Time trends in lifestyle, risk factor control and use of evidence-based medications in patients with coronary heart disease in Europe: results from three EUROASPIRE surveys, 1999 – 2013, of the European Society of Cardiology

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Brief title: Time trends in risk factor management in CHD patients

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Abstract

Background The EUROASPIRE cross-sectional surveys describe time trends in lifestyle and risk factor control among coronary patients between 1999 and 2013 in Belgium, Czech Republic, Finland, France, Ireland, The Netherlands, Poland, Slovenia and the United Kingdom as part of the EuroObservational Research Programme under the auspices of European Society of Cardiology.

Objectives To describe time trends in lifestyle, risk factor control and the use of evidence-based medication in coronary patients across Europe.

Methods The EUROASPIRE II (1999-2000), III (2006-2007) and IV (2012-13) surveys were conducted in the same geographical areas and selected hospitals in each country. Consecutive patients (≤70 years) after CABG, PCI or an acute coronary syndrome identified from hospital records were interviewed and examined ≥6 months later with standardized methods.

Results Of 12,775 identified coronary patients 8456 (66.2%) were interviewed. Proportion of current smokers was similar across the three surveys. Prevalence of obesity increased by 7%. The prevalence of raised blood pressure (≥140/90 mmHg or ≥140/80 mmHg with diabetes) dropped by 8% from III to IV, and therapeutic control of blood pressure improved with 55% of patients below target in IV. The prevalence of LDL-C≥2.5 mmol/l decreased by 44%. 75% were above the target LDL-C<1.8 mmol/l in IV. The prevalence of self reported diabetes increased by 9%. The use of evidence-based medications increased between II and III surveys but did not change between III and IV surveys.

Conclusions Lifestyle habits have deteriorated over time with increases in obesity, central obesity and diabetes and stagnating rates of persistent smoking. Although blood pressure and lipid management improved they are still not optimally controlled and the use of evidence-based medications appears to have stalled apart from the increased use of high intensity statins. These results underline the importance of offering coronary patients access to modern preventive cardiology programmes.

Key words: EUROASPIRE, coronary patients, prevention, guideline implementation

Abbreviation list

EUROASPIRE = EUROpean Action on Secondary and Primary prevention In order the Reduce Events

CVD = cardiovascular disease

SBP = systolic blood pressure

DBP = diastolic blood pressure

MI = Myocardial Infarction

LDL-C = low-density lipoprotein cholesterol

BMI = body mass index

ACE = angiotensin-converting enzyme

ARBs = angiotensin-receptor blockers

WHO = World Health Organisation

Introduction

In 2012 the 194 World Health Organisation (WHO) member states adopted a global target to reduce premature mortality from non-communicable diseases (NCDs) by 25% by 2025 (1). Cardiovascular disease (CVD) accounts for a majority of NCDs mortality and is preventable. The WHO adopted targets to achieve this ambition embracing lifestyle, risk factors and the use of essential medicines and technologies, including preventive and rehabilitative care for those with established CVD. Since 1996 the EUROASPIRE (European Action on Secondary and Primary Prevention by Intervention to Reduce Events) surveys have described the management of coronary patients using comparable methodologies over time (2-8). The same nine countries participated in EUROASPIRE II (1999-2000) (3), EUROASPIRE III (2007-2008) (5) and EUROASPIRE IV (2012-2013) (7,8). These three surveys included a total of 12,775 consecutive patients with established coronary artery disease of whom 8,456 were interviewed at least six months after their initial hospitalisation and form the basis for 14-year time trend analyses in lifestyle and therapeutic management compared to targets set by the most recent Joint European Societies Cardiovascular Prevention Guidelines in Clinical Practice (9). The comparison between EUROASPIRE I, II and III surveys showed an increase in obesity, no change in smoking and poor blood pressure and lipids control despite the substantial increase in blood pressure and lipid-lowering drugs. In EUROASPIRE IV, we looked at the lifestyle and medical risk factors and the use of evidence-based medication as it was important to determine whether the adverse lifestyle and risk factors time trends continued and whether the practice of preventive cardiology has improved by comparison with the previous surveys.

