Associations of exercise frequency and cardiorespiratory fitness with symptoms of depression and anxiety - a cross-sectional study of 36,595 adults

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ABSTRACT

Introduction: Regular exercise has been associated with better mental health, but relationships of cardiorespiratory fitness (CRF) with mental health symptoms are less certain. We conducted a large cross-sectional study to examine associations of exercise frequency and objectively measured CRF with symptoms of depression and anxiety.

Methods: Data originates from the Swedish Health Profile Assessment (HPA) database, a general health assessment offered to all employees working for companies or organizations connected to occupational and health services. Participants reported the frequency (last 30 days) of structured exercise and completed a 6-min VO₂max test on a cycle ergometer to determine CRF. Data on relevant covariates including leisure-time sedentary behavior were also collected. The study outcome was self-reported frequent (often/very often) symptoms of depression/anxiety.

Results: Complete data from 36,595 participants were analyzed (41% female, mean age = 42 years). In fully-adjusted models, compared to those in the lowest exercise frequency category (never/sometimes), those exercising 1–2 times/week and ≥3 times/week had 0.75 (95% CI = 0.68–0.82) and 0.72 (95% CI = 0.65–0.79) lower odds of reporting frequent depression/anxiety symptoms, respectively. For CRF, crude models indicated a dose-response with the odds of frequent depression/anxiety symptoms reducing with higher CRF levels (low versus medium and high, respectively). No associations were found after adjustment for leisure-time sedentary behavior.

Conclusions: Exercising at least 1–2 times per week is associated with lower odds of depression/anxiety symptoms. Leisure-time sedentary behavior attenuates relationships of CRF with depression/anxiety symptoms.

1. Introduction

Depression and anxiety are prevalent psychiatric conditions associated with marked socio-occupational impairment and somatic co-morbidity (Correll et al., 2017), including a high prevalence of cardiovascular disease (Batelaan, Seldenrijk, Bot, van Balkom, & Penninx, 2016). Mood disorders are often preceded by a ‘prodromal’ period, characterized by increasingly frequent symptoms of sadness, lowered mood, and heightened anxiety (Karsten et al., 2011). Universal prevention strategies commonly target these sub-threshold symptoms, with the aim of curtailing transitions to major depression or an anxiety disorder (Beyond Blue, 2020).

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Physical activity and its sub-set, exercise, are widely promoted as effective prevention strategies for depression and anxiety (Hallgren et al., 2017; McDowell, Gordon, Andrews, MacDonnacha, & Herring, 2018). In a review of prospective studies (n = 49; 266,939 participants) Schuch et al. (2018) found that, compared to those with low levels of physical activity, those with high levels had lower odds of developing depression (AOR = 0.83, 95% CI = 0.79–0.88). Comparable effect sizes were seen across different age groups and geographic regions. Beneficial relationships have also been reported in prospective studies of anxiety symptoms and disorders (McDowell, Dishman, Gordon, & Herring, 2019). A recent Mendelian randomization study (Choi et al., 2019), and meta-analysis of randomized controlled trials (Gordon et al., 2018; Gordon, McDowell, Lyons, & Herring, 2017), suggest causal relationships between exercise and mental health symptoms.

Despite this evidence, there is active discussion in the literature concerning the relative importance of exercise ‘dose’ and the role of cardiorespiratory fitness (CRF) in these relationships. Exercise dose refers to the combined intensity, duration and frequency of exercise. Of these three components, the frequency of exercise is particularly important in helping novice exercisers to establish and maintain new lifestyle routines (Lachman, Lipsitz, Lubben, Castaneda-Sceppa, & Jette, 2018). Regular exercise could have stronger neurobiological effects than infrequent exercise (Dunn & Jewell, 2010; Dunn, Trivedi, Kampert, Clark, & Chambless, 2005). From a behavioral perspective, regular exercise might also have stronger reinforcing properties, leading to better adherence and ultimately greater psychological benefits (Hallgren, Moss, & Gatin, 2010). While several experimental studies have assessed the effects of exercise dose or exercise intensity on depressive symptoms (Dunn et al., 2005; Helgadottir, Hallgren, Ekblom, & Forsell, 2016), observational studies of associations between exercise frequency and symptoms of depression and anxiety are scarce (McDowell et al., 2019; Schuch et al., 2018). These studies could inform mental health promotion strategies, and potentially enhance the effectiveness of exercise prescriptions for those presenting with symptoms of mood disorders.

