Association between physical exercise and mental health in 1·2 million individuals in the USA between 2011 and 2015: a cross-sectional study

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Summary

Background Exercise is known to be associated with reduced risk of all-cause mortality, cardiovascular disease, stroke, and diabetes, but its association with mental health remains unclear. We aimed to examine the association between exercise and mental health burden in a large sample, and to better understand the influence of exercise type, frequency, duration, and intensity.

Methods In this cross-sectional study, we analysed data from 1 237 194 people aged 18 years or older in the USA from the 2011, 2013, and 2015 Centers for Disease Control and Prevention Behavioral Risk Factors Surveillance System survey. We compared the number of days of bad self-reported mental health between individuals who exercised and those who did not, using an exact non-parametric matching procedure to balance the two groups in terms of age, race, gender, marital status, income, education level, body-mass index category, self-reported physical health, and previous diagnosis of depression. We examined the effects of exercise type, duration, frequency, and intensity using regression methods adjusted for potential confounders, and did multiple sensitivity analyses.

Findings Individuals who exercised had 1·49 (43·2%) fewer days of poor mental health in the past month than individuals who did not exercise but were otherwise matched for several physical and sociodemographic characteristics (W=7·42×10^{10}, p<2·2×10^{-16}). All exercise types were associated with a lower mental health burden (minimum reduction of 11·8% and maximum reduction of 22·3%) than not exercising (p<2·2×10^{-16} for all exercise types). The largest associations were seen for popular team sports (22·3% lower), cycling (21·6% lower), and aerobic and gym activities (20·1% lower), as well as durations of 45 min and frequencies of three to five times per week.

Interpretation In a large US sample, physical exercise was significantly and meaningfully associated with self-reported mental health burden in the past month. More exercise was not always better. Differences as a function of exercise were large relative to other demographic variables such as education and income. Specific types, durations, and frequencies of exercise might be more effective clinical targets than others for reducing mental health burden, and merit interventional study.

Funding Cloud computing resources were provided by Microsoft.

Introduction

Physical exercise is associated with several positive health benefits, including reduced overall mortality,[1] improved musculoskeletal health and stress regulation,[2] and reduced risks of cardiovascular disease, obesity, stroke, and cancer.[1] Research into the effect of exercise on mental health has provided conflicting results. On the basis of pooled effects from randomised controlled clinical trials,[3–5] and associations among patients identified in national registry data,[6,7] most studies consider exercise an effective treatment for mild and moderate depression, either alone[8] or in an adjunctive capacity.[9] However, other randomised controlled trials do not support this hypothesis,[10] and evidence from longitudinal observational studies is inconsistent, with positive associations reported in adults[7,11,12] but not in adolescents.[13] Among many of these studies, it has been argued that more exercise is better, primarily on the basis of the inverse relationship between leisure-time physical activity and mental health[14] and better outcomes in the higher exercise groups of dose-comparison randomised controlled trials.[9]

One factor that might explain conflicting results is the use of small (or non-representative) samples. Such studies lack statistical power to examine the effect of exercise type, since only a few types of exercise are likely to be represented, and few individuals will engage in each type. This lack of large samples also made it difficult to determine the specificity of the association. That is, how do other features of exercise—such as frequency, intensity, or duration—relate to mental health and how does that relationship vary across the full range of possible frequencies or durations?[15] To the extent that people have preferences for specific exercise

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Research in context

Evidence before this study

We searched PubMed for all papers in English published before March 18, 2018, using the medical subject heading major topic search term ("depression" OR "depressive disorder, major") and the medical subject heading term "exercise". We retrieved and scanned 856 articles, and then focused on the 269 articles that were most relevant based on their titles. All articles deemed not to be relevant based on their titles were excluded. Abstracts of the remaining articles were reviewed to identify potentially relevant articles, and, on the basis of this selection, we read full-text articles.

Exercise has been associated with lower depressive symptoms compared with no exercise. A particular focus has been on walking interventions to improve mental health in elderly samples, but associations have also been reported in both cross-sectional and longitudinal studies of adolescents and adults. Randomised controlled trials suggest that exercise is an effective treatment for depression either alone or in an adjunctive capacity, but sample sizes are typically very small and have included few types, durations, and frequencies of exercise. Clear dose–response relationships remain elusive. The largest meta-analysis of physical exercise and depression included 89 894 individuals but was not able to explore individual participant-level effects of type, duration, frequency, or intensity.

