Title: Health Related Quality of Life in Coronary Patients and Its Association With their Cardiovascular Risk Profile : Results from the EUROASPIRE III survey

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Conflict of interest

None declared.

Keywords: Coronary heart disease, Quality of life, Secondary prevention

Abstract

Background:

Cardiovascular patients are likely to have an impaired health-related quality of life (HRQoL) due to functional and psycho-social limitations. The main objective of this study was to assess the distribution of HRQoL scores in coronary heart disease (CHD) patients across 22 European countries and to identify factors associated with the variation between patients.

Methods:

Data from the EUROASPIRE III survey (European Action on Secondary and Primary Prevention by Intervention to Reduce Events), on 8734 patients, were used. Patients with a diagnosis of CHD (coronary artery bypass graft (CABG), percutaneous coronary intervention (PCI), acute myocardial infarction (AMI) or myocardial ischaemia) were interviewed and examined at least 6 months after their acute coronary event. Quality of life of each patient was measured using 2 standardized questionnaires: the EuroQoL-5D (EQ-5D) and the 12-item short form health survey (SF-12v2).

Results:

HRQoL values differed significantly across countries. Lower HRQoL estimates were found in women, older patients, less educated, patients with myocardial infarction or ischaemia as recruiting diagnosis, patients with a history of stroke and patients who suffered from a recurring CHD event. In addition, HRQoL was significantly associated with current smoking, central obesity, lack of exercise and inappropriate HbA1c control in patients with diabetes. Furthermore the number of risk factors is inversely associated with HRQoL.

Conclusion:

Overall, a large heterogeneity was observed in HRQoL values between countries and patient groups. There seems to be a significant association between quality of life and patient characteristics with lifestyle risk factors as important determinants of HRQoL.

Introduction

Cardiovascular disease (CVD) remains the most common cause of disease burden in Europe, with coronary heart disease (CHD) being the single most important cause of death(1). Conventional treatment focuses mainly on functional outcomes, survival and extending life. However, morbidity and mortality rates are incomplete measures of outcome, since they do not reflect all aspects of health. Many patients consider the quality of the additional life years gained equally important as the length of life. Indeed, the goal of today's medicine should be to increase both patients' quantity and quality of life(2). In response, assessment of health-related quality of life (HRQoL) has been increasingly integrated in daily clinical practice. HRQoL is a subjective measure of overall well-being and reflects how a disease and its symptoms are perceived by a patient. Although there is no universal agreement on what constitutes HRQoL, current assessment focuses on the domains of social functioning, physical functioning and psychological functioning(3).

CHD patients are known to have an impaired HRQoL(4). Recent studies have shown a significant influence of HRQoL on long-term outcomes. Poor HRQoL has been shown to predict morbidity and mortality in patients with CHD, even when controlling for standard risk factors(5-7).

The aim of our study was to examine the relationship between the cardiovascular profile of coronary patients and their HRQoL. Data were derived from the EUROASPIRE III (European Action on Secondary and Primary Prevention by Intervention to Reduce Events) survey wherein two commonly used instruments were employed to assess patient's HRQoL: the EQ-5D (EuroQol-5D) and the SF-12v2 (12-item Short-Form Health Survey).

Methods

Study population and data collection

The details of the EUROASPIRE III study have been reported elsewhere(8). In brief, EUROASPIRE III, performed in 2006-07 in patients with established CHD, was a cross-sectional study to determine whether the European recommendations on CVD prevention were being followed in everyday clinical practice. Patients aged between 18 and 80 years, hospitalized for coronary artery bypass graft (CABG), percutaneous coronary intervention (PCI), acute myocardial infarction (AMI) or myocardial ischaemia, hereafter referred to as the recruiting diagnosis, were retrospectively identified from diagnostic registers, hospital discharge lists or other sources at 76 different hospital centres across 22 European countries: Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Poland, Romania, Russian federation, Slovenia, Spain, The Netherlands, Turkey, and the United Kingdom (UK). Data collection was conducted by trained research staff using standardized methods and instruments. In total, 8,966 patients (participation rate=73%) were interviewed and examined at least 6 months and not later than 3 years after their initial hospital admission (mean=1.24 years). Informed consent was obtained from each patient and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki (9).

Patient characteristics and risk factors assessed

The interview contained questions on personal and demographic details; medical and in particularly cardiovascular history (i.e. having a history of stroke or suffering from a recurrent coronary event between the recruiting diagnosis and the moment of interview); reported lifestyle and risk factor management related to smoking, exercise (regular exercise defined as 20-60 min, 3-5 x/week), blood pressure, lipids, glucose and medication. In addition, height, weight and waist circumference were measured in light indoor clothes without shoes, as well as blood pressure, heart rate and breath carbon monoxide. Venous blood was tested for serum total cholesterol, HDL-cholesterol, triglycerides, plasma glucose and HbA1c, the latter two were only measured in patient with self-reported diabetes(8). LDL was calculated

according to the Friedewald formula. The risk factor targets used, were based on the European guidelines on cardiovascular prevention(10). A raised blood pressure was defined as systolic blood pressure (SBP)/diastolic blood pressure (DBP) ≥ 140/90 mmHg (≥ 130/80 mmHg in patients with diabetes). A Raised total cholesterol was defined as total cholesterol ≥ 4.5 mmol/L. Raised LDL-cholesterol (LDL-C) was defined as LDL-C ≥ 2.5 mmol/L and Low HDL-cholesterol (HDL-C) was defined as HDL-C <1/1.2 mmol/L for men/women. Raised fasting glucose was defined as fasting glucose ≥ 6.1 mmol/L among patients with self-reported diabetes and raised HbA1c as HbA1c ≥ 6.5% among patients with self-reported diabetes. Low physical activity was defined as less than 20 min moderate physical activity, three times a week. Central obesity was defined as waist circumference > 102/88 cm (men/women).

