JYU DISSERTATIONS 561

Ilkka Raatikainen

Associations between Physical Activity, Mental and Somatic Morbidity, and Health Care Utilization in Depressed Patients

UNIVERSITY OF JYVÄSKYLÄ
FACULTY OF SPORT AND
HEALTH SCIENCES

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ERRATA

- **Page 20, 2.1.2 Depression / Definition of depression, first chapter:**
  "According to the WHO (2020)" **should be:** "According to the WHO (2020a)"

- **Page 21, 2.1.2 Depression / Prevalence of depression, second chapter:**
  "(World Health Organization, 2020)" **should be**: "(World Health Organization, 2020a)"

- **Page 22, 2.1.3 Physical activity in depression, last chapter:**
  "(Table" **should be:** "(Table 1)"

ABSTRACT

Raatikainen, Ilkka
Associations between physical activity, mental and somatic morbidity, and health care utilization in depressed patients
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The aim of this thesis was to examine the relationships between physical activity (PA) and depression, more precisely leisure-time physical activity (LTPA) in relation to psychiatric and somatic comorbidity, subsequent health care utilization (HCU), future depressive symptoms, and total PA among depressed patients, as well as the association between PA and coping with home chores.

This thesis is based on data of population-based cross-sectional and longitudinal cohort study, the Finnish Depression and Metabolic Syndrome in Adults (FDMSA) and its five-year follow-up which were conducted within municipalities in the Central Finland Hospital District between 2008–2016. The study population was enrolled from patients ≥35 years old with depressive symptoms who scored ≥10 on the Beck Depression Inventory (BDI). Of the 760 patients, 447 received a depression diagnosis and from these 258 took part in the follow-up study. Participants' psychiatric diagnoses were confimed by structured interview (M.I.N.I.). All participants completed a standard self-administered questionnaire on their socioeconomic background, factors related to health, morbidity, depressive symptoms, and PA. Participants' LTPA were assessed with the questions categorized into three levels (low, moderate, and high) and their total PA was assessed via a short version of the International Physical Activity Questionnaire (IPAQ). All participants also underwent a health examination at baseline. The study nurses captured HCU from participants' health records.

LTPA level was not associated with psychiatric comorbidities or HCU among depressed patients. Higher PA levels were associated with lower cardiovascular disease, obesity, and depressive symptoms among depressed patients. Baseline LTPA did not predict the future improvement of depression, but it predicted the future total PA among depressed patients. Higher PA levels were related to lower home presenteeism among depressed patients.

To conclude, PA can mitigate the risk factors associated with mental and somatic morbidity and promote health in depressed patients. However, the role of PA in depressed patients' HCU is not clear. Therefore, PA should be considered and recommended in clinical practices and guidelines as an adjunctive treatment for depression.

Keywords: physical activity, depression, health care utilization, presenteeism

TIIVISTELMÄ (ABSTRACT IN FINNISH)

Raatikainen, Ilkka
Liikunta-aktiivisuuden yhteys psyykkiseen ja somaattiseen sairastavuuteen sekä terveyspalvelujen käyttöön masentuneilla
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Tämän väitöskirjatutkimuksen tavoitteena oli tutkia masennuspotilaiden vapaa-ajan liikunta-aktiivisuuden yhteyttä psyykkiseen ja somaattiseen sairastavuuteen, terveyspalvelujen käyttöön, myöhempään masennukseen ja kokonaisliikunta-aktiivisuuteen sekä kotona selviytymiseen.

Väitöskirjatutkimus perustuu Keski-Suomen sairaanhoitopiirin kunnissa vuosina 2008–2016 tehdyn väestöpohjaisen poikkileikkaus- ja pitkittäiskohorttitutkimuksen, Masennus- ja metabolinen oireyhtymä Suomessa, aineistoon. Tutkimuspopulaatio koostui ≥35-vuotiaista, joilla oli masennusoireita ja jotka saivat ≥10 pistettä Beckin masennusinventaariossa (BDI). 760 potilaasta 447 sai masennusdiagnoosin ja näistä 258 osallistui seurantatutkimukseen. Osallistujien psykiatriset diagnoosit varmennettiin strukturoidulla haastattelulla (M.I.N.I.). Tietoja tutkittavien sosioekonomisesta taustasta, terveyteen liittyvistä tekijöistä, sairauksista, masennusoireista sekä liikunta-aktiivisuudesta kerättiin vakiomuotoisella itsearviointikyselylomakkeella. Liikunta-aktiivisuus luokiteltiin kolmeen tasoon (matala, kohtalainen tai korkea). Tutkittavien kokonaisliikunta-aktiivisuutta arvioitiin kansainvälisen liikuntakyselyn (IPAQ) lyhyellä versiolla. Kaikille osallistujille tehtiin myös terveystarkastus lähtötilanteessa. Terveyspalvelujen käyttö kerättiin tutkittavien terveystiedoista.

Vapaa-ajan liikunta-aktiivisuus ei ollut yhteydessä psyykkisiin liitännäissairauksiin tai terveyspalvelujen käyttöön masentuneilla. Korkeampi liikunta-aktiivisuus oli yhteydessä alhaisempaan sydän- ja verisuonisairastavuuteen, vähäisempään lihavuuteen ja vähäisimpiin masennusoireisiin masentuneilla. Lähtötilanteen vapaa-ajan liikunta-aktiivisuus ei ennustanut paranemista masennuksesta mutta ennusti tulevaa kokonaisliikunta-aktiivisuuden tasoa. Korkeampi liikunta-aktiivisuus oli myös yhteydessä parempaan kotona selviytymiseen.

Tulosten mukaan liikunta-aktiivisuus voi vähentää ja lieventää psyykkiseen ja somaattiseen sairastavuuteen liittyviä riskitekijöitä ja edistää masennuspotilaiden terveyttä. Sen sijaan, liikunta-aktiivisuuden yhteys terveyspalvelujen käyttöön on epäselvä. Tulosten perusteella liikuntaa tulisi suositella kliinisissä käytännöissä ja ohjeistuksissa yhdessä muiden masennuksessa käytettyjen hoitomuotojen kanssa.

Asiasanat: liikunta, masennus, terveyspalvelujen käyttö, presenteeismi

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Jyväskylä 2.9.2022
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ORIGINAL PUBLICATIONS AND AUTHOR CONTRIBUTION

This dissertation is based on the following original publications referred to in the text by Roman numerals I–IV.

I Raatikainen, I., Vanhala, M., Mäntyselkä, P., Heinonen, A., Koponen, H., Kautiainen, H., & Korniloff, K. (2018). Does level of leisure time physical activity, in a sample of patients with depression, predict health care utilization over a subsequent 5-year period? Findings from a Finnish cohort study. *Mental Health and Physical Activity*, *15*, 40–44. https://doi.org/10.1016/j.mhpa.2018.06.007

II Raatikainen, I., Mäntyselkä, P., Vanhala, M., Heinonen, A., Koponen, H., Kautiainen, H., & Korniloff, K. (2019). Leisure time physical activity and its relation to psychiatric comorbidities in depression. Findings from Finnish Depression and Metabolic Syndrome in Adults (FDMSA) study. *Journal of Affective Disorders*, *259*, 150–153. https://doi.org/10.1016/j.jad.2019.08.039

III Raatikainen, I., Vanhala, M., Mäntyselkä, P., Heinonen, A., Kautiainen, H., Koponen, H., & Korniloff, K. (2021). Relationship between physical activity and predicted home presenteeism among participants with depressive symptoms with and without clinical depression. Findings from Finnish Depression and Metabolic Syndrome in Adults (FDMSA) study. *The European Journal of Psychiatry*. *35*(2), 75–82. https://doi.org/10.1016/j.ejpsy.2020.12.005

IV Raatikainen, I., Mäntyselkä, P., Heinonen, A., Vanhala, M., Kautiainen, H., Koponen, H., & Korniloff, K. (2021). Does baseline leisure-time physical activity level predict future depressive symptoms or physical activity among depressive patients? Findings from a Finnish five-year cohort study. *Nordic Journal of Psychiatry*, *75*(5), 356–361. https://doi.org/10.1080/08039488.2020.1862296

Additionally, previously unpublished results are included in the thesis.

The author of this dissertation, who is the first author of these publications, was mainly responsible for designing the studies, analyzing the data, interpreting the results, writing the manuscripts, and managing the review prosess during publication prosedures. The statistical analyses were conducted with the help of research group statistician. The author was privileged to use pre-existing data.

FIGURES

TABLES

ABBREVIATIONS

aRR	Adjusted incidence rate ratio
AUDIT	Alcohol Use Disorders Identification Test
BDI	Beck depression inventory
BMI	Body mass index
Cl	Confidence interval
CVD	Cardiovascular disease
DM	Diabetes mellitus
DS	Depressive symptoms
DSM	Diagnostic and Statistical Manual of Mental Disorders
ED	Emergency department
FDMSA	Finnish Depression and Metabolic Syndrome in Adults
GAD	General anxiety disorder
HCU	Health care utilization
HDL	High-density lipoprotein
HR	Hazard ratio
ICD	International Classification of Diseases
IPAQ	International Physical Activity Questionnaire
LDL	Low-density lipoprotein
LTPA	Leisure-time physical activity
M.I.N.I.	Mini-International Neuropsychiatric Interview
MADRS	Montgomery-Åsberg Depression Rating Scale
MDD	Major depressive disorder
MET	Metabolic equivalent
MetS	Metabolic syndrome
mmHG	Millimeter of mercury
MOPA	Moderate-intensity physical activity
MVPA	Moderate and vigorous physical activity
OCD	Obsessive-compulsive disorder
OGTT	Oral glucose tolerance test
OR	Odds ratio
PA	Physical activity
PHP	Predicted home presenteeism
PHQ	Patient Health Questionnaire
Q	Quartile/quintile
RCT	Randomized controlled trial
RR	Relative risk
SD	Standard deviation
TRD	Treatment resistant depression
US	United States
VAS	Visual analogue scale
WHO	World Health Organization

CONTENTS

1 INTRODUCTION

Depression is the third most common disease worldwide and is projected to become the most common disease by 2030 (Mathers & Loncar, 2006). Depression is the greatest incapacitating disease in the world and its costs represent a major social burden (Whiteford et al., 2013). Depression is a highly recurrent and chronic disease in some patients, which is thought to be caused by both hereditary and environmental (Sullivan et al., 2000) as well as personality factors (Brunes et al., 2013). In addition, unfavorable lifestyles and a number of somatic diseases have been found to be linked to an increased risk of depression (Ali et al., 2006; Korniloff et al., 2010, 2012). Over the past few years, evidence of the link between depression and other diseases has strengthened. Depression has been found to increase the risk of somatic diseases such as type 2 diabetes, cardiovascular disease (CVD), and of premature mortality (Koponen et al., 2010; Penninx et al., 2013; Whiteford et al., 2013). Depression and related psychiatric comorbidities have also been shown to significantly increase pain sensations, impair functional capacity, and reduce quality of life (Bair et al., 2003, 2008). Despite effective treatments, only a minority of people with depression receive appropriate and adequate treatment due to lack of resources, lack of skilled specialists, social stigma, and diagnosed factors (World Health Organization, 2020a).

The total annual cost to society of depression is enormous. The costs of depression can be divided into direct costs for treating the disease (use of health resources), indirect costs (absence due to sickness, retirement, reduced work intensity, premature deaths) and intangible costs (deterioration of quality of life, reduction in life expectancy) (Larg & Moss, 2011; Luppa et al., 2007). Depression in Europe has been calculated to cost €250 for every European per year (Sobocki et al., 2006). According to several studies, indirect costs of depression are higher than direct costs. For example, an extensive study carried out in 2006 (Sobocki et al., 2006) found that the indirect cost of depression in Europe in 2004 accounted for an estimated 64% of the total cost of depression of €118 billion. Similarly, in the US the indirect cost of depression formed roughly 55% ($112 billion) of the total cost of depression in 2010 (Greenberg et al., 2015). Depression also causes high levels of absence from work. In Finland depression is the most common

reason for sickness allowances (Kela, 2019) and disability retirement (Finnish Centre for Pensions, 2017). In Finland, the average length of a depressed patient's continuous absence due to illness is from 12 to 17 weeks (Kaila et al., 2012; Sorvaniemi et al., 2003). However, one third of patients with depression do not stay on sick leave for this, even though their ability to work is at least partially reduced (Kaila et al., 2012). Although only about 20–30% of patients with depression seek treatment and receive help (Hämäläinen et al., 2008), patients with depression have been found to use health services more than non-depressed patients (Kleinberg et al., 2013). According to a recent study, investing in the treatment of depression would make national economic sense, as more comprehensive treatment of depression pays for itself fourfold in better health and working capacity (Chisholm et al., 2016).

Physical activity can affect not only the physical condition and health of the individual, but also their mental health (Hassmén et al., 2000). Exercise has been shown in several studies to have a preventive and decreasing effect on depression and depressive symptoms (DS) (Hassmén et al., 2000; Korniloff et al., 2010, 2012; Sieverdes et al., 2012; Teychenne et al., 2008) The more frequent and intense exercise is, the more DS it reduces (Cooney et al., 2013). The link between exercise and depression has also been found to be bidirectional: increased PA reduces depression, while depression reduces PA (Da Silva et al., 2012; Sieverdes et al., 2012). PA can also influence societal health costs. Physically active persons use fewer health services (Lordan & Pakrashi, 2014; Woolcott et al., 2010) and their institutionalization is lower than that of physically inactive persons (Souza et al., 2015). In addition, the net cost of social and health services for physically active persons is lower than that of physically inactive persons (Vuori et al., 2010).

Although PA is beneficial both in terms of preventing and treating depression, and in terms of reducing societal costs, studies have not yet examined the effects of PA on comorbidities, coping at home, and social costs in depressed people. It is therefore justified to determine whether PA is related to these factors among people with clinical depression and DS.

2 REVIEW OF THE LITERATURE

2.1 Physical activity and depression

2.1.1 Physical activity

Definitions of physical activity

The most widely accepted definition of physical activity (PA) is any bodily movement produced by skeletal muscles that requires energy expenditure (Caspersen et al., 1985; Vuori et al., 2010; World Health Organization, 2022). PA can be considered as any such movement that increases energy expenditure over resting energy expenditure (Bangsbo et al., 2019; Bouchard et al., 2012) and is often characterized in terms of intensity from low to moderate to vigorous (Bangsbo et al., 2019). According to Vuori et al. (2010), PA refers solely to physical and physiological events and does not include expectations for the PA's causes, psychological effects, or social consequences. PA can be divided into work-related PA, sports, fitness, household work and other similar activities and can be described according to its duration and intensity (Caspersen et al., 1985). Total PA consists of actual PA and other daily physical activities (Leppäluoto et al., 2012). According to the WHO (2022), PA refers to all movement including during leisure time, for transport, or as part of a person's work. PA is linked to the physical and mental health condition of the individual (Caspersen et al., 1985; Vanhees et al., 2005; World Health Organization, 2022). PA plays a role in the prevention, treatment, and rehabilitation of numerous common diseases, syndromes, and symptoms, as well as in maintaining and improving functional capacity (Huttunen, 2022; Vuori, 2011), mental health, quality of life and well-being (World Health Organization, 2022). PA of both moderate and vigorous intensity improves health (World Health Organization, 2022).

PA is the opposite of physical inactivity and sedentary behavior; it can reduce their detrimental effects, i.e., the risk of morbidity and mortality and increased economic burden (Ding et al., 2016; Ekelund et al., 2016). PA can also be distinguished according to its aims. PA and exercise may aim to affect physical

fitness and health, produce experiences, or serve essential optional tasks (Vuori et al., 2010). As physical fitness refers to excellent performance, especially endurance and muscle strength, important health issues related to fitness include low blood pressure and blood cholesterol, ideal weight, musculoskeletal health, and joint mobility (Huttunen, 2022). When PA is used to achieve better physical fitness, it is a question of physical exercise, and when health fitness is the primary objective, we talk about exercise for health (Huttunen, 2022).

The effects of PA and exercise include training effects, i.e., changes in body structures and functions due to load responses and biological effects, e.g., the need for physiological overload, the need to increase load to increase the effects, specificity, the reversibility of effects after the load has ended or decreases, and the individual variation of the effects (Vuori, 2011). The load response is not always physiological, as some of the health effects of exercise are psychological (Vuori, 2011). These training, biological, and psychological effects must be recognized in order to plan and implement the PA program (Vuori, 2011).

Recently, a broader definition of PA has been proposed: "Physical activity involves people moving, acting and performing within culturally specific spaces and contexts, and influenced by a unique array of interests, emotions, ideas, instructions and relationships" (Piggin, 2020, p. 5). This holistic approach challenges the current and traditionally definitions of PA as it allows the lived experiences of people to be recognized (Piggin, 2020).

Leisure-time physical activity

In the literature, leisure-time physical activity (LTPA) is defined as PA that an individual engages in during his/her free time (Steinbach & Graf, 2008), which is not related to regular work, housework, or transportation activities (Meseguer et al., 2009) and increases the total daily energy expenditure (Bouchard et al., 2012). The chosen LTPA is driven by individual's personal needs and interests (Bouchard et al., 2012). PA can be considered as an umbrella term that encompasses all the total daily physical activities of which LTPA is one part, alongside transport, domestic, and work-related activities (Bangsbo et al., 2019).

Assessment of physical activity

PA is multidimensional, and complex to measure, as its various domains are often misunderstood (Warren et al., 2010). Inappropriate or crude measures of PA may have serious implications, lead to misleading results, and/or underestimate effect size (Warren et al., 2010). PA or exercise can be measured objectively using devices or subjectively using self-assessment questionnaires. Objective methods for measuring PA include various activity and accelerometers, as well as heart rate monitoring or pedometers (Husu et al., 2016, 2018; Vähä-Ypyä, Vasankari, Husu, Suni, et al., 2015; Vanhees et al., 2005; Warren et al., 2010) and accelerometers measuring oxygen consumptions (Vähä-Ypyä, Vasankari, Husu, Mänttäri, et al., 2015). Subjective self-assessment of PA can be carried out either retrospectively or prospectively through interviews, surveys, questionnaires, and diaries (Vanhees et al., 2005; Warren et al., 2010). With the development of technology and digitalization, new methods, applications, and devices for measuring PA are

constantly being developed, such as the latest wearable technology that collect information about a person's PA.

Before these new technologies were developed, large-scale objective measurements of PA have been costly, time-consuming, and difficult to carry out, so self-reported questionnaires have often been used to assess PA, especially in epidemiological studies (Lamonte & Ainsworth, 2001; Vanhees et al., 2005). Objective measurement of PA with new technologies is becoming more and more feasible, also in large study populations (Husu et al., 2018; Vähä-Ypyä, Vasankari, Husu, Mänttäri, et al., 2015). Objective measurements (such as accelerometry) are better able than self-reported questionnaires to capture the intensity, duration, and frequency of daily PA and exercise, even in short activity bouts (Bonomi et al., 2009; Esliger & Tremblay, 2007; Troiano et al., 2008)

At population level and in large study samples with the few questions, PA can be categorized in different categories (e.g., low-intensity, moderate, vigorous or active/inactive) and monitor the changes in PA on population level (Sallis & Saelens, 2000; Vanhees et al., 2005). PA surveys should include questions about the duration, frequency, and forms (e.g., work, leisure, transport, fitness, sports) (Van Poppel et al., 2010). The advantage of questionnaires, in addition to affordability, is their easier implementation in a large body of research (Lamonte & Ainsworth, 2001; Van Poppel et al., 2010; Vanhees et al., 2005). Thus, in large population studies, self-reported questionnaires are feasible methods to assess PA (Korniloff, 2013).

Although self-reported methods have several limitations, such as their tendency to overestimation (Hagströmer et al., 2007; Luke et al., 2011), interpretation, recall and socially desirable biases (Warren et al., 2010) and weaker reliability and relevance compared to objective methods (Shephard, 2003), their reliability and validity have been found to be sufficiently good at describing and classifying PA roughly at group and population level (Aires et al., 2003; Van Poppel et al., 2010).

No single method of measuring PA can be considered superior, and every method has advantages and disadvantages (Van Poppel et al., 2010; Warren et al., 2010). While objective measurements are more accurate and reliable, they are not practical in large population-based studies. Measurement methods are often selected in a trade-off between the degree of validity and feasibility, but the method must be suitable for the aims of the study to avoid crude or misleading outcome data (Warren et al., 2010).

Recommendations for physical activity

The PA recommendation for adults (aged 18–64) established by the WHO (2020b) is: "1) all adults should undertake regular PA; 2) adults should do at least 150–300 minutes of moderate-intensity aerobic PA, or at least 75–150 minutes of vigorous-intensity aerobic PA, or an equivalent combination of moderate- and vigorous-intensity activity throughout the week, for the substantial health benefits; 3) adults should also do muscle-strengthening activities at moderate or greater intensity that involve all major muscle groups on two or more days a week, as these provide additional health benefits; 4) adults may increase

moderate-intensity aerobic PA to more than 300 minutes, or do more than 150 minutes of vigorous-intensity aerobic PA, or an equivalent combination of moderate- and vigorous-intensity activity throughout the week for additional health benefits". PA can include recreational or LTPA (play, games, sports, or planned exercise), transportation (wheeling, walking, and cycling), work or household chores, in daily occupational, educational, home and community settings (World Health Organization, 2020b). The WHO states the following on good practice: "1) doing some PA is better than doing none; 2) if adults are not meeting these recommendations, doing some PA will benefit their health; and 3) adults should start by doing small amounts of PA, and gradually increase the frequency, intensity, and duration over time" (World Health Organization, 2020b). Current Finnish recommendations for PA are in line with the those of the WHO. The Finnish Current Care Recommendation (Duodecim, 2016) also emphasizes that PA should include exercise that maintains joint mobility and balance.

According to a previous Finnish national survey, FinHealth 2017, only half of the Finnish adult population achieved the national recommended PA level and one third were physically inactive (Borodulin et al., 2018). As during recent decades in Finland, the total PA has remained fairly stable, the LTPA has increased among the general population and occupational PA has decreased respectively (Borodulin et al., 2016). In FinHealth 2017 survey, 73% of men and 71% of women reported having LTPA and it was common in all age groups. Ageing decreased LTPA more among women than among men (Borodulin et al., 2018). As sedentary behavior has become more common during recent years, the survey results showed that one third of Finnish adults reported spending over 3 hours per day on "screen time," although this proportion has decreased in the last few years (Borodulin et al., 2018).

2.1.2 Depression

Definition of depression

According to the WHO (2020), depression is a common mental disorder characterized by depressed mood, decreased interest, pleasure, and self-feeling, increased feelings of guilt, insomnia, loss of appetite, fatigue, decreased activity, and difficulty concentrating. Depression includes *recurrent depressive disorder*, which involves repeated depressive episodes, and *bipolar affective disorder*, which typically consists of both manic and depressive episodes separated by periods of normal mood. Depression can be chronic or repetitive and can significantly impair an individual's ability to work, function, and cope with daily activities. Depression can encounter an individual at any stage of life, from childhood to old age. At worst, depression can lead to death. Depression is classified by the quality and quantity of its symptoms as mild, moderate, or severe. People with mild cases can be treated without medication, but in moderate to severe depression, medical and other treatments such as therapy are often required (World Health Organization, 2020a). The causes of depression include complex interactions between social, psychological, and biological factors. Life events

such as childhood adversity, loss, and unemployment contribute to and may catalyze the development of depression (World Health Organization, 2020a).

Assessment of depression

The diagnosis of depression is usually based on the International Classification of Diseases (ICD-10) (World Health Organization, 2021) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (American Psychiatric Association, 2020) (Pedersen et al., 2001). The severity of depression is assessed and classified in ICD-10 according to the number of symptoms as mild (4–5 symptoms), medium (6–7 symptoms) and severe (8–10 symptoms) (Duodecim, 2021). The severity of depression can also be assessed by means of various symptom monitors, such as Hamilton's depression scale, the Montgomery-Åsberg Depression Rating Scale (MADRS), Beck's depression scale (BDI), 9-question Patient Health Questionnaire (PHQ-9) or according to depressive related impairment (Duodecim, 2021).

Prevalence of depression

Globally, it has been estimated that more than 264 million people of all ages have depression and that women are more affected than men (James et al., 2018; World Health Organization, 2020a). Of Finnish citizens, approximately 5 to 9% have depression yearly (Markkula et al., 2015; Markkula & Suvisaari, 2018; Pirkola et al., 2005) and the increase in prevalence in the past few years has been significant for women, but not for men (Markkula & Suvisaari, 2018).

When it is long-lasting and/or moderate or severe in intensity, depression may become a serious health condition which can cause great suffering and poor function at work, home, or school (World Health Organization, 2020). At worst depression can lead to suicide, and close to 800 000 people every year die by suicide. Among younger people (aged 15–29) suicide is the second leading cause of death (World Health Organization, 2020a).

2.1.3 Physical activity in depression

Many resent studies have demonstrated the positive associations of PA and exercise on treatment and prevention of depression. For example, PA was found to be associated with reduced risk of depression (Gallegos-Carrillo et al., 2013; Mammen & Faulkner, 2013; Schuch et al., 2018) and of DS (Kvam et al., 2016; Sieverdes et al., 2012). In their meta-analysis of thirty-nine eligible randomized controlled trials (RCT), Rosenbaum et al. (2014) demonstrated that PA reduced DS in people with mental illness. Also reduced lifetime LTPA was found to be linked with higher occurrence of DS, especially in older age (Korniloff et al., 2012). The recent meta-analysis of prospective cohort studies about PA and incidence of depression concluded that the available evidence supports the notion that PA can confer protection against the emergence of depression regardless of age and geographical region (Schuch et al., 2018).

While moderate to vigorous PA was found to be related more strongly to decreased likelihood of depression than low PA (Cooney et al., 2013; Teychenne

et al., 2008), the protective effects against depression may be achieved even with low-intensity PA (Teychenne et al., 2008). According to Mammen and Faulkner (2013), any PA intensity, including low levels such as walking < 150 min/week, may prevent future depression. In recent 13-year cohort study of 25 520 Swedish adults with major depressive disorder (MDD), those whose habitual PA levels exceeded the duration recommended for general health had a 29% reduced risk of depression onset (Hallgren et al., 2019). A recent large nationwide US study demonstrated that physically active individuals had nearly 43% fewer poor mental health days than inactive ones during the past month (Chekroud et al., 2018). The positive effects of physical exercise on depression can be equal to medication or other treatments such as psychotherapy (Cooney et al., 2013) and PA could a be viable adjunctive treatment in combination with antidepressants (Kvam et al., 2016). Earlier studies have demonstrated that the association between PA and depression is bidirectional. As PA can reduce DS, DS can correspondingly reduce PA (Da Silva et al., 2012; Sieverdes et al., 2012).

My recent unpublished systematic literature search for original studies investigating associations between PA and DS/depression had the following inclusion criteria: 1) cross-sectional or prospective/retrospective cohort study; 2) published in English; 3) original and peer reviewed; 4) conducted between 2010 and 2020; 5) study population are adults; 6) the authors reported an association between PA and DS/depression using odds ratios; 7) the study is open access.

A total of 1660 articles (from the Medline Ovid, Web of Science and Cinahl databases) were found in this systematic literature search. After screening titles and abstracts based on the inclusion criteria, 57 articles remained. On full text examination, 34 more articles were excluded. Finally, 23 articles were included (Table

TABLE 1 Summary table of observational studies (2010–2020) that have examined the association between physical activity and depressive symptoms/depression (regression analysis, odds ratio).

