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The effect of the 2019 ESC/EAS dyslipidaemia guidelines on low-density lipoprotein cholesterol goal achievement in patients with acute coronary syndromes: The ACS EuroPath IV project

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ABSTRACT

Aims: To evaluate the effect of the ESC/EAS 2019 dyslipidaemia guidelines on patient management of lipid-lowering therapy in patients with acute coronary syndrome (ACS), through a survey designed to compare post-ACS patient management in 2022 with that in 2018.

Methods: Online questionnaires focused on lipid profile and medications were used to gather data from 2650 ACS patients in 6 European countries, treated between March–June 2022 (ACS EuroPath IV survey). These data were compared with data collected from 2650 patients who participated in the ACS EuroPath I survey (conducted in 2018).

Results: Lipid testing was performed in 90% of patients and was done sooner after admission in 2022 versus 2018 (mean 1.4 vs 1.7 days). Increased testing for non-HDL-C, lipoprotein(a), and ApoB was observed over time. At discharge, most patients (≥90%) were receiving lipid-lowering therapy. Prescribing patterns differed, with a higher proportion of patients receiving statin plus ezetimibe combination therapy in 2022 versus 2018 (34% vs 13%). LDL-C levels were lower in 2022 versus 2018 at admission and at 1st, 2nd and 3rd post-discharge follow-up points. More patients achieved low-density lipoprotein cholesterol (LDL-C) goals in 2022 versus 2018 at the first follow-up (average 14 vs 16 weeks since discharge; <70 mg/dL [1.8 mmol/L]: 34% vs 20%; <55 mg/dL [1.4 mmol/L]: 18% vs 10%) and at subsequent follow-up points.

Conclusion: LDL-C goal achievement has improved since the release of the 2019 guidelines, but lipid management in post-ACS patients remains suboptimal.

Abbreviations: ACS, acute coronary syndrome; ApoA1, Apolipoprotein A1; ApoB, Apolipoprotein B; ASCVD, atherosclerotic cardiovascular disease; CV, cardiovascular; EAS, European Atherosclerosis Society; ESC, European Society of Cardiology; FH, familial hypercholesterolaemia; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LLT, lipid-lowering therapy; MI, myocardial infarction; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor; UK, United Kingdom.

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1. Introduction

Despite the availability of effective treatments, patients who have experienced an acute coronary syndrome (ACS) remain at very high risk of death, as well as of recurrent cardiovascular (CV) events. [1–3] Relative risk for all-cause death and cardiovascular outcomes was estimated to be at least 30% greater in patients who had previously experienced a myocardial infarction (MI) compared with the general population at both 1–3 years and 3–5 years post-MI. [1] However, improved outcomes can be achieved with better and timely management of risk factors, such as low-density lipoprotein cholesterol (LDL-C) level. [4,5]

The European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS) recommendations for lipid-lowering therapy (LLT) for patients with ACS were updated in 2019. [5] This update was motivated by results from recent large randomised placebo-controlled clinical studies showing that the addition of either ezetimibe or anti-PCSK9 monoclonal antibodies to statin therapy is associated with further reduction in atherosclerotic cardiovascular disease (ASCVD) risk, correlating with absolute LDL-C reduction. [5] The updated guidelines lowered the recommended LDL-C goals for very high CV risk patients from 70 mg/dL (1.8 mmol/L) to 55 mg/dL (1.4 mmol/L). [5,6]

The ongoing ACS EuroPath project (including the ACS EuroPath I, II and III initiatives) was designed to review clinical practice for post-ACS lipid management. [7,8] The ACS EuroPath I survey was conducted in 2018, including 555 cardiologists from 7 European countries, capturing data on patients with ACS ($n = 2775$). Survey results showed that lipid screening and management were suboptimal, and there was a lack of physicians' compliance with ESC/EAS 2016 guidelines. [7] However, the impact of the new evidence recapitulated in the revised ESC/EAS 2019 guidelines on clinical practice is not known. The ACS EuroPath IV survey was thus designed to compare post-ACS patient management in 2022 with that in 2018 (i.e. before and after the ESC/EAS guideline update) and to evaluate changes in cardiologists' therapeutic approaches to lipid management and goal achievement in ACS patients.

2. Methods

The 2018 survey was performed in 7 European countries (France, Germany, Italy, Spain, the United Kingdom (UK), the Netherlands, and Switzerland). The 2022 survey was performed in 6 European countries (including all of the above with the exception of Switzerland). Exactly the same methodology, recruitment criteria, and questionnaires were used in both surveys. Data were collected between April and May 2018 (EuroPath I) and March and June 2022 (EuroPath IV).

2.1. Recruitment

Panel recruitment was blinded, and respondents were anonymised. There was no relationship between respondents and any parties. Cardiologists selected for survey participation represented 25–47% of all cardiologists in the corresponding country. The first part of the online survey was a screening questionnaire, which determined whether the respondent matched the criteria for inclusion into the study. The key screening criteria were: 1) general cardiologist or interventional cardiologist status; 2) 3–40 years in practice; 3) >50% of time spent in direct patient care; 4) >15 ACS patients treated per month.

2.2. Methodology

Data were collected through a 40-min online questionnaire (Supplementary Information: Section 1), completed independently by respondents. The questionnaire included a Patient Record Form section, in which respondents provided data collected from their last 5 patients with ACS. Data were collected for the acute or the follow-up phase of the ACS. The acute phase was defined as the period from hospital admission to discharge (patients who have been hospitalised and subsequently discharged within <1 month, with a hospitalisation phase of <7 days). The follow-up phase was defined as the period from discharge until 12 months of follow up (patients discharged from hospital and receiving follow-up management after an ACS that occurred between 12 and 18 months ago).

