

Type 2 diabetes prevention from research to practice:

the SLIMMER lifestyle intervention

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ABSTRACT

INTRODUCTION

Diabetes is a worldwide epidemic, causing a high disease and economic burden. Type 2 diabetes, the most common form of diabetes, is associated with overweight and obesity and an unfavourable lifestyle, including unhealthy diet and physical inactivity. Over the last two decades, many large-scale experimental trials have shown that type 2 diabetes can be delayed or prevented by lifestyle modification in high-risk subjects. This evidence has been translated and implemented in interventions in real-world settings, however, no (cost)effective diabetes prevention programme in Dutch primary health care was available at the start of the current project in 2008. Therefore the SLIMMER study (SLIM iMplementation Experience Region Noord-en Oost-Gelderland) was started in which the SLIM intervention, revealing a 47% diabetes risk reduction, was translated to Dutch primary health care. The aim of this thesis was to implement the SLIMMER intervention in Dutch primary health care and to evaluate its (cost)effectiveness and implementation.

METHODS

In 2010–2011, the SLIMMER intervention was tested for its feasibility and desired impact in a one-year pilot study ($n = 31$) with process evaluation, including quantitative and qualitative methods. From 2011 to 2014, the SLIMMER intervention was implemented on a larger scale in Dutch public health and primary health care. A randomised controlled trial was conducted ($n = 316$), including subjects aged 40 to 70 years with impaired fasting glucose or high risk of diabetes. The 10-month SLIMMER intervention involved a dietary and physical activity programme, including case management and a maintenance programme. The control group received usual health care. A logic model of change was composed to link intervention activities with intervention outcomes in a logical order. Primary outcome was fasting insulin. Measurements were performed at baseline and after 12 and 18 months and covered quality of life, clinical and metabolic risk factors (e.g. glucose tolerance, serum lipids, body fatness, and blood pressure), and eating and physical activity behaviour. Furthermore, 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 in semi-structured interviews with health care professional ($n = 45$) and intervention participant questionnaires ($n = 155$). Moreover, cost-effectiveness analyses were performed from both a societal and a health care perspective. Participants completed questionnaires to assess health care utilisation, participant out-of-pocket costs, and productivity losses.

RESULTS

The pilot study showed that participants lost on average 3.5 kg ($p = 0.005$) of their body weight. Both participants and health care professionals were satisfied with the intervention, which was implemented as planned and appeared to be suitable for application in practice. Refinements were identified and made prior to further implementation. The randomised controlled trial showed that after 12 and 18 months, the intervention group significantly improved weight ($\beta = -2.7$ kg (95% CI: -3.7;-1.7) and $\beta = -2.5$ kg (95% CI: -3.6;-1.4), respectively), and fasting insulin ($\beta = -12.1$ pmol/l (95% CI: -19.6;-4.6) and $\beta = -8.0$ pmol/l (95% CI: -14.7;-0.53), respectively) compared with the control group. Intervention subjects improved weight and glucose tolerance, independent of manner of recruitment (laboratory glucose test or Diabetes Risk Test). Furthermore, intake of total and saturated fat decreased and fibre intake increased in the intervention group compared with the control group, both at 12 and 18 months ($p < 0.05$). The DHD-index score – indicating adherence to the Dutch dietary guidelines – was significantly higher in the intervention group than in the control group, both at 12 and at 18 months ($p < 0.05$). Vigorous activities and physical fitness improved both at 12 and at 18 months. Finally, beneficial changes in several domains of quality of life were found both at 12 and at 18 months, although not all domains reached statistical significance. From the process evaluation it was revealed that it was possible to recruit the intended high-risk population, and the SLIMMER intervention was very well received by both participants and health care professionals. 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. The cost-effectiveness analysis showed that, from a societal perspective, the incremental costs of the SLIMMER lifestyle intervention were €547 and that the incremental effect was 0.02 QALY, resulting in an incremental cost-effectiveness ratio (ICER) of 28,094/QALY. When cost-effectiveness was calculated from a health care perspective, the ICER decreased to 13,605/QALY, with a moderate probability of being cost-effective (56% at a willingness to pay (WTP) of €20,000/QALY and 81% at a WTP of €80,000/QALY).

CONCLUSION

In conclusion, this study showed that a thorough preparation of translation and implementation has led to a cost-effective intervention to prevent type 2 diabetes which is feasible to implement in Dutch primary health care. In fact, our clinical effects were larger than those in most other real-world intervention programmes, and most effects sustained at 18 months. Furthermore, we showed that a higher intervention dose and participant acceptability were associated with improved health outcomes and dietary behaviour. Further research is needed on effects and costs over longer follow-up, effective intervention components, and consequences of suggested adaptations of the programme on intervention effectiveness. The results of this study provide valuable insights that can contribute to structural embedding and funding of effective diabetes prevention programmes in Dutch primary health care.

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The background of the page is a light gray color. It is decorated with a pattern of white circles of various sizes, some of which are solid and others are outlines. In the center of the page, there is a faint, stylized illustration of a person with their arms raised, possibly in a gesture of celebration or triumph. The person is wearing a dark cap and a light-colored shirt. The overall aesthetic is clean and modern.

Chapter 1

General introduction

DIABETES MELLITUS

Diabetes mellitus is a chronic non-communicable metabolic disorder of glucose homeostasis that occurs when the pancreas is no longer able to produce insulin (β -cell dysfunction), or when the body is resistant to insulin (insulin resistance) [1, 2]. The body needs insulin to absorb glucose from the blood into the cells of the body to produce energy. Insulin deficiency and insulin resistance will lead to increased levels of glucose in the blood. There are three main types of diabetes. Type 1 diabetes is caused by an autoimmune reaction in which the β -cells in the pancreas do not produce insulin anymore. Type 2 diabetes is characterised by insulin resistance and relative insulin deficiency. The third type, gestational diabetes, consists of high blood glucose levels during pregnancy [1].

The history of diabetes mellitus dates back to ancient times when symptoms and remedies for treatment of excessive urination were described for the first time [3]. The physician Aretaeus (130-200 AC) was the first to use the term *diabetes*, derived from the Greek word for siphon, which means 'the flow of liquids through tubes'. Later, the Greek word *mellitus*, meaning 'the smell, colour, and flavour of honey', was added to the name, to reflect the sweet taste and smell of patients' urine [3]. At that time, diabetes mellitus was a rare disease. Nowadays, diabetes is expanded to a worldwide epidemic with 382 million people affected in 2013 [1]. It is estimated that this number will increase to 592 million by 2035. In the Netherlands, 834.100 people were diagnosed with diabetes in 2011. Furthermore, it is estimated that about 25% of people with diabetes have not been diagnosed yet and thus are unaware of their disease [4].

Type 2 diabetes is the most common form of diabetes, accounting for 90% of all diabetes cases [4]. Genetic factors and environmental aspects together are important determinants of the development of diabetes [2]. Type 2 diabetes usually occurs in adults but nowadays is increasingly seen in children and adolescents [1]. Type 2 diabetes may remain undiagnosed for many years, leading to severe complications like retinopathy, nephropathy, neuropathy, and cardiovascular diseases [5]. It was estimated that 5.1 million people aged between 20 and 79 years died from diabetes in 2013, accounting for 8.4% of global all-cause mortality among people in this age group [1]. In addition to this disease burden, diabetes causes a large economic burden. Diabetes costs at least USD 548 billion in health expenditure in 2013, accounting for 10.8% of total health care expenditure worldwide [1]. In the Netherlands, diabetes health care costs amounted 1.7 billion Euros in 2011, which is 1.9% of total health care expenditure [4].

DIAGNOSIS OF TYPE 2 DIABETES AND PREDIABETES

According to the World Health Organization (WHO), diabetes is defined as fasting plasma glucose ≥ 7.0 mmol/l (126 mg/dl) or 2-hour plasma glucose ≥ 11.1 mmol/l (200 mg/dl) (see Table 1.1) [6]. In 2011, WHO concluded that HbA1c can also be used as a diagnostic test for diabetes in which an HbA1c of 6.5% is recommended as the cut-off point [7]. As the onset of type 2 diabetes is gradual, most individuals progress through a state of prediabetes (intermediate hyperglycaemia), a high-risk state for diabetes development and adverse outcomes. Prediabetes is typically defined as blood glucose concentrations higher than normal, but lower than diabetes thresholds. According to WHO, individuals at risk have one or both prediabetic conditions: impaired fasting glucose (IFG), defined as fasting plasma glucose (FPG) concentration of 6.1 to 6.9 mmol/l (110 to 125 mg/dl) and, if measured, a 2-hour plasma glucose of < 7.8 mmol/l (140 mg/dl); and impaired glucose tolerance (IGT), defined as an FPG concentration of < 7.0 mmol/l (126 mg/dl) and a 2-hour plasma glucose concentration of ≥ 7.8 and < 11.1 mmol/l (140 and 200 mg/dl), measured during a 75 g oral glucose tolerance test [6]. In 2013, 316 million people worldwide, or 6.9% of adults, were estimated to have IGT and this number is expected to increase to 471 million, or 8% of the adult population, by 2035 [1]. In 2010, approximately 8% of the Dutch population aged 30-70 years had prediabetes (IFG or IGT) [8]. Around 5-10% of people with prediabetes become diabetic every year and up to 70% of individuals with prediabetes will eventually develop diabetes [9].

Table 1.1. Diagnostic criteria for diabetes and intermediate hyperglycaemia (according to the World Health Organization) [6, 7].

Type 2 diabetes		
Fasting glucose (mmol/l) ^a	OR	≥ 7.0 mmol/l (126 mg/dl)
2-hour glucose (mmol/l) ^{a,b}		≥ 11.1 mmol/l (200 mg/dl)
HbA1c		$\geq 6.5\%$
Impaired Fasting Glucose (IFG)		
Fasting glucose (mmol/l) ^a	AND ^c	6.1 to 6.9 mmol/l (110 to 125 mg/dl)
2-hour glucose (mmol/l) ^{a,b}		< 7.8 mmol/l (140 mg/dl)
Impaired Glucose Tolerance (IGT)		
Fasting glucose (mmol/l) ^a	AND	< 7.0 mmol/l (126 mg/dl)
2-hour glucose (mmol/l) ^{a,b}		≥ 7.8 and < 11.1 mmol/l (140 and 200 mg/dl)

^a Venous plasma glucose concentration.

^b Measured two hours after ingestion of 75 g oral glucose load.

^c If only fasting glucose concentration is measured, IGT cannot be excluded.

RISK FACTORS FOR TYPE 2 DIABETES

Type 2 diabetes is caused by a combination of genetic factors and environmental aspects [2]. Several genetic variants that are associated with type 2 diabetes have been identified, however, their contribution to the development of type 2 diabetes is modest (5-10%) [10]. Other non-modifiable risk factors are for example advancing age, ethnicity, family history of diabetes, and maternal diabetes [1]. The rapidly increasing incidence rates of diabetes, however, suggest a particularly important role for environmental aspects in the development of diabetes. This paragraph summarises the evidence for the major risk factors of type 2 diabetes, namely overweight and obesity, unhealthy diet, and physical inactivity.

Overweight and obesity

Overweight, and especially obesity, is a major risk factor for the development of type 2 diabetes [11, 12], especially when the excess adiposity is centrally distributed [13]. In obese subjects, adipose tissue releases increased amounts of fatty acids, glycerol, hormones, pro-inflammatory cytokines, and other factors that are involved in the development of insulin resistance [13]. There is convincing evidence for the association between excessive weight gain, central adiposity, and the development of type 2 diabetes. This association has been shown in several longitudinal studies in different populations, with a striking increase in risk apparent with increasing levels of Body Mass Index, waist circumference, or waist-to-hip ratio [14]. The risk of developing type 2 diabetes is almost three times higher when being overweight and seven times higher when being obese compared with normal weight persons [15]. Several randomised controlled trials have shown that weight loss could reduce the risk of progression from IGT to type 2 diabetes, even when there is a relatively small reduction in weight [16-20].

Unhealthy diet

The composition of diet seems to be an important factor in the prevention of type 2 diabetes. Both international and national guidelines recommend a diet with increased dietary fibre and whole grains intake and reduced calorie and saturated fat intake [14, 21-23]. A diet high in carbohydrates can have adverse metabolic consequences by raising triglycerides and reducing high-density lipoprotein (HDL) cholesterol [24]. Carbohydrates can be divided in whole grains and other less-refined complex carbohydrates (e.g. dietary fibre), and highly refined starches and sugars [25]. Several prospective studies showed a reduced risk for high intake of dietary fibre from grains on the development of type 2 diabetes [26-30]. The evidence for the association between

dietary fibre and type 2 diabetes is graded as probable because it is not clear which form of dietary fibre causes the effect [14].

The total amount of dietary fat has been shown to have only a minor, and in most studies even no effect on the risk of developing type 2 diabetes [14, 29, 31, 32]. There is, however, probable evidence for a moderate association between total fat intake and body weight [33]. The quality of dietary fat intake appears to be more important than the quantity [29]. Several reviews showed that saturated fat intake was associated with an increased risk of type 2 diabetes [29, 34, 35]. A recent systematic review, however, did not find any clear associations between intake of saturated fat and type 2 diabetes [33]. Epidemiologic studies generally did not find an association between monounsaturated fatty acid (MUFA) intake and type 2 diabetes [27, 33, 36], but MUFA had a beneficial effect on insulin sensitivity and fasting insulin concentration [33, 34]. There is possible evidence of a relationship between polyunsaturated fatty acid (PUFA) intake and reduced risk of type 2 diabetes [31, 32, 34, 35]. Furthermore, there is possible evidence that trans fatty acids are positively associated with a risk of type 2 diabetes [29, 34, 35]. Mechanisms underlying the relationship between dietary fat and risk of type 2 diabetes are still unclear, but potential mechanisms include alteration of cell membrane functioning, regulation of gene expression and enzyme activities, and influencing inflammation status [35].

Dietary protein intake is suggested to have positive effects on weight loss, weight maintenance, and glycaemic control due to its effect on satiety, appetite, and insulin sensitivity [37, 38]. In contrast, several long-term observational studies reported an association between high protein intake and increased risk of type 2 diabetes [39, 40]. Recently, a large European cohort study showed that high total and animal protein intake was associated with a modest elevated risk of type 2 diabetes [41]. Research suggests that the source of protein intake might be of relevance. Type 2 diabetes risk was associated with higher meat consumption, especially red and processed meat [42-44]. High intakes of dairy products, low-fat dairy products, and cheese were associated with a decreased risk of type 2 diabetes [45]. No consistent evidence exists on the association between fish consumption and the risk of type 2 diabetes, possibly due to heterogeneity among populations [46, 47].

Moderate alcohol intake (1-2 drinks per day) has been associated with reduced risk of type 2 diabetes [48, 49]. The mechanisms behind this association are unclear, but

there are several factors that may explain the relationship, including increases in insulin sensitivity after low levels of alcohol consumption [50]. A prospective study showed that moderate alcohol consumption combined with healthy lifestyle behaviours add to a decreased risk of type 2 diabetes [51].

In conclusion, there is no definite consensus on which dietary treatment is most appropriate to prevent development of type 2 diabetes and weight gain [37, 52]. Lifestyle interventions, however, have shown that an increased intake of dietary fibre and a reduced intake of total fat and saturated fat in combination with modest weight reduction and increased physical activity could reduce the risk of type 2 diabetes in subjects with glucose intolerance even many years after the end of the intervention [16-18, 53-56].

Physical inactivity

Physical inactivity is the fourth leading cause of global mortality [57] and data show that 31% of the world's adult population is physically inactive [58]. Evidence shows that physical inactivity increases the risk of coronary heart disease, type 2 diabetes, and breast and colon cancer, and shortens life expectancy [59]. Additionally, physical activity is a key determinant of energy expenditure, thereby contributing to energy balance and weight control [57]. Worldwide it was estimated that physical inactivity causes 7% of the burden of disease from type 2 diabetes [59]. Several studies have shown that increased physical activity can reduce the risk of type 2 diabetes [16-18, 60, 61]. A potential mechanism for the beneficial effects of physical activity is that it increases glucose uptake into active muscles, which improves insulin sensitivity [62]. Furthermore, physical activity may help produce weight loss, thereby contributing to improved insulin sensitivity. The American Diabetes Association and the American College of Sports Medicine have stated that a combination of aerobic exercise training and resistance training should be undertaken to prevent type 2 diabetes in high-risk adults [63, 64]. In these guidelines, it is advised to perform at least 150 min/week of moderate-intensity aerobic physical activity, spread over at least three days per week with no more than two consecutive days without exercise. In addition, these guidelines suggest that moderate or vigorous resistance training that involves the major muscle groups should be undertaken at least twice weekly on non-consecutive days [63]. A recent meta-analysis showed that interventions with combined aerobic and resistance training might be the most efficacious exercise modality to improve glycaemic control and blood lipids compared to the isolated effects of either aerobic or resistance training [65].

PREVENTION OF TYPE 2 DIABETES BY LIFESTYLE MODIFICATION

Type 2 diabetes can be prevented when modifiable risk factors are avoided. Lifestyle modification, therefore, could be a successful strategy to tackle the diabetes epidemic. This paragraph summarises evidence on diabetes prevention from lifestyle interventions in experimental and real-world settings and their effects on the long term.

Lifestyle interventions in experimental settings

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 many individuals at high risk. In 1986, the Chinese Da Qing IGT and diabetes study was one of the first studies to investigate whether diet and exercise interventions in subjects with IGT could delay the development and reduce the incidence of type 2 diabetes [55]. Five hundred seventy-seven subjects with IGT were randomised into one of four groups: diet-only, exercise-only, diet plus exercise, or control group. Follow-up examinations were conducted over a 6-year period to identify subjects who developed type 2 diabetes. At six years, there was an overall reduction in the incidence of diabetes of 31% in the diet-only group, 46% in the exercise-only group, and 42% in the diet plus exercise group [55]. After 23 years of follow-up, diabetes incidence in the intervention group (all three active treatment groups combined) was significantly lower than in the control group (73 vs. 90%) [56]. In the Finnish Diabetes Prevention Study (DPS) it was aimed to evaluate whether an intensive diet plus exercise programme could prevent or delay type 2 diabetes [16]. In this large trial, 522 subjects with overweight and IGT were randomised to either the lifestyle intervention group or the control group. The lifestyle intervention, with a median follow-up period of four years, involved tailored advice aimed at weight reduction, total and saturated fat intake reduction, and increased fibre intake and physical activity. After four years of intensive intervention, the relative risk reduction was 58% [16]. Seven years after baseline, a 43% reduction in the relative risk was shown and after 13 years from baseline, there was a 38% risk reduction [53]. The US Diabetes Prevention Program (DPP) was developed to evaluate the efficacy of both an intensive lifestyle intervention and standard lifestyle recommendations combined with metformin in preventing or delaying the development of type 2 diabetes [66]. A total of 3,234 subjects with elevated fasting and post-load plasma glucose concentrations were randomised into one of three groups: lifestyle modification group, metformin, or control group. The lifestyle modification programme consisted of a 16-lesson curriculum covering diet, exercise, and behaviour modification and was aimed to achieve and maintain a weight reduction of at least 7% of initial body weight, and to achieve and

maintain a level of moderate-intensity physical activity of at least 150 minutes per week. The mean follow-up period was 2.8 years. At the end of the study period, the lifestyle intervention reduced diabetes incidence by 58% and metformin by 31% compared with the control group [17]. Ten years after randomisation, diabetes incidence was reduced by 34% in the lifestyle group and 18% in the metformin group compared with the control group [54]. In the Netherlands, the Study on Lifestyle intervention and Impaired glucose tolerance Maastricht (SLIM) was designed to evaluate the effect of a combined diet and physical activity intervention programme on glucose tolerance in subjects with IGT [67, 68]. A total of 147 subjects were randomised to the lifestyle intervention group or the control group. The lifestyle intervention, with a mean follow-up period of 4.1 years (range 3-6 years), consisted of personal advice on dietary intake and physical activity and participants were encouraged to participate in a combined aerobic and resistance exercise programme. This study has shown 58% reduction in diabetes risk after three years of intervention and 47% reduction at the end of the intervention [18, 68].

Lifestyle interventions in real-world settings

The evidence from studies in experimental settings calls for translation and implementation of diabetes prevention programmes in real-world settings to guide diabetes prevention policies. As real-world settings are complex and limited in finances and resources, it is a challenge to implement cost-effective and sustainable interventions [69-71]. Real-world diabetes prevention programmes have been investigated in several studies. Multiple reviews showed significant reductions in weight but inconclusive results for metabolic indicators of diabetes risk, such as blood glucose or HbA1c [70-74]. In 2003-2008, the Finnish National Program for the Prevention of Type 2 Diabetes (FIN-D2D) was one of the first large-scale nationwide diabetes prevention programme in the world, aimed to include prevention of diabetes and reduction of cardiovascular risk factor levels among high-risk individuals in daily routines in health care centres and occupational health care clinics [75]. Altogether 10,149 individuals at high risk of diabetes were identified and followed up for one year. The lifestyle intervention consisted of either individual counselling visits or group sessions, focused on weight control, dietary intake, and exercise. After one-year follow-up, weight loss was on average 1.1 kg, waist circumference reduced by 1.3 cm, blood pressure decreased, and the lipid profile changed in a less atherogenic direction. Altogether 17.5% of the subjects lost $\geq 5\%$ weight. Diabetes risk reduced by 69% in the group who lost $\geq 5\%$ weight compared with the group who maintained weight [75]. The US DPP has been translated and implemented in many real-world settings like community environments and health care facilities.

Ali *et al.* summarised 28 lifestyle interventions that were modelled on the DPP [76]. These programmes consisted of individual or group sessions, or a combination of both, and the median study duration was twelve months. Across all studies, mean weight change was -3.99% at 12-month follow-up [76]. In the Netherlands, several studies were conducted in primary health care settings. Most of these studies showed modest, albeit non-significant, changes in body weight and no changes in risk factors like dietary intake and physical activity [77-80].

Maintenance of lifestyle modification

To ensure diabetes prevention, lifestyle modifications need to be maintained in the long term. Lifestyle interventions that were conducted in experimental settings have shown that reduced diabetes risk can be sustained over long term, up to 23 years after baseline [53, 54, 56]. However, current evidence for sustainability and long-term clinical benefits of lifestyle interventions in real-world settings is limited [70, 73, 81]. It has been shown that maintaining weight loss reduced diabetes incidence [19, 20], however, it is well-known that weight regain is common [82, 83], even in successful lifestyle interventions [53, 54]. Factors that might facilitate maintenance of behaviour change are social support, self-efficacy, and relapse prevention strategies, while comorbidities, lack of time, and psychological stress are perceived as barriers for maintenance [84-86].

EXPLAIN INTERVENTION EFFECTIVENESS

A comprehensive evaluation approach is required, as interventions in real-world settings are often complex and not delivered in tightly controlled environments [87, 88]. Within this approach, the scope of evaluation research needs to be broadened from assessing only effectiveness to also getting insight in intervention characteristics (e.g. setting, delivery mode, intervention provider), intervention components (e.g. behaviour change techniques and strategies), and intervention implementation [89, 90]. This will provide insight in the so-called 'black-box', that is identify aspects that explain what works, how, and why [87, 88]. Therefore, studies need to include a process evaluation to establish the validity of the hypothesised causal processes for behaviour change, and taxonomies can be used to describe behaviour change techniques used to modify these processes [90]. Several systematic reviews on dietary or physical activity interventions (or both), showed that greater intervention effectiveness was associated with targeting both diet and physical activity [90], mobilising social support [90], and the use of behaviour change techniques (e.g. self-monitoring, relapse prevention, and individual tailoring) [90-92]. Furthermore, effectiveness was associated with using

self-regulatory techniques (goal setting, self-monitoring, and providing feedback on performance) [90, 92] and providing higher intensity interventions [74, 90, 93]. There were no clear associations between intervention effectiveness and setting, delivery mode, delivery provider, or study population [74, 90, 93].

ECONOMIC EVALUATION OF TYPE 2 DIABETES PREVENTION

In addition to insight into effective intervention components, it is also important to gain insight into costs and benefits of lifestyle interventions for several reasons. Firstly, diabetes causes a large economic burden [1] and resources are limited [69]. Secondly, policymakers need to be provided with information to make a decision whether or not to sustain and implement lifestyle interventions in the real world [94]. A review found evidence for cost-effectiveness of diabetes prevention interventions in experimental settings [95], including the DPP and DPS lifestyle interventions [96, 97]. Also the Dutch SLIM study proved to be cost-effective: the cost-effectiveness ratio for the lifestyle intervention was € 3,900–5,500 per QALY [98]. Although evidence is accumulating that lifestyle modification may be cost-effective in prediabetic patients, information on cost-effectiveness of interventions implemented in community and primary health care settings is limited [99]. Evidence from well-conducted pragmatic trials is needed to gain insight into cost-effectiveness of diabetes prevention interventions in real-world settings. Nowadays, this information becomes more and more available. Recently, a systematic review found that diet and physical activity programmes, mostly based on the DPP and DPS studies, were cost-effective from a health care perspective [99]. However, a Dutch study that investigated the cost-effectiveness of a primary care lifestyle intervention for prevention of type 2 diabetes and cardiovascular disease showed that the intervention was cost-saving without being effective [100]. Another Dutch study, on the prevention of weight gain among employees, failed to reveal cost-effectiveness too [101]. It should be considered that comparing results of economic evaluations is difficult because of the diverse nature of lifestyle interventions and methodological differences [102].

THE SLIMMER STUDY: RATIONALE AND OBJECTIVES

Although prevention of type 2 diabetes by lifestyle modification has been shown to be effective, translation and implementation of a (cost-)effective diabetes prevention programme in Dutch primary health care was lacking at the start of this study. Therefore the SLIMMER study (SLIM iMplementation Experience Region Noord- en Oost-Gelderland) was started in which the SLIM intervention, revealing a 47% risk reduction

[18], was translated to Dutch primary health care. The SLIMMER study was aimed to reduce the risk of developing type 2 diabetes by improving lifestyle behaviour in subjects at high risk. The SLIMMER study was a randomised, controlled intervention study, carried out in Apeldoorn and Doetinchem, two cities in the eastern part of the Netherlands, by a consortium of Wageningen University and the community health service Noorden Oost-Gelderland. The project was coordinated by the community health service in close collaboration with both municipalities. The SLIMMER intervention, which resembled the SLIM intervention [18], was a 10-month combined lifestyle intervention consisting of a dietary and physical activity component, including case management and a maintenance programme. The SLIMMER intervention was implemented in Dutch public health and primary health care, involving general practitioners and their practice nurses, dietitians, physiotherapists, and sports clubs.

The overall objectives of the SLIMMER study were (1) to translate the SLIM intervention into the SLIMMER intervention and implement this SLIMMER intervention in Dutch primary health care, and (2) to investigate the effectiveness of the SLIMMER intervention in Dutch primary health care.

During the first phase of the SLIMMER study (2008-2010), the evidence-based SLIM intervention [18] was translated into the SLIMMER intervention (Figure 1.1). This was done in a joint decision-making process between SLIM intervention developers and local health care professionals. This translational process has been described by Jansen *et al.* [103]. During the second phase (2010-2011), the SLIMMER intervention was pilot-tested ($n = 31$) in the municipality of Apeldoorn, using a one group pre-test post-test design. During the last phase (2011-2014), a large-scale implementation of the SLIMMER intervention ($n = 316$) was conducted, using a randomised controlled design. A maintenance programme has been developed and integrated into the 10-month SLIMMER intervention, which has been described by Elsman *et al.* [104]. Process, effect and economic evaluations have been performed.

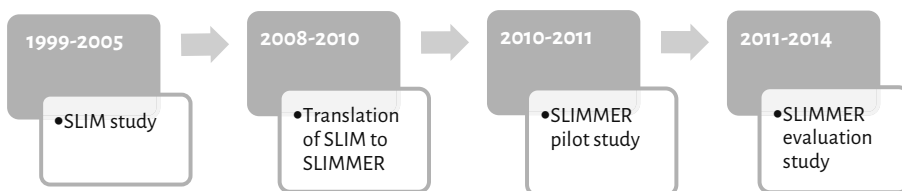


Figure 1.1. Timeline of the SLIMMER project.

In this thesis the following research objectives are addressed:

1. To describe and investigate the feasibility and impact of the SLIMMER intervention in Dutch primary health care (*Chapters 2 and 3*).
2. To investigate the effectiveness of the SLIMMER intervention in Dutch primary health care on behavioural determinants, eating and physical activity behaviour, health, and quality of life (*Chapters 4 and 5*).
3. To examine the implementation of the SLIMMER intervention in Dutch primary health care (*Chapter 6*).
4. To assess the cost-effectiveness of the SLIMMER intervention in Dutch primary health care (*Chapter 7*).

OUTLINE OF THIS THESIS

This thesis is based on a pilot study and a randomised controlled trial conducted between 2010 and 2014 in Apeldoorn and Doetinchem in the Netherlands in adults at high risk of developing type 2 diabetes.

Chapter 2 gives an overview of the translation of the SLIM diabetes prevention intervention to a Dutch real-world setting, with special attention for the roles of general practitioners and other professionals in implementing lifestyle intervention programmes in primary health care. Furthermore, it is discussed what is known from literature about translation of trials to primary health care and what the role perception is of professionals working in primary health care.

Chapter 3 describes the effect of the SLIMMER pilot study ($n = 31$) on the feasibility and desired impact. Furthermore, refinements are identified that are made prior to further implementation and evaluation.

Chapter 4 presents the background and methods of the SLIMMER randomised controlled trial investigating the effectiveness of an intensive lifestyle intervention in

primary health care. A logic model of change which links intervention activities with intervention outcomes in a logical order is given, as well as a detailed description of the study design, setting, study population, lifestyle intervention programme, and the evaluation design.

Chapter 5 describes results of the randomised controlled trial ($n = 316$) in which effectiveness of the SLIMMER intervention on clinical and metabolic risk factors, dietary intake, physical activity, and quality of life after 12 months was assessed. In addition, results on maintenance of effects after 18 months are described.

Chapter 6 presents results of the process evaluation, using an extensive evaluation plan with quantitative and qualitative methods. This chapter describes how the SLIMMER intervention was delivered and received in Dutch primary health care and how this could explain intervention effectiveness.

Chapter 7 describes the economic evaluation of the SLIMMER intervention. Cost-effectiveness of the SLIMMER intervention compared with usual health care was assessed from both a societal and health care perspective. Sensitivity analyses were performed to assess cost-effectiveness using different input parameters.

Chapter 8 summarises the main findings of this thesis and discusses methodological issues. The results are discussed in a broader perspective and implications for primary health care, Dutch health policy, and future research are given.

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Chapter 2

Translating the SLIM diabetes prevention intervention into SLIMMER: implications for the Dutch primary health care

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ABSTRACT

All over the world, prevalence and incidence rates of type 2 diabetes mellitus are rising rapidly. Several trials have demonstrated that prevention by lifestyle intervention is (cost-) effective. This calls for translation of these trials to primary health care. This article gives an overview of the translation of the SLIMMER diabetes prevention intervention to a Dutch real-life setting and discusses the role of primary health care in implementing lifestyle intervention programmes. Currently, a 1-year pilot study, consisting of a dietary and physical activity part, performed by three GPs, three practice nurses, three dieticians and four physiotherapists is being conducted. The process of translating the SLIM lifestyle intervention to regular primary health care is measured by means of the process indicators: reach, acceptability, implementation integrity, applicability and key factors for success and failure of the intervention. Data will be derived from programme records, observations, focus groups and interviews. Based on these results, our programme will be adjusted to fit the role conception of the professionals and the organization structure in which they work.

INTRODUCTION

All over the world, prevalence and incidence rates of type 2 diabetes mellitus (T2DM) are rising rapidly [1]. This trend is also seen in the Netherlands. It is expected that the number of people with diagnosed diabetes will double to 1.3 million in 2025, accounting for 8% of the total population [2]. This rising problem contributes to a large disease and economic burden. In 2005, the costs for diabetes care amounted to a total of 813.8 million Euros, accounting for 1.2% of the total health care costs in the Netherlands [3]. In addition, ~30% of the Dutch population aged ≥ 60 years suffers from pre-diabetes [impaired glucose tolerance (IGT) and/or impaired fasting glucose] and approximately one-third to two-thirds of them are expected to develop T2DM within 6 years [4].

Theoretically, over 50% of the expected increase in the number of diabetes patients can be avoided by prevention, especially when focussing on high-risk groups with pre-diabetes [2]. Several international trials have demonstrated a 29-67% reduction in the incidence of T2DM for adults with IGT who participated in lifestyle interventions targeting dietary behaviour and activity pattern [5-9]. The potential for cost savings due to such interventions is also considerable. Roumen *et al.* [10] concluded in their review that, in general, the implementation of lifestyle intervention as a therapy to prevent and postpone T2DM and its complications looks promising, and cost-effectiveness seems acceptable.

The Dutch SLIM study (Study on Lifestyle intervention and Impaired glucose tolerance Maastricht) was designed to investigate whether a combined diet and physical activity intervention programme could improve glucose tolerance in subjects with a high risk for developing T2DM. In total, 147 subjects with IGT were randomly allocated to either the intervention or control group. The intervention programme, based on the Diabetes Prevention Study (DPS), was developed in 1999, using a combination of theories, such as Stages of Change model [11] and the Theory of Planned Behaviour [12], and tools such as motivational interviewing [13] and goal setting. The intervention group received personal dietary advice by a skilled dietician, trained in motivational interviewing and goal setting, based on the Dutch guidelines for a healthy diet, during a 1-hour counselling session every 3 months. Additionally, subjects were advised to increase their level of physical activity to at least 30 minutes a day for at least 5 days a week. A body weight loss of 5-7% was the objective. Moreover, subjects were encouraged to participate in a combined aerobic- and resistance exercise programme at an intensity of at least 70% of their maximal peak oxygen consumption ($\text{VO}_{2\text{max}}$). Control subjects were only briefly

informed about the beneficial effects of a healthy diet and physical activity, whereas no individual advice was provided [14, 15]. The SLIM study was effective in improving dietary composition, increasing VO_2 max and reducing diabetes risk by 47% over a mean period of 4.1 years at costs generally acceptable to society [15-17].