Health-related Quality of life assessment

In order to assess patients' HRQoL, they were asked to fill out 2 self-administered questionnaires: EQ-5D and SF-12v2. In each country, questionnaires were administered in the official language. Validity of these scales has been reported previously(11).

The EQ-5D is an easy to complete brief instrument that contains a self classifier ($EQ\text{-}5D_{index}$) covering 5 dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) and a visual analogue scale (EQ-VAS). In the current analyses only the EQ-VAS was included. The EQ-VAS is a vertical scale, ranging from 0 (worst imaginable) to 100 (best imaginable) on which the respondent is asked to indicate their current HRQOL state.

The SF-12v2 consists of 12 Likert scale questions, covering 8 dimensions: general health, physical functioning, role-physical, bodily pain, vitality, social functioning, role-emotional and mental health. Both physical (PCS-12) and mental functioning (MCS-12) components can be assessed. The scores were standardized by a common scoring algorithm, ranging between 0 and 100, with lower scores

representing worse and higher scores representing better health(12). The SF-12v2 was not administered in Hungary. In Germany, the SF-36 was used instead of the SF-12v2(13).

Statistical analyses

All analyses were based on generalized linear mixed models in order to account for the clustering of patients within countries. The association between patient characteristics and HRQoL was initially adjusted for gender, age and educational level. A further adjustment for age, gender, educational level, recruiting diagnosis, diabetes, history of stroke, recurring coronary events, smoking, physical activity and central obesity was applied. To investigate the relation between uncontrolled risk factors and HRQoL, in patients being medically treated, adjustment for gender, age, recruiting diagnosis, educational level, diabetes and history of stroke and recurring events was performed.

Likewise the relation between the number of risk factors and HRQoL was investigated. In an additional analysis the number of risk factors was considered as a continuous variable, hence a linear regression analysis was performed. In both analyses adjustment for patient characteristics was applied.

Significance levels were set at $p<0.05$. All statistical analyses were performed using the IBM SPSS statistical software (version 20.0).

Results

HRQoL data (full information on at least 1 HRQoL instrument) were available for 8734 patients (table 1). About three quarters (74.6%) of patients included in our analyses were male (n=6516). The average age of patients was 63.2 years (SD=9.5). About 60% of patients included, had a cardiac revascularisation as recruiting diagnosis, 19.5% was diagnosed with AMI.

[insert Table 1 here]

The overall mean PCS-12 and MCS-12 were 42.14 (SD=10.15) and 49.15 (SD=10.22) respectively. For the EQ-VAS a mean value of 66.42 (SD=18.84) was observed (table 2).

Comparison of the HRQoL scores across countries indicated substantial differences, even after adjustment for age, gender and education ($p<0.001$) (figure 1). There was a tendency towards a poorer HRQoL in patients residing in Eastern European countries.

[insert Figure 1 here]

Likewise, gender, age and educational level were significantly associated with HRQoL, with men having a better self-perceived HRQoL compared to women, younger patients scoring higher on physical health and overall well-being, and those with lower education levels having worse HRQoL compared to those with higher levels of education (table 2 and 3). Furthermore, significantly lower HRQoL vales were found in patients with self-reported diabetes and higher values in those having undergone cardiac surgery or angioplasty, except for MCS-12, where no significant differences were found between diagnostic categories. In addition, cardiovascular history was also significantly associated with lower HRQoL measures, except for MCS-12, on which recurring events did not have any impact. Finally, better control of lifestyle parameters (central obesity, smoking, physical activity) was significantly associated with HRQoL (except for MCS-12 in central obesity). Based on the regression coefficients from table 3, these lifestyle parameters seem to be as important as cardiovascular history, gender or educational level.

[insert Table 2 here]

[insert Table 3 here]

Furthermore, HRQoL was significantly associated with certain cardiovascular risk factors in those patients being medically treated (table 4). Regarding blood pressure the associations with the different HRQoL measures were found to be non-significant or to go in the opposite direction, with worse HRQoL being associated with better blood pressure values. Regarding total cholesterol a significant association was seen with MCS-12. No significant relation was found with LDL-cholesterol and fasting glucose, whereas HbA1c was significantly associated with all HRQoL measures in patients with diabetes.

[insert Table 4 here]

Looking at the number of CVD risk factors (blood pressure, total cholesterol, smoking, physical activity, central obesity) revealed that an increase in the amount of risk factors was associated with a gradual decrease in HRQoL even after adjustment for patient characteristics (table 5). Fitting a multiple linear model showed that each additional risk factor was associated with a 0.872 ($p<0.001$) decrease in PCS-12, a 0.326 ($p=0.002$) decrease in MCS-12 and a 1.368 ($p<0.001$) decrease on the EQ-VAS.

