RESEARCH REPORT

Use of statins and beta-blockers after acute myocardial infarction according to income and education

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J Epidemiol Community Health 2007;**61**:1091–1097. doi: 10.1136/jech.2006.055525

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Received 4 October 2006
Revised 29 November 2006
Accepted 21 January 2007

Objective: To study the initiation of and long-term refill persistency with statins and beta-blockers after acute myocardial infarction (AMI) according to income and education.
Design and setting: Linkage of individuals through national registers of hospitalisations, drug dispensation, income and education.
Participants: 30 078 patients aged 30–74 years surviving first hospitalisation for AMI in Denmark between 1995 and 2001.
Main outcome measures: Initiation of statin or beta-blocker treatment (out-patient claim of prescriptions within 6 months of discharge) and refill persistency (first break in treatment lasting at least 90 days, and re-initiation of treatment after a break).
Results: When simultaneously estimating the effect of income and education on initiation of treatment, the effect of education attenuated and a clear income gradient remained for both drugs. Among patients aged 30–64 years, high income (adjusted hazard ratio (HR) 1.27; 95% confidence interval (CI) 1.19–1.35) and medium income (HR 1.13; 95% CI 1.06–1.20) was associated with initiation of statin treatment compared with low income. The risk of break in statin treatment was lower for patients with high (HR 0.73; 95% CI 0.66–0.82) and medium (HR 0.82; 95% CI 0.74–0.92) income compared with low income, whereas there was a trend in the opposite direction concerning a break in beta-blocker treatment. There was no gradient in re-initiation of treatment.
Conclusion: Patients with low compared with high income less frequently initiated preventive treatment post-AMI, had worse long-term persistency with statins, but tended to have better persistency with beta-blockers. Low income by itself seems not to be associated with poor long-term refill persistency post-AMI.

Patients with low socioeconomic status (SES) have a high prevalence of cardiovascular risk factors and high mortality from heart disease; therefore, secondary prevention with evidence-based therapy in patients with low SES is of importance.[1–5] Nevertheless, initiation of and refill persistency with these drugs according to SES have not been thoroughly investigated, and the few studies on this topic have mainly been on selected populations, involving contextual or single measures of SES.[6–11] Socioeconomic indicators are found to be partly independent determinants of health instead of being interchangeable,[12 13] and recently we have demonstrated that income and education independently affect mortality after an acute myocardial infarction (AMI).[2] The importance of patient factors, such as education and income, to the treatment after AMI needs to be studied further to improve the understanding of the mechanisms leading to social inequality in the prognosis after AMI.

To further understand the influence of SES on secondary prevention after MI, we performed a nationwide study of the initiation of and long-term refill persistency with statins and beta-blockers according to income and education. Our study included all patients in Denmark, aged 30–74 years, who had been discharged alive after an AMI between 1995 and 2001. We linked individuals through national registries of hospitalisation, drug dispensation, income and education.

METHODS

Setting

Health care in Denmark is built on the Nordic welfare model and is a tax-financed public service, with a small privately financed sector. Denmark's healthcare system provides free access, with no payment, to hospitals and general practitioners.[14] During hospital admission, drug use is free, whereas out-patient drug use is partially reimbursed. In the study period, approximately 75% of expenditures to statins and beta-blockers were reimbursed for patients with AMI by public health insurance, independently of income. Post-AMI, short-term out-patient medical control and follow-up is, for the majority of patients, provided by the treating hospital, whereas long-term follow-up is provided by the general practitioner.[15] Every citizen in Denmark is provided with a unique, permanent civil registration number, which is used for administrative purposes; this number allows linkage of individuals among registers.

Study population

Through the Danish National Hospital Register, which contains data on all hospitalisations in Denmark since 1978,[16] we identified all patients aged 30–74 years old who were discharged alive after hospitalisation for first AMI (primary diagnosis of AMI (International Classification of Diseases (ICD) version 10, codes I21.x) between 1 January 1995 and 31 December 2001. To study survivors of a first AMI, we included only patients with no previous diagnosis of AMI during the 17 years before the index AMI, which is the longest possible period for all patients (using ICD-8 code 410 for 1978–1994).

Co-morbidity is a potential confounder for initiation of secondary preventive medication and we used the register to identify co-morbidity at the index admission and at admissions up to 1 year previously. The conditions that we, a priori, defined as potentially influencing a decision to treat were: congestive heart failure, cardiogenic shock, arrhythmia, pulmonary oedema, malignancy, diabetes mellitus, renal failure and cerebrovascular disease. Conditions defined as potential contraindications to treatment were: liver disease (potential contraindication for statin treatment) and chronic obstructive lung disease and asthma (potential contraindications for beta-blocker treatment). Furthermore, we identified type of admitting hospital (invasive cardiac care centre, main regional hospital or local community hospital) and whether revascularisation procedures (coronary-artery bypass surgery or percutaneous coronary intervention) were performed within 6 months of admission. Living alone has been associated with having a negative influence on positive health practices, hence we identified cohabitation status (living alone/not living alone).[17] Information on patients' vital status was obtained from the Civil Registration System.

