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Effects of cardiac rehabilitation on risk factor management and quality of life in patients with ischemic heart disease: A multicenter cross-sectional study

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**Short title:** Participation in cardiac rehabilitation and CVD risk factor management
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Key words: cardiac rehabilitation, ischemic heart disease, propensity score matching, risk factors, secondary cardiovascular prevention
**What’s new**

The benefits of cardiac rehabilitation (CR) programs on the management of risk factors in patients with chronic coronary syndromes is underreported in Poland. This is the first multicenter study to investigate the referral to, and participation patterns of, CR in Poland. We found the rate of referral to CR in Poland was low, particularly in the elderly, unemployed, and in patients having undergone elective percutaneous coronary intervention (PCI). There was a significant positive effect of CR on aspects of secondary prevention approximately one year after the acute coronary event or elective revascularization; smoking habit, blood glucose level, and quality of life. The observed effects may be limited by the fact that patients only participated in a single period of CR. Therefore, we suggest a single program of CR should be accompanied by a more prolonged schedule to sustain such benefits.
Abstract

Introduction: While cardiac rehabilitation (CR) improves survival outcomes in patients with ischemic heart disease (IHD), the long-term benefits of a short-term program are still discussed.

Objectives: To assess the impact of CR on risk factor management in a multicenter real-life registry of patients with IHD.

Patients and methods: We included patients aged ≤80 years who had been hospitalized due to an ACS or for a myocardial revascularization procedure and interviewed 6–18 months later. Risk factors control was compared for patients who participated in CR and those who did not participate in CR. Propensity score matching (PSM) was used to account for differences in patient characteristics between groups.

Results: Of total 1,012 patients (28.6% females) interviewed, 35.6% were referred for CR, with 76.1% of them completing program. Those referred were younger ($P < 0.001$), employed ($P < 0.001$), have presented with ST-segment elevation myocardial infarction (STEMI) ($P < 0.001$) have hypertension ($P < 0.001$), and be current smokers ($P < 0.001$). Logistics regression revealed that patients who participated in CR were more likely to stop smoking (OR 2.42, CI 1.33 - 4.14), achieve acceptable glucose control (OR 1.70, CI 1.02 - 2.83), and better quality of life ($\beta 0.12$, CI 0.00 to 0.24) compared to those who did not participate in CR.

Conclusions: CR is moderately effective if performed only once and without a continuous support program. Further efforts to increase referrals for CR in IHD patients must be accompanied by a long-term strategy to sustain the beneficial effects.
Introduction

Cardiac rehabilitation (CR) is one of the core elements of secondary prevention in patients with ischemic heart disease (IHD), aiming to improve risk factors, reduce hospital readmission, and produce a more favorable survival outcome. Two large meta-analyses of 34 and 18 randomized controlled trials have shown that CR reduces recurrent cardiovascular (CV) events and improves mortality rates in patients with myocardial infarction [1, 2]. CR has also been shown to improve patients’ quality of life and ability to recommence work quickly [1].

International guidelines recommend that all patients who have had a planned revascularization procedure or suffer from acute coronary syndrome (ACS), chronic stable angina, or heart failure should engage in a CR program to reduce subsequent events [3, 4]. Moreover, recently revised practice guidelines urge for a “comprehensive rehabilitation” program covering a range of aspects: exercise training aimed at improving clinical profiles (optimization of blood pressure, lipid and glucose levels, and weight), healthy heart education (appropriate diet and stopping smoking), and psychological counseling to reduce stress and improve quality of life [3, 5, 6]. These comprehensive efforts are intended to foster better CV risk management than could be achieved by supervised exercise alone.

However, referrals to CR programs and the impact of such programs in the real world has been suboptimal [9], in both Europe [10] and the USA [11]. A summary of a large cross-sectional survey carried out by the pan-European group EUROASPIRE (European Action on Secondary and Primary Prevention by Intervention to Reduce Events) reported that CR referral rates and hence participation rates in Europe remain
low [12, 13]. Thus, there is a need for urgent action to increase referral and enrollment rates in CR programs.

In Poland, cardiovascular disease (CVD) is one of the major causes of mortality, accounting for 46% of total deaths in 2010 [7], with nearly half of these attributable to IHD. To address this serious situation, healthcare experts have been trying to promote a preventive approach through CR and lifestyle changes. In addition there has been an increase in the efforts to manage care for patients with IHD, including increased access to CR programs [8]. To our knowledge there has not been any multicenter studies performed to investigate disparities in referral rates and participation in CR and understand the effectiveness of CR in Poland.

This study assessed the effectiveness of CR in a patient population enrolled in a CR program in 14 cardiology centers from four different regions of Poland, all of which participated in EUROASPIRE.

