CLINICAL RESEARCH STUDY

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Protective Effect of Regular Physical Activity on Depression After Myocardial Infarction: The HUNT Study

Linda Ernstsen, RN, PhD,[a,b] Vegar Rangul, PhD,[c,d] Javaid Nauman, PhD,[b] Bjarne M. Nes, PhD,[b] Håvard Dalen, MD, PhD,[e,f] Steinar Krokstad, MD, PhD,[d,g] Carl J. Lavie, MD, PhD,[h] Steven N. Blair, PED,[i] Ulrik Wisløff, PhD[b]

[a]Department of Nursing Science, Faculty of Health and Social Science, Sør-Trøndelag University College, Trondheim, Norway; [b]K.G. Jebsen Center of Exercise in Medicine, Department Circulation and Medical Imaging, Faculty of Medicine, Norwegian University of Science and Technology, Trondheim, Norway; [c]Faculty of Health Science, Nord-Trøndelag University College, Levanger, Norway; [d]HUNT Research Centre, Department of Public Health and General Practice, Faculty of Medicine and [e]MI Lab & Department of Circulation & Medical Imaging, Norwegian University of Science and Technology, Trondheim, Norway; [f]Levanger Hospital and [g]Psychiatric Department, Levanger Hospital, Health Trust Nord-Trøndelag, Levanger, Norway; [h]Department of Cardiovascular Diseases, John Ochsner Heart and Vascular Institute, Ochsner Clinical School—The University of Queensland School of Medicine, New Orleans, La; [i]Department of Exercise Science, University of South Carolina, Columbia, SC.

ABSTRACT

PURPOSE: To study if physical activity within the recommended level over time was associated with risk of developing depression after the first myocardial infarction in older adults.

METHODS: Men (n = 143) and women (n = 46) who had reached the age of 60 years in 2006-2008 who participated in the Nord-Trøndelag Health Study (HUNT1, 1984-1986; HUNT2, 1995-1997; HUNT3, 2006-2008) without any mental illness or cardiovascular disease at baseline in HUNT2 and who experienced their first myocardial infarction before HUNT3 were included. Based on the patterns of physical activity from HUNT1 to HUNT2, the sample was divided into 4 groups: persistently inactive, from active to inactive, from inactive to active, and persistently active. The primary outcome, post-myocardial infarction depression symptoms, was measured with the Hospital, Anxiety and Depression Scale in HUNT3.

RESULTS: In HUNT3, 11% of participants had depression. After multivariable adjustment, those who were persistently active had significantly lower odds of being depressed (odds ratio 0.28; 95% confidence interval, 0.08-0.98) compared with those who were persistently inactive. Additionally, a significant test for trend ($P = .033$) of lowering odds of depression was observed across all 4 categories of physical activity patterns at baseline.

CONCLUSIONS: In this small sample of initially healthy adults, we observed a long-term protective effect of regular physical activity on the development of depression following myocardial infarction.

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KEYWORDS: Depression; Myocardial infarction; Physical activity

Physical inactivity is the fourth leading cause of death worldwide,[1] and several epidemiological studies support a reciprocal relationship between physical activity and depression.[2-5] Results from a meta-analyses and systematic review on physical exercise intervention in depressive disorders suggest that physical exercise as

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Requests for reprints should be addressed to Linda Ernstsen, RN, PhD, Department of Nursing Science, Sør-Trøndelag University College, NO-7004 Trondheim, Norway.

E-mail address: linda.ernstsen@hist.no

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treatment for depression has a moderate to large effect.[4,6]

Depression is an independent risk factor for incident cardiovascular disease,[7] and patients with established cardiovascular disease including heart failure and, particularly, coronary heart disease, who are moderately or severely depressed have markedly higher risk of dying compared with those who are not depressed.[8-12] So far, no medical treatment of depression in patients with cardiovascular disease has improved cardiac outcomes,[13] other than, possibly, formal exercise training programs.[10,14,15] Recent results suggest that almost 4 million coronary heart disease disability-adjusted life years can be attributed to major depression in 2010: 3.5 million years of life lost and 250,000 years of life lived with a disability.[16] In the face of shifting demographics with an ageing population, cardiovascular disease and mental health both hold enormous public health importance. The benefits of physical activity in cardiovascular disease prevention in healthy populations are well established,[17,18] and recent results suggest that patients who are regularly active after myocardial infarction have half the risk of dying compared with inactive patients.[19] Additionally, studies of cardiac rehabilitation and exercise training following major coronary heart disease events have reported marked benefits of this therapy to reduce psychological stress, including depression,[4,10] and depression-related and stress-related increased mortality.[4,10,14,15,20]