Internationally, more examples of diabetes prevention interventions are available. The Finnish DPS was the first large, well-controlled long-term lifestyle intervention to prevent diabetes. A total of 522 middle-aged, overweight subjects with IGT [based on two oral glucose tolerance tests (OGTTs)] were randomly allocated to either a control or intervention group. The control group received only general advice about healthy lifestyle at baseline. The intervention group had seven individual sessions with a study nutritionist during the first year and a session every 3 months thereafter aimed at reducing weight by consuming a healthy diet. Intervention subjects were also guided individually to increase their physical activity. After a mean follow-up time of 3.2 years, the risk of diabetes was reduced by 58% in the intervention group. After an extended follow-up time of in total 7 years, the relative risk reduction was still 43% [7]. Furthermore, the lifestyle intervention was estimated to be cost saving for the health care payer and highly cost-effective for society as a whole [18].

The US Diabetes Prevention Program (DPP) compared the efficacy of an intensive lifestyle intervention (intervention group) with standard lifestyle recommendations (control group). A total of 3234 high-risk subjects with IGT and slightly elevated fasting plasma glucose (FPG) were recruited. Lifestyle intervention in this study was primarily undertaken by case managers called lifestyle coaches. The main goal of the DPP was to achieve and maintain a 7% weight reduction by consuming a healthy, low-calorie low-fat diet and to engage in physical activities of moderate intensity ≥ 150 minutes/week. The lifestyle intervention commenced with a 16-session core curriculum with basic information about nutrition, physical activity and behavioural self-management, followed by a post-core adherence/maintenance phase. The DPP showed a 58% risk reduction at 2.8 years mean follow-up [19]. Furthermore, the lifestyle intervention showed to be cost-effective from both a health system and a societal perspective [20, 21].

Although diabetes prevention studies are available, they are not easily applicable in public health practice. This is due to the fact that experimental trials are designed to answer scientific questions on the relation between lifestyle and diabetes. They are

designed to secure a high internal validity, not to achieve a high external validity. They are therefore carried out under strictly controlled conditions that do not resemble everyday real-life. Thus, implementing these interventions in daily practice may require changes in, e.g. subject screening and selection; intervention frequency and duration; intervention strategy and materials and skills of professionals who deliver the intervention. These changes do have implications for the intervention (cost-) effectiveness.

In this article, we give an overview of the translation of the SLIM diabetes prevention intervention to a Dutch real-life setting, with special attention for the roles of GPs and other professionals in implementing lifestyle intervention programmes in primary health care. We will discuss what is known from literature about translation of trials to primary health care, and the role conception of professionals working in primary health care; how the SLIM lifestyle intervention will be translated into the SLIMMER intervention in order to be applicable in a Dutch primary health care setting and what the role of primary health care professionals is in implementing lifestyle interventions.

TRANSLATING TRIALS INTO PRIMARY HEALTH CARE

Recently, all over the world, diabetes prevention trials are being implemented into daily practice. One example is the translation of the Finnish DPS to several Finnish and Australian primary health care community and workplace settings. The Finnish 'National Program for the Prevention of Type 2 Diabetes' (FIN-D2D), based on the DPS, has been implemented in health care centres and occupational health care outpatient clinics [22]. Altogether 2798 individuals at high risk for diabetes were identified in the general population by nurses with the Finnish diabetes risk score (FINDRISC; scoring ≥ 15 points). High-risk individuals underwent an oral glucose tolerance test; the nurse or GP referred eligible individuals to a lifestyle intervention that focussed on weight management and physical activity. Several intervention alternatives were provided, like group intervention, individual intervention and self-initiated actions. The lifestyle interventions were delivered mostly by public health nurses in collaboration with local multi-professional teams. After 1 year of follow-up, the study showed beneficial changes in cardiovascular disease risk factors and glucose tolerance in both sexes [22, 23]. Furthermore, the Finnish 'Good Ageing in Lahti Region' (GOAL) study, also based on the DPS, was implemented in primary health care centres [23]. In each primary health care centre, patients with already-identified risk factors were referred to the study nurse. Risk status was screened with the FINDRISC score; patients with a score

≥12 point were recruited to the trial [24]. The intervention consisted of six sessions of task-oriented socio-behavioural group counselling by public health nurses over a period of 8 months. The study showed that a significant risk reduction at 12 months in weight, body mass index and serum total cholesterol was maintained at 36 months [25]. A comparable lifestyle intervention, based on the Finnish GOAL study, was conducted in Australian primary health care setting: the Greater Green Triangle (GGT) Diabetes Prevention Project. Patients were opportunistically screened by study nurses at local general practices with the FINDRISC score (scoring ≥12 points). The intervention was delivered by trained study nurses, dieticians and physiotherapists and found reductions in risk factors approaching those observed in clinical trials [26]. The DPS was also implemented in a Finnish airline company. Finnair employees were invited for an annual health examination, including physical examinations, laboratory tests, questionnaires and counselling by an occupational health nurse or physician [23]. The FINDRISC score, fasting blood glucose and/or glucose tolerance test were used to classify participants as having a low, increased or high risk of T2DM. Those with an increased or high risk were referred to a diabetes nurse or a nutritionist for individual counselling. Results of the effectiveness are not yet available [23].

Also the US DPP lifestyle intervention has been translated to a variety of settings, including YMCAs (Young Men's Christian Associations), churches, primary care practice settings and health care settings [27]. Prevention screening assessments included collection of medical and family history, fasting lipid and glucose levels, blood pressure, height, weight and waist circumference. The goals and key learning objectives of the DPP curriculum have been maintained, but modifications to the DPP lifestyle intervention on implementation were made, including offering group delivery rather than individual delivery, reducing the number of core-curriculum sessions from 16 to 12, concentrating on healthy-food choices rather than the food pyramid specifically, emphasizing initially on fat intake and calories instead of fat intake only and introducing pedometer use during core sessions instead of during maintenance phase. The manual was also updated to reflect current standards [27]. The findings show improvements in dietary and physical behaviour that are comparable to those achieved in the DPP [27-31].

In short, international studies translated clinical diabetes prevention trials to a specific context, taking the health care system of the country concerned into account, as recommended by the IMAGE evidence-based guidelines on type 2 diabetes

prevention [32]. However, although international and Dutch effective studies exist, translation to Dutch practice is still lacking.

TRANSLATING SLIM INTO SLIMMER

In the Netherlands, a project has been started to implement the SLIM intervention in a real-life setting. This project is called SLIMMER (SLIM iMplementation Experience Region gelre-ijssel) and consists of three steps: (i) translation of the SLIM intervention to practice, together with professionals from prevention and primary health care, (ii) implementation of the modified intervention in a 1-year pilot study by three general practices, guided by process evaluation and (iii) extension of the SLIMMER intervention in primary health care, guided by effect evaluation and cost-effectiveness analyses.

In this article, we focus on the second step, the first step will be described in detail in a separate article currently under construction. In short, a modified Delphi technique was used with the aim of reaching a consensus between SLIM researchers and local health care professionals on the adaptations needed to make the SLIM intervention applicable in a Dutch real-life setting. In three rounds, key elements of the SLIM intervention were identified, rated for applicability and adapted.

Pilot implementation, guided by process evaluation

In the second step, we will test the adapted SLIMMER intervention for its actual applicability in a Dutch primary health care setting. For this, a 1-year pilot study is currently being conducted in three general practices. A process evaluation is included, in order to assess reach, acceptability, implementation integrity, applicability and key factors for success and failure of the intervention. Elaborated information and data will be given in a forthcoming article on the results of the pilot study. Therefore, here subjects and methods will be described briefly.

Recruitment of subjects

Participants for the pilot were recruited by three GPs in the municipality of Apeldoorn (Figure 2.1) from their patient registration database in August and September 2010. Apeldoorn has been selected as pilot municipality because it can be considered as an average, middle-sized Dutch city (population 156000), representative for Dutch real-life setting in general. The three selected GPs were assumed to be representative for their professional group in Apeldoorn and are considered as local pioneers in the field of diabetes prevention. Each GP selected a sample of patients aged 40-65 years with

impaired fasting glucose (fingerprick fasting capillary blood glucose >5.6 and <6.0 mmol/l or fasting venous blood glucose >6.1 and <6.9 mmol/l). Exclusion criteria were: not being able to speak the Dutch language; cognitive dysfunction or any co-morbidity that made participation in a lifestyle intervention impossible.



Figure 2.1. Map of the Netherlands with pilot municipality Apeldoorn.

The GPs sent all eligible patients a letter and flyer to inform them about the SLIMMER programme and to invite them for an information meeting. Two weeks after sending the invitation letter, practice nurses called the patients to invite them again for the information meeting and to motivate them to participate if necessary. A short non-response survey was conducted in case patients were not willing to participate. Finally, an information meeting was organized by the practice nurse in collaboration with the GP, a dietician and a physiotherapist. During this meeting, patients were given all details of the programme. They were also introduced to the professionals involved in the programme. After the information meeting, patients gave their written informed consent.

Lifestyle intervention programme

The adapted SLIMMER intervention resembles the SLIM intervention (described in the introduction). In short, the programme consists of a dietary and physical activity part (Table 2.1). Six times per year, a skilled dietician gives personal dietary advice (30-60 minutes per visit; in total 4 hours/year per participant) based on the Dutch guidelines for a healthy diet 2006 [33]. Individual consults instead of group-based consults are used because this is in accordance with the Dutch regular primary health care. The Dutch guidelines for a healthy diet refer to a carbohydrate intake of >50% of energy consumed (E%), a total fat intake of 30-35 E%, a saturated fat intake of <10 E%, a fibre intake of >30 g/day and a protein intake of 1.2 g/kg body weight per day. Topics that are being discussed during visits are the Dutch guidelines for a healthy diet, artificial sweeteners and special occasions, e.g. a party. If desired, spouses can join the visits. In addition, the dietician organizes a group session aimed at sharing experiences, motivating each other and discussing the topic of label reading. Subjects are being encouraged to quit smoking, and if necessary drink less alcohol. A body weight loss of 5-10% is the objective. Furthermore, the dietician encourages subjects to increase their physical activity level to at least 30 minutes a day for at least 5 days a week. The dietician uses motivational interviewing to assist individuals aiming to achieve a positive attitude towards changes in diet and physical activity. Goals for behavioural change are being set every visit, evaluated in the next visit and, if necessary, adjusted.

The physical activity part consists of a combined aerobic- and resistance exercise programme at the physiotherapist's practice, in which subjects participate at an intensity of at least 60-90% of their maximal peak oxygen consumption (VO_2max). The training sessions with a duration of 1 hour are group-based and supervised by a physiotherapist. Subjects have free access to these training sessions and are stimulated to participate for at least 1 hour/week. In addition, the physiotherapist gives individual advice on how to increase daily physical activity (walking, cycling, swimming or running), based on the PACE questionnaire (adapted version based on van Sluijs *et al.* [34]), and goals are set.

Table 2.1. Details of the SLIMMER lifestyle intervention programme.

Lifestyle intervention programme – 1 year
<i>Dietary intervention</i> <ul style="list-style-type: none">• Six times/year individual nutrition advice by dietician• Based on Dutch dietary guidelines• One group session on label reading• Goal: 5-10% weight reduction
<i>Physical activity intervention</i> <ul style="list-style-type: none">• Weekly group sessions by physiotherapist• Combined aerobic- and resistance exercise programme• Individual advice on physical activity in daily life• Goal: increase physical activity to at least 30 minutes/day on at least 5 days/week

Process evaluation

Process evaluation will be performed to investigate how the intervention was implemented, what activities occurred under what conditions, by whom and with what level of effort. Process measures, among others based on the indicators as defined by Nutbeam [35], are:

- Reach: did the programme reach all of the target population?
- Acceptability: is the programme acceptable to the target population and the health professionals who delivered the intervention?
- Implementation integrity: was the programme implemented as planned? Why or why not?
- Applicability: does the programme fit into the health care structure, the social and cultural environment, the organizational system of local health and welfare organizations and professional working standards?
- Key factors for success and failure.

To investigate programme reach, programme records are used to assess the number of implemented activities and the number of attending participants. Dropouts and unreached eligible subjects are examined to assess whether this group differs from those participating and to identify reasons for non-participation.

To assess acceptability, implementation integrity and applicability, multiple methods will be used: observations, semi structured interviews and focus groups. Key factors for success and failure will be derived from all methods used in the process evaluation.

Based on literature and observation methods used in other interventions, a structured observation method has been developed. The following activities of the pilot

intervention will be observed: the information meeting for patients and the visits to the practice nurse, dietician and physiotherapist. The following aspects of these activities will be studied: acceptability and appropriateness of the location; the use of materials; course of the meeting or visit (which parts were discussed, when and how well?); involvement, communication and skills of the professionals; enthusiasm, motivation and appreciation of participants and the mood and feelings of the observer.

In addition, focus group sessions will be used to assess acceptability of the intervention to professionals as well as participants and implementation integrity of the intervention. Focus group sessions will be held with participating professionals (GPs and practice nurses, dieticians and physiotherapists) and participating patients separately. An item list will be developed to guide these sessions. Questions relate to experiences with several parts of the intervention, the use of materials, communication, barriers and facilitations. An experienced focus group leader will guide the focus group sessions. Furthermore, semi structured interviews will be held with some of the professionals and participants to obtain more in-depth information on acceptability, implementation integrity, applicability and key factors for success and failure. An item list will be developed to guide the interviews, covering topics like expectations, experiences and suggestions for modifications. One of the researchers will guide the interviews.

Measures of health effects are also included in the pilot study to evaluate whether the measurements will be acceptable to the patients in the effectiveness study (Step 3 in the translational process). The following measurements are included: body weight, waist and hip circumference, FPG values, blood pressure, medical history, aerobic fitness (SteepRamp test), motivation for physical activity (PACE questionnaire) and dietary behaviour. Other effect measures, like glucose and cholesterol, are not included because measuring these indicators is not the aim of the pilot study.

Data of the process evaluation will be used in order to optimize the programme for the Dutch real-life setting. Finally, the intervention will be expanded, guided with an effect evaluation and cost-effectiveness analyses, including all the above-mentioned health indicators (this is Step 3 of the translational process).

THE POSITION OF PRIMARY HEALTH CARE

Primary health care professionals have an important role in implementing lifestyle intervention programmes. Hiddink *et al.* [36] recognized that GPs are trusted sources

of nutrition information by adults because they had a high referral score, high perceived expertise and they reached nearly all segments of the population. This view is shared by the Heelsum Collaboration on Nutrition in Primary Care, as described by van Weel: 'opportunity through regular contacts with patients (continuity of care), central position in the health care system and trust with "their" patients' [37]. Over the last years, a tendency can be seen for the GP as nutrition counsellor towards gatekeeper of the health care system, working together with other professionals from primary health care and public health [38-41]. Generally, GPs have an interest in nutrition and perceive themselves as being able to give dietary advice in the treatment and prevention of coronary heart disease [42]. However, GPs experience barriers for giving nutrition guidance to their patients, most importantly not being trained in nutrition, lack of time to address nutrition issues and GPs perception that patients lack motivation to change lifestyle and/or dietary patterns [43, 44]. These main barriers were also found by Kushner [45] and Helman [46]. Therefore, a promising possibility is to transfer the dietary and/or physical activity advice to other disciplines in primary health care in order to alleviate the responsibilities of the GP as is done in SLIMMER. In addition, we see a movement towards synergy between primary health care and public health over the last years [41]. This has been expanded in the sixth Heelsum International Workshop themed 'Practice-based evidence for weight management: alliance between primary care and public health' [47].

Within combined lifestyle interventions, it is important that one professional has the lead and the overview over the programme. This is indicated as case management. The case manager should work together with all the professionals involved in the alliance between primary health care and public health. Which professional should have the role of case manager in combined lifestyle interventions is a matter of discussion. In a Dutch lifestyle intervention, the BeweegKuur programme, the lifestyle advisor is the pivot of the intervention. Often the lifestyle advisor is a practice nurse, who is designing an individual exercise programme and providing coaching and supervision [48]. Also in the UK Counterweight programme, it is the practice nurse who plays a key role in the delivery of the lifestyle intervention, with initial guidance, training and facilitation by weight management advisors (all state-registered dietitians, who are proactive, creative and specially trained in health promotion and obesity management) [49]. In the US DPP, the intervention is undertaken by lifestyle coaches. The majority of these lifestyle coaches are registered dietitians, registered nurses and diabetes educators but also social workers, exercise specialists, pharmacists, physicians, psychologists and

emergency services technicians [27]. In the SLIMMER intervention, it is the GP who acts as a spider in the web, given his/her role as gatekeeper of the health care system, and works together with allied forces. GPs select eligible subjects and refer them to dieticians because they are one of the most important nutritional information sources for GPs [50]. In addition, GPs refer the subjects to physiotherapists for physical activity advice and support. GPs have the final responsibility for the quality of the delivered care, but practice nurses are the case managers in the SLIMMER intervention. They motivate subjects to participate in the intervention programme and they are in contact with the dieticians and physiotherapists. Which professional is in the best position of being a case manager depends on several factors like type of lifestyle intervention activities, time, money, interest, expertise and competences.

Regarding the collaboration between primary health care professionals and public health, both the community health service and local authorities are important partners within the last profession. The community health service may act as coordinator of the lifestyle intervention programme and has the health promotion expertise that is needed. The local authorities can bring several partners, from different disciplines and professions, together. Furthermore, they can secure the lifestyle intervention programme into local policy.

The tendency towards an alliance between primary health care and public health especially fits to the Dutch health care system. Currently, the Dutch primary health care sector and prevention sector are two different worlds since they are based on separate laws and financial systems. However, one of the main topics of the Dutch Public Health Act is to join forces of primary health care and public health, so that prevention is incorporated in the health care system [51]. Also Green [52] described the urgent need for an alliance between primary health care and public health. Avendonk *et al.* [53] described how the Dutch College of General Practitioners evaluated the situation and published the guidelines for obesity. Therefore, we consider the accomplishment of an alliance between primary health care and public health, such as established in the SLIMMER intervention, as a promising development and a necessary step in diabetes prevention.

CONCLUSION

Several trials, such as SLIM, DPS and DPP, have demonstrated that prevention of diabetes by lifestyle intervention is (cost-) effective. However, translation of diabetes prevention trials to Dutch real-life setting is lacking. Therefore, the SLIMMER project was developed in order to translate the SLIM intervention into Dutch daily practice, together with professionals from prevention and primary health care. Currently, the adapted SLIMMER intervention is being implemented in a pilot study and guided with a process evaluation in order to assess reach, acceptability, implementation integrity, applicability and key factors for success and failure. Based on these results, the programme will be optimized to fit the role conception of the professionals and the organization structure in which they work. Especially in the Dutch health care system, we consider collaboration between professionals from primary health care and public health needed now more than ever to combat the rising problem of diabetes.

DECLARATION

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The background of the page features a faint, light gray illustration of a person in a dynamic, almost dancing pose. The person is surrounded by numerous circles of varying sizes, some of which are highlighted with a white outline, creating a sense of movement and energy. The overall aesthetic is clean and modern.

Chapter 3

Feasibility and potential impact of the adapted SLIM diabetes prevention intervention in a Dutch real-life setting: the SLIMMER pilot study

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ABSTRACT

Objective

Pilot-testing of the adapted Study on Lifestyle intervention and Impaired glucose tolerance Maastricht (SLIM) and to determine its feasibility and likelihood of achieving desired impact.

Methods

Pilot intervention study (a 10-month combined lifestyle intervention) using a one group pre-test post-test design with on-going process measures (i.e. reach, acceptability, implementation integrity, and applicability) and several health outcomes (e.g. body weight).

Results

In total, 31 subjects participated in the SLIMMER (SLIM iMplementation Experience Region Noord- en Oost-Gelderland) intervention. Participant weight loss was -3.5 kg ($p = 0.005$). Both participants and health care professionals (i.e. practice nurses, dieticians, and physiotherapists) were satisfied with the intervention. The intervention was implemented as planned and appeared to be suitable for application in practice. Refinements have been identified and will be made prior to further implementation and evaluation.

Conclusion

Implementation of the SLIMMER intervention is feasible in a Dutch real-life setting and it is likely to achieve desired impact. Practising and optimising the intervention creates local support for SLIMMER among stakeholders.

Practice implications

Performing a pilot study on the basis of a structured approach is a meaningful step in the process of optimising the feasibility and potential impact of an evidence-based intervention in a real-life setting.

INTRODUCTION

Many experimental studies, such as the Finnish Diabetes Prevention Study (DPS), the US Diabetes Prevention Program (DPP), and the Dutch Study on Lifestyle intervention and Impaired glucose tolerance Maastricht (SLIM), have shown that moderate changes in diet and physical activity (PA) lead to a substantial and sustained reduction in the incidence of type 2 diabetes mellitus for individuals with impaired glucose tolerance (IGT) [1-8]. This evidence calls for an increase in the implementation of lifestyle interventions in public health practice in order to maximise possible health gains for individuals with IGT in society. Interventions which have been developed in experimental settings, however, are not necessarily suitable for implementation in real-life settings because these settings differ substantially [9-11]. Translation of lifestyle interventions from research to practice is, therefore, needed whereby effectiveness must be preserved. On the other hand, adaptations are inevitable within this translational process from research to practice, and this may have unknown consequences for the effectiveness of the intervention.

Translations from experimental interventions to real-life settings have previously been shown to be feasible. However, they appeared to have limited clinical benefits, possibly due to less control, less intensive methods, or practical issues of noncompliance [11, 12]. No experimental interventions have to date been translated to real-life settings in The Netherlands. For this project, the evidence-based SLIM intervention was translated into the SLIMMER intervention, which is designed to be applicable in a Dutch real-life setting [13]. To this end, the five-step guidance of McKleroy *et al.* has been applied, providing a systematic approach to adapt the intervention to and imbed it in a real-life setting while maintaining the scientific integrity that makes the intervention effective [14]. Firstly, core elements of the SLIM intervention were identified (*step 1: assess*) and consensus on suggested adaptations was achieved between SLIM intervention developers and local health care professionals in a joint decision making process (*step 2: select*). These adaptations were then incorporated in the new SLIMMER manual (*step 3: prepare*). These first three steps of McKleroy's guidance [14] have been described in detail elsewhere [15]. The next step in the adaptation process is to pilot-test the adapted intervention. The aim of this article is to describe the pilot-testing of the adapted SLIM intervention and to determine its feasibility (i.e. reach, acceptability, implementation integrity, and applicability) and likelihood of achieving desired impact. This was done in a 10-month lifestyle intervention, guided by process and outcome evaluation. The results from this pilot-test will be used to refine the adaptation and will serve as input for McKleroy's final and fifth step [14] of implementation and evaluation.

METHODS

This pilot study is part of a larger project called SLIMMER (SLIM iMplementation Experience Region Noord- en Oost-Gelderland (formerly called Region Gelre-IJssel)), which aims to implement an effective diabetes prevention intervention in a Dutch real-life setting.

Study design

This 10-month pilot intervention study ran from August 2010 until July 2011, using a one group pre-test post-test design with on-going process measures. Both qualitative and quantitative data collection approaches were used to investigate the feasibility of SLIMMER and the likelihood of achieving its desired impact. The study received ethical approval from the Medical Ethical Committee of Wageningen University.

Participants

Participants for the pilot study were recruited from August to September 2010 by three general practitioners (GPs) in the municipality of Apeldoorn from their patient registration database. Each GP selected a random sample of patients from the database aged 40 through 65 years with impaired fasting glucose (finger prick fasting capillary blood glucose >5.6 and <6.0 mmol/l or fasting venous plasma glucose >6.1 and <6.9 mmol/l [16]). Exclusion criteria were: not being able to speak and understand the Dutch language; cognitive dysfunction; or any comorbidity that made participation in a lifestyle intervention impossible. Recruitment of the participants has been described in detail elsewhere [13]. In short, GPs sent eligible patients a letter and flyer to inform them about the SLIMMER intervention and to invite them to an information meeting in their neighbourhood with all health care professionals involved (GP, practice nurse, dietician, and physiotherapist). Two weeks after sending the invitation letter, practice nurses called the patients to invite them to the information meeting again, and to motivate them to participate if necessary. During the information meeting, patients were given all details of the programme and afterwards they gave their written informed consent. A short non-response survey was conducted in case patients were not willing to participate.

Lifestyle intervention programme

The SLIMMER intervention resembled the SLIM intervention [17] and consisted of a dietary and physical activity component. In addition, the SLIMMER intervention fitted in with daily routines of Dutch GPs, practice nurses, dieticians, and physiotherapists.

Therefore, only minimal training, provided during a special two-hour SLIMMER kick-off training, was required to assure adequate delivery of the intervention by the health care professionals. Relevant details of the SLIMMER intervention are described below and additional details can be found elsewhere [13, 15].

Dietary intervention

Dietary recommendations were based on Dutch dietary guidelines [18]. A dietician gave tailored dietary advice during six individual consultations within the 10-month intervention period (30–60 min per consultation; in total 4 h per participant). If desired, spouses could join consultations. In addition, the dietician organised one group session aimed at sharing experiences, motivating each other, and discussing the topic of label reading. Subjects were encouraged to drink less alcohol, quit smoking if necessary, increase daily physical activity, and to participate in the physical activity intervention. The dietician, trained in motivational interviewing [19], assisted individuals to achieve a positive attitude towards changes in diet and physical activity. Goals for behaviour change were set every consultation, evaluated in the next consultation, and if necessary adjusted. The objective of the dietary intervention was to adopt, step by step, a sustainable healthy dietary pattern according to Dutch dietary guidelines.

Physical activity intervention

The physical activity intervention consisted of a combined aerobic and resistance exercise programme (proportion 2:1) at the physiotherapist's practice. Weekly training sessions with a duration of 1 h were group-based and supervised by a skilled physiotherapist. Sports groups were formed based on day and time preferences of the subjects and availability of the physiotherapists. Subjects had free access to the training sessions and were stimulated to participate for at least 1 h per week. In addition, the physiotherapist gave tailored advice on how to increase physical activity in daily life (e.g. bicycling, walking, gardening) and goals were set. The objective of the physical activity intervention was to increase the physical activity level of the participants to at least 30 min a day during at least five days a week.

Outcome and process measures

An outcome and process evaluation was performed to investigate feasibility and likelihood of the intervention. Several health outcomes and four process measures commonly used in process evaluations were included: reach, acceptability, implementation integrity, and applicability [20–23]. Process evaluation data were

collected and used to optimise the intervention programme. Outcome and process measures are described below. A detailed evaluation plan including measures and time points of data collection is provided in Additional file 3.1.

Outcome measures

Health care professionals performed health measures at baseline (T_0) and at the end of the intervention (T_1) to assess likelihood of achieving desired impact. Fasting plasma glucose was measured by practice nurses using a finger prick according to guidelines of the Dutch College of General Practices [16]. Furthermore, practice nurses measured blood pressure twice on the left arm with an electronic monitor. The average of two measurements was recorded. Dieticians measured body weight to the nearest 0.1 kg and height to the nearest 0.5 cm. Body Mass Index (BMI) was measured as the ratio of weight and height squared (kg/m^2). Waist and hip circumference were measured by dieticians to the nearest 0.5 cm. Waist circumference was obtained at the level midway between the lowest rib and the iliacal crest. Hip circumference was measured as the maximum circumference over the buttocks. Waist and hip measurements were performed in duplicate and the average of two measurements was recorded. Medication use was recorded by practice nurses in each of the following categories: hypertension, hypercholesterolemia, hypertriglyceridemia, and cardiovascular diseases. Fitness was measured using the SteepRamp Test [24, 25]. Physiotherapists performed this test on a calibrated cycle ergometer. After 3 min of unloaded cycling (at 25 W), the load was increased by 25 W every 10 s. Subjects were instructed to cycle with a pedal frequency between 60 and 80 rounds per minute (rpm). The test ended when pedal frequency fell below 60 rpm. Obtained maximal workload (the maximum short exercise capacity), time cycled at that load, and heart rate at the end of the test were reported. Maximal oxygen uptake (VO_2max) was estimated as follows: $\text{VO}_2\text{max (l/min)} = 0.0067 \text{ SteepRamp Wmax} + 0.358$ [24, 25]. Participants filled in questionnaires on perceived health, smoking, and physical activity. Perceived health was measured with the question “How would you rate your health, in general?” with answer categories poor, fair, good, very good, and excellent. This question was taken from the Short-Form Health Survey (SF-36), which has been shown to be a practical, reliable, and valid tool for both general and chronic disease populations in The Netherlands [26, 27]. Smoking was measured with the question “Do you smoke (sometimes)?” with answer categories yes, no but I used to (more than 15 years ago), no but I used to (less than 15 years ago), and no I never smoked. Physical activity was measured with the question “On how many days per week are you usually physically active for at least 30 minutes?” with answer categories ranging from

less than one day per week to 7 days per week. Questions on smoking and physical activity were measured according to standards of the national surveillance system for adults and the elderly in The Netherlands [28]. These national standards are based on best available scientific insights, experiences of local community health services, and expert opinions. Alcohol intake, fruit intake, and vegetable intake were assessed by a validated food frequency questionnaire [29].

Process measures

Reach was defined as 'the proportion of intended target audience that participated in the intervention'. Data on socio-demographic characteristics of participants and non-participants were collected according to standards of the national surveillance system for adults and the elderly in The Netherlands [28].

Acceptability was defined as 'the extent to which participants and health care professionals (i.e. practice nurses, dieticians, and physiotherapists) are satisfied with the intervention'. Participants' acceptability was assessed using questionnaires and evaluation forms. Furthermore, a focus group meeting ($n = 10$, duration of 1.5 h) was conducted to collect more in-depth information on acceptability [30]. Two participants of each sports group were randomly selected and invited by one of the researchers (GD). In case a participant was not able or willing to participate, another randomly selected participant was invited. A semi-structured focus group guide was developed. An experienced focus group leader (CdR) guided the meeting and one of the researchers (GD) assisted the focus group leader and took notes. Acceptability of health care professionals was assessed using telephone semi-structured interviews (practice nurses, $n = 3$, average duration of 17 min) and face-to-face semi-structured interviews (dieticians, $n = 3$, and physiotherapists, $n = 4$, average duration of 67 min). All health care professionals that implemented the SLIMMER intervention were invited to the interviews by one of the researchers (GD) and they were all willing to participate. A semi-structured interview guide was developed and all interviews were conducted by one of the researchers (GD).

Implementation integrity was defined as 'the extent to which the intervention was implemented as planned'. Professionals' implementation integrity was assessed by semi-structured inter-views ($n = 10$), as described above. Furthermore, a structured observation method was developed to track several intervention activities and aspects. The observations were performed by one of the researchers (GD).

Applicability was defined as 'the extent to which an intervention process can be implemented in the real-life setting'. Semi-structured interviews with professionals were conducted ($n = 10$), as described above.

Information on intervention optimisation was obtained from the collected process data as described above. Refinements in the adaptation process will be made prior to further implementation and evaluation in a real-life setting, the fifth step of McKleroy's guidance [14].

Analyses

Quantitative data were analysed using IBM SPSS Statistics version 19. Non-participants were compared with participants for gender, age, perceived health, and education level, using an independent samples *t*-test. Ten-month changes in health outcomes were assessed using paired samples *t*-tests for continuous variables, McNemar's chi-square tests for categorical variables, and Wilcoxon signed-rank tests for ordinal variables. Relative effect sizes were calculated using Cohen's *d* [31]. Qualitative data were analysed using an inductive approach [32]. The focus group discussion with participants and interviews with dieticians and physiotherapists were tape-recorded and transcribed. During interviews with practice nurses and observations, notes were taken and then transcribed. Transcripts were coded into topics and read multiple times by the first author until themes emerged.

RESULTS

Reach

The SLIMMER pilot study included a total of 31 participants (i.e. a response rate of 57%), with an average of 10 patients per GP practice (range 6–13). On average, participants were 54 years old, had a low level of education (46%), and a family history of diabetes (63%; see Table 3.1). Twenty of the 54 patients did not respond to the invitation (Figure 3.1). Reasons for this non-response were lack of time (28%), lack of interest (24%), reporting of 'I already have a healthy lifestyle' (17%), not reached by practice nurse (14%), not able due to physical or mental problems (10%), and reporting of 'It is of no importance to me' (7%). Three more patients were excluded because they no longer had impaired fasting glucose. Non-participants were slightly older, perceived their health as being better, and were lower educated than participants (Table 3.1). During the SLIMMER pilot study, two participants dropped out (i.e. a drop-out rate of 7%) because of personal

circumstances and health constraints. In total, 13 health care professionals worked together to implement the SLIMMER intervention: three GPs, three practice nurses, three dieticians, and four physiotherapists. They jointly organised three information meetings, at which 23 participants were present (i.e. a participation rate of 74%). On average participants received 5.2 (SD 1.7; range 0–6) consultations by dieticians and 34.1 (SD 16.7; range 0–64) sports lessons. Dieticians organised three group meetings at which 21 participants were present (i.e. a participation rate of 68%).

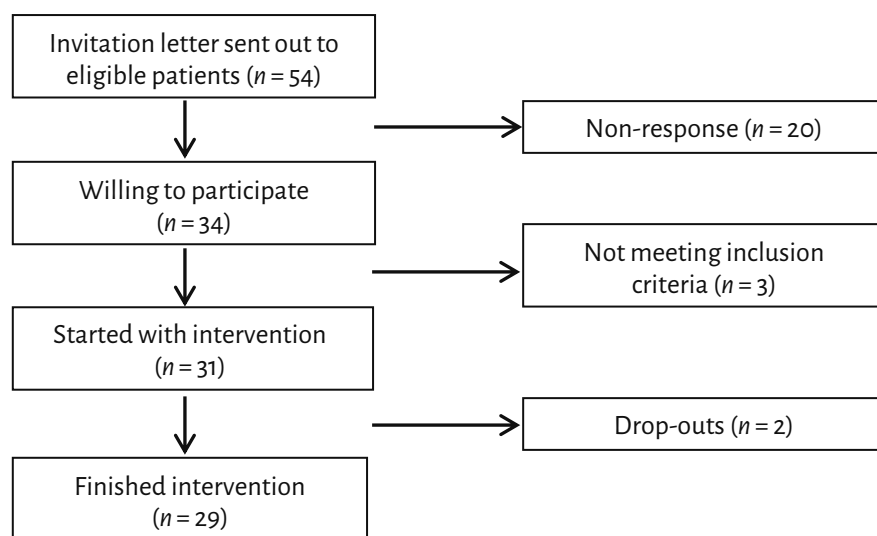


Figure 3.1. Participant flow diagram of the SLIMMER pilot intervention.

