



Long distance ski racing is associated with lower long-term incidence of depression in a population based, large-scale study

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ABSTRACT

Physical activity has been proposed to be beneficial for prevention of depression, although the importance of exercise intensity, sex-specific mechanisms, and duration of the effects need to be clarified. Using an observational study design, following 395,369 individuals up to 21 years we studied whether participation in an ultralong-distance cross-country ski race was associated with lower risk of developing depression. Skiers (participants in the race) and matched non-skiers from the general population (non-participants in the race) were studied after participation (same year for non-participation) in the race using the Swedish population and patient registries. The risk of depression in skiers ($n = 197,685$, median age 36 years, 38% women) was significantly lower, to nearly half of that in non-skiers (adjusted hazard ratio, HR 0.53) over the follow-up period. Further, a higher fitness level (measured as the finishing time to complete the race, a proxy for higher exercise dose) was associated with lower incidence of depression in men (adjusted HR 0.65), but not in women. Our results support the recommendations of engaging in physical activity as a preventive strategy decreasing the risk for depression in both men and women. Furthermore, the exercise could reduce risk for depression in a dose-dependent matter, in particular in males.

1. Introduction

Depressive disorders are highly prevalent in most societies all around the world. Globally, depression constitutes one of the largest burdens of disability (Collaborators, 2016). The lifetime prevalence depression is estimated to be 5–10% (Kessler et al., 2009) and together with other mental disorders accounting for 21–32% of the total years lived with disability (Vigo et al., 2016). Even though several pharmacological treatment strategies targeting depression, including selective serotonin reuptake inhibitors, have become available over the past century, many patients still suffer from side-effects such as sexual dysfunction and gastrointestinal problems (Wang et al., 2018; Souery et al., 2007) or lack of effects (Rush, 2007). Numerous studies have pointed out physical activity as a promising strategy to reduce the burden of depressive disorders (Schuch et al., 2018; Pedersen and Saltin, 2015). Interestingly, interventional studies have shown that

exercise can reduce symptoms of depression (Hennings et al., 2013; Wegner et al., 2014; Khanzadea et al., 2015; Stanton et al., 2016). However, there are also studies, showing no additional effect of exercise compared to antidepressant medication alone (Danielsson et al., 2013; Kvam et al., 2016) or cognitive behavioral therapy alone (Bernard et al., 2018).

Furthermore, several studies have proposed exercise to have protective effects when it comes to development of depression (Sui et al., 2009; Jonsdottir et al., 2010; Aberg et al., 2012; Mammen and Faulkner, 2013; McPhie and Rawana, 2015; Schuch et al., 2018). A recent meta-analysis of prospective cohort studies, demonstrated that physical activity was protective against development of depression across all ages and also across different geographical regions (Schuch et al., 2018). Conversely, it has been pointed out that the association between higher level of physical activity and subsequent lower incidence of depression might be due to the fact of reverse

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causation. Individuals already having undiagnosed depression tend to be less engaged in physical activities as a consequence of symptoms such as reduced mood (Vancampfort et al., 2015; Busch et al., 2016). Indeed, exercise has to the large part been proposed as a treatment for individuals suffering from mild to moderate depression and not for more severe cases, where failure of adherence to exercise programs due to depressive symptoms might be an important limitation (Vancampfort et al., 2015; Firth et al., 2016).

To date, many studies investigating the effects of physical activity are conducted on small study populations and only have a few years of follow-up time (Khanzada et al., 2015; Schuch et al., 2018). This might increase the risk of biased results if several participants reporting low physical activity at baseline, due to yet undiagnosed depression, indeed get diagnosed within the next few years. Therefore, studies taking these potential barriers to engage in exercise in the initial phase of a yet undiagnosed depressive disorder into account are of great importance.

