

Cardiac rehabilitation goal attainment after myocardial infarction with versus without diabetes: A nationwide registry study

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ABSTRACT

Background: Patients with first-time myocardial infarction (MI) and diabetes mellitus (DM) constitute a vulnerable subgroup of cardiovascular (CV) patients for which secondary prevention is particularly important. We investigated if patients with versus without DM differ in attaining four main lifestyle-related cardiac rehabilitation (CR) targets, one-year post-MI.

Methods: This national cohort study (2006–2015) identified individuals with and without DM at hospital admission in the Swedish cardiac registry, SWEDEHEART. CR goal attainment was assessed one year later. The study population included 47,907 unique patients with first-time MI <75 years at baseline (61.8 mean age, 26.7% women, 14.6% with DM). After imputation, propensity score matching was performed. Analyses were conducted with logistic regression.

Results: In the matched population, having DM was associated (OR [95% CI]) with lower odds of attaining the one-year post-MI CR goal for both smoking cessation (0.90 [0.81, 0.99]) and attendance in exercise training (0.88 [0.83, 0.95]), yet with higher odds of the <1.8 mmol LDL-C target (1.28 [1.19, 1.36]), and similar odds for the <140 mm Hg systolic blood pressure target (0.97 [0.91, 1.04]). In addition, women with DM were particularly unlikely to attend exercise training.

Conclusions: Patients with first-time MI and DM are less likely to attain two of four selected CR goals compared to those without DM. The particularly low exercise training attendance by women with DM is of concern. Possibilities for tailored interventions targeting behavioural change for this high-risk group, including focused efforts to increase exercise training attendance in women with DM, should be investigated.

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1. Introduction

Cardiovascular (CV) disease (CVD) and diabetes mellitus (DM) are major global health burdens, accounting for >20 million deaths annually [1]. Myocardial Infarction (MI) is the most common acute result of coronary artery disease (CAD). In the general population, DM is a major risk factor for the development of CAD and MI [2]. In 2015, approximately 415 million people aged 20–79 had DM worldwide, with an estimated global health cost of 673 billion US dollars [3]. The prevalence is increasing primarily due to increased type 2 DM (T2DM) [4], characterised by chronic hyperglycaemia caused by impaired insulin secretion or action which results from the interaction of genetic variants [5] and environmental factors, primarily sedentary lifestyles [6]. Long-term T2DM and

inadequate glycaemic control contribute to the development of vascular complications [7]. Moreover, those with DM experience a greater mortality during the acute phase of MI and a higher morbidity post-MI [8–10]. Data from the Framingham heart study 1950–2005 suggests that the risk for CV mortality is two-fold higher in patients with DM [11] and evidence from the Minnesota Heart Survey showed that the in-hospital death rate after admission for acute MI was 1.5 times higher in those with DM compared with non-DM patients [12].

The purpose of cardiac rehabilitation (CR) is to decrease morbidity and mortality, and improve quality of life post MI [13,14]. Guidelines for CR uniformly recommend behavioural/lifestyle interventions targeting smoking cessation, regular exercise training and increased daily physical activity, maintaining a healthy body weight, optimal control of risk factors (blood pressure, cholesterol and glucose control), and adherence to cardioprotective drug therapies [15]. Many of these behavioural/lifestyle interventions are also recommended for prevention and treatment of DM [16,17]. Despite the importance of CR there is

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evidence of gender disparity, with previous reports from a European population-based study [18] and a meta-analysis [19] that women are less frequently referred to CR than men. The higher mean age of women in these studies may in part explain this difference.

Following an MI, those with DM constitute a high-risk subpopulation for which lifestyle changes involving the patient's own behavioural changes seem particularly crucial. However, we are unaware of any study that has compared the relative success of attaining important behaviour-related lifestyle goals during CR – in MI patients with and without DM.

Using linked nationwide registries including the unselected Swedish quality registry on CAD (SWEDEHEART), we applied propensity score matching on demographic, clinical, and socioeconomic baseline variables and thereafter estimated the associations between having DM or not at hospital admission for first-time MI and the subsequent goal attainment at one-year of four major CR goals; smoking cessation, attendance in exercise training, as well as low density lipoprotein cholesterol (LDL-C) < 1.8 mmol/L or a 50% reduction from an untreated baseline value, and systolic blood pressure (SBP) < 140 mm Hg.