**Patients and methods**

POLASPIRE is a parallel program run by Polish centers involved in EUROASPIRE V. In total, 403 patients chosen from the POLASPIRE survey contributed to the Polish subset of EUROASPIRE V. The detailed methodology of this survey has been previously described [14, 15]. A multicenter cross-sectional study was conducted between 2016 and 2017 on Polish patients from four geographical areas (Krakow, Katowice, Warszawa, Bialystok) and from 14 cardiology departments. For each department, medical records were reviewed retrospectively of patients aged between 18 and 80 years who had been hospitalized for (i) coronary artery bypass graft surgery (CABG), (ii) elective percutaneous coronary intervention (PCI), (iii) acute myocardial infarction (AMI; ICD-10 I21, I22) or (iv) unstable angina. Eligible patients were invited...
for an interview and follow-up examination 6 to 18 months after being discharged. In addition to the patients from the EUROASPIRE V database, we also enrolled additional patients from participating centers during the same period, using the same methodology, inclusion, and exclusion criteria.

**Cardiac rehabilitation management**

Patients were asked to report their level of participation in CR at the time of the interview using the following options: i) did not attend; ii) attended at least one session; iii) attended more than half of the sessions; or iv) completed all of the recommended sessions. In Poland, full participation means that patients received a comprehensive program of in-hospital rehabilitation of between 2 to 6 weeks duration, which included exercise training, dietary guidance, medication review, smoking cessation advice, and stress management. Due to the design of the study and the short duration of enrollment, we only included participants in the treatment group who declared that they completed all of the CR sessions, to reliably assess the effects of CR.

**Study variables**

We used interviews to obtain participants’ self-reported information on a range of health and lifestyle-related issues, detailed below. Each patient’s body mass index (BMI) was calculated using their height and weight measured in a straight standing position, excluding shoes and heavy items. Obesity was defined as a body mass index (BMI) \( \geq 30 \text{kg/m}^2 \). A low educational level was defined as having completed only primary school level education or less. A persistent smoker was defined as a patient reported to have been a smoker in the month before the index event who was either still smoking at the time of the interview or who had an exhaled carbon monoxide
level exceeding 10 parts per million (ppm). Blood pressure was measured twice on the right arm in a sitting position at five-minute intervals, and the mean was used for analyses. Increased blood pressure was defined as blood pressure $\geq 140/90$ mmHg.

Total cholesterol, high-density lipoprotein cholesterol (HDL-C) low-density lipoprotein cholesterol (LDL-C), triglycerides, and glycated hemoglobin (HbA1c) were measured in fasting venous blood samples. An elevated LDL-C concentration was defined as $\geq 1.8$ mmol/L, and HbA1c was considered acceptable if lower than 7%, as per the relevant guidelines [5]. Depression and anxiety were assessed using the Hospital Anxiety and Depression Scale (HADS) with a score of lower than 8 points considered normal. Quality of life was assessed using a Health-Related Quality of Life (HRQoL) questionnaire consisting of two domains; physical (10 items) and emotional (four items). Generic health status was assessed using the EQ-5D questionnaire which comprises a 5-dimension code describing the patient’s state of health in five domains, which was converted into a single index ranging from “0” (dead) to “1” (perfect health), with Germany used as the country of reference [16].

**Follow up and outcome assessment**

The main outcome in this study was the achievement of risk factor management goals and self-reported lifestyle changes at interview. The secondary outcome was the interactions between CR participation and time points.

**Ethics**

All patients provided written informed consent to take part in the study. The study was approved by the local ethics committees in each regional center.

**Propensity score matching method**
We performed propensity score matching (PSM) to account for potential bias resulting from an imbalance in the covariate distribution between the groups that had been referred to and who participated in CR and those who were not referred and did not participate in CR; both of which could be influenced by decisions by physicians and patients. We used multivariable logistic regression to obtain a propensity score (PS) for each CR participant and then were able to search the database for non-referred CR patients with the same or nearly the same PS match [17]. The variables included in generating the PS were age at index event, gender, center code, type of event, education status, obesity, BMI, and smoking status.

**Statistical methods**

The distribution of study variables was analyzed using the Shapiro Wilk’s test, with a P value of >0.05 indicating a normal distribution. Categorical variables were described using proportion and compared using the Chi-Square test. Continuous variables were expressed using mean and median values and compared using the Mann-Whitney U test for data without a normal distribution and Student’s t-test for variables with a normal distribution.

To compare the distribution of the baseline characteristics of patients who had been referred to CR with those not referred to CR we used the Chi-Square test.

Multivariable logistic regression was used to identify predictors of CR participation in those referred to CR. Univariable logistic and linear regression models were constructed to estimate the effect of CR in those who participated in CR and those who did not participate in CR from the dataset of propensity score-matched groups.

A generalized linear model (GLM) was used, rather than a simple linear regression model, to adequately account for correlated data due to repeated measurements (pre
and post) of the same study subjects. This model encompassed three parameters: CR effect which describes baseline difference between participated in CR and did not participate in CR groups, secondly time effect describes interview-baseline difference for patients did not participate in CR [participated in CR was coded as 1, and did not participate in CR as 0], lastly main effects “time-CR interaction effect” describes how time effect in CR group differs from no CR group. The interaction term between the main effects, to highlight differences between the CR groups in terms of changes in the outcome variables during the period of observation.

