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# Organizational and patient-level predictors for attaining key risk factor targets in cardiac rehabilitation after myocardial infarction: The Perfect-CR study\*

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### ABSTRACT

*Background:* Benefits of cardiac rehabilitation (CR) programme components on attaining risk factor targets post-myocardial infarction (MI) and their predictive strength relative to patient characteristics remain unclear. We aimed to identify organizational and patient-level predictors of risk factor target attainment at one-year post-MI. *Methods:* In this observational study data on CR organization at 78 Swedish CR centres was collected and merged with patient-level registry data (n=7549). Orthogonal partial least squares discriminant analysis identified predictors (Variables of Importance for the Projection (VIP) values >0.8) of attaining low-density lipoprotein-cholesterol (LDL-C) <1.8 mmol/L, blood pressure (BP) <140/90 mmHg and smoking abstinence.

Results: The strongest predictors (VIP [95% CI]) for attaining LDL-C and BP targets were offering psychosocial management (2.14 [1.78–2.50]; 2.45 [1.91–2.99]), having a psychologist in the CR team (1.62 [1.36–1.87]; 2.05 [1.67–2.44]), extended opening hours (2.13 [2.00–2.27]; 1.50 [0.91–2.10]), adequate facilities (1.54 [0.91–2.18]; 1.89 [1.38–2.40]), and having a medical director (1.70 [0.91–2.48]; 1.46 [1.04–1.88]). The strongest patient-level predictors of attaining LDL-C and/or BP targets were low baseline LDL-C (3.95 [3.39–4.51]) and having no history of hypertension (2.93 [2.60–3.26]), respectively, followed by exercise-based CR participation (1.38 [0.66–2.10]; 1.46 [1.14–1.78]). For smoking abstinence, the strongest organizational predictor was varenicline being prescribed by CR physicians (1.88 [0.95–2.80]) and patient-level predictors were participation in exercise-based CR (2.47 [2.07–2.88]) and group education (1.92 [1.43–2-42]), and no cardio-vascular disease history (2.13 [1.78–2.48]).

Conclusions: We identified multiple CR organizational and patient-level predictors of attaining risk factor targets post-MI. These results may influence the future design of comprehensive CR programmes.

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**Table 1**Baseline patient-level registry data.

