

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<u>http://bmjopen.bmj.com</u>).

If you have any questions on BMJ Open's open peer review process please email <u>info.bmjopen@bmj.com</u>

# **BMJ Open**

# Temporal trends in cardiovascular risk factors, lifestyle, and secondary preventive medication for patients with myocardial infarction attending cardiac rehabilitation in Sweden 2006-2019: a registry-based cohort study

Journal:	BMJ Open
Manuscript ID	bmjopen-2022-069770
Article Type:	Original research
Date Submitted by the Author:	01-Nov-2022
Complete List of Authors:	Leosdottir, Margret; Lund University, Department of Clinical Sciences Malmö; Skanes universitetssjukhus Malmo, Department of Cardiology Hagstrom, Emil; Uppsala University, Department of Medical Sciences, Cardiology; Uppsala Clinical Research Center Hadziosmanovic, Nermin; Uppsala University, Department of Medical Sciences, Cardiology Norhammar, Anna; Karolinska Institutet; Capio Sankt Görans Sjukhus Lindahl, Bertil; Uppsala University, Department of Medical Sciences, Cardiology; Uppsala Clinical Research Center Hambraeus, Kristina; Falun Hospital, Department of Cardiology Jernberg, Tomas; Danderyd University Hospital, Department of Clinical Sciences Bäck, Maria; Linköping University, Department of Medical and Health Sciences, Division of Physiotherapy; Sahlgrenska University Hospital, Department of Occupational Therapy and Physiotherapy
Keywords:	Myocardial infarction < CARDIOLOGY, REHABILITATION MEDICINE, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Coronary heart disease < CARDIOLOGY, Risk management < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

SCHOLARONE<sup>™</sup> Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

reliez oni

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Temporal trends in cardiovascular risk factors, lifestyle, and secondary preventive medication for patients with myocardial infarction attending cardiac rehabilitation in Sweden 2006-2019: a registry-based cohort study

Margret Leosdottir <sup>a,b</sup>, Emil Hagström <sup>c,d</sup>, Nermin Hadziosmanovic<sup>c</sup>, Anna Norhammar<sup>e,f</sup>, Bertil Lindahl<sup>c,d</sup>, Kristina Hambraeus<sup>g</sup>, Tomas Jernberg<sup>h</sup> and Maria Bäck<sup>i,j</sup>, for the SWEDEHEART-CR study group

<sup>a</sup>Department of Clinical Sciences Malmö, Faculty of Medicine, Lund University, Malmö, Sweden; <sup>b</sup>Department of Cardiology, Skane University Hospital, Malmö, Sweden; <sup>c</sup>Department of Medical Sciences, Cardiology, Uppsala University, Uppsala, Sweden; <sup>d</sup>Uppsala Clinical Research Centre, Uppsala, Sweden; <sup>e</sup>Institution of Medicine, Karolinska Institute at Karolinska University Hospital, Solna, Sweden; <sup>f</sup>Capio S:t Göran hospital, Stockholm, Sweden; <sup>g</sup>Department of Cardiology, Falun Hospital, Falun, Sweden; <sup>h</sup>Department of Clinical Sciences, Danderyd Hospital, Karolinska Institute, Stockholm, Sweden; <sup>i</sup>Department of Medical and Health Sciences, Division of Physiotherapy, Linköping University, Linköping, Sweden; <sup>j</sup>Department of Occupational Therapy and Physiotherapy, Sahlgrenska University Hospital, Gothenburg, Sweden

**Correspondence:** Margret Leosdottir, Department of Cardiology, Skane University Hospital, Jan Waldenströms gata 15 plan 3, 20502 Malmo, Sweden. Telephone number +46 732 561 536, margret.leosdottir@med.lu.se.

## Word count: 3927

## Abstract

**Objectives.** Registries have been highlighted as means to improve quality of care. Here we describe temporal trends in risk factors, lifestyle, and preventive medication for patients after myocardial infarction (MI) registered in the quality registry SWEDEHEART.

**Design.** A registry-based cohort study.

Setting. All coronary care units and cardiac rehabilitation (CR) centres in Sweden.

**Participants.** Patients attending a CR visit at one-year post-MI 2006-2019 were included (n=81363, 18-74 years, 74.7% men).

**Outcome measures.** Outcome measures at one-year follow-up included blood pressure (BP) <140/90 mmHg, low-density lipoprotein-cholesterol (LDL-C) <1.8 mmol/L, persistent smoking, overweight/obesity, central obesity, diabetes prevalence, inadequate physical activity, and prescription of secondary preventive medication. Descriptive statistics and testing for trends were applied.

**Results.** The proportion of patients attaining the targets for BP <140/90 mmHg increased from 65.2% (2006) to 86.0% (2019), and LDL-C <1.8 mmol/L from 29.8% (2006) to 66.9% (2019, p<0.0001 both). While smoking at the time of MI decreased (32.0% to 26.5%, p<0.0001), persistent smoking at one-year was unchanged (42.8% to 43.2%, p=0.672) as was the prevalence of overweight/obesity (71.9% to 72.9%, p=0.559). Central obesity (50.5% to 57.0%), diabetes (18.2% to 27.2%) and patients reporting inadequate levels of physical activity (57.0% to 61.5%) increased (p<0.0001 for all). From 2007, >90.0% of patients were prescribed statins and approximately 98% antiplatelet and/or anticoagulant therapy. Angiotensin-converting enzyme inhibitor/angiotensin receptor blocker prescription increased from 68.7% (2006) to 80.2% (2019, p<0.0001).

**Conclusions.** While little change was observed for persistent smoking and overweight/obesity, large improvements were observed for LDL-C and BP target achievements and prescription of preventive medication for Swedish patients after MI 2006-2019. Compared to published results from patients with coronary artery disease in Europe during the same period, these improvements were considerably larger. Continuous auditing and open comparisons of CR outcomes might possibly explain some of the observed improvements and differences.

Abstract word count: 299

 **Keywords:** Cardiac rehabilitation, risk factors, registry, myocardial infarction, secondary prevention, SWEDEHEART it c

## **Article summary**

*Strengths and limitations of this study* 

- In this paper we report changes over time in risk factor burden, lifestyle variables, and • secondary preventive medication for patients attending cardiac rehabilitation (CR) in Sweden between 2006 and 2019. Comparisons to published results from patients with coronary artery disease in Europe during the same period are presented.
- The major strength of the study is the broad representability and national coverage of • data, but all patients who suffered a myocardial infarction (MI) and were followed in the Swedish quality registry SWEDEHEART were included. More than 75% of all MI patients under the age of 75 are registered in SWEDEHEART and attend a one-year CR follow-up visit.
- Using descriptive statistics and testing for trends, proportion of patients attaining blood pressure (BP) <140/90 mmHg, low-density lipoprotein-cholesterol (LDL-C) <1.8

### **BMJ** Open

mmol/L, persistent smoking, overweight/obesity, central obesity, diabetes prevalence, inadequate physical activity, and prescription of secondary preventive medication were explored.

• The major limitation of the study is the lack of data describing MI patients not attending CR and on those ≥75 years of age.

## Introduction

Treating cardiovascular risk factors and adopting healthy behaviours after myocardial infarction (MI) is the most effective way to reduce recurrent cardiovascular events (1, 2). Based on abundant and continuously accumulating evidence, the European Society of Cardiology (ESC) regularly publishes guidelines on cardiovascular disease prevention in clinical practice (3). Secondary prevention is usually provided through cardiac rehabilitation (CR) - a complex intervention entailing the optimal use of cardio-protective medication, exercise training, behavioural modification, patient education, and psychosocial counselling (4). In the latest ESC prevention guidelines, participation in CR post-MI is given the highest possible recommendation and level of evidence (3). Still, implementing the guidelines in clinical practice has proven to be a challenge, with goal attainment in CR being far from optimal (5, 6). Especially it seems challenging to reach lifestyle associated targets such as being adequately physically active and active smokers at the time of the MI being abstinent from smoking. Furthermore, only marginal improvements have been observed in goal attainment for blood pressure (BP) and low-density lipoprotein cholesterol (LDL-C) during the last ten years despite increasing availability of more effective pharmacotherapy (5).

Systematically monitoring quality of care, structure, and process of delivery within CR has been highlighted as a possible way to increase prevention target attainment (7-11). The Swedish Web-system for Enhancement and Development of Evidence-based care in

Heart disease Evaluated According to Recommended Therapies (SWEDEHEART) is a nationwide quality registry that records patient characteristics, treatments, and outcomes of consecutive patients with MI admitted to coronary care units in Sweden (12). Registration of CR quality and process-based metrics for patients after an MI started in 2005. Since 2006 data has been collected for patients under the age of 75 at two routine follow-up visits within CR - at two-months and one-year post-MI (13, 14). Referrals to CR are automatically generated through the electronic registry system for all MI patients and since 2016 more than 75% of all eligible patients, who are alive at one-year after the acute event, attend the one-year CR follow-up visit (15). Data from SWEDEHEART is available online and is updated continuously, facilitating open comparisons between CR programs in the country (16).

The objective of this study was to describe temporal trends 2006-2019 in risk factor prevalence, lifestyle, and prescription of secondary preventive medication at one-year after MI for patients attending CR in Sweden, hypothesising that a national quality registry can contribute to improving outcomes in CR.

## Methods

## Patient population and settings

In this retrospective registry-based cohort study, data on all patients i) with a Swedish national identification number, ii) aged 18-74 years, iii) admitted for a first time or recurrent MI (ICD codes I21, I22 or I23), and iv) having a one-year CR follow-up visit registered in SWEDEHEART between January 1<sup>st</sup> 2006 and December 31<sup>st</sup> 2019 were used. Since patients with recurrent MI are included in SWEDEHEART, the same patient can be registered on several occasions, although not more than once per year since each individual patient can only generate one SWEDEHEART-based follow-up per year. Until 2018 it was mandatory to register patients <75 years of age, while registration of those 75 years or older was optional.

#### **BMJ** Open

For this reason, we chose to apply the age limit of 18-74 years throughout the whole period in the current study. No other exclusion criteria were applied.

## Patient involvement

Patients were not involved in the design or conduct of the current study. The SWEDEHEART registry's steering group has, however, included a patient representative for many years. The steering group is involved in decisions concerning variables included in the registry and how results generated from registry data are disseminated to the general public.

#### Data collection

## Hospitalization data

Detailed description of the SWEDEHEART registry has previously been published (12, 13). In short, the registry includes more than 100 variables collected during hospitalization, describing patient characteristics and acute MI care (12). These include age, sex, smoking status (current smoker, previous smoker [stopped smoking >1 month] or never smoker), history of diabetes, hypertension, atherosclerotic cardiovascular disease (ASCVD: MI, percutaneous coronary intervention [PCI], coronary artery by-pass grafting [CABG] or stroke), and current pharmacotherapy, collected from electronic medical records and by self-report. Data on race/ethnicity is not available in SWEDEHEART. Height (cm) and weight (kg) is collected, measured during hospitalization or self-reported, and body-mass index (BMI, kg/m<sup>2</sup>) calculated. Waist circumference is not measured during hospitalization. Systolic and diastolic blood pressures (BP, mmHg) are registered. Blood samples collected include total cholesterol (HDL-C), fasting plasma glucose, and HbA1c (for patients with diabetes only). In SWEDEHEART, estimated LDL-C according to the Friedewald formula: LDL-C = total

cholesterol – HDL-C – (0,45 x triglycerides) is used to minimize inter-laboratory differences in LDL-C (17). In case of triglycerides >4.5 mmol/L or missing values on total cholesterol, HDL-C, or triglycerides, directly measured LDL-C is used instead. In the SWEDEHEART user manual it is recommended that laboratory measures are performed according to local laboratory routines.

## Cardiac rehabilitation data

Approximately 80 variables are collected at CR visits at two-months (time frame 6-10 weeks) and one-year (time frame 11-13 months) post-MI (13). These include weight and waist circumference, systolic and diastolic BP, blood samples (lipids, fasting plasma glucose, and in patients with diabetes HbA1c), smoking status and current pharmacotherapy. Additionally, patients report how many days during the last week they have been physically active for a minimum of 30 minutes (at least 10 minutes at a time) at an intensity that will induce shortness of breath and a slightly increased pulse, corresponding to a brisk walk.

All data in SWEDEHEART is registered online. Data validity is continuously monitored, with sampling confirming >95% agreement with data from medical records (12, 13).

## *Exposure and outcome variables*

Exposure in this study was defined as the calendar year of the one-year follow-up visit. Outcome variables at one-year follow-up included the following: BP <140/90 mmHg (both systolic and diastolic BP targets fulfilled, same goal irrespective of diabetes status); LDL-C <1.8 mmol/L; diabetes prevalence; persistent smoking (proportion of smokers at the time of MI who were still smoking at one-year follow-up); inadequate physical activity (being physically active [as defined above] <5 days/week); overweight/obesity (BMI  $\ge$ 25 kg/m<sup>2</sup>); central obesity (waist circumference  $\ge$ 102 cm for men and  $\ge$ 88 cm for women); prescription of secondary

#### **BMJ** Open

preventive medication: lipid lowering drugs (statins and/or ezetimibe), angiotensin converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARB), beta blockers, antiplatelet agents (acetylsalicylic acid [ASA] and/or P2Y<sub>12</sub>-receptor antagonists) and anticoagulants (warfarin or direct oral anticoagulants).

## Statistical analysis

The distribution of continuous variables was assessed by visual inspection of histograms and Q-Q plots. Most continuous variables were non-normally distributed, and are presented as medians (quartile 1, quartile 3), apart from delta values which are presented as means ±standard deviations (SD). Data for categorical variables is presented as percentages. Trend tests were performed using Cochrane-Armitage trend test for categorical variables and Wilcoxon type test for continuous variables. To compare data between years 2006 and 2019, Chi-square test was used for categorical variables and Wilcoxon rank sum test for continuous variables. Outcomes were analysed as dichotomized variables. Median values for continuous outcome variables and mean delta values between baseline (time of index event) were also analysed. For waist circumference delta was based on the two-month and one-year follow-up visit measurements. No imputation was performed on missing data. Data was analysed using SAS version 9.4 (SAS Institute, Cary, North Carolina, USA). A 2-sided p value of <0.05 was considered statistically significant.

# Ethical considerations

The need for signed informed consent by patients for inclusion in Swedish quality registries has collectively been waived in Sweden. Upon hospital admission, MI patients are informed verbally and in writing by a nurse or physician about data being collected and entered in the registry. However, all patients have the right to deny registration and the right upon request to be removed from the registry at any time. Opt-out is extremely rare, counting less than ten cases per year. The study complies with the Declaration of Helsinki and was approved by The Swedish Ethical Review Authority (registration number: 2019-04277).

## Results

## Patient characteristics during hospitalization

Between 2006 and 2019, 81363 MI cases were registered in SWEDEHEART, representing 78679 individual patients 18-74 years of age at the time of the acute event who subsequently attended a one-year follow-up registry visit within CR. Patients were predominantly male, the proportion increasing slightly during the period from 73.5% in 2006 to 75.2% in 2019 (p-trend <0.0001). The median (q1, q3) age was 63.0 (57.0, 69.0) years in 2006 and 65.0 (58.0-70.0) years in 2019 (p-trend < 0.0001). Further patient characteristics can be seen in Fig. 1 and Tables S1-S3. The most prominent changes observed during the period were a decrease in the proportion of smokers from 32.0% to 26.5% (p-trend < 0.0001), an increase in the proportion of overweight and obese patients (BMI  $\geq 25$  kg/m<sup>2</sup>) from 70.7% to 74.1% (p-trend <0.0001), and an increase in the use of lipid-lowering drugs (statins and/or ezetimibe) (24.5% to 28.6%, ptrend=0.004) or antihypertensive drugs (ACEi/ARB, beta blockers, diuretics and/or calcium channel blockers) (47.6% to 51.2%, p-trend <0.0001) prior to admission (Fig. 1). The proportion of patients being revascularized (by PCI or CABG) during hospitalization and the proportion being prescribed statins, ezetimibe, ACEi/ARB, and P2Y<sub>12</sub>-receptor antagonist therapy at discharge increased during the observed period (p-trend <0.0001 for all), while the proportion receiving beta blockers at discharge decreased (p-trend <0.0001) (Table S3).

Blood pressure, lipids, and diabetes

Page 11 of 46

#### **BMJ** Open

The proportion of patients achieving BP <140/90 mmHg at the one-year follow-up visit increased from 65.2% in 2006 to 86.0% in 2019 (p-trend <0.0001) (Fig 2). Regarding LDL-C, 29.8% were treated to the <1.8 mmol/L target in 2006, increasing to 66.9% in 2019 (p-trend <0.0001), with 30.4% having an LDL-C of <1.4 mmol/L in 2019 (Fig 2). Mean delta values for systolic and diastolic BP and LDL-C between hospitalization and one-year follow-up also increased during the observed period (p for trend <0.0001 for all) (Fig. 3). The one-year median SBP, DBP, total cholesterol, LDL-C, and triglycerides decreased over the period, while HDL-C remained unchanged (Table S4).

The prevalence of diabetes at the one-year follow-up increased from 18.2% in 2006 to 27.2% in 2019 (p-trend <0.0001) (Fig. 4). Between 2006 and 2013 there was a minimal difference between the prevalence of diabetes at hospitalization and at one-year follow-up ( $\pm$ 1%-point). Since 2014, however, the difference increased, in 2019 being 4.6%-points higher at the one-year follow-up. HbA1c (patients with diabetes only) at the one-year follow-up decreased from 56 mmol/mol to 52 mmol/mol (p-trend <0.0001) while the delta value between hospitalization and one-year remained unchanged (Tables S4-S5). Fasting glucose at one-year (all patients) increased from 5.7 mmol/L to 6.0 mmol/L over the period (p-trend <0.0001) (Table S4).