Research, year, and country	Setting and design	Sample size, age(s) and gender distribution	Physical activity defined as	OR (95% CI) [1]	Findings
Asztalos et al., 2010 Belgium	Population-based cross-sectional study	6803 adults 25 to 64 years women 51%	Vigorous (>60 min/week) Moderate (>150 min/week) Walking (>120 min/week) PA below the recommended level	0.58 (0.41; 0.83) [2] 0.68 (0.47; 0.97) [2] - 1.00	Positive association regardless of the intensity of PA, differences between men and women.
Brunes et al., 2013 Norway	Population-based cross-sectional study 2006–2008	38 743 adults ≥19 years women 56%	Frequency (0, <1, 1, 2–3, >3 times/week) Duration (<15, 15–30, 30–60, >60 min) Intensity (low, moderate, high)	Women: OR decreases as the frequency, duration, and intensity increase Men: U-shaped relationship with frequency and duration, OR decreased with intensity	A positive connection with regular exercise. Personality can have an effect.
Chang et al., 2016 Iceland	25-year longitudinal follow-up study	4140 adults mean age 52 ±7 years women 57%	Active Inactive	0.65 (0.43; 0.83) 1.00	Midlife PA is associated with lower DS 25 years later.

Research, year, and country	Setting and design	Sample size, age(s) and gender distribution	Physical activity defined as	OR (95% CI) [1]	Findings
Da Silva et al., 2012 United Kingdom	8-year prospective cohort research, bidirectional 1985–1993	10 308 government officials 35 to 55 years women 32%	Regular PA according to recommendations Irregular PA below recommendations	0.71 (0.54; 0.99) [4] 1.00	Regular PA has a positive association. The association between PA and depression is bidirectional.
Dugan et al., 2015 Unites States of America	10-year longitudinal study Recruiting between 1995–1997	2891 women 42 to 52 years at baseline	PA meeting guidelines PA below guidelines Inactive	0.52 (0.40; 0.70) 0.81 (0.67; 0.98) 1.00	Higher PA is associated with lower levels of DS persistently over 10 years. Reaching moderate-intensity PA levels during midlife may protect from DS.
Gallegos-Carrillo et al., 2013 Mexico	6-year longitudinal follow-up study 1998–2006	1335 employees of all ages women 78%	High PA Moderate PA Physically inactive	0.46 (0.25; 0.87) [4] 0.57 (0.34; 0.93) [4] 1.00	The incidence of depression is lower among those who are more physically active. PA protects against depression.

Research, year, and country	Setting and design	Sample size, age(s) and gender distribution	Physical activity defined as	OR (95% CI) [1]	Findings
Hallgren et al., 2020 Sweden	Cross-sectional study 2017–2019	36 595 participants 16 to 80 years women 41%	Exercise frequency Never/Sometimes 1–2 times/week ≥3 times/week	(Model 3, fully adjusted) 1.00 0.75 (0.68; 0.82) 0.72 (0.65; 0.79)	Exercising at least 1–2 times per week is associated with lower odds of depression/anxiety symptoms. Sedentary behavior reduces the relationship.
Harvey et al., 2018 Norway	11-year longitudinal follow-up study	33 908 individuals ≥20 years women 50%	Amount per week: None Up to 30 minutes 31–59 minutes 1–2 hours 2–4 hours More than 4 hours	1.44 (1.17; 1.78) - - 1.00 - -	Any intensity of LTPA provides protection against future depression.
Jacka et al., 2011 Australia	Epidemiological research 2000, 2006	2152 adults 20 to 97 years	PA during childhood Physical inactivity during childhood	1.00 1.35 (1.01; 1.74)	Physical inactivity during childhood increases the risk of depression in adulthood.

Research, year, and country	Setting and design	Sample size, age(s) and gender distribution	Physical activity defined as	OR (95% CI) [1]	Findings
Marques et al., 2020 14 Europe countries	Cross-sectional and prospective study 2011, 2015	32 392 adults ≥50 years women 58%	MPA VPA	Cross-sectionally: OR is lower when engaging in MPA or VPA at least once a week in both gender Prospectively: PA predicts lower depression scores in both gender	PA is inversely associated with depression, both cross-sectionally and prospectively. PA seems to provide a positive effect on both prevention and treatment of depression.
Mc Dowell et al., 2018 Ireland	Cross-sectional study	10 122 adults of all ages pooled data women 55%	PA guidelines Meeting PA guidelines Not meeting PA guidelines PA tertiles High Middle Low	 0.56 (0.47; 0.66) 1.00 0.49 (0.40; 0.59) 0.74 (0.60; 0.83) 1.00	Meeting the PA guidelines and incerased volumes of MVPA are associated with lower odds of elevated DS.
Noh et al., 2015 South Korea	Register study 2011	12 350 adults ≥20 years women 53%	Vigorous Moderate Walking Physically inactive	1.00 - - 1.49 (1.14; 1.93)	Efficacious and vigorous exercise protects against depression better than lower-intensity PA.

Research, year, and country	Setting and design	Sample size, age(s) and gender distribution	Physical activity defined as	OR (95% CI) [1]	Findings
Padmapriya et al., 2016 Singapore	Population-based cohort study 2009–2010	1144 pregnant women ≥20 years	Sufficient level of PA (MET≥600 min/week) Insufficient level of PA (MET<600 min/week)	0.54 (0.31; 0.94) 1.00	Sufficient PA is associated with reduced risk of antenatal depression symptoms.
Pavey et al., 2013 Australia	Longitudinal follow-up study 1996–2010	11 285 women 46 to 52 years	MVPA (MET≥2000 min/week) MOPA (MET≥2000 min/week) Physically inactive	0.54 (0.47; 0.63) 0.65 (0.56; 0.75) 1.00	High levels of PA (MET) have an effect on depression.
Sieverdes et al., 2012 United States of America	Cross-sectional study 1996–2006	9580 men, 20 to 87 years	High (MET≥1000 min/week) Moderate (MET 500–999) Low (MET 1–499) Inactive (MET 0)	0.49 (0.40; 0.61) 0.49 (0.38; 0.62) 0.76 (0.60; 0.95) 1.00	PA has an inverse relation to DS.
Song et al., 2012 United States of America	Cross-sectional study	4058 adults ≥20 years women 51%	High Moderate Low Passive	- 0.72 (0.54; 0.97) - 1.00	Moderate exercise (30 min or more per day 3 times/day) is inversely related to the risk of depression.

Research, year, and country	Setting and design	Sample size, age(s) and gender distribution	Physical activity defined as	OR (95% CI) [1]		Findings
Souza et al., 2015 Brazil	Cross-sectional study	6924 adults ≥60 years women 66%	PA Physical inactivity	1.00 1.28 (1.05; 1.57)		PA is linked to an increased risk of depression and can lead to self-care neglect and hospital stays.
Stubbs et al., 2016 Low- and middle-income countries, World Health Survey	Cross-sectional study 2002–2004	178 867 people 18 to 69 years women 50%	High/meet PA recommendations Low/not meet recommendations	1.00 1.42 (1.24; 1.63)		People with depression engage in lower levels of PA.
Suija et al., 2013 Finland	Cross-sectional study	Cohort study of births in 1966 1997–1998 5497 participants at age 31 women 51%	Q5 (26.2–84.0 MET hours/week) Q4 (13.8–26.1) Q3 (7.4–13.7) Q2 (1.7–7.4) Q1 (≤1.6)	0.92 (0.65; 1.31)[2] 0.96 (0.68; 1.35) 1.00 1.10 (0.79; 1.53) 1.74 (1.29; 2.26)	1.05 (0.80; 1.38)[3] 0.99 (0.76; 1.29) 1.00 1.30 (1.00; 1.70) 1.36 (1.05; 1.75)	PA is inversely associated with the prevalence of depression in young Finnish adults.

Research, year, and country	Setting and design	Sample size, age(s) and gender distribution	Physical activity defined as	OR (95% CI) [1]		Findings
Teychenne et al., 2010 Australia	Cross-sectional study 2007–2008	3645 women 18 to 45 years	LTPA [5]			High weekly leisure and commuting exercise is linked to a lower risk of depression in women. Physical exercise, partly in combination with someone, is linked to a lower risk of depression. Excessive stationary, sitting, and screen time are similarly linked to an increased risk of depression in women.
			>3.4 hours/week	0.65 (0.56; 0.76)		
			41 min – 3.4 hours/week	0.67 (0.57; 0.80)		
			<40 min/week	1.00		
			Transport PA [6]			
			>2.5 hours/week	0.82 (0.69; 0.98)		
			<30 min/week	1.00		
			Social context of LTPA			
			part together with someone	0.69 (0.53; 0.89)		
			all alone	1.00		
			Stationary/seating [7]			
			<30.7 hours/week	1.00		
			>54.5 hours/week	1.28 (1.06; 1.53)		
			Work-related PA	-		
			Domestic PA	-		
Torres et al., 2013 United States of America	Cross-sectional study 2001–2003	2849 Afro-Americans 40 to 43 years women 64%	Often	0.41 (0.25; 0.69)[2]	0.42 (0.24; 0.72)[3]	Increased LTPA is inversely linked to DS in Afro-Americans.
			Sometimes	0.49 (0.28; 0.88)	-	
			Rarely	-	0.59 (0.40; 0.86)	
			Never	1.00	1.00	

Research, year, and country	Setting and design	Sample size, age(s) and gender distribution	Physical activity defined as	OR (95% CI) [1]	Findings
Vallance et al., 2011 United States of America	Cross-sectional study 2005–2006	2862 adults ≥20 years women 50% overweight 68%	Moderate-to-vigorous PA Q4 (>36 min/day) Q3 (19.22–6 min/day) Q2 (8.52–9.22 min/day) Q1 (<8.52 min/day)	 0.37 (0.20; 0.70) 0.49 (0.26; 0.93) 0.55 (0.34; 0.89) 1.00	Increasing the intensity of PA and reducing stationarity are positively linked to depression, at least in overweight individuals.
Wang et al., 2019 China	Longitudinal study	9118 adults ≥45 years women 51%	Frequency Intensity Duration Volume	Women: Lower OR with lower frequency, shorter duration, and moderate amount of MPA Men: Higher OR with higher frequency, longer duration, and overlong time on VPA	The association between PA and depression depend on intensity and gender.

CI = confidence interval, DS = depressive symptoms, MET = metabolic equivalent, OR = odds ratio, PA = physical activity, LTPA= leisure-time physical activity, MOPA = moderate-intensity physical activity, highest (MET) category, MPA = moderate physical activity, MVPA = moderate and vigorous physical activity, top (MET) class, Q = quartile/quintile, VPA = vigorous physical activity, 1.00 = reference group, - = result not statistically significant, [1] adjusted and only statistically significant results if reported ($p < 0.05$), [2] men, [3] women, [4] follow-up, [5] total time/week (walking, moderate and vigorous exercise combined), [6] total time/week (cycling and walking combined), [7] total time/week (computer time, TV viewing time, and sitting combined)

Of the articles found, 12 were cross-sectional studies, 8 were follow-up studies, ranging from 6 to 25 years, one was a cross-sectional and longitudinal follow-up study, one was reported as epidemiological research, and one as a register study. Most studies included women and men, but three of studies concerned women only and one study was of men only. The studies examined the association of PA level, duration, intensity, and format with depression or DS and the links were expressed using odds ratios. In some studies, inverse associations were examined and found.

While many of these recent observational studies (Table 1) indicate that more vigorous and higher levels of PA are more positively associated with depression (Asztalos et al., 2010; Brunes et al., 2013; Gallegos-Carrillo et al., 2013; Hallgren et al., 2020; Marques et al., 2020; Mc Dowell et al., 2018; Noh et al., 2015; Pavey et al., 2013; Suija et al., 2013; Teychenne et al., 2010; Torres et al., 2013; Vallance et al., 2011; Wang et al., 2019), studies suggest that reaching the recommended PA level and regular PA and exercise is already beneficial for the treatment and prevention of depression (Asztalos et al., 2010; Brunes et al., 2013; Da Silva et al., 2012; Mc Dowell et al., 2018; Padmapriya et al., 2016; Sieverdes et al., 2012; Song et al., 2012). According to study of Harvey et al. (2018), even any mount of LTPA can predict protection against future depression.

There is a gender difference. The strength of association between PA and depression may differ between women and men according to PA frequency, duration, and intensity (Brunes et al., 2013; Wang et al., 2019). For example, women with the longest duration of PA and men with highest intensity of PA may have the strongest association (Brunes et al., 2013), although the risk for depression may increase for men spending too long on vigorous PA (Wang et al., 2019). Personality may also affect the association: extrovert individuals may be more social and physically active than introvert persons (Brunes et al., 2013). The association between PA and depression is bidirectional (Da Silva et al., 2012; Sieverdes et al., 2012); depressed people engage in lower levels of PA (Stubbs et al., 2016). Doing PA with others might be better than exercising alone (Teychenne et al., 2010). Earlier studies also shows that childhood PA (Jacka et al., 2011) and midlife PA can protect against future depression (Chang et al., 2016; Dugan et al., 2015). To conclude, adequate, regular, and meaningful exercise, either alone or with others, seems to be crucial, while the form of PA does not seem to be so decisive.

2.2 Comorbidities, physical activity, and depression

2.2.1 Psychiatric comorbidities in depression

Depression is often associated with multiple psychiatric comorbidities: approximately 70% of individuals with depression have at least one psychiatric comorbidity (Kessler et al., 2003). Most commonly major depression disorder (MDD) is accompanied with anxiety disorder, substance abuse, and/or impulse control disorder (Kessler et al., 2003). Depression with psychiatric comorbidities is found to affect the individual's everyday life by increasing the sensation of pain and reducing one's performance and quality of life (Bair et al., 2008).

2.2.2 Somatic comorbidities in depression

Many previous studies have established the association between depression and somatic diseases. Depression has been found to be linked with elevated risk of obesity, diabetes, stroke, and CVD (Penninx, 2017; Penninx et al., 2013). In various meta-analyses of longitudinal studies, depression was found to increase the risk of diabetes (relative risk RR=1.60) (Mezuk et al., 2008), obesity (RR=1.58) (Luppino et al., 2010), stroke (RR=1.34) (Dong et al., 2012), hypertension (RR=1.42) (Meng et al., 2012), dementia (RR=1.96) (Cherbuin et al., 2015) and as well as risk of subsequent overall mortality (RR=1.81) (Cuijpers et al., 2014). For the onset of CVD depression can pose up to 80–90% elevated risk (Nicholson et al., 2006) and according to recent review of Doyle et. al. (2015), beyond increasing the risk of CVD onset, depression also increases the risk of cardiovascular mortality when CVD has already emerged. Again, the connection between depression and somatic comorbidity is bidirectional: depression may predispose metabolic syndrome (MetS) and vice versa (Koponen et al., 2008; Vanhala et al., 2009).

2.2.3 Physical activity, psychiatric and somatic comorbidities in depression

In most previous studies of the associations between (LT)PA and depression, psychiatric comorbidities have not been considered, or they are often excluded. Thus, there is a still some lack of knowledge about PA and its effects on psychiatric comorbidities in depression. The connection with PA and risk factors for somatic disease are better established in the literature. For example, the prevalence of simultaneous MetS and DS among depressed people was found to be higher with low LTPA (Korniloff et al., 2010). At least moderate LTPA can also reduce and prevent CVD and all-cause mortality (Barengo et al., 2017). PA may also reduce the risk of depression and somatic disorders in elderly patients (Korniloff et al., 2012).

2.3 Health care utilization, physical activity, and depression

2.3.1 Health care utilization and health care costs in depression

Definition of health care services

In Finland, health services are located in different sectors (Ministry of Social Affairs and Health, 2021) and aim to promote and maintain the health, well-being, work, functional capacity, and social safety of the population and to reduce health inequalities. In Finland, health services are divided into municipal health care (primary and specialized health care), occupational health care, and private health care.

According to the definition of the Finnish Ministry of Social Affairs and Health (2021), primary health care refers to health surveillance of the population organized by the municipality, the promotion of health, and various services provided in municipal health care centers. Specialized medical care refers to medical examinations and treatments in accordance with specialties. Most specialized medical services are provided in hospitals. The patient's status, rights, and time limits for access to treatment are regulated by law (Ministry of Social Affairs and Health, 2021).

Finnish employers are responsible for providing occupational health care for their employees. Occupational health care includes mandatory preventive health care and voluntary medical care services for working people. Private health services complement municipal services. A municipality or joint municipal authority may purchase services from private service providers (Keskimäki et al., 2019; Ministry of Social Affairs and Health, 2021).

Health care utilization

Depression is associated with increased health care utilization (HCU). Previous studies (Table 2) have demonstrated that depressed people use health care services up to 1.5 to 3 times more than non-depressed people (Kleinberg et al., 2013) and that only a minority of depressed people seek help (Byatt et al., 2016; Kim et al., 2015; Kleinberg et al., 2013). Depression can increase the risk of HCU among people who have cancer (Lo et al., 2013; Mausbach & Irwin, 2017), CVD (Chamberlain et al., 2011; Hornung et al., 2019), diabetes (Chan et al., 2012), knee and hip arthroplasty surgery (Gold et al., 2016), are overweight (Atlantis et al., 2012), and obese (Nigatu et al., 2017). Comorbidities (Bhattarai et al., 2013) alongside depression and lifetime history of depression (Lee et al., 2020) as well as the severity of depression (Ghafoori et al., 2014; McIntyre et al., 2020; Pálinkás et al., 2019) also tend to increase HCU. Among older people, depression was found to increase the risk of institutional care (Shin et al., 2012). Yet depressed older people appear to use preventive measures less than non-depressed people do (Shin et al., 2012). Gender, age, and socioeconomic status also appear to be linked to depressed people's HCU, with more common use of mental health services in women, middle-aged people, and those with the highest education and employment (Kim et al., 2015). Absence from work during depression was

found to increase risk of hospitalization and other health care visits up to 7 times more compared to the individual being at work while having depression (Gangan & Yang, 2018). A summary of recent observational studies on the association between depression and HCU is presented in Table 2.

According to the FINHealth 2017 survey, in Finland, 9% of women and 8% of men used health care services during the last 12 months due to mental health disorders (Suvisaari & Lindfors, 2018). HCU is most common among women aged 30–39 and 50–59. In the 30–39 age group, women used health care services twice as much as men. The lowest use of services was among people aged 60 years or over. One third of these were people with DS. HCU due to mental health problems is more common among highly educated citizens. HCU with mental health disorders has been stable since 2011 in the Finnish population (Suvisaari & Lindfors, 2018).

TABLE 2 Summary table of observational studies (2010–2020) that have examined the link between depression and the use of health services.

Research, year, and country	Setting and design	Sample size, age(s) and gender distribution	Health service use	OR/RR/HR/average difference (CI 95%)[1]	Conclusions
Atlantis et al,. 2012 Australia	Population-based follow-up study 1998, 2004, 2008	2747 persons ≥15 years women 55%	Use of health services 1 month In different categories of BMI	On average, 0.8–1.0 (60–72%) more visits, if depression	Depression, together with unhealthy BMI, increases HCU.
Bhattarai et al., 2013 United Kingdom	Cohort study 2004–2010	299 912 adults 30 to 100 years women 50%	HCU 1 year (general and specialist, prescriptions, institutional periods) together and without ancillary diseases	On average, 5.8 (3.9; 7.7) more visits, if ancillary diseases	Depression increases HCU in combination with comorbidities.
Byatt et al., 2016 United States of America	Population-based cohort study 2005–2012	463 pregnant women 20 to 44 years	Mental HCU during past 12 months	OR 3.5 (1.1; 11.0) if depressed	Depression increases the risk of mental health care use. Only 12% of depressed reported mental health care use.
Chamberlain et al., 2011 United States of America	Cohort study 1979–2009	799 cardiovascular disease patients, mean age 67.9 (±13.9) years women 45%	Institutionalization among cardiovascular patients (with depression) over the average follow-up period (6.2 years)	HR 1.28 (1.08; 1.51) HR 1.35 (1.08; 1.71)[2]	Depression increases the risk of institutionalization in cardiovascular patients.

Research, year, and country	Setting and design	Sample size, age(s) and gender distribution	Health service use	OR/RR/HR/average difference (CI 95%)[1]	Conclusions
Chan et al., 2012 Taiwan	Population-based cross-sectional study 2002–2003	1260 diabetic, mean age 63.7 (±12.2) years of which 127 with depression, of these women 60%	Retinal studies Kidney studies Outpatient visits Chinese medicine treatments Institutional care First aid visits Health checks	OR 1.61 (1.09; 2.37)[3] OR 2.35 (1.56; 3.54)[3] OR 2.11 (1.22; 3.67)[3] OR 1.31 (0.72; 2.40)[3] OR 2.09 (1.39; 3.16)[3] OR 1.63 (1.06; 2.50)[3] OR 1.15 (0.78; 1.69)[3]	Depression is linked to an increased risk of using health services in diabetics.
Gangan & Yang, 2018 United States of America	Retrospective cross-sectional study 2011–2014	3478 individuals with self-reported depression 18 to 64 years women 65%	Hospitalization and other health care visits according to work absence status	OR 7.11 (3.12; 16.2)	Work absence with depression increases the risk of hospitalization and other health care visits.
Ghafoori et al., 2014 United States of America	Cross-sectional study Mixed methods study	178 trauma sufferers >18 years women 34%	Current use of mental health services	OR 1.05 (1.00; 1.09)	The more severe the depression and the lower the trauma experience, the more likely it is to use mental health services.

Research, year, and country	Setting and design	Sample size, age(s) and gender distribution	Health service use	OR/RR/HR/average difference (CI 95%)[1]	Conclusions
Gold et al., 2016 United States of America	Retrospective cohort study 2007–2010	132 422 total knee arthroplasty and 65 071 total hip arthroplasty adults, >50 years women 63% / 59%	90-day hospital readmission when depression		Depression is associated with higher risk of readmission after THA and TKA.
			Total knee arthroplasty (TKA)	OR 1.21 (1.13; 1.29)	
			Total hip arthroplasty (THA)	OR 1.24 (1.13; 1.35)	
Hornung et al., 2019 Germany	Follow-up study 2012–2014	949 coronary heart disease patients mean age 63.8 (±10.1) women 20%	HCU during following 30 days after treatment in coronary heart disease unit		Depression increases risk of outpatient visits but not re-admission after hospitalization for cardiac care.
			Outpatient visit	OR 2.36 (1.75; 3.18)	
			Re-hospitalization	-	
Kim et al., 2015 South Korea	Population-based cross-sectional study 2011–2012	21 644 depressed adults ≥19 years women 70%	Use of mental health services for depressed people		Less than a fifth of depressed people use mental health services. Gender, age, and socioeconomic status are linked to the use of mental health services.
			Men (vs. women)	OR 0.73 (0.63; 0.85)	
			Elderly (vs. middle-aged)[m]	OR 0.67 (0.54; 0.83)	
			Elderly (vs. middle-aged)[w]	OR 0.69 (0.58; 0.83)	
			Low level of education (vs. high)[w]	OR 0.80 (0.64; 0.99)	
			Unemployment[m]	OR 0.55 (0.45; 0.67)	
			Unemployment[w]	OR 0.81 (0.72; 0.91)	

Research, year, and country	Setting and design	Sample size, age(s) and gender distribution	Health service use	OR/RR/HR/average difference (CI 95%)[1]	Conclusions
Kleinberg et al., 2013 Estonia	Cross-sectional study 2006–2008	6105 depressed adults Aged 18 to 84 women 52%	HCU among people who are depressed for 12 months (vs. non-depressed) Family doctor visits Calls to the emergency room Visits to the emergency room Institutional care	 OR 1.42 (1.06; 1.90) OR 2.80 (2.15; 3.64) OR 1.20 (0.84; 1.73) OR 2.10 (1.62; 2.73)	Depressed people use 1.5–3 times more health services than non-depressed ones. Only one-third of depressed people seek help.
Lee et al., 2020 South Korea	Cross-sectional study 2009–2013	499 492 individuals with at least one comorbidity women 55% [t] mean age 63.3 (±13.3)[t]	Comorbidity treatment (vs. without DS) Lifetime history of depression with current DS[m] Lifetime history of depression with current DS[w]	 OR 1.21 (1.00; 1.47) OR 1.13 (1.02; 1.25)	Depressed individuals with lifetime history of depression use treatment services more than non-depressed individuals. Major illnesses tend to decrease treatment seeking for medical conditions.
Lo et al., 2013 Canada	Retrospective study 2002–2008	680 cancer patients >18 years women 48%	Before the depression assessment Primary health care, not mh After the depression measurement Primary health care, mh Oncology	 RR 1.23 (1.00; 1.50) RR 2.35 (1.18; 4.66) RR 0.78 (0.65; 0.94)	Depression increases primary care visits and reduces oncologist visits for depressed people.

Research, year, and country	Setting and design	Sample size, age(s) and gender distribution	Health service use	OR/RR/HR/average difference (CI 95%)[1]	Conclusions
Mausbach & Irwin, 2017 United States of America	Retrospective study 2011	5055 outpatients with cancer diagnosis mean age 59.0 (±13.9)[d] women 58% [d] mean age 60.9 (±14.2)[nd] women 51% [nd]	One year health care visits Annual non-mental health care visits ED visit Overnight hospitalization 30-day hospital re-admission	 aRR 1.76 (1.61; 1.93) OR 2.25 (1.97; 3.04) OR 1.81 (1.49; 2.20) OR 2.03 (1.48; 2.79)	Depression among cancer patients is associated with greater HCU.
McIntyre et al., 2020 Canada	Retrospective longitudinal cohort study 2005–2007	277 TRD patients mean age 52 (±16) women 53%	HCU All cause outpatient visits Emergency unit visits Depression related visits to GP Psychiatrist visits	(TRD vs. Non-TRD) 38.2 vs. 24.2 2.7 vs. 2.0 3.06 vs. 1.63 5.88 vs. 1.95	TRD patients have more demand on healthcare resources than non-TRD patients.
Nigatu et al., 2017 Netherlands	Longitudinal 6 years follow-up study 2004–2013	2706 persons 18 to 65 years women 66%	HCU (obesity with MD/anxiety vs. non-obese and non-depressed) Primary care visits Specialty care visits Hospitalization	 OR 1.83 (1.44; 2.34) OR 1.31 (1.06; 1.61) OR 1.79 (1.40; 2.29)	Obesity along with depression/anxiety leads to higher HCU and health care costs over time.

