Estimating treatment effects of physical activity on subcategories of mental health: A propensity score analysis among a global sample of 341,956 adults

Christopher Huong, BA & Denver M. Y. Brown, PhD

Department of Psychology, The University of Texas at San Antonio

Author Note

Christopher Huong: christopher.huong@utsa.edu, 0009-0008-6986-7784

Denver Brown: denver.brown@utsa.edu, 0000-0003-4078-8253

Correspondence concerning this article should be addressed to Christopher Huong, Department of Psychology, One UTSA Circle, Main Building 2.306, San Antonio, TX 78249, USA. E-mail: christopher.huong@utsa.edu. We have no conflicts of interest to disclose.

CRediT Author Statement: **Christopher Huong**: formal analysis, writing – original draft, methodology (equal). **Denver Brown**: conceptualization, methodology (equal), writing – review and editing

Keywords: mental health, well-being, physical activity, exercise, machine learning

Estimating treatment effects of physical activity on subcategories of mental health: A propensity score analysis among a global sample of 341,956 adults

Introduction

Suboptimal mental well-being and mental health problems have proven to be a significant burden on the global population. Approximately 29% of individuals have experienced a common mental disorder during their lifetime, with a 9.6%, 12.9%, and 10.7% lifetime prevalence for mood, anxiety, and substance-use disorders, respectively [1]. The global burden of mental disorders was estimated at 125.3 million disability-adjusted life-years (DALY) in 2019 – an increase from 80.8 million DALYs in 1990 [2]. Moreover, lost productivity due to poor mental health is estimated to cost the global economy $2.5T annually and is projected to more than double over the next decade, reaching $6T by 2030 [3]. The COVID-19 pandemic may also have conferred a toll on population mental health and well-being worldwide. Evidence from reviews is somewhat mixed, but findings suggest there has been an increase in depressive and anxiety symptoms most consistently in younger cohorts [4–8]. Collectively, it is clear that mental health problems and poor mental well-being are a growing issue in society today, but certain subpopulations may experience an even greater toll.

Emerging evidence in addition to recent findings from the COVID-19 pandemic suggests younger age cohorts of adults may be at the greatest risk for poor mental health and well-being [9,10]. For example, a recent study showed that younger adults living in the US consistently report the lowest scores on all domains of mental well-being, including happiness, health, meaning and purpose, character, social relationships, and financial stability, with a linear pattern of improvements in well-being observed with increased age [11]. These findings are in contrast to previous work that had demonstrated an inverted-U relationship between age and mental well-being in which mental well-being was lowest in middle adulthood [12]. Further, the onset of an estimated half of first mental disorders occurs by age 18, which speaks to the pervasiveness of mental health challenges experienced when transitioning into early adulthood [13]. Evidently, more research is needed to better understand these age-related trends from a global perspective, including a focus on protective factors that may moderate the relationship between age and mental well-being.

Physical activity is one aspect of our lifestyle that has received increasing attention for its potential to promote mental well-being as well as assist in the prevention and management of mental health disorders. Observational and experimental evidence has consistently shown a relationship between higher levels of physical activity and benefits across various mental health outcomes, including, but not limited to depression [14–16], anxiety [17,18], and general mental health and well-being [19]. For example, in a large cross-sectional dataset of over 1.2M adults living in the United States, Chekroud et al [20] showed that engaging in physical activity in the past month was associated with 43.2% lower self-reported days with poor mental health over that period. Despite these robust findings, particularly for depression and anxiety, physical activity remains an underutilized treatment tool among clinical practitioners [21]. The inclusion of physical activity – albeit as an alternative and/or complementary treatment – in several recent national guidelines for the treatment of depression holds promise for promoting greater uptake in primary care services [22–24].

While evidence supports the importance of physical activity for preventing and/or reducing a range of mental health problems and improving overall well-being, for some other psychiatric symptoms and disorders (e.g., bipolar disorder, schizophrenia), the evidence is less suggestive of benefits, or remains unclear [25–27]. More recently, however, researchers have demonstrated that there is considerable overlap in symptomatology across the most commonly classified mental health disorders, which illustrates the complexity and heterogeneous nature of mental health as a construct [28,29]. Such knowledge has sparked the development of novel measures – the Mental Health Quotient (MHQ) for example – to address these considerations. Yet, due to their recency, these instruments have seldom been utilized.

One promising avenue in which comprehensive measures of mental health can be applied is in studies examining the specific aspects of mental health that physical activity may especially favor. Findings stemming from such studies have the potential to improve precision in the treatment of mental health problems and therefore may have important implications for clinical outcomes [30,31]. Determining whether physical activity is associated with differential effects for certain aspects of mental health across the lifespan is but one fruitful area of inquiry to pursue for the purpose of improving population-level mental health and well-being.