Further, the impact of fitness level or exercise dose on risk of depression has not been thoroughly investigated and existing studies so far show inconsistent results (Noh et al., 2015; Balchin et al., 2016; Harvey et al., 2018; Helgadottir et al., 2017). Some studies show that only exercise above a certain intensity have beneficial effects (Noh et al., 2015; Balchin et al., 2016), whereas others reveal no impact of intensity levels (Harvey et al., 2018). There are even studies in which the most beneficial effects are seen in exercise of lower intensities (Helgadottir et al., 2017). However, none of these studies analyze the impact of exercise intensity on incident depression in both men and women separately. Depression affects women more and it has been shown that the effect of physical activity on mental disorders might differ between men and women (Mikkelsen et al., 2010). Hence, investigating also the effects of physical activity also in women in a large-scale study with long-term follow up is needed.

To minimize the impact of any possible symptoms of undiagnosed mental illnesses on study results, it is important to follow a large number of subjects over a long time after initial exposure. Increasing the time of follow-up and excluding those who develop mental disorders within the first years after baseline are two ways of decreasing the risk for this type of bias. The aim of this study was to investigate the association between ultralong-distance ski racing and subsequent diagnosis of depression in a large scale, population-based cohort, in a long-term perspective. In addition, we also aimed to investigate the impact of fitness level as a measurement of exercise dosage on depression in men and women separately. As our treated cases, we used participants in the world's largest long-distance cross-country ski race (Vasaloppet). We matched the participants in the ski race with non-skiers from the general population, to include a total of 395,369 subjects in the study. Anderson et al. revealed that 93% of 5000 endurance skiers answering an online questionnaire reported freedom of depression (Anderson et al., 2017). To the best of our knowledge, no prospective studies have investigated the effect of skiing on development of depression. We hypothesized that there would be a lower risk of developing depression in the participants of the ski race compared to the general population that would also manifest long-term after participation.

2. Methods

2.1. Study design

This observational study was approved by the Ethical Review Board in Uppsala, Sweden, Dnr 2010/305. The cases in the study population comprise all Swedes who took part in the world's largest long-distance (30 to 90 km), cross-country ski race (Vasaloppet) between 1989 and 2010 ($n = 197,685$), together with frequency-matched, individuals from the general population ($n = 197,684$) (Supplementary Materials, Fig. 1). Frequency matching was done by Statistics Sweden to draw non-skier controls from the population registry according to age group

(five-year intervals), sex, region of residency, and year of participation in ski race as previously described (Hallmarker et al., 2018). Individuals participating in Vasaloppet were considered physically active and were denominated skiers. According to previous studies, on average, Vasaloppet skiers smoke less, have a healthier diet, and lower mortality than the general Swedish population (Farahmand et al., 2003; Carlsson et al., 2007). The majority of Vasaloppet skiers exercise for at least 4 h a week (Carlsson et al., 2007) and on average they have higher leisure time physical activity than the general Swedish population (Farahmand et al., 2003). In general, Vasaloppet skiers have higher fitness levels, with VO₂max 45–80 ml/kg per minute, compared to around 35 ml/kg per minute in the general population (Hallmarker et al., 2016). To reduce bias due to inability to participate in the race because of poor physical health, all individuals (skiers and non-skiers) with severe disease were excluded as previously described (e.g. cancer, chronic neurologic disease, dementia, heart- and lung disease) (Hallmarker et al., 2016). Participants with dementia (all cause, Alzheimer's disease (AD), vascular dementia (VaD), Parkinson's disease dementia, Lewy body dementia, senile dementia), Parkinson's disease, meningitis/encephalitis, epilepsy, psychiatric disorders (depressive episode, schizophrenia, bipolar disorder, anxiety disorders and mental disorders due to the use of alcohol) were additionally excluded from the study (see Supplementary Material Table 1). If skiers participated in several races, the first race was the only one considered and set as baseline. If a non-skier participated in the ski race after baseline it contributed with data for the skiers population from the time of participation in the ski race until the end of follow-up period.

The participants were monitored for participation as well as finishing time in the race in three categories with finishing time of 100–150, 150–200 and above 200% of the winning finishing time for each sex respectively as previously described (Hallmarker et al., 2015). The finishing time analysis was used as a measurement of physical fitness and a proxy for the more extreme doses of exercise during their preparation before the race, as previously explained (Andersen et al., 2013). Information on date of birth, sex, and education level were derived from Swedish registries (Swedish National Patient Registry for diagnoses and Statistics Sweden for socio-economic data) (Hallmarker et al., 2018). The total study cohort ($n = 395,369$) was followed in the Swedish National Patient Registry (described below) throughout 2010.

