: An Incremental Cost-Effectiveness Ratio of €2988 ($3385)/point increase in SPPB was found. The intervention has an 82.4% probability of being cost-effective at a Willingness to Pay (WTP) of €12.000 ($13.559)/point increase in SPPB. No change in quality of life was found according to EQ-5D-5L. Interviews, however, revealed a wide range of function-related perceived benefits.

Conclusions and implications: At a WTP of €12.000 ($13.559)/point increase in SPPB, the intervention was found to have an 82.4% probability of being cost-effective. Because generic quality of life questionnaires seem unable to detect subtle changes in public health interventions, future studies are advised to include targeted and specific questionnaires.

INTRODUCTION

The proportion of the world's population aged 60 years and older is expected to increase from 12% to 22% between 2015 and 2050.[2] Ageing is often accompanied by conditions such as frailty and sarcopenia, leading to an increased risk of falls, hospitalization, and decreased quality of life.[13,153,190] Additionally, the ability to perform daily tasks tends to impair, and the need for help tends to increase, adding up to loss of independence.[152] Besides, ageing and its consequences are associated with increased healthcare costs.[13,15] In the USA, annual personal healthcare spending for adults aged 65 years and older has increased between 1992 and 2017 from $16.906 to $18.620 per person.[191] Older adults already accounted for 36% of total healthcare spending in 2016 and this number is expected to increase.[192] Specifically in the Netherlands, healthcare costs in older care are expected to increase by 153% (from 17 billion in 2015 to 43 billion in 2040).[16] These health and economic burdens ask for preventive strategies to counteract age-related impairments and to contribute to independence of older adults.

Previous research has shown that the combination of dietary protein supplementation and resistance exercise (RE) is an effective strategy to prevent sarcopenia and improve physical functioning.[21–23,31,74] Most of these effects were observed in a clinical, controlled setting, and cannot directly be translated to the practice setting. Therefore, the efficacious, clinical program ProMuscle[25] was adapted and pilot-tested for the practice setting, resulting in the ProMuscle in Practice intervention (PiP). Adaptations included i.e. replacing the protein supplementation by an extensive nutrition program guided by a dietitian and the provision of protein-rich products.[26] PiP was implemented by physiotherapists and dieticians in the practice setting. After 12 and 24 weeks, community-dwelling older adults in the intervention group significantly improved muscle strength, muscle mass, and physical functioning compared to control participants.[28] Meaningful between group differences were reported, i.e. a change on SPPB of 0.5 points (95%-CI: 0.1 - 0.9) and a change on the chair rise test of 1.4 seconds (95%-CI: -2.3 - -0.4) after 24 weeks.

The next step in development of PiP is to assess the cost-effectiveness of the intervention. To date, cost-effectiveness studies of similar interventions aiming to improve muscle strength, muscle mass, and physical functioning have not been conducted. However, economic evaluations of comparable interventions in older adults aiming to prevent falls are available, showing variable results regarding cost-effectiveness.[75–77] A recent systematic review included 12 exercise-based falls prevention programs, in which different methods and willingness to pay thresholds were used. Ten studies used Cost Effectiveness Analysis and/or Cost Utility Analysis as method for economic evaluation and two studies reported medical costs as cost-utility. They reported four interventions to be cost-effective, three interventions as potentially cost-effective and six interventions to be not cost-effective on preventing falls.[77] Despite positive effects on falls prevention, reviews reported no or minimal effects on quality of life using generic questionnaires such as EQ-5D-5L or SF-36, indicating the importance to assess perceived benefits.[75,77]

Thus, findings on cost-effectiveness of falls prevention programs are inconsistent and to date, no study has investigated the cost-effectiveness of a lifestyle intervention combining RE and an increased protein intake for older adults. Besides, limited changes in quality of life were found using generic questionnaires. Therefore, this study aims to assess the cost-effectiveness of the PiP intervention, and gain insights into benefits regarding health-related quality of life.

METHODS

Study design

The current study was a trial-based cost-effectiveness analysis complemented with interviews. Economic evaluation was performed from the societal perspective with a time horizon of 24 weeks. The healthcare perspective was included as sensitivity analysis. The study design and sample size calculation of PiP are described in detail elsewhere.[27,28] In short, the Randomized Controlled Trial (RCT) was implemented in a phased manner in five Dutch municipalities between 2016 and 2018 (first the intervention was implemented at location 1, a few months later implementation started at location 2, etc.).

Study population

Researchers recruited older adults via local media. Interested older adults received an extensive information brochure and were invited to an information meeting. After that, researchers screened older adults according to the inclusion criteria. Older adults' general practitioners checked the exclusion criteria, i.e. renal insufficiency, allergy/sensitivity to milk proteins or being lactose intolerant, diagnosed COPD, cancer, or unregulated diabetes type 1 or 2 (see supplementary table 1). Included participants (n=168) were randomly assigned to the intervention or control group (stratified for sex and frailty), based on a randomisation scheme generated by an independent researcher. The study protocol was approved by the Wageningen University Medical Ethics Committee, and all subjects gave written informed consent before the start of the study. PiP is registered at the Dutch Trial Register (identifier NTR6038).

Description of the intervention

The intervention consisted of a 12-week intensive support program, followed by a 12-week moderate support program. The intensive support program included twice weekly group based progressive RE, primarily focused on the leg muscles, supervised by physiotherapists. Dietitians advised participants individually to increase their protein intake to 25 grams per main meal, via an intake consultation, a contact moment in the first week, and an evaluation consultation in week 6. Besides, for the duration of 12 weeks, intervention participants received protein-rich foods, such as dairy foods, to incorporate in their diet.

After the first 12 weeks, intervention group participants were encouraged to continue with the optional moderate support program, to maintain their adapted lifestyle pattern. The program consisted of group-based RE 1-2 times a week at local fitness centres or physiotherapist practices and a nutrition course, comprising five group-based workshop meetings. An extensive description of the intervention is provided in supplementary material 1.

The control group received usual healthcare during the first 24 weeks and were asked to retain their habits regarding exercise and diet. After 24 weeks, the control group was offered to participate in the moderate support intervention. In the current study, we compared data from the first 24 weeks of the intervention and control group.

DATA COLLECTION AND OUTCOMES

Measures

Participants visited the research centre at baseline (T0), and after 12 (T1) and 24 weeks (T2). Measurements were performed by un-blinded trained researchers and research-assistants, following standardized protocols. Only the EQ-5D-5L questionnaire was additionally self-reported in week 6 and 18.

Physical functioning

The Short Physical Performance Battery (SPPB) was used to measure physical functioning (score 0-12, 12 represents the best score). The test consists of three components, each with a maximum of 4 points: a standing balance, repeated chair-rise and gait speed test.[163] Repeated chair-rise test in seconds was analysed separately, because of its high correlation with lower body strength and functioning.[164] Less seconds on the chair-rise test represented a better performance.

Quality of life

The EQ-5D-5L questionnaire was used to measure health-related quality of life.[193] The questionnaire consists of five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has five answer categories: no problems (level 1), slight (2), moderate (3), severe (4) and extreme problems (5). The five dimensions and five levels lead to a health state score at each time point. The health state scores were then recalculated to a health utility (for example, a health score of 11111 indicates full health and has utility 1). The recalculation was performed using a 'tariff', that was based on an EQ-5D-5L valuation study conducted in the Netherlands.[194] Health utilities were multiplied by the time spent in the health state, to estimate Quality Adjusted Life Years (QALYs). Adding these scores established the total QALY for the 24-week period, with a maximum of 0.46 (24/52) for a person with the best possible health state at all measurement points.[194]

Healthcare use, out-of-pocket costs, and productivity losses

A healthcare use questionnaire was developed before start of the study, based on the iMTA Medical Cost Questionnaire.[195] It included cost categories that were deemed relevant for community-dwelling older adults (general practitioner, homecare, informal care, dietitian, physiotherapist, occupational therapist, hospitalisation, residential care, rehabilitation care, outpatient clinic and medication use). Out-of-pocket costs included sports club memberships, purchase of sport equipment, and other out-of-pocket payments related to the intervention, such as braces or crutches. Productivity losses were measured using questions from the Productivity Cost Questionnaire.[196] Data on healthcare use, out-of-pocket costs, and productivity losses was collected in week 0, 12, and 24. In between measurements (week 1-12, and week 13-24) participants used a cost diary to keep track of their healthcare use, out-of-pocket costs, and productivity losses. Participants brought these diaries to the measurements to improve recall and accuracy in filling out the questionnaires. Trained researchers conducted measurements in a standardized manner, not differentiating between intervention and control participants.

Costs

Healthcare costs, out-of-pocket costs, and productivity losses

We used 2017 healthcare price levels, because the intervention was mainly delivered in that year. The *Dutch guideline for costing analysis in healthcare* was used to assess cost prices per unit for healthcare related costs and productivity losses for unpaid work.[197,198] As this guideline included costs from 2014, those were adapted to 2017 levels applying Dutch consumer price index figures. Costs for medication use, sports club membership, sports equipment and out-of-pocket payments were individualised. Detailed unit cost per category can be found in supplementary table 2.

Intervention costs

Bottom-up micro-costing was used to estimate intervention costs (golden standard).[197] Intervention costs were calculated per participant, and separately for the intensive and moderate support program. During the intensive program, healthcare professionals registered their working hours. These hours were multiplied by unit prices (hourly wage costs) for the specific professional. Intervention materials (for example, protein-rich products) were valued according to market prices. Fitness equipment was valued by the purchase price minus the selling price and divided by the number of participants in the intensive support intervention. Rent of rooms for RE training sessions were valued according to average renting prices for sports facilities in the five municipalities.

During the moderate support program, nutrition workshop supervisors registered their hours, which were multiplied by unit prices for dieticians. Costs for RE sessions at local sports centres were incorporated by including charges for sports club membership. Research-related study costs were excluded.

Interviews

After completion of the intervention, researchers conducted semi-structured interviews with four intervention participants per municipality (n=20 in total) and with healthcare professionals, comprising physiotherapists (n=18) and exercise trainers (n=9). Detailed information on methods regarding interviewing are described elsewhere.[29] Interview questions were used from the interview guide that was pretested during the pilot study.[26] In the current study, only data providing insights into perceived benefits were included. This information was obtained by asking interviewees whether they noticed effects or changes in participants.

DATA ANALYSES

Quantitative analyses

Baseline characteristics were analysed using independent samples t-test or Mann Whitney U test for continuous data, and Pearson's chi-squared test or Fisher's exact tests for categorical data. Data were analysed according to the intention-to-treat principle (ITT). Multiple imputation models were used to impute missing cost and outcome data (10.2%

on average). Data was analysed with SPSS version 23 (IBM Corp., Armonk, NY).

Qualitative analyses

Qualitative data were analysed using Atlas.ti version 8. Interviews were audiotaped and transcribed verbatim. One researcher (EJIvD) analysed transcripts of interviews with healthcare professionals and one research assistant (LB) analysed transcripts of interviews with participants. Transcripts and analyses were checked by a third researcher (BD). Detailed information on coding is provided elsewhere.[29] Perceived benefits of the intervention were classified according to the seven domains of the SarQol questionnaire.[199]

Economic analyses

The incremental cost-effectiveness ratio (ICER) was calculated by dividing the difference in costs by the difference in effects between the intervention and control group. The ICER was separately calculated for effects in SPPB, chair-rise test, and QALY (difference in effect between intervention and control group after 24 weeks) using bootstrap analyses with 5000 simulations. The ICERs were calculated from the societal perspective, including intervention costs, direct healthcare costs, patient- and family costs and other costs. The time horizon was 24 weeks. Therefore, no discounting was applied in this study.

Cost-effectiveness planes and cost-effectiveness acceptability curves were plotted. The latter indicate the probability of the intervention to be cost-effective compared to usual care, according to threshold values for willingness to pay (WTP). In the Netherlands, threshold values of €20.000 to €80.000 per QALY are used.[200] Currently, no threshold values are determined for SPPB or chair-rise test.

Sensitivity analyses

Sensitivity analyses comprised calculating ICERs from a healthcare perspective, including intervention costs and direct healthcare costs, and performing economic analyses for complete cases. Complete cases comprised participants with complete data for costs and included study outcomes.

RESULTS

Table 1 presents baseline characteristics of the intervention and control group. No significant differences were found between the two groups. Baseline SPPB score was 10.1 ± 1.7 and baseline utility value for participants' health status was 0.86 ± 0.11.

Table 1. *Baseline characteristics of participants of the ProMuscle in Practice intervention.*

	Intervention group (n=82)	Control group (n=86)
Sex, female, n (%)	51 (62%)	51 (59%)
Age, y	74.7 ± 5.8	75.9 ± 6.5
Frailty status (n, %)		
Non-frail	41 (50%)	39 (45%)
Pre-frail	39 (48%)	42 (49%)
Frail	2 (2%)	5 (6%)
Bodyweight (kg)	76.3 ± 14.4	75.6 ± 13.6
Height (cm)	167.6 ± 9.0	169.2 ± 9.3
Education level, n (%)[a]		
Low	2 (2%)	4 (5%)
Intermediate	54 (66%)	42 (49%)
High	26 (32%)	40 (47%)
Ethnicity: native Dutch, n (%)	79 (96%)	81 (94%)
Care use, n (%)	11 (13%)	16 (19%)
Alcohol use		
Drinker (≥1 d/wk), n (%)	52 (63%)	59 (69%)
no. of glasses/day	1.5 ± 0.8	1.9 ± 1.2
Smoking, n (%)		
Never smoked	32 (39%)	30 (35%)
Stopped >1 y ago	46 (56%)	53 (62%)
Current or stopped in last year	4 (5%)	7 (3%)
Morbidities, n (%)		
Diabetes	9 (11%)	9 (11%)
Arthrosis	38 (46%)	42 (49%)
Fractures	3 (4%)	4 (5%)
Other	69 (84%)	67 (78%)
SPPB total score (0-12)	10.1 ± 1.4	10.1 ± 2.0
Standing balance, points (0-4)	3.7 ± 0.6	3.6 ± 0.7
4-meter gait speed, s	4.2 ± 0.9	4.2 ± 1.2
Repeated chair rise, s	13.7 ± 3.4	13.1 ± 3.9
Health status score (0-1)	0.87 ± 0.10	0.86 ± 0.13

Data is presented as mean ± SD unless otherwise noted. [a]Educational level, based on the Development of the Older Persons and Informal Caregivers Survey Minimal Dataset (TOPICS-MDS) questionnaire, low: primary school (less than 6 classes, 6 classes or full primary school), intermediate: secondary education or vocational school, high: higher vocational education or university.

Costs

Table 2 and 3 show the total costs during the 24-week study period in the intervention and control group. Average intervention costs were €1119 per participant, comprising €1014 for the intensive support intervention and €105 for the moderate support intervention. Direct healthcare costs were lower for the intervention compared to control group (€1336 and €1697, respectively). The total cost difference between the two groups was €890 for the societal perspective.

Table 2. *Mean (SD) costs for intervention and control participants over the total 24-week study period: Intervention costs*

	Unit costs in € ($)*	Intervention (n=82) Mean total costs € ± SD ($ ± SD)*	Control (n=86) Mean total costs € ± SD ($ ± SD)*
Intensive support intervention			
Recruitment	13 p.p.* (15)	13 ± 0 (15 ± 0)	0 ± 0
Materials	4 p.p.* (4)	4 ± 0 (5 ± 0)	0 ± 0
Fitness equipment	82 p.p.* (93)	82 ± 0 (93 ± 0)	0 ± 0
Protein-rich products	Individualized	264 ± 74 (299 ± 84)	0 ± 0
Rent of rooms	12 per hour (13)	55 ± 9 (62 ± 10)	0 ± 0
Physiotherapist hours (RE sessions)	34 per hour (38)	450 ± 88 (509 ± 100)	0 ± 0
Dietitian hours (consultations)	34 per hour (38)	145 ± 46 (164 ± 52)	0 ± 0
Subtotal		1014 ± 167 (1147 ± 189)	0 ± 0
Moderate support intervention			
RE sessions at local sports centre	5 per session (5)	55 ± 20 (62 ± 23)	0 ± 0
Nutrition workshop	10 per session (11)	50 ± 9 (57 ± 10)	0 ± 0
Materials	1 p.p.* (1)	1 ± 0 (1 ± 0)	0 ± 0
Subtotal		105 ± 27 (119 ± 31)	0 ± 0
Subtotal intervention costs		1119 ± 171 (1266 ± 194)	0 ± 0

p.p.: per participant.

**Currency exchange rates accessed on July 6, 2020: €1 = US$1.12990.*

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Table 3. Mean (SD) costs for intervention and control participants over the total 24-week study period

	Unit costs € ($)*	Intervention (n=82) Mean total costs € ± SD ($ ± SD)*	Care use intervention group n (%)	Control (n=86) Mean total costs € ± SD ($ ± SD)*	Care use control group n (%)
Direct health care costs					
General practitioner	Suppl. table 2	131 ± 199 (148 ± 225)	69 (84%)	137 ± 132 (155 ± 149)	75 (87%)
Homecare	Suppl. table 2	328 ± 649 (371 ± 734)	24 (29%)	483 ± 1131 (547 ± 1280)	27 (31%)
Consultations dietitian	34 per hour (38)	3 ± 7 (2 ± 8)	19 (23%)	2 ± 9 (2 ± 10)	14 (16%)
Consultations physiotherapist	34 per hour (38)	101 ± 184 (114 ± 208)	36 (44%)	157 ± 222 (178 ± 251)	46 (54%)
Consultations occupational therapist	34 per hour (38)	7 ± 16 (8 ± 18)	16 (20%)	15 ± 53 (17 ± 60)	16 (19%)
Hospital admission	489 per day (553)	259 ± 494 (293 ± 559)	24 (29%)	258 ± 703 (292 ± 795)	20 (23%)
Intensive care admission	2068 per day (2340)	40 ± 230 (45 ± 260)	11 (13%)	6 ± 26 (7 ± 29)	4 (5%)
Ambulance transportation	529 per ride (598)	32 ± 96 (36 ± 109)	17 (21%)	37 ± 114 (42 ± 129)	17 (20%)
Residential care admission	172 per day (195)	44 ± 102 (50 ± 115)	14 (17%)	82 ± 401 (93 ± 454)	12 (14%)
Residential care treatment	69 per half day (78)	1 ± 2 (1 ± 2)	10 (12%)	1 ± 8 (1 ± 9)	5 (6%)
Rehabilitation care admission	472 per day (534)	0 ± 0 (0 ± 0)	0 (0%)	0 ± 0 (0 ± 0)	0 (0%)
Rehabilitation care treatment	157 per hour (178)	3 ± 18 (3 ± 20)	11 (13%)	1 ± 2 (1 ± 2)	4 (5%)
Consultations outpatient clinic	93 per hour (106)	212 ± 242 (240 ± 274)	55 (67%)	164 ± 197 (186 ± 223)	51 (59%)
Medication use	Individualised	174 ± 153 (197 ± 173)	76 (93%)	356 ± 1347 (403 ± 1524)	76 (88%)
Subtotal		1336 ± 1466 (1510 ± 1656)		1697 ± 2656 (1917 ± 3001)	

***Table 3** continued.*

	Unit costs € ($)*	Intervention (n=82) Mean total costs € ± SD ($ ± SD)*	Care use intervention group n (%)	Control (n=86) Mean total costs € ± SD ($ ± SD)*	Care use control group n (%)
Patient and family costs					
Sports club membership	Individualised	47 ± 56 (45 ± 63)	46 (56%)	68 ± 88 (77 ± 100)	50 (58%)
Sports equipment	Individualised	20 ± 32 (23 ± 36)	35 (43%)	14 ± 43 (16 ± 49)	25 (29%)
Out-of-pocket payments	Individualised	155 ± 244 (175 ± 276)	66 (81%)	130 ± 251 (147 ± 284)	63 (73%)
Informal care	14 per hour (16)	259 ± 649 (293 ± 734)	34 (42%)	141 ± 332 (160 ± 376)	28 (33%)
Subtotal		*481 ± 815 (544 ± 921)*		*353 ± 520 (399 ± 588)*	
Other costs					
Productivity loss unpaid work	14 per hour (16)	18 ± 58 (20 ± 66)	66 (81%)	13 ± 35 (15 ± 40)	63 (73%)
Subtotal		*18 ± 58 (20 ± 66)*		*13 ± 35 (15 ± 40)*	
Total costs - Societal perspective		*2953 ± 2055 (3341 ± 2325)*		*2063 ± 2858 (2334 ± 3233)*	
Total costs - Healthcare perspective		*2455 ± 1479 (2774 ± 1671)*		*1697 ± 2656 (1917 ± 3001)*	

**Currency exchange rates accessed on July 6th, 2020: 1 EUR = 1.12990 USD.*

6

Effectiveness

Physical functioning - SPPB

After 24 weeks, an incremental effect in physical functioning of 0.3 SPPB points was found (95%-CI: -0.2; 0.8), presented in table 4. Effects in intervention and control group separately are presented in supplementary table 3. The incremental effect in complete cases was 0.6 SPPB points (95%-CI: 0.0; 1.2) (supplementary table 3).

Physical functioning - Chair-rise test

The intervention group improved chair-rise test performance over time, whereas the control group decreased their performance (supplementary table 3). Mean difference between the two groups was 1.2 seconds (95% CI 0.4; 2.1) according to ITT (table 4) and 1.5 seconds (95% CI 0.4; 2.6) in complete cases (supplementary table 3).

Quality adjusted life years

According to ITT as well as complete case analyses, no significant changes between groups were found in QALY (table 4, supplementary table 3).

Benefits of the program according to interviewees

Table 5 presents the perceived benefits of the intervention mentioned by the interviewees, classified according to the seven domains of the SarQol questionnaire.[199] A broad variety of positive effects due to the intervention were mentioned, including an improvement in strength, vitality, mental state, balance, ability to walk, climb the stairs and cycle, and a reduction in fatigue during daily activities.

Table 4. *Results of cost-effectiveness analyses including SPPB, chair-rise test and QALY as outcome measure from the societal perspective.*

	n	Incremental effect	Incremental costs € ($)	ICER* € ($) /outcome	Probability cost-effective (WTP† €20.000 ($22.654) / outcome) %	Probability cost-effective (WTP† €80.000 ($90.603) / outcome) %
SPPB‡	168	0.3	891 (1007)	2988 (3385)	85.4	88.9
Chair-rise test§	168	1.2	891 (1007)	728 (946)	99.4	99.4
QALY||	168	0.0	891 (1007)	7.337.501 (8.290.642)	4.5	18.9

**ICER: Incremental Cost-Effectiveness Ratio. †WTP: Willingness to pay. ‡SPPB: Short Physical Performance Battery. §Chair-rise test: analyses were performed with inverse minus/plus signs, to better present effects. ||QALY: Quality Adjusted Life Years.*

Cost-effectiveness

Physical functioning - SPPB

From the societal perspective, an ICER of €2988/point increase in SPPB was found according to ITT analyses (table 4). Figure 1A presents the cost-effectiveness plane with 5000 bootstrap simulations. Most simulations were situated in the north-eastern part of the cost-effectiveness plane, meaning an additional health effect was associated with additional costs. Figure 1B presents the cost-effectiveness acceptability curve, showing that the probabilities of the intervention being cost-effective are 82.4% and 85.4% at a WTP of respectively €12.000 and €20.000/point increase in SPPB.

Physical functioning - Chair-rise test

An ICER of €728/second improvement in chair-rise test was found according to ITT analyses (table 4). There was a 99.4% probability of the intervention being cost-effective at a WTP of €20.000/second improvement in chair-rise test.

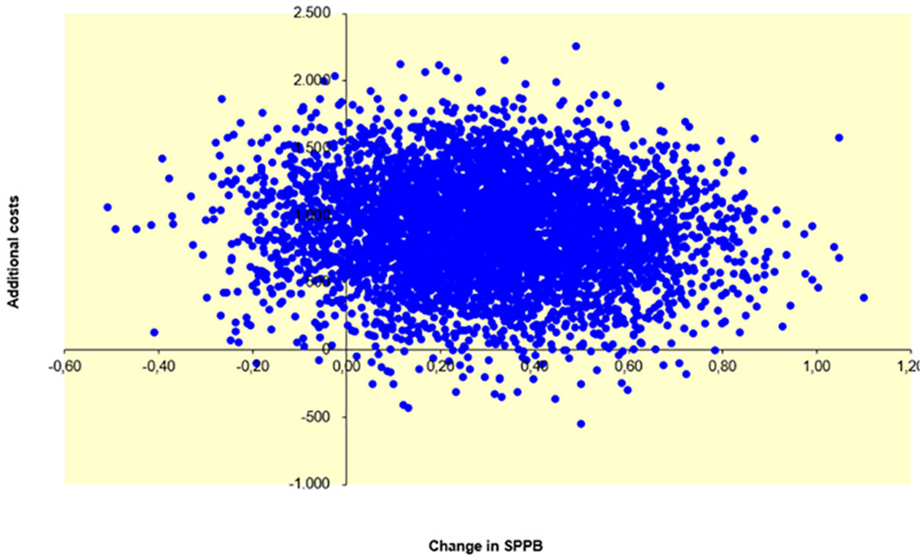
Quality of life

An ICER of €7.337.501/QALY was found (table 4) and the corresponding cost-effectiveness plane and cost-effectiveness acceptability curve were presented (figure 1C+1D, respectively). The ICER was found to be high due to the lack of difference in QALYs between intervention and control group.