Income and education

From the statistics on tax-related income provided by Statistics Denmark,[18] we obtained gross income, comprising all income subject to taxation (wages and salaries, all types of benefits and pensions), for each patient and cohabiting partner. Patients with a cohabiting partner were categorised according to their average income. Patients' incomes were categorised into tertiles of increasing amounts, according to average income in the 5 years before the year of admission for AMI to account for yearly variations in income and the potentially adverse effect of admission on income. Information on the highest level of completed education was retrieved from the Integrated Student Registry of Statistics Denmark. Due to the Danish registration of education in the period investigated, a large proportion of people above 75 years of age do not have their highest achieved education registered, hence the age limit of 75 years was chosen. Patients were divided into three groups according to length of education: >12 years (short-, medium- and long-term higher education), 10–12 years (vocational education and upper secondary school) and <10 years (primary and lower secondary school).

National prescription register

The national prescription register (Registry of Medicinal Product Statistics) contains information on out-patient prescription drug use by all citizens of Denmark since 1995, but does not contain information on in-hospital drug use. Each prescription record contains detailed information on the drug dispensed (anatomical therapeutic classification (ATC) system name, strength and package size), the date and the civil registration number of the person purchasing the drug. From this database, we retrieved all prescriptions claimed by the AMI patients for statins (ATC: C10AA) and beta-blockers (ATC: C07) in the period 1995–2002. As the prescribed daily dosage is not recorded in the national prescription register, we calculated the dose of each prescription from the average dose given during up to three consecutive prescriptions. Excess tablets were allowed to be accumulated for up to three previous consecutive prescriptions at any time. On the basis of these assumptions, we calculated whether patients at any time had tablets available or not. We defined a patient as receiving treatment if tablets were available. This method is described in more detail elsewhere.[19]

Initiation and refill persistency

Initiation of treatment within 6 months of discharge was established by identifying those who claimed at least one prescription at a pharmacy within this period. As measures of refill persistency, we used break in treatment and re-initiation of treatment after a break. Break in treatment was defined as a break of at least 90 days occurring within 4 years of first prescription claim (the point in time when 90 days had elapsed with no tablets available). We have previously found that less than one-half of post-AMI patients who had a break in statin or beta-blocker treatment of 90 days or more re-initiated treatment within 1 year, whereas more than two-thirds re-initiated treatment after a break of less than 90 days.[19] We therefore used this break duration as the cut-off point for poor adherence. Re-initiation of treatment after a break was defined as a new claim of a prescription at a pharmacy within 1 year of the break.

Statistical analyses

Due to age-specific differences in income and education, we stratified, a priori, the population into two age groups: 30–64 years and 65–74 years in all the analyses. To analyse differences in proportion in baseline characteristics between income or education levels, we tested for linear trends in logistic regression models. The proportion of patients claiming a prescription within 6 months of discharge had a first break in treatment and claimed a prescription after a break were determined by the Kaplan–Meier method with censoring for death. To analyse the effect of income and education on treatment, three analyses using Cox multivariable proportional hazard models were performed for each drug: (1) time to first prescription claim at a pharmacy within 6 months of discharge as outcome (all patients), adjusted for the baseline characteristics; age, sex, cohabitation status, period, use of respective drug within 6 months before index admission (dichotom variable), co-morbidity including contraindications and if revascularisation procedures were performed. Furthermore, we adjusted for patients' residence at county level and clustering at the hospital level; (2) time to first break of at least 90 days within 4 years of initiation as outcome (only for patients who initiated treatment within 6 months of discharge), adjusted for the same baseline characteristics as above; and (3) time to new claim of a prescription at a pharmacy within 1 year of the first break as outcome (only patients who experienced a break), adjusted for baseline characteristics as above. In all the analyses, patients were censored if they died or reached the end of observation period (31 December 2002). The model assumptions; linearity of continuous variables, proportional hazards and lack of interaction were tested and found valid unless otherwise indicated. All analyses were performed with SAS version 9.1 (SAS Institute Inc, Cary, North Carolina, USA).

Ethics

The Danish Data Protection Agency approved the design of the study, and data were made available to us in such a way that individuals could not be identified. The project did not require approval by the regional committee on biomedical research ethics.

RESULTS

A total of 30 078 patients of 30–74 years old were discharged alive after a first hospitalisation for AMI in 1995–2001. Information on income and education was available for 97% of the patients. The study population consisted of 17 182 patients of 30–64 years old and 11 978 patients of 65–74 years old.

Baseline

Table 1 presents the clinical and demographic characteristics stratified by age group, income and educational level. For both age groups, a higher proportion of patients with low than high income or education were women, were living alone, had

Table 1 Baseline characteristics of patients surviving a first hospitalisation for acute myocardial infarction in the period 1995–2001 stratified by age, income and education

