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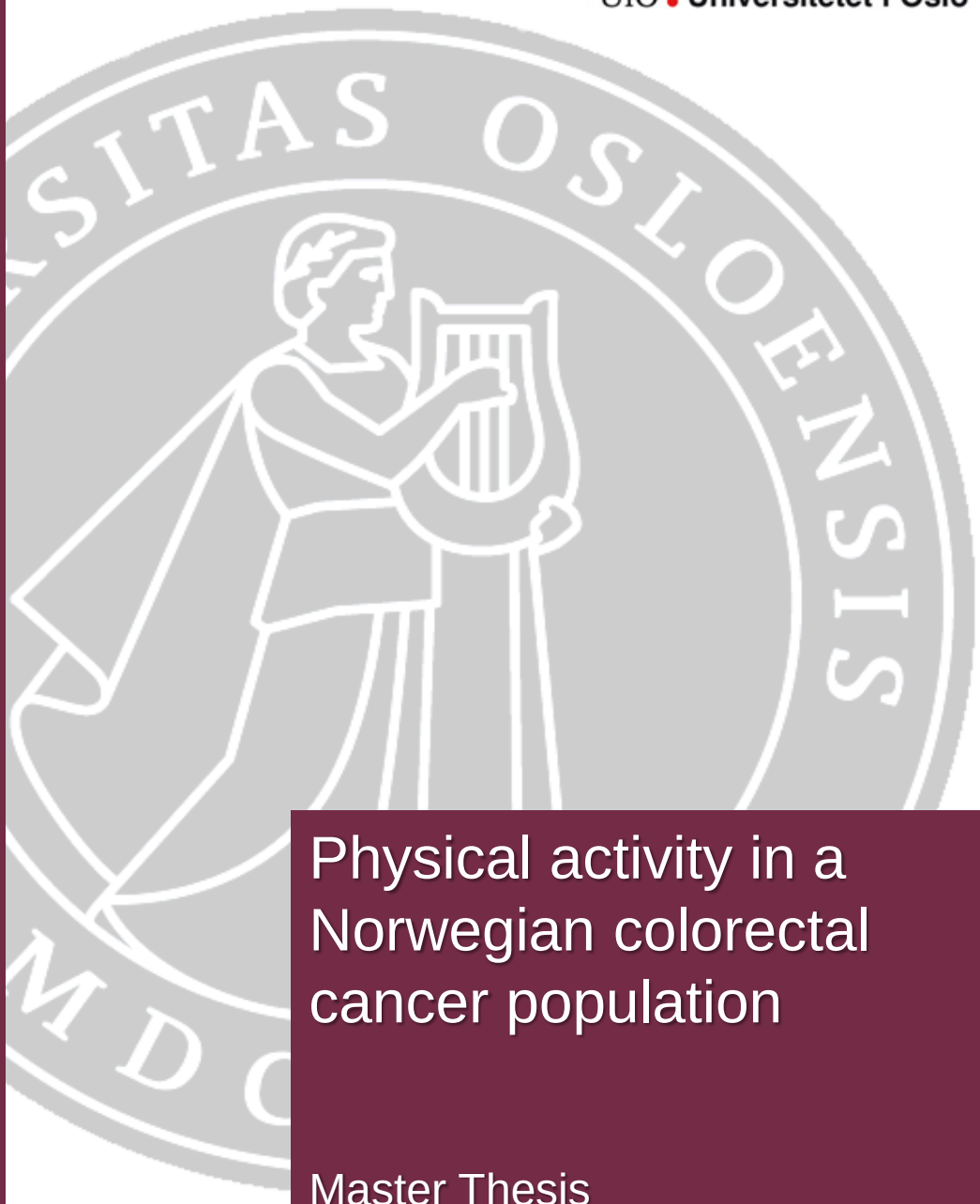

Physical activity in a Norwegian colorectal cancer population

Master Thesis

by

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Faculty of Medicine
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May 2018

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Abstract

Objective: Physical activity is a strong modifier of cancer risk and other health related outcomes. Thus a central challenge in studying the impact of diet in randomized clinical trials is to control the impact of physical activity. The major aim of this master thesis was to examine the effect of a one-year diet and lifestyle intervention on physical activity among patients with colorectal cancer (CRC). The effects on physical function and muscle mass were also investigated. In addition, associations between clinical, demographic and anthropometric factors, and physical activity and sedentary time were investigated.

Subjects and methods: The participants constitute of a subpopulation (n=167) within a large ongoing randomized controlled trial in Norwegian CRC patients (CRC-NORDIET study). The participants were aged 50-80 years and diagnosed with TNM-stage I-III. The intervention group received an intensive one-year dietary intervention program based on the Norwegian food-based dietary guidelines. Both groups received the similar general advice and incentives regarding physical activity. Physical activity was assessed with the SenseWear armband. Physical function was assessed using the 6-min walking test (6MWT), 30-second sit-to-stand test (30STS) and hand-grip strength. Body composition was measured with Bioelectric Impedance Analysis (BIA) and Dual-Energy-X-ray Absorptiometry (DXA).

Results: The one-year dietary intervention had no differential impact on physical activity between the groups. No changes were observed in the level of physical activity among the total study population, however, the CRC-NORDIET participants significantly increased their level of physical function. At baseline, the level of physical activity was affected by gender, age, BMI, severity of disease, treatment, cancer location, surgery and education. Physical activity was also positively correlated with physical function and muscle mass, where those with the highest level of physical activity performing better on the tests and having higher muscle mass.

Conclusions: The results from this thesis indicate no additional effect of a one-year dietary and lifestyle intervention on physical activity in CRC patients. However, a significant increase in physical function was observed for the total study population.

List of abbreviations

6MWT	6 Minute Walking Test
30STS	30-Second Sit-to-Stand test
ANOVA	Analysis of Variance
ANCOVA	Analysis of Covariance
BIA	Bioelectrical Impedance Analysis
BMI	Body Mass Index
CRC	Colorectal Cancer
CRC-NORDIET	The Norwegian Dietary Guidelines and Colorectal Cancer Survival Study
DXA	Dual-energy X-ray Absorptiometry
NFBDG	Norwegian Food-Based Dietary Guidelines
RCT	Randomized Controlled Trial
SD	Standard Deviation
TNM	Tumor Node Metastasis
WCRF/AICR	World Cancer Research Fund/ American Institute for Cancer Research
WHO	World Health Organization

List of figures

List of tables

Table of Contents

1 Introduction

This master thesis is conducted within the 'Norwegian Dietary Guidelines and Colorectal Cancer Survival Study' (CRC-NORDIET), which is an ongoing multicentre randomized controlled, parallel two-arm intervention trial. The CRC-NORDIET study investigates the effect of the Norwegian food-based dietary guidelines (NFBDG) on overall mortality, cancer recurrence, relapse and comorbidities among patients treated for colorectal cancer (CRC) (1).

1.1 Cancer incidence and survival

With 14 million new cases in 2012, cancer is the second leading cause of death worldwide, and was responsible for 8.8 million deaths in 2015 (2). During the next two decades, the number of new cases is expected to increase with 70 % (3). Lung, liver and stomach cancer is the most common causes of cancer deaths globally (2). The continuous increase in cancer incidence and mortality is largely because of an aging and growing world population, and an increase in behaviors known to be risk factors for developing cancer like smoking, physical inactivity and "westernized" diet (4).

In Norway 32 827 new cases of cancer were registered in 2016 (5). The most common cancers were prostate, female breast, lung and colon, and these accounts for half of the total cancer mortality (5). Over 90 % of cancers in men, and 85 % of cancers in women are diagnosed among those 50 years and older (5). In 2015, there were 10 944 deaths from cancer, this accounts for 25 % of all deaths in Norway (5). Among Norwegian men, cancer is the most common cause of death (6).

The National Coalition for Cancer Survivorship (NCCS) and the National Cancer Institute define a person as a cancer survivor from the moment of a cancer diagnosis and throughout the rest of his or hers life (7). This means that an individual diagnosed with cancer, is a cancer survivor. NCCS has later expanded the definition to also include family, friends and voluntary caregivers who are affected of the diagnosis in any way (7). Despite that more people gets a cancer diagnosis, screening, detection and treatment is getting better, which increases the amount of cancer survivors (5, 8). In 2016, there were 262 884 cancer survivors in Norway, this is 80 000 more than in 2005 (5). The cancer types with most survivors is prostate, breast, melanoma and colon (5).

1.2 Colorectal cancer

1.2.1 Colon and rectum

Cancer is a disease initiated by the uncontrolled division and survival of abnormal cells. Colorectal cancer comprises cancers occurring in the colon or rectum region (9).

The colon and rectum, together with the cecum and anal tract constitute the large intestine (10). The colon is approximately 150-180 centimeter long and consists of four sections: the ascending colon, the transverse colon, the descending colon and the sigmoid colon (9) (**Figure 1**). As the food travels through the colon, water and nutrients are absorbed from undigested foods (11). The colon contains a large number of bacteria that has an important role in fermentation of undigested carbohydrates to short fatty acids, the synthesis of vitamin B and K and the metabolism of bile acids and other sterols (10-12). The mucous membrane that lines the colon consists of lymphoid cells that is a part of the body's immune defense (11). Muscle contractions, peristalsis, moves the waste products from the colon and towards rectum where it is stored until it exits the body (11, 13). The majority of tumors present in the colon is in the area of the sigmoid colon and the ascending colon, in addition to the cecum (14).

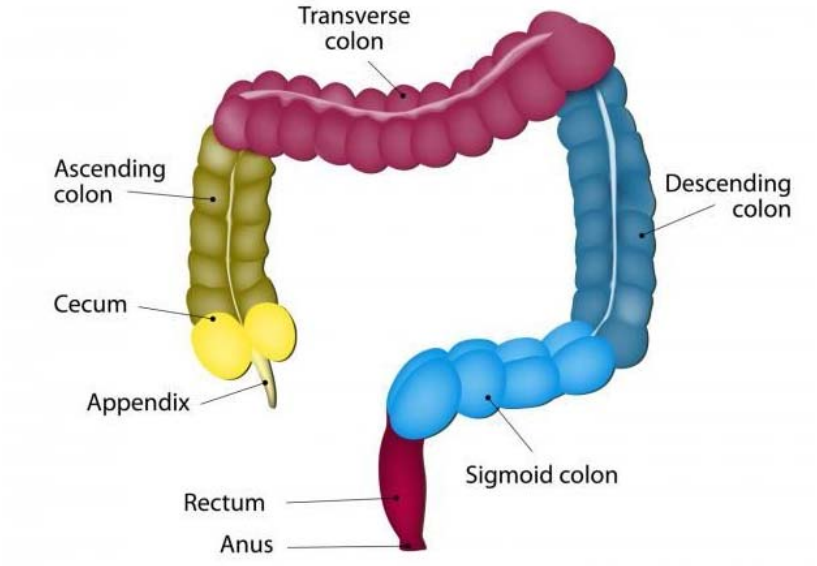

Figure 1: Anatomy of the large intestine.
The large intestine consists of the cecum, the colon, the rectum and the anal canal. The colon is devided into four sections, the ascending, the transverse, the descending and the sigmoid colon. Picture from dreamsteame.com.

1.2.2 Epidemiology

CRC is the third most common cancer in the world, with 1.36 million new cases in 2012; this is approximately 10 % of all new cases of cancer (15). CRC is the fourth leading cause of cancer death worldwide, accounting for almost 700 000 deaths in 2012 (2). By 2030, the number of new cases is expected to increase with 60 % to more than 2.2 million (16). CRC is most common in countries with a high or very high human development index (HDI) (16), and Norway is one of the countries in the world with highest rate, especially among women (2).

In Norway, CRC is the second most common cancer type when looking at men and women in total, with 4343 new cases in 2016 (5). Of these, 3003 was colon cancer and 1340 was rectal cancer. Rectal cancer is most common among men, while colon cancer is the more common subtype among women (5). The incidence of colon cancer is still increasing, but the rectal cancer rates seem to be stable. Compared with other Nordic and European countries, the incident rates in Norway are high, and the treatment of CRC has been estimated to be the most expensive cancer to treat in Norway (5). Also in Norway, the number of cases are expected to increase in the years to come, this is mainly due to aging of the population (17).

The stage at which the cancer is diagnosed affects the survival, with later-stage diagnosis having poorer survival. The five-year survival rate is 90 % for CRC diagnosed at an early stage compared with 13 % for those diagnosed at a late stage (11). The incidence of CRC has been increasing over the years, but due to the improved treatment and detection methods, and the aging and growing of the population, more patients live longer after being diagnosed with cancer (5, 18, 19). The five-year survival for CRC is now around 65 % in Norway (5).

1.2.4 Pathogenesis

Cancer develops in a complex interaction between genetics, environment, lifestyle and different biological processes (20).

CRC can start either in the colon or in the rectum, and most cases begin as a polyp on the inner lining of the colon or rectum. Over time, from 5 to 15 years or more, some of these polyps can become cancerous (13, 14). Approximately 96 % of CRC is adenocarcinomas (13).

1.2.3 Risk factors

Risk factors for CRC can be both environmental and inherited (21). In approximately 70 % of all CRC cases, there are no family history of CRC (21). Between 5-10 % of CRC's are consequences of recognized hereditary conditions, with familial adenomatous polyposis (FAP) and hereditary non-polyposis colorectal cancer (HNPCC) being most common (11). Twenty percent of the cases occur in people who have a family history of CRC (11). Individuals from families with a history of CRC have increased risk of developing CRC, but the risk is even higher in those with an inherited predisposition (21).

The risk of CRC increases with age and is most common among those over 50 years (9, 17). The median age at diagnosis for colon and rectal cancer in Norway is 73 and 69 years respectively (5). In addition, inflammatory bowel diseases like Crohn's disease and ulcerative colitis increases the risk of developing CRC and are together with FAP and HNPCC among the three most common high risk conditions for CRC (8, 22). People with type 2 diabetes also have an increased risk of developing CRC, even if the common risk factors with CRC are taken into account (9).

However, most cases of CRC develops sporadically without any genetically disposition (23). There are several modifiable lifestyle-related risk factors for CRC; these include smoking and other use of tobacco, medication, diet, physical activity, and body composition (8, 11). It is estimated that about 47% of all CRC cases could be prevented by improving lifestyle (8, 15). In the colorectal cancer 2017 report (11) they concluded that there is strong evidence suggesting that processed meat, red meat, alcohol intake over 30 g per day, body fatness and abdominal fatness, and factors leading to greater adult attained height increases the risk for CRC. Physical activity is stated as a convincing factor that decreases the risk of colon cancer, however no conclusion was drawn for rectal cancer. In addition, there is strong evidence that consumption of foods containing dietary fiber and wholegrain, dairy products and calcium supplements (200-1000mg) probably protects against CRC (11).

1.2.5 Diagnose

CRC can be both symptomatic and asymptomatic. In the early stage most patients are asymptomatic, and the cancer will often be detected through screening (24). The presence of symptoms usually indicates a more advanced tumor, growing into the lumen or adjacent structures (24, 25). Hence, location of tumor have a great impact on the presence and extent of symptoms (17).

Typical symptoms and signs associated with CRC include blood in the stool, abdominal pain, unexplained iron deficiency anemia, weight loss and changes in bowel habits like diarrhea and constipation (17, 24). However, these symptoms are not specific for CRC and can therefore be difficult to interpret (17, 26, 27). In some cases the cancer is detected because of an acute abdomen with ileus, major bleedings or intestinal perforation (17).

Screening is an important factor to reduce the CRC mortality by both decreasing the incidence and increasing the likelihood of survival (9, 28). There is however uncertainty on which screening method is the best in a public health perspective (17).

Along with the registration of medical history, rectal exploration and palpation of the abdomen are standard procedures when CRC is suspected. If there is blood in the stool this is investigated further with blood tests (14). If the patient is suspected to have CRC, the primary method for assessing colon cancer and the most accurate diagnostic test is colonoscopy (17, 24). When assessing possible rectal cancer, rectoscopy is commonly used (17). With both methods, biopsy is taken to determine the diagnosis (17).

1.2.6 Staging

Staging is a process used to determine the extent and the location of the cancer, and is being used to help plan the treatment and to predict a person's prognosis (29).

There are several cancer staging systems worldwide, but the most common and useful staging system is the Tumor-Node-Metastasis (TNM) system, maintained by the American Joint Committee on Cancer (AJCC) and the International Union for Cancer Control (UICC) (30). Letters and numbers from the staging do however not always mean the same for every cancer, therefore different versions of the classification system exists for most of the different cancer

types (29). The TNM-classification for CRC provides more detail than other staging systems and applies to all carcinomas arising in the colon and rectum (30).

For CRC, the TNM system describes the size of the primary tumor and weather it has reach nearby structures (T), spread to nearby lymph nodes (N), or metastasized to other organs (M) (31). Numbers or letters after T, N and M are used to give more details about each factor, where higher number indicates higher severity (31). The values given for T, N and M are combined to determine the overall stage (0 to IV), where stage IV is the most severe (29). Some of the stages are also divided into the subgroups A, B and C (31). See **Table 1** for an overview.

Table 1: Staging of CRC according to the TNM system.

TNM staging	T	N	M
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
	T2	N0	M0
Stage IIA	T3	N0	M0
Stage IIB	T4	N0	M0
Stage IIIA	T1, T2	N1	M0
Stage IIIB	T3, T4	N1	M0
Stage IIIC	Any T	N2	M0
Stage IV	Any T	Any N	M1

T: Indicates the size and extent of the primary tumor. Tis: in situ cancer/pre-cancer.
N: Indicates the extent of spread to the lymph nodes nearby. N0: No lymph nodes containing cancer cells.
M: Indicates whether the cancer has spread to distant parts of the body. M0: No distant cancer spread.
Table adapted from the American Joint Committee on Cancer (AJCC).

1.2.7 Treatment

The choice of treatment strategy for CRC will depend on the tumor characteristics, stage and location, in addition to the patient's age, health and preferences (9, 17, 32).

Both patients with colon and rectal cancer that has not spread to other parts of the body are often treated with surgery (9, 33, 34). The surgery involves resection of the tumor-bearing bowel segment with adequate margins and the removal of regional lymph nodes where the cancer might has spread (17). This can include removal of the entire colon, parts of the colon, or removal of the rectum (32). Surgery can be performed open or laparoscopic, where the latter has been shown to be associated with less pain, faster return of bowel function and shorter duration of hospital stay, especially for rectal cancer (35, 36). No differences between these techniques is reported for long-term outcomes (37).

Many CRC patients will receive a colostomy or ileostomy after the surgery. For most of the patients, this is a temporary solution until the bowel heals. Some patients will however need a permanent ostomy, this is more common in rectal than colon cancer patients (9, 32, 38).

Some patients will also receive additional therapy like radiation and chemotherapy before and/or after surgery. This is especially used if the cancer has spread to the lymph nodes, if the cancer is more advanced or if there is high risk of recurrence (18, 39, 40). Radiation therapy can be used to treat CRC before or after surgery to prevent recurrence, in people who are not healthy enough to have surgery, or if the cancer has spread to other areas (39). Chemotherapy can be given after surgery to kill any remaining cancer cells, or before surgery to shrink the cancer, or if the cancer has metastasized (40). It is more common with additional therapy, especially radiation therapy, for rectal cancer than in colon cancer (32).

About one-half of CRC survivors will have difficulties with chronic diarrhea. Bowel dysfunction is also common among rectal cancer survivors. In addition, some may experience bladder dysfunction, sexual dysfunction, and negative body image (32). Nausea and vomiting are side effects that can be experienced among patient undergoing cancer treatment, in addition to chemotherapy-induced peripheral neuropathy (41). Some patients can also experience symptoms that can affect the intake of nutrients, such as anorexia, early satiety, changes in taste and smell, as well as disturbance of the bowel (19, 41). The widespread of these symptoms will depend on the type of cancer and the stage at diagnosis (41).

1.2.8 Comorbidity

Comorbidity is defined as the “coexistence of disorders in addition to a primary disease of interest” (42).

About 40 % of CRC patients have at least one comorbidity at the time of diagnosis, with the most common conditions being diabetes, chronic obstructive pulmonary disease, cognitive heart failure and cerebrovascular disease (43). Among Australian CRC patients, the number of patients having comorbidity is reported to be even higher, about 80 % (44). CRC patients also have an increased risk of developing additional comorbidities like diabetes, hypertension, pulmonary disease and cerebrovascular disease after diagnosis (45-48). The prevalence of comorbid conditions increases with age and elderly CRC patients have an increased frequency of comorbid conditions compared with younger patients (47, 48). In addition, the prevalence has been found to increase with lower socioeconomic status (46). Comorbid conditions in CRC patients can affect treatment and may have a negative impact on short- and long-term outcomes after surgery like survival (42, 45, 46, 49, 50).

1.3 Physical activity

According to WHO, physical activity is defined as any bodily movement produced by skeletal muscles that requires energy expenditure (51). Physical activity therefore includes both exercise as well as movements done as part of playing, working, active transportation (e.g. walking or cycling), household chores and recreational activity (51).

There are several positive effects of regular and adequate levels of physical activity in adults and elderly. Men and women who are more physically active have reduced risk of hypertension, coronary heart disease, stroke, diabetes, metabolic syndrome, breast and colon cancer and depression compared with less active. In addition, they have a higher level of cardiorespiratory and muscular fitness, and increased bone mass density. For older adults physical activity can also improve bone and functional health, and cognitive function, in addition to reduce the risk of falls. Physical activity is important for energy balance and weight control as it is a key determinant of energy expenditure (52).

In many countries, especially in middle and high-income countries, the general level of physical activity has decreased and many uses a lot of time in sedentary recreations (8). However, trend data among adults suggest that the decrease applies for occupational activity, and that there has been an increase in leisure-time activity (53). Physical inactivity (i.e. the lack of physical activity) is the fourth leading risk factor for global mortality accounting for 6 % of deaths globally (52), and is estimated to be the main cause for around 21-25 % of breast and colon cancers, 27 % of diabetes and 30 % of ischemic heart disease burden (54).

The reduction in the level of physical activity have a great impact on the prevalence of non-communicable diseases like cardiovascular disease, diabetes and cancer, and their risk factors like raised blood pressure, raised blood sugar and overweight (52).

