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Longitudinal associations between physical activity and depression scores in Swedish women followed 32 years.

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Running title: Physical activity and depression scores in women

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Abstract

Objective: Physical activity is negatively associated with depressive symptoms. However, few studies consider dynamic associations of changes in physical activity and reciprocal relationships. This study aimed to perform comprehensive evaluations of relationships between physical activity and depression scores in women followed from mid- to late-life.

Method: The Prospective Population Study of Women in Gothenburg, Sweden provided repeated measures of self-reported physical activity and depressive symptoms between 1974-2005 (baseline N=676, 84.5 % response rate). Depressive symptoms were assessed using the Montgomery-Åsberg Depression Rating Scale and physical activity was evaluated by the Saltin-Grimby Physical Activity Level Scale. Latent growth curve analyses were used to evaluate associations of change and cross-lagged models were used to study the reciprocal relationship between physical activity and depression scores.

Results: At baseline, lower levels of physical activity were related to higher depression scores. Individuals with decreasing physical activity over time evidenced higher depression scores at 32 year follow-up. Higher average baseline depression score was related to declining levels of physical activity at subsequent examinations.

Conclusion: Reduced physical activity may be a long-term consequence of depression. It is important to address individual changes in physical activity and not merely absolute levels of physical activity in relationship to depression.

Keywords: Physical activity; depression scores; change; women

Significant outcomes

- Average depression symptomatology significantly increased across time, and there were significant between-person differences in modified MADRS score at baseline and change over time.
- On a within-person level, women who reported a decreasing physical activity over time also reported higher depression scores.
- Higher depression scores predicted less subsequent physical activity. These results highlight the need to consider within-person changes and not merely current levels of physical activity.

Limitations

- Since all members of the sample are female, White, and living in Sweden, the external validity of the study is limited.
- Even though directions of effects were analysed in cross-lagged models, the observational study design limits the possibility to draw conclusions about directionality.
- The self-reported single item provided a less than optimal measure of physical activity.

Introduction

A growing evidence base suggests that physical activity is important for mental health (1, 2). Numerous studies show associations between physical activity and features of depression in both women and men, and across culturals and age groups (1, 3, 4). Cross-sectional studies show inverse associations between physical activity and depression score (5, 6). Physical activity is reported to have protective (5, 7-10) and even therapeutic (2, 10-12) effects on depression status. However, this relationship is not supported by all studies (6, 13), thus a causal relationship between physical activity and depression remains unclear (5, 14-17). Most studies examine how a baseline level of physical activity predicts subsequent depression (6-8, 18), and few have targeted reciprocal effects across time (5, 15, 17). Furthermore, few studies investigate dynamic associations of changing physical activity levels and depression scores over time (5, 17, 19-20). As a result, within-person fluctuation of physical activity or depression scores is not considered. The need for more thorough models investigating the relationship between physical activity and depression has recently been emphasized (21).

Aims of the study

The aim of our study was to investigate associations between leisure time physical activity and depression scores in a prospective population-based study of women followed for 32 years. First, cross-sectional baseline associations of physical activity and depression scores were evaluated. Second, baseline level of physical activity was associated with the subsequent trajectory of depression scores over time. Third, within-person change from baseline level of physical activity was associated with deviations from the individual's predicted trajectory of depression scores. Finally, the reciprocal relationship between physical activity and depression scores was evaluated over time.

Methods

Study population

These analyses originate from the Prospective Population Study of Women (PPSW) in Gothenburg which began in 1968 with a representative sample of 1462 women (participation rate 90%) living in

Gothenburg and born in 1908, 1914, 1918, 1922, and 1930 (22). The sample was obtained from the Revenue Office Register and women born on specific dates were invited to take part in the study. PPSW is a multi-disciplinary longitudinal study with seven follow-up examinations over 44 years. A representative subsample of 899 women was invited to take part in a psychiatric examination at baseline in 1968, and 800 participated (89%). The psychiatric examinations in 1974 (N=676, 84.5 % response rate) provided baseline data for the current study, and follow-ups were conducted in 1992 (N=590), 2000 (N=651), and 2005 (N=527). The study was approved by the Ethics Committee for Medical Research of the University of Gothenburg and has been performed according to the ethical standards outlined in the Helsinki declaration. All participants or close relatives gave informed consent before taking part of the study.

