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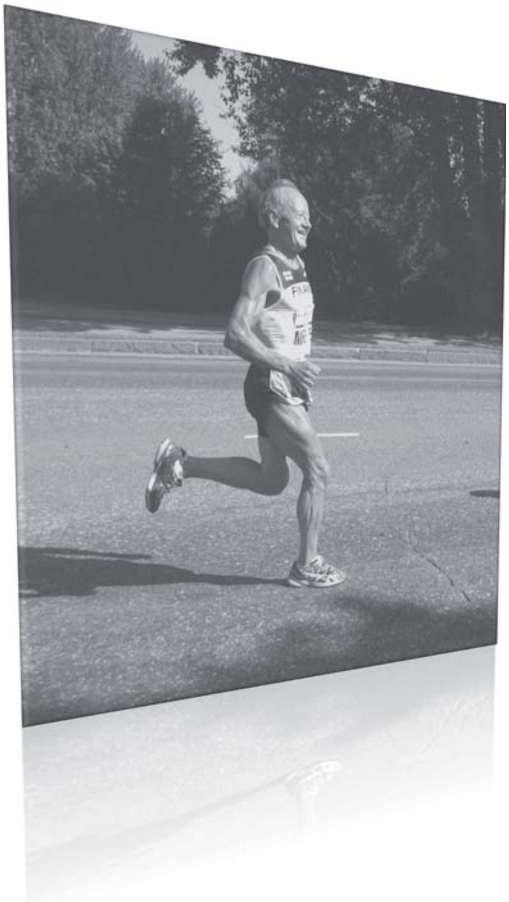
Katariina Korniloff

Interrelationships of Physical Activity and Depressive Symptoms with Cardiometabolic Risk Factors



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ABSTRACT

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The aim of this thesis was to examine the relationships between physical activity (PA) and health, more specifically PA in relation to depressive symptoms (DS) and cardiometabolic risk factors, also in a lifetime perspective, and further perceived barriers to PA. Additionally this thesis reveals the occurrence of unintentional injuries related to PA level and DS.

The participants were randomly selected from the National Population Register in August 2007 and invited by mail to a clinical examination. Of the 4500 persons aged 45-74 years, 64% participated in the health examination. All participants completed a standard questionnaire, including questions on cardiometabolic risk factors, health behaviour, functional ability, unintentional injuries and somatic diseases. PA was assessed with the self-administered short version of the International Physical Activity Questionnaire, with a question about leisure-time physical activity (LTPA), and retrospective recall of lifetime historical LTPA frequency from age 15 years onwards. Depressive symptoms (DS) were assessed by the Beck Depression Inventory (BDI-21), and the cut-off point for mild depression was ≥10/63.

The physically inactive participants presented more commonly with health risk factors and DS. In addition, the rate of simultaneous metabolic syndrome and DS was more than fivefold higher among the participants with low LTPA, than among those in the high LTPA group. Lack of time proved to be the main reason for inactivity, while among those with DS and metabolic syndrome the main reason for inactivity was illness or disability. Lifetime LTPA seemed to be associated with occurrence of DS and somatic diseases in later life. The presence of DS found to increase the prevalence of unintentional injuries.

To conclude, PA plays a significant role relation to DS and cardiometabolic risk factors. Health-related risk factors seem to accumulate in inactive individuals. Therefore, promoting LTPA over the lifespan would be beneficial with respect to DS and somatic diseases.

Keywords: physical activity, depressive symptoms, chronic disease, health, risk factors

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Jyväskylä, April 2013

Katariina Korniloff

LIST OF ORIGINAL PUBLICATIONS

The thesis is based on the following original papers, which will be referred to in the text by their Roman numerals:

I Korniloff K, Vanhala M, Koponen H, Kautiainen H, Järvenpää S, Peltonen M, Mäntyselkä P, Saaristo T, Kampman O, Oksa H, Häkkinen A. Depressive symptoms are related to physical activity and cardiometabolic risk factors in a population-based sample of adult male and female. The FIN-D2D survey. Submitted for publication.

II Mäntyselkä P, Korniloff K, Saaristo T, Koponen H, Eriksson J, Puolijoki H, Timonen M, Sundvall J, Kautiainen H, Vanhala M. 2011. Association of depressive symptoms with impaired glucose regulation, screen detected type 2 diabetes and previously known type 2 diabetes –the Finnish D2D survey. Diabetes Care 34(1): 71-9.

III Korniloff K, Vanhala M, Kautiainen H, Koponen H, Peltonen M, Mäntyselkä P, Oksa H, Kampman O, Häkkinen A. 2012. Lifetime leisure-time physical activity and the risk of depressive symptoms at the age of 65–74. The FIN-D2D survey. Preventive Medicine 54(5): 313–315.

IV Korniloff K, Häkkinen A, Koponen H, Kautiainen H, Järvenpää S, Peltonen M, Mäntyselkä P, Saaristo T, Kampman O, Oksa H, Vanhala M. 2012. Relationships between depressive symptoms and self-reported unintentional injuries: the cross-sectional population–based FIN-D2D survey. BMC Public Health 12: 516.

V Korniloff K, Häkkinen A, Kautiainen H, Koponen H, Peltonen M, Mäntyselkä P, Oksa H, Kampman O, Vanhala M. 2010. Leisure-time physical activity and metabolic syndrome plus depressive symptoms in the FIN-D2D survey. Preventive Medicine 51(6): 466-70.

Additionally, previously unpublished results are included in the thesis.

ABBREVIATIONS

ANOVA	Analysis of variance
BMI	Body mass index
BDI	Beck depression inventory
BDNF	Brain-Derived Neurotrophic Factor
CES-D	Center for Epidemiologic Studies Depression Scale
CRP	C-reactive protein
CVD	Cardiovascular disease
DEPS	Depression Scale
DS	Depressive symptoms
DSM	Diagnostic and Statistical Manual of Mental Disorders
FPG	Fasting plasma glucose
FIN-D2D	The Finnish type 2 diabetes survey
GEE	Generalizing estimating equations
GPAQ	Global physical activity questionnaire
HDL	High–density lipoprotein
HPA	Hypothalamic–pituitary–adrenal
ICD-10	International Classification of Diseases
IGT	Impaired glucose tolerance
IGR	Impaired glucose regulation
IFG	Impaired fasting glycaemia
IQR	Inter quartile ranges
IPAQ	International physical activity questionnaire
kg	Kilogram
LDL	Low-density lipoprotein
LTPA	Leisure-time physical activity
m^2	Square meter
MET	Metabolic equivalent
MetS	Metabolic syndrome
mmHg	Millimeter of mercury
mmol/L	Millimole per liter
MONICA	Multinational monitoring of trends and determinants in cardiovascular disease
NHANES	National Health and Nutrition Examination Survey
NCEP	National Cholesterol Education Program
RCT	Randomized controlled trial
SD	Standard deviation
SDS	The Zung Self-Rating Depression Scale
ST2D	Screen-detected type 2 diabetes
T2D	Type 2 diabetes
WHO	World Health Organization

CONTENTS

1 INTRODUCTION

Depression is a common, highly recurrent disorder, which further often becomes chronic and leads to long-term disability. Depression affects every fifth person during their lifespan; consequently, it is a significant illness with regard to public health and the economy. By 2020, it is predicted that depression will be the second leading public health problem next to cardiovascular diseases (CVD) in the developed countries due to its tendency to cause premature death and disability (Murray and Lopez, 1997). Typically treatment of depression includes anti-depressant medication and often also psychotherapy or counseling, with a 60-80% success rate (Möller and Henkel, 2005). According to one study, after initial medical treatment, only one-third of depressed participants went into remission. Thus, there is a need for alternative treatment and, above all, a need for the prevention of depressive disorders.

One such adjunct or alternative treatment that has been proposed is physical activity (PA). There is plausible evidence that PA can play a substantial role in the prevention and management of depressive symptoms (DS) (Teychenne et al., 2008). DS, also called minor depression, do not meet the full criteria for major depression but instead, present a high risk for developing depression.

However, along with economic growth, our lifestyles have become increasingly sedentary (Lanningham-Foster et al., 2003), as demands to be physically active have diminished since the middle of the last century, largely due to increasing industrialization. Technological developments like machinery, engines and vehicles have replaced physical labor, resulting in a reduction in human energy consumption. As a result of today's diminished demands on energy consumption a global health problem has emerged. The prevalence of DS and cardiometabolic risk factors are growing worldwide, resulting in a significant threat from the perspective of public health. Thus, an intervention, such as lifestyle counseling at an early stage with encouragement to engage in regular PA, would be an important non-pharmacological and low-cost alternative in preventing and treating DS and cardiometabolic risk factors.

Although physical inactivity is undoubtedly a common etiological factor in the development of both cardiometabolic risk factors and DS (Laaksonen et al., 2002b; Teychenne et al., 2008), only little is known about the effect of the simultaneous presence of cardiometabolic risk factors and DS on physical activity. Thus, purpose of this thesis was to examine the relationships between physical activity, depressive symptoms and cardiometabolic risk factors in a cross-sectional population-based study of Finnish participants aged 45-74 years. In addition, this study applies the life course perspective to examine how PA during the lifespan affects somatic and mental health in later life.

2 REVIEW OF THE LITERATURE

2.1 Physical activity

The human body has evolved over the centuries to be physically active as in order to obtain food and earn a living (Booth et al., 2008). However, the demand to be physically active has diminished both at home and at in the workplace, and in transportation. It has been shown that, in the general population, adults spend at least half, and up to two-thirds of their waking hours being sedentary (Dunstan et al. 2012). Thus being sedentary, mainly due to prolonged sitting at work and during commuting and leisure, has become a serious health risk, which is associated with obesity, increased risk for cardiovascular disease, mental disorders and hypertension (Thorp et al., 2011). However, to maintain physical and mental health, it is important to engage in frequent physical activity. Compensation for the reduced energy consumption of modern working life should be made by increasing leisure-time physical activity; however, not all have succeeded in doing this, since as many as one-third of adults worldwide are inactive (Hallal et al., 2012).

2.1.1 Definition of physical activity

Physical activity (PA) was defined in 1985 as 'any bodily movement produced by skeletal muscles that results in energy expenditure' (Caspersen et al., 1985). Resting metabolic rate together with the thermic response to food and physical activity constitute this caloric expenditure. Of this, the resting metabolic rate accounts for about 65% and thermic response to food accounts for about 10%. Physical activity-associated energy expenditure is on average 25-35% in sedentary persons, and may amount to as much as 75% of daily energy expenditure in highly active persons (Westerterp, 1998).

Total physical activity is composed of several components, such as work load, commuting physical activity, domestic chores and leisure-time physical activity (LTPA). Leisure-time physical activities are functions which are not required for the necessary functions of daily living or work, and are performed at a person's own discretion. Such functions include sports participation, exercise training, and recreational activities.

In addition, physical activity is commonly described according to the following different dimensions. Frequency is the amount of PA events during a specific time period, usually determined per week or month. Intensity refers to the strenuousness of physical activity, and duration to the amount of time spent on a single bout of physical activity (Bouchard et al., 2006). Intensity of physical activity is often expressed as the metabolic equivalent (MET), which is a unit used to estimate the amount of oxygen used during physical activity. 1 MET refers to the rate of energy expenditure at rest. A higher MET value indicates a higher level of intensity of physical activity.

2.1.2 Physical activity assessments

Physical activity is multidimensional, and is a complex behavior to measure. It can be measured by self-reports, also called subjective methods, using methods such as questionnaires, diaries or recalls, or by objective measures such as accelerometers and pedometers, heart rate monitoring, direct observation and doubly labeled water (Warren et al., 2010). No single method of measuring physical activity ranks above all the others. All the methods used have both advantages and disadvantages. An advantage of objective measures is likely to be more accurate results compared to self-report methods, but objective measures are not practical for most epidemiological studies with a large population-based sample.

Self-reported methods to assess physical activity are the most widely used. They are easy and not time-consuming in clinical practice. They are also the cheapest and easiest to use in studies with large samples, but they are also the least accurate. However, in large population-based studies, the questionnaire is the only feasible method to assess physical activity. With a questionnaire it is possible to categorize people into different PA levels and to monitor changes in PA on the population-level (Sallis and Saelens, 2000). However, self-reported measures have several limitations. For instance, they are dependent on respondents' interpretations and their cognitive capability of recall, and might also suffer from socially desirable bias (Warren et al., 2010).

PA questionnaires vary in their complexity from single-item questions to interviewer-administered surveys of lifetime physical activity over a selected time frame (Pereira et al., 1997). Questionnaires with a short time frame are less vulnerable to recall bias and easier to validate with objective measures. However, the longer the time period is, the more likely it will be to reflect habitual activity patterns. Differences also concern whether the questionnaire assesses total PA, including work load, commuting physical activity, domestic chores and leisure-time physical activity or only part of it. Nowadays, with the decline in work load in most industrialized countries, the assessment of LTPA has become more important. LTPA level can be evaluated by the duration and intensity of leisure-time activities, by the measurement of energy expenditure, or by cardiorespiratory capacity. Although the measurement of LTPA with heart-rate monitoring or accelerometers would provide more accurate results, it is not feasible in large studies. In population studies with a large sample, assessment of LTPA with a questionnaire might be the only suitable method available.

The assessment tool used should have certain psychometric properties. To be reliable, the method should be reproducible independently of the assessor. Additionally, the method should be validated against an objective method or gold standard (criterion validity). Self-report questionnaires fulfill these properties variously; reliability varies from moderate to good and criterion validity from poor to moderate (Warren et al., 2010).

In the late 1990s, the International Physical Activity Questionnaire (IPAQ) (Bauman et al., 2009) was developed for conducting population-level surveillance, allowing international comparisons of total PA between countries. The questionnaire assesses the time spent doing moderate- and vigorous-intensity activities across all the domains of leisure-time, work, transportation, and household tasks as well as sitting behavior (Craig et al., 2003). Currently, several countries have adopted the IPAQ as their national surveillance system, supporting an internationally comparable estimate of PA.

Physical activity is closely related with physical fitness, and thus change in PA habits is likely to induce modification in physical fitness as well. Physical fitness is an indicator of health, functional ability and wellbeing, and it has been defined as "a set of attributes that people have or achieve that relates to the ability to perform physical activity" (Caspersen et al., 1985). Measuring physical fitness objectively requires extensive investment, as the requisite laboratories and equipment, time and personnel should be available. Self-rated physical fitness, in turn, is a quick and easy way of measuring physical fitness in large population-based studies and, moreover, single question-based physical fitness has proved to be almost as accurate in estimating physical fitness as objective methods (Germain and Hausenblas, 2006).

2.1.3 Physical activity levels in population

Several cross-sectional studies have investigated PA level in Finland with questionnaire. A national physical activity study of 5 500 Finnish participants aged 19-65 during the years 2009–2010 showed that both LTPA frequency and intensity had increased since the early 2000s (The Finnish Olympic Committee, 2010). On the basis of the national FINRISK studies of Finnish 25- to 64-year-old citizens, repeated every five years, the prevalence LTPA has increased more during the last decades among females than males. Instead, commuting PA declined steadily from year 1972 to 2007 among females, while among males the decline stopped in the early nineties and little change has been observed since. Physical work load has also dramatically decreased from the 1990s onwards.

To be sufficiently active for health benefits, adults should accumulate 150 minutes moderate-intensity or 75 minutes of vigorous-intensity aerobic LTPA each week and, in addition, muscle-strengthening and balance training two times a week (Haskell et al., 2007). In the Finnish health behavior study by

Helakorpi et al. (2010), the proportion of those who reached the LTPA recommendations was 11% among females and 12% among males, while the proportion of those who accumulated the aerobic part of the recommendations was 50% among females and 47% among males. Consequently, although participating in LTPA has become more popular, a significant proportion of the Finnish population is not active enough to obtain health benefits.

Furthermore, whether one is physically active enough, can also be evaluated according to one's total physical level. Based on the review of total PA levels reported from 122 countries, a third of adults worldwide do not reach the recommended levels of total PA, and 31% of adults are inactive (Hallal et al., 2012).