2.2. The Swedish national patient registry

Data on psychiatric and somatic diagnoses were retrieved from the Swedish National Patient Registry. Since 1987 it provides information on all primary and secondary diagnoses in patients attending hospital-based care in Sweden. The register covers 99% of all hospital-based diagnoses, both somatic and psychiatric. Primary care diagnoses are not included in the registry, but they are imported into the patient registry as soon as the patient becomes an inpatient. Since 2001, this registry also covers out-hospital diagnoses made in hospital clinics closely related to primary care. Depressive disorders were defined according to the International Classification of Diseases (ICD), tenth revision (ICD10, Socialstyrelsen) or ninth revision (ICD9, Socialstyrelsen). Diagnoses included are depressive episode (F32, F33, F34, F38, F399/296B, 296X, 29620, 29800).

2.3. Statistical analyses

We used R statistical software package for analyses. P-values < 0.05 were considered statistically significant. Demographic data are presented as median and interquartile range (IQR) or numbers (n) and percent (%). Numeric group differences were estimated with Mann-Whitney U test and categorical with Pearson's χ^2 test. Cox regression models were used to compare risk of depression for Vasaloppet skiers vs non-skiers. Risk of depressive disorders are presented as hazard ratios

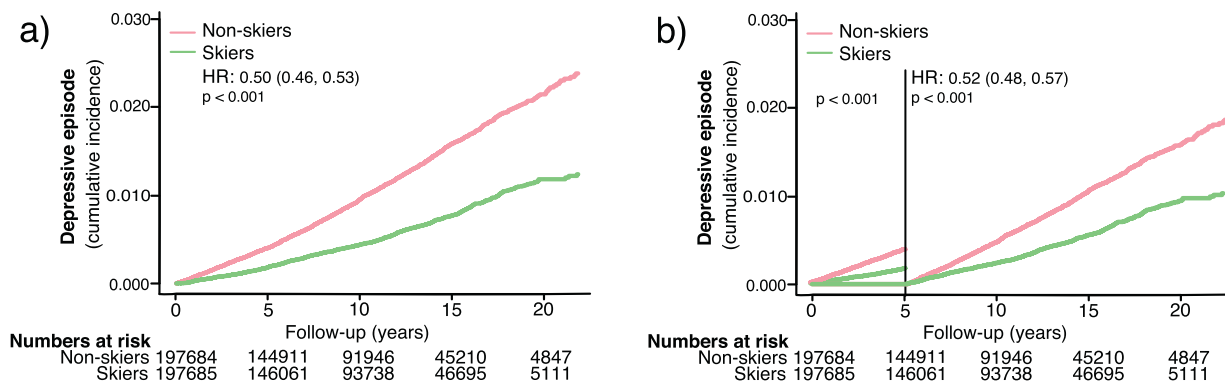


Fig. 1. The risk of developing depressive episodes in Vasaloppet skiers compared to non-skiers (a) and the risk of developing depressive episodes more than 5 years after completing the ski race (b). HR represents hazard ratios from an unadjusted cox regression.

(HR) with 95% confidence intervals (CI). Numbers at risk were derived from survival tables specifying number of individuals entering each five-year interval, as presented in the graph. The time variable was calculated as years between participation in the ski race (and the same year for the matched non-skier) and event or censoring. The event was defined as date of first registered depression diagnosis in the Patient Registry. Censoring appeared when subjects died or at time of register outtake/end of follow-up. Information on date of death for deceased study individuals was available through the Causes of Death Register (CDR), held at the National Board of Health and Welfare. Schoenfeld residuals were modeled graphically to assess the proportionality assumption. Sex was suggested to be a possible effect modifier, therefore men and women were also analyzed separately. The impact of finishing time (fitness level) was assessed by trichotomizing the finishing time to 100–150%, 150–200% and above 200% of the winning finishing time for men and women separately. Adjustments were done for age, sex and education in the adjusted cox model. In sensitivity analyses, all individuals who developed depression within five years of inclusion were excluded.