2. Method

2.1. Registries and data

Different national registries were linked for the present study. The national quality health registries are clinical registries of unselected patient populations, aimed at including all cases of a particular ailment occurring in the country.

The national quality Registry of Information and Knowledge about Swedish Heart Intensive Care Admissions (SWEDEHEART:RIKS-HIA) gathers data on >100 variables, including diagnosis of MI, medications, acute care clinical variables, demographics, and more, through registration of hospital admissions for acute MI at all Coronary Care Units (CCU) in Sweden with national population coverage >90% for patients <80 years [20]. Discharge diagnoses according to ICD-10 codes I21–I23 are based on established myocardial infarction criteria including clinical symptoms, ECG readings, laboratory values and cardiac imaging. RIKS-HIA is randomly audited showing >95% concordance with hospital health record data. RIKS-HIA registers MI cases from all hospitals in Sweden with national population coverage >90% for those <80 years [20].

The national quality registry for Secondary Prevention after Heart Intensive Care Admission (SWEDEHEART:SEPHIA) seeks to register all surviving cases treated for MI < 75 years old in Sweden. SEPHIA gathers information on >40 variables, on traditional risk factors, a range of behavioural interventions, patient-reported variables including psychological functioning and others. The SEPHIA nationwide coverage of eligible patients is >75%, registered at 97% of Swedish hospitals. SEPHIA is also randomly audited, showing >95% concordance with hospital health record data. Two CR visits are registered in SEPHIA: 6–10 weeks (SEPHIA1) and 12–14 months (SEPHIA2) post MI [20].

Statistics Sweden (SCB) is the agency entrusted with the official national statistics. SCB maintains the individual data on educational attainment, country of birth, income, and more. SCB has excellent coverage of the entire Swedish population with annual repeated measurements on socioeconomic status (SES) variables [21].

2.2. Patient selection

See Fig. 1 for details on the flow of patients through the present study. Out of all 192,059 MI admissions registered in RIKS-HIA from 1st Jan 2006 through 31st December 2015, the final study population of 47,907 unique patients with first-time MI < 75 years of age that were alive at SEPHIA1 and attending CR were selected.

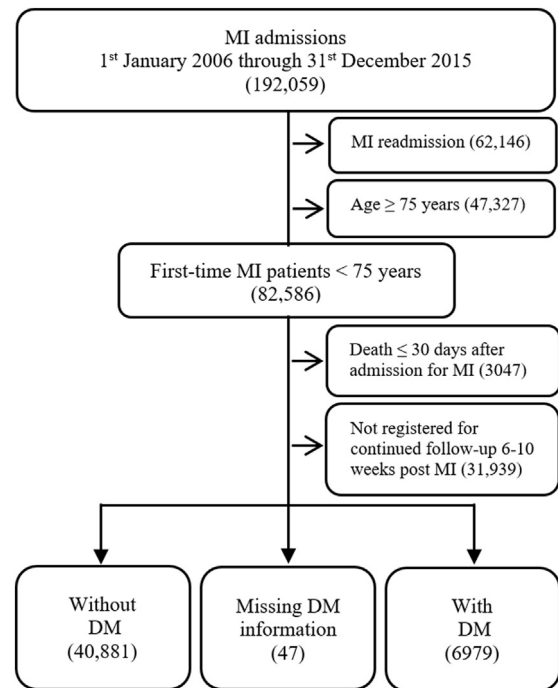


Fig. 1. The study population. Patient counts are in parentheses. DM, diabetes mellitus; MI, myocardial infarction.

2.3. Exposure and outcomes

The exposure condition was having DM (~90% of all having T2DM) as registered at the index hospitalisation. Some patients with first-time MI are newly diagnosed with DM at this instance, but only a relatively minor portion of them are likely to escape registration. The chosen four CR goal attainment outcomes were all assessed at the one-year post MI follow-up at SEPHIA2 and defined as follows; smoking abstinence, attendance in exercise training, LDL-C < 1.8 mmol/L or a 50% reduction from an untreated baseline value, and SBP < 140 mm Hg. Both smoking and participation in exercise training are considered directly behavioural, whereas LDL-C and SBP are considered indirectly, and only to a lesser extent, behavioural.