The primary purpose of the present study was to estimate the treatment effect of physical activity engagement on overall mental health in a large global sample, as well as various subcategories of mental health, while statistically accounting for a range of observed covariates using a machine learning technique underutilized in exercise psychology and behavioral medicine. The secondary purpose of this study was to examine whether differential effects of physical activity are observed on indicators of mental health across age cohorts.

Methods

The reporting of the methods and results in this study adhere to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cross-sectional studies. [32]

Study Sample and Data Collection. This cross-sectional study used data from the Global Mind Project (GMP; formally the Mental Health Million Project), an on-going online study with the purpose of assessing global mental well-being through administration of the Mental Health Quotient. The sample for our present study included 341,956 participants from 229 countries who completed the GMP survey between December 31st, 2021 and October 14th, 2022. The start of this period coincided with the launch of Version 3 of the MHQ. Additional information concerning the GMP and recruitment strategy may be found elsewhere [33]. This study involved secondary analysis of existing non-identifiable data and therefore Institutional Research Ethics Board approval was not required.

Measures

Mental health. The MHQ is a 47-item instrument designed to assess a comprehensive range of common attributes found across widely used existing mental health assessment tools in a single questionnaire to estimate overall mental well-being and functioning in the population. Items were developed by consolidation of 170 symptoms coded from 126 commonly used assessment tools covering depression, anxiety, bipolar disorder, ADHD, post-traumatic stress disorder, obsessive-compulsive disorder, addiction, schizophrenia, eating disorders and autism spectrum disorder. The MHQ is unique from other psychiatric tools in that the items assess level of functioning and impact on one’s life associated with each mental health element, as opposed to frequency, duration, or severity of symptoms. The questionnaire took an average of 14 minutes for participants to complete.

Responses from the 47 items were used to compute the MHQ, which represents an overall score of mental health and well-being. The MHQ originally ranged from -100 to +200, however, the lower limit was recently expanded to -166 to improve the distribution of scores that previously demonstrated a floor effect at the lower bound. Scores on the MHQ can be classified into six levels of functioning, with negative scores indicating clinical risk and positive scores representing normal range: Clinical (≤-50), At Risk (-50 to <0), Enduring (0 to <50), Managing (50 to <100), Succeeding (100 to <150) and Thriving (150 to 200). To compute the overall score, individual item responses were weighted to reflect the nonlinearity of risk associated with increases in symptom severity, as well as the differential risk associated with different symptoms (e.g., suicidal thoughts vs irritability).

In addition to the overall MHQ score, scores for six broad subcategories of mental health and well-being were computed: Core Cognition (e.g., executive functioning and other cognitive processes), Adaptability and Resilience (e.g., creativity and flexibility), Mood and Outlook (e.g., emotional regulation, optimism), Drive and Motivation (e.g., sustained interest, persistence), Social Self (e.g., maintaining relationships, self-image), and Mind-Body Connection (e.g., physical functioning, psychosomatic wellbeing). Subcategory scores ranged from -100 to +200, and were computed by a weighted average of scores from 10 to 24 relevant symptom items based on a review of cognitive and brain functioning models. Further details on the development, full descriptions, and psychometric properties of the MHQ can be found elsewhere [33,34],

Physical activity. Participants responded to single item that asked: "How regularly do you engage in physical exercise (30 minutes or more)?" Response options included "Rarely/never"; "Less than once a week"; "Once a week"; "Few days a week"; and "Every day". In line with Chekroud et al. [28], responses to the physical activity frequency item were recoded into binary groups with participants who reported "Rarely/never" coded as the control (inactive; no exposure to physical activity), and all other responses coded as the treated (physically active; exposure to physical activity).

Covariates. To adjust for potential confounders, the following covariates were considered for inclusion in our analysis: age, biological sex, gender identity, ethnicity, educational attainment, employment status, relationship status, frequency of adequate sleep, frequency of socializing, diagnosis of a medical condition (Y/N), whether they are currently seeking mental health treatment (Y/N), and whether they reported a significant traumatic childhood or adult experience (Y/N). Data inspection revealed considerable missingness for ethnicity (84.2%) and gender identity (98.5%) due to only having been included on surveys for individuals who reported residing in certain countries, and therefore these variables were excluded. All responses in which participants answered “Prefer not to say” were recoded as missing.