Regular exercise promotes higher CRF and both factors are shown to independently have beneficial effects on somatic health (Myers et al., 2015). The extent to which these related factors also confer independent mental health benefits is unclear. A small number of observational studies have examined associations of CRF with depression and anxiety symptoms, but their findings have been inconsistent. In one systematic review and meta-analysis (Papasavvas, Bonow, Alhashemi, & Micklewright, 2016) four cross-sectional studies were identified, with sample sizes of 37, 53, 131 and 2428, respectively. Two of the included studies found an inverse association between higher CRF and depression (Rice, Katzel, & Waldstein, 2010; Valtonen et al., 2009), while two studies showed no association (Raso, Natale, Duarte, Greve, & Shephard, 2012; Stewart et al., 2003). Recently, Kendola, Ashdown-Franks, Hendrikse, Sabiston, and Stubbs (2019) systematically evaluated the relationship between CRF and the incidence of common mental health disorders in prospective cohort studies. Compared to high CRF, low and medium CRF were associated with 47% and 23% greater risk of these disorders, respectively. However, only four eligible studies were included and heterogeneity was substantial in the meta-analysis. Moreover, one study used an estimated CRF algorithm (Shigdel, Stubbs, Sui, & Ernstsen, 2019), and two studies involved the same participant sample (Aberg et al., 2012; Nyberg et al., 2018), highlighting the need for more research using objective measures of CRF. If changes in CRF are associated with mental health symptoms, then CRF might be an important biomarker to identify at-risk groups or a benchmark for exercise-based treatments.

Several factors are shown to be associated with both exercise and depressive symptoms, including body mass, smoking, and pain (Craft, Perrin, Freund, & Culppepper, 2008). Recently, we have also shown that leisure-time sedentary behaviors (e.g. TV-viewing) are inversely associated with depressive symptoms after adjustment for physical activity levels (Hallgren et al., 2018). This suggests that sedentary behavior is an important co-variante in studies of relationships between exercise and mental health.

Further studies measuring associations of both exercise frequency and CRF with symptoms of depression and anxiety are needed to determine their relative importance in the prevention of common mental health symptoms. We examined cross-sectional relationships of exercise frequency and objectively measured CRF (assessed as maximal oxygen consumption, VO2max) with self-reported symptoms of depression and anxiety. As these symptoms are more prevalent among females (McLean, Asmaani, Litz, & Hofmann, 2011; Parker & Brotchie, 2010), and sex differences in CRF have been reported previously (Ekblom-Bak et al., 2019), a secondary aim was to explore possible sex differences in these relationships.

2. Materials and methods

2.1. Study population

Data originate from the Swedish Health Profile Assessment (HPA) database, managed by the HPI Health Profile Institute (Stockholm, Sweden: www.hpihealth.se/). HPA includes a one-page questionnaire about lifestyle and health experiences during the last 30 days, measurement of anthropometrics and blood pressure, estimation of VO2max from a submaximal fitness test on a cycle ergometer, and a brief dialogue with a HPA ‘coach’ (with qualifications in allied health science) to promote wellbeing. The HPA is offered nationally to employees working for companies or organizations connected to occupational (e.g. employee wellness, ergonomics and occupational therapy) or health related services. Participation is voluntary and free-of-charge. Although HPA has been running since 1976, we based our analyses on data collected from January 2017 (when questions on relevant co-variates were first introduced) to June 2019. The total initial sample comprised 50,264 participants before removal of missing co-variante data (described below). The final fully adjusted sample included 18,429 unique cases. The original study complies with the guidelines of the Declaration of Helsinki. The Research Ethics Vetting Board in Stockholm approved the original study and all subjects gave informed consent. Informed consent was obtained from participants after the procedure was fully explained.