Measurement of depression score

Psychiatric examinations were semi-structured and performed by psychiatrists (1974, 1992) or psychiatric nurses (2000, 2005). The Montgomery-Åsberg Depression Rating Scale (MADRS) (23) was used to rate symptoms and signs of depression during the preceding month. The early version employed at baseline in 1974 lacked one of the 10 original MADRS items (reduced appetite). The MADRS score used in this study is therefore referred to as modified MADRS score, and included reported and observed depressed mood, inner tension, reduced sleep, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts. Each symptom is rated from 0 (no symptoms) to 6 (severe symptoms), yielding a maximum score of 54.

Physical activity

At each examination, participants were asked about level of physical activity in their leisure time based on the Saltin-Grimby Physical Activity Level Scale (24). This scale is a combined frequency-intensity measure including the following options: (1) “Almost totally inactive” (e.g. reading, watching TV, going to the movies), (2) “Some physical activity at a minimum of 4 hours/week” (e.g. bicycling, walking to/from workplace or during leisure time, walking with family), (3) “Regular physical activity” (e.g. gardening, golfing, running, keep-fit exercise, tennis, dancing), and (4) “Regular intense

physical activity and contests" (e.g. running several times/week, swimming several times/week, competitive sports.

Diagnoses of dementia

In 1974, clinical dementia diagnoses were made by the examining psychiatrist. From the 1992 examination a diagnosis of dementia was made based on the psychiatric examination and a close informant interview using a symptom algorithm according to Diagnostic and Statistical Manual of Mental Disorders, third version revised (DSM-III-R) criteria (25). For individuals lost to follow-up, the diagnosis of dementia was made by geriatric research psychiatrists in consensus conferences after examination of data from medical records and the Swedish Hospital Discharge Register (26). In this study women with dementia were excluded in subanalyses.

Covariates

Potential covariates included age, marital status (married or cohabiting versus not married or cohabiting), education (defined as compulsory education, i.e. 6 years in those born 1914-22 and 7 years in those born 1940, versus at least one year of post-compulsory education), social group (socioeconomic status based on the husband's occupation for married women and own occupation for unmarried women, and defined as high, medium or low), smoking status last year (never/former smoker versus current smoker), alcohol habits (drinking wine and hard liquor: never/seldom versus quite often-very often), menopausal status (pre versus post), mean body mass index (weight in kilogram divided by length in meter squared), hypertension (defined as self-reported history of being diagnosed by doctor), cardiovascular disease (self-reported), stroke (self-reported), cancer (self-reported), diabetes (self-reported treated diabetes mellitus), aching joints (yes/no), and activities of daily living (ADL; no impairment versus needing help with bathing, feeding, dressing, transfer or toileting), and were chosen based on previous literature. Potential confounders were evaluated using linear regression models. Only variables showing association ($p<0.1$) with both physical inactivity and depressive symptoms were included in the final models (i.e. age, marital status, education, and smoking status).

Statistical analyses

Latent growth curve models (LGCM) were used in this study (27). LGCM have several advantages compared to more traditional methods of analysing longitudinal data, such as general linear models (GLM) (28, 29). First, LGCM target true changes by correcting for measurement error by including residual values. Second, LGCM consider both between-person and within-person variability. In addition, latent growth curve models take different time intervals into consideration given the way they are set up. In other words, time intervals themselves are modelled. In this study, LGCM was used to model average baseline value (intercept mean) and change (slope mean) in depression scores across four measurement time-points over 32 years, as well as differences between persons in intercept variance and change (slope variance). Baseline measures of age, education, physical activity, smoking status, and marital status were used as time-invariant covariates in models of baseline depression score and change in depression scores over time. Age and level of physical activity were mean-centred to the baseline mean to improve interpretation. Moreover, change from baseline in mean-centred physical activity was used as a time-varying covariate to model how within-person change in physical activity was related to within-person change in depression scores.

Finally, cross-lagged models were used to study the reciprocal relationship between physical activity and depression scores. The strategy used was to compare the fit of four different models: (a) a baseline model, including only prediction between levels of depression and physical activity at subsequent occasions (e.g., prediction from depression 1974 to 1992, from 1992 to 2000 and similarly for physical activity), (b) a "physical activity-to-depression-model", including prediction between levels of depression at subsequent occasions and prediction from physical activity to subsequent depression scores; (c) a "depression-to-physical activity-model", including prediction between levels of physical activity at subsequent occasions (e.g., from physical activity 1974 to 1992, from 1992 to 2000 and so on), and prediction from depression scores to subsequent physical activity, and (d) a reciprocal model, including both prediction from depression to physical activity and vice versa.