1.3.1 Physical activity recommendations

The Norwegian Directorate of Health recommend at least 150 minutes of moderate intensity activity, 75 minutes of vigorous intensity activity or a combination of these (moderate-to-vigorous activity) throughout the week for adults and older adults (55). This is consistent with other international guidelines (52, 56, 57). Moderate-to-vigorous activity is defined as: moderate activity + (vigorous activity*2). The activity should be performed in bouts of at

least 10 minutes duration. Two times a week it is recommended to do activities that is muscle-strengthening. It is also recommended to reduce sedentary time, and break up long periods of sitting with light activity (55). When elderly people are unable to perform the recommended amount of physical activity, they should be as physically active as their abilities and conditions allows (58).

Higher volumes of activity than 150 minutes per week, up to 300 minutes per week, are associated with additional health benefits (52, 55). Evidence shows that vigorous intensity not provides any additional health benefit compared with moderate intensity activity, it therefore seems that the total energy consumption has a greater impact on the effect than the intensity (20, 52).

The intensity of physical activity can be divided into levels based on metabolic equivalents (METs), such as vigorous (>6 METs), moderate (3-6 METs), and light (≥1.5-3 METs) (59, 60). MET values describe intensity relative to a person's resting metabolic rate, and is defined as the amount of oxygen consumed while sitting at rest and is equal to 3,5 ml O2 per kg body weight x min (8, 61). MET take factors like a person's basal energy expenditure, age, sex, size, skill, and level of fitness into account, as these factors affect the energy costs of any particular activity (8). Intensity can also be defined by heart rate; vigorous activity is defined as increased heart and breathing rates up to 80 % or more of its maximum, moderate activity increases heart rate to around 60-70 % of its maximum, whereas light activity only have minor effects on heart and breathing rates (8). The combination of frequency, intensity, and duration will determine the total physical activity levels (8).

A study conducted in Norwegian healthy adults aged 20-85 years, showed that only one in five people met the national physical activity recommendations (62). Compared to other European countries (Sweden, Portugal, England) participants from Norway had the highest percentages of meeting physical activity recommendations. However, Norway also showed the highest level of sedentary time (63).

1.3.2 Physical activity and CRC

It is well established that physical activity plays a vital role in preventing the risk of CRC (8, 11, 64). Physical activity during and after a cancer diagnosis is considered to be safe (65). Several studies have proposed that physical activity can improve physical functioning, quality of life and cancer-related fatigue, in addition to decrease all-cause and colorectal-specific mortality (65-68). However several barriers to perform physical activity among CRC survivors have been reported. These include the effects of cancer and cancer treatment (e.g. stoma, chronic diarrhea, and neuropathy), sleeplessness and fatigue, digestion issues, lack of time, work responsibilities, older age and no interest or dislike of sports (69-71).

Recommendations for cancer survivors

In the WCRF second expert report 2007 (8), it is recommended that cancer survivors follows the same recommendations as for cancer prevention regarding diet, healthy weight and physical activity. This is consistent with other reports were they recommend cancer survivors to follow the same guidelines as for healthy adults, and return to normal activities as soon as possible after surgery and during treatment. However, it is important that they take precautions and adjust their activity level to their abilities and health status (56, 65, 72). For all cancer survivors it is recommended to maintain or increase muscle mass during and after treatment (65).

Patients having an ostomy are recommended to follow advices from the physician before participating in contact sports and weight training. For resistance training, patients with a stoma should start with low resistance and progress slowly. It is also important that these patients avoid excessive intra-abdominal pressure (65).

Among cancer survivors, it is reported that approximately 30-50 % meets the physical activity guidelines (73). When looking at CRC survivors, only one third reached the recommended amount of activity (73, 74). This is lower than many of the other cancer survivor groups (73).

Pre-diagnosis physical activity

Conflicting results is reported from studies that have examined the association between pre-diagnosis physical activity and CRC outcomes (75). However, a meta-analysis from 2013 with five prospective cohort studies found that patients who participated in any amount of physical activity before diagnosis had a 25% reduction in CRC-specific mortality and 26% reduction in all-cause mortality compared to those who did not participate in any physical activity. The risk reduction was highest among those with the highest amount of activity, but this meta-analysis may suggest that even a small amount of physical activity before cancer diagnosis leads to favorable survival outcomes (75). This is consistent with findings from a large cohort study in Europe, where greater adherence with the recommendations from WCRF/AICR on diet, physical activity, and body fatness prior to diagnosis was associated with improved survival among CRC patients (76).

In a recent systematic review of Boereboom *et al.* (77), they concluded that there is no evidence that pre-operative physical activity improves post-operative outcomes such as recovery or survival in CRC patients.

Post-diagnosis physical activity

Recently more studies have been investigating the association between post-diagnosis physical activity and the risk of recurrence and mortality among CRC survivors. This has led to fairly consistent conclusions that increasing level of physical activity significantly improves overall mortality. Physical activity might also have an impact on CRC-specific mortality (68). In a meta-analysis of six prospective cohort studies of Je *et al.* (75), they found that there was a 26% reduced risk for CRC-specific mortality and a 32% reduced risk for overall mortality in patients who were in any physical activity after diagnosis compared with patients with no physical activity. The risk reduction was highest among those with the highest amounts of activity (75).

A literature review from van Zutphen *et al.* (78) showed that previous meta-analyses examinig the association between physical activity and all-cause mortality found that the highest level of post-diagnostic physical activity versus the lowest are associated with 40% lower risk.

Baade *et al.* (79) investigated the association between changes in physical activity and mortality outcome in CRC patients. They found that an increase in activity level of > 2 h/week between 5 and 12 months post-diagnosis was associated with a 31% lower risk of all-cause mortality and a 36% lower risk of CRC-specific mortality (79). This is consistent with the findings in a meta-analysis of Otto *et al.* were increased physical activity from pre- to post-diagnosis or at post-diagnosis only, was associated with a reduced risk of CRC and overall mortality rate (80).

Findings also suggest that there is a positive association between physical activity and quality of life, and fatigue among cancer survivors (81, 82). In addition, physical activity may also influence the management of the treatments side effects and expedite recovery from the acute effects of treatments like chemotherapy-induced peripheral neuropathy (83-85). It can also reduce the likelihood of cancer recurrence or the development of other chronic diseases (83, 84).

Recovery time and level of physical activity among cancer survivors

There are great differences in recovery time among CRC patients, which can have an impact on the level of physical activity after CRC diagnosis. The location of the tumor, type and duration of the treatment, the adverse effects of treatment, presence of ostomy and comorbidity, the patient's age and several socio-demographic factors can affect recovery and levels of physical activity. In addition, physical functioning and the level of physical activity before surgery will matter (65, 86, 87). In patients over 60 years of age undergoing abdominal surgery, less than 50 % were recovered to baseline physical functioning after 6 months (88). This is consistent with findings among CRC patients were about half of the patients had recovered to preoperative functioning after 6 months (86). However, the exercise pattern among CRC patients is expected to increase during post treatment period. Courneya and Friedenreich (89) found that exercise levels in CRC patients decreased from pre-diagnosis to active treatment, but increased again during post-treatment period. This pattern especially applies for moderate, vigorous, and total physical activity, whereas the light activity is better maintained throughout treatment (89). The same pattern has been found in an Australian study (90).

Van Zutphen *et al*. (86) studied the patient-reported recovery of physical functioning after CRC surgery. They found that patients who increased their physical activity level 6 months post-diagnosis, were 43 % more likely to recover physical function compared with those who kept the activity levels stable. Higher levels of physical activity after surgery compared with before surgery were also positively associated with recovery (86). The patients who followed the recommendations for physical activity, but not increased their activity level did not experience improved recovery. This might suggests that it is the change in physical activity since cancer diagnosis, rather than the total amount of activity, that is associated with physical functioning (89).

The role of physical activity in the cancer process

Physical activity affects a variety of biological processes, like energy metabolism, levels of sex hormones, hyperinsulinemia, insulin resistance, leptin, prostaglandins, C-reactive protein, reduces immune function and can influence the cells ability for DNA repair (20). Studies suggests that physical activity also can prevent cancer by affecting many stages during the process of carcinogenesis, including both tumor initiation and progression (91).

The possible biological mechanisms of physical activity in relation to CRC have proposed to be effects on immune function, oxidative damage, and the insulin axis. Oxidative DNA damage and inflammatory cytokines may also be affected (92). A decline in interleukin-1 receptor antagonist levels after short periods with exercise is also observed (93). Alterations in the insulin axis may play a role in the effect of physical activity on the development and the recurrence of CRC. In an Australian prospective cohort study they found that increasing levels of Insulin-like growth factor-binding protein-3 (IGFBP-3) was associated with improved survival from CRC among those who were physically active prior to diagnosis (94). The authors proposed that the beneficial effects of physical activity in reducing CRC mortality might occur through interactions with the insulin-like growth factor axis. Insulin-like growth factor 1 is central to the regulation of growth process by complexing with IGFBP-3 in the circulation and limiting tumorgenic potential (94).

In CRC survivors, pre-diagnosis levels of C-peptide have also been correlated with mortality outcomes. Higher levels of C-peptide were associated with increased risk of mortality (95). Physical activity may also lower CRC risk by reducing transit time through the intestine, and thereby the time the intestinal epithelium is exposed to potential carcinogens (20).

1.3.3 Sedentary behavior

Many healthy adults and cancer survivors do not meet the physical activity recommendations. A study from Norway found that adults and elderly people spend the majority of time being sedentary, in average 62% of their time awake (62). Sedentary behavior is defined as any waking behavior characterized by an energy expenditure ≤1.5 METs, while in a sitting, reclining, or lying position (96). Being sedentary is shown to be a health risk itself, independently of physical activity levels (97). Considering that 150 minutes of moderate physical activity per week is about 2 % of our daily time awake, the remaining 98% of our waking time can be spent in sedentary behavior and light intensity activity. Meeting the guidelines for physical activity does therefore not make up for a sedentary lifestyle, and thus being sedentary is not consistent with being physical inactive (98, 99).

Several studies have found an increase in sedentary behavior and sitting time after cancer diagnosis (100), and this is possibly associated with higher mortality (101). Among CRC survivors, only pre-diagnosis sitting time has been found to be associated with higher risk of all-cause mortality, whereas post-diagnosis sedentary time has been associated with CRC-specific mortality (78). Campbell *et al.* (102) reported that 6 hours or more of leisure time spent sitting pre-diagnosis was significantly associated with higher all-cause mortality and post-diagnosis sitting time was significantly associated with CRC-specific mortality. This is consistent with findings from Arem *et al.* (66) where those reporting 5 hours or more of TV-watching pre-diagnosis had a 22% increased risk of all-cause mortality.

1.3.4 Exercise interventions

The majority of exercise interventions conducted among CRC survivors have shown improvements in the physical activity parameters (103). Most of the studies are telephone-guided and home-based interventions. These studies have had low dropout rates and good adherence, suggesting that these kinds of interventions are feasible and well tolerated by CRC survivors (103).

In the 'CanChange' study (44), a two-armed RCT among CRC patients, participants were randomized to either a telephone-delivered health coaching intervention or to follow usual care. The results indicated significant intervention effects for moderate physical activity.

Moreover, the intervention group was also more likely to meet the physical activity recommendations (44).

In a home-based physical activity intervention by Pinto *et al.* (104) among CRC survivors, the level of activity and motivational readiness improved at 3 months in the intervention group compared with the control group. These group differences were attenuated with time. The intervention group also increased their submaximal aerobic fitness at 3, 6 and 12 months compared to the control group.

The 'CHALLENGE' (Colon Health and Life-Long Exercise Change) trial (105) is an ongoing RCT examining the effects of a 3 year structured exercise program compared with health education materials on disease-free survival among colon cancer survivors. Results from the first year of the intervention shows that the exercise group reported a greater increase in recreational physical activity than the control group. The exercise group also had a greater increase in the 6-minute walking test (6MWT) and the 30-second sit-to-stand test (30STS).

The CRC-NORDIET is primarily a dietary intervention, not an exercise intervention. However, both study groups receives similar advices on physical activity. This is done in order to control for any confounding effect of physical activity in attempt to isolate the effect of the diet intervention. Although, the general advices given on physical activity should, in theory, result in similar changes in the two groups, the individual dietary counseling given to the participants in the dietary intervention group might impose an additional effect on physical activity.

2 Aims for this master thesis

This master thesis is a subproject within the ongoing Norwegian Dietary Guidelines and Colorectal Cancer Survival Study (CRC-NORDIET). The primary aim of this master thesis was to examine whether the CRC patients receiving individual nutritional counseling will have an additional effect on the level of physical activity compared to the control group. The secondary aims were to investigate the effect of the intervention on physical function, sedentary time and muscle mass and investigate the association between clinical and demographic factors and physical activity and sedentary time.

The primary endpoint of this master thesis was:

- Investigate whether the change in physical activity from baseline to 12-months follow up is different between the intervention group and the control group.

The secondary endpoints of this master thesis were:

- Investigate whether the change in physical function and muscle mass from baseline to 12-months follow up is different between the intervention group and control group.
- Investigate whether the level of physical activity, sedentary time, physical function and muscle mass changes for the total study population independent of study groups.
- Investigate the impact of demographic and clinical factors such as gender, age, socioeconomic factors, smoking, severity of the disease, treatment type, surgery, cancer location, BMI, and stoma on physical activity and sedentary time at baseline in the total study group.
- Investigate the association between physical activity and physical function and body composition.

3 Subjects and methods

3.1 The CRC-NORDIET study

This master thesis was conducted from August 2017 to May 2018.

3.1.1 Study design

The CRC-NORDIET study is a multicenter, randomized controlled trial, with two parallel study arms, initiated in June 2012. Patients were invited to the baseline of the study within two to nine months after surgery, and randomized to one of the two groups. The dietary intervention group receives individual dietary counseling and general advices regarding physical activity. The dietary advices are in accordance with the Norwegian food-based dietary guidelines (NFBDG) and focuses on anti-inflammatory and antioxidant-rich foods. In addition, the dietary intervention group receives a grocery discount cards, delivery of free food items, a cooking course, telephone-based counseling, and access to a website with detailed information about the NFBDG, recipes, advice for treatment-related symptoms and more. The control group receives a booklet with general dietary advice and the same general advices on physical activity as the intervention group. Both groups are invited to an inspiration day at the study center and receive written reports from the sampling performed during the first intervention year.

The dietary intervention consists of an intensive 12 months period, followed by a 14 years follow-up period. During the first year, the participants meet at the study center, which is located at the Department of Nutrition, University of Oslo, three times; at baseline, and 6 and 12 months after baseline. At every visit the participants undergo several physical and biological measurements. These include blood pressure, venous blood samples, anthropometry, body composition and physical function. The participants are also asked to fill out a number of questionnaires regarding demographic characteristics, diet, physical activity, comorbidities, health related quality of life and fatigue. For the participants in the intervention group, three additional follow-ups by telephone are also performed during the first year. All participants are invited to similar follow-up visits 3, 5, 7, 10 and 15 years after baseline. See **Figure 2** for an overview of the study design.

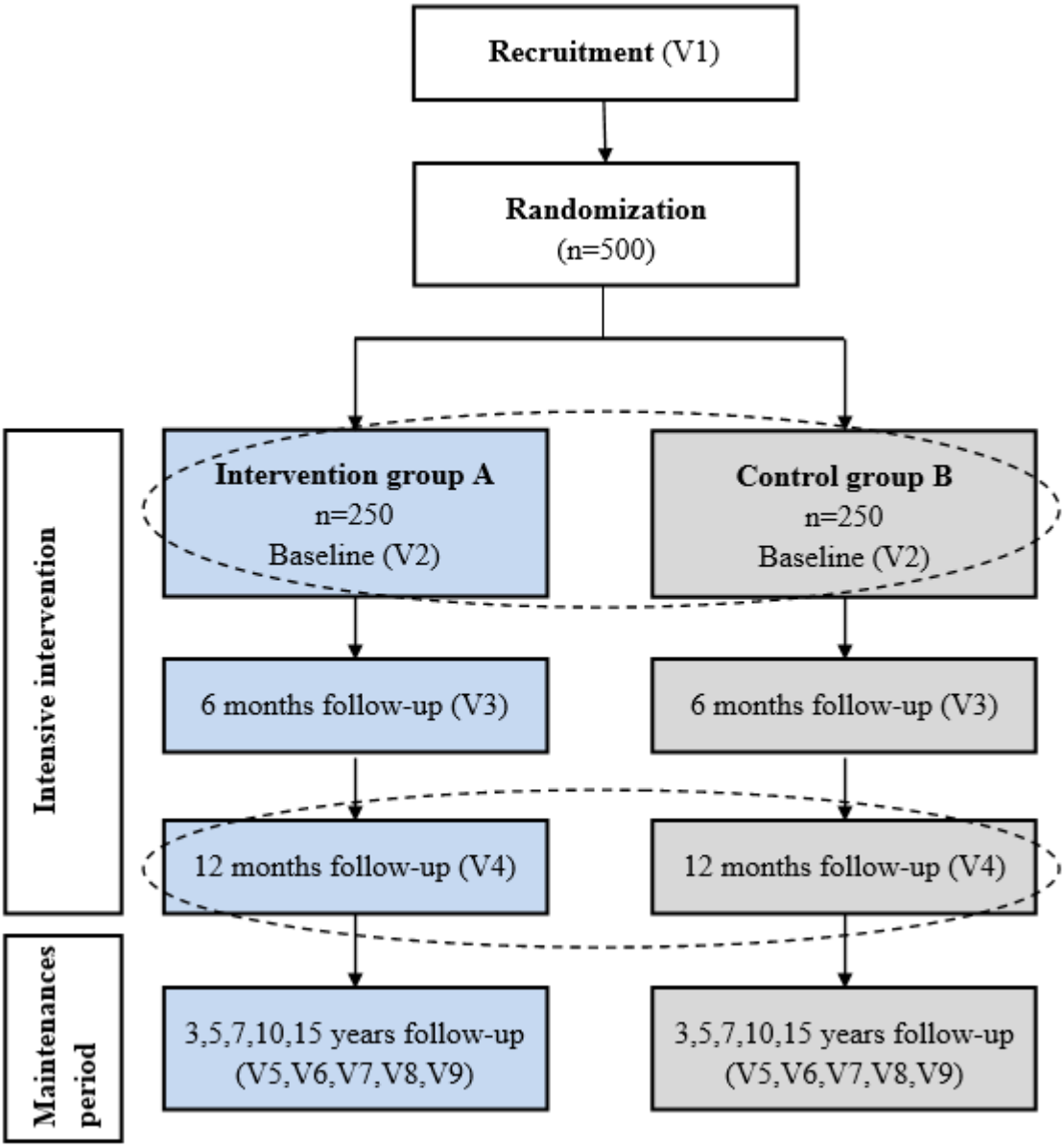

Figure 2: Overview of the CRC-NORDIET study design

The intervention consists of an intensive 12 months period, followed by a 14 years maintenance period. Patients are invited (V1) after surgery for CRC. The participants are invited to the study centre for baseline visit two to nine months post-surgery. Participants are then follow-up 3, 5, 7, 10 and 15 years after baseline. At every visit the participants undergo several physical and biological measurements, in addition to filling out a number of questionnaires. This master thesis includes measurements performed at the time-points in the dotted circles, V2 and V4. This figure is adapted and edited with permission (1).

3.1.2 Recruitment

Recruitment of participants started in 2012 and is estimated to last until end of year 2019. The participants are recruited from two hospitals within the South-Eastern Regional Health Authority; Oslo University Hospital and Akershus University Hospital two to eight months after surgery. Research investigators and hospital personnel determine which patients are eligible for inclusion to the study. Subjects are invited to the study through telephone, and receive a postal invitation letter together with a consent form and an FFQ if they are interested in participating. From the start and until January 2015, the participants were invited face-to-face in the hospitals before surgery. Baseline visit have to be within nine months from surgery.

3.1.3 Intervention strategy – physical activity

The advices given on physical activity in this study is in accordance with the Norwegian recommendations on physical activity (55). The participants receive a booklet on how to be physically active in daily life and advice on how to reach the recommended amount of activity.

The CRC-NORDIET study also has an agreement with "Active against cancer" (106). This private foundation works to establish physical activity as an integral part of cancer treatment. The organization has established training studio ("Pusterommet") at several hospitals in Norway. "Pusterommet" offers guidance and individualized physical activity to cancer patients both during and after cancer treatment. The study participants are encouraged to utilize this offer.

All participants are invited to an inspiration day within the first 12 months of the intervention. Both groups are offered equal focus on physical activity, whereas the dietary intervention group also receives special attention on dietary recommendations. The participants also get the opportunity to meet the employees at "Active against cancer" and "Pusterommet" which presents the facilities and exercise program offered to all cancer patients in the hospitals. In addition, lectures about physical activity incorporated in daily life are held by the researchers from CRC-NORDIET study.

3.2 Subjects

Men and women aged 50 to 80 years, newly treated for primary invasive CRC are invited to the CRC-NORDIET study. Inclusion criteria for participation are established primary adenocarcinoma in the colon or rectum including diagnosis with ICD-10 codes C18-C20 and TMN-stage I-III (1). Patients unable to read and understand Norwegian or patients participating in other studies that affect the participation in CRC-NORDIET study are excluded. In addition, patients unable to perceive information and understand the intervention due to dementia or altered mental status are also excluded from the study.

3.2.1 Subjects in this current master thesis

In this current master thesis, participants from the CRC-NORDIET study who had attended baseline and one-year follow-up prior to 1.january 2018 and had worn the SenseWear armband at both visits (i.e. baseline and 12-months follow-up visit) were eligible for inclusion. In January 2018, a total of 438 participants had given their written consent to participate in the study, of which 324 had attended baseline. Moreover, 167 participants fulfilled the inclusion criteria and were therefore included in this master thesis (**Figure 3**).