Statistical Analysis

All data preprocessing and statistical analyses were done using the statistical software R version 4.1.2 [35] and RStudio (Version 2022.07.2). First, distributions of covariates were balanced between the non-exposure (i.e., Inactive) and exposure (i.e., Physically Active) groups using propensity score weights estimated with generalized boosted modeling (GBM) [36,37], and implemented in the R Package *WeightIt* [38]. The propensity score is defined as “the conditional probability of assignment to a particular treatment given a vector of observed covariates” [39]. Weighting was preferred over matching procedures for the purpose of preserving sample size. Propensity scores weights were computed based on the Average Treatment effect on the Control (ATC) estimand, which is used to estimate the hypothetical average treatment effect on those who did not receive the treatment. In other words, it is the expected effect of physical activity on those in the sample who are inactive, which would help inform the clinical question of whether mental health practitioners should encourage physical activity in inactive patients. This research question is relevant for mental health practitioners given that individuals with mental health disorders have been shown to be more sedentary and less active than population norms [40]. Treatment effects estimated with propensity score adjustment are unbiased when the strong ignorability assumption is met (i.e., when there are no unobserved confounders, and all observed confounders are included in the model) [39].

GBM is a non-parametric iterative machine learning method which, as implemented in the present study, combines boosting (the sequential combination of weak learners to improve predictions by adapting the errors of the previous model) and regression trees (the weak learners) to generate a smoothed function of estimated propensity scores. This method automatically accommodates non-linearity and complex interactions, and has been shown in previous studies to outperform traditional parametric models such as logistic regression [36,41,42]. Several tuning parameters were selected to achieve covariate balancing, as suggested by McCaffrey et al [36]. The Bernoulli distribution was chosen for the loss function the boosted model was to minimize, as our treatment variable was coded as a binary exposure. The number of trees was determined by minimizing the average standardized absolute mean difference in the covariates. The maximum number of trees was set to 10,000 by default, and increased to 20,000 if covariate balancing was not achieved. Missing data was handled by surrogate splitting as described in the *WeightIt* R package documentation [38]. Though unlikely to significantly improve the performance of our procedure [43] weights above 99% were winsorized to reduce potential bias from extreme values. Diagnostics were used to ensure covariates were adequately balanced by assessing the weighted absolute standardized difference in means of covariates between treatment and control group.

For our main analysis, propensity weights were fed into a regression model to estimate the ATC for physical activity on seven outcomes: overall MHQ score, and its six subcategories, Core Cognition, Adaptability and Resilience, Mood and Outlook, Drive and Motivation, Social

Self, and Mind-Body Connection. To explore whether the effect of physical activity on mental health differs across age groups, we performed the same analysis on each age group (18-24, 25-34, 35-44, 45-54, 55-64, 65-74, 75-84, 85+ years of age) for the MHQ and its six subcategories. Lastly, we estimated the marginal interaction effects of age and physical activity on MHQ to investigate whether an age gradient for mental health exists, and how this may be moderated by physical activity status. In all models, participants were nested within country to account for potential clustering effects.

Several sensitivity analyses were performed to determine whether the inferences of the main analyses were biased due to model misspecification or handling of missing data [44,45]. First, we computed propensity score weighted regression models that included further adjustment for the full covariate set to allow for doubly robust estimation [46]. Second, instead of handling covariate missingness by surrogate splitting, we first implemented multiple imputation (MI) before the GBM estimation of propensity scores. Third, we estimated ATCs using MI and covariate balancing propensity score (CBPS) weighting, which may outperform GBM if there is a non-complex relationship between treatment and outcome [47]. MI and CBPS are described in greater detail in the Supplementary Materials (Section A). Doubly robust estimation was also computed for these models by including the full covariate set in the multiply imputed, CBPS or GBM-weighted regression models. Akin to our main analyses, participants were nested within country for all models.

Results

Descriptive statistics. After dropping two cases due to Arabic responses not translating properly, the final sample included 341,956 participants, and was predominantly female (55.3%; 43.5% male, 0.2% other/intersex), post-secondary educated (47.5% with a bachelor’s or graduate degree; 32.6% high school or less), employed (47.8%; 32.1% studying or retired, 8.7% unemployed), married (42.5%; 24.9% single), and physically active to some degree (60.4%). The sample was also representative across the adult lifespan (18-24 and 55-64 were the most common age ranges selected at 18.91% and 18.50% of the sample, respectively). The mean score for the MHQ was 67.93 ± 72.70 SD, which would be considered "Managing" as per the MHQ's six levels of functioning. Full descriptive statistics for the sample demographic characteristics, covariates, physical activity, MHQ, and the six subcategories for each age group can be found in Supplementary Materials Table 1.

After adjusting for propensity score weighting, the effective sample for the treated (active) group was reduced to 140,633.8 (68.13% of unadjusted), yielding an overall effective sample size of 276,158.8 (80.76% of original sample). The effective sample size is the "approximately the number of observations from a simple random sample that yields an estimate with sampling variation equal to the sampling variation obtained with the weighted comparison observation", and can be interpreted as a conservative lower bound for the adjusted size of the weighted sample [48]. Diagnostics indicated that covariate balance was successfully achieved after GBM and CBPS weighting procedures were implemented (see Supplementary Materials, Section B).