Research, year, and country	Setting and design	Sample size, age(s) and gender distribution	Health service use	OR/RR/HR/average difference (CI 95%)[1]	Conclusions
Pálinkás et al., 2019 Hungary	Linkage study 2013–2016	2027 patients with hypertension and/or diabetes mean age 60.3 (± 13) women 64%	Outpatient service use	OR 1.60 (1.11; 2.31) (untreated severe depression)	Untreated depression increases HCU and related expenses. Screening for depression in hypertension and DM patients in primary care is reasonable and feasible.
Shin et al., 2012 South Korea	Longitudinal cohort study 2008	5137 adults ≥60 years women 57%	Health care Outpatient visits Institutional care Prevention Health checks	 OR 1.22 (1.18; 1.27) OR 1.19 (1.11; 1.24) OR 0.82 (0.77; 0.86)	Depression increases the risk of HCU and institutional care but reduces the use of preventive health care measures in older people.

aRR = adjusted incidence rate ratio, BMI = body mass index, CI = confidence interval, DM = diabetes mellitus, DS = depressive symptoms, GP = general practice, HCU = health care utilization, HR = hazard ratio, MD = mental disorder, mh = mental health, OR = odds ratio, RR = risk ratio, THA = total hip arthroplasty, TKA = total knee arthroplasty, TRD = treatment resistant depression, [1] adjusted value, statistical significance $p < 0.05$, [2] depression and anxiety combined, [3] p-values not mentioned, [m] men, [w] women, [t] used comorbidity disease treatment, [d] depressed, [nd] non-depressed

Health care cost

The annual cost of depression to society is enormous, totaling hundreds of billions per year. Sobocki et al. (2006) calculated that depression cost approximately €250 per year per European citizen. In the US the incremental cost of depression to society has increased in first decade of 21st century roughly 21% from $173 billion to over $210 billion, where comorbidities account for the largest portion of the growing burden (Greenberg et al., 2015). With severity of depression the costs also tend to rise (Chow et al., 2019; Ho et al., 2013; Tomonaga et al., 2013). The indirect costs of depression are many times higher than the direct costs. According to studies conducted in different countries, the indirect costs formed from 60% up to 90% of all costs (Chang et al., 2012; Ho et al., 2013; Sado et al., 2011; Salvador-Carulla et al., 2011; Tomonaga et al., 2013). In Europe in 2006 indirect cost consisted of 64% of all costs of depression (Sobocki et al., 2006). In Finland, depression in the most significant reason for payment of sickness allowances (Kela, 2019) and disability retirement (Finnish Centre for Pensions, 2017). The real cost of depression to society is likely to be much higher than reported simply because proper diagnosis and treatment do not reach everyone with depression and preventive or other intangible costs have not been taken into account in the calculations (Chang et al., 2012; Ho et al., 2013; Luppa et al., 2007; Sado et al., 2011; Salvador-Carulla et al., 2011; Tomonaga et al., 2013).

2.3.2 Health care utilization and physical activity in depression

PA has found to be associated with HCU in that physically active individuals seem to use health care services less than inactive ones (Fonseca et al., 2010; Kang & Xiang, 2017; Kaul et al., 2017; Lordan & Pakrashi, 2014; Rocca et al., 2015), though socioeconomic factors and self-rated health may reduce this association (Rocca et al., 2015). The association is also gender specific. Spika & Breyer (2020) found that women with high LTPA levels have 22% more physician visits; this association was not found among men, indicating that high LTPA does not necessarily mean lower HCU. Physically active individuals may use more preventive health care services, however, which may reduce their need for secondary and tertiary HCU (Kang & Xiang, 2017).

Among older people physical inactivity has been reported to increase the risk of hospitalization and depression and to decrease outpatient visits (Souza et al., 2015). Among patients with coronary heart disease, DS were associated with reduced PA and increased contact to mental care specialists (Hohls et al., 2020). While depression is associated with increased HCU (e.g., Kleinberg et al., 2013) and the benefits of PA for treating and preventing depression are well documented (Gallegos-Carrillo et al., 2013; Korniloff et al., 2012; Sieverdes et al., 2012), there is a lack of studies that have examined the relations between PA, HCU, and depression simultaneously. A summary of recent observational studies (2010–2020) that have examined the associations between PA and HCU is presented in Table 3.

TABLE 3 Summary table of observational studies (2010–2020) that have examined the associations between physical activity and the use of health services (regression analysis).

Research, year, and country	Setting and design	Sample size, age (group) and gender distribution	Physical activity defined as	OR (95% CI) [1] for HCU	Connection to health services
Fonseca et al., 2010 Brazil	Cross-sectional study 2006–2008	620 employees mean age 38.5 ±10.5 women 11%	Work-related PA LTPA excluding sport	1.25 (0.99; 1.58)[2] 0.76 (0.57; 1.02)[2]	Work-related PA may be linked to an increased risk of HCU and LTPA is similarly linked to the reduced risk of using health services, but the results are not statistically significant.
Kang & Xiang, 2017 United States of America	Cross-sectional study 2007–2011	117 361 adults ≥18 years women 52%	Physical activity vs. inactivity Preventive health service use Office-based visit Outpatient visit Inpatient visit Emergency room visit Home health care visit	 From 1.06 to 1.34 1.05 (1.01; 1.10) - 0.80 (0.75; 0.86) 0.93 (0.90; 0.98) 0.66 (0.57; 0.80)	Promoting regular PA may reduce secondary and tertiary HCU and heath care costs. Physically active individuals use more preventive health care services.
Kaul et al., 2017 United States of America	Cross-sectional study 2010–2014	4920 cancer survivors 18 to 64 years women 65%	Physical activity vs. inactivity Emergency department visits Hospital discharge	 -0.06 (-012; -0.01)[3] -	Physically active individuals have fewer ED visits and lower total health care costs than inactive ones.

			Outpatient visit	-	
Research, year, and country	Setting and design	Sample size, age (group) and gender distribution	Physical activity defined as	OR (95% CI) [1] for HCU	Connection to health services
Rocca et al., 2015 Sweden	Cross-sectional study 2012	28 028 participants 18 to 80 years women 54%	LTPA Sedentary Physically active Moderate exercise Vigorous exercise	 1.00 0.89 (0.81; 0.96) 0.74 (0.67; 0.81) 0.65 (0.60; 0.72)	The risk for HCU decreases with increasing levels of LTPA, though socioeconomic factors, and especially self-rated health, attenuate this association.
Spika & Breyer, 2020 Germany	Longitudinal cohort study 2012, 2016, 2017	2096 participants ≥18 years women 40%	Total PA LTPA Transport PA Work-related PA	Women: 22% more physician visit with high LTPA Men: no associations	LTPA is not necessarily associated with lower HCU.
Souza et al., 2015 Brazil	Cross-sectional study	6924 adults ≥60 years women 66%	Outpatient visits in last 6 months Institutional care periods in last 12 months More than one institutional care period (Effect of physical inactivity on these)	0.81 (0.69, 0.94) 1.41 (1.18, 1.67) -	Physical inactivity is linked to an increased risk of depression and can lead to neglect of self-care and increased periods in institutions.

CI = confidence interval, statistical significance $p < 0.05$, ED = emergency department, HCU = health care utilization, LTPA = leisure-time physical activity, OR = odds ratio, PA = physical activity, [1] adjusted value, [2] = univariate analysis, [3] = marginal effect, - = result not statistically significant

2.4 Presenteeism, physical activity, and depression

2.4.1 Definition of presenteeism

The concept of presenteeism in the literature is ambiguous and a generally accepted definition is still lacking (Lohaus & Habermann, 2019). Presenteeism as the opposite of absenteeism (being away) is something like being present but not necessarily fully capable of doing things. Again, presenteeism can be health related or not. For example, it can refer to working longer than necessary to show high commitment (Lowe, 2020) or it can refer to attending and going to work sick or injured (Johns, 2010; Lowe, 2020). In his review, Johns (2010, p. 521) has identified nine different definitions for presenteeism: "1) attending work, as opposed to being absent; 2) exhibiting excellent attendance; 3) working elevated hours even when unfit; 4) being reluctant to work part-time rather than full time; 5) being unwell but exhibiting no sickness or absenteeism; 6) going to work despite feeling unwell; 7) going to work despite feeling unwell or experiencing other events that normally compel absence; 8) reduced productivity at work due to health problems; and 9) reduced productivity at work due to health problems or other events that distract a person from full productivity". Therefore, the concept of presenteeism can vary on the point of view or study approach.

2.4.2 Home presenteeism

As most studies have focused on work-related presenteeism, there is little research available on presenteeism at home. In their studies Soliman et al. (2017) and Kumar et al. (2003) have used terms "household presenteeism" and "presenteeism at home" to describe a situation leading to loss of productivity in planned housework or home chores. The focus of home presenteeism is on an individual's everyday life apart from work; it describes how much a person's health disorders or harms affect their ability of a person to cope and perform everyday chores at home.

2.4.3 Presenteeism and physical activity in depression

Previous studies have shown that depression is associated with work-related presenteeism causing vast losses of productivity in the workplace due to the affected person's reduced functional capacity (Evans-Lacko & Knapp, 2016; Lépine & Briley, 2011). In a recent large prevalence study conducted in the US, depression, general anxiety, and other mental disorders were among the top health conditions that cause the highest estimated daily productivity loss and annual cost per person (Allen et al., 2018).

Promoting PA can help prevent and reduce health-related work presenteeism, as employees with sufficient PA or with better physical fitness were found to have less work limitations and increased work ability (Justesen et al., 2017; Walker et al., 2017a, 2017b). However, knowledge of relationships

between depression, PA, and home presenteeism is still lacking. As these intangible factors which are associated with the impact of illness on quality of life are often difficult to estimate accurately in monetary terms they are often disregarded in studies (Luppa et al., 2007).

2.5 Summary of the literature

Globally depression places an enormous burden on both society and individuals. Only a minority of those affected seek and receive adequate help. Depression is more common among women than men, and it can encounter an individual at any stage of life. Depression can greatly limit an individual's ability to work and function in everyday life and it can significantly reduce a person's quality of life. At worst depression can lead to death. Mild forms of depression can be treated well with adequate treatments such as medication. Depression is a risk factor for many somatic diseases such as CVD, diabetes, obesity, and dementia, and it is often accompanied by multiple psychiatric comorbidities. Depression is also associated with increased HCU, but people with severe depression may miss health appointments and this reduced HCU could lead hospitalization. Depression was found to be linked to productivity losses due to absence from work or reduced work capability but there is limited evidence on how depression affects the ability to cope with home chores.

There is plausible evidence from large number of studies that regular and sufficient PA can mitigate depression and that, in general, physically active individuals use fewer health care services compared to inactive ones, though socioeconomic factors, self-perceived health status, and gender may influence these connections. There is also evidence that promoting PA can be beneficial for preventing and reducing health-related work presenteeism.

PA, depression, psychiatric and somatic comorbidities, HCU, and coping with daily tasks are linked to form complex and multilevel networks. In each factor, the influence on/by PA is more or less bidirectional. So, impact on one factor is reflected in the other. As recent studies have limited scope to some but not all of these factors, there is need to investigate PA and depression together with HCU, somatic and psychiatric comorbidities, and home presenteeism.

3 PURPOSE OF THE STUDY

The purpose of this study was to examine the associations between physical activity, mental and somatic morbidity, and health care utilization in depressed patients in a population-based cross-sectional and longitudinal cohort study conducted in Finland between 2008 and 2016.

The detailed objectives of the study were to examine:

1. Leisure-time physical activity and its relation to psychiatric comorbidities and somatic diseases in depression. (Study II)
2. The association between leisure-time physical activity and subsequent health care utilization among depressed patients. (Study I)
3. The association between baseline leisure-time physical activity and future depressive symptoms and physical activity among depressed patients. (Study IV).
4. Relationship between physical activity and predicted home presenteeism and severity of depression among participants with depressive symptoms with and without clinical depression. (Study III)

4 MATERIAL AND METHODS

This study is part of the population-based cross-sectional and longitudinal cohort study, the Finnish Depression and Metabolic Syndrome in Adults (FDMSA) and its five-year follow-up. The study examines clinical and sosiodemograghic factors related to depression and metabolic syndrome in Finnish adults aged 35 and over.

4.1 Study participants and design

The study was conducted within the municipalities in the Central Finland Hospital District with a total catchment area of 274 000 inhabitants. FDMSA baseline data was collected between 2008 and 2011 and its follow-up data between 2012 and 2016. At baseline, 760 patients with DS were recruited, and those who scored ≥10 in the 21-item Beck Depression Inventory (BDI-21), were aged 35 or older, and were either self-referred or had been referred by general practitioners to depression nurse case managers. Using a structured interview (M.I.N.I.), a diagnosis of depression was confirmed in 447 participants. Of these, 258 participants took part in the follow-up study. The inclusion criteria, the data used, and participants are presented in Figure 1. The FDMSA data collection timeline and collected data utilized in Studies I–IV are presented in Figure 2 and outcome variables of each study in Table 4. More detailed information can be found in the individual articles.

All the participants signed an informed consent form. The ethical permission for the study was approved by the Ethics Committee of the Central Finland Hospital District.

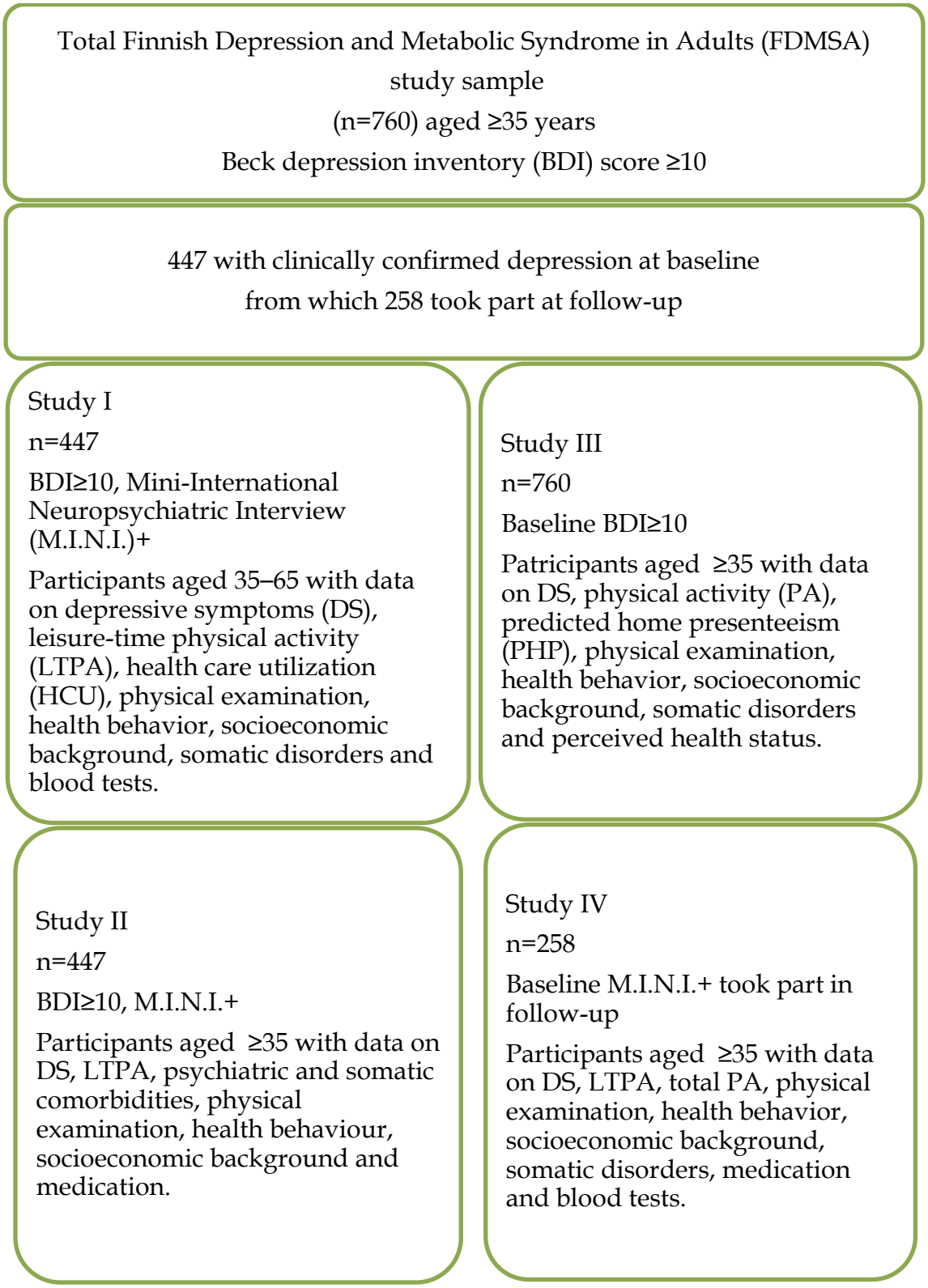

FIGURE 1 Study samples in articles I–IV.

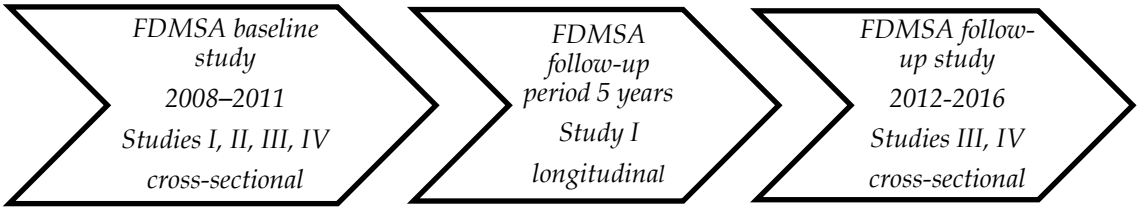

FIGURE 2 Finnish Depression and Metabolic Syndrome in Adults (FDMSA) data collection timeline and collected data utilized in Studies I–IV.

TABLE 4 The primary and secondary outcome variables of Studies I–IV.

Variables	Study I	Study II	Study III	Study IV
Primary outcome variables				
Depression	x	x	x	x
Leisure-time physical activity	x	x		x
Total physical activity			x	x
Health care utilization	x			
Psychiatric comorbidities		x		
Home presenteeism			x	
Secondary outcome variables				
Physical examination	x	x	x	x
Health behavior	x	x	x	x
Socioeconomic background	x	x	x	x
Somatic disorders	x	x	x	x
Antidepressant use		x		x
Perceived health status			x	
Blood tests	x			x

4.2 Measurements

Measurements included a self-administered questionnaire containing questions on participants' socioeconomic background, health and morbidity related factors, DS and PA, objective measured anthropometric measurement, and collection of health care visits.

4.2.1 Physical activity

Leisure-time physical activity (LTPA) was assessed by the question: How often do you do physical activity at least for half an hour so that you are out of breath and sweating? Answers were classified into three levels: low (twice per month or less), moderate (once or twice per week), or high (three times per week or more). Self-reported LTPA has shown a high correlation with physical fitness as measured by maximal oxygen uptake (Aires et al., 2003).

Total physical activity (PA) was assessed at follow-up by using the self-administered short version of the International Physical Activity Questionnaire (IPAQ), which was included in the self-administered questionnaire. IPAQ was developed as an instrument for cross-national monitoring of PA (Booth, 2000) and it has proven to be valid and reliable method to collect PA data in cross-sectional studies (Craig et al., 2003). The IPAQ short form consists of seven questions about participants' PA (in work, leisure time, commuting, exercising, or sport) during the last seven days. Participants were asked to assess their PA as vigorous (hard physical effort that really affects one's breathing), moderate (moderate physical effort that somewhat affects breathing) and walking sessions lasting at least 10 minutes in days per week, hours per day, and minutes per day. In addition, daily sitting time (hours and minutes per day) were also assessed. Answers were classified as IPAQ grades (low, moderate, high) via the IPAQ scoring protocol (Grupo IPAQ, 2019). At follow-up answers for PA were converted and expressed as metabolic equivalent (MET) (Jetté et al., 1990) hours per week (Study IV).

4.2.2 Depressive symptoms and psychiatric diagnosis

Depressive symptoms (DS) were captured using the 21-item self-report Beck Depression Inventory (BDI) questionnaire (Beck et al., 1961) consisting of symptoms and attitudes related to depression. To calculate the total score, the items are summed, with a range from 0 to 63. The cut-off point was set to ≥10 which indicates at least mild depression (Koponen et al., 2008, 2015a; Korniloff et al., 2010; Väänänen et al., 2008).

Psychiatric diagnosis and number of psychiatric comorbidities were confirmed and obtained with a diagnostic Mini-International Neuropsychiatric Interview (M.I.N.I.) (Sheehan et al., 1998) delivered by trained study nurse during the study visit.

Severity of depression symptoms was evaluated alongside with BDI questionnaire using the Montgomery-Åsberg Depression Rating Scale (MADRS) (Montgomery & Asberg, 1979) (Study I).

4.2.3 Somatic disorder

Information on participants' previously diagnosed somatic disorders such as diabetes mellitus, cardiovascular and lung diseases were collected via a self-administered study questionnaire.

4.2.4 Health care utilization

Data on HCU were collected by two study nurses from participants' health care records for the first five years after the first study visit and calculated as person years. The frequency of visits and phone call contacts, and days of hospitalization were calculated separately for primary and specialized health care. Health professionals were categorized as a physician (general practitioner or specialized physician), psychiatrist, psychologist, depression nurse, substance abuse nurse or other (e.g., social worker, nutritionist).

4.2.5 Home presenteeism

Home presenteeism (defined in this thesis as how much housework or household chores are disturbed or affected by subjects' diseases and disorders at home) was captured by a visual analogue scale (VAS) question: How much have your diseases and symptoms affected your necessary housework and household chores at home during the last month? Each participant was asked to mark the position to describe his/her agreement with the statement along a continuous line between two end points. For the analysis answers were scored from 0 ("not at all") to 100 ("completely blocked").

4.2.6 Anthropometric measurement

The physical examination during the study visits included measurements of the participant's weight/body mass, height, waist circumference, and blood pressure. Weight and height were measured with the participant wearing light clothing and were accurate to the nearest 0.5 cm and 0.1 kg, respectively. Waist circumference was measured to the nearest 1.0 cm at the midpoint between the lateral iliac crest and the lowest rib. Blood pressure was measured twice by trained nurses after 15 minutes at rest with a mercury sphygmomanometer and the participant in the sitting postition. The Body Mass Index (BMI) was defined as person's weight (kg) divided by the square of the height (m). The WHO has defined a person as overweight as when their BMI ≥25 and obese with BMI ≥30, respectively (World Health Organization, 2019).

4.2.7 Collection of blood samples

Fasting blood samples were drawn after 12 h of fasting to determine glucose and lipid levels (Koponen et al., 2015b). Glucose tolerance was tested using an oral glucose tolerance test (OGTT).

4.2.8 Other health-related and socioeconomic variables

Smoking and alcohol use
Smoking was assessed by asking whether the participant currently smoked or not. Participants' drinking habits were evaluated by an alcohol use disorders identification test in its three-question screening version (AUDIT-C) (Babor et al., 2001). AUDIT-C is a brief practical and valid primary care screening test for heavy drinking and/or active alcohol abuse or dependence (Bush et al., 1998). Participants were asked to answer the following three questions: How often did you have a drink containing alcohol (1 = never; 2 = monthly or less; 3 = 2 to 4 times a month; 4 = 2 to 3 times a week; 5 = 4 or more times a week)? How many drinks did you have on a typical day when you were drinking (1 = 1 to 2 drinks; 2 = 3 to 4 drinks; 3 = 5 to 6 drinks; 4 = 7 to 9 drinks; 5 = 10 or more drinks)? How often did you have 6 or more drinks on one occasion in the past year (1 = never; 2 = less than monthly; 3 = monthly; 4 = weekly; 5 = daily or almost daily)? The AUDIT-C was scored on a scale 0 to 12 (where response option 1 = 0 points, 2 = 1 point, 3 = 2 points, 4 = 3 points, and 5 = 4 points). Generally, men scoring 4 (women 3) or more are considered potential hazardous/heavy drinkers and the higher the score, the more likely drinking is affecting to one's health and safety (Babor et al., 2001; Bush et al., 1998).

Socioeconomic characteristics such as employment status (employed, unemployed, student, or retired), years of education, and marital status were collected via a self-administered questionnaire.

Antidepressant use was collected via a study questionnaire.

Measurements are described more detailed in studies I–IV.

4.3 Statistical methods

The results were presented as means with standard deviations (SD) or as counts with percentages. In studies III and IV statistical comparisons between the depression groups were performed using the t-test for continuous variables and Pearson's chi-square test for categorical variables.

Statistical significance for the unadjusted analyses of linearity across the LTPA categories were evaluated using the Cochran-Armitage test, Cuzick test, and analysis of variance with an appropriate contrast. Adjusted analyses of linearity (orthogonal polynomial) were evaluated using generalized linear models (e.g., analysis of co-variance, regression models, and logistic models) with appropriate distribution and link function. Models included age, gender, years of education, marital status, comorbidities, and household income as covariates (Study I, II).

The adjusted relationship between the PA level and the depression status with home presenteeism was analyzed using a two-way analysis of variance. A possible nonlinear relationship between the BDI score and home presenteeism was assessed using 4-knot-restricted cubic spline regression. The models included age, gender, marital and working status, years of education, smoking, BMI, and comorbidities as covariates. Correlation coefficients with 95% confidence intervals (CI) were calculated by using the Pearson method. (Study III).

The adjusted hypothesis of linearity (orthogonal polynomial) was evaluated using generalized linear models (analysis of covariance and logistic models), with the appropriate distribution and link function. Models included age, gender, years of education, diabetes, and BDI as covariates. Rank-based (Spearman) partial correlations were calculated between baseline and follow-up LTPA, adjusted for age, gender, years of education, and diabetes. Confidence intervals for the correlation was obtained by bias-corrected bootstrapping (5000 replications). (Study IV).

The bootstrap method was used when the theoretical distribution of the test statistics was unknown or in the assumptions were violated (e.g., non-normality). The normality of variables was evaluated graphically and with the Shapiro–Wilk W test. All analyses were performed using STATA 14.0 (Study I, II) and STATA 16.0. (Study III, IV).

5 RESULTS

5.1 Characteristics of participants

Participants' baseline sociodemographic and clinical characteristics according to each study setting are presented in Table 5.

The study sample consist of 760 participants with DS. The majority of participants were women (n=514; 68%). Participants' mean age at baseline was 53 (SD 10). At baseline 447 participants had received a depression diagnosis (Study I, II), with the mean age 51 (SD 10). The majority of those who had a confirmed diagnosis of depression were women (n=312, 70%). From these with confirmed clinical depression at baseline, 258 patients took part in five-year follow-up (Study IV) with the mean age 52 (SD 10) at baseline. The majority at follow-up were women (n=195, 76%).

At baseline, from whole study population (n=760) most of the participants were living in a relationship (64%) and were employed (43%) or retired (45%) with the mean years of education 11.5 (SD 3.3). The majority of participants diagnosed with depression (n=447) were living in a relationship (60%) and were employed (45%) with the mean years of education 11.0 (SD 3.0). The relative portion of smokers was higher (32%) among those participants who had received a depression diagnosis (Study I, II) than among the whole study population (17%) (Study III). Participants' mean BMI at baseline was 27.5 (SD 5.2) for the whole study population and 28.0 (SD 5.9) for those with a depression diagnosis. Most of the participants (from 74% to 77%) consumed five or fewer doses of alcohol per week regardless of having a depression diagnosis or not.

The most prevalent somatic diseases among participants with DS at baseline were lung diseases (14%), DM (12%) and CVD (9%) (Study III). The relative portion of CVD (16%) and DM (14%) increased with depression diagnosis (Study I, II).

Depressive symptoms were more severe among participants who had a depression diagnosis, with the mean BDI scores 23.4 (SD 8.2) (Study I, II) and

23.2 (SD 7.8) (Study IV); participants without a depression diagnosis had a lower mean BDI score of 13.3 (SD 10.7) (Study III). In the whole study population (n=760; study III) 37% of participants used antidepressant at baseline while among those who received a depression diagnosis (n=447; Study I, II) the portion of antidepressant users was 68%.

At baseline, from the whole study population (n=760; study III) 17% of participants reported a low level of LTPA, 43% a moderate, and 39% a high level. Among those who received depression diagnosis at baseline (n=447; study I, II) proportions were 25% for low, 41% for moderate, and 34% for high levels of LTPA. Among those patients (n=258; Study IV) with confirmed clinical depression at baseline who took part in five-year follow-up, the proportions were 23% for low, 41% for moderate, and 36% for high LTPA level, respectively.

TABLE 5 Participants' baseline sociodemographic and clinical characteristics.