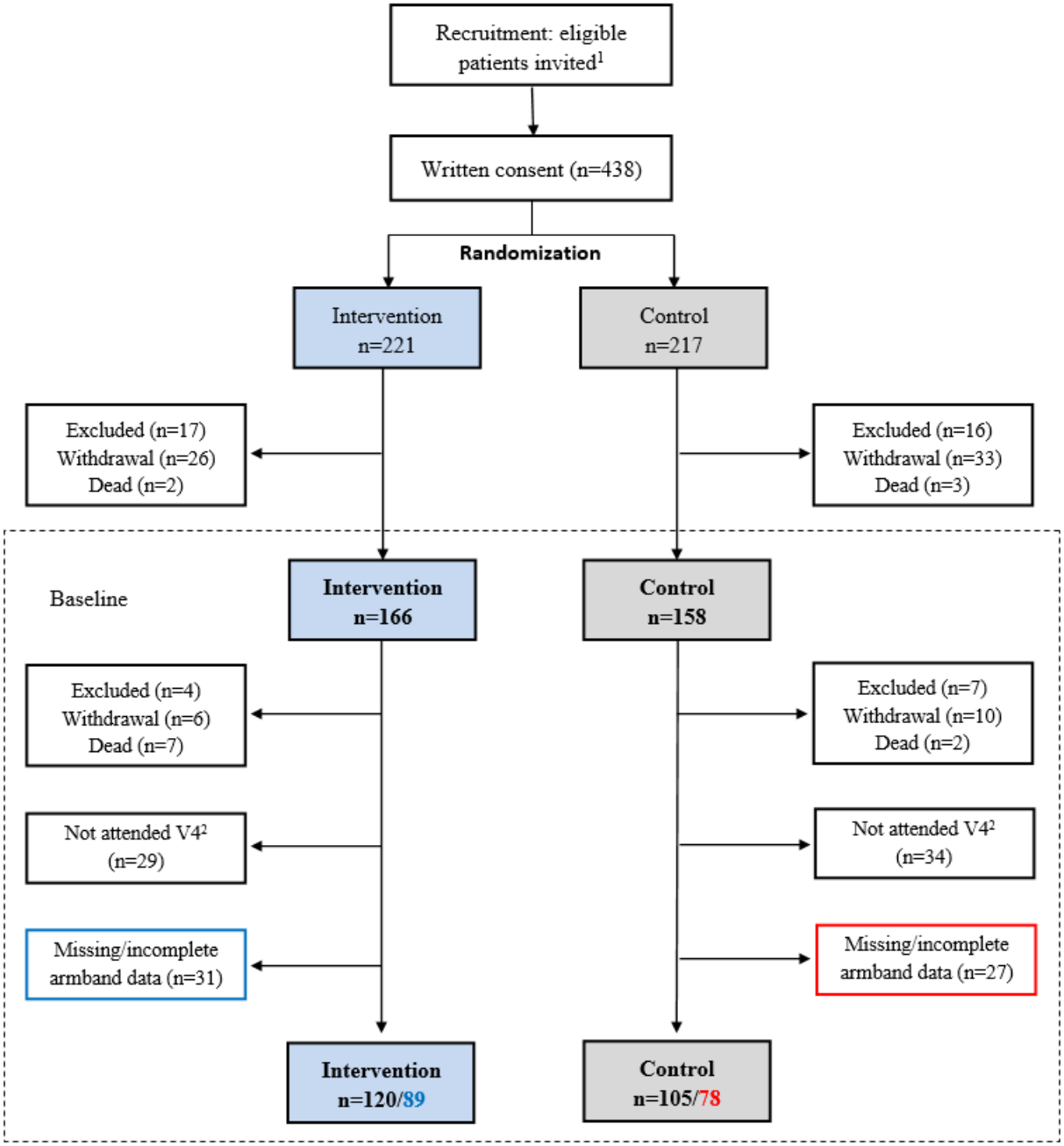

Figure 3: Flow chart for participants included in this master thesis.
By December 2017, 324 out of the 438 patients that had agreed to participate in the CRC-NORDIET study had reached baseline. In total 225 participants had attended to the 12-months follow-up visit. Out of these, 167 participants had armband data at both visits, and were included in the analysis. The numbers highlighted in blue and red represents the participants in the intervention- and control group, respectively, in this current master thesis. [1]Number not available, [2]Not attended 12-months follow-up in time before master thesis data collection ended. Complete dataset: armband data available from both baseline and 12-months follow-up.

3.3 Methods

All measurements performed in the CRC-NORDIET study that was relevant for this master thesis is presented in detail in this chapter.

3.3.1 Subject characteristics

Demographic data

Information regarding age, gender, marital status, highest completed education and present working status was self-reported by the participants by using a short questionnaire at baseline.

Clinical characteristics

Tumor location, TNM-status, type of surgery and additional treatment (i.e. neoadjuvant or adjuvant) were collected from medical records.

Presence of ostomy was obtained from data registered at the anthropometric measurements. The participant smoking status was registered when the SenseWear armband was prepared, as this information is pre-programmed into the armband before use. The presence of comorbid conditions were collected by using a questionnaire developed in-house at every visit. The comorbidities included in the questionnaire were myocardial infarction, angina pectoris, heart failure, other heart disease, stroke, kidney disease, asthma, chronic obstructive pulmonary disease, diabetes (type I and II), psoriasis, hand eczema, other cancer diseases, rheumatoid arthritis, Bechterew's disease, osteoporosis, fibromyalgia and arthrosis.

Anthropometric measures

In this master thesis, anthropometric measures include weight, height, body mass index, waist and hip circumference and body composition. Data on anthropometric measures were collected at every visit by trained researchers. All measurements were performed with light clothes, empty pockets and shoes removed.

Body weight was measured by using either a non-slip Marsden M-420 Digital Portable Floor Scale (Marshden, Rotherdam, South Yorkshire, United Kingdom) or a digital wireless

measuring station for height and weight, Seca 285 (Seca, Birmingham, United Kingdom) (107). Weight was recorded at the nearest 0.1 kg. Height was measured by using either a mechanical height rod (Kern MSF-200) (108) or Seca 285 (107), and recorded to the nearest 0.1 cm.

The weight and height were used to calculate BMI, which is defined as a person's weight in kilograms (kg) divided by the square of height in meters (m) (kg/m^2). As the WHO BMI thresholds (109) for overweight and obese have been proposed as too restrictive for older people (110), the CRC-NORDIET study has determined the normal BMI as BMI 20-27 for patients aged 50-80 years (1).

Waist circumference was measured at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest. Hip circumference was measured around the widest portion of the hips. Both measurements were performed without clothes, except for underwear, over the area of measurement.

Body composition was measured with Bioelectric Impedance Analysis (BIA), BIA 101 (SMT Medical, Würzburg, Germany) and with the iDXA (GE Healthcare Lunar, Buckinghamshire, United Kingdom). BIA use the resistance (Rz) and reactance (Xc) to calculate body composition compartments such as muscle mass, fat mass and fat free mass. The measurements were conducted on the patient's right side as described by the manual. Patients with pacemaker were excluded from this measurement. The percentage muscle mass, fat mass and fat free mass was calculated and used in the analysis. In addition, Dual-Energy-X-ray Absorptiometry (DXA) was used to retrieve data on lean mass. The advantages of DXA compared to Computed Topography (CT) is the use of smaller doses of ionizing radiation to produce pictures of the body composition compartments inside the body. The DXA scans were administered by trained research technicians following manufacturer guidelines. In this master thesis, the measures of the lean soft-tissue masses for the arms and the legs, in addition to total lean body mass were used.

3.4 Assessment of physical activity and function

In this master thesis, assessment of physical activity and function includes objective measurement of physical activity by the SenseWear armband, hand-grip strength, 30STS, and 6MWT. All tests were conducted at every visit.

3.4.1 SenseWear armband

The physical activity monitor SenseWear Armband Mini (BodyMedia, Pittsburg, Pennsylvania, USA) was used to record physical activity both day and night, sedentary time and steps during seven consecutive days (111). The SenseWear armband monitors physiological data such as heat flux, galvanic skin response, 3-axis accelerometer and skin temperature. The participants were instructed to wear the armband all day, including while sleeping, to remove it only for brief periods for showering or water activities, and to continue their normal activity level. The armband was placed around the triceps muscle halfway on the upper non-dominant arm. Participants were provided with a written guidance sheet on how to use the SenseWear armband. A priori, we defined a valid day of recording if the wear time was ≥ 80% of 24-h sampling period (i.e. 19.2 hours/day). The armband was pre-programmed by the researcher with information on age, gender, height, weight, smoking status and handedness. Contraindications for using the SenseWear were having a pacemaker, going through radiotherapy or known allergy/irritable skin. All data was retrieved from the armband to the computer by using SenseWear Professional Software Version 7.0 BodyMedia Inc (Pittsburg, Pennsylvania, USA).

The SenseWear armband is a reliable method for assessing activity levels and energy expenditure and is validated in adults, older adults and cancer patients against doubly labeled water, indirect calorimetry and other accelerometers (112-116).

The activity intensities were integrated into algorithms, providing estimates of energy expenditure expressed in METs. Light intensity were defined as 1.6-2.9 MET, moderate intensity as 3-5.9 METs and vigorous intensity as >6 METs, as calculated by Ainsworth *et al.* (59, 60). Sedentary time was defined as all daily activities ≤1.5 METs, including nighttime (a priori defined as midnight to 6.00 a.m.). The SenseWear armband records all intensities in 1-minute periods, which were translated into different categories such as light, moderate,

vigorous and moderate-to-vigorous physical activity. The total physical activity during a day corresponds to the sum of light, moderate and vigorous physical activity. All activities were calculated as minutes per day, except for sedentary time which was calculated as hours per day.

3.4.2 30-second sit-to-stand test

The 30-second sit-to-stand test (30STS) is performed by using a straight back chair without armrests, and with a solid seat at the height of 45 cm. The same chair was used for all measurements (1). The participants are instructed to sit on the chair with arms folded across their chest and feet placed parallel on the floor. During 30 seconds, the participants should stand up to a fully extended position and sit down as quickly and frequently as possible. The total number of full stands was registered (117).

This test is used a measure of lower extremity strength and endurance (118).

3.4.3 6- min walking test

The 6-min walking test (6MWT) was performed indoor, with a walking course of 30 meter, along a flat, straight, enclosed corridor with a hard surface. The participants are walking forth and back as many times as possible in 6 min. The total length of walking (in meters) is recorded. The participant's blood pressure is measured prior to the test; in addition the heart rate is monitored before, during and after the test. By using the Borg scale 6-20 (119), the participants perceived exertion are registered both before and after the test. The Borg scale is a 15-point scale ranging from 6 (very, very light) to 20 (very, very hard), and is a valid tool for monitoring exercise intensity (120).

The 6MWT assesses the submaximal level of functional capacity and reflects the functional exercise level for daily physical activity (121). It is also used as an indicator of functional aerobic capacity and endurance. It is mostly used among patients with lung and heart problem, but it is also reliable and valid for individuals with other conditions (122, 123). In older people, the 6MWT may be a general indicator of overall physical function and mobility (124). The 6MWT has also been used as a predictor of morbidity and mortality. There has been reported a significant correlation between 6MWT and peak oxygen uptake (121). The walking distance decreases with increasing age (125).

3.4.4 Handgrip strength

The maximal strength of hand-grip (kg) was measured by using the MAP 80 KI Hand grip dynamometer (KERN & SOHN GmbH, Balingen, Germany) and measured as described in the manufacturers protocol (108). The elbow should be flexed at 90 degrees and the arm should not be supported by the armrest. For women a 40 kg-spring was used, and for men a 80 kg-spring. The grip strength was measured with one punch and repeated three times on each hands, switching arm between each measure. The maximum hand-grip strength in both left and right hand were recorded.

This test is a method for assessing muscle strength in the upper extremities (126). Studies has also shown that impaired handgrip strength can be an indicator of increased postoperative complications, length of hospitalization and mortality, in addition to decreased muscle mass and physical function (127-130).

3.5 Determination of required sample size

In order to detect a mean change in physical activity of 4 ± 13.8 min/day (mean difference ± SD) between the two study groups from baseline to 12-months follow-up, a sample size of 157 subjects in each group was required to achieve a significance level of 5 % and power of 80 % (44).

The sample size calculation of the entire CRC-NORDIET population is designed to detect 25 % reduction in primary endpoints (i.e. disease free survival and overall survival) after 5, 10 and 15 years, requiring a total sample size of 250 in each group (i.e. a total of 500 subjects) (1). The recruitment of patients is estimated to continue until 2020, to reach the 500 participants needed in the study.

3.6 Statistical analyses

All statistical analyses were conducted using IBM SPSS Statistics for Windows, version 25.

Continuous variables that are normally distributed are presented as mean with standard deviation (SD), whereas non-normally distributed data are presented as median with 25^{th} and 75^{th} percentile (p25, p75). Categorical variables are presented as frequencies with percentages, n (%). Results were considered statistical significant if the p–value were below 0.05. Normality was assessed for all data by evaluating histograms, normal Q-Q Plots and the Kolmogorov-Smirnov test. The Kolmogorov-Smirnov test indicates normality when the result is non-significant. The Normal Q-Q Plot suggests a normal distribution when the line is reasonable straight.

The changes from baseline to 12-months between the two study groups were investigated using one-way between groups analysis of covariance (ANCOVA) for normally distributed variables to 'control' for the baseline differences between the groups if the assumptions were fulfilled. When the assumptions for ANCOVA were violated, independent samples t-test was used. Mann-Whitney U Test was used when comparing differences in continuous variables between independent groups (such as the intervention group versus the control group) on non-normally distributed data. Categorical variables were compared by the Pearson chi-square test and Fisher exact test. Cases with missing values were excluded pairwise.

When investigating changes in continuous data from baseline to 12-months follow-up for the total study population; paired-samples t-test was used for normally distributed variables, and Wilcoxon signed-rank test on non-normally distributed variables.

When comparing differences in categorical variables with more than two groups, one-way analysis of variance (ANOVA) with post-hoc tests was used if the variables were normally distributed. Kruskall-Wallis test was used for non-normally distributed variables, pairwise comparison with Bonferroni correction was used to correct for multiple testing in Post-Hoc analysis.

Correlation analyses with Pearson or Spearman`s rank order correlation was used to explore the relationship between physical activity and anthropometric measures, physical function and body composition. In addition to the correlation between the measurements from DXA and physical function were explored. A correlation coefficient below 0.3 was categorized as small, between 0.3 and 0.5 as medium, and above 0.5 as large correlation (131).

3.7 Ethics

The “Norwegian Dietary Guidelines and Colorectal Cancer Survival Study” is registered on the National Institutes of Health ClinicalTrials.gov (ID no. NCT01570010), and approved by The National Committee for Medical and Health Research Ethics in Norway (REC no. 2011/836).

3.8 My contributions in the CRC-NORDIET Study

Work assignment	Description	Responsibility
Recruitment of patients	• Invite patients via telephone after surgery	Master student CRC-NORDIET research team
Baseline and follow-up visits at the study center	• Admission and discharge of patients • Dietary consultations • Nutritional screening with PG-SGA • Anthropometric measurements • Advise about physical activity • Guidance in handling of questionnaires	Master student CRC-NORDIET research team
Follow-up phone calls (short and long-time)	• Dietary consultations via telephone	Master student Clinical nutritionist
Inspiration day	• Preparing and participating in inspiration day for both groups	Master student CRC-NORDIET research team
Plot data into online database, LabKey	• Plot data from PG-SGA schemes • Plot data from dietary consultations	Master student CRC-NORDIET research team
SenseWear armband	• Transfer the data from the armband to the computer • Making reports to the participants	Master student CRC-NORDIET research team
Make and copying materials to the participants	• Paperback with information, recipes, recommendations regarding diet and physical activity.	Master student CRC-NORDIET research group
Statistical analyses	• Analyze data with relevant statistical methods in SPSS	Master student Under supervision

4 Results

The study sample for this master thesis includes the participants that attended their 12-months follow-up visit prior to January 1st 2018. A total of 167 participants had complete armband data at both baseline and 12-months, and were included in the analyses (Figure 3). As the recruitment of participants for the main CRC-NORDIET study is still ongoing, the results presented in this master thesis are only preliminary and the interpretation must be done accordingly.

4.1 Subject characteristics

Information on several demographic and clinical features were collected at baseline for the entire study population, these are presented in **Table 2** and **Table 3**.

4.1.1 Demographic characteristics

Demographic characteristics for the participants at baseline are presented in **Table 2**.
Out of the 167 participants included in the study sample, 83 were men and 84 were women. The mean age of the participants was 66.1 years and most of them were in the middle age group from 60 to 69 years (43%). The lowest proportion of subjects (22%) was found in the youngest age group 50-59 years, whereas 35% were in the oldest age group. More than half of the study population (55%) had completed college or university education, while 37% and 8% had high school and primary-secondary school as their highest educational level respectively. Most of the participants were married or cohabitant (71%). Approximately half of the participants were retired (51%), 32% were still working part or full time, and the remaining 17% were on sick leave, in rehabilitation or had other reasons for not working. Seven percent were smokers.

Table 2: Demographic characteristics at baseline for the CRC-NORDIET population

	Count (%) (n=167)
Age[1a]	66.1 (±7.6)
Age group[1]	
50-59	37 (22.2)
60-69	71 (42.5)
70-80	59 (35.3)
Gender [1]	
Men	83 (49.7)
Women	84 (50.3)
Marital status[2]	
Married/cohabitant	98 (71.0)
Divorced	22 (15.9)
Widowed	8 (5.8)
Single	10 (7.2)
Highest education completed[3]	
Primary-lower secondary	11 (7.9)
High school	52 (37.4)
College/university	76 (54.7)
Work status[3]	
Working[4]	44 (31.7)
Retired	71 (51.1)
On sick leave, rehabilitation	18 (12.9)
Other[5]	6 (4.3)
Smoking status[1]	
Smoker	12 (7.2)
Non-smoker	155 (92.8)

[a]Age presented as mean with standard deviation (SD), [1]Data available for all participants (n=167), [2]Data available for n=138, [3]Data available for n=139, [4]Working full or part time, [5]Staying at home, unemployed or receiving temporary/permanent disability benefit.

4.1.2 Clinical characteristics

The clinical characteristics for the population at baseline are presented in **Table 3.**
The average BMI for the total study group was 26.2kg/m^2, and the greatest proportion of subjects (44%) was in the BMI-category that corresponds to overweight according to WHO. The mean time between surgery and baseline visit was 4 months. Cancer of the colon (C.18) was the most common cancer diagnosis in the population (53%), 39% of the subjects was diagnosed with rectal cancer (C.20) and the remaining (8%) with rectosigmoid cancer (C.19). The most common TNM stage were stage II with 38%, but the distribution between the three categories were quite similar, with 31% in both stage I and III. A total of 12% of the patients received neoadjuvant treatment and 21% received adjuvant treatment. Laparoscopic surgery was the most common type of surgery (48%). Twenty-eight percent of the study population had ostomy at baseline. Thirty-six percent of the participants reported to have one additional disease at baseline, whereas 29% reported having two or more. Among the comorbidities registered, other cancers and muscle and skeletal diseases (rheumatoid arthritis, Bechterew's, osteoporosis, fibromyalgia and osteoarthritis) were the most common, with 23% of the subjects in both. This were followed by cardiovascular diseases (15%) (myocardial infarction, angina pectoris, heart failure, cerebral stroke and hemorrhage), respiratory diseases (11%) (asthma and chronic obstructive pulmonary disease), and diabetes (11%).

Table 3: Clinical characteristics at baseline for the CRC-NORDIET population

	Count (%) (n=167)
BMI[1]	26.2 (±4.8)
BMI-categories[2]	
<18.5	3 (1.8)
18.5-24.9	62 (37.1)
25-29.9	74 (44.3)
>30	28 (16.8)
Time since surgery[1]	4.0 (±1.7)
Tumor localization[3]	
C18 Colon	73 (52.6)
C19 Rectosigmoid	10 (8.0)
C20 Rectum	54 (39.4)
TNM-stage[4]	
I	38 (30.6)
II	47 (37.9)
III	39 (31.5)
Treatment	
Neoadjuvant[5]	16 (11.9)
Adjuvant[6]	28 (21.5)
Type of surgery[7]	
Laparoscopic	61 (48.4)
Open surgery	50 (39.7)
Laparoscopic converted to open	15 (11.9)
Ostomy[8]	42 (28.2)
Comorbidities[9]	
Cardiovascular disease	20 (14.7)
Respiratory disease	15 (11.0)
Muscle and skeletal disease	32 (23.5)
Kidney disease	4 (2.9)
Diabetes I/II	15 (11.0)
Skin disease	11 (8.1)
Other cancer	32 (23.5)
Number of comorbidities[9]	
0	48 (35.3)
1	49 (36.0)
≥2	39 (28.7)

[1]Data available for all participants (n=167) presented as mean with standard deviation (SD). [2]BMI categories: Body Mass Index-categories defined by WHO. Data available for: n=137[3], n=124[4], n=134[5], n=130[6], n=126[7], n=149[8], n=136[9].

4.2 Effect of the intervention

As the primary aim for this master thesis was to assess whether a change in physical activity from baseline to 12-months follow up is different between the intervention group and the control group, data on this is presented in **Table 6**. Of the 167 participants, 89 had been randomized to the intervention group and 78 to the control group.

4.2.1 Comparison of the groups – baseline demographic and clinical characteristics

In order to check if the randomization had been successful, a set of demographic and clinical characteristics at baseline were compared between the two groups. Demographic characteristics of the participants who completed the one-year intervention are displayed in **Table 4**, and the clinical characteristics are presented in **Table 5.**

No differences were found at baseline between the study groups regarding the demographic parameters recorded (Table 4). This included age, gender, marital status, education level, work status and smoking status.

The groups were also similar with regard to the clinical characteristics measured in this study (Table 5).

Table 4: Demographic characteristics at baseline for the intervention and control group

	Intervention (n=89)	**Control** (n=78)	**p-value**
Age[1a]	65.5 (±7.3)	66.8 (±7.9)	0.298
Age groups[1]			0.171
50-59	20 (22.5)	17 (21.8)	
60-69	43 (48.3)	28 (35.9)	
70-80	26 (29.2)	33 (42.9)	
Gender[1]			0.591
Men	42 (47.2)	41 (52.6)	
Women	47 (52.8)	37 (47.4)	
Marital status[2]			0.324
Married/cohabitant	58 (76.3)	40 (64.5)	
Divorced	9 (11.8)	13 (21.0)	
Widowed	3 (3.9)	5 (8.1)	
Single	6 (7.9)	4 (6.5)	
Highest education completed[3]			0.495
Primary-lower secondary	7 (9.2)	4 (6.3)	
High school	25 (32.9)	27 (42.9)	
College/university	44 (57.9)	32 (50.8)	
Work status[3]			0.956
Working[4]	24 (31.6)	20 (31.7)	
Retired	38 (50.0)	33 (52.4)	
On sick leave, rehabilitation	10 (13.2)	8 (12.7)	
Other[5]	4 (5.3)	2 (3.2)	
Smoking status[1]			0.082
Smoker	3 (3.4)	9 (11.5)	
Non-smoker	86 (96.6)	69 (88.5)	

[a]Age presented as mean with standard deviation (SD), [1]Data available for all participants (n=167), [2]Data available for n=138, [3]Data available for n=139, [4]Working full or part time, [5]Staying at home, unemployed or receiving temporary/permanent disability benefit.
For categorical data, Chi-square test or Fisher`s exact test were performed to determine the difference between the groups. For continuous and normal distributed data, independent-samples T-test was performed.