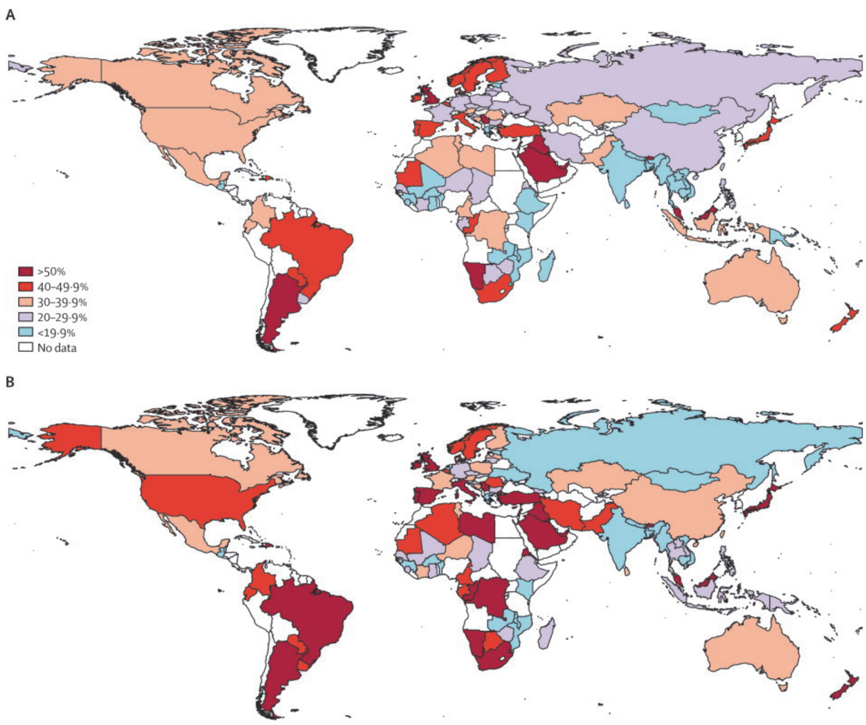

FIGURE 1 Physical inactivity in adults (15 years or older) worldwide in men (A) and women (B). (From Hallal et al. 2012 with permission of Elsevier)

The recommended level of total PA is consistent with the general LTPA-based public health recommendations taking into account of basal level of activity of daily living with an additional 30 minutes of LTPA (Bauman et al., 2009). Physical activity levels vary among different populations and regions worldwide (Figure 1). The prevalence of inactivity is 40-50% in the Nordic countries, which is relatively high when compared globally, except for females in Finland and both genders in Denmark (inactivity rate 30-40%). In a global review, females were more inactive (34%) than males (28%) and further, inactivity was shown to increase with age (Hallal et al., 2012). The report reveals that people in Europe and in America are among those who participate least in vigorous PA and who also have one of the highest rates of inactivity worldwide (Hallal et al., 2012). In contrast, people in the South Asia region have the highest participation rate in vigorous total PA and the lowest prevalence of inactivity.

This review, which represents 89% of the world's population, is first of its kind to take into account total physical activity (leisure-time, occupational, housework, and commuting PA) measured with the international physical activity questionnaire (IPAQ) and the global physical activity questionnaire (GPAQ) (Hallal et al., 2012). Previously, when defined according to leisure-time physical activity, PA level was shown to be higher among those with higher income compared to those with lower income (Trost et al., 2002). However, because IPAQ and GPAQ take into account total PA level, physical inactivity has been found to be substantially higher in the high income countries compared to low income countries.

2.2 Depressive symptoms

2.2.1 Definition of depressive symptoms

Depressive symptoms (DS) are characterized by the presence of various signs and symptoms which have a multidimensional effect on health and well-being. These are low levels of mood and lack of energy, low self-worth, feelings of guilt, deprived concentration, lack of interest or pleasure, and disrupted appetite or sleep. The diagnosis of depression, in turn, is based on a mental status examination by a psychiatrist, and defined according to the number of symptoms and their duration in accordance with various diagnostic classifications, of which the most common are the ICD-10 (World Health Organization, 1993) and DSM-IV (American Psychiatric Association, 1994).

Depressive symptoms refer to lower mood states lacking clinical significance; however, the criteria for DS are the same as those for depression, but the number of symptoms necessary for a diagnosis is smaller. Additionally, those with DS have increased risk for developing depression (Cuijpers and Smit, 2004; Horwath et al., 1994), and thus constitute an important target group for the prevention of depression. In Finland, 11–21% of persons have depressive symptoms (DS) assessed according to the Beck Depression Inventory (BDI$\geqslant$10 points) (Vanhala et al., 2009; Väänänen et al., 2008). The US population-based National Health and Nutrition Examination Survey (NHANES) showed that about 1 in 5 adults, i.e. 42.1 million Americans, screened positive for DS (Shim et al., 2011). Across Europe, in turn, there is marked variation in the prevalence of DS. A meta-analysis of 13 808 participants conducted in the year 1999 reported an overall prevalence of DS in Europe of 12%, 14% for females and 9% for males (Copeland et al., 1999). Furthermore, the prevalence of DS has been shown to increase with age (Stordal et al., 2003); this is likely to become a major problem in the future due to higher life expectancy.

Several risk factors for depression and DS have been shown to exist. These include unhealthy lifestyle habits, such as alcohol consumption and smoking. Also, previous depression, somatic diseases, lower socio-economic status and sudden negative life events, stress and anxiety may increase the risk for depression (Fryers 2005).

2.2.2 Assessment of depressive symptoms

Several tools are available for the assessment of depressive symptoms and depression, both for clinical diagnoses and population screening. The content of the items in the assessment tools are based on the definition of depression and its diagnostic criteria as a clinical syndrome. Assessment methods can be divided into self-reports and clinician-rated methods. Each type has its advantages and disadvantages, and thus the most appropriate method should be selected according to the measurement goal and the time resources available, and the target population. Below is an overview of some frequently used self-reported methods to measure depressive symptoms in epidemiological studies.

The Beck Depression Inventory (BDI) is one of the most widely used self-report measures to identify and assess DS among health care professionals and researchers. The BDI construct of 21 items on cognitive, affective and physiological symptoms reflecting the symptoms of depression most often reported by depressed psychiatric patients (Beck et al., 1961). The BDI is used to screen for the presence of DS, for diagnostic purposes, to measure variability in the severity of depression, and for monitoring the effectiveness of treatment. The BDI has been translated into many languages, and its psychometric properties have been widely studied in both clinical and non-clinical samples, and have been shown to be excellent (Lasa et al., 2000; Richter et al., 1998). In addition to its successful validation in several other countries (Shaw et al., 1985), the effectiveness of the BDI as a screening measure for depression has also been studied in Finland (Nuevo et al., 2009b; Seppälä et al., 2010). The BDI was found to have acceptable or moderate sensitivity (70.1%) and specificity (73.7%) for detecting depression in a general population sample. These findings provide additional support for the reliability and validity of the BDI, demonstrating that it can be a useful instrument for identifying the presence of depression among the Finnish population.

Another widely used self-report assessment tool is the Center for Epidemiologic Studies Depression Scale (CES-D) (Radloff, 1977). The CES-D is a 20-item rating scale developed to assess DS in the general population. It is used mostly in epidemiological studies, in treatment studies and in measuring change over time. The CES-D has been shown to be a valid and reliable tool in epidemiological studies (Radloff, 1977). In population-based studies, the sensitivity of the scale has proved to be 60% and its specificity 86% (Myers and Weissman, 1980).

The Zung Self-Rating Depression Scale (SDS) is among the most popular self-rating depression scales (ZUNG, 1965). It was developed to evaluate the level of depression among patients with a diagnosis of depressive disorder. It is a 20-item questionnaire covering affective, psychological, and somatic symptoms associated with depression. Many studies have reported on the psychometric properties of the tool in different cultures, such as in Finland and Japan (Kivela and Pahkala, 1986; Sakamoto et al., 1998).

In Finnish primary health care, the Depression Scale (DEPS) has been widely used for over 15 years, and it is also recommended by the Finnish Evidence-Based Treatment Guideline for Depression as well (Current Care Guideline). It is 10-item questionnaire which sensitivity (75%) and specificity (88%) were evaluated before implementation by the Finnish Medical Society Duodecim (Duodecim). However, a recent Finnish study found that the DEPS has only some limited ability to distinguish in primary care patients, and its ability to measure the severity of depression is questionable (Poutanen et al., 2010).

Self-report questionnaires are commonly used in epidemiological studies on account of their cost- and time-saving properties. However, they cannot take the place of a comprehensive clinical interview for confirming a diagnosis of depression.

2.2.3 Physical activity and depressive symptoms

The effect of physical activity on depression and depressive symptoms has been widely studied. It is known that physical activity is inversely associated with depression levels. Numerous studies have been published on the effects of both aerobic and anaerobic exercise, and strength training on depressiveness among different age categories, with a wide variety of intervention types and settings. Perhaps the main problems of these studies are the small sample sizes of different study arms and the motivation of the volunteer participants to adhere to a PA program.

Perhaps the best known study on PA and DS is that conducted by Paffenbarger et al., who examined 31 000 students over 26 years, from 1962 to 1988 (Paffenbarger et al., 1994). The study showed that students who were physically active reported lower DS than those who were physically inactive. A recent Cochrane meta-analysis of 32 randomized controlled trials (RCT) on PA and depression with 1 858 participants found that depressive symptoms significantly decreased among the participants who received exercise therapy in comparison to controls (Rimer et al., 2012). The difference in the effect between the groups was about three points on the Beck Depression scale. However, when only studies with adequate allocation concealment, intention-to-treat analysis and blinded outcome assessors were analyzed, the effect size was clinically small and no longer statistically significant. The meta-analysis concluded that PA seems to alleviate DS, but further research is needed (Rimer et al., 2012). However, even low doses of PA have been shown to have a protective effect against the likelihood of depression (Teychenne et al., 2008; Rethorst et al., 2009), and the beneficial effects of exercise on DS can be achieved even without improvements in fitness (Rimer et al., 2012).

There are also studies comparing the effect of PA with other treatments of DS. When the effects of PA and antidepressants were compared in a meta-analysis, no difference was found (Rethorst et al., 2009). A similar result was found between exercise and cognitive therapy (Rethorst et al., 2009). Bright-light therapy, in turn, has yielded somewhat controversial results. One study found that both exercise and bright-light effectively relieved DS (Leppämäki et al., 2002), whereas in another study bright-light therapy was not as beneficial as PA in reducing DS (Pinchasov et al., 2000). Additionally, the combination of light exposure and PA treatments has shown beneficial effects in alleviating DS (Leppamaki et al., 2004; Partonen et al., 1998).

The association between PA and DS seems to be bidirectional, as DS are associated with deleterious health-related behavior. For example, both total and leisure-time physical activities are shown to decline as a consequence of DS, probably due to low motivation and lack of initiative (Roshanaei-Moghaddam et al., 2009). Another study showed that emerging depression is most likely to co-occur with a person's change from being physically active to being sedentary, and that depression was associated with a decrease in PA (van Gool et al., 2003).

For the purposes of the present research, a systematic literature search was performed (from the index date of the database up to October 2012) for original studies investigating associations between physical activity and depressive symptoms. Articles were considered for inclusion in the systematic review if 1) the authors reported data from an original, peer-reviewed study (i.e., not case reports, comments, letters, meeting abstracts, or review articles); 2) the study was a cross-sectional or prospective cohort study with a noninstitutional middle-aged or older adult population (age >45 years); 3) the authors reported an association between the two conditions and 4) the study was published in English. In the case of multiple publications from the same study, only the most recent paper or article was included.

A total of 304 articles were found in this systematic literature search. After screening titles and abstracts based on the aforementioned criteria, 41 articles remained. After examining those articles in full text, 14 articles were excluded. Finally, 27 articles were included (Table 1).

TABLE 1 Summary table of observational studies examining the association between physical activity and depressive symptoms.

Authors	**Subjects, N Age**	**Study design**	**Association**
Almeida et al., 2011	20 677 ≥60	cross-sectional	+ DS was independently associated with physical inactivity
Backmand et al., 2003	1 336 46–92	cross-sectional	+ PA has a protective effect against DS; an increase of one MET-unit (hour/day) statistically significantly decreased the risk for DS by 8 %
Brown et al., 2005	9 207	6-year follow-up	+ Relationship between increasing PA and decreasing DS
Cassidy et al., 2004	278 ≥70	cross-sectional	+ Physically active women were half as likely to have DS when compared to their physically inactive counterparts
Chen et al., 2012	2 727 ≥65	cross-sectional	+ LTPA but not NLTPA (N=non) was significantly associated with DS
Choi et al., 2008	188 18-64	cross-sectional	+ Time spent in LTPA had negative associations with DS
Fukukawa et al., 2004	1151 40-79	2-year follow-up	+/- Daily walking predicted fewer DS (65-79 years old) not 40-64
Galper et al., 2006	1277 female 5451 male 20-88	cross-sectional	+ Dose-response associations between the level of physical activity and both CES-D and GWB scores
Hamer et al., 2009	4323 ≥46	4-year follow-up	+ Moderate and vigorous PA decreased the odds for DS
Kamphuis et al., 2007	909 male 70-90	cross-sectional	+ Men with more DS were less physically active than men with few DS
Ku et al., 2012	1160 ≥67	11-year follow-up	+ PA was negatively associated with changes in DS. DS were not related to change in PA
Lampinen et al., 2000	663 ≥65	8-years follow- up	+ Reduced intensity of physical exercise during the 8 years associated with more DS at follow-up
Lee and Park, 2008	645 ≥65	1-year follow-up	+ Significantly less DS were observed with PA
Lindwall et al., 2011	17 593	2-year follow-up	+ Reciprocal prospective relationship between PA and DS
Pitsavos et al., 2005	3042 20-89	cross-sectional	+ Physically active men and women were less likely to report DS
Piwonski et al., 2010	13 545 20-74	cross-sectional	+ Inactivity was significantly and independently related to DS
Reichert et al., 2011	379 60-79	cross-sectional	+ More intense PA was related to lower prevalence of DS. PA was inversely related to DS in males, but not in females
Rosqvist et al., 2009	645 81-87	cross-sectional	+ Risk of physical inactivity was higher among persons with DS compared with non-depressed people

Salguero et al., 2011	436 60-98	cross-sectional	+ PA was related to decreased DS
Sieverdes et al., 2012	9580 male 20-87	cross-sectional	+ A significant inverse relationship between PA categories and DS
van Gool et al., 2003	1280 55-85	6-year follow-up	+ Emerging depression associated with change from being physically active to being sedentary
Wada et al., 2006	11 724 18-69	cross-sectional	+ DS were significantly associated with PA less than once a week
Wise et al., 2006	35 224 female 21-69	2-year follow-up	+ Leisure time vigorous physical activity was associated with a reduced odds of DS
Woo et al., 2002	2 032 ≥70	3-year follow-up	+ Inverse relationship between DS and increasing PA
Xue et al., 2012	433 female 70-79	12-years follow-up	+ DS were associated with sedentary behavior and/or a fast decline in activity.
Yang et al., 2012	935 30-45	8-year follow-up	+ Sustained participation in LTPA was inversely associated with DS
Yoshiuchi et al., 2006	184 65-85	1-year follow-up	+ PA showed significant negative correlations with DS

Of the 27 articles found, 14 were cross-sectional studies and 13 were follow-up studies ranging from 1 to 12 years. Most studies included both females and males, but two studies concerned females only and two males only. Primarily, the studies examined the effect of PA on DS, and an inverse association between PA and DS was found, in both the cross-sectional and follow-up studies. The study by Chen et al. (2012) found that LTPA was associated with DS, whereas domestic and work-related physical activities were not. In study of Fukukawa et al. (2004), daily walking predicted fewer DS at the 2-year follow-up among older adults, but not among middle-aged adults. Some studies investigated the impact of DS on PA. Emerging depression was found to be associated with a change from being physically active to being sedentary (van Gool et al., 2003) and furthermore, DS were associated with a fast decline in PA (Xue et al., 2012). In their 11-year follow-up, Ku et al. (2012) found that PA was negatively associated with changes in DS, whereas DS were not related to change in PA. In one study, a gender difference emerged: PA was inversely related to DS in males, but not in females (Reichert et al., 2011). A reciprocal prospective relationship between PA and DS was also reported (Lindwall et al., 2011).

2.2.4 Mechanisms behind the interaction of physical activity and depressive symptoms

Despite extensive investigation regarding the relationship between PA and DS, the underlying mechanisms are not completely understood. Several possible biochemical, physiological and psychological mechanisms that have been proposed to be behind the beneficial effect of PA on DS are shown in Figure 2.

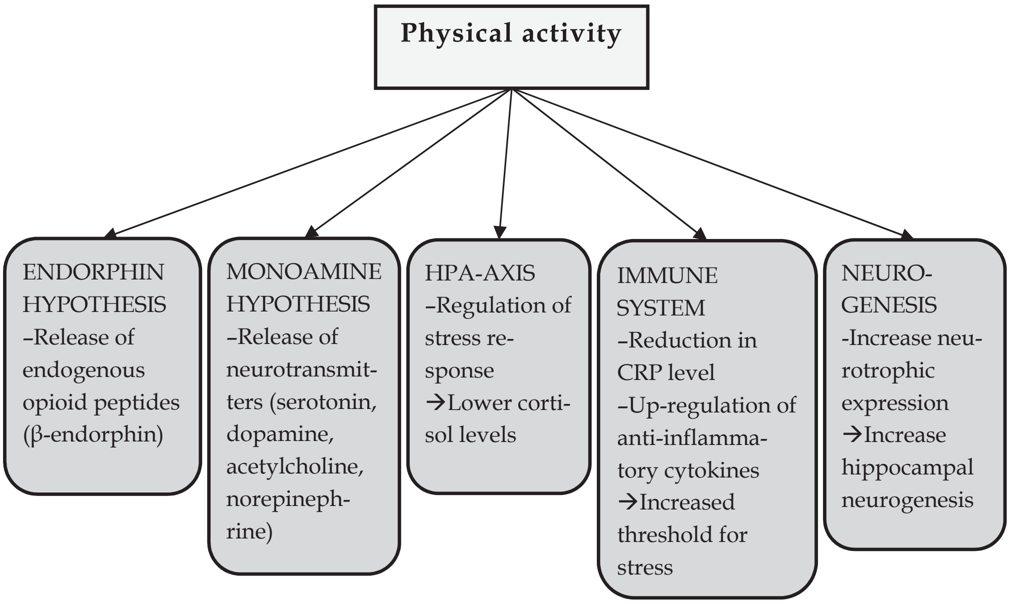

FIGURE 2 Physiological effects of physical activity on depression.