Mplus version 7.1 (Muthen & Muthen, 1998–2012) was used to analyse the data with the maximum likelihood (ML) and robust maximum likelihood (MLR) estimators. Missing data were handled using full maximum likelihood (FIML) estimator, which is default in Mplus. Based on recommendations of

Hu and Bentler, 1999 (30), the following fit indexes were used: (a) Satorra-Bentler chi-square statistics, (b) Bentler's comparative fit index (CFI) (31) and (c) the root mean square error of approximation (32). For CFI, values close to .95 or greater indicate a well-fitting model (30). For RMSEA, values less than .05 indicate a good fit, whereas values up to .08 represent a reasonable fit (32). When considering confounders, only variables related to both physical activity and depression score at a level of $p<0.05$ were included in the conditional model.

Results

Table 1 shows characteristics of the 676 women who participated in the psychiatric examinations in 1974. Cross-sectional relationships between modified MADRS scores and physical activity levels at each examination wave are shown in Figure 1. The linear latent growth curve model of depression scores without covariates fitted the data well, $\chi 2= 11.19$ (5df), CFI=0.97; RMSEA: 0.043 (0.000-0.077). The mean modified MADRS score at baseline was 4.0 (of 54) and the model estimated a yearly increase of about 0.10 points over the observation period (0.10, SE=0.01, p<.001). There were substantial between-person differences in modified MADRS score at baseline (intercept variance 24.93, SE=5.49, p<.001), as well as between-person change over time (slope variance 0.02, SE=0.01, p<.05). The final model with both time-varying (physical activity change) and time-invariant covariates fitted data adequately, $\chi 2= 52.75$ (26df), CFI=0.90; RMSEA: 0.039 (0.024-0.054).

Table 1 here

Figure 1 here

Level or change in physical activity in relation to level or change in depression scores are presented in table 2. Lower mean baseline level of physical activity was related to higher mean modified MADRS score at baseline in 1974. No association was observed between baseline physical activity and change in average modified MADRS score during follow-up. In within-person analyses, a decrease in physical activity during follow-up compared to baseline was associated with higher depression scores during

32-year follow-up. Exclusion of women with dementia at any examination (n=40) did not change the results in any essential aspects (data not shown).

Table 2 here

The baseline cross-lagged model fitted data adequately, $\chi 2$= 65.13 (18df), CFI=0.91; RMSEA: 0.042 (0.032-0.054). The autoregressive estimates (i.e., previous level predicting subsequent levels of the same variable) for both depression scores and physical activity were all significant but generally lower for physical activity (β = 0.18-0.35) compared with depression scores (β = 0.48-0.57), indicating that depression scores were more stable across time compared with physical activity. Cross-sectional higher physical activity was related to lower depression score in 1974 (ϕ = -.17, p <.001), 1992 (ϕ = -.28, p <.001), and 2000 (ϕ = -.10, p <.05), but not in 2005. When adding cross-lagged predictions from physical activity to subsequent depression scores, model fit did not improve significantly ($\Delta \chi^2$=1.92/ 3 df; p>.05). None of the cross-lagged predictions were significant. However, when adding predictions from depression scores to subsequent physical activity, the model fit did improve significantly, ($\Delta \chi^2$=11.90/ 3 df, p<.01). More specifically, higher depression scores reported in examinations preceding physical activity measures, predicted lower physical activity in 1992 (β = -.13, p < .01), and 2000 (β = -.11, p < .05), but not in 2005 The reciprocal model demonstrated better fit compared with 1) the baseline, ($\Delta \chi 2$=13.78/ 6 df, p<.05), and 2) the physical activity-to-depression model ($\Delta \chi 2$=11.86/ 3 df, p<.01), but not compared to the depression-to-physical activity model ($\Delta \chi 2$=1.88/ 3 df, p>.05).

Discussion

Our study is the first to examine dynamic associations of within-person change between physical activity and depression scores in a non-clinical sample of women assessed at repeated occasions over three decades using latent growth curve modelling and cross-lagged analyses. Furthermore, on a within-person level, women who reported a decreasing physical activity over time also reported higher depression scores over time. Finally, cross-lagged analyses indicated that higher depression scores predicted less subsequent physical activity but not vice versa.