The multiple imputation method was used to deal with missing values (ranging between 5 and 20 percent). All the variables mentioned were included in the imputation model, and 10 imputation sets were then created [18, 19]. The imputation set was used to analyze and report study outcomes in both univariable regression model and generalized linear model.

Two-tailed P values of less than 0.05, and a 95% CI for odds ratios that did not include 1, were considered statistically significant. All analyses were performed using IBM SPSS statistics software, version 25 (IBM, Armonk, New York, USA).

Results

We analyzed a total of 1,012 patients who were interviewed 6 to 18 months after their index event and who had provided complete information on their participation in CR (Table 1). Of these, female patients accounted for less than 30%; the median age of patients at the time of hospitalization was 65 years old, and the majority of the patients had been hospitalized in teaching hospitals (83%). Almost 40% of the patients had been recruited following elective PCI (n = 377). Other common index events were: non-ST elevation myocardial infarction (NSTEMI), accounting for 217 (21.4%).
unstable angina with 215 (21.2%) and ST-elevation myocardial infraction (STEMI) with 160 (15.8%) of the patients analyzed (Table 1). Overall, one third of the patients had been referred to a CR program (35.6%), and 76.1% of these completed all the recommended sessions.

Physicians were more likely to refer younger patients than older patients; median age 62 (57 - 68) vs. 67 (61 - 72), and employed patients vs. unemployed patients ($P$ <0.001) to CR. The rates of CR referral and participation differed considerably between regions (Figure 1). Clinically, the patients referred were more likely to have presented with STEMI ($P$ <0.001), CABG ($P$ <0.001) or hypertension ($P$ <0.001), and were more likely to be taking angiotensin converting enzyme (ACE) inhibitors ($P$ <0.001), diuretics ($P$ <0.001) and anticoagulants ($P$ <0.001) at the time of hospital discharge. One-third of smokers at the time of the index event (35.1%) were referred to CR ($P$ <0.001). Among the patients referred to CR, obese patients were twice as likely to participate in CR (OR 2.32, 95% CI 1.07 to 5.00) than the non-obese. In addition, a higher level of education was marginally associated with CR participation (OR 2.05, 95% CI 0.99 to 4.27) (Table 2). After PSM we found out that patients who participated in CR were twofold more likely to stop smoking (OR 2.42, 95% CI 1.33 to 4.14) and to achieve appropriate glucose control (OR 1.70, 95% CI 1.02 to 2.83) than those who did not participate in CR (Table 3). A marginal improvement was observed in the physical domain of the quality of life score in patients who participated in CR ($\beta$ coefficient = 0.12, 95% CI 0.00 to 0.24). Overall, there were no significant changes in the risk control variables (outcomes) time-changes between the patients who participated in CR and those who did not (Table 4). We further performed sensitivity analyses to examine the effects of PSM compared to conventional methods, which showed that both produced very similar results.
Discussion

Our research revealed several interesting findings regarding CR referrals in Poland. First, the rate of referrals between 2016 and 2017 years was relatively low, with only 35.6% of relevant cardiac patients referred for CR. Second, there were significant disparities in CR referral rates between regions, but little or no difference between teaching and non-teaching hospitals. Third, CR was most often recommended for those with AMI (STEMI = 28.9% and NSTEMI = 28.3%). Obesity was a strong predictor of participation in CR. Finally, patients who participated in CR were twice as likely to quit smoking, achieve a favorable glucose concentration, and have an improved quality of life (in the physical domain) than those who did not take part in CR.

The challenge is that, despite growing evidence from meta-analyses, systematic reviews, and multicenter studies showing that CR improves the prognosis for IHD patients in terms of reduced hospital re-admissions, recurrent events, and mortality [2, 20, 21, 22], there is still a low acceptance of CR overall in Poland. Our results confirm that there is a huge gap in referrals and enrollments between hospital discharge and participation in CR. Only just over one-third (35.6%) of the study patients were advised to participate in CR after their index CV event, of whom just under 77% completed full sessions: in other words, fewer than 30% of the study population completed the recommended CR sessions. These figures on CR participation in Poland are even lower than those in both the EUROASPIRE III and IV reports covering 27 countries in Europe, which similarly showed a low proportion of patients (≤ 50%) being advised to take part in CR and only around one-third doing so [12, 13]. These differences in participation levels could be due to the patient’s clinical profile, health care systems, and the accessibility of CR services in different countries.
Another finding from our study is that CR was most often assigned to patients with acute conditions, particularly those diagnosed with STEMI (65.0%) or NSTEMI (47.0%), while the referrals for those who had undergone planned PCI were lower (24.1%). In contrast, a study from the USA using data from the ACTION-Get registry showed that about 50% of patients were being referred for CR overall, with enrollment rates of 84.5% for patients with STEMI, 75.9% for those with NSTEMI, and 60.0% for those having undergone PCI [23].