In the first place, endogenous opioids, such as endorphins are hypothesized to be the mediating factor between PA and enhanced mental health (Grisel et al., 2008). Although PA stimulates the production of endorphins, there is only little evidence of a correlation between increased endorphin levels following PA and a reduction in DS (Dishman and O'Connor, 2009). Therefore, alternative hypotheses have been favored recently. The monoamine hypothesis is based on the fact that PA induces the release of several neurotransmitters, such as serotonin, dopamine, acetylcholine and norepinephrine by increasing the activity of some subtypes of receptors for the transmitters (Sarbadhikari and Saha, 2006). These transmitters are diminished with depression, and thus anti-depressant medication is based on these ingredients (Deslandes et al., 2009). This hypothesis gives preliminary support for the use of PA in alleviating DS (Brosse et al., 2002).

Other proposed mechanisms include exercise-driven changes in the hypothalamic–pituitary–adrenal (HPA) axis that regulates the stress response (Eyre and Baune, 2012). In depression the function of the HPA axis is imbalanced. Depressed patients tend to exhibit higher baseline basal cortisol levels and non-suppression in cortisol secretion denoting hyperactivity of HPA axis (Pariante and Lightman, 2008). Although PA activates also the HPA axis, this exercise-induced stress response is different from the threat-induced activation of the HPA-axis in depression. There is substantial evidence that PA is related to lower reactivity of the sympathetic nervous system and HPA axis. Lower stress-related cortisol increase and cardiovascular reactivity, and more rapid cardiovascular recovery have been found among physically active persons compared to those who are less active (Crews and Landers, 1987; Jackson and Dishman, 2006; Rimmele et al., 2007; Spalding et al., 2004).

One proposed mechanism of action is the anti-inflammatory effect of regular physical activity on the immune system, as depression is associated with low-graded inflammation (Rethorst et al., 2011). This hypothesis is supported by longitudinal studies, which showed that regular training induces a reduction in CRP (C-reactive protein) level, and also by studies conducted under laboratory conditions (Beavers et al., 2010; Petersen and Pedersen, 2005). Exercise is proposed to up-regulate anti-inflammatory cytokines resulting in an increased immune system threshold for stress. Hence, physical activity could be effective in reducing chronic inflammation, especially in individuals with chronic diseases associated with a state of elevated low grade inflammation (Hallberg et al., 2010).

In addition, PA is involved in neurogenesis in the hippocampus. Depression, aging and stress have been demonstrated to decrease neurotrophic expression and hippocampal neurogenesis, while antidepressants and exercise have favorable effects on these (Cotman et al., 2007; Duman, 2005; Erickson et al., 2012). One such influential factors is Brain-Derived Neurotrophic Factor (BDNF), a protein which supports neuron survival and contributes to growth and differentiation of new neurons and synapses, as low levels of BDNF has been shown to occur with depression (Duman and Monteggia, 2006; Karege et al., 2002). In contrast, PA has proved to normalize depression-derived decreed BDNF (Laske et al., 2010).

Four main psychological mechanisms of action have been proposed. Physical activity has been stated to provide ‘time out’; this is known as the distraction hypothesis (Daley, 2002). PA allows the depressed person to take time out from his or her worries. The second explanation is achievement of a sense of mastery with the successful completion of physical activities (Daley, 2002). Improved self-esteem and self-image attained through PA have also been suggested as possible therapeutic mechanisms (Kirkcaldy et al., 2002). Finally, an increased opportunity for social interaction may play some role in the relationship between physical activity and depression (Fox, 1999).

Consequently, improvement in mental health due to physical activity is probably based on some or all of the pathways mentioned. Hence, the relationship between PA and depressive symptoms may rest upon such multiple mechanisms, while they may also be reciprocal. People who experience reduced depressive symptoms may be more likely to continue a physically active lifestyle.

2.3 Association between physical activity and cardiometabolic risk factors

There is a consensus that a physically active lifestyle results in positive health-related outcomes. However, the relationship between PA and health is rather complex. As early as 1948, the World Health Organization defined heath as "a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity" (World Health Organization, 1948). With physical activity it is possible to affect all these three dimensions of health: physical, mental and social health. Thus, physical activity is indicated in the treatment of numerous medical disorders (Pedersen and Saltin, 2006). Physical activity has both acute health effects which occur in the hours after a physical activity session, and chronic effects which, in turn, occur over time.

2.3.1 Effect of physical activity on cardiometabolic risk factors

There is plenty of evidence for the beneficial effect of PA on cardiometabolic risk factors which, without intervening, turn into cardiovascular diseases and type 2 diabetes. The beneficial effects of physical activity on blood pressure is well documented among both normotensive (Cornelissen and Fagard, 2005; Kelley et al., 2001) and hypertensive (systolic blood pressure >140mmHg; diastolic blood pressure >90mmHg) individuals (Pescatello et al., 2004). The decrease in blood pressure after PA typically lasts 4-10 hours after the exercise session, but this acute effect of exercise may last up to 22 hours (Pedersen and Saltin, 2006). Repeated exercise, in turn, can lead to chronic adaptations. Repeated aerobic exercise three times per week for four weeks at 60-70% of maximum work lasting 40 minutes induced a significant reduction in blood pressure which persisted for a period of one week after cessation of exercise (Meredith et al., 1990). Another study on the effect of exercise on blood pressure showed that blood pressure was significantly reduced both after acute (30 min at 65% maximum oxygen consumption) and after 8 weeks of chronic aerobic exercise (4 times per week, 30 min per session, 65% of maximum oxygen consumption), denoting that the acute and chronic effects of exercise appeared at the same level (Liu et al., 2012). A significant reduction also occurred after 5 weeks of training, but not after one or three weeks. Thus, in order to achieve long lasting effect on blood pressure, the training should be long-term. A review article published in 2006 showed that with aerobic exercise it is possible to decrease both systolic blood pressure (by 3-3.84 mmHg among normotensive and 15 mmHg among hypertensive participants) and diastolic blood pressure (by 2-2.58 mmHg among normotensive and 4 mmHg among hypertensive participants) (Pedersen and Saltin, 2006). The antihypertensive effect of PA is considered to be based on neurohumoral, vascular and structural adaptation. In addition, PA reduces sympathetically induced vasoconstriction and decreases catecholamine levels (Pedersen and Saltin, 2006).

Individuals with hypertension often also have dyslipidemia, including some abnormality in the blood lipid (e.g. cholesterol and triglyceride) levels. Strong evidence of the beneficial effect of PA on the blood lipid profile has been reported in the literature (Pedersen and Saltin, 2006). A meta-analysis of 51 studies, conducted in 2001, showed that HDL increased by 3.7%, LDL decreased by 5% and triglyceride concentration decreased by 3.7% (Leon and Sanchez, 2001). The PA interventions included aerobic exercise 3-5 times per week with duration of 30 minutes in the majority of the studies. Similar results were found in a RCT, which, in addition showed that a high amount of exercise (32 km jogging/week at 65–80% of maximum oxygen consumption) had a significantly better effect on lipid profile than a low amount of exercise (19km jogging/week at 65–80% of maximum oxygen consumption) (Kraus et al., 2002). Thus, based on the literature, the amount of PA should be high and intensity moderate or high to achieve a favorable lipid profile (Pedersen and Saltin, 2006). In addition, in their RCT, Slentz et al. (2007) studied the effect of six months exercise training on plasma lipoproteins at 16–24 h, 5 days, and 15 days after the last training session. They showed that the beneficial effects of exercise found at 24 h were largely sustained at both 5 and 15 days after the last exercise cessation. The study also observed that moderate-intensity exercise had favorable effects on triglycerides and vigorous-intensity on HDL metabolism (Slentz et al., 2007). The possible mechanisms underlying the relationship between PA and lipid profile may be the fact that lipid metabolism increases due to exercise, and thus muscles are able to use lipids to a greater extent, instead of glycogen (Pedersen and Saltin, 2006).

Furthermore, glucose tolerance has been shown to be better among those who are physically active (Dunstan et al., 2004). Most studies on lifestyle modification and impaired glucose tolerance include interventions with combined exercise and diet, and thus isolated effect of exercise is difficult to determine. However, Tuomilehto et al. (2001) provided some indication of an independent effect of exercise in their RCT, which studied Finnish participants with impaired glucose tolerance. They found that participants in the intervention group with moderate 30-minute bout of daily exercise combined with diet managed to reduce the risk for type 2 diabetes by 58% in a 3.2-year follow up. During that period, the weight loss of the participants was only modest (Tuomilehto et al., 2001). Another study randomized over three thousand participants with impaired glucose tolerance into metformin treatment, lifestyle modification and placebo and, found a similar reduction in the risk for type 2 diabetes among those in the lifestyle group, as was reported in the Finnish study (Knowler et al., 2002). In addition, the lifestyle intervention was more effective than metformin. The beneficial effect of PA on glucose tolerance is based on the ability to enhance insulin sensitivity and contraction-induced glucose uptake in the muscle (Dela et al., 1993). Further, PA has a favorable effect on endothelial dysfunction, which is common among those with insulin resistance.

Consequently, in all these cardiometabolic risk factors, PA has proved to have a beneficial effect (Wannamethee et al., 2000; Warburton et al., 2006).

Based on the literature, the amount of exercise for those with these cardiometabolic risk factors should mainly follow the general PA recommendations for the general population: 150 minutes of moderate-intensity or 75 minutes of vigorous-intensity aerobic LTPA each week, with the addition of muscle-strengthening and balance training two times a week (Haskell et al., 2007). Muscle-strengthening training should not be forgotten, as skeletal muscle seems to have several beneficial effects through the endocrine system. Muscle mass has been identified as a secretory organ as it is shown to produce, express and release cytokines and other peptides called myokines (Pedersen, 2011). With these peptides, muscles are able to communicate with other organs, such as adipose tissue, liver, pancreas, bones and brain. Myokines are involved in muscle hypertrophy, fat oxidation, immune system, and endothelial function of the vascular system (Pedersen and Febbraio, 2012). However, to induce all this to act, muscle contraction is needed (Pedersen and Febbraio, 2012). Consequently, the low output of myokines associated with loss of muscle contraction may provide a potential mechanism for the association between physical inactivity and cardiometabolic risk factors. Adipose tissue, however, is also an active endocrine and an immune organ with metabolically active cells, which in turn promotes and exacerbates cardiometabolic risk factors (Bays, 2012).

PA has a central role in prevention of cardiometabolic risk factors, the prevalence of which in Finland are as high as 64% for raised cholesterol, 58% for overweight, 49% for raised blood pressure, 23% for obesity and 10% for raised blood glucose (World Health Organization, 2005).

2.3.2 Metabolic syndrome

Cardiometabolic risk factors can be addressed together as metabolic syndrome (MetS). MetS is known as the clustering of several metabolic abnormalities, including a combination of abdominal obesity, hypertension, dyslipidemia, insulin resistance, and hyperglycemia, which are often accompanied by a proinflammatory state (Grundy et al., 2005; Laaksonen et al., 2004), in turn also increasing the risk for developing type 2 diabetes (Ford et al., 2008; Laaksonen et al., 2002a) and cardiovascular diseases (Sattar et al., 2008; Wang et al., 2007). The prevalence of MetS depends partly on the definition used, but age, gender, race and ethnicity are relevant factors (Cornier et al., 2008). Approximately one-fourth of the adult European and Latin American populations have MetS (Grundy, 2008), while in the United States the prevalence is as high as 39% among adults (Churilla et al., 2007). The prevalence in Finland is 12% among people aged 24-39 (Yang et al., 2008), rising to as high as 45% among middle-aged people (aged 45-64) (Hu et al., 2008). The prevalence of MetS is rapidly increasing worldwide (Grundy, 2008; Zimmet et al., 2005), which makes it major public health problem due to the increased risk for type 2 diabetes and CVD.

As metabolic syndrome is a cluster of different abnormalities instead of single disease, it has resulted in the development of multiple concurrent definitions. It was first defined by the World Health Organization (WHO) in 1998 (Alberti and Zimmet, 1998), since when several definitions have been proposed by different working medical societies (Table 2). The main criteria in the WHO definition were insulin resistance, impaired glucose tolerance (IGT) or type 2 diabetes. In addition, two of the following parameters were required: hypertension, hypertriglyceridemia or low HDL-cholesterol, obesity, and microalbuminuria (Alberti and Zimmet, 1998).

TABLE 2 Most commonly used definitions of metabolic syndrome.

	WHO (1988)	**EGIR (1999)**	**NCEP/ATPI II (2001)**	**IDF (2005)**	**AHA/NHL BI (2005)**
Required	Type 2 diabetes or IFG or IGT	Fasting-insulin in top 25%	-	Abdominal obesity with ethnicity-specific values	-
Additionally	and ≥2 of:	and ≥2 of:	≥3 of:	and ≥2 of:	≥3 of:
Fasting glucose (mmol/l)		≥6.1	≥6.1	≥5.6	≥5.6
HDL cholesterol (mmol/l)	<0.9 males, <1.0 females	<1.0	<1.03 males, <1.29 females	<1.03 males, <1.29 females	<1.03 males, <1.29 females
Triglycerides	≥1.7	≥2.0	≥1.7	≥1.7	≥1.7
Obesity	Waist/hip ratio > 0.90 in males, >0.85 in females, or BMI > 30 kg/m²	Waist ≥ 94 cm males, ≥ 80 cm females	Waist ≥ 102 cm males, ≥ 88 cm females		Waist ≥ 102 cm males, ≥ 88 cm females
Blood pressure (mmHg)	≥ 140/90 or drug treatment	≥ 140/90 or drug treatment	≥ 130/85 or drug treatment	≥ 130/85 or drug treatment	≥ 130/85 or drug treatment
Microalbuminuria	urinary-albumin ≥ 20 µg/min				

IFG=impaired fasting glucose, IGT=impaired glucose tolerance, HDL=high-density cholesterol

The European Group for the study of Insulin Resistance (EGIR), in turn, excluded microalbuminuria as an integral component of the MetS in 1999, while it required hyperinsulinemia to be present (Balkau and Charles, 1999). In 2001, the National Cholesterol Education Program Adult Treatment Panel III (NCEP/ATPIII) introduced alternative criteria for defining MetS, including three of the following as mandatory components: central obesity, blood lipids, hypertension, and fasting glucose (Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, 2001). Thus, it differed from the previous definitions in that insulin resistance was not a necessary diagnostic component, thus making it possible to capture those at high risk for both cardiovascular diseases and diabetes.

Thereafter, the International Diabetes Federation (IDF) published their own criteria in 2005 which modified the NCEP/ATPIII criteria (Alberti et al., 2005). The IDF emphasized central obesity as the major underlying risk factor for MetS, introducing abdominal obesity measured with waist circumference as a prerequisite of the diagnosis. Further, IDF took account of ethnic differences in the correlation between abdominal obesity and other metabolic syndrome risk factors.

Furthermore, the American Heart Association (AHA) and the National Heart, Lung, and Blood Institute (NHLBI) updated the MetS criteria (Grundy et al., 2005). The AHA/NHLBI criteria, in contrast to the IDF criteria, are largely based on the NCEP/ATP III criteria, which have been widely adopted in the US. Only the threshold for IFG was reduced, to correspond with the American Diabetes Association (ADA) criteria for IFG (Genuth et al., 2003). Thus, it is also called the revised NCEP/ATPIII.

Despite wide and profound development work on the definition of MetS, there is still a lack of commonly and universally accepted criteria for MetS. Currently, the NCEP/ATP III and IDF are the most widely used definitions. These definitions focus specifically on central obesity. In contrast, the other criteria largely focus on insulin resistance.

2.3.3 Pathogenesis of metabolic syndrome and association with physical activity

The pathogenesis of the MetS still remain partly unclear, but there is undoubted evidence that sedentary behavior, an unhealthy diet, and overweight and obesity are factors underlying the development of MetS (Laaksonen et al., 2004; Teran-Garcia and Bouchard, 2007). Additionally, abdominal obesity and insulin resistance are undoubtedly key elements in the pathophysiology of MetS, and behind both of these elements, hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis is proposed to play a central role (Pasquali et al., 1998; Wajchenberg, 2000). The HPA axis is a complex neuroendocrine system with interaction between the hypothalamus, the pituitary gland and the adrenal glands. It comprises the stress system and regulates several body processes. One of the reasons for hyperactivity of the HPA axis is chronic stress. Chronic stress with increased cortisol levels is known to contribute to the development of many somatic diseases and to the development of MetS as well (Björntorp and Rosmond, 1999; Chalew et al., 1995; Chrousos, 2000). Also, insulin resistance and altered lipid profile, as diagnostic components of MetS, are suggested to have some involvement in higher cortisol levels (Andrews and Walker, 1999).