We observed that women reporting a lower level of physical activity in 1974 had higher concurrent depression scores, a finding in line with previous cross-sectional studies (5, 6). Previous studies have investigated associations of change between latent variables of physical activity and depression scores (5, 17, 19-20), and our result support the findings from these studies. However, these studies used data from only two time points (5), did not consider within-person change (17, 19) or had shorter follow-ups (between 2 and 11 years) (17, 19-20).

Several studies have investigated directionalty of the relationship between physical activity and symptom burden of depression. Most of these studies focused specifically on older adults (5, 15-17) while few also included middle-aged persons (14). Results from these studies are mixed. Our finding that higher depression scores predicted lower levels of physical activity but not vice versa is supported by one previous study that used walking as a measurement of physical activity (15), and studies focusing on consequences of depression that report physical inactivity as an outcome of depression (33). In contrast, other studies reported that lower physical activity predicted higher depression scores, but depression scores did not predict physical activity in older adults (14, 17). However, this was not observed in middle-aged adults (14), indicating a potential influence of age on the relationship between physical activity and depression and highlighting the importance of examining this association by age group in future studies. Finally, three recent studies gave support for a reciprocal relationship between physical activity and depression scores (5, 16, 18), and two of these (5, 16) used similar analytical approaches as this study. Differences between studies in sample sizes, length of follow-up, baseline ages, measurement methods, and other aspects may partly explain the inconsistent findings. Further studies investigating the reciprocal relationship between physical activity and depression scores are needed.

Mean levels of depression scores were in the expected range for the healthy population (34). No relationship was found between physical activity at baseline and subsequent change in mean depression scores, a finding that is supported by one other study (6). Most previous studies reporting that physical activity has a protective effect against depression or depression scores evaluated level of depression at follow-up rather than change in depression score (5, 7, 8).

There are a number of both biological and psychosocial hypotheses to explain the relationship between depression and physical activity. Current biological hypotheses focus on altered brain plasticity, neuroimmune effects, increased monoaminergic neurotransmission, and effects on the hypothalamic-pituitary-adrenocortical axis (35). Psychosocial hypotheses include socialization, social reinforcement, behavioural activation, self-evaluations, sense of mastery, and distraction from negative thoughts and emotion (35-36). Conditions for a physically active life are also dependent of several factors. For example, home and workplace built environments impact on cardiorespiratory fitness (37).

Reduced physical activity should be emphasized as a long term consequence of depressive symptoms and not merely as a temporary characteristic of the syndrome. This is important for several reasons. Depression scores predict subsequent physical inactivity. By focusing on this issue when managing depression, the risk for long term inactivity may be decreased. Further, inactivity associated with depression scores places this already vulnerable group at increased risk for negative consequences associated with low physical activity. For example, low physical activity is reported to mediate the relationship between depressive symptoms and disability in older adults (38), and may also be a reason why depressed elderly have an increased risk for stroke and cardiovascular disorders as well as an increased overall mortality (39). Furthermore, it is important to identify depressive symptoms in later life to prevent other severe consequences of sedentary behaviour. Finally, reduced physical activity is associated with an increase in burden of depressive symptoms. Evidence is mounting for the beneficial effects of physical activity for physical, mental, and social health in older adults. Health care professionals should work to promote physical activity in this group (40). In light of our findings, it is important to address individual changes and not merely current levels of physical activity. In the present study analyses were not stratified by age due to lack of power. Further it was not possible to stratify for sex as all participants were women. However, future studies of change should address age and sex, and examine the potential moderating effects of age and sex in the longitudinal relationships between physical activity and depression. Studies employing more modern and structured measurements of physical activity are needed.

Strengths and limitations

Strengths of these analyses include that the PPSW is a representative, systematically selected and well-characterized population sample of women followed for over three decades. Second, psychiatric examinations were performed by psychiatrists or psychiatric nurses. Third, statistical analyses considered both between- and within-person changes in physical activity and depression scores across time. In addition, analyses of the reciprocal relationship between physical activity and depression scores were included. These types of models are rarely used in this field.