## Lifestyle

The prevalence of persistent smoking, inadequate physical activity, overweight/obesity, and central obesity at one-year post-MI can be seen in Fig. 4. Persistent smoking, i.e., the proportion of smokers at the time of MI who were still smoking at the one-year follow-up, remained unchanged over the period (42.8% in 2006 and 43.2% 2019, p-trend=0.672). The proportion of patients reporting inadequate physical activity increased during the observed period from 57.0% to 61.5% (p-trend <0.0001). While the prevalence of patients who were overweight or obese at hospitalization increased, the proportion at one-year follow-up was similar (71.9% to

72.9%, p-trend=0.559). In 2006-2015 an increase in BMI between baseline and one-year follow-up was observed (between 0.04 and 0.30 kg/m<sup>2</sup>), while in 2016-2019 the difference was negative (between -0.01 and -0.15 kg/m<sup>2</sup>, p-trend <0.0001) (Table S5). The prevalence of central obesity increased from 50.5% in 2006 to 57.0% in 2019 (p-trend <0.0001). Yearly median values at one-year follow-up for number of days during the last week the patients had been physically active, BMI, and waist circumference are shown in Table S4.

## Secondary preventive medication

The use of secondary preventive medication at the one-year follow-up visit can be seen in Fig. 5. Since 2007 more than 90% of all patients were prescribed statins. Between 4% and 6% of the patients were prescribed ezetimibe prior to 2014 where after its use increased successively to 29.8% in 2019 (p-trend <0.0001). Approximately 98% were prescribed either an antiplatelet or anticoagulant therapy throughout the period, with the proportion of patients receiving anticoagulant therapy doubling from 6.4% in 2006 to 12.0% in 2019 (p-trend <0.0001). ACEi/ARB prescription increased from 68.7% to 80.2% (p-trend <0.0001) while the use of beta blockers decreased from 86.4% to 76.7% (p-trend <0.0001).

## Discussion

In this study of temporal trends in risk factor control and use of secondary preventive medication in post-MI patients attending CR in Sweden 2006-2019, a considerable improvement in BP and LDL-C goal achievement and use of evidence-based pharmacotherapy was observed. On the other hand, changes in lifestyle were less encouraging, with the proportion of persistent smokers at one-year remaining unchanged, and prevalence of inadequate physical activity, central obesity, as well as diabetes increasing.

## Blood pressure, lipids, and diabetes

In the EUROASPIRE surveys patients aged 18-79 years with coronary artery disease (CAD) were interviewed and examined at approximately one year after a first or recurrent coronary event (acute MI, unstable angina, or revascularization), to determine whether guidelines on CR were followed in clinical practice (5, 6). The III-V surveys were conducted over a period approximately matching our current study period (EUROASPIRE III 2006-2007, IV 2012-2013 and V 2016-2017), the patients had similar initiating events, and the mean age and gender proportions were comparable to the SWEDEHEART population (Table S6), giving a good opportunity to compare our results to European data. In our study, the proportion of patients achieving the BP goal of <140/90 mmHg increased from 65.2% to 86.0% between 2006 and 2019, compared to an increase from 44.0% to 58.0% between EUROASPIRE III and V (Fig. 6) (5, 6). As such, the proportion of patients achieving the BP goal was considerably higher (approximately 20%-points) during the whole period in SWEDEHEART. There was an even larger difference in the proportion of patients reaching the LDL-C target of <1.8 mmol/L, increasing from 29.8% (2006) to 66.9% (2019) (37%-point improvement) in SWEDEHEART, compared to 20.9% vs 29.0% (8%-point improvement) between EUROASPIRE III and V (Fig. 6). One reasonable explanation for the large difference in proportion of patients achieving treatment targets for BP and LDL-C in SWEDEHEART compared to EUROASPIRE could be that all patients in our study participated in CR to some extent, compared to 35-40% in the EUROASPIRE cohorts (18, 19). Participation in CR has been shown to increase adherence to secondary preventive medication and the proportion of patients reaching risk factor goals (20) as well as improving prognosis (2). Somewhat contradictory though, data from EUROASPIRE IV on risk factor target achievement showed no difference in the proportion of patients reaching targets for BP and LDL-C when comparing attenders and non-attenders in CR (19). Another possible explanation for the more pronounced improvement in target attainment in

SWEDEHEART compared to EUROASPIRE might be the possibility of continuous self-audit of publicly available data for CR centres reporting to SWEDEHEART, as only a minority of the countries participating in EUROASPIRE had quality registries or audits comparable to SWEDEHEART. Among patients with CAD attending CR in Austria, where a well-functioning CR registry has been in use since 2001 (7), 85% of patients between 2005 and 2015 reached the systolic BP goal of <140 mmHg (21). Similarly, according to annual reports from the Danish CR Database on patients with CAD attending CR, which started in 2015, the proportion of patients reaching the LDL-C goal of <1.8 mmol/L increased from 54% in 2015 to 63% in 2019 (22, 23), figures aligning well with our results for the same years. The joint observations from these three registries (SWEDEHEART, Austrian registry and Danish Registry) support the conclusion that benchmarking quality improvement at a local and national level, and providing opportunities for open comparisons between centres, can positively impact quality of care (7, 24, 25).

An interesting observation in our data was the increased difference in diabetes prevalence between hospitalization and one-year follow-up towards the end of the observed period. Also, median HbA1c values among patients with diabetes decreased. This possibly reflects heightened awareness and more structured routines for diagnosing diabetes in patients after an MI, with patients with milder forms of glucose disturbances being diagnosed. More patients being diagnosed should in the long-term positively impact prognosis (26, 27). The increase in fasting glucose values in the whole population, paralleled by increased prevalence of central obesity, further underlines the importance of vigilant screening and treatment of diabetes in the post-MI population.

Lifestyle

Page 15 of 46

#### **BMJ** Open

Approximately 30% of patients were smokers at the time of the index event in both the SWEDEHEART registry and the EUROASPIRE surveys. The proportion of persistent smokers at one-year after the event, however, was generally higher in EUROASPIRE than in SWEDEHEART (Fig. S1) (5, 28). The fact that Sweden has the lowest proportion of daily smokers in Europe might partly explain the higher success rate for smoking cessation in our data. In contrary with the lack of difference in BP and LDL-C target achievement between CR attenders and non-attenders in EUROASPIRE, there was a substantial difference between attenders and non-attenders in smoking cessation rates, with 47% and 43% of CR attenders being persistent smokers in EUROASPIRE III (2006-2007) and IV (2011-2012), compared to 54% and 53% of the non-attenders (18, 19). The corresponding figures in SWEDEHEART (all patients defined as attenders) during the same years were 42% (2006-2007) and 45% (2011-2012). In both cohorts, however, there was no improvement in smoking cessation rates during the observed periods. The same can be seen in the British National Audits for CR (NACR) 2016-2019 (29) and the Danish CR Database 2015-2019 (23). Observational studies have shown that smoking cessation post-MI results in a 36% relative risk reduction in total mortality (30). The smoking cessation rates among CR attenders in the EUROASPIRE surveys and patients registered in SWEDEHEART, when compared to the considerably higher figures for non-attenders from EUROASPIRE, underline the importance of CR attendance for supporting tobacco abstinence. At the same time, it is discouraging to see no improvement in smoking cessation rates in any of the reviewed datasets.

The proportion of patients reporting insufficient physical activity at the one-year follow-up increased during the observed period. As different questionnaires for assessing physical activity have been used in the surveys and audits cited here, direct comparisons cannot be made. Generally, though, in EUROASPIRE, the level of physical activity in all surveys was

suboptimal and did not improve between surveys (5, 6), while the proportion of patients classified as physically active increased somewhat in the NACR reports 2016-2019 (29).

While the prevalence of overweight/obesity at the time of the MI increased during the study period, the proportion of overweight/obese patients at the one-year follow-up visit remained unchanged (72-73%). This might partly be explained by a slight weight gain between hospitalization and one-year follow-up during the first half of the observed period, while a minimal weight loss was observed during the latter half. The clinical relevance of this observation is, however, uncertain. No change in the proportion of obese patients was observed in NACR 2016-2019 (29) or the EUROASPIRE surveys, where just over 80% were overweight or obese (5, 6) (Fig. S1). The prevalence of central obesity was similar in our study and in EUROASPIRE and increased to the same extent (by approximately 10%-points) during the observed period (5, 6).

In a recently published paper based on data from EUROASPIRE IV and V, poor adherence to lifestyle changes were addressed (20). The authors concluded that while adherence to lifestyle advice was better among patients who had attended CR, an increased focus on behavioural change within CR to address unhealthy lifestyles is strongly needed. With all patients in our cohort having participated in CR to some extent, data on lifestyle being monitored and openly compared annually in the SWEDEHEART registry, and no visible change for the better seen for more than a decade, our results strongly support this conclusion.

#### Cardioprotective medication

According to our study the use of lipid lowering drugs was high during the whole period. More than 90% of the patients were prescribed statins at the one-year follow-up visit throughout the observed period and ezetimibe use increased rapidly after 2015, reaching 29.8% in 2019. In 2015-2109 more than 94% of all patients were prescribed statins and/or ezetimibe. Meanwhile,

Page 17 of 46

#### **BMJ** Open

the use of lipid lowering therapy including statins, ezetimibe, fibrates, bile acid sequestrants, and nicotinic acid, increased from approximately 80% of patients in EUROASPIRE III to 84% in EUROASPIRE V (5, 28, 31) (Fig. S2). In the CR attendance analyses from the EUROASPIRE III and IV surveys, compared to non-attenders, the proportion of CR attenders on lipid lowering therapy was considerably higher, or 83% vs 78% (EAIII) and 88% vs 85% (EAIV), respectively (18, 19). Data on the use of cardioprotective medication from the Austrian registry or the British National Audit for CR (NACR) has to our knowledge not been published. In annual reports from the Danish CR database, during 2016-2019, between 93-96% of CAD patients were prescribed statins at the end of CR (23). According to our study the use of ACEi/ARB increased from 64.9% in 2006 to 79.5% in 2019 while patients prescribed ACEi/ARB in EUROASPIRE III was 71% and 75% in EUROASPIRE V (Fig. S2) (5, 28, 31). In the EUROASPIRE III and IV, the use of ACEi/ARB and BP-lowering medication was significantly higher in CR attenders than in non-attenders, although the difference was not as large as for lipid lowering treatment (18, 19). While conclusions about the influence of auditing on cardioprotective medication prescription in Sweden are hard to draw, generally it can be concluded that the use of cardioprotective medication in our and other surveys has been high and has increased both in Sweden and Europe in general during the observed period.

# Strengths and limitations

The major strength of this study is the broad representability and national coverage of data, with more than 75% of all MI patients under the age of 75 being registered in SWEDEHEART and attending a one-year CR follow-up visit since 2016. At the same time, a major limitation is the lack of data describing MI patients not attending CR and on those  $\geq$ 75 years of age. This might have led to a positive bias in the results. Also, the coverage on center-level during the first years was low and representability therefore not as extensive. Comparing

our data with other survey and audit data is limited by differences in patient selections, different rates of CR participation, time of follow-up, differences in measurement methods (i.e., questionnaires, self-report), and definitions (i.e., physical inactivity).

#### Conclusion

Between 2006-2019, an increasing proportion of patients in Sweden reached secondary preventive goals for BP and LDL-C one year after an MI. The proportion of patients treated with evidence-based secondary preventive medication also increased. Both levels of BP and LDL-C, as well as use of pharmacological treatment were comparable with data from other similar European quality registries or audits used on a national level for benchmarking. The trends were more favourable than that observed in EUROASPIRE, data from which represents several European countries where audits were not widely available. The results may indicate that national quality registries can contribute to improving outcomes in CR. Less encouraging, no changes were seen the proportion of current smokers at the time of the MI who are abstinent at one-year, more patients reported inadequate levels of physical activity, and the proportion of patients with central obesity and diabetes increased, as was observed in EUROASPIRE. These observations bare witness of a large unmet need to prioritize patient support to improve lifestyle after an MI.

## Acknowledgements

None.

# Funding

#### **BMJ** Open

This research received no specific grant from any funding agency in the public, commercial or non-for-profit sectors.

## **Data sharing statement**

The data used in this study is based on the SWEDEHEART registry. Access to data from the registry needs to be applied for and third-party data usage is not allowed, irrespective of whether the data contain potentially identifying or sensitive data or not. Instead, given ethical study approval from the Swedish Ethical Review Authority, access to SWEDEHEART data supporting the present findings can be applied for from the Uppsala Clinical Research Center (UCR) in Sweden. Further information can be found on the UCR <u>www.ucr.uu.se/en</u>/ and Swedish Ethical Review Authority <u>etikprovningsmyndigheten.se</u>/ websites.

One co-author (NH) had primary responsibility for the study data and takes responsibility for its integrity and the data analysis. Analytical methods and other study material are available upon reasonable request to the corresponding author.

#### A competing interests statement

All authors except NH are or have been engaged in the SWEDEHEART registry. Otherwise, the authors have no conflicts of interest to declare.

## **Author contributions**

M.L., E.H., and M.B. contributed to the conception and design of the work. A.N., B.L., K.H. and T.J. offered medical expertise and guidance. N.H. conducted all data analysis. M.L. drafted the manuscript. All other authors critically revised the manuscript. All approved the final version of the manuscript.

## **Figure legends**

Fig. 1. Patient characteristics as registered during MI hospitalization for patients attending the one-year follow-up visit within CR in Sweden 2006-2019. <sup>a</sup>BMI ≥25 kg/m<sup>2</sup>; <sup>b</sup>prior MI, PCI, CABG, or stroke; <sup>c</sup>ACE inhibitors/ARB, beta blockers, diuretics and/or calcium channel blockers; <sup>d</sup>statins and/or ezetimibe. ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; ASCVD, atherosclerotic cardiovascular disease (MI, PCI, CABG or stroke); BMI, body mass index; CABG, coronary artery bypass grafting; MI, myocardial infarction; N, number; PCI, percutaneous coronary intervention.

**Fig. 2.** Proportion of patients achieving targets for BP and LDL-C at the one-year follow-up visit 2006-2019. The p-value for trend from 2006 to 2019 was <0.0001 for both BP and LDL-C. BP, blood pressure; LDL-C, low-density lipoprotein cholesterol.

**Fig. 3.** Mean delta values between hospitalization and the one-year CR follow-up visit for systolic and diastolic BP (upper panel) and LDL-C (lower panel) by year 2006-2019. The p-value for the trend from 2006 to 2019 was <0.0001 for all. DBP, diastolic blood pressure; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure.

Fig. 4. Prevalence of persistent smoking (proportion of active smokers at the time of MI who were still smoking), inadequate physical activity, overweight/obesity, and diabetes at one-year post-MI. <sup>a</sup>BMI  $\geq$ 25 kg/m<sup>2</sup>; <sup>b</sup>waist circumference  $\geq$ 102 cm for men and  $\geq$ 88 cm for women; <sup>c</sup>physically active  $\geq$  30 minutes for less than 5 days a week. BMI, body mass index; MI, myocardial infarction.

**Fig. 5.** Proportion of patients at one-year follow-up for each year 2006-2019 treated with statins, ezetimibe, ACEi or ARB, beta blockers, antiplatelet (acetylsalicylic acid or  $P2Y_{12}$ -receptor

## **BMJ** Open

antagonists) or anticoagulant therapy (warfarin or direct oral anticoagulants). ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker.

**Fig. 6.** Management of BP and LDL in SWEDEHEART (left panel) and EUROASPIRE (right panel) (5, 6). \*Different definitions of BP treatment goals for patients with diabetes were adapted in the EUROASPIRE surveys (III <130/80 mmHg, IV 140/80 mmHg, V <140/85 mmHg), while the definition <140/90 mmHg was adapted for patients with and without diabetes in SWEDEHEART. BP, blood pressure; LDL-C, low-density lipoprotein cholesterol.

# References

1. Björck L, Rosengren A, Bennett K, Lappas G, Capewell S. Modelling the decreasing coronary heart disease mortality in Sweden between 1986 and 2002. *Eur Heart J*. 2009;30(9):1046-56.

2. Salzwedel A, Jensen K, Rauch B, et al. Effectiveness of comprehensive cardiac rehabilitation in coronary artery disease patients treated according to contemporary evidence based medicine: Update of the Cardiac Rehabilitation Outcome Study (CROS-II). *Eur J Prev Cardiol*. 2020;27(16):1756-74.

3. Visseren FLJ, Mach F, Smulders YM, et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. *Eur Heart J.* 2021;42(34):3227-337.

4. Ambrosetti M, Abreu A, Corra U, et al. Secondary prevention through comprehensive cardiovascular rehabilitation: From knowledge to implementation. 2020 update. A position paper from the Secondary Prevention and Rehabilitation Section of the European Association of Preventive Cardiology. *Eur J Prev Cardiol*. 2020:2047487320913379.

5. Kotseva K, De Backer G, De Bacquer D, et al. Lifestyle and impact on cardiovascular risk factor control in coronary patients across 27 countries: Results from the

European Society of Cardiology ESC-EORP EUROASPIRE V registry. *Eur J Prev Cardiol.* 2019;26(8):824-35.

Kotseva K, De Bacquer D, Jennings C, et al. Time Trends in Lifestyle, Risk Factor
Control, and Use of Evidence-Based Medications in Patients With Coronary Heart Disease in
Europe: Results From 3 EUROASPIRE Surveys, 1999-2013. *Glob Heart*. 2017;12(4):315-22
e3.

7. Poffley A, Thomas E, Grace SL, et al. A systematic review of cardiac rehabilitation registries. *Eur J Prev Cardiol.* 2017;24(15):1596-609.

8. Aktaa S, Batra G, Wallentin L, et al. European Society of Cardiology methodology for the development of quality indicators for the quantification of cardiovascular care and outcomes. *Eur Heart J Qual Care Clin Outcomes*. 2022;8(1):4-13.

9. Aktaa S, Gencer B, Arbelo E, et al. European Society of Cardiology Quality Indicators for Cardiovascular Disease Prevention: developed by the Working Group for Cardiovascular Disease Prevention Quality Indicators in collaboration with the European Association for Preventive Cardiology of the European Society of Cardiology. *Eur J Prev Cardiol.* 2022;29(7):1060-71.