Abdominal obesity, with its accompanying adipose tissue, acts as an endocrine organ which secretes hormones and proteins essential in the regulation of cardiovascular risk factors and, further, produces inflammatory cytokines which, in turn, induce insulin resistance (Mohamed-Ali et al., 1998; Perseghin et al., 2003).

With daily lifestyle habits, including diet, PA, alcohol consumption and smoking, it is possible to affect the factors behind MetS. Recommendations for the prevention of MetS include increased PA (including aerobic and resistance exercise), a healthy diet, and weight loss (Alberti et al., 2006; Grundy et al., 2005; Lakka and Laaksonen, 2007). Many studies have reported beneficial effects of PA on MetS. These have mainly been cross-sectional epidemiological studies, but a few prospective studies and, more recently, RCT studies have also been published (Wang et al., 2012). Lakka et al. (2003) showed, in their population-based cross-sectional study of 1 069 middle-aged males that those with low levels of LTPA are more likely to have MetS. In addition, they suggested that a sedentary lifestyle and poor cardiorespiratory fitness can be considered features of MetS. Ilanne-Parikka et al. (2010), in turn, followed 486 middle-aged overweight female and male with impaired glucose tolerance over an average of 4.1 years (Ilanne-Parikka et al., 2010). They found that an increase in moderate to vigorous LTPA (from 1.4 to 2.5 hours per week in females and from 2.3 to 3.1 in males) decreased the likelihood of developing MetS and increased the likelihood of resolving MetS. Moreover, these changes were independent of changes in diet and body weight. Kukkonen-Harjula et al. (2005), in turn, found in their randomized trial that combined diet counseling with PA did not alleviate MetS more than diet counseling alone. Wang et al. (2012) studied the effect of a 12-month PA and a nonexercise health education intervention in an elderly sample. Their randomized controlled trial showed that the use of medications to treat MetS components may weaken the effect of PA on MetS among the elderly. The prevalence of MetS was reduced, but the PA intervention did not reduce the prevalence of MetS more than the nonexercise health education intervention. However, in the subgroup of participants not taking any medication for treating components of MetS, those in the PA intervention had lower odds of having MetS in comparison to those with the health education intervention. Lakka & Laaksonen (2007) concluded in their review that although RCTs with the prevention or treatment of the MetS as the main outcome are lacking, extensive evidence confirms the favorable effect of PA on the risk factors behind type 2 diabetes and MetS. They suggest the general PA recommendations for the population to be valid also among those with MetS but however, taking into account possible individual contraindications for vigorous PA and resistance training should take into account.

2.4 Summary of the literature

Almost one-third of the adult populations globally are insufficiently active for health benefits. This is partly a consequence of lack of engagement in LTPA and increased sedentary behavior during occupational and domestic activities. The highest prevalence of insufficient PA occurs in the high-income countries. Inactivity and sedentary behavior have, in turn, contributed to the growing burden of lifestyle-related diseases, such as cardiovascular diseases and type 2 diabetes, and to a cluster of these diseases risk factors, metabolic syndrome. In addition, there is plausible evidence of deleterious effect of low PA on mental health; depressive symptoms are more prevalent among those with a low PA level. Moreover, depressive symptoms are associated with somatic diseases as well.

Thus, these factors are clearly linked to each other. Furthermore, fairly extensive studies have been conducted on these links, although mainly by studying the relationship between just two factors. However, on the population level, there is a lack of evidence on the simultaneous investigation of physical inactivity, cardiometabolic risk factors and depressive symptoms – factors which, if serious action is not taken, may ultimately present an unmanageable burden.

3 PURPOSE OF THE STUDY

The purpose of this thesis was to analyze the interrelationships of physical activity and depressive symptoms with cardiometabolic risk factors in a cross-sectional population-based study conducted in Finland in the year 2007.

The specific aims of this thesis were to study:

1. The relationships between physical activity and self-rated fitness and health. (additional data)
2. Physical activity level in relation to depressive symptoms and cardiometabolic risk factors. (Studies I, II and additional data)
3. The association between lifetime physical activity and occurrence of depressive symptoms in older age. (Study III)
4. The significance of physical activity level related to the prevalence of unintentional injuries and presence of depressive symptoms. (Study IV)
5. The association between physical activity and the simultaneous presence of metabolic syndrome and depressive symptoms. (Study V)

4 MATERIAL AND METHODS

This thesis is based on a cross-sectional population study, the FIN-D2D survey, which monitors cardiometabolic risk factors in Finnish adults aged 45 to 74 years.

4.1 Study participants and design

The study was carried out in the hospital districts of Central Finland, Pirkanmaa, and South Ostrobothnia between October and December 2007. A random sample of 4 500 subjects aged 45–74 years, stratified according to gender, 10-year age groups (45–54, 55–64 and 65–74 years) and the three geographical areas, was selected from the National Population Register in August 2007. The study participants were invited by mail to a clinical examination. Of the 4 500 persons, 64% participated in the health examination. The data analyzed in this thesis are based on those 2 868 participants. Non-responders were on average 1.4 years younger than responders ($p<0.001$), and females were more likely to participate than males (67% vs. 61%, $p<0.001$). The participation rate in the articles of this thesis varies due to the differing availability of the study variables between articles. The study samples and inclusion criteria in the articles are presented in Figure 3. More detailed information can be found in the individual articles.

All the participants signed an informed consent form. Ethical permission for the study was granted by the Hospital District of Helsinki and the Uusimaa ethics committee.

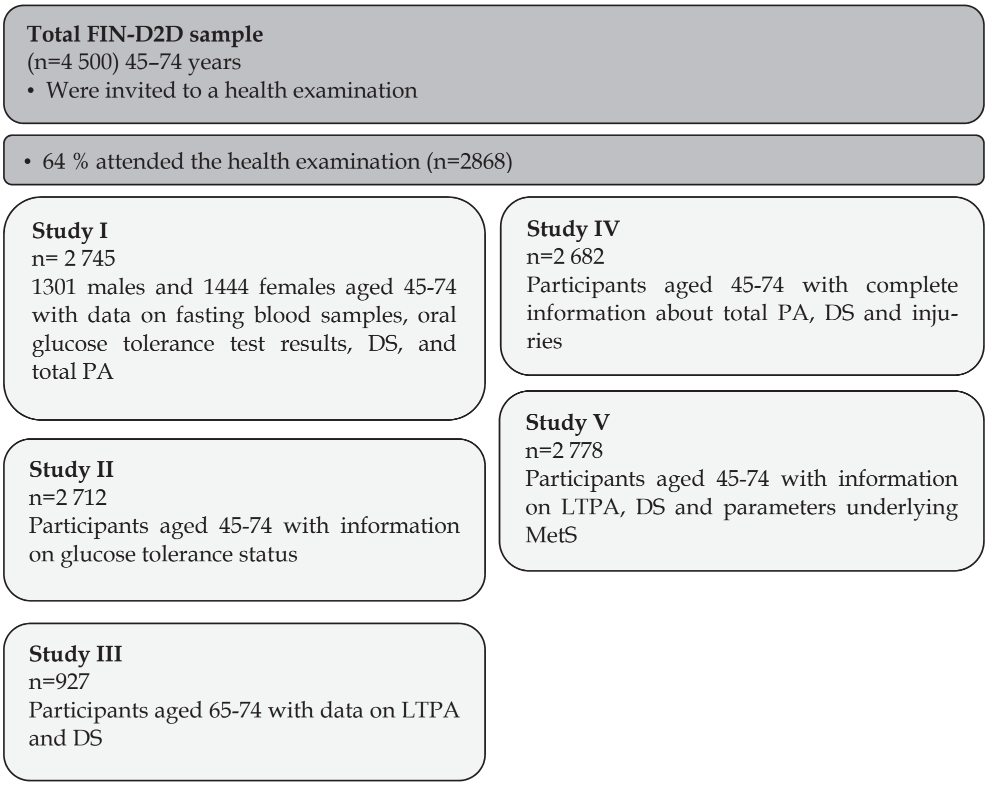

FIGURE 3 Study samples in articles I-V.

4.2 Measurements

Measurements included both self-rated questionnaires on health, lifestyle factors, depressive symptoms and physical activity, and objectively measured cardiometabolic risk factors.

4.2.1 Physical activity

Total physical activity
Total physical activity (PA) was assessed using the self-administered short version of the International Physical Activity Questionnaire (IPAQ). The questionnaire estimates the frequency, intensity, and duration of PA in leisure time and at home, and also includes occupational and commuting PA over the previous seven days (Bauman et al., 2009; Craig et al., 2003; Papathanasiou et al., 2010). Total daily PA in MET-min (Metabolic Equivalent; 1 MET = resting energy expenditure) was calculated according to the official IPAQ scoring protocol

(www.ipaq.ki.se). In the analysis, total PA was divided into three categories (low, < 600; moderate, 600-2999; and high, ≥ 3000) or into tertiles based on MET-min week^{-1}, where the high category represents the recommended level of total PA (Bauman et al., 2009).

Leisure-time physical activity

Leisure-time physical activity (LTPA) was assessed with the question: "How much physical activity do you engage in leisure-time?" The response options were: In my leisure-time I 1) read, watch television and do things which do not need physical activity; 2) walk, ride a bicycle or move in other ways requiring physical activity at least for four hours a week; 3) do physical activities to maintain my condition such as jogging, cross-country skiing, aerobics, swimming or ball-games at least three hours a week; and 4) practice for competitions in running, cross country skiing, orienteering, ball games, or other physically heavy sports several times a week. LTPA was classified as follows: low (category 1), moderate (category 2) and high (categories 3 and 4). The questionnaire on LTPA has shown a high correlation with physical fitness, as measured by maximal oxygen uptake, and its validity against serum cholesterol and BMI has proved to remain stable over 25 years (Aires et al., 2003; Saltin, 1977).

Lifetime leisure-time physical activity

Lifetime history of LTPA was assessed with the following question: "How often in your leisure-time did you exercise (including jogging, cross-country skiing, cycling, swimming, walking, pole/Nordic walking, aerobics, ball games, ice hockey, etc.) at age of 15–24, 25–34, 35–44, 45–54 and 55–64 years, and how often do you exercise at present". The response options were: over 5 times a week, 4–5 times a week, 2–3 times a week, once a week, 1–3 times a month, less than once a month and I cannot exercise because of an illness or disability.

4.2.2 Depressive symptoms

Depressive symptoms (DS) were assessed by using the Beck Depression Inventory (BDI) (Beck et al., 1961), which is a 21-item self-report questionnaire consisting of symptoms and attitudes related to depression. The items are summed to form a total score, with a range from 0 to 63. The cut–off point for DS was 10, which indicates at least mild depression (Koponen et al., 2008; Väänänen et al., 2008). Participants with DS ≥ 10 were offered a possibility to meet a psychiatrist for further examination.

4.2.3 Cardiometabolic risk factors

Alcohol use

Alcohol-specific questions inquired about the frequency of occasions during the past 12 months the respondent had drunken alcohol to feel inebriated. Alcohol consumption was classified into four categories as follows: never, occasionally, at least once a month, and at least once a week.

Hypertension

Hypertension was indicated if systolic blood pressure was ≥130 mmHg or diastolic ≥85 mmHg or participants were having treatment for previously diagnosed hypertension. Blood pressure was measured with a mercury sphygmomanometer twice in a sitting position after a minimum of 15 minutes of acclimatization.

Dyslipidemia

Dyslipidemia was analyzed using a fasting venous blood specimen and entailed at least one of the following: elevated low-density lipoprotein (LDL) cholesterol (>3.0 mmol/L) or triglyceride concentration (>2.0 mmol/L), decreased high-density lipoprotein (HDL) cholesterol concentration (<1.0 mmol/¥), and the use of cholesterol-lowering agents or a ratio of LDL and HDL >4 (Castelli et al., 1992). A fasting venous blood specimen was drawn into a gel serum tube for serum cholesterols, triglycerides and glucose. The serum and plasma were separated within one hour by centrifuging at room temperature. After that, the samples were aliquoted into storage tubes and stored at a minimum of -20°C. Later, the samples were transported frozen to the National Institute for Health and Welfare and stored at -70 C° until analyzed in the same laboratory.

Glucose profile

Impaired glucose tolerance (IGT) was defined as a fasting plasma glucose (FPG) level of < 7.0 mmol/L and a two-hour glucose value of 7.8-11.0 mmol/L. Impaired fasting glycemia (IFG) was defined if FPG was 6.1-6.9 mmol/L and the two-hour glucose value was < 7.8 mmol/L (James et al., 1997). Having both IGT and IFG is considered as having impaired glucose regulation (IGR). The subjects were defined as having screen-detected type 2 diabetes (ST2D) if they had not previously been diagnosed with type 2 diabetes and their FPG was ≥ 7.0 mmol/L or 2-h glucose ≥ 11.1 mmol/L at the clinical examination (James et al., 1997). The subjects were defined as having previously known type 2 diabetes (T2D) if they reported a history of diabetes. Subjects who did not have these glucose regulation abnormalities or previously known diabetes were defined as having normal glucose regulation. Accordingly, the glucose regulation categories were: impaired glucose tolerance, impaired fasting glycemia, screen-detected diabetes and previously known diabetes.

Metabolic syndrome

MetS was defined according to the NCEP criteria (Grundy et al., 2005), which include the presence of at least three of the following: abdominal obesity (waist circumference ≥ 102 cm in men and ≥ 88 cm in women), high blood pressure (≥ 130 mm Hg systolic or ≥ 85 mm Hg diastolic or use of blood pressure-lowering agents), hypertriglyceridemia (serum triglycerides ≥ 1.70 mmol/L), low HDL cholesterol (serum HDL cholesterol < 1.03 mmol/L in male or < 1.3 mmol/L in female) or high fasting glucose (≥ 5.6 mmol/L or use of glucose-lowering agents).

4.2.4 Other health-related variables

Chronic diseases

Information about chronic diseases and disorders diagnosed by a physician during the past 12 months was captured with a questionnaire and categorized into groups of cardiovascular, respiratory, and musculoskeletal diseases. Chronic pulmonary diseases included asthma and chronic obstructive pulmonary disease. Heart diseases included ischemic heart disease and chronic heart failure. Chronic musculoskeletal disorder included arthritis and other chronic joint disorders and chronic back disease. A comorbidity sum score, which included chronic musculoskeletal, pulmonary and heart diseases and cancer, was also calculated.

Functional ability

Functional ability was evaluated with modified functional ability questionnaire (Katz et al., 1963; Katz et al., 1970; Lawton and Brody, 1969; McWhinnie, 1981). Answers (1 am able without difficulties; 2 am able but it is difficult; 3 cannot) were summed in a total score, which accounted for physical functioning index. For the analysis, the total score was standardized on a scale of 0-10, with higher numbers indicating worse functioning.

Unintentional injury

The questionnaire asked about unintentional injuries which had required medical attention during the past 12 months, and divided them into the following four groups: traffic injuries, home injuries, sports or exercise injuries, and other leisure-time injuries. The questionnaire also asked about the number of activity-loss days after injury, which indicates difficulties coping with daily activities.

Self-rated physical fitness and risk of developing chronic diseases

The participants were asked about their physical fitness as follows: "How do you rate your current physical fitness". The five response options were: extremely good, quite good, satisfactory, quite bad, and extremely bad. Responses were categorized as follows: poor, satisfactory and good physical fitness. The subjects were also asked to estimate their self-rated risk (low, moderate, and high) of developing cardiovascular disease, type 2 diabetes and depression during the lifespan.

4.3 Statistical methods

The results are presented as means with standard deviations (SD), medians with interquartile ranges (IQR), or as counts with percentages. The most important descriptive values were expressed with 95 per cent confidence intervals (95% CI). Comparisons between groups were made using t-test, chi-square test, analysis of variance (ANOVA). Statistical significance for the hypotheses of linearity was evaluated by using generalized linear models with an appropriate distribution and link function. In the case of violation of the assumptions (non-normality), a bootstrap-type or permutation test was used. Univariate and multivariate logistic regression models was used to estimate odds ratios (OR) or adjusted proportions with their 95% CI. Repeated measures for continuous outcomes were analyzed using a generalized estimating equations (GEE) model with the unstructured correlation structure. Odds ratios were converted into the effect sizes with cut-off points 1.47 for a small effect and 2.47 for a moderate effect (Chinn, 2000). Statistical analyses were performed using Stata statistical software, release 12.0 (StataCorp, College Station, Texas).