Possible limitations also need to be considered. The sample size is relatively small, and all members of the sample are female, White, and living in Sweden, thereby limiting sex, ethnic, and cultural generalizability. Due to lack of information in the baseline examination, only nine out of ten MADRS items were considered, making it difficult to compare mean MADRS scores with previous studies. The MADRS was initially designed to measure change of severity in depressive symptoms in clinical settings. However, this scale has been considered an acceptable screening tool for depression in the healthy population (34). Although the inclusion of MADRS as a continuous scale in a population-based study may be discussed, the use of a continuous scale affords a stronger platform for examining more complex associations of dynamic change in depression and other variables (such as physical activity using time-varying covariate models as in the present study). Using categorically defined depression based on a particular MADRS cutoff would provide a considerable less optimal solution when looking at dynamic associations of change and reciprocal relationships across time.

The physical activity variable used in this study involves only frequency and intensity; other important components such as duration or type are lacking. Furthermore, there is potential overlap between categories 2 and 3. Together these weaknesses resulted in a less than optimal measure of total quantity of physical activity in the present study. In addition, participants are not equally distributed among the four activity groups and the number of participants in some groups is small. The limited variance associated with the physical activity item might be viewed as a potential weakness, in particular linked to using measure in change analyses that are sensitive to change. Also, the physical activity measure pertains to the entire past year, while depressive symptomatology was rated during the past month only. However, our result did demonstrate that detecting change in physical activity using this simple item was possible and the activity change demonstrated meaningful associations with

change in depressive symptoms. This scale was included in the study over 45 years ago and has been retained in its original version for comparison over time. While this is a strength for making comparisons over time, it is also a limitation as new types of exercise and new methods for assessing physical activity have appeared during the long period of follow-up. Nevertheless, the scale has shown predictive validity in relation to cardiovascular risk factors (41), and it is straightforward and easy for the participants to comprehend compared to some of the new instruments used in the field today.

MADRS scores were not available prior to 1974 and we were unable to study effects of depressive symptomatology earlier in life. Although numerous confounders were considered the potential for residual confounding is obvious. Finally, attrition due to loss of follow-up or death is an issue that must be considered in follow-up studies. Participants might be more physically active and less depressed than non-participants, and mortality is associated with both physical activity and depression. Data from the 2000 examination of the study performed at the clinic show that compared to participants, surviving non-participants had higher BMI, Waist-to-hip ratio, and blood pressure, lower education and were more likely to be smokers at the baseline examination in 1968, but inclusion of home visits attenuated these differences (42).

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Declaration of interest

PG reports no disclosures or conflicts of interest.

ML reports no disclosures or conflicts of interest.

DR G reports no disclosure or conflicts of interest.

SÖ reports no disclosure or conflicts of interest.

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References

1. BIDDLE SJ, ASARE M. Physical activity and mental health in children and adolescents: a review of reviews. Br J Sports Med 2011;**45**:886-95.
2. JOSEFSSON T, LINDWALL M, ARCHER T. Physical exercise intervention in depressive disorders: Meta-analysis and systematic review. Scand J Med Sci Sports 2014;**24**:259-72.
3. GALLEGOS-CARRILLO K, FLORES YN, DENOVA-GUTIERREZ E et al. Physical activity and reduced risk of depression: Results of a longitudinal study of Mexican adults. Health Psychol 2013;**32**:609-15.
4. AIHARA Y, MINAI J, AOYAMA A, SHIMANOUCHI S. Depressive symptoms and past lifestyle among Japanese elderly people. Community Ment Health J 2011;**47**:186-93.
5. LINDWALL M, LARSMAN P, HAGGER MS. The reciprocal relationship between physical activity and depression in older European adults: a prospective cross-lagged panel design using SHARE data. Health Psychol 2011;**30**:453-62.
6. KRITZ-SILVERSTEIN D, BARRETT-CONNOR E, CORBEAU C. Cross-sectional and prospective study of exercise and depressed mood in the elderly : the Rancho Bernardo study. Am J Epidemiol 2001;**1**53:596-603.
7. BRUNET J, SABISTON CM, CHAITON M et al. The association between past and current physical activity and depressive symptoms in young adults: a 10-year prospective study. Ann Epidemiol 2013;**23**:25-30.
8. STRAWBRIDGE WJ, DELEGER S, ROBERTS RE, KAPLAN GA. Physical activity reduces the risk of subsequent depression for older adults. Am J Epidemiol 2002;**156**:328-34.
9. ABERG MA, WAERN M, NYBERG J et al. Cardiovascular fitness in males at age 18 and risk of serious depression in adulthood: Swedish prospective population-based study. Br J Psychiatry 2012;**201**:352-9.
10. BERK M, SARRIS J, COULSON CE, JACKA FN. Lifestyle management of unipolar depression. Acta Psychiatr Scand 2013;**127**(Suppl 443):38-54.