10. Thomas RJ, Balady G, Banka G, et al. 2018 ACC/AHA Clinical Performance and Quality Measures for Cardiac Rehabilitation: A Report of the American College of Cardiology/American Heart Association Task Force on Performance Measures. *J Am Coll Cardiol.* 2018;71(16):1814-37.

11. Brittish Association for Cardiovascular Prevention and Rehabilitation. The BACPR standards and core components for cardiovascular disease prevention and rehabilitation (3rd edition). London, England; 2017.

## **BMJ** Open

12.	Jernberg T, Attebring MF, Hambraeus K, et al. The Swedish Web-system for
enhanceme	ent and development of evidence-based care in heart disease evaluated according to
recommen	ded therapies (SWEDEHEART). Heart. 2010;96(20):1617-21.
13.	Back M, Leosdottir M, Hagstrom E, et al. The SWEDEHEART secondary
prevention	and cardiac rehabilitation registry (SWEDEHEART CR registry). Eur Heart J
Qual Care	<i>Clin Outcomes.</i> 2021;7(5):431-7.
14.	Hambraeus K, Tyden P, Lindahl B. Time trends and gender differences in
prevention	guideline adherence and outcome after myocardial infarction: Data from the
SWEDEH	EART registry. Eur J Prev Cardiol. 2016;23(4):340-8.
15.	Jernberg T, Boberg B, Back M, et al. SWEDEHEART Annual Report 2019.
Uppsala, S	weden: Uppsala Clinical Research Center; 2019.
16.	Vasko P, Alfredsson J, Back M, et al. SWEDEHEART Annual report 2020.
Annual rep	oort. Uppsala, Sweden: Uppsala Clinical Research Center (UCR); 2021.
17.	Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of
low-densit	y lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge.
Clin Chem	2. 1972;18(6):499-502.
18.	Kotseva K, Wood D, De Backer G, et al. Use and effects of cardiac rehabilitation
in patients	with coronary heart disease: results from the EUROASPIRE III survey. Eur J Prev
Cardiol. 20	013;20(5):817-26.
19.	Kotseva K, Wood D, De Bacquer D, et al. Determinants of participation and risk
factor cont	rol according to attendance in cardiac rehabilitation programmes in coronary patients
in Europe:	EUROASPIRE IV survey. Eur J Prev Cardiol. 2018;25(12):1242-51.
20.	De Bacquer D, Astin F, Kotseva K, et al. Poor adherence to lifestyle
recommen	dations in patients with coronary heart disease: results from the EUROASPIRE
surveys. E	ur J Prev Cardiol. 2021.

21. Reich B, Benzer W, Harpf H, et al. Efficacy of extended, comprehensive outpatient cardiac rehabilitation on cardiovascular risk factors: A nationwide registry. *Eur J Prev Cardiol.* 2020;27(10):1026-33.

22. Zwisler AD, Rossau HK, Nakano A, et al. The Danish Cardiac Rehabilitation Database. *Clin Epidemiol*. 2016;8:451-6.

23. Thomsen KK. Danish Cardiac Rehabilitation Registry Annual Report. 2019.

24. Paton JY, Ranmal R, Dudley J, and R. C. S. Committee. Clinical audit: still an important tool for improving healthcare. *Arch Dis Child Educ Pract Ed*. 2015;100(2):83-8.

25. Abreu A, Frederix I, Dendale P, et al. Standardization and quality improvement of secondary prevention through cardiovascular rehabilitation programmes in Europe: The avenue towards EAPC accreditation programme: A position statement of the Secondary Prevention and Rehabilitation Section of the European Association of Preventive Cardiology (EAPC). *Eur J Prev Cardiol.* 2020.

26. Feldman AL, Griffin SJ, Fharm E, et al. Screening for type 2 diabetes: do screendetected cases fare better? *Diabetologia*. 2017;60(11):2200-9.

27. Ogmundsdottir Michelsen H, Sjolin I, Schlyter M, et al. Cardiac rehabilitation after acute myocardial infarction in Sweden - evaluation of programme characteristics and adherence to European guidelines: The Perfect Cardiac Rehabilitation (Perfect-CR) study. *Eur J Prev Cardiol.* 2020;27(1):18-27.

28. Kotseva K, Wood D, De Backer G, et al. EUROASPIRE III: a survey on the lifestyle, risk factors and use of cardioprotective drug therapies in coronary patients from 22 European countries. *Eur J Cardiovasc Prev Rehabil.* 2009;16(2):121-37.

Doherty P. National Audit of Cardiac Rehabilitation - Annual Statistical Reports
 York, U.K.; 2016-2019.

## **BMJ** Open

3	
4	
5	
6	
7	
, 8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
27	
23	
23	
25	
25	
20	
27	
20	
29	
21	
27	
2∠ 22	
22 24	
24 25	
33 26	
30 27	
3/	
38	
39	
40	
41	
42	
43	
44	
45	
40	
4/	
48	
49 50	
50	
51	
52	
53	
54	
55	
56	
57	
58	

59 60 30. Critchley JA, Capewell S. Mortality risk reduction associated with smoking cessation in patients with coronary heart disease: a systematic review. *JAMA*. 2003;290(1):86-97.

31. Kotseva K, Wood D, De Bacquer D, et al. EUROASPIRE IV: A European Society of Cardiology survey on the lifestyle, risk factor and therapeutic management of coronary patients from 24 European countries. *Eur J Prev Cardiol*. 2016;23(6):636-48.









BMJ Open





#### Page 31 of 46



**SWEDEHEART EUROASPIRE** For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

# **Supplementary material**

Temporal trends in cardiovascular risk factors, lifestyle, and secondary preventive medication for patients with myocardial infarction attending cardiac rehabilitation in Sweden 2006-2019: lyce. a registry-baseu co...

Page 33 of 46

BMJ Open

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	p for trend
N	2502	3942	5223	4948	4720	5368	5976	6530	6432	6831	7121	7073	7269	7428	
Age (years)	63 (57, 69)	63 (57, 69)	63 (57, 69)	63 (57, 69)	63 (57, 69)	64 (57, 69)	64 (57, 69)	64 (57, 69)	64 (57, 69)	64 (57, 69)	65 (57, 70)	64 (57, 70)	65 (58, 70)	65 (58, 70)	< 0.0001
N missing	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Systolic BP	150 (130,	147 (130,	145 (130,	146 (130,	147 (130,	149 (130,	150 (130,	150 (130,	150 (131,	150 (132,	150 (133,	150 (132,	150 (133,	150 (130,	< 0.0001
(mmHg)	170)	165)	165)	165)	165)	168)	170)	170)	170)	170)	170)	170)	170)	169)	
N missing	293	406	479	456	308	7	18	36	48	51	44	2	3	4	
Diastolic BP	85 (74,	85 (75, 98)	85 (75, 97)	85 (75, 97)	85 (75, 96)	85 (75, 98)	87 (76,	88 (77,	88 (78,	89 (79,	89 (78, 99)	89 (79,	90 (79,	89 (79,	< 0.0001
(mmHg)	100)						100)	100)	100)	100)		100)	100)	100)	
N missing	330	471	529	509	410	130	176	213	290	299	261	227	352	454	
Total cholesterol	5.0 (4.3,	5.0 (4.2,	4.9 (4.2,	5.0 (4.2,	5.1 (4.3,	5.1 (4.3,	5.1 (4.3,	5.1 (4.3,	5.0 (4.2,	5.0 (4.2,	5.0 (4.2,	5.0 (4.1,	5.0 (4.1,	4.9 (4.0,	< 0.0001
(mmol/L)	5.8)	5.8)	5.7)	5.8)	5.9)	6.0)	6.0)	6.0)	5.9)	5.8)	5.9)	5.8)	5.9)	5.7)	
N missing	329	554	788	833	835	1108	1185	1280	1204	1088	947	835	686	727	
LDL-C	3.0 (2.3,	3.0 (2.3,	3.0 (2.3,	3.1 (2.3,	3.2 (2.5,	3.2 (2.5,	3.2 (2.5,	3.2 (2.4,	3.1 (2.3,	3.1 (2.3,	3.1 (2.3,	3.0 (2.2,	3.0 (2.2,	3.0 (2.2,	< 0.0001
(mmol/L)	3.7)	3.7)	3.7)	3.8)	3.9)	3.9)	4.0)	3.9)	3.9)	3.8)	3.9)	3.8)	3.8)	3.8)	
N missing	471	844	1008	972	1001	1272	1420	1678	1395	1234	1028	927	629	663	
HDL-C	1.2 (1.0,	1.2 (1.0,	1.1 (0.9,	1.1 (0.9,	1.1 (0.9,	1.1 (0.9,	1.1 (0.9,	1.1 (1.0,	1.1 (1.0,	1.1 (0.9,	1.1 (0.9,	1.2 (1.0,	1.2 (0.9,	1.1 (0.9,	0.003
(mmol/L)	1.4)	1.4)	1.4)	1.3)	1.3)	1.4)	1.4)	1.4)	1.4)	1.4)	1.4)	1.4)	1.4)	1.4)	
N missing	455	821	898	886	941	1214	1330	1519	1374	1188	987	901	746	766	

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

2502 .5 (1.1, .2) 91 .7 (5.6, .4) 13	3942         1.5 (1.1,         2.1)         769         6.6 (5.7,         8.3)	5223           1.5 (1.1,           2.1)           897           6.7 (5.7,	4948 1.5 (1.1, 2.1) 901	4720 1.4 (1.1, 2.0) 923	5368 1.4 (1.0, 2.0)	5976 1.4 (1.0, 1.9)	6530 1.4 (1.0,	6432 1.4 (1.0,	6831 14(10	7121	7073	7269	7428	
.5 (1.1, .2) 91 .7 (5.6, .4) 13	1.5 (1.1,         2.1)         769         6.6 (5.7,         8.3)	1.5 (1.1,         2.1)         897         6.7 (5.7,	1.5 (1.1, 2.1) 901	1.4 (1.1, 2.0) 923	1.4 (1.0, 2.0)	1.4 (1.0, 1.9)	1.4 (1.0,	1.4 (1.0,	14(10	14(10	1 1 (1 0			1
.2) 91 .7 (5.6, .4) 13	2.1) 769 6.6 (5.7, 8.3)	2.1) 897 6.7 (5.7,	2.1) 901	2.0) 923	2.0)	1.9)			,	1.4 (1.0,	1.4 (1.0,	1.4 (1.0,	1.4 (1.0,	< 0.0001
91 .7 (5.6, .4) 13	769 6.6 (5.7, 8.3)	897 6.7 (5.7,	901	923			1.9)	2.0)	2.0)	2.0)	2.0)	2.0)	2.0)	
.7 (5.6, .4) 13	6.6 (5.7, 8.3)	6.7 (5.7,			1170	1318	1599	1500	1601	1488	1460	1481	1472	
.4) 13	8.3)		6.8 (5.7,	6.7 (5.8,	6.8 (5.8,	6.7 (5.8,	6.7 (5.9,	6.8 (5.9,	6.8 (5.9,	6.9 (5.9,	6.9 (5.9,	6.9 (5.9,	7.0 (6.0,	< 0.0001
13		8.4)	8.5)	8.3)	8.5)	8.4)	8.5)	8.5)	8.6)	8.7)	8.7)	8.6)	8.8)	
	332	452	363	324	727	1034	1147	1014	767	762	643	812	1011	
J/A	N/A	N/A	N/A	N/A	59.0 (50.0,	59.0 (48.0,	58.0 (50.0,	61.0 (50.0,	60.0 (50.0,	59.0 (48.0,	56.0 (48.0,	56.0 (48.0,	57.0 (48.0,	0.012
					71.0)	73.0)	73.0)	74.0)	77.0)	74.0)	69.0)	72.0)	69.0)	
84	730	977	996	852	776	872	1059	949	1071	1113	980	973	1012	
6.7 (24.6,	26.9 (24.7,	26.9 (24.5,	26.9 (24.5,	27.0 (24.7,	27.1 (24.7,	27.2 (24.7,	27.2 (24.7,	27.2 (24.8,	27.2 (24.7,	27.4 (24.8,	27.4 (24.9,	27.5 (24.9,	27.5 (24.9,	< 0.0001
9.4)	29.7)	29.7)	29.8)	29.9)	30.0)	30.1)	30.1)	30.1)	30.1)	30.5)	30.4)	30.5)	30.7)	
93	955	898	861	862	316	263	167	183	166	205	169	207	234	
sterol; LI	DL-C, low	-density li	poprotein	s index; в	P, blood p	per; N/A, 1	, fasting, F	ilable; q1	, lower qua	artile; q3, u	-C, nign-d	tile.	oprotein	
84 6. 9. 99: 99: 99: 99: 99: 99: 99: 99: 99:	4 .7 (24.6, .4) <u>3</u> nts with ærol; LI	4       730         .7 (24.6, 26.9 (24.7, .4) 29.7)       29.7)         3       955         nts with diabetes of cerol; LDL-C, low	4       730       977         .7 (24.6, 26.9 (24.7, 26.9 (24.5, 29.7))       29.7)       29.7)         3       955       898         1ts with diabetes only. BMI, cerol; LDL-C, low-density li	4       730       977       996         .7 (24.6, 26.9 (24.7, 26.9 (24.5, 26.9 (24.5, 26.9 (24.5, 26.9 (24.5, 26.9 (24.5, 26.9 (24.5, 29.7) 29.8))))       29.7)       29.8)         3       955       898       861         nts with diabetes only. BMI, body masterol; LDL-C, low-density lipoprotein	4       730       977       996       852         .7 (24.6, 26.9 (24.7, 26.9 (24.5, 26.9 (24.5, 27.0 (24.7, 29.7) 29.7) 29.8)       29.9)       29.9)         3       955       898       861       862         nts with diabetes only. BMI, body mass index; B         cerol; LDL-C, low-density lipoprotein cholestero         For peer review o	4       730       977       996       852       776         .7 (24.6, 26.9 (24.7, 26.9 (24.5, 26.9 (24.5, 27.0 (24.7, 27.1 (24.7, 29.7) 29.7) 29.8)       29.9)       30.0)         3       955       898       861       862       316         its with diabetes only. BMI, body mass index; BP, blood p         cerol; LDL-C, low-density lipoprotein cholesterol; N, numl	4       730       977       996       852       776       872         .7 (24.6, 26.9 (24.7, 26.9 (24.5, 26.9 (24.5, 27.0 (24.7, 27.1 (24.7, 27.2 (24.7, 29.7) 29.7) 29.8)       29.9)       30.0)       30.1)         3       955       898       861       862       316       263         nts with diabetes only. BMI, body mass index; BP, blood pressure; F, zerol; LDL-C, low-density lipoprotein cholesterol; N, number; N/A, not server the server of	4       730       977       996       852       776       872       1059         .7 (24.6, 26.9 (24.7, 26.9 (24.5, 26.9 (24.5, 27.0 (24.7, 27.1 (24.7, 27.2 (24.7, 27.2 (24.7, 29.7) 29.7) 29.8)       29.9)       30.0)       30.1)       30.1)         3       955       898       861       862       316       263       167         tts with diabetes only. BMI, body mass index; BP, blood pressure; F, fasting; H         cerol; LDL-C, low-density lipoprotein cholesterol; N, number; N/A, no data ava	4       730       977       996       852       776       872       1059       949         7 (24.6, 26.9 (24.7, 26.9 (24.5, 26.9 (24.5, 27.0 (24.7, 27.1 (24.7, 27.2 (24.7, 27.2 (24.7, 27.2 (24.8, 29.7)       29.7)       29.8)       29.9)       30.0)       30.1)       30.1)       30.1)       30.1)         3       955       898       861       862       316       263       167       183         its with diabetes only. BMI, body mass index; BP, blood pressure; F, fasting; HbA1c, her       its with diabetes only. BMI, body mass index; BP, blood pressure; F, fasting; HbA1c, her         cerol; LDL-C, low-density lipoprotein cholesterol; N, number; N/A, no data available; q1,	4       730       977       996       852       776       872       1059       949       1071         7       (24.6, 26.9 (24.7, 26.9 (24.5, 26.9 (24.5, 27.0 (24.7, 27.1 (24.7, 27.2 (24.7, 27.2 (24.7, 27.2 (24.8, 27.2 (24.7, 29.9) 30.0) 30.1)       30.	4       730       977       996       852       776       872       1059       949       1071       1113         7       (24.6, 26.9 (24.7, 26.9 (24.5, 26.9 (24.5, 29.9)       29.9 (24.7, 27.1 (24.7, 27.2 (24.7, 27.2 (24.7, 27.2 (24.8, 27.2 (24.7, 27.4 (24.8, 29.7)       29.7 (24.8, 29.7)       29.8 (29.9)       30.0)       30.1 (1	4       730       977       996       852       776       872       1059       949       1071       1113       980         7       (24.6, 26.9 (24.7, 26.9 (24.5, 26.9 (24.5, 29.9))       29.9)       30.0)       30.1)       30.1)       30.1)       30.1)       30.1)       30.1)       30.1)       30.1)       30.1)       30.1)       30.1)       30.4)         3       955       898       861       862       316       263       167       183       166       205       169         its with diabetes only. BMI, body mass index; BP, blood pressure; F, fasting; HbA1c, hemoglobin A1c; HDL-C, high-d       erol; LDL-C, low-density lipoprotein cholesterol; N, number; N/A, no data available; q1, lower quartile; q3, upper quartile; q4, upper quartile; q4, upper quartile; q4, upper qu	4       730       977       996       852       776       872       1059       949       1071       1113       980       973         7       (24.6, 26.9 (24.7, 26.9 (24.5, 26.9 (24.5, 29.9))       26.9 (24.7, 27.1 (24.7, 27.2 (24.7	4       730       977       996       852       776       872       1059       949       1071       1113       980       973       1012         7 (24.6, 26.9 (24.7, 26.9 (24.5, 26.9 (24.5, 27.0 (24.7, 27.1 (24.7, 27.2 (24.7, 27.2 (24.7, 27.2 (24.7, 27.2 (24.7, 27.4 (24.8, 27.4 (24.9, 27.5 (24.9, 27.
Page 35 of 46