5 RESULTS

5.1 Characteristics of females and males in relation to physical activity

The mean age (SD) of all the participants (N=2868) was 59.6 (8.4) years. The median of total PA in MET min week^{-1} was 2 079 for females and 2 373 for males. The recommended level of total PA (3 000 MET min week^{-1}) was reached by 38 % of females and by 43% of males. Table 2 shows the sociodemographic and clinical data for females and males according to the total physical activity tertile groups in MET min week^{-1} (groups: I=lowest PA, II=moderate PA and III=highest PA). For females, years of education were highest and prevalence of smokers lowest among those in the moderate PA group. Females with the lowest PA had a higher BMI value and prevalence of MetS and DS, worse functional ability and lower frequency of LTPA at the age of 15-24 years in comparison to those with the highest PA. (Additional data)

Among males, similar differences between the PA groups existed, except that the lowest prevalence of smokers was in the highest PA group. Household income differed between groups among males, as those with highest PA also had the highest household income. In addition, the males with the lowest PA had highest prevalence of CVD.

TABLE 3 Demographic and clinical data according to total physical activity tertiles (groups: I=low PA, II=moderate PA and III=high PA) in MET min week^{-1} in females and males assessed with International Physical Activity Questionnaire (IPAQ).

Females

	Total physical activity (IPAQ), MET min week^{-1} (min-max)			p-value
	I n=480	II n=482	III n=482	
MET (min week^{-1})	(<1280)	(1280–3545)	(>3545)	
Age, mean (SD)	58.9 (8.5)	59.5 (8.6)	58.9 (7.7)	0.44
Education years, mean (SD)	11.8 (3.9)	11.9 (3.7)	11.3 (3.4)	0.033
Marriage or common law marriage, (%)	354 (74)	340 (71)	341 (71)	0.46
Household income (1000€), mean (SD)	21,3 (11,1)	22,2 (11,5)	21,2 (12,0)	0.38
Smokers, n (%)	105 (22)	77 (16)	102 (21)	0.042
Alcohol users, n (%)	363 (78)	391 (82)	381 (80)	0.18
BMI, mean (SD)	28.2 (5.9)	27.1 (5.1)	27.2 (4.9)	0.0036
Metabolic syndrome, n (%)	265 (55)	234 (49)	226 (47)	0.024
Depressive symptoms, n (%)	107 (22)	78 (16)	63 (13)	<0.001
Chronic diseases, n (%)				
Cardiovascular disease	173 (37)	172 (36)	152 (32)	0.25
Respiratory disease	41 (9)	45 (9)	39 (8)	0.82
Musculoskeletal disease	162 (35)	167 (35)	158 (34)	0.89
Comorbidity sum, mean (SD)	0.52 (0.67)	0.53 (0.68)	0.48 (0.65)	0.40
Functional ability, mean (SD)	1.45 (1.83)	0.97 (1.35)	0.82 (1.22)	<0.001
LTPA frequency at the age of 15-24 years in months, mean (SD)	11.6 (8.8)	12.4 (9.3)	14.2 (9.3)	<0.001

Males

MET (min week^{-1})	(<1348)	(1348–4260)	(>4260)	
Age, mean (SD)	59.7 (8.6)	59.7 (8.5)	60.6 (8.2)	0.21
Education years, mean (SD)	11.0 (3.6)	11.7 (4.0)	10.6 (3.3)	<0.001
Marriage or common law marriage, (%)	337 (78)	362 (84)	360 (83)	0.068
Household income (1000€), mean (SD)	21,0 (12,0)	23,3 (12.3)	21.4 (11.5)	0.0068
Smokers, n (%)	125 (29)	103 (24)	95 (22)	0.048
Alcohol users, n (%)	369 (86)	382 (89)	365 (85)	0.31
BMI, mean (SD)	28.2 (4.6)	27.1 (4.2)	27.1 (3.8)	<0.001
Metabolic syndrome, n (%)	267 (62)	242 (56)	214 (49)	<0.001
Depressive symptoms, n (%)	81 (19)	42 (10)	37 (9)	<0.001
Chronic diseases, n (%)				
Cardiovascular disease	179 (42)	164 (39)	141 (33)	0.030
Respiratory disease	37 (8)	28 (7)	36 (9)	0.44
Musculoskeletal disease	128 (30)	115 (27)	113 (27)	0.47
Comorbidity sum, mean (SD)	0.61 (0.77)	0.51 (0.70)	0.49 (0.68)	0.037
Functional ability, mean (SD)	1.08 (1.64)	0.66 (1.12)	0.48 (0.84)	<0.001
LTPA frequency at the age of 15-24 years in months, mean (SD)	12.9 (9.7)	14.2 (9.5)	14.9 (9.8)	0.013

5.2 Self-rated physical fitness and risk of developing chronic diseases in relation to total physical activity

A linear trend was observed in self-rated physical fitness in relation to total physical activity (IPAQ) in both females and males in all the age categories, except for females in the age category 55-59. Those who rated their fitness poor had the lowest total physical activity level, and those who rated their fitness good had the highest total physical activity level (Figure 4, additional data).

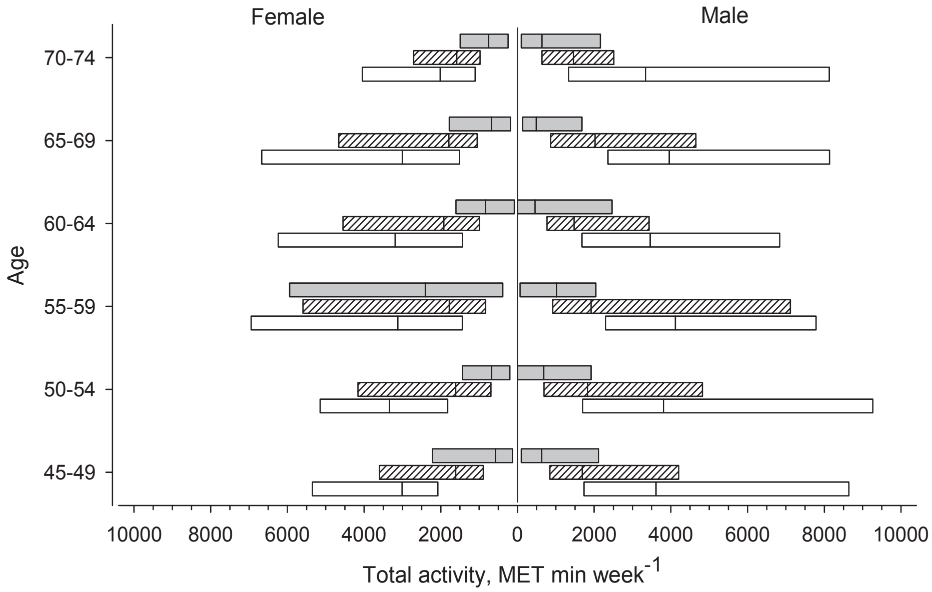

FIGURE 4 Self-rated fitness in relation to total physical activity (IPAQ) mean (IQR) in females and males according to age. The grey bar denotes poor, the striped bar satisfactory and the white bar good physical fitness.

In order to investigate the association between total physical activity and perceived risk of developing chronic diseases, participants were asked to evaluate their risk of cardiovascular disease, type 2 diabetes and depression. Table 4 shows that the females and males, who rated their risks low, were physically the most active. Among both genders, total PA median decreased with increasing self-rated risk for contracting these diseases.

TABLE 4 Self-rated risk of developing chronic diseases in relation to total physical activity (International Physical Activity Questionnaire, IPAQ) in metabolic equivalent (MET) -minutes in males and females.

Perceived risk	Female N (%)	IPAQ, MET min week^{-1} Median (IQR)		Male N (%)	IPAQ, MET min week^{-1} Median (IQR)	
CVD						
Present	61 (4)	1386 (678,2880)		108 (9)	1413 (516,3627)	
High	256 (18)	1939 (707,4185)		208 (16)	1608(686,4506)	
Moderate	736 (52)	1971 (929,4590)		556 (44)	2400 (1026,6368)	
Low	362 (26)	2616 (1200,5544)		395 (31)	2880 (1293,6930)	
p for linearity			<0.001			<0.001
DM						
Present	64 (5)	1288 (530,2240)		77 (6)	1386 (594,2979)	
High	181 (13)	1746 (693,3990)		116 (9)	1727 (768,4506)	
Moderate	571 (41)	2079 (942,4986)		448 (35)	2365 (837,6168)	
Low	591 (42)	2316 (1116,4865)		626 (49)	2717 (1166,6228)	
p for linearity			<0.005			<0.001
Depression						
Present	15 (1)	1386 (594,2079)		11 (1)	396 (0,6834)	
High	71 (5)	1173 (318,2970)		49 (4)	1188 (594,3066)	
Moderate	306 (22)	1917 (873,4365)		219 (17)	1928 (918,5280)	
Low	1017 (72)	2148 (1065,4851)		988 (78)	2463 (1053,5900)	
p for linearity			<0.006			<0.002

CVD, cardiovascular disease; DM, diabetes mellitus

5.3 Physical activity level, depressive symptoms and cardiometabolic risk factors

5.3.1 Depressive symptoms in relation to leisure-time physical activity and cardiometabolic risk factors

When the study participants were assessed in relation to DS, differences between those with and without DS were observed in LTPA and in the prevalence of cardiometabolic risk factors (table 5, additional data). (More details in study I.) Prevalence of low LTPA was statistically significantly higher in both females (33%) and males (37%) with DS in comparison with the participants without DS (15% and 17%, respectively) ($p<0.001$ in both genders). The prevalence of DS among the participants in the low LTPA category was about threefold higher in both genders in comparison with the participants in the high LTPA category.

Glucose profile among males with DS was unfavorable compared to males without DS (table 5). Males with DS had higher prevalence of type 2 diabetes and impaired glucose tolerance ($p<0.001$). In addition, differences in lipid profile were found between those with and without DS in both genders. The prevalence of dyslipidemia was higher in both genders, total cholesterol lower in males, and triglycerides higher in females for those with DS compared to those without DS (table 5).

TABLE 5 Leisure-time physical activity (LTPA) and glucose and lipid profile according to gender and depressive symptoms.

Variables	Female Depressive symptoms			Male Depressive symptoms		
	Not present N=1196	Present N=248	p-value	Not present N=1141	Present N=160	p-value
LTPA category			<0.001			<0.001
Low	182 (15)	83 (33)		197 (17)	60 (37)	
Moderate	729 (61)	136 (55)		667 (58)	83 (52)	
High	285 (24)	29 (12)		280 (25)	17 (11)	
Glucose profile, n (%)			0.42			<0.001
Normal	665 (56)	130 (53)		420 (37)	53 (33)	
T2D	51 (4)	16 (7)		66 (6)	26 (16)	
ST2D	93 (8)	25 (10)		149 (13)	17 (11)	
IGT	213 (18)	42 (17)		197 (17)	33 (21)	
IFG	156 (13)	32 (13)		298 (26)	30 (19)	
Lipid profile						
Dyslipidemia, n (%)	292 (24)	88 (36)	<0.001	448 (39)	81 (51)	0.006
Total cholesterol, mean (SD)	5.52 (0.96)	5.62(0.99)	0.18	5.36 (1.01)	5.13 (0.97)	0.007
HDL cholesterol, mean (SD)	1.56 (0.34)	1.52 (0.32)	0.055	1.32 (0.32)	1.28 (0.30)	0.073
Triglycerides, mean (SD)	1.24 (0.58)	1.42 (0.72)	<0.001	1.49 (1.02)	1.53 (0.85)	0.59

T2D, type 2 diabetes; ST2D, screen-detected type 2 diabetes; IGT, impaired glucose tolerance; IFG, impaired fasting glycemia

In addition, the prevalence of low LTPA and DS was analyzed in subjects with normal glucose regulation (NGR), impaired glucose regulation (IGR, including impaired fasting glycemia and impaired glucose tolerance), screen-detected (previously unknown) diabetes, and previously known type 2 diabetes. The prevalence of low LTPA was highest among those with previously known diabetes (32%) than among participants with screen-detected diabetes (26%), IGR (18%), and NGT (16%). The prevalence of DS was highest among the participants with previously known diabetes (26.4%) than among those with screen-detected diabetes (14.8%), IGR (13.7%) and NGR (14.4%). (Study II)

5.3.2 Depressive symptoms in relation to total physical activity and cardiometabolic risk factors

To examine more deeply the relationship between physical activity and DS, females and males were divided into three total PA categories (low, moderate and high). Figure 5 shows that in both females and males the proportion of subjects with DS decreased linearly with increasing total PA categories (age-adjusted p<0.001). (Study I)

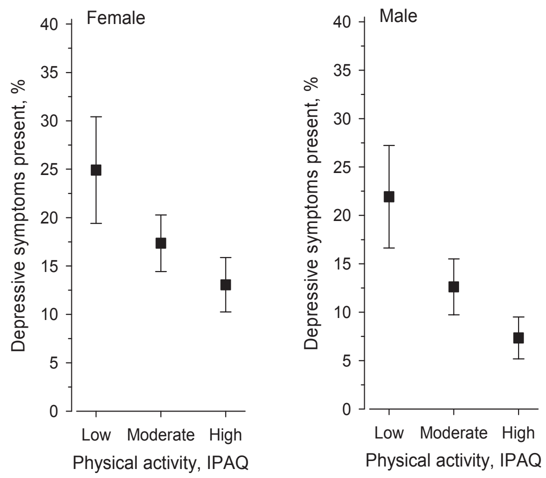

FIGURE 5 Age adjusted percentage (%) of depressive symptoms in physical activity categories (IPAQ).

In order to determine the impact of age on total PA among those with and without DS, females and males were stratified into 5-year age groups (Figure 6) (additional data). Among all the participants, the mean (95% CI) of total physical activity (IPAQ) was 3 028 (4 263) MET min per week among those with DS and 3 864 (4 742) among those without DS in females (p=0.006), and the corresponding values were 2 908 (4763) and 4 953 (6 203) in males (p<0.001) (age adjusted p=0.013). Total PA was lower among those with DS compared to those without DS in all age categories for both genders.

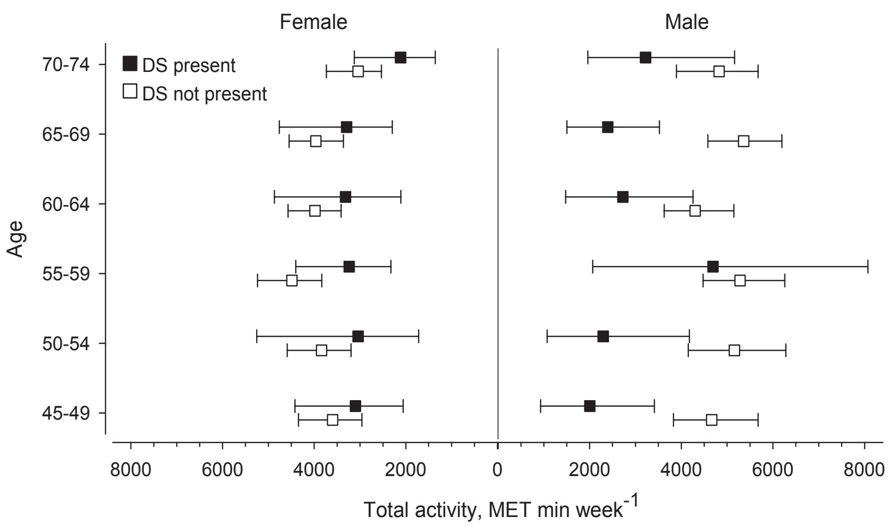

FIGURE 6 Mean (CI 95%) total physical activity in metabolic equivalent (MET) -minutes per week among females and males according to age. (DS=depressive symptoms)

To gain further insight into other possible factors related to DS in addition to total PA, associations between sociodemographic and clinical factors, and DS were estimated using a logistic regression model where variables were entered into the model simultaneously (additional data).

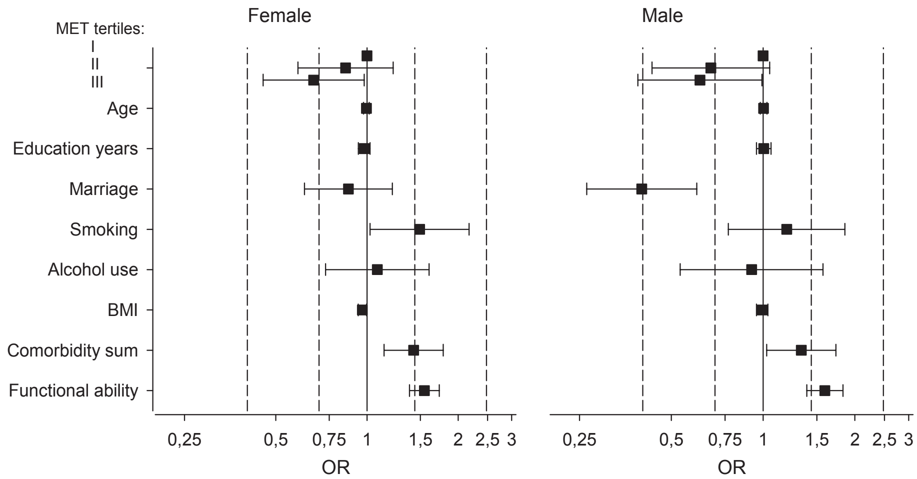

FIGURE 7 Logistic regression model for depressive symptoms among males and females. Small (1.47/0.68) and moderate (2.47/0.40) effect sizes are illustrated with dotted lines.