Health outcomes

At the end of the intervention, self-reported days of physical activity (i.e. at least 30 min/day physically active) increased from four to five ($p = 0.005$; Table 3.2). No changes in alcohol, fruit, and vegetable intake were observed. Minor changes in medication use were observed. On average, body weight was 3.5 kg lower and significant reductions in waist and hip circumference were noted. Fasting glucose increased slightly, albeit non-significantly. Diastolic blood pressure, but not systolic blood pressure, was significantly reduced. VO_2 max significantly improved after the intervention ($p < 0.001$). Perceived health increased significantly ($p = 0.005$).

Acceptability, implementation integrity, applicability, and intervention optimisation

The participants' questionnaire on acceptability was completed by 90% at baseline and 77% at follow-up and all attending participants filled in the short evaluation form after the group meeting with the dietician. On average, participants evaluated the overall intervention programme with a 7.7 (SD 0.6) out of 10 and the individual intervention elements were positively evaluated by most participants (Table 3.3).

In general, participants and professionals were satisfied with the intervention programme, although some improvements were mentioned. Overall, the intervention was implemented as planned. Some parts of the protocol, however, were omitted or adjusted by health care professionals. This mostly concerned measurements and planning aspects regarding intervention elements. The intervention appeared suitable for application in practice as most health care professionals indicated that it was not very different from their regular functioning and professional performance. However, there were some organisational difficulties.

Table 3.1. Baseline characteristics of participants (N = 31) and non-participants (N = 23) of the SLIMMER pilot intervention^{a,b}.

	Participants	Non-participants
Gender	(n = 31)	(n = 23)
Male	15 (48)	10 (43)
Female	16 (52)	13 (57)
Age (mean (SD))	(n = 31)	(n = 23)
	54.1 (8.5) years (range 36-68y)	58.3 (4.6) years (range 48-66y)
Perceived health	(n = 28)	(n = 16)
Poor / Fair	9 (32)	2 (12)
Good	19 (68)	11 (69)
Very good / Excellent	0 (0)	3 (19)
Education level ^c	(n = 28)	(n = 14)
None / primary education	2 (7)	3 (22)
Low education	11 (39)	8 (57)
Intermediate education	6 (22)	2 (14)
High education	9 (32)	1 (7)
Ethnicity	(n = 27)	
Native	25 (93)	
Non-native	2 (7)	
Marital status	(n = 28)	
Married / cohabitating	25 (89)	
Unmarried	1 (4)	
Divorced	2 (7)	
Widowed	0 (0)	
Employment status	(n = 28)	
Fulltime job	13 (47)	
Part time job	6 (21)	
No paid job	9 (32)	
Family history of diabetes	(n = 27)	
Yes	17 (63)	
No	10 (37)	
History of hyperglycaemia	(n = 15)	
Yes	7 (47)	
No	8 (53)	

^a Data are n (%) unless otherwise indicated.

^b Missing values because of incomplete measurements and drop-out of n = 2.

^c Education level was based on the highest level of education completed and divided in four categories: none/primary (primary school or less), low (lower vocational education), intermediate (medium vocational education, high school), and high (higher vocational education, university).

Table 3.2. Ten-month changes in health outcomes of the SLIMMER pilot intervention (N = 31).

	<i>n</i> ^a	Baseline	$\Delta T_i - T_o$ ^b	<i>p</i> -value	Effect size
Physically active (number of days per week)	22	4 (2.2)	+1 (1.5)	0.005	0.49
Alcohol intake (g/day)	23	7.1 (8.5)	-0.82 (3.0)	0.206	-0.09
Dietary intake (g/day)	23				
Fruit intake		149.0 (103.9)	-1.23 (84.1)	0.945	-0.01
Vegetable intake		165.4 (90.7)	-20.6 (80.0)	0.231	-0.26
Smoking (<i>n</i>)	23	6	-2	0.500	-0.22
Medication use (<i>n</i>)	28				
Hypertension		18	0	1.000	0
Hypercholesterolemia		10	+1	1.000	0.06
Hypertriglyceridemia		0	+1	–	–
Cardiovascular diseases		6	-2	0.625	-0.19
Body weight (kg)	24	85.9 (17.9)	-3.5 (5.4)	0.005	-0.20
BMI (kg/m ²)	23	29.0 (4.1)	-1.2 (1.9)	0.006	-0.30
Waist circumference (cm)	23	104.4 (13.7)	-4.2 (5.1)	0.001	-0.31
Hip circumference (cm)	23	109.8 (7.9)	-2.8 (4.3)	0.005	-0.34
Fasting plasma glucose (mmol/l)	28	6.1 (0.5)	0.3 (0.8)	0.062	0.51
Blood pressure (mmHg)	28				
Systolic		134.9 (10.3)	-4.4 (14.5)	0.118	-0.36
Diastolic		84.6 (8.3)	-5.9 (8.8)	0.001	-0.74
SteepRamp Test	27				
VO ₂ max (l/min)		2.3 (0.6)	+0.4 (0.4)	<0.001	0.58
Perceived health (<i>n</i>)	23				
Poor / Fair		8	-6	0.005	n.a. ^c
Good		15	+4		
Very good / Excellent		0	+2		

^a Missing values because of incomplete measurements and drop-out of *n* = 2.

^b Change between baseline (*T_o*) and follow-up (*T_i*), data are expressed as mean (SD) or *n*.

^c n.a. = not applicable.

Looking in detail at acceptability, implementation integrity, and applicability, seven themes emerged. Most of these themes were related to intervention elements (i.e. information meeting, physical activity intervention, dietary intervention). In addition, the themes measurements and the need for a coordinating professional were identified. Additional file 3.2 provides a detailed overview of all seven themes. Based on these themes, improvements will be made to refine the adaptation process. Both the themes and the improvements are described below.

1. The information meeting was positively evaluated by both participants and professionals, but the organisation of such a meeting proved to be time-consuming and costly for both participants and professionals. The information meeting will be replaced by brochures, providing all details of the SLIMMER intervention programme.

2. The formation of physical activity groups was an important aspect of the physical activity intervention. In practice, the formation of these groups was logistically more difficult than expected. Therefore, instead of forming groups based on day and time preferences of participants, groups will be formed based only on the availability of physiotherapists. It is expected that limiting the options for participants will speed up the formation of physical activity groups.
3. The nutrition intervention included a fixed number of six consultations but it appeared that more flexibility in the number of consultations was desired by both participants and dieticians. More flexibility, therefore, will be provided by determining a minimum of five and a maximum of eight consultations with a maximum of 4 h per participant.
4. Several important findings were related to measurements conducted by health care professionals. It appeared that in practice, some measurements were not performed according to the protocol or not easily applicable, and that different devices were used. Therefore, measurements will be shifted from health care professionals to a research centre for the future cost-effectiveness evaluation study. Furthermore, fasting plasma glucose will be measured using a venepuncture because this might be more reliable than a finger prick [33], and the SteepRamp Test will be replaced by the six-minute walk test [34] because the SteepRamp Test was difficult to perform and was not suitable for all participants.
5. It was identified that there was a need for an independent health care professional who could take action towards professionals and participants in case of difficulties. The practice nurse, therefore, will be designated as case manager of the project to motivate and stimulate participants and to facilitate contact between dieticians and physiotherapists.
6. Monitoring (i.e. repeated measurements during the intervention) appeared to be important to both participants and professionals as it contributes to participants' motivation and professionals' evaluation purposes. Monitoring of behaviour change, therefore, will be expanded and described more explicitly in the SLIMMER manual.
7. The importance of maintaining a healthy lifestyle and how to achieve this was recognised by both the participants and the professionals. Suggestions for a maintenance programme were provided by both participants and professionals and some health care professionals have already taken initiatives themselves. Therefore, a maintenance programme will be added to the lifestyle intervention programme to guide participants in the process of maintaining lifestyle behaviour change in an independent and sustainable manner.

Table 3.3. Participants' acceptability of SLIMMER pilot intervention elements (N = 31)^a.

Intervention elements	Mean participants' acceptability (SD)
Information meeting (n = 21)	
Grade ^b	7.5 (0.8) (range 7-10)
The information meeting was very useful to me ^c	4.2 (0.4) (range 4-5)
I learned a lot from the information meeting ^c	3.2 (0.6) (range 2-4)
I understood the information I received ^c	4.0 (0.4) (range 3-5)
Consultations by dietician (n = 24)	
By participating in SLIMMER...	
I had a motivation to start eating healthy ^c	3.7 (0.9) (range 2-5)
I could focus on eating more healthy ^c	3.7 (0.8) (range 2-5)
Group meeting by dietician (n = 21)	
Grade ^b	8.2 (0.7) (range 7-9)
Sports lessons by physiotherapist (n = 24)	
By participating in SLIMMER...	
I had a motivation to be physically active ^c	4.0 (0.9) (range 1-5)
I could be physically active with a goal ^c	3.8 (0.9) (range 1-5)
I liked to take part in sports together with others ^c	4.1 (0.7) (range 2-5)
Overall intervention (n = 23)	
Grade ^b	7.7 (0.6) (range 7-9)

^a Missing values because of incomplete measurements and drop-out of n = 2.

^b Grading on a scale ranging from 1 to 10.

^c Scale from 1 (I totally disagree) to 5 (I totally agree).

DISCUSSION AND CONCLUSION

Discussion

In this pilot-test of the adapted SLIM intervention, the aim was to determine the feasibility and likelihood of achieving the desired impact. Several improvements in health outcomes were observed. Furthermore, as indicated in the findings, this SLIMMER pilot study was successful in both the inclusion and retention of patients from a high-risk group for diabetes. Both participants and professionals were satisfied with the SLIMMER intervention. Overall, the intervention was implemented as planned and appeared to be suitable for application in practice. Some improvements regarding measurements, planning aspects of intervention elements, and organisational matters were mentioned. Refinements in the adaptation process will be made prior to further implementation and evaluation.

Results of this SLIMMER pilot study are comparable to results of the effective SLIM study [35]. Improvements in body weight, BMI, waist circumference, and VO₂ max were slightly higher in the SLIMMER pilot study than in the SLIM study, whereas fasting plasma glucose slightly increased in the pilot study compared to a decrease in the SLIM study (+0.3 mmol/l vs. -0.1 mmol/l) [35]. However, results of the SLIMMER study should be

interpreted with caution as results are only based on a pilot study with a small sample size. The main goal of this pilot study was to test feasibility of the SLIMMER intervention in practice. Further investigation of effectiveness of the intervention is needed. The SLIMMER intervention may be more successful in primary health care than other interventions because of the intensity of this SLIMMER intervention, the deployment of health care professionals with specific expertise and skills rather than general lifestyle coaches, and the group-based sports lessons which contribute to social support.

Several lessons were learned based on the quantitative and qualitative results of this pilot study. Firstly, this pilot study showed that a structured approach with outcome and process measurements is appropriate to test and optimise the feasibility of an intervention. As indicated by Dombrowski *et al.*, performing a pilot study is important and meaningful because challenges for refinement become clear [36]. Furthermore, a pilot study can be valuable as practising and optimising the intervention might increase chances for success [37]. Secondly, local support among stakeholders is created by initiating a local steering committee who takes responsibility for the implementation process of the intervention. Thirdly, a case manager should be appointed to enhance participant compliance and the feasibility of the implementation. A recent Dutch study showed that practice nurses are highly involved in diabetes care and that patients are satisfied with this care [38]. Because of this and the fact that general practices act as gatekeepers of the health care system and work together with allied forces [13, 39], practice nurses seem to be in the best position to be case managers. Fourthly, monitoring appeared to be an important aspect of the intervention. The need for monitoring was also recognised in several other studies [36, 40]. Fifthly, including a maintenance programme appeared to be important, as losing weight is relatively easy, whereas maintaining weight loss is a more difficult task [36, 41, 42]. Sixthly, it seemed that non-participants were slightly older, perceived their health as better, and were lower educated than participants. This indicates that special attention should be given to recruitment and retention of subjects with a lower socio-economic status. Furthermore, translating findings of this pilot study to other ethnic groups should be done with caution, as most participants were Dutch.

The small study size is a limitation, although this is acceptable for a pilot study [14, 37]. Furthermore, all data were collected and analysed by one researcher which could cause subjectivity in qualitative data interpretation. The researcher, however, was aware of this, worked in a structured way, and discussed analyses and results with two co-authors.

Conclusion

This pilot study shows that implementation of the SLIMMER diabetes prevention intervention is feasible in a Dutch real-life setting and that it is likely to achieve the desired impact. Moreover, practising and optimising the intervention creates local support among stakeholders. Results of this pilot study have led to several improvements regarding measurements, planning aspects of intervention elements, and organisational matters that facilitate the next step of implementation and evaluation of the SLIMMER intervention.

Practice implications

This study shows that performing a pilot study on the basis of a structured approach is a meaningful step in the process of optimising the feasibility and potential impact of an evidence-based intervention in a real-life setting. Implementation of the SLIMMER intervention in Dutch real-life setting is feasible and it is likely to achieve the desired impact.

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The authors declare that they have no competing interest.

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Additional file 3.1. Effect and process evaluation plan of the SLIMMER pilot intervention.

Measure	Evaluation question	Topics measured	Instrument and time point (by whom)	Scale
Effect evaluation				
<i>Health measures</i>	What are the effects of the intervention?	Fasting plasma glucose, blood pressure, weight, height, BMI, waist- and hip circumference, SteepRamp test (VO ₂ max), medication use, perceived health, smoking, physical activity, alcohol intake, fruit and vegetable intake	Registration forms <ul style="list-style-type: none"> At baseline and follow-up (professionals) Questionnaires <ul style="list-style-type: none"> At baseline and follow-up (participants) 	Registration of actual values Multiple choice
Process evaluation				
<i>Reach</i>	What proportion of the intended target group participated in the SLIMMER programme (i.e. response rate)? How many activities were implemented and how many participants attended (i.e. participation rate)? What was the drop-out rate?	Number of eligible patients, patients willing to participate, patients who started intervention Attendance rate at information meetings, group meetings with dietician, consultations, and sports lessons Number of drop-outs and reason for drop-out	Registration forms <ul style="list-style-type: none"> during recruitment (practice nurse) Registration forms <ul style="list-style-type: none"> during intervention (research team, dieticians, physiotherapists) Project logbook <ul style="list-style-type: none"> during intervention (research team) Project logbook <ul style="list-style-type: none"> at baseline (research team) Questionnaires <ul style="list-style-type: none"> at baseline (participants) Non-response form <ul style="list-style-type: none"> during recruitment (practice nurse) Non-response form <ul style="list-style-type: none"> during recruitment (practice nurse) 	Open-ended questions Registration of participant names Notes from researchers Registration of actual numbers Multiple choice Multiple choice
	How many professionals were involved in implementing the SLIMMER intervention? What were characteristics of participants and non-participants?	Number of GPs, practice nurses, dieticians and physiotherapists involved in implementation Gender, age, perceived health, education level, ethnicity, marital status, employment status, family history of diabetes mellitus, history of hyperglycaemia		
	What were barriers to recruiting participants?	What is your most important reason to not participate?		

Additional file 3.1. Continued.

Measure	Evaluation question	Topics measured	Instrument and time point (by whom)	Scale
<i>Acceptability</i>	How satisfied were participants with the information meeting?	Grade for information meeting	Questionnaire • at baseline (participants)	1 (very bad) – 10 (very good)
		Statements: • The information meeting was very useful to me • I learned a lot from the information meeting • I understood the information I received	Questionnaire • at baseline (participants)	5-point Likert scale
		How did you perceive the information meeting?	Focus group meeting • at follow-up (participants)	Open-ended questions
	How satisfied were participants with the dietary intervention?	<i>Consultations</i> Statements: • By participating in SLIMMER, I had a motivation to start eating healthily • By participating in SLIMMER I could focus on eating more healthily	Questionnaire • at follow-up (participants)	5-point Likert scale
		How did you perceive the consultations? How do you see the future? Can you maintain your behaviour?	Focus group meeting • at follow-up (participants)	Open-ended questions
		<i>Group meeting</i> Grade for group meeting	Evaluation form • after group meeting (participants)	1 (very bad) – 10 (very good)
	How satisfied were participants with the physical activity intervention?	Statements: • By participating in SLIMMER, I had a motivation to be physical active • By participating in SLIMMER I could be physical active with a goal • By participating in SLIMMER I liked to take part in sports together with others	Questionnaire • at follow-up (participants)	5-point Likert scale
		How do you perceive the sports lessons? How do you see the future? Can you maintain your behaviour?	Focus group meeting • at follow-up (participants)	Open-ended questions
	How satisfied were participants with the total SLIMMER intervention?	Grade for total intervention	Questionnaire • at follow-up (participants)	1 (very bad) – 10 (very good)

Additional file 3.1. Continued.

Measure	Evaluation question	Topics measured	Instrument and time point (by whom)	Scale
	How satisfied were professionals with the SLIMMER programme?	Did you enjoy participating in SLIMMER? What went (less) well implementing SLIMMER? How did you perceive the implementation of SLIMMER? What are strengths and weaknesses of SLIMMER? How do you see the maintenance phase after SLIMMER has ended?	Semi-structured interviews during the intervention (professionals)	Open-ended questions
<i>Implementation integrity</i>	Is the intervention carried out according to the pre-specified plan?	How did the information meeting / measurements / consultations / sports lessons go? What did you do? Observation of course of intervention elements / professional / participant(s) / materials	Semi-structured interviews during the intervention (professionals) Observations during the intervention (research team)	Open-ended questions Tick registration form
	How often are protocol or parts of protocol omitted? Which parts are omitted?	Did you implement [intervention element] as planned according to the protocol or did you omit or adjust anything?	Semi-structured interviews during the intervention (professionals) Observations during the intervention (research team) Project logbook during the intervention (research team)	Open-ended questions Tick registration form Notes of researchers
<i>Applicability</i>	Does SLIMMER fit into the professional functioning and working standard of GPs, practice nurses, dieticians, and physiotherapists?	Does the programme suit your own knowledge, skills, and experience? Are there differences between your regular functioning and working standards and those in SLIMMER?	Semi-structured interviews during the intervention (professionals)	Open-ended questions
	Are the essential resources for implementing SLIMMER available in the local setting?	Did you have all facilities and materials available that were needed to implement SLIMMER?	Semi-structured interviews during the intervention (professionals)	Open-ended questions

Additional file 3.2. Themes on acceptability, implementation integrity, and applicability of participants ($n = 10$) and health care professionals ($n = 10$) of the SLIMMER pilot intervention.

Themes	Acceptability	Implementation integrity	Applicability
Information meeting	Professionals perceived the information meeting as important because it enabled them to explain things to patients and to get to know and motivate them, facilitating a conscious decision on whether to participate or not Professionals perceived the role of the GP as important because a GP has natural authority. Participants could ask questions and get further explanations during the information meeting.	Collaboration between professionals was not always optimal.	Organisation of the information meeting proved to be difficult because it was time-consuming and costly for professionals and participants.
Start physical activity (PA) intervention	Participants' opinions on the importance of a GP during the meeting ranged from important because their GP is familiar and GP does it right', to not important because the GP has no role in further intervention programme. It was not clear to professionals when PA intervention would start. Participants found it demotivating that there was a long period between inclusion in study and actual start of PA intervention.	The PA intervention started later than planned because formation of physical activity groups was time-consuming.	Physiotherapists indicated that it is difficult to form physical activity groups because it interfered with their own planning and capacity.
Consultations dietician	Dieticians missed latitude in the planning of consultations. Participants found it a pity that they could not have more than six consultations if this was necessary, or less if it was not necessary.	Dieticians did not adhere strictly to the six consultations that were planned for each participant according to protocol.	Dieticians are used to having more latitude in planning the number of consultations, according to needs of participants.
Measurements	Professionals would not have problems with measurements conducted in a research centre instead of performing them themselves, as long as they get access to results of these measurements.	Waist- and hip measurements were not measured according to protocol. Professionals used different devices to measure glucose, blood pressure, and physical fitness.	The SteepRamp Test was not suitable for all participants and was difficult to measure according to protocol.

Additional file 3.2. Continued.

Themes	Acceptability	Implementation integrity	Applicability
Need for a coordinating professional	Professionals would appreciate contact with each other to discuss results and problems with participants, but they did not seek contact with each other.	One participant never started the nutrition programme but no one noticed.	Having the practice nurse as case manager fits into the role that a GP practice has as gatekeeper of the health care system.
Monitoring	<p>Professionals perceived repeated measurements as important to meet information needs of the participants, to provide insights into progress, and to contribute to motivation.</p> <p>Professionals perceived repeated measurements as useful for monitoring results, raising issues, and adapting treatment plans.</p> <p>Participants wanted a higher frequency of multiple repeated measurements (glucose, physical fitness). Overall, they indicated it motivated them.</p>	<p>Waist- and hip measurements were not measured according to protocol.</p> <p>Professionals differed in type and frequency of measurements performed.</p>	<p>Most professionals were used to performing repeated measurements for evaluation purposes.</p>
Maintenance	<p>Professionals thought it would be good to add a maintenance programme to the SUMMER programme in which participants are supported in maintaining a healthy lifestyle on their own. They think it is the responsibility of participants to maintain a healthy lifestyle.</p> <p>Participants had the intention to continue practising some sport, although they were afraid of relapsing into unhealthy behaviour. They need to be motivated, and want to practise sport with someone else. They enjoyed experiencing sports other than fitness.</p> <p>Participants wanted to be monitored by someone after the intervention, for example a practice nurse, every three months. Professionals also thought monitoring by practice nurses was a good idea.</p>	<p>Physiotherapists let participants experience sports other than fitness (e.g. Nordic Walking or squash).</p>	<p>Professionals already offered handles to participants to maintain a healthy lifestyle: e.g. dieticians offered continuation of consultations paid by health insurance, and a half-yearly check; physiotherapists offered sports other than fitness, a list with sports clubs, fitness at a reduced price, and a one-on-one conversation to identify the wishes of participants.</p>



Chapter 4

SLIMMER: a randomised controlled trial of diabetes prevention in Dutch primary health care: design and methods for process, effect, and economic evaluation

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ABSTRACT

Background

Implementation of interventions in real-life settings requires a comprehensive evaluation approach. The aim of this article is to describe the evaluation design of the SLIMMER diabetes prevention intervention in a Dutch real-life setting.

Methods/Design

The SLIMMER study is a randomised, controlled intervention study including subjects aged 40 through 70 years with impaired fasting glucose or high risk of diabetes. The 10-month SLIMMER intervention involves a dietary and physical activity intervention, including case management and a maintenance programme. The control group receives usual health care and written information about a healthy lifestyle. A logic model of change is composed to link intervention activities with intervention outcomes in a logical order. Primary outcome is fasting insulin. Measurements are performed at baseline and after 12 and 18 months and cover quality of life, cardio-metabolic risk factors (e.g. glucose tolerance, serum lipids, body fatness, and blood pressure), eating and physical activity behaviour, and behavioural determinants. A process evaluation gives insight in how the intervention was delivered and received by participants and health care professionals. The economic evaluation consists of a cost-effectiveness analysis and a cost-utility analysis. Costs are assessed from both a societal and health care perspective.

Discussion

This study is expected to provide insight in the effectiveness, including its cost-effectiveness, and delivery of the SLIMMER diabetes prevention intervention conducted in Dutch primary health care. Results of this study provide valuable information for primary health care professionals, researchers, and policy makers.

BACKGROUND

Diabetes mellitus is one of the most challenging health problems of the 21st century [1]. Randomised controlled trials of lifestyle interventions have shown that a healthy diet and increased physical activity reduce the incidence of type 2 diabetes mellitus (T2DM) in impaired glucose tolerance patients [2-5]. This evidence calls for translation and implementation of diabetes prevention programmes in real-life settings to guide diabetes prevention policies. As real-life settings are complex and limited in finances and resources, it is a challenge to implement effective and sustainable interventions [6-8]. Multiple reviews that included studies conducted in several real-life settings, showed significant reductions in weight and waist circumference but inconclusive results for metabolic indicators of diabetes risk, such as blood glucose or HbA1c [7-10].

A comprehensive evaluation approach is required, as interventions in real-life settings are often complex and not delivered in tightly controlled environments [11, 12]. Within this approach, the scope of evaluation research needs to broaden from assessing only effectiveness to also getting insight in the delivery of an intervention. This will provide insight in the so-called 'black box', that is identify aspects that explain what works, how, and why [11, 12]. Therefore, studies need to include a process evaluation to establish the validity of the hypothesised causal processes for behaviour change and taxonomies can be used to describe behaviour change techniques used to modify these processes [13].

To date no effective diabetes prevention programme has been implemented in Dutch primary health care [14-17]. Therefore, the Study on Lifestyle intervention and Impaired glucose tolerance Maastricht (SLIM), revealing a 47% risk reduction [5], was translated into the SLIMMER intervention (SLIM iMplementation Experience Region Noord- en Oost-Gelderland). Translation of this intervention was done in a joint decision making process between SLIM intervention developers and local health care professionals [18]. Pilot-testing of the adapted intervention showed that implementation of the SLIMMER intervention was feasible in a Dutch real-life setting and that it was likely to achieve desired impact [19]. These results serve as input for the next step of broader implementation and evaluation of the intervention in a real-life setting.

The aim of this article is to describe the evaluation design of the SLIMMER diabetes prevention intervention in a Dutch real-life setting. This was done using a logic model describing the hypothesised causal pathway, including process indicators, behavioural determinants, and behavioural and health outcomes. The SLIMMER study will address

the following research questions:

1. Which effects can be measured regarding behavioural determinants, eating and physical activity behaviour, health, and quality of life? (effect evaluation)
2. How is SLIMMER delivered and received in a real-life setting? (process evaluation)
3. How can results be interpreted in terms of costs and benefits? (economic evaluation)

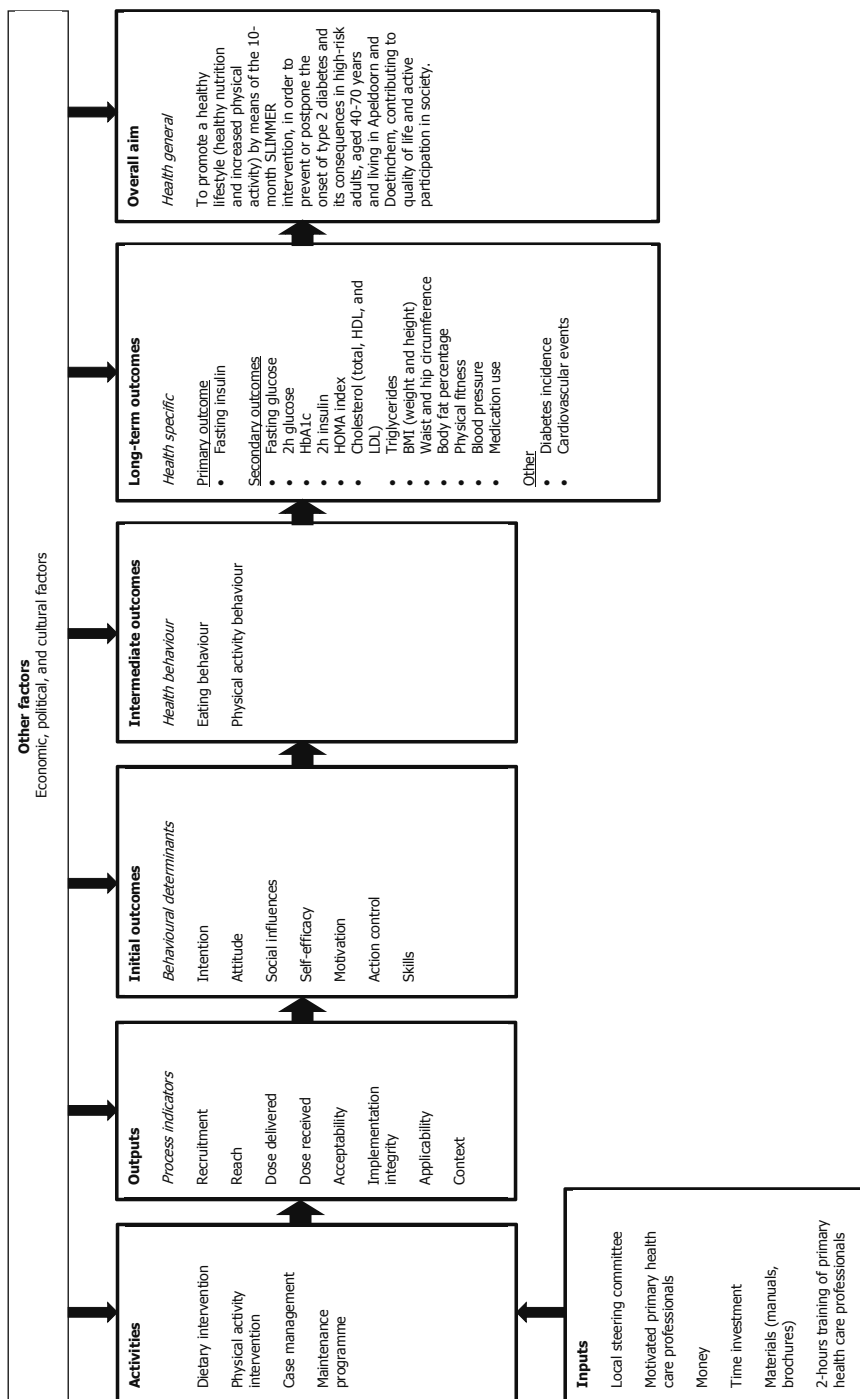


Figure 4.1. Logic model of change for the SLIMMER intervention.

METHODS/DESIGN

Logic model

For this study, a logic model of change is composed to link intervention activities, their mechanisms of change (i.e. behavioural determinants), expected behaviours, and intervention outcomes in a logical order. A logic model facilitates the understanding of intervention effectiveness and provides insights for further improvements [20, 21]. Figure 4.1 shows the logic model of change for the SLIMMER intervention. The overall aim of the intervention is to prevent or postpone T2DM and its consequences and to increase quality of life. On the long-term, improvement in fasting insulin is taken as the primary outcome, whereas improvements in cardio-metabolic risk factors (e.g. glucose tolerance, serum lipids, body fatness, and blood pressure) are defined as secondary outcomes. Improvements in eating behaviour and physical activity behaviour are intermediate outcomes. Eating behaviour is measured as nutrient intake and food intake. Physical activity behaviour is operationalised as mode, frequency, duration, intensity, and activity score. Improvements in intention, attitude, social influences, self-efficacy, motivation, action control, and skills are formulated as initial outcomes. These outcomes are achieved if sufficient outputs are delivered in terms of recruitment, reach, dose delivered, dose received, acceptability, implementation integrity, applicability, and context.

Study design

The SLIMMER study is a randomised, controlled intervention study, carried out in the Netherlands by a consortium of Wageningen University (WU, Wageningen) and the Community Health Service Noord- en Oost-Gelderland (GGD NOG, Apeldoorn). The total duration of the study is 1.5 years with an intervention period of 10 months. Recruitment of participants took place from October 2011 to September 2012. After baseline measurements, participants are randomly allocated to the intervention or control group, using block randomisation on the level of general practitioners (GPs) and stratification for gender. Couples are allocated to the same group to avoid contamination. Randomisation was performed by an independent dietician of the division of Human Nutrition (WU, Wageningen). The SLIMMER study has been registered with ClinicalTrials.gov (Identifier NCT02094911) since March 19, 2014. The WU Medical Ethics Committee approved the study protocol and all subject gave their written informed consent before the start of the intervention.

Setting

This study is carried out in Apeldoorn and Doetinchem, two average, middle-sized Dutch cities, located in the eastern part of the Netherlands. The SLIMMER intervention is implemented in Dutch public health and primary health care, involving GPs and their practice nurses, dieticians, physiotherapists, and sports clubs. Within the study setting, GPs are organised in a formal network to deliver coordinated diabetes care. The majority of dieticians is employed by a home care organisation, only few are self-employed. No regional organisation or network for physiotherapists exists. All GPs have natural referral lines with at least one dietician and in most cases with one physiotherapy practice in the neighbourhood. This existing structure is used for implementation of the SLIMMER intervention. Furthermore, the project is coordinated by the community health service in close collaboration with both municipalities. Sports clubs are organised in a municipal sports stimulation organisation, which has an important role in the maintenance programme.

Sample size calculation

The sample size calculation for this study is estimated based on changes in fasting insulin, observed in SLIM after one year [22]. In the SLIM study, mean difference in fasting insulin between groups was 2.9 mU/l with a standard deviation of 5.3 mU/l [22]. Because SLIMMER is conducted in a real-life setting instead of a controlled setting, it is estimated to achieve 75% of this result, that is an expected difference in fasting insulin between intervention and control group of 2.175 mU/l. Because we expect a larger SD in real-life setting, we use 6 mU/l. To adjust for clusters (i.e. general practices), an intra-cluster correlation of 0.055 is used [23]. Based on results of SLIM [22] and the SLIMMER pilot study [19], we expect a drop-out rate of 10%. Assuming an alpha of 0.05, power of 80%, and two-sided test, a sample size of 145 subjects per group is required.

Study population

GPs and practice nurses have selected patients aged 40 through 70 years suffering from impaired fasting glucose (IFG: i.e. fasting plasma glucose concentration 6.1–6.9 mmol/l [24]) in the past five years from their patient registration database. Patients are recruited using either laboratory glucose test or the Dutch Diabetes Risk Test [25]. Patients are considered for participation if they still suffer from IFG or if the test score indicates an elevated or high risk of T2DM (i.e. a score of ≥ 7 points). Inclusion and exclusion criteria (Table 4.1) are checked by GPs using electronic medical records. GPs have invited eligible patients to participate in the SLIMMER study. A short non-response survey is conducted in case patients are not willing to participate.