Variables	Study I, II	Study III	Study IV
Number	447	760	258
Women, n (%)	312 (70)	514 (68)	195 (76)
Age, years (SD)	51 (10)	53 (10)	52 (10)
Years of education (SD)	11.0 (3.0)	11.5 (3.3)	11.1 (3.0)
Married or cohabited, n (%)	266 (60)	490 (64)	141 (55)
Employment status, n (%)			
Employed	202 (45)	328 (43)	122 (47)
Unemployed	113 (25)	86 (11)	54 (21)
Student	11 (2)	6 (1)	7 (3)
Retired	121 (27)	340 (45)	75 (29)
BMI, mean (SD)	28.0 (5.9)	27.5 (5.2)	28.7 (5.7)
Smoking, n (%)	142 (32)	129 (17)	56 (22)
Disease, n (%)			
CVD	73 (16)	70 (9)	25 (10)
Lung	42 (9)	103 (14)	41 (16)
DM	64 (14)	91 (12)	44 (17)
Blood pressure (mmHg), mean (SD)			
Systolic	131 (16)	130 (15)	130 (15)
Diastolic	82 (11)	81 (10)	81 (10)
Plasma Glucose 0h (mmol/l), mean (SD)	5.88 (1.45)	5.68 (1.02)	5.70 (1.06)
Total cholesterol (mmol/l), mean (SD)	5.09 (1.02)	5.08 (0.94)	5.13 (0.99)
LDL cholesterol (mmol/l), mean (SD)	3.05 (0.93)	3.10 (0.85)	3.11 (0.90)
HDL cholesterol (mmol/l), mean (SD)	1.57 (0.48)	1.57 (0.43)	1.55 (0.41)
Alcohol, doses per week, n (%)			
None	95 (21)	137 (18)	53 (21)
1–5	251 (56)	421 (56)	141 (55)
6–9	41 (9)	88 (12)	28 (11)
≥10	60 (13)	100 (13)	36 (14)
BDI score, mean (SD)	23.4 (8.2)	13.3 (10.7)	23.2 (7.8)
Antidepressant, n (%)	305 (68)	282 (37)	178 (69)

LTPA, n (%)			
Low	111 (25)	129 (17)	60 (23)
Moderate	185 (41)	330 (43)	106 (41)
High	151 (34)	296 (39)	92 (36)

BMI body mass index, BDI Beck depression inventory, CVD cardiovascular disease, DM diabetes mellitus, HDL high-density lipoprotein, LDL low-density lipoprotein, LTPA leisure-time physical activity

For participants (n=447) who had a clinically confirmed diagnosis of depression at baseline, LTPA did not associate with sociodemographic factors such as working status, marital status, years of education, or health habits (smoking or alcohol use). Details are described in the original Studies I and II.

From 258 patients with confirmed clinical depression at baseline who took part in five-year follow-up, DS (BDI ≥10) were observed in 76 patients (29%). The participants with DS in follow-up had fewer years of education (p=0.035), had more DS (p=0.011), and had higher prevalence of DM (p=0.014) at baseline than those participants without DS. The study results are described in more detail in original Study IV.

5.2 Leisure-time physical activity and psychiatric and somatic comorbidities

5.2.1 Leisure-time physical activity and psychiatric comorbidities

One-fifth (23%) of participants diagnosed with depression (n=447) had no psychiatric comorbidity. More than one third (38%) of the participants had one comorbidity, 22% had two, and 17% had at least three psychiatric comorbidities. The most common psychiatric comorbidities were general anxiety disorder (GAD) and suicidal thoughts, which were present among half or more of the depressed patients. Participants with one or more psychiatric comorbidities were younger (50 vs. 53 years) and smoked more often (34% vs. 23%, p=0.023) than those without psychiatric comorbidities. There were no difference in gender, BMI, or years of education among participants with or without psychiatric comorbidities. The prevalence of psychiatric comorbidities among all depressed participants is presented according to the LTPA tertiles in Table 6.

LTPA level was not related to number of psychiatric comorbidities (p=0.24) among depressed patients, although lower levels of LTPA were linearly associated with higher BDI (p<0.001) and MADRS (p=0.002) values. While 68% (n=305) of participants used antidepressants, linear association between the LTPA level and antidepressant use was not observed (p=0.53).

TABLE 6 Psychiatric comorbidities among depressed patients according to baseline leisure-time physical activity level.

Variables	Total N=447	Leisure-time physical activity Low N=111	Moderate N=185	High N=151	P-value for linearity*
GAD, n (%)	250 (56)	68 (61)	101 (54)	81 (54)	0.62
Suicidal, n (%)	218 (49)	60 (54)	86 (46)	72 (48)	0.97
Panic disorder, n (%)	111 (25)	26 (23)	46 (25)	39 (26)	0.24
Alcohol abuse or dependence, n (%)	65 (15)	17 (15)	25 (14)	23 (15)	0.93
Social phobia, n (%)	71 (16)	20 (18)	30 (16)	21 (14)	0.83
Hypomania, n (%)	55 (12)	16 (14)	17 (9)	22 (15)	0.57
Posttraumatic stress disorder, n (%)	27 (6)	9 (8)	13 (7)	5 (3)	0.41
Agoraphobia, n (%)	28 (6)	9 (8)	9 (5)	10 (7)	0.84
OCD, n (%)	26 (6)	8 (7)	7 (4)	11 (7)	0.45
Bulimia or anorexia, n (%)	11 (2)	7 (6)	1 (1)	3 (2)	0.68
Psychosis, n (%)	7 (2)	3 (3)	2 (1)	2 (1)	0.69
Number of psychiatric comorbidities, mean (SD)	1.5 (1.3)	1.6 (1.4)	1.4 (1.2)	1.4 (1.2)	0.24
Number, n (%)					
0	102 (23)	23 (21)	44 (24)	35 (23)	
1	169 (38)	37 (33)	77 (42)	55 (36)	
2	99 (22)	28 (25)	38 (21)	33 (22)	
≥3	77 (17)	23 (21)	26 (14)	28 (19)	

*Adjusted for gender, age, BMI, BDI, and antidepressant use
BDI Beck depression inventory, BMI body mass index, GAD generalized anxiety disorder, OCD obsessive-compulsive disorder

5.2.2. Leisure-time physical activity and somatic comorbidities

For the somatic disorders, the study results revealed that the proportion of subjects with CVD (p=0.036) and obesity (p=0.006) decreased linearly across increasing LTPA categories. A higher level of LTPA was also linearly associated with lower BMI (p=0.005), lower triglyceride (p=0.025), and higher HDL (p=0.002) values. Also, a higher level of LTPA was linearly associated with decreased waist circumference among women (p=0.002), but not men (p=0.22). More details are given in Studies II and II.

5.3 Leisure-time physical activity and health care utilization

Participants' five-year health care records were examined to determine the number of visits to primary and specialized health care units. The study results revealed that the depressed patients' LTPA level was not related to HCU after the results were adjusted for age, gender, years of education, marital status, comorbidities, and household income. During five-year follow-up, participants mostly used physician services, phone calls, and depression nurse services, while lesser use was made of services provided by a psychologist or substance abuse nurse. Participants' HCU is presented in Table 7.

TABLE 7 Health care utilization per person year among depressed patients according to leisure-time physical activity during five-year follow-up.

Variables	Leisure-time physical activity			
	Low N=111 Mean (SD)	Moderate N=185 Mean (SD)	High N=151 Mean (SD)	P-value for linearity*
Physician	3.57 (4.16)	3.21 (3.15)	3.70 (3.29)	0.94
Psychiatrist	0.48 (0.73)	0.38 (0.90)	0.32 (0.71)	0.37
Psychologist	0.26 (0.79)	0.41 (1.90)	0.53 (2.13)	0.14
Depression nurse	2.18 (2.12)	2.07 (2.54)	1.92 (1.95)	0.32
Substance abuse nurse	0.41 (2.18)	0.77 (4.52)	0.29 (2.25)	0.71
Other professionals	1.82 (2.64)	1.83 (2.31)	2.03 (2.62)	0.73
Hospitalization days	1.07 (4.70)	0.75 (2.03)	1.08 (3.28)	0.88
Phone calls	2.59 (3.16)	2.50 (2.75)	2.60 (3.02)	0.69

*Adjusted for age, gender, years of education, marital status, comorbidities, and household income (median < €30 000).

There was no interaction between LTPA and working status with respect to total health care visits (p=0.63) among the depressed patients, although those who were not working had more total visits (p=0.043) after the results were adjusted for age, gender, years of education, marital status, comorbidities, and household income (Figure 3).

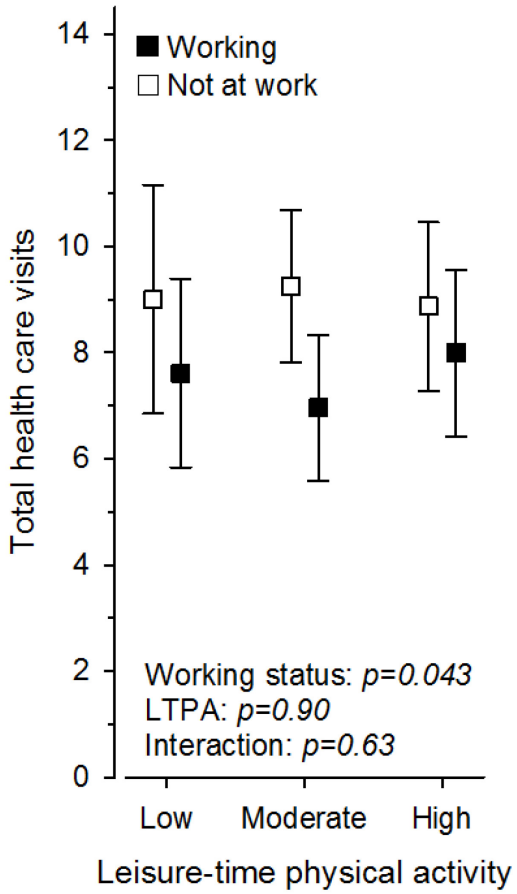

FIGURE 3 Total health care visits (physician + psychiatrist + psychologist + depression nurse + substance abuse nurse + other professionals) according to leisure-time physical activity (LTPA) and working status. Adjusted for age, gender, years of education, marital status, comorbidities, and household income (median < €30 000). Means with 95% confidence intervals.

5.4 Leisure-time physical activity, future depressive symptoms and total physical activity

5.4.1 Leisure-time physical activity and future depressive symptoms

Baseline LTPA was not associated with the DS status at the five-year follow-up (Figure 4). The adjusted (for age, gender, years of education, diabetes, and BDI) odds ratio (OR) for future depression was 1.71 (95% CI: 0.61 to 4.79) for participants with moderate LTPA and 1.00 (95% CI: 0.35 to 2.85) for participants with high LTPA, as compared with low LTPA at baseline. Crude OR were 1.2 (95% CI: 0.61 to 2.38) and 0.73 (95% CI: 0.35 to 1.52) for participants with moderate or high LTPA and low LTPA, respectively. Removing the BDI adjustment did not change the result.

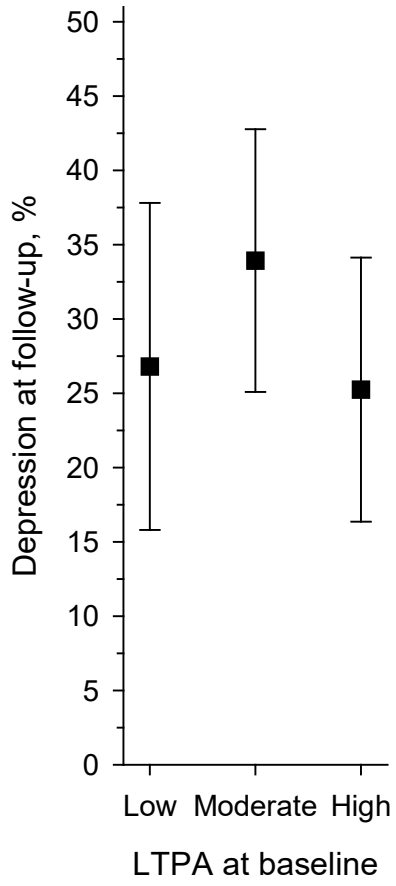

FIGURE 4 Proportion (%) of participants with depressive symptoms (Beck depression inventory (BDI) score ≥10) at follow-up according to baseline leisure-time physical activity (LTPA) level. Adjusted for baseline age, gender, years of education, diabetes, and BDI (with 95% confidence intervals).

5.4.2 Leisure-time physical activity and future physical activity

When investigating LTPA's impact on future PA, the study results showed that higher baseline LTPA levels were associated with higher PA in the future. Those participants with higher LTPA levels had more metabolic equivalent hours (METh) of PA per week at follow-up than those with lower baseline LTPA levels (β=0.15 [95% CI: 0.03 to 0.27], p for linearity =0.021) (Figure 5a) and this association did not differ for different follow-up DS status (Figure 5b). The adjusted correlation (for age, gender, years of education, and diabetes) between baseline and follow-up LTPA did differ according to follow-up DS status: for participants with DS, it was 0.52 (95% CI: 0.34 to 0.71) and for participants without DS it was 0.32 (95% CI: 0.18 to 0.46), respectively.

At the follow-up, among the participants without DS, 34% had low, 30% had moderate, and 36% had high PA levels (expressed as IPAQ grade). Among those participants with DS, 37% had low, 32% had moderate, and 32% had a high PA classification.

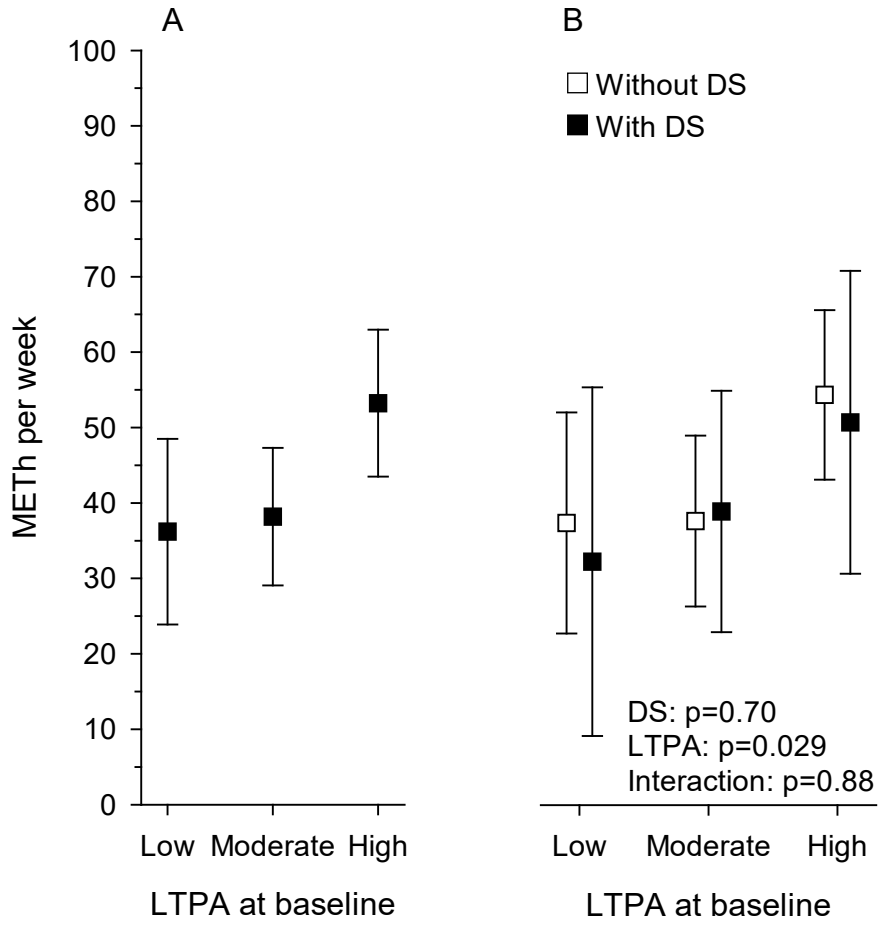

FIGURE 5 (a) Participant (all) physical activity expressed as metabolic equivalent hours (METh) per week at follow-up according to baseline leisure-time physical activity (LTPA) level. Adjusted for baseline age, gender, years of education, diabetes, and Beck depression inventory score. (b) Participant (separate with and without depressive symptoms (DS)) physical activity expressed as METh per week at follow-up according to baseline LTPA level. Adjusted for baseline age, gender, years of education, and diabetes. Means with 95% confidence intervals.

5.5 Physical activity and home presenteeism

Participants' PA and its relation to coping with everyday home chores (home presenteeism) were assessed. The results showed that depressed participants without clinical depression were more physically active than those with depression diagnosis. The IPAQ scores were higher among participants without depression (mean 43.8, SD 44.8) than among those with depression (mean 35.4, SD 44.1) which indicate lower PA among those with depression (p=0.046). Among participants without depression 28% of subjects had low, 35% moderate, and 37% high IPAQ grades; participants with depression had 42%, 30%, and 28% respectively. In the whole study population, PA level was linearly related to home presenteeism (p for linearity <0.001). The mean home presenteeism scores

by PA level were 37.7 (SD 32.7) in low PA, 21.4 (SD 25.6) in moderate PA, and 15.8 (SD 23.4) in high PA.

Higher PA levels were related to lower home presenteeism score among both those without depression ($p<0.001$) and with depression ($p=0.021$) after adjusting the results for age, gender, marital, and working status, years of education, smoking, BMI and comorbidities (Figure 6). Home presenteeism scores were higher among participants with depression than among those without depression at all PA levels ($p<0.001$). However, there was no interaction between IPAQ grade and depression status with respect to home presenteeism ($p=0.47$).

Overall, the mean home presenteeism was lower among those without depression (18.8, SD 25.2) than among those with a depression diagnosis (51.5, SD 29.3) ($p=0.002$).

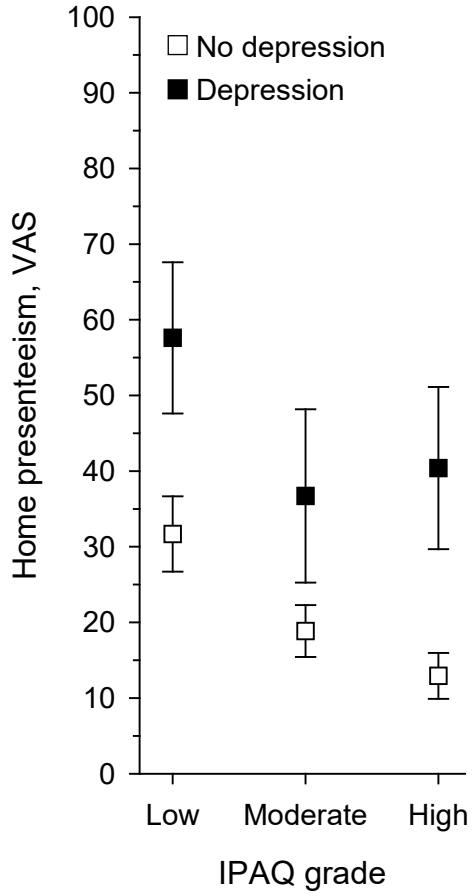

FIGURE 6 Mean home presenteeism (with 95% confidence intervals) according to physical activity level (International Physical Activity Questionnaire (IPAQ) grade) and depression status (depression vs. no depression). Adjusted for age, gender, marital and working status, years of education, smoking, body mass index, and comorbidities.

BDI scores correlated with predicted home presenteeism (PHP) (r=0.60, 95% Cl: 0.56 to 0.65, adjusted for age, gender, marital and working status, years of education, smoking, BMI, and comorbidities). The higher the BDI score was, the higher the PHP was in all PA levels (Figure 7). Also, higher the PA level was, the lower the mean PHP score was, respectively (Figure 7).

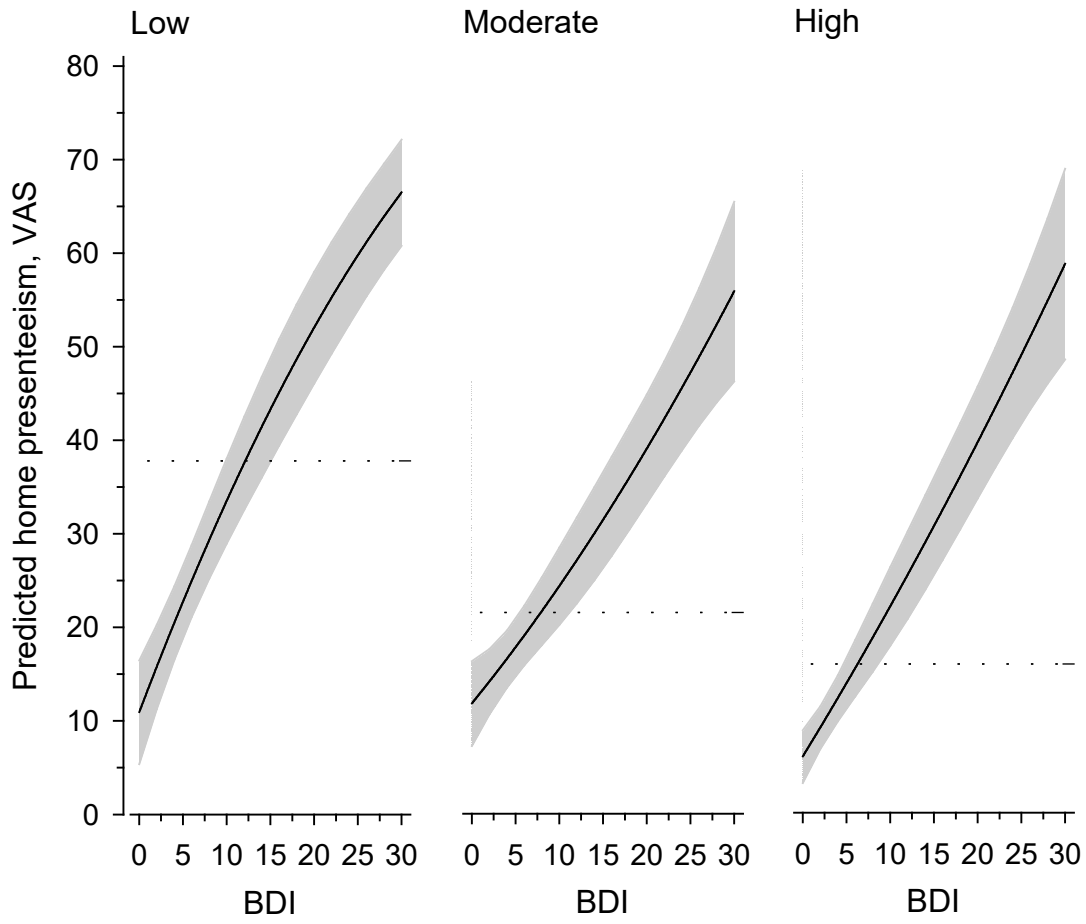

FIGURE 7 Home presenteeism as a function of the Beck depression inventory (BDI) score according to physical activity levels (low, moderate, high). The curves were derived from 4-knot restricted cubic spline regression models. The models were adjusted for age, gender, marital and working status, years of education, smoking, body mass index, and comorbidities. The gray area represents 95% confidence intervals.

6 DISCUSSION

This population-based study of a sample of adult depressed patients in Finland showed that LTPA level was not associated with number of psychiatric comorbidities, subsequent HCU, or future onset of depression. Instead the study results showed that higher PA levels were associated with lower CVD, obesity, DS and better blood lipid levels, as well as higher future PA and better coping with home chores.

6.1 Leisure-time physical activity and its influence on psychiatric and somatic comorbidities among depressed patients

According to the study results, among adult depressed patients in the Finnish population LTPA is not related to psychiatric comorbidities, although those with higher LTPA levels appear to have fewer DS. Indeed, the participants with higher LTPA had lower BMI, incidence of CVD, and obesity, and better blood lipid levels.

As PA has a positive impact on mental health in general, it would have been expected to influence psychiatric comorbidities. We know that depression is often accompanied by multiple psychiatric comorbidities and particularly GAD (Kessler et al., 2003). Also in this study, the most common psychiatric comorbidity was GAD, affecting 56% of participants.

There are several potential reasons why LTPA showed no association with psychiatric comorbidities. In their meta-analysis Bartley et al. (2013) found that current evidence does not support aerobic exercise to be superior to other treatments for anxiety disorders. So, while PA is efficacious in reducing depression, it might have lesser impact on situations when depression is accompanied with anxiety. Also, while PA is generally useful for mental health, there is evidence that more exercise is not always better and that the optimal amount might lie between 30 and 60 minutes per day three times a week (Chekroud et al., 2018). Depression can itself reduce PA (Da Silva et al., 2012;

Sieverdes et al., 2012) and as neurotic disorders might force one to move more, this could diminish these effects. This impact of neurotic disorders may have affected this study, but it was not possible to identify those who exercise more. These are some possible reasons why LTPA seems not to have a positive effect on psychiatric comorbidities in this study.

Neurobiological changes which are related to depression may play a role. For example, PA could work as a "scaffolding" factor in hypothalamic-pituitary-adrenal-axis homeostasis, neurotransmitters, neurogenesis, and inflammatory markers supporting amelioration processes (Archer et al., 2015). Further, one can speculate that neurotic disorders might purely associate more with mind rather than body. This could partly explain why PA's positive health effects more clearly associate with depression itself, but not depression with additional psychiatric disorders. PA can reduce DS, but not necessarily psychiatric comorbidities.

The study findings that LTPA has positive effects on health-related factors such as DS and CVD confirm and are in line with earlier study findings (Barengo et al., 2017; Korniloff et al., 2010). People with severe mental illness and low LTPA levels have an increased risk of CVD and mortality (Vancampfort et al., 2017). In the light of the facts that depression itself forms a risk factor for many of these somatic diseases such as obesity, diabetes, and CVD (Penninx et al., 2013), and with other psychiatric disorders could dramatically increase pain sensation, lower individuals' quality of life (Bair et al., 2008), and increase the mortality risk (Walker et al., 2015), this study finding, and connection is significant.

Though LTPA does not necessarily affect the quantity or quality of additional psychiatric comorbidities – at least this connection is not clear – it surely has a positive connection to other somatic comorbidities and/or the health-related risk factors accompanying depression. The study findings underline the importance of overall health promotion and health care in which PA potentially plays a crucial role.

6.2 Leisure-time physical activity and its influence on health care utilization among depressed patients

This study found that LTPA level is not related with subsequent HCU among depressed patients, although it found a positive association between higher levels of LTPA and many health-related-factors such as obesity, blood lipid levels, and depression severity. The health care resources that depressed patients use most often are physician services. Therefore, it seems that the positive effects of PA do not directly transfer to HCU among depressed individuals, at least in the short term.

This result is somewhat unexpected and contrasts with some previous findings summarized in Tables 1 to 3. Earlier studies found that even though only a minority of depressed people seek and receive adequate help from health care

institutions, depression generally increases HCU (see Table 2). Further studies have suggested that while increased PA can confer from depression and reduce DS (see Table 1), it may also reduce health care visits among population (see Table 3). The reason for this disharmony may be the multidimensional structure of health and health behavior, of which PA is only one part.

There are some plausible explanations for this discrepancy between the present and earlier study findings. The influence of PA on HCU may vary depending on gender and on how individuals perceive their own health. For example, people who perceive their health as poor are three times more likely to use health care services than people who perceive it as good (Rocca et al., 2015). This could attenuate the effect of PA on HCU, and it is reasonable to expect this to be the case among depressed people. Gender also has an effect: women with higher LTPA levels visit health care service more often than less active women, but this association was not found among men (Spika & Breyer, 2020). Also, physically active individuals have shown to utilize more preventive health care services and less secondary and tertiary health services than physically inactive individuals (Kang & Xiang, 2017). Depressed people seek and receive help from health care poorly (Byatt et al., 2016; Kim et al., 2015; Kleinberg et al., 2013) and depression itself can reduce one's capability for self-care, making one more likely to neglect health care visits and to be hospitalized, respectively (Souza et al., 2015). The reverse is also the case: physically active lifestyle and higher levels of LTPA were related to better self-care capacity and psychological well-being, such as sense of coherence and feelings of social integration (Hassmén et al., 2000). Further, a stronger sense of coherence is found to be associated with better capability to cope with everyday tasks (Portegijs et al., 2014). Thus, physically active individuals are likely feeling more self-confident and could be more active in self-care than physically inactive ones. This again may lead to better and more efficacious use of health care services. These previous findings may explain, at least partly, the similar frequency of HCU among depressed patients in our study regardless of LTPA level.

