DIETARY PROTEIN AND RESISTANCE EXERCISE TRAINING FOR COMMUNITY-DWELLING OLDER ADULTS

Intervention adaptation, implementation and effectiveness

Ellen J.I. van Dongen

Dietary protein and resistance exercise training for community-dwelling older adults

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CHAPTER 1

General introduction

THE IMPACT OF AGING?

In the coming 30 years it is expected that the global population of adults aged ≥ 60 years will double, reaching 2.1 billion adults in 2050 [1]. Aging is associated with increasing healthcare costs due to e.g. decline in muscle mass and strength [2, 3], development of morbidities, and increased dependence on care [4]. In 2016 about half of the Dutch total healthcare expenses went to adults aged 65 years or over [4]. It is estimated that health care costs in elderly care in the Netherlands will increase from 17 billion in 2015 to 45 billion in 2040, as it is estimated that one-fourth of the population will be aged 65 years or over by then [5].

With the reformation of long-term care in the Netherlands in 2015, more emphasis is placed on facilitating older adults to age in their own homes with a good quality of life [4, 6]. In the Netherlands, 94% of adults aged 65 years and over still live at home [4]. Average health care expenses of older adults living at home are almost three times lower than for older adults who do not live independently [4]. Therefore strategies supporting healthy ageing among older adults may reduce or postpone the dependence on care and related costs. The World Health Organisation (WHO) defines healthy ageing as "the process of developing and maintaining the functional ability that enables wellbeing in older age" [7]. For healthy aging, it is important that older adults are supported in maintaining their independence and their ability to perform activities of daily living (ADL) at home. This enables older adults to continue active participation in society [8, 9]. The Dutch government, municipalities, and societal organisations have joint forces in the 'Elderly Care Pact', which aims to improve the care and living-situation of community-dwelling older adults [6]. One of the three focus points of this Pact is the program 'Longer at Home', which emphasises the role of local stakeholders in enabling older adults to live independently at home longer with a good quality of life [6].

Preventive activities that aim to maintain the function and independence of older adults need to focus on signalling and preventing declines in function, and on individuals' own possibilities of improving self-reliance [10]. Such preventive actions are highly relevant, as the age-related decline in skeletal muscle mass and muscle strength contributes to decreased functional capacity [11] (sarcopenia, see box 1). The decline in muscle strength with aging is larger (2.5-4% a year) than the decline in lean

body mass (0.5-1.0% a year), but both declines are gradual [12, 13]. The loss of muscle mass and strength is associated with reduced quality of life and jointly increase the risk of losing independence [14].

Box 1. Sarcopenia

Sarcopenia is the age related loss of skeletal muscle mass and strength and/or physical performance [11, 14-18]. The in 2018 revised sarcopenia definition from the European Working Group on Sarcopenia in Older People 2 (EWGSOP2) uses low muscle strength as a primary indicator of sarcopenia [19]. Factors that contribute to the onset of sarcopenia are i.e. diseases, physical inactivity and/or poor dietary intake, and smoking [11, 20-22]. According to the SarcoPhAge study, the estimated global sarcopenia prevalence amounts to 13.7% in people aged ≥ 65 years [23]. European estimates indicate that sarcopenia prevalence will increase between 2016 and 2045, reaching prevalence rates of 12.9% - 22.3% in 2045 [24]. In general, sarcopenia prevalence increases with age, and is slightly higher in women and in persons who have more comorbidities or who are malnourished [23]. In 2016, sarcopenia was given an ICD-10 code, meaning that it is recognized as a reportable condition that requires treatment [25]. EWGSOP2 has specified cut-off points for low strength, low muscle quantity, and low performance, to identify and characterize sarcopenia [19].

LIFESTYLE FACTORS

Dietary protein intake and resistance exercise are the two major elements that can be used to counteract the loss of muscle mass, strength, and physical functioning.

Dietary protein intake

Ageing may be associated with a decline in dietary energy and food intake, and a concomitant decline in nutrient intake [26]. Research has provided evidence that dietary protein intake is associated with improvements in or preservation of muscle mass, muscle strength, and function in older adults [21, 27, 28]. There are general dietary guidelines for older adults [29], and for older adults with malnutrition [30], but the current Dutch Health Council and European Food Safety Authority recommendations state no specific dietary recommendations for protein, fat, or carbohydrates for older adults [29, 31, 32]. The current Recommended Dietary

Allowance (RDA) for protein intake for all adults is 0.8 grams/per kg bodyweight/day (g/kg/day) [31, 33]. In the Netherlands, average habitual protein intake of community-dwelling older adults was 1.0 g/kg/day [34]. Expert groups recommend increased protein intakes for older adults to maintain muscle mass and function, with recommended protein intakes of 1.0 to 1.2 g/kg/day for older adults, and intakes of ≥ 1.2 g/kg/day for older adults who are regularly physically active [35-38]. Additionally, in older adults muscles are less responsive to anabolic stimuli (i.e. food intake), which is termed anabolic resistance [39]. There is growing evidence that consumption of 25-30 grams of protein per meal for older adults is beneficial for muscle protein synthesis [40-45]. Consumption of more meals with ≥30 grams of protein was associated with greater leg lean body mass and muscle strength in adults with a mean age of 60 years [41]. Food consumption data show that on average protein intakes at breakfast and lunch of community-dwelling older adults are below 25 grams (~11 grams and ~21 grams respectively), whereas at dinner average protein intake reaches ~27 grams [34, 46]. There is especially room for improvement in dietary protein intake at breakfast and lunch in this population.

Resistance-type exercise

In general, older adults demonstrate lower physical activity levels as compared to younger adults [47]. Regular physical activity at moderate intensity in older adults is associated with protection of certain chronic diseases, maintaining muscle strength [48], prevention of ADL disability [49], and with lower risk of all-cause mortality in frail community-dwelling older adults [50]. Especially muscle strengthening exercise, or resistance exercise, is shown to be an effective exercise type to prevent or treat the deterioration of muscle function [51], prevent physical disability [52], and to improve muscle strength [51, 53, 54], gait speed [55], and lean body mass [56]. Further, a higher training intensity, a longer training period, and a training frequency of two times a week are most effective in improving muscle strength in older adults [57]. The updated Dutch Physical Activity Norm for older adults (aged ≥ 55 years) published in 2017 includes two guidelines: 1) perform moderate intensity exercise for at least 150 minutes a week, and 2) perform muscle- and bone strengthening exercises, combined with balance exercises, at least twice a week [58]. This norm is in line with international physical activity recommendations [59-62]. A study across European countries showed that on average 58-59% of adults aged ≥ 65 years comply to the moderate intensity exercise guideline [63]. Not many European data is published on compliance to the

muscle strengthening guidelines, but results from the Scottish Health Survey indicate that only 12-14% of adults aged 65-74 year and 4-9% of adults aged ≥ 75 year comply with these guidelines [64]. In the Netherlands, 72.9% of adults aged ≥ 65 years reports to comply with the muscle- and bone-strengthening exercise guideline, but only 37% of older adults report to be compliant with the full physical activity guideline [65]. These findings imply there is room for improvement.

Combined lifestyle intervention

The combination of sufficient protein intake and resistance exercise is assumed to elicit most benefits for older adults in counteracting the loss of muscle mass, strength, and function. Meta-analyses have shown that protein supplementation in combination with prolonged resistance training in older adults is associated with gains in fat free mass [66-69] and leg strength [67-69], although some studies have found conflicting results [70, 71]. The additional effect of combining the two strategies might depend on e.g. level of frailty of the older adults, habitual dietary protein intake level, type of protein supplementation, and exercise frequency and intensity. For older adults, expert groups recommend to combine an increased protein intake (1.0 - 1.5 g/kg/day) with progressive resistance exercise to optimize muscle function and decrease strength loss [36, 38, 42]. There is a need for preventive programs that combine these two strategies, to counteract the age-related decline in function [72]. In the Netherlands, a variety of interventions for older adults is registered in online intervention databases. The majority of these interventions for older adults which are registered in the Centre of Healthy Living (RIVM) database are focused on fall prevention, general physical activity, social cohesion, or loneliness [73]. In addition, there are several nutritional interventions for older adults, which mainly focus on improving the nutritional status or general lifestyle [74]. Most of these interventions have not provided enough evidence to be registered in the database as 'effective'. In addition, most available interventions in the database do not include the combination of nutrition and resistance exercise, and do not specifically target prevention of functional decline. To date, only few interventions that combine nutrition and exercise for community-dwelling older adults are actually implemented and disseminated in practice. To contribute to the demand for feasible interventions in practice, the ProMuscle in Practice project is initiated. This project will be described in more detail later in this introduction.

DIFFERENCE BETWEEN EFFICACY AND EFFECTIVENESS

Numerous trials have been conducted to test efficacy of combined resistance exercise and dietary interventions for older adults. These trials show efficacy of interventions under optimum conditions, in a homogenous study population, with a standardised intervention delivered by research staff in a highly controlled manner [75-77]. It is, however, difficult to extrapolate the findings of these efficacy studies to practice, as these studies focus mostly on internal validity [76]. Often, efficacious interventions are not directly suitable for implementation in real-life settings [78], as there are differences between characteristics of the clinical and practice setting [76]. For implementation in real-world settings, interventions should be suitable to fit in these practice settings by dealing with contextual factors (i.e. organisational structure, financial aspects), and allow some extent of intervention flexibility [76]. One way to develop effective real-world interventions is through systematic translation of efficacious interventions to practice. Translation means intervention adaptation to ensure that the intervention fits the practice setting while retaining the essential elements that make the intervention effective [79, 80]. Such translation efforts from clinical research to healthcare practice are important for achieving integration of interventions into practice.

ADAPTING INTERVENTIONS TO PRACTICE

Translating efficacious combined lifestyle interventions to practice requires attention to intervention content and implementation, the target population, and the evaluation design.

Intervention content and implementation

For interventions to be successful in practice and to achieve compliance and maintenance, the intervention content should match with participants needs and should take into account barriers and facilitating factors for the desirable lifestyle behaviour. Research identified important drivers to comply with protein-rich food consumption, such as fit with existing dietary habits, knowledge of the benefits of dietary protein, and specific product properties (i.e. taste, convenience in use) [81]. Furthermore, encouragement by significant others and paramedics have been shown to motivate older adults to participate in nutritional interventions [82]. Therefore, in practice it would be preferred to include professional guidance and incorporate regular protein-rich foods in the dietary pattern of the older adults [42], instead of using

specific dietary supplements as commonly done in efficacy research (i.e. [83-89]). With regard to resistance exercise, important facilitating factors for compliance include customized support or supervision by paramedics [81, 82, 90], social aspects of an exercise program [81, 91, 92], and the experience of physical improvement [81, 82]. Additionally, tailoring a physical activity intervention to participants and providing information about local exercise opportunities might be important for long-term behaviour maintenance [93]. Barriers for participating in a lifestyle intervention are often related to costs [81] or personal factors such as health conditions or cognitive abilities [90].

In practice, lifestyle interventions will be implemented by healthcare professionals instead of by research staff, and implementation will most likely be less strictly according to a protocol compared to efficacy research. Besides tailoring the intervention to the participants' needs, interventions should also be acceptable and feasible for the implementing healthcare professionals, and be adopted by organisations in different settings [76]. Factors such as attitudes of implementers and resources available within the organisation have to be taken into consideration [94], as they influence the intervention implementation [95], and the implementation in turn influences intervention outcomes [96]. For example, when an intervention does not fit within the daily work of implementers, they may perceive the intervention to be inappropriate [94], causing reduced motivation to implement the intervention. Intervention content and activities should therefore match the designated implementers. For interventions to be effective in impacting the health outcome, implementers of the intervention should use relevant behaviour change techniques to change participant behaviour by targeting certain behavioural determinants [97-99]. Examples of techniques that have been used in interventions for older adults are tailoring [100] and goal setting [93]. Thus, for implementation to succeed, the intervention should be acceptable to implementers and organisations, and a training for the implementers should be developed to sufficiently prepare them for implementing the essential elements of the intervention.

Target population

Another point of attention for practice interventions is the target population. Efficacy studies usually include a very specific and homogeneous target population [76], for example physically frail older adults, with strict exclusion criteria on comorbidities. But

for interventions to be more broadly applicable in practice, they should ideally be made available to and match with a broader audience [76, 79]. For example, older adults that might experience the first signs of reduced muscle strength or minor difficulties in activities of daily living might also benefit from an intervention that was efficacious in a frail population. Effectiveness research is, however, necessary to test whether the intervention also obtains comparable results in a broader audience as in efficacy research. In addition, for a project to be profitable in practice, the population from which to recruit potential participants in a certain municipality or community should be large enough to recruit sufficient participant numbers to form exercise groups. Too strict inclusion criteria or screening procedures may impede recruitment and make it more time-consuming to identify eligible participants, reducing intervention feasibility in practice.

Evaluation

Evaluating interventions in practice requires an extensive evaluation approach, that should match the objectives from these complex interventions [101]. An important evaluation aim is to assess intervention effectiveness when implemented in a real-life setting by healthcare professionals. The effectiveness outcomes should be carefully selected for two reasons. First, the outcomes should be suitable to compare effectiveness in practice with the results obtained in the efficacy study. Furthermore, the outcomes should be of interest for future implementers and relevant stakeholders, to stimulate further use of the intervention after the study. In addition to assessing effectiveness, it is necessary to collect information about what happens during intervention delivery in practice. This information can be used to determine whether a possible lack of effectiveness is due to a weak intervention or inadequate delivery [102]. A process evaluation can open this "black box" of effectiveness research [102], to obtain insight in when, how, and why interventions work [103]. Process evaluation is particularly important for multicentre trials, as implementation will likely differ between sites [104]. Gathering information on implementation effectiveness in addition to intervention effectiveness is necessary to draw conclusions about the real effect of the intervention [94]. The Medical Research Council framework provides a useful guidance for process evaluation of complex interventions, including focus on implementation, context, and mechanisms of impact [103]. Process evaluations can include a range of process indicators, focussing on i.e. whether the target audience was reached and to what extent they engaged with the intervention, whether the intervention was

acceptable and implemented as planned, and the influence of contextual factors on implementation or outcomes [94, 103, 105-107]. It is important that data collection is planned before the actual intervention starts, and that data are collected at the level of the participant, implementer, and context, since there may be interactions between these levels that contribute to the complexity of the intervention [103, 108].

FROM PROMUSCLE TO PROMUSCLE IN PRACTICE

To address the gap in real-world interventions for older adults combining both resistance exercise and nutrition, the ProMuscle project is initiated. ProMuscle combines dietary protein supplementation with resistance exercise training for frail older adults [89]. In 2010 an efficacy trial started in an academic setting, using highly structured training protocols, standardized protein supplements, and implementation by research staff. This efficacy trial elicited positive results on study outcomes under highly controlled circumstances [89]. Building on the design and findings of the ProMuscle study, we embark on a series of consecutive steps, aiming to develop an effective and feasible intervention that can be implemented in practice to contribute to improved function and independence of community-dwelling older adults (Figure 1.1). The first step is to adapt the ProMuscle intervention to fit the Dutch practice setting, by combining insights from researchers, healthcare professionals, and the target group. Subsequently, the adapted intervention will be pilot tested to assess feasibility and to select relevant outcome measures before studying intervention effectiveness [103, 108, 109]. As a next step, a multicentre effectiveness study will be performed, in which the final adapted intervention will be tested for effectiveness, implementation, and cost-effectiveness in practice. The intervention will include a period with intensive support, as well as a period focused on maintaining the new lifestyle. This multicentre effectiveness study will be performed in five municipalities in the Netherlands, in collaboration with local care organisations, primary care professionals, fitness centres, and municipalities (Figure 1.2). After the effectiveness study, the focus will shift to intervention optimization, broader implementation, and sustainability in practice.

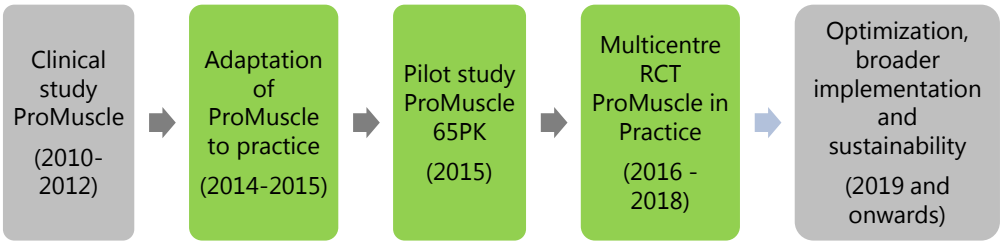

Figure 1.1 Timeline of the ProMuscle in Practice project; the current thesis focuses on the middle three steps.

Figure 1.2 The effectiveness study of ProMuscle in Practice will be conducted in the Province of Gelderland (marked with black line) in the Netherlands. The municipalities in which the study will be conducted are presented in chronological order, with collaborating care organisations and municipalities.

AIM AND OUTLINE OF THIS THESIS

The aims of the current thesis are 1) to provide more insight in translating an efficacious nutrition and exercise intervention for community-dwelling older adults to practice, and 2) to evaluate effectiveness and feasibility of implementing the adapted combined lifestyle intervention in practice. Chapter 2 to 5 build on a previously conducted clinical

efficacy trial on a combined dietary protein supplementation and resistance exercise training intervention for frail older adults [89], as shown in Figure 1, and describe the process of bringing this efficacious intervention to practice. Firstly, in **Chapter 2**, we describe the systematic adaptation of this efficacious clinical intervention to fit the practice setting, and the feasibility testing of this adapted intervention in practice in a pilot study. The results from this adaptation and pilot study provide insight to further improve the intervention's fit in practice. Subsequently, a multicentre randomised controlled effectiveness study is initiated, including an effectiveness-, process-, and economic evaluation of the ProMuscle in Practice intervention. The design and methods of this study and the intervention are described in detail in **Chapter 3**. The ProMuscle in Practice intervention consists of a 12-week intensive support intervention and an optional 12 week moderate support intervention. The results of the effectiveness evaluation of this intervention are presented in **Chapter 4**. This chapter describes effects on outcomes, i.e. physical functioning, muscle strength, lean body mass, and quality of life, when comparing the intervention group that received the ProMuscle in Practice intervention to a control group that received no intervention. The results of the process evaluation of this combined intervention are described in **Chapter 5**. In this chapter we explore the implementation (including recruitment, reach, dose received, acceptability, fidelity, and applicability) and contextual factors of the intensive support and moderate support intervention in the five study locations. In **Chapter 6** we present the process evaluation of the SLIMMER lifestyle intervention, which was also adapted from an efficacious intervention. The SLIMMER diabetes prevention program combines physical activity with dietary advice for adults aged 40-70 years old at risk of type 2 diabetes. The process evaluation also focuses on the process indicators as described for chapter 5, with addition of explaining intervention effectiveness. In the last chapter of this thesis, **Chapter 7**, the main findings of this thesis are summarized and discussed. The results are placed into a broader context and implications for public health and suggestions for future research are provided.

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CHAPTER 2

Translation of a tailored nutrition and resistance exercise intervention for elderly people to a real-life setting: adaptation process and pilot study

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ABSTRACT

Background: Combining increased dietary protein intake and resistance exercise training for elderly people is a promising strategy to prevent or counteract the loss of muscle mass and decrease the risk of disabilities. Using findings from controlled interventions in a real-life setting requires adaptations to the intervention and working procedures of healthcare professionals (HCPs). The aim of this study is to adapt an efficacious intervention for elderly people to a real-life setting (phase one) and test the feasibility and potential impact of this prototype intervention in practice in a pilot study (phase two).

Methods: The Intervention Mapping approach was used to guide the adaptation in phase one. Qualitative data were collected from the original researchers, target group, and HCPs, and information was used to decide whether and how specified intervention elements needed to be adapted. In phase two, a one-group pre-test post-test pilot study was conducted (n=25 community-dwelling elderly), to elicit further improvements to the prototype intervention. The evaluation included participant questionnaires and measurements at baseline (T0) and follow-up (T1), registration forms, interviews, and focus group discussions (T1). Qualitative data for both phases were analysed using an inductive approach. Outcome measures included physical functioning, strength, body composition, and dietary intake. Change in outcomes was assessed using Wilcoxon signed-rank tests.

Results: The most important adaptations to the original intervention were the design of HCP training and extending the original protein supplementation with a broader nutrition programme aimed at increasing protein intake, facilitated by a dietician. Although the prototype intervention was appreciated by participants and professionals, and perceived applicable for implementation, the pilot study process evaluation resulted in further adaptations, mostly concerning recruitment, training session guidance, and the nutrition programme. Pilot study outcome measures showed significant improvements in muscle strength and functioning, but no change in lean body mass.

Conclusion: The combined nutrition and exercise intervention was successfully adapted to the real-life setting and seems to have included the most important effective intervention elements. After adaptation of the intervention using insights from the pilot study, a larger, controlled trial should be conducted to assess cost-effectiveness.

BACKGROUND

In aging societies, increased attention is being given to strategies to maintain independent functioning among older adults. Sarcopenia, the age-related loss of muscle mass and strength in elderly people [1-3], contributes to loss of physical functioning [3] and subsequently increases challenges to living at home independently in the long term [4]. Meta-analyses showed that the combination of resistance-type exercise training and dietary protein supplementation augments muscle mass and improves strength and physical performance [5, 6] and proved a promising strategy to counteract sarcopenia. In the Netherlands, a randomised double-blind placebo controlled trial investigated the impact of daily protein supplementation during twice-weekly resistance-type exercise training in (pre-)frail older adults. This RCT was performed in an academic setting, facilitating high compliance, and the intervention activities, including the training sessions, were implemented by researchers. All participants performed the resistance exercise twice a week, and participants consumed either a dairy protein drink or a placebo drink after both breakfast and lunch every day. The study's findings were promising and showed a significant increase in muscle mass and strong improvements in muscle strength and physical performance after 12 and 24 weeks of intervention [7]. Implementing this efficacious intervention in real-life practice may benefit the health of community-dwelling elderly people. However, since efficacy interventions differ from effectiveness interventions, it is not certain that these findings can be directly translated into a real-life setting [8], for instance communities or care organisations. To increase the likelihood of achieving similar effects in a real-life setting, the efficacious intervention should be adapted to fit the practice setting.

To our knowledge, adaptation processes for combined nutrition and exercise interventions for community-dwelling elderly have not been described elsewhere. Real-life-setting interventions usually require some flexibility [8] in order to fit with disparate settings. In the adaptation process therefore, the balance between fidelity to the original programme and fit with the new setting should be carefully monitored [9-11]. The most essential, effective elements of the original intervention should be maintained, but the intervention needs to fit in the new setting, i.e. the healthcare professionals' (HCPs) working procedures [12] and organisational structure. Furthermore, in real-life settings, the intervention might be made available to a broader

audience than the very restricted target group in the experimental trial [12]. Reporting the adaptation process adds to the current knowledge on making evidence-based interventions suitable for real-life setting implementation, such as implementation by HCPs from care organisations. Following this adaptation process, a feasibility and pilot phase should be conducted before performing a large-scale effectiveness evaluation [13, 14]. Information from the pilot study can be used to test the feasibility of the adapted intervention in practice and provides insight to further improve the intervention and optimise the evaluation design.

The aim of the current study is to adapt an existing efficacious experimental nutrition and exercise intervention for (frail) elderly people to a real-life setting (phase one) and to test the feasibility and potential impact of this prototype intervention in the new setting (phase two). Describing the adaptation process and pilot testing the adapted intervention will elicit valuable insights into the successful translation of efficacious interventions to real-life practice. The results of this adaptation and pilot study will be used to further refine the prototype intervention to fit the real-life practice setting and to prepare the intervention for effectiveness testing.

METHODS

The adapted intervention was designed in phase one, resulting in the prototype intervention as described in the results section. In phase two, this prototype intervention was tested for feasibility, and the potential impact of the adapted intervention in the real-life setting was assessed.

Phase one: Design prototype intervention

In the first phase, Intervention Mapping (IM), a framework for systematic planning and adaptation of theory- and evidence-based health promotion interventions, was used to guide the adaptation to the new setting [15]. The original intervention was not systematically designed or explicitly based on behaviour change theories and behaviour change evidence. The adaptation consisted of six steps: 1) needs assessment, 2) adaptation of goals and objectives, 3) adaptation of methods and practical applications, 4) revision of programme materials, 5) planning implementation, and 6) planning evaluation [15]. In each step, we assessed whether and how the original intervention needed to be adapted to fit the new, real-life setting. Throughout

adaptation, four perspectives were taken into account: relevant stakeholders, theories and supporting evidence, the implementation context, and a socioecological perspective [16]. The results of IM steps 2–5 are described in the phase one results section, IM step 6 is discussed as part of the second phase.

The adaptation process started with the involvement of all relevant stakeholders, including the intended audience (frail) older adults. As part of the needs assessment, a literature study was undertaken to obtain insight into the new implementation setting and to explore determinants of participation in exercise programmes and eating behaviour (protein intake) amongst elderly people. All available documents relating to the original intervention were studied, and a semi-structured interview was conducted with two researchers from the original intervention.

Subsequently, semi-structured focus group discussions were conducted with professionals (n=5 dieticians, n=3 physiotherapists) to assess whether original intervention elements would align with their standard working procedure (applicability). If they did not, the professionals were asked to provide suggestions for change. A discussion leader (EvD) and a note-taker were present during each focus group. In addition, EvD conducted semi-structured interviews with participants from the original intervention (n=13) and possible future participants (n=9), to gain insight into their experiences, needs, and desires. Interview guides for these interviews were created based on predefined intervention elements.

The results were iteratively discussed (via e-mail and face-to-face) with researchers, HCPs, and food product developers until consensus was reached about adaptations to the intervention. Researchers focused on ensuring that proposed adaptations by HCPs would not influence effectiveness. Food product developers were involved in the discussion about the nutrition programme and the selection of protein-rich products to replace standard protein drinks. The findings from these discussions relating to all IM steps are summarised in Table 2.1. They were used to design the adapted intervention taking the defined behaviour and behavioural determinants into account [16] and to develop intervention materials. Ethical approval for phase one was obtained from the Social Sciences Ethical Committee of Wageningen University.

Phase two: Pilot testing the prototype intervention in practice

The pilot study was a one group pre-test post-test 12 week intervention trial among 25 elderly persons. The prototype intervention as developed in phase one was implemented during the pilot study. No sample size calculation was required as the study focused mostly on assessing the implementation process [17]. Ethical approval for the pilot study was obtained from the Medical Ethical Committee of Wageningen University. The trial was registered at clinicaltrials.gov (number NL51834.081.14). Before the start of the intervention, HCPs received implementation manuals and a short training session.

Participants

Participants were originally recruited and provided with information via community nurses from the care organisation in the city of Harderwijk, the Netherlands. As this did not evoke enough responses for participation, a broader group of potential participants was approached and finally recruited via local organisations (e.g. choirs for the elderly) and an ad in the local newspaper. After home screening and informed consent, the participants' general practitioner (GP) gave a final authorisation, based on the medical exclusion criteria (Figure 2.1). Eligible participants were invited for the baseline measures and afterwards assigned to one of four training groups. All the community-dwelling elderly participants (aged ≥ 65 years, living in Harderwijk) were experiencing loss of muscle strength or difficulties in walking, climbing stairs, or rising from a chair.

Process and outcome measures

The pilot study focused primarily on process measures to study feasibility and on a number of outcome measures to assess the potential impact of the intervention in a real-life setting.

Process measures

The process evaluation focused on five process indicators. Recruitment/reach refers to the procedures to attract participants and the participants' characteristics [18]. Dose received is defined as the extent to which participants were involved in intervention activities [18]. Acceptability indicates the extent to which the participants and the HCPs were satisfied with the intervention [19]. Applicability refers to the extent to which the intervention can be implemented in the real-world setting [20]. Implementation

integrity concerns the extent to which the intervention was implemented as planned in the implementation manuals [18, 21]. Data were collected using a participant questionnaire at baseline (T0) and after 12 weeks (T1), semi-structured interviews with HCPs (T1, n=2 dieticians, n=4 physiotherapists, n=1 coordinator within implementing organisation), and two focus group discussions with participants (T1, n=6 and n=8). Guides for the interviews with professionals were based on the process indicators acceptability, applicability, and integrity, and followed the content of the implementation manual. Focus group discussions with participants were less structured and assessed acceptability with regard to the exercise and nutrition intervention. EvD facilitated the focus group discussion, and a note-taker was present. To check integrity, EvD and a research assistant conducted structured observations, and the HCPs completed registration forms during the intervention. Dieticians recorded the discussed topics and advice during the consultations on registration forms. To assess the indicator dose received, physiotherapists recorded attendance and exercise intensity, and the number of repetitions during the training sessions, on registration forms. Furthermore, participants had to monitor their intake of the protein products at the designated meal occasions, using specific calendars every week during the trial.

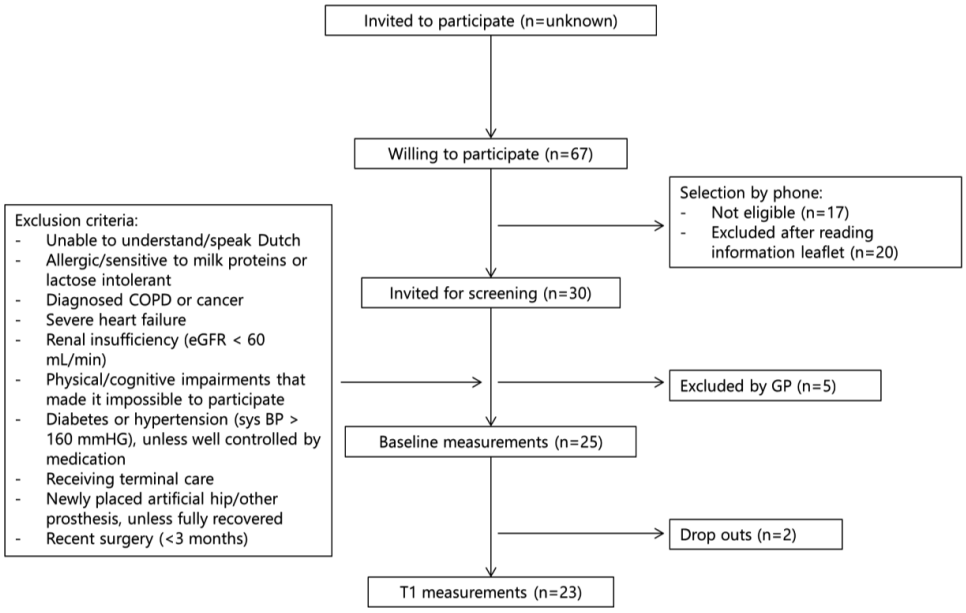

Figure 2.1 Participant flow diagram of the pilot intervention and exclusion criteria.

Outcome measures

At baseline (T0), the Fried frailty criteria [22] and socio-demographics were assessed. Height was measured twice (to the nearest 0.1 cm) at T0 and weight was measured twice (to the nearest 0.1 kg) at T0 and T1. All other outcomes were measured once at T0 and T1. Muscle strength was tested using 3 Repetition Maximum (3RM) measures at the Leg Press and Leg Extension machines (Technogym, Rotterdam, the Netherlands), recalculated to 1 Repetition Maximum (1RM) using the assumption that 3RM weight is 90% of 1RM. At baseline, a 3RM estimation was performed to familiarize participants with the training machines and to estimate their maximal strength. At baseline also a 3RM confirmation was performed, using the estimated maximal strength of the estimation to more accurately measure the 3RM. At T1, 3RM confirmation was performed, since 3RM weight could be estimated from their training schedules. Body composition (total lean mass, appendicular lean mass, and total fat mass) was measured using Dual-energy X-ray absorptiometry (DEXA) at Wageningen University, and bio-impedance analysis (Tanita BC-418, measuring fat free mass (FFM)), both in a non-fasting state. Physical functioning was assessed by the Short Physical Performance Battery (SPPB) [23], Timed Up-and-Go test (TUG, using the faster of two attempts) [24], and a six-minute walking test (6MWT, metres walked in six minutes) [25]. Activities of Daily Living (ADL) was measured using 22 items to assess basic (6 items), instrumental (11 items), and mobility ADL (5 items), scored on a scale of 0 (unable to perform) to 3 (able to perform without difficulty) (based on [26-30]). Quality of Life was assessed using the Short Form 36 (SF-36) [31, 32]. Summary scores for physical (physical component summary (PCS)) and mental (mental component summary (MCS)) health (scores ranging from 0–100) were calculated. All measures were performed by trained research assistants or qualified physiotherapists. Questionnaires were completed either independently by the participants or with the researchers' assistance. Dietary intake was assessed using three-day food diaries, completed on random days. The researchers gave oral and written instructions about completing the food diaries. The T1 diaries were checked by a trained research dietician (n=20 by telephone, n=2 face-to-face) and coded (type of food and amount), and energy and macronutrient intakes were calculated with Compleat (food calculation programme developed by the Division of Human Nutrition; Wageningen University), using NEVO-online version 2013/4.0 [33]. The T0 diaries were coded together with the T1 diaries, using assumptions from the T1 diary check, e.g. relating to portion sizes and product brands. Overall intake and intake per meal occasion were checked.

Data analysis

The qualitative data from the interviews and focus groups in both phases were tape recorded and transcribed verbatim. All transcripts were checked with the audio recording. Using an inductive approach [34], two researchers read the transcripts to identify important themes with regard to the intervention's acceptability, applicability, and integrity. Coding schemes were based on those themes. Data were coded and analysed using Atlas.ti (version 7). Analysed data were used to determine whether elements of the intervention should be changed or not, and, if yes, what should be changed. These results are presented in the results section as a rationale for intervention adaptation, for both phase one and phase two.

Outcome measures were analysed using SPSS (version 22.0). Descriptives were presented as mean and standard deviation (SD), mean and 95% Confidence Interval (95% CI), or percentage. Changes in outcome measures after 12 weeks were tested by Wilcoxon signed-rank tests.

RESULTS

Phase one: Intervention adaptation

Phase one resulted in the prototype intervention, consisting of a combined resistance exercise and nutrition programme for elderly participants and a training programme for the HCPs on recruitment and implementation. Table 2.1 presents the 5 IM steps of the adaptation process with in column one the original intervention, in columns two and three the adaptations made in phase one, and in columns 4 and 5 the adaptations made in phase two. If an element was not adapted, it can be assumed that this element was applicable and acceptable for both the participants and the HCPs.

There were four major changes to the original intervention in the prototype intervention. First, behaviour change goals for both participants and HCPs were specified, as these were not explicitly specified in the original intervention. Second, theoretical methods (general techniques for influencing change in determinants of behaviour [16]) were identified to provide a theoretical foundation for the intervention's activities. These included tailoring (matching the intervention to participant characteristics [35]), persuasive communication (using arguments to guide

Table 2.1 Adaptation of intervention elements for each IM step resulting from phase one and phase two.

Original intervention	**Phase one – design prototype intervention**		**Phase two – pilot test prototype intervention**	
Original intervention elements	**Adapt?**	**Adaptation to original intervention** **Rationale**	**Adapt?**	**Adaptation to prototype intervention** **Rationale**
Intervention Mapping step 2: Adaptation of target population and objectives based on needs assessment (step 1)				
Target group: - age ≥ 65 years - (pre)frail - community-dwelling	Yes	Homecare-receiving clients of care organisation *Clients of care organisation where implementing HCP work.* No screening on (FRIED) frailty criteria *Simplified inclusion criteria as frailty screening is not part of regular HCP work. Assumed that care-dependent elderly are also (pre)frail.*	Yes	Broader population from the community, focus on experienced muscle weakness *Pilot had difficulty recruiting homecare clients. PTs and OR indicate better to focus on elderly who are (pre)frail or heading towards frailty; staying close to target group of original intervention.*
Specified exclusion criteria, checked by research physician	Yes	Similar exclusion criteria, but checked by participants' own GP *Check by GP resembles real-life situation and allows large-scale implementation.*	No	
No explicit behavioural outcomes for participants	Yes	Behavioural outcomes and objectives were defined *Behavioural outcome: participants initiate and maintain participation in the exercise and nutrition intervention. As different behaviours were targeted, i.e. changing and maintaining nutrition and exercise behaviours, outcomes were specified in more detail.*	No	
Intervention Mapping step 3: Adaptation of methods and practical applications (Techniques, instruments, and methods)				
Progressive training: - work towards 75% of 1RM - check 1RM every four weeks → Method: Tailoring	Yes	Still progressive, but check 3RM and recalculate to 1RM *Implementing PTs were not confident in using 1RM in this TG; using 3RM and recalculating to 1RM is acceptable measure of strength.*	Yes	Only check 1RM at week 6 *PTs perceived 4-weekly 1RM checks as too intensive for PPs.* More focus on reaching 75% of 1RM *Training intensity in pilot not always up to 75% of 1RM.*

Table 2.1 Continued.

Original intervention	Phase one – design prototype intervention		Phase two – pilot test prototype intervention	
Original intervention elements	**Adapt?**	**Adaptation to original intervention Rationale**	**Adapt?**	**Adaptation to prototype intervention Rationale**
Trainers - encourage and motivate participants - explain purpose of exercises/nutrition → Method: Persuasive communication, arguments	No		No	
Tailored personal exercise schedule → Method: Tailoring	No		Yes	Still tailored exercise scheme, but ensure that physiotherapists train at the intensity desired in the protocol *PTs did not always use 1RM to change intensity. PTs changed lay-out of individual schedules, so it is easier to track progress.*
Monitoring protein intake using calendars → Method: Self-monitoring	Yes	Still use calendar, but now with more options to indicate consuming cheese/yoghurt/drink *DTs also perceived this as suitable and feasible way to monitor intake.*	Yes	Add more detailed monitoring, make it easier to complete calendar *Monitoring intake was not always easy for DTs due to mixed quality of completed calendars. E.g. make calendar more personally programmed, ask about compensation during meals.*
One flavour protein drink (250 mL) containing 15 g protein/drink	Yes	Range of protein-rich products (not only drinks) instead of just one drink → Method: facilitation *DTs expect that choice from a range of ordinary products would fit better with regular dietary habits and thus increase compliance. However, DTs doubt whether it is feasible to provide personalised advice*	Yes	Focus more on energy content of products *PPs experienced weight increase, so energy content of products should be taken into account in advice.*

Table 2.1 Continued.

Original intervention	Phase one – design prototype intervention		Phase two – pilot test prototype intervention	
Original intervention elements	**Adapt?**	**Adaptation to original intervention** **Rationale**	**Adapt?**	**Adaptation to prototype intervention** **Rationale**
		over a longer period of time (maybe in the future better work with 'standardised' advice).		Try to incorporate more variety in products during trial *Some PPs missed product variation during trial.*
Two protein drinks a day (just after breakfast and lunch), aiming for intake of 25 g of protein per meal	Yes	DTs check during which meals protein intake should be increased and provide tailored advice on which products and portion sizes to take (in agreement with participant preferences) → Method: Tailoring *DTs and product developers emphasise the importance of tailoring protein products to individual needs and desires.*	No	
Handing out protein drinks for whole week at training, by researcher → Method: Facilitation	Yes	Protein products for whole week organised per person by DT, distributed at training by PT *Most convenient according to DT and PT, also for product storage; DT knows personal advice and PT can distribute after training session.*	Maybe	*PPs were satisfied with receiving products for the week during training. Logistics depend on whether products are provided or whether the participants should purchase them themselves.*
Arranged free transport to all trainings by volunteers → Method: Facilitation	Yes	Participants should come to training on their own *In real-life setting, more emphasis on independence. Create the training location in the community, near the participants.*	No	
Intervention Mapping step 4: Revision of programme materials (Intervention design: Delivery mode, intensity, materials)				
General				
Programme of 24 weeks	Yes	Prototype intervention of 12 weeks *Researchers saw great improvement in outcomes after 12 weeks in experimental trial. HCPs perceive this as a sufficient period to test implementation of the prototype intervention.*	Yes	Intensive intervention of at least 12 weeks, with addition of a maintenance programme *Maintenance programme was requested by HCPs and PPs, focusing on both exercise and nutrition. Some PPs indicated that 12 weeks of 'obligations' was long enough.*

Table 2.1 Continued.

Original intervention	Phase one – design prototype intervention		Phase two – pilot test prototype intervention	
Original intervention elements	**Adapt?**	**Adaptation to original intervention Rationale**	**Adapt?**	**Adaptation to prototype intervention Rationale**
				PTs indicated that around 12 weeks participants reach an 'optimum'.
Information materials: leaflet (easy language, large font, clear information)	Yes	Adapt materials to practice setting. DTs also provide printed overview of individual advice *DTs are used to doing this with their clients, to help them remember advice.*	No	
Contact person for questions was researcher	Yes	Contact person for training was PT, for dietary intervention was DT *It is likely that these are the first persons participants will ask questions about the nutrition/exercise programme.*	Maybe	*Depends on organisational structure in implementing organisation.*
Training sessions				
Training twice a week, one hour per session	No		No	
Training supervised by researcher, assisted by trained students	Yes	Training supervised by PT, assisted by assistant PTs *(Geriatric) PTs are skilled professionals who can implement this programme in real-life. Researchers think that presence of a skilled supervisor during training sessions is important. OPs indicated that enthusiasm, social skills, and the ability to stimulate participants were important trainer qualities.*	No	
No intake consultation by trainer	Yes	Intake by PTs before start intervention *PTs perceive this as necessary to gain knowledge on possible health problems/injuries.*	No	

Table 2.1 Continued.