Significant differences are indicated at the 95% confidence level and are not reported where samples sizes are <30. Outliers were defined as being ±3 standard deviations away from the mean and were excluded (for numeric questions only; number of excluded respondents varied by question).

3. Results

The 2022 survey included a total of 2650 ACS patients; of these, 929 (35%) were in the acute phase and 1721 (65%) in the follow-up phase. The 2018 survey included a total of 2775 ACS patients, 2650 of whom were included in this analysis: 900 (34%) in the acute phase and 1750 (66%) in the follow-up phase. A total of 530 physicians participated in the survey in each year. Among participating physicians in 2022, 137 (26%) were interventional cardiologists and 393 (74%) were general cardiologists; in 2018, 122 (23%) were interventional cardiologists and 408 (77%) were general cardiologists.

Patient characteristics were similar between 2022 and 2018 (Table 1). The mean age and the proportion of males did not differ, and patients in the 2022 population included fewer current smokers and had more comorbidities compared to those in 2018. There were more patients with a previous CV event in 2022 compared to 2018 (13% vs 11%), but fewer were only medically managed (i.e. they did not undergo percutaneous coronary intervention; 12% in 2022 vs 17% in 2018). Patient characteristics by acute and follow-up status in 2022 are detailed in Supplementary Table 1.

3.1. Acute and follow-up phase

Lipid testing was similar in 2022 and 2018 (90% of patients; Fig. 1A) but occurred sooner after admission (1.4 vs 1.7 days) in 2022. Testing of non-high-density lipoprotein cholesterol (non-HDL-C), lipoprotein(a) and apolipoprotein B (ApoB) was significantly more prevalent in 2022 (Fig. 1A). LLT was prescribed during hospitalisation in ≥90% of cases in both surveys. Prescribing patterns changed over time, with a higher proportion of patients receiving statin plus ezetimibe combination

Table 1
Patient characteristics in 2022 and 2018.

	2022	2018	*P* value
Number of patients (n)	2650	2650	
Acute ACS (n)	929	900	
Post ACS (n)	1721	1750	
Age (years), mean ± SD	64.5 ± 12.2	65.4 ± 12.5	0.01
Male sex, n (%)	1778 (67)	1756 (66)	0.52
Smokers, n (%)	1949 (74)	1897 (72)	0.11
Current smokers	899 (34)	1022 (39)	**0.00***
Former smokers	1050 (40)	875 (33)	**0.00***
Comorbidities, n (%)			
Obesity	857 (32)	752 (28)	**0.00***
Diabetes	1032 (39)	951 (36)	**0.02***
Hypertension	1912 (72)	1989 (72)	0.67
Familial hypercholesterolaemia	213 (8)	198 (7)	0.44
Previous CV event	348 (13)	284 (11)	**0.01***
Stable CAD	359 (14)	382 (14)	0.36
Polyvascular disease	256 (10)	214 (8)	**0.04***
Family history of premature CV disease	885 (33)	778 (29)	**0.00***

Key patient characteristics in 2018 and 2022 are depicted.
*Significant difference between wave average.
Data derived from answers to questionnaire sections: P1, P2, P3, P4, P5a.
ACS, acute coronary syndrome; CAD, coronary artery disease; CV, cardiovascular; SD, standard deviation.

