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EUROASPIRE IV: Educational level and risk factor control in patients with coronary heart disease

A report from the European Society of Cardiology survey in 24 countries in Europe

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Objective To ascertain in which way conventional risk factors, readiness to modify behaviour and to comply with recommended medication, and the effect of this medication were associated with education in patients with established coronary heart disease (CHD).

Methods The EUROASPIRE IV (EUROpean Action on Secondary Prevention by Intervention to Reduce Events) study was a cross-sectional survey undertaken in 24 European countries to ascertain how recommendations on secondary CHD prevention are being followed in clinical practice. Consecutive patients, men and women ≤80 years of age who had been hospitalized for an acute coronary syndrome or revascularization procedures, were identified retrospectively. Data were collected through an interview with examinations at least six months after hospitalization.

Results A total of 7937 patients (1934 women) were evaluated. Patients with primary education were older, with a larger proportion of women. The control of risk factors, as defined by JES 4 and JES 5 guidelines, was significantly better with higher education for current smoking (p=0.001), overweight and obesity (p=0.047 and p=0.029 respectively), low physical activity (p<0.001) and low HDL-cholesterol (p=0.011) in men, and for obesity (p=0.005), high blood pressure (p<001), low physical activity (p=0.001), diabetes (p<0.001) and low HDL-cholesterol (p=0.023) in women. Taking high education as reference, a significantly higher risk was observed in men for overweight, smoking, low HDL and low physical activity, and in women for overweight, obesity, diabetes, high blood pressure, low HDL and low physical activity. Patiens with primary and secondary education were more often treated with diuretic and antidiabetic drugs, other significant differences in drug use were not found.

Conclusions: Particular risk communication and control are needed in secondary CHD prevention for patients with lower educational status.

Keywords: educational level and CHD risk factors, educational level and risk factors control, coronary heart disease, secondary prevention, EUROASPIRE IV study

Summary: Our study, performed in 2012-2013, found the differences in cardiovascular risk factors prevalence and control according to educational level, most pronounced in women and in risk factors obesity and diabetes. Compared to previous studies, the differences in cardiovascular risk factors prevalence and control according to educational level remained relatively stable. This study indicates the need to pay special attention to coronary patients with low education, possibly with obesity and diabetes control as a major target.

INTRODUCTION

Socioeconomic status (SES) is an accepted and important factor influencing cardiovascular and coronary heart disease (CHD) morbidity and mortality.[1-4] Socioeconomic status is a complex phenomenon composed by many variables, with education, income and occupation being the the most important measures.[5] Higher education enables access to better social, professional, economic, cultural, and psychological position and helps to reach a higher SES. Over time, also due to difficulties in obtaining and comparing some other socioeconomic characteristics (e.g. income, property, job position in due time), education has become the most commonly used measure of SES in epidemiological studies. In developed countries, these studies have consistently shown an inverse relation between education and lifestyle-related risk factors as well as between education and the risk of cardiovascular and CHD disease and mortality.[5-14] Among various SES measures, a low level of education was most consistently related to CHD risk factors and CHD morbidity and mortality.[5 6 12]

The short- and long- term mortality after an acute myocardial infarction (AMI) and the risk of reinfarction increases with lower SES and education.[13 14] Secondary prevention of CHD is of paramount importance,[15 16] yet the relation between educational level and coronary risk factors control and secondary medical prevention after acute coronary syndromes and coronary revascularization procedures has been studied only occasionally.[17-19] An analysis based on the EUROASPIRE II (1999-

2000) study (EUROpean Action on Secondary Prevention by Intervention to Reduce Events) found lower global coronary risk in patients with higher education, but virtually the same effectiveness of treatment in all educational groups.[17] Other studies investigating drug use in secondary prevention found no major differences in drug use according to education levels.[18 19] The recent EUROASPIRE IV survey, carried out in 2012-2013 in 24 European countries allows to assess the extent to which educational status is actually associated with lifestyle factors, implementation of recommended lifestyle changes and pharmacotherapies, as recommended by the recent European guidelines on secondary CHD prevention.[20 21] It also offers an unique opportunity to compare the recent EUROASPIRE IV data with the EUROASPIRE II results and to find whether the social differences as defined by educational status are getting more or less pronounced in patiens with established CHD.