Original intervention	**Phase one – design prototype intervention**		**Phase two – pilot test prototype intervention**	
Original intervention elements	**Adapt?**	**Adaptation to original intervention** **Rationale**	**Adapt?**	**Adaptation to prototype intervention** **Rationale**
Training - one trainer per two participants (individual exercise - same trainers all sessions	No		Yes	No 1-on-1 guidance, more flexible *According to PTs two trainers for six participants was (more than) sufficient, especially after the first few weeks. Flexible guidance was successful during pilot. PPs were satisfied with guidance. PTs work schedule did not allow same trainer every training session, but two different trainers was feasible.*
Training in mixed groups of maximally six elderly	No		No	
Training in gym location equipped for the trial at university	Yes	Gym location in local community, near the elderly *TG wanted training location close by. Depends on the possibilities of the care organisation; a meeting room was transformed to a gym for the intervention period as other locations were occupied.*	No	
Training session structure: - warming-up, resistance exercises, cooling-down - six training machines - no specific exercise order	No		Yes	Group-based cooling-down (stretching) *PTs added group-based stretching to enable group cohesion. According to PPs, it was a nice way to close the session.*
Researcher organised individual training schedules and trainings	Yes	Individual training schedules organised by PTs *The PTs organise the training and complete the individual training schedules during/after the training sessions. Fits their regular work.*	No	

Table 2.1 Continued.

Original intervention	Phase one – design prototype intervention		Phase two – pilot test prototype intervention	
Original intervention elements	**Adapt?**	**Adaptation to original intervention Rationale**	**Adapt?**	**Adaptation to prototype intervention Rationale**
Nutrition intervention				
Only short explanation of protein drinks at start intervention by research dietician (no real consultation)	Yes	Face-to-face consultations with DT before intervention and midway through, added (phone) consultation when needed → Method: persuasive communication, arguments *As the nutrition programme in the prototype is more extensive, DT guidance is needed to explain the need of the nutrition programme and provide advice on the protein-rich products. Individual consultations ensured two-way communication. A midway evaluation opportunity is added to evaluate and adjust the advice if necessary.*	Yes	Add contact opportunity at start intervention and include monitoring of weight and dietary compliance *DTs had to inform PPs about the protein advice again when they were handing out products. Weight gain, indicated as problem by PPs, should be monitored. PPs indicated that they sometimes compensated for the protein-rich products. Therefore, DTs should closely monitor weight and dietary compliance.*
Intervention Mapping step 5: Planning implementation				
No involvement of other organisations	Yes	Involvement of care organisation to implement intervention *Building support by discussions with organisation and involving them in adaptation process.*	No	
Recruitment by researchers, using letters to all community-dwelling elderly ≥65 years of selected cities	Yes	Recruitment by homecare nurses and care organisation's communication department *The care organisation is also partly responsible for recruiting enough participants as it is implementing the programme.*	Yes	Provide more management support for recruiting HCPs *Pilot showed that recruitment through homecare nurses needs more attention.*
No protocol for dieticians or physiotherapists	Yes	Implementation protocol and registration forms developed for dieticians and physiotherapists *Including detailed information describing implementation of the dietary and exercise intervention. Includes detailed training protocol for*	No	

Table 2.1 Continued.

Original intervention	Phase one – design prototype intervention		Phase two – pilot test prototype intervention	
Original intervention elements	**Adapt?**	**Adaptation to original intervention** **Rationale**	**Adapt?**	**Adaptation to prototype intervention** **Rationale**
		PTs, although they were already familiar with exercises.		
Implementing students trained by principal researcher	Yes	HCPs who recruit and implement intervention are trained by principal researcher *HCPs receive training before the intervention starts, to inform them about the implementation manual content and to train them to implement the intervention as planned. Also, the DTs and PTs meet one another during this training session, thus easing collaboration during the intervention.* Organise interdisciplinary discussion halfway through the implementation period with all implementing HCPs *HCPs indicated need to exchange experiences, so implementation could be altered if needed.*	No	
Sustainability not taken into consideration	No		Yes	Include care organisation and municipalities in project *To ensure prolonged use of intervention, after (cost)- effectiveness is shown.*

HCPs = healthcare professionals. PTs = physiotherapists. OR = original intervention researchers. GP = general practitioner. 1RM = 1 repetition maximum strength. TG = target population of the intervention in real-life setting. 3RM = 3 repetition maximum strength. PPs = Pilot study participants. DTs = dieticians. OPs = original intervention participants.

an individual towards adoption of an action [36]), and facilitation (creating an environment that reduces barriers to action [37]). Third, an extensive nutrition programme with a dietician replaced the protein supplementation in the original intervention. In order to fit better with the participants' regular dietary pattern, protein intake was to be increased using a range of protein-rich products, instead of just one drink. Guidance by a dietician was perceived necessary to enable the participants to perform this nutrition intervention. Finally, a training programme for implementing professionals was designed to ensure quality implementation. As the original intervention had not been implemented in practice, the training programme for HCPs was an element of the adapted intervention.

Several elements were already applicable to the practice setting or were important to retain according to, e.g., the researchers. For example, HCPs were already used to encouraging and motivating elderly people, and this was also perceived as important by the original intervention's participants. Physiotherapists and researchers agreed that progressive training and two training sessions of one hour a week were important to achieve results and that in a frail elderly population intensive guidance and a small training group were important. Physiotherapists and researchers deemed it necessary to use a tailored training schedule based on 1RM and individual possibilities. The original study participants perceived the group-based training and being informed about improvements in strength during four-weekly 1RM checks as motivating. Furthermore, monitoring intake of protein products was seen as important, and dieticians perceived calendars to be the easiest way to monitor this.

The adapted prototype intervention consisted of the following parts:

Resistance exercise intervention: The participants performed progressive resistance exercise twice a week (one day's rest in between) for one hour, guided by physiotherapists. Training groups consisted of 5–7 participants. Each training session included warming-up (5 minutes easy biking on a home trainer, 60 rpm), six strength exercises (leg press, leg extension, lat pulldown, vertical row, chest press, and pec dec), and cooling-down (5 minutes easy biking on a home trainer, 60 rpm), similar to the exercise protocol in the original study. Training schedules were based on personal maximum strength tests. According to the protocol, the leg exercises were performed with 4 sets of 8-12 repetitions, and physiotherapists should increase the intensity from

50% to 75% of 1RM. The other exercises were also performed in 4 sets with 8-12 repetitions, but in a less progressive manner.

Nutrition intervention: The nutrition programme included two consultations with a dietician (at the beginning and halfway through), and an additional consultation if needed. Dieticians formulated a personally tailored nutrition intervention with protein-rich dairy products for breakfast and lunch (the second bread-meal), aiming to achieve an intake of 25 g of protein to evoke the most optimal muscle protein synthesis response in these main meals. Participants received the recommended protein products, such as cheese, dairy drinks, and Greek yoghurt, for free during the study. These products were either supplements to their meals or substitutes for other products.

Training for recruiting professionals: The care organisation's homecare nurses were instructed about recruitment at a training session of approximately 30 minutes and given an information leaflet explaining the intervention and their recruitment tasks. The nurses invited care-receiving elderly persons to participate in the intervention. The progress of the recruitment phase was monitored, and nurses received a recruitment reminder via e-mail.

Training for implementing professionals: Before the intervention started, the participating physiotherapists and dieticians received their implementation manuals and a training session of 1.5 h to instruct them on the intervention and implementation. Halfway through the intervention, both professional groups compared their experiences with implementing the programme in an interdisciplinary discussion on problems and solutions.

Phase two: Pilot study

Phase two described the evaluation results of the tested prototype intervention, including the resulting adaptations to the intervention as presented in columns four and five of Table 2.1.

Reach/recruitment

In total, 67 persons indicated interest in participating in the intervention (eight through homecare nurses, 59 through other recruitment means). After screening by the researcher and a check for exclusion criteria by their GP, 25 participants were eligible to participate and started with the baseline measures (Figure 2.1). Non-eligible participants (n=42) did not differ from included participants, with a mean age of 73.5

± 7.4 years (n=36) and 40.5% males. After three weeks, two participants dropped out, due to health issues and time constraints. All remaining 23 participants completed the measures after the intervention (T1).

Eligible participants were on average 74 years old, and 36% were male (Table 2.2). Eleven participants were non-frail, twelve were pre-frail, and two were frail based on the Fried frailty criteria [22]. All participants were of Dutch ethnicity, and half lived with a partner. At baseline, participants were very motivated to participate in the intervention (score of 4.6 on a scale of 1–5). Fifteen participants did not receive care, and the others received mostly domestic help and/or informal care.

Table 2.2 Baseline characteristics of participants (N=25) of the pilot intervention.

Characteristic	**Mean ± SD or N (%)**
Age	74.1 ± 6.8
Gender: Male	9 (36)
Frailty status	
– Non-frail	11 (44)
– Pre-frail	12 (48)
– Frail	2 (8)
Education level[a]	
– Low	10 (40)
– Intermediate	14 (56)
– High	1 (4)
Ethnicity: Native Dutch	25 (100)
Marital status: Married/living together	13 (52)
Motivation at baseline [b]	4.6 ± 0.7
Alcohol: Drinker (≥ 1 day/week)	14 (56)
Smoking: Current smoker [c]	2 (8)
One or more morbidities[d]	23 (92)

[a] Based on the highest level of education completed, divided into three categories: low (primary school or less), intermediate (lower/medium vocational education, high school), and high (higher vocational education, university). [b] Scale 1 (totally unmotivated) – 5 (very motivated). [c] Current smoker or stopped smoking < 1 year ago. [d] Diagnosed by GP in last 12 months. Main morbidities are: high blood pressure (n=11), joint pain (n=8), visual impairments (n=8), and back problems (n=6).

Acceptability and dose received

The intervention received high acceptability ratings from both the participants and professionals (8.7 and 7.6, respectively). Focus group discussions and the T1

questionnaire showed that participants were pleased with both the exercise and the nutrition programme. They described the professionals' guidance, the (group) ambiance during training sessions, tailoring of the exercise programme, being informed about strength increases, and the characteristics of the supplementary products as positive points. However, small points for improvements related to short intervals between the two training days, some inappropriate training machines for their age group, lack of variation in protein products, and too high consumption amounts of the products, as well as undesired weight gain. They expected that maintaining a protein-rich diet after the project would be quite easy, and they would use similar products to the ones received during the intervention. With regard to continuing to exercise, participants indicated that they wanted to do so in small groups with likeminded older adults, with supervision, and without very high costs.

Professionals were very positive about, among other things, the combination of exercise and nutrition, and the participants' enthusiasm, but indicated some factors for improvement, as shown in Table 2.1. They perceived the interdisciplinary group discussion as a very useful way to compare experiences and elicit points for attention in the last six weeks of the intervention.

Participants attended on average 86.4% of training sessions, and all participants received both an intake (mean duration 30 minutes, n=20) and a midway evaluation consultation (mean duration 16 minutes, around week 6, n=21) with the dietician. According to the registration forms, only one participant received an additional consultation. The dietician adjusted the advice for 10 participants (43.5%) during the evaluation consultation, mainly because of suspected weight gain. Intensity of the leg exercises was on average 62% of 1RM, in three sets. Self-reported data from participants showed that they consumed the recommended products during on average 94% of meals (Table 2.3).

Integrity

A broader recruitment strategy than initially planned was used, because not enough participants were recruited among homecare clients. Overall, HCPs implemented the programme as planned in the implementation manuals, although Table 2.1 shows some adjustments to the protocol during the pilot. The physiotherapists did not

Table 2.3 Participants' and professionals' acceptability of the pilot intervention and dose received by participants.

	Participants (mean ± SD)	**Professionals (mean ± SD)**
Overall intervention	n=23	n=7
Acceptability	8.7 ± 0.7	7.6 ± 0.6
Because of my participation in this project…		
I received a lot of individual attention (1–5)[a]	4.2 ± 0.8	
I feel stronger (1–5) [a]	3.7 ± 1.1	
I feel better physically (1–5) [a]	3.7 ± 0.9	
I feel better mentally (1–5) [a]	3.6 ± 1.0	
Exercise programme		n=4
Acceptability	8.9 ± 0.8	7.5 ± 0.4
Because of my participation in this project…		
I enjoyed exercising (1–5) [a]	4.5 ± 0.7	
I could exercise with a goal (1–5) [a]	4.3 ± 0.7	
How satisfied were you with…		
the fact that the exercises were in a training group? (1–5) [b]	5.0 ± 0.2	
the duration of the training sessions (1 h)? (1–5) [b]	4.9 ± 0.3	
the supervision during the training sessions? (1–5) [b]	4.9 ± 0.5	
the exercises you had to perform? (1–5) [b]	4.8 ± 0.4	
the division of the training sessions over the week? (1–5) [b]	4.1 ± 1.1	
Nutrition programme		n=2
Acceptability	8.4 ± 1.0	7.5 ± 0.7
How satisfied were you with…		
the extent to which the dietician took your dietary preferences into account? (1–5) [b]	4.6 ± 0.8	
the possibility to adjust the advice? (1–5) [b,c]	4.7 ± 0.7	
the intake consultation with the dietician? (1–5) [b]	4.5 ± 0.9	
the midway evaluation consultation? (1–5) [b,c]	4.6 ± 0.8	
the products the dietician recommended? (1–5) [b]	4.5 ± 0.8	

	Dose received
Exercise programme	
Training attendance (# of sessions, (% of total))	19.9 (86.4%)
Exercise intensity (% of 1RM) – Leg Press (mean ± SD)	61.4 ± 6.4
Exercise intensity (% of 1RM) – Leg Extension (mean ± SD)	62.4 ± 12.4
Nutrition programme	
Participants receiving intake (n (%))	23 (100%)
Participants receiving evaluation consultation (n (%))	23 (100%)
Compliance with taking products (mean ± SD) [d]	94.2 ± 8.1

[a] Score 1 (totally disagree) - 5 (totally agree). [b] Score 1 (very dissatisfied) - 5 (very satisfied). [c] n=22. [d] Percentage of meals during which recommended products were consumed; based on an average of 53 days of completed calendars.

engage in real intake consultations, as researchers provided them with the relevant background information about participants. The 1-on-1 guidance was omitted in the first weeks of the intervention, because having less structured group guidance was a better fit with their usual way of working and most participants did not need such structured guidance as they were quite fit and independent. Participants indicated that they appreciated the guidance received during the training sessions, and therefore this adaptation to the manual was not seen as a problem. The newly added group-based cooling-down was perceived as pleasant by the participants, as it was also a moment of interaction and laughter. Physiotherapists indicated that they motivated and encouraged participants, provided positive feedback during the training sessions, and showed the 1RM progression to the participants; this was also welcomed and confirmed by the participants.

Some participants had an intake consultation with the dietician in the first week of the intervention instead of before the programme started. Also, it appeared that the intake consultation alone did not provide the participants with enough information on how and when to take the products, so extra contact was needed at the start to repeat the explanation of the nutrition intervention. Moreover, participants asked the dietitians small questions if the latter happened to be around during training sessions. Furthermore, participants' complaints triggered the dieticians to pay specific attention to weight gain, and they monitored participants' weight during the follow-up consultation. Also, some participants indicated that they missed variety in the products provided and sometimes skipped foods from their 'regular' diet, so variation in products and close monitoring of weight and dietary compliance is a point for attention in the future.

Applicability

All professionals perceived the intervention as matching their professional skills and knowledge and were willing to continue working with this programme. However, as can be seen in Table 2.1, there were some points for improvement, such as adaptations to the format of individual training schedules and training machines that are more suited to an elderly population. Also, the HCPs emphasised specific skills that HCPs should have when implementing this intervention: good communication skills, familiarity with the participants and their comorbidities/level of ability, and ability to

motivate participants. For the training sessions, physiological knowledge is needed to prevent injuries.

Outcome measures

Participants increased significantly in leg strength during the intervention, with an average increase of 24.9% in leg press strength and 39.1% in leg extension strength. No change in total lean mass and a non-significant decrease in appendicular lean mass were observed, whereas weight and total fat mass increased significantly. Participants showed significant improvements in all three physical functioning tests. There were no significant changes in basic, instrumental, mobility (data not shown) or total ADL. Participants showed a slight, non-significant increase in the PCS of the SF-36. Results from the three-day food diaries showed that participants significantly increased their daily protein intake to 1.2 g of protein/kg-bodyweight/day. Protein intake increased significantly during breakfast and lunch to 24.1 and 29.9 g, respectively. On the days the diaries were completed, the desired intake of 25 g of protein per meal (breakfast and lunch) was achieved by, respectively, 45.5% and 86.4% of participants (compared to, respectively, 13.6% and 22.7% at baseline) (Table 2.4).

DISCUSSION

This adaptation and pilot study showed that a highly structured experimental intervention can be successfully adapted for implementation in a real-life setting. Adaptations to the experimental intervention related mostly to the design of training for implementing and recruiting professionals, design of a dietician-guided nutrition programme, and organisation of the training sessions. The prototype intervention was perceived as highly acceptable by both participants and professionals, and applicable to implement in Dutch healthcare practice. Furthermore, the findings of the pilot study showed indications of positive impact on muscle strength and physical performance, but not on muscle mass, in older adults. The pilot study also provided insight into intervention elements that may need further adaptation, such as the recruitment strategy and parts of the HCP training to implement the intervention.

Table 2.4 Twelve-week changes in health outcomes and dietary intake of the pilot intervention participants.

	N	**Baseline** mean (95%CI)	**ΔT1-T0** [a] mean (95%CI)	***p*-value** [b]
Strength [c]				
– 1RM Leg press (kg)	23	137.4 (120.8-154.0)	31.7 (20.6-42.8)	0.000
– 1RM Leg extension (kg)	22	52.6 (44.2-60.9)	17.8 (13.6-22.0)	0.000
Anthropometrics				
– Weight (kg)	23	85.1 (79.0-91.3)	0.9 (0.2-1.5)	0.007
– Total lean mass (kg)	23	48.8 (44.7-53.0)	-0.1 (-0.6-0.3)	0.447
– Appendicular lean mass (kg)	23	21.4 (19.3-23.4)	-0.3 (-0.6-0.0)	0.073
– FFM (kg)	20	52.4 (47.4-57.4)	0.4 (-0.7-1.4)	0.513
– Body mass index	23	29.4 (28.0-30.9)	0.3 (0.1-0.5)	0.009
– Total fat mass (kg)	23	33.2 (29.5-36.9)	0.7 (0.1-1.4)	0.029
SPPB				
– Total score	23	9.1 (8.3-9.9)	0.7 (0.0-1.3)	0.047
– 4m walk (sec)	23	4.1 (3.8-4.4)	0.1 (-0.4-0.5)	0.831
– Repeated chair rise (sec)	18	17.6 (15.2-19.9)	-3.6 (-5.8- -1.4)	0.002
TUG (sec)	23	10.6 (9.1-12.2)	-1.3 (-1.8- -0.8)	0.000
6MWT (m)	23	384.5 (357.9-411.1)	27.5 (12.8-42.3)	0.002
ADL (total score) [d]	23	2.8 (2.7-2.9)	0.0 (-0.1 – 0.0)	0.407
Quality of life [e]				
– MCS	23	57.2 (54.0-60.5)	0.4 (-2.9-3.6)	0.879
– PCS	23	42.9 (38.5-47.3)	2.7 (-0.3-5.8)	0.073
Dietary intake				
– Energy (MJ)	21	7.6 (6.6-8.7)	0.7 (-0.1-1.5)	0.106
– Protein (g)	21	79.9 (67.6-92.3)	23.1 (10.2-36.0)	0.003
– Protein (g/kg-bw/day)	21	0.96 (0.81-1.12)	0.29 (0.13-0.45)	0.002
– Protein breakfast (g)	21	15.1 (11.5-18.6)	9.0 (3.9-14.0)	0.003
– Protein lunch (g) [f]	21	19.4 (15.8-23.1)	10.5 (6.2-14.7)	0.000
– Protein dinner (g)	21	37.1 (31.7-42.5)	-0.7 (-5.0-3.7)	0.986
– Protein (en%)	21	17.8 (15.5-20.2)	3.5 (1.6-5.4)	0.002
– Fat (en%)	21	31.2 (28.2-34.2)	0.6 (-3.5-4.8)	0.715
– Carbohydrates (en%)	21	46.0 (41.9-50.0)	-5.9 (-10.1--1.7)	0.004

[a] Change between baseline (T0) and follow up (T1). [b] Wilcoxon signed-rank test. [c] Baseline score is 1RM estimation, as 1RM confirmation was not documented. [d] Mean of score of basic, instrumental, and mobility ADL, score range 0 (cannot do)–3 (can do completely independently). [e] MCS is Mental Component Summary, PCS is Physical Component Summary. [f] Lunch is second bread-meal.

Adapting evidence-based health promotion interventions can be a challenge, especially if the interventions are not systematically described [13] and not based on social psychological theories, and if evaluation studies measuring their efficacy do not take into account both internal and external validity [9]. Efficacy trials that use a very strict protocol and are delivered in research settings by research staff are not directly appropriate for implementation in practice [9]. Successful adaptation requires insight into the ideas and implementation experiences of the designers of the original intervention, as well as support from the intended implementers of the intervention. A systematic adaptation approach provides insight into effective intervention elements by establishing which parts of the intervention have to remain, and which elements need adaptation to fit the new setting.

Although the prototype intervention was mostly feasible to implement as planned, the pilot study evaluation elicited some adaptations to improve fit to the practice setting and HCP working procedures. As the nutrition intervention was added to the prototype intervention, the pilot provided valuable suggestions to improve feasibility. Points for attention in subsequent intervention implementation are monitoring body weight, adding sufficient product variety, monitoring compliance, and providing ample guidance at the start of the programme. The physiotherapists adapted implementation of the training sessions to allow more flexibility and leave room for social interactions in the group. It is expected that, with the adaptations in phase two, the prototype intervention is ready to be tested on effectiveness in practice. However, when the intervention is implemented by other organisations, it is expected that commitment to properly adopt and implement the intervention will have to be created among the organisation's professionals [8] and that the implementation manuals will have to be fine-tuned to the specific organisation on aspects such as organisational structure and HCP task divisions.

Recruitment for the pilot study required some effort, as often reported in studies in elderly populations [38]. Relying on homecare nurses to recruit the specific group of homecare-receiving elderly did not go as intended, and the fact that participants had to travel somewhere to attend the group training sessions might have led to recruitment of a broader, possibly fitter, group of participants than when only homecare recipients were included. This pilot showed that both non-frail and pre-frail individuals experienced benefit from the intervention with regard to physical

functioning and strength (data not shown). As stated by Glasgow et al. [8], practice trials should work in, and appeal to, a broad target audience. Although all participants were positive about the intervention, recruitment of non-care-receiving elderly was easier, and professionals indicated that it would require more effort to implement the intervention if only (pre-)frail individuals were involved. Selecting the ideal target group for this intervention means finding a balance between elderly persons who are very willing to participate and those for whom the original intervention was developed but are more difficult to reach. Given these issues, the proposed effectiveness trial will focus on the original intervention target group, (pre-)frail elderly. In order to facilitate recruitment, the pilot participants' positive experiences might be included in the recruitment materials to make the programme more attractive. Also, extra attention will be given to training homecare nurses about recruitment.

The pilot study showed indications of positive effects on several outcome measures. Strength and physical functioning improved, as also found in both groups in the original intervention [7]; this accords with Cermak et al.'s meta-analysis of protein supplementation and resistance-type exercise training [5]. The changes in leg strength results are comparable to findings reported in Peterson et al.'s meta-analysis of the effect of resistance exercise on muscular strength in older adults [39], with a 29% and 33% increase in leg press and knee extension strength, respectively. Compliance was high for both the nutrition and the exercise intervention in the pilot, although training intensity (62% of 1RM and only three sets instead of four) was slightly lower than in the original. Even though the pilot study participants were not all (pre-)frail and the intervention was implemented in a more flexible way, our results give indications of retained effectiveness in practice. The pilot did not detect changes in lean body mass in the participants, whereas it is assumed that exercise [40] and sufficient protein intake [41] increase muscle protein synthesis and muscle mass accretion in elderly people. A possible explanation for not finding an increase in muscle mass might be the protein intake, which was still low for breakfast. The original study resulted in a slightly higher protein intake than the pilot study [7]. Previous studies suggest that 25–30g protein per main meal is needed to maximally stimulate muscle protein synthesis and increase muscle mass in older adults [42]. In addition, DEXA measurements were performed in a non-fasting state, with no standardisation of meals or drinks, and not at the same time of day at both time points. This may have influenced

the accuracy of the measures. These aspects should be taken into consideration in the proposed effectiveness study.

Even though the current study gave indications of potential impact of this adapted intervention in a real-life setting, further research is needed to test the (cost)-effectiveness of the up-scaled intervention in practice. As implementation can differ between settings, it is important to test the effectiveness of the adapted intervention in multiple locations and within multiple organisations. Maintenance of intervention implementation should be ensured on both the professional and the organisational level [12]. Establishing a broad network of stakeholders is important to facilitate future continuation of the project. This network should include implementing care organisations, the target group, and possible other stakeholders in the field of nutrition and/or exercise. Funding is another important issue to be addressed by the involved stakeholders to ensure further implementation of the intervention in the local setting. Pilot participants indicated that they would like to continue, so ideally a follow-up programme should be developed. This should facilitate a fluent transfer to regular exercise and nutrition guidance in order to help participants to sustain their newly adopted healthy lifestyle after the intervention. Additional research is needed to assess specific participant needs in maintaining this lifestyle.

Strengths and limitations

Although the size of the current study was not intended to provide sufficient power to detect differences in outcomes, and no control group was included, most of the outcome measures showed significant, positive effects. This indicates that translation of the intervention was successful and that effective elements of the intervention were retained. Furthermore, as the evaluation showed that in general the intervention was applicable and acceptable for the professionals and participants, it seems that a good balance was achieved between integrity to the original intervention and fit with the new setting. Limitations of the pilot include testing feasibility in only one location and not fully reaching the desired target population of homecare-receiving elderly. Nevertheless, the pilot provided essential insights into aspects to consider in recruiting (pre-)frail elderly, and motivating the target population remains a point for attention in the proposed effectiveness study.

CONCLUSION

The clinical intervention was successfully adapted from a research setting to a real-life setting in Dutch primary healthcare using a concise Intervention Mapping approach, and perceived implementation feasibility was tested in a pilot study. Proposed adaptations to the prototype intervention after the pilot study relate mainly to guidance by physiotherapists and dieticians. The study showed potential impact on muscle strength and physical functioning outcomes, indicating effectiveness after adaptation. As the results from the pilot study are promising, in the next phase the adapted intervention will be tested for (cost-)effectiveness in a larger, multicentre randomised controlled trial.

Trial registration number: ClinicalTrials.gov NL51834.081.14 (April 22, 2015)

Keywords: Adaptation, Feasibility, Resistance exercise, Protein-rich products, Elderly, Real-life setting

List of abbreviations

1RM: 1 repetition maximum; 3RM: 3 repetition maximum; 6MWT: Six minute walking test; 95% CI: 95% Confidence interval; ADL: Activities of daily living; BMI: Body mass index; DEXA: Dual-energy X-ray absorptiometry; DTs: Dieticians; FFM: Fat free mass; GP: General practitioner; HCPs: Healthcare professionals; IM: Intervention Mapping; MCS: Mental component summary; NEVO: Dutch nutrient composition table; OPs: Original intervention participants; OR: Original intervention researchers; PCS: Physical component summary; PPs: Pilot study participants; PTs: Physiotherapists; SD: Standard deviation; SF-36: Short Form 36; SPPB: Short Physical Performance Battery; TG: Target population of the intervention in real-life setting; TUG: Timed Up-and-Go test.

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Authors' contributions

EvD carried out the study, analysed the data, and drafted the manuscript. EvD, JL, MT, JS, LdG, and AH were involved in designing the study, interpreting the data, and revising the manuscript. JL assisted in analysing the data from phase one of the study. All authors read and approved the final manuscript.

Competing interests

FrieslandCampina provided materials and protein products during the trial. Care organisation ZNWV provided staff to implement the intervention.

Ethics and consent to participate

Ethical approval for phase one was obtained from the Social Sciences Ethical Committee of Wageningen University. Ethical approval for the pilot study was obtained from the Medical Ethical Committee of Wageningen University. All pilot study participants signed a consent form during screening.

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CHAPTER 3

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

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ABSTRACT

Background: Exercise and nutrition are important for older adults to maintain or to regain their muscle mass, function, strength, and ultimately quality of life. The effectiveness of combined resistance exercise and diet interventions is commonly evaluated in controlled clinical studies, but evidence from real-life settings is lacking. This article describes the effectiveness, process, and economic evaluation design of a combined nutrition and exercise intervention for community-dwelling older adults in a Dutch real-life setting.

Methods: The ProMuscle in Practice study is a randomised controlled multicentre intervention study, conducted in five municipalities in the Netherlands. Two hundred community-dwelling older adults (≥65 years) who are frail or pre-frail based on Fried frailty criteria or who experience strength loss are randomised over an intervention and control group by municipality. In the first 12-week intensive support intervention, participants in the intervention group perform resistance exercise training guided by a physiotherapist twice a week and increase protein intake by consuming protein-rich products under the supervision of a dietitian. Afterwards, they continue with a 12-week moderate support intervention. The control group receive only regular care during the two 12-week periods. Effect outcomes are measured at all locations at baseline, 12 weeks, 24 weeks, 36 weeks and only at three locations at 52 weeks. The primary outcome is physical functioning (Short Physical Performance Battery). Secondary outcomes include leg muscle strength, lean body mass, activities of daily living, social participation, food intake, and quality of life. Qualitative and quantitative implementation process data are collected during the intervention. Healthcare use and intervention costs are registered for the economic evaluation.

Discussion: Evaluating the effects, implementation, and costs of this combined intervention provides valuable insight into the feasibility of this intervention for community-dwelling older adults and into the intervention's ability to improve or to maintain physical functioning and quality of life.

BACKGROUND

Age-related loss of muscle mass and function, also known as sarcopenia [1-3], is a major scientific and public health problem. Sarcopenia prevalence ranges from 1 to 29% for community-dwelling older adults [4]. This geriatric condition increases the risk of adverse outcomes, such as physical disability, lower quality of life, and mortality [1], and impacts the ability to live independently. Furthermore, sarcopenia greatly influences healthcare expenses: in the Netherlands healthcare costs of community-dwelling sarcopenic older adults are €11,000 higher per year than costs of non-sarcopenic older adults [5]. Metabolic changes, physical inactivity, and insufficient dietary intake are causal factors in the development of sarcopenia [1, 3].

There is accumulating evidence that sarcopenia can be counteracted with lifestyle changes. Reviews and meta-analyses have shown that interventions including resistance exercise (RE) and dietary strategies towards improving protein intake effectively increase muscle outcomes in older adults [6-9]. However, as these interventions are mostly implemented in highly controlled settings, no conclusions can be drawn about their effectiveness when implemented in a real-life setting. There are large differences between controlled clinical settings and real-life settings. In real-life settings, interventions are implemented by healthcare professionals working in a variety of organisations and settings, rather than by researchers. Therefore, some flexibility in implementation should be allowed in real-life settings [10] to account for the local context (i.e. organisation structure, responsibilities, capacity) and the needs of the target group. Slight deviations from the intervention protocol to tailor the intervention to the local setting are therefore likely. Consequently, there is a need to translate these efficacious clinical interventions to real-life healthcare and community settings and investigate their effectiveness in practice.

In a real-life setting therefore, a more extensive evaluation approach is required to show effectiveness when compared to a clinical efficacy study. The evaluation should focus on effect outcomes that are of interest for future implementers or stakeholders in order to increase the chances of implementation continuing after the effectiveness study. Furthermore, a process evaluation is needed to describe what happens during implementation, to explain intervention effects [11], and to allow continuous optimisation of implementation protocols. Lastly, healthcare costs related to

intervention effects should be assessed in an economic evaluation, as this is important to support sustainable implementation of the intervention and to embed the intervention in the policy of care organisations or local governments. Although some studies on different physical activity and/or diet interventions in older adults include all three evaluation components [12, 13], most studies report only effect evaluations [14-16]. There is thus a lack of information on the other evaluation components for the implementation of a resistance exercise and diet intervention to counteract sarcopenia in practice. Therefore, we translated an effective resistance exercise and dietary protein nutrition intervention for community-dwelling older adults [17] to fit the practice setting [18]. As a next step, this paper describes the design of the multicentre effectiveness study on this adapted resistance-type exercise and nutrition intervention for community-dwelling older adults in Dutch healthcare practice. The objectives of this study are to examine 1) the effectiveness of a combined resistance exercise and nutrition intervention for community-dwelling older adults on i.e. physical functioning, muscle strength, muscle mass, quality of life, and social participation (effectiveness evaluation); 2) implementation integrity, acceptability, applicability, and dose received of the intervention (process evaluation); and 3) the cost-effectiveness of the ProMuscle in Practice intervention in a real life-setting, compared to usual care (economic evaluation).

METHODS/DESIGN

Study design

This study is a randomised controlled multicentre intervention study, in five different municipalities in the Netherlands. The duration of the study is 36 weeks in two municipalities (Apeldoorn and Ede) and 52 weeks in three municipalities (Epe, Ermelo/Putten, and Harderwijk). The intervention comprises resistance exercise training with a focus on the leg muscles and a diet intervention focused on increasing protein intake. For the intervention group, this includes a 12-week intensive support intervention period (weeks 1–12) followed by a 12-week moderate support intervention period (weeks 13–24). The control group receives no intervention (weeks 1–24) to allow comparison with the intervention group in this period, followed by the delayed moderate support intervention (weeks 25–36). Participants receive no additional support after the 24-week intervention period in the intervention group and the 12-week intervention period in the control group, see Figure 3.1. Effect measures

and healthcare cost measures are performed every 12 weeks, and process measures are performed continuously during the study. The ProMuscle in Practice study has been registered at Netherlands Trial Register (NTR6038) since 30 August 2016. The Wageningen University Medical Ethics Committee approved the study protocol and all participants provide written informed consent before the start of the study.

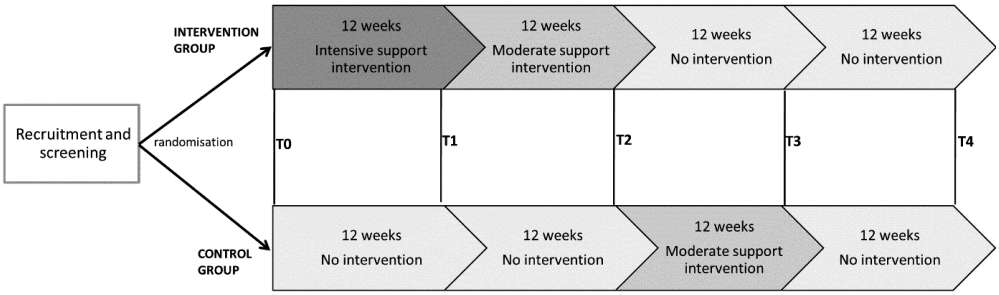

Figure 3.1 Study design and measurements (T0, T1, T2, T3, and T4) per intervention location.
The 12-week intensive support intervention consists of resistance exercise training sessions twice a week under the supervision of a physiotherapist, focused on the major muscle groups, and increasing dietary protein intake to 25 grams per main meal under the supervision of a dietitian. The moderate support intervention comprises optional resistance exercise sessions at local facilities (e.g. fitness centre or sports hall) and five group-based nutrition workshops. T0, T1, T2, and T3 measurements are taken in all five intervention municipalities, T4 measurements are performed only in Epe, Ermelo/Putten, and Harderwijk.

Setting

The study is carried out in five municipalities in the province of Gelderland, the Netherlands. These include three small cities (10,000–100,000 inhabitants: Epe, Ermelo/Putten, and Harderwijk) and two cities (>100,000 inhabitants: Apeldoorn and Ede). The intensive support intervention is delivered by healthcare professionals from four regional care organisations (Zorggroep Apeldoorn, Viattence, Zorggroep Noordwest-Veluwe, and Opella). The moderate support intervention is designed by the community health service in collaboration with the selected municipalities and local organisations, such as a sports-promoting agency or prevention centre. These local organisations and the municipal health service deliver this moderate support intervention.

Sample size calculation

The sample size calculation is based on the difference in change in Short Physical Performance Battery (SPPB) score between the intervention and control group after 12 weeks in the experimental ProMuscle trial of 1.2 with a standard deviation of 1.4 [17]. Because the current study is performed in a real-life setting instead of a highly controlled research setting, only 75% of the previously observed change in SPPB score is expected. Furthermore, we take into account a drop-out of 30% within the first 12 weeks. Assuming an alpha of 0.05, power of 90%, and a two-sided test, a sample size of 78 participants per group is required. To account for clustering effects, we aim for 100 participants per research group. Participants are equally divided over the five locations, so each location should provide 40 participants (i.e. 20 intervention and 20 control participants).

Study population and recruitment

The study population consists of community-dwelling older adults, 65 years or over, from the selected municipalities (Apeldoorn, Epe, Ermelo/Putten, Harderwijk, and Ede). Participants are mainly recruited through announcements and adverts in local newspapers, posters in public spaces and meeting centres, via homecare nurses of the care organisations, and in collaboration with local organisations for older adults. Recruitment strategies may differ between the different intervention locations. All interested older adults receive an extensive information brochure and are invited to an information meeting. If they remain interested, they are invited for a screening visit in their municipality to evaluate eligibility for study participation based on the inclusion and the exclusion criteria (Table 3.1). After signing an informed consent, potential participants complete Fried's frailty test [19], a medical questionnaire, and the 4-item Simplified Nutritional Appetite Questionnaire (SNAQ) [20]. If a person is non-frail, an additional screening questionnaire is administered to check whether this person experiences difficulty in daily activities due to loss of muscle strength. If a person fits the inclusion criteria, that person's general practitioner (GP) performs a check on eligibility based on the exclusion criteria. The GP informs the researchers whether the person can participate safely, and, if the GP approves, the researchers include the person in the study. After inclusion, participants are randomly allocated to the intervention or the control group at each location, stratified by gender and frailty status. Couples are allocated to the same group to prevent contamination. The researchers randomise the participants based on a randomisation scheme constructed

by an independent person from the division of Human Nutrition of Wageningen University (Netherlands).

Table 3.1 Inclusion and exclusion criteria for the ProMuscle in Practice study.

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 [19]
	- Do not perform whole body resistance exercises for >30 minutes on 2 or more days per week, and report loss of muscle strength
	Having signed informed consent
Exclusion criteria	Having an allergy to, or being sensitive to, milk proteins or being lactose intolerant
	Diagnosed COPD or cancer
	Diagnosed diabetes type 1 or type 2, that is unstable, not well regulated with medication, or the participant is not able to notice hypoglycaemia
	Diagnosed hypertension (systolic blood pressure > 160 mmHG) that is not well regulated with medication
	Severe heart failure
	Renal insufficiency (eGFR < 30 ml/min)
	Having physical impairments that prevent them from participating in the exercise training
	Having cognitive impairments that prevent them from understanding and completing questionnaires
	Receiving terminal care
	Having a newly fitted artificial hip or knee prosthesis, unless fully recovered
	Having recent surgery (<3 months) scars that the exercises might stress

Logic model

We created a logic model for the intervention (Figure 3.2) showing intervention activities and their proposed mechanism of change in outcomes such as behaviour or health [11]. Adequate implementation of the intervention activities is expected to improve dietary and exercise behaviour (intermediate outcomes), which in turn will affect health-specific long-term outcomes such as physical functioning and muscle strength. The overall aim of the intervention is to prevent or postpone loss of independence and to contribute to quality of life.

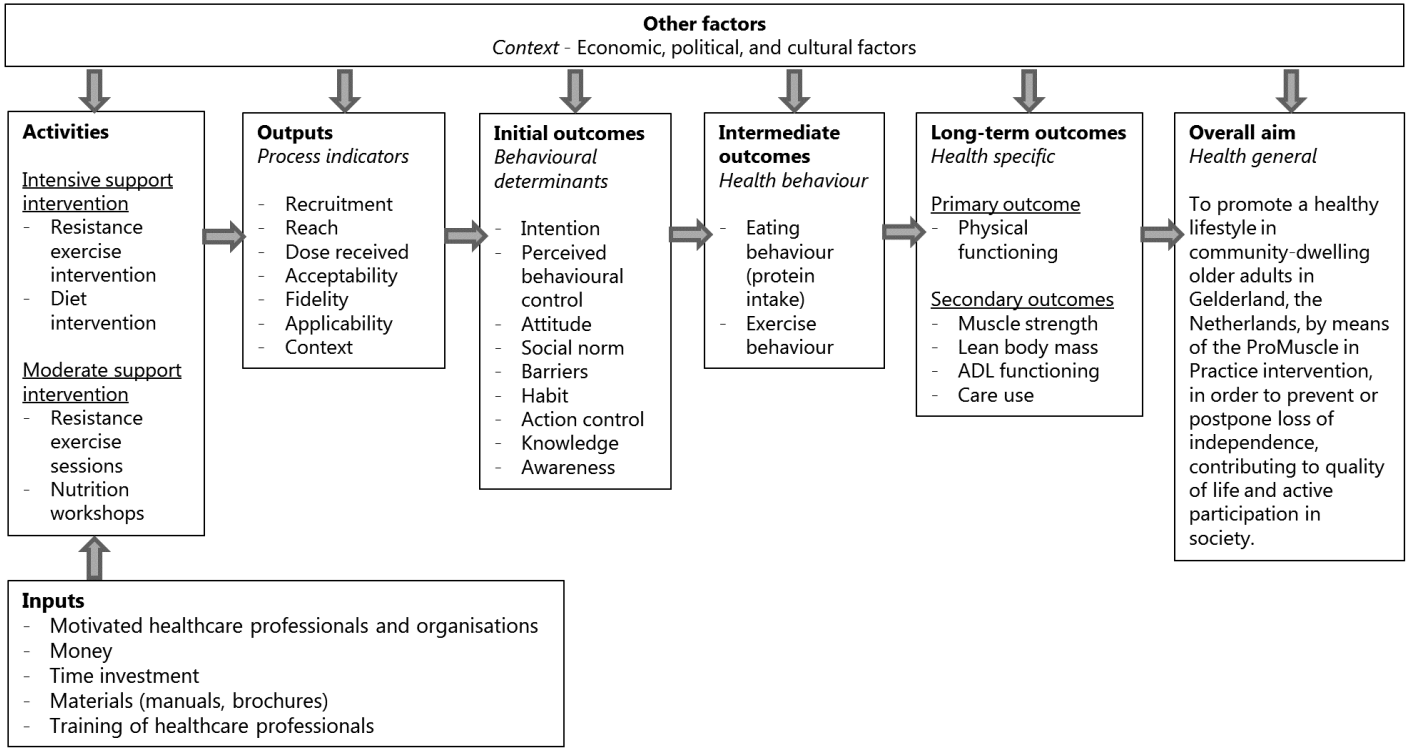

Figure 3.2 Logic model of change for the ProMuscle in Practice intervention.