In summary, there are significant disparities in the levels of CR referral and participation between the USA, Europe, and specifically Poland. What is not clear is whether these low referral and participation rates are due to low physician awareness of the benefits of CR; limited access to CR facilities; patients declining to participate; or a combination thereof. The fact that CR services after ACS or PCI are covered by the public healthcare system in Poland [8] makes it all the more surprising that CR has been so underused. One possible explanation is that, as one of the fastest-aging societies in the EU with 5.9 million people aged 65 and over [7], basic health care facilities and hospitals may face problems in managing these large numbers of patients and the costs of treatment involved. As a consequence, hospitals may try to keep the number of admissions and basic health care referrals to a minimum, and prioritize those most in need [7]. Also, there is evidence that the poor uptake of CR may be due to the reluctance of physicians to refer patients; to a lack of CR facilities; and/or to a lack of funding [1, 23, 24]. In Poland, this was the motivation for the introduction of a country-wide program of managed care after myocardial infarction, including compulsory CR programs [5]. The hope is that this program will improve communication between physicians and patients, which in turn may improve the uptake of CR as well as optimize secondary prevention.
Further noteworthy observations from our study are that younger, employed, smoking patients, and those on ACE inhibitors were more likely to be advised to take part in CR. Advising patients in employment to participate in CR makes sense since CR can help cardiac patients to improve their condition and quality of life to a point where they can go back to work. Concerning age, physicians are perhaps less inclined to refer the elderly for CR due to frailty, as well due to possible difficulties they might face in commuting to the hospital [5]. To reduce these age-related disparities, alternative approaches such as home-based CR for elderly and frail patients should be considered and ideally included in a country-wide program.

Our findings show that more than half of the patients participating in CR were smokers, which is consistent with the results of EUROAPSiRE IV (OR 1.48, 95% CI 1.25 to 1.74). Moreover, those participating in CR were more than twice as likely to give up smoking than non-participants. There is previous evidence from landmark trials that smoking may even outweigh the beneficial effects of statins, with the risk of mortality observed in non-smokers not taking statins being similar to that of smokers taking statins [27]. Ours and other’s [13] results showing the beneficial impact of CR programs on individuals giving up smoking could help boost efforts to encourage more persistent smokers to participate in CR and attend sessions regularly.

Our study confirms the positive effects of CR. It showed about a two-fold reduction of average blood glucose levels (HbA1c <7%) in those taking part and completing all the sessions. Moreover, patients who participated in CR showed marginal increases in HRQoL in at least one domain. This finding is similar to two earlier observational studies that reported significant improvements in quality of life after 6 months [28] and after 1 year [29]. However, neither of these studies adjusted for confounding factors, unlike our study, which applied comprehensive adjustments through the PSM method.
Our results therefore provide substantial novel evidence to confirm these findings. However, the observed effects on the attainment of secondary prevention targets are still smaller than expected. We need to search for innovative strategies to improve and sustain the beneficial effects of CR [30].

This study is subject to several limitations. The main one is potential recall bias, given that the bulk of the data on CR participation and its effects was obtained from patients’ self-reported questionnaires. Another limitation is that patients volunteered to participate in the study, so individuals more concerned about their health might have been more likely to participate. Finally, since the data was gathered in Poland the results may not be representative of all countries.

Nonetheless, our findings contribute to the evidence supporting the introduction of the managed healthcare policy for IHD patients in Poland, which aims to increase CR uptake and participation rates in Poland as well as involving multidisciplinary teams (physicians, nurses, exercise scientists, nutritionists, and psychologists) to improve the prognosis of patients with IHD [8, 21]. Our statistical approach, using the PSM method to control confounding variables as well as systematically dealing with missing values using multiple imputations, greatly enhances the statistical power and strength of the study findings, notwithstanding the modest size of the sample groups.

**Conclusions**

The present study showed that a relatively small number of patients with IHD are referred for CR in Poland. Most patients had an improved lifestyle after participation in CR, with the main identified long-term benefits being an increase in the rates of those giving up smoking and a better quality of life score in the physical domain. Our
findings point to an urgent need to incorporate CR into optimized long-term care programs to help sustain the benefits for patients with IHD.

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Contribution statement: SS and KK contributed equally. KK, PJ, SS, JJ & PS contributed to the conceptualization and design of the study. KK, PJ, ZG, DK, MH, DC, AP, MS, ML contributed to the data acquisition and interpretation. SS, KK, PS & JJ contributed to the data analysis and interpretation. The draft manuscript was prepared by SS & KK, and critically checked and approved by KK. All authors critically revised and approved the final manuscript.