3. Results

3.1. Ski race participation is associated with lower incidence of depression

Demographic data comparing the Vasaloppet skiers and non-skiers are presented in Table 1. A total of 395,369 individuals were followed over 3975,881 person years. After a median follow-up of 10 (IQR 5–15) years, a total of 3075 individuals were newly diagnosed with depression. The occurrence of comorbidity with other psychiatric disorders did not differ between Vasaloppet skiers and non-skiers (Supplementary Table 2). Participation in the long-distance ski race was associated with a lower risk of developing depression in the follow-up compared to non-skiers (unadjusted HR 0.50, 95% CI 0.46–0.53, Table 2, Fig. 1a). Skiers

Table 2

Association between physical activity and incident mental disorders, based on participation in a long-distance ski race (skiers) compared to non-skiers.

Depressive episode	Unadjusted model	Adjusted model*
Physical activity	HR (95% CI)	HR (95% CI)
Nr events	3075	3040
Non-skiers (Reference)	1	1
Skiers	0.50 (0.46–0.53)	0.53 (0.49–0.58)
Excluding psychiatric diagnoses < 5 years		
Nr events	2029	2003
Non-skiers (Reference)	1	1
Skiers	0.52 (0.48–0.57)	0.56 (0.51–0.62)

HR: hazard ratio, CI: confidence interval.

Cox regression models showing HR for risk of depressive disorders.

* Model adjusted for age, sex, and education.

had higher education than non-skiers (Table 1), but adjustments for age, sex and education, did not alter the results (adjusted cox model, Table 2). The effect remained even when individuals that developed depression within five years of the ski race (baseline) were excluded (unadjusted HR 0.52, 95% CI 0.48–0.57, Table 2, Fig. 1b). Taken together, ski race participation was associated with a relative risk reduction of 50% for developing depression.

3.2. Both male and female Vasaloppet skiers have lower incidence of depression

The association between ski race participation and lower incidence of depression was seen in both men and women (unadjusted HR 0.52, 95% CI, 0.47–0.57 for men and unadjusted HR 0.47, 95% CI, 0.42–0.53 for women, Fig. 2a–b).

Table 1

Characteristics of the study population, presented for the whole cohort and by skiers and non-skiers separately.

	All n = 395,369	Skiers n = 197,685	Non-skiers n = 197,684
Characteristics 1989–2010	Median (IQR) or n (%)	Median (IQR) or n (%)	Median (IQR) or n (%)
Age at baseline, y	36.0 (29.0–46.0)	36.0 (29.0–46.0)	36.0 (29.0–46.0)
Women	149,796 (38)	74,897 (38)	74,899 (38)
Education:			
Primary/elementary school (≤ 8 y)	49,344 (13)	14,538 (7.4)	34,806 (18)***
Secondary school/high school (9–12 y)	17,6571 (45)	76,635 (39)	99,936 (51)
Higher education/university (≥ 13 y)	16,6133 (42)	10,6147 (54)	59,986 (31)
Depression at follow-up	3075	1030	2045***

IQR: interquartile range, y: years, n: numbers.

*** $p < 0.001$. Group difference between skiers and non-skiers, estimated with Wilcoxon test (numeric variables) and Pearson's χ^2 test (categorical variables). Only significant differences are noted in the table.

