UNIVERSITY OF COPENHAGEN
FACULTY OF HEALTH AND MEDICAL SCIENCES

PhD Thesis
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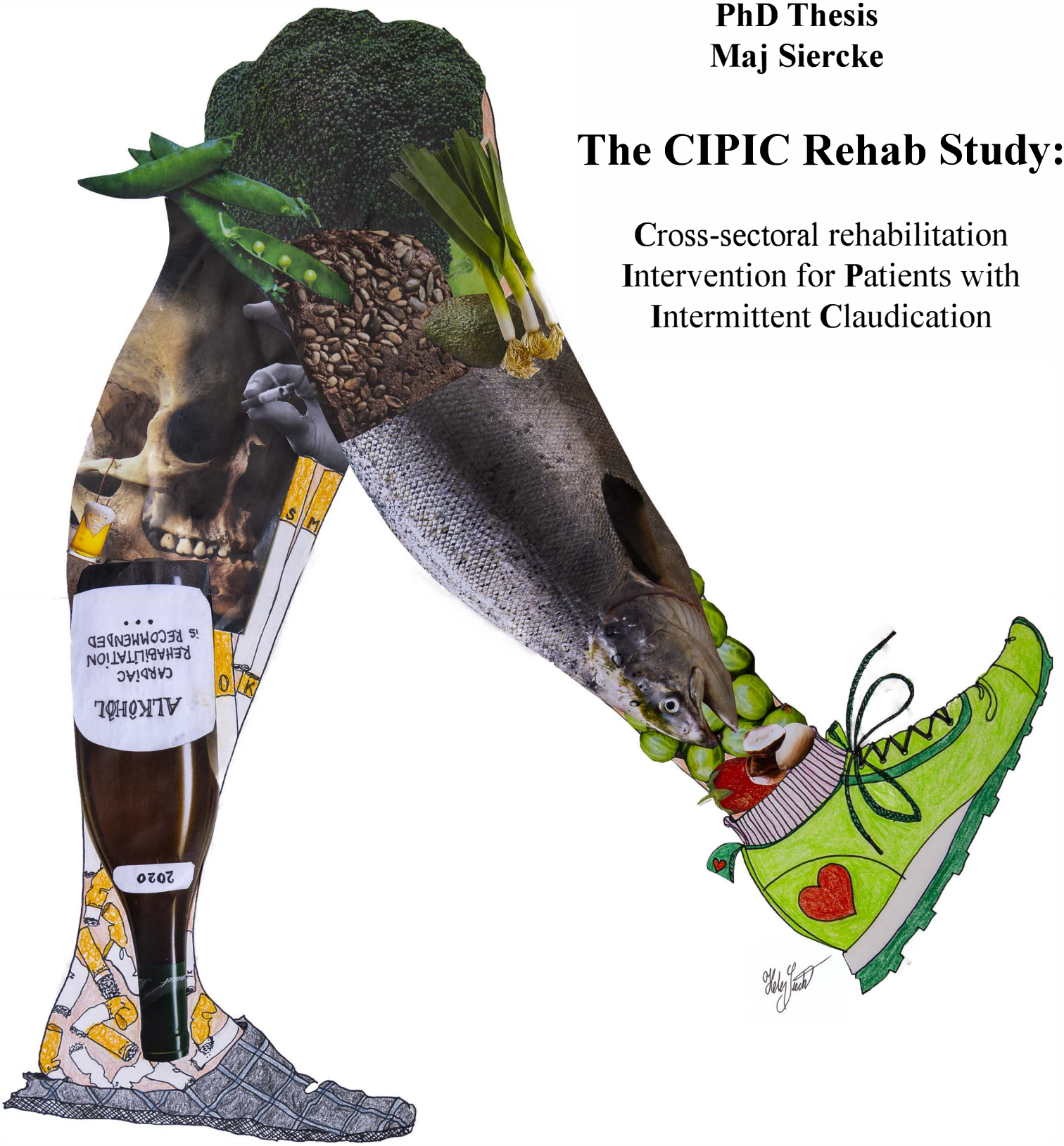
The CIPIC Rehab Study:

Cross-sectoral rehabilitation Intervention for Patients with Intermittent Claudication



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Title:
The CIPIC Rehab Study -Cross-sectoral rehabilitation for patients with intermittent claudication

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Preface and Acknowledgements

Firstly, I want to express my gratitude for having had the privilege of being a PhD student during the last three years at the Department of Vascular Surgery, Rigshospitalet. This PhD thesis was made possible by the great scientific guidance of my supervisor, professor MD, head of department **Henrik Sillesen,** and leading head nurse **Margit Roed** who was, and still is, visionary and insistent on finding a way to make this project possible. I would like to thank my principal supervisor **Selina Kikkenborg Berg** for her helpful scientific guidance. I also would like to thank my co-supervisor, **Malene Missel,** for her great knowledge and guidance in the field of qualitative scientific research, and **Lise Pyndt Jørgensen** for her insight into power calculations and treadmill tests. A special thank you to **Dorthe Overgaard** for her helpful guidance in mixed methods research. I gratefully acknowledge the financial support donated by Danish Regions, Capital Region of Denmark - Center for Clinical Research and Prevention, the Danish Nurses Organization, and Novo Nordisk Foundation.

The journey before I became a PhD student has been long. Life-long learning has always been an important part of my life. In my working life, I have been 12 years at the Department of Cardiology, Herlev Hospital, where I became the leader and developer of an interdisciplinary rehabilitation programme on the basis of work carried out in my Master's Thesis. At that time, the first thoughts about a PhD came to my mind in the field of cardiology. Instead, I worked for 12 years as a senior lecturer at the School of Nursing, University College Copenhagen – always with a focus on clinical training, acute and cardiac care, and rehabilitation. A Master's in learning and innovative change qualified me to do a PhD study. My interest was in unintended events in health care, and I had an excellent cooperation with Professor **Henning Boje Andersen** from the Technical University of Denmark on that subject and the possibility of a research project. Many thanks to Henning who encouraged me to go further on, and for hosting me as a participant in his research environment when I became a PhD student.

In June 2017, I went to a job interview at the Department of Vascular Surgery for this PhD project. At that time, I thought if they do not hire me for this project, it would be because I simply was not meant to do a PhD. Fortunately, I was hired and began at the department in September 2017… and the rest is history. However, the point is that I had returned to the cardiovascular field and development of a cardiac rehabilitation programme, now for patients with intermittent

claudication. Project leadership from earlier was very helpful in launching the project in time with the Healthcare Centre in Albertslund Municipality. However, it also took all my time - more than full time for several months, and therefore my enrolment at the University of Copenhagen did not start before January 2019, with all the great PhD courses. Clinical research is not possible without help from positive colleagues. Thank you to **all the staff** in the Vascular outpatient Department who helped me find patients, cheering me on and celebrating milestones along the way. It meant a lot. Thank you to **Signe Westh Christensen** for assisting follow-up treadmill tests – you were never more than a text message and four floors away. Thank you to **Prashanth Sivapalan, Louise Holm, Line Højlund** and **Cecilie Bannebjerg** for helping me with data registration, budding nurses to be proud of. A special thank you to **Lau Caspar Thygesen** for assisting me with statistical analyses and support and to **Peter Kristian Lundø for** technical image support. Thank you to **Lise Koefoed** for always being helpful and your great sense of humour. Thank you to the very helpful "PhD office": Alexander Zielinski, Magdalena Broda, Karin Yeung and Majken Lyhne Jessen. I also want to thank **Lise Westerlin** and **Sally Jakobsen** for their support, especially through hard times in my private life in 2019. Thank you to my friends and family for love and support. Especially thank you to amazing **Jan Kinch, Morten Glavind, Søsserr Grimshaw-Aagaard** and **Pernille Thomsen** for "lifesaving" support. A special thank you to my twin sister **Helen Siercke** who made a little artwork for my thesis's front page. I will sincerely thank all patients who have participated in my research. My thesis would not have been possible without your support. Normally the preface would end by the last dot above, but a state of emergency came to our society. My PhD was put on hold for a period while I went to COVIMA at Rigshospitalet, working as a nurse with COVID-19 patients. It was hard work in 8-hour shifts dressed in very warm protective equipment. In this state of emergency, it was quite an experience, unrealistic and like being in a bad dream. The cooperation and team spirit were amazing and despite so many compromises along the way, there is a lot to be proud of. It reminded me why I became a nurse and why I will always be proud of it. In that journey through COVID-19, I was lucky that I only lost five patients to follow up due to the lockdown at this strange time in history when many Consort Flow Diagrams around the world must contain "lost to follow up - because of the COVID-19 crisis".

Maj Siercke, Copenhagen, June 2021

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List of abbreviation

CIPIC	**C**ross-sectoral rehabilitation **i**ntervention for **p**atients with **i**ntermittent **c**laudication
IC	Intermittent claudication
PAD	Peripheral Artery Disease
ABI	Ankle-brachial index
SET	Supervised Exercise Training/Therapy
PWD	Pain-free walking distance
MWD	Maximal walking distance
RCT	Randomised Clinical Trial
CONSORT	Consolidated standards of reporting trials
COREQ	Consolidated Criteria for Reporting Qualitative Research
HADS	Hospital Anxiety and Depression Scale
VascuQol	The Vascular Quality of Life Questionnaire (VQ6)
TLFB	The Alcohol Timeline Follow back

List of scientific papers

The thesis is based on three scientific papers, which can be found in the appendices.

I. Siercke M, Jørgensen LP, Missel M, Thygesen LC, Blach PP, Sillesen H, Berg SK. Cross-sectoral rehabilitation intervention for patients with intermittent claudication versus usual care for patients in non-operative management - the CIPIC Rehab Study: study protocol for a randomised controlled trial. Trials. 2020;21:105.

II. Siercke M, Jørgensen LP, Missel M, Thygesen LC, Møller SP, Sillesen H, Berg SK. Cardiovascular rehabilitation increases walking distance in patients with intermittent claudication -Results of the CIPIC Rehab study: a randomised controlled trial. European Journal of Vascular and Endovascular Surgery, May 20 2021. In press: https://www.sciencedirect.com/science/article/pii/S1078588421002999

III. Spurred by pedometers, unity and fun exercise: A qualitative study of participation in rehabilitation for patients with intermittent claudication (the CIPIC Rehab study) Journal of Vascular Nursing, June 7 2021. In press: https://www.sciencedirect.com/science/article/pii/S1062030321000510

Dansk resumè (Summary in Danish)

Formålet med denne afhandling er at skabe evidens-baseret viden som beslutningsgrundlag for at tilbyde patienter med åreforkalkning i benene – såkaldt vindueskiggersyndrom (claudicatio intermittens) rehabilitering. Patientgruppen lider af krampende lægsmerter, reduceret gangdistance, fysisk inaktivitet, reduceret helbredsrelateret livskvalitet og social isolation som kan føre til forværring af sygdommen. Hovedparten af patienterne formår ikke at træne på egen hånd da træning er smertefuld og kræver vedholdenhed for at have effekt. Selvom tilstanden på sigt er lige så dødelig som kræft og hjertesygdom, er det en patientgruppe som ikke får tilbudt rehabilitering på lige fod med hjertepatienter som er indskrevet i Sundhedsloven og indgår i Sundhedsstyrelsens forløbsprogrammer for rehabilitering af hjertesygdomme.

Eksisterende kvantitativ forskning (Cochrane-review) har påvist at superviseret fysisk træning er effektivt til at lindre symptomer, mindske hjertekar sygdom, øge livskvalitet og er omkostningseffektivt. Langt de fleste eksisterende studier er foregået i et klinisk set-up med gangtræning på et gangbånd, 1 time 3 x om ugen, hvor fysioterapeuter har understøttet patientens træning. Disse randomiserede kliniske kontrollerede studier er velegnede til at vise effekten af træningen, men efterlader et hul i viden om hvordan et rehabiliteringsforløb skal sammensættes når det skal omsættes i det virkelige liv. Eksisterende systematiske kvalitative studier har opsummeret patienternes opfattelse af barriere, aktiviteter og sygdomsopfattelse og er blevet brugt med det formål at udvikle et relevant patientcentreret program i en kommunal setting. Forskningsprocessen blev udført i følgende faser:

I studie protokollen præsenteres rationale og design af *the CIPIC Rehab Study*: En tværsectoriel rehabiliterings intervention for patienter med claudicatio intermittens (Artikel I).

I studie 1 blev der gennemført et randomiseret klinisk forsøg, hvor patienterne blev allokeret til enten et kommunalt hjerterehabiliterings program tilpasset patienter med claudicatio intermittens eller vanlig behandling. Resultater blev målt på gangdistance, livskvalitet og livsstil. (Artikel II).

I studie 2 blev det undersøgt hvordan patienter med claudicatio intermittens oplevede at deltage i et specialiseret komunalt hjerterehabiliterings program og de forskellige komponenter i rehabiliterings programmet (Artikel III).

Konklusion

Studiet viser at rehabiliteringsprogrammet, som var målrettet patienter med claudicatio intermittens i kommunalt regi, har en statistisk og klinisk effekt på gangdistance, fysisk aktivitet, kost og helbredrelateret livskvalitet, men ikke på smertefri gangdistance og rygning.
Patienterne blev motiveret af varieret og sjov træning faciliteret af fysioterapeuter i kommunalt regi. Træning med andre patienter som en selv, og undervisning af sygeplejerske og diætist, blev opfattet som betydningsfulde faktorer i programmet. Skridttæller blev anset som et stærkt motiverende instrument for den daglige gangtræning, og fremdrift i gangbåndstesten motiverede til at fortsætte træningen. Koordinering via karkirurgisk sygeplejerske med direkte telefonnummer skabte patienttryghed når der var brug for råd og vejledning omkring sygdommen og eventuel klinisk kontrol. Patienterne havde et stærkt ønske om opfølgende træningsmuligheder efter de 12 uger, også med egenbetaling.

English summary

The aim of this thesis is to create evidence-based knowledge about how to set up a rehabilitation programme for patients with atherosclerosis in the legs – intermittent claudication. These patients suffer from cramping leg pain, reduced walking distance, physical inactivity, reduced health-related quality of life, and social isolation, leading to worsening of the disease. The majority of patients are unable to exercise on their own as exercise is painful and requires persistence to be effective. Although the condition is as deadly as heart disease, patients with intermittent claudication are not offered rehabilitation that is as comprehensive as the rehabilitation provided for patients with heart disease (the Danish Health Authority stipulates that patients with heart disease are offered a 12-week structured rehabilitation intervention).
Existing high-level quantitative research on intermittent claudication (Cochrane review) has shown that supervised physical exercise effectively relieves symptoms, reduces cardiovascular disease, increases quality of life, and is cost-effective. The majority of existing studies have taken place in clinical set-ups with supervised exercise training on a treadmill, 1 hour 3 times a week, where physiotherapists have supported the patient's training. These randomised, controlled clinical trials are suitable for demonstrating the effect of the training, but leave a gap in the knowledge on how to set up an effective rehabilitation programme in real-life settings. Existing systematic qualitative studies have summarised patients' perceptions of barriers, activities and disease perception and their results were used in the present study to develop a relevant patient-centred programme in a

municipal setting. A study protocol was developed, and the research process was carried out in the following phases:

The study protocol presented the rationale and design of the CIPIC Rehab study: a **C**ross-sectoral rehabilitation **I**ntervention for **P**atients with **I**ntermittent **C**laudication (Paper I).

Study 1 examined whether a cardiac rehabilitation programme in a community-based setting for patients with intermittent claudication (IC) affects walking ability, quality of life, and changes in health behaviour. The trial investigated a cross-sectoral cardiovascular rehabilitation programme compared with usual care for patients in non-operative management (Paper II)

Study 2 explored how patients with intermittent claudication experience participating in a community-based cardiovascular rehabilitation programme and the various components of the rehabilitation programme (Paper III).

Conclusion

The CIPIC Rehab Study shows that a specialised rehabilitation programme for patients with intermittent claudication in a community-based setting has a statistical and clinical effect on walking distance, physical activity, diet and health-related quality of life, but not on pain-free walking distance and smoking. The patients were motivated by varied and fun training facilitated by municipal physiotherapists and in a setting close to the patients' homes. Patients reported that training with patients similar to themselves and teaching by a nurse and dietitian were perceived as significant positive factors in the programme. Pedometers were a highly motivating instrument for the daily exercise, and progress in the treadmill test motivated patients to continue exercising. Coordination of the patients' participation in the programme by a vascular nurse (to whom patients had a direct telephone number) created a feeling of safety for the patients, as they were able to access advice and guidance about the disease and possible clinical control when needed. The patients had a strong desire for follow-up training options after the 12 weeks, even if they would have to pay for it.

1.0 Introduction

1.1 Scientific background

Cardiovascular disease caused by atherosclerosis is one of the leading causes of morbidity and mortality worldwide (1). Peripheral arterial disease (PAD) is a chronic occlusive arterial disease caused by progressive atherosclerosis (2). The majority of patients with PAD suffer from intermittent claudication (IC). The symptoms of IC are defined as reproducible lower extremity muscular pain that occurs during walking and is relieved by short periods of rest. Patients with IC have lower mobility and activity levels, reduced health-related quality of life, and reduced walking capacity because of burning muscle pain in the legs (3, 4). Those symptoms can result in social isolation, impacting health behaviour and worsening the disease with the risk of atherosclerotic complications and death (2-8). In Western Europe and the USA, 2% of the population of the age of 50-60 years are affected by IC, and this increases to 6-7% in the age range of 65-75 years (9). Intermittent claudication is a marker of systemic atherosclerosis, and is associated with cardiovascular mortality rates of 42% at five years and 65% at ten years. Patients with PAD have a 20% risk of myocardial infarction or stroke, and a 10% risk of death in 5 years. The cumulative 10-year amputation rate is 10% (10). In general mortality from cardiovascular disease has declined, but the social inequality of cardiovascular disease in terms of incidence and mortality has increased, which is also a fact for patients with IC (11). Social inequality is also reflected in the public health care system, as described below.

In Denmark, patients with ischemic heart disease or heart failure are by legislation offered a 12-week structured rehabilitation intervention including supervised exercise training, a smoking cessation course, and advice about healthy diet. This offer does not include patients with IC. Only a few hospitals and municipalities include patients with IC in rehabilitation and most of them fail to meet current guidelines (12). Specific rehabilitation for patients with IC is almost non-existent in Denmark, which has led to call for recommendations of structured, systematic rehabilitation for patients with IC to be acted upon (12).

Current practice in Danish hospitals only involves brief spoken and written advice to patients about quitting smoking, healthy diet and walking exercise in combination with preventive medications with statins and antiplatelet therapy (13, 14). Studies indicate that many patients with IC are not motivated to make health behaviour changes (6, 7, 15).

Non-adherence to the recommended health behaviour changes increases the risk of progression from IC to critical ischaemia and limb amputation (2). Intermittent claudication also has economic costs due to hospitalisation, reduces patient's capacity to be active, and has detrimental consequences for individual patients (16, 17).

Qualitative studies show that patients' treatment beliefs and lack of knowledge and education about IC can be some of the reasons for the associated detrimental consequences for the individual patients (15). Patients with IC are able to adopt exercise programmes if health care providers provide more explicit instructions and address outcome expectations alongside support throughout the process of health behaviour changes (15).

Studies report that patient education about general atherosclerotic disease and nurse-led follow-up programmes can motivate patients and give them competences to participate more and make decisions that promote health-related self-care (18, 19). Hospital-based rehabilitation can be challenging for patients due to time spent on logistics and transportation, which indicates that intervention in a local community setting can improve patients' motivation and adherence to rehabilitation programmes (20, 21). There is a lack of studies that explore the effect of specialised rehabilitation programmes for patients with IC, while the applicability of the existing evidence in the field is limited. Rehabilitation programmes for patients with IC in community-based settings are scarce, and knowledge about how to set up such programmes effectively is poor (22, 23).

1.2 Non-operative therapies for intermittent claudication.

Current guidelines for patients with peripheral arterial disease recommend risk factor modification: tobacco, diet, exercise, and pharmacologic therapies (5, 24).

It is well known that smoking cessation increases walking distances and reduces risk of amputation in patients with PAD (10). Walking exercise is recommended as non-operative therapy for IC, and prescribes walking until onset of leg pain, resting, and then resuming walking.

Multiple randomised trials have shown that 30–60 minutes of walking exercise 3 days per week for six months increases walking distance by more than 100% (10). Findings from a Cochrane review have shown that patients participating in a supervised exercise programme increased their walking ability more than patients who followed a home-based exercise programme or just received advice about walking (25).

Another Cochrane review concludes that patients with IC need to exercise regardless of whether their treatment is non-operative management or revascularisation (26). The CLEVER Study that compared medical therapy and good advice with stent revascularisation and supervised exercise showed a significant positive effect of exercise at 6 and 18 months into treatment (27). Cholesterol-lowering therapy improves pain-free walking distance and reduces cardiovascular events (28). In addition to cholesterol-lowering and lifelong antiplatelet treatment, pharmacological treatment should also target hypertension and glycaemic control (10). Programmes with supervised exercise therapy/training (SET) effectively improve quality of life, walking distance, alleviating symptoms, and reducing cardiovascular risk factors. Studies have also shown that SET is relatively inexpensive and cost-efficient compared with invasive therapies (17, 25, 26, 29). In research about supervised exercise therapy, the intervention typically consists of treadmill walking. However, alternative forms of training such as strength or cardio training also have beneficial effects on walking capacity and quality of life. A Cochrane review of five studies and 135 randomised patients found no clear evidence of the difference between supervised walking exercise compared with other types of exercise. Only a few studies compare alternative forms of training with the standard of supervised walking exercise in different settings. Randomised controlled trials are required to evaluate the effect on a larger scale (30).

1.3 Diagnostic methods for peripheral arterial disease

The ankle-brachial index (ABI) is a non-invasive method for diagnosing lower extremity artery disease. A low ABI score is a strong marker of generalised atherosclerosis and cardiovascular risk. The ABI indicates the ratio of lower to upper extremity Doppler recorded systolic pressures. The systolic pressures are normally higher at the ankle than in the brachial arteries. A normal ABI is 1.10 to 1.40. An ABI $\leq$ 0.90 is associated with increased risk of cardiovascular death, higher rates of cardiovascular events and higher rates of functional impairment (24, 31). For vascular diagnosis, Duplex ultrasound is often used in combination with ABI. Ultrasound is used to detect and localise vascular lesions and to quantify their extent and severity (24). There are several types of treatment options for patients with IC, including lifestyle change, drug therapy, angioplasty, and bypass surgery. The mainstay of treatment for patients with claudication remains advice to stop smoking and doing exercise while modifying other cardiovascular risk factors.

A systematic review of 33 trials examined the effect of exercise on lower limb haemodynamics in individuals with mild to moderate claudication. The review found that the underlying factors that exercise may affect are distribution of blood flow to the legs, which increases and is more effective, use of oxygen, which expands, and anaerobic metabolism, which is reduced. Exercise did not improve the ABI and was therefore not included as a measurement in the CIPIC Rehab Study (32).

1.4 Supervised exercise training

Worldwide, supervised exercise for IC treatment is an underutilised tool, and only few of all diagnosed IC patients receive efficient and structured supervised exercise training. An exception to this general lack of SET programmes is the Netherlands which, due to the organisation of its healthcare system and the role of healthcare insurance companies, has an obligation to include everyone in basic healthcare insurance (33, 34). Popplewell *et al.* and Gommans *et al.* identify reasons for the reluctance to universally adopt SET (35, 36). Firstly, there is patient resistance, due to the effort and responsibility SET places on patients rather than the "quick fix" offered by surgery. Secondly there is a lack of access to SET, and a lack of reimbursement and funding in the health care system. Another contributor to the lack of adoption of SET is clinicians performing surgery within the fee-for-service model (37). Furthermore, in the "*Guidelines on the Diagnosis and Treatment of Peripheral Arterial Disease"* by the European Society of Cardiology (ECS) and European Society for Vascular Surgery (ESVS), there are recommendations about "*Treatment approach"* regarding medical therapy that includes antihypertensive, lipid-lowering and antithrombotic drugs, optimal glucose level control, risk factor management, smoking cessation, healthy diet, weight loss and regular exercise, but no guidelines on how to set up a rehabilitation programme (24).

1.5 Assumptions and rationale of the study

The **C**ross-sectoral rehabilitation **I**ntervention for **P**atients with **I**ntermittent **C**laudication (The CIPIC Rehab Study) which was tested in this trial, assumed that the existing Danish cardiac rehabilitation set-up could be adapted to benefit patients with IC in a cross-sectorial intervention between hospital and community. To examine the benefits of a specialised cardiovascular rehabilitation programme based on the existing cardiac rehabilitation, a randomised controlled trial (RCT) was necessary. For rehabilitation interventions to succeed in the future, we need more

information on patient's experiences of participating in rehabilitation including qualitative data. The reasoning for this methodology is that the quantitative data and their following analysis provide a broad understanding of the effects of IC rehabilitation. The qualitative data and their analysis enhance and explain the statistical results by investigating participants' opinions more deeply.

2.0 Aims

2.1 Overall aims

The overall aims of the studies present in the PhD thesis were to quantitively and qualitatively investigate the effect and patient experiences of a cross-sectoral cardiovascular rehabilitation programme targeted a population of patients conservatively treated for IC. This aim was thus to create a comprehensive foundation for recommendations on effective and patient centred future rehabilitation programmes for this specific patient population.

2.2 Specific aims

The specific aims of the studies are as follows:

To present the rationale and design of the CIPIC Rehab Study, which examines the effect of a cross-sectoral rehabilitation programme versus usual care for patients in non-operative management for IC (Paper I).

Study 1: To examine whether a cardiac rehabilitation programme in a community-based setting for patients with intermittent claudication (IC) affects walking ability, quality of life, and changes in health behaviour. The trial investigated a cross-sectoral cardiovascular rehabilitation programme compared with usual care for patients in non-operative management (Paper II).

Study 2: To explore how patients with intermittent claudication experiences participating in a community-based cardiovascular rehabilitation programme and the various components of the rehabilitation programme (Paper III).

3.0 Methods

The methods used in the PhD project are described in this section.

3.1 Theoretical inspiration

3.2 Albert Bandura

The foundation for the rehabilitation intervention used in the present study was inspired by Albert Bandura's Social Cognitive Theory, in which self-efficacy is a central component (38). Bandura describes self-efficacy as: *'Belief in one's capabilities to organise and execute the courses of action required to produce given attainments'* (Bandura, 1997 p. 3) *(38)*. The degree of self-efficacy is proportional to the opportunity to succeed and is not an innate competency but one that needs to be learned. A person's assessment of self-efficacy controls the acts and the actions that will be used. If someone experiences success in overcoming a challenge, then their self-belief that they are capable of succeeding in a new circumstance increases (38).