Conflict of interest: None declared
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Table 1. Baseline characteristics and treatment profile of patients referred, and not referred, for cardiac rehabilitation at time of hospitalization.

| Variable                        | Total (n = 1012) | Cardiac rehabilitation status | *P value |
|---------------------------------|------------------|-------------------------------|----------|
|                                 |                  | Not referred (n = 652) | Referred (n = 360) |
| Age at index event, median (IQR)| 65 (60 - 71)     | 67 (61-72)                   | 62 (57-68) | <0.001 |
| Center, n (%)                   |                  |                              | 0.57     |
| Non-teaching hospitals          | 172 (17.0)       | 114 (17.5)                   | 58 (16.1) |
| Teaching hospitals              | 840 (83.0)       | 538 (82.5)                   | 302 (83.9) |
| Region, n (%)                   |                  |                              | <0.001   |
| Białystok                       | 238 (23.5)       | 75 (11.5)                    | 163 (45.3) |
| Kraków                          | 398 (39.3)       | 296 (45.4)                   | 102 (28.3) |
| Katowice                        | 150 (14.8)       | 102 (15.6)                   | 48 (13.3)  |
| Warsaw                          | 226 (22.3)       | 179 (27.5)                   | 47 (13.1)  |
| Gender, n (%)                   |                  |                              | 0.25     |
| Male                            | 723 (71.4)       | 458 (70.2)                   | 265 (73.6) |
| Female                          | 289 (28.6)       | 194 (29.8)                   | 95 (26.4)  |
| Education status, n (%)         |                  |                              | 0.52     |
| Primary level                   | 125 (12.5)       | 84 (12.9)                    | 41 (11.5)  |
| Higher level                    | 879 (87.5)       | 565 (87.1)                   | 314 (88.5) |
| Unknown                         | 8                | 3                             | 5         |
| Employment status, n (%)        |                  |                              | <0.001   |
|                  | Unemployed | Employed | Unknown |
|------------------|------------|----------|---------|
|                  | 663 (66.1) | 471 (72.2)| 192 (54.7)|
| Employment Status|            |          |         |
|                  | 340 (33.9) | 181 (27.8)| 159 (45.3)|
|                  | 9          | 0        | 9       |
| Index event, n (%)|            |          | <0.001  |
| CABG             | 43 (4.2)   | 19 (2.9) | 24 (6.7) |
| PCI              | 377 (37.3) | 286 (43.9)| 91 (25.3)|
| STEMI            | 160 (15.8) | 56 (8.6) | 104 (28.9)|
| NSTEMI           | 217 (21.4) | 115 (17.6)| 102 (28.3)|
| UA               | 215 (21.2) | 176 (27.0)| 39 (10.8)|
| Previous event, n (%)|          |          |         |
| CABG             | 75 (13.6)  | 58 (14.2)| 17 (12.0)| 0.50   |
| PCI              | 333 (60.8) | 241 (59.2)| 92 (65.2)| 0.20   |
| AMI              | 255 (47.0) | 195 (48.4)| 60 (43.2)| 0.28   |
| UA               | 55 (10.4)  | 47 (12.02)| 8 (5.7) | 0.03   |
| Angina pectoris  | 206 (39.0) | 172 (44.1)| 34 (24.6)| <0.001 |
| Stroke           | 58 (10.7)  | 45 (11.2)| 13 (9.4) | 0.55   |
| PAD              | 42 (7.8)   | 33 (8.2) | 9 (6.4)  | 0.49   |
| Heart Failure    | 40 (7.5)   | 37 (9.3) | 3 (2.2)  | <0.001 |
| Smoking habit, n (%)|          |          | <0.001  |
| Non-smoker       | 356 (38.8) | 236 (39.5)| 120 (37.6)|
| Former smoker    | 312 (34.0) | 225 (37.6)| 87 (27.3)|
| Current smoker   | 249 (27.2) | 137 (22.9)| 112 (35.1)|
| Unknown          | 54         | 41       | 95      |
| Obesity, n (%)   | 395 (39.0) | 265 (40.6)| 130 (36.1)| 0.05   |
|                                       | Group 1 | Group 2 | Group 3 | P      |
|---------------------------------------|---------|---------|---------|--------|
| Weight, kg,                           | 82.7 (74.0 - 94.0) | 83.0 (74.0 - 93.0) | 82.5 (74.0 - 94.0) | 0.86   |
| BMI, kg/m²,                            | 29.0 (26.2 - 32.2) | 29.0 (26.2 - 32.1) | 28.9 (26.0 - 32.6) | 0.96   |
| Diabetes, n (%)                        | 317 (31.3) | 200 (30.7) | 117 (32.5) | 0.24   |
| Hypertension, n (%)                    | 880 (87.0) | 587 (90.0) | 293 (81.4) | <0.001 |
| SBP, mmHg,                             | 136 (123 - 150) | 136.0 (123.5 - 150.0) | 135.0 (120.7 - 150.0) | 0.18   |
| DBP, mmHg,                             | 80 (72 - 88) | 80 (74 - 88) | 80 (71 - 88) | 0.32   |
| Hyperlipidemia, n (%)                  | 817 (80.7) | 524 (80.4) | 293 (81.4) | 0.51   |
| LDL-C, mmol/L,                         | 2.4 (1.8 - 3.3) | 2.4 (1.7 - 3.2) | 2.5 (1.9 - 3.4) | 0.00   |
| HDL-C, mmol/L,                         | 1.1 (0.9 - 1.3) | 1.1 (0.9 - 1.4) | 1.1 (0.9 - 1.3) | 0.02   |
| Triglycerides, mmol/L,                 | 1.3 (0.9 - 1.8) | 1.2 (0.9 - 1.8) | 1.3 (0.9 - 1.8) | 0.38   |
| Medication prescribed, n (%)           |         |         |         |        |
| Antiplatelets                          | 999 (98.7) | 643 (98.6) | 356 (98.9) | 0.71   |
| Beta-blockers                          | 931 (92.0) | 599 (91.9) | 332 (92.2) | 0.84   |
| ACE inhibitors                         | 773 (76.4) | 478 (73.3) | 295 (81.9) | <0.001 |
| Statins                                | 960 (94.9) | 614 (94.2) | 346 (96.1) | 0.18   |
|                         | n (%)  | n (%)  | n (%)  | P-value |
|-------------------------|--------|--------|--------|---------|
| Calcium channel blockers| 272 (26.9) | 188 (28.8) | 84 (23.3) | 0.05    |
| Diuretics               | 512 (50.6) | 309 (47.4) | 203 (56.4) | <0.001  |
| Anticoagulants          | 147 (14.5)  | 114 (17.5)  | 33 (9.2)   | <0.001  |