METHODS

Sample selection and data collection

The design and protocol of the EUROASPIRE surveys are described in detail elsewhere.[22-25] The cross sectional EUROASPIRE IV study was conducted between May 2012 and April 2013 in the following 24 European countries: Belgium, Bulgaria, Bosnia and Hercegovina, Croatia, Cyprus, the Czech Republic, Finland, France, Germany, Greece, Ireland, Latvia, Lithuania, the Netherlands, Poland, Romania, Russia, Serbia, Slovenia, Spain, Sweden, Turkey, Ukraine, and the United Kingdom. Within each country, one or more geographical areas with a defined population (at least half a million people) were selected. Each area included at least one hospital offering interventional cardiology and cardiac surgery, and one or more hospitals admitting patients with AMI and coronary ischaemia. One or more hospitals in such an area were included into the study, so that any patient presenting within the area with acute symptoms of coronary disease, or requiring revascularization, had an approximately equal chance of being included.

Consecutive patients, men and women $\leq$ 80 years of age at the time of their index event or procedure, with the following first or recurrent diagnoses or treatment for CHD were retrospectively identified from registers, hospital records, and discharge lists or other sources: (i) elective or emergency coronary artery bypass grafting

(CABG), (ii) elective or emergency percutaneous intervention (PCI), (iii) acute myocardial infarction, STEMI or non-STEMI (AMI: ICD-10 I21, I22), and (iv) acute myocardial ischaemia (ischaemia).

The study interview and examination took place at least 6 months and no more than 3 years after the index event. In each country, the objective was to identify a sufficient number of coronary patients in order to obtain prospective interview data on 400 living patiens.

Patient interview and examination.

The survey was performed in compliance with the standard EUROASPIRE IV study protocol. At interview, the respondents were asked about their history including their personal and demographic characteristics, personal and family history of cardiovascular disease, data on adherence to principles of a healthy lifestyle, and pharmacotherapy. The number of years spent at school and the highest education degree obtained were also recorded. Standardized measurements were made as per protocol using calibrated devices, blood samples were obtained, and the patients completed questionnaires.

a) Body weight was measured in light-fabric attire without footwear (SECA 701 scales, SECA GmbH, Hamburg, Germany) with an accuracy of 0.1 kg, body height using a stadiometer (SECA model 220) with an accuracy of 0.5 cm. Waist circumference was measured using a metal tape measure at mid-distance between the spina iliaca anterior and the lower edge of the ribcage.
b) Blood pressure (BP) was measured by a physician twice after at least 10-minute rest in the sitting position on the right arm using an automated digital Omron M6 sphygmomanometer (Omron, Healthcare Ltd, Milton Keynes, UK). In cases where the difference between the first and second measurements was greater than 10 mmHg, BP was measured twice again. As the final value the mean of the first or last two measurements was calculated.
c) Carbon monoxide levels in expired air were measured in ppm using a smokerlyser device (Micro +, Bedfont Scientific, Upchurch, United Kingdom). Smoking at the time of interview was defined as smoking self-reported by the patient and/or breath CO levels > 10 ppm.
d) Blood samples were obtained by venipuncture after at least 12-hour fasting. The

serum separated from venous blood samples was stored at -70°C to be subsequently shipped (frozen) to the central laboratory at the Disease Risk Unit, National Institute for Health and Welfare, Helsinki, Finland. The central laboratory performed analyses using a clinical chemical analyzer (Architect c8000, Abbott Laboratories, Abbott Park, Illinois, USA). Total cholesterol (TC) was determined enzymatically, HDL-cholesterol (HDL-C), and triglycerides (TG) using kits manufactured by Abbott Laboratories (USA), LDL-cholesterol (LDL-C) levels were calculated using a modified Friedewald method (i.e., TC – HDL-C – TG/2.2). Venous blood glucose was determined by a photometric point-of-care technique (Glucose 201, Hemocue^{R}, Ängelholm, Sweden, with a coefficient of variation of 2.8%). The definition of diabetes was self-reported diabetes at interview based on a history of diabetes diagnosed by a physician. In those without a history of diabetes, fasting plasma glucose levels $\geq$ 7.0 mmol/L were defined as new-onset diabetes. The Helsinki-based laboratory participates in the Lipid Standardization Program run by the Centers for Disease Control and Prevention (CDC), Atlanta, USA, and the Program of External Quality Assessment run by Labquality, Helsinki, Finland.