Of the contacts with different professionals, depressed patients most often visited a physician, then made phone calls to a health professional, and thirdly used the services of a depression nurse. This is a line with previous studies which have demonstrated that depressed patients prefer their family doctor or physicians in primary care and visit them more often than, e.g., a psychiatrist (Kleinberg et al., 2013; Lo et al., 2013). This finding is important for knowledge management in health care. Gathering data and information from past and current HCU improves planning, managing, organizing, and targeting health care resources more efficaciously for depressed individuals in the future.

The study finding that depressed patients who are working use public health care services less than those who are not working can be, at least partly explained by the use of occupational health services among working participants. This factor was not possible to assess in this thesis. Finnish workplaces are compelled by law to arrange occupational health services. At its narrowest these services include only preventive measures to support working capacity but,

depending on employer will and contracts, they can include a variety of medical care treatments. When available, employees can choose to use occupational health services instead of public primary health care services.

It is also important to note that as LTPA was positively associated with health-related factors such as lower BMI, obesity, and blood cholesterol levels, this association could reduce HCU by depressed individuals, since depression alongside obesity was found to increase HCU and health care related costs respectively (Penninx et al., 2017).

The study finding that there is no association between LTPA and sociodemographic factors such as working status, marital status, years of education or health habits (smoking or alcohol use) among participants diagnosed with depression can be viewed in the light of some earlier research. LTPA can positively impact on DS independently of sociodemographic characteristics such as age, gender, education, family, social status, living environment (Marques et al., 2019); thus, LTPA can benefit everyone with depression or DS, regardless of social background.

6.3 Leisure-time physical activity as a predictor for future depressive symptoms and total physical activity among depressed patients

There is quite strong evidence in the literature that PA can be an efficacious element for reducing and treating, preventing, and protecting against depression (Hallgren et al., 2019; Kvam et al., 2016; Schuch et al., 2018). There is also some evidence that childhood PA may reduce depression risk in adulthood (Jacka et al., 2011) and promoting lifetime LTPA could reduce DS in older age (Korniloff et al., 2012).

This protective effect could have been expected to show up in this study. However, baseline LTPA levels did not predict future improvement in DS among depressed patients in the findings. To some extent, this is in line with earlier study findings, at least among older participants. Wassink-Vossen et al. (2018) demonstrated in their two-year follow-up study that in younger adults, PA predicted future remission of depressive disorder, but not in older adults. Also, Kaseva et al. (2016) have demonstrated that earlier PA does not necessarily contribute to progression of depression more than current adulthood PA. Further, a recent systematic review of meta-analyses of randomized controlled trials examined the effect of exercise interventions on the onset of depression or DS in the general population (Hu et al., 2020). The review suggested that while exercise interventions seem to have a beneficial effect on DS in a wide age range in the general population and low-intensity exercise could be as effective as high-intensity exercise, there is no evidence for the impact of exercise on the onset of depression (Hu et al., 2020).

While PA can be efficacious method against depression, it might not be suitable for everyone. While some individuals with depression or DS may benefit less from other treatments and medications, others may benefit less from PA due to different psychological, biological, clinical and/or social moderators (Schuch & Stubbs, 2019). Social support from friends, family, and health professionals, as well as autonomous motivation may play a key role in PA and exercise adherence (Schuch & Stubbs, 2019). It is also important to note that depression fluctuates, which means that the severity of symptoms may vary over time. In turn, this may diminish the positive effect of PA over time.

Baseline LTPA can predict future PA. This is consistent with the finding that PA level stays rather stable and rarely changes much over time (Wassink-Vossen et al., 2018). A depressed person's PA level may reflect that person's traits rather than their state of depression (Wassink-Vossen et al., 2018). Given the longitudinal and reciprocal relationship between low PA and severity of depression and anxiety symptoms and greater odds for chronicity (Hiles et al., 2017), this is an important finding. Once a physically active way of life is achieved, it is more likely to be maintained (Wassink-Vossen et al., 2018).

In this light, it is important that health professionals endorse lifelong PA, and promote it during patient visits alongside other health care measures, to create better odds for protection against depression in the future.

6.4 Physical activity and predicted home presenteeism among depressed patients

In the present results, regardless of clinically confirmed depression, physically active people with depression seemed to cope better in their daily home chores than those who were less active. PA was inversely related to predicted home presenteeism (PHP) as those participants with high PA experienced less discomfort and difficulties managing their necessary household chores than participants with lower PA. Also, depression diagnosis and severity of symptoms predicted greater difficulties in coping with chores at home.

This study is one of the first to illuminate the connections between PA, depression, and presenteeism at home. The concept of presenteeism itself is still ambiguous (Lohaus & Habermann, 2019) and its aspects include productivity losses, some health related and some not (Johns, 2010); the term was originally used to describe being present at work, but not fully functional capability or capacity. The terms household presenteeism (Soliman et al., 2017) or presenteeism at home (Kumar et al., 2003), which have been used to describe the difficulties to do home chores due to illnesses, are more rarely used or studied.

Depression can cause vast productivity losses at work, as numerous studies have shown (Allen et al., 2018; Evans-Lacko & Knapp, 2016; Lépine & Briley, 2011; Lohaus & Habermann, 2019) and there is some evidence that PA can reduce the costs which presenteeism might cause (Justesen et al., 2017; Walker et al., 2017b).

This thesis shows that the same can apply to a home environment. Physically active participants coped better with their daily home activities than their physically inactive counterparts, despite the impact of depression. PA can affect an individual's mental well-being by increasing sense of coherence and social integration (Hassmén et al., 2000), which are related to better coping with common daily tasks (Portegijs et al., 2014). Thus, we can assume that physically active individuals may feel more self-confident, and this could mean better self-care and capability to seek help and protect them from social isolation. All this could make it easier for an individual to manage their daily tasks. Since depressed patients may spend a substantial amount of time at home alone and their social network may have shrunk, they are at potential risk for social isolation, too, which makes this finding even more important.

The study results indicate that, in the same way as PA can reduce health-related presenteeism at work (Justesen et al., 2017; Walker et al., 2017a, 2017b) and endorse employees psychosocial health (Brown et al., 2011), sufficient PA may also play an important role in reducing home presenteeism.

6.5 Methodological considerations

The data used here was drawn from a population-based, cross-sectional, and longitudinal cohort study, the Finnish Depression and Metabolic Syndrome in Adults (FDMSA) and its five-year follow-up, which examines clinical and sociodemograghic factors related to depression and metabolic syndrome in Finnish adults aged 35 and over. The FDMSA study protocol and design has been described in detail elsewhere (Koponen et al., 2015a, 2015b). This data provided an unique opportunity to examine the relationships between PA, HCU, coping at home, psychiatric and somatic morbidity, and depression in the same framework. With the geographically representative catchment area of 274 000 inhabitants in Central Finland the participant sample offers an overview of the Finnish population. Thus, the study results can be considered generalizable to Finnish adult population, but as the lower age limit was 35 years, the generalization of these results to younger persons are questionable. Further, as the sample size was drawn from a single health care district instead of nationwide spread, this could limit the generalizability to some extent.

The main strengths of this study were the use of diagnostic interview, exact counts of HCU visits, and long follow-up period. As BDI with a cut-off score of 10 points was used to assess the severity of DS, the depression diagnosis was confirmed by using the diagnostic structured interview (M.I.N.I.). To estimate participants' HCU, study nurses extracted the exact counts of contacts and their frequencies during the five-year follow-up from the health records. As many recent studies have focused on PA's immediate or short-term effects on depression, this five-year longitudinal study design extended the time perspective. Using IPAQ to assess participants' total PA follow-up point can be considered as another study strength. IPAQ has proven to be a valid and reliable

method, which is widely used and accepted in cross-sectional studies to assess PA (Craig et al., 2003). The unique and novel approach of this study is to explore the associations between PA, depression, and home presenteeism in same setting. Home presenteeism has been rather rarely studied and mentioned in literature before.

The main limitation of this study, alongside the questionable generalizability to younger individuals, is its use of self-reported LTPA. Despite being cost-effective and easy to use in large observational studies, self-administered questionnaires are prone to recall biases, overestimation, and socially desirable effects. Participants may have overestimated, been unsure about, or not clearly remembered their PA. Nevertheless, self-reported LTPA has shown a high correlation with objective measured PA among adults (Aires et al., 2003) and it is widely used in large population-based studies (Aires et al., 2003; Barengo et al., 2004; Borodulin et al., 2008). Despite its known disadvantages, self-rated PA can separate physically inactive from active individuals in a population. Again, the purpose of this study was not to assess the exact frequency or intensity of LTPA, but to broadly categorize participants' everyday PA habits, which was achievable via self-reported LTPA. Also, the single assessment point of LTPA at baseline can be considered to be one weakness as LTPA may have changed during follow-up. The study focused particularly on LTPA and did not account the other forms of PA which could be accumulated throughout the day. Some participants may have active jobs or busy family lives having therefore less time for LTPA and still be active in terms of total PA. This can consider as a limitation.

In this study the women and men are analyzed together not separately. As there could be differences between males and females for DS, this can consider as a limitation. Level of depression also needs some consideration. Individuals with mild symptoms may experience their LTPA differently compared individuals with more severe symptoms. This phenomenon could not be verified in this study. Also, the role of PA intensity in the inter-relationship with depression was not investigated in this study. Whether one category (mild, moderate, vigorous) is more important than other waits therefore for future explorations.

Using a self-administered VAS questionnaire to assess participants' difficulties in home chores due to depression may have some weaknesses also. Although widely used in cross-sectional studies for the patients with motor or cognitive limitations and among older persons, the VAS questionnaire could be difficult to complete (Lazaridou et al., 2018). The VAS questionnaire is prone to spreading, meaning that the respondents may use all areas on the valuation scale, especially when multiple health states are valued on the same scale, and context has an effect, as the level of the other items that are being valued influence the average ratings of the item (Brazier & Ratcliffe, 2017). Endpoint bias may occur, when respondents place their health states further away from the top and bottom of the scale than is suggested by direct comparison of differences (Brazier & Ratcliffe, 2017). Further, the concept of "worst imaginable" may be difficult to

understand and assess: one can never know whether the present feeling or experience is the "worst" (Correll, 2007).

Lastly, to evaluate participants' HCU during follow-up time, data were gathered from the municipal primary care records and secondary care (hospital) records, but it was not possible to gather information from occupational health care records. Participants who were working may choose occupational health services instead of public primary health care.

6.6 Practical implications and future directions

The study findings emphasize the role of PA as feasible method in treating and preventing depression. According to the study results, PA seems to have a positive association with DS and many health-related risk factors. Higher PA levels are associated with lower severity of DS, reduced obesity, and CVD as well as better blood lipid levels. These findings are in line with and corroborate those of previous studies (Barengo et al., 2017; Korniloff et al., 2010).

Nevertheless, the association between PA and subsequent HCU among depressed individuals as well as PA's relation to psychiatric comorbidities alongside depression are not clear. In line with earlier study findings, depressed patients used the following public health care services most physician visits, phone calls, and visits to depression nurses. Contrary to some earlier findings and expectations, however, PA did not decrease overall HCU among depressed individuals. Therefore, it seems that the positive health effects of PA do not transfer directly to subsequent use of health resources. Reasons include other health conditions that may reduce the positive effects of PA in the long term. Keeping in mind the fact that depressed patients seek and receive adequate treatment poorly (Hämäläinen et al., 2008; Kim et al., 2015; Kleinberg et al., 2013), better physical condition may promote better self-care, help and treatment seeking. In this context, the finding that PA did not reduce depressed participants' HCU is not a bad sign. Better and more comprehensive treatment of depression lowers the overall burden on society and individuals. Knowing how depressed patients use health care resources helps health professionals to plan future resources and to implement treatment more cost-effectively.

The lack of association between PA and psychiatric comorbidity is at least partly explained by the complexity of mental illnesses. Depression seldom appears alone (Kessler et al., 2003) and the impact of PA may be reduced by psychiatric comorbidities (Bartley et al., 2013). Also, PA is not necessarily suitable for everyone and more exercise not always better (Chekroud et al., 2018). For the future we need more extensive research to gain better understanding about the relevance of LTPA in depression with psychiatric comorbidities.

While depression is known to cause vast productivity loss at work (Allen et al., 2018; Evans-Lacko & Knapp, 2016; Lépine & Briley, 2011), the study showed that this is also true at home. Participants with clinically diagnosed depression coped less well than those without a depression diagnosis in their daily activities.

While PA improves employees' mental well-being (Brown et al., 2011) and reduces health-related presenteeism at work (Justesen et al., 2017; Walker et al., 2017a, 2017b), the study showed that this is also true at home.

Sufficient PA helps people to cope better with home chores despite depression. This is a novel and important finding as most recent studies of presenteeism, PA, and/or depression focus on work. The finding outlines the importance of being physically active in managing daily activities. Home presenteeism is a term that needs more precise clarification, and more investigations into the connections between PA, depression, and home presenteeism are urgently needed. Hopefully, this study will raise questions and attract interest in exploring this topic further.

PA should be considered as an essential part of health professionals' clinical practice and additional method to treat and prevent depression. PA counseling and exercise guidance should be imbedded more firmly in every health professional's encounter with individuals who have depression. As the positive effects of PA on depression and health-related risk factors are well understood, as is the connection between HCU and both PA and depression separately, more studies are needed to explore the connections between PA, depression, and HCU together. The effect of PA on both psychiatric comorbidities and home presenteeism among depressed individuals should be a topic for future research.

7 MAIN FINDINGS AND CONCLUSIONS

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

1. LTPA level was not associated with psychiatric comorbidities among depressed patients although physically active depressed patients had fewer depressive symptoms. Higher levels of PA were associated with lower levels of CVD and obesity among depressed patients.
2. LTPA level did not predict future HCU among depressed patients. Although higher levels of LTPA were positively associated with health-related factors such as BMI, DS, and blood lipid levels, it seems that these health benefits of PA do not transfer directly to HCU. Of the health services depressed patients most often used the services of physicians.
3. Baseline LTPA did not predict the future improvement of depression, but it predicted the future total PA among depressed patients.
4. Higher PA levels were related to lower home presenteeism among depressed patients. Physically active depressed patients coped better with their daily home chores despite DS or clinical depression.

To conclude, these findings indicate that both leisure-time and total physical activity can reduce and mitigate the risk factors associated with mental and somatic morbidity and promote health in depressed patients. However, the role of physical activity in depressed patients' health care utilization is not so clear. Although higher physical activity seems not to decrease or influence on depressed patients' subsequent health care utilization, have any association with number of psychiatric comorbidities, or predict future improvement of depression, other health-related risk factors seem to accumulate in inactive depressed patients. Again, those depressed patients with higher levels of physical activity appeared to have fewer depressive symptoms and cope better with home chores. Thus, the positive effects of physical activity on overall health might be more important for depressed patients' everyday life and total societal burden in the long term than for the direct short-term and narrow impact on

depression. Many other factors influence depression, and promoting physical activity alone is obviously not enough. Therefore, physical activity should be considered and recommended in clinical practices and guidelines as an adjunctive treatment for depression.

YHTEENVETO (SUMMARY IN FINNISH)

Masennus on kolmanneksi yleisin sairaus maailmanlaajuisesti ja sen on ennustettu nousevan yleisimmäksi sairaudeksi vuoteen 2030 mennessä. Masennus on suurin toimintakyvyttömyyttä aiheuttava sairaus maailmassa ja sen kustannukset yhteiskunnalle ovat miljardiluokkaa. Arviolta vain 20–30 % sairastuneista hakee ja saa asianmukaista apua. Masennus on yleisempää naisilla kuin miehillä ja se voi kohdata yksilön missä tahansa elämänvaiheessa. Masennus voi rajoittaa huomattavasti yksilön työkykyä ja toimintakykyä jokapäiväisessä elämässä ja se voi myös merkittävästi heikentää ihmisen elämänlaatua. Pahimmillaan masennus voi johtaa kuolemaan. Lieviä masennuksen muotoja voidaan hoitaa hyvin asianmukaisilla hoidoilla, kuten lääkityksellä. Masennus on myös riskitekijä monille somaattisille sairauksille, kuten sydän- ja verisuonitaudeille, diabetekselle, liikalihavuudelle ja dementialle, ja siihen liittyy usein useita muita psykiatrisia oheissairauksia. Masennus on yhteydessä myös terveyspalvelujen käyttöön. Toisaalta masennus voi lisätä terveyspalvelujen käyttöä, ja toisaalta ne, jotka kärsivät esimerkiksi vakavasta masennuksesta, voivat laiminlyödä terveyspalvelukäyntinsä ja tämä voi johtaa sairaalahoitoon. Masennuksen on todettu myös liittyvän työstä poissaoloihin sekä alentuneeseen työkykyisyyteen mutta on vain vähän näyttöä siitä, miten masennus liittyy kykyyn selviytyä kotitöistä. Monista tutkimuksista on näyttöä siitä, että säännöllinen ja riittävä liikunta voi suojata masennukselta ja että yleensä fyysiset aktiiviset käyttävät vähemmän terveydenhuollon palveluja kuin passiiviset. On myös näyttöä siitä, että liikunnan edistäminen voi olla hyödyllistä työ- ja toimintakyvyn ylläpysymisen kannalta. Liikunta, masennus, psykiatriset ja somaattiset liitännäissairaudet, terveydenhuollon käyttö sekä päivittäisistä askareista selviytyminen liittyvät toisiinsa muodostaen monitahoisia ja moniulotteisia tasoja ja yhteyksiä. Koska monissa viimeaikaisissa tutkimuksissa on näitä yhteyksiä tutkittu vain kapealaisesti, onkin tarpeellista tutkia liikuntaa ja masennusta yhdessä terveyspalvelujen käytön, somaattisten ja psykiatristen oheissairauksien sekä kotona selviytymisen kanssa.

Tässä väitöskirjatutkimuksessa tutkittiin fyysisen aktiivisuuden, masennuksen, psykiatrisen ja somaattisen sairastavuuden, terveydenhuollon käytön sekä kotona selviytymisen välisiä yhteyksiä aikuisilla masennuspotilailla. Tutkimusaineisto on osa Masennus- ja metabolinen oireyhtymä Suomessa -tutkimusta, joka toteutettiin Keski-Suomen sairaanhoitopiirin alueella 2008–2016. Tutkimusjoukko koostui aikuisista (≥ 35 vuotiaista) masennusoireisista potilaista, jotka saivat Beckin masennusoirekyselystä (BDI) 10 pistettä tai yli. Tutkittavien masennusdiagnoosi varmennenttin strukturoidulla kyselylomakkelle (M.I.N.I). 760 tutkitusta 447 osallistujaa sai masennusdiagnoosin lähtötilanteessa ja näistä 256 osallistui seurantatutkimukseen viiden vuoden kuluttua. Kaikki osallistujat täyttivät vakiomuotoisen kyselylomakkeen, joka sisälsi kysymyksiä osallistujien sosioekonomisesta taustasta, terveyteen, sairastuvuuteen, masennusoireisiin ja liikunta-aktiivisuuteen liittyvistä tekijöistä. Vapaa-ajan liikunta-aktiivisuutta arvioitiin kysymyksillä, jotka oli luokiteltu kolmeen tasoon (alhainen, kohtalainen ja korkea) ja lisäksi liikunnan kokonaismäärää kansainvälisen liikuntakyselyn

(IPAQ) lyhyen version avulla. Kaikki osallistujat osallistuivat myös terveystarkastukseen lähtötilanteessa. Terveytarkastuksessa tutkittavilta mitattiin pituus, paino, vyötärönympärys ja verenpaine sekä otettiin sokeri- ja rasva-aineenvaihduntaa kuvaavia laboratoriokokeita. Tiedot terveyspalvelujen käytöstä tutkimushoitajat keräsivät osallistujien terveystiedoista.

Tutkimustulokset osoittivat, että vapaa-ajan liikunta-aktiivisuus ei ollut yhteydessä psyykkisiin liitännäissairauksiin tai terveyspalvelujen käyttöön masennuspotilailla. Sen sijaan liikunta-aktivisuus oli yhteydessä somaattiseen sairastavuuteen ja masennuoireisiin siten, että fyysisesti aktiivisilla masennuspotilailla oli vähemmän sydänsairauksia, lihavuutta sekä lievempiä ja vähemmän masennusoireita. Tutkimustulokset osoittivat lisäksi, että lähtötilanteen korkeampi liikunta-aktiivisuus ei ollut yhteydessä myöhäisempään masennuksen esiintyvyyteen, mutta oli yhteydessä myöhäisempään kokonaisliikunta-aktiivisuuteen. Lähtötilanteen korkeampi vapaa-ajan liikunta-aktiivisuus ennusti korkeampaa liikunta-aktiivisuutta myös tulevaisuudessa. Niinikään korkeampi liikunta-aktiivisuus oli tutkimustulosten mukaan yhteydessä parempaan kotona selviytymiseen masennuoireisilla riippumatta siitä, oliko heillä masennusdiagnoosi tai ei.

Tämä laaja väestöpohjainen poikkileikkaus- ja pitkittäiskohorttitutkimus osoitti, että liikunta-aktiivisuudella voidaan vähentää ja lieventää masennuspotilaiden psyykkiseen ja somaattiseen sairastavuuteen liittyviä riskitekijöitä. Sen sijaan liikunta-aktiivisuuden yhteys terveyspalvelujen käyttöön on epäselvä. Vaikka korkeampi liikunta-aktiivisuus ei näytä vähentävän tai vaikuttavan terveyspalvelujen käyttöön tai psyykkisiin liitännäissairauksiin tai ennustavan myöhempää paranemista masennuksesta, voivat liikunta-aktiivisuuden myönteiset terveysvaikutukset pitkällä aikavälillä olla lyhytaikaisempia tärkeämpiä elämänlaadun ja myös kustannusten valossa. On myös selvää, että monet muut tekijät vaikuttavat masennuksen taustalla ja että pelkästään liikunta-aktiivisuuden edistäminen ei riitä. Siksi liikunta-aktiivisuuden merkitys masennuksen ennaltaehkäisyssä ja hoidossa tulee tiedostaa ja liikuntaa tulisikin suositella kliinisissä käytännöissä ja potilaskohtaamisissa sekä -ohjeissa yhdessä muiden masennushoitojen kanssa.

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ORIGINAL PAPERS

I

DOES LEVEL OF LEISURE TIME PHYSICAL ACTIVITY, IN A SAMPLE OF PATIENTS WITH DEPRESSION, PREDICT HEALTH CARE UTILIZATION OVER A SUBSEQUENT 5-YEAR PERIOD? FINDINGS FROM A FINNISH COHORT STUDY

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Does level of leisure time physical activity, in a sample of patients with depression, predict health care utilization over a subsequent 5-year period? Findings from a Finnish cohort study

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ABSTRACT

Objectives: The main aim of this study was to investigate the association between leisure time physical activity (LTPA) and health care utilization (HCU) and furthermore, socio-demographic and clinical factors according to LTPA level among depressed patients based on data drawn from the Finnish Depression and Metabolic Syndrome in Adults (FDMSA) -study (2009–2016).

Methods: 447 depressed patients aged 35–65 from municipalities within the Central Finland Hospital District participated in this study. Depressive symptoms (DS) were determined with the Beck Depression Inventory ($\geq$10 points) and the psychiatric diagnosis confirmed with a diagnostic interview (M.I.N.I.). Severity of depression was evaluated using the Montgomery-Åsberg Depression Rating Scale (MADRS). LTPA was assessed using a self-reported questionnaire. Use of health services was counted from participant's health care records.

Results: Of the 447 depressed patients, 25% reported their LTPA level as low, 41% as moderate and 34% as high. Among depressed patients, higher levels of LTPA were linearly associated with lower BDI ($p < 0.001$), MADRS ($p = 0.002$), BMI ($p = 0.005$), triglyceride ($p = 0.025$) and higher HDL ($p = 0.002$) values. LTPA level was not related to health care utilization among depressed patients. The health services most used were physician services.

Conclusions: According to this study, the level of LTPA in baseline does not predict the future use of health care services among depressed patients in Finnish adult population. Although higher levels of LTPA are positively associated with many health-related factors, promoting PA alone is not enough when aiming to manage and modify HCU among depressed patients.

1. Introduction

Depression is the leading cause of disability worldwide (Whiteford et al., 2013) and it has been estimated that it will be the most common illness globally by the year 2030 (Mathers & Loncar, 2006). People suffering from mental illnesses such as depression have over a two-fold higher mortality risk and ten years shorter life expectancy than the general population (Walker, McGee, & Druss, 2015). Depressive symptoms can also predispose to metabolic syndrome (Vanhala, Jokelainen, Keinänen-Kiukaanniemi, Kumpusalo, & Koponen, 2009). Although effective treatments are available, only a minority of people suffering from depression seek and receive appropriate treatment (Hämäläinen, Isometsä, Sihvo, Pirkola, & Kiviruusu, 2008; Kim, Cho, Park, & Park, 2015; Kleinberg, Aluoja, & Vasar, 2013). There are many

Abbreviations: BDI (−21), Beck Depression Inventory; BMI, Body Mass Index; DS, depressive symptoms; FDMSA-study, Finnish Depression and Metabolic Syndrome in Adults-study; GDP, Gross Domestic Product; HCU, heath care utilization; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LTPA, leisure-time physical activity; MADRS, Montgomery-Åsberg Depression Rating Scale; M.I.N.I., Mini-International Neuropsychiatric Interview; mmHg, millimeter of mercury; mmol/l, millimoles per liter; OGTT, Oral Glucose Tolerance Test; PA, physical activity; SD, standard deviation; SPI, Social Progress Index

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reasons for this, including lack of resources, lack of trained health care providers, social stigma associated with mental disorders and inaccurate assessment (World Health Organization, 2015).

Depression is also associated with increased health care utilization. According to Kleinberg et al. (2013), depressed people use health care services from 1.5 to 3 times more often than the non-depressed. Depression has been shown to increase the risk of HCU among people with unhealthy BMI (Atlantis, Goldney, Eckert, Taylor, & Phillips, 2012) and among patients with diabetes (Chan, Lin, Chau, & Chang, 2012), cancer (Lo et al., 2013) and cardiovascular diseases (Chamberlain et al., 2011). Both hereditary and environmental factors are thought to play a role in depression (Sullivan, Neale, & Kendler, 2014). In addition, an unhealthy life style characterized, for example, by physical inactivity (Korniloff, 2013), long-lasting dissatisfaction with life (Rissanen, 2016) and many somatic diseases have been found to be associated with increased risk of depression (Ali, Stone, Peters, Davies, & Khunti, 2006; Korniloff et al., 2010, 2012).