Figure 7 shows that high total PA (p for PA linearity=0.039) decreased, and smoking, high comorbidity sum score and low functional ability increased the risk for DS in females. In addition to high and moderate total PA (p for PA linearity=0.046), marriage also decreased the risk for DS, and low functional ability increase the risk for DS in males. Although the odds ratios for the associations were statistically significant, the effect sizes remained small, except for the effect size of marriage among males, which was moderate.

5.4 Life-time leisure-time physical activity and depressive symptoms

Of the 927 participants aged 65-74, the prevalence of DS was 19.3 %. The participants with DS showed a higher prevalence of females (58.7% vs. 47.3%, p=0.006), use of antidepressants (11% vs. 4%, p<0.001), and prevalence of cardiovascular diseases (59% vs. 50%, p=0.044) and musculoskeletal diseases (53% vs. 35%, p<0.001) than the participants without DS. In addition, those with DS had significantly lower functional ability, quality of life and frequency of LTPA compared to those without DS. (More details in Study III)

The difference in LTPA frequency between those with and without DS was visible already from age 45 years onwards. Figure 8 shows that the frequency of LTPA was highest at ages 15–24 years, when it was 14.6 times monthly in both the DS present and not-present groups. At the ages of 25–34 years, the frequencies had decreased to 10.9 and 11.9 times monthly in the DS present and not-present groups, and at the age of 65–74 years the corresponding frequencies were 8.6 and 11.9. The frequency of LTPA was significantly lower among those with DS compared with those without DS at ages 45–54 (p=0.029), 55–64 (p<0.001), and 65–74 years (p<0.001), but not for those younger than 45 years.

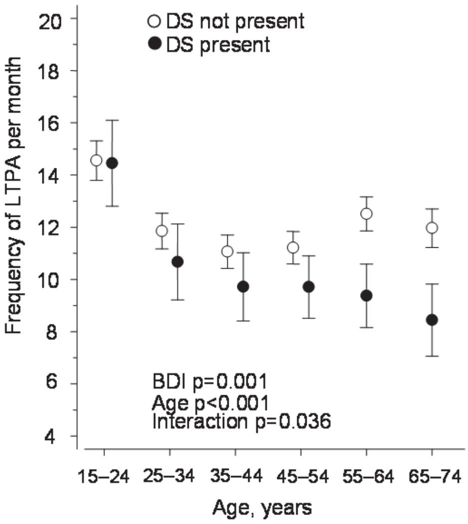

FIGURE 8 Gender-adjusted mean (95% confidence intervals) profiles of lifetime leisure time physical activity (LTPA) frequency per month in participants aged 65–74 years with (black circle) or without (open circle) presence of depressive symptoms according to the Beck Depression Inventory (BDI-21).

5.5 Unintentional injuries in relation to physical activity and depressive symptoms

Of the 2 682 participants 301 (11%) reported at least one unintentional injury which had required medical attention during the past 12 months (Study IV). The prevalence of subjects with an unintentional injury was 17.0% (95% CI: 13.5% to 21.1%) among participants with DS and 10.2% (95% CI: 9.0% to 11.5%) among participants without DS (age- and gender-adjusted p<0.001). The prevalence of unintentional injuries among those with low total PA was 10.3% (95% CI: 7.7% to 13.4%), among those with moderate PA 10.8% (95% CI: 9.1% to 12.8%), and among those with high PA 12.0% (95% CI: 10.1% to 14.1%) (age- and gender adjusted p=0.55). The mean (range) number of activity-loss days after injury was 22 (0–365) days in participants with DS and 7 (0–120) days in participants without DS (p=0.009).

Figure 9 shows main effects and interaction of total PA and DS on unintentional injuries.

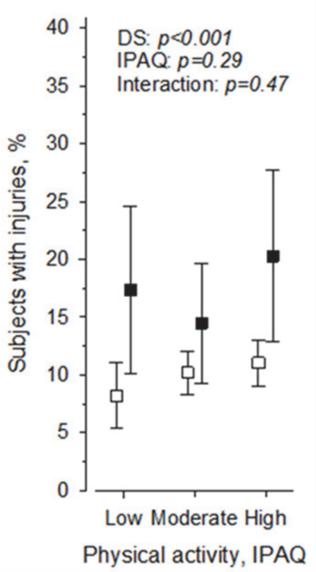

FIGURE 9 Age- and gender-adjusted percentage of subjects with unintentional injuries in physical activity categories according to depressive symptoms (DS). Percentages with 95% confidence intervals in participants with (black square) or without (open square) depressive symptoms are shown.

To further analyze the factors related to unintentional injuries, important determinants of injuries were added one at the time to the univariate regression model and, in addition, a multivariate logistic regression model was used with forward stepwise selection. The univariate logistic regression analysis showed that age, BMI, DS, functional ability, cardiovascular disease, respiratory disease, and musculoskeletal disorders were significantly related to a higher risk of injuries, but PA level was not. In the forward stepwise multivariate model, the relationship between unintentional injuries and DS, functional ability, and musculoskeletal disorders remained significant (Table 6).

TABLE 6 Univariate and multivariate stepwise logistic regression models for unintentional injuries.

	Univariate		Multivariate[a]	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age	1.02 (1.00 to 1.03)	0.034		
Male gender	1.09 (0.86 to 1.38)	0.49		
Body mass index	1.03 (1.00 to 1.05)	0.032		
Education years	1.00 (0.97 to 1.03)	0.93		
Depressive symptoms	1.80 (1.34 to 2.43)	<0.001	1.52 (1.11 to 2.10)	0.010
Use of antidepressants	1.24 (0.76 to 2.02)	0.38		
Functional ability	2.31 (1.62 to 3.30)	<0.001	1.74 (1.15 to 2.61)	0.008
Cardiovascular diseases	1.50 (1.18 to 1.92)	<0.001		
Respiratory diseases	1.59 (1.09 to 2.33)	0.016		
Musculoskeletal diseases	1.63 (1.27 to 2.08)	<0.001	1.38 (1.06 to 1.80)	0.018
IPAQ		0.27[b]		
< 600	1 (reference)			
600–2999	1.06 (0.74 to 1.51)			
≥ 3000	1.19 (0.84 to 1.70)			
Alcohol use		0.24[b]		
Never	1 (reference)			
Occasionally	1.19 (0.91 to 1.55)			
At least once a month	1.15 (0.78 to 1.68)			
At least once a week	1.24 (0.74 to 2.08)			

OR, odds ration; CI, confidence interval; IPAQ, International Physical Activity Questionnaire
a: Forward stepwise selection. Only those variables which entered the model are shown.
b: p for linearity

5.6 Physical activity, metabolic syndrome and depressive symptoms

5.6.1 Metabolic syndrome

Cardiometabolic risk factors can be viewed by clustering them into the metabolic syndrome. The prevalence of MetS among all participants was 53.1% (95% CI: 51.2 to 55.0), among females 50.9% and males 55.8%. Associations between sociodemographic and clinical factors, and MetS were estimated using logistic regression model where the variables were entered into the model simultaneously (additional data).

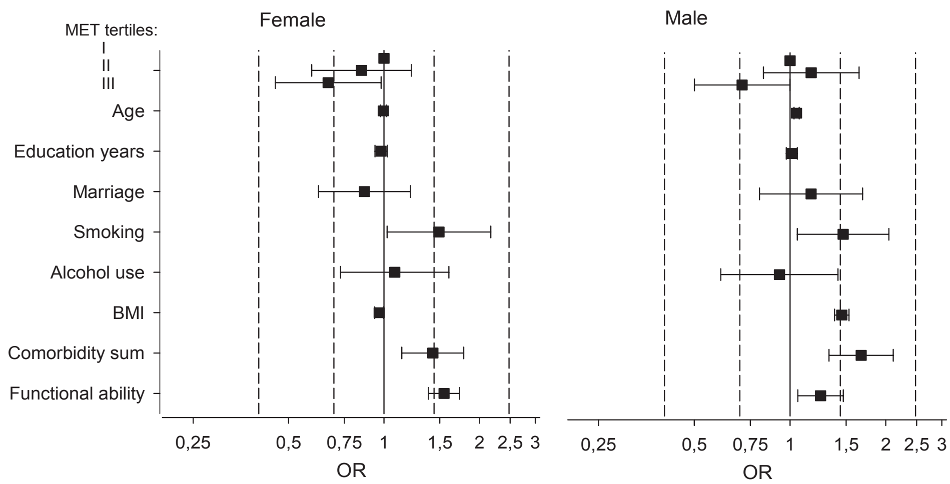

FIGURE 10 Logistic regression model for metabolic syndrome among males and females. Small (1.47/1.47) and medium (2.47/0.40) effect sizes are illustrated with dotted lines.

Figure 10 shows that high total PA decreases the risk of MetS, and smoking, high comorbidity sum score and low functional ability increase the risk of MetS in females, and that high total PA decreases, and smoking, high BMI and comorbidity sum score increases the risk of MetS in males. Although the odds ratios were statistically significant in these associations, the effect sizes remained small.

5.6.2 Physical activity and simultaneous presence of metabolic syndrome and depressive symptoms

The prevalence of simultaneous MetS and DS was 9.6% (95% CI: 8.6 to 10.8) in the total study group (Study V). Almost two-thirds (64%) of the participants with DS had MetS, and 18% of those with MetS had DS.

Among the participants with simultaneous MetS and DS, 43% reported their LTPA level to be low, 49% moderate, and 8% high (Figure 11A). Participants with DS only or MetS only were similarly distributed among the LTPA levels. There was a significant difference in LTPA between the participants with both MetS and DS compared to those with no DS or MetS. In the group with simultaneous MetS and DS, 43% reported low LTPA compared with 12% in the group without either MetS or DS (age- and gender adjusted p<0.001) (Figure 11B).

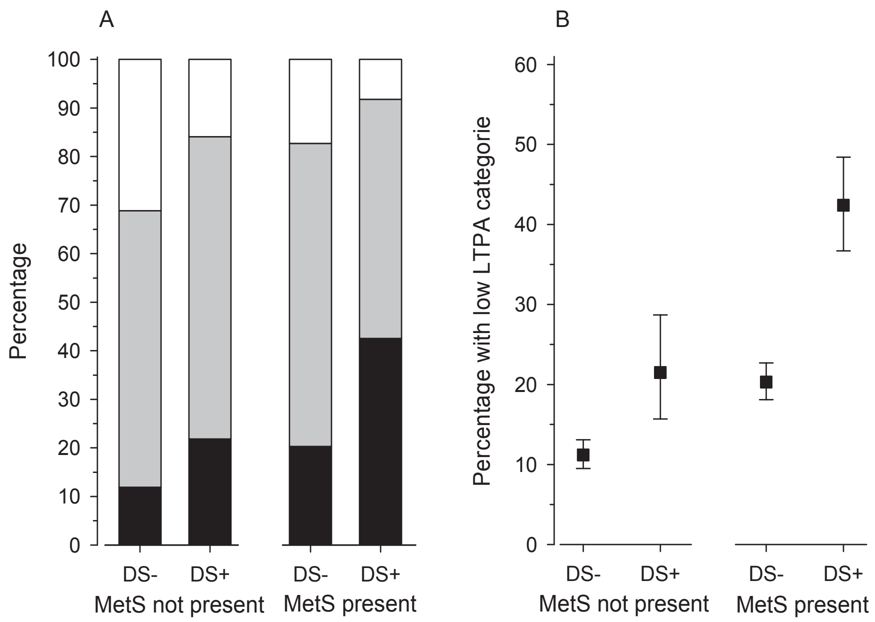

FIGURE 11 A. Leisure-time physical activity categories (LTPA) according to metabolic syndrome (MetS) and depressive symptoms (DS: + present; - not present). The black bar denotes low, the grey bar moderate and the white bar high physical activity level. B. Age- and gender–adjusted percentage (with 95% confidence intervals) of the study population in the low LTPA categories according to MetS and DS.

5.6.3 Awareness of insufficient physical activity and underlying causes

When asked participants opinion of their leisure-time physical activity, 56% of all the participants answered that they are not active enough in their leisure-time. The corresponding proportion was 74% among those with DS, 64% among those with MetS, and 46% among those without either DS or MetS. The main reasons for inactivity among all participants who reported not being active enough were reported to be lack of time, presence of illness or disability, and lack of company to engage in sport with (Table 7). Furthermore, among the participants with DS and with MetS, the main reason for inactivity was illness or disability. Over one-third of those without either DS or MetS reported the reason to be lack of time. However, 31% of all participants, 24% of those with DS, 30% of those with MetS, and 32% among those without either DS or MetS reported some other reason for inactivity. About one-half of all the other reasons for inactivity were reported to be inefficiency and laziness among those with DS and those with MetS, while the corresponding value among those without either DS or MetS was less than one-third. In contrast, cost was not considered to be an obstacle to participating LTPA. (additional data)

TABLE 7 Reasons for insufficient leisure-time physical activity among participants who reported not being active enough; all (1567), participants with DS (312), participants with MetS (937), and participants without either DS or MetS (256). One responder may have several reasons for inactivity.

Reason for inactivity	All n (%)	DS n (%)	MetS n (%)	DS and MetS not present n (%)
I do not have time	478 (26)	61 (16)	237 (21)	230 (36)
Sport equipment is too expensive	16 (1)	4 (1)	13 (1)	4 (1)
Sport facilities are far away or otherwise difficult to reach	86 (5)	17 (4)	49 (4)	37 (6)
Charges are too high	51 (3)	12 (3)	32 (3)	19 (3)
I feel I am not sufficiently familiar with the skills needed in sports	52 (3)	12 (3)	35 (3)	13 (2)
I do not have friends or a group to engage in sport with	159 (9)	46 (12)	96 (8)	53 (8)
I do not like sports	83 (4)	20 (5)	64 (6)	22 (3)
I have an illness or disability which limits physical activity	333 (18)	122 (32)	268 (24)	59 (9)
Some other reason	563 (31)	93 (24)	349 (30)	207 (32)

6 DISCUSSION

This study of a population-based sample of Finnish females and males aged 45-74, showed that low levels of physical activity were associated with depressive symptoms and further, the accumulation of cardiometabolic risk factors. Also, lifetime leisure-time physical activity seemed to be associated with the occurrence of DS and somatic diseases in later life. The rate of simultaneous metabolic syndrome and DS was over fivefold higher among participants with low LTPA than among those with high LTPA. Moreover, physically inactive participants were aware of their low fitness and the possibility of lifestyle dependent diseases.

6.1 Physical activity and health

When studying the trends of total PA in relation to the sociodemographic and clinical variables, an association was found between total PA and years of education. In both genders, those with the lowest education in years also had the highest total PA. Thus, according to this finding, the higher work load commonly associated with low education, measured in years, seems to play an important part in total PA. This finding is in agreement with Hallal et al. (2012), who showed that physical inactivity is more common in the high income countries than low income countries. Total PA appears to be significant in terms of health as well. In particular, obesity and obesity-related disorders, including MetS and DS, among both genders, and CVD among males, were more common among those with the lowest total PA levels. These results corroborate the findings of a great deal of the previous work in this field (Knight, 2012). Also, functional ability was undoubtedly worse and frequency of LTPA at age 15-24 lower among those with the lowest total PA in comparison to those with the highest PA.

6.1.1 Awareness of one's own fitness and risk for diseases

The present results indicate that both the female and male participants seemed to understand and account for their physical fitness level by reference to their PA level. Participants with low PA levels estimated their physical fitness as low, while those with high PA levels estimated their fitness as high. These findings are in line with some previous studies revealing that people have rather accurate perceptions of their actual physical fitness (Germain and Hausenblas, 2006; Okano et al., 2003). Physical fitness can be considered to reflect functional ability and the ability to perform daily activities. Moreover, self-reported physical fitness might also be reflected by the presence of chronic diseases, as shown by an earlier Finnish study with a sample of about 20% of the working-age population (Miilunpalo et al., 1997). The study revealed that chronic diseases were more prevalent among females (87%) and males (83%) who rated their fitness as low in comparison to those who rated their fitness as high (20%, 30%).

This study also showed that those who were physically active perceived their risk for developing cardiovascular diseases, diabetes and depression as lower compared to the perceived risk of those with low total PA. Thus, the connection between inactivity and these chronic diseases was understood, as also was the connection between PA and health. In Finland, and elsewhere in the world, a number of national projects are under way that aim to increase citizen awareness of the effects of a healthier diet and physically active lifestyle (Aittasalo et al., 2007; Coppell et al., 2009; Lindström et al., 2010; Saaristo et al., 2007). Based on results of the present thesis, it seems that these national implementation projects are achieving good results, since the risks attached to an inactive lifestyle were identified. However, the proportion of the present participants who rated their risk for CVD and diabetes as moderate or high was as high as 70% and 54% for females, and 60% and 44% for males. Moreover, the median of PA level of those who rated their risk as low did not reach the sufficient recommended value of PA, as the borderline value for being sufficiently active is 3000 MET minutes in the IPAQ (Guidelines for Data Processing and Analysis of the International Physical Activity Questionnaire (IPAQ)). Thus, it is questionable whether it has been fully understood among the general population what it means to be a sufficiently physically active citizen.