e) Venous blood glucose was determined by photometry (Glucose 201, Hemocue^{R}, Ängelholm, Sweden). Diabetic patients were defined as those reporting diabetes diagnosed previously by a physician whereas new-onset diabetes was defined as fasting glucose levels $\geq$ 7.0 mmol/l not previously detected in their personal history.

f) Standardized IPAQ (International Physical Activity Questionnaire) (26) was completed for each patient to quantify the level of physical activity.

Data management and statistical analyses

Data excerpted from the medical records of patients and those obtained during interview were entered into electronic Case Report Forms (CRFs), which were forwarded to the data processing center (Euro Heart Survey Department, European Heart House, Nice, France), checked for completeness, internal consistency, and accuracy to be subsequently processed.

Patients were divided into three educational groups: primary education defined as primary school or less, secondary education characterized as secondary school level, and high education defined as university/college levels or equivalent. The number of years spent in full time education for educational level reached varied among participating countries. The median was 8 years (IQR=6-10 years) for primary, 12 years (IQR=11-13 years) for secondary and 16 years (IQR=15-18 years) for high education.

Risk factors control targets not reached were categorized according to 2007 and 2012 European guidelines on cardiovascular disease prevention in clinical practice (JES 4 and JES 5)[20 21] as follows: overweight = BMI ≥ 25kg/m², obesity = BMI ≥ 30kg/m²; smoking = self-reported smoking or CO in breath > 10 ppm; diabetes = self-reported diabetes; high blood pressure = systolic blood pressure ≥ 130 mmHg and/or diastolic blood pressure ≥ 80 mmHg (JES4) and systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg (140/80 mmHg in patients with diabetes) (JES5); high total cholesterol = TC ≥ 4.5 mmol/l (JES4); high LDL-cholesterol = LDL-cholesterol ≥ 2.5 mmol/L (JES4) and LDL-cholesterol ≥ 1.8 mmol/L (JES5); low HDL cholesterol = HDL-C < 1mmol/L in men and < 1.2 mmol/L in women; low physical activity = lowest level of physical activity according to IPAQ.

All statistical analyses were undertaken using SAS statistical software in the Department of Public Health, Ghent University, Belgium. Analyses were based on generalized linear mixed models in order to account for the clustering of patients within countries. All analyses were adjusted for age and gender. The analyses on cardiovascular risk factors by educational level (table 4) were additionally adjusted for diagnosis and BMI. From the logistic models, adjusted odds ratio (OR) and 95% confidence intervals (CI) were calculated.

Ethical issues

The study was performed in conformity with the principles of Good Clinical Practice; the study protocol was approved by the respective local ethics committees, and all participants signed their informed consent forms. Data were stored in accordance with the applicable regulations.

RESULTS

Sample structure

After reviewing N=16426 hospitalization medical records, a total of N=7998 patients (48.7%) were interviewed, of whom N=7937 provided valid data on educational level. Mean time between the index event (i.e., acute coronary event and/or revascularization) and the interview was 1.35 years.

Distribution of educational levels by gender and age is presented in Table 1. The proportion of primary, secondary, and high educational level in the whole sample was 17.45%, 60.25%, and 22.3%, respectively. This proportion varied across different countries. The proportion of primary education was higher in females and in patients over 60 years and lower in patients who underwent an interventional procedure (PCI or CABG).