BMJ Open

2 3 4	Table S2. Patient char	acteristic	es during	g hospita	lization (	categoric	al variab	les) by y	ear. Data	are prese	ented as 1	numbers	(N) and j	proportion	ns (%).	3
5 6	Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	p for trend
7 8	N	2502	3942	5223	4948	4720	5368	5976	6530	6432	6831	7121	7073	7269	7428	
9	Male sex	73.5%	74.4%	73.1%	73.7%	74.1%	74.5%	74.6%	74.1%	76.2%	75.3%	74.5%	76.2%	75.1%	75.2%	< 0.0001
10	N missing	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
12 13	Current smoking	32.0%	32.6%	32.4%	32.1%	30.8%	30.4%	30.4%	30.1%	28.9%	28.5%	28.0%	27.6%	27.4%	26.5%	< 0.0001
14 15	N missing	99	150	161	171	130	215	128	143	124	132	145	145	172	177	
16	Overweight/obese (BMI ≥25 kg/m2)	70.7%	71.5%	70.2%	69.8%	72.1%	71.6%	71.9%	72.1%	73.3%	72.0%	73.2%	74.1%	74.0%	74.1%	< 0.0001
17 18	N missing	793	955	898	861	862	316	263	167	183	166	205	169	207	234	
19 20	Obese (BMI ≥30 kg/m2)	22.8%	23.8%	23.4%	23.9%	24.3%	25.4%	26.0%	25.9%	26.0%	26.4%	28.7%	27.9%	29.0%	29.5%	< 0.0001
21	N missing	793	955	898	861	862	316	263	167	183	166	205	169	207	234	
23	Use of antihypertensive drugs*	47.5%	47.9%	49.1%	49.9%	48.0%	48.4%	49.2%	49.4%	49.2%	49.4%	49.8%	50.3%	48.9%	50.5%	< 0.0001
24 25	N missing	6	13	9	24	15	41	26	33	31	23	84	85	92	99	
26 27	Use of lipid lowering drugs <sup>†</sup>	24.5%	25.0%	26.5%	28.8%	27.7%	28.4%	28.4%	28.8%	27.6%	27.9%	27.7%	28.0%	26.9%	28.6%	0.004
28	N missing	8	17	15	30	20	44	29	39	29	31	94	103	102	131	
29 30	Prior diabetes diagnosis	19.3%	18.5%	18.7%	20.1%	18.1%	18.8%	18.9%	20.3%	19.7%	20.5%	21.7%	21.1%	21.5%	22.6%	< 0.0001
31 32	N missing	0	0	1	0	0	2	0	1	0	6	1	2	13	21	
33 34	Prior ASCVD diagnosis‡	23.3%	24.5%	23.8%	23.8%	22.8%	22.8%	26.5%	28.2%	26.5%	26.9%	27.4%	28.2%	27.2%	27.9%	< 0.0001
35	N missing	0	0	0	0	0	2	0	0	0	0	0	0	0	0	

\*ACE inhibitor, ARB, beta blocker, diuretics, and/or calcium channel blocker. †Statins and/or ezetimibe. ‡MI, PCI, CABG or stroke. ACE,

angiotensin converting enzyme; ARB, angiotensin receptor blocker; ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index;

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate; MI, myocardial infarction; PCI, percutaneous coronary intervention.

 For peer review only

 BMJ Open

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	p for trer
N	2502	3942	5223	4948	4720	5368	5976	6530	6432	6831	7121	7073	7269	7428	
STEMI	39.3%	38.8%	36.4%	38.9%	39.7%	39.2%	37.6%	37.2%	38.9%	38.9%	38.6%	38.9%	40.4%	40.5%	< 0.000
N missing	0	1	2	69	52	48	55	5	0	0	0	0	0	0	
Revascularized* during hospitalization	65.1%	71.5%	71.1%	71.1%	76.4%	87.3%	82.2%	83.9%	86.0%	88.6%	88.5%	89.6%	90.6%	90.3%	< 0.000
N missing	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Discharge medication			I	1	1	I	1	I	I	1		<u> </u>		1	1
Statin	90.4%	93.5%	94.7%	95.7%	96.7%	96.8%	97.1%	96.8%	97.3%	97.7%	97.5%	97.3%	96.9%	97.0%	< 0.000
N missing	1	2	4	1	1	2	1	4	5	2	0	2	2	8	
Ezetimibe	1.3%	1.5%	2.0%	2.0%	1.5%	1.6%	1.5%	1.5%	1.6%	1.5%	2.4%	3.1%	4.2%	5.1%	< 0.000
N missing	3	7	16	7	4	4	3	8	7	2	1	0	798	4	
ACE-inhibitor/ARB	64.3%	67.1%	72.4%	75.6%	78.9%	82.5%	82.8%	84.0%	83.9%	85.1%	85.1%	85.8%	85.3%	84.7%	< 0.000
N missing	3	6	6	2	3	9	3	5	6	3	3	1	2	4	
Beta blocker	92.2%	90.6%	92.3%	93.1%	92.8%	93.2%	92.1%	91.9%	90.9%	90.2%	90.3%	89.7%	88.2%	81.5%	< 0.000
N missing	2	3	7	0	0	3	2	0	3	2	1	1	2	4	
Acetylsalicylic acid	94.0%	96.2%	95.9%	96.2%	96.6%	96.9%	97.6%	97.2%	96.3%	96.2%	95.9%	96.2%	95.9%	95.3%	0.114
N missing	1	1	3	0	0	2	2	1	4	1	9	3	5	5	
P2Y <sub>12</sub> -receptor antagonist	79.3%	84.0%	84.5%	86.0%	89.2%	87.4%	82.8%	85.3%	89.9%	90.5%	91.2%	90.9%	90.7%	91.0%	< 0.0001
N missing	0	0	0	0	0	0	0	0	0	0	0	0	1	1	

7													2010	2010	6
Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	p for trend
N	2502	3942	5223	4948	4720	5368	5976	6530	6432	6831	7121	7073	7269	7428	
DAPT/DAT/TAT	78.1%	83.9%	84.2%	85.8%	88.6%	87.5%	83.3%	85.3%	89.8%	90.7%	91.2%	91.2%	91.1%	91.5%	<0.0001
N missing	1	1	3	0	0	2	2	1	4	1	9	3	5	5	
*Percutaneous coronar	y interve	ntion or	coronary	artery by	pass gra	fting. AC	E, angio	tensin co	nverting	enzyme	; ARB, a	ingioten	sin recep	tor	
blocker: DAPT. dual a	ntiplatele	et therapy	: DAT. o	lual antit	hromboti	ic therapy	7: N. num	nber: N/A	. no data	availab	le: STEN	ЛI. ST-е	elevation		
myocardial infarction;	TAT, tri	ple antith	irombotic	therapy.											

Page 39 of 46

BMJ Open

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	p for trend
N	2502	3942	5223	4948	4720	5368	5976	6530	6432	6831	7121	7073	7269	7428	
Systolic BP (mmHg)	130 (120,	130 (120,	130 (120,	130 (120,	130 (120,	130 (120,	130 (120,	130 (120,	130 (120,	130 (120,	130 (120,	130 (120,	130 (120,	128 (120,	< 0.0001
	145)	140)	140)	140)	140)	140)	140)	140)	140)	140)	138)	138)	137)	135)	
N missing	869	1308	1351	996	711	945	999	675	381	339	262	196	234	219	
Diastolic BP (mmHg)	80 (70,	78 (70,	80 (70,	76 (70,	80 (70,	80 (70,	80 (70,	80 (70,	79 (70,	78 (70,	77 (70,	77 (70,	76 (70.	76 (70.	< 0.0001
	82)	80)	80)	80)	80)	80)	84)	82)	82)	80)	80)	81)	81)	80)	
N missing	871	1314	1364	999	715	947	1008	689	392	344	267	201	238	226	
Total cholesterol (mmol/L)	4.2 (3.6,	4.1 (3.6,	4.1 (3.6,	4.2 (3.7,	4.1 (3.6,	4.2 (3.6,	4.1 (3.6,	4.0 (3.5,	3.8 (3.3,	3.7 (3.2,	3.6 (3.2,	3.5 (3.1,	3.4 (3.0,	3.3 (2.9,	< 0.0001
	4.8)	4.7)	4.6)	4.7)	4.7)	4.8)	4.7)	4.6)	4.4)	4.3)	4.2)	4.1)	4.0)	3.8)	
N missing	690	1383	1819	1664	1117	1152	1162	759	410	434	407	345	381	370	
LDL-C (mmol/L)	2.1 (1.7,	2.2 (1.8,	2.2 (1.7,	2.3 (1.9,	2.2 (1.8,	2.2 (1.8,	2.2 (1.8,	2.1 (1.7,	1.9 (1.6,	1.8 (1.5,	1.8 (1.4,	1.7 (1.4,	1.7 (1.4,	1.6 (1.3,	< 0.0001
	2.6)	2.6)	2.6)	2.7)	2.7)	2.7)	2.7)	2.5)	2.4)	2.3)	2.2)	2.1)	2.1)	1.9)	
N missing	729	1443	1891	1745	1247	1238	1310	837	439	419	338	244	255	224	
HDL-C (mmol/L)	1.3 (1.1,	1.2 (1.0,	1.2 (1.0,	1.2 (1.0,	1.2 (1.0,	1.2 (1.0,	1.2 (1.0,	1.2 (1.0,	1.2 (1.0,	1.2 (1.0,	1.2 (1.0,	1.2 (1.0,	1.2 (1.0,	1.2 (1.0,	0.552
	1.5)	1.4)	1.4)	1.4)	1.4)	1.5)	1.5)	1.5)	1.5)	1.5)	1.5)	1.5)	1.4)	1.4)	
N missing	714	1423	1860	1720	1180	1217	1253	850	481	627	679	644	667	641	
Triglycerides (mmol/L)	1.4 (1.0,	1.3 (1.0,	1.3 (1.0,	1.4 (1.0,	1.3 (1.0,	1.3 (1.0,	1.3 (1.0,	1.3 (1.0,	1.2 (0.9,	1.2 (0.9,	1.2 (0.9,	1.2 (0.9,	1.2 (0.9,	1.1 (0.8,	< 0.0001
	1.9)	1.9)	1.9)	1.9)	1.8)	1.8)	1.8)	1.8)	1.7)	1.7)	1.6)	1.7)	1.6)	1.6)	
N missing	720	1415	1869	1701	1204	1192	1286	907	727	966	1153	1139	1259	1175	

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	p for tren
N	2502	3942	5223	4948	4720	5368	5976	6530	6432	6831	7121	7073	7269	7428	
F-glucose (mmol/L)	5.7 (5.2,	5.7 (5.2,	5.7 (5.2,	5.7 (5.2,	5.7 (5.3,	5.8 (5.3,	5.8 (5.3,	5.9 (5.4,	5.9 (5.4,	6.0 (5.5,	6.0 (5.5,	6.0 (5.5,	6.0 (5.5,	6.0 (5.5,	< 0.0001
	6.5)	6.4)	6.6)	6.5)	6.5)	6.6)	6.6)	6.8)	6.7)	6.7)	6.8)	6.8)	6.7)	6.8)	
N missing	893	1391	1820	1639	1374	1777	2128	1923	1953	2332	2376	2598	2830	3006	1
HbA1c (mmol/mol)*	56.0	56.5	56.0	55.0	55.0	56.0	58.0	57.0	54.0	55.0	55.0	54.0	53.0	52.0	<0.0001
	(49.0,	(49.0,	(48.0,	(48.0,	(49.0,	(49.0,	(50.0,	(48.0,	(47.0,	(46.0,	(47.0,	(46.0,	(46.0,	(46.0,	
	68.0)	68.0)	66.0)	67.0)	69.0)	68.0)	70.0)	69.0)	67.0)	66.0)	66.0)	66.0)	63.0)	64.0)	
N missing	165	215	242	274	267	372	407	496	595	676	735	755	801	868	
BMI (kg/m2)	26.8	27.1	27.2	27.1	27.2	27.2	27.4	27.2	27.2	27.3	27.4	27.4	27.4	27.4	0.0007
	(24.7,	(24.7,	(24.8,	(24.7,	(24.8,	(24.8,	(24.8,	(24.8,	(24.8,	(24.6,	(24.7,	(24.8,	(24.8,	(24.8,	
	29.7)	30.0)	30.1)	30.0)	30.2)	30.2)	30.4)	30.3)	30.2)	30.3)	30.6)	30.6)	30.5)	30.6)	
N missing	1203	1694	1899	1751	1462	1292	1583	1442	1367	1589	1782	1874	2396	2630	
Waist circumference (cm)	99 (92,	100 (93,	100 (92,	100 (93,	100 (93,	100 (93,	100 (93,	100 (93,	101 (93,	101 (93,	101 (93,	101 (94,	101 (93,	101 (94,	<0.0001
	106)	107)	107)	107)	108)	108)	108)	108)	109)	109)	110)	110)	110)	109)	
N missing	1306	1799	2111	1771	1409	1822	2079	2246	2138	2551	2984	3301	3789	4403	
Physical activity (days)**	4 (1, 7)	4 (1, 7)	4 (1, 7)	4 (1, 7)	3 (1, 7)	4 (1, 7)	3 (1, 6)	3 (1, 7)	3 (1, 7)	4 (1, 7)	3 (1, 7)	3 (1, 6)	3 (1, 6)	3 (1, 6)	<0.0001
N missing	140	237	551	377	24	112	59	55	40	37	56	35	59	68	
*Patients with di	abetes only.	** Days	during th	le last we	ek of phy	vsical act	ivity (at ]	least 30 n	ninutes p	er day). E	BMI, bod	y mass ir	ndex; BP	blood	
nressure: F fasti	ng HhAlcl	remoglol	$\sin A1c^{-1}$		i . high <b>.</b> den	, sity linor	rotein ch	alesteral	· I DI -C	low-den	sity linor	, protein cl	olestero	ŀN	
	1		, , , , , , , , , , , , , , , , , , ,		ingii den				, LDL C	, 10 w den	sity npop		loiestero	l, 1 <b>\</b> ,	

 BMJ Open

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	p for trend
Systolic BP (mmHg)	-25.2	-25.2	-24.5	-25.4	-25.8	-26.5	-26.5	-26.9	-28.5	-28.4	-29.9	-29.5	-29.9	-30.2	<0.0001
	(25.8)	(26.0)	(26.0)	(25.8)	(25.9)	(25.7)	(25.5)	(26.0)	(26.4)	(25.3)	(25.2)	(25.5)	(25.1)	(24.9)	
Diastolic BP (mmHg)	-16.6	-16.7	-16.1	-17.2	-16.2	-16.2	-16.0	-16.7	-17.2	-17.5	-18.1	-17.9	-18.4	-20.1	< 0.0001
	(13.5)	(14.7)	(14.6)	(14.5)	(14.1)	(14.2)	(14.6)	(14.6)	(14.8)	(14.2)	(14.4)	(14.3)	(14.0)	(14.3)	
LDL-C (mmol/L)	-0.83	-0.75	-0.83	-0.78	-0.89	-0.91	-0.93	-1.02	-1.10	-1.13	-1.23	-1.24	-1.26	-1.29	< 0.0001
	(1.11)	(1.05)	(1.10)	(1.12)	(1.11)	(1.13)	(1.17)	(1.21)	(1.16)	(1.17)	(1.19)	(1.18)	(1.21)	(1.20)	
F-glucose (mmol/L)	-1.59	-1.40	-1.46	-1.52	-1.46	-1.47	-1.36	-1.30	-1.40	-1.37	-1.42	-1.37	-1.45	-1.62	0.670
	(3.33)	(3.02)	(3.08)	(3.16)	(3.17)	(2.85)	(3.02)	(3.10)	(3.17)	(3.08)	(3.11)	(2.87)	(3.11)	(3.39)	
HbA1c (mmol/mol) *	N/A	N/A	N/A	N/A	N/A	-1.5 (-	-1.0 (-	-2.0 (-	-1.0 (-	0.0 (-8.0,	-1.0 (-	0.0 (-7.0,	0.0 (-7.0,	-1.0 (-9.0,	0.297
						9.0, 5.0)	11.0, 5.0)	10.0, 4.0)	10.0, 3.0)	6.0)	9.0, 5.0)	6.0)	5.0)	4.0)	
3MI (kg/m2)	0.24	0.17	0.30	0.23	0.25	0.23	0.21	0.09	0.06	0.04	-0.03	-0.01	-0.11	-0.15	< 0.0001
	(1.80)	(1.91)	(1.80)	(1.88)	(1.86)	(1.91)	(1.91)	(1.91)	(1.88)	(2.06)	(2.00)	(1.97)	(2.09)	(2.11)	
*Patients with	diabetes only.	BMI, bo	dy mass :	index; Bl	P, blood j	pressure;	CCU, co	ronary ca	re unit; F	F, fasting;	HbA1c,	hemoglo	bin A1c;	LDL-C,	
low-density lip	oprotein chole	esterol: N	. number	; N/A, no	o data ava	ailable: S	D, standa	rd deviat	tion.						
5 1	1	,		, ,			,								

Table S6. Patient demographics for the EUROASPI	IRE surveys III, IV and V (1-3).
---	----------------------------------

Survey	Years conducted	Number of	% men	Number of participating	Number of participating	Median (IQR) time
		patients		centres	countries	(years) after index event
III	2006-2007	8966	73%	76	22	1.2 (1.0-1.8)
IV	2011-2012	7998	76%	78	24	1.4 (1.0-1.9)
V	2016-2017	8261	74%	131	27	1.1 (0.8-1.6)
iqk, inter q	quaitite failige.					