Altogether, the present literature suggests that there might be a causal relationship between physical activity and depression, both in healthy individuals and in patients with cardiovascular disease.[4,14,20] However, we have not been able to find any prospective studies that have assessed the association of long-term exposure of physical activity in apparently healthy individuals before incident myocardial infarction and the risk of developing post-myocardial infarction depression. The aim of the current study is therefore to explore whether different behavioral patterns of leisure-time physical activity level in adulthood are associated with the presence of depressive symptoms following first-time myocardial infarction.

CLINICAL SIGNIFICANCE

- Regular physical activity (PA) is associated with lower risk of post-myocardial infarction (MI) depression.
- MI patients with long-standing low PA require close attention to prevent depression.
- MI patients with low PA may particularly benefit from exercise training programs.

METHODS

Study Population

The Nord-Trøndelag Health Study (HUNT) is a Norwegian population-based general health study conducted in 1984-1986 (HUNT1),[21] 1995-1997 (HUNT2),[22] and 2006-2008 (HUNT3).[23] Data were collected from questionnaires, blood samples, and clinical measurements. All participants included in the present study had reached the age of 60 years when participating in HUNT3, and they had been hospitalized with their first myocardial infarction after baseline in HUNT2. Change in physical activity level from HUNT1 to HUNT2 was the independent variable at baseline in HUNT2. Depressive symptoms measured 10 years later in HUNT3 were the independent variable. Of the 529 participants experiencing their initial myocardial infarction after baseline and who had participated in all 3 surveys (1984-2008), we excluded individuals with missing information on physical activity level in HUNT1 (n = 78) and HUNT2 (n = 56), with prevalent depression and anxiety (n = 83), a history of stroke (n = 5) and cancer (n = 6), or missing data on any of the confounders (n = 80) at baseline in HUNT2. We also excluded those with missing data on depressive symptoms at HUNT3 (n = 32). The final analysis included 189 individuals (ages 48-85 years; 24% women and 76% men).

Baseline Data

Disease history/health status at baseline (HUNT2) was measured by asking for diabetes, any limiting long-standing illness, regular use of any medication the last year, any use of sedatives the last month, and measuring hypertension, hyperlipidemia (defined as total serum cholesterol ≥5.0 mmol/L), and body mass index (weight [kg]/height [m^2]). Information about diabetes mellitus was collected with the question: “Do you have or have you had diabetes?” (yes/no). Any limiting long-standing illness was monitored by asking “Do you suffer from any long-standing somatic or psychiatric illness, disease, or disability?” (yes/no). Health behavior was measured by smoking (current smoker, former smoker, and never smoker) and alcohol consumption over a 2-week period (abstainers, 0 drinks, 1 ≤5 drinks, and ≥6 drinks). The diagnosis of hypertension was defined as systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg, or as self-report of current use of antihypertensive medication. Socioeconomic status was measured as educational level.

Physical Activity Level

On the basis of the international guidelines recommending that adults participate in daily physical activity,[24] both questionnaires were dichotomized into “active” or “inactive” depending on whether physical activity level was ≥150 min/week or <150 min/week, respectively (see Appendix, available online). Physical activity was assessed by different questions in HUNT1 and HUNT2. The summary indices used to compute the cut-off values for meeting the recommended level of physical activity level are based on the work of Kurtze et al[25,26] on the validation of self-reported physical activity in

HUNT1 and HUNT2. Those who were active at both time points were "persistently active," those who decreased from active and became inactive were "decreasing." Those who moved from being inactive to active were classified as "increasing," and those who were inactive at both time points were "persistently inactive."