Table 5: Clinical characteristics at baseline for the intervention and control group

	Intervention (n=89)	**Control** (n=78)	**p-value**
BMI[1]	25.8 (±4.7)	26.6 (±4.8)	0.241
BMI-categories[2]			0.070
<18.5	0 (0.0)	3 (3.8)	
18.5-24.9	39 (43.8)	23 (29.5)	
25-25.9	38 (42.7)	36 (46.2)	
>30	12 (13.5)	16 (20.5)	
Tumor localization[3]			0.508
C18 Colon	38 (52.8)	34 (52.3)	
C19 Rectosigmoid	4 (5.6)	7 (10.8)	
C20 Rectum	30 (41.7)	24 (36.9)	
Time since surgery[1]	3.9 (±1.6)	4.3 (±1.8)	0.101
TNM-stage[4]			0.676
I	23 (33.8)	15 (26.8)	
II	24 (35.3)	23 (41.1)	
III	21 (30.9)	18 (32.1)	
Treatment			
Neoadjuvant[5]	10 (14.1)	6 (9.5)	0.416
Adjuvant[6]	14 (20.0)	14 (23.3)	0.645
Type of surgery[7]			0.633
Laparoscopic	36 (52.2)	25 (43.9)	
Open surgery	25 (36.2)	25 (43.9)	
Laparoscopic converted to open	8 (11.6)	7 (12.2)	
Function score?			
Ostomy[8]	27 (32.9)	15 (22.4)	0.215
Comorbidities[9]			
Cardiovascular disease	8 (10.7)	12 (19.7)	0.218
Respiratory disease	8 (10.7)	7 (11.5)	1.000
Muscle and skeletal disease	21 (28.0)	11 (18.0)	0.246
Kidney disease	3 (4.0)	1 (1.6)	0.628
Diabetes I/II	6 (8.0)	9 (14.8)	0.329
Skin disease	6 (8.0)	5 (8.2)	1.000
Other cancer	18 (24.0)	14 (23.0)	1.000
Number of comorbidities[9]			0.935
0	27 (36.0)	21 (34.4)	
1	26 (34.7	23 (37.7)	
≥2	22 (29.3)	17 (27.9)	

[1]Data available for all participants (n=167) presented as mean with standard deviation (SD).
[2]BMI-categories: Body Mass Index-categories defined by WHO. Data available for: n=137[3], n=124[4], n=134[5], n=130[6], n=126[7], n=149[8], n=136[9].
For categorical data, Chi-square test or Fisher`s exact test was performed to determine the difference between the groups. For continuous and normally distributed data, independent-samples T-test was performed.

4.2.2 Effects of the intervention on physical activity

The amount of total, light, moderate, vigorous and moderate-to-vigorous physical activity, sedentary time, and steps at baseline and the change from baseline to 12 months for the intervention group and the control group are presented in **Table 6**.

The effect of the intervention on physical activity was evaluated by comparing the 12 months change in several physical activity intensities, sedentary time, steps and average METs between the intervention group and the control group (Table 6).

There was no difference between the groups with regard to change in the different intensities of physical activity from baseline to 12-months follow-up, indicating that the dietary component of the intervention did not have any impact on physical activity. The changes between the groups were investigated using ANCOVA for normally distributed variables if the assumptions were fulfilled. No difference in the change between the groups for total physical activity, sedentary time and average METs were found based on this method. There were no differences between the groups at baseline in the variables regarding physical activity (data not shown).

4.2.3 Effects of the intervention on physical function and body composition

The physical function and body composition measurements at baseline and the change from baseline to 12 months for both groups are presented in **Table 7**.

When comparing the change during the one-year intervention, no significant differences were found between the study groups. The changes between the groups were investigated using ANCOVA for normally distributed variables if the assumptions were fulfilled, no differences in the change between the groups were found using this method. There were no differences between the groups at baseline for physical function or body composition measures from BIA. The percent of total lean body mass calculated from DXA was also similar at baseline for both groups, whereas arm skeletal muscle mass and leg skeletal muscle mass differed significantly. The control group had higher values of both arm and leg skeletal muscle mass compared with the intervention group ($p=0.008$ and $p=0.05$, respectively) (data not shown).

Table 6: Effects of the intervention in physical activity for the intervention and control group.

	Intervention group		Control group		
	Baseline	Change[1]	Baseline	Change[1]	**p-value change**
Total PA (min/day)	296.3 (±99.6)	5.0 (±72.8)	293.2 (±91.3)	-6.2 (±65.6)	0.240
LPA (min/day)	193.0 (147.3, 247.7)	0.7 (-38.2, 35.4)	183.9 (151.2, 223.8)	1.7 (-28.2, 35.4)	0.974
MPA (min/day)	79.0 (48.0, 136.6)	-1.2 (-28.4, 24.7)	81.9 (43.5, 140.7)	-4.3 (-36.8, 18.0)	0.286
VPA (min/day)	1.0 (0.0, 3.8)	0.0 (-0.4, 1.5)	0.7 (0.0, 2.4)	0.0 (-0.7, 0.8)	0.424
MVPA (min/day)	84.0 (48.3, 145.3)	1.2 (-25.6, 30.9)	85.7 (44.2, 143.5)	-4.2 (-41.4, 18.4)	0.209
Total sedentary time (h/day)	18.5 (±1.7)	-0.0 (±1.2)	18.6 (±1.6)	0.1 (±1.2)	0.204
Steps per day (1000steps/day)	6.4 (4.1, 8.6)	0.2 (-1.1, 1.9)	6.0 (4.2, 8.9)	-0.1 (1.6, 1.0)	0.186
Average METs	1.3 (±0.2)	0.0 (±0.1)	1.3 (±0.2)	0.0 (±0.1)	0.126

Data available for all participants. All variables are presented as median with percentiles (p25, p75), except for total PA, sedentary time and average METs which is presented as mean with standard deviation (SD).

ANCOVA was used to compare the change between the intervention and control group with controlling for baseline values on normally distributed data, otherwise Mann-Whitney U-test was used.

[1]Change from baseline to 12 months follow-up visit.

Abbreviations: PA = physical activity, LPA = total light intensity physical activity, MPA = total moderate intensity physical activity, VPA = total vigorous intensity physical activity, MVPA = total moderate-to-vigorous intensity physical activity, MET = metabolic equivalent.

Table 7: Effects of the intervention in physical function and body composition for the intervention and control group.

		Intervention group		Control group		
	n[1] (V2/V4)	Baseline	Change[2]	Baseline	Change[2]	**p-value change**
Sit-to-stand test	149/162	15.7 (±4.9)	2.2 (±3.7)	15.6 (±4.8)	1.8 (±3.0)	0.473
6 min walking test (m)	120/99	588.7 (±83.2)	37.0 (±66.3)	566.5 (±109.9)	32.1 (±32.5)	0.661
Max hand-grip strength (right)(kg)	166/165	32.0 (±9.5)	1.3 (±3.3)	32.4 (±10.1)	0.9 (±3.4)	0.417
Max hand-grip strength (left)(kg)	165/164	29.3 (±8.7)	1.2 (±3.8)	29.9 (±10.1)	1.3 (±3.2)	0.739
Muscle mass BIA (%)	160/165	43.7 (±7.6)	1.5 (±3.9)	43.4 (±6.7)	1.3 (±4.0)	0.695
Fat mass BIA (%)	160/165	31.8 (±8.0)	1.4 (±3.3)	31.6 (±7.7)	1.5 (±3.5)	0.877
Fat free mass BIA (%)	160/165	68.2 (±8.0)	-1.4 (±3.3)	68.4 (±7.7)	-1.5 (±3.5)	0.900
Total lean body mass DXA (%)	58/106	63.3 (57.2, 67.2)	-0.7 (-2.8, 0.6)	63.4 (58.1, 67.7)	-1.1 (-3.3, 0.4)	0.431
Arm skeletal muscle mass DXA (kg)	58/106	4.9 (3.7, 6.2)	0.1 (0.0, 0.3)	5.9 (4.1, 7.3)	0.0 (-0.2, 0.2)	0.168
Leg skeletal muscle mass DXA (kg)	58/106	15.6 (12.3, 17.1)	-0.1 (-0.5, 0.6)	18.6 (13.5, 20.4)	0.1 (-0.2, 0.8)	0.293

Values are presented as mean with standard deviation (SD), except for the DXA measures that is presented as median with percentiles (p25, p75). ANCOVA was used to compare the change between the intervention and control group with controlling for baseline values on normally distributed data, except for on 6-min walking test were the assumptions were violated and independent samples t-test was used. Mann-Whitney U-test was used on the non-normally distributed data.

[1]Number of participants with available data at baseline (V2) and 12-months follow up (V4) for the total study population.

[2]Change from baseline to 12 months follow-up visit.

4.2.4 Effect of the 12 months intervention for the total study population

Because both groups received the same advices and incentives on physical activity, the effects of time and gender in the total study population were investigated further for the total study population.

Physical activity

The effect of time, from baseline to 12 months on physical activity and sedentary time was investigated by performing paired analysis (**Table 8**). There was no significant change from baseline to 12-months follow-up in neither of the physical activity measurements for the total study population.

Physical function and body composition

Table 9 presents the changes from baseline to 12-months follow-up in physical function and body composition for the total study population.

For all the physical function measures, which include 30STS, 6MWT and hand-grip strength, significant increases from baseline to 12-months follow-up were found for the total study population.

Both fat mass and muscle mass, obtained through BIA increased significantly during the intervention period. Fat-free mass decreased significantly. A significant decrease from baseline to 12-months follow-up was observed for total lean body mass, whereas an increase was found for arm skeletal muscle mass, both obtained by DXA scan. No change was found for leg skeletal muscle mass.

Anthropometric measures

Within the total CRC-NORDIET population, significant changes were observed for weight, BMI, waist circumference and hip circumference during the 12 months intervention. All the measures increased during the intervention period (Table 9).

Table 8: Change in physical activity for the total study population during the intervention period.

	Baseline	Change[1]	p-value change
Total PA (min/day)	294.9 (±95.5)	-0.2 (±69.5)	0.971
LPA (min/day)	189.6 (149.7, 237.5)	1.2 (-35.4, 30.7)	0.973
MPA (min/day)	81.6 (44.0, 139.0)	-2.3 (-33.2, 20.3)	0.338
VPA (min/day)	0.8 (0.0, 3.5)	0.0 (-0.5, 1.0)	0.182
MVPA (min/day)	85.0 (45.0, 143.6)	-1.5 (-28.1, 25.0)	0.640
Sedentary time (h/day)	18.6 (±1.7)	0.0 (±1.2)	0.665
Steps (1000 steps/day)	6.2 (4.1, 8.7)	0.06 (-1.4, 1.3)	0.635
Average METs	1.3 (±0.2)	0.0 (±0.1)	0.250

Data available for all participants. Values are presented as median with percentiles (p25, p75), except for total PA, sedentary time and average METs which is presented as mean with standard deviation (SD).
Paired samples t-test was used to investigate the change from baseline to 12 months on normally distributed data, otherwise Wilcoxon signed rank test was used.
[1]Change from baseline to 12 months follow-up visit.
Abbreviations: PA: physical activity, LPA: total light intensity physical activity, MPA: total moderate intensity physical activity, VPA: total vigorous intensity physical activity, MVPA: total moderate-to-vigorous intensity physical activity, MET: metabolic equivalent.

Table 9: Effects of the intervention in anthropometry, physical function and body composition in the total study population

	n[1] (V2/V4)	Baseline	Change[2]	p-value change
Anthropometry				
Weight (kg)	167/166	77.9 (±16.8)	1.9 (±5.4)	<0.001**
BMI(kg/m^2)	167/166	26.2 (±4.8)	0.6 (±1.8)	<0.001**
Waist circumference (cm)	167/166	93.3 (±14.5)	0.6 (±5.7)	0.033*
Hip circumference (cm)	167/166	100.7 (±9.5)	1.1 (±4.7)	0.003*
Physical function				
Sit-to-stand test (30STS) (n)	149/162	15.6 (±4.8)	2.0 (±3.4)	<0.001**
6 min walking test (6MWT) (m)	120/99	578.7 (±96.4)	35.1 (±55.3)	<0.001**
Max hand-grip strength (right)(kg)	166/165	32.2 (±9.8)	1.1 (±3.3)	<0.001**
Max hand-grip strength (left)(kg)	165/164	29.6 (±9.4)	1.2 (±3.5)	<0.001**
Body composition				
Muscle mass BIA (%)	160/165	43.4 (±7.4)	1.4 (±3.9)	<0.001**
Fat mass BIA (%)	160/165	31.5 (±7.8)	1.4 (±3.4)	<0.001**
Fat free mass BIA (%)	160/165	68.3 (±7.8)	-1.4 (±3.3)	<0.001*
Total lean body mass DXA (%)	58/106	63.3 (57.9, 67.4)	-0.9 (-3.1, 0.5)	0.001*
Arm skeletal muscle mass DXA (kg)	58/106	5.2 (4.0, 6.6)	0.1 (-0.1, 0.2)	0.037*
Leg skeletal muscle mass DXA (kg)	58/106	16.3 (13.4, 19.8)	0.1 (-0.3, 0.7)	0.263

*p-value<0.05, **p-value<0.001. Values are presented as mean with standard deviation (SD), except for the DXA measures that are presented as median with percentiles (p2, p75).
Paired samples t-test was used to investigate the change from baseline to 12 months on normally distributed data, otherwise Wilcoxon signed rank test was used.
[1]Number of participants with available data at baseline (V2) and 12-months follow-up (V4).
[2]Change from baseline to 12 months follow-up visit.

4.3 Impact of gender and clinical factors for physical activity and function at baseline

4.3.1 Impact of gender on physical activity

Table 10 presents the data extracted from the SenseWear armband at baseline, for the total population and separated by gender. At baseline the total physical activity level for the CRC-NORDIET study population was 4.9 hours per day. When dividing this into intensity levels, most of the physical activity performed was of light intensity, followed by moderate intensity which contributed to approximately one third of the total physical activity. Little time was spent in vigorous intensity activity. The participants spent the majority of the day being sedentary, in total 77% of the day included sleeping. Total steps per day were measured to be 6258 and the average METs per day was 1.3. The participants had high compliance with wearing the armband to measure the physical activity, with the armband being used 98.0±1.8% (mean ± SD) of the time during 6.0±0.7 (mean ± SD) days of monitoring.

When comparing the physical activity levels in men and women, men were found to spend significantly more time in moderate, vigorous, and moderate-to-vigorous physical activity than women ($p=0.012$, $p<0.001$ and $p=0.004$, respectively). There were no significant differences between the genders in total physical activity, sedentary time, steps or METs, but a trend towards women spending more time in light physical activity than men ($p=0.069$).

Table 10: Physical activity at baseline for the total study group

	All (n=167)	Men (n=83)	Women (n=84)	p-value[1]
Total PA (min/day)[2]	294.0 (±96.0)	294.0 (±90.0)	294.0 (±102.0)	0.809
LPA (min/day)[3]	189.6 (149.7, 237.5)	177.7 (146.7, 216.0)	198.3 (149.9, 251,9)	0.069
MPA (min/day)[3]	81.6 (44.0, 139.0)	89.8 (58.5, 149.6)	68.5 (38.2, 120.2)	0.012*
VPA (min/day)[3]	0.8 (0, 3.5)	1.5 (0.33, 6.2)	0.2 (0.0, 1.6)	<0.001**
MVPA (min/day)[3]	85.0 (45.0, 143.6)	99.3 (61.5, 163.2)	69.2 (38.4, 127.1)	0.004*
Sedentary time (h/day)[2]	18.6 (±1.7)	18.5 (±1.5)	18.6 (±1.8)	0.623
Steps (1000steps/day)[3]	6.2 (4.1, 8.7)	6.4 (4.1, 9.0)	5.9 (3.9, 8.0)	0.269
Average METs/day[2]	1.3 (±0.2)	1.4 (±0.2)	1.3 (±0.2)	0.706

*: p-values <0.05, **: p-value <0.001. [1]Difference between the genders, [2]Data presented as mean with standard deviation (SD), [3]Data presented as median and percentiles (p25, p75).
Independent samples t-test was performed to determine differences between the genders for normally distributed data. Mann-Whitney U-test was performed for the non-normally distributed data.
Abbreviations: PA: physical activity, LPA: light intensity physical activity, MPA: moderate intensity physical activity, VPA: vigorous intensity physical activity, MVPA: moderate-to-vigorous intensity physical activity, MET: metabolic equivalent.

4.3.2 Impact of gender on physical function and body composition

Table 11 presents the measurements regarding physical function and body composition from BIA and DXA at baseline for the total study population and by gender.

The average stands measured in the 30STS test was 15.6. In the 6MWT, the subjects walked in average 578.7 meters. The maximum hand-grip strength for the right hand was 32.2 kg and 29.6 kg for the left hand. The muscle mass measured by BIA at baseline was 43.4%, the fat mass was 31.5%, and the fat-free mass was 68.3%. Data from the DXA scan was only available for 58 participants at baseline. The total lean body mass measured by DXA was 63.3%, and the leg and arm skeletal muscle mass were 16.3 kg and 5.2 kg, respectively.

When looking at men and women separately, it was significant difference between the genders for all variables. The men had higher mean values in all of the variables, except for in fat mass.

Table 11: Physical function and body composition from BIA and DXA at baseline for the total study group

	All	Men	Women	p-value[1]
Physical function				
Sit-to-stand test (30STS) (n)[2]	15.6 (±4.8)	16.5 (±5.0)	14.9 (±4.6)	0.043*
6-min walking test (6MWT) (m)[3]	578.7 (±96.4)	606.8 (±101.6)	553.3 (±84.4)	0.002*
Max hand-grip strength (right) (kg)[4]	32.2 (±9.8)	39.9 (±6.7)	24.5 (±5.3)	<0.001**
Max hand-grip strength (left) (kg)[5]	29.6 (±9.4)	36.8 (±6.9)	22.5 (±5.0)	<0.001**
BIA[6]				
Muscle mass (%)	43.4 (±7.4)	46.9 (±6.1)	40.2 (±6.7)	<0.001**
Fat mass (%)	31.5 (±7.8)	28.1 (±5.8)	35.3 (±8.0)	<0.001**
Fat free mass (%)	68.3 (±7.8)	71.9 (±5.8)	64.7 (±8.0)	<0.001**
DXA[7]				
Total lean body mass (%)	63.3 (57.9, 67.4)	66.2 (62.8, 70.2)	61.4 (54.6, 64.2)	0.001*
Leg skeletal muscle mass (kg)	16.3 (13.4, 19.8)	19.9 (18.1, 21.4)	13.5 (12.0, 14.9)	<0.001**
Arm skeletal muscle mass (kg)	5.2 (4.0, 6.6)	6.6 (6.1, 7.4)	4.0 (3.7, 4.9)	<0.001**

*: p-value <0.05, **: p-value<0.001.
Data presented as mean with standard deviation (SD) for all variable, except from the variables from DXA which is presented as median with percentiles (p25, p75). [1]Difference between the genders.
Data available for: n=149[2], n=120[3], n=166[4], n=165[5], n=160[6], n=58[7].
Independent samples t-test was performed to determine differences between the genders for normally distributed variables, whereas Mann-Whitney U-test was performed on non-normally distributed data.

4.3.3 Impact of demographic characteristics, clinical factors and anthropometric measures on physical activity

Many factors may influence the level of physical activity in the CRC-NORDIET population. The following parameters were tested for correlation with the different physical activity intensities and sedentary time: anthropometric (weight, BMI, waist- and hip circumference), body composition (fat-mass, muscle mass, fat-free mass, lean body mass), demographic characteristics (age, work, marital status, education, smoking), clinical characteristics (TNM-stage, tumor localization, adjuvant treatment, operation type, ostomy, comorbidity) and physical function (6MWT, 30STS, hand-grip strength).

Association between physical activity and demographic characteristics

At baseline, there was no difference between the age groups for total-, light-, moderate-, moderate-to-vigorous physical activity or sedentary time (**Figure 4A)**. However there was a significant difference in vigorous physical activity across the age groups (p=0.042) (**Figure 4B**). Because the amount of time spent in vigorous physical activity (green color) is small and thus not visible in Figure 4A, a separate diagram as produced to indicate the difference between the age groups. Post-hoc analysis revealed that those in the oldest age group spent less time in vigorous intensity compared to the middle age group (p=0.045). The median time in vigorous physical activity among the oldest participants was 0.3 (0.0, 2.6) and 1.5 (0.2, 4.2) among those between 60-69 years.