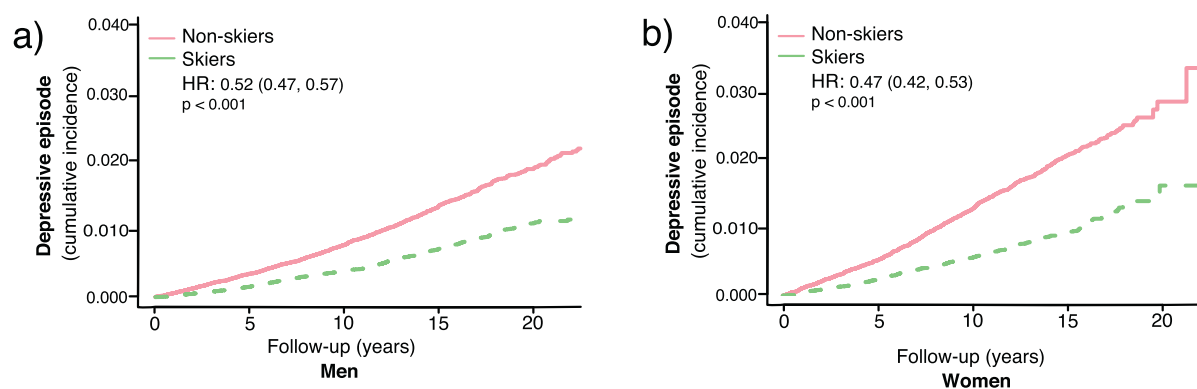


Fig. 2. The risk of developing depressive episodes in Vasaloppet skiers compared to non-skiers in men (a) and women separately (b). HR represents hazard ratios from an unadjusted cox regression.

3.3. The impact of exercise dose on incident depression is sex-specific

Men completing the race with shortest finishing time (a proxy for the effect of extreme exercise) had an even lower incidence of depression compared to slower Vasaloppet skiers (unadjusted HR 0.65, 95% CI, 0.49–0.87, Table 3, Fig. 3a). This was not the case among women, where the finishing time did not have any significant impact (unadjusted HR 1.14, 95% CI, 0.77–1.70, Table 3, Fig. 3b). Adjustments for age, sex and education, did not alter the results (adjusted Cox model, Table 3). These associations remained even when excluding cases that developed depression within the first five years (unadjusted HR 0.61, 95% CI, 0.44–0.86 for men, Table 3, Fig. 3c-d).

4. Discussion

In a large, population-based study on nearly 400,000 individuals, followed over nearly 4 million person years, we found that higher baseline participation in physical exercise was associated with a significant lower risk of the development of depression, one of the most prevalent psychiatric disorders. Our results were highly significant and showed relative risk reductions of around 50% for depression. Of high importance, our results were the same even when we excluded all cases of depression that occurred during the first five years after the baseline event. This minimizes the risk that our results were due to a selection bias towards more psychiatrically healthy individuals at baseline in the

group participating in the ski race. Furthermore, our analysis of ski race finishing time (a proxy for the level of fitness) revealed a sex-specific impact of the dose of exercise on incident depression, where we found fast male Vasaloppet skiers to have lower risk of depression compared to slow male skiers.

Our study setup offered a unique possibility to study the effect of a physical active life-style on the development of depression in a very large study population over a long period of time.

We used the unique national patient registries available in Sweden, which is one of the largest in the world covering diagnoses set on the entire population since 1964.

By use of this registry, we were able to exclude all subjects (skiers and non-skiers) that had psychiatric diseases or somatic disorder that could impact physical activity prior to the baseline participation in the long-distance ski race (Hallmarker et al., 2016) (See supplementary material, Table 1). We carefully matched the Vasaloppet skiers with non-skiers based on sex, age and geographic location. Psychiatric diagnoses set after baseline for participation in the world's largest ski race were extracted. This enabled us to follow the participants up to 21 years after participation. As such, this is the largest population wide epidemiological study to date including both men and women, confirming an effect of physical exercise on the later development of depression seen in previous studies (Aberg et al., 2012; Mammen and Faulkner, 2013; Khanzada et al., 2015; Schuch et al., 2018). In addition to these studies, our study takes into consideration the impact of exercise dose and

Table 3
Association between ski race finishing time and incident mental disorders in men and women.

Depressive episode	Men	Women
Finishing time (% of winning time)	HR (95% CI)	HR (95% CI)
Unadjusted model		
+ 200% (Reference)	1	1
150–200%	0.94 (0.78, 1.14)	0.84 (0.67, 1.05)
100–150%	0.65 (0.49, 0.87)	1.14 (0.77, 1.70)
Adjusted model*		
+ 200% (Reference)	1	1
150–200%	0.91 (0.75, 1.09)	0.83 (0.66, 1.04)
100–150%	0.65 (0.49, 0.87)	1.11 (0.74, 1.66)
Excluding psychiatric diagnoses <5 years		
Unadjusted model		
+ 200% (Reference)	1	1
150–200%	0.94 (0.75, 1.17)	0.83 (0.62, 1.11)
100–150%	0.61 (0.44, 0.86)	1.12 (0.69, 1.82)
Adjusted model*		
+ 200% (Reference)	1	1
150–200%	0.89 (0.71, 1.11)	0.84 (0.63, 1.12)
100–150%	0.60 (0.43, 0.84)	1.13 (0.69, 1.86)

HR: hazard ratio, CI: confidence interval.