Added value of this study

In this study of a representative US sample of 1·2 million individuals, representing the largest study of its kind to date, we showed that exercising was associated with reduced self-reported mental health burden, an effect that was consistent across a range of sociodemographic characteristics including age, race, gender, household income, and education level. Although all exercise types were better than no exercise, we found that certain exercises were much more strongly associated with reduced mental health burden than others. More exercise was not always associated with better mental health, and we found evidence for optimal ranges of duration (45 min) and frequency (between three and five times per week). These differences were large relative to other modifiable factors (eg, education and income) that are known to be associated with mental health. These analyses were statistically well powered and controlled for a wider range of person-level covariates than previous studies, including aspects of physical health and body-mass index. The dose–response relationships were highly non-linear, which might explain inconsistencies across previous studies of exercise and mental health.

Implications of all the available evidence

The characteristics of exercise (ie, type, duration, and frequency) might play an important part in the association between exercise and mental health burden. The association was also observed in a subsample of individuals who reported no previous diagnosis of depression, suggesting that the benefit might not be restricted to clinical populations. These findings could offer a platform for future research into the role of exercise in reducing mental health burden in a more efficient manner both in randomised clinical trials and at a population level.

types, it is important to understand whether all types are equally beneficial (ie, individuals should choose their favourite), or whether it would help to inform people that certain forms of exercise have advantages over others.

Because depression is now the leading cause of global disability burden,[16] there is a pressing need to identify modifiable factors that influence mental health burden and which can be the target of population health campaigns to reduce this burden. We examined the association between exercise and mental health. The goal was to measure patterns of mental health burden across a diverse set of exercise types, durations, and frequencies while accounting statistically for a range of sociodemographic and physical health characteristics.

See Online for appendix

Methods

Data sources and dataset description

In this cross-sectional study, we analysed data from the Behavioral Risk Factor Surveillance System survey collected by the Centers for Disease Control and Prevention through a telephone survey of individuals aged 18 years or older across all 50 states in the USA between 2011 and 2015. We aggregated data from 2011, 2013, and 2015—because the survey included a module about patterns of physical exercise in those years—which resulted in a dataset of responses from 1 439 696 individuals that included information on participants' demographics, physical health, mental health, and health-related behaviours. Since relatively few data were missing, we took a complete cases approach to missingness (appendix). Individuals with missing data were excluded. Participants self-reported a previous diagnosis of depression or depressive episode on the basis of the following question: "Has a doctor, nurse, or other health professional EVER told you that you have a depressive disorder, including depression, major depression, dysthymia, or minor depression?"

Outcome variable

We measured mental health burden according to participants' self-report for the question: "Now thinking about your mental health, which includes stress, depression, and problems with emotions, for how many days during the past 30 days was your mental health not good?"

Data preprocessing

Participants were asked: "During the past month, other than your regular job, did you participate in any

physical activities or exercises such as running, calisthenics, golf, gardening, or walking for exercise?" Participants who answered yes to this question were then asked: "What type of physical activity or exercise did you spend the most time doing during the past month?" A total of 75 types of exercise were represented in the sample, which were grouped manually into eight exercise categories to balance a diverse representation of exercises with the need for meaningful cell sizes (appendix).

Participants indicated the number of times per week or month that they did this exercise and the number of minutes or hours that they usually spend exercising in this way each time. We harmonised weekly and monthly frequency responses into times per month by multiplying weekly responses by four, and converted durations from hours into minutes. To reduce the possibility of spurious outliers, we applied a 99% winsorisation to the frequency and duration responses, such that responses of more than 360 min and 76 times per month were adjusted to be equal to these 99th percentile values. Finally, to reduce sparsity and minimise estimation errors, exercise durations were rounded to the nearest 15 min and exercise frequencies were rounded to the nearest 2 days per month.

Statistical analysis

We adjusted analyses for the effect of individual-level covariates, including age, race, gender, marital status, income, education level, employment status, body-mass index (BMI) category, self-reported physical health, and previous diagnosis of depression. Herein, we refer to these variables as the full covariate set.