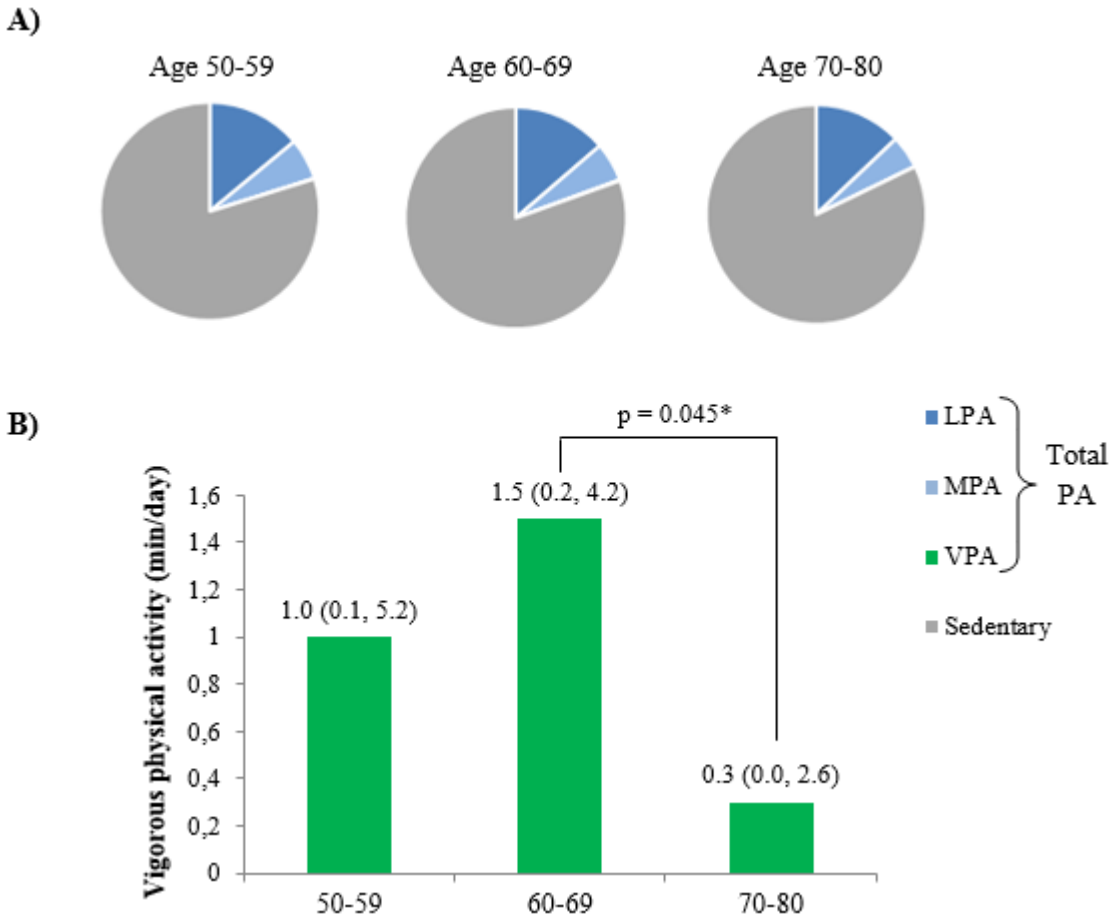

Figure 4, A-B: The distribution of physical activity across the age groups at baseline.
A) The circular chart show the distribution of sedentary time (grey), total physical activity (Total PA), light physical activity (LPA) (blue), moderate physical activity (MPA) (light blue), and vigorous physical activity (VPA) (green) during a day (24 hours) in the age groups; 50-59 (n=37), 60-69 (n=71) and 70-80 (n=59) years.
B) Time spent in vigorous physical activity for the three different age groups. The variables are presented as median with percentiles (p25, p75) and p-value from pairwise comparison between the two oldest age groups. *: p-value <0.05.

Between the three different education groups, there was a significant difference in moderate and moderate-to-vigorous physical activity (p=0.026 and p=0.041, respectively). Those with high-school as highest completed education had significantly lower time in moderate and moderate-to-vigorous physical activity compared to those in the collage/university group (p=0.024 and p=0.034, respectively) (**Figure 5**). No differences between the groups were found for the other physical activity intensities, total physical activity or sedentary time.

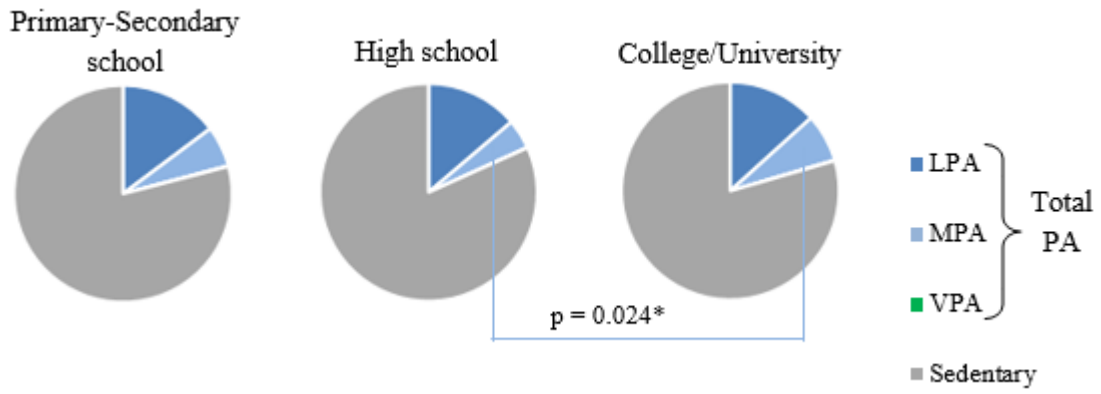

Figure 5: The distribution of physical activity across the education groups at baseline.
The circular chart show the distribution of sedentary time (grey), total physical activity (total PA), light physical activity (LPA) (blue), moderate physical activity (MPA) (light blue) and vigorous physical activity (VPA) (green) during a day (24 hours) in the three different education groups; primary-secondary school (n=11), high-school (n=52) and college/university (n=76). P-value from pairwise comparison between the education groups. *: p-value <0.05.

Smoking, work situation and marital status were not correlated to physical activity or sedentary time (data not shown).

Association between physical activity and clinical characteristics

When exploring the impact of TNM-stage on the level of total physical activity, the sum of light, moderate and vigorous physical activity, there was a statistically significant difference for the three TNM-stages (p=0.019). Post-hoc comparison indicated that the mean score for those with TNM-stage III (4.3±1.5) was significantly different from those with TNM-stage II (5.1±1.8) and TNM-stage I (5.1±1.3) (p=0.031 and p=0.044, respectively) (**Figure 6A**). There were also significant differences in moderate physical activity across the three different TNM-stages (p=0.047). Post-hoc analyses revealed that the subjects in TNM-stage III had a

significantly lower median score than the other two groups. However, this difference did not remain significant after Bonferroni adjustment for moderate physical activity, but there was a trend towards difference between those with TNM-stage III and I (p=0.067). Because the amount of time spent in vigorous physical activity (green color) is small and thus not visible in Figure 6A, a separate diagram was produced to indicate the difference between the TNM groups. A significant difference was found across the groups (p=0.005) and post hoc analysis revealed that TNM III was significantly different from both TNM I and TNM II (p=0.005 and p=0.051 respectively) (**Figure 6B**).

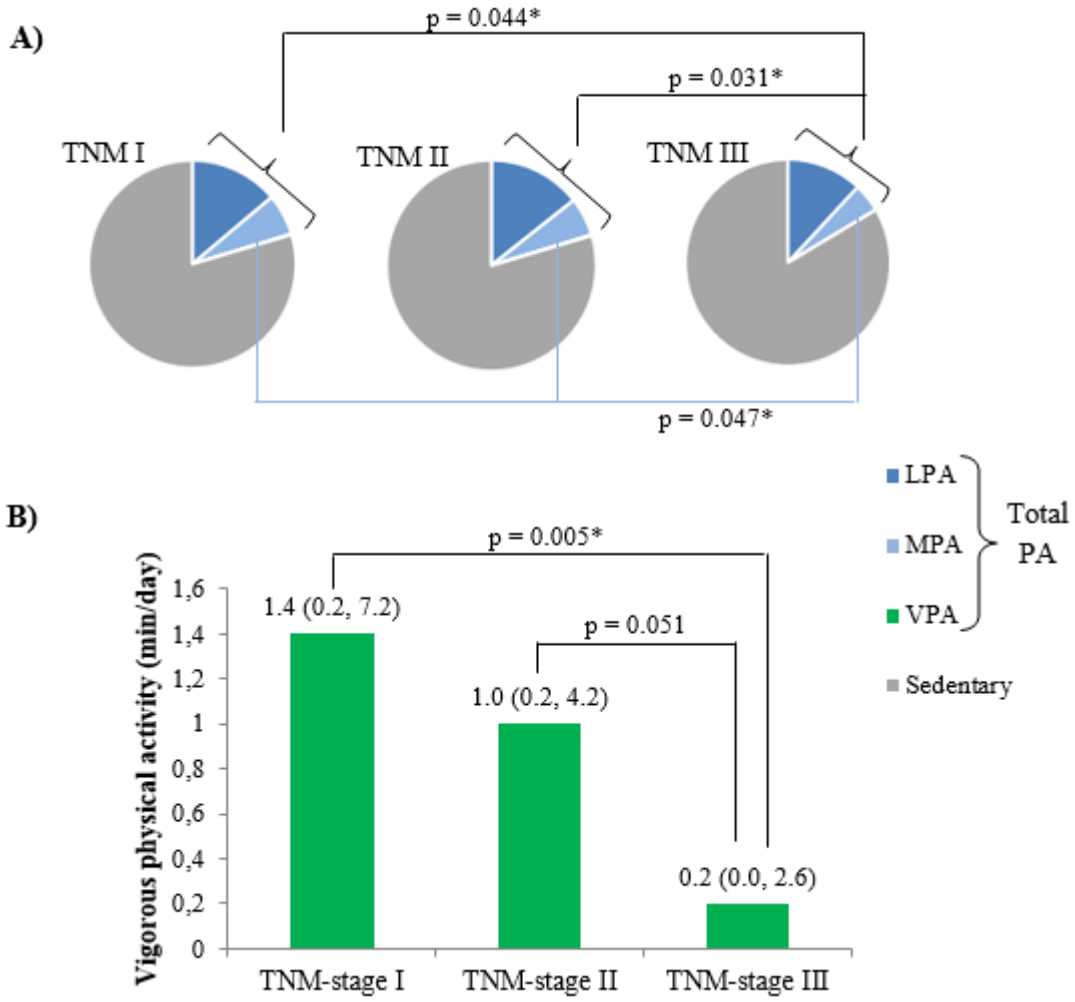

Figure 6, A-B: The distribution of physical activity across the TNM-stages at baseline.
A) The circular chart show the distribution of sedentary time (grey), total physical activity (Total PA), light physical activity (LPA) (blue), moderate physical activity (MPA) (light blue) and vigorous physical activity (VPA) (green) during a day (24 hours) in the three TNM-stages; I (n=38), II (n=47) and III (n=39).
B) Time spent in vigorous physical activity for the three different TNM-stages. The variables are presented as median with percentiles (p25, p75) and p-values from pairwise comparison between the groups.
*: p-value <0.05.

With regard to the physical activity in the different cancer location groups, no difference were found between the groups in light-, moderate-, moderate-to-vigorous activity or sedentary time (**Figure 7A**). However, significant differences between the groups were found for vigorous physical activity (p=0.025). Post-hoc analysis revealed that those diagnosed with rectal cancer spent more time in vigorous intensity compared to those with colon cancer (p=0.021). The median time in vigorous physical activity among those with colon cancer was 0.3 (0.0, 2.6) and 1.3 (0.2, 5.8) among those with rectal cancer (**Figure 7B)**.

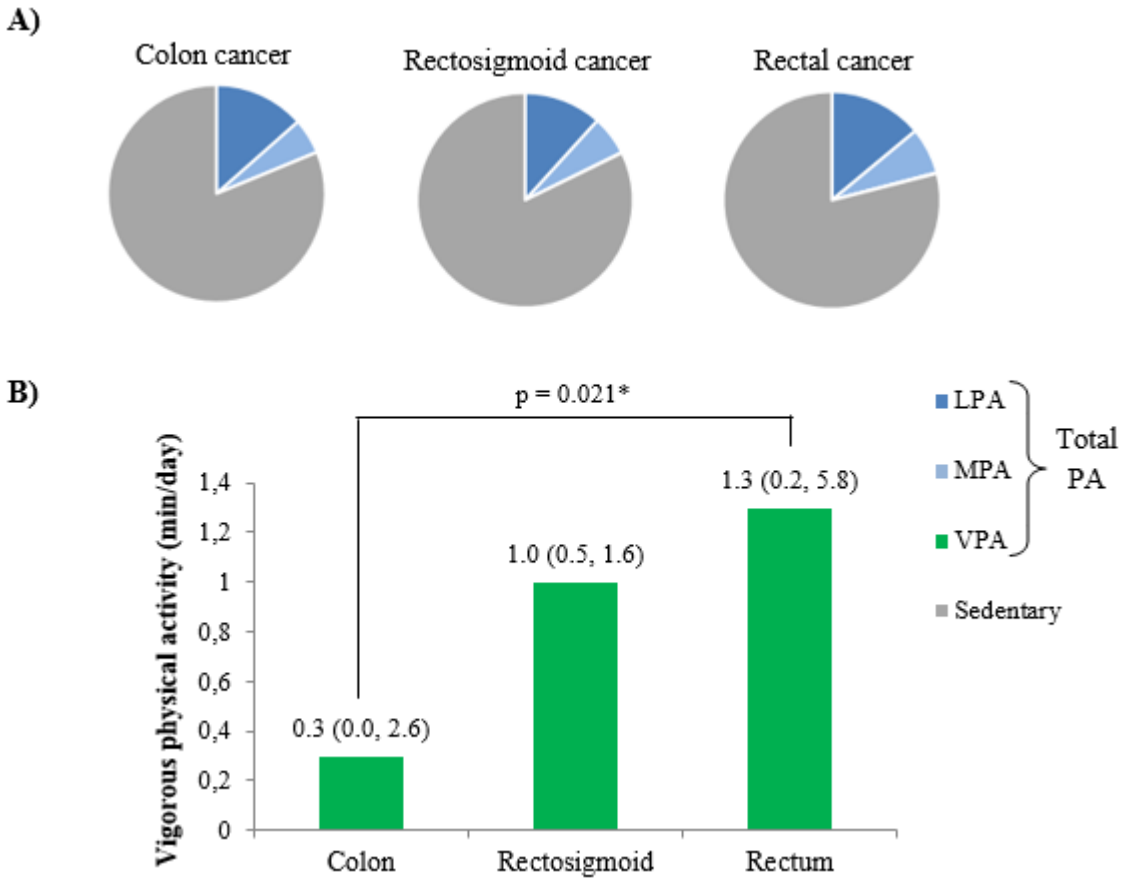

Figure 7, A-B: The distribution of physical activity in the different cancer location groups at baseline.
A) The circular charts show the distribution of sedentary time (grey), total physical activity (Total PA), light physical activity (LPA) (blue), moderate physical activity (MPA) (light blue) and vigorous physical activity (VPA) (green) during a day (24 hours) in the three cancer location groups; colon cancer (n=72), rectosigmoid cancer (n=11) and rectal cancer (n=54).
B) Time spent in vigorous physical activity for the three different cancer location groups. The variables are presented as median with percentiles (p25, p75) and p-value from pairwise comparison between the groups. *: p-value <0.05.

Receiving adjuvant treatment was associated with lower time in total physical activity (p=0.011), moderate physical activity (p=0.003) and moderate-to-vigorous physical activity (p=0.005), and significantly higher sedentary time (p=0.026) when comparing those who received treatment with those who did not (**Figure 8A).** Time in vigorous physical activity was also significantly different in the two groups (p<0.001). Median time in vigorous physical activity were 0.0 (0.0, 1.0) among those receiving adjuvant treatment and 1.0 (0.2, 5.2) in the no treatment group (**Figure 8B**).

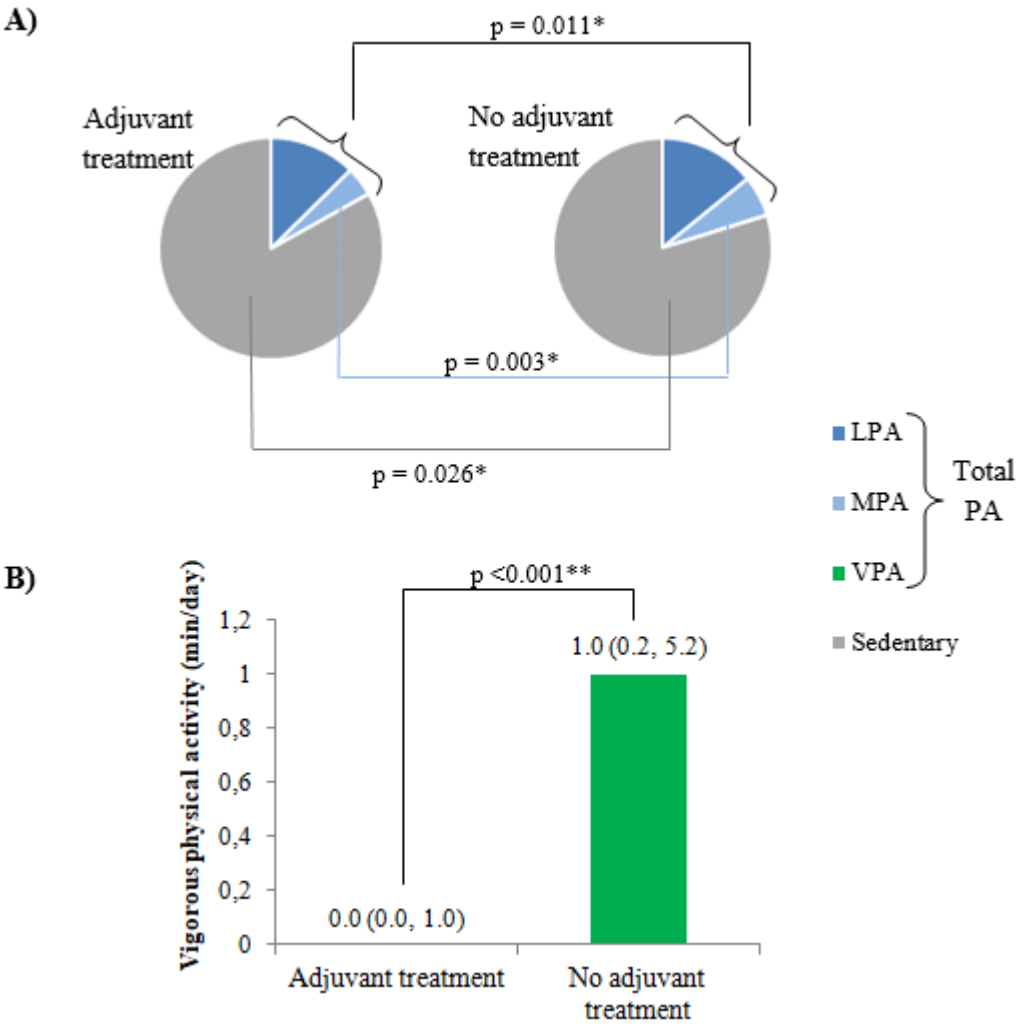

Figure 8, A-B: The distribution of physical activity among those receiving adjuvant treatment and those who not receive adjuvant treatment at baseline.
A) The circular charts show the distribution of sedentary time (grey), total physical activity (Total PA), light physical activity (LPA) (blue), moderate physical activity (MPA) (light blue) and vigorous physical activity (VPA) (green) during a day (24 hours) in the two treatment groups; adjuvant treatment (n=28) and no adjuvant treatment (n=102).
B) Time spent in vigorous physical activity for the treatment groups. The variables are presented as median with percentiles (p25, p75) and p-values from pairwise comparison between the groups.
*: p-value <0.05, **: p-value <0.001.

Analysis revealed that the level of total physical activity, light physical activity and sedentary time was significantly different across the three types of surgeries that are performed to remove the tumor (p=0.014, p=0.017, and p=0.017 respectively) (**Figure 9**). Post-hoc analysis found that those who had a surgery that was planned to be laparoscopic, but were converted to open spent significantly less time in total physical activity compared with both those who received laparoscopic and open surgery (p=0.016 and p=0.019 respectively). They also had significantly lower time in light physical activity than those who had open surgery (p=0.015). Sedentary time was significantly higher for this group compared to the other two groups (p=0.017 and p=0.030 respectively). No differences between the groups were found for moderate or vigorous physical activity.

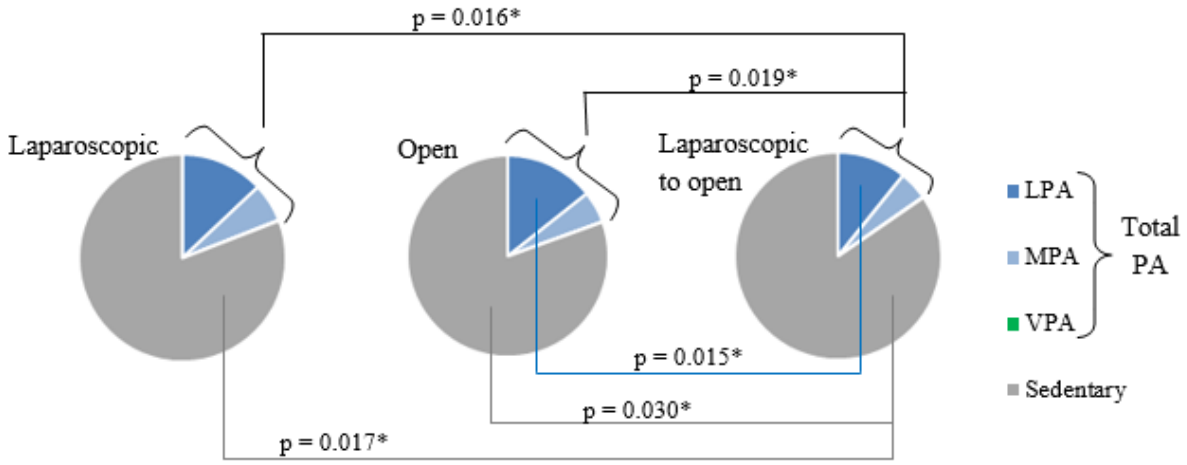

Figure 9: The distribution of physical activity across the different surgery types at baseline. The circular charts show the distribution of sedentary time (grey), total physical activity (Total PA), light physical activity (LPA) (blue), moderate physical activity (MPA) (light blue) and vigorous physical activity (VPA) (green) during a day (24 hours) among the three different surgery groups; laparoscopic (n=61), open (n=50) and laparoscopic to open (n=15). *: p-value <0.05.