6.1.2 Perceived barriers to physical activity

Majority of the participants (62% of females, 57% of males) did not reach the recommended level of total PA. The main perceived barrier to being physically active was lack of time among those without DS or MetS. This is in line with another population-based study which found lack of time to be associated with physical inactivity, in addition to dislike of exercising, tiredness, and lack of company and money (Reichert et al., 2007). Additionally, the study revealed that lack of time seemed to be a substantial reason for inactivity since the more hours daily that were reported to be otherwise occupied, the greater the perception of lack of time, and lower the proportion of sufficiently active individuals.

Work or study commitments also emerged as the most frequently perceived barrier to increased physical activity among Europeans (Zunft et al., 1999).

In addition to lack of time, laziness turned out to be surprisingly frequently cited reason for inactivity among the Finnish population aged 45-74 in this study. Similar results were found in a study on the sedentariness of the European population, as loss of energy appeared to be the most frequently perceived barrier cited among the Finnish population for not increasing participation in PA (Zunft et al., 1999). Nineteen percent of the Finnish respondents selected this barrier in comparison to 11% of the EU average.

Those with DS or MetS reported illness or disability as the main reason for inactivity. Consequently, having DS or MetS highlights the role of diseases as a reason for inactivity, with lack of time as a significantly less meaningful factor.

On the other hand, a rather high proportion of all the participants reported some other reason for inactivity. Thus, it might be appropriate to modify the questionnaire to take account of this.

6.2 Physical activity, depressive symptoms and metabolic syndrome

6.2.1 Interrelationship between physical activity and health

This population-based survey showed that both females and males with DS had lower LTPA levels. Thus, the highest LTPA level was related to a lower DS risk in this study. The proportion of participants without DS who reached this level was about twofold higher in both genders than that among those with DS. These results are in line with those of a previous systematic review, which reported an inverse association between physical activity and the likelihood of depressive symptoms (Teychenne et al., 2008). In addition to LTPA, total physical activity was also linearly related to DS in this study. The prevalence of DS decreased with increasing total PA. When the groups with and without DS were compared, the difference in total PA in MET minutes was higher for males than females. However, a significant difference between those with and without DS was found in every age category studied in both genders. Total PA was also significantly associated with DS when other confounding factors, such as glucose and lipid abnormalities, were included in the analysis.

When cardiometabolic risk factors were evaluated in relation to DS, dyslipidemia emerged as a significant determinant in both genders, with triglyceride values significant only in females and total cholesterol in males. Earlier results on the relationship between DS and lipid profile are inconsistent. For total cholesterol, both lower and higher levels have been shown to be related to depression (Partonen et al., 1999; Shin et al., 2008; Äijänseppä et al., 2002), while in the present study males with DS had a lower level of total cholesterol compared to those without DS. Moreover, there is evidence that higher triglyceride values are associated with depression (Ergün et al., 2004), as demonstrated in this study for females. However, normal levels of triglycerides may also be related to DS (Lehto et al., 2010). Moreover, these obesity-related cardiometabolic risk factors have been shown to be risk factors for future depression, as the study by Hamer et al. suggests that it is not obesity alone that is associated with DS, but rather metabolic health (Hamer et al., 2012). They showed that their metabolically unhealthy obese participants had increased risk for DS, whereas obese participants who were metabolically healthy did not. In addition, the association between DS and physical inactivity may play some role, as it was shown to have deleterious effects on the blood lipid profile (Pedersen and Saltin, 2006).

Previous studies have shown that cardiometabolic risk factor accumulation as well as DS and inactivity increase the risk for type 2 diabetes (Muhtz et al., 2009; Venables and Jeukendrup, 2009). Furthermore, it is widely recognized that depression is more common among subjects with diabetes than in the general population (Anderson et al., 2001). This phenomenon was seen in this study as well. One fourth of those with T2D had DS, while the prevalence of DS was similar between the NGT and screen-detected diabetes groups and substantially lower than in those with T2D. These results suggest that the knowledge of having T2D, but not the disease itself, may be related to the increase in low LTPA and DS. This finding corroborates earlier studies suggesting that depression is not more prevalent among those with screen-detected diabetes or impaired glucose tolerance (Icks et al., 2008; Knol et al., May 2007), and that there is no association between depressive symptoms and unrecognized glucose intolerance (Rhee et al., 2008). The prevalence of participants with low LTPA was twofold among those with previously known type 2 diabetes mellitus compared to those with normal glucose tolerance (NGT). The proportion of participants with low LTPA seemed to be lower also among those with screen-detected diabetes in comparison to those with T2D. This finding contrasts with that reported in an earlier study by Karjalainen et al., (2008) according to which females, although not males, with known type 2 diabetes were more physically active than those with screen-detected T2D. The explanation they proposed for this was a more adaptive attitude towards diabetes among females. Similar results might have been obtained in the present study, if females and males had been analyzed separately.

The above-mentioned cardiometabolic risk factors can be examined together through metabolic syndrome. In the present population–based sample, over half of the participants had MetS, and the prevalence of MetS was higher in men than in women. In a previous study, the prevalence of MetS (based on the NCEP definition from year 2001) in the Finnish population aged 45-64 had increased from 48.8 to 52.6% in men and from 32.2 to 39.1 in women during 1992-2002 (Hu et al., 2008). The results of the present study confirm these findings of an increasing prevalence of MetS in both genders, particularly among women. However, the possibility of some systematic error cannot be excluded, when comparing the results of this study to those of Hu et al. (2008), due to up-per age limit used in this study, and some differences in the methods used. However, the prevalence of MetS in the Finnish population appears to be high in international comparisons (Ford et al., 2002; Grundy, 2008; Park et al., 2003; Vaughan et al., 2009). This study discovered that total PA is associated with increased risk for MetS on the population level, and the factors associated with the increased prevalence of MetS were smoking and chronic diseases in both genders, obesity among males and low functional ability among females.

The present data show that the rate of simultaneous MetS and DS was over fivefold higher in the low compared to high LTPA group. The simultaneous presence of MetS and DS was associated with a fourfold increased frequency of low LTPA in comparison to subjects without DS and MetS, and with a more than twofold increased frequency of low LTPA compared to participants with only DS or only MetS. The factors underlying the strong relationship found here between PA, DS and MetS may be biological or psychological. Due to the cross-sectional design of this study, a causal conclusion cannot be draw about which factor was first: inactivity or DS and MetS. However, there is evidence of a bi-directional association between MetS and DS; MetS predisposes to DS and vice versa (Bjorntorp, 2001; Koponen et al., 2008; Vanhala et al., 2009). In addition, physical inactivity has been shown to be a risk factor for cardiovascular disease, hypertension, obesity and impaired glucose and lipid metabolism (Blair et al., 1989; Paffenbarger et al., 1986; Petersen et al., 2004), and it has also been shown to contribute to the progression of MetS (Ilanne-Parikka et al., 2010; Johnson et al., 2007; Laaksonen et al., 2002b; Vaughan et al., 2009; Wang et al., 2012; Yang et al., 2008) and DS (Chen et al., 2012; Rethorst et al., 2009; Teychenne et al., 2008).

Chronic diseases are non-infectious and non-transmissible between persons. The four main behavioral risk factors that contribute to chronic diseases are stated to be tobacco use, the harmful alcohol consumption, unhealthy diet and physical inactivity (World Health Organization, 2011). In this study, differences in the prevalence of chronic diseases in relation to total PA level were found only among males. The prevalence of CVD was higher for males with low total PA than for those with a high level of PA. In addition, chronic diseases were related to DS in the present study. Among females, in particular, the relationship seemed to be strong. This result is in line with a previous finding showing that individuals with chronic diseases are on average 1.5–2 times more often depressed (Beekman et al., 1997). Moreover, the relationship between depression and chronic diseases has shown to be linear. Egede (2007), compared the odds ratios for major depression in patients with one, two and three chronic diseases compared to a reference group with no chronic diseases, and reported odds ratios of 2.22, 3.90 and 6.52 for one, two and three diseases, respectively. In addition, lower functional ability related to DS among both genders might be also a consequence of associated chronic diseases as well as of a low PA level. However, the present findings of an association between total PA and DS regardless other confounding factors, supports the view that the increased prevalence of DS among subjects with low total PA is not explained simply by their excessive disease burden.

6.2.2 Mechanisms of interaction

The tendency of depressive symptoms and metabolic syndrome to cluster can, at least partly, be explained by common pathogenetic mechanisms. Figure 12 shows the possible potential connections between PA, DS and MetS. This study did not clarify the involvement of the HPA-axis and inflammation as unifying factors and thus, the following connections in this regard draw on studies published by other researchers.

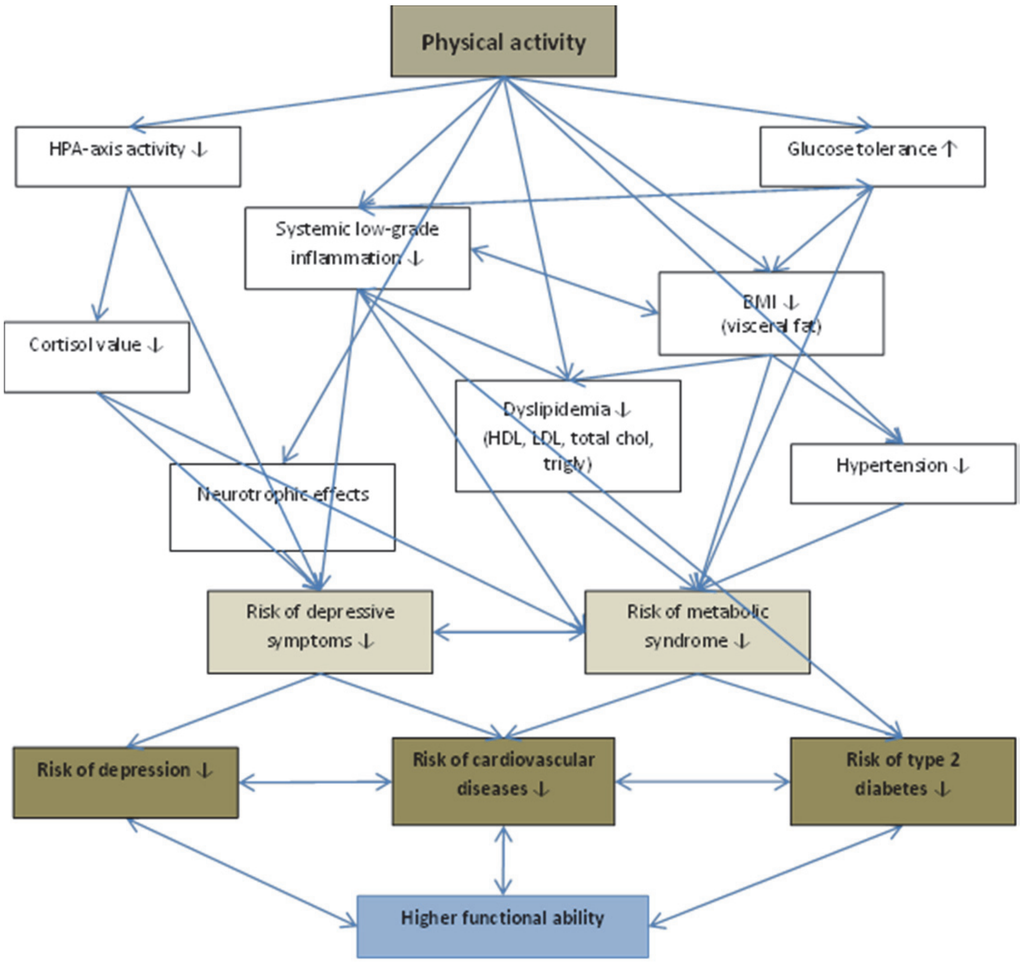

FIGURE 12 Potential connections between physical activity, depressive symptoms and metabolic syndrome.

High BMI values, as well as excess central obesity have been shown to be major cardiometabolic risk factors (van Dis et al., 2009). Obesity, especially visceral adiposity, is associated with insulin resistance. According to observational studies, obesity is a major determinant of premature mortality and a risk factor for the most significant causes of death, such as type II diabetes, cardiovascular disease and various types of cancer (Wyatt et al., 2006). Furthermore, increased central obesity has been found during follow-up in depressed persons (Weber-Hamann et al., 2006). This accumulation was seen in participants with depressive symptoms in this study as well, while, on the contrary, participants with high levels of PA were less obese than their counterparts with low levels of PA.

Impaired glucose tolerance and high BMI, in turn, are associated with systemic low-grade inflammation (Bastard et al., 2006; Herder et al., 2009). Systemic low-grade inflammation includes increased circulating levels of pro-inflammatory and anti-inflammatory cytokines (Bruunsgaard and Pedersen, 2003). Chronic inflammation has been shown to be associated with chronic diseases (Pedersen, 2009; Probst-Hensch, 2010) and further, contributes to the development of atherosclerosis, insulin resistance, and neurodegeneration (Handschin and Spiegelman, 2008). In addition, inflammation may induce dyslipidemia as well, as it stimulates lipid release into the blood stream (Esteve et al., 2005). Adipose tissue is highly sensitive to inflammatory signals, and releases inflammatory markers itself; thereby further stimulating dyslipidemia (Rajala and Scherer, 2003).

Also inactivity induces visceral fat accumulation leading to activation of a network of inflammatory pathways, which in turn has been shown to promote the development of DS (Pedersen, 2009). On the contrary, PA is suggested to protect against diseases associated with low-grade systemic inflammation, as exercise increases muscle production of cytokines and IL-6, which in turn have anti-inflammatory effects (Petersen and Pedersen, 2005). Observational studies have showed an inverse relationship between PA and inflammatory biomarkers, while data from randomized-controlled trials are somewhat limited, and the results inconclusive (Beavers et al., 2010).

One potential pathway to explain this connection can be found in the endocrine system. DS have been associated with physiological abnormalities that may have metabolic consequences, including HPA–axis hyperactivity which in turn induces cortisol secretion, causing abdominal obesity and dyslipidemia (Anagnostis et al., 2009; Björntorp and Rosmond, 2000; Faith et al., 2002; Stunkard et al., 2003; Veen et al., 2009). In addition to DS, this hyperactivity of the HPA-axis has also been reported in individuals with MetS (Bjorntorp, 2001).

However, in addition to biological factors, psychological factors may play an important role as well. People with DS are commonly unable to maintain a healthy lifestyle, which may lead to increased cardiometabolic risk factors, such as fat accumulation and obesity, resulting eventually in inactivity due to physical difficulty. On the other hand, MetS, commonly associated with obesity, causes discomfort, decreased self-esteem and difficulty in engaging in physical activity, particularly in public places, which in turn contribute to the isolation and the development of DS. Thus, inactivity may also be the primary factor linking these factors, as it is known to increase the risk for MetS and DS (Laaksonen et al., 2002b; Teychenne et al., 2008).

There is evidence that a physically-active lifestyle reduces the risk for functional limitations (Lahti et al., 2010) and improves the quality of life (Vuillemin et al., 2005). As the population ages, understanding how to remain healthy and maintain one's physical abilities become increasingly important. The possible overall strong health benefit of physical activity in the development of diseases seems to be a sum effect mediated via different mechanisms. Consequently, sufficient PA may be a key factor in maintaining health.

6.3 Association between lifetime physical activity and occurrence of depressive symptoms in older age

This study revealed a relationship between reduced LTPA from the age of 45 years and increased prevalence of DS at the age of 65–74 years. Those with DS had significantly lower LTPA frequency from age 45 years onwards compared with those without DS. This finding indicates that maintaining LTPA throughout the lifespan may prevent DS later in life. Previous studies confirm that PA protects against the likelihood of DS and depression over the short term (Teychenne et al., 2008). However, this study provides evidence of benefits throughout the life course. Among participants with DS, the frequency of LTPA decreased throughout adulthood, reaching the lowest frequency at age 65–74 years. In contrast, those without DS at the ages of 65–74 years managed to maintain their LTPA frequency from the age of 25 years.

On the other hand, due to the retrospective nature of the data and in the absence of information about the age of onset of DS, these results may also reflect earlier onset of DS. Depression is a chronic disorder, which frequently occurs already in adolescence (Merikangas et al. 2010), thus the impact of DS over the lifespan on the PA habits is possible. This phenomenon was revealed in recent review, where depression was shown to be a significant risk factor for sedentary lifestyle and decreased PA (Roshanei-Moghaddam et al. 2009).

The birth cohort used in these analyses (65 to 74 years in 2007) has been accustomed to a physically-active lifestyle since childhood. However, PA habits have changed over time due to the development of automation and the information-based society. Children and adolescents nowadays are unlikely to achieve the same amount of overall activity as people in the previous generation at the same age. Because PA level is rather stable from childhood to adulthood (Biddle et al., 2010), the decreasing tendency for LTPA among adolescents is a cause for concern (Knuth and Hallal, 2009). Furthermore, a Finnish study of the general population showed that the strongest predictor of being physically active at the 22-year follow-up was participation in physical activity at baseline

(Borodulin et al., 2012). Based on this and another recently published study, insufficient PA could have deleterious consequences on health in older age (Jacka et al., 2011).