Categorical data presented as n (%) and continuous data is presented as median (IQR)

International System of Units (SI) conversion factors: to convert HDL and LDL from mg/dL to mmol/L, values were multiplied by 0.02586; to convert triglyceride level from mg/dL to mmol/L, values were multiplied by 0.01129.

Categorical data is presented as % and continuous median, 25th and 75th percentile, P-values are reported by excluding missing values; primary educational level denotes at most primary school level education, higher educational level denotes completion of secondary school, high school, technical or vocational training, college, or postgraduate study.

Abbreviations: STEMI = ST-elevation myocardial infarction; CABG = coronary artery bypass graft; PCI = percutaneous coronary intervention; AMI = acute myocardial infarction; UA = unstable angina; PAD = peripheral artery disease; BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; LDL-C = low-density lipoprotein cholesterol; HDL-C = high-density lipoprotein cholesterol; ACE inhibitor = angiotensin converting enzyme inhibitor.
Table 2. Association between patient characteristics and participation in cardiac rehabilitation in those referred for cardiac rehabilitation.

| Variable                        | Overall (n = 360) | Did not Participate in CR (n = 86) | Participated in CR (n = 274) | P value (group comparison) | Multivariable OR (95% CI) |
|---------------------------------|-------------------|-----------------------------------|-----------------------------|---------------------------|--------------------------|
| Age at diagnosis, median (IQR)  | 62 (57 - 68)      | 62 (58 - 68)                      | 62 (57 - 68)                | 0.92                      | 0.99 (0.96 to 1.03)      |
| Center, n (%)                   |                   |                                   |                             |                           |                          |
| Non-teaching hospitals          | 58 (16.1)         | 18 (20.9)                         | 40 (14.6)                   | 1.00                      |                          |
| Teaching hospitals              | 302 (83.9)        | 68 (79.1)                         | 234 (85.4)                  | 1.70 (0.87 to 3.29)       |                          |
| Gender, n (%)                   |                   |                                   |                             | 0.30                      |                          |
| Female                          | 95 (26.4)         | 19 (22.1)                         | 76 (27.7)                   | 1.00                      |                          |
| Male                            | 265 (73.6)        | 67 (77.9)                         | 198 (72.3)                  | 0.76 (0.42 to 1.40)       |                          |
| Index event, n (%)              |                   |                                   |                             | 0.88                      |                          |
| Planned revascularization       | 115 (31.9)        | 28 (32.6)                         | 87 (31.8)                   | 1.00                      |                          |
| ACS                             | 245 (68.1)        | 58 (67.4)                         | 187 (68.2)                  | 1.02 (0.58 to 1.80)       |                          |
|                                |          |          |          |
|--------------------------------|----------|----------|----------|
| **Education status, n (%)**    |          |          | 0.10     |
| Primary level                 | 41 (11.5)| 14 (16.5)| 27 (10.0)| 1.00     |
| Higher level                  | 314 (88.5)| 71 (83.5)| 243 (90.0)| 2.05 (0.99 to 4.27) |
| Unknown                       | 5        | 1        | 4        |
| **Occupation status, n (%)**  |          |          | 0.70     |
| Unemployed                     | 192 (54.7)| 45 (52.9)| 147 (55.3)| 1.00     |
| Employed                      | 159 (45.3)| 40 (47.1)| 119 (44.7)| 0.90 (0.48 to 1.66) |
| Unknown                        | 9        | 8        | 1        |
| **Smoking habit, n (%)**      |          |          | 0.42     |
| Non-smoker or former smoker   | 207 (64.9)| 46 (63.0)| 161 (65.4)| 1.00     |
| Current smoker                | 112 (35.1)| 27 (37.0)| 85 (34.6)| 1.04 (0.57 to 1.87) |
| Unknown                        | 41       | 13       | 28       |
| **Hypertension, n (%)**       |          |          | 0.47     |
| No                             | 34 (10.4)| 10 (12.5)| 24 (9.7) |
| Yes                            | 293 (89.6)| 70 (87.5)| 223 (90.3)|          |
| Unknown                        | 33       | 6        | 27       |
| Condition          | No     | Yes    | Unknown |
|--------------------|--------|--------|---------|
| **Hyperlipidemia, n (%)** | 29 (9.0) | 293 (91.0) | 38 (11.7) |
| No                 | 29 (9.0) | 6 (7.9) | 23 (9.3) |
| Yes                | 293 (91.0) | 70 (92.1) | 223 (90.7) |
| Unknown            | 38 (11.7) | 10 (1.0) | 28 (1.0) |
| **Obesity, n (%)**  |        |        | 0.01    |
| No                 | 159 (55.0) | 47 (67.1) | 112 (51.1) |
| Yes                | 130 (45.0) | 23 (32.9) | 107 (48.9) |
| Unknown            | 71 (2.2) | 16 (2.1) | 55 (2.5) |
| **Diabetes, n (%)** |        |        | 0.62    |
| No                 | 198 (62.9) | 46 (60.5) | 152 (63.6) |
| Yes                | 117 (37.1) | 30 (39.5) | 87 (35.4) |
| Unknown            | 45 (1.5) | 10 (1.3) | 35 (1.5) |