[insert Table 5 here]

Discussion

In this study, including 8734 stabilized CHD patients from 22 European countries, we aimed to analyse the association between HRQoL and patient characteristics. As expected the overall HRQoL scores in our cohort of CHD patients were lower compared to the general population(14) and similar to previously reported results(4). Furthermore, consistent with previous research and compared to the general population, having CHD seemed to have a limited influence on the mental health status, in contrast to the physical component and the overall health(4).

Our analyses revealed that patient characteristics were significantly associated with HRQoL. Firstly, patients from Eastern European countries were more likely to have an impaired HRQoL. Similar findings have been previously reported in the general population with lower overall subjective well-being scores in less prosperous countries(15). Secondly, in accordance with the literature, CHD women reported lower HRQoL results than men(4;16-22), an observation which was also seen in the general population(4;23). With regard to age, a significant association - with younger patients reporting a better HRQoL - was observed with the PCS-12 and the EQ-VAS. Likewise other research groups found higher HRQoL values in younger CHD patients(17;21;22;24). Xie and colleagues reported similar results regarding the physical score, however for the mental score and the EQ-5D, better values were found in older CHD patients(4).

Patients with self-reported diabetes were more likely to have a worse HRQoL. Similarly Xie *et al.* reported significantly lower HRQoL outcomes on both the SF-12 and the EQ-5D in these patients whereas Peterson *et al.* reported a 3 point lower score on PCS-12 in patients with diabetes(4;25). In addition, similar to the results reported by Lee *et al.*, lower educated patients had significantly lower HRQoL outcomes(24). Analyses also revealed significantly higher HRQoL scores in patients undergoing revascularization as recruiting diagnosis, confirming previous studies(26-29). Other significant predictors

of impaired HRQoL were: having a history of stroke or suffering from a recurring coronary event. Several studies have shown a negative influence of stroke on HRQoL(4;30-33). Recurring cardiovascular events are also known to cause a decrease in HRQoL, although to a smaller extent than the HRQoL reduction associated with initial events(33).

Lifestyle risk factors were significantly associated with HRQoL. In line with the literature, central obesity was associated with a decrease in HRQoL(24;34;35). In addition, we found an association between HRQoL and physical activity, with better HRQoL outcomes in physically active persons. Similarly, Sevinc *et al.* reported a higher HRQoL in coronary patients who are active or exercise regularly, compared to sedentary patients(28). Finally, a significant association between HRQoL and current smoking was seen(36;37). In contrast to some authors stating that smoking cessation does not improve HRQoL significantly, we have found significantly higher HRQoL in quitters, similar to non-smokers (data not shown)(38-40). These results stress the importance of promoting healthy lifestyle changes in coronary patients, not only to prevent recurrent events but also to increase patients' HRQoL. Our findings are in line with the latest European recommendations on CVD prevention, promoting multimodal, behavioral interventions in CHD patients(41). The interventions should include promotion of healthy lifestyle based on cognitive-behavioral strategies, through behavioral change including nutrition, exercise, smoking cessation, coping with the illness and improving medication adherence.

When looking at the relation between HRQoL and CVD risk factors in patients being treated, less pronounced differences were seen across different risk groups. A negative association was found between SF-12v2 and raised blood pressure, which was eliminated after adjustment for medication intake. Indeed about 28% of the EUROASPIRE III patients was taking nitrates and 30% was taking diuretics at the time of the interview, medication which is often given in patients with angina and heart failure respectively, two conditions that are associated with a substantial decrease in HRQoL(21;42). Some previous studies did find a correlation between HRQoL and blood pressure, with worse HRQoL in

hypertensive patients whereas others did not find any association(28;42-44). An uncontrolled total cholesterol was significantly associated with a worse MCS-12, whereas no association was found with LDL-cholesterol. Similarly, Sevinç *et al.*, found no significant association between HRQoL and cholesterol(28). HbA1c but not fasting glucose was significantly associated with HRQoL with worse health outcomes in those with a lower HRQoL. The latter observation was in accordance with published literature(24). Khanna *et al.* found a significant association between HbA1c and diabetes-specific HRQoL whereas Lau *et al*., only found an effect on the mental score of SF-12(45;46). Furtemore, in accordance with the literature, the number of risk factors was inversely associated with HRQoL(47). These results reaffirm the high importance of a holistic approach regarding risk factor prevention.

Our analyses did not include the EQ-$5D_{index}$ since country-specific weights to calculate the EQ-$5D_{index}$ were not available for all 22 countries. However, when performing the analyses using the UK weights for all the countries, similar results as reported were found (data not shown).

The EUROASPIRE III study is one of the largest surveys throughout Europe assessing patients' subjective HRQoL in a stable coronary population. Data collection was organized in a standardized way and HRQoL was measured by means of 2 different widely used HRQoL instruments. In order to account for HRQoL differences inherent to the centre, multilevel analyses were used. The major limitation of our study is its cross-sectional design, therefore no statement about causality, only about the association between HRQoL and different characterstics, can be made. Furthermore, results should be interpreted with caution since most of the data were self-reported. Additionally, results are not country representative as the survey was carried out in selected geographical areas in each country.