The theory involves that knowledge is developed in relation to others in a local environment. The individual's actual capacity to operate and learning is related to those essential factors. Therefore, we arranged both group sessions and individual sessions. Participant strategies to increase self-efficacy in physical activity under progressively challenging conditions was operationalised in task-specific terms to reflect participants' degree of confidence, for example self-monitoring with pedometer, goal setting about daily physical activity, and feedback on goal progress, problem-solving barriers, and on small changes. Sharing stories of success with peers, sharing information and managing exercise discomfort, vicarious experiences and verbal persuasion were also crucial in relation to participants' degree of self-efficacy (39, 40).

In accordance with Bandura's theory, three overall principles were applied in the rehabilitation intervention:

1) Self-efficacy in own ability by gaining knowledge and support from health professionals
2) Self-efficacy by being with other patients with IC in a local setting
3) Self-efficacy by support from the surroundings

Self-care is strongly influenced by attitudes and beliefs and the patient's confidence in the ability to perform self-care such as self-efficacy. An approach to increase the degree of self-efficacy focuses on behaviour, interaction, and the individual's ability to make health behaviour changes, by learning new skills and by adapting knowledge obtained by observing peers and listening to health care professionals that encourage positive health behaviour and expectations (39, 40).

Consequently, the CIPIC Rehab Study included the individual, the group, spouses, and surroundings. Bandura's social cognitive model of self-efficacy relies on confidence in ability, support from others than oneself, and social support from spouses as a condition to make changes in health behaviour (41).

3.3 Self-care in chronic illness

A middle-range theory of self-care of chronic illness will be used to discuss the findings in the CIPIC Rehab Study. Self-care is described as an extremely challenging process that includes key barriers to and facilitators of self-care – these are: *experience and skill; motivation; cultural beliefs and values; confidence; habits; functional and cognitive abilities; support from others; and access to care (41)*. These factors are all essential to consider when developing or improving interventions. Self-care is considered essential in managing chronic illness, and most patients wish for relief from the symptoms caused by their disease. Patients with higher levels of self-care have better quality of life and lower mortality (41). The health care professional's intention is to motivate patients to engage in self-care, and by understanding the process used by patients performing self-care, the health care professional can identify where the patients struggle – such knowledge about self-care processes might improve outcomes in tailored interventions for chronic illness (42).

Self-care is defined as *"a process of maintaining health through health-promoting practices and managing illness"* (Riegel et al.,2012 p 195) *(42).* Barbara Riegel et al. offer an operational definition of the concept of self-care, built on three key concepts: self-care maintenance, self-care monitoring and self-care management. The three concepts are closely related, and sufficient self-care encompasses all three behaviours. *"The goal of self-care maintenance is to maintain health and prevent symptoms exacerbations, the goal of self-care monitoring is recognition that a change has occurred, and the goal of self-care management is effective treatment of symptoms"* (Riegel et al., 2019 p 208) (43). The middle-range theory of self-care of chronic illness can assist health professionals in assessment and identifying individual factors that hinder patients' engagement in self-care (43).

3.4 Scientific framework

The CIPIC Rehab Study used a pragmatic approach that sought to create meaning and improvements in a local community-based context, and at the same time aimed to create knowledge that may also be useful in a broader context (44). In the study, functional pragmatism was an underlying method for investigation and involved focusing on the practical and feasible rather than the theoretical foundation (44). This approach means that the participants' experiences of participation in a tailored rehabilitation programme are essential. Their expertise, opinions, and activities are examined to be used and implemented in daily practice. Detecting challenges with the rehabilitation programme and addressing solutions were in focus of the study (45-47). Focus group interviews seeking to understand the subjective meanings of experiences by individuals and value using inductive logic (48). The quantitative aims were implicitly framed from postpositivist assumptions with its deductive methodology to be able to generate reason and effect (determinism) and being able to limit a position to a set of variables (reductionism), being able to meaningfully measure a concept such as, e.g. walking distance (measurements) and assessing theory testing by deductive logic (48).

3.5 Definition of rehabilitation

World Health Organization (WHO) defines rehabilitation as "*a set of interventions designed to optimise functioning and reduce disability in individuals with health conditions in interaction with their environment"* (49). In relation to cardiovascular diseases, WHO notes that rehabilitation, including exercise training and education on healthy living, can reduce the impact of health conditions, complement medical and surgical interventions, and help to reduce, manage or prevent complications. Rehabilitation helps minimise or slow down the effects of a cardiovascular disease or other complications by equipping people with self-management strategies and the assistive products they require. Rehabilitation is also described as an investment with cost benefits for both individuals and society: *"It can help to avoid costly hospitalisation, reduce hospital length of stay, and prevent re-admissions. Rehabilitation also enables individuals to participate in education and gainful employment, remain independent at home, and minimise the need for financial or caregiver support"* (WHO, 2020 (49).

3.6 Study protocol of the CIPIC Rehab Study (Paper I)

The protocol was designed to qualify the design of the study and explore the existing quantitative and qualitative research in the field and applied the methodology of a state-of-the-art review (50). The findings considered the most current research in the field and provided knowledge and new perspectives on rehabilitation for patients with IC as well as identifying areas in need of further research. The main characteristics of topics from review articles were derived to address current matters and identify potential opportunities for contemporary research. Exploring the existing research has no formal quality assessment but provides current knowledge and research that makes it possible to prioritise further research in the field. The state-of-the-art review was performed as described by Grant and Booth (50) but not displayed in the paper due to word limits. A PubMed and CHINAHL database search was performed, in which each search consisted of 'peripheral arterial disease', 'intermittent claudication', 'supervised exercise training', and 'rehabilitation, combined with the terms: 'systematic review', 'pedometer', 'community', 'health technology', 'cross-sectorial, 'hospital', 'health behaviour changes', both as MeSH term and as a free-text. All abstracts were extracted, and if it was relevant, the entire article was accessed and used to qualify the protocol for the CIPIC Rehab Study.

The advantage of doing a study protocol was that it created a higher level of transparency in the research process, however, a more precise description of the framework than present in the paper was needed. The study was designed as a complex intervention with several interacting components with no sharp boundary between simple and complex interventions (51).

The quantitative and qualitative data were collected and analysed on its own tradition (52) p. 104-115. In the protocol paper, qualitative explorative data was described as focus group interviews and brief individual interviews as a part of a separate questionnaire survey. The design was updated throughout the study period, and the ancillary questions performed as brief individual interviews were later left out as the data collection method was insufficient to use in the qualitative study.

A planned post doc study will perform the described mixed method to investigate how qualitative data about rehabilitation for patients with intermittent claudication do provide an enhanced understanding of the quantitative experimental results.

In the following information of the various instruments will be presented under each study.

4.0 Study 1 (Paper I and II)

With the purpose of investigating a cross-sectoral rehabilitation programme for patients with intermittent claudication compared with usual care, an RCT study was conducted over a period of one and a half years (December 5, 2017, to May 14, 2019).

4.1 Participants

We included 118 newly diagnosed patients with IC where invasive treatment was not indicated. The patients included in the study had all been diagnosed at the Department of Vascular Surgery, Rigshospitalet prior to inclusion in the study. Patients diagnoses were made on the basis of their medical history, ankle-brachial index (ABI), and/or ultrasound scanning.

4.2 Eligibility criteria

All patients were consecutively included. Patients aged more than 18 years and able to speak and understand Danish and able to provide informed written consent were included if they were able to perform physical exercise. Exclusion criteria were: Failure to understand and cooperate according to the trial instructions; comorbidity complicating physical activity and exercise training; and lack of informed consent.

4.3 Setting

The setting was one hospital: Department of Vascular Surgery outpatient clinic, Copenhagen University Hospital, Rigshospitalet and one municipal healthcare centre: Albertslund Healthcare Centre, The Capital Region of Denmark.

4.4 Recruitment

Patients were pre-screened and if the diagnosis was confirmed, they were asked about recruitment to the study by the nurses at the outpatient clinic, either at the initial consultation or afterwards by email, letter or telephone by the primary investigator.

All patients at the outpatient Clinic of Vascular Surgery, Rigshospitalet who lived in the eight municipalities in the western part of the Greater Copenhagen area were invited to participate, and all data were collected at the outpatient Clinic of Vascular Surgery and the Healthcare Centre.

4.5 Sample size and randomisation

Randomisation was conducted after the baseline data collection to either the intervention group or the control group. The expected average baseline value of maximal walking distance was set to 120 m with a detected 50% improvement (60 metres). The standard deviation of the maximal walking test was set at 100 m, based on an expected improvement in the walking ability of

approximately 50% to 200%. With a 5% significance level and 80% power, 88 patients were needed to detect an improvement of 60 metres in the maximal walking test. With an expected drop-out rate of 25%, we included 118 patients in total, with 59 patients in the intervention group and 59 patients in the control group.

4.6 Blinding

An independent statistician did blind computer-generated block randomisation. The follow-up treadmill walking test was completed by a research assistant blinded as to the patients' group associations, and all the statistical analyses were blinded.

4.7 Variables and data sources

The study included data from patients' medical records, treadmill tests and questionnaires.

Data were collected at baseline and measurements were repeated at 6 and 12 months.

Data consisted of demographics and clinical data: smoking habits, alcohol consumption, medication, nutritional screening, bloodwork, physical activity and general condition of the patient's legs. Comorbidity was measured by Charlson Comorbidity Index (53). Each comorbidity category has an associated weight from 1 to 6, and the sum results in a comorbidity score for each patient. A score of zero indicates that no comorbidities were found.

4.8 Treadmill walking test

Maximal walking distance and pain-free walking distance were measured by a treadmill test described in a protocol: 3.2 km/hour with a 2% increase every 2 minutes. The limit of pain-free walking distance was measured when the first sign of claudication pain in the legs emerged and the total claudication distance was measured when the test had to stop due to the maximal intensity of tolerable claudication pain in the legs (54).

4.9 Questionnaires

Health-related quality of life was measured by the Danish validated version of the Vascular Quality of Life Questionnaire VascuQol (VQ6)(55) with a six-item questionnaire as a PAD-specific instrument to evaluate the quality of life outcomes. Each item scored 1-4 with a total sum of 6-24, where a higher value indicates better health status (56). VQ6 was developed by Morgan et al. and first published in 2001 (57). The VascuQoL questionnaire has been translated to several languages, and we contacted M.B. Morgan directly for permission and access to the Danish validated version.

Depression and anxiety were measured by the Danish validated version of the Hospital Anxiety and Depression Scale (HADS)(58, 59). HADS comprises 14 items with two subscales, HADS-A for anxiety and HADS-D for depression. Cut-off values for both HADS-A and HADS-B are 8-10, indicating the possible presence of a mood disorder, and $\geq$ 11 indicating the probable existence of a mood disorder.

A Danish validated diet questionnaire measured diet with a fat score and a fish-fruit-green score (60). To achieve the term "healthy", each score must be at least 75%.

Daily physical activity was measured by self-reported number of times per week of walking or physical exercise activity of at least 30 minutes, as recommended by the Danish Health authorities (61).

4.10 Statistical methods

The association between all variables and outcomes were investigated, and general regression models for the continuous outcomes and logistic regression models for binary outcomes were used. Intention to treat principle, adjustment for baseline values, sex and age, mixed general and generalised models, interaction groups, sensitivity analyses, significance level of 0.05 and multiple testing with no p-value were used as described in papers I and II.

4.11 Interventions

The intervention began at the outpatient Clinic of Vascular Surgery at Rigshospitalet (Copenhagen) and continued at the health care centre in the municipality of Albertslund, as illustrated in **Table 1**. Two physiotherapists experienced in cardiac rehabilitation, and with specific insight into IC developed and conducted the supervised exercise training, see appendix (Supplementary **Table S1**. Exercise protocol).

Table 1. **Content of the rehabilitation intervention** (Copy from paper 3)

Baseline at the Vascular Surgery outpatient clinic Pedometer and logbook for self-monitoring steps to motivate physical activity, and access to a direct telephone number to the Vascular nurse*. Rehabilitation sessions in the community Physiotherapist: 24 one-hour group sessions over 12-weeks consisting of supervised strength and cardiovascular exercise (up to 10 participants/group). 2-hour group education about IC and coordination of patient enrolments on smoking cessation courses in the municipality + spouses (Vascular Nurse*). Dietician: 2-hour group education about diet and IC, and access to individual counselling. + spouses. After 12 weeks Individual motivational text message (up to the 12-month follow-up) designed with the participant (Vascular nurse*) 6- and 12-month follow-ups at the Vascular Surgery outpatient clinic Vascular nurse*: Individual counselling related to the RCT treadmill test and a questionnaire about health behaviour.

*Primary investigator. IC= Intermittent claudication.

Initially, all the patients in the CIPIC Rehab Study had received usual care before recruitment, which was: advice about keeping on walking and on smoking cessation, and prescriptions for cholesterol-lowering and antiplatelet medication, which is currently standard care in most of Denmark. Usual care included an information brochure about IC, walking exercise, smoking cessation, medication and a logbook for steps. At the outpatient clinic, an old-school pedometer that counted steps was handed out to the patients in the intervention group, and they were asked to self-report daily steps in a logbook. There was no initial goal-setting. The patients brought their logs to the first and last consultation with the physiotherapist and to their consultation with the nurse at the outpatient Clinic for Vascular Surgery. The consultations included conversations about daily steps and motivational factors, and individual goals for physical activity were set. Walking behaviour was a focus of the consultations, which were used to persuade patients to increase or maintain daily physical exercise at a level of at least 30 min/day. The intervention included two weekly exercise sessions for 12 weeks in groups of up to ten patients. The exercises involved different types of physical activity designed to help the patients increase physical activity and set goals for walking ability in daily life. The group received training from a vascular nurse about the pathophysiology of IC, medication, health behaviour, disease management, quality of life and coping with the disease, in order to provide emotional support, improve coping skills and prepare

the patients for expected symptoms and sensations, for example when burning leg pain is a part of the treatment for getting better. Cross-sectorial coordination of the patients' participation in the programme was managed by a vascular nurse, to whom patients had a direct telephone number. After completing the 12 weeks exercise programme, the patients were offered personalised motivational follow-up text messages, and the content, frequency and duration of this were agreed upon individually. The group also received training from a clinical dietician about healthy diet and atherosclerosis, and in addition the patients had access to individual consultations with the dietician.

A smoking cessation course was not a direct part of the intervention, but at the education session with the vascular nurse the patients were informed about existing smoking cessation courses in their respective municipalities so they could coordinate signing up for a course with other participants.

5.0 Study 2 (Paper I and III)

With the purpose to explore how patients with intermittent claudication experiences participating in a community-based cardiovascular rehabilitation programme and the various components of the rehabilitation programme, a qualitative study was conducted.

5.1 Participant for the focus group interviews

Study 2 included patients who had participated in the intervention. Participants for Study 2 were recruited post-intervention the day they ended their 12-weeks of exercise with a follow-up test by the physiotherapist in the healthcare centre. Recruitment was based on the following eligibility criteria:

- Been part of the same training team at the same period from start to stop (which was the first ten participants).
- Participation in post-intervention follow-up by a physiotherapist (Six-minute walking test and sit to stand test) (62, 63).
- Willing to participate in a focus-group interview of about one hour, 6-months post-intervention.

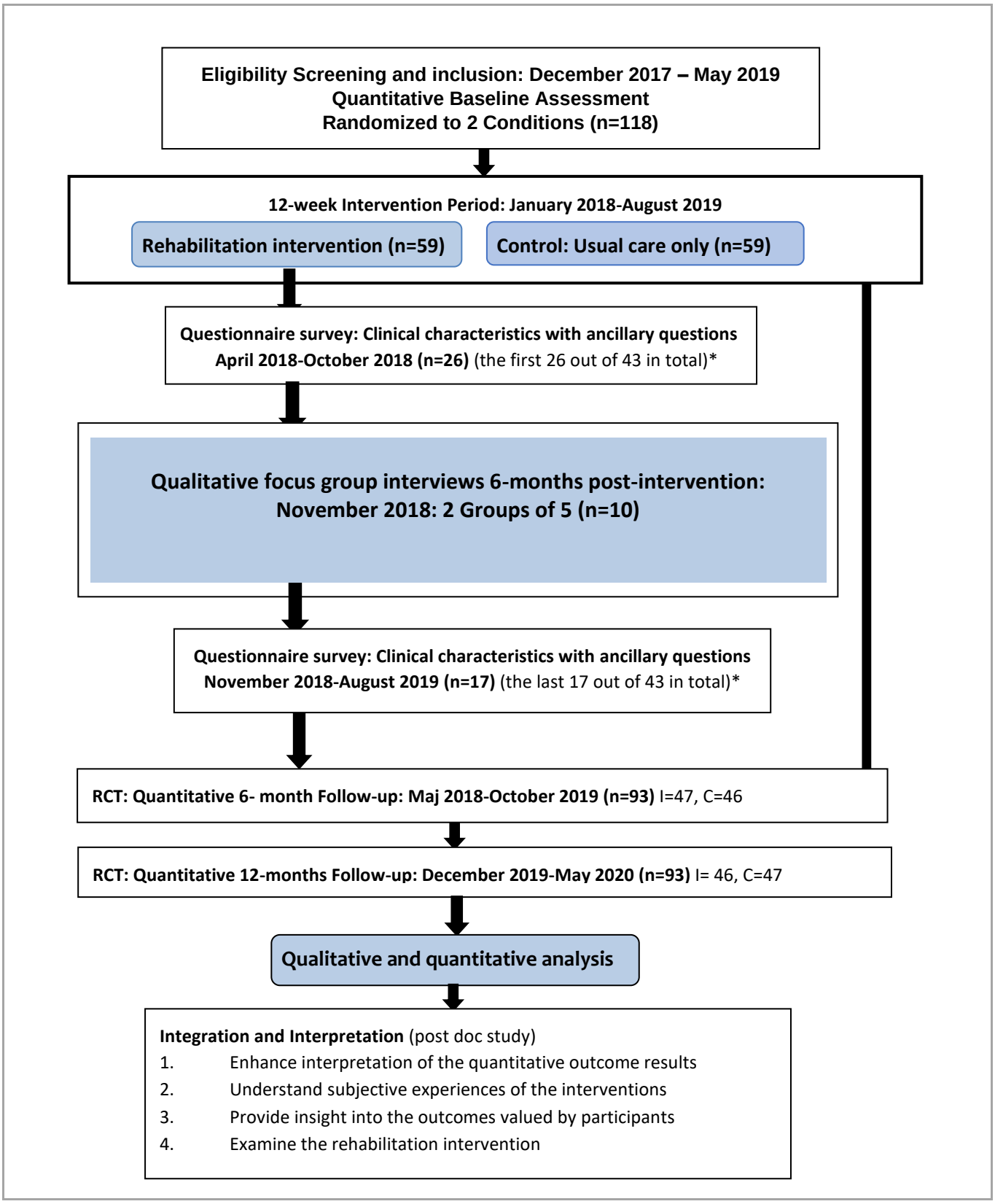
The goal was to include five to eight participants in each focus group with size dependent on information power from the two focus-group interviews (64) (52)(p-70-75). The participants received written and oral information specific to study 2, and all signed a written consent form.

5.2 Participants for questionnaire survey

All patients who completed the intervention were planned to participate in a brief questionnaire survey to register clinical characteristics, level of participation in the intervention, and answer ancillary questions (see Supplementary **Table S2**: 3 Months' Survey. Over a period of sixteen months (April 9, 2018, to August 5, 2019, data was collected the day the participant completed the intervention, see timeline **Figure 1**.

Figure 1. Timeline diagram of the CIPIC Rehab Study.

*All participants who completed the intervention were included (= n 43) before or after the conducted focus-group interviews. I = Intervention group. C= Control group



5.3 Data collection and analysis

The research questions in the semi-structured interview guide and the questionnaire survey were developed and based on systematic reviews on the conceptualisation of a patient-centred programme, as well as three qualitative studies that explore patient experiences of living with IC (6, 15, 19, 20, 22). The focus group interviews were conducted on November 21th, 2018, and lasted around 60 minutes. The PhD student conducted the focus group interviews in cooperation with two assistant facilitators at the health care centre to ensure rich and detailed data collection. A practical guide for performing focus-group interviews in applied research was followed carefully (65), Chapter 5. The focus group interviews were audio-recorded and written down to text accurately. Thematic analysis was used as an organized methodology to examining information from the interviews (65-67)

6.0 Results

A summary of the results from each paper is present in this section. A more comprehensive description of the results can be found in papers II and III.

6.1 Study 1

Cardiovascular Rehabilitation Increases Walking Distance in Patients With Intermittent Claudication. Results of the CIPIC Rehab Study: A Randomised Controlled Trial.

We included 118 patients in the trial, with 59 patients in each group. We analysed data from 93 patients after 6 and 12 months: 47 patients in the control group and 46 patients in the intervention group after six months, and 46 patients in the control group, and 47 patients in the intervention group after 12 months. Forty-three participants completed the rehabilitation programme. The number of patients was sufficient regarding a 5% significance level and 80% power, where a total number of 88 patients were needed to detect an improvement of 60 metres in maximal walking distance.

There were minor baseline differences between the intervention and usual care group, and the groups were comparable, see **Table 2.**

Table 2. Baseline demographic and clinical characteristics

Abbreviations: SD, standard deviation; IQR, interquartile range.

Variable	Control Group N=59		Intervention Group N=59	
Female	26	(44%)	23	(39%)
Age, *mean (SD)*	70.1	(7.3)	70.5	(7.0)
BMI, *mean (SD)*	26.2	(6.0)	26.8	(4.3)
Smoking				
Current smoker	25	(42%)	28	(47%)
Former smoker	29	(49%)	27	(46%)
Never smoker	5	(8%)	4	(7%)
Pack-years, *mean (SD)*	50.2	(31.5)	42.9	(27.6)
Physical activity				
Times per week doing exercise at least 30 minutes				
0 times	32	(54%)	42	(71%)
1-2 times	15	(25%)	9	(15%)
3-6 times	8	(14%)	7	(12%)
7+ times	3	(5%)	1	(2%)
Times per week walking at least 30 minutes				
0 times	24	(41%)	26	(44%)
1-2 times	6	(10%)	7	(12%)
3-6 times	10	(17%)	9	(15%)
7+ times	19	(32%)	17	(29%)
Physical activity at least 30 minutes daily	21	(36%)	18	(31%)
Alcohol				
Alcohol intake (drinks/week), *mean (SD)*	10.3	(12.6)	10.4	(13.4)
Medications				
Aspirin	36	(61%)	42	(71%)
Clopidogrel	17	(29%)	10	(17%)
Anticoagulation (DOAC)	1	(2%)	2	(3%)
Anticoagulation (Vitamin K-antagonists)	0	(0%)	2	(3%)
Statins	54	(92%)	51	(86%)
Charlson comorbidity score				
No comorbidity (Score 0)	31	(53%)	42	(71%)
Mild comorbidity (Score 1)	15	(25%)	7	(12%)
Moderate comorbidity (Score 2)	9	(15%)	5	(8%)
Severe comorbidity (Score 3+)	4	(7%)	5	(8%)

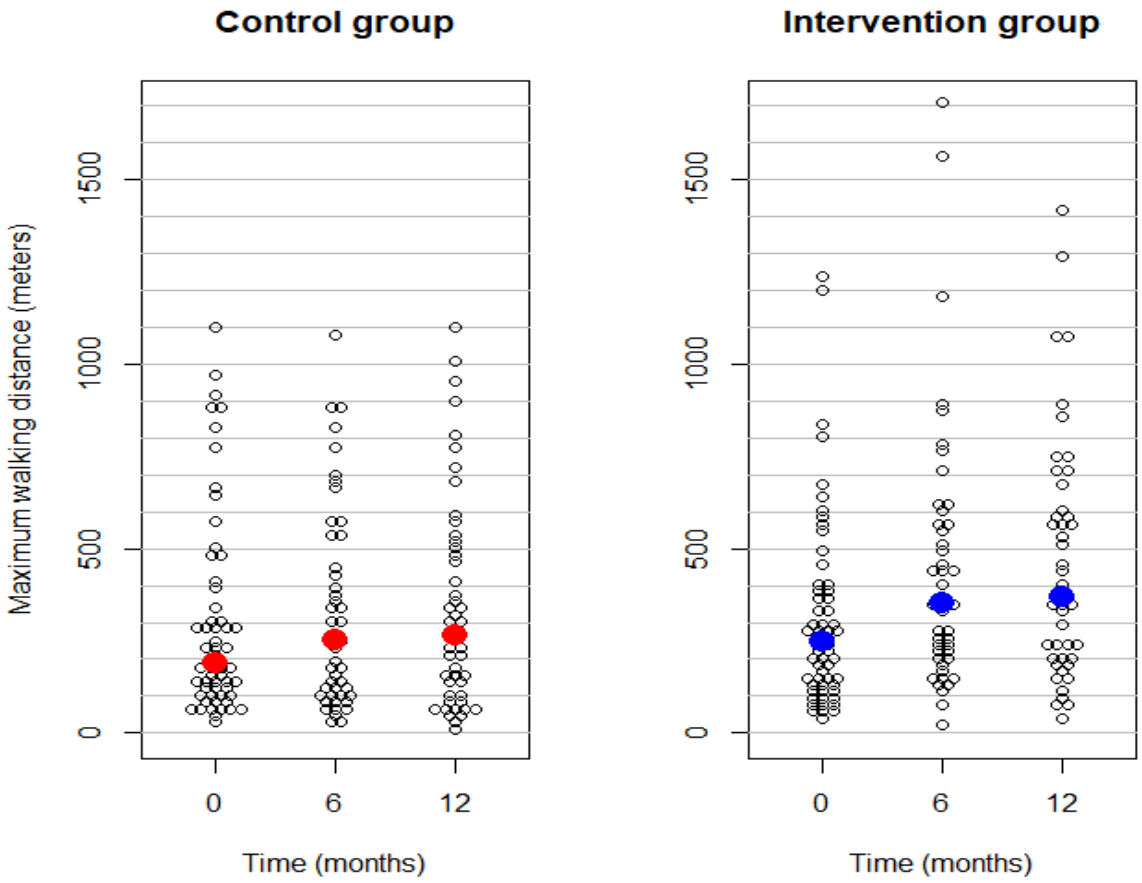
Clinical profile				
Diabetes	7	(12%)	11	(19%)
Myocardial infarction	8	(14%)	9	(15%)
Congestive heart failure	6	(10%)	6	(10%)
Cerebrovascular disease	8	(14%)	7	(12%)
Chronic pulmonary disease	14	(24%)	8	(14%)
Renal disease	0	(0%)	0	(0%)
Psoriasis	5	(8%)	2	(3%)
Prolapsed disc	7	(12%)	7	(12%)
Atrial flutter/fibrillation	5	(8%)	5	(8%)
Spinal stenosis	4	(7%)	3	(5%)
Osteoporosis	4	(7%)	3	(5%)
Back pain (undiagnosed)	1	(2%)	2	(3%)
Osteoarthritis	9	(15%)	6	(10%)
Hypertension				
Medically treated hypertension	42	(71%)	44	(75%)
Treadmill-test PWD (Pain-Free-Walking-Distance), metres				
Mean (SD)	157.9	(168.8)	151.5	(145.7)
Median (IQR)	96.5	(52-175)	115	(54-175)
Treadmill-test MWD (Maximal-Walking-Distance), metres				
Mean (SD)	300.7	(273.7)	309.9	(255.1)
Median (IQR)	188	(107-393)	248	(130-384)
Quality of life questionnaires				
VacuQol (VQ6), *mean (SD)*	14.7	(3.0)	14.6	(4.0)
HADS-A >= 8 (Anxiety)	7	(12%)	11	(19%)
HADS-D >= 8 (Depression)	5	(8%)	8	(14%)
Blood work				
Haemoglobin, *mean (SD)*	8.7	(1.0)	8.8	(0.9)
Hba1c, *mean (SD)*	39.4	(5.6)	42.4	(8.1)
Creatinine, *mean (SD)*	82.1	(20.9)	87.0	(25.7)
Total Cholesterol, *mean (SD)*	4.2	(0.9)	4.4	(0.9)
Cholesterol LDL, *mean (SD)*	2.0	(0.8)	2.3	(0.8)
Cholesterol HDL, *mean (SD)*	1.5	(0.6)	1.4	(0.5)
Triglyceride, *mean (SD)*	1.6	(0.8)	1.9	(1.7)
CRP, *mean (SD)*	2.9	(4.3)	5.3	(11.7)

6.2 Results - primary outcome

Maximal walking distance increased in both groups at six months but increased 37% more in the intervention group compared to the control group (95% CI: 1.10-1.70; P=0.005), see **Table 3**. The intervention group had higher median scores on maximal walking distance at baseline: 248 metres in the intervention group versus 188 metres in the control group. Improvement at the 6-month follow-up was 350.5 metres in the intervention group versus 253 metres in the control group. **Figure 2** illustrates each distinct maximal walking distance in metres and the outliers.