To investigate the association between exercise and mental health, we compared self-reported mental health burden between those who exercised in the past month and those who did not. We used a non-parametric exact matching procedure[17] to account for differences across the full covariate set (appendix). Non-parametric two-sample Wilcoxon rank-sum tests were used to assess for differences in mental health burden between these matched groups (figure 1). Since a previous diagnosis of depression could have an extremely strong association with current mental health burden, we did separate matched sample analyses for individuals who had been diagnosed with depression in the past and those with no previous diagnosis of depression. Finally, to ensure that the findings were not an artifact of covariate adjustment, we did sensitivity analyses without matching procedures (appendix pp 16–18).

With a large sample of participant-level data, this sample afforded a detailed comparison between the various types of exercise in which individuals engage. We analysed the effect of exercise type using a hurdle-at-zero negative binomial regression. We confirmed the presence of zero-inflation with a Vuong test comparing a negative binomial regression with a hurdle-at-zero negative binomial regression. To account for the fact that participants self-select into various exercise types, we applied a multinomial propensity weighting procedure that uses generalised boosted regression trees to estimate poststratification propensity scores. In this case, these scores reflect the probability that an individual will be assigned to a specific exercise type, given the full covariate set. Propensity scores were then winsorised at a 99% level to minimise the impact of excessive values, and then included as weights in the hurdle regression analyses exploring the association between exercise type and mental health burden. Finally, coefficients from the count model were compared for different exercise types to identify which one was associated with the lowest mental health burden, given that an individual had a non-zero mental health burden (appendix).

Some mindfulness-based exercises, such as yoga or tai chi, are touted as particularly beneficial for mental health. We explored this notion in a post-hoc analysis, in which we grouped exercise types as yoga or tai chi (mindful exercises), walking, all other exercises, and no

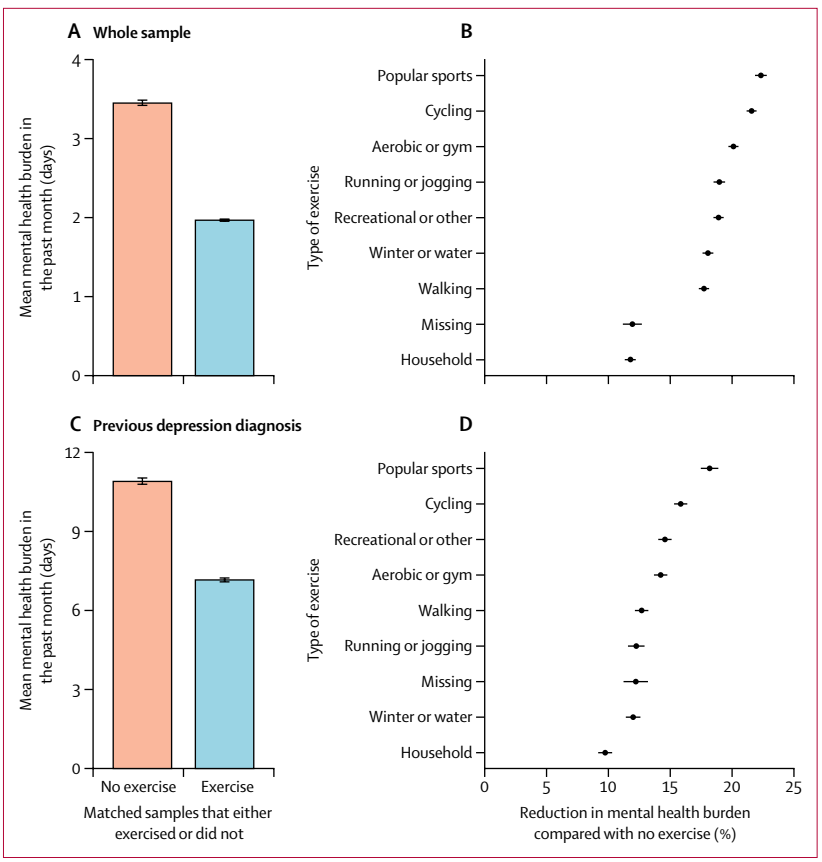

Figure 1: **Cross-sectional data from more than 1·2 million individuals in the USA**
(A) In samples matched for a range of physical and sociodemographic characteristics, individuals who exercised had a 1·49 day (43·2%) reduction in mental health burden. (B) Relative to no exercise, individuals who engaged in popular sports, cycling, or aerobic and gym exercises had the lowest mental health burden. Even walking was associated with a 17·7% reduction in mental health burden relative to not exercising (C). Among individuals with a previous diagnosis of depression, those who exercised had 3·75 fewer days (34·5%) of poor mental health each month, with a similar ranking of exercise types (D). Error bars represent 95% CIs.