2.2. Study outcome: frequent symptoms of depression and anxiety

The primary outcome was assessed with a single question: ‘During the past 30 days...I experience worry, depressed mood, or anxiety...’ with five response alternatives; Never, Rarely, Sometimes, Often, Very often. As previously reported (Hallgren, Nguyen, et al., 2020b), the last two categories were merged and coded as ‘1’ indicating frequent symptoms of depression/anxiety. The remaining responses were merged and coded as ‘0’ (i.e. does not have frequent symptoms of depression/anxiety).

2.3. Exposures

Exercise frequency: This was assessed with the question: ‘During the past 30 days...I exercise/train...’ with eight response alternatives; Never, Sometimes, 1 time/week, 2 times/week, 3 times/week, 4 times/week, 5 times/week, >6 times/week. Based on the distribution of these scores, which included low frequencies in the highest two categories, these were re-coded as: Never/sometimes, 1–2 times/week, and >3 times/week.

Cardiorespiratory fitness: This was assessed as VO2max, expressed as ml/min/kg, estimated from heart rate response after completing the Åstrand 6-min submaximal exercise test on a Monarch cycle ergometer (Åstrand, 1960). VO2max test scores were divided into three groups (low, medium and high) based on the inter-quartile range. In previous validation studies on adult population samples, we have shown small and
non-significant mean differences between estimated VO$_{2\text{max}}$ using the Åstrand test and directly measured VO$_{2\text{max}}$ during treadmill running (Björkman, Eklom-Bak, Ekblom, & Eklom, 2016).

2.4. Covariates

Based on previous evidence of associations of exercise and CRF with depression (Hallgren, Nguyen, et al., 2020b; Zhai, Zhang, & Zhang, 2014) and anxiety (Teychenne, Costigan, & Parker, 2015), the variables listed below were included in the statistical models. Furthermore, in light of recent studies showing robust inverse associations between leisure-time sedentary behavior and depression (Huanga, Gana, Wang, Caoa, & Lu, 2019), this variable was also included to explore possible attenuating effects.

**Age and sex:** These were self-reported and included as continuous and categorical variables, respectively.

**Education level:** This was not directly assessed in the HPA survey, but derived by converting occupation codes from the Swedish Standard Classification of Occupation (2012) into three education levels: Primary school, Secondary school, University/vocational. A detailed description of the conversion method is presented elsewhere (Eklom-Bak, Bak, Eklom, Anderson, Wallin, & Eklom, 2018).

**Body mass index:** Weight was assessed with a calibrated scale in lightweight clothing to the nearest 0.5 kg. Height was measured to the nearest 0.5 cm using a wall-mounted stadiometer. With these two variables, body mass index (BMI; kg/m$^2$) was calculated, then categorised according to the WHO’s classification for adults; normal weight (<25), overweight (25–<30), and obese (≥30).

**Smoking:** This was assessed by asking participants how often during the past 30 days they smoked tobacco (cigarettes), with the response alternatives: ≥20/day, 11–19/day, 1–10/day, Occasionally, Never. The first three responses were merged as ‘daily smokers’ (versus occasional, and non-smoker).

**Use of pain medication:** This was assessed with the question ‘During the past 30 days… I use pain medicines…’ with five response alternatives (Very often, Often, Sometimes, Rarely, Never). This question was included as a continuous variable.

**Leisure-time sedentary behavior:** This was assessed with the question ‘During the past 30 days… I sit still during my leisure-time…’ with five response alternatives: Almost always, 75% of the time, 50% of the time, 25% of the time, Almost never. Due to the small proportion of responses to the lowest and highest categories, these were merged into: high (≥75% of the time), medium (50% of the time), and low (<25% of the time).

