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REGULAR EXERCISE BEHAVIOUR AND INTENTION AND SYMPTOMS OF ANXIETY AND DEPRESSION IN CORONARY HEART DISEASE PATIENTS ACROSS EUROPE: RESULTS FROM THE EUROASPIRE III SURVEY

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	22 European countries were interviewed on average 15 months after hospitalisation. Whether patients exercised or intended to exercise regularly was assessed using the Stages of Change questionnaire in 8,330 patients. Symptoms of anxiety and depression were evaluated using the Hospital Anxiety and Depression Scale. Total physical activity was measured by the International Physical Activity Questionnaire in patients from a subset of 14 countries. Results: Overall, 50.3% of patients were not intending to exercise regularly, 15.9% were intending to exercise regularly, and 33.8% were exercising regularly. Patients with severe symptoms of depression less frequently exercised regularly than patients with symptoms in the normal range (20.2%, 95% confidence interval (CI) 14.8–26.8 vs. 36.7%, 95% CI 29.8–44.2). Among patients not exercising regularly, patients with severe symptoms of depression were less likely to have an intention to exercise regularly (odds ratio 0.62, 95% CI 0.46–0.85). Symptoms of anxiety did not affect regular exercise intention. In sensitivity analysis, results were consistent when adjusting for total physical activity. Conclusions: Lower frequency of regular exercise and decreased likelihood of exercise intention were observed in CHD patients with severe depressive symptoms. Severe symptoms of depression may preclude CHD patients from performing regular exercise.

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Diederick Grobbee, MD, PhD
Editor-in-Chief
European Journal of Preventive Cardiology

Berlin, 2nd August 2016

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Dear Prof Grobbee,

We are delighted that the revised version of our paper is now suitable for acceptance for the *European Journal of Preventive Cardiology*.

Regarding the final comments by Reviewer #1 we amended the labels of Table S1 and S3 to make it clear that estimated mean percentages are presented. In addition, minor changes were made to table and figure headings and legends to add clarity. Further, as suggested by the reviewer, we kept previous references #19 to #20 for scales used to measure main variables and previous reference #22, a paper that examined the same study topic. All changes were implemented using the track changes function.

Thank you for the careful consideration of our work.

We are looking forward to the publication.

Yours sincerely,

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Response to Reviewer #1

Comment:

The mean percentages shown in supplementary tables S1 and S3 are imprecise and do not add up corresponding to a direct division calculation. This is probably due to the fact that they have been estimated by regression analysis as stated in the methods section. As this is confusing I suggest to either delete the N¨s columns or to calculate the direct percentages.

Response:

We agree that the percentage signs in Tables S1 and S2 suggest that the corresponding values can be calculated from the numbers also presented in these tables. We thus replaced % by p̂ and refer with an asterisk to the legend stating that mean percentages with 95% confidence intervals were estimated in logistic regression models.

Comment:

Previous references 18, 19 and 20 should be kept in spite of exceeding the maximum number of references set by the journal as they provide the key references for the scales used to measure the main variables in the study. In addition, reference 22 also should be kept, as it is a previous study examining the same topic as this paper.

Response:

Done

Title Page

REGULAR EXERCISE BEHAVIOUR AND INTENTION AND SYMPTOMS OF ANXIETY AND DEPRESSION IN CORONARY HEART DISEASE PATIENTS ACROSS EUROPE: RESULTS FROM THE EUROASPIRE III SURVEY

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Word count: 4,38~~0~~8 including title and author names/affiliations (n=193), abstract (n=250), keywords (n=9), main text (n=2847), figure/table legends (n=168~~8~~1) and references (n=921~~828~~)

Abstract

Background: Regular exercise lowers the risk of cardiovascular death in coronary heart disease (CHD) patients. We aimed to investigate regular exercise behaviour and intention in relation to symptoms of anxiety and depression in CHD patients across Europe.

Design: Multicentre cross-sectional survey

Methods: In the EUROASPIRE III survey, 8,966 CHD patients <80 years of age from 22 European countries were interviewed on average 15 months after hospitalisation. Whether patients exercised or intended to exercise regularly was assessed using the Stages of Change questionnaire in 8,330 patients. Symptoms of anxiety and depression were evaluated using the Hospital Anxiety and Depression Scale. Total physical activity was measured by the International Physical Activity Questionnaire in patients from a subset of 14 countries.

Results: Overall, 50.3% of patients were not intending to exercise regularly, 15.9% were intending to exercise regularly, and 33.8% were exercising regularly. Patients with severe symptoms of depression less frequently exercised regularly than patients with symptoms in the normal range (20.2%, 95% confidence interval (CI) 14.8–26.8 vs. 36.7%, 95% CI 29.8–44.2). Among patients not exercising regularly, patients with severe symptoms of depression were less likely to have an intention to exercise regularly (odds ratio 0.62, 95% CI 0.46–0.85). Symptoms of anxiety did not affect regular exercise intention. In sensitivity analysis, results were consistent when adjusting for total physical activity.