6.4 Physical activity level, prevalence of unintentional injuries and present of depressive symptoms

Physical activity and depressive symptoms play a role in the phenomenon of unintentional injuries as well. Although increased PA, particularly increased strength and balance training, has proved beneficial in terms of decreasing fall-related injuries and preventing fractures (Kannus et al., 2005), it may also have some deleterious consequences. A high level of PA has been shown to be associated with an increased risk for activity-related injury (Hootman et al., 2001). However, a physically active lifestyle seems to provide some protection against injuries other than activity-related ones (Carlson et al., 2006; Hootman et al., 2001). In the present study, unintentional injuries were studied in relation to total PA, and maybe therefore PA was not among the factors that explain unintentional injuries.

On the contrary, DS were strongly related to unintentional injuries. The proportion of subjects with unintentional injuries was almost double among those with DS compared with those without DS. This is in line with previous findings, as a number of studies have found DS to be associated with unintentional injury (Nordstrom et al., 2001; Patten et al., 2010; Poole et al., 1997; Tiesman et al., 2006). In fact, DS have been reported to increase the risk of injury by 41 % (Tiesman et al., 2006). It is also evident that result of an unintentional injury risk for DS increases (Scaf-Klomp et al., 2003). Hence, this phenomenon seems to be bidirectional as demonstrated in a national representative study (Patten et al., 2010).

Those with DS also had higher amounts of activity loss days after unintentional injuries. This finding is in line with results of Wan et al. (2006), who reported longer lengths of hospital stay in mentally ill participants after unintentional injury. One explanation behind this longer recovery period might be that the presence of DS affects perceived disability by lowering the sense of complete recovery after injury (Tiesman et al., 2006). Another explanation may be the lower functional ability among those with DS reported in this study, as functional ability has proved to be highly predictive for recovery after injury (Kempen et al., 2003).

The reasons behind the relationship between DS and unintentional injuries can be speculated. In the analysis, a variety of known confounders was controlled, including antidepressant use. Most of the previous studies examining injuries and mental health have reported antidepressant medication to be a risk factor for injuries (Modén et al., 2011; Woolcott et al., 2009), whereas this was not found in the present study. In addition, Tiesman et al. (2006) found that DS are a risk factor for injury, regardless of the use of antidepressants. Hence, there may be some alternative explanations for the relationship which was not explored in this study. Possibly, increased daytime sleepiness and a lack of concentration among those with DS may act as mediating factors (Maglione et al., 2012).

In addition, functional ability and musculoskeletal diseases were related to unintentional injuries. Functional ability worsens as a result of musculoskeletal diseases (Roux et al., 2005) and likely due to other somatic diseases as well. Therefore increased PA could be beneficial with respect to injury prevention, as PA has proven to be strictly related to functional ability (Hillsdon et al., 2005; Manini and Pahor, 2009). PA contributes favourably to balance, muscle strength, and neuromuscular control (Haskell et al., 2007), which in turn improve functional ability. A recently published injury prevention report encourages adults to maintain and increase their sporting and physical activity behaviours and suggests that they take up activities appropriate for their age and individual level of fitness and experience (Martin-Diener et al., 2010). Furthermore, the report emphasizes the importance of sufficient PA among elderly people for maintaining independency and reducing falls and fractures (Martin-Diener et al., 2010).

6.5 Methodological considerations

The present study utilized the population-based Finnish type 2 diabetes (FIN-D2D) survey, which provided excellent opportunity to examine PA habits in relation to mental and cardiometabolic health in a large sample of females and males aged 45-74. The FIN-D2D survey was a part of a national project for the prevention of type 2 diabetes, and covered a population of 1.5 million during the years 2003-2008 (Saaristo et al., 2007). The specific aims were to improve the screening of people at risk for diabetes and detection of undiagnosed diabetes. The data of the present study derive from the FIN-D2D survey, in order to evaluate heath behavior and the prevalence of DS and cardiometabolic risk factors. The sample size of 4 500 citizens with age and gender stratification together with moderate and acceptable participation rate gives an overview of the Finnish population. Consequently, the study sample, and thus also the results of this study can be considered generalizable to the Finnish population, but due to the lower age limit of 45 in this study, the results cannot be generalized to younger individuals. Furthermore, the sample was drawn from three health care districts instead of a national random sample, which could to some extent limit generalizability.

The effect of selection bias on the results, however, needs to be considered due to participation rate of 64% in this study. Typically, those who do not participate in surveys are younger males, and also persons who are less healthy. The non-responders in this study were somewhat younger than the responders and more likely to be female. Thus, it cannot directly be assumed that they have worse overall health status.

Due to the cross-sectional design of this study, the direction of the relationships cannot be evaluated. The study design does not either allow causal relationships to be made between of PA, DS and the cardiometabolic risk factors.

Several self-rated questionnaires and questions were used in this study, some of which have been validated while others are widely used and well-known measurement tools. Both the BDI questionnaire used to assess DS and the IPAQ used to assess total PA have been validated and are widely used, which also allows comparison of the results with those of other studies (Bauman et al., 2009; Nuevo et al., 2009a). Self-rated PA is a common way to assess PA in large population samples, and is considered to be comparable in outcome to objectively measured PA among adults. Also the LTPA assessment method used in this study is widely used in assessing LTPA in large population-based studies (Aires et al., 2003; Barengo et al., 2004; Borodulin et al., 2008). The LTPA question included multiple-choice response options. A disadvantage of the question is that it does not allow identification of the participants whose level of activity is above the health recommendations. The question is, however, effective in separating the inactive from the active population. Retrospective ascertainment of LTPA over decades might also increase the risk of recall bias, especially among those with DS, as they might project apathy or low motivation to earlier points in the lifecycle. Moreover, self-reported questionnaires have the potential for error in judgment; recall difficulties, misinterpretation of questions, and socially desirable responses.

A diagnostic interview would be the primary method for detecting DS. However, the BDI (with a cut-off score of 10 points) has proved to be an applicable method for assessing DS in various adult populations (Räikkönen et al., 2007; Timonen et al., 2005), although it was not initially constructed as a diagnostic scale. In addition, the information about injuries was collected retrospectively, meaning that participants do not necessarily remember all the injuries they had sustained during the previous 12 months. However, because we limited unintentional injuries only to those needing medical attention, the possibility of this source of error is minimized.

In the health examination, the objective measurements were done by nurses who were specially trained to carry out the study protocol as recommended to ensure validity of the measurements (World Health Organization, 1988). Further, all the specimens taken were transported frozen to the National Institute for Health and Welfare and stored at -70 C° until analyzed in the same laboratory.

The main strength of this study is the large representative population sample of middle-aged men and women, resulting a substantial number of participants. Other strengths include the novel findings of the role of lifetime LTPA on DS at older ages, and the distribution of LTPA levels with the co-occurrence of MetS and DS.

6.6 Practical implications and future directions

The findings of an association between low levels of PA and DS and cardiometabolic risk factors in this study corroborate the findings of previous studies. However, this study provides insight into the accumulation of deleterious health behavior, DS and health risk factors, and exposes the possible common mechanisms behind the accumulation. The hypothesis of shared etiologies is supported by evidence that the presence of one chronic disease in a person is often associated with an increased risk for developing additional health conditions (Probst-Hensch, 2010). Although we cannot know whether PA is a reason or consequence in this study, we can assume that being physically active enough for health benefits is enormously important.

With PA, it is possible to directly address the underlying causes of DS and also to determinants of MetS, and to break the vicious circle which seems to exist around MetS, DS and inactivity. The fact that two-thirds of participants with DS also had MetS is noteworthy. In these patients, health behavior modification is extremely challenging, while interference is highly relevant. Pharmacotherapy to treat the factors behind MetS and DS may cause negative side-effects such as weight gain. In addition, medication only treats symptoms, not underlying reasons. Early phase interventions, even among relatively low-risk individuals, may significantly reduce the progression to DS or MetS. Moreover, health care professionals should be able to identify patients who may benefit from a psychological intervention before focusing on lifestyle modifications.

Furthermore, although PA has become a recommended form of prevention and treatment of depression in the public heath guidelines in Finland, with similar recommendations existing in the UK and Austria (Rethorst et al., 2009; Current Care Guideline, 2004), there is a lack of research supporting a specific dose-response relationship between PA and DS. Further studies are needed to specify the appropriate duration, frequency, and intensity of PA to alleviate DS.

In addition to the direct effects of physical activity on health, physical activity has beneficial influence on social interaction and other health behaviors as well. Participating in physical activity offers an opportunity to interact with others, the community, and the environment, and thus decrease antisocial behavior. This social interaction may nevertheless be restricted among those with low income, as they are more likely to live in environments that do not support PA, and access to transport to reach PA facilities may be difficult. In addition, a physically active lifestyle tends to be associated with other positive health behaviors like healthy eating and nonsmoking (Cavill et al., 2006).

This study reveals that chronic diseases and depression can no longer be considered in isolation. Increasing awareness of the underlying common risk factors provides an opportunity to strengthen the role of PA in disease prevention. It is important for better public health to understand the common risks for diseases, their causal links and underlying biological mechanisms. Health care professionals should be more aware of physical activity's possibilities in prevention and treatment of diseases. Furthermore, based on the literature, PA should be intensive enough to trigger the underlying protective physical mechanisms.

As the connection between insufficient PA and chronic diseases seemed to be well understood, and simultaneously laziness turned out to be frequently cited reason for inactivity based on this study, internal motivation appears to be essential factor in order to be physically more active. It is also important to consider that for inactive people with DS, lifestyle modifications appear to be more challenging. More studies are needed to understand how to motivate and activate those with DS, and most of all how to commit them to be physically active. Randomized controlled trials are needed to study whether the effect of PA on cardiometabolic risk factors is similar to those with DS compared to the effect on those without DS. It would give more accurate information about the dose of PA needed to alleviate DS. More trials are also needed to investigate PA effect on common pathogenetic mechanisms of DS and MetS.

7 MAIN FINDINGS AND CONCLUSIONS

The main findings in the present study can be summarized as follows:

1. Physically inactive participants more commonly had health risk factors and depressive symptoms than their active counterparts. Furthermore, they were aware of their low fitness and higher risks for type 2 diabetes, cardiovascular diseases and depression. Lack of time was cited as the main reason for inactivity, while among those with DS and with MetS the main reason for inactivity was illness or disability.
2. Participants with depressive symptoms also had worse cardiometabolic risk factor profiles and lower total PA levels than participants without DS.
3. Lifetime leisure-time physical activity seemed to be associated with the occurrence of DS and somatic diseases in later life.
4. The presence of DS was related to increased prevalence of unintentional injuries. In addition, lower functional ability and musculoskeletal diseases were significantly related to the occurrence of unintentional injuries. Surprisingly, physical activity was unrelated to the unintentional injuries.
5. The rate of coincident MetS and DS was over fivefold higher among participants with low LTPA compared to those in the high LTPA group.

To conclude, the results of the present study indicate that both LTPA and total PA play a significant role in relation to DS and cardiometabolic risk factors. Health-related risk factors seem to accumulate in inactive individuals. Despite the fact that they are aware of the consequences of their inactive lifestyle, lack of time was reported to be the main reason for physical inactivity, particularly among those without DS or MetS. As national health education seems to achieve its goal, at least at the level of consciousness, alternative ways should be developed to convert inactive individuals into active ones, just sufficiently for them to derive somatic and mental health benefits.

YHTEENVETO (FINNISH SUMMARY)

Fyysisen aktiivisuuden yhteys masennusoireiden ja kardiometabolisten riskitekijöiden samanaikaiseen esiintyvyyteen

Depressio on keskeinen kansanterveydellinen ongelma. Maailman terveysjärjestön mukaan länsimaissa siihen sairastuu vuosittain 5% väestöstä, elämänaikaisen esiintyvyyden ollessa jopa 10–15%. Masennustilaa ennakoivat tavallisesti masennusoireet, missä masennuksen oirekriteerit eivät vielä täyty, mutta riski masennukseen sairastumiselle on suuri. Alhaisen fyysisen aktiivisuuden on todettu olevan yhteydessä sekä masennukseen että masennusoireisiin. Yhtenä syynä alhaiseen aktiivisuuteen voidaan pitää yhteiskunnan teollistumista ja automatisoitumista. Terveyden kannalta liian vähän liikkuvien suuri osuus on omalta osaltaan lisännyt kardiometabolisten riskitekijöiden esiintyvyyttä aiheuttaen yhä kasvavan kansanterveydellisen uhkan. Kardiometaboliset riskitekijät edetessään johtavat lopulta sydän- ja verisuonitautien ja diabeteksen puhkeamiseen. Vaikka vähäisen liikunnan on todettu olevan altistava tekijä sekä masennukselle että diabetekselle ja sydän- ja verisuonitaudeille, ei tutkimuksia juurikaan ole tehty näiden tekijöiden samanaikaisesta esiintyvyydestä.

Tässä väitöskirjatyössä tutkittiin fyysisen aktiivisuuden, masennusoireiden ja kardiometabolisten riskitekijöiden välisiä yhteyksiä suomalaisessa aikuisväestössä. Tutkimusaineisto on osa D2D-väestötutkimusta, mikä valikoitui satunnaisotannan perusteella väestörekisteristä vuonna 2007 Etelä-Pohjanmaan, Keski-Suomen ja Pirkanmaan sairaanhoitopiirien alueilta. Terveystarkastukseen kutsuttiin 4500 45–74-vuotiasta naista ja miestä, joista 64% osallistui. Heiltä mitattiin pituus, paino ja vyötärönympärys, sekä otettiin sokeri- ja rasva-aineenvaihduntaa kuvaavia laboratoriokokeita. Lisäksi tutkittavat täyttivät terveyskäyttäytymistä, terveydentilaa, toimintakykyä, tapaturmia ja somaattisia sairauksia koskevan kyselylomakkeen. Fyysisen aktiivisuuden arviointiin käytettiin kansainvälistä kokonaisfyysisen aktiivisuuden kyselyä IPAQ (International Physical Activity Questionnaire), mikä mahdollisti fyysisen aktiivisuuden luokittelun MET (metabolic equivalent) – arvojen perusteella kolmeen luokkaan. Lisäksi kartoitettiin viimeaikaista sekä elämänaikaista vapaa-ajan liikuntaa. Masennusoireita arvioitiin Beckin depressioasteikon avulla.

Tutkimustulokset osoittivat, että masennusoireisilla oli enemmän kardiometabolisia riskitekijöitä ja alhaisempi fyysinen aktiivisuus verrattuna henkilöihin, joilla ei ollut masennusoireita. Masennusoireiden esiintyvyys oli kolme kertaa yleisempää vähän liikkuvien keskuudessa kun heitä verrattiin paljon liikkuviin. Elämänaikaista vapaa-ajanliikuntaa tarkasteltaessa havaittiin, että vähäinen liikunta 45-vuoden iästä eteenpäin altisti masennusoireille sekä sydän- ja tuki- ja liikuntaelinsairauksille myöhemmällä iällä. Lisäksi rasva- ja sokeriaineenvaihdunnan häiriöt sekä alhaisempi toimintakyky olivat yhteydessä masennusoireisiin. Tutkimustulokset paljastivat myös, että vähän liikkuvat tiedostivat alhaisen kuntotasonsa, ja suurentuneen riskinsä sairastua tyypin 2 diabetekseen, sydän- ja verisuonisairauksiin ja masennukseen. Pääsyitä liikkumattomuudelle ilmoitettiin olevan ajan puute ja jokin sairaus tai vamma. Tapaturmia tarkasteltaessa todettiin, että niiden esiintyvyys oli korkeampaa masennusoireisilla (17%) verrattuna henkilöihin, joilla ei ollut masennusoireita (10%). Lisäksi masennusoireisilla tapaturmista toipuminen oli kolme kertaa hitaampaa.

Tämä laaja väestöotokseen perustuva tutkimus osoitti, että alhainen fyysinen aktiivisuus on merkittävä tekijä terveyteen liittyvien riskitekijöiden kasaantumiselle. Tulosten perusteella voidaan todeta myös, että liikkumattomuuden terveydelliset riskit tiedostetaan väestötasolla. Nämä suuremmassa sairastumisriskissä olevat tulisi löytää heidän terveyden seuraamiseksi ja toisaalta mahdollisuuksien kartoittamiseksi. Olisi hyvä tiedostaa, että vähäisetkin kardiometaboliset riskitekijät yhdessä vähentyneen arjen fyysisen aktiivisuuden kanssa voivat johtaa elintapasairauksien määrän kasvuun, ja kasvattavat osaltaan myös mielenterveysongelmien riskiä. Liikunnallisen elämäntavan ja vapaa-ajan liikunnan merkitystä ei tulisi unohtaa suunniteltaessa elintapasairauksien ennaltaehkäisyä ja sairauksien hoitoa.

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