2.4. Covariates

To account for confounding and obtain baseline precision, covariates included in the propensity score were selected based on a directed acyclic graph (Supplemental material), and included age, sex, smoking (never/former/current smoker), physical activity (number of ≥30 minute sessions of at least moderate physical activity per week), occupational status (working/sick-leave/unemployed/retired/student or other), highest attained education (primary/secondary/higher), household income adjusted for family composition (quintiles; 1–5), admission year, hospital size based on number of treated patients (tertiles of n patients per hospital per year; small/medium/large), country of birth (foreign/Sweden), body mass index (BMI), hypertension, previous stroke, left ventricular ejection fraction (LVEF), and discharge medications. Discharge medications consisted of anticoagulants, angiotensin II receptor blockers (ARB), angiotensin-converting enzyme (ACE) inhibitors, beta blockers, calcium antagonists, digitalis, diuretics, long acting nitrates, other antiplatelets, statins, and other lipid lowering agents. Additionally, at baseline registered participation in the general CR education (called the heart school), physical exercise training and specific types of CR programmes promoting smoking cessation, a healthy diet, and stress reduction were included as covariates.

2.5. Ethical considerations

After linkage, the National Board of Health and Welfare sent pseudonymised data to the researchers after formal application-and-approval. The SWEDEHEART registry is sanctioned by Swedish law, and all patients are informed of their inclusion and their right to have their data erased at any time. It is extremely rare that anyone requests to have their data erased (~single digit numbers/year, if any at all). Informed consent is waived as it was not feasible. The Regional Ethical Review Board in Uppsala, Sweden approved the present study (2013/478).

2.6. Statistical analysis

Additional details of the statistical analysis are available in the Data Supplement. In summary, numerical variables are presented as mean (SD) and categorical variables as count (%) if not further specified.

Missing values were assumed to be missing dependent on measured variables (MAR), rather than missing completely at random (MCAR), and imputation through *k* Nearest Neighbour (*k*NN) was performed with *k* = 2 [22,23]. We thereafter applied propensity score analysis [24,25], using binomial logistic regression to estimate the probability for having DM at baseline for each patient given the covariates. On this probability, exposed patients (with DM) were then matched without replacement 1:1 with unexposed patients (without DM) using nearest neighbour matching within 0.2 SD caliper matching. Primary analysis was thereafter performed with this matched population, in which binomial logistic regression was again used, but now for estimating odds ratios (OR) with 95% confidence intervals (CI) for each of the four outcomes. Statistical significance was set to 5%. Separate sensitivity analyses were performed through (a) complete case analysis, (b) additional matching on specific components of CR, and (c) conditioning on those also registered at the SEPHEA2 follow-up (CR

Table 1
Descriptives summary of the study population, by group, and with missing values.