Conclusions: Lower frequency of regular exercise and decreased likelihood of exercise intention were observed in CHD patients with severe depressive symptoms. Severe symptoms of depression may preclude CHD patients from performing regular exercise.

Abstract word count: 250

Keywords

Coronary heart disease; Exercise; Physical activity; Anxiety; Depression

Introduction

Physical inactivity is a leading cause of the global disease burden and, along with smoking, one of the most important modifiable risk factors.[1] Convincing epidemiological evidence supports the conclusion that regular exercise decreases the risk of cardiovascular disease.[2] The benefit of regular exercise in the secondary prevention of coronary heart disease (CHD) is well documented: aerobic exercise training reduces the medium to long term risk of cardiovascular death by 25% when compared to usual care.[3] Indeed, exercise and drug interventions may be equally effective in the prevention of mortality outcomes among CHD patients.[4] The long-term benefit of regular exercise among CHD patients increases with the number of weekly sessions.[5] Higher exercise levels elicit greater cardio-protective effects and more strongly reduce the cardiovascular risk of CHD patients.[6] Low risk of cardiovascular events during high- and moderate intensity exercise training supports its adoption for secondary prevention.[7] Accordingly, patients with a previous acute coronary event or procedure should undergo regular exercise of moderate-to-vigorous intensity.[8]

Elevated symptoms of anxiety and depression worsen the clinical course and prognosis of cardiovascular disease, but may not represent independent cardiovascular risk factors.[9, 10] Psychobiological mediators possibly linking anxiety and depression with cardiovascular outcomes in CHD patients are unfavourable lifestyle factors: in particular, lack of regular exercise has been shown to largely explain the adverse association between depressive symptoms and cardiovascular events.[11] Moreover, regular exercise and symptoms of anxiety and depression seem to be interrelated: notably, depression and anxiety symptoms have been prospectively associated with reduced levels of physical exercise.[12, 13] However, we are not aware of any prior multicentre study that systematically evaluated to what extent symptoms of anxiety and depression impact regular exercise among CHD patients. The aim of the present study, therefore, was to investigate regular exercise behaviour and intention in relation to

symptoms of anxiety and depression in CHD patients across Europe. For this purpose, we took the opportunity to analyse data from the EUROASPIRE III survey (EUROpean Action on Secondary and Primary Prevention through Intervention to Reduce Events) conducted in patients previously hospitalised for coronary events and procedures.

Methods

Study participants

The EUROASPIRE III survey among CHD patients is a cross-sectional study conducted in 2006–2007 in 76 study centres in 22 European countries. Patients hospitalised for coronary artery bypass graft (CABG), percutaneous coronary intervention (PCI), acute myocardial infarction (AMI) and myocardial ischemia were retrospectively identified from hospital records.[14] Trained research staff reviewed 13,935 medical records and interviewed 8,966 patients <80 years of age at least 6 months after hospitalisation for their index event or procedure. Information on study centres and organisations is provided in the Supplementary data as Material S1. The study was approved by local ethics committees. Study participants provided written informed consent.

Regular exercise behaviour and intention

Whether patients exercised or intended to exercise regularly was assessed using the Stages of Change (SoC) short form questionnaire. Figure 1 shows the questionnaire including definition of regular exercise, question and answer choices, and the scoring scheme. Study centres in all 22 countries that participated in EUROASPIRE III contributed SoC data for analysis. We categorized patients not intending to exercise regularly (precontemplation stage), patients intending to exercise regularly in the next 30 days or 6 months (contemplation and preparation stage, respectively) and patients exercising regularly for less or more than 6 months (action and maintenance stage, respectively).[15, 16, 17]

Symptoms of anxiety and depression

Symptoms of anxiety and depression during the last 7 days were evaluated using the Hospital Anxiety and Depression Scale (HADS). The HADS is a 4-point Likert scale (range 0–3) with 7 items being related to anxiety and 7 items to depression. Item scores are added to obtain the summary scores on anxiety (HADS-A) and depression (HADS-D) separately, ranging between 0 and 21. A score <8 is considered to be in the normal range, scores from 8 to 10 (moderate symptoms) indicate a possible disorder and a score ≥11 (severe symptoms) indicates a probable disorder.[17]

Covariates

Covariates were socio-demographic and clinical characteristics (age at interview, sex, educational level, current smoking, diabetes, obesity) and factors possibly influencing physical performance (diagnostic group, history of stroke, recurrent CHD, cardiac rehabilitation, longstanding illness, disability or infirmity, time since hospitalisation). Ten-year age groups were used in the analysis. Educational levels considered were primary, secondary, intermediate and higher education. Smoking was self-reported and validated by carbon monoxide in breath (Bedfont Scientific, Model Micro 4 Smokerlyser, Kent, UK) using ≤10 ppm as cut-off value. Diagnosis of diabetes was reported by the patient. Body height and weight were measured using calibrated instruments. Obesity was defined as a body mass index ≥30 kg/m^2. Information on cardiac rehabilitation was assessed by asking: 'Were you advised to follow a cardiac prevention/rehabilitation programme within 3 months of discharge following the index event or procedure?' and 'If yes, did you attend the cardiac rehabilitation programme offered?' Diagnostic groups were patients' index events or procedures. History of stroke was self-reported stroke prior and/or following hospital admission for the index event or procedure. Recurrent CHD was self-reported hospitalisation for PCI, CABG, AMI or myocardial ischemia since the index event. Longstanding illness, disability or infirmity was assessed by asking: 'Do you have any long-standing illness, disability or infirmity? By long- standing it is meant

anything that has troubled you over a period of time, or that is likely to affect you over a period of time?' Total physical activity in the last 7 days was assessed using the International Physical Activity Questionnaire (IPAQ) short form in patients from 14 countries.[18]