Depressive Symptoms

Symptoms of anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS).[27] The psychometric properties of the Norwegian translation of HADS were found to be excellent in the Nord-Trøndelag Health Study.[28] The scale consists of 7 items that cover anxiety symptoms (HADS-A) and 7 items covering depressive symptoms (HADS-D) on a 4-point Likert scale. No somatic items are included. An optimal balance between sensitivity and specificity seems to be achieved when a case is defined by a score of 8 or more on both HADS-A and HADS-D.[27] Those who filled in 5 or 6 items were also included in the study, and their scores were based on the sum of completed items multiplied by 7/5 or 7/6, respectively. Of note, for simplicity, we use the term depression to present the respective symptoms and not clinical diagnoses of mental health.

Data Analyses

Differences in baseline data among the 4 groups of change in physical activity level from HUNT1 (1984-1986) to HUNT2 (1995-1997) were assessed by one-way analysis of variance for continuous variables. Pearson chi-squared statistic was used for categorical variables, and Fischer's exact test was used in cases were expected values of categorical variables were $\leq$5. For continuous variables where Shapiro-Wilk test and Q−Q-plots indicated that the normal distribution was violated, we used the nonparametric Kruskal−Wallis one-way analysis of variance. Further, to assess any trend in the response variable by pattern on physical activity level, we used the nonparametric Jonckheere-Terpstra test. Due to the small sample size, we restricted our multivariable adjustments to 4 confounders that are related to both physical activity level and depressive symptoms: age, sex, systolic blood pressure, and any limiting long-standing illness. Logistic regression models computed the odds of elevated depression post myocardial infarction (HADS-D $\geq$8), with odds ratios (ORs) and 95% confidence intervals (CIs) in 4 different models.

Tests of linear trend were conducted by entering the 4-category physical activity pattern variable as the independent variable into the regression model as an ordinal term. To assess if sex and age modified the association, we computed 2 interaction terms (physical activity pattern*sex, and physical activity pattern*age), which were analyzed separately in a fully adjusted model. We assessed analyses with multiple imputation of missing data, however, as the results did not support a better model fit, we report the results from the sample with complete cases. Data were analyzed using the Statistical Package for the Social Sciences, version 20 for Windows (SPSS Inc, Chicago, IL), and all tests were 2-sided.

RESULTS

Baseline descriptive data are presented in **Table 1**. Of the 189 participants included, 46 (24%) were women. In general, the majority of covariates did not differ significantly between the categories of physical activity pattern, except for smoking (P = .049), with most smokers among those being persistently inactive (41.3%). The Kruskal-Wallis H test showed that there was a statistically significant difference between at least 2 of the groups in systolic blood pressure, χ^2 (3) = 7.92, P = .048, and time since myocardial infarction, χ^2 (3) = 8.98, P = .030. The Jonckheere-Terpstra test for systolic blood pressure was significant (P = .035), and Kendall's Tau_b indicated that there was a decreasing trend in systolic blood pressure by increasing level of pattern of physical inactivity.

When the outcome post-myocardial infarction depression was measured in HUNT3, the mean years since first myocardial infarction for the total sample was 5.3 (SD = 3.2). The prevalence of high depressive symptoms (HADS-D $\geq$8) in HUNT3 was 7.5% (n = 5) among those who were persistently active, 9.1% (n = 4) among those who changed from being inactive to being active, 12.5% (n = 4) in those who changed from being active to inactive, and with the highest occurrence of 17.4% (n = 8) among those who maintained being persistently inactive (**Figure**), but Fisher's exact test indicated that these differences were not statistically significant (P = .098).

In the multivariable analyses (**Table 2**), the category "persistently inactive" was set as the reference group. In the first model, with adjustment only for age and sex, the likelihood of being depressed post myocardial infarction was not significant for any groups. Adding systolic blood pressure to the first model made no significant difference. After additional adjustment for body mass index, those being persistently active showed a reduced likelihood (OR 0.28; 95% CI, 0.08-0.98) of having depressive symptoms after first myocardial infarction compared with those who were persistently inactive. The inclusion of any limiting longstanding in Model 4 made no contribution to the association between physical activity pattern and post-myocardial infarction depression. The linear test for trend (P = .033) was significant, indicating a benefit of physical activity in midlife on the likelihood of developing depressive symptoms post myocardial infarction.