2.5. Statistical analyses

Baseline characteristics of the fully adjusted sample were calculated using descriptive statistics (mean, standard deviation (SD), percentage). To assess associations of exercise and CRF with frequent symptoms of depression/anxiety, data were analyzed in two steps. First, separate logistic regression models were run to assess the crude, partly-adjusted (Model 2: age, gender, smoking, pain medication, BMI), and fully-adjusted (Model 3: model 2 plus leisure-time sedentary behavior) associations of each exposure variable (i.e. exercise frequency and CRF) with the primary outcome. These are shown as odds ratios (ORs) with 95% confidence intervals (CIs) and corresponding p-values. To assess a potential dose-response relationship between exercise frequency and symptoms of depression/anxiety, ‘Never/sometimes’ was used as the reference category and compared to the remaining two categories; 1–2 times/week, and ≥ 3 times/week. Similarly, the ‘Low’ CRF group was used as the reference category and compared to ‘Medium’ and ‘High’. Recognizing that both CRF levels and the prevalence of depression/anxiety symptoms may differ by sex (Eklom-Bak et al., 2019; Parker & Brotchie, 2010) we included a sex interaction term in the partly (Model 2) and fully-adjusted analyses (Model 3). In a second analytic step, fully-adjusted models were run separately within each of the three exercise frequency and CRF categories, respectively. This enabled associations of exercise frequency with symptoms of depression/anxiety to be assessed within low, medium, and high CRF levels. Analyses were performed using SPSS version 25, and R version 3.5.2.

3. Results

3.1. Missing data

Of the initial sample consisting of 50,264 people, missing data on relevant co-variates ranged from 0.1% (Age) to 36% (CRF). For the Education variable, 52% of cases were missing. This occurred due to the process (described above) of converting occupational codes into education levels. As some occupations could not be coded, the conversion process was not always possible. We therefore conducted two sets of analyses, (1) primary analyses without the Education variable included, shown below (n = 36,595), and (2) sensitivity analyses with the Education variable included (n = 18,429). Results from sensitivity analyses are shown in Supplementary Table 1 (exercise frequency) and 2 (CRF), respectively. Differences between participants with and without the Education variable are shown in Supplementary Table 3.

3.2. Participant characteristics

Characteristics of the study sample are shown in Table 1. Participants were predominantly middle-aged (mean age = 41.7 years, SD = 11.5)

| Characteristic                             | n (%)   |
|--------------------------------------------|---------|
| Gender (Female), n (%)                     | 15,077 (41.2) |
| Age mean (SD); [range]                     | 41.7 (11.5); [16–80] |
| Education, n (%)                           |         |
| Primary school                             | 1427 (3.9) |
| Secondary school                           | 18,187 (49.7) |
| University                                 | 16,980 (46.4) |
| Smoking status, n (%)                      |         |
| Non-smoker                                 | 30,703 (83.9) |
| Occasional smoker                          | 3220 (8.8) |
| Daily smoker                               | 2671 (7.3) |
| Body Mass Index (BMI), n (%)               |         |
| Normal weight                              | 16,174 (44.2) |
| Overweight                                 | 13,832 (37.8) |
| Obese                                      | 6587 (18.0) |
| Pain medication, n (%)                     |         |
| Never                                      | 7831 (21.4) |
| Rarely                                     | 19,139 (52.3) |
| Sometimes                                  | 7209 (19.7) |
| Often                                      | 1610 (4.4) |
| Very often                                 | 805 (2.2) |
| Leisure-time sedentary behavior, n (%)     |         |
| Low (<25% of the time)                     | 19,431 (53.1) |
| Medium (50% of the time)                   | 12,552 (34.3) |
| High (>75% of the time)                    | 4611 (12.6) |
| Exercise frequency                         |         |
| Never/Sometimes                            | 11,820 (32.2) |
| 1-2 times/week                             | 10,905 (29.8) |
| ≥ 3 times/week                             | 13,869 (37.9) |
| VO$_{2\text{max}}$ ml/min/kg; mean (SD), [range] | 35.8 (10.0), [15.0–77.9] |
| Cardiorespiratory fitness (VO$_{2\text{max}}$) categories |         |
| Low (14.9–28.3 ml/min/kg)                  | 9148 (25.0) |
| Medium (28.4–41.7 ml/min/kg)               | 18,297 (50.0) |
| High (41.8–77.9 ml/min/kg)                 | 9148 (25.0) |
| Frequent symptoms of depression/anxiety No (Never/Rarely/Sometimes) | 33,594 (91.8) |
| Yes (Often/Very often)                     | 3001 (8.2) |
and there were more males (58.8%). Approximately half of the sample was university educated, and the majority were non-smokers. In total, 8.2% of the sample reported experiencing frequent ('Often/Very often') symptoms of depression/anxiety (11.6% males; 5.8% males). Thirty-two percent of the participants exercised 'Never/Sometimes', 29.8% exercised 1–2 times/week, and 37.9% exercised ≥3 times/week. Cardiorespiratory fitness scores were normally distributed and comparable to other population based surveys of Swedish adults (Ekblom, Engstrom, & Ekblom, 2007). CRF values did not differ significantly between males and females at any level (mean score, low, medium, or high).