In conclusion, patient characteristics such as age, gender, educational level, physical activity, smoking status, central obesity and comorbidities seem to be significantly associated with HRQoL in coronary

patients. In addition HRQoL, especially the physical health components and the overall self-perceived well-being, seems to decrease significantly with an increasing number of risk factors.

References

(1) Allender S, Scarborough P, Peto V, R et al. European Cardiovascular Disease Statistics. 2008.

(2) Oldridge N, Saner H, McGee HM. The Euro Cardio-QoL Project. An international study to develop a core heart disease health-related quality of life questionnaire, the HeartQoL. Eur J Cardiovasc Prev Rehabil 2005 Apr;12(2):87-94.

(3) Swenson JR, Clinch JJ. Assessment of quality of life in patients with cardiac disease: the role of psychosomatic medicine. J Psychosom Res 2000 Apr;48(4-5):405-15.

(4) Xie J, Wu EQ, Zheng ZJ, Sullivan PW, Zhan L, Labarthe DR. Patient-reported health status in coronary heart disease in the United States: age, sex, racial, and ethnic differences. Circulation 2008 Jul 29;118(5):491-7.

(5) Rumsfeld JS, MaWhinney S, McCarthy M, et al. Health-related quality of life as a predictor of mortality following coronary artery bypass graft surgery. Participants of the Department of Veterans Affairs Cooperative Study Group on Processes, Structures, and Outcomes of Care in Cardiac Surgery. JAMA 1999 Apr 14;281(14):1298-303.

(6) Grool AM, van der GY, Visseren FL, de Borst GJ, Algra A, Geerlings MI. Self-rated health status as a risk factor for future vascular events and mortality in patients with symptomatic and asymptomatic atherosclerotic disease: the SMART study. J Intern Med 2012 Jan 18.

(7) Spertus JA, Jones P, McDonell M, Fan V, Fihn SD. Health status predicts long-term outcome in outpatients with coronary disease. Circulation 2002 Jul 2;106(1):43-9.

(8) Kotseva K, Wood D, De Backer G, De Bacquer D, Pyorala K, 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 Apr;16(2):121-37.

(9) Coats AJ, Shewan LG. Statement on authorship and publishing ethics in the international journal of cardiology. Int J Cardiol 2011 Dec 15;153(3):239-40.

(10) De Backer G, Ambrosioni E, Borch-Johnsen K, et al. European guidelines on cardiovascular disease prevention in clinical practice. Third Joint Task Force of European and Other Societies on Cardiovascular Disease Prevention in Clinical Practice. Eur Heart J 2003 Sep;24(17):1601-10.

(11) De Smedt D, Clays E, Doyle F, et al. Validity and reliability of three commonly used quality of life measures in a large European population of coronary heart disease patients. Int J Cardiol 2012 Jun 28.

(12) Ware J, Kosinski M, Turner-Bowker D, Gandek B. How to Score Version 2 of the SF-12 Health Survey (With a Supplement Documenting Version 1). Lincoln, RI: QualityMetric Incorporated; 2002.

(13) Wee CC, Davis RB, Hamel MB. Comparing the SF-12 and SF-36 health status questionnaires in patients with and without obesity. Health Qual Life Outcomes 2008;6:11.

(14) König HH, Bernert S, Angermeyer MC et al. Comparison of population health status in six european countries: results of a representative survey using the EQ-5D questionnaire. Med Care 2009;47(2):255-61.

(15) The EuroQol Group's International Task Forceon Self-Reported Health. Measuring Self-Reported Population Health: An International Perspective based on EQ-5D. EuroQol Group; 2004.

(16) Agewall S, Berglund M, Henareh L. Reduced quality of life after myocardial infarction in women compared with men. Clin Cardiol 2004 May;27(5):271-4.

(17) Brink E, Grankvist G, Karlson BW, Hallberg LR. Health-related quality of life in women and men one year after acute myocardial infarction. Qual Life Res 2005 Apr;14(3):749-57.

(18) Duenas M, Ramirez C, Arana R, Failde I. Gender differences and determinants of health related quality of life in coronary patients: a follow-up study. BMC Cardiovasc Disord 2011;11:24.

(19) Emery CF, Frid DJ, Engebretson TO, et al. Gender differences in quality of life among cardiac patients. Psychosom Med 2004 Mar;66(2):190-7.

(20) Philips Bute B, Mathew J, Blumenthal JA, et al. Female gender is associated with impaired quality of life 1 years after coronary artery bypass surgery. Psychosomatic medicine 2003;65:944-51.

(21) Pragodpol P, Ryan C. Critical Review of Factors Predicting Health-Related Quality of Life in Newly Diagnosed Coronary Artery Disease Patients. J Cardiovasc Nurs 2012 Apr 9.

(22) Schweikert B, Hahmann H, Leidl R. Validation of the EuroQol questionnaire in cardiac rehabilitation. Heart 2006 Jan;92(1):62-7.