Methods

Study design

EUROASPIRE II, III and IV were cross-sectional surveys conducted from 1999-2013 in Belgium, the Czech Republic, Finland, France, Ireland, the Netherlands, Poland, Slovenia and United Kingdom. The surveys were undertaken in the same

geographical areas including at least one hospital offering interventional cardiology and cardiac surgery, and one or more acute hospitals receiving patients with acute myocardial infarction (MI) and unstable angina. A sample of hospitals was taken in such a way that any patient presenting within the geographical area with acute symptoms of coronary disease, or requiring revascularisation in the form of balloon angioplasty or coronary artery surgery, had an approximately equal chance of being included in the patient sample. Countries where the surveys were undertaken in different areas were excluded. The number of centres in the three surveys was 26, 27 and 32 respectively, from the same geographical areas.

Study population

Consecutive patients, men or women [≥18 years and <70 years at the time of identification], with first or recurrent clinical diagnosis for coronary heart disease (see below) were *retrospectively* identified from diagnostic registers, hospital discharge lists or other sources: (i) coronary artery bypass grafting, (ii) percutaneous coronary intervention, (iii) acute MI, and (iv) unstable angina. The starting date for identification was >6 months ≤3 years prior to the study interview.

Data collection

Information on personal and demographic details, self reported lifestyle and medication was obtained at interview. Central training of data collectors ensured quality of data collection according to a written protocol, using standardised methodologies for all measurements, equipment calibrated according to the manufacturer's recommendations, and a central laboratory for total and HDL-cholesterol and triglycerides (see appendix). The LDL-C concentration was calculated using Friedewald's formula in all surveys (13).

Statistical analyses

A total of 2,100 interviewed patients were required from each of the three EUROASPIRE surveys to demonstrate differences in prevalence of at least 5% between surveys with 90% power at the 0.05 significance level. Frequency of risk

factors, lifestyles and drug use by survey, country, gender and age at interview are therefore reported at a European level only using descriptive statistics. Clustering of patients within centres was taken into account using multilevel modelling. A random coefficient model allowed for variation in time trends of risk factor frequencies between countries. P-values for evaluating the null hypothesis of equality in risk factor frequencies between surveys were based on Wald-type tests. Tukey's method for correcting P-values and confidence intervals was used to account for multiplicity in pairwise comparisons of surveys. Potential confounding due to differences in distributions of age and gender between surveys was adjusted for in all models. All statistical analyses were done with SAS statistical software (version 9.3).

Results

Patient characteristics

12,775 patients were consecutively identified and 8,456 interviewed (66.2%): 3,320 patients in EUROASPIRE II (1999-2000), 2,632 in EUROASPIRE III (2006-2007) and 2,513 in EUROASPIRE IV (2012-13) (Table 1). Interview rates were 67.5%, 63.6% and 51.4% respectively, slightly lower in females and those aged ≥60 years. A comparison of those attending for interview with those who did not showed that the interview participation rate was lower in women, in younger patients (except EUROASPIRE II), for those with acute myocardial infarction or unstable angina not revascularised. Median (interquartile range) times between the index event and interviews for the three surveys were 1.45(1.14-1.90), 1.22(0.98-1.63) and 1.39(1.00-1.92) years. The trends in lifestyle, risk factors and medications, stratified by the time between recruiting event and interview (less or more than the median of 1.3 years), were very similar for all variables. None of the two-way interactions between survey and time between recruiting event and interview was significant at P=0.10 level.

Study outcomes

The prevalence of current smoking, defined as the proportion of all patients smoking at the time of interview, did not differ across the surveys, with the highest rates in youngest (<50 years) patients, in both men and women (Table 2a). About half of

patients were persistent smokers having reported they were smoking in the month prior to their index event and still smoking at the time of interview. Among these smokers a large majority (81.4%, 67.4%, 72.5%; p=0.19) had attempted to quit following their coronary event. The use of pharmacotherapy for smoking cessation was low and did not change over time.