Figure 2. Bee-swarm plot

Standardised treadmill walking test in control and intervention groups at time points 0 (baseline) and 6 and 12 (6 and 12 months after randomisation). Median values at the three-time points shown in coloured dots.



6.3 Results - secondary outcome

Pain-free walking distance increased numerically in the intervention group at six months (28% (95%CI:0.99-1.65)), but the difference was not significant between the groups (P= 0.06), see **Table 3**. Physical activity estimated as odds ratio for minimum 30 daily minutes at six months was significantly higher in the intervention group (OR: 5.59;95% CI: 1.66-8.82, P=0.002), see **Table 3**. Healthy diet score showed that only five patients in the intervention group achieved the term "healthy" with a score of at least 75% in the fat score and the fish-fruit-green score, but differences in the scores analysed separately showed a significantly higher score in the intervention group at 6 and 12 months (P<0001), see **Table 4**.

Table 3. Results log-linear model

Continuous primary and secondary outcomes and logistic regression for binary secondary outcomes measured at six months. Available case analysis (Adapted from paper 2)

	Median (mean) and n (%) value at baseline		Median (mean) and n (%) value at 6 months		Exp(estimate) (95%CI) (1)	p-value	Cohen d (2)
	Control group (n=59)	Intervention group (n=59)	Control group (n=47)	Intervention group (n=46)			
Primary outcome							
Maximum walking distance (3)	188 (300.7)	248 (309.9)	253 (325.4)	350.5 (447.6)	1.37 (1.10-1.70)	0.005	0.38
Secondary outcomes							
Pain-free walking distance (4)	96.5 (157.9)	115 (151.5)	96 (165.8)	133.5 (207.9)	1.28 (0.99- 1.65)	0.06	0.29
Healthy diet	0 (0%)	1 (2%)	0 (0%)	5 (11%)	NA (5)	NA	
Physical activity	21 (36%)	18 (31%)	15 (32%)	24 (52%)	5.59 (1.66-18.82)	0.002	

(1) Main effect of intervention adjusted for sex, age (continuous), and baseline value (time 0). The estimate is the exponential log-transformed mean difference for maximum walking distance and pain-free walking distance, meaning the relative extra metres in the intervention group compared to the control group. For physical activity, the estimate is the odds ratio. Analyses on the median.
(2) Cohen's d is the estimate from the log-transformed model divided by the standard deviation of the log-transformed baseline value.
(3) Sensitivity analyses with removal of outliers (Cook's d above 0.1 (n=1) also showed statistically significant differences (p=0.004).
(4) No outliers were identified after log-transforming this outcome (Cook's d below 0.1 for all observations).
(5) NA, not estimable since no outcomes in the control group.

6.4 Results - explorative outcomes

Maximal walking distance was sustained over time at 12 months with 263.5 metres in the control group versus 370 metres in the intervention group. P-value (P=0.0201), and the interaction over time was different in the two groups and was bigger over time, see **Table 4**. Physical activity was still significantly higher in the intervention group after 12 months (P=0.01), see **Table 4**.

General self-reported condition in the legs compared to baseline showed a better outcome in the intervention group. At six months, 9% in the control group and 28% in the intervention group felt that the condition was much better. At 12 months, 22% in the control group and 36% in the intervention group felt the condition was much better, see **Table 5.**

Vascular quality of life (VQ6) increased significantly in the intervention group compared with the control group at 6 and 12 months (P=0.02). The anxiety and depression scale (HADS-A and HADS-D) showed no significant differences between the groups, see **Table 4**.

There were no significant differences in alcohol consumption and smoking cessation between the intervention group compared to the control group, even though there were more non-smokers in the intervention group at 12 months. There were 42% smokers in the control group at baseline and 47% smokers in the intervention group. After 12 months, there were still 42% smokers in the control group, but only 40 % in the intervention group, see **Table 4**.

Table 4. Explorative outcomes measured at 0, 6 and 12 months

Results of linear and logistic mixed models. The estimates are the crude proportions, medians or means and proportions with outcomes in intervention and control groups. Available case analysis

(Adapted from paper 2)

		0 months		6 months		12 months		
	N (1)	Control	Intervention	Control	Intervention	Control	Intervention	p-value (2)
Explorative outcomes								
Maximum walking distance, *median*	303	188	248	253	350.5	263.5	370	0.02 (3)
Pain-free walking distance, *median*	303	96.5	115	96	133.5	140	170	0.25 (4)
Physical activity, *%*	301	36%	31%	32%	52%	25%	52%	0.01
Vascular Quality of Life Questionnaire, *means*	303	14.7	14.6	15.6	17.3	16.0	17.1	0.02
HADS-A >= 8, *%*	303	12%	19%	11%	17%	15%	21%	0.96
HADS-D >= 8, *%*	303	9%	14%	6%	4%	2%	4%	0.76
Smoking status, *%*	299	42%	47%	38%	43%	42%	40%	0.58
High alcohol consumption (5), *%*	304	24%	17%	28%	13%	20%	11%	0.58
Fat score, *mean*	303	0.55	0.56	0.55	0.66	0.57	0.71	<0.0001
Fish-fruit-green score, *mean*	303	0.43	0.43	0.40	0.53	0.41	0.55	<0.0001

(1) N is the number of observations where each person can have up to three observations.

(2) P-value from interaction term between intervention group and time (0, 6 and 12 months). Adjusted for sex and age (continuous).

(3) p-value based on analyses on log-transformed maximum walking distance

(4) p-value based on analyses on log-transformed pain-free walking distance

(5) >21 weekly units for men; >14 weekly units for women.

Table 5. Self-reported general condition in the legs compared to baseline

General condition in the legs	6 months		12 months	
	Control (n=47)	Intervention (n=46)	Control (n=46)	Intervention (n=47)
Much better	9%	28%	22%	36%
Better	17%	20%	4%	18%
A little better	11%	28%	24%	25%
Almost the same	45%	22%	37%	11%
A little worse	11%	2%	7%	7%
Worse	4%	0%	2%	2%
Much worse	4%	0%	4%	0%

Table 6 shows that a higher percentage of the intervention group participated in a smoking cessation course.

Table 6. Participated in a smoking cessation course

SCC* before baseline		SCC at 6 months		SCC at 12 months	
Control (n=28)	Intervention (n=24)	Control (n=20)	Intervention (n=20)	Control (n=19)	Intervention (n=19)
36%	33%	10%	20%	5%	11%

*SCC= smoking cessation course

6.5 Per-protocol analyses

The per-protocol analyses of the primary and secondary outcomes consist of 39 patients who achieved at least 70% of the exercise sessions and additionally performed a treadmill test at six months. These outcomes make estimates and differences stronger in favour of the intervention group with a further 50 metres longer walking distance that increased 45% more in the intervention group than the control group (95% CI: 1.17-1.80; P=0.001). Improvement at the 6-month follow-up was 400 metres in the intervention group versus 253 metres in the control group. The overall conclusion was thus more robust but not changed, see **Table 7.**

Table 7. Per protocol version

Results log-linear model with continuous primary and secondary outcomes and logistic regression for binary secondary outcomes measured at six months. Per protocol and available case analysis

	Median (mean) and n (%) value at baseline		Median (mean) and n (%) value at 6 months		Exp (estimate) (95%CI) (1)	p-value	Cohen d (2)
	Control group (n=59)	Intervention group (n=41)	Control group (n=47)	Intervention group (n=39)			
Primary outcome							
Maximum walking distance	188 (300.7)	281 (350.6)	253 (325.4)	400 (479.7)	1.45 (1.17-1.80)	0.001	0.45
Secondary outcomes							
Pain-free walking distance	96.5 (157.9)	138 (161.5)	96 (165.8)	147 (223.8)	1.32 (1.02-1.73)	0.04	0.33
Healthy diet	1 (2%)	0 (0%)	0 (0%)	5 (13%)	NA (3)	NA	
Physical activity	21 (36%)	12 (29%)	15 (32%)	20 (51%)	6.50 (1.69-25.03)	0.002	

(1) Main effect of intervention adjusted for sex, age (continuous), and baseline value (time 0). The estimate is the exponential log-transformed mean difference for maximum walking distance and pain-free walking distance, meaning the relative extra metres in the intervention group compared to the control group. For physical activity, the estimate is the odds ratio.

(2) Cohen's d is the estimate from the log-transformed model divided by the standard deviation of the log-transformed baseline value.

(3) NA, not estimable since no outcomes in the control group.

6.6 Study 2

Spurred by pedometers, unity and fun exercise: A qualitative study of participation in rehabilitation for patients with intermittent claudication (The CIPIC Rehab study)

The patients' perspectives on participating in the intervention were as described in paper 3, illuminated into four themes: *1)The shared community, 2) Pushing your own limits, 3) Spurred by pedometers and health professionals, and 4) Continuing new habits own on your own.* These four themes are presented one by one in the following.

6.7 The shared community

The social part and the community-based setting of the rehabilitation was essential for the participants. They described how a unique “team spirit” and being together with other patients with the same disease helped them to complete the training sessions and motivates them to maintain physical activity. Sharing experiences and observing others succeed with the training encouraged them to exercise and “go on” when it was challenging. A sense of community appeared when the patients were having fun and kept an eye on each other.

The patients found it challenging to do the training independently and expressed gratitude about being a part of a specialised programme with education and exercise.

6.8 Pushing your own limits

The participants described that the main challenge during physical activity was a painful feeling of “muscles burning up”. They were supported by the physiotherapist, which encouraged them to continue exercise despite cramping pain in the calves. During the training sessions, the participants had experienced that they could delay the onset of pain if they pushed their own limits. Competition and fun exercise helped the participant to continue despite their cramping leg pain.

The participant described that continuity and structure in the programme increased the daily level of physical activity. Through the education sessions with the vascular nurse, the participants had learnt about the benefits of doing exercise, which was experienced as essential for managing the disease. The participant's new experiences and knowledge about atherosclerosis and its causes became vital in managing life with intermittent claudication. Support from fellow patients, physiotherapists, vascular nurses, and dietitian helped the participant find strategies to handle daily life.

6.9 Spurred by pedometer and health professionals

The participants explained how the healthcare centre's local setting influenced motivation and adherence to participate. Transportation time and parking issues at Rigshospitalet would have hindered participation. The main part of the participants explained that a local setting was essential, and otherwise, they would have dropped out of the programme.

The participants were motivated and compelled by being waited for and valued when the health professional designed a specialised programme for them. With exciting and playful competition, the different kinds of exercise taught the patients what type of training they like and helped them relieve the feeling of cramping leg pain during the exercise.

The participants highlighted the pedometer as a solid motivational instrument. The logbook and the daily numbers at the pedometer spurred the participants to be more physically active. The ability to perform daily walking increased and they were independently competing with themselves about their individual goals.

6.10 Continuing new habits on your own

The participants were inspired by the different kinds of exercise and the affiliation to group training with fellow patients as an influential motivational factor.

The participants found it challenging to continue training independently and felt unhappy when the three months of the exercise were ended, described by some patients as a *"mental downturn."* The education session with the dietician was evaluated as helpful to get knowledge about how food can impact health. Basic knowledge about healthy food was experienced limited for some of the patients who found the content of the education cession a little bit overwhelming. Therefore they suggested separating the sessions into two parts, allowing practising and preparing questions between the sessions. The dietician was very young, and some of the participants described that they found age and life experience essential to "relate" and being "in eye level". Lifestyles changes like eating habits could be challenging, especially when the immediate effect doesn't appear, and there is a lack of knowledge about how the function of the human body is. The participants described how they found that education sessions could guide them and gave increased knowledge about claudication, how to treat the disease, and why medication is necessary.

The participants found it useful to know that pain in the legs while exercising is an essential part of the treatment to help the legs make new collateral blood circulation. Another crucial aspect increasing the feeling of security was that they had a direct mobile number to the vascular nurse from the outpatient clinic, allowing them to call when they need counselling about intermittent claudication.

7.0 Discussion

The main findings from this project were that a specialised cardiac rehabilitation programme for patients with IC in a community setting improved walking distance, physical activity, healthy diet and health-related quality of life in the intervention group compared with the control group after 6 and 12 months. The programme comprised cross-sectoral cooperation between an outpatient vascular clinic and a health care centre in the community. The effect on walking distance, physical activity and quality of life was aligned with results from supervised exercise programmes that have proven efficient for minimizing symptoms, improving walking distance, reducing cardiovascular risk factors and increasing health-related quality of life (26), but with the absence of evidence about how to set up a rehabilitation programme (22). Complex interventions include several interacting components with no sharp boundary between simple and complex interventions (51). Social activities can be difficult to investigate using quantitative methods alone. Qualitative investigation can help design interventions and enhance knowledge of the structures and impacts of complex interventions in health care. In the CIPIC Rehab study, we included several elements that could act both independently and interdependently to examine the mechanism of the "active ingredient" of the intervention (68).

In the following, the primary, secondary and explorative outcomes from the study will be discussed, and the plan for the mixed methods post-doc study will be explained in section 8.4 under reflexivity.

7.1 Walking distance and supervised exercise training

In the CIPIC Rehab Study, walking distance increased 37% more in the intervention group compared to the control group. Per protocol analyses showed a further 47 metres longer walking distance that increased 45% more in the intervention group compared with the control group (walking advice group). Improvement at the 6-month follow-up increased from 281-400 metres (mean 129 metres) in the intervention group versus 188-253 (mean 24 metres) in the control

group. Over the past 30 years, treadmill-based SET programs have been shown improvement in walking ability assessed by graded treadmill testing, and meta-analyses of 25 randomized trials show statistically significant 180 metres (95% CI, 130-238) improvement in maximal walking distance (69). A multicenter randomized trial by Nicolaï and college included 304 patients with intermittent claudication. Patients were randomized to exercise therapy in the form of"go home and walk" advice (WA) (as the control group in the CIPIC Rehab Study), SET (treadmill) or SET (treadmill) with feedback (performance-based accelerometer) provided by a local physiotherapist. The median change (interquartile range) in walking distance measured by treadmill between 12 months and baseline in meters was 110 (0-300) in the walking advice group, 310 (145-995) in the SET group, and 360 (173-697) in the SET with feedback group (P<.001 WA vs SET) (70). Another study with structured home-based walking exercise intervention found improvement in the 6-min walking test from 41 to 53 metres at six months follow-up compared to a control group. In that study, the intervention improved the 6-minute walking distance more than it improved maximal walking distance at a treadmill test. In contrast, a supervised treadmill exercise intervention improved treadmill walking more than it improved the 6-minute walking test. So, SET on a treadmill improved walking distance more than the community-based programme we used in the CIPIC Rehab Study. However, it may be discussed if a supervised treadmill exercise intervention specifically trains the participants to the treadmill walking measure, whereas a structured intervention focuses on over-ground walking. Clinically meaningful change in the 6-minute walking test distance has been defined: A small change has been defined as 20 m, and a large meaningful change has been defined as 50 m; however, these findings of meaningful change were not derived specifically from people with PAD. A systematic review of recruitment for RCT of SET for PAD concluded that 69% of 1541 eligible participants with PAD refused participation, and many refused because of the burdensome requirements of SET programmes (71). For the large number of patients who find the demands of SET too difficult, a community-based cardiovascular rehabilitation programme in a local setting as the CIPIC Rehab Study could be a realistic and successful alternative, even though the effect on walking distance is not as high as in a supervised treadmill exercise intervention. According to ESVS guidelines, a treadmill test is a good instrument for quantitative functional assessment and an excellent tool for follow-up after exercise (72). In the CIPIC Rehab Study, we found that the treadmill test was useful as a motivational tool. At the 6-

and 12-month follow-ups, many of the patients were surprised about the improvement in walking distance, because they expressed a feeling of non-improvement in walking ability. When the treadmill test showed an improvement in walking distance, the patients walked out of the door with new energy to continue the training. An explanation might be that making collaterals in the limbs is a slow process over 3-6 months and time blurs the memory of how challenging walking was half a year ago. In the CIPIC Rehab Study, there were no significant differences in pain-free walking distance between the intervention group and the control group. A meta-analysis from nine studies with 391 participants demonstrated overall progress in pain-free walking distance in the exercise group compared with the no exercise group (MD 82.11 m, 95% CI 71.73 to 92.48, P < 0.00001) (32). These studies were based on supervised exercise training on a treadmill three times/week and improvements were seen for up to two years. The fact that we did not find a significant increase in pain-free walking distance (though it did increase numerically) might be related to the more light and mixed form of exercise, two times/week, which could delay collateral formation in the limbs. However, this form of exercise suits patients with IC and will probably contribute to long-lasting effects in the future. The main part of studies on supervised exercise is performed in hospital outpatient clinics with limited capacity and implementation, and patients' adherence to outpatient clinics is low (22). A standard programme consists of 45-60 minutes of exercise on a treadmill, three times a week, for 12 weeks. Transportation to the outpatient clinic is often time-consuming and expensive for the patients and doesn't fit patients in a job. In community-based programmes with exercise on a treadmill, high dropout rates of 40% are seen (73). The treadmill-based exercise is relatively painful, may be perceived as boring, and could therefore explain some of the high dropout rates. Based on findings of typical SET programmes, Kruidenier *et al.* suggest that a minor pain-full exercise approach could be more appealing to patients and result in improved compliance and minor dropout rates (73). Examples of minor pain-full ways of training in addition to those used in our study could include circuit training, strength training or bicycling in combination with different kinds of walking exercises.

7.2 Patient-reported outcomes and knowledge

Patient experiences about living with IC, and outcomes of physical programmes designed to improve walking distance and cardiovascular risk factors of patients with IC, have been published (19, 26), but patient-reported advice and experience on setting up rehabilitation programmes are inadequate. The qualitative part of the study provided insight into patients' rehabilitation

experiences. Previous research has indicated that patients with IC lack information and knowledge about their disease (18). In general, we found that it was a challenge in this patient group to ascertain the knowledge they needed about IC and how the human body works. Social inequality, lower education levels in the patient group, and their cultural and social environment could all be a part of the reason for this. Studies have confirmed that health literacy is independently associated with self-care behaviour (74). In general, patients with peripheral arterial disease are over-represented in low socio-economic groups (2), impacting self-care ability. Therefore, the supervised exercise support group in the local community was an essential aspect of the CIPIC Rehab Study.

A study by Wann-Hansson and Wennick confirms that there is individual variation in demographics and experiences that impact how patients with intermittent claudication obtain knowledge and how they are trying to find a way through insecurity, beliefs and facts (18).

These differences in knowledge are probably related to health inequality and the ability to adapt information. At a larger macro-level, communities and countries are affected by social inequality and health literacy. Across education and gender groups in 23 OECD countries inequality in longevity is evidenced by a gap in life expectancy between highly educated and poorly educated people. Cardiovascular disease is the most common cause of death for all groups and genders above the age of 65 years, but it is also the factor that displays the largest mortality inequality between highly educated and poorly educated elderly groups (75). The recent report from the Danish Health Authority *Social inequalities in health and illness -the development in Denmark in the period 2010-2017* (76) shows that people with a shorter education experience more illness, feel greater consequences of disease and die earlier than people with higher education. The report focuses on the fact that health and illness are systematically unequally distributed in society. Social position and living conditions impact human health, illness, life expectancy, and health-related quality of life. There is inequality in relation to who is affected by illness and the consequences of illness in the form of return to work and survival. This inequality is manifested in risk factors such as smoking, obesity, poorer mental health and multi-disease conditions, contact with health services, and clinical research has described the accumulation of risky health behaviour in lower socioeconomic groups. Some of the reasons for this are these groups' reduced

coping skills, lower personal resilience, poorer working conditions, poor communication skills, stressful situations, negative life events and impact from the environment (77).

Knowledge of the disease is important because exercise by a patient will be hindered if the patient does not know that leg pain while walking is a necessary part of their treatment and if the patient does not know how to go about such walking exercises. Such knowledge is necessary to help patients successfully through their rehabilitation, thus dissemination of this knowledge formed part of the self-efficacy strategy in the CIPIC Rehab Study. However, knowledge alone cannot achieve health behaviour changes. Patients experience influence knowledge, and they need to have skills to set a plan, make goals, and understand advice, instructions, and health information. Patients need the ability to use information and apply it in a context. Skills for self-care in practice must fit into their daily lives (41).

In the CIPIC Rehab Study, goal setting and making plans based on patients' experiences with exercise and managing leg pain increased self-care. When participants in the CIPIC Rehab Study were able to transfer new knowledge to their own lives, their self-efficacy increased, and in Bandura's words, they became more skilled in controlling their own motivation, behaviour, and social environment (38). After 12 weeks of rehabilitation, the participants highlighted that they wished to continue with their exercise group since it influenced their self-care and self-efficacy. Self-care advice might contradict cultural beliefs based on prioritized values and blocked values (43). Cultural beliefs as factors might be important knowledge to include in rehabilitation interventions for patients with IC.

7.3 Motivational factors

Motivation is higher when the patient engages in an activity for pleasure instead of engaging because of recommendations by others (41). Lack of motivation to change is powerful but is only one of many complex factors influencing behaviour change (78). In the CIPIC Rehab Study, patients were motivated and engaged through the various forms of exercise, having fun, playing and competing, and when they learned what kind of exercise suited them best. These factors showed that early and clear benefits in an exercise-based rehabilitation programme can be motivational, and habits and daily routines influence self-care. To incorporate self-care into everyday life, education should include strategies that encourage self-efficacy, learning, and employing the recommendations to daily life. For example, this can be done by a focus on eating habits and social relationships. Patients reported that they made their decisions about self-care based on the values

they prioritize, plus personal feelings and life circumstances. Motivation could also be socially based and related to benefits from society. Treatment beliefs about the necessity of medications or beliefs about an illness are significant predictors of self-care (43). Medication is also an essential part of the treatment of atherosclerosis and palliative treatment of leg pain. In the CIPIC Rehab Study, participants highlighted that sessions with the nurse and dietitian were important and gave them helpful information, for example about collateral circulation, and *"when it hurts, it is doing good"*, why medication with antiplatelet therapy and cholesterol-lowering medication is essential and how simple advice about healthy diet could be incorporated in daily life.

Participants in our study stated the importance of support from health professionals in a local context with a frame of interaction and learning from observing fellow patients, leading to manage the disease and exercise despite the cramping leg pain. By being in the same situation, they experienced that their self-confidence to do the training improved, which is an experience that has also have been seen in studies with other patient populations (79, 80). The findings here are coherent with Bandura's social cognitive theory of self-efficacy, where interaction with others, behaviour, ability to perform, and learning new competencies are essential. Intervention strategies should provide training and guidance, progressive goal setting, verbal reinforcement, demonstrate desired behaviours, and reduce anxiety about taking action by pushing the patients' limits (40, 81, 82). In addition, Bandura's theory of self-efficacy can explain the benefits of exercising in groups. He states that interaction with other patients with the same disease may result in health behaviour change and the ability to perform and learn new skills.

7.4 Local setting

The CIPIC Rehab Study illuminates how nurse-led follow-up programmes can be experienced as supportive and meaningful for patients and that such programmes should be held in a local community-based setting, as indicated in other studies (18-21). The local environment is crucial because joining a hospital-based supervised exercise programme can be problematic for patients due to logistics and transportation time (20). In addition, McDermott and colleagues found that intervention in the local community improved patients' motivation and adherence (21).

Our results concur with Bandura's theory about self-efficacy, where support in the local community does matter. The CIPIC Rehab Study also points out that the patients wished for further training after the 12-week rehabilitation programme, as they found it difficult to continue

on their own, and that they were motivated by the fact that the physiotherapist at the exercise sessions stood there waiting for them. Therefore, it is essential to consider how the programme can be followed up in the community to continue the training after the initial 12 weeks. Studies indicate that peer mentor models can support exercise (83). A recent Danish study in cardiac rehabilitation by Pedersen et al. imply that it would be advantageous for a future rehabilitation programme to involve peers for social support (84).

The present study results could imply that cross-sectorial and multidisciplinary rehabilitation intervention could benefit the patients' pain management. The European Society of Cardiology guidelines support this view, in that they recommend that patients with IC receive supervised exercise therapy because it is more cost-effective than unsupervised exercise (24). However, such cross-sectoral and multidisciplinary rehabilitation interventions still face the general problem that supervised exercise therapy is not reimbursed or available everywhere, and concrete recommendations for interventions are lacking in the guidelines such as the aforementioned (24).

7.5 Anxiety and depression

The HADS score showed no significant differences between the intervention and the control group, but high anxiety scores (>=8) were found in both groups. Depression is associated with cardiac, cerebrovascular, and peripheral diseases. High prevalence of anxiety and depressive disorders among patients with PAD have previously been found. A cohort study found that up to 24.4% of patients with PAD suffer from anxiety, and 27.6% suffer from depression (85). Despite those findings, anxiety and depression are underdiagnosed in clinical practice and not adequately treated (86). The presence of depression or anxiety is a risk factor for developing cardiovascular disease. Therefore, it is necessary in clinical practice to address anxiety and depression in patients with PAD, and a more dedicated intervention focusing on these issues may influence the results (87). It is well known that depression, anxiety and cognitive impairment can decrease the patient's ability and interest in self-care (41), and these studies indicate that poor self-care is affected by even low levels of depressive symptoms. In the CIPIC Rehab Study, anxiety was present in 11-21% of the participants, and depression was present in 2-14% of the participants in the 12-month period, and an intervention that was more focused on alleviating anxiety and depressive disorders could have had an impact on the results of the intervention.