Cox regression models showing HR for risk of depressive disorders in men and women respectively.

* Model adjusted for age and education.

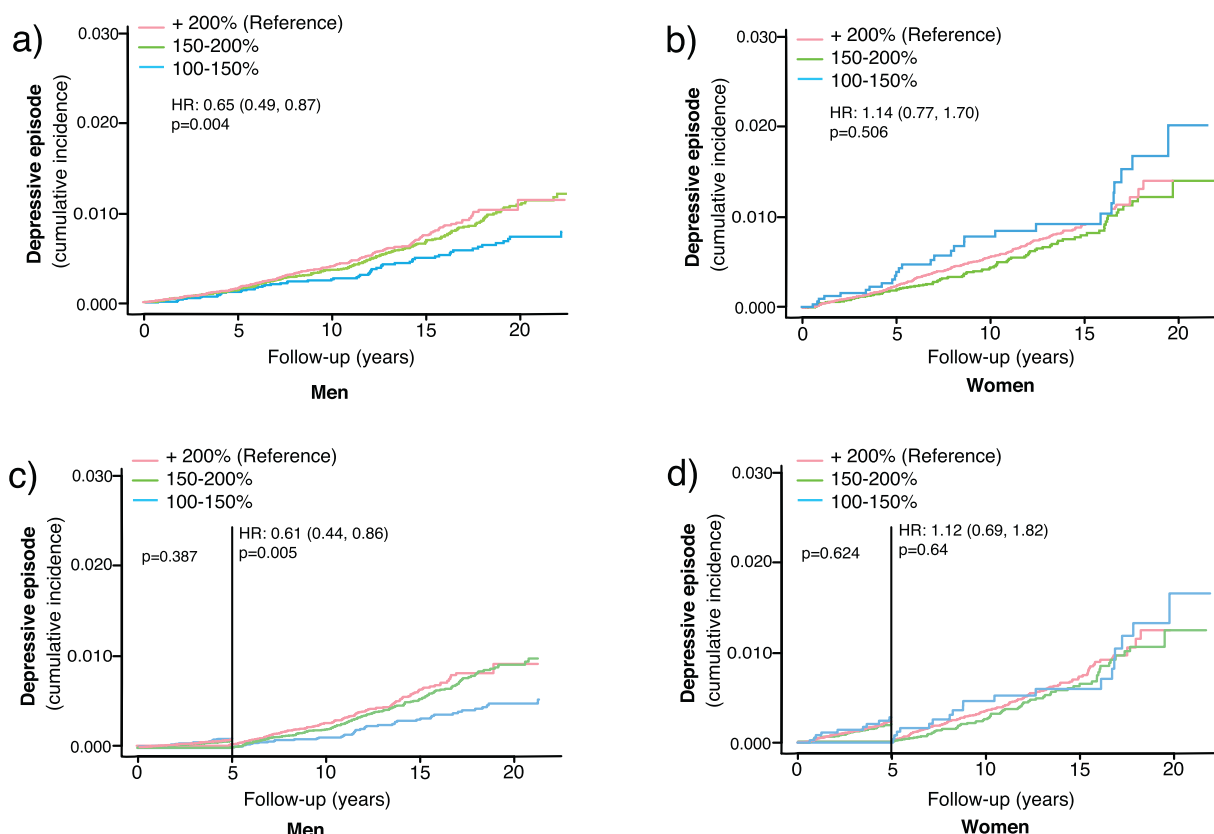


Fig. 3. The impact of ski race finishing time on the risk of developing depressive episodes in skiers in men (a) and women separately (b). The impact of ski race finishing time on the risk of developing depressive episodes more than 5 years after completing the ski race in men (c) and women (d). HR represents hazard ratios from an unadjusted cox regression for the fastest (100–150% of winning finishing time) group, using +200% as the reference group.

differences between men and women.