Demographics	lex AMI	year follow-up	value*	index AMI	year follow-up	value**
Demographics Age (years ±SD) 62 Gender, male (%) Distance between home and CR centre (kilometres ±SD) Country or region of birth (%) Born in Sweden Born in Nordic countries (outside of Sweden) Born in Europe (outside of Nordic countries) Born outside of Europe Employment status (%) Unskilled workers Skilled workers Assistant non-manual employees High / intermediate salary employees Self-employed Other employment Marital status (%) Living with partner Living alone Education attainment (%) Under 10 years (compulsory school only) 10–12 years (Upper school) Over 12 years (college/university level) Household adjusted income (%) Low Medium-low Medium Medium-high	9165	7549		2653	2170	
Age (years ±SD)  Gender, male (%) Distance between home and CR centre (kilometres ±SD)  Country or region of birth (%) Born in Sweden Born in Nordic countries (outside of Sweden) Born in Europe (outside of Nordic countries) Born outside of Europe  Employment status (%) Unskilled workers Skilled workers Assistant non-manual employees High / intermediate salary employees Self-employed Other employment  Marital status (%) Living with partner Living alone Education attainment (%) Under 10 years (compulsory school only) 10–12 years (Upper school) Over 12 years (college/university level) Household adjusted income (%) Low Medium-low Medium Medium-high						
Gender, male (%) Distance between home and CR centre (kilometres ±SD) Country or region of birth (%) Born in Sweden Born in Nordic countries (outside of Sweden) Born in Europe (outside of Nordic countries) Born outside of Europe Employment status (%) Unskilled workers Skilled workers Assistant non-manual employees High / intermediate salary employees Self-employed Other employment Marital status (%) Living with partner Living alone Education attainment (%) Under 10 years (compulsory school only) 10–12 years (Upper school) Over 12 years (college/university level) Household adjusted income (%) Low Medium-low Medium Medium-high	$0.9 \pm 8.6$	$62.6 \pm 8.7$	0.05	$60.2 \pm 8.8$	$60.0 \pm 8.7$	0.52
Distance between home and CR centre (kilometres ±SD)  Country or region of birth (%)  Born in Sweden  Born in Nordic countries (outside of Sweden)  Born in Europe (outside of Nordic countries)  Born outside of Europe  Employment status (%)  Unskilled workers  Skilled workers  Assistant non-manual employees  High / intermediate salary employees  Self-employed  Other employment  Marital status (%)  Living with partner  Living alone  Education attainment (%)  Under 10 years (compulsory school only)  10–12 years (Upper school)  Over 12 years (college/university level)  Household adjusted income (%)  Low  Medium-low  Medium-low  Medium-high	75.0	76.0	0.13	70.5	70.7	0.86
(kilometres ±SD)  Country or region of birth (%) Born in Sweden Born in Nordic countries (outside of Sweden) Born in Europe (outside of Nordic countries) Born outside of Europe Employment status (%) Unskilled workers Skilled workers Assistant non-manual employees High / intermediate salary employees Self-employed Other employment Marital status (%) Living with partner Living alone Education attainment (%) Under 10 years (compulsory school only) 10–12 years (Upper school) Over 12 years (college/university level) Household adjusted income (%) Low Medium-low Medium Medium-high	N/A	$21.4 \pm 26.6$		N/A	$20.7 \pm 25.1$	
Country or region of birth (%) Born in Sweden Born in Nordic countries (outside of Sweden) Born in Europe (outside of Nordic countries) Born outside of Europe Employment status (%) Unskilled workers Skilled workers Skilled workers Assistant non-manual employees High / intermediate salary employees Self-employed Other employment Marital status (%) Living with partner Living alone Education attainment (%) Under 10 years (compulsory school only) 10–12 years (Upper school) Over 12 years (college/university level) Household adjusted income (%) Low Medium-low Medium Medium-high						
Born in Sweden  Born in Nordic countries (outside of Sweden)  Born in Europe (outside of Nordic countries)  Born outside of Europe  Employment status (%)  Unskilled workers  Skilled workers  Assistant non-manual employees  High / intermediate salary employees  Self-employed  Other employment  Marital status (%)  Living with partner  Living alone  Education attainment (%)  Under 10 years (compulsory school only)  10–12 years (Upper school)  Over 12 years (college/university level)  Household adjusted income (%)  Low  Medium-low  Medium  Medium-high			0.33			0.80
Born in Nordic countries (outside of Sweden) Born in Europe (outside of Nordic countries) Born outside of Europe Employment status (%) Unskilled workers Skilled workers Assistant non-manual employees High / intermediate salary employees Self-employed Other employment Marital status (%) Living with partner Living alone Education attainment (%) Under 10 years (compulsory school only) 10–12 years (Upper school) Over 12 years (college/university level) Household adjusted income (%) Low Medium-low Medium Medium-high	80.1	81.1		71.0	72.1	
Sweden) Born in Europe (outside of Nordic countries) Born outside of Europe Employment status (%) Unskilled workers Skilled workers Skilled workers Assistant non-manual employees High / intermediate salary employees Self-employed Other employment Marital status (%) Living with partner Living alone Education attainment (%) Under 10 years (compulsory school only) 10–12 years (Upper school) Over 12 years (college/university level) Household adjusted income (%) Low Medium-low Medium Medium-high	5.0	4.6		6.6	6.1	
Born in Europe (outside of Nordic countries) Born outside of Europe Employment status (%) Unskilled workers Skilled workers Assistant non-manual employees High / intermediate salary employees Self-employed Other employment Marital status (%) Living with partner Living alone Education attainment (%) Under 10 years (compulsory school only) 10–12 years (Upper school) Over 12 years (college/university level) Household adjusted income (%) Low Medium-low Medium Medium-high						