Additional adjustments for hypertension, total cholesterol, diabetes, medication use, smoking habits, alcohol consumption, education, marital status, and time since first myocardial infarction gave almost the same results as in Model 4 (**Table 2**), indicating that those who were persistently active had significantly lower odds of post-myocardial infarction depression (OR 0.22; 95% CI, 0.05-0.88) compared with those who were persistently inactive

Table 1 Unadjusted Baseline Characteristics by Patterns of Physical Activity Habits From HUNT1 (1984-1986) to HUNT2 (1995-1997), n =189

	Categories of Change in Physical Activity Habits From 1984-1986 to 1995-1997				
	Stable Active (n = 67)	From Inactive to Active (n = 44)	From Active to Inactive (n = 32)	Stable Inactive (n = 46)	*P*-Value
Age, y (SD)	62.3 (7.4)	62.4 (7.4)	60.0 (8.3)	61.1 (7.2)	.447
Women	16 (23.9)	6 (13.6)	10 (31.3)	14 (30.4)	.212
High total cholesterol*	63 (94.0)	42 (95.5)	29 (90.6)	43 (93.5)	.861
Hypertension†	55 (82.1)	35 (79.5)	19 (59.4)	32 (69.6)	.069
Systolic blood pressure‡ (mean, SD)	153 (20.5)	150 (19.8)	141 (18.8)	148 (20.5)	.048§
Body mass index‖ (mean, SD)	26.4 (2.5)	27.4 (3.2)	27.5 (3.6)	27.3 (3.8)	.201
Diabetes	3 (4.5)	0 (0)	0 (0)	0 (0)	.281¶
Any limiting long-standing illness	20 (29.9)	13 (29.5)	12 (37.5)	19 (41.3)	.544
Regularly use of prescribed drugs the last year	34 (50.7)	18 (40.9)	18 (56.3)	22 (47.2)	.593
Use of sedatives last month	10 (14.9)	4 (9.1)	3 (9.4)	6 (13.0)	.802¶
Current smoking	20 (29.9)	12 (27.3)	4 (12.5)	19 (41.3)	.049¶
Alcohol intake ≥6 per 2 wk	7 (10.4)	6 (13.6)	3 (9.4)	4 (8.7)	.897¶
Primary education	21 (31.3)	18 (40.9)	6 (18.8)	16 (34.8)	.227
Years since first MI (mean, SD)	5.6 (3.2)	4.4 (3.0)	4.5 (3.2)	6.1 (3.2)	.030§

Data are presented as mean (SD) and numbers (%) if not otherwise stated.
HUNT = Nord-Trøndelag Health Study; MI = myocardial infarction.
*Total cholesterol ≥5.0 mmol/L.
†Systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg or as self-report of current use of antihypertensive medication.
‡mm Hg.
§Kruskal—Wallis test.
‖Weight (kg)/height (m)^2.
¶Fisher's exact test.

(data not shown). There was no significant interaction between age and pattern of physical activity (P = .933) and between sex and pattern of physical activity (P = .950).

DISCUSSION

The main finding of this study was that maintaining a recommended level of physical activity in adulthood into older age was significantly associated with lower odds of having depressive symptoms after first incident myocardial infarction. To our knowledge, this is the first study accounting for a protective effect of stable physical activity on post-myocardial infarction depression.

Although we have not been able to find similar studies on the association between pattern of physical activity and post-myocardial infarction depression, some studies support our finding of a protective effect for people meeting the recommended level of physical activity on the development of depressive symptoms after myocardial infarction in the general population. Longitudinal results from the Maastricht Aging Study found that 1169 healthy adults who reported more than 30 minutes per day of physical activity on average at baseline had a 48% lower risk of being depressed at follow-up than respondents who reported not engaging in physical activity at baseline (relative risk 0.52; 95% CI, 0.29-0.92). Furthermore, respondents who reported engaging in physical activity at both baseline and follow-up were at 44% lower risk of subsequent depression than those who reported not engaging in physical activity at either baseline or follow-up. In agreement with our findings, change in physical exercise level (initiating or discontinuing physical exercise between baseline and follow-up) in the Maastricht Aging Study was not significantly associated with depressive symptoms at follow-up.[29] In a systematic review, 25 of the 30 prospective studies from nonclinical community samples found a significant inverse relationship between baseline physical activity level and follow-up depression.[5] The recent Aerobics Center Longitudinal Study,[30] in which 4802 adults were followed for

