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Management of dyslipidaemia in patients with coronary heart disease: Results from the ESC-EORP EUROASPIRE V survey in 27 countries

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HIGHLIGHTS

- Most patients with established coronary artery disease have suboptimal lipid management.
- More professional strategies are needed aiming at lifestyle changes and LLT adapted to the need of the individual patient.
- The striking variability between countries and centers with several examples of well managed patients illustrates that the present conditions can be improved.

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ABSTRACT

Background and aims: One of the objectives of the ESC-EORP EUROASPIRE V survey is to determine how well European guidelines on the management of dyslipidaemias are implemented in coronary patients.
Methods: Standardized methods were used by trained technicians to collect information on 7824 patients from 130 centers in 27 countries, from the medical records and at a visit at least 6 months after hospitalization for a coronary event. All lipid measurements were performed in one central laboratory. Patients were divided into three groups: on high-intensity LDL-C-lowering-drug therapy (LLT), on low or moderate-intensity LLT and on no LLT.
Results: At the time of the visit, almost half of the patients were on a high-intensity LLT. Between hospital discharge and the visit, LLT had been reduced in intensity or interrupted in 20.8% of the patients and had been started or increased in intensity in 11.7%. In those who had interrupted LLT or had reduced the intensity, intolerance to LLT and the advice of their physician were reported as the reason why in 15.8 and 36.8% of the cases, respectively. LDL-C control was better in those on a high-intensity LLT compared to those on low or moderate intensity LLT. LDL-C control was better in men than women and in patients with self-reported diabetes.
Conclusions: The results of the EUROASPIRE V survey show that most coronary patients have a less than optimal management of LDL-C. More professional strategies are needed, aiming at lifestyle changes and LLT adapted to the need of the individual patient.

1. Introduction

Despite significant progress in secondary prevention of coronary heart disease (CHD) over the past decades, the incidence of recurrent events remains a problem for many patients and the society. In a Swedish national registry with more than 100,000 patients, post acute myocardial infarction (AMI) recurrent events were observed in 18% of the cohort during the first year following the index event and in 20% during the following three years among those who remained free of recurrent events during the first year [1].

The consequences are high numbers of premature mortality, of disability adjusted life years (DALYs) and of avoidable health care costs. More efforts to improve secondary prevention of CHD are needed. Evidence that an efficient risk factor control has great potential in avoiding unnecessary cardiovascular events has recently been documented in a large Swedish cohort study [2].

The European Society of Cardiology has since 1994 a comprehensive program of cardiovascular disease (CVD) prevention by developing and updating guidelines and implementation strategies. All this is regularly evaluated through the European Society of Cardiology – Eurobservational Research Programme (ESC-EORP) EUROASPIRE (European Action on Secondary and Primary Prevention by Intervention to Reduce Events) surveys. The EUROASPIRE IV survey incorporated the EuroHeart Survey on Diabetes to create the first European Survey of CVD prevention and diabetes. The aim of the prevention guidelines and the results from the EUROASPIRE I-IV surveys have been extensively communicated [3–16]. The most recent survey (EUROASPIRE V) in coronary patients took place in 2016–17 in 27 countries and the overall results have been reported [17].

In recent guidelines on CVD prevention in clinical practice [8] it is recommended to treat all patients with established CHD using lifestyle changes and cardio-protective drug therapies. Regarding the control of dyslipidaemia, achieving a low-density-lipoprotein cholesterol (LDL-C) level of < 1.8 mmol/L (70 mg/dL) is recommended or a reduction of at least 50% if the baseline LDL-C level is between 1.8 and 3.5 mmol/L (70–135 mg/dL). Non-HDL-cholesterol (Non-HDL-C) is regarded as a secondary target with a treatment goal of < 2.6 mmol/L (100 mg/dL). Trials have provided evidence that high-intensity LDL-C-lowering drug therapies (LLT) are more effective than low-intensity LLT at reducing recurrent events in coronary patients [18–20]. In an observational study a graded association was observed between the intensity of statin therapy and total mortality in patients with atherosclerotic CVD [21]. The safety and efficacy of the use of high-intensity LLT to achieve low levels of LDL-C in patients with CHD has been well documented [22].