Born outside of Europe  Employment status (%) Unskilled workers Skilled workers Skilled workers Assistant non-manual employees High / intermediate salary employees Self-employed Other employment Marital status (%) Living with partner Living alone Education attainment (%) Under 10 years (compulsory school only) 10–12 years (Upper school) Over 12 years (college/university level) Household adjusted income (%) Low Medium-low Medium Medium-high	7.1	6.9		10.7	10.5	
Employment status (%) Unskilled workers Skilled workers Assistant non-manual employees High / intermediate salary employees Self-employed Other employment Marital status (%) Living with partner Living alone Education attainment (%) Under 10 years (compulsory school only) 10–12 years (Upper school) Over 12 years (college/university level) Household adjusted income (%) Low Medium-low Medium Medium-high	7.8	7.4		11.6	11.3	
Unskilled workers Skilled workers Assistant non-manual employees High / intermediate salary employees Self-employed Other employment Marital status (%) Living with partner Living alone Education attainment (%) Under 10 years (compulsory school only) 10–12 years (Upper school) Over 12 years (college/university level) Household adjusted income (%) Low Medium-low Medium Medium-high			0.88			0.94
Skilled workers Assistant non-manual employees High / intermediate salary employees Self-employed Other employment Marital status (%) Living with partner Living alone Education attainment (%) Under 10 years (compulsory school only) 10–12 years (Upper school) Over 12 years (college/university level) Household adjusted income (%) Low Medium-low Medium Medium-high	24.5	27.9		35.9	36.5	
Assistant non-manual employees High / intermediate salary employees Self-employed Other employment Marital status (%) Living with partner Living alone Education attainment (%) Under 10 years (compulsory school only) 10–12 years (Upper school) Over 12 years (college/university level) Household adjusted income (%) Low Medium-low Medium Medium-high	17.2	20.0		21.5	20.7	
High / intermediate salary employees Self-employed Other employment Marital status (%) Living with partner Living alone Education attainment (%) Under 10 years (compulsory school only) 10–12 years (Upper school) Over 12 years (college/university level) Household adjusted income (%) Low Medium-low Medium Medium-high	10.3	12.0		11.0	11.8	
Self-employed Other employment Marital status (%) Living with partner Living alone Education attainment (%) Under 10 years (compulsory school only) 10–12 years (Upper school) Over 12 years (college/university level) Household adjusted income (%) Low Medium-low Medium Medium-high	21.8	25.8		15.2	15.2	
Other employment  Marital status (%) Living with partner Living alone  Education attainment (%) Under 10 years (compulsory school only) 10–12 years (Upper school) Over 12 years (college/university level) Household adjusted income (%) Low Medium-low Medium Medium-high	6.8	7.7		6.9	6.9	
Marital status (%) Living with partner Living alone Education attainment (%) Under 10 years (compulsory school only) 10–12 years (Upper school) Over 12 years (college/university level) Household adjusted income (%) Low Medium-low Medium Medium-high	6.1	6.6		9.5	8.9	
Living with partner Living alone Education attainment (%) Under 10 years (compulsory school only) 10–12 years (Upper school) Over 12 years (college/university level) Household adjusted income (%) Low Medium-low Medium Medium-high	0.1	0.0	0.03	5.0	0.9	0.20
Living alone  Education attainment (%)  Under 10 years (compulsory school only)  10–12 years (Upper school)  Over 12 years (college/university level)  Household adjusted income (%)  Low  Medium-low  Medium  Medium-high	56.8	58.6	0.00	44.4	46.3	0.20
Education attainment (%) Under 10 years (compulsory school only) 10–12 years (Upper school) Over 12 years (college/university level) Household adjusted income (%) Low Medium-low Medium Medium-high	43.1	41.4		55.6	53.7	
Under 10 years (compulsory school only) 10–12 years (Upper school) Over 12 years (college/university level) Household adjusted income (%) Low Medium-low Medium Medium-high	73.1	41.4	0.33	33.0	33.7	0.90
10–12 years (Upper school) Over 12 years (college/university level) Household adjusted income (%) Low Medium-low Medium Medium-high	27.7	27.2	0.55	33.4	32.8	0.50
Over 12 years (college/university level)  Household adjusted income (%)  Low  Medium-low  Medium  Medium-high	48.5	49.2		51.1	51.3	
Household adjusted income (%) Low Medium-low Medium Medium-high	22.6	23.6		15.5	15.9	
Low Medium-low Medium Medium-high	22.0	23.0	0.001	13.3	13.9	0.24
Medium-low Medium Medium-high	20.0	17.8	0.001	29.6	27.1	0.24
Medium Medium-high					20.6	
Medium-high	20.0 20.0	19.4 20.0		21.1 20.3	20.8	
	20.0	21.5		16.1	17.6	
nigii	20.0	21.2		12.8	13.8	
Diels feetene musuious discoses and tune of MI	20.0	21.2		12.8	13.8	
Risk factors, previous diseases, and type of MI	28.9	29.4	0.76			
Active smoker (%)				146 + 20	147 + 20	0.00
, 0	$50 \pm 28$	$151 \pm 28$	0.19	$146 \pm 29$	$147 \pm 29$	0.88
	$8 \pm 16$	$88 \pm 16$	0.29	$88 \pm 17$	$88 \pm 17$	0.91
	$0 \pm 1.1$	$3.1 \pm 1.1$	0.30	$3.1 \pm 1.1$	$3.2 \pm 1.1$	0.45
	$0 \pm 4.7$	$28.0 \pm 4.6$	0.99	$27.5 \pm 4.9$	$27.6 \pm 4.8$	0.89
History of hypertension (%)	48.3	47.1	0.25	41.8	41.5	0.95
History of CVD (%)	27.5	24.5	< 0.01	23.1	20.5	0.03
History of DM (%)	24.2	22.5	< 0.01	21.1	20.3	0.01
STEMI (%)	37.6	39.1		46.6	48.1	0.27
LVEF during admission (%)		50.0	0.20	60.0	64.1	0.86
Normal (≥50%)	57.7	59.0		63.0	64.1	
Mildly reduced (40–49%)	18.5	18.7		20.3	20.3	
Moderately - severely reduced (≤39%)	11.9	11.2		14.1	13.3	
Medication at discharge (%)				05.		
Platelet inhibitors <sup>a</sup>	98.8	99.2	0.06	99.1	99.4	0.12
Lipid-lowering therapy <sup>b</sup>	96.9	97.9	< 0.01	98.0	98.4	0.37
ACEi or ARB	84.7	85.8	0.10	84.2	84.9	0.51
Beta blockers	89.6	89.9	0.90	90.7	90.9	0.86
CR programme participation (%)						
Participated in EBCR	42.0	50.6	< 0.01	35.5	43.1	< 0.01
Participated in group education	39.2	46.9	0.92	30.2	36.2	0.95
Participated in professional tobacco	N/A	N/A		14.4	17.5	0.99