	Age 30–64 years								Age 65–74 years							
	Income tertile				Educational level				Income tertile				Educational level			
	High	Medium	Low	p	High	Medium	Low	p	High	Medium	Low	p	High	Medium	Low	p
Number	5738	5723	5721		2323	7199	7660	*	4000	3990	3988		1107	3453	7418	*
%	33.4	33.3	33.3		13.5	41.9	44.6		33.4	33.3	33.3		9.2	28.8	61.9	
Male (%)	84.2	77.7	67.4	*	82.7	84.3	67.1	*	74.0	64.4	55.1	*	79.0	77.4	56.4	*
Mean age (years)	53.0	53.7	56.1	*	53.9	53.6	55.1	*	68.9	69.6	70.5	*	69.5	69.3	69.8	*
Mean observation period (years)	4.1	4.3	4.0	*	4.1	4.1	4.1		3.7	3.5	3.7		3.6	3.5	3.7	
Living alone (%)	19.5	17.3	35.1	*	21.9	20.4	28.0	*	28.0	34.3	30.7	*	24.9	25.5	34.5	*
Drug use before admission†																
Statins (%)	4.5	4.2	5.1		4.5	4.5	4.7		4.6	4.8	3.9		5.1	5.0	4.1	*
Beta-blockers (%)	9.9	9.9	11.5	*	9.8	10.7	10.4		14.0	13.7	14.8		13.5	14.0	14.4	
Co-morbidity‡																
COPD + asthma (%)	1.1	1.8	4.8	*	1.4	2.0	3.4	*	5.0	8.5	9.8	*	4.9	6.1	9.0	*
Congestive heart failure (%)	3.0	3.1	5.6	*	3.7	3.6	4.3		7.4	10.1	11.4	*	8.5	8.8	10.2	*
Arrythmia (%)	3.1	3.4	3.7		3.3	3.5	3.3		7.6	7.5	8.4		8.6	7.7	7.8	
Cerebrovascular disease (%)	1.0	1.4	2.3	*	1.5	1.3	1.8		3.1	3.4	4.5	*	1.9	3.3	4.1	*
Pulmonary oedema	0.1	0.2	0.5	*	0.1	0.2	0.4	*	0.7	0.6	1.0		0.7	0.9	0.7	
Diabetes (%)	5.2	6.9	10.3	*	5.5	6.5	8.9	*	7.3	8.5	10.9	*	6.2	8.0	9.7	*
Renal failure (%)	0.4	0.7	1.2	*	0.5	0.6	1.0	*	1.0	1.1	1.2		1.3	1.3	1.0	
Liver disease (%)	0.1	0.1	0.3	*	0.3	0.1	0.2		0.1	0.1	0.3		0.2	0.3	0.1	
Malignancy (%)	0.5	0.8	1.1	*	0.8	0.8	0.8		2.3	2.4	2.1		2.5	2.4	2.2	
Cardiogenic shock (%)	0.2	0.2	0.4		0.1	0.3	0.3		0.5	0.5	0.7		0.3	0.5	0.6	
Admitting hospital type																
Cardiac care centre (%)	16.2	15.0	15.1		19.5	15.2	14.5	*	16.5	14.1	13.8	*	18.4	16.4	13.5	*
Main regional hospital (%)	64.3	61.6	60.9	*	62.1	63.6	61.1	*	62.5	60.4	58.0	*	60.3	64.2	58.4	*
Local hospital (%)	19.5	23.4	23.9	*	18.5	21.2	24.5	*	21.1	25.5	28.2	*	21.3	19.3	28.1	*
Revascularisation§	38.0	33.2	28.1	*	37.6	35.0	30.0	*	28.1	25.2	18.6	*	30.6	27.8	21.2	*

COPD, chronic obstructive pulmonary disease

*$p<0.05$ in univariate test for trend between income levels or educational levels.

†Claim of prescription within 6 months before index admission.

‡International Classification of Diseases (ICD) version 10 codes: COPD + asthma, J40.x-J46.x; congestive heart failure, I50.x; arrythmia, I46.x-I49.x; cerebrovascular disease, I60.x-I69.x; pulmonary oedema, J18.2, J81.x; diabetes, E10.x-E14.x; renal failure, N17.x-N19.x, I12.x, I13.x, R34.x, T85.8, T85.9, Z99.2; liver disease, K70.x-K77.x; malignancy, C00.x-C97.x; cardiogenic shock, R57.x.

§Coronary-artery bypass surgery or percutaneous coronary intervention within 6 months of admission (Danish version of the Nordic Classification of Surgical Procedures: KFN.x).

comorbid conditions and did not receive revascularisation procedures.

Initiation of treatment

Of all patients aged 30–74 years, who were discharged alive after first hospitalisation for AMI in 1995, 15.7% and 55.7% claimed a prescription at a pharmacy within 6 months of discharge for statin and beta-blockers, respectively. In 2002, these numbers increased to 67.9% and 87.1%, respectively. During the entire period, the proportion of patients claiming a statin or beta-blocker prescription within 6 months of discharge decreased with decreasing income or education (figure 1). Tables 2 and 3 shows the adjusted hazard ratios for initiation of statins and beta-blockers, respectively. For example, among patients aged 30–64 years old, 54.0%, 47.5% and 41.4% with high, medium and low income, respectively, and 52.2%, 49.3% and 44.8% with high, medium and low education, respectively, claimed a prescription for statins within 6 months of discharge. When adjusting for baseline characteristics only (Model 1 in table 2), both income and education had a significant effect on the initiation of statin treatment. When the effects of income and education were estimated simultaneously, the effect of income remained significant, whereas the effect of education became non-significant (Model 2 in table 2). There was a significant interaction between gender and income concerning the initiation of statin treatment among patients aged 30–64 years, such that the income gradient was greater for men than for women. For men, the hazard ratio was 1.33 (95% CI 1.24–1.42) and 1.17 (1.09–1.26) for high and medium income versus low income, and for women the hazard ratio was 1.16 (1.02–1.32) and 1.11 (1.00–1.24) for high and medium income versus low income. There was no interaction between year of AMI and income or education concerning initiation of either treatments, indicating that even though the overall proportion receiving treatment increased during the period, the income and educational gradient were unchanged.

