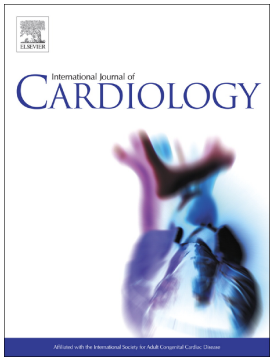

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Use of guideline-recommended management in established coronary heart disease in the observational DYSIS II study

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[1] This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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Contributors: JF, DL, BMA, PB and AKG created the study design, the study hypothesis, wrote the protocol, selected the countries, analyzed the data and wrote the manuscript.

MH performed the statistical analysis.

GMDF, AV, CAB, LDB, MV-R, WA, FTC, KKP, ME, and PB contributed to patient recruitment and participated in writing the paper.

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ABSTRACT

Background: Guidelines recommend lifestyle modification and medications to control risk factors in coronary heart disease (CHD). Using data from the observational DYSIS II study, we sought to evaluate the use of guideline-recommended treatments at discharge for acute coronary syndromes or in the chronic phase for CHD, and participation in rehabilitation/secondary prevention programs.

Methods and results: Between 2013 and 2014, 10,661 patients (3867 with ACS, 6794 with stable CHD) were enrolled in 332 primary and secondary care centers in 18 countries (Asia-Pacific, Europe, Middle East/Africa). Patients with incident ACS were younger and more likely to be smokers than patients with recurrent ACS or stable CHD (both p<0.0001). Sedentary lifestyle was common (44.4% of ACS patients; 44.2% of stable CHD patients); 22.8% of ACS patients and 24.3% of stable CHD patients were obese. Prevalence of low high-density lipoprotein cholesterol (<40 mg/dL in men/50 mg/dL in women) was 46.9% in chronic CHD and 55.0% in ACS. Rates of secondary prevention medications were lower among CHD versus ACS (all p<0.0001): antiplatelet 94.3% vs 98.0%, beta-blocker 72.0% vs 80.0%, lipid-lowering therapy 94.7 vs 97.5%, and angiotensin-converting enzyme inhibitors/angiotensin-receptor blockers 69.4% vs 73.7%, respectively. Attendance at cardiac rehabilitation (16.8% of patients with a first ACS, 10.8% with recurrent ACS) or a secondary prevention program (3.7% of ACS and 11.7% of stable CHD patients) was infrequent.

Conclusions: The high prevalence of risk factors in all CHD patients and reduced rates of secondary prevention medications in stable CHD offer areas for improvement.

Translational aspects: The findings of DYSIS II may reinforce the importance of adopting a healthy lifestyle and prescribing (by clinicians) and adhering (by patients) to evidence-based medications in the management of coronary heart disease, not only during the short-term but also over the longer term after a cardiac ischemic event. The results may help to increase the proportion of ACS patients who are referred to cardiac rehabilitation centres.

Abbreviations

ACS, Acute coronary syndrome; CHD, coronary heart disease; CKD, chronic kidney disease; DYSIS II, Dyslipidemia International Study II; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LLT, lipid-lowering therapy; MDRD, Modification of Diet in Renal Disease; NSTEMI, non−ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction.

1 Introduction

Cardiovascular disease, comprising ischemic heart disease and stroke, is the leading cause of mortality worldwide [1]. Of the 56.4 million deaths in 2015, cardiovascular disease accounted for 15 million [1]. Major efforts are needed on a global scale to reduce mortality and morbidity from cardiovascular disease. Acute coronary syndrome (ACS) presents as a spectrum of clinical conditions encompassing unstable angina, non−ST-segment elevation myocardial infarction (NSTEMI) and ST-segment elevation myocardial infarction (STEMI). During the acute phase of ACS, which generally lasts around 2 months [2, 3], patients are at very high risk for recurrent events [4, 5]. The likelihood of such an event can be reduced by using secondary prevention strategies [2, 6], but some patients retain a substantial long-term residual risk. In the REACH Registry, the risk of cardiovascular death, myocardial infarction or stroke increased annually in patients with a previous myocardial infarction (but without prior stroke or transient ischemic attack), from 4.7% in the first year and reaching 15.1% by 4 years of follow-up [7]. Factors associated with a recurrence were congestive heart failure, polyvascular disease, diabetes, atrial fibrillation or flutter, and older age, whereas statin use was associated with a lower risk. These findings emphasize the benefit of intensive secondary prevention strategies to minimize residual risk. The situation is further complicated by decreasing adherence to secondary prevention treatments after discharge from hospital [8-14]. European guidelines advocate immediate reperfusion with primary angioplasty or fibrinolytic therapy for STEMI, and an invasive strategy for NSTEMI patients with moderate-risk to very high-risk characteristics [14, 15]. Lifestyle modification and early uptake of evidence-based drugs to control risk factors are also recommended [14-18]. Several large national [19] and multinational [13, 20, 21] observational studies have indicated that patients with coronary heart disease (CHD) are still inadequately treated, with wide variations in adherence to evidence-based medicine, leading to failure to achieve treatment targets and optimize risk factor reduction. Given the global impact of CHD, robust contemporary data from across the globe are needed for the spectrum of conditions that manifest as CHD. The DYSIS II (Dyslipidemia International Study II) was a multinational observational study in adults with established CHD, presenting as either an ACS or stable CHD [22]. The aim of this analysis was to document patterns of secondary prevention, including evidence-based drug use and cardiac rehabilitation in several world regions (Asia, Europe and the Middle East).

2 Methods

2.1 Study design and patient population

DYSIS II was a multinational observational study in adults with established CHD. The study design has been described [22]. Eighteen countries in Asia (Hong Kong, India, Indonesia, Philippines, Singapore, South Korea, Taiwan, Vietnam), Europe (Belgium, France, Greece, Ireland, Italy, Russia), and the Middle East (Jordan, Lebanon, Saudi Arabia, United Arab Emirates) enrolled patients into the study between 2013 and 2014. Two distinct samples were enrolled: patients hospitalized with an ACS and patients with stable CHD.

The study was conducted in accordance with good epidemiological and clinical practice, and all applicable laws, rules and regulations, and was approved by the authorities in all participating countries. Patients provided written informed consent to participate.

2.2 Patients with an ACS

Acute care centers and site investigators were geographically distributed to be representative of the acute and ambulatory treatment of secondary prevention in each of the countries. Study enrollment was designed to include a representative cohort of lipid-treated patients at the time of the acute event. Physicians were encouraged to include patients consecutively. Eligibility criteria for ACS patients were age ≥18 years; hospitalization for an ACS (STEMI, left bundle branch block, NSTEMI, or unstable angina) at the time of enrollment; full lipid profile performed on blood drawn within 24 hours of admission; and treatment with lipid-lowering therapy (LLT) for ≥3 months or no treatment with LLT at the time of the lipid test. Data were collected by clinical examination and from medical charts at admission to the hospital and at discharge.

2.3 Patients with stable CHD

Physicians were representative of those managing patients for secondary cardiovascular prevention in the countries involved in DYSIS II, and included internists, cardiologists, general practitioners, and endocrinologists. To avoid selection bias, participating centers were strongly encouraged to enroll all consecutive patients who fulfilled the inclusion criteria. Eligibility criteria for patients with stable CHD were age ≥18 years, stable CHD, and attendance at a single physician outpatient appointment. CHD was defined as the presence of 1 or more of the following: >50%

stenosis on coronary angiography or computed tomography; previous percutaneous coronary intervention; previous coronary artery bypass graft; and history of ACS >3 months previously. Patients were required to have had a fasting lipid profile done within the previous 12 months, either while on LLT for ≥3 months or while not on any LLT. Patients with a history of ACS within the previous 3 months and patients enrolled in clinical trials involving medication were excluded.

2.4 Data collected and study definitions

Data on patient characteristics, risk factors, treatments (LLT and selected concomitant pharmacological therapies) and laboratory values were collected using a web-based data collection form developed by Institut für Herzinfarktforschung, Ludwigshafen, Germany. Demographic and clinical variables collected at enrollment included age, sex, body mass index, sedentary lifestyle, smoking status, family history of CHD, hypertension, type 2 diabetes mellitus, history of ACS, myocardial infarction, unstable angina, chronic kidney disease (CKD), congestive heart failure, stroke (ischemic or hemorrhagic), and peripheral vascular disease.

Obesity was defined as a body mass index >30 kg/m². Hypertension was defined as the treating physician's diagnosis or use of blood pressure-lowering medication or sitting blood pressure >140/90 mmHg. Diabetes was defined as current treatment for diabetes, a previous diagnosis of diabetes, or a fasting plasma glucose value ≥126 mg/dL. Sedentary lifestyle was defined as <20−30 minutes of walking on <3−4 days per week. Use of selected classes of cardiovascular medications (antiplatelets, beta-blockers, LLT, angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers) and laboratory values of hemoglobin A1c and glucose at admission were recorded. History of CKD was checked by the investigator on the case report form. Renal function was measured using estimated glomerular filtration rate, calculated using the Modification of Diet in Renal Disease (MDRD) study equation [23]. An estimated glomerular filtration rate (eGFR) of <60 mL/min/1.73 m² indicated patients with renal dysfunction (ranging from mild to severe, and including renal failure).

The lipid profile included measurements of serum levels of high-density lipoprotein cholesterol (HDL-C) and triglycerides. Low HDL-C was defined as <40 mg/dL in men and <50 mg/dL in women, and high triglycerides as >150 mg/dL or >200 mg/dL. Residual (or atherogenic) dyslipidemia was defined as a composite of high triglycerides (>200 mg/dL) and low HDL-C [24].

2.5 Statistical analysis

Assuming a prevalence of lipid abnormalities (low-density lipoprotein cholesterol [LDL-C] ≥1.8 mmol/L/70 mg/dL) between 20% and 60%, a sample size of 7500 would allow the survey to estimate the prevalence with a given precision of ±1.25% (range of 95% CI 2.5%). This size guarantees sufficient information for estimating the prevalence in smaller subgroups (e.g. CKD with a prevalence of 30% and precision of +2.3% (range of 95% CI 4.6%).

Continuous variables are presented as mean (standard deviation [SD]) or median (interquartile range [IQR]), and categorical variables as number (percentage). All values are reported among patients with available data. Patients in the ACS population were divided into subgroups based on whether the ACS was a first or a recurrent event (defined as previous CHD, myocardial infarction, stable or unstable angina, congestive heart failure, heart transplant or valvular heart disease). Demographic and clinical variables at admission were compared using chi-square or Mann-Whitney-Wilcoxon tests. LDL-C target value attainment was assessed by pre-ACS risk classification and then, with all patients classified as very high risk, by time point (admission and follow-up). Lipid profiles and types of LLT used at admission and follow-up were assessed descriptively. A P-value <0.05 was considered statistically significant. SAS version 9.3 (Cary, NC, USA) was used for all the statistical analyses.

3 RESULTS

3.1 Study Population

A total of 10 661 patients with established CHD from 18 countries were enrolled in DYSIS II. Of these patients, 6794 had stable disease and 3867 had an ACS, 49.4% of whom had a recurrent event. Baseline characteristics of the study population according to type of CHD are detailed in Table 1 and the online supplementary appendix table 1. Patients with a first ACS event had a high prevalence of cardiovascular risk factors (Graphical abstract); they were younger than patients with a recurrent event or with stable CHD and had a lower prevalence of CKD and hypertension and a less frequent history of stroke, peripheral vascular disease, and heart failure. Patients with a first ACS also had a lower prevalence of family history of CHD, obesity, and sedentary lifestyle, but a much higher rate of current smoking and of serum plasma glucose values ≥126 mg/dL (7 mmol/L) versus those with a recurrent

event and patients with stable disease. Half of the ACS patients had metabolic syndrome (Adult Treatment Panel III) versus 37.0% of those with stable CHD.

Mean (SD) eGFR in the overall population with stable CHD was 79.9 (25.6) mL/min/1.73 m² (56.4 [32.2] mL/min/1.73 m² in patients with CKD). Corresponding data in the ACS population were 83.7 (28.3) mL/min/1.73 m² (65.6 [47.3] mL/min/1.73 m²). In the overall population, the prevalence of renal dysfunction was lowest in patients with an ACS (17.7% vs 20.2%), driven by a 13.8% rate in those with a first event. A similar pattern was observed in the subgroup with CKD.

Low HDL-C values were reported in 55.0% of ACS patients and in 46.9% of stable CHD patients, and triglyceride values >200 mg/dL in 18.9% and 14.1%, respectively. Residual dyslipidemia was identified in 12.9% of ACS patients and in 9.3% of stable CHD patients.

3.2 Secondary Prevention Medications

As shown in Table 2, the use of secondary prevention medications was higher in ACS patients (recorded at discharge from hospital) than in patients with stable CHD (reported as chronic use) (all p<0.0001). The percentage of patients who did not receive secondary prevention treatments at discharge after an ACS is illustrated in the Graphical abstract. Most patients were taking antiplatelet therapy (either aspirin or a P2Y12 inhibitor); the rate was highest among patients with a recurrent ACS, slightly lower among those with a first event, and lowest in those with stable CHD (p<0.0001). Almost one third of patients with stable disease were on dual antiplatelet therapy compared with 86.1% of patients with an ACS. The rate of beta-blocker use was similar in ACS patients with a first or recurrent event (both at 80%), compared with 72.0% of patients with stable CHD. The use of angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers was highest in patients with recurrent ACS.

LLT, most commonly statins, was being taken by 97.5% of ACS patients and by 94.7% of patients with stable CHD. The mean statin dose, calculated in atorvastatin dose equivalents, was higher in ACS patients (Fig. 1A). The use of combination LLT therapy comprising a statin and nonstatin (most often ezetimibe) was highest in stable CHD patients and lowest in patients with a first ACS (15.6% vs 6.5%, respectively; p<0.0001). The use of combination therapy with a statin plus ezetimibe is illustrated in Fig. 1B.

3.3 Cardiac Rehabilitation and Patient Education

Cardiac rehabilitation (for ACS patients) was infrequent (Graphical abstract), with 16.8% of those with a first event versus only 10.8% with a recurrent event participating in a program (Table 3). In stable CHD, 11.7% of patients reported participating in a disease management program or patient education program for CHD, and 6.6% in a similar program for diabetes. The rates of ACS patients were lower, at 3.7% and 3.5%, respectively.

3.4 Geographic variations

Patient profiles and secondary prevention strategies, according to geographic region, are detailed in online supplementary appendix tables 2 to 10. In Europe, the mean statin dose (atorvastatin dose equivalent) was 27 ± 20 in stable CHD and 34 ± 24 in recurrent ACS, and 17.7% and 10.5%, respectively, were on combination LLT (online Table 3); 40.9% of patients with a first ACS were referred for cardiac rehabilitations versus 23.2% with a recurrent ACS (online Table 4). Patients in the Middle East had very high rates of use of coronary medications and were on a moderate- or high-intensity statin dose (mean atorvastatin dose equivalent: 44 ± 19 in ACS and 30 ± 18 in stable CHD); 19.2% of patients with stable CHD and 18.1% with a recurrent ACS were on combination LLT therapy (online Table 6). However, only 6.5% of Middle Eastern patients with an ACS were referred for a cardiac rehabilitation program (online Table 7). The mean statin dose in the Asian population was 20 ± 15 in stable CHD and 29 ± 19 in patients with a recurrent ACS; and 12.0% and 5.2%, respectively, were on combination LLT (online Table 9). A minority (4.2%) of Asian patients with an ACS were referred for a cardiac rehabilitation program (online Table 10).

4 Discussion

The multinational observational DYSIS II study provides insights into the clinical profile and management of patients with established CHD from Asia, Europe and the Middle East. Our study shows that substantial proportions of patients with CHD are current smokers, particularly ACS patients with a first event, are obese and have a sedentary lifestyle, and consequently have hypertension and diabetes mellitus. Of concern is that only a small percentage of patients participate in a cardiac rehabilitation or prevention program. Furthermore, the use of evidence-based therapies was lower in patients with stable disease, with approximately 1 in 5 patients not taking aspirin and 1 in 10 not taking

statin. These findings indicate opportunities for improvement in the management of patients with CHD in several geographic regions.

The EUROASPIRE IV study [25], undertaken in 24 European countries and involving 16 426 coronary patients aged <80 years, reported disappointing rates of adherence to secondary prevention standards, including smoking cessation, healthy diet and physical activity. Furthermore, despite high levels of use of evidence-based therapies for CHD, therapeutic targets were not achieved in a substantial proportion of these high-risk patients, and one-half were not advised to participate in cardiac prevention and rehabilitation programs. Our present findings from DYSIS II, involving patients not only from Europe but also from the Middle East and Asia, show similar overall patterns to patients in EUROASPIRE IV, with a high prevalence of risk factors such as current smoking, hypertension and diabetes. Additionally, they provide insights into the use of cardiac medications and patient lifestyle factors after a first and a subsequent ACS event, and also among patients with stable CHD. Of note, the rates of use of cardiac medications were high among patients in the Middle East, whereas lower rates (and lower intensity of statin therapy) were observed in Asia.

The DYSIS II study has already shown that despite generally high rates of LLT, albeit at a low to moderate intensity dose, only 26% of ACS patients and 31% of patients with stable CHD achieve the recommended LDL-C levels of <70 mg/dL (<1.8 mmol/L) [26]. The authors reported that use of higher doses of statins and/or combination therapy is likely to improve attainment of lipid goals and thus reduce cardiovascular morbidity and mortality. Our present study from DYSIS II adds further to these findings, highlighting suboptimal achievement of risk factor goals, and of adherence to secondary prevention medications during the chronic stage of disease, combined with limited attendance at cardiac prevention programs.

There is a clear and established epidemiological relationship between high HDL-C and reduced risk of myocardial infarction [27]. However, this relationship does not appear to hold true for patients with very high HDL-C levels [28], and data from genome-wide association studies failed to demonstrate an effect of high HDL-C on CHD risk [29]. In terms of pharmacotherapy, neither DAL-OUTCOME [30] nor AIM-HIGH [31], two major randomized outcome trials designed to test the effect of pharmacological HDL-C raising, showed any decrease in cardiovascular effects versus control. The recently completed and published REVEAL trial [32] confirmed this finding, in which anacetrapib lowered LDL-C and raised HDL-C level, but the 9% risk reduction corresponded to lowering only the

apolipoprotein B fractions. In our present study, a high percentage of patients had elevated triglycerides and/or low HDL-C values, both of which are independently associated with elevated CHD risk [5, 33]. The prevalence of these 2 conditions together (i.e., 'residual dyslipidemia') is common in patients with type 2 diabetes, CKD, abdominal obesity, insulin resistance, or who have a sedentary lifestyle [34, 35]. In our study, 9.3% of patients with stable CHD and 12.9% with an ACS had residual dyslipidemia. Whereas no evidence yet exists to identify target values, patients with residual dyslipidemia may derive cardiovascular benefit from lifestyle interventions (e.g., increased levels of physical activity to increase HDL-C levels) and pharmacotherapy [34]. Addressing residual dyslipidemia may therefore facilitate a reduction in the substantial cardiovascular risk that persists in patients with established CHD [36].

We observed clear gaps between evidence-based guideline recommendations and use of cardiac medications. Fourteen percent of patients with a recent ACS did not receive dual antiplatelet therapy, which is recommended in such patients in the absence of contraindications [37]. Almost all patients in our study received an ACE inhibitor or ARB, whereas approximately 1 in 5 patients did not receive a beta-blocker. This apparent failure to adhere to guideline recommendations may not have direct consequences for most patients, as its value in reducing cardiovascular morbidity and mortality appears limited after concomitant administration of a renin–angiotensin–aldosterone system inhibitor and statin [38].

In the present study, 8.8% of patients with stable CHD and 7% with an ACS had CKD, and are therefore a high priority for intensive advice about all risk factors [39]. A systematic review [40] and a large meta-analysis [41] confirmed the benefits of statin therapy in CKD. The randomized SHARP [42] trial demonstrated a 17% proportional reduction in major atherosclerotic events (nonfatal myocardial infarction or coronary death, nonhemorrhagic stroke, or any arterial revascularization procedure) of simvastatin plus ezetimibe in 9270 patients with CKD (stage 3A to 5 with no known history of myocardial infarction or coronary revascularization).

Adherence to behavioral advice (i.e., diet, exercise and smoking cessation) after an ACS is associated with a lower risk of recurrent cardiovascular events, including myocardial infarction, stroke and death [43]. Clark *et al* reported that programs of education, counselling and/or exercise lower the risk of death and myocardial infarction in patients with CHD [44]. These findings emphasize the importance of behavioral modification in the prevention of recurrent events after an ACS.

Consequently, patients hospitalized for an ACS should be referred for cardiac rehabilitation, comprising exercise training, risk factor modification, education, and psychological support to improve outcomes, and patients with stable CHD should undergo prevention programs for therapy optimization, adherence, and risk factor management to reduce the risk of a recurrence [15, 34]. The results of our study indicate suboptimal participation in such specialized prevention programs, particularly for ACS patients in the Middle East and Asia, for reasons we are unable to further investigate. Limited availability of such programs, and differences in national guidelines and standards, legislation and reimbursement factors, are likely to explain in part the low uptake. However, the results from several systematic reviews showed that exercise-based cardiac rehabilitation decreased the rate of hospital readmissions and improved health-related quality of life versus usual care after myocardial infarction or revascularization, with the potential to reduce mortality over the longer term [45]. Increasing the rates of referral and attendance at such cardiac prevention programs has the potential to improve clinical outcomes in patients with CHD, but can be limited by a lack of resources or differences in national or local practices. Efforts should, however, be made to address the reasons for the low rates of physician referral and/or patient attendance. These include electronic prompts or automatic referrals, structured follow-up by healthcare providers, early initiation of referral after discharge from hospital, and availability of nurse-led programs [34]. Additionally, the use of electronic communication and information technology to support remote clinical care (‘telerehabilitation’) may be useful in effecting changes in patient behavior, but evidence from randomized trials is needed to confirm the benefits reported to date [46, 47].

4.1 Limitations

DYSIS II offers insights into recent treatment practices in established CHD in several world regions, some of which have not been extensively studied. As an observational study, it is, however, subject to several limitations, including missing data. The eGFR values are, for example, limited by the absence of ethnicity data. Additionally, information on contraindications to secondary prevention medications, and tolerability issues that led to treatment cessation, was not available. Whereas attempts were made to involve healthcare providers who were representative of the physicians treating patients with established CHD, the data are pooled from countries with widely varying

healthcare systems, cultural practices, and ethnic compositions; these wide variations also preclude direct comparisons between countries.

5 Conclusion

The results from this observational study in patients with established CHD from Asia, Europe and the Middle East illustrate good adherence to evidence-based medications during the acute stage of disease, but also areas for improvement in their long-term management − when they achieve a more stable ischemic profile − and in the control of cardiovascular risk factors. The high prevalence of tobacco smoking, sedentary lifestyle, obesity, and consequently diabetes, and reduced rates of secondary prevention medications, is worrisome, given the high risk for future events in patients with CHD, and offers several areas for better risk factor control. This may be achieved through increased attendance at cardiac rehabilitation and prevention programs. Such programs offer simple approaches that target smoking cessation and weight control, encourage appropriate physical activity and adherence to secondary prevention medications, and educate patients about the value of their own behaviors in reducing the risk of recurrent ischemic events.

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Figure legend

Fig. 1 (A) Statin dose in AED (per US Federal Drug Administration) in CHD patients (chronic treatment) and in ACS patients (at discharge from hospital); and (B) use of combination therapy with ezetimibe plus statin. ACS indicates acute coronary syndrome; AED, atorvastatin equivalent dose; CHD, coronary heart disease.

Table 1

Patient demographics, medical history, and risk factors

Characteristics	CHD patients (N=6794)	ACS patients (recurrent event) (N=1911)	ACS patients (first event) (N=1956)	p value (3-way)[a]	All ACS patients (N=3867)	p value (CHD vs all ACS)[a]
Age (years)	65.3 (10.8) (N=6794)	64.1 (11.6) (N=1888)	60.6 (12.4) (N=1932)	<0.0001	62.3 (12.1) (N=3820)	<0.0001
Men	79.1 (5375)	76.1 (1455)	76.5 (1497)	<0.01	76.3 (2952)	<0.001
Medical history						
CKD	8.8 (597/6794)	9.6 (184/1910)	4.3 (85/1956)	<0.0001	7.0 (269/3866)	<0.001
Hypertension	75.5 (5130/6794)	82.3 (1572/1911)	73.2 (1432/1956)	<0.0001	77.7 (3004/3867)	<0.05
Diabetes mellitus	48.8 (2899/5940)	60.1 (982/1634)	56.7 (947/1670)	<0.0001	58.4 (1929/3304)	<0.0001
Stroke (ischemic or hemorrhagic)	5.4 (361/6680)	6.1 (115/1877)	4.2 (82/1932)	<0.05	5.2 (197/3809)	0.61
Peripheral vascular disease	9.1 (607/6670)	7.0 (132/1894)	2.8 (55/1937)	<0.0001	4.9 (187/3831)	<0.0001
COPD	6.1 (409/6664)	5.9 (111/1890)	3.8 (73/1939)	<0.001	4.8 (184/3829)	<0.01
Congestive heart failure	12.0 (809/6726)	10.9 (204/1871)	0	<0.0001	5.3 (204/3815)	<0.0001
Risk factors						
Family history of CHD	32.4 (1931/5969)	27.2 (477/1752)	23.9 (441/1846)	<0.0001	25.5 (918/3598)	<0.0001
BMI >30 kg/m² (obesity)	24.3	26.2	19.5	<0.0001	22.8	0.09

	(1641/6761)	(500/1905)	(377/1938)		(877/3843)	
Current smoking	12.2	20.9	33.3	<0.0001	27.2	<0.0001
	(830/6794)	(399/1911)	(652/1956)		(1051/3867)	
Sedentary lifestyle	44.2	47.0	41.8	<0.01	44.4	0.88
	(2836/6414)	(813/1731)	(739/1767)		(1552/3498)	
Metabolic syndrome (ATP	37.0	50.1	50.3	<0.0001	50.2	<0.0001
III)	(1307/3537)	(342/683)	(381/757)		(723/1440)	
Waist circumference	92.5 (13.3)	91.7 (15.4)	91.3 (13.6)	0.09	91.5 (14.4)	<0.05
(women) (cm)	(N=930)	(N=217)	(N=241)		(N=458)	
Waist circumference	96.7 (12.2)	96.1 (13.6)	94.0 (12.6)	<0.0001	95.0 (13.1)	<0.0001
(men) (cm)	(N=3728)	(N=708)	(N=770)		(N=1478)	
Dyslipidemia						
Triglycerides >150	31.0	37.0	37.6	<0.0001	37.3	<0.0001
mg/dL	(2104/6792)	(706/1910)	(734/1954)		(1440/3864)	
Triglycerides >200	14.1	18.6	19.2	<0.0001	18.9	<0.0001
mg/dL	(961/6792)	(356/1910)	(375/1954)		(731/3864)	
HDL-C <40 mg/dL in	46.9	57.0	53.0	<0.0001	55.0	<0.0001
men/50 mg/dL in	(3184/6793)	(1089/1911)	(1036/1955)		(2125/3866)	
women						
Residual dyslipidemia[b]	9.3	13.1	12.8	<0.0001	12.9	<0.0001
	(630/6791)	(250/1910)	(250/1953)		(500/3863)	

Variables are presented as % (n), % (n/N) or mean (SD).

[a]Chi-squared test, Kruskal-Wallis test or Mann-Whitney-Wilcoxon test.

[b]Triglycerides >200 mg/dL and HDL-C <40 mg/dL in men/50 mg/dL in women.

ACS indicates acute coronary syndrome; ATP, Adult Treatment Panel; BMI, body mass index; CHD, coronary heart disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; HDL-C, high-density lipoprotein cholesterol; SD, standard deviation.

Table 2

Coronary medications[a]

Medication	CHD patients (N=6794)	ACS patients (recurrent event) (N=1911)	ACS patients (first event) (N=1956)	p value (3-way)[b]	All ACS patients (N=3867)	p value (CHD vs all ACS)[b]
Antiplatelet therapy (aspirin or $P2Y_{12}$ inhibitor)	94.3 (6394/6781)	98.4 (1876/1906)	97.6 (1908/1954)	<0.0001	98.0 (3784/3860)	<0.0001
Aspirin	82.7 (5609/6781)	94.7 (1805/1906)	95.3 (1862/1954)	<0.0001	95.0 (3667/3860)	<0.0001
Other antiplatelet	44.0 (2987/6794)	88.1 (1683/1910)	89.8 (1757/1956)	<0.0001	89.0 (3440/3866)	<0.0001
DAPT (aspirin + $P2Y_{12}$ inhibitor)	32.4 (2198/6781)	84.6 (1612/1906)	87.6 (1711/1954)	<0.0001	86.1 (3323/3860)	<0.0001
Beta-blocker	72.0 (4867/6760)	80.3 (1524/1899)	79.7 (1551/1947)	<0.0001	80.0 (3075/3846)	<0.0001
Lipid-lowering medication	94.7 (6433/6792)	98.3 (1876/1909)	96.7 (1891/1956)	<0.0001	97.5 (3767/3865)	<0.0001
Statin treatment	92.5 (6287/6794)	97.7 (1867/1910)	96.4 (1885/1956)	<0.0001	97.1 (3752/3866)	<0.0001
Statin dose[c] (mg/day)	25 (18) (N=6261)	34 (21) (N=1853)	38 (24) (N=1877)	<0.0001	36 (23) (N=3730)	<0.0001
Median (IQR)	20 (10, 40)	40 (20, 40)	40 (20, 40)	−	40 (20, 40)	−
Range	5−160	5−160	5−160	−	5−160	−
Statin monotherapy	77.9 (5286/6783)	88.3 (1677/1900)	89.8 (1756/1955)	<0.0001	89.1 (3433/3855)	<0.0001
Non-statin monotherapy	1.2 (81/6783)	0.5 (9/1900)	0.3 (6/1955)	<0.001	0.4 (15/3855)	<0.0001

Statin + non-statin	15.6 (1057/6783)	9.5 (181/1900)	6.5 (128/1955)	<0.0001	8.0 (309/3855)	<0.0001
Statin + ezetimibe	9.9 (670/6794)	6.0 (114/1910)	3.7 (73/1956)	<0.0001	4.8 (187/3866)	<0.0001
ACE or ARB inhibitor	69.4 (4672/6733)	76.2 (1440/1891)	71.3 (1382/1939)	<0.0001	73.7 (2822/3830)	<0.0001

Variables are presented as % (n/N) or mean (SD) unless otherwise stated.

[a]Chronic medication in CHD patients and medication at discharge from hospital in ACS patients.

[b]Chi-squared test, Kruskal-Wallis test or Mann-Whitney-Wilcoxon test.

[c]Mean (SD) statin dose calculated in atorvastatin dose equivalent.

ACE indicates angiotensin-converting enzyme; ACS, acute coronary syndrome; ARB, angiotensin-receptor blocker; CHD, coronary heart disease; DAPT, dual antiplatelet therapy; IQR, interquartile range; SD, standard deviation.

Table 3

Cardiovascular prevention program attended by DYSIS II patients

	CHD patients (N=6794)	ACS patients (recurrent event) (N=1911)	ACS patients (first event) (N=1956)	p value (3-way)[a]	All ACS patients (N=3867)	p value (CHD vs all ACS)[a]
Cardiac rehabilitation program	−	10.8 (184/1699)	16.8 (295/1754)	−	13.9 (479/3453)	−
Current participation in disease management program or patient education program for CHD	11.7 (768/6549)	4.9 (87/1787)	2.6 (49/1893)	<0.0001	3.7 (136/3680)	<0.0001
Current participation in disease management program or patient education program for diabetes	6.6 (436/6564)	3.7 (68/1817)	3.2 (60/1892)	<0.0001	3.5 (128/3709)	<0.0001

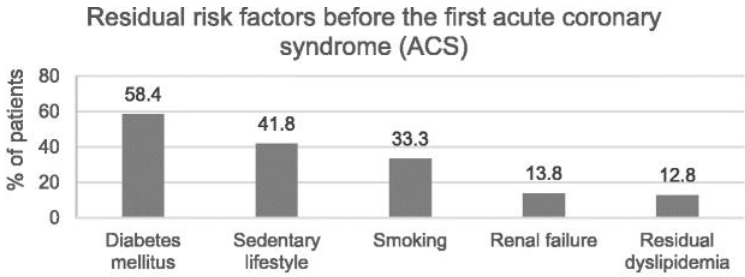
Variables are presented as % (n/N).

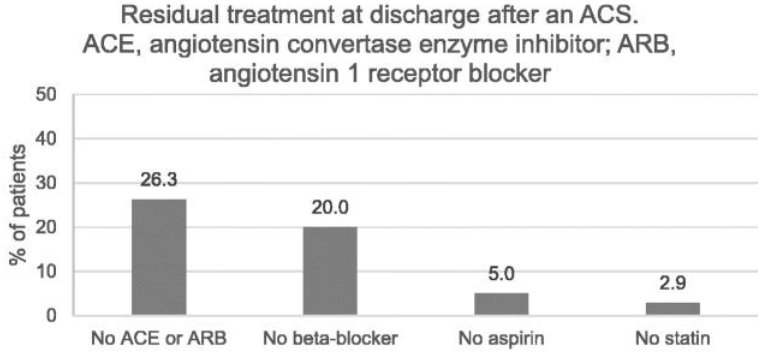
[a]Chi-squared test, Kruskal-Wallis test or Mann-Whitney-Wilcoxon test.

ACS indicates acute coronary syndrome; CHD, coronary heart disease.

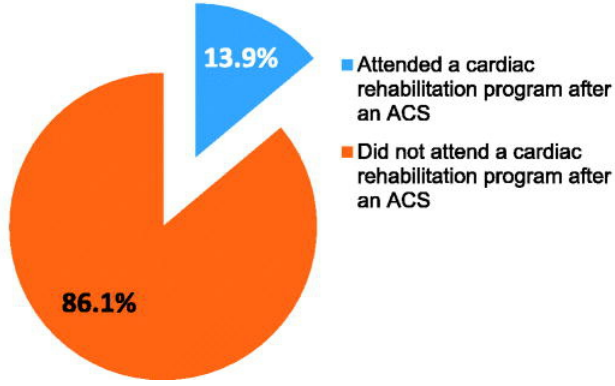
Highlights

- Our study shows good adherence to medications during the acute stage of coronary heart disease.
- Long-term management of CHD remains suboptimal.
- The high prevalence of risk factors offers areas for better risk factor control.





Management of secondary prevention: attendance of cardiac rehabilitation after an ACS



Graphics Abstract

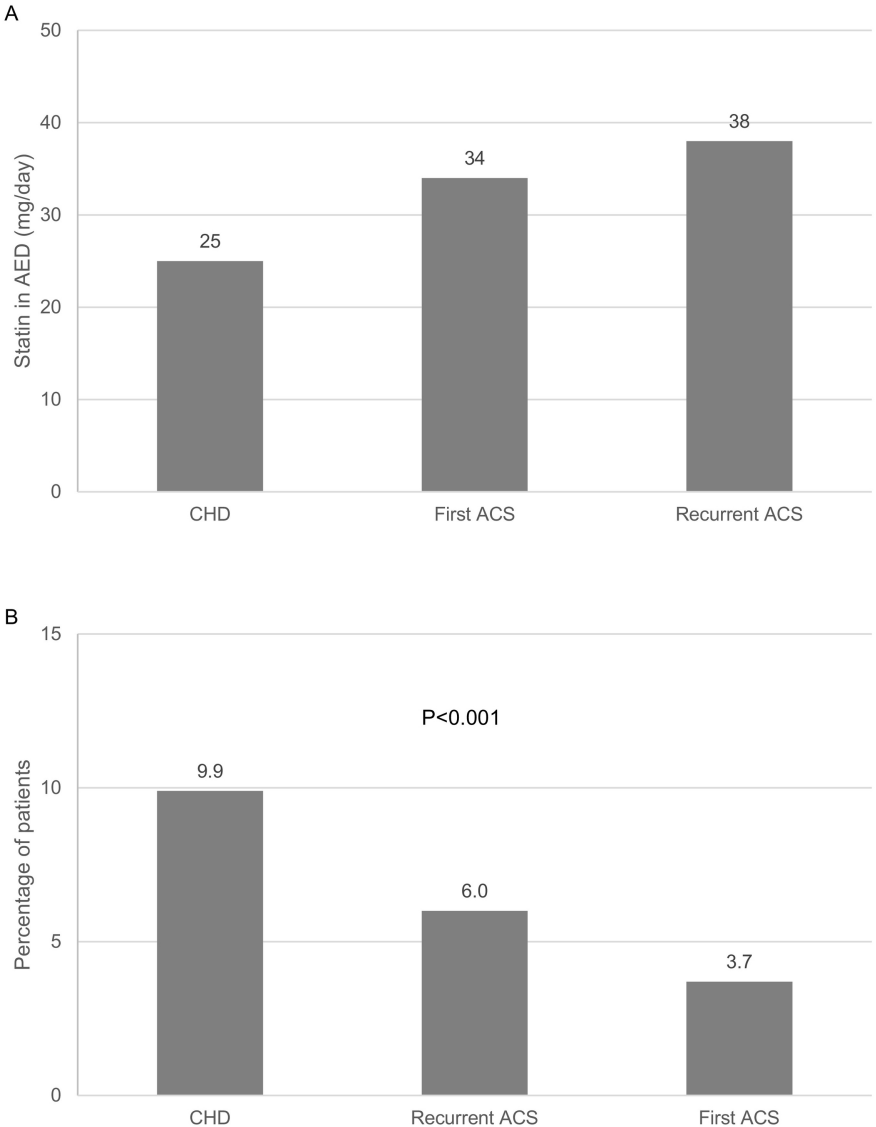

A
Statin in AED (mg/day)
50
40
30
20
10
0
25
34
38
CHD
First ACS
Recurrent ACS
B
Percentage of patients
15
10
5
0
P<0.001
9.9
6.0
3.7
CHD
Recurrent ACS
First ACS

Figure 1