Our study is important because it provides new information about the effect of physical activity on development of depressive disorders in both men and women, in addition to the discoveries made by Åberg et al. Indeed, in their study, following over 1 million men in the Swedish population for a period of up to 40 years, physical fitness was associated with a lower incidence of depression (Åberg et al., 2012). However, their study did not assess the effects of physical activity on development of depression in women. This additional analysis included in our study is of great importance, since the incidence/prevalence is significantly higher in women. Furthermore, the effect of physical activity on mental disorders may differ between men and women (Mikkelsen et al., 2010). Importantly, we found an association of physical activity on incidence of mental disorders in both men and women. Our study revealed that the impact of physical activity on the risk for depression lasts over long time, and remained even when we excluded cases during the first 5 years following inclusion in the study (Table 2). This is in line with a recent study by Choi et al., which investigated the relationship between physical activity and depression (Choi et al., 2019). They demonstrated additional evidence for objectively measured physical activity to be protective against later risk for depression.

Our study demonstrates an impact of the dose of exercise on the incidence of depression. Interestingly, this effect differed between men and women. Notably, men with higher dose of exercise had even lower incidence of depression, whereas no such tendency could be seen for women in our study. This emphasizes the importance of evaluating the effect of physical exercise in men and women separately. Our findings on the impact of exercise dose on depression are in line with other studies investigating the effect on depressive symptoms (Asztalos et al., 2010; Balchin et al., 2016; Craft et al., 2014; Helgadottir et al., 2017; Meyer et al., 2016). Indeed, higher intensities of exercise has been

shown to specifically reduce depression in men (Balchin et al., 2016), whereas the intensities did not matter for women (Meyer et al., 2016). In a randomized controlled trial demonstrating that the most beneficial effects on depression was seen in the group with the lightest form of exercise, 74% of the participants were women (Helgadottir et al., 2017). The reasons for these discrepancies between men and women were not possible to investigate in our study. However, it has been shown that the reasons for having high levels of physical activity among women might be a better predictor of mental well-being than the exercise per se (Craft et al., 2014). Notably, women reporting aims such as weight loss and body toning as reasons for exercising tended to have lower quality of life compared to those reporting such as improving health as reasons (Craft et al., 2014). Interestingly, the same pattern was not detected in men. In addition, only self-reported level of physical activity and not objectively measured fitness level was shown to be related to depressive symptoms (Lindwall et al., 2012). Hence, it is tempting to speculate that psychological reasons behind the exercise results might be a confounding factor and explain at least some of these differences, although we lack this kind of data in our study. To that adds also a need of gaining more knowledge in the potential mechanisms behind the beneficial effects of exercise and how these might differ between men and women.

Even though this epidemiological study did not attempt to assess the mechanisms by which exercise may exert protective effects on the development of depression, many experimental studies have done so in the past. A large wealth of studies indicate that inflammation is involved in the pathogenesis of neuropsychiatric disorders (Hallberg et al., 2010; Shelton et al., 2011; Dahl et al., 2014; Wang and Miller, 2018). Thus, a main proposed mechanisms by which exercise might be protective might be by reducing the amount of inflammation in the body (Hallberg et al., 2010), and ultimately in the brain. Other

studies indicate that beneficial effects of exercise might be mediated by increased levels of neurotrophic factors (Callaghan et al., 2017). Exercise may also affect the regulation of the hypothalamic pituitary adrenal (HPA) axis (Svensson et al., 2015; Phillips, 2017), known to be altered in depression (Lopez-Duran et al., 2009). Further, exercise is also known to induce endorphins, proven to contribute to the perception of well-being (Mikkelsen et al., 2017). However, long-term effects of exercise on molecular mechanisms involved in depression still need to be elucidated (Millischer et al., 2017). To further address these questions, animal models are of great importance in the first phase. In addition to the above-mentioned molecular effects, exercise also have significant psychological and psychosocial effects as previously discussed by Nieman et al. (Nieman, 2002). Importantly, Nieman mention how exercise might facilitate distraction from negative thoughts and also how it contributes to the persons increased perceived self-significance as being physically active is regarded as doing something good according to the society.