Break in treatment

Concerning break in statin treatment, there was an inverse relation with both income and education for patients 30–64 years old, such that a higher proportion of patients with low than high income or education had a break (figure 1). After adjustment for baseline characteristics only, this effect was significant for both income and education (Model 1 in table 2), whereas after mutual adjustment (Model 2 in table 2), only the effect of income remained significant. Among elderly patients, no significant relationship between income or education and first break in statin treatment was found. Concerning beta-blockers, a higher proportion of patients with high than low income or education had breaks. After adjustment, the effect of education was significant for young patients and the effect of income was significant for elderly patients (table 3).

Re-initiation of treatment after a break

There was no relationship between income or education and re-initiation of statin treatment among younger patients. A higher, though non-significant, proportion of elderly patients with high income or education re-initiated statin treatment. Similarly, for beta-blockers, a higher proportion of patients with low income or education re-initiated treatment, although when simultaneously adjusting for income and education this effect was non-significant (Model 2 in table 3).

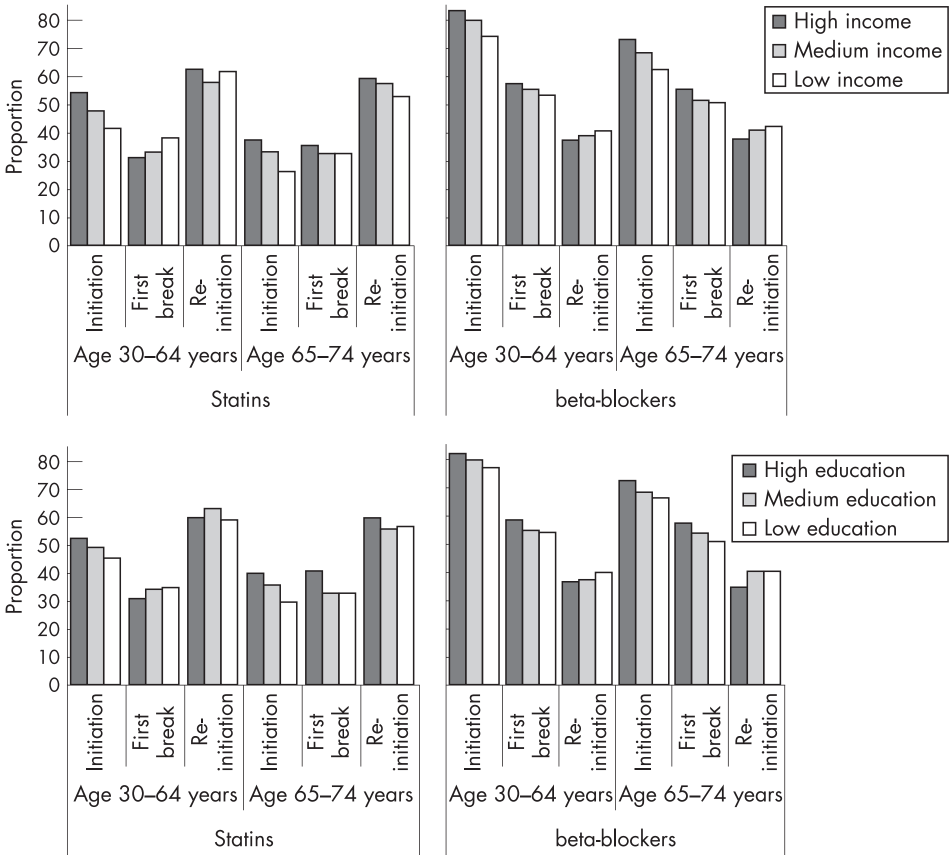

Figure 1 Patients surviving an AMI who claimed a statin or beta-blocker prescription at a pharmacy within 6 months of discharge, having a break of at least 90 days within 4 years of first claim, and re-initiating treatment within 1 year of first break, stratified by age group, income and education (proportions determined by Kaplan–Meier method with censoring for death).

Table 2 Predictors of initiation, first break of at least 90 days and re-initiation after a break of statin treatment among patients aged 30–64 years and 65–74 years who survived a first hospitalisation for acute myocardial infarction in the period 1995–2001