Categorical data presented as n (%) and continuous data is presented as median (IQR)

*a* Multivariable model adjusted by: age at index event, center, gender, index event, education status, occupation status, smoking habit, obesity, and diabetes. Missing value treated as “unknown” subcategory in multivariable logistics regression model.

Abbreviations: IQR = interquartile range; ACS = acute coronary syndrome; OR = odds ratio; CI = confidence interval; CR = cardiac rehabilitation.
Table 3. Patient characteristics and risk factors by participation in cardiac rehabilitation at the time of hospital interview using univariable regression model

|                              | No CR (n = 274) | CR (n = 274) | OR (95% CI) | B coefficient (95% CI) | P value |
|------------------------------|-----------------|--------------|-------------|------------------------|---------|
| Stopped smoking             | 31 (33.0)       | 49 (54.4)    | 2.42 (1.33 to 4.14) | -                      | 0.00    |
| Physically active           | 49 (18.6)       | 36 (13.7)    | 0.71 (0.44 to 1.13) | -                      | 0.15    |
| Bodyweight                  |                 |              |             |                        |         |
| BMI <25 kg/m²               | 38 (14.1)       | 40 (14.8)    | 1.07 (0.66 to 1.73) | -                      | 0.76    |
| BMI <30 kg/m²               | 149 (55.2)      | 158 (58.5)   | 1.14 (0.81 to 1.60) | -                      | 0.45    |
| Weight, kg                  | 85.8 (75.3 - 94.9) | 85.0 (75 - 94) | -            | -0.23 (-2.79 to 2.31) | 0.85    |
| BMI, kg/m²                  | 29.4 (26.7 - 32.7) | 29.0 (26.4 - 32.5) | -            | 0.32 (-0.48 to 1.12) | 0.43    |
| Blood pressure              |                 |              |             |                        |         |
| BP <140/90 mmHg             | 238 (87.8)      | 237 (87.5)   | 0.96 (0.57 to 1.61) | -                      | 0.89    |
|                          |     |     |     |     |     |
|--------------------------|-----|-----|-----|-----|-----|
| **SBP, mmHg**            | 131 (120 - 146) | 130 (120 - 145) | -   | -1.06 (-4.29 to 2.16) | 0.51 |
| **DBP, mmHg**            | 80 (73 - 87) | 80 (73.5 - 87.5) | -   | 0.49 (-1.27 to 2.26) | 0.58 |
| **Cholesterol control**  |     |     |     |     |     |
| **LDL-C <1.8 mmol/L**    | 109 (40.7) | 95 (35.1) | 0.78 (0.55 to 1.11) | -   | 0.17 |
| **LDL-C, mmol/L**        | 1.90 (1.54 - 2.60) | 2.0 (1.6 - 2.59) | -   | 0.03 (-0.12 to 0.18) | 0.70 |
| **HDL, mmol/L**          | 1.23 (1.06 - 1.47) | 1.24 (1.03 - 1.49) | -   | -0.01 (-0.07 to 0.04) | 0.58 |
| **Triglycerides, mmol/L**| 1.29 (0.95 - 1.79) | 1.27 (0.91 - 1.76) | -   | -0.05 (-0.24 to 0.14) | 0.59 |
| **Glucose control**      |     |     |     |     |     |
| **HbA1c <7%**            | 195 (81.9) | 224 (88.5) | 1.70 (1.02 to 2.83) | -   | 0.04 |
| Medication       | 6.0 (5.6 - 6.4) | 5.8 (5.6 - 6.2) | - | 0.02 (-0.46 to 0.52) | 0.90 |
|------------------|-----------------|-----------------|---|----------------------|------|
| Antiplatelets    | 250 (92.3)      | 262 (95.6)      | 1.83 (0.88 to 3.80) | - | 0.10 |
| Beta-blockers    | 235 (86.7)      | 248 (90.5)      | 1.46 (0.85 to 2.49) | - | 0.16 |
| ACE inhibitors   | 192 (70.8)      | 208 (75.9)      | 1.29 (0.88 to 1.89) | - | 0.18 |
| Lipid-lowering   | 241 (88.9)      | 246 (89.8)      | 1.09 (0.63 to 1.88) | - | 0.74 |
| Quality of life  |                 |                 |               |       |      |
| Anxiety          | 8 (3.0)         | 10 (3.8)        | 1.25 (0.48 to 3.23) | - | 0.63 |
| Depression       | 32 (11.9)       | 39 (14.7)       | 1.27 (0.77 to 2.11) | - | 0.33 |
| Emotional        | 2.0 (1.5 - 2.2) | 2.0 (1.5 - 2.2) | - | 0.00 (-0.09 to 0.90) | 0.94 |
| Physical         | 2.2 (1.7 - 2.7) | 2.4 (1.8 - 2.8) | - | 0.12 (0.00 to 0.24) | 0.05 |
| EQ-5D QoL | 0.9 (0.8 - 0.9) | 0.9 (0.8 - 0.9) | - | 0.00 (-0.01 to 0.02) | 0.65 |