Physical Activity. Propensity score weighted models demonstrated physical activity was associated with significant ($p < 0.01$) treatment effects on overall MHQ scores (ATC = 17.86; 95% CI: 15.07-20.64), which coincided with a small effect size calculated using standard deviations from the unweighted data (standardized mean difference (SMD) = 0.25). Physical activity was also associated with significant treatment effects for each of the six MHQ subcategories: Core Cognition (ATC = 16.33; 95% CI: 13.87-18.78; SMD = 0.25), Adaptability and Resilience (ATC =17.57; 95% CI: 14.83-20.31; SMD = 0.26), Drive and Motivation (ATC = 15.86; 95% CI: 12.87-18.86; SMD = 0.24), Mood and Outlook (ATC = 15.27; 95% CI: 12.53-18.01; SMD = 0.22), Social Self (ATC = 13.02; 95% CI: 10.18-15.85; SMD = 0.17), and Mind-Body Connection (ATC = 19.25; 95% CI: 16.66-21.84; SMD = 0.31).

Physical Activity and Age. Figures 1 and 2 show the effects of PA on overall MHQ scores and each subcategory by each age group. Briefly, overall trends showed significant beneficial effects of physical activity on overall MHQ scores and each MHQ subcategory across each age group. Larger effects were observed for young and middle-aged adults as well as those 85+ years of age. Inspection of the estimated effects on the six MHQ subcategories suggest that younger age groups may experience more favorable effects from physical activity for Core Cognition and Adaptability and Resilience, as compared to the other older age groups. All ATCs and standard errors can be found in Supplementary Materials Table 2.

Figures 3 and 4 show the predicted values of overall MHQ scores and each of the six subcategories as a function of age and physical activity engagement, demonstrating consistent increases in mental health with aging, with the exception of 75-84 to 85+ where mental health appears to plateau as evidenced by non-significant changes in both the Inactive and Active groups. Being physically active was associated with consistently higher mental health across all age groups.

Sensitivity analyses. Our sensitivity analyses (see Table 1) demonstrated convergence of the estimated treatment effects of physical activity on mental health across each of the alternative statistical techniques employed when compared to the main GBM results.

Discussion

The purpose of the present study was to estimate the treatment effects of physical activity engagement on a comprehensive indicator of mental health and its subcategories, and whether these effects may differ across age cohorts. Our findings revealed a significant small effect of self-reported physical activity on overall mental health and well-being. Sensitivity analyses revealed this effect was robust after adjusting for covariates using several different statistical methods. These findings are consistent with the existing evidence that has demonstrated beneficial associations between physical activity and various psychological outcomes including severe mental disorders [40], cognitive function [49,50], emotional skills [51], resilience [52], and quality of life [19,53]. Our results also align with previous work that has shown favorable effects of physical activity on indicators of mental health are consistent across the adult lifespan [54,55]. Taken together, these findings further underscore the importance of promoting a physically activity lifestyle to improve population mental health and well-being, which has the potential to significantly reduce the forecasted growing economic costs associated with poor mental health over the next decade.

Findings from the present study also contribute to the body of literature investigating associations between physical activity and mental health through examining specific subcategories of mental health and well-being. Our results showed robust and consistent beneficial effects of physical activity on each of the six subcategories of the MHQ, although it should be noted that physical activity appears to have a significantly stronger relationship with Mind-Body Connection compared to Social Self as evidenced by non-overlapping 95% CIs. The Mind-Body Connection subcategory, in which the largest effects were observed for physical activity, contains items assessing aspects of well-being with benefits robustly related to physical activity, such as pain [56,57], sleep [58,59], appetite regulation [60,61], and fatigue [62,63].

Conversely, the smallest effect was shown for Social Self, which includes aspects of well-being with less established and robust associations to physical activity such as empathy, communication skills and relationship building [64,65]. Although physical activity is a social pursuit for many, one potential explanation for a smaller effect of physical activity on Social Self is that some individuals prefer to engage in independent activities such as running or cycling alone, thus negating the potential social benefits associated with more group-oriented activities such as team sports and exercise classes. Nevertheless, these findings suggest that physical activity may confer benefits for all aspects of mental health and well-being, with small differences favoring psychophysiological over social aspects.

This study also addressed a knowledge gap regarding a dearth of evidence investigating potential differential effects of physical activity on certain aspects of mental health and well-being across the adult lifespan. Evidence indicated that young and middle-aged adults may experience greater benefits for their overall mental health from physical activity engagement in comparison to older adults. It should be noted that adults 85+ years of age appear to be an exception; however, this group also had the largest confidence interval likely due to a relatively smaller sample. As average levels of physical activity tend to be higher among young and middle-aged adults than older adults [66], a more sedentary lifestyle may be especially indicative of impairment in younger cohorts. Core Cognition, Drive and Motivation, and Adaptability and Resilience followed the same trend as overall MHQ scores, and thus these specific aspects of mental health and well-being may be more amenable to benefits from adopting a more active lifestyle, whereas the other subcategories seem to demonstrate relatively consistent benefits from physical activity across the adult lifespan. Finally, differences between inactive and active groups across ages were most pronounced in the 85+ age group as evidenced by the largest average marginal effect across all subcategories. This finding makes it clear that physical activity engagement is especially important for maintaining better mental health and well-being in the latest stages of life.