	All (N = 47,907)	Without DM (N = 40,881)	With DM (N = 6979)	Missing ^a (N = 47)
Demographics				
Men (%)	35,104 (73.3)	30,149 (73.7)	4917 (70.5)	0
Age, years (mean (SD))	61.7 (8.7)	61.6 (8.7)	63.0 (8.3)	0
Clinical variables at baseline				
Current smoker (%)	14,892 (31.8)	13,069 (32.7)	1809 (26.8)	16,006
BMI (mean (SD))	27.6 (4.5)	27.3 (4.3)	29.6 (5.1)	4096
Physical activity ^b (median [IQR])	5.0 [2.0, 7.0]	5.0 [2.0, 7.0]	3.0 [0.0, 7.0]	2
Hypertension (%)	19,248 (40.3)	14,542 (35.7)	4691 (67.5)	197
Previous stroke (%)	1670 (3.5)	1168 (2.9)	499 (7.2)	211
LVEF (%)				6752
≥50%	27,467 (66.7)	23,776 (67.5)	3663 (62.4)	
40–49%	8316 (20.2)	7085 (20.1)	1223 (20.8)	
30–39%	4225 (10.3)	3498 (9.9)	722 (12.3)	
<30%	1147 (2.8)	885 (2.5)	262 (4.5)	
Hospital size, tertiles (%)				
<334 cases/year	144 (0.3)	123 (0.3)	21 (0.3)	0
334–976 cases/year	5535 (11.6)	4675 (11.4)	857 (12.3)	
≥977 cases/year	42,228 (88.1)	36,083 (88.3)	6101 (87.4)	
Medication at discharge				
ACE inhibitors (%)	31,796 (66.4)	27,360 (67.0)	4405 (63.2)	38
AR blockers (%)	6688 (14.0)	4786 (11.7)	1898 (27.2)	29
Oral anticoagulantia (%)	2369 (4.9)	1888 (4.6)	478 (6.9)	32
Other antiplatelets (%)	43,284 (90.4)	37,249 (91.1)	5993 (85.9)	20
Beta blockers (%)	43,843 (91.5)	37,361 (91.4)	6438 (92.3)	14
Calcium antagonists (%)	5759 (12.0)	4110 (10.1)	1648 (23.6)	18
Digitalis (%)	405 (0.8)	294 (0.7)	108 (1.5)	12
Diuretics (%)	6899 (14.4)	4813 (11.8)	2080 (29.8)	13
Statins (%)	46,416 (96.9)	39,699 (97.1)	6674 (95.7)	9
Other lipid lowering agents (%)	598 (1.2)	411 (1.0)	185 (2.7)	38
Nitrates (%)	2185 (4.6)	1566 (3.8)	616 (8.8)	59
Socioeconomic variables				
Foreign born	5044 (11.1)	4092 (10.5)	949 (14.4)	2426
Education, tertiles (%)				
Primary	14,741 (31.0)	12,225 (30.1)	2500 (36.3)	402
Secondary	22,412 (47.2)	19,194 (47.3)	3199 (46.4)	
Higher	10,352 (21.8)	9147 (22.5)	1193 (17.3)	
Income, quintiles (%)				
1 (low)	6158 (12.9)	4997 (12.3)	1158 (16.7)	308
2	5664 (11.9)	4613 (11.4)	1045 (15.1)	
3	8667 (18.2)	7249 (17.8)	1402 (20.2)	
4	12,716 (26.7)	10,966 (27.0)	1740 (25.1)	
5 (high)	14,394 (30.2)	12,795 (31.5)	1587 (22.9)	
Occupation status (%)				
Working	20,770 (45.5)	18,538 (47.5)	2215 (33.8)	2290
Sick-leave	1358 (3.0)	1098 (2.8)	258 (3.9)	
Unemployed	1089 (2.4)	909 (2.3)	180 (2.7)	
Retired	22,194 (48.7)	18,299 (46.9)	3870 (59.0)	
Student/other	206 (0.5)	166 (0.4)	39 (0.6)	

First-time MI cases ≤75 years of age with scheduled continued CR. Hospital size tertiles are derived from *n* patients per year. Income is the median the year before the MI adjusted for family composition. ACE, angiotensin-converting enzyme; AR, angiotensin receptor; BMI, body mass index; CR, cardiac rehabilitation; DM, diabetes mellitus; IQR, inter-quartile range; LDL-C, low-density lipoprotein; LVEF, left ventricular ejection fraction; N, patient count; SBP, systolic blood pressure; SD, standard deviation.

^a Imputed before primary analyses.

^b Number of ≥30 min sessions of at least moderate exercise per week.

completers). Analyses were performed in R version 3.4.1 [26] using packages *base*, *caret*, *cobalt*, *data.table*, *dummies*, *foreign*, *forestplot*, *haven*, *MASS*, *MatchIt*, *matrixStats*, *mice*, *plyr*, *stats*, and *VIM*.

3. Results

Summary statistics for the 47,907 included patients are available in Table 1. At baseline, 6979 (14.6%) had DM.

3.1. Main analysis

After propensity score matching, exposed and unexposed patients were balanced on the included covariates (Supplement, Figs. A2–3). Crude logistic regression estimates (OR, [95% CI], P) calculated with this matched population showed that patients with DM at baseline – compared to patients without DM – were less likely to attain the CR target goal for both smoking cessation (0.90, [0.81, 0.99], $P = 0.035$) and exercise training attendance (0.88, [0.83, 0.95], $P < 0.001$) one year later at SEPHIA2. On the contrary, patients with DM at baseline were more likely to attain the LDL-C target (1.28, [1.19, 1.36], $P < 0.001$), compared to those without DM. There was no association between DM at baseline and SBP target attainment (0.97, [0.91, 1.04], $P = 0.415$).