Statistical analysis

Mean percentages of SoC by HADS-A and HADS-D and odds ratios (ORs) of intending to exercise regularly with 95% confidence intervals (CIs) were estimated using logistic regression analysis. Models allowed for random variation in regression intercepts between countries. To estimate the effects of HADS-A and HADS-D on regular exercise intention, a minimal sufficient adjustment set that comprised the above-mentioned covariates was determined using directed acyclic graphs (Supplementary data, Figure S1). In sensitivity analysis, multivariable associations of HADS-A and HADS-D with exercise intension were examined in patients from the subset of 14 countries with IPAQ data. All patients without missing data on HADS-A and HADS-D were considered in univariate analyses and patients without missing data on all covariates entered the multivariable analysis. Statistical tests were two-tailed, and an alpha level of 0.05 was chosen to indicate statistical significance. SAS software version 9.4 (SAS Institute Inc., Cary, NC) was used.

Results

Study population

Overall, the number of patients with available data on SoC was 8,330 (Figure S2 in the Supplementary data shows the study population by data availability). Compared to patients with missing/unclassifiable SoC data, patients with available SoC data showed lower HADS-A [median (IQR), 5 (3–8) vs. 6 (4–10)] and HADS-D [median (IQR), 4 (2–7) vs. 5 (3–8)] scores.

Frequency distributions of SoC

Overall, 50.3% of patients (in precontemplation stage) were not intending to exercise regularly, 15.9% (in contemplation and preparation stage) were intending to exercise regularly,

and 33.8% (in action and maintenance stage) were exercising regularly. The mosaic plots in Figure 2 show the frequency distribution of SoC by HADS-A and HADS-D score. The frequency of exercising regularly decreases and the frequency of not intending to exercise regularly increases with increasing HADS-D score (Figure 2B). This distribution pattern is less pronounced with increasing HADS-A score (Figure 2A). Compared to patients with symptoms of depression in the normal range (HADS-D <8), patients with severe symptoms (HADS-D ≥11) less frequently exercised regularly (20.2%, 95% CI 14.8–26.8 vs. 36.7%, 95% CI 29.8–44.2). Table S1 in the Supplementary data provides further mean percentages of SoC by HADS-A and HADS-D as shown in Figure 2.

Associations of HADS-A and HADS-D with exercise intention

Among the subgroup of patients not exercising regularly, the Table presents univariate and multivariable associations of HADS-A and HADS-D with exercise intention. In the univariate analysis, severe symptoms of anxiety (OR 0.76, 95% CI 0.62–0.93) and moderate (OR 0.71, 95% CI 0.58–0.85) and severe (OR 0.53, 95% CI 0.41–0.68) symptoms of depression were inversely associated with intending to exercise regularly. Table S2 in the Supplementary data shows univariate associations of covariates with intending to exercise regularly.

In the multivariable analysis, only severe depressive symptoms decreased the likelihood of intending to exercise regularly (OR 0.62, 95% CI 0.46–0.85), whereas the univariate associations of severe anxiety and moderate depressive symptoms were attenuated (Table). No statistically significant interaction was observed between HADS-A and HADS-D.

Sensitivity analysis

The sensitivity analysis included patients from the subset of 14 countries with IPAQ data (total physical activity, N=4,438). Overall, 23.1%, 37.6%, and 39.4% respectively had a low, moderate and high IPAQ level. Patients with severe symptoms of depression more

frequently had a low IPAQ level than patients with depressive symptoms in the normal range (41.4%, 95% CI 30.2–53.8 vs. 19.3%, 95% CI 13.2–27.3, Table S3 in Supplementary data).

When further adjusting multivariable associations of HADS-A and HADS-D with exercise intention for IPAQ categories in patients not exercising regularly (N=2,632), similar results were observed as in the main analysis: in patients with severe depressive symptoms, the likelihood of intending to exercise regularly was lower as compared to patients with symptoms in the normal range (OR 0.60, 95% CI 0.39–0.91, p=0.017).

Discussion

In the present study, we report on the frequency of regular exercise behaviour and intention and on associations of exercise intention with regard to symptoms of anxiety and depression among patients with CHD across Europe. Only one fifth of patients with severe symptoms of depression exercised regularly, compared to almost two fifths of patients with symptoms in the normal range. Severe depressive symptoms had a detrimental effect on planned regular exercise, lowering the likelihood of intending to exercise regularly by 40%. Symptoms of anxiety did not independently affect intention to exercise regularly.

