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Nicolas Kjerulf and Susanne Grøn

The effects of active commuting by bike on cardiorespiratory fitness and body composition in healthy, sedentary and overweight adults
A randomized controlled trial

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Co-advisors: Martin Bæk Petersen and Mads Rosenkilde Larsen
Department of Biomedical Sciences
Submitted: June 30th 2016.
Forord

Dette kandidat speciale er udarbejdet på afdeling for Systembiologisk forskning, Biomedicinsk Institut, det Sundhedsvidenskabelige Fakultet, Københavns Universitet. Det er baseret på data fra projektet GO ACTIWE, som er en del af det multidisciplinære projekt Governing Obesity.


Det var vores ønske at arbejde kvantitativt med systembiologisk forskning, samt at være en del af et forskningsteam. Det ønske har vi til fulde fået opfyldt, og vi er glade over den tillid, som vi er blevet mødt med, når vi er blevet sat til at udføre opgaver i projektet. Vi har haft mange interessante samtaler og diskussioner og mødt stor hjælpomhed, som har bidraget til en fantastisk læreproces, der rækker langt ud over selve afhandlingen. Endelig har vi med opholdet på BMI i højere grad fået et tilhørsforhold til Københavns Universitet, end det var tilfældet som stud. scient. san.

Nicolas Kjerulf og Susanne Grøn
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1. Abstract

Introduction: A sedentary lifestyle is associated with poor cardiorespiratory fitness (CRF) and obesity, both predictors of cardiovascular disease (CVD) and all-cause mortality. Previous studies have shown that active commuting by bike (ACB) is associated with reduced risk of diabetes, CVD and all-cause mortality. More knowledge on health effects of ACB in the sedentary and obese adult population is needed to guide health professionals and policy makers on recommendations and public health initiatives.

Aims: To investigate the effects of ACB on CRF and body composition in sedentary, overweight or obese, but healthy adults. A further aim was to describe exercise characteristics during ACB and investigate the association between self-selected intensity (SSI) and change in CRF.

Study design: A randomized controlled trial with a per protocol analysis

Methods and materials: In total, 53 adult, sedentary, overweight participants were randomly assigned to either “no change in lifestyle” (CON, n=18) or six months of ABC (BIKE, n=35) with a daily exercise energy expenditure of 320 and 420 kcal for females and males, respectively. At baseline and post intervention, CRF (V̇O₂max) was measured using standard open circuit spirometry system (Oxycon Pro, Jaeger). Fat mass (FM), percentage of android fat mass (%AFM) and fat free mass (FFM) was measured using dual-energy X-ray absorptiometry (DXA). Outcomes were analyzed with analysis of covariance, and effect reported as between-group differences adjusted for baseline values.

Results: In BIKE, 18 participants (51%) completed the intervention, and 17 were included in the analysis as well as 16 controls. The mean increase in V̇O₂max in BIKE compared to CON was 402 ml O2/min (95% CI: 197-606), corresponding to a 16% increase. BIKE participants’ mean loss of FM was 4.9 kg (95% CI: 1.8 to 7.9) with no concomitant loss of FFM. A 4% (95% CI: 1 to 7) mean reduction of AFM was found. Mean SSI (%V̇O₂max) was 53% with a range of 41-65%, placing 13 participants in the moderate exercise zone and four in the vigorous exercise zone. No association between SSI and changes in V̇O₂max was found.

Conclusion: Completing a six-month intervention of active commuting by bike with an exercise volume corresponding to the recommended minimum for physical activity induced a clinically significant improvement of cardiorespiratory fitness as well as a healthy weight loss, in healthy, overweight, sedentary adults. The mean self-selected intensity was moderate.
2. Resumé

**Introduktion:** En fysisk inaktiv livsstil er associeret med lav kardiorespiratorisk fitness (CRF) og overvægt, begge prædiktorer for kardiovaskulær sygdom (CVD) og død af alle årsager. Tidligere studier har vist sammenhæng mellem aktiv cykeltransport til arbejde (ACB) og reduceret helbredsrisiko. Der er behov for mere viden om den sundhedsfremmende effekt af ACB hos fysisk inaktive og overvægtige raske voksne, for at sundhedsprofessionelle og politikere kan inddrage ACB i anbefalinger på individ og befolkningsniveau.

**Formål:** At undersøge effekten af ACB på CRF og kropssammensætning hos raske, fysisk inaktive og overvægtige voksne. Derudover at beskrive træningskarakteristika under ACB, og at undersøge sammenhængen mellem selvvalgt træningsintensitet (SSI) og ændring i CRF.

**Studie design:** Et randomiseret, kontrolleret studie med en per-protokol analyse.

**Metode and materialer:** I alt 53 voksne, stillesiddende og overvægtige/fede deltagere blev randomiseret til enten uændret livsstil (CON, n=18) eller seks måneders ACB med et dagligt trænings energiforbrug (ExEE) på 320 Kcal for kvinder og 420 Kcal for mænd (BIKE, n= 35). Før og efter interventionen blev CRF (V̇O₂maxR) målt med et standard åbent-kredsløb spirometrisk system (Oxycon Pro, Jaeger). Fedtmasse (FM), procent android fedtmasse (%AFM) og fedtfri masse (FFM) blev målt med dual-energy X-ray absorptiometry (DXA), og analyseret justeret for baseline værdier med kovarians analyse. Effekten blev angivet som forskelle mellem grupperne.

**Resultater:** I BIKE gennemførte 18 (51%) interventionen, og 17 blev inkluderet i analysen sammen med 16 i CON. Den gennemsnitlige V̇O₂maxR øgning i BIKE var 402 ml O2/min (95% CI: 197-606), svarende til 16%. Den gennemsnitlige reduktion i FM var 4.9 kg (95% CI: 1.8 to 7.9) uden samtidigt tab af FFM. AFM reduceredes 4% (95% CI: 1 to 7). SSI (%V̇O₂maxR) var i gennemsnit 53%, med en range på 41-65%. Dermed trænede 13 med moderat intensitet, og fire med høj intensitet. Der blev ikke fundet en association mellem SSI og ændring i V̇O₂maxR.

**Konklusion:** Seks måneders aktiv cykeltransport til arbejde med en træningsmængde svarende til minimumsanbefalingerne for fysisk aktivitet medførte en klinisk relevant fremgang i kardiorespiratorisk fitness, og et sundt vægttab hos raske, overvægtige/fede, fysisk inaktive voksne. Den gennemsnitlige selvvalgte træningsintensitet hos deltagerne var moderat.
3. Introduction

Physical inactivity is associated with obesity and poor cardiopulmonary fitness (CRF) and is a predictor of cardiovascular disease (CVD) (1), type 2 diabetes (2,3), and metabolic syndrome (4). Poor CRF and obesity have been found to increase all-cause mortality (5,6). Observational studies have shown health benefits from initiating physical activity (PA) in sedentary adults, as shown by Li et al. who found a 20-30% reduced risk of CVD with a moderate vs. low level of PA in a meta-analysis with 790,000 healthy adult individuals (7).

The global prevalence of obesity is increasing (8), and more than one third of the global population is insufficiently physically active to maintain health (9). Thus, both national health authorities and the World Health Organization (WHO) recommend all adults (age 18-66 years) to engage in moderate-intensity aerobic PA for a minimum of 30 minutes per day on 5 days per week or vigorous-intensity aerobic activity for a minimum of 20 minutes on 3 days a week (1,10,11). These recommendations emphasize a dose-response relationship between exercise volume or intensity and reduction in disease risk and obesity (12). However, experimental studies have not always confirmed this relationship: an 11-week study in overweight sedentary men showed almost similar fat mass (FM) loss and metabolic health benefits from 60 minutes of daily exercise as opposed to 30 minutes per day. However, in the same study increases in fat free mass (FFM) were only seen with the highest dose exercise (13,14).

While most physical activity interventions are carried out as leisure time physical activity (LTPA), active commuting by bike (ACB) may be an effective way for individuals to increase PA in sustainable lifestyle routines. Two Finnish observational studies found that ACB reduced the risk of CVD for women, and reduced risk of diabetes for both genders (15,16). A Danish observational study with adult administrative or industrial workers showed a reduced risk of all-cause mortality from ACB (17). Furthermore, a British cross-sectional study showed that ACB was associated with a significantly reduced BMI and body fat percentage (18). Experimental studies investigating causal effects of ACB on health risk factors are few and show large heterogeneity in exercise volumes and outcomes (19), as well as differences in the participants’ self-selected intensity (SSI) (20,21).

For health professionals and health authorities to be able to include ACB in recommendations and public health initiatives, more knowledge on ACB exercise characteristics and effects on CRF and body composition is needed.
4. Study aims

The aim of this thesis was to investigate the effects of a six-month intervention of ACB on CRF and body composition, in a healthy, sedentary, overweight and adult study population. As a part of this investigation, we aimed to describe the exercise characteristics of ACB, in particular participants’ SSI, and investigate the association between SSI and changes in CRF.

This thesis used data from the randomized controlled trial (RCT) Governing Obesity: Active Commuting To Improve health and Wellbeing in Everyday life (GO ACTIWE). To allow for elaborate discussion of the results, we performed a brief systematic review of interventional studies with ACB on the physical health effects in healthy adults.

4.1 Hypotheses

We hypothesized the following:

ACB would improve $\dot{V}O_{2\text{max}}R$.
ACB would reduce FM and increase muscle mass.
Average SSI during ACB would be approximately 60% of $\dot{V}O_{2\text{max}}R$.
A positive association between SSI and change in $\dot{V}O_{2\text{max}}R$ would be found.

5. Background

5.1 Definitions and outcome relevance

5.1.1 Physical activity and inactivity

Physical inactivity is defined by not meeting the international recommendations on physical activity (PA) (1). PA is defined by the World Health Organization (WHO) as: “any bodily movement produced by skeletal muscles that require energy expenditure – including activities undertaken while working, playing, carrying out household chores, travelling, and engaging in recreational pursuits” (1). When structured and aimed at maintaining or increasing the body’s capacity to perform, PA is termed “exercise” (1).
5.1.2 Cardiorespiratory fitness

The term cardiorespiratory fitness (CRF) is defined by WHO as “A health-related component of physical fitness; the ability of the circulatory and respiratory systems to supply oxygen during sustained physical activity” (1). CRF may be measured directly as the maximum uptake of oxygen (volume per time unit; $\dot{V}O_2\text{max}$), or indirectly through heart rate monitoring under the assumption that a linear relationship between heart rate (HR) and $\dot{V}O_2$ uptake exists (22,23). In the present thesis CRF is used interchangeably for measures of aerobic fitness and presented as either $\dot{V}O_2\text{max}$ or $\dot{V}O_2\text{maxR}$, as either absolute measure (ml O2/min) or as relative to body weight (ml O2/kg/min).