Limitations of the study include that we do not have any detailed information about the physical activity in the cohort. The information we use as a proxy of physical activity is the baseline participation in the long-distance ski race (30–90 km). The race is physically demanding and requires arduous preparation, assuring that the participants in the race had led an active life-style with preparatory exercise long-term prior to the race. It is likely that the reference group of non-skiers thereby to some extent include physically active as well and this may attenuate the true association. However, the exercise habits of the participants in this classical ski race have been characterized and described as more physically active compared to the general population in (Farahmand et al., 2003; Carlsson et al., 2007). Furthermore, as with many other sports, the ski racers spend a substantial amount of time outdoors, being exposed to natural light, a factor associated with reduced risk of depression. A synergistic effect of being outdoor and exercising has been proposed in alleviating depression (Lahart et al., 2019). Natural environment has been shown to improve coping with psycho-physiological stress (Berto, 2014; Ulrich et al., 1991). However, a systematic review revealed that physical activity had a more important effect than light therapy, suggesting that the activity per se is of substantial importance (Cooney et al., 2013). Skiing is a winter activity and individuals with seasonal mood disorders might have difficult to participate. To this adds the possible limitation for those with asthma to participate in skiing. However, recent report indicate that a substantial amount of Vasaloppet skiers manage to participate in the ski race despite having asthma (Nasman et al., 2018). Further, a meta-analysis of prospective studies indicates that it was more likely that having depression predicted subsequent development of asthma than vice versa (Gao et al., 2015). We tried to reduce the impact of the above mentioned potential bias by excluding all individuals diagnosed with depression prior to baseline, and also within the first five years from baseline.

Moreover, our study is based on diagnoses found in the Swedish Patient Registry, which does not cover all diagnoses. Due to the long follow-up time we assume that many diagnoses set in primary care would have been imported to this registry. Another limitation is that our study does not isolate physical activity as a truly independent factor. For instance, it has been shown before that Vasaloppet skiers may have a healthier lifestyle including less smoking and better diet, than a control population of non-skiers (Farahmand et al., 2003; Carlsson et al., 2007). We cannot adjust for smoking, weight or alcohol consumption since that information is not available in the Swedish Patient Registry. However, when we adjust for age, sex and education in our statistical models, the results were not altered. Additionally, we demonstrate that faster Vasaloppet skiers had lower incidence of depression, implicating that the association between physical activity and lower incidence of depression can be attributable to the physical fitness level per se. We used finishing time as a proxy for fitness level/dose of exercise as previously described (Hallmarker et al., 2015). Further, it

has been shown that physical performance level (work output measured in W/kg) before participation in Vasaloppet predicts the finishing time of the skier (Mygind et al., 2015). However, it should be mentioned that also other factors, such as race experience and pacing strategy affects the finishing time (Carlsson et al., 2016; Nikolaidis et al., 2018).

Last, but not least, if these findings should be implemented in healthcare, one also has to take into account the reasons preventing patients with depression from engaging in physical activity. Most researchers agree that physical activity is beneficial for this group of patients, but in order to find strategies for motivating patients in engaging in more physical activities, factors preventing them from doing so must be determined more in detail. In our study, we take this factor into account by excluding patients with psychiatric disorders prior to baseline and also cases newly diagnosed within the first five years after baseline. Nevertheless, this is important for reducing potential bias also when designing future studies.

In conclusion, our study on 395,369 individuals in the Swedish population indicates that participating in this long distance ski race is associated with a substantially lower risk of developing depression. The effect was of similar size in men and women, and persisted even when removing the first five years after baseline from the analysis. In addition, we detected an impact of exercise dose on incidence of subsequent depression that differed between men and women. Our results indicate that the effects of physical activity may be greater than previously estimated and warrants additional experimental studies characterizing the neurobiological mechanisms by which exercise impacts mental health.

Data statements

Database for the Vasaloppet cohort with disease incidence belong to Uppsala Clinical Research Center and can be made available upon request.

Declaration of Competing Interest

No author reports conflict of interests.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2019.112546.

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