The objectives of this report is to describe the lipid profile of coronary patients from 27 countries, the management of elevated LDL-C levels, the change that occurred in LLT between hospital discharge and what was actually taken at the time of the interview. Reasons for reducing the dosage or for stopping the LLT were enquired as well. Finally, the management of dyslipidaemia in these coronary patients was looked after according to patient characteristics.

2. Materials and methods

The hospital arm of the EUROASPIRE V surveys patients with documented CHD. National coordinators of 27 countries (Belgium, Bosnia & Herzegovina, Bulgaria, Croatia, Czech Republic, Egypt, Finland, Germany, Greece, Ireland, Italy, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, the Netherlands, Poland, Portugal, Romania, Russian Federation, Serbia, Slovenia, Spain, Sweden, Turkey, Ukraine and the United Kingdom) identified within their country one to three geographical areas, each with a population of at least half a million inhabitants. Within these areas, hospitals were identified in which patients with CHD were hospitalized. The number of geographical areas depended on the country size. In each participating hospital consecutive patients aged > 18 and < 80 years, who had been hospitalized at least 6 months and at most 2 years prior to the scheduled interview, were identified. The reason for hospitalization was an elective CABG, an elective PCI or an acute coronary syndrome (ACS). The eligible patients were invited for an interview and in those who participated, some information from the medical records was retrieved.

Participants were seen by centrally trained research technicians who used standardized methods to collect information through questionnaires and interviews among which questions on adopted lifestyle changes since the hospital stay and on the actual use of and adherence to lipid lowering drugs (generic name and total daily dosage). They also measured blood pressure, body weight and height and breath CO with similar instruments in all centers. High-intensity LDL-lowering therapies were defined as daily dosages that are on average associated with a reduction of LDL-C of at least 50%. All other lipid lowering drug therapies were considered as of 'low or intermediate intensity'.

Venous blood samples were taken after an overnight fast in the sitting position with light stasis into a tube containing clot activator (Vacutainer SST II Advanced, Becton Dickinson) for lipid assays. Serum was separated by centrifuging at 2000 g for 10 min at room temperature. After that serum was aliquoted into 2 bar-code-labelled tubes and stored locally at a minimum of −70 °C and then transported frozen to the central laboratory (Biochemistry Laboratory, National Institute for Health and Welfare, Helsinki, Finland) where all measurements were performed on a clinical chemistry analyzer (Architect c8000; Abbott Laboratories, Abbott Park, Illinois, USA). Total cholesterol (TC), HDL-cholesterol (HDL-C) and triglycerides (TG) were analysed in serum, with the following methods: enzymatic methods for total cholesterol and triglycerides and a homogenous method for direct measurement of HDL cholesterol. Non-HDL-C was calculated as TC-(HDL-C) and LDL-C using the Friedewald formula in patients with fasting TG < 4.5 mmol/L (400 mg/dL). The laboratory takes part in Lipid Standardization Program organized by CDC, Atlanta, Georgia, USA and External Quality Assessment Schemes organized by Labquality, Helsinki, Finland and is accredited by the Finnish Accreditation Service. It fulfils the requirements of the standard SFS-EN ISO/IEC 17025:2005. During the course of the study, comprising four months in 2017, the coefficient of variation (mean ± SD) and systematic error (bias) (mean ± SD) were 1.2% ± 0.1 and 0.0% ± 1.0 for total cholesterol, 1.9% ± 0.5 and −0.1% ± 2.4 for HDL cholesterol, 1.3% ± 0.2 and −1.8% ± 2.0 for triglycerides, respectively.

In the large majority of the patients the untreated baseline LDL-C level was not known; therefore it was not possible to calculate the % reduction from baseline and the LDL-C goal was set for all patients at < 1.8 mmol/L (70 mg/dL).