Numbers are presented as percentages (%) or means and standard deviations ( $\pm$ SD). p-values are presented for \* Patients with index MI vs. Patients with a one-year follow-up and \*\* Active smokers with index MI vs. Active smokers at baseline with a one-year follow-up.

SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL-C, low-density lipoprotein-cholesterol; CVD, cardiovascular disease; HbA1c, Haemoglobin A1c; DM, diabetes mellitus, BMI, body mass index; MI, myocardial infarction; STEMI, ST-elevation myocardial infarction; LVEF, left ventricular ejection fraction; ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin-II receptor blocker; CR, cardiac rehabilitation; EBCR, exercise-based CR.

<sup>&</sup>lt;sup>a</sup> Platelet inhibitors included acetylsalicylic acid, clopidogrel, ticlopidine, prasugrel, ticagrelor or other. <sup>b</sup>Lipid-lowering therapy included statins, ezetimibe, fibrates or other LLT.

### 1. Introduction

Cardiac rehabilitation (CR) is a multidisciplinary intervention with clearly defined core components, including patient assessment, management of cardiovascular risk factors, physical activity and dietary counselling, prescription of exercise training, psychosocial management, and vocational support [1,2]. CR carries the highest possible recommendation in the current European guidelines on cardiovascular disease (CVD) prevention [3] and evidence from meta-analyses have affirmed its effectiveness [4–6].

However, considerable heterogeneity in CR service delivery exists across programmes [4,5]. While the framework for optimal CR in the era of modern cardiology is well described, the individual benefits of various programme components and their relative predictive strength for attaining risk factor targets are still largely unknown [2].

Treatment target attainment also varies substantially. In the repeated cross-sectional EUROASPIRE (European Action on Secondary and Primary Prevention through Intervention to Reduce Events) surveys [7], target attainment for key risk factors varied considerably between programmes [8-10]. Similar outcome variation has been observed in the nationwide SWEDEHEART (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart disease Evaluated According to Recommended Therapies) quality registry, that records individual-level baseline characteristics, treatments, and follow-up data of all patients admitted with a myocardial infarction (MI) to coronary care units in Sweden [11]. In 2020, the proportion of patients that attained the low-density lipoprotein-cholesterol (LDL-C) target of <1.8 mmol/L varied between 50% and 96% across centres, for systolic blood pressure (BP) attaining the <140 mmHg target varied between 64% to 98%, and for smoking abstinence the proportion varied between 22% and 100% [11]. Whether heterogeneity in CR delivery can explain some of this variation is unknown.

Through combining unique survey data from all CR centres in Sweden with patient-level data from SWEDEHEART, the present study aimed to identify organizational and patient-level predictors for attaining treatment targets for LDL-C, BP, and smoking abstinence at one-year post-MI in a nationwide cohort of patients who participated in CR.

### 2. Methods

This was an observational survey- and registry-based study. The study complies with the Declaration of Helsinki was reviewed and approved by the Ethics Committee at Lund University (2336–001). The need for signed consent by patients for inclusion in Swedish quality registries has collectively been waived. Upon hospital admission MI patients are informed verbally and in writing by a nurse or physician about SWEDEHEART.

### 2.1. Organizational centre-level survey data

Data on CR organization was derived from the survey-based Perfect-CR study, evaluating service delivery at Swedish CR centres. Details of the study procedure have previously been published [12]. In short, a web-based questionnaire was sent out in November 2016 to all 79 CR centres in Sweden reporting to SWEDEHEART at the time (95% of all CR centres in Sweden) [13]. The respondents were instructed to provide answers that reflected the everyday operation at the centre during 2016. The response rate was 100% and missing data minimal (Table 1). One centre shut down weeks after the survey was performed and was excluded from further analysis [12]. In total, 71 organizational variables representing guidelines-recommended standards of CR delivery were used in the current analysis. The variables included *Structure-based metrics*, *Process-based metrics*, and *Quality metrics*, categorized as suggested by European Association of Preventive Cardiology [2]. All variables and their definitions are listed in Supplementary Table S1.

### 2.2. Patient-level registry data

The patient population in the current study was defined by the discharge date after hospital admission (01.11. 2015 to 31.10. 2016). The date interval was selected by matching the time during which patients attended CR (first 3-6 months after discharge) with the time interval the answers in the Perfect-CR survey represented. Inclusion criteria were: 1) discharged alive after suffering type-1 MI, 2) age 18–74 years, and 3) attending a one-year follow-up CR visit. Data was extracted from the SWEDEHEART and Statistics Sweden registries. Twenty-six patient-level variables were used in the current analysis (Supplementary Table S2). Geographical distance (kilometres) to the CR centre was estimated using coordinates of the central point of each patient's postal code as a proxy for their address, from which the driving distance to the CR centre was calculated by a commercially available algorithm using Google Maps. Patient-level data was linked using the unique Swedish personal identification number allocated to every Swedish citizen. Organizational data was then merged with patient-level data based on at which CR centre each patient had their follow-up.

### 2.3. Study outcomes

Attaining targets for LDL-C, BP, and smoking abstinence (for current smokers at baseline only) at one-year post-MI were the outcomes for the study. Outcome variable data was retrieved from SWEDEHEART. LDL-C and BP target attainment was defined according to the 2016 European guidelines as <1.8 mmol/L (yes/no) and < 140/90 mmHg (yes/no), respectively [14]. Smoking status was self-reported. Abstinence was defined as not smoking during  $\geq 1$  month (yes/no) prior to the follow-up visit.