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml



Figure S1. Lifestyle factors at one-year in SWEDEHEART (left panel) and EUROASPIRE (right panel) where comparable data in the two cohorts

was available (1-3). <sup>a</sup>Body mass index  $\geq$ 25 kg/m<sup>2</sup>; <sup>b</sup>waist circumference  $\geq$ 102 cm for men and  $\geq$ 88 cm for women.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml



**Figure S2.** Proportion of patients at one-year follow-up for each year 2006-2019 in SWEDEHEART treated with lipid lowering therapy (statins or ezetimibe), ACEi or ARB, beta blockers or antiplatelet therapy (ASA or  $P2Y_{12}$ -receptor antagonists). Corresponding data from the EUROASPIRE III-V surveys shown on the right panel of the figure (1-3). In EUROASPIRE lipid lowering drugs included statins, ezetimibe, fibrates, bile acid sequestrants and nicotinic acid.

ACEi, angiotensin converting enzyme inhibitors; ARB, angiotensin receptor blockers; ASA, acetylsalicylic acid.

 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

#### References

1. Kotseva K, De Backer G, De Bacquer D, Ryden L, Hoes A, Grobbee D, et al. Lifestyle and impact on cardiovascular risk factor control in coronary patients across 27 countries: Results from the European Society of Cardiology ESC-EORP EUROASPIRE V registry. Eur J Prev Cardiol. 2019;26(8):824-35.

 Kotseva K, Wood D, De Backer G, De Bacquer D, Pyorala K, Keil U, et al.
 EUROASPIRE III: a survey on the lifestyle, risk factors and use of cardioprotective drug therapies in coronary patients from 22 European countries. Eur J Cardiovasc Prev Rehabil.
 2009;16(2):121-37.

Kotseva K, Wood D, De Bacquer D, De Backer G, Ryden L, Jennings C, et al.
EUROASPIRE IV: A European Society of Cardiology survey on the lifestyle, risk factor and therapeutic management of coronary patients from 24 European countries. Eur J Prev Cardiol. 2016;23(6):636-48.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

### STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Page No
Title and abstract	1	( <i>a</i> ) Indicate the study's design with a commonly used term in the title or the	1-2
		(b) Provide in the abstract an informative and balanced summary of what was	2-3
		done and what was found	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-7
Participants	6	( <i>a</i> ) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5-7
		( <i>b</i> ) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
Data sources/	8*	For each variable of interest, give sources of data and details of methods of	5-7
measurement		assessment (measurement). Describe comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	N/A
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-8
Statistical methods	12	( <i>a</i> ) Describe all statistical methods, including those used to control for confounding	8
		(b) Describe any methods used to examine subgroups and interactions	
		(c) Explain how missing data were addressed	
		(d) If applicable, explain how loss to follow-up was addressed	
		( <u>e</u> ) Describe any sensitivity analyses	
Results			
Participants	13*	<ul> <li>(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed</li> <li>(b) Give reasons for non-participation at each stage</li> <li>(c) Consider use of a flow diagram</li> </ul>	9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9 and Tables S1-3
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	S4

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Main results	16	( <i>a</i> ) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-11 Fig 1-5 Tables S1-5
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Table S6 Figures S1-2
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16-17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	11-17
Other informati	on		
Funding	22	Give the source of funding and the role of the funders for the present study and, if	N/A

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

applicable, for the original study on which the present article is based

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

# **BMJ Open**

#### Temporal trends in cardiovascular risk factors, lifestyle, and secondary preventive medication for patients with myocardial infarction attending cardiac rehabilitation in Sweden 2006-2019: a registry-based cohort study

Journal:	BMJ Open
Manuscript ID	bmjopen-2022-069770.R1
Article Type:	Original research
Date Submitted by the Author:	28-Feb-2023
Complete List of Authors:	Leosdottir, Margret; Lund University, Department of Clinical Sciences Malmö; Skanes universitetssjukhus Malmo, Department of Cardiology Hagstrom, Emil; Uppsala University, Department of Medical Sciences, Cardiology; Uppsala Clinical Research Center Hadziosmanovic, Nermin; Uppsala University, Department of Medical Sciences, Cardiology Norhammar, Anna; Karolinska Institutet; Capio Sankt Görans Sjukhus Lindahl, Bertil; Uppsala University, Department of Medical Sciences, Cardiology; Uppsala Clinical Research Center Hambraeus, Kristina; Falun Hospital, Department of Cardiology Jernberg, Tomas; Danderyd University Hospital, Department of Clinical Sciences Bäck, Maria; Linköping University, Department of Medical and Health Sciences, Division of Physiotherapy; Sahlgrenska University Hospital, Department of Occupational Therapy and Physiotherapy
<b>Primary Subject Heading</b> :	Cardiovascular medicine
Secondary Subject Heading:	Rehabilitation medicine
Keywords:	Myocardial infarction < CARDIOLOGY, REHABILITATION MEDICINE, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Coronary heart disease < CARDIOLOGY, Risk management < HEALTH SERVICES ADMINISTRATION & MANAGEMENT
	·

## SCHOLARONE<sup>™</sup> Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

reliez oni

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Temporal trends in cardiovascular risk factors, lifestyle, and secondary preventive medication for patients with myocardial infarction attending cardiac rehabilitation in Sweden 2006-2019: a registry-based cohort study

Margret Leosdottir <sup>a,b</sup>, Emil Hagström <sup>c,d</sup>, Nermin Hadziosmanovic<sup>c</sup>, Anna Norhammar<sup>e,f</sup>, Bertil Lindahl<sup>c,d</sup>, Kristina Hambraeus<sup>g</sup>, Tomas Jernberg<sup>h</sup> and Maria Bäck<sup>i,j</sup>, for the SWEDEHEART-CR study group

<sup>a</sup>Department of Clinical Sciences Malmö, Faculty of Medicine, Lund University, Malmö, Sweden; <sup>b</sup>Department of Cardiology, Skane University Hospital, Malmö, Sweden; <sup>c</sup>Department of Medical Sciences, Cardiology, Uppsala University, Uppsala, Sweden; <sup>d</sup>Uppsala Clinical Research Centre, Uppsala, Sweden; <sup>e</sup>Institution of Medicine, Karolinska Institute at Karolinska University Hospital, Solna, Sweden; <sup>f</sup>Capio S:t Göran hospital, Stockholm, Sweden; <sup>g</sup>Department of Cardiology, Falun Hospital, Falun, Sweden; <sup>h</sup>Department of Clinical Sciences, Danderyd Hospital, Karolinska Institute, Stockholm, Sweden; <sup>i</sup>Department of Medical and Health Sciences, Division of Physiotherapy, Linköping University, Linköping, Sweden; <sup>j</sup>Department of Occupational Therapy and Physiotherapy, Sahlgrenska University Hospital, Gothenburg, Sweden

**Correspondence:** Margret Leosdottir, Department of Cardiology, Skane University Hospital, Jan Waldenströms gata 15 plan 3, 20502 Malmo, Sweden. Telephone number +46 732 561 536, margret.leosdottir@med.lu.se.

#### Word count: 4080

#### Abstract

**Objectives.** Registries have been highlighted as means to improve quality of care. Here we describe temporal trends in risk factors, lifestyle, and preventive medication for patients after myocardial infarction (MI) registered in the quality registry SWEDEHEART.

**Design.** A registry-based cohort study.

Setting. All coronary care units and cardiac rehabilitation (CR) centres in Sweden.

**Participants.** Patients attending a CR visit at one-year post-MI 2006-2019 were included (n=81363, 18-74 years, 74.7% men).

**Outcome measures.** Outcome measures at one-year follow-up included blood pressure (BP) <140/90 mmHg, low-density lipoprotein-cholesterol (LDL-C) <1.8 mmol/L, persistent smoking, overweight/obesity, central obesity, diabetes prevalence, inadequate physical activity, and prescription of secondary preventive medication. Descriptive statistics and testing for trends were applied.

**Results.** The proportion of patients attaining the targets for BP <140/90 mmHg increased from 65.2% (2006) to 86.0% (2019), and LDL-C <1.8 mmol/L from 29.8% (2006) to 66.9% (2019, p<0.0001 both). While smoking at the time of MI decreased (32.0% to 26.5%, p<0.0001), persistent smoking at one-year was unchanged (42.8% to 43.2%, p=0.672) as was the prevalence of overweight/obesity (71.9% to 72.9%, p=0.559). Central obesity (50.5% to 57.0%), diabetes (18.2% to 27.2%) and patients reporting inadequate levels of physical activity (57.0% to 61.5%) increased (p<0.0001 for all). From 2007, >90.0% of patients were prescribed statins and approximately 98% antiplatelet and/or anticoagulant therapy. Angiotensin-converting enzyme inhibitor/angiotensin receptor blocker prescription increased from 68.7% (2006) to 80.2% (2019, p<0.0001).

**Conclusions.** While little change was observed for persistent smoking and overweight/obesity, large improvements were observed for LDL-C and BP target achievements and prescription of preventive medication for Swedish patients after MI 2006-2019. Compared to published results from patients with coronary artery disease in Europe during the same period, these improvements were considerably larger. Continuous auditing and open comparisons of CR outcomes might possibly explain some of the observed improvements and differences.

Abstract word count: 299

Keywords: Cardiac rehabilitation, risk factors, registry, myocardial infarction, secondary prevention, SWEDEHEART it c

#### **Article summary**

*Strengths and limitations of this study* 

- The major strengths of the study are the broad representability and national coverage of • data including all patients <75 years of age who suffered a myocardial infarction (MI) and were followed in the Swedish quality registry SWEDEHEART.
- Major modifiable cardiovascular risk factors were included; blood pressure levels, lowdensity lipoprotein cholesterol levels, smoking habits, self-reported physical activity, overweight, obesity, central obesity, as well as prescription of secondary preventive medication.
- The major limitations of the study are the lack of data on MI patients not attending CR and on those  $\geq$ 75 years of age.

#### **BMJ** Open

• Also, comparing our data with other survey and audit data is limited by differences in patient selections, different rates of CR participation, time of follow-up, and differences in measurement methods.

#### Introduction

Treating cardiovascular risk factors and adopting healthy behaviours after myocardial infarction (MI) is the most effective way to reduce recurrent cardiovascular events (1, 2). Based on abundant and continuously accumulating evidence, the European Society of Cardiology (ESC) regularly publishes guidelines on cardiovascular disease prevention in clinical practice (3). Secondary prevention is usually provided through cardiac rehabilitation (CR) - a complex intervention entailing the optimal use of cardio-protective medication, exercise training, behavioural modification, patient education, and psychosocial counselling (4). In the latest ESC prevention guidelines, participation in CR post-MI is given the highest possible recommendation and level of evidence (3). Still, implementing the guidelines in clinical practice has proven to be a challenge, with goal attainment in CR being far from optimal (5, 6). Especially it seems challenging to reach lifestyle associated targets such as being adequately physically active and active smokers at the time of the MI being abstinent from smoking. Furthermore, only marginal improvements have been observed in goal attainment for blood pressure (BP) and low-density lipoprotein cholesterol (LDL-C) during the last ten years despite increasing availability of more effective pharmacotherapy (5).

Systematically monitoring quality of care, structure, and process of delivery within CR has been highlighted as a possible way to increase prevention target attainment (7-11). The Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies (SWEDEHEART) is a nationwide quality registry that records patient characteristics, treatments, and outcomes of

consecutive patients with MI admitted to coronary care units in Sweden (12). Registration of CR quality and process-based metrics for patients after an MI started in 2005. Since 2006 data has been collected for patients under the age of 75 at two routine follow-up visits within CR - at two-months and one-year post-MI (13, 14). Referrals to CR are automatically generated through the electronic registry system for all MI patients and since 2016 more than 75% of all eligible patients, who are alive at one-year after the acute event, attend the one-year CR follow-up visit (15). Data from SWEDEHEART is available online and is updated continuously, facilitating open comparisons between CR programs in the country (16).

The objective of this study was to describe temporal trends 2006-2019 in risk factor prevalence, lifestyle, and prescription of secondary preventive medication at one-year after MI for patients attending CR in Sweden, hypothesising that a national quality registry can contribute to improving outcomes in CR.

elle

#### Methods

#### Patient population and settings

In this retrospective registry-based cohort study, data on all patients i) with a Swedish national identification number, ii) aged 18-74 years, iii) admitted for a first time or recurrent MI (ICD codes I21, I22 or I23), and iv) having a one-year CR follow-up visit registered in SWEDEHEART between January 1<sup>st</sup> 2006 and December 31<sup>st</sup> 2019 were used. Since patients with recurrent MI are included in SWEDEHEART, the same patient can be registered on several occasions, although not more than once per year since each individual patient can only generate one SWEDEHEART-based follow-up per year. Until 2018 it was mandatory to register patients <75 years of age, while registration of those 75 years or older was optional. For this reason, we chose to apply the age limit of 18-74 years throughout the whole period in the current study. No other exclusion criteria were applied.

#### Patient and Public Involvement statement

Patients were not involved in the design or conduct of the current study. The SWEDEHEART registry's steering group has, however, included a patient representative for many years. The steering group is involved in decisions concerning variables included in the registry and how results generated from registry data are disseminated to the general public.

#### Data collection

#### Hospitalization data

Detailed description of the SWEDEHEART registry has previously been published (12, 13). In short, the registry includes more than 100 variables collected during hospitalization, describing patient characteristics and acute MI care (12). These include age, sex, smoking status (current smoker, previous smoker [stopped smoking >1 month] or never smoker), history of diabetes, hypertension, atherosclerotic cardiovascular disease (ASCVD: MI, percutaneous coronary intervention [PCI], coronary artery by-pass grafting [CABG] or stroke), and current pharmacotherapy, collected from electronic medical records and by self-report. Data on race/ethnicity is not available in SWEDEHEART. Height (cm) and weight (kg) is collected, measured during hospitalization or self-reported, and body-mass index (BMI, kg/m<sup>2</sup>) calculated. Waist circumference is not measured during hospitalization. Systolic and diastolic blood pressures (BP, mmHg) are registered. Blood samples collected include total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), fasting plasma glucose, and HbA1c (for patients with diabetes only). In SWEDEHEART, estimated LDL-C according to the Friedewald formula: LDL-C = total cholesterol – HDL-C – (0,45 x triglycerides) is used to minimize inter-laboratory differences in LDL-C (17). In case of triglycerides >4.5 mmol/L or missing values on total cholesterol, HDL- C, or triglycerides, directly measured LDL-C is used instead. In the SWEDEHEART user manual it is recommended that laboratory measures are performed according to local laboratory routines.

#### Cardiac rehabilitation data

Approximately 80 variables are collected at CR visits at two-months (time frame 6-10 weeks) and one-year (time frame 11-13 months) post-MI (13). These include weight and waist circumference, systolic and diastolic BP, blood samples (lipids, fasting plasma glucose, and in patients with diabetes HbA1c), smoking status and current pharmacotherapy. Additionally, patients report how many days during the last week they have been physically active for a minimum of 30 minutes (at least 10 minutes at a time) at an intensity that will induce shortness of breath and a slightly increased pulse, corresponding to a brisk walk.

All data in SWEDEHEART is registered online. Data validity is continuously monitored, with sampling confirming >95% agreement with data from medical records (12, iner 13).

#### *Exposure and outcome variables*

Exposure in this study was defined as the calendar year of the one-year follow-up visit. Outcome variables at one-year follow-up included the following: BP <140/90 mmHg (both systolic and diastolic BP targets fulfilled, same goal irrespective of diabetes status); LDL-C <1.8 mmol/L; diabetes prevalence; persistent smoking (proportion of smokers at the time of MI who were still smoking at one-year follow-up); inadequate physical activity (being physically active [as defined above] <5 days/week); overweight/obesity (BMI  $\ge 25$  kg/m<sup>2</sup>); central obesity (waist circumference  $\geq 102$  cm for men and  $\geq 88$  cm for women); prescription of secondary preventive medication: lipid lowering drugs (statins and/or ezetimibe), angiotensin converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARB), beta blockers, antiplatelet

#### **BMJ** Open

agents (acetylsalicylic acid [ASA] and/or  $P2Y_{12}$ -receptor antagonists) and anticoagulants (warfarin or direct oral anticoagulants). Registration of the use of proprotein convertase subtilisin/kexin 9 (PCSK9) inhibitors started in SWEDEHEART in 2017. As information on use prior to 2017 was not available, as well as the use being minimal in the first years (0.5-1.5%) we decided to include only statins and ezetimibe in the definition of lipid lowering therapy (15).

#### Statistical analysis

The distribution of continuous variables was assessed by visual inspection of histograms and Q-Q plots. Most continuous variables were non-normally distributed, and are presented as medians (quartile 1, quartile 3), apart from delta values which are presented as means ±standard deviations (SD). Data for categorical variables is presented as percentages. Trend tests were performed using Cochrane-Armitage trend test for categorical variables and Wilcoxon type test for continuous variables. To compare data between years 2006 and 2019, Chi-square test was used for categorical variables and Wilcoxon rank sum test for continuous variables. Outcomes were analysed as dichotomized variables. Median values for continuous outcome variables and mean delta values between baseline (time of index event) were also analysed. For waist circumference delta was based on the two-month and one-year follow-up visit measurements. No imputation was performed on missing data. Data was analysed using SAS version 9.4 (SAS Institute, Cary, North Carolina, USA). A 2-sided p value of <0.05 was considered statistically significant.

#### Results

Patient characteristics during hospitalization

Between 2006 and 2019, 81363 MI cases were registered in SWEDEHEART, representing 78679 individual patients 18-74 years of age at the time of the acute event who subsequently attended a one-year follow-up registry visit within CR. Patients were predominantly male, the proportion increasing slightly during the period from 73.5% in 2006 to 75.2% in 2019 (p-trend <0.0001). The median (q1, q3) age was 63.0 (57.0, 69.0) years in 2006 and 65.0 (58.0-70.0) vears in 2019 (p-trend <0.0001). Further patient characteristics can be seen in Fig. 1 and Tables S1-S3. The most prominent changes observed during the period were a decrease in the proportion of smokers from 32.0% to 26.5% (p-trend < 0.0001), an increase in the proportion of overweight and obese patients (BMI  $\geq 25$  kg/m<sup>2</sup>) from 70.7% to 74.1% (p-trend <0.0001), and an increase in the use of lipid-lowering drugs (statins and/or ezetimibe) (24.5% to 28.6%, ptrend=0.004) or antihypertensive drugs (ACEi/ARB, beta blockers, diuretics and/or calcium channel blockers) (47.6% to 51.2%, p-trend <0.0001) prior to admission (Fig. 1). The proportion of patients being revascularized (by PCI or CABG) during hospitalization and the proportion being prescribed statins, ezetimibe, ACEi/ARB, and P2Y<sub>12</sub>-receptor antagonist therapy at discharge increased during the observed period (p-trend <0.0001 for all), while the proportion receiving beta blockers at discharge decreased (p-trend <0.0001) (Table S3).