7.6 Quality of life

Quality of life improved after intervention in the CIPIC Rehab Study measured by the Vascular Quality of Life questionnaire VascuQoL (VQ6), a disease-specific instrument to evaluate quality of life outcomes (55). Improvement in MWD and better health-related quality of life have also been found in a Cochrane review by Laurent *et al.,* who compared supervised walking exercise with other kinds of activity as bicycling and exercise in strength training equipment, and found improvement in MWD and health-related quality of life (30).

7.7 Health behaviour changes

In the CIPIC Rehab Study, a typical behaviour among patients before intervention would have been to promote rest instead of walking despite pain, or, prior to participating in the intervention, a patient would not have believed in the positive effects of exercise, medication or of stopping smoking. Daily routines and new habits are important self-care factors (41). In the CIPIC Rehab Study, some of the patients adopted new routines, while other patients struggled to adopt new self-care habits. During the rehabilitation programme and individual goal setting, the participants learned and experienced how to change their habits in a process of increased self-efficacy. Sharing in group sessions and meeting other patients in the same situation were perceived as supportive. Almost none of the patients with IC ate healthy food, measured by a diet score (60), but small changes over time were possible. We found a low percentage of “healthy” in the diet score during the study in both groups. However, improvement in the diet score was seen in the intervention group. The impact was relatively small, measured by the score of at least 75% in the diet score to achieve the term “healthy”, but there was a significant improvement in the score for the intervention group compared with the control group.

In the CIPIC Rehab study, patients with a daily intake of fruit and vegetables were deficient, associated with increased cardiovascular mortality. A large study from 2002 with 100,191 participants found that all-cause mortality, including cardiovascular mortality, increased if there were a low adherence to dietary guidelines. Cardiovascular mortality was 30% higher, non-cardiovascular mortality was 54% higher, and all-cause mortality was 43% higher than those with very high compliance (88). However, some small and spontaneous changes can occur, indicating that there may be a willingness to modify nutritional behaviours. But in general, patients with IC have sub-optimal dietary intake and continue to consume poor diets (89), and the intervention in our study also failed to change participants’ diet habits in a more significant manner. An analysis

of dietary habits and nutritional counselling after coronary artery bypass grafting reports how food was experienced as a nutritional jungle for patients, and how they were influenced by previous nutritional habits – especially men stood out as having challenges in understanding the importance of healthy food and changing habits (90). The gender aspect is particularly interesting in relation to the IC population, as men represent most such patients (56-61% men in the CIPIC Rehab Study).

A systematic review of behaviour change concludes that it can be challenging to maintain adapted behaviour such as exercise over time (91). In that context, the 12-month follow-up in the CIPIC Rehab Study might not be long enough. Another issue is that unhealthy behaviours are often learned early in life, and habits are hard to change (92). In the CIPIC Rehab Study, the dietician was female, young and fit, and some of the participants, therefore, expressed a feeling of not being met as equals and not being understood from their own context. An intervention that addresses these issues and extends further than a 12-month period might likely have a more successful outcome than the present study.

Performing self-care requires functional ability to engage in the required behaviours. Many patients with IC suffer from other chronic illnesses that might be associated with cognitive deficits that can make self-care particularly challenging (41).

In general, multimorbidity in older adults with cardiovascular disease is well documented, with associated higher health care costs for medication, hospitalization and health care provider visits. Poor clinical outcomes, reduced quality of life, frailty and reduced functional ability are some of the consequences (93, 94). In the CIPIC Rehab Study, there were no specific interventions related to those patients with multimorbidity. Thus, a more person-centred focus might have impacted the results.

Individuals perform Self-care, but their families or social network are essential in helping about communication, decision making, and support (41). Social support was a part of the intervention in the CIPIC Rehab Study and spouses were invited to participate in the sessions with the nurse and dietician. In the CIPIC Rehab Study, participants' easy access to a vascular nurse at the outpatient clinic was highlighted by participants as important and related to supporting self-care. Other studies of exercising in groups for patients with other diagnoses such as heart disease and cancer have also highlighted the group community as a special place for understanding and as a

supportive atmosphere, as well as highlighting how the group might be significant in terms of the patients' social capital (95, 96).

Self-care is often influenced to some degree by providers. In concordance with the findings in the CIPIC Rehab Study, the qualitative study by Liljeroos et al. on perceived caring needs in patient-partner dyads affected by heart failure reports that patients and their partners found it important to receive guidance and education by health care professionals throughout the treatment of their illness (97). Further, they highlight that visits to an outpatient clinic and easy access to telephone support were important, as was having a healthcare provider that involved the patient's partner in matters concerning well-being (97). The study finds that patients need a relative to be present at the clinic visits, to reduce insecurity, receive information and ask questions (97).

There were some minor differences between groups in health behaviour during the study. Some of the reasons could be that health behaviour by nature is challenging to change. Another reason regarding smoking might be that we did not offer a smoking cessation course as a part of the specialised cardiovascular rehabilitation programme. The participants were informed and given cards with contact information about their local smoking cessation course, but the participants must arrange the contact and course registration independently. Smoking cessation in this group is difficult, and there were no significant differences between the intervention group or the control group.

A systematic review and meta-analysis by Aveyard *et al.* conclude that the method "very brief advice", where the healthcare provider takes the initiative and directly registers patients on a smoking cession course, without giving any advice, is more effective than providing patients with advice about courses and leaving them to enrol themselves (98, 99). If we had used the "very brief advice" method at the outpatient vascular clinic, it might have resulted in more patients who stopped smoking. Future studies could also build on other research findings that have shown promising interventions to promote changes in health behaviour that combine training and environment, education, knowledge, and persuasion with economic incentives and restrictions (100).

7.8 Technology

In the CIPIC Rehab Study, we found that the pedometer given to patients was a strong motivational tool when used in combination with logbooks and self-efficacy strategies. The effectiveness of pedometer interventions with goal setting and logbook for steps to promote walking has been documented in systematic and meta-analytic reviews that report such interventions can increase daily steps by approximately 2000 to 2500 steps per day (101). The benefits of self-care and self-efficacy strategies have also been reported in a randomised clinical trial that used pedometers, which was found to be more effective than interventions that did not include theoretical strategies (39).

In the CIPIC Rehab Study, receiving text messages was something that the patients found generated some guilty feelings about not doing enough exercise. Still, the majority wished to continue with the messages because they had a sincere desire to be more physically active and the text message helped them to continue. These findings are supported by research carried out by Hoffmann Pii (2014), who carried out interviews with IC patients at the Vascular Surgery outpatient Clinic at Rigshospitalet. Some of the patients in her study especially asked for "professional expert guidance" and wanted something that gave them a guilty conscience; the study concludes that *this disciplinary understanding of motivation is not easily aligned with the critique of the paternalistic and disciplinary attitude of the professional-centred approach from which the nurses wish to distance themselves* (p 226) (102). In the future, it is quite clear that an individual approach to each patient is necessary, and the model "one size fits all" must be revised to accommodate the wish of some patients for a disciplinary approach.

In the research field of self-care, there are high expectations that technology and eHealth can support health behaviour changes and help individuals perform self-care. EHealth's positive outcomes have shown improved self-care, self-efficacy, healthy behaviour, quality of sleep, diet, physical activity, mental health, medication, and adherence to treatment in chronically ill populations with extensive need for self-care (103).

In the field of self-care research, it is recommended to measure variables and find other studies to identify measuring of relevant factors. In the CIPIC Rehab Study, we used psychometric instruments as an approach to facilitate comparison of results in combination with demographical factors, socio-economic factors, disease-related factors and multimorbidity (104).

8.0 Strengths and limitations

8.1 External validity

The external validity in the term of generalizability and transferability in the CIPIC Rehab Study is high since its patient population was selected in accordance with the Clinical Practice Guidelines on *Diagnosis and Treatment of Peripheral Arterial Diseases* (24).

We randomised about one-third of potential eligible patients and this may represent bias. When we compared the patients in the intervention group to the control group, there were no significant differences between the groups. The 12 weeks of exercise was in the daytime, and ten patients couldn't participate because of their jobs, while others prefer self-training.

Self-training is an essential part of the treatment. Even though the main part of patients needs supervised training, some patients can do exercise independently and adapt other advice about healthy behaviour. This fact might explain the improvements in maximal walking distance in both groups of the randomised study. A rehabilitation programme with a flexible timespan targeting participants in jobs might result in a more significant percentage of younger patients.

8.2 Internal validity

The internal validity is high since we used blinding, randomisation and a study protocol.

The primary outcome maximal walking distance was performed using a standardised treadmill walking test, with a time-related random day to day variation of the test. However, group affiliation was blinded in the follow-up test, and the circumstances were the same during the tests for both groups. In addition, detection bias was minimized using an instruction manual to guide the research assistant during the treadmill test.

The CIPIC Rehab Study used maximal walking distance measured by treadmill test as the primary outcome, as it is regarded as a well-founded tool (105). Some PAD studies use the measurement of the ankle-brachial index (ABI) before and after exercise interventions. However, the ABI measurement was not chosen, as the Cochrane review by Lane et al. concludes that exercise does not improve the ABI (32). Clinical and demographic data on non-participants were sparse due to the Danish legislation on informed and signed consent. Self-reported questionnaires were used to measure secondary and explorative outcomes. This kind of subjective investigation relies on the participant's memories which carries the risk of recall bias. Data were interpreted independently by the researchers in the study, and two blinded statisticians performed the dataset analyses.

We used validated instruments (VascuQol, HADS, diet questionnaire etc.) and data collected face-to-face improved the patients' participation in the data collection. All 32-item in the checklist: *Consolidated Criteria for Reporting Qualitative Research* was used for detailed and comprehensive qualitative study reporting when paper III was published (106).

8.3 Credibility

In the qualitative study, interpretive and theoretical validity was ensured by applying the participants' expressions as they were told and involving theory on self-efficacy. The trustworthiness of the study was increased by investigator triangulation in all steps of the analysis discussing findings to agree on the interpretation of data. Credibility was improved by using thematic analysis as a well-established research method (67). Description of the setting, the participants and the themes in rich detail established credibility (107). We could have increased the validity by bringing the data and interpretations backwards to the participants in the study so they could have confirmed the trustworthiness of the data and review the findings from the focus group interviews (107). Patients in the study appreciate participating in the rehabilitation programme, and they knew the interviewer from the data collection and education sessions. This may have hindered criticism and affected the patients' explanations of the programme's advantages more positively. The nonappearance of criticism may also be associated with the context of the rehabilitation programme. The opportunity to participate in a specialised rehabilitation programme might give the patients a feeling of being valued and taken care of in a secured environment with a well-specified programme.

The participants in the focus groups interviews were the first patients that began the 12 weeks of exercise at precisely the same time, and therefore they knew each other well, which improved the possibilities of comfort during the interviews.

Focus group conversations can lead to group consensus, which may impact the findings, however "information power"(64) was reached and shown to the aim of the study. The themes revealed from the focus group interviews are overlapping each other, and are not exhaustive. Other researchers analyses of the same dataset might result in different themes; however, it is a premise in this kind of study.

8.4 Reflexivity

The challenges of combining methods are to develop a certain form of joint analysis of the set of data without losing the characteristics of each type of data. One approach has been to analyse each collection of data within its own paradigm. The value of combining methods can contribute to improve the precision of research results and produce new knowledge through a combination of the results from different methodologies (108). The mixed methods paper is not included in this PhD and is planned to be performed in the postdoc period due to the limited timeframe of the PhD period. The individual questionnaire survey with ancillary questions was planed as an ad on to the quantitative instrument, and the items generally do not result in a rigorous context-based qualitative data set, also called “mixed methods light” (52)(p 73). Data from the ancillary questions were therefore left out in the qualitative study. However, the qualitative data provides emergent themes and interesting quotes that can explain the quantitative findings in a planned postdoc study. Validated scales were used in the quantitative research. Complex interventions have many possibilities to combine various elements that are more than the results of each study component. The design of the CIPIC Rehab study might have been more transparent if we had used a qualitative exploratory evaluating design (47, 48, 52, 108-117), (52) p. 72-74, 101-116, and the Medical Research Council (MRC) guidelines on developing and evaluating complex interventions with its framework of four phases: development, feasibility/piloting, evaluation, and implementation (51). However, the CIPIC Rehab study design was in line (except piloting) with the MRC phases and the key questions asked in evaluating complex interventions: Are they effective in everyday practice? How does the intervention works? What are the effective ingredients, and how are they exerting effect? (51). Complex studies with randomised clinical trials are the most excellent to evaluate the effect of interventions. However, there can be some challenges regarding the methods in multidimensional and context-based interventions (118).

High-quality interventions needed to be adequately evaluated in detail with those factors that might have influenced the results. The extra costs of doing a mixed methods study with integration and analysis would possibly be balanced by superior descriptive power and insight into the intervention's generalizability (118). The pre-planned mixed methods study will therefore be explained in the following.

8.5 Plan for the postdoc study

The planned mixed methods study will be built on datasets from participants who participated in studies 1 and 2. In study 1, the quantitative component investigated walking distance, QoL and changes in health behaviour, and in study 2, the qualitative part explored the patient experiences of participation in the rehabilitation intervention and evaluated the rehabilitation intervention to get information about how the ideal rehabilitation programme should be. The planned postdoc study wants to combine the quantitative and qualitative findings to determine additional information about clinical outcomes in the CIPIC Rehab study. A contextual evaluation of the randomised clinical trial and its complex interventions will be performed to examine the implementation of the components in the rehabilitation programme (118).

9.0 Conclusion

As described in paper 1, The overall aim of this thesis was to investigate if a specialised cross-sectorial rehabilitation programme for patients with IC between the Department of Vascular Surgery, Rigshospitalet and the Healthcare Center in Albertslund community affects walking distance, health-related quality of life and incentive lifestyle changes. In the CIPIC rehab study, we found that the 12-weeks rehabilitation programme increased the patients walking distance.

The results showed a statistically and clinically significant impact on the patient's ability to walk a longer distance measured on a treadmill after 6 and 12 months. In addition, the patients increased their daily physical activity, had a better health-related quality of life, and improved their diet in a more healthy way. There were only minor changes in pain-free walking distance and smoking cessation in favour of the intervention group, but not statistically significant.

The qualitative investigation aimed to elucidate patients' experiences of participation in an existing community-based cardiac rehabilitation programme adapted for patients with intermittent claudication.

The CIPIC rehab study found that a local environment as a context for rehabilitation is essential for the patients to achieve support to manage the disease. By being with other patients with IC, the patients could be encouraged to go further on with the exercise when burning leg muscles appear. In combination with fun exercise facilitated by physiotherapists, motivation and adherence were increased. The patient's use of a pedometer was an independently motivational factor to increase daily physical activity. The components in the rehabilitation programme were evaluated positively

by the participants and were essential for even minor positive changes in health behaviour. When the 12 weeks of exercise were completed, the patients were on their own without support from fellows patients, and the ongoing independently exercise without guidance from physiotherapists was challenging.

9.1 Implication for practice

Community-based cardiac rehabilitation programmes have been established in many Danish municipalities and, with minor changes, could easily be adapted for patients with intermittent claudication.

Based on the findings of the CIPIC Rehab Study, recommendations for a specialised rehabilitation programme for patients with intermittent claudication include:

- Community-based setting in the patients' local health care centre with easy access for transportation and logistics with a flexible time span.
- Interdisciplinary rehabilitation programme with physiotherapist, vascular nurse, and dietician.
- Direct telephone number to the vascular nurse and access to counselling about the disease while needed.
- Pedometer and logbook handed out at the department of vascular surgery when diagnosed with intermittent claudication.
- Treadmill test before and after the 12 weeks of exercise, and as clinical follow-up test as recommended by the European Society for Vascular Surgery.
- Possibility to continue group training in the local community.

9.2 Implications for future research

Health behaviour is by nature challenging to change. As health care professionals, we are often very ambitious about giving information and advice about changes in health behaviour, even though studies indicate that up to 65% of patients with IC do not change their health behaviour. In the CIPIC Rehab Study, participants were able to grasp simple advice, for example dietary advice about integrating whole grains, nuts and fish into their diets. Likewise, patients made minor improvements in physical activity by acting on advice about "home activity" such as using a stair step or stool to do up and down walking exercise on-site when the weather was too bad for outdoor activities, or by acting on advice to park their car a bit further from the stores in order to increase their steps per day.

Future research should consider the possible benefits of integrating such 'easy to grasp' advice for patients into rehabilitation programmes, which concurs with the successful "very brief advice" method in smoking cessation and the findings in the present study that showed that simple advice about healthy food was reported by patients as beneficial to their self-care – in sum these findings could be summed up as what one might call a "less is more" concept for the advice given in rehabilitation programmes. Further research could investigate how the "less is more" concept could be applied to rehabilitation programmes in order to develop more simple advice for patients on how to implement healthy behaviour in their daily lives. A combination of such "less is more" advice and cross-sectorial rehabilitation interventions as described in the CIPIC Rehab Study would probably increase physical activity and healthy diets among patients and contribute to patients' feeling of doing the right thing, which may well lead to long-term improvement in their health behaviour.

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Appendices

Paper 1

Paper 2

Paper 3

Table S1. Exercise Protocol.

Table S2. 3 Months' Survey

PAPER 1

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Trials

STUDY PROTOCOL Open Access

Cross-sectoral rehabilitation intervention for patients with intermittent claudication versus usual care for patients in non-operative management - the CIPIC Rehab Study: study protocol for a randomised controlled trial

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Abstract

Introduction: Intermittent claudication (IC) caused by peripheral artery disease (PAD) is a common cardiovascular disease. Patients with IC have reduced walking capacity, restricted activity levels and mobility, and reduced health-related quality of life. The disease leads to social isolation, the risk of cardiovascular morbidity, and mortality. Non-operative management of IC requires exercise therapy and studies show that supervised exercise training is more effective than unsupervised training, yet many patients with IC lack motivation for changes in health behaviour. No studies investigating the effects of existing cardiac rehabilitation targeted patients with IC have been published. The aim of this article is to present the rationale and design of the CIPIC Rehab Study, which examines the effect of a cross-sectoral rehabilitation programme versus usual care for patients in non-operative management for IC.

Methods and analysis: A randomised clinical trial aims to investigate whether cardiac rehabilitation for patients with IC in non-operative management versus usual care is superior to treatment as usual. The trial will allocate 118 patients, with a 1:1 individual randomisation to either the intervention or control group.
The primary outcome is maximal walking distance measured by the standardised treadmill walking test. The secondary outcome is pain-free walking distance measured by the standardised treadmill walking test, healthy diet measured by a fat-fish-fruit-green score, and level of physical activity measured by an activity score within official recommendations. Statistical analyses will be blinded.
Several exploratory analyses will be performed. A mixed-method design is used to evaluate qualitative and quantitative findings. A qualitative and a survey-based complementary study will be undertaken to investigate patients' post-discharge experiences. A qualitative post-intervention study will explore experiences of participation in rehabilitation.

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Discussion: The study is the first to assess the effect of a cardiac rehabilitation programme designed for patients with IC. The study will describe how to monitor and improve rehabilitation programmes for patients with IC in a real-world setting. Mixed-method strategies can allow for both exploration and generalisation in the same study, but the research design is a complex intervention and any effects found cannot be awarded a specific component.

Trial Registration: Retrospectively registered in Clinicaltrials.gov identifier: NCT03730623.

Keywords: Intermittent claudication, Cross-sectoral rehabilitation, Physical exercise,

Background

Peripheral artery disease (PAD) is a chronic occlusive arterial disease caused by progressive atherosclerosis [1]. The most common symptom is intermittent claudication (IC), defined as a cramping leg pain that occurs during walking and is relieved by a short period of rest. IC affects 2% of the population (age 50–60) and increases with age to 6–7% (age 65–75) of the population in Western Europe and the USA [2]. Patients with IC have diminished walking capacity, restricted activity levels and mobility, and reduced health-related quality of life [3, 4]. It leads to social isolation and, unless health behaviour and relevant medications are prescribed, it may lead to worsening of disease with the risk of atherosclerotic complications and death [1, 3–8]. Motivation is an important but neglected factor as studies indicate that many patients with IC are not motivated for health behaviour changes in accordance with current recommendations [6, 7, 9]. Due to the risk of complications and limited patency of revascularisation (depending on procedure and anatomic location), current guidelines recommend that patients not requiring surgical revascularisation due to critical limp ischaemia be managed conservatively without surgical intervention [10]. Current practice for managing IC in Danish hospital settings involves brief advice to 'stop smoking and keep walking', combined with preventive medications including cholesterol-lowering treatment with statins and antiplatelet therapy [10, 11]. Non-adherence to these recommendations increases the risk of progression from IC to critical ischaemia and limb amputation [1]. It also produces a substantial economic burden on society due to reduced working ability, hospitalisation, and associated personal and social consequences for the individual patient [12, 13]. A recent Cochrane review [14] concluded that for patients with IC exercise is important regardless of whether treatment is revascularisation or overall conservative management. Supervised exercise training (SET) programmes are effective for alleviating symptoms, increasing walking distance, reducing cardiovascular risk factors and improving quality of life. Additionally, SET is relatively inexpensive and cost-efficient compared with other more invasive therapies [13–16]. Although evidence for SET is strong, studies exploring the effects of cross-sectoral rehabilitation intervention on patients treated for IC are lacking. IC rehabilitation is still poorly implemented and knowledge about how to set up an effective programme in a community-based setting is poor [17, 18].

Rehabilitation

Secondary prevention initiatives including rehabilitation for patients with PAD are recommended in current guidelines [5, 19]. Community-based supervised exercise appears to be at least as effective as exercise programmes provided in hospital settings [20]. Importantly, a study recently reported that attending a hospital-based supervised exercise programme was difficult for patients due to time spent on transportation and logistics [21]. This indicates that intervention in the local community improves patients' motivation and adherence [22]. Therefore, given the evidence for the beneficial effect of supervised exercise training for patients after acute coronary syndrome, the hypothesis is that patients with IC could also benefit with regard to maximal walking distance (MWD), pain-free walking distance (PWD), health-related quality of life, and physical function. Patients' perspectives on participating in the intervention could shed light on the factors that facilitate or hinder exercise and recommended health behaviour. Knowledge of this may increase both the quality and patient adherence to the conservative management of IC, thereby attenuating the burden of disease and improving quality of life for patients with IC.

Study objectives

The objectives of the trial are to investigate the effects of a cross-sectoral exercise and lifestyle intervention based on the established rehabilitation programme for patients with ischaemic heart disease versus usual care without rehabilitation in patients with IC. The primary hypothesis is that, compared with the control group, a specialised rehabilitation programme for the intervention group improves MWD in the treadmill walking test after the completed intervention. The three secondary hypotheses are that PWD, diet and level of physical activity improve in the intervention group compared with the control group after 6 and 12 months. Exploratory analyses will test the

hypothesis that IC rehabilitation improves quality of life, health behaviour, physical activity and reduces anxiety and depression after 6 and 12 months. The effects, benefits, and motivational factors of conservative management will be examined and patient experiences of the intervention, including factors that support or hinder adherence to the intervention explored.

Design

The CIPIC Rehab Study is designed to develop evidence-based knowledge on rehabilitation among patients with IC. It is a cross-sectoral, multidisciplinary, randomised clinical trial designed to examine the effects of an IC rehabilitation programme compared with usual care for patients in non-operative treatment for IC. Accordingly, the trial combines quantitative and qualitative research methods. The mixed methods are integrated by applying the explanatory sequential design [23, 24]. The rationale for this approach is that the quantitative findings provide a general understanding of the research problem through statistical results, and qualitative findings refine and explain the results by exploring participants' views in greater detail. Qualitative research coupled with randomised controlled trials can contribute to developing and evaluating complex healthcare interventions; it may be particularly useful in evaluating interventions that involve social and behavioural processes that are difficult to explore or capture using quantitative methods alone [25, 26]. A pragmatic world view is the philosophy underpinning the study [23].

Study population and eligibility criteria

Consecutive patients at the Department of Vascular Surgery at the Rigshospitalet in Copenhagen, Denmark will be screened for inclusion and approached for study participation.

Inclusion criteria are: patients with newly diagnosed IC treated conservatively; age $\geq$ 18 years; speak and understand Danish; able to provide informed written content; citizens of the eight municipalities of Greater Copenhagen belonging to the Healthcare Centre; and able to perform physical exercise. Exclusion criteria are: failure to understand and cooperate according to the trial instructions; co-morbidity complicating physical activity and exercise training, and lack of informed content.

Study procedure

When the informed content is signed, baseline data will be collected including a questionnaire administrated by the primary investigator. After baseline data collection, randomisation is conducted. Computer-generated block randomisation in four blocks has been done by an independent statistician and delivered in envelopes blinded from investigators. Randomisation is conducted by ongoing inclusion numbers marked on the envelopes.

Control group – usual care

Patients randomised to the control group will initially receive the department's usual, brief advice about exercise therapy (walking), smoking cessation, and preventive medical treatment with antiplatelet therapy and statins. The IC patients will receive written information about medication, walking exercise, and a logbook for self-reporting of walking behaviour in the outpatient clinic at the Department of Vascular Surgery, Rigshospitalet. Patients in the control group will follow standard follow-up procedure for patients treated for IC.

Experimental intervention group

The intervention group initially receives the usual care in the outpatient clinic at the Department of Vascular Surgery; additionally, patients' home communities offer courses in smoking cessation. Patients will receive a pedometer and be asked to self-report walking behaviour and steps in a logbook. The patient brings the logbook to the consultation with the physiotherapist, who initiates the startup training, supplies the motivation and explains the goal for the physical activity. Patients in the intervention group will follow the specialised cardiac rehabilitation programme for patients with IC. The intervention is based on experiences of cardiac rehabilitation and guidelines of the Danish National Board of Health and European Society of Cardiology [19]. Theories about personalised feedback and self-efficacy will be used as a method for encouraging behavioural changes to improve health outcomes [27].

Physical exercise training component

Training sessions will take place at a Healthcare Centre within the municipality of Greater Copenhagen. The main goal of the exercise is to improve the patient's physical capacity and health behaviour, such that this subsequently results in physical and psychological health benefits. Supervised exercise training is also targeted, relieving the fear and uncertainty the patient may feel towards physical activity. Two specialised cardiac rehabilitation physiotherapists with specific insight into IC will plan and supervise participants' exercise. This entails patients actively engaging, in groups with up to ten in 24 supervised physical exercise sessions, each lasting one hour with two weekly sessions. The exercises include varied forms of physical exercise all combined to accommodate the patients' own goals regarding walking distance. The physiotherapists will administer and record a six-minute walking test and 30-second chair stand test prior to and at completion of the intervention. Pedometer and self-reported walking behaviour are a part of

the consultation used to increase or sustain daily physical exercise at least 30 minutes per day. The results will be used as part of an individual motivational interview with each patient after completion of the 24 training sessions.