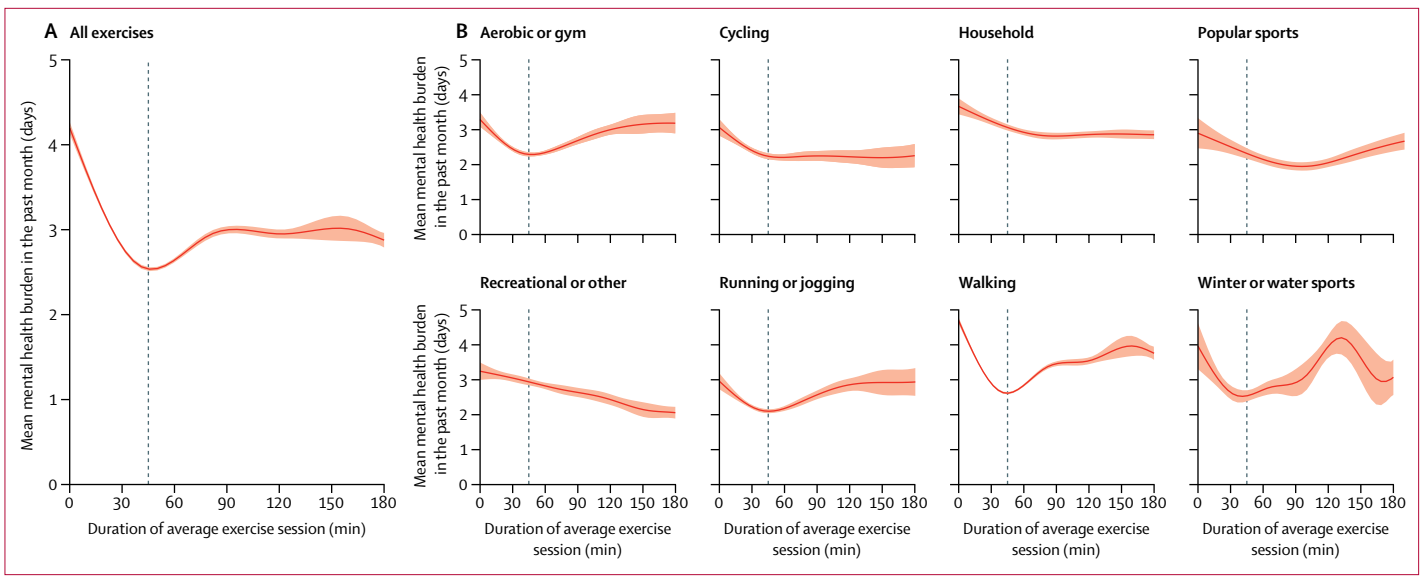

Figure 2: **Mental health burden as a function of exercise duration**
(A) Across the whole sample, individuals who exercised for approximately 45 min per session had the lowest mental health burden. Durations less than 45 min were associated with higher mental health burden, and durations longer than 60 min were generally not better than 45 min. (B) This pattern was broadly consistent across several exercise categories. Lines represent smoothed conditional means with generalised additive model smoothing, with ribbons representing 95% CIs. Dashed lines indicate exercise durations of 45 min.

exercise. As before, we used a hurdle-at-zero negative binomial regression to analyse the effect, included a winsorised propensity weight for these four levels of exercise type, and compared coefficients from the count model to determine whether the mindful exercises were associated with a greater reduction in mental health burden than other forms of exercise.