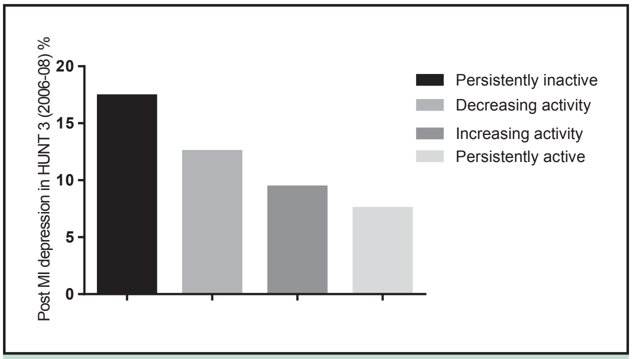

Figure Distribution of post-MI depression at HUNT3 by categories of physical activity pattern from HUNT1 to HUNT2. MI = myocardial infarction; HUNT = Nord-Trøndelag Health Study.

Table 2 Odds Ratios (OR) and 95% Confidence Intervals (CI) of Depressive Symptoms (HADS-D ≥8) Measured in HUNT3 (2006-2008) After First Myocardial Infarction (MI) by Changes in Physical Activity Patterns From HUNT1 (1984-1986) and HUNT2 (1995-1997) Before First MI, with Sequential Adjustment

	Model 1		Model 2		Model 3		Model 4	
Categories of Physical Activity Pattern	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Persistently inactive (n = 46)	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference
Decreasing activity level (n = 32)	0.71	0.19-2.61	0.79	0.21-2.98	0.82	0.21-3.10	0.82	0.21-3.10
Increasing activity level (n = 44)	0.41	0.11-1.49	0.40	0.11-1.46	0.38	0.10-1.41	0.37	0.10-1.42
Persistently active (n = 67)	0.35	0.11-1.17	0.32	0.10-1.09	0.28	0.08-0.98*	0.28	0.08-0.98*
Test for trend	P = .067		P = .048*		P = .032*		P = .033*	

Model 1: adjusted for age and sex.
Model 2: adjusted for Model 1 + systolic blood pressure.
Model 3: adjusted for Model 2 + body mass index.
Model 4: adjusted for Model 3 + any limiting long-standing illness.
HADS = Hospital, Anxiety and Depression scale; HUNT = Nord-Trøndelag Health Study.
*P <.05.

9 years, found that the association between sedentary behaviors and depressive symptoms was statistically significant only among those not meeting the recommended level of physical activity. These findings add support for a long-term association between level of physical activity and development of depressive symptoms.

Still, the course of depressive symptoms after myocardial infarction is influenced by time since incident myocardial infarction. In a prospective study from HUNT,[31] the authors found that women had a high initial risk for both anxiety and depression, with a decrease after 2 years post myocardial infarction, while there were no such risks for men; but more surprisingly, that the risk for depression in men increased after 2 years post myocardial infarction. In a recent study, the mental progress of 288 patients hospitalized with myocardial infarction was monitored using self-reports after 3, 6, 12, and 18 months.[32] The authors found that 13.6% of myocardial infarction patients reported high levels of depression at baseline, but after 3-18 months, these patients were not more depressed than the Norwegian reference population. Additionally, prospective results from the HUNT Study found that the level of depressive symptoms at HUNT2 was a significant and independent predictor of myocardial infarction at HUNT3; but having a myocardial infarction had only a marginal effect on depressive symptoms at HUNT3, and time since myocardial infarction was not a significant predictor of post-myocardial infarction depression.[33] Thus, our finding that 11% of the total sample was depressed after myocardial infarction may not be related to the former experience of myocardial infarction.

Nevertheless, twin studies suggest that approximately 40% of the attributable risk of depression can be explained by genetic variation,[34] and that the heritability of exercise in the adult generation is estimated at 42%.[35] Thus, it is plausible that our findings of a protective effect from stable physical activity level on post-myocardial infarction depression is influenced by nonenvironmental factors, or by genetic dispositions in combination with the exposure to specific environments.