When investigating the impact of BMI on the level of physical activity, there were significantly differences across the four BMI-categories for all the physical activity measures. Post-hoc analysis revealed that there was significant difference in total physical activity between BMI-category 2 and 4 ($p<0.001$), and BMI-category 3 and 4 ($p=0.002$). For sedentary time there was also significantly difference between BMI-category 2 and 4 (<0.001), and BMI-category 3 and 4 ($p=0.002$) (**Figure 10A**). For moderate physical activity and moderate-to-vigorous physical activity there were significant difference between BMI-category 1 and 4, 2 and 4, and 2 and 3. When comparing the different BMI-categories with regard to light physical activity, a significant difference was found between BMI-category 3 and 4 ($p=0.016$). For vigorous physical activity there were significant difference between BMI-category 1 and 4 ($p=0.044$), 2 and 4 ($p<0.001$), in addition to 2 and 3 ($p=0.039$) (**Figure 10B**). In conclusion, the activity level decreased with increasing BMI-category, whereas the sedentary time increased.

No association was found between physical activity and ostomy, time since surgery, or comorbidities (data not shown).

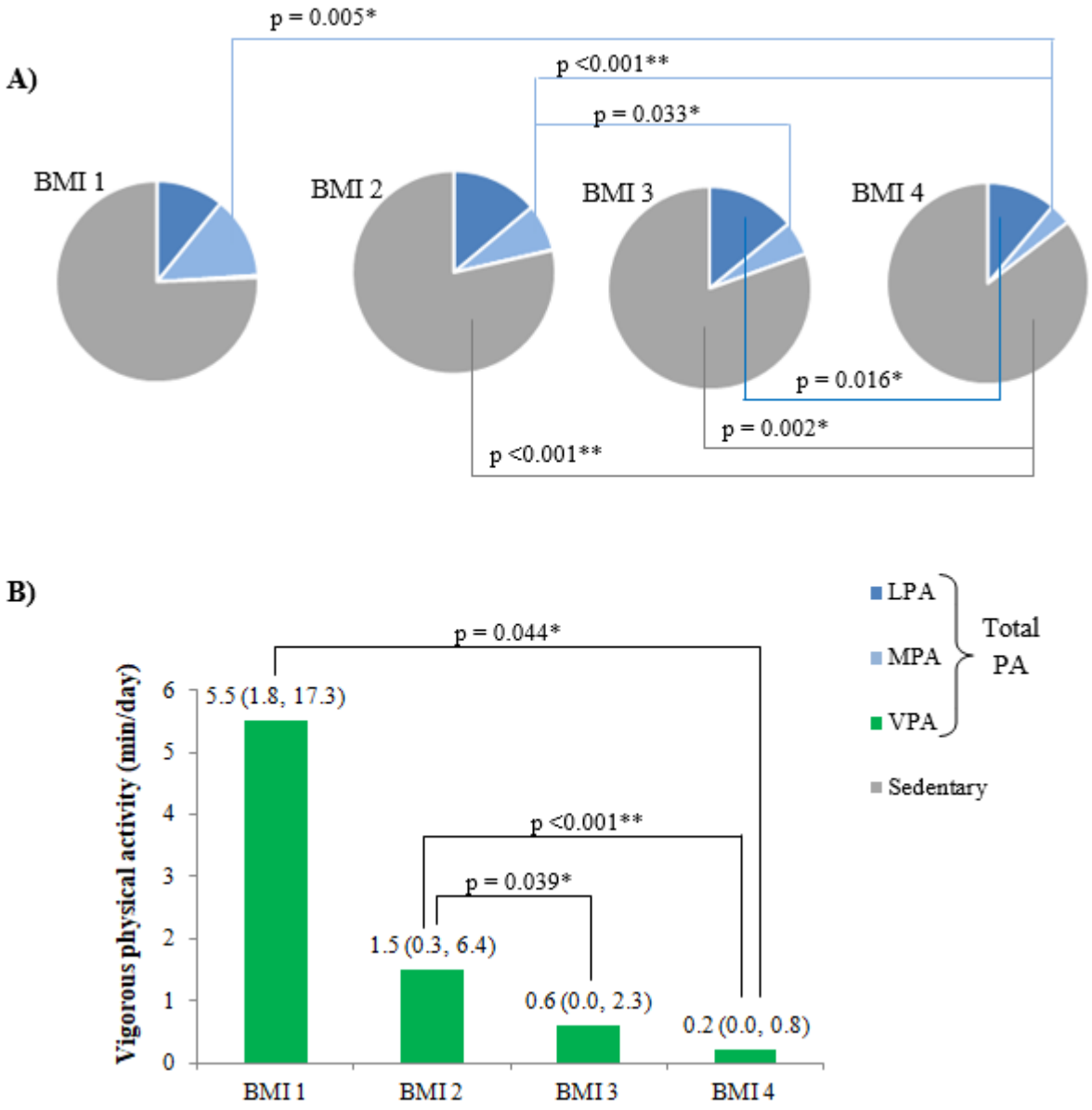

Figure 10, A-C: The distribution of physical activity across the BMI-categories at baseline.
A) The circular charts show the distribution of sedentary time (grey), total physical activity (total PA), light physical activity (LPA) (blue), moderate physical activity (MPA) (light blue) and vigorous physical activity (VPA) (green) in the four different BMI-categories: 1 (<18.5 kg/m^2) (n=3), 2 (18.5-24.9 kg/m^2) (n=62), 3 (25-29.9 kg/m^2) (n=74) and 4 (>30 kg/m^2) (n=28).
B) Time spent in vigorous physical activity for the BMI-categories. The variables are presented as median with percentiles (p25, p75), except for BMI 1 which is presented as median with max and min because n=3.
*: p-value <0.05, **: p-value <0.001.

Correlation between physical activity and anthropometric measures

The correlation between the physical activity measures and anthropometric measures including weight, BMI, waist circumference and hip circumference is displayed in **Table 12.** A significant and negative correlation was found between the anthropometric measures and all the physical activity measures except for light physical activity. The correlation coefficient indicated that the correlation varied between small and medium. A significant positive, medium correlation was found between sedentary time and all of the anthropometric measures. However, between vigorous physical activity and weight there was a trend towards a small correlation, but this were not significant ($p=0.067$). In conclusion, the higher weight, BMI, waist circumference and hip circumference, the lower were the time spent in moderate and vigorous physical activity, whereas the sedentary time were higher.

Correlation between physical activity and physical function

The correlation between the physical activity measures and the physical function measures; hand-grip strength, 30STS and 6MWT, are displayed in **Table 12.** A significant positive correlation was found between both left and right hand-grip strength and moderate, vigorous, and moderate-to-vigorous physical activity. The correlation coefficient indicated small to medium correlation. The correlation between the 30STS and total physical activity, moderate, vigorous, and moderate-to-vigorous physical activity were significantly positive, with a correlation coefficient that indicated medium to large correlation. A significant and medium negative correlation was found between sedentary time and the 30STS. A similar pattern as for the 30STS was also seen for the 6MWT. None of the measures correlated with light physical activity.

Correlation between physical activity and body composition

The correlation between the physical activity measures and fat mass, muscle mass, fat-free mass and total lean body mass is displayed in **Table 12.** The body composition measures significantly correlated with all of the physical activity measures except for light physical activity. The correlation coefficient indicated that the correlation varied between medium and large. The correlation between total physical activity, moderate, vigorous, and moderate-to-vigorous physical activity and muscle mass, fat-free mass and total lean body mass was positive. Fat-mass were negatively correlated with total physical activity, moderate, vigorous,

and moderate-to-vigorous physical activity. For sedentary time, the opposite were seen, i.e. the higher muscle mass, fat-mass and lean body mass, the less time is spent sedentary, whereas with higher fat-mass, the amount of sedentary time is higher.

Table 12: Correlation between physical activity and anthropometry, physical function and body composition.

	Total PA		LPA		MPA		VPA		MVPA		Sedentary	
	r	p-value	rho	p-value	rho	p-value	rho	p-value	rho	p-value	r	p-value
Weight (kg)	-0.313	<0.001**	-0.117	0.133	-0.265	0.001*	-0.143	0.065	-0.256	0.001*	0.314	<0.001**
BMI (kg/m^2)	-0.384	<0.001**	-0.084	0.281	-0.439	<0.001**	-0.350	<0.001**	-0.447	<0.001**	0.395	<0.001**
Waist circumference (cm)	-0.380	<0.001**	-0.170	0.028	-0.337	<0.001**	-0.217	0.005*	-0.333	<0.001**	0.369	<0.001**
Hip circumference (cm)	-0.330	<0.001**	-0.023	0.768	-0.426	<0.001**	-0.419	<0.001**	-0.435	<0.001**	0.354	<0.001**
Hand-grip strength right (kg)	0.065	0.404	-0.069	0.378	0.191	0.014*	0.305	<0.001**	0.225	0.004*	-0.074	0.341
Hand-grip strength left (kg)	0.087	0.265	-0.058	0.462	0.203	0.009*	0.295	<0.001**	0.227	0.003*	-0.110	0.160
Sit-to-stand test (30STS) (n)	0.378	<0.001**	0.062	0.450	0.496	<0.001**	0.470	<0.001**	0.522	<0.001**	-0.345	<0.001**
6 min walking test (6MWT) (m)	0.483	<0.001**	0.148	0.107	0.573	<0.001**	0.568	<0.001**	0.588	<0.001**	-0.469	<0.001**
Muscle mass BIA (%)	0.331	<0.001**	0.033	0.678	0.469	<0.001**	0.496	<0.001**	0.492	<0.001**	-0.311	<0.001**
Fat mass BIA (%)	-0.392	<0.001**	0.024	0.759	-0.553	<0.001**	-0.545	<0.001**	-0.574	<0.001**	0.386	<0.001**
Fat-free mass BIA (%)	0.393	<0.001**	-0.023	0.776	0.554	<0.001**	0.544	<0.001**	0.575	<0.001**	-0.387	<0.001**
Total lean mass DXA (%)	0.484	<0.001**	0.166	0.213	0.504	<0.001**	0.626	<0.001**	0.522	<0.001**	-0.453	<0.001**

*: p-value <0.05, **: p-value <0.001.
Normally distributed data are analyzed with Pearson's correlation, r = correlation confident. Non-normally distributed variables are analyzed Spearman`s correlation, rho = correlation coefficient.
Abbreviations: PA = physical activity, LPA = total light intensity physical activity, MPA = total moderate intensity physical activity, VPA = total vigorous intensity physical activity, MVPA = total moderate-to-vigorous intensity physical activity, BMI = body mass index.

4.3.4 Association between lean mass and physical function

The correlation between arm skeletal muscle mass and hand-grip strength and the correlation between leg skeletal muscle mass and 30STS were investigated. In addition, the correlation with total lean body mass for both hand-grip strength, 30STS and 6MWT were explored. This is presented in **Table 13** and **Table 14**.

We found that there was a significant and strong correlation between arm skeletal muscle mass and both left and right hand-grip strength for the total study population at both baseline and 12-months follow-up (Table 13). This was also seen when investigating men and women separately. Furthermore, a medium and significant correlation was also seen between hand-grip strength and total lean body mass for the total study population. However, this association was not observed when separating the genders, except for a significant medium correlation among men at 12-months follow-up (Table 13).

When investigating leg skeletal muscle mass, no significant correlation were found with the 6MWT or the 30STS (Table 14). A medium to strong significant correlation were found both between 30STS and total lean body mass, and 6MWT and total lean body mass. However, among men at baseline, no significant correlation were found (Table 14).

Table 13: Correlation between hand-grip strength, and arm skeletal muscle mass and total lean body mass measured by DXA

		Baseline		12 months		Baseline		12 months	
		rho	p-value	rho	p-value	rho	p-value	rho	p-value
	n (V2/V4)[1]	Arm skeletal muscle mass (kg)				Total lean body mass (%)			
Max hand-grip strength (right) (kg)	58/104	0.854	<0.001**	0.889	<0.001**	0.404	0.002*	0.458	<0.001**
Men	28/46	0.548	0.003*	0.558	<0.001**	0.166	0.398	0.430	0.003*
Women	30/58	0.387	0.035*	0.710	<0.001**	0.109	0.565	-0.074	0.583
Max hand-grip strength (left) (kg)	58/103	0.851	<0.001**	0.870	<0.001**	0.475	<0.001**	0.485	<0.001**
Men	28/45	0.555	0.002*	0.535	<0.001**	0.143	0.469	0.309	0.039*
Women	30/58	0.338	0.068	0.677	<0.001**	0.351	0.057	0.113	0.399

*: p-value <0.05, **: p-value <0.001.
rho = Spearman's correlation coefficient.
[1]Number of participants with available data at baseline (V2) and 12-months follow up (V4) for the total study population.

Table 14: Correlation between 30STS and 6MWT, and leg skeletal muscle mass and total lean body mass measured by DXA.

		Baseline		12 months		Baseline		12 months	
		rho	p-value	rho	p-value	rho	p-value	rho	p-value
	n (V2/V4)[1]	Leg skeletal muscle mass (kg)				Total lean body mass DXA (%)			
Sit-to-stand test (30STS) (n)	58/103	0.036	0.786	0.138	0.163	0.430	0.001**	0.531	<0.001**
Men	28/46	-0.128	0.517	-0.014	0.926	0.292	0.139	0.494	<0.001**
Women	30/57	-0.102	0.592	-0.023	0.867	0.613	<0.001**	0.473	0.001*
6 min walking test (6MWT) (m)	47/57	0.262	0.075	0.190	0.156	0.528	<0.001**	0.527	<0.001**
Men	25/27	0.248	0.231	-0.065	0.746	0.189	0.400	0.534	<0.001**
Women	22/30	0.276	0.213	0.131	0.490	0.749	<0.001**	0.491	0.020*

*: p-value <0.05, **: p-value <0.001.
rho = Spearman's correlation coefficient.
[1]Number of participants with available data at baseline (V2) and 12-months follow up (V4) for the total study population.

5 Discussion

Physical activity is shown to have beneficial effects on CRC progression and health-related outcomes post-surgery. Therefore, both study groups in the CRC-NORDIET study were offered equal recommendations and incentives on physical activity to control the impact of physical activity and 'isolate' the health effects on the diet intervention.

However, it could be possible that the dietary intervention would impose an additional effect on physical activity. The primary aim of this master thesis was therefore to explore if the 12-months dietary intervention had a differential effect on the amount of physical activity in the intervention group as compared to the control group. Moreover, physical function was investigated from baseline to 12 months in both study groups. Associations between physical activity and demographic, clinical and anthropometric characteristics were also investigated.

The results from this master thesis indicated no additional effect of a one-year dietary intervention on the level of physical activity. However, significant improvements in the measurements of physical function (i.e. 30STS, 6MWT and hand-grip strength) were seen for the total study population. Several factors affected the level of the different physical activity intensities in addition to sedentary time, such as gender, age, BMI, TNM-stage, tumor localization, operation type, adjuvant treatment and education.

5.1 Methodological considerations

5.1.1 Study population

In this master thesis the CRC-NORDIET population was found to have a high baseline level of physical activity compared to that of healthy Norwegian individuals (132). This might indicate that the study is limited by selection bias, which is common for RCTs investigating lifestyle (133, 134). Willingness to participate increases with higher education and already a focus on a healthy lifestyle, resulting in enrolling of healthier participants as compared to the population from which they are drawn. This can result in failing to recruit those subjects who

would have had the highest benefit in participating in the study (135). This is a known problem and previous studies have found that cancer patients with greater comorbidity and lower socioeconomic status is often underrepresented in RCTs (133). In a Norwegian lifestyle intervention in cancer patients undergoing chemotherapy, the 'I CAN' study (136), a higher baseline physical activity level among the completers vs. the dropouts were observed. In addition more completers vs. dropouts were non-smokers and had healthier dietary habits. Selection bias may thus affect the generalisability of the results from the study (137).

In the CRC-NORDIET study a commonly mentioned reason for not participating were having side effects from the cancer, surgery or treatment like symptoms, fatigue, pain, and thus not feeling healthy or well enough to participate (unpublished data). Therefore those with the poorest health conditions and those who might had benefit the most of participating in the study, may not have been included, leading to selection bias.

5.1.2 Physical activity assessments

Time spent in different physical activity intensities varies greatly among different objective physical activity assessments, in addition different activity monitors record different aspects of physical activity such as acceleration, position changes, heart rate, and so on. Therefore it may be a challenge comparing results of physical activity from different studies (114).

In the CRC-NORDIET study, the participants' daily physical activity was recorded by the SenseWear armband, in addition, self-reported physical activity was collected through a questionnaire. The physical activity questionnaire used in the CRC-NORDIET study has been validated with the SenseWear armband as reference method by Henriksen *et al.* (138), and found to under-report all intensities of physical activity This might have been due to few questions to report physical activity in the questionnaire, resulting in less opportunity to report all physical activity. Additionally, the SenseWear armband monitors all time in all intensities of physical activity during all day and night. Consequently, total time in different intensities of physical activity will be larger as compared to a few questions in the questionnaire. Several of the intervention studies on physical activity among CRC survivors have also used questionnaires. Vassbakk-Brovold *et al*. (139) compared a different physical activity questionnaire (IPAQ-sf) with the SenseWear armband in cancer patients undergoing chemotherapy, and found that the patients reported significantly higher levels of moderate and

vigorous physical activity when using the questionnaire. The IPAQ-sf contained more questions regarding physical activity than the questionnaire used in Henriksen *et al.* Additionally, Vassbakk-Brovold *et al.* emphasized that cancer patients may feel breathlessness at lighter intensities than normal, resulting in over-reporting of physical activity.

The SenseWear armband was preferred in the CRC-NODIET study to objectively measure physical activity and sedentary time as it is practical, relatively inexpensive and easy-to-use. In addition, it has been validated against both indirect calorimetry in cancer patients and healthy adults (113, 114) and doubly labeled water in healthy adults and older adults (112, 116, 140), and showed to be a valid and reliable measurement method. However, the SenseWear armband may slightly overestimate the level of physical activity when compared to indirect calorimetry (114). Berntsen *et al.* (114) found that the armband overestimated time in moderate-to-vigorous activity with 2.9%. Other studies have also found that the SenseWear armband is not as sensitive in estimating the level of physical activity at high intensities as lower intensities (141, 142). However, most other monitors used to measure physical activity in clinical trials either under- or over-estimate the physical activity levels (114).

When four commonly used monitors were compared with indirect calorimetry, ActiGraph showed similar overestimation of moderate-to-vigorous activity as the SenseWear armband with 2.5 % overestimation. Ikcal and ActiReg on the other hand were found to underestimate time in moderate-to-vigorous activity with 11.6% and 98.7%, respectively (114).

Calabro *et al.* (143) who also compared different activity monitors found that multi-sensor monitors like SenseWear armband and Actiheart provided more accurate estimates on sedentary, light and moderate intensity activities compared to accelerometry-based activity monitors like ActiGraph and ActivPAL.

Although discomfort in wearing (i.e. skin irritation) the SenseWear armband has been reported in previous studies (144), the armband was well tolerated among the participants in the present study.

5.1.3 Statistics

ANCOVA adjusts each participant's follow-up score for his or her baseline score, and thereby is not affected by any baseline differences between the groups (145). As the model uses two measurements (i.e. baseline and follow-up) for each participant instead of only one (i.e. the change between baseline and follow-up), this method has great statistical power. A frequently used model in the ANCOVA analyses is the one by Vickers and Altman (145): Follow-up score = constant + a x baseline score + b x group.

The ANCOVA could not be applied on all of the variables regarding physical activity, physical function and body composition in the current thesis because of violation of several of the models assumptions. The Mann-Whitney test was therefore performed in order to compare the change over time (Follow-up score – baseline score) between the two study groups. The change score does not control for baseline imbalance because of regression to the mean, however, for most of the measures in the present thesis there were no significant differences between the groups at baseline.

5.1.4 Sample size

The power calculation for assessing intervention effects on physical activity in this master thesis was based on the effect size obtained in a telephone-delivered multiple health behavior change RCT (CanChange) in CRC survivors (44) (see Method section, section 3.5). A sample size of 157 subjects in each group was required to achieve a significant level of 5 % and power of 80 % to show this effect. In the present master thesis, we were able to include about half of this size (i.e. 89 and 78 subjects from the intervention and control group, respectively), which reduces the power to detect the estimated effect size.

However, it is important to note that in the 'CanChange' study the controls received no intervention on physical activity. Because both groups in the CRC-NODIET study received similar advices on physical activity, in order to isolate the effect of the diet, it is likely that we would not obtain similar differences between the groups.

For these reasons the lack of reduction in power should be taken into consideration when interpreting the results from this master thesis.

5.2 Discussion of the results

5.2.1 Participant characteristics

The CRC-NORDIET study population is slightly younger than the average age at CRC diagnosis in Norway (5). However, compared with other intervention studies among CRC survivors, our study population is approximately similar with regard to age, gender distribution, smoking and marital status (44, 90, 105, 146). The CRC-NORIDET study population had a higher education level and a lower share of smokers as compared to the general Norwegian population (147). Most of the CRC-NORDIET participants had completed education at the university or college level, which is in accordance with other cancer survivors participating in intervention studies (136, 146). More than half of the participants in this study were overweight or obese, which is in line with findings from other studies involving CRC patients (44, 146), but much higher than the general Norwegian population (i.e. 28% people with a BMI over 25 kg/m^2 in 2015) (147).

Colon cancer was the most common cancer type in this present study, which is along with the general Norwegian CRC-population (5), as well as other studies among CRC survivors (44, 146). With regard to comorbidity, both prevalence and the type of diseases in the present study are similar with findings among other CRC patients (47), but the prevalence has been reported to be even higher in the 'CanChange' study (44). Proportion of patients within the TNM-stages I-III in CRC-NORIDET population was similar as in the population of the 'CanChange' study (44). The number of participants receiving adjuvant treatment was also quite similar in these two studies. However, other studies have reported a higher share of the patients with more severe cancer stages and a higher share of patients receiving adjuvant treatment (105, 146).

In conclusion, the CRC-NORDIET population seems quite comparable to other CRC-populations as well as comparable to the general Norwegian population. However, the CRC-NORDIET participants are slightly healthier than other CRC-populations with regard to severity of disease, comorbidities and adjuvant treatment.