	Statins					
	Initiation		**First break**		**Re-initiation**	
	Model 1	**Model 2**	**Model 1**	**Model 2**	**Model 1**	**Model 2**
	HR (95% CI)	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**
Age 30–64 years						
Income						
High	1.28 (1.21–1.36)	1.27 (1.19–1.35)	0.71 (0.64–0.79)	0.73 (0.66–0.82)	1.03 (0.89–1.19)	1.01 (0.86–1.18)
Medium	1.13 (1.07–1.20)	1.13 (1.06–1.20)	0.82 (0.73–0.91)	0.82 (0.74–0.92)	0.93 (0.80–1.07)	0.91 (0.79–1.06)
Low*	1	1	1	1	1	1
p value†	<0.0001	<0.0001	<0.0001	<0.0001	0.30	0.32
Education						
High	1.12 (1.05–1.20)	1.03 (0.96–1.11)	0.79 (0.69–0.90)	0.87 (0.75–1.00)	1.07 (0.89–1.28)	1.05 (0.86–1.27)
Medium	1.08 (1.02–1.13)	1.04 (0.99–1.09)	0.91 (0.83–1.00)	0.95 (0.87–1.05)	1.13 (1.00–1.27)	1.13 (1.00–1.27)
Low*	1	1	1	1	1	1
p value†	0.0009	0.36	0.002	0.13	0.16	0.16
Age 65–74 years						
Income						
High	1.23 (1.13–1.34)	1.19 (1.08–1.30)	0.96 (0.81–1.15)	0.94 (0.79–1.13)	1.19 (0.94–1.51)	1.16 (0.91–1.49)
Medium	1.12 (1.03–1.22)	1.11 (1.02–1.20)	0.93 (0.78–1.10)	0.93 (0.78–1.10)	1.20 (0.94–1.52)	1.19 (0.94–1.51)
Low*	1	1	1	1	1	1
p value†	<.0001	0.001	0.69	0.69	0.27	0.33
Education						
High	1.24 (1.11–1.38)	1.17 (1.04–1.31)	1.14 (0.93–1.40)	1.15 (0.93–1.43)	1.15 (0.86–1.53)	1.11 (0.82–1.50)
Medium	1.09 (1.01–1.18)	1.06 (0.98–1.15)	0.92 (0.79–1.08)	0.93 (0.80–1.08)	0.99 (0.80–1.22)	0.97 (0.79–1.21)
Low*	1	1	1	1	1	1
p value†	0.0004	0.03	0.15	0.14	0.57	0.70

Model 1: Effects of income and education are estimated separately with adjustment for baseline characteristics.
Model 2: Effects of income and education are estimated simultaneously with adjustment for baseline characteristics.
*Reference
†Test that all categories within variable are equal.

Table 3 Predictors of initiation, first break of at least 90 days and re-initiation after a break of beta-blocker treatment among patients aged 30–64 years and 65–74 years who survived a first hospitalisation for acute myocardial infarction in the period 1995–2001

	Beta-blockers					
	Initiation		First break		Re-initiation	
	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Age 30–64 years						
Income						
High	1.14 (1.09–1.18)	1.12 (1.08–1.17)	1.04 (0.97–1.11)	1.02 (0.96–1.10)	0.89 (0.80–0.99)	0.91 (0.82–1.02)
Medium	1.07 (1.02–1.11)	1.06 (1.02–1.10)	1.01 (0.95–1.08)	1.01 (0.95–1.08)	0.98 (0.88–1.08)	0.99 (0.89–1.09)
Low*	1	1	1	1	1	1
p value†	<0.0001	<0.0001	0.48	0.79	0.06	0.20
Education						
High	1.08 (1.03–1.14)	1.04 (0.99–1.09)	1.09 (1.01–1.17)	1.08 (0.99–1.17)	0.89 (0.78–1.00)	0.92 (0.81–1.05)
Medium	1.04 (1.01–1.08)	1.02 (0.99–1.06)	0.98 (0.93–1.03)	0.97 (0.92–1.03)	0.92 (0.84–1.01)	0.93 (0.85–1.02)
Low*	1	1	1	1	1	1
p value†	0.002	0.24	0.02	0.03	0.07	0.25
Age 65–74 years						
Income						
High	1.18 (1.12–1.24)	1.19 (1.12–1.25)	1.12 (1.03–1.23)	1.11 (1.01–1.22)	0.94 (0.81–1.08)	0.95 (0.82–1.11)
Medium	1.07 (1.01–1.12)	1.07 (1.02–1.13)	1.02 (0.93–1.11)	1.01 (0.93–1.11)	1.05 (0.91–1.21)	1.05 (0.91–1.21)
Low*	1	1	1	1	1	1
p value†	<0.0001	<0.0001	0.02	0.05	0.28	0.42
Education						
High	1.06 (0.98–1.13)	0.98 (0.91–1.06)	1.10 (0.98–1.23)	1.05 (0.93–1.18)	0.86 (0.70–1.05)	0.88 (0.72–1.09)
Medium	0.99 (0.94–1.03)	0.96 (0.92–1.01)	1.05 (0.97–1.13)	1.03 (0.95–1.12)	1.05 (0.93–1.20)	1.06 (0.93–1.21)
Low*	1	1	1	1	1	1
p value†	0.20	0.25	0.23	0.68	0.15	0.21

Model 1: Effects of income and education are estimated separately with adjustment for baseline characteristics.
Model 2: Effects of income and education are estimated simultaneously with adjustment for baseline characteristics.
*Reference
†Test that all categories within variable are equal.

Dosages

Sixty-four per cent of the patients received simvastatin, 20% pravastatin, 12% atorvastatin and 4% other statins. The median dosage of simvastatin, pravastatin and atorvastatin during the observation period was 20 mg (interquartile range (IQR) 13–23 mg), 40 mg (IQR 20–40 mg) and 10 mg (IQR 10–20 mg), respectively. There were no significant differences in statin dosage between income or education groups. Eighty per cent of the patients received metoprolol, 8% atenolol, 6% bisoprolol and 6% other beta-blockers. The median dosage of metoprolol, atenolol and bisoprolol was 85 mg (50–100 mg), 50 mg (29–56 mg) and 5 mg (5–7 mg), respectively. There was only a significant difference in metoprolol dosage between the income groups ($p = 0.02$), such that patients with high, medium and low income received 83 mg (50–100 mg), 85 mg (50–100 mg) and 88 mg (50–100 mg), respectively.