Supervised exercise training programme

The exercise training protocol will consist of a 10–15-minute warm-up, followed up by a 45–50-minute combination of strength and circuit training. The exercise training programme is based on national guidelines for cardiac rehabilitation [28]. The warm-up will be based on either bicycling, with a focus on using the forefoot when pedalling, or walking in different variations, i.e. walking on toes, heels, walking sideways, walking lunges and walking at different paces. In strengthening the large muscle groups, there will be a primary focus on the leg muscles. The strength exercises for the upper body will primarily be performed as an intermission, in the exercise for the lower body. Different exercise equipment will be used to create resistance in the exercise training, i.e. elastic bands, body bars, dumb bells, and strength-training machines. The exercise will vary from 1×15, 2×15, and 3×10 repetitions, based on low to moderate intensity of 40–60% of the maximum muscle strength [28]. The circuit training will primarily be based on activity for the lower limbs, i.e. walking and running at different paces and variations, walking combined with an exercise, i.e. high knee lifts, kick backs, calf raises, and different relay races in teams. The circuit training will also involve interval training, of varying lengths, depending on both the different exercises and the patients' individual limits due to lower limb pain. Two of the sessions will be based on using and practising pole striding at a nearby outdoor training park. In addition to the physical activity component, the programme will also contain components of health education for improving the self-efficacy of physical activity in the patients and therefore seek to affect health behaviour. Five of the sessions will contain 10–15 minutes of health education, which will include the use of tools developed by Steno Diabetes Center, Copenhagen, Denmark. These tools were developed for supporting patients in making long-term health-related changes, and for the use of health professionals in health education for patients with chronic illness [29]. Furthermore, the health education will contain motivational, group-based dialogue with the patients about their health behaviour and ability to participate in physical activity in their own neighbourhood. There will also be motivational conversations concerning the patients' daily use of and achievements with the pedometer and logbook handed out to each patient at the start of the intervention.

Education in groups and individual consultation

The aim of the intervention is to provide emotional support, improve coping skills, and to respond to physical symptoms. Education and information about the disease prepares the patient for expected symptoms and sensations, and dialogue and shared reflections facilitate strategies for coping with symptoms and experiences associated with the condition, for example when leg pain is part of the treatment for getting better. The group education is a two-hour-long session, about the pathophysiology of IC, medications, health behaviour, disease management, quality of life, and coping with the disease. The principal investigator (MS), who is an experienced cardiac rehabilitation nurse with specific knowledge of IC to ensure protocol compliance, will perform the intervention. Information given will also be based on national guidelines and standard treatment of patients with IC. A clinical dietician will advise participants in a two-hour-long group session about healthy diet and atherosclerosis, and in addition give access to individual consultation.

Albert Bandura's Social Cognitive-Behavioral Theory and self-efficacy inspires the intervention. Its focus is on the dynamic interaction of person and behaviour; the individual's actual ability to perform the appropriate behaviour; learning a new skill or knowledge by observing others; external responses to the individual's behaviour that either encourage or discourage the behaviour expectations: the anticipated consequences of a behaviour; and self-efficacy: the person's confidence in his or her ability to perform a behaviour [27, 30]. Consequently, the individual, the group, spouses, and surroundings in a rehabilitation setting are important. Spouses are therefore invited to participate in group sessions as well as in individual sessions.

Studies show that text messages can facilitate lifestyle changes [31–33]. After completion of exercise training, participants are offered personalised motivational follow-up text messages. The content, frequency, and duration of the text messages are agreed upon individually for the next 8 months and will be reassessed at follow-ups after 3 and 6 months.

Outcomes and data collection

Data will be collected at admission, discharge, 6 months and 12 months administrated by the primary investigator (see Table 1). The primary and the secondary outcomes reflect the primary modifiable factors of the intervention, and a number of explorative outcomes will be collected to evaluate the effect and meaning of the intervention (see Table 2). The post-discharge experiences of patients in the intervention group will be explored through semi-structured qualitative interviews. Patient flow is illustrated in Fig. 1.

Table 1 The CIPIC Rehab Study - exploratory quantities subjected to post hoc analysis

Quantity	Time of measure	Type of quantity
Demographic		
Sex	Baseline	Binary (M/F)
Age, height, weight, body mass index (BMI)	Baseline	Continuous
Marital, occupational, educational status	Baseline	Categorical
Clinical		
Charlson Comorbidity Index [34]	Baseline, 6, 12	Categorical
Hypertension	Baseline 6, 12	Binary (Y/N)
Smoking+ Fagerströms test, (Alcohol Timeline Followback)	Baseline, 6, 12	Categorical
Medication (routine drugs; antiplatelet; statins and other medication)	Baseline, 6, 12	Categorical
Nutritional screening 'HjerteKost': fat-fish-fruit-green score [35]	Baseline, 6, 12	Categorical
Paraclinical		
Blood work (biomarkers, cholesterol, HBa1C, Hg, thyroid)	Baseline, 6, 12	Continuous
Physical function		
The standardised treadmill walking test [36, 37]	Baseline, 6, 12	Continuous
Six-minute walking test (before and after supervised exercise training) [38]	Baseline, 3	Continuous
Sit to stand test (before and after supervised exercise training) [39]	Baseline, 3	Continuous
Level of physical activity (0–7 times a week)	Baseline, 6, 12	Categorical
Questionnaires		
HADS, Hospital Anxiety and Depression Scale [40]	Baseline, 6, 12	Categorical
VascuQol, Vascular Quality of Life questionnaire [41]	Baseline, 6, 12	Categorical
PAM13, 13-item Patient Activation Measure [42]	Baseline, 6, 12	Categorical
Pedometer, text message (intervention group)	3 months, 6	Binary (Y/N)
Participation in dietician and nurse session (intervention group)	3 months	Binary (Y/N)

M/F male/female, *Y/N* yes/no

Primary outcome

MWD will be measured by the standardised treadmill walking test based on a graded protocol (3.2 km/hour with 2% increase every 2 minutes). Treadmill assessment has the highest reliability when using a graded protocol together with outcome measurements, such as initial claudication distance and absolute claudication distance. Results of treadmill testing are expressed as the initial claudication distance, the moment claudication pain begins and the absolute claudication distance, the moment the test has to stop due to the maximal level of bearable claudication pain [36, 37]. The follow-up treadmill walking test will be performed by a research assistant blinded as to the patients' group affiliations.

Secondary outcome

PWD will be measured by the standardised treadmill walking test as described above and with a numeric rating scale for pain [37, 43]. Daily physical activity is measured by self-reported number of times per week of walking or physical exercise activity of at least 30 minutes, as recommended by the National Board of Health [44]. Diet will be measured by a diet questionnaire (HjerteKost), a validated Danish instrument with 19 items. The scale offers two scores, a fat and a fish-fruit-green score, each of which can range from 0 to 18. To be able to achieve the term 'healthy' the score must be at least 75% in both the fat and the green scores [35]. The instrument is validated and recommended by the National Board of Health [28].

Exploratory outcomes

Smoking is measured by self-reported smoking behaviour by the Fagerström Test for Nicotine Dependence. The self-administered questionnaire has good internal validity and a good correlation with nicotine levels as an instrument for measuring addiction to tobacco [45].

Table 2 Focus group - interview topics

Supervised exercise training: physiotherapist. Content and education
Education session: nurse and dietician. Content and education
Patients' experiences of participating in the intervention group.
Knowledge and uncertainty about IC
Experiences of factors and barrier that supported or hindered adherence to the intervention.
Factors that influence coping strategy, persistent lifestyle changes
Importance of environment and togetherness with similar patients
Empathy, support and motivation
Risk factor management
Coping behaviours
Change interventions
Attitudes, beliefs, how to handle the pain
Feeling better mentally
Accessibility and compliance
Self-monitoring goal setting
Exercise logbook and pedometers. Motivational text message.
Specific walking advice to promote self-managed walking
Quality of life
Solution behaviour change techniques
Patient satisfaction of participate in the IC rehabilitation programme and point out if any suggestions for changes.

Alcohol consumption will be measured by the Alcohol Timeline Followback (TLFB). TLFB has been shown to be a psychometrically sound assessment instrument for obtaining retrospective daily estimates of alcohol consumption. TLFB has been extensively evaluated in various settings, over varying reporting intervals and with diverse drinker populations and has been found to have very good measurement properties [46, 47].

The Hospital Anxiety and Depression Scale (HADS)

HADS is a 14-item instrument that measures symptoms of anxiety (HADS-A) and depression (HADS-D). The scale offers two subscales, each of which can range from 0 to 21. Scores of 0–7 for either subscale are regarded as normal; 8–10 suggest the presence of a mood disorder; and 11 and above suggest the probable presence of a mood disorder. This tool has been translated and validated in many countries and its capacity to detect anxiety and depressive disorders is widely recognised [48].

The Vascular Quality of Life questionnaire (VascuQoL)

VascuQoL (VQ6) is a PAD-specific instrument recommended as one of the preferred questionnaires when evaluating quality of life outcomes in patients with PAD. The VQ6 is a six-item questionnaire, developed using a

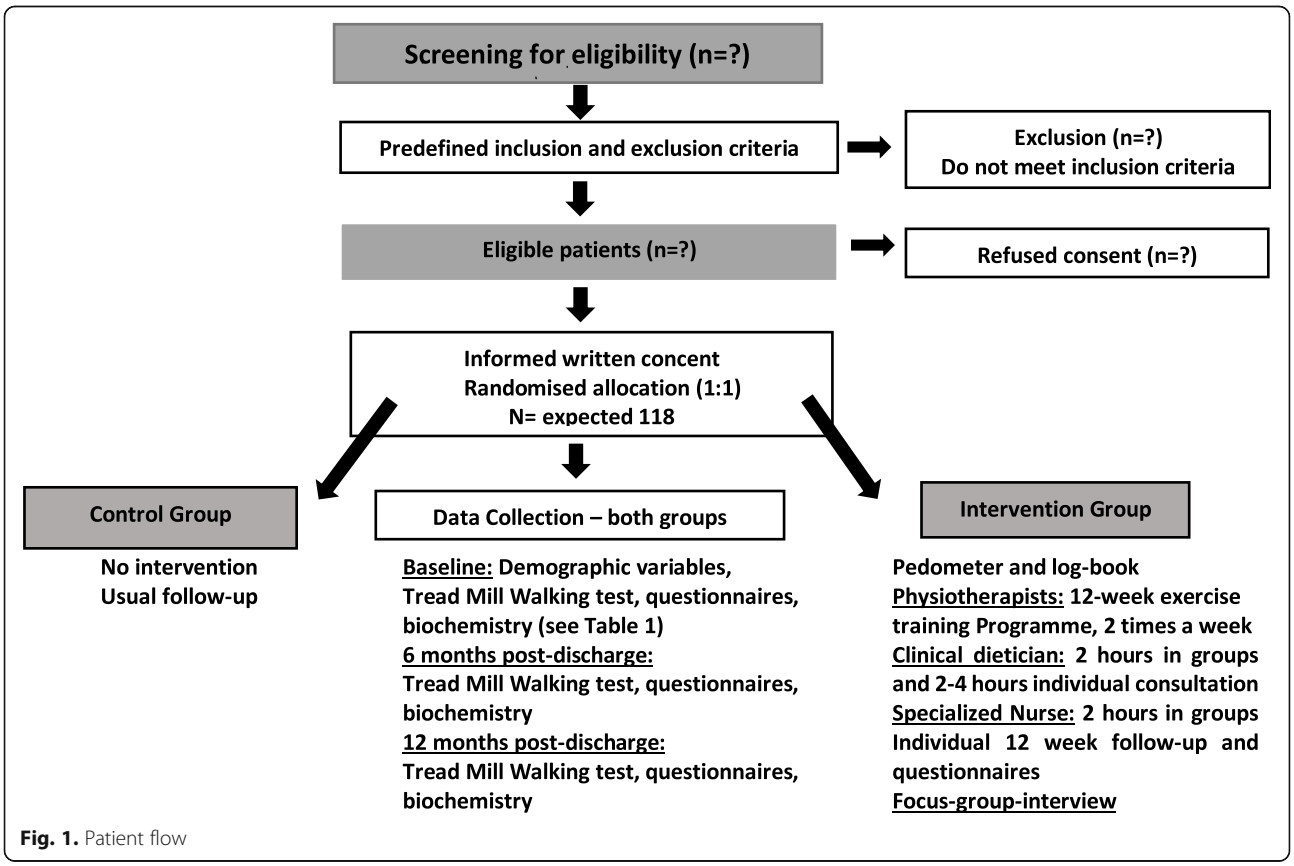

Fig. 1. Patient flow

combination of qualitative and quantitative methodology. The VQ6 has acceptable to good psychometric properties regarding data quality, scale assumptions, targeting, validity and reliability. Further, VQ6 seems to be easy to use and comprehend within the target population of patients with PAD [41].

The Patient Activation Measure (PAM)

PAM-13 is a 13-item instrument for evaluating educational interventions aimed at improving patient engagement. Patient activation specifies the level of patients' engagement and may contribute to better self-management, higher engagement in treatment and greater patient satisfaction. The European translations of PAM-13 resulted in four instruments with good psychometric capabilities for measuring patient activation. All items have five possible responses with scores ranging from 0 to 4: (1) disagree strongly, (2) disagree, (3) agree, (4) agree strongly or (0) not applicable [42, 49].

Complementary studies

Numerous data will be collected to evaluate the effect and meaning of the intervention.

Quantitative data

The quantitative study consists of an individual questionnaire survey conducted as interview by the principal investigator. The survey including data about feasibility: participation (number of times), use of pedometer (yes/no), logbook (yes/no) and to what extent it has motivated daily physical exercise, exercise choice after the course, and text messages (yes/no). Results from the physiotherapist six-minute walking test and 30-second chair stand test, before and after in metres/number are also included.

Qualitative explorative data

As a part of the study, brief individual interviews exploring course satisfaction, suggestions for changes, and the relevancy of the various rehabilitation components will be conducted. Furthermore, focus group interviews of patients participating in the intervention group will also be conducted. Prior to interviewing, an interview guide will be developed. It will be used to help explore patient experiences of training and teaching sessions, factors helping or hindering improvement in health behaviour, the use of the pedometer, logbook, and text message influenced motivation/adherence, patient satisfaction with the intervention and suggestions for future rehabilitation programmes. Research questions will be developed using knowledge from existing qualitative studies in the field and the individual brief interviews [6, 7, 9, 15, 17, 50, 51] (see Table 2). The focus group interviews will be conducted by the principal investigator (MS) and two assistant moderators that register key points and takes field notes [52]. Patients will be recruited during their 3- and 6-month follow-ups at the Healthcare Centre or at the Department of Vascular Surgery as a convenience sampling with consecutive recruitment of participants according to the groups in which they exercised during the training sessions. To embrace the potential impact of any team spirit developed during the training session, we consider focus groups and recruitment of participants according to training groups to be relevant. The interviews will be held in well-known surroundings in the Healthcare Centre. The size of the focus groups will be five to eight participants to secure an opportunity for each person to share insights, experiences and observations. Smaller groups allow more in-depth conversation and afford each person a greater opportunity to speak. 'Information power' will guide the adequate sample size and the number of focus group interviews [52].

Data collection and data analysis

The interviews will be audio recorded and transcribed verbatim. Interviews are anticipated to last approximately one hour. Thematic analysis according to Braun & Clarke will be used to analyse data [53]. This means combining a coding analysis with the content of the focus group discussion [11, 13]. Derivation of themes will be identified by an exploratory analysis to present selected patterns relevant for the study aim and collected data. Numbers of data coders, description of the coding tree, software program, illustrated themes/findings, quotation identification, consistency between the data presented and the findings, as well as the clarity of major and minor findings will be a part of the analysis [54, 55]. The thematic analysis will be used as a systematic approach to the analysis of quality data from the focus group interviews. That involves identifying themes or patterns of meaning by coding and classifying data textually, according to themes and interpreting the resulting thematic structures by seeking commonalties, relationships, overarching patterns, theoretical constructs, or explanatory principles [56].

Statistical analysis

A trial-independent statistician will make a blind analysis of the data and the primary and secondary analyses will be performed according to the intention-to-treat principle. We will use general regression models for the continuous outcomes and logistic regression models for binary outcomes. In the analysis of the primary outcome, the outcome (MWD at 6 months) will be analysed with adjustment for baseline MWD, sex or age (included continuously). For the three secondary outcomes – PWD distance, level of physical activity and diet at 6 months – the analysis will be done similarly with adjustment for

baseline values, sex and age (continuous). As exploratory analyses of MWD, PWD, smoking behaviour, diet and patient-related outcome measures, mixed general and generalised models with repeated measurements will be used including measurements at baseline, 6 and 12 months in the same model. These models will also be used for all other explorative outcomes. In these models, the interaction between intervention group and time is of primary interest, indicating different developments after intervention start. In the case of significant results in the primary outcome, sensitivity analyses will be performed to estimate the potential effect of data missing at random by a worst-case scenario. Let X be the group where a beneficial effect is observed, and Y be the other group. Missing values in group X will be imputed by the minimum value found in the material and missing values in group Y will be imputed by the maximum value found. The primary outcome will be tested first using a significance level of 0.05. Analyses of the secondary and exploratory outcome measures as planned above will be analyzed with no p value adjustment due to multiplicity. Instead, the interpretation of these results will be assessed in the light of multiple testing, i.e. statistically significant effects will be interpreted in the context of increased risk of type I error. The clinical effect size will be reported by Cohen's d. Per protocol analyses of the primary and secondary outcomes will be performed.

Sample size and power calculation

The expected average baseline value of MWD has been set to 120 m with a detected 50% improvement (60 m). There is a wide variance in MWD in this patient group and consequently the standard deviation (SD) is set at 100 m, based on an expected improvement in walking ability of approximately 50% to 200% [18]. With a 5% significance level and 80% power, it will thus be necessary to include 88 patients to detect an improvement of 60 m in MWD in the intervention group at the 12-month follow-ups, compared with the control group. Owing to the previously mentioned risk of co-morbidities, combined with an expected drop-out, a drop-out of 25% must be expected, therefore the investigators plan to include 118 patients in total (59 in each group).

Discussion

This randomised clinical trial is the first to examine the effect of a cross-sectoral exercise and health behaviour intervention based on the established cardiac rehabilitation programme for patients with IC. The CIPIC Rehab Study will provide evidence on the rehabilitation needs of patients treated conservatively for IC, ánd insight into the patient benefits and motivational factors of conservative management experiences of the intervention. The results can be used to make recommendations for a specialised IC rehabilitation programme, which healthcare professionals and policymakers may use to make qualified, evidence-based decisions in everyday clinical practice and as a foundation for national and international guidelines. With a positive outcome, some of the possible effects could be lower morbidity and a decrease in the use of the public health system. This is advantageous for both patients and society. Whether it produces neutral, negative or positive results the study will have implications for clinical practice and follow-up care for patients treated for IC. The study has been designed to meet the criteria for high quality in non-pharmacological randomised clinical trials [57] with central randomisation, blinded assessment of the exercise outcome, and blinded analysis by a study-independent statistician. Detailed information on the intervention received and usual care will be collected, including self-initiated exercise training during the trial period. The secondary outcomes of self-rated mental health are subjective by nature [58–60]. The trial is designed with multiple statistical comparisons, therefore results of the explorative analyses will be interpreted with caution.

Trial status

Recruitment began on 1 April 2017 and end of the 12-month follow-up of all patients will be completed in april 2020 in accordance to protocol number: H-17004183/clinicaltrials.gov.

Inclusion was initiated on 5 December 2017 and completed in 28 June 2019. End of the 12-month follow-up of all patients will be completed at the end of June 2020. The results of the trial and complementary studies will be published in relevant international peer-reviewed journals. Authorship will be determined according to the guidelines of the International Committee of Medical Journal Editors.

Supplementary information

Supplementary information accompanies this paper at https://doi.org/10.1186/s13063-019-4032-x.

Additional file 1. SPIRIT 2013 checklist.

Abbreviations

HADS: Hospital Anxiety and Depression Scale; IC: Intermittent claudication; M/F: Male/Female; MWD: Maximal walking distance; PAD: Peripheral artery disease; PAM13: Patient Activation Measure; PWD: Pain-free walking distance; SET: Supervised exercise training; TLFB: Alcohol Timeline Followback; VascuQol: Vascular Quality of Life questionnaire

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Author contributions
MS, LPJ and HS conceived the idea of the study. MS initiated the study design and implementation. LCT designed the statistical analysis plan in collaboration with MS and SKB. PPB designed the supervised exercise training programme. All authors designed the trial, developed the protocol, revised the manuscript critically and have given their final approval of the version to be published.

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Availability of data and materials
Not applicable.

Ethics approval and consent to participate
The study complies with the Declaration of Helsinki and was approved by the regional research ethics committee (J. No.: H-17004183) and the Danish Data Protection Agency (J. No.: 2012-58-0004). Informed written content has been provided and signed.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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Publisher's Note

PAPER 2

RANDOMISED CLINICAL TRIAL

Cardiovascular Rehabilitation Increases Walking Distance in Patients With Intermittent Claudication. Results of the CIPIC Rehab Study: A Randomised Controlled Trial

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WHAT THIS PAPER ADDS

This study adds to knowledge that cardiac rehabilitation programmes for patients with intermittent claudication increase walking distance, health related quality of life, physical activity, and healthy diet. Based on this study, recommendations for a specialised rehabilitation programme for patients with intermittent claudication include supervised exercise training as an interdisciplinary intervention in a local community setting with physiotherapists, a specialist vascular nurse, and dietician; a pedometer as a strong motivational tool for patients to increase daily walking; follow up training after 12 weeks and cross sector coordination by vascular nurse; and patient access to a telephone number.

Objective: To examine whether a cardiac rehabilitation programme in a community based setting for patients with intermittent claudication (IC) affects walking ability, quality of life, and changes in health behaviour. The trial investigated a cross sector cardiovascular rehabilitation programme compared with usual care for patients having non-operative management.

Methods: The trial allocated 118 patients, with 1:1 individual randomisation to either an intervention or control group. Data were collected at a department of vascular surgery and at a healthcare centre in Denmark. The rehabilitation intervention consisted of usual care plus 12 weeks of exercise training, pedometer, health education, and text messages. The primary outcome was maximum walking distance at six months measured by treadmill walking test. The secondary outcomes were maximum walking distance at 12 months and pain free walking distance measured by treadmill walking test, healthy diet, level of physical activity, and quality of life (QoL) at six and 12 months.

Results: In the intervention group, 46 participants were analysed, with 47 in the control group. Following three months of rehabilitation, a 37% difference (95% CI 1.10 − 1.70; $p = .005$) was found between groups in maximum walking distance at six and 12 months, in favour of the intervention group. The same positive effect was found in physical activity, QoL, and healthy diet, but was not statistically significant in pain free walking distance and smoking.

Conclusion: A specialised community based cardiac rehabilitation programme for patients with IC showed statistically and clinically significant effects on maximum walking distance, physical activity, quality of life, and healthy diet, but not on pain free walking distance and smoking, compared with usual care without rehabilitation.

Keywords: Cardiovascular rehabilitation, Intermittent claudication, Pedometer, Quality of life, Randomised controlled trial, Walking distance
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INTRODUCTION

Peripheral artery disease (PAD) is a chronic occlusive disease in the lower limb arteries caused by progressive atherosclerosis.[1] The prevalence of PAD is increasing and

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affects more than 200 million people globally and > 10% of the population aged > 70 years.[2] The most common symptom is intermittent claudication (IC), which is defined as a cramping leg pain that occurs during walking and is relieved by a short period of rest. Patients with IC have diminished walking capacity, restricted activity levels and mobility, and reduced health related quality of life.[3] This can lead to social isolation and worsening of the disease with increasing risk of atherosclerotic complications and death.[4] Because of the risk of complications and limited patency of revascularisation, conservative management should be attempted as first line treatment in patients without critical limb ischaemia.[5]

According to the most recent *Cochrane Review*, supervised exercise training (SET) can be effective in alleviating symptoms, increasing walking distance, reducing cardiovascular events, and improving quality of life. Such programmes are also relatively inexpensive and cost effective, compared with other more invasive IC therapies.[6,7] Although evidence for the health benefits of SET is strong, rehabilitation is still poorly implemented and studies exploring how to set up effective community based IC rehabilitation interventions are lacking.[8] Current practice for managing IC in Danish hospital settings involves brief advice to "stop smoking and keep walking", combined with preventive medications including cholesterol lowering treatment with statins and antiplatelet therapy, and this quality does not live up to the recommended SET evidence.[5]

The aim of this trial was to investigate the effects of a cross sector (community/hospital) exercise and lifestyle intervention based on an already established community based rehabilitation programme for patients with ischaemic heart disease compared with the effects of usual care without rehabilitation in patients with IC.

Cardiac rehabilitation programmes have been offered for more than a decade with a mix of exercise and education sessions twice a week for 12 weeks, and are established in Denmark, Sweden, and the UK.[9,10] Different kinds of exercise type and intensity for older people with cardiovascular diseases are recommended by the European Society of Cardiology.[11]

The primary hypothesis was that compared with the control group, a specialised rehabilitation programme in a community based setting for patients with IC (intervention group) improves maximum walking distance in a treadmill walking test after the completed intervention.

METHODS

The design and methods of the CIPIC Rehab Study have been described in a previous design paper[12] and are summarised here. The trial also incorporates a qualitative component, details of which will be published elsewhere. The trial has been registered at clinicaltrials.gov (NCT03730623). The trial complies with the Declaration of Helsinki and was approved by the local ethics committee (J. No.:H-17004183) and the Danish Data Protection Agency (J.No.:2012—58—0004).

Setting and recruitment

Consecutive patients at the Department of Vascular Surgery in Copenhagen, Denmark (Rigshospitalet) were screened for inclusion and approached for study participation. The setting was one hospital and one municipal healthcare centre in the Capital Region of Denmark. None of the patients had any interventions before recruitment.

Inclusion criteria were conservatively treated patients with newly diagnosed IC using clinical assessment and ankle brachial index; age > 18 years; speaks and understands Danish; able to provide informed written content; citizens of one of eight municipalities of Greater Copenhagen belonging to the local healthcare centre; and expected to be able to manage transportation and perform exercise. Exclusion criteria were failure to understand and cooperate according to the trial instructions; comorbidity complicating physical activity and exercise training; and lack of informed consent.

Rehabilitation

The rehabilitation began in the outpatient clinic and continued in the healthcare centre, with an experienced cardiac physiotherapist with specialised knowledge of patients with IC. All patients were followed by the investigator and a direct telephone number to counselling was provided to both groups to secure access to counselling if needed.