5.1.3 Body composition

Fat mass (FM) is defined as “all extractable lipids from adipose or other body tissues”, measured in kg (22). Reference values for percentages of FM (%FM) relative to the total body mass are 15% and 27% for normal weight adult males and females, respectively (22). The risk of adverse effects on health increases when %FM values exceed 20 and 30% for males and females, respectively (22). The association between %FM and risk of metabolic syndrome ($\geq$ 3 of 5 risk factors: abdominal obesity, dyslipidaemia, high blood pressure or high fasting plasma glucose concentrations) at various BMI levels was investigated in an American observational study including 4684 adult Caucasian men and women (24). For individuals with a BMI of 30 kg/m² a concomitant FM of 30.8 % for females and 29.1 % FM for males was associated with health risk (24).

Android fat mass (AFM) is defined as “fat in the abdominal region distributed both subcutaneously and viscerally between the organs” (22). In a literary review Després described variations in abdominal fat distribution, and suggested that positive associations between the fat distribution and metabolic risk factors for CVD exists, where an increase in AFM increases the risk of CVD (25). In two interventional studies, Ross et al. demonstrated that viscerally distributed AFM was strongly associated with insulin resistance in obese men and women (26,27).

Fat free mass (FFM) is defined as “the total body mass with FM subtracted, and consists of internal organs, bones, connective tissues and muscle” (22). Assuming that the non-fat, non-muscular tissue mass change very little with short-term exercise, changes in FFM is an excellent
surrogate measure of changes in muscle mass. Sufficient muscle mass is necessary for human function in performing activities of daily living, and active muscles are important for metabolic activity and health (28). Sufficient muscle mass and regular activation of muscles has been found to prevent insulin resistance and dyslipidaemia (29). In addition, active muscle is an important site for oxidation of fat and carbohydrates, and thus important in weight management (30).

5.1.4 Dose-response relationship of exercise components and health risk factors
Exercise volume (total exercise energy expenditure, ExEE) is composed of three components: intensity, duration and frequency (12,22). A practical method of quantifying aerobic work is by the number of metabolic equivalents of task (MET) used during the activity. By convention, one MET is defined as “the amount of oxygen consumed while sitting at rest, equal to 3.5 ml O2 per kg body weight x min” (31). Relevant units of exercise intensity corresponding to the terminology of exercise intensity zones used in health recommendations are presented in Table 1 (11).

<table>
<thead>
<tr>
<th>Exercise zone</th>
<th>%VO2maxR / %HRR</th>
<th>% VO2max</th>
<th>% HRmax</th>
<th>METs</th>
</tr>
</thead>
<tbody>
<tr>
<td>very light</td>
<td>&lt;30</td>
<td>&lt;37</td>
<td>&lt;57</td>
<td>&lt;2</td>
</tr>
<tr>
<td>light</td>
<td>30-39</td>
<td>37-45</td>
<td>57-63</td>
<td>2.0-2.9</td>
</tr>
<tr>
<td>moderate</td>
<td>40-59</td>
<td>46-63</td>
<td>64-76</td>
<td>3.0-5.9</td>
</tr>
<tr>
<td>vigorous</td>
<td>60-89</td>
<td>64-90</td>
<td>77-95</td>
<td>6.0-8.7</td>
</tr>
<tr>
<td>high</td>
<td>&gt;89</td>
<td>&gt;90</td>
<td>&gt;95</td>
<td>&gt;8.7</td>
</tr>
</tbody>
</table>

Adapted from the American College of Sports Medicine (ACSM) guidelines. VO2maxR=VO2max reserve, HRmax=maximal heart rate, HRR=heart rate reserve, MET=metabolic equivalent of task (means of all adults)

A clear dose-response relationship has been found between exercise volume or intensity and increase in CRF in healthy sedentary adults (11,32). Ross et al. found that increased intensity at a fixed exercise volume increased CRF, but that increasing the intensity did not result in further reductions in abdominal obesity (33,34). Thus, sedentary healthy adults may experience greater increases in CRF with moderate or vigorous versus low intensity exercise (12).
5.2 Brief systematic review

To gain further insights into the causal effects of ACB in adults, we performed a systematic review on ACB outcomes related to physical health. The aim was to answer the following research question: “What are the effects of active commuting by bike on physical health outcomes in healthy adults, as investigated by interventional studies?”

5.2.1 Methods

This systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for reporting of systematic reviews (35).

Literature search and selection

Searches were performed on March 14th 2016 on three major databases: PubMed, Embase (OVID) and CINAHL (EBSCOhost) for original peer-reviewed articles, using the following combination of search terms for active commuting and bicycling: commut* OR active travel* AND biking OR bicycle OR bike OR cycling. Inclusion criteria were: Interventional studies, interventions of ACB, study population of healthy, sedentary adults (any BMI) and, physical health outcome. Exclusion criteria were: Disease in the participants, non-original studies, non-interventional (observational) studies, and non-work related commuting. Filter was used for Ages: +19 (PubMed) or equivalent filters in Embase or CINAHL (18-64 yrs.). No limits were applied for year of publication or language, but articles in other than English, German or Scandinavian languages were excluded. Duplicates were removed from CINAHL and Embase in relation to the PubMed search by using the “Exclude MedLine records” function. Titles and abstracts were screened independently by both authors, and any disagreement in the initial appraisal between the authors was discussed until consensus.
Fig 1. Flowchart of literature search

Records identified through database search (n = 460)

- Medline n=179
- Embase n=233
  (201 duplicates with Medline)
- Cinahl n=48
  (26 duplicates with Medline)

Additional records identified through other sources (n = 0)

Records after duplicates removed (n =233)

Records screened (n =233)

- Records excluded (n=222)
  based on title or abstract (n=188)
  based on design (n=34)

Full-text articles assessed for eligibility (n =11)

- Full-text articles excluded, with reasons (n=3)
  Not relevant health outcome (n=1)
  Insufficient reporting of results (n=1)
  Relevant outcome reported in other included study (n=1)

Studies included in systematic review (n = 8)


**Data extraction and evaluation**

Articles found eligible were read in full detail by both authors independently and data was extracted using a data extraction sheet designed by the authors. Data on physical health outcome variables were extracted, and if possible presented as differences between intervention and control groups in means with 95% confidence interval (CI). Study quality and risks of bias were assessed independently by both authors with the use of the Quality Assessment Tool for Quantitative Studies, from the Effective Public Health Practice Project (EPHPP) (36). It consists of six components; 1) study participants’ representativeness of the target population, 2) study design, 3) control of confounding, (4) blinding of outcome assessors and participants, (5) reliability and validity of the data-collection tools, and (6) number of withdrawals and drop-outs. Disagreements between the authors were discussed until consensus was achieved. The Grading of Recommendations Assessment, Development and Evaluations approach (GRADE) was used to evaluate the strength of evidence of each outcome across studies. We graded the level of evidence considering issues of bias, indirectness, inconsistency or imprecision of results (37).

**5.2.2 Findings**

The flow of the literature search and inclusion is presented in Figure 2. The search identified 233 original studies after duplicates were removed. Screening of titles and abstracts lead to exclusion of 222 studies, therefore 11 studies were assessed for eligibility by full text reading (20,38-47). One study by de Geus et al. was excluded as the aim was not to assess a health outcome, but rather intensity during ACB, and its secondary outcome on CRF was reported in a later study (20). Mutrie et al. aimed to investigate if a self-help intervention could change workers’ active commuting behavior, which we decided was irrelevant for answering our research question (47). Finally, a study by Marshall was excluded as it did not report data and results in a transparent and sufficient manner, and we were unable to get in contact the author by mail for clarification on sample sizes and results (46).

**Study and population characteristics**

The eight included studies represented five controlled trials, as two studies by de Geus et al. used data from administrative workers in a 12 month intervention in Belgium (40,41), and the studies by Hemmingsson et al. and Eriksson et al. use data with obese women in an 18 month intervention in Sweden (42-44). Of the five trials, four used a randomized design, and the trial...
by de Geus et al. used a quasi-randomized design based on home-to-work distance (40,41). Interventions took place in Denmark, Finland and Holland in the remaining studies, thus only European populations were represented. Average sample size was 92 participants (range: 48-122). Study populations were similar: mixed-gender, adults in the late thirties to mid-forties, sedentary and healthy, except for the study population used by Eriksson et al. and Hemmingsson et al., which was all-female, slightly older and overweight/obese with abdominal obesity (42-44). The interventions ranged in duration from 10 weeks to 78 weeks, with weekly doses of ACB ranging from 12 to 90 km per week, or with no upper limit. All cycling intensities were self-selected. Intervention compliance ranged from 34% to 87.5%.

**Cardiorespiratory fitness**

Five studies reported changes in CRF as \( \dot{V}O_{2\text{max}} \), either absolute (ml O2/min) or relative to body weight (ml O2/kg/min) and consistently showed CRF improvements. In the one-year intervention by de Geus (2008), the increase took place in the first six months, with no further significant change in the next six months (40). The increase in \( \dot{V}O_{2\text{max}} \) from ACB in the study by Hendriksen et al. was significant for men only in the first six months (6.9%) (39). Møller et al. showed the greatest effect in the shortest intervention duration (12.5% increase in eight weeks), however it was a per protocol analysis as opposed to the other studies which used intention to treat analysis, and with a 24% drop out rate in the intervention group (45). Hendriksen et al. and de Geus et al. (2009) used maximum power output (Pmax; watt/min or watt/min/kg) as outcome (39,41). Both studies showed an increase in Pmax of 13% and 6.5% respectively.

Dose-response between ACB and CRF was investigated by Hendriksen et al., de Geus et al. (2009) and Møller et al. showing positive correlations between ACB distance or ExEE and CRF (39,41,45). In addition, Eriksson et al. showed a dose-response relationship between cycling distance and left ventricular systolic dimension (44).
### Table 2. Data extraction sheet.

**Author, year, country, aim**

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Population</th>
<th>Intervention</th>
<th>Results (primary and secondary outcome)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oja; 1991 Finland</td>
<td>RCT stratified for gender, fitness level and home-work distance: 1)walking to work (range 2-4.9 km); 2)walking or cycling (range 5-6.9 km); 3)cycling to work (range 7-20 km). Finally randomized to intervention or control group.</td>
<td>Sedentary non-commuters (n=71); Men = 40; mean age 40 yrs; mean BMI 25; Women = 31; mean age 38 yrs.; mean BMI 24</td>
<td>2x 10 weeks of walking or cycling to and from work, all workingdays.</td>
<td>Exercise characteristics: Walking: 3.4 km/trip; 35 min/trip; mean HR 121; mean intensity %VO2 max 53%; Cycling: 9.7 km/trip; 32 min/trip; mean HR 133; mean intensity %VO2 max 65%; Intervention group had 78% compliance. CRF VO2 max (l/min) increased 0.08 l/min [0.01; 0.15] for Intervention; and decreased -0.02 [-0.08; 0.06] for controls; insign. diff. between groups p=0.07; VO2 max (ml/min/kg) increased 1.2 ml/min/kg [0.2; 2.2] for Intervention; controls unchanged; p=0.02. The increase in VO2max (l/min) was significant for cyclist only with 0.1 [0.11; 0.27] vs. walkers 0.05 [-0.02 ; 0.12]; between groups p=0.01. No gender effects. <strong>Body weight</strong> remained stable. <strong>Blood lipids</strong> Total cholesterol and triglycerides insignificant difference. HDL increased 0.08 mmol/l [0.03; 0.14] for Intervention vs. 0.01 [-0.04; 0.07] for controls; trend of difference p=0.06. No gender effects.</td>
</tr>
<tr>
<td>Hendriksen; 2000 the Netherlands.</td>
<td>RCT stratified for sex and age Controls crossed over to intervention after 6 months. Secondary aim: to identify a dose-response relationship between the changes in Wmax and VO2max for frequency, distance, and intensity of cycling.</td>
<td>Healthy, sedentary administrative employees aged 25 - 56 years N=122; men n=87, women n=35, mean age 37; Mean BMI: women 25.5, men 24.5</td>
<td>Commuter cycling, min. 3 km each way, min.3 days/week, duration: 6 months. Control: no change in lifestyle After 6 months, controls were asked to commute by bike for 6 months.</td>
<td>Exercise characteristics: Distance: average one-way trip 9.4 km for men and 6.4km for women. Bouts/week 3.3 times /week for men and 3 times /week for women. Avg. intensity: 68 % HRmax / 55% VO2 max for men; 75% HRmax / 65% VO2 max for women. CRF after 6 months: VO2max/kg: Cycling 4% vs controls -1% (p&lt;0.01). Mean change in the intervention group was 6.1% (p&lt;0.01) for men, -2.2% (not significant) for women. In the control group both men and women significantly reduced VO2max/kg. When the control group did AC from 6 to 12 months, they increased 6.9% (men) and 9.5% (women) (p&lt;0.01). Maximal external power Wmax/kg increased 13% (P&lt;0.01) for Intervention group, and remained unchanged in the control group. When the control group did AC from 6 to 12 months, they saw a similar increase (p&lt;0.01) <strong>Body weight</strong> no change. <strong>Dose-response</strong> subjects with the lowest initial fitness levels scored the largest gains, and for them a single trip distance of 3 km was enough to lead to a gain of about 14% in the Wmax. An increase in the cycling distance from 3 to 6 km produced more gain than increasing the distance from 15 to 18 km. <strong>Blood lipids</strong> No significant difference. <strong>Body composition</strong> No sig. change in weight and BMI over time between groups. <strong>Blood lipids</strong> No significant between group changes in total cholesterol, Triglycerides, HDL, LDL, VLDL, CrP.</td>
</tr>
<tr>
<td>De Geus et al; Belgium</td>
<td>Quasi-randomized controlled study. Randomization according to distance between work and home. Living 2-15 km from work and travelling &gt; 3 times/week led to inclusion in the intervention group. Others were in control group.</td>
<td>Healthy adults, untrained &lt; than 3h PA/week and non-AC for 6 months, VO2peak below 50th percentile. Intervention (n=73): mean BMI 26 ± 4, Mean age 43± 5</td>
<td>Biking to work, 2-15 km x 2, minimum 3/week, 12 months. Controls: remained sedentary.</td>
<td>Exercise characteristics: Compliance (cycling ≥ 3 times a week to work) was 38% during the first 6 months and 34% during the second 6 months. Decreased motivation or weather? Average frequency 3.9 bouts/week and 250 min/week. <strong>Body composition</strong> No sig. change in weight and BMI over time between groups. <strong>Blood lipids</strong> No significant between group changes in total cholesterol, Triglycerides, HDL, LDL, VLDL, CrP.</td>
</tr>
</tbody>
</table>
Aim (2009): to examine the effect of cycling to work on physical performance; and the minimum weekly energy expenditure needed for fitness improvement based on the dose–response relationship between total caloric expenditure and fitness changes.

Hemmingson et al; 2009

Sweden

RCT

Randomization with stratification for age and WC.

Healthy female volunteers (30–60 years) with abdominal obesity (waist circumference 88–120 cm); Working away from the home ≥ 3 days/week, with no medical contraindications for PA.

Not sedentary prior to participation.

2.5% normal weight, 42.5% overweight, 55% obese.

Mean WC 103.8 cm. Mean Sagittal Abdominal Diameter (SAD) 23.5.

N=120.

Study period 78 weeks.

Control (standard care):

Two 2-hour group sessions at baseline and 6 months, to encourage participants to walk a minimum of 10,000 steps a day as well as PA generally, including AC. A pedometer was given participants.

Intervention: 78 weeks of standard care with the addition of an intensive behavioral counseling package with a health educator to increase ACB (min. 2 km/day) and walking min. 10,000 steps per day. A pedometer and a new bicycle was given participants.

Exercise characteristics (primary outcome)

Drop-out rate: Intervention 10%, controls 25%.

Cycling distance: In the IG it increased with seasonal fluctuations, highest mean recorded cycling distance during 7 days 36.7 km/day. 38.7% cycled > 2 km/day; 24.8% cycled > 4 km/day. CG: 8.9% cycled > 2 km/day, 4.6% ≥ 4 km/day. Significant between group difference for increase in cycling (p<0.001).

Walking: increased from 8692 to 10.129 and from 8249 to 9086 steps/day for intervention and controls respectively, within group difference p< 0.001. Between group difference p=0.10.

Secondary outcome

Body composition: no between group differences.

WC: mean difference in intervention group at 26 weeks -2.2 cm. [-3.3 ; -1.1] and at 78 weeks -2.1 cm; 95 % CI [-3.4 ; -0.8]

SAD decreased in the intervention group at 26 weeks -1.1 cm. [-1.5 ; -0.8] and at 78 weeks -1.0 cm [-1.3 ; -0.7].

Body weight unchanged for both groups.

Hemmingson et al; 2011

Sweden

Aim: to quantify the separate effects of walking and bicycling on fasting insulin and homeostatic model assessment – insulin resistance (HOMA-IR).

Pooled prospective cohort analysis of data from a randomized trial on active commuting with cycling and walking vs walking only (n=98).

Healthy female volunteers (30 to 60 years) with abdominal obesity (waist circumference 88–120 cm); Working away from the home ≥ 3 days/ wk, and with no medical contraindications for PA

See above (Hemmingson et al; 2009)

Data obtained after 26 weeks of intervention.

Exercise characteristics

Cycling 10 km/day in addition to walking

Insulin resistance (IR)

Fasting serum insulin and homeostatic model assessment (HOMA-IR): increased bicycling by 10 km/week was associated with reductions in fasting serum insulin (β = –10.9, P = .042) adjusted, but not HOMA-IR. Walking was not associated with IR, % body fat reduced; (p= 0.04)

Eriksson et al; 2010

Sweden.

Single arm, single blinded study (Secondary analysis of

Healthy middle-aged (30–60 years old) women with

An intensive 26 week behavioral program to

Exercise characteristics

Walking increased from 8950 steps per day at baseline to 10 750 steps per day at
Same cohort as Hemmingsson.

Aim: to determine the impact of low intensity training on cardiac morphology and function in women with abdominal obesity and with a sedentary lifestyle.

Intervention group data from RCT

Abdominal obesity [waist circumference (WC) > 88 cm] N=50

Mean age 47±7.5 years; mean BMI 30±2.8; mean WC 103.2±7.8 cm. Mean Blood pressure BP systolic 127±15 mm Hg, Mean BP diastolic 80±8 mm Hg.

Increase PA by walking and cycling AC (the same as Hemmingsson et al.; 2009 using data from the first 26 weeks)

6 months (P = 0.00003)
Cycling increased to 5 km per day at 2 and 4 months; but decreased to 3.2 km per day at 6 months (P = 0.0438).

WC
Mean WC decreased significantly from 103.3±7.9 to 100.8±8.4 cm, P = 0.0003

BP
Systolic BP decreased 7±15 mmHg, p=0.0002; and diastolic BP decreased 2±8 mm Hg, p=0.0003.

Heart function measured by TEE (transthoracic echocardiography)

No significant change in LV mass.
Mean longitudinal systolic function (RV TAPSE) increased from 22.00±3.30 to 23.05±3.59 mm, P = 0.015; and a trend for positive change in LV MAPSE.

WC was negatively correlated to RV TAPSE, suggesting increase in longitudinal function in patients with largest decrease in WC.

Dose-responsen
Increased cycling distance was associated with reduced LV systolic dimension independently of changes in walking, WC, systolic and diastolic blood pressure Beta= 0.45, P = 0.04, and with RV diastolic dimension Beta= 0.33, P = 0.03.

Møller et al., 2011, Denmark

Aim: to investigate the short term effect of 8 weeks of commuter cycling on VO2max and CRF in a heterogeneous sample of untrained men and women in various occupational affinities.

Secondary outcomes were body fat and blood pressure.

Hypothesis: a min. of 20 min of daily commuter cycling would lead to a 10% increase in VO2max.

RCT
“4 block randomization procedure”, stratified for gender, age and daily cycling distance.

Per protocol; Gender pooled analysis adjusted for baseline, age and gender.

Healthy industrial and administrative workers (n=48). No regular cycling or LTPA for past 3 months.

Men (n=34), mean age 44.3 years ±9.4), mean BMI 27.6.

Women (n=14) mean age 45.9 years±6.6, BMI 24.9.

Intervention: n= 25 (25% dropout)

Controls; n= 23
5 participants used medication for high BP

Min. 20 min of daily commuter cycling with self-selected intensity during a period of 8 weeks (i.e. estimated distance=25 km/week assuming an average speed of 15 km/h).

Controls: no change.

Exercise characteristics Intervention group:

Avg. 40 min/day, average speed 15 km/h. 24% dropouts.
Controls: 31.9 km cycling/week. 0% dropouts.

Primary (No gender diff., pooled analysis)
VO2max (ml/min) Sig. change in VO2max between groups=206 ml O2/min; p= 0.005.
VO2 max increased 12.5% in Intervention group vs. 4.6 for controls.

CRF (ml O2/min/kg) significant (p=0.003) increased in Intervention vs. controls.
Change between groups= 2.6 ml O2/min/kg; p=0.003.

Dose-response:
A relatively strong dose–response relationship between amount of cycling and change in maximal oxygen uptake (β=0.73, R2=0.46 and p=0.002).

Secondary

Body fat by skinfold thickness (mm) (m. triceps brachii, m. biceps brachii, subscapularly, superior to the spina iliaca anterior superior, abdominal, and front thigh): change in sum of skinfolds between groups =12.1 mm; p= 0.026.

Blood pressure
Systolic and diastolic: no significant between group difference.

Results as mean [95% confidence interval] or mean (p-value alpha level 0.05). RCT= randomized controlled trial; CRF= cardiorespiratory fitness; VO2 = volume of oxygen consumption; ITT= intention to treat; BP= blood pressure; WC= waist circumference; SAD= sagittal abdominal distance; RV/LV= right or left ventricular. R= correlation coefficient.
Body composition

Three studies investigated body composition; De Geus et al. (2008) found no difference in weight and BMI between the intervention and the control group, however the study population was only borderline overweight (40). Hemmingsson et al. investigating a study population of obese women reported no between group difference in body weight, but found a reduction in waist circumference, and a reduction in Sagittal Abdominal Distance (SAD) (42). Møller et al. measured body fat by sum of skinfold thickness at eight different body locations, and found a significant between group difference (45).

Other health outcomes

Blood lipids were assessed in two studies, Oja et al. and de Geus (2008) et al. showing no effect (38,40). Resting blood pressure was assessed in three studies; Møller et al. and de Geus et al. (2008) found no between group difference in BP (40,45), whereas Eriksson found a small reduction in BP at six months, but the single arm study design did not allow for comparison with a control group (44). Insulin resistance was investigated by Hemmingson et al. (2011) who found a dose response relationship between cycling volume and reductions in fasting serum insulin (43). Eriksson et al. investigated changes in cardiac morphology and heart function with TEE (transthoracic echocardiography), and found improved systolic function (44).
<table>
<thead>
<tr>
<th>Paper</th>
<th>Selection bias</th>
<th>Study design (RCT)</th>
<th>Confounders</th>
<th>Blinding</th>
<th>Data collection</th>
<th>Withdrawals/dropouts</th>
<th>Overall QA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oja 1991</td>
<td>Moderate (recruited from survey on ACB)</td>
<td>Strong</td>
<td>Strong</td>
<td>Weak</td>
<td>Strong</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
<tr>
<td>Hendriksen 2000</td>
<td>Weak (selected workplaces)</td>
<td>Strong</td>
<td>Strong</td>
<td>Weak</td>
<td>Strong</td>
<td>Strong</td>
<td>Weak</td>
</tr>
<tr>
<td>De Geus 2008</td>
<td>Moderate (quasi randomization)</td>
<td>Strong</td>
<td>Moderate</td>
<td>Weak</td>
<td>Strong</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
<tr>
<td>De Geus 2009</td>
<td>Moderate (quasi randomization)</td>
<td>Strong</td>
<td>Moderate</td>
<td>Weak</td>
<td>Strong</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
<tr>
<td>Hemmingsson 2009</td>
<td>Strong</td>
<td>Strong</td>
<td>Strong</td>
<td>Moderate</td>
<td>Strong</td>
<td>Strong</td>
<td>Strong</td>
</tr>
<tr>
<td>Hemmingsson 2011</td>
<td>Strong</td>
<td>Moderate (Non-randomized cohort)</td>
<td>Weak</td>
<td>Weak</td>
<td>Strong</td>
<td>Moderate</td>
<td>Weak</td>
</tr>
<tr>
<td>Eriksson 2010</td>
<td>Strong</td>
<td>Moderate (Non-randomized cohort)</td>
<td>Weak</td>
<td>Weak</td>
<td>n/a</td>
<td>Weak</td>
<td>Weak</td>
</tr>
<tr>
<td>Møller 2011</td>
<td>Moderate (self referral from work)</td>
<td>Strong</td>
<td>Strong</td>
<td>Moderate (blinding of assessors)</td>
<td>Strong</td>
<td>n/a (per protocol)</td>
<td>Strong</td>
</tr>
</tbody>
</table>

Abbreviations: QA = quality assessment; EPHPP = Effective Public Health Practice Project. All studies received lower score due to lack of participant blinding. n/a = not applicable.
5.2.3 Study quality

The study quality is presented in Table 3. Study quality was rated strong in two studies, as they had no weak ratings, with strong study designs, relevant outcome and data collection methods (42,45). Only these two studies were powered with respect to a predefined primary outcome, and the general lack of power calculations across the remaining studies may have increased the risk of false negative results. The study by Eriksson et al. was graded weak as it was a non-controlled cohort, without information of blinding on assessors (44). By the nature of the interventions a double blind design was inapplicable, but report of assessor blinding was absent in most studies, thus introducing the risk of observer bias.

5.2.4 Summary of findings

Summary of findings and evaluation of the evidence level for each outcome is presented in Table 4. High quality evidence was found for an improvement of CRF with ACB with a dose-response relationship between volume of ACB, and CRF. Moderate quality evidence was found for reductions in waist circumference and blood pressure. Low quality evidence was found for other outcomes, which were investigated in only single studies with weak ratings of quality.
Table 4. Evidence profile and summary of findings.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>N (studies)</th>
<th>Summary of effect</th>
<th>Quality of the evidence (GRADE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiopulmonary Function</td>
<td></td>
<td></td>
<td>High: strong design RCTs with dose-response design, primary outcome. Consistent results across 4 studies of moderate quality.</td>
</tr>
<tr>
<td>Power max</td>
<td>210 (2)</td>
<td>Increased 6.5% (p&lt;0.01)&lt;sup&gt;4&lt;/sup&gt;; 13 % (p&lt;0.01)&lt;sup&gt;2&lt;/sup&gt; Active vs. Passive commuting increased (p=0.07)&lt;sup&gt;7&lt;/sup&gt;; Cycling vs. Walking increased (p&lt;0.01)&lt;sup&gt;1&lt;/sup&gt;. VO2 peak 1.2% at 6 months (p&lt;0.01), but insig. 12 months&lt;sup&gt;4&lt;/sup&gt;. Increased 206 ml O2/min (p=0.005)&lt;sup&gt;7&lt;/sup&gt;.&lt;sup&gt;8&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>VO2 peak / max</td>
<td>333 (4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VO2max (ml/kg/min)</td>
<td>71 (1)</td>
<td>1.2 ml/kg/min [0.2; 2.2] (p=0.02)&lt;sup&gt;1&lt;/sup&gt;. 11% increase (p&lt;0.01)&lt;sup&gt;2&lt;/sup&gt;. Increased (p&lt;0.01)&lt;sup&gt;4&lt;/sup&gt;. Increased 2.6ml/kg/min (p=0.003)&lt;sup&gt;8&lt;/sup&gt;.</td>
<td></td>
</tr>
<tr>
<td>Dose response</td>
<td>312 (4)</td>
<td>Volume increased effect (β=0.73, R2=0.46 and p=0.002)&lt;sup&gt;4&lt;/sup&gt;. EE&gt; 1000 kcal women and 1500 kcal men (R=0.40)&lt;sup&gt;4&lt;/sup&gt;. Increased effect by distance &gt;3 km. 14% with low baseline fitness&lt;sup&gt;7&lt;/sup&gt;. Increased distance improved dBP (p=0.04) and right ventricular dimension (p=0.03)&lt;sup&gt;7&lt;/sup&gt;. Effect for cycling vs. walking&lt;sup&gt;1&lt;/sup&gt; (Cycling intensities were on average 55-65% VO2 max., walking lower approx. 50% VO2 max).</td>
<td></td>
</tr>
<tr>
<td>Body composition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body weight</td>
<td>310 (5)</td>
<td>No changes in body weight&lt;sup&gt;12&lt;/sup&gt;&lt;sup&gt;3&lt;/sup&gt;&lt;sup&gt;5&lt;/sup&gt;&lt;sup&gt;6&lt;/sup&gt;&lt;sup&gt;7&lt;/sup&gt;</td>
<td>Very low Secondary outcome in non-obese population, only obese participants in one study.</td>
</tr>
<tr>
<td>WC</td>
<td>120 (2)</td>
<td>-2.2 cm [-3.3;-1.1] at 26 weeks; -2.1 cm [-3.4;-0.8]at 78 weeks&lt;sup&gt;1&lt;/sup&gt;&lt;sup&gt;3&lt;/sup&gt; &lt;sup&gt;4&lt;/sup&gt;-2.5 cm (p=0.003)&lt;sup&gt;9&lt;/sup&gt;</td>
<td>Moderate Secondary outcome, consistent results.</td>
</tr>
<tr>
<td>Skinfold and SAD</td>
<td>168 (2)</td>
<td>SAD <code>-1.1 cm [-1.5;-1.8] at 26 weeks and </code>-1.0 [-1.3;-0.7] at 78 weeks&lt;sup&gt;4&lt;/sup&gt;&lt;sup&gt;8&lt;/sup&gt;. Sum of skinfolds `-12.1 mm (p=0.026)&lt;sup&gt;9&lt;/sup&gt;</td>
<td>Low Imprecison of results - secondary outcome.</td>
</tr>
<tr>
<td>Body fat percentage</td>
<td>98 (1)</td>
<td>Reduced (p= 0.04)&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Low Imprecision of results</td>
</tr>
<tr>
<td>Other outcome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood pressure</td>
<td>190 (3)</td>
<td>Reduced diastolic BP (p&lt;0.01)&lt;sup&gt;4&lt;/sup&gt;. Reduced dbp (p=0.0002); sbp(p= 0.0003) and resting BP (p&lt;0.01)&lt;sup&gt;7&lt;/sup&gt;. No difference&lt;sup&gt;8&lt;/sup&gt;</td>
<td>Moderate Inconsistency, primary outcome in 2 studies.</td>
</tr>
<tr>
<td>Blood lipids</td>
<td>163 (2)</td>
<td>No difference&lt;sup&gt;1&lt;/sup&gt;&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Low Imprecision of results</td>
</tr>
<tr>
<td>Heart function</td>
<td>50 (1)</td>
<td>Increased systolic function (p = 0.015)&lt;sup&gt;7&lt;/sup&gt;</td>
<td>Low Weak design, but dose-response between cycling distance and change. Indirectness of outcome measure (ECHO cardiography).</td>
</tr>
<tr>
<td>Insulin resistance</td>
<td>98 (1)</td>
<td>Reduced fasting serum insulin; β = –10.9 (p = 0.042)&lt;sup&gt;7&lt;/sup&gt;</td>
<td>Low Study design, Impression of result</td>
</tr>
</tbody>
</table>

Summary of significant results in mean change with [95% confidence interval] and (p-value alfa level 0.05) in between group differences for total groups (no gender subgroups). N= number of participants; RCT= randomized controlled trial; EE= energy expenditure; WC= waist circumference. SAD= saggital Diameter. <sup>1</sup>= Oja et al. <sup>2</sup>= Hendriksen et al.; <sup>3</sup>= de Geus et al. 2008; <sup>4</sup>= de Geus et al. 2009; <sup>5</sup>=Hemmignsson et al. 2009; <sup>6</sup>= Hemmignsson et al. 2011; <sup>7</sup>= Eriksson et al. <sup>8</sup>= Møller et al.
6. Materials and methods

Data for the analysis in this thesis was collected from the GO ACTIWE project, Dep. of Biomedical Sciences, Faculty of Health and Medical Sciences, University of Copenhagen. The project aims and protocol can be found on: www.go.ku.dk and on www.clinicaltrials.gov (Identifier: NCT01962259).

6.1 Purpose and design of GO ACTIWE

Active Commuting to Improve health and Wellbeing in Everyday life (GO ACTIWE) was a randomized controlled trial conducted in Copenhagen, Denmark from October 2013 to May 2016. The overall aim was to investigate effects of lifestyle routine physical activity interventions on health factors in sedentary, overweight and healthy adults, with peripheral insulin sensitivity as the primary outcome. Other aims were to investigate differences in effect and long-term compliance between high and low exercise intensity LTPA, and ACB.

6.2 Recruitment and randomization

Participants were recruited by advertising in media and relevant web pages, and screened for eligibility before block-randomization in a 2:2:2:1 ratio to moderate intensity LTPA, vigorous intensity LTPA, cycling to work (BIKE) or control (CON). The project was powered to show changes in peripheral insulin sensitivity (clamp), $\dot{V}O_{2max}$ and visceral fat mass (MR-scan) with a power for Type I error of 85% with 140 randomized participants, hereof 40 in BIKE and 20 in CON, with a 20% drop out rate. Due to difficulty in recruitment, the original one-year length of the intervention was reduced to six months. The present thesis used data from the BIKE and CON groups only, and result were analyzed for four outcomes: CRF, FM, FFM and percentage of fat in the android region (%AFM) at six months.

6.3 Eligibility criteria

Inclusion criteria:

- Healthy overweight or grade 1 obese men and women (BMI 25-35 kg/m²)
- Fat mas above 32% for women and above 25% for men
- Age 20-45 years
Sedentary lifestyle (self-reported) and CRF <40 and 45 ml O₂/kg/min for women and men, respectively.

Non-smoking

Caucasian

Willing to accept random allocation to control group or one of three interventions.

Exclusion criteria:
Chronic use of medicine, smoking, fasting plasma glucose > 6.1 mmol/L, blood pressure > 140/90 mm Hg, abnormal resting or working ECG, parents or siblings with diagnosed type 2 diabetes, for women: pregnancy or planning of pregnancy within the coming year.

6.4 Ethical considerations
All participants were given verbal and written information about the purpose, intervention, randomization and test procedures. Participants were informed about any discomfort or nuisance associated with participation, and they were provided with written information on participants’ rights in research projects (48). Participants were included after giving written consent according to the declaration of Helsinki II to participate in the study, which was approved by the Ethics Committee for Medical Research in Copenhagen (File no. H-4-2013-108). CON participants were offered individualized lifestyle guidance and a 12-month membership in a fitness center after the six-month intervention period.

6.5 Intervention
The BIKE intervention consisted of commuter cycling 9-15 km per day for women or 11-17 km per day for men, five days per week. Exercise induced energy expenditure (ExEE) per day was 320 kcal ± 25% and 420 kcal± 25% for females and males, respectively. Participants uploaded exercise data regularly and were in dialog with study personnel throughout the intervention period regarding adjustments of exercise volume, practical assistance with the bicycles, the use and calibration of heart rate monitors, booking of tests days etc. CON participants were instructed to remain sedentary.

6.6 Data collection for the present thesis
Outcome measurements were collected at baseline and six months. Participants performed additional VO₂max tests at 1.5 months and three months, the results of which were used for
monitoring SSI and adjusting exercise volume. All data were collected by researchers or trained project personnel, imported to Excel and validated by two independent researchers. No assessor blinding was used. Data analysis was not initiated until after the last participants’ last visit.

6.6.1 Cardiorespiratory fitness

\( \dot{V}O_{2\text{max}} \) test

Maximal oxygen consumption \( \dot{V}O_{2\text{max}} \) (ml O2/min) was measured using a standard open circuit spirometry system (Oxycon Pro, Jaeger, Würzburg, Germany) with a pre-set graded exercise test on an electronically braked bicycle (Lode Excalibur, Groningen, Netherlands). Before each test the Oxycon PRO was calibrated, and a heart rate monitor (Polar RC3, Polar Electro Oy, Kempele, Finland) was synchronized with the computer. All tests were performed afternoons, participants had fasted for six hours and had not exercised on that day, nor the day before. Participants were instructed to cycle “as long as possible” with approximately 80-100 revolutions per minute to exhaustion to reach their maximum capacity. Shoes and face-masks were fitted individually. The test protocol warm-up consisted of three levels of three-minute workloads of 30/40 Watt (W), 60/80 W and 90/120 W for females/males, respectively. Heart rate at these set points were later used to establish SSI by the best-fitted line between HR and \( \dot{V}O_2 \). The workload was then increased with 25W increments every minute and continued until appearance of exhaustion, oxygen consumption levelling off despite increased load, or a respiratory exchange rate of >1.15. Mean oxygen consumption was calculated from the three highest, but not the last, measurements in the test. This test is considered gold standard with excellent validity when using the above mentioned criteria for reaching maximal exhaustion (49). In a study with young adults the test-retest reliability was found to be good with a test-retest correlation coefficient of 0.96 and a standard deviation of the difference of 8% (50).

Resting metabolic rate

RMR was measured with an Oxycon PRO REE respiratory calorimetry system (Oxycon Pro, Jaeger, Würzburg, Germany), and heart rate was measured with a POLAR heart rate monitor (Polar RC3, Polar Electro Oy, Kempele, Finland). The test was performed in the morning, in a quiet temperate room. Participants were fasting and had not exercised on that morning, nor on the day before. Oxygen consumption was measured with a hood covering the head for 20 min. with the participant resting undisturbed lying in a bed with covers and without sleeping. Mean oxygen
consumption (\( \dot{V}O_2 \), ml/min) was calculated from measurements in the last five minutes of the test period.

**Calculation of \( \dot{V}O_{2\max R} \) and technical error**

\( \dot{V}O_{2\max R} \) was calculated as: \( \dot{V}O_{2\max R} = \dot{V}O_{2\max} - \text{RMR} \).

The technical error (TE) of the \( \dot{V}O_{2\max R} \) estimate was calculated using the method outlined by Bouchard et al. (51), and used by Ross et al. in a study of exercise intensity and CRF (33): TE equals the square root of the sum of squared differences of repeated measures, divided by the total number of paired samples multiplied by two. CRF response was defined as individual CRF gain above the TE and, as suggested by Bouchard, CRF adverse response was defined conservatively as individual CRF decrease below 2 x TE (51).

### 6.6.2 Body composition

Weight was measured on an electronic scale (kg), and height measured on a stadiometer (cm). BMI was calculated as body mass/height\(^2\) (kg/m\(^2\)).

The body composition measures of FM, %AFM and FFM were assessed using a dual-energy X-ray absorptiometry scanner (DPX-IQ X-ray bone densitometer 4.7e; Lunar Corporation, Madison, WI, USA) calibrated before each test for functionality and accuracy. Tests were performed mornings, participants were dressed lightly, were fasting and had not exercised on the day, nor the day before. The participant was positioned supine on the midline of the scanner with cushions and straps for stabilization to lie completely still. Total body composition analysis was selected and weight, height, age, gender and race were registered. FM was reported in kg and percentage of total body mass. FFM was calculated as total body mass subtracted by FM and reported in kg. %AFM was measured using the LUNAR preset cut positions for the android region, which was defined as depicted in Figure 2 (52). The marked upper box (pink) represents the android region defined caudally by the pelvis line (not visible), laterally by arm lines (green), and cranially by the 20\% point between the pelvis line and the neckline (green). %AFM was recorded as percentage of fat in the android region. The DXA scan measurements have been found to have a standard error of the estimate of 2.8\% for this measurement in Caucasian adults (53).
6.6.3 Exercise monitoring

During the entire intervention all cycling bouts were recorded by participants with a GPS based heart rate monitor (Polar RC3, Polar Electro Oy, Kempele, Finland). GPS position, duration, speed and heart rate were recorded and uploaded regularly to the research group with the web-based software tool PolarPersonalTrainer.com. Time and heart rate were recorded only when the participant was moving; when not moving (e.g. at stoplights) the monitor was automatically paused. Participants´ daily ExEE was calculated by an algorithm within the Polar heart rate monitor, using age, gender, weight, height, and $\dot{V}O_2\text{max}$. Bodyweight and $\dot{V}O_2\text{max}$ was updated after each $\dot{V}O_2\text{max}$ test. SSI was determined using the best fitted line between HR and $\dot{V}O_2\text{max}$ from the $\dot{V}O_2\text{max}$ test chronologically closest ($\pm$ 3-6 weeks) to the time interval.

Level of compliance (% ExEE) was calculated as total ExEE divided by planned total ExEE, multiplied by 100. Planned total ExEE was calculated as daily ExEE multiplied by 5, multiplied by 26 weeks. Planned exercise-free days before and on test days were subtracted. The ExEE in the first two weeks of the intervention was increased gradually, with first two and then three days of cycling.

All training files from the polarpersonaltrainer.com training log, were visually inspected for technical errors (i.e. poor skin/sensor contact) and data was exported to EXCEL 2010 (Microsoft Corporation, One Microsoft Way, Redmond, WA 98052-6399, USA). Missing data due to equipment failure were replaced with standard values of 320 or 420 Kcal for females and males, respectively.

6.7 Statistics

6.7.1 Descriptive data

Baseline characteristics were described by gender, height, weight, age, BMI, CRF, and percentage of FM for BIKE and CON, respectively. Data was visually inspected for normality, and reported as means with 95% reference intervals (RI) if normally distributed, otherwise as median and range. Statistical differences between the total BIKE and CON group baseline characteristics were tested with unpaired t-tests, alfa level 0.05.

Exercise characteristics for the entire six month intervention period in BIKE were described by SSI, distance (km per day), duration (min per day), speed (km per hour), and compliance to intervention, as means with 95% RI for the total BIKE group, as well as for men and women, respectively.
SSI over time was expressed as mean % of $\dot{V}O_{2\text{max}}$ reserve for six time intervals during the intervention, evenly spaced between the $\dot{V}O_{2\text{max}}$ tests: 0-0.75; 0.75-2.25; 2.25-3; 3-4.5 and 4.5-6 months.

### 6.7.2 Analytical data

Linear regression was used to describe the association between SSI and changes in $\dot{V}O_{2\text{max}}R$ for the total group of BIKE participants. The regression coefficient was reported with a 95% CI for the slope. Assumptions (normality, homogeneity and linearity) required for linear regression were tested prior to analysis.

The effect of BIKE was investigated in a per protocol analysis with four outcomes: $\dot{V}O_{2\text{max}}R$, FM, FFM and %AFM, using an analysis of covariance (ANCOVA). The ANCOVA is a method of multiple regression allowing analysis of one outcome defined by two or more explanatory variables.

Despite randomization, differences in baseline characteristics may be expected due to inter-individual biological variation, as well as due to small sample size. Thus, we adjusted for baseline values of outcome in the total group analysis. The advantage is that controlling for baseline variation increases the accuracy of the estimates and the likelihood of detecting a difference.

**Example regression line:**

$$\dot{V}O_{2\text{max}}R_{\text{post}} = B_0 + B_1 \times \text{intervention (CON = 0)} + B_2 \times \dot{V}O_{2\text{max}}R_{\text{pre}}$$

To investigate any gender effect, sub analyses were performed for females and males, respectively, also with adjustment for baseline values. If visual inspection of the data (Cooks distance) showed extreme observations, the effect of these were tested by removing the observation(s) and running a secondary analysis. Results that changed the conclusions of the investigations (i.e. change of statistical significance) were presented. To test the assumptions underlying an ANCOVA, residuals of data were inspected for normal distribution, homogeneity and linearity by a visual test. Also, if data were found not to be normally distributed transformation would be considered.

All analyses are performed with statistical software: SAS 9.4, SAS Institute Inc., 100 SAS Campus Drive, Cary, NC 27513-2414, USA
7. Results

7.1 Enrollment

Enrollment, allocation and follow-up in the GO ACTIWE project took place as shown in Figure 3. Due to a slow recruitment process, only 130 participants were randomized to the four groups. A total of 35 participants were allocated to BIKE, and 18 of these completed the intervention. However at the deadline of data collection for this thesis, post-intervention tests were available for only 17 of the 18 completers, so 17 were included in this per protocol analysis. Two adverse events during cycling were registered: one participant suffered an arm fracture; another was run over and hurt his knee. Both continued and finished the intervention.

Figure 3. Flow of participants.
7.2 Baseline characteristics

Baseline characteristics are presented in Table 5. No statistically significant differences between the BIKE and CON total group means were found. Participants matched the inclusion criteria, and female and male participants were evenly distributed in the two groups, which indicate that the stratification and randomization process was successful. Dropouts were evenly distributed among genders in BIKE.

| Table 5. Baseline characteristics of participants completing BIKE and CON |
|-----------------|-----------------|-----------------|-----------------|
| **BIKE**        | **Total (n=17)** | **Women (n=9)** | **Men (n=8)**   |
| Age (years)     | 35.3 [21.0; 45.0] | 33.2 [21; 45]   | 37.6 [32; 44]   |
| Height (cm)     | 173 [160; 187]   | 169 [160; 177]  | 177 [171; 187]  |
| Weight (kg)     | 90.7 [73.8; 109.9]| 87.1 [73.8; 109.9]| 94.7 [81.5; 104.2]|
| BMI (kg/m²)     | 30.3 [26.6; 35.2] | 30.6 [26.6; 35.2] | 30.1 [26.6; 34.1]|
| Fat mass (%)    | 38.9 [24.6; 48.5] | 45.2 [40.9; 48.6] | 32.4 [24.6; 43.2]|
| CRF (ml/min/kg) | 29.5 [21.2; 36.6] | 27.0 [21.2; 32.5] | 32.4 [25.2; 36.6]|
| **CON**         | **Total (n=16)** | **Women (n=7)** | **Men (n=9)**   |
| Age (years)     | 34.9 [23; 44]    | 36.0 [24.6; 44.0] | 34.0 [23.0; 43.0]|
| Height (cm)     | 176 [171; 181]   | 169 [163; 174]   | 181 [176; 186]   |
| Weight (kg)     | 93.2 [78.0; 19.7] | 85.6 [78.0; 93.3] | 99.2 [79.3; 119.7]|
| BMI (kg/m²)     | 30.1 [26.6; 34.4] | 30.1 [27.1; 34.4] | 30.1 [26.6; 32.5]|
| Fat mass (%)    | 39.0 [29.8; 52.2] | 45.2 [42.1; 52.2] | 34.2 [29.8; 44.6]|
| CRF (ml/min/kg) | 29.5 [20.5; 39.6] | 23.8 [20.5; 26.5] | 33.9 [27.0; 39.6]|

Abbreviations: BIKE = Intervention group, CON = control group, BMI = body mass index, CRF = Cardiorespiratory fitness. Data are mean and (95% Reference Interval). Significance test of total group differences performed with unpaired t-test, alfa level 0.05.


7.3 Exercise characteristics

Average SSI, distance and duration per day of commuting as well as compliance was reported in Table 6. Participants in BIKE cycled on average 13.9 km per day (95% RI: 8.8 – 19.4). The daily mean time spent cycling was 47 minutes (95% RI: 33 – 62), with an average speed of 17.8 km per hour (95% RI: 13.9-22.9). Only small differences were seen between females and males in daily distance and duration, but males appeared to cycle faster than females (no analysis was performed). Both female and male participants met the requirements for their total ExEE with a mean compliance of 97%.

Table 6 Exercise characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total (n=17)</th>
<th>Females (n=9)</th>
<th>Males (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSI (%VO2 maxR)</td>
<td>53.2 [40.9; 65.1]</td>
<td>53.3 [45.5; 64.5]</td>
<td>53.2 [40.9; 65.1]</td>
</tr>
<tr>
<td>Distance (km/day)</td>
<td>13.9 [8.8; 19.4]</td>
<td>12.2 [8.8; 15.0]</td>
<td>15.7 [12.1; 19.4]</td>
</tr>
<tr>
<td>Duration (min/day)</td>
<td>47.0 [33.3; 61.8]</td>
<td>44.0 [34.7; 59.7]</td>
<td>50.5 [33.3; 61.8]</td>
</tr>
<tr>
<td>Speed (km/hour)</td>
<td>17.8 [13.9; 22.9]</td>
<td>16.7 [14.4; 21.1]</td>
<td>19.0 [13.9; 22.9]</td>
</tr>
<tr>
<td>ExEE compliance (% kcal)</td>
<td>97.1 [86.9; 107.3]</td>
<td>97.4 [86.9; 107.3]</td>
<td>96.8 [92.2; 101.3]</td>
</tr>
</tbody>
</table>

Mean and [95% reference interval]. SSI = Self selected intensity; VO2 maxR = VO2 max reserve; ExEE = exercise energy expenditure.

7.3.1 Description of participants’ self-selected exercise intensity over time

Figure 4 shows the group mean SSI as well as individual mean SSIs (% VO2maxR) in the six different time intervals during the intervention. The mean SSI over time ranged between 50% and 56% of VO2maxR, with no apparent pattern or trend. Large intra-individual variations were seen throughout the intervention period: the largest variations in SSI were seen in a female participant who ranged between 38.8% and 72.6% over time, and in one male participant who ranged from 48.5% to 75.9%.
7.3.2 Self-selected intensity and exercise intensity zones

Mean SSI for the entire intervention period was 53%, with an inter-individual variation (range) of 41-65%. Figure 5 shows the distribution of female and male participants in the different intensity zones, with demarcations depicting moderate and vigorous exercise zones. Based on their mean SSI, 13 BIKE participants performed moderate intensity exercise during ACB and the remaining four performed vigorous intensity exercise. Gender distribution showed that male participants exercised in a broader range of SSI, with two male participants exercising in the lower range of moderate intensity (40-44% of VO$_{2max}$R) vs. none of the females. Three males performed vigorous intensity ACB (60-69% of VO$_{2max}$R) vs. one female. No participants exercised in the higher range of vigorous exercise (70-89% of VO$_{2max}$R).
7.3.4 The association between self-selected intensity and change in $\dot{V}O_{2\text{max}}R$

No association between SSI and change in $\dot{V}O_{2\text{max}}R$ was found with linear regression. The slope of the best fitted line and the 95% CI was 13 ml O2/min, 95% CI [-10; 36], $p=0.2446$, depicted in Figure 6, with 95% confidence intervals shaded in blue.

Figure 5. Distribution of BIKE participants’ mean self selected intensity with moderate and vigorous exercise intensity zones depicted (11).

Figure 6. Linear regression showing association between average self selected intensity over 6 months (SSI, %VO2maxR) and change in VO2 max reserve ($\Delta$VO2maxR, ml O2/min). Shaded blue area = 95% confidence interval.
7.4 Effects of active commuting by bike

7.4.1 Cardiorespiratory fitness

The differences between BIKE and CON on all outcomes are reported in Table 7. The analysis of covariance showed that BIKE participants had a significant increase in $\dot{V}O_{2\text{max}}R$ compared to CON. Sub analysis for gender showed significant positive results for males ($p=0.0039$), but only borderline significance for females ($p=0.0692$). One extreme observation was seen: a female BIKE participant who showed a large improvement in $\dot{V}O_{2\text{max}}R$ of 749 ml O2/min. An analysis without this observation changed the result for females to a significant improvement of 273 ml O2/min (95% CI [3; 543], $p=0.0479$).

The number of BIKE participants in the “very low” CRF category (females <29 and males < 35 ml O2/kg/min) changed from nine individuals to three (54).
### Tabel 7. Effects of active commuting by bike.

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>6 months</th>
<th>Between group diff.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>VO₂ max reserve (ml/min)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BIKE</td>
<td>2438 [2196; 2680]</td>
<td>2788 [2471; 3106]</td>
<td>402 (197; 606) *</td>
</tr>
<tr>
<td>CON</td>
<td>2534 [2148; 2921]</td>
<td>2478 [2090; 2867]</td>
<td></td>
</tr>
<tr>
<td>BIKE females</td>
<td>2126 [1832; 2421]</td>
<td>2373 [2045; 2701]</td>
<td>303 [-28; 333]</td>
</tr>
<tr>
<td>CON females</td>
<td>1817 [1674; 1960]</td>
<td>1801 [1537; 2064]</td>
<td></td>
</tr>
<tr>
<td>BIKE males</td>
<td>2790 [2565; 3015]</td>
<td>2356 [2891; 3621]</td>
<td></td>
</tr>
<tr>
<td>CON males</td>
<td>3092 [2779; 3406]</td>
<td>3005 [2643; 3367]</td>
<td></td>
</tr>
<tr>
<td><strong>FM (kg)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BIKE</td>
<td>35.1 [30.7; 39.6]</td>
<td>32.1 [27.5; 36.7]</td>
<td>-4.9 [-7.9; -1.8]*</td>
</tr>
<tr>
<td>CON</td>
<td>36.1 [32.8; 39.3]</td>
<td>38.0 [33.2; 42.7]</td>
<td></td>
</tr>
<tr>
<td>BIKE females</td>
<td>39.5 [33.8; 45.3]</td>
<td>35.9 [29.3; 42.6]</td>
<td>-6.4 [-12.3; -0.5]*</td>
</tr>
<tr>
<td>CON females</td>
<td>38.8 [34.0; 43.5]</td>
<td>41.7 [34.4; 48.9]</td>
<td></td>
</tr>
<tr>
<td>BIKE males</td>
<td>30.2 [24.0; 36.4]</td>
<td>27.8 [21.5; 34.2]</td>
<td>-3 [-5.6; 0.6]</td>
</tr>
<tr>
<td>CON males</td>
<td>34.0 [29.1; 38.8]</td>
<td>35.1 [28.2; 42.0]</td>
<td></td>
</tr>
<tr>
<td><strong>% AFM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BIKE</td>
<td>49.2 [46.2; 52.2]</td>
<td>46.0 [41.3; 50.6]</td>
<td>-4.0 [-7.0; -1.0]*</td>
</tr>
<tr>
<td>CON</td>
<td>49.2 [46.2; 52.2]</td>
<td>49.9 [46.6; 53.3]</td>
<td></td>
</tr>
<tr>
<td>BIKE females</td>
<td>47.5 [43.1; 52.0]</td>
<td>49.7 [44.4; 55.0]</td>
<td>-4.8 [-10.4; 0.8]</td>
</tr>
<tr>
<td>CON females</td>
<td>53.0 [49.8; 56.2]</td>
<td>54.3 [50.0; 58.6]</td>
<td></td>
</tr>
<tr>
<td>BIKE males</td>
<td>44.9 [38.8; 51.0]</td>
<td>41.8 [33.7; 50.0]</td>
<td>-3.2 [-7.0; 0.6]</td>
</tr>
<tr>
<td>CON males</td>
<td>46.3 [42.3; 50.3]</td>
<td>46.6 [42.2; 50.9]</td>
<td></td>
</tr>
<tr>
<td><strong>FFM (kg)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BIKE</td>
<td>55.5 [49.7; 61.3]</td>
<td>56.3 [50.5; 62.1]</td>
<td>0.6 [-0.8; 1.9]</td>
</tr>
<tr>
<td>CON</td>
<td>57.2 [51.0; 63.4]</td>
<td>57.4 [51.2; 63.5]</td>
<td></td>
</tr>
<tr>
<td>BIKE females</td>
<td>47.5 [43.0; 52.0]</td>
<td>48.5 [44.1; 52.8]</td>
<td>0.9 [-1.6; 3.3]</td>
</tr>
<tr>
<td>CON females</td>
<td>46.9 [43.6; 50.4]</td>
<td>47.0 [43.6; 50.4]</td>
<td></td>
</tr>
<tr>
<td>BIKE males</td>
<td>64.5 [57.0; 72.0]</td>
<td>65.2 [57.3; 73.0]</td>
<td>0.4 [-1.2; 2.0]</td>
</tr>
<tr>
<td>CON males</td>
<td>65.2 [58.5; 71.9]</td>
<td>65.4 [59.0; 71.9]</td>
<td></td>
</tr>
</tbody>
</table>

Baseline and 6 months outcome values, and between group difference at 6 months adjusted for baseline (ANCOVA). All results presented in means [95% confidence intervals]. BIKE= intervention group, CON= control group. FM= fat mass; %AFM= percentage android fat mass; FFM= fat free mass.
Cardiorespiratory fitness response and non-response

The TE of the $\dot{V}O_{2\text{max}}R$ estimate was calculated to 117 ml O2/min. Using the TE as the cutoff for positive response and 2 x TE as the cutoff for adverse response, we categorized the BIKE participants. Twelve of 17 BIKE participants were categorized as positive responders, four were categorized as non-responders, and one as an adverse responder, see Figure 7.

![Figure 7: Individual responses in $\dot{V}O_{2\text{max}}$ reserve ($\dot{V}O_{2\text{max}}R$) in BIKE participants. Positive responders in green, negative responders in red, non-responders in black.](image)

7.4.2 Body composition

A reduction was seen in FM (p= 0.0030) and %AFM (p= 0.0098) for the total group of BIKE participants compared to CON. FFM was unchanged (p=0.3820).

In the gender sub analysis, BIKE females showed reduction in FM (p= 0.0347), and borderline significant reduction in %AFM (p=0.0863). No change was seen in FFM (p= 0.4690). In males, borderline significance was seen in FM (p=0.0937) and %AFM (p=0.0891). However, in the sub analysis one extreme observation was identified: a male in the control group with a fat mass loss of 6.1 kg. Removing this outlier from the analysis changed the result for males to a reduction in FM of 4.08 kg (95% CI [0.9; 7.1], p=0.016). The FFM was found to be unchanged in males as well (p=0.5862).
8. Discussion

8.1 Primary findings
The primary findings of this thesis were substantial improvement of CRF, as well as reductions in FM and %AFM with no change in FFM, in BIKE participants compared to CON participants.

The improvement in CRF was in line with the findings in our systematic review, which showed strong evidence for improvements in CRF following ACB interventions, and low to moderate evidence for the changes in FM and %AFM. BIKE participants in the present RCT were found to exercise with a mean SSI of 53% (range: 41%-65%), however no association between SSI and change in CRF was found.

8.2 Intervention exercise volume meets official recommendations
In BIKE, the mean daily exercise duration of 47 minutes on five working days a week corresponds to an average of 34 minutes of daily exercise if spread out on seven days a week. Thus, the exercise dose matches closely the minimum Danish PA recommendations of 30 min/day of moderate intensity aerobic exercise seven days a week (10,54), and exceeds the minimum dose recommended by ACSM of 30 min/day five days a week (11). The recommended minimum exercise dose is an arbitrary threshold, taking in to account the scientific evidence, but also educational and motivational considerations, with the intention to target the least physically active individuals (54).

Meeting the recommendations should reduce the risk of disease and premature death, but further health gains may be achieved with higher doses, in a dose responsive manner (12,54). According to the dose-response investigations by Hendriksen et al., individuals with the lowest fitness level will experience CRF gains by cycling only 3 km per day (39). Moreover de Geus et al. (2009) in their study on ACB estimated that gains in $\dot{V}O_{2peak}$ occur when ExEE exceeds approximately 1000 and 1500 kcal per week for sedentary women and men, respectively (41). In this study, the mean 97% compliance to the intervention corresponded to a weekly mean ExEE of 1552 Kcal for females, and 2100 Kcal for males, which should then be sufficient to induce an effect.

8.3 Self-selected intensity was mainly moderate
The mean SSI of the BIKE participants of 53% $\dot{V}O_{2maxR}$ with a range from 41-65% places the majority of participants in the moderate intensity exercise zone during ACB, see Table 1 and Figure
5. De Geus et al. (2008) found a considerably higher mean SSI during ACB of 79% of \( \dot{V}O_{2\text{max}} \), corresponding to vigorous exercise, in a similar mixed-gender population (20). However, intensity was measured during a single field test, which may have introduced bias from the participants being influenced by the test procedure. This was supported by the fact that participants cycled significantly faster (13%, p<0.01) during the field test (20.1 km/hour) as opposed to the rest of their ACB intervention (17.8 km/h) (40). The average speed of the BIKE participants’ commutes of 17.8 km/h [95% CI: 16.4 ; 19.2], corresponds well with the intervention mean in the study by de Geus et al., although differences in routes should be noted: de Geus’ participants cycled in rural areas, whereas most BIKE participants cycled in an urban environment (40). Even though the heart rate monitors were programmed to pause recordings when participants were at a stop, traffic and stoplights may have influenced their SSI. Oja et al., in their 2 x 10 week ACB intervention study, measured mean SSI at four different time intervals and found it to range between 57% and 65% of \( \dot{V}O_{2\text{max}} \), corresponding to moderate exercise intensity (21). Similarly, participants in the study by Hendriksen et al. cycled with a mean SSI (%\( \dot{V}O_{2\text{max}} \)) of 57% for males and 65% for females (39). In light of this is seems reasonable to assume that most healthy sedentary adults who start ACB will do so with a mean SSI in the moderate zone, which according to ACSM is between 40 and 59% of \( \dot{V}O_{2\text{max}R} \) (11), see Table 1.

In this study, the mean SSI over six months may not truly reflect the amount of time spent exercising in the different intensity zones. The large intra-individual variations over the six months support this hypothesis. Further, we have not analyzed the single bike trips to investigate whether the subjects were exercising at a fixed intensity, or with intervals of different intensities. As such, we have no precise measure of the total amount of time spent in the different exercise zones. However, we have as part of the data validation in GO-ACTIWE visually inspected graphic depictions of the intensity of every single bike commute made by the participants. Based on this, it is our impression that the participants were cycling at steady intensities on their commutes. According to the ACSM recommendations, healthy individuals who meet the minimum recommended PA doses of moderate intensity exercise will have further health benefits if 2-3 weekly bouts of minimum 10 minutes of vigorous intensity (60-89% of \( \dot{V}O_{2\text{max}R} \)) are introduced (11). In future studies on SSI during ACB it may be relevant to investigate the frequency of vigorous intensity bouts.
8.4 Changes in cardiorespiratory fitness are clinically significant

Our most important finding was an increase in $\dot{V}O_{2\text{max}}R$ of 402 ml O2/min [95% CI: 197; 606] in BIKE compared to CON, corresponding to an increase of 16% [95% CI: 8; 24]. This result is in line with the results reported in the systematic review included in this thesis, demonstrating consistent improvements in CRF, as well as an exercise volume-CRF dose response relationship (38,39,41,45).