Lifestyle intervention programme

The SLIMMER intervention resembles the SLIM intervention [5], which was based on the Finnish Diabetes prevention Study [4]. The SLIM intervention used a combination of theories, such as Stages of Change model [26] and Theory of Planned Behaviour [27], and tools, such as motivational interviewing [28] and goal setting. SLIMMER is a 10-month combined lifestyle intervention consisting of a dietary and physical activity component, including case management and a maintenance programme. The SLIMMER intervention conforms regular functioning and professional performance of Dutch GPs, practice nurses, dieticians, and physiotherapists. Minimal training and a detailed manual are provided during a two-hour SLIMMER kick-off training for health care professionals. In total, 25 general practices, 11 dieticians, nine physiotherapy practices, and 15 sports clubs are participating in the SLIMMER study. An overview of core tasks and competences of these professionals is given in Additional file 4.1. Details of the lifestyle intervention programme are described below.

Table 4.1. Inclusion and exclusion criteria for the SLIMMER study.

Inclusion criteria	Age 40 through 70 years Impaired fasting glucose (IFG; i.e. fasting plasma glucose concentration 6.1-6.9 mmol/l) [24] in the past 5 years according to the patient registration database, OR risk score ≥ 7 points based on the Dutch Diabetes Risk Test [25] Willing and able to participate in the study for at least 1.5 years Able to speak and understand the Dutch language
Exclusion criteria	Known diabetes mellitus Any chronic illness that makes 1.5-years survival improbable, interferes with glucose tolerance, or makes participation in a lifestyle intervention impossible Any severe cardiovascular disease (including history of cardiac dysrhythmia), unless general practitioner gives agreement Medication known to interfere with glucose tolerance (mainly systemic glucocorticoids and pituitary gland/hypothalamus hormones) Any mental or physical disability that will hinder participation in a lifestyle intervention Severe psychiatric disease Patients showing bad compliance in the past Participation in another regular vigorous exercise and/or dietary programme, i.e.: <ul style="list-style-type: none">Intensive physical activity programme: any physical activity programme offered by a physiotherapist and/or patients sporting at least three times a week at own initiativeIntensive dietary programme: patients who visited a dietician at least three times during the last year Patients who participated in the SLIMMER pilot study

Dietary intervention

The dietary intervention is consisting of tailored dietary advice during individual consultations and one group session and is aimed to adopt, step by step, a sustainable

healthy dietary pattern according to the Dutch dietary guidelines [29]. Furthermore, it is aimed to help participants to achieve 5-10% weight loss. Dietary recommendations are based on Dutch dietary guidelines [29], focussed on people at risk of developing diabetes. Dietary advice is given by a dietician from primary health care, trained in motivational interviewing [28] and using positive feedback. The number of consultations is flexible, ranging from five to eight (30-60 minutes per consultation; maximum of 4 hours per participant), and dependent on needs of participants. If desired, spouses could join consultations. In addition, the dietician organises one group session aimed at sharing experiences, motivating each other, and discussing the topic of label reading. Subjects are encouraged to drink less alcohol, quit smoking if necessary, increase daily physical activity, and to participate in the physical activity intervention. To stimulate self-management of participants, goals for behaviour change are set each consultation, evaluated in the next consultation, and if necessary adjusted. Halfway and at the end of the intervention, behaviour change is more extensively evaluated by dieticians to motivate participants, prevent drop-out, and discuss progression and goals.

Physical activity intervention

The physical activity intervention is consisting of a combined aerobic and resistance exercise programme at the physiotherapist's practice and is aimed to obtain and maintain an active lifestyle, that is moderate-intensity physical activity for at least 30 minutes per day on at least five days a week. Physical activity recommendations are based on Dutch guidelines for physical activity and type 2 diabetes [30]. Participants have free access to group-based training sessions and are stimulated to participate for at least one hour per week (maximum of two hours per week). Training sessions are given by a physiotherapist from primary health care and tailored to individual needs, desires, and opportunities. In addition, physiotherapists give tailored advice on how to increase physical activity in daily life (e.g. bicycling, walking) and goals are set. After three, six and ten months, behaviour change is monitored by physiotherapists (e.g. weight, waist circumference, and body fat percentage) aimed to motivate participants, prevent drop-out, and discuss progression and goals.

Case management

Practice nurses are appointed as case managers of the intervention programme to enhance participant compliance and the feasibility of the implementation. They refer participants to the dietician and physiotherapist at the start of the intervention. Furthermore, they have the overview of the programme and work together with

dieticians and physiotherapists. Four weeks after the start of the intervention and halfway the intervention, practice nurses contact dieticians, physiotherapists, and participants of the intervention group to facilitate contact among health care professionals, to detect and solve problems, and to motivate and support participants.

Maintenance programme

A maintenance programme is added to the combined lifestyle intervention to guide participants in the process of maintaining lifestyle behaviour change in an independent and sustainable manner. This maintenance programme includes 1) intermediate evaluations (e.g. measurement of weight, waist circumference, and body fat percentage) by dieticians and physiotherapists to provide feedback and stimulate self-management; 2) sports clinics at local sports clubs to introduce participants to different sports activities; 3) final interviews with dieticians and physiotherapists at the end of the intervention to give positive feedback, discuss behaviour maintenance, and to set goals; 4) return visit with dieticians and physiotherapists to motivate and support participants in maintaining a healthy lifestyle; and 5) monitoring by practice nurses (i.e. discuss and monitor behaviour change during consultations at the general practice).

Control group

Subjects in the control group receive usual health care as provided by GPs and practice nurses. Furthermore, they receive a minimal intervention at the start of the study, consisting of written information about beneficial effects of a healthy diet and increased physical activity, whereas no individual advice or programme is provided. No additional appointments are scheduled, apart from visits for follow-up measurements.

Outcomes

Clinical assessments are performed by trained research assistants in research centres in Apeldoorn and Doetinchem. Furthermore, process and economic data are collected. Participants are measured at baseline (T_0), after the intervention (12 months, T_1), and six months after ending the intervention (18 months, T_2). At each time point, participants are invited to two sessions on different days: one in the morning and one in the afternoon. Additional file 4.2 gives an overview of indicators, methods, and time points of the data collection.

Effect evaluation

Socio-demographic characteristics

Participants fill in questionnaires on socio-demographic characteristics. Data on age, gender, education, ethnic background, marital status, job status, and smoking are collected according to standards of the national surveillance system for adults and the elderly in the Netherlands [31]. These national standards are based on best available scientific insights, experiences of local community health services, and expert opinions. Family history of diabetes is measured with a question from the Dutch Diabetes Risk Test [25]. Data on disease history are collected based on questions from the CoDAM study (Cohort study Diabetes and Atherosclerosis Maastricht) [32]. Non-response data (i.e. age, gender, reason for non-participation, perceived health, and education) are collected during the recruitment period by practice nurses.

Overall outcomes

Quality of life is assessed by the Short-Form Health Survey (SF-36), which proved to be a practical, reliable, and valid tool for both general and chronic disease populations in the Netherlands [33, 34].

Long-term outcomes

A standard oral glucose tolerance test (OGTT; glucose load 75 g) is performed by a trained nurse after at least 10 hours of fasting. Fasting and 2 h plasma glucose levels, HbA1c, and serum lipids (cholesterol (total, HDL, and LDL), and triglycerides) are determined at SHO laboratory in Velp, the Netherlands. For fasting and 2 h serum insulin, all blood samples are analysed within one run after 18 months. An index for insulin resistance is calculated from fasting plasma glucose and insulin concentration, using the homeostasis model assessment (HOMA index) [35]. Body mass index (BMI) is calculated as the ratio of weight and height squared (kg/m^2). Waist circumference is obtained at the level midway between the lowest rib and the iliacal crest. Hip circumference is measured as the maximum circumference over the buttocks. Body fat percentage is measured by bio-impedance analysis (Tanita BC-418). Physical fitness is measured by the six-minute walk test [36], measuring the distance that participants walk within six minutes, which is an indicator of physical functional capacity. This is simple, safe, and inexpensive sub-maximal exercise test [37]. In addition to distance, heart beat rate after six minutes and rating of perceived exertion are obtained using the 6-20 category Borg scale [38]. Blood pressure and heart beat rate at rest are measured using the Omron Digital

Blood Pressure Monitor HEM-907. Self-reported use of medication (name, frequency, and duration of medication use) is determined using a questionnaire [39]. Diabetes incidence is based on data of self-reported medication use which are verified by GPs. Cardiovascular events are based on self-reported data measured by a questionnaire [32]. Procedures of measurements are described in protocols.

Intermediate outcomes

Eating behaviour is operationalised as nutrient intake and food intake. Nutrient intake is assessed by a validated Food Frequency Questionnaire (FFQ) [40, 41]. FFQs are checked by trained research assistants. Average daily nutrient intakes are calculated by multiplying frequency of consumption by portion size and nutrient content per gram using the Dutch food composition table of 2006 [42]. Six food intake behaviours are formulated based on Dutch food-based dietary guidelines [43] and common dietician practices in the SLIMMER pilot study [19]: 1) eating 200 grams of fruit every day; 2) eating 200 grams of vegetables every day; 3) eating more whole grain bread; 4) eating less unhealthy snacks; 5) replacing fat bread spreads with lean bread spreads; and 6) drinking less soft drinks. These food intake behaviours are measured by an FFQ [40, 41]. Physical activity behaviour is measured using the Short Questionnaire to Assess Health-enhancing physical activity (SQUASH), including questions on commuting activities, leisure time activities, household activities, and activities at work [44]. Physical activity behaviour is operationalised as mode, frequency, duration, intensity, and activity score (i.e. total minutes of activity * intensity score). The SQUASH is a short, simple, reliable, and valid measure for categorising adults to their level of physical activity [44, 45]. In addition, a question on sedentary behaviour is added, based on the Activity Questionnaire for Adults and Adolescents (AQuAA) [46].

Initial outcomes

A questionnaire is developed to measure behavioural determinants, as no validated questionnaires are available to measure determinants of specific nutrition and physical activity behaviours in adults at high risk of T2DM. To inform the development of the questionnaire, the Theoretical Domains Framework [47, 48] is used in which behaviour change techniques, used in the SLIMMER intervention, are linked to behavioural determinants. The final questionnaire contains items on intention, attitude, social influences, self-efficacy, motivation, action control, and skills. Items are based on questions and scales described by Fishbein and Ajzen [49], Lakerveld *et al.* [50], and Helmink *et al.* [51].

Process evaluation

To assess how the SLIMMER intervention is delivered and received in a real-life setting, data from both participants and health care professionals are collected. A process evaluation plan is designed based on strategies of Steckler and Linnan [52], Saunders *et al.* [53], Nutbeam [54], and Wang *et al.* [55]. Process measures include recruitment, reach, dose delivered, dose received, acceptability, implementation integrity, applicability, and context. These process measures are assessed using the project logbook, non-response surveys, participant questionnaires, registration forms, attendance lists, and semi-structured interviews with health care professionals.

Economic evaluation

Costs and effects of the SLIMMER intervention are compared with those of the usual care. Economic evaluation is performed from a societal perspective, taking all costs and benefits into account. In addition, a health care perspective is considered, in which only direct medical costs are taken into account. As in the effect evaluation, a time horizon of 1.5 years is used. Both a cost-effectiveness analysis (CEA) and a cost-utility analysis (CUA) are performed. The CEA presents clinical outcomes in terms of reduction of fasting insulin. The CUA presents outcomes in terms of quality-adjusted life years (QALYs), determined by the SF-6D health state classification, a preference-based single index derived from the SF-36 [56, 57]. Intervention costs, health care costs, medication costs, patient costs, as well as productivity losses are assessed. In order to estimate intervention costs, time spent by different types of staff involved (practice nurses, dieticians, physiotherapists, providers of sports clinics, and project coordinator) and materials are identified by means of the project logbook, attendance lists, and registration forms. Volumes of health care use, medication use, absence from work, and other expenses are identified by means of participant questionnaires and registration forms. Costs associated with resources used are valued following Dutch guidelines for costing research within health economic evaluations [58, 59]. If no standard cost prices are available, cost estimates from literature are used. All costs are expressed as year 2012 Euros. Where necessary, costs are indexed to the baseline year, as suggested in the Dutch manual [58, 59]. Costs and effects in the second year are discounted at Dutch standard discounting rates of 4% (costs) and 1.5% (effects).

Data analysis

Quantitative data analyses are performed following the intention-to-treat procedure. If necessary, data are transformed and analyses are adjusted for baseline measurements

and possible differences between groups at baseline. To adjust for clustering on GP level, multilevel analyses are performed. To determine differences in effects between groups, multivariate analysis techniques are performed. Two-sided P values are calculated and a significance level of 0.05 is applied.

Qualitative data analyses are performed using an inductive approach [60]. Interviews with health care professionals are audiotaped and transcribed verbatim. All transcripts are read by two researchers individually to identify frequently emerging themes. These themes are used to create a coding scheme for analysis of data. Quotes are used to describe aspects of how the intervention is delivered and received.

Differences in costs and effects between intervention and control group are expressed as incremental cost-effectiveness ratios (ICERs). ICERs are plotted on a cost-effectiveness plane, a four quadrant diagram with a horizontal axis representing effect differences between the intervention and control group and the vertical axis representing costs differences between groups. In addition, a cost-effectiveness acceptability curve is constructed, which shows the probability that the SLIMMER intervention is cost-effective for a range of cost-effectiveness thresholds. Sensitivity analyses are conducted to assess robustness of results.

DISCUSSION

Implementation of diabetes prevention interventions in real-life settings requires a comprehensive evaluation approach. The design of the SLIMMER intervention described in this paper offers an appropriate evaluation strategy. Firstly, the logic model will facilitate understanding of the intervention effectiveness by assessing outcomes at several levels. Furthermore, the randomised design was adapted to be suitable for application in primary health care practice by incorporating block randomisation on GP level. Secondly, more attention is given to the process of intervention delivery, which is important for real-life, and thus less standardised, interventions. Thirdly, the economic evaluation will provide policy makers with valuable information on costs and benefits of an intervention.

In conclusion, this study is expected to provide insight in the effectiveness, including its cost-effectiveness, and delivery of the SLIMMER diabetes prevention intervention conducted in Dutch primary health care. Furthermore, it is expected that this study will facilitate our understanding on intervention components and characteristics that are

associated with effectiveness. Results of this study provide valuable information for primary health care professionals, researchers, and policy makers.

AUTHORS' CONTRIBUTIONS

GD designed the evaluation study, collected and processed all data, and drafted the manuscript. SCJ and JTB participated in the study design and implementation in public health and primary health care, and helped to draft the manuscript. AH, GJH, and EJM made major revisions to the manuscript. All authors contributed to the development of the SLIMMER intervention, and read and approved the final manuscript.

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Additional file 4.1. Overview of core tasks and competences of primary health care professionals involved in the SLIMMER intervention.

1. PRACTICE NURSE

Goal

To select eligible patients with a high risk of type 2 diabetes mellitus (T2DM) from the electronic patient registration database and motivate them to participate in the SLIMMER study. Practice nurses inform patients on the risk of developing diabetes and how to reduce this risk by a healthy lifestyle.

Core tasks

1. To select patients with a high risk of T2DM, based on inclusion and exclusion criteria.
2. To inform patients about risk factors of T2DM and the importance of a healthy lifestyle; to motivate patients to participate in the SLIMMER study; to advise patients, taking into account their environment, needs, and opportunities.
3. To act as case manager to enhance participant compliance and the feasibility of the implementation. Practice nurses contact dieticians, physiotherapists, and participants of the intervention group to facilitate contact among health care professionals, to detect and solve problems, and to motivate and support participants.

Competences

- Stimulating patients towards a healthy lifestyle
- Good conversation and motivational skills
- Good listening skills
- Good coaching skills
- Monitoring progress of participants
- Being able to empathise with specific situation of participants
- Good coordination skills regarding role of case manager



2. DIETICIAN

Goal

To guide participants towards an improved dietary pattern, based on Dutch dietary guidelines and focussed on people at risk of developing diabetes. Aim is to adopt a sustainable healthy dietary pattern step by step.

Core tasks

1. To carry out intakes to gather relevant information (e.g. dietary pattern, experiences, needs, environment) and set goals together with participants.
2. To formulate dietary advices to discuss during the individual consultations. It is important to support and motivate participants, to make an inventory of barriers and facilitators, and to set goals together with participants.
3. To organise a group session, aimed at sharing experiences, motivating each other, and discussing the topic of label reading (practice with comparing products on fat and sugar content).

Competences

- Conducting anamnesis of current dietary pattern
- Formulating tailored dietary advice
- Being able to empathise with specific situation of participants
- Stimulating participants towards a healthy lifestyle
- Good conversation and motivational skills (motivational interviewing techniques)
- Recognising and analysing barriers for healthy nutrition behaviour
- Applying dietary guidelines adequately
- Giving information on relation between nutrition and glucose tolerance
- Collecting data on dietary advice, progress and condition of participants
- Monitoring dietary pattern and compliance to dietary advices
- Detecting and tackling problems with new dietary pattern
- Building confidence with participants
- Improving participants' self-consciousness by listening and asking the right questions
- Guiding participants in a step-by-step behaviour change
- Helping participants get insight into their motivation
- Teaching participants new skills in a creative manner
- Organising and executing group session

3. PHYSIOTHERAPIST

Goal

To guide participants towards an improved physical activity pattern, based on Dutch guidelines for physical activity and type 2 diabetes. Aim is to obtain and maintain an active lifestyle, that is moderate-intensity physical activity for at least 30 minutes per day on at least five days a week, and (re-)discover pleasure of being physically active.

Core tasks

1. To carry out an intake to get insight in physical activity pattern, wishes, knowledge, opportunities, and experiences of participants.
2. To conceive a tailored physical activity programme based on information of the intake, consisting of weekly, group-based training lessons with both aerobic and resistance exercise. Besides individual coaching during the lessons, attention will be given to the group and team wise activities.
3. To stimulate and advise on tailored physical activity in daily life, taking into account opportunities and barriers of participants.
4. To guide participants to local sports clubs to maintain lifestyle behaviour change in an independent and sustainable manner. During the physical activity intervention, attention will be given to the period after ending the intervention.

Competences

- Being aware of Dutch guidelines for physical activity and type 2 diabetes
- Conducting anamnesis of current physical activity pattern
- Advising and stimulation of participants towards a healthy physical activity pattern
- Giving information on relation between physical activity and glucose tolerance
- Stimulating participants to participate in the SLIMMER exercise intervention
- Stimulating and advising participants to additional physical activity in daily life
- Detecting and tackling problems regarding the exercise intervention
- Monitoring compliance to physical activity advices



Additional file 4.2: Overview of indicators, methods, and time points of data collection.

Outcomes	Indicators	Method	Time points		
			Baseline (T ₀)	12 months (T ₁)	18 months (T ₂)
Socio-demographics	Age, gender, education, ethnic background,	Participant questionnaire [31]	X		
	Non-response data (age, gender, education, perceived health, reason for non-participation,)	Non-response survey [31]	X		
	Marital status, job status, smoking	Participant questionnaire [31]	X	X	X
	Family history of diabetes	Participant questionnaire [25]	X	X	X
	Disease history	Participant questionnaire [32]	X	X	X
Overall	Quality of life	SF-36 questionnaire [33, 34]	X	X	X
Long-term	Fasting and 2h insulin, fasting and 2h glucose, HbA1c, HOMA index	Oral Glucose Tolerance Test (OGTT)	X	X	X
	Cholesterol (total, HDL, LDL), triglycerides	Oral Glucose Tolerance Test (OGTT)	X	X	X
	Body weight, height, Body mass index (BMI), waist and hip circumference	Anthropometry	X	X	X
	Body fat percentage	Bio-impedance analysis (Tanita BC-418)	X	X	X
	Physical fitness	Six-minute walk test [36]; Borg scale [38]	X	X	X
	Blood pressure	Omron Digital Blood Pressure Monitor HEM-907	X	X	X
	Medication use	Participant questionnaire [39]	X	X	X
	Diabetes incidence	Participant questionnaire [39]	X	X	X
	Cardiovascular events	Participant questionnaire [32]	X	X	X
	Economic indicators <ul style="list-style-type: none">• health care use• absence from work	Participant questionnaire	X	X	X

Additional file 4.2. Continued

Outcomes	Indicators	Method	Time points		
			Baseline (T ₀)	12 months (T ₁)	18 months (T ₂)
Intermediate	Nutrient intake				
	Food intake behaviours	Food Frequency Questionnaire [40, 41]	X	X	X
	• eating 200 grams of fruit every day				
	• eating 200 grams of vegetables every day				
	• eating more whole grain bread	Food Frequency Questionnaire [40, 41]	X	X	X
	• eating less unhealthy snacks				
	• replacing fat bread spreads with lean bread spreads				
	• drinking less soft drinks				
	Physical activity behaviour	SQUASH [44]	X	X	X
	• mode				
Initial	• frequency				
	• duration				
	• intensity				
	• activity score				
	• compliance to physical activity guidelines				
	Sedentary behaviour	AQuAA [46]	X	X	X
	Social participation	Participant questionnaire		X	X
	Behavioural determinants	Participant questionnaire (items based on [49-51])	X	X	X
	• intention				
	• attitude				
	• social influences				
	• self-efficacy				
	• motivation				
	• action control				
	• kills				

Additional file 4.2. Continued

Outcomes	Indicators	Method	Time points		
			Baseline (T ₀)	12 months (T ₁)	18 months (T ₂)
Outputs	Recruitment (procedures used to approach and attract participants at individual or organisational levels)	Project logbook	X		
	Reach (proportion of intended target audience that participated in an intervention)	Participant questionnaire, non-response survey, attendance lists	X	X	
	Dose delivered (number of amount of intended units of each intervention or component delivered or provided by interventionists)	Registration forms	X	X	X
	Dose received (extent to which participants actively engage with, interact with, are receptive to, and use materials or recommended resources)	Participant questionnaire, registration forms, attendance lists		X	X
	Acceptability (extent to which participants and health care professionals are satisfied with the intervention)	Participant questionnaire, semi-structured interviews with professionals		X	X
	Implementation integrity (extent to which the intervention was implemented as planned)	Semi-structured interviews with professionals	X	X	
	Applicability (extent to which an intervention process could be implemented in the real-life setting)	Semi-structured interviews with professionals	X	X	
Economic	Context (aspects of the larger physical, social, and political environment that either directly or indirectly affects intervention implementation)	Participant questionnaire, semi-structured interviews with professionals	X	X	X
	Intervention costs	Project logbook, registration forms, attendance lists	X	X	X
	<ul style="list-style-type: none"> personnel (practice nurses, dieticians, physiotherapists, providers of sports clinics, project coordinator) materials 				
	Patient costs (e.g. sports expenditures, time costs)	Participants questionnaire, registration forms	X	X	X
	Willingness-to-pay	Participant questionnaire	X	X	X

The background of the page features a faint, light-colored illustration of a person in a yoga pose, specifically a standing balance pose with one leg raised. The person is surrounded by numerous water droplets of various sizes, creating a soft, ethereal effect. The overall color palette is light and airy, with shades of gray and white.

Chapter 5

Effect and maintenance of the SLIMMER diabetes prevention lifestyle intervention in Dutch primary health care: a randomised controlled trial

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Hiddink, EJM Feskens

Submitted

ABSTRACT

Objective

To assess the effectiveness of the SLIMMER combined dietary and physical activity lifestyle intervention on clinical and metabolic risk factors, dietary intake, physical activity, and quality of life after 12 months, and to investigate whether effects sustained six months after the active intervention period ended.

Research Design and Methods

SLIMMER was a randomised controlled intervention, implemented in Dutch public health and primary health care. In total, 316 subjects aged 40–70 years with increased risk of type 2 diabetes were randomly allocated to the intervention group (10-month dietary and physical activity programme) or the control group (usual health care). All subjects underwent an oral glucose tolerance test and physical examination, and filled in questionnaires. Identical examinations were performed at baseline and after 12 and 18 months. Primary outcome was fasting insulin.

Results

The intervention group showed significantly greater improvements in anthropometry and glucose metabolism. After 12 and 18 months, differences between intervention and control group were -2.7 kg (95% CI: -3.7; -1.7) and -2.5 kg (95% CI: -3.6; -1.4) for weight, and -12.1 pmol/l (95% CI: -19.6; -4.6) and -8.0 pmol/l (95% CI: -14.7; -0.53) for fasting insulin. Furthermore, dietary intake, physical activity, and quality of life improved significantly more in the intervention group than in the control group.

Conclusions

The Dutch SLIMMER lifestyle intervention is effective in the short and long term in improving clinical and metabolic risk factors, dietary intake, physical activity, and quality of life in subjects at high risk of diabetes.

INTRODUCTION

Universal consensus exists on the need to translate and implement evidence from landmark clinical trials on combined lifestyle interventions to prevent type 2 diabetes in real-world settings [1]. Recent reviews on studies conducted in such settings showed limited results, with significant reductions in weight and waist circumference but inconclusive results for metabolic indicators of diabetes risk, such as blood glucose or HbA1c [2-4]. Furthermore, current evidence on the sustainability and long-term clinical benefits of such interventions is limited [2-4]. To date, no evidence-based diabetes prevention interventions have been effectively implemented in Dutch primary health care [5, 6], while the Study on Lifestyle intervention and Impaired glucose tolerance Maastricht (SLIM), conducted in an experimental setting, had earlier revealed a 47% diabetes risk reduction [7]. We therefore used the SLIM intervention as a starting point for implementation and translated this into the SLIMMER intervention (SLIM iMplementation Experience Region Noord- en Oost-Gelderland). This translation was done jointly by SLIM intervention developers and local health care professionals [8]. Pilot-testing of the adapted intervention showed its implementation was feasible in Dutch primary health care and that it was likely to achieve the desired impact [9]. These results served as input for the broader implementation and evaluation of the intervention [10]. In this study, we assess the effectiveness of the SLIMMER intervention on clinical and metabolic risk factors, dietary intake, physical activity (PA), and quality of life after 12 months. Moreover, the aim is to investigate whether effects sustained six months after the active intervention period ended.

RESEARCH DESIGN AND METHODS

Study design

The SLIMMER study's design and 10-month lifestyle intervention programme have been described in detail elsewhere [10]. In short, SLIMMER was a randomised, controlled intervention study, conducted in the cities of Apeldoorn and Doetinchem (the Netherlands). It was implemented in Dutch public health and primary health care, involving 25 general practices – general practitioners (GPs) and their practice nurses –, 11 dietitians, 16 physiotherapists, and 15 sports clubs. The study protocol was approved by the Wageningen University Medical Ethics Committee, and all subjects gave their written informed consent before the study started.

Study population

Study subjects were recruited by GPs and practice nurses from their patient registration database, using either a laboratory glucose test or the Dutch Diabetes Risk Test [11]. The inclusion criteria were 1) aged between 40 and 70 years at screening, 2) impaired fasting glucose (IFG; 6.1–6.9 mmol/l) [12] or an elevated/high risk of type 2 diabetes (a Diabetes Risk Test score of ≥ 7 points) [11], 3) willing and able to participate in the study for at least 1.5 years, and 4) 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. Recruitment took place between October 2011 and September 2012 in three consecutive groups for logistical reasons.

In total, 1,009 individuals aged 40–70 years without diabetes mellitus were initially identified from the patient registration database (Figure 5.1). Of these, 590 (58%) fulfilled all criteria and were invited to participate. In total, 316 subjects (54%) were willing to participate and underwent an oral glucose tolerance test (OGTT) and physical examination at baseline.

After baseline measurements, participants were randomly allocated to the intervention or control group (allocation ratio 1:1), using block randomisation at GP level and stratification for sex. Couples were allocated to the same group to avoid contamination. An independent dietician from the Division of Human Nutrition, Wageningen University, performed the randomisation. One of the researchers (GD) assigned participants to the intervention or the control group.

Intervention

The SLIMMER combined lifestyle intervention resembled the SLIM intervention [7], which was based on the Finnish Diabetes Prevention Study [13], and consisted of a dietary and a PA component, delivered by primary health care professionals (GPs, practice nurses, dieticians, and physiotherapists) [10]. Furthermore, case management and a maintenance programme were included. The dietary intervention consisted of tailored dietary advice given by a dietician, during 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 [14]. Furthermore, the intervention aimed to help overweight participants to achieve 5–10% weight loss. The PA intervention was delivered by physiotherapists as weekly group-based combined aerobic and resistance training sessions, based on the Dutch guidelines for PA and type 2 diabetes [15]. The aim

was to obtain and maintain an active lifestyle, which includes moderate-intensity PA for at least 30 minutes per day on at least five days a week. Furthermore, case management was performed by practice nurses (contacting intervention participants and health care professionals by phone) to enhance participant compliance and feasibility of implementation.

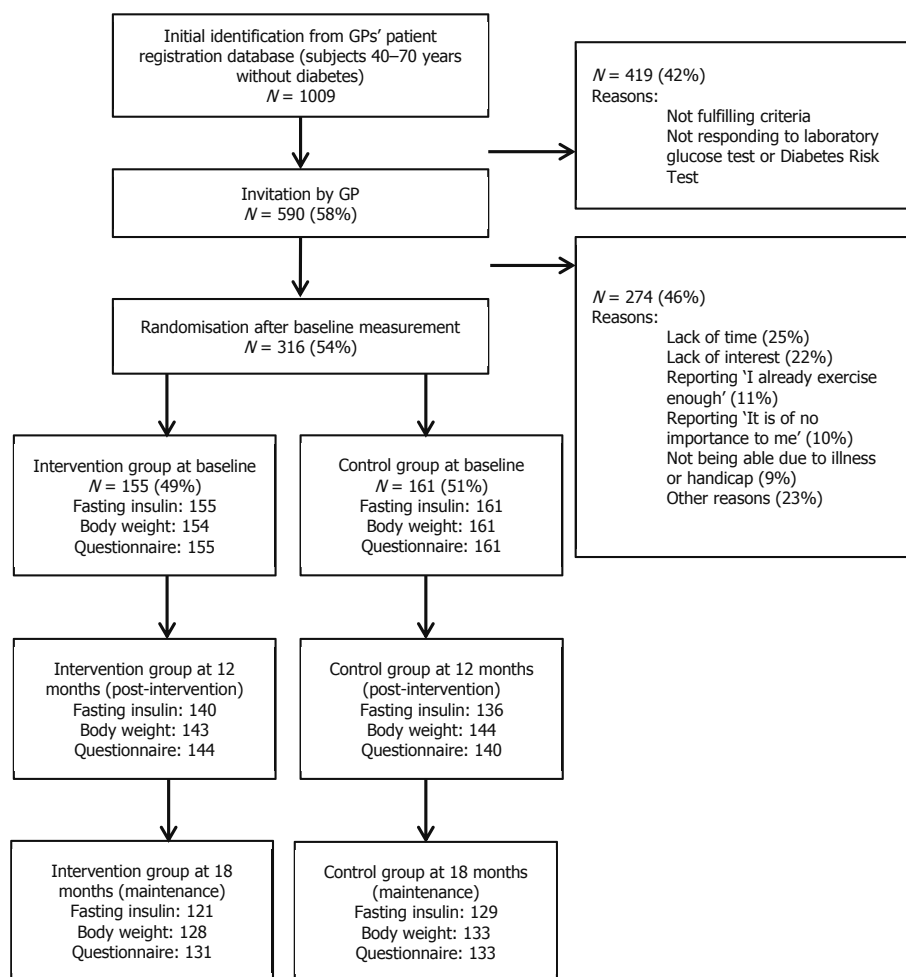


Figure 5.1. Flow diagram.

In addition to the core dietary and PA intervention, a maintenance programme was delivered, starting in the last phase of the 10-month intervention period and lasting up to three months thereafter. This programme comprised sports clinics at local sports

clubs, concluding meetings with the dietician and physiotherapist, and a return session with the physiotherapist, dietician, and the PA group [16]. This programme was added to guide participants in the process of maintaining lifestyle behaviour change in an independent and sustainable manner.

Control group subjects received usual health care as provided by GPs and practice nurses (yearly monitoring of blood glucose, according to the guidelines of the Dutch College of General Practices) [17]. Furthermore, at baseline they received written information on the beneficial effects of a healthy diet and increased PA. No additional appointments were scheduled, apart from visits for follow-up measurements.

Data collection and outcomes

Baseline measurements were taken between February and October 2012. All study subjects underwent an oral glucose tolerance test (OGTT) and physical examination, and filled in questionnaires. Identical examinations were performed at baseline, after 12 months (at the end of the intervention), and after 18 months (six months after the end of the intervention; see Additional file 5.1). These procedures have previously been described in detail [10].

The primary outcome was fasting insulin, determined on the basis of a standard OGTT with a glucose load of 75g, performed by trained nurses after at least 10 hours of fasting. Fasting and 2-h plasma glucose levels, HbA_{1c}, and serum lipids (cholesterol (total, HDL, and LDL) and triglycerides) were determined at SHO laboratory in Velp, the Netherlands. For fasting insulin, all blood samples were analysed within one run after 18 months. An index for insulin resistance was calculated from fasting plasma glucose and insulin concentration, using the homeostasis model assessment (HOMA-IR) [18]. Diabetes was classified based on World Health Organisation recommendations [12, 19] and standards of the American Diabetes Association [20]. Normoglycaemia was defined as fasting glucose <6.1 mmol/l and 2-h glucose <7.8 mmol/l; isolated IFG was defined as fasting glucose 6.1–6.9 mmol/l and 2-h glucose <7.8 mmol/l; impaired glucose tolerance was defined as fasting glucose <7.0 mmol/l and 2-h glucose 7.8–11.0 mmol/l; and diabetic values were defined as fasting glucose ≥7.0 mmol/l, 2-h glucose ≥11.1 mmol/l, HbA_{1c} ≥6.5%, or using diabetes medication. Clinical assessments were performed by trained research assistants in research centres in Apeldoorn and Doetinchem according to standardised procedures. BMI was calculated as the ratio of weight and height squared (kg/m²). Waist circumference was obtained at the level midway between the lowest

rib and the iliac crest. Blood pressure was measured using the Omron Digital Blood Pressure Monitor HEM-907.