Previous studies

To the best of our knowledge, this is the first multicentre study investigating the association of anxiety and depression with regular exercise in CHD patients. Our results support the findings of a previous study that prospectively investigated depressive symptoms and regular exercise in 502 patients hospitalized for coronary syndromes in the United Kingdom: HADS-D score prior to hospital discharge was inversely associated with taking regular exercise 12 months later.[12] Our results further concur with findings of a prospective analysis in the Whitehall II study, where symptoms of anxiety and/or depression at baseline decreased the probability of exercising regularly as assessed twice during an 8-year follow-up period.[13] Of note, this study also showed that regular exercise at baseline reduced the likelihood of

depressive symptoms at follow-up examinations, suggesting that the association between depressive symptoms and regular exercise is bi-directional. Indeed, other studies in general population samples similarly observed adverse prospective associations between regular exercise and incident depressive symptoms.[19~~6~~, 20] Accordingly, we refrained from examining cross-sectional associations of symptoms of anxiety and depression with current regular exercise, and analysed associations of HADS with intention to exercise regularly, excluding patients who already exercised. Our data show a marked difference in regular exercise between patients with severe symptoms of depression and patients with symptoms in the normal range as well as a considerable effect of severe depressive symptoms on intention to exercise regularly. This suggests that depressive symptoms represent a major barrier to exercise behaviour change in CHD patients. Investigating the directionally opposite association than the one investigated in the present study, our group previously reported higher HADS-A and HADS-D scores in overweight/obese patients intending to exercise regularly when compared to patients not intending to become physically active.[21~~17~~] Thus, in line with general population studies, previous results from EUROASPIRE together with the findings of the present study provide further evidence for a bi-directional association between depressive symptoms and regular exercise.

Stages of change

Among patients with stable CHD, aerobic exercise training is recommended ≥3 times a week and 30 minutes per session by current European guidelines on cardiovascular disease prevention.[8] This recommendation is largely consistent with the assessment of regular exercise by the SoC questionnaire (3 to 5 times per week for 20-60 minutes per session). According to the transtheoretical model, individuals advance through the "stages of change" (from which the name of the SoC questionnaire is derived) until they successfully adapt a new health behaviour.[22~~18~~] A study validating SoC against exercise behaviour demonstrated accurate stage

distinction by moderate and strenuous exercise.[23,19] A meta-analysis of studies investigating predictors of exercise behaviour showed a large effect size for the relationship between exercise intention and actual exercise uptake.[24,40] A meta-analysis of studies on regular exercise SoC showed that stage membership well defines the progress of change, concluding that future studies should investigate the moderators and mediators of stage transition.[25,1] In this regard, the present study identified severe depressive symptoms as a barrier to advancement from the precontemplation stage (not intending) to the contemplation and preparation stage (intending to exercise).

The level of total physical activity (not only exercise, but all types of activities) is a possible confounding factor in the association of symptoms of anxiety and depression with intention to exercise regularly. As outlined above, it was measured using the IPAQ, which covers a wide range of physical activity domains and is recommended for use in large study samples.[26,2] In sensitivity analysis, a low IPAQ level was more frequently observed in patients with severe depressive symptoms. Importantly, however, the multivariable association of severe depressive symptoms with intention to exercise regularly persisted after further adjustment for IPAQ level, indicating that the effect is independent from total physical activity.

Implications and perspectives

Our results show that a majority of CHD patients are not intending to exercise regularly and emphasise the need of novel preventive strategies to enhance motivational readiness and finally lifestyle change. Randomized controlled trials on the efficacy of SoC-matched exercise interventions have shown positive effects on regular exercise in healthy individuals and CHD patients.[27,3, 28,4] A systematic review of intervention studies to increase the adherence to regular exercise in cardiac rehabilitation concluded - due to heterogeneous results - that practice recommendations could not be made.[29,5] The authors of that study, however, inferred from their findings that “individually tailored approaches may increase the likelihood of success”. Based

on a large sample of CHD patients from 22 countries, our study results could be helpful in designing future behavioural interventions for exercise promotion that may need to be specifically tailored to patients with severe symptoms of depression. As an important take home message for cardiologists, general practitioners, specialist nurses and other allied professionals, we would like to emphasise the adverse association of depressive symptoms with regular exercise in CHD patients.

Limitations

As study limitations we note the following. Firstly, regular exercise was assessed simultaneously with symptoms of anxiety and depression. Secondly, the thresholds used by the instruments for assessing regular exercise and total physical activity ignore the benefit of low-volume exercise among individuals at risk of cardiovascular disease.[28] Thirdly, we lacked medical data on functional status and relied on information provided by the patients on long-standing illness, disability or infirmity. Fourth, our study sample can be looked at as survivors of a hypothetical cohort of CHD patients. Back in time, it is likely that these survivors exercised and intend to exercise more frequently and exhibited sever symptoms of depression less frequently than non-survivors. Thus, our study may overestimate the frequency of regular exercise and exercise intention, but underestimate the association of HADS-D with exercise intention in that hypothetical cohort.