Sensitivity analyses

Results of economic analyses from the healthcare perspective were in line with analyses from the societal perspective. Analyses of complete cases resulted in an ICER of €1945/point increase in SPPB (n=101). The probabilities of the intervention being cost-effective at WTPs of €5.000 and €20.000/point increase in SPPB are respectively 92.9% and 99.1%. For the chair-rise test, results of complete case analyses were in line with ITT analyses.

A)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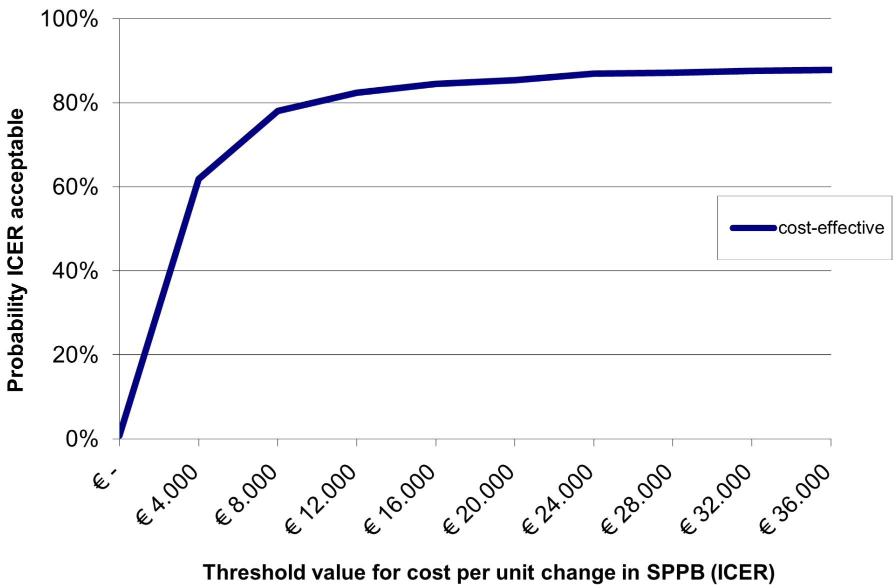
B)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Threshold value for cost per unit change in SPPB (ICER)
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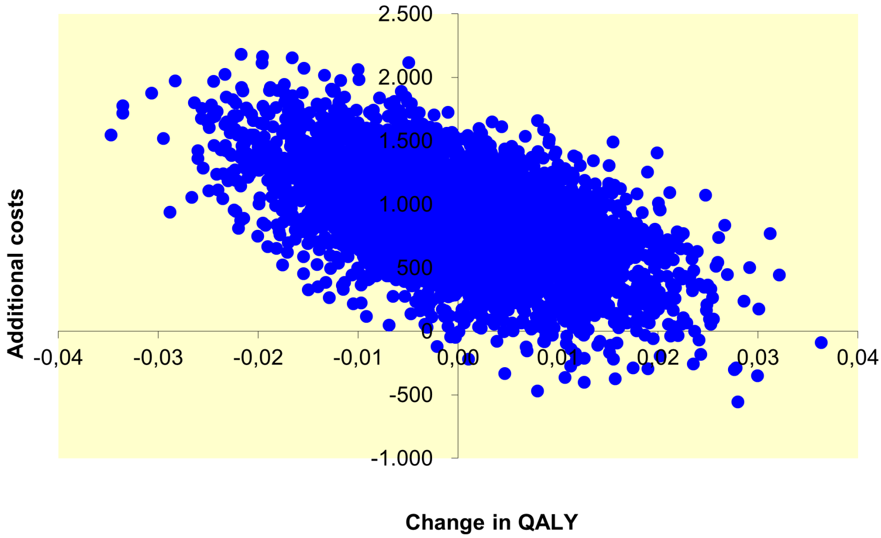
C)



D)

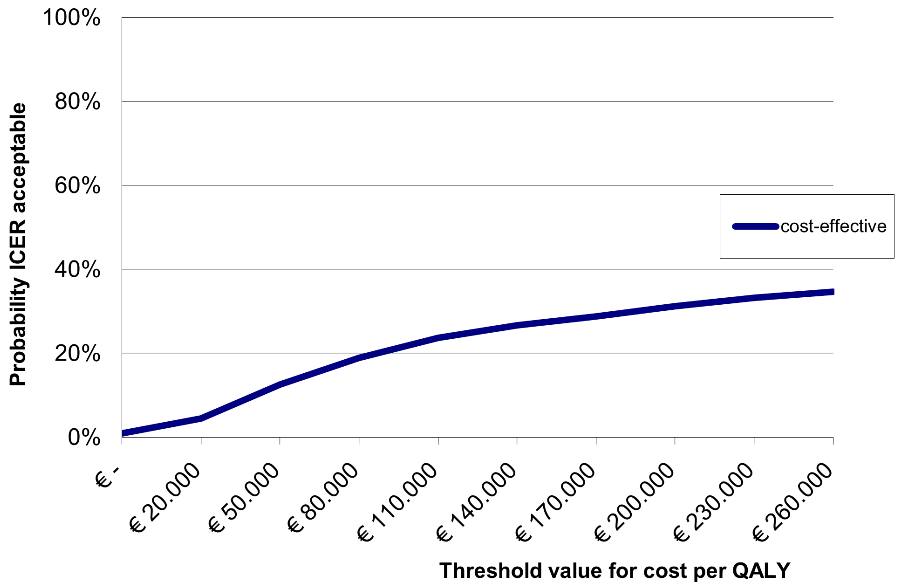


Figure 1. *Cost-effectiveness of the ProMuscle in Practice intervention compared to usual care, including SPPB (A, B) and QALY (C, D) as outcome measures. (A, C) Cost-effectiveness plane including 5000 bootstrap simulations. (B, D) Cost-effectiveness acceptability curve for change in, respectively, physical functioning or QALY (WTP/outcome).*

Table 5. *Overview of perceived benefits of the ProMuscle in Practice intervention from interviews with participants (n=20), physiotherapists (n=18), and exercise trainers (n=9) classified according to domains of the SarQol questionnaire.*

SarQol domains	**Aspects mentioned by participants during interviews* Due to the ProMuscle in Practice intervention, participants…**	**Aspects mentioned by physiotherapists during interviews† Physiotherapists mentioned that due to the ProMuscle in Practice intervention, participants...**	**Aspects mentioned by exercise trainers during interviews‡ Exercise trainers mentioned that due to the ProMuscle in Practice intervention, participants…**
Physical and mental health	▸ Perceived an increased strength in their arms, legs or back (n=4) ▸ Felt really good/fit/vital, their energy level increased; physically as well as mentally (n=6) ▸ Noticed that working out is very important for the mind, and very relaxing (n=1)	▸ Perceived an increased strength in their legs or arms (n=5) ▸ Felt fitter than before the program (n=4) ▸ Felt better, felt very well (n=2)	▸ Perceived an increased strength (n=2) ▸ Felt the program is good for their mental state (n=1) ▸ Felt very well (n=1)
Locomotion		▸ Increased their walking ability (n=5)	▸ Moved much more freely than before the program (n=1)
Body composition		▸ Had visible muscle growth, their skin was tighter (n=3)	
Functionality	▸ Increased their ability to walk the stairs (is easier now) (n=2) ▸ Felt less stiff in the morning, and it was easier to get up and start the day (n=2) ▸ Noticed their muscles were activated (n=1)	▸ Perceived an improved balance (n=2) ▸ Increased their ability to walk the stairs (n=7) ▸ Perceived they were standing more firmly and surely (n=4)	▸ Perceived an improvement in balance (n=2) ▸ Perceived that the performance of the exercises is easier now (n=2) ▸ Increased their ability to walk the stairs (n=2) ▸ Increased their ability to get out of bed (n=1)

Table 5 continued.

SarQol domains	**Aspects mentioned by participants during interviews*** **Due to the ProMuscle in Practice intervention, participants…**	**Aspects mentioned by physiotherapists during interviews†** **Physiotherapists mentioned that due to the ProMuscle in Practice intervention, participants...**	**Aspects mentioned by exercise trainers during interviews‡** **Exercise trainers mentioned that due to the ProMuscle in Practice intervention, participants…**
Activities of daily living	▸ Were able to work in the garden for a longer period (n=1) ▸ Perceived an increased strength in their arms (it is now possible to open a jar) (n=1)	▸ Reduced pain symptoms (n=2) ▸ Increased their ability to get out of the bathtub (n=2) ▸ Increased their ability to get dressed, tie their shoes (n=3) ▸ Increased their ability to get up from a chair (n=2) ▸ Were able to sustain activities for a longer period and suffer less from fatigue (N=6)	▸ Mentioned that their shoulder injury has disappeared due to the exercises (n=1) ▸ Increased their ability to carry bags with groceries (n=1) ▸ Increased their ability to perform ADL (n=1)
Leisure activities	▸ Increased their ability to cycle (is easier now) (n=4) ▸ Noticed their energy level to carry out activities increased (n=1)	▸ Mentioned that cycling is easier, goes faster, is without pain now, can be sustained for a longer period and without the use of electrical support (n=8) ▸ Carried out more activities, e.g. more walks in the neighbourhood (n=2)	▸ Increased their ability to cycle (n=1)
Fears		▸ Increased their self-assurance (n=2)	

n=number of participants/physiotherapists/exercise trainers that mentioned the aspect.

**In total 20 participants were interviewed, but three did not participate in the moderate support program. 13 out of 17 participants mentioned benefits of the intervention.*

†In total 18 physiotherapists were interviewed. In one interview the topic of intervention effects was not discussed. The remaining 17 physiotherapists noticed benefits of the intervention. ‡In total 9 exercise therapists were interviewed. One of the exercise trainers did not keep track of intervention effects. Seven of the exercise trainers noticed benefits of the intervention.

DISCUSSION

The current study showed that the PiP intervention has an 82.4% probability of being cost-effective at a WTP of €12.000/point increase in SPPB. This probability was 99.4% at a WTP of €20.000/second increase on the chair-rise test. No change in QALY on EQ-5D-5L was found, whereas interviews revealed a broad range of function- and quality of life-related perceived benefits.

Quality of Life

Comparable interventions targeted at fall prevention reported inconsistent results regarding cost-effectiveness, and often found no change in quality of life.[75–77] We as well found no change in QALY using EQ-5D-5L, for which the explanation is twofold. On the one hand, the mean health status of our study population at baseline was 0.86 ± 0.11, being slightly higher than the health status of a Dutch reference population aged 70 years and over (0.85 ± 0.15).[194] The relatively high baseline health status may represent a ceiling effect, limiting room for improvement. Often, public health interventions lead to limited changes in quality of life[201]. On the other hand, a generic questionnaire was used to measure quality of life. Although generic questionnaires are often used in economic evaluations and enable comparison of results between clinical studies, they seem to be insensitive to capture subtle changes in quality of life in older adults, as reported by cross-sectional studies[202–204], a systematic review[205] and meta-analyses.[206,207] So generic questionnaires are useful when investigating i.e. a diseased population in medical studies, but it seems that preventive interventions might need another approach.[208] For this reason, we additionally included performance measures. Conducting interviews led to a comprehensive overview of practical examples regarding perceived benefits. The qualitative results from the interviews were reflected by the quantitative results, showing improvements on muscle strength, lean body mass, and physical functioning.[28] Additionally, comparable interventions consisting of protein intake and resistance exercise show positive effects that are in line with our quantitative as well as qualitative results, including benefits on i.e. physical health, body composition, locomotion, and functionality.[23,31]

Specific questionnaires are needed to capture subtle changes in quality of life, and therefore quality of life questionnaires targeting particular conditions seem more suitable.[172,209,210] A broad range of specific instruments for musculoskeletal health is already available, including questionnaires for osteoporosis, arthritis and sarcopenia.[209,210] The SarQol is a validated quality of life questionnaire specifically for sarcopenic older adults.[199,211–213] In our study, participants as well as professionals indicated a wide range of function-related perceived benefits due to the intervention (table 5). These benefits corresponded with the domains of the target specific SarQol questionnaire. Whereas measures such as EQ-5D-5L might not be able to detect the range of effects of a preventive intervention on the short term, adding targeted and specific quality of life instruments seems to be valuable.[213]

SPPB

Cost-effectiveness analyses resulted in an ICER of €2988/point increase in SPPB. The intervention has an 82.4% probability of being cost-effective at a WTP of €12.000/point increase in SPPB. An even higher probability (99.4%) of being cost-effective was found for the chair rise test at a WTP of €20.000/second improvement. No WTP thresholds are yet available for physical functioning outcomes. However, we can put value to these results, by clarifying the meaning of 1-point change in SPPB and by elaborating on care related costs. Individuals with a lower SPPB score are predicted to have adverse outcomes such as decreased mobility, disability, hospitalization, nursing home admission and even death.[163,214–218] More specifically, Volpato and colleagues showed that 1-point increase in SPPB score at hospital discharge was associated with a 14% reduction of the risk of new hospitalizations and death combined over a 12-month period.[215] In line with this, Miller and colleagues showed that every 1-point increase in baseline SPPB score was related to 5% decreased risk of hospitalization, 12% decreased risk of subsequent mortality and 21% decreased risk of nursing home placement over a 36-months follow-up period.[217] Costs related to nursing home placement including daytime activities are €168 per day, adding up to €61.320 per year.[198] Besides, total healthcare costs for older adults in a nursing home including treatment are ten times higher than for community-dwelling older adults in the Netherlands (€84.300 vs. €7338 per person per year, respectively).[219–221] These findings show that an investment of €12.000 for one-point improvement in SPPB score could lead to lower hospitalization, nursing home admission and mortality and its associated costs in the long run.

Health care costs

A time period of 24 weeks is relatively short to capture changes in healthcare use, especially in preventive intervention programs.[208,222] Direct healthcare costs over the 24-week study period were higher in the control compared to the intervention group (€1697 ± 2656 vs. €1336 ± 1466, respectively). Specifically, control participants had higher costs for physiotherapist consultations compared to intervention participants. Additionally, homecare and medication use were higher in the control group, although those differences were mainly caused by a few participants having rather high costs compared to average. Future studies should include an extended follow-up period to measure possible changes in costs and effects on the long term. As healthcare utilization data was collected using questionnaires, both under- and overreporting may occur.[223,224] To enhance accuracy in collecting healthcare utilization data, we collected data every 3 months and participants used cost diaries to keep track of their healthcare use in between measurements.

Intervention costs

Costs for the intensive support intervention were relatively high compared to the moderate support program (€1014 vs. €105 per person, respectively). However, when implementing the intervention in the real-life setting, costs are lower. For the 12-week PiP implementation program, offered at several physiotherapist practices from 2019 onwards, participants were charged €210. The lower costs for the implementation program compared to the intensive intervention resulted from several factors. First of all, costs for purchasing fitness equipment and rent of rooms were eliminated, since the implementation program was conducted in the physiotherapist practice, that already provided access to equipment and rooms. Secondly, dietitian consultations were reimbursed by health insurance, as three hours of dietitian consultations per year are included in health insurance in the Netherlands.[225] Lastly, costs for protein-rich products were lower during the implementation program. In the current analysis, we included costs for protein-rich products according to market prices. During the moderate support program, participants had to purchase their own protein-rich products and 58% indicated no increased costs. The remaining 42% had average additional costs of €7 per week (€84 for 12 weeks). It is expected that costs of protein-rich products are comparable during the moderate support program and the implementation program. Overall, organising the PiP implementation program results in lower costs compared to costs of the PiP intervention.

CONCLUSIONS AND IMPLICATIONS

The PiP intervention resulted in a positive change in physical functioning and was found to have an 82.4% probability of being cost-effective at a WTP of €12.000/point increase in SPPB. The EQ-5D-5L questionnaire did not measure any changes, whereas interviews revealed a range of function-related benefits. Because generic quality of life questionnaires seem less suitable to capture effects of preventive health interventions such as PiP, future studies are advised to include targeted and specific questionnaires.

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CHAPTER 6 - SUPPLEMENTARY MATERIAL

Supplementary material 1. *Extended description of the intervention.*

The intervention consisted of a 12-week intensive support program, followed by a 12-week moderate support program. The intensive support program included twice weekly progressive RE, primarily focused on the leg muscles. Each session had a duration of 1 hour, was group-based (4-7 participants) and was supervised by physiotherapists according to PiP manuals. Training sessions consisted of a warm-up, resistance exercises (leg press, leg extension, lat pulldown, vertical row, and chest press) and a warm-down. The intensity of the exercises started with 3 to 4 sets of 15 repetitions (50% of 1-repetition maximum (1RM)) and extended to 4 sets of 8-12 repetitions (75-80% of 1RM) in weeks 7 to 12. Additionally, a dietitian advised participants to increase their protein intake to 25 grams per main meal, via individual consultations (at baseline, in the first week, and after 6 weeks). The dietitian provided information on the importance of a protein-rich diet and advised participants on how to achieve a protein intake of at least 25 grams during breakfast, lunch, and dinner. Additionally, participants received protein-rich dairy products, cakes, or desserts, fitting with their preferences, to incorporate in their diet.

After the first 12 weeks, participants of the intervention group were encouraged to continue with the optional moderate support program, to maintain their adapted lifestyle pattern. Local fitness centers provided group based RE training 1-2 times a week. Physiotherapists and other skilled trainers supervised the progressive RE sessions. Each training session had a duration of one hour and was mainly focused on leg muscles but also included additional balance or functional exercises. Strength exercises were described in a manual, but the type of exercises differed per location. Next to this, a health promotor and a dietitian conducted a nutrition workshop, comprising five 1,5-hour meetings. During each meeting, participants received information on dietary protein, they shared experiences, and prepared and tasted protein-rich dishes.

Supplementary table 1. *Inclusion and exclusion criteria of the ProMuscle in Practice intervention.*

Inclusion criteria
‣ Aged 65 years or over
‣ Living independently in one of the selected municipalities (Apeldoorn, Epe, Ermelo/Putten, Harderwijk, Ede)
‣ Mastery of the Dutch language
Meet one of the two following criteria:
‣ Score 1 or more points on the Fried frailty criteria[153]
‣ Experience difficulties in daily activities and being inactive (ie, not participate in RE > 30 minutes a day on more than 2 days a week
Exclusion criteria
‣ Allergy/sensitivity to milk proteins or being lactose intolerant
‣ Diagnosed COPD or cancer
‣ Diagnosed diabetes Type 1 or 2 or hypertension (systolic blood pressure > 160 mmHG) that is unstable or not well regulated with medication
‣ Severe heart failure
‣ Renal insufficiency (eGFR < 30 ml/min)
‣ Physical or cognitive impairment that hinder participation
‣ Receiving terminal care
‣ Not fully recovered from newly fitted artificial hip or knee prosthesis
‣ Recent surgery (<3 months)

***Supplementary table* 2.** *Detailed description of unit costs not mentioned in table 2.*

Direct healthcare costs	Unit costs in € ($)
General practitioner	
Visit to practice	33.9 per visit (38.3)
Phone contact for medical prescription	17.4 per contact (19.7)
Phone consultation	17.4 per consultation (19.7)
Home visit	51.3 per visit (58.0)
Visit to practice (outside working hours)	109.9 per visit (124.2)
Home care	
Domestic help	20.5 per hour (23.2)
Medication/support stockings assistance	51.3 per hour (58.0)
Personal care	51.3 per hour (58.0)
Nursing care	74.9 per hour (84.6)

***Supplementary table* 3.** *Total change over 24 weeks in SPPB, chair-rise test, and QALY for the total study population and for complete cases*

	Intervention group Mean ± SD	Control group Mean ± SD	Mean difference (95% CI)
Total study population	**n=82**	**n=86**	
SPPB* (points)	0.2 ± 1.5	-0.1 ± 1.5	0.3 (-0.2; 0.8)
Chair-rise test† (sec)	0.8 ± 2.8	-0.4 ± 2.8	1.2 (0.4; 2.1)
Total QALY† over 24 weeks	0.37 ± 0.06	0.37 ± 0.06	0.00 (-0.02; 0.02)
Complete cases	**n=51**	**n=50**	
SPPB* (points)	0.4 ± 1.4	-0.2 ± 1.5	0.6 (0.0; 1.2)
Chair-rise test (sec)	0.9 ± 2.6	-0.5 ± 3.0	1.5 (0.4; 2.6)
Total QALY† over 24 weeks	0.37 ± 0.06	0.37 ± 0.06	0.00 (-0.02; 0.02)

**SPPB: Short Physical Performance Battery. †Chair-rise test: analyses were performed with inverse minus/plus signs, to better present effects. §QALY: Quality Adjusted Life Years*

7

General discussion

The decline in muscle mass, muscle strength and physical functioning in older adults can be counteracted by resistance exercise and an increased protein intake. The lifestyle intervention ProMuscle in Practice includes these two elements and was found to be effective in improving older adults' muscle health. However, the ageing population is characterized by a large variability, not only in terms of personal characteristics, ethnicity and health status, but also in its responsiveness to treatments or interventions. In order to fit the needs and possibilities of older adults, and to serve a broad population with regards to health promotion, the heterogeneity in health and responsiveness needs to be assessed. In addition, organisational and contextual factors are expected to influence responsiveness to lifestyle interventions. Therefore, the aim of this thesis was threefold: 1) To study the sarcopenia prevalence, dietary protein intake, and underlying behavioural and environmental factors affecting protein intake in ethnic minorities in the Netherlands (chapter 2, 3), 2) To study personal, organizational, and other contextual factors affecting responsiveness to a diet and exercise intervention (chapter 4, 5), and 3) To study the cost-effectiveness of ProMuscle in Practice (chapter 6). In the current chapter, the results are placed in perspective according to the wider framework of literature, and implications and recommendations for practice and future studies are provided.

MAIN FINDINGS

Sarcopenia prevalence was found to be sex- and ethnic-specific. A cross-sectional study of the HELIUS data **(chapter 2)** revealed that sarcopenia prevalence was found to be lowest in Turkish women and men (2.4% and 29.8% respectively) and highest in South-Asian Surinamese women and men (30.5% and 61.3% respectively). Within each ethnic subgroup, sarcopenia prevalence differed substantially between men and women. Besides, a higher protein intake was associated with a 4% lower odds of sarcopenia in the total group and across ethnic groups, being only significant in the South-Asian Surinamese group. **Chapter 3** showed that 40-60% of the Dutch, South Asian Surinamese, African Surinamese, and Moroccan older adults did not reach the dietary protein recommendation (1.0 g/kg bodyweight/day). Major sources of protein intake were found to be ethnic-specific. In addition, focus group discussions revealed that participants of all ethnic subgroups appeared to have little knowledge and awareness of protein and its role in ageing.

Intervention effects were found to be subgroup specific. **Chapter 4** was dedicated to answering the question 'Who benefits most from the ProMuscle in Practice intervention?'. In-depth analyses showed that participants aged 75 years and younger and women benefited to a great extent from the intervention, as they improved significantly on nearly every outcome. Effects in participants with and without a mobility-impairing disorder (frailty, sarcopenia, or osteoarthritis) were comparable, indicating that the intervention is suitable for older adults regardless of having a mobility-impairing disorder.

Intervention effects were not only found to be subgroup specific, but also context specific. **Chapter 5** presents the effects and contextual factors of the ProMuscle intervention in three different contexts: the controlled setting (ProMuscle), the real-life setting (ProMuscle in Practice) and the real-life setting of the implementation pilots (ProMuscle Implementation Pilots). We found varying effects across the three settings, with the highest effects in the Implementation Pilots. Improvements on chair-rise performance were found in ProMuscle (-2.0 ± 7.0 sec, p=0.186), ProMuscle in Practice (-0.8 ± 2.9 sec, p=0.019) and the Implementation Pilots (-3.3 ± 4.2 sec, p=0.001). Similar results were found for leg strength in ProMuscle (32.6 ± 24.8 kg, p<0.001), ProMuscle in Practice (17.0 ± 23.2 kg, p<0.001) and the Implementation pilots (47.8 ± 46.8 kg, p<0.001). The variation in effects across settings can be explained by several aspects, including room for adapting and tailoring the intervention, the availability of and access to facilities, the involvement of experienced professionals, and participant characteristics.

Next to reporting group specific prevalences of sarcopenia and group- and context specific effects of lifestyle interventions, gaining insights into costs of such interventions is of major importance. In **chapter 6**, the cost-effectiveness and perceived benefits of the ProMuscle in Practice intervention were assessed. Results show an Incremental Cost-Effectiveness Ratio of €2988 per point increase in the Short Physical Performance Battery (SPPB). The intervention has an 82.4% probability of being cost-effective at a willingness to pay of €12.000 per point increase in SPPB. No change in quality of life was found using the EQ-5D-5L questionnaire; however, interviews revealed a wide range of function-related perceived benefits.

MICRO, MESO, MACRO

One size does not fit all. This statement applies to the implementation of public health interventions, as such interventions are not being implemented in a vacuum. Their success is affected by contextual aspects at numerous levels related to participants, intervention providers, organizations, communities, and policies. As introduced in chapter 1 of this thesis, factors related to public health interventions can be categorized according to three levels: micro, meso, and macro. The micro level includes personal characteristics of the target population, the meso level includes the organization and its professionals, and the macro level includes the external setting on the societal level. Variety within these levels can lead to heterogeneity in effect sizes of interventions. In this chapter, for each level, results are first placed in perspective and implications for future research are provided. Next, implications for practice are elaborated on.