There was no change in the level of leisure time physical activity. Proportions of patients reaching recommended levels (vigorous physical activity for at least 20 minutes once or more times a week) were 37.3%, 33.8% and 41.8%; p=0.78) across the three surveys.

Prevalence of overweight did not differ across the surveys (Table 2b). However, prevalence of obesity increased from 31.9% in EUROASPIRE II to 38.5% in EUROASPIRE IV (p=0.007) with the greatest difference between survey III and IV. The same trend was observed for central obesity.

Prevalence of raised blood pressure dropped from 53.5% to 44.5% (p=0.01) between EUROASPIRE II and EUROASPIRE IV. The prevalences of very high blood pressure (systolic≥160 mmHg and/or diastolic≥100 mmHg) also dropped (21.9%, 16.8% and 12.8%; p=0.0006). Therapeutic control of blood pressure in patients using blood pressure lowering drugs improved with 55% of patients below target in EUROASPIRE IV (Table 3a).

The prevalence of raised total cholesterol decreased using either ≥4.5 mmol/l (77.0%, 40.6%, 32.8%; p<0.0001) or ≥4.0 mmol/l (89.3%, 62.6%, 54.3%; p<0.0001) as cut-points, and so did the prevalence of elevated LDL-C≥2.5 mmol/l (78.0%, 42.9%, 33.5%; p<0.0001). Using ≥1.8 mmol/l to define elevated LDL-C the decline over time is also present with 75.3% of patients being above the target <1.8 mmol/l in the most recent survey. Among all patients treated with lipid lowering drugs the proportion with LDL-C<1.8 mmol/l increased by 20% between survey II and IV (Table 3b). Although the proportion of patients on lipid-lowering drugs was similar between EUROASPIRE III and IV the use of high intensity statins (Atorvastatin 40-80mg or Rosuvastatin 20-40mg or Simvastatin 80mg) increased from 23.0% to 45.1%.

The prevalence of self reported diabetes increased (18.5%, 23.8% to 27.2%; p=0.004).

The use of evidence-based medications in the surveys is described in Tables 4a and 4b. The frequency of evidence-based medications use increased between EUROASPIRE II and III but did not change between EUROASPIRE III and IV surveys.

Discussion

The EUROASPIRE cross-sectional surveys undertaken on three occasions over a period of 14 years describe time trends in risk factor control and use of evidence-based medications among coronary patients. Lifestyle factors are deteriorating with increasing prevalences of obesity and central obesity and corresponding increases in the prevalence of diabetes mellitus. The control of blood pressure and LDL-C has improved over this period but most patients have still not achieved the guideline targets. The proportion of patients on evidence-based medications did not change between 2006 and 2013 although the use of high-intensity statins almost doubled. By comparison with standards set in the European guidelines on CVD prevention there is still considerable potential to reduce the risk of recurrent disease and improve survival.

There is a wealth of scientific evidence from meta-analyses of randomised controlled trials and observational studies that secondary prevention and cardiac rehabilitation are effective in reducing both cardiovascular and total mortality (11-14). The comprehensive, multifactorial approach to reduce total cardiovascular risk is strongly underlined in European and US guidelines on cardiovascular prevention (9,15). Recent studies such as EUROACTION and GOSPEL provide scientific evidence that structured, multidisciplinary programmes achieve healthier lifestyles and more effective risk factor control compared to usual care (16,17). In contrast the reality of cardiac rehabilitation provision, as described in EUROASPIRE III, varies widely. Only 45% of the patients were advised to attend and only 36% of those

eligible participated (18). These patients had by comparison to non-participants, improved lifestyle and risk factor management after one year. A health economics analysis from EUROASPIRE III showed that preventive care for coronary patients is cost effective for different health economies across Europe (19). Yet, despite the evidence for cost effectiveness the results of the European Cardiac Rehabilitation Inventory Survey show that provision of high quality services is limited because of lack of government funding, no professional guidelines or health service infrastructure (20).

The EUROASPIRE surveys show that the prevalence of persistent smokers did not change over the years but, importantly, that most smokers attempt to quit after their coronary event indicating a genuine wish to do so. This intention is more likely to be successful if supported by a smoking cessation specialist using evidence-based pharmacotherapy (21,22). Yet only a minority of the participants in EUROASPIRE received support and drugs for smoking cessation.

Obesity and central obesity have increased together with diabetes mellitus across the three surveys with an increased risk of recurrent macrovascular disease, microvascular disease and further reduction in life expectancy. In a mortality follow-up of the EUROASPIRE I cohort of 5,216 coronary patients the independent modifiable risk factors associated with an increased risk of dying were smoking, cholesterol and poor glucose control (23). The potential to reduce that risk in diabetes is considerable by combining lifestyle and risk factors control and evidence-based medications (24,25).

In contrast blood pressure and lipid control are improving although many patients are still not achieving the targets set in the current 2012 Joint European Societies Guidelines on CVD Prevention despite high prescription rates for evidence-based medications. These rates are comparable to trial populations such as the REACH registry and the STABILITY study, but considerably higher than the PURE study including the high-income countries (26-28). Yet, there appears to be a ceiling to prescribing with no increase in the proportions of patients on any of the blood pressure or lipid lowering drugs between EUROASPIRE III and IV. However, the progress was being made, as there was a two-fold increase in the proportion of

patients on high intensity statins between EUROASPIRE III and IV. The next steps for reducing the risk of recurrent disease could be by optimizing the dose of evidence-based medications and improving patient adherence.

By comparison with earlier multinational studies in Europe and the United States the prevalence and control of cardiovascular risk factors is comparable. (29-32). The nine-year trends (1998-2006) in achievement of risk factor goals in patients with cardiovascular disease showed that adherence to guidelines was suboptimal and lower in Europe than in the United States (29). In patients with CVD and diabetes type 2 NHANES reported significant improvements in blood pressure, LDL-cholesterol and triglycerides but only modest improvements in lifestyle factors.

Strengths and limitations

The EUROASPIRE surveys are conducted in selected geographic regions which are not nationally representative and the centres selected within each region include at least one offering interventional cardiology and cardiac surgery but not necessarily all centres. Therefore there is a conservative bias because the reality of secondary prevention practice outside these specialist centres will be poorer than described by EUROASPIRE. The interview rates across all three surveys combined was 66% but this is not a true participation rate as it was not possible to identify all those who had moved away or died and these patients are still included in the denominator. The falling interview rate may reflect falling participation in medical research generally (33), for which there are many reasons including increasing restrictions by ethics committees on how patients are recruited, and patients less willing to volunteer. However, this introduces a similar conservative bias because non-responders are more likely to be persistent smokers with unhealthier diets and an even more sedentary lifestyle. This is supported by a comparison of patient characteristics at hospital discharge in those who attended for interview with those who did not in the countries participated in EUROASPIRE IV. The interview participation rate was significantly lower in women, in smokers and in those with abnormal glucose metabolism (7). Therefore the evidence-practice gap between guideline recommendations for lifestyle, medical risk factors and evidence-based medications and patient management described by these EUROASPIRE surveys is likely to be much wider.

Conclusions

The adverse lifestyle factors trends described by the EUROASPIRE surveys in patients surviving the development of coronary disease, characterised by high levels of persistent smoking and inexorable increases in obesity, central obesity and diabetes, will mitigate to some extent the gains made in improving blood pressure and lipid control. The progress with lipids management and the use of evidence-based medications that has been made since 1999 has slowed down in the past five years. A modern preventive cardiology programme could bring together all elements of 'cardiac rehabilitation' and 'secondary prevention' to deliver one comprehensive service addressing all aspects of lifestyle, medical risk factor control and prescription of, and adherence with, evidence-based medications. All cardiovascular patients should be guaranteed access to modern preventive cardiology programmes in every country in order to gain, beyond those initial life saving treatments, longer, healthier and productive lives.