(23) Franco OH, Wong YL, Kandala NB, et al. Cross-cultural comparison of correlates of quality of life and health status: the Whitehall II Study (UK) and the Western New York Health Study (US). Eur J Epidemiol 2012 Apr;27(4):255-65.

(24) Lee DT, Choi KC, Chair SY, Yu DS, Lau ST. Psychological distress mediates the effects of socio-demographic and clinical characteristics on the physical health component of health-related quality of life in patients with coronary heart disease. Eur J Prev Cardiol 2012 Jun 7.

(25) Peterson PN, Spertus JA, Magid DJ, et al. The impact of diabetes on one-year health status outcomes following acute coronary syndromes. BMC Cardiovasc Disord 2006;6:41.

(26) Kim J, Henderson RA, Pocock SJ, Clayton T, Sculpher MJ, Fox KA. Health-related quality of life after interventional or conservative strategy in patients with unstable angina or non-ST-segment elevation myocardial infarction: one-year results of the third Randomized Intervention Trial of unstable Angina (RITA-3). J Am Coll Cardiol 2005 Jan 18;45(2):221-8.

(27) Lukkarinen H, Hentinen M. Treatments of coronary artery disease improve quality of life in the long term. Nurs Res 2006 Jan;55(1):26-33.

(28) Sevinc S, Akyol AD. Cardiac risk factors and quality of life in patients with coronary artery disease. J Clin Nurs 2010 May;19(9-10):1315-25.

(29) Weintraub WS, Spertus JA, Kolm P, et al. Effect of PCI on quality of life in patients with stable coronary disease. N Engl J Med 2008 Aug 14;359(7):677-87.

(30) Leach MJ, Gall SL, Dewey HM, Macdonell RA, Thrift AG. Factors associated with quality of life in 7-year survivors of stroke. J Neurol Neurosurg Psychiatry 2011 Dec;82(12):1365-71.

(31) Paul SL, Sturm JW, Dewey HM, Donnan GA, Macdonell RA, Thrift AG. Long-term outcome in the North East Melbourne Stroke Incidence Study: predictors of quality of life at 5 years after stroke. Stroke 2005 Oct;36(10):2082-6.

(32) Saarni SI, Harkanen T, Sintonen H, et al. The impact of 29 chronic conditions on health-related quality of life: a general population survey in Finland using 15D and EQ-5D. Qual Life Res 2006 Oct;15(8):1403-14.

(33) Schwander B, Gradl B, Zollner Y, et al. Cost-utility analysis of eprosartan compared to enalapril in primary prevention and nitrendipine in secondary prevention in Europe--the HEALTH model. Value Health 2009 Sep;12(6):857-71.

(34) Jarvinen O, Julkunen J, Tarkka MR. Impact of obesity on outcome and changes in quality of life after coronary artery bypass grafting. World J Surg 2007 Feb;31(2):318-25.

(35) Oreopoulos A, Padwal R, McAlister FA, et al. Association between obesity and health-related quality of life in patients with coronary artery disease. Int J Obes (Lond) 2010 Sep;34(9):1434-41.

(36) Haddock CK, Poston WS, Taylor JE, Conard M, Spertus J. Smoking and health outcomes after percutaneous coronary intervention. Am Heart J 2003 Apr;145(4):652-7.

(37) Taira DA, Seto TB, Ho KK, K et al. Impact of smoking on health-related quality of life after percutaneous coronary revascularization. Circulation 2000 Sep 19;102(12):1369-74.

(38) Hoogwegt MT, Hoeks SE, Pedersen SS, et al. Smoking cessation has no influence on quality of life in patients with peripheral arterial disease 5 years post-vascular surgery. Eur J Vasc Endovasc Surg 2010 Sep;40(3):355-62.

(39) Quist-Paulsen P, Bakke PS, Gallefoss F. Does smoking cessation improve quality of life in patients with coronary heart disease? Scand Cardiovasc J 2006 Feb;40(1):11-6.

(40) Wiggers LC, Oort FJ, Peters RJ, Legemate DA, de Haes HC, Smets EM. Smoking cessation may not improve quality of life in atherosclerotic patients. Nicotine Tob Res 2006 Aug;8(4):581-9.

(41) Perk J, De BG, 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 May 3.

(42) Herlitz J, Brandrup-Wognsen G, Caidahl K, et al. Determinants for an impaired quality of life 10 years after coronary artery bypass surgery. Int J Cardiol 2005 Feb 28;98(3):447-52.

(43) Carvalho MA, Silva IB, Ramos SB, Coelho LF, Goncalves ID, Figueiredo Neto JA. Quality of life of hypertensive patients and comparison of two instruments of HRQOL measure. Arq Bras Cardiol 2012 Apr 5;0.

(44) Soini EJ, Davies G, Martikainen JA, Hu HX, Tunceli K, Niskanen L. Population-based health-economic evaluation of the secondary prevention of coronary heart disease in Finland. Curr Med Res Opin 2010 Jan;26(1):25-36.