Many recent studies have demostrated that physically active compared to physically in-active people utilize health care services less (Fonseca, Nobre, Pronk, & Santos, 2010; Lordan & Pakrashi, 2014; Vuori, Taimela, & Kujala, 2010) and have lower lifetime net costs of health care and social services (Vuori et al., 2010). Recent studies have also demostrated the usefulness of physical activity and exercise in the treatment and prevention of depression (Gallegos-Carrillo et al., 2013; Korniloff et al., 2012; Sieverdes et al., 2012) and that the positive effects of physical exercise can equal those of other methods of treatment or medication (Cooney, Dwan, & Mead, 2014). Souza, Fillenbaum, and Blay (2015) reported an association of physical inactivity with both higher risk of depression and higher risk of hospitalization, and also with decreased outpatient visits, among older people.

In sum, physical activity (PA) is a cheap and effective way to treat and prevent many diseases and it decreases the use of health care services. However, studies on whether increased physical activity reduces the use of health care services, and therefore health care costs, among depressed patients are lacking. As the primary aim of FDMSA Study was to investigate association between depression and metabolic syndrome, we also have studied relations between leisure time physical activity and depression. Thus, the main aim of this preset study was to investigate the association between HCU and leisure time physical activity (LTPA) and furthermore, socio-demographic and clinical factors, among depressed patients. The study was an exploration of data collected in FDMSA -study.

2. Materials and methods

2.1. Participants

The data used in this study were drawn from the Finnish Depression and Metabolic Syndrome in Adults (FDMSA) study and its 5-year follow-up (2012–2016). The FDMSA -study protocol/design has been reported in some earlier studies (Auvinen et al., 2018; Koponen, Kautiainen, Leppanen, Mantyselka, & Vanhala, 2015a; Koponen, Kautiainen, Leppänen, Mäntyselkä, & Vanhala, 2015b; Korniloff et al., 2017). The study was conducted in municipalities within the Central Finland Hospital District in Finland with catchment area of 274 000 inhabitants. The study population was enrolled from patients (n = 730) with depressive symptoms who scored ≥10 in the 21- item Beck Depression Inventory (BDI-21), were over 35 years of age and were either self-referred or had been referred by general practitioners to depression nurse case managers, who conducted a diagnostic structured interview (M.I.N.I.). Of this study population, 447 received a diagnosis of depression. The study protocol was approved by the Ethics Committee of the Central Finland Hospital District prior to the commencement of the study. All participants signed an informed written consent.

2.2. Data sources

At baseline, all the participants completed a standard self-administered questionnaire that contained questions about their health and health behavior. The questionnaire also contained questions on participants' socio-economic background such as marital status, years of education, household income, employment status, comorbid diseases, smoking habits and LTPA.

LTPA was assessed with the question:" How often do you do physical activity at least for half an hour so that you are out of breath and sweating?" Answers were classified as follows: low (twice per month or less), moderate (once or twice per week), or high (three times per week or more). Self-reported LTPA has shown a high correlation with physical fitness as measured by maximal oxygen uptake (Aires, Selmer, & Thelle, 2003).

Depressive symptoms were captured using the Beck Depression Inventory (BDI) (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961) with a cut-off point of ≥10 (Koponen, Jokelainen, Keinanen-Kiukaanniemi, Kumpusalo, & Vanhala, 2008; Korniloff K et al., 2010; Väänänen, Buunk, Kivimäki, Vahtera, & Koskenvuo, 2008). The psychiatric diagnosis was confirmed with a diagnostic Mini-International Neuropsychiatric Interview (M.I.N.I.) (Sheehan et al., 1998). Severity of depression was evaluated using the Montgomery-Åsberg Depression Rating Scale (MADRS) (Montgomery & Åsberg, 1979).

Fasting blood samples were drawn after 12 h of fasting for glucose and lipid determination (Koponen, Kautiainen, Leppänen, Mäntyselkä, & Vanhala, 2015a). Glucose tolerance was tested using an oral glucose tolerance test (OGTT). The physical examination during the study visit also included measurements of the participants' weight, height, waist circumference and blood pressure. Weight and height were measured with the participant wearing light clothing and was accurate to the nearest 0.5 cm and 0.1 kg, respectively. Waist circumference was measured to the nearest 1.0 cm at the midpoint between the lateral iliac crest and the lowest rib. Blood pressure was measured twice by trained nurses after a 15-min rest time with a mercury sphygmomanometer with the participant in the sitting position.

Data on health care utilization were collected by two research nurses from participants' health care records over a 5-year period and calculated as person years. The frequency of visits and phone call contacts, and days of hospitalization were calculated separately for primary and specialized health care. Health care professionals were categorized as a physician (general, practitioner or specialized physician), psychiatrist, psychologist, depression nurse, substance abuse nurse or other (e.g. social worker, nutritionist).

2.3. Statistical methods

The results were presented as means with standard deviations (SD) or as counts with percentages. Statistical significance for the unadjusted hypothesis of linearity across the LTPA categories were evaluated using the Cochran-Armitage test for trend and analysis of variance with an appropriate contrast. Adjusted hypothesis of linearity (orthogonal polynomial) were evaluated using generalized linear models (e.g. analysis of co-variance and logistic models) with appropriate distribution and link function. Models included age, gender, years of education, marital status, comorbid diseases and household income as covariates. In the case of violation of the assumptions (e.g. non-normality), a bootstrap-type method was used (10 000 replications) to estimate standard errors. The normality of variables was evaluated by the Shapiro-Wilk W test. All analyses were performed using STATA 14.1.

3. Results

At baseline, 25% of the 447 participants with depression reported a low level of LTPA, 41% a moderate level and 34% a high level. A lower level of LTPA was linearly associated with higher BMI (p = 0.005),

Table 1
Depressed patients' socio-demographic and clinical characteristics at baseline.

Variables	Low N = 111	Moderate N = 185	High N = 151	p for linearity
Number of females, n (%)	82 (74)	129 (70)	101 (67)	0.23
Age in years, mean (SD)	49 (9)	52 (10)	51 (10)	0.055
BMI, mean (SD)	28.9 (6.3)	28.4 (6.0)	26.9 (5.2)	0.005
Waist circumference (cm), mean (SD)				
Males	101 (11)	100 (14)	97 (14)	0.22
Females	96 (16)	93 (15)	89 (13)	0.002
Blood pressure (mmHg), mean (SD)				
Systolic	131 (15)	131 (15)	131 (17)	0.91
Diastolic	83 (12)	81 (10)	82 (11)	0.90
Plasma Glucose 0 h (mmol/l), mean (SD)	5.79 (1.15)	6.12 (1.93)	5.66 (0.80)	0.85
Total cholesterol (mmol/l), mean (SD)	5.18 (1.07)	5.05 (0.91)	5.08 (1.11)	0.54
LDL cholesterol (mmol/l), mean (SD)	3.15 (0.96)	3.01 (0.84)	3.03 (1.00)	0.42
HDL cholesterol (mmol/l), mean (SD)	1.48 (0.45)	1.55 (0.46)	1.67 (0.50)	0.002
Triglyceride (mmol/l), mean (SD)	1.50 (0.88)	1.41 (0.98)	1.25 (0.62)	0.025
Smoking, n (%)	47 (42)	49 (26)	46 (30)	0.067
Years of education, mean (SD)	11.0 (2.9)	11.3 (3.0)	10.8 (3.1)	0.57
Living in a relationship, n (%)	68 (61)	103 (56)	95 (63)	0.69
Working status, n (%)				0.29
Employed	55 (50)	84 (45)	63 (42)	
Unemployed	32 (29)	41 (22)	40 (26)	
Student	4 (4)	4 (2)	3 (2)	
Retired	20 (18)	56 (30)	45 (30)	
Household income below median (< 30.000), n (%)	66 (59)	108 (58)	85 (56)	0.60
Comorbidities, mean (SD)	0.56 (0.82)	0.65 (0.94)	0.75 (0.99)	0.076
BDI score, mean (SD)	25.4 (8.6)	23.4 (8.2)	21.9 (7.7)	< 0.001
MADRS score, mean (SD)	23.5 (5.8)	21.5 (6.5)	21.5 (5.3)	0.002

BMI body mass index, LDL low-density lipoprotein, HDL high-density lipoprotein, BDI beck depression inventory, MADRS montgomery-åsberg depression rating scale.

triglyceride (p = 0.025), BDI (p < 0.001) and MADRS (p = 0.002) and lower HDL (p = 0.002) values (Table 1). In turn, a higher level of LTPA was also linearly associated with decreased waist circumference among females (p = 0.002), but not males (p = 0.22).

The regression analysis revealed that LTPA level was not related to health care utilization among the depressed patients after adjusting the results for age, gender, years of education, marital status, comorbid diseases and household income. The health resources mostly used by the participants were physician services, phone calls and depression nurse services. Lesser use was made of psychologist and substance abuse nurse services (Table 2).

In addition, subgroup analyses (working vs. not at work) showed no interaction between LTPA and working status with respect to total health care visits (p = 0.63) among the depressed patients, although those not working had more total visits (p = 0.043) after the results were adjusted for age, gender, years of education, marital status, comorbid diseases and household income (Fig. 1).

4. Discussion

4.1. Main findings and study implications

This study showed that LTPA level was not associated with HCU among the studied sample of depressed individuals. This result is contrary to previous findings. Many recent studies have reported that while increased LTPA is beneficial in the care and prevention of depression (Gallegos-Carrillo et al., 2013; Korniloff et al., 2012; Sieverdes et al., 2012), it can, in general, also reduce HCU (Fonseca et al., 2010; Lordan & Pakrashi, 2014) among population. This discrepancy may be due to the multidimensional structure of health and health behavior in which PA is only one factor.

Depression can reduce a patient's overall capacity for self-care (Souza et al., 2015). It is known that depressed people seek for help poorly and that approximately only one-fifth to one-third of them have adequate treatment (Hämäläinen et al., 2008; Kim et al., 2015; Kleinberg et al., 2013). A physically active lifestyle in turn, is associated with better capacity for self-care (Hassmen, Koivula, & Uutela, 2000). Level of LTPA can affect aspects of psychological well-being such as

Table 2
Health care utilization per person years among depressed patients according to leisure-time physical activity level during the 5-year follow-up (FDMSA follow up 2012–2016).

Variables	Low N = 111 Mean (SD)	Moderate N = 185 Mean (SD)	High N = 151 Mean (SD)	p for linearity
Physician	3.57 (4.16)	3.21 (3.15)	3.70 (3.29)	0.94
Psychiatrist	0.48 (0.73)	0.38 (0.90)	0.32 (0.71)	0.37
Psychologist	0.26 (0.79)	0.41 (1.90)	0.53 (2.13)	0.14
Depression nurse	2.18 (2.12)	2.07 (2.54)	1.92 (1.95)	0.32
Substance abuse nurse	0.41 (2.18)	0.77 (4.52)	0.29 (2.25)	0.71
Other professionals	1.82 (2.64)	1.83 (2.31)	2.03 (2.62)	0.73
Hospitalization days	1.07 (4.70)	0.75 (2.03)	1.08 (3.28)	0.88
Phone calls	2.59 (3.16)	2.50 (2.75)	2.60 (3.02)	0.69

Adjusted for age, gender, years of education, marital status, comorbid diseases and household incomes (med < 30 000).

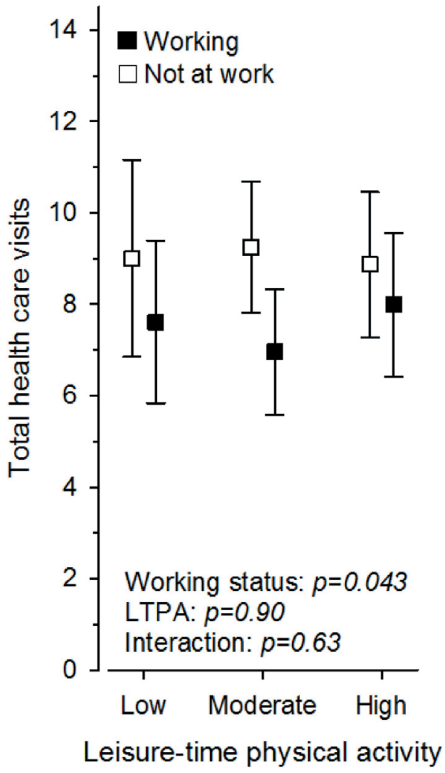

Fig. 1. Total health care visits according to LTPA and working status. Physician + Psychiatrist + Psychologist + Depression nurse + Substance abuse nurse + Other professionals. Adjusted for age, gender, education years, marital status, comorbid diseases and household income (median < 30 000).

sense of coherence and feelings of social integration (Hassmen et al., 2000). In turn, a stronger sense of coherence is related to better coping with common daily activities (Portegijs et al., 2014). Thus, physically active people are likely to feel more self-confident and be more active in self-care in general. This may also lead to more effective use of health care resources (Souza et al., 2015) and, further, be one explanation for our findings of a similar frequency of health care visits regardless of the level of LTPA among depressed patients.

However, this study showed that PA was positively associated with many health-related factors such as obesity, blood fat levels and severity of depression. First, higher levels of LTPA were associated with increased HDL, decreased BMI and triglyceride, and lower waist circumference in women among the depressed participants in this study, as reported earlier (Besson et al., 2009; Sofi et al., 2007). This is important for overall health and lowering risk for metabolic syndrome and other diseases such as heart diseases and diabetes (Grundy et al., 2005). Second, and more importantly, higher levels of PA were also associated with decreased severity of depression among the depressed participants. This suggest that LTPA can be a considerable and useful method to treat and prevent depression, as has also been shown in previous studies (Gallegos-Carrillo et al., 2013; Korniloff et al., 2012; Sieverdes et al., 2012). Cicek et al. (2015) have demonstrated that average BDI scores can be over 4 points lower in participants who engaged in active exercise one hour or more per week (8.93) than in sedentary controls (13.18). However, it is important to remember that association between PA and depression is bidirectional (Sieverdes et al., 2012): physical inactivity can increase the risk for depression and depression can reduce physical activity. The present participants with more severe depression may have been less physically active due to the severity of their depression. Additionally, any effect of LTPA may be washed out by greater effects of other physical health conditions on long-term HCU.

In contrast to some previous studies which have suggested that people with low socioeconomic status are more physically inactive (Laaksonen, Prattala, Helasoja, Uutela, & Lahelma, 2003; Souza et al., 2015) we did not find any association between LTPA level and socioeconomic factors such as marital status, years of education, household income or working status. There may be many reasons for this. For example, in Finland and the other Nordic countries social security and health insurance are in general quite good while socioeconomic differences are relatively narrow compared, for example, with some Anglo-American or Asian countries. When social progress and the distribution of social equity between its citizens is measured using the Social Progress Index (SPI) instead of Gross Domestic Product (GDP), Finland is the highest ranked country in the world while the other Nordic countries are all in the top ten (Porter, Stern, & Green, 2016). In addition, the present participants may be among the minority of depressives who have sought and received help for depression. These two factors may explain the absence of socio-economic differences in LTPA levels.

In this study, the HCU services most used by the present sample of depressed patients were physician services, phone calls and depression nurse services and, to a lesser extent, psychologist and substance abuse nurse services. These findings are in line with those of some previous studies (Kleinberg et al., 2013; Wang et al., 2005), which have demonstrated that depressed patients visited their family doctors or general practitioners more often than, for example, seeking help directly from a psychiatrist. To more effectively manage and organize health care resources to meet future demands, it is vital to know how they are currently used. This would also make it possible to better target suitable and adequate health services for depressive patients.

Subgroup analyses revealed that patients who were not working made more health care visits than those who were working. This difference could be due to utilization by the latter of occupational health care, a factor we were unable to assess. Individuals who have a comprehensive occupational health care service can choose whether to use this instead of primary health care.

Depression is world's leading cause of disability and its societal costs are huge. On the other hand, benefits of PA are well known both in prevention and healing in depression. Although this study showed many positive relationships of PA on health and depression, these benefits did not transfer directly to HCU. Therefore, when aiming to modify and manage the HCU of depressed patients, it is not enough to promote PA alone. Alongside increasing PA, we need deeper knowledge and understanding of both the hereditary and environmental factors as well as personality traits behind illness.

4.2. Study strengths and limitations

The strengths of this study include its geographically representative sample of subjects (catchment area of 274 000 inhabitants) and its long follow-up time with exact counts and frequencies of participants' HCU extracted from health records instead of rough estimates. One strength of this study is also the use of diagnostic interview (M.I.N.I) to confirm depression diagnosis (instead using only BDI). The main limitations are the robustness of self-reported LTPA and the single baseline measurement of the levels of LTPA and depression, as they may have changed during the follow-up. Though, in this study, we didn't try to estimate exact frequency or intensity of each participants PA instead of crude categorization of LTPA lifestyle. Moreover, as already stated, this study does not include visits to occupational health care. However, we were able to conduct the analysis separately for both working and non-working depressives. The relationship between LTPA and HCU in the two subgroups was similar and no interaction was observed between working status and LTPA. Furthermore, the use of a self-reported questionnaire to assess LTPA is vulnerable to overestimation by participants. Nonetheless, as self-reported questionnaire of LTPA used in this study does not tell the exact amount, frequency or intensity of LTPA, the method is widely used in large population-based studies (Aires et al., 2003; Barengo et al., 2004; Borodulin, Laatikainen, Juolevi, & Jousilahti, 2008). Finally, the study population was middle aged and older, and thus the results cannot be generalized to younger persons Also, health care service systems and structures are different in different countries and accessibility to health care services differs and thus, as the study was geographically representative in Finland, caution must be made for generalisability to other countries because of different health care systems and accestability to public health care services.

4.3. Conclusions

According to this study, the level of LTPA in baseline does not predict the future use of health care services among depressed patients in Finnish adult population. Although higher levels of LTPA are positively associated with many health-related factors, these benefits do not transfer directly to HCU. It may be possible that any effect of LTPA is dimished by greater effects of other physical health conditions in long-term.Therefore, promoting PA is not enough when aiming to manage and modify HCU of depressed patients. Deeper understanding behind the illness and also further research are needed to find out how to manage the use and availability of health care services more effectively.

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Conflicts of interest

The authors declare that they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.mhpa.2018.06.007.

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II

LEISURE TIME PHYSICAL ACTIVITY AND ITS RELATION TO PSYCHIATRIC COMORBIDITIES IN DEPRESSION. FINDINGS FROM FINNISH DEPRESSION AND METABOLIC SYNDROME IN ADULTS (FDMSA) STUDY

by

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Short communication

Leisure time physical activity and its relation to psychiatric comorbidities in depression. Findings from Finnish Depression and Metabolic Syndrome in Adults (FDMSA) study

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ABSRACT

Purpose: The study aim was to examine association between leisure time physical activity (LTPA) and psychiatric comorbidities among people with depression.
Methods: Total 447 patients aged 35 years and older suffering from depressive symptoms (DS) and who were confirmed depression positive participated this study. The study was conducted between 2008 and 2011 in municipalities within Central Finland Hospital District. DS were determined with Beck Depression Inventory (BDI-21) with cutoff score ≥10 and psychiatric diagnoses were confirmed by Mini-International Neuropsychiatric Interview (M.I.N.I.). LTPA, other diseases as well as use of antidepressant were captured by self-reported questionnaire. Participants also took part in physical examination. The associations between LTPA and psychiatric comorbidities were analyzed using generalized linear models.
Results: LTPA level was not related to number of psychiatric comorbidities (after adjustment for age, gender, BMI, BDI and use of antidepressant $p = 0.24$) among depressed patients. The higher levels of LTPA were linearly associated with lower cardiovascular diseases ($p = 0.036$) and obesity ($p = 0.006$) as well as fewer DS ($p < 0.001$) among depressed patients.
Limitations: Possibility of LTPA level overestimation and study results generalizability to younger persons.
Conclusions: According to this study, LTPA level is not associated with psychiatric comorbidities among depressed patients in Finnish adult population. However, our results showed that the higher the LTPA level was, the less the participants suffered from depressive symptoms. In addition, higher levels of physical activity were associated with fewer heart diseases and obesity outlining the importance of overall health-care and health promotion although other forms of treatment are also needed.

1. Introduction

Depression is one of the most disability causing illnesses in the world (Whiteford et al., 2013) and its economical and individual burden are huge. Depression is often associated with one or more other psychiatric disorder and together they can impact one's life dramatically. Over 70% of depression diagnosed patients have at least one other psychiatric comorbidity (Kessler et al., 2003). Patient suffering from mental illnesses has over two-fold higher risk of early death compare to people in general and their life expectancy is ten years

Abbreviations: BDI (-21), Beck Depression Inventory; BMI, Body Mass Index; CVD, cardiovascular disease; DM, diabetes mellitus; DS, depressive symptoms; FDMSA-study, Finnish Depression and Metabolic Syndrome in Adults- study; GAD, generalized anxiety disorder; HPA-axis, hypothalamic-pituitary-adrenal -axis; LTPA, leisure-time physical activity; M.I.N.I., Mini-International Neuropsychiatric Interview; OCD, obsessive-compulsive disorder; PA, physical activity; SD, standard deviation; US, United States; vs, versus

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shorter (Walker et al., 2015). Depression together with psychiatric comorbidities are found to increase the sensation of pain and decrease one's performance and quality of life (Bair et al., 2008). Depression is also associated with increased risk of many somatic diseases such as obesity, diabetes and cardiovascular diseases (Penninx et al., 2013).

According to recent knowledge leisure time physical activity (LTPA) is useful for treating and preventing depression. Physical activity reduces depressive symptoms (DS) in people with mental illness (Rosenbaum et al., 2014) and physically active individuals have lower risk for depression in the future compared to in-active ones (Mammen and Faulkner, 2013; Schuch et al., 2018). According to review of Mammen and Faulkner (2013) any physical activity (PA) level, including low levels (e.g., walking <150 min/weeks), may prevent for future depression. Recent large United States (US) nationwide study (Chekroud et al., 2018) has revealed that physical exercised and physically active individuals had nearly 43% fewer poor mental health days than those who not in the past month. The relationship between PA and depression is also bidirectional, increased PA can reduce depressive symptoms as well as depression itself can reduce PA (Sieverdes et al., 2012).

As depression is often associated with multiple psychiatric comorbidities (Kessler et al., 2003), it is still largely unknown whether or how amount of LTPA is related to psychiatric comorbidities among depressive patients. Depression by itself and particularly with additional psychiatric comorbidities is not only individual misery but huge societal burden (Mrazek et al., 2014;Sobocki et al., 2006) and therefore it is sensible to figure out means and factors to resolve or at least reduce these negative effects of illness. Most of the previous studies investigating the relationship between depression and LTPA have not took psychiatric comorbidity into account or psychiatric comorbidities are excluded. Thus, the main aim of this study as a part of Finnish Depression and Metabolic Syndrome Study (FDMSA) is to explore the relationship between LTPA and psychiatric comorbidities among depressive diagnosed patients.

2. Materials and methods

2.1. Participants

The study data were drawn from the Finnish Depression and Metabolic Syndrome in Adults (FDMSA) study which was conducted between 2008 and 2011 in municipalities within Central Finland Hospital District with catchment area of 274 000 inhabitants. The population of this study were enrolled from 35 years of age or older patients ($n = 730$) with depressive symptoms determined with Beck Depression Inventory (BDI-21) with cutoff score ≥10. Participants were self-referred or referred by general practitioners to depression nurse case managers and who's psychiatric diagnoses were confirmed by diagnosis structured interview (M.I.N.I.) conducted by depression nurse case managers. Total 447 patients received a diagnosis of depression. The Ethics Committee of the Central Finland Hospital District approved the study protocol prior to the commencement of the study. All participants signed an informed written consent.

2.2. Data sources

All participants filled out a standard self-administered questionnaire containing questions about previously diagnosed somatic disorders, use of antidepressant, smoking habits, number of alcohol doses per week and leisure time physical activity (LTPA). Data on participants' socioeconomical background such as years of education, marital and employment status were also collected via questionnaire. Participants also took part on physical examination during the study visit. The physical examination included measurements of participants' weight and height during the study visit. Weight and height were measured in light clothing and was accurate to the nearest 0.5 cm and 0.1 kg, respectively. The body mass index (BMI) was defined as person's weigth (body mass) divided by the square of the heigth. Obesity were defined when BMI ≥ 30 (World Health Organization, 2018).

LTPA was assessed by asking:“ How often do you do physical activity at least for half an hour so that you are out of breath and sweating?” Answers were classified into three levels: low (twice per month or less), moderate (once or twice per week), or high (three times per week or more). In previous studies self-assessed LTPA has shown a high correlation with physical fitness as measured by maximal oxygen uptake (Aires et al., 2003).

The severity of depressive symptoms (DS) was captured using the 21-item Beck Depression Inventory (BDI-21) (Beck et al., 1961), which was completed by the participants. The cut-off point was set to ≥ 10 (Koponen et al., 2015). The psychiatric diagnosis and number of other psychiatric comorbidities were confirmed and obtained with a diagnostic Mini-International Neuropsychiatric Interview (M.I.N.I.) (Sheehan et al., 1998) delivered by trained study nurse.

2.3. Statistical methods

The results were presented as means with standard deviations (SD) or as counts with percentages. Statistical significance for the unadjusted analyses of linearity across the LTPA categories were evaluated using the Cochran-Armitage test, Cuzick test and analysis of variance with an appropriate contrast. Adjusted analyses of linearity (orthogonal polynomial) were evaluated using generalized linear models (e.g. analysis of co-variance, regression models and logistic models) with appropriate distribution and link function. Models included age, gender, years of education, marital status, comorbid diseases and household income as covariates. In the case of violation of the assumptions (e.g. non-normality), a bootstrap-type method was used (10 000 replications) to estimate standard errors. The normality of variables was evaluated by the Shapiro–Wilk W test. All analyses were performed using STATA 14.1.

3. Results

Table 1 shows the socio-demographic and clinical characteristics of the participants according to LTPA levels. BMI ($p = 0.005$) and depressive symptoms ($p < 0.001$), and further proportion of subjects with cardiovascular diseases ($p = 0.036$) and obesity ($p = 0.006$) decreased linearly across increasing LTPA categories. Although antidepressant was used by 68% ($n = 305$) of participants, there were no linear association between the LTPA level and use of antidepressant ($p = 0.53$), nor with other clinical or socio-demographic characteristics either (Table 1).

The prevalence of psychiatric comorbidities among all depressed participants ($n = 447$) were as follow: generalized anxiety disorder (GAD) 56%, suicidal 49%, panic disorder 25%, social phobia 16%, alcohol abuse or dependence 15%, hypomania 12%, agoraphobia 6%, posttraumatic stress reaction 6%, obsessive-compulsive disorder (OCD) 6%, bulimia or anorexia 2% and psychosis 2% (Table 2). Only one-fifth (23%) of the participants had no psychiatric comorbidity. More than one third (38%) of the participants had one comorbidity, 22% had two and 17% had at least three psychiatric comorbidities. Participants with one or more psychiatric comorbidities were younger (50 years vs. 53 years) and smoked more often (34% vs. 23%, $p = 0.023$) than those without psychiatric comorbidities. Instead there were no difference in gender, BMI or educational years among participants with or without psychiatric comorbidities.

The statistical analysis revealed that LTPA level was not related to number of psychiatric comorbidities ($p = 0.24$). In addition, there was no significant linear relationship between the prevalence of psychiatric comorbidities and physical active level after adjusting the results for age, gender, BMI, BDI score and use of antidepressant (Table 2).

Table 1
Depressed patients' socio-demographic and clinical characteristics at baseline.