#### Blood pressure, lipids, and diabetes

The proportion of patients achieving BP <140/90 mmHg at the one-year follow-up visit increased from 65.2% in 2006 to 86.0% in 2019 (p-trend <0.0001) (Fig 2). Regarding LDL-C, 29.8% were treated to the <1.8 mmol/L target in 2006, increasing to 66.9% in 2019 (p-trend <0.0001), with 30.4% having an LDL-C of <1.4 mmol/L in 2019 (Fig 2). Mean delta values for systolic and diastolic BP and LDL-C between hospitalization and one-year follow-up also increased during the observed period (p for trend <0.0001 for all) (Fig. 3). The one-year median

#### **BMJ** Open

SBP, DBP, total cholesterol, LDL-C, and triglycerides decreased over the period, while HDL-C remained unchanged (Table S4).

The prevalence of diabetes at the one-year follow-up increased from 18.2% in 2006 to 27.2% in 2019 (p-trend <0.0001) (Fig. 4). Between 2006 and 2013 there was a minimal difference between the prevalence of diabetes at hospitalization and at one-year follow-up ( $\pm$ 1%-point). Since 2014, however, the difference increased, in 2019 being 4.6%-points higher at the one-year follow-up. HbA1c (patients with diabetes only) at the one-year follow-up decreased from 56 mmol/mol to 52 mmol/mol (p-trend <0.0001) while the delta value between hospitalization and one-year remained unchanged (Tables S4-S5). Fasting glucose at one-year (all patients) increased from 5.7 mmol/L to 6.0 mmol/L over the period (p-trend <0.0001) (Table S4).

#### Lifestyle

The prevalence of persistent smoking, inadequate physical activity, overweight/obesity, and central obesity at one-year post-MI can be seen in Fig. 4. Persistent smoking, i.e., the proportion of smokers at the time of MI who were still smoking at the one-year follow-up, remained unchanged over the period (42.8% in 2006 and 43.2% 2019, p-trend=0.672). The proportion of patients reporting inadequate physical activity increased during the observed period from 57.0% to 61.5% (p-trend <0.0001). While the prevalence of patients who were overweight or obese at hospitalization increased, the proportion at one-year follow-up was similar (71.9% to 72.9%, p-trend=0.559). In 2006-2015 an increase in BMI between baseline and one-year follow-up was observed (between 0.04 and 0.30 kg/m<sup>2</sup>), while in 2016-2019 the difference was negative (between -0.01 and -0.15 kg/m<sup>2</sup>, p-trend <0.0001) (Table S5). The prevalence of central obesity increased from 50.5% in 2006 to 57.0% in 2019 (p-trend <0.0001). Yearly median values at one-year follow-up for number of days during the last week the patients had been physically active, BMI, and waist circumference are shown in Table S4.

#### Secondary preventive medication

The use of secondary preventive medication at the one-year follow-up visit can be seen in Fig. 5. Since 2007 more than 90% of all patients were prescribed statins. Between 4% and 6% of the patients were prescribed ezetimibe prior to 2014 where after its use increased successively to 29.8% in 2019 (p-trend <0.0001). Approximately 98% were prescribed either an antiplatelet or anticoagulant therapy throughout the period, with the proportion of patients receiving anticoagulant therapy doubling from 6.4% in 2006 to 12.0% in 2019 (p-trend <0.0001). ACEi/ARB prescription increased from 68.7% to 80.2% (p-trend <0.0001) while the use of beta blockers decreased from 86.4% to 76.7% (p-trend <0.0001). The decrease was mostly driven by a decrease in use among patients with preserved ejection fraction (from 85.1% in 2006 to 70.5% in 2019, p for difference <0.0001), while the use in patients with reduced ejection fraction was unchanged (87.8% in 2006 compared to 88.6% in 2019, p for difference = 0.540).

#### Discussion

In this study of temporal trends in risk factor control and use of secondary preventive medication in post-MI patients attending CR in Sweden 2006-2019, a considerable improvement in BP and LDL-C goal achievement and use of evidence-based pharmacotherapy was observed. On the other hand, changes in lifestyle were less encouraging, with the proportion of persistent smokers at one-year remaining unchanged, and prevalence of inadequate physical activity, central obesity, as well as diabetes increasing.

#### Blood pressure, lipids, and diabetes

In the EUROASPIRE surveys patients aged 18-79 years with coronary artery disease (CAD) were interviewed and examined at approximately one year after a first or recurrent coronary

Page 13 of 46

#### **BMJ** Open

event (acute MI, unstable angina, or revascularization), to determine whether guidelines on CR were followed in clinical practice (5, 6). The III-V surveys were conducted over a period approximately matching our current study period (EUROASPIRE III 2006-2007, IV 2012-2013 and V 2016-2017), the patients had similar initiating events, and the mean age and gender proportions were comparable to the SWEDEHEART population (Table S6), giving a good opportunity to compare our results to European data. In our study, the proportion of patients achieving the BP goal of <140/90 mmHg increased from 65.2% to 86.0% between 2006 and 2019, compared to an increase from 44.0% to 58.0% between EUROASPIRE III and V (Fig. 6) (5, 6). As such, the proportion of patients achieving the BP goal was considerably higher (approximately 20%-points) during the whole period in SWEDEHEART. There was an even larger difference in the proportion of patients reaching the LDL-C target of <1.8 mmol/L, increasing from 29.8% (2006) to 66.9% (2019) (37%-point improvement) in SWEDEHEART, compared to 20.9% vs 29.0% (8%-point improvement) between EUROASPIRE III and V (Fig. 6). One reasonable explanation for the large difference in proportion of patients achieving treatment targets for BP and LDL-C in SWEDEHEART compared to EUROASPIRE could be that all patients in our study participated in CR to some extent, compared to 35-40% in the EUROASPIRE cohorts (18, 19). Participation in CR has been shown to increase adherence to secondary preventive medication and the proportion of patients reaching risk factor goals (20) as well as improving prognosis (2). Somewhat contradictory though, data from EUROASPIRE IV on risk factor target achievement showed no difference in the proportion of patients reaching targets for BP and LDL-C when comparing attenders and non-attenders in CR (19). Another possible explanation could be the higher proportion of patients being prescribed lipid lowering therapies in our study as compared to EUROASPIRE. Between 2015 and 2019 94-95% of patients were prescribed statins and/or ezetimibe, with the corresponding proportion in EUROASPIRE V (2016-2017) being 84%, out of which only 50% were prescribed high-

intensity lipid lowering drugs (5). In a study using Swedish registry data, the proportion of AMI patients receiving high-intensity stating post-MI during 2014-2016 was 91.3% (21). An additional explanation for the more pronounced improvement in target attainment in SWEDEHEART compared to EUROASPIRE, as well as a more pronounced use of potent lipid lowering therapy, might be the possibility of continuous self-audit of publicly available data for CR centres reporting to SWEDEHEART, as only a minority of the countries participating in EUROASPIRE had quality registries or audits comparable to SWEDEHEART. Among patients with CAD attending CR in Austria, where a well-functioning CR registry has been in use since 2001 (7), 85% of patients between 2005 and 2015 reached the systolic BP goal of <140 mmHg (22). Similarly, according to annual reports from the Danish CR Database on patients with CAD attending CR, which started in 2015, the proportion of patients reaching the LDL-C goal of <1.8 mmol/L increased from 54% in 2015 to 63% in 2019 (23, 24), figures aligning well with our results for the same years. The joint observations from these three registries (SWEDEHEART, Austrian registry and Danish Registry) support the conclusion that benchmarking at a local and national level, and providing opportunities for open comparisons between centres, can positively impact quality of care (7, 25, 26).

An interesting observation in our data was the increased difference in diabetes prevalence between hospitalization and one-year follow-up towards the end of the observed period. Also, median HbA1c values among patients with diabetes decreased. This possibly reflects heightened awareness and more structured routines for diagnosing diabetes in patients after an MI, with patients with milder forms of glucose disturbances being diagnosed. More patients being diagnosed should in the long-term positively impact prognosis (27, 28). The increase in fasting glucose values in the whole population, paralleled by increased prevalence of central obesity, further underlines the importance of vigilant screening and treatment of diabetes in the post-MI population.

# Lifestyle

Approximately 30% of patients were smokers at the time of the index event in both the SWEDEHEART registry and the EUROASPIRE surveys. The proportion of persistent smokers at one-year after the event, however, was generally higher in EUROASPIRE than in SWEDEHEART (Fig. S1) (5, 29). The fact that Sweden has the lowest proportion of daily smokers in Europe might partly explain the higher success rate for smoking cessation in our data. In contrary with the lack of difference in BP and LDL-C target achievement between CR attenders and non-attenders in EUROASPIRE, there was a substantial difference between attenders and non-attenders in smoking cessation rates, with 47% and 43% of CR attenders being persistent smokers in EUROASPIRE III (2006-2007) and IV (2011-2012), compared to 54% and 53% of the non-attenders (18, 19). The corresponding figures in SWEDEHEART (all patients defined as attenders) during the same years were 42% (2006-2007) and 45% (2011-2012). In both cohorts, however, there was no improvement in smoking cessation rates during the observed periods. The same can be seen in the British National Audits for CR (NACR) 2016-2019 (30) and the Danish CR Database 2015-2019 (24). Observational studies have shown that smoking cessation post-MI results in a 36% relative risk reduction in total mortality (31). The smoking cessation rates among CR attenders in the EUROASPIRE surveys and patients registered in SWEDEHEART, when compared to the considerably higher figures for non-attenders from EUROASPIRE, underline the importance of CR attendance for supporting tobacco abstinence. At the same time, it is discouraging to see no improvement in smoking cessation rates in any of the reviewed datasets.

The proportion of patients reporting insufficient physical activity at the one-year follow-up increased during the observed period. As different questionnaires for assessing physical activity have been used in the surveys and audits cited here, direct comparisons cannot

be made. Generally, though, in EUROASPIRE, the level of physical activity in all surveys was suboptimal and did not improve between surveys (5, 6), while the proportion of patients classified as physically active increased somewhat in the NACR reports 2016-2019 (30).

While the prevalence of overweight/obesity at the time of the MI increased during the study period, the proportion of overweight/obese patients at the one-year follow-up visit remained unchanged (72-73%). This might partly be explained by a slight weight gain between hospitalization and one-year follow-up during the first half of the observed period, while a minimal weight loss was observed during the latter half. The clinical relevance of this observation is, however, uncertain. No change in the proportion of obese patients was observed in NACR 2016-2019 (30) or the EUROASPIRE surveys, where just over 80% were overweight or obese (5, 6) (Fig. S1). The prevalence of central obesity was similar in our study and in EUROASPIRE and increased to the same extent (by approximately 10%-points) during the observed period (5, 6).

In a recently published paper based on data from EUROASPIRE IV and V, poor adherence to lifestyle changes were addressed (20). The authors concluded that while adherence to lifestyle advice was better among patients who had attended CR, an increased focus on behavioural change within CR to address unhealthy lifestyles is strongly needed. With all patients in our cohort having participated in CR to some extent, data on lifestyle being monitored and openly compared annually in the SWEDEHEART registry, and no visible change for the better seen for more than a decade, our results strongly support this conclusion.

#### *Cardioprotective medication*

According to our study the use of lipid lowering drugs was high during the whole period. More than 90% of the patients were prescribed statins at the one-year follow-up visit throughout the observed period and ezetimibe use increased rapidly after 2015, reaching 29.8% in 2019. In

Page 17 of 46

#### **BMJ** Open

2015-2109 more than 94% of all patients were prescribed statins and/or ezetimibe. Meanwhile, the use of lipid lowering therapy including statins, ezetimibe, fibrates, bile acid sequestrants, and nicotinic acid, increased from approximately 80% of patients in EUROASPIRE III to 84% in EUROASPIRE V (5, 29, 32) (Fig. S2). In the CR attendance analyses from the EUROASPIRE III and IV surveys, compared to non-attenders, the proportion of CR attenders on lipid lowering therapy was considerably higher, or 83% vs 78% (EAIII) and 88% vs 85% (EAIV), respectively (18, 19). Data on the use of cardioprotective medication from the Austrian registry or the British National Audit for CR (NACR) has to our knowledge not been published. In annual reports from the Danish CR database, during 2016-2019, between 93-96% of CAD patients were prescribed statins at the end of CR (24). According to our study the use of ACEi/ARB increased from 64.9% in 2006 to 79.5% in 2019 while patients prescribed ACEi/ARB in EUROASPIRE III was 71% and 75% in EUROASPIRE V (Fig. S2) (5, 29, 32). In the EUROASPIRE III and IV, the use of ACEi/ARB and BP-lowering medication was significantly higher in CR attenders than in non-attenders, although the difference was not as large as for lipid lowering treatment (18, 19). While conclusions about the influence of auditing on cardioprotective medication prescription in Sweden are hard to draw, generally it can be concluded that the use of cardioprotective medication in our and other surveys has been high and has increased both in Sweden and Europe in general during the observed period.

#### Strengths and limitations

The major strength of this study is the broad representability and national coverage of data, with more than 75% of all MI patients under the age of 75 being registered in SWEDEHEART and attending a one-year CR follow-up visit since 2016. At the same time, a major limitation is the lack of data describing MI patients not attending CR and on those  $\geq$ 75 years of age and results cannot be generalized to these groups. Even though the mean age in

our data was similar to EUROASPIRE, the age range differed somewhat (our data 18-74 years vs 18-79 years in EUROASPIRE), which might have led to a slight overestimation of the results. Also, the coverage on center-level during the first years was low and representability therefore not as extensive. Comparing our data with other survey and audit data is limited by differences in patient selections, different rates of CR participation, time of follow-up, differences in measurement methods (i.e., questionnaires, self-report), and definitions (i.e., physical inactivity).

#### Conclusion

Between 2006-2019, an increasing proportion of patients in Sweden reached secondary preventive goals for BP and LDL-C one year after an MI. The proportion of patients treated with evidence-based secondary preventive medication also increased. Both levels of BP and LDL-C, as well as use of pharmacological treatment were comparable with data from other similar European quality registries and national level audits used for benchmarking. The trends were more favourable than those observed in EUROASPIRE, data from which represents several European countries where audits were not widely available. The results may indicate that national quality registries can contribute to improving outcomes in CR and add evidence to the importance of auditing and benchmarking as means to improve quality of care. Less encouraging, no changes were seen the proportion of current smokers at the time of the MI who are abstinent at one-year, more patients reported inadequate levels of physical activity, and the proportion of patients with central obesity and diabetes increased, as was observed in EUROASPIRE. These observations bare witness of a large unmet need to prioritize patient lifestyle support after an MI, which should be improved to provide patients with adequate risk reduction.

#### Acknowledgements

None.

#### **Statements**

#### Contributorship

M.L., E.H., and M.B. contributed to the conception and design of the work. A.N., B.L., K.H. and T.J. offered medical expertise and guidance. N.H. conducted all data analysis. M.L. drafted the manuscript. All other authors critically revised the manuscript. All approved the final version of the manuscript.

#### *Funding statement*

This research received no specific grant from any funding agency in the public, commercial or non-for-profit sectors.

#### Competing of Interests

All authors except NH are or have been engaged in the SWEDEHEART registry. Otherwise, the authors have no conflicts of interest to declare.

#### *Ethics approval*

The need for signed informed consent by patients for inclusion in Swedish quality registries has collectively been waived in Sweden. Upon hospital admission, MI patients are informed verbally and in writing by a nurse or physician about data being collected and entered in the registry. However, all patients have the right to deny registration and the right upon request to be removed from the registry at any time. Opt-out is extremely rare, counting less than ten cases

per year. The study complies with the Declaration of Helsinki and was approved by The Swedish Ethical Review Authority (registration number: 2019-04277).

#### Data sharing

The data used in this study is based on the SWEDEHEART registry. Access to data from the registry needs to be applied for and third-party data usage is not allowed, irrespective of whether the data contain potentially identifying or sensitive data or not. Instead, given ethical study approval from the Swedish Ethical Review Authority, access to SWEDEHEART data supporting the present findings can be applied for from the Uppsala Clinical Research Center (UCR) in Sweden. Further information can be found on the UCR <u>www.ucr.uu.se/en</u>/ and Swedish Ethical Review Authority <u>etikprovningsmyndigheten.se</u>/ websites.

One co-author (NH) had primary responsibility for the study data and takes responsibility for its integrity and the data analysis. Analytical methods and other study material are available upon reasonable request to the corresponding author.

#### **Figure legends**

Fig. 1. Patient characteristics as registered during MI hospitalization for patients attending the one-year follow-up visit within CR in Sweden 2006-2019. <sup>a</sup>BMI ≥25 kg/m<sup>2</sup>; <sup>b</sup>prior MI, PCI, CABG, or stroke; <sup>c</sup>ACE inhibitors/ARB, beta blockers, diuretics and/or calcium channel blockers; <sup>d</sup>statins and/or ezetimibe. ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; ASCVD, atherosclerotic cardiovascular disease (MI, PCI, CABG or stroke); BMI, body mass index; CABG, coronary artery bypass grafting; MI, myocardial infarction; N, number; PCI, percutaneous coronary intervention.

#### **BMJ** Open

**Fig. 2.** Proportion of patients achieving targets for BP and LDL-C at the one-year follow-up visit 2006-2019. The p-value for trend from 2006 to 2019 was <0.0001 for both BP and LDL-C. BP, blood pressure; LDL-C, low-density lipoprotein cholesterol.