### 3.3. Associations of exercise (last 30 days) with frequent symptoms of depression and anxiety

In crude models, a dose-response relationship was found. Compared to those in the lowest exercise frequency category (Never/sometimes), those exercising 1–2 times/week and ≥3 times/week had 0.67 (95% CI = 0.62–0.74) and 0.56 (95% CI = 0.52–0.62) lower odds of reporting frequent symptoms of depression/anxiety, respectively. In partly-adjusted models, these results remained stable. In fully adjusted analyses (Fig. 2), mean CRF scores (total and within each of the three CRF categories) did not differ significantly between males and females. The sex interaction term was not significant in any models (p > 0.32).

### 3.4. Associations of cardiorespiratory fitness with frequent symptoms of depression and anxiety

In crude models, compared to those with low CRF, those with medium and high CRF had 0.88 (95% CI = 0.81–0.97) and 0.86 (95% CI = 0.77–0.95) lower odds of reporting frequent symptoms of depression/anxiety, respectively. In partly-adjusted models, compared to those with low CRF, those with high CRF had 0.83 (95% CI = 0.73–0.95) lower odds of depression/anxiety symptoms. In fully adjusted models that included leisure-time sedentary behavior, there was no association (Table 3). When analyses were run separately within each of the three exercise frequency categories, the results were comparable to the pooled analyses (Fig. 1). Mean CRF scores (total and within each of the three CRF categories) did not differ significantly between males and females. The sex interaction term was not significant in any models (p > 0.38). Results from sensitivity analyses with the Education variable included were almost identical to those shown here (Supplementary Tables 2 and 3).

### 4. Discussion

In this large cross-sectional study involving employed adults, we found that participation in at least 1–2 exercise sessions per week was associated with lower odds of reporting frequent symptoms of depression and anxiety. After adjustment for potential confounders, including leisure-time sedentary behavior (Hallgren, Nguyen, et al., 2020a), no associations were found between objectively measured CRF levels and frequent symptoms of depression/anxiety. Sex did not appear to moderate these relationships.

To optimize the effectiveness of exercise-based prevention and treatment strategies for mental health, information is needed regarding the optimal frequency of exercise, and the relative importance of CRF. To our knowledge, no previous studies have assessed relationships of both exercise frequency and CRF with symptoms of depression and anxiety in the same population. Our findings suggest that exercise frequency may have a stronger association with common mental health symptoms than CRF, where the association was nullified by leisure-time sedentary behavior. While exercise frequency and CRF were positively correlated (r = 0.32), they appear to have somewhat independent relationships with mental health symptoms; a finding also reported in studies of the relationship between physical activity, CRF, and somatic health (Myers et al., 2015). A related observation is that some forms of structured exercise (e.g., resistance training) are shown to be effective treatments for mood disorders and related symptoms (Gordon et al., 2017), yet may not significantly improve CRF levels. Taken together, this suggests that high CRF may not be necessary to prevent common mental health symptoms. Instead, regular participation in a preferred form of structured exercise may be of greater relative importance.