We formally analysed the effects of exercise duration and frequency using a generalised additive model to allow us to observe non-linear relationships with mental health burden. The model used penalised cubic regression splines for exercise duration and for frequency, with parametric regressors to control for the full covariate set. We then plotted the fitted smoothed coefficients for duration and frequency, with 95% CIs. To explore how the effect varies across exercise types, we plotted the relationship between mental health burden and exercise duration (figure 2) and frequency (figure 3), first for the whole sample and then independently for each exercise type using smoothed conditional means (generalised additive model smoothing with penalised cubic regression splines) and 95% CIs.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Our analyses were based on 1 237 194 (86·0%) of all (1 439 696) participants. The mean mental health burden was 3·36 days (SD 7·7) of poor mental health in the past month (median 0 [IQR 0–2]). In an analysis of 852 068 matched individuals (627 510 [73·6%] of whom exercised), we found that exercise was associated with a 1·49 day (43·2%) lower self-reported mental health burden per month (W=7·42×10^{10}, p<2·2×10^{-16}) for individuals who exercised than those who did not. We repeated the same analysis specifically for matched individuals with (110 194; 71 111 [64·5%] of whom exercised) and without (741 874; 556 399 [75·0%] of whom exercised) a previous depression diagnosis. The effect was larger among individuals who reported a previous depression diagnosis, in whom exercise was associated with a 3·75 day (34·5%) lower mental health burden (W=1·61×10^{9}, p<2·2×10^{-16}), than among people who reported a previous diagnosis of depression but did not exercise. The association between exercise and mental health burden was seen across the full age span, for men and women, across all racial groups and all levels of household income (appendix pp 7–13).

Mental health burden also varied as a function of exercise type. Results were similar, and conclusions the same, for a zero-inflated negative binomial regression model. All types of exercise were associated with a reduction in mental health burden (minimum reduction of 11·8%, p<2·2×10^{-16} for all exercise types; figure 1B) compared with no exercise. The strongest associations were found for popular sports (22·3% lower), cycling (21·6% lower), and aerobic and gym exercises (20·1% lower). A similar ranking was found when we analysed the previous depression subsample alone (figure 1D; appendix p 26). In both analyses, even engaging in household chores was associated with at