Categorical data presented as n (%) and continuous data is presented as median (IQR)

Abbreviations: HbA1c = glycated hemoglobin; ACE inhibitor = angiotensin converting enzyme inhibitor; HADS = hospital anxiety and depression scale; HRQL = health-related quality of life; EQ-5D QoL = Euro quality of life questionnaire of 5 dimension;

a Completed all the recommended sessions; b for patients smoking in the month before the recruiting event; c patient exercise >20 minutes per week; d odds ratio reported for propensity score-matched population; e beta coefficients reported for propensity score-matched population.
Table 4. Interaction between cardiac rehabilitation participation and time point on risk factors using a generalized linear model.

|                      | No CR (n = 274) | CR group (n = 274) | Interaction between CR and measurement time (95% CI) | P value* |
|----------------------|-----------------|-------------------|------------------------------------------------------|---------|
|                      | Baseline        | Interview         | Baseline     | Interview         |                                                     |         |
| Weight, kg           | 85.9 (15.0)     | 85.4 (15.0)       | 84.9 (4.9)   | 85.1 (15.3)       | 0.32 (-1.58 to 2.23) \(^{a}\)                       | 0.74    |
| SBP, mmHg            | 139 (20)        | 133 (19)          | 136 (21)     | 132 (18)          | 1.57 (-2.60 to 5.75) \(^{a}\)                       | 0.46    |
| DBP, mmHg            | 82 (11)         | 80 (10)           | 79 (12)      | 80 (10)           | 3.17 (0.81 to 5.53) \(^{a}\)                        | 0.00    |
| LDL, mmol/L          | 2.7 (1.3)       | 2.2 (1.0)         | 2.7 (1.1)    | 2.2 (0.9)         | -0.02 (-0.25 to 0.20) \(^{a}\)                      | 0.83    |
| HDL, mmol/L          | 1.2 (0.4)       | 1.2 (0.3)         | 1.1 (0.3)    | 1.2 (0.3)         | 0.02 (-0.05 to 0.10) \(^{a}\)                       | 0.52    |
| Triglycerides, mmol/L| 1.5 (1.2)       | 1.5 (1.3)         | 1.5 (0.9)    | 1.4 (0.9)         | -0.00 (-0.20 to 0.13) \(^{a}\)                      | 0.93    |
| Antiplatelet         | 268 (98.9)      | 250 (92.3)        | 270 (98.5)   | 262 (95.6)        | 2.42 (0.54 to 10.90) \(b\)                         | 0.24    |
| Beta blocker         | 250 (92.3)      | 235 (86.7)        | 253 (92.3)   | 248 (90.5)        | 1.44 (0.78 to 2.66) \(b\)                          | 0.24    |
| ACE inhibitors       | 198 (73.1)      | 192 (70.8)        | 227 (82.8)   | 208 (75.9)        | 0.72 (0.47 to 1.11) \(b\)                          | 0.14    |
Statin | 262 (96.7) | 241 (88.9) | 264 (96.4) | 246 (89.8) | 1.20 (0.44 to 3.29) \(^b\) | 0.71

Categorical data presented as n (%) and continuous data is presented as mean (SD)

*P-value derived from the interaction between cardiac rehabilitation and measurement time point; \(^a\) beta coefficient for continuous outcomes; \(^b\) Odds ratio for categorical outcomes.

Abbreviations: see table 1 and 2

**Figure 1.** Referrals and participation in a cardiac rehabilitation program by regions. Referred CR bars show the percentage of all enrolled patients in that region who were referred to the CR center according to the discharge letter and patient’s history. Participated bars present the percent of patients who were referred for CR that actually participated in a full CR programme.