Another possible interpretation is that the benefits of CRF on mental health symptoms only become apparent when comparing those with very low CRF to those with moderate CRF. Studies of the relationship between CRF and somatic health suggest that most of the benefits are gained through modest improvements in CRF among those with very low baseline fitness levels (Blair et al., 1996). All participants in this study were employed, and employment status is linked to higher average CRF (Van Domelen et al., 2011). Thus, it is possible that our study did not include enough participants with low CRF levels to observe associations with depression and anxiety symptoms.

Our findings regarding CRF differ from those reported in a longitudinal Swedish study. To determine whether CRF at 18 years of age was associated with future risk of being diagnosed with an affective disorder, Aberg et al. (2012) prospectively followed 1,117,292 adolescents with no history of mental illness for 3–40 years. In fully adjusted models, low CRF (compared to medium and high) was associated with increased risk for clinician-diagnosed depression. Similarly, a recent cross-sectional study (n = 26,615; mean age = 55.7 years) found that, compared to those with low non-exercise estimated (e) CRF levels, those with medium and high eCRF had 21% and 26% lower odds of depression, respectively (Shigdel et al., 2019). In prospective analyses (n = 14,020; mean age = 52.2 years) the odds were 22% and 19% lower for the same comparisons. These disparate findings could be attributable to several factors, including differences in study design, participant mean age, measurement of the primary outcome (clinical depression versus symptoms of depression/anxiety), and adjustment for different co-variates in the statistical models. Unlike previous studies, we included leisure-time sedentary behavior in the fully-adjusted models, as it is shown to be inversely associated with symptoms of depression (Hallgren, Dunstan, & Owen, 2020b; Hallgren, Nguyen, et al., 2020a).
Inclusion of this co-variate may have reduced residual confounding.

Our finding that ‘regular’ exercise (defined here as ≥1–2 times/week) is associated with lower odds of depression/anxiety symptoms, compared to exercising ‘never/sometimes’, is broadly consistent with previous observational studies. Prospective data from the British Whitehall II study (n = 9,309, 8 year follow-up) demonstrated that, compared to non-regular exercise, regular moderate intensity exercise lasting at least 2.5 h/week was associated with lower odds of future depression and anxiety symptoms (Da Silva et al., 2012). Although exercise duration was not assessed in this study, it is reasonable to assume that for most people, exercise lasting ‘2.5 h/week or more’ implies a frequency of at least 1–2 times/week. However, the Whitehall II study results contrast with a recent prospective study involving 33,908 ‘healthy’ adults followed over 11 years, where just 30 min/week of moderate exercise was associated with lower odds of developing depression (Harvey et al., 2017). Longer average weekly durations of exercise (lasting 1–2 h, 3–4 h, and 5–6 h, respectively) did not confer additional protective effects.

Regular exercise influences a range of biological and psychosocial processes implicated in the pathophysiology of mood disorders. Underlying mechanisms include neurogenesis, monoamine synthesis, reduced systemic inflammation and oxidative stress, and regulation of the endocrine system (Kandola, Ashdown-Franks, Hendrikse, et al., 2019). Emerging research suggests that exercise could also improve the

Fig. 1. Associations of exercise frequency (last 30 days) with frequent symptoms of depression/anxiety measured within three strata of cardiorespiratory fitness (n = 36,595).