5.2.2 Physical activity and physical function at baseline

The level of physical activity in the CRC-NORDIET compared to general Norwegian older adults and other CRC populations

Compared to older adults in Norway, the level of moderate-to-vigorous activity was higher in the CRC-NORDIET population; whereas the level of light activity and steps per day was lower (132). Lohne-Seiler *et al.* (132) measured the level of physical activity among Norwegian older adults aged 65-85 years using accelerometer, and found that the participants spent 10 min more in light activity and walked 400 more steps than observed in the CRC-NORDIET study. Furthermore, the level of moderate-to-vigorous activity was 57 min lower than observed in the present study (132). However, the age span in the study of Lohne-Seiler *et al*. appeared to be narrower than the present study and did not include the ages of 50-64 years. In addition they used a different method to measure activity. It is also worth mentioning that the values are presented in median in our study, whereas in mean in the study of Lohne-Seiler *et al*.

Most of the studies conducted on CRC patients have used self-reported data on physical activity from questionnaires, which is not totally comparable with the objective measurement used in the present master study. The physical activity level in the CRC-NORIDET population was higher than most CRC studies, which might reflect the different assessments used. In the 'CanChange' study (44), which included participants that is quite similar with our population, the physical activity at baseline (6 months after diagnosis) was measured with the Godin Leisure-Time Exercise Questionnaire. They found that mean time in moderate-to-vigorous activity was 58 min/week and 52 min/week in the intervention and control group respectively. This is much lower than observed in our study considered that the populations have quite similar characteristics. The same questionnaire was used in another study among CRC survivors by Courneya *et* al. (146), which documented higher amounts of time in moderate-to-vigorous activity (i.e. 91 min/week and 97 min/week in the intervention and control group, respectively) than the 'CanChange' study. Moreover, a higher share of the participants in the study of Courneya *et al*. were in cancer stage III and IV and received adjuvant treatment compared with the CRC-NORDIET population. In the 'I CAN' study (139) among Norwegian cancer patients with different cancer types (colorectal, breast and prostate) undergoing chemotherapy, physical activity were measured with both a

questionnaire and the SenseWear armband at baseline. Time spent in moderate-to-vigorous physical activity was 182 min/week. Although all of these patients underwent chemotherapy, the physical activity was higher than the other previously mentioned studies, but lower than the present study. Again, this can reflect the different methods for assessing physical activity.

In conclusion, our CRC population had a higher level of moderate-to-vigorous physical activity that what has previously been reported among CRC survivors, although the comparison of the studies are difficult as different methods for assessing physical activity is used. Another reason for the large differences in physical activity among different studies, might also be that Norwegian cancer survivors are more physically active than those in other countries (i.e. Australia and Canada).

The recommendations for physical activity from The Norwegian Directorate of Health is at least 150 min/week of moderate-to-vigorous physical activity performed in bouts of at least 10 min (55). Since calculation of physical activity measured in 10-min bouts were not available in the present master thesis, a correct estimate of percentage of the participants reaching the recommendations for physical activity was therefore not possible. However, 93 % of the CRC-NORDIET participants fulfilled the recommendation of at least 150 min/week when including all time in moderate-to-vigorous physical activity. In a pooled analysis from four European countries, including Norway, the percentage of adults aged 25-75 years reaching the recommendation for physical activity was approximately 70 % when based on total time in moderate-to-vigorous activity (63). However, the percentage of adults reaching the recommendations decreased to approximately 30 % when based on 10-min bouts of moderate-to-vigorous activity (63). Similar finding were also seen when only investigating the results from Norway (62). Therefore, the number of participants in the CRC-NORDIET study reaching the physical activity recommendations most likely is much lower than found when using total time in moderate-to-vigorous activity.

The average METs can be used to say something about a subject's general activity level. Although the level of physical activity is relatively high in the CRC-NORDIET population compared to healthy adults and cancer survivors, the average METs for the total study population this was found to be 1.3, which corresponds to a sedentary and relatively inactive lifestyle (148).

Physical function in the CRC-NORDIET study compared to general Norwegian older adults and other CRC-populations

Generally, physical function in the present study appeared to be lower as compared to an age-matched healthy Norwegian population (149). For instance, the participants in the present study performed less number of stands in the 30STS as compared to the Norwegian reference population (i.e. ranging from 17-24 for women and 19-25 for men as compared to 14.9 for women and 16.5 for men in the present study). Both men and women in the CRC-NORDIET study were within the range of distance walked in the 6MWT by the reference population. Regarding hand-grip strength, both men and women were in the lower layer of what would have been expected. The right hand-grip strength in the Norwegian reference population ranged from 24.3-30.3 kg for women and 40.1-47.8 kg for men, whereas in the CRC-NORDIET study this was found to be 24.5 kg for women and 39.9 kg for men.

In the 'CHALLENGE' study (105) among high-risk stage II- III colon cancer survivors, the mean distance walked in the 6MWT at baseline were 535 meter and 522 meter in the intervention and control group respectively. The mean number of stands from the 30STS was 13.4 and 14.1 in the intervention group and control group, respectively, which is lower than the CRC-NORDIET population in the present study. Tomruk *et al.* (150) reported the distance walked in the 6MWT to be even lower, 383 meter.

Longer distance walked in the 6MWT and better result in the 30STS was reported in a cross-sectional study among stage II-III CRC survivors approximately 1.4 years after diagnosis (i.e. 589 meter and 22 stands) (151), which is higher than in the present study. In an exercise intervention among stage II-III CRC survivors undergoing chemotherapy by Lin *et al.* (152), they assessed hand-grip strength and 6MWT approximately 1 month after surgery. They found that participants in the intervention group walked 491 meters and the control group walked 506 meters. The handgrip-strength was 28.8 and 29.5 in the intervention and control group respectively. Both distance walked and hand-grip strength was lower in this study compared to the CRC-NORDIET population. This might indicate that time since diagnosis may be of importance when measuring physical function in CRC populations.

In conclusion, our CRC population had a physical function level that is slightly lower than the general Norwegian population with the same age span, but had higher function level compared to other cancer populations.

5.2.3 Changes in physical activity and physical function from baseline to 12-months

Physical activity

No differences were seen between intervention and control group with regards to the change in the level of physical activity, steps, average METs and sedentary time. Since both groups received similar advice regarding physical activity, this was expected. However, since the dietary intervention group receives higher intensity of contact with the researchers from the CRC-NORDIET study than the control group due to more intervention strategies, it may promote physical activity to a greater extent than the control group. Results from the current master thesis indicated that this was not the case. Moreover, an increase in the level of physical activity during the 12 months intervention period in the total study group could have been expected, as both groups received similar advises on physical activity. In contrast to the findings in the present study, several previous intervention studies focusing on physical activity has reported changes in physical activity during the intervention period (44, 105, 153).

Those who choose to participate in a lifestyle study are often highly motivated to improve their health behaviors. As this was a relatively health and active population at baseline compared to Norwegian older adults (132) and other CRC-population (44, 139, 146), it could be speculated that the activity level already was good, and therefore difficult to improve. Studies have stated that the physical activity level after a CRC surgery is lower than before diagnosis, and that the activity level increases gradually in the post-treatment period (89). As few of the participants received adjuvant treatment and many of the participants had low grade CRC (stage I-II), it might have been that 4 months from surgery to baseline was enough time for the participants to recover after surgery. Consequently, the present study therefore was not able to detect the expected increase in physical activity after CRC surgery.

Contrary to our findings, the ‘CanChange’ study (44) found a significant difference between the intervention and control group in moderate and moderate-to-vigorous physical activity after 12 months. The intervention group received telephone-delivered health coaching sessions over 6 months focusing on physical activity, weight management, dietary intakes, alcohol and smoking habits. The control group only received freely available brochures on CRC, diet and physical activity. They also found that the sedentary time significantly

decreased from baseline to 12 months in both the intervention and control group, with no between-group differences with regard to change. The intervention group significantly decreased sedentary time with 1.21 hours after 12 months, and the control group with 0.55 hours (154).

Also in contrast to the results from the present study, the 'CHALLENGE' study (105) involving high-risk stage II and III colon cancer patients observed a significant difference for self-reported recreational physical activity between the intervention group and the control group after one year intervention. The intervention group received a structured exercise program, whereas the control group received general health education materials. Both groups were found to increase the amount of physical activity, but the increase observed for the intervention group was significantly higher than for the control group.

Grimmett *et al.* (153) conducted a 12-week feasibility study among CRC patients who had recently completed treatment, and investigated the effects of an intervention combining printed materials and telephone consultations to target multiple behavioral changes. Self-reported measures of physical activity increased significantly in both moderate and vigorous physical activity after the intervention, which is in contrast to the findings in the present study. Additionally, physical activity measured with accelerometer showed an increase of total activity in 10 min bouts and number of steps at follow-up compared with baseline.

In line with our results, the 'I CAN' study (136) among Norwegian cancer patients (breast, colorectal, prostate, others) undergoing chemotherapy did not find any significant changes in self-reported physical activity from baseline to end of study. This study aimed to increase adherence to healthy lifestyle behaviors and the participants received information about lifestyle recommendations and were offered monthly individual lifestyle counseling over a 12-month period.

Both the 'CanChange' study and the 'CHALLENGE' study mentioned above also observed changes in physical activity from baseline to follow-up in the control group. Some authors explain this with the population being highly motivated and are likely to have joined a behavior change study because they want to make changes. In addition, receiving education materials and having fitness testing can also contribute to a change in this group (44, 105). It was therefore unexpected to not observe any change in the physical activity among the CRC-NORIDET participants during the one year intervention period.

As described above, many previous studies have observed an increase in physical activity and a decrease in sedentary time during exercise and lifestyle interventions. However, there are some important differences between these studies and the CRC-NORDIET study. None of these studies, except for one, has used objective measurement for assessing physical activity, but only questionnaires. The participants also had lower level of physical activity at baseline; it therefore might be easier to achieve an increase in the activity level. In addition, the CRC-NORDIET study was not designed to detect changes in physical activity as physical activity was a secondary outcome.

Physical function

Despite no changes in physical activity from baseline to 12-months, the total CRC-NORDIET population significantly increased in all measures of physical function during the 12 months, both 6MWT, hand-grip strength and 30STS. They also increased their muscle mass and fat mass measured by BIA and the arm skeletal muscle mass measured by DXA. No change was observed for leg skeletal muscle mass, and there were no differences in change from baseline to 12 months between the intervention and control group.

One of the reasons for the lack of change in physical activity and the observed change in physical function might be related to the time of inclusion. The mean time since surgery was 4 months; this might have been enough time for the participants to have regained their activity level, but not their muscle strength and functional capacity regarding strength and endurance. Among elderly undergoing abdominal surgery, the hand-grip strength was found to be lower postoperatively compared to preoperatively. The grip-strength increased from 3 weeks after surgery to 6 months, but was at this point still lower than before surgery (88). The time from diagnosis might therefore be an important factor in detecting changes in physical function. Improvement in general health, more energy and better nutritional status could be other explanations for the observed change in physical function.

The findings of improved physical function among the participants in the current thesis are in line with other studies among CRC-patients. However, contrary to our findings, these studies have also observed significant differences between the study groups. In the ‘CHALLENGE’ study (105) among high risk stage II and III colon cancer survivors they observed an increase in the 6MWT from baseline to one year with 59 and 31 meters in the intervention and control group respectively. It was a significant difference between the two study groups. In the 30STS

they found that the number of stands increased with 4.1 in the intervention group and 2.5 in the control group from baseline to one year. The observed changes among the participants in the control group in the 'CHALLENGE' study is in line with the changes observed for both study groups in the CRC-NORDIET study. Similarly, a multicenter, telephone-based physical activity intervention conducted among breast and colorectal cancer survivors (Active After Cancer Trial) (155) found that both the exercise and control group experienced increases in 6MWT. From baseline to 16 weeks, the exercise group increased with 57 meters, whereas the control group increased with 25 meters, the difference between the groups was significant.

Also in line with the results in the current thesis, a supervised-exercise intervention among stage II-III CRC patients undergoing chemotherapy by Lin *et al.* (152) observed an increase in 6MWT and hand-grip strength in both the exercise and control group from baseline to 3 months, with no significant difference between the groups. The exercise group increased with 59 meter in the 6MWT and 1.74 kg in hand-grip strength, whereas the control group increased with 45 meter and 1.91 kg. Furthermore, the exercise group also achieved a significant increase in physical activity, but this was not found in the control group. This might indicate that the increase in physical function in CRC survivors is independent of changes in physical activity.

Another possible reason for the observed improvements in the measurements of physical function in the total CRC-NORDIET population might be due to learning effect. As the 6MWT, 30STS and hand-grip strength was completed at every visit to the study center, a possible learning effect may have occurred between baseline and one-year follow-up, because the participants benefit from the experience of the first time. Other studies have shown that walking distance tend to increase with repeated tests. It is proposed that a learning effect occurs because of familiarity with the test, improved pacing, habituation to dyspnea, recognition of the limits of the test and because of the desire to improve from last time (156, 157). The extent of the reported learning effect varies from study to study. Most of the previous studies have conducted the repeated measures on the same day or with a few weeks or months between, and not 6 months as in our study. However, whether the learning effect persists for this long time is uncertain. Factors known to potentially influence results of walking tests includes learning, motivation, and methodological variables as instruction, encouragement and disruptions while walking (158). Since it has been shown that a learning effect is observed in the performance of walk tests, studies indicate that practice sessions are

necessary to establish optimal performance, instead of just a single walk as in this present study (159).

5.2.4 Factors associated with physical activity

The results of this master thesis revealed that the level of physical activity to various extents were affected by gender, age, BMI, TNM-stage, cancer location, operation type, adjuvant treatment and education.

Our results are in line with previous reports in CRC populations where gender, BMI, age, education and treatment have been found to affect the adherence to physical activity and the likelihood of meeting the recommendations after CRC diagnosis (160-162). However, contrary to our findings, comorbidities, stoma, work situation and smoking has also been found to affect physical activity (160-162). Higher physical activity has been reported by CRC survivors who were younger, unmarried, higher educated, wealthier, employed, non-smokers, social drinkers, not treated with radiation therapy, in better health and had less comorbidity (74).

Gender

In the present study, men were found to spend more time in moderate and vigorous intensity activity compared to women, whereas women spent more time in light physical activity compared to men. This is consistent with findings among healthy Norwegian and US older adults (132, 163). Among Norwegian older adults (132), men were also found to accumulate more minutes in sedentary time than women, in contrast to the present study which did not find any differences between the genders in sedentary time. A suggested reason for why women was found spending more time in light activity might be related to spending more time doing lifestyle intensity activities, such as walking, household chores, and gardening (62). Supporting our findings, studies among CRC survivors has also found that men reported more time in moderate and vigorous activity than women and that men were more likely to meet the physical activity guidelines post-diagnosis (162, 164).

Age

Age was found to affect the level of vigorous activity in the CRC-NORDIET population, with the middle age group having a significantly higher level of time in high intensity activity compared to the oldest age group. This is in accordance with previous findings among healthy adults and older adults, but these studies has also found that the level of total, light and moderate physical activity and sedentary time decreases with increasing age (63, 132, 165, 166). This was however not found in the present study. Similar results are also seen among cancer patients. A longitudinal population-based cohort among CRC survivors found that those who were 55-74 years reported significantly more time in moderate-to-vigorous physical activity compared to those ≥ 75 years old (164). In addition, being physical active after cancer treatment is found to be negatively associated with being ≥ 65 years old (161). The lack of association between age and the other physical activity intensities except for vigorous could be explained by selection bias. The oldest participants in the CRC-NODIET study might represent the healthiest CRC patients among the elderly group in Norway (see method discussion, section 5.1.1).

BMI

In the present study, the level of physical activity for all intensities was found to decrease with increasing BMI. In addition, level of sedentary time increased with increasing BMI. The level of moderate physical activity in the lowest BMI-category in the present study was very high and was found to be significantly different from moderate physical activity in the highest BMI-category. However, there were only three participants in this group, which is important to have in mind when interpreting these results.

The results in the present study is in accordance with findings from other studies in healthy adults and older adults were overweight and obese spend less time in physical activity compared to normal weight (167, 168). Loyen *et al.* (63) assessed the levels of sedentary time and physical activity in four European countries. Being overweight and obese was consistently associated with more sedentary time, less physical activity and not reaching the recommendations for physical activity. Among cancer survivors, increasing weight were negatively associated with being physically active after treatment, and associated with lower time in moderate-to-vigorous activity (160, 161, 169).

TNM-stage and adjuvant treatment

In the CRC-NORDIET population, activity level decreased with higher TNM-stage and with adjuvant treatment, which indicate that physical activity accompanies severity of disease. This result could be expected as receiving adjuvant treatment can be accompanied with side-effects than can affect the ability to be physically active. Those with a higher burden of disease might also more often experience side-effects after surgery than can influence the activity level. This is supported by a previous study involving breast cancer survivors, of which cancer stage was negatively associated with physical activity (169). Also among CRC patients, receiving adjuvant therapy was associated with a decrease in physical activity after diagnosis (162). However, in the 'CanChange' study (160), they did not find that treatment or cancer stage were associated with being sufficiently physical active. The level of light intensity activities did not differ between the groups in the present study; this might indicate that those who receive adjuvant treatment are able to maintain the regular daily activity, but not the more strenuous activity. In the present study, TNM-stage and treatment regime were closely related as adjuvant chemotherapy was mainly given to patients with advanced cancer (TNM-III).

Surgery and cancer location

Results from this present study found that the level of vigorous physical activity were lower among those diagnosed with colon cancer compared to rectal cancer. In addition, the level of total physical activity was lower among those who had a surgery that was planned to be laparoscopic, but were converted to open. It is suggested that it is higher complication rate among patients who have a converted operation (170), this might lead to more side-effects after surgery and therefore affect the level of physical activity. Among CRC survivors in Netherland, they found that those diagnosed with rectal cancer was less physically activity compared to those with colon cancer (171), which is in contrast to the findings in the present study.

Education

Among the CRC-NORDIET participants, those with high-school education accumulated less time in moderate and moderate-to-vigorous activity compared to those with university/college education. This is somewhat different from finding in other studies. Mostly, those with the highest education level are found to be the most physically active, whereas those with the

lowest education level is the least active (63, 74, 161, 162). Even though those with the highest education level are more likely to meet the physical activity recommendation, they are also found to be more sedentary (63). This might be because they have a desk job and therefore spend a great part of the day seated, but might also be more prone to exercise and therefore are more likely to meet the physical activity recommendations. Those with low education on the other hand, might have a more active job, and therefore spend more time in light activity and less time sedentary compared to more educated. It has also been suggested that higher levels of education could indirectly raise awareness of the importance of exercise and its potential health benefits (172).

Correlation between physical activity and anthropometry, physical function and body composition.

All of the anthropometric, physical function and body composition measures correlated with moderate and vigorous intensity physical activity, whereas none correlated with light activity. This indicated that a certain level of intensity is required to achieve the beneficial effect. On the other hand, sedentary time correlated with all measures except for hand-grip strength.

Higher levels of moderate and vigorous physical activity were associated with better status on the physical function measures and higher muscle mass. Stronger correlations were found between physical activity and 6MWT and 30STS compared to handgrip strength, this might be expected as these tests are more related to the everyday movements that most of the participants does (walking, housework, get up and down from a seated position, and so on).

In line with findings in the current master thesis, studies among older adults have investigated the association of physical activity with several measures of physical function, including hang-grip strength, chair rise and 6MWT, and found that those who spent more time in moderate-to-vigorous activity perform better in these tests (173-175). On the other hand, those who spent more time sedentary tended to perform worse across the same measures (173, 174). Cooper *et al.* (176) investigated the relationship between physical activity and hand-grip strength among adults aged ≥ 60 years. They found a significant positive association between moderate-to-vigorous activity and hand-grip strength, which is in line with the present study. Furthermore, they showed that those who maintained or improved their muscle strength were more likely to increase their level of physical activity over time, whereas those who increased their level of physical activity did not increase their muscular strength.

Several components may explain the observed association between physical activity and function. Physical activity can increase strength, flexibility, endurance, balance and coordination, which all are determinants of functional status (177, 178).

5.2.5 Association between lean mass and physical function

Hand-grip strength was significantly correlated with both arm skeletal muscle mass and total lean body mass. This is consistent with previous finding, and although grip strength is a direct measure of hand strength it has also been used as an overall measure of body strength and lean body mass (179-181).

We did not, however, find any correlation between leg skeletal muscle mass and 30STS or 6MWT. Similar results were seen in a cohort among older men and women were leg skeletal muscle mass were not associated with lower extremity function measured by walking and repeated chair stands (180). Moreover, total lean body mass was found to be significantly correlated with both 30STS and 6MWT among the CRC-NORDIET participants, which is consistent with findings in older adults (182).

The reason why leg skeletal muscle mass did not correlated with 30STS or 6MWT might be because these tests are more complex and rely on more than just leg strength. Trunk strength, balance and endurance are also needed to perform these exercises (20, 179). This might also be the reason why total lean body mass were significantly correlated with 30STS and 6MWT. Balance, mobility and walking ability often become poorer with increasing age (20), and this might affect the participant's effort in the 30STS and 6MWT, whereas the hand-grip measure don't require much more than strength. This is also emphasized in the Norwegian recommendations for physical activity, as it is stated that adults over 65 years with poor balance or reduced mobility should perform balance exercises or strength training 3 or more times a week (55).

In a US population of older adults aged 60-69 years, the level of total lean body mass among men was 67%, which is quite similar as in the present study with 66%. However, the lean mass among US women were found to be 56%, which is slightly lower than among the women in the CRC-NORDIET study with 61% (183).

Compared with a population of older adults with mean age 75 years, leg muscle mass was found to be higher in the present study (i.e. 15.2 kg for men and 10.9 kg for women compared to 19.9 and 13.5 in the present study) (180). The leg and arm skeletal muscle mass in the present study were however more similar with a younger population with mean age approximately 45 years. Leg skeletal muscle mass in this study were 21.1 kg in men and 14.5 kg in women, whereas arm skeletal muscle mass were 7.2 kg in men and 4.1 kg in women (184). This might indicate that the muscle mass in the CRC-NORDIET population is quite good.

5.2.6 Strengths and limitations of this master thesis

An important strength in the current master thesis and the CRC-NORDIET as a whole is the low lost to follow-up rates from baseline to 12 months. By December 2017, only 10 % in the intervention group and 12 % in the control group were lost to follow-up.