MICRO LEVEL

Results in perspective and implications for research

Personal characteristics that might lead to heterogeneity in responsiveness to diet and exercise interventions include the distribution of age, sex, disease, and ethnicity in the target population. Starting with age, chapter 4 showed that older adults aged 75 years and younger were found to improve on physical functioning, leg strength, and lean body mass. Specifically, the increase in lean body mass was significantly higher in participants aged 75 years and younger (+1.9%) compared to participants aged 75 years and older (+0.1%). We were among the first to compare effects of diet and exercise interventions in subgroups of adults aged 65 years and older. Recent meta-analyses primarily compared effects of diet and exercise interventions in younger (<45-50 y) vs. older adults (>45-50 y).[21,31] Meta-analyses reported similar effects in leg strength for those younger and older adults.[21,31] However, effects in fat free mass (FFM) were either found to be similar across ages[21] or greater in younger compared to older adults.[31] It is known that in both younger and older adults, skeletal muscles are sensitized by resistance exercise to dietary protein ingestion.[226] However, the sensitivity to anabolic stimuli, such as exercise and protein intake, is reduced in older adults, also called anabolic resistance.[42,167,168] Moore and colleagues (2015) showed that the amount of protein needed to maximally stimulate myofibrillar protein synthesis is higher in older compared to younger men (0.40 vs. 0.24 g/kg/meal, respectively).[42] Therefore, older adults may need more protein compared to younger adults to reach similar effects in response to resistance exercise.[45,167] This might explain the larger improvements in younger compared to older adults in response to diet and exercise interventions. Most studies investigated the effect of diet and exercise interventions in younger vs. older adults, instead of subgroups of older adults. Besides, the variation in results (in terms of confidence intervals) in the older subgroups indicates the presence of heterogeneity. This should be further investigated and therefore, more research should be targeted on comparing the effects of such interventions in subgroups of older adults (>65 years). If our results are to be confirmed, and subgroups of older adults respond differently to such interventions, it might be suitable to further adjust the intervention to specific age groups.

A second factor at the micro level is sex. The sex-based differences in sarcopenia prevalence were already highlighted in chapter 2. In addition, chapter 4 presented sex-related differences in intervention effects. Women improved significantly in physical functioning, leg press and leg extension strength, but not in lean body mass, whereas men improved significantly in lean body mass and leg extension strength only. Significant sex-based differences were only found in leg press strength: women increased 22.8 kg on leg press strength (95% CI: 12.9; 32.8), compared to 7.4 kg in men (95% CI: -3.8, 18.6). Meta-analyses reported either no sex-based differences in leg muscle strength[49] or an increase in men but not in women[23] in response to a diet and exercise intervention. According to effects in FFM or lean body mass, two meta-analyses were in line with our results and reported no sex-based differences in response to a diet and exercise intervention in FFM or lean body mass change.[41,49] Another meta-analysis found a significant increase in lean body mass in men but not in women.[23] Summarizing, meta-analyses show inconsistency concerning sex-based differences in response to diet and exercise interventions. This inconsistency can be due to variety in included studies, specifically intervention characteristics, such as length of the intervention and type of RE or protein intake, and variety in methodological aspects, such as inclusion criteria leading to differences in participant characteristics (i.e. residential situation or health status).[23,31,41,49] Besides, several of the meta-analyses included fewer studies conducted in women then in men, limiting the evidence in older women and complicating comparability between sexes.[23,31,41] Several implications for research can be connected to these findings. Overall, sex-differences in response to diet and exercise interventions may be present. Our results indicate stronger improvements in women compared to men. This can partially be explained by the fact that women in our study population had a lower starting point in terms of leg muscle strength compared to men. This is in line with other studies, in which it is estimated that muscle strength of women is about 40-60% of that of men.[227–229] The lower starting point in terms of muscle strength leaves more room for improvement. As mechanisms underlying these sex differences remain unclear, future research should focus on gaining insights into these mechanisms. Besides, fewer studies have been performed in women. More research in women should be conducted to close this gap and allow for a fair comparison between the sexes.

A third factor at the micro level is ethnicity. Chapter 2 and 3 show ethnic specificity in terms of dietary protein intake, cultural determinants related to dietary protein intake, sarcopenia prevalence and the association between dietary protein intake and sarcopenia prevalence. To be specific, dietary protein intake ranged from 0.96 g/kg BW/d in African Surinamese women to 1.38 g/kg BW/d in Turkish men. Besides, food products contributing mostly to daily protein intake were found to be ethnic-specific. Additionally, sarcopenia prevalence ranged from 2.4% in Turkish women to 61.3% in South-Asian Surinamese men. Qualitative data showed that all ethnic groups seemed to lack knowledge and awareness of the importance of protein for healthy ageing. Besides, cultural background appeared to determine food choices, eating habits, and beliefs about health behaviours. In line with our results, food intake in general, and dietary protein intake in particular, is found to be influenced by cultural and social aspects.[68,69] These aspects appear to be ethnic-specific. For example, traditions and hospitality were found to be important cultural aspects that influence food consumption in certain ethnic groups.[68,69] In addition, sarcopenia prevalence was found to be ethnic-specific. Although variations in skeletal muscle mass and muscle strength across ethnic minority groups were indicated in multiple studies,[61,62,105,107,108] variations in sarcopenia prevalence have only been documented for certain ethnic groups.[80] The variation across ethnic groups might be due to several aspects, including biological factors such as genes or body composition, distribution of chronic diseases, and health-related behaviours such as physical activity levels.[61,62,80,105] However, underlying mechanisms are yet unclear and need further investigation. Overall, it is important to further identify, unravel and tackle differences in health status across ethnic minorities. As presented in this paragraph, first steps in identifying and unravelling differences in health status and underlying health behaviours across ethnic minority groups have been made. Ethnic-specific interventions seem to be justified for tackling sarcopenia. However, few studies focused on tackling health disorders, such as sarcopenia, in ethnic minorities. Therefore, future studies should investigate the effects of diet and exercise interventions in ethnic minority groups, to counteract sarcopenia. First steps in the right direction are being made: The ProMIO 2.0 study is currently investigating the effectiveness and implementation of a diet and exercise intervention for older ethnic minorities.[230]

A fourth factor at the micro level is health status. Research has shown that a major part of older adults suffer from morbidity and disability, and in particular encounter mobility-related impairments.[8,231] Besides, as interindividual variability regarding functional status and mobility increases over the life course, heterogeneity in mobility is present in the ageing population. Mobility-impairing conditions that are common in older adults include frailty, sarcopenia, and osteoarthritis. Chapter 4 showed that older adults with and without a mobility-impairing disorder responded equally to our diet and resistance exercise intervention. This implies that both groups can benefit from the intervention. Evidence from other studies on the effects of diet and resistance exercise interventions in older adults with mobility-impairing disorders differs according to the disorder studied. Regarding frailty, results are rather straightforward: reviews show that older adults who were (pre-)frail seem to benefit from diet and exercise interventions.[25,50,51,82] However, heterogeneity in mobility levels was found to be present within a group of very frail older adults.[8] The authors suggest that very frail older adults should not be treated as a homogeneous group, and suitable public health interventions should be designed in order to fit this heterogeneous population. Regarding sarcopenia, studies are often targeted at preventing sarcopenia. However, studies that did include older adults with sarcopenia reported improvements on muscle mass, muscle strength, and physical functioning in response to a diet and resistance exercise intervention.[41,49] Last, studies on the effects of diet and resistance exercise interventions including older adults who suffer from osteoarthritis are often postoperative and include participants who underwent total joint replacement. Results are predominantly positive and include improvements in muscle mass, muscle strength, and functional outcomes.[52] Thus, diet and exercise interventions seem to be effective not only in healthy older adults but also in subgroups suffering from mobility-impairing disorders. As described previously, the ageing population is heterogeneous in terms of health status and presence of diseases. The incidence of a disease or the occurrence of a fracture can have detrimental effects for older adults. This is elaborated on in Box 1.

Box 1. The downward spiral

In general, when ageing, the risk of developing chronic diseases is increased and multi-morbidity is relatively common.[6,232] Diseases that are associated with ageing include, but are not limited to, cardiovascular disease, osteoporosis, dementia and diabetes.[232] Sarcopenia, characterized by a decrease in muscle strength and muscle mass, is also common with increasing age.[13] The consequences of sarcopenia include a decrease in physical functioning, mobility limitations, falls, hospitalization and mortality.[13,17,109] In the presence of sarcopenia, a catabolic crisis, such as the onset of additional diseases or a fracture, can have detrimental effects.[13,232] To illustrate this, figure 1 compares the *traditional sarcopenia* process with a *catabolic crisis* process. In the first situation, the loss of lean muscle mass with ageing can be depicted as a decreasing, more or less straight, slope. In the second situation, when the ageing process is interrupted by crises, such as an acute illness or a fracture, the loss of lean muscle mass with ageing is accelerated. Recovery from such crises is often limited and incomplete.[233] A faster decline in muscle loss enhances risk of mobility limitations, disablement and bed rest. In turn, the lower activity levels lead to an increased loss of muscle mass, resulting in a downward spiral.

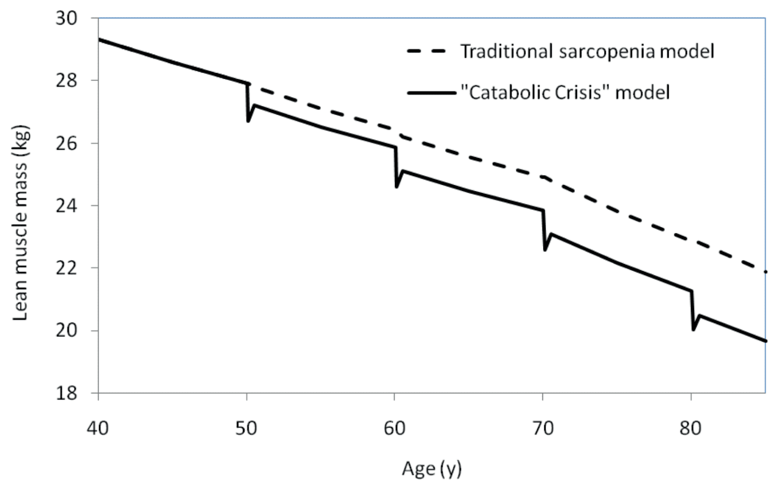


Figure 1. *Catabolic crisis. From English et al (2010)*[233]

7

Implications for practice

The heterogeneity in the ageing population and the interindividual differences in effects of lifestyle interventions lead to several implications for practice at the micro level. Firstly, our results show that a diet and exercise intervention leads to sex- and age-specific effects in older adults. Besides, dietary protein intake and sarcopenia prevalence were found to be sex- and ethnic-specific. In contrast to our results, literature remains inconclusive. Therefore, implications for practice include the necessity to consider diversity in age, sex, ethnicity, and health status when developing lifestyle interventions or lifestyle-related recommendations. Take for example the recommendations in terms of exercise and protein intake for older adults. In 2017, the Dutch Health Council reevaluated the exercise guidelines. Older adults are now advised to perform moderate or heavy exercise for 2.5 hours per week and conduct muscle- and bone strengthening exercises two times per week. Besides, they are advised to conduct exercises to improve balance.[234] In 2021, the Dutch Health Council reassessed the dietary reference intakes for protein. The advice for adults (>18 years) involves a protein intake of 0.83 g/kg/d, in which no distinction has been made for younger and older adults. Expert groups in other countries recommend older adults to increase their protein consumption to 1.0-1.2 g/kg/d,[235–237] which is in line with recommendations from scientific expert groups.[129,135,238] So on the one hand, older adults are advised to enhance their exercise levels. On the other hand, the benefits of increasing protein intake when increasing physical activity are not fully recognized, as the protein recommendations specifically for older adults were not raised.[239] The advice from the Health Council is targeted at healthy older adults. However, the current protein recommendation is expected to be insufficient for older adults who are frail or who suffer from underlying disorders. Again, this highlights the importance of tailoring. It is important to consider the potential influence of factors such as age, sex, ethnicity, and health status during the development of recommendations or lifestyle interventions. In this way, advice and lifestyle interventions could be tailored even more to the needs of specific subgroups of older adults.

Secondly, from our results and other studies it appeared that ethnic minorities are more likely to have an unfavorable health status compared to the majority population. Besides, their knowledge and awareness on the importance of ageing-related health behaviors such as an increased protein intake is often lacking. In addition, cultural aspects seemed to influence health-related behaviors. Therefore, it is necessary to adjust the ProMuscle in Practice intervention to ethnic minorities, taking social and cultural aspects into account. Literature shows that behavioral health interventions are more likely to result in statistically significant effects when a set of cultural adaptations was applied and if family values were considered.[120] With regard to food consumption, family, traditions, and hospitality play a major role.[68,69] In order to provide a fitting advice to increase protein intake in an ethnic minority group, food culture and ethnic-specific dietary intake should be considered. Although our research mainly focused on dietary intake, exercise is also subject to cultural-related perspectives. Cultural sensitivity plays a role, for example, when religious practices demand men and women to exercise separately.[240,241] Besides, some ethnic minorities prefer culture-specific exercises, which were also found to enhance participation of ethnic minorities in physical activity programs. Cultural aspects can be intertwined in exercises, for example through including specific music or traditional dance into a warming up.[242] Other effective strategies to align with specific cultures, include targeting interventions to older adults from a similar cultural and linguistic background, or appointing a trainer that speaks the language and empathizes with the values of the older adults.[241,242] In order to offer an effective and target group-specific diet and exercise intervention for older ethnic minorities, it is necessary to study (cost-)effectiveness and implementation of such an intervention. This is currently being investigated with the ProMIO 2.0 study.[230]

Thirdly, our results as well as those of other studies indicate that diet and exercise interventions are effective in healthy older adults as well as in subgroups suffering from mobility-impairing disorders. However, ageing is associated with a range of chronic diseases and multimorbidity is common. In light of the ProMuscle in Practice intervention, the presence of chronic diseases asks for customization. This is elaborated on in Box 2.

Box 2. Heterogeneity in health status demands customization

In this box, the difference in offering ProMuscle in Practice to older adults with and without diseases is highlighted. The first paragraph describes older adults with limited diseases. The second group describes older adults with one or multiple diseases, which is illustrated by two diseases common with ageing.

Noncomplex health status

Positive effects of the ProMuscle interventions have been found in (pre-)frail older adults who are living at home, and have limited additional disorders.[25,28,82] Cooperation of a physiotherapist, dietitian and general practitioner would be sufficient to guide such a population during ProMuscle in Practice. Ideally, the role of the general practitioner consists of assessing the older adult's health status by performing a medical check before participation. During the first 12-week program, the physiotherapist and dietitian adjust the intervention to the level and needs of the participants. After the first 12-week intervention, older adults can continue their changed habits under less intensive guidance, such as a sports or fitness instructor, and a dietitian or lifestyle coach.

Complex health status

When participants are suffering from one or multiple diseases, their health status is often more complex and guidance during ProMuscle in Practice would be more extensive. One disease that is common with ageing, is type 2 diabetes mellitus (T2DM). Older adults with T2DM have a two to three times increased risk of evolving physical disability compared to older adults without T2DM.[243,244] Besides, sarcopenia has been indicated as a cause as well as a consequence of T2DM.[245,246] In addition, T2DM in older adults is known to be heterogenous, in terms of severity of the disease, presence of comorbidities, and functional status of the older adults.[247] These factors contribute to the complexity of the situation and should be considered in case of management and treatment of T2DM in older adults. Other common diseases in the ageing population are cognitive disorders, such as dementia. Healthy lifestyle behaviours, such as physical activity and a healthy diet, have been associated with a reduced risk of cognitive decline in healthy older adults.[248–250] However, large-scale RCTs should confirm the efficacy of multidomain interventions, such as exercise and diet combinations, in delaying cognitive impairment in older adults.[251,252] T2DM and dementia are only two examples of diseases that are prevalent in the ageing population. When diseases are present, the situation is often more complex, and other professionals need to be involved in guiding ProMuscle in Practice. Again, the general practitioner plays a role in assessing eligibility for the intervention by checking the medical status of the participants. At this stage, it might also be possible that another treatment or intervention is more suitable than ProMuscle in Practice. If the participant is enrolled in ProMuscle in Practice, specialized care and supervision is necessary, and the geriatric physiotherapist comes in. A geriatric physiotherapist is specialized in the care for vulnerable older adults with a more complex health status.[253] As highlighted before, older adults suffering from a disease can be considered as a heterogeneous group, because a specific disorder can affect people in different ways.[8,247] Therefore, a geriatric physical therapist should not only have deep knowledge of the specialty content, he or she should also be creative in adjusting the intervention to more complex needs of participants.[253] The dietitian should guide the older adults' to increase their protein intake, taking into account the possible influence of or interaction with disorders that are present.

MESO LEVEL

Results in perspective and implications for research

The meso level, also referred to as the 'inner setting', includes the organization in which the intervention is being conducted, and its professionals.[32,70] Variety within this level can result in heterogeneity in effect sizes of interventions.[254,255] Chapter 5 shows that implementing the ProMuscle in Practice intervention in different settings, led to different results. Effects on chair-rise test and leg press strength were found in the controlled setting, remained present in the real-life setting and were even more pronounced in the real-life setting of the implementation pilots. Several factors contributed to the variation in effects and are related to the organization, the professionals involved and the target population. Aspects related to the target population are already covered at the micro level and will not be discussed in the current section. Aspects related to the organization and its professionals will be discussed in more detail below.

In line with our results, other studies also report that implementing interventions in different organizations, likely results in varying outcomes.[254–256] An example is the implementation of a physical activity promotion program for older adults into three varying community organizations (CHAMPS III program).[255] Results showed a trend towards an increased physical activity level at two of the three organizations. The authors suggested that the variety in effects across settings is likely associated with variety in participant characteristics, the content of the intervention, and practicalities related to the intervention such as scheduling conflicts.[255] According to the Consolidated Framework for Implementation Research (CFIR; figure 2), *structural characteristics* of an organization could also influence intervention effects.[70] Within the CHAMPS III program, organizations differed in size, goal, infrastructure and clients, which might have influenced the effects.

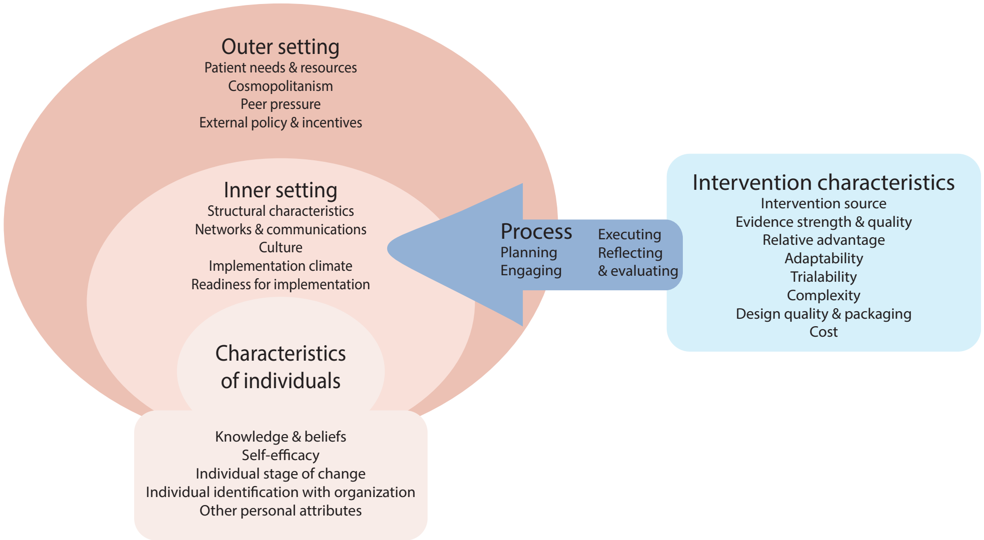


Figure 2. *Overview of the Consolidated Framework for Implementation Research (CFIR). Adapted from Damschroder et al (2009)*[70]

Switching back to CFIR, another aspect that contributes to variation in intervention effects across settings according to this framework, is *readiness for implementation*. This is related to the organization's commitment of implementing an intervention. It consists of three subcategories: available resources, access to information and knowledge, and leadership engagement.[70] These aspects also contributed to the variation in effects of the ProMuscle interventions across settings. In the real-life setting of the implementation pilots, facilities, and resources such as a safe, spacious training room with training machines were available, information and knowledge related to the intervention was accessible, and leadership was highly involved and committed to conduct the intervention. In line with this, these factors were also highlighted in a recent study, which investigated factors that influence implementation of a community-based health promotion intervention for older adults.[71] An increasing number of studies has focused on assessing factors that contribute to successful implementation in practice, since implementation can be a complex process that requires time and resources, and nevertheless can be unsuccessful.[257–260] These studies have shown that an essential early step is to examine the organizational readiness for implementation or change. Readiness for change refers to "the extent to which organizational members are psychologically and behaviorally prepared to implement organizational change".[258–261] A large number of tools are available to assess readiness for change. However, most of them have not been tested for validity or reliability, and most of them were developed for a specific setting and population, which limits generalizability.[259,260] Therefore, it is important to either assess an existing tool for validity and reliability, or develop a valid and reliable tool that can be generalized to a broader population. Aforementioned challenges make selecting an appropriate tool complicated and time-consuming. However, multiple decision support instruments have been developed, which aim to aid implementers in choosing a readiness assessment tool.[262,263] Using such a tool will estimate an organization's level of readiness for change and can prevent investing unnecessary resources.[262] Therefore, in future studies, an organization's readiness for change should be assessed before starting an intervention.

An important factor that influences an intervention's implementation success at the level of the organization is the professional.[70] Professionals that were involved in the ProMuscle Implementation Pilots could be indicated as 'first users' or champions. Champions are individuals that are dedicated to support the implementation and are characterised by their perseverance and strong believe in the intervention.[70,184,185] They play an important role in the process of implementing an intervention and therefore belong to the subdomain *engaging* under the domain *process* of the CFIR (figure 2).[70] As champions are often highly committed to and an expert on the intervention, their involvement is associated with the intervention's success.[70,186,255] This is reflected by literature, as systematic reviews indicated the involvement of champions as an important feature that influences implementation.[186,264] Although champions are one of the key factors related to implementation success, their presence alone is not sufficient to induce change. Together with other aspects at the level of the intervention, the target population, and the inner and the outer setting, champions are deemed essential to implementation success.[186] To deepen this finding, a suggestion for future research includes exploring the questions *how* and *why* champions are important to implementation success.

Implications for practice

The ProMuscle in Practice intervention was conducted at physiotherapist and dietitian practices including community-dwelling older adults. Professionals that conducted the Implementation pilots were already involved in the ProMuscle in Practice study. These professionals can be referred to as *innovators* or *early adopters*, according to the diffusion of innovations model.[189] They were among the first to adopt a new intervention in their system. Besides, they were highly motivated, skilled, and committed to conduct the intervention and can therefore also be classified as *champions*. Their involvement most likely affected the intervention's implementation and eventually its effects in a positive way. Next, to enhance the number of locations that offer the ProMuscle in Practice intervention, it is necessary to additionally involve the *early* and *late majority*.[189] However, as each category of adopters is associated with a different set of characteristics, they may need another approach in terms of communication strategies. Whereas in general, innovators would conduct an intervention because it was proven to be effective and developed by scientists, the late majority places more trust in their fellows' subjective experiences with an intervention, which are communicated through personal networks.[189] Tailored strategies should be deployed to involve professionals belonging to different adoption stages. In practice, this can be translated to informational meetings and networks in which professionals that are experienced with ProMuscle in Practice inform or educate professionals that are interested in starting with the intervention. This and other strategies should be investigated in the context of implementing ProMuscle in Practice in the Netherlands.

In order to reach a broader population, such as older adults with multiple diseases, the intervention could also be implemented in different settings.[254] An example of such a setting is a nursing home. Before implementation, it is important to check if the intervention is the best possible and fitting intervention for the subgroup. Implementing an intervention in such a setting accompanies an organization-wide change and involves multiple levels of the organization.[265,266] Besides, most residents have a combination of medical disorders and need assistance with multiple activities of daily living.[267,268] In addition, often a large number of staff, including several disciplines, work in a nursing home.[269] In addition, staff turnover is found to be high. This leads to changing, poorly instructed personnel, which restricts the ability to offer a person-centred intervention.[270–272] Next to the aforementioned barriers, multiple enablers are found to enhance implementation success. As mentioned before, tailoring the intervention and the corresponding training activities to the organizational context, to the values and working procedures of staff and to the needs and abilities of the residents increases the changes of implementing change in a nursing home.[266,272,273] Before implementing ProMuscle in Practice in another setting, barriers and enablers specific to implementation of such an intervention in that setting should be investigated. After that, a study is needed to investigate the effectiveness and implementation of the intervention in the new setting.

So, the next step is to involve new organizations and professionals in implementing the intervention. Different strategies should be used to involve them, and the intervention should be adapted to fit the setting, its individuals, and the target group. The importance of adaptations for an intervention's success is further highlighted in Box 3. Besides, before starting the implementation, the organizational readiness for change should be assessed, preferably using a reliable and valid tool.