Table 3
Associations of cardiorespiratory fitness (VO₂max) with self-reported frequent symptoms of depression/anxiety (n = 36,595).

| Fitness level | Crude Model | Model 2 | Model 3 |
|---------------|-------------|---------|---------|
|               | OR 95% CI   | p       | OR 95% CI | p | OR 95% CI  | p |
| Low           | 0.88 0.81-0.95 | 0.011   | 0.91 0.81-1.00 | 0.063 | 0.99 0.89-1.11 | 0.975 |
| Medium        | 0.86 0.77-0.95 | 0.005   | 0.83 0.73-0.95 | 0.012 | 1.01 0.88-1.16 | 0.827 |
| High          | 1.01 0.88-1.16 | 0.827   | 1.01 0.88-1.16 | 0.827 |

Model 2 adjusted for: age, gender, smoking status, BMI, use of pain medication, exercise-gender interaction. Model 3 adjusted for Model 2 co-variates plus leisure-time sedentary behavior. Cardiorespiratory fitness levels correspond to the following values: Low = 14.9–28.3 ml/kg/min; Medium = 28.4–41.7 ml/kg/min; High = 41.8–77.9 ml/kg/min. OR = Odds Ratio; CI = Confidence Interval.
Fig. 2. Associations of cardiorespiratory fitness (VO$_{2\text{max}}$) with frequent symptoms of depression/anxiety measured within three strata of exercise frequency (n = 36,595).
suggests that prolonged sedentary behaviors which are mentally ‘passive’ (e.g. TV-viewing) are detrimentally related to depression, while mentally-active behaviors (e.g. reading) could have protective mental health effects (Hallgren, Nguyen, et al., 2020). As noted, exercise dose is comprised of three elements, and we have measured only one component (i.e. frequency). While the average frequency of exercise tends to increase with longer average durations of training, making them potentially comparable in this sense, exercise intensity could have associations with depression/anxiety symptoms that are largely independent of exercise frequency and duration. Finally, it is recognized that BMI is a relatively poor indicator of the percent of body fat. Waist and hip circumference are more accurate indicators of overweight and obesity (Adab, Pallan & Wincup, 2018).

In conclusion, our findings suggest that participation in regular (>1–2 times/week) exercise is associated with lower odds of frequent symptoms of depression/anxiety. The association between CRF and these symptoms was substantially attenuated when leisure-time sedentary behavior was included as a co-variariate. Taking into account the limitations noted above, the results suggest that regular exercise may be sufficient to reduce the risk of depression/anxiety symptoms at the population level. However, as poor mental health is consistently associated with somatic co-morbidity (Correll et al., 2017), it may be advisable to promote exercise routines that improve CRF in those with identified low levels. Prospective studies of these relationships are needed. Studies examining associations of exercise intensity, duration and frequency with common mental health symptoms are also warranted.

Author contributions

MH conceived the study and wrote the first draft; TTDN and MH conducted the statistical analyses. All co-authors contributed substantive comments that were incorporated into the manuscript. PW manages the database on which the study is based.

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Supplementary Table 1
Associations of exercise frequency (last 30 days) with frequent symptoms of depression/anxiety (n = 18,429)

| Exercise frequency | Crude Model | Model 2 | Model 3 |
|--------------------|-------------|---------|---------|
|                    | OR 95% CI   | p       | OR 95% CI | p       | OR 95% CI | p       |
| Never/Sometimes    | 1 -         | -       | 1 -       | -       | 1 -       | -       |
| 1-2 times/week     | 0.66 0.61–0.71 | <0.001 | 0.66 0.58–0.76 | <0.001 | 0.73 0.64–0.81 | <0.001 |
| ≥3 times/week      | 0.56 0.52–0.60 | <0.001 | 0.58 0.51–0.66 | <0.001 | 0.74 0.66–0.83 | <0.001 |

Model 2 adjusted for: age, gender, smoking status, BMI, use of pain medication, exercise-gender interaction. Model 3 adjusted for Model 2 co-variates plus leisure-time sedentary behavior. OR= Odds Ratio; CI = Confidence Interval.