3.2. Sensitivity analyses

Sensitivity analyses were performed and are further detailed in Fig. 2. Sensitivity analysis 1 only matched complete cases with DM ($N = 3076$) and without DM ($N = 20,455$) and yielded similar estimates as in the main analysis regarding all four CR outcomes but with lower precision due to weakened statistical power. In sensitivity analysis 2, re-matching of patients with DM ($N = 6979$) with those without DM ($N = 40,881$) then also including specific CR interventions at baseline (heart school, physical exercise training, anti-stress course, smoking cessation course, and dietary course participation) produced similar estimates as in the main analysis for DM regarding one-year goal attainment for all four CR outcomes. Sensitivity analysis 3 re-matched patients with DM ($N = 6886$) and those without DM ($N = 40,235$) that were scheduled for CR at SEPHIA1 and also attended SEPHIA2 (CR completers) and did also corroborate the main analysis findings for all point estimates, although the association with smoking cessation had lower precision.

3.3. Stratified analyses

Stratified analyses in men and women are available in Table 2 for which matching was separately done by sex not including the sex covariate. These analyses showed that women with DM had particularly low odds of attaining the CR target for exercise training yet displayed a trend of being more likely to attain the target for SBP, compared to

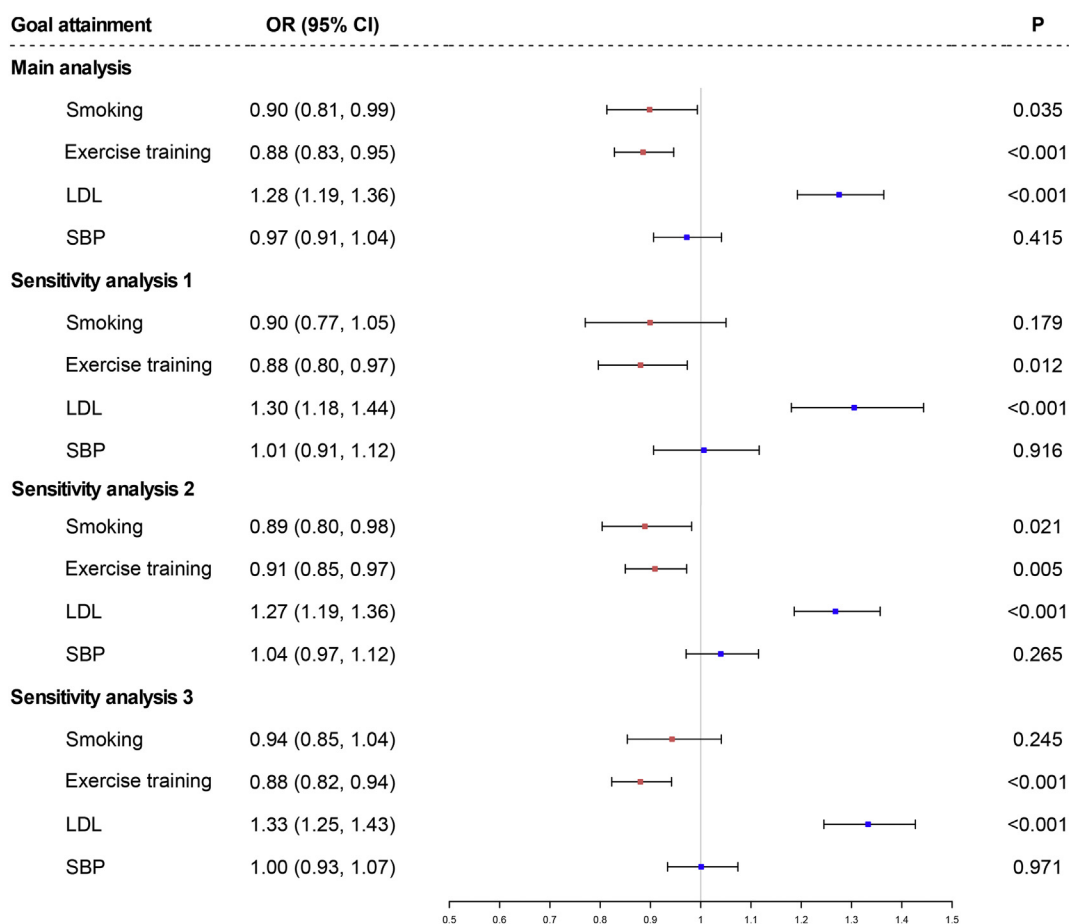


Fig. 2. Forest plot of study outcome estimates from the propensity score matched population separated by type of analysis. Goal attainment estimates are for first-time MI patients with DM (exposed) compared to those without DM (unexposed). Points and whiskers are point estimate OR and 95% CI, respectively. Nearest neighbour matched 1:1 without replacement on patient logit probability for DM at baseline with 0.2 SD calipers. CI, confidence interval; CR, cardiac rehabilitation; Main analysis matched exposed ($N = 6979$) with unexposed ($N = 40,881$). Sensitivity analysis 1: Complete case analysis matched exposed ($N = 3076$) with unexposed ($N = 20,455$). Sensitivity analysis 2: After additional matching on specific components of CR (attending heart school, anti-stress course, smoking cessation course, diet course, and attendance in exercise training) this analysis compared exposed ($N = 6979$) with unexposed ($N = 40,881$). Sensitivity analysis 3: Conditioning on CR completers (scheduled for continued CR at SEPHIA1 and also attending SEPHIA2). Matched exposed ($N = 6886$) with unexposed ($N = 40,235$). DM, diabetes mellitus; LDL-C, low-density lipoprotein; MI, myocardial infarction; SBP, systolic blood pressure.

Table 2
Study outcome estimates by men and women after propensity score matching.

	Men with DM vs without DM	Women with DM vs without DM
Smoking	0.89 (0.79, 1.01)	0.89 (0.75, 1.07)
Exercise training	0.95 (0.88, 1.03)	0.77 (0.68, 0.88)
LDL-C	1.23 (1.14, 1.34)	1.16 (1.02, 1.31)
SBP	0.97 (0.89, 1.05)	1.13 (0.99, 1.27)

First-time MI cases ≤ 75 years of age with scheduled continued CR by sex. Estimates (OR with 95% CI) are obtained after separate propensity score matching 1:1 with 0.2 SD calipers. Exposed men (N = 4922) are matched with unexposed men (N = 30,182), exposed women (N = 2063) are matched with unexposed women (N = 10,740). DM, diabetes mellitus; LDL-C, low-density lipoprotein; N, patient count; SBP, systolic blood pressure; SD, standard deviation.

women without DM. Regarding both smoking and LDL-C targets, the estimates were similar to the main analysis.

4. Discussion

The present nationwide study showed that patients with first-time MI that also had DM at the start of CR were less likely to both abstain from smoking and to attend exercise training as part of CR, but were more likely to attain their LDL-C target one year later. There was no difference between groups for attaining the SBP target. These results were largely corroborated in sensitivity analyses. In stratified analyses, women with DM were particularly unlikely to attend exercise training, compared to women without DM.

Previous research has shown that patients with first-time MI and DM have a greater mortality and morbidity risk compared to those without DM [2,7–12]. One interpretation of this may be that patients with DM are adequately medicated regarding both their SBP and LDL-C, as well as generally having a lower LDL-C [27], but that they fail to a greater extent to achieve two of the most important lifestyle/behavioural changes post MI. Given the substantially higher mortality and morbidity risk post MI for those patients that have DM, their relative failure regarding the CR goal of both smoking cessation and attending exercise training likely contributes to their worse prognosis. Consequently, this subpopulation would likely benefit from targeted intervention focusing on behavioural change, that might be of higher intensity than suggested by current clinical consensus [14,17]. In addition, pharmacotherapy to boost smoking cessation could possibly be prescribed more frequently [28]. Recent technological development in video communication may also be leveraged with these patients for physiotherapist-led exercise training in the patient's home environment. Traditional centre-based versus home-based training seem to be comparatively effective according to a recent Cochrane review [29], yet it is indeed possible that patient preferences in the subpopulation under study may favour home-based training. In summary, behavioural change constitutes a challenge and how to best accomplish it for the high-risk subpopulation with both MI and DM remains an important area of future clinical research, especially given the worldwide projected increase in DM [3,4]. Such future research would likely benefit from building on the present findings when focused on possible causal reasons as to why patients with MI and DM display this distinct pattern of CR goal attainment.

One clinical way forward in the near future may be to strengthen efforts to enrol more women with DM into exercise training, as this patient subgroup showed particularly low attendance compared to women without DM. It is usually said that women with MI are in general older and more ill than men with MI [18,19], and perhaps women with DM need exercise training programmes better tailored to them. Yet, the present study controlled for age and several disease severity variables, so the low exercise training attendance by women with DM cannot readily be explained by those factors. We also controlled for the average rate of moderate physical exercise at baseline. The study may have benefited from actual biometric exercise capacity

measurements (e.g. METS) at baseline, since women with DM may in comparison be particularly sedentary. However, the variables indicative of baseline exercise capacity that were indeed adjusted for must constitute valid proxies for exercise capacity at baseline.

4.1. Limitations and strengths

The validity of statistical analysis with observational data is always under latent threat from residual confounding. However, by using data from different unselected population registries and propensity score matching, we were able to minimise residual confounding, not only with respect to the comprehensive set of clinical covariates, but also regarding demographic and SES variables. Despite these statistical control efforts, there may be remaining unobserved heterogeneity between the two groups causing differences in goal attainment. One such possible residual confounder is the patients' cognitive ability [30,31], however, much of such confounding from cognitive ability is controlled for indirectly through matching that included the three major SES covariates educational attainment, income, and occupation status. It is also possible that patients with DM have additional risk factors and comorbidities, including a less healthy diet, greater alcohol consumption, greater stress, greater inflammation, small vessels disease, clotting factors, infarct location, infarct severity and more that are not measured directly in the present study. Some of these factors are however likely controlled for indirectly through included proxies, such as the inclusion of BMI, SES, and smoking actually indirectly controlling for a substantial portion of possible diet and alcohol consumption confounding. Infarction severity is also reflected to a substantial extent in the LVEF which is controlled for. Still, such unmeasured confounding may remain, impacting on these patients' ability to attend exercise training programmes and cease smoking and should be investigated in future studies. Future studies may also further investigate higher-order effects between DM, smoking, and exercise training as these factors are likely in part interacting.

Misclassification of DM is in theory a potential problem but the estimates in different sensitivity analyses were only marginally different from the main analysis estimates. Having some diabetic patients differentially misclassified as non-diabetic in the present study would attenuate the estimates towards the null. The robustness in the present study across differing analyses that included patients that were both more or less compliant to CR also suggests, together with the known high-quality data from Swedish registries, that bias was minimal in comparison with previous studies not having access to this type of data. In addition, as some patients did not attend the first SEPHIA1 visit, it is possible that this introduced some selection bias. Then, such bias is likely to be conservative regarding the present estimates since DM is likely to be more prevalent and more severe in CR non-attendees. There is also the possibility for time and place dependent effects beyond those dealt with through the present matching on admission year and size of treating hospital. Data on whether patients were offered home-based exercise training programmes was not registered in SEPHIA during the time-period included in the present study which may have blurred our estimates. Furthermore, the present findings are from a specific subpopulation of the total Swedish patient population with MI which limits the generalisability of our findings to other populations. The present age of patients was also slightly lower than usual, primarily due to the SEPHIA age cut-off and our deliberate subselection of patients with first-time MI. As both DM prevalence and associated difficulties in goal target attainment during CR increase with age, our group comparison estimates may be conservative relative to if we had also included patients with reinfarction.

The main strengths of our study stem from the large high-quality dataset of this important subpopulation obtained from interlinked real-world population registries, allowing us to obtain precise estimates, thoroughly adjust for various confounders using appropriate

statistical methods, and perform complementary sensitivity analyses strengthening the validity of the main findings.

5. Conclusion

The present results suggest that the high-risk subgroup of patients with first-time MI which also suffer from DM are less likely to attain the CR lifestyle targets for both smoking cessation and attending exercise training during the first year post MI. Conversely, these patients were more likely to reach the CR target for LDL-C, and there were no group differences for the SBP target. Hence, patients with MI and DM seem adequately medicated, yet are simultaneously exposed to higher lifestyle-related risk during their critical, first year of CR post MI. Possibilities for targeted post-MI care focused on behavioural change for this high-risk subgroup, including a focus on promoting exercise training for women with DM, should be investigated further.

5.1. Contributions, acknowledgements, sources of funding, and disclosure

JW and AM designed the study. JW, AM, CH, EO, EH, and ML interpreted the findings, critically revised the manuscript, and approved its final form and submission. JW analysed data. JW and AM drafted the manuscript. We are grateful to the SWEDEHEART/RIKS-HIA patients. This work was supported by the Swedish Research Council for Health, Working Life and Welfare [2014-4947], the Vårdal Foundation [2014-0114], and is part of the strategic research programme U-CARE [2009-1093].

Conflicts of interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijcard.2019.04.049>.

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