Control group: usual care

Patients in the control group followed standard procedure for patients treated for IC[5] and received the department of vascular surgery's usual, brief advice about walking exercise and smoking cessation, and were given preventive medical treatment with antiplatelet therapy and statins. The patients received written information about medication, walking exercise, and a logbook for self reporting walking behaviour.

Intervention group

The intervention group initially received the usual care. Additionally, patients' home municipalities offered courses in smoking cessation. Patients received a pedometer and were asked to self report walking behaviour and steps in a logbook. The patients brought their logbooks to the consultations with the physiotherapist. These consultations included a dialogue about motivational factors and initiation of the training, and informed patients about the goal of the physical activity.

Group course and individual consultation

The group course was a two hour session about the pathophysiology of IC, medications, health behaviour and disease management. Group sessions and the individual consultation were performed by an experienced nurse with

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specific knowledge of IC, based on guidelines.[13] Spouses were invited to participate in group sessions as well as in the individual consultations. A clinical dietician ran a two hour group session about healthy diet and atherosclerosis and offered individual consultations.

Supervised exercise training

Two physiotherapists with specific insight into IC developed and conducted the supervised exercise training. The programme was based on the established cardiac rehabilitation programme according to guidelines,[9] with a primary focus on the leg muscles.

The programme was initiated continuously and offered two weekly exercise sessions for 12 weeks. Patients were required to actively engage in groups of up to 10 patients from the programme. The exercises included varied forms of physical exercise combined to accommodate the patients' own goals regarding walking distance. To increase or sustain daily physical exercise at a level of at least 30 min/day, pedometer and self reported walking behaviour were included in the discussions with patients at their individual consultations.

Outcome evaluation

Both groups underwent outcome assessments at six and 12 months post randomisation.

Primary outcome: maximum walking distance

Maximum walking distance (MWD) was measured by the standardised treadmill walking test based on a graded protocol: 3.2 km/hour with 2% increase every two minutes.[13]

Secondary outcome: pain free walking distance, daily physical activity and diet

Pain free walking distance (PWD) was measured by the standardised treadmill walking test as described above and with a numeric rating scale for pain. Daily physical activity was measured by self reported number of times per week of walking or physical exercise activity of at least 30 minutes.[14] Diet was measured by a diet questionnaire with a fat score and a fish-fruit-green score. To achieve the term "healthy", each score had to be at least 75%.[15]

Exploratory outcomes

Before the treadmill tests at six and 12 months, self reported general condition in the legs compared with baseline was measured. Smoking and alcohol consumption were measured by self reported behaviour.[16,17] The Hospital Anxiety and Depression Scale (HADS)[18] was used to detect symptoms of anxiety and depression (scores $\geq$ 8). The Vascular Quality of Life Questionnaire (VQ6) was used as a disease specific instrument to evaluate QoL, where a higher value indicates better health status.[19]

Randomisation and blinding

The trial allocated 118 patients, with 1:1 individual randomisation to either the intervention group or control group.

When the informed consent was signed, baseline data were collected, and randomisation conducted. Computer generated block randomisation in four blocks was generated by an independent statistician and delivered in envelopes blinded from the investigator. Randomisation was conducted by ongoing inclusion numbers marked on the envelopes. In trials with rehabilitation intervention it is not possible to blind patients and healthcare professionals. However, primary outcome measures and statistical analyses were blinded, and follow up treadmill walking tests were performed by a research assistant blinded to the patients' group.

Statistical analysis

The analyses were performed as intention to treat analysis with use of general linear regression models and logistic regression models. Primary and secondary outcomes were analysed with adjustment for baseline values, sex, and age with a significance level of .050. For all continuous outcomes, violation of the assumption of normally distributed residuals were solved by log transformation of the outcome. Sensitivity analyses were conducted by removal of outliers (Cook's d above 0.1). The exploratory outcomes measured at 0, 6, and 12 months were analysed with linear and logistic mixed models with each participant included as a random effect. In these analyses the interaction between intervention group and time was the significance test of interest. These models were adjusted for sex and age. Exploratory outcomes were assessed as multiple testing with significant effects interpreted in the context of increased risk of type I error. Clinical effect size reported by Cohen's d.[12] Analyses were performed using SAS 9.4.

The expected average baseline value of maximum walking distance was estimated to 120 metres (m) with a detected 50% improvement (60 m), and the standard deviation (SD) was set at 100 m, based on an expected improvement in walking ability of approximately 50% to 200%.[20] Expected dropout rate was set to 25%. With a 5% significance level and 80% power, a total of 88 patients (44 in each group) was needed to detect an improvement of 60 m in MWD in the intervention group.

RESULTS

Between April 2017 and May 2019, 333 patients diagnosed with IC and having non-operative management were screened. A total of 215 patients were excluded, and 118 patients gave consent and were randomised with 59 in each

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group. During the trial, 12 patients from the intervention group and 13 patients from the control group withdrew their consent. The three month intervention was completed by 43 participants. Six patients withdrew before the SET intervention, and 10 patients dropped out after beginning the SET, corresponding to a dropout rate of 17% (see Fig. 1).

Baseline

There were small differences between the intervention and usual care groups at baseline (Table 1). Mean age was 70 years and slightly more than one third were female. Groups were comparable with small baseline differences in smoking, alcohol intake, physical activity, comorbidity, psychological measurements, and medication (Table 1). Participants and non-participants in the trial were comparable with respect to age and sex: mean age ± SD non-participants 68.6 ± 9.0, mean age participants 70.2 ± 7.1 ($p = .13$). Sex distribution was the same in both groups: non-participants 36.9% female and 63.1% male, participants 41.5% female and 58.5% male ($p = .48$).

Primary outcome

MWD increased in both groups at six months, but statistically significantly more in the intervention group compared with the control group as measured by the standardised treadmill walking test. The intervention group had higher median MWD scores at baseline (248 m *vs.* 188 m in the control group), but also had greater improvement at the six month follow up (350.5 m *vs.* 253 m in the control group) (37%; 95% CI 1.10 — 1.70; $p = .005$) and group difference corresponded to a Cohen's d of 0.38 with a small to medium effect size (Table 2).

In the per protocol analyses of the primary and secondary outcomes, 39 patients were included who completed at least 70% of the exercise sessions and also participated in the treadmill follow up test at six months. These findings make estimates and differences stronger in favour of the intervention group with a further 50 m greater walking distance that increased 45% more in the intervention group compared with the control group (95% CI 1.17 — 1.80; $p = .001$). Improvement at the six month follow up was 400 m in the intervention group *vs.* 253 m in the control group, but this does not change the conclusions (Table 3).

Secondary outcomes

PWD distance increased further in the rehabilitation group compared with the usual care group at six months (28%; 95% CI 0.99 — 1.65), but the difference was not statistically significant ($p = .060$) (Table 2).

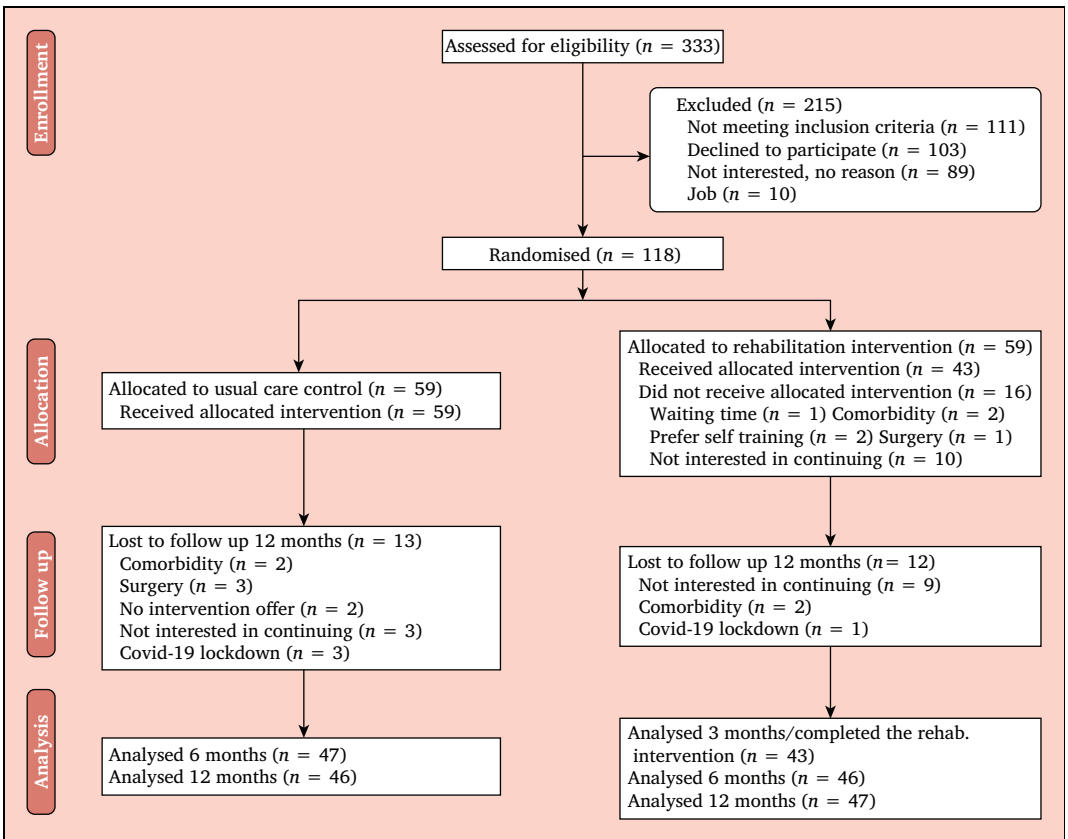

Figure 1. Consolidated Standards of Reporting Trials (CONSORT) study flow diagram of the CIPIC Rehab Study of patients with intermittent claudication receiving usual care (Control) or additional cardiovascular rehabilitation programme (Intervention), 5 December 2017 — 18 May 2020.

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Table 1. Baseline demographic and clinical characteristics of 118 patients with intermittent claudication included in the CIPIC Rehab Study for usual care (Control group) or additional cardiovascular rehabilitation programme (Intervention group)

Variable	Control group (n = 59)	Intervention group (n = 59)
Female sex	26 (44)	23 (39)
Age − y	70.1 ± 7.3	70.5 ± 7.0
BMI − kg/m^2	26.2 ± 6.0	26.8 ± 4.3
Smoking		
Current smoker	25 (42)	28 (47)
Former smoker	29 (49)	27 (46)
Never smoker	5 (8)	4 (7)
Pack years	50.2 ± 31.5	42.9 ± 27.6
Physical activity		
Exercise of 30 min/w		
0 times	32 (54)	42 (71)
1−2 times	15 (25)	9 (15)
3−6 times	8 (14)	7 (12)
≥ 7 times	3 (5)	1 (2)
Walking of 30 min/w		
0 times	24 (41)	26 (44)
1−2 times	6 (10)	7 (12)
3−6 times	10 (17)	9 (15)
≥ 7 times	19 (32)	17 (29)
Physical activity ≥ 30 min/d	21 (36)	18 (31)
Alcohol intake − drinks/w	10.3 ± 12.6	10.4 ± 13.4
Medications		
Aspirin	36 (61)	42 (71)
Clopidogrel	17 (29)	10 (17)
DOAC	1 (2)	2 (3)
Vitamin K-antagonists	0 (0)	2 (3)
Statins	54 (92)	51 (86)
Charlson comorbidity score		
0, no comorbidity	31 (53)	42 (71)
1, mild	15 (25)	7 (12)
2, moderate	9 (15)	5 (8)
≥ 3, severe	4 (7)	5 (8)
Diabetes	7 (12)	11 (19)
Myocardial infarction	8 (14)	9 (15)
Congestive heart failure	6 (10)	6 (10)
Cerebrovascular disease	8 (14)	7 (12)
Chronic pulmonary disease	14 (24)	8 (14)
Renal disease	0 (0)	0 (0)
Psoriasis	5 (8)	2 (3)
Prolapsed disc	7 (12)	7 (12)
Atrial flutter/fibrillation	5 (8)	5 (8)
Spinal stenosis	4 (7)	3 (5)
Osteoporosis	4 (7)	3 (5)
Back pain, undiagnosed	1 (2)	2 (3)
Osteoarthritis	9 (15)	6 (10)
Medically treated hypertension	42 (71)	44 (75)
Treadmill test PWD − m		
Mean	157.9 ± 168.8	151.5 ± 145.7
Median	96.5 (52−175)	115 (54−175)
Treadmill test MWD − m		
Mean	300.7 ± 273.7	309.9 ± 255.1
Median	188 (107−393)	248 (130−384)
VascuQol-6 score	14.7 ± 3.0	14.6 ± 4.0
HADS-A ≥ 8	7 (12)	11 (19)
HADS-D ≥ 8	5 (8)	8 (14)
Haemoglobin − mmol/L	8.7 ± 1.0	8.8 ± 0.9
HbA1c − %	39.4 ± 5.6	42.4 ± 8.1
Creatinine − µmol/L	82.1 ± 20.9	87.0 ± 25.7
Total cholesterol − mmol/L	4.2 ± 0.9	4.4 ± 0.9
Cholesterol LDL − mmol/L	2.0 ± 0.8	2.3 ± 0.8
Cholesterol HDL − mmol/L	1.5 ± 0.6	1.4 ± 0.5
Triglyceride − mmol/L	1.6 ± 0.8	1.9 ± 1.7
CRP − mg/L	2.9 ± 4.3	5.3 ± 11.7

Data are presented as n (%), mean ± standard deviation or median (interquartile range). DOAC = direct oral anticoagulant; PWD = pain free walking distance; MWD = maximum walking distance; VascuQol = Vascular Quality of Life Questionnaire; HADS = Hospital Anxiety and Depression Scale; HbA1c = glycated haemoglobin; LDL = low density lipoprotein; HDL = high density lipoprotein; CRP = C reactive protein.

Physical activity estimated as the odds ratio (OR) for a minimum of 30 daily minutes of physical activity at six months was significantly higher in the rehabilitation group compared with the usual care group (OR 5.59; 95% CI 1.66 − 18.82; p = .002) (Table 2).

None of the participants in the control group and only five participants in the intervention group achieved the term "healthy" with a score of at least 75% after six months (Table 2). Separate analyses of the healthy diet questionnaire showed significantly higher scores for fat and the fish-fruit-green scores (p < .001) in the intervention group at six and 12 months (Table 4).

Exploratory outcomes

The results of the linear and logistic mixed models with exploratory outcomes measured at zero, six, and 12 months are presented in Table 3.

After 12 months there was a statistically significant lasting effect on MWD in the intervention group (p = .020), but no statistically significant difference in PWD (p = .24). Physical activity was statistically significantly higher in the intervention group after 12 months (p = .010) (Table 3). At six months, the general self reported condition in the legs compared with baseline was that 9% of those in the control group and 28% in the intervention group felt that this was much improved. By 12 months, this had risen to 22% of those in the control group and 36% in the intervention group.

The VQ6 scores were statistically significantly better in the rehabilitation group compared with the usual care group at six and 12 months (p = .020). There were no statistically significant differences between the groups in anxiety and depression scale (HADS), alcohol consumption, and smoking (Table 3).

DISCUSSION

To the present authors' knowledge, the present study is the first to show that a specialised cardiac rehabilitation

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Table 2. Results log linear model with continuous primary and secondary outcomes and logistic regression for binary secondary outcomes measured at six months in 118 patients with intermittent claudication receiving usual care (Control group) or additional cardiovascular rehabilitation programme (Intervention group). Available case analysis of the CIPIC Rehab Study

	Baseline		Six months		Exp(estimate) (95% CI)*	p	Cohen's d†
	Control group (n = 59)	Intervention group (n = 59)	Control group (n = 47)	Intervention group (n = 46)			
Primary outcome							
Maximum walking distance‡	188 [300.7]	248 [309.9]	253 [325.4]	350.5 [447.6]	1.37 (1.10–1.70)	.005	0.38
Secondary outcomes							
Pain free walking distance§	96.5 [157.9]	115 [151.5]	96 [165.8]	133.5 [207.9]	1.28 (0.99–1.65)	.060	0.29
Healthy diet	0 (0)	1 (2)	0 (0)	5 (11)	NA‖	NA	
Physical activity	21 (36)	18 (31)	15 (32)	24 (52)	5.59 (1.66–18.82)	.002	

Data are presented as median [mean] or *n* (%) unless stated otherwise. CI = confidence interval; NA = not available.
* Main effect of intervention adjusted for sex, age (continuous), and baseline value (time 0). For maximum walking distance and pain free walking distance, the estimate is the exponential log transformed mean difference meaning the relative extra metres in intervention group compared with control group. For physical activity, the estimate is the odds ratio.
† Cohen's d is the estimate from the log transformed model divided by the standard deviation of the log transformed baseline value.
‡ Sensitivity analyses with removal of outliers (Cook's d > 0.1, $n = 1$) also showed statistically significant differences ($p = .004$).
§ No outliers were identified after log transforming this outcome (Cook's d < 0.1 for all observations).
‖ NA, not estimable as no outcomes in control group.

programme in a community setting improves walking distance in patients with IC. The programme comprised cross sector cooperation between an outpatient clinic and a healthcare centre in the community. Additionally, physical activity, healthy diet, and QoL improved compared with usual care after six and 12 months.

The effects on walking distance, physical activity, and QoL are in line with that resulting from SET programmes, which have proven effective for alleviating symptoms, increasing walking distance, reducing cardiovascular risk factors, and improving QoL,[7] but there is a lack of evidence on how to set up such programmes.[8] Most studies on SET are performed in hospital outpatient clinics and have limitations for implementation, capacity, and adherence.[8] A typical programme includes 45–60 minutes treadmill based exercise, three times a week, for 12 weeks, and is time consuming and expensive, with high dropout rates of 40%.[21] The treadmill based exercise on such a typical programme is relatively painful and can be perceived as boring, which could explain some of the high dropout rates. Cardiac

Table 3. Log linear model with continuous primary and secondary outcomes and logistic regression for binary secondary outcomes measured at six months in 118 patients with intermittent claudication receiving usual care (Control group) or additional cardiovascular rehabilitation programme (Intervention group). Per protocol and available case analysis of the CIPIC Rehab Study

	Baseline		Six months		Exp(estimate) (95% CI)*	p	Cohen's d†
	Control group (n = 59)	Intervention group (n = 41)	Control group (n = 47)	Intervention group (n = 39)			
Primary outcome							
Maximum walking distance	188 [300.7]	281 [350.6]	253 [325.4]	400 [479.7]	1.45 (1.17–1.80)	.001	0.45
Secondary outcomes							
Pain free walking distance	96.5 [157.9]	138 [161.5]	96 [165.8]	147 [223.8]	1.32 (1.02–1.73)	.040	0.33
Healthy diet	1 (2)	0 (0)	0 (0)	5 (13)	NA‖	NA	
Physical activity	21 (36)	12 (29)	15 (32)	20 (51)	6.50 (1.69–25.03)	.002	

Data are presented as median [mean] or *n* (%) unless stated otherwise. CI = confidence interval; NA = not available.
* Main effect of intervention adjusted for sex, age (continuous), and baseline value (time 0). For maximum walking distance and pain free walking distance, the estimate is the exponential log transformed mean difference meaning the relative extra metres in the intervention group compared with the control group. For physical activity, the estimate is the odds ratio.
† Cohen's d is the estimate from the log transformed model divided by the standard deviation of the log transformed baseline value.
‖ NA, not estimable as no outcomes in control group.

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Table 4. Results of linear and logistic mixed models with exploratory outcomes measured at 0, 6 and 12 months in 118 patients with intermittent claudication receiving usual care (Control) or additional cardiovascular rehabilitation programme (Intervention). The estimates are the crude proportions, medians or means and proportions with outcome in intervention and control groups. Available case analysis of the CIPIC Rehab Study

	n*	0 months		6 months		12 months		p value†
		Control	Intervention	Control	Intervention	Control	Intervention	
Exploratory outcomes								
Median maximum walking distance	303	188	248	253	350.5	263.5	370	.020‡
Median pain free walking distance	303	96.5	115	96	133.5	140	170	.25§
Physical activity − %	301	36	31	32	52	25	52	.010
Mean Vascular Quality of Life Questionnaire	303	14.7	14.6	15.6	17.3	16.0	17.1	.002
HADS-A $\geq$ 8 − %	303	12	19	11	17	15	21	.96
HADS-D $\geq$ 8 − %	303	9	14	6	4	2	4	.76
Smoking status − %	299	42	47	38	43	42	40	.58
High alcohol consumption‖ − %	304	24	17	28	13	20	11	.58
Mean fat score	303	0.55	0.56	0.55	0.66	0.57	0.71	<.001
Mean fish-fruit-green score	303	0.43	0.43	0.40	0.53	0.41	0.55	<.001

HADS = Hospital Anxiety and Depression Scale.
* n is the number of observation where each person can have up to three observations.
† p value from interaction term between intervention group and time (0, 6 and 12 months). Adjusted for sex and age (continuous).
‡ p value based on analyses on log transformed maximum walking distance.
§ p value based on analyses on log transformed pain free walking distance.
‖ > 21 weekly units for men; > 14 weekly units for women.

IC rehabilitation exercise can adapt a larger group of patients compared with treadmill exercise because of limited numbers of treadmills per SET. Therefore, the cost of cardiac rehabilitation including dietician and nurse sessions is not more expensive.

The different kind of exercise is adapted and less time consuming and is beneficial in combination with risk factor reduction sessions with a nurse and dietician. The cost of SET alone, and a typical cardiac rehabilitation programme as in this study is 600 € per patient, while a simple iliac cardiovascular procedure costs approximately 9 000 €.[22,23]

The 12 week cardiac rehabilitation programme tested in the present study has been offered to patients with ischaemic heart disease for more than a decade. Rehabilitation has never been offered to PAD patients, as unfortunately they are not considered to be at the same high risk as patients with coronary artery disease, despite the fact that mortality from PAD is similar to that of coronary heart disease and that the mortality is caused by the same underlying condition.[1]

The significant findings on MWD and better QoL are in accordance with findings in a *Cochrane Review* by Lauret *et al.*, who compared SET with alternative modes of exercise therapy including cycling, strength training, and upper arm ergometry, and found improvement in MWD and QoL.[24] The effect on walking distance is also in accordance with findings in a *Cochrane Review* by Lane *et al.*, who found that exercise for IC improved MWD by 108.99 m (95% CI 38.20 − 179.78).[25] Based on these findings, Kruidenier *et al.* suggest that a more pain free mode of training would be more attractive to patients and result in better compliance and lower dropout rates.[21]

The HADS score showed no statistically significant differences, but high anxiety scores ($\geq$ 8) were found in both groups. High prevalence of anxiety and depressive disorders among patients with PAD has been found previously,[26] and such disorders are underdiagnosed in clinical practice and, hence, not properly treated.[27] Both anxiety and depression are risk factors for cardiovascular diseases. There is a need to address anxiety and depression in patients with PAD, and a more focused intervention addressing these issues may have more impact on outcomes.[28]

Improvement in the diet score was found in the intervention group; however, a low percentage of "healthy" was detected in both groups. Very few participants ate vegetables and fruit every day. A recent study of 100 191 adults found that cardiovascular, non-cardiovascular, and all cause mortality increased gradually with increasing non-adherence to dietary guidelines. Cardiovascular mortality was 30% higher, non-cardiovascular mortality 54% higher, and all cause mortality 43% higher compared with those with very high adherence.[29] Despite evidence to support the benefits of dietary modification in risk reduction, adults with IC continue to consume poor diets.[30] There could be several reasons for the lack of differences between groups at the six month stage of the programme. Health behaviour is, by nature, difficult to change. A smoking cessation course was not a specific part of the design in the programme. The participants were informed about local smoking cessation courses and given cards with contact information. A systematic review and meta-analysis by Papadakis *et al.* concludes that the method "Very brief advice" where the initiative and direct registration to a smoking cession course is taken by the healthcare provider without giving any advice is effective,[31] and this method may have improved the outcome.

Limitations

External validity is high as this population was included following Clinical Practice Guidelines on Diagnosis and Treatment of

Peripheral Arterial Diseases from 2017. However, about one third of potential eligible patients were randomised and this may represent bias. Even though there were no statistically significant differences between participants and non-participants in age and sex, some of the reasons for not participating included being in a job or doing self training. Self training is an important part of the treatment, and some of the patients can do it on their own, which might also explain improvements in MWD in both groups of the trial. A larger percentage of younger participants might welcome a rehabilitation programme with a flexible timespan.

The primary outcome MWD was obtained using a standardised treadmill walking test with random temporal variation from day to day and for the time of day the test was performed. However, these conditions were the same for both groups and group affiliation was blinded in the follow up treadmill test. Furthermore, to minimise detection bias, a manual was developed to guide the research assistant during the test. MWD measured by treadmill test was chosen as the primary outcome as a reliable measuring tool.[13]

Some studies use measurement of ankle brachial index before and after exercise interventions but were deselected in accordance with a *Cochrane Review* by Lane *et al.*, who concluded that exercise does not improve the ABI.[25] The secondary and exploratory outcomes were measured by self reported questionnaires. This kind of patient reported outcome is, by nature, subjective and relies on patient memory, which carries the risk of recall bias. Data management and analysis were conducted by two blinded statisticians independently of the researchers who interpreted data.

In conclusion, the present study showed that a specialised community based three month cardiovascular rehabilitation programme improved maximum walking distance, physical activity, quality of life, and healthy diet, but not pain free walking distance and smoking, compared with usual care without rehabilitation.

Guidelines on cardiac rehabilitation, for example from the European Society of Cardiology, Danish Health Authority, and British Heart Foundation, can be used as inspiration for how to set up a rehabilitation programme for patients with IC.

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CONFLICT OF INTEREST

None.

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APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvs.2021.04.004.

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PAPER 3

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Spurred by pedometers, unity and fun exercise: A qualitative study of participation in rehabilitation for patients with intermittent claudication (The CIPIC Rehab study)

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Aim: To explore how patients with intermittent claudication experiences participating in a community-based cardiovascular rehabilitation program and the various components of the rehabilitation program.
Background: Intermittent claudication is a condition associated with progressive atherosclerosis that affects daily life. Most patients with intermittent claudication do not exercise even though exercise is essential in the treatment of this condition. Rehabilitation is reported to be effective in alleviating symptoms, increasing walking distance, reducing cardiovascular events, and improving quality of life. Patients' perspectives are important when designing such programs, however, this aspect has not previously been investigated.
Design: A qualitative study.
Methods: Patients with intermittent claudication (n=10) participating in a rehabilitation program were interviewed in two focus groups. Pragmatic philosophy inspired the approach. Data were analyzed using qualitative thematic analysis, and emerging themes were discussed according to self-efficacy theory.
Results: Participants experienced social support from other patients, which motivated them to exercise. The intervention encouraged the patients' management of leg pain, while a local setting and a pedometer were important motivational factors to keep adherence to the program. The participants' experiences of the rehabilitation program are expressed in four themes revealed from the qualitative analysis: 1) the shared community, 2) pushing your own limits, 3) spurred by pedometers and health professionals, and 4) continuing new habits on your own. The participants found the components in the rehabilitation program meaningful, but encountered difficulties in continuing on their own after completion of the program.
Conclusion: A specialized community-based cardiovascular rehabilitation program for patients with intermittent claudication can be supportive for patients suffering from intermittent claudication.
Relevance to clinical practice: The qualitative results can be used to guide development of existing cardiac rehabilitation programs targeted patients with intermittent claudication in a community setting.