As the body of literature examining associations between physical activity and mental health continues to grow, it is imperative that researchers adopt statistical best practices that can reduce bias and strengthen our inferences. Matching and weighting techniques have received little attention in the fields of exercise psychology and behavioral medicine to date. For example, an advantage of utilizing propensity scores over controlling for covariates in a traditional multivariable linear regression is that the propensity model can deal with non-linear relationships between the covariates and outcome, as well as higher order interactions, and the GBM can handle these interaction terms non-parametrically when estimating the propensity score. As different propensity score estimation methods may perform differentially based on different assumptions and approaches to handle missing data [44,45,47], we utilized several combinations of methods in our sensitivity analyses. Our sensitivity analysis revealed minimal deviance in the estimated effects of physical activity on overall MHQ scores across the various covariate adjustment and missing data procedures that were implemented – effect sizes were equivalent ranging from an SMD of 0.25 to 0.26. Using these various propensity score estimation techniques helped to improve our confidence that the estimated effect was not biased due to misspecification of the propensity model. In doing so, these estimates strengthen the inferences we can make about the relationship between physical activity and mental health. Though strong causal inferences are not indicated by cross-sectional observations, our results converge with existing intervention studies. For example, previous meta-analyses of randomized controlled trials on exercise and depression found pooled effect sizes ranging from 0.62 to 0.98 [16,67,68].

Compared to previous intervention research however, our findings may underestimate the true effect of physical activity due to issues related with self-report (e.g., overestimating ones physical activity). Regardless, the present findings support and extend the existing literature on the benefits of physical activity engagement across various aspects of mental health.

Despite several strengths, there are several limitations with the current study. Firstly, unlike randomization, propensity score weighting does not adjust for unobserved covariates [69]. An unbiased treatment effect assumes that all potential confounders are observed, which is unlikely to be the case in any observational study. Additionally, the covariates included in this analysis were restricted by what was included in the GMP survey. Adjusting for a partial set of confounders may reduce bias, but it is unknown to what extent. Second, the MHQ and its subcategories have yet, to our knowledge, been validated in an independent sample. It would be interesting, for example, to investigate whether the MHQ and its subcategories predict the onset or course of distinct mental disorders. Third, physical activity was self-reported, which can introduce recall errors – particularly among older adults who are more prone to cognitive decline – and social desirability effects [70]. However, researchers need to balance feasibility with practicality and therefore using a self-reported measure of physical activity may be best suited for data collection with a sample of this size and geographic dispersion. Lastly, the GMP has used convenience sampling to recruit participants, targeted towards individuals who used mental health-related search terms in Google and Facebook. Although the present sample includes individuals from over 200 countries, it may not truly be globally representative, as it would have also overlooked individuals living in regions with limited to no internet access.

Conclusion

This cross-sectional study estimated treatment effects of physical activity on several aspects of mental health among a large global sample of adults using advanced covariate balancing techniques to reduce bias in our estimates. Our results demonstrate a significant small effect of self-reported physical activity on a comprehensive measure of overall mental health and well-being, in addition to similar benefits across several specific subcategories of mental health. The strongest associations between physical activity and mental health appear to occur during the early and middle-aged adult life stages, with effects becoming weaker into old age. These findings further support the growing body of evidence promoting the benefits of physical activity on various aspects of mental health and well-being among the population.

References

1. Steel Z, Marnane C, Iranpour C, et al.: The global prevalence of common mental disorders: a systematic review and meta-analysis 1980–2013. Int J Epidemiol. 2014; 43:476–493.
2. Collaborators G 2019 MD, others: Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Psychiatry. 2022; 9:137–150.
3. Health TLG: Mental health matters. Lancet Glob Health. 2020; 8:e1352.
4. Samji H, Wu J, Ladak A, et al.: Mental health impacts of the COVID-19 pandemic on children and youth–a systematic review. Child Adolesc Ment Health. 2022; 27:173–189.
5. Prati G, Mancini AD: The psychological impact of COVID-19 pandemic lockdowns: a review and meta-analysis of longitudinal studies and natural experiments. Psychol Med. 2021; 51:201–211.
6. Robinson E, Sutin AR, Daly M, Jones A: A systematic review and meta-analysis of longitudinal cohort studies comparing mental health before versus during the COVID-19 pandemic in 2020. J Affect Disord. 2022; 296:567–576.
7. Kauhanen L, Wan Mohd Yunus WMA, Lempinen L, et al.: A systematic review of the mental health changes of children and young people before and during the COVID-19 pandemic. Eur Child Adolesc Psychiatry. 2022; .
8. Santomauro DF, Mantilla Herrera AM, Shadid J, et al.: Global prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020 due to the COVID-19 pandemic. The Lancet. 2021; 398:1700–1712.