DISCUSSION

In this population-based nationwide study, we have demonstrated a clear gradient between income and initiation of evidence-based preventive treatment post-AMI. Patients with low income less frequently initiate statin as well as beta-blocker treatment. We have shown that the effect of education disappears after adjustment for income, implying that income mediates the effect. Below the age of 65 years, the risk of break in statin treatment was higher among patients with low than high income in the mutual adjusted model. There was no income or educational difference in re-initiation of statin treatment, indicating that even though a higher proportion of low-income patients had a break, they did not resume treatment to a higher degree than high-income patients, thereby demonstrating poorer refill persistency than high-income patients. Interestingly, refill persistency with beta-blockers tended to be better for patients with low than high income or education. Even though it has been repeatedly shown that low SES is associated with lifestyle factors that increase the risk of heart disease,[3] it is less evident how low SES affects healthcare behaviour, such as compliance with heart medication treatment.[20] Recently, it has been concluded that the findings with regard to an association between SES and adherence to treatment are inconsistent.[20] This also applies to our findings that long-term refill persistency is not worse for patients with low SES, as measured by income and education, concerning all preventive medications post-AMI.

The initiation of secondary preventive treatment after an AMI in Denmark is usually provided by the treating hospital and long-term follow-up provided by the general practitioner.[15] The physician is responsible for providing the first prescription initiating treatment, hence physician characteristic may be more important regarding initiation than patient characteristics. Physicians may prescribe fewer necessary drugs to patients of low SES, because they expect poor adherence or because these patients tend to have more co-existing conditions. Ko *et al.*[21] found that prescription of statins diminish as the cardiovascular risk factors increase, and others have found that clinicians who care for patients with chronic diseases become less attentive when managing the necessities of other concurrent conditions due to constraints in time, expertise and preferences.[22] Income was the strongest predictor regarding initiation of treatment, so it might be speculated that the cost of the drug was responsible for the gradient found. If this was the case, we would not expect to find the same gradient for both drugs as beta-blockers were inexpensive during the period investigated, whereas statins were more costly with a price approximately five times that of beta-blockers. The price of the drug prescribed does not appear on the prescription but is only obtainable after ordering the drug at the pharmacy; therefore, it is more likely that patients might repel from reiterating a prescription due to the high cost experienced from earlier dispensing. It seems more likely that physicians less frequently prescribe secondary preventive drugs to patients with lower SES than that patients with lower SES refrain from filling the first prescription due to the price of the drug.

Patient characteristics are important concerning long-term refill persistency and characteristics associated with poor adherence have been found to be presence of psychological problems, cognitive impairment, treatment of asymptomatic disease, lack of belief in benefit in treatment, lack of insight into the illness, cost of medication and co-payment.[20] Physicians may also contribute to poor adherence by failing to adequately explain the benefits and side effects of a medication, not giving consideration to the patient's lifestyle or the cost of medication, and having poor therapeutic relationships with their patients, all of which may have a larger impact on patients with low SES.[20] We found that low-income patients had a higher risk of breaks in statin treatment than high-income patients, whereas the refill persistency with beta-blockers was better among patients with low income. The higher price of statins compared with beta-blockers could be a disincentive for continuous statin use among low-income patients, implying that the cost of the drug could be an important factor regarding long-term refill persistency. Ellis *et al.*[23] also found that increasing the co-payment of statins was associated with decreasing adherence, which agrees with our findings. It is also likely that the willingness of treating an asymptomatic condition may be better in patients with high SES, whereas patients with high SES may be less likely to accept the more common side effects of beta-blockers compared with patients with lower SES, who have been found to be less willing to be involved in the decision-making process and to take responsibility for the treatment choices.[24] Symptom relief by beta-blockers, such as anti-anginal effects and blood-pressure lowering, could be more pronounced among patients with low income or education due to their higher co-morbidity, and this could contribute to the higher persistency with beta-blockers that is found among these patients.

Cardiovascular risk factors, such as high blood pressure and high blood cholesterol levels, are more prevalent among Danish men and women of lower compared with higher SES.[1] Hence, even though guidelines on statin and beta-blocker use post-AMI changed during the study period, nothing indicates that the reduced use of secondary preventive drugs post-AMI among patients with low SES was appropriate. Our study implies that inequity in use of secondary preventive drugs exists in Denmark, and that an effort is needed to ensure that all people, regardless of SES, receive recommended medical treatment post-AMI. This applies both to therapists and public-health policy-makers. Physicians need to be more focused on initiating proper treatment to all groups, and it seems that the higher price of recommended drugs could be a disincentive to taking these drugs for longer periods among patients of low SES.

Comparison with other studies

Few studies have examined socioeconomic differences in use of secondary preventive drugs, and those that have were either cross-sectional,[6–8 11] used contextual measures of SES,[7–10] or investigated selected or non-representative populations.[6 9 10 25] A recent cross-sectional study found a gradient in statin use according to occupation among Danish patients with cardiovascular disease, such that a higher proportion of top managers used statins compared with basic-level workers.[11] The cross-sectional survey EUROASPIRE II found less use of statins and beta-blockers after discharge with cardiovascular disease by patients with a short education than by those with a longer education.[6] Wei *et al.* found no association between a contextual socioeconomic deprivation score and adherence to either statins or beta-blockers in a small sample of post-AMI patients in Scotland.[9 10] Many countries have implemented specific systems to counter the potential negative effects of drug payment, and in most European countries more than 50% of out-patient prescriptions are reimbursed from public funds,[26] and our results on overall refill persistency to these drugs are similar to those found in other countries.[9 10 27 28] Our study was confined to AMI patients in Denmark. Although the extent to which our findings are generalisable to other jurisdictions and disease settings is unknown, our study is comprehensive, consisting of all AMI patients of 30–74 years old in Denmark. Therefore, we believe that our findings would be generalisable to other jurisdictions that have similar drug-reimbursement policies to Denmark.