Introduction

Intermittent claudication (IC) is a classic symptom of peripheral artery disease (PAD), a common vascular disease caused by progressive atherosclerosis, that refer to symptoms in the lower extremities. Cases of PAD are rising, and the disease affects more than 200 million people globally and more than 10% of the population aged over 70 years[1]. In addition to age, smoking, hypertension, hypercholesterolemia, and diabetes are the main reason for atherosclerosis leading to increasing cases of PAD[1]. Among patients with PAD, 50–80% suffer from IC, which is defined as cramping leg pain that occurs during walking and is relieved by a short period of rest[2]. Up to 65% of patients with IC do not exercise, even though exercise is an important part of the treatment. Some of the reasons might be related to social inequality and low socioeconomic status, which can lead to social isolation, poor qual-

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ity of life, and disease progression[3-5]. Evidence from the latest Cochrane review shows that supervised exercise training (SET) programs are effective in alleviating symptoms of IC, increasing walking distance, reducing cardiovascular events, and improving quality of life[6]. In addition, SET is also relatively inexpensive and cost effective compared with other more invasive treatment therapies for IC[6,7]. While Cochrane review documents the positive effects of SET for IC patients, knowledge is still lacking on how to set up a program in a community-based setting[8]. There is a lack of knowledge on the perspectives of patients with IC in relation to rehabilitation and on the approaches that may affect patients' adherence to such programs[8]. A common reason for lack of adherence to walking exercise programs is exertional leg pain. It is suggested that involving patients by addressing incoherent illness and treatment beliefs, outcome expectations, and providing clearer instruction, alongside support throughout the behavior-change process, which could enable individuals with IC to adopt a regimen of walking[3]. Patients with IC seem to lack knowledge about atherosclerotic disease and how it can affect their behavior. Nurse-led programs can be an effective way of giving patients the competence to make decisions about their health-related behavior and enabling them to participate more fully in their rehabilitation[9,10]. Furthermore, a study has indicated that patients with IC do not consider conservative management to be a treatment that is as effective as surgery, and perhaps this perception affects the degree of motivation and adherence[3]. Time spent on transportation and logistics attending a supervised exercise program can be difficult for the patients, indicating that a local, community-based interventions may improve patients' motivation and adherence to such rehabilitation programs[11,12].

On this background, a mixed method study with a randomized clinical trial was developed to test the efficacy of a rehabilitative intervention for patients with IC[13]. Testing of efficacy can be measured using selected physiological and other relevant instruments, which is important knowledge when looking at the effect size. These instruments do however not tell anything about how patients participating in such interventions perceive the program, including any barriers and motivational factors. Shedding light on the participants' perspective is better captured during qualitative approaches. The objective of this qualitative study was therefore to explore patients' experiences of participation in a community-based rehabilitation program and the various components of the rehabilitation program.

Material and methods

Design

The CIPIC Rehab study present in this paper is the qualitative part of a larger mixed methods study designed to examine a community-based cardiac rehabilitation program for patients with IC in which 118 patients were randomized to rehabilitation or usual care. In accordance with recommendations, the findings will be reported separately[14], and results from the mixed methods integration will be published in another paper[15]. This study presents a qualitative investigation of patient perceptions of participation in the intervention[13].

Theoretical framework

Functional pragmatism as an approach to the research underpins this study and implies a focus on the practical and achievable, rather than the theoretical or ideal[16]. This means that the participants' experiences of participation in rehabilitation, their knowledge, beliefs and actions are all viewed in terms of their practical uses and successes. Identifying problems within the components in the rehabilitation program and finding solutions to these problems were a key part of the approach in this study[17-20]. For the present study, this pragmatic approach sought to create meaning and improvements in a local community-based context, and at the same time aimed to create knowledge that may also be useful in a wider context[16].

The intervention

Albert Bandura's theory on self-efficacy[21] inspired the design of this intervention. Therefore group sessions and individual counseling were included in the intervention, as theory on self-efficacy implies that knowledge, interactions with others, the individual's actual ability to perform, and learning a new skill in the local environment all contribute to enhancing an individual's self-efficacy. Further measures that were implemented to increase the patients' self-efficacy included self-monitoring with pedometers, patients keeping logbooks of steps, and patients setting goals for daily physical activity. All the measures aimed to motivate patients to perform physical activity, believe in their own ability and adopt healthy habits. The participants received feedback on their progress towards goals and on barriers to problem-solving, and received encouragement and feedback on even small changes in health behavior[21,22].

The rehabilitation intervention comprised usual care with information on stop smoking and keep walking combined with exercise that was supervised by physiotherapists, and furthermore included patient education carried out by a dietician and a vascular nurse. The participants were provided with a pedometer and were offered personalized motivational text messages designed in cooperation with the participants. The SET included various forms of physical exercise as described in a protocol. The intervention took place in a healthcare center in the Capital Region of Denmark, see Table 1. The program was based on the established cardiac rehabilitation program according to guidelines[23] with a primary focus on the leg muscles. The patients were actively engaged in groups of up to ten patients and the exercises included varied forms of physical exercise adapted to accommodate the patients' own goals regarding walking distance. To increase or sustain daily physical exercise at a level of at least 30 min/day, pedometer and self-reported walking behavior were included in the dialogue with patients at their individual consultations.

Participants

Forty-three participants completed the rehabilitation program. On this background, to increase depth of the participants experiences two focus-groups interviews were conducted. The first ten participants from the intervention group participated in qualitative focus group interviews. They were recruited at the 3-month follow-up in the healthcare center as a purposeful sample to explore patients' experiences of participation in the intervention[24]. The included participants were more than 18 years old with newly diagnosed IC that was being treated conservatively. All participants were residents in one of the eight local municipalities of Greater Copenhagen that fell under the healthcare center's catchment area. All patients in the CIPIC Rehab study had a mobile phone even though it was not a criterion for inclusion.

Data collection

The pragmatic philosophy underpinning the present study shaped the investigation such that participants were asked about

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Table 1
Content of the rehabilitation intervention.

Baseline at the Vascular Surgery outpatient clinic
Vascular nurse* handed out a pedometer and logbook for self-monitoring steps to motivate physical activity. Participant access to a direct telephone number to the Vascular nurse*.
Rehabilitation sessions in the community
Physiotherapist: 24 one-hour group sessions over 12-weeks consisting of supervised strength and cardiovascular exercise (up to 10 participants/group).
Vascular Nurse*: 2-h group education about IC and coordination of patient enrolments on smoking cessation courses in the municipality + spouses.
Dietician: 2-h group education about diet and IC, and access to individual counseling. + spouses.
After 12 weeks
Vascular nurse*: Individual motivational text message (up to the 12-month follow-up) designed with the participant.
6- and 12-month follow-ups at the Vascular Surgery outpatient clinic
Vascular nurse*: Individual counseling related to the RCT treadmill test and a questionnaire about health behavior.

*Vascular nurse= primary investigator/first author. IC= Intermittent claudication.

Table 2
Topics for interviews.

- Experiences with pedometer, logbook, and text messages
- Experiences with supervised exercise training
- Experiences with education about IC and healthy diet
- Experiences with barriers, support, and motivation
- Experiences of participating in rehabilitation
- Perception of knowledge about IC
- Perceptions of environment and togetherness with similar patients

actions they had described as participants in the rehabilitation program, and about how they experienced the consequences of these actions.

The participants were informed about the investigator's background as a vascular nurse, PhD fellow, and the purpose of the research. The focus group interviews were moderated by the first author and two assistant moderators unknown to the participants who captured key points to obtain rich descriptive information that would ensure that all topics that arose during the interview were adequately illuminated[24]. There were five participants in each focus group, who all knew the vascular nurse from the inclusion in the study and the 2-h group session. In order to create unity and to secure a safe environment as possible for the focus group, the participants were matched with others who had been part of the same training team at the same period, and the interviews were held in well-known surroundings in the healthcare center. There was a total of five participants in each focus group that was chosen to ensure each person has an opportunity to share insights and observations about the intervention and be able to share their experiences to allow for more in-depth conversation[24]. A semi-structured interview guide was developed prior to the focus group interviews and topics are shown in Table 2. (see supplementary Table S1, interview guide). The research questions in the semi-structured interview guide drew on the conclusions from 26 out of 43 post-intervention evaluating surveys and systematic reviews on the conceptualization of a patient-centered program, as well as three qualitative studies that explore patient experiences of living with IC[3,4,8,10,11]. The model by Malterud et al. was used to suggest an adequate number of participants for the focus group interviews to demonstrate new knowledge referring to the aim of the study and to achieve "Information power"[25][20, 25](p-70–75). Focus group interviews were conducted in Danish and quotes were translated after identifying and interpreting repeated patterns of meaning in the interview data. The manuscript was examined by a professional proofreader with full edit to ensure correct translation.

These studies point out the important patient aspects on rehabilitation to consider while planning a program, summarized as: provide a treatment and management plan at the point of diagnosis, written information about the condition with specific and consistent advice on walking and behavior change. Education and ongoing support and motivation on how to handle the pain while walking and coping behavior. Knowledge and uncertainty about IC, empathy, attitudes, beliefs, feeling better mentally, accessibility and compliance, environment, self-monitoring and goal setting, and quality of life.

The purpose of conducting focus group interviews was to better understand the participants' perceptions and experiences when their options were gathered and shared in the group. By creating a supportive environment, the participants were encouraged to share perceptions and points of view without being pressured to reach consensus. This environment aimed to allow the patients to freely discuss experiences of participating in the rehabilitation program. These open-forum discussions were designed to generate comprehensive information on the participants' perspectives[24].

The focus group interviews were conducted on November 21th, 2018, and lasted around 60 minutes.

Data analysis

The interviews were audio recorded and transcribed verbatim. The thematic analysis as described by Braun and Clarke was used as a systematic approach to analyze data from the interviews. This inductive analysis was data driven in a process that coded the data without trying to fit them into a pre-existing coding frame or any analytical preconceptions[26]. The thematic analysis strategy sought to identify common themes and relationships within the transcribed interviews by identifying and interpreting repeated patterns of meaning in the interview data.

The thematic analysis was carried out in six phases: 1) Familiarizing with the data: Transcribing data, reading and re-reading the data and noting down initial ideas. 2) Generating initial codes: Coding features of interest in a systematic way across the entire data set, and collating data codes. 3) Searching for themes: Collating codes into potential and relevant themes. 4) Reviewing themes: Checking if the themes worked in relation to the coded extracts and the entire data set and generating a thematic analysis. 5) Defining and naming themes: Ongoing analysis to refine the specifics of each theme, and the overall story the analysis tells, generating clear definitions and names for each theme. 6) Producing the report with selection of vivid, compelling extract examples[26](p 87). Familiarization of data, coding, searching for themes, reviewing themes, and defining themes were performed by two authors independently of each other.

Ethical considerations

The study complies with the Declaration of Helsinki and was approved by the regional research ethics committee (J. No.:H-17004183) and the Danish Data Protection Agency (J.No.:2012-58-

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Table 3
Demographics and clinical characteristics.

Baseline characteristics	Group 1 n=5	Group 2 n=5	All n=43
Age m (range)	71(63–76)	72(65–83)	70(55–83)
Sex n (%) Male/female	3(60)/2(40)	5(100)/0(0)	27(63)/16(37)
Living alone n (%)	3(60)	1(20)	22(51)
Risk factors and co-morbidity n (%)			
Smoker	3	3	23(53)
Ex-smoker	2	1	17(40)
COPD			7(16)
Hypertension	4	3	31(72)
Heart disease	2		9(21)
Diabetes		1	8(19)
Stroke			5(12)
Rheumatoid arthritis			5(12)
Cancer			2(5)
Health technology at 3 months			
Uses pedometer	5	5	41(95)
Uses logbook for steps	5	5	39 (91)
Text messages 1-2 times a week	5	3	27 (63)

0004). The participants provided signed informed consent after receiving written and oral information about the study. To ensure transparency the reporting followed the Consolidated Criteria for Reporting Qualitative Research guidelines[27].

Results

The participant demographics, clinical characteristics, use of pedometer, logbook, and text messages are illustrated in Table 3.

In the following, the findings of the inductive thematic analysis will be presented, and subsequently a discussion of the findings related to theoretical perspectives will follow.

The patient perspectives are illuminated in four themes describing the experiences of participating in the rehabilitation program:

1)The shared community, 2) Pushing your own limits, 3) Spurred by pedometers and health professionals, and 4) Continuing new habits on your own.

The shared community

Participation in the rehabilitation program was experienced as being part of a community with a special "team spirit". The patients expressed how exercising with others with the same disease was of great importance for their identity and motivation due to their sharing of experiences in the group. The social part of exercising made the patients have fun while they were keeping an eye on each other. This sense of community gave the participants energy and encouraged them to exercise:

"…It's like it's more rewarding doing everything when you share and do it together..." (I); *"…Yes, we are all in the same boat"* (B). Another part of being "in the same boat" was the patients' awareness of the fact that there was usually no rehabilitation program provided for them as patients with IC, as opposed to patients with cardiac diseases, who were provided with systematic rehabilitation programs. The patients were frustrated about training alone and expressed gratitude about being offered training sessions*: "…for otherwise one had been completely alone in the world and frustrated..*(F); *"…I actually think I would have given up at that time…"*(J); *"…and that's what we all say, if it hadn't happened, we had never moved on…"*(G). The team spirit in the rehabilitation program helped to create a community for the patients that made it easier for them to manage their disease and motivated them to participate in the program. They described how having fun, playing and competition relieved the feeling of burning leg muscles while exercising. Furthermore, the participants described how they were motivated by the fact that they would look forward to what the physiotherapists would come up with next time: "…It was different things we all did every time. For example we would fill out a pools [betting] coupon, and then we would do 10 exercises in between filling out the coupon…" (B); "…we were split into teams and competed. It was childish and so on. It's that kind of thing I think is fun every time…" (F).

Pushing your own limits

The participants narrated how they experienced significant pain during physical activity. The pain was described as *"now my muscles are burning up"* and occurred after starting physical activity. During the rehabilitation program, the participants expressed how they were encouraged and supported by the physiotherapist to exercise despite their leg pain. They explained how they had become convinced that training was an important aspect of managing their disease because they had learned about the benefits of exercising despite the pain, and because they had experienced being able to push their limits and delay the onset of leg pain. They described how they learned through their new experiences and the possibilities it gave them to act. The participants described how knowledge about the disease became an important part of managing life with a chronic condition. Participants recounted how they managed the overall challenge of their daily life with leg pain and how they were able to find their own strategies with the support of the rehabilitation team and their fellow patients: *"…it hurts right away, but I am walking anyway, because I've been told it helps – that it should cure me"*(D); *"…so, I try to ignore it. And what the heck, now I can walk one kilometer without my muscles burning up..."* (F). Furthermore, patients described how competition between members of the patient group motivated them to continue the exercise despite their leg pain. In a similar vein, they described how the physiotherapists were able to motivate them to push on: *"…actually you need to be whipped on"* (H); *"…It is just to get pushed forward"* (B). By participating in the exercise group, patients discovered how to continue despite pain and how to push their own limits: *"…when walking on the treadmill, I know when the burning comes, and I slow down the speed instead of stopping"* (G). Continuity in participation is also expressed as an important factor: *"…if you don't have the exercise as we did and do it 2-3 times a week and sometimes skipping it, it goes down…"* (G).

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Spurred by a pedometer and health professionals

The participants described how they felt motivated due to the location. If the rehabilitation program had been run at a hospital, the transportation and logistics would have hindered their participation, and they would therefore have chosen to decline to participate. Other motivating aspects described as important for participation were that the health professionals stood there waiting for them, which gave the participants a sense of being important, but also obligated them to show up. They experienced the pedometers and logbooks as personal motivational tools, and described how it had helped them become aware of their own ability to perform exercise and how they could compete with themselves about their own goals. The participants pointed out that they regarded the pedometer as a powerful instrument for motivation and they felt obliged to walk when they saw the numbers on the pedometer:

"…I am using the pedometer, looking at it every day... I am completely dependent on that pedometer (B); "…I put it on in the morning and put it on the kitchen table before I go to bed..." (F).

The logbook was used by almost all the participants, for some of them it was only in the beginning they found it meaningful, when they used it to map their walking route routine. Others used the logbook every day and found it helped to motivate them to go out for a walk and do something about their daily-steps goal: *"…The logbook is great, and spurred me into action… "…I look at it to find out how far I am. And my step average is 9000 steps daily"* (E); *"…at 11.45 p.m. my alarm rings on my phone and I find the logbook and write down...that logbook means everything for me…"* (F). The participants expressed that they found getting personal text messages rather cozy, but also had some mixed feelings about receiving them. When ending the program, they described an ambivalence about being a patient with IC. They wished to do something about the condition by doing exercise on their own, but explained it was difficult in real life when the rehabilitation program was over, which could lead to feelings of guilt: (G). *"…Every Monday when I receive a text message, I feel guilty because I haven't walked as much as I should have, but I don't want to stop receiving the text messages…"because I want to be able to walk again..."* (G).

Continuing new habits on your own

All participants highlighted the variation in forms of exercise as a motivational factor. The varied forms of exercise taught the participants what kind of exercise fitted them best. Following on from these experiences from the group exercising, the participants expressed a wish to continue in the group setting after the initial 12 weeks because they felt it was difficult to exercise on their own and they felt sad about missing their exercise community: *"…something is missing afterward. Walking alone is not the same …"*(G); *"I had a mental downturn when it stopped…"* (F). The participants also described how they found it useful to learn about healthy food from a dietician. Some of the participants found that their basic knowledge about healthy food was limited and suggested splitting the dietician's sessions in two: *"…then you could maybe have time to ask her questions and prepare some questions for the next time…"* (A). If it had been possible to split the sessions, the participants would have had an opportunity to practice some of the advice in real life after a first session, and then prepare questions in preparation for a second dietary advice session. Patients also pointed out that they felt it important that the dietician could meet them as an equal: *"…age and life experience and the ability to know who we are…"* (F). Participants also described difficulties in changing their eating habits when they could not feel the difference in their body or on their health: *"…yes, I've started eating herring every day, but I can't feel any difference…"* (A). While this statement points to a lack of knowledge about how the body works, participants did find it important to learn more about IC, medication, and treatment. They described how understanding the "why and how" of IC and their bodies made a difference in managing life with IC. The participants expressed that the knowledge they received from the program helped them to know that they would not damage anything while walking with pain: *"…in my head it helps a lot to know, now you are making…[collateral circulation]…now it is good…"* (D); *"…It occurred to me…when it hurts it is doing good…"*(J).

The participants also pointed out the importance of a personal contact with a specialized nurse from the outpatient clinic, and the importance of being able to get in touch directly by phone whenever they needed it. Even though the patients did not use this possibility very much, it gave them a sense of security and was experienced as important when they needed counseling about disease-specific topics.

Discussion

This study is the first investigation IC patients' experiences of participation in a community-based rehabilitation program and sheds light on how various components of the program helped and guided the patients to perform health behavior changes. The European Society of Cardiology guidelines recommend that patients with IC receive SET but it is not available everywhere and concrete recommendations for designing and implementing interventions are lacking in the guidelines[28].

A scientific statement from the American Heart Association about optimal exercise programs for patients with PAD provides a great deal of guidance in different kinds of exercise modes and recommends that future studies should focus on identifying optimal exercise programs for patients with PAD; delineating biological pathways by which exercise improves walking performance in PAD[29].

This study contributes with significant perspectives from patients with IC who participated in a tailored rehabilitation program, and it is suggested that the knowledge from these perspectives can be incorporated in the further development of guidelines on designing and implementing interventions.

The theme of *the shared community* found in the present study illuminates the patients' descriptions of how exercising in groups invited them to share stories of success with peers and share information on managing exercise discomfort. The theoretical perspective on self-efficacy posits the feeling of being with others with the same condition supports the individual's ability to actually make changes and therefore such a shared community might be a motivational factor for increasing patients' self-efficacy[21,22]. Our study illuminated that being with others who experience that health behavior changes are possible was a motivational factor that guided the participants to increase self-efficacy and make health behavior changes themselves. Further to this, the participants' accounts of being "in the same boat" highlighted how they experienced that the community in the group led to feelings of increased personal confidence in performing the exercise. A study of group-based exercise for cancer patients illuminated in continuation of this, how patients gained access to resources that derived from human interaction in the exercise group, and how their illness and treatment became easier to manage when shared with others in the same situation[30].

The participants described how during the intervention they became able to *push their own limits* and were able to continue walking and exercising despite pain when the physiotherapist encouraged and supported them. Participants in this study expressed the importance of social support, dynamic interaction, and knowl-

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edge from observing others as motivational factors to do exercise and manage their leg pain. These aspects might shed light on how individuals with IC are able to push their own limits, develop and adapt new habits to postpone pain based on their perceived positive outcomes. The participants "taking action" impacted their belief in their own abilities positively as well as enhancing the possibility of increased self-efficacy, as described in self-efficacy theory[21,31,32]. The basic premise of Banduras Social cognitive theory is that people learn not only through their own experiences, but also by observing the actions of others and the results of those actions. In this study, self-control, reinforcement, and self-efficacy included goal-setting, self-monitoring, and behavioral contracting. The participant was both an agent for change and responder to change. According to the theory, the Intervention was not only targeted individuals but were also affected by interpersonal, organizational, and environmental factors influencing health behavior[31].

The theme *spurred by a pedometer and health professionals* illuminates how the pedometer was perceived as a strong motivational tool for the participants when adapting to physical activity, and furthermore, the participants described how they felt important because the health professionals were waiting for them. Feeling spurred on and at the same time expected and important was particularly motivating. The local setting was important because attending a more distant hospital-based supervised exercise program can be difficult for patients due to time spent on transportation and logistics. The local setting was also important as a motivational self-efficacy factor, in that the local setting created a sense of community. McDermott and colleagues found that intervention in the local community might improve patients' motivation and adherence[12]. Those findings can be further unfolded in relation to the present study by applying Bandura's theory about self-efficacy. According to this, support in the local community matters, not only because of the logistic factors previously mentioned, but because the local community setting may lend itself to creating a supportive and persistent environment after the rehabilitation program has ended. These aspects are described by Bandura as important mechanisms when changing habits and include both cognitive and social processes[33]. The opposing emotions described by participants in relation to receiving personal motivational text messages demonstrate that health behavior changes by nature are difficult. Health professionals must thus balance healthcare advice in a manner that fits the individual patient in order to maintain the individual patient's motivation. When the participants had to *continue their new habits on their own*, they expressed how difficult it was to exercise on their own. These challenges impacted three areas of their self-efficacy: believing in their own abilities, being with others in a shared community, and the support from the environment. One risks that these significant motivational areas might be missing in cases where participants are left to move on by themselves after completion of a group rehabilitation program at a time when new habits have not yet been settled, and can still quickly become repressed. Furthermore, the participants in our study suggested how the session about healthy food should be split in two. An approach that allows time for practice between dietary advice sessions, cooking sessions and visits to a local supermarket could provide more supportive cognitive solutions[23].

The participants' understanding about the IC, medication and treatment made them believe in their own ability to make changes in their health behavior. Self-efficacy can be compromised if participants do not understand how the human body works. For example, in relation to the presence of atherosclerosis in the whole body, to the fact that eating healthy food and doing exercise is not a quick fix to such health problems. Social inequality, lower education levels in a patient group, cultural, and social environment can be influential factors, and awareness regarding these aspects is needed in a rehabilitation program.

The design of the study was based on systematic review to conceptualize a relevant and patient-centered program, and three qualitative studies about experiences, knowledge and beliefs of patients with IC[3,4,11]. A study by Wann-Hansson and Wennick confirms differences in knowledge in this patient group. They find that nurse-led follow-up programs can increase patients' knowledge about the disease and thus help patients navigate through treatment, uncertainty, and differentiate between beliefs and facts[9].

Some similar topics from the three qualitative studies was also found in The CIPIC rehab study: "*importance of a group setting*", *"feeling of togetherness with similar patients"*, *feeling frustrated about the disease*, "*increased blood flow*". *"feeling better mentally"*, and *"believe that it would make a difference while walking exercise"*. The present study succeeds with the rehabilitation program based on these earlier studies, and that the studied rehabilitation program was "modeled after" a well-established cardiac rehabilitation program in a community-based setting.

The present study also points out that the patients wished for further training after the 12-week rehabilitation program, as they found it difficult to continue on their own. It is therefore important to consider how the program can be followed up after the initial 12 weeks. Studies indicate that peer mentor models can support rehabilitation[34,35]. Future programs could include peers who are fellow patients that have completed previous rehabilitation programs and understand how it is to suffer from IC, and who could act as role models in how to manage health behavior changes and increase self-efficacy.

Methodological considerations

Interpretive and theoretical validity in this study were ensured by using the participants' own words and by including theory on self-efficacy[36]. The patients in the study were grateful to participate in the intervention and the interviewer was well known from the inclusion in the study and the 2-hour group education. This may have influenced the patients' descriptions of the benefits of their participation in a positive manner and may have hindered criticism of the program. The absence of criticism may also be related to the context. The participants might have been grateful for the opportunity to participate in a well-defined program, giving them a sense of security and worth. The participants in the focus groups were the first ten patients that began and ended the intervention, and therefore they knew each other well, which enhanced the chances of being at a high level of comfort in the group. Focus group discussions can lead to group consensus, which may influence the results, however, information power[25] was achieved and demonstrated new knowledge in relation to the aim of the study. The pragmatic philosophy identified the components in the rehabilitation program, their consequences, experiences, and solutions. A phenomenological-hermeneutical approach could have shed light on human perception and lived experiences without preconception of the results in a narrative way[37], however when investigating motivational factors in a rehabilitation intervention, the pragmatic philosophical approach was deemed appropriate.

Conclusion

The study highlights that a community-based rehabilitation program can be supportive for patients suffering from IC. Participants experienced social support from other patients, which facilitated them in adhering to exercise. The intervention encouraged the patients' management of leg pain, while a local setting and the pedometer were important for motivation. Participants found

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it difficult to continue exercising on their own after the initial 12 weeks, but found the components in the rehabilitation program meaningful. These qualitative results can be used to guide development of existing cardiac rehabilitation programs targeted at patients with IC in a community setting. Knowledge about human behavior as described by Albert Bandura's self-efficacy theory is well known, and combined with the empirical findings from the present study and existing knowledge on cardiac rehabilitation, it might be possible to design long-term rehabilitation interventions that work in a real-life setting.