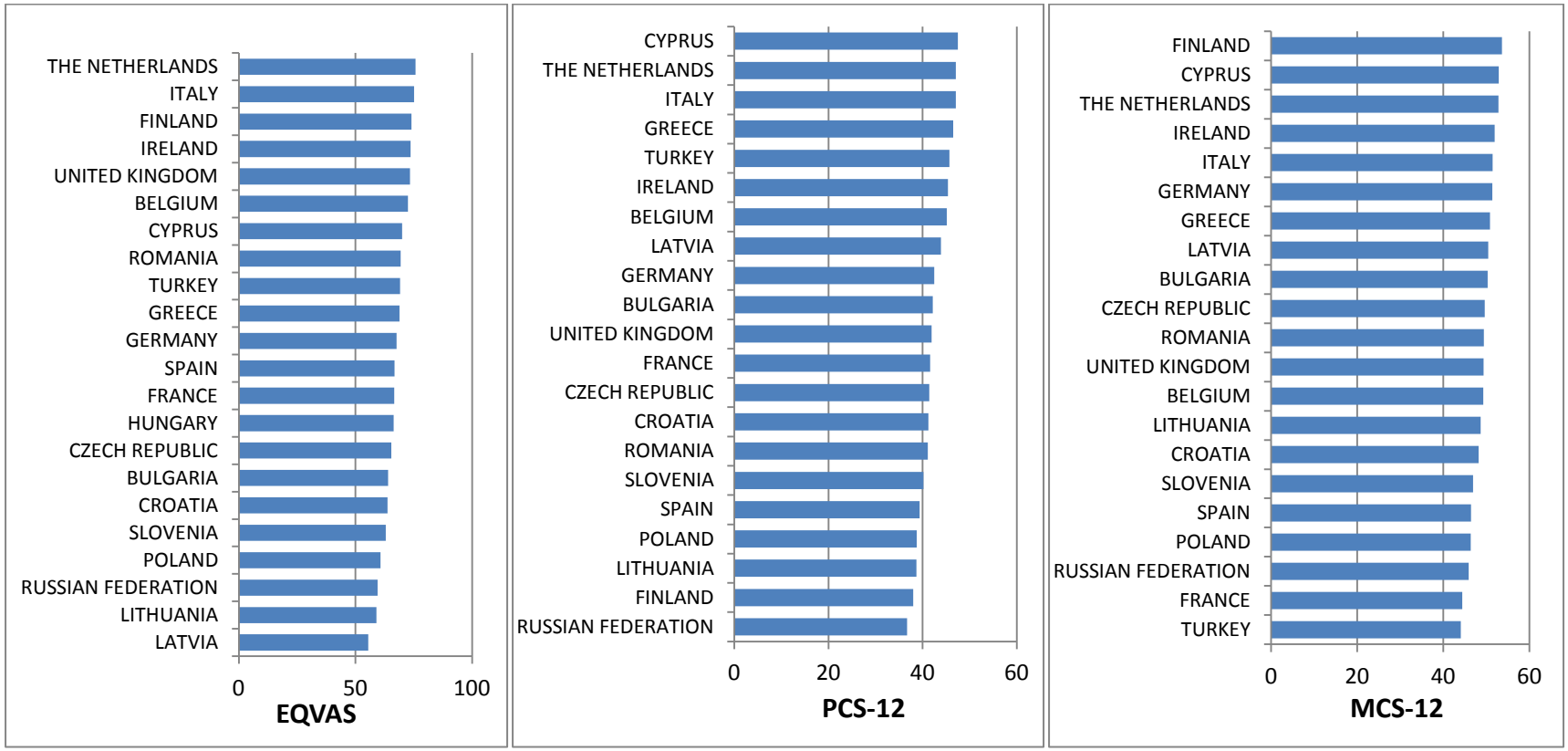
(45) Khanna A, Bush AL, Swint JM, Peskin MF, Street RL, Naik AD. Hemoglobin A1c improvements and better diabetesspecific quality of life among participants completing diabetes self-management programs: A nested cohort study. Health Qual Life Outcomes 2012 May 14;10(1):48.

(46) Lau CY, Qureshi AK, Scott SG. Association between glycaemic control and quality of life in diabetes mellitus. J Postgrad Med 2004 Jul;50(3):189-93.

(47) Li C, Ford ES, Mokdad AH, Balluz LS, Brown DW, Giles WH. Clustering of cardiovascular disease risk factors and health-related quality of life among US adults. Value Health 2008 Jul;11(4):689-99.

Table 1: Patient characteristics at the time of the interview (n=8734)			
	Men (n=6516)	Women (n=2218)	All (n=8734)
Age in years, Mean (SD)	62.3(9.5)	65.9(8.9)	63.2(9.5)
Age categories			
<50 years	10.6%(688/6516)	5.0%(112/2218)	9.2%(800/8734)
50-59 years	29.5%(1924/6516)	19.9%(442/2218)	27.1%(2366/8734)
60-69 years	37.4%(2440/6516)	40.1%(890/2218)	38.1%(3330/8734)
≥70 years	22.5%(1464/6516)	34.9%(774/2218)	25.6%(2238/8734)
Recruiting Diagnosis			
CABG	20.5%(1339/6516)	17.1%(379/2218)	19.7%(1718/8734)
PTCA	43.1%(2806/6516)	35.3%(782/2218)	41.1%(3588/8734)
AMI	19.2%(1248/6516)	20.7%(459/2218)	19.5%(1707/8734)
Ischaemia	17.2%(1123/6516)	27.0%(598/2218)	19.7%(1721/8734)
Education			
Primary education	22.5%(1456/6480)	33.4%(737/2207)	25.2%(2193/8687)
Secondary education	57.3%(3714/6480)	54.9%(1211/2207)	56.7%(4925/8687)
High education	20.2%(1310/6480)	11.7%(259/2207)	18.1%(1569/8687)
Diabetes	22.6%(1459/6454)	29.8%(657/2203)	24.4%(2116/8657)
Raised fasting glucose	90.7%(943/1040)	87.4%(396/453)	89.7%(1339/1493)
Raised HbA1c	60.9%(592/972)	73.8%(321/435)	64.9%(913/1407)
History of stroke	4.1%(268/6500)	5.7%(127/2212)	4.53%(395/8712)
Recurrent CHD after recruiting diagnosis	14.1%(912/6483)	11.4%(251/2204)	13.4%(1163/8687)
Central obesity	45.7%(2940/6433)	73.4%(1609/2193)	52.7%(4549/8626)
Current smoker	19.0%(1234/6500)	10.9%(242/2214)	16.9%(1476/8714)
Low physical activity	63.9%(3880/6073)	72.8%(1483/2038)	66.1%(5363/8111)
Raised total cholesterol	47.7%(2936/6155)	62.0%(1309/2111)	51.4%(4245/8266)
On lipid lowering medication (LLM)	80.3%(5210/6487)	77.9%(1718/2205)	79.7%(6928/8692)
Raised total cholesterol in treated patients	41.4%(2035/4912)	56.8%(929/1637)	45.3%(2964/6549)
Raised LDL-cholesterol	52.6%(2511/4770)	61.3%(980/1598)	54.8%(3491/6368)
Raised LDL-cholesterol in patients on LLM	46.5%(1797/3865)	55.0%(697/1267)	48.6%(2494/5132)
Raised Blood pressure	54.5%(3544/6503)	60.8%(1347/2215)	56.1%(4891/8718)
On antihypertensive medication	67.1%(4350/6481)	80.3%(1778/2215)	70.5%(6128/8696)
Raised Blood Pressure in medically patients	61.4%(2665/4341)	66.3%(1176/1775)	62.8%(3841/6116)

Figure 1: Crude mean HRQoL outcomes across EUROASPIRE III countries



* Adjusted for age, gender, educational level, recruiting diagnosis, diabetes, history of stroke and recurring events ($p<0.001$)

Table 2: Association between patient characteristics and different HRQoL instruments (Mean (SD))

	PCS-12	MCS-12	EQ-VAS
All	42.14(10.15)	49.15(10.22)	66.42(18.84)
Gender			
Male	43.20(10.02)	49.93(9.96)	67.85(18.59)
Female	38.82(9.84)	46.75(10.64)	62.22(18.94)
	p<0.001*	p<0.001	p<0.001
Age			
< 50 yrs	45.59(9.96)	48.84(10.51)	71.43(18.18)
50-59 yrs	43.31(10.10)	48.94(10.22)	67.48(18.73)
60-69 yrs	42.16(9.99)	49.57(10.19)	66.72(18.66)
≥ 70 yrs	39.56(9.89)	48.90(10.13)	63.03(18.90)
	p<0.001	p=0.034	p<0.001
Recruiting diagnosis			
CABG	42.53(10.03)	50.23(9.88)	66.85(19.43)
PTCA	43.03(10.06)	49.27(10.18)	67.92(18.50)
AMI	41.83(10.13)	48.58(10.24)	65.64(18.56)
ISCHAEMIA	40.04(10.18)	48.47(10.53)	63.63(18.88)
	p<0.001	p=0.214	p=0.011
Educational level			
Primary	40.95(10.36)	47.98(10.89)	64.87(20.00)
Secondary	41.95(10.04)	49.27(10.08)	66.44(18.55)
High	44.28(9.88)	50.44(9.53)	68.32(18.00)
	p<0.001	p<0.001	p<0.001
Diabetes			
No	42.94(9.97)	49.48(10.03)	67.34(18.57)
Yes	39.46(10.27)	48.10(10.76)	63.50(19.43)
	p<0.001	p<0.001	p<0.001
Central Obesity			
No	43.53(9.98)	49.67(9.96)	68.33(18.45)
Yes	40.87(10.11)	48.73(10.44)	64.76(18.99)
	p<0.001	p=0.246	p<0.001
Smoking			
No	42.04(10.14)	49.37(10.00)	66.56(18.71)
Yes	42.64(10.17)	48.06(11.18)	65.71(19.40)
	p=0.004	p<0.001	p<0.001
Physical activity			
<20min, 3x/week	40.79(10.19)	48.69(10.39)	64.39(19.12)
≥20 min, 3x/week	45.52(9.28)	50.54(9.58)	71.08(17.22)
	p<0.001	p<0.001	p<0.001
History of stroke			
No	42.39(10.08)	49.24(10.16)	66.80(18.77)
Yes	36.92(10.42)	47.17(11.30)	58.43(18.83)
	p<0.001	p=0.001	p<0.001
Recurring coronary event after IE			
No	42.34(10.13)	49.26(10.15)	66.76(18.85)
Yes	40.90(10.19)	48.47(10.59)	64.25(18.64)
	p<0.001	p=0.109	p<0.001