Risk profile and risk factors control

The distribution of quantitative risk factors by educational level and gender is given in Table 2. Men and women with primary education were older than those with secondary and high education. In women educational level was inversely associated with an increase in BMI, waist circumference, systolic and diastolic blood pressure, fasting triglycerides, and fasting glucose. No such consistent trend was found in men. A positive trend with education was found concerning HDL-C in both genders.
The control of risk factors, as defined by JES 4 and JES 5 guidelines, is shown in Table 3. In men, worse control of overweight and obesity, smoking, low HDL-C and low physical activity were associated with lower educational levels. In women, worse control of obesity, diabetes, high blood pressure, low HDL-C and low physical activity were significantly associated with lower educational levels.
Adjusted odds ratios and 95% confidence intervals for the association between education and categorical risk factors are given in Table 4. Taking high education as reference, the lower educational levels (secondary and primary education) increased the relative risk of all factors. In men a significantly increased risk was observed for overweight (OR 1.22 and 1.29 for secondary and primary education respectively), obesity (OR 1.20 for secondary education), smoking (OR 1.30 and 1.55 for secondary and primary education respectively), diabetes (OR 1.18 for secondary education), low HDL-CH (OR 1.33 for primary education) and low physical activity (OR 1.72 for primary education). In women a significantly higher risk was observed for overweight (OR 1.50 for primary education), obesity (OR 1.74 for primary

education), diabetes (OR 1.53 and 2.22, for secondary and primary education), high blood pressure (OR 1.36 and 2.06, for secondary and primary education, for JES 5 and OR 1,45 and 1.76 for secondary and primary education for JES 4, respectively), low HDL-CH (OR 1.6 for primary education) and low physical activity (OR 1.88 and 2.75 for secondary and primary education).

Drugs used for secondary prevention

Use of secondary preventive medication according to educational level is presented in Table 5. No major differences in drug use were found, only patients with primary and secondary education were more often treated with diuretics and antidiabetic drugs.

Proportion of patients who reached target values for blood pressure, total cholesterol and HbA1c are shown in Table 6. Blood pressure targets were reached more often with higher educational level, total cholesterol targets were reached non significantly more often with lower educational level. No differences were observed in terms of diabetes control.

Comparison with the EUROASPIRE II Study

Compared to the previous EUROASPIRE II report (1999-2000),[17] the differences in cardiovascular risk factors prevalence and control according to educational level remained relatively stable. The differences in risk factors control according to education decreased in men and increased in women, and the treatment modalities became more equal across the educational levels.

DISCUSSION

Education as the most used, reliable and stable measure of SES is known to be related not only to general and cardiovascular, but also to acute and chronic CHD morbidity and mortality. This relation is inverse in developed countries, persons with low education are at greater risk.[1-4 6 9-14] There are considerable differences in this relation between men and women, older and younger patients, and between various countries. In former communist countries, where social differences were not so much pronounced, education is the most discriminating social factor in CHD morbidity and mortality.[27] The differences are attributed mainly to variations of CHD risk, but also to confounding factors.

It is well established that persons with low SES and education have a higher prevalence of overweight and obesity, smoking, diabetes, high blood pressure, and hyperlipidaemia. This has been consistently found in epidemiological as well as clinical studies in both genders, in most age groups, and virtually in all European countries.[5-8 10 17 28-31] It has also been shown that the knowledge about cardiovascular risk factors is positively associated with higher educational level and vice versa.[32] As cardiovascular risk factors, according to some studies, may explain most differences in CHD morbidity and mortality between different social groups, control of these factors, either by lifestyle modification or through medical drug treatments, is essential, especially in secondary CHD prevention.

Compliance with recommendations on life-style changes in patients with established CHD remains low[25] and is inversely related to social and educational status.[16 17] Hospital stay for acute coronary events such as AMI became very short now. Substantially less time is left for guiding the patient and educating on secondary prevention measures during the hospitalization. Recommendations and further follow-up are too often restricted only to drug prescription. This might be particularly significant for patiens with a low educational level. When health care is well accessible and costs of drug treatments are entirely, or for the most part, covered by the obligatory health insurance, as common in European countries (no major-out-of-pocket payments), then use of recommended drugs must not be socially graded. Still, compliance with treatment may vary due to other sociopsychological factors.