Variables	Total	Leisure time physical activity			*P*-value*
	N = 447	Low *N* = 111	Moderate *N* = 185	High *N* = 151	
Female, n (%)	312 (70)	82 (74)	129 (70)	101 (67)	0.23
Age, years (SD)	51 (10)	49 (9)	52 (10)	51 (10)	0.055
BMI, mean (SD)	28.0 (5.9)	28.9 (6.3)	28.4 (6.0)	26.9 (5.2)	0.005
Obesity, (BMI ≥30), n (%)	143 (32)	43 (39)	65 (35)	35 (23)	0.006
Education years (SD)	11.0 (3.0)	11.0 (2.9)	11.2 (3.1)	10.8 (3.1)	0.50
Married or cohabited, n (%)	266 (60)	68 (61)	103 (56)	95 (66)	0.23
Employment status, n (%)					0.28
Employed	202 (45)	55 (50)	84 (45)	63 (42)	
Unemployed	113 (25)	32 (29)	41 (22)	40 (26)	
Student	11 (2)	4 (4)	4 (2)	3 (2)	
Retired	121 (27)	20 (18)	56 (30)	45 (30)	
Smoking, n (%)	142 (32)	47 (42)	49 (26)	46 (30)	0.067
Alcohol, doses per week, n (%)					0.99
None	95 (21)	25 (23)	35 (19)	35 (23)	
1–5	251 (56)	62 (56)	109 (59)	80 (53)	
6–9	41 (9)	6 (5)	19 (10)	16 (11)	
≥10	60 (13)	18 (16)	22 (12)	20 (13)	
BDI score, mean (SD)	23.4 (8.2)	25.4 (8.6)	23.4 (8.2)	22.0 (7.7)	<0.001
Antidepressant, n (%)	305 (68)	75 (68)	123 (66)	107 (71)	0.53
Disease, n (%)					
Neurological	11 (2)	4 (4)	2 (1)	5 (3)	0.99
Cancer	3 (1)	0 (0)	2 (1)	1 (1)	0.58
CVD	73 (16)	10 (9)	34 (18)	29 (19)	0.036
Rheumatic	15 (3)	4 (4)	9 (5)	2 (1)	0.25
Lung	42 (9)	10 (9)	12 (6)	20 (13)	0.18
DM	64 (14)	18 (16)	23 (12)	23 (15)	0.90

BDI beck depression inventory, CVD cardiovascular disease, DM diabetes mellitus.
* p for linearity across the LTPA categories.

4. Discussion

4.1. Main findings and study implications

Our findings suggested that LTPA is not associated with psychiatric comorbidities in patients with depressive symptoms. However, as in line with some earlier findings (Barengo et al., 2017; Korniloff et al., 2010) our study showed that LTPA had positive association with such health-related factors as DS obesity and CVD in depressive patients. This is important, since it has been shown in recent review that people with severe mental illness with low LTPA has increased risk of cardiovascular disease and premature mortality (Vancampfort et al., 2017).

Because PA, in general, has positive effect on mental health, it would be expected that these positive effects of PA are reflected on psychiatric comorbidities as well. Although, for example Bartley et al. (2013) have concluded in their meta-analysis that current evidence does not support the use of aerobic exercise as an effective treatment for anxiety disorders as compared to other treatment. In our study, the majority of study participants suffered from GAD (56%) and as PA seems to be useful in depression it may have lesser impact on depression with anxiety disorder (Bartley et al., 2013). This could be one reason why LTPA does not seem to have positive association with psychiatric comorbidities in this study.

There are also neurobiological changes associated with depression e.g. in hypothalamic-pituitary-adrenal (HPA)- axis homeostasis, neurotransmitters, neurogenesis and inflammatory markers where PA could work as a "scaffolding" factor that support amelioration processes (Archer et al., 2014). Again, neurotic disorders might "purely" associate more with "mind" than "body". This could also explain, at least partly, why positive health effects of PA associated more clearly with pure depression but not depression with additional psychiatric disorders and that PA can reduce depressive symptoms but not necessarily psychiatric comorbidities.

Recent study of Chekroud et al. (2018) has also revealed that while physical exercise is in general useful for mental health, more exercise is not always better and that the optimal amount lies between 30 and 60 min per day three to five times a week. As depression itself can reduce PA (Sieverdes et al., 2012), neurotic disorders might force one to move more and therefore neutralize depressions effects on PA. This phenomenon might be reflected in our study also because we were not able to catch those who exercise "more". Nor we did not use objective PA measurement instead of subjective assessment nor we didn't know

Table 2
Psychiatric comorbidities among depressed patients according to leisure-time physical activity level at baseline.

Variables	Total	Leisure time physical activity			*P* for linearity*
	N = 447	Low *N* = 111	Moderate *N* = 185	High *N* = 151	
GAD, n (%)	250 (56)	68 (61)	101 (54)	81 (54)	0.62
Suicidal, n (%)	218 (49)	60 (54)	86 (46)	72 (48)	0.97
Panic disorder, n (%)	111 (25)	26 (23)	46 (25)	39 (26)	0.24
Alcohol abuse or dependence, n (%)	65 (15)	17 (15)	25 (14)	23 (15)	0.93
Social phobia, n (%)	71 (16)	20 (18)	30 (16)	21 (14)	0.83
Hypomania, n (%)	55 (12)	16 (14)	17 (9)	22 (15)	0.57
Posttraumatic stress reaction, n (%)	27 (6)	9 (8)	13 (7)	5 (3)	0.41
Agoraphobia, n (%)	28 (6)	9 (8)	9 (5)	10 (7)	0.84
OCD, n (%)	26 (6)	8 (7)	7 (4)	11 (7)	0.45
Bulimia or anorexia, n (%)	11 (2)	7 (6)	1 (1)	3 (2)	0.68
Psychosis, n (%)	7 (2)	3 (3)	2 (1)	2 (1)	0.69
Number of psychiatric comorbidities, mean (SD)	1.5 (1.3)	1.6 (1.4)	1.4 (1.2)	1.4 (1.2)	0.24
Number, n (%)					
0	102 (23)	23 (21)	44 (24)	35 (23)	
1	169 (38)	37 (33)	77 (42)	55 (36)	
2	99 (22)	28 (25)	38 (21)	33 (22)	
>=3	77 (17)	23 (21)	26 (14)	28 (19)	

GAD generalized anxiety disorder, OCD obsessive-compulsive disorder.
* p for linearity across the LTPA categories, adjusted for gender, age, BMI, BDI and use of antidepressant.

what kind of PA lifestyle each participant had before the study due to cross sectional study design. This may have affected to these results also.

With these study findings without more extensive investigation we cannot say what is the relevance of LTPA in depression in terms of psychiatric comorbidities. While these findings can increase and widen our knowledge about factors related to depression, it also raises questions about methods and tools which are suitable in prevention and treatment of illness. As PA has many health benefits in depression it´s suitability as treatment method to reduce psychiatric comorbidities associated with depression are arguable. Therefore, further research and more knowledge from the underlying factors behind these study findings are needed.

4.2. Strengths and limitations

The main strength of this study is the use of diagnostic interview (M.I.N.I.) to confirm depression and psychiatric comorbidities. Another strength of this study is national representative study population with catchment area of 274 000 inhabitants. Main limitation lies on the self-reported LTPA which may prone to overestimation by participants. Although, a self-reported questionnaire has proven to be a valid and reliable method to measure PA in cross-sectional studies (Aires et al., 2003) and in this study design we were not trying to estimate exact amount and intensity of PA instead of crude LTPA level categorization. Moreover, generalization of study results to younger persons cannot be done due to study population of 35 and older in this study. Also, generalizability to other countries might be questionable as in Finnish society social equity is in very high level and for example physical education and health promotion as well as health services are well organized compared many other countries.

5. Conclusion(s)

LTPA level was not associated with psychiatric comorbidities among depressive diagnosed patients. This may suggest a different pathophysiology in depression and anxiety disorders as the level of LTPA was inversely associated with depressive symptoms. However, higher levels of physical activity associated with fewer heart diseases and obesity highlights the importance of LTPA promotion in the treatment of comorbid depression although other forms of treatment for comorbid anxiety disorders are also needed.

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CRediT authorship contribution statement

Ilkka Raatikainen: Writing - original draft. **Pekka Mäntyselkä:** Conceptualization, Methodology, Project administration, Writing - review & editing. **Mauno Vanhala:** Conceptualization, Methodology, Writing - review & editing. **Ari Heinonen:** Supervision, Writing - review & editing. **Hannu Koponen:** Conceptualization, Methodology, Writing - review & editing. **Hannu Kautiainen:** Data curation, Formal analysis, Software, Writing - review & editing. **Katariina Korniloff:** Conceptualization, Methodology, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2019.08.039.

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III

RELATIONSHIP BETWEEN PHYSICAL ACTIVITY AND PREDICTED HOME PRESENTEEISM AMONG PARTICIPANTS WITH DEPRESSIVE SYMPTOMS WITH AND WITHOUT CLINICAL DEPRESSION. FINDINGS FROM FINNISH DEPRESSION AND METABOLIC SYNDROME IN ADULTS (FDMSA) STUDY

by

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ORIGINAL ARTICLE

Relationship between physical activity and predicted home presenteeism among participants with depressive symptoms with and without clinical depression. Findings from Finnish Depression and Metabolic Syndrome in Adults (FDMSA) study

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KEYWORDS
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Abstract
Background and objectives: Depression can pose a major threat to an individual's ability to cope with daily activities. The aim of this study was to explore the relationship between physical activity (PA) and predicted home presenteeism (PHP) among depressive participants. The relationship between PHP and the severity of depressive symptoms was also investigated.
Methods: A total of 760 participants with depressive symptoms (DS) aged ≥35 years participated in this study. The study was conducted between 2008 and 2016 in municipalities within the Central Finland Hospital District. DS were determined with the 21-item Beck Depression Inventory (BDI-21) with a cutoff score ≥10, and psychiatric diagnoses were confirmed by the Mini-International Neuropsychiatric Interview (M.I.N.I.). PA, home presenteeism and other social-clinical factors were captured by standard self-administered questionnaires.

Abbreviations: AUDIT, alcohol use disorders identification test; BDI (-21), Beck Depression Inventory; BMI, Body Mass Index; CI, confidence intervals; CVD, cardiovascular disease; DM, diabetes mellitus; DS, depressive symptoms; EQ5D, European quality of life five dimensions questionnaire; FDMSA-study, Finnish Depression and Metabolic Syndrome in Adults-study; HT, hypertension; IPAQ, International Physical Activity Questionnaire; IPW, inverse probability weighting; LD, lung disease; MDD, major depressive disorder; Migr, migraine; M.I.N.I., Mini-International Neuropsychiatric Interview; MSD, musculoskeletal disorder; PA, physical activity; PHP, predicted home presenteeism; SD, standard deviation; VAS, visual analogue scale; YLD, years lived with disability.

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Results: Higher PA levels were associated with lower PHP (adjusted) among depressive patients with ($p < 0.001$) and without clinical depression ($p = 0.021$). In addition, DS (adjusted BDI) correlated with PHP ($r = 0.60$, 95% CI: 0.56–0.65) in such a way that the higher the BDI was, the higher the PHP was. Moreover, home presenteeism were higher among depression diagnosed participants than those without ($p = 0.002$).
Conclusion: According to this study, PA is associated with PHP among depressive patients in the Finnish adult population. PA seems to promote the ability to cope better with daily activities at home despite DS or a depression diagnosis. These findings outline the importance of being physically active regarding independency of daily activities, and thus, should be considered in clinical practices when treating depressive patients.

Introduction

With population aging and increasing life expectancy also years living with disease and disability increase among population. Globally, major depressive disorder (MDD) is one of the leading causes of years lived with disability (YLD),[1] and depression has been estimated to be the most common global illness by the year 2030.[2] In the Finnish population, depression is the most significant cause of sickness allowances[3] and disability retirement.[4]

Beside economic burden to society, depression is a huge individual misery.[5] Depression is often accompanied by other health conditions, such as other psychiatric comorbidity,[6] elevated experience of pain and decreased quality of life.[7] Depression can also increase the risk for many somatic diseases, such as obesity, diabetes and cardiovascular diseases.[8] For example, in the Finnish adult population (≥30 years), only approximately one third of people who are suffering from depression seek and receive adequate treatment from health care units.[9]

Current evidence of benefits of physical activity (PA) and exercise on treatment and prevention of depression is quite clear. PA can decrease depressive symptoms (DS)[10] and also lower the risk for depression in the future.[11] As physical exercise is an effective intervention for depression it also could be a viable adjunct treatment in combination with antidepressants.[12]

In most literature, presenteeism describes the situation in which a subject works while being sick; it is workplace or occupation-related and often associated with productivity loss.[13] Household presenteeism or presenteeism at home are terms that describe the productivity losses in planned housework or tasks at home.[14,15] The focus of home presenteeism is an individual's everyday life apart from work; it describes the situation or level of how much a person's health disorders or harms the ability of a person to cope and perform everyday home chores. Although presenteeism is a global phenomenon, a generally accepted definition and consistent measurement methods are lacking.[16] In this study, home presenteeism consists of performing housework or household chores while sick in a home environment from the point of view of how much these home tasks are disturbed or affected by subjects' diseases and disorders.

From previous studies, we know that depression is associated with (work-related) presenteeism, which causes vast workplace productivity losses.[17,18] A recent large U.S.-based prevalence study has revealed that depression, general anxiety and other mental health disorders are among the top health conditions that cause the highest estimated daily productivity loss and annual cost per person.[19] Recent studies also suggest that promoting PA can help prevent and reduce health-related work presenteeism.[20–22] Instead, the knowledge of associations between depression and home presenteeism and how PA is related to these factors is lacking. One reason for this gap in research might be the difficulty in the accurate monetary quantification of these intangible factors that are associated with sufferers' quality of life due to illnesses and therefore they are often disregarded in studies.[23] In summary, as increasing number of individuals are absenting (unemployment, sick leave or disability retirement) from work life due to depression and further, in a light of PA's positive effect on both depression and work-related presenteeism, PA may have an important role in the everyday home tasks of depressed individuals.

Thus, the aim of this study as a part of the Finnish Depression and Metabolic Syndrome Study (FDMSA) was to explore the relationship between physical activity (PA) and predicted home presenteeism (PHP) among depressive patients. In addition, the relationship between PHP and the severity of depressive symptoms was also investigated.

Materials and methods

Design

Data of the Finnish Depression and Metabolic Syndrome in Adults (FDMSA) baseline study (2008–2011) and its follow-up study (2012–2016), which were conducted within the municipalities in the Central Finland Hospital District with a catchment area of 274,000 inhabitants, were used in this study.[24] Participants' DS and clinical depression were confirmed in the FDMSA baseline study stage, and other study results were captured at the FDMSA five-year follow-up stage.

In the FDMSA follow-up study, all participants completed a standard self-administered questionnaire that contained

questions about previously diagnosed somatic disorders, home presenteeism, smoking and drinking habits, PA, sleep, quality of life and perceived pain. Data on participants' socio-economical background, such as years of education and marital and employment status were also collected via questionnaire.

Participants

The study population was enrolled from patients with DS (n = 760) who scored ≥10 in the 21-item Beck Depression Inventory (BDI-21)[25] and who were 35 years of age or older at the baseline FDMSA-study stage (2008–2011). Participants were either self-referred or referred by general practitioners to depression nurse case managers, and participants' psychiatric diagnoses were confirmed by trained depression nurse case managers using the diagnostic structured Mini-International Neuropsychiatric Interview (M.I.N.I.).[26] The study protocol was approved by the Ethics Committee of the Central Finland Hospital District prior to the commencement of the study. All participants signed an informed written consent.

Of the 760 participants with depressive symptoms who were included in the analysis, clinical depression was confirmed in 124 participants (16%). The majority of participants were female (n = 514; 68%).

Physical activity questionnaire

PA was assessed by using the International Physical Activity Questionnaire (IPAQ), short-form questionnaire. The IPAQ was developed as an instrument for cross-national monitoring of physical activity[27] and has proven to be valid and reliable method for collecting PA data in cross-sectional studies.[28] The short-form IPAQ consists of seven questions about participants' PA (during work, leisure time, commuting, exercising or sports) during the last seven days. Participants were asked to assess their participation in at least ten minutes of vigorous PA (difficult physical effort that causes rapid breathing) and moderate PA (moderate physical effort that causes slower breathing) and walking sessions as days per week, hours per day and minutes per day. In addition, their daily sitting time (hours and minutes per day) was also assessed. All answers were classified as IPAQ grades (low, moderate, and high) via the IPAQ scoring protocol.[29]

Depressive symptoms and psychiatric diagnosis

The severity of participants DS were captured using the 21-item Beck Depression Inventory (BDI-21)[25] with a cut-off point ≥10.[24] The psychiatric diagnoses were confirmed and obtained with the diagnostic Mini-International Neuropsychiatric Interview (M.I.N.I.),[26] which was delivered by a trained study nurse.

Anthropometric measurements

The Body Mass Index (BMI) was defined as person's weight (kg) divided by the square of the person's height (m). The World Health Organization (WHO) has defined overweight as BMI ≥ 25 and obesity when BMI ≥ 30 respectively.[30]

Smoking and alcohol use

Smoking was assessed by asking whether a subject currently smokes or not. Participants' drinking habits were evaluated by an alcohol use disorders identification test and its three-question screening version (AUDIT-C).[31] AUDIT-C is a brief, practical and valid primary care screening test for heavy drinking and/or active alcohol abuse or dependence.[32] Subjects were asked to answer the following questions: ''How often did you have a drink containing alcohol (1 = never; 2 = monthly or less; 3 = 2–4 times a month; 4 = 2–3 times a week; 5 = 4 or more times a week)?'', ''How many drinks did you have on a typical day when you were drinking (1 = 1–2 drinks; 2 = 3–4 drinks; 3 = 5–6 drinks; 4 = 7–9 drinks; 5 = 10 or more drinks)?'' and ''How often did you have 6 or more drinks on one occasion in the past year (1 = never; 2 = less than monthly; 3 = monthly; 4 = weekly; 5 = daily or almost daily)?'' The AUDIT-C was scored on a scale from 0 to 12 (response option 1 = 0 points; 2 = 1 point; 3 = 2 points; 4 = 3 points; 5 = 4 points). Generally, men who receive a score of 4 or higher (a score of 3 or higher for women) is considered potential hazardous/heavy drinkers, and the higher is the score, the more likely drinking will affect a person's health and safety.[31,32]

Home presenteeism

Home presenteeism is defined as doing housework or household chores while sick. It is an evaluation of how much housework or household chores are disturbed or affected by subjects' diseases and disorders.[14,15] In this study, home presenteeism was evaluated by a visual analogue scale (VAS) and asking the following question: ''How much have your diseases and symptoms affected your necessary housework and household chores at home during the last month (extreme options were ''not at all'' or ''completely blocked'')?'' Each participant was asked to mark the position that describes his/her agreement to this question along a continuous line between these two end points. For the analysis, the answers were scored from 0 (''not at all'') to 100 (''completely blocked'').

Quality of life

Quality of life was evaluated by using the European Quality of Life Five Dimension (three-level version) (EQ-5D-3 L) questions.[33] EQ-5D is a standardized measure of health status that provides a simple, generic measure of health for clinical and economic appraisal. The three-level version of EQ-5D (EQ-5D-3 L) is the most widely used instrument for measuring the health-related quality of life.[34] EQ-5D has found to be responsive to changes related to depression severity and health status and appropriate for estimating utility in depression treatment.[35] In this study, the response options were recalculated (1 = 0 point, 2 = 1 point and 3 = 2 points) and expressed as an average per patient.

Sleeping

Participants' quality of sleep were evaluated by asking the following question: ''How tired do you feel during the first 30 min after you have woken up in the morning (1 = very tired; 2 = quite tired; 3 = quite rested; 4 = feel fresh)?'' The answers ''quite rested'' and ''feel fresh'' were linked to the assessment that a participant received a sufficient amount of sleep.

Pain assessment

Participants' perceived pain during the last seven days were assessed on a scale from 0 to 10 using questions. Average pain intensity was represented by a score range from 0 (''no pain'') to 10 (''worst imaginable pain''). Pain interference during the last seven days, when pain had disturbed daily activities in the home or outside the home, was represented by a score range from 0 (''no interference'') to 10 (''total interference'').

Statistical methods

The results were presented as means with standard deviations (SD) or as counts with percentages. Statistical comparisons between the depression groups were performed using the *t*-test for continuous variables and Pearson's chi-square test for categorical variables. The adjusted relationship between the PA level and the depression status with home presenteeism was analyzed using a two-way analysis of variance. A possible nonlinear relationship between the BDI score and home presenteeism was assessed by using 4-knot-restricted cubic spline regression. The models included age, gender, marital and working status, educational years, smoking, BMI and comorbid diseases as covariates. The bootstrap method was used when the theoretical distribution of the test statistics was unknown or in the case of a violation of the assumptions (e.g., non-normality). Correlation coefficients with 95% confidence intervals (CI) were calculated by using the Pearson method. The normality of variables was evaluated graphically and with the Shapiro–Wilk W test. All analyses were performed using STATA 16.0.

Results

Table 1 shows the socio-demographic and clinical characteristics of the study population. Participants with clinical depression were less likely to be in a relationship, had less years of education, were more likely to be unemployed or retired, and smoked more and had a higher BMI than depressive participants without a depression diagnosis. Among the participants who were diagnosed with depression the prevalence of diabetes, musculoskeletal disorders and lung diseases were higher than among depressive participants without a depression diagnosis. The number of subjects who received enough sleep were significantly lower among participants with a depression diagnosis and their health-related quality of life was poorer than depressive participants without a depression diagnosis. In addition, perceived pain (intensity and interference) was significantly more severe for participants who were diagnosed with depression compared to participants without a depression diagnosis (Table 1).

The mean home presenteeism was lower among participants without depression (18.8, SD 25.2) than those with a depression diagnosis (51.5, SD 29.3) ($p = 0.002$).

Depressive participants without clinical depression were more physically active than those with a depression diagnosis. Among the participants without depression, 28% of subjects had low, 35% moderate and 37% high IPAQ grade while participants with depression had 42%, 30% and 28% respectively. The mean sum of IPAQ score was higher for participants without depression (43.8, SD 44.8) than those with depression (35.4, SD 44.1) indicating lower PA among those with depression ($p = 0.046$). In the whole study population, the PA level was linearly related to home presenteeism (p for linearity <0.001). Low, moderate and high mean home presenteeism scores by PA level were 37.7 (SD 32.7), 21.4 (SD 25.6) and 15.8 (SD 23.4), respectively.

Fig. 1 shows that higher PA levels were related to lower home presenteeism scores in both groups: among participants without depression ($p < 0.001$) and participants with depression ($p = 0.021$) after adjusting the results for age, gender, marital and working status, educational years, smoking, BMI and comorbid diseases. Home presenteeism scores were higher among participants with depression compared to those without depression in all PA levels ($p < 0.001$). Instead, there was no interaction between IPAQ grade and depression status with respect to home presenteeism ($p = 0.47$).

In addition, the subgroups analysis (Fig. 2) revealed that BDI scores correlate with PHP ($r = 0.60$, 95% CI: 0.56 to 0.65) after adjusting the results for age, gender, marital and working status, educational years, smoking, BMI and comorbid diseases. The higher the BDI score was, the higher the PHP was as well. The same tendency in the correlations between BDI scores and PHP was observed for all PA levels: low ($r = 0.60$, 95% CI: 0.50 to 0.68), moderate ($r = 0.49$, 95% CI: 0.39 to 0.58) and high ($r = 0.63$, 95% CI: 0.54 to 0.70). Also, the higher the PA level was, the lower the mean PHP score was respectively (Fig. 2).

Discussion

Main findings and study implications

The study results showed that PA was inversely associated with PHP among depressive participants with and without clinical depression. Those participants with a higher PA level had less difficulties and coped better with their necessary daily housework and household chores than those patients with lower PA activity. Also, depression diagnosis and severity of depressive symptoms were factors that predicted higher discomfort and difficulties in coping with daily tasks.

Consistent with previous studies,[6–8] our study results indicate that clinically diagnosed depression was related to greater BMI as well as other comorbid diseases, poorer quality of life, increased perceived pain and insufficient sleep. Also, depression diagnosed participants' socioeconomic fac-

Table 1 Socio-demographic and clinical characteristics of study population at follow-up; patients with depression symptoms without depression diagnosis and with a depression diagnosis.

Variables	No depression N = 636	Depression N = 124	P value
Female, n (%)	434(68)	80(65)	0.42
Age, mean (SD)	59(10)	60(10)	0.91
Living in relationship, n (%)	424(67)	66(53)	0.004
Working status, n (%)			<0.001
Working	300(47)	34(27)	
Unemployed	66(10)	20(16)	
Retired	270(42)	70(56)	
Education years, mean (SD)	11.7(3.3)	10.5(3.0)	<0.001
Body Mass Index (kg/m^2), mean (SD)	27.3(5.0)	29.0(6.0)	<0.001
Smoking, n (%)	94(15)	35(28)	<0.001
Drinking habits (AUDIT-C), mean (SD)	2.6(2.4)	2.9(3.2)	0.23
Chronic conditions, n (%)			
Hypertension	207(33)	50(40)	0.094
Cardiovascular disease	58(9)	12(10)	0.84
Diabetes mellitus	65(10)	26(21)	<0.001
Musculoskeletal disorder	241(38)	71(57)	<0.001
Lung disease	77(12)	26(21)	0.008
Migraine	79(12)	18(15)	0.52
Sufficient sleep, n (%)	458(72)	32(26)	<0.001
Health-related quality of life (EQ5D), mean (SD)	0.805(0.188)	0.565(0.254)	<0.001
Pain, mean (SD)			
Intensity	3.0(2.4)	5.2(2.4)	<0.001
Interference	2.6(2.6)	5.2(2.9)	<0.001

AUDIT-C: alcohol use disorders identification test (three question screening version); EQ5D: European quality of life five dimensions questionnaire; SD: standard deviation.

tors and health behavior were poorer than those participants without a depression diagnosis. These facts may form a significant risk for a person's future health as well as increase the societal burden of depression.[5] For example, depression alongside obesity has found to increase health care utilization and health care-related costs.[36]

Depression can also cause a substantial productivity loss in work[17–19]; according to this study, it is also obvious in the home environment. Among our study population, managing daily home tasks was harder for participants diagnosed with depression as well as participants with a higher severity of DS. We also know that depression can lower a person's quality of life[7] and this association was also found in our study as well. One important finding of our study was that participants who were more physically active suffered less discomfort from diseases and symptoms and managed their housework and household chores better than the inactive participants in both groups (among those with and without a depression diagnosis). PA can positively affect a person's psychological well-being, such as sense of coherence and social integration,[37] which again is related to better coping with common daily activities.[38] Thus, physically active people may have more self-confidence, which may protect them, for example, from social isolation and lead to better self-care and help-seeking in addition to better management with common daily tasks. This is important, especially among people who suffer from depressive disorders and spend a substantial amount of time at home (live alone, unemployed or retired) because their social network may have shrunk. These people have a greater risk of social isolation.

As we know from previous studies, PA and exercise is effective and beneficial for preventing depression as well as reducing DS and that association between PA and depression is bidirectional.[10–12] PA may not directly decrease health care utilization (at least not in the short term) among depressive patients[39]; however, promoting lifetime PA may mean reduced risk for depression and somatic diseases for elderly patients.[40] Our study results indicate that, in the same way that PA has a positive relation to an employee's psychosocial health[41] and can reduce health-related presenteeism at work,[20–22] it can also be beneficial for reducing home presenteeism as well. In this scope and according to our study results, it seems clear that PA can have an important role in improving a person's health and quality of life and help depressive patients manage everyday tasks in their home environments.