Socio-demographic characteristics (age, sex, education level, ethnic background, smoking, and family history of diabetes) were collected by participant questionnaires. These data were collected according to standards of the national surveillance system in the Netherlands [21] and an existing questionnaire [11]. Self-reported medication use was determined using a questionnaire [22]. Non-response data (age, sex, reason for non-participation, perceived health, and education level) were collected during the recruitment period by practice nurses.

Dietary intake (nutrient intake and food intake) was assessed by a validated Food Frequency Questionnaire (FFQ) [23]. FFQs were checked by trained research assistants. Average daily nutrient intakes were calculated by multiplying frequency of consumption by portion size and nutrient content per gram using the 2011 Dutch food composition table [24]. Food intake behaviours were formulated based on Dutch food-based dietary guidelines [25] and common dietician practices in the SLIMMER pilot study [9]. Adherence to the Dutch dietary guidelines [14] was calculated, based on the Dutch Healthy Diet Index (DHD-index) [26]. The original DHD-index consisted of 10 components representing the guidelines, whereas for the current study we adapted the index and included eight components: PA, vegetable, fruit, fibre, fish (EPA and DHA), saturated fat, trans-fatty acids, and alcohol. Two components ('acidic drinks and foods' and 'sodium') were excluded because no data were available on these components. 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) [27]. The durations (minutes per week) of total and light-, moderate-, and vigorous-intensity physical activities were calculated. Level of compliance with the PA guidelines (moderate-intensity PA for at least 30 minutes per day on at least five days a week) was represented as inactive (0 days), semi-active (1–4 days), or norm-active (at least 5 days) [28]. Furthermore, physical fitness was measured as the distance covered in metres during the six-minute walk test [29].

Quality of life was assessed by the Short-Form Health Survey (SF-36), which has proved to be a practical, reliable, and valid tool for both general and chronic disease

populations in the Netherlands [30]. The questions were organised into one item on health transition and eight scales for, respectively, physical functioning, role limitations due to physical health problems, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems, and general mental health. The eight scales were converted to a 0–100 scale indicating worst to best possible health. Scores were summarised into the physical component summary score and the mental component summary score.

Statistical analysis

A sample size of 145 subjects per group was required to detect differences between groups in fasting insulin, assuming an alpha of 0.05, power of 80%, two-sided test, and an expected drop-out rate of 10%. After exclusion of subjects because of missing data on fasting insulin or BMI at baseline or 12 months ($n=16$ in the intervention group and $n=25$ in the control group), data collected from 275 subjects were used for statistical analysis. Participants who dropped out were not substantially different from the completers in baseline characteristics, except that drop-outs were more often divorced than completers (25% vs. 6% in the intervention group and 28% vs. 5% in the control group). Furthermore, the HOMA-IR was higher in intervention drop-outs than in completers (3.1 ± 2.8 vs. 2.0 ± 1.1 , $p = 0.053$), whereas this was lower in control drop-outs than in completers (1.5 ± 0.6 vs. 2.0 ± 1.2 , $p = 0.015$).

Continuous variables are presented as mean \pm SD and categorical variables as percentages. Natural log transformations were used in the event of skewed distributions. Differences within groups were tested for statistical significance with paired samples t tests for normally distributed variables and Wilcoxon signed-rank tests for non-normally distributed variables. Differences between groups were tested for statistical significance with independent samples t tests for normally distributed variables and Mann-Whitney tests for non-normally distributed variables, χ^2 tests, and ANCOVA adjusting for baseline value, sex, recruitment phase, and medication use if applicable. Additional analyses showed similar results when subjects on medication were excluded. We included an interaction term in the ANCOVA models to test whether the association between treatment and outcome measures differed by sex. All primary analyses were performed according to the intention-to-treat principle: participants were analysed in the groups to which they were originally randomly assigned, regardless of whether or not they actually participated in the intervention. All analyses were performed using IBM SPSS Statistics version 22.

RESULTS

Baseline results

Study subjects and non-responders (those who were not willing to participate) were similar in terms of sex, age, and education level. However, 90% of the non-responders perceived their health as good or even better, against 79% of the study subjects. 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 being able due to illness or handicap (9%).

Table 5.1 shows the baseline characteristics of the 275 subjects. No differences in baseline characteristics between study groups were found. On average, subjects were 61 years old, and most had a low education level, were Dutch, and had a family history of diabetes. Of the total, 48% were overweight ($\text{BMI} \geq 25$ and $< 30 \text{ kg/m}^2$), 42% were obese ($\text{BMI} \geq 30 \text{ kg/m}^2$), and 15% had a cardiovascular disease in the past (data not shown). Dietary intake was similar between groups both in terms of nutrient intake and food intake, and both groups had similar adherence to the Dutch dietary guidelines. Moderate-to-vigorous-intensity PA was comparable between groups and 80% of participants were classified as norm-active. Health-related quality of life was comparable in both groups, with scores around 50 for both physical and mental component scores.

Results on clinical and metabolic risk factors

Table 5.2 summarises changes in clinical and metabolic risk factors after 12 and 18 months. Beneficial changes were observed in the intervention group compared with the control group. At 12 months, mean weight reduction was 3.4% in the intervention group and 0.3% in the control group ($p < 0.001$). Furthermore, waist circumference reduction was greater in the intervention group. Fasting insulin declined more in the intervention group than in the control group (-12.6 vs. 0.6 pmol/l , $p = 0.005$). Also, greater improvements were seen in fasting glucose (-0.2 vs. -0.01 mmol/l), 2-h glucose (-0.5 vs. 0.2 mmol/l), HbA1c (-0.15 vs. -0.07%), and HOMA-IR (-0.29 vs. 0.02) in the intervention group than in the control group ($p < 0.05$). Compared to baseline, more subjects had normoglycaemia (19% vs. 25% in the intervention group and 15% vs. 20% in the control group) and fewer intervention subjects (32% vs. 27%) than control subjects (28% vs. 31%) had diabetic values.

Table 5.1. Baseline characteristics of participants in the SLIMMER intervention ($n = 275$)^a.

	INT ($n = 139$)	CON ($n = 136$)
<i>Socio-demographics</i>		
Sex ($n, \%$)		
Male	75 (54)	69 (51)
Female	64 (46)	67 (49)
Age (years)	61.1 ± 6.1	61.2 ± 6.6
Education level ($n, \%$) ^b		
Low	74 (53)	73 (54)
Middle	39 (28)	26 (19)
High	26 (19)	37 (27)
Ethnicity ($n, \%$)		
Dutch	123 (88)	123 (90)
Western non-Dutch	12 (9)	9 (7)
Non-western non-Dutch	4 (3)	4 (3)
Family history of diabetes ($n, \%$)		
No	46 (33)	57 (42)
First degree	66 (48)	62 (46)
Second degree	27 (19)	17 (12)
Smoking status ($n, \%$)		
Yes	21 (15)	26 (19)
Ex-smoker	86 (62)	78 (57)
No, never	32 (23)	32 (24)
<i>Clinical and metabolic risk factors</i>		
Weight (kg)	89.5 ± 17.0	87.8 ± 15.2
BMI (kg/m^2)	30.2 ± 4.5	29.9 ± 4.8
Waist circumference (cm)		
Male	109.3 ± 12.2	107.4 ± 10.2
Female	101.0 ± 12.0	100.0 ± 12.9
Fasting glucose (mmol/l)	6.6 ± 0.6	6.6 ± 0.6
2-h glucose (mmol/l) ^c	8.2 ± 2.8	8.0 ± 2.5
Fasting insulin (pmol/l)	87.8 ± 48.2	86.0 ± 52.8
HOMA-IR	2.0 ± 1.1	2.0 ± 1.2
HbA1c ($\%$ (mmol/mol))	5.8 ± 0.4 (40.3 ± 3.9)	5.8 ± 0.4 (40.1 ± 4.0)
Total cholesterol (mmol/l)	5.5 ± 1.1	5.5 ± 1.2
HDL cholesterol (mmol/l)	1.5 ± 0.4	1.4 ± 0.4
LDL cholesterol (mmol/l)	3.5 ± 1.0	3.6 ± 1.0
Triglycerides (mmol/l)	1.7 ± 0.9	1.6 ± 0.8
Blood pressure (mmHg) ^c		
Systolic	133.0 ± 15.5	131.0 ± 13.5
Diastolic	77.5 ± 10.7	75.6 ± 8.7
<i>Dietary intake</i>		
Energy intake (kcal/d)	1986.3 ± 576.1	2040.7 ± 634.2
Saturated fat (en%)	11.8 ± 2.2	11.9 ± 2.3
Fibre (g/1000 kcal)	11.0 ± 2.6	11.1 ± 2.4
Alcohol (en%)	4.8 ± 5.7	4.3 ± 5.2

Table 5.1. Continued

	INT (<i>n</i> = 139)	CON (<i>n</i> = 136)
Fruit intake incl. fruit juices (g/d)	186.1 ± 119.9	206.5 ± 140.0
Vegetable intake (g/d)	149.3 ± 96.6	137.8 ± 84.7
Fibre intake from total bread intake (%)	5.6 ± 1.0	5.8 ± 1.2
Fat intake from total bread spread intake (%)	21.0 ± 6.4	19.6 ± 6.1
Snack intake (kcal/d)	278.5 ± 208.2	323.0 ± 272.7
Soft drink intake (kcal/d)	56.3 ± 69.6	48.5 ± 60.1
Dutch Healthy Diet index (0–80 scale)	58.8 ± 9.5	58.7 ± 9.0
<i>Physical activity (PA)</i>		
Total PA (min/week)	2254 ± 1337	2306 ± 1232
Light PA (min/week)	1307 ± 1094	1331 ± 970
Moderate PA (min/week)	593 ± 692	559 ± 552
Vigorous PA (min/week)	354 ± 427	417 ± 450
Physical fitness (m) ^c	454.0 ± 58.0	455.5 ± 57.7
<i>Quality of life</i>		
Physical component score	50.1 ± 8.2	49.8 ± 7.9
Mental component score	50.1 ± 10.3	50.7 ± 8.1

^a Data are *n* (%) or mean ± SD.

^b Education level was based on the highest level of education completed and divided in three categories: low (no, primary or lower secondary school), middle (higher secondary school or intermediate vocational school), and high (higher professional education or university level).

^c 2-h glucose INT *n* = 138, CON *n* = 136; systolic blood pressure INT *n* = 138, CON *n* = 135; diastolic blood pressure INT *n* = 138, CON *n* = 135; physical fitness INT *n* = 138, CON *n* = 136.

No significant differences in serum lipids between groups were observed. Systolic and diastolic blood pressure reduced in both groups. However, no significant differences between groups were noted.

No differences in outcomes were observed between subjects recruited by laboratory glucose test (*n* = 130) or by Diabetes Risk Test (*n* = 110), except for fasting glucose at 12 months: in subjects recruited by laboratory glucose test, fasting glucose was significantly lower in the intervention group than in the control group (β = -0.4, 95%CI -0.6;-0.1), whereas there was no effect on fasting glucose in subjects recruited by Diabetes Risk Test (β = -0.0, 95%CI -0.2;0.2; *p* for interaction = 0.016; Additional file 5.2).

At 18 months, reductions in weight, waist circumference, fasting glucose, 2-h glucose, fasting insulin, HbA1c, and HOMA-IR were sustained in favour of the intervention group (Table 5.2). Even more subjects than at 12 months had normoglycaemia (44% in the intervention group and 38% in the control group).

Table 5.2. Changes in clinical and metabolic risk factors from baseline to 12 months ($n = 275$) and 18 months ($n = 240$)^a.

	From baseline to 12 months			From baseline to 18 months		
	INT	CON	β (95%CI) ^b	INT	CON	β (95%CI) ^b
<i>n</i>	139	136		118	122	
Weight (kg)	-3.0 \pm 5.1 ^c	-0.3 \pm 3.6	-2.7 (-3.7; -1.7)	-2.9 \pm 5.1 ^c	-0.4 \pm 3.7	-2.5 (-3.6; -1.4)
BMI (kg/m ²)	-1.0 \pm 1.7 ^c	-0.1 \pm 1.2	-0.9 (-1.3; -0.6)	-1.0 \pm 1.7 ^c	-0.1 \pm 1.3	-0.8 (-1.2; -0.5)
Waist circumference (cm)						
Men	-5.4 \pm 5.1 ^c	-2.0 \pm 4.8 ^c	-3.2 (-4.8; -1.6)	-4.9 \pm 5.6 ^c	-2.4 \pm 5.7 ^c	-2.3 (-4.3; -0.3)
Women	-5.2 \pm 6.0 ^c	-0.8 \pm 4.2	-4.4 (-6.1; -2.6)	-3.8 \pm 6.7 ^c	-0.2 \pm 4.9	-3.4 (-5.5; -1.3)
Fasting glucose (mmol/l)	-0.2 \pm 0.7 ^c	-0.0 \pm 0.7	-0.2 (-0.3; -0.0)	-0.6 \pm 0.6 ^c	-0.4 \pm 0.6 ^c	-0.2 (-0.3; -0.0)
2-h glucose (mmol/l) ^c	-0.5 \pm 2.2 ^c	0.2 \pm 2.6	-0.8 (-1.3; -0.3)	-1.0 \pm 2.1 ^c	-0.3 \pm 2.5 ^c	-0.7 (-1.2; -0.1)
Fasting insulin (pmol/l)	-12.6 \pm 36.9 ^c	0.6 \pm 38.1	-12.1 (-19.6; -4.6)	-17.9 \pm 35.5 ^c	-9.3 \pm 38.5 ^c	-8.0 (-14.7; -0.53)
HOMA-IR	-0.29 \pm 0.85 ^c	0.02 \pm 0.86	-0.28 (-0.46; -0.11)	-0.45 \pm 0.81 ^c	-0.25 \pm 0.85 ^c	-0.19 (-0.34; -0.02)
HbA1c (% (mmol/mol))	-0.15 \pm 0.21 ^c (-1.67 \pm 2.29 ^c)	-0.07 \pm 0.23 ^c (-0.74 \pm 2.49 ^c)	-0.09 (-0.14; -0.04) (-0.99 (-1.55; -0.42))	-0.17 \pm 0.21 ^c (-1.86 \pm 2.31 ^c)	-0.06 \pm 0.45 ^c (-0.62 \pm 4.95 ^c)	-0.11 (-0.20; -0.02) (-1.18 (-2.14; -0.21))
Total cholesterol (mmol/l)	-0.07 \pm 0.88	-0.10 \pm 0.96	0.02 (-0.16; 0.20)	-0.17 \pm 0.83 ^c	-0.16 \pm 1.00	-0.04 (-0.24; 0.16)
HDL cholesterol (mmol/l)	0.02 \pm 0.18	0.01 \pm 0.15	0.01 (-0.03; 0.05)	0.01 \pm 0.21	0.04 \pm 0.18 ^c	-0.02 (-0.07; 0.02)
LDL cholesterol (mmol/l)	-0.05 \pm 0.82	-0.14 \pm 0.88	0.05 (-0.11; 0.21)	-0.05 \pm 0.78	-0.06 \pm 0.95	-0.06 (-0.25; 0.14)
Triglycerides (mmol/l)	-0.08 \pm 0.67	0.03 \pm 0.73	-0.09 (-0.25; 0.07)	-0.01 \pm 0.63	0.03 \pm 0.57	-0.02 (-0.16; 0.13)
Systolic blood pressure (mmHg) ^c	-2.8 \pm 11.4 ^c	-1.8 \pm 11.4	-0.3 (-2.8; 2.2)	-1.9 \pm 12.9	-2.7 \pm 11.6 ^c	1.0 (-2.0; 3.9)
Diastolic blood pressure (mmHg) ^c	-4.0 \pm 7.4 ^c	-2.4 \pm 7.0 ^c	-1.0 (-2.6; 0.6)	-2.6 \pm 8.4 ^c	-2.7 \pm 6.9 ^c	0.1 (-1.7; 1.9)

^a Data are mean \pm SD or β (95% CI).^b β (95% CI) for fasting glucose, 2-h glucose, fasting insulin, HOMA-IR, HbA1c, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, systolic and diastolic blood pressure were adjusted for medication use.^c From baseline to 12 months: 2-h glucose: INT $n = 134$, CON $n = 132$; systolic and diastolic blood pressure: INT $n = 136$, CON $n = 130$; From baseline to 18 months: 2-h glucose: INT $n = 113$, CON $n = 118$; systolic and diastolic blood pressure: INT $n = 113$, CON $n = 119$.^d Significant difference within group ($p < 0.05$).

Table 5.3. Changes in dietary intake and physical activity from baseline to 12 months (*n* = 272) and 18 months (*n* = 239)^a.

<i>n</i>	From baseline to 12 months ^b			From baseline to 18 months ^b		
	INT	CON	β (95%CI)	INT	CON	β (95%CI)
<i>Dietary intake</i>						
Energy intake (kcal/d)	-233.5 ± 452.5 ^c	-178.8 ± 538.7 ^c	-93.2 (-186.3; -0.2)	-226.3 ± 453.7 ^c	-255.3 ± 518.8 ^c	-5.2 (-104.3; 93.9)
Total protein (en%)	0.7 ± 2.6 ^c	0.3 ± 2.29	0.4 (-0.2; 0.9)	0.8 ± 2.7 ^c	0.7 ± 2.6 ^c	0.2 (-0.4; 0.8)
Total fat (en%)	-1.5 ± 5.1 ^c	-0.4 ± 4.5	-1.2 (-2.2; -0.1)	-1.6 ± 5.4 ^c	-0.1 ± 5.1	-1.6 (-2.8; -0.4)
Saturated fat (en%)	-0.9 ± 2.3 ^c	-0.2 ± 2.0	-0.7 (-1.2; -0.3)	-1.0 ± 2.3 ^c	-0.1 ± 1.9	-0.9 (-1.4; -0.4)
Total carbohydrates (en%)	1.0 ± 5.1 ^c	0.3 ± 4.7	0.6 (-0.4; 1.7)	0.9 ± 5.0	-0.2 ± 5.2	1.0 (-0.2; 2.2)
Fibre (g/1000 kcal)	1.2 ± 2.5 ^c	0.5 ± 2.1 ^c	0.6 (0.1; 1.1)	1.2 ± 2.7 ^c	0.3 ± 2.0	0.9 (0.4; 1.5)
Alcohol (en%)	-0.6 ± 2.8 ^c	-0.3 ± 2.7	-0.2 (-0.8; 0.4)	-0.4 ± 2.7 ^c	-0.2 ± 3.4	-0.1 (-0.8; 0.6)
Fruit intake incl. fruit juices (g/d)	20.2 ± 116.8 ^c	-28.5 ± 126.6 ^c	38.6 (14.3; 62.9)	7.4 ± 125.4	-23.8 ± 141.6	23.6 (-4.0; 51.3)
Vegetable intake (g/d)	6.1 ± 83.0	2.6 ± 78.7	8.4 (-8.6; 25.4)	15.7 ± 91.9 ^c	2.2 ± 80.9	19.3 (1.0; 37.6)
Fibre intake from total bread intake (%)	0.4 ± 1.5 ^c	-0.0 ± 1.1	0.3 (0.0; 0.5)	0.4 ± 1.6 ^c	0.1 ± 0.9	0.3 (0.0; 0.6)
Fat intake from total bread spread intake (%)	-3.3 ± 6.2 ^c	-0.5 ± 5.6	-2.1 (-3.3; -0.9)	-3.9 ± 6.8 ^c	-0.5 ± 6.5	-2.6 (-4.1; -1.1)
Snack intake (kcal/d)	-59.6 ± 146.0 ^c	-72.3 ± 222.0 ^c	-15.0 (-44.5; 14.6)	-45.4 ± 175.6 ^c	-93.1 ± 239.8 ^c	14.8 (-22.0; 51.7)
Soft drink intake (kcal/d)	-15.6 ± 66.9 ^c	-13.7 ± 55.4 ^c	2.2 (-9.1; 13.6)	-21.9 ± 57.4 ^c	-10.6 ± 52.3 ^c	-8.0 (-18.5; 2.6)
High-fat dairy intake (g/d)	-18.0 ± 55.6 ^c	-7.6 ± 51.1 ^c	-11.6 (-21.7; -1.6)	-16.3 ± 52.1 ^c	-13.7 ± 46.8 ^c	-6.5 (-16.1; 3.1)
Low-fat dairy intake (g/d)	20.8 ± 157.0 ^c	-12.9 ± 158.7	33.7 (-0.3; 67.6)	12.5 ± 182.1	-2.3 ± 127.4	16.3 (-22.7; 55.2)
Dutch Healthy Diet index (0-80 scale)	3.6 ± 7.9 ^c	0.3 ± 7.7	3.4 (1.7; 5.0)	3.8 ± 7.8 ^c	0.3 ± 7.8	3.8 (2.1; 5.5)
<i>Physical activity (PA)</i>						
Total PA (min/week)	152.5 ± 1346.5	-80.1 ± 1225.3	229.9 (-47.3; 507.1)	159.2 ± 1552.6	98.8 ± 1094.6	55.0 (-258.5; 368.6)
Light PA (min/week)	89.7 ± 970.4	26.4 ± 997.0	70.4 (-139.9; 280.8)	33.7 ± 1270.8	56.7 ± 875.2	-21.5 (-267.9; 225.0)
Moderate PA (min/week)	-2.9 ± 649.6	-26.3 ± 531.0	39.7 (-81.8; 161.2)	17.9 ± 684.4	28.2 ± 609.1	0.8 (-149.3; 150.8)
Vigorous PA (min/week)	65.7 ± 415.7 ^c	-80.2 ± 412.7 ^c	118.3 (33.8; 202.8)	107.6 ± 429.7 ^c	13.9 ± 317.3	82.0 (-7.9; 171.9)
Physical fitness (m)	25.1 ± 38.7 ^c	2.3 ± 37.4	22.6 (13.5; 31.7)	32.8 ± 47.2 ^c	10.0 ± 40.8 ^c	22.3 (10.7; 33.9)

^a Data are mean ± SD or β (95% CI).

^b From baseline to 12 months: dietary intake: INT *n* = 138, CON *n* = 134; physical activity (min/week): INT *n* = 139, CON *n* = 133; physical fitness: INT *n* = 137, CON *n* = 130; From baseline to 18 months: dietary intake: INT *n* = 116, CON *n* = 122; physical activity (min/week): INT *n* = 117, CON *n* = 122; physical fitness: INT *n* = 105, CON *n* = 118.

^c Significant difference within group (*p* < 0.05).

Table 5.4. Changes in quality of life from baseline to 12 months ($n = 271$) and 18 months ($n = 233$)^a.

	From baseline to 12 months			From baseline to 18 months		
	INT	CON	β (95%CI)	INT	CON	β (95%CI)
<i>n</i>	138	133		115	118	
Health transition	15.8 \pm 26.5 ^b	0.4 \pm 23.2	14.5 (10.0; 18.9)	12.2 \pm 25.5 ^b	-0.2 \pm 21.8	10.9 (5.9; 16.0)
General health	5.5 \pm 15.3 ^b	3.0 \pm 14.6 ^b	2.7 (-0.3; 5.7)	7.0 \pm 15.6 ^b	2.4 \pm 15.8	4.4 (0.9; 7.9)
Physical functioning	3.4 \pm 13.1 ^b	0.2 \pm 12.1	3.1 (0.2; 5.9)	2.7 \pm 14.4 ^b	-1.0 \pm 14.0	3.4 (-0.1; 6.8)
Role physical	4.7 \pm 36.1	-0.4 \pm 35.8	4.3 (-3.1; 11.8)	3.5 \pm 40.3	2.1 \pm 36.5	0.3 (-7.9; 8.5)
Role emotional	4.8 \pm 34.5	3.1 \pm 29.9	-0.5 (-6.8; 5.8)	9.0 \pm 37.3 ^b	-1.6 \pm 34.6	8.1 (0.6; 15.5)
Social functioning	2.2 \pm 20.3	-1.0 \pm 17.1	2.5 (-1.4; 6.5)	2.5 \pm 18.8	-2.3 \pm 19.0	4.5 (0.3; 8.7)
Bodily pain	2.6 \pm 21.2	-0.1 \pm 19.7	3.7 (-0.7; 8.0)	1.2 \pm 21.8	0.5 \pm 18.6	1.3 (-3.4; 6.0)
Vitality	4.5 \pm 12.3 ^b	2.1 \pm 12.6	2.7 (-0.1; 5.5)	3.7 \pm 11.4 ^b	1.2 \pm 14.5	3.1 (-0.2; 6.4)
Mental health	2.8 \pm 10.0 ^b	-0.6 \pm 12.1	3.4 (1.0; 5.7)	3.4 \pm 11.8 ^b	0.9 \pm 12.4	2.7 (-0.2; 5.6)
Physical component score	1.5 \pm 7.4 ^b	0.3 \pm 6.2	1.4 (-0.1; 2.9)	0.9 \pm 7.7 ^b	0.4 \pm 7.1	0.5 (-1.2; 2.3)
Mental component score	1.6 \pm 7.6 ^b	0.4 \pm 6.9	1.0 (-0.5; 2.5)	2.4 \pm 8.3 ^b	-0.1 \pm 8.7	2.5 (0.6; 4.5)

^a Data are mean \pm SD or β (95% CI).^b Significant difference within group ($p < 0.05$).

Results on dietary intake and PA

At 12 months, intake of energy, fat, and saturated fat was reduced; intake of fibre increased more in the intervention group than in the control group (Table 5.3). No significant differences in intake of protein, carbohydrates, and alcohol between groups were observed. Fruit intake increased significantly in the intervention group but decreased in the control group. No significant difference in vegetable intake between groups was found. Generally, similar results were observed when food groups were expressed per 1000 kcal. The DHD-index score improved significantly more in the intervention group than in the control group (3.6 vs. 0.3, $p < 0.001$, Table 5.3).

At 18 months, no effect on energy and protein intake was found, whereas intake of fat and saturated fat reduced even more than at 12 months in the intervention group compared with the control group (Table 5.3), especially in men (data not shown). Furthermore, the effect on fibre intake continued at 18 months. No significant difference in fruit intake between groups was observed anymore, in contrast to vegetable intake, which was significantly higher in the intervention group than in the control group (15.7 vs. 2.2 g, $p = 0.039$). Also at 18 months, the DHD-index score was significantly higher in the intervention group than in the control group.

At 12 months, the intervention group spent more time on vigorous activities compared with baseline, whereas this decreased in the control group (65.7 vs. -80.2 min/week, $p = 0.006$; Table 5.3). Furthermore, the intervention group improved more on physical fitness than the control group (covered distance 25.1 vs. 2.3 m, $p < 0.001$).

At 18 months, the intervention group further increased time spent on vigorous activities. However, the control group also slightly improved (Table 5.3). Especially women in the intervention group spent more time on vigorous activities than women in the control group (at 12 months p for interaction = 0.055, and at 18 months p for interaction = 0.051). Furthermore, the improvement in physical fitness was maintained in favour of the intervention group (Table 5.3).

Results on quality of life

At 12 months, the item 'health transition' and the sub-scales 'physical functioning' and 'general mental health' improved in the intervention group compared with the control group ($p < 0.05$; Table 5.4). Additional analyses showed that the sub-scale 'role limitations due to physical health problems' improved in women in the intervention group but not in

men (p for interaction = 0.014). No significant differences in physical component score or mental component score between groups were observed (Table 5.4).

At 18 months, the effect on health transition continued and, additionally, significant effects were found for 'general health perceptions', 'role limitations due to emotional problems', and 'social functioning' in favour of the intervention group (Table 5.4). Moreover, the mental component score significantly improved in the intervention group compared with the control group (2.4 vs. -0.1), but no effect was found on the physical component score.

CONCLUSIONS

The aim of this study was to assess the effectiveness and maintenance of the SLIMMER lifestyle intervention after 12 and 18 months in Dutch primary health care. It was shown that the SLIMMER intervention improved body weight, clinical and metabolic risk factors, dietary intake, physical activity, and quality of life. Furthermore, it was shown that most of these improvements sustained at 18 months.

It is often shown that the effectiveness of lifestyle interventions in real-world settings is limited compared with experimental settings [3], due to the real world's complexity and limited finance and resources [31]. The SLIMMER lifestyle intervention, however, showed a weight reduction of 3.0 kg after 12 months, which is comparable with that in the original SLIM study (-2.8 kg) [7]. Furthermore, our study found better improvements in several clinical and metabolic risk factors, such as weight, BMI, waist circumference, fasting and 2-h glucose, and HbA1c, compared with most other real-world programmes [3-5]. These results were found in two primary health care settings that are representative of Dutch primary health care.

Weight reduction during our study can be indicated as modest. However, it might be relevant, as several studies have shown that even modest weight reduction can reduce the risk of diabetes [32, 33]. In the US Diabetes Prevention Program, it was shown that diabetes incidence can be reduced by around 16% for each kilogram of weight lost [32]. Given the weight loss seen in the SLIMMER intervention group compared with the control group, we would expect around a 43% reduction in type 2 diabetes attributable to weight loss at 12 months, and a 40% reduction at 18 months, which is comparable with the 47% risk reduction in the SLIM study [7]. A review of 36 studies assessing diabetes prevention in real-world settings revealed a 26% risk reduction,

which is lower than our results, possibly because of the less intensive nature of many included interventions [4].

Weight reduction is maintained at 18 months. This is remarkable, as it is well known that weight regain following the end of an intensive lifestyle programme is common within five years [34], even in successful lifestyle interventions [35, 36]. This result might partly be explained by the inclusion of a maintenance programme following the intensive lifestyle programme. It is suggested that such a maintenance programme could enhance intervention effectiveness because of the use of specific behaviour change techniques such as goal-setting, self-monitoring, and relapse prevention [37]. However, data on weight loss maintenance in real-world trials is limited, as very few studies report outcomes beyond 12 months [4]. Our study investigated maintenance after six months. However, benefits over extended follow-up should be further investigated.

Our results indicate that the SLIMMER intervention was successful in improving overall dietary patterns and several nutrient intakes, such as total fat, saturated fat, and fibre intake. Furthermore, vigorous physical activities were more improved in the intervention group than in the control group. The Dutch Aphrodite lifestyle intervention found beneficial effects only for total physical activities and fibre intake [5]. A systematic review of diabetes prevention interventions in the real world, however, concluded that, overall, changes in diet and PA are poorly reported, and that more research is needed [4].

Several factors in our lifestyle programme compared to others could have contributed to intervention effectiveness. Firstly, the SLIMMER intervention was highly intensive, with weekly sports lessons and regular dietary consultations for 10 months. Several reviews found that increased intervention effectiveness was associated with higher intervention intensity [3, 4, 37]. Secondly, lifestyle advice in our study was provided by dietitians and physiotherapists rather than by the more general lifestyle coaches in other studies, such as GPs or practice nurses (or both) and lay community educators [37]. Specialist professionals are more specifically educated for, and more experienced in, delivering nutritional or physical activity advice, and this may have contributed to intervention effectiveness. Moreover, several international reviews concluded that a wide staff range delivers effective interventions [4, 37]. Thirdly, the thorough preparation of the SLIMMER intervention may have contributed to its effectiveness [38]. Much attention was paid to carefully translating the intervention programme to the real world in a joint decision-making process with intervention developers and

local health care professionals [8], followed by pilot-testing of the adapted intervention programme [9] prior to implementation and evaluation.

The randomised design, comprehensive evaluation approach (outcomes at several levels), and validated methods to measure dietary intake and PA allow us to draw solid conclusions on the SLIMMER intervention's effectiveness. By investigating outcomes at several levels (dietary intake and PA alongside clinical and metabolic risk factors), we now have more insight into determinants contributing to diabetes prevention, such as intakes of fat, saturated fat, and fibre, and vigorous activities. Although we observed beneficial changes in quality of life, many were non-significant. Therefore, a disease-specific questionnaire might have been used rather than the SF-36 questionnaire, as such a generic instrument is less responsive to changes in health-related quality of life [39].

Risk scores might be good tools to screen people at high risk of type 2 diabetes in primary health care. They are non-invasive, easy, and cheap compared with fasting plasma glucose measurements. The Diabetes Risk Test used in the current study is based on the FINDRISC questionnaire, which has been shown to be capable to predict undiagnosed diabetes and prediabetes [40]. As shown in our study, intervention subjects improved weight and glucose tolerance, independent of manner of recruitment (fasting plasma glucose or Diabetes Risk Test). This is in line with Ashra *et al.*'s review [4].

In summary, this study has shown that the Dutch SLIMMER lifestyle intervention is effective in the short and long term in improving clinical and metabolic risk factors, dietary intake, physical activity, and quality of life in subjects at high risk of diabetes. More insight into longer-term effects of the intervention on maintenance and cost-effectiveness is needed and important for sustainable diabetes prevention. The results provide valuable information for primary health care professionals, researchers, and policymakers.