Relevance to clinical practice

Based on this study, recommendations for a specialized IC rehabilitation program should include an interdisciplinary intervention with a physiotherapist, vascular nurse and dietician in a local community setting. Further recommended requirements include cross-sectoral coordination by a vascular nurse and patient access to a telephone number for counseling in relation to the program. Rehabilitation began at the department of vascular surgery where a logbook for steps and a pedometer are given to the patient. The logbook for steps and pedometer was a strong motivational tool, and therefore it is recommended to provide a pedometer for the patients. Follow-up exercise training in the local community after 12 weeks is important and could be continued in a local association.

Limitations

An inherent limitation of qualitative studies is their lack of generalizability. However, the findings are viewed as generalizable for IC patients. The study only included the voices of the participant. Leaving out the voice of other relevant parties, such as physiotherapists, dieticians, politicians and administrators in the health care sector. Even though all stakeholders could not be included in this mixed methods study, the voice of the patient was heard. Complex interventions have many potentials "active ingredients", that combine different components in a whole that is more than the sum of its parts. Randomized controlled trials are the most rigorous way to evaluate the effectiveness of interventions, regardless of their complexity. Because of their multifaceted nature in a social context, complex interventions pose methodological challenges[14]. "Good" randomized controlled trials have been defined as those having a high-quality intervention, adequate evaluation of the intervention and its delivery, documentation of external factors that may influence the outcome, and culturally sensitive intervention[14]

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Authors' contributions

The first author was responsible for the qualitative study design and data collection. The first and the last author did the initial data analysis. The final data analysis was discussed and consented to by all authors. All authors were responsible for drafting of the manuscript, revision and approval of the final manuscript.

Declaration of Competing Interest

None

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jvn.2021.06.001.

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TABLE S1.
EXERCISE PROTOCOL

	Supplementary Table S1. Exercise protocol. The CIPIC Rehab Study
Session	Activities
1.	Warm-up: Different ways of walking (15 minutes)[i] **Primary exercise equipment: Step bench** <u>Position - Standing:</u> - Different variations of stepping up and down on the step bench (e.g. forward, sideway, stepping sideways over the step bench, stepping sideways down on each side of the step bench) - Quick sprint on the spot - 30 seconds - squat 3 x 10 <u>Position: Lying down on exercise mat on the floor:</u> Following exercises are conducted in sets of 3 x 10: - Pelvic lift - Sit-ups - Side-lying internal and external hip rotation (the clam) - Side-lying hip abduction with stretched leg.
2.	Warm-up: Different ways of walking (15 minutes) **Circular training: 6 different exercises, each performed for 2 minutes.** **2 rounds with different exercises.** First round: 1) Walk overstep benches lined up on a row (3-4 pcs.). Shift between forward and sideways walking 2) Walk over low hurdles lined up on a row (6-7 pcs.). shift between forward and sideways walking 3) Farmer walk with dumbbells (2 or 3 kg) 4) Walking while dribbling with a big swiss ball 5) Standing up and sitting down on a chair 6) Walking forward with sliders under both feet Second round: 1) Quick stepping up and down on a step bench 2) Walk over low hurdles lined up on a row (6-7 pcs). Shift between forward and sideways walking 3) Walking on toes (calf raise) while carrying dumbbells (2 or 3 kg) 4) Walking while dribbling with a big swiss ball 5) Standing up and sitting down on a chair 6) Small quick steps with sliders under feet
3.	Warm-up: Bicycling (15 minutes)[ii] **Pool coupon with 13 questions about physical activity. Before answering a question on the coupon, the patient must do the following exercises, equivalent to each question:** 1) Stairs (2-3 floors) 2) Sit-ups 20 repetitions 3) Stairs (2-3 floors) 4) Back lift 20 repetitions 5) Stairs (2-3 floors) 6) Pelvic lift 20 repetitions 7) Stairs (2-3 floors)

	8) Push-ups 20 repetitions 9) Stairs (2-3 floors) 10) Squat 20 repetitions 11) Stairs (2-3 floors) 12) Walking lunges 13) Stairs (2-3 floors)
4.	Warm-up: Different ways of walking (15 minutes) **Primary exercise equipment: Swiss ball** <u>Position: Following exercises are done while sitting on a swiss ball:</u> - Introduction in correct posture/alignment while sitting on the swiss ball. - Walking on the spot - Sidestep - Walking forward and backwards - Jumping jack (legs only) - Balancing: lift one leg at a time and keep balance on the swiss ball - Hop while sitting on the ball and stop the movement after direction from the therapist - Straight leg raising - Balancing on toes while sitting on the swiss ball <u>Position: Following exercises are done laying down (supine) on an exercise mat on the floor:</u> - Pelvic lift with legs resting on the swiss ball 2 x 15 - Sit-ups with legs on the swiss ball 2 x 15 - Swiss ball placed between legs. Knee extension/flexion (lifting the swiss ball up and down) 2 x 15 - Lift the swiss ball up and place it between arms in front of the upper body, press arms/hands in adduction and hold the pressure in 15 seconds. 2 repetitions - Laying supine with lower legs resting on the swiss ball. Do a pelvic lift and contract your hamstrings and pull the ball towards you as far as possible 2 x 15 - Laying supine with legs on the swiss ball and do sideways sit-ups 2 x 15 <u>Position: Following exercises is done standing up:</u> - Stand in front of a wall and have the swiss ball in front of your upper body and press the ball against the wall, while rolling the ball up and down 2 x15 - Wall squat with a swiss ball: stand with the ball as back support against a wall. Bend your knees about 90 degrees and push back up 2 x 15 - Stand and dribble the swiss ball - 30 seconds - Hold the swiss ball between your hands/arms while doing a core rotation from side to side. 10 repetitions - Hold the swiss ball between your hands/arms and lift the ball over the head and down to the floor. 10 repetitions <u>Exercise between two patients:</u> - 1 patient hold the swiss ball in front of the upper body, while the other patient boxes into the swiss ball. 2 x 30 seconds
5.	Warm-up: Bicycling (15 minutes) **Exercise after a training-DVD[iii] developed for heart disease. The DVD contains standing exercises, that are possible for the patients to do at home.** 3 different exercise programs each of 10 minutes.

6.	Warm-up: Bicycling (15 minutes) **Primary exercise equipment: Sliders**[iv] Different types of walking/sliding with the sliders under feet - quick/small steps, long steps, sideways walking. <u>Position - Standing on the sliders:</u> Lunges in different directions - Forward - Backwards - Sideway Standing facing a wall while leaning against the wall with hands pressing the sliders against the wall, slide hands/arms up and down, slide arms in circles, slide in a V-shape.
7.	Warm-up: Bicycling (15 minutes) **Exercise in strength training equipment.** **Circular training in 8 different machines. Preforming in each machine for 1 minute and 30 seconds.** **2 rounds.** 1) Step machine 2) Standing back row 3) Leg curl 4) Chest press 5) Leg press 6) Pull down 7) ThoraxTrainer 8) Crosstrainer
8.	Warm-up: Different ways of walking (15 minutes) <u>Exercises performed on an exercise mat on the floor:</u> Following exercises are conducted in sets of 2 x 15: - Diagonal lift of arms and legs - standing on all fours - Standing on knees and shift between standing and sitting down - Isometric quadriceps hold while standing on knees - pelvic lift - sit-ups Sprint exercise done all together: All the patients and therapists stands in a circle (e.g. 10 persons all together). The aim of the game is that all the participants have to say a number from 1 to e.g. 10 in the correct order (1,2,3,4…10). All of the participants have to sprint on the spot until every participants have said a number and reached the number for participants (e.g. 10). It is up to each participant to determine when to say the next number in the order. The longer it takes to reach the final number (e.g. 10), the longer all the participants have to stand and sprint on the spot. <u>Exercises performed on an exercise mat on the floor:</u> Following exercises are conducted in sets of 2 x 15: - Side-lying clam - Side-lying hip abduction - Sitting straight leg raise

9.	Warm-up: Different ways of walking (15 minutes) **Exercise equipment: Resistance band (TheraBand[v])** <u>Position: Standing</u> Following exercises are conducted in sets of 2 x 15: - Back rowing - shoulder extension with stretched arms - sprint on the spot - standing chest press - sprint on the spot while shadow boxing **Exercise equipment: Resistance band - mini[vi]** Side steps with mini elastic bands around feet - 2 x 25 steps to each side (left and right) **Exercise equipment: Resistance band (TheraBand)** Following exercises are conducted while standing with both feet on the TheraBand, which gives resistance in the exercise Following exercises are conducted in sets of 2 x 15: - Biceps curl - Shoulder abduction - Squat Different ways off walking 3 min. **Exercise equipment: resistance band – mini** Following exercises are conducted in sets of 2 x 15: - Standing high knee drills with a mini resistance band around both feet - Standing butt kicks with a mini resistance band around feet The mini resistance band is placed around the wrists. Walking on the while moving stretched arms up and down in front of the body while doing small shoulder abduction/adduction movements Calf raise 2 x 15
10.	Warm-up: Bicycling for 15 minutes. During the last 3 minutes of the warm-up, the patients raise resistance on the bike every half minute. **Exercise equipment: Bodybar[vii]** <u>Position: Standing</u> Following exercises are conducted in sets of 3 x 10: - Biceps curl - Upright row - Squat Relay race with small bean bags: 2-3 patients on each team: 40 bean bags gets spread out in one end of the gym hall. The patients stands in the other end. The patients on each team shift in running down to the other end of the hall, pick up a bean bag and run back to the team before the next patient runs after a bean back. The relay race is finished when all the bean bags are picked up by the patients. OBS: the patients are only allowed to pick up one bean bag at a time. **Exercise equipment: Bodybar** <u>Position: Standing</u> Following exercises are conducted in sets of 3 x 10: - Triceps curl - Side bend with resistance from Bodybar

	- Sumo squat Relay race with small bean bags – and return of the bean bags: The patients get divide into the same teams as before, but now they must return the bean bags that they picked up earlier. The patients run one team play at a time, down to the other end of the hall and place a bean bag at the end, and returns to the teammates.
11.	Warm-up: Bicycling (15 minutes) **Four different relay races** Teams of maximum 3 patients per team **1. Exercise equipment: Sliders** - Walk/slide forward with sliders under feet to the other end of the gym hall. At the end do 10 squats. Afterwards, walk/slide forward back to the other team players with sliders under feet. *It is now the next team players turn to do the same exercise. This is done until all the team players on the team have done the first exercise. When all the team players have done the first exercise, they continue to the next exercise (described below).* - Walk/slide sideways with sliders under feet to the other end of the gym hall. At the end do 10 Ski jumping (Hop alternately forward on one leg and back on the other leg). Afterwards, walk/slide sideways back to the other team players with sliders under their feet - Walk/slide backwards with sliders under feet to the other end of the gym hall. At the end do 10 jumping jacks. Afterwards, walk/slide backwards back to the other team players with sliders under their feet *When all team players have done all three exercises, they are done with the relay race. After a short break, they continue to the next relay race.* **2. Exercise equipment: Hula Hoop** *The relay must be performed as described above (relay 1).* - Use the hula hoop as a skipping rope, skip through the hula hoop. At the end of the hall stand with the hula hoop around your waist and do 10 high knee drills (the knees lifts up to the hula hoop). Afterwards, run back to the team players again by skipping in the hula hoop. - Run to the end of the gym hall while pushing/rolling the hula hoop by your side. At the end of the hall, lift the hula hoop from the floor and up over your head and back down to the floor 10 times. Afterwards, run back to team players by pushing/rolling the hula hoop by your side. **3. Exercise equipment: Giant Four-in-a-row game.** - The patients get divided into two groups and play against each other. One team has 21 bright yellow rings, and the other team has 21 vibrant green rings. On each team the players take turns strategically dropping in a ring from the top of the ring box; Be the first to arrange 4 rings of your colour in a row (horizontally, vertically, or diagonally) to win, but watch out, because your opponent will try to block your moves. The game is placed in the opposite end of the gym hall, so the patients must run back and forth when placing a ring in the game. When all the rings are placed you count which team has the most four-in-a-row. **4. Exercise equipment: Aires balance beam + low hurdles** *The relay must be performed as described above (relay 1).* - Following equipment are placed after each other on a track: a) Airex balance beam (approx.. 1,6 m) b) 4 low hurdles

	The patients starts by walking on a line on an Airex balance beam followed up by walking forwards over 4 hurdles. When they reach the end of the gym hall they turn around and do the same exercises back. - The patients starts by walking on heels approx. 3 m. afterwards they walk sideways over 4 hurdles. When they reach the end of the gym hall they turn around and do the same exercises back.
12.	Warm-up: Bicycling (7 minutes) + 6-minute walk test conducted in the gym hall on a 40 m. circular test track **Primary exercise equipment: Swiss ball** <u>Position: laying on an exercise mat on the floor</u> Following exercises are conducted in sets of 2 x 15 - Pelvic lift – conducted with legs resting on the swiss ball. - Sit-ups – conducted with legs resting on the swiss ball. - Lying on back with the swiss ball between legs, hip held in 90 degrees flexion, shift between flexion and extension of knees. - Hip crossover with legs resting on the swiss ball - Pelvic lift and thigh curl with the swiss ball - Supine side bend while legs are resting on the swiss ball 5 x 5 seconds: Supine hold the swiss ball over the upper body and squeeze the ball with both hands. Supine hold the swiss ball in front of the body and move the ball over the head and to each side – 5 times in each direction. Boxing in the swiss ball, while another patient holds the swiss ball 2 x 30 seconds
13.	Warm-up: Bicycling (15 minutes) **Pool coupon with 13 questions about healthy diet. Before answering a question on the coupon, the patient must do the following exercises equivalent to each question:** 1) Walk/run 100 m 2) Pelvic lift 20 repetitions 3) Walk/run 100 m 4) Sit-ups 20 repetitions 5) Walk/run 100 m 6) Back lift 20 repetitions 7) Walk/run 100 m 8) squat w/ dumbbells 20 repetitions 9) Walk/run 100 m 10) push-ups 20 repetitions 11) Walk/run 100 m 12) Lunges w/ dumbbells 20 repetitions 13) Walk/run 100 m
14.	Warm-up: Different ways of walking (15 minutes) **Exercise equipment: TheraBand** Following exercises are conducted in sets of 2 x 15 - Biceps curls - Triceps press - Side bend - Squat

	Game: Tail tag Each patient tucks a 'tail' (e.g. a mini elastic band) into the back of their shorts or pants. The patients now have to walk/run around the gym hall trying to capture the tails of the other patients whilst also keeping their own 'tail' safe. The therapist gives the patients three minutes to capture as many tails from each other. If patients have a tail stolen from them, they continue and try and steal a tail off somebody else in the game. After three minutes the patient with the most tails wins. **Exercise equipment: mini elastic band** Sidesteps with a mini elastic band around feet 15 steps each direction Following exercises are conducted in sets of 1 x 15 - High knee drills with an elastic band around feet - Butt kicks with an elastic band around fee
15.	Warm-up: Bicycling (15 minutes) **Game: Walking Bingo with exercises** The patients get divide into two teams. Each team gets a bingo card plate with 10 numbers. In the other end of the gym hall, each team has a pile of 20 pieces of paper, which has either a number – equal to a number on their bingo card plate – or an exercise. One patient at a time run/walk down to the pile of paper and pull up a number. If the patient pulls up a number, they run/walk back with the number, and place it on the bingo card plate. If the patient pull up an exercise all of the team players has to do the exercise before it's the next patient in turn to walk/run to the end of the gym hall to pulls up a new piece of paper. The game continues to one of the teams has a full plate. The exercises in the pile: Jumping jack x 10 Lunges x 10 Ski jumping (Hop alternately forward on one leg and back on the other leg) x 10 Sprint on the spot 30 seconds Elbow to knee x 20 Push-up x 10 High knee drills on the spot x 20 Squat x 10 Box and sprint on the spot x 20 Hand too heel x 20 **Game: Walking and finding the right number** Each patient gets a bingo card plate with 10 numbers. They now must walk individually around the gym hall and find the numbers on their card in the correct order. The numbers are 'hidden' under a disc cone, so the patients have to walk right up to the cone, to see the number. When the patients have found all the numbers they are finished.
16.	Warm-up: Bicycling (10 minutes) **Exercise equipment: Sliders** <u>Position – walking/sliding:</u> Walk/slide with feet on the sliders – walk with small steps – walk with big/long steps Walk/slide forward Walk/slide backwards Walk/slide sideways

	Walking/slide lunges Standing/slide twist <u>Position – laying down on an exercise mat on the floor:</u> Different exercises for the upper body, core, and lower body <u>Position – Standing:</u> Twist Jumping jack Ski jumping (Hop alternately forward on one leg and back on the other leg)
17.	Warm-up: Bicycling (15 minutes) **Circular training in strengthening machines. Preforming in each machine for 1 minute and 30 seconds.** First round: 1) Step machine 2) Standing rowing 3) Leg curl 4) Chest press 5) Leg press 6) Pull down 7) ThoraxTrainer 8) Crosstrainer Second round: 1) Step machine 2) Standing rowing 3) Leg curl 4) Chest press 5) Leg press 6) Dips 7) Rowing machine 8) Crosstrainer
18.	Warm-up: Bicycling (10 minutes) **Circular training: 2 rounds. Every exercise is performed for 1 minute and 30 seconds:** 1) Skipping in hula hoop - Use the hula hoop as a skipping rope, skip through the hula hoop 2) Sit-ups 3) Jump on trampoline 4) Skipping with a skipping rope 5) Back lift **6)** Hip bridge heel slide out
19.	Warm-up: Different ways of walking (15 minutes) **Primary exercise equipment: Bodybar** <u>Position- Standing:</u> Following exercises are conducted in sets of 3 x 10: - Bicep curl - Squat (while holding the Bodybar in both hands) calf raise (while holding the Bodybar in both hands) - Shoulder press

	- Lunges - Side bend (first to the right side 10 rep. and afterwards to the left side 10 rep.) <u>Position - Supine:</u> Following exercises are conducted in sets of 3 x 10: - Chest press - Triceps press - Pelvic lift with Bodybar resting across pelvic
20.	Warm-up: Bicycling (15 minutes) **Pool coupon with 13 questions about Intermittent claudication. Before answering a question on the coupon, the patient must do the following exercises equivalent to each question:** 1) Walk/run 100 m 2) Diagonal lift standing on all fours 20 repetitions 3) Walk/slide with sliders 100 m 4) Sit-ups 20 repetitions 5) Walk/run 100 m 6) Pelvic lift 20 repetitions 7) Walk/slide sideways 50 m + walk/run 50 m 8) Biceps curls w/ dumbbells 20 repetitions 9) Walk/run 100 m 10) Lunges 20 repetitions 11) Walk w/high knee drills 25 m, walk w/ butt kicks 25 m, run 50 m 12) calf raise w/ dumbbells 20 repetitions 13) Walk/run 100 m
21.	Warm-up: Bicycling (10 minutes) **Three different relay races** Teams of maximum 3 patients per team. **1. Exercises equipment: Sliders** - Walk/slide forward with sliders under feet to the other end of the gym hall. At the end do 20 steps on the spot. Afterwards, walk/slide forward back to the other team players with sliders under feet. *It is now the next team players turn to do the same exercise. This is done until all the team players on the team have done the first exercise. When all the team players have done the first exercise, they continue to the next exercise (described below).* - Walk/slide sideways with sliders under feet to the other end of the gym hall. At the end do 10 squats. Afterwards, walk/slide sideways back to the other team players with sliders under feet. - Walk/slide backwards with sliders under feet to the other end of the gym hall. At the end do 10 jumping jacks. Afterwards, walk/slide backwards back to the other team players with sliders under their feet *When all team players have done all three exercises, they are done with the relay race. After a short break, they continue to the next relay race.* **2. Exercise equipment: Skipping rope** *The relay must be performed as described above (relay 1).* - Jump rope forward with the skipping rope to the other end of the gym hall. At the end do 10 sit-ups. Afterwards, jump rope forward back to the other team players. - Jump rope backward with the skipping rope to the other end of the gym hall. At the end do 10 back bends. Afterwards, jump rope backwards to the other team players.

	- Jump rope sideways with skipping rope to the other end of the gym hall. At the end do 10 diagonal lift of arms and legs - standing on all fours. Afterwards, jump rope backwards back to the other team players. *When all team players have done all three exercises, they are done with the relay race.* **3. Exercise equipment: Badminton racket + balloon + airex balance beam** *The relay must be performed as described above (relay 1).* - Jungle the balloon with a badminton racket to the other end of the gym hall. At the end take the balloon and lift it from the ground and up over your head 10 times. Afterwards jungle the balloon back to the other team players - Balance on the Airex Balance Beam at the end do 10 high knee lifts. Afterwards, balance on the Airex Balance Beam back to your team players.
22.	*Nordic walking outdoor.* Each patient gets a set of Nordic walking poles. They get an introduction to how to walk correctly with the poles. The exercise is conducted outside, by walking around in the outdoor environment. During the walking, different exercises are conducted as an active break: (e.g. High knee drills, standing butt kicks, calf raising, squats).
23.	Warm-up: Different ways of walking (15 minutes) **Primary exercise equipment: Step bench + dumbbells** <u>Position - Standing:</u> Following exercises are conducted in sets of 3 x 10: - Step forward up and down from the step bench while doing biceps curls with dumbbells - Sideways step up and down from step bench while doing shoulder abduction with dumbbells 15 quick steps on step bench 15 rep. <u>Position - Laying supine on step bench:</u> Following exercises are conducted in sets of 3 x 10: - Dumbbell flyes - Triceps press - Sit-ups <u>Position - Standing:</u> Different ways of stepping up and down on step bench: forward while doing high knee drills, forward while doing butt kicks, sideways. <u>Position - Laying supine on an exercise mat on the floor:</u> Following exercises are conducted in sets of 3 x 10: - Pelvic lift - Hip abduction/adduction while the hip is held in 90 degrees flexion - Shoulder flexion/ extension with stretched arms 15 quick steps on step bench 15 rep.
24.	*Exercise conducted outdoor by using a nearby outdoor training park.* Warm-up: Walking to the training park – approx. 15 minutes walking. **Exercise equipment: Training park, with the ability to conduct circular training with 9 different exercises.** Each exercise is performed for 1 minute and 15 seconds.

	1) Sit-ups 2) Standing and throwing and grabbing a ball clamped tightly on a steel-string 3) Back bend 4) Step up and down 5) Stand up and sit down on a bench 6) Squat with weight resistance 7) Dips 8) Standing balance on a balance board 9) Standing calf raise 10) Push-ups

[i] Includes different types off walking in a gym hall. One round in the gym hall is approx. 40 meters. Eg. walking and doing forward/backward arm swings, walking lunges, walking on toes, walking on heals, shift in walking phase (quick/slow/normal), walking sideways, walking with high knee lifts, walking with butt kicks.
During the warm-up, there is a focus on the patients continue walking despite experiencing pain in their legs/lower body. The warm-up is conducted in a big gym hall.

[ii] The warm-up by bicycling is done on an exercises bike. The patients get instructions in using the forefoot, and thereby activates the calf muscles. During the warm-up, there is a focus on the patients continue bicycling despite experiencing pain in their legs.

[iii] Training DVD – *Tænd og træn dit hjerte*. (Hjerteforeningen) https://hjerteforeningen.dk/alt-om-dit-hjerte/livet-med-hjerte-kar-sygdom/motion-og-hjerte-kar-sygdom/taend-og-traen-dit-hjerte/

[iv] A slider is a piece of cloth/carpet which has a side that makes it possible to glide/slide over a surface i.e floor or wall, without any friction.

[v] Theraband:

[vi] Resistance band – mini:

[vii] Bodybar:

TABLE S2.
3 MONTH'S SURVEY

Table S2 3 months survey The CIPIC Rehab Study

3 Months' Survey

Health-Related

How will you describe your general condition in your legs now, compared to 3 months ago?

- □ Much better
- □ Better
- □ A little bit better
- □ Almost the same
- □ A little worse
- □ Worse
- □ Much worse

Intervention

Results of the 6 minutes walking test. Distance before intervention_____ Distance after intervention____

Results of 30-second chair stand test numbers before intervention____Numbers after intervention____

Participation in the sessions

24 exercise sessions with a physiotherapist twice a week:

Participated in all sessions □ Not participated in all sessions □

How many times did you not participate?

Why did you not participate?

Did you participate in the 2-hour session with a vascular nurse? Yes □ No □

Did you participate in the 2-hour session with a dietician Yes □ No □

Did you receive individual guidance from the dietician? Yes □ No □

Exercise

What kind of exercise do you want to continue now the rehabilitation is over?

Walks

How often do you walk at least 30 minutes a day?

Number of times per week:

0 □ 2 □ 4 □ 6 □ >7 □

1 □ 3 □ 5 □ 7 □

Are you generally more physically active compared to 3 months ago? (In addition to the intervention training)

Yes □ No □

Smoking

Did you smoke at the inclusion? □ Do you smoke now? □ No, I have not been smoking for ____months

Do you smoke more now? □ Less □ Same quantity as 3 months ago? □

How much tobacco do you smoke daily?
(1 cigarette = 1 g, 1 cigar = 4 g, 1 pipe = 3 g, 1 cheroot = 3 g)

□ Less than 10 grammes □ 22-30 grammes
□ 11-21 grammes □ More than 30 grammes

Have you participated in a smoking cessation course during the last 3 months?
Yes □ No □

Would you be interested in a smoking cessation course, if offered?

Yes □ No □

Did you use any kind of the below medication regularly for more than the latest 3 months?

□ Nicotine patch
□ Nicotine gum
□ Nicotine lozenges
□ E- cigarettes
□ Ingen. None
□ Nicotine inhalator
□ Nicotine nose spray
□ Varenicilin (Champix) □ Bupropion (Zyban, Wellbutrin)
□ Snuff

Others
□ Write which
_____

Motivation

How great impact did the pedometer have on the level of your daily physical activity?

□ Very great impact
□ Some impact
□ No impact
□ Did not use a pedometer

How great was the impact of the logbook on your daily activity?

□ Very great impact
□ Some impact
□ No impact
□ Did not use a pedometer

Do you want to continue using a pedometer? □ No □ Yes - What is your daily target? _____

Rehabilitation programme

Is there anything during the course that was particularly meaningful to you? □ No □ Yes

If yes, please write what was particularly meaningful to you:

Have you any suggestions as to an ideal rehabilitation programme? Or other comments?

If you had to decide the ideal course, what would it be?

Do you want to receive text messages on your mobile phone?

No □

Yes □ How often? /time/days?

What kind of text? What will motivate you to for instance physical activity, smoking stop, change of diet? Who should be involved, if anybody? – Society, club, training mate, target for number of steps? Encouragement by smoking desire, visiting XX, etc. What is important?