Supplementary Table 2
Associations of cardiorespiratory fitness (VO₂max) with self-reported frequent symptoms of depression/anxiety (n = 18,429)

| Fitness level | Crude Model | Model 2 | Model 3 |
|---------------|-------------|---------|---------|
|                | OR 95% CI   | p       | OR 95% CI | p       | OR 95% CI | p       |
| Low           | 1 -         | -       | 1 -       | -       | 1 -       | -       |
| Medium        | 0.89 0.81–0.98 | 0.017  | 0.91 0.80–1.01 | 0.067 | 1.06 0.90–1.23 | 0.489 |
| High          | 0.83 0.73–0.93 | 0.002  | 0.82 0.72–0.93 | 0.013 | 1.01 0.81–1.24 | 0.942 |

Model 2 adjusted for: age, gender, smoking status, BMI, use of pain medication, exercise-gender interaction. Model 3 adjusted for Model 2 co-variates plus leisure-time sedentary behavior. Cardiorespiratory fitness levels correspond to the following values: Low = 14.9–28.3 ml/kg/min; Medium = 28.4–41.7 ml/kg/min; High = 41.8–77.9 ml/kg/min. OR= Odds Ratio; CI = Confidence Interval.
### Supplementary Table 3

| Characteristic                  | Missing Education n (%) | With Education N (%) |
|--------------------------------|-------------------------|----------------------|
| **Female**, n (%)              | 10,343 (39.6)           | 10,263 (42.5)        |
| Age mean (SD); [range]         | 42.44 (11.62); [16–80]  | 42.56 (12.03); [16–80]|
| **Smoking**, n (%)             |                         |                      |
| Non-smoker                     | 21,942 (84.7)           | 19,944 (83.0)        |
| Occasional smoker              | 2268 (8.8)              | 2127 (8.9)           |
| Daily smoker                   | 1694 (6.5)              | 1947 (8.1)           |
| **Body Mass Index (BMI)**, n (%)|                         |                      |
| Normal weight                  | 10,598 (45.5)           | 10,229 (42.9)        |
| Overweight                     | 8737 (37.5)             | 9076 (38.1)          |
| Obese                          | 3955 (17.0)             | 4518 (19.0)          |
| **Pain medication**, n (%)     |                         |                      |
| Very often                     | 481 (1.9)               | 588 (2.4)            |
| Often                          | 1055 (4.1)              | 1148 (4.8)           |
| Sometimes                      | 5010 (19.3)             | 4830 (20.1)          |
| Rarely                         | 13,838 (53.4)           | 12,262 (51.0)        |
| Never                          | 5509 (21.3)             | 5197 (21.6)          |

**Leisure-time sedentary behavior** n (%)

| Characteristic                  | Mean (SD)  |
|--------------------------------|-------------|
| High (Always)                   | 3535 (13.6) | 2746 (11.4) |
| Medium (50% of the time)        | 9007 (35.9) | 7805 (32.5) |
| Low (Never/25% of the time)     | 13,069 (50.4) | 13,467 (56.1) |

**Exercise frequency**

| Characteristic                  | Mean (SD)  |
|--------------------------------|-------------|
| Never/Sometimes                 | 8129 (31.4) | 7896 (33.3) |
| 1–2 times/week                  | 7905 (30.5) | 7699 (29.1) |
| At least 3 times/week           | 9849 (38.1) | 9034 (37.6) |
| VO2 max ml/kg/min mean (SD)     | 36.12 (10.09) | 35.67 (10.03) |
| [range]                         | (14.95–77.78) | (14.95–97.04) |

| **Fitness** (categories of VO2 max) | Mean (SD)  |
|-------------------------------------|-------------|
| Low                                 | 3520 (19.3) | 3828 (20.7) |
| Medium                              | 10,968 (60.1) | 11,078 (59.9) |
| High                                | 3768 (20.6) | 3576 (19.3) |

**Frequent symptoms of depression/anxiety**

| Characteristic                  | Mean (SD)  |
|--------------------------------|-------------|
| No (Never/Rarely/Sometimes)    | 23,563 (91.0) | 22,024 (91.7) |
| Yes (Often/Very often)         | 2335 (9.0) | 1996 (8.3) |

*Significantly different r < 0.01.  
Kandola et al., 2019.
M. Hallgren et al.

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