11. DANIELSSON L, NORAS AM, WAERN M, CARLSSON J. Exercise in the treatment of major depression: A systematic review grading the quality of evidence. Physiother theory Pract 2013;**29**:573-85.

12. STURM J, PLÖDERL M, FARTACEK C et al. Physical exercise through mountain hiking in high-risk suicide patients. A randomized crossover trial. Acta Psychiatr Scand 2012;**126**: 467–475.

13. JOHNSON CC, MURRAY DM, ELDER JP et al. Depressive symptoms and physical activity in adolescent girls Med Sci Sports Exerc 2008;**40**:818-26.

14. FUKUKAWA Y, NAKASHIMA C, TSUBOI S et al. Age differences in the effect of physical activity on depressive symptoms. Psychol Aging 2004;**19**:346-51.

15. PERRINO T, MASON CA, BROWN SC, SZAPOCZNIK J. The relationship between depressive symptoms and walking among Hispanic older adults: a longitudinal, cross-lagged panel analysis. Aging Ment Health 2010;**14**:211-9.

16. STAVRAKAKIS N, DE JONGE P, ORMEL J, OLDEHINKEL AJ. Bidirectional prospective associations between physical activity and depressive symptoms. The TRAILS Study. J Adolesc Health 2012;**50**:503-8.

17. KU PW, FOX KR, CHEN LJ, CHOU P. Physical activity and depressive symptoms in older adults: 11-year follow-up. Am J Prev Med 2012;**42**:355-62.

18. AZEVEDO DA SILVA M, SINGH-MANOUX A et al. Bidirectional association between physical activity and symptoms of anxiety and depression: the Whitehall II study. Eur J Epidemiol 2012;**27**:537-46.

19. MOTL RW, BIRNBAUM AS, KUBIK MY, DISHMAN RK. Naturally occurring changes in physical activity are inversely related to depressive symptoms during early adolescence. Psychosom Med 2004;**66**:336-42.

20. LINDWALL M, GERBER M, JONSDOTTIR I, BÖRJESSON M, AHLBORG JR G. The relationships of change in physical activity with change in depression, anxiety, and burnout: A longitudinal study of Swedish healthcare workers. Health Psychol 2013; **33**;1309-18.

21. DE JONGE P, ROEST AM. Depression and cardiovascular disease: the end of simple models. Br J Psychiatry 2012;**201**:337-8.

22. BENGTSSON C, BLOHME G, HALLBERG L et al. The study of women in Gothenburg 1968-1969-a population study. General design, purpose and sampling results. Acta Med Scand 1973; **193**: 311-18.

23. MONTGOMERY SA, ASBERG, M. A new depression scale designed to be sensitive to change. Br J Psychiatry 1979;**134**:382-9.

24. SALTIN B, GRIMBY G. Physiological analysis of middle-aged and old former athletes. Comparison with still active athletes of the same ages. Circulation 1968;**38**:1104-15.

25. APA. Diagnostic and statistical manual of mental disorders, third edition - revised (DSM-III-R). AMERICAN PSYCHIATRIC ASSOCIATION, 1987, Washington DC.

26. GUO X, WAERN M, SJOGREN K et al. Midlife respiratory function and Incidence of Alzheimer's disease: a 29-year longitudinal study in women. Neurobiol Aging 2007;**28**:343-50.

27. MEREDITH W, TISAK, J. Latent curve analysis. Psychometrika 1990;**55**:107-22.

28. DUNCAN TA, DUNCAN SC, STRYCKER LA. An introduction to latent variable growth curve modeling: Concepts, issues, and applications (2nd ed.). Lawrence Erlbaum Associates Publishers, Mahwah, NJ, 2006.

29. MCARDLE JJ. Latent variable modeling of differences and changes with longitudinal data. Annu Rev Psychol 2009;**60**:577-605.

30. HU L, BENTLER PM. Cutoff Criteria for Fit Indexes in Covariance Structure Analysis: Conventional Criteria Versus New Alternatives. Struct Equasion Mode 1999;**6**:1-55.

31. BENTLER, PM. Comparative fit indexes in structural models. Psychol Bull 1990;107:238-246.

32. BROWN MW, CUDECK R. CFI versus RMSEA: A comparison of two fit indexes for structural equation modeling. Struct Equasion Mode 1993;**6**:369-379.