The detail of a dose—response relationship on the inverse association between level of physical activity and depressive symptoms is not yet clear, and future longitudinal studies of the trajectories of physical activity before myocardial infarction and post-myocardial infarction depression are needed to confirm our results. However, data from formal cardiac rehabilitation and exercise training programs after myocardial infarction and other major coronary heart disease events is supportive, showing that these programs substantially reduce the prevalence of depression and other psychological stress, generally by >50%,[4,10,14,15,36] and reduce depression-related increased mortality by over 30%.[4,15,20] In fact, Blumenthal et al[37] found an intervention of 4 months of aerobic exercise (3 times/week) in patients with coronary heart disease just as effective as antidepressant medication; and further, that improvements in cardiovascular biomarkers were present only among those who exercised.

Strengths and Limitations of the Study

The main strengths of our study were the prospective design, with a long and highly reliable follow-up period, the use of myocardial infarction from hospital data, and the extensive data on psychosocial, behavioral, and biomedical factors. However, several important limitations of our study should be noted. There is a methodological challenge, because physical activity is measured differently in the HUNT1 and HUNT2 surveys, and physical activity was measured with self-report, rather than objective measures. But the physical activity questions have shown high reliability and acceptable validity,[25] and the dichotomization as active and inactive provides good information on physical activity.

Further, the small sample size was reflected through overlapping 95% CIs, as well as particularly wide CIs within each category of physical activity pattern in the multivariable analyses. Thus, one should be cautious when drawing conclusions based on the estimates in our study.

Even with adjustment for time since myocardial infarction, it is possible that exposure to reinfarction, diagnosed heart failure, other stressful life events (eg, losing one's spouse or close friends as a natural consequence of ageing), or number of chronic diseases after baseline may have influenced our results. However, results from a randomized controlled study on exercise capacity and everyday activity in older heart failure patients found no evidence that the severity of left ventricular systolic dysfunction predicted exercise capacity, but that psychosocial factors such as depressive symptoms contribute to the variance in physical exercise.[38]

Old age and mental health problems are strongly related to nonparticipation in population-based studies, which were confirmed in 2 nonresponder studies from HUNT 2.[22,39] If a significant number of those who could have been included did not participate in HUNT3 due to poor mental health, our sample is artificially small, with possible underestimation of any associations.

CONCLUSIONS

In a small sample of initially healthy individuals participating in 3 health surveys with 10-year intervals, we found that persistent patterns of physical activity level before being diagnosed with their first myocardial infarction significantly decreased the odds of post-myocardial infarction depression, which further supports the promotion of physical activity throughout the health care system. Despite the methodological limitations of the study, we believe that the results add important aspects to the existing literature concerning the long-term protective effect of regular physical activity on the development of depressive symptoms post myocardial infarction that merit further investigation.