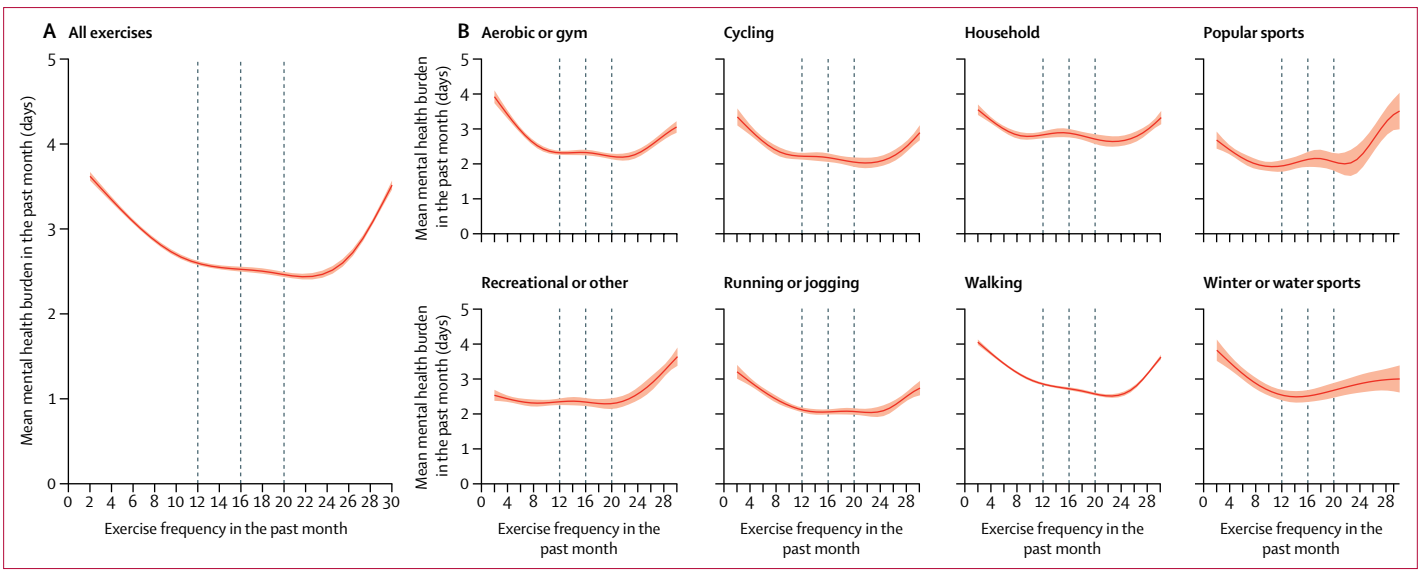

Figure 3: **Mental health burden as a function of exercise frequency**
(A) Across the whole sample, individuals who exercised between three and five times per week had the lowest mental health burden. (B) The pattern was remarkably consistent across most exercise groups. Frequencies of less than three per week (12 times per month), or more than five per week (20 times per month) were associated with greater mental health burden. Lines represent smoothed conditional means using generalised additive model smoothing with cubic regression splines, with ribbons representing 95% CIs. Dashed lines indicate exercise frequencies of three, four, and five times per week (12, 16, and 20 times per month).

least a 9·7% reduction in days of poor mental health (about 0·4 days per month). An exploratory post-hoc analysis revealed that mindful exercises (yoga and tai chi) were associated with a significantly greater reduction in mental health burden than not exercising (22·9%), walking (17·4%), or engaging in any other exercise (17·8%; appendix p 35).

These associations were larger than many modifiable social or demographic factors. For example, the absolute improvement (*vs* no education) was only 17·8% higher for graduating college than graduating high school (appendix p 22). Relative to individuals with a normal BMI, obese individuals had an approximately 4% worse mental health burden. Even a household income of more than US$50 000 was associated with only 17% lower mental health burden than an income of $15 000 (appendix p 22).

We observed significant and non-linear relationships between mental health burden and both exercise duration and frequency, while controlling for the full covariate set. Smoothed regression splines revealed that exercise durations between 30 min and 60 min (peaking around 45 min) were associated with the lowest mental health burden (appendix p 45). This pattern of optimal duration was broadly consistent across many exercise types (figure 2B). In general, small reductions were seen for individuals who exercise longer than 90 min, and durations of more than 3 h were associated with worse mental health burden than exercising for either 45 min or not exercising at all.

We also observed U-shaped relationships between exercise frequency and mental health burden, whereby individuals who exercise between three and five times a week had a lower mental health burden than those who exercised fewer than three or more than five times (appendix p 46). Once again, this pattern was broadly consistent across all exercise types (figure 3), and existed for all levels of exercise intensity (light, moderate, or vigorous exercise), with vigorous exercise associated with a more favourable burden than either light or moderate exercise (appendix p 49). In units commonly used in public health guidelines, people exercising between 120 min and 360 min per week had the lowest mental health burden (appendix p 50).

Discussion

This study shows a meaningful association between exercise and mental health, in the largest cross-sectional sample to date, even after adjusting for several sociodemographic and physical health characteristics that themselves are known to contribute to mental health burden. Individuals who exercised had about 1·5 (about 43%) fewer days of poor mental health in the past month than individuals who did not exercise, but were otherwise similar in terms of age, race, gender, marital status, income, employment status, education level, BMI category, self-reported physical health, and previous diagnosis of depression. Furthermore, this association was strongest for individuals who exercised for between 30 min and 60 min per session, three to five times per week. Engaging in popular (team) sports and cycling was associated with the lowest mental health burden, both in the whole sample and in the subsample of individuals with a previous diagnosis of depression.

More exercise was not always better—extreme ranges of more than 23 times per month, or longer than 90 min per session, were associated with worse mental health.

These effects were large relative to other modifiable factors. The difference in mental health burden between individuals who participated in popular (team-based) sports versus those who do not exercise was approximately the same as the difference in mental health burden between individuals who obtain a college degree (*vs* high school alone) or between individuals with a difference in household income of more than US$25 000.

It is plausible that these findings are causal because they are consistent with randomised controlled trials indicating positive effects of exercise on mental health outcomes,[15] anxiety,[14,18] and post-traumatic stress disorder,[19] as well as cohort studies suggesting that exercise protects against the incidence of depression.[11,12] In research samples, exercise has been shown to specifically relieve symptoms of fatigue and amotivated behaviour in individuals with major depressive disorder, with changes in motivated behaviour tightly coupled to changes in severity of depressive symptoms.[20] Our finding that popular sports, mostly team based, were associated with the lowest mental health burden is in line with studies showing that social activity promotes resilience to stress and reduces depression,[21] and the prosocial benefits of minimising social withdrawal and feelings of isolation might contribute an additional benefit for mental health over other forms of physical exercise. That mindful exercises (ie, yoga and tai chi) were associated with lower mental health burden than walking or other exercises supports literature around the benefits of mindfulness-based techniques for mental health.[22] These data suggest that all exercise groups, including social and non-social forms, were associated with lower mental health burden.