When interpreting the results, it is important to note that the concept of presenteeism in the literature is ambiguous. In general, presenteeism can refer either to working longer than necessary, e.g., to show high commitment[42] or it can refers to attending and going to work sick or injured.[13,42] For example, in his review, Johns[13] has identified nine different definitions for presenteeism: (1) attending work, as opposed to being absent; (2) exhibiting excellent attendance; (3) working elevated hours even when unfit; (4) being reluctant to work part-time rather than full time; (5) being unhealthy but exhibiting no sickness or absenteeism; (6) going to work

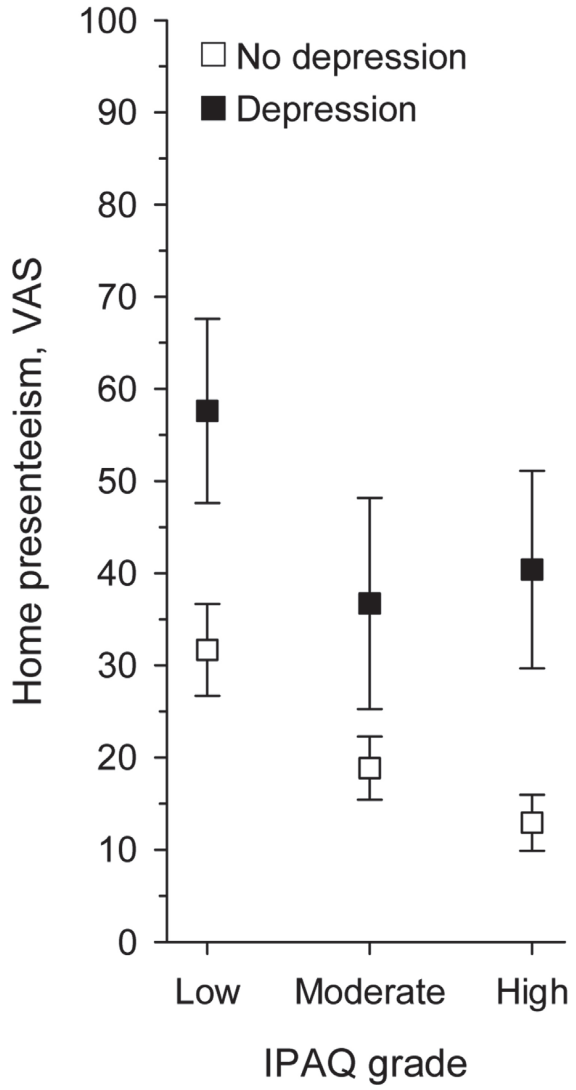

Figure 1 Mean home presenteeism (with 95% confidence intervals) according to physical activity level (IPAQ grade) and depression status (depression vs. no depression). Adjusted for age, gender, marital and working status, educational years, smoking, BMI and comorbid diseases.

despite feeling unhealthy; (7) going to work despite feeling unhealthy or experiencing other events that normally compel absence; (8) reduced productivity at work due to health problems; and (9) reduced productivity at work due to health problems or other events that distract a person from full productivity. Therefore, the term presenteeism can be considered health-related or not health-related and can vary depending on the point of view or study approach.

As most recent studies focus on work-related presenteeism, it is important to illuminate the impact of illness on household chores and daily activities as well. Moreover, the concept of presenteeism, including home presenteeism, needs further clarification in future studies. Our study is one of the first to study and measure home presenteeism in association with PA and illness.

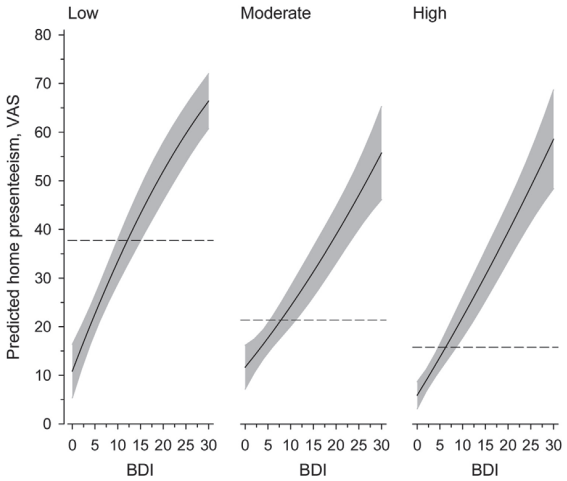

Figure 2 Relationships of home presenteeism as a function of the BDI in PA levels (low, moderate, high). The curves were derived from a 4-knot restricted cubic splines regression model. The models were adjusted for age, gender, marital and working status, educational years, smoking, BMI and comorbid diseases. The gray area represents 95% confidence intervals.

Strengths and limitations

The novelty of this study is the study design and approach to explore associations between PA, depression, and home presenteeism. The main strength of this study is the use of a diagnostic interview (M.I.N.I.) to confirm depression and the use of the IPAQ method to assess participants PA. The IPAQ is widely used and accepted, valid and reliable proof method for evaluating PA in cross-sectional studies.[28] Another strength of this study is the nationally representative study population with a catchment area of 274,000 inhabitants. The main limitation of this study is its generalizability. Because the study population included patients who were 35 years or older, the generalizability to younger persons is questionable. Also, different global health care infrastructures (such as accessibility, screening and prevention methods or funding of health care, etc.) must be considered when interpreting these study findings in a wider international context.

Although the VAS has been demonstrated to be a valid and reliable measurement in cross-sectional studies, some caution must also be taken when using the self-administered VAS questionnaire. In the literature, some limitations of the VAS have been raised. For example, the VAS may be difficult to fulfill among patients with perceptual-motor problems or cognitive limitations and among the elderly.[43] The VAS may also be prone to spreading (respondents use all areas on the valuation scale, especially when multiple health states are valued on the same scale) and context effects (average rating for items is influenced by the level of the other items that are being valued) and endpoint bias (health states at the top and bottom of the scale are placed further apart on the scale than as suggested by a direct comparison of differences).[44] Again, the concept ''worst imaginable ....'' may be difficult to understand, as the respondent can never know whether the present experience is the ''worst''.[45]

Furthermore, as Despiegel et al.[46] pointed out in their review, the recommendations for presenteeism tools (such as VAS-based tools) must consider the instrument properties, such as ease of use and monetization ability, as well as study type.[46] Also, the responsiveness of the tool and impact of mood disorders on self-reported assessments must be taken into account.[46]

Conclusions

According to this study, PA is associated with PHP among patients with depressive symptoms with and without clinical depression in the Finnish adult population. Higher levels of PA seem to help patients cope better with daily activities at home despite their depression or depressive symptoms. On the contrary, the participants with higher depressive symptoms had more difficulties and coped worse with their necessary household chores than those with lower DS levels. These findings outline the importance of being physically active regarding the independency of daily activities, and thus, should be considered in clinical practices when treating depressive patients.

Ethical considerations

The study protocol was approved on the 17th of April 2007 by the Ethics Committee of Central Finland Central Hospital.

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Conflict of interest

The authors declare that they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ejpsy.2020.12.005.

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IV

DOES BASELINE LEISURE-TIME PHYSICAL ACTIVITY LEVEL PREDICT FUTURE DEPRESSIVE SYMPTOMS OR PHYSICAL ACTIVITY AMONG DEPRESSIVE PATIENTS? FINDINGS FROM A FINNISH FIVE-YEAR COHORT STUDY

by

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ARTICLE

Does baseline leisure-time physical activity level predict future depressive symptoms or physical activity among depressive patients? Findings from a Finnish five-year cohort study

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ABSTRACT

Objectives: The aims of this study were to investigate whether baseline leisure-time physical activity (LTPA) is associated with future recovery from depression among patients with a depression diagnosis and whether baseline LTPA is associated with total physical activity after five years of follow-up.

Methods: A total of 258 patients aged ≥35 years with clinically confirmed depression at baseline participated. The study was conducted between 2008 and 2016 in municipalities within the Central Finland Hospital District. Depressive symptoms (DS) were determined with the Beck Depression Inventory (BDI) with a cutoff score ≥10, and depression diagnoses were confirmed by the Mini-International Neuropsychiatric Interview (MINI). Blood pressure and anthropometric parameters were measured and blood samples for glucose and lipid determinations were drawn at baseline. LTPA, physical activity, and other social and clinical factors were captured by standard self-administered questionnaires at baseline and the five-year follow-up point.

Results: Of the 258 patients, 76 (29%) had DS at follow-up. Adjusted odds ratio (OR) for future DS was 1.43 (confidence interval [CI] 0.69–2.95) for participants with moderate LTPA and 0.92 (CI 0.42–2.00) for participants with high LTPA, compared with low LTPA at baseline. Higher baseline LTPA levels were associated with higher total physical activity in the future (β=0.14 [95% CI: 0.02–0.26] for linearity = 0.024).

Conclusion: Baseline LTPA did not affect the five-year prognosis of depression among depressed patients in a Finnish adult population. Because the baseline LTPA level predicted the future total physical activity, it could be included as a part of the overall health management and treatment of depression in clinical practices.

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Introduction

The benefits of physical activity for the treatment and prevention of depression are well known. Engaging in physical exercise or having a physically active lifestyle can reduce depressive symptoms (DS) and also reduces the risk of developing depression [1–3]. In their Cochrane review, Cooney et al. [4] concluded that physical exercise may have at least a moderate-sized effect for reducing DS and that physical exercise may be as effective as psychological therapies or medications. Similarly, Mammen and Faulkner [5] stated in their review that any physical activity level, including low levels, such as walking, may prevent future depression. In turn, Ringen et al. [6] found in their recent study that among inpatients with severe mental illness, low levels of physical activity were significantly associated with more severe depression.

Recent studies have also shown that independently of sociodemographic characteristics, leisure-time physical activity (LTPA) can benefit everyone with DS regardless of age, gender, education, family, social status, or living environment [7]. In the body of literature, LTPA is defined as physical activity that an individual engages in during free time [8] that is not related to regular work, housework, or transportation activities [9]. In addition, lifetime physical activity has been shown to be linked to depression in such a manner that childhood physical activity may reduce the risk of depression in adulthood [10]. Furthermore, promoting lifetime LTPA may reduce DS in older age [11]. In the literature, physical activity is defined as any bodily movement

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produced by skeletal muscles that result in energy expenditure. Studies have shown that in daily life, physical activity can be categorized as occupational, sports, conditioning, household, or other activities [12], and physical activity is used as an umbrella term that encompasses all daily physical activities in which LTPA is one part of total daily physical activity.

Because recent studies have suggested that physical activity and LTPA alone or as adjuncts to other treatments (medication and psychotherapy) [2] are promising and plausible methods of treating and preventing depression and DS, it is relevant to explore whether self-assessed LTPA levels can predict future depression among those who have already been diagnosed as depression positive. Thus, the aims of this study, as a part of the Finnish Depression and Metabolic Syndrome in Adults (FDMSA) study, were to investigate whether baseline LTPA is associated with future recovery from depression among patients with a depressive diagnosis and whether baseline LTPA is associated with total physical activity after five years of follow-up.

Materials and methods

The study data from this prospective cohort study were drawn from the FDMSA baseline study (2008–2011) and its follow-up study (2012–2016), which were conducted within the municipalities in Central Finland Hospital District with a catchment area of 274,000 inhabitants. The Ethics Committee of the Central Finland Hospital District approved the study protocol prior to the commencement of the study. The study enrollment was based on written and oral patient information. All participants signed a written informed consent form before any study procedures commenced. The study population was enrolled from the group of new and old mild to moderately depressed patients who were experiencing a new depressive episode, were 35 years or older, and who scored $\geq$10 on the BDI. Participants were self-referred or referred by general practitioners to depression nurse case managers. Participants' psychiatric diagnoses were confirmed by a diagnostic structured interview, the Mini-International Neuropsychiatric Interview (MINI), administered by trained depression nurse case managers.

At the baseline, a total of 706 referred patients scored 10 or more on the BDI. From these, 447 patients met the criteria for clinical depression (major depressive episode, major depressive episode with melancholic features, dysthymia) after the diagnostic interview. Of these, 258 patients took part through the follow-up stage, and those participants whose BDI scores were 10 or over at follow-up were classified as having DS. Depression (and Type 2 diabetes) are more prevalent in the Finnish population after 35 years of age; therefore, in this study, the authors decided to focus on the $\geq$35 year age group [13]. The age limit of 35 years was also chosen to obtain a stable study population, which facilitates having a more prolonged follow-up [14]. By including self-referred patients along with general practitioner referred patients, we obtained a representative sample comprising both mild and more severely depressive participants [13,14].

At baseline, all participants filled out a standard self-administered questionnaire containing questions about their socioeconomic background, health, and health behaviors, previously diagnosed somatic disorders, and LTPA. Participants also took part in a physical examination and collection of blood samples. Moreover, participant DS was assessed, and clinical depression was confirmed. At the five-year follow-up, participants filled out the same standard self-administered questionnaire. Participants' DS, clinical depression, and total physical activity were also assessed at the five-year follow-up.

Participant LTPA was assessed by asking 'How often do you participate in physical activity for at least half an hour so that you are out of breath and sweating?' Answers were classified into three levels: low (twice per month or less), moderate (about once or twice per week), or high (three times per week or more). In previous studies, self-assessed LTPA has shown a high correlation with physical fitness as measured by maximal oxygen uptake [15].

At follow-up participants' total physical activity was assessed using the short-form International Physical Activity Questionnaire (IPAQ). The IPAQ was developed as an instrument for cross-national monitoring of physical activity [16], and it has been proved to be a valid and reliable method of collecting physical activity data in cross-sectional studies [17]. The IPAQ short form consists of seven questions about physical activity (in work, leisure time, commuting, exercising, or for sport) during the previous seven days. Participants were asked to assess the number of times they had engaged in at least 10 min of vigorous activity (hard physical effort that makes one's breathing labored), moderate activity (moderate physical effort that makes breathing a little difficult), or walking, as days per week, hours per day, and minutes per day. Further, daily sitting time as hours and minutes per day were also assessed. Answers were then classified as IPAQ grades (low, moderate, high) via the IPAQ scoring protocol [18]. At the five-year follow-up, answers for physical activity were converted and expressed as metabolic equivalent (MET) [19] hours per week (METh).

The severity of DS was captured using the 21-item Beck Depression Inventory (BDI) [20] completed by participants. The cutoff point was set at $\geq$10 [13]. The psychiatric diagnosis was confirmed with the diagnostic Mini-International Neuropsychiatric Interview (MINI), version 5.0.0 [21], delivered by a trained study nurse. In Finland, depression nurse case managers are an important part of the basic health care team, and they primarily organize the treatment of depressed patients together with the general practitioners [13]. The patients were treated according to the current Finnish treatment guidelines for depression, meaning with antidepressive medications and/or psychotherapy [13].

At baseline, the participant's weight, height, and blood pressure were measured. Weight and height were measured with the participant wearing light clothing and were accurate to the nearest 0.5 cm and 0.1 kg, respectively. Blood pressure was measured twice after 15 min rest time with a mercury sphygmomanometer and the patient in a sitting position. The physical examination was conducted by trained study

Table 1. Participants' baseline social and clinical characteristics according to follow-up categorization as with or without depressive symptoms (DS).

	DS at follow-up		
Variables	No $N = 182$	Yes $N = 76$	*p*-Value
Female, *n* (%)	142 (78)	53 (70)	0.16
Age, years (SD)	51 (10)	52 (10)	0.54
Body mass index (kg/m^2), mean (SD)	27.9 (5.4)	28.7 (6.0)	0.26
Education, years, mean (SD)	11.4 (3.0)	10.5 (3.1)	0.035
Blood pressure (mmHg), mean (SD)			
Systolic	130 (16)	131 (12)	0.55
Diastolic	81 (10)	81 (10)	0.79
Total cholesterol (mmol/l), mean (SD)	5.13 (0.99)	5.13 (1.01)	0.97
HDL cholesterol (mmol/l), mean (SD)	1.54 (0.40)	1.56 (0.42)	0.73
LDL cholesterol (mmol/l), mean (SD)	3.13 (0.93)	3.08 (0.86)	0.70
Triglyceride (mmol/l), mean (SD)	1.32 (0.72)	1.39 (0.86)	0.54
Plasma glucose (mmol/l), mean (SD)	5.64 (0.85)	5.84 (1.44)	0.17
Married or cohabiting *n* (%)	115 (63)	43 (57)	0.32
Employment status *n* (%)			0.15
Employed	94 (52)	28 (37)	
Unemployed	36 (20)	18 (24)	
Student	5 (3)	2 (3)	
Retired	47 (26)	28 (37)	
Smoking, *n* (%)	52 (29)	26 (34)	0.37
Alcohol, servings per week, *n* (%)			
None	34 (19)	19 (25)	
1–5	105 (58)	36 (47)	
6–9	18 (10)	10 (13)	
$\geq$10	25 (14)	11 (14)	
BDI score, mean (SD)	22.4 (8.0)	25.1 (7.3)	0.011
BDI $\geq$10, *n* (%)	71 (39)	72 (94)	
Antidepressant, *n* (%)	122 (67)	56 (74)	0.29
Disease, *n* (%)			
Neurological disease	5 (3)	0 (0)	0.33
Cardiovascular disease	30 (16)	13 (17)	0.96
Rheumatic disease	7 (4)	3 (4)	0.99
Lung disease	16 (9)	10 (13)	0.29
Diabetes mellitus	16 (9)	15 (20)	0.014
LTPA, *n* (%)			0.30
Low	42 (23)	18 (24)	
Moderate	70 (38)	36 (47)	
High	70 (38)	22 (29)	

BDI: Beck Depression Inventory; HDL: high-density lipoprotein; LDL: low-density lipoprotein; LTPA: leisure-time physical activity.

nurses [22]. The body mass index (BMI) was defined as the person's weight (kg) divided by the square of the height (m). The World Health Organization (WHO) has defined overweight as a BMI $\geq$25 and obesity as a BMI $\geq$30 [23].

The blood samples were drawn between 8:00 a.m. and 11:00 a.m. after 12 h of fasting, for glucose and lipid determination. Serum total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides, and plasma glucose were analyzed using Modular Analytics SWA (Hitachi High-Technologies Corporation, Tokyo, Japan) [13,13,24].

Statistical analysis

Data are presented as means with standard deviation (SD) or as counts with percentages. Statistical comparisons between DS groups were made using a t-test for continuous variables and Pearson's chi-square for categorical variables. The adjusted hypothesis of linearity (orthogonal polynomial) was evaluated using generalized linear models (analysis of covariance and logistic models), with the appropriate distribution and link function. Models included age, gender, years of education, diabetes, and BDI as covariates. The bootstrap method was used when the theoretical distribution of the test statistics was unknown or in the case of violation of the assumptions (e.g. non-normality). Rank-based (Spearman) partial correlations were calculated between baseline and follow-up LTPA, adjusted for age, sex, years of education and diabetes. Confidence intervals for the correlation was obtained by bias-corrected bootstrapping (5000 replications). The normality of variables was evaluated graphically and with the Shapiro–Wilk W-test. The Stata 16.0 statistical package (StataCorp LP, College Station, TX, USA) was used for the analysis.

Results

A total of 258 patients with confirmed clinical depression at baseline and who took part in the five-year follow-up were included in the analysis. Of these, DS (BDI $\geq$10) was confirmed in 76 patients (29%). The majority of participants were female ($n = 195$, 76%). Table 1 shows the baseline sociodemographic and clinical characteristics of the participants according to the

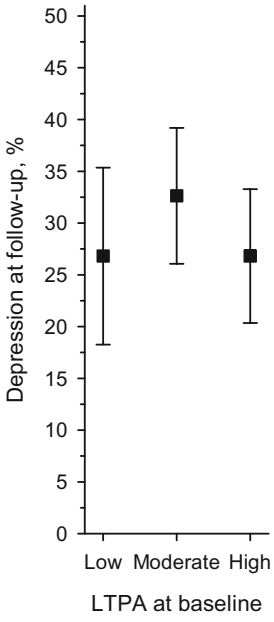

Figure 1. Proportion (%) of participants with DS (BDI score ≥10) at follow-up according to baseline LTPA level. Adjusted for baseline age, gender, years of education, diabetes, and BDI. BDI: beck depression inventory; DS: depressive symptoms; LTPA: leisure-time physical activity.

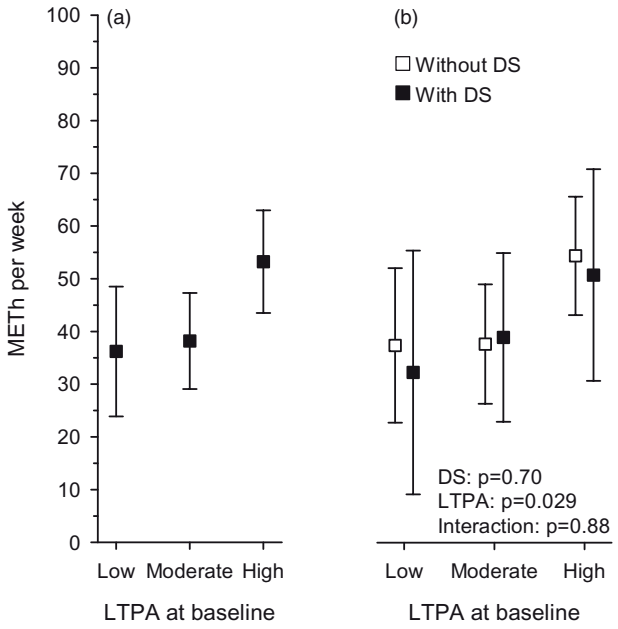

Figure 2. (a) Participant (all) physical activity expressed as METh per week at follow-up according to baseline LTPA level. Adjusted for baseline age, gender, years of education, diabetes, and BDI. (b) Participant (separate with DS and without DS) physical activity expressed as METh per week at follow-up according to baseline LTPA level. Adjusted for baseline age, gender, years of education, and diabetes. BDI: beck depression inventory; DS: depressive symptoms; LTPA: leisure-time physical activity; METh: metabolic equivalent hours per week.

follow-up DS status. Those participants with DS at the follow-up had fewer years of education ($p = 0.035$), more DS ($p = 0.011$), and higher prevalence of diabetes ($p = 0.014$) at baseline than those participants without DS.

In a comparison of the main baseline characteristics (age, gender, BDI level) of those who participated and those who did not participate in the follow-up, there was no statistically significant difference between the groups.

Statistical analysis revealed that the baseline LTPA level (adjusted for age, sex, years of education, diabetes, and BDI) was not associated with the DS status at the five-year follow-up (Figure 1). Age, sex, years of education, diabetes and BDI adjusted odds ratio (OR) for future depression was 1.71 (CI 0.61–4.79) for participants with moderate LTPA and 1.00 (CI 0.35–2.85) for participants with high LTPA, as compared with low LTPA at baseline. Crude OR were 1.2 (CI 0.61–2.38) and 0.73 (CI 0.35–1.52) for participants with moderate or high LTPA and low LTPA, respectively. The result did not change even though the BDI adjusting was removed.

Instead, higher baseline LTPA levels were associated with higher physical activity in the future. Those participants with higher LTPA levels had more METh per week at follow-up than those with lower baseline LTPA levels [$\beta = 0.15$ (95% CI: 0.03–0.27) for linearity $=0.021$] (Figure 2(a)), and this association did not differentiate between follow-up DS status (Figure 2(b)). Correlation (adjusted for age, sex, years of education, and diabetes) between baseline and follow-up LTPA split by follow-up DS status was for participants with DS 0.52 (95% CI: 0.34–0.71) and 0.32 (95% CI: 0.18–0.46) for participants without DS, respectively.

At the follow-up, among the participants without DS, 34% had low, 30% had moderate, and 36% had high physical activity levels (expressed as IPAQ grade). Among those participants with DS, 37% had low, 32% had moderate, and 32% had a high physical activity classification.

Discussion

This study showed that baseline LTPA levels did not predict an improvement in DS among depressive patients at a five-year follow-up. However, baseline LTPA did predict future total physical activity. Moreover, baseline depressive diagnosed participants who still had DS at the five-year follow-up had fewer years of education and poorer health status (more diabetes and DS) at baseline.

Our study findings are in line to a certain extent with some earlier studies. While physical activity has been found to be an effective method of reducing depression, as well as preventing and protecting against depression [1–3], in our study sample, earlier physical activity levels were not related to a subsequent recovery from depression. On the other hand [25], for example, found in their recent study after a two-year follow-up that physical activity predicts future remission of depressive disorder only in younger adults but not in older depressive patients. Our findings are in line with the findings from [25] on older depressive patients. Also, although physical activity can be a protective factor and effective treatment method for depression, it might not be favorable for everyone. Some individuals may benefit less from physical activity and exercise in the same way that some benefit less from other treatments of depression, such as medication, due to different biological, clinical, psychological, and/or social moderators [26]. Again, autonomous motivation and social support from the patient's friends and

family, as well as from health professionals, may play the key role in exercise adherence [26]. From earlier studies, we also know that the course of depression fluctuates and the severity of DS can vary over time [27–29].

Our finding that baseline LTPA was associated with the future total physical activity level is consistent with findings that physical activity stays relatively stable and the level of physical activity rarely changes over time [25]. The physical activity level of depressed patients might also reflect a trait (feature of one's personality) instead of the state of depression [25]. Also, according to a study by [20], as compared with adulthood physical activity, an earlier physical activity history does not contribute to the progression of DS to a greater degree. Further, there is evidence of a longitudinal and bi-directional relationship between a low physical activity and the severity of depression and anxiety symptoms and odds for disorders chronicity [31]. In this light, our findings are important because being physically active can create better odds of successful protection from depression, and thus, health professionals should encourage their patients to engage in physical activity by endorsing it in everyday life and as an add-on to other treatments for depression. Once a physically active lifestyle has been gained and stabilized, the probability of it being a permanent situation is more plausible [25].

Earlier studies have shown that depression is often associated with other illnesses [32,33], a poorer living environment, and lower socioeconomic status [34,35]. This kind of association was found in our study as well with years of education, diabetes, and DS. Our finding that depressed patients had more diabetes is in line with the recent knowledge that diabetes is a risk factor for depression and that depression is more prevalent in people with diabetes [36]. In addition, the fact that depression may remain underdiagnosed when comorbid with diabetes underlines the importance of properly identifying and treating both illnesses [36].

In Finland, LTPA has increased in recent decades among the general population, but total physical activity has remained fairly stable [37]. According to the recent Finnish national FinHealth 2017 survey, one-third of the Finnish adult population were physically inactive, and approximately only half of the population achieved the national recommended physical activity level [38]. Given that in our study sample, only one-third of the participants achieved the same level, it seems that depressive patient physical activity is lower than in the overall Finnish population. This could be one reason for the diminishing effects of physical activity on future DS among our study sample.

Overall, in light of earlier studies, it seems that factors other than physical activity alone influence the remission of DS. Patient traits, socioeconomic background, and other somatic illnesses such as diabetes might be, together or individually, more important elements of individual well-being and health than is a physically active lifestyle. Nonetheless, promoting physical activity is especially important because it certainly has positive impacts on overall health and well-being and seldom has any adverse effects.

Because many recent studies have focused mainly on the immediate or short-term effects of physical activity on depression, the main strength of this study is its five-year longitudinal design, nationally representative capture, and depression confirmation. In this study, we also had a nationally representative study population with a catchment area of 274,000 inhabitants. Another study strength is that we used a structured diagnostic interview (MINI) to confirm depression. The main limitations lie in the possibility of LTPA and total physical activity overestimation by participants and the study results' generalizability. As the study population included only patients 35 years or older, the generalizability to younger persons is questionable. Also, follow-up was at only one time point, which can be considered a weakness because many depression patients cycle between periods. Again, one study weakness is the lack of data on intra- and inter-observer variability.

Conclusion

Baseline LTPA did not affect the five-year prognosis of depression among depressed patients in a Finnish adult population. However, as baseline LTPA predicted future physical activity, those in clinical practice should consider including it as a part of overall health management and the treatment of depression.

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