Box 3. The importance of adaptations

A key factor for an intervention's success is the room for adapting and tailoring the intervention to the local context.[70,73,179,180,254,256,274] Adaptation can be defined as the process of intervention modification to fit specific characteristics and needs of a new context and enhance intervention acceptability, while retaining the basic components of the intervention.[180,254] It appears from literature that the main reasons for adaptations to evidence-based public health interventions in community settings include fitting to a specific culture or a specific target population.[274] Small adjustments to the intervention can be made to increase suitability to fit a certain subgroup such as the younger older adults, the oldest old, men or women. Examples of adaptations include the intervention's intensity and type of additional exercises. Healthcare professionals are familiar with their community and are therefore able to fit the intervention to the needs and preferences of the local community, also called tailoring.[73] Tailoring an intervention leads to improved program outcomes, better implementation, and was found to be a key element for success in physical activity and dietary interventions.[46,73,181–183] In addition, as each organization accompanies different characteristics, adapting an intervention to a specific organization is of importance. If the intervention does not fit the setting, individuals involved in implementation are likely to resist the intervention.[70] This is in line with our results, which show increased effects when the intervention was adapted to the real-life setting of the implementation pilots.

On the other side of adapting an intervention, is retaining fidelity of an evidence-based intervention. A balance between the two should be pursued: maintaining effective core elements of the intervention while permitting room for adaptations to enhance implementation success.[275–277]

MACRO LEVEL

Results in perspective and implications for research

As the ageing population is expected to increase, the prevalence of age-related disorders, such as sarcopenia, and accompanied health care costs are also expected to increase.[2,13,15,152,153,190] Specifically in the Netherlands, health care costs in older care are expected to increase by 153%: from €17 billion in 2015 to €43 billion in 2040.[16] As discussed before, an effective way of counteracting sarcopenia is the combination of resistance exercise and increased dietary protein intake.[10,21,22,24,52] Maintaining muscle mass and muscle strength will contribute to the prevention of mobility-related disorders and may in turn save costs. As every health innovation accompanies a price tag, an important topic of the macro level is the financial aspect, including sources and funding. To make decisions on investments in health care, an economic evaluation of a treatment or intervention can be performed. An economic evaluation shows whether the benefits of an intervention outweigh the costs.[278] Different outcomes can be included in such an evaluation. We conducted a cost-utility analysis, comparing the costs of the intervention to the effects in quality of life using Quality Adjusted Life Years (QALY). Willingness to pay threshold values are available and range from €20.000 to €80.000 per QALY.[200] Besides, we conducted a cost-effectiveness analysis using the Short Physical Performance Battery (SPPB) as an outcome measure reflective of physical functioning. However, willingness to pay values for SPPB are currently not known. This makes it more difficult to interpret the results and draw conclusions on the cost-effectiveness of the intervention.

Chapter 6 provides insights in the cost-effectiveness and perceived benefits of the ProMuscle in Practice intervention. An Incremental Cost-Effectiveness Ratio of €2988 per point increase in SPPB was found. Besides, the intervention was found to have an 82.4% probability of being cost-effective at a willingness to pay of €12.000 per point increase in SPPB. Although no willingness to pay threshold for SPPB is available, we can put value to these numbers. A 1-point increase in SPPB baseline score was related to a 21% decreased risk of nursing home placement over a 36-month follow-up period.[217] Costs related to nursing home placement can add up to €61.320 on a yearly basis.[198] Besides, total health care costs for older adults in a nursing home including treatment are 10 times higher than for community-dwelling older adults in the Netherlands (€84.300 vs. €7338 per person per year, respectively).[219–221] In addition to the detrimental impact of losing independence on older adults' daily life and health, these findings emphasize the cost-related consequences. Investing in a health promotion intervention such as ProMuscle in Practice contributes to maintaining independence of the ageing population and can possibly save costs on the long term. More research is needed to substantiate this. Besides, it is important to guarantee comparability between preventive interventions when conducting economic evaluations. In addition, research on suitable and valid methods to assess quality of life in the field of public health is needed.

Chapter 6 presents an important finding related to the cost-effectiveness of ProMuscle in Practice. No change in QALY was found using the EQ-5D-5L questionnaire, however, interviews revealed a wide range of function-related perceived benefits. First, several methods can be used to assess quality of life. Generic quality of life questionnaires measuring QALY are often used in curative or clinical services, for example when studying the effects of a drug in a diseased population.[279] However, in preventive interventions, generic QALY-related measures were found to be insensitive to capture subtle changes in quality of life in older adults.[202–207,279] Second, the goal in a curative setting is often to *improve* quality of life. However, the goal in the field of public health is often different, as preventive interventions are primarily targeted at *maintaining* one's quality of life while preventing a decrease in health status. Therefore, public health and preventive interventions often lead to limited change in, often an already high level of, quality of life.[201] Preventive interventions such as ProMuscle in Practice are for instance aimed at maintaining older adults' physical functioning status; an aim that is different to and more specific than improving one's quality of life. Therefore, evaluating preventive interventions using generic QALY measures potentially underestimates the benefits of such interventions.[280] This will lead to incorrect results in terms of cost-effectiveness and will hamper proper decision making on priorities in public health practice.[279] For this reason, other methodological approaches might be more suitable when conducting an economic evaluation in the field of public health.[208,279] One of these methods is using a topic-specific questionnaire. A specific questionnaire is more likely to capture subtle changes in quality of life, and therefore quality of life questionnaires targeting particular conditions seem more suitable.[172,208–210] In our field of study, a wide range of such questionnaires, related to musculoskeletal health, are already available.[209,210] One specific example is the SarQol: a validated quality of life questionnaire specifically for sarcopenic older adults.[199,211–213] Results in chapter 6 indicate that this questionnaire would be suitable to be used in interventions such as ProMuscle in Practice. Although generic QALY measures are frequently being used in the field of health economics, there should be more room and attention for using specific quality of life measures in the field of public health. This will lead to estimating relevant effects, which in turn will provide an appropriate economic evaluation, and a solid base for deciding on priorities in public health practice. For researchers or implementers in a specific field such as sarcopenia-related research, it might be most important to compare (cost-)effectiveness of interventions aiming to decrease or prevent sarcopenia. Interventions that are all aimed at sarcopenia, could use the same topic-specific quality of life questionnaire, such as SarQol. This allows for comparison between interventions in the same field. The downside of using various topic-specific quality of life related questionnaires in interventions, is the limited comparability. For policy makers, it might be relevant to compare the cost-effectiveness based on the same outcome of several interventions that differ in topic. In this way, he or she can make a proper decision on health-related investments. An alternative to topic-specific quality of life questionnaires is using a single all-purpose well-being index that measures quality of life from a broader perspective.[208,281] An example is the ICE-CAP-O, which is based on the capability approach.[282,283] This measure is used to value health benefits for older people and was found to be useful in public health interventions.[201,282] The advantage of such a measure is allowing for comparison across a broad range of interventions, across social care as well as health care.

Implications for practice

The macro level is not only related to costs, but it additionally includes the wider framework of policies. Political support plays a role as well, as it influences implementation of health promotion programmes. Overall, the national government is responsible for the quality and the efficiency of public health care and for creating the national health policy note every four years.[284] 'Healthy ageing' was indicated as one of the four priority areas in the Dutch National Health policy note 2020-2024, published by the Ministry of Health, Welfare and Sport.[285] One of the specific ambitions is that in 2024, relatively more older adults feel vital, so they can maintain participation in society. An important step in reaching this ambition is the development of a coherent offer of prevention, care, and support together with all involved parties.

As the benefits of a preventive intervention are sometimes not immediately visible, and can be present at multiple domains, it is often unclear who is financially responsible for such interventions. To clarify this, we will outline who is responsible for prevention, and thus for stimulating implementation of interventions such as ProMuscle in Practice. According to the Dutch National Institute for Public Health and the Environment, the aim of prevention is to ensure that people stay healthy by promoting and protecting their health. In addition, it aims to prevent diseases and complications of diseases as early as possible.[286] The population can be divided in several subgroups based on health: healthy people, people with an increased health risk, and people with a health problem or disorder. The primary target group of ProMuscle in Practice falls within the subgroup of people with an increased health risk. Municipalities are responsible for local health policy and health promotion of their inhabitants. According to legal frameworks, older adults with an increased health risk can receive preventive interventions from the Public health act (Dutch: Wpg), and the Social support act (Dutch: Wmo).[284] Within these acts, municipalities are responsible for local health policy, elderly healthcare, social participation, and health promotion. In practice, municipalities are often not able to work on health promotion on their own. Multidisciplinary collaboration including all relevant stakeholders is needed to reach the right target population. Examples of such parties are municipal health services, community centers, general practitioners, health care insurances, sports associations, community sports coaches, physiotherapist and dietitian practices, welfare organizations, volunteer organizations, and the target group (ie, older adults). These parties should collaborate on a local level to facilitate effective interventions, such as ProMuscle in Practice, to contribute to vitality of older adults.[285] To stimulate this, national as well as local policy should be aimed at maintaining health and preventing health decline, especially in the elderly population.

Opportunities for financing

The collaboration between municipalities, health care insurances, care- and welfare organizations regarding prevention in 2020 has recently been evaluated. It appeared that the themes *prevention* and *lifestyle* have received increased attention within municipalities and health care insurances. Besides, these organizations find each other more often and develop collaborations. The quality of the collaboration between municipalities and health care insurances differs from place to place. In practice, it appears that different forms of prevention intermingle, which causes indistinctness in terms of responsibility. Besides, financial resources are often not structural, and it is unclear for municipalities and health care insurances who is responsible for which costs. Part of the solution would be to increase possibilities within policy regulations or by providing structural supplies, for example an overarching, common budget for prevention. This will contribute to more structural and secured prevention strategies.[287] In line with this, Health KIC indicates that the health care system should shift from 'fixing and treating diseases' to 'maintaining good health'. The *parcel model* (Dutch: Kavelmodel) provides an opportunity for this. Within this model, the conditions for health of inhabitants are organized within a defined geographical area. To realize this, a shift in organization, financing, and monitoring is needed. Regarding organization, focus will be on cross-domain collaborations, and identifying the needs and potential of the area together with the inhabitants. In terms of financing, an investment fund will provide opportunities for parties to receive a single investment to realize their ideas, such as implementing a health promotion intervention in order to improve health of the inhabitants. Regarding monitoring, effective and non-effective aspects of health interventions will be identified. In addition, disease, as well as perceived health across the life course, will be monitored. In the end, this model should make sure that health is self-evident, and a basic principle for the design of the society. This would enable inhabitants to make healthy choices and enable health care professionals to focus on their clients.[288]

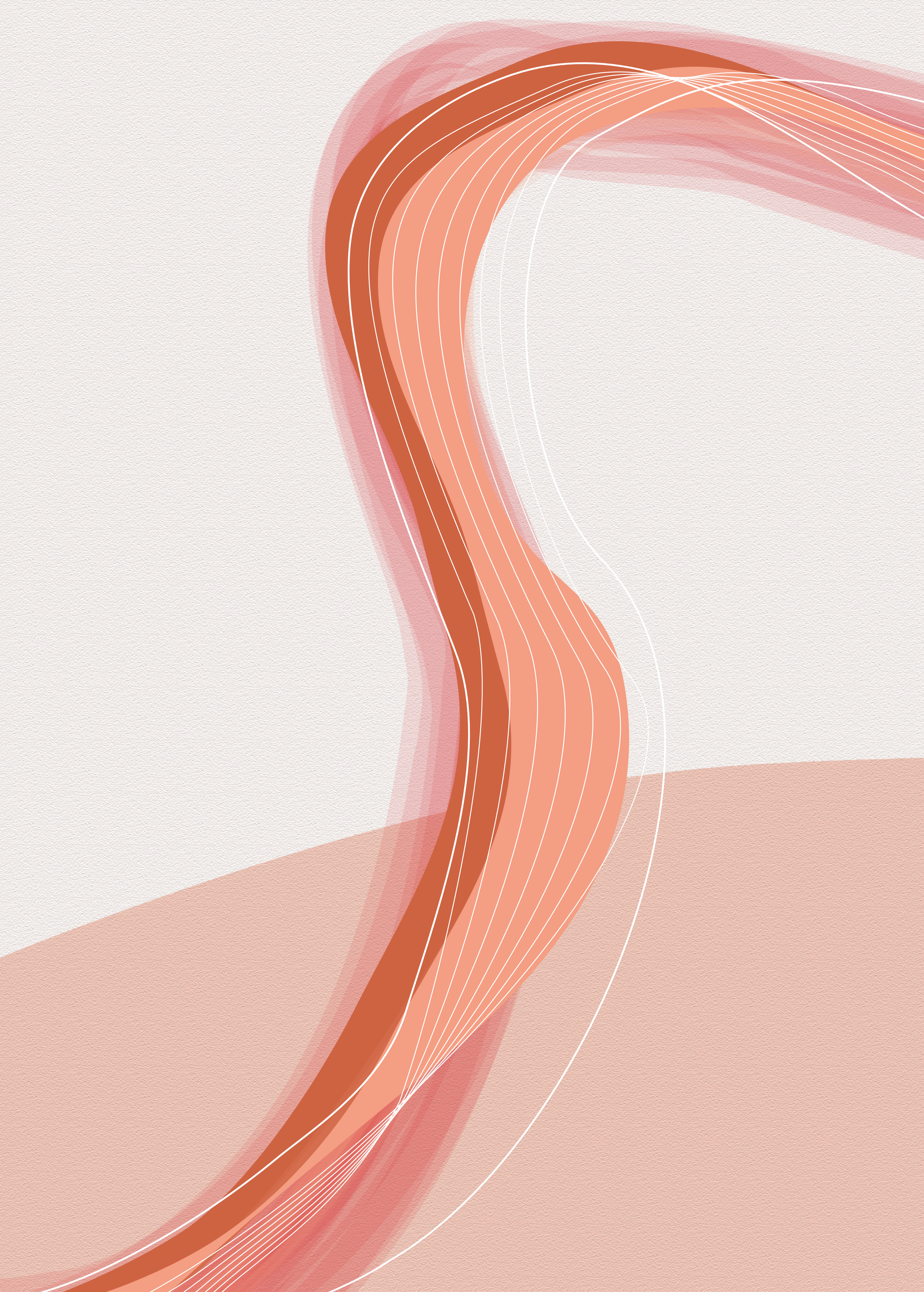
The importance of prevention is also highlighted in the scientific world. A recent paper, published in the Lancet, indicated the essence of prevention over recovery.[289] It states that it is best to prevent a decrease in functioning rather than trying to fix it afterwards.[289–291] Therefore, it is essential to implement effective exercise programs for older adults. In terms of financial opportunities, physical trainers could be included in the health-care system in order to promote healthy ageing.[289] In this way, a cost-related threshold for offering a diet and exercise intervention such as ProMuscle in Practice, will be removed for professionals. In addition, costs for participation in such an intervention will be lowered for the target population as well.

Overall, the focus on prevention should be enhanced. One way to contribute to the prevention of disease and maintaining health is offering lifestyle interventions at a local level. Local, multidisciplinary networks can be used to stimulate the implementation of lifestyle interventions. In terms of financing, opportunities include more structural supplies, cross-domain collaborations and budgets, and a reimbursement from the health-care system for offering an exercise program for professionals such as physical trainers. Regarding the implementation of ProMuscle in Practice, multidisciplinary collaborations and financial aspects are currently being investigated in practice with the ProMuscle Implementation study (PUMP-fit study).

Overall conclusion

The results of this thesis emphasize the presence of heterogeneity in older adults' health status, lifestyle, and in their responsiveness to preventive interventions. Indeed, one size does not fit all. Lifestyle interventions should be adapted to specific target groups in order to increase the fit. Additionally, professionals should tailor the intervention to specific needs and abilities of the participant. At the micro level, we found that personal characteristics including age, sex, and health status might lead to heterogeneity in responsiveness to diet and exercise interventions. Regarding frailty, sarcopenia, and osteoarthritis, no differences in responsiveness were found. Besides, sarcopenia prevalence, dietary protein intake, and its underlying behavioral determinants were found to be ethnic-specific. Cultural background appeared to determine food choices, eating habits, and beliefs about health behaviors. At the meso level, we found that heterogeneity in effects and implementation of an intervention is related to the setting, organization, and its professionals. Positive effects of the intervention were found in the clinical and in the real-life setting but were even more pronounced in the real-life setting of the implementation pilots. At the macro level, we found heterogeneity in results of the economic evaluation. The variation was due to the measure used to conduct the economic evaluation of the ProMuscle in Practice intervention.

Placing our results in the larger body of literature leads to several conclusions and implications. First, the potential influence of factors such as age, sex, ethnicity, and health status should be considered during the development of lifestyle recommendations aiming to improve functional health later in life. Second, to reach a large group of older adults, additional organizations and professionals should be involved in implementing ProMuscle in Practice, using tailored strategies to include them. All in all, the implementation of interventions should be adjusted to fit the target population, organization, its professionals, and the overall setting. Third, the focus on prevention should be enhanced. National government and municipalities can take the lead in offering health promotion interventions targeted at older adults, while exploring financial opportunities. Local multidisciplinary networks could stimulate the implementation of interventions such as ProMuscle in Practice, aiming to maintain proper physical functioning of older adults. In this way, we contribute to the independence of the ageing population, and make sure they can maintain a vital life.



References

REFERENCES

1. WHO. The global health observatory - Life expectancy at birth (years). Accessed January 12, 2021. https://www.who.int/data/gho/data/indicators/indicator-details/GHO/life-expectancy-at-birth-(years)

2. WHO. Factsheet Ageing and Health. Accessed January 12, 2021. https://www.who.int/news-room/fact-sheets/detail/ageing-and-health

3. Carnes BA, Olshansky SJ. Heterogeneity and its biodemographic implications for longevity and mortality. *Exp Gerontol*. 2001;36(3):419-430. doi:10.1016/S0531-5565(00)00254-0

4. Stone ME, Lin J, Dannefer D, Kelley-Moore JA. The continued eclipse of heterogeneity in gerontological research. *Journals Gerontol - Ser B Psychol Sci Soc Sci*. 2017;72(1):162-167. doi:10.1093/geronb/gbv068

5. Beard JR, Bloom DE. Towards a comprehensive public health response to population ageing. *Lancet*. 2015;385(9968):658-661. doi:doi:10.1016/S0140-6736(14)61461-6.

6. Yashin AI, Arbeev KG, Arbeeva LS, et al. How the effects of aging and stresses of life are integrated in mortality rates: insights for genetic studies of human health and longevity. *Biogerontology*. 2016;17(1):89-107. doi:10.1007/s10522-015-9594-8

7. Mitnitski A, Howlett SE, Rockwood K. Heterogeneity of Human Aging and Its Assessment. *Journals Gerontol - Ser A Biol Sci Med Sci*. 2017;72(7):877-884. doi:10.1093/gerona/glw089

8. Montero-Odasso M, Bergman H, Béland F, Sourial N, Fletcher JD, Dallaire L. Identifying mobility heterogeneity in very frail older adults. Are frail people all the same? *Arch Gerontol Geriatr*. 2009;49(2):272-277. doi:10.1016/j.archger.2008.09.010

9. Webber SC, Porter MM, Menec VH. Mobility in older adults: A comprehensive framework. *Gerontologist*. 2010;50(4):443-450. doi:10.1093/geront/gnq013

10. Morley JE. Sarcopenia in the elderly. *Fam Pract*. 2012;29(1):i44-i48. doi:10.1093/fampra/cmr063

11. Mitchell WK, Williams J, Atherton P, Larvin M, Lund J, Narici M. Sarcopenia, dynapenia, and the impact of advancing age on human skeletal muscle size and strength; a quantitative review. *Front Physiol*. 2012;3:1-18. doi:10.3389/fphys.2012.00260

12. Goodpaster BH, Park SW, Harris TB, et al. The loss of skeletal muscle strength, mass, and quality in older adults: The Health, Aging and Body Composition Study. *Journals Gerontol - Ser A Biol Sci Med Sci*. 2006;61(10):1059-1064. doi:10.1093/gerona/61.10.1059

13. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: Revised European consensus on definition and diagnosis. *Age Ageing*. 2019;48(1):1-16. doi:10.1093/ageing/afy169

14. Mayhew AJ, Amog K, Phillips S, et al. The prevalence of sarcopenia in community-dwelling older adults, an exploration of differences between studies and within

definitions: a systematic review and meta-analyses. *Age Ageing*. 2019;48(1):48-56. doi:10.1093/ageing/afy106

15. Bruyère O, Beaudart C, Ethgen O, Reginster JY, Locquet M. The health economics burden of sarcopenia: a systematic review. *Maturitas*. 2019;119:61-69. doi:10.1016/j.maturitas.2018.11.003

16. Hilderink H, Verschuuren M. *Public Health Foresight Study 2018: A Healthy Prospect, Synthesis*.; 2018.

17. Ethgen O, Beaudart C, Buckinx F, Bruyère O, Reginster JY. The Future Prevalence of Sarcopenia in Europe: A Claim for Public Health Action. *Calcif Tissue Int*. 2017;100(3):229-234. doi:10.1007/s00223-016-0220-9

18. Fries JF. Aging, natural death, and the compression of morbidity. *N Engl J Med*. 1980;303(3):130-135. doi:10.1056/nejm198007173030304

19. Fries JF, Bruce B, Chakravarty E. Compression of morbidity 1980-2011: A focused review of paradigms and progress. *J Aging Res*. 2011;2011. doi:10.4061/2011/261702

20. Cruz-Jentoft AJ, Sayer AA. Sarcopenia. *Lancet*. 2019;393(10191):2636-2646. doi:10.1016/S0140-6736(19)31138-9

21. Cermak NM, Res PT, Groot LC De, Saris WHM, Loon LJC Van. Protein supplementation augments the adaptive response of skeletal muscle to resistance type exercise training a meta analysis. *Am J Clin Nutr*. 2012;96:1454-1464. doi:10.3945/ajcn.112.037556.

22. Finger D, Goltz FR, Umpierre D, Meyer E, Rosa LHT, Schneider CD. Effects of Protein Supplementation in Older Adults Undergoing Resistance Training: A Systematic Review and Meta-Analysis. *Sport Med*. 2015;45(2):245-255. doi:10.1007/s40279-014-0269-4

23. Liao C De, Tsauo JY, Wu YT, et al. Effects of protein supplementation combined with resistance exercise on body composition and physical function in older adults: A systematic review and meta-analysis. *Am J Clin Nutr*. 2017;106(4):1078-1091. doi:10.3945/ajcn.116.143594

24. Hou L, Lei Y, Li X, et al. Effect of Protein Supplementation Combined With Resistance Training on Muscle Mass, Strength and Function in the Elderly: A Systematic Review and Meta-Analysis. *J Nutr Heal Aging*. 2019;23(5):451-458. doi:10.1007/s12603-019-1181-2

25. Tieland M, Dirks ML, van der Zwaluw N, et al. Protein Supplementation Increases Muscle Mass Gain During Prolonged Resistance-Type Exercise Training in Frail Elderly People: A Randomized, Double-Blind, Placebo-Controlled Trial. *J Am Med Dir Assoc*. 2012;13(8):713-719. doi:10.1016/j.jamda.2012.05.020

26. Van Dongen EJ, Leerlooijer JN, Steijns JM, Tieland M, De Groot LC, Haveman-Nies A. Translation of a tailored nutrition and resistance exercise intervention for elderly people to a real-life setting: adaptation process and pilot study. *BMC Geriatr*.

2017;17(1):1-15. doi:10.1186/s12877-017-0413-8

27. Van Dongen EJI, Haveman-Nies A, Wezenbeek NLW, Dorhout BG, Doets EL, De Groot LCPGM. Effect, process, and economic evaluation of a combined resistance exercise and diet intervention (ProMuscle in Practice) for community-dwelling older adults: Design and methods of a randomised controlled trial. *BMC Public Health*. 2018;18(1):1-12. doi:10.1186/s12889-018-5788-8

28. van Dongen EJI, Haveman-Nies A, Doets EL, Dorhout BG, de Groot LCPGM. Effectiveness of a Diet and Resistance Exercise Intervention on Muscle Health in Older Adults: ProMuscle in Practice. *J Am Med Dir Assoc*. Published online 2020:1065-1072. doi:10.1016/j.jamda.2019.11.026

29. van Dongen EJI, Doets EL, de Groot LCPGM, Dorhout BG, Haveman-Nies A. Process Evaluation of a Combined Lifestyle Intervention for Community-Dwelling Older Adults: ProMuscle in Practice. *Gerontologist*. Published online 2020:1-17. doi:10.1093/geront/gnaa027

30. Daly RM. Dietary Protein, Exercise and Skeletal Muscle: Is There a Synergistic Effect in Older Adults and the Elderly? In: Weaver, C., Daly, R., Bischoff-Ferrari H, ed. *Nutritional Influences on Bone Health*. Springer, Cham; 2016. doi:10.1007/978-3-319-32417-3

31. Morton RW, Murphy KT, McKellar SR, et al. A systematic review, meta-analysis and meta-regression of the effect of protein supplementation on resistance training-induced gains in muscle mass and strength in healthy adults. *Br J Sports Med*. 2018;52(6):376-384. doi:10.1136/bjsports-2017-097608

32. Pfadenhauer LM, Gerhardus A, Mozygemba K, et al. Making sense of complexity in context and implementation: The Context and Implementation of Complex Interventions (CICI) framework. *Implement Sci*. 2017;12(1):1-17. doi:10.1186/s13012-017-0552-5

33. Grol R. Successes and Failures in the Implementation of Evidence-Based Guidelines for Clinical Practice. *Med Care*. 2001;39(8):46-54. doi:10.1097/00005650-200108002-00003

34. Craig P, Ruggiero E Di, Frohlich KL, et al. Taking account of context in population health intervention research: guidance for producers, users and funders of research. Published online 2018. doi:10.3310/CIHR-NIHR-01

35. Watson DP, Adams EL, Shue S, et al. Defining the external implementation context: An integrative systematic literature review. *BMC Health Serv Res*. 2018;18(1):1-14. doi:10.1186/s12913-018-3046-5

36. Dahlgren G, Whitehead M. *Policies and Strategies to Promote Social Equity in Health. Background Document to World Health Organisation - Strategy Paper for Europe*.; 2007.

37. Lysdahl K., Mozygemba K, Chilcott J., Brönneke JB, Hofmann B. Guidance for assessing effectiveness, economic aspects, ethical aspects, socio-cultural aspects and legal aspects in complex techonologies. 2016;(306141):1-166.

38. Mendel, Peter, Merideth Lisa S, Schoenbaum Michael, Sherbourne Cathy, Wells KB. Interventions in Organizational and Community context: a Framework for building evidence. *Adm Policy Ment hlth*. 2008;35(1-2):21-37. doi:10.1007/s10488-007-0144-9.Interventions

39. Dahlgren G, Whitehead M. *European Strategies for Tackling Social Inequities in Health: Levelling up Part 2.*; 2006.

40. Martone AM, Marzetti E, Calvani R, et al. Exercise and Protein Intake: A Synergistic Approach against Sarcopenia. *Biomed Res Int*. Published online 2017. doi:10.1155/2017/2672435

41. Hidayat K, Chen GC, Wang Y, et al. Effects of milk proteins supplementation in older adults undergoing resistance training: A meta-analysis of randomized control trials. *J Nutr Heal Aging*. 2018;22(2):237-245. doi:10.1007/s12603-017-0899-y

42. Moore DR, Churchward-Venne TA, Witard O, et al. Protein ingestion to stimulate myofibrillar protein synthesis requires greater relative protein intakes in healthy older versus younger men. *Journals Gerontol - Ser A Biol Sci Med Sci*. 2015;70(1):57-62. doi:10.1093/gerona/glu103

43. Kumar V, Selby A, Rankin D, et al. Age-related differences in the dose-response relationship of muscle protein synthesis to resistance exercise in young and old men. *J Physiol*. 2009;587(1):211-217. doi:10.1113/jphysiol.2008.164483

44. Churchward-Venne TA, Holwerda AM, Phillips SM, van Loon LJC. What is the Optimal Amount of Protein to Support Post-Exercise Skeletal Muscle Reconditioning in the Older Adult? *Sport Med*. 2016;46(9):1205-1212. doi:10.1007/s40279-016-0504-2

45. McKendry J, Currier BS, Lim C, McLeod JC, Thomas ACQ, Phillips SM. Nutritional supplements to support resistance exercise in countering the sarcopenia of aging. *Nutrients*. 2020;12(7):1-29. doi:10.3390/nu12072057

46. Olanrewaju O, Kelly S, Cowan A, Brayne C, Lafortune L. Physical activity in community dwelling older people: A systematic review of reviews of interventions and context. *PLoS One*. 2016;11(12):1-19. doi:10.1371/journal.pone.0168614

47. Colonetti T, Grande AJ, Milton K, et al. Effects of whey protein supplement in the elderly submitted to resistance training: systematic review and meta-analysis. *Int J Food Sci Nutr*. 2017;68(3):257-264. doi:10.1080/09637486.2016.1232702

48. Anton S, Hida A, Mankowski R, et al. Nutrition and Exercise in Sarcopenia. *Curr Protein Pept Sci*. 2017;17(December). doi:10.2174/1389203717666161227144349

49. Liao C De, Chen HC, Huang SW, Liou TH. The Role of Muscle Mass Gain Following Protein Supplementation Plus Exercise Therapy in Older Adults with Sarcopenia and Frailty Risks: A Systematic Review and Meta-Regression Analysis of Randomized Trials. *Nutrients*. 2019;11(10):1-23. doi:10.3390/nu11081713

50. Liao C De, Lee PH, Hsiao DJ, et al. Effects of protein supplementation combined with exercise intervention on frailty indices, body composition, and physical function in frail older adults. *Nutrients*. 2018;10(12):1-30. doi:10.3390/nu10121916

51. Jadczak AD, Makwana N, Luscombe-Marsh N, Visvanathan R, Schultz TJ. Effectiveness of exercise interventions on physical function in community-dwelling frail older people: an umbrella review of systematic reviews. *JBI database Syst Rev Implement reports*. 2018;16(3):752-775. doi:10.11124/JBISRIR-2017-003551

52. Liao C De, Wu YT, Tsauo JY, et al. Effects of protein supplementation combined with exercise training on muscle mass and function in older adults with lower-extremity osteoarthritis: A systematic review and meta-analysis of randomized trials. *Nutrients*. 2020;12(8):1-19. doi:10.3390/nu12082422

53. Schellingerhout R. *Gezondheid En Welzijn van Allochtone Ouderen*.; 2004.

54. Denktaş S, Koopmans G, Birnie E, Foets M, Bonsel G. Ethnic background and differences in health care use: a national cross-sectional study of native Dutch and immigrant elderly in the Netherlands. *Int J Equity Health*. 2009;8(1):35. doi:10.1186/1475-9276-8-35

55. Nielsen SS, Krasnik A. Poorer self-perceived health among migrants and ethnic minorities versus the majority population in Europe: A systematic review. *Int J Public Health*. 2010;55:357-371. doi:10.1007/s00038-010-0145-4

56. Franse CB, Van Grieken A, Qin L, Melis RJF, Rietjens JAC, Raat H. Ethnic differences in frailty: A cross-sectional study of pooled data from community-dwelling older persons in the Netherlands. *BMJ Open*. 2018;8(8):1-10. doi:10.1136/bmjopen-2018-022241

57. Snijder MB, Agyemang C, Peters RJ, Stronks K, Ujcic-Voortman JK, Van Valkengoed IGM. Case Finding and Medical Treatment of Type 2 Diabetes among Different Ethnic Minority Groups: The HELIUS Study. *J Diabetes Res*. 2017;2017. doi:10.1155/2017/9896849

58. Perini W, Kunst AE, Snijder MB, Peters RJG, van Valkengoed IGM. Ethnic differences in metabolic cardiovascular risk among normal weight individuals: Implications for cardiovascular risk screening. The HELIUS study. *Nutr Metab Cardiovasc Dis*. 2019;29(1):15-22. doi:10.1016/j.numecd.2018.09.004

59. Marty E, Liu Y, Samuel A, Or O, Lane J. A review of sarcopenia: Enhancing awareness of an increasingly prevalent disease. *Bone*. 2017;105:276-286. doi:10.1016/j.bone.2017.09.008

60. Han A, Bokshan S, Marcaccio S, DePasse J, Daniels A. Diagnostic Criteria and Clinical Outcomes in Sarcopenia Research: A Literature Review. *J Clin Med*. 2018;7(4):70. doi:10.3390/jcm7040070

61. Rush EC, Goedecke JH, Jennings C, et al. BMI, fat and muscle differences in urban women of five ethnicities from two countries. *Int J Obes*. 2007;31(8):1232-1239. doi:10.1038/sj.ijo.0803576

62. Silva AM, Shen W, Heo M, et al. Ethnicity-Related Skeletal Muscle Differences Across the Lifespan. *Am J Hum Biol*. 2010;22(1):76-82. doi:10.1002/ajhb.20956

63. Greenhall GHB, Davenport A. Screening for muscle loss in patients established on peritoneal dialysis using bioimpedance. *Eur J Clin Nutr*. 2017;71(1):70-75. doi:10.1038/ejcn.2016.202

64. Van Der Kooi ALLF, Snijder MB, Peters RJG, Van Valkengoed IGM. The association of handgrip strength and type 2 diabetes mellitus in six ethnic groups: An analysis of the HELIUS study. *PLoS One*. 2015;10(9):1-11. doi:10.1371/journal.pone.0137739

65. Bos V. Ethnic Inequalities in Mortality in the Netherlands and the Role of Socioeconomic Status. Published online 2005.

66. Gilbert PA, Khokhar S. Changing dietary habits of ethnic groups in Europe and implications for health. *Nutr Rev*. 2008;66(4):203-215. doi:10.1111/j.1753-4887.2008.00025.x

67. Osei-Kwasi HA, Nicolaou M, Powell K, et al. Systematic mapping review of the factors influencing dietary behaviour in ethnic minority groups living in Europe: A DEDIPAC study. *Int J Behav Nutr Phys Act*. 2016;13(1). doi:10.1186/s12966-016-0412-8

68. Nicolaou M, Doak CM, van Dam RM, Brug J, Stronks K, Seidell JC. Cultural and Social Influences on Food Consumption in Dutch Residents of Turkish and Moroccan Origin: A Qualitative Study. *J Nutr Educ Behav*. 2009;41(4):232-241. doi:10.1016/j.jneb.2008.05.011

69. Jager MJ, Van Der Sande R, Essink-Bot ML, Van Den Muijsenbergh METC. Views and experiences of ethnic minority diabetes patients on dietetic care in the Netherlands - A qualitative study. *Eur J Public Health*. 2019;29(2):208-213. doi:10.1093/eurpub/cky186

70. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: A consolidated framework for advancing implementation science. *Implement Sci*. 2009;4(1):1-15. doi:10.1186/1748-5908-4-50

71. Sims-Gould J, McKay HA, Hoy CL, et al. Factors that influence implementation at scale of a community-based health promotion intervention for older adults. *BMC Public Health*. 2019;19(1):1-12. doi:10.1186/s12889-019-7984-6

72. Ministerie van Volksgezondheid Welzijn en Sport. *Programma Langer Thuis*.; 2018. doi:10.1007/s40718-015-0025-3

73. Durlak JA, DuPre EP. Implementation matters: A review of research on the influence of implementation on program outcomes and the factors affecting implementation. *Am J Community Psychol*. 2008;41(3-4):327-350. doi:10.1007/s10464-008-9165-0

74. Hanach NI, McCullough F, Avery A. The Impact of Dairy Protein Intake on Muscle Mass, Muscle Strength, and Physical Performance in Middle-Aged to Older Adults with or without Existing Sarcopenia: A Systematic Review and Meta-Analysis. *Adv Nutr*. 2019;10(1):59-69. doi:10.1093/advances/nmy065

75. Davis, J.C., Robertson, M.C., Ashe, M.C., Liu-Ambrose, T., Khan, K.M., Marra CA. Does a home-based strength and balance programme in people aged ≥80 years provide the best value for money to prevent falls? A systematic review of economic evaluations of falls prevention interventions. *Br J Sports Med*. 2010;44:80-89. doi:10.1136/bjsm.2008.060988

76. Matchar DB, Eom K, Duncan PW, et al. A Cost-Effectiveness Analysis of a Randomized Control Trial of a Tailored, Multifactorial Program to Prevent Falls Among the Community-Dwelling Elderly. *Arch Phys Med Rehabil*. 2019;100(1):1-8. doi:10.1016/j.apmr.2018.07.434

77. Winser SJ, Chan HTF, Ho L, et al. Dosage for cost-effective exercise-based falls prevention programs for older people: A systematic review of economic evaluations. *Ann Phys Rehabil Med*. Published online 2019. doi:10.1016/j.rehab.2019.06.012

78. CBS. Prognose: 18,4 miljoen inwoners in 2060. Published 2017. Accessed January 9, 2019. https://www.cbs.nl/nl-nl/nieuws/2017/51/prognose-18-4-miljoen-inwoners-in-2060

79. Cruz-Jentoft AJ, Landi F, Schneider SM, et al. Prevalence of and interventions for sarcopenia in ageing adults: A systematic review. Report of the International Sarcopenia Initiative (EWGSOP and IWGS). *Age Ageing*. 2014;43(6):748-759. doi:10.1093/ageing/afu115

80. Du K, Goates S, Arensberg MB, Pereira S, Gaillard T. Prevalence of Sarcopenia and Sarcopenic Obesity Vary with Race / Ethnicity and Advancing Age. 2018;15:175-183.

81. Fielding RA, Vellas B, Evans WJ, et al. Sarcopenia: An Undiagnosed Condition in Older Adults. Current Consensus Definition: Prevalence, Etiology, and Consequences. International Working Group on Sarcopenia. *J Am Med Dir Assoc*. 2011;12(4):249-256. doi:10.1016/j.jamda.2011.01.003

82. Tieland M, van de Rest O, Dirks ML, et al. Protein Supplementation Improves Physical Performance in Frail Elderly People: A Randomized, Double-Blind, Placebo-Controlled Trial. *J Am Med Dir Assoc*. 2012;13(8):720-726. doi:10.1016/j.jamda.2012.07.005

83. Layne AS, Hsu F-C, Blair SN, et al. Predictors of Change in Physical Function in Older Adults in Response to Long-Term, Structured Physical Activity: The LIFE Study. *Arch Phys Med Rehabil*. 2017;98(1):11-24.e3. doi:10.1016/j.apmr.2016.07.019

84. Hita-Contreras, F., Bueno-Notivol, J., Martinez-Amat, A., Cruz-Diaz, D., Hernandez, A.V., Perez-Lopez FR. Effect of exercise alone or combined with dietary supplements on anthropometric and physical performance measures in community-dwelling elderly people with sarcopenic obesity: A meta-analysis of randomized controlled trials. *Maturitas*. 2018;116:24-35. doi:10.1016/j.maturitas.2018.07.007

85. Van Erp-Baart MAJ, Westenbrink S, Hulshof KFAM, Brussaard JH. Assessment of dietary intake among Moroccan women and Surinam men. *Ethn Heal*. 2001;6(2):145-154. doi:10.1080/13557850120068478

86. Stronks, K., Snijder, M.B., Prins, M., Schene, A.H., Zwinderman AH. Unravelling the impact of ethnicity on health in Europe: the HELIUS study. *BMC Public Health*. 2013;13(402).

87. Snijder MB, Galenkamp H, Prins M, et al. Cohort profile: The Healthy Life in an Urban Setting (HELIUS) study in Amsterdam, the Netherlands. *BMJ Open*. 2017;7(12):1-12. doi:10.1136/bmjopen-2017-017873

88. Beukers MH, Dekker LH, De Boer EJ, et al. Development of the HELIUS food frequency questionnaires: Ethnic-specific questionnaires to assess the diet of a multiethnic population in the Netherlands. *Eur J Clin Nutr*. 2015;69(5):579-584. doi:10.1038/ejcn.2014.180

89. Willett W. *Nutritional Epidemiology*. 3rd ed. Oxford University Press; 2013.

90. Stronks, K., Kulu-Glasgow, I., Agyemang CO. The utility of "country of birth" for the classification of ethnic groups in health research: the Dutch experience. *Ethn Heal*. 2009;14:255-269.

91. Janssen I, Heymsfield SB, Baumgartner RN, Ross R. Estimation of skeletal muscle mass by bioelectrical impedance analysis. *J Appl Physiol*. 2000;89(2):465-471. doi:10.3945/ajcn.115.119925.

92. Janssen I, Baumgartner RN, Ross R, Rosenberg IH, Roubenoff R. Skeletal Muscle Cutpoints Associated with Elevated Physical Disability Risk in Older Men and Women. *Am J Epidemiol*. 2004;159(4):413-421. doi:10.1093/aje/kwh058

93. *Dutch Food Composition Table 2011*. National Institute for Public Health and the Netherlands Nutrition Centre; 2011.

94. Nicolaou M, Gademan MGJ, Snijder MB, et al. Validation of the SQUASH physical activity questionnaire in a multi-ethnic population: The HELIUS study. *PLoS One*. 2016;11(8):1-14. doi:10.1371/journal.pone.0161066

95. Kemper HCG, Ooijendijk WTM, Stiggelbout M. Consensus over de Nederlandse norm voor gezond bewegen. *Tijdschr voor gezondheidswetenschappen*. 2000;78(3):180-183.

96. Willett WC, Howe GR, Kushi HK. Adjustment for total energy intake in epidemiologic studies. *Am J Clin Nutr*. 1997;65(Suppl):1220S-8S.

97. Coutinho LMS, Scazufca M, Menezes PR. Methods for estimating prevalence ratios in cross-sectional studies. *Rev Saude Publica*. 2008;42(6):992-998.

98. Dodds RM, Syddall HE, Cooper R, et al. Grip strength across the life course: Normative data from twelve British studies. *PLoS One*. 2014;9(12):1-15. doi:10.1371/journal.pone.0113637

99. Guerra RS, Amaral TF. Comparison of hand dynamometers in elderly people. *J Nutr Heal Aging*. 2009;13(10):907-912. doi:10.1007/s12603-009-0250-3

100. Khalil SF, Mohktar MS, Ibrahim F. The theory and fundamentals of bioimpedance analysis in clinical status monitoring and diagnosis of diseases. *Sensors (Switzerland)*. 2014;14(6):10895-10928. doi:10.3390/s140610895

101. Sergi G, De Rui M, Stubbs B, Veronese N, Manzato E. Measurement of lean body mass using bioelectrical impedance analysis: a consideration of the pros and cons. *Aging Clin Exp Res*. 2017;29(4):591-597. doi:10.1007/s40520-016-0622-6

102. Brantlov S, Jødal L, Lange A, Rittig S, Ward LC. Standardisation of bioelectrical impedance analysis for the estimation of body composition in healthy paediatric populations: a systematic review. *J Med Eng Technol*. 2017;41(6):460-479. doi:10.1080/03091902.2017.1333165

103. Kyle, U.G., Genton, L., Karsegard, L., Slosman, D.O., Pichard C. Single prediction equation for bioelectrical impedance analysis in adults aged 22-59 years. *Nutrition*. 2001;17:248-253. doi:10.3109/03091902.2010.543751

104. Buckinx F, Landi F, Cesari M, et al. Pitfalls in the measurement of muscle mass: a need for a reference standard. *J Cachexia Sarcopenia Muscle*. 2018;9(2):269-278. doi:10.1002/jcsm.12268

105. Wagner DR, Heyward VH. Measures of body composition in blacks and whites : a comparative review. *Am J Clin Nutr*. 2000;71(May):1392-1402. doi:10.1093/ajcn/71.6.1392

106. Deurenberg P, Yap M, Van Staveren WA. Body mass index and percent body fat: A meta analysis among different ethnic groups. *Int J Obes*. 1998;22(12):1164-1171. doi:10.1038/sj.ijo.0800741

107. Heymsfield, S.B., Peterson, C.M., Thomas, D.M., Heo MSJJM. Why are there race/ethnic differences in adult body mass index-adiposity relationships? A quantitative critical review. *Obes Rev*. 2016;17(3):262-275. doi:10.1111/obr.12358

108. Shaw SC, Dennison EM, Cooper C. Epidemiology of Sarcopenia: Determinants Throughout the Lifecourse. *Calcif Tissue Int*. 2017;101(3):229-247. doi:10.1007/s00223-017-0277-0

109. Abellan Van Kan G. Epidemiology and consequences of sarcopenia. *J Nutr Heal Aging*. 2009;13(8):708-712. doi:10.1007/s12603-009-0201-z

110. Anujuo K, Agyemang C, Snijder MB, et al. Contribution of short sleep duration to ethnic differences in cardiovascular disease: Results from a cohort study in the Netherlands. *BMJ Open*. 2017;7(11):1-9. doi:10.1136/bmjopen-2017-017645

111. Chen LK, Liu LK, Woo J, et al. Sarcopenia in Asia: Consensus report of the Asian working group for sarcopenia. *J Am Med Dir Assoc*. 2014;15(2):95-101. doi:10.1016/j.jamda.2013.11.025

112. Chen LK, Lee WJ, Peng LN, Liu LK, Arai H, Akishita M. Recent Advances in Sarcopenia Research in Asia: 2016 Update From the Asian Working Group for Sarcopenia. *J Am Med Dir Assoc*. 2016;17(8):767.e1-767.e7. doi:10.1016/j.jamda.2016.05.016

113. Houston DK, Nicklas BJ, Ding J, et al. Dietary protein intake is associated with lean mass change in older, community-dwelling adults: The Health, Aging, and Body Composition (Health ABC) study. *Am J Clin Nutr*. 2008;87(1):150-155. doi:10.1093/ajcn/87.1.150

114. Huang RY, Yang KC, Chang HH, Lee LT, Lu CW, Huang KC. The association between total protein and vegetable protein intake and low muscle mass among the community-dwelling elderly population in Northern Taiwan. *Nutrients*. 2016;8(6). doi:10.3390/nu8060373

115. Sahni S, Mangano KM, Hannan MT, Kiel DP, McLean RR. Higher Protein Intake Is Associated with Higher Lean Mass and Quadriceps Muscle Strength in Adult Men and Women. *J Nutr*. 2015;145(7):1569-1575. doi:10.3945/jn.114.204925

116. Radavelli-Bagatini S, Zhu K, Lewis JR, Dhaliwal SS, Prince RL. Association of Dairy Intake with Body Composition and Physical Function in Older Community-Dwelling Women. *J Acad Nutr Diet*. 2013;113(12):1669-1674. doi:10.1016/j.jand.2013.05.019

117. Mangano KM, Sahni S, Kiel DP, Tucker KL, Dufour AB, Hannan MT. Dietary protein is associated with musculoskeletal health independently of dietary pattern: The Framingham Third Generation Study. *Am J Clin Nutr*. 2017;105(3):714-722. doi:10.3945/ajcn.116.136762

118. Meng X, Zhu K, Devine A, Kerr DA, Binns CW, Prince RL. A 5-year cohort study of the effects of high protein intake on lean mass and BMC in elderly postmenopausal women. *J Bone Miner Res*. 2009;24(11):1827-1834. doi:10.1359/jbmr.090513

119. Ong S, Woo J, Parikh P, et al. Addressing nutritional requirements of ageing consumers in Asia-recommendations from an expert workshop. *Asia Pac J Clin Nutr*. 2019;28(2):204-213. doi:10.6133/apjcn.201906_28(2).0001

120. Nierkens V, Hartman MA, Nicolaou M, et al. Effectiveness of Cultural Adaptations of Interventions Aimed at Smoking Cessation, Diet, and/or Physical Activity in Ethnic Minorities. A Systematic Review. *PLoS One*. 2013;8(10). doi:10.1371/journal.pone.0073373

121. NIDI. *Bevolking 2050 in Beeld; Drukker, Diverser En Dubbelgrijs*.; 2020.

122. Reus-Pons M, Kibele EU, Janssen F. Differences in healthy life expectancy between older migrants and non-migrants in three European countries over time. *Int J Public Health*. 2017;62(5):531-540.

123. El Fakiri F, Bouwman-Notenboom J. *Gezondheid van Oudere Migranten in de Vier Grote Steden*.; 2016.

124. Reus-Pons M, Mulder CH, Kibele EU, Janssen F. Differences in the health transition patterns of migrants and non-migrants aged 50 and older in southern and western

Europe (2004–2015). *BMC Med*. 2018;16(1):57. doi:10.1186/s12916-018-1044-4

125. Dorhout BG, Overdevest E, Tieland M, et al. Sarcopenia and its relation to protein intake across older ethnic populations in the Netherlands: the HELIUS study. *Ethn Heal*. 2020;0(0):1-16. doi:10.1080/13557858.2020.1814207

126. Bauer JM, Verlaan S, Bautmans I, et al. Effects of a Vitamin D and Leucine-Enriched Whey Protein Nutritional Supplement on Measures of Sarcopenia in Older Adults, the PROVIDE Study: A Randomized, Double-Blind, Placebo-Controlled Trial. *J Am Med Dir Assoc*. 2015;16(9):740-747. doi:10.1016/j.jamda.2015.05.021

127. Dillon EL, Sheffield-Moore M, Paddon-Jones D, et al. Amino acid supplementation increases lean body mass, basal muscle protein synthesis, and insulin-like growth factor-I expression in older women. *J Clin Endocrinol Metab*. 2009;94(5):1630-1637. doi:10.1210/jc.2008-1564

128. Solerte SB, Gazzaruso C, Bonacasa R, et al. Nutritional Supplements with Oral Amino Acid Mixtures Increases Whole-Body Lean Mass and Insulin Sensitivity in Elderly Subjects with Sarcopenia. *Am J Cardiol*. 2008;101(11A):69E-77E. doi:10.1016/j.amjcard.2008.03.004

129. Deutz NEP, Bauer JM, Barazzoni R, et al. Protein intake and exercise for optimal muscle function with aging: recommendations from the ESPEN Expert Group. *Clin Nutr*. 2014;33(6):929-936. doi:10.1016/j.clnu.2014.04.007

130. World Health Organization. *Protein and Amino Acid Requirements in Human Nutrition: Report of a Joint FAO/WHO/UNU Expert Consultation*.; 2007.

131. van Vliet S, Burd NA, van Loon LJ. The skeletal muscle anabolic response to plant-versus animal-based protein consumption. *J Nutr*. 2015;145(9):1981-1991. doi:10.3945/jn.114.204305

132. Gorissen SH, Remon D, van Loon LJ. The muscle protein synthetic response to food ingestion. *Meat Sci*. Published online 2015. doi:10.1016/j.meatsci.2015.05.009

133. Paddon-Jones D, Rasmussen BB. Dietary protein recommendations and the prevention of sarcopenia. Published online 2009. doi:10.1097/MCO.0b013e32831cef8b

134. van der Gaag M, van der Heide I, Spreeuwenberg PM, Brabers AE, Rademakers JJ. Health literacy and primary health care use of ethnic minorities in the Netherlands. *BMC Health Serv Res*. 2017;17(1):350. doi:10.1186/s12913-017-2276-2

135. Bauer J, Biolo G, Cederholm T, et al. Evidence-based recommendations for optimal dietary protein intake in older people: A position paper from the prot-age study group. *J Am Med Dir Assoc*. 2013;14(8):542-559. doi:10.1016/j.jamda.2013.05.021

136. Tieland M, van Loon LJ, de Groot LC. Dietary protein intake in Dutch elderly people: a focus on protein sources. *Nutrients*. 2015;7(12):9697-9706. doi:10.3390/nu7125496

137. Gilbert JA, Bendsen NT, Tremblay A, Astrup A. Effect of proteins from different sources on body composition. *Nutr Metab Cardiovasc Dis*. 2011;21(SUPPL. 2):B16-B31. doi:10.1016/j.numecd.2010.12.008

138. Muilwijk M, Stenvers DJ, Nicolaou M, Kalsbeek A, van Valkengoed IG. Behavioral Circadian Timing System Disruptors and Incident Type 2 Diabetes in a Nonshift Working Multi-Ethnic Population. *Obesity*. 2020;28(S1):S55-S62. doi:10.1002/oby.22777

139. Arnal MA, Mosoni L, Boirie Y, et al. Protein pulse feeding improves protein retention in elderly women. *Am J Clin Nutr*. 1999;69(6):1202-1208. doi:10.1093/ajcn/69.6.1202

140. Bouillanne O, Curis E, Hamon-Vilcot B, et al. Impact of protein pulse feeding on lean mass in malnourished and at-risk hospitalized elderly patients: A randomized controlled trial. *Clin Nutr*. 2013;32(2):186-192. doi:10.1016/j.clnu.2012.08.015

141. Areta JL, Burke LM, Ross ML, et al. Timing and distribution of protein ingestion during prolonged recovery from resistance exercise alters myofibrillar protein synthesis. *J Physiol*. 2013;591(9):2319-2331. doi:10.1113/jphysiol.2012.244897

142. Mamerow MM, Mettler JA, English KL, et al. Dietary protein distribution positively influences 24-h muscle protein synthesis in healthy adults. *J Nutr*. 2014;144(6):876-880. doi:10.3945/jn.113.185280

143. Bartholomew LK, Markham CM, Ruiter RAC, Fernandez ME, Kok G, Parcel GS. *Planning Health Promotion Programs - an Intervention Mapping Approach*. Four. Jossey-Bass; 2016. doi:10.7748/ns.32.6.33.s38

144. Ahluwalia J, Baranowski T, Braithwaite R, Resnicow K. Cultural sensitivity in public health: defined and demystified. *Ethn Dis*. 1999;9(1):10-21.

145. Bhasin S, Apovian CM, Travison TG, et al. Effect of protein intake on lean body mass in functionally limited older men: a randomized clinical trial. *JAMA Intern Med*. 2018;178(4):530-541. doi:10.1001/jamainternmed.2018.0008

146. Chan R, Leung J, Woo J, Kwok T. Associations of dietary protein intake on subsequent decline in muscle mass and physical functions over four years in ambulant older Chinese people. *J Nutr Health Aging*. 2014;18(2):171-177. doi:10.1007/s12603-013-0379-y

147. Verreijen AM, Engberink MF, Houston DK, et al. Dietary protein intake is not associated with 5-y change in mid-thigh muscle cross-sectional area by computed tomography in older adults: The Health, Aging, and Body Composition (Health ABC) Study. *Am J Clin Nutr*. 2019;109(3):544-553. doi:10.1093/ajcn/nqy341

148. Tieland M, Franssen R, Dullemeijer C, et al. The Impact of Dietary Protein or Amino Acid Supplementation on Muscle Mass and Strength in Elderly People: Individual Participant Data and Meta-Analysis of RCT's. *J Nutr Heal Aging*. 2017;21(9):994-1001. doi:10.1007/s12603-017-0896-1

149. Bonnefoy M, Cornu C, Normand S, et al. The effects of exercise and protein-energy supplements on body composition and muscle function in frail elderly individuals: a long-term controlled randomised study. *Br J Nutr*. 2003;89(5):731-739. doi:10.1079/bjn2003836

150. Kim H, Suzuki T, Saito K, et al. Exercise and thermal therapy for community-dwelling japanese elderly women with chronic knee pain: A randomized controlled trial. *J Am Geriatr Soc*. 2012;60(S164).

151. Anne Nelson E, Dannefer D. Aged Heterogeneity: Fact or Fiction? The Fate of Diversity in Gerontological Research. *Gerontologist*. 1992;32(1):17-23. doi:10.1093/geront/32.1.17

152. Rantakokko M, Mänty M, Rantanen T. Mobility decline in old age. *Exerc Sport Sci Rev*. 2013;41(1):19-25. doi:10.1097/JES.0b013e3182556f1e

153. Fried LP, Tangen CM, Walston J, et al. Frailty in Older Adults: Evidence for a Phenotype. *Journals Gerontol Ser A Biol Sci Med Sci*. 2001;56(3):M146-M157. doi:10.1093/gerona/56.3.M146

154. Stuck AE, Walthert JM, Nikolaus T, Büla CJ, Hohmann C, Beck JC. Risk factors for functional status decline in community-living elderly people: a systematic literature review. *Soc Sci Med*. 1999;48(4):445-469. doi:10.1016/S0277-9536(98)00370-0

155. Statline - Prognose bevolking; geslacht en leeftijd, 2020-2060. Published 2019. Accessed November 4, 2020. https://opendata.cbs.nl/statline/#/CBS/nl/dataset/84646NED/table?ts=1604479523506

156. Churchward-Venne TA, Tieland M, Verdijk LB, et al. There are no nonresponders to resistance-type exercise training in older men and women. *J Am Med Dir Assoc*. 2015;16(5):400-411. doi:10.1016/j.jamda.2015.01.071

157. Ahtiainen JP, Walker S, Peltonen H, et al. Heterogeneity in resistance training-induced muscle strength and mass responses in men and women of different ages. *Age (Omaha)*. 2016;38(1):1-13. doi:10.1007/s11357-015-9870-1

158. Hubal MJ, Gordish-Dressman H, Thompson PD, et al. Variability in muscle size and strength gain after unilateral resistance training. *Med Sci Sports Exerc*. 2005;37(6):964-972. doi:10.1249.01.mss.0000170469.90461.5f

159. de Zwart AH, van der Leeden M, Roorda LD, et al. Dietary protein intake and upper leg muscle strength in subjects with knee osteoarthritis: data from the osteoarthritis initiative. *Rheumatol Int*. 2019;39(2):277-284. doi:10.1007/s00296-018-4223-x

160. Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. *Lancet*. 2019;393(10182):1745-1759. doi:10.1016/S0140-6736(19)30417-9

161. Fransen, M., McConnell, S., Hernandez-Molina, G., Reichenbach S. Exercise for osteoarthritis of the hip. *Annu Rev Gerontol Geriatr*. 2014;36(1):155-168. doi:10.1891/0198-8794.36.155

162. Fransen M, McConnell S, Harmer AR, Van Der Esch M, Simic M, Bennell KL. Exercise for osteoarthritis of the knee: A Cochrane systematic review. *Br J Sports Med*.

2015;49(24):1554-1557. doi:10.1136/bjsports-2015-095424

163. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: Association with self-reported disability and prediction of mortality and nursing home admission. *Journals Gerontol*. 1994;49(2). doi:10.1093/geronj/49.2.M85

164. Jones CJ, Rikli RE, Beam WC. A 30-s chair-stand test as a measure of lower body strength in community-residing older adults. *Res Q Exerc Sport*. 1999;70(2):113-119. doi:10.1080/02701367.1999.10608028

165. Brzychi M. Strength testing - Predicting a one-rep max from reps-to-fatigue. *J Phys Educ Recreat Danc*. 1993;64(1):88-90. doi:10.1080/07303084.1993.10606684

166. Fry CS, Rasmussen BB. Skeletal muscle protein balance and metabolism in the elderly. *Curr Aging Sci*. 2011;4(3):260-268. doi:10.2174/1874609811104030260

167. Breen L, Phillips SM. Skeletal muscle protein metabolism in the elderly: Interventions to counteract the "anabolic resistance" of ageing. *Nutr Metab*. 2011;8(1):68. doi:10.1186/1743-7075-8-68

168. Burd NA, Gorissen SH, Van Loon LJCC. Anabolic resistance of muscle protein synthesis with aging. *Exerc Sport Sci Rev*. 2013;41(3):169-173. doi:10.1097/JES.0b013e318292f3d5

169. Da Boit M, Sibson R, Meakin JR, et al. Sex differences in the response to resistance exercise training in older people. *Physiol Rep*. 2016;4(12):1-8. doi:10.14814/phy2.12834

170. Burd NA, Tang JE, Moore DR, Phillips SM. Exercise training and protein metabolism: Influences of contraction, protein intake, and sex-based differences. *J Appl Physiol*. 2009;106(5):1692-1701. doi:10.1152/japplphysiol.91351.2008

171. Guralnik JM, Ferrucci L, Pieper CF, et al. Lower extremity function and subsequent disability: Consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. *Journals Gerontol - Ser A Biol Sci Med Sci*. 2000;55(4):221-231. doi:10.1093/gerona/55.4.M221

172. Guralnik J, Bandeen-Roche K, Bhasin SAR, et al. Clinically Meaningful Change for Physical Performance: Perspectives of the ICFSR Task Force. *J frailty aging*. 2020;9(1):9-13. doi:10.14283/jfa.2019.33

173. Perera S, Mody SH, Woodman RC, Studenski SA. Meaningful change and responsiveness in common physical performance measures in older adults. *J Am Geriatr Soc*. 2006;54(5):743-749. doi:10.1111/j.1532-5415.2006.00701.x

174. Glasgow RE, Vinson C, Chambers D, Khoury MJ, Kaplan RM, Hunter C. National institutes of health approaches to dissemination and implementation science: Current and future directions. *Am J Public Health*. 2012;102(7):1274-1281. doi:10.2105/AJPH.2012.300755

175. Burnes B. Emergent change and planned change - Competitors or allies? The case of XYZ construction. *Int J Oper Prod Manag*. 2004;24(9):886-902. doi:10.1108/01443570410552108

176. Collins FS. Reengineering Translational Science: The Time Is Right. *Sci Transl Med*. 2011;3(90):1-7.

177. Cruz-Jentoft AJ, Franco A, Sommer P, et al. Silver paper: The future of health promotion and preventive actions, basic research, and clinical aspects of age-related disease. *Eur J Ageing*. 2009;6(1):51-57. doi:10.1007/s10433-009-0108-x

178. Simmons R, Fajans P, Ghiron L. *Scaling up Health Service Delivery: From Pilot Innovations to Policies and Programmes*. Vol 123.; 2009. doi:10.1016/j.puhe.2009.05.012

179. Milat AJ, Bauman A, Redman S. Narrative review of models and success factors for scaling up public health interventions. *Implement Sci*. 2015;10(1):1-11. doi:10.1186/s13012-015-0301-6

180. Gray SM, McKay HA, Hoy CL, et al. Getting Ready for Scale-Up of an Effective Older Adult Physical Activity Program: Characterizing the Adaptation Process. *Prev Sci*. 2020;21(3):355-365. doi:10.1007/s11121-019-01085-3

181. Zubala A, MacGillivray S, Frost H, et al. *Promotion of Physical Activity Interventions for Community Dwelling Older Adults: A Systematic Review of Reviews*. Vol 12.; 2017. doi:10.1371/journal.pone.0180902

182. Craig P, Dieppe P, Macintyre S, Mitchie S, Nazareth I, Petticrew M. Developing and evaluating complex interventions: The new Medical Research Council guidance. *Bmj*. 2008;337(7676):979-983. doi:10.1136/bmj.a1655

183. Herrema AL, Westerman MJ, van Dongen EJ, Kudla U, Veltkamp M. Combined protein-rich diet with resistance exercise intervention to counteract sarcopenia: A qualitative study on drivers and barriers of compliance. *J Aging Phys Act*. 2017;26(1):106-113. doi:https://doi.org/10.1123/japa.2017-0126

184. Greenhalgh T, Robert G, Bate P. How to spread good ideas: A systematic review of the literature on service delivery and organisation. *A Syst Rev …*. Published online 2004:426.

185. Maidique MA. Entrepreneurs, Champions, and Technological Innovation. *Sloan Manag Rev*. 1980;21(2):59-76.

186. Miech EJ, Rattray NA, Flanagan ME, Damschroder L, Schmid AA, Damush TM. Inside help: An integrative review of champions in healthcare-related implementation. *SAGE Open Med*. 2018;6:205031211877326. doi:10.1177/2050312118773261

187. Dorhout BG, Doets EL, van Dongen EJI, de Groot LCPGM, Haveman-Nies A. In-depth analyses of the effects of a diet and resistance exercise intervention in older adults: who benefits most from ProMuscle in Practice? *J Gerontol A Biol Sci Med Sci*. Published online 2021. doi:10.1093/gerona/glab104

188. Pablos-Mendez A, Chunharas S, Lansang MA, Shademani R, Tugwell P. Knowledge Translation in Global Health. Bulletin of the World Health Organization. Published 2005. Accessed April 1, 2021. https://www.who.int/bulletin/volumes/83/10/editorial21005html/en/

189. Rogers EM. *Diffusion of Innovations*. 4th editio. The Free Press; 1995.

190. Morley John E., Baumgartner Richard N., Roubenoff Ronenn, Mayer Jean NSK. Sarcopenia, From the chicago meetings. *J Lab Clin Med*. 2001;137(4):231-243. doi:10.1067/mlc.2001.113504

191. Federal Interagency Forum on Aging-Related Statistics. *Older Americans 2020: Key Indicators of Well-Being*.; 2020.

192. Sawyer B, Claxton G. How do health expenditures vary across the population? Chart collections. Published 2016. Accessed November 20, 2020. https://www.healthsystemtracker.org/chart-collection/health-expenditures-vary-across-population/#item-start

193. Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res*. 2011;20(10):1727-1736. doi:10.1007/s11136-011-9903-x

194. Versteegh, Matthijs M. Vermeulen KM, Evers SMAA, de Wit GA, Prenger R, Stolk EA. Dutch Tariff for the Five-Level Version of EQ-5D. *Value Heal*. 2016;19(4):343-352. doi:10.1016/j.jval.2016.01.003

195. iMTA. Questionnaires for the measurement of costs in economic evaluations. https://www.imta.nl/questionnaires/

196. Bouwmans C, Hakkaart-van Roijen L, Koopmanschap M, Krol M, Severens H, Brouwer W. *Productivity Cost Questionnaire - Manual*.; 2013.

197. IJzerman MJ. *Richtlijn Voor Het Uitvoeren van Economische Evaluaties in de Gezondheidszorg*.; 2016.

198. Hakkaart-van Roijen L, van der Linden N, Bouwmans C, Kanters T, Swan Tan S. *Richtlijn Voor Het Uitvoeren van Economische Evaluaties in de Gezondheidszorg. Bijlage 1: Kostenhandleiding: Methodologie van Kostenonderzoek En Referentieprijzen Voor Economische Evaluaties in de Gezondheidszorg*.; 2016.

199. Beaudart C, Biver E, Reginster JY, et al. Development of a self-administrated quality of life questionnaire for sarcopenia in elderly subjects: The SarQoL. *Age Ageing*. 2015;44(6):960-966. doi:10.1093/ageing/afv133

200. Council for Public Health and Care. *Rechtvaardige En Duurzame Zorg [Fair and Sustainable Care]*.; 2007.

201. Lorgelly PK, Lawson KD, Fenwick EAL, Briggs AH. Outcome measurement in economic evaluations of public health interventions: A role for the capability approach? *Int J Environ Res Public Health*. 2010;7(5):2274-2289. doi:10.3390/

ijerph7052274

202. Silva Neto LS, Karnikowski MGO, Osório NB, et al. Association between sarcopenia and quality of life in quilombola elderly in Brazil. *Int J Gen Med*. 2016;9:89-97. doi:10.2147/IJGM.S92404

203. Beaudart C, Reginster JY, Petermans J, et al. Quality of life and physical components linked to sarcopenia: The SarcoPhAge study. *Exp Gerontol*. 2015;69:103-110. doi:10.1016/j.exger.2015.05.003

204. Woo T, Yu S, Adams R, Visvanathan R. The Association Between Sarcopenia and Quality of Life is Different in Community Dwelling Older Australian Men and Women. *Geriatr Med Care*. 2018;2(1):1-6. doi:10.15761/gmc.1000113

205. Liu C-J, Latham NK. Progressive resistance strength training for improving physical function in older adults. *Cochrane database Syst Rev*. 2009;(3):CD002759. doi:10.1002/14651858.CD002759.pub2

206. Chou CH, Hwang CL, Wu YT. Effect of exercise on physical function, daily living activities, and quality of life in the frail older adults: A meta-analysis. *Arch Phys Med Rehabil*. 2012;93(2):237-244. doi:10.1016/j.apmr.2011.08.042

207. Robertson MC, Campbell AJ, Gardner MM, Devlin N. Preventing injuries in older people by preventing falls: A meta-analysis of individual-level data. *J Am Geriatr Soc*. 2002;50(5):905-911. doi:10.1046/j.1532-5415.2002.50218.x

208. Weatherly H, Drummond M, Claxton K, et al. Methods for assessing the cost-effectiveness of public health interventions: Key challenges and recommendations. *Health Policy (New York)*. 2009;93(2-3):85-92. doi:10.1016/j.healthpol.2009.07.012

209. Rizzoli R, Reginster J, Arnal J, Bautmans I. Quality of Life in Sarcopenia and Frailty. *Calcif Tissue Int*. 2014;93(2):101-120. doi:10.1007/s00223-013-9758-y.

210. Beaudart C, Biver E, Bruyère O, et al. Quality of life assessment in musculo-skeletal health. *Aging Clin Exp Res*. 2018;30(5):413-418. doi:10.1007/s40520-017-0794-8

211. Beaudart C, Biver E, Reginster JY, et al. Validation of the SarQoL®, a specific health-related quality of life questionnaire for Sarcopenia. *J Cachexia Sarcopenia Muscle*. 2017;8(2):238-244. doi:10.1002/jcsm.12149

212. Geerinck A, Bruyère O, Locquet M, Reginster JY, Beaudart C. Evaluation of the Responsiveness of the SarQoL® Questionnaire, a Patient-Reported Outcome Measure Specific to Sarcopenia. *Adv Ther*. 2018;35(11):1842-1858. doi:10.1007/s12325-018-0820-z

213. Tsekoura M, Billis E, Tsepis E, et al. The Effects of Group and Home-Based Exercise Programs in Elderly with Sarcopenia: A Randomized Controlled Trial. *J Clin Med*. 2018;7(12):480. doi:10.3390/jcm7120480

214. Pavasini R, Guralnik J, Brown JC, et al. Short Physical Performance Battery and all-cause mortality: Systematic review and meta-analysis. *BMC Med*. 2016;14(1):1-9.

doi:10.1186/s12916-016-0763-7

215. Volpato S, Cavalieri M, Sioulis F, et al. Predictive value of the Short Physical Performance Battery following hospitalization in older patients. *Journals Gerontol - Ser A Biol Sci Med Sci*. 2011;66 A(1):89-96. doi:10.1093/gerona/glq167

216. Guralnik JM, Ferrucci L, Simonsick EM, Salive ME, Wallace RB. Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. *N Engl J Med*. 1995;332(9):556-562. doi:10.1056/NEJM199503023320902

217. Miller, D.K., Wolinsky, F.D., Andresen, E.M., Malmstrom, T.K., Miller JP. Adverse outcomes and correlates of change in the short physical performance battery over 36 months in the African American Health Project. *J Gerontol A Biol Sci Med Sci*. 2008;63(5):487-494. doi:10.1016/j.physbeh.2017.03.040

218. Perera S, Studenski S, Chandler JM, Guralnik JM. Magnitude and patterns of decline in health and function in 1 year affect subsequent 5-year survival. *Journals Gerontol - Ser A Biol Sci Med Sci*. 2005;60(7):894-900. doi:10.1093/gerona/60.7.894

219. Van Dijk, C., Van den Burg, M., Dik, J.W., Heim N. *Ouderenzorg 2013-2016. Deel 1 - Zorgggebruik En Zorgkosten van Ouderen*.; 2018.

220. van Dijk CE, van den Burg M, Dik JW, Heim N. *Ouderenzorg 2013-2016. Deel 2 - Zorggebruik En Zorgkosten van Thuiswonende Ouderen*.; 2018.

221. van Dijk CE, van den Burg M, Dik JW, Heim N. *Ouderenzorg 2013 - 2016. Deel 3 - Zorggebruik En Zorgkosten Voorafgaand Aan En Tijdens Verblijf in Intramurale Verpleging En Verzorging*.; 2018.

222. De Wit G, Tariq L, Van Gils P, Panneman M. *Over Euro En Effect: Handleiding Voor Economisch Evaluatieonderzoek Bij Gezondheidsbevordering*.; 2010.

223. Bhandari A, Wagner T. Self-reported utilization of health care services: Improving measurement and accuracy. *Med Care Res Rev*. 2006;63(2):217-235. doi:10.1177/1077558705285298

224. Wallace E, Moriarty F, McGarrigle C, Smith SM, Kenny RA, Fahey T. Self-report versus electronic medical record recorded healthcare utilisation in older community-dwelling adults: Comparison of two prospective cohort studies. *PLoS One*. 2018;13(10):1-13. doi:10.1371/journal.pone.0206201

225. Alle verzekerde zorg onderwerpen - Diëtetiek (Zvw). Zorginstituut Nederland. Accessed May 29, 2020. https://www.zorginstituutnederland.nl/Verzekerde+zorg/dietetiek-zvw

226. Biolo G, Tipton KD, Klein S, Wolfe RR. An abundant supply of amino acids enhances the metabolic effect of exercise on muscle protein. *Am J Physiol - Endocrinol Metab*. 1997;273(1 36-1). doi:10.1152/ajpendo.1997.273.1.e122

227. Chen G, Liu L, Yu J. A Comparative Study on Strength between American College Male and Female Students in Caucasian and Asian Populations. *Sport Sci Rev*.

2012;21(3-4):153-165. doi:10.2478/v10237-012-0015-5

228. Miller AEJ, Macdougall JD, Tarnopolsky MA, Sale DG. Gender differences in strength and muscle fiber characteristics. *Eur J Appl Physiol*. 1993;66:254-262. doi:https://doi.org/10.1007/BF00235103

229. Frontera WR, Hughes VA, Lutz KJ, Evans WJ. A cross-sectional study of muscle strength and mass in 45- to 78-yr-old men and women. *J Appl Physiol*. 1991;71(2):644-650. doi:10.1152/jappl.1991.71.2.644

230. NWO. ProMIO 2.0: Een krachtig leefstijlprogramma voor migranten ouderen. Published 2020. Accessed July 5, 2021. https://www.nwo.nl/en/projects/raakmkb12033

231. Gill TM, Gahbauer EA, Han L, Allore HG. Trajectories of Disability in the Last Year of Life. *N Engl J Med*. 2010;362(13):1173-1180. doi:10.1056/nejmoa0909087

232. Jaul E, Barron J. Age-Related Diseases and Clinical and Public Health Implications for the 85 Years Old and Over Population. *Front Public Heal*. 2017;5. doi:10.3389/fpubh.2017.00335

233. English KL, Paddon-Jones D. Protecting muscle mass and function in older adults during bed rest. *Curr Opin Clin Nutr Metab Care*. 2010;13(1):34-39. doi:10.1097/MCO.0b013e328333aa66

234. de Gezondheidsraad. Beweegrichtlijnen 2017. Published 2017. Accessed August 26, 2021. https://www.gezondheidsraad.nl/documenten/adviezen/2017/08/22/beweegrichtlijnen-2017

235. Fogelholm M. New Nordic Nutrition Recommendations are here. *Food Nutr Res*. 2013;57(1). doi:10.3402/fnr.v57i0.22903

236. Richter M, Baerlocher K, Bauer JM, et al. Revised Reference Values for the Intake of Protein. *Ann Nutr Metab*. 2019;74(3):242-250. doi:10.1159/000499374

237. Food Safety Authority of Ireland. *Scientific Recommendations for Food-Based Dietary Guidelines for Older Adults in Ireland*.; 2021.

238. Dorrington N, Fallaize R, Hobbs DA, Weech M, Lovegrove JA. A Review of Nutritional Requirements of Adults Aged ≥65 Years in the UK. *J Nutr*. 2020;150(9):2245-2256. doi:10.1093/jn/nxaa153 Abstract

239. Gezondheidsraad. *Voedingsnormen Voor Eiwitten - Referentiewaarden Voor de Inname van Eiwitten*.; 2021.

240. Franco MR, Tong A, Howard K, et al. Older people's perspectives on participation in physical activity: A systematic review and thematic synthesis of qualitative literature. *Br J Sports Med*. 2015;49(19):1268-1276. doi:10.1136/bjsports-2014-094015

241. Ige-Elegbede J, Pilkington P, Gray S, Powell J. Barriers and facilitators of physical activity among adults and older adults from Black and Minority Ethnic groups in the UK: A systematic review of qualitative studies. *Prev Med Reports*.

2019;15(February):100952. doi:10.1016/j.pmedr.2019.100952

242. Belza B, Walwick J, Shiu-Thornton S, Schwartz S, Taylor M, LoGerfo J. Older adult perspectives on physical activity and exercise: Voices from multiple cultures. *Prev Chronic Dis*. 2004;1(4):1-12.

243. Gregg EW, Beckles GLA, Williamson DF, et al. Diabetes and physical disability among older U.S. adults. *Diabetes Care*. 2000;23(9):1272-1277. doi:10.2337/diacare.23.9.1272

244. Gregg EW, Mangione CM, Cauley JA, et al. Diabetes and Incidence of Functional Disability in Older Women. *Diabetes Care*. 2002;25(1):61-67. doi:10.2337/diacare.25.1.61

245. Park SW, Goodpaster BH, Strotmeyer ES, et al. Decreased muscle strength and quality in older adults with type 2 diabetes: The health, aging, and body composition study. *Diabetes*. 2006;55(6):1813-1818. doi:10.2337/db05-1183

246. Mesinovic J, Zengin A, De Courten B, Ebeling PR, Scott D. Sarcopenia and type 2 diabetes mellitus: A bidirectional relationship. *Diabetes, Metab Syndr Obes Targets Ther*. 2019;12:1057-1072. doi:10.2147/DMSO.S186600

247. Bellary S, Kyrou I, Brown JE, Bailey CJ. Type 2 diabetes mellitus in older adults: clinical considerations and management. *Nat Rev Endocrinol*. Published online 2021. doi:https://doi.org/10.1038/s41574-021-00512-2

248. Jackson PA, Pialoux V, Corbett D, et al. Promoting brain health through exercise and diet in older adults: a physiological perspective. *J Physiol*. 2016;594(16):4485-4498. doi:10.1113/JP271270

249. WHO. Fact sheet Dementia. Published 2020. Accessed August 26, 2021. https://www.who.int/news-room/fact-sheets/detail/dementia

250. Liu T, Li N, Hou Z, et al. Nutrition and exercise interventions could ameliorate age-related cognitive decline: a meta-analysis of randomized controlled trials. *Aging Clin Exp Res*. 2020;(0123456789). doi:10.1007/s40520-020-01730-w

251. Lisko I, Kulmala J, Annetorp M, Ngandu T, Mangialasche F, Kivipelto M. How can dementia and disability be prevented in older adults: where are we today and where are we going? *J Intern Med*. 2021;289(6):807-830. doi:10.1111/joim.13227

252. Baranowski BJ, Marko DM, Fenech RK, Yang AJT, Macpherson REK. Healthy brain, healthy life: A review of diet and exercise interventions to promote brain health and reduce alzheimer's disease risk1. *Appl Physiol Nutr Metab*. 2020;45(10):1055-1065. doi:10.1139/apnm-2019-0910

253. Guccione AA, Wong RA, Avers D. *Geriatric Physical Therapy*. Third edit. Elsevier Mosby; 2012.

254. Movsisyan A, Arnold L, Evans R, et al. Adapting evidence-informed complex population health interventions for new contexts: a systematic review of guidance.

Implement Sci. 2019;14(105):1-20. doi:https://doi.org/10.1186/s13012-019-0956-5

255. Stewart AL, Gillis D, Grossman M, et al. Diffusing a research-based physical activity promotion program for seniors into diverse communities: CHAMPS III. *Prev Chronic Dis*. 2006;3(2):1-16.

256. Evans RE, Craig P, Hoddinott P, et al. When and how do "effective" interventions need to be adapted and/or re-evaluated in new contexts? the need for guidance. *J Epidemiol Community Health*. 2019;73(6):481-482. doi:10.1136/jech-2018-210840

257. Chaudoir SR, Dugan AG, Barr CHI. Measuring factors affecting implementation of health innovations: A systematic review of structural, organizational, provider, patient, and innovation level measures. *Implement Sci*. 2013;8(22). doi:10.1186/1748-5908-8-22

258. Gagnon MP, Labarthe J, Légaré F, et al. Measuring organizational readiness for knowledge translation in chronic care. *Implement Sci*. 2011;6(72):1-10. doi:10.1186/1748-5908-6-72

259. Khan S, Timmings C, Moore JE, et al. The development of an online decision support tool for organizational readiness for change. *Implement Sci*. 2014;9(56):1-7. doi:10.1186/1748-5908-9-56

260. Weiner BJ, Amick H, Lee S-YD. Conceptualization and Measurement of Organizational Readiness for Change: A Review of the Literature in Health Services Research and Other Fields. *Med Care Res Rev*. 2008;65(4):379-436. doi:https://doi.org/10.1177/1077558708317802

261. Weiner BJ. A theory of organizational readiness for change. *Implement Sci*. 2009;4(67):1-9. doi:10.1186/1748-5908-4-67

262. Timmings C, Khan S, Moore JE, Marquez C, Pyka K, Straus SE. Ready, Set, Change! Development and usability testing of an online readiness for change decision support tool for healthcare organizations. *BMC Med Inform Decis Mak*. 2016;16(24):1-10. doi:10.1186/s12911-016-0262-y

263. Gagnon MP, Attieh R, Dunn S, et al. Development and content validation of a transcultural instrument to assess organizational readiness for knowledge translation in healthcare organizations: The OR4KT. *Int J Heal Policy Manag*. 2018;7(9):791-797. doi:10.15171/ijhpm.2018.17

264. Li SA, Jeffs L, Barwick M, Stevens B. Organizational contextual features that influence the implementation of evidence-based practices across healthcare settings: A systematic integrative review. *Syst Rev*. 2018;7(1). doi:10.1186/s13643-018-0734-5

265. Brodtkorb K, Skaar R, Slettebø Å. The importance of leadership in innovation processes in nursing homes: An integrative review. *Nord J Nurs Res*. 2019;39(3):127-136. doi:10.1177/2057158519828140

266. Rosemond CA, Hanson LC, Ennett ST, Schenck AP, Weiner BJ. Implementing person-centered care in nursing homes. *Health Care Manage Rev*. 2012;37(3):257-266.

doi:10.1097/HMR.0b013e318235ed17

267. Moore KL, Boscardin WJ, Steinman MA, Schwartz JB. Age and sex variation in prevalence of chronic medical conditions in older residents of U.S. nursing homes. *J Am Geriatr Soc*. 2012;60(4):756-764. doi:10.1111/j.1532-5415.2012.03909.x

268. Zimmerman S, Shier V, Saliba D. Transforming nursing home culture: Evidence for practice and policy. *Gerontologist*. 2014;54(SUPPL 1). doi:10.1093/geront/gnt161

269. Jones AL, Dwyer LL, Bercovitz AR, Strahan GW. *The National Nursing Home Survey: 2004 Overview*. Vol 13.; 2009.

270. Collier E, Harrington C. Staffing characteristics, turnover rates, and quality of resident care in nursing facilities. *Res Gerontol Nurs*. 2008;1(3):157-170. doi:10.3928/00220124-20091301-03

271. Castle NG, Engberg J. Staff turnover and quality of care in nursing homes. *Med Care*. 2005;43(6):616-626. doi:10.1097/01.mlr.0000163661.67170.b9

272. Scalzi CC, Evans LK, Barstow A, Hostvedt K. Barriers and Enablers to Changing Organizational Culture in Nursing Homes. *J Nurs Adm*. 2006;30(4):368-372. doi:10.1097/00005110-200605000-00010

273. Tyler DA, Lepore M, Shield RR, Looze J, Miller SC. Overcoming Resistance to Culture Change: Nursing Home Administrators' Use of Education, Training, and Communication. *Gerontol Geriatr Educ*. 2014;35(4):321-336. doi:10.1080/02701960.2013.837049

274. Escoffery C, Lebow-Skelley E, Haardoerfer R, et al. A systematic review of adaptations of evidence-based public health interventions globally. *Implement Sci*. 2018;13(125). doi:10.1186/s13012-018-0815-9

275. Castro FG, Barrera Jr. M, Martinez Jr. CR. The Cultural Adaptation of Prevention Interventions: Resolving Tensions Between Fidelity and Fit. *Prev Sci*. 2004;5(1):41-45. doi:10.1023/b:prev.0000013980.12412.cd

276. Bopp M, Saunders R, Lattimore D. The Tug-of-War: Fidelity Versus Adaptation Throughout the Health Promotion Program Life Cycle. *J Prim Prev*. 2013;34(3):193-207. doi:10.1007/s10935-013-0299-y

277. McKay H, Mackey D, Gray S, et al. Translational Formative Evaluation before Scale-up of a Physical Activity Intervention for Older Men. *Transl J Am Coll Sport Med*. 2019;4(14):106. doi:10.1249/TJX.0000000000000090

278. Zwaap J, Knies S, van der Meijden C, Staal P, van der Heiden L. *Cost-Effectiveness in Practice*.; 2015.

279. Kelly MP, McDaid D, Ludbrook A, Powell J. Economic appraisal of public health interventions. In: *NHS, Health Development Agency*. ; 2005:1-8.

280. Makai P, Brouwer WBF, Koopmanschap MA, Stolk EA, Nieboer AP. Quality of life instruments for economic evaluations in health and social care for older people: A systematic review. *Soc Sci Med*. 2014;102:83-93. doi:10.1016/j.socscimed.2013.11.050

281. Van Leeuwen KM, Bosmans JE, Jansen APD, et al. Comparing measurement properties of the EQ-5D-3L, ICECAP-O, and ASCOT in frail older adults. *Value Heal*. 2015;18(1):35-43. doi:10.1016/j.jval.2014.09.006

282. Coast J, Flynn TN, Natarajan L, et al. Valuing the ICECAP capability index for older people. *Soc Sci Med*. 2008;67(5):874-882. doi:10.1016/j.socscimed.2008.05.015

283. Payne, K., McAllister, M., Davies LM. Valuing the economic benefits of comlex interventions: when maximising health is not sufficient. *Health Econ*. 2013;22:258-271. doi:10.1002/hec.2795

284. Heijink R, Struijs J. Preventie in het zorgstelsel: wat kunnen we leren van het buitenland? Published 2016. Accessed August 20, 2021. https://www.rivm.nl/publicaties/preventie-in-zorgstelsel-wat-kunnen-we-leren-van-buitenland-eerste-inventarisatie-op

285. Ministerie van Volksgezondheid Welzijn en Sport. Gezondheid breed op de agenda [National paper on health policy 2020-2024. Published 2020. Accessed August 26, 2021. https://www.rijksoverheid.nl/documenten/rapporten/2020/02/29/gezondheid-breed-op-de-agenda

286. Volksgezondheidenzorg.info. Dossier Preventie. Wat is preventie? Published 2021. Accessed June 30, 2021. https://www.volksgezondheidenzorg.info/onderwerp/dossier-preventie/wat-preventie#node-wat-verstaan-we-onder-preventie

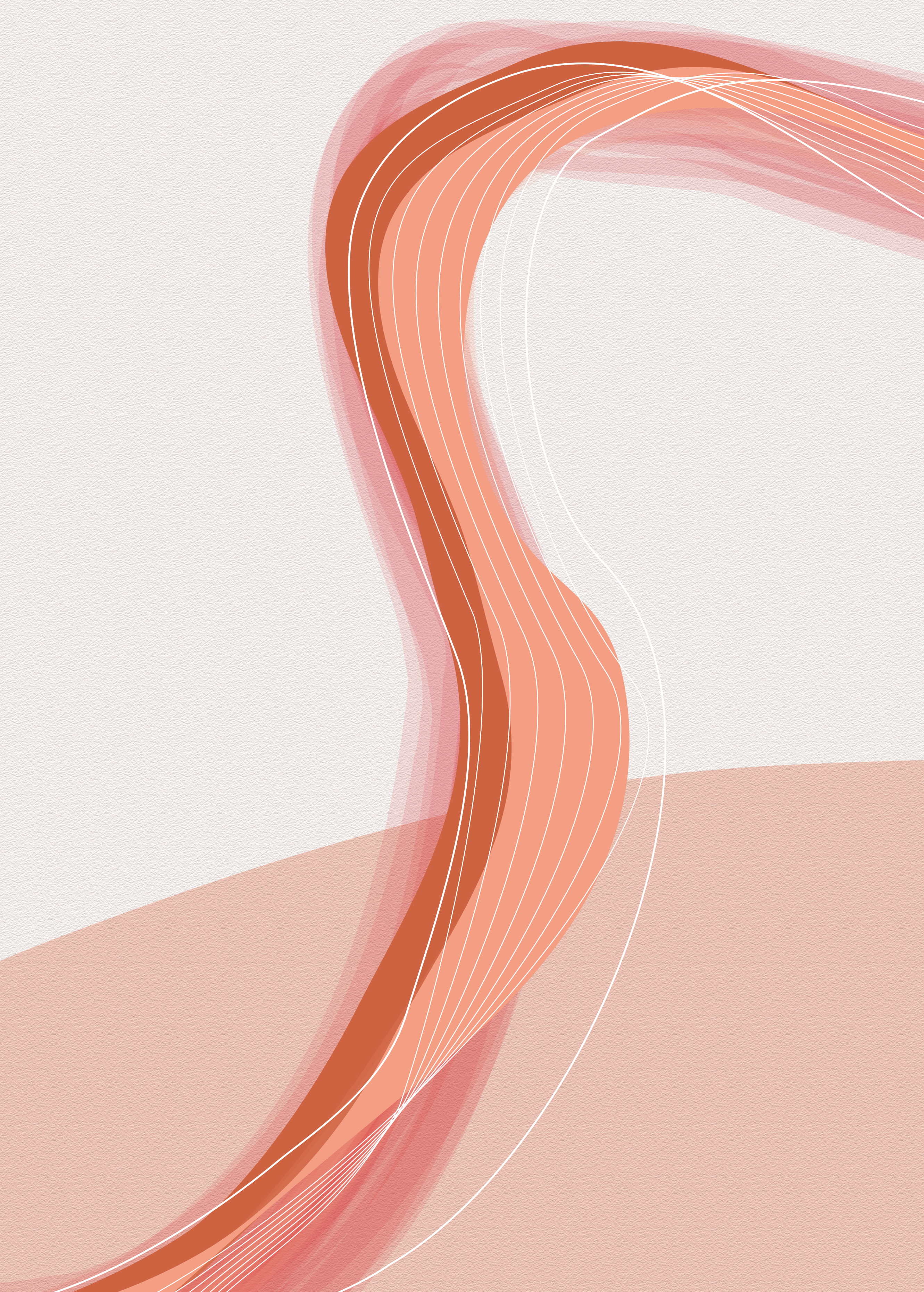
287. Kemper PF, Lemmens LC, de Bekker A. Evaluatie Preventie in het Zorgstelsel. RIVM, Centrum voor Voeding, Preventie en Zorg. Published 2020. Accessed August 20, 2021. https://www.rivm.nl/documenten/evaluatie-preventie-in-zorgstelsel-2020

288. HealthKIC. Wat is het Kavelmodel? HeatlhKIC Community. Published 2021. Accessed September 9, 2021. https://www.kic.nl/wat-is-kic/het-kavelmodel

289. Izquierdo M, Duque G, Morley JE. Physical activity guidelines for older people: knowledge gaps and future directions. *Lancet Heal Longev*. 2021;2(6):e380-e383. doi:10.1016/S2666-7568(21)00079-9

290. Covinsky KE, Pierluissi E, Johnston CB. Hospitalization-associated disability "She was probably able to ambulate, but i'm not sure." *JAMA - J Am Med Assoc*. 2011;306(16):1782-1793. doi:10.1001/jama.2011.1556

291. Sáez de Asteasu ML, Martínez-Velilla N, Zambom-Ferraresi F, et al. Inter-individual variability in response to exercise intervention or usual care in hospitalized older adults. *J Cachexia Sarcopenia Muscle*. 2019;10(6):1266-1275. doi:10.1002/jcsm.12481



Summary

SUMMARY

Global life expectancy has increased tremendously over the past decades, and so has the number of older adults. Preferably, these later years are spent in good health living independently at home, rather than suffering from physical and mental declines. However, a common consequence of ageing is the decrease in muscle mass, muscle strength and physical functioning. Diet and exercise interventions have been proven to be effective in counteracting this deterioration in health status in (pre-)frail older adults. However, the ageing population can be referred to as a heterogeneous population. Not only in terms of personal characteristics, ethnicity, and health status, but also in its responsiveness to treatments or interventions. To be able to serve a wide population, it is important to assess heterogeneity in older adults' health status and subsequently study the heterogeneity in responsiveness to diet and exercise interventions. Besides, factors on the organisational and contextual level are expected to influence responsiveness to lifestyle interventions. Therefore, the aim of this thesis was threefold: 1) To study the sarcopenia prevalence, dietary protein intake, and underlying behavioural and environmental factors affecting protein intake in ethnic minorities in the Netherlands, 2) To study the personal, organisational, and other contextual factors affecting responsiveness to a diet and exercise intervention, and 3) To study the cost-effectiveness of ProMuscle in Practice.

Chapter 2 and 3 focused on the Healthy Life in an Urban Setting (HELIUS) study: a large cohort which includes participants from Dutch, South Asian Surinamese, African Surinamese, Turkish, Moroccan, and Ghanaian ethnic origin living in Amsterdam. Chapter 2 includes the results of a cross-sectional study of the HELIUS data, presenting the sarcopenia prevalences and its relation to protein intake in ethnic minorities in the Netherlands. The results show that sarcopenia prevalence varies across sexes and ethnic groups, being lowest in Turkish women and men and highest in South-Asian Surinamese women and men. Besides, higher protein intake was associated with a 4% lower odds of sarcopenia in the population and across ethnic groups, being only significant in the South-Asian Surinamese group.

In chapter 3 we investigated the dietary protein intake and underlying behavioural and environmental factors affecting protein intake in ethnic minority populations. The dietary protein recommendation (1.0 g/kg bw/day) was not met by 40-60% of the Dutch, South Asian Surinamese, African Surinamese, and Moroccan older adults. Major sources of protein intake were found to be ethnic-specific. In addition, focus group discussions revealed that participants appeared to have little knowledge of and awareness on protein and its role in ageing.

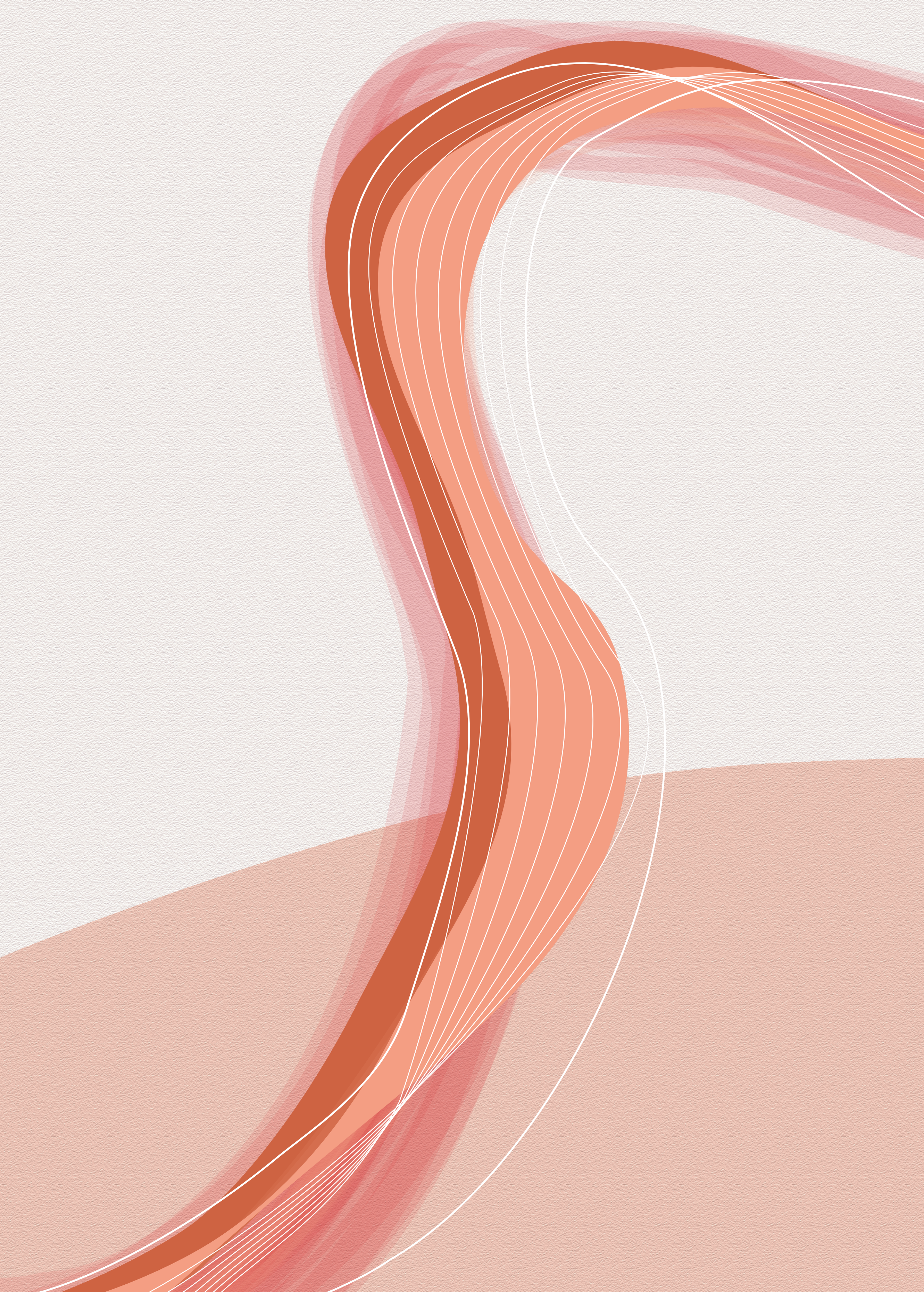
Chapter 4, 5 and 6 focused on the ProMuscle intervention, a diet and exercise intervention targeted at older adults. In chapter 4 we investigated which subgroup benefited most from the ProMuscle in Practice intervention. Results of in-depth analyses show that participants aged 75 years and younger and women benefited to a great extent from the intervention, as they improved significantly on nearly every outcome. Effects in participants with and without a mobility-impairing disorder (frailty, sarcopenia, or osteoarthritis) were comparable, indicating that the intervention is suitable for older adults regardless of having a mobility-impairing disorder.

In chapter 5, the effects and contextual factors of the three successive ProMuscle

interventions are pooled and compared in a mixed-methods study. The intervention was conducted in the controlled setting (ProMuscle), real-life setting (ProMuscle in Practice) and real-life setting of the implementation pilots (ProMuscle Implementation Pilots). Quantitative results show that the intervention led to improvements on chair-rise performance and leg strength in each setting, with the largest improvements in the ProMuscle Implementation Pilots. Qualitative results show that room for adapting and tailoring the intervention, the availability of and access to facilities, the involvement of experienced professionals, and participant characteristics might contribute to explaining the variation in effects across settings.

In chapter 6, we investigated the cost-effectiveness of ProMuscle in Practice and its perceived benefits regarding quality of life. Results show an Incremental Cost-Effectiveness Ratio of €2988 per point increase in the Short Physical Performance Battery (SPPB). The intervention has an 82.4% probability of being cost-effective at a willingness to pay of €12.000 per point increase in SPPB. No change in quality of life was found using the EQ-5D-5L questionnaire, however, interviews revealed a wide range of function-related perceived benefits. Evaluating preventive interventions using QALY measures could underestimate the benefits of such interventions. For this reason, other methods, such as topic-specific questionnaires, might be more suitable when conducting an economic evaluation in the field of public health.

Overall, we can conclude that one size does not fit all. This thesis emphasizes the importance of considering heterogeneity in the older population. Personal characteristics, organizational aspects, and the general setting influence the effects of lifestyle interventions. Adapting ProMuscle in Practice to the needs and possibilities of older adults, to the working procedures and facilities of professionals, while considering economic aspects is of major importance for a successful intervention and implementation. Successfully implementing an effective intervention such as ProMuscle in Practice will lead to an increased physical functioning status in older adults. As a results, older adults are more likely to maintain their independence and live longer at home in a healthy and vital way.