Conclusions

In conclusion, our results indicate that severe symptoms of depression may preclude CHD patients from performing regular exercise. Strategies for regular exercise promotion may need to specifically target CHD patients with severe depressive symptoms across Europe.

Acknowledgements

The EUROASPIRE Study Group is grateful to all the hospitals in which the study was carried out. Their administrative staff, physicians, nurses, and other personnel helped us in many ways and we very much appreciate this. We are particularly grateful to the patients who participated in the study.

Declaration of conflicting interests

Dr. De Smedt was financially supported by the Research Foundation Flanders. Dr. Reiner reports personal fees from AstraZeneca, personal fees from Abbott, personal fees from Aegirion, and other from Sanofi, outside the submitted work; Dr. Kotseva reports grants from European Society of Cardiology, during the conduct of the study; grants from Hoffman La Roche, from Boehringer Ingelheim, outside the submitted work; Dr. Wood reports grants from Astra Zeneca, Bristol Myers Squibb, Glaxo SmithKline, Pfizer, Sanofi-Aventis, Servier Laboratories, Merck, Sharp and Dohme (MSD)/Schering-Plough, personal fees from Bristol Myers Squibb Merck, Sharp and Dohme/Schering Plough, Pfizer, Zentiva, during the conduct of the study; grants from Pfizer, grants from Hoffman La Roche, Merck Sharp and Dohme, Bristol-Myers Squibb Emea Sarl, AstraZeneca, GlaxoSmithKline, personal fees from Astra Zeneca, Merck Sharp and Dohme, Kowa Pharmaceuticals, Zentiva, Ranexa, Sanofi, Pfizer, personal fees from Merck Sharp and Dohme, outside the submitted work; Dr. Keil reports grants from Pfizer, MSD and AstraZeneca, for projects generated within EUROASPIRE III. All other authors declare that there is no conflict of interest.

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Squibb; GlaxoSmithKline; Pfizer; Sanofi-Aventis; and Servier; Sponsors: Merck/Schering-Plough; and Novartis.

Authorship

CP, JW, JH, DDB, DDS, GDB, ZR, ZF, KK, DW, and UK contributed to the conception or design of the work. CP, JW, JH, DDB, DDS, GDB, ZR, JPE, ZF, DG, CJ, KK, and UK contributed to the acquisition, analysis, or interpretation of data for the work. CP drafted the manuscript. JW, JH, DDB, DDS, GDB, ZR, JPE, ZF, DG, CJ, KK, and UK critically revised the manuscript. All gave final approval. CP, JW, JH, DDB, DDS, GDB, ZR, ZF, DG, KK, DW, and UK agree to be accountable for all aspects of work ensuring integrity and accuracy.

Figure legends

Figure 1: Stages of Change short form questionnaire

Figure 2: Mosaic plots showing the frequency distribution of Stages of Change by HADS-A (Figure 2A, N=8,000) and HADS-D (Figure 2B, N=8,039) score

HADS, Hospital Anxiety and Depression Scale (HADS-A [Anxiety] and HADS-D [Depression])

1=Precontemplation stage (not intending to exercise regularly)

2=Contemplation and preparation stage (intending to exercise regularly)

3= Action and maintenance stage (exercising regularly)

~~Mean proportions from logistic regression models with country modelled as a random effect.~~

Regular exercise is any *planned* physical activity (e.g. brisk walking, aerobics, jogging, bicycling, swimming, rowing, etc.) performed to increase physical fitness. Such activity should be performed *3 to 5 times* per week for *20-60 minutes* per session. Exercise does not have to be painful to be effective but should be done at a level that increases your breathing rate and causes you to break a sweat.

- Question and aswer choices

Do you exercise regularly according to that definition?
- Yes, I have been for MORE than 6 months (choice #1)
- Yes, I have been for LESS than 6 months (choice #2)
- No, but I intend to in the next 30 days (choice #3)
- No, but I intend to in the next 6 months (choice #4)
- No, and I do NOT intend to in the next 6 months (choice #5)
- Don't Know/ Unsure (choice #6)

- Scoring scheme

- answerd with choice #1: stage = Maintenance
- answerd with choice #2: stage = Action

} Exercising regularly

- answerd with choice #3: stage = Preparation
- answerd with choice #4: stage = Contemplation

} Intending to exercise regularly

- answerd with choice #5: stage = Precontemplation } Not intending to exercise regularly
- answerd with choice #6: stage = Unclassifiable

Table: Univariate and multivariable associations of HADS-A and HADS-D with intending to exercise regularly in patients not exercising regularly

		Univariate associations					Multivariable associations				
		N	n	OR	95% CI	p-value	N	n	OR	95% CI	p-value
HADS-A	<8	3,510	891	1.00	Reference	–	3,351	858	1.00	Reference	–
	8–10	980	226	0.90	0.75–1.07	0.228	936	216	1.06	0.87–1.29	0.562
	≥11	789	163	0.76	0.62–0.93	0.009	739	149	0.99	0.77–1.27	0.951
HADS-D	<8	3,879	1,016	1.00	Reference	–	3,683	974	1.00	Reference	–
	8–10	889	180	0.71	0.58–0.85	0.001	847	172	0.82	0.67–1.01	0.067
	≥11	538	85	0.53	0.41–0.68	<0.001	496	77	0.62	0.46–0.85	0.003

HADS, Hospital Anxiety and Depression Scale (HADS-A [Anxiety] and HADS-D [Depression]); OR, odds ratio; CI, confidence interval.