*p-value adjusted for age, gender, educational level

Table 3: Results of multilevel linear regression analyses for the association between patient characteristics and HRQOL

	PCS-12		MCS-12		EQ-VAS	
PATIENT CHARACTERISTICS	***β (SE)****	***p-value***	***β (SE)****	***p-value***	***β (SE)****	***p-value***
Intercept	56.709(1.033)	<0.001	50.347(1.016)	<0.001	84.60(1.88)	<0.001
Age	-0.153(0.012)	<0.001	0.011(0.013)	0.407	-0.183(0.023)	<0.001
Gender						
Male	Reference		Reference		Reference	
Female	-2.154(0.267)	<0.001	-2.749(0.289)	<0.001	-2.878(0.499)	<0.001
Educational level						
Primary education	-0.971(0.293)	0.001	-0.570(0.315)	0.071	-2.046(0.549)	<0.001
Secondary education	Reference		Reference		Reference	
High education	2.231(0.296)	<0.001	1.144(0.320)	<0.001	2.635(0.558)	<0.001
Recruiting diagnosis						
CABG	0.518(0.305)	0.090	0.604(0.329)	0.067	0.999(0.574)	0.082
PTCA	Reference		Reference		Reference	
AMI	0.115(0.315)	0.714	0.681(0.339)	0.045	1.677(0.606)	0.006
Ischaemia	-1.588(0.337)	<0.001	0.282(0.363)	0.436	-0.210(0.629)	0.739
Diabetes						
No	Reference		Reference		Reference	
Yes	-2.535(0.261)	<0.001	-1.160(0.281)	<0.001	-2.911(0.486)	<0.001
History of stroke						
No	Reference		Reference		Reference	
Yes	-3.591(0.520)	<0.001	-1.456(0.561)	0.009	-5.426(0.979)	<0.001
Recurrent coronary event after recruiting diagnosis						
No	Reference		Reference		Reference	
Yes	-1.688(0.319)	<0.001	-0.580(0.344)	0.093	-2.251(0.604)	<0.001
Smoking						
No	Reference		Reference		Reference	
Yes	-0.917(0.301)	0.002	-1.622(0.325)	<0.001	-2.062(0.570)	<0.001
Physical activity						
≥20 min, 3x/week	Reference		Reference		Reference	
<20min, 3x/week	-3.094(0.243)	<0.001	-1.121(0.262)	<0.001	-4.384(0.456)	<0.001
Central obesity						
No	Reference		Reference		Reference	
Yes	-1.528(0.228)	<0.001	0.042(0.246)	0.865	-1.887(0.432)	<0.001

*β (SE) = regression coefficient (standard error)

Table 4: Association between uncontrolled cardiovascular risk factors different HRQoL instruments (mean (SE))			
	PCS-12	MCS-12	EQ-VAS
Raised blood pressure in treated patients			
No	38.24(0.80)*	47.04(0.73)	62.17(1.38)
Yes	39.28(0.78)	47.65(0.71)	63.01(1.35)
	p<0.001**	p=0.040	p=0.099
Raised total cholesterol in treated patients			
No	39.35(0.79)	47.90(0.71)	63.84(1.42)
Yes	39.11(0.79)	47.22(0.72)	62.96(1.43)
	p=0.329	p=0.011	p=0.056
Raised LDL-cholesterol in treated patients			
No	39.40(0.84)	47.30(0.74)	63.08(1.50)
Yes	39.43(0.84)	46.82(0.74)	62.65(1.50)
	p=0.909	p=0.104	p=0.408
Raised fasting glucose in diabetes patients			
No	37.75(1.33)	44.50(1.26)	58.43(2.34)
Yes	37.58(1.10)	45.05(0.95)	58.83(1.84)
	p=0.839	p=0.559	p=0.809
Raised HbA1c in diabetes patients			
No	39.01(1.18)	47.43(1.17)	61.90(2.04)
Yes	37.55(1.13)	45.62(1.10)	59.15(1.92)
	p=0.013	p=0.006	p=0.013

*adjusted mean

**p-value adjusted for age, gender, educational level, recruiting diagnosis, diabetes, history of stroke and coronary recurring events

Table 5: HRQoL means (SD) in relation to the number of risk factors			
Number of risk factors	PCS-12	MCS-12	EQVAS
0	46.11(9.76)	50.80(9.22)	72.85(17.23)
1	44.38(9.79)	50.01(9.62)	70.25(18.07)
2	42.15(10.16)	49.49(10.16)	66.68(18.44)
3	41.27(10.07)	48.62(10.33)	64.82(18.90)
4	39.73(9.88)	47.98(10.76)	61.99(19.64)
5	38.21(9.73)	46.85(12.37)	60.47(18.06)
p-value	<0.001*	0.023	<0.001

*p-value adjusted for age, gender, educational level, recruiting diagnosis, diabetes, history of stroke and recurring coronary events

Risk factors included are: raised blood pressure, raised total cholesterol, current smoking, low physical activity and central obesity