**Fig. 3.** Mean delta values between hospitalization and the one-year CR follow-up visit for systolic and diastolic BP (upper panel) and LDL-C (lower panel) by year 2006-2019. The p-value for the trend from 2006 to 2019 was <0.0001 for all. DBP, diastolic blood pressure; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure.

**Fig. 4.** Prevalence of persistent smoking (proportion of active smokers at the time of MI who were still smoking), inadequate physical activity, overweight/obesity, and diabetes at one-year post-MI. <sup>a</sup>BMI  $\geq$ 25 kg/m<sup>2</sup>; <sup>b</sup>waist circumference  $\geq$ 102 cm for men and  $\geq$ 88 cm for women; <sup>c</sup>physically active  $\geq$  30 minutes for less than 5 days a week. BMI, body mass index; MI, myocardial infarction.

**Fig. 5.** Proportion of patients at one-year follow-up for each year 2006-2019 treated with statins, ezetimibe, ACEi or ARB, beta blockers, antiplatelet (acetylsalicylic acid or  $P2Y_{12}$ -receptor antagonists) or anticoagulant therapy (warfarin or direct oral anticoagulants). ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker.

**Fig. 6.** Management of BP and LDL in SWEDEHEART (left panel) and EUROASPIRE (right panel) (5, 6). \*Different definitions of BP treatment goals for patients with diabetes were adapted in the EUROASPIRE surveys (III <130/80 mmHg, IV 140/80 mmHg, V <140/85 mmHg), while the definition <140/90 mmHg was adapted for patients with and without diabetes in SWEDEHEART. BP, blood pressure; LDL-C, low-density lipoprotein cholesterol.

#### References

1. Björck L, Rosengren A, Bennett K, Lappas G, Capewell S. Modelling the decreasing coronary heart disease mortality in Sweden between 1986 and 2002. *Eur Heart J*. 2009;30(9):1046-56.

2. Salzwedel A, Jensen K, Rauch B, et al. Effectiveness of comprehensive cardiac rehabilitation in coronary artery disease patients treated according to contemporary evidence based medicine: Update of the Cardiac Rehabilitation Outcome Study (CROS-II). *Eur J Prev Cardiol*. 2020;27(16):1756-74.

3. Visseren FLJ, Mach F, Smulders YM, et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. *Eur Heart J.* 2021;42(34):3227-337.

4. Ambrosetti M, Abreu A, Corra U, et al. Secondary prevention through comprehensive cardiovascular rehabilitation: From knowledge to implementation. 2020 update. A position paper from the Secondary Prevention and Rehabilitation Section of the European Association of Preventive Cardiology. *Eur J Prev Cardiol*. 2020:2047487320913379.

5. Kotseva K, De Backer G, De Bacquer D, et al. Lifestyle and impact on cardiovascular risk factor control in coronary patients across 27 countries: Results from the European Society of Cardiology ESC-EORP EUROASPIRE V registry. *Eur J Prev Cardiol.* 2019;26(8):824-35.

6. Kotseva K, De Bacquer D, Jennings C, et al. Time Trends in Lifestyle, Risk Factor Control, and Use of Evidence-Based Medications in Patients With Coronary Heart Disease in Europe: Results From 3 EUROASPIRE Surveys, 1999-2013. *Glob Heart*. 2017;12(4):315-22 e3.

7. Poffley A, Thomas E, Grace SL, et al. A systematic review of cardiac rehabilitation registries. *Eur J Prev Cardiol.* 2017;24(15):1596-609.
Page 23 of 46

### **BMJ** Open

8. Aktaa S, Batra G, Wallentin L, et al. European Society of Cardiology methodology for the development of quality indicators for the quantification of cardiovascular care and outcomes. *Eur Heart J Qual Care Clin Outcomes*. 2022;8(1):4-13.

9. Aktaa S, Gencer B, Arbelo E, et al. European Society of Cardiology Quality Indicators for Cardiovascular Disease Prevention: developed by the Working Group for Cardiovascular Disease Prevention Quality Indicators in collaboration with the European Association for Preventive Cardiology of the European Society of Cardiology. *Eur J Prev Cardiol.* 2022;29(7):1060-71.

10. Thomas RJ, Balady G, Banka G, et al. 2018 ACC/AHA Clinical Performance and Quality Measures for Cardiac Rehabilitation: A Report of the American College of Cardiology/American Heart Association Task Force on Performance Measures. *J Am Coll Cardiol.* 2018;71(16):1814-37.

11. Brittish Association for Cardiovascular Prevention and Rehabilitation. The BACPR standards and core components for cardiovascular disease prevention and rehabilitation (3rd edition). London, England; 2017.

12. Jernberg T, Attebring MF, Hambraeus K, et al. The Swedish Web-system for enhancement and development of evidence-based care in heart disease evaluated according to recommended therapies (SWEDEHEART). *Heart.* 2010;96(20):1617-21.

13. Back M, Leosdottir M, Hagstrom E, et al. The SWEDEHEART secondary prevention and cardiac rehabilitation registry (SWEDEHEART CR registry). *Eur Heart J Qual Care Clin Outcomes*. 2021;7(5):431-7.

14. Hambraeus K, Tyden P, Lindahl B. Time trends and gender differences in prevention guideline adherence and outcome after myocardial infarction: Data from the SWEDEHEART registry. *Eur J Prev Cardiol.* 2016;23(4):340-8.

15. Jernberg T, Boberg B, Back M, et al. SWEDEHEART Annual Report 2019.Uppsala, Sweden: Uppsala Clinical Research Center; 2019.

16. Vasko P, Alfredsson J, Back M, et al. SWEDEHEART Annual report 2020.Annual report. Uppsala, Sweden: Uppsala Clinical Research Center (UCR); 2021.

17. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem.* 1972;18(6):499-502.

18. Kotseva K, Wood D, De Backer G, et al. Use and effects of cardiac rehabilitation in patients with coronary heart disease: results from the EUROASPIRE III survey. *Eur J Prev Cardiol.* 2013;20(5):817-26.

19. Kotseva K, Wood D, De Bacquer D, et al. Determinants of participation and risk factor control according to attendance in cardiac rehabilitation programmes in coronary patients in Europe: EUROASPIRE IV survey. *Eur J Prev Cardiol.* 2018;25(12):1242-51.

20. De Bacquer D, Astin F, Kotseva K, et al. Poor adherence to lifestyle recommendations in patients with coronary heart disease: results from the EUROASPIRE surveys. *Eur J Prev Cardiol.* 2021;29(2):383-395.

21. Svensson MK, Sorio Vilela F, Leosdottir M, et al. Effects of lipid-lowering treatment intensity and adherence on cardiovascular outcomes in patients with a recent myocardial infarction: a Swedish register-based study. *Ups J Med Sci.* 2022;127.

22. Reich B, Benzer W, Harpf H, et al. Efficacy of extended, comprehensive outpatient cardiac rehabilitation on cardiovascular risk factors: A nationwide registry. *Eur J Prev Cardiol.* 2020;27(10):1026-33.

23. Zwisler AD, Rossau HK, Nakano A, et al. The Danish Cardiac Rehabilitation Database. *Clin Epidemiol*. 2016;8:451-6.

24. Thomsen KK. Danish Cardiac Rehabilitation Registry Annual Report. 2019.

### **BMJ** Open

25. Paton JY, Ranmal R, Dudley J, and R. C. S. Committee. Clinical audit: still an important tool for improving healthcare. *Arch Dis Child Educ Pract Ed*. 2015;100(2):83-8.

26. Abreu A, Frederix I, Dendale P, et al. Standardization and quality improvement of secondary prevention through cardiovascular rehabilitation programmes in Europe: The avenue towards EAPC accreditation programme: A position statement of the Secondary Prevention and Rehabilitation Section of the European Association of Preventive Cardiology (EAPC). *Eur J Prev Cardiol.* 2020.

27. Feldman AL, Griffin SJ, Fharm E, et al. Screening for type 2 diabetes: do screendetected cases fare better? *Diabetologia*. 2017;60(11):2200-9.

28. Ogmundsdottir Michelsen H, Sjolin I, Schlyter M, et al. Cardiac rehabilitation after acute myocardial infarction in Sweden - evaluation of programme characteristics and adherence to European guidelines: The Perfect Cardiac Rehabilitation (Perfect-CR) study. *Eur J Prev Cardiol.* 2020;27(1):18-27.

29. Kotseva K, Wood D, De Backer G, et al. EUROASPIRE III: a survey on the lifestyle, risk factors and use of cardioprotective drug therapies in coronary patients from 22 European countries. *Eur J Cardiovasc Prev Rehabil.* 2009;16(2):121-37.

Doherty P. National Audit of Cardiac Rehabilitation - Annual Statistical Reports
 York, U.K.; 2016-2019.

31. Critchley JA, Capewell S. Mortality risk reduction associated with smoking cessation in patients with coronary heart disease: a systematic review. *JAMA*. 2003;290(1):86-97.

32. Kotseva K, Wood D, De Bacquer D, et al. EUROASPIRE IV: A European Society of Cardiology survey on the lifestyle, risk factor and therapeutic management of coronary patients from 24 European countries. *Eur J Prev Cardiol.* 2016;23(6):636-48.









BMJ Open





### Page 31 of 46



**SWEDEHEART EUROASPIRE** For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

## **Supplementary material**

Temporal trends in cardiovascular risk factors, lifestyle, and secondary preventive medication yocardina. for patients with myocardial infarction attending cardiac rehabilitation in Sweden 2006-2019:

Page 33 of 46

# Table S1. Patient characteristics during hospitalization (continuous variables) by year. Data are presented as median values (q1, q3).

BMJ Open

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	p for trend
N	2502	3942	5223	4948	4720	5368	5976	6530	6432	6831	7121	7073	7269	7428	
Age (years)	63 (57, 69)	63 (57, 69)	63 (57, 69)	63 (57, 69)	63 (57, 69)	64 (57, 69)	64 (57, 69)	64 (57, 69)	64 (57, 69)	64 (57, 69)	65 (57, 70)	64 (57, 70)	65 (58, 70)	65 (58, 70)	< 0.0001
N missing	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Systolic BP	150 (130,	147 (130,	145 (130,	146 (130,	147 (130,	149 (130,	150 (130,	150 (130,	150 (131,	150 (132,	150 (133,	150 (132,	150 (133,	150 (130,	< 0.0001
(mmHg)	170)	165)	165)	165)	165)	168)	170)	170)	170)	170)	170)	170)	170)	169)	
N missing	293	406	479	456	308	7	18	36	48	51	44	2	3	4	
Diastolic BP	85 (74,	85 (75, 98)	85 (75, 97)	85 (75, 97)	85 (75, 96)	85 (75, 98)	87 (76,	88 (77,	88 (78,	89 (79,	89 (78, 99)	89 (79,	90 (79,	89 (79,	< 0.0001
(mmHg)	100)						100)	100)	100)	100)		100)	100)	100)	
N missing	330	471	529	509	410	130	176	213	290	299	261	227	352	454	
Total cholesterol	5.0 (4.3,	5.0 (4.2,	4.9 (4.2,	5.0 (4.2,	5.1 (4.3,	5.1 (4.3,	5.1 (4.3,	5.1 (4.3,	5.0 (4.2,	5.0 (4.2,	5.0 (4.2,	5.0 (4.1,	5.0 (4.1,	4.9 (4.0,	< 0.0001
(mmol/L)	5.8)	5.8)	5.7)	5.8)	5.9)	6.0)	6.0)	6.0)	5.9)	5.8)	5.9)	5.8)	5.9)	5.7)	
N missing	329	554	788	833	835	1108	1185	1280	1204	1088	947	835	686	727	
LDL-C	3.0 (2.3,	3.0 (2.3,	3.0 (2.3,	3.1 (2.3,	3.2 (2.5,	3.2 (2.5,	3.2 (2.5,	3.2 (2.4,	3.1 (2.3,	3.1 (2.3,	3.1 (2.3,	3.0 (2.2,	3.0 (2.2,	3.0 (2.2,	< 0.0001
(mmol/L)	3.7)	3.7)	3.7)	3.8)	3.9)	3.9)	4.0)	3.9)	3.9)	3.8)	3.9)	3.8)	3.8)	3.8)	
N missing	471	844	1008	972	1001	1272	1420	1678	1395	1234	1028	927	629	663	
HDL-C	1.2 (1.0,	1.2 (1.0,	1.1 (0.9,	1.1 (0.9,	1.1 (0.9,	1.1 (0.9,	1.1 (0.9,	1.1 (1.0,	1.1 (1.0,	1.1 (0.9,	1.1 (0.9,	1.2 (1.0,	1.2 (0.9,	1.1 (0.9,	0.003
(mmol/L)	1.4)	1.4)	1.4)	1.3)	1.3)	1.4)	1.4)	1.4)	1.4)	1.4)	1.4)	1.4)	1.4)	1.4)	
N missing	455	821	898	886	941	1214	1330	1519	1374	1188	987	901	746	766	

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	p for tren
N	2502	3942	5223	4948	4720	5368	5976	6530	6432	6831	7121	7073	7269	7428	
Triglycerides	1.5 (1.1,	1.5 (1.1,	1.5 (1.1,	1.5 (1.1,	1.4 (1.1,	1.4 (1.0,	1.4 (1.0,	1.4 (1.0,	1.4 (1.0,	1.4 (1.0,	1.4 (1.0,	1.4 (1.0,	1.4 (1.0,	1.4 (1.0,	< 0.000
(mmol/L)	2.2)	2.1)	2.1)	2.1)	2.0)	2.0)	1.9)	1.9)	2.0)	2.0)	2.0)	2.0)	2.0)	2.0)	
N missing	391	769	897	901	923	1170	1318	1599	1500	1601	1488	1460	1481	1472	
F-glucose	6.7 (5.6,	6.6 (5.7,	6.7 (5.7,	6.8 (5.7,	6.7 (5.8,	6.8 (5.8,	6.7 (5.8,	6.7 (5.9,	6.8 (5.9,	6.8 (5.9,	6.9 (5.9,	6.9 (5.9,	6.9 (5.9,	7.0 (6.0,	< 0.000
(mmol/L)	8.4)	8.3)	8.4)	8.5)	8.3)	8.5)	8.4)	8.5)	8.5)	8.6)	8.7)	8.7)	8.6)	8.8)	
N missing	213	332	452	363	324	727	1034	1147	1014	767	762	643	812	1011	
HbA1c	N/A	N/A	N/A	N/A	N/A	59.0 (50.0,	59.0 (48.0,	58.0 (50.0,	61.0 (50.0,	60.0 (50.0,	59.0 (48.0,	56.0 (48.0,	56.0 (48.0,	57.0 (48.0,	0.012
(mmol/mol)*						71.0)	73.0)	73.0)	74.0)	77.0)	74.0)	69.0)	72.0)	69.0)	
N missing	484	730	977	996	852	776	872	1059	949	1071	1113	980	973	1012	
BMI (kg/m2)	26.7 (24.6,	26.9 (24.7,	26.9 (24.5,	26.9 (24.5,	27.0 (24.7,	27.1 (24.7,	27.2 (24.7,	27.2 (24.7,	27.2 (24.8,	27.2 (24.7,	27.4 (24.8,	27.4 (24.9,	27.5 (24.9,	27.5 (24.9,	< 0.000
	29.4)	29.7)	29.7)	29.8)	29.9)	30.0)	30.1)	30.1)	30.1)	30.1)	30.5)	30.4)	30.5)	30.7)	
N missing	793	955	898	861	862	316	263	167	183	166	205	169	207	234	
cho	lesterol; L	DL-C, low	-density li	poprotein	cholestero	ıl; N, numł	ber; N/A, r	io data ava	ailable; q1,	lower qua	artile; q3, 1	upper qua	rtile.	- <b>P</b> - <b>O</b> - <b>D</b>	

Page 35 of 46

BMJ Open

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	p for trend
N	2502	3942	5223	4948	4720	5368	5976	6530	6432	6831	7121	7073	7269	7428	
Male sex	73.5%	74.4%	73.1%	73.7%	74.1%	74.5%	74.6%	74.1%	76.2%	75.3%	74.5%	76.2%	75.1%	75.2%	<0.0001
N missing	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Current smoking	32.0%	32.6%	32.4%	32.1%	30.8%	30.4%	30.4%	30.1%	28.9%	28.5%	28.0%	27.6%	27.4%	26.5%	<0.0001
N missing	99	150	161	171	130	215	128	143	124	132	145	145	172	177	
Overweight/obese (BMI ≥25 kg/m2)	70.7%	71.5%	70.2%	69.8%	72.1%	71.6%	71.9%	72.1%	73.3%	72.0%	73.2%	74.1%	74.0%	74.1%	<0.0001
N missing	793	955	898	861	862	316	263	167	183	166	205	169	207	234	
Obese (BMI ≥30 kg/m2)	22.8%	23.8%	23.4%	23.9%	24.3%	25.4%	26.0%	25.9%	26.0%	26.4%	28.7%	27.9%	29.0%	29.5%	< 0.0001
N missing	793	955	898	861	862	316	263	167	183	166	205	169	207	234	
Use of antihypertensive drugs*	47.5%	47.9%	49.1%	49.9%	48.0%	48.4%	49.2%	49.4%	49.2%	49.4%	49.8%	50.3%	48.9%	50.5%	< 0.0001
N missing	6	13	9	24	15	41	26	33	31	23	84	85	92	99	
Use of lipid lowering drugs†	24.5%	25.0%	26.5%	28.8%	27.7%	28.4%	28.4%	28.8%	27.6%	27.9%	27.7%	28.0%	26.9%	28.6%	0.004
N missing	8	17	15	30	20	44	29	39	29	31	94	103	102	131	
Prior diabetes diagnosis	19.3%	18.5%	18.7%	20.1%	18.1%	18.8%	18.9%	20.3%	19.7%	20.5%	21.7%	21.1%	21.5%	22.6%	<0.0001
N missing	0	0	1	0	0	2	0	1	0	6	1	2	13	21	
Prior ASCVD diagnosis‡	23.3%	24.5%	23.8%	23.8%	22.8%	22.8%	26.5%	28.2%	26.5%	26.9%	27.4%	28.2%	27.2%	27.9%	<0.0001
N missing	0	0	0	0	0	2	0	0	0	0	0	0	0	0	

\*ACE inhibitor, ARB, beta blocker, diuretics, and/or calcium channel blocker. †Statins and/or ezetimibe. ‡MI, PCI, CABG or stroke. ACE,

angiotensin converting enzyme; ARB, angiotensin receptor blocker; ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index;

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

**BMJ** Open

CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate; MI, myocardial infarction; PCI, percutaneous coronary intervention.