The biggest difference from this intervention to other ACB interventions identified in the systematic review was the fixed-volume exercise dose with higher daily ExEE, as opposed to minimum criteria volumes. Interestingly, the effect on CRF in this study was approximately double that of the effect of 206 ml O2/min (CI’s not reported) found in the study by Møller et al. who also used a per protocol design but a much shorter intervention (8 weeks) (45). Participants cycled on average 40 min/day, very similar to the mean in this study of 47 min/day (45). So the larger effect size in the present study may be attributed to the longer study duration (26 weeks vs. 8 weeks). This is supported by Ross et al. who found that CRF response to moderate intensity exercise (60 min/day, 50% of $\dot{V}O_{2\text{max}}$) levelled off at 16 weeks (33). This indicates that the subjects in Møller et al. may not have reached a new CRF steady state, but also that further gains in CRF may not be expected from the subjects in the present study, were they to continue the intervention.

Kodama et al. in a meta-analysis investigated the association between CRF and risk of CVD or all-cause mortality (55). In populations with low CRF (<7.9 METs) it was shown that an increase in CRF of one MET reduced the risk of CVD with 15%, and the risk of all-cause death with 13%. This evidence is supported by observational studies that suggest an exponentially increasing risk of death in individuals with a “very low” CRF below 35 ml O2/kg/min for males and 29 for females (54). The CRF improvements in the present study are considered clinically significant, as the number of participants with a “very low” fitness level changed from 9 out of 17 before the intervention to 3 out of 17 after. In addition, the mean change in CRF corresponds to approximately 1.4 MET. According to Kodama, this suggests an 18% reduced risk of CVD and an all-cause mortality risk reduction of 20% in the BIKE participants with the lowest baseline CRF.

Among the 17 BIKE participants, we found that four were classified as CRF non-responders, and one as a CRF adverse responder. Other studies have shown that not all individuals respond to aerobic exercise with an increase in CRF (56). Importantly though, these CRF non-responders may still have received health benefits from the intervention, in the form of increased metabolic fitness,
e.g. reduced insulin resistance and improved blood lipid profile. Investigating this, however, lies outside the scope of the present thesis.

By closer examination of data pertaining to the single adverse responder in our investigation, we found that the male participant maintained his CRF from baseline to three months, and then lost 300 ml O2/min from three months to six months. Correspondingly, his SSI dropped from moderate in the beginning of the intervention to light in the last 4.75 months, see Figure 4. It is possible that a drop in total activity level during the last three months of the intervention is the cause of the adverse response, but lack of data prevents us from testing this hypothesis.

8.5 Effects on CRF in females and males

Separate analysis by gender showed a statistical significant increase in CRF for males only, despite both genders exercising with similar duration and mean SSI. Males had a larger mean absolute increase than females (549 vs. 303 ml O2/min), which is expected from their larger body sizes. The gender difference in CRF relative to body weight was much smaller: 5.6 ml O2/kg/min for males vs. 4.1 ml O2/kg/min for females. This difference may be explained by biological gender differences in the response to aerobic exercise (57), or to gender-cultural differences e.g. that females may commute differently from males, with less bouts of vigorous exercise. Finally, this study was not powered to explore gender differences, and it is very likely that the number of participants is too low to detect statistically significant differences. This hypothesis is supported by the fact that removing a female outlier with a very large increase in CRF from the analysis made the CRF increase for the female group statistically significant.

8.6 No association between self-selected intensity and change in VO2maxR

Our analysis demonstrated no significant association between SSI and changes in VO2maxR. Thus, our hypothesis that this association would be found is rejected. This contradicts theories on exercise physiology, which predict a dose response on CRF with increasing exercise (22). Ross et al. showed a clear intensity-CRF dose response in a 24 week isocaloric ExEE intervention, with exercise intensity of either 50% or 75% of VO2peak (33). Several explanations may account for the lack of association in the present study: 1) The range of SSI of 41%-65% of VO2maxR may have been be too small to reliably detect an association. 2) The mean SSI over six months does not detect spikes of vigorous intensity exercise, and may not truly reflect the amount of time spent exercising vigorously. 3) The number of participants was not large enough to detect an association. Future
studies aiming to investigate the association between SSI and changes in CRF should adopt a method of assessing SSI that more precisely estimates the time spent in different exercise zones, and with a sample size large enough to reach significant statistical power.

8.7 Body composition changes indicate a healthy weight loss

Fat mass and android fat mass decreased

Another important finding in this thesis was the reduction of FM and %AFM as a result of ACB. Loss of android fat is clinically relevant, because excess android fat and in particular fat with a visceral distribution is associated with adverse metabolic functions, e.g. increased risk of insulin resistance (25). Recent studies indicate that aerobic exercise facilitates abdominal fat loss better than diet alone (58). The health implications of this, besides a favorable weight loss, is an improved metabolic fitness associated with improved blood lipids, glucose tolerance and reduced insulin resistance (59). Measurements of AFM in this thesis were performed with a DXA scanner that could not differentiate visceral from subcutaneous fat. Future studies aiming to assess these changes in body composition will need to employ more sensitive methods e.g. MRI scans.

In the ACB intervention study by Hemmingsson a significant reduction was seen in waist circumference in obese women (42). Møller et al. showed changes in body composition by reductions in subcutaneous tissue by skinfold test, following a much shorter intervention of 12 weeks (45). These studies as well as the present study, support our hypothesis that healthy, sedentary and overweight/obese adults who commence ACB lose FM.

An observational study by Zhu et al. found an increased risk of having metabolic syndrome with percentages of body fat above 30.8% and 29.1% for Caucasian women and men (24). At baseline, all of the BIKE participants except three males were above this threshold. After the intervention, only one participant had reduced FM enough to be removed from this high-risk category. It is unknown whether the BIKE participants reached a new steady state during the intervention, or whether a further decrease in FM may be expected, were they to continue ACB.

Fat free mass was preserved, not increased

Our hypothesis that BIKE participants would increase their FFM as a result of ACB is rejected, as no change in FFM between groups was seen. Interventions with weight loss induced by diet alone typically result in a proportionate loss of both FM and FFM (13), whereas moderate amounts of
regular exercise effectively induce weight loss by loss of FM with less or no concomitant loss of FFM (60). The loss of FM achieved by PA represents according to Rosenkilde et al. a “healthy weight loss”, with conservation of the metabolically active muscle tissue (13). Accordingly, efforts to treat obesity and the related metabolic abnormalities have increasingly focused on changing body composition through a combination of exercise and diet rather than by diet alone, to preserve or even increase FFM. Increases in FFM can be achieved by including strength training in the exercise regime (22).

8.8 Methodological discussion: strengths and limitations

The main strength of this study is the randomized controlled design and the precise measurement methods used to assess CRF and body composition. Assessors were not blinded in this study, which increased the risk of information bias generated by the assessors. The ŔO2max test in particular is sensitive to the amount of encouragement given by the assessor. In this thesis, outcome measures and statistical analysis methods were chosen and described in a synopsis (see appendix 1) before data was obtained and analysis performed, to avoid the temptation to hunt for significant results.

Precision of outcome measurements

The estimation of ŔO2maxR by direct measurement using the Jaeger OXYCON PRO apparatus is gold standard today. This is reflected in the small TE of 117 ml O2/min corresponding to only 5% of mean ŔO2maxR baseline values.

SSI was calculated using the best fitted line between HR and ŔO2max. This best fitted line was plotted during the ŔO2max test warm-up, using fixed power outputs originally designed for ECG testing. This introduces the possibility of error in the estimation of exercise intensity, since ideally the power outputs should be designed to fit each participant’s fitness level individually.

DXA scan has excellent validity in body composition assessment and high test-rest reliability. The precision of the measurement of %AFM in the present study however was limited by the use of preset regional boundaries of the abdomen in the LUNAR DPX-IQ X-ray (52). These boundaries were not specifically designed for this investigation.

For several BIKE participants the Polar RC3 heart rate equipment showed periodic instability in measurements of heart rate or GPS, making some of the measurements invalid. Also, BIKE participants would sometimes forget to use the watch during commuting. Both types of incidents
resulted in standard trainings (ExEE of 320/420 Kcal, no other data) being inserted instead of the actual measurements. This is likely to have increased the random error of the estimate.

8.9 Systematic review: strengths and limitations

The quality of the systematic review is strengthened by the transparent use of the PRISMA guidelines, and the EPHPP and GRADE methods to assess the quality of included studies and the evidence levels of results (35-37). Both inclusion and extraction of data was performed independently by two reviewers, with disagreements discussed until consensus, strengthening the credibility of decisions. In the future, if more studies on the subject emerge, it will be relevant to pool results.

8.10 Ethical considerations

Two adverse events during this intervention raise the question of safety in ACB. Future studies should include a risk assessment and risk prevention strategy, when planning ACB interventions. Allocating obese individuals who are motivated for a change in lifestyle to a sedentary control group may cause detrimental health effects from missing an open window of motivation to exercise. However, control participants were offered membership of a fitness center and guidance after their participation in the project.

9. Conclusion

In conclusion, completing a six-month intervention of active commuting by bike with an exercise volume corresponding to minimum recommendations on PA induces a clinically significant improvement of cardiorespiratory fitness as well as a healthy weight loss, in healthy, sedentary and overweight adults. Mean self-selected intensity of the participants during cycling was moderate. No dose response was found between self-selected intensity and cardiorespiratory fitness, but methodological weaknesses call for a cautious interpretation of this result.
10. Perspectives

The study population of healthy, sedentary, overweight or obese adults are comparable to a large part of the global population. Today more than one third of the adult population in Western societies are either overweight or obese, and prevalence is predicted to rise (61-63). More than one third of the global population does not meet the recommendations for physical activity (9). Cycling is particularly common and feasible in Denmark and in many Northern European cities; however some countries may face considerable barriers to ACB, of both cultural and infrastructural nature. Nevertheless a health impact assessment of active transportation in Europe, USA, Australia and New Zealand by Mueller et al. concluded that health benefits clearly outweighed detrimental effects of traffic incidents and pollution (64). The large number of drop-outs in this study (17 out of 35 or 49%) was an indication that serious barriers to ACB may exist for individuals in the target population, even in Copenhagen. Future studies should aim to assess efficiency of ACB interventions, employing intention to treat analysis.
11. References