Strengths and weaknesses of the study

The main strength of this study is the population-based design, with complete follow-up over several years. This approach allows study of a real population representing all socioeconomic groups, irrespective of their position in the labour market, the health insurance system or the admitting hospital, thereby avoiding selection bias. By using information on both income and education at the individual level, we avoided the potential misclassification that is inherent in the use of contextual measures of SES. Patients with low income may be more likely to live in deprived areas, where the quality of care may be less optimal but – as we adjusted for area of living – this effect is unlikely to explain our results. The validity of AMI as the primary diagnosis in the National Patient Registry is good; the predictive value is 94% (80% being definite and 14% possible AMI), with a sensitivity of 80% (93% for non-fatal and 56% for fatal AMI).[29] The national prescription register relies on data collected from pharmacies in a homogeneous, automatic fashion nationwide, and reimbursement to pharmacies is linked to reporting through the register. The validity of the register has been found to be good;[30] furthermore, one of the most reliable objective measures of adherence in large patient groups is failure to refill a prescription.[20 31] The weakness of the study is that the registries do not contain information about adverse reactions or allergies, which might explain why treatment was not initiated or was terminated early. In addition, we do not know how many patients started treatment in hospital and discontinued after discharge, and we were unable to differentiate between non-adherence by patients and non-prescription by physicians. We did not have information on whether individuals were receiving supervised care or living in supervised care facilities, which would probably yield better adherence. This would only apply to a small proportion of people aged 30–64 years; hence, in our opinion, accounting for this would not affect our results for this age group—it would apply to a higher proportion of patients aged 65–74 years. Furthermore, some of the challenges of characterising the SES of elderly people are that retirement affects income and that older persons are more likely to have received less education.[32] Therefore, our results concerning patients above 65 years of age should be interpreted with more caution than the results for patients below the age of 65 years, as a more precise classification of SES can be expected in the younger age groups.

CONCLUSION

In Denmark, a country with a healthcare system built on the Nordic welfare model, post-AMI patients with low income less frequently receive secondary preventive treatment with statins and beta-blockers. Long-term refill persistency with statins was lower for patients with low income than high income, whereas concerning beta-blockers, long-term refill persistency was better for patients with low than high income or education. Low SES is associated with less frequent initiation of secondary

What is already known on this subject

Patients with low socioeconomic status have a high prevalence of cardiovascular risk factors and high mortality from heart disease. Secondary prevention after acute myocardial infarction (AMI) with evidence-based therapy is important in this group of patients. The importance of patient factors, such as education and income, to the treatment after AMI needs to be studied further to improve the understanding of the mechanisms leading to social inequality in the prognosis after AMI.

What this study adds

Patients with low income suffering an AMI less frequently receive secondary preventive treatment with statins and beta-blockers. Long-term refill persistency with statins was lower for patients with low than high income, whereas concerning beta-blockers, long-term refill persistency was better for patients with low than high income or education.

preventive medication post-AMI, but is not by itself associated with poorer long-term refill persistency.

ACKNOWLEDGEMENTS
The study was supported by the Danish Heart Foundation, grant no: 05-10-B19-A699-22244F and by Denmark's Ministry of Interior and Health.

CONTRIBUTORS

Jeppe N. Rasmussen was responsible for designing the study, analysing and interpreting data, drafting the manuscript and final approval of the version to be published. He also acts as guarantor.
Søren Rasmussen was responsible for collecting data, analysing and interpreting data and critically revising the manuscript.
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The study sponsors had no involvement in study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the article for publication.

Competing interests: Several of the authors have given industry-sponsored lectures and taken part in clinical trials sponsored by the industry, but there are no specific conflicts of interest related to the current article.

Ethical approval: The project did not require approval by the regional committee on biomedical research ethics.