9. Oswalt SB, Lederer AM, Chestnut-Steich K, Day C, Halbritter A, Ortiz D: Trends in college students' mental health diagnoses and utilization of services, 2009–2015. J Am Coll Health. 2020; 68:41–51.
10. Keyes KM, Gary D, O'Malley PM, Hamilton A, Schulenberg J: Recent increases in depressive symptoms among US adolescents: trends from 1991 to 2018. Soc Psychiatry Psychiatr Epidemiol. 2019; 54:987–996.
11. Chen Y, Cowden RG, Fulks J, Plake JF, VanderWeele TJ: National data on age gradients in well-being among US adults. JAMA Psychiatry. 2022; 79:1046–1047.
12. Blanchflower DG, Oswald AJ: Is well-being U-shaped over the life cycle? Soc Sci Med. 2008; 66:1733–1749.
13. Solmi M, Radua J, Olivola M, et al.: Age at onset of mental disorders worldwide: large-scale meta-analysis of 192 epidemiological studies. Mol Psychiatry. 2022; 27:281–295.
14. Gordon BR, McDowell CP, Hallgren M, Meyer JD, Lyons M, Herring MP: Association of efficacy of resistance exercise training with depressive symptoms: meta-analysis and meta-regression analysis of randomized clinical trials. JAMA Psychiatry. 2018; 75:566–576.
15. Pearce M, Garcia L, Abbas A, et al.: Association between physical activity and risk of depression: a systematic review and meta-analysis. JAMA Psychiatry. 2022; .
16. Schuch FB, Vancampfort D, Richards J, Rosenbaum S, Ward PB, Stubbs B: Exercise as a treatment for depression: a meta-analysis adjusting for publication bias. J Psychiatr Res. 2016; 77:42–51.
17. Aylett E, Small N, Bower P: Exercise in the treatment of clinical anxiety in general practice–a systematic review and meta-analysis. BMC Health Serv Res. 2018; 18:1–18.

18. McDowell CP, Dishman RK, Gordon BR, Herring MP: Physical activity and anxiety: a systematic review and meta-analysis of prospective cohort studies. Am J Prev Med. 2019; 57:545–556.

19. Marquez DX, Aguiñaga S, Vásquez PM, et al.: A systematic review of physical activity and quality of life and well-being. Transl Behav Med. 2020; 10:1098–1109.

20. Chekroud SR, Gueorguieva R, Zheutlin AB, et al.: Association between physical exercise and mental health in 1· 2 million individuals in the USA between 2011 and 2015: a cross-sectional study. Lancet Psychiatry. 2018; 5:739–746.

21. Ekkekakis P: Why Is exercise underutilized in clinical practice despite evidence it is effective? Lessons in pragmatism from the inclusion of exercise in guidelines for the treatment of depression in the British National Health Service. Kinesiol Rev. 2020; 10:29–50.

22. Kendrick T, Pilling S, Mavranezouli I, et al.: Management of depression in adults: summary of updated NICE guidance. BMJ. 2022; 378:o1557.

23. Stubbs B, Vancampfort D, Hallgren M, et al.: EPA guidance on physical activity as a treatment for severe mental illness: a meta-review of the evidence and Position Statement from the European Psychiatric Association (EPA), supported by the International Organization of Physical Therapists in Mental Health (IOPTMH). Eur Psychiatry. 2018; 54:124–144.

24. Malhi GS, Bassett D, Boyce P, et al.: Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders. Aust N Z J Psychiatry. 2015; 49:1087–1206.

25. Brokmeier LL, Firth J, Vancampfort D, et al.: Does physical activity reduce the risk of psychosis? A systematic review and meta-analysis of prospective studies. Psychiatry Res. 2020; 284:112675.
26. Ashdown-Franks G, Firth J, Carney R, et al.: Exercise as medicine for mental and substance use disorders: a meta-review of the benefits for neuropsychiatric and cognitive outcomes. Sports Med. 2020; 50:151–170.
27. Melo MCA, Daher EDF, Albuquerque SGC, de Bruin VMS: Exercise in bipolar patients: a systematic review. J Affect Disord. 2016; 198:32–38.
28. Borsboom D, Cramer AO, Schmittmann VD, Epskamp S, Waldorp LJ: The small world of psychopathology. PloS One. 2011; 6:e27407.
29. Newson JJ, Pastukh V, Thiagarajan TC: Poor separation of clinical symptom profiles by DSM-5 disorder criteria. Front Psychiatry. 2021; 12:775762.
30. Iniesta R, Malki K, Maier W, et al.: Combining clinical variables to optimize prediction of antidepressant treatment outcomes. J Psychiatr Res. 2016; 78:94–102.
31. Fried EI, Nesse RM: Depression sum-scores don't add up: why analyzing specific depression symptoms is essential. BMC Med. 2015; 13:1–11.
32. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP: The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. The Lancet. 2007; 370:1453–1457.
33. Newson JJ, Thiagarajan TC: Assessment of population well-being with the mental health quotient (MHQ): development and usability study. JMIR Ment Health. 2020; 7:e17935.
34. Newson JJ, Pastukh V, Thiagarajan TC: Assessment of Population Well-being With the Mental Health Quotient: Validation Study. JMIR Ment Health. 2022; 9:e34105.