N corresponds to the total number of patients, n corresponds to the number of patients intending to exercise.

Odds ratios with 95% confidence intervals from logistic regression analysis with not intending to exercise regularly as the reference category and country modelled as a random effect. Multivariable associations from a single logistic regression model adjusted for age at interview, sex, diagnostic

group, educational level, current smoking, diagnosis of diabetes, obesity, cardiac rehabilitation, history of stroke, recurrent coronary heart disease, longstanding illness, disability or infirmity, and time since hospitalisation.

References

1. Collaborators GBDRF, Forouzanfar MH, Alexander L, et al. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet*. 2015; 386: 2287-323.

2. World Health Organisation. Joint WHO/FAO Expert Consultation on Diet, Nutrition and the Prevention of Chronic Diseases. *WHO Technical Report Series* Geneva, 2003.

3. Heran BS, Chen JM, Ebrahim S, et al. Exercise-based cardiac rehabilitation for coronary heart disease. *Cochrane Database Syst Rev*. 2011: CD001800.

4. Naci H and Ioannidis JP. Comparative effectiveness of exercise and drug interventions on mortality outcomes: metaepidemiological study. *BMJ*. 2013; 347: f5577.

5. Moholdt T, Wisloff U, Nilsen TI and Slordahl SA. Physical activity and mortality in men and women with coronary heart disease: a prospective population-based cohort study in Norway (the HUNT study). *Eur J Cardiovasc Prev Rehabil*. 2008; 15: 639-45.

6. Mora S, Cook N, Buring JE, Ridker PM and Lee IM. Physical activity and reduced risk of cardiovascular events: potential mediating mechanisms. *Circulation*. 2007; 116: 2110-8.

7. Rognmo O, Moholdt T, Bakken H, et al. Cardiovascular risk of high- versus moderate-intensity aerobic exercise in coronary heart disease patients. *Circulation*. 2012; 126: 1436-40.

8. Perk J, De Backer G, Gohlke H, et al. European Guidelines on cardiovascular disease prevention in clinical practice (version 2012). The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts). Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur Heart J*. 2012; 33: 1635-701.

9. Nicholson A, Kuper H and Hemingway H. Depression as an aetiologic and prognostic factor in coronary heart disease: a meta-analysis of 6362 events among 146 538 participants in 54 observational studies. *Eur Heart J*. 2006; 27: 2763-74.

10. Roest AM, Martens EJ, Denollet J and de Jonge P. Prognostic association of anxiety post myocardial infarction with mortality and new cardiac events: a meta-analysis. *Psychosomatic medicine*. 2010; 72: 563-9.

11. Whooley MA, de Jonge P, Vittinghoff E, et al. Depressive symptoms, health behaviors, and risk of cardiovascular events in patients with coronary heart disease. *JAMA*. 2008; 300: 2379-88.

12. Allan JL, Johnston DW, Johnston M and Mant D. Depression and perceived behavioral control are independent predictors of future activity and fitness after coronary syndrome events. *J Psychosom Res*. 2007; 63: 501-8.

13. Azevedo Da Silva M, Singh-Manoux A, Brunner EJ, et al. Bidirectional association between physical activity and symptoms of anxiety and depression: the Whitehall II study. *Eur J Epidemiol*. 2012; 27: 537-46.

14. Kotseva K, Wood D, De Backer G, De Bacquer D, Pyorala K and Keil U. EUROASPIRE III: a survey on the lifestyle, risk factors and use of cardioprotective drug therapies in coronary patients from 22 European countries. *Eur J Cardiovasc Prev Rehabil*. 2009; 16: 121-37.

15. Prochaska JO and DiClemente CC. Stages and processes of self-change of smoking: toward an integrative model of change. *J Consult Clin Psychol*. 1983; 51: 390-5.

16. Prochaska JO and Velicer WF. The transtheoretical model of health behavior change. *American journal of health promotion : AJHP*. 1997; 12: 38-48.

17. Zigmond AS and Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983; 67: 361-70.

18. Guidelines for Data Processing and Analysis of the International Physical Activity Questionnaire (IPAQ). Available at: https://sites.google.com/site/theipaq/scoring-protocol (Assessed: 2nd August 2016).

196. Wiles NJ, Haase AM, Gallacher J, Lawlor DA and Lewis G. Physical activity and common mental disorder: results from the Caerphilly study. *Am J Epidemiol*. 2007; 165: 946-54.