Many of the intervention studies on physical activity conducted among CRC survivors have used different physical activity questionnaires or accelerometer to assess the level of activity. A major strength in the CRC-NORIDET study is therefore the use of an objective measurement, the SenseWear armband, which has been found to be more valid than questionnaires and accelerometers in assessing physical activity.

The equal distribution of baseline clinical and demographic characteristics between the two study groups indicates that the randomization has been successful.

In this master thesis, the physical activity has only been assessed at two occasions during the one-year intervention period. Changes in the activity level on other time points during this year, or between surgery and baseline have therefore not been detected. The CRC-NORDIET participants have also used the SenseWear armband 6 months after baseline, however, this data is not included in the present master thesis. It is also a possibility that the participants increased their activity level when wearing the armband, due to the Hawthorne effect which proposes that the participants improve aspects of their behavior as a response to being studies (139).

The lack of power to detect a change in physical activity is an important limitation in this master thesis. However, when the CRC-NORDIET has included the planned 500 participants, it will have the power to detect a possible intervention effect. In addition, the CRC-NORDIET study does not include a control group who are not receiving advises on physical activity.

6 Conclusion

The major aim of this master thesis was to examine the effect of a one-year dietary and lifestyle intervention following CRC surgery on physical activity.

The interim results indicate no additional effect of the dietary intervention on physical activity. However, a significant increase was observed in all measures of physical function among the total CRC-NORDIET population. The physical activity level in the CRC-NORDIET population at baseline, mean 4 months after surgery, was higher compared to Norwegian older adults and other CRC populations.

Several factors were found to be important for the physical activity level at baseline, such as gender, age, disease burden, treatment, cancer location and education. Physical activity was found to be negatively correlated to BMI and fat mass. On the other hand, physical activity was positively correlated with physical function, muscle mass and total lean mass.

The lack of observed intervention effects on physical activity may be related to a high level of physical activity at baseline, a healthier CRC population compared to previous studies or the lack of power to detect a change in physical activity between the groups. The observed changes in physical function among the total CRC-NORDIET population, despite no change in physical activity, may be explained by learning effect, improvement in general health or more energy. It is also possible that it takes more time to recover physical function compared to physical activity after surgery, so that the observed changes might be part of the natural recovery process.

The findings in this thesis indicate that the physical activity level in the CRC-NORIDET study is kept similar among the two study groups, which was the intention when designing the CRC-NORIDET study.

7 Future perspectives

The results from this master thesis did not find any change in the level of physical activity during the one-year intervention period. However, the future dataset from the CRC-NORDIET study with larger sample size (n=500), will have the power to detect changes in physical activity as calculated in the sample size chapter in this current master thesis, and might reveal effects of the intervention on physical activity.

The SenseWear armband has the ability to assess physical activity in 10 min bouts, this was however not available in the present thesis. The inclusion of this data would give valuable information about adherence to the recommendations of physical activity.

As the baseline measure in the present study was 4 months after surgery, changes before this time point can have been missed. The inclusion of physical activity and physical function assessments both before, and right after surgery would give a more detailed picture of the change in physical activity and physical function after a CRC surgery. Future studies should aim to include the whole timeline from diagnosis to one year after surgery.

It would also be interesting to include a control group who don't receive any advice regarding physical activity. This is planned to be conducted in the CRC-NORDIET study with time, by recruiting a matched reference group consisting of healthy subjects, representing the general Norwegian population. This will give valuable information on how the CRC-NORDIET population differs from the general Norwegian population, not only regarding physical activity and physical function, but also for other important outcomes in the study.

Several factors were found to affect the level of physical activity among the study participants, this could give an indication on which patients might need or benefit of advice and guidance on physical activity.

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Appendixes

Appendix 1	SenseWear armband user manual for the participants
Appendix 2	Ethical approval for the CRC-NORDIET study (several adjustments in the protocol have later been approved by the ethical committee)
Appendix 3	Informed consent to participate in the CRC-NORDIET study

Appendix 1: SenseWear armband user manual for the participants

UNIVERSITETET I OSLO
DET MEDISINSKE FAKULTET

Deltaker-Brukerveiledning for Armband

SenseWear Armband Mini (model MF-SW)

Når må ikke Armband benyttes

- Ved kjent metallallergi, eksem eller lett irritabel hud
- Under strålebehandling
- Dersom du har pacemaker
- Sammen med annet utstyr som kan forårsake elektromagnetiske forstyrrelser (på sykehus, ved bruk av pulsklokke osv.)

Bruk av Armband

Hvordan ha den på:

- Festes på baksiden av venstre overarm (triceps), Armband-logoen skal peke oppover mot skulderen og sølv-sensorene på undersiden av Armband skal være i kontakt med huden. Overarmen skal være ren, tørr og uten krem/olje ol. Stroppen strammes så den sitter komfortabelt, men stramt nok så Armband ikke sklir nedover armen, det skal være plass til to fingre under stroppen.
- Brukes **7 dager** i strekk: **23t/døgn** med 1 time hvor den er tatt av.
- Armband slår seg PÅ automatisk og begynner å lagre data innen 10 min etter at den er tatt på armen, Aktiveringen indikeres av en rekke lyd-toner (det er ingen AV- og PÅ knapp)
- *Når armband kan benyttes*: når deltakeren sover, trener og ellers ved daglige rutiner.
- *Når Armband ikke kan benyttes*: I dusjen eller på svømming – **tåler ikke vann!!!**

Renhold:

Rengjør Armband etter å ha svettet eller dersom den blir synlig skitten.

- *Rengjøring av Armband:*

  Den siden som berører huden tørkes av med en fuktig klut med mild såpe, sørg deretter for å fjerne såperester og tørk til slutt med en tørr klut

! Farer ved bruk

- Hudirritasjon (rapportert hos < 1 % av brukerne) Viktig å følge rådene for hvordan Armband skal rengjøres og festes rundt armen. Hvis hudirritasjonen skulle vedvare – avslutt bruken av Armband og eventuelt konsulter med fastlegen.

Husk å sende tilbake Armband i medfølgende returkonvolutt etter avsluttet bruk!

Takk ☺

Appendix 2: Ethical approval for the CRC-NORDIET study (several adjustments in the protocol have later been approved by the ethical committee)

UNIVERSITETET I OSLO

DET MEDISINSKE FAKULTET

Professor Rune Blomhoff
Institutt for medisinske basalfag
Universitetet i Oslo
Postboks 1046 Blindern
0316 Oslo

Regional komité for medisinsk og helsefaglig forskningsetikk sør-øst C (REK sør-øst C)
Postboks 1130 Blindern
NO-0318 Oslo

Telefon: 22 84 46 67

E-post: post@helseforskning.etikkom.no
Nettadresse: http://helseforskning.etikkom.no

Dato: 29.04.2011
Deres ref.:
Vår ref.: 2011/836 (oppgis ved henvendelse)

Typisk norsk!

Vi viser til søknad mottatt til frist 22.03.2011 om forhåndsgodkjenning av ovennevnte forskningsprosjekt. Søknaden er blitt vurdert av Regional komité for medisinsk og helsefaglig forskningsetikk i henhold til lov av 20. juni 2008 nr. 44, om medisinsk og helsefaglig forskning (helseforskningsloven) kapittel 3, med tilhørende forskrift om organisering av medisinsk og helsefaglig forskning av 1. juli 2009 nr 0955.

Både økt forekomst og overlevelse etter behandling gjør at et økende antall personer lever med en tidligere kreftdiagnose. Disse personene har større sannsynlighet for å utvikle andre livsstilssykdommer enn resten av befolkningen i samme alder. Man ønsker i denne studien å undersøke hvordan et endret kosthold påvirker helsetilstanden og utvikling av livsstilssykdommer etter behandling for tykk- og endetarmskreft. Kostholdet i studien er basert på de nye kostrådene fra Helsedirektoratet og matvarer som i epidemiologiske- og eksperimentelle studier er vist å hemme inflammasjon eller oksidativt stress, og med et fokus på norske matvaner. Kostholdsintervensjonen kombineres med intensiv oppfølging, som er nødvendig for høy compliance til kosten.

Prosjektleder: Rune Blomhoff
Forskningsansvarlig: Universitetet i Oslo, Medisinsk fakultet

Forskningsetisk vurdering
Komiteen har ingen forskningsetiske innvendinger til studien i seg selv, men mener prosjektleder bør vurdere å oversette og benytte den engelske tittelen *Effect of the new Norwegian food based dietary guidelines on chronic diseases in colorectal cancer survivors*, da denne tittelen oppleves å bedre beskrive formålet med prosjektet. Tittelen skal også endres på informasjonsskrivet.

Det anføres på s. 564 i den vitenskapelige protokollen: *Total genome transcriptomics, low density gene arrays as well as RT-PCR will be performed on white blodd cells (WBC) taken from the participants during visits to the study centre or hospital. Gene expression profiling will also be performed on tissue samples of tumor and neighboring healthy tissues removed during surgery.*

Komiteen bemerker at dersom det skal gjøres helgenomsekvensering i prosjektet, kan man risikere å komme over utilsiktede funn med prediktiv verdi for både pasient og pårørende. Komiteen mistenker at prosjektet kan komme til å falle inn under bestemmelsene i bioteknologiloven, men gjør oppmerksom på at søker selv plikter å avklare dette med Helsedirektoratet ved tvil. Komiteen forutsetter at det finnes beredskap for å håndtere eventuelle uventede funn.

Forskningsbiobank
Det søkes om å opprette en spesifikk forskningsbiobank med navn *The Norwegian Foods Study* i prosjektet.

Ansvarshavende for forskningsbiobanken er Rune Blomhoff. Forskningsansvarlig er Institutt for Medisinske Basalfag, Universitetet i Oslo.

Biobanken vil bestå av blodprøver.

Biobanken planlegges å vare til 2040. Deretter skal materialet behandles i henhold til helseforskningslovens § 30.

Biologisk materiale vil utføres til utlandet i henhold til helseforskningslovens § 29. Deltakerne er orientert om dette i informasjonsskriv.

Informasjonsskriv og samtykkeerklæring
Det anføres i informasjonsskrivet til deltakerne at *studiens målsetning er at du skal forbedre dine kostvaner og at du skal nærme deg kostrådene som utgitt av Helsedirektoratet.* Komiteen oppfatter ikke at dette er formålet med studien. Formålet med studien er å undersøke hvordan et endret kosthold påvirker helsetilstanden og utvikling av livsstilssykdommer etter behandling for tykk- og endetarmskreft. Denne informasjonen må således rettes.

Ut fra dette setter komiteen følgende vilkår for prosjektet:
1. Tittel på studien skal endres i informasjonsskrivet, for bedre å reflektere studiens formål.
2. Informasjonsskriv skal revideres i tråd med det ovennevnte.

Vedtak:
Prosjektet godkjennes under forutsetning av at ovennevnte vilkår oppfylles.

Komiteen godkjenner opprettelse av forskningsbiobanken *The Norwegian Foods Study*, i tråd med det som er angitt i prosjektsøknaden. Biobankregisteret vil bli underrettet ved kopi av dette brev

I tillegg til vilkår som fremgår av dette vedtaket, er tillatelsen gitt under forutsetning av at prosjektet gjennomføres slik det er beskrevet i søknaden og protokollen, og de bestemmelser som følger av helseforskningsloven med forskrifter.

Tillatelsen gjelder til 31.12.2040. Opplysningene skal deretter slettes eller anonymiseres, senest innen et halvt år fra denne dato. Prosjektet skal sende sluttmelding på eget skjema, jf. helseforskningsloven § 12, senest et halvt år etter prosjektslutt.

Komiteens avgjørelse var enstemmig.

Forskningsprosjektets data skal oppbevares forsvarlig, se personopplysningsforskriften kapittel 2, og Helsedirektoratets veileder for *Personvern og informasjonssikkerhet i forskningsprosjekter innenfor helse- og omsorgssektoren:*
http://www.helsedirektoratet.no/samspill/informasjonssikkerhet/norm_for_informasjonssikkerhet_i_helsesektoren_232354

Hvis forskningsbiobanken opphører, nedlegges eller overtas av andre, skal det søkes REK om tillatelse, jf. helseforskningloven § 30.

Komiteens vedtak kan påklages til Den nasjonale forskningsetiske komité for medisin og helsefag, jf. Forvaltningslovens § 28 flg. Eventuell klage sendes til REK sør-øst. Klagefristen er tre uker fra mottak av dette brevet.

Med vennlig hilsen

Arvid Heiberg (sign.)
professor dr. med.
leder

Tor Even Svanes
seniorrådgiver

Kopi: Universitetsdirektøren, universitetsdirektørens kontor, Pb 1072 Blindern, INTERNPOST
Biobankregisteret v/ nina.hovland@fhi.no

Vi ber om at alle henvendelser sendes inn via vår saksportal:
http://helseforskning.etikkom.no eller på e-post til: post@helseforskning.etikkom.no. Vennligst oppgi vårt saksnummer/referansenummer i korrespondansen.

Appendix 3: Informed consent to participate in the CRC-NORDIET study

UiO : Universitetet i Oslo
Medisinsk Fakultet/Institutt for medisinske basalfag/Avdeling for ernæringsvitenskap

Invitasjon til å delta i Typisk norsk-studien

- om hvordan endringer i kostholdet kan påvirke helsetilstanden etter behandling for tykktarm- eller endetarmskreft

Du mottar dette brevet i forbindelse med din behandling ved Oslo Universitetssykehus, Akershus Universitetssykehus eller Vestre Viken. I samarbeid med Professor Rune Blomhoff ved Avdeling for ernæringsvitenskap på Universitetet i Oslo ønsker vi å undersøke hvordan et endret kosthold etter kirurgisk behandling for tykktarm- eller endetarmskreft, påvirker helsetilstanden og utvikling av livsstilssykdommer. Kostholdet i studien er basert på de nye matvarebaserte kostrådene fra Helsedirektoratet og annen nyere forskningslitteratur.
Vedlagt finner du relevant informasjon om undersøkelsen, og vi ber deg lese gjennom denne.

Hva innebærer studien?
Dersom du blir med i studien vil du bli trukket ut til å delta i en av to grupper.
Les mer om hva dette innebærer på neste side.

Gruppe A vil få følgende tilbud:
- Kosthold
- Fysisk aktivitet

Gruppe B vil få følgende tilbud:
- Fysisk aktivitet

For å bli med i studien ber vi deg om å fylle ut vedlagte Samtykkeerklæring og Spørreskjema om kosthold og sende begge til oss i vedlagte svarkonvolutt

Les «Mer informasjon om Typisk norsk-studien» på de neste sidene.

Din deltagelse i denne undersøkelsen vil ikke forandre på behandlingen du skal få, men vil gi verdifull kunnskap til bruk i behandling av tykktarms- eller endetarmskreft i fremtiden.

Med vennlig hilsen

Rune Blomhoff, Prosjektleder
Professor ved Avd. for ernæringsvitenskap
Universitetet i Oslo og Avd for klinisk service,
Oslo Universitetssykehus

Sigbjørn Smeland
Klinikkleder for klinikken; Kreft-, kirurgi og transplantasjonsklinikken
Oslo Universitetssykehus

Oslo universitetssykehus

Postadresse:
E-post: typisk-norsk@medisin.uio.no
Telefon: 22851520 eller 932 00 727
http://www.med.uio.no/imb/om/organisasjon/avdelinger/ernering/index.html

Mer informasjon om Typisk norsk-studien

Hva innebærer studien?

Hvis du deltar i studien betyr det noen besøk på Studiesenteret ved Avdeling for ernæringsvitenskap, Universitetet i Oslo i løpet av studieperioden. Der vil det bli tatt blodprøver, blodtrykksmåling, måling av kroppssammensetning, måling av høyde og vekt, samt tester av fysisk funksjon og test av blodsukkernivå etter inntak av sukker. I tillegg ønsker vi at du fyller ut spørreskjema om kosthold, bakgrunnsinformasjon, samt helsetilstand som for eksempel sykdom, ernæringsstatus, fysisk aktivitet og livskvalitet. Du kan også bli spurt om å gi urin og feces prøver i løpet av studien. Alle prøvetakingene er frivillige. Prøvene og målingene vil bli gjort ved studiestart, og noen av dem vil bli gjentatt ved 6 måneder, 1, 3, 5, 7, 10 og 15 år. Dersom du blir med i studien vil du bli trukket ut til å delta i en av to grupper:

Gruppe A vil få følgende tilbud:
- Kosthold
- Fysisk aktivitet

Gruppe B vil få følgende tilbud:
- Fysisk aktivitet

Tilbud om kosthold:
Inspirasjonsmøter, matlagingskurs, utdeling av gratis matvarer, rabattordninger på enkelte matvarer, tilgang på klinisk ernæringsfysiolog, egen nettside.

Tilbud om fysisk aktivitet:
Råd om fysisk aktivitet og tilrettelagt treningstilbud med mulighet for både individuell trening og gruppetrening.

Frivillig deltakelse

Din deltagelse i denne undersøkelsen vil ikke forandre på behandlingen du skal få, men kan gi verdifull kunnskap til bruk i behandling av tykktarms- eller endetarmskreft i fremtiden. Din deltagelse er frivillig og du kan når som helst trekke deg. Dersom du ønsker å delta, undertegner du samtykkeerklæringen på siste side. Dersom du ikke vil delta i studien eller senere trekker deg, får du den behandlingen og oppfølgingen som vanligvis blir gitt til pasienter med samme diagnose som deg.
Hvis ny informasjon blir tilgjengelig som kan påvirke din villighet til å delta i studien, vil du så raskt som mulig bli orientert.

Mulige fordeler og ulemper

Du vil få tilbud om fysisk aktivitet og/eller kosthold ledet av kyndig fagpersonell.
Vi forventer ikke komplikasjoner som følge av de gitte endringene i kostholdet, men dersom eventuelle komplikasjoner allikevel skulle oppstå, ber vi om at du rapporterer disse tilbake til oss ved disse anledningene og kontakter din lege.

Kompensasjon til deltakere
Deltakere vil få dekket reiseutgifter (med offentlig transport) ved innkalling til Studiesenteret.

Personvern
Prøvene tatt av deg og informasjonen som registreres om deg skal kun brukes slik som beskrevet i hensikten med studien. Alle opplysningene og prøvene vil bli behandlet uten navn og fødselsnummer eller andre direkte gjenkjennende opplysninger. En kode knytter deg til dine opplysninger og prøver gjennom en navneliste. Ved å samtykke til deltakelse i studien, samtykker du til at relevante opplysninger fra din journal ved Oslo universitetssykehus (f.eks CT-bilder, diagnose, behandling o.l.) blir utlevert til Universitetet i Oslo. Du samtykker også til at opplysninger om deg blir hentet fra Dødsårsaksregisteret, Reseptregisteret, Kreftregisteret (inkludert Nasjonalt kvalitetsregister for tykk- og endetarmskreft), Hjerte- og karregisteret og Norsk Pasientregister. Det er kun autorisert personell knyttet til studien som har adgang til navnelisten og som kan finne tilbake til deg. Navnelisten fra studien vil bli slettet når studien er gjennomført og resultatene publisert, senest i 2040. Det vil ikke være mulig å identifisere deg i resultatene av studien når disse publiseres. Dersom du trekker deg fra studien, kan du kreve å få slettet innsamlede prøver og opplysninger, med mindre opplysningene allerede er inngått i analyser eller brukt i vitenskapelige publikasjoner. Ved Studiesenteret er avdelingsleder databehandlingsansvarlig i henhold til personopplysningsloven/helseregisterloven.

Biobank
Prøvene som blir tatt og informasjonen fremkommer av denne studien vil bli lagret i en forskningsbiobank ved Avdeling for ernæringsvitenskap, Universitetet i Oslo. Hvis du sier ja til å delta i studien, gir du også samtykke til at det biologiske materialet og analyseresultater inngår i biobanken. Forskningsansvarlig for biobanken er Instituttleder Jan G. Bjålie, Institutt for medisinske basalfag, Det Medisinske Fakultet, Universitetet i Oslo. Biobanken er godkjent av Regional Komite for forskningsetikk. Biobanken planlegges å vare til 2040. Etter dette vil materiale og opplysninger bli destruert og slettet etter interne retningslinjer.

Utlevering av materiale og opplysninger til andre
Hvis du sier ja til å delta i studien, gir du også ditt samtykke til at prøver og avidentifiserte opplysninger utleveres til Department of Chronic Disease Prevention, National Institute for Health and Welfare i Finland ved professor Iris Erlund som er en samarbeidspartner i prosjektet.

Rett til innsyn og sletting av opplysninger om deg og sletting av prøver
Hvis du sier ja til å delta i studien, har du rett til å få innsyn i hvilke opplysninger som er registrert om deg. Du har videre rett til å få korrigert eventuelle feil i de opplysningene vi har registrert.

Forsikring
Du er forsikret i henhold til reglene i "Lov om produktansvar" og "Pasientskadeloven".

Informasjon om utfallet av studien
Resultatene fra studien vil bli offentlig tilgjengelig ved publisering i medisinske vitenskapelige tidsskrift.

Økonomi og sponsorer
Studien og biobanken er finansiert gjennom forskningsmidler fra Forskningsrådet og Helse Sør-Øst. Deltakere i Gruppe A vil få utdelt en startpakke med brosjyrer og enkelte matvarer, og et rabattkort på enkelte matvarer hos utvalgte dagligvarekjeder og produsenter. Utvalget er basert på varer studiegruppen ønsker å fokusere på, og er ikke bestemt av sponsor. Sponsorer har rett til å reklamere med bidrag til studien, men ingen enkeltprodukter vil kunne markedsføres direkte basert på resultater fra studien.

Studien er godkjent av Regional komite for medisinsk og helsefaglig forskningsetikk (saksnr.2011/836).

Har du spørsmål om studien?
Ta gjerne kontakt med en av oss i studiegruppen:

Hege Berg Henriksen eller Siv Kjølsrud Bøhn:

Prosjekttelefon: 932 00 727, e-postadresse: typisk-norsk@medisin.uio.no

Samtykkeerklæring til deltakelse i "Typisk norsk-studien"

Jeg er villig til å delta i undersøkelsen.

_____

Underskrift av deltager Dato

Navn med blokkbokstaver:_____

Adresse:_____

Jeg kan kontaktes per (fyll gjerne ut flere alternativer):

☐ Epost _____
Epostadresse

☐ SMS _____
Mobilnummer

☐ Telefon _____
Telefonnummer