Height and weight were measured in light indoor clothes without shoes using SECA scales 701 and measuring stick model 220. Obesity was defined as a BMI ≥30 kg/m^2. Smoking at the time of interview was defined as self-reported smoking, and/or a breath carbon monoxide (CO) exceeding 10 ppm; breath CO was measured using a Smokerlyser device (Micro + Bedfont Scientific, UK). Regular physical activity was defined as physical activity of at least 30 min duration on average 5 times a week. Low educational level was defined as 'no formal schooling, less than primary school or primary school completed'.

2.1. Data management

Data management was undertaken by the EORP at the European Heart House, Sophia-Antipolis, France. All data were collected electronically through web based data entry using a unique identification number for country, centre and individual. The data were submitted via the Internet to the data management centre where checks for completeness, internal consistency and accuracy were run. All data were stored under the provisions of the National Data Protection Regulations.

Table 1
Lipid profile according to gender and age at interview.

	TC ≥ 4.5 mmol/L	HDL-C < 1.0/1.2 mmol/L for men/women	Non-HDL-C ≥ 2.6 mmol/L	TG ≥ 1.7 mmol/L	LDL-C ≥ 1.8 mmol/L	LDL-C ≥ 2.6 mmol/L
	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)
All	35.5 (2780/7824)	40.8 (3194/7824)	63.3 (4953/7824)	33.3 (2450/7351)	71.0 (5375/7575)	33.4 (2531/7575)
Men	31.5 (1831/5813)	38.7 (2251/5813)	60.4 (3512/5813)	32.5 (1767/5443)	68.6 (3853/5620)	30.4 (1707/5620)
Women	47.2 (949/2011)	46.9 (943/2011)	71.7 (1441/2011)	35.8 (683/1908)	77.9 (1522/1955)	42.2 (824/1955)
Age < 50 yrs	37.2 (271/729)	51.3 (374/729)	67.6 (493/729)	41.0 (286/697)	72.7 (499/686)	36.0 (247/686)
Age 50–59 yrs	36.5 (697/1911)	45.4 (868/1911)	66.7 (1275/1911)	37.9 (679/1792)	72.6 (1327/1827)	36.0 (658/1827)
Age 60–69 yrs	36.6 (1096/2992)	40.9 (1225/2992)	63.9 (1913/2992)	35.0 (983/2812)	71.4 (2079/2911)	33.8 (985/2911)
Age ≥ 70 yrs	32.7 (716/2192)	33.2 (727/2192)	58.0 (1272/2192)	24.5 (502/2050)	68.3 (1470/2151)	29.8 (641/2151)

2.2. Statistical analyses

Descriptive statistics (mean, standard deviation, median, interquartile range, proportion) were used to describe patient characteristics, lipid profiles, dietary changes and the use of lipid-lowering drug therapies. The association between patient characteristics and the therapeutic control of lipids was statistically evaluated according to mixed logistic modelling, the latter accounting for the clustering of patients within centers. A two-sided $p < 0.05$ was considered as indicating statistical significance. All data analyses were undertaken using SAS statistical software release 9.4 (SAS Institute Inc., Cary, North Carolina, USA) at the Department of Public Health, Ghent University, Belgium.

2.3. Ethical procedures

National coordinators were responsible for obtaining Local Research Ethics Committees approvals. Written, informed consent was obtained from each participant by the investigator by a signed declaration. The research assistants signed in the Case Record Form verifying that informed consent was obtained. The original signed declaration consent was stored in the patient file.

3. Results

Overall 16,208 patients were identified from consecutive lists of hospitalized patients of whom 8261 (56%) took part in the interview. For the purpose of this analysis on the management of dyslipidaemia full results were available in 7824 patients from 130 centers in 27 countries. They were on average 63.6 years of age (SD: 9.6 years) and 25.7% were females. Smoking was prevalent in 18.5% of these patients; 38% were obese and 35% did not engage in regular physical activity. The median time between hospital discharge and interview was 1.12 years (P25-P75 0.82–1.57 years).

In Table 1, the lipid profile is presented according to gender and age at interview. The lipid profile was on average less optimal in women compared to men with higher levels of TC, LDL-C and non-HDL-C. The proportion with low HDL-C levels was higher in women compared to men. The lipid profile was on average less optimal in young compared to older patients. These lipid profiles are given across the participating countries in Supplementary Table 1, illustrating the large heterogeneity between countries in the proportions with elevated TC, LDL-C and non-HDL-C. The differences in residual risk related to low HDL-C and high TG were also very large between countries. There were also considerable differences in the lipid profile between patients from different centers within a given country; for instance in country X the prevalence of LDL-C < 1.8 mmol/L (70 mg/dL) in patients on LLT was 24% in centre A and 41% in centre B.

In Table 2, the proportions of the patients on lipid lowering drugs at the interview are given according to gender and age. Almost half of the patients (n = 3811) were on a high-intensity LLT (men = 51.3%; women = 46.0%). The high-intensity LLT related in 72% to atorvastatin 40–80 mg/d and in 20% to rosuvastatin 20–40 mg/d while 8% were on combinations of statins with ezetimibe. Only 15 patients (0.4% of all those on high-intensity LLT) from 7 different countries were treated with PCSK9 inhibitors with or without statins and/or ezetimibe. The combination of atorvastatin 40–80 mg/d or rosuvastatin 20–40 mg/d with ezetimibe 10 mg/d was reported by 211 patients (5.5% of all those on a high-intensity LLT and 2.7% of all patients); in them the LDL-C goal of < 1.8 mmol/L (70 mg/dL) was achieved in 52%.

On the question “how often they took their lipid lowering drugs as prescribed by their doctor”, 92% answered all or nearly all of the time, a proportion that varied between countries from 70 to 98%.

In Supplementary Table 2, the use of LLT is presented across participating countries illustrating a large variation with high-intensity LLT used in > 80% of the patients in some countries compared to < 10% in other countries.

Changes in LLT between what was prescribed at hospital discharge to what was actually used at the visit are presented in Table 3. There were no changes in 67.5% and in this group 5% were never on a LLT, 20.2% remained on a low/moderate intensity LLT and 42.3% on a high-

Table 2
LDL-C lowering drug therapies according to gender and age at interview.

	LDL-C lowering therapy, % (n)		
	All	Low or moderate intensity	High intensity
All	84.3 (6514/7732)	34.1 (2603/7632)	49.9 (3811/7632)
Men	85.6 (4920/5746)	34.1 (1935/5671)	51.3 (2910/5671)
Women	80.3 (1594/1986)	34.1 (668/1961)	46.0 (901/1961)
Age < 50 yrs	80.4 (580/721)	28.7 (205/715)	51.6 (369/715)
Age 50–59 yrs	84.4 (1593/1888)	32.3 (601/1860)	51.8 (964/1860)
Age 60–69 yrs	83.6 (2472/2958)	33.5 (979/2921)	49.8 (1456/2921)
Age ≥ 70 yrs	86.3 (1869/2165)	38.3 (818/2136)	47.8 (1022/2136)

Table 3
Change in the LDL-C-lowering therapies from discharge to interview.

Prescribed at hospital discharge	Used at the time of interview	% (n)
No LLT	No LLT	5.0 (374/7528)
Low/Moderate intensity LLT	Low/Moderate intensity LLT	20.2 (1521/7528)
High intensity LLT	High intensity LLT	42.3 (3181/7528)
High intensity LLT	Low/Moderate intensity LLT	10.0 (755/7528)
High intensity LLT	No LLT	6.2 (463/7528)
Low/moderate intensity LLT	No LLT	4.6 (350/7528)
No LLT	Low/moderate intensity LLT	3.9 (297/7528)
No LLT	High intensity LLT	3.2 (241/7528)
Low/moderate intensity LLT	High intensity LLT	4.6 (346/7528)

LLT: LDL-C-lowering therapies.

intensity LLT. The LLT was reduced in intensity in 10.0% of the patients and completely interrupted in another 10.8% while LLT was initiated in 7.1% and increased in intensity among 4.6%.

In patients who reported a change from high-intensity LLT to low/moderate intensity LLT or from any LLT to no LLT, intolerance to statins was given as the main reason (15.8%). Another 36.8% reported that the change was based on the advice of their physician without any detailed explanation. A refusal to take statins was reported by another 14.3% and 33.1% had other reasons or was unsure of the reason of the change. In those who reported statin intolerance muscular pain was reported as the main symptom (62%) while non-muscular adverse events occurred in 14%, other adverse effects in 21% and 3% were uncertain.

The control of LDL-C is presented in Table 4 for two different treatment targets (< 1.8 and < 2.6 mmol/L [< 70 and < 100 mg/dL]) as well as for non-HDL-C at < 2.6 and < 3.4 mmol/L (< 100 and < 130 mg/dL) according to different patient characteristics.

Lipid control seemed to be better in men than in women and improved somewhat by increasing age and with higher education. There was no relation between LDL-C control and BMI categories or physical activity while smoking was systematically associated with unfavorable lipid levels. In patients with self-reported diabetes LDL-C and to a lesser extent non-HDL-C were better controlled. Both lipid fractions were better controlled in patients on LLT compared to those not on LLT and the control was better in those on high-intensity LLT than those on low/moderate LLT.

In Fig. 1, a comparison is made between patients at goal for LDL-C and those not at goal with respect to other lipid fractions that influence the residual risk of recurrent events: 9.4% of the patients who were at goal for LDL-C were not at goal for non-HDL-C while 30% of those at goal for non-HDL-C were not at goal for LDL-C. A low HDL-C was more

Table 4
Lipid control according to patient characteristics.

	Lipid control, % (n)			
	LDL-C < 1.8 mmol/L	LDL-C < 2.6 mmol/L	Non-HDL-C < 2.6 mmol/L	Non-HDL-C < 3.4 mmol/L
Men	32.3 (1561/4835)	69.6 (3913/5620)	39.6 (2301/5813)	71.6 (3577/4999)
Women	23.1 (377/1635)	57.8 (1131/1955)	28.3 (570/2011)	61.7 (1036/1679)
Age < 50 yrs	27.7 (165/596)	64.0 (439/686)	32.4 (236/729)	63.3 (400/632)
Age 50–59 yrs	28.5 (436/1531)	64.0 (1169/1827)	33.3 (636/1911)	66.2 (1061/1602)
Age 60–69 yrs	29.9 (737/2465)	66.2 (1926/2911)	36.1 (1079/2992)	68.9 (1744/2531)
Age ≥ 70 yrs	31.9 (600/1878)	70.2 (1510/2151)	42.0 (920/2192)	73.6 (1408/1913)
Low educational level[a]	33.9 (323/954)	72.7 (800/1101)	41.0 (465/1133)	73.8 (725/982)
Higher educational level	29.3 (1615/5516)	65.8 (4180/6353)	36.2 (2378/6560)	68.3 (3888/5696)
BMI < 25 kg/m^2	28.1 (349/1240)	65.2 (917/1407)	41.7 (595/1426)	70.8 (889/1255)
BMI 25–29.9 kg/m^2	29.5 (843/2856)	67.8 (2230/3290)	37.8 (1279/3384)[d]	70.1 (2061/2939)
BMI ≥ 30 kg/m^2	31.4 (746/2374)	66.1 (1844/2790)	33.3 (971/2918)[f]	66.9 (1663/2484)
Not currently smoking	31.0 (1655/5340)	67.9 (4211/6198)	38.4 (2447/6377)	70.9 (3891/5491)
Currently smoking[b]	25.0 (283/1130)[e]	60.5 (833/1377)[c]	29.3 (424/1447)[f]	60.8 (722/1187)[f]
Physical activity on target[c]	31.3 (712/2274)	66.5 (2981/4484)	36.0 (1664/4628)	72.1 (1692/2347)
Physical activity not on target[c]	29.2 (1226/4196)	72.0 (1709/2374)	42.1 (1032/2451)	67.4 (2921/4331)
No self-reported diabetes	26.3 (1234/4691)	64.9 (3503/5395)	35.9 (1980/5515)	68.7 (3293/4794)
Self-reported diabetes	39.6 (704/1779)[f]	70.8 (1496/2114)[f]	38.6 (866/2243)	70.1 (1320/1884)
No LLT	13.9 (126/907)	32.1 (373/1162)	15.4 (188/1218)	36.6 (348/950)
Low/moderate LLT +	26.3 (573/2178)[f]	66.9 (1688/2524)[f]	33.5 (872/2603)[f]	69.1 (1550/2242)[f]
High intensity LLT +	36.6 (1239/3385)[f]	77.2 (2857/3701)[f]	45.2 (1724/3811)[f]	77.9 (2715/3486)[f]

[a] 'No formal schooling', 'Less than primary school' or 'Primary school completed'.
[b] Self-reported smoking or CO in breath > 10 ppm.
[c] Regular physical activity of at least 30 min duration on average 5 times a week; +LLT = LDL-C lowering drug therapies.
[d] $p < 0.01$.
[e] $p < 0.001$.
[f] $p < 0.0001$ (after adjustment for gender and age at interview and taking clustering of patients within centers into account).

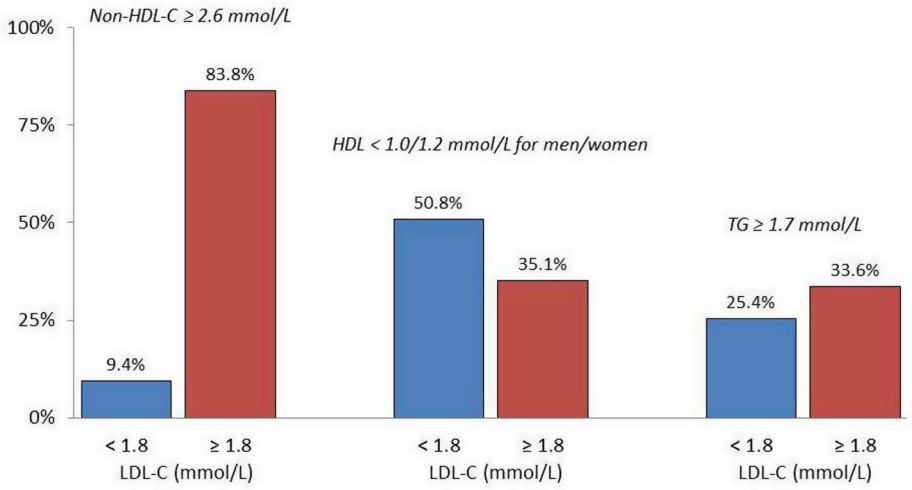

Fig. 1. Elevated non-HDL-C and TG and low HDL-C levels in patients at goal or not at goal for LDL-C.

frequently observed in patients at goal for LDL-C compared to the group not at goal for LDL-C and the reverse was true for elevated TG.

4. Discussion

The EUROASPIRE V survey clearly shows that the overall lipid control was unsatisfactory in a large proportion of patients as reflected by elevated levels of TC, LDL-C, non-HDL-C and TG and low levels of HDL-C. Unfortunately, other fractions such as apo B and Lp(a) were not measured. This situation was on average worse in women and in young patients. Moreover, there was a substantial variation in these lipid profiles between patients from different participating countries and between patients from different centers within a country; this illustrates that it is possible to achieve targets and that standard of care is an important factor.

4.1. Lifestyle related issues

The causes of the poor adherence to guideline recommended management are multiple. An optimal control of dyslipidaemia requires both lifestyle changes and LLT adapted to individual demands. Given the international, multicenter design of EUROASPIRE V it was not possible to organize a full quantitative dietary survey. A high quality diet is essential in secondary prevention not only for LDL-C control as documented in patients with CAD in the Nurses' Health study and the Health Professionals Follow-up study [23] as well as in the OASIS-5 trial [24]. Residual risk reduction in patients with CHD can also be achieved with smoking cessation and with regular physical exercise [25,26]. These lifestyles were poorly adapted in the patients of EUROASPIRE V [17].

4.2. Lipid lowering drugs

Present recommendations advocate, irrespective of the LDL-C level, prescription of LLT to all patients with documented CHD if not contraindicated. In EUROASPIRE V an average of 84% of all patients were on LLT, varying between the 27 countries from 75 to 98%. The corresponding average proportions were 80% (varying from 38 to 92%) in EUROASPIRE III (22 countries; 2006–7) and 86% (varying from 72 to 97%) in EUROASPIRE IV (24 countries; 2012–13) [12,27].

The results of EUROASPIRE V may be considered as 'real life data' reflecting contemporary practice in contrast with observations in clinical trials presenting patient populations subjected to selection bias and strict control of drug intake.

The present findings are unfortunately not unique. In the STABILITY trial [28] 97% of 15 828 patients with stable CHD from 39 countries on five continents were on statins and 29% of them had a LDL-C $>$ 2.5 mmol/L. This should be compared with 84% on LLT and 33% at a LDL-C $\geq$ 2.6 mmol/L in EUROASPIRE V. In similarity with EUROASPIRE V regional results in STABILITY differed considerably suggesting that other factors such as lifestyle, prescription inertia, insufficient drug dosage and patient compliance are important. In a retrospective examination of LLT in a real world cohort performed in 2014 in the United Kingdom, 79% of 91 470 patients with atherosclerotic CVD (mean age 73 years) received statin treatment whereof 31% atorvastatin 80 mg o.d. or the equivalent. A total of 31% had a LDL-C $<$ 1.8 mmol/L (70 mg/dL) and 12% a non-HDL-C of $<$ 2.6 mmol/L (100 mg/dL) [29]. The SURF survey included 10 186 patients with CHD (29% women) from 79 centers in 11 countries. One fifth were not taking any LLT therapy and only 30% reached a LDL-C $<$ 70 mg/dL ($<$ 1.8 mmol/L) [30].

In the DYSIS study, 10,587 statin-treated patients with CVD were selected in 2008–9 in 11 Western-European countries and in Canada. LDL-C was $<$ 2.5 mmol/L (100 mg/dL) in 58%. High potency statins (equivalent to 80–160 mg/d of simvastatin) was used by 14% of all high-risk patients. Importantly, higher statin dose was the single greatest modifiable predictor of LDL-C at goal. In these statin-treated patients a low HDL-C ($<$ 1.0 mmol/L [39 mg/dL] in men and $<$ 1.2 mmol/L [46 mg/dL] in women) was found in 31% and elevated TG ($\geq$ 1.7 mmol/L [$\geq$ 150 mg/dL]) in 39% [31]. In the International Cholesterol Management Practice Study (ICLPS) in 18 countries outside Western-Europe 4842 patients at very-high cardiovascular risk and on a stable lipid lowering therapy were enrolled in 2015–16. Almost all of them were on statins with 33% on high-intensity statins. A total of 32% of all these very-high risk patients achieved a LDL-C of $<$ 1.8 mmol/L (70 mg/dL) [32]. The uniform experience from these trials and most recently from the EUROASPIRE V survey is that considerable efforts should be invested in improving lipid management in patients with coronary artery disease manifestations.

More potent statins reduce morbidity and mortality after an acute myocardial infarction (AMI) more effectively than less potent statins [18,33–35]. This is reflected in the 2011 and the 2016 EAS/ESC guidelines for the management of dyslipidaemia [36,37]. Both recommend that high dose statins should be initiated early after admission in all patients with acute coronary syndrome without contraindications or a history of intolerance regardless of the LDL-C value. In EUROASPIRE V 88% of all patients were discharged on LLT whereof 59% on high-intensity treatment. Of 4340 US patients hospitalized for an AMI 2005–8 in the TRIUMPH study 87% of 2776 statin naïve patients were prescribed a statin and among patients who arrived on a

submaximal statin dose 26% had their therapy intensified. Only 140 were on a maximal dose at entry. Among all patients without a contraindication 23% were discharged on maximal statin therapy but there was a large in between hospitals variability in this respect [38].