It has previously been argued that more exercise is better, given the inverse relationship between leisure-time physical activity and mental health.[14] The detail in this survey, coupled with the large sample size, allowed us to examine these claims with more precision in terms of frequency and duration and more representativeness in terms of the variety of exercises that people engage in. These data suggest that the argument that more is better fails to hold beyond certain volumes, and that exercising beyond 6 h per week is associated with worse mental health (appendix p 50). Moreover, the U-shaped curves seen for both frequency and duration suggest that motivation to exercise is not enough to explain the association between exercise and mental health. An observational study[11] of more than 30 000 individuals suggested that merely exercising for 1 h per week was sufficient to see a lasting benefit in depressive symptoms. We replicated this association of sufficiency, but note the optimal association in these data was between 2 h and 6 h per week.

The cross-sectional nature of this study, however, limits the ability to establish the direction of causality for the association between exercise and mental health. Although this concern is partially mitigated by randomised controlled trials indicating positive effects of exercise on mental health,[15] at least one longitudinal observational study has suggested that the association might be bidirectional.[7] In other words, inactivity might be both a symptom of and contributor to poor mental health, whereas activity might be an indicator of and contributor to resilience. Although covariates and propensity weighting adjustments can control for observable effects of several sociodemographic and physical characteristics on exercise assignment and also on mental health burden, these procedures cannot account for confounding by unmeasured factors. Since we only considered participants' responses about their primary exercise, we might have underestimated the duration and frequency of exercise if they routinely engage in two or more regimes. Additionally, since the dose of exercise was not randomised, it is possible that subgroups at the high end of exercise dose might be enriched for psychopathological risk beyond socioeconomic risks (eg, individuals with obsessive characteristics or personality traits).

An important next step for this line of research is to collect longitudinal passive mobile[23] or wearable sensor data (eg, Fitbit [Fitbit; San Francisco, CA, USA]), which are not affected by self-report, to investigate the precise association between the actual frequency, duration, and intensity of exercise and mental health burden. Such devices could also allow us to measure physical exertion during both work hours and leisure and hence parse out effects relating to exertion versus an appropriate balance in leisure time. Since mental health burden varied as a function of exercise patterns in this sample as well as a function of socioeconomic background, it could be possible to personalise exercise recommendations[24,25] in order to identify what format of exercise will best help an individual to reduce their mental health burden.

This study relies on a participant's own assessment of mental health burden in a given month, without use of structured interviews or standardised rating scales to determine mental health burden. Although the use of participant-reported outcomes has many advantages, we were not able to relate current mental state (eg, measured by the Patient Health Questionnaire or Hamilton Depression Rating Scale) to exercise with this approach. This outcome offers broad insight into patient's perceived mental health condition, but it precludes identification of specific contributions to overall burden, such as depression, anxiety, or stress. Use of standardised rating scales in a large-scale study would allow more finely grained investigation of the association between exercise and specific symptoms or clusters of symptoms, and help to contextualise effects measured in days per month against known clinical severity ratings.

Contributors

AMC had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. AMC obtained funding. AMC, JHK, and RG devised the study concept and design. AMC, SRC, ABZ, MP, HMK, and JHK drafted the manuscript. All authors critically revised the manuscript for important intellectual content. SRC, RG, and AMC did the statistical analysis. All authors acquired, analysed, and interpreted data, and provided administrative, technical, and material support. AMC and JHK supervised the study.