20. Brown WJ, Ford JH, Burton NW, Marshall AL and Dobson AJ. Prospective study of physical activity and depressive symptoms in middle-aged women. *American journal of preventive medicine*. 2005; 29: 265-72.

2117. De Smedt D, Clays E, Annemans L, et al. The association between self-reported lifestyle changes and health-related quality of life in coronary patients: the EUROASPIRE III survey. *European journal of preventive cardiology*. 2014; 21: 796-805.

2218. Marcus BH and Simkin LR. The transtheoretical model: applications to exercise behavior. *Medicine and science in sports and exercise*. 1994; 26: 1400-4.

2319. Schumann A, Estabrooks PA, Nigg CR and Hill J. Validation of the stages of change with mild, moderate, and strenuous physical activity behavior, intentions, and self-efficacy. *International journal of sports medicine*. 2003; 24: 363-5.

240. Hausenblas HA, Carron AV and Mack DE. Application of the theory of planned behavior to exercise behavior: a meta-analysis. *J Sport Exerc Psychol*. 1997: 35-61.

251. Marshall SJ and Biddle SJ. The transtheoretical model of behavior change: a meta-analysis of applications to physical activity and exercise. *Annals of behavioral medicine : a publication of the Society of Behavioral Medicine*. 2001; 23: 229-46.

262. Craig CL, Marshall AL, Sjostrom M, et al. International physical activity questionnaire: 12-country reliability and validity. *Medicine and science in sports and exercise*. 2003; 35: 1381-95.

273. Zhu LX, Ho SC, Sit JW and He HG. Effect of a Transtheoretical Model-Based Stage-Matched Exercise Intervention on Exercise Behavior and Angina in Patients With Coronary Heart Disease: A Randomized Controlled Trial. *The Journal of cardiovascular nursing*. 2014.

284. Prochaska JO, Evers KE, Castle PH, et al. Enhancing multiple domains of well-being by decreasing multiple health risk behaviors: a randomized clinical trial. *Population health management*. 2012; 15: 276-86.

295. Karmali KN, Davies P, Taylor F, Beswick A, Martin N and Ebrahim S. Promoting patient uptake and adherence in cardiac rehabilitation. *Cochrane Database Syst Rev*. 2014; 6: CD007131.

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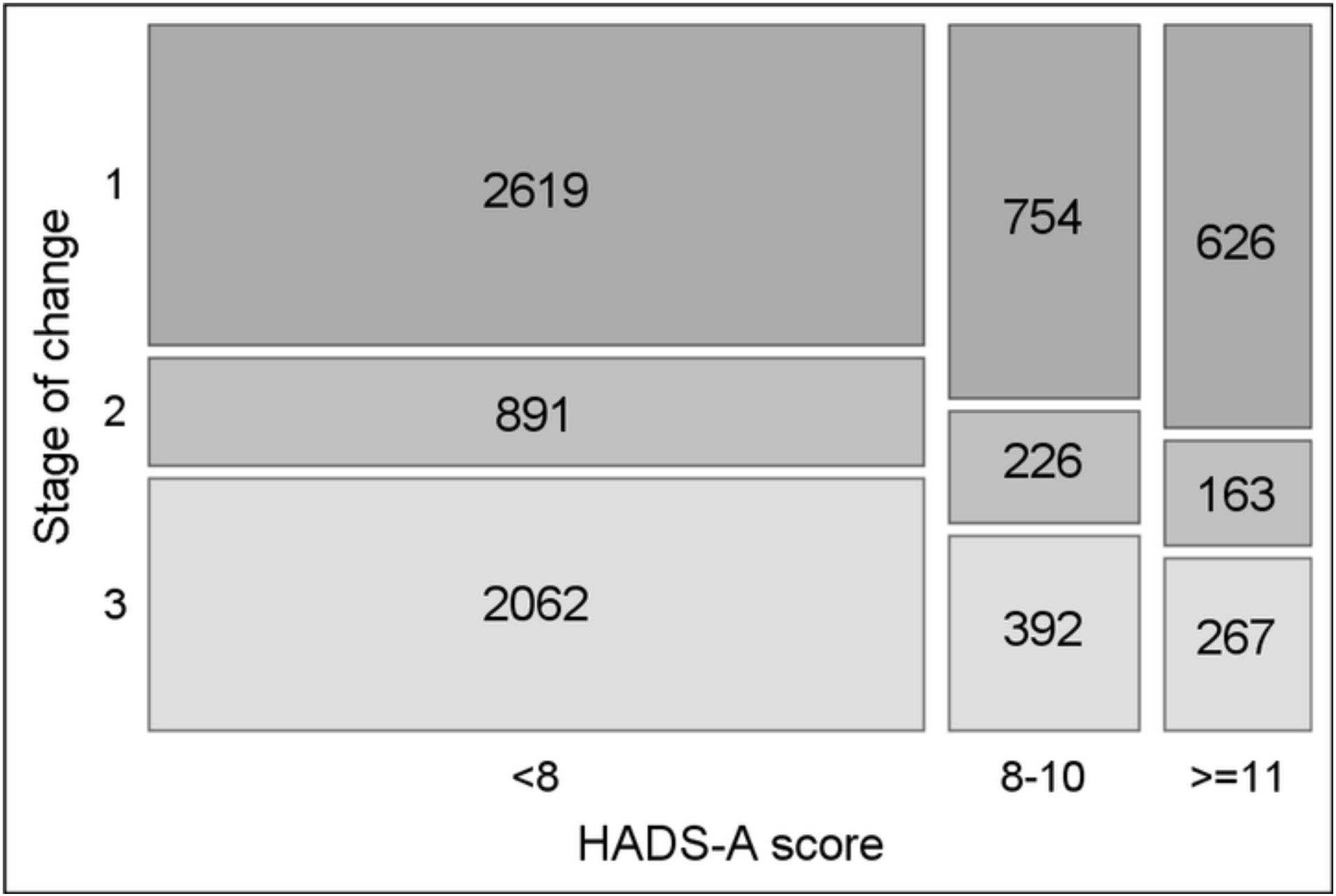
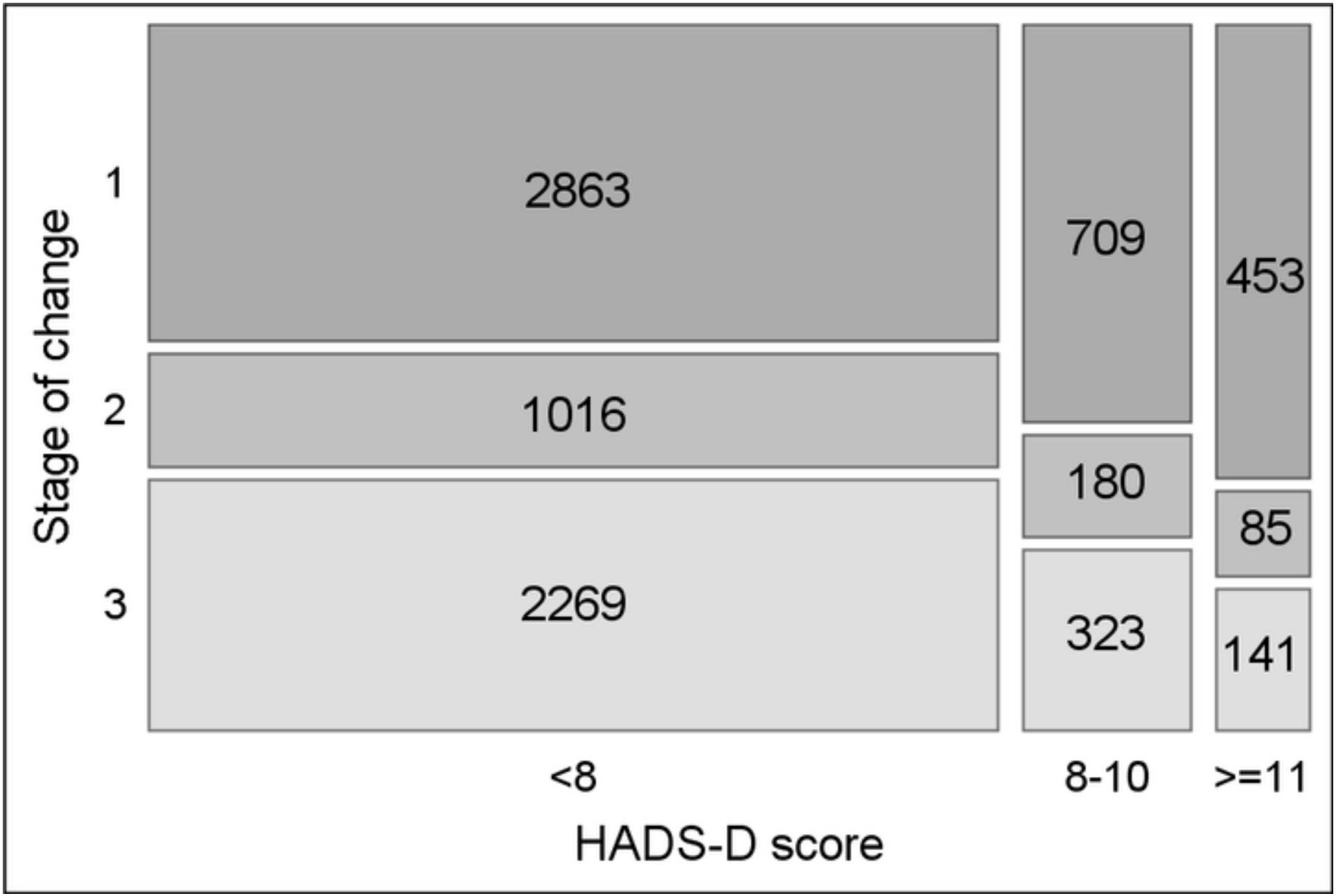


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