In patients at extremely high CVD risk it is recommended to reduce LDL-C by at least 50% or towards even lower targets than < 1.8 mmol/L (70 mg/dL) [39,40]. If that can not be achieved with maximally tolerated high-intensity statins alone it is recommended to add ezetimibe and, if needed, a PCSK9 inhibitor. In EUROASPIRE V only 55% of all participants were discharged on a high-intensity statin and at interview only 2.7% were on a combination of a high-intensity statin with ezetimibe. It is clear that substantial improvements can be achieved by an up titration of statin therapy and by using combined LLT in a large proportion of patients with CVD.

PCSK9 inhibitors were used in only 15 patients from 7 countries in EUROASPIRE V. This relates probably to the fact that in 2016–17 the availability of these drugs was limited. Even in early 2019 only 14 of the 27 EUROASPIRE V countries had access to these drugs. The efficacy of PCSK9 inhibitors has been demonstrated [19,20] but the high cost, based on the 2018 prices, remains a barrier to its clinical application.

In addition, results from the REDUCE-IT trial do suggest that lowering of other lipid components may improve outcomes in selected groups of patients [41].

4.3. Gender and age

An important finding in EUROASPIRE V is that women were less treated with LLT and less often received high-intensity LLT than men. This was also reflected in their lipid profile. Only 23% of the women had a LDL-C < 1.8 mmol/L (70 mg/dL) compared to 32% in men. This confirms observations made in EUROASPIRE IV [24] and are congruent with the observation that women with CHD are less likely to receive state-of the art evidence-based treatment than men [42,43]. One way to improve the secondary prevention, including optimal LDL-C control in female patients would be to incorporate them in multidisciplinary cardiac rehabilitation programs, presently less frequently prescribed to women compared to men [44]. Another interesting finding is that on average young compared to older patients have more elevated levels of TC, LDL-C, non-HDL-C and TG and low levels of HDL-C. The reason might be that their physicians underestimate their actual CV risk and that they are less well informed on their ideal lipid target levels [45].

4.4. Physician inertia

It is worrying that the proportion of patients without LLT in EUROASPIRE V had increased from 12% at the time of hospital discharge to 16% about one year later and that the proportion on high-intensity LLT had decreased from 58 to 50%. The reasons why practitioners often prefer low/moderate intensity instead of high-intensity LLT are complex. It is reasonably influenced by the fear of adverse effects with confusing information on side effects of statins as a contributory factor. Recent observations on the safety of attaining even very low levels of LDL-C [19] should re-assure physicians and together with the greater gain that can be achieved in terms of secondary prevention all this should be an incentive to prescribe high-intensity LLT in almost all coronary patients and in the maximal tolerated dose if necessary to achieve the LDL-C target.

4.5. Concluding remarks

The results of the EUROASPIRE V survey clearly demonstrate that most patients with established coronary artery disease have suboptimal lipid management and, most worrisome, LDL-C levels far from those, based on very solid evidence, recommended by available guidelines. The causes are multiple and in an immediate need of professional strategies aiming at lifestyle changes and adequate use of available LLT adapted to the need of the individual patient. Among such strategies the present data strongly underlines the need for improved education of the profession and the patients and a structured care according to principles that are well established, however, less well put in place. The striking variability between countries and centers with several examples of well managed patients serves as evidence that the present conditions can be improved.

Conflicts of interest

No competing interests for G. De Backer, D. De Bacquer, E. Mirrakhimov and D. Wood. P. Jankowski has received honoraria, research and conference grants from, KRKA, MSD, Pfizer, SanofiAventis, Servier, Zentiva. Ž Reiner has received honoraria for lectures from Sanofi Aventis and from Akcea. L.Tokozoglu has had financial interests, arrangements or affiliations with Actelion, Amgen, Sanofi, Pfizer, Novonordisk, MSD, Recordati, Kowa, Abbott, Novartis, Mylan, Bayer, Servier and Sanovel. L Rydén has received honoraria and research grants from Amgen, Bayer AG, Boehringer Ingelheim, MSD, Novo Nordisk and Sanofi. K. Kotseva received consultancy fees from Amgen.

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Appendix A. Supplementary data

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