The EUROASPIRE I-IV studies have shown a high prevalence of modifiable lifestyle-related risk factors like smoking and obesity, and biomedical factors like hypertension, hyperlipidaemia, and diabetes in patients with established coronary heart disease. These studies also presented data on adherence to lifestyle changes and implementation of drug treatments. Basically, from 1995-1996 to 2012-2013, a major decrease in high blood pressure and high total and LDL-C, a substantial increase in obesity and diabetes prevalence, and a remarkable increase in the use of cardioprotective medications were documented. The unhealthy lifestyle behaviours of these patients did not improve and even deteriorated in some aspects. Use of cardioprotective medication increased, but remained only partly effective.[22-25]

Our study shows that the level of education in patients with established CHD who need secondary prevention is negatively associated with most risk factors, and that these associations, except for smoking, are more significant in women than in men. Worse control of most risk factors, as defined by JES 4 and JES 5 guidelines, was found in persons with lower education. On the other hand, most cardioprotective drugs were used in our patients fairly equally across the educational spectrum and the effectiveness of such treatment did not differ substantially.

Based on our results, we have to stress a discriminative role of education in CVD risk factors control in women and only partly in men. As patients with lower education have higher CHD morbidity and mortality, especially of acute CHD forms (e.g. reinfarctions), one would expect that patients with primary education will be in greater need of treatments. But we found fairly similar treatment in all educational strata. This could mean, that the patients with primary education are actually undertreated.

Because the median of years spent at school in different countries considerably varied and overlapped, we divided the sample by educational level reached into primary, secondary, and high school categories. The number of years spent at study and highest educational level reached were included into the patients interview questionnaire. The reported educational level reached is probably a better proxy for individual SES than the number of years spent at school, because the achieved higher educational level generally results in a better working position, higher income, and a higher social status. We preferred educational status to income or working position, which are affected by large economical differences among participating countries, are less reliably specified and fluctuate considerably during the life. Since older patients (65-80 years) were also involved in the study, a considerable part of them was already retired. Educational status as a proxy for SES has the advantage of being an exact, reliable, and in middle and older, fixed measure.

The strengths of this study are the wide scope of European countries virtually covering the whole continent and its strict protocol, which allows international and longitudinal comparisons.

The study has also several limitations. We are reporting on a sample of European coronary patients, who have survived their index event for at least six months and have attended the interview. Unlike PCI, CABG and AMI (STEMI and non-STEMI), the term acute myocardial ischaemia remained poorly validated as clinical and ECG signs of myocardial ischaemia in the absence of myocardial necrosis and mostly relied on physicians´ judgment in discharge summary. All other data presented in this study were obtained at interview.

Observed differences in risk factors and treatment are not representative for the entire populations of participating countries, because patients were recruited mainly from tertiary cardiac centers and university hospitals. The implementation of secondary preventive measures may be therefore overestimated, compared to the country-wide situation. Conversely, the inclusion of minor hospitals without interventional facilities could make the differences between educational groups even more pronounced. In general, the regional differences in coronary care in European countries with developed systems of acute coronary care (transportation to direct PCI, etc.) and advanced revascularization programs, diminish.[33]

The educational systems in European countries vary. Classifying patients into primary, secondary, and high education still does not exclude overlaps between primary and secondary, as well as between secondary and high education.

Based only on patients´ reports at interview, the data on use of secondary preventive medications may be overestimated and could further explain the limited effectiveness of treatments. The same may apply to data on compliance with lifestyle changes such as diet or physical activities.

The comparison with the EUROASPIRE II has considerable limitations due to different countries involved and different control tarets pusued.

CONCLUSIONS

The EUROASPIRE I–IV data have shown that evidence based secondary preventive measures in coronary patients remain underused in Europe. In our study, patients with lower education were at a higher global cardiovascular risk than those with higher education. The differences were more pronounced in women. The major differences were found in risk factors obesity and diabetes, which appear to be interrelated. The medical treatments are fairly similar but are only partly efficient in all educational strata. When compared to the EUROASPIRE II Education Substudy (1999-2000), our study has found only modest changes. This study indicates the need to pay special attention to coronary patients with low education, possibly with obesity and diabetes control as a major target.

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Competing interest: [to be added]

Authors' contribution [to be added]

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