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References

1. Kohl HW 3rd, Craig CL, Lambert EV, et al. The pandemic of physical inactivity: global action for public health. *Lancet*. 2012;380(9838): 294-305.
2. Roshanaei-Moghaddam B, Katon WJ, Russo J. The longitudinal effects of depression on physical activity. *Gen Hosp Psychiatry*. 2009;31(4): 306-315.
3. Azevedo Da Silva M, Singh-Manoux A, Brunner E, et al. Bidirectional association between physical activity and symptoms of anxiety and depression: the Whitehall II study. *Eur J Epidemiol*. 2012;27(7): 537-546.
4. Swift DL, Lavie CJ, Johannsen NM, et al. Physical activity, cardiorespiratory fitness, and exercise training in primary and secondary coronary prevention. *Circ J*. 2013;77(2):281-292.
5. Mammen G, Faulkner G. Physical activity and the prevention of depression: a systematic review of prospective studies. *Am J Prev Med*. 2013;45(5):649-657.
6. Josefsson T, Lindwall M, Archer T. Physical exercise intervention in depressive disorders: meta-analysis and systematic review. *Scand J Med Sci Sports*. 2014;24(2):259-272.
7. Huffman JC, Celano CM, Beach SR, Motiwala SR, Januzzi JL. Depression and cardiac disease: epidemiology, mechanisms, and diagnosis. *Cardiovasc Psychiatry Neurol*. 2013;2013:695925.
8. Moraska AR, Chamberlain AM, Shah ND, et al. Depression, healthcare utilization, and death in heart failure: a community study. *Circ Heart Fail*. 2013;6(3):387-394.
9. Carney RM, Freedland KE. Depression in patients with coronary heart disease. *Am J Med*. 2008;121(11 Suppl. 2):S20-S27.
10. Lavie CJ, Milani RV, O'Keefe JH, Lavie TJ. Impact of exercise training on psychological risk factors. *Prog Cardiovasc Dis*. 2011;53(6):464-470.
11. Figueredo VM. The time has come for physicians to take notice: the impact of psychosocial stressors on the heart. *Am J Med*. 2009;122(8): 704-712.
12. Lichtman JH, Froelicher ES, Blumenthal JA, et al. Depression as a risk factor for poor prognosis among patients with acute coronary syndrome: systematic review and recommendations: a scientific statement from the American Heart Association. *Circulation*. 2014;129(12): 1350-1369.
13. Freedland K, Carney R. Depression as a risk factor for adverse outcomes in coronary heart disease. *BMC Med*. 2013;11(1):131.
14. Milani RV, Lavie CJ. Reducing psychosocial stress: a novel mechanism of improving survival from exercise training. *Am J Med*. 2009;122(10):931-938.
15. Milani RV, Lavie CJ, Mehra MR, Ventura HO. Impact of exercise training and depression on survival in heart failure due to coronary heart disease. *Am J Cardiol*. 2011;107(1):64-68.
16. Charlson F, Moran A, Freedman G, et al. The contribution of major depression to the global burden of ischemic heart disease: a comparative risk assessment. *BMC Med*. 2013;11(1):250.
17. Wisløff U, Nilsen TIL, Drøyvold WB, Mørkved S, Slørdahl SA, Vatten LJ. A single weekly bout of exercise may reduce cardiovascular mortality: how little pain for cardiac gain? 'The HUNT study, Norway'. *Eur J Cardiovasc Prev Rehabil*. 2006;13(5): 798-804.
18. Haskell WL, Blair SN, Hill JO. Physical activity: health outcomes and importance for public health policy. *Prev Med*. 2009;49(4):280-282.
19. Gerber Y, Myers V, Goldbourt U, Benyamini Y, Scheinowitz M, Drory Y. Long-term trajectory of leisure time physical activity and survival after first myocardial infarction: a population-based cohort study. *Eur J Epidemiol*. 2011;26(2):109-116.
20. Milani RV, Lavie CJ. Impact of cardiac rehabilitation on depression and its associated mortality. *Am J Med*. 2007;120(9):799-806.
21. Holmen J, Midthjell K, Bjartveit K, et al. *The Nord-Trøndelag Helath Survey 1984-86. Purpose, Background and Methods. Participation, Non-participation and Frequency Distributions*. Verdal, Norway: Statens institutt for folkehelse, Senter for sammfunnsmedisinsk forskning; 1990.
22. Holmen J, Midthjell K, Krüger Ø, et al. The Nord-Trøndelag Health Study 1995-97 (HUNT 2): objectives, contents, methods and participation. *Nor J Epidemiol*. 2003;13(1):19-32.
23. Krokstad S, Langhammer A, Hveem K, et al. Cohort profile: the HUNT Study, Norway. *Int J Epidemiol*. 2013;42(4):968-977.
24. World Health Organization. Global recommendations on physical activity for health. Available at: http://whqlibdoc.who.int/publications/2010/9789241599979_eng.pdf?ua=1. 2010. Accessed January 20, 2015.
25. Kurtze N, Rangul V, Hustvedt B-E, Flanders W. Reliability and validity of self-reported physical activity in the Nord-Trøndelag Health Study (HUNT 2). *Eur J Epidemiol*. 2007;22(6):379-387.
26. Kurtze N, Rangul V, Hustvedt B-E, Flanders WD. Reliability and validity of self-reported physical activity in the Nord-Trøndelag Health Study — HUNT 1. *Scand J Public Health*. 2008;36(1):52-61.

27. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale: an updated literature review. *J Psychosom Res*. 2002;52(2):69-77.
28. Mykletun A, Stordal E, Dahl AA. Hospital Anxiety and Depression (HAD) scale: factor structure, item analyses and internal consistency in a large population. *Br J Psychiatry*. 2001;179(6):540-544.
29. van Gool CH, Kempen GI, Bosma H, van Boxtel MP, Jolles J, van Eijk JT. Associations between lifestyle and depressed mood: longitudinal results from the Maastricht Aging Study. *Am J Public Health*. 2007;97(5):887-894.
30. Sui X, Brown WJ, Lavie CJ, et al. Associations between television watching and car riding behaviors and development of depressive symptoms: a prospective study. *Mayo Clin Proc*. 2015;90(2):184-193.
31. Bjerkeset O, Nordahl HM, Mykletun A, Holmen J, Dahl AA. Anxiety and depression following myocardial infarction: gender differences in a 5-year prospective study. *J Psychosom Res*. 2005;58(2):153-161.
32. Hanssen TA, Nordrehaug JE, Eide GE, Bjelland I, Rokne B. Anxiety and depression after acute myocardial infarction: an 18-month follow-up study with repeated measures and comparison with a reference population. *J Cardiovasc Risk*. 2009;16(6):651-659.
33. Langvik E, Hjemdal O. Symptoms of depression and anxiety before and after myocardial infarction: the HUNT 2 and HUNT 3 study. *Psychol Health Med*. 2015;20(5):560-569.
34. Rice F, Harold G, Thapar A. The genetic aetiology of childhood depression: a review. *J Child Psychol Psychiatry*. 2002;43(1):65-79.
35. De Moor MH, Willemsen G, Rebollo-Mesa I, Stubbe JH, De Geus EJ, Boomsma DI. Exercise participation in adolescents and their parents: evidence for genetic and generation specific environmental effects. *Behav Genet*. 2011;41(2):211-222.
36. Lavie CJ, Milani RV. Adverse psychological and coronary risk profiles in young patients with coronary artery disease and benefits of formal cardiac rehabilitation. *Arch Intern Med*. 2006;166(17):1878-1883.
37. Blumenthal JA, Sherwood A, Babyak MA, et al. Exercise and pharmacological treatment of depressive symptoms in patients with coronary heart disease: results from the UPBEAT (Understanding the Prognostic Benefits of Exercise and Antidepressant Therapy) study. *J Am Coll Cardiol*. 2012;60(12):1053-1063.
38. Witham MD, Argo IS, Johnston DW, Struthers AD, McMurdo ME. Predictors of exercise capacity and everyday activity in older heart failure patients. *Eur J Heart Fail*. 2006;8(2):203-207.
39. Torvik F, Rognmo K, Tambs K. Alcohol use and mental distress as predictors of non-response in a general population health survey: the HUNT study. *Soc Psychiatry Psychiatr Epidemiol*. 2012;47(5):805-816.

SUPPLEMENTAL DATA

Supplemental tables accompanying this article can be found in the online version at http://dx.doi.org/10.1016/j.amjmed.2015.08.012.

APPENDIX

Indices of the Computation of Moderate to Vigorous Physical Activity Level (MVPA) Based on the Questions on Leisure Time Physical Activity in HUNT1 and HUNT2.

The cut of a MVPA meeting the recommended level of weekly physical activity was set to a sum score ≥2.5 in HUNT1 and HUNT2. See also references.[25,26]

Recodes in HUNT1

By exercise we mean going for walks, skiing, swimming, and working out/sports

How Often Do You Exercise? (on the Average)	Values	Scores
Never	1	0
Less than once a wk	2	0.5
Once a wk	3	1
2-3 times a wk	4	2.5
Nearly every d	5	5
If You Exercise as Often as Once or Several Times a Week: How Hard Do You Exercise?	**Values**	**Scores**
Take it easy, I don't get out of breath or break a sweat	1	1
I push myself until I'm out of breath and break into a sweat	2	2
I practically exhaust myself	3	3
For How Long Do You Exercise Each Time?	**Values**	**Scores**
Less than 15 min	1	0.10
15-29 min	2	0.38
30 min-1 h	3	0.75
More than 1 h	4	1

Recodes in HUNT2

How has your leisure-time physical activity been the last year?

Imagine an average week through the year. The distance to and from work is considered as leisure time.

Low Physical Activity, Hours per Week? (Not Out of Breath/Sweat)	Values	Scores
None	1	0
Less than 1 h	2	0.5
1 - 2 h	3	1.5
3 h or more	4	3
Vigorous Physical Activity, Hours per Week? (Out of Breath/Sweat)	**Values**	**Scores**
None	1	0
Less than 1 h	2	1
1-2 h	3	3
3 h or more	4	6