33. ROSHANAEI-MOGHADDAM B, KATON WJ, RUSSO J. The longitudinal effects of depression on physical activity. Gen Hosp Psychiatry 2009;**31**:306-15.

34. KIJÆRGAARD M, ARFWEDSON WANG C E, WATERLOO K, JORDE R. A study of the psychometric properties of the Beck Depression Inventory-II, the Montgomery and Asberg Depression Rating Scale, and the Hospital Anxiety and Depression Scale in a sample from a healthy Population. Scand J Psychology 2014;**55**:83–89.

35. ERICKSON KI, GILDENGERS AG, BUTTERS MA. Physical activity and brain plasticity in late adulthood. Dialogues Clin Neurosci 2013;**15**: 99-108.

36. BROSSE AL, SHEETS ES, LETT HS, BLUMENTHAL JA. Exercise and the treatment of clinical depression in adults: recent findings and future directions. Sports Med 2002; **32**:741-60.

37. HOEHNER CMET, ALLEN P, BARLOW CE, et al. Understanding the independent and joint associations of the home and workplace built environments on cardiorespiratory fitness and body mass index. Am J Epidemiology 2013;**178**:1094-105.

38. LEE Y, PARK K. Does physical activity moderate the association between depressive symptoms and disability in older adults? Int J Geriatr Psychiatry 2008; 23:249-56.

39. KRUK J. Physical activity in the prevention of the most frequent chronic diseases: an analysis of the recent evidence. Asian Pac J Cancer Prev 2007;8:325-38.

40. RETHORST CD, TRIVEDI MH. Evidence-based recommendations for the prescription of exercise for major depressive disorder. J Psychiatric Pract 2013;19:204-12.

41. RODJER L, JONSDOTTIR IH, ROSENGREN A et al. Self-reported leisure time physical activity: a useful assessment tool in everyday health care. BMC public health 2012;**12**:693.

42. LISSNER L, SKOOG I, ANDERSSON K et al. Participation bias in longitudinal studies: experience from the Population Study of Women in Gothenburg, Sweden. Scand J Prim Health Care 2003;**21**:242-7.

Table 1. Characteristics of Women with Initial and Follow-up assessments, Gothenburg, Sweden, Who Participated in Baseline Psychiatric Examinations in 1974 (N=676)

	n (%) or Mean (SD)			
Birth cohort (age at baseline), n (%)				
1914 (60 years)	79 (11.7)			
1918 (56 years)	248 (36.7)			
1922 (52 years)	264 (39.1)			
1930 (44 years)	85 (12.6)			
Age at baseline, Mean (SD)	53.4 (0.2)			
Modified MADRS score[a], Mean (SD)				
1974	4.0 (0.2)			
1992	6.0 (0.3)			
2000	5.1 (0.3)			
2005	6.2 (0.3)			
Education, n (%)				
<6 years	475 (70.5)			
Marital status n (%)				
Married	528 (78.1)			
Smoking status n (%)				
Smoker previous year	245 (36.2)			
Level of physical activity[b], n (%)	**1**	**2**	**3**	**4**
1974	149	424	102	1 (0.1)
1992	(22.0)	(62.7)	(15.2)	0 (0.0)
2000	116	200	119	1 (0.5)
2005	(26.7)	(46.0)	(27.3)	0 (0.0)
	42 (16.8)	146	61 (24.4)	
	21 (13.5)	(58.3)	52 (33.3)	
		83 (53.2)		

Abbreviations: MADRS, Montgomery Asberg Depression Rating Scale; SD, standard deviation.

[a] The MADRS item "Reduced appetite" is excluded from the rating scale.

[b] Based on the Saltin-Grimby Physical Activity Level Scale (Saltin & Grimby, 1968): 1 = almost totally inactive, 2 = some physical activity at a minimum of 4 hours/week, 3 = regular physical activity, 4 = regular intense physical activity and contests.