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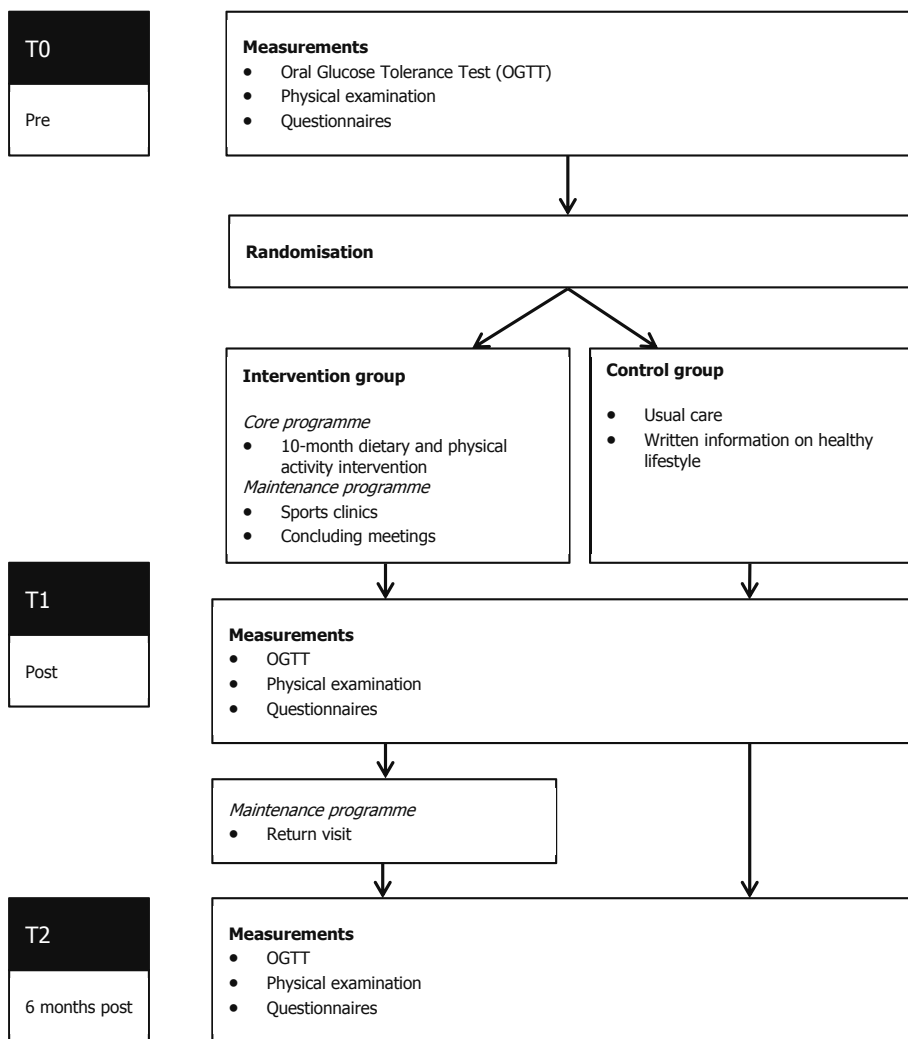
AUTHOR CONTRIBUTIONS

GD designed the evaluation study, collected and processed all data, and drafted the manuscript. SCJ and JTB participated in the study design and implementation in public health and primary care, and helped to draft the manuscript. AH, GJH, and EJMf made major revisions to the manuscript. MW and RVB helped to draft the manuscript. All authors contributed to the development of the SLIMMER intervention, and read and approved the final manuscript. EJMf is the guarantor of this work, and as such, had full access to all data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Additional file 5.1. Timeline of the SLIMMER intervention.

Additional file 5.2. Changes in clinical and metabolic characteristics from baseline to 12 months ($n = 240$) by manner of recruitment^a

	Laboratory glucose test (IFG)			Diabetes Risk Test (risk score)		
	INT	CON	β (95%CI) ^b	INT	CON	p-value for interaction
<i>n</i>	64	66		57	53	
Weight (kg)	-3.5 ± 4.7 ^d	-0.5 ± 2.5	-2.9 (-4.2; -1.6)	-3.0 ± 4.9 ^d	0.5 ± 4.2	0.612
BMI (kg/m ²)	-1.2 ± 1.6 ^d	-0.2 ± 0.9	-1.0 (-1.4; -0.6)	-1.0 ± 1.6 ^d	0.2 ± 1.4	0.764
Waist circumference (cm)	-5.7 ± 5.3 ^d	-1.3 ± 3.6 ^d	-4.3 (-5.9; -2.8)	-5.2 ± 5.8 ^d	-0.9 ± 5.5	0.775
Fasting glucose (mmol/l)	-0.2 ± 0.7 ^d	0.1 ± 0.7	-0.4 (-0.6; -0.1)	-0.1 ± 0.6	-0.1 ± 0.6	0.016
2-h glucose (mmol/l) ^c	-0.5 ± 2.2	0.4 ± 3.2	-1.2 (-2.1; -0.3)	-0.4 ± 2.5	-0.0 ± 1.6	0.613
Fasting insulin (pmol/l)	-16.4 ± 38.8 ^d	3.1 ± 33.2	-14.2 (-25.6; -2.8)	-10.2 ± 37.3	-0.4 ± 46.4	0.746
HOMA-IR	-0.38 ± 0.89 ^d	0.08 ± 0.78	-0.35 (-0.61; -0.08)	-0.23 ± 0.85	-0.01 ± 1.02	0.862
HbA1c (%) (mmol/mol)	-0.19 ± 0.20 ^d (-2.06 ± 2.16 ^d)	-0.07 ± 0.28 ^d (-0.73 ± 3.07 ^d)	-0.12 (-0.21; -0.04) (-1.35 (-2.29; -0.41))	-0.12 ± 0.21 ^d (-1.28 ± 2.55 ^d)	-0.07 ± 0.15 ^d (-0.74 ± 1.64 ^d)	0.138 0.138
Total cholesterol (mmol/l)	-0.12 ± 0.81	-0.06 ± 0.94	-0.04 (-0.30; 0.21)	-0.18 ± 0.79	-0.05 ± 1.01	0.834
HDL cholesterol (mmol/l)	0.04 ± 0.16	0.03 ± 0.13	0.02 (-0.03; 0.07)	-0.00 ± 0.20	0.00 ± 0.16	0.461
LDL cholesterol (mmol/l)	-0.15 ± 0.77	-0.15 ± 0.89	-0.00 (-0.24; 0.23)	-0.05 ± 0.75	-0.06 ± 0.87	0.898
Triglycerides (mmol/l)	-0.07 ± 0.56	0.10 ± 0.80	-0.18 (-0.41; 0.06)	-0.20 ± 0.71	0.01 ± 0.72	0.932
Systolic blood pressure (mmHg) ^c	-2.9 ± 12.0	-0.7 ± 12.2	-1.6 (-5.7; 2.4)	-2.0 ± 11.0	-3.1 ± 10.4 ^d	0.224
Diastolic blood pressure (mmHg) ^c	-4.3 ± 7.9 ^d	-2.4 ± 7.1 ^d	-0.6 (-3.1; 1.8)	-3.3 ± 7.1 ^d	-2.3 ± 7.1 ^d	0.856

^a Data are mean ± SD or β (95% CI).

^b β (95% CI) for fasting glucose, 2-h glucose, fasting insulin, HOMA-IR, HbA1c, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, systolic and diastolic blood pressure were adjusted for medication use.

^c Laboratory glucose test: 2-h glucose: INT $n = 61$, CON $n = 62$; systolic and diastolic blood pressure: INT $n = 62$, CON $n = 62$; Diabetes Risk Test: 2-h glucose: INT $n = 53$, systolic and diastolic blood pressure: INT $n = 56$, CON $n = 53$.

^d Significant difference within group ($p < 0.05$).

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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^{*}These authors contributed equally to the contents of the manuscript

Submitted

ABSTRACT

Background

A comprehensive evaluation approach is required to identify the combination of most effective intervention components for preventing type 2 diabetes. A process evaluation can enhance confidence in conclusions about intervention effectiveness. The aim of this article is twofold: first, to investigate how the SLIMMER intervention was delivered and received in Dutch primary health care, and, second, how this could explain intervention effectiveness.

Methods

SLIMMER was a randomised controlled trial for diabetes prevention, implemented in Dutch primary health care. The intervention consisted of a 10-month combined dietary and physical activity intervention, including case management and a maintenance programme. In total, 316 subjects at increased risk of developing type 2 diabetes were included. 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 in semi-structured interviews with health care professionals ($n = 45$) and intervention participant questionnaires ($n = 155$).

Results

It was possible to recruit the intended high-risk population, and the SLIMMER intervention was very well received by both participants and health care professionals. 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, however, to physical activity behaviour.

Conclusions

This 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, but not with physical activity behaviour. Furthermore, targeting both diet and physical activity, using behaviour change techniques, focusing on behaviour maintenance, tailoring

the intervention, and using a multidisciplinary approach might have facilitated intervention 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.

BACKGROUND

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 developing type 2 diabetes [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 to 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 dietician, 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 health care [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: first, to investigate how the SLIMMER intervention was delivered and received in Dutch primary health care, and, second, 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 average, 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 (T_0), at the end of the intervention (12 months, T_1), and six months after the end of the intervention (18 months, T_2). The study took place between 2011 and 2014. The intervention was implemented in Dutch primary health care, involving general practitioners (GPs), practice nurses, dieticians, 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 GPs and practice nurses (this ranged from no consultations to 1–4 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 (WU) 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 GPs 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 1) aged between 40 and 70 years at screening, 2) impaired fasting glucose (IFG; 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], 3) willing and able to participate in the

study for at least 1.5 years, and 4) 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. GPs invited eligible subjects to participate in the SLIMMER study, and a short non-response survey was conducted if subjects 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 GPs, 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 (HCPs) involved in implementation of the intervention. This training was attended by 68% of general practices, 82% of dietitians, and all physiotherapy practices. HCPs that did not attend the training session were visited individually. HCPs 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 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 minutes per day at least five days a 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 stimulated to participate for at least one hour per week (maximum of two hours per week; a total of 40–80 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 dietician and the physiotherapist at the start of the programme. Furthermore, they contacted dieticians, physiotherapists, and intervention participants twice during the programme to facilitate contact among HCPs, detect and solve problems, and motivate and stimulate 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 1) intermediate evaluations by dieticians and physiotherapists to provide feedback and stimulate self-management, 2) 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), 3) final interviews with dieticians and physiotherapists to provide positive feedback and discuss behaviour maintenance (goal setting and self-monitoring) and relapse prevention, 4) a return visit with dieticians 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 HCPs and intervention participants were collected between baseline (T_0) and the end of the intervention (T_1), 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 (GD). A semi-structured interview guide was developed, and all interviews were conducted by one of the researchers (GD).

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]. Drop-outs were defined as participants that had both no T_1 -measurement for fasting insulin and/or BMI, and dropped out of the dietary and PA programme before the end of the intervention.

Table 6.1. Details of the SUMMER 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	<ul style="list-style-type: none"> • 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 fibres, sweeteners, special occasions, and relation 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	<ul style="list-style-type: none"> • 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
	Intake	1 (individual)	30	<ul style="list-style-type: none"> • Aim: obtain information on current PA, needs, abilities, motivation, and barriers to PA • Set goals
	Sports lessons	40–80 (group-based)	60 (per lesson)	<ul style="list-style-type: none"> • Aim: achieve moderate-intensity PA for at least 30 minutes per day at least five days a week • 2/3rd of training is aerobic exercise (60–70% of VO₂max) • 1/3rd of training is resistance exercise (55–60% of 1RM, with 3x15 repetitions, for major muscle groups) • Offer group-based activities • Individually tailored guidance • Improve level of ability
Case management	Advice on PA during leisure time	-	-	<ul style="list-style-type: none"> • Aim: stimulate 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
	Contact with health care professionals and participants	2 phone calls (individual)	-	<ul style="list-style-type: none"> • Aim: monitor participants' progress • Facilitate contact among health care professionals • Detect and solve problems • Motivate and stimulate participants

Table 6.1. Continued

Intervention components	Sub-components	Number	Time (min)	Details
Maintenance programme	Intermediate evaluations by dietitians and physiotherapists	3 (individual)	-	<ul style="list-style-type: none"> • 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)	<ul style="list-style-type: none"> • 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)	-	<ul style="list-style-type: none"> • Aim: strengthen participants' self-efficacy and motivation • 1 final interview with dietitian during last consultation and 1 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	<ul style="list-style-type: none"> • Aim: prevent relapse and motivate and support participants to maintain behaviour change • Dietician 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

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 HCPs 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. HCPs' acceptability of the intervention was assessed using semi-structured telephone interviews. All HCPs were invited by one of the researchers (GD) three months after starting the intervention (practice nurses, $n = 19$, average duration 27 min; dieticians, $n = 11$, 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; dieticians, $n = 9$, 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 (GD). Acceptability of the intervention by participants and by HCPs was rated on a 7-point or a 10-point Likert 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 HCPs 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 HCPs, 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 minutes) 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 (T_1).

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 (T_0) and after the intervention (T_1). 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 Food Frequency Questionnaire (FFQ) [36, 37]. The FFQs 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, vegetable, fruit, fibre, fish (EPA and DHA), saturated fat, trans-fatty acids, and alcohol. Per component, the score ranges between zero and 10, resulting in a total score between zero (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 IBM SPSS Statistics version 22 with complete cases for the item of interest (ranging from 78 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 HCPs were audiotaped and transcribed verbatim. All transcripts were read by two researchers (EJvD and GD) 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, 25 general practices (GPs and practice nurses), 11 dietitians, nine physiotherapist practices (including 16 physiotherapists), and 15 sports clubs were involved in the implementation of the SLIMMER intervention. Selection of patients from the GP 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 between SLIMMER participants and non-responders were observed (Table 6.2). On average, participants were 61 years old and most of them were less educated, Dutch, and had a family history of diabetes. Of all participants, 48% were overweight (BMI 25–29.9 kg/m²) and 43% were obese (BMI ≥ 30 kg/m²). No significant baseline differences between the intervention and the control group were found (Table 6.2). In total, 10 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 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 38 sports lessons of one hour with the physiotherapist. The goal of participating at least once a week (≥ 40 times in total) in the PA intervention was achieved by 41% of participants. Regarding

the case management component of the intervention, 75% 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 dietician and physiotherapist, three months after the end of the intervention.

Acceptability

Overall, participants and HCPs were highly satisfied with the SLIMMER intervention, with mean acceptability ratings 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). HCPs 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 HCPs, 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. HCPs 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 showed:

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 ($n = 175$)
n (male/female) ^a	81/74	80/81	87/87
Age (years)	60.7 \pm 6.4	61.0 \pm 6.5	60.9 \pm 7.0
Education (%) ^{b,c}			
Low	54	51	52
Middle	26	21	27
High	20	28	21
Perceived health (%) ^d			
Poor/fair	21	21	10
Good	68	70	74
Very good/excellent	11	9	16
Ethnicity (%)			
Dutch	88	89	
Western non-Dutch	9	8	
Non-Western non-Dutch	3	3	
Employment status (%)			
No paid job	54	52	
Part-time job (<32 h/week)	18	22	
Full-time job (\geq 32 h/week)	28	26	
Family history of diabetes (%)			
No	32	42	
First degree	49	45	
Second degree	19	13	
BMI (kg/m ²) ^e	30.4 \pm 4.7	30.0 \pm 4.8	
Fasting insulin (pmol/l)	93.3 \pm 64.3	82.5 \pm 50.2	

^a Non-responders $n = 174$.

^b INT $n = 155$, CON $n = 160$, and non-responders $n = 96$.

^c 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).

^d Non-responders $n = 115$.

^e INT $n = 154$, CON $n = 161$.

Table 6.3. Dose of the SLIMMER intervention components received by the intervention group ($n = 155$)^a.

Intervention component	Intervention manual	Dose received
<i>Dietary intervention</i>		
Individual consultations		
Number	5–8 (incl. intake)	5.6 ± 1.4
Total time (hours)	Max. 4 hours	3.4 ± 0.8
Group meeting (%)	Attend 1 group meeting	67
<i>Physical activity intervention</i>		
Number of sports lessons	At least once a week = 40 times	38 ± 20.8
<i>Case management</i>		
Phone calls by practice nurse (%) ^b	Twice	
Never		24
Once		48
Twice		28
<i>Maintenance programme</i>		
Number of clinics	2–7	2.3 ± 1.9
Final interview (%) ^c	Materials provided during last consultation with dietician	61
Return visit (%)	Attend 1 return visit	58

^a Data are mean ± SD or %.^b $n = 143$.^c Based on the number of participants receiving materials on maintenance distributed during final interview.**Table 6.4.** Acceptability (score 0–100) of the SLIMMER intervention by the intervention group ($n = 144$) and health care professionals ($n = 44$)^a.

	Participants	Professionals
<i>Overall</i>		
Total SLIMMER intervention	82 ± 11 ^b	80 ± 5
<i>Dietary intervention</i>		
Individual consultations	77 ± 21	78 ± 6 ^c
Group meeting	80 ± 8 ^d	
<i>Physical activity intervention</i>		
Sports lessons	84 ± 20 ^e	78 ± 7 ^f
<i>Case management</i>		
Contact with practice nurse	66 ± 21 ^e	
<i>Maintenance programme</i>		
Indicates final interview with dietician as helpful (%)	76 ^g	
Indicates final interview with physiotherapist as helpful (%)	68 ^g	
Sports clinics	77 ± 20 ^h	
Return visit	80 ± 13 ^g	

^a Data are mean ± SD or %.^b $n = 142$; ^c $n = 9$ dieticians; ^d $n = 99$; ^e $n = 143$; ^f $n = 8$ physiotherapists; ^g $n = 78$, percentage of participants that perceived the advice during the final interview as helpful; ^h $n = 118$.

Dietary intervention – In general, participants and dietitians were satisfied with the individual consultations with the dietitian, with mean scores 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 advices.

PA 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 HCPs 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 HCPs' guidance 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.

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.

PA 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 dieticians 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, e-mails 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 HCPs other than the phone calls was reported.

Maintenance programme – Dieticians 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 dieticians 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 dieticians and physiotherapists perceived an equal distribution of tasks. However, not all suggested measurements were performed by all HCPs.

Applicability

Most HCPs 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 dieticians and physiotherapists for lifestyle advice instead of providing this advice themselves. Some dieticians indicated that normally they were more flexible in planning consultations. Furthermore, dieticians perceived dietary consultations as difficult if participants themselves did not feel the need for these (compulsory) consultations or lacked motivation. All HCPs indicated that it was possible to implement SLIMMER in daily practice, although they foresaw financial barriers. Furthermore, they indicated that contact between dieticians 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 associated with a higher DHD-index score, albeit non-significantly ($p = 0.067$). 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

This 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 HCPs. 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, however, 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.

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].

Table 6.5. Associations between process indicators (dose received and acceptability) and intervention effectiveness ($n = 144$)^{a,b}.

	Δ fasting insulin (pmol/l) $T_1 - T_0$		Δ weight (kg) $T_1 - T_0$		Δ DHD-index $T_1 - T_0$		Δ vigorous activities (min/week) $T_1 - T_0$	
	β (SE)	p -value	β (SE)	p -value	β (SE)	p -value	β (SE)	p -value
Dietary consultations (min)	-0.06 (0.08)	0.407	-0.004 (0.01)	0.770	0.03 (0.02)	0.067	1.39 (0.86)	0.108
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

^a Associations are adjusted for baseline value, sex, and recruitment phase.

^b There are 0–4 missing values per analysis because of incomplete data.

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 and change in dietary behaviour, but not with change in 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. 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 *et al.* [51] found GPs 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 HCPs providing data on implementation of the intervention. Furthermore, interviews were conducted by the researcher who was also the contact person for HCPs during the study. However, HCPs 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 HCPs, 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 HCPs (90%) participated in interviews.

CONCLUSIONS

In summary, this 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.

AUTHORS' CONTRIBUTIONS

GD designed the process evaluation study. GD and EJVd collected and analysed the data and drafted the manuscript. SCJ and JtB participated in the study design and implementation in public health and primary care, and helped to draft the manuscript. JMH, JNL, AH, GJH, and EJMF made major revisions to the manuscript. All authors contributed to the development of the SLIMMER intervention, and read and approved the final manuscript.

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The background of the page features a faint, light gray illustration of a hand holding a heart. Surrounding this central image are numerous water droplets of varying sizes, some with soft halos, creating a clean and medical aesthetic.

Chapter 7

Cost-effectiveness of the SLIMMER diabetes prevention intervention in Dutch primary health care

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CJ Hiddink, EJM Feskens, GA de Wit

Submitted

ABSTRACT

Background

Although evidence is accumulating that lifestyle modification may be cost-effective in prediabetic patients, information on the cost-effectiveness of interventions implemented in public health and primary health care settings is limited. Evidence from well-conducted pragmatic trials is needed to gain insight into the realistic cost-effectiveness of diabetes prevention interventions in real-world settings.

Objective

To assess the cost-effectiveness of the SLIMMER lifestyle intervention targeted at patients at high risk of developing type 2 diabetes compared with usual health care in a primary care setting.

Research Design and Methods

Three hundred and sixteen high-risk subjects were randomly assigned to the SLIMMER lifestyle intervention or to usual health care. Costs and outcome assessments were performed at the end of the intervention (12 months) and six months thereafter (18 months). Costs were assessed from a societal perspective. Patients completed questionnaires to assess health care utilisation, participant out-of-pocket costs, and productivity losses. Quality Adjusted Life Years (QALY) were calculated based on the SF-36 questionnaire. Cost-effectiveness planes and acceptability curves were generated using bootstrap analyses.

Results

The cost-effectiveness analysis showed that the incremental costs of the SLIMMER lifestyle intervention were €547 and that the incremental effect was 0.02 QALY, resulting in an incremental cost-effectiveness ratio (ICER) of 28,094/QALY. When cost-effectiveness was calculated from a health care perspective, the ICER decreased to 13,605/QALY, with a moderate probability of being cost-effective (56% at a willingness to pay (WTP) of €20,000/QALY and 81% at a WTP of €80,000/QALY).

Conclusions

The SLIMMER lifestyle intervention to prevent type 2 diabetes had a low to moderate probability of being cost-effective, depending on the perspective taken.

INTRODUCTION

Nowadays, diabetes is recognised as a major public health problem as it leads to a high disease and economic burden, with 5.1 million deaths and a health expenditure of USD 548 billion (11% of total health expenditure) globally in 2013 [1]. Diabetes is associated with an unfavourable lifestyle, including obesity, poor diet, and physical inactivity [1]. Although evidence is accumulating that lifestyle modification may be cost-effective in prediabetic patients, information on the cost-effectiveness of interventions implemented in public health and primary health care settings is limited [2]. Evidence from well-conducted pragmatic trials is needed to gain insight into the realistic cost-effectiveness of diabetes prevention interventions in real-world settings. The Dutch SLIM intervention, revealing a 47% diabetes risk reduction [3], proved to be cost-effective [4]. This intervention has been translated from the experimental setting into a real-world intervention, called SLIMMER [5-7]. The aim of the current study is to assess the cost-effectiveness of the SLIMMER lifestyle intervention compared with usual health care in a primary care setting. We recently reported the effects of the SLIMMER intervention: significantly greater improvements in anthropometry, glucose metabolism, dietary intake, physical activity, and quality of life were seen in the intervention group than in the control group, both at 12 and at 18 months [8]. Here, we report on the cost-effectiveness analysis conducted alongside this pragmatic randomised trial.

RESEARCH DESIGN AND METHODS

Study design

The design of the SLIMMER study has been published in detail elsewhere [6]. In short, the SLIMMER study is a randomised controlled trial carried out in Dutch primary health care between 2011 and 2014. We performed an economic evaluation from a societal perspective.

Study population and setting

Twenty-five general practices (general practitioners (GPs) and practice nurses) recruited patients aged between 40 and 70 years at increased risk of diabetes, defined as having impaired fasting glucose (IFG; 6.1-6.9 mmol/l [9]) or an elevated/high risk of type 2 diabetes (a Diabetes Risk Test score of ≥ 7 points [10]). The study was conducted in the Dutch cities Apeldoorn and Doetinchem. The SLIMMER intervention was implemented in primary health care, involving GPs and their practice nurses, dietitians, physiotherapists, and local sports clubs. 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).

Randomisation procedure

After baseline measurement, 316 participants were randomly allocated to the intervention or to the control group, using block randomisation at GP level and stratification for sex. Spouses were allocated to the same group to avoid contamination. An independent dietician from the Division of Human Nutrition, Wageningen University, performed the randomisation.

Lifestyle intervention

The SLIMMER lifestyle intervention resembled the SLIM intervention [3] and consisted of a dietary and physical activity intervention, including case management and a maintenance programme. The dietary intervention consisted of five to eight individual consultations and one group session with a dietician during 10 months. The physical activity intervention was delivered by physiotherapists as weekly group-based training sessions for 10 months. Furthermore, case management was performed by practice nurses and consisted of keeping in contact with both health care professionals and intervention participants throughout the intervention period. In addition to this core programme, a maintenance programme was delivered during the last phase of the intervention period and continued up to three months after the end of the intervention. This maintenance programme comprised of sports clinics at local sports clubs and concluding meetings with the dietician and physiotherapist during the core programme of 10 months, and a return session with the dietician, physiotherapist, and the physical activity group three months after the end of the intervention [11].

Control group

The control group received the usual health care provided by GPs and practice nurses, i.e. yearly monitoring of blood glucose, according to the guidelines of the Dutch College of General Practitioners [12]. Furthermore, at baseline, the control subjects received written information on the beneficial effects of a healthy diet and increased physical activity.

Data collection and outcomes

Measurements

Participants visited the research centre for measurements at baseline, directly after the intervention (12 months), and at 18 months. Participants completed questionnaires at each visit to assess health care utilisation, participant out-of-pocket costs, productivity losses, and quality of life. The present cost-effectiveness analysis (CEA) includes effects and costs over the total 18-month study period.

Volumes of resources used

Data on volumes of health care utilisation (general practitioner, dietician, physiotherapist, consultations at outpatient clinic, and hospitalisation), use of medication, and participant out-of-pocket costs (sports club memberships and sports equipment) were obtained from participant questionnaires. Productivity losses (related to both absence from work (absenteeism) and less productivity while working (presenteeism)) were measured using the Short Form Health and Labour Questionnaire (SF-HLQ) [13].

Cost prices

We used 2012 price levels and indexed prices when necessary using the consumer price indices from Statistics Netherlands [14]. Discounting was not applied because of the short timeframe of 18 months. A detailed description of cost prices is given in Additional file 7.1.

Intervention costs

Bottom-up micro-costing analysis was used to estimate intervention costs. Selection and recruitment of participants cost €37 per participant. Intervention materials were valued using charges paid. Training of GPs and practice nurses and supervision by a project coordinator cost €133 per participant. The volumes of individual and group dietary sessions, physical activity sessions, and the return session were collected by attendance registration. These volumes were multiplied by unit prices for each component of the lifestyle intervention. Cost prices per unit were retrieved from the Dutch guideline for costing analysis in health care [15, 16].

Utilities and quality adjusted life years (QALY)

The Short-Form Health Survey (SF-36) [17, 18] was used to assess quality of life at every visit to the research centre. Health utilities were determined by the SF-6D health state

classification [19], a preference-based single index derived from the SF-36. QALYs were calculated by multiplying health utilities by the amount of time a participant spent in a particular health state. Transitions between health states were linearly interpolated.

Statistical analyses

Intention to treat analyses were performed. Missing cost and outcome data (16%) were imputed with multiple imputation techniques, using Fully Conditional Specification and Predictive Mean Matching procedures. The imputation model included age, sex, baseline health status, randomisation group, and available costs and outcomes at each measurement. Baseline characteristics were compared with an independent samples *t* test for normally distributed data, a Mann-Whitney test for non-normally distributed data, and a Pearson's chi-squared test for categorical data.

Economic analyses

The incremental cost-effectiveness ratio (ICER) was calculated as the difference in costs divided by the difference in QALYs between the intervention and the control group using a bootstrap analysis with 1000 simulations. From the bootstrap analysis, a cost-effectiveness plane was plotted, where each quadrant indicates whether the intervention is more or less effective and more or less expensive than usual health care. Furthermore, cost-effectiveness acceptability curves (CEACs) were plotted to illustrate the uncertainty of cost-effectiveness estimates. The CEAC shows the probability that the SLIMMER intervention is cost-effective compared with usual health care, for a range of threshold values for willingness to pay (WTP) per additional QALY. In the Netherlands, threshold values of €20,000 to €80,000 per QALY are commonly used [20].

Sensitivity analyses

Sensitivity analyses were performed to assess cost-effectiveness using different input parameters. In the first sensitivity analysis, cost-effectiveness was calculated from a health care perspective, taking into account only intervention costs and direct health care costs. The second sensitivity analysis was restricted to participants with complete cost and effect data, that is, complete cases. In the third sensitivity analysis, intervention costs were reduced. If the SLIMMER intervention would be implemented regularly in health care, the project coordinator would be redundant, therefore these costs were excluded.

RESULTS

For the economic analysis, data for 288 (91%) SLIMMER study participants were available (Figure 7.1). Twenty-eight participants were excluded because they did not complete a single questionnaire nor were other measurements available. As shown in Table 7.1, baseline characteristics were similar between the intervention and the control group.

Costs

Table 7.2 shows costs of the intervention and the control subjects. Total costs of the intervention were €677 per participant. Costs for the intervention, participant out-of-pocket costs, and costs for absenteeism were higher in the intervention group than in the control group, whereas costs for hospitalisation, medication, and presenteeism were lower. The incremental cost difference between groups was €547.

QALYs

Participants' health status at baseline was comparable between the intervention and the control group, whereas it was higher in the intervention group than in the control group after 12 and 18 months, albeit non-significantly. Total QALY over the 18-month study period was 0.02 (-0.01; 0.05) higher in the intervention group than in the control group (Table 7.3).

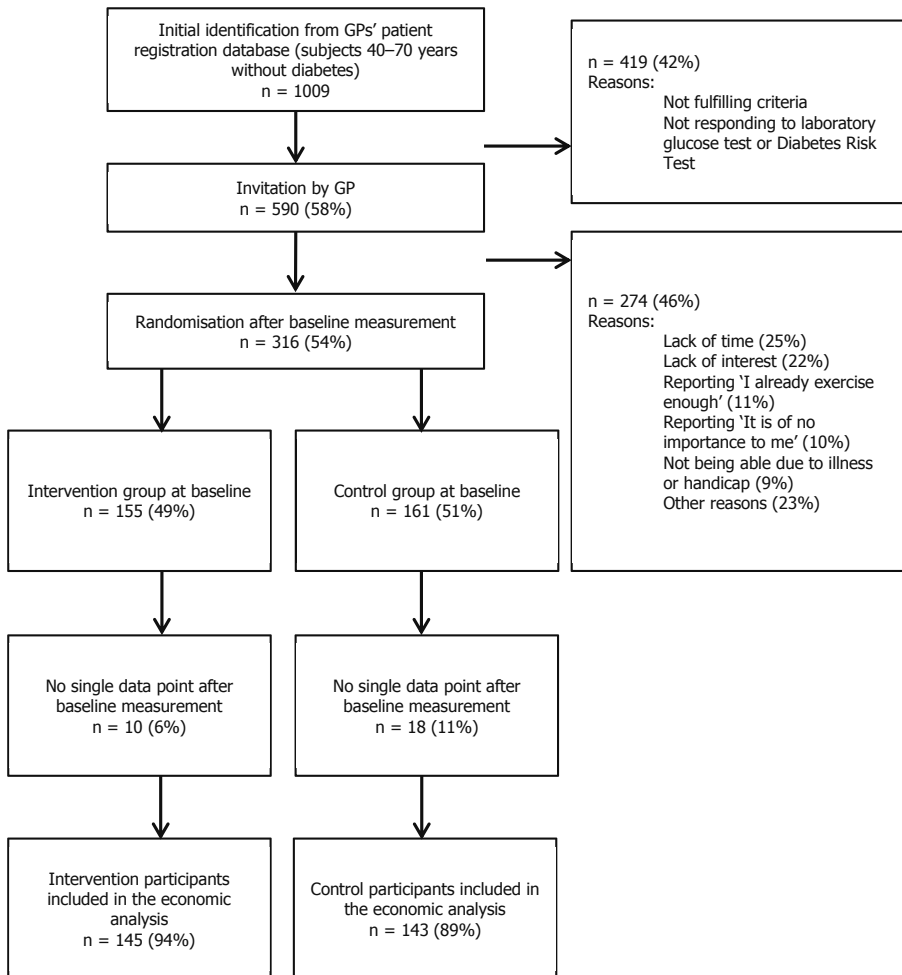


Figure 7.1. Flow diagram of the SLIMMER randomised controlled trial, for cost-effectiveness analyses.

Economic analyses

The higher costs and effects in the intervention group compared with the control group resulted in an ICER of 28,094/QALY (Table 7.4). From the bootstrap analysis, it appeared that most simulations showed higher costs for the intervention as well as small positive QALY differences between the intervention and the control group (Additional file 7.2). Figure 7.2 shows that, if society is willing to pay either €20,000 or €80,000 per additional QALY, the probability that the intervention will be cost-effective is 43% and 70%, respectively.

Table 7.1. Baseline characteristics of the SLIMMER study participants included in the cost-effectiveness analyses ^a.

	Intervention (<i>n</i> = 145)	Control (<i>n</i> = 143)
Sex (<i>n</i> female, %)	67 (46%)	71 (50%)
Age (years)	60.9 ± 6.0	61.1 ± 6.5
Education level (<i>n</i> , %)		
Low	77 (53%)	76 (53%)
Middle	40 (28%)	28 (20%)
High	28 (19%)	39 (27%)
Ethnicity (<i>n</i> , %)		
Dutch	128 (88%)	129 (90%)
Western non-Dutch	13 (9%)	11 (8%)
Non-western non-Dutch	4 (3%)	3 (2%)
Family history of diabetes (<i>n</i> , %)		
No	46 (32%)	61 (43%)
First degree	70 (48%)	65 (45%)
Second degree	29 (20%)	17 (12%)
Paid job (<i>n</i> , %)	67 (46%)	68 (48%)
Smoking (<i>n</i> , %)	22 (15%)	27 (19%)
BMI (kg/m ²) ^b	30.3 ± 4.6	29.9 ± 4.8
Waist circumference (cm) ^b		
Male	109.1 ± 12.2	107.8 ± 10.1
Female	101.3 ± 12.9	99.9 ± 12.6
Fasting glucose (mmol/l)	6.6 ± 0.6	6.5 ± 0.6
2-h glucose (mmol/l) ^b	8.2 ± 2.8	8.0 ± 2.5
Fasting insulin (pmol/l)	89.6 ± 51.7	84.8 ± 52.2
SF-6D health state	0.79 ± 0.12	0.79 ± 0.10

^a Data are mean ± SD, or *n* (%). ^b INT *n* = 144, CON *n* = 143

Sensitivity analyses

The sensitivity analyses for complete cases and reduced intervention costs revealed similar results as the base case analysis (Table 7.4). However, when cost-effectiveness was calculated from a health care perspective, the ICER decreased to 13,605/QALY (Table 7.4). The probability of the intervention being cost-effective was 56% at a WTP of €20,000/QALY and 81% at a WTP of €80,000/QALY (Figure 7.3).

Table 7.2. Mean (standard error of the mean) costs for intervention and control subjects.

		Intervention (n = 145)	Control (n = 143)
	Unit costs (€)	Mean total costs € (SEM)	Mean total costs € (SEM)
Intervention costs			
Selection and recruitment by practice nurse	37.08 per participant	37 (0)	0 (0)
Materials	15.65 per participant	16 (0)	0 (0)
Project coordinator	133.02 per participant	133 (0)	0 (0)
Individual consultations with dietician	28.64 per hour	101 (1)	0 (0)
Group session with dietician	6.20 per session	4 (0)	0 (0)
Group-based training sessions with physiotherapist	8.06 per session	319 (13)	0 (0)
Sports clinics at local sports club	24.69 per sports clinic	60 (4)	0 (0)
Return session with dietician and physiotherapist	8.92 per session	6 (0)	0 (0)
<i>Subtotal</i>		677 (16)	0 (0)
Direct health care costs			
Consultations general practice	Additional file 7.1	118 (12)	190 (16)
Consultations dietician	28.64 per hour	2 (1)	9 (4)
Consultations physiotherapist	38.18 per hour	111 (26)	94 (21)
Consultations health care specialist	76.38 per visit	291 (41)	272 (35)
Hospital days	484.72 per day	426 (146)	637 (374)
Medication	Individualised	369 (38)	526 (55)
<i>Subtotal</i>		1,317 (178)	1,728 (414)
Direct non-health care costs			
Sports club membership	Individualised	233 (35)	224 (31)
Sports equipment	Individualised	151 (28)	112 (36)
<i>Subtotal</i>		384 (49)	336 (48)
Indirect non-health care costs			
Absence from work	Individualised	1,995 (714)	1,285 (574)
Less productivity while working	Individualised	500 (180)	975 (367)
<i>Subtotal</i>		2,495 (763)	2,261 (730)
Total costs (€)			
Societal perspective	-	4,872 (854)	4,325 (887)
Health care perspective	-	1,993 (178)	1,728 (414)

Table 7.3. Mean health-related quality of life at the end of the intervention (12 months) and at 18-month follow-up and the QALYs for the intervention and the control group.

	Intervention (<i>n</i> = 145)	Control (<i>n</i> = 143)	Mean difference
	Mean (SEM)	Mean (SEM)	Mean (95% CI)
SF-6D health status			
Baseline	0.79 (0.01)	0.79 (0.01)	-0.001 (-0.03; 0.02)
12 months	0.81 (0.01)	0.79 (0.01)	0.02 (-0.002; 0.05)
18 months	0.80 (0.01)	0.79 (0.01)	0.01 (-0.02; 0.04)
QALY total over 18 months	1.20 (0.01)	1.19 (0.01)	0.02 (-0.01; 0.05)

Table 7.4. Results of sensitivity analyses.

	Sample size per group		Incremental effect	Incremental costs	ICER	Dominance		Probability cost-effective (WTP ^a €20,000/QALY)		Probability cost-effective (WTP ^a €80,000/QALY)	
	Intervention	Control				€ /QALY	%	%	%	%	%
Societal perspective	145	143	0.02	547	28,094		30	43		70	
Health care perspective	145	143	0.02	265	13,605		26	56		81	
Complete cases	123	119	0.02	600	24,586		32	48		75	
Reduced intervention costs	145	143	0.02	414	21,266		34	47		73	

^a WTP = Willingness to pay.

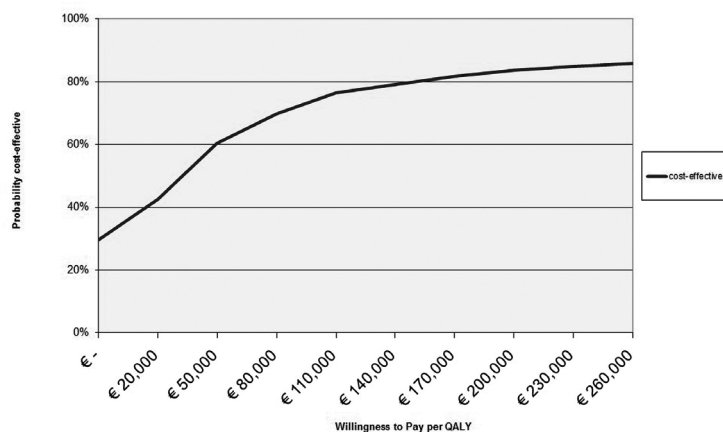


Figure 7.2. Cost-effectiveness acceptability curve of the SLIMMER intervention compared to usual health care, from a societal perspective.

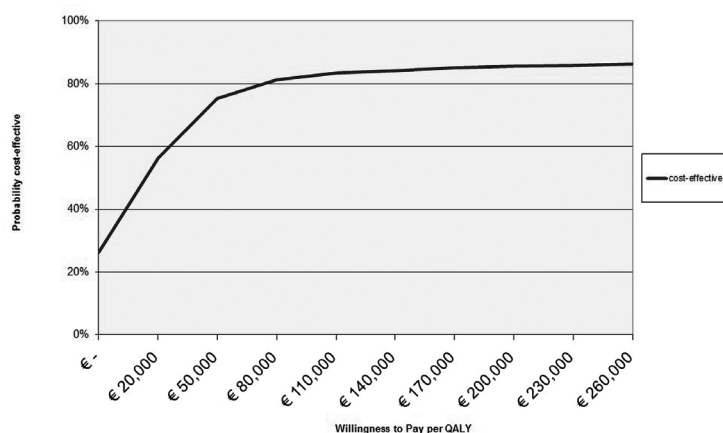


Figure 7.3. Cost-effectiveness acceptability curve of the SLIMMER intervention compared to usual health care, from a health care perspective.

DISCUSSION AND CONCLUSION

The current study showed that the SLIMMER intervention was both more costly and more effective than usual health care. As expected, the intervention group had a lower health care utilisation and reported less presenteeism than the usual care group. From a societal perspective, the ICER was 28,094/QALY, reflecting a relatively low probability of 43-70% at usual Dutch threshold values of WTP per QALY. From a health care perspective, the ICER was 13,605/QALY, with a moderate probability of being cost-effective (56% at a WTP of €20,000/QALY and 81% at a WTP of €80,000/QALY).

Nowadays, more and more insight into the cost-effectiveness of diabetes prevention programmes is becoming available. Recently, a systematic review found a median ICER for diet and physical activity programmes of \$13,761/QALY, from a health care perspective [2]; this is comparable to our ICER. Most of the studies included in that review were based on the US Diabetes Prevention Program or the Finnish Diabetes Prevention Study (DPS), like our DPS-based SLIMMER study. However, a Dutch study that investigated the cost-effectiveness of a primary care lifestyle intervention for prevention of type 2 diabetes and cardiovascular disease showed that the intervention was cost-saving without being effective [21]. Another Dutch study, on the prevention of weight gain among employees, failed to reveal cost-effectiveness too [22].

The higher costs in the intervention group were due mainly to costs of the intervention programme. We should therefore consider possibilities to reduce these intervention costs, like appointing sports instructors instead of higher-salaried physiotherapists. The Greaves *et al.*'s review [23] showed that a wide range of providers can deliver effective interventions. Furthermore, the provision of group-based dietary consultations could be considered, as Li *et al.*'s review showed that group-based interventions were less costly and more cost-effective than individual-based interventions [2]. In addition, an even more individually tailored intervention approach could be used by referring participants earlier to regular sports clubs when they are ready to do so, rather than adhering strictly to the programme's schedule. These adaptations were not taken into account in the sensitivity analysis because the impact of changes in the intervention on its effectiveness is currently unknown. Further research on this issue is necessary.

Costs for health care utilisation, mainly hospitalisation and medication use, and presenteeism were lower in the intervention group than in the control group. This was also found in the DPP study [24] and the Dutch Hoorn Prevention study [21]. The reduced direct health care costs indicate that the benefits of this intervention may be attractive for health insurance companies. Out-of-pocket costs were €48 higher in the intervention group than in the control group. We separately asked participants about their willingness to pay for the intervention. On average, they reported that they would be willing to pay €97 (data not shown). The additional out-of-pocket costs of €48 therefore appear to be acceptable for participants. Unexpectedly, costs for absenteeism were higher in the intervention group than in the control group. More detailed inspection of the causes of absenteeism revealed that these productivity losses were in general

unrelated to physical fitness or diabetes, but for example to fever. Hence, the higher productivity costs in the intervention group could be a coincidental finding.

Limitations of the study should be considered. First, data were collected intermittently to reduce participant burden, but this may be associated with a slight inaccuracy in data reporting, and in cost estimates as a consequence [25]. Second, besides monetary investments, participants have to make a time investment, which was not taken into account in the current analysis. Third, we included costs and effects during the intervention period up to six months after the end of the intervention. Although the intervention was not cost-saving, beneficial effects on intermediate outcomes were found. Improvements in weight, fasting insulin, dietary intake, and physical activity were observed at 12 months, and most of these improvements were sustained at 18 months [8]. In Li *et al.*'s review, it was shown that programmes were most cost-effective in the longer term, indicating that short-term studies are limited in their ability to capture the full range of an intervention's health benefits and cost savings [2]. Therefore, more insight into longer-term cost-effectiveness is needed, and the results of our study should be modelled to a lifetime horizon. We expect more favourable cost-effectiveness on the longer term because diabetes will be postponed or prevented, leading to cost savings in the future.

A strength of the current study is the use of a randomised design in a real-world setting. Furthermore, data were complete for 84% of the measurements. In the event of missing values, multiple imputation techniques were used, which is a status quo method for dealing with missing data [26]. Moreover, we performed the CEA from a societal perspective as recommended by the Dutch guideline for costing analysis in health care [15, 16]. In addition, we performed the evaluation from a health care perspective, the perspective most relevant to health insurance companies which may consider to reimburse the intervention programme.

In summary, our results indicate that the SLIMMER intervention is more cost-effective from a health care perspective than from a societal perspective. Costs were higher in the intervention group, mostly due to costs of the intervention programme and higher productivity losses. Intervention costs could be decreased to a certain extent to further enhance the cost-effectiveness of the SLIMMER intervention.

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Additional file 7.1. Detailed description of cost prices.

Cost prices of intervention implementers (practice nurse, dietician, and physiotherapist), the project coordinator, and sports clubs' instructors (giving sports clinics) were retrieved from the Dutch guideline for costing analysis in health care [15, 16].

Cost prices of health care utilisation (general practice, dietician, physiotherapist, health care specialist, and hospital days) were retrieved from the Dutch guideline for costing analysis in health care [15, 16]. An overview of exact cost prices can be found in Table 7.2 and Table 7.A1.

Cost prices of medication were based on summary cost prices for average daily dosages as used in the Netherlands, according to the *Pharmacotherapeutic Compass* [27], augmented by the 3-month delivery tariff charged by pharmacies.

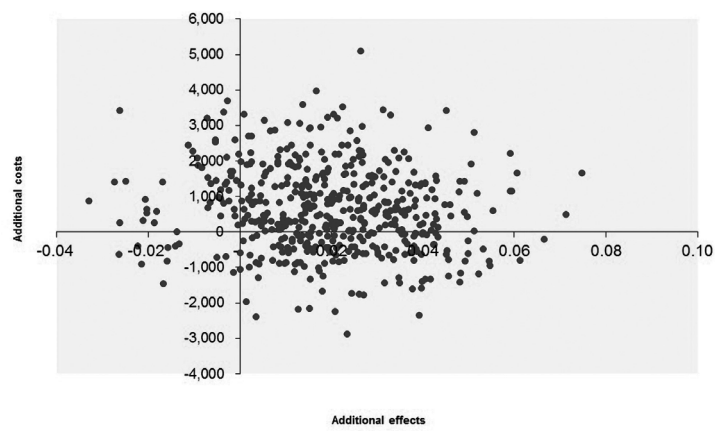
The participant out-of-pocket costs were valued as indicated by the participants themselves.

Productivity losses were assessed with the friction cost approach [15, 16], using a friction period of 115 days. For all participants with a paid job, age- and sex-standardised productivity costs per hour were used, following the Dutch guideline for costing analysis in health care [15, 16].

Table 7.A1. Unit costs for cost categories not mentioned in Table 7.2

Unit costs (€)	
Direct health care costs	
General practice	
Visit to practice	29.70 per visit
Phone consultation	14.85 per consultation
Home visit	45.61 per visit
Phone contact for medical prescription	14.85 per contact

Additional file 7.2. Cost-effectiveness plane from 1000 bootstrap simulation for the SLIMMER intervention compared to usual health care.



The background of the page is a light gray color. It is decorated with a pattern of white circles of various sizes, some of which are slightly blurred, giving a sense of depth. In the center of the page, there is a faint, stylized illustration of a person with their arms outstretched, possibly representing a person in a state of joy or freedom. The person is also rendered in a light gray color, blending with the background.

Chapter 8

General discussion

MAIN FINDINGS

The overall objective of this project was to improve the lifestyle behaviour in high-risk subjects in order to reduce the risk of developing type 2 diabetes. The main findings of this research project as described in **chapters 2 to 7** are summarised in Table 8.1.

The literature in **chapter 2** showed that, all over the world, clinical diabetes prevention trials have been translated to daily practice. In Dutch practice, however, this was still lacking. Therefore, the SLIM intervention – conducted in an experimental setting and revealing a 47% diabetes risk reduction – was translated to practice, and the adapted intervention, called SLIMMER, was tested in a one-year pilot study. Collaboration between professionals from primary health care and public health was considered necessary to prevent diabetes.

A pilot study ($n = 31$) with process evaluation was conducted to test the feasibility and desired impact of the SLIMMER intervention (**chapter 3**). This study showed that inclusion and retention of high-risk subjects was successful and that both participants and health care professionals were satisfied with the SLIMMER intervention. Overall, the intervention was implemented as planned and appeared to be suitable for application in practice. Some improvements were identified and refinements were made prior to further implementation and evaluation.

The evaluation design of the SLIMMER intervention was described in **chapter 4**. A logic model of change was composed to link intervention activities, their mechanisms of change, expected behaviours, and intervention outcomes in a logical order. The SLIMMER intervention consisted of a 10-month dietary and physical activity intervention, including case management and a maintenance programme. Effect, process, and economic evaluations were performed.

The effectiveness of the SLIMMER intervention was tested in a randomised controlled trial (**chapter 5**). We found that, after 12 and 18 months, the intervention group significantly improved weight ($\beta = -2.7$ kg and $\beta = -2.5$ kg, respectively) and fasting insulin ($\beta = -12.1$ pmol/l and $\beta = -8.0$ pmol/l, respectively) compared with the control group. Furthermore, intake of total and saturated fat decreased and fibre intake increased more in the intervention group than in the control group, both at 12 and at 18 months ($p < 0.05$). Fruit intake increased at 12 but not at 18 months, whereas vegetable intake increased at 18 but not at 12 months. The DHD-index score, indicating adherence to

the Dutch dietary guidelines, was significantly higher in the intervention group than in the control group, both at 12 and at 18 months ($p < 0.05$). Improvements in vigorous activities and physical fitness were found, both at 12 and at 18 months. Finally, beneficial changes in several domains of quality of life were found both at 12 and at 18 months, although not all domains reached statistical significance.

As described in **chapter 6**, the process evaluation showed that 316 high-risk subjects were recruited and that the intervention was very well received by both participants and health care professionals. The intervention programme was to a large extent implemented according to the manual and fitted well within the regular functioning and professional performance of health care professionals. Higher dose received and participant acceptability were related to improved health outcomes and dietary behaviour, but not to physical activity behaviour. Furthermore, targeting both diet and physical activity, using behaviour change techniques, focusing on behaviour maintenance, tailoring the intervention, and adopting a multidisciplinary approach may have facilitated intervention effectiveness.

The economic evaluation in **chapter 7** showed that the SLIMMER intervention was both more costly and more effective than usual health care. From a societal perspective, the incremental cost-effectiveness ratio (ICER) was 28,094/QALY, reflecting a relatively low probability of 43–70% at usual Dutch threshold values of willingness to pay (WTP) per QALY. From a health care perspective, the ICER decreased to 13,605/QALY, with a moderate probability of being cost-effective (56% at a WTP of €20,000/QALY and 81% at a WTP of €80,000/QALY). Intervention costs could be decreased to a certain extent to further enhance cost-effectiveness.

Table 8.1. Summary of the main findings of this thesis.

Objective	To give an overview of the translation of the SLIM intervention to a Dutch real-life setting and discuss the role of primary health care in implementing lifestyle intervention programmes.
Methods	Literature overview
Findings	<ul style="list-style-type: none"> • A one-year pilot study was conducted, consisting of a dietary and physical activity part, and guided by process evaluation, to test the applicability of the adapted SLIM intervention in Dutch primary health care. • Collaboration between professionals from primary health care and public health is needed to prevent diabetes.
Objective	To describe and investigate the feasibility and impact of the SLIMMER intervention in Dutch primary health care.
Methods	Pilot study with a one group pre-test post-test design, guided by process evaluation
Findings	<ul style="list-style-type: none"> • 31 subjects participated in the intervention with mean weight loss of 3.5 kg. • Both participants and health care professionals were satisfied with the intervention. • The intervention was implemented as planned and appeared to be suitable for application in practice. • Improvements were identified and refinements are made prior to further implementation and evaluation.
Objective	To describe the evaluation design of the SLIMMER diabetes prevention intervention in a Dutch real-life setting.
Methods	Study protocol
Findings	<ul style="list-style-type: none"> • A logic model of change was composed to link intervention activities with intervention outcomes in a logical order. • Subjects at high risk of diabetes were randomly allocated to the intervention (10-month combined dietary and physical activity intervention, including case management and maintenance programme) or to the control group (usual health care). • The intervention is guided by effect, process, and economic evaluation.
Objective	To investigate the effectiveness of the SLIMMER intervention in Dutch primary health care on clinical and metabolic risk factors, dietary intake, physical activity, and quality of life after 12 and 18 months.
Methods	Randomised controlled trial
Findings	<ul style="list-style-type: none"> • Improvements in clinical and metabolic characteristics after 12 and 18 months <ul style="list-style-type: none"> - Significantly more weight loss in intervention group than in control group ($\beta=-2.7$ kg at 12 months, $\beta=-2.5$ kg at 18 months). - Significantly greater decrease in fasting insulin in intervention group than in control group ($\beta=-12.1$ pmol/l at 12 months, $\beta=-8.0$ pmol/l at 18 months). - Intervention subjects improved weight and glucose tolerance, independent of manner of recruitment. • Improvements in dietary intake, physical activity, and quality of life.
Objective	To investigate how the SLIMMER intervention was delivered and received in Dutch primary health care and how this could explain intervention effectiveness.
Methods	Process evaluation
Findings	<ul style="list-style-type: none"> • In total, 316 subjects at high risk of developing type 2 diabetes were recruited. • Actual dose received was in line with the planned dose according to the manual. • The SLIMMER intervention was very well received by both participants and health care professionals. • The intervention programme was to a large extent implemented according to the manual. • In general, the SLIMMER intervention was not very different from health care professionals' regular functioning and professional performance. • Higher dose received and participant acceptability were related to improved health outcomes and dietary behaviour, but not to physical activity behaviour.

Table 8.1. Continued

Objective	To assess the cost-effectiveness of the SLIMMER intervention compared with usual health care in Dutch primary health care.
Methods	Economic evaluation alongside a randomised controlled trial
Findings	<ul style="list-style-type: none">• Incremental costs were €547 and the incremental effect was 0.02 QALY.• From a societal perspective, the incremental cost-effectiveness ratio (ICER) was 28,094/QALY, with a low probability of being cost-effective (43% at a willingness to pay (WTP) of €20,000/QALY and 70% at a WTP of €80,000/QALY).• From a health care perspective, the ICER was 13,605/QALY, with a moderate probability of being cost-effective (56% at a WTP of €20,000/QALY and 81% at a WTP of €80,000/QALY).

METHODOLOGICAL CONSIDERATIONS

Research in practice

Efficacy trials, such as the Finnish Diabetes Prevention Study (DPS) [1], the US Diabetes Prevention Program (DPP) [2], and the Dutch Study on Lifestyle intervention and Impaired glucose tolerance Maastricht (SLIM) [3], provided us with convincing evidence on type 2 diabetes prevention by lifestyle interventions in high-risk subjects. Such trials show us the performance of interventions under highly controlled and more or less ideal conditions and maximise the likelihood of observing an intervention effect, if there is one. Although this has several methodological advantages and increases internal validity, the circumstances are far from those of the real world [4]. The diabetes prevention interventions in these efficacy trials were intensive, prohibitively expensive, and used highly standardised protocols, thereby not reflecting real-world circumstances. Therefore, these studies were translated to real-world settings and tested in effectiveness trials. Such trials account for external factors that may moderate the intervention's effect, reflecting real-world conditions, and can therefore be more relevant to primary health care and policy [4]. Effectiveness trials have a higher external validity than efficacy trials, resulting in better generalisability.

Several steps are needed for an efficacious intervention to become effective in the real world. A thorough adaptation of an efficacious intervention and pilot-testing of this adapted intervention are important steps. When an intervention is being translated from research to practice, adaptations are inevitable because of the substantial differences between those settings. These adaptations, however, might have consequences for intervention effectiveness. Few studies, however, describe how and which adaptations have been made [5]. In the SLIMMER study, firstly, we adapted the efficacious SLIM study [3] to Dutch primary health care. Core elements of the SLIM intervention

were identified, and consensus on suggested adaptations was achieved between intervention developers and local health care professionals in a joint decision-making process [6]. Secondly, the adapted intervention was tested in a pilot study (chapter 3). Several studies have shown that pilot-testing before large-scale implementation is valuable, as challenges for refinement become clear, recruitment and retention may improve, there may be fewer deviations from the budget, and chances for success may increase [7-9]. The thorough preparation of the SLIMMER intervention, including the abovementioned steps, may have contributed to its effectiveness.

The distinction between efficacy and effectiveness trials is a continuum rather than a dichotomy [4]. In this respect, the SLIMMER intervention can be positioned closer to an effectiveness trial. The intervention was implemented in a primary health care setting and delivered by representative usual providers (general practitioners (GPs), practice nurses, dieticians, and physiotherapists) who did not need much additional training as the intervention fitted well within their regular functioning and professional performance (chapter 6). GPs referred participants to the intervention programme and used their natural referral lines, as is normal practice in the Netherlands. Active case finding for high-risk patients, as was done in our study, does not conform to daily practice. However, most practice nurses perceived this active approach as useful (data not shown). Furthermore, a standardised protocol was used, but this was applied with flexibility in order to tailor the intervention to participants' needs and wishes. No additional resources or equipment were needed to implement the intervention. In conformity with normal practice in the Netherlands, the control group received the usual health care provided by GPs and practice nurses (yearly monitoring of blood glucose, according to the guidelines of the Dutch College of General Practitioners) [10].

Conducting research in practice often has implications for the study design. Performing a randomised controlled trial, which is considered the gold standard for determining the effects of a treatment, is often difficult. However, we were able to use a randomised design and individuals rather than groups were randomised. We adapted the randomised design to make it suitable for application in primary health care practice by incorporating block randomisation at GP level (chapter 4). This was done in order to motivate GPs to participate in the study and ensured that each GP had both intervention and control participants. We attempted to reduce contamination within general practices by paying special attention to this during the SLIMMER kick-off training for

health care professionals. By means of the randomised design, we were able to attribute the observed improvements (chapter 5) to the SLIMMER intervention.

It is often said that 'it takes 17 years to turn original clinical research to the benefit of patients' [11]. This means that uptake of an intervention into clinical guidelines requires perseverance. When we look at the SLIMMER intervention, this is indeed the case. The SLIM study started in 1999 [3], and 17 years later, which is actually today, the SLIMMER intervention is not yet included in primary health care standards. However, the results of this study provide valuable insights that can contribute to this uptake.

Theoretical basis

If we are to understand how interventions work, we must understand the causal mechanisms hypothesised to explain intervention effectiveness [12]. Therefore, theories are often used as a basis for lifestyle intervention development. However, evidence on the association between using theory and increased effectiveness is mixed [13, 14]. The original SLIM study used a combination of theories such as the Stages of Change model [15] and the Theory of Planned Behaviour [16].

In the SLIMMER study, insight into causal mechanisms was gained in two ways. Firstly, behaviour change techniques used in the SLIMMER intervention were identified and linked to behavioural determinants by means of the Theoretical Domains Framework [17, 18]. These determinants were then linked to intermediate and long-term outcomes in a logic model (chapter 4) to describe how changing determinants could possibly lead to behaviour change and improved health outcomes. In addition, a maintenance programme for the SLIMMER intervention was designed using the Intervention Mapping protocol [19]. Specific behaviours and determinants for maintenance were identified and then linked to behaviour change techniques and practical applications [20]. Greaves *et al.*'s review [13] showed that the use of behaviour change techniques (e.g. goal-setting and self-monitoring) was associated with increased intervention effectiveness. These techniques were also used in the SLIMMER intervention, thereby possibly contributing to intervention effectiveness. Greaves *et al.* [13] recommend a planned approach to intervention design, such as the Intervention Mapping protocol [19] used in our study. As discussed below, further research into the relation between behavioural determinants and health outcomes in the SLIMMER intervention is needed. Secondly, a process evaluation was performed to gain insight into the relationship between specific intervention activities and outcomes [21]. This provided

us with valuable information on intervention elements that were probably linked to intervention effectiveness, such as a highly intensive intervention programme, focusing on behaviour maintenance, and tailoring the intervention (chapter 6).

Evaluation design

A comprehensive evaluation approach, including effect, process, and economic evaluations, was used to investigate causal processes for behaviour change. An effect evaluation was used to gain insight into outcomes on several levels (behaviour, health, quality of life). A process evaluation was conducted to assess how the intervention was delivered and received and how this could explain intervention effectiveness. Finally, an economic evaluation was performed to provide valuable information on costs and benefits of the intervention. A logic model was composed to describe the hypothesised causal pathway. This facilitated the understanding of intervention effectiveness and provided insights for further improvements, as discussed below.

Furthermore, triangulation of qualitative and quantitative data – gathered by a combination of multiple methods from both participants and health care professionals – increased the credibility and validity of our results. This gave us a profound understanding of the delivery of the intervention and possible aspects that could explain intervention effectiveness.

Generalisability to other individuals and settings

The generalisability of intervention results to other individuals and settings can be very dependent on these factors [22]. Our study participants were not substantially different from non-responders and drop-outs (chapter 5), and, as they were recruited by GPs who reach nearly all segments of the population [23], they can be considered as a representative sample of patients in the Netherlands. Furthermore, our study focussed on high-risk subjects and our study participants indeed could be classified as such, as most of them were of an advancing age (mean of 61 years), were overweight or obese (48% and 42%, respectively), and had a family history of diabetes (63%). Also, subjects with a low socioeconomic status (SES) were successfully reached (53% of the participants had a low SES) (chapter 5). The prevalence of type 2 diabetes is especially high among low SES subjects [24], and this group is often hard to reach [25, 26]. The fact that this group was successfully reached might be due to the fact that participants were recruited by GPs, who reach nearly all segments of the population [23], including those with a low SES. However, the number of subjects with no education or only primary

school (lowest SES group) was rather low in our study (9%). Furthermore, only 11% of the study participants were of non-Dutch origin (chapter 5). Therefore, the results of our study might not apply to subjects with the lowest SES or to ethnic minorities, and the intervention programme might need to be tailored to the specific needs of these groups. This issue is currently being addressed in the Dutch MetSLIM study [27]. In this study, the original SLIM intervention has been adapted to the needs of these specific groups by providing activities for men and women separately, paying attention to price concerns, and providing the programme in the neighbourhood.

The SLIMMER intervention was implemented in two primary health care settings that are considered representative of Dutch primary health care. This was verified during the translational process by checking whether adaptations made to SLIM corresponded with national health care practices, and the result was positive [6]. However, intervention implementation in more rural and remote areas might require additional adaptations as facilities might not be available in the neighbourhood. Participants were recruited by GPs and practice nurses, and this fits in their role as gatekeepers of the Dutch health care system [28]. Implementation of this intervention could therefore be generalised to countries with similar health care systems, such as the UK and Scandinavian countries, whereas implementation in countries with different systems might need adaptations.

RESULTS IN PERSPECTIVE

The feasibility and potential impact of the intervention were optimised by conducting a pilot study (chapter 3), as was also shown in the BRIDGES programme, in which several diabetes translational research studies were implemented in real-world settings [7]. From our pilot study, we learned that local support among stakeholders was created by initiating a local steering committee who took responsibility for the intervention's implementation process. This was also recognised in the BRIDGES programme, where strong networks were seen as an enhancer for implementing and disseminating interventions [7].

An overview of clinical diabetes prevention trials that were translated into practice was given in chapter 2. Since then, increasing attempts have been made to translate interventions to real-world settings. However, the translation of efficacious interventions into routine practice remains a challenge [29]. In chapter 5, we showed that the SLIMMER intervention improved body weight and several clinical and metabolic risk factors, both at 12 and at 18 months. In general, these improvements were stronger than

in most other real-world programmes [29-32]. On the basis of the weight loss results in our study, we estimated that diabetes risk could be reduced by 43% at 12 months and by 40% at 18 months. This is comparable to the 47% risk reduction in the original SLIM study [3] and higher than the 26% risk reduction that was revealed in a review of 36 real-world studies [29]. Possibly, the high intensity of our intervention programme has contributed to its effectiveness, as was shown in chapter 6.

In a recent review, it was stated that effects of dietary intake and physical activity on diabetes prevention in real-world settings are poorly reported in the literature [29]. In chapter 5, we reported in detail on effects on dietary intake and physical activity. We found beneficial changes in intakes of fat, saturated fat, and fibre, and vigorous activities. The literature has shown that fat intake, especially saturated fat, is probably associated with an increased risk of type 2 diabetes, although evidence is mixed [33-37], and that dietary fibre intake [34, 38-41] and increased physical activity [1-3, 42, 43] could reduce this risk.

Our process evaluation revealed that higher intervention intensity (dose received) was associated with weight loss and change in dietary behaviour, but not with change in physical activity behaviour (chapter 6); this is in line with other studies [13, 29, 44, 45]. However, no clear evidence exists for a particular minimum threshold for intervention intensity [13]. Also, higher participant satisfaction was associated with increased weight loss in our study. Mean participants' acceptability rating for the overall SLIMMER intervention was 82 out of 100. This is slightly higher than in the Dutch Beweegkuur lifestyle intervention, with an acceptability rating of 7.7 out of 10 [46]. In general, results on process outcomes are difficult to compare between studies, 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. Other intervention components that might be associated with increased intervention effectiveness were observed in our process evaluation, like targeting both diet and physical activity, using behaviour change techniques, focusing on behaviour maintenance, tailoring the intervention, and adopting a multidisciplinary approach. These intervention components were also found in Greaves *et al.*'s review [13].

In chapter 7, we showed that the SLIMMER intervention was more cost-effective from a health care perspective than from a societal perspective (ICERs were 28,094/QALY and 13,605/QALY, respectively). Costs were higher in the intervention group, mostly due to costs of the intervention programme and higher productivity losses. A recent systematic

review found a median ICER for diet and physical activity programmes of \$13,761/QALY, from a health care perspective [47]; this is comparable to our ICER. One Dutch primary care lifestyle intervention proved to be cost-saving without being effective [48], and another Dutch study failed to show cost-effectiveness [49].

IMPLICATIONS FOR PRIMARY HEALTH CARE

Our study showed that the SLIMMER intervention was effective in improving diabetes risk factors in the short and the long term (chapter 5), feasible to implement in primary health care (chapter 6), and cost-effective from a health care perspective (chapter 7). However, several other prerequisites must be met before a sustainable intervention can be implemented in routine practice.

Firstly, an infrastructure is needed to scale up intervention implementation. Local prevention structures need to be built in which an alliance between public health and primary health care is achieved [50]. This alliance was also emphasised in WHO European Region's health policy framework *Health 2020: A European policy framework and strategy for the 21st century* [51]. A Dutch study on promoting collaboration between public health and primary care showed that local stakeholders were open to collaboration and perceived collaboration as positive [52]. A study on global translational diabetes research showed that having a collaboration between several sectors enhanced intervention implementation [7]. In our study, a local steering committee was formed, in which local authorities, the public health service (community health service), the regional supporting organisation for primary care (ROS), and primary health care professionals worked together and took responsibility for the intervention's implementation process. The initiation of this local steering committee created local support among stakeholders (chapter 3). Often, a third party, such as the community health service in our study, is of added value in bringing several parties together [53]. It has, however, been shown that sustaining an alliance is difficult [53]. Within the Dutch BeweegKuur lifestyle intervention, local networks in over 120 municipalities were formed in which primary health care, public health, and local sports clubs worked together [54]. Further implementation of the SLIMMER intervention might make use of these networks.

Secondly, an intervention should fit into the regular functioning and performance of health care professionals. Intervention effectiveness might not be achieved if intervention providers are unfamiliar with the intervention approach [55]. Furthermore, it is likely that deviating from regular functioning and performance will require more

training, threaten implementation integrity, and lower professional motivation. Health care professionals in our study indicated that the SLIMMER intervention was not very different from their regular functioning and professional performance and that a two-hour kick-off training session was sufficient to make them well-informed and prepared for the implementation (chapter 6).