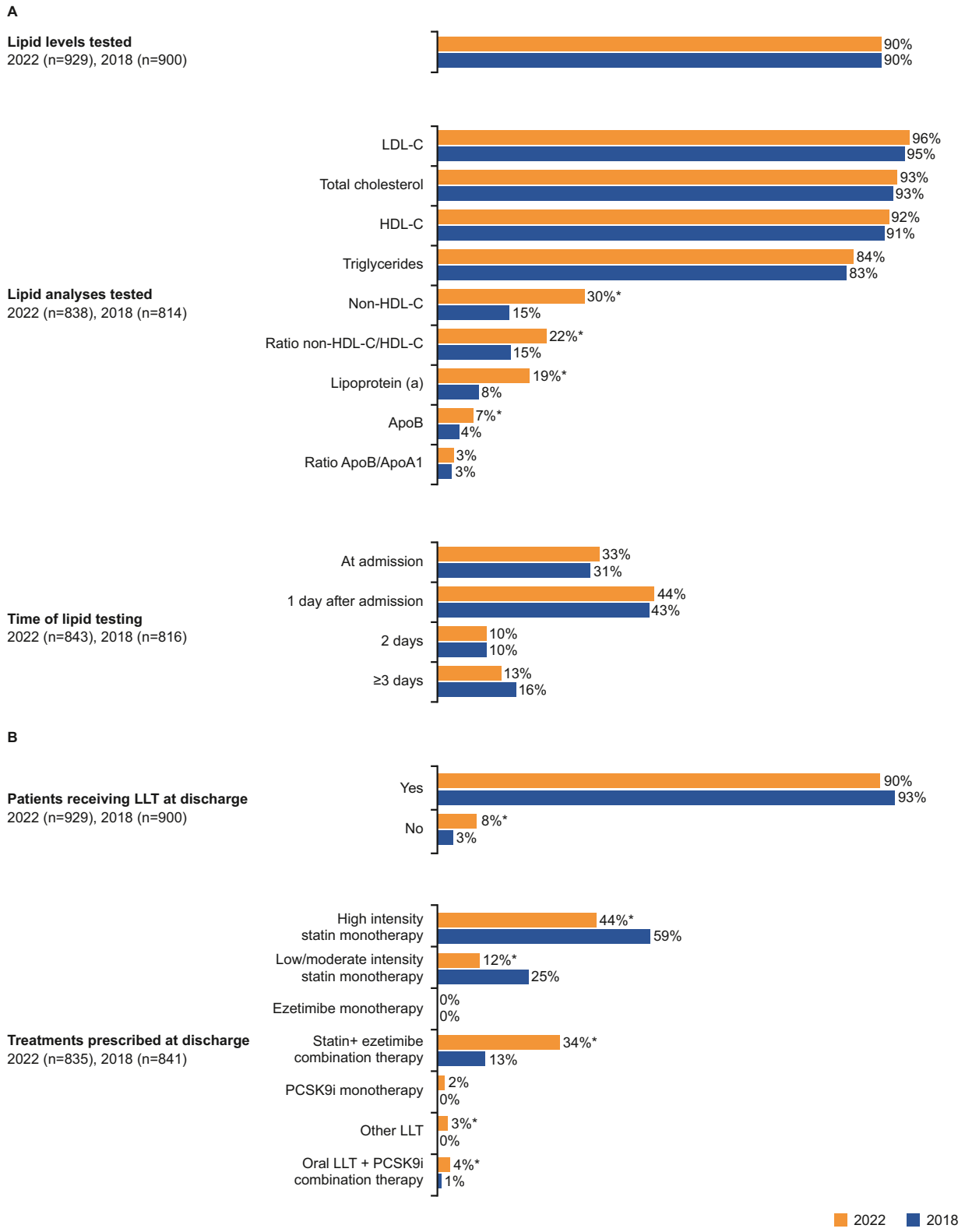

Fig. 1. Lipid testing in the acute and follow-up phases. A: Lipid testing in the acute phase (% of patients). B: Pharmacological approach at discharge.
Fig. 1A: lipid testing status, types of lipid analyses and time of lipid testing are depicted.
Fig. 1B: proportion of patients receiving LLT at discharge and treatments prescribed at discharge are depicted.
*Significant difference between 2022 and 2018.
Data derived from answers to questionnaire sections: P12a, P12b and P13 (Fig. 1A); P17, P22B (Fig. 1B).
ApoA1, Apolipoprotein A1; ApoB, Apolipoprotein B; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LLT, lipid-lowering therapy; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor.

therapy at discharge in 2022 versus 2018 (34% vs 13%) and fewer patients receiving high (44% vs 59%) or low/moderate intensity statin monotherapy (12% vs 25%; Fig. 1B) alone. LDL-C levels were lower in 2022 versus 2018 in the acute phase and at all follow-up points (Table 2). As the number of follow-up consultations increased in 2022, so did treatment intensification, with greater use of statin and ezetimibe combination therapy and PCSK9 inhibitor (PCSK9i) monotherapy compared to 2018 (Fig. 2). More patients had achieved guideline-recommended LDL-C goals in 2022 at the first follow-up (<70 mg/dL [1.8 mmol/L]: 34% vs 20%; <55 mg/dL [1.4 mmol/L]: 18% vs 10%) and at 2nd and 3rd follow-up points (Fig. 3; Supplementary Table 2). In 2022, there were 213 patients with familial hypercholesterolaemia (FH) in comparison to 198 patients in 2018 (Supplementary Table 3). The type of FH screening also differed between the years, with more genetic testing and less clinical assessment in 2022 compared to 2018 (Supplementary Fig. 1).

3.2. Ranking of risk factors by physicians, lipid targets and management protocols

In 2022, physicians ranked high LDL-C levels in the top 3 priority risk factors when managing post-ACS patients, after smoking and diabetes (Fig. 4). Of all cardiologists surveyed, 26% set an LDL-C goal of <55 mg/dL and 68% expected a ≥ 50% reduction from baseline, to be achieved in 2–3 months. However, 5% of cardiologists would not typically set an LDL-C level or LDL-C reduction goal (Fig. 5). A vast majority (81%) strongly agreed that most patients with the highest risk profiles should systematically get more intensive LLT with statins and ezetimibe during the acute phase (Supplementary Fig. 2).

Lipid management protocols at discharge were implemented in 43% of cases. Over half of cardiologists reported high value of lipid management guidance in general. Treatment recommendations were generally not specific to patient type: 69% of respondents confirmed that they used the same guidance for all post-ACS patients, but 46% thought guidance should vary by patient type and be primarily based on LDL-C levels. At discharge, a rehabilitation programme was recommended more often in 2022 than in 2018 (62% vs 49%; Supplementary Fig. 3). Most discharge letters currently include LLT prescribed at discharge, LDL-C goal, recommended timeframe for first follow-up consultation and recommended timing for lipid profile re-evaluation (Supplementary Fig. 4).

Table 2
LDL-cholesterol serum concentrations over time.

LDL-C in mg/dL, mean ± SD	2022	2018	P value
Prior to most recent event	*n* = 1050 133 ± 56	*n* = 991 142 ± 59	**0.00***
At admission/during acute phase but before discharge	*n* = 1244 125 ± 54	*n* = 1160 143 ± 89	**0.00***
Chronic phase			
Follow-up visit 1	*n* = 1070 85 ± 45	*n* = 937 101 ± 49	**0.00***
Follow-up visit 2	*n* = 613 71 ± 37	*n* = 595 87 ± 41	**0.00***
Follow-up visit 3	*n* = 220 67 ± 33	*n* = 257 83 ± 41	**0.00***

LDL-C levels in 2018 and 2022 (pre-event, at admission/acute phase and during chronic phase) are depicted.
*Significant difference between wave average.
Data derived from answers to questionnaire sections: P6, P14, P32_4.
LDL-C, low-density lipoprotein cholesterol; SD, standard deviation.

4. Discussion

The effects of guideline recommendations on patient care are incompletely known. To the best of our knowledge, this study is the first comparing two similar cohorts of patients with ACS before and after the 2019 ESC/EAS updated guidelines for management of dyslipidaemias. The results of this comparison of post-ACS patient management data from 2018 and 2022 show that goal attainment and awareness of LDL-C in post-ACS patients has improved since the 2019 update. However, a second important finding was that lipid management in post-ACS patients remains suboptimal across Europe.