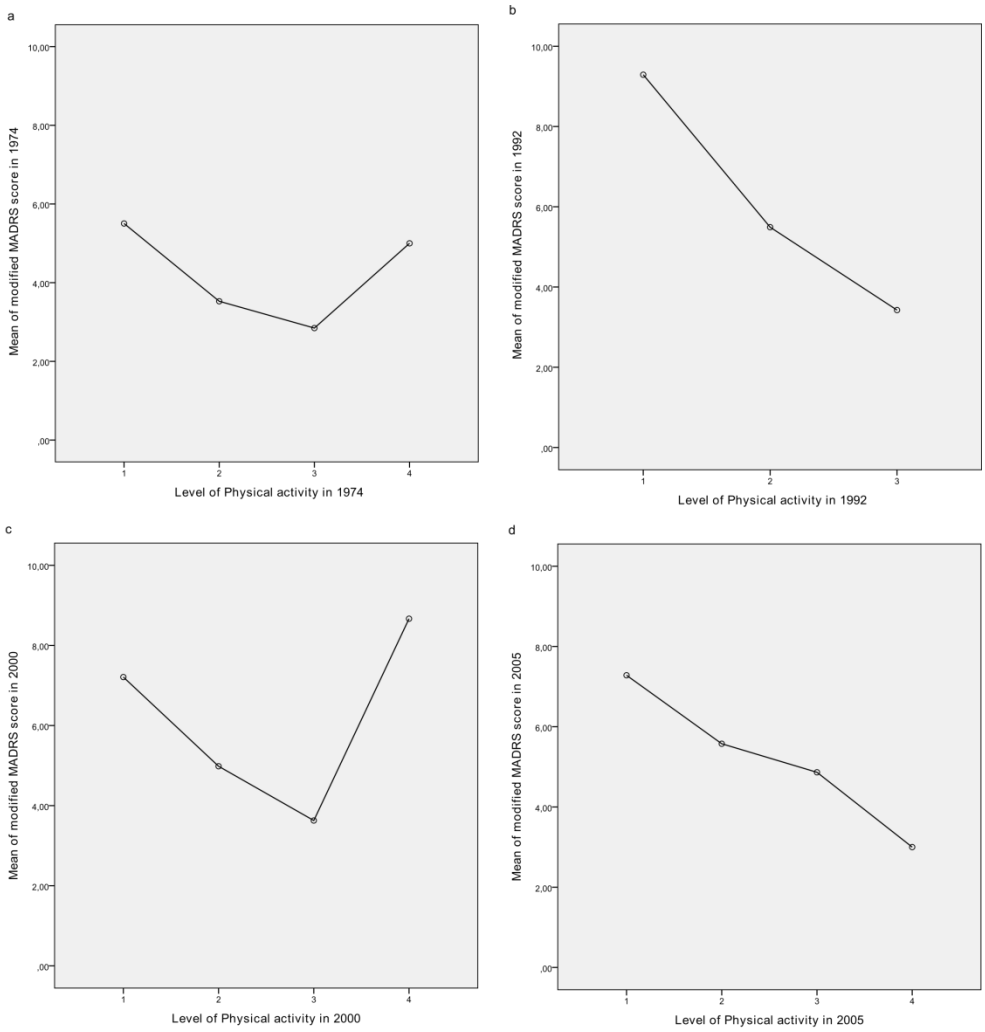

Figure 1: panel a-d. Mean modified MADRS score by level of physical activity

Table 2. Results from Latent Growth Curve Models Showing Level or Change in Physical Activity on Level or Change in Depression Scores in Women, Gothenburg, Sweden, followed between 1974 and 2005

	Empty model[a] *b* (SE)	***Conditional model***[a,b] *b* (SE)
Prediction of depression Intercept[c]		
Physical activity level at baseline	-1.53 (0.36)*	-1.28 (0.36)**
Age at baseline (years)	-	0.08 (0.05)
Education >6 years	-	-0.53 (0.48)
Marital status at baseline (Married)	-	-1.04 (0.53)*
Smoking status (Smoker)	-	1.18 (0.45)*
Prediction of depression Slope[d]		
Physical activity level baseline	-0.03 (0.02)	-0.03 (0.02)
Age at baseline (years)	-	-0.003 (0.002)
Education >6 years	-	0.02 (0.024)
Marital status at baseline (Married)	-	0.05 (0.028)
Smoking status at baseline (Smoker)	-	0.03 (0.03)
Within-person change in physical activity	-0.98 (0.27)*	-1.00 (0.28)*

Abbreviations: SE, standard error.

[a]Using a latent growth curve model (LGCM).

[b]Controlling for age at baseline, education, marital status at baseline and smoking status.

[c]Mean depression score at baseline.

[d]Change in depression scores 1974-1992-2000-2005.

*Significant at a level of $P < 0.05$.

**Significant at a level of $P < 0.001$.