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Appendix A. Data collection and data management

Data Collection

Measurements were made with the following instruments:

a) Height and weight in light indoor clothes without shoes (SECA scales and measuring stick, model number 707 in EUROASPIRE II and SECA scales 701 and measuring stick model 220 in EUROASPIRE III and IV). Overweight was defined as a body mass index (BMI)≥25 kg/m2 and obesity as a BMI≥30 kg/m2.

b) Waist circumference was measured using a metal tape applied horizontally at the point midway in the mid-axillary line between the lowest rim of the rib cage and the tip of the hip bone (superior iliac crest) with the patient standing. Central obesity was defined as a waist circumference of ≥88 cm for women and ≥102 cm for men.

c) Blood pressure was measured twice on the right upper arm in a sitting position using an automatic digital sphygmomanometers (Omron 711 in EUROASPIRE II, Omron M5-I in EUROASPIRE III and Omron M6 in EUROASPIRE IV) and the mean was used for all analyses. Raised blood pressure was defined as systolic blood pressure (SBP)≥140 mmHg and/or diastolic blood pressure (DBP)≥90 mmHg in patients with no diabetes, and SBP≥140 mmHg and/or DBP≥80 mmHg in patients with diabetes.

d) Breath carbon monoxide was measured in ppm using a smokerlyser (Bedfont Scientific, Model EC50 in EUROASPIRE II, Bedfont Scientific, Model Micro4 in EUROASPIRE III and Bedfont Scientific, Model Micro+ in EUROASPIRE IV). Smoking at the time of interview was defined as self-reported smoking and/or a breath carbon monoxide exceeding 10 ppm. Persistent smoking was defined as smoking at interview among patients who reported smoking in the month prior to the index event.

e) Venous (fasting) blood was drawn for serum total and HDL-cholesterol and triglycerides. Elevated LDL-cholesterol (LDL-C) concentration was defined as ≥1.8 mmol/l (70 mg/dl)

f) Leisure time physical activity was assessed with the following question: Which of the following four best describes your level of activity outside

work? (i) no physical activity weekly; (ii) only light physical activity in most weeks; (iii) vigorous physical activity at least 20 minutes once or twice a week; (iv) vigorous physical activity for at least 20 minutes three or more times a week.

The monitors in EUROASPIRE II (Omron 711) and III (Omron M5-I) were compared in 100 patients and blood pressures from survey II had to be adjusted: corrected SBP = observed SBP - 0.95 mmHg; corrected DBP = observed DBP + 1.42 mmHg. According to the manufacturer no conversion formula is required for measurements obtained by Omron M6 and Omron M5-I.

In EUROASPIRE II, serum from venous blood was used for lipid measurements. The samples were stored at ≤-20°C. Total cholesterol measurements were performed at the Department of Medicine, University of Manchester, UK on a Cobas Mira S auto-analyser (Roche Diagnostics) using Unimate 7 (Roche) cholesterol reagent. The coefficient of variation for total cholesterol was 1.2% during the study. In EUROASPIRE III and IV serum from venous samples were stored at -70°C. Total cholesterol was measured at the central laboratory at the Disease Risk Unit, National Institute for Health and Welfare, Helsinki, Finland on a clinical chemistry analyser (Architect c8000, Abbott Laboratories, Abbott Park, Illinois, USA using enzymatic method for measuring). Since the methods used for cholesterol measurement in EUROASPIRE II and III differed, the performance of the methods was compared by re-measuring a total of 183 samples from EUROASPIRE II in the EUROASPIRE III central laboratory and no significant difference was found (mean difference 0.011 mmol/l, 95%CI -0.050 to +0.029) between these laboratories. Data from the external quality assessment programs demonstrated no systematic error in the cholesterol method during the study.

Self reported diabetes at interview was based on a history of diabetes diagnosed by a physician.

Written, informed consent was obtained from each patient and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's ethics research committee.

Data management

In EUROASPIRE II, all data were stored electronically using a unique identification number for country, centre and individual. Data from each country was transferred to the Co-ordinating Centre (Cardiovascular Medicine, National Heart and Lung Institute, Imperial College London, UK). In EUROASPIRE III and IV data were also collected electronically and submitted via Internet to the data management centre at European Heart House, Sophia Antipolis, France. Data were checked for completeness, internal consistency and accuracy. All data were stored under the provisions of the National Data Protection Regulations.