Overall, LDL-C control improved between 2018 and 2022, and lipid testing was conducted more often. The increase in non-HDL-C, lipoprotein(a) and ApoB testing from 2018 to 2022 likely reflects the ESC/EAS 2019 guidelines, which recommend non-HDL-C testing for risk assessment, particularly in people with high triglyceride (TG) levels, diabetes mellitus, obesity or very low LDL-C levels. [5] A greater proportion of patients achieved both <70 mg/dL (1.8 mmol/L) and < 55 mg/dL (1.4 mmol/L) LDL-C goals in 2022 than in 2018. The improvements in LDL-C level/goal attainment indicate that guideline changes have had an impact on management; however, the proportion of patients achieving <55 mg/dL goal in 2022 was still low, suggesting the need for further improvement.

More patients were receiving combination therapy at discharge and during follow-up in 2022 compared to 2018 (particularly statins in combination with ezetimibe: 34% vs 13% at discharge and 38% vs 16% at 1st follow-up point). The use of anti-PCSK9 monotherapy was also greater in 2022 compared to 2018 (8% vs 2% at 1st follow-up, 11% vs 3% at 2nd follow-up and 12% vs 4% at 3rd follow-up point). The newer guidelines recommend prescription of PCSK9i for patients at very high-risk not achieving their goal on a maximum tolerated dose of statin and ezetimibe. [5] This new recommendation is based on the results of the ODYSSEY OUTCOMES and FOURIER studies, which suggest that PCSK9i therapy combined with potent LLT may safely reduce CV risk [9,10] In the ODYSSEY OUTCOMES study (which included 18,924 post-ACS patients), a 15% relative reduction in the primary composite outcome (i.e. death from coronary heart disease, non-fatal MI, ischaemic stroke, or unstable angina requiring hospitalisation) and a 15% reduction in risk of all-cause death were observed after a median follow-up of 2.8 years. [9] The FOURIER study (which included 27,564 patients with ASCVD and LDL-C ≥ 70 mg/dL receiving statin therapy) observed a 15% reduction in the primary composite outcome (i.e. CV death, MI, stroke, hospitalisation for unstable angina, or coronary revascularisation) after a median follow-up of 2.2 years; no reduction was observed in all-cause mortality. The 2022 results are consistent with this change in guidelines, and the reductions in LDL-C levels seen in this survey are likely to be linked, at least in part, to both the higher levels of prescription of combined LLT and the higher use of PCSK9 inhibitors. Nevertheless, the number of patients receiving PCSK9 inhibitors at the first follow-up visit was low (8%).

Interestingly, a ranking of CV risk factors based on the physician's perception highlighted smoking and diabetes as the most important risk factors to consider when managing post-ACS patients, with elevated LDL-C level considered less important in comparison. Of note, 5% of clinicians would not set a goal for LDL-C reduction at all. Overall, it appears that cardiologists across Europe still accept suboptimal LDL-C levels for ACS patients, despite evidence on the causal role of LDL-C in ASCVD from clinical trials and knowledge from mechanistic studies that retention of low LDL-C and other cholesterol-rich lipoproteins within the arterial wall is a key initiating event in atherogenesis and an important factor in atherosclerosis progression. [5,11] Results from the 2022 survey indicate greater awareness of combination therapies among cardiologists compared with 2018. A recent ESC/EAS survey indicated that physicians in Europe (mainly cardiologists [>50%]) are generally in favour of the updated guidance, but acknowledge that the new goal levels are often not attained. [12] Thus, the data identify key topics for

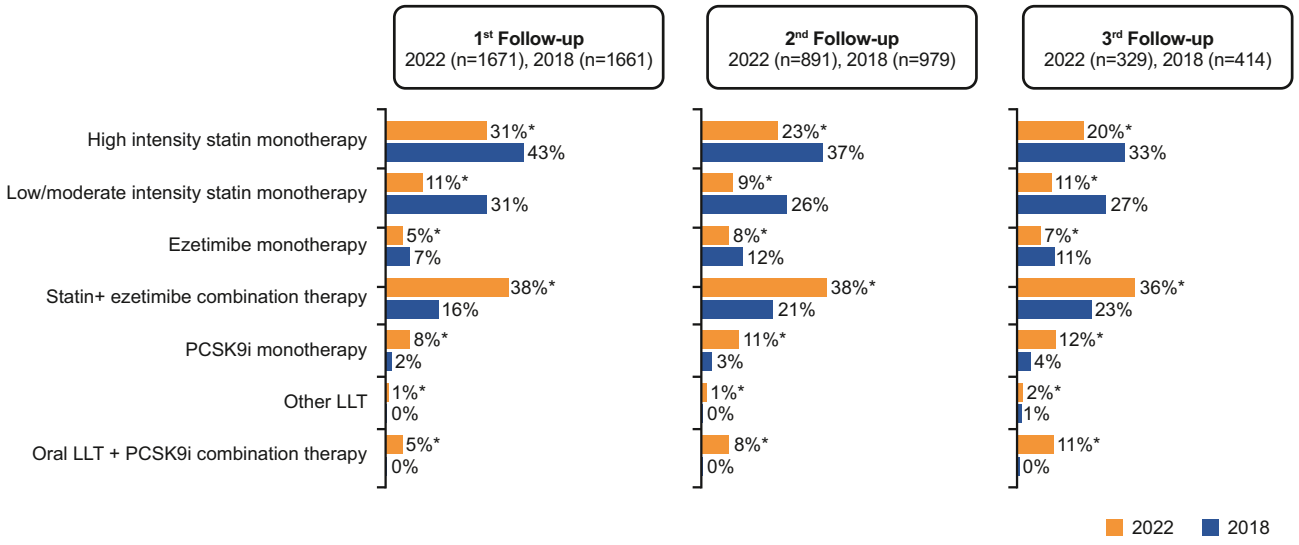

Fig. 2. Pharmacological approach during chronic phase.
Pharmacological approach at 1st, 2nd and 3rd follow-ups during chronic phase is depicted.
*Significant difference between 2022 and 2018.
Data derived from answers to questionnaire sections: P32_3, P32_7.
LLT, lipid-lowering therapy; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor.

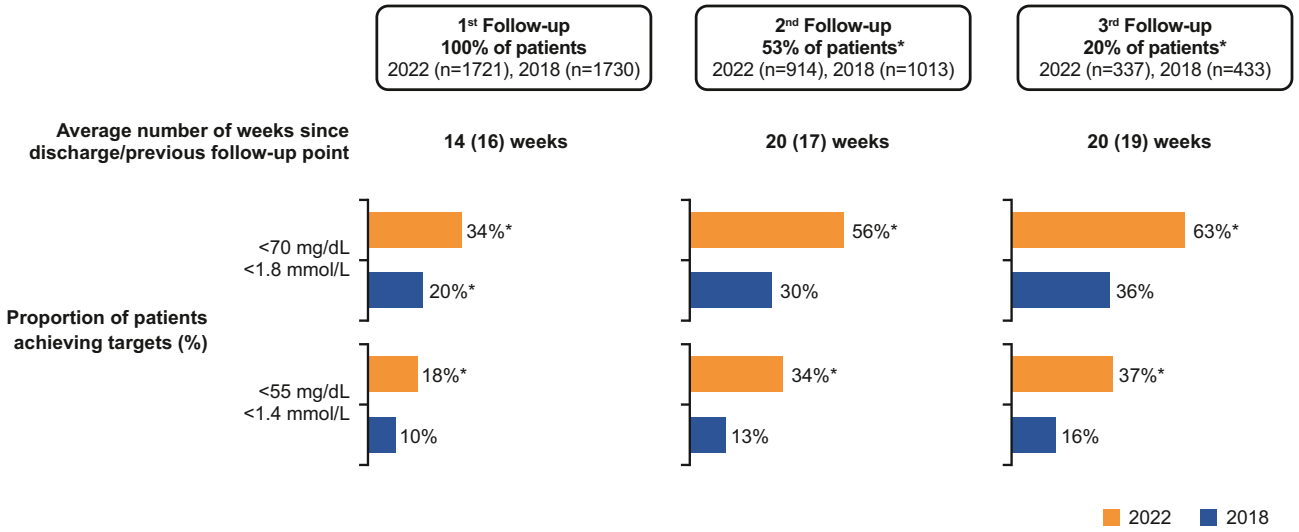

Fig. 3. Achievement of LDL-C goals at follow-up visits.
Achievement of LDL-C goals at 1st, 2nd and 3rd follow-up visits is depicted.
*Significant difference between 2022 and 2018.
Data derived from answers to questionnaire sections: P31, P32_3, P32_4.
LDL-C, low-density lipoprotein cholesterol.

medical education to support the implementation of the 2019 ESC/EAS lipid guidelines and to improve patient management approaches.

Patients with FH are at increased CV risk due to their lifelong exposure to elevated LDL-C levels. The prevalence of FH is significantly higher among patients with ACS, representing an opportunity to identify patients with FH and initiate screening in family members. [13] In the 2022 survey, the population with FH was greater than in 2018. This may indicate increased awareness for this condition, which may have led to increased screening rates. Genetic testing was limited, which is a barrier to establishing accurate prevalence figures.

The results of the ACS EuroPath I–III project showed that lipid management was suboptimal and found a lack of physicians' compliance with the ESC/EAS 2016 guidelines. [7] Similar results were observed in other registries, including in the EUROASPIRE V survey (conducted between 2016 and 2017; 7824 patients from 27 countries), which assessed dyslipidaemia management in coronary heart disease patients. [14] Here, high-intensity LLT was reported in less than half of the patients at admission; LDL-C control was better in those on high-intensity LLT compared with those on low- or moderate-intensity LLT. [14] However, another survey of treatment patterns and LDL-C goal attainment in Germany in 2012–2014 found that approximately 80% of ASCVD patients on moderate−/high-intensity statins had LDL-C $\geq$ 70 mg/dL. [15] Despite low attainment of LDL-C goals, very few patients in the described studies changed their treatment regimens. [14,15] Similarly, the DA VINCI study (conducted between 2017 and 2018) demonstrated that among high- and very high-risk patients receiving preventative LLT, fewer than half achieved 2016 LDL-C goals. [16]

This analysis has limitations. Participating respondents may not be

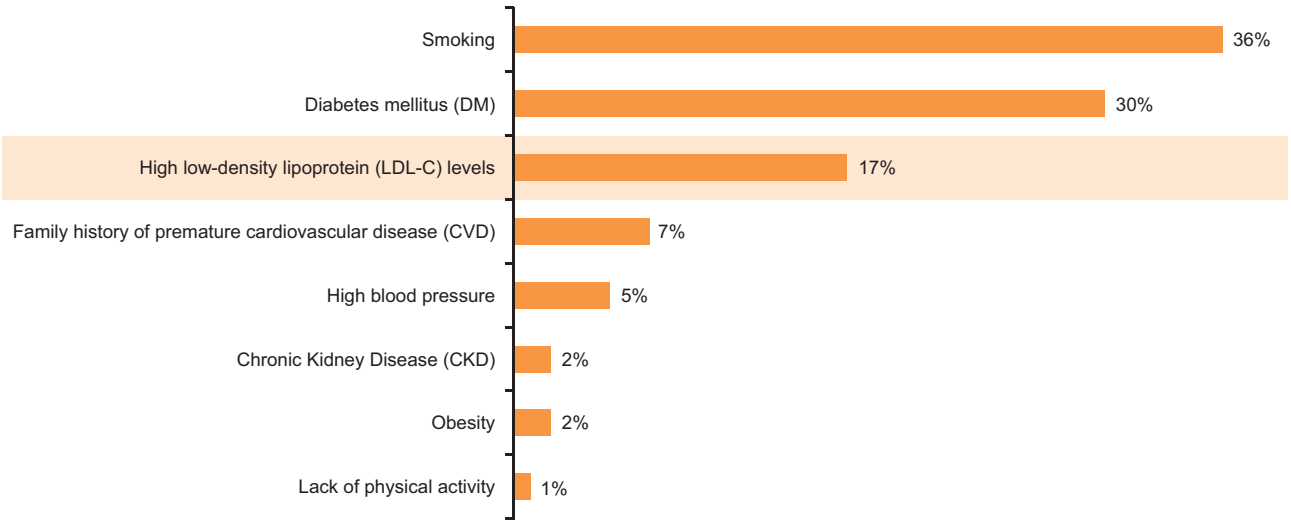

Fig. 4. Priority order of risk factors when managing post-ACS patients.
Assessment of priority order of risk factors when managing post-ACS patients is depicted.
Data from 2022 only (n = 530), ranked from highest to lowest priority.
Data derived from answers to questionnaire sections: X1.

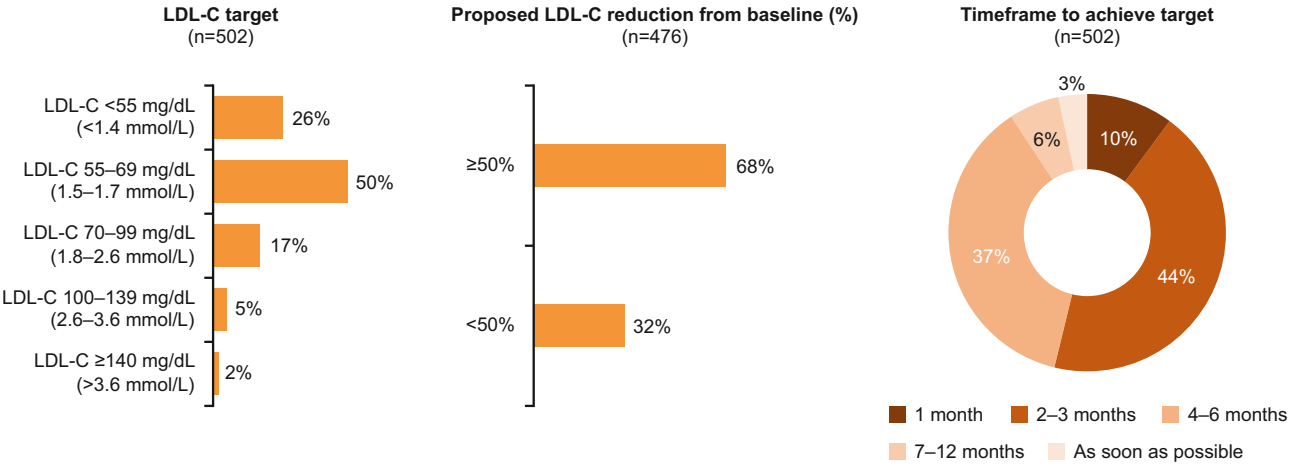

Fig. 5. Recommendations of HCPs for LDL-C goals and timeframe for achievement.
HCP recommendations for LDL-C goals and appropriate timeframes for achievement are depicted.
Data from 2022 only.
Note: 5% of respondents would not typically set an LDL-C goal or % of LDL-C levels reduction. No HCPs recommended a timeframe >12 months or stated that they did not know what timeframe to select.
HCP, healthcare professional; LDL-C, low-density lipoprotein cholesterol.

representative of all treating physicians in general, but this limitation is common to other surveys [14]. The evaluations were based on information provided by physicians, which might induce a selection bias. The data from the six European countries included may not reflect other countries in the world. Nevertheless, the results of these two large surveys provide a valuable snapshot of the current clinical practice and the unique opportunity to assess the impact of the ESC/EAS 2019 guidelines. The results clearly indicate the need for better upstream approaches to LDL lowering after an ACS, including the need for increasing awareness of LDL as a risk factor, early implementation of strategies of combination therapy and better communication among stakeholders to ensure persistent attention to LDL goals after discharge. Implementation of the practical protocols in place should be assessed as part of site certification. Specific lipid management recommendations should be provided in the discharge letter and increased awareness of LDL-C treatment goals for the very high-risk patient population is required. Timing of the first follow-up visit should be set during first 4–6 weeks after discharge from hospital in order to monitor LDL-C levels and intensify lipid lowering treatment if the treatment goal has not been achieved. A recommendation should be made in the discharge letter for general practitioners to continue to monitor their patients' progress with lipid lowering treatment over the long term (i.e. at the second follow-up and beyond), as this will hopefully ensure that the patient receives the most appropriate treatment and thus make it more likely that they will achieve therapeutic goal. We also recommend that many post-ACS patients would benefit from undergoing cardiac rehabilitation (per European guideline recommendations), as this has been shown to promote patient adherence to their post-ACS treatment regimen and to reduce post-ACS mortality [5,17,18].

In conclusion, LDL-C control and goal achievement has improved between 2018 and 2022 in the specified countries, which is encouraging. However, patient management is still suboptimal, identifying very important opportunities to further improve patient outcomes after an ACS.

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Author contributions

All authors had access to relevant data, and participated in the writing, review and approval of the manuscript. All authors were involved in study concept and design, acquisition of data, analysis, and interpretation of data, drafting of the manuscript and critical revision of the manuscript for important intellectual content.

Ethics statement

Participants in all surveys provided informed written consent for their information to be collected and used for market research, and also used on an aggregated basis for external publication purposes.

CRediT authorship contribution statement

Ulrich Laufs: Conceptualization, Methodology, Investigation, Writing – original draft, Writing – review & editing, Visualization, Supervision. **Alberico Luigi Catapano:** Conceptualization, Methodology, Investigation, Writing – review & editing, Supervision. **Raffaele De Caterina:** Conceptualization, Investigation, Writing – review & editing, Supervision. **François Schiele:** Conceptualization, Investigation, Writing – review & editing, Supervision. **Alessandro Sionis:** Conceptualization, Investigation, Writing – review & editing, Supervision. **Azfar Zaman:** Conceptualization, Investigation, Writing – review & editing, Supervision. **J. Wouter Jukema:** Conceptualization, Investigation, Writing – review & editing, Supervision.

Declaration of Competing Interest

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Data availability

Qualified researchers may request access to patient level data and related study documents including the clinical study report, study protocol with any amendments, blank case report form, statistical analysis plan, and dataset specifications. Patient level data will be anonymised and study documents will be redacted to protect the privacy of our trial participants. Further details on Sanofi's data sharing criteria, eligible studies, and process for requesting access can be found at https://www.vivli.org/.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vph.2023.107141.

References

[1] S. Johansson, A. Rosengren, K. Young, E. Jennings, Mortality and morbidity trends after the first year in survivors of acute myocardial infarction: a systematic review, BMC Cardiovasc. Disord. 17 (1) (2017) 53, https://doi.org/10.1186/s12872-017-0482-9.

[2] B. Ibanez, S. James, S. Agewall, M.J. Antunes, C. Bucciarelli-Ducci, H. Bueno, A.L. P. Caforio, F. Crea, J.A. Goudevenos, S. Halvorsen, G. Hindricks, A. Kastrati, M. J. Lenzen, E. Prescott, M. Roffi, M. Valgimigli, C. Varenhorst, P. Vranckx, P. Widimsky, E.S.C.S.D. Group, 2017 ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: the task force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC), Eur. Heart J. 39 (2) (2018) 119–177, https://doi.org/10.1093/eurheartj/ehx393.

[3] M. Alings, O. Descamps, B. Guillon, M. Leosdottir, A.P. Maggioni, L. Recasens, W. S. Speidl, R.V. Tripodi, U. Landmesser, A.L. Catapano, A. Pirillo, Implementation of clinical practices and pathways optimizing ACS patients lipid management: Focus on eight European initiatives, Atheroscler Suppl 42 (2020) e59–e64, https://doi.org/10.1016/j.atherosclerosissup.2021.01.010.

[4] Q. Wang, C. Liang, Role of lipid-lowering therapy in low-density lipoprotein cholesterol goal attainment: focus on patients with acute coronary syndrome, J. Cardiovasc. Pharmacol. 76 (6) (2020) 658–670, https://doi.org/10.1097/FJC.0000000000000914.

[5] F. Mach, C. Baigent, A.L. Catapano, K.C. Koskinas, M. Casula, L. Badimon, M. J. Chapman, G.G. De Backer, V. Delgado, B.A. Ference, I.M. Graham, A. Halliday, U. Landmesser, B. Mihaylova, T.R. Pedersen, G. Riccardi, D.J. Richter, M. S. Sabatine, M.R. Taskinen, L. Tokgozoglu, O. Wiklund, 2019 ESC/EAS guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk, Eur. Heart J. 41 (1) (2020) 111–188, https://doi.org/10.1093/eurheartj/ehz455.

[6] A.L. Catapano, I. Graham, G. De Backer, O. Wiklund, M.J. Chapman, H. Drexel, A. W. Hoes, C.S. Jennings, U. Landmesser, T.R. Pedersen, Ž. Reiner, G. Riccardi, M.-R. Taskinen, L. Tokgozoglu, W.M.M. Verschuren, C. Vlachopoulos, D.A. Wood, J. L. Zamorano, M.-T. Cooney, E.S.D. Group, ESC/EAS guidelines for the Management of Dyslipidaemias, Eur. Heart J. 37 (39) (2016) 2999–3058, https://doi.org/10.1093/eurheartj/ehw272.

[7] U. Landmesser, A. Pirillo, M. Farnier, J.W. Jukema, U. Laufs, F. Mach, L. Masana, T. R. Pedersen, F. Schiele, G. Steg, M. Tubaro, A. Zaman, P. Zamorano, A.L. Catapano, Lipid-lowering therapy and low-density lipoprotein cholesterol goal achievement in patients with acute coronary syndromes: The ACS patient pathway project, Atheroscler. Suppl. 42 (2020) e49–e58, https://doi.org/10.1016/j.atherosclerosissup.2021.01.009.

[8] A. Sionis, A.L. Catapano, G.M. De Ferrari, D. Dudek, J.W. Jukema, U. Landmesser, A. Pirillo, F. Schiele, A. Zaman, J.L. Zamorano, Improving lipid management in patients with acute coronary syndrome: the ACS lipid EuroPath tool, Atheroscler Suppl 42 (2020) e65–e71, https://doi.org/10.1016/j.atherosclerosissup.2021.01.011.

[9] G.G. Schwartz, P.G. Steg, M. Szarek, D.L. Bhatt, V.A. Bittner, R. Diaz, J. M. Edelberg, S.G. Goodman, C. Hanotin, R.A. Harrington, J.W. Jukema, G. Lecorps, K.W. Mahaffey, A. Moryusef, R. Pordy, K. Quintero, M.T. Roe, W.J. Sasiela, J. F. Tamby, P. Tricoci, H.D. White, A.M. Zeiher, O.O. Committees, Investigators, Alirocumab and Cardiovascular Outcomes after Acute Coronary Syndrome, N. Engl. J. Med. 379 (22) (2018) 2097–2107, https://doi.org/10.1056/NEJMoa1801174.