Declaration of interests

SRC and ABZ declare no competing interests. RG discloses consulting fees for Palo Alto Health Sciences and Mathematica Policy Research, and a provisional patent submission (US Patent and Trademark Office [USPTO] docket number Y0087.70116US00) by Yale University (New Haven, CT, USA). MP is an adviser to Spring Care (New York City, NY, USA), a behavioural health startup. He has received royalties for an article about methamphetamine in UpToDate (Wolters Kluwer; Waltham, MA, USA), and received grant support from Janssen Pharmaceuticals. HMK was a recipient of a research grant, through Yale University, from Medtronic and the US Food and Drug Administration to develop methods for post-market surveillance of medical devices; is a recipient of research agreements with Medtronic and Johnson & Johnson (Janssen), through Yale University, to develop methods of clinical trial data sharing; works under contract with the Centers for Medicare & Medicaid Services to develop and maintain performance measures that are publicly reported; chairs a Cardiac Scientific Advisory Board for UnitedHealth; is a participant/participant representative of the IBM Watson Health Life Sciences Board; is a member of the Advisory Board for Element Science and the Physician Advisory Board for Aetna; and is the founder of Hugo, a personal health information platform. JHK has been a consultant for AstraZeneca Pharmaceuticals, Biogen, Biomedisyn Corporation, Bionomics (Australia), Concert Pharmaceuticals, Heptares Therapeutics (UK), Janssen Research & Development, L.E.K. Consulting, Otsuka America Pharmaceutical, Spring Care Inc, Sunovion Pharmaceuticals, Takeda Industries, and Taisho Pharmaceutical Co; is on the scientific advisory boards of Bioasis Technologies, Biohaven Pharmaceuticals, Blackthorn Therapeutics, Broad Institute of Massachusetts Institute of Technology and Harvard University (Boston, MA, USA), Cadent Therapeutics, Lohocla Research Corporation, Pfizer Pharmaceuticals, and Stanley Center for Psychiatric Research at the Broad Institute; has stock in ArRETT Neuroscience, Blackthorn Therapeutics, Biohaven Pharmaceuticals Medical Sciences, and Spring Care; and has stock options with Biohaven Pharmaceuticals Medical Sciences. He has the following patents and inventions: Seibyl JP, Krystal JH, Charney DS, Dopamine and noradrenergic reuptake inhibitors in treatment of schizophrenia, US patent number 5,447,948, Sept 5, 1995; Coric V, Krystal JH, Sanacora G, Glutamate modulating agents in the treatment of mental disorders, US patent number 8,778,979, July 15, 2014; Coric V, Krystal JH, Sanacora G, Glutamate agents in the treatment of mental disorders, US patent application number 15/695,164, Sept 5, 2017. Charney D, Krystal JH, Manji H, Matthew S, Zarate C, Intranasal administration of ketamine to treat depression, US patent number 14/197,767, March 5, 2014; Charney DS, Manji HK, Krystal JH, Matthew SJ, Zarate CA, Intranasal administration of ketamine to treat depression, US application or Patent Cooperation Treaty International application number 14/306,382, filed on June 17, 2014; Zarate C, Charney DS, Manji HK, Mathew, Sanjay J, Krystal JH, Methods for treating suicidal ideation, US patent application number 14/197,767 filed on March 5, 2014, by Yale University Office of Cooperative Research; Arias A, Petrakis I, Krystal JH, Composition and methods to treat addiction, provisional use patent application number 61/973/961 filed on April 2, 2014, by Yale University Office of Cooperative Research; Chekroud A, Gueorguieva R, Krystal JH, Treatment selection for major depressive disorder, June 3, 2016, USPTO docket number Y0087.70116US00, provisional patent submission by Yale University; and Yoon G, Petrakis I, Krystal JH, Compounds, compositions and methods for treating or preventing depression and other diseases, US provisional patent application number 62/444,552, filed on Jan 10, 2017, by Yale University Office of Cooperative Research OCR 7088 US01. He has received non-federal research support from AstraZeneca Pharmaceuticals, which provides the drug saracatinib for research related to US National Institute on Alcohol Abuse and Alcoholism grant Center for Translational Neuroscience of Alcoholism (CTNA-4), and from Pfizer Pharmaceuticals, which provides an investigational drug, PF-03463275, for research related to US National Institutes of Health grant Translational Neuroscience Optimization of GlyT1 Inhibitor. AMC holds equity in Spring Care. He is lead inventor on three patent submissions relating to treatment for major depressive disorder (USPTO docket number Y0087.70116US00, USPTO provisional application number 62/491,660, and USPTO provisional application number 62/629,041). He has consulted for Fortress Biotech on antidepressant drug development.

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