### 2.4. Statistical methods

Baseline characteristics are presented as means (SD) or medians (IQR) for continuous variables and counts (%) for categorical variables. Missing data was assumed to be missing at random [15], and k Nearest Neighbour imputation was performed with k set low (k = 3) [16]. Outcome data were not imputed. A multivariable discriminant analysis was performed by Orthogonal Projection to Latent Structures Discriminant Analysis (OPLS-DA) [17] using the non-linear iterative partial least squares (NIPALS) algorithm that allows for the analysis of wide data matrices. OPLS-DA uses Q<sup>2</sup> (goodness of prediction), calculated using leave-one-out cross-validation (LOOCV) resampling, to determine the number of independent (orthogonal) components to extract. OPLS-DA computes the influence of every X-variable on patient outcome (Y) resulting in Variables of Importance for the Projection (VIP) as well as their respective loading on the first principal component. VIP is a weighted sum of each individual X-variable in the model. In our study variables with a VIP value >0.8 and a confidence interval (CI) excluding zero were considered to have influence on the projection and, thus, be predictive of outcomes. To aid in interpretation of the VIP value the loading value was used, which indicates whether the variables were negative or positive predictors of the outcome. Thereafter, a set of crude logistic regression models were fitted to estimate the unadjusted association of each predictor to the three outcome variables. Point estimate odds ratios (OR) and 95% CI are presented. Baseline characteristics were calculated using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp, Armonk, NY). The OPLS-DA was performed using SIMCA P+, version 15.0.2.0 (Sartorius Stedim Data Analytics AB, MKS, Umeå, Sweden). Covariate imputation and logit modelling was performed in R, version 4.0.3 (The R Foundation for Statistical Computing, Vienna, Austria).

# 3. Results

Details of CR organization at the 78 CR centres included in Perfect-

CR have previously been published [12,18]. In short, all CR programmes were phase II in an out-patient setting. The median (IQR) programme duration was 6.5 (2.5, 12.0) months. Only eight centres (10.3%) offered home-based CR as an alternative to a centre-based programme. Almost all centres (76, 97.4%) offered supervised exercise-based CR (EBCR), most commonly including two one-hour sessions per week for a minimum of 12 weeks. Seventy-five out of the 78 centres (96.2%) had a multidisciplinary team constituting a nurse, a physician, and a physiotherapist. Additionally, a psychologist or social worker and a dietician were a part of the CR team at 71 (91.0%) and 66 (84.6%) of the centres, respectively. The programme was led by a medical director at 59 (75.6%) of the centres. Further details on CR organization are summarized in Supplementary Table S3.

In Fig. 1, a flowchart of patients in the study is displayed. Patient-level baseline characteristics are displayed in Table 1. Baseline characteristics stratified by outcome, and number of missing values for each variable, are presented in Supplementary tables S4-S6.

### 3.1. Organizational and patient-level predictors of risk factor outcomes

Variables with a VIP value >0.8 and a CI excluding zero from the OPLS-DA are displayed in Fig. 2 (LDL-C and BP) and Fig. 3 (smoking abstinence). Exact VIP [95% CI] and loading [95% CI] values for all variables, as well as the logistic regression estimates (OR and [95% CI])

are listed in Supplementary tables S7–9. Main results for each outcome are summarized below.

### 3.1.1. LDL-C and BP

The five strongest Structure-based metrics predicting patients being at LDL-C target were: the CR team having a medical director responsible for the programme, having written protocols for physician's coronary care unit discharge consults, a psychologist or social worker being part of the CR team, the CR team reporting satisfaction with facilities, and the CR nurses having written protocols on how to adjust lipid-lowering medication (Fig. 2). The same five variables were also the strongest Structure-based metric predictors for attaining the BP target (Fig. 2). The strongest Process-based metrics for LDL-C and BP were: assessing and counselling patients regarding psychosocial health (LDL-C and BP), having extended opening hours at the CR centre (LDL-C and BP), offering an individual assessment with a physiotherapist before starting EBCR (BP), during this visit performing a symptom-limited exercise test (LDL-C and BP) and providing the patients with an exercise log to register their physical activity (BP), individually evaluating the patient's need for a physician consultation during CR follow-up (LDL-C), and continuity in nurse-patient contact during follow-up (LDL-C) (Fig. 2). For *Quality metrics*, patient coverage and the CR centre being situated at a university hospital were identified as predictors of attaining both LDL-C and BP targets. The strongest patient-level predictors for attaining

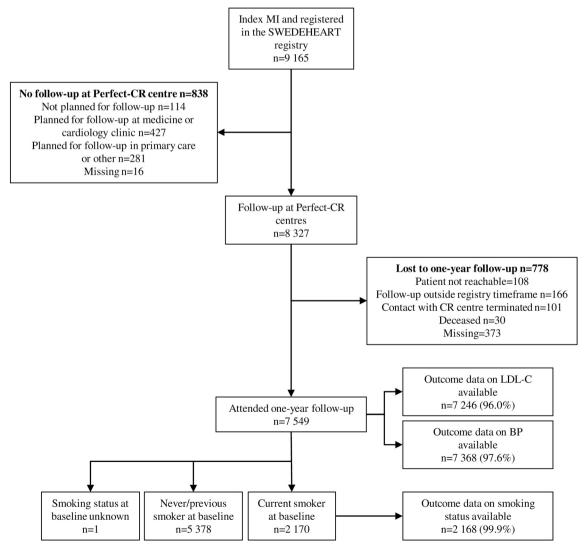


Fig. 1. Flow diagram of the study population.

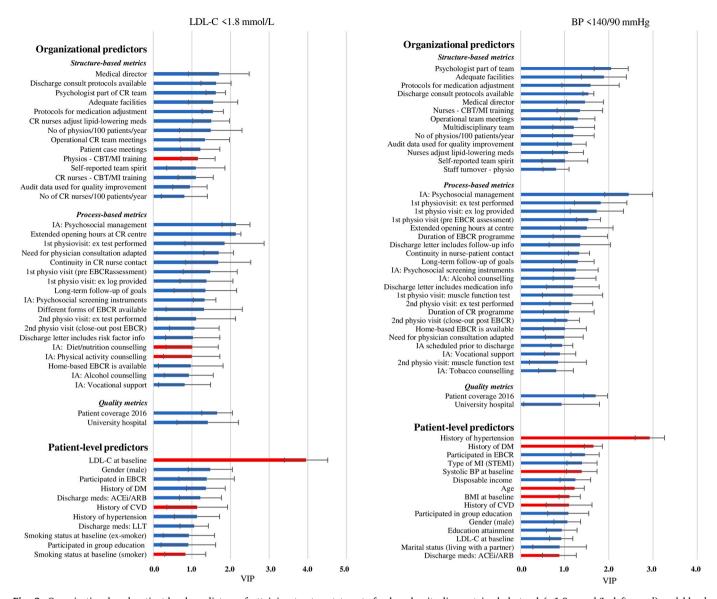


Fig. 2. Organizational and patient-level predictors of attaining treatment targets for low-density lipoprotein-cholesterol (<1.8 mmol/L, left panel) and blood pressure (<140/90 mmHg, right panel) at one-year after myocardial infarction. Negative predictors are shown in red. Only variables with VIP values >0.8 and confidence intervals not including zero are displayed.

CR, cardiac rehabilitation; CBT, cognitive behavioural therapy; MI, motivational interviewing, IA, initial assessment; physio, physiotherapist; ex, exercise, EBCR, exercise-based cardiac rehabilitation; LLT, lipid-lowering treatment (statins, ezetimibe, fibrates or other LLT), DM, diabetes mellitus; ACEi, angiotensin converting enzyme inhibitors; ARB, angiotensin II receptor blockers; MI, myocardial infarction; STEMI, ST-elevation MI; LDL-C, low-density lipoprotein cholesterol; BP, blood pressure; BMI, body mass index; CVD, cardiovascular disease. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

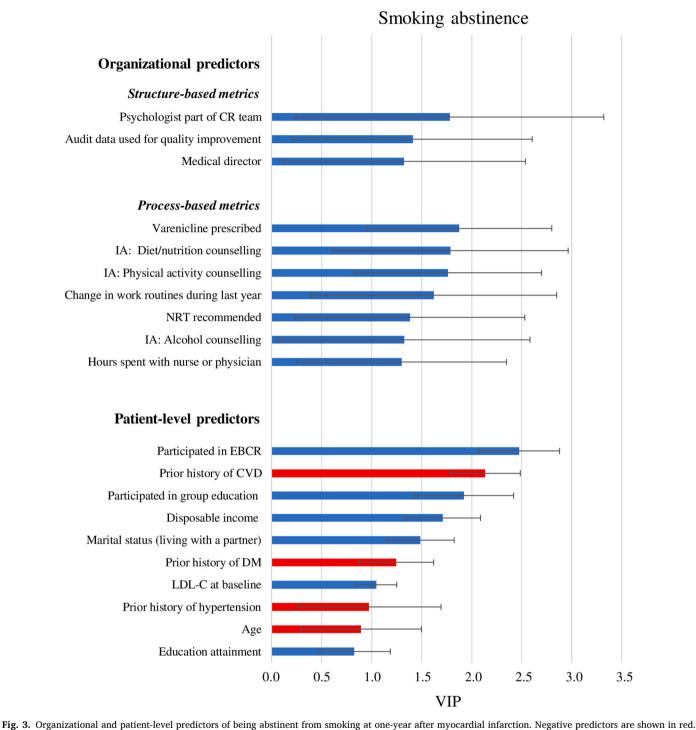
LDL-C targets at one-year were LDL-C at baseline (negative predictor), male gender, having participated in EBCR, and having a history of diabetes mellitus (DM). For attaining the BP target the strongest patient-level predictors were history of hypertension and DM (both negative predictors), having participated in EBCR, and having had an ST-elevation MI.

# 3.1.2. Smoking abstinence

Out of the Structure-based metrics having a psychologist or social worker in the CR team, using audit data for quality improvement, and having a medical director positively predicted smoking abstinence at one-year post-MI (Fig. 3). Out of the Process-based metrics CR centre physicians prescribing varenicline to current smokers, diet/nutritional and physical activity counselling being provided at the initial assessment and recommending the use of nicotine replacement therapy to

currently smoking patients were the strongest predictors (Fig. 3). The strongest patient-level predictors included having participated in EBCR and group education, having a history of CVD (negative predictor), household disposable income and living with a partner (Fig. 3).

Out of the variables identified as predictive by the OPLS-DA the majority were also significant in the logistic regression for LDL-C (91.1%) and BP (81.1%) (Supplementary tables S7–8). There was a larger discrepancy between the OPLS-DA and logistic regression for smoking abstinence (55.0% consistency), with confidence intervals being wide for many variables (Supplementary Table S9). Whether the association between exposure and outcome was positive or negative in the OPLS-DA and logistic regression was 100% consistent for all outcomes.



Only variables with VIP values >0.8 and confidence intervals not including zero are displayed. CR, cardiac rehabilitation; IA, initial assessment; EBCR, exercise-based CR; MI, myocardial infarction; STEMI, ST-elevation MI; LDL-C, low-density lipoprotein cholesterol; CVD, cardiovascular disease; DM, diabetes mellitus. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

# 4. Discussion

In this study, using unique nationwide CR organizational and patient-level registry data, we found multiple organizational and patient-level variables to be predictive of patients attaining recommended targets for LDL-C and BP, and for current smokers at baseline being abstinent at one-year post-MI.

# 4.1. LDL-C and BP

One of the strongest *structure-based metrics* predicting patients being at target for both LDL-C and BP was to have a medical director. Even though a medical director in the CR team is recommended by European guidelines, supporting evidence is limited [19]. Studies from other medical fields, however, have shown that clear leadership is associated with improved patient outcomes and quality of care [20]. Also, including a psychologist in the CR team was a strong predictor for both

outcomes. The prevalence of mental health disorders among CVD patients is high, and for post-MI patients with mental health disorders, interdisciplinary cooperation in patient care is recommended [3].

Several predictors indicating an importance of training and autonomy of CR nurses were identified as meaningful, including nurses having written protocols for medication adjustment, independently adjusting lipid lowering medication, and having formal training in motivational interviewing. Studies of patients undergoing surgery or having DM have shown that having autonomous nurses was associated with better risk factor outcomes and decreased mortality rates [21,22]. Other structurebased variables of importance were having adequate facilities, operational team meetings and patient case meetings. Also, using audit data for quality improvement was predictive of both outcomes, strengthening prior conclusions on the importance of auditing for quality improvement in cardiac care [23]. Interestingly, hours spent with a nurse and/or physician during follow-up were not predictive of attaining LDL-C or BP targets, and the number of nurses in staff was only predictive of attaining LDL-C. These results indicate that the composition and competence of the CR team, teamwork and leadership might be more important for reaching treatment targets than the number of hours spent with the individual patient. In addition, patient coverage and the centre being situated at a university hospital being predictive of LDL-C and BP indicates the importance of adequate referral routines and highly educated staff.

Concerning process-based metrics, the strongest predictor was to have psychosocial management as a part of the initial nurse assessment. Using screening instruments to evaluate psychosocial health was also predictive, supporting the notion to focus on psychosocial health of post-MI patients. Psychosocial risk factors such as low socio-economic status, social isolation, depression, and anxiety have been shown to worsen the prognosis in patients with established coronary heart disease and act as barriers to lifestyle changes and treatment adherence, decreasing the effects of CR [24]. Here, psychosocial management is referred to as the initial assessment by a CR nurse. European guidelines recommend that screening for psychosocial risk factors be done by any member of the multidisciplinary team best suited according to each institutions' resources and preferences. If psychosocial risk factors are identified the patient should be referred to a psychologist or behavioural expert and, as previously stated, having a psychologist as a part of the multidisciplinary team was predictive of both outcomes. Other predictive processbased metrics including flexible opening hours at the CR centre, continuity in nurse-patient care, long-term follow-up of goals, and the need for physician consultation being adapted to patient needs, reflect a CR organization that provides care tailored to patient needs. Evidence supports the application of individualized CR where the approach to behavioural change is person-centred [4,5].

Interestingly, ten out of eleven EBCR variables included in the analysis were positive predictors for reaching LDL-C and/or BP targets. EBCR participation improves risk factors and reduces hospital readmissions, cardiovascular morbidity, and mortality [25–27]. Our results further highlight the importance of well-equipped, well-staffed, and flexible EBCR programmes, offering individualized consultations with physiotherapists, testing of aerobic and muscular capacity, a variety of group-training sessions, and possibility for home-based EBCR [1].

Diet/nutritional and physical activity counselling at the initial assessment, as well as physiotherapists having formal training in motivational interviewing, were negative predictors of LDL-C target attainment at one-year. The reason for this is ambiguous but could be methodological. As such, there was near-zero variance in physical activity counselling at the initial assessment. Also, the VIP and loading values for all three variables were in the lower range and should be interpreted with caution.

Baseline LDL-C was, not surprisingly, the strongest negative *patient-level predictor* for attaining the LDL-C treatment target. Likewise, a history of hypertension was the strongest negative predictor of reaching BP targets. EBCR participation was a strong patient-level predictor for both

outcomes, further underlining the importance of EBCR. Also, patients participating in interactive group education were more likely to attain LDL-C and BP targets. This is in line with previous studies showing that post-MI patients who receive education have fewer cardiovascular events [28,29]. As expected, lipid-lowering therapy at discharge was predictive of attaining LDL-C target at one-year. Adequate lipid-lowering therapy initiated early is crucial to reach LDL-C targets and improve prognosis [3]. However, our results show that multiple organizational predictors, where there is ample room for improvement, were of equal or larger importance for patients reaching LDL-C targets as being prescribed lipid-lowering therapy at discharge. As such, the importance of adequate structure and process of CR delivery for aiding patients in reaching treatment targets should not be disregarded.

### 4.2. Smoking abstinence

Considerably fewer organizational predictors were identified as meaningful for smoking abstinence at one-year post-MI. One possible reason is the lower number of patients included in the analysis, diminishing the discriminatory power of the analyses and the precision of predictor estimates. For structure-based metrics, as for LDL-C and BP having a psychologist in the CR team, using audit data for quality improvement, and having a medical director were predictors of smoking abstinence at one-year. Of the process-based metrics the strongest predictors included varenicline being prescribed by the centre physicians and recommending nicotine replacement therapy. Varenicline has been shown to increase the likelihood of achieving smoking abstinence, but the treatment is highly underutilized in CR [8,12,30]. Time spent with a nurse or physician during the first year post-MI was predictive for smoking abstinence, indicating that smokers perhaps should be designated more face-to-face time during follow-up. This is corroborated by our data that participation in group education and in EBCR were positive predictors of smoking abstinence, both involving face-to-face contact with the patient. Other patient-level predictors for smoking abstinence included variables indicating a favourable socioeconomic status, and negative predictors included age, history of CVD, DM, and hypertension. These variables have previously been identified as predictors for CR attendance [31]. All these attributes are simultaneously non-modifiable by the CR team. The results indicate that smokers are a vulnerable patient group and may benefit from more individually adjusted CR compared to non-smokers.

# 4.3. Strengths and limitations

Our study included data from a nationwide cohort with 100% response rate on CR centre-level and high patient coverage. However, 778 (9.3%) patients were lost to follow-up which excludes patients who died and, perhaps, patients who were less prone to treatment adherence. Also, generalisability is limited due to the age cut off (18-74 years) as well as due to use of risk factor targets followed at the time that subsequently have been changed. The results can only be applied to CR centres in Sweden. OPLS-DA has the advantage of being able to analyse all variables together, allowing us to look for patterns in prediction and investigate relations between all variables in a single context. Thus, by using OPLS-DA more variables could be included in the analysis than what is possible in traditional regression models. At the same time, results should be interpreted as exploratory, and patterns of predictors and variable clusters should be interpreted from a bird's eye view rather than focusing on each single predictor identified. Also, being an observational study, no conclusions can be drawn on causality. A limitation of the study lies in how all predictors are put together in one model. This is however also a strength allowing the result output to be more data driven. The approach was also complemented with traditional regression analysis estimates per each single predictor, with generally high consistency. We then proceeded to apply human subject matter expertise in interpreting the results. This seemed a more valid approach given

the sheer number of possible predictors to be accounted for and the explicit goal of the paper also accounting for unique predictors from the Perfect-CR survey. Although NIPALS, and consequently OPLS-DA can overfit to data, we did apply both (a) resampling in the form of LOOCV to counter the risk of overfitting and (b) crude log-linear regression as a sensitivity analysis.

### 5. Conclusions

We identified multiple organizational predictors of importance for attaining targets for LDL-C and BP at one-year post-MI in Swedish patients who had attended a CR programme. For smoking abstinence, patient-level variables were more predictive and mostly non-modifiable. Building up a multiprofessional CR team with strong leadership, interdisciplinary teamwork, regular auditing, flexible and person-centred patient care may positively influence patient risk factor outcomes. These results can contribute to optimally organizing CR programme delivery in the era of modern cardiology, making the best possible use of limited human and economic resources.

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# CRediT authorship contribution statement

Halldora Ögmundsdottir Michelsen: Formal analysis, Investigation, Writing – original draft, Writing – review & editing, Visualization. Peter Henriksson: Methodology, Formal analysis, Data curation, Writing - review & editing, Visualization. John Wallert: Formal analysis, Methodology, Data curation, Validation, Writing - review & editing, Visualization. Maria Bäck: Conceptualization, Writing - review & editing. Ingela Sjölin: Investigation, Writing - review & editing. Mona Schlyter: Investigation, Writing - review & editing. Emil Hagström: Conceptualization, Writing - review & editing. Anna Kiessling: Conceptualization, Methodology, Writing - review & editing. Claes Held: Conceptualization, Writing - review & editing. Emma Hag: Conceptualization, Writing - review & editing. Lennart Nilsson: Conceptualization, Writing - review & editing. Alexandru Schiopu: Writing - review & editing, Supervision. M. Justin Zaman: Conceptualization, Writing - review & editing. Margret Leosdottir: Conceptualization, Methodology, Formal analysis, Investigation, Writing - review & editing, Visualization, Supervision, Project administration, Funding acquisition.

### Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi. org/10.1016/j.ijcard.2022.09.012.

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