35. R Core Team: R: A Language and Environment for Statistical Computing. Vienna, Austria: R Foundation for Statistical Computing, 2022.
36. McCaffrey DF, Ridgeway G, Morral AR: Propensity score estimation with boosted regression for evaluating causal effects in observational studies. Psychol Methods. 2004; 9:403.
37. Friedman JH: Greedy function approximation: a gradient boosting machine. Ann Stat. 2001; 1189–1232.
38. Greifer N: WeightIt: Weighting for Covariate Balance in Observational Studies. 2022.
39. Rosenbaum PR, Rubin DB: The central role of the propensity score in observational studies for causal effects. Biometrika. 1983; 70:41–55.
40. Vancampfort D, Firth J, Schuch FB, et al.: Sedentary behavior and physical activity levels in people with schizophrenia, bipolar disorder and major depressive disorder: a global systematic review and meta-analysis. World Psychiatry. 2017; 16:308–315.
41. Tu C: Comparison of various machine learning algorithms for estimating generalized propensity score. J Stat Comput Simul. 2019; 89:708–719.
42. Lee BK, Lessler J, Stuart EA: Improving propensity score weighting using machine learning. Stat Med. 2010; 29:337–346.
43. Lee BK, Lessler J, Stuart EA: Weight trimming and propensity score weighting. PloS One. 2011; 6:e18174.
44. Cham H, West SG: Propensity score analysis with missing data. Psychol Methods. 2016; 21:427.

45. Coffman DL, Zhou J, Cai X: Comparison of methods for handling covariate missingness in propensity score estimation with a binary exposure. BMC Med Res Methodol. 2020; 20:1–14.

46. Funk MJ, Westreich D, Wiesen C, Stürmer T, Brookhart MA, Davidian M: Doubly robust estimation of causal effects. Am J Epidemiol. 2011; 173:761–767.

47. Setodji CM, McCaffrey DF, Burgette LF, Almirall D, Griffin BA: The right tool for the job: Choosing between covariate balancing and generalized boosted model propensity scores. Epidemiol Camb Mass. 2017; 28:802.

48. Ridgeway G, McCaffrey DF, Morral AR, et al.: Toolkit for weighting and analysis of nonequivalent groups: a tutorial for the R TWANG package. Rand Santa Monica, Calif, 2022.

49. Bidzan-Bluma I, Lipowska M: Physical Activity and Cognitive Functioning of Children: A Systematic Review. Int J Environ Res Public Health. 2018; 15:800.

50. Carvalho A, Rea IM, Parimon T, Cusack BJ: Physical activity and cognitive function in individuals over 60 years of age: a systematic review. Clin Interv Aging. 2014; 661–682.

51. Laborde S, Dosseville F, Allen MS: Emotional intelligence in sport and exercise: A systematic review. Scand J Med Sci Sports. 2016; 26:862–874.

52. Shanahan L, Steinhoff A, Bechtiger L, et al.: Emotional distress in young adults during the COVID-19 pandemic: evidence of risk and resilience from a longitudinal cohort study. Psychol Med. 2022; 52:824–833.

53. Schuch FB, Vancampfort D, Rosenbaum S, Richards J, Ward PB, Stubbs B: Exercise improves physical and psychological quality of life in people with depression: A meta-

analysis including the evaluation of control group response. Psychiatry Res. 2016; 241:47–54.

54. Cunningham C, O'Sullivan R, Caserotti P, Tully MA: Consequences of physical inactivity in older adults: A systematic review of reviews and meta-analyses. Scand J Med Sci Sports. 2020; 30:816–827.
55. de Oliveira L da SSCB, Souza EC, Rodrigues RAS, Fett CA, Piva AB: The effects of physical activity on anxiety, depression, and quality of life in elderly people living in the community. Trends Psychiatry Psychother. 2019; 41:36–42.
56. Rice D, Nijs J, Kosek E, et al.: Exercise-induced hypoalgesia in pain-free and chronic pain populations: state of the art and future directions. J Pain. 2019; 20:1249–1266.
57. Shiri R, Falah-Hassani K: Does leisure time physical activity protect against low back pain? Systematic review and meta-analysis of 36 prospective cohort studies. Br J Sports Med. 2017; 51:1410–1418.
58. Lederman O, Ward PB, Firth J, et al.: Does exercise improve sleep quality in individuals with mental illness? A systematic review and meta-analysis. J Psychiatr Res. 2019; 109:96–106.
59. Kredlow MA, Capozzoli MC, Hearon BA, Calkins AW, Otto MW: The effects of physical activity on sleep: a meta-analytic review. J Behav Med. 2015; 38:427–449.
60. Beaulieu K, Hopkins M, Blundell J, Finlayson G: Homeostatic and non-homeostatic appetite control along the spectrum of physical activity levels: An updated perspective. Physiol Behav. 2018; 192:23–29.

61. Beaulieu K, Hopkins M, Blundell J, Finlayson G: Does habitual physical activity increase the sensitivity of the appetite control system? A systematic review. Sports Med. 2016; 46:1897–1919.
62. Pilutti LA, Greenlee TA, Motl RW, Nickrent MS, Petruzzello SJ: Effects of exercise training on fatigue in multiple sclerosis: a meta-analysis. Psychosom Med. 2013; 75:575–580.
63. Bower JE: Cancer-related fatigue—mechanisms, risk factors, and treatments. Nat Rev Clin Oncol. 2014; 11:597–609.
64. Pels F, Kleinert J: Loneliness and physical activity: A systematic review. Int Rev Sport Exerc Psychol. 2016; 9:231–260.
65. Shima T, Jesmin S, Nakao H, et al.: Association between self-reported empathy and level of physical activity in healthy young adults. J Phys Fit Sports Med. 2021; 10:45–49.
66. Van Der Zee MD, Van Der Mee D, Bartels M, De Geus EJ: Tracking of voluntary exercise behaviour over the lifespan. Int J Behav Nutr Phys Act. 2019; 16:1–11.
67. Cooney GM, Dwan K, Greig CA, et al.: Exercise for depression. Cochrane Database Syst Rev. 2013; .
68. Josefsson T, Lindwall M, Archer T: Physical exercise intervention in depressive disorders: Meta-analysis and systematic review. Scand J Med Sci Sports. 2014; 24:259–272.
69. Joffe MM, Rosenbaum PR: Invited commentary: propensity scores. Am J Epidemiol. 1999; 150:327–333.
70. Sallis JF, Saelens BE: Assessment of physical activity by self-report: status, limitations, and future directions. Res Q Exerc Sport. 2000; 71:1–14.

Tables and Figures

Table 1. Sensitivity analysis. Reported ATC effects and standard errors on MHQ

MHQ	GBM	Doubly Robust GBM	MI + GBM	Doubly Robust MI + GBM	MI + CBPS	Doubly Robust MI + CBPS
ATC	17.86	17.74	17.75	17.77	18.15	17.87
SE	1.43	0.99	0.28	0.23	0.28	0.22
SMD	0.25	0.25	0.25	0.25	0.26	0.25

Figure 1. ATC's of physical activity on overall MHQ and subcategories scores across age groups. Error bars represent 95% CIs.

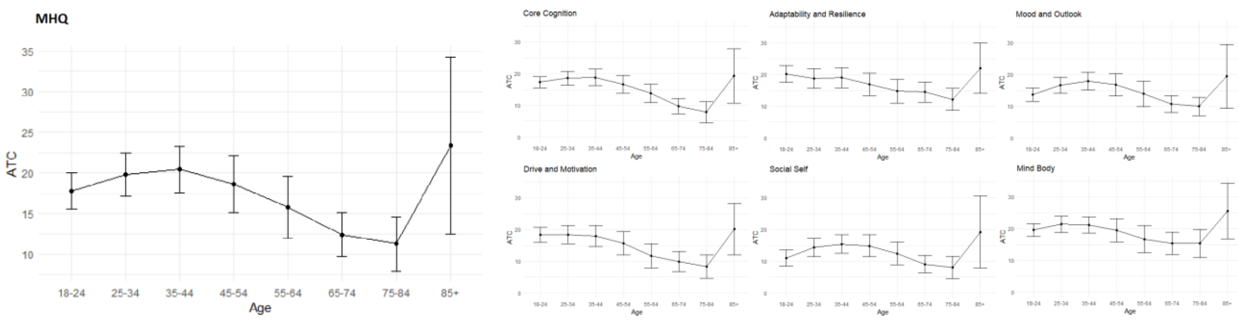

Figure 2. Marginal effects on MHQ and subcategories by age for inactive and active groups with 95% CIs. Levels of subcategory scores ranged from -100 to +200.