REFERENCES

1 **Osler M**, Gerdes LU, Davidsen M, *et al.* Socioeconomic status and trends in risk factors for cardiovascular diseases in the Danish MONICA population, 1982–1992. *J Epidemiol Community Health* 2000;**54**:108–13.
2 **Rasmussen JN**, Rasmussen S, Gislason GH, *et al.* Mortality after acute myocardial infarction according to income and education. *J Epidemiol Community Health* 2006;**60**:351–56.
3 **Kaplan GA**, Keil JE. Socioeconomic factors and cardiovascular disease: a review of the literature. *Circulation* 1993;**88**:1973–98.
4 **Alter DA**, Naylor CD, Austin P, *et al.* Effects of socioeconomic status on access to invasive cardiac procedures and on mortality after acute myocardial infarction. *N Engl J Med* 1999;**341**:1359–67.
5 **Salomaa V**, Niemela M, Miettinen H, *et al.* Relationship of socioeconomic status to the incidence and prehospital, 28-day, and 1-year mortality rates of acute coronary events in the FINMONICA Myocardial Infarction Register Study. *Circulation* 2000;**101**:1913–8.
6 **Mayer O Jr**, Simon J, Heidrich J, *et al.* Educational level and risk profile of cardiac patients in the EUROASPIRE II substudy. *J Epidemiol Community Health* 2004;**58**:47–52.
7 **Packham C**, Robinson J, Morris J, *et al.* Statin prescribing in Nottingham general practices: a cross-sectional study. *J Public Health* 1999;**21**:60–4.
8 **Stocks NP**, Ryan P, McElroy H, *et al.* Statin prescribing in Australia: socioeconomic and sex differences. A cross-sectional study. *Med J Aust* 2004;**180**:229–31.
9 **Wei L**, Wang J, Thompson P, *et al.* Adherence to statin treatment and readmission of patients after myocardial infarction: a six year follow up study. *Heart* 2002;**88**:229–33.
10 **Wei L**, Flynn R, Murray GD, *et al.* Use and adherence to beta-blockers for secondary prevention of myocardial infarction: who is not getting the treatment? *Pharmacoepidemiol Drug Saf* 2004;**13**:761–6.
11 **Thomsen RW**, Johnsen SP, Olesen AV, *et al.* Socioeconomic gradient in use of statins among Danish patients: population-based cross-sectional study. *Br J Clin Pharmacol* 2005;**60**:534–42.
12 **Geyer S**, Hemstrom O, Peter R, *et al.* Education, income, and occupational class cannot be used interchangeably in social epidemiology. Empirical evidence against a common practice. *J Epidemiol Community Health* 2006;**60**:804–10.
13 **Lahelma E**, Martikainen P, Laaksonen M, *et al.* Pathways between socioeconomic determinants of health. *J Epidemiol Community Health* 2004;**58**:327–32.
14 **Christiansen T**. Organization and financing of the Danish health care system. *Health Policy* 2002;**59**:107–18.
15 **Zwisler AD**, Traeden UI, Videbaek J, *et al.* Cardiac rehabilitation services in Denmark: still room for expansion. *Scand J Public Health* 2005;**33**:376–83.
16 **Andersen TF**, Madsen M, Jorgensen J, *et al.* The Danish National Hospital Register. A valuable source of data for modern health sciences. *Dan Med Bull* 1999;**46**:263–8.
17 **Yarcheski A**, Mahon NE, Yarcheski TJ, *et al.* A meta-analysis of predictors of positive health practices. *J Nurs Scholarsh* 2004;**36**:102–8.
18 **Statistics Denmark**. Containing detailed statistical information on the Danish society. http://www.dst.dk/HomeUK.aspx25-5-, 2006.
19 **Gislason GH**, Rasmussen JN, Abildstrom SZ, *et al.* Long-term compliance with beta-blockers, angiotensin-converting enzyme inhibitors, and statins after acute myocardial infarction. *Eur Heart J* 2006;**27**:1153–8.
20 **Osterberg L**, Blaschke T. Adherence to medication. *N Engl J Med* 2005;**353**:487–97.
21 **Ko DT**, Mamdani M, Alter DA. Lipid-lowering therapy with statins in high-risk elderly patients: The treatment-risk paradox. *JAMA* 2004;**291**:1864–70.
22 **Redelmeier DA**, Tan SH, Booth GL. The treatment of unrelated disorders in patients with chronic medical diseases. *N Engl J Med* 1998;**338**:1516–20.
23 **Ellis JJ**, Erickson SR, Stevenson JG, *et al.* Suboptimal statin adherence and discontinuation in primary and secondary prevention populations. *J Gen Intern Med* 2004;**19**:638–45.
24 **Vick S**, Scott A. Agency in health care. Examining patients' preferences for attributes of the doctor-patient relationship. *J Health Econ* 1998;**17**:587–605.
25 **Avorn J**, Monette J, Lacour A, *et al.* Persistence of use of lipid-lowering medications: a cross-national study. *JAMA* 1998;**279**:1458–62.
26 **Ess SM**, Schneeweiss S, Szucs TD. European healthcare policies for controlling drug expenditure. *Pharmacoeconomics* 2003;**21**:89–103.
27 **Jackevicius CA**, Mamdani M, Tu JV. Adherence with statin therapy in elderly patients with and without acute coronary syndromes. *JAMA* 2002;**288**:462–7.
28 **Benner JS**, Glynn RJ, Mogun H, *et al.* Long-term persistence in use of statin therapy in elderly patients. *JAMA* 2002;**288**:455–61.
29 **Madsen M**, Davidsen M, Rasmussen S, *et al.* The validity of the diagnosis of acute myocardial infarction in routine statistics: A comparison of mortality and hospital discharge data with the Danish MONICA registry. *J Clin Epidemiol* 2003;**56**:124–30.
30 **Gaist D**, Sorensen HT, Hallas J. The Danish prescription registries. *Dan Med Bull* 1997;**44**:445–8.
31 **Steiner JF**, Prochazka AV. The assessment of refill compliance using pharmacy records: methods, validity, and applications. *J Clin Epidemiol* 1997;**50**:105–16.
32 **House JS**, Lepkowski JM, Kinney AM, *et al.* The social stratification of aging and health. *J Health Soc Behav* 1994;**35**:213–34.