Intervention

The intervention consists of an intensive support intervention (12 weeks, intervention group only) and a moderate support intervention (12 weeks, separately for the intervention group and the control group).

Intensive support intervention

The intensive support intervention is based on an efficacious clinical trial [17] and adapted to fit the real-life setting [18]. The adapted intervention uses a combination of behaviour change methods for the healthcare professionals (HCP) and participants, such as tailoring, persuasive communication, and self-monitoring [18], see also Additional file 3.1. The intensive support intervention is implemented by physiotherapists and dietitians from local care organisations. The researchers provide a 1 h general information meeting, a more detailed 1.5 h training session, and detailed implementation manuals to the HCPs before the intervention starts. If desired, HCPs can contact HCPs in another intervention location for additional information, e.g. tips and tricks for implementing the resistance exercise training. Halfway through the programme, HCPs at each location have a joint peer discussion. Furthermore, the research team functions as a helpdesk during the trial. For an extensive overview of core HCP tasks and behaviour change methods, see Additional file 3.1.

Resistance exercise intervention – Under the supervision of physiotherapists, participants undertake progressive resistance exercise training twice a week. Each training session lasts one hour, and training groups consist of about six participants. Every training session starts with a warm-up using a home trainer (bike) for five minutes or a warm-up under the physiotherapist's guidance. Afterwards, participants perform exercises using the following machines: leg press, leg extension, lat pulldown, vertical row, and chest press (Technogym BV, Rotterdam, The Netherlands) to target the major muscle groups. The session ends with a group-based warm-down including stretch exercises. The objective of the resistance exercise intervention is that participants increase the training load for the leg exercises from 50% of their one-repetition maximum (1-RM) (four sets of 10–15 repetitions) at baseline to 75% of their 1-RM (four sets of 8–12 repetitions) in weeks 7 to 12. Before the intervention starts, participants perform a maximum strength test on the leg press and the leg extension machine. The physiotherapists use the outcome of this test to tailor individual resistance-exercise programmes. Participants perform the other exercises at a lower intensity up to a

maximum of approximately 60% of their 1-RM (three sets of 15 repetitions), with optional small increases in training load. Physiotherapists can add exercises to train coordination or balance, but most emphasis should be placed on progressively training the leg muscles. The physiotherapists should also ensure that participants take enough rest between exercises and check regularly whether participants have any problems or complaints. If a participant has complaints or injuries, physiotherapists are allowed to deviate from the training protocol provided. At week 6, physiotherapists test the maximum leg strength (3-RM) again and recalculate this to the 1-RM. Physiotherapists can use this 3-RM to monitor progression in training and to evaluate the training programme with the participants.

Diet intervention – The objective of the dietary intervention is to ensure that participants have a protein intake of at least 25 g at each main meal (breakfast, lunch, and dinner). Before the start of the 12-week intervention, the dietitian formulates tailored advice based on a 3-day food diary. Dietitians provide this tailored advice during an individual 30-minute intake consultation, while also discussing regular dietary habits and preferences. The dietitian recommends mainly dairy-based protein-rich products, such as cheese, drinks, yoghurt. These are provided for free during these 12 weeks. These products can be used in addition to the regular diet, or as a substitute for dietary components, and are meant to help the participants increase daily protein intake. Participants receive these products each week during one of the training sessions. The first time the products are handed out, the dietitian is present to provide additional explanations or answer questions. Around week 6 of the intervention period, the dietitian has an individual 15-minute evaluation consultation with the participants to discuss experiences, possible complaints, and how participants can maintain the increased protein intake after the end of the first 12-week period. The dietary advice can be adjusted if needed, and the participants' weight is also monitored. During the 12-week intervention period, participants are asked to indicate on a checklist whether they have consumed the recommended protein-rich products. They hand in this checklist every week at the training session, and the dietitian can use these checklists to monitor compliance with consuming the recommended products and see whether an additional (phone) consultation is needed.

Moderate support intervention

The intervention group starts the moderate support intervention after the intensive intervention. The control group receives this moderate support intervention only after 24 weeks of being a regular care control group, without receiving the intensive support intervention. The aim of the moderate support intervention is to encourage participants to continue consuming sufficient protein at main meals and engaging in resistance exercise training. About four weeks before the moderate support intervention starts, participants receive an information leaflet that includes information on available activities including both exercise sessions and dietary workshops, and suggestions about including (home) exercises and protein-rich products in their daily routine. Healthcare professionals from the intensive support intervention encourage the intervention group to participate. Participants could choose to join all, some, or none of the activities offered.

Resistance exercise sessions – Group exercise sessions take place twice a week at local sports clubs, gyms, or in collaboration with care sport connectors (brokers whose role is to connect the primary care and the sports sector). The trainers offer an exercise programme that includes strength exercises focusing on the legs, based on a manual designed for the moderate support intervention. The exercise sessions are group based and under professional guidance. Financial support for the moderate support intervention may be provided by municipalities or organisations, and participants have to pay nothing or a reduced price for the exercise sessions. At one or more meetings, the municipal health service instructs the trainers who implement the exercise sessions. Trainers also receive an implementation manual for this moderate support intervention. The trainers and the municipal health service have a midterm evaluation meeting before the control group starts the intervention. The municipal health service and the research team also serve as a helpdesk during the intervention period.

Nutrition workshops – Five 1.5-h nutrition workshops are organised in each municipality by the municipal health service, based on a newly developed course guide. During these workshops, participants receive information on how to incorporate protein-rich foods in their diet, share experiences, cook and taste protein-rich meals (breakfast, lunch, dinner), visit a supermarket (optional), and can experiment with a newly developed e-health app. The nutrition course is offered free of charge for both study groups. Intervention participants no longer receive free protein-rich food products.

These workshops are implemented by a health promotion employee of the municipal health service, in collaboration with a dietitian to answer nutrition-related questions. As the health promotion employee is involved in designing the workshops, no additional training is provided for this intervention.

Newsletter – Once participants receive the intensive or moderate support intervention, they also receive a bi-monthly newsletter via e-mail, sent out by the community health service. The newsletter includes information about the study and interventions at the different locations, and stories from study participants or researchers.

Outcomes

All participants are measured at baseline (T0), after 12 weeks (T1), after 24 weeks (T2), and after 36 weeks (T3). A selection of outcomes is also measured after 52 weeks (T4) at three intervention locations. At T0, T1, and T2, participants visit the research location in Wageningen once in the morning and the research location in their municipality once in the afternoon (on different days). The T3 and T4 measures are taken during one afternoon visit in their municipality. Participants are invited for the measurements by regular mail and are phoned if necessary. Participants receive a small financial compensation after completion of the final measurement. Un-blinded trained researchers and assistants take the measurements according to standardised protocols. Table 3.2 provides an overview of outcomes, indicators, methods, and time points.

Socio-demographic characteristics – Socio-demographic characteristics are assessed at baseline through a questionnaire based on The Development of the Older Persons and Informal Caregivers Survey Minimal DataSet (TOPICS-MDS) questionnaire [21], including questions on age, gender, education level, ethnicity, living situation, marital status, dental or swallowing problems, receiving formal or informal care, diseases, smoking, alcohol consumption, history of physical activity, and (past) occupation. Participant height is measured at baseline only, participant weight is collected at all time points. Weight and height are measured twice, and if there is too much disagreement between the two measures (> 0.1 kg or > 0.3 cm), a third measure is performed. Body Mass Index (BMI) is calculated from these measures. Olfactory function is checked at baseline using the Sniffin' Sticks odour identification test [22]. At baseline, participants are asked to indicate the main functionalities associated with meals consumed at breakfast or lunch on a 26-item questionnaire based on questions

Table 3.2 Overview of indicators, methods, and time points of data collection.

			-T1 (Enrolment)	T0 week 0		T1 week 12		T2 week 24		T3 week 36		T4[c] week 52	
Enrolment	**Indicators**	**Method**		**INT[a]**	**CON[b]**	**INT**	**CON**	**INT**	**CON**	**INT**	**CON**	**INT**	**CON**
		Informed consent	X										
Eligibility screen	Frailty state[d]	Fried frailty criteria [19], medical questionnaire, additional screening questionnaire (optional)	X										
Allocation				X	X								
Outcomes	**Indicators**	**Method**											
Socio-demographics	Age, gender, education, ethnic background, marital status, job status, smoking	Participant questionnaire [21]		X	X								
	Disease history	Participant questionnaire [21]		X	X								
	Height	Stadiometer		X	X								
	Nutritional status[d]	SNAQ [20]	X										
	Olfactory function	Sniffin' sticks [22]		X	X								
	Meal functionalities	Questionnaire [23]		X	X								
Overall	Quality of life	EQ-5D-5L [24][e]		X	X	X	X	X	X	X	X	X	X
Long-term	Physical functioning / fitness	SPPB [25], TUG [26, 27], 6MWT [28]		X	X	X	X	X	X	X	X	X	X
		Basic Lower Extremity function questionnaire [29]		X	X	X	X	X	X		X		

Table 3.2 Continued.

			-T1 (Enrolment)	T0 week 0		T1 week 12		T2 week 24		T3 week 36		T4[c] week 52	
Enrolment	**Indicators**	**Method**		**INT[a]**	**CON[b]**	**INT**	**CON**	**INT**	**CON**	**INT**	**CON**	**INT**	**CON**
	Lower extremity strength	3RM on leg press and leg extension		X	X	X	X						
		Knee extension with hand held dynamometer (MicroFET)		X	X	X	X	X	X	X	X	X	X
	Body composition (lean mass, fat mass, hydration status) and weight	DXA, BIS		X	X	X	X	X	X				
		Weighing scales		X	X	X	X	X	X	X	X	X	X
	Social participation	Social Role Domain questionnaire [30]		X	X	X	X	X	X		X		
Intermediate	Dietary / protein intake	3-day food diaries		X	X	X	X	X	X		X		
		Urinary nitrogen[f]		X	X	X	X	X	X				
	Physical activity	LAPAQ [31]		X	X	X	X	X	X		X		
		Actigraph[g]		X	X								
Initial	Behavioural determinants	Participant questionnaire (based on [32-39])		X	X	X	X	X	X				

[a] Intervention participants. [b] Control participants. [c] Only in Epe, Ermelo/Putten, and Harderwijk. [d] Measured during screening. [e] Also collected through regular post at T0.5 (week 6) and T1.5 (week 18). [f] Collected once at one of the time points for each participant, not collected in Apeldoorn. [g] Collected in a random subsample of participants.

from den Uijl et al. [23]. Protein intake is validated by urinary nitrogen from a single 24-hour urine sample. All participants without incontinence problems from four intervention locations are asked to collect their urine once, on one of the days they fill in the food diary (either at T0, T1, or T2). Urine completeness is checked using the Para-AminoBenzoic Acid (PABA) marker [40].

Effectiveness evaluation

Overall outcome – Quality of life is measured by the EQ-5D-5L questionnaire [24], completed at T0, T0.5 (week 6), T1, T1.5 (week 18), T2, T3, and T4. This questionnaire is used to calculate Quality Adjusted Life Year (QALY) [41]. Additionally, a Visual Analogue Scale (VAS) is used to assess perceived health (scale 0–100), with 100 being the best possible health.

Long-term outcomes – The primary outcome of this study is the Short Physical Performance Battery (SPPB), a measure of physical functioning including three aspects: standing balance, gait speed, and a repeated chair rise test [25]. Two other tests of physical functioning are included; the Timed Up-and-Go test (TUG, [26, 27]) and the six minute walking test (6MWT) [28]. The 6MWT is a measure of fitness, and the number of metres walked in six minutes on a straight track of 10 metres is recorded. The use of a walking aid is permitted in all three tests and should then be used at all time points. The SPPB, TUG, and 6MWT are measured at T0, T1, T2, T3, and T4 in both groups.

Lower extremity muscle strength is measured through 3 Repetition Maximum tests (3-RM) at T0 and T1, on both a leg press and a leg extension machine (Technogym BV, Rotterdam, The Netherlands). At baseline, first a familiarisation session including a maximum strength estimation test is performed, and a week later a maximum strength confirmation test is performed, aiming to achieve a 3-RM. The 3-RM confirmation scores (kg) are recalculated to 1 Repetition Maximum (1-RM), based on Brzycki's formula [42]. Additionally, at T0, T1, T2, T3, and T4, knee extension force is measured using a hand-held dynamometer (MicroFET) with belt-stabilisation of the lower leg. A male researcher performs three repeated tests alternating both legs to define maximum strength in Newton.

Body composition is measured through total-body Dual Energy X-ray Absorptiometry (DXA) scans (Lunar Prodigy Advance, GE Health Care, Madison, WI). Total body lean mass, appendicular lean mass (sum of leg and arm lean mass), and fat mass are used as outcomes. Additionally, hydration status is assessed by Bio

Impedance Spectroscopy (BIS, using a SFB7 impedance analyser from ImpediMed Limited, Pinkenba QLD, Australia). The BIS and DXA are conducted in the morning at T0, T1, and T2. Participants are asked to consume a standardised, light breakfast on the scan days and to defecate just before the measurements.

Activities of daily living (ADL) and social participation are measured at T0, T1, and T2 in both groups, and at T3 in the control group. ADL is measured through the Late Life Functional Disability Index related to Basic Lower Extremity Function [29]. Fourteen daily activities can be scored on a 5-point scale, ranging from 'no difficulty' to 'I cannot do this'. Three additional items are included for participants who use a walking aid (e.g. a walker). The scores obtained for each question are added to a total raw score that equals a scaled score of basic lower extremity function; the higher the score, the better the ADL function [43]. Furthermore, participants complete the 5-item SARC-F questionnaire [44] and an additional question on knee pain from the Knee injury and Osteoarthritis Outcome Score questionnaire [45].

Social participation is measured through the Social Role Domain questions of the Late Life Functional Disability Index [30]. The questionnaire includes 16 items that ask both the frequency of performing different social activities (5-point scale ranging from 'very often' to 'never') and the difficulty participants perceive performing those activities (5-point scale ranging from 'not at all' to 'very much'). Similar to the ADL questions, a total score is calculated that equals a scaled score [43]. The ADL questionnaire and the Social participation questionnaire have been translated to Dutch and were pretested in an older adult population (n=5 and n=6, respectively).

Intermediate outcomes – Dietary intake, with a special interest in protein intake, is measured through 3-day food diaries. Participants receive written and verbal (telephone) instructions and complete the diaries on three randomly allocated days (two weekdays [Monday–Thursday] and one weekend day [Friday–Sunday]). At T0, a trained research dietitian visits the participants at home, preferably within a week of completing the diary. The diary is checked, and measures are taken from common household items that people use to consume protein-rich foods (e.g. glasses, cups), according to a standardised protocol. At all other time points, diaries are checked by telephone by a trained research dietitian within a week of completion. Food consumption data are coded (type of food and amount) and energy and macronutrient intakes are calculated with Compleat (food calculation programme developed by the

Division of Human Nutrition, Wageningen University). Additionally, a question on (vitamin D) supplement use is included.

Physical activity is measured by the LASA Physical Activity Questionnaire (LAPAQ) [31]. Additionally, Accelerometers (Actigraph GT3X) are used in a random subsample of participants at baseline, who were asked to wear the accelerometers on their hip for seven consecutive days.

Initial outcomes – Participants complete a self-developed questionnaire on behavioural determinants of dietary protein intake at T0, T1, and T2. Behaviour is formulated as 'eating protein-rich products at breakfast and lunch'. Items to measure intention, perceived behavioural control, attitude, and social norms are based on scales described in the literature [32-35]. Items on barriers to eating protein-rich foods are based on items formulated to assess barriers related to physical activity [38]. Items to assess habits are adapted from the Self Report Index of habit strength [39]. Action control items are based on questions used by den Braver et al. [36]. To assess knowledge, participants are asked to indicate whether products frequently consumed by older adults (informed by Ocké et al. [37]) are rich in protein. Additionally, awareness of protein-rich foods and health is assessed with two items. This questionnaire has been pre-tested in a sample of older adults (n=4).

Process evaluation

Data from both participants and healthcare professionals are collected to assess intervention implementation at the different locations for both the intensive support intervention and the moderate support intervention. This evaluation is guided by the RE-AIM framework, the Medical Research Council guidelines for process evaluation [11], and the Conceptual model for implementation research [46]. Process measures include the indicators recruitment, reach, dose received, acceptability (for implementers and participants), fidelity, applicability (appropriateness or feasibility), and context [11, 46-51]. Process evaluation methods include a project logbook, registration forms, and attendance lists completed by HCPs, participant questionnaires (T0, T1, T2, T3, and T4) and semi-structured interviews (T2 and T3), semi-structured interviews with HCPs (T1 and T3), and structured observations of the intervention components (between T0 and T3).

Economic evaluation

For the economic evaluation, additional information on care use and costs is collected. Participants complete a questionnaire to assess healthcare utilisation, participant out-of-pocket costs, and productivity losses, the latter based on the Productivity Cost Questionnaire [52]. To facilitate recall during measurements, participants record their care use in a cost diary in the period between measurements. The direct and indirect healthcare costs are recalculated using the standard prices for cost research in healthcare, provided by the Dutch Healthcare Institute [53]. Outcomes of the SPPB and the EQ-5D (QALY) are used to assess incremental cost-effectiveness and cost-utility, respectively. Intervention costs are registered by the researchers and the involved HCPs from the care organisations (type and duration of care provided).

Statistical analysis

Quantitative data analyses are performed using the intention-to-treat principle. Descriptives are presented as mean and standard deviation, mean and 95% confidence interval, or percentage. If necessary, not normally distributed data are transformed. Linear mixed model analysis is used to assess differences in changes between the intervention group and the control group, with a significance level of 0.05. Analysis is adjusted for possible differences between the two groups at baseline and other possible confounders. Additionally, subgroup analysis is performed (e.g. per-protocol analysis or based on frailty state or socio-economic background).

Qualitative data (interviews) are audiotaped and transcribed verbatim. Transcripts are checked before analysis and are analysed using an inductive approach in ATLAS.ti.

For the economic evaluation, an incremental cost-effectiveness ratio (ICER) is calculated using a bootstrap analysis, based on costs and effects, in an analysis with a societal and healthcare perspective. In the societal perspective, all costs and benefits of the intervention are included, irrespective of who pays and who gets the benefit [54]. Cost-effectiveness planes and cost-effectiveness acceptability curves are plotted. Additionally, sensitivity analysis is performed.

DISCUSSION

This article described the comprehensive approach to evaluate a combined exercise and nutrition intervention to prevent sarcopenia in a real-life setting, including an effectiveness, a process, and an economic evaluation. The intervention focuses on resistance exercise for the major muscle groups and the consumption of at least 25 g of protein at the three main meals. It comprises an intensive support intervention and a moderate support intervention. The intensive support intervention is aimed at initiating behaviour change under the supervision of healthcare professionals, whereas the moderate support intervention provides support to sustain the behaviour change, making use of local facilities. To our knowledge, this is the first multi-component evaluation of a combined dietary and exercise intervention for community-dwelling older adults in a real-life setting.

When an intervention is being tested in a real-life setting, the ultimate aim is to enable its broad dissemination once effectiveness is shown. To achieve that, besides being effective and cost-effective, an intervention must be shown to be acceptable and feasible in order to achieve citizen and stakeholder support and structural financing. We have, therefore, included a broad range of effectiveness outcomes that are relevant for research, policy, and practice. The process evaluation adopts a mixed-methods approach, combining information from questionnaires, interviews, registration forms, and observations. This extensive process evaluation approach is expected to provide a clear insight into the delivery of the intervention and why this intervention is or is not effective in improving outcomes. With this, the intervention can be further improved to facilitate future implementation and dissemination. Furthermore, this study design allows us to make multiple comparisons of effects within one study. As most interest lies in the effectiveness of the combination of the intensive support intervention and the moderate support intervention during the first 24 weeks, we only include a control group in that period. The control group receives the moderate support intervention after these 24 weeks. By offering this, we allow the control group also to benefit from the intervention, and it also allows us to gain valuable information regarding the effectiveness of this less intensive intervention on the study outcomes. Furthermore, the follow-up measurements 12 or 24 weeks after the end of the moderate support intervention provide insight into the intervention's long-term effects.

We aim to investigate effects and costs in physically frail older adults, as we expect frail older adults to benefit most from this intervention. We know that reaching and recruiting frail older adults for studies is challenging [55], and our pilot study showed that the intervention seems beneficial for a less frail population also [18]. Therefore, we include a broader population of older adults who are not necessarily frail but who do experience loss of muscle strength. Furthermore, the study population will probably include individuals who are highly motivated to change their dietary and exercise behaviour. This might be beneficial for compliance but also induces selection bias, making it more difficult to generalise findings to the overall population of Dutch community-dwelling older adults. As we expect differences between the different municipalities, we randomise participants per intervention location. In this way, we aim to achieve an overall comparable intervention and control group. A downside of this design is that participants randomised into the control group might potentially refrain from participation or change their exercise or dietary habits by themselves, even though we ask them not to do so.

The moderate support intervention is a newly developed programme that has not yet been tested on acceptability, feasibility, or effectiveness. The content of this programme is more practice-based, and no detailed implementation guidelines are used. We expect more variation in the implementation and content of the moderate support intervention between the different locations than in the implementation and content of the intensive support intervention. This makes it challenging to compare the effectiveness of the overall moderate support intervention. Therefore, this moderate support intervention receives extra attention in the process evaluation. This allows us to describe in detail how the intervention is tailored to the different contexts [11] and to obtain insight into best practices and factors for success or failure.

In conclusion, this study will provide valuable insight into the effectiveness, implementation, and cost-effectiveness of a combined exercise and nutrition intervention for community-dwelling older adults in five real-life settings. The results of this study are relevant for large-scale dissemination and implementation of this intervention in practice.

Trial registration: Netherlands Trial Register (NTR6038) since 30 August 2016.

Keywords: Sarcopenia, Resistance exercise, Dietary protein intake, Community-dwelling older adults, Real-life setting, Evaluation, Physical functioning

Abbreviations

1-RM: One-repetition maximum; 3-RM: Three-repetition maximum; 6MWT: Six minute walking test; ADL: Activities of daily living; BIS: Bio Impedance Spectroscopy; BMI: Body Mass Index; DXA: Dual Energy X-ray Absorptiometry; GP: General practitioner; HCPs: Healthcare professionals; ICER: Incremental cost-effectiveness ratio; LAPAQ: LASA Physical Activity Questionnaire; PABA: Para-AminoBenzoic Acid; QALY: Quality Adjusted Life Year; RE: Resistance exercise; SNAQ: Simplified Nutritional Appetite Questionnaire; SPPB: Short Physical Performance Battery; TOPICS-MDS: The Development of the Older Persons and Informal Caregivers Survey Minimal DataSet; TUG: Timed Up-and-Go test; VAS: Visual Analogue Scale.

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Authors' contributions

EVD, AH, ELD, NLW, and LDG designed the evaluation study. EVD, NLW, and BD collected the data. EVD drafted the manuscript. AH, ELD, LDG, NLW, and BD provided suggestions to improve the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The Wageningen University Medical Ethics Committee approved the study protocol, and all participants provide written informed consent before the start of the study.

Competing interests

The authors declare that they have no competing interests.

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Additional file 3.1 Overview of the intensive support intervention and the moderate support intervention.

Intensive support intervention

DIETITIAN

Objective of the diet intervention:

To advise and guide participants about consuming extra dietary protein in their daily dietary pattern, achieving intakes of 25–30 grams of protein with each main meal.

Key attention points for the dietitian:

- Provide insight into options to increase dietary protein intake;
- Remove barriers for participants regarding adequate dietary protein consumption;
- Empower and strengthen participants' self-efficacy;
- Motivate participants to consume extra dietary protein.

Core tasks of the dietitian:

1. Perform intake consultation (30 minutes) and provide advice to participant
    a. Broadly discuss the dietary intake pattern based on the completed 3-day food diary;
    b. Discuss the participant's complaints regarding nutrition and digestion;
    c. Explain relation between dietary protein intake and physical functioning;
    d. Measure participant's body weight;
    e. Provide advice concerning dietary protein intake, taking the participant's preferences into account, and explain when to consume which protein-rich products;
    f. Explain how to fill in calendar to monitor compliance;
    g. Explain that the project has a duration of 24 weeks and that the participant should aim for long-term behaviour change.

2. Additional contact moment the first time that participants receive protein-rich products
    a. Hand out the bag with the advised protein-rich products;
    b. If needed, answer participant's questions and repeat the tailored advice, including information on portion sizes and when to consume which protein-rich product.

3. Signal problems and non-compliance
    a. Signal problems and non-compliance by checking the calendars every two weeks;
    b. If needed, discuss problems and experiences in a (phone) consultation;
    c. Motivate participant to consume protein-rich products and prevent drop-out;

d. Provide clear information and instructions on, and assess facilitators and barriers for, consuming protein-rich products.

4. Perform midterm evaluation consultation (15 minutes) and prepare participants for the moderate support intervention period

a. Evaluate the previous six weeks with the participant concerning consumption of protein-rich products;
b. Discuss experiences and compliance with the dietary advice with the participant, including an explanation that it is not desirable to compensate for the protein-rich products at mealtimes;
c. If relevant, discuss complaints concerning the consumption of the protein-rich products;
d. Measure participant's body weight and check potential weight change;
e. If needed, adjust the advice concerning dietary protein intake;
f. Motivate participant to consume protein-rich products and prevent drop-out;
g. Explain the nutrition workshops within the moderate support intervention period in more detail and discuss with the participant how to independently maintain a protein-rich dietary intake pattern.

PHYSIOTHERAPIST

Objective of the resistance exercise intervention:

To supervise participants during the performance of progressive resistance-type exercises, working from 50% of 1 Repetition Maximum (1-RM) to 75–80% of 1-RM. The physiotherapist tailors the training sessions to the participants' physical possibilities and motivates them to perform the exercises correctly.

Key attention points for the physiotherapist:

- Train participants' load ability by increasing the training load. Attention should be paid to the balance between load ability and training load;
- Supervise resistance-type exercise sessions, with exercises focused on the major muscle groups;
- Remove barriers for participants;
- Motivate participants and promote having fun during exercise;
- Improve group coherence;
- Empower and strengthen participant's self-efficacy;
- Provide ideas about being more physically active in daily life;

- Inform participants about the moderate support intervention on time and motivate them to participate.

Core tasks of the physiotherapist:

1. Map physical possibilities, complaints, or constraints of participants
   a. Make an inventory of the participants' expectations concerning the training sessions;
   b. Analyse motivation and potential constraints for participating in the training sessions;
   c. Provide a good introduction and familiarise participants with the machines, ensure that they feel comfortable doing the exercises.

2. Design and implement the ProMuscle in Practice resistance-exercise intervention
   a. Ensure that there are at least two days of rest between the two training sessions;
   b. Take individual participants' load ability into account when starting the intervention;
   c. Take the training protocol as guideline when performing the progressive exercise intervention;
   d. Stimulate and motivate participant, provide positive feedback;
   e. Answer participant's questions about the intervention or discuss these questions with the dietitian;
   f. Motivate participant to be physically active in daily life;
   g. Stimulate group feeling, e.g. by performing a group-based warm-down;
   h. Collect the calendars every week and pass them on to the dietitian.

3. Perform an intermediate evaluation (week 6)
   a. Perform a maximum strength test (3-RM) with the participant and tailor the training protocol accordingly. Inform participants of their progress;
   b. Discuss participant's experiences with the training sessions during the intervention period;
   c. Motivate participant to perform the resistance exercises and prevent drop-out;
   d. Explain the content of the moderate support intervention to the participants and motivate them to continue with resistance exercises sessions or give tips on being physically active.

Moderate support intervention

NUTRITION WORKSHOPS

Objective of the nutrition workshops:

The nutrition workshop leader will discuss theory about nutrition, facilitate the exchange of experiences with nutrition between participants, facilitate creating and tasting different protein-rich meals, and discuss homework assignments.

Course content of the individual nutrition workshops:

Workshop	Goals	Activities
1. General information on protein-rich nutrition and resistance exercise	• Participants know that exercise in combination with protein-rich nutrition contributes to maintaining or improving muscle mass and strength; • Participants can name a few examples of protein-rich products.	1. Welcome 2. Introduction round 3. Introduction protein-rich nutrition 4. Introduction resistance exercise 5. Explain homework assignment and give preview of second workshop
2. Breakfast and introduction ProMuscle mobile application	• Participants can mention protein-rich products that contribute to the protein-content of their breakfast; • Participants can explain how to read nutrition labels and how to define the protein-content of a product based on the label; • Participants are able to make a healthy and protein-rich breakfast; • Participants plan to consume sufficient protein at breakfast at home more often.	1. Welcome 2. Discuss previous workshop and homework assignment 3. Discuss breakfast 4. Discuss product labels 5. Make breakfast and taste the different dishes 6. Explain homework assignment and give preview of third workshop 7. Explain the ProMuscle mobile application (optional)

3. Lunch	• Participants can mention protein-rich products that contribute to the protein-content of their lunch; • Participants can explain what the labels on products mean; • Participants are able to explain the differences between types of dairy products; • Participants are able to make a tasty and protein-rich lunch; • Participants plan to consume sufficient protein at lunch at home more often.	1. Welcome 2. Discuss previous workshop and homework assignment 3. Discuss lunch 4. Make lunch and taste the different dishes 5. Explain homework assignment and give preview of fourth workshop
4. Dinner	• Participants can mention protein-rich products that contribute to the protein-content of their dinner; • Participants are familiarised with different types of protein-rich products; • Participants are able to explain the differences between types of dairy products; • Participants are able to make a tasty and protein-rich dinner.	1. Welcome 2. Discuss previous workshop and homework assignment 3. Discuss dinner 4. Make dinner and taste the different dishes 5. Closure
5. Supermarket visit (optional)	• None specified.	None specified

RESISTANCE EXERCISE SESSIONS

General key attention points:

- Create a nice atmosphere during the exercise sessions
- Supervise and motivate participants
- Ensure that participants have faith in the supervision and their own abilities
- Remove fear of performing the exercises
- Build a personal connection with the participants
- Stress that participants exercise for their own health!

Specific key points for sports hall (no training machines available):

- Provide progressive resistance-type exercise sessions, so the intensity of exercises should increase (mostly by increasing number of repetitions). Intensity can be also increased with elastic bands or free weights.
- Perform exercises for the major muscle groups, with most emphasis on the leg muscles (20–25 minutes in each training session). Exercises for chest, back, shoulders, and core can be somewhat progressive, but pay attention to individual load ability and participant experiences. The intensity of these exercises should not negatively influence the training intensity of the leg exercises.
    - Leg exercises: 3 sets, 10–15 repetitions, exercises should be moderate to high intensity
    - Other exercises: 15 repetitions, exercises should be of mild intensity.
- Safety in performance of exercises is key. Complex exercises that require balance should be done only under supervision.
- Make sure participants breathe out with concentric movements and breathe in with eccentric movements.
- Ensure sufficient rest between the different exercises.

Specific key points for fitness centre (training machines available):

- Provide progressive resistance-type exercise sessions, so the intensity of exercises should increase (mostly by increasing weights or number of repetitions).
- Perform exercises for the major muscle groups, with most emphasis on the leg muscles (20–25 minutes in each training session). Exercises for chest, back, shoulders, and core can be somewhat progressive, but pay attention to individual load ability and participant experiences. The intensity of these exercises should not negatively influence the training intensity of the leg exercises.
    - Leg exercises: 3–4 sets, 10–15 repetitions, exercises should be moderate to high intensity

    - Other exercises: 3 sets, 15 repetitions, exercises should be of mild intensity.
- Ensure that the right number of sets and repetitions is performed.
- Older adults should train at a high intensity for a maximum of 45 minutes per training session.
- Eccentric movement should take 2 seconds, concentric movement 1 second.
- Safety in performance of exercises is key. Complex exercises that require balance should be done only under supervision.

Structure of a training session:

1. Warm-up with the group (5–10 minutes). If possible, use game elements to incorporate fun.
    a. Optional for gym: warm-up on an exercise machine if a group warm-up is not possible for participants.
2. Performance of resistance-type exercises. Explain the exercises and let the participants perform them individually, but under supervision.
    - For the sports halls: try to include 5 different exercises each week, of which 3 leg exercises (3 sets per exercise, 10 repetitions for the leg exercises, 15 repetitions for the other exercises). Pay attention to balance (use chairs if necessary). Supervise participants if necessary, depending on the participant's level.
    - For the fitness centre: For the leg press and leg extension machine, build intensity from 65% of 1-RM in week 1 to 75% 1-RM in week 12. Upper body exercises should be performed at around 60% of 1-RM.
3. Warm-down with the group; stretching and balance exercises to improve group cohesion

Supplemental table 3.1 Overview of behaviour change methods and practical applications used to change the behavioural determinants during the intensive support intervention and the moderate support intervention.

Determinant	Methods	Definition	Practical application
General methods	Tailoring	Matching the intervention or components to previously measured characteristics of participants	Intensive support intervention: • Physiotherapist tailors the intensity of the resistance exercises to each participant's capabilities (based on strength measurement at baseline and in week 6). • Dietitian provides personalised advice to increase protein intake based on current dietary intake and participant's preferences. Moderate support intervention: • Trainers tailor intensity of exercises to the capabilities of the participants.
	Persuasive communication	Guiding individuals and environmental agents towards the adoption of an idea, attitude, or action by using arguments or other means	Intensive support intervention: • Physiotherapist explains the importance of resistance-type exercises for older adults and being physically active in daily life. Physiotherapist encourages participant to perform the resistance-type exercises. • Dietitian explains the importance of adequate dietary protein intake in combination with resistance-type exercise during the intake and evaluation consultation. Dietitian encourages participant to increase protein intake. Moderate support intervention: • Nutrition workshop leader explains the importance of consuming adequate amounts of dietary protein.
	Feedback	Giving information to individuals and environmental agents regarding the extent to which they are accomplishing learning or performance, or the	Intensive support intervention: • Physiotherapist provides positive feedback during the training sessions and during the mid-term evaluation following the midterm strength measurement. Physiotherapist also provides feedback on correct execution of the exercises. • Dietitian provides feedback during evaluation consultation on the extent to which the dietary intake goal is met. Moderate support intervention:

		extent to which performance is having an impact	• Trainer provides positive feedback during training sessions concerning performance of the exercises. • Nutrition workshop leader might provide feedback during the workshops concerning dietary habits or product choices.
	Facilitation	Creating an environment that makes the action easier or reduces barriers to action	<u>Intensive support intervention:</u> • Resistance exercise sessions and consultations with dietitian are in the municipality where participants live. • Participants receive protein-rich products to incorporate in their diet every week after one of the training sessions. <u>Moderate support intervention:</u> • Resistance exercise sessions and nutrition workshops are in the municipality where the participants live. • To ensure continuity, the resistance exercise sessions are preferably scheduled on the same day as the training sessions in the intensive support intervention. • Ideally, the nutrition workshops are at the same location as the consultations with the dietitian during the intensive support intervention.
	Reinforcement	Linking a behaviour to any consequence that increases the behaviour rate, frequency, or probability.	<u>Intensive support intervention:</u> • Physiotherapist praises the participant for performing the exercises correctly or for increasing intensity. <u>Moderate support intervention:</u> • Trainer praises the participant for performing the exercises correctly or for increasing intensity.
	Belief selection	Using messages designed to strengthen positive beliefs, weaken negative beliefs, and introduce new beliefs	• During recruitment, interested older adults are told why resistance exercise and dietary protein intake are important for maintaining or increasing muscle strength. • A short film shown during information meetings depicts other older adults who are performing the resistance-type exercises and who are positive. <u>Intensive support intervention:</u>

			• Physiotherapist convinces participants that they are able to perform the resistance exercises and increase exercise intensity. Moderate support intervention: • Nutrition workshop leader shows participants that consuming adequate protein is feasible, by providing examples of protein-rich products and easy protein-rich meal recipes.
Perceived behavioural control / Barriers / Action control	Guided practice	Prompting individuals to rehearse and repeat the behaviour various times, discuss the experience, and provide feedback	Intensive support intervention: • At the start of the intensive support intervention, physiotherapist shows how to do the resistance exercises, explains the exercises, and provides feedback when the participant does the exercises. Moderate support intervention: Not applicable.
	Self-monitoring of behaviour	Prompting the person to keep a record of specified behaviours	Intensive support intervention: • Participants indicate daily on a calendar whether they consumed the protein-rich products. Moderate support intervention: • Participants can register on the mobile application (app) how much protein they consumed and whether they performed resistance exercises.
	Goal setting	Prompting planning what the person will do, including a definition of goal-directed behaviours that result in the target behaviour	Intensive support intervention: • Dietitian explains that the goal is to consume 25 grams of protein at each main meal and discusses with the participant how this can be achieved by changing dietary habits at the main meals. Moderate support intervention: • Nutrition workshop leader reminds participants of the goal to consume 25 grams of protein at each main meal and discusses and demonstrates within the group how this can be achieved.

	Set tasks on a gradient of difficulty	Setting easy tasks and increasing difficulty until target behaviour is performed	Intensive support intervention: • Physiotherapist starts the intensive support intervention with a familiarisation period, using low intensity. Later, the intensity is slowly increased to improve the participant's strength, based on the training protocol provided. Moderate support intervention: Not applicable.
	Planning coping responses	Getting the person to identify potential barriers and ways to overcome these	Intensive support intervention: • Physiotherapist might discuss barriers to performance of the resistance exercises and how to deal with them. • During the intake and evaluation consultation, dietitian might discuss difficult situations concerning following the dietary advice (e.g. holiday or disliking products) and how to deal with that. Moderate support intervention: • Trainers might discuss barriers to performance of the resistance exercises and how to deal with them. • Nutrition workshop leader might discuss barriers to consuming adequate dietary protein and ask participants to think of ways to overcome these barriers.
Attitude	Direct experience	Encouraging a process whereby knowledge is created through the interpretation of experience	Intensive support intervention: • Physiotherapist guides participants in performing resistance-type exercises and, by doing the exercises, participants find that they can perform the exercises and increase training intensity. • Dietitian evaluates protein intake during evaluation consultation and shows participants that they were able to consume sufficient dietary protein. Moderate support intervention: • Nutrition workshop leader lets participants practice with reading labels and preparing protein-rich meals.
	Arguments	Using a set of one or more meaningful	Intensive support intervention:

		premises and a conclusion	• Physiotherapist explains importance of resistance-type exercise for older persons. • Dietitian explains importance of consuming adequate dietary protein in combination with resistance-type exercise. <u>Moderate support intervention:</u> • Nutrition workshop leader explains importance of consuming adequate dietary protein.
Social support	Stimulate communication to mobilise social support	Prompting communication about behaviour change in order to provide instrumental and emotional social support	<u>Intensive support intervention:</u> • Physiotherapist encourages interaction between participants by providing a group-based warm-up and/or warm-down and conversation during training sessions. <u>Moderate support intervention:</u> • Trainers can facilitate interaction by providing a group-based warm-up or warm-down of the exercise sessions. • Nutrition workshop leader encourages interaction between participants by asking questions and prompting exchange of experiences in the group.
	Provide opportunities for social comparison	Facilitating observation of non-expert others in order to evaluate one's own opinions and performance abilities	<u>Intensive support intervention:</u> • Training sessions are in a group, where participants can compare themselves with, or observe, peers performing the same exercises. <u>Moderate support intervention:</u> • Training sessions are in a group, participants can still compare themselves with their peers. • Participants share experiences during the nutrition workshops and can either learn from others or be an example to others.
Awareness	Framing	Using gain-framed messages, emphasising the advantages of performing the	• Participants receive information during recruitment stating gain-framed information concerning the benefits of participating in this project. <u>Intensive support intervention:</u> Not applicable. <u>Moderate support intervention:</u>

		healthy behaviour, or loss-framed messages, emphasising the disadvantages of not performing the healthy behaviour.	Not applicable.
	Consciousness raising	Providing information, feedback, or confrontation about the causes, consequences, and alternatives for a problem or a problem behaviour	<u>Intensive support intervention:</u> • Dietitian discusses the 3-day food diary during the intake consultation, explains the meals at which protein intake can be improved, and discusses solutions with the participant. <u>Moderate support intervention:</u> • Nutrition workshop leader provides examples of protein-rich meals and protein-rich products.
Knowledge	Discussion	Encouraging consideration of a topic in open informal debate	<u>Intensive support intervention:</u> Not applicable. <u>Moderate support intervention:</u> • Nutrition workshop leader facilitates discussion on nutrition-related topics.
	Elaboration	Stimulating the learner to add meaning to the information that is processed	• Participants receive information on resistance exercises and the nutrition intervention during recruitment, in the information leaflet, or at an information meeting. <u>Intensive support intervention:</u> • Physiotherapist might explain about the resistance-type exercises during the training sessions. • Dietitian provides information on nutrition during the intake consultation and the evaluation consultation and, if needed, during the additional contact moment.

			<u>Moderate support intervention:</u> • Nutrition workshop leader provides information on nutrition during the workshops.
Habit	Planning coping responses	Getting the person to identify potential barriers and ways to overcome these	See 'Coping response' concerning PBC / Barriers / Action Control

CHAPTER 4

Effectiveness of a diet and resistance exercise intervention on muscle health in older adults: ProMuscle in Practice

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ABSTRACT

Objectives: Clinical studies show that resistance exercise (RE) and a protein-rich diet can counteract the age-related decline of muscle mass, strength, and physical performance. The aim of the ProMuscle in Practice study was to test effectiveness of a RE and dietary protein intervention for older adults implemented in a real life setting.

Design/settings/participants: A randomised controlled multicentre intervention design, including 168 community-dwelling older adults (75 ± 6 years). A 12-week intensive support intervention including progressive RE supervised by physiotherapist and dietitian guidance on increasing protein intake was followed by a voluntary 12-week moderate support intervention focusing on continuing the adapted lifestyle pattern.

Methods: Compliance (RE attendance, protein intake) was measured through attendance lists and 3-day food records. Physical functioning (Short Physical Performance Battery (SPPB), Timed Up-and-Go (TUG), six minute walking test (6MWT), and activities of daily living (ADL)), leg strength (3-Repetition Maximum, knee extension strength), lean body mass, and quality of life (EQ-5D-5L) were measured at baseline, after 12 and 24 weeks.

Results: The intervention group increased protein intake and attended 83.6% of training sessions. SPPB score increased in intervention participants (from 10.1 ± 0.2 to 10.4 ± 0.2 at week 12 and 10.6 ± 0.2 at week 24), where control participants decreased (time x treatment interactions $P < .05$). Improvements in the intervention group compared to controls were also observed for TUG, leg strength and lean body mass at both time points (time x treatment interactions $P < .05$). No difference between groups was found for 6MWT, ADL and quality of life.

Conclusions and Implications: Our study demonstrates the effectiveness of ProMuscle in Practice on improving muscle health related outcomes in community-dwelling older adults in a real life setting. Further research should explore feasibility of implementation in real-life, as well as improving compliance and long-term behaviour maintenance.

INTRODUCTION

The age-related loss of skeletal muscle mass and strength increases the risk of adverse outcomes, such as physical disability, poor quality of life, and loss of independence [1]. Reviews and meta-analyses have well established that resistance exercise (RE) and protein supplementation are promising strategies to improve muscle related outcomes in older adults [2-9]. These findings are generally based on clinical research performed under controlled circumstances, and with minimal attention to establishing behaviour change. In real-life settings, interventions are not implemented by researchers, but in existing healthcare structures by healthcare professionals. Consequently, the intervention as described in the implementation manuals may need adaptation to fit the working procedures of these professionals, which can influence intervention effectiveness [10]. As there is a need for preventive strategies to manage age-related decline of muscle mass and function [11], intervention strategies should be tested for effectiveness in practice.

The current study aims to do so, by building on the efficacious clinical intervention ProMuscle, combining resistance exercise and protein supplementation [12]. This intervention was systematically adapted in collaboration with researchers and healthcare professionals to fit the practice setting, and then pilot tested [13]. The aim of the current study was to evaluate effectiveness of this combined dietary protein and resistance exercise intervention for community-dwelling older adults on physical functioning, muscle strength, lean body mass, and quality of life when implemented in practice. This intervention includes an intensive support intervention implemented by physiotherapists and dietitians, and a subsequent voluntary moderate support intervention to offer older adults the opportunity to continue the newly adopted dietary and exercise behaviours.

METHODS

Research design

This randomised controlled multicentre intervention study ran from November 2016 till November 2018. Five study centres were included that started in a phased manner. Study duration was 36 to 52 weeks per centre. In this article we focus on effectiveness of the intensive support intervention and the subsequent moderate support intervention (two 12-week periods). The study is registered at the Dutch Trial Register

(identifier NTR6038). The study protocol was approved by the Wageningen University Medical Ethics Committee. Study design, sample size calculation, and intervention description have been published in detail elsewhere [14].

Participants

In five Dutch municipalities (Apeldoorn, Epe, Ermelo/Putten, Harderwijk, Ede) we recruited community-dwelling older adults aged ≥ 65 years through local media. Interested older adults were screened to evaluate eligibility on the following inclusion criteria: master the Dutch language, being frail, pre-frail, or experience difficulty in daily activities and being inactive (defined as: not participate in RE > 30 minutes a day on more than 2 days a week). The older adults' general practitioner (GP) checked the exclusion criteria (Figure 4.1). In total, 168 older adults were randomised to an intervention and control group (stratified for gender and frailty state) and started the study. All included participants provided written informed consent before participation.

Intervention

The 12-week intensive support intervention was directly followed by a 12-week voluntary moderate support intervention. Participants in the control group received no intervention and were asked to refrain from changes in their dietary and exercise behaviour.

Intensive support intervention

Participants joined progressive RE training sessions twice a week at local care organisations in groups of 4-7 participants. Physiotherapists supervised the training sessions according to provided manuals. Each 60-minute session consisted of a warm-up, resistance exercises (leg press, leg extension, lat pulldown, vertical row, and chest press (Technogym, the Netherlands)), and a warm-down (stretching). Workload of leg exercises started with 3-4 sets of 15 repetitions (50% of 1-Repetition Maximum (1RM)), and increased towards 4 sets of 8-12 repetitions (75-80% of 1RM) in weeks 7-12.

A dietitian implemented the dietary protein intervention, consisting of an intake consultation, a contact moment during the first week, and an evaluation consultation during week 6. The dietitian informed participants on the importance of dietary proteins and advised participants on achieving a protein intake of 25 grams during breakfast, lunch, and dinner. Participants received dairy foods and/or protein-rich cakes or desserts of their preference, to incorporate in their diet.

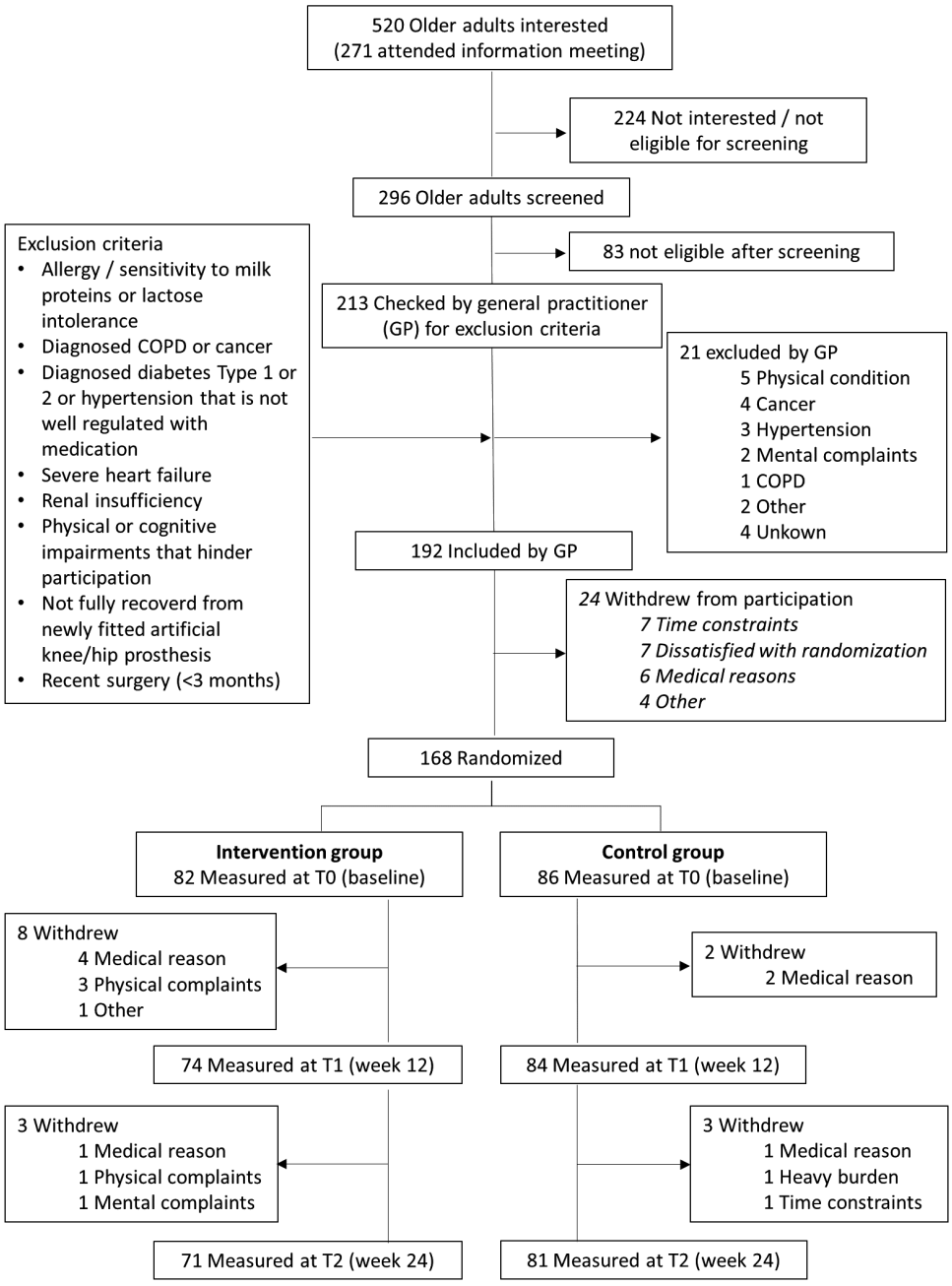

Figure 4.1 Flow diagram of participants of the ProMuscle in Practice intervention.

Moderate support intervention

The 12-week voluntary moderate support intervention was included to facilitate continuing the adapted lifestyle pattern. Group-based RE (1-2 times a week) was offered at local fitness centres, with primary care physiotherapists, or with care-sport connectors employed by the municipality. Skilled trainers of these organisations were instructed to perform RE with focus on the legs, and were encouraged to add e.g. balance or functional exercises.

Additionally, a health promotor and a dietitian provided a nutrition course on dietary protein, consisting of five 1.5 hour meetings at a local centre. During the course participants learned theory, prepared and tasted protein rich dishes, and shared experiences with the other course attendees.

Intervention participants also received a newsletter of the project through e-mail every 2-3 months.

Measures

All outcomes were measured at baseline (week 0, T0), after the intensive support intervention (week 12, T1), and after the moderate support intervention (week 24, T2). Data were collected by trained, unblinded researchers and research assistants.

Baseline characteristics – Frailty state [15] and nutritional status (Short Nutritional Appetite Questionnaire, SNAQ, [16]) were recorded during screening. Participant characteristics such as age, sex, education level, diagnoses with morbidities, were collected at baseline [17]. Participants also completed the SARC-F questionnaire to assess sarcopenia risk [18].

Compliance – Attendance of dietitian consultation and RE trainings, and training intensity were assessed through attendance lists and registration forms. Dietary protein intake was assessed through 3-day food records, on three randomly assigned days (two weekdays, one weekend day). Trained research dietitians checked the records during a home visit at baseline, including taking measures from common household items used to consume protein-rich foods (e.g. glasses, cups), and through telephone at T1 and T2. Dietary intake was coded and macronutrient and energy intakes were calculated with Compleat (food calculation programme developed by the Division of Human Nutrition & Health, Wageningen University).

Primary outcome – The Short Physical Performance Battery (SPPB) was the primary outcome of this study, consisting of a balance test, a gait test, and a repeated chair rise test [19].

Secondary outcomes – Additional physical functioning outcomes were the Timed-Up-And-Go test (TUG, [20]) and the six minute walking test (6MWT) [21]. Lower limb muscle strength was measured through a 3-Repetition Maximum test (3RM) on leg press and leg extension machines (T0 and T1 only) and with a hand-held dynamometer measuring knee extension strength (MicroFET, all time points). For 3RM, at baseline first a familiarization session was performed before the actual test. 3RM scores were recalculated to 1RM using the formula of Brzycki [22]. Lean body mass (LBM), appendicular lean mass (ALM), and fat mass (FM) were measured through Dual X-ray Absorptiometry (DXA, Lunar Prodigy Advance, GE Health Care, Madison, WI). Scans were performed in the morning, participants were asked to consume a standardised breakfast and to defecate shortly before the scan. Hydration state was assessed trough Bio-electrical Impedance Spectroscopy (BIS, using SFB7 ImpediMed Limited).

Furthermore, quality of life was assessed with the EQ-5D-5L questionnaire [23]. Results of the questionnaire were used to calculate Quality Adjusted Life Years (QALY, [24]). Self-perceived health status score (0-100), part of the EQ-5D-5L, was evaluated separately. Functioning in activities of daily living (ADL) was measured with the Basic Lower Extremity Function questionnaire from the Late Life Function & Disability Index [25]. Frequency and capability in participating in socially defined life's tasks was measured through the Social Role Domain questionnaire [26]. ADL and social participation scores were recalculated to standardised scores, with higher scores indicating better ADL functioning, and more frequent engagement and less limitations in socially defined life tasks.

Statistical methods

Data were analysed with SPSS version 23. Descriptive statistics are shown as means with standard deviations or as percentages. Baseline differences between the intervention and control group were analysed using independent t-test or Mann Whitney U tests for continuous data, and χ^2 tests or Fishers exact tests for categorical data. Data were analysed according to the intention-to-treat principle. Linear mixed models analysis was used to analyse difference in changes between the intervention

and control group after the intensive support intervention (week 12) and for the full intervention period (week 12 and week 24). Time, treatment and their interaction were specified as fixed factors, subjects were defined as random factors. A random intercept model was used for all outcomes, with Variance Component covariance structure. Covariables age, gender, education level, municipality (for full intervention period analysis only), and hydration state (for LBM, ALM, and FM only) were tested. These covariables were not included in the final model as they did not affect the estimates of the interaction effect by more than 10% compared to the crude model (adjusted model see Supplementary Table 4.1). Estimated means and 95% confidence intervals, and the estimates of the interaction between time and treatment in the crude model are presented.

RESULTS

Study population baseline characteristics did not significantly differ between the intervention and control group (Table 4.1). During the intensive support intervention 10 participants (5.9%) dropped out, mainly because of medical reasons or physical complaints.

Compliance

In the intensive support intervention, participants attended on average 83.6% of the training sessions. Average training intensity was 63% of 1RM for leg press and 62% for leg extension. Intake consultations with the dietitian were done with 98.8% of participants, and evaluation consultations with 91.5%. In the moderate support intervention, 56.1% of participants joined training sessions, attending on average 63.6% of these sessions. The nutrition course was followed by 59.8% of the participants, attending on average 76.8% of the meetings (data of Epe was missing).

At baseline, average protein intake in the intervention group was 83.0 gram (1.1 gram/kilogram per bodyweight/day, g/kg/day), and on average 14.7 gram during breakfast, 21.5 gram during lunch, and 35.6 gram during dinner, Table 4.2. During the 12 week intensive support intervention, participants in the intervention group increased daily protein intake to 108.9 gram (1.5 g/kg/day). During the following moderate support intervention this declined to 97.2 gram per day (1.3 g/kg/day), which was still higher as compared to baseline. Protein intake significantly increased during

Table 4.1 Baseline characteristics of participants of the ProMuscle in Practice intervention.

	Intervention group (n=82)	**Control group (n=86)**
Age, mean ± SD	74.7 ± 5.8	75.9 ± 6.5
Males, n (%)	31 (37.8)	35 (40.7)
Frailty status, n (%)		
Non-frail	41 (50.0)	39 (45.3)
Pre-frail	39 (47.6)	42 (48.8)
Frail	2 (2.4)	5 (5.8)
Bodyweight (kg) , mean ± SD	76.3 ± 14.4	75.6 ± 13.6
Height (cm) , mean ± SD	167.6 ± 9.0	169.2 ± 9.3
BMI (kg/m^2) , mean ± SD	27.1 ± 4.8	26.3 ± 4.0
Level of education, n (%)*		
Low	2 (2.4)	4 (4.7)
Intermediate	54 (65.9)	42 (48.8)
High	26 (31.7)	40 (46.5)
Ethnicity: Native Dutch, n (%)	79 (96.3)	81 (94.2)
Living situation, n (%)		
Alone	32 (39)	30 (34.9)
Together	50 (61)	56 (65.1)
Care use, n (%)	11 (13.4)	16 (18.6)
Alcohol use		
Drinker (≥1 day/week), n (%)	65 (79.3)	70 (81.4)
# of glasses/day, mean ± SD†	1.6 ± 0.8	1.9 ± 1.2
Smoking, n (%)		
Never smoker	32 (39.0)	30 (34.9)
Stopped > 1 year ago	46 (56.1)	53 (61.6)
Current / stopped in last year	4 (4.9)	3 (3.5)
Morbidities, n (%)		
Diabetes	9 (11.0)	9 (10.5)
Arthrosis	38 (46.3)	42 (48.8)
Fracture	3 (3.7)	4 (4.7)
Other	69 (84.1)	67 (77.9)
Swallowing problems, n (%)	10 (12.2)	6 (7.0)
Dental problems, n (%)	5 (6.1)	6 (7.0)
Nutrition status (SNAQ), n (%)‡		
Significant risk of weight loss >5 within 6 months (< 14 points)	4 (4.9)	7 (8.1)
≥ 14 points	77 (93.9)	79 (91.9)
SARC-F score ≥ 4, n (%)§||	13 (15.9)	14 (16.3)
Current physiotherapist guidance (yes), n (%)	15 (18.3)	21 (24.4)
Currently on a diet (yes), n (%)	10 (12.2)	10 (11.6)
History of sports (yes), n (%)	70 (85.4)	69 (80.2)
Total physical activity (min/day), mean ± SD§	109.5 ± 83.5	106.1 ± 77.1

SNAQ – Short Nutritional Appetite Questionnaire. * Low level of education: primary school or less, intermediate level: secondary professional education or vocational school, high level: higher vocational education, university. † Intervention group n=64, control group n=70. ‡ Intervention group n=81. § Control group n=85. || SARC-F score ≥ 4 is predictive of sarcopenia.

breakfast and lunch, reaching 25.4 gram and 31.1 gram respectively in week 12, and 21.9 gram and 27.0 gram respectively in week 24. Dietary protein intake in the control group did not change over time (difference in change between intervention and control group P < 0.001).

Primary and secondary outcomes

The intervention group significantly increased on our primary outcome measure SPPB score, as well as in secondary outcome measures TUG, gait speed, repeated chair rise, leg muscle strength, LBM and ALM, compared to the control group (Table 4.3, Figure 4.2). Between baseline and 12 weeks, there was a significant positive effect on SPPB score of the intervention compared to control (Time x treatment effect β 0.5 (95% CI 0.0–0.9), P = .043). In line with these results, also secondary outcomes gait speed (P = .008), repeated chair rise (P = .001), TUG (P = .006), and the leg strength measures (P < .001) improved in the intervention group as compared to control. In the intensive support period, the intervention group increased also in LBM (β 0.6 (95% CI 0.2–0.9), P = .001), ALM (β 0.5 (95% CI 0.1–0.8), P = .008), and bodyweight (β 0.7 (95% CI 0.2–1.2), P = .004) compared to the control group, while there were no changes in fat mass (P > .05) in both groups. When considering the full 24 weeks study period including both the intensive and moderate support intervention, there was a significant positive change in physical functioning, leg strength and lean body mass in the intervention group as compared to the control group (Table 4.3). We observed no differences in change between the groups for 6MWT, quality of life, ADL, and social participation.

DISCUSSION

This study demonstrates that community-dwelling older adults can improve physical functioning, leg muscle strength, and lean body mass following a 12-week intensive dietary protein and RE intervention implemented in practice. The subsequent 12-week moderate support intervention contributed to the maintenance of the effects as compared to baseline.

Table 4.2 Dietary intake at baseline (T0), week 12 (T1) and week 24 (T2), and the interaction terms time x treatment for week 12 (analysis with T0-T1 only), and week 12 and 24 (analysis with T0-T1-T2). Crude estimated means with 95% Confidence intervals are shown per group and time point, β-coefficients and 95% Confidence intervals are shown for the time x treatment interaction.

	Control group			Intervention group			T0-T1	T0-T1-T2		
	Week 0 Mean (95% CI)	Week 12 Mean (95% CI)	Week 24 Mean (95% CI)	Week 0 Mean (95% CI)	Week 12 Mean (95% CI)	Week 24 Mean (95% CI)	Time x Treatment β (95% CI)	Week 12 Time x Treatment β (95% CI)	Week 24 Time x Treatment β (95% CI)	Overall Time x Treatment p-value
Energy intake (MJ)	8.5 (8.1-8.9)	8.2 (7.8-8.6)	8.1 (7.7-8.5)	8.3 (7.9-8.7)	8.8 (8.4-9.2)	8.9 (8.5-9.3)	0.8 (0.3-1.3)**	0.8 (0.2-1.3)**	0.9 (0.4-1.5)**	0.001
Protein intake (g) ††	79.9 (75.7-84.1)	76.7 (72.4-81.0)	77.6 (73.2-82.0)	83.0 (78.7-87.4)	108.9 (104.4-113.5)†	97.2 (92.6-101.7)†‡	29.2 (22.5-35.9)***	29.1 (22.8-35.4)***	16.4 (10.0-22.8)***	< 0.001
Protein intake (g/kg/day) ††	1.08 (1.01-1.15)	1.04 (0.97-1.11)	1.06 (0.99-1.13)	1.12 (1.05-1.19)	1.46 (1.38-1.53)†	1.29 (1.21-1.36)†‡	0.37 (0.28-0.46)***	0.38 (0.29-0.46)***	0.19 (0.10-0.28)***	< 0.001
Protein intake at breakfast (g) ††	13.1 (11.4-14.8)	12.8 (11.1-14.6)	13.5 (11.7-15.3)	14.7 (12.9-16.4)	25.4 (23.5-27.2)†	21.9 (20.0-23.7)†‡	11.1 (8.8-13.3)***	11.0 (8.7-13.3)***	6.8 (4.5-9.1)***	< 0.001
Protein intake at lunch (g) ††	21.5 (19.6-23.5)	21.6 (19.6-23.5)	20.6 (18.6-22.7)	21.5 (19.5-23.5)	31.1 (29.0-33.2)†	27.0 (24.9-29.1)†‡	9.6 (6.4-12.8)***	9.6 (6.4-12.7)***	6.4 (3.2-9.6)***	< 0.001
Protein intake at dinner (g) ††	33.7 (31.1-36.3)	32.9 (30.3-35.6)	34.3 (31.5-37.0)	35.6 (33.0-38.3)	39.3 (36.5-42.1)	38.5 (35.7-41.3)	4.5 (-0.1-9.1)	4.5 (0.1-8.9)*	2.4 (-2.1-6.9)	0.14
Protein intake (en%) ††	16.2 (15.5-16.8)	16.1 (15.5-16.7)	16.5 (15.8-17.1)	17.0 (16.4-17.6)	21.4 (20.7-22.1)†	19.1 (18.4-19.8)†‡	4.5 (3.5-5.5)***	4.5 (3.5-5.5)***	1.8 (0.8-2.8)**	< 0.001
Fat intake (en%)	35.7 (34.5-37.0)	35.1 (33.9-36.4)	34.9 (33.6-36.1)	34.5 (33.2-35.7)	33.3 (31.9-34.6)	36.1 (34.8-37.5)‡	-0.6 (-2.7-1.4)	-0.6 (-2.6-1.4)	2.5 (0.5-4.6)*	0.006
Carbohydrate intake (en%)	41.5 (40.2-42.7)	42.3 (41.0-43.6)	42.1 (40.8-43.4)	42.7 (41.4-44.0)	40.1 (38.7-41.4)†	39.6 (38.2-40.9)†	-3.5 (-5.4- -1.5)***	-3.5 (-5.3- -1.7)***	-3.8 (-5.7- -1.9)***	< 0.001

95% CI – 95% Confidence interval. MJ – mega joule. en% - energy percentage. g/kg/day – gram per kilogram bodyweight per day. Treatment: control group is reference. Time: baseline is reference. n=168.

* Significant time*treatment effect (P<0.05), ** Significant time*treatment effect (P<0.01), *** Significant time*treatment effect (P<0.001)

† Significant Time effect (P<0.05) compared to T0. ‡ Significant time effect (P<0.05) compared to T1. || Treatment effect (P<0.05) at T1. †† Treatment effect (P<0.05) at T1 and T2.

Table 4.3 Study outcomes at baseline (T0), week 12 (T1) and week 24 (T2), and the interaction terms time x treatment for week 12 (analysis with T0-T1 only), and week 12 and 24 (analysis with T0-T1-T2). Crude estimated means with 95% Confidence intervals are shown per group and time point, β-coefficients and 95% Confidence intervals are shown for the time x treatment interaction.

	Control group			Intervention group			T0-T1	T0-T1-T2		
	Week 0 Mean (95% CI)	Week 12 Mean (95% CI)	Week 24 Mean (95% CI)	Week 0 Mean (95% CI)	Week 12 Mean (95% CI)	Week 24 Mean (95% CI)	Time x Treatment β (95% CI)	Week 12 Time x Treatment β (95% CI)	Week 24 Time x Treatment β (95% CI)	Overall Time x Treat-ment p-value
Physical functioning										
SPPB total score[a]	10.2 (9.8-10.5)	9.9 (9.6-10.3)	10.1 (9.7-10.5)	10.1 (9.7-10.5)	10.4 (10.0-10.8)	10.6 (10.2-10.9)	0.5 (0.0-0.9)*	0.5 (0.0-0.9)*	0.5 (0.1-0.9)*	0.039
4 meter gait speed (sec)[a]	4.2 (4.0-4.4)	4.4 (4.2-4.6)†	4.1 (3.9-4.3)‡	4.2 (4.0-4.4)	4.1 (3.9-4.3)	4.0 (3.7-4.2)†	-0.3 (-0.6- -0.1)**	-0.3 (-0.6- -0.1)**	-0.2 (-0.4-0.0)	0.022
Repeated chair rise time[b] (sec)	13.2 (12.3-14.0)	14.0 (13.1-14.8)	13.6 (12.7-14.4)	13.7 (12.9-143.5)	12.9 (12.1-13.8)	12.8 (11.9-13.6)	-1.6 (-2.5- -0.6)**	-1.6 (-2.5- -0.7)**	-1.4 (-2.3- -0.4)**	0.001
TUG (sec)[a]	9.6 (9.0-10.2)	9.9 (9.3-10.5)	9.8 (9.2-10.5)	9.5 (8.8-10.1)	9.0 (8.4-9.7)	9.1 (8.4-9.7)	-0.7 (-1.2- -0.2)**	-0.7 (-1.2- -0.2)**	-0.6 (-1.1- -0.1)*	0.007
6MWT (meter)[a]	373.0 (355.9-390.0)	368.4 (351.2-385.5)	368.3 (350.9-385.7)	368.2 (350.7-385.6)	375.9 (358.2-393.7)	369.7 (351.8-387.6)	12.4 (-0.8-25.7)	12.4 (-1.4-26.1)	6.2 (-8.1-20.5)	0.21
ADL (score)	71.7 (68.6-74.8)	73.8 (70.7-77.0)	74.5 (71.3-77.7)	70.5 (67.4-73.7)	74.0 (70.7-77.3)†	73.9 (70.5-77.2)†	1.3 (-2.0-4.6)	1.3 (-2.2-4.8)	0.5 (-3.1-4.1)	0.77
Social participation (frequency)[a]	51.5 (50.4-52.5)	50.7 (49.7-51.8)	50.2 (49.1-51.2)†	50.4 (49.4-51.5)	50.6 (49.5-51.7)	50.1 (49.0-51.2)	0.9 (-0.3-2.1)	0.9 (-0.3-2.1)	1.0 (-0.2-2.2)	0.20
Social participation (limitation)	77.5 (74.3-80.7)	76.9 (73.7-80.1)	77.5 (74.2-80.7)	73.7 (70.5-77.0)	75.8 (72.4-79.1)	76.2 (72.9-79.6)	2.4 (-1.6-6.5)	2.6 (-1.4-6.6)	2.5 (-1.5-6.5)	0.35
Body composition										
Lean body mass (kg)[c]	47.8 (45.8-49.9)	47.9 (45.9-49.9)	47.7 (45.7-49.8)	47.5 (45.5-49.6)	48.2 (46.1-50.2)†	47.9 (45.8-50.0)†	0.6 (0.2-0.9)**	0.6 (0.2-1.0)**	0.4 (0.1-0.8)*	0.008

Table 4.3 Continued.

	Control group			Intervention group			T0-T1	T0-T1-T2		
	Week 0 Mean (95% CI)	Week 12 Mean (95% CI)	Week 24 Mean (95% CI)	Week 0 Mean (95% CI)	Week 12 Mean (95% CI)	Week 24 Mean (95% CI)	Time x Treatment β (95% CI)	Week 12 Time x Treatment β (95% CI)	Week 24 Time x Treatment β (95% CI)	Overall Time x Treat-ment p-value
Appendicular lean mass (kg)[c]	20.5 (19.5-21.5)	20.4 (19.4-21.4)	20.5 (19.5-21.5)	20.5 (19.5-21.6)	20.9 (19.9-21.9)	20.7 (19.7-21.8)	0.5 (0.1-0.8)**	0.5 (0.2-0.8)**	0.2 (-0.1-0.5)	0.013
Fat mass (kg)[c]	23.9 (21.9-25.9)	23.8 (21.8-25.7)	23.8 (21.8-25.8)	25.2 (23.2-27.2)	25.4 (23.4-27.4)	25.6 (23.6-27.6)	0.3 (-0.2-0.9)	0.3 (-0.2-0.9)	0.5 (0.0-1.1)	0.14
Bodyweight (kg)[a]	75.6 (72.6-78.6)	75.4 (72.4-78.4)	75.4 (72.4-78.4)	76.3 (73.2-79.3)	76.8 (73.7-79.8)	76.7 (73.6-79.7)	0.7 (0.2-1.2)**	0.7 (0.2-1.2)*	0.6 (0.1-1.2)*	0.023
Muscle strength										
Leg Press strength (kg)§‖	123.4 (114.3-132. 6)	124.5 (115.3-133.7)	N/A	128.3 (119.1-137.5)	145.8 (136.4-155.3)†	N/A	16.5 (9.1-23.8)***	N/A	N/A	N/A
Leg Extension strength (kg)§	67.6 (62.6-72.6)	65.7 (60.6-70.7)	N/A	66.9 (61.8-71.9)	76.5 (71.4-81.7)†	N/A	11.6 (7.9-15.2)***	N/A	N/A	N/A
Knee extension strength (Newton)††[b]	301.1 (278.5-323.7)	326.9 (303.9-349.8)†	315.5 (292.4-338.5)	309.9 (287.0-332.9)	373.2 (349.8-396.6)†	355.0 (331.3-378.7)†‡	36.4 (17.8-54.9)***	37.5 (18.8-56.3)***	30.8 (11.5-50.0)**	<0.001
Quality of life										
QALY[a]	0.87 (0.84-0.89)	0.87 (0.84-0.89)	0.87 (0.84-0.89)	0.87 (0.84-0.89)	0.89 (0.86-0.91)	0.87 (0.84-0.89)	0.02 (-0.01-0.05)	0.02 (-0.01-0.05)	0.00 (-0.03-0.03)	0.32
Health score[a]	82.9 (80.4-85.4)	83.2 (80.7-85.7)	84.3 (81.8-86.9)	82.9 (80.4-85.5)	83.7 (81.1-86.4)	81.9 (79.2-84.6)	0.5 (-2.7-3.6)	0.5 (-2.7-3.7)	-2.4 (-5.7-0.9)	0.19

95% CI – 95% Confidence interval. SPPB – Short Physical Performance Battery. TUG – Timed Up-and-Go. 6MWT – Six minute walk test. ADL – Activities of Daily Living. QALY – Quality Adjusted Life Year. Treatment: control group is reference. Time: baseline is reference. [a] n=168. [b] n=167. [c] n=165.

* Significant time*treatment effect (P<0.05), ** Significant time*treatment effect (P<0.01), *** Significant time*treatment effect (P<0.001)

† Significant Time effect (P<0.05) compared to T0. ‡ Significant time effect (P<0.05) compared to T1. § Estimated means are calculated for T0-T1.

‖ Treatment effect (P<0.05) at T1. †† Treatment effect (P<0.05) at T1 and T2.

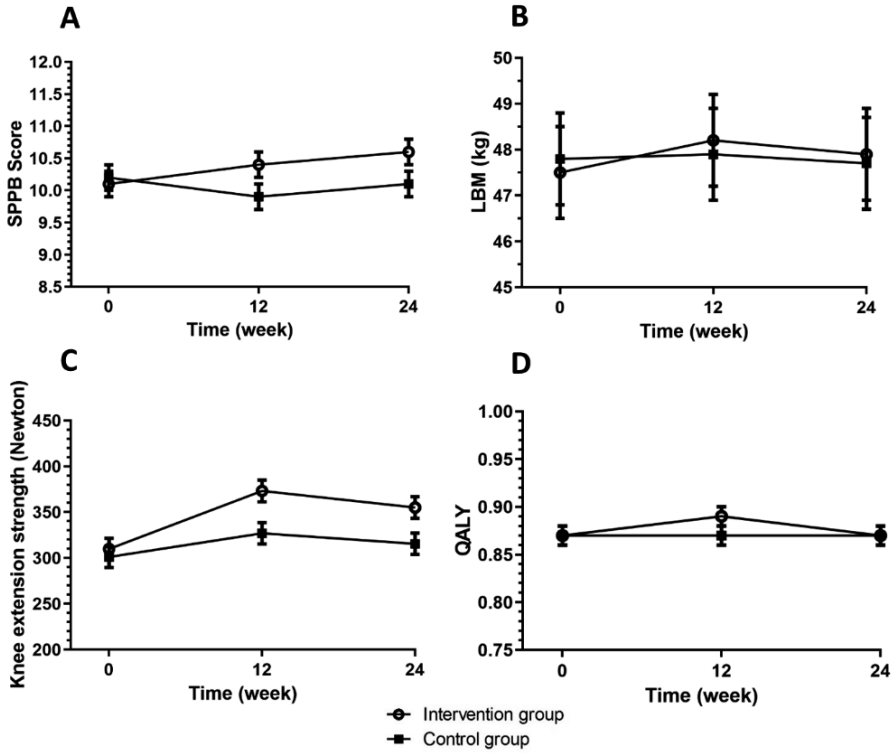

Figure 4.2 Crude model estimated mean and SEM for SPPB score (a), Lean body mass (kg, b), knee extension strength (Newton, c) and QALY (d). There was a significant time x treatment interaction for SPPB score, lean body mass, and knee extension strength for week 12 (P = .043, P = .001, and P < .001 respectively), and for the full intervention period (P = .039, P = .008, and P < .001 respectively).

We tested effectiveness of an adapted efficacious intervention on increasing protein intake in combination with RE for community-dwelling older adults, fully implemented by healthcare professionals. Our intensive support intervention was based on the efficacious clinical trial as described by Tieland et al [12], a highly controlled intervention that included pre-frail and frail older adults. To study effectiveness in real life our study population also included non-frail older adults, and our intervention was implemented by local healthcare professionals. Drop-out rate was lower than expected (6% instead of expected 30% in week 1-12) [14] and those who dropped out may not have been able to adhere to the programme, as they had similar baseline demographics but scored lower at baseline outcomes than persons who did not drop out. Adherence as compared to the efficacy study was better for protein intake and

comparable for RE [12]. Mean protein intake shifted from 1.0 g/kg/day at baseline to 1.5 g/kg/day at week twelve, with largest increases at breakfast and lunch, and exercise attendance was 84% with average training intensity of 63% of 1RM. The control group participants were asked to refrain from major changes in their lifestyle, and analysis showed that they did not change dietary intake or total physical activity during the 24 week period (data not shown).

Differences in intervention effects on SPPB, muscle strength and muscle mass between the efficacy and effectiveness study can be explained by the less structured implementation by HCP in practice and differences in population characteristics. Increases in SPPB score and leg strength in the intervention group in the first 12 weeks were smaller than those in the study by Tieland et al. (improvements of 0.3 versus 1.3 SPPB points, 14-23% versus 37-43% for leg strength respectively) [12]. Other combined RE and diet studies found no overall SPPB difference between the intervention and control groups [27, 28], though effects were found for other physical performance outcomes such as repeated chair rise [28] and gait speed [29, 30]. We observed improvements in SPPB score as well as in these sub-tests, although average improvements in all physical performance outcomes were small. Ceiling effects might have played a role for SPPB score in these high functioning adults with a high baseline score (>10) [31, 32]. Furthermore, we observed a 0.6 kg increase in LBM in the intervention group during the intensive support intervention, whereas the clinical study observed an increase of 1.2 kg LBM after 12 weeks [12]. Maintaining lean mass with aging is important to prevent loss of physical performance and metabolic conditions [33]. The extent of the improvements in LBM and strength in our study were comparable to another intervention including non-research staff implemented exercise and dietitian counselling [34]. Moreover, the intervention effects as reported were similar when performing the analysis with complete cases, confirming robustness of results. Despite the intervention adaptations affecting the effectiveness, we were still able to evoke relevant improvements on muscle health parameters when implementing the intervention in practice.

The improvement in objectively measured strength and performance did not translate into improved ADL, compared to the control group. The lower extremity functioning focused ADL questionnaire was shown to correlate moderately to strongly with SPPB and TUG [35], and is a relevant measure that depicts how difficult participants perceive

performance of daily activities. Exercise interventions in frail older adults can improve ADL functioning [36]. Potentially the intervention would have had a larger impact on ADL with addition of functional exercises or in a frail population with lower baseline ADL scores. Additionally, we explored effects on quality of life using the EQ-5D-5L questionnaire, which is often used for economic evaluation of health care interventions [37]. However, in this study population and with this intervention we observed no change in quality of life. Results on quality of life following other RE interventions for older adults are inconclusive [7, 12, 36, 38]. Potentially, the questions in the EQ-5D-5L are too general to captures subtle changes in perceived fitness or vitality as would be expected from participation in the intervention. Process evaluation results may provide insight in potential perceived improvements related to quality of life that were not detected by the EQ-5D-5L.

The moderate support intervention was followed by 56-60% of participants, and compliance was lower than for the intensive support intervention. The moderate support intervention manuals were not standardised, and therefore exercise intervention content varied between municipalities [14]. As opposed to the dietary intensive support intervention, participants no longer received protein-rich foods during the moderate support intervention. Protein intake in the moderate support intervention (1.3 g/kg/day) was lower than in the intensive support intervention, although it was still higher than baseline. Increasing protein intake using regular foods instead of supplements seemed feasible, although participants did not maintain the high intake levels without provision of foods and intensive guidance. Despite the lower compliance and intensity, the moderate support intervention ensured that the outcomes did not drop back to baseline scores after 24 weeks in intention-to-treat analysis, although the outcomes might decrease slightly over time. Yet a recent study demonstrated that effects on muscle mass and strength fade away on the long term without supervised training [39], which underlines the need of continuous support for long term compliance and effectiveness.

CONCLUSIONS AND IMPLICATIONS

This study shows that a combined intensive resistance exercise and dietary protein intervention for older adults, implemented in a real-life setting, is effective in improving physical functioning, leg strength, and lean body mass. A moderate support

intervention focused on behaviour maintenance seems suitable to prevent these effects from dropping back to baseline values. We demonstrated that effectiveness can be retained when implementing an efficacious intervention in practice, albeit effects are smaller than in a clinical setting. Further research is needed to explore best practices and feasibility of implementation in a real-life setting, as well as improving compliance and long-term behaviour maintenance.

Trial registration number: Dutch Trial Register, identifier NTR6038 (30 August 2016).

Keywords: Physical functioning, Strength, Lean body mass, Dietary protein, Resistance exercise

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Conflicts of interest
The authors declare that there are no conflicts of interest.

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Supplementary Table 4.1 Study outcomes at baseline (T0), week 12 (T1) and week 24 (T2), and the interaction terms time x treatment for week 12 (analysis with T0-T1 only), and week 12 and 24 (analysis with T0-T1-T2). Adjusted estimated means with 95% Confidence intervals are shown per group and time point, β-coefficients and 95% Confidence intervals are shown for the time x treatment interaction.

	Control group			Intervention group			T0-T1	T0-T1-T2		
	Week 0 Mean (95% CI)	Week 12 Mean (95% CI)	Week 24 Mean (95% CI)	Week 0 Mean (95% CI)	Week 12 Mean (95% CI)	Week 24 Mean (95% CI)	Time* Treatment β (95% CI)[1]	Week 12 Time* Treatment β (95% CI)[2]	Week 24 Time * Treatment β (95% CI)[2]	Overall Time * Treatment p-value[2]
Physical functioning										
SPPB total score[a]	10.2 (9.9-10.6)	10.0 (9.7-10.4)	10.2 (9.8-10.5)	10.2 (9.8-10.5)	10.4 (10.1-10.8)	10.6 (10.2-11.0)	0.5 (0.0-0.9)*	0.5 (0.0-0.9)*	0.5 (0.1-0.9)*	0.038
4 meter gait speed (sec)[a]	4.1 (3.9-4.3)	4.3 (4.1-4.5)†	4.0 (3.8-4.2)‡	4.2 (4.0-4.4)	4.1 (3.9-4.3)	3.9 (3.7-4.1)†	-0.3 (-0.6- -0.1)**	-0.3 (-0.6- -0.1)**	-0.2 (-0.4-0.0)	0.023
Repeated chair rise time[b] (sec)	13.1 (12.3-13.9)	13.9 (13.1-14.7)	13.5 (12.7-14.4)	13.5 (12.7-14.3)	12.7 (11.9-13.6)	12.6 (11.7-13.4)	-1.6 (-2.5- -0.6)**	-1.6 (-2.5- -0.7)**	-1.4 (-2.4- -0.4)**	0.001
TUG (sec)[a]	9.5 (9.0-10.0)	9.8 (9.2-10.3)	9.7 (9.2-10.2)	9.4 (8.8-9.9)	9.0 (8.4-9.5)	9.0 (8.4-9.6)	-0.7 (-1.2- -0.2)**	-0.7 (-1.2- -0.2)**	-0.6 (-1.1- -0.1)*	0.007
6MWT (meter)[a]	380.9 (366.1-395.6)	376.0 (361.1-391.0)	376.0 (360.8-391.2)	372.2 (356.7-387.6)	379.8 (364.0-395.5)	373.8 (357.9-389.8)	12.5 (-0.8-25.7)	12.4 (-1.4-26.2)	6.5 (-7.8-20.8)	0.21
ADL (score)	72.3 (69.3-75.3)	74.5 (71.4-77.5)	75.1 (72.0-78.2)	70.7 (67.5-73.8)	74.0 (70.8-77.3)†	74.0 (70.7-77.2)†	1.3 (-2.1-4.6)	1.2 (-2.3-4.7)	0.5 (-3.1-4.1)	0.78
Social participation (frequency)[a]	51.4 (50.4-52.4)	50.7 (49.7-51.7)	50.1 (49.1-51.1)†	50.2 (49.2-51.2)	50.4 (49.4-51.5)	49.9 (48.8-51.0)	0.9 (-0.3-2.1)	1.0 (-0.2-2.2)	1.0 (-0.2-2.2)	0.19
Social participation (limitation)	78.1 (74.9-81.3)	77.5 (74.3-80.7)	78.1 (74.9-81.3)	73.7 (70.4-77.0)	75.7 (72.3-79.1)	76.1 (72.7-79.6)	2.4 (-1.6-6.4)	2.6 (-1.4-6.6)	2.5 (-1.6-6.5)	0.35
Body composition										
Lean body mass (kg)[c3]	49.6 (48.5 - 50.7)	49.7 (48.5-50.8)	49.6 (48.4-50.7)	49.3 (48.2-50.5)	50.0 (48.8-51.1)†	49.7 (48.5-50.9)†	0.6 (0.3-1.0)**	0.6 (0.2-1.0)**	0.4 (0.0-0.8)*	0.010

Supplementary Table 4.1 Continued

Appendicular lean mass (kg)[c3]	21.4 (20.9-21.9)	21.3 (20.8-21.9)	21.4 (20.9-22.0)	21.4 (20.9-22.0)	21.8 (21.2-22.3)	21.6 (21.1-22.2)	0.4 (0.1-0.8)*	0.4 (0.1-0.8)**	0.2 (-0.1-0.6)	0.027
Fat mass (kg)[c3]	24.0 (22.0-26.0)	23.9 (21.9-25.8)	23.9 (21.9-25.8)	24.7 (22.6-26.7)	24.9 (22.8-27.0)	25.1 (23.1-27.2)	0.3 (-0.2-0.9)	0.4 (-0.2-0.9)	0.6 (0.0-1.1)*	0.12
Weight (kg)[a]	77.2 (74.4-80.0)	77.0 (74.2-79.8)	77.0 (74.2-79.8)	77.3 (74.4-80.2)	77.8 (74.9-80.7)	77.7 (74.8-80.6)	0.7 (0.2-1.2)**	0.7 (0.2-1.2)*	0.6 (0.1-1.2)*	0.024
Muscle strength										
Leg Press strength (kg)§‖	127.9 (120.5-135.2)	128.9 (121.4-136.3)	N/A	131.0 (123.3-138.7)	148.2 (140.3-156.1)†	N/A	16.2 (8.9-23.5)***	N/A	N/A	N/A
Leg Extension strength (kg) §‖	71.0 (67.8-74.3)	69.2 (65.9-72.4)	N/A	70.2 (66.8-73.6)	79.7 (76.2-83.2)†	N/A	11.4 (7.8-15.0)***	N/A	N/A	N/A
Knee extension strength (Newton) ‖ †† [b]	316.5 (301.3-331.7)	341.9 (326.1-357.6)†	330.6 (314.7-346.5)	322.6 (306.9-338.4)	385.7 (369.3-402.1)†	367.4 (350.7-384.2)†‡	36.2 (17.8-54.6)***	37.7 (19.0-56.4)***	30.7 (11.6-49.8)**	<0.001
Quality of life										
QALY [a]	0.87 (0.85-0.90)	0.87 (0.85-0.90)	0.87 (0.85-0.90)	0.87 (0.85-0.90)	0.89 (0.86-0.92)	0.87 (0.84-0.90)	0.02 (-0.01-0.05)	0.02 (-0.01-0.05)	0.00 (-0.03-0.03)	0.33
Health score[a]	83.2 (80.6-85.7)	83.4 (80.9-86.0)	84.5 (81.9-87.2)	82.9 (80.3-85.6)	83.7 (80.9-86.4)	81.9 (79.1-84.7)	0.4 (-2.7-3.6)	0.5 (-2.8-3.7)	-2.4 (-5.7-0.9)	0.19
Dietary intake										
Energy intake (MJ) [a]	8.7 (8.3-9.0)	8.4 (8.0-8.8)	8.2 (7.9-8.6)	8.5 (8.1-8.9)	9.0 (8.6-9.4)	9.1 (8.6-9.5)	0.8 (0.2-1.3)**	0.8 (0.2-1.3)**	1.0 (0.4-1.5)***	0.001
Protein intake (g) †† [a]	81.3 (77.1-85.5)	78.0 (73.7-82.3)	79.2 (74.8-83.7)	85.4 (81.0-89.8)	111.4 (106.8-116.0) †	99.2 (94.5-103.9) †‡	29.2 (22.4–36.1)***	29.4 (22.9-35.8)***	15.9 (9.3-22.5)***	<0.001
Protein intake (g/kg/d) †† [a]	1.08 (1.01-1.15)	1.04 (0.96-1.11)	1.06 (0.98-1.13)	1.14 (1.07-1.21)	1.47 (1.40-1.55) †	1.31 (1.23-1.39) †‡	0.37 (0.28–0.47)***	0.38 (0.29-0.47)***	0.19 (0.10-0.28)***	<0.001

Supplementary Table 4.1 Continued

Protein intake at breakfast (g) †† [a]	13.4 (11.7-15.1)	13.1 (11.4-14.9)	13.9 (12.1-15.7)	15.6 (13.8-17.4)	26.5 (24.7-28.4) †	22.9 (21.0-24.8) †‡	11.2 (9.0–13.5)***	11.3 (8.9-13.6)***	6.8 (4.5-9.1)***	<0.001
Protein intake at lunch (g) †† [a]	22.1 (20.2-24.0)	21.9 (19.9-23.9)	21.4 (19.3-23.4)	22.3 (20.3-24.3)	31.7 (29.5-33.8) †	27.5 (25.3-29.6) †‡	9.6 (6.4–12.7)***	9.6 (6.4-12.7)***	5.9 (2.7-9.2)***	<0.001
Protein intake at dinner (g) || [a]	34.2 (31.5-36.8)	33.4 (30.7-36.1)	34.7 (31.9-37.5)	36.2 (33.4-38.9)	39.8 (36.8-42.7)	38.5 (35.6-41.5)	4.3 (-0.4–9.0)	4.4 (-0.1-8.9)	1.8 (-2.8-6.4)	0.16
Protein intake (en%) †† ‡‡ [a]	16.1 (15.5-16.8)	16.0 (15.4-16.7)	16.6 (15.9-17.2)	17.1 (16.5-17.8)	21.6 (20.9-22.3) †	19.1 (18.4-19.8) †‡	4.5 (3.5 – 5.5)***	4.5 (3.5-5.5)***	1.6 (0.5-2.6)**	<0.001
Fat intake (en%) [a]	35.6 (34.4-36.8)	35.0 (33.7-36.2)	34.7 (33.4-35.9)	34.4 (33.2-35.7)	33.3 (32.0-34.6)	36.0 (34.7-37.4) ‡	- 0.5 (-2.5 – 1.6)	-0.5 (-2.5-1.5)	2.6 (0.6-4.6)*	0.009
Carbohydrate intake (en%) [a]	41.5 (40.2-42.8)	42.5 (41.2-43.8)	42.2 (40.9-43.6)	42.6 (41.3-43.9)	39.9 (38.5-41.3) †	39.4 (38.0-40.8) †	- 3.6 (-5.6 - -1.7)***	-3.7 (-5.6- -1.8)***	-4.0 (-5.9- -2.1)***	<0.001

95% CI – 95% Confidence interval. SPPB – Short Physical Performance Battery. TUG – Timed up and Go. 6MWT – Six minute walk test. ADL – Activities of Daily Living. QALY – Quality Adjusted Life Year. g/kg/day – Gram per kilogram bodyweight per day. En% - energy percentage. Treatment: control group is reference. Time: baseline is reference.

[1]Adjusted for: Age, education level (low/intermediate vs high), sex. [2] Adjusted for: Age, education level (low/intermediate vs high), sex, municipality. [3] Additionally adjusted for ratio extracellular water / total body water. [a] n=168. [b] n=167. [c] n=165.

* Significant time*treatment effect (P<0.05), ** Significant time*treatment effect (P<0.01), *** Significant time*treatment effect (P<0.001)

† Significant Time effect (P<0.05) compared to T0. ‡ Significant time effect (P<0.05) compared to T1. § Estimated means are calculated for T0-T1.

|| Treatment effect (P<0.05) at T1. †† Treatment effect (P<0.05) at T1 and T2. ‡‡ Treatment effect (P<0.05) at T0.

CHAPTER 5

Process evaluation of a combined lifestyle intervention for community-dwelling older adults: ProMuscle in Practice

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ABSTRACT

Background and Objectives: The ProMuscle in Practice intervention combines resistance exercise training and dietary protein intake for community-dwelling older adults, implemented by healthcare professionals. This study aimed to evaluate implementation and context of this intervention in Dutch healthcare practice.

Research Design and Methods: We conducted a randomised controlled multicentre intervention study, in five Dutch municipalities. Eighty-two older adults received the 12-week intensive support intervention (resistance exercise training and individual dietary counselling) and the optional 12-week moderate support intervention (resistance exercise training and a nutrition course). Mixed method data were collected from both participants and healthcare professionals (n=36) on process indicators recruitment, dose received, acceptability, fidelity, applicability, and context.

Results: Overall, the intervention was feasible to implement and accepted by participants and healthcare professionals. About two-thirds of participants continued with the moderate support intervention after the first twelve weeks. Mean dose received for the training sessions was 83.6% in the intensive intervention and 63.6% in the moderate intervention, >90% for individual dietitian consultations, and 76.8% for the nutrition course. The intensive support intervention was implemented with high fidelity, whereas for the moderate support intervention resistance exercise trainings varied in implementation between exercise providers.

Discussion and Implications: A combined resistance exercise training and dietary protein intervention for community-dwelling older adults can be successfully implemented in practice. Well-tailored interventions, intensive supervision by skilled healthcare professionals, social aspects, fidelity and fit within real-world settings appeared essential for successful implementation. These elements are important for continuous intervention optimization, to accomplish broader and successful implementation.

BACKGROUND AND OBJECTIVES

The age related decline in muscle mass, strength and physical functioning can be counteracted by implementing effective resistance exercise training and dietary protein interventions in practice [1-3]. Implementing such complex lifestyle interventions in practice should take into account that the setting and the organisational and professional context influence the intervention and its outcomes [4, 5]. Tailoring the intervention to the local context can increase intervention effectiveness [6], but to sustain implementation it should be reported what was tailored and why [4]. Besides focusing on organisational and implementer factors, participant engagement with and acceptability of the intervention is also important for intervention success [4]. Most randomized controlled trials on intervention effectiveness report attendance or intervention compliance (i.e. [7-9]), but seldom report on acceptance, context, or the underlying intervention theory. To promote broader adoption of effective interventions, it is necessary to understand what works, for whom, and under what conditions [4, 10].

An efficacious combined resistance exercise training and protein supplementation intervention [8] was previously adapted to ProMuscle in Practice, to fit in the practice setting [11]. A multicentre real-life study has shown that the ProMuscle in Practice intervention is effective in improving physical functioning, muscle strength, and body composition when implemented in a multicentre real-life study [12], but these effects vary per setting and intervention period. To obtain insight in how the ProMuscle in Practice intervention produced these results, a process evaluation is performed to assess implementation, and to identify mechanisms of impact or contextual factors that can explain variance in effectiveness outcomes [4, 13]. Therefore, the aim of this study is to investigate implementation and context of the total ProMuscle in Practice intervention for community-dwelling older adults in Dutch healthcare practice.

RESEARCH DESIGN AND METHODS

Study design and setting

The ProMuscle in Practice randomised controlled multicentre intervention study was conducted between September 2016 and November 2018 in five municipalities in the Netherlands. Study duration was 36 weeks in municipalities Apeldoorn and Ede, and 52 weeks in Epe, Ermelo/Putten, and Harderwijk. The study protocol was approved by

the Wageningen University Medical Ethics Committee, the Netherlands, and all participants gave their written informed consent before participation. The study is registered with The Dutch Trial Register (NTR, number 6038) since 30 August 2016. Study design, and intervention theory and description have been reported in detail elsewhere [14].

Study population

The study population consisted of community-dwelling older adults (65 years or over) that were mainly recruited through local media. Screening of interested persons was performed in two rounds. In the first round, researchers evaluated whether they met one of two inclusion criteria: 1) being pre-frail or frail based on the Fried frailty criteria [15], or 2) experiencing difficulty in selected activities of daily living (ADL) tasks and not performing resistance exercises ≥ 2 times a week. If so, in the second round, ,the general practitioner (GP) checked the specified exclusion criteria mainly regarding the presence of specific medical conditions [14]. After inclusion, participants were randomly allocated to the intervention or control group at each location. This article focuses on the intervention group only, as intervention participants engaged both with the intensive support intervention and moderate support intervention.

Intervention

The intervention consisted of a 12-week intensive support intervention and a subsequent voluntary 12-week moderate support intervention [14].

Intensive support intervention

The intensive support intervention was based on previous studies [8, 11] and included a resistance exercise component and a dietary protein component, implemented by physiotherapists and dietitians of local care organisations. These healthcare professionals (HCP) received a 1.5 h training session by one of the researchers and detailed implementation manuals before the intervention started. In week 6 of the intervention, HCP at each location had a one-hour joint-peer discussion.

Participants performed progressive resistance exercise twice a week, one hour per session, supervised by physiotherapists. Training sessions were performed in groups of 4-6 participants. Each training consisted of a warm-up, five strength exercises (leg press, leg extension, lat pulldown, vertical row, and chest press), and warm-down.

Training intensity of the leg exercises was based on personal maximum strength tests (1 repetition maximum (1RM)). Leg exercises were performed progressively with 4 sets that ranged between 8-15 repetitions over the intervention period, and intensity was increased from 50% of 1RM in week 1 to 75% of 1RM in week 12. Physiotherapists used a maximum strength test (3RM) in week six to further tailor the training intensity. Physiotherapists motivated participants to perform the exercises correctly and with progressive intensity, built participants' confidence in performing resistance exercise, and promoted social cohesion during the training sessions.

In the diet intervention dietitians counselled to achieve intake of at least 25 grams of protein per main meal, based on 3-day food diaries completed before the start of the intervention. They provided a tailored advice to participants during a 30-minute intake consultation before the intervention started. Participants received mainly dairy-based protein-rich foods to complement or to replace parts of their diet, in agreement with participants' preferences. The dietitian was present to answer questions when the participants first received the foods, and held an individual evaluation consultation with participants in week six in which they could adjust the dietary advice and discussed the continuation with consuming protein-rich foods after the intensive intervention. Furthermore, dietitians monitored food consumption compliance through a weekly checklist completed by participants, and discussed barriers and facilitators for increasing protein intake.

Moderate support intervention

The aim of this follow-up intervention was to guide participants towards behaviour maintenance concerning resistance exercise and a protein-rich diet. This optional program started directly after the intensive support intervention, and was designed by the municipal health service in collaboration with local organisations and municipalities. Approximately three weeks before the start, participants received a leaflet that included information on the moderate support program, and suggestions to include (home) exercise and protein-rich foods in their daily routine. For the training program, exercise groups (twice a week) were initiated at local gymnastic clubs, fitness centres, or physiotherapy practices. All trainers offered a group-based exercise program including strength exercises described in a general manual, but the type of exercises and professional guidance differed per location. In some municipalities participants had to pay a small contribution to participate in the exercise sessions.

A nutrition course was organised by the municipal health service, and implemented by a health promotor and dietitian. The course consisted of five workshops, in which participants interacted, prepared dishes rich in protein (breakfast, lunch, dinner), and visited a supermarket. Additionally, participants received a 2-3 monthly newsletter through e-mail about the program.

Data collection and outcomes

Background characteristics

Background characteristics were assessed through a questionnaire at baseline, including questions on age, education level, living situation, care use, morbidities [16], current physiotherapist or dietitian guidance, and history of physical activity.

Process evaluation

The process evaluation was informed by the Medical Research Council guidelines for process evaluation [4] and the Conceptual Framework for Implementation Research [17, 18]. We collected mixed method data from participants and HCP on several process indicators related to the domains implementation and context of the MRC framework [4], see Table 5.1. For implementation we focused on the process indicators recruitment, reach, dose received, acceptability, fidelity, and applicability [4, 5, 19-22]. Additionally, maintenance was assessed at the organisational and individual level [23]. Lastly, context includes aspects in the environment that influenced implementation or effectiveness [4, 5].

Data analysis

Quantitative data were analysed using SPSS version 23. Differences between background characteristics of the drop-outs and completers were tested using independent samples t-tests, χ^2 tests, or Fisher's exact test. Descriptive statistics were used to analyse acceptability and dose received, and data were presented in mean and standard deviation, or frequency and percentage. Qualitative data were analysed using an inductive approach in Atlas.ti version 8. All interviews were audiotaped and transcribed verbatim. All transcripts were checked with the audio recording before analysis to remove transcribing errors. Transcripts of HCP interviews were analysed by EJIvD and transcripts of intervention participants were analysed by a research assistant (LB) to identify important themes within the specified process indicators of Table 5.1 and for professionals also within their specified tasks (suppl. File of [14]).

Table 5.1 Overview of process indicators, definitions, and data collection within the process evaluation of ProMuscle in Practice for the intensive support intervention and moderate support intervention.

Process indicator Definition	**Methods -** **Intensive support intervention**	**Methods -** **Moderate support intervention**
Recruitment Procedures used to attract participants [19]	- Project logbook - Registration forms - Participant questionnaire T0 (incl. reasons to participate)	N/A
Reach Extent to which intended audience comes into contact with the intervention [4]	- Project logbook - Registration forms	- Project logbook - Registration forms
Dose received Quantity of the intervention that was implemented and the extent to which participants actively engaged in intervention activities [4]	- Attendance lists of training sessions and dietitian consultations - Registration forms on training intensity and topics discussed within dietitian consultations	- Attendance lists of training sessions and nutrition course sessions
Acceptability Extent to which the participants and HCP[a] were satisfied with the intervention [21]	- Participant questionnaire T0[b] (incl. motivation to participate on Likert-type scale 1-5, reasons for participation) - Participant questionnaire T1[c] (incl. general acceptability score (1-10), acceptability on specific aspects of diet and exercise intervention (Likert-type scale 1-5), open questions on intervention acceptability, and perceived confidence in performing the desired behaviour after completing the intensive support intervention (Likert-type scale 1-5)). - Semi-structured interviews with HCP at T1 – 18 physiotherapists / interns, 8 dietitians (incl. questions on intervention acceptability).	- Participant questionnaire T1 (incl. motivation to participate on Likert-type scale 1-5) - Participant questionnaire at T2[d] (incl. general acceptability score (1-10), acceptability on specific aspects of diet and exercise intervention (Likert-type scale 1-5), open questions on intervention acceptability) - Participant questionnaire T2 and T3[e] (incl. perceived confidence in performing the desired behaviour after completing the moderate support intervention (Likert-type scale 1-5)). - Semi-structured interviews with participants at T2 focused on the moderate support intervention (n=4 per municipality, both males and females, including participants who participated in none, one or more of the intervention components). - Semi-structured interviews with HCP at T2 – 9 trainers, 2 nutrition course leaders (incl. questions on intervention acceptability).
Fidelity Extent to which the intervention was implemented as planned [4, 19, 20]	Focused on whether the intervention was implemented as planned according to the structured manuals. - Semi-structured interviews with HCP at T1 (incl. questions on whether, how and why they deviated from the intervention	Focused on what was actually implemented and how the intervention as described in the general manual was adapted to local context. - Semi-structured interviews with HCP at T2 (incl. questions on intervention content and adaptations to local context). - Structured observations - Project meetings minutes

Table 5.1 Continued.

Process indicator Definition	**Methods -** **Intensive support intervention**	**Methods -** **Moderate support intervention**
	protocol). - Registration forms of training intensity and dietitian consultations - Structured observations - Project meetings minutes	
Applicability Extent to which the intervention fitted in the real-world setting [22]	- Semi-structured interviews with HCP at T1 (incl. questions on whether the intervention fitted their regular working procedures).	- Semi-structured interviews with HCP at T2 (incl. questions on whether the intervention fitted their regular working procedures).
Maintenance (Organisation level) / sustainability Extent to which a program is sustained over time within the organisation or community [23]	N/A	- Project logbook - Project meeting minutes - Semi-structured interviews with HCP at T2 (incl. questions on possibility for intervention sustainability within their organisation).
Maintenance (Individual level) Extent to which a program becomes an enduring part of the behavioural repertoire of an individual [23]	N/A	- Participant questionnaire T2 and T3 (incl. questions on maintenance of exercise and dietary behaviour)
Context Larger physical, organisational, social environment that could influence intervention implementation [4] and intervention outcomes [5]	- Participants questionnaire T1 (incl. questions on whether they followed a diet or participated in other exercise programs) - Semi-structured interviews with HCP at T1 (incl. question on contextual factors that either facilitated or hindered intervention implementation). - Project logbook - Project meeting minutes - Semi-structured interview with project coordinator (n=1) that initiated adoption of part of the intervention	- Participants questionnaire T2 (incl. questions on whether they followed a diet or participated in other exercise programs) - Semi-structured interviews with participants at T2 (incl. questions on reasons for (non)-participation) - Semi-structured interviews with HCP at T2 (incl. question on contextual factors that either facilitated or hindered intervention implementation). - Project logbook - Project meeting minutes - Semi-structured interviews with project coordinators (n=2) that initiated adoption of part of the moderate support intervention

[a] HCP = healthcare professionals. [b] T0 – baseline. [c] T1 – week 12, directly after the intensive support intervention. [d] T2 – week 24, directly after the moderate support intervention. [e] T3 – week 36, twelve weeks after the moderate support intervention finished.

RESULTS

Recruitment and reach

Of the 296 screened older adults, 192 were initially included in the study by the GP (supplementary Figure 5.1). Persons were mainly excluded because they were too fit, too active, or because they met one or more of the exclusion criteria related to diseases. Twenty-four participants withdrew between randomization and baseline measures, starting the baseline measures with 168 individuals, of which 82 participants were included in the intervention group. Main reasons for participation were contribution to science (n=56), personal interest (n=53), and personal improvement (n=44).

Table 5.2 shows baseline characteristics of the total intervention group, and of the intervention participants that completed the trial versus those who dropped-out. Mean age was 74.7 years, nearly two-thirds were women, and half of the population was non-frail. The eleven participants who dropped-out did not significantly differ from the completers in any of the baseline characteristics, although 36% of drop-outs already received physiotherapist guidance at baseline as compared to 16% of completers. Reasons for drop-outs were mostly medical or physical complaints (Supplementary Figure 5.1).

Intensive support intervention

Implementation

Dose

Twelve out of 18 trainers (66.7%) and all eight dietitians attended the 1.5 hr training session before the intervention. Participants attended on average 83.6% of the delivered training sessions (Table 5.3). In agreement with the protocol, exercise intensity progressed on average from 47% of 1RM in week 1 to 75% of 1RM in week 12. In the diet intervention, 98.8% of intervention participants received the intake consultation with the dietitian (average duration 31 minutes), and 91.5% of participants received the evaluation consultation (average duration 20 minutes). Sixty-six percent of participants used the checklist as a reminder and tool to provide insight in dietary intake.

Table 5.2 Baseline characteristics of intervention participants, and of completers and drop-outs within the intervention group of the ProMuscle in Practice intervention.

	Total intervention group (n=82)	**Completers (n=71)**	**Drop-outs before T2 (n=11)**
Age, mean ± SD	74.7 ± 5.8	74.6 ± 5.7	75.7 ± 6.5
Males, n (%)	31 (37.8)	29 (40.8)	2 (18.2)
Frailty status, n (%)			
Non-frail	41 (50.0)	36 (50.7)	5 (45.5)
Pre-frail	39 (47.6)	33 (46.5)	6 (54.5)
Frail	2 (2.4)	2 (2.8)	0 (0.0)
Level of education, n (%) [a]			
Low	2 (2.4)	1 (1.4)	1 (9.1)
Intermediate	54 (65.9)	49 (69.0)	5 (45.5)
High	26 (31.7)	21 (29.6)	5 (45.5)
Living situation (together / alone), n (%)			
Alone	32 (39.0)	26 (36.6)	6 (54.5)
Together	50 (61.0)	45 (63.4)	5 (45.5)
Care use, n (%)	11 (13.4)	8 (11.3)	3 (27.3)
Morbidities, n (%)			
Diabetes	9 (11.0)	7 (9.9) [b]	2 (18.2)
Arthrosis	38 (46.3)	32 (45.1)	6 (54.5)
Fracture	3 (3.7)	2 (2.8)	1 (9.1)
Other	69 (84.1)	61 (85.9)	8 (72.7)
Current physiotherapist guidance (yes), n (%)	15 (18.3)	11 (15.5)	4 (36.4)
Currently on a diet (yes), n (%)	10 (12.2)	9 (12.7)	1 (9.1)
History of sports (yes), n (%)	70 (85.4)	60 (84.5)	10 (90.9)

[a] Low level of education: primary school or less, intermediate level: secondary professional education or vocational school, high level: higher vocational education, university. [b] Completers n=70

Acceptability

Acceptability scores of the intensive support intervention of both participants and HCP can be found in Table 5.3. Intervention participants and HCP were highly motivated to start with the intervention. At the end of the study, overall satisfaction with the intervention programme was rated with a grade 8.3 ± 0.9 by participants and 7.8 ± 0.8 by HCP.

When addressing the exercise component of the intervention, participants and HCP were both satisfied (score 8.3 ± 1.1 and 7.3 ± 0.8 respectively). Positive points according to participants were the group-based program and the physiotherapist guidance. A

suggestion for improvement according to both participants and HCP was increasing variation in exercises next to the resistance exercises. HCP were satisfied with the training session they received beforehand, and with the clear manuals and registration forms, which contained enough information to be able to start with the intervention.

The diet intervention was also appreciated by participants and HCP (7.5 ± 1.3 and 7.5 ± 1.1 respectively), although on average participants scored the diet intervention lower than the exercise intervention. Positive aspects were the consultations with the dietitian and the fact that the dietitian took participants' dietary preferences into account in the advice. Both participants and HCP indicated that the number of protein-rich foods added to the diet was high, and that it would be better to include more variation.

In general, HCP felt sufficiently involved in the intervention. They perceived the joint peer-discussion in week six as useful, as it helped to exchange experiences with the other professionals and to discuss bottlenecks with regard to implementation.

Fidelity and Applicability

Resistance exercise

Overall, the exercise intervention was implemented as planned, with physiotherapists following the progressive training protocol (Table 5.3) and supporting and motivating participants. Physiotherapists indicated that group coherence was achieved automatically, but that they also facilitated this by starting conversations within the group, or by performing a group-based warm-up or warm-down. There were at least two rest days between the training sessions, group size varied between four and seven participants, and there were two or three trainers per group. Physiotherapists were assisted by interns or remedial therapists at all locations.

A deviation from the manual was that physiotherapists did not map the abilities and constraints of participants at the beginning of the intervention program, although in their daily work they would do so. They indicated that they received the information about participants' strength and medical information too late from the researchers, which caused difficulties with tailoring the training intensity at the start of the training program.

Physiotherapists deviated from the training protocol when necessary, i.e. in case of physical complaints. In the last weeks of the intervention period physiotherapists reported less progression in the training intensity because participants had reached their maximum. In some locations other or adjusted resistance exercises were performed for part of the intervention period, as some of the training machines did not function properly. At all locations an intermediary 3RM measure was performed around week 6, used to evaluate training progression and inform participants about their training progress.

Dietary protein intervention

About half of the intake consultations were performed after the start of the intervention period, in contrast to before the intervention, as was stated in the manual (Table 5.3). All dietitians formulated the dietary advice together with the participant, and dietitians spoke about most of the required topics during the intake. The contact moment in the first training week was not performed as planned, as this was done mostly in later weeks. Participants addressed questions about the dietary intervention mostly to the physiotherapists in the first weeks. Dietitians performed evaluation consultations around week 6 with the majority of participants, upon which dietary advice was adjusted for 37% of participants and 76% of participants were informed about the moderate support intervention.

Fit with target group and with HCP working procedures

HCP expressed that the intervention fitted well with the target population. They mentioned that participants noticed positive effects of the intervention, especially in ADL functioning and perceived fitness (e.g. climbing the stairs or rising from a chair was easier, and they were less tired after walking). HCP indicated that the intervention fitted their regular working procedures, as dietitians and physiotherapist have the required competencies, including people skills and knowledge. The involved HCP worked mostly with a more frail population in long-term care facilities or in rehabilitation, and indicated that this intervention would fit best in primary care with regard to the target population. The involved HCP would like to continue working with the intervention. Preconditions for further continuation are sufficient time available to implement the project, and recruiting the community-dwelling target population.

Table 5.3 Dose received and acceptability of the intensive support intervention for participants and healthcare professionals.

Dose received	**Dose according to protocol**	**Received by participants**
Number of exercise sessions attended, n (%) [a]	24 sessions	19.7 (83.6)
Mean intensity of the exercises (% of 1RM) [b]		
Leg press	Not specified	63
Leg extension	Not specified	62
Mean intensity at week 1 (% of 1RM) [cd]	50% of 1RM	47
Mean intensity at week 5 (% of 1RM) [cd]	60-75% of 1RM	66
Mean intensity at week 12 (% of 1RM) [ce]	70-80% of 1RM	75
Mean number of sets per exercise (mean) [fb]		
Leg press	4 sets	3.5
Leg extension	4 sets	3.5
Mean number of repetitions per set (mean) [b]	Varies over time	
Leg press	(range: 8 – 15	12.4
Leg extension	repetitions)	12.3
Number of participants that received intake consultation, n (%) [g]	100%	81 (98.8)
Intake consultation performed before week 1, n (%) [g]	100%	35 (42.7)
Number of participants that received evaluation consultation, n (%) [g]	100%	75 (91.5)
Evaluation consultation performed in week 5, 6 or 7, n (%) [g]	100%	67 (81.7)
Dietary advice adjusted during evaluation consultation, n (%) [g]	Optional	30 (36.6)
Dietitians informed participants about moderate support intervention during evaluation consultation, n (%) [g]	100%	62 (75.6)
Number of participants that received an additional consultation, n (%)	Optional	9 (11.0)
	Participants	**Healthcare professionals**
Motivation to start intensive support intervention		
Exercise sessions, mean ± SD	4.6 ± 0.5 [h]	8.3 ± 0.8 [i]
Diet intervention, mean ± SD	4.4 ± 0.7 [h]	8.3 ± 0.3 [i]
Acceptability [j]		
Overall score (scale 1-10), mean ± SD	8.3 ± 0.9	7.8 ± 0.8
Resistance exercise sessions (scale 1-10), mean ± SD	8.3 ± 1.1	7.3 ± 0.8
Satisfaction with..., mean ± SD[k]		
Physiotherapist explanation of the exercises and training programme	4.7 ± 0.5	*N/A*
Guidance by the physiotherapist during the training sessions	4.7 ± 0.6	*N/A*
The exercises	4.6 ± 0.6	*N/A*
Exercising in a group	4.8 ± 0.4	*N/A*
Extent to which they were being informed of personal training progress	4.2 ± 1.0	*N/A*
Extent to which they were being informed about the moderate support intervention	3.7 ± 1.0	*N/A*
Diet intervention (scale 1-10), mean ± SD	7.5 ± 1.3	7.5 ± 1.1
Satisfaction with..., mean ± SD [k]		

Table 5.3 Continued.

	Participants	Healthcare professionals
Intake consultation with the dietitian	4.1 ± 0.9	*N/A*
Evaluation consultation with the dietitian	4.1 ± 0.9	*N/A*
Number of protein-rich foods to consume daily	3.8 ± 1.1	*N/A*
Filling out the checklist every day	3.7 ± 1.1	*N/A*
Extent to which they were being informed about the moderate support intervention	3.6 ± 1.0	*N/A*

[a] In Apeldoorn, Epe, Ermelo, Harderwijk 24 training sessions were offered, in Ede 22 training sessions. [b] Average of week 0, week 5 and week 12. [c] Combined for leg press and leg extension machine. [d] Percentage of 1RM as measured during the baseline measurements. [e] Percentage of 1RM as measured in week 6 of the intervention. [f] Excluding data from Ede. [g] Based on completed registration forms (n=71 – 81), proportion of 82 intervention participants. [h] Scale 1 = not motivated at all, 5 = very motivated. [i] Scale 1 = not motivated at all, 10 = very motivated. [j] Participants n=74, professionals overall acceptability n=26, resistance exercise acceptability n=18 physiotherapists, diet intervention acceptability n=8 dietitians. [k] Scale 1 = not satisfied at all, 5 = very satisfied.

Context

The care organisations that adopted the intensive support intervention were recruited mainly through existing networks of the municipal health service or the Nutrition & Healthcare Alliance. Most HCP indicated in the interviews that it was their own choice to partake in intervention implementation. Factors that impeded the implementation as identified in the interviews were logistic issues concerning the protein-rich foods for the dietitians, and issues with training machines, training location, and time to implement the intervention for the physiotherapists. Facilitating contextual factors were having a 15 minute break between the training groups, supporting management that made sufficient time available, and inclusion of motivated participants. In general, HCP were satisfied with the multidisciplinary collaboration, although in several locations physiotherapists indicated that they would have preferred more contact with the dietitians, as the physiotherapists did not always know how to handle questions about the diet intervention.

Moderate support intervention

Implementation

Table 5.4 and Supplementary table 5.1 show an overview of the moderate support intervention components offered per municipality. Four municipalities offered sessions in a fitness centre, one municipality in a sports hall, and three municipalities with a primary care physiotherapist. Type of exercises performed and costs for participants

varied between municipalities. The nutrition course had the same general format at all municipalities.

Transfer to moderate support intervention

Participants were informed on the options within the moderate support intervention approximately 4-to-5 weeks before the start through a letter and a leaflet, except in Apeldoorn where the options were confirmed at a late stage and participants were informed only 2 weeks before the start. Participants were relatively satisfied with the information they received about the moderate support intervention from physiotherapists and dietitians (Table 5.2), and were motivated to participate. Their confidence in being able to continue with resistance-type exercises and consuming protein-rich foods after the intensive support intervention was somewhat positive (3.7 ± 1.2 and 4.1 ± 0.9 on a scale of 1-5, respectively). HCP were satisfied with the moderate support intervention content, as it focused on the combination of diet and exercise, and included sufficient guidance and low costs. However, HCP indicated that they were not timely informed on the exact content and involved organisations of the moderate support intervention, so they had difficulty properly informing the participants about the program.

Dose received

Some exercise providers offered two sessions a week, while others offered one session a week (Table 5.4). Each exercise option was attended by 4-8 participants per municipality (56.1% of all intervention participants attended one or more exercise sessions), who attended between 43.8% and 83.3% of delivered sessions (mean 63.6%) (Table 5.4, see also Supplementary table 5.1). Main reasons for joining the exercise sessions were for their health, practical location or time (in the morning), and social aspects (social interaction or continuing together with their intensive support intervention training group). The nutrition course was attended by 3-13 participants per municipality (59.8% of participants in total), who attended on average 76.8% of the course sessions (data of Epe is missing) (Table 5.5). During the moderate support intervention period, the majority of participants indicated to have tried to consume 25 grams of protein during breakfast (n=54) or lunch (n=50). The newsletter was read by 58 participants, and the majority of these participants found the newsletter useful. Main reasons for non-participation in the moderate support intervention were inconvenient planning, having no interest in nutrition, having physical complaints, a preference for

exercising outside, or because not all intensive support intervention group members continued.

Acceptability

Sixty-six participants completed the questionnaire after the moderate support intervention. Participants' average acceptability of the total moderate support intervention was 8.1 ± 1.3 (n=58), and the majority of participants could fit the moderate support intervention well within their daily life (n=52) and perceived it to be of added value (n=49). All HCP were motivated to implement the group-based training sessions or nutrition course (Supplementary table 5.1 and Table 5.5), and felt involved with the project. However, both nutrition course leaders indicated that they missed a connection with the overall project and the exercise providers of the moderate support intervention, and missed insight in the diet intervention of the first 12 weeks.

Exercise sessions

On average, participants and exercise trainers were satisfied with the exercise sessions, mean scores 8.4 ± 1.2 and 8.1 ± 0.7 respectively. Participants were overall satisfied with the type of exercises, supervision, and group-based training. When comparing the types of exercise options, both participant and trainer satisfaction with exercise in a sports hall was lower than satisfaction with fitness centres and with primary-care physiotherapists. From the questionnaire and interviews it emerged that participants perceived the exercise intensity to be lower at the sports hall compared to the fitness or physiotherapist, and somewhat less matching with RE from the intensive support intervention.

Similarly to the intensive support intervention, trainers considered it positive that the project made older adults aware of the importance of both resistance exercise and nutrition, that the trainings were in groups, and that they saw improvements in ADL, balance and exercise intensity of participants.

Nutrition course

Participants were satisfied with the group-based nutrition course (mean score 8.1 ± 0.8), the information, and the activities during the course (Table 5.5 and 5.6). In the questionnaire and interviews participants indicated they learned new things about protein-rich foods and meals, became more aware of the importance of a protein-rich

diet, and obtained more insight in their protein intake. A point of improvement could be the addition of more general dietary advice instead of focusing mostly on proteins. In addition, some participants indicated that they would have preferred more personal diet advice.

The nutrition course leaders were moderately satisfied with the nutrition course (mean score 6.8 ± 0.8), with least satisfaction for the first course in Apeldoorn, as the leader experienced it as a sort of try-out. Strong points were the practical aspects of the course, and the fact that it was organised in the local setting of participants.

Fidelity and applicability

Exercise intervention

Exercise providers used the manuals as inspiration, and based the training session content on possibilities within their setting and participants' abilities. In the first intervention location Apeldoorn, the manual was still in development, so these trainers did not have access to a list with exemplar resistance exercises. The majority of trainers added other types of exercise to sessions, such as balance or functional exercises, cardio, exercises in circuit form, or sport games (Table 5.4). All trainers except the fitness trainer in Apeldoorn indicated to have increased training intensity, although some trainers indicated that it was difficult to keep track of the intensity level of the participants. For the majority of providers there was a trainer present focusing solely on the training group, while the fitness trainer in Apeldoorn was supervising the whole fitness centre (30-40 persons) and thus not really involved with the participants.

During the sessions, trainers explained exercises, paid attention to correct performance of the exercises, or checked whether exercise intensity could be increased. To motivate participants, trainers tried to make participants see their training success and stimulated them to increase intensity. Several trainers tried to facilitate group cohesion, e.g. by stimulating a coffee moment after the training, by performing exercises together, or by having a joint start-up moment (Supplementary table 5.1).

Table 5.4 Overview of the exercise sessions per municipality in the moderate support intervention, including data on dose received and acceptability.

Exercise sessions	**Apeldoorn**		**Epe**		**Ermelo**		**Harderwijk**	**Ede**
Exercise options implemented	Sports hall (1x/week)	Fitness (1x/week)	Physio-therapist (1x/week) [a]	Fitness (2x/week)	Fitness (2x/week)	Physio-therapist (2x/week)	Fitness (2x/week)	Physio-therapist (2x/week)
Costs for participants	Free of charge	Free of charge	12.50 euro /month	12.50 euro /month	15 euro /month	15 euro /month	15 euro /month	30 euro /month
Implemented by [b]	Neighbour-hood sport coach and intern	Fitness trainer and intern	Physio-therapist	Fitness trainer	Fitness trainer and other fitness trainer	Physio-therapist	Fitness trainer and other fitness trainer	Medical fitness instructor
Training session content								
Resistance exercises (RE)	Squat, Step-up, push-up, other exercises for arms, abdomen, back	Exercises for leg muscles, back, chest.	Leg press (LP), lunge, squat, lat pulldown	LP, leg extension (LE), leg curl, lunge, step-up, calf exercises, abductor, adductor	LP, LE, total body strength exercises	LP, LE, lunge, step-up, exercise for trunk muscles	LP, LE, leg curl, abductor, adductor, chest press, lat pulley	LP, LE, leg curl, abductor, back extension, biceps curl, chest press, abdomen exercise, vertical row, triceps pushdown, squat, lunge
Use of training machines for resistance exercises	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Other exercises	Game activities (simple vs more difficult) / balance exercises	Cardio	Balance exercises / cardio (e.g. home trainer, stepper)	Balance exercises (e.g. with bosu ball)	N/A	Cardio / balance / walking exercises if needed	1 minute maximum bike-test	N/A

Table 5.4 Continued.

	Apeldoorn		Epe		Ermelo		Harderwijk	Ede
Dose received								
Number of participants joined (% of total) [c]	5 (41.7)	4 (33.3)	4 (22.2)	8 (44.4)	8 (50.0)	6 (37.5)	8 (44.4)	5 (27.8)
Number of training sessions delivered	12	12	12	24	24	24	24	24
Mean # of sessions attended (%)	6.0 (50.0)	5.3 (43.8)	10.0 (83.3)	17.4 (72.4)	17.9 (74.5)	17.3 (72.2)	13.5 (56.3)	11.4 (47.5)
Acceptability								
Professionals								
Acceptability (score 1-10)	7	7.5	8	8	8.25	9	9	8
Participants								
Acceptability (score 1-10), Mean ± SD	7.8 ± 1.0 n=4	6.7 ± 2.3 n=3	8.7 ± 1.5 n=3	9.0 ± 0.9 n=8	8.8 ± 1.2 n=8	8.6 ± 0.9 n=5	8.6 ± 1.1 n=7	8.0 ± 0.0 n=4
Satisfaction with the type of exercises (score 1-5), Mean ± SD [d]	4.0 ± 1.2	3.3 ± 2.1	5.0 ± 0.0	4.9 ± 0.4	4.9 ± 0.4	5.0 ± 0	4.9 ± 0.4	4.5 ± 1.0

[a] Combination of physiotherapist and Sports hall (not included in table) was 12.50/month. [b] Underlined professionals is interviewee. [c] Based on attendance registration (attended 1 or more sessions). [d] Scale 1 = not satisfied at all, 5 = very satisfied.

Table 5.5 Overview of nutrition course per municipality in the moderate support intervention, including data on dose received and acceptability.

Nutrition course	**Total**	**Apeldoorn**	**Epe**	**Ermelo**	**Harderwijk**	**Ede**
Costs for participants	N/A	Free of charge	Free of charge	Free of charge	Free of charge	Free of charge
Implemented by [a]	N/A	Health promoter #1 and dietetics student #1	Health promoter #1	Health promoter #2 and dietetics student #2	Health promoter #2 and dietitian #1	Health promoter #2 and dietitian #2
Content of 5th session [b]	N/A	N/A	N/A	With welfare worker, tasting foods made by course leader	N/A	Tasting foods made by participants
Dose received						
N participants joined (% of total)	49 (59.8)	3 (25.0)	12 (66.7) [c]	13 (81.3)	11 (61.1)	10 (55.6)
Number of workshops delivered	4-5	4	4	5	4	5
Mean # of workshops attended (%)	3.5 (76.8)	3.7 (91.7)	Unknown	3.4 (68.3)	3.3 (82.5)	3.8 (76.0)
Acceptability						
Professionals						
Motivation to start (scale 1-10), mean ± SD	8.5 ± 0.7 [d]	8 [e]	8 [e]	9 [g]	9 [g]	9 [g]
Acceptability (scale 1-10), mean ± SD	6.8 ± 0.8 [f]	6 [e]	7.5 [e]	7 [g]	7 [g]	7 [g]
Participants						
Acceptability (scale 1-10), mean ± SD	8.1 ± 0.8 (n=41)	7.7 ± 0.6 (n=3)	7.3 ± 0.8 (n=10)	8.6 ± 0.6 (n=10)	8.5 ± 0.5 (n=11)	8.2 ± 0.6 (n=7)

[a] Underlined professionals is interviewee. [b] Fifth course meeting was a follow-up meeting. In Ermelo a welfare-worker was invited during this follow-up meeting. [c] Based on persons that indicated to want to try the course at least once; no data available on whether they actually attended the course. [d] One score for health promotor 1 and one score for health promotor 2. [e] Health promoter #1. [f] Two scores for health promotor 1 and one score for health promotor 2. [g] Health promoter #2; one grade for all locations.

Table 5.6 Participants' acceptability of the moderate support intervention components, for the exercise sessions also clustered for sports hall, fitness or physiotherapist.

EXERCISE SESSIONS	Total (n=43)[a]	Sports hall (n=5)	Fitness (n=27)	Physiotherapist (n=12)
Participants motivation to start, mean ± SD [a]	3.9 ± 1.0	N/A	N/A	N/A
Participants acceptability (scale 1-10), mean ± SD	8.4 ± 1.2	7.8 ± 1.0	8.5 ± 1.4	8.4 ± 0.9
Satisfaction with.. [b]				
Type of exercise	4.7 ± 0.8	4.0 ± 1.2	4.7 ± 0.8	4.8 ± 0.6
Supervision during training sessions	4.9 ± 0.3	5.0 ± 0.0	4.8 ± 0.4	5.0 ± 0.0
Group-based training	4.8 ± 0.4	4.8 ± 0.4	4.8 ± 0.4	4.8 ± 0.4

NUTRITION COURSE	Total (n=41)
Participants motivation to start, mean ± SD [b]	4.0 ± 0.8
Participants acceptability, mean ± SD	8.1 ± 0.8
Because of participating in the nutrition course.. [c]	
I gained more insight in personal protein intake	4.1 ± 1.2
Gained ideas on protein-rich meals	4.1 ± 1.0
Learned new things about protein-rich nutrition	4.1 ± 1.1
Know how to use the info in daily life	4.1 ± 1.0
Satisfaction with.. [d]	
Information received during the dietary workshops	4.8 ± 0.5
Group-based dietary workshops	4.9 ± 0.3
The preparation of protein-rich breakfast meals?	4.7 ± 0.5
The preparation of protein-rich lunch meals?	4.7 ± 0.6
The preparation of protein-rich dinner meals?	4.7 ± 0.5
Viewing product labels	4.7 ± 0.6

[a] One participant joined both the sport centre and fitness, so is included once in the total grade. [b] Scale 1 (not motivated at all) - 5 (very motivated). [c] Score 1 (totally disagree) – 5 (totally agree). [d] Score 1 (very unsatisfied) – 5 (very satisfied).

Nutrition course

Two course leaders were consecutively involved in the nutrition course, and they received assistance from a dietitian or dietetics student during course sessions (Table 5.5). The first course leader developed the course manual, and the second course leader made several adjustments, i.e. changing recipes and developing slideshows. From the third location onwards the participants received the slideshows, materials, and recipes after the course.

Session duration of 1.5 hours was perceived as rather short by the course leaders, especially when cooking the recipes. During the sessions, the leaders started with a recap of the previous session. The discussed theory focused mostly on dietary proteins,

also including plant-based proteins, and some information was provided on the overall diet as participants requested this. Course leaders indicated in the interview that social interaction was very important, and that participants generally were eager to give examples and to discuss their dietary habits. The fifth workshop was cancelled in three municipalities as participants were not interested in a supermarket visit, and was held in Ermelo and Ede several weeks after meeting four.

Fit with target group and HCP working procedures
According to HCP, both the exercise sessions and the nutrition course were suitable for the target group. In the questionnaire, all except three participants indicated that the intensity of exercises was just right, and not too light or heavy. Participants noted a difference in the information they received from the dietitian in the intensive support intervention (mainly dairy-focused) and the information as included in the nutrition course (i.e. broader information on protein, reading labels).

HCP indicated that the intervention fitted with their working procedures. All trainers except the neighbourhood sports coach in Apeldoorn were used to supervise group-based trainings, and work with this target group. Some mentioned differences from their normal work, for example that they would usually perform an individual intake with participants or would use a different build-up of sets and repetitions. Nutrition course leaders were also used to work in health promotion and education.

Context
Most involved exercise organisations were existing contacts of the different Municipalities or Sportservice in Ede. Financial support was asked from some municipalities for parts of the intervention, or received from the project, resulting in no costs for the participants for the nutrition course.

Some factors that hindered implementation of the exercise intervention were identified. In the beginning it was hard for trainers to divide attention over the participants with explaining the exercises in larger groups. The neighbourhood sports coach indicated that he would have liked to have additional materials (e.g. free weights) to enable more resistance exercises in the sports hall. Some trainers missed information on physical complaints or medical issues, and suggested that in future implementation they would do an intake at the start. Facilitating factors were that in Epe, Ermelo, and

Harderwijk trainers noted that people tended to know each other and that there was more social cohesion as these were small cities.

According to the nutrition course leaders, it was preferred to schedule the four main sessions in subsequent weeks, and the optional fifth sessions a few weeks later. A group size of 8-10 participants was ideal, as this allowed bonding with participants and exchanging experiences within the group. While most courses were now implemented within long-term care buildings, one course leader suggested that selecting a more inspirational location (e.g. cooking studio) would be preferred.

Maintenance

All primary care physiotherapists and fitness centres (except Apeldoorn) indicated that they could continue to use this project in their daily work, and would like to do so. The neighbourhood sports coach indicated that the project should be more structurally embedded within their municipality, as they now struggled to refer participants to suitable exercise opportunities with sport clubs. After the study, some of the involved fitness centres and primary care physiotherapists decided to continue the project or training group, and indicated that several participants became a member of their organisation. However, for other participants, membership costs were a barrier for continuation. The nutrition course was not sustained over time. One of the course leaders indicated that there should have been more emphasis on ensuring sustainability, for example by letting a person from the local network implement the course, or by collaborating with local cooking clubs. One nutrition course leader suggested that providing participants with materials (e.g. poster, list) with the most relevant information and a list of protein-rich foods, might help to continuously remind them of dietary proteins after the course.

The majority of participants indicated that the moderate support intervention helped them to continue with resistance exercise (n=45) and consuming protein-rich foods (n=52). At the end of the moderate support intervention participants were slightly more motivated to continue consuming protein-rich foods (score 4.3 ± 0.6 on scale 1 (not motivated) – 5 (very motivated)) than to continue with RE (score 3.8 ± 1.1). In agreement, participants had plans to continue with eating protein-rich meals (n=61) and performing resistance exercise (n=51) after the moderate support intervention.

Twenty-there out of 65 participants who completed the week 36 questionnaire performed resistance exercises at home, and 27 at another location (mostly fitness centre or physiotherapist practice), in the period after the moderate support intervention (week 24-36). The majority of participants indicated to have paid attention to the amount of protein in foods (n=46) and to have deliberately bought foods rich in protein (n=49) in this period. The majority of participants still indicated to have plans to continue with consuming dietary protein (n=59) or resistance exercises (n=44) in the future, and participants were on average most confident to continue with consuming sufficient dietary protein.

DISCUSSION AND IMPLICATIONS

The aim of this comprehensive process evaluation was to obtain insight in implementation and context of the ProMuscle in Practice RE and dietary protein intervention. The intensive support intervention was implemented with high dose received and fidelity, and was accepted by both participants and implementing HCP. The moderate support intervention had lower attendance rates, and especially the exercise session content and acceptability showed high variability across settings.

Based on this process evaluation, we can suggest key elements of the intervention and implementation that explain how the intervention produces change, also known as the mechanisms of impact [4]. We observed high dose received for the intensive support intervention, comparable to the original clinical study [8], and lower and more variable dose received for the moderate support intervention. The lower dose received in the moderate support intervention could indicate that participants felt less obliged to join all sessions, as it was an optional intervention, or that intervention content did not always match with participants needs. We observed that not all participants continued with the moderate support intervention, suggesting that the transfer to this intervention period was not optimal. One possible explanation for this is that HCP from the first period were informed too late about the moderate support intervention content, and were therefore not able to sufficiently motivate participants to continue. Lack of information is a barrier to participating in physical activity programs [24], emphasising the need for sufficient information supply about the follow-up program. Another explanation for non-continuation with the moderate support intervention were practical aspects, such as inconvenient location or lack of time, which is in line

with other research [25]. However, as increased contact frequency within combined lifestyle interventions is associated with increased intervention effectiveness [26], increasing adherence over time is important. For future intervention continuation, more attention should be paid to a better transfer to community facilities and overcoming barriers experienced by participants for this transfer.

Intervention acceptability may be a prerequisite to achieve high dose received. Overall, participants were satisfied with both intervention periods. Participants appreciated the group-based nature of the intervention, even though they did not indicate the social aspect to be an important reason to participate at baseline. Although evidence of the impact of social support on intervention effectiveness is conflicting [26, 27], studies investigating motivators and preferences of older adults for participating in physical activity or nutritional programs identified fun and social interaction as important factors [25, 28, 29]. Especially the presence of like-minded peers seems to be beneficial [30], and these findings support importance of the social aspect within the intervention. In our study, it appeared that there was most room for social interaction in the moderate support intervention, e.g. during circuit-form training, coffee after the training, and during activities of the nutrition course. HCP have an important role in facilitating social cohesion and stimulating communication to create social support. Furthermore, promoting continuation of the intervention with the same group may be helpful to achieve long-term behaviour change.

Other intervention elements that contributed to intervention acceptability for participants were tailoring the intervention and intensive HCP supervision. Most tailoring occurred within the intensive support intervention, as this intervention included more intensive training guidance and individual dietary advice. A person-centred approach was identified as an important element for physical activity intervention effectiveness for older adults [25, 27]. However, at the start of both the intensive support and moderate support intervention, HCP often could not tailor the program to participants capabilities or needs as they lacked information on medical issues of participants. Therefore, HCP from both intervention periods would prefer to perform an intake at the start, like they would normally do. Performing a multidisciplinary intake beforehand could possibly prevent drop-out, and elicit input for specific types of exercise (e.g. balance, functional) that could help participants to achieve their goals. Based on our results, intensive professional supervision is needed

to tailor the intervention, and to apply the other behaviour change techniques (e.g. feedback, goal setting) that are necessary to change participants' behaviour [14]. Goal setting [25, 31] and feedback [32] are examples of behaviour change techniques that can positively impact intervention effectiveness. A combination of education and behavioural activities, may work best for older adults to improve physical activity behaviour [33]. Although face-to-face contact with a professional is not necessary for physical activity intervention effectiveness [25, 33], it can increase the effect size [25], with more intensive contact with HCP resulting in higher effect sizes [34]. We therefore consider professional supervision essential for our target group and contributing to intervention acceptability.

The diet intervention in the intensive support intervention included a personal, tailored approach including facilitation with protein-rich foods, whereas the moderate support intervention used a less individual approach. We saw largest increases in dietary protein intake in the first period, with only slight decreases in protein intake in the second 12 weeks [12]. This indicates that participants were reasonably able to maintain their increased protein intakes after cessation of receiving protein-rich foods, although on average reaching the 25 gram threshold over time seems to be most difficult for the breakfast meal. Qualitative research shows that fit of dietary protein foods with older adults habits and knowledge of health benefits are important drivers for consuming protein-rich foods [35], which are aspects incorporated in the intervention. However, food choice in older adults is a complex interplay between numerous factors [36], and thus sufficient tailoring of dietary advice is needed to improve dietary patterns. Tailoring of dietary advice was incorporated in the intensive support period, but enabling the dietitian to be more often present during the training sessions to answer questions may be helpful, as the checklists proved to be unsuccessful. In addition to group-based training also tailored support during the diet intervention is necessary to achieve sufficient protein intakes over time. Overall, largest intervention effects and acceptability were seen in the intensive support intervention (van Dongen et al., submitted), which might indicate that a more tailored and intensively supervised intervention is most effective in improving health outcomes and achieving participant satisfaction.

This multicentre design allowed us to get insight into intervention fit and adaptations to context in several locations. In general, HCP indicated the intervention to fit their

working procedures, an important prerequisite to achieve implementation success. Implementation fidelity differed between the intensive support intervention and the moderate support intervention, mostly for the exercise sessions. Physiotherapists generally adhered to the implementation manuals in the first 12 weeks, whereas, as expected, we observed more variation in training content in the second 12 weeks. The latter intervention was not previously tested and the manuals were not very strict, so we expected more implementation variation. In the moderate support intervention the main focus was still on resistance training, but sessions included also other types of exercises. This matched with wishes from participants, who missed variation in exercises during the intensive support intervention. Adapting or selecting only parts of an intervention might support intervention sustainability in daily practice, as the implementers can fit the intervention to the needs of themselves and the participants [6]. Overall, the moderate support exercise intervention fitted best within fitness centres or primary care physiotherapy practices. Based on our results, we propose that the moderate support intervention exercise sessions should include skilled supervisors that monitor progress and provide feedback, training in groups, and a combination of RE on training machines and additional exercises.

Besides implementation fidelity and fit in the real-life setting, multidisciplinary collaboration also contributes to implementation success. The physiotherapists and dietitians in general had good contact in the intensive support intervention, as they worked in the same organisation and appreciated the joint peer discussion. However, cohesion between the exercise and nutrition part of the moderate support intervention was lacking, and exercise trainers and health promotors missed a connection with the first intervention period. Targeting both exercise and nutrition in this intervention is a strength [26], which was also confirmed by the healthcare professionals. Further intertwining the exercise and nutrition aspects in both intervention periods, and strengthening the collaboration between all involved organisations may make the intervention more coherent.

Some strengths and limitations related to the study design should be mentioned. We believe that the high fidelity to content and overall high acceptability by HCP and participants was due to the systematic intervention adaptation and piloting process [11]. A strength of this study was the comprehensive process evaluation that used suitable frameworks to guide evaluation efforts. Secondly, the involved organisations

could be viewed as early adopters [37] and might therefore not fully represent other healthcare organisations in the Netherlands. Nevertheless, multiple practice organisations were involved in the different municipalities, proving that it is possible to successfully implement the intervention in practice. Currently, the intensive support intervention was implemented in secondary care, while based on the target population and the professionals this intervention would fit better within primary care or within public health. Additionally, as the intervention had a phased start in the different municipalities, the intervention, materials, and recruitment procedures were continuously improved during the study. We expect that the later intervention locations benefitted from this ongoing improvement in e.g. number of recruited participants and the organisation of the moderate support intervention.

Concluding, the ProMuscle in Practice intervention was feasible to implement and generally acceptable to both community-dwelling older adults and implementing healthcare professionals. The intensive support intervention was implemented with high dose received and fidelity, whereas for the moderate support intervention the dose received and implementation were more variable between settings. Key elements that we assume contribute to intervention success were tailored interventions, intensive supervision by skilled healthcare professionals, social aspects, implementation fidelity, the fit within the real-world setting, and multidisciplinary collaboration. The moderate support intervention should receive due attention in future implementation to achieve optimal participant engagement and intervention delivery including key intervention elements. Continuous intervention optimization, while taking into account the key intervention elements, is warranted for broader implementation of this combined intervention for community-dwelling older adults.

Key words:
Dietary protein, nutrition, resistance exercise training, implementation

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Conflict of interest
We have no conflict of interest to declare.

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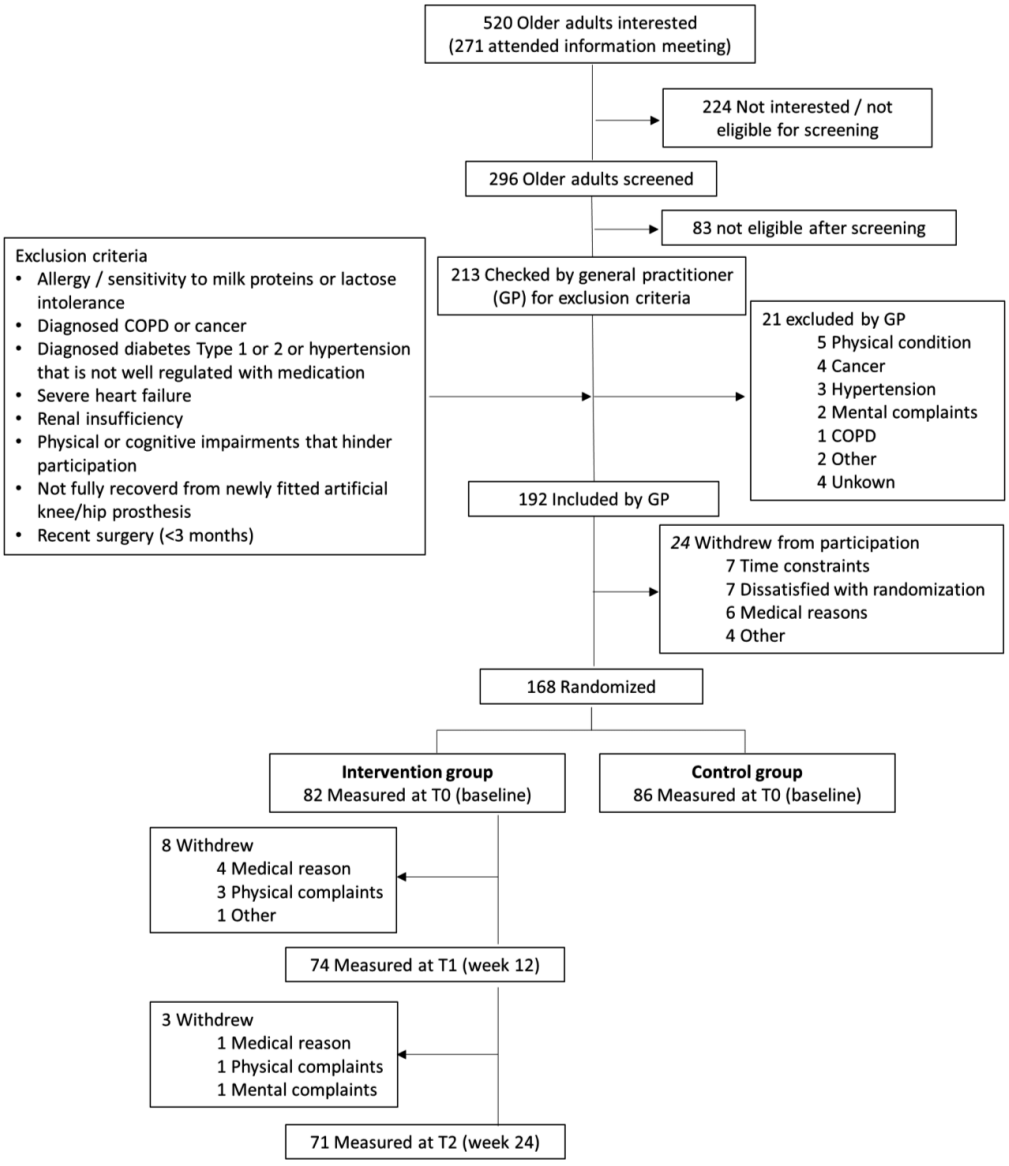

Supplementary figure 5.1 Flow chart of the ProMuscle in Practice study, including follow-up in the intervention group.

Supplementary table 5.1 Additional information on the exercise sessions per municipality in the moderate support intervention, including data on dose received and acceptability.

Exercise sessions	**Apeldoorn**		**Epe**		**Ermelo**		**Harderwijk**	**Ede**
Exercise options explored in the municipality	Sports hall (sport stimulation organisation), two fitness centres		Sports hall (Welfare organisation Epe), care organisation from intensive support intervention (physiotherapist), fitness centre		Fitness centre, two primary care physiotherapists practices, neighbourhood sport coach		Fitness centre	Fitness centre, physio-therapist, gymnastics organisation
Exercise options implemented	Sports hall (1x/week)	Fitness (1x/week)	Physio-therapist (1x/week)	Fitness (2x/week)	Fitness (2x/week)	Physio-therapist (2x/week)	Fitness (2x/week)	Physio-therapist (2x/week)
Training session content								
Warm-up (WU)	Sports / games, group-based	Unknown	Exercises sitting / standing, group-based	Home trainer cycling / rowing / walking / cross trainer	Cardio	Exercises in a cirle (walking, side-steps, half lunges, passing around a ball), group-based	Home trainer cycling / rowing	Cardio
Warm-down (WD)	Only in the last few weeks. Stretching, group-based	Unknown	Practicing the homework exercises, group-based	Sometimes stretching, group-based	Cardio and stretching, group-based	Stretching, group-based	One minute slow home trainer cycling after bike-test	Cardio
Use of other materials	Balls, benches, floor mats, gymnastic vaulting box	Unknown	Balance pillow, pylon, ball	Step-block, bosu ball, sticks for balance	Unknown	Unknown	Unknown	Sticks for balance
Participants received training schedule on paper	No	Yes	No	Yes	Yes	Yes [a]	Yes	Yes

Supplementary table 5.1 Continued.

	Apeldoorn		Epe		Ermelo		Harderwijk	Ede
Resistance exercises (RE) duration	Time: 20-25 min for total body RE.	Time: unknown.	Time: 15-20 min for leg exercises.	Time: unknown.	Time: 40 min for total body RE.	Time: 20 min for leg exercises.	Time: unknown.	Time: 35-45 min for total body RE.
Sets x repetitions for RE, and progression in RE intensity	3x10. Increases in difficulty based on participants' abilities	Unknown	3x15. No progression in intensity	4x15, 3x15, 4x12 (depending on exercise). Weight was increased (machines) / increases in difficulty (other exercises)	3x15 to 2x8. Weight was increased for leg exercises	4x12. Weight was increased from week 3 onwards, and were adjusted further after 3RM halfway	From 3x15 towards 3x8. Exercise intensity was increased from week 6 onwards	From 3x15 to 3x10 to 3x12 to 4x10 to 4x12. Weight was increased when possible
Stimulation of group cohesion	Games during session (e.g. competition), group-based WU and WD	Not done	Not necessary, as there already was a group feeling. Group-based WU and WD	Circuit training, coffee moment after training	Group-based WD, coffee moment after training	Group-based WU and WD, encouraged to drink coffee after training	Group-based start with conversation	Stimulate social interaction during training sessions. Once a week exercises in a group (squat, lunge)
<u>Dose received</u>								
# of participants who stopped with exercise in this period (when)	0	0	0	0	1 (week 7)	0	2 (week 1, week 4)	1 (week 4)
Mean # of lessons attended (%) – without participants who	*N/A*	*N/A*	*N/A*	*N/A*	*19 (79.2)*	*N/A*	*17.3 (72.2)*	*13.8 (57.3)*

Supplementary table 5.1 Continued.

Exercise sessions	Apeldoorn		Epe		Ermelo		Harderwijk	Ede
stopped with exercise								
Acceptability								
Professionals								
Motivation to start (score 1-10)	8.5	Unknown	8	8	7.75	9	9	9
Participants								
Satisfaction with the trainer supervision (score 1-5), Mean ± SD [b]	5.0 ± 0.0	3.0 ± 1.7	5.0 ± 0.0	5.0 ± 0.0	4.9 ± 0.4	5.0 ± 0	4.7 ± 0.5	5.0 ± 0
Did the exercises sessions match with intensive support intervention?								
Yes / a bit, n (%)	3 (60.0)	3 (75)	3 (100)	7 (87.5)	8 (100)	5 (100)	6 (85.7)	4 (100)
No, n (%)	2 (40.0)	1 (25)	0	1 (12.5)	0	0	1 (14.3)	0

[s] Exercises (intensity and sets & reps) are loaded onto a card that has to be inserted in every training machine. [b] Scale 1 = not satisfied at all, 5 = very satisfied.

CHAPTER 6

Process evaluation of a randomised controlled trial of a diabetes prevention intervention in Dutch primary health care: the SLIMMER study

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ABSTRACT

Objective: To investigate (i) how the SLIMMER intervention was delivered and received in Dutch primary health care and (ii) how this could explain intervention effectiveness.

Design: A randomised controlled trial was conducted and subjects were randomly allocated to the intervention (10-month combined dietary and physical activity intervention) or the control group. A process evaluation including quantitative and qualitative methods was conducted. Data on process indicators (recruitment, reach, dose received, acceptability, implementation integrity and applicability) were collected via semi-structured interviews with health-care professionals (n=45) and intervention participant questionnaires (n=155).

Setting: SLIMMER was implemented in Dutch primary health care in twenty-five general practices, eleven dietitians, nine physiotherapist practices and fifteen sports clubs.

Subjects: Subjects at increased risk of developing type 2 diabetes were included.

Results: It was possible to recruit the intended high-risk population (response rate 54%) and the SLIMMER intervention was very well received by both participants and health-care professionals (mean acceptability rating of 82 and 80, respectively). The intervention programme was to a large extent implemented as planned and was applicable in Dutch primary health care. Higher dose received and participant acceptability were related to improved health outcomes and dietary behaviour, but not to physical activity behaviour.

Conclusions: The present study showed that it is feasible to implement a diabetes prevention intervention in Dutch primary health care. Higher dose received and participant acceptability were associated with improved health outcomes and dietary behaviour. Using an extensive process evaluation plan to gain insight into how an intervention is delivered and received is a valuable way of identifying intervention components that contribute to implementation integrity and effective prevention of type 2 diabetes in primary health care.

INTRODUCTION

Over the last two decades, many large-scale randomised controlled trials have shown that type 2 diabetes can be delayed or prevented by lifestyle intervention in individuals at high risk of this disease [1-8]. Many of these interventions have been implemented in real-world settings and have shown significant reductions in weight but inconclusive results for metabolic indicators of diabetes risk [9-12]. However, implementation of interventions in the real world is often complex, as they are not delivered in controlled environments and thus are influenced by a multitude of factors (e.g. limited resources and finance). Therefore, a comprehensive evaluation approach is required to identify the combination of most effective intervention components for preventing type 2 diabetes [9, 10, 13, 14]. The scope of the evaluation approach needs to be broadened from only assessing effectiveness to also getting insight into the delivery of an intervention, that is, elucidating the aspects that explain what works, how, and why [15, 16]. A process evaluation, therefore, can enhance confidence in conclusions about intervention effectiveness [17].

Several reviews have identified intervention components associated with increased intervention effectiveness. A review by Greaves *et al*. [18] showed that greater intervention effectiveness in dietary and physical activity (PA) interventions to prevent type 2 diabetes was associated with targeting both diet and PA, mobilising social support, using behaviour change techniques (e.g. self-monitoring, goal setting, relapse prevention, and individual tailoring), and having a clear plan to support maintenance of behaviour change. Also, providing higher intensity interventions was associated with greater intervention effectiveness [18, 19]. There were no clear associations between intervention effectiveness and setting, delivery mode (e.g. group-based, individual, or mixed), delivery provider, or study population [18, 19]. Another systematic review on interventions to increase PA in adults aged 55-70 years found no relationship between intervention effectiveness and delivery mode or intervention intensity. However, it was concluded that tailoring the intervention to participants may be important [20]. Furthermore, a meta-regression on weight management programmes showed that greater weight loss was associated with counting calories (self-monitoring), providing at least some contact with a dietitian, and facilitating social comparisons [21].

In the Netherlands, the original Study on Lifestyle intervention and Impaired glucose tolerance Maastricht (SLIM) [4] was translated into the SLIMMER diabetes prevention intervention (SLIM iMplementation Experience Region Noord- en Oost-Gelderland) for Dutch primary healthcare [22], pilot-tested [23], implemented on a large scale and tested in a randomised controlled trial. This intervention proved to be effective: improvements in fasting insulin, weight reduction, dietary intake, and PA were found at the end of the intervention (12 months), and these were maintained at 18 months [24]. The aim of this article is twofold: to investigate (i) how the SLIMMER intervention was delivered and received in Dutch primary healthcare, and (ii) how this could explain intervention effectiveness. This was done by conducting a process evaluation including several process measures (recruitment, reach, dose received, acceptability, implementation integrity, and applicability).

METHODS

Study design and setting

The SLIMMER study was a randomised controlled intervention study, carried out in Apeldoorn and Doetinchem, two middle-sized cities located in the eastern part of the Netherlands. The total duration of the study was 1.5 years with an intervention period of 10 months and measurements at baseline (T0), at the end of the intervention (12 months, T1), and six months after the end of the intervention (18 months, T2). Recruitment took place between October 2011 and September 2012 in three consecutive groups for logistical reasons. The last measurements were performed in March 2014. The intervention was implemented in Dutch primary healthcare, involving general practitioners, practice nurses, dietitians, physiotherapists, and local sports clubs. Subjects were randomised to either the SLIMMER intervention or the control group. Subjects in the control group received usual health care as provided by general practitioners and practice nurses (this ranged from no consultations to one to four consultations per year) and written information on a healthy lifestyle. The study design and lifestyle intervention programme have been reported in detail elsewhere [25]. 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 SLIMMER study is registered with ClinicalTrials.gov (identifier NCT02094911).

Study population

Study subjects were recruited by general practitioners and practice nurses from their patient registration database, using either a laboratory glucose test or the Dutch Diabetes Risk Test [26]. The inclusion criteria were (i) aged between 40 and 70 years at screening; (ii) impaired fasting glucose (6.1-6.9 mmol/l) [27] or an elevated/high risk of type 2 diabetes (a Diabetes Risk Test score of ≥7 points) [26]; (iii) willing and able to participate in the study for at least 1.5 years; and (iv)) able to speak and understand the Dutch language. Exclusion criteria were, amongst others, known diabetes and any severe cardiovascular or psychiatric disease. Criteria were checked using electronic medical records. General practitioners invited eligible patients to participate in the SLIMMER study and a short non-response survey was conducted if patients were not willing to participate.

Lifestyle intervention programme

The SLIMMER intervention resembled the original SLIM intervention [4] and consisted of a 10-month combined dietary and PA lifestyle intervention, including case management and a maintenance programme. The SLIMMER intervention was suitable for application in practice, as it was not very different from the regular functioning and professional performance of Dutch general practitioners, practice nurses, dietitians, and physiotherapists [23]. Minimal training and a detailed implementation manual were provided during a two-hour SLIMMER kick-off training session for health-care professionals (HCP) involved in implementation of the intervention. This training was attended by 68% of general practices, 82% of dietitians, and all physiotherapy practices. HCP who did not attend the training session were visited individually. HCP indicated that they felt well informed and prepared to implement the intervention after this training session. The standardised SLIMMER intervention was tailored to participants' individual needs. Details of the SLIMMER lifestyle intervention programme are given in Table 6.1 and described below.

Dietary intervention

The dietary intervention consisted of individually tailored dietary advice given in five to eight individual consultations and one group session. The aim was to adopt, step by step, a sustainable healthy dietary pattern according to the Dutch dietary guidelines [28]. Furthermore, it was aimed to reduce body weight by 5–10%. Dietary advice was given by a primary health-care dietitian, trained in motivational interviewing and using

Table 6.1. Details of the SLIMMER lifestyle intervention programme according to the implementation manual.

Intervention components	Sub-components	Number	Time (min)	Details
Dietary intervention	Consultations (incl. intake)	5–8 (individual)	max. 240	- Aim: adopt sustainable healthy dietary pattern; 5–10% weight loss - 60 min intake consultation to obtain information on social and environmental factors, perform dietary assessment, and set goals - Formulate treatment plan (including goals and advice) - Inform, advise, and guide participants in adapting dietary pattern - Based on Dutch dietary guidelines [28] - Discuss topics: Dutch dietary guidelines, fats, carbohydrates and fibre, sweeteners, special occasions, and explain the relation between nutrition and glucose tolerance - Make use of motivational interviewing and positive feedback - Spouses could join - Set, evaluate, and adjust goals - Divide consultations over 10 months
	Group meeting	1 (group-based)	90	- Aim: share experiences, motivate one another, and provide information - Discuss topic: label reading - Compare products on fat and sugar content - Plan this group meeting halfway through the intervention
Physical activity (PA) intervention	Intake	1 (individual)	30	- Aim: obtain information on current PA, needs, abilities, motivation, and barriers to PA - Set goals
	Sports lessons	40–80 (group-based)	60 (per lesson)	- Aim: achieve moderate-intensity PA for at least 30 min/d at least five days per week - 2/3rd of training is aerobic exercise (60–70% of VO_2max) - 1/3rd of training is resistance exercise (55–60% of 1 repetition maximum, with 3x15 repetitions, for major muscle groups) - Offer group-based activities - Individually tailored guidance - Improve level of ability
	Advice on PA during leisure time	-	-	- Aim: encourage participants to be physically active during leisure time - Discuss PA possibilities during leisure time - If necessary: formulate an individual plan for PA during leisure time

Table 6.1 Continued.

Intervention components	Sub-components	Number	Time (min)	Details
Case management	Contact with health-care professionals and participants	2 phone calls (individual)	-	- Aim: monitor participants' progress - Facilitate contact among health-care professionals - Detect and solve problems - Motivate and encourage participants
Maintenance programme	Intermediate evaluations by dietitians and physiotherapists	3 (individual)	-	- Aim: keep participants motivated, prevent drop-out (at 3, 6, and 9 months) - Provide feedback and discuss experiences with programme - Assess individual progress (using measurements of weight, waist circumference, and body fat percentage) - Evaluate personal goals and adjust goals if necessary - Stimulate self-management
	Sports clinics	2–7 (group-based)	60 (per clinic)	- Aim: introduce participants to different types of sports and sports organisations to achieve sustainable behaviour change - During times of regular sport lessons
	Final interview dietitian / physiotherapist	2 (individual)	-	- Aim: strengthen participants' self-efficacy and motivation - One final interview with dietitian during last consultation and one final interview with physiotherapist during last sports lesson - Provide positive feedback - Discuss behaviour maintenance (goal setting and self-monitoring) - Inform about relapse prevention
	Return visit	1 (group-based)	60	- Aim: prevent relapse and motivate and support participants to maintain behaviour change - Dietitian and physiotherapist are present - Discuss behaviour maintenance during last 3 months/share experiences - Measurements of weight, waist circumference, and body fat percentage - Discuss relapse and relapse prevention - Provide tips for behaviour maintenance

positive feedback. Goals for behaviour change were set with participants at each consultation, evaluated in the next one, and adjusted if necessary.

Physical activity intervention

The PA intervention consisted of a combined aerobic and resistance exercise programme, supervised by a physiotherapist. The aim was to obtain and maintain an active lifestyle, that is, moderate-intensity PA for at least 30 min/d at least five days per week. PA recommendations were based on Dutch guidelines for PA in type 2 diabetes patients [29]. Participants had free access to group-based training sessions and were encouraged to participate for at least one hour per week (maximum of two hours per week; a total of forty to eighty lessons). In addition, physiotherapists gave individually tailored advice on how to increase PA during leisure time and goals were set.

Case management

Practice nurses were appointed as case managers of the intervention programme to enhance participant compliance and the feasibility of implementation. They referred participants to the dietitian and the physiotherapist at the start of the programme. Furthermore, they contacted dietitians, physiotherapists, and intervention participants twice during the programme to facilitate contact among HCP, detect and solve problems, and motivate and encourage participants.

Maintenance programme

A maintenance programme was added to the combined lifestyle intervention to guide participants in the process of maintaining lifestyle behaviour change in an independent and sustainable manner [30]. This maintenance programme was implemented during the last two months of the intervention period and consisted of (i) intermediate evaluations by dietitians and physiotherapists to provide feedback and stimulate self-management; (ii) sports clinics at local sports clubs to introduce participants to several sports activities (the number of sports clinics ranged between two to seven per participant); (iii) final interviews with dietitians and physiotherapists to provide positive feedback and discuss behaviour maintenance (goal setting and self-monitoring) and relapse prevention; (iv) a return visit with dietitians and physiotherapists three months after the end of the intervention to motivate and support participants in maintaining a healthy lifestyle. The fifth and final element of the maintenance programme was monitoring by practice nurses after the end of the intervention. This involved discussing

and monitoring participants' behaviour change during regular consultations at the general practice in the following months and years. This element was therefore beyond the scope of the process evaluation.

Data collection and outcomes

A process evaluation including quantitative and qualitative methods was conducted. Data from both HCP and intervention participants were collected between baseline (T0) and the end of the intervention (T1), and during the return visit three months after the end of the intervention.

Process measures

A process evaluation plan was designed based on evaluation strategies of Steckler and Linnan [31], Saunders *et al.* [32], Nutbeam [33], and Wang *et al.* [34]. Process evaluation data were collected and used to investigate how the SLIMMER intervention was delivered and received in Dutch primary health care, and to explain intervention effectiveness. The following process measures were included and are described below: recruitment, reach, dose received, acceptability, implementation integrity, applicability, and context.

Recruitment was defined as procedures used to approach and attract participants [31]. Recruitment procedures and barriers were evaluated using semi-structured telephone interviews with practice nurses, three months after the intervention started (n=19, average duration 27 min). All practice nurses involved in the implementation of the SLIMMER intervention were invited to these interviews by one of the researchers (G.D.). A semi-structured interview guide was developed, and all interviews were conducted by one of the researchers (G.D.).

Reach was defined as the proportion of the intended target audience that participated in the intervention [31]. To assess the number of subjects willing to participate, the project logbook was consulted. Data on socio-demographic characteristics of both participants and non-responders were collected with a survey according to Dutch national standards [35]. Dropouts were defined as participants who had both no T1 measurement for fasting insulin and/or BMI, and dropped out of the dietary and PA programme before the end of the intervention.

Dose received was defined as the extent to which participants actively engaged in intervention activities [31]. The following items were assessed from registration forms: the number and total minutes of dietary consultations; the number of one-hour sports lessons, case management phone calls, and sports clinics; the number of participants attending final interviews; the number of participants attending the dietary group meeting; and the number of participants attending the return visit.

Acceptability was defined as the extent to which participants and HCP were satisfied with the intervention [32]. Participants' acceptability of the intervention was assessed using evaluation forms after the dietary group meeting, sports clinics, and return visit, and questionnaires at the end of the intervention. Acceptability of the intervention by HCP was assessed using semi-structured telephone interviews. All HCP were invited by one of the researchers (G.D.) three months after starting the intervention (practice nurses, *n*=19, average duration 27 min; dietitians, *n*=11, average duration 34 min; physiotherapists, *n*=15, average duration 31 min) and at the end of the intervention (practice nurses, *n*=11, average duration 23 min; dietitians, *n*=9, average duration 28 min; physiotherapists, *n*=12, average duration 25 min). A semi-structured interview guide was developed, and all interviews were conducted by one of the researchers (G.D.). Acceptability of the intervention by participants and by HCPs was rated on a 7-point or a 10-point scale. To make results comparable, all acceptability ratings were expressed as a percentage of maximum.

Implementation integrity was defined as the extent to which the intervention was implemented as planned [31, 33]. Applicability was defined as the extent to which the intervention process could be implemented in a real-world setting [34]. These measures were assessed by semi-structured interviews and questionnaires with HCP as described above.

Context was defined as aspects of the larger physical, social, and political environment that either directly or indirectly affect intervention implementation [31]. Participant questionnaires and semi-structured interviews with HCP, as described above, were used to investigate aspects that affect intervention implementation. Our analysis regarding context aspects provided no additional information to that elicited in relation to acceptability, integrity, and applicability.

Explain intervention effectiveness

To explain intervention effectiveness, associations between process measures (dose received and acceptability) and health outcomes and lifestyle behaviours (fasting insulin, weight, dietary intake, and PA) were investigated. Dose received was defined as attending dietary consultations (in number of consultations) and as attending sports lessons (in number of lessons). Participants' acceptability of the total SLIMMER intervention (score 1–10) was ascertained in a questionnaire at the end of the intervention (T1).

To assess health outcomes, clinical assessments were performed by trained research assistants in research centres in Apeldoorn and Doetinchem. This has been described in detail elsewhere [24, 25]. In short, participants were measured at baseline (T0) and after the intervention (T1). A standard oral glucose tolerance test (glucose load 75 g) was performed by a trained nurse after at least 10 hours of fasting. Fasting serum insulin, our primary outcome [25], was determined at SHO laboratory in Velp, the Netherlands. Dietary intake was assessed by a validated FFQ [36, 37]. The FFQ were checked by trained research assistants. Adherence to the Dutch dietary guidelines was calculated with an adapted Dutch Healthy Diet Index (DHD-index) [24, 38, 39], which included eight components; namely, PA, vegetables, fruit, fibre, fish (EPA and DHA), saturated fat, *trans*-fatty acids, and alcohol. Per component, the score ranged between 0 and 10, resulting in a total score between 0 (no adherence) and 80 (complete adherence). PA was measured using the validated Short Questionnaire to Assess Health-enhancing physical activity (SQUASH), including questions on commuting activities, leisure time activities, household activities, and activities at work [40, 41]. The duration (minutes per week) of vigorous-intensity physical activities was calculated.

Data analysis

Quantitative data were analysed using the statistical software package IBM SPSS Statistics version 22 with complete cases for the item of interest (ranging from seventy-eight to 155 intervention participants per analysis). Differences between intervention and control participants and non-responders (those who were invited but not willing to participate) were tested for statistical significance with independent samples *t* tests, one-way ANOVA, and Chi-square tests. Descriptive statistics were used to analyse dose received and acceptability and applicability scores. Associations between process

measures and health outcomes and lifestyle behaviours were assessed with linear regression analysis, adjusted for baseline value, sex, and recruitment phase.

Qualitative data analyses were performed using an inductive approach [42]. Interviews with HCP were audiotaped and transcribed verbatim. All transcripts were read by two researchers (E.J.I.v.D. and G.D.) individually to identify frequently emerging themes within predefined topics and these were discussed until agreement was reached. These themes were used to create a coding scheme in the qualitative data analysis software package Atlas.ti version 7.

RESULTS

Recruitment and reach

In total, twenty-five general practices (general practitioners and practice nurses), eleven dietitians, nine physiotherapist practices (including sixteen physiotherapists), and fifteen sports clubs were involved in the implementation of the SLIMMER intervention. Selection of patients from the general practitioners registration database was perceived as difficult and time consuming by some practice nurses, but others perceived it as easy. Patients were often difficult to reach, but most practice nurses were persistent in trying to contact participants. Of the 590 subjects that were eligible and invited, 316 subjects (response rate 54%) were willing to participate. For those not willing to participate, the most important reasons for non-response were lack of time (25%), lack of interest (22%), reporting 'I already exercise enough' (11%), reporting 'It is of no importance to me' (10%), and not able due to illness or handicap (9%). No significant differences in baseline characteristics were observed between SLIMMER participants and non-responders or between the intervention and the control group (Table 6.2). On average, participants were 61 years old and most of them had a low education level, were Dutch, and had a family history of diabetes. Of all participants, 48% were overweight (BMI 25–29.9 kg/m^2) and 43% were obese (BMI ≥ 30 kg/m^2). In total, ten participants (7%) dropped out of the intervention, mostly during the first ten weeks of the intervention period.

Dose received

Table 6.3 describes the dose of the SLIMMER intervention received by intervention participants. Overall, actual dose received was in line with the planned dose according

Table 6.2 Baseline characteristics of participants (*n*=316) and non-responders (*n*=175) in the SLIMMER intervention[*].

	Intervention group (*n*=155)		**Control group (*n*=161)**		**Non-responders (*n*=175)**	
	Mean or %	**SD**	**Mean or %**	**SD**	**Mean**	**SD**
n (male/female)[†]	81/74		80/81		87/87	
Age (years)	60.7	6.4	61.0	6.5	60.9	7.0
Education (%)[‡,§]						
Low	54.0		51.0		52.0	
Middle	26.0		21.0		27.0	
High	20.0		28.0		21.0	
Perceived health (%)[‖]						
Poor/fair	21.0		21.0		10.0	
Good	68.0		70.0		74.0	
Very good/excellent	11.0		9.0		16.0	
Ethnicity (%)						
Dutch	88.0		89.0			
Western non-Dutch	9.0		8.0			
Non-Western non-Dutch	3.0		3.0			
Employment status (%)						
No paid job	54.0		52.0			
Part-time job (<32 h/week)	18.0		22.0			
Full-time job (≥32 h/week)	28.0		26.0			
Family history of diabetes (%)						
No	32.0		42.0			
First degree	49.0		45.0			
Second degree	19.0		13.0			
BMI (kg/m^2)[¶]	30.4	4.7	30.0	4.8		
Fasting insulin (pmol/l)	93.3	64.3	82.5	50.2		

BMI, Body Mass Index. [*] Data are mean and SD or %. [†] *n*=174 for non-responders. [‡] *n*=155 for intervention group, *n*=160 for control group, and *n*=96 for non-responders. [§] Education level was based on the highest level of education completed and divided in three categories: low (primary school or less, lower vocational education), middle (medium vocational education, high school), and high (higher vocational education, university). [‖] *n*=115 for non-responders. [¶] *n*=154 for intervention group and *n*=161 for control group.

to the manual. Most participants in the intervention group (84%) received five or more individual consultations with the dietitian. On average, 5.6 consultations with a total duration of 3.4 hours were attended. Participants attended on average thirty-eight sports lessons of one hour with the physiotherapist. The goal of participating at least once a week (forty or more times in total) in the PA intervention was achieved by 41% of participants. Regarding the case management component of the intervention, 76% of participants indicated that they had contact at least once with the practice nurse, with 28% of participants having contact twice. More than two-thirds of the participants

(71%) attended at least one sports clinic at a local sports club, with an average number of 2.3 clinics attended per participant. Sixty-one percent of participants attended the final interviews and received materials on maintenance, and 58% attended the return visit with the dietitian and physiotherapist, three months after the end of the intervention.

Table 6.3 Dose of the SLIMMER intervention components received by the intervention group (n=155)[*].

		Dose received	
Intervention component	**Intervention manual**	**Mean**	**SD**
Dietary intervention			
Individual consultations			
Number	5–8 (incl. intake)	5.6	1.4
Total time (hours)	Max. 4 h	3.4	0.8
Group meeting (%)	Attend 1 group meeting	67.0	
Physical activity intervention			
Number of sports lessons	At least once a week = 40 times	38.0	20.8
Case management			
Phone calls by practice nurse	Twice		
(%)[†]		24.0	
Never		48.0	
Once		28.0	
Twice			
Maintenance programme			
Number of clinics	2–7	2.3	1.9
Final interview (%)[‡]	Materials provided during last consultation with dietitian	61.0	
Return visit (%)	Attend 1 return visit	58.0	

[*] Data are mean and SD or %. [†] n=143. [‡] Based on the number of participants receiving materials on maintenance distributed during final interview

Acceptability

Overall, participants and HCP were highly satisfied with the SLIMMER intervention, with mean acceptability rating of 82 and 80, respectively (Table 6.4). Physiotherapists' scores decreased a little over time, mostly because they experienced the organisation of sports clinics during the last phase of the intervention period as not always optimal (e.g. clinics at times deviating from regular sports lesson times). HCP were convinced of the added value of the SLIMMER intervention, were positive about the communication with the project team and the multidisciplinary nature of the programme, and perceived the intensive guidance of participants as a strength. According to HCP, inclusion criteria might be sharpened, as several participants already

had a healthy lifestyle at the start of the intervention and therefore could not improve much more, resulting in low motivation in these participants. HCP felt involved in the SLIMMER intervention, although practice nurses indicated that the focus of their involvement was mostly at the beginning of the project. Data on acceptance of the specific intervention components are presented below.

Dietary intervention

In general, participants and dietitians were satisfied with the individual consultations with the dietitian, with mean score of 77 and 78, respectively (Table 6.4). Participants were also positive about the number of consultations, the guidance of the dietitian, and the tailoring of advice.

Physical activity intervention

Both participants and physiotherapists were positive about the weekly sports lessons, scoring a mean appreciation of 84 and 78, respectively (Table 6.4). Participants were satisfied with physiotherapists' guidance and appreciated the programme being tailored to their personal needs. Furthermore, participants preferred group-based sports lessons. Four HCP indicated that the fact that sports lessons were group-based was important for support and motivation.

Case management

Participants were reasonably satisfied with the contact with practice nurses (score of 66; Table 6.4). Several practice nurses indicated that, besides monitoring progress, showing their engagement with participants was an important aspect of phone calls with participants.

Maintenance programme

Overall, participants perceived final interviews with the dietitian and physiotherapist as helpful (76% and 68%, respectively; Table 6.4), and they were satisfied with the sports clinics and return visit (score of 77 and 80, respectively; Table 6.4). They appreciated guidance of HCP during the return visit, and the fact that this meeting was group-based. Physiotherapists thought sports clinics were a good way to introduce participants to several sports and to reduce barriers to joining a sports club.

Table 6.4 Acceptability (score 0–100) of the SLIMMER intervention by the intervention group (*n*=144) and healthcare professionals (*n*=44)[*].

	Participants		Professionals	
	Mean or %	**SD**	**Mean or %**	**SD**
Overall				
Total SLIMMER intervention	82.0[†]	11.0	80.0	5.0
Dietary intervention				
Individual consultations	77.0	21.0	78.0[‡]	6.0
Group meeting	80.0[§]	8.0		
Physical activity intervention				
Sports lessons	84.0[‖]	20.0	78.0[¶]	7.0
Case management				
Contact with practice nurse	66.0[‖]	21.0		
Maintenance programme				
Indicates final interview with dietitian as helpful (%)	76.0[**]			
Indicates final interview with physiotherapist as helpful (%)	68.0[**]			
Sports clinics	77.0[††]	20.0		
Return visit	80.0[††]	13.0		

[*] Data are mean and SD or percentage. [†] *n*=142. [‡] *n*=9 dietitians. [§] *n*=99. [‖] *n*=143. [¶] *n*=8. Physiotherapists. [**] *n*=78, percentage of participants that perceived the advice during the final interview as helpful. [††] *n*=118

Implementation integrity

Dietary intervention

The number of consultations, time schedule, and topics to discuss were individually tailored to participants' wishes and needs, and goals were set and evaluated during consultations. Some dietitians deviated from the Dutch dietary guidelines by advising a low-carbohydrate diet. Motivational interviewing was used by all dietitians, albeit to a varying extent, and all dietitians gave positive feedback to participants. Sometimes not all components of the group meeting were implemented because of lack of time.

Physical activity intervention

Both aerobic and resistance exercises were incorporated and implemented according to the manual. Intensity of training and type of exercise were individually tailored on the basis of test results or physiotherapists' judgement. Goals were set at the start of the PA intervention, and physiotherapists provided feedback during sports lessons. Tailored advice on PA in daily life was given. However, physiotherapists indicated that not all participants needed this stimulation. Furthermore, physiotherapists stated that they were able to give individual guidance during sports lessons, unless groups were

too large. Group cohesion was facilitated by most physiotherapists during joint exercises at the end of the sports lessons.

Case management

Referral of participants to dietitians and physiotherapists was perceived as easy and normal by most practice nurses. Most practice nurses have had contact with HCPs and participants as part of their case management role. Sometimes, emails were used instead of phone calls to save time, and in some cases case management was omitted because of lack of time. Although case management was aimed at solving problems and motivating participants, practice nurses almost never had to do this. No contact and collaboration between HCP other than the phone calls was reported.

Maintenance programme

Dietitians and physiotherapists provided feedback on participants' progress during intermediate evaluations, according to the manual. Physiotherapists indicated that the intensity of sports clinics did not always match participants' level of ability and that some sports clinics were less intensive than regular SLIMMER sports lessons. Furthermore, they suggested that it would be better to introduce sports clinics earlier in the programme to slowly familiarise participants with a variety of sports. All dietitians and physiotherapists conducted final interviews with participants and discussed maintenance of behaviour change by giving advice on self-monitoring (e.g. weigh yourself regularly) and goal setting (e.g. make an action plan). Furthermore, they informed participants about relapse prevention (e.g. contact HCP if needed). Overall, the return visit was implemented as planned according to the manual, and dietitians and physiotherapists perceived an equal distribution of tasks. However, not all suggested measurements were performed by all HCP.

Applicability

Most HCP indicated that in general the SLIMMER intervention was not very different from their regular functioning and professional performance. Some practice nurses, however, indicated deviations from their daily practice, mainly regarding a different role perception in that they referred participants to dietitians and physiotherapists for lifestyle advice instead of providing this advice themselves. Some dietitians indicated that normally they were more flexible in planning consultations. Furthermore, dietitians perceived dietary consultations as difficult if participants themselves did not feel the

need for these (compulsory) consultations or lacked motivation. All HCP indicated that it was possible to implement SLIMMER in daily practice, although they foresaw financial barriers. Furthermore, they indicated that contact between dietitians and physiotherapists was limited because their respective networks do not overlap and therefore better collaborations need to be built in order to be able to work in a multidisciplinary way.

Explain intervention effectiveness

A higher dose of sports lessons, that is, higher attendance at the PA programme, was associated with increased weight loss (p=0.001; Table 6.5). A higher dose of dietary consultations was not associated with a higher DHD-index score. Participants' acceptability of the intervention was associated with beneficial changes in fasting insulin (p=0.044) and weight (p<0.001). Neither dose received nor acceptability was associated with changes in vigorous activities.

DISCUSSION

The current process evaluation gave insight into how the SLIMMER intervention was delivered and received in Dutch primary health care and how this could explain intervention effectiveness. We were able to recruit the intended high-risk target population and the SLIMMER intervention was very well received by both participants and HCP. The intervention programme was to a large extent implemented as planned and was applicable in Dutch primary health care. Dose received and acceptability were related to health outcomes and dietary behaviour, but not to PA behaviour.

We designed and used an extensive process evaluation plan to evaluate implementation and provide insight into the effectiveness of the SLIMMER intervention. Nowadays, the value of process evaluation within trials is recognised, and recently the Medical Research Council developed guidance on process evaluation of public health interventions [17]. Several studies have investigated intervention implementation [43-48]; however, results are difficult to compare because a systematic approach to process evaluation has not been used and consequently a wide range of process indicators and methods are reported in publications.

Table 6.5. Associations between process indicators (dose received and acceptability) and intervention effectiveness of the SLIMMER intervention (*n*=144)[*,†].

	Δ fasting insulin (pmol/l) T1-T0			Δ weight (kg) T1-T0			Δ DHD-index T1-T0			Δ vigorous activities (min/week) T1-T0		
	β	SE	*p*-value	β	SE	*p*-value	β	SE	*p*-value	β	SE	*p*-value
Dietary consultations (number)	-3.36	2.38	0.159	-0.48	0.38	0.207	0.85	0.52	0.102	26.54	27.50	0.336
Sports lessons (number)	-0.23	0.13	0.072	-0.07	0.02	0.001	0.02	0.03	0.527	0.73	1.61	0.651
Participant acceptability (score 1–10)	-4.51	2.21	0.044	-1.40	0.36	0.000	0.60	0.53	0.257	32.60	28.68	0.258

Δ, change; T1, end of the intervention; T0, baseline; DHD-index, Dutch Healthy Diet Index. [*] Associations are adjusted for baseline value, sex, and recruitment phase. [†] There are zero to four missing values per analysis because of incomplete data.

Recruitment of participants was perceived as difficult and time consuming by some practice nurses. Issues related mainly to improper registration of blood glucose values in the patient registration database and to technical problems retrieving information from this database. However, the response rate (54%) was comparable with the SLIMMER pilot study (57%) [23].

Participants' acceptability was high with mean acceptability scores around 80 on a scale of 0-100. Participants appeared to be least satisfied with the practice nurse. This could be explained by the minor role of the practice nurse in the intervention programme, making it more difficult for participants to remember or recognise this.

The high implementation integrity might be due to the careful and long initial period of translating [22] and pilot-testing the SLIMMER intervention [23] and the fact that we built on existing structures in primary health care. We believe that implementation becomes more successful if capacity is built and networks are formed among local partner organisations.

To ensure intervention effectiveness, it is essential to include the intervention components most strongly associated with effectiveness [18]. Our regression analysis showed that higher intervention intensity (dose received) was associated with weight loss, but not with change in dietary and PA behaviour. This is in line with results of several systematic reviews [18-20, 49], although other reviews found no associations with intervention intensity [21, 50]. As no clear evidence exists for a particular minimum threshold for intervention intensity [18], more research is needed to determine the optimum. Explanations for not finding an association between intervention intensity and dietary behaviour might include the fact that adherence to the Dutch dietary guidelines was already high at baseline or that there was not much variation in the number of consultations between participants. Not finding an association between intervention intensity and PA behaviour might be explained by the fact that vigorous activities, as an outcome indicator, does not cover all physical activities. Furthermore, participants who perform vigorous activities during the sports lessons might compensate this in their leisure time. In addition, our analysis showed that higher participant satisfaction was associated with increased weight loss. Appreciation of the programme might be important for intervention compliance. This in turn leads to a

higher intervention intensity, which we have shown was associated with better outcomes.

The intervention effectiveness might also have been facilitated by other components incorporated in the SLIMMER intervention, as suggested Greaves *et al.*'s [18] review: targeting both diet and PA, using behaviour change techniques (goal setting, self-monitoring, relapse prevention), and focusing on behaviour maintenance. Furthermore, the high level of individual tailoring of the dietary and PA programme, which was appreciated by participants, might have contributed to effectiveness [20]. Also, deploying specialists – dietitians and physiotherapists – rather than generalists for lifestyle counselling may have contributed to intervention effectiveness. A systematic review by van Dillen and Hiddink [51] found general practitioners and practice nurses, who are considered generalists, able to provide lifestyle counselling in primary health care. However, they provided rather general lifestyle advices and experienced lack of time and competency issues. Therefore, cooperation with specialists was needed and recommended [51]. Another systematic review suggested that a wide range of staff could deliver effective interventions [18]. Therefore, a multidisciplinary approach with both specialists and generalists, such as in our study, might be the best way to utilise expertise fully, thereby contributing to intervention effectiveness.

A limitation of the study might be the risk of recall bias by HCP providing data on implementation of the intervention. Furthermore, interviews were conducted by the researcher who was also the contact person for HCP during the study. However, HCP were not hesitant to criticise the intervention and to mention points for improvement. Our study has several strengths. First, we used an extensive process evaluation plan, including several process indicators measured both quantitatively and qualitatively. This provided a profound understanding of the delivery of the intervention and gave insight into possible aspects that might explain intervention effectiveness. Second, triangulation is considered a strength of our study. By the combination of multiple methods (registration forms, questionnaires, semi-structured interviews), incorporating both participants and HCP, and by two researchers analysing the data independently, the credibility and the validity of our results have been increased. Third, our study had a high response rate from participants and professionals who provided input for the process evaluation: 50–100% of participants provided data dependent on the item of interest and almost all involved HCP (90%) participated in interviews.

CONCLUSIONS

In summary, the present study has shown that it is feasible to implement a diabetes prevention intervention in Dutch primary health care. Higher dose received and participant acceptability were associated with improved health outcomes and dietary behaviour, but not with PA behaviour. Furthermore, targeting both diet and PA, using behaviour change techniques, focusing on behaviour maintenance, tailoring the intervention and using a multidisciplinary approach might have facilitated effectiveness. Using an extensive process evaluation plan to gain insight into how an intervention is delivered and received is a valuable way of identifying intervention components that contribute to implementation integrity and effective prevention of type 2 diabetes in primary health care.

Trial registration number: ClinicalTrials.gov NCT02094911

Keywords: Process evaluation, Lifestyle intervention, Diabetes, Prevention, Primary health care, Randomised controlled trial

Abbreviations

ANOVA: Analysis of Variance; DHD-index: Dutch Healthy Diet index; FFQ: food frequency questionnaire; HCP: healthcare professionals; PA: physical activity; SLIMMER: SLIM iMplementation experience Region Noord- en Oost-Gelderland; SQUASH: Short Questionnaire to Assess Health-enhancing physical activity; WU: Wageningen University.

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Conflict of interest

None.

Authorship

E.J.I.v.D. and G.D. contributed equally to the contents of the manuscript. G.D. designed the process evaluation study. G.D. and E.J.I.vD collected and analysed the data and drafted the manuscript. S.C.J. and J.t.B. participated in the study design and

implementation in public health and primary care, and helped to draft the manuscript. J.M.H., J.N.L., A.H.-N., G.J.H. and E.J.M.F. made major revisions to the manuscript. All authors contributed to the development of the SLIMMER intervention, and read and approved the final manuscript.

Ethics of human subject participation

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the Wageningen University Medical Ethics Committee. Written informed consent was obtained from all subjects.

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CHAPTER 7

General discussion

MAIN FINDINGS

The overall objectives of the current thesis were to gain insight in translating an efficacious nutrition and exercise intervention for community-dwelling older adults to practice, and to evaluate effectiveness and feasibility of implementing the adapted combined lifestyle intervention in practice. Chapters 2 to 5 describe the steps we took to adapt an existing, efficacious intervention for older adults to practice. First, adaptations were made to the clinical resistance exercise and protein supplementation intervention using input from researchers, healthcare professionals, and older adults (**Chapter 2**). Most important adaptations concerned the dietary intervention, organisation of the resistance exercise training sessions, and the development of materials and training for healthcare professionals who will implement the intervention. The small-scale 12-week pilot study showed that the adapted intervention was perceived feasible to implement and was generally accepted by professionals and participants. However, further refinements to the intervention and procedures were made using insights of the pilot study, for example in recruitment procedures. Subsequently, a multicentre randomised controlled intervention study was designed, with the objective to study effectiveness, cost-effectiveness, and the implementation process of the adapted intervention in practice (**Chapter 3**). We found that the intensive support intervention (week 1-12) implemented in a real-life setting was effective in improving physical functioning, muscle strength, and lean body mass in the intervention group when compared to a usual care control group (**Chapter 4**), although effects were smaller than in the clinical setting. Our moderate support intervention (week 13-24) was successful in preventing these effects from dropping back to baseline scores, but future attention is warranted to increase compliance and to optimize implementation of this intervention. A process evaluation provided us with insight in intervention implementation in the different municipalities (**Chapter 5**). Both the intensive support intervention and the moderate support intervention were acceptable to participants and professionals, and fitted within professionals' working procedures. Important intervention aspects that may have contributed to intervention success include intensive supervision by healthcare professionals, tailoring of the intervention to individual participants, the social aspect, multidisciplinary collaboration, and fit within the real-life setting. The SLIMMER diabetes prevention lifestyle intervention (**Chapter 6)** was also adapted from an efficacious intervention to practice using a similar trajectory. Process evaluation results show that this intervention was also well

received by participants and primary-care professionals, and was to a large extent implemented as planned. For this intervention it was shown that implementation was related to intervention effectiveness.

MOVING RESEARCH TO PRACTICE

This thesis described the process of moving an efficacious intervention for older adults to practice. In other words, getting research discoveries implemented by healthcare professionals and integrated in healthcare practice [1, 2]. The intervention ProMuscle in Practice focuses on counteracting the age-related decline in muscle mass, strength, and physical function, to preserve mobility and independence. In agreement with comparable research trajectories of moving efficacy research to effectiveness research [2-4], the time between the initial efficacy study ProMuscle (2009) and implementation in practice following the effectiveness study (2019) is approximately 10 years. This time was needed as we followed a trajectory including three steps addressing 1) intervention adaptation and feasibility, 2) intervention effectiveness, and 3) the implementation process.

Adaptation

As a first step, the efficacious intervention had to be adapted to make it appropriate for implementation in the real-life context [5, 6]. Although adaptations might happen spontaneously when interventions are moved to a different setting [7], a systematic adaptation approach like Intervention Mapping (IM) [8] gives insight in this adaptation process and increases the chance of future implementation success. By reporting the separate adaptation steps and rationale for decisions made, we explained how the intervention reached its current form. This information is relevant for research on other comparable interventions, and for further intervention improvement of the adapted intervention. A strength of the IM approach used in Chapter 2 is the involvement of stakeholders in the adaptation process. This involvement increases the likelihood that the adapted intervention fits in the new setting, while it retains the intervention components that contributed to intervention efficacy. In each step we compared the original efficacious intervention with the new real-life setting, and adjusted the intervention when necessary, using input from researchers, healthcare professionals, and the target group. As a final adaptation step we tested feasibility of the intervention in practice in a pilot study [9, 10]. This pilot study (Chapter 2) provided valuable insights

in the intervention aspects that required further adaptation to improve fit and acceptability, before moving to assessing intervention effectiveness.

During IM adaptation, behavioural determinants of health behaviours of the older adults were identified (e.g. attitude, self-efficacy). Subsequently, behaviour change techniques (BCT) to change these determinants were identified and incorporated in the intervention, such as tailoring an intervention, providing feedback, or setting goals [11]. IM provided us with a structure to retrospectively specify the underlying intervention theory, which was necessary as the original efficacious intervention was not designed on the level of behaviour change. This intervention theory, or proposed mechanism of action of an intervention [12], hypothesizes how the intervention activities produce change in effectiveness outcomes. We summarized the intervention theory in an intervention logic model (Chapter 3), which links inputs and intervention activities with desired intervention outcomes, and guided our intervention evaluation [9].

Effectiveness

In the randomised controlled multicentre intervention study we assessed intervention effectiveness when implemented in practice (Chapter 4). We observed positive intervention effects on dietary protein intake, and on physical functioning, muscle strength, and lean body mass. However, our effects were smaller than the effects seen in the efficacy study [13]. Smaller effects in real-life settings as compared to efficacy studies can be expected, as the effects of the intervention in practice can be influenced by factors related to the implementation, the study population, and the context [14]. Nevertheless, the observed improvements in muscle related outcomes are substantial, considering a general decline in muscle strength and lean body mass with aging [15, 16]. More research is warranted to investigate whether these improvements retain or even increase when the resistance exercise training and protein-rich diet are continued over time.

The intervention aim of increasing protein intake during the main meals was achieved in the effectiveness study. As compared to the efficacy intervention, the diet intervention was highly adapted in ProMuscle in Practice. Instead of providing participants with one type of protein supplement twice a day, a dietitian provided dietary advice to incorporate regular protein-rich foods in the dietary pattern. The foods used in our intervention belonged to product groups often consumed by Dutch

older adults [17]. Matching the advice to the participants' dietary pattern and dietary preferences is important to achieve behaviour change, and we expected that ordinary protein-rich foods would be suitable to incorporate in the participants' diet. In Chapter 4 we observed comparable increases in dietary protein intake using ordinary foods as compared to the efficacy study which used protein supplements [13], confirming our expectation.

Implementation process

In Chapter 4 we concluded that the ProMuscle in Practice intervention was still effective when implemented in practice, which indicates that the adaptation and the implementation had been successful. The SLIMMER intervention also retained effectiveness when implemented in practice [18]. The process evaluations from chapter 5 and 6 provide valuable insights into key elements that most likely contributed to intervention effectiveness. Both the ProMuscle in Practice intervention and the SLIMMER intervention obtained high acceptability and dose received, and the healthcare professionals generally implemented the intervention according to the guidelines. Healthcare professionals reported some deviations from the manual, such as less case-management phone calls by the practice nurse, not discussing all aspects within the dietary counselling, and difficulty with providing individual guidance in large training groups. Furthermore, not all participants joined the maintenance interventions, and the maintenance program exercise sessions were of lower training intensity as compared to the first intervention periods. Although some deviations were made because of practical aspects, many deviations happened to tailor the intervention to the participants or to the setting. Based on our research, we propose several essential elements for combined lifestyle interventions that can contribute to intervention success. The main promising elements identified in this thesis relate to supervision by healthcare professionals, tailoring, social support, focus on long-term behaviour change, multidisciplinary collaboration (between exercise, nutrition and primary care professionals), and intervention fit within the real-life setting. The importance of several of these elements for intervention acceptability or effectiveness is confirmed by other studies. Research revealed that face-to-face delivery and an individualised approach are important implementation factors for dietary and physical activity programs for older adults [19-23]. In addition, social support and social interaction are widely supported facilitators for lifestyle interventions [22, 24, 25], and older adults show a preference for exercising in groups with people of their age [26]. Focusing both on

nutrition and exercise within a lifestyle intervention [27, 28], and involvement of multidisciplinary professionals are promising intervention elements [29]. The chances of individuals continuing with an exercise program increase when the intervention includes behaviour change techniques, such as improving self-efficacy, regular feedback on performance, and positive reinforcement [30]. The link between individual intervention components and intervention outcomes is not clear [31], as most interventions, including the interventions in this thesis, included all or a combination of these aspects. We suggest that these promising elements should be considered in future lifestyle interventions in practice with older adults.

Three topics require attention for future implementation of combined lifestyle interventions in practice: the balance between fidelity and fit, the intervention intensity and support level, and long term intervention success.

Balance between fidelity and fit

A topic of debate in the field of implementation science is how to balance fidelity to intervention description and adapting interventions to fit the local setting [32] or individuals. We concluded in Chapters 5 and 6 that the interventions were implemented with generally high fidelity, although there were indications that adjusting the intervention to individuals or the context was needed. Related to this, the used definition of intervention fidelity may be reconsidered. Fidelity can be seen as implementing the intervention completely as planned in the protocol [33], leaving little room for flexibility. However, in real-life settings slight deviations from the protocol are common. Therefore it is suggested that the function of intervention elements should be standardised and described in the protocols, while the form in which these elements are delivered can vary in different contexts [34]. In other words, the underlying behaviour change method should be implemented, but the form in which healthcare professionals implement this method does not have to be standardised over all intervention settings. In both process evaluations described in this thesis, we noted that healthcare professionals generally mentioned to have implemented the prescribed behaviour change techniques (e.g. tailoring, goal setting), but the way in which they did so probably varied between professionals, individual participants, and settings. Implementing interventions in varied real-life settings does require some degree of flexibility [4], but there is limited evidence to guide implementers into how to be flexible within implementation [35]. Some scholars suggest to already incorporate

potential adaptation in the intervention design, to facilitate both program fit and fidelity [32]. For example, the SLIMMER manuals already describe that the number and content of dietitian consultations can be tailored according to participants' needs. We postulate that interventions should be clearly described for healthcare professionals in terms of behaviour change techniques that should be used, but at the same time these descriptions should indicate limited aspects that are open for adaptation to context or to participants. Further research is however necessary to provide insight into possible adaptations to interventions without negatively impacting effectiveness.

Intervention intensity and support level

Intervention intensity and the level of support within lifestyle interventions are important factors from a public health and economic perspective, as they relate to intervention costs. Process evaluation results from ProMuscle in Practice and SLIMMER show that professional and intensive supervision, and tailoring of the intervention is appreciated by participants. For ProMuscle in Practice, the intensive support intervention was most intensive, with 2-3 trainers present per small exercise training group, and dietitians providing individual consultations. This intensive supervision allowed the healthcare professionals to tailor the intervention to the participants' needs and situation. A prerequisite for this is that healthcare professionals should have the required competences needed to implement the intervention. Several reviews show a dose-response relation between intervention intensity (dose received) and effectiveness [21, 27], but it remains difficult to specify the minimum dose required to achieve behaviour change or change in health outcomes. In SLIMMER, a higher attendance of sports lessons was associated with increased weight loss, supporting the proposed dose-response relation. Most combined exercise and protein supplementation interventions for community-dwelling older adults included two (e.g. [13, 36, 37]) or three (e.g. [38-42]) training sessions a week, and achieved comparable attendance rates as our effectiveness study. Even more, in frail older adults, exercise training less than twice a week was not enough to achieve functional improvement [43]. Two to three training sessions a week have been associated with larger improvements in strength and muscle hypertrophy in older adults as compared to one training session per week [44]. It should be considered, however, that a more intensive intervention, with specialist professionals and high contact frequency, will also be more expensive. In addition, randomly removing intervention parts to reduce the intervention costs almost certainly impedes intervention effectiveness [35]. More

research is thus needed to identify a minimal intervention dose still resulting in intervention effectiveness. Regardless, we argue that lifestyle interventions for older adults should be implemented by competent health care professionals, with frequent contact moments.

Long-term intervention success

Finally, the overall aim of lifestyle interventions is achieving long-term success, both related to behaviour change of participants as well as to intervention sustainability. With regard to the first aspect, interventions need to incorporate components focussing on the maintenance of behaviour. Both the ProMuscle in Practice and the SLIMMER intervention included a follow-up period aimed at establishing maintenance of behaviour change. For SLIMMER, the maintenance period was developed using an Intervention Mapping approach, including a theory base for the intervention content and activities [45]. Whereas for ProMuscle in Practice, the moderate support intervention was based on facilities and networks within the community, and on insights from the Municipal health service. For both interventions we signal that not all participants join the maintenance program, as described in Chapters 5 and 6. In SLIMMER 71% of participants joined at least one sports clinic and 58% attended the return visit with the healthcare professionals. For ProMuscle in Practice, 56% of participants joined at least one of the exercise sessions in the moderate support intervention, and 60% attended the nutrition course. We identified several possible reasons for participants to discontinue with the intervention, including practical aspects, insufficient information, or health issues. Studies that have measured behaviour maintenance show that it is possible to achieve maintenance to some extent [46, 47], although these findings might be positively biased as follow-up measures will most likely include the healthy participants [46]. The extent to which behaviour maintenance is achieved will almost certainly impact long-term intervention effectiveness on health outcomes. After structured physical exercise intervention cessation, participants do not maintain the increased physical activity levels, and participants should be supported to continue on the long-term [48]. Research has shown that without continuous support after exercise interventions effectiveness drops [30, 47, 49].

Changing dietary behaviours and establishing new dietary habits also requires sufficient attention, as there are multiple aspects that influence older adults' dietary

habits [50]. Habitual protein intake at baseline within the ProMuscle in Practice effectiveness trial was on average above the RDA of 0.8 gram/kilogram-bodyweight/day. In the efficacy study, pilot study, and effectiveness study protein intake increased at breakfast and lunch, the meals in which community-dwelling older adults usually consume the lowest amount of protein [17, 51]. The intensive support intervention in practice used dietary counselling and regular protein-rich foods, and was equally able to increase dietary protein intakes as was the efficacy intervention that used protein supplements only. However, we observed a small decrease in protein intake after the moderate support intervention, suggesting that attention is needed to maintaining a high protein intake over time, without intensive supervision and delivery of protein-rich foods. Continuous focus on providing older adults with useful tools to guide food selection or with practical advice on suitable food products may be helpful [52], and therefore attempts should be made to increase participation rates for the moderate support intervention nutrition course.

All in all, long-term behaviour maintenance is possible, but is often not measured [46], and support is needed to accomplish behaviour maintenance. Analysis of data collected in ProMuscle in Practice at week 36 and 52 (3 and 6 months after the intervention, respectively) can provide insight into maintenance of effectiveness and behaviour after intervention cessation. When aiming to increase participation rates for the maintenance interventions, we expect that only offering intervention sessions is not sufficient. There should be attention for stimulating and facilitating participants to continue with the program over time. For example, facilitation can include embedding the intervention within communities so the social connections created in the intervention can be sustained and there is no need for transition to other facilities [53].

In addition, intervention sustainability should be a point of attention from the start of intervention planning [54]. However, in many projects it is common practice to focus on program effectiveness and feasibility first, before thinking about planning sustainability. Sustainability refers to intervention continuation and long-term adoption of the intervention by the involved organisations [55]. Key elements that are important for sustainability of public health interventions include planning of sustainability at an early stage of implementation, seeking commitment and engagement, building capacity within organisations and communities, and ensuring funding opportunities [54]. For both interventions described in this thesis, commitment

and engagement from several local stakeholders was ensured during the study. At the moment of writing, SLIMMER is still being implemented by local organizations. An important factor contributing to sustainability of SLIMMER is the coordinating role of the municipality health service, as this organisation continued to coordinate the intervention after the research finished, and has strong connections to local policy makers. After the ProMuscle in Practice study finished, several involved organisations have incorporated the intervention within their organisation, and are attracting more participants to join. These continued interventions after the studies described in this thesis still elicit evaluation data and information on adaptation, two of the key elements for sustainability [54]. Another aspect related to sustainability is ensuring that structural finance, and governmental funding can support preventive interventions. From a public health perspective, municipalities can play a role in providing facilities needed to implement the intervention, such as financial support for subgroups of municipality residents, or employment of neighbourhood sports coaches. When the intervention is positioned in primary care, the municipalities may provide financial support from the Social Support Act. Or when an intervention will be implemented more as indicated prevention, as is done with SLIMMER, the intervention can be refunded from the Healthcare Insurance Act. The target group and intervention aim will define where the intervention can be positioned and what financing opportunities are relevant.

METHODOLOGICAL CONSIDERATIONS

Study design and measurements

A major strength of the trajectory used in this thesis is the continuous building on previous research, including optimizing the research procedures and the intervention. The design of the pilot study (Chapter 2) was partly informed by the efficacy study that this project built on, such as the study duration, outcomes to assess, and screening methods. The pilot study was a valuable opportunity to test evaluation methods and procedures, and to optimize these before conducting the multicentre effectiveness study. Firstly, we obtained insight in relevant evaluation questions within the process evaluation. We used the obtained knowledge to optimize interview guides and registration forms for professionals. In addition, we were able to further sharpen the questionnaires for participants based on topics that were perceived important. The measures used in the process evaluation are mostly self-developed to match the intervention content and selected process indicators, which makes comparison with

other studies difficult. In both process evaluations described in this thesis we used a combination of quantitative and qualitative data from participants and healthcare professionals, to increase credibility of our findings. Secondly, within the pilot study we could assess whether the used effectiveness measures were suitable for this intervention and this target group. For example, following the pilot study, we decided to further standardize the measurement procedures, and to change the questionnaire to measure activities of daily living. A strength of the effectiveness study was that we used validated and frequently used methods to assess intervention effectiveness, allowing comparison with other studies.

The intervention design of the ProMuscle in Practice study (Chapter 3) provided insight in effectiveness, implementation, and cost-effectiveness, which is needed before the step to routine uptake can be taken. We employed a study design in which the primary aim was to assess intervention effectiveness, while additionally data were collected on implementation in the real-world setting. Another term for such a trial is an 'effectiveness-implementation hybrid design' [56]. This design makes the study more valuable in terms of public health impact than standard effectiveness-only trials [56], and can decrease the time between efficacy research and uptake in routine healthcare [4, 57]. In addition, the use of a multicentre design further contributed to external validity of the research, as we obtained insight in implementation in a variety of settings.

Diet intervention

The dietary advice was aimed at increasing protein intake during the three main meals and involved mainly animal protein, such as dairy products. We based our aim on evidence from the efficacy study intervention as well as on recommendations to ingest 25-30 grams of protein per meal to overcome the anabolic threshold [58-63]. However, research on most optimal protein distribution during the day is inconclusive, as there is evidence for benefits of an evenly distributed (spread) protein intake over the day [64-67] as well as evidence for benefits of a more skewed (pulse) protein intake [68, 69]. With regard to protein-source, animal-source protein is considered high quality, and contain high proportions of essential amino acids [70]. Proteins that are rich in leucine, such as whey proteins or dairy, are superior to other protein sources in stimulating muscle protein synthesis [71]. It may be interesting to assess whether other

protein distribution patterns or protein sources result in similar or even better feasibility, acceptability, and intervention effectiveness.

Target population

The original ProMuscle intervention included physically pre-frail and frail older adults [13], whereas both the pilot study (Chapter 2) and the practice study (Chapter 3-5) included non-frail, pre-frail and frail older adults. Thus, these real-life studies included a different target group, which in general functioned better at baseline compared to the efficacy study population. In our multicentre effectiveness study we aimed to include a broad population, as interventions in a real-life setting should ideally be made available for a broad audience [4]. However, recruitment procedures during evaluation studies do not always match real-life procedures. For the SLIMMER study, the target population was clearly defined and could easily be identified using a laboratory glucose test or a Dutch Diabetes Risk test; tests that are common in the general practitioner practice. After the SLIMMER study, the target population was extended, also making the intervention available for adults with obesity. For the ProMuscle in Practice study, the Fried frailty screening [72] and some additional questions were used by researchers to identify eligible participants. These screening tools are not commonly used in primary care, and it can thus be debated whether these screening procedures are applicable for future intervention implementation. In addition, as with most randomised controlled trials, selection bias may have occurred, as both studies described in this thesis had a long duration and were quite time-consuming for participants. By including highly motivated participants the adherence and acceptability may be higher than they will be in real-life implementation.

For future implementation in practice, specifying the target population is a major issue. As the Dutch Physical Activity Guidelines recommend muscle strengthening activities for all adults aged ≥ 55 years, the ProMuscle in Practice intervention may be suitable for a broad target population of older adults. In this thesis we showed feasibility and effectiveness of the ProMuscle in Practice intervention in a broad target group of community-dwelling older adults, and additional subgroup analysis may provide insight in effectiveness in specific subgroups. For future dissemination of the intervention some differentiation in subgroups is warranted, as characteristics of the target group have implications for intervention implementation, effectiveness, and costs. For example, frail older adults may need a personalised strength training

program [73], and intensive supervision especially at the start to improve training progression [43], whereas more vital individuals might be able to move to a regular exercise provider sooner and might be open to using e-health tools to monitor behaviour. Potentially, for a more frail target group the intervention would fit better within primary care settings, whereas for a non-frail population the intervention could be positioned within public health. Positioning of the intervention also has consequences for potential reimbursement of intervention costs, as for example primary care falls within the Social Care Act. A way to make the intervention suitable for different subgroups is to further develop the intervention into specific 'modules'. These modules can also include different routes of referring older adults to the intervention, for example practice nurses referring the more frail individuals, or welfare workers informing older adults about the intervention. These modules would preferably be developed in collaboration with relevant stakeholders from practice, and they should still include the key elements of the intervention, but then adjusted to the specific target population.

IMPLICATIONS FOR PUBLIC HEALTH AND POLICY

This research shows that the multidisciplinary ProMuscle in Practice lifestyle intervention is an effective and feasible way of targeting muscle related outcomes of community-dwelling older adults. The need for preventive programs in practice is evident, considering that the Dutch government aims to stimulate older adults to live in their own home independently as long as possible , which requires good health and functioning, and considering that sarcopenia increases health care expenses [74]. There are several implications of this research for public health, and for further dissemination of the intervention. The main important aspects relate to creating awareness, coordination, referral of the target group, multidisciplinary collaboration, and intervention availability.

Create awareness amongst older adults

One important prerequisite for further intervention dissemination to be successful is awareness of the relevance of combining exercise and dietary protein intake amongst older adults. In Chapter 5 we observed that the reason to participate in this intervention was not always their own health or personal interest, while these reasons are important for the intervention to succeed in practice. Moreover, to be able to reach a broad target

group for the intervention, all older adults should be aware of the importance to engage in resistance exercise and to optimize dietary protein intake. Increasing the awareness on the health benefits of exercise may be a relevant strategy to improve participation in exercise programs [75]. Although there are physical activity guidelines for older adults (55+) and dietary guidelines [76, 77], there is currently no combined physical activity and dietary guideline that is broadly communicated to the general public. Combining these guidelines and clearly communicating them to the relevant target groups could be a first step. Professionals from primary care (i.e. general practitioners, practice nurses, or paramedics) and from public health (i.e. consultants for older adults, neighbourhood sport coaches, or welfare workers) have an important role in informing older adults about the importance of resistance exercise and sufficient dietary protein intake. This requires that also professionals are sufficiently aware of the importance of these aspects for healthy aging.

Coordination and local network

It is important to identify a coordinating party that directs further implementation of the intervention in practice. The studies described in Chapters 5 and 6 were implemented in a Dutch healthcare practice, involving a variety of organisations in different municipalities. The coordination of the ProMuscle in Practice intensive support intervention was done by the researchers, whereas the coordination of the moderate support intervention and of the SLIMMER intervention were done by the municipal health service. The municipal health service is an example of an organisation that can take on this coordinating role also in the future, as they often coordinate projects, bring organisations together, or serve as an advisor [78]. A coordinating party has several tasks, including being the owner of the intervention, guiding and monitoring evaluation and implementation, taking the lead in embedding the intervention in the local context, and securing intervention quality. Furthermore, scaling-up of the intervention can elicit further adaptations to the intervention for it to fit in the local contexts, and the coordinator can take the lead in monitoring these adaptations and the consequences for effectiveness. In addition, it is important to connect to local initiatives or existing networks in the implementation efforts. Other organisations that could be involved in further dissemination, for example in a steering group, are municipalities or regional supporting organisations for primary care (ROS), as they also have extensive local networks. By involving the municipal health service and local authorities, the collaboration between primary health care and public health

is strengthened. Overall, involving relevant organisations within the local network can strengthen intervention dissemination and continuous implementation.

Referral

In both ProMuscle in Practice as well as in SLIMMER, the general practitioner or practice nurse had a role in recruitment or screening. General practitioners, and more specifically practice nurses, come in contact with (older) adults that could benefit from these lifestyle intervention. In the Netherlands, referral to local exercise facilities by general practitioners is low. This is mainly due to restricted knowledge on where to refer to, even though general practitioners have a positive attitude towards referring [79]. Involvement of neighbourhood sports coaches or local coordinators may improve referral rates. It is, however, important that persons are referred to opportunities or facilities focussing both on exercise and nutrition, instead of only one of these aspects. Building on results of Chapter 6, practice nurses are a suitable professional group to be a case manager, identifying potential participants, keeping contact with participants, and following up on referral. A review confirmed the importance of a case manager during a community-based intervention to prevent disability in activities of daily living in community-dwelling older adults [29]. When an intervention is embedded within public health, other professionals might be involved in referral, such as consultants of older adults or welfare workers. As discussed earlier, for referral it is important that the target group is clearly defined, and that identifying potential participants can be done easily using simple tools.

Multidisciplinary collaboration

Results in this thesis support the claim that lifestyle interventions for older adults should be implemented by skilled healthcare professionals. Both Chapter 5 and Chapter 6 support the necessity of having professionals implement the interventions for these target groups, as this contributes to acceptability and tailoring of the interventions. Implementation manuals for both interventions clearly describe competencies needed to successfully implement the intervention. Our process evaluations indicate that multidisciplinary collaboration is key, as nutrition and exercise are two intertwined elements within lifestyle interventions that strengthen each other. In the Netherlands, the focus for preventive actions is on an integral approach, and on making connections between relevant stakeholders [80]. Multidisciplinary collaboration is emphasised for paramedics, but in practice this is not always done. During the

intensive support intervention in Chapter 5, physiotherapists and dietitians were generally satisfied with the multidisciplinary collaboration, which was facilitated by the fact that they were working within the same organisation. However, in the moderate support intervention and in SLIMMER, there was less or no collaboration between exercise and diet professionals, and it was recommended that better collaboration should be ensured. Even more, the collaboration should ideally be extended to other involved professionals from primary care or public health. Successful coordinated action between organisations requires effort to achieve involvement, communication, and collaboration [81]. A coordinator could stimulate the collaboration between different professionals to increase cohesion within these combined lifestyle interventions, e.g. by facilitating joint peer discussions or formation of a working group.

Intervention registration in database

Before broader dissemination of the intervention, the intervention manuals should be made suitable for further use in practice, outlining the essential intervention elements, and potentially differentiating between different subgroups. Submitting interventions in intervention databases will facilitate further dissemination. Currently, SLIMMER is already included in the Dutch Centre of Healthy Living (RIVM) database, and ProMuscle in Practice should also be submitted to this database. Featuring in the intervention database will make the intervention visible and available for interested organisations, and provides opportunities for strengthening the evidence of the intervention.

FUTURE RESEARCH

Following the research described in this thesis, there are still some questions left unanswered. These issues relate to achieving more insight in intervention optimization, optimizing long-term adherence to the intervention, further testing of the intervention theory, and optimizing implementation.

Intervention optimization

The ProMuscle in Practice intervention as tested in Chapters 4 and 5 already went through several adaptation steps as described in Chapter 2. The effectiveness study elicited insight in key intervention elements, but also provided insight in points of improvement. The moderate support intervention was not evaluated before, and can be optimized using insights from the practice study. Further research should be

conducted to assess whether and how these points of improvement can be taken into account for further intervention optimization. For example, it can be studied how the content of the exercise trainings can be optimized, as it was clear that sufficient variation in exercises is important for participants. For ProMuscle in Practice, organisations have shown interest to use the intervention in different settings, i.e. in rehabilitation or in long-term care settings, or in different populations, i.e. in migrants. Process evaluations can provide insight in conditions or adaptations needed to successfully implement the intervention and achieve the intervention aims [33]. By guiding and monitoring future implementation efforts, more evidence can be gathered to potentially support the effectiveness and to support making the intervention available for more practice organisations.

Optimizing long-term adherence

Further research is needed to investigate how we can ensure that participants continue with the intervention over time. As described earlier, in Chapters 5 and 6 we observed that not all participants continued with the maintenance programs. It is relevant to further explore the underlying reasons for this, as well as what intervention strategies could be employed to improve long-term adherence. Although research has identified several intervention elements that are positively associated to adherence of lifestyle interventions, it should be investigated to what extent these elements are applicable to the target population of these interventions.

Further testing of intervention theory

In the process evaluation of ProMuscle in Practice we identified several intervention components that are expected to influence intervention success. However, we cannot yet conclude whether the intervention had effect on the outcomes through the pathway as depicted in the intervention logic model in Chapter 3. Further analysis is needed to test whether the intervention had effect on health outcomes through changing the proposed behavioural determinants that would impact the health behaviours. Data were collected on behavioural determinants, such as attitude, self-efficacy and intention. For the SLIMMER intervention evidence was established on how changes in behavioural determinants mediated change in health behaviours [82]. Mediation analysis on ProMuscle in Practice data could provide insight in how the intervention produced change in the outcomes, and through that provide more insight in the underlying mechanism of the intervention.

Optimizing implementation

Lastly, there are several issues to study for future intervention dissemination. Examples of these issues are exploring who will be a coordinating party, who will be the intervention owner, and what type of structure or work group should be created to manage further intervention dissemination. In addition, more research may provide insight in how to better fit the intervention with a variety of implementers. The current intervention adaptation process did take into account input from healthcare professionals, but we did not thoroughly explore the barriers, facilitators, and attitudes of these implementers. Mapping these aspects and incorporating these in the healthcare professional training will most likely benefit implementation in the future. This can, for example, be explored using the Implementation Mapping protocol, which is an addition to Intervention Mapping. With Implementation Mapping we could select suitable implementation strategies to be used in achieving intervention adoption, implementation, but also scale-up [83].

CONCLUSION

In this thesis, we have demonstrated that it is possible to adapt an efficacious lifestyle intervention for community-dwelling older adults, combining resistance exercise and dietary protein, to a real-life setting. Systematic intervention adaptation is necessary to translate efficacious interventions to fit the practice setting, using input from researchers, healthcare professionals, and the target group. The combined resistance exercise training and dietary protein intervention was effective in improving physical functioning, muscle strength, and lean body mass when implemented in a real-life setting. The intervention was highly acceptable to participants and professionals, and was generally implemented with high dose received and with high fidelity. Further attention is warranted, however, to optimize long-term adherence to the intervention to achieve behaviour maintenance. Combining implementation findings from ProMuscle in Practice and SLIMMER, key elements for success of combined lifestyle intervention include implementation by skilled healthcare professionals, tailoring of the intervention, social aspects, implementation fidelity and applicability, multidisciplinary collaboration, and focus on behaviour maintenance.

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SUMMARY

Recently, there is increasing attention for stimulating older adults to age in their own homes in good health and with a good quality of life. For independent living it is essential to preserve physical functioning and the ability to perform activities of daily living. However, ageing is accompanied by a decline in skeletal muscle mass and muscle strength, which are linked to decreased functional capacity. Strategies to prevent the loss of muscle mass, strength, and physical functioning include dietary protein intake and resistance exercise. Expert groups recommend protein intakes for older adults of 1.0-1.2 gram/kilogram-bodyweight/day, and it is suggested that consuming 25-30 gram of protein per meal is beneficial for muscle health. In addition, physical activity guidelines for adults aged ≥ 55 year recommend performing muscle-strengthening exercises twice a week. The combination of increased dietary protein intake and resistance exercise is assumed to elicit largest benefits in counteracting the loss of muscle mass, strength, and functioning. Although there is extensive evidence on the efficacy of these two strategies for older adults, there is a need for feasible and effective interventions implemented in a real-life setting. Therefore, the aims of this research were to 1) provide insight in translating an efficacious dietary protein and resistance exercise training intervention for community-dwelling older adults to practice, and 2) to evaluate effectiveness and implementation feasibility of adapted lifestyle interventions in a real-life setting. The main findings of this research as described in chapters 2-6 are summarized below.

An efficacious intervention, consisting of resistance exercise training and protein supplementation, was systematically adapted to fit the practice setting (Chapter 2). Most important adaptations to make the intervention fit the real-life setting were related to the design of a training for healthcare professionals that implement the intervention, and the inclusion of dietary counselling by a dietitian focused on incorporating protein-rich foods in the diet of older adults. Subsequently, the adapted intervention was tested for feasibility and potential impact in a 12-week pilot study, including 25 community-dwelling older adults. This pilot study showed that the intervention was well received by both the participants and the healthcare professionals, and was perceived feasible to implement in Dutch healthcare practice. Based on these results, further improvements were made to the recruitment process, guidance during the training sessions, and the diet intervention. In addition, the one-group pre-test post-test pilot study showed that there were indications for intervention effectiveness on muscle strength and functioning, suggesting that the most important

effective intervention elements were retained in the intervention during the adaptation process.

Subsequently, a randomised controlled multicentre intervention study was designed (Chapter 3), involving a target population of non-frail, pre-frail, and frail community-dwelling older adults. The ProMuscle in Practice intervention consisted of two 12-week periods. The first 12-week intensive support intervention consisted of group-based resistance exercise training supervised by physiotherapists twice a week, and dietitian guidance aimed at increasing dietary protein intake during the main meals using protein-rich foods. Afterwards, participants could continue with the optional 12-week moderate support intervention, aimed to encourage participants to continue with their adapted lifestyle. This period consisted of group-based exercise sessions at different exercise providers, and a nutrition course. To guide evaluation, the theory underlying the intervention was summarized in an intervention logic model. The aims of the intervention study were to assess 1) effectiveness, 2) implementation outcomes, and 3) cost-effectiveness of the intervention (not part of this thesis).

Effectiveness of the combined intensive support and moderate support intervention were evaluated in a 24-week multicentre study (Chapter 4). Participants were randomly allocated to an intervention group (n=82) and a control group (n=86) per municipality. Effect measurements were conducted at baseline, after 12 weeks and after 24 weeks, and included physical functioning, leg muscle strength, lean body mass, and quality of life. Intervention participants increased their dietary protein intake during breakfast (from 14.7 grams to 25.4 grams at week 12 and 21.9 grams at week 24) and lunch (from 21.5 grams to 31.1 grams at week 12 and 27.0 grams at week 24) following the intervention. Resistance exercise training attendance was higher in the intensive support intervention as compared to the moderate support intervention. In the first twelve weeks, the Short Physical Performance Battery score increased in the intervention group, but decreased in the control group (β 0.5 (95% CI 0.0–0.9)). Secondary outcomes gait speed (β 0.3 (95% CI -0.6- -0.1)), repeated chair rise (β -1.6 (95% CI -2.5- -0.6)), Timed Up-and-Go (β -0.7 (95% CI -1.2- -0.2)), lean body mass (β 0.6 (95% CI 0.2–0.9)), and the leg strength measures ($P < .001$) improved in the intervention group as compared to the control group. For the full 24 week intervention period, there was a significant positive change in physical functioning, leg strength, and lean body mass in the intervention as compared to the control group. No

difference in change between groups was observed for the six minute walking test, functioning in activities of daily living, and quality of life.

The evaluation of the implementation process of the ProMuscle in Practice intervention was described in Chapter 5. Mixed method data were collected from intervention participants (n=82) and healthcare professionals (n=36), before the intervention, after the intensive support intervention (week 12), and after the moderate support intervention (week 24). Process indicators assessed in this study were recruitment, dose received, acceptability, fidelity, applicability, and context. Overall, both intervention periods were feasible to implement and well received by participants and healthcare professionals. Dose received was high for the intensive support intervention (83.6% training session attendance, >90% dietitian consultations received). About two-third of participants continued with the optional moderate support intervention, and a lower dose received was observed for this intervention period (63.6% of training sessions, 76.8% for nutrition course). The intensive support intervention was overall implemented as planned, and the moderate support intervention resistance exercise training sessions varied in implementation between providers. Intervention elements contributing to intervention success included tailoring of the intervention, intensive supervision by healthcare professionals, social aspects, implementation fidelity, and applicability of the intervention.

These and other elements contributed to the intervention success of the SLIMMER diabetes prevention study. This intervention was also adapted from an efficacious intervention to implement in practice. Chapter 6 described how this intervention was delivered and received upon implementation in Dutch primary care, and how this could explain intervention effectiveness. SLIMMER consisted of 10 months of combined dietary and physical activity guidance by dietitians and physiotherapists, case management by a practice nurse, and a maintenance program. Data on process indicators were collected through participant questionnaires (n=155) and semi-structured interviews with healthcare professionals (n=45). The intended target population of adults at risk of developing type 2 diabetes was recruited. The intervention was very well received by both the participants and the professionals (mean acceptability rating of 82 and 80 on a scale of 1-100, respectively), and was to a large extent implemented as planned. The intervention was perceived applicable to implement in Dutch primary care. A higher intervention dose received was associated

with increased weight loss and with dietary behaviour change, and participant acceptability was related to health outcomes.

Thus, according to the ProMuscle in Practice and the SLIMMER study, it is possible to systematically adapt an efficacious combined exercise training and dietary intervention to practice. Although in ProMuscle in Practice the observed effects were smaller than in the original efficacy study, this study demonstrated that an adapted combined intervention can retain effectiveness on physical functioning, muscle strength, and lean body mass when implemented in a real-life setting. In addition, both the ProMuscle in Practice intervention and the SLIMMER intervention were feasible to implement in Dutch healthcare practice and highly accepted by participants and professionals. Promising intervention elements that can contribute to lifestyle intervention success include implementation by skilled healthcare professionals, tailoring of the intervention, incorporating social aspects, multidisciplinary collaboration, fit in the real-life setting, implementation fidelity, and focus on behaviour maintenance. These combined lifestyle interventions are thus valuable and feasible preventive strategies to implement in practice. However, there are some issues that need to be considered for future implementation, such as balancing fidelity and fit during implementation, optimal intervention intensity and support level, focus on long-term intervention success and sustainability, and specifying the target population for this intervention in practice. These issues can be addressed in collaboration with relevant stakeholders from research, practice, and policy. Future research can provide insight in optimization of the intervention and its implementation, in improving long-term adherence, and in testing the intervention theory.

SAMENVATTING

Ouderen worden gestimuleerd om zo lang mogelijk zelfstandig thuis te wonen, in goede gezondheid en kwaliteit van leven. Voor zelfstandig wonen is het belangrijk dat de fysieke functie en de mogelijkheid tot het uitvoeren van activiteiten van het dagelijks leven behouden blijven. Echter, veroudering gaat samen met een afname van skeletspiermassa en spierkracht, en daarbij ook een achteruitgang in functionele capaciteit. Strategieën om deze afname in spiermassa, kracht en fysieke functie tegen te gaan zijn onder andere het verbeteren van de eiwitinname en het introduceren van krachttraining. Expertgroepen adviseren een eiwitinname voor ouderen van 1.0-1.2 gram/kilogram-lichaamsgewicht/dag. Daarnaast lijkt een eiwitinname van 25-30 gram eiwit per maaltijd gunstig te zijn voor de spiergezondheid. Verder wordt in de beweegrichtlijnen voor volwassenen van 55 jaar of ouder aanbevolen om twee keer per week spierversterkende oefeningen te doen. Naar verwachting biedt de combinatie van een verhoogde eiwitinname en krachtoefeningen de grootste voordelen in het tegengaan van het verlies van spiermassa, kracht en fysiek functioneren. Hoewel er veel bewijs is van het effect van deze twee strategieën bij ouderen, is er behoefte aan uitvoerbare en effectieve interventies in de praktijk. Daarom zijn de doelen van dit onderzoek om 1) inzicht te krijgen in het aanpassingsproces van een klinisch effectieve interventie met eiwitsuppletie en krachttraining voor zelfstandig wonende ouderen naar de praktijk, en 2) de effectiviteit en uitvoerbaarheid van aangepaste leefstijlinterventies te evalueren in de praktijk. De belangrijkste bevindingen van dit onderzoek zoals beschreven in Hoofdstuk 2-6 zijn hieronder weergegeven.

Een eerder bewezen, effectieve interventie voor fragiele ouderen, bestaande uit krachttraining en eiwitsuppletie, is systematisch aangepast om beter aan te sluiten bij de praktijksetting (Hoofdstuk 2). De belangrijkste aanpassingen waren het ontwikkelen van een training voor de gezondheidsprofessionals die de interventie uitvoeren en het toevoegen van een voedingsprogramma waarin een diëtist advies geeft over hoe de ouderen eiwitrijke voedingsmiddelen kunnen opnemen in hun voedingspatroon. Vervolgens is de aangepaste interventie getest op haalbaarheid en potentiele impact in een pilotstudie van 12 weken, onder 25 zelfstandig wonende ouderen. Deze pilotstudie wees uit dat de interventie goed ontvangen werd door zowel de deelnemende ouderen als de gezondheidsprofessionals, en dat de interventie uitvoerbaar was in de Nederlandse gezondheidszorgpraktijk. Op basis van de resultaten van het pilotonderzoek zijn verdere verbeteringen aangebracht in de wervingsprocedure, de begeleiding tijdens de krachttrainingen en het voedings-

programma. Verder liet de *one-group pre-test post-test* pilotstudie zien dat er indicaties waren voor effecten van de interventie op spierkracht en fysieke functie, waardoor we veronderstellen dat de belangrijkste effectieve interventie-elementen behouden zijn tijdens het aanpassingsproces.

Vervolgens is een gerandomiseerd, gecontroleerd multicenter interventieonderzoek opgezet (Hoofdstuk 3), met als doelgroep zelfstandig wonende ouderen (≥ 65 jaar) met een verschillend niveau van lichamelijke kwetsbaarheid. De ProMuscle in de Praktijk interventie bestond uit twee perioden van 12 weken. De eerste 12-weekse intensief begeleide interventie bestond uit twee keer per week krachttraining in groepjes onder supervisie van fysiotherapeuten, en begeleiding van een diëtist om met behulp van eiwitrijke voedingsmiddelen de eiwitinname tijdens de hoofdmaaltijden te verhogen. Na deze interventie konden deelnemers doorgaan met de optionele 12-weekse matig intensief begeleide interventie, welke als doel had om deelnemers te ondersteunen in het vasthouden van hun aangepaste leefstijl. Deze interventieperiode bestond uit trainingen in groepjes bij verschillende beweegaanbieders en een voedingscursus. De onderliggende interventietheorie is samengevat in een logisch model, dat gebruikt is om de evaluatie van de interventie te sturen. De doelen van deze interventiestudie waren het evalueren van 1) de effectiviteit, 2) de implementatie, en 3) de kosteneffectiviteit van de interventie (geen onderdeel van deze thesis).

De effectiviteit van de gecombineerde intensief begeleide interventie en matig intensief begeleide interventie is geëvalueerd in een multicenter onderzoek (Hoofdstuk 4), in vijf gemeenten in Gelderland. Deelnemers werden per gemeente gerandomiseerd over een interventiegroep (n=82) en een controlegroep (n=86). Effectmetingen werden uitgevoerd op baseline, na 12 weken en na 24 weken, en omvatten metingen voor o.a. fysiek functioneren, beenspierkracht, vetvrije massa, en kwaliteit van leven. Deelnemers in de interventiegroep verhoogden hun eiwitinname tijdens het ontbijt (van 14.7 gram naar 25.4 gram in week 12 en 21.9 gram in week 24) en tijdens de lunch (van 21.5 gram naar 31.1 gram in week 12 en 27.0 gram in week 24). De opkomst tijdens de trainingssessies was hoger tijdens de intensief begeleide interventie dan tijdens de matig intensief begeleide interventie. In de eerste twaalf weken ging de interventiegroep vooruit in *Short Physical Performance Battery* score, terwijl de controlegroep wat achteruit ging (β 0.5 (95% CI 0.0–0.9)). De secundaire uitkomsten loopsnelheid (β 0.3 (95% CI -0.6- -0.1)), herhaalde stoeltest (β -1.6 (95% CI -2.5- -0.6)),

Timed Up-and-Go (β -0.7 (95% CI -1.2- -0.2)), vetvrije massa (β 0.6 (95% CI 0.2–0.9)), en beenspierkracht (verschillende metingen, P < .001) verbeterden ook tijdens deze 12 weken in de interventiegroep vergeleken met de controlegroep. Voor de volledige interventieperiode van 24 weken was er een significante positieve verandering in lichamelijk functioneren, beenspierkracht, en vetvrije massa in de interventiegroep ten opzichte van de controlegroep. We zagen geen verschil in verandering tussen de groepen voor de zes minuten wandeltest, functioneren in activiteiten van dagelijks leven, en kwaliteit van leven.

Hoofdstuk 5 beschrijft de evaluatie van het implementatieproces van de ProMuscle in de Praktijk interventie. We hebben m*ixed method* data verzameld van interventiedeelnemers (n=82) en gezondheidsprofessionals (n=36), zowel vóór de interventie, na de intensief begeleide interventie (week 12), en na de matig intensief begeleide interventie (week 24). De volgende procesindicatoren zijn gemeten in dit onderzoek: werving, ontvangen dosis, acceptatie, *fidelity* (de mate waarin de interventie is uitgevoerd zoals gepland), toepasbaarheid binnen de praktijksetting, en context. Over het algemeen was het interventieprogramma in beide perioden goed uitvoerbaar en werd het programma goed gewaardeerd door deelnemers en gezondheidsprofessionals. De ontvangen dosis was hoog voor de intensief begeleide interventie (83.6% van de krachttrainingen zijn bijgewoond, >90% van de deelnemers heeft de consulten met de diëtist gehad). Ongeveer twee-derde van de deelnemers ging door met de optionele matig intensief begeleide interventie, en bij deze interventie was de ontvangen dosis lager dan in de eerste twaalf weken (63.6% van de trainingen en 76.8% van de voedingscursusbijeenkomsten zijn bijgewoond). De intensief begeleide interventie was grotendeels uitgevoerd zoals beschreven in de draaiboeken. De uitvoering van de trainingen van de matig intensief begeleide interventie verschilde per beweegaanbieder. Op basis van deze bevindingen verwachten wij dat de volgende interventie-elementen hebben bijgedragen aan het succes van de interventie: advies op maat (*tailoring)*, intensieve begeleiding door gezondheidsprofessionals, het sociale aspect, uitvoer van de interventie zoals gepland, en de toepasbaarheid van de interventie in de praktijk.

Deze en andere elementen hebben ook bijgedragen aan het interventiesucces in de SLIMMER diabetes preventie studie. De SLIMMER interventie was ook aangepast van een klinisch effectieve interventie naar de praktijk. Hoofdstuk 6 beschrijft hoe deze

interventie is uitgevoerd en ontvangen bij implementatie in de Nederlandse eerstelijns gezondheidszorg, en hoe dit de interventie-effectiviteit kan verklaren. SLIMMER bestond uit 10 maanden gecombineerde voeding- en beweegbegeleiding door diëtisten en fysiotherapeuten, casemanagement door een praktijkondersteuner huisarts en een uitstroomprogramma. We hebben data verzameld middels deelnemer-vragenlijsten (n=155) en semigestructureerde interviews met gezondheidszorg-professionals (n=45). Uit de resultaten bleek dat het gelukt was om de doelgroep van volwassenen met risico op het ontwikkelen van type 2 diabetes te werven. De interventie werd goed ontvangen door deelnemers en professionals (gemiddelde acceptatie respectievelijk 82 en 80, op een schaal van 1-100). De interventie was grotendeels uitgevoerd zoals gepland, en was toepasbaar in de Nederlandse eerstelijns gezondheidszorg. Een hogere ontvangen dosis was geassocieerd met groter gewichtsverlies en met verandering in voedingsgedrag, en de mate waarin deelnemers de interventie waardeerden was geassocieerd met gezondheidsuitkomsten.

Op basis van de ProMuscle in de Praktijk en SLIMMER onderzoeken kunnen we concluderen dat het mogelijk is om een klinisch effectieve interventie bestaande uit training en een voedingsprogramma systematisch aan te passen aan de praktijk. Hoewel bij ProMuscle in de Praktijk de effecten kleiner waren dan in de oorspronkelijke klinische studie, heeft het onderzoek aangetoond dat een aangepaste interventie effectiviteit kan behouden op lichamelijke functie, spierkracht en vetvrije massa, wanneer deze wordt uitgevoerd in de praktijk. Verder was zowel ProMuscle in de Praktijk als SLIMMER uitvoerbaar in de Nederlandse gezondheidszorgpraktijk, en goed gewaardeerd door zowel deelnemers als professionals. Veelbelovende interventie-elementen die kunnen bijdragen aan het succes van leefstijlinterventies zijn uitvoering door gekwalificeerde gezondheidsprofessionals, op maat aanbieden van de interventie, het incorporeren van sociale aspecten, multidisciplinaire samenwerking tussen de professionals, toepasbaarheid van de interventie in de praktijksetting, uitvoeren van de interventie zoals gepland en de focus op gedragsbehoud. Deze gecombineerde leefstijlinterventies zijn zodoende waardevolle en goed uitvoerbare preventieve strategieën om te implementeren in de praktijk. Daarentegen zijn er enkele aandachtspunten geformuleerd voor verdere implementatie, zoals het zoeken van een evenwicht tussen *fidelity* en *fit* tijdens implementatie, de optimale intensiteit en begeleidingsniveau van de interventie, het richten op lange-termijn succes van de interventie, borgen van de interventie, en het specificeren van de interventiedoelgroep

in de praktijk. Deze zaken kunnen worden aangepakt in samenwerking met relevante partijen vanuit zowel onderzoek, praktijk, als beleid. Toekomstig onderzoek kan meer inzicht verschaffen in het optimaliseren van de interventie en de implementatie, het verbeteren van langdurige naleving van de interventie en het testen van de onderliggende interventietheorie.

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Ellen

ABOUT THE AUTHOR

CURRICULUM VITAE

Ellen Johanna Ine van Dongen was born on July 14, 1988 in Tilburg, the Netherlands. In 2006 she received her secondary school diploma from St. Odulphus Lyceum in Tilburg.

After obtaining her BSc degree in Nutrition and Health at Wageningen University in 2009, she worked as a student assistant at Wageningen University and travelled to Australia and New Zealand. In 2010 she continued with a MSc at Wageningen University, specializing in Public Health Nutrition. She conducted her major thesis with the Municipal Health Service in Apeldoorn (GGD Noord- en Oost-Gelderland), where she developed and validated effect evaluation questionnaires for the '*cursus Evenwicht*', for overweight children and their parents. She conducted her minor thesis at the department of Communication and Innovation Studies at Wageningen University, assessing behavioural determinants of university freshmen students' sport behaviour. Thereafter, Ellen completed her internship with Taste Lessons (in Dutch: *Smaaklessen*), performing the process evaluation of the Taste Lesson nutrition education curriculum at primary schools. After obtaining her MSc degree in 2012, Ellen was appointed as a junior researcher at Wageningen University & Research. She was involved in evaluation studies on Taste Lessons and the SLIMMER diabetes prevention intervention, and in a qualitative study in health professionals on malnutrition in older adults. In 2015 she started as a PhD fellow, working both at the Division of Human Nutrition & Health at Wageningen University and at the Food, Health & Consumer Research group at Wageningen Food & Biobased Research. Her PhD project is described in this thesis, and focused on the adaptation, implementation and effectiveness of a combined diet and resistance exercise training intervention for community-dwelling older adults in a real-life setting.

She joined the educational programme of the Graduate School VLAG and was secretary of the VLAG PhD Council. Furthermore, she attended (international) conferences and courses, was involved in teaching and supervising MSc students and interns, and coordinated the MSc course 'Public Health Nutrition' in 2015. Ellen co-authored a book chapter on Quality Control in the book 'Epidemiology in Public Health Practice'. In 2019 she was selected to participate in the 25th Essentials seminar of the European Nutrition Leadership Platform.

LIST OF PUBLICATIONS

Publications in peer-reviewed journals

EJI van Dongen, A Haveman-Nies, NLW Wezenbeek, BG Dorhout, EL Doets, CPGM de Groot. 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)

DSM ten Haaf*/**EJI van Dongen***, MAH Nuijten, TMH Eijsvogels, CPGM de Groot, MTE Hopman. Protein intake and distribution in relation to physical functioning and quality of life in community-dwelling elderly people: acknowledging the role of physical activity. *Nutrients* (2018)

AL Herrema, MJ Westerman, **EJI van Dongen**, U Kudla, M Veltkamp. Qualitative Analysis of drivers and barriers to adhering to an exercise-protein intervention designed to counteract sarcopenia. *J Aging Phys Act* (2018)

EJI van Dongen, JN Leerlooijer, JM Steijns, M Tieland, CPGM de Groot, A Haveman-Nies. Translation of a tailored nutrition and resistance exercise intervention for elderly people to a real-life setting: adaptation process and pilot study. *BMC Geriatrics* (2017)

MCE Battjes-Fries, A Haveman-Nies, GG Zeinstra, **EJI van Dongen**, HJ Meester, R van den Top-Pullen, P van't Veer, C de Graaf.
Effectiveness of Taste Lessons with and without additional experiential learning activities on children's willingness to taste vegetables. *Appetite* (2017)

EJI van Dongen*/G Duijzer*, SC Jansen, J Ter Beek, JM Huijg, JN Leerlooijer, GJ Hiddink, EJ Feskens, A Haveman-Nies. Process evaluation of a randomised controlled trial of a diabetes prevention intervention in Dutch primary health care: the SLIMMER study. *Public Health Nutrition* (2016)

MCE Battjes-Fries, **EJI van Dongen**, RJ Renes, HJ Meester, P van 't Veer, A Haveman-Nies. Unravelling the effect of the Dutch school-based nutrition programme Taste Lessons: the role of dose, appreciation and interpersonal communication. *BMC Public Health* (2016)

MCE Battjes-Fries, A Haveman-Nies, **EJI van Dongen**, HJ Meester, R van den Top-Pullen, C de Graaf, P van 't Veer. Effectiveness of Taste Lessons with and without additional experiential learning activities on children's psychosocial determinants of vegetables consumption. *Appetite* (2016)

C Ziylan, A Haveman-Nies, **EJI van Dongen**, S Kremer, CPGM de Groot. Dutch nutrition and care professionals' experiences with undernutrition awareness, monitoring, and treatment among community-dwelling older adults: a qualitative study. *BMC Nutrition* (2015).

EJI van Dongen, C Pieterse, A Haveman-Nies. Ontwikkeling van een onderbouwd evaluatie-instrument voor de practice-based interventie 'cursus Evenwicht'. *Tijdschrift voor gezondheidswetenschappen* (2014)

Other publications

C Rots-de Vries, J Helmink, **EJI van Dongen**. Perform Quality Control. Book chapter in: *Epidemiology in public health practice*, 2017. Wageningen Academic Publishers, Wageningen.

MCE Fries, **EJI van Dongen**, A Haveman-Nies. Evaluatie van Smaaklessen: heeft Smaaklessen effect op determinanten van gezond en bewust eetgedrag. *Report for Dutch Ministry of Economic Affairs* (2013)

Submitted manuscripts

EJI van Dongen, A Haveman-Nies, EL Doets, BG Dorhout, CPGM de Groot. Effectiveness of a diet and resistance exercise intervention on muscle health in older adults: ProMuscle in Practice.

EJI van Dongen, EL Doets, CPGM de Groot, BG Dorhout, A Haveman-Nies. Process evaluation of a combined lifestyle intervention for community-dwelling older adults: ProMuscle in Practice.

Abstracts in scientific journal or proceedings

NLWJ Wezenbeek, **EJI van Dongen,** L O'Callaghan, EL Doets, A Haveman-Nies, CPGM de Groot. Effectiviteit van een interventieprogramma met eiwitrijke voeding en krachttraining in een praktijkomgeving: Een multicenter gerandomiseerde en gecontroleerd onderzoek - Voorlopige resultaten. *In: 14e Nationaal Gerontologie-congres, Ede.* (2017)

EJI van Dongen, A Haveman-Nies, CAB Tieland, CPGM de Groot. ProMuscle 65PK: uitvoerbaarheid en potentiele impact van een voeding- en beweegprogramma voor ouderen in de praktijk. *Tijdschrift voor Gerontologie en Geriatrie 46. - p. 231 - 231.* (2015)

MCE Fries, A Haveman-Nies, **EJI van Dongen,** HJ Meester, C de Graaf; P van 't Veer. Effectiveness of school-based nutrition programme Taste Lessons with and without experience-oriented activities on children's determinants of behaviour towards vegetable consumption: a quasi-experimantal study. *Abstract from International Society of Behavioral Nutrition and Physical Activity (ISBNPA), Edinburgh, United Kingdom, 117-117.* (2015)

C Ziylan, **EJI van Dongen,** S Kremer, A Haveman-Nies, CPGM de Groot. Excerpts from Dutch public health professionals' experiences with malnutrition among the elderly. *In: 12e Nationaal Congres Nederlandse Vereniging Voor Gerontologie - Kennisnetwerk Ouder Worden en Samenleving. - p. 246 - 246.* (2014)

OVERVIEW OF COMPLETED TRAINING ACTIVITIES

Discipline specific activities	Institute and location	Year
Courses and workshops		
Masterclass 'Public Health Interventions in real-life settings'	AGORA/ VLAG, Wageningen, NL	2012
Masterclass 'Evaluation of public health interventions in real-life settings'	AGORA/VLAG, Wageningen, NL	2013
Energy Metabolism and Body Composition in nutrition and health research*, oral presentation*	VLAG/HNH (WU)/HAP (WU)/ HB (MU), Wageningen, NL	2016
Masterclass 'How to evaluate intervention in public health practice'	AGORA/VLAG, Wageningen, NL	2016
Masterclass 'Evaluation and adaptation of public health interventions: the role of context'*, oral presentation*	VLAG/SSG WUR/Research-NL, Wageningen, NL	2018
Conferences and meetings		
Landelijk Congres Bewegen in de Langdurige Zorg	Studie Arena, Bussum, NL	2014
HAPS seminar 'Social context of healthy aging'	RUG (HAPS), Groningen, NL	2014
Congres 'Ambitie in Transitie'	AGORA/Caransscoop, Apeldoorn, NL	2014
Food for Thought wetenschapsavond	Alliantie Voeding in de Zorg (ZGV), Ede, NL	2014
Eat2Move project Sportkantine meeting*, oral presentation*	Eat2Move, Ede, NL	2015
Gerontologiecongres*, oral presentation*	NVG-KNOWS, Ede, NL	2015
Geriatriedagen*, oral presentation*	NVG-KNOWS/V&VN/De Fysiotherapeut, Den Bosch, NL	2016
Symposium Activiteitenbegeleiders Geriatrie (ZGV)*, oral presentation*	GOAZ, Ede, NL	2016
Dag van de Fysiotherapeut*, poster presentation*	KNGF, Utrecht, NL	2016
FItVAK Voeding & leefstijl (FC Institute)*, oral presentation*	FC Institute/Fit!vak, Driebergen, NL	2016
Innovating healthcare: an implementation science perspective	Trimbos Academie, Amsterdam, NL	2017
Werkconferentie Gezond Ouder Worden*, oral presentation*	GGD-NOG/AGORA, Ermelo, NL	2017
WEON 2017	VVE, Antwerpen, BE	2017
Improving implementation practice	Nederlands Implementatie Collectief, Amsterdam, NL	2018
Lab meeting - Wayne State University*, oral presentation*	Wayne State University, Detroit MI, USA	2018

Wageningen PhD Symposium*, oral presentation*	WPC, Wageningen, NL	2018
Congres Diagnose Voeding & Gezondheid: 'Samen innoveren voor een vitaler Nederland'*, oral presentation*	Diagnose Voeding & Gezondheid, Utrecht, NL	2018
Implementation Science Conference: Improving Implementation Practice	NIC/Trimbos Instituut/Amsterdam UMC, Utrecht, NL	2019
Ouderen en Voeding congres*, oral presentation*	GerCare/ NVKG/Alliantie voeding in de zorg/NVFG/NVD/ DGO/V&VN/EDOMAH/WUR, Ede, NL	2019
International Association of Gerontology and Geriatrics European Region Congress 2019 (IAGG-ER) *, two oral presentations*	IAGG-ER, Gothenborg, SE	2019

General courses and workshops	**Institute and location**	**Year**
Data Management	WGS, Wageningen, NL	2014
Project and Time Management	WGS, Wageningen, NL	2014
PhD Carrousel workshops	WGS, Wageningen, NL	2016
ICH Good Clinical Practice (GCP) basic course	PROFESS, Wageningen, NL	2016
Mixed Model Analysis	VLAG, Wageningen, NL	2017
Scientific Writing	WGS, Wageningen, NL	2018
Reviewing a Scientific Paper	WGS, Wageningen, NL	2018
Guiding and Supervising BSc and MSc students	WGS, Wageningen, NL	2018
Nutritional Leadership Workshop	NAV, Den Bosch, NL	2018
Career Orientation	WGS, Wageningen, NL	2018
European Nutritional Leadership Platform – Essentials Program	ENLP, Luxemburg, LU	2019

Optional courses and activities	**Institute and location**	**Year**
PhD Study Tour USA*, oral presentation*	HNH/VLAG, Wageningen	2015
Preparing PhD research proposal	VLAG, Wageningen	2016
Literature and discussion groups: 'Rothman lunch', 'Paperclip club', 'Muscle meeting', 'Consumer Understanding Expertise meeting WFBR'	HNH/WFBR, Wageningen	2014-2018
VLAG PhD Council	VLAG, Wageningen	2016-2018

Colophon

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Propositions

1. An adapted efficacious lifestyle intervention for older adults can retain effectiveness when implemented in practice.
   (this thesis)

2. Intensive supervision and tailoring are key in lifestyle interventions for older adults.
   (this thesis)

3. Fitness trackers can help to increase physical activity levels, but the wearer should be motivated to engage with the feedback. (Based on *Maher et al., BMC Public Health, 2017, 1:15*)

4. Healthy ageing has a different meaning for older adults than for researchers. (Based on *Patzelt et al., BMC Geriatrics, 2016, 16:210*)

5. You learn most from supervising students that are most unlike yourself.

6. It is often overlooked that researchers influence the intervention they study.

Propositions belonging to the thesis, entitled:

Dietary protein and resistance exercise training for community-dwelling older adults
Intervention adaptation, implementation, and effectiveness

Ellen J.I. van Dongen
Wageningen, 14 November 2019