From CLINICAL SCIENCE AND EDUCATION, SÖDERSJUKHUSET

Karolinska Institutet, Stockholm, Sweden

SUPPORT FOR PHYSICAL ACTIVITY IN INDIVIDUALS WITH PREDIABETES AND TYPE 2 DIABETES IN PRIMARY CARE
- THE SOPHIA STEP STUDY

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Stockholm 2018

Published by Karolinska Institutet.

ISBN 978-91-7831-139-2

Printed by Eprint AB 2018

Institutionen för klinisk forskning och utbildning, Södersjukhuset

Support for physical activity in individuals with prediabetes and type 2 diabetes in primary care -the Sophia Step Study

AKADEMISK AVHANDLING

Som för avläggande av medicine doktorsexamen vid Karolinska Institutet offentligen försvaras i Erfors- & Weitnersalen, Sophiahemmet Högskola, Valhallavägen 91, ingång R, plan 2, Stockholm

Torsdagen den 11 oktober 2018 kl. 9.30

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To Irma, Viggo and Erling

"Reach as high as you can, and then reach a little higher. There you will find magic and possibility. And maybe even cookies."

Marc Jones

ABSTRACT

A health promoting-care approach includes supporting the individual to increase control over and to improve his or her health to obtain the best possible wellbeing and quality of life. In prediabetes and type 2 diabetes regular physical activity is of pronounced importance for preventing complications and premature death as well as to enhance quality of life. Supporting the individual in self-management of physical activity and establishing new routines in daily life is a major challenge for the health-care system. There is a need for feasible, low-cost intervention programs to support physical activity in type 2 diabetes care.

The overall aim of this thesis was to design and evaluate the implementation of an intervention in primary care intended to support individuals with prediabetes or type 2 diabetes to become physically active on a regular basis. A secondary aim was to explore the theoretical associations of replacing prolonged sedentary time with time being sedentary but taking breaks, engaging in light intensity physical activity or moderate and vigorous physical activity with health parameters.
Study I was a study protocol describing the assessment protocol and the theoretical framework underlying the randomized controlled trial Sophia Step Study. Study II was a process evaluation study describing the context of the Sophia Step Study and evaluating the implementation during the first 6 months of intervention. Intervention delivery and dose received were obtained through the process of continuous dialogue with the diabetes specialist nurses, attendance records and data on the number days for step registration and step goal. Changes in physical activity behavior were measured objectively for 159 participants by accelerometers and health outcomes by blood samples, anthropometry and blood pressure. Study III was a qualitative interview study reporting the experiences of 18 adhering participants´ after attending 2 years of the Sophia Step Study. Study IV employed a cross-sectional design that included 124 individuals with prediabetes or type 2 diabetes. The study investigated the associations of reallocating sedentary time in bouts (>60 min) to sedentary time in non-bouts (<60 min), light intensity physical activity and to moderate and vigorous physical activity with cardiometabolic risk factors.

The participants in the Sophia Step Study were randomized into one of three parallel groups: a multicomponent intervention (A) entailing individual consultations with a diabetes specialist nurse based on motivational interviewing and physical activity on prescription, group meetings and self-monitoring of steps; a single component intervention (B) encompassing self-monitoring of steps; or a control group (C) entailing usual care except for the assessments that were included in the study *(study I)*. Between April 2013 and October 2016 159 persons were recruited. The interventions were feasible to implement in primary care with a low dropout rate (3%) at 6 months and high fidelity to the study protocol, except for the physical activity on prescription component. There was a high grade of delivery and dose among those enrolled in the study. Group A increased mean daily steps with 1097 steps (CI: 232, 1962), group B increased mean daily steps with 1242 steps (CI: 313, 2171) and the control group (C) decreased mean daily steps with 457 step (CI:-1164, 250). Clinical improvements after 6 months were found in the two intervention groups, while the control group showed mixed results *(study II)*.
In total 18 participants with high adherence to the interventions and study assessments were interviewed in *study III*. The health check-ups were described as personalized, giving feedback on health outcomes and positive reinforcement. Overall, the participants felt that they received good care throughout the study. The self-monitoring of steps, the group sessions and the health check-ups were recalled as resources that increased motivation for physical activity, led to the establishment of new daily routines and in empowering them to take control over their own health. *Study IV* demonstrated that modeling reallocation of 30 min of objectively measured time from sedentary time in 60 min bouts to moderate and vigorous physical activity was beneficially associated with BMI (b = -1.46 95% CI: -2.60, -0.33 kg/m^2), waist circumference (b = -4.30 95% CI: -7.23, -1.38 cm), and HDL cholesterol b = 0.11 95% CI: 0.02, 0.21 mmol/l). No associations of reallocating sedentary time from long bouts to shorter bouts or to light intensity physical activity were seen. Accumulating time in moderate and vigorous physical activity was beneficial, independent of the behavior it replaced.

In conclusion, this thesis shows that it is possible to implement self-monitoring of steps both with and without counseling support as a strategy to support individuals with prediabetes or type 2 diabetes in the primary care setting. The two interventions were effective in increasing physical activity after 6 months. Self-monitoring of steps, feedback on health outcomes and a personalized approach were highly valued by the individuals and should be considered in primary care. The thesis also confirmed that modeling replacement of sedentary time with time in moderate and vigorous physical activity showed beneficial associations with HDL cholesterol, waist circumference and BMI levels in individuals with prediabetes or type 2 diabetes.

SAMMANFATTNING

Hälsofrämjande vård innebär att ge stöd till individen att själv ta kontroll över sin egen hälsa och förbättra den för att uppnå välbefinnande och livskvalitet. Vid prediabetes och typ 2 diabetes är regelbunden fysisk aktivitet särskilt effektivt för att förebygga komplikationer, förtida död och ökad livskvalitet. Att ge stöd för etablering av nya rutiner och regelbunden fysisk aktivitet är en utmaning för vården.

Huvudsyftet med denna avhandling var att utforma och implementera en randomiserad kontrollerad studie med syfte att ge stöd för fysisk aktivitet till personer med prediabetes och typ 2 diabetes inom primärvården. Ytterligare ett syfte var att teoretiskt undersöka hälsosamband med att byta ut tid i långvarigt stillasittande mot tid i stillasittande med pauser, tid i lätt aktivitet och tid i aktivitet med måttlig intensitet.

Studie I beskriver utformandet av interventionen och forskningsprojektet Sophia Step Study i ett studieprotokoll. Deltagarna i Sophia Step Study randomiserades till en av tre grupper, A, B eller C. Deltagarna i grupp A fick stöd för beteendeförändring från sin diabetessjuksköterska i form av individuella samtal baserade på motiverat samtal och fysisk aktivitet på recept, gruppträffar och en stegräknare med tillhörande hemsida för egenmätning av steg. Deltagare i grupp B fick samma stegräknare och tillhörande hemsida för egenmätning av steg. Deltagare i grupp C var en kontrollgrupp som fick sedvanlig vård förutom hälsokontrollerna som ingick i studien.

Studie II och III var delar av en processutvärdering av Sophia Step Study. Studie II avsåg att beskriva kontexten och utvärdera implementeringen av studien under de första 6 månaderna. Mellan april 2013 och oktober 2016 rekryterades 159 deltagare. Det var få bortfall (3%) och deltagarna visade hög följsamhet till interventionerna. Alla komponenter utom fysisk aktivitet på recept implementerades enligt protokollet. Antalet dagliga steg ökade i genomsnitt med 1097 steg/dag i interventionsgrupp A och med 1242 steps steg/dag i grupp B och minskade i kontrollgruppen med i genomsnitt 457 steg/dag. Båda interventionsgrupperna visade på förbättrade kliniska variabler jämfört med kontrollgruppen efter 6 månader, även om dessa inte var statistiskt signifikanta.

Studie III var en kvalitativ intervjustudie, med syfte att utvärdera deltagarnas erfarenheter efter av två års deltagande i Sophia Step Study. Totalt 18 deltagare som fullföljt två år av Sophia Step Study med hög följsamhet i alla tre grupperna intervjuades. Resultatet visade att de regelbundna kontrollerna som ingick i studiedeltagandet ansågs vara individuellt anpassade och gav återkoppling på hälsostatus, positiv förstärkning och en känsla av att vara omhändertagen. Gruppträffarna, egenmätning av steg och hälsokontrollerna uppskattades för att de lett till ökad motivation för fysisk aktivitet, etablering av nya rutiner och kontroll över den egna hälsan.

Studie IV var en tvärsnittsstudie med 124 individer med prediabetes eller typ 2 diabetes. Studien visade statistiskt signifikanta positiva samband mellan att byta ut långvarigt stillasittande mot fysisk aktivitet på måttlig intensitet med BMI, midjemått och HDL-kolesterol. Inga samband mellan att byta 30 minuter i långvarigt stillasittande mot stillasittande med pauser eller fysisk aktivitet på lätt intensitet fanns. Däremot var det fördelaktigt att samla tid i måttligt intensiv aktivitet oavsett vad man byter tiden från.

Sammanfattningsvis visar avhandlingen att det är möjligt att implementera egenmätning av steg med och utan individuella samtal och gruppträffar som hälsofrämjande åtgärd för individer med prediabetes och typ 2 diabetes i primärvården. I båda interventionerna ökade den genomsnittliga fysiska aktiviteten efter 6 månader. Egenmätning av steg, återkoppling på hälsoutfall och ett personligt bemötande värderades högt bland deltagarna och bör övervägas inom primärvården. Avhandlingen stärker också evidensen för att ett teoretiskt byte av stillasittande tid mot tid i måttlig fysisk aktivitetsnivå är positivt relaterat med HDL kolesterol, midjemått och BMI hos individer med prediabetes och typ 2 diabetes.

LIST OF SCIENTIFIC PAPERS

I. Rossen J, Yngve A, Hagströmer M, Brismar K, Ainsworth B, Iskull C, Möller P, and Johansson U-B. Phyiscal activity promotion in the primary care setting in pre-and type 2 diabetes- the Sophia Step Study.
BMC Public Health. 2015; 15 (647).
https://doi.org/10.1186/s12889-015-1941-9

II. Rossen J, Hagströmer M, Yngve A, Brismar B, Ainsworth A, and Johansson U-B. Process evaluation of the Sophia Step Study- a three-armed randomized controlled trial using self-monitoring of steps with and without counselling in prediabetes and type 2 diabetes.
Submitted manuscript

III. Rossen J, Lööf H, Yngve A, Hagströmer M, Brismar K and Johansson U-B. This is why I'm doing a lot of exercise' — a qualitative study of participant's experiences of the Sophia Step Study.
International Diabetes Nursing. 2017;14 (2-3): 99-104.
https://doi.org/10.1080/20573316.2018.1437940

IV. Rossen J, Buman MP, Johansson U-B, Yngve A, Ainsworth B, Brismar B. Hagströmer M. Reallocating bouted sedentary time to non-bouted sedentary time, light activity and moderate-vigorous physical activity in adults with prediabetes and type 2 diabetes.
PLOS ONE. 2017; 12 (7): e0181053.
https://doi.org/10.1371/journal.pone.0181053

INNEHÅLL

LIST OF ABBREVIATIONS

BCT	Behavior change technique
BMI	Body mass index
CI	Confidence Interval
cpm	Counts per minute
FaR®	Fysisk aktivitet på recept
LPA	Light intensity physical activity
MI	Motivational interviewing
MVPA	Moderate and vigorous intensity physical activity
RCT	Randomized controlled trial
SB	Sedentary behavior
SB20	Sedentary behavior in bouts of 20 min: being sedentary with no break for 20 min
SB40	Sedentary behavior in bouts of 40 min: being sedentary with no break for 40 min
SB60	Sedentary behavior in bouts of 60 min: being sedentary with no break for 60 min
WC	Waist circumference

1 INTRODUCTION

Physical activity has well-recognized preventive effects on type 2 diabetes and its comorbidities cardiovascular diseases. Regular physical activity is thus a central component of type 2 diabetes self-management and prevention (1, 2). Still, a majority of the populations with prediabetes and type 2 diabetes do not reach the recommended levels of physical activity (3-5). A challenge for the health care professionals lies in supporting the establishment of regular physical activity habits that are maintained over longer time (6).

A large number of studies in physical activity have shown that it is possible to increase physical activity and improve clinical parameters by interventions in primary care in the short term (7-9). However, evidence for long-term (>12 months) effectiveness is still limited and few interventions are both effective in improving physical activity and clinical parameters and pragmatic for clinical implementation (10, 11). Available studies are heterogeneous and often limited details are reported on intervention components, delivery, fidelity, reach and context, which make evidence synthesis problematic. Thus, evidence for specific features associated with greater effectiveness, maintenance and transferability into the healthcare systems is needed (4, 8, 11-13). For interventions to be comparable, reproducible and credible for health care policies and guidelines, it is necessary to make explicit the context, implementation factors and the mechanisms of effect of specific intervention components (12, 14). It is also fundamental to evaluate the interventions from the perspectives of the individuals (15, 16).

Sedentary behavior (SB) has gained considerable attention in the past decade as being associated with detrimental health effects (17, 18). It is however unclear whether these detrimental health effects are due to too much total sedentary time, mostly due to prolonged sedentary time or because of lack of being physically active. While it is clear that moderate and vigorous physical activity (MVPA) is beneficial, less is known about the effects of light intensity physical activity (LPA) and the whole-day pattern of sedentary and physically active behaviors (19, 20).

This thesis investigates whether it is feasible to implement self-monitoring of steps, group counselling, motivational interviewing (MI) and physical activity on prescription as means to support physical activity in the primary care setting. It describes the intervention design, the context and implementation of two levels of interventions targeted for individuals with prediabetes and type 2 diabetes. Furthermore, the thesis explores whether physical activity and clinical parameters are improved after 6-month intervention and how the individuals experience the interventions. Additionally, the thesis investigates potential health associations of replacing prolonged sedentary time with disrupted sedentary time, or with LPA or MVPA.

2 BACKGROUND

2.1 PREVALENCE OF PREDIABETES AND TYPE 2 DIABETES AND CRITERIA FOR DIAGNOSIS

Approximately 425 million people worldwide have diabetes, whereof more than 90% have type 2 diabetes. This number is estimated to increase to 629 million by 2045. In addition, it is estimated that another 352 million individuals have impaired glucose tolerance (prediabetes) and consequently, at high risk of developing type 2 diabetes (21)**.**

Screening for individuals with high risk for developing type 2 diabetes to identify adult high-risk target populations is an important step towards prevention and delaying disease progress. Suggested methods to detect individuals with or at risk for type 2 diabetes, are a single blood test determining fasting blood glucose or fasting HbA_{1c} (impaired glucose metabolism), or an oral glucose tolerance test (impaired glucose tolerance) (21, 22)**.** HbA_{1c} as diagnostic instrument for diabetes was implemented in Sweden in 2014. Although, there is a discussion on whether HbA_{1c} should be used for screening as it may fail to detect individuals with prediabetes, it is commonly used today (23, 24). Table 1 presents diagnostic criteria for diabetes and prediabetes.

Table 1. Diagnostic criteria for diabetes and prediabetes.

	ADA[1]			WHO[2]	
	HbA_{1c} (mmol/mol)	Fasting plasma glucose (mmol/l)	2-hour plasma glucose (IGT) (mmol/l)	Fasting plasma glucose (mmol/l)	2-hour plasma glucose (mmol/l)
Diabetes	≥48	≥7.0	≥11.1	≥7.0	≥11.1
Prediabetes	39-46	5.6–6.9	7.8–11.0	6.1-6.9	≥7.8–11.0

[1] The American Diabetes Association, ADA (25)
[2] The World Health Organization, WHO (26)

Type 2 diabetes is a heterogeneous disease with a varied pathogenesis underlying the elevated blood glucose and risk for complications and comorbidities. It has been known for some years that treatment effect can be enhanced if the treatment is tailored to the specific form of diabetes. Recently a research group suggested that type 2 diabetes should be classified into five sub-groups of (27):

- Severe autoimmune diabetes (SAID): earlier age at onset, poor metabolic control, insulin deficiency, relatively low body mass index (BMI) and presence of GADA (Glutamic acid decarboxylase antibodies);
- Severe insulin-deficient diabetes (SIDD): earlier age at onset, low insulin secretion, poor metabolic control, relatively low BMI and GADA negative;
- Severe insulinresistant diabetes (SIRD): insulin resistance and high BMI;
- Mild obesity-related diabetes (MOD): no insulin resistance but high BMI;
- Mild age-related diabetes (MARD): older age at onset and only modest metabolic derangements.

The classification was based on a sample of 8980 Swedish individuals with newly diagnosed type 2 diabetes. MARD was the most common type of type 2 diabetes in the sample whereas SAID was the least common type (27).

2.2 PREVENTION OF TYPE 2 DIABETES AND CARDIOVASCULAR DISEASE

Having either prediabetes or type 2 diabetes increases the risk of comorbidities such as cardiovascular disease and premature death (1, 28) . Diabetes, together with its complications places a financial burden on the healthcare system not to mention all the suffering for the affected individuals. Referral to behavior programs should take place both for individuals with type 2 diabetes and for those with prediabetes to lower the risk of cardiovascular disease and diabetes complications in these two groups (29-33). Large prospective studies have been undertaken to investigate the preventive effects of lifestyle change on both type 2 diabetes and cardiovascular incidence. The Da Qing study in China, The Diabetes Prevention Program in the USA and the Finish Diabetes Prevention Study laid the groundwork for the argument that diabetes is preventable with changes in diet and physical activity and/or weight reduction at a public health level (34-36).

Not only to prevent type 2 diabetes, but also in the treatment plan of type 2 diabetes, a healthy diet and regular physical activity play an important role in reducing weight and other cardiovascular risk factors (2). The Look Ahead trial was a large (n=5145) randomized controlled trial (RCT) evaluating cardiovascular events and mortality of a lifestyle intervention in individuals with type 2 diabetes and overweight. The trial was successful in decreasing weight and improving cardiorespiratory fitness, blood glucose control, blood lipids and blood pressure. Moreover, improvements and significant differences between intervention and control group remained over 9 years (37). The study was discontinued after a median follow-up of 9.6 years because of failure to detect a difference between the intervention and control group for cardiovascular morbidity and mortality. Several papers have been published since with post hoc analysis of the data in an attempt to explain the failure of detecting significant differences in cardiovascular morbidity and mortality between the groups. There was an overall low rate of cardiovascular events in both groups and it is possible that the participants in the control group were health conscious and had good metabolic control. The Look Ahead trial was indeed successful and provided strong evidence for health benefits from lifestyle changes, such as improved quality of life, less sleep apnea, less sexual dysfunction, less severe diabetic kidney disease and retinopathy and less depression. All this occurred with a lower health care cost (38).

2.3 PHYSICAL ACTIVITY, SEDENTARY BEHAVIOR AND TYPE 2 DIABETES

2.3.1 Physical activity and the type 2 diabetes condition

It is evident that regular physical activity has a variety of benefits, including reduced risk of type 2 diabetes, cardiovascular disease and premature death (3, 39). Physical activity is a central component of diabetes care (1, 40). The effect of physical activity in individuals with type 2 diabetes has recently been quantified and is estimated to contribute to a 30 to 40% reduced risk for cardiovascular mortality (41). For individuals with type 2 diabetes there is a dose-response relationship for physical activity and cardiovascular mortality with some reduced risk when engaging in physical activity compared to no activity and larger risk reduction when engaged in higher levels of physical activity (42, 43).

Physical activity, in comparison with drugs, has positive simultaneous effects on several cardiovascular risk factors (e.g. overweight and obesity, blood pressure and blood lipids) and HbA_{1c} (39, 41). Furthermore, physical activity has low risks and few side effects. When performed on a regular basis, physical activity enhances metabolic control by improving insulin sensitivity and blood glucose control (39, 44). Aerobic training is more effective than resistance training in improving HbA_{1c} and blood glucose but combined training is even more favorable (45, 46). The effects of a bout of aerobic physical activity on insulin action and glucose tolerance depend on the intensity of the physical activity and duration of the bout. Health effects of a bout of physical activity (e.g. lower blood pressure and improved insulin sensitivity) last between 24 and 72 hours. Continuous regular activity is thus an important component, in order to keep repeating the effects (39, 47).

Walking is the form of aerobic activity that is most frequently performed and moderate intensity walking is often referred to as it is practical and convenient for most individuals. Amount of daily steps reflects the total daily walking and running and is strongly associated with cardiometabolic risk factors in cross-sectional studies (48-50).

2.3.2 Physically active and SBs

Physical activity is a complex multidimensional behavior that people undertake daily; such behavior occurs in combination with SB. Both behaviors – physically active and SB - are influenced by physiological, psychological and environmental determinants (51), which are distinct between the two behaviors (52). SB implies that no movements are made by large muscle groups and is performed in different posture positions (lying down, sitting and standing).

When being physically active locomotor movements are involved. Any movement results in energy expenditure, regular locomotor movement is health enhancing leading to physical fitness and health (51). Movement is performed under different types of activity such as walking at various speeds, carrying loads, cleaning, bicycling, performing sports or playing with children at different levels of intensity. Physical activity is a behavior resulting in movement while SB is defined no or very little movement. Movement performed in a continuum of different intensities with a corresponding dose-response effect is illustrated in Figure 1. The figure also illustrates how the behaviors are distinct and affected by physiological, psychosocial and environmental determinants.

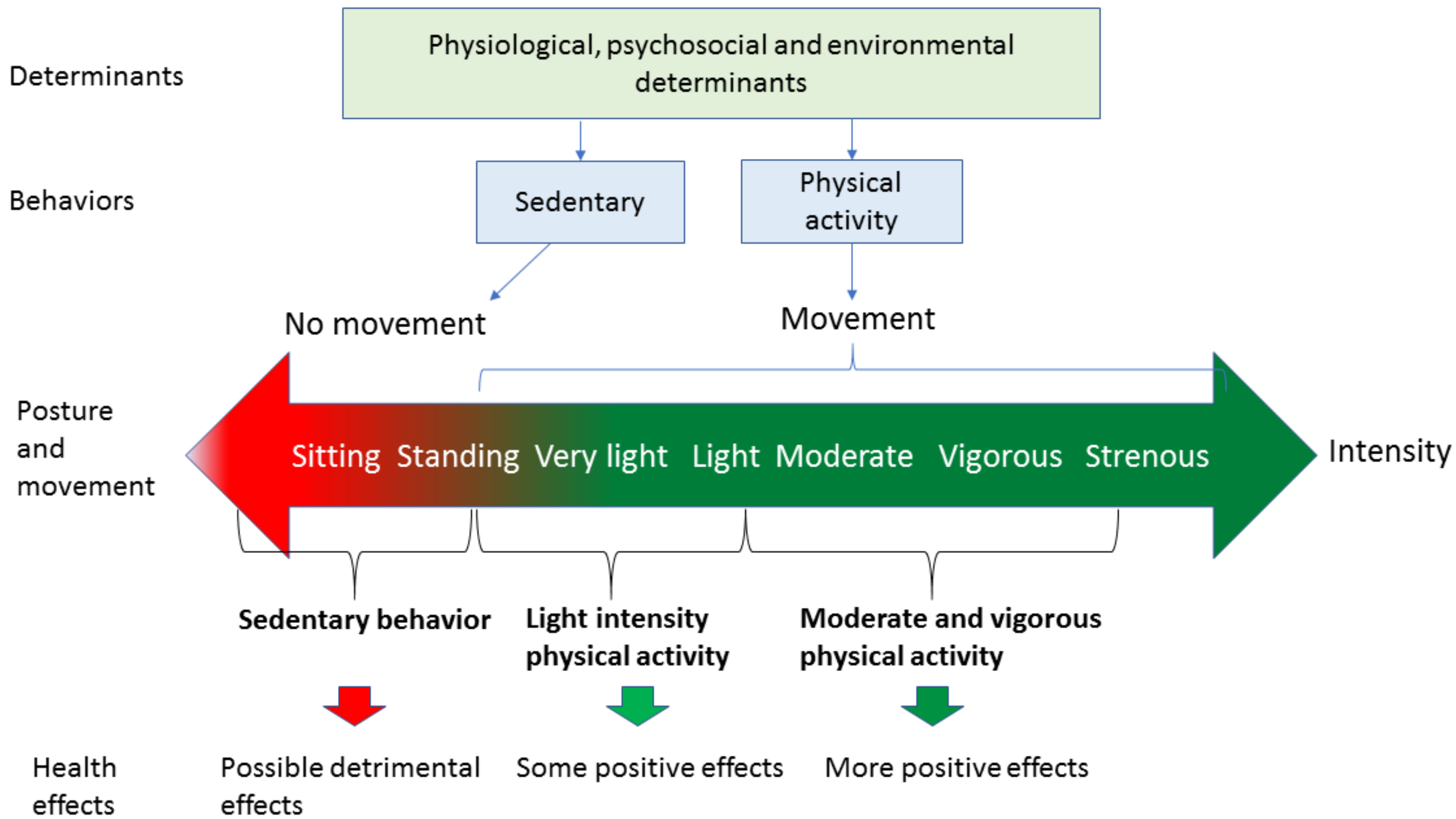

Figure 1. Illustration of how determinants, sedentary and physically active behaviors, postures and movement at different intensities lead to various health effects.

A common definition for physical activity is Caspersen, Powell, and Christenson's definition: "Physical activity- any bodily movement produced by skeletal muscles that results in energy expenditure" (Caspersen 1985, p. 129). This wide definition is problematic and the authors did suggest that energy expenditure should preferably be categorized. Categories could be based on activities performed during the day such as during sleep, at work and at leisure time (e.g. sports, conditioning exercises and household tasks); on physical activity intensity such as light, moderate, or heavy intensity; on whether the activity is willful or compulsory; or on whether it is weekday or weekend activity. It was proposed that the different ways of subdividing physical activity are correct as long as the subdivisions are mutually exclusive and that they correctly sum up the total caloric expenditure due to physical activity (53).

Today, physical activity is commonly divided into categories of intensities: light intensity physical activity (LPA), moderate intensity physical activity (MPA) and vigorous physical activity (VPA). In most adult populations very little VPA is performed and moderate and vigorous physical activity are often collapsed into one category referred to as moderate and vigorous physical activity (MVPA).

In research and in guidelines, intensity of physical activity is often expressed in terms of percentage VO_2 max, percentage of maximal heart rate, or in metabolic equivalent (MET) values. MET is a way to express absolute intensity as the energy cost of a physical activity type (i.e. brisk walking or vacuum cleaning) and is defined as the ratio of metabolic rate (the rate of energy consumption) during a specific activity to a reference metabolic rate. The reference value (1 MET) most often used is the amount of energy spent when sitting quietly (54).

SB is commonly defined as "any waking behavior characterized by an energy expenditure ≤ 1.5 METs while in a sitting or reclining posture" (p.450), as proposed by The Sedentary Behavior Research Network in 2012 (55). In 2017, the Sedentary Behavior Research Network published a conceptual model that included a movement-based terminology across the 24-hour movement and non-movement behaviors Additional definitions were established for: physical inactivity, stationary behavior, standing, screen time, non-screen-based SB, sitting, reclining, lying and SB pattern. It was also proposed that SB should be separated from sleep which includes lying, reclining and sitting postures. Physical activity may also include lying, reclining and sitting behaviors if energy expenditure exceeds 1.5 METs (56). Thus, SB is complex and when studying SB, defining what is measured and choosing the appropriate measurement method are crucial.

Studies in the field of physical activity and SB are methodologically heterogonous, and despite the enormous number of studies on the topic, some issues (e.g. recommend intensity of physical activity and sedentary time) are still being debated. Inconsistencies in findings may often be attributed to inconsistencies in, for example, definitions, type of activity measured, measurement method, cut-off levels for physical activity intensity, health outcome, confounders and whether adjustment for time in other activities has been made.

2.3.3 Duration, dose, bouts, frequency and type of physical activity and breaks in sedentary behavior

The complexity of physical activity behavior makes it difficult to monitor and interpret. When establishing the relationship between physical activity and health it is important to consider the total dose of activity. Individuals display various patterns of physical activity at different intensities during the day, the week and over the year. A dose of physical activity is the sum of duration and intensity, which is often summed over a day or a week. Because different intensities have different health effects, the spectrum of intensities needs to be considered when summarizing a dose. While it is central to reflect on both the total time and intensity of activity, it has also been discussed whether each bout of a performed activity should reach a certain duration (e.g. 10 min in MVPA) in order to count (57). Mode or type and frequency of activity are additional dimensions of physical activity that should be regarded when quantifying physical activity (58).

Concerning SB, it is important to quantify not only total sedentary time, but also how often breaks in sedentary time are taken, duration of the breaks, and the type of physical activity that is performed during the break (standing, light activity or moderate and vigorous physical activity) given that the varying activities has different health effects (20).

2.3.4 Physical activity intensity

Most research in physical activity links health outcomes with time spent in MVPA (or exercise) (39, 59). Less is known about the effects of LPA (also referred to as non-exercise physical activity), that does not necessarily reach moderate intensity level. Contemporary lifestyle has resulted in a large proportion of waking time spent performing SBs. Many of the activities that used to be spent ambulatory (e.g. standing, lifting light objects and walking slowly at work, in transportation, during household duties, gardening and grocery shopping) have been substituted by sedentary activities (sitting or reclining).

Cross-sectional studies on general populations reveal that spending time in LPA instead of being sedentary is associated with reduced mortality (60-62), and increased physical health and wellbeing (63). Thus, increasing time in LPA and reducing sedentary time may give additional health benefits over the recommended dose of MVPA.

Globally, a majority of individuals with type 2 diabetes do not reach recommended levels of physical activity and display high levels of sedentary time (4). It is therefore currently being discussed whether, in the case of preventing and treating type 2 diabetes, reducing sedentary time by increasing time in LPA should be encouraged as a more realistic approach than the present recommended dose of MVPA (19). Recommending reduced or interrupted sedentary time and increased time in LPA can be a start to become more active. A recent large international cross-sectional study on a population with prediabetes revealed similar health benefits from total physical activity as for MVPA, and that accumulating total physical activity during a day is as important as receiving the intensity of MVPA (5).

For the general population, there is a clear dose-response relationship for the intensity of physical activity and health outcomes. Thus, even though LPA has health advantages, MVPA is more time efficient and stronger related to mortality (60, 61, 64).This finding also held when total volume (instead of time in LPA or MVPA) of physical activity was investigated on a general population (62). This finding is important to consider in that working hours, job strain and stress are inversely related to physical activity level (65).

2.3.5 Sedentary behavior

Sitting and SB have gained much attention over the years, especially during the past decade since it was highlighted as a health hazard and risk factor for cardiometabolic disease, type 2 diabetes and premature mortality in the early 2010s (18, 66). SB has now been proposed to be a distinct risk factor for type 2 diabetes, insulin resistance and cardiovascular and all-cause mortality independent of time spent in physical activity (18, 64, 67-70).

The mechanisms underlying the deleterious effects of SB are not clear. However, spending a majority of waking time sedentary contributes to less energy expenditure and increase risk for overweight and obesity, which are known risk factors for type 2 diabetes (71). Total sedentary time has also been associated with poorer insulin sensitivity (69). A frequently cited study showed that lipoprotein lipase activity in the quadriceps muscle is diminished when contractile activity is reduced, leading to lower absorption of fat from circulating lipoproteins (71).

Breaking up sedentary time, on the other hand has shown some beneficial associations for example with cardiovascular disease risk and metabolic risk in cross-over studies (72, 73), with triglycerides in a meta-analysis of cross-sectional studies (69) and with glucose metabolism (unadjusted for total sedentary time) and obesity metrics in a meta-analysis that included observational and experimental studies (74). During 2016 and 2017 a large number of epidemiological, cross-over, experimental and interventions studies looking at reducing or interrupting sedentary time were conducted. A discussion is ongoing as to whether it is the break per se or the physical activity performed during the break that has the positive effects (20).

Despite the large number of studies on sedentary research in the past years some argue still that it is too early to draw conclusions and formulate guidelines for sedentary time. Previous studies are too heterogeneous with respect to study design, the definitions used for SB, measurement methods, cut-off levels, adjustment for physical activity, study population and health outcome (20).

When studying and interpreting associations and effects of SB, it is important to separate the results from different study populations and disease. For example for persons with impaired glucose tolerance taking breaks in sedentary time seems more beneficial than for the general healthy population (72, 75). While most agree that little physical activity and too much sitting are harmful, there is conflicting evidence as to whether very active individuals benefit from being less sedentary. Five large meta-analyses demonstrate that moderate to vigorous physical activity may attenuate the hazardous risk of being sedentary (i. e. being sedentary may not be as harmful for those that are very active) (64, 70, 76).

2.3.6 Adjusting for time in other activities over 24 hours or total waking time

A concern that has been underlined recently is that the health effects of being sedentary, or on the other hand being more active, also depends on what activity is being replaced (60, 77-79). Because time is constant, spending less time in one behavior inevitably means spending more time in another behavior and vice versa. An example is a person who decreases time in SB. This time usually spent in SB is instead spent sleeping, in LPA or in MVPA. The behaviors are interdependent: it may be the activity that is replaced (more time spent in sleep, LPA or MVPA) that brings the associated effects. Thus, it is imperative to clarify the activity that is replaced when investigating associations, or effects, of physical activity (60).

An isotemporal substitution paradigm of sleep, SB and physical activity has been suggested to model associations with health of reallocating time in one behavior for time in another (79). The model considers that time is limited (isotemporal) and that the activity intensities are dependent. A limitation when using isotemporal substitution on cross-sectional data is that the model is data driven and merely model reallocation of time. Therefore, intervention and mechanistic studies are needed to establish causal relationships between SB, physical activity and sleep with health parameters.

2.3.7 Recommendations on physical activity and sedentary behaviors

Recommendations on physical activity for people with type 2 diabetes are similar to those for the general population. The recommendations have changed just slightly during the past 10 years. In 2010 the American College of Sports Medicine jointly with the American Diabetes Association (ADA) recommended individuals with type 2 diabetes to undertake at least 150 min per week of aerobic exercise at moderate intensity or greater (47). There is a dose-response relationship and if the activity is performed at a vigorous intensity level the time can be reduced to 75 min per week. To reach the total dose the two intensities can also be combined over the week. The aerobic activity should be performed in bouts of at least 10 min and be spread throughout the week on at least three occasions, with no more than 2 days between activity bouts. In addition to aerobic exercise resistance training should be undertaken at least 2-3 days per week. In the position statement released by the ADA in 2016 the recommendations for MVPA did not change. However, encouragement of increased total daily non-exercise activities were added and flexibility and balance training for older individuals with diabetes were underlined (47, 80, 81). Additional recommendations for interrupting sitting with bouts of LPA every 30 min and decrease total amount of time spent sedentary were also added in the updated position statement (39). These same recommendations were outlined also in the American Diabetes Association Standards of Medical Care in Diabetes 2018 (40).

The Swedish recommendations provided in Physical Activity in the Prevention and Treatment of Disease Prevention (Swedish: Fysisk aktivitet vid sjukdomsprevention, FYSS), updated in 2015, provides similar recommendations as those of the ADA, except for the exclusion of bouts of at least 10 min (80). Of note, the former Swedish recommendations from 2008 included recommendations for 30 min of every day non-exercise activities in addition to 20-60 min of activities at moderate intensity 3-5 days per week (80). These recommendations on non-exercise activities were removed from the 2016 version, in contrast to the recent ADA guidelines, in which recommendation for non-exercise activities additional to 150 min per week of MVPA was added (39).

The 2018 Physical Activity Guidelines Advisory Committee Scientific Report summarizes the scientific evidence with the purpose to guide updated recommendations for physical activity. In the report it is noted that the evidence for beneficial health effects of physical activity for individuals with type 2 diabetes has been strengthened since the 2008 report. There is now stronger evidence both for types of activity (aerobic exercise and resistance training or, preferably, combined) and for diverse health outcomes (mortality, HbA_{1c}, BMI, blood pressure, lipids). The report concludes that reaching bouts of 10 min of activity is not necessary but collecting at least 150 min per week ideally up to 300 min per week of MVPA and to substitute time in SB is the essential message (41).

Nowadays, step counters are widely used to self-monitor physical activity and increase motivation to be physically active. The optimal number of steps for a population with type 2 diabetes is not known. A recommendation for the number of steps proposed by Tudor-Locke and co-authors for healthy adults is 7100-11000 steps per day (82). The recommendation is similar for healthy older adults and individuals with disability and/or chronic illness with a proposal of 7000-10000 steps per day (83). A cadence (walking speed) of 100 steps per min, which is at a brisk pace, corresponds to MVPA. To reach the guidelines for physical activity at least 15000 steps per week (e.g., 3000 steps per day for five days) should be accumulated at a cadence of 100 steps/min (83).

Less than 5000 steps per day have been proposed as a sedentary lifestyle and number of days with < 5000 steps should be avoided (84). For an initially inactive population, it is appropriate to work with gradual increases based on the current number of steps (83). Many individuals (especially with impaired glucose tolerance) are physically inactive and a more realistic approach (rather than to reach 150 min of MVPA per week) is to use a stepped approach and start with substituting sedentary time to LPA time (85, 86).

2.4 SUPPORT FOR PHYSICAL ACTIVITY IN DIABETES CARE

2.4.1 Support for self-management of physical activity

Individuals with diabetes should be at the center of self-management care, and the role of the educator is to make that work in a more manageable manner (87). Diabetes self-management education is defined as “the ongoing process of facilitating the knowledge, skill, and ability necessary for prediabetes and diabetes self-care” (p.S145 Haas et al. Diabetes Care 2014) (88). Diabetes self-management support is “Activities that assists the person with prediabetes or diabetes in implementing and sustaining the behaviors needed to manage his or her condition on an ongoing basis beyond or outside of formal self-management training. The type of support provided can be behavioural, educational, psychological or clinical” (p.S145 Haas, Diabetes Care 2014) (88). Various approaches to deliver of self-management education and support can be equally effective and flexibility using various approaches has been recommended specifically for physical activity interventions (14, 88).

If priority is given by the health care services to encourage individuals to be more physically active, the results are often promising (89). However, reaching the majority of a population and maintaining long-term effects are challenging and dependent on several influencing factors such as the motivation of and the circumstances around both the health care professionals and the person (9, 90). A recent systematic review and meta-analysis established that both structured and lifestyle behavioral interventions are effective in increasing physical activity in individuals with type 2 diabetes. Face-to-face support and more contacts were associated with greater improvements. Long intervention duration and frequent contacts improved efficacy for HbA_{1c} (10). Such interventions are costly and demanding and often not pragmatic for clinical implementation (11).

In primary care, to minimize the usage of cost and time, brief interventions are recommended to support inactive individuals to become more physically active (91-93). Brief interventions are time efficient, inexpensive and low demanding. Examples of brief interventions are: giving advice only, advice with pedometer or written prescription/referral, or short counselling with or without pedometers and prescription/referral. In a systematic review of reviews summarizing the evidence of brief interventions in promoting physical activity in primary care it was concluded that brief interventions were efficient in increasing self-reported physical activity in the short term (4-12 weeks). However, the evidence was insufficient for long-term effectiveness, and mixed for contact time and follow-up, intervention duration, inclusion of written materials or prescriptions, and for provider training (9).

A recent systematic review summarized the effectiveness of physical activity interventions on objectively measured physical activity in adult populations with type 2 diabetes. Exercise consultation, behavioral/cognitive consultation, consultation on continuous glucose monitoring and motivational phone calls were all effective interventions in increasing objectively measured physical activity (94). Despite variations between the reviewed studies in terms of sample size, intervention dose, delivery methods, length of follow-up and country, there were similar improvements in physical activity across the studies. Personalized health care (face-to-face consultations, and/or cognitive behavioral sessions) was a predictor for effectiveness (94). Tailoring the needs of each individual has also been suggested as a strong predictor for success within the health care services (89) and individualization is stressed in the National Standards for Diabetes Self-Management Education and Support (88).

2.4.2 Counselling physical activity

2.4.2.1 Motivational interviewing

MI is a person-centered counselling style developed to support people wishing to change their behavior (95). MI explores ambivalence and stimulates an intrinsic motivation for change. The counsellor uses open questions to engage the individual, to help focus and to evoke and plan change. More information and advice are given but only if the person requests additional help. Change talk is applied and aims to confirm and encourage what the person suggests. The counsellor uses open questions to engage the individual, to help focus and to evoke and plan change. More information and advice are given but only if the persons request additional help. Change talk is applied and aims to apply and encourage what the person suggests. The counsellor collaborates with the persons; it is up to the persons if they want to change and to suggest what they would like to change. All individuals have their own life story with experiences and preferences. Only the individuals themselves can change; as a health professional, one can assist based on where the individual is in the process of change (95). MI is suitable as a support method to modify unwanted behaviors. It has become a core element in the curricula of many health professional educational programs in Sweden, and several educational organizations offer training in MI (96).

Despite the vast number of courses offered in MI, evidence in the efficacy of MI specifically for self-managing physical activity in type 2 diabetes is scarce. A systematic review and meta-analysis published in 2014 showed that there is a small effect of MI with improvements in physical activity for individuals with chronic health conditions. The effects became stronger when treatment fidelity was considered. The optimal dose (frequency and duration of a MI session) could not be determined because of lack of reported details and variations between the studies. Of the 10 studies included in this systematic review, none included persons with diabetes (97). A review article also published in 2014, including nine studies with adult type 1 diabetes and type 2 diabetes populations, concluded that MI in diabetes type 1 and 2 self-management has potential to improve metabolic control (HbA_{1c}). MI was most effective if tailored to the individual's unique character and circumstances and based on values and perceived relevance for the individual (98). In a systematic review published in 2016, evidence and gaps of MI on behavior change outcomes in type 2 diabetes populations were explored. Six RCTs targeting and measuring physical activity were identified. None of these studies showed significant positive results for MI on self-reported physical activity. The authors discussed possible bias because of heterogeneous designs, methods and measures used in the studies as well as variations in recruitments and lack of fidelity measures (99). A recent review article consisted of nine studies with focus on type 2 diabetes self-management and measuring physical activity as an outcome. Of the nine studies, four reported significant outcomes on physical activity. In contrast with the studies showing no positive results, the studies showing efficacy targeted not more than two type 2 diabetes self-management behaviors, considered delivered dose (two or more sessions, at least once monthly and/or > 30 min counselling duration), and in two of the four studies that reported significant outcomes, counsellors were MI proficient (100). In total, only three studies provided details on fidelity and therefore comparisons and interpretation regarding the lack of significant results should be done with caution.

2.4.2.2 Group support

Using groups to support individual behavior change is a cost-effective and widely used method. Well-planned group counselling sessions led by health professionals have been shown to be effective and useful in diabetes care (101-103). In the group setting there is a unique opportunity for the participants to share information, to encourage and elicit change talk and to teach and follow-up goal-setting, barrier identification and problem solving. Social support, a component that is easily implemented in group consulting, has been shown to be important for successful lifestyle change (101). In a systematic review made by the Swedish Council of Health Technology Assessment one of the main conclusions was that group education, led by a committed team of professionals with expert competence and acquainted with the methods used, can substantially reduce HbA_{1c} after 1-2 years (104). Two recent systematic reviews support this evidence for group-based self-management as more effective in reducing HbA_{1c} than individual counselling sessions (105, 106).

2.4.3 Self-monitoring of physical activity

Pedometers are simple low-cost devices that assist in the self-monitoring of steps. Pedometers are efficient in increasing people's motivation to be more active by behavior goal setting, feedback on performance and prompt review of behavioral goals (107). Pedometers have the potential to increase the number of steps with approximately 2000 daily steps per person (108, 109), physical activity (110), and modest weight loss (111). The evidence for pedometers in improving metabolic parameters in individuals with type 2 diabetes is mixed (110, 112, 113). Yet, in a meta-analysis pedometers and other forms of activity trackers in combination with counselling were effective in improving HbA_{1c} (109). Most studies have a duration of ≤6 months, but there is evidence from single studies for 12- month's effects on steps per day, physical activity and SB by pedometer-based behavioral modification programs in individuals with type 2 diabetes (102, 114).

2.4.4 Physical activity on prescription

Physical activity (or exercise) on prescription was introduced in the early 2000s as a method to strengthen the message that physical activity is important and to bring physical activity on an equal status with medication. In Sweden the method Physical Activity on Prescription (FaR®) was developed and has partly been implemented in the Swedish primary care system (115). FaR® is applied to introduce the recommendations for physical activity as treatment outlined in FYSS (80) and for individual behavioral goal-setting. Individualized consultation forms the basis of FaR® in which individual preconditions and preferences are discussed. A prescription is outlined in collaboration between the health professional and the person. A referral to a sport club or a gym with an educated staff can be included if the person wishes such arrangements (115). Follow-up is an important feature of FaR®. Few studies are available evaluating FaR® and they are heterogenous in terms of study population, duration, outcome measured and measurements method and study quality. A Health Technology Assessment report summarizing the current evidence for FaR® and similar methods, was recently published. The authors considered FaR® promising for use in Swedish primary care setting with some evidence for improvements in physical activity, body weight, waist circumference, and glucose metabolism (116).

There is limited evidence for the effectiveness and cost-effectiveness for physical activity on prescription and in populations with type 2 diabetes. It is not clear, however, whether it depends on the method itself, the way that the method is implemented or the heterogeneity of the available studies (117). In the UK and Australia exercise referral schemes (referral to an exercise professional) are recommended to be used, and extensive research is in the process of evaluating efficacy, effectiveness and implementation.

2.4.5 Theories on behavior change

Effective interventions are often grounded in a theoretical framework (118). Theories and models for behavior change can assist in structuring a program and make it explicit. There are numerous behavior change theories and models that have been shown to be effective in changing behavior. The Health Belief Model was introduced already in the 1950s and has been widely used since for several health issues and behaviors (119). The model assists in raising awareness of a risk behavior and increases intention and motivation to change. Constructs included are perceived severity of the disease and its complications, perceived susceptibility for a disease, perceived benefits of changing behavior, perceived barriers for behavior change, cues for action and self-efficacy. Stages-of-change model, also known as the transtheoretical model, is one of the most applied theories in physical activity interventions. The model assists in moving individuals forward in their readiness for change and targets the needs of individuals depending on their readiness to act. It helps in preparing and planning a change in behavior and provides tools for action, maintenance and relapse prevention. The model focuses on constructs such as: provide personal information, raise awareness, encourage and assist in goal-setting, action planning, set graded tasks, give feedback, identify barriers, problem solving, plan social support, prompt rewards on progress and success, teach to use cues and relapse prevention (120). Social cognitive theory is another commonly applied theory. Social cognitive theory adds the dimension that behaviors are dynamic and reciprocal. This dimension refers to behaviors being changeable and interactive: personal factors and the environment can change behaviors and behaviors may change personal factors and the environment. The social cognitive theory includes the components reciprocal determinism, self-efficacy, behavioral capability, expectations, observational learning (role modeling) and reinforcements (121) .

It is probable that the theoretical constructs that are helpful for short-term behavior change differ from those assisting inthe maintenance of new behaviors. In a systematic review Kwashnika et al. synthesized the evidence for theoretical explanations in behavior change maintenance across health behaviors. A thematic analysis resulted in five themes explaining behavior change maintenance. The themes were: maintenance motives, self-regulation, habits, resources and environmental and social influence. As in most cases, the theoretical models and thus the constructs applied for maintenance were the same as those for behavior change. However, the direction and value of the constructs were changed for the maintenance phase. For example, for behavior change, motivation focuses on the behavior change per se and may be driven by the risks of the old behavior and expected benefits of changing. For maintenance, motivation may be enhanced when focus is on endorsing the new behavior: on behavior enjoyment, satisfaction with behavioral outcomes and congruence of the new behavior with the individual's own identity, beliefs and values (122).

2.4.6 Behavior change techniques

The constructs applied by the use of behavior change theories in interventions are the factors believed to lead to change. These are also referred to as mechanisms, mediators, active ingredients or behavior change techniques (BCTs). Because of heterogeneous vocabulary and use of concepts, it has been difficult to summarize the evidence. Accordingly, Susan Michie and her colleagues developed and published a taxonomy, the CALO-RE taxonomy (123, 124). This taxonomy has now been revised into a hierarchically clustered version: The BCT Taxonomy version 1 (BCTTv1), including 96 BCTs (125). These taxonomies have contributed to a common terminology and improved means of evaluation and replicability of interventions and compilation of evidence (124-126). A BCT is defined as "an observable, replicable, and irreducible component of an intervention designed to alter or redirect causal processes that regulate behavior; that is, a technique is proposed to be an 'active ingredient' (124). Within the promotion of physical activity, there is growing evidence for the use of certain BCTs in interventions.

Several systematic reviews and meta-analyses have identified BCTs to be efficient in increasing self-efficacy, physical activity behavior and HbA_{1c} (127-129). Table 2 summarizes the most effective BCTs found in reviews on populations with type 2 diabetes, obesity and healthy adults. Considerations should be taken to the results of the reviews, as the findings depend on whether they have applied the CALO-RE taxonomy or the BCTTv1 taxonomy.

Table 2. Overview over systematic reviews reporting most effective BCTs for behavior change on self-efficacy for physical activity, physical activity, weight and HbA_{1c}.

Author, year of publication and population	**Outcome**	**BCTs found to be most effective**
Williams et al., 2011 Healthy adults	Physical activity and self-efficacy for physical activity	*Action planning, provide instruction and reinforcing effort towards behavior*
Greaves et al., 2011 Type 2 diabetes	Physical activity and weight loss	*Self-monitoring, specific goal-setting, relapse prevention, social support and support maintenance of the behavior change*
Avery et al., 2012 Type 2 diabetes	HbA_{1c}	*Provide information on the consequences specific to the individual, prompt the target behavior; prompt focus on past success; behavioral goal setting, provide information on where and when to perform physical activity, apply follow-up prompts; prompt review of behavioral goals; plan social support/social change; time management and barrier identification/problem-solving*
Olander et al., 2013 Obese adults	Physical activity	*Teach to use prompts/cues, prompt practice, and prompt rewards contingent on effort or progress towards behavior*
Avery et al., 2015 Type 2 diabetes	Physical activity and HbA_{1c}	*Prompt focus on past success, barrier identification/problem solving, use of follow-up prompts, and provide information on where and when to perform physical activity*
Cradock et al., 2017 Type 2 diabetes	HbA_{1c} and weight (through diet and physical activity)	*Action planning, instruction on how to perform a behavior, demonstration of the behavior, behavioral practice or rehearsal*

2.5 DESIGNING AND EVALUATING PHYSICAL ACTIVITY BEHAVIOR CHANGE INTERVENTIONS

2.5.1 Developing interventions

The development of a behavior change intervention should be based on the identification of a problem and its determinants preferably both as perceived by individuals and health professionals and by statistical and scientific means. Existing research should be scrutinized to clarify what is already known about similar interventions; what has had effects and what has not. Next, is the development of a theory: a rationale for the expected change and how/why the change is likely to be achieved. Several decisions need to be made regarding the intervention, the evaluation and the reporting thereof. Examples of decisions include type of study design, delivery method (e.g. by health professionals, through leaflets, e-based), intervention components/strategies (e.g. consultation, pedometers, supervised exercise), dose (how much and how often) and duration. Evaluation features to be decided upon are: primary and secondary outcomes; measurement methods, number of assessments and duration between assessments. A study protocol describing the intervention should be developed and be as detailed as possible to ease the fidelity to the intended protocol, enhance transparency, and reduce bias in the reporting of results (16, 130, 131).

The RCT design is considered the gold standard in medical and intervention research (131). Randomization refers to the random allocation of the subjects into parallel groups of treatment or control/placebo groups. The groups differ only with respect to the treatment received and are thus comparative (controlled). Randomization and blinding are the most important features to reduce bias of a trial (132). Blinding refers to not knowing what group a study participant is allocated to and a trial can be blinded to the participant, the health professional, the research staff and the person performing the statistical analyses. Other problems of interventions that will interfere with the results are missing data and drop-outs. The CONSORT (CONsolidated Standards of Reporting Trials) 2010 guideline provides guidance and a checklist for the full reporting of RCTs with the ultimate aim to increase transparency and to allow for the readers to assess the validity of a trial. The CONSORT also includes a flow chart showing the flow of participants throughout the recruitment and intervention process (133).

Several health outcomes are often of interest when evaluating an intervention, which may cause a problem as multiple testing will likely provide statistically significant results by random chance. To choose an outcome variable to report when knowing which one is showing statistically significant result is considered as research fraud (132). Such deceit is now being avoided by the registration of a trial and specification of the primary outcome of interest and expected change on beforehand.

The application of the RCT design in behavior change interventions raises some difficult challenges. It is problematic to blind behavior change interventions and to control human behaviors. In behavior change interventions it becomes crucial to be aware of the degree of implementation of a trial: Was the intervention delivered in the intended way? Are the participants doing as they were educated or supported to do? The CONSORT was therefore extended to include a checklist for information to include when reporting a randomized trial assessing non-pharmacologic treatments.

The extended checklist includes, for example, how bias due to not being able to use a blinding procedure are limited, detailed information about the providers of the intervention and assessment of adherence to the intervention. The extended CONSORT builds on the template for intervention description and replication (TiDieR) checklist that was developed to encourage and improve the reporting of interventions (not only RCTs). Key features of interventions (such as duration, dose or intensity, means of delivery, processes and monitoring) were all too often poorly reported and thus interventions were not replicable. The TiDieR checklist includes 12 items to be reported (134).

2.5.2 Process evaluation

Process evaluation assesses whether an intervention was implemented as planned and is ideally completed before outcome evaluation (16). In complex behavioral interventions of long duration, it is paramount to explore intermediate results and factors that may interfere with the results (12, 16, 130). Process evaluation assists in deciding whether to change or adjust intervention components; to stop allocation to any of the arms or even to discontinue the intervention if it is not being implemented or having adverse effects or causing negative results. (132). In addition, it provides details on factors that should be made explicit to enhance best practice and guide policy and guidelines, including feasibility, degree of reach, implementation and adherence to study protocol (fidelity) (12, 14, 16). Furthermore, by providing implementation quality, fidelity and dose received, an understanding and interpretation of variations of the final outcomes are made possible. For instance, whether specific components contributed significantly to the overall or specific outcomes or whether the intervention was better suited to or did not work for subgroups of the population (16).

Process evaluation preferably applies both quantitative methods and qualitative research methods. Quantitative methods are used to measure such factors as reach, delivery and exposure to an intervention, whereas qualitative methods are more appropriate when exploring participant and deliverer satisfaction, barriers and facilitators to fidelity to the study protocol, and formal and contextual features of intervention fidelity (16).

Frameworks for process evaluation have been developed and are recommended to be used to conceptualize the fidelity of interventions. A frequently applied framework in physical activity interventions is the reach, effectiveness, adoption, implementation and maintenance (RE-AIM) framework (135). The RE-AIM approach is suitable for planning and evaluating large scale implementation programs, in which the researchers have little involvement. Another framework suitable also for smaller scale RCTs is provided by the Medical Research Council guidance. This framework focuses on three themes: implementation, mechanisms and context. Implementation incorporates the implementation process (how delivery is achieved) including fidelity, dose, adaptation, and reach (who received what). Mechanisms incorporate mediators for change, participants responses to and interaction with intervention components, and unexpected pathways and concerns. Context refers to any external factors that may act as barriers or facilitators of the intervention implementation and of the intervention effects (12).

Process evaluation features reported to a limited degree for type 2 diabetes self-management and physical activity interventions for adults (136, 137). A feature that is commonly reported is intervention dose, often reported as adherence, but there is a large variation in the reporting of intervention implementation.

2.5.3 The Hawthorne effect

The Hawthorne effect refers to the fact that people will modify their behavior simply because they take part in a research study (138, 139). Such assessment reactivities can be explained by several factors: increased reflections on the behavior, reminders of the behavior by frequent study measurements and enhanced efforts for change when randomized to a control group (as hopes and allocation preferences may have been present) (138). When studying cognitions, emotions and behaviors, it is difficult to distinguish the effects of the program from the added Hawthorne effects of being monitored and studied (138, 139). Differences in follow-up procedures and adherence between the interventions arms can affect the result and must be taken into account when interpreting the results of an intervention (138, 140). This process can be better understood when assessment extent and procedures are transparent and reasons for participation and participation effects are explored (138, 140).

2.5.4 Qualitative research

Mediating factors for behavior change are often cognitive in nature (e.g. changed attitudes and increased awareness and motivation). Cognitions, thoughts and experiences are difficult to evaluate using quantitative methods and qualitative inquiry is considered more appropriate to explore mechanisms for behavior change (12, 15, 130). By using interviews with open questions, in contrast to pre-set questions used in questionnaires, the individual’s reflections and perceptions can be explored (15). Qualitative inquiries can also underscore implementation factors, informal patterns and unexpected interactions (15). In addition, they may be helpful in separating the effects of the intervention from the subtle effects that taking part in a research study may have on participant behavior (139).

Content analysis is a suitable method to sort and abstract data in the form of text material, and to describe a phenomenon without a large extent of interpretation (141). Content analysis with a qualitative approach is commonly applied in health care and public health research. Qualitative analysis is made by either an inductive or a deductive approach. An inductive approach is well suitable to describe lived experiences and to give detailed and unanticipated descriptions. By using a non-theory-driven inductive approach, going from the specific to the general, it is possible to recognize patterns, interrelationships and themes emerging from the data and thereby the synthesis of larger statements. A deductive approach is appropriate when studying a phenomenon from a theoretical standpoint, and thus perform the analysis based on a pre-decided framework (15,132, 142).

2.5.5 Measuring physical activity

2.5.5.1 Self-reported measurement

Historically, self-report instruments (e.g. questionnaires and activity logs) have been the most frequently applied tools to assess physical activity behavior. Many of the health associations of physical activity are based on self-reported data. Examples of typically used questionnaires are the International Physical Activity Questionnaire (IPAQ) (143) and the Stanford Brief Activity Survey (144). MET values are often summed over a short period (e.g. 1 week), and represents the energy expended from time spent in physical activity. Both questionnaires (but also activity logs) have limitations, including recall bias, over reporting and interpretation difficulties. Moreover, they are not well suited to measure energy expenditure or total physical activity (145).

2.5.5.2 Objective measurements

Pedometers, or step counters are low-cost valid instruments to assess total ambulatory movement in simple outputs (steps). They cause little burden on the participant and are easily interpreted. Limitations are that simple pedometers cannot measure intensity, duration or type of activity and fail to capture various activities such as swimming and cycling (58, 146). Another limitation is that if the individuals are registering the steps by themselves the measurements are not fully objective. Nowadays a large number of wearables counting steps are available and steps, in addition, can be collected from smartphones and similar devices.

In the past 15 years, ambulatory assessment tools (e.g. accelerometers and various forms of activity trackers) have become abundant (58). These tools are objective and reduce the human error in reporting bias and recall. From accelerometers energy expenditure, activity intensity, duration and total volume of physical activity can be obtained. A large quantity of data can be stored, which makes it possible to follow individuals over long periods at a rather low participant burden. Limitations with accelerometers are that they are based on algorithms to quantify physical activity, they fail to capture non-ambulatory movements (e.g. cycling, load carrying and resistance training) and are not sensitive for SB and running (58, 146). To differentiate between sitting and standing the accelerometer can be put on the thigh or inclinometers can be used (147, 148).

Outputs from accelerometers can be given as energy expenditure, types of activity or counts per min (cpm). Table 3 lists examples of conventionally used categories for MET values and accelerometer counts based on healthy individuals. Cut-offs in Table 3 are given as absolute intensities: they do not consider the individual's relative intensity or perceived intensity that is dependent on the individual's fitness level. When applying cut-off values it is important to use values that are valid for the study population in question.

In many adult populations physical activity of vigorous intensity is performed to a limited extent by few individuals and the two categories moderate and vigorous intensity are often combined into one category (moderate and vigorous intensity physical activity). Using the cut-off values for moderate intensity proposed by Freedson et al., 1998 (149), and MET values of 3 can be compared to a walking speed of 4.0 km/h or 100 steps/min on flat ground (150, 151).

To acquire the entire picture of physical activity patterns of a population it is necessary to use complementary assessment methods. Questionnaires, diaries and interviews serve as good complements to accelerometers or pedometers to obtain information on context, dimensions and domains, as well as to determine factors related to physical activity (e.g. physical and social environment, intention and motivation) (58)

Heart rate is a direct physiological measure with a strong relationship to energy expenditure for MVPA. However, limitations with heart rate monitors are that for light intensity physical activity other factors (e.g. caffeine consumption, emotional state and temperature) may influence the heart rate and heart rate is affected by medications (e.g. betablockers). Multi-sensor systems combining physiological and mechanical sensors are becoming available and are look encouraging for the future (58, 146).

Table 3. Frequenly used cut-off values for categories of absolute physical activity intensity.

	Sedentary	Light intensity physical activity	Moderate intensity physical activity	Vigorous intensity physical activity
MET range[1]	≤ 1.5	1.6-2.9	3-5.9	≥ 6
Activity counts[2] (cpm)	≤ 99[3]	100-1951 100-759[5]	1952-5724[4] ≥ 2020[5]	≥ 5725[4]

[1]Ainsworth, Haskell et al., 1993(54), [2] Strath, Kaminsky et al., 2013 (58), [3]Matthews et al., 2008 (152), [4]Freedson et al., 1998 (149), [5]Troiano et al., 2008

3 RATIONALE FOR THE THESIS AND RESEARCH QUESTIONS

Scalable methods to support self-management of physical activity are needed in primary care to prevent type 2 diabetes, the progression of the disease and cardiovascular disease. Major concerns today are how to support individuals to make the lifestyle changes needed to manage the condition at a low cost, as well as how to implement such interventions into clinical practice (6). Self-monitoring of steps is a low-cost method, with low effort needed from health care professionals in terms of time and training. However, few studies exist on the effects of self-monitoring of steps on objectively measured physical activity and cardiometabolic risk factors and for long-term effects (9, 94). Self-monitoring of steps combined with MI, group counselling and FAR® may increase compliance and motivation to be more effective in the long term. To better inform guidelines and training curricula for health professionals, more evidence is needed on the effectiveness of combining the methods, on long-term effects and on implementation factors such as fidelity and mediators for behavior change (9).

SB has proposed detrimental health effects whereas physical activity is health enhancing (39, 69). While MVPA has clear health benefits the effects of LPA and interrupted SB is not as well-studied. Besides, the behaviors are interrelated and thus if one behavior is reduced the effects may be because of the behavior that it is replaced with, not by the reduction per se. In previous research time in the other behaviors has often been adjusted for in the past 10 years, but it is rare that health associations of the replacement of behaviors have been considered.

Research questions:

Study II: Is it feasible to implement self-monitoring of steps and individual and group counselling as support for physical activity in the primary care setting? To what degree is self-monitoring of steps and individual and group counselling implemented after 6 months? How effective is the self-monitoring of steps with or without individual and group counselling on physical activity behavior and health outcomes after 6 months intervention? Do the effects differ contingent on age, gender and diagnose?

Study III: How do the participants experience the support for physical activity based on the self-monitoring of steps and individual and group counselling?

Study IV: What are the health associations of modeling replacing bouted (prolonged) sedentary time with interrupted sedentary time, LPA or MVPA?

4 AIMS

4.1 OVERALL AIM

The overall aim of this thesis was to design and evaluate the implementation of a RCT in primary care, with the purpose to support individuals with prediabetes and type 2 diabetes to become regularly physically active (Study, II and III).

A secondary aim was to explore the theoretical associations of replacing prolonged sedentary time with interrupted sedentary time, LPA and MVPA with health parameters (study IV).

4.2 SPECIFIC AIMS OF THE STUDIES

The specific aims were:

Study I: To describe the design and recruitment procedure, methods and the theoretical framework for the physical activity promotion program Sophia Step Study.

Study II: To undertake a process evaluation to describe the implementation, context and physical activity behavior and health outcomes in the first 6 months of the Sophia Step Study.

Study III: To report a qualitative exploration of adhering participants' experiences after attending two years of the Sophia Step Study.

Study IV: To investigate the associations of reallocating sedentary time in bouts (>60 min) to sedentary time in non-bouts, LPA and MVPA with cardiometabolic risk factors in a population diagnosed with prediabetes or type 2 diabetes.

5 METHODS

5.1 STUDY DESIGN

The studies included in this thesis all apply different study designs: study I was a study protocol, describing the background, theoretical framework, design, intervention and evaluation protocol of the Sophia Step Study; study II was a process evaluation of a three-armed randomized controlled trial; study III was a qualitative interview study and study IV was a cross-sectional study exploring the associations of SB and physical activity with cardiometabolic risk factors.

5.2 RECRUITMENT PROCESS, INCLUSION AND EXCLUSION CRITERIA

5.2.1. Study II, III and IV

Recruitment of participants took place in seven waves at the primary care centers Husläkarmottagningen (study II, III and IV) and Försäkringsmottagningen (study II and VI) at Sophiahemmet and at Smedby hälsocentral (study VI). Patients diagnosed with prediabetes and type 2 diabetes meeting eligibility criteria were informed about the study, given a leaflet and were invited to participate. This was made by applying consecutive and convenience sampling techniques; asking all eligible patients at a planned visit at the health care center, or by telephone. Patients showing interest received a letter with further information and were subsequently phoned by the diabetes specialist nurse and asked a set of inclusion/exclusion questions. If they fulfil the inclusion criteria they were booked for a baseline study visit. Inclusion and exclusion criteria are displayed in Table 4. These were the same for study II, III and IV.

Table 4. Inclusion and exclusion criteria applied in study II, III and IV.

Inclusion criteria	Exclusion criteria
- Prediabetes (HbA_{1c} > 39-<47 mmol/mol and/or fasting glucose >5.6 mmol/l) or diagnosed with type 2 diabetes with a duration of ≥1 year.	- On insulin since the last 6 months
- 40-80 years	- Additional disease prohibiting physical activity
- Ability to communicate in Swedish	- Myocardial infarction in the past 6 months
	- Repeated hypoglycemia or severe hypoglycemia in the past 12 months
	- Serum creatinine >140 mmol/l
	- Diabetic foot ulcer or risk of ulcer (severe peripheral neuropathy)
	- Being classified as very physically active according to the Stanford Brief Activity Survey (144)
	- Having no access to internet.

5.2.2 Study III

For study III additional criteria were applied based on purposeful sampling with criterion-based selection (including only participants with ≥ 60% attendance at group counseling sessions, ≥ 80% of days with registered steps and ≥75% study assessments). The selection was also time-based as only participants from the third and fourth waves were included. In all, 22, of 36 participants were contacted list wise for interview by telephone or email until maximum variation was reached in terms of intervention group, sex and diagnosis (pre-diabetes and type 2 diabetes).

5.3 PROCEDURES AND DATA COLLECTION

Data used for respective study in this thesis are described in table 5.

5.3.1 Procedure study I

The principles of the public health nutrition practice bi-cycle was used as a planning method when designing the project (16). After the problem (low physical activity levels in individuals with type 2 diabetes) had been identified and discussed with health professionals the following steps followed in an intertwined manner: a search for evidence on the magnitude of the problem in Sweden and possible determinants; a thorough literature search on evidence based methods for physical activity promotion in type 2 diabetes care; and several design meetings were held within the research group and with a company providing a website for step-monitoring. The meetings led to a detailed project plan, approval from the board for medical ethics was obtained and funding was allocated. A pilot group including 14 participants started in April 2013, the trial was registered at ClinicalTrials.gov (NCT02374788) and the full study protocol was published in 2015. The CONSORT 2010 statement and the Declaration of Helsinki were followed when conducting the study protocol.

5.3.2 Procedure and data collection study II and IV

5.3.2. Baseline assessment and randomization

For study II and IV baseline data from the RCT Sophia Step Study was used. The study assessments took place at Husläkarmottagningen and Försäkringsmottagningen at Sophiahemmet (study II and IV) and Smedby hälsocentral (study II). All baseline assessments were performed by the diabetes specialist nurse, sometimes assisted by the project manager. At the baseline study visit the participants also meet a physician, who were responsible for excluding study participation. After the visit to the physician the participant was randomized to an intervention group by the use of sealed envelopes. A schedule for the two-year study assessments was handed out and times for the following appointments were booked.

5.3.2.2 Objective physical activity measures

At the study visit, an ActiGraph GT1M accelerometer, instructions for placement on the lower back and a paper-based diary to log wear time, was handed out whilst also instructed. At the following visits some participants were either asked to pick up the accelerometer at the reception when coming to leave blood sample or it was handed out during the visit. Participants were asked to hand in the accelerometer at the next visit, at the group session, to drop by to leave it at the reception, or they were given a prepaid envelope to send it back.

5.3.2.3 Blood samples

Fasting blood samples were collected at the laboratory at the respective health center. Participants were asked to leave blood samples a week prior to the appointment for each study assessment, to allow for the physician to have the results and appraise on possible exclusion before randomization. This also allowed for the diabetes specialist nurse to give feedback on the results at the following visits.

5.3.2.4 Anthropometrics, blood pressure, medication, comorbidity

The assessments that were made at the appointment with the diabetes specialist nurse included anthropometrics, resting blood pressure and questions about medications and health condition. Anthropometrics included sagittal abdominal diameter measured by Holstein Kahn (153), waist circumference measured by SECA 2 cm above the umbilicus (154), weight measured by Tanita (Model TBF 300A, Arlington Heights, IL), and height (at baseline assessment only). Blood pressure was measured with Omron M6 Comfort after 10 min rest in a seated position (155). Verification for comorbidity and medication in the medical record was made at baseline and changes thereof were asked for at the following visits. At each assessment it was also asked about regular strength training.

5.3.2.5 Questionnaire

An emailed questionnaire was sent by the project manager prior to each appointment and a reminder was sent automatically to participants who had not completed the questionnaire after two weeks. At the study visit the diabetes specialist nurse checked if the participant could access the questionnaire. If not, it was either emailed once more, or a paper-based version was handed out together with a prepaid envelop for return. Questions on dietary patterns were based on a food frequency questionnaire validated for Swedish populations (156). Sleep was assessed by a question on sleep quality.

5.3.2.6 Implementation and context

Study II was a process evaluation designed according to the Medical Research Council Guidance of process evaluation of complex interventions (12). Fidelity to the intervention protocol (study II) was checked continuously by meetings and emails between project staff and the diabetes specialist nurses. Issues with pedometers and the website were discussed and solved if possible. Implementation was also measured as dose received: attendance at individual consultations, attendance at group consultations, registration of steps and having an individual step goal. Numbers of study assessment visits were also tracked. The quality of the MI sessions and follow-up of FaR® were assessed by 1-10 point scales and short log with reflections on the consultations.

5.3.3 Procedure and data collection study III

Eligible participants that consented to be interviewed were booked by e-mail or telephone for a time and place for an individual face-to-face interview. An interview guide was developed in collaboration with the principal investigator, the author and an external researcher based on the study purpose, similar studies and experience from colleague researchers. Three pilot interviews with participants from respective intervention group were conducted and briefly analyzed, to allow for changes to the interview guide. No changes were deemed necessary and the pilot interviews were included in the later analysis. The interviews were conducted in a private room near the health care center by an experienced interviewer who was external to the study. All interviews were audio-recorded and transcribed verbatim.

Table 5. Methodological descriptions of the studies.

	Study I	Study II	Study III	Study IV
Aim	To describe the design, recruitment procedure, methodology and the theoretical framework for the physical activity promotion program Sophia Step Study.	To undertake a process evaluation to describe the implementation, context and physical activity behavior and health outcomes of the first 6 months in the Sophia Step Study.	To explore adhering participants' experiences after two years' study participation in the Sophia Step Study.	To investigate the potential associations of reallocating 30 min sedentary time in long bouts (>60 min) to sedentary time in non-bouts, LPA and MVPA with cardiometabolic risk factors in a population diagnosed with prediabetes or type 2 diabetes.
Design	Study protocol	Process evaluation of a randomized controlled trial	Qualitative interview study	Cross-sectional
Participants	Not applicable	159 individuals with prediabetes and type diabetes from health care centers at Sophiahemmet and Smedby health care center	18 individuals with prediabetes and type 2 diabetes from a health care center at Sophiahemmet	124 individuals with prediabetes and type 2 diabetes from health care centers at Sophiahemmet
Data-sampling	Not applicable	Field notes, attendance records, step registration, accelerometry, blood samples, anthropometry, questionnaire	Face-to face semi-structured individual interviews	Accelerometry, blood samples, anthropometry, questionnaire
Data	Not applicable	Age, gender, diagnose, intervention dose, steps, MVPA, LPA, SB, HbA_{1c}, fasting plasma glucose, triglycerides, HDL cholesterol, C-peptide, resting blood pressure, weight and sagittal abdominal diameter	Transcribed audio-recorded interviews	MVPA, LPA, sedentary time, breaks in SB, HbA1c, fasting plasma glucose, triglycerides, HDL cholesterol, C-peptide, resting blood pressure, weight and waist circumference
Analysis	Not applicable	Descriptive statistics, paired sample t-tests, linear mixed models	Manifest qualitative content analysis with an inductive approach	Descriptive statistics, multiple regression models

5.4 DATA PROCESSING

5.4.1 Quantitative data

5.4.1.1 Objectively measured physical activity

Data on physical activity and SB was collected using ActiGraph GT1M accelerometer (ActiGraph, Pensacola, FL) (58, 157). It was sampled at 10 hz and summarized over 1 minute. The data was downloaded using ActiLife v.6.13.1 software and underwent the following stages of data cleaning and extraction in both studies:

1. Wear time was validated towards participants' wear time log to decide on a cut-off for valid time the accelerometers were worn. For both studies >90 min with consecutive zero accelerometer counts was counted as non-wear time and was not used. During the 90 min, peaks of two minutes with nonzero counts were included, to allow for moving the accelerometer. This was in line with the validation study by Choi et al. on a population of older adults of similar age (158).

2. Next step was to decide on number of days and amount of time per day to include in the analysis. This is a critical step; we wanted to include as many participants as possible not to lose power, whilst capturing a valid picture of daily activities. The number of participants providing at least 9, 10 or 11 hours per day and 3, 4 or 5 valid days was summarized to check the amount with valid data. Based on this, only participants with ≥10 hours per day for at least 3 days were included in the analyses. This is a commonly applied cut-off point and validated to provide a decent picture of average daily activities (159).

3. Valid wear time was then divided into sedentary and physical activity intensity categories. Frequently used thresholds for SB, low LPA, high LPA, and MVPA were applied and correlation analyses were run. These samples showed that, to best separate physical activity intensities and categorize the data, the thresholds: <100 (cpm) for SB (152); LPA (100-1,951 cpm) and MVPA (≥1,952 cpm) (149) were applicable.

4. Sedentary time was further split into bouted (prolonged/uninterrupted) periods of sedentary time and non-bouted (interrupted) sedentary time. For study II three sets of data was prepared with sedentary time divided in bouted periods of sedentary time and non-bouted sedentary time (Figure 2). Bouted sedentary time was defined as > 60, > 40 and > 20 min bouts of < 100 cpm with allowance for breaks ≥100 cpm <1 min and non-bouted sedentary time as all other time ≤ 99 cpm.
In study IV the split of sedentary time was based on >30 min bouted periods of sedentary time and non-bouted sedentary time (≤30 min sedentary), hence bouted sedentary time was defined as >30 min bouts of <100 cpm with allowance for breaks ≥100 cpm <1 min and non-bouted sedentary time as all other time ≤ 99 cpm.

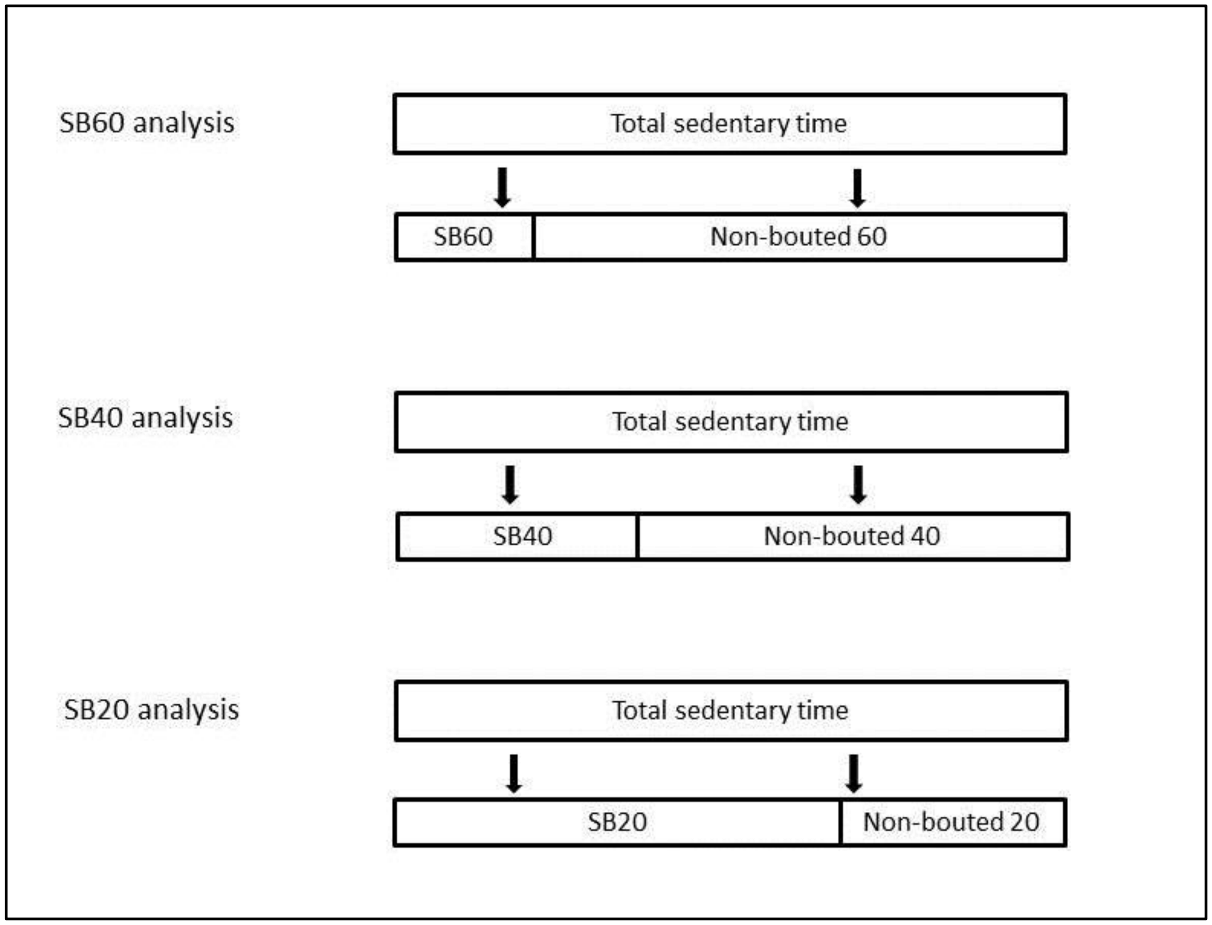

Figure 2. Description of how accelerometer measured sedentary time was divided in bouted time of length > 60 (SB60), > 40 (SB40) and > 20 (SB20) min and non-bouted sedentary time.

5.4.1.2 Blood samples

Blood samples were determined by following methods: HbA_{1c} with immunologic MonoS method, Unimate (Roche Diagnostics, Basel, Schweiz). Plasma glucose with a glucose oxidase method, triglycerides by enzymatic method, LDL and HDL by using a homogeneous method, Apolipoprotein-A1 and Apolipoprotein B by turbimetric method and C-peptide by immunometric method using two monoclonal antibodies and detection with electrochemiluminiscense using a Modular E system (Beckman Coulter, Inc.).

5.4.2 Qualitative data (study III)

The recorded interviews were transcribed verbatim by a separate researcher (not performing the interviews). Content analysis with an inductive approach was applied to analyze the transcribed interviews (142, 160). This was made by the interviewer who had not been involved in the intervention and was objective to the theoretical framework underpinning the intervention. In the first step the text material was sorted in units of analyses, separated by group allocation and interview question. The answers of each interview question were reduced to meaning units and summarized to condensed units and coded as illustrated by the examples in table 6. The codes were compared for their similarities and differences and abstracted into categories (160).

Table 6. Examples of how the answers were condensed from meaning-bearing units and coded.

Interviewer, question	Meaning-bearing unit	Condensed unit	Code
”*Could you tell us about your experiences from participating in the Sophia Step Study?”*	*” Yes, first of all, I'm excited that I took part in this study, and my experience is that we were weighed and that you have checked everything possible. Blood pressure and everything else. No, I feel as though I was in very good hands.”*	A positive description that a professional care provider was available. There has been confidence in the professionals who have closely monitored the study participants' physiological measurements.	Confidence in the study's recurrent (individual) health checks at the diabetes clinic.
"In what way do you think the pedometer has been supportive of your physical activity?"	*”I love my little measuring device (pedometer)! I would like to do at least 10,000 (steps) every day. Then, I actually have it (the pedometer) with me all the time; well, wait now, today I have only gone 7000 (steps). I have to go another round. So, it's clear there is a little competition with myself”*	A strong positive attitude to the step counter is recorded. The step counter has acted as a daily checker, a motivator, and is depicted as an aid to achieve the established physical goals.	A significant external resource towards a healthy physical activity level.
”Now that you have completed the study, what are your thoughts about participating in the Sophia Step Study?"	*”It has kept me on track, which I feel is natural, and I'm not going to break this pattern. I can break my legs, as one might say. No, but it has become a part of my daily routine. No, I do not intend to depart from this path."*	It describes an altered mind structure through participating in the study, and it establishes an attitude towards maintaining this new daily healthy living routine.	An attitude to maintain a healthy level of physical activity.

5.5 STATISTICAL ANALYSES

All statistical analyses were run using IBM SPSS version 23 or 24 (SPSS Inc., Chicago, IL).

5.5.1 Descriptive statistics and t-tests

In study II, III and IV descriptive statistics were applied to display the studied population groups. Independent sample t-tests and Chi square tests were applied to test between group differences and paired sample t-test to test within group differences (study II).

5.5.2 Covariate and correlation analysis

To rule out confounders to adjust for in the main analysis of study IV covariate analysis were run to test the correlations between the possible confounder and the studied health parameters. To avoid multicollinearity, correlation analyses were performed to study the correlations between physical activity intensities.

5.5.3 Multiple linear regressions

In study IV multiple regression analyses were applied to determine the associations between time in different activity behaviors and health parameters. The linear regression analyses were applied in steps. In all steps the analysis were controlled for wear time and age and for covariates if the covariate analysis showed a p-value < 0.2. In the first step, the single model, health associations of different behaviors were explored without controlling for time in other activity behavior. In the second analysis, partition model, health associations of different intensities were explored while controlling for time in the other activity behavior. In the third step, isotemporal substitution was applied. The health associations of different behavior were explored while controlling for substituting the time in one activity behavior with total time (Figure 3). This is modeling the “real life” situation as time is isotemporal (finite) (79).

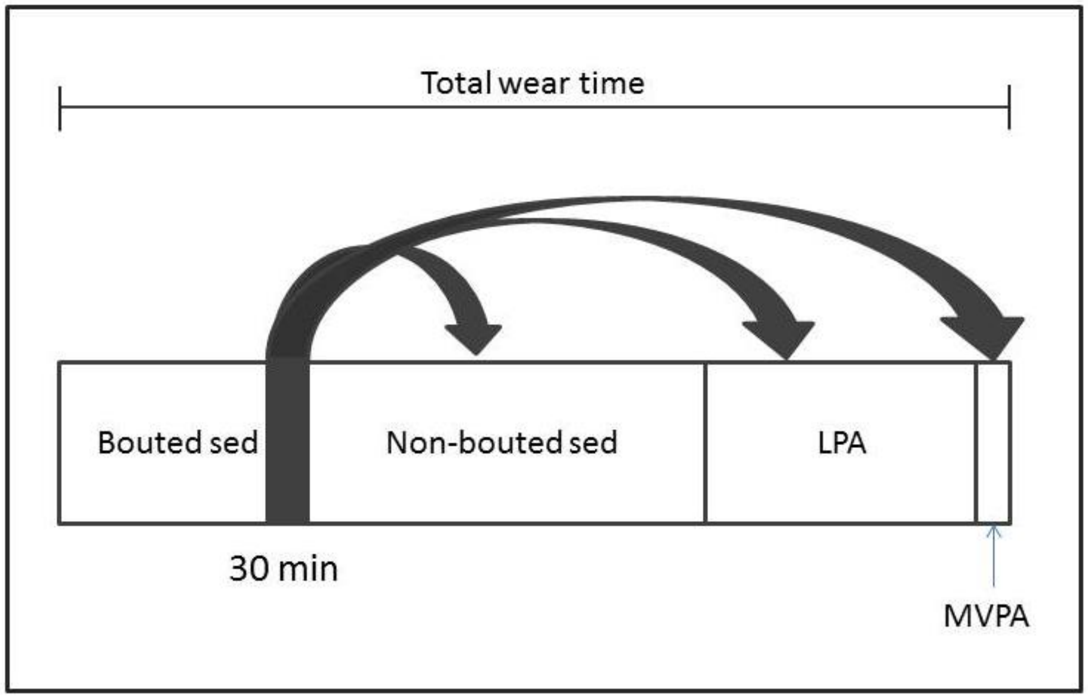

Figure 3. The isotemporal modeling of substituting 30 minutes in one activity behavior to another activity behavior.

5.5.4 Mixed linear regressions

In study II mixed linear regression models were applied to test the effects of belonging to respective intervention group on health outcomes and to estimate the effect of the predictors age, gender and diagnose (161).

5.6 ETHICAL CONSIDERATIONS

The Sophia Step Study was approved by the Regional Ethical Review Board in Stockholm, Sweden, 2012/1570-31/3 (study II, III and IV) and 2015/2075-32 (study III) and registered at Clinical Trials (NCT02374788). Participation was made on a voluntary basis, participants were informed written and orally about the projects and that they could resign participation without giving any reason. Informed consent was collected from all participants at baseline measurements (study II and IV) and at the interviews (study III). The ethical principles of the World Medical Association Declaration of Helsinki for medical research involving human subjects (2013) and Personuppgiftslagen (PUL) were followed assuring anonymity and confidentiality of the participants, and handling of data. After May 25th 2018 the General Data Protection Regulation was applied as a replacement for of PUL.

6 RESULTS

6.1 SUMMARY OF THE MAIN RESULTS

Study I was a study protocol that was not meant to provide experimental results. The outcome was an agreed protocol for an RCT. The planning process culminated in deciding: 1) a theoretical basis for the intervention, 2) intervention components, 3) primary and secondary outcomes, 4) evaluation methods and 5) number and time points for the study assessments. The logic underlying the Sophia Step Study, i.e. how the inputs and intended components should result in increased physical activity and cardiometabolic risk reduction is summarized in Figure 4. The figure also depicts the assumed mediators for effects and how mediators, physical activity outcome and cardiometabolic risk outcome should be evaluated.

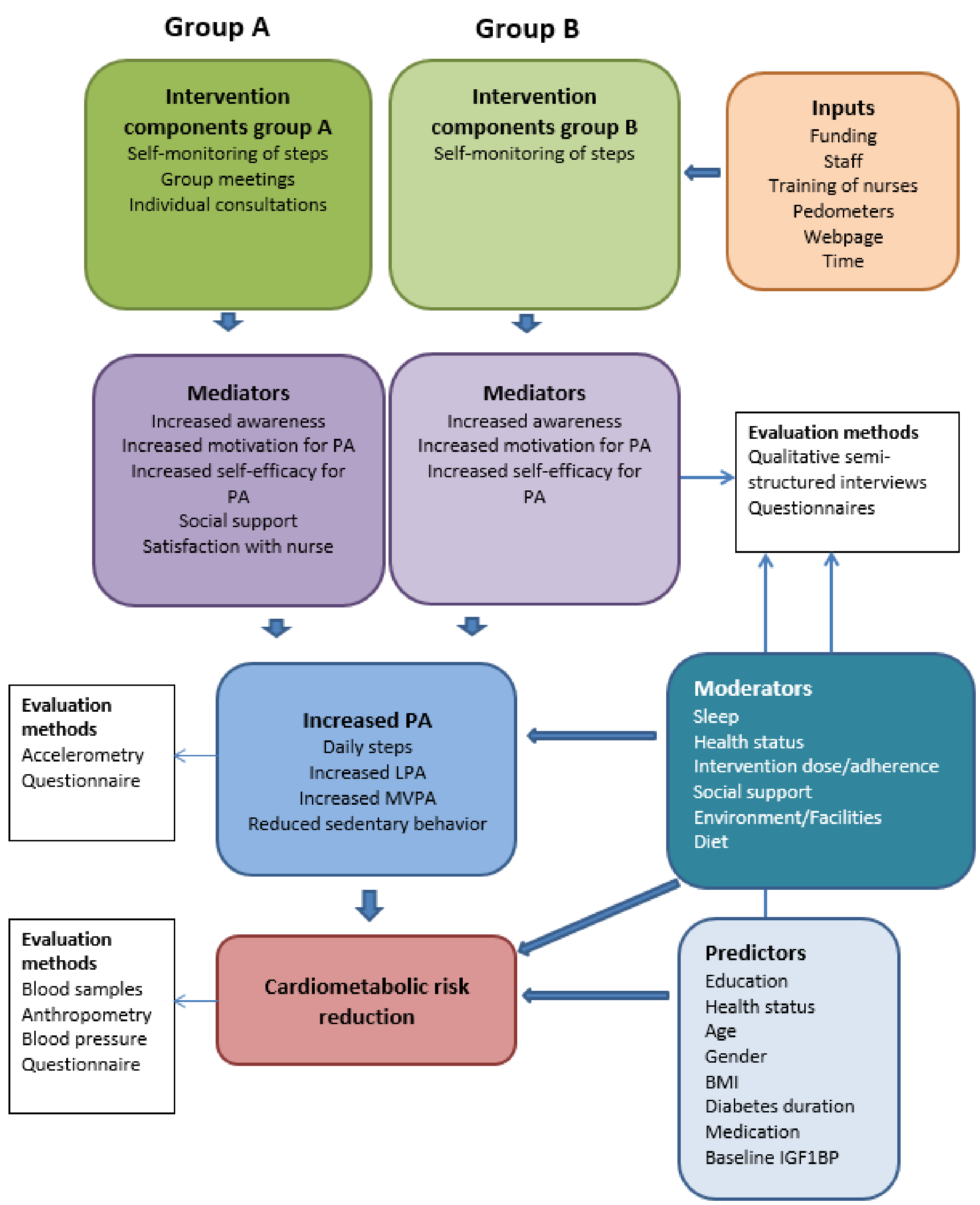

Figure 4. The logic underlying the Sophia Steps Study.

Study II showed that the interventions could be feasibly implemented in three primary care settings with high fidelity to the study protocol, a high grade of delivery and readily reaching those individuals that enrolled in the interventions. Between April 2013 and October 2016 159 participants were deemed eligible and consented to participate. The response rate was approximately 48%. The enrolled participants (mean age 64 years ±7.4 years, 24% prediabetes, 44% female, 55% university education and 71% living with a partner) were well-controlled in terms of their diabetes at baseline and baseline daily steps were 6757 ± 2955. Six months after the intervention, 68% of the participants in intervention group A reached the highest possible scores (9 and 10) for dose received. In intervention group B 84% reached the highest possible scores (3 and 4). The two intervention groups increased mean daily steps and the control group decreased mean daily steps. The study also demonstrated clinical feasibility of the intervention with the two intervention groups improving clinical variables while the controls showed mixed results.

Study III was a qualitative study, based on interviews with participants who adhered to their respective intervention protocols: 7 participants from group A, 6 from group B and 5 from group C. The study resulted in two main categories and five subcategories illustrating the participants' experiences of taking part in the Sophia Step Study (Figure 5). The two main categories were "Professional management" and "An internal journey". The participants were grateful to take part in a research study that seemed to be exclusively designed for them. The health check-ups were described as personalized, with positive reinforcement that resulted in a sense of being watched over. The participants described the pedometers, the group sessions and the health check-ups as resources that motivated them to become physically active. The individual and group consultations were in a personal and friendly style that provided emotional support through an open and honest sharing of experiences and struggles. Being part of the study was described as a personal cognitive process. Study participation led to a heightened awareness of physical activity and increased motivation to be physically active. Strategies to implement new daily routines for physical activity and to overcome barriers to be physical active were established during the course of the study. The participants reported some problems and concerns, including pedometers lacking reliability, other participants talking too much during group consultations, not performing as expected or desired, and concerns over other participants not reporting steps as expected.

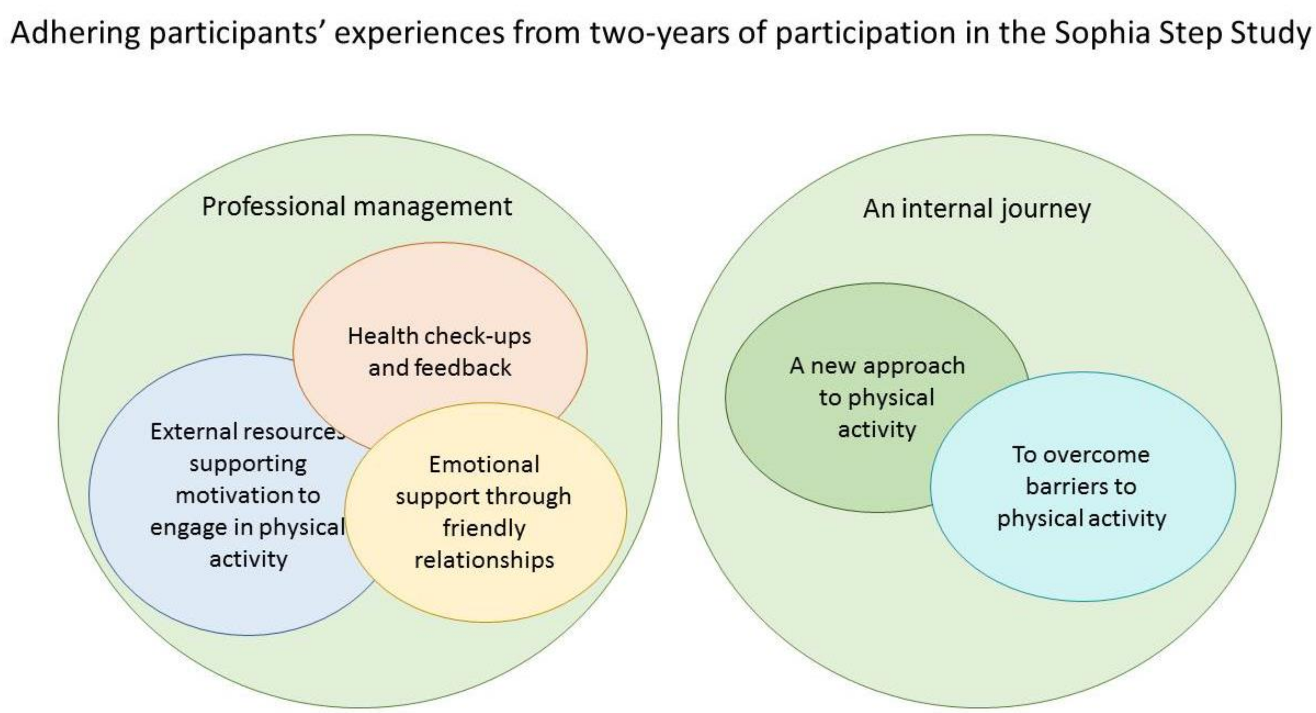

Figure 5. Content analysis resulted in two main categories and five sub-categories.

Study IV demonstrated that modeling substitution of 30 min in the form of objectively measured time from SB in bouts >60 min to MVPA was beneficially associated with BMI (b = -1.46 95% confidence interval (CI): -2.60, -0.33 kg/m^2), waist circumference (b = -4.30 95% CI: -7.23, -1.38 cm), and HDL cholesterol (b = 0.11 95% CI: 0.02, 0.21 mmol/l) in individuals with prediabetes and type 2 diabetes. The associations were of similar size for the 60 min sedentary bout and sedentary non-bout time (interrupted sitting). There were no statistically significant health benefits observed in reallocating time from long-bout sedentary time to non-bout sedentary time. The same associations were observed when sedentary time was in bouts of >40, and >20 min, with the addition that reallocating time from LPA to MVPA was associated with lower waist circumference, lower BMI and higher HDL cholesterol.

Intervention group A participants walking during a group session.

6.2 STUDY POPULATION AND CONTEXT

Three samples of the population with prediabetes and type 2 diabetes were used in this thesis. Table 7 lists demographics of the three samples and, for comparison, from the Swedish National Diabetes Register. For most variables the three samples show similar patterns in the three samples. Study II included participants from Smedby, whereas study III and IV only included participants that were recruited at Sophiahemmet. The sample in study II had a somewhat lower number of persons with university education.

Table 7. Demographics of the three study samples and from the Swedish National Diabetes Register.

Baseline variable	**Study II** **Process evaluation**	**Study III** **Qualitative**	**Study IV** **Cross-sectional**	**National Diabetes Register**[1]
n	159	18	124	371148
Age, years	64.4 (7.4)	66.6 (4.5)	63.8 (7.5)	68.5
Female, %	44%	38.9%	50%	
Prediabetes, %	25%	27.8%	27%	
Diabetes duration[1], years	8.4 (6.0)	9.5 (7.4)	7.8 (5.2)	
Daily smoker	6%	6%	5%	
University education	49 %	50%	60%	
Living with partner	71%	66.7%	70%	
HbA_{1c}, IFCC mmol/L, all	49 (11)	51 (14)	48 (11)	
HbA_{1c}, type 2 diabetes participants	52 (11)	56 (13)	52 (11)	54 (53.4–53.8)
Fasting glucose, mmol/l	7.8 (1.9)	7.4 (1.8)	7.4 (1.6)	
C-Peptide, nmol/L	1.1 (0.4)	0.9 (0.4)	1.1 (0.8)	
HDL cholesterol, mmol/L	1.4 (0.4)	1.4 (0.4)	1.4 (0.4)	
LDL cholesterol, mmol/L	2.9 (1.0)	3.1 (0.9)	3.0 (1.0)	2.6 (2.6–2.6)
Triglycerides, mmol/L	1.7 (0.8)	1.9 (1.1)	1.7 (0.9)	
Body mass index, kg/m^2	29.9 (4.4)	29.2 (4.6)	29.7 (4.6)	29.9 (29.8–30.0)
Waist circumference, men, cm	107.0 (10.3)	110.2 (14.0)	108.0 (11.3)	
Waist circumference, women, cm	99.3 (12.5)	91.3 (14.5)	99.3 (12.8)	
Sagittal abdominal diameter, cm	24.2 (3.4)	23.5 (4.2)	23.7 (3.3)	
Systolic blood pressure, mmHg	132.6 (15.2)	131.4 (15.6)	130.6 (15.1)	134.2 (133.8–134.6)
Diastolic blood pressure, mmHg	83.5 (9.3)	80.4 (9.0)	83.1 (9.3)	76.6 (76.3–76.9)

Table 8 shows physical activity and dietary patterns for baseline values of the three samples and table 9 lists medical treatment and comorbidities if the three samples.

Table 8. Physical activity and dietary patterns of the three samples.

Baseline variable	**Study II Process evaluation**	**Study III Qualitative**	**Study IV Cross-sectional**
Accelerometer wear time, min/day	833 (79)	847 (54)	834 (80)
Steps/day	6757 (2955)	7099 (2225)	7169 (2948)
> 5000 steps/day	68%	76.5%	74%
> 7100 steps/day	42%	52.9%	48.2%
Moderate to vigorous intensity physical activity[5]	31.1 (23.7)	32.8 (17.3)	34.1 (24.1)
Time in MVPA bouts, min/day[2]	14.9 (17.2)	13.3 (12.0)	16.2 (17.3)
Light physical activity, min/day[1]	222.5 (63.1)	229.8 (47.4)	224.4 (63.1)
Total sedentary time, min/day[1]	579.0 (84.4)	684.7 (86.6)	576.1 (82.0)
Time in sedentary bouts min/day[3]	273.3 (103.1)	277.8 (101.1)	263.6 (96.6)
> 22 min MVPA/day	56%	64.3%	66.4%
Vegetables, daily servings	1.5 (1.0)	1.7 (1.3)	1.6 (1.0)
Percentage whole wheat bread of consumed bread	80 (31)	80 (30)	80 (30)
Cooking fat quality, mostly butter	28%	33.3%	29%

The table presents mean (standard deviation), or proportion (%).
[1]Total accumulated min/day (> 1 min), thresholds for physical activity intensity are <100 counts/min for sedentary (SB), 100 to 1951 counts/min for light intensity physical activity (LPA) and >1952 counts/min for moderate to vigorous physical activity (MVPA).
[2] Bouts of >10 min duration of moderate to vigorous physical activity.
[3] Sedentary time was divided into 30 min sedentary bouts and other sedentary time.

Table 9. Medical treatment and comorbidities of the three samples.

Baseline variable	Study II Process evaluation	Study II Qualitative	Study IV Cross-sectional
Insulin	13%	11%	8%
Sulfonylurea	15%	28%	13%
Metformin	56%	50%	57%
Other anti-diabetic drugs	9%	0 %	12%
Statins	55%	56%	66%
Beta-blocker	23%	18%	23%
ARB or ACE medication	51%	66.7%	46%
Hypertension	75%	94%	73%
Hyperlipidemia	76%	89%	76%
Other CVD	28%	22%	24%
COPD	10%	6%	18%
Inflammatory diseases	5%	6%	4%
Cancer in past 5 years	6%	11%	7%
Other disease	22%	6%	21%

6.3 INTERVENTION DESIGN (study I)

6.3.1 Theoretical framework

Sophia Step Study was set-up as a three-armed RCT, randomizing the participants into either a multi-component intervention group (A), a single component intervention group (B) or a control group (C) (Figure 6). The multicomponent intervention (A) consisted of individual consultations, group meetings and self-monitoring of steps. The single component intervention (B) consisted of self-monitoring of steps, and group C served as a control group. Interventions A and B were theory-based and applied several BCTs intended to facilitate behavior change (124). The intervention was grounded on three theoretical models for behavior change: stage of change theory (120), health belief model (119) and social cognitive theory (121). From each of the respective theory several BCTs were assumed to be applied by the intervention components. Figure 6 illustrates how the initial ideas, backed with scientific evidence, previous experience and discussions resulted in three intervention components and the BCTs from respective theory.

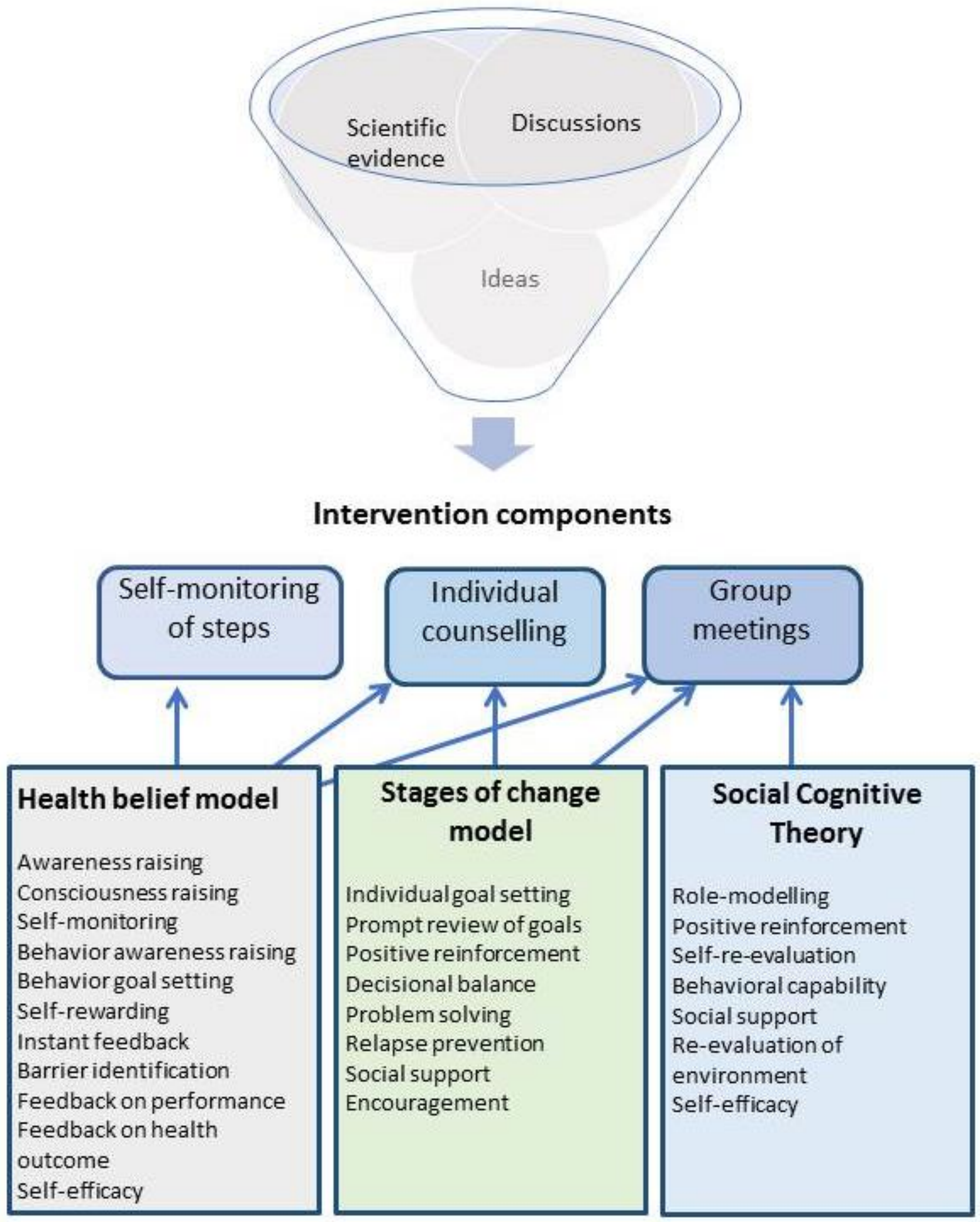

Figure 6. The theoretical foundation of the Sophia Step Study illustrating the intervention components and how they relate to the theoretical models and BCTs.

6.3.2 Intervention components, study assessments and outcomes

6.3.2.1 Self-monitoring of steps

Participants in group A and B were offered a pedometer (model Yamax Digiwalker SW 200) (Figure 7). The participants were given the pedometer together with a diary and instructions on how to log in to the webpage (www.steg.se) to register steps. The webpage contained features such as a voluntary individual goal setting, feedback on performance compared with the individual goal and to a “healthy goal” of 7000 steps/day, graphical summaries of the own steps, distance walked and calories burned over a week, average steps over the calendar year, total distance walked on a simulated map and social comparison (anonymously participants saw a total summary of the performance of other participants in the same group and their position in a ranking of total steps). Figure 7 describes a diagram over a participant’s steps during 1-year period.

Figure 7. The pedometer model Yamax 200 and an example of graphical feedback from the webpage were offered to all participants in group A and B.

6.3.2.2. Individual consultations

In total 10 individual consultations during two years were offered. These consultations were planned to take from 45 to 60 min. They were based on MI (95) in the sense that the diabetes specialist nurses were trained in using the method. Step performance and the outcomes from the health assessments served as a basis for the consultations. The diabetes specialist nurses were familiar with the FaR® method (physical activity on prescription) and were asked to apply this method and to follow-up whenever a prescription was outlined.

6.3.2.3 Group meetings

The group session program in Sophia Step Study was inspired by the IMAGE Toolkit, which was based on evidence-based guidelines and curriculum developed by a large EU funded collaborating project (the IMAGE project) (162). A program for the group session was planned and tested in a pilot sample. At the first group session the individuals were given a handbook for an individual action plan and information about the risk of hypoglycemia that could occur during physical activity. The group sessions started with a walk for 20-30 min and were then continued in a small room with a round table. The first sessions started with information about the benefits of physical activity and behavior change and the group leader asking open questions. Subsequently the group sessions progressed with the participants describing the status of their behavior change. Throughout the session, the participants were given time to discuss and ask questions while at the same time the group leader was structuring and managing the core content. The second session consisted of instructions for Nordic walking, correct technique for walking was instructed and practiced. The fourth session took place at a gym, where instructions were given and the participants practiced a home-based program for strength training. The strength training program was developed in collaboration with a personal trainer and a physiotherapist. In total 12 group meetings were offered over 2 years.

6.3.2.4 Control setting

The participants in the control group were given standard care, except for taking part in a research study. The controls came regularly for study assessments, received feedback on health outcomes and were asked to fill out a questionnaire on five separate occasions. At the last assessments, they were asked if they had used a pedometer or any other activity tracker in the past 2 years.

6.3.2.4 Study duration, assessment frequency and outcome

Intervention duration was 2 years, with more intense support during the first 6 months of the intervention and focus on maintenance thereafter. Primary outcome was HbA_{1c} and secondary outcomes included steps, MVPA and a number of cardiometabolic biomarkers and anthropometric parameters. Study assessments were performed at week 8, 12, 16 and month 6, 12, 18 and 24.

6.4 IMPLEMENTATION OF SOPHIA STEP STUDY (study II and III)

6.4.1 Fidelity, delivery and reach

The process evaluation followed a framework to structure the procedure in which the reporting included context, fidelity, delivery, adaptations and reach. The results from the process evaluation of the first 6 months of implementation of the Sophia Step Study are outlined in Table 10. The context of the Sophia Steps Study is described in terms of a description of the study population in section 6.2.

Table 10. Process evaluation features and results for each intervention component.

Implementation feature	Intervention component			
	Pedometer + website	**Individual MI consultations**	**FaR®**	**Group consultations**
What was delivered	Delivered as planned	Delivered as planned	Applied occasionally	Delivered as planned
Notes	Some issues with the pedometers and usernames to the website occurred. If a pedometer did not work correctly a new device was given or mailed. Some participants chose to use other activity trackers.	The nurses reported some difficulty focusing on physical activity.	The diabetes specialist nurses felt that applying FaR® was not necessary, because the method was overlapping with MI and an application of a step goal	
Who delivered	Diabetes specialist nurses distributed out the pedometers, instructions and usernames for the website.	Diabetes specialist nurses introduced in the theoretical models and trained in MI.	Diabetes specialist nurses trained in the FaR® method.	The group meetings were led by a project staff at Sophiahemmet and a diabetes specialist nurse at the rural primary care center.

	Pedometer + website	Individual MI consultations	FaR®	Group consultations
Dose delivered	6 months step-registration	4 consultations	Data missing	5-6 group sessions
Notes	Reminders were sent every 6 weeks by text messages to participants who had not registered their steps onto the webpage for the past 6 weeks. Pedometers that did not seem to work properly were replaced. Some participants chose to use another activity tracker for step counting. Problems with lost passwords and browsers were solved.	Individual consultations were offered to all group A participants within ± 2 weeks from the scheduled week. The nurses were generous by offering to reschedule the appointments to suit the participant. The quality of the MI talks was not possible to evaluate.	Prescriptions were not logged to the extent that made it possible to evaluate.	One group session was cancelled for the group from the insurance clinic, because of too few participants. Fewer participants than expected came to the group sessions, otherwise the sessions followed the intended program. The discussions were structured by content but shaped by the individuals in the respective groups.
Dose received ***Group A***	89 % registered steps on >67% of the possible days; 84 % had a step goal.	89 % came to all four individual consultations; 9 % came to three individual consultations.	Data missing	72 % came to at least four (or three in the case of the insurance clinic) group sessions.
Group B	96 % registered steps on >67% of the possible days; 71 % had a step goal.	84 % came to all four study assessments; 13 % came to three study assessments.	Not applicable	Not applicable
Group C		80 % came to all four study assessments; 13 % came to three study assessments.	Not applicable	Not applicable

6.4.2 Mechanisms of impact

The possible mechanisms of impact were studied indirectly in study III by exploring the experiences of participating in a research study. Participants adhering to the 2-year interventions and the control group protocol repeatedly described many of the intended BCTs during the interviews. This is illustrated by some examples of the participants' remarks about the study participation in figure 8.

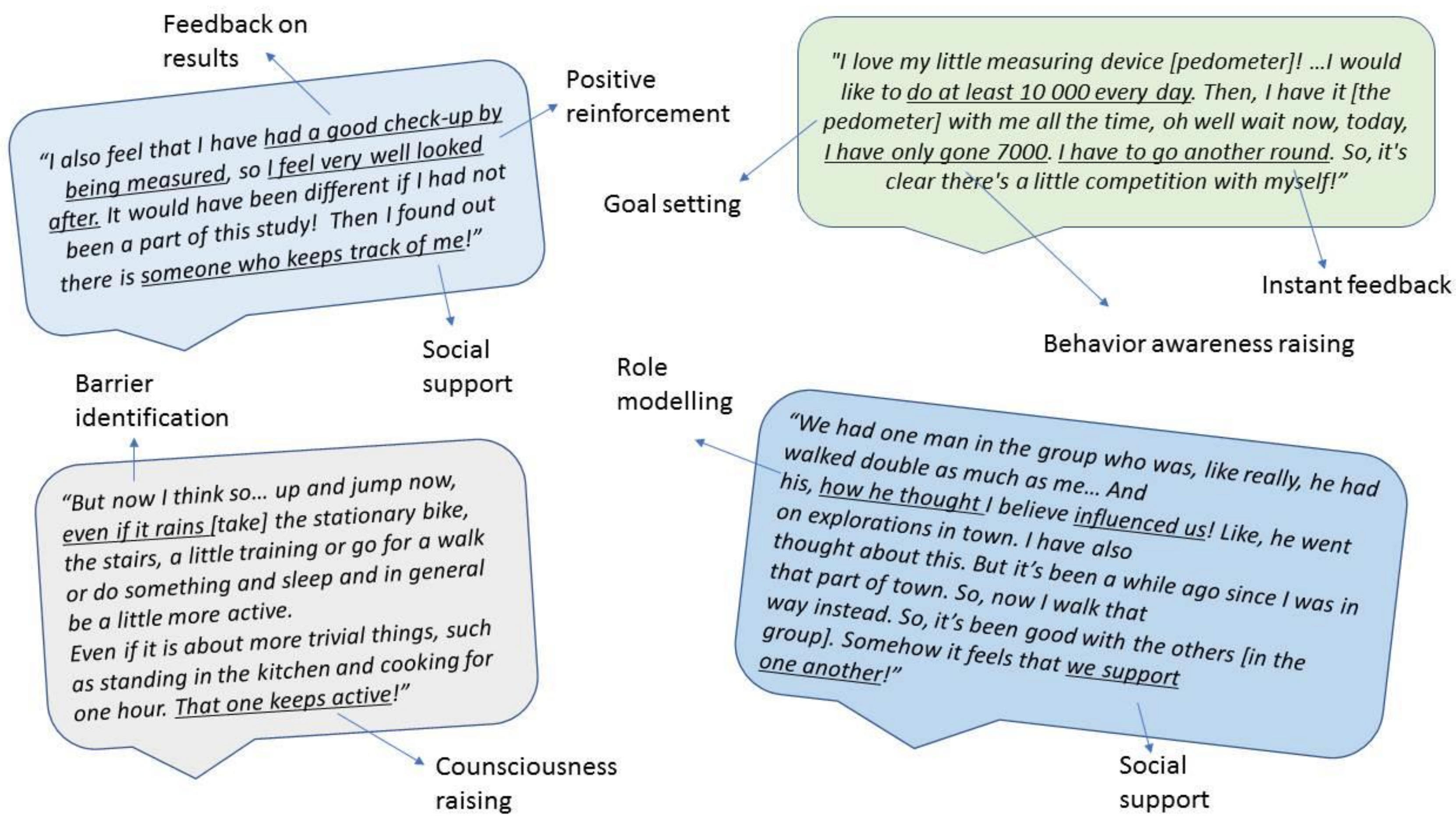

Figure 8. Participants' quotations and examples of the BCTs mentioned by the participants'.

The qualitative analysis was performed using an inductive approach. In a process evaluation it is of interest to explore whether the intervention components and mechanisms were applied. In an ad hoc application of a deductive approach (not included in the manuscript), the results from study III were compared with the intended BCTs. Figure 9 displays the BCTs that were intended to be applied in the Sophia Step Study, the experiences that were reported by the interviewed participants in study III and the BCTs evaluated as implemented in an ad hoc analysis.

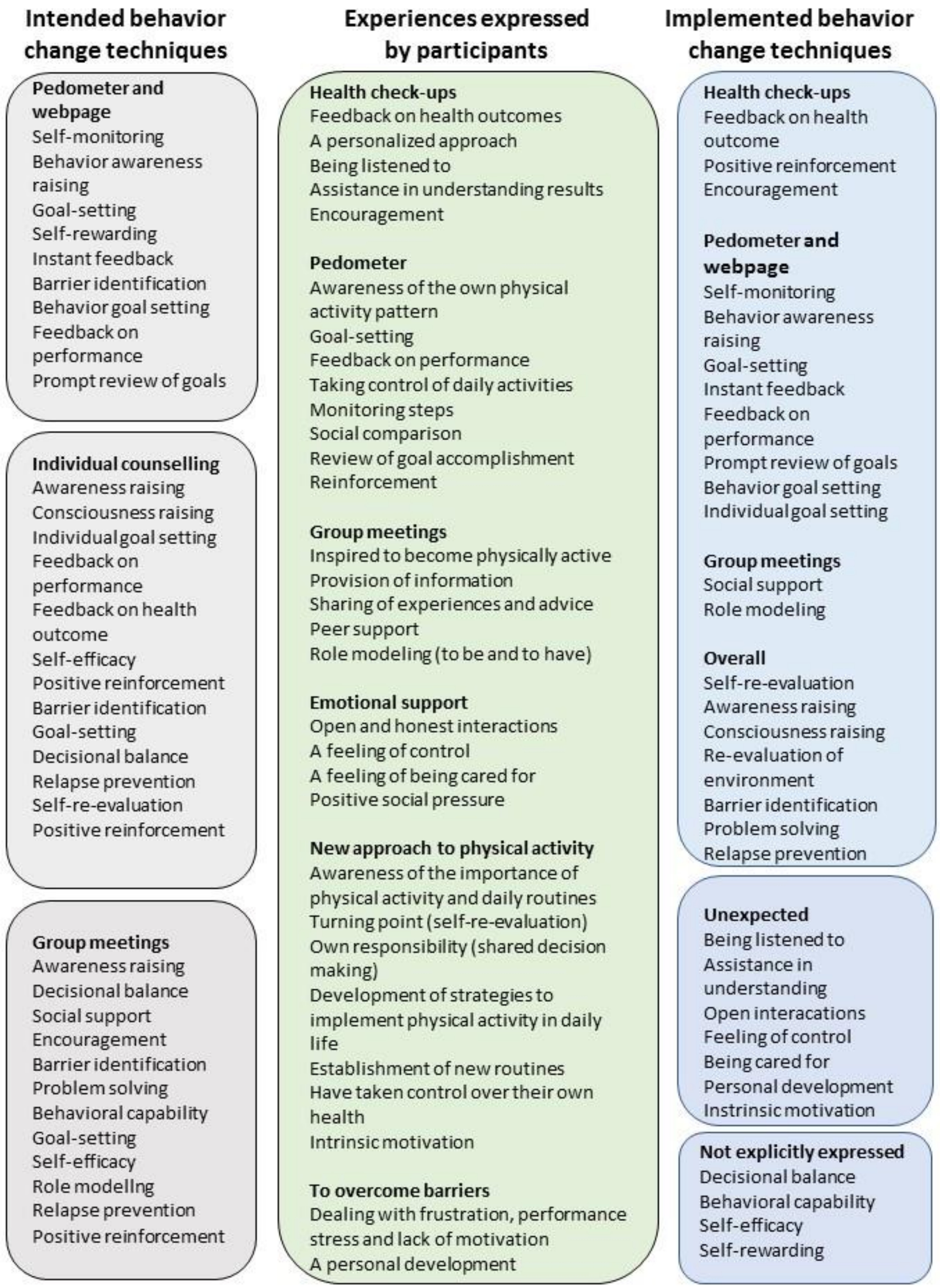

Figure 9. The intended BCTs (first column), participants' expressed experiences (middle column) and implemented BCTs (last column).

6.5 PHYSICAL ACTIVITY BEHAVIOR AND HEALTH OUTCOMES (study II)

6.5.1 Changes in physical activity behavior

After 6 months of intervention, the trends favor the two intervention groups (A and B) regarding physical activity measures. Mean (CI) change in number of daily steps was 1097 (232, 1962) in group A, 1242 (313, 2171) in group B and -457 (-1164, 250) in group C. Mean (CI) change in MVPA was 6.1 (-0.0, 12.2), 7.4 (-0.9, 15.6) and -6.3 (-11.2, -1.5) min per day in group A, B and C respectively. Time spent sedentary changed with mean (CI) -0.3 (-27.0, 26.5), -7.8 (-21.8, 6.1), and 14.4 (-17.0, 45.8) min per day respectively. Figure 10 shows the percentage in each group reaching the recommended levels of steps and MVPA at baseline and after 6 months post intervention.

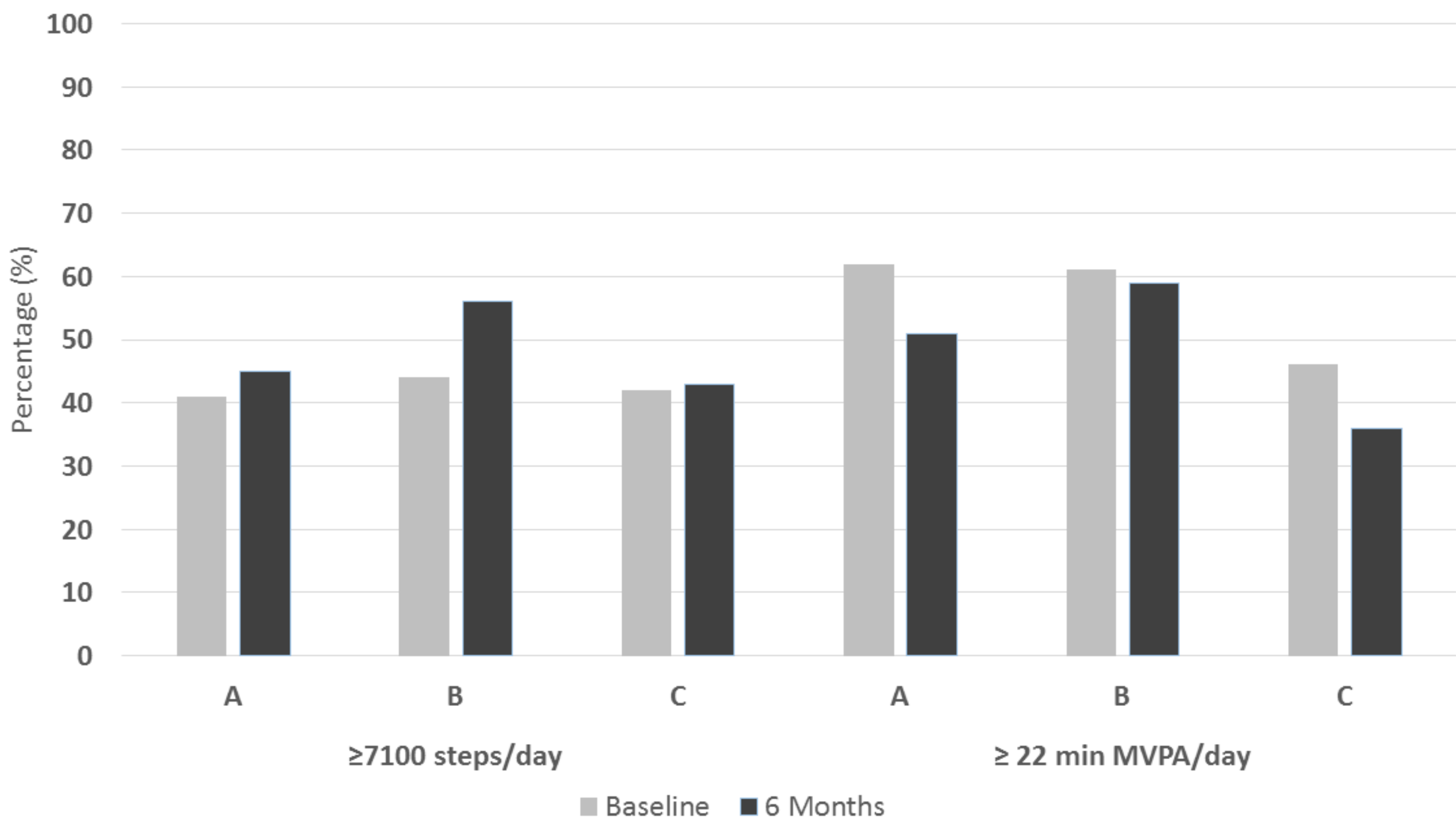

Figure 10. The percentage in each of the three groups reaching recommended daily levels of steps and MVPA at baseline and after 6 months of intervention.

6.5.2 Changes in clinical biomarkers

Mean (CI) change in HbA_{1c} was -2.32 (-4.65, 0.01) in group A, -0.93 (-2.60, 0.75) in group B and -1.44 (-3.47, 0.58) in group C. Figure 11 displays the trends for several cardiometabolic risk factors up to 6 months intervention.

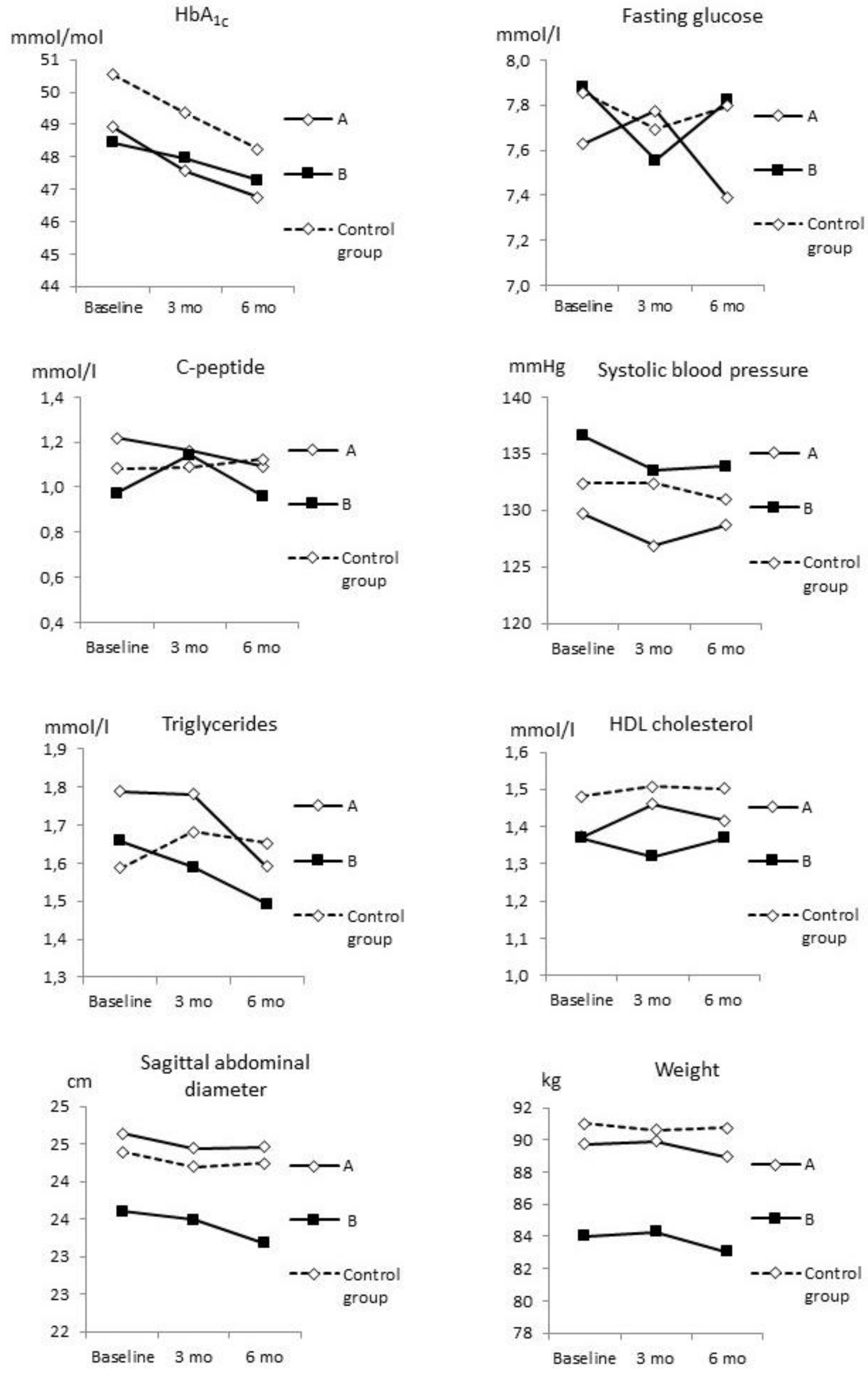

Figure 11. Clinical variables at baseline, 3 months and 6 months for respective group.

6.5.3 Between group differences

In study II between group differences at 6 months of intervention were analyzed using linear mixed models. To obtain the effects of gender, diagnosis and age stratified linear mixed models were run for these predictors. Forest plots for the total sample and the stratified analyses are presented for selected outcome variables in Figure 12 and 13.

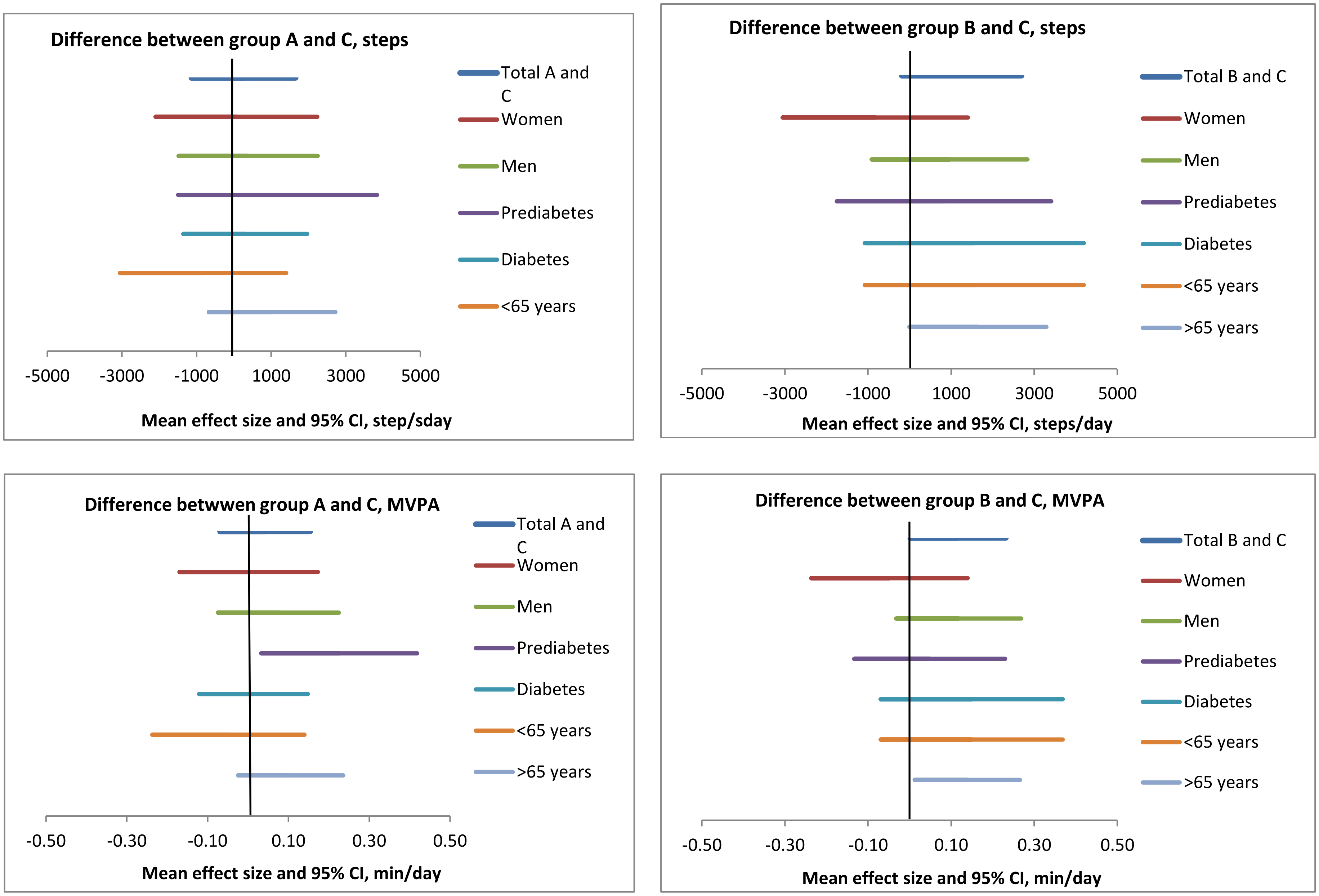

Figure 12. Confidence intervals for mean effect size for between-group differences in the total sample and when stratified by gender, diagnosis and age.

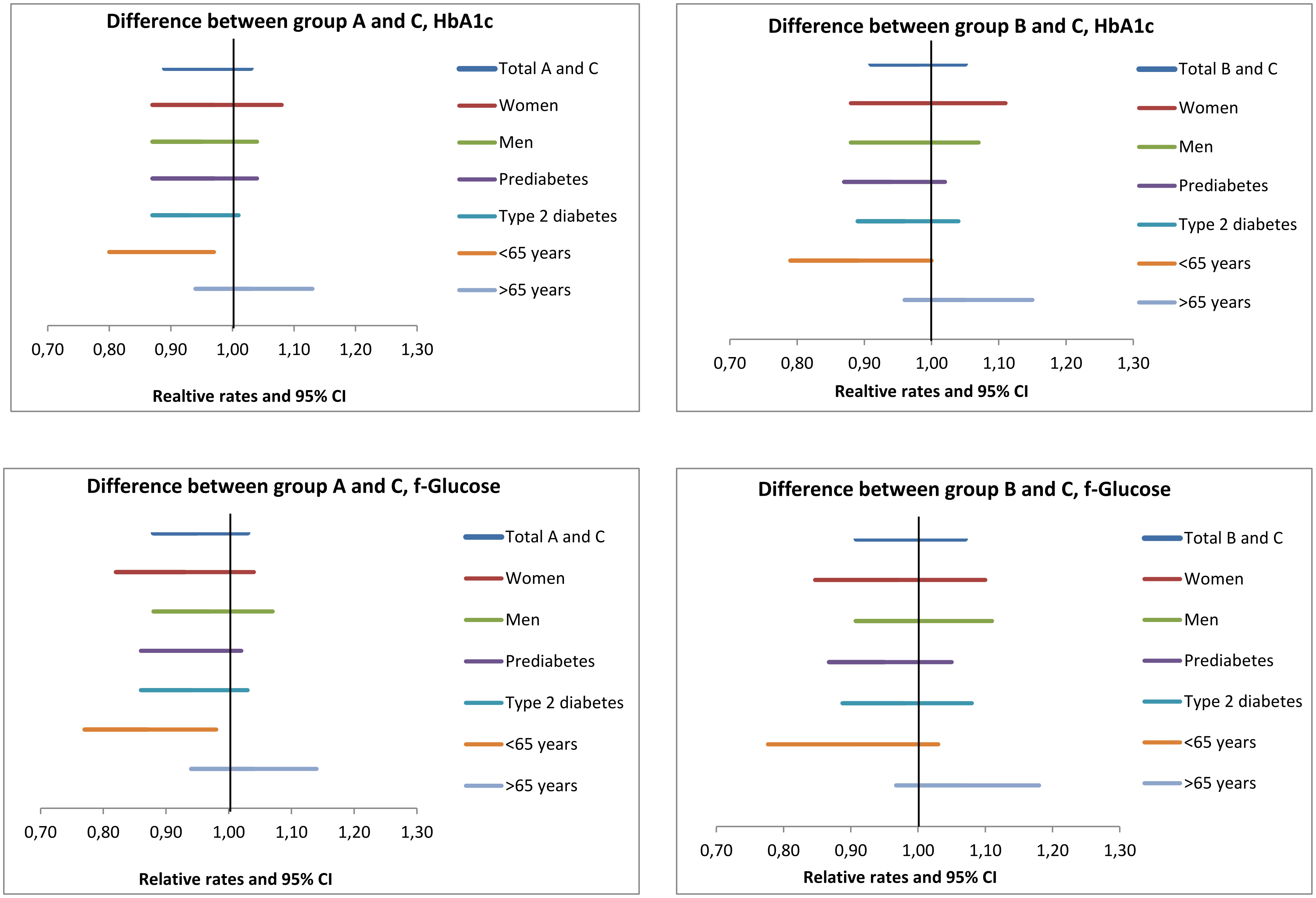

Figure 13. Confidence intervals for relative rate for between-group differences in the total sample and when stratified by gender, diagnosis and age.

6.6 HEALTH ASSOCIATIONS OF SEDENTARY TIME IN VARIOUS BOUT LENGHTS AND PHYSICAL ACTIVITY OF LIGHT AND MODERATE TO VIGOROUS INTENSITY (study IV)

Study IV investigated the health associations of substituting prolonged sedentary time by modeling reallocation of sedentary time with time in other activity intensities, including interrupted sedentary time.

In study IV the results of sedentary time in 60 min bouts were displayed and discussed. It is unknown when breaks in sedentary time should be taken and secondary analyses with sedentary time in bouts of 20 and 40 min were therefore performed. The purpose was to investigate the health associations of taking breaks after sitting in 60-, 40- and 20 min intervals. The results from these analyses were provided as supplements in the manuscript. Here, the results from the partition and isotemporal analyses for all three subsets of sedentary time are presented for the three health outcomes (HDL, BMI and waist circumference).

6.6.1 Health associations of sedentary time and physical activity

In the single model, in which no adjustments were made for time in other activities, statistically significant ($p<0.05$) detrimental associations were found for total sedentary time and HDL, waist circumference and BMI. MVPA was beneficially associated with HDL, waist circumference and BMI. For LPA and sedentary time split in bouts and non-bouts the results were mixed and for the other outcome variables the effects were small or non-significant.

In the partition model adjustments were made for time in other activities. The negative health effects of sedentary time remained, but the effects were no longer statistically significant ($p<0.05$). In contrast, the beneficial associations of 30 min of MVPA with higher HDL, lower waist circumference and lower BMI were strengthened, with statistically significant results remaining for all three variables. Figure 14, 15 and 16 displays the regression coefficients from the partition model for HDL, waist circumference and BMI, respectively. Although small, there was a tendency with negative associations for sedentary time in bouts with HbA_{1c} (relative rate 1.02), and positive associations of sedentary time in non-bouts with fasting plasma glucose (relative rate 0.98) (not shown).

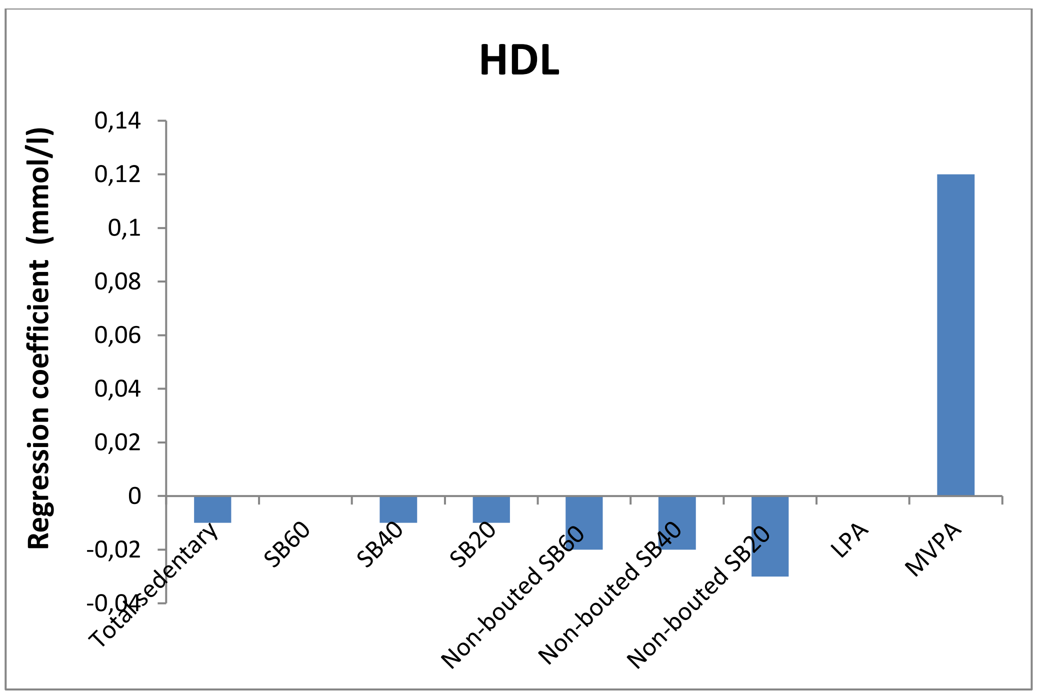

Figure 14. Associations of sedentary and physical activity time with HDLcholesterol, adjusted for time in other activities.

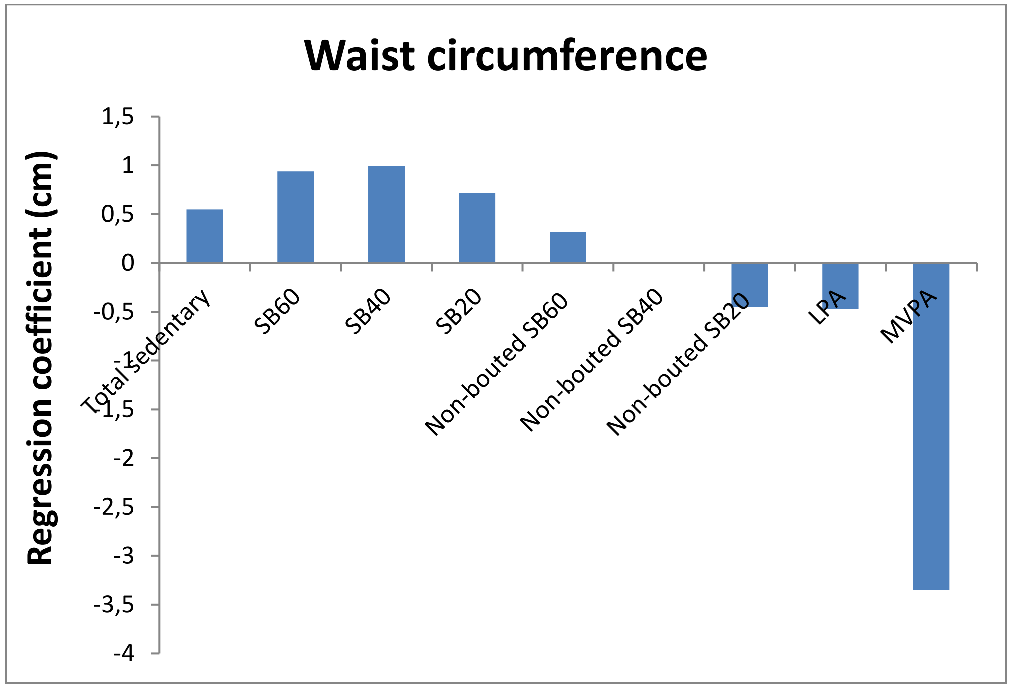

Figure 15. Associations of sedentary and physical activity time with waist circumference, adjusted for time in other activities.

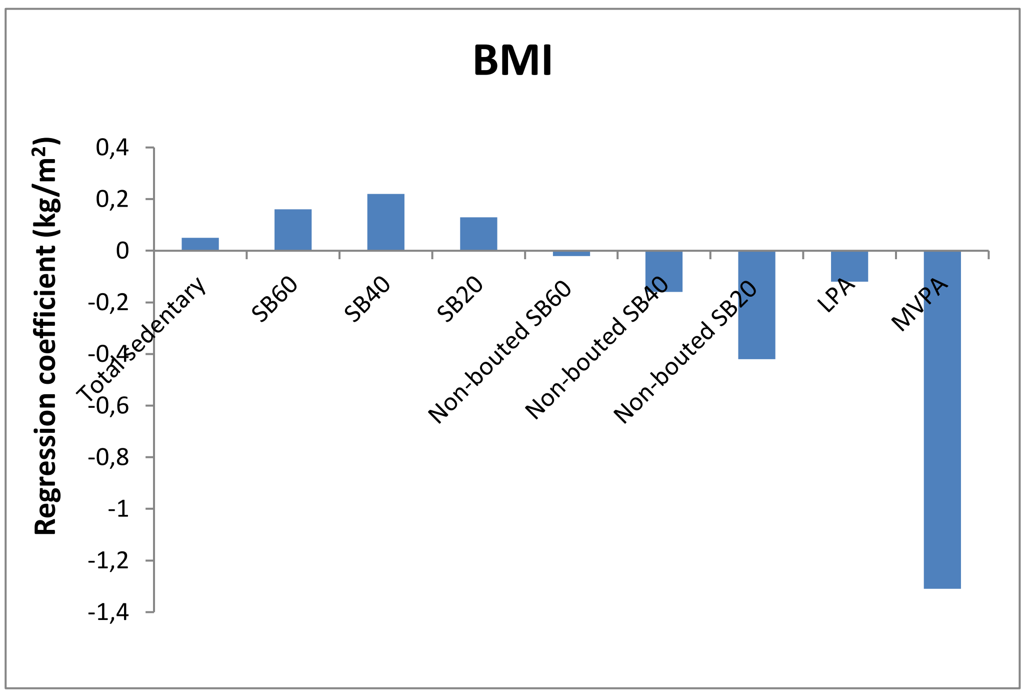

Figure 16. Associations of sedentary and physical activity time with BMI, adjusted for time in other activities.

6.6.2 Health associations of sedentary time and physical activity adjusted for substituted activity

By modeling reallocation of 30 min sedentary time to MVPA (isotemporal model) the beneficial associations from the partition model with higher HDL, lower waist circumference and lower BMI were even stronger. The same associations were observed when sedentary bout time was > 60 -, > 40- and > 20 min (Figure 17, 18 and 19). No associations were seen for HbA_{1c} and fasting glucose.

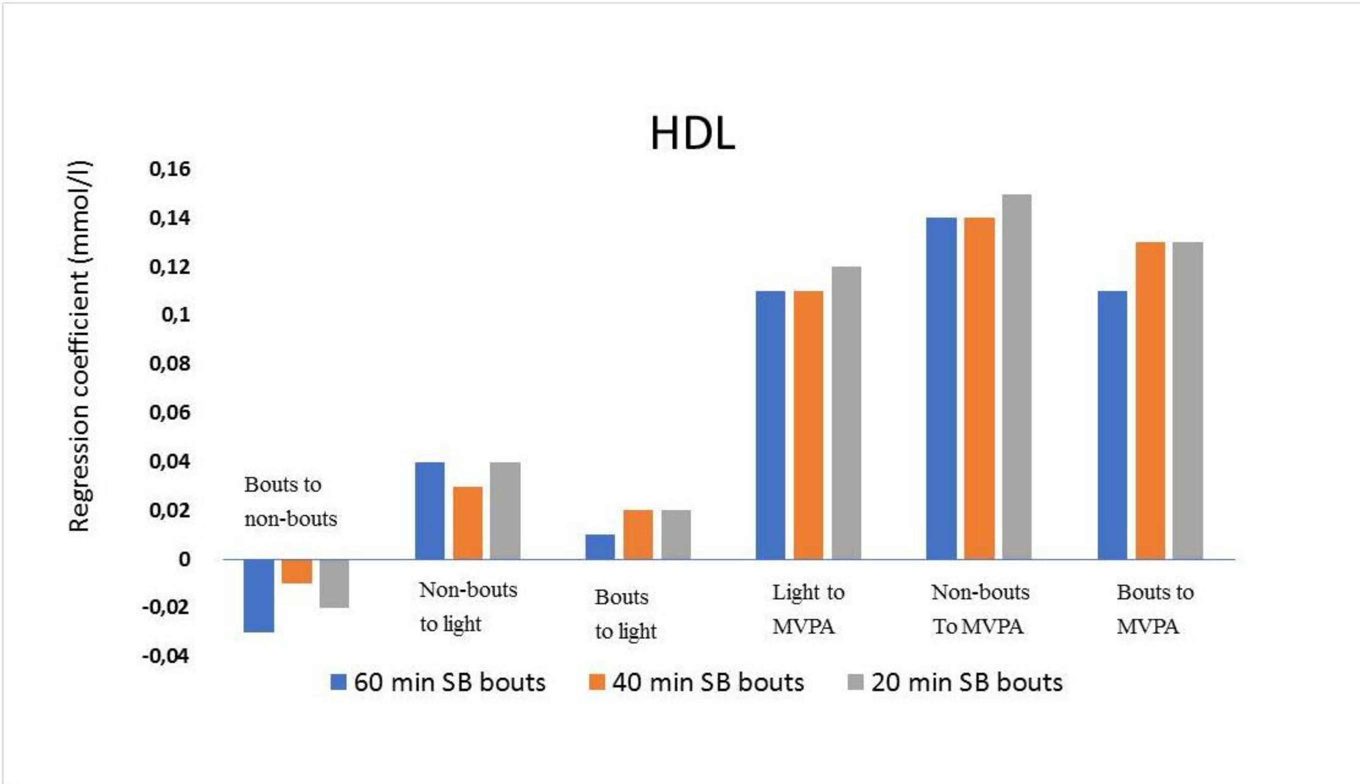

Figure 17. Effects on HDL cholesterol of reallocating 30 min from one sedentary or physically active behavior to another.

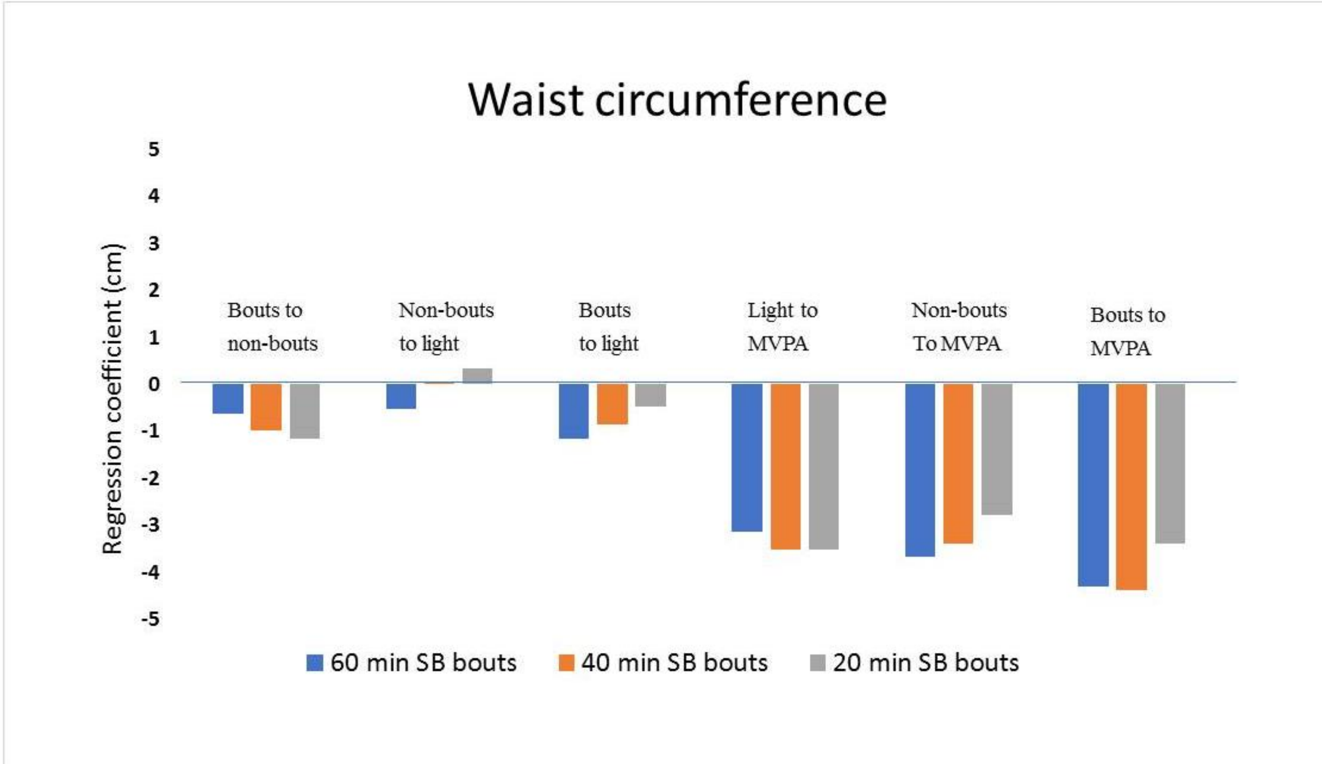

Figure 18. Effects on waist circumference of reallocating 30 min from one sedentary or physically active behavior to another.

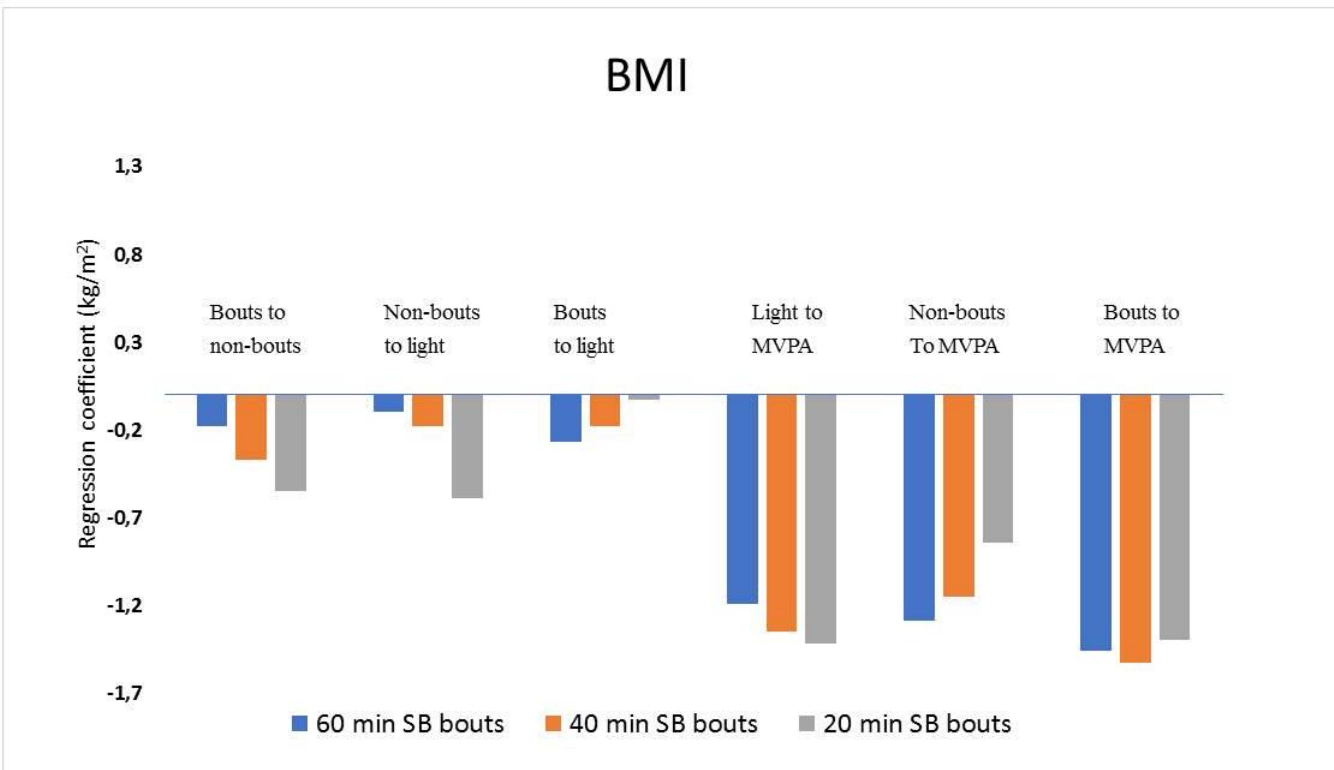

Figure 19. Effects on BMI of reallocating 30 min from one sedentary or physical active behavior to another.

7 DISCUSSION

By October 2016 159 participants had been recruited to the Sophia Step Study and randomized into one of three parallel groups: a multicomponent intervention (A); a single component intervention (B); or a control group (C). The interventions were feasible to implement in the primary care setting with low drop-out rate, high fidelity to the study protocol and a high grade of delivery and dose among those that enrolled. Both intervention groups increased mean daily steps while the control group decreased mean daily steps after 6 months intervention. The health check-ups were described as personalized, providing feedback on health outcomes, positive reinforcement, and resulting in a sense of being taken care of. The participants recalled self-monitoring of steps, the group sessions and the health check-ups as resources that increased motivation for physical activity and lead to establishment of new daily routines and in taking control over the own health.

Modeling reallocation of objectively measured time from sedentary time in bouts to moderate and vigorous physical activity was beneficially associated with HDL cholesterol, waist circumference and BMI.

7.1 INTERVENTION DESIGN OF THE SOPHIA STEP STUDY

7.1.1 Intervention components

In 2011 the Swedish National Board for Health and Welfare recommended health services to support self-management of physical activity by offering an advisory dialogue (Swedish: rådgivande samtal) to physically inactive persons (92). Further advice included recommending the use of a pedometer and/or to prescribe FaR®. A few years earlier, the Swedish Agency for Health Technology Assessment and Assessment of Social Services recommended applying group education in diabetes care (104). Sophia Step Study evaluated a structured use of these recommended methods in type 2 diabetes care. It will not be possible to elucidate the separate effects of MI, FaR® and group consultations in the Sophia Step Study, but it is possible to evaluate the effects of a multicomponent approach. Evidence suggests efficacy of these methods in improving physical activity and that perhaps applying a personalized approach and tailoring the needs of the individual, together with a minimum dose, are the core components of effective support (89, 94). The Swedish Board of Social Health and Welfare has concluded that MI is not recommended as means to improve metabolic control and weight reduction in diabetes care because of its limited effects (163). Yet, evidence on the efficacy and pragmatic application of physical activity support methods is still scarce (11).

The purpose of intervention B was to evaluate whether self-monitoring of steps alone is effective to support self-management of physical activity. Whereas intervention A is staff demanding, intervention B is a brief intervention and a more pragmatic approach for scaling up. The evidence behind the intervention B was largely drawn from the study of Bravata et al. which was one of the first systematic reviews demonstrating efficacy of pedometers on increased physical activity levels (164). At the time of planning the Sophia Step Study few pedometer interventions had been undertaken in a diabetes care setting. Today, both systematic reviews and meta-analyses have shown the efficacy of pedometers and other forms of activity trackers in increasing daily steps and reducing weight even in the population with type 2 diabetes (108,110,111).

In many pedometer studies it varies how, and if, steps were actually self-monitored over time, or if pedometer feedback was only displayed from a day-to-day basis. In the Sophia Step Study the feature of self-registration of steps onto a webpage added the possibility for the participant to view their own step pattern graphically illustrated over the week, month and year, as well as to compare their performance with that of others. The webpage (steg.se) was previously used in a workplace intervention (ASUKI step) with promising results for blood pressure benefit in healthy adults (165). Combining a pedometer with a webpage as in the Sophia Step Study, corresponds to the new generation of step counters that are integrated with software in smartphones, smart watches, bracelets and other handheld devices. During the past years, the use of activity trackers has exploded, where self-monitoring of steps has proven to be a promising tool for the self-management of physical activity (166). Currently, a vast number of trials internationally, and at least one trial in Sweden, the DiaCert-study, is evaluating the use of a mobile phone application in diabetes care (167). It is probable that activity trackers become a part of diabetes self-management in the near future and therefore it becomes crucial to explore, not only the efficacy, but also the mediating factors, participants' experiences and potential side effects of self-monitoring of physical activity.

Sophia Step Study was designed to examine the effects of long-term use of self-monitoring of steps and to explicate the role of counseling on increased physical activity and maintenance. Two studies have had similar set-ups. Walking for wellbeing was an RCT with two intervention groups: one group received pedometers and brief advice on physical activity and the other group received pedometers with more intense counseling. The study was undertaken in a general population in primary care in Scotland. Both interventions were effective in increasing steps over time (at 12, 24 and 48 weeks) and there was no significant difference between the two intervention groups (114). The PACE-UP trial is another study that provided a pedometer with or without counselling. The study took place in a general population in primary care practices in London. After 12 months both intervention groups increased mean daily steps with a similar amount compared to the control group (642 steps/day without counseling and 677 step/day with counselling more than the controls). Yates el al evaluated a three-hour physical activity education session with or without pedometers, compared with a control group in individuals with impaired glucose tolerance. The group receiving the education and pedometers increased physical activity levels compared with the control group after 3, 6 and 12 months while the group without pedometers increased physical activity compared with the control group only after 12 months. Intervention effects on fasting glucose and 2-hour glucose were evident at 3, 6 and 12 months but only in the pedometer group (168). Bjørgås et al. evaluated the effects of using a physical activity diary with or without a pedometer. Physical activity was not measured, but both groups significantly improved weight, $HbA_{1c,}$ fasting glucose, triglycerides, HDL and glucose 24 weeks after the intervention with no effect between the groups (169). The authors conclude that pedometers did not enhance the effect above the intervention with advice and a physical activity diary. It may well be that the physical activity diary, together with the four study assessments resulted in a ceiling effect.

7.1.2. Intervention duration and dose

Study duration was decided to last 2 years, to allow for behavior change to occur and to be maintained. For many individuals, finding motivation to change is a difficult and slow process. Many circumstances around the individual can affect readiness for change, or the possibility to be active: for example, work conditions, their health and that of relatives, or that the weather or the winter season may reduce motivation for physical activity. Support therefore needs to be a continued process of establishing conditions for change. For the first 6 months of the intervention individual consultations and group meetings were planned on a more frequent basis. The second focused on maintenance strategies. The Sophia Step Study allowed for long-term treatment and tracking of physical activity behavior and cardiometabolic outcomes over a 2-year period, which is rather unique (14).

7.1.3 Intervention outcomes

HbA_{1c} is the most commonly used outcome measure for diabetes treatment and was chosen as a primary outcome to allow for direct comparisons with other treatments. Fasting glucose, insulin, C-peptide, IGF BP1 and ApoA1 and ApoB were selected as secondary outcomes. These biomarkers will help explore the effects of volume and intensity of physical activity on the complex pattern of glucose metabolism. The risk for cardiovascular disease is elevated in individuals with type 2 diabetes and known cardiovascular risk factors HDL cholesterol, LDL cholesterol, triglycerides and blood pressure were also measured. Several obesity measures were chosen (weight, BMI, waist circumference, sagittal abdominal diameter and percentage body fat) to evaluate the effects of the intervention on overweight and obesity, as these are closely linked to glucose metabolism. All these cardiometabolic biomarkers play separate roles in diabetes progression and cardiovascular risk. Thus it is important to understand the effects of physical activity on each of these markers separately as well in combination (170, 171). Health related quality of life was also included as an intervention outcome of Sophia Step Study. The choice of HbA_{1c} as primary outcome for prediabetes can be discussed. For participants included based on elevated fasting glucose an effect on HbA_{1c} cannot be expected.

Evidence of the effect of pedometers on cardiometabolic risk factors (e.g. HbA_{1c},) is mixed (108, 110). Several factors may explain this miscellany of results. For instance, the level of physical intensity or volume needed to impact on cardiometabolic risk factors may not be achieved by the use of pedometers. This will be possible to explore in the Sophia Step Study by using accelerometers to evaluate change in physical activity. Furthermore, obtained intervention dose, sleep, other health conditions and changes in diet and medications may function to mask the effects of the intervention and hence subgroups may not be susceptible to response. In the planned 12- and 24- month evaluations of the Sophia Step Study such moderators and predictors will be explored.

7.1.4. Logic model

The theoretical models stages of change model, health belief model and the social cognitive theory were chosen as a basis for the interventions. The three models complement each other well and serve to structure the interventions and in understanding behavior change. The health belief model was intended to be applied to increase determination and motivation for physical activity, mainly during the early phase (first 6 months) of the intervention (119). The stages of change model was applied, for instance, with decisional balance, goal-setting, action planning, barrier identification and relapse prevention, but as a whole to understand the individual´s readiness for change and tailor the support to the specific needs of the individual (120). Social cognitive theory was primarily employed during the group sessions and added BCTs, such as role modeling and skills training, as well as the approach that physical activity behavior is dynamic, changeable and that there exists an interaction between the individual, the behavior and the environment (121).

The BCTs that were anticipated to be used in the interventions in Sophia Step Study were drawn from Tudor Locke's explanation of why pedometers work (107) and from the constructs of the theoretical models, interpreted to be consistent with the CALO-RE taxonomy (124). Several of the chosen BCTs had been identified as efficient in increasing physical activity and improve HbA_{1c} in systematic reviews (101, 118, 127). Commonly applied BCTs are goal-setting, action planning, self-monitoring of behavior, barrier identification, instructions on how to perform a behavior, use of follow-up prompts and social support (105, 118). However, the most common BCTs are not necessarily the most effective (105). Improvements in HbA_{1c} have been associated with the use of a larger number of BCTs (>10) (105, 118). Though, the quality of reporting BCTs and fidelity in the use of BCTs are often poor and conclusions cannot yet be drawn for either specific BCTs or efficacy of a larger number of BCTs. Fidelity in relation to each of the BCTs was not planned to be measured in the Sophia Step Study and thus it may not be possible to contribute to the evidence of the most effective BCTs. However, questions on self-efficacy and support for physical activity are included in the questionnaire and planned to be evaluated in future studies.

7.2 THE CONTEXT OF THE SOPHIA STEP STUDY

7.2.1 Recruitment

Enrollment of participants to the Sophia Step Study took a longer time than expected. The planned recruitment method was consecutive, but changed to convenience sampling over the course of the study. The response rate was 48%, i.e. 52% were excluded or denied participation. Most frequent grounds for exclusion were: already highly active or the patient´s health condition did not allow. Most common reasons for denying participation were time constraints, health condition and already active/don't need, which is in congruence with reasons reported in previous studies (172-174). The participants from the insurance clinic showed a lower enrollment rate and lower adherence than the two primary care centers. Patients are listed at the insurance clinic by their employer and it can be speculated that this group of patients in general is younger and busier. Response rates in similar interventions studies ranged from 19-54% (112, 168, 172, 174-176). Concerns that should be investigated are how to include individuals with health conditions that requires supervision for physical activity and how to reach and motivate those that feel they don't have time.

7.2.2 Study population

In the Sophia Step Study it was decided to recruit not only individuals being diagnosed with type 2 diabetes but also those diagnosed with prediabetes. The reason for including both groups of diagnosis was to implement the guidelines to offer a treatment plan also for individuals with prediabetes (177). The findings of study II showed that applying the same intervention for individuals with prediabetes and type 2 diabetes is appropriate. Combining the two diagnosis groups is a pragmatic approach to enhance both primary and secondary prevention of type 2 diabetes. Yet, this strategy of mixing the two groups of diagnosis makes comparisons with other studies somewhat more complicated and the two groups may differ in motivation and response. The group with prediabetes had more females, was more physically active, consumed more fiber-rich bread and displayed a better cardiovascular risk profile at baseline. There were no differences between the diagnosis groups with respect to age, smoking, other diseases, educational level or living with partner.
The three samples displayed baseline values similar to the Swedish National Diabetes Register with the mean HbA_{1c} marginally lower in study II and IV and marginally higher in study III. Mean age of all three samples were slightly lower which can be explained by the inclusion criteria of 40-80 years of age.

A large proportion of the individuals in study II (56%) reached >22 min of MVPA per day at baseline, which can be considered equal with the recommended levels of MVPA, if the recommended level of 150 min of weekly MVPA is averaged over 7 days. The mean baseline steps in study II was 6757 steps per day. In similar intervention trials in populations with type 2 diabetes, mean daily steps range from 4775-7160 steps per day (168, 174, 175, 178, 179). Hence, a large number of participants enrolling in intervention trials are likely not sedentary (<5000 steps/day) and many are probably already reaching 7100 steps/day.

This fact raises a number of concerns: the Stanford Brief Activity Questionnaire applied to exclude already active individuals may not be sensitive enough to exclude high active individuals, inactive persons were not reached, the participants may have raised their level of physical activity during the week wearing an accelerometer, and the intervention should perhaps be better tailored to the individual levels of physical activity. For those already reaching 150 min/week MVPA per week focus should be on increased volume or intensity, as it is underlined in the recommendations that 150 min MVPA per week is a minimum and higher intensity of physical activity probably provides superior effects on metabolic control (180, 181). Besides, resistance training is also included in the recommendations and could be the next step to include as a regular habit (39, 80). Depending on the individual focus of the support could also be on maintenance of the current physical activity level.

7.2.3 Control setting

A factor that influences the efficacy of an RCT is what the controls receive during the study. The number of study assessments and attendance by the controls was therefore described in study II. The questionnaires that the participants were asked to complete at baseline and after 12 weeks included questions on e.g. physical activity and dietary habits, social support for physical activity and self-efficacy for physical activity. Being asked these questions may have influenced the participants´ awareness and motivation to comply and physical activity, including those in the control group. Another factor that can have biased the control group is the contamination effect of receiving feedback on health outcomes and meeting the same diabetes specialist nurse, who was educated in MI. The results from the qualitative analysis in study III revealed that simply participating in the study and receiving feedback on their results were greatly appreciated the participants. It became clear that the control group did not receive usual care with "only" study assessments, as formulated in the study protocol (study I). In fact, the controls received an intervention with regular contact and check-ups by a diabetes specialist nurse. The fact that being part of a research study affects the motivation to comply and may induce behavior change per se is well-known (138, 139). Thus, the participants in the control group may have gained motivation and improved their lifestyle habits during the course of the study. In the case of Sophia Step Study, the treatment that being part of the research study brings, follows the same protocol for the three groups and the effects of being part of a research study can be ruled out.

7.2.4 Concurrent trends

Factors that may influence the outcomes of a study can be from the social and physical environment that occurred during the course of the study (12). This possibility was not discussed in the manuscript because of limited space. Nevertheless, a general increased use of activity trackers in the society, changes in infrastructure with more bike paths and dietary trends (e.g. 5-2 diet) occurred during the study period. To control for the use of activity trackers by the controls they were asked at the last study assessment (24-months assessment) whether they had used any activity monitoring device during the past two years. Another development that has occurred during the study period of Sophia Step Study is the prescription of new diabetic drugs and technical devices to monitor blood glucose and blood pressure levels (182).

7.3 THE IMPLEMENTATION OF THE SOPHIA STEP STUDY

7.3.1 Delivery

Overall, the intervention components were delivered as expected and fidelity to the study protocol was high. An exception was prescribing physical activity according to FaR®. Grading the delivery of FaR® and MI after the individual consultations was not done frequently and therefore it was not possible to evaluate the delivery as planned. From the frequent dialogues with the diabetes specialist nurses during the study, it became apparent that the reason for not applying FaR® was that asking about steps and applying MI were concurring with FaR®. Thus, FaR® seemed to be doing the same thing. Applying MI was also reported as challenging. It was especially challenging with respect to goal setting and in keeping the focus on physical activity. Important constructs of MI are to let the person decide on what to focus on and to encourage the choices that the individuals make, even if they decide not to change (95). The counsellor may feel like not performing well because progress is always not so obvious. There are methods to qualitatively evaluate MI sessions, such as the Motivational Interviewing Treatment Integrity Code (MITI 4) (183). This option was considered, but not made during the Sophia Step Study.

The results from study III indicate that self-monitoring of steps, and group and individual consultations were aptly delivered. The participants' expressed experiences also indicated that many of the essential components of MI were delivered. For example, a friendly atmosphere, encouragement and a personal turning point with increased awareness, motivation for physical activity and the establishment of new routines can be regarded as being results of delivered MI. A limitation of using study III as a measure of fidelity is that participants from the different intervention groups were not separated in the analysis and only seven participants from intervention group A were interviewed. In addition, only participants from the first two blocks of recruited participants were interviewed, these participants all met the same diabetes specialist nurse.

An important part of intervention delivery is to report on the training of the intervention providers (136). The three nurses involved in the Sophia Step Study were all acquainted with MI and FaR® through courses provided or paid for by their employers. They were only briefly introduced (1-2 hours) to the theoretical background of the interventions. The prior knowledge and skills of the three nurses probably varied owing to educational background, experiences and interests, which would reflect the actual in primary care context. The knowledge and skills of the intervention providers of the Sophia Step Study were not evaluated, which is a limitation in the evaluation of delivery. In a process evaluation of a similar physical activity intervention in routine diabetes care fidelity to was evaluated through email contacts, intervention session summaries and interviews with participants and the health professionals. The intervention was feasible to implement with high delivery and appreciated by the participants. Reasons for succeeding in delivering the intervention were reported to be the positive relationship between the participants and the health professionals delivering the consultations, the individual approach of meeting the individuals´ needs and the flexibility in follow-up support offered (telephone, email or face-to face) (184).

7.3.2 Dose received and reach

The intervention dose received reached high percentages in both intervention groups from all three centers and compliance to the treatment scheme offered was high. Few studies reporting dose received for interventions that promote physical activity in primary care are available. However, studies that do report treatment compliance show similar results with a high dose in enrolled participants. The PACE-UP up trial was a pedometer-based walking intervention in primary care centers in South London. A process evaluation following the Medical Research Council (MRC) guidance framework was undertaken to evaluate the implementation of the 12-week intervention. The dose was regarded as high with 86 % attending two of three sessions with the nurse, 80 % returning the diary as planned and 85% reporting steps to a satisfying degree (185). Higher dose and fidelity to the study components were associated with taking more steps and higher levels of MVPA after 3- and 12-months follow-ups. The SLIMMER study was a 10-month intervention targeting individuals with prediabetes taking place in the Dutch public health and primary care setting. The intervention comprised both physical activity and diet components. In the SLIMMER study the physical activity component was gym-based and included an aerobic and resistance exercise program and advice to increase physical activity in daily life. Acceptability of the study was high (score of 80 on a 1-100 scale) and high adherence to the physical activity component was related to greater weight loss; however dose received and acceptability were not associated with increased self-reported physical activity (172). A further study evaluating dose received showed high attendance to the offered consultations and high overall protocol fidelity after 12 months intervention (184).

The drop-out rate after 6 months in the Sophia Step Study was 3%. In similar interventions in routine diabetes care drop-out rates after 6 months were 1% (179) 4%, (176), 7% (186), 8% (184) and 30% (175). These data reflect the fact that persons who enroll are generally highly motivated and engaged in behavior change interventions in physical activity.

Although intervention fidelity and dose received are central features of an intervention and may explain lack of significant effects, it has rarely been investigated in relation to intervention outcomes (97, 137). The rigorous assessment of dose received in the Sophia Step Study will make associations of intervention dose with behavior and health outcomes possible.

7.4 THE BEHAVIORAL MECHANISMS OF THE SOPHIA STEP STUDY

The results of study III indicates that many of the intended BCTs were attained and recognized by the participants and can be considered as delivered through the intervention. The PACE-UP trial was a similar study evaluating the use of pedometers with and without nurse support in primary care. In a qualitative study it was elaborated by telephone interviews upon which of the many BCTs that were implemented through the PACE-UP trial. Similar to the findings in study III the nurse support group revealed greater use of several BCTs and that self-monitoring was particularly embraced by group B receiving self-monitoring of steps only. The BCTs that were most often mentioned by participants in the PACE-UP trial were: prompting self-monitoring, review of goals and outcomes, providing feedback, providing information about the link between behavior and health, providing specific information about how, where and when to, increase walking, planning social support/change and relapse prevention (187). Comparisons between the studies are difficult because of different methods of analysis. By applying an inductive approach in the content analysis, other aspects, rather than the intended BCTs, were also explored in study III, including a feeling of control, being listened to, the friendly style of the support being open and interactive and a personal development. These would probably not have been explored with a deductive approach or by the use of a questionnaire. The practice nurses providing the PACE-UP intervention were, similar to the nurses in the Sophia Step Study, briefly trained in the use of BCTs, which implies that many BCTs can be embraced by participants through primary care routine with just little additional training.

A few other studies have explored the experiences from participating in physical activity interventions in type 2 diabetes care. In the SLIMMER study participants with prediabetes reported in a questionnaire that they appreciated the guidance from the physiotherapists and especially that the program was tailored to their individual needs (172). Linmans et al. interviewed type 2 diabetes participants to explore the experiences of an intensified lifestyle intervention. The participants reported being enthusiastic and highly motivated to improve their lifestyle thanks to the intervention and the extra consultations delivered by the diabetes specialist nurse (173). Similarly, Matthews et al., reported high satisfaction with the intervention in type 1 and 2 diabetes individuals: the participants named that the approach and the helpfulness of the providers. They also reported that the provision of pedometers and diaries was especially motivational, informative and useful (184). From the PACE-UP trial (on general primary care patients) participants' barriers and facilitators to engage in the physical activity intervention were evaluated through interviews. The main findings were that almost all participants, irrespective of change in activity levels, felt that they had benefitted both physically and psychologically from the intervention and had succeeded in their goals (187). The results of study III added to this body of evidence that personalized support is appreciated by participants motivated to change physical activity behaviors and should therefore be a key of the self-management of process.

A few studies have performed mediator analyses for increased physical activity in interventions in type 2 diabetes. Van Dyck et al., for instance, revealed that change in physical activity after 12 months was mediated by coping with relapse, changes in social norms and social modeling from family members (188). In the SLIMMER study change in physical activity after 18 months was mediated by change in action control and motivation and psychological profile (189). Finally, in the HEALD study no single theoretical construct significantly mediated the increase in steps (190).

In study III the participants' experiences were not analyzed separated by group allocation. Comparisons between the three groups should therefore be made consciously. Yet, when similarities and differences between the groups were studied, it became evident that the participants in group A mostly talked about the group consultations and the interactions and emotional support gained from these activities. Group B participants primarily talked about the pedometer and the self-monitoring of steps. The inclusion of participants from the control group in study III and the aim to explore the experiences from participation in a research study rather than to explore the experiences from participation in an intervention/treatment can be discussed. The reason behind the chosen aim was to have an open mindset in relation to the interventions, and to allow for the experiences of taking part in a research study to be explored.

7.5 EFFECTS OF THE SOPHIA STEP STUDY ON PHYSICAL ACTIVITY BEHAVIOR AND HEALTH OUTCOMES

After 6 months, the two intervention groups showed improvements in physical activity behavior and clinical outcomes. The mean value after 6 months had improved for all variables in the two intervention groups while the control group showed a mixed pattern of results. Some variables indicated statistically significant changes at $p<0.05$ (increased steps in group A and B, decreased MVPA in group C, increased LPA in group B and C, decreased triglycerides in group A and B and decreased weight in group B). These results were drawn from paired sample t-tests and were not adjusted for potential confounders. Also, multiplicity was not considered and the significant results may be purely by chance (random error). Previous comparable pedometer interventions showed somewhat larger increases in mean daily steps after 6 months: 1220 (178), 1281 (179), 1481 (175), 2093 (168) and 2744 (102) steps/day.

The intervention effect, comparing the variation in variables over time between the intervention groups and the control group, showed statistically significant effects ($p<0.05$) after 6 months only for group B and only for MVPA and C-peptide. The linear mixed model adjusts for baseline values and the accelerometer derived values were adjusted for changes in wear time. Many of the participants (56%) included in the Sophia Step Study were already physically active at baseline (>22 min MVPA) and the mean clinical values meet the national target. It may be challenging to increase the physical activity levels in the participants that were already active and it may be questioned what results should then be expected from the intervention. It has previously been concluded that physical activity interventions are more effective in inactive target groups (8). In study II the proportion of the participants reaching 7100 steps increased from baseline to 6 months in all three groups. In contrast, the percentage of the participants reaching 22 min MVPA per day decreased slightly in all groups after 6 months. A possible explanation is that self-monitoring of steps leads to collecting steps rather than time in MVPA. Lower intensity exercise is not as effective as higher intensity exercise, or combined aerobic and resistance training, on HbA_{1c} and thus self-monitoring of steps may not be an optimal method to improve glucose metabolism (180, 181). Van Dyck and colleagues found that enhanced glucose control was realized in those who achieved an increase of > 4000 steps/day over baseline values, which is a rather high increase (191).

Applying stratified analyses provides the estimated effect for particular groups and the results can be compared with other studies using, for example, adults >65 years of age or only individuals diagnosed with diabetes. Such analyses also assist in predicting and understanding the outcomes based on the population mix. In the sample used in the Sophia Step Study the outcomes after 6 months varied slightly between participants older and younger than 65 years and between those diagnosed with prediabetes and those diagnosed with type 2 diabetes. Although older participants (>65 years) appear to respond marginally better on physical activity outcomes (steps and MVPA), younger participants seem to respond better on the clinical variables. This finding indicates that expectations of results and magnitude of intervention effect should be interpreted in relation to the study population groups, especially older vs. younger age groups. The implications are that when evaluating effects of an intervention, or summarizing evidence in a meta-analysis, it is crucial to be clear about the specific population group and understand that the response in question may differ for subgroups. Explanations for larger behavioral effects on older participants may be that being retired and at an older age brings a higher disease engagement and prioritizing of their health. To reach more motivated individuals newly retired individuals could be a potential target group. At the same time, for better response on clinical parameters and preventive effects lower age groups should be targeted. In the results of study II there seem to be no major effect differences between participants with prediabetes and those with type 2 diabetes. Likewise, there was no gender difference after 6 months intervention.

7.6 HEALTH ASSOCIATIONS OF REALLOCATING SEDENTARY AND PHYSICALLY ACTVIVE BEHAVIORS

Study IV employed a cross-sectional design aimed to explore the relationship of changing time from being sedentary in longer periods to break up sedentary time, or to be physically active, with cardiometabolic parameters. In the single model sedentary time was significantly ($p<0.05$) negatively associated and MVPA was positively associated with many health parameters. In the partition model, when adjustments were made for time in other activity behaviors, the negative health effects of sedentary time, though no longer significant, still remained. This finding contrasts with several other (larger) studies, which provided negative health effects of sedentary time independent of time spent in moderate to vigorous physical activity (69). The conflicting findings may be explained by the small sample size in our study, different measurement methods and protocol, that our participants were rather active at moderate intensity levels and had few sedentary bouts. In addition, both diabetes and prediabetes participants were included and that they were well-controlled in terms of their cardiometabolic condition. Whether SB is associated with cardiometabolic risk factors independent of the time spent in physical activity has been questioned and needs to be supported by objective measures, causality and plausible mechanisms (20).

The results of the partition model in study IV suggest that MVPA is associated with HDL, waist circumference and weight, independent of the total time spent in SBs and LPA. HbA_{1c} and fasting glucose showed mixed associations (Supplementary Table 3 in the article), which are difficult to explain. The mixed associations may be due to the participants being well-controlled by medications and the rather crude adjustment method for medications that was applied. Another explanation is that type 2 diabetes has several pathophysiological causes and individuals respond differently to physical activity depending on their actual type of diagnose (27).

In the isotemporal models, substituting time in one activity behavior while adjusting for total time was simulated. This method better corresponds better to reality, given that time is constant. The health effects of substituting sedentary time with MVPA were strong and clinically relevant for HDL, waist circumference and BMI. Replacing bouted sedentary time with interrupted sedentary time or with LPA showed beneficial associations, although not at a statistically significant level. A noteworthy tendency was that shortening time in sedentary bouts from 60 to 40 to 20 min seemed beneficial for waist circumference and BMI, but not for HDL. Hence, the results of study IV for the obesity measures show a possible gradient with positive effects of breaking up sedentary time in shorter bouts.

Studies that have controlled for substituted (reallocated) time in populations with type 2 diabetes or prediabetes all provide similar benefits of MVPA (78, 192-195). Associations of the health effects of reallocating sedentary time to light intensity physical activity and to sedentary time in shorter bouts are inconsistent (78, 192-195). The results from the isotemporal model in study IV illustrate beneficial effects of spending time in MVPA, regardless of what type of activity that is replaced. Important to consider is that time in MVPA was accumulated and every minute counted. This observation supports the recommendations to collect min in MVPA over the day and bouts of 10 min are not needed for effects on obesity measures and HDL. The level of the effect is also important to consider from a time management perspective. For example, it is three times more beneficial on waist circumference to spend time in MVPA rather than in LPA. The implication is that all physical activity is beneficial, but for the obesity parameters and HDL cholesterol, it is more time effective to spend time in MVPA corresponding to a walking speed of 4 km/h. However, study IV applied a cross-sectional design and causal relationships for the obesity parameters can therefore not be determined.

7.7 METHODOLOGICAL CONSIDERATIONS

7.7.1 External validity

The samples used in this thesis were all based on the inclusion and exclusion criteria for the Sophia Step Study. Yet, individuals with conditions contraindicative to physical activity, not able to communicate in Swedish or not having access to the internet were excluded. For study III and IV the participants were all recruited from Sophiahemmet, which is located in central Stockholm. The serving area of the two health care centers Husläkarmottagningen and Försäkringsmottagningen at Sophiahemmet is not restricted and patients are from the entire Stockholm area. In study II participants were also recruited from a rural part of Sweden. Nevertheless, it is likely that population groups such as low income groups, unemployed and immigrants were underrepresented in the Sophia Step Study. Thus the findings of this thesis should not be generalized to groups of different socioeconomic status or to other population areas.

It is probable that there was a selection bias in that half of the individuals initially asked denied enrollment. The fact that many of the included participants already were physically active reflects that highly motivated individuals were reached. This may affect the results as the intervention was tailored to inactive individuals, focusing on increasing daily steps. However, the multiple component intervention (A) included several BCTs that intended to enhance individualization and maintenance of physical activity. The hypothesis that the multi-component intervention should be superior to the single-component intervention after two years intervention still needs to be confirmed or rejected. In all three study samples the distribution between men and women were satisfying and the samples with type 2 diabetes displayed mean health values close to the mean values in the National Diabetes Register. Among individuals with prediabetes women were slightly overrepresented. In addition, the individuals with prediabetes were more active and had a higher intake of fiber rich bread, which may reflect that they were more health concerned.

7.7.2 Internal validity

The Sophia Step Study was an RCT designed to be implemented in primary care, where the diabetes specialist nurses would apply the intervention without much additional education and support. Feasibility was tested at three primary care settings and, as such, it can be considered as an effectiveness trial. However, with frequent study assessments during the first 6 months (week 0, 8, 12, 16 and 24) that followed a strict measurement protocol, it was a rather controlled setting and it may be questioned if it is practically and cost-effective to implement at a large scale format. An important finding of study III was that the frequent study assessments and feedback on health outcomes were highly appreciated by the participants, including the control group participants. A more pragmatic approach to deliver the follow-ups of health assessments could for example be by the use of telephone or digital forms for communication.

There was a contamination bias in the Sophia Steps Study as the control group met the same diabetes specialist nurse during the study. The health check-ups were possible mediators for behavior change in all three groups and may influence the efficacy of the intervention. This could have been avoided by choosing a different study design, such as cluster randomization or step wedged design (130). The participants from study III are essential given that the qualitative evaluation of the Sophia Step Study was based on this sample. Study III participants were more males, slightly older and fewer had a university education compared to the sample of study II. Additionally, these participants only represent one primary care center and the findings of study III cannot be generalized to the full Sophia Step Study

A limitation of the interview design as a mean to explore mechanisms is that it is not possible to quantify the mediating effects that the different BCTs had on physical activity behavior. A more frequently applied method to evaluate the implementation of intervention components and BCTs is the use of questionnaires. With a quantitative measure of the degree of implementation of BCTs the direct mediating effects of BCTs on behavior change could have been investigated.

The choice of objective measures to measure physical activity and SB is a strength of study II and IV. Nevertheless, the GT1M accelerometers that were used measure ambulatory movements (vertical accelerations) and some forms of activities such as cycling, swimming and resistance training were not captured. This may have underestimated physical activity levels in study II and IV. In addition, accelerometers placed on the hip are not sensitive enough to separate sitting from standing and standing was probably classified as SB. It is possible that breaks in SB and standing have beneficial metabolic effects which may explain the mixed pattern on these variables that was seen in study II and IV (196, 197). Adjusting for breaks (< 1 minute) in sedentary time should be made to rule out the influence of breaks in sitting on metabolic parameters.

Study measurements are snap shots, generating values that are assumed to reflect the typical values of the individual. In study II and IV physical activity was measured over a week and for some participants valid data was provided for only 4 days. Likewise, blood samples were drawn at one single occasion. Fasting glucose, triglycerides, HDL cholesterol and blood pressure are influenced by physical activities and dietary intake that occurred on the day before the measurement is taken. It is possible that the participants changed their behaviors while wearing the accelerometer and prior to the study measurement appointment. Individuals with type 2 diabetes are often educated to be aware of how their lifestyle patterns influence blood glucose. In addition, the fact of being studied may generate motivation to perform well. By excluding participants with accelerometer data on less than three days the bias of performing more physical activity than usual is reduced. HbA_{1c} is reflecting long term blood glucose levels and is thus a more reliable measure of blood glucose metabolism. In the planned two-year efficacy analyses of Sophia Step study, after total 9 study assessments, these effects of performing well may have levelled off.

Missing data is a potential bias to RCTs and should be considered carefully. The bias of values missing at random is reduced by the application of linear mixed model as statistical mean to evaluate the intervention effect. The drop-out rate after 6 months intervention in study II was low and did not allow for statistical analyses to explore differences between drop-outs and adherers. In behavioral intervention it is possible that those who don't improve drop-minout. In the case of drop-outs in study II, 4 out of 6 dropped out before the first assessment after baseline and reasons for dropout were lack of time and worsened health condition.

7.7.3 Trustworthiness

Credibility and conformability of the findings in study III was assured by close collaboration between three researchers, all being familiar with the whole by both listening to the interviews and reading the entire text material. The researchers individually reflected upon the categories and triangulation was made by going back and forth between categories, the condensed material and the units of analyses and discussed them. By this procedure the risk of missing or too rapidly interpreting aspects decreased (160). In qualitative research the pre-understanding of the researcher is a critical factor that can bias the result. The pre-understanding differed between the three authors, a fact that reduced bias and enriched and deepened the discussions, the triangulations and subsequently the analysis and the results. The choice of recruiting an external researcher for all interviews and for performing the content analysis was to assure objectively towards the participants and the theoretical background

7.8 PRACTICAL AND FUTURE IMPLICATIONS

This thesis suggests that self-monitoring of steps combined with regular feedback on health outcomes has potential for self-managing of physical activity in prediabetes and type 2 diabetes. Next step is to evaluate the 2-year outcomes of Sophia Step Study: to investigate the long-term implementation and maintenance effects of self-monitoring of steps with and without counselling support. The Sophia Step Study intervention model should also be evaluated in other population groups and contexts, including exploration of the perceptions of individuals and health care professionals. It is possible that with interventions, such as those provided in Sophia Step Study, individuals with high motivation and ability to self-manage physical activity are reached. Therefore, experiences and perceptions of drop-outs and low-adhering participants in Sophia Step Study and similar interventions should be explored. Based on knowledge about drop-outs' and low-adherers' motivation, capabilities and opportunities strategies for how to engage less motivated persons can be developed and evaluated.

The efficacy of MI as support for self-monitoring of physical activity in prediabetes and type 2 diabetes needs further investigation. MI should be evaluated through a rigor evaluation protocol and appropriate evaluating methods together with objectively measured physical activity. In previous research MI has frequently been complemented with other intervention components or combined with dietary interventions. Thus, it still needs to be evaluated to what extent MI is effective without other intervention components, or whether a combination is most effective.

The method FaR® is recognized in the Swedish primary care context and is based on the same theoretical models as Sophia Step Study. Self-monitoring of steps and/or individual and group consultations can be provided as an alternative to FaR®. Similar to medical treatment, the treatment that is most effective may vary between individuals. Whether it is FaR®, self-monitoring of steps or individual and group consultations, the most effective support is perhaps the one the individual choses themselves, the support that suits them for the moment. The intervention components included in Sophia Step Study are recommended for use in the Swedish primary care at present and the extent to which they are implemented should be evaluated based on a framework for process evaluations.

Activity monitors and health apps have become popular in the past years and self-monitoring of physical activity is easily available and frequently applied today. Another ongoing development is the release of "my pages" by the National Diabetes Register through which clinical data is becoming readily available for the patients. There is potential to collect data on steps and other physical activity parameters to serve as a basis for a personalized consultation with the health professional. Indeed, digital technology (e.g. including e-health in combination with for example activity trackers and feedback on behaviors and health outcome) is promising for the support of self-monitoring of physical activity. This development should be carefully evaluated in terms of implementation factors and reach, short and long term health outcomes, individuals'' experiences and side effects (e.g. performance stress, inability to understand the results, digital overload and enhanced inequality in health and provision of health care). In addition, there is a need to investigate what BCTs and interface designs that are most effective for increased motivation and maintenance of physical activity when self-monitoring of steps is delivered digitally.

To further increase the understanding of the effects that diverse physical activity and sedentary patterns have on different health outcomes considerations should be made for bout length and interrupted time of the different behaviors. Moreover, the effects of changes in physical activity and sedentary patterns on biomarkers such as insulin, IGF BP1, and adiponectin should be investigated.

8 CONCLUSION

Sophia Step Study was developed to evaluate support for physical activity in the primary care setting. The intervention model, including self-monitoring of steps with and without individual counselling and group meetings, was shown feasible to implement in the primary care context. Adherence to the intervention components was high in both intervention groups and was well appreciated by the participants. The two interventions were effective in increasing physical activity after 6 months.

Self-monitoring of steps, feedback on health outcomes and a personalized approach is highly valued for self-management of physical activity by the individuals and should be considered in primary care. Self-monitoring of steps, feedback on health outcomes and group counselling increased awareness of physical activity, stimulated self-reevaluation and problem solving and promoted establishment of new routines for physical activity in daily life.

In addition, the thesis also confirmed that modeling replacement of sedentary time with time in moderate and vigorous physical activity showed beneficial associations with HDL cholesterol, waist circumference and BMI levels in individuals with prediabetes and type 2 diabetes.

9 ACKNOWLEDGEMENTS

I wish to express my sincere appreciation:

To the funders of my thesis work: the **Sophiahemmet Foundation; The Swedish Diabetes Foundation; King Gustav V and Queen Victoria's Order of Freemasons Research Foundation; Vårdalsstiftelsen; Skandia; and The Sibling Svensson's Foundation for Medical Research.**

To **Karolinska Institutet**, Department of Clinical Sciences and Education, Södersjukhuset, especially head of the department **Per Tornvall**, director of studies **Buster Mannheimer and Christer Svensen** for the opportunity to become a PhD student and **Jeanette Öhrman** for all assistance and support.

To **Pernilla Hillerås and Jan-Åke Lindgren**, for believing in this PhD project and offering me employment and workplace at Sophiahemmet University. **Johanna Adami and Susanne Georgsson,** for continued employment and support.

There are so many people to whom I would like to express my sincere and warmest gratitude for making it possible to realize my PhD studies and this thesis.

First of all, I would like to thank all **the participants of the Sophia Step Study**. Not only have you provided me with highly valued data, you have also given me experience and many enjoyable and unforgettable moments.

My supervisors **Unn-Britt Johansson, Maria Hagströmer and Agneta Yngve**, thank you for your engagement, support, patience, for sharing your knowledge and experiences and for believing in me. It has been an honor to work with the three of you. You are my role-models.

I have also been privileged to have such excellent and experienced co-authors. Thank you **Kerstin Brismar, Barbara Ainsworth, Matthew Buman and Helena Lööf** for valuable inputs and interesting discussions.

The diabetes specialist nurses **Christina Iskull, Elisabeth Duggin and Linda Åberg** who delivered the interventions and assisted with data collection. Thank you for your engagement in the Sophia Step Study and for being so easy to work with. It has been a pleasure to work with the three of you! The heads of the primary care centers, **Hilmar Geber**, **Maarit Korkeila Lidén** and **Anna-Karin Alvunger** for being supportive of the study.

Jan Sjöbeck and Charlotte Lindström at Select Wellness. I have appreciated the smooth communication and fast support throughout the years with steg.se.

Peter Seger, Peter Aspelin, Peter Möller, and Susanne Amsberg, for the initial ideas to Sophia Step Study and for making the study possible at first hand.

Marina Dyfverman and Pia Robertsson Ronkainen for valuable support with the printed materials and figures. **Christina Jansson and Caroline Lagerman,** who assisted with support for the on-line survey.

The statisticians **Hans Järnbert Pettersson**, Department of Clinical Sciences and Education, Södersjukhuset, KI and **Marcus Thuresson**, Statisticon, for valuable guidance. **Leslie Shaps**, Proofreading, Editing & Translation (PET) Global Services, for responsible and effective reading, editing and commenting in a friendly style.

The staff at the lab and the reception at Husläkarmottagningen for assisting with blood samples and handing out accelerometers.

My mentor and dear friend **Bettina Ehrenblad** for support and long discussions in all kinds of matters. I truly appreciate your engagement and wise advices.

My former colleagues **Kamilla Nylund, Johan Faskunger, Christel Lynch, Eric Poortvliet, Susanna Kugelberg, Emma Patterson, Patrick Bergman and Lydia Kwak** for shaping me as a researcher and teacher in public health, physical activity and behavior change. Together, although spread out, I believe that we will accomplish changes to the better. We are the veaklings!

Master students **Hanna Jisser, Michael Gäfvert, Morten Sjölander and Leonhard Thunn Hohenstein** for intellectual and fun moments, for assistance with data collection, data entering and support in group sessions.

Poorna Anandavian, the meetings with you have been highlight moments in my PhD process. I have truly enjoyed our meetings at the coffee shop at aula Medica.

Åsa Norman, Matthias Lidin, my peer PhD students at KI, for support and sharing frustrating moments during the PhD process, and for discussions and fun moments at courses, seminars and conferences.

My dear and fun attic colleagues: **Sandra Doveson, Anna Akselsson, Anders Linde, Maja Holm** for all serious and unserious discussions in all kinds of matters and for all the laughter and fun moments.

All other **colleagues at Sophiahemmet,** the support and friendship you have given me during this period is highly appreciated.

My friends outside of research, especially **Sara, Lotta, Ingela, Stina, Pernilla, Kattis, Petra, Cissi and Marie J with families**, I'm so happy to have all of you in my life. **Frida and Jamie** for being the best of neighbors, for keeping up with the twins and for showing interest in my work.

My fantastic **Andersson family** with all my siblings, nephews, nieces, sisters- and brothers in law and dogs, you are fabulous people and dogs every single one of you.

Mum, **Marie-Louise**, for evoking my interest in health and physical activity and for being a role model in so many ways. Thanks also for assisting at home when I have been away for conferences.

My late father, **Bosse**, for always supporting my choices and for making me believe I can do whatever I want to if I only work hard. You are truly missed.

My three fantastic children**, Irma, Viggo and Erling**, for being flexible with dinner habits and taking responsibility in school mornings and afternoons. Thanks for bringing joy, for being curious about my work and for all your brilliant questions and ideas. You give me perspective to on what I am doing, and to what is important in life. I'm so proud of the three of you.

My awesome husband **Flemming** for always being supportive, for having patience during the more stressful periods and with the extra load of household responsibilities that you have had when I have been away. Thanks a lot for that. I love you.

10 REFERENCES

1. Authors/Task Force M, Ryden L, Grant PJ, Anker SD, Berne C, Cosentino F, et al.. ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: the Task Force on diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and developed in collaboration with the European Association for the Study of Diabetes (EASD). Eur Heart J. 2013;34:3035-87
2. American Diabetes Association. 4. Lifestyle Management: Standards of Medical Care in Diabetes. Diabetes Care. 2018;41:S38-S50
3. Zethelius B, Gudbjornsdottir S, Eliasson B, Eeg-Olofsson K, Cederholm J, Swedish National Diabetes R. Level of physical activity associated with risk of cardiovascular diseases and mortality in patients with type-2 diabetes: report from the Swedish National Diabetes Register. Eur J Prev Cardiol. 2014;21:244-51
4. Kennerly AM, Kirk A. Physical activity and sedentary behaviour of adults with type 2 diabetes: a systematic review. Practical Diabetes. 2018;35:86
5. Swindell N, Mackintosh K, McNarry M, Stephens JW, Sluik D, Fogelholm M, et al.. Objectively Measured Physical Activity and Sedentary Time Are Associated With Cardiometabolic Risk Factors in Adults With Prediabetes: The PREVIEW Study. Diabetes Care. 2018;41:562-9
6. Finer S, Robb P, Cowan K, Daly A, Robertson E, Farmer A. Top ten research priorities for type 2 diabetes: results from the Diabetes UK-James Lind Alliance Priority Setting Partnership. Lancet Diabetes Endocrinol. 2017;5:935-6
7. Orrow G, Kinmonth A-L, Sanderson S, Sutton S. Effectiveness of physical activity promotion based in primary care: systematic review and meta-analysis of randomised controlled trials. BMJ. 2012;344
8. Sanchez A, Bully P, Martinez C, Grandes G. Effectiveness of physical activity promotion interventions in primary care: A review of reviews. Prev Med. 2015;76 Suppl:S56-67
9. Lamming L, Pears S, Mason D, Morton K, Bijker M, Sutton S, et al.. What do we know about brief interventions for physical activity that could be delivered in primary care consultations? A systematic review of reviews. Prev Med. 2017;99:152-63
10. Mosalman Haghighi M, Mavros Y, Fiatarone Singh MA. The Effects of Structured Exercise or Lifestyle Behavior Interventions on Long-Term Physical Activity Level and Health Outcomes in Individuals With Type 2 Diabetes: A Systematic Review, Meta-Analysis, and Meta-Regression. J Phys Act Health. 2018;15:697-707
11. Luoma KA, Leavitt IM, Marrs JC, Nederveld AL, Regensteiner JG, Dunn AL, et al.. How can clinical practices pragmatically increase physical activity for patients with type 2 diabetes? A systematic review. Transl Behav Med. 2017;7:751-72
12. Moore GF, Audrey S, Barker M, Bond L, Bonell C, Hardeman W, et al.. Process evaluation of complex interventions: Medical Research Council guidance. BMJ: 2015;350
13. Reis RS, Salvo D, Ogilvie D, Lambert EV, Goenka S, Brownson RC. Scaling up physical activity interventions worldwide: stepping up to larger and smarter approaches to get people moving. Lancet. 2016;388:1337-48
14. Matthews L, Kirk A, Macmillan F, Mutrie N. Can physical activity interventions for adults with type 2 diabetes be translated into practice settings? A systematic review using the RE-AIM framework. Transl Behav Med. 2014;4:60-78
15. Patton MQ. Qualitative research & evaluation methods : integrating theory and practice. Thousand Oaks, California: SAGE Publications, Inc.; 2015.
16. Hughes R, Margetts BM. Practical public health nutrition [Elektronisk resurs]. Chichester, West Sussex, U.K.: Wiley-Blackwell; 2011.
17. Henson J, Dunstan DW, Davies MJ, Yates T. Sedentary behaviour as a new behavioural target in the prevention and treatment of type 2 diabetes. Diabetes Metab Res Rev. 2016;32 Suppl 1:213-20
18. Dunstan DW, Howard B, Healy GN, Owen N. Too much sitting--a health hazard. Diabetes Res Clin Pract. 2012;97:368-76

19. Dempsey PC, Owen N, Yates TE, Kingwell BA, Dunstan DW. Sitting Less and Moving More: Improved Glycaemic Control for Type 2 Diabetes Prevention and Management. Curr Diab Rep. 2016;16:114
20. Stamatakis E, Ekelund U, Ding D, Hamer M, Bauman AE, Lee I-M. Is the time right for quantitative public health guidelines on sitting? A narrative review of sedentary behaviour research paradigms and findings. Br J Sports Med. 2018
21. Federation ID. IDF Diabetes Atlas 8th Edn. Brussels, Belgium: 2017.
22. Bluher S, Markert J, Herget S, Yates T, Davis M, Muller G, et al.. Who should we target for diabetes prevention and diabetes risk reduction? Curr Diab Rep. 2012;12:147-56
23. Hellgren MI, Daka B, Jansson PA, Lindblad U, Larsson CA. Insulin resistance predicts early cardiovascular morbidity in men without diabetes mellitus, with effect modification by physical activity. Eur J Prev Cardiol. 2015;22:940-9
24. Use of glycated haemoglobin (HbA1c) in the diagnosis of diabetes mellitus Abbreviated report of a WHO consultation. Geneva: World Health Organisation; 2011.
25. American Diabetes Associations. Standards of Medical Care in Diabetes—2010. Diabetes Care. 2010;33:S11-S61
26. WHO. Definitions and Diagnosis of Diabetes Mellitus and intermediate hyperglycemia - Report of a WHO/IDF Consultation. Geneva, Switzerland: 2006.
27. Ahlqvist E, Storm P, Karajamaki A, Martinell M, Dorkhan M, Carlsson A, et al.. Novel subgroups of adult-onset diabetes and their association with outcomes: a data-driven cluster analysis of six variables. Lancet Diabetes Endocrinol. 2018;6:361-9
28. ADA. 8. Cardiovascular Disease and Risk Management: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018;41:S86-S104
29. Schwarz PE, Greaves CJ, Lindstrom J, Yates T, Davies MJ. Nonpharmacological interventions for the prevention of type 2 diabetes mellitus. Nat Rev Endocrinol. 2012;8:363-73
30. Tuomilehto J, Schwarz PE. Preventing Diabetes: Early Versus Late Preventive Interventions. Diabetes Care. 2016;39 Suppl 2:S115-20
31. American Diabetes Association. 2. Classification and Diagnosis of Diabetes. Diabetes Care. 2015;38:S8-S16
32. American Diabetes Association. 4. Lifestyle Management: Standards of Medical Care in Diabetes. Diabetes Care. 2018;41:S38-S50
33. American Diabetes Association. 8. Cardiovascular Disease and Risk Management: Standards of Medical Care in Diabetes. Diabetes Care. 2018;41:S49-S57
34. Pan XR, Li GW, Hu YH, Wang JX, Yang WY, An ZX, et al.. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. Diabetes Care. 1997;20:537-44
35. Lindstrom J, Ilanne-Parikka P, Peltonen M, Aunola S, Eriksson JG, Hemio K, et al.. Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study. Lancet. 2006;368:1673-9
36. Diabetes Prevention Program Research Group. Reduction in the Incidence of Type 2 Diabetes with Lifestyle Intervention of Metformin. The New England Journal of Medicine.2002;346:393-403.
37. Wing RR, Bolin P, Brancati FL, Bray GA, Clark JM, Coday M, et al.. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. The N Engl JMed. 2013;369:145-54
38. Pi-Sunyer X. The Look AHEAD Trial: A Review and Discussion Of Its Outcomes. Curr Nutr Rep. 2014;3:387-91
39. Colberg SR, Sigal RJ, Yardley JE, Riddell MC, Dunstan DW, Dempsey PC, et al.. Physical Activity/Exercise and Diabetes: A Position Statement of the American Diabetes Association. Diabetes Care. 2016;39:2065-79
40. ADA. 4. Lifestyle Management: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018;41:S38-S50
41. Committee PAGA. 2018 Physical Activity Guidelines Advisory Committee Scientific Report: U.S. Public Health Service, Department of Health and Human Services; 2018. Available from: https://health.gov/paguidelines/second-edition/report.aspx.

42. Sadarangani KP, Hamer M, Mindell JS, Coombs NA, Stamatakis E. Physical activity and risk of all-cause and cardiovascular disease mortality in diabetic adults from Great Britain: pooled analysis of 10 population-based cohorts. Diabetes Care. 2014;37:1016-23
43. Kodama S, Tanaka S, Heianza Y, Fujihara K, Horikawa C, Shimano H, et al.. Association between physical activity and risk of all-cause mortality and cardiovascular disease in patients with diabetes: a meta-analysis. Diabetes Care. 2013;36:471-9
44. Snowling NJ, Hopkins WG. Effects of different modes of exercise training on glucose control and risk factors for complications in type 2 diabetic patients: a meta-analysis. Diabetes Care. 2006;29:2518-27
45. Umpierre D, Ribeiro PA, Kramer CK, Leitao CB, Zucatti AT, Azevedo MJ, et al.. Physical activity advice only or structured exercise training and association with HbA1c levels in type 2 diabetes: a systematic review and meta-analysis. JAMA. 2011;305:1790-9
46. Schwingshackl L, Missbach B, Dias S, Konig J, Hoffmann G. Impact of different training modalities on glycaemic control and blood lipids in patients with type 2 diabetes: a systematic review and network meta-analysis. Diabetologia. 2014;57:1789-97
47. Colberg SR, Albright AL, Blissmer BJ, Braun B, Chasan-Taber L, Fernhall B, et al.. Exercise and type 2 diabetes: American College of Sports Medicine and the American Diabetes Association: joint position statement. Exercise and type 2 diabetes. Med Sci Sports Exerc. 2010;42:2282-303
48. Sisson SB, Camhi SM, Church TS, Tudor-Locke C, Johnson WD, Katzmarzyk PT. Accelerometer-determined steps/day and metabolic syndrome. Am J Prev Med. 2010;38:575-82
49. Jennersjo P, Ludvigsson J, Lanne T, Nystrom FH, Ernerudh J, Ostgren CJ. Pedometer-determined physical activity is linked to low systemic inflammation and low arterial stiffness in Type 2 diabetes. Diabet Med. 2012;29:1119-25
50. Tudor-Locke C, Schuna JM, Jr., Han HO, Aguiar EJ, Green MA, Busa MA, et al.. Step-Based Physical Activity Metrics and Cardiometabolic Risk: NHANES 2005-2006. Med Sci Sports Exerc. 2017;49:283-91
51. Pettee Gabriel KK, Morrow JR, Jr., Woolsey AL. Framework for physical activity as a complex and multidimensional behavior. J Phys Act Health. 2012;9 Suppl 1:S11-8
52. Keadle SK, Conroy DE, Buman MP, Dunstan DW, Matthews CE. Targeting Reductions in Sitting Time to Increase Physical Activity and Improve Health. Med Sci Sports Exerc. 2017;49:1572-82
53. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. Public Health Rep. 1985;100:126-31
54. Ainsworth BE, Haskell WL, Leon AS, Jacobs DR, Jr., Montoye HJ, Sallis JF, et al.. Compendium of physical activities: classification of energy costs of human physical activities. Med Sci Sports Exerc. 1993;25:71-80
55. Letter to the editor: standardized use of the terms "sedentary" and "sedentary behaviours". Appl Physiol Nutr Metab. 2012;37:540-2
56. Tremblay MS, Aubert S, Barnes JD, Saunders TJ, Carson V, Latimer-Cheung AE, et al.. Sedentary Behavior Research Network (SBRN) – Terminology Consensus Project process and outcome. Int J Behav Nutr Phys Act. 2017;14:75
57. Saint-Maurice PF, Troiano RP, Matthews CE, Kraus WE. Moderate-to-Vigorous Physical Activity and All-Cause Mortality: Do Bouts Matter? J Am Heart Assoc. 2018;7
58. Strath SJ, Kaminsky LA, Ainsworth BE, Ekelund U, Freedson PS, Gary RA, et al.. Guide to the assessment of physical activity: Clinical and research applications: a scientific statement from the American Heart Association. Circulation. 2013;128:2259-79
59. Chaput J-P, Carson V, Gray CE, Tremblay MS. Importance of All Movement Behaviors in a 24 Hour Period for Overall Health. Int J Environ Res Public Health. 2014;11:12575-81
60. Matthews CE, Moore SC, Sampson J, Blair A, Xiao Q, Keadle SK, et al.. Mortality Benefits for Replacing Sitting Time with Different Physical Activities. Med Sci Sports Exerc. 2015;47:1833-40
61. Dohrn IM, Kwak L, Oja P, Sjostrom M, Hagstromer M. Replacing sedentary time with physical activity: a 15-year follow-up of mortality in a national cohort. Clin Epidemiol. 2018;10:179-86

62. Saint-Maurice PF, Troiano RP, Berrigan D, Kraus WE, Matthews CE. Volume of Light Versus Moderate-to-Vigorous Physical Activity: Similar Benefits for All-Cause Mortality? J Am Heart Assoc. 2018;7

63. Buman MP, Hekler EB, Haskell WL, Pruitt L, Conway TL, Cain KL, et al.. Objective light-intensity physical activity associations with rated health in older adults. Am J Epidemiol. 2010;172:1155-65

64. Ekelund U, Steene-Johannessen J, Brown WJ, Fagerland MW, Owen N, Powell KE, et al.. Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonised meta-analysis of data from more than 1 million men and women. Lancet. 2016

65. Bauman AE, Reis RS, Sallis JF, Wells JC, Loos RJF, Martin BW. Correlates of physical activity: why are some people physically active and others not? Lancet. 2012;380

66. Owen N, Healy GN, Matthews CE, Dunstan DW. Too much sitting: the population health science of sedentary behavior. Exerc Sport Sci Rev. 2010;38

67. Wilmot EG, Edwardson CL, Achana FA, Davies MJ, Gorely T, Gray LJ, et al.. Sedentary time in adults and the association with diabetes, cardiovascular disease and death: systematic review and meta-analysis. Diabetologia. 2012;55:2895-905

68. Edwardson CL, Gorely T, Davies MJ, Gray LJ, Khunti K, Wilmot EG, et al.. Association of sedentary behaviour with metabolic syndrome: a meta-analysis. PLoS One. 2012;7:e34916

69. Brocklebank LA, Falconer CL, Page AS, Perry R, Cooper AR. Accelerometer-measured sedentary time and cardiometabolic biomarkers: A systematic review. Prev Med. 2015;76:92-102

70. Biswas A, Alter DA. Sedentary Time and Risk for Mortality. Ann Intern Med. 2015;162:875-6

71. Hamilton MT, Hamilton DG, Zderic TW. Role of low energy expenditure and sitting in obesity, metabolic syndrome, type 2 diabetes, and cardiovascular disease. Diabetes. 2007;56:2655-67

72. Healy GN, Dunstan DW, Salmon J, Cerin E, Shaw JE, Zimmet PZ, et al.. Breaks in sedentary time: beneficial associations with metabolic risk. Diabetes Care. 2008;31:661-6

73. Healy GN, Matthews CE, Dunstan DW, Winkler EA, Owen N. Sedentary time and cardio-metabolic biomarkers in US adults: NHANES 2003-06. Eur Heart J. 2011;32:590-7

74. Chastin SF, Egerton T, Leask C, Stamatakis E. Meta-analysis of the relationship between breaks in sedentary behavior and cardiometabolic health. Obesity (Silver Spring, Md). 2015;23:1800-10

75. Dunstan DW, Kingwell BA, Larsen R, Healy GN, Cerin E, Hamilton MT, et al. Breaking up prolonged sitting reduces postprandial glucose and insulin responses. Diabetes Care. 2012;35:976-83

76. Chau JY, Grunseit AC, Chey T, Stamatakis E, Brown WJ, Matthews CE, et al. Daily sitting time and all-cause mortality: a meta-analysis. PLoS One. 2013;8:e80000

77. Buman MP, Winkler EA, Kurka JM, Hekler EB, Baldwin CM, Owen N, et al.. Reallocating time to sleep, sedentary behaviors, or active behaviors: associations with cardiovascular disease risk biomarkers, NHANES 2005-2006. Am J Epidemiol. 2014;179:323-34

78. Hamer M, Hackett RA, Bostock S, Lazzarino AI, Carvalho LA, Steptoe A. Objectively assessed physical activity, adiposity, and inflammatory markers in people with type 2 diabetes. BMJ Open Diabetes Res Care. 2014;2:e000030

79. Mekary RA, Feskanich D, Malspeis S, Hu FB, Willett WC, Field AE. Physical activity patterns and prevention of weight gain in premenopausal women. Int J Obes (Lond). 2009;33:1039-47

80. Yrkesföreningar för fysisk aktivitet. FYSS 2017: Fysisk aktivitet i sjukdomsprevention och sjukdomsbehandling.[3., rev.uppl.]2016.

81. American Diabetes Association. 1. Strategies for Improving Care. Diabetes Care. 2015;39:S6

82. Tudor-Locke C, Craig CL, Brown WJ, Clemes SA, De Cocker K, Giles-Corti B, Hatano Y, Inoue S, Matsudo SM, Mutrie N, Oppert J-M, Rowe DA, Schmidt MD, Schofield GM, Spence JC, Teixeira PJ, Tully MA, Blair SN: How many steps/day are enough? For adults. Int J Behav Nutr Phys Act. 10.1186/1479-5868-8-79.

83. Tudor-Locke C, Craig CL, Aoyagi Y, Bell RC, Croteau KA, De Bourdeaudhuij I, et al.. How many steps/day are enough? For older adults and special populations. Int J Behav Nutr Phys Act. 2011;8:80

84. Tudor-Locke C, Craig CL, Thyfault JP, Spence JC. A step-defined sedentary lifestyle index: <5000 steps/day. Appl Physiol Nutr Metab. 2013;38:100-14

85. Dempsey PC, Owen N, Biddle SJ, Dunstan DW. Managing sedentary behavior to reduce the risk of diabetes and cardiovascular disease. Curr Diab Rep. 2014;14:522

86. Prince SA, Saunders TJ, Gresty K, Reid RD. A comparison of the effectiveness of physical activity and sedentary behaviour interventions in reducing sedentary time in adults: a systematic review and meta-analysis of controlled trials. Obesity Reviews. 2014;15:905-19

87. Inzucchi SE, Bergenstal RM, Buse JB, Diamant M, Ferrannini E, Nauck M, et al.. Management of hyperglycemia in type 2 diabetes: a patient-centered approach: position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care. 2012;35:1364-79.

88. Haas L, Maryniuk M, Beck J, Cox CE, Duker P, Edwards L, et al.. National standards for diabetes self-management education and support. Diabetes Care. 2014;37 Suppl 1:S144-53

89. Vuori IM, Lavie CJ, Blair SN. Physical activity promotion in the health care system. Mayo Clin Proc. 2013;88:1446-61

90. Lion A, Vuillemin A, Thornton JS, Theisen D, Stranges S, Ward M. Physical activity promotion in primary care: a Utopian quest? Health Prom Int. 2018;Jun 8.

91. Physical activity: brief advice for adults in primary care. NICE National Institute for Health and Care Excellence, 2013.

92. Socialstyrelsen. Nationella riktlinjer för sjukdomsförebyggande metoder. The National Board of Health and Welfare, Sweden. 2011.

93. Socialstyrelsen. Nationella riktlinjer för prevention och behandling vid ohälsosamma levnadsvanor [Elektronisk resurs]. Stockholm: 2017. [28 August 2018] Availaible from https://www.socialstyrelsen.se/riktlinjer/nationellariktlinjer/preventionochbehandlingvidohalsosammalevnadsvanor

94. Alothman S, Yahya A, Rucker J, Kluding PM. Effectiveness of Interventions for Promoting Objectively Measured Physical Activity of Adults With Type 2 Diabetes: A Systematic Review. Journal of physical activity & health. 2017;14:408-15

95. Miller WR, Rollnick S. Motivational interviewing : helping people change. New York, NY: Guilford Press; 2013.

96. Utbildning.se. Kurser i motiverande samtal (MI). [28 August 2018]. Availaible from: https://www.utbildning.se/kurs/motiverande-samtal

97. O'Halloran PD, Blackstock F, Shields N, Holland A, Iles R, Kingsley M, et al.. Motivational interviewing to increase physical activity in people with chronic health conditions: a systematic review and meta-analysis. Clin Rehab. 2014;28:1159-71

98. Christie D, Channon S. The potential for motivational interviewing to improve outcomes in the management of diabetes and obesity in paediatric and adult populations: a clinical review. Diabetes Obes Metab. 2014;16:381-7

99. Ekong G, Kavookjian J. Motivational interviewing and outcomes in adults with type 2 diabetes: A systematic review. Pat Educ Coun. 2016;99:944-52

100. Soderlund PD. Effectiveness of motivational interviewing for improving physical activity self-management for adults with type 2 diabetes: A review. Chronic Illn. 2018;14:54-68

101. Greaves CJ, Sheppard KE, Abraham C, Hardeman W, Roden M, Evans PH, et al.. Systematic review of reviews of intervention components associated with increased effectiveness in dietary and physical activity interventions. BMC Public Health. 2011;11:119

102.De Greef K, Deforche B, Tudor-Locke C, De Bourdeaudhuij I. Increasing physical activity in Belgian type 2 diabetes patients: a three-arm randomized controlled trial. Int J Behav Med. 2011;18:188-98

103.Deakin T, McShane CE, Cade JE, Williams RD. Group based training for self-management strategies in people with type 2 diabetes mellitus. Cochrane Database Syst Rev. 2005:CD003417

104.Patientutbildning vid diabetes : en systematisk litteraturöversikt. Stockholm: Statens beredning för medicinsk utvärdering; 2009.

105.Cradock KA, G OL, Finucane FM, Gainforth HL, Quinlan LR, Ginis KA. Behaviour change techniques targeting both diet and physical activity in type 2 diabetes: A systematic review and meta-analysis. Int J Behav Nutr Phys Act. 2017;14:18

106.Odgers-Jewell K, Ball LE, Kelly JT, Isenring EA, Reidlinger DP, Thomas R. Effectiveness of group-based self-management education for individuals with Type 2 diabetes: a systematic review with meta-analyses and meta-regression. Diabet Med. 2017;34:1027-39

107.Tudor-Locke C, Lutes L. Why do pedometers work?: a reflection upon the factors related to successfully increasing physical activity. Sports Med (Auckland, NZ). 2009;39:981-93

108.Qiu S, Cai X, Chen X, Yang B, Sun Z. Step counter use in type 2 diabetes: a meta-analysis of randomized controlled trials. BMC Med. 2014;12:36

109.Vaes AW, Cheung A, Atakhorrami M, Groenen MTJ, Amft O, Franssen FME, et al.. Effect of 'activity monitor-based' counseling on physical activity and health-related outcomes in patients with chronic diseases: A systematic review and meta-analysis. Annals of Medicine. 2013;45:397-412

110.Baskerville R, Ricci-Cabello I, Roberts N, Farmer A. Impact of accelerometer and pedometer use on physical activity and glycaemic control in people with Type 2 diabetes: a systematic review and meta-analysis. Diabet Med. 2017;34:612-20

111.Cai X, Qiu SH, Yin H, Sun ZL, Ju CP, Zugel M, et al.. Pedometer intervention and weight loss in overweight and obese adults with Type 2 diabetes: a meta-analysis. Diabet Med. 2016;33:1035-44

112.De Greef K, Deforche B, Tudor-Locke C, De Bourdeaudhuij I. A cognitive-behavioural pedometer-based group intervention on physical activity and sedentary behaviour in individuals with type 2 diabetes. Health Educ Res. 2010;25:724-36

113.Jennersjo P, Ludvigsson J, Lanne T, Nystrom FH, Ostgren CJ. Pedometer-determined physical activity level and change in arterial stiffness in Type 2 diabetes over 4 years. Diabet Med. 2016;33:992-7

114.Fitzsimons CF, Baker G, Gray SR, Nimmo MA, Mutrie N. Does physical activity counselling enhance the effects of a pedometer-based intervention over the long-term: 12-month findings from the Walking for Wellbeing in the west study. BMC Public Health. 2012;12:206

115.FaR® : individanpassad skriftlig ordination av fysisk aktivitet. Östersund: Statens folkhälsoinstitut; 2011.

116.Borjesson M, Arvidsson D, Blomqvist Å, Daxberg e-l, Jonsdottir I, Lundqvist S, et al.. Efficacy of the Swedish model for physical activity on prescription. Västra Götalandsregionen, Sahlgrenska Universitetssjukhuset, HTA-Centrum: 2018.

117.Pavey TG, Anokye N, Taylor AH, Trueman P, Moxham T, Fox KR, et al.. The clinical effectiveness and cost-effectiveness of exercise referral schemes: a systematic review and economic evaluation. Health Technol Assess. 2011;15:i-xii, 1-254

118.Avery L, Flynn D, van Wersch A, Sniehotta FF, Trenell MI. Changing Physical Activity Behavior in Type 2 Diabetes: A systematic review and meta-analysis of behavioral interventions. Diabetes Care. 2012;35:2681-9

119.Rosenstock IM, Strecher VJ, Becker MH. Social learning theory and the Health Belief Model. Health Educ Q. 1988;15:175-83

120.Prochaska JO, DiClemente CC, Norcross JC. In search of how people change. Applications to addictive behaviors. Am Psychol. 1992;47:1102-14

121.Bandura A. Social foundations of thought and action : a social cognitive theory. Englewood Cliffs, N.J.: Prentice-Hall; 1986.

122.Kwasnicka D, Dombrowski SU, White M, Sniehotta F. Theoretical explanations for maintenance of behaviour change: a systematic review of behaviour theories. Health Psychol Rev. 2016;10:277-96

123.Abraham C, Michie S. A taxonomy of behavior change techniques used in interventions. Health Psychol. 2008;27

124. Michie S, Ashford S, Sniehotta FF, Dombrowski SU, Bishop A, French DP. A refined taxonomy of behaviour change techniques to help people change their physical activity and healthy eating behaviours: the CALO-RE taxonomy. Psychol Health. 2011;26:1479-98

125. Michie S, Richardson M, Johnston M, Abraham C, Francis J, Hardeman W, et al.. The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: building an international consensus for the reporting of behavior change interventions. Ann Behav Med : a publication of the Society of Behavioral Medicine. 2013;46:81-95

126. Presseau J, Ivers NM, Newham JJ, Knittle K, Danko KJ, Grimshaw JM. Using a behaviour change techniques taxonomy to identify active ingredients within trials of implementation interventions for diabetes care. Implement Sci. 2015;10:55

127. Williams SL, French DP. What are the most effective intervention techniques for changing physical activity self-efficacy and physical activity behaviour--and are they the same? Health Educ Res. 2011;26:308-22

128. Olander EK, Fletcher H, Williams S, Atkinson L, Turner A, French DP. What are the most effective techniques in changing obese individuals' physical activity self-efficacy and behaviour: a systematic review and meta-analysis. Int J Behav Nutr Phys Act. 2013;10:1-15

129. Avery L, Flynn D, Dombrowski SU, van Wersch A, Sniehotta FF, Trenell MI. Successful behavioural strategies to increase physical activity and improve glucose control in adults with Type 2 diabetes. Diabet Med. 2015;32:1058-62

130. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M. Developing and evaluating complex interventions: the new Medical Research Council guidance. Int J Nurs Stud 2013;50:587-92

131. Fraser MW. Intervention research: developing social programs. Oxford: Oxford University Press; 2009.

132. Greenfield T, Greener S. Research Methods for Postgraduates. Chichester, UK: John Wiley & Sons; 2016.

133. Schulz KF, Altman DG, Moher D. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. BMJ. 2010;340

134. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al.. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. BMJ.2014;348

135. Glasgow RE, Vogt TM, Boles SM. Evaluating the public health impact of health promotion interventions: the RE-AIM framework. Am J Public Health. 1999;89:1322-7

136. Lambert JD, Greaves CJ, Farrand P, Cross R, Haase AM, Taylor AH. Assessment of fidelity in individual level behaviour change interventions promoting physical activity among adults: a systematic review. BMC Public Health. 2017;17:765

137. Schinckus L, Van den Broucke S, Housiaux M. Assessment of implementation fidelity in diabetes self-management education programs: A systematic review. Patient Educ Couns. 2014;96:13-21

138. McCambridge J, Kypri K, Elbourne D. In randomization we trust? There are overlooked problems in experimenting with people in behavioral intervention trials. J Clin Epidemiol. 2014;67:247-53

139. MacNeill V, Foley M, Quirk A, McCambridge J. Shedding light on research participation effects in behaviour change trials: a qualitative study examining research participant experiences. BMC Public Health. 2016;16:91

140. McCambridge J, Witton J, Elbourne DR. Systematic review of the Hawthorne effect: new concepts are needed to study research participation effects. J Clin Epidemiol. 2014;67:267-77

141. Krippendorff K. Content analysis : an introduction to its methodology. Thousand Oaks, Calif. ;: SAGE; 2013.

142. Elo S, Kyngas H. The qualitative content analysis process. J Adv Nurs. 2008;62:107-15

143. Craig CL, Marshall AL, Sjostrom M, Bauman AE, Booth ML, Ainsworth BE, et al.. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc. 2003;35:1381-95

144. Taylor-Piliae RE, Norton LC, Haskell WL, Mahbouda MH, Fair JM, Iribarren C, et al.. Validation of a new brief physical activity survey among men and women aged 60-69 years. Am J Epidemiol. 2006;164:598-606

145. Ainsworth BE, Macera C, editors. Physical activity and public health practice. Boca Raton, Fla: CRC Press: 2012.

146. Ainsworth B, Cahalin L, Buman M, Ross R. The current state of physical activity assessment tools. Prog Cardiovasc Dis. 2015;57:387-95

147. Steeves JA, Bowles HR, McClain JJ, Dodd KW, Brychta RJ, Wang J, et al.. Ability of thigh-worn ActiGraph and activPAL monitors to classify posture and motion. Med Sci Sports Exerc. 2015;47:952-9

148. Grant PM, Ryan CG, Tigbe WW, Granat MH. The validation of a novel activity monitor in the measurement of posture and motion during everyday activities. Br J Sports Med. 2006;40:992-7

149. Freedson PS, Melanson E, Sirard J. Calibration of the Computer Science and Applications, Inc. accelerometer. Med Sci Sports Exerc. 1998;30:777-81

150. Tudor-Locke C, Han H, Aguiar EJ, Barreira TV, Schuna Jr JM, Kang M, et al.. How fast is fast enough? Walking cadence (steps/min) as a practical estimate of intensity in adults: a narrative review. Br J Sports Med 2018;52:776

151. Ainsworth BE, Haskell WL, Herrmann SD, Meckes N, Bassett DR, Jr., Tudor-Locke C, et al.. 2011 Compendium of Physical Activities: a second update of codes and MET values. Med Sci Sports Exerc. 2011;43:1575-81

152. Matthews CE, Chen KY, Freedson PS, Buchowski MS, Beech BM, Pate RR, et al.. Amount of time spent in sedentary behaviors in the United States, 2003-2004. Am J Epidemiol. 2008;167:875-81

153. Hoenig MR. MRI sagittal abdominal diameter is a stronger predictor of metabolic syndrome than visceral fat area or waist circumference in a high-risk vascular cohort. Vasc Health Risk Manag. 2010;6:629-33

154. Mason C, Katzmarzyk PT. Variability in waist circumference measurements according to anatomic measurement site. Obesity (Silver Spring, Md). 2009;17:1789-95

155. Topouchian JA, El Assaad MA, Orobinskaia LV, El Feghali RN, Asmar RG. Validation of two automatic devices for self-measurement of blood pressure according to the International Protocol of the European Society of Hypertension: the Omron M6 (HEM-7001-E) and the Omron R7 (HEM 637-IT). Blood Press Monit. 2006;11:165-71

156. Sepp H, Becker W. Enkätfrågor om kost och fysisk aktivitet bland vuxna – Underlag till urval av frågor i befolkningsinriktade enkäter. [In Swedish] The National Food Agency, Sweden. 2004.

157. Kelly LA, McMillan DGE, Anderson A, Fippinger M, Fillerup G, Rider J. Validity of actigraphs uniaxial and triaxial accelerometers for assessment of physical activity in adults in laboratory conditions. BMC Medical Physics. 2013;13:5-

158. Choi L, Liu Z, Matthews CE, Buchowski MS. Validation of accelerometer wear and nonwear time classification algorithm. Med Sci Sports Exerc. 2011;43:357-64

159. Hart TL, Swartz AM, Cashin SE, Strath SJ. How many days of monitoring predict physical activity and sedentary behaviour in older adults? Int J Behav Nutr Phys Act. 2011;8:62

160. Graneheim UH, Lundman B. Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness. Nurse Educ Today. 2004;24:105-12

161. Gueorguieva R, Krystal JH. Move over ANOVA: progress in analyzing repeated-measures data and its reflection in papers published in the Archives of General Psychiatry. Arch Gen Psychiatry. 2004;61:310-7

162. Lindström J, Neumann A, Sheppard KE, Gilis-Januszewska A, Greaves CJ, Handke U, et al.. Take Action to Prevent Diabetes – The IMAGE Toolkit for the Prevention of Type 2 Diabetes in Europe. Horm Metab Res. 2010;42:S37-S55

163. Socialstyrelsen. Motiverande samtal enligt MI-metoderna (MI, AMI och MET) i syfte att förbättra glukoskontrollen: [cited 2018 23 August]. Available from: http://www.socialstyrelsen.se/nationellariktlinjerfordiabetesvard/sokiriktlinjerna/diabetes1.

164. Bravata DM, Smith-Spangler C, Sundaram V, Gienger AL, Lin N, Lewis R, et al.. Using pedometers to increase physical activity and improve health: a systematic review. JAMA. 2007;298:2296-304

165. Soroush A, Der Ananian C, Ainsworth BE, Belyea M, Poortvliet E, Swan PD, et al.. Effects of a 6-Month Walking Study on Blood Pressure and Cardiorespiratory Fitness in U.S. and Swedish Adults: ASUKI Step Study. Asian J Sports Med. 2013;4:114-24

166. Phillips SM, Cadmus-Bertram L, Rosenberg D, Buman MP, Lynch BM. Wearable Technology and Physical Activity in Chronic Disease: Opportunities and Challenges. Am J Prev Med. 2018;54:144-50

167. Bonn SE, Alexandrou C, Hjörleifsdottir Steiner K, Wiklander K, Östenson C-G, Löf M, et al.. App-technology to increase physical activity among patients with diabetes type 2 - the DiaCert-study, a randomized controlled trial. BMC Public Health. 2018;18:119

168. Yates T, Davies M, Gorely T, Bull F, Khunti K. Effectiveness of a pragmatic education program designed to promote walking activity in individuals with impaired glucose tolerance: a randomized controlled trial. Diabetes Care. 2009;32:1404-10

169. Bjorgaas MR, Vik JT, Stolen T, Lydersen S, Grill V. Regular use of pedometer does not enhance beneficial outcomes in a physical activity intervention study in type 2 diabetes mellitus. Metabolism. 2008;57

170. Cersosimo E, Triplitt C, Solis-Herrera C, Mandarino LJ, DeFronzo RA. Pathogenesis of Type 2 Diabetes Mellitus. In: De Groot LJ, Chrousos G, Dungan K, Feingold KR, Grossman A, Hershman JM, et al.., editors. Endotext. South Dartmouth MA: MDText.com, Inc.; 2000.

171. Booth FW, Roberts CK, Thyfault JP, Ruegsegger GN, Toedebusch RG. Role of Inactivity in Chronic Diseases: Evolutionary Insight and Pathophysiological Mechanisms. Physiological reviews. 2017;97:1351-402

172. van Dongen EJ, Duijzer G, Jansen SC, Ter Beek J, Huijg JM, Leerlooijer JN, et al.. Process evaluation of a randomised controlled trial of a diabetes prevention intervention in Dutch primary health care: the SLIMMER study. Public Health Nutr. 2016:1-12

173. Linmans JJ, van Rossem C, Knottnerus JA, Spigt M. Exploring the process when developing a lifestyle intervention in primary care for type 2 diabetes: a longitudinal process evaluation. Public Health. 2015;129:52-9

174. Plotnikoff RC, Karunamuni N, Courneya KS, Sigal RJ, Johnson JA, Johnson ST. The Alberta Diabetes and Physical Activity Trial (ADAPT): a randomized trial evaluating theory-based interventions to increase physical activity in adults with type 2 diabetes. Ann Behav Med 2013;45:45-56

175. Johnson ST, Mundt C, Qiu W, Soprovich A, Wozniak L, Plotnikoff RC, et al.. Increase in Daily Steps After an Exercise Specialist Led Lifestyle Intervention for Adults With Type 2 Diabetes In Primary Care: A Controlled Implementation Trial. J Phys Act Health. 2015;12:1492-9

176. De Greef KP, Deforche BI, Ruige JB, Bouckaert JJ, Tudor-Locke CE, Kaufman JM, et al.. The effects of a pedometer-based behavioral modification program with telephone support on physical activity and sedentary behavior in type 2 diabetes patients. Patient Educ Couns 2011;84:275-9

177. Socialstyrelsen. Nationella riktlinjer för diabetesvården 2010 : stöd för styrning och ledning.Socialstyrelsen. Stockholm:; 2010.

178. Dasgupta K, Rosenberg E, Joseph L, Cooke AB, Trudeau L, Bacon SL, et al.. Physician step prescription and monitoring to improve ARTERial health (SMARTER): A randomized controlled trial in patients with type 2 diabetes and hypertension. Diabetes Obes Metab. 2017;19:695-704

179. Andrews RC, Cooper AR, Montgomery AA, Norcross AJ, Peters TJ, Sharp DJ, et al.. Diet or diet plus physical activity versus usual care in patients with newly diagnosed type 2 diabetes: the Early ACTID randomised controlled trial. Lancet. 2011;378:129-39

180. Liubaoerjijin Y, Terada T, Fletcher K, Boule NG. Effect of aerobic exercise intensity on glycemic control in type 2 diabetes: a meta-analysis of head-to-head randomized trials. Acta Diabetol. 2016;53:769-81

181. Rohling M, Herder C, Roden M, Stemper T, Mussig K. Effects of Long-Term Exercise Interventions on Glycaemic Control in Type 1 and Type 2 Diabetes: a Systematic Review. Exp Clin Endocrinol Diabetes 2016;124:487-94

182. Information från Läkemedelsverket nr 4 2017 [Elektronisk resurs]: Läkemedelsverket; 2017. [28 August 2018]. Availaible from: https://lakemedelsverket.se/upload/halso-och-sjukvard/behandlingsrekommendationer/Information-fran-lakemedelsverket-nr-4-2017-behandlingsrekommendation.pdf

183. Moyers TB, Rowell LN, Manuel JK, Ernst D, Houck JM. The Motivational Interviewing Treatment Integrity Code (MITI 4): Rationale, preliminary reliability and validity. J Subst Abuse Treat. 2016;65:36-42

184. Lynsay M, Alison K, Mary M, Nanette M, Ann G, Andrew K. The feasibility of a physical activity intervention for adults within routine diabetes care: a process evaluation. Practical Diabetes. 2017;34:7-12a

185. Furness C, Howard E, Limb E, Cook DG, Kerry S, Wahlich C, et al.. Relating process evaluation measures to complex intervention outcomes: findings from the PACE-UP primary care pedometer-based walking trial. Trials. 2018;19:58

186. De Greef K, Deforche B, Tudor-Locke C, De Bourdeaudhuij I. A cognitive-behavioural pedometer-based group intervention on physical activity and sedentary behaviour in individuals with type 2 diabetes. Health Educ Res 2010.Oct;25(5):724-36.

187. Normansell R, Smith J, Victor C, Cook DG, Kerry S, Iliffe S, et al.. Numbers are not the whole story: a qualitative exploration of barriers and facilitators to increased physical activity in a primary care based walking intervention. BMC Public Health. 2014;14:1272

188. Van Dyck D, De Greef K, Deforche B, Ruige J, Tudor-Locke CE, Kaufman JM, et al.. Mediators of physical activity change in a behavioral modification program for type 2 diabetes patients. Int J Behav Nutr Phys Act. 2011;8:105

189. den Braver NR, de Vet E, Duijzer G, Ter Beek J, Jansen SC, Hiddink GJ, et al.. Determinants of lifestyle behavior change to prevent type 2 diabetes in high-risk individuals. Int J Behav Nutr Phys Act. 2017;14:78

190. Johnson ST, Lubans DR, Mladenovic AB, Plotnikoff RC, Karunamuni N, Johnson JA. Testing social-cognitive mediators for objective estimates of physical activity from the Healthy Eating and Active Living for Diabetes in Primary Care Networks (HEALD-PCN) study. Psychol Health Med 2016;21:945-53

191. Van Dyck D, De Greef K, Deforche B, Ruige J, Bouckaert J, Tudor-Locke CE, et al.. The relationship between changes in steps/day and health outcomes after a pedometer-based physical activity intervention with telephone support in type 2 diabetes patients. Health Educ Res. 2013;28:539-45

192. Yates T, Henson J, Edwardson C, Dunstan D, Bodicoat DH, Khunti K, et al.. Objectively measured sedentary time and associations with insulin sensitivity: Importance of reallocating sedentary time to physical activity. Prev Med. 2015;76:79-83

193. Falconer CL, Page AS, Andrews RC, Cooper AR. The Potential Impact of Displacing Sedentary Time in Adults with Type 2 Diabetes. Med Sci Sports Exerc. 2015;47:2070-5

194. Healy GN, Winkler EA, Brakenridge CL, Reeves MM, Eakin EG. Accelerometer-derived sedentary and physical activity time in overweight/obese adults with type 2 diabetes: cross-sectional associations with cardiometabolic biomarkers. PLoS One. 2015;10:e0119140

195. Ekblom-Bak E, Ekblom O, Bergstrom G, Borjesson M. Isotemporal substitution of sedentary time by physical activity of different intensities and bout lengths, and its associations with metabolic risk. Eur J Prev Cardiol. 2016;23:967-74

196. Sardinha LB, Magalhães JP, Santos DA, Júdice PB. Sedentary Patterns, Physical Activity, and Cardiorespiratory Fitness in Association to Glycemic Control in Type 2 Diabetes Patients. Front Physiol. 2017;8

197. Healy GN, Winkler EAH, Owen N, Anuradha S, Dunstan DW. Replacing sitting time with standing or stepping: associations with cardio-metabolic risk biomarkers. Eur Heart J. 2015;36:2643