Thirdly, multidisciplinary teams are needed to effectively implement diabetes prevention programmes [56]. In our study, GPs, practice nurses, dieticians, physiotherapists, and local sports clubs together implemented the SLIMMER intervention (chapter 4), and they appreciated its multidisciplinary nature (chapter 6). GPs are in a unique position to provide guidance for diabetes prevention because of their high referral score, high perceived expertise, and reach to nearly all segments of the population [23], and almost 75% of the Dutch population has yearly contact with a GP [57]. However, GPs perceive barriers to giving their patients nutrition and physical activity guidance, such as time constraints and lack of self-efficacy [58-62]. Nowadays, practice nurses support GPs and provide an increasing proportion of preventive lifestyle advice [63]. Although they are knowledgeable and patients are satisfied with their care, they perceive the same barriers as GPs. Therefore, they need to cooperate with dieticians and physiotherapists who are specialists in the area of nutrition and physical activity [63], as was done in our study. As GPs act as gatekeepers of the health care system [28], they have natural referral lines with dieticians, and often also with physiotherapists (chapter 4). However, our health care professionals indicated that multidisciplinary collaboration, especially collaboration with physiotherapists, could be improved (chapter 6); this is in line with another Dutch study on diabetes care [64]. Health care professionals in our study indicated that collaboration between them was better and easier when physical distances were short, that is, when they all worked in the same building. This was also perceived as a facilitator among Dutch health care professionals in another study [64]. Furthermore, GPs' referral of patients to local sports facilities is low because knowledge of these facilities is limited [65], and this might also be true for other health care professionals [66]. In our study, local sports clubs were organised in a municipal sports stimulation organisation (chapter 4). This organisation provided an overview of local sports facilities, which was used during the intervention. Such overviews can guide participants from primary health care towards local sports facilities. In addition to such overviews, the use of community liaison workers with knowledge of the local situation, such as the Dutch neighbourhood sports coaches, may facilitate contact with local sports facilities and thereby increase referral of participants to these facilities [65, 66].

Adding a psychologist or psychological care to the intervention programme might have been beneficial for several participants. Several of our health care professionals indicated that, for some participants, psychological care was needed before lifestyle changes could be made (data not shown). The literature shows that obese people with depression, anxiety, family problems, or problems at work are more likely to drop out of intervention programmes and are less likely to successfully complete a programme [67–69]. These barriers might first have to be resolved before people are able and willing to change their lifestyle. A disadvantage, however, is that adding a psychologist or psychological care may increase intervention costs.

Fourthly, non-invasive, easy, and cheap screening for people at high risk of type 2 diabetes is needed, as this is the first step in the prevention of this disease. In our study, a two-stage screening approach was used, consisting of identifying high-risk subjects from GPs' patient registration databases followed by fasting plasma glucose testing or the Dutch Diabetes Risk Test (chapter 4); this is in line with the guidelines of the Dutch College of General Practitioners [70]. We found improvements in weight and glucose tolerance, independent of manner of recruitment (chapter 5); this is in line with a review by Ashra *et al.* [29]. Our results therefore suggest that risk scores, such as the Dutch Diabetes Risk Test, might be feasible and effective for screening in primary health care to identify and recruit people at high risk of type 2 diabetes. In order to implement SLIMMER in routine practice, a coordinated screening action is needed. The guidelines of the Dutch College of General Practitioners [70] advise using opportunistic screening (case finding) for diabetes at most once every three years; this is supported by a cost-effectiveness study [71]. Therefore, it might be advisable to start a new SLIMMER intervention every three years.

Fifthly, high-risk subjects should be selected properly. Our health care professionals suggested applying a stricter selection of those at risk in order to include those most able and willing to change. In our study, several participants already had a healthy lifestyle at the start of the intervention (chapter 6), and this left less room for improvement. Furthermore, some participants had a low motivation to change (chapter 6). Therefore, additional screening on intrinsic motivation could identify participants who are sufficiently motivated to take part in the intervention [72], thereby potentially leading to increased effectiveness.

Sixthly, our pilot study recognised the need for a case manager, an independent health care professional who could take action towards professionals and participants in the event of difficulties, and thereby enhance participant compliance and the feasibility of intervention implementation (chapter 3). Practice nurses were appointed as case managers and participants were satisfied with their care (chapter 6); this is in line with another study [73]. However, practice nurses indicated that problems appeared incidentally, and it was almost never necessary to motivate participants (chapter 6). Possibly, the availability of such a person might be sufficient to ascertain and solve problems, if needed.

Seventhly, the economic evaluation showed that incremental costs arose mainly from costs of the intervention programme (chapter 7), and financial barriers were foreseen by health care professionals (chapter 6) as a possible limitation to intervention implementation. Therefore, possibilities for reducing intervention costs should be considered. In chapter 7, we suggested appointing sports instructors instead of higher-salaried physiotherapists. Greaves *et al.*'s review [13] showed that a wide range of providers can deliver effective interventions. As stated above, we conclude that GPs and practice nurses should not be appointed as lifestyle counsellors, and this seems to be confirmed by two Dutch studies on lifestyle interventions to prevent type 2 diabetes that were not effective [32, 74]. Furthermore, we could consider providing group-based dietary consultations, as Li *et al.*'s review showed that group-based interventions were less costly and more cost-effective than individual-based interventions [47]. Moreover, an even more individually tailored intervention approach could be used to reduce costs. In this approach, participants are referred earlier to regular sports facilities when they are ready to do so, rather than adhering strictly to the programme's schedule. Another possibility for reducing costs is to shorten the intervention period. However, our dose-response analysis showed that effectiveness was associated with increased dose of the intervention received (chapter 6), but the optimum intervention intensity and duration are not yet known. Two Dutch studies with a lower intervention intensity than ours found no effect [32, 74]. All these suggestions for reducing intervention costs require a joint approach by intervention developers, health care professionals, and other parties concerned in order for such adaptations to be implemented successfully.

IMPLICATIONS FOR DUTCH HEALTH POLICY

In the Netherlands, the Ministry of Health, Welfare, and Sport is responsible for the national prevention policy. In the government policy document *Health nearby*, diabetes

is indicated as one of the main priorities, and an alliance between primary health care and prevention is advocated [75]. A new health policy plan is expected from the Dutch government in autumn of 2015, in which diabetes is still indicated as a main priority [76]. Because an alliance between primary health care and prevention does not naturally exist in the Netherlands, the government supported the realisation of local network structures within the Beweegkuur lifestyle intervention [75]. These structures can be used by other initiatives, such as the SLIMMER intervention. Furthermore, local governments have an important role in formulating local health priorities and collaborating with health insurance companies in order to finance health care together [75]. Recently, the National Prevention Programme was launched, in which integration of prevention within primary health care has a prominent place [77].

In addition to policies, standards for prevention of type 2 diabetes in primary health care have been developed by the Dutch Diabetes Federation [78] and the Dutch College of General Practitioners [70, 79, 80]. In conformity with these standards, individuals at increased risk are identified, given general lifestyle advices, and referred to local intervention initiatives. In the Netherlands, the Centre for Healthy Living – part of the National Institute for Public Health and the Environment – has a recognition system in which lifestyle interventions are rated for their quality, effectiveness, and feasibility [81]. This system can help primary health care and public health professionals to refer individuals to effective interventions.

Despite these developments, to date there has been no structural embedding of diabetes prevention interventions in daily routines. Furthermore, structural funding is lacking. Our health care professionals perceived this as a barrier to implementation (chapter 6); this result confirmed findings of the Beweegkuur study [46] and the Heartbeat 2 study [82]. Traditionally, little money has been spent on prevention, and prevention is even considered as not 'sexy' [53]. The Dutch government does not support the inclusion of combined lifestyle interventions in the basic insurance scheme but suggests collaboration between local governments, health insurance companies, and other local parties to co-finance prevention initiatives [75]. Currently, regional collaborations between municipalities and health insurance companies are being explored, and these offer prospects for the future of SLIMMER. The results of our study (chapters 5, 6, and 7) therefore provide valuable insights that can contribute to the structural embedding and funding of effective diabetes prevention programmes in Dutch primary health care.

IMPLICATIONS FOR FUTURE RESEARCH

Although our results contribute to the knowledge on effective implementation of a diabetes prevention intervention in primary health care, we can conclude that further research is needed.

Firstly, more insight is needed into the effects of our intervention over extended follow-up in order to determine whether effects are maintained. As discussed in chapter 5, most of the outcomes in our study improved and were sustained after 18 months. It is well known, however, that maintaining these results over a longer period is difficult [83]. Weight reduction during our study was modest, but it is likely to be relevant, as several studies have shown that even modest weight reduction can reduce the risk of diabetes [84, 85]. On the basis of this weight reduction, we estimated subsequent diabetes risk reduction. However, following our participants over a longer time period to investigate whether diabetes is actually prevented would provide us with more precise and actual information on the reduction in risk.

Secondly, further investigation of effective intervention components is needed in order to identify the most effective intervention programme at lowest cost. In chapters 5 and 6, several factors were identified that were associated with increased effectiveness. The optimal combination of intervention components, however, remains unclear. Combining data on effective intervention components from several other Dutch studies (e.g. Aphrodite [32], Hoorn study [74], Beweegkuur [86], GOAL [87], IJSCO [88], NDF Road Map [89], DH!AAN [90], and MetSLIM [27]) could provide valuable insights.

Furthermore, investigating behavioural determinants and their relation to health is important in order to gain more insight into mechanisms of change. Behavioural determinants were linked to behaviour change techniques used in the SLIMMER intervention, and several of these techniques (e.g. social support, goal-setting, relapse prevention) have been associated with increased intervention effectiveness [13]. Knowing which behaviour change techniques contribute to improved health helps to identify effective intervention components.

Moreover, insight into dietary intake and physical activity is needed to identify the aspects of the intervention that are most strongly associated with decreasing diabetes risk [13]. Furthermore, changes in dietary intake and physical activity need to be perceived as

feasible by participants. Our study investigated changes in dietary intake and physical activity and provided us with more insight into determinants contributing to diabetes prevention, such as intake of fat, saturated fat, and fibre, and vigorous activities (chapter 5). These changes were moderate but feasible to achieve and may have contributed to beneficial changes in weight and glucose tolerance, thereby contributing to diabetes prevention. As noted by Ashra *et al.*, however, overall effects of dietary intake and physical activity on diabetes prevention in real-world settings are poorly reported in the literature [29].

Thirdly, it is important to evaluate the consequences of the above-suggested adaptations of the intervention programme on intervention effectiveness. This could provide useful information on an optimal intervention strategy for diabetes prevention.

Fourthly, more insight into longer-term cost-effectiveness is needed, and therefore the results of our study should be modelled to a lifetime horizon. We expect more favourable cost-effectiveness on the longer term because our study found beneficial effects on intermediate outcomes (chapter 5), indicating that diabetes will be postponed or prevented, leading to cost savings in the future. This is supported by Li *et al.*'s review which showed that interventions were most cost-effective in the longer term, indicating that short-term studies have are limited in their ability to capture the full range of intervention's health benefits and cost savings [47]. Furthermore, it is shown that lifestyle interventions are much more cost-effective than many diabetes treatment interventions, such as intensive glycaemic control [91].

OVERALL CONCLUSION

In conclusion, this study showed that a thorough preparation of translation and implementation has led to a cost-effective intervention to prevent type 2 diabetes which is feasible to implement in Dutch primary health care. In fact, our clinical effects were larger than those in most other real-world intervention programmes, and we provided additional insight into dietary intake and physical activity. Further research is needed on effects and costs over longer follow-up, effective intervention components, and consequences of suggested adaptations of the programme on intervention effectiveness. The results of this study provide valuable insights that can contribute to the structural embedding and funding of effective diabetes prevention programmes in Dutch primary health care.

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Summary

Diabetes is a worldwide epidemic, causing a high disease and economic burden. Type 2 diabetes, the most common form of diabetes, is associated with an unfavourable lifestyle, including overweight and obesity, unhealthy diet, and physical inactivity. Over the last two decades many large-scale experimental trials have shown that type 2 diabetes can be delayed or prevented by lifestyle modification in high-risk subjects. This evidence has been translated and implemented in interventions in real-world settings, however, this remains a challenge. At the time this project started, translation and implementation of a (cost-)effective diabetes prevention programme in Dutch primary health care was lacking. Therefore the SLIMMER study (SLIM iMplementation Experience Region Noord- en Oost-Gelderland) was started in which the SLIM intervention, revealing a 47% diabetes risk reduction, was translated to Dutch primary health care. The overall objective of this study was to improve the lifestyle behaviour in high-risk subjects in order to reduce the risk of developing type 2 diabetes. The main findings of this research project as described in **chapters 2 to 7** are summarised below.

The literature in **chapter 2** showed that, all over the world, clinical diabetes prevention trials have been translated to daily practice. In Dutch practice, however, this was still lacking. Therefore, the SLIMMER project was started in which the SLIM intervention was translated to practice. The adapted SLIM intervention, called SLIMMER, consisted of a 10-month combined dietary and physical activity programme. A one-year pilot study was conducted to test its applicability in Dutch primary health care, guided by a process evaluation. Collaboration between professionals from primary health care and public health was considered necessary to prevent diabetes.

When diabetes prevention programmes are translated to real-world settings, adaptations are inevitable and this may have unknown consequences for effectiveness of the intervention. Therefore, a pilot study with process evaluation was conducted to test the feasibility and desired impact of the SLIMMER intervention (**chapter 3**). The pilot study ($n = 31$) showed that inclusion and retention of high-risk subjects was successful and that both participants and health care professionals were satisfied with the SLIMMER intervention. Overall, the intervention was implemented as planned and appeared to be suitable for application in practice. Some improvements regarding measurements, planning aspects of intervention elements, and organisational matters were identified. Refinements (e.g. including monitoring, a case manager, and a maintenance programme) were made prior to further implementation and evaluation.

A comprehensive evaluation approach is required, as interventions in real-world settings are often complex and not delivered in tightly controlled environments. The evaluation design of the SLIMMER intervention was described in **chapter 4**. A logic model of change was composed to link intervention activities, their mechanisms of change (i.e. behavioural determinants), expected behaviours, and intervention outcomes in a logical order. The SLIMMER intervention consisted of a 10-month dietary and physical activity intervention, including case management and a maintenance programme. The effectiveness of the intervention was tested in a randomised controlled trial, including outcomes at several levels: quality of life, health outcomes, dietary and physical activity behaviours, and behavioural determinants. In addition, a process evaluation was conducted to assess how the SLIMMER intervention was delivered and received in Dutch primary health care. Furthermore, an economic evaluation was performed, both from a societal and health care perspective.

The effect of the SLIMMER diabetes prevention intervention in Dutch primary health care on clinical and metabolic risk factors (primary outcome fasting insulin), dietary intake, physical activity, and quality of life after 12 and 18 months, was tested in a randomised controlled trial (**chapter 5**). We found that after 12 and 18 months, the intervention group significantly improved weight ($\beta = -2.7$ kg and $\beta = -2.5$ kg, respectively) and fasting insulin ($\beta = -12.1$ pmol/l and $\beta = -8.0$ pmol/l, respectively) compared with the control group. Intervention subjects improved weight and glucose tolerance, independent of manner of recruitment (laboratory glucose test or Diabetes Risk Test). Furthermore, intake of total and saturated fat decreased and fibre intake increased in the intervention group compared with the control group, both at 12 and at 18 months ($p < 0.05$). Fruit intake increased at 12 but not at 18 months, whereas vegetable intake increased at 18 but not at 12 months. The DHD-index score—indicating adherence to the Dutch dietary guidelines—was significantly higher in the intervention group than in the control group, both at 12 and at 18 months ($p < 0.05$). Vigorous activities and physical fitness improved both at 12 and at 18 months. Finally, beneficial changes in several domains of quality of life were found both at 12 and at 18 months, although not all domains reached statistical significance.

As described in **chapter 6**, a process evaluation was conducted to gain insight into how the SLIMMER intervention was delivered and received and to identify intervention components that contribute to intervention effectiveness. The process evaluation showed that 316 high-risk subjects were recruited. The actual dose that intervention

subjects received was in line with the planned dose according to the manual. Overall, participants and health care professionals were highly satisfied with the SLIMMER intervention, with mean acceptability ratings of 82 and 80 (out of 100), respectively. The intervention programme was to a large extent implemented according to the manual and fitted well within the regular functioning and professional performance of health care professionals. Higher dose received and participant acceptability were related to improved health outcomes and dietary behaviour, but not, however, to physical activity behaviour. Furthermore, targeting both diet and physical activity, using behaviour change techniques, focusing on behaviour maintenance, tailoring the intervention, and adopting a multidisciplinary approach may have facilitated intervention effectiveness.

The economic evaluation in **chapter 7** showed that the SLIMMER intervention was both more costly and more effective than usual health care. As expected, the intervention group had a lower health care utilisation and reported less presenteeism than the usual health care group. The cost-effectiveness analysis showed that the incremental costs of the SLIMMER lifestyle intervention were €547 and the incremental effect was 0.02 QALY, resulting in an incremental cost-effectiveness ratio (ICER) of 28,094/QALY. From a health care perspective, the ICER decreased to 13,605/QALY, with a moderate probability of being cost-effective (56% at a willingness to pay (WTP) of €20,000/QALY and 81% at a WTP of €80,000/QALY). Intervention costs could be decreased to a certain extent to further enhance cost-effectiveness.

In conclusion, this study showed that a thorough preparation of translation and implementation has led to a cost-effective intervention to prevent type 2 diabetes which is feasible to implement in Dutch primary health care. In fact, our clinical effects were larger than those in most other real-world intervention programmes, and we provided additional insight into changes in dietary intake and physical activity. Further research is needed on effects and costs over longer follow-up, effective intervention components, and consequences of suggested adaptations of the programme on intervention effectiveness. The results of this study provide valuable insights that can contribute to the structural embedding and funding of effective diabetes prevention programmes in Dutch primary health care.



Samenvatting

Diabetes is een wereldwijde epidemie die gepaard gaat met een grote ziektelast en hoge kosten. Type 2 diabetes, de meest voorkomende vorm van diabetes, is geassocieerd met een ongunstige leefstijl, waaronder overgewicht en obesitas, ongezonde voeding en lichamelijke inactiviteit. In de afgelopen twee decennia hebben vele grote studies aangetoond dat type 2 diabetes in hoog-risico personen uitgesteld of voorkomen kan worden door leefstijlverandering. Dit bewijs is verkregen in een onderzoeks-setting en dit is vervolgens vertaald naar interventies in de dagelijkse (zorg)praktijk. De implementatie van dergelijke interventies blijft echter een uitdaging. Op het moment dat het huidige project startte, bestond er nog geen vertaling en implementatie van een (kosten)effectief diabetes preventie programma in de Nederlandse eerstelijnszorg. Daarom is de SLIMMER studie (SLIM iMplementation Experience Region Noord- en Oost-Gelderland) gestart. In deze studie is de SLIM-interventie, die het risico op diabetes met 47% verlaagde, vertaald is naar de Nederlandse eerstelijnszorg. Het doel van de SLIMMER studie was het verbeteren van het leefstijlgedrag in hoog-risico personen om zo het risico op type 2 diabetes te verminderen. De belangrijkste bevindingen van dit onderzoeksproject, zoals beschreven in de **hoofdstukken 2 tot en met 7**, worden hieronder samengevat.

De literatuur in **hoofdstuk 2** laat zien dat klinische diabetespreventie studies wereldwijd zijn vertaald naar de dagelijkse praktijk. Echter, in de Nederlandse praktijk ontbrak dit nog. Daarom werd het SLIMMER project gestart, waarin de SLIM-interventie werd vertaald naar de praktijk. Het SLIMMER-project bestond uit een gecombineerd voedings- en beweegprogramma van 10 maanden. Samenwerking tussen zorgverleners uit de eerstelijnszorg en de publieke gezondheidszorg werd noodzakelijk geacht om diabetes te voorkomen. Ook het aanstellen van een casemanager die samenwerkt met alle betrokken zorgverleners werd noodzakelijk geacht.

Aanpassingen zijn onvermijdelijk wanneer diabetespreventie programma's naar de dagelijkse (zorg)praktijk worden vertaald. Dit kan mogelijk gevolgen hebben voor de effectiviteit van de interventie. Daarom werd een pilotstudie met een procesevaluatie uitgevoerd om de haalbaarheid en de gewenste impact van de SLIMMER-interventie te testen (**hoofdstuk 3**). De pilotstudie ($n = 31$) toonde aan dat de werving en het behoud van hoog-risico personen in de interventie succesvol was en dat zowel deelnemers als zorgverleners (praktijkondersteuners, diëtisten en fysiotherapeuten) tevreden waren met de SLIMMER-interventie. Over het algemeen werd de interventie uitgevoerd zoals gepland en bleek deze ook geschikt te zijn voor toepassing in de praktijk.

Enkele verbeteringen ten aanzien van metingen, planning van interventie-elementen en organisatorische zaken werden gesignaleerd. Aanpassingen aan het SLIMMER programma (bijvoorbeeld het toevoegen van monitoring, een casemanager en een uitstroomprogramma) werden gedaan voorafgaand aan verdere implementatie en evaluatie.

Een uitgebreide evaluatie is nodig, omdat interventies in de dagelijkse (zorg) praktijk vaak complex zijn en niet worden uitgevoerd in een volledig gecontroleerde omgeving. Het evaluatiedesign van de SLIMMER-interventie wordt in **hoofdstuk 4** beschreven. Een logisch model werd samengesteld om interventie-activiteiten, hun mechanismen voor verandering (gedragsdeterminanten), verwachte gedragingen en interventie-uitkomsten op een logische manier met elkaar te verbinden. De SLIMMER-interventie bestond uit een voedings- en beweegprogramma van 10 maanden, inclusief casemanagement en een uitstroomprogramma. Deelnemers kregen persoonlijke adviezen van een diëtist en sportten tenminste een keer per week in een speciaal SLIMMER groepje onder leiding van een fysiotherapeut. Ook maakten ze kennis met lokale sportverenigingen. De controlegroep kreeg de gebruikelijke zorg van de huisarts. De effectiviteit van de interventie werd getest in een gerandomiseerde gecontroleerde studie, met uitkomsten op verschillende niveaus: kwaliteit van leven, gezondheidsuitkomsten, voedings- en beweeggedrag en gedragsdeterminanten. Daarnaast werd een procesevaluatie uitgevoerd om te onderzoeken hoe de SLIMMER-interventie werd uitgevoerd en ontvangen in de Nederlandse eerstelijnszorg. Aanvullend werd een economische evaluatie uitgevoerd, zowel vanuit een maatschappelijk perspectief als een gezondheidszorg perspectief.

Door middel van de gerandomiseerde gecontroleerde studie werd onderzocht wat het effect van de SLIMMER-interventie was op klinische en metabole risicofactoren (primaire uitkomstmaat nuchter serum insulinegehalte), voedingsinname, lichamelijke activiteit en kwaliteit van leven na 12 maanden en zes maanden na afloop van de interventie (**hoofdstuk 5**). We vonden na 12 en 18 maanden significante verbeteringen in de interventiegroep ten opzichte van de controlegroep in gewicht ($\beta = -2.7$ kg en $\beta = -2.5$ kg, respectievelijk) en nuchter insuline ($\beta = -12.1$ pmol/l en $\beta = -8.0$ pmol/l, respectievelijk). Personen in de interventiegroep verbeterden hun gewicht en glucosetolerantie onafhankelijk van de manier van werving (via een glucosetest of via de Diabetes Risico Test). Verder verminderde de inname van totaal en verzadigd vet en steeg de inname van vezels in de interventiegroep in vergelijking met de controlegroep,

zowel op 12 als 18 maanden ($p < 0.05$). Fruitconsumptie nam toe na 12 maanden, maar niet na 18 maanden, terwijl groenteconsumptie toenam na 18 maanden, maar niet na 12 maanden. De DHD-index score, die aangeeft in welke mate men voldoet aan de Nederlandse voedingsrichtlijnen, was significant hoger in de interventiegroep dan in de controlegroep, zowel op 12 als 18 maanden ($p < 0.05$). Zware fysieke activiteiten en fysieke fitheid verbeterden zowel na 12 maanden als na 18 maanden. Tot slot werden gunstige veranderingen in verschillende domeinen van kwaliteit van leven gevonden, zowel na 12 als na 18 maanden, maar niet in alle domeinen was het effect statistisch significant.

Zoals beschreven in **hoofdstuk 6**, werd een procesevaluatie uitgevoerd om inzicht te krijgen in hoe de SLIMMER-interventie was uitgevoerd en ontvangen, en om interventie-componenten te identificeren die bijdragen aan effectiviteit van de interventie. De procesevaluatie liet zien dat 316 hoog-risico personen zijn geworven. Het daadwerkelijke aantal voedingsconsulten en sportlessen (dosis) dat interventiepersonen hebben ontvangen, was in lijn met de geplande dosis zoals beschreven in het draaiboek. Over het geheel waren deelnemers en zorgverleners zeer tevreden met de SLIMMER-interventie, met gemiddelde tevredenheidsscores van respectievelijk 82 en 80 (op een schaal van 1 tot 100). Het interventie-programma werd in grote lijnen uitgevoerd volgens het draaiboek en paste goed binnen het reguliere functioneren en professionele handelen van zorgverleners. Een hogere ontvangen dosis en een hogere tevredenheid bij deelnemers waren gerelateerd aan betere gezondheidsuitkomsten en voedingsgedrag, maar niet aan beweeggedrag. Andere factoren die mogelijk hebben bijgedragen aan de effectiviteit van de interventie waren: een programma dat zowel op voeding als bewegen was gericht, het gebruik van gedragsveranderingstechnieken, de focus op gedragsbehoud, het op maat aanbieden van de interventie ('tailoring') en de multidisciplinaire aanpak.

De economische evaluatie in **hoofdstuk 7** liet zien dat de SLIMMER-interventie zowel duurder als effectiever was dan reguliere zorg. Zoals verwacht had de interventiegroep een lager zorggebruik en rapporteerde deze groep minder arbeidsproductiviteitsverlies dan de controlegroep. De kosteneffectiviteitsanalyse liet zien dat de netto kosten van de SLIMMER-interventie €547 bedroegen en dat het netto effect 0.02 QALY was. Dit resulteerde in een netto kosteneffectiviteitsratio (ICER) van €28,094/QALY. Vanuit een gezondheidszorg perspectief daalde de ICER tot 13,605/QALY, met een matige kans dat de interventie kosteneffectief zou zijn (56% bij een betalingsbereidheid van €20,000/

QALY en 81% bij een betalingsbereidheid van €80,000/QALY). Interventiekosten zouden tot een bepaalde hoogte kunnen worden beperkt om de kosteneffectiviteit verder te vergroten, zoals het aanstellen van een goedkopere sportinstructeur in plaats van een fysiotherapeut, het aanbieden van groepsconsulten bij de diëtist en het nog meer op maat maken van het programma.

Samenvattend heeft deze studie laten zien dat een gedegen voorbereiding van de vertalingen implementatie heeft geleid tot een kosteneffectieve interventie ter preventie van type 2 diabetes, die uitvoerbaar is in de Nederlandse eerstelijnszorg. Daarbij waren onze klinische effecten groter dan in de meeste andere interventieprogramma's in de dagelijkse (zorg)praktijk. We hebben daarnaast de veranderingen in voedingsinname en beweging inzichtelijk gemaakt. Verder onderzoek is nodig naar de effecten en kosten op de langere termijn, de effectieve interventie-componenten en de gevolgen van de voorgestelde aanpassingen van het programma op de effectiviteit van de interventie. De resultaten van deze studie bieden waardevolle inzichten die kunnen bijdragen aan de structurele verankering en financiering van effectieve diabetespreventie programma's in de Nederlandse eerstelijnszorg.



About the author

CURRICULUM VITAE

Geerke Duijzer was born on July 8, 1985 in Dordrecht, the Netherlands. After completing secondary school at Heerenlanden College in Leerdam, she started her study Nutrition and Health at Wageningen University. As part of her studies, she conducted a first Master thesis at Nairobi University, entitled “The effect of using different food groupings on the association of dietary diversity and nutrient adequacy among women in Kenya”. Her second Master thesis was performed at the community health service Noord- en Oost-Gelderland (former GGD Gelre-IJssel) in Apeldoorn. She investigated the effect of several overweight interventions focusing on youth. The results were presented at the Dutch Public Health Congress (NCVGZ, 2009) and at the European Congress on Obesity (ECO, 2009). Furthermore, with this master thesis Geerke has won the NVVL-prize 2010 for the best scientific Master thesis. After that, Geerke did her internship at Danone Research in Wageningen. She investigated the relationship between behavioural and baby nutrition aspects and infant development. Geerke obtained her Master’s degree with two majors in Public Health Nutrition, and Nutritional and Public Health Epidemiology in September 2009. Immediately after her graduation, she was appointed as a research assistant at the Division of Human Nutrition, Wageningen University, where she contributed to the book “Epidemiology in public health practice”. In September 2010, she started as a PhD fellow at the Academic Collaborative Centre AGORA, a collaboration between Wageningen University and community health service Noord-en-Oost-Gelderland of which the results are described in this thesis. Her research focussed on the implementation and evaluation of the SLIMMER diabetes prevention intervention in Dutch primary health care. She joined the educational programme of the Graduate School VLAG, attended several (international) conferences and courses, and was involved in teaching and supervising students at MSc level. In 2010-2011, she was a co-organisier (chairwoman) of the PhD study tour for PhD fellows of the Division of Human Nutrition to Mexico and the west coast of the USA. Currently, she is appointed as an epidemiologist at the community health service Noord- en Oost-Gelderland.

LIST OF PUBLICATIONS

PUBLICATIONS IN PEER-REVIEWED JOURNALS

JMHuijg, EDusseldorp, WAGebhardt, MWVerheijden, NVanderZouwe, BJCMiddelkoop, **G Duijzer**, MR Crone. Factors associated with physical therapists' implementation of physical activity interventions in the Netherlands. *Physical Therapy* 2015;95:539.

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SUBMITTED MANUSCRIPTS

AJ Bukman, **G Duijzer**, A Haveman-Nies, SC Jansen, J ter Beek, GJ Hiddink, EJM Feskens. Is success of the SLIMMER diabetes prevention intervention modified by socioeconomic status? A randomised controlled trial.

G Duijzer, AJ Bukman, A Meints-Groenveld, A Haveman-Nies, SC Jansen, J Heinrich, GJ Hiddink, EJM Feskens, GA de Wit. Cost-effectiveness of the SLIMMER diabetes prevention intervention in Dutch primary health care.

EJ van Dongen^{*}/**G Duijzer**^{*}, SC Jansen, J ter Beek, JM Huijg, JN Leerlooijer, GJ Hiddink, EJM Feskens, A Haveman-Nies. Process evaluation of a randomised controlled trial of a diabetes prevention intervention in Dutch primary health care: the SLIMMER study.

^{}These authors contributed equally to the contents of the manuscript.*

G Duijzer, A Haveman-Nies, SC Jansen, J ter Beek, R van Bruggen, M Willink, GJ Hiddink, EJM Feskens. Effect and maintenance of the SLIMMER diabetes prevention lifestyle intervention in Dutch primary health care: a randomised controlled trial.

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S Ngala, **G Duijzer**, AM Mwangi, I Brouwer. The effect of food groupings on the association of dietary diversity and nutrient adequacy of women in Kenya. *European Journal of Clinical Nutrition* 2009;63:S23.

GC Pieterse, **G Duijzer**, A Haveman-Nies. Effectevaluatie van overgewichtactiviteiten gericht op de jeugd: Okido en Evenwicht. *Tijdschrift voor Gezondheidswetenschappen* 2009;87.

OVERVIEW OF COMPLETED TRAINING ACTIVITIES



Discipline specific activities	Institute and location	Year
Courses and workshops		
Introduction to public health economy	NSPOH, Amsterdam	2010
Masterclass 'Public health interventions in real-life settings: the AGORA experience'	VLAG/AGORA, Wageningen	2010
Masterclass 'Multilevel analysis'	VLAG, Wageningen	2011
Introduction to structural equation modeling using Mplus	Utrecht University, Utrecht	2012
Introduction to multilevel analysis	Utrecht University, Utrecht	2012
Masterclass 'How to develop effective interventions in public health practice'	VLAG/AGORA, Wageningen	2012
Methodology in health economic evaluation	UMC Utrecht/Julius Centre, Utrecht	2013
Masterclass 'Confounding'	VLAG, Wageningen	2014
Conferences and meetings		
PREVENT-2010: National congress structured prevention of chronic diseases	NDDO Education Foundation, Oegstgeest	2010
European public health conference ^a	EUPHA, Amsterdam	2010
Heelsum VI: Practice-based evidence for weight management ^a	Heelsum Collaboration, Heelsum	2010
Dutch public health congress (NCVGZ)	Amsterdam	2011
Behaviour change symposium	Maastricht University, Maastricht	2011
Multidisciplinary symposium dieticians cooperation Netherlands ^a	DCN, Utrecht	2011
Annual meeting NWO nutrition	NWO, Deurne	2011
World congress on prevention of diabetes and its complications ^a	Madrid (Spain)	2012
NVDO young investigators meeting ^a	NVDO, Zaltbommel	2013
Dutch public health Congress (NCVGZ) ^a	Ede	2013
National diabetes day	NDF, Den Haag	2014
Dutch public health Congress (NCVGZ)	Rotterdam	2014
Public lecture 'Nutrition, diabetes and my doctor ^a	VLAG, Wageningen	2014
Expert meeting on implementation of diabetes prevention interventions in real-life settings ^a	CNAMTS, Paris (France)	2014
Annual Dutch diabetes research meeting ^a	NVDO, Oosterbeek	2014
FENS European nutrition conference ^a	FENS, Berlin (Germany)	2015
World diabetes congress ^b	IDF, Vancouver (Canada)	2015

General courses and workshops	Institute and location	Year
Teaching and supervising thesis students	DO, Wageningen	2009
24 th Edition of the PhD introduction week	VLAG, Baarlo	2010
PhD Competence assessment	WGS, Wageningen	2011
Information literacy including EndNote introduction	WUR library, Wageningen	2011
Mini-symposium 'How to write a world class paper'	WUR library, Wageningen	2011
Interviewing techniques	YRM/WUR, Wageningen	2011
Workshop 'Successful presenting'	Mennen Training & Consultancy, Wageningen	2011
Techniques for writing and presenting a scientific paper	WGS, Wageningen	2012
Career assessment	WGS/Meijer & Meijaard, Wageningen	2014
Career perspectives	WGS, Wageningen	2015
Optional courses and activities	Institute and location	Year
Preparing PhD research proposal	VLAG, Wageningen	2010
Literature and discussion groups: 'Epi-research club', 'Methodology club', 'Rothman lunch', 'Paperclip club'	HNE, Wageningen	2010-2015
PhD tour organising committee	HNE/VLAG, Wageningen	2010-2011
PhD study tour Mexico & USA ^{a,b}	HNE/VLAG, Wageningen	2011
PhD study tour Australia ^a	HNE/VLAG, Wageningen	2013

^a oral presentation given; ^b poster presentation given



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Geerke
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