[10] M.S. Sabatine, R.P. Giugliano, A.C. Keech, N. Honarpour, S.D. Wiviott, S. A. Murphy, J.F. Kuder, H. Wang, T. Liu, S.M. Wasserman, P.S. Sever, T.R. Pedersen, Evolocumab and clinical outcomes in patients with cardiovascular disease, N. Engl. J. Med. 376 (18) (2017) 1713–1722, https://doi.org/10.1056/NEJMoa1615664.

[11] B.A. Ference, H.N. Ginsberg, I. Graham, K.K. Ray, C.J. Packard, E. Bruckert, R. A. Hegele, R.M. Krauss, F.J. Raal, H. Schunkert, G.F. Watts, J. Borén, S. Fazio, J. D. Horton, L. Masana, S.J. Nicholls, B.G. Nordestgaard, B. van de Sluis, M.-R. Taskinen, L. Tokgözoğlu, U. Landmesser, U. Laufs, O. Wiklund, J.K. Stock, M. J. Chapman, A.L. Catapano, Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European atherosclerosis society consensus panel, Eur. Heart J. 38 (32) (2017) 2459–2472, https://doi.org/10.1093/eurheartj/ehx144.

[12] K.C. Koskinas, A.L. Catapano, C. Baigent, L. Tokgozoglu, F. Mach, Current perceptions and practices in lipid management: results of a European Society of Cardiology/European atherosclerosis society survey, Eur, J Prev Cardiol 28 (18) (2022) 2030–2037, https://doi.org/10.1093/eurjpc/zwaa156.

[13] Y. Yu, L. Chen, H. Zhang, Z. Fu, Q. Liu, H. Zhao, Y. Liu, Y. Chen, Association Between Familial Hypercholesterolemia and Risk of Cardiovascular Events and Death in Different Cohorts: A Meta-Analysis of 1.1 Million Subjects, Front Cardiovasc Med 9 (2022) 860196, https://doi.org/10.3389/fcvm.2022.860196.

[14] G. De Backer, P. Jankowski, K. Kotseva, E. Mirrakhimov, Z. Reiner, L. Ryden, L. Tokgozoglu, D. Wood, D. De Bacquer, E.V. collaborators, C. Writing, C. Scientific Steering/ Executive, c. Coordinating, c. Diabetes, c. Data management, c. Statistical analysis, l. Central, o.i. Study centres, p. other research, Management of dyslipidaemia in patients with coronary heart disease: Results from the ESC-EORP EUROASPIRE V survey in 27 countries, Atherosclerosis 285 (2019) 135–146, https://doi.org/10.1016/j.atherosclerosis.2019.03.014.

[15] K.M. Fox, M.-H. Tai, K. Kostev, M. Hatz, Y. Qian, U. Laufs, Treatment patterns and low-density lipoprotein cholesterol (LDL-C) goal attainment among patients receiving high- or moderate-intensity statins, Clin. Res. Cardiol. 107 (5) (2018) 380–388, https://doi.org/10.1007/s00392-017-1193-z.

[16] K.K. Ray, B. Molemans, W.M. Schoonen, P. Giovas, S. Bray, G. Kiru, J. Murphy, M. Banach, S. De Servi, D. Gaita, I. Gouni-Berthold, G.K. Hovingh, J.J. Jozwiak, J. W. Jukema, R.G. Kiss, S. Kownator, H.K. Iversen, V. Maher, L. Masana, A. Parkhomenko, A. Peeters, P. Clifford, K. Raslova, P. Siostrzonek, S. Romeo, D. Tousoulis, C. Vlachopoulos, M. Vrablik, A.L. Catapano, N.R. Poulter, D.V. study, EU-Wide Cross-Sectional Observational Study of Lipid-Modifying Therapy Use in Secondary and Primary Care: the DA VINCI study, Eur. J. Prev. Cardiol. 28 (11) (2021) 1279–1289, https://doi.org/10.1093/eurjpc/zwaa047.

[17] M. Ambrosetti, A. Abreu, U. Corra, C.H. Davos, D. Hansen, I. Frederix, M.C. Iliou, R.F. Pedretti, J.P. Schmid, C. Vigorito, H. Voller, M. Wilhelm, M.F. Piepoli, B. Bjarnason-Wehrens, T. Berger, A. Cohen-Solal, V. Cornelissen, P. Dendale, W. Doehner, D. Gaita, A.B. Gevaert, H. Kemps, N. Kraenkel, J. Laukkanen, M. Mendes, J. Niebauer, M. Simonenko, A.O. Zwisler, Secondary prevention through comprehensive cardiovascular rehabilitation: From knowledge to implementation. 2020 update. A position paper from the Secondary Prevention and Rehabilitation Section of the European Association of Preventive Cardiology, Eur. J. Prev. Cardiol. (2020), https://doi.org/10.1177/2047487320913379.

[18] B. Rauch, C.H. Davos, P. Doherty, D. Saure, M.I. Metzendorf, A. Salzwedel, H. Voller, K. Jensen, J.P. Schmid, E.A.o.P.C.i.c.w.t.I.o.M.B. Cardiac Rehabilitation Section, D.o.M.B.U.o.H. Informatics, M. the Cochrane, I.o.G.P.H.-H.U.D.G, Endocrine disorders group, the prognostic effect of cardiac rehabilitation in the era of acute revascularisation and statin therapy: A systematic review and meta-analysis of randomized and non-randomized studies - the Cardiac Rehabilitation outcome study (CROS), Eur, J Prev Cardiol 23 (18) (2016) 1914–1939, https://doi.org/10.1177/2047487316671181.