Samenvatting

SAMENVATTING

Niet alleen de wereldwijde levensverwachting steeg de afgelopen decennia enorm, ook het aantal ouderen nam toe. Hoewel de jaren op latere leeftijd bij voorkeur zelfstandig thuiswonend en in goede gezondheid doorgebracht worden, wordt veroudering nog vaak gekenmerkt door lichamelijke en geestelijke aftakeling. Een voorbeeld van zo'n lichamelijke verandering is de afname van spiermassa, spierkracht en lichamelijk functioneren. Een van de strategieën die deze verslechtering van de gezondheidstoestand kan tegengaan, is de combinatie van krachttraining en eiwitrijke voeding. Voedings- en beweeginterventies zijn effectief gebleken in het verbeteren van de spiergezondheid bij (pre-)kwetsbare ouderen. De vergrijzende bevolking kan echter worden gekarakteriseerd als een heterogene populatie. Niet alleen wat betreft persoonlijke kenmerken, etniciteit en gezondheidstoestand, maar ook wat betreft de respons op behandelingen of interventies. Om een brede populatie te kunnen bereiken met interventies, is het van belang de heterogeniteit in de gezondheidsstatus van ouderen te bestuderen. Daarnaast is het van belang de heterogeniteit in de respons op voedings- en beweeginterventies te bestuderen. Ook wordt verwacht dat factoren op organisatorisch en contextueel niveau de respons op leefstijlinterventies beïnvloeden. Daarom was het doel van dit proefschrift drieledig: 1) Het bestuderen van de sarcopenie prevalentie, eiwitinname, en onderliggende gedrags- en omgevingsfactoren die de eiwitinname beïnvloeden in etnische minderheden in Nederland, 2) Het bestuderen van persoonlijke, organisatorische, en andere contextuele factoren die de respons op een voedings- en beweeginterventie beïnvloeden, en 3) Het bestuderen van de kosteneffectiviteit van ProMuscle in de Praktijk.

Hoofdstuk 2 en 3 richtten zich op de Healthy Life in an Urban Setting (HELIUS) studie: een groot cohort met deelnemers van Nederlandse, Zuid-Aziatisch Surinaamse, Afrikaans-Surinaamse, Turkse, Marokkaanse en Ghanese etnische afkomst die in Amsterdam wonen. Hoofdstuk 2 bevat de resultaten van een cross-sectionele studie van de HELIUS data. Hierin presenteren we de sarcopenie prevalenties en de relatie tussen sarcopenie en eiwitinname in etnische minderheden in Nederland. De resultaten laten zien dat de prevalentie van sarcopenie varieert tussen mannen en vrouwen, en tussen de etnische groepen. De prevalentie is het laagst bij Turkse vrouwen en mannen en het hoogst bij Zuid-Aziatisch Surinaamse vrouwen en mannen. Bovendien was een hogere eiwitinname geassocieerd met een 4% lagere kans op sarcopenie in de gehele groep en in de verschillende etnische groepen. Deze associatie was alleen significant in de Zuid-Aziatisch Surinaamse groep.

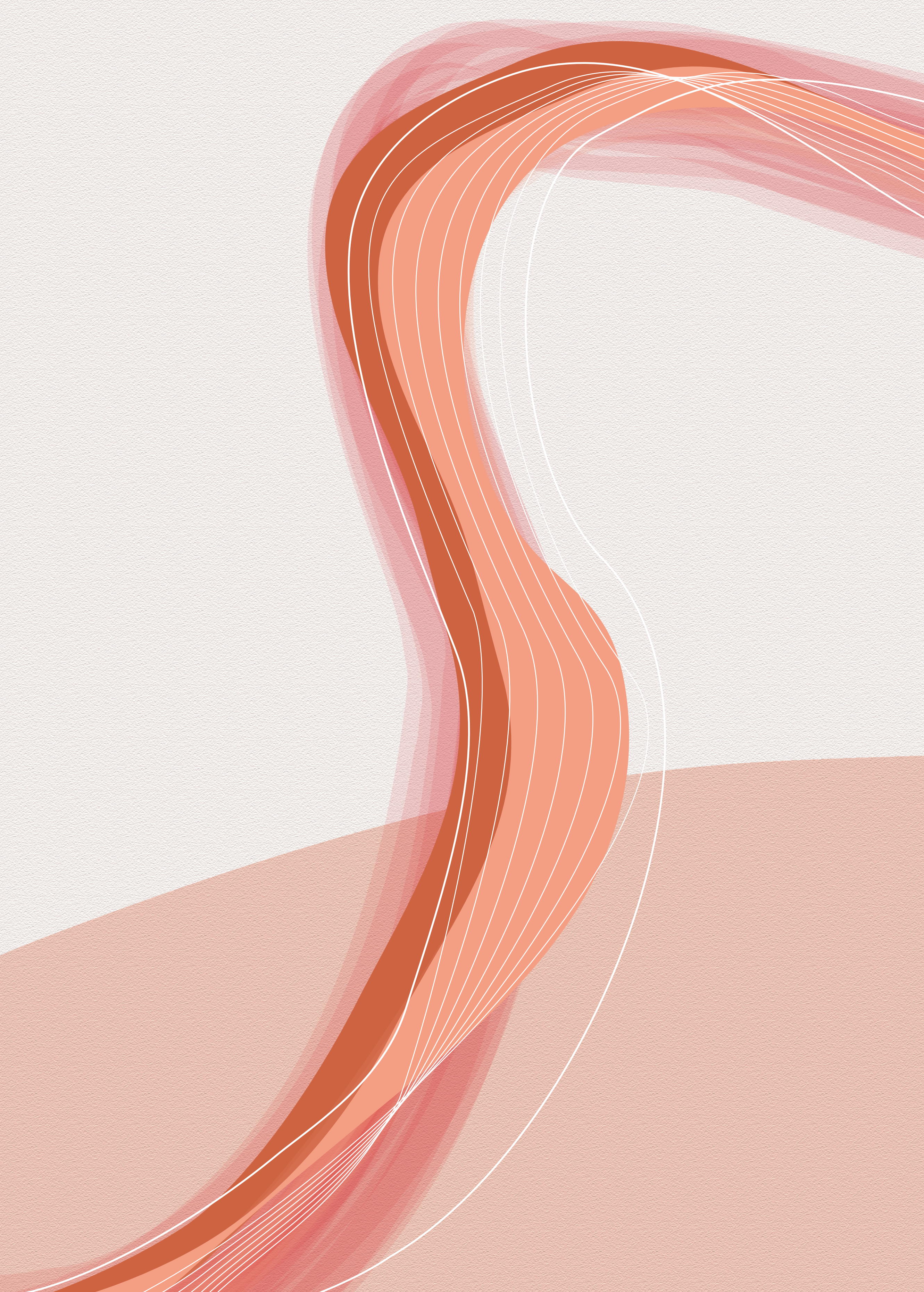
In hoofdstuk 3 onderzochten we de eiwitinname en onderliggende gedrags- en omgevingsfactoren die van invloed zijn op de eiwitinname van etnische minderheden. De aanbevolen hoeveelheid eiwit (1.0 g/kg lichaamsgewicht/dag) werd niet gehaald door 40-60% van de Nederlandse, Zuid-Aziatisch Surinaamse, Afrikaans-Surinaamse, en Marokkaanse ouderen. De belangrijkste eiwitbronnen bleken te verschillen per etniciteit. Bovendien wezen de focusgroepen uit dat kennis en bewustzijn over eiwitten en de rol ervan bij het ouder worden beperkt was bij de deelnemers.

Hoofdstuk 4, 5 en 6 richtten zich op de ProMuscle interventie, een voedings- en beweeginterventie voor ouderen. In hoofdstuk 4 hebben we onderzocht welke subgroep het meeste baat had bij de ProMuscle in de Praktijk interventie. De resultaten van verdiepende analyses laten zien dat deelnemers jonger dan 75 jaar en vrouwen in hoge mate profiteerden van de interventie, aangezien zij op bijna elke uitkomst significant verbeterden. De effecten bij deelnemers met en zonder een mobiliteitsbeperkende aandoening (fragiliteit, sarcopenie, of osteoartritis) waren vergelijkbaar. Dit wijst erop dat de interventie geschikt is voor ouderen, ongeacht of ze een mobiliteitsbeperkende aandoening hebben.

In hoofdstuk 5 zijn de effecten en contextuele factoren van de drie opeenvolgende ProMuscle interventies gebundeld en vergeleken in een mixed-methods studie. De interventie is uitgevoerd in de gecontroleerde setting (ProMuscle), de praktijksetting (ProMuscle in de Praktijk) en de praktijksetting van de implementatie pilots (ProMuscle Implementatie Pilots). Kwantitatieve resultaten tonen aan dat de interventie in elke setting heeft geleid tot verbeteringen op stoeltest-prestaties en beenspierkracht, met de grootste verbeteringen in de ProMuscle Implementatie Pilots. Kwalitatieve resultaten laten zien dat ruimte voor het aanpassen en op maat maken van de interventie, de beschikbaarheid van en toegang tot faciliteiten, de betrokkenheid van ervaren professionals, en kenmerken van deelnemers de variatie in effecten tussen de settings deels kunnen verklaren.

In hoofdstuk 6 onderzochten we de kosteneffectiviteit van ProMuscle in de Praktijk en de ervaren voordelen met betrekking tot kwaliteit van leven. De resultaten laten een kosteneffectiviteitsratio zien van €2988 per punt toename in de Short Physical Performance Battery (SPPB). De interventie heeft een waarschijnlijkheid van 82,4% dat deze kosteneffectief is bij een betalingsbereidheid van €12.000 per punt toename in SPPB. Er werd geen verandering in kwaliteit van leven gevonden op basis van de EQ-5D-5L vragenlijst (in QALY), maar met behulp van interviews werd een scala aan functie-gerelateerde ervaren voordelen in kaart gebracht. Het evalueren van preventieve interventies met behulp van QALY kan de voordelen van dergelijke interventies onderschatten. Daarom zouden andere methoden, zoals thema-specifieke vragenlijsten, geschikter kunnen zijn bij het uitvoeren van een economische evaluatie in het domein van de publieke gezondheid.

We kunnen concluderen dat er niet één uniforme aanpak is. Deze dissertatie benadrukt het belang van het in acht nemen van heterogeniteit in de oudere populatie. Persoonlijke kenmerken, organisatorische aspecten en de algemene setting beïnvloeden de effecten van leefstijlinterventies. Het aanpassen van ProMuscle in de Praktijk aan de behoeften en mogelijkheden van ouderen, aan de werkwijze en faciliteiten van professionals, en het rekening houden met financiële aspecten is van groot belang voor een succesvolle interventie en implementatie. Het succesvol implementeren van een effectieve interventie zoals ProMuscle in de Praktijk draagt bij aan het verbeteren van het fysiek functioneren van ouderen. Hierdoor is de kans groter dat ouderen hun zelfstandigheid behouden en langer gezond en vitaal thuis kunnen blijven wonen.



Dankwoord

DANKWOORD

Het laatste hoofdstuk dat ik schrijf, en tegelijkertijd het onderdeel dat vaak als eerste gelezen wordt: het dankwoord. Als ik terugkijk op de afgelopen vier jaar, lijkt het echt voorbij gevlogen. Ik heb het ervaren als een geweldige tijd en het was een proces waarin ik enorm veel geleerd heb, uiteraard met de nodige ups and downs. Dank dat jullie er waren om de ups met mij te vieren en de downs te relativeren!

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En dan het ProMuscle Dreamteam dat betrokken was bij de uitvoer van ProMuscle in de Praktijk: wauw, wat is er veel werk verzet! Jullie bijdrage aan het onderzoek was enorm, en daarvoor wil ik jullie bedanken. Allereerst Ellen, jij bent een echte doorzetter en keiharde werker. Ik heb veel bewondering voor jouw inzet, motivatie en nauwkeuige werkwijze. Ik heb veel geleerd van je en ben blij dat we dit samen hebben gedaan. Er was altijd ruimte voor gezelligheid, maar ook om onze frustraties te delen als iets niet volgens plan liep. Volgens mij waren we een topteam! Het onderzoeksteam was natuurlijk niet compleet zonder Saskia, Sandra, Meeke, Mariska, Odette, Irene, en Ilse. Wat hebben jullie veel ouderen gebeld, gemeten, opgehaald in de vroege uurtjes en ga zo maar door. Super bedankt voor jullie inzet, toewijding en betrokkenheid bij het onderzoek. En daarnaast: bedankt voor de gezellige tijd in Axis! Diederik, het leiden van zo'n enorme studie is wel voor jou weggelegd. Mijn complimenten hiervoor! Ik heb je inzet en manier van werken altijd heel erg gewaardeerd. Anne, wat fijn dat je betrokken was bij het onderzoek. De planning en logistiek is niet een gemakkelijke taak, maar toen het in jouw handen lag, konden we het compleet loslaten.

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Terug naar Wageningen Universiteit, waar ik een hele rij collega's wil bedanken. Ik had het geluk om zowel bij Human Nutrition & Health als bij Consumption & Healthy Lifestyles een werkplek te hebben. Ook al betekent dit soms extra overleggen, het betekent vooral dubbel zo veel leuke collega's en activiteiten.

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'Oude' kamergenoten van 1055: Carlijn, Guido, Paulina, Rachelle. Niet voor niets stond 1055 bekend als de 'loudest room': het was altijd gezellig met jullie! Rachelle, bedankt dat ik je altijd kon vragen voor een 'Engelse check'! En huidige kamergenoten van 1055: Eva, Ina, Maria, Matjaz, Max, en Michele. Met jullie is het er zeker niet minder gezellig op geworden! Speciale shout-out voor levensreddende acties wanneer je tas met vragenlijsten iets zwaarder is dan ingeschat. En niet te vergeten: de overload aan 'Celebrations'. Die hebben me zeker door de laatste maanden van mijn PhD gesleept!

Floortje, van bestuursgenootjes, via dispuutsgenootjes naar collega's. Naast dat het vooral erg gezellig was, verliep de samenwerking met jou bij onderwijstaken altijd heel soepel. Ik kan wel zeggen dat we een top team zijn!

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Allang geen roomies in 4069 meer, maar nu veel meer dan dat: Amy, Lotte, en Christel. Wat ben ik blij dat ik jullie tijdens mijn PhD heb leren kennen. Met jullie kan ik alles delen: niet alleen de hoogtepunten, maar ook de frustraties in het leven van een PhD'er. Na een avondje borrelen (en dansen) met jullie ben ik weer volledig opgeladen. Wanneer staat de volgende gepland? ;)

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En dan Bellatores: Anica, Iris, Katja, Laura, Nynke, Viola en Wies. We hebben net ons lustrum gevierd en ik heb nu al zin in de komende tien jaar met jullie. Wandelingen over de campus, avonden borrelen en weekendjes weg: het voelt altijd als thuiskomen met jullie. Jullie begrijpen me als de beste, zeker wat betreft 'PhD life'. Meiden: ik ben super blij met jullie als vriendinnen en weet zeker dat we nog vele lustra zullen vieren samen!

Viola, jij verdient een aparte vermelding in dit dankwoord. Je hebt ontzettend veel tijd besteed aan de voorkant en titelpagina's van mijn proefschrift. Wat was het fijn om hier samen met jou aan te werken, je begreep precies wat ik wilde. Het kiezen van kleuren was al een proces op zich: Ziekenhuiskleuren, legertinten, vies geel, en babykaartkleuren: we hebben alles gehad en ze waren zeker niet allemaal succesvol. Naast je hulp vond ik het vooral heel gezellig om dit samen te doen en ik ben super blij met het resultaat!

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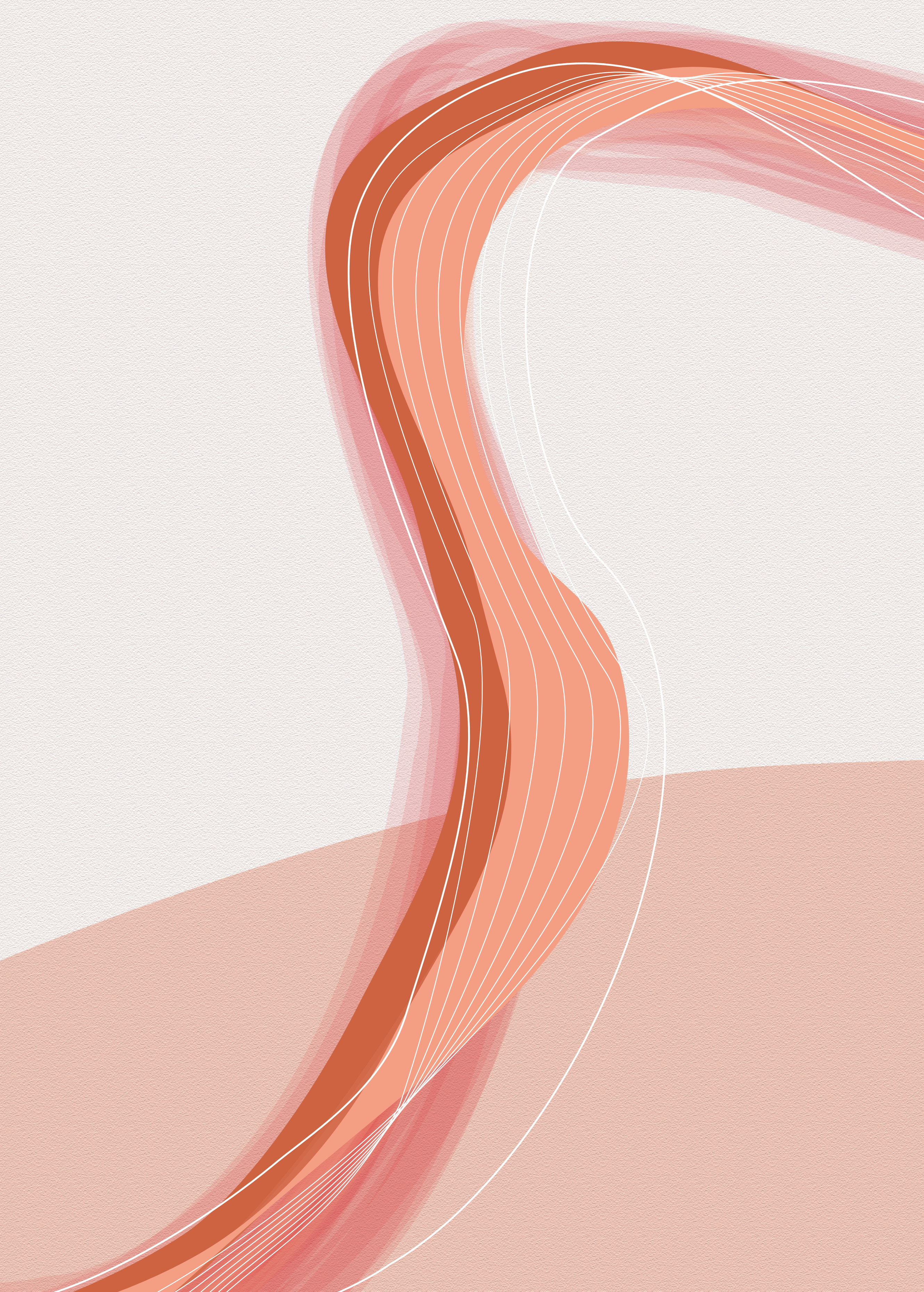

About the author

CURRICULUM VITAE

Berber Gijsbertha Dorhout was born on January 25th, 1993 in Surhuisterveen, the Netherlands. She grew up in Surhuizum living with her parents, brother and sister. After obtaining her secondary school diploma from Lauwers College in Buitenpost in 2011, she started her Bachelor studies Nutrition and Health at Wageningen University & Research. In the third year of the Bachelor, she spend a semester at the University of Eastern Finland in Kuopio for her minor studies. After achieving her Bachelor degree, she continued with the master studies in Nutrition and Health at Wageningen University & Research. She specialized in Epidemiology and Public Health. Her thesis was focused on the protein intake of older adults, and this enlarged her passion for research in the sector of public health, especially for the target group of older adults. During her internship at GGD Noord- en Oost Gelderland she studied aspects of a healthy living environment and setting up a research panel. After graduating in 2017, she started her PhD with a focus on nutrition and exercise in the aging population. Specifically, she worked on a lifestyle intervention targeted at older adults, called ProMuscle in Practice. During her PhD she worked at both Human Nutrition and Health and Consumption and Healthy Lifestyles at Wageningen University & Research. She presented her results at national as well as international conferences. Besides, she was involved in teaching, supervising thesis students, and she coordinated the courses Public Health Nutrition and Evaluation of Public Health Interventions.

In the beginning of 2021, she started working on the systematic and sustainable implementation of the ProMuscle in Practice intervention in collaboration with UMC Utrecht and Hogeschool Utrecht. In September 2021, she started working as a researcher at Hogeschool Utrecht. From November 2021 onwards she additionally started as postdoctoral researcher at Wageningen University & Research. Both jobs are focused on the implementation of ProMuscle in Practice.

LIST OF PUBLICATIONS

Publications

Dorhout BG, Doets E, van Dongen EJI, de Groot CPGM, Haveman-Nies A (2021). In-depth analyses of the effects of a diet and resistance exercise intervention in older adults: who benefits most from ProMuscle in Practice? J Gerontol A Biol Sci Med Sci. doi:10.1093/gerona/glab104

Dorhout BG, Haveman-Nies A, van Dongen EJI, Wezenbeek N, Doets E, Bulten A, de Wit A, de Groot CPGM (2021). Cost-effectiveness of a Diet and Resistance Exercise Intervention in Community-Dwelling Older Adults: ProMuscle in Practice. J Am Med Dir Assoc. doi.org/10.1016/j.jamda.2020.12.036

Overdevest E, **Dorhout BG**, Nicolaou M, van Valkengoed IGM, Haveman-Nies A, Oztürk H, de Groot CPGM, Tieland M, Weijs PJM (2021). Dietary Protein Intake in Older Adults from Ethnic Minorities in the Netherlands, a Mixed Methods Approach. Nutrients, 13(1). doi:10.3390/nu13010184

Dorhout BG, Overdevest E, Tieland M, Nicolaou M, Weijs PJM, Snijder MB, Peters RJG, van Valkengoed IGM, Haveman-Nies A, de Groot CPGM (2020). Sarcopenia and its relation to protein intake across older ethnic populations in the Netherlands: the HELIUS study. Ethnicity & Health. doi:10.1080/13557858.2020.1814207

van Dongen EJI, Doets EL, de Groot CPGM, **Dorhout BG**, Haveman-Nies A (2020). Process Evaluation of a Combined Lifestyle Intervention for Community-Dwelling Older Adults: ProMuscle in Practice. Gerontologist, 60(8): 1538-54. doi:10.1093/geront/gnaa027

van Dongen EJI, Haveman-Nies A, Doets EL, **Dorhout BG**, de Groot CPGM (2020). Effectiveness of a Diet and Resistance Exercise Intervention on Muscle Health in Older Adults: ProMuscle in Practice. J Am Med Dir Assoc, 21(8): 1065-72.e3. doi:10.1016/j.jamda.2019.11.026

van Dongen EJI, Haveman-Nies A, Wezenbeek NLW, **Dorhout BG**, Doets EL, de Groot CPGM (2018). Effect, process, and economic evaluation of a combined resistance exercise and diet intervention (ProMuscle in Practice) for community-dwelling older adults: design and methods of a randomised controlled trial. BMC Public Health, 18(1): 877. doi:10.1186/s12889-018-5788-8

Submitted manuscripts for publication

Dorhout BG, de Groot CPGM, van Dongen EJI, Doets E, Haveman-Nies A. Effects and contextual factors of a diet and resistance exercise intervention vary across settings: an overview of three successive ProMuscle interventions.

OVERVIEW OF COMPLETED TRAINING ACTIVITIES

Discipline specific activities	Organizing institute and location	Year
Nationaal Gerontologiecongres	NVG Knows, Ede	2017
Health Technology Assessment	UMC Utrecht, Utrecht	2018
Werkgroep Voedingsgewoonten	WeVo, Maastricht	2018
Masterclass Public evaluation and adaptation of public health interventions	VLAG, Wageningen	2018
Werkgroep Voedingsgewoonten	WeVo, Zwolle	2018
International Association of Gerontology and Geriatrics Congress	IAGG-er, Gothenburg, Sweden	2019
2e nationaal ouderen en voeding congres	Gercare consulting, Ede	2019
Conference nutrition disparity and equity	Edema-Steenberg, Wageningen	2019
The Dutch Society for Research on Ageing meeting	DUSRA, Leiden	2019
Symposium Pioneering Nutrition	WUR, Wageningen	2019
Symposium Towards healthy and environmentally sustainable diets for European consumers	TIFN, WUR, Wageningen	2019
International Conference on Frailty and Sarcopenia Research	International Academy Nutrition and Ageing, online	2020
Congres Arts en Leefstijl	Vereniging arts en leefstijl, online	2020
Conferentie - een nieuwe generatie ouderen, langer thuis	Ministerie VWS, online	2020
Symposium Physicians Implement Exercise = Medicine (PIE=M)	UMCG, Amsterdam UMC, online	2020
EuroVision of Implementation - An Introductory Workshop to Implementation	EIE2021, online	2021
European Implementation Event	EIE2021, online	2021

Discipline specific activities	Organizing institute and location	Year
Teaching an online course	ESD, Wageningen	2017
Supervising BSc and MSc thesis students	ESD, Wageningen	2018
Brain training	WGS, Wageningen	2018
The essentials of scientific writing and presenting	WGS, Wageningen	2018
Introduction to R	VLAG, Wageningen	2019
Scientific writing	WGS, Wageningen	2019
Career orientation	WGS, online	2020
Reviewing a scientific manuscript	WGS, online	2020
How to Create Impactful Infographics and Data Visuals	YoungWUR, online	2020
PhD carousel - workshop storytelling	WGS, online	2021

Discipline specific activities	Organizing institute and location	Year
Preparation of research proposal	Wageningen	2017
Research meetings Nutritional Biology	Wageningen	2017-2021
Research seminars Consumption and Healthy Lifestyles	Wageningen	2017-2021
PhD study tour to Canada	Canada	2019
Developing knowledge clips on economic evaluation	Wageningen	2021

COLOPHON

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