.nerular filt.

## BMJ Open

numbers (N) and p	roportions (9	6).													
Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	p for trend
N	2502	3942	5223	4948	4720	5368	5976	6530	6432	6831	7121	7073	7269	7428	
STEMI	39.3%	38.8%	36.4%	38.9%	39.7%	39.2%	37.6%	37.2%	38.9%	38.9%	38.6%	38.9%	40.4%	40.5%	< 0.0001
N missing	0	1	2	69	52	48	55	5	0	0	0	0	0	0	
Revascularized* during	65.1%	71.5%	71.1%	71.1%	76.4%	87.3%	82.2%	83.9%	86.0%	88.6%	88.5%	89.6%	90.6%	90.3%	<0.0001
hospitalization															
N missing	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Discharge medication															
Statin	90.4%	93.5%	94.7%	95.7%	96.7%	96.8%	97.1%	96.8%	97.3%	97.7%	97.5%	97.3%	96.9%	97.0%	<0.0001
N missing	1	2	4	1	1	2	1	4	5	2	0	2	2	8	
Ezetimibe	1.3%	1.5%	2.0%	2.0%	1.5%	1.6%	1.5%	1.5%	1.6%	1.5%	2.4%	3.1%	4.2%	5.1%	< 0.0001
N missing	3	7	16	7	4	4	3	8	7	2	1	0	798	4	
ACE-inhibitor/ARB	64.3%	67.1%	72.4%	75.6%	78.9%	82.5%	82.8%	84.0%	83.9%	85.1%	85.1%	85.8%	85.3%	84.7%	<0.0001
N missing	3	6	6	2	3	9	3	5	6	3	3	1	2	4	1
Beta blocker	92.2%	90.6%	92.3%	93.1%	92.8%	93.2%	92.1%	91.9%	90.9%	90.2%	90.3%	89.7%	88.2%	81.5%	<0.0001
N missing	2	3	7	0	0	3	2	0	3	2	1	1	2	4	
Acetylsalicylic acid	94.0%	96.2%	95.9%	96.2%	96.6%	96.9%	97.6%	97.2%	96.3%	96.2%	95.9%	96.2%	95.9%	95.3%	0.114
N missing	1	1	3	0	0	2	2	1	4	1	9	3	5	5	1
P2Y <sub>12</sub> -receptor antagonist	79.3%	84.0%	84.5%	86.0%	89.2%	87.4%	82.8%	85.3%	89.9%	90.5%	91.2%	90.9%	90.7%	91.0%	< 0.0001
N missing	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

															6
Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	p for trend
N	2502	3942	5223	4948	4720	5368	5976	6530	6432	6831	7121	7073	7269	7428	
DAPT/DAT/TAT	78.1%	83.9%	84.2%	85.8%	88.6%	87.5%	83.3%	85.3%	89.8%	90.7%	91.2%	91.2%	91.1%	91.5%	< 0.0001
N missing	1	1	3	0	0	2	2	1	4	1	9	3	5	5	
*Percutaneous coror	nary interve	ntion or	coronary	artery by	pass gra	fting. AC	E, angio	tensin co	nverting	enzyme	; ARB, a	ngioten	sin recep	tor	1
blocker; DAPT, dua	l antiplatele	et therapy	; DAT, c	lual antit	hromboti	ic therapy	; N, num	ber; N/A	, no data	availab	le; STEN	AI, ST-e	elevation		
myocardial infarctio	n; TAT, tri	ple antith	rombotic	c therapy.											
			-		L., (4										
								1000111/	انتم مانام مدينا	a traa l					

Page 39 of 46

BMJ Open

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	p for trend
N	2502	3942	5223	4948	4720	5368	5976	6530	6432	6831	7121	7073	7269	7428	_
Systolic BP (mmHg)	130 (120,	130 (120,	130 (120,	130 (120,	130 (120,	130 (120,	130 (120,	130 (120,	130 (120,	130 (120,	130 (120,	130 (120,	130 (120,	128 (120,	< 0.0001
	145)	140)	140)	140)	140)	140)	140)	140)	140)	140)	138)	138)	137)	135)	
N missing	869	1308	1351	996	711	945	999	675	381	339	262	196	234	219	
Diastolic BP (mmHg)	80 (70,	78 (70,	80 (70,	76 (70,	80 (70,	80 (70,	80 (70,	80 (70,	79 (70,	78 (70,	77 (70,	77 (70,	76 (70.	76 (70.	< 0.0001
	82)	80)	80)	80)	80)	80)	84)	82)	82)	80)	80)	81)	81)	80)	
N missing	871	1314	1364	999	715	947	1008	689	392	344	267	201	238	226	
Total cholesterol (mmol/L)	4.2 (3.6,	4.1 (3.6,	4.1 (3.6,	4.2 (3.7,	4.1 (3.6,	4.2 (3.6,	4.1 (3.6,	4.0 (3.5,	3.8 (3.3,	3.7 (3.2,	3.6 (3.2,	3.5 (3.1,	3.4 (3.0,	3.3 (2.9,	< 0.0001
	4.8)	4.7)	4.6)	4.7)	4.7)	4.8)	4.7)	4.6)	4.4)	4.3)	4.2)	4.1)	4.0)	3.8)	
N missing	690	1383	1819	1664	1117	1152	1162	759	410	434	407	345	381	370	
LDL-C (mmol/L)	2.1 (1.7,	2.2 (1.8,	2.2 (1.7,	2.3 (1.9,	2.2 (1.8,	2.2 (1.8,	2.2 (1.8,	2.1 (1.7,	1.9 (1.6,	1.8 (1.5,	1.8 (1.4,	1.7 (1.4,	1.7 (1.4,	1.6 (1.3,	< 0.0001
	2.6)	2.6)	2.6)	2.7)	2.7)	2.7)	2.7)	2.5)	2.4)	2.3)	2.2)	2.1)	2.1)	1.9)	
N missing	729	1443	1891	1745	1247	1238	1310	837	439	419	338	244	255	224	
HDL-C (mmol/L)	1.3 (1.1,	1.2 (1.0,	1.2 (1.0,	1.2 (1.0,	1.2 (1.0,	1.2 (1.0,	1.2 (1.0,	1.2 (1.0,	1.2 (1.0,	1.2 (1.0,	1.2 (1.0,	1.2 (1.0,	1.2 (1.0,	1.2 (1.0,	0.552
	1.5)	1.4)	1.4)	1.4)	1.4)	1.5)	1.5)	1.5)	1.5)	1.5)	1.5)	1.5)	1.4)	1.4)	
N missing	714	1423	1860	1720	1180	1217	1253	850	481	627	679	644	667	641	
Triglycerides (mmol/L)	1.4 (1.0,	1.3 (1.0,	1.3 (1.0,	1.4 (1.0,	1.3 (1.0,	1.3 (1.0,	1.3 (1.0,	1.3 (1.0,	1.2 (0.9,	1.2 (0.9,	1.2 (0.9,	1.2 (0.9,	1.2 (0.9,	1.1 (0.8,	< 0.0001
	1.9)	1.9)	1.9)	1.9)	1.8)	1.8)	1.8)	1.8)	1.7)	1.7)	1.6)	1.7)	1.6)	1.6)	
N missing	720	1415	1869	1701	1204	1192	1286	907	727	966	1153	1139	1259	1175	

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	p for trend
N	2502	3942	5223	4948	4720	5368	5976	6530	6432	6831	7121	7073	7269	7428	
F-glucose (mmol/L)	5.7 (5.2,	5.7 (5.2,	5.7 (5.2,	5.7 (5.2,	5.7 (5.3,	5.8 (5.3,	5.8 (5.3,	5.9 (5.4,	5.9 (5.4,	6.0 (5.5,	6.0 (5.5,	6.0 (5.5,	6.0 (5.5,	6.0 (5.5,	< 0.0001
	6.5)	6.4)	6.6)	6.5)	6.5)	6.6)	6.6)	6.8)	6.7)	6.7)	6.8)	6.8)	6.7)	6.8)	
N missing	893	1391	1820	1639	1374	1777	2128	1923	1953	2332	2376	2598	2830	3006	
HbA1c (mmol/mol)*	56.0	56.5	56.0	55.0	55.0	56.0	58.0	57.0	54.0	55.0	55.0	54.0	53.0	52.0	< 0.0001
	(49.0,	(49.0,	(48.0,	(48.0,	(49.0,	(49.0,	(50.0,	(48.0,	(47.0,	(46.0,	(47.0,	(46.0,	(46.0,	(46.0,	
	68.0)	68.0)	66.0)	67.0)	69.0)	68.0)	70.0)	69.0)	67.0)	66.0)	66.0)	66.0)	63.0)	64.0)	
N missing	165	215	242	274	267	372	407	496	595	676	735	755	801	868	
BMI (kg/m2)	26.8	27.1	27.2	27.1	27.2	27.2	27.4	27.2	27.2	27.3	27.4	27.4	27.4	27.4	0.0007
	(24.7,	(24.7,	(24.8,	(24.7,	(24.8,	(24.8,	(24.8,	(24.8,	(24.8,	(24.6,	(24.7,	(24.8,	(24.8,	(24.8,	
	29.7)	30.0)	30.1)	30.0)	30.2)	30.2)	30.4)	30.3)	30.2)	30.3)	30.6)	30.6)	30.5)	30.6)	
N missing	1203	1694	1899	1751	1462	1292	1583	1442	1367	1589	1782	1874	2396	2630	
Waist circumference (cm)	99 (92,	100 (93,	100 (92,	100 (93,	100 (93,	100 (93,	100 (93,	100 (93,	101 (93,	101 (93,	101 (93,	101 (94,	101 (93,	101 (94,	< 0.0001
	106)	107)	107)	107)	108)	108)	108)	108)	109)	109)	110)	110)	110)	109)	
N missing	1306	1799	2111	1771	1409	1822	2079	2246	2138	2551	2984	3301	3789	4403	
Physical activity (days)**	4 (1, 7)	4 (1, 7)	4 (1, 7)	4 (1, 7)	3 (1, 7)	4 (1, 7)	3 (1, 6)	3 (1, 7)	3 (1, 7)	4 (1, 7)	3 (1, 7)	3 (1, 6)	3 (1, 6)	3 (1, 6)	<0.0001
N missing	140	237	551	377	24	112	59	55	40	37	56	35	59	68	
*Patients with dia	abetes only.	** Days	during th	e last we	ek of phy	ysical act	ivity (at ]	least 30 n	ninutes p	er day). E	BMI, bod	y mass in	idex; BP,	blood	
pressure; F, fastin	ng; HbA1c, l	nemogloł	oin A1c;	HDL-C, I	high-den	sity lipor	orotein ch	nolesterol	;LDL-C	, low-den	sity lipor	orotein ch	nolesterol	; N,	
number: N/A, no	data availah	ole: a1. lo	wer quar	tile: a3. i	ipper au	artile					• • •				
	dutu u vunut	10, 41, 10	wer quur	une, 45, v	apper qui										

 BMJ Open

ear	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	p for trend
vstolic BP (mmHg)	-25.2	-25.2	-24.5	-25.4	-25.8	-26.5	-26.5	-26.9	-28.5	-28.4	-29.9	-29.5	-29.9	-30.2	< 0.0001
<i>(</i>	(25.8)	(26.0)	(26.0)	(25.8)	(25.9)	(25.7)	(25.5)	(26.0)	(26.4)	(25.3)	(25.2)	(25.5)	(25.1)	(24.9)	
viastolic BP (mmHg)	-16.6	-16.7	-16.1	-17.2	-16.2	-16.2	-16.0	-16.7	-17.2	-17.5	-18.1	-17.9	-18.4	-20.1	<0.0001
	(13.5)	(14.7)	(14.6)	(14.5)	(14.1)	(14.2)	(14.6)	(14.6)	(14.8)	(14.2)	(14.4)	(14.3)	(14.0)	(14.3)	
DL-C (mmol/L)	-0.83	-0.75	-0.83	-0.78	-0.89	-0.91	-0.93	-1.02	-1.10	-1.13	-1.23	-1.24	-1.26	-1.29	< 0.0001
10	(1.11)	(1.05)	(1.10)	(1.12)	(1.11)	(1.13)	(1.17)	(1.21)	(1.16)	(1.17)	(1.19)	(1.18)	(1.21)	(1.20)	
glucose (mmol/L)	-1.59	-1.40	-1.46	-1.52	-1.46	-1.47	-1.36	-1.30	-1.40	-1.37	-1.42	-1.37	-1.45	-1.62	0.670
	(3.33)	(3.02)	(3.08)	(3.16)	(3.17)	(2.85)	(3.02)	(3.10)	(3.17)	(3.08)	(3.11)	(2.87)	(3.11)	(3.39)	
[bA1c (mmol/mol) *	N/A	N/A	N/A	N/A	N/A	-1.5 (-	-1.0 (-	-2.0 (-	-1.0 (-	0.0 (-8.0,	-1.0 (-	0.0 (-7.0,	0.0 (-7.0,	-1.0 (-9.0,	0.297
						9.0, 5.0)	11.0, 5.0)	10.0, 4.0)	10.0, 3.0)	6.0)	9.0, 5.0)	6.0)	5.0)	4.0)	
MI (kg/m2)	0.24	0.17	0.30	0.23	0.25	0.23	0.21	0.09	0.06	0.04	-0.03	-0.01	-0.11	-0.15	< 0.0001
	(1.80)	(1.91)	(1.80)	(1.88)	(1.86)	(1.91)	(1.91)	(1.91)	(1.88)	(2.06)	(2.00)	(1.97)	(2.09)	(2.11)	
											1				

**BMJ** Open

# Table S6. Patient demographics for the EUROASPIRE surveys III, IV and V (1-3).

Survey	Years conducted	Number of	% men	Number of participating	Number of participating	Median (IQR) time
		patients		centres	countries	(years) after index event
III	2006-2007	8966	73%	76	22	1.2 (1.0-1.8)
IV	2011-2012	7998	76%	78	24	1.4 (1.0-1.9)
V	2016-2017	8261	74%	131	27	1.1 (0.8-1.6)
TQR, mer g	luar the range.					

 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml



Figure S1. Lifestyle factors at one-year in SWEDEHEART (left panel) and EUROASPIRE (right panel) where comparable data in the two cohorts

was available (1-3). <sup>a</sup>Body mass index  $\geq$ 25 kg/m<sup>2</sup>; <sup>b</sup>waist circumference  $\geq$ 102 cm for men and  $\geq$ 88 cm for women.

BMJ Open



**Figure S2.** Proportion of patients at one-year follow-up for each year 2006-2019 in SWEDEHEART treated with lipid lowering therapy (statins or ezetimibe), ACEi or ARB, beta blockers or antiplatelet therapy (ASA or  $P2Y_{12}$ -receptor antagonists). Corresponding data from the EUROASPIRE III-V surveys shown on the right panel of the figure (1-3). In EUROASPIRE lipid lowering drugs included statins, ezetimibe, fibrates, bile acid sequestrants and nicotinic acid.

ACEi, angiotensin converting enzyme inhibitors; ARB, angiotensin receptor blockers; ASA, acetylsalicylic acid.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

## References

1. Kotseva K, De Backer G, De Bacquer D, Ryden L, Hoes A, Grobbee D, et al. Lifestyle and impact on cardiovascular risk factor control in coronary patients across 27 countries: Results from the European Society of Cardiology ESC-EORP EUROASPIRE V registry. Eur J Prev Cardiol. 2019;26(8):824-35.

 Kotseva K, Wood D, De Backer G, De Bacquer D, Pyorala K, Keil U, et al.
 EUROASPIRE III: a survey on the lifestyle, risk factors and use of cardioprotective drug therapies in coronary patients from 22 European countries. Eur J Cardiovasc Prev Rehabil.
 2009;16(2):121-37.

Kotseva K, Wood D, De Bacquer D, De Backer G, Ryden L, Jennings C, et al.
EUROASPIRE IV: A European Society of Cardiology survey on the lifestyle, risk factor and therapeutic management of coronary patients from 24 European countries. Eur J Prev Cardiol. 2016;23(6):636-48.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

# STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Page No
Title and abstract	1	( <i>a</i> ) Indicate the study's design with a commonly used term in the title or the	1-2
		(b) Provide in the abstract an informative and balanced summary of what was	2-3
		done and what was found	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-7
Participants	6	( <i>a</i> ) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5-7
		( <i>b</i> ) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
Data sources/	8*	For each variable of interest, give sources of data and details of methods of	5-7
measurement		assessment (measurement). Describe comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	N/A
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-8
Statistical methods	12	( <i>a</i> ) Describe all statistical methods, including those used to control for confounding	8
		(b) Describe any methods used to examine subgroups and interactions	
		(c) Explain how missing data were addressed	
		(d) If applicable, explain how loss to follow-up was addressed	
		( <u>e</u> ) Describe any sensitivity analyses	
Results			
Participants	13*	<ul> <li>(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed</li> <li>(b) Give reasons for non-participation at each stage</li> <li>(c) Consider use of a flow diagram</li> </ul>	9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9 and Tables S1-3
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	S4

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Main results	16	( <i>a</i> ) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-11 Fig 1-5 Tables S1-5
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Table S6 Figures S1-2
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16-17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	11-17
Other informati	on		
Funding	22	Give the source of funding and the role of the funders for the present study and, if	N/A

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

applicable, for the original study on which the present article is based

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml