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This is an accepted version of a paper published in *European Journal of Clinical Pharmacology*. This paper has been peer-reviewed but does not include the final publisher proof-corrections or journal pagination.

Citation for the published paper:

Sjölander, M., Eriksson, M., Glader, E. (2012)

"Social stratification in the dissemination of statins after stroke in Sweden"

European Journal of Clinical Pharmacology

URL: <http://dx.doi.org/10.1007/s00228-012-1454-8>

Access to the published version may require subscription.

Permanent link to this version:

<http://urn.kb.se/resolve?urn=urn:nbn:se:umu:diva-61918>

<http://umu.diva-portal.org>

Title: Social stratification in the dissemination of statins after stroke in Sweden

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Keywords: brain infarction, secondary prevention, statins, socioeconomic status, ethnic groups

Word count: 4857

Abstract

Purpose: Since 2005, statins have been recommended to patients with ischemic stroke. The objective of this study was to analyse how statin treatment has been disseminated in different patient groups (age, sex, socioeconomic status and country of birth) in Sweden 2004–2009.

Methods: The Swedish Stroke Register, Riks-Stroke, has been linked to the Longitudinal Integration Database for Health Insurance and Labour Market Studies. Approximately 85% of stroke patients in Sweden are included in Riks-Stroke. Odds ratios for statin prescribing were calculated using a multivariable logistic regression model including age, sex, socioeconomic status and risk factors.

Results: 108 950 ischemic stroke patients were discharged alive from hospital. The proportion with statins at discharge increased from 32.9% in 2004 to 60.1% in 2009. Patients with secondary school or university education had slightly higher odds (OR 1.07, 95% CI 1.04–1.11 and OR 1.05, 95% CI 1.01–1.10 respectively) compared with patients with primary school education. Patients on a high income were prescribed more statins compared with low income (OR 1.24, 95% CI 1.19–1.28). Compared with patients born in Sweden, patients born in other countries were prescribed more statins (OR 1.07, 95% CI 1.01–1.14, OR 1.31, 95% CI 1.22–1.40 and OR 1.20, 95% CI 1.08–1.34 respectively).

Conclusions: Statin prescribing after ischemic stroke has increased from 2004 to 2009.

Results also show a social stratification in the dissemination of statins. Patients with higher income and education received more statins, and patients born in Sweden received less statins.

Introduction

Studies from the 1990s provide evidence that statins (HMG-CoA reductase inhibitors) reduce the risk of stroke in patients with coronary heart disease (CHD) and in patients at high risk of cardiovascular disease [1-3]. In 2002, results from The Heart Protection Study showed that statin treatment for patients with a previous stroke reduce the risk of subsequent major vascular events [4]. The SPARCL study concludes that statins also reduce the overall incidence of strokes and of cardiovascular events in patients with a recent stroke or TIA without previous CHD [5].

A meta-analysis shows no evidence of differences in treatment effects across patient groups [6]. An updated Cochrane Review, first published in 2002, recommend that all ischemic stroke or TIA patients should receive statins [7]. The Swedish stroke guidelines also recommend secondary preventive treatment with statins in ischemic stroke patients, irrespective of risk-factor level [8].

The objective of health care in Sweden is, according to the Swedish Health and Medical Services Act of 1982, to provide good health and good care on equal terms to the whole population [9]. Generally, both health and health care in Sweden are good, but data still shows health and health-care related differences between different groups in society [10].

Socioeconomic status, often indicated by measures of income, education and occupation, is often used to measure an individual's social position in society. Ethnicity is also a source of status ranking. There is a structure of socioeconomic inequality in society, which is strongly related to health, disease and death [11, 12]. This relation between socioeconomic status and health has been proven not only for the poorest patients, but there is a social gradient in health [13]. Two studies from Sweden show a higher stroke incidence and stroke mortality in patients with lower socioeconomic status [14, 15]. The health of populations has been more

strongly affected by social and economic welfare than by health care. Still, resources for health care have shown to vary inversely with needs, what is sometimes referred to as the inverse care law [16].

Data from Riks-Stroke, the Swedish Stroke Register, and data from Statistics Sweden is used to explore how statin treatment after stroke has disseminated and been implemented in Swedish stroke care.

The main hypothesis is that there are differences in prescribing of statins at discharge from hospital between the patient groups (age, sex, socioeconomic status and country of birth) and that the rate at which statin prescribing after stroke has been implemented varies between patient groups.

Materials and Methods

This hospital-based study includes patients registered in Riks-Stroke [17]. Riks-Stroke was established in 1994, and it covers all hospitals in Sweden admitting patients with acute stroke since 1998. Basic patient characteristics, stroke risk factors and outcome variables, including drugs prescribed at discharge for secondary prevention, have been recorded in the register by all hospitals admitting acute stroke patients. The coverage of the register was, during the study period, estimated to be approximately 85% [18].

Data from Riks-Stroke has, through the personal identification number, been merged with data from the Longitudinal Integration Database for Health Insurance and Labour Market Studies (LISA), Statistics Sweden, in order to retrieve individualised information on patients' highest level of education, income and country of birth [19].

Patient selection

Included in this study were adult patients, from the age of 18, who had had an ischemic stroke (ICD-10 I63) between 1 April 2004 and 31 December 2009 and who were registered in Riks-Stroke (statin treatment after stroke has been registered in the same way since 1 April 2004).

Variable definitions

The main outcome variable was prescribing of statins at discharge from hospital, measured as a proportion of patients with a statin prescription registered in Riks-Stroke.

Patients' highest level of education and disposable income, taken from the LISA database, were used as indicators of socioeconomic status. Education was grouped into primary school (up to nine years in compulsory school) (reference category), secondary school (the upper levels of comprehensive school) or university level. Disposable income was individualised from family income, registered for the calendar year before the year of the stroke, and

recalculated using the Consumer Price Index for 2009. Income was grouped into tertiles: low income (reference category), medium income and high income.

Country of birth was grouped into Sweden (reference category), Nordic countries (except Sweden), Europe (except the Nordic countries) and other countries.

The age groups used were 18–59 (reference category), 60–69, 70–79 and 80+. Level of consciousness was categorised as ‘Alert’ (reference category), ‘Drowsy’ and ‘Unconscious’.

Variables for dependency in Activities of Daily Living (ADL), smoking, history of stroke, atrial fibrillation, history of diabetes and antihypertensive medication at the onset of stroke, were categorised as either ‘Yes’ or ‘No’ with ‘No’ as reference category.

The project was approved by the Ethical Review Board at Umeå University.

Statistical analyses

The proportion of patients who received statin treatment after stroke have been presented for groups defined by year of stroke onset, age group, sex, socioeconomic status and country of birth. Age-adjusted logistic regression was used for group comparisons. Age was included as a categorical variable (age groups), and the results have been presented as odds ratios (OR) with 95% confidence intervals (CI).

Multiple logistic regression was used to simultaneously test the effect of several factors on the probability of receiving statin treatment. Tested factors were selected based on expected clinical relevance. Variables included from the stroke register were age, sex, smoking, ADL-dependency, history of stroke, atrial fibrillation, history of diabetes, antihypertensive medication at onset of stroke and level of consciousness on admission. For variables with more than 10% missing values, a ‘missing’ category was included in logistic regression models, but OR were not presented in the results.

The rate at which statin treatment was implemented in different groups has mainly been presented graphically by plotting the change in proportion over time. In addition, the two-way interaction terms (year-by-age-group, year-by-sex, year-by-education, year-by-income, year-by-country-of-birth) were included in the multivariable model to test if there was a difference in the rate of dissemination.

Statistical analyses were performed using SPSS 19.0.0.1.

Results

From 1 April 2004 until 31 December 2009, 108 950 patients (from the age of 18) who had had an ischemic stroke were registered in the Swedish Stroke Register. Of these, 108 015 had valid information on prescribing of statins at discharge from hospital. The proportion of patients discharged from hospital with a statin prescription increased from 32.9% in 2004 to 60.1% in 2009 (Table). The proportions of statin treatment over time are presented graphically for different patient groups in figures 1–5.

The age group with the largest proportion with a statin prescription were patients aged 60–69, with 67.1%, and the age group with the smallest proportion were patients aged 80+, with 27.2% (OR 1.26, 95% CI 1.20–1.33 and OR 0.35, 95% CI 0.33–0.37 respectively) (Table). Patients aged 70–79 had the highest increase in prescribing over time compared with patients aged 18–59 ($p < 0.001$) (Figure 1). Since the level of statin prescribing was so much lower in the 80+ age group, figures 2–5 have been separated into two panels with patients aged 18–79 years old in one panel and patients aged 80+ years old in the other.

More men than women were prescribed statins, 52.1% compared with 40.5% (OR 0.88, 95% CI 0.85–0.90) (Table). The relative difference in prescribing between men and women decreased over time ($p = 0.038$), although the absolute difference remained at a similar level (Figure 2).

Socioeconomic status

A larger proportion of patients with a high level of education were prescribed statins (Table). Among patients with a university education, 57.3% were prescribed a statin, in secondary school the figure was 55.7% and in patients with a primary school education 48.0% received a statin. The adjusted odds were slightly higher for patients with secondary or university education (OR 1.07, 95% CI 1.04–1.11 and OR 1.05, 95% CI 1.01–1.10 respectively)

compared with primary school education, but the difference in prescribing between secondary school education and primary school decreased over time ($p=0.032$) (Figure 3). More patients (56.6%) in the highest income tertile were prescribed statins compared with patients with the lowest income (40.1%) (OR 1.24, 95% CI 1.19–1.28), but there was no difference between low and medium income (OR 1.02, 95% CI 0.99–1.06) (Table 1). No interactions over time were found for income ($p=0.343$) (Figure 4).

Country of birth

Data showed different proportions of statin use after stroke when considering patients' country of birth. Patients born in Sweden had the lowest proportion statin prescribing 45.6%, and patients born in Europe had the highest, 54.9% (Table). When adjusting for patient-related factors, the odds of statin prescription were higher when born in the Nordic countries (OR 1.07, 95% CI 1.01–1.14), Europe (OR 1.31, 95% CI 1.22–1.40) and in countries outside of Europe (OR 1.20, 95% CI 1.08–1.34) compared with Sweden. Prescribing to patients born outside of Europe increased more over time compared with prescribing to patients born in Sweden ($p=0.004$) (Figure 5).

Excluding individual risk factors (history of stroke, smoking, atrial fibrillation, diabetes, antihypertensive medication) in the multivariable logistic regression had no substantial affect on the OR of remaining variables (data not presented).

Missing data

For the main outcome, prescribing of statins to patients being discharged from hospital, 0.9% of patients had missing data. The variables with highest proportion of missing data were education (15.2%) and smoking (10.0%). For other variables, the highest proportion of missing data was 1.3% (antihypertensive treatment).

Discussion

This analysis of data from more than 100 000 Swedish stroke patients showed that prescribing of statins after stroke has increased in all studied patient groups from 2004 to 2009. Patients over the age of 80 were less likely to receive statins for secondary prevention compared with other age groups. This has also been found in other studies [20, 21]. In the national guidelines, there is no upper age limit for patients to be prescribed statins after stroke. Discussions have taken place about benefits and risks, cost-effectiveness and problems with polypharmacy in the highest age groups [22]. Scientific data on stroke prevention with statins for patients over 80 years of age was limited at the beginning of the study period because of the exclusion or under-representation of this patient group in most clinical trials. More recent reviews, however, conclude that although the evidence is stronger for secondary prevention with statins after CHD than after stroke, the recommendation of statin treatment after ischemic stroke should be applied also to the very elderly [23, 24]. Data showed that the proportion prescribed statins in the 80+ group has been steadily increasing from 2004 to 2009.

The differences between men and women are known from prior studies on data from this register [25-27]. The difference persisted after controlling for the fact the women were, on average, 4.4 years older when they suffered a stroke. However, this study also showed that differences in prescribing between men and women decreased over time.

Both higher education and higher income were associated with higher prescribing of statins, indicating more statins were given to patients with higher socioeconomic status. A Swedish study on drugs bought by patients with a myocardial infarction (MI) also showed slightly higher use of statins in patients with the highest level of education compared with the lowest level of education [28]. Another Swedish study on MI showed that a larger proportion of high-income patients collected lipid-lowering drugs from pharmacies after being discharged

from hospital compared with low-income patients [29]. Socioeconomic differences are not unique to Swedish stroke care. In an international review the evidence is strongest for mortality and incidence of stroke but there is evidence also for outcome and stroke severity [30]. Differences in risk factors, and accordingly prevention of risk factors, are probably part of a complex mechanism for socioeconomic differences in stroke.

Variables used as indicators of socioeconomic status are often based on income, education and occupation. To use occupation seemed less appropriate in this case since the majority of stroke patients would be classified as retired. There is often a correlation between different indicators of socioeconomic status. In this case we have controlled for both education and income. Correlation between education and income has been tested (Spearman's Rho) and the results showed a low correlation ($r=0.091$, $p<0.001$).

As previously mentioned, a Swedish study on patients with MI showed lower levels of statin use in patients born outside Sweden [28]. This is contrary to our findings in stroke patients. The study on MI is, however, based on sales data, and our study is based on prescription data. There might be differences between patient groups based not only on what drugs are prescribed, but also on what drugs patients decide to purchase. Even though statins in Sweden are subsidized and included in the high-cost-threshold, they are not for free (Swedish citizens pay a total maximum equivalent to 260 EUR per 12 month period for subsidized drugs). Therefore, patients' affordability is more likely to be a problem when considering if patients do not purchase drugs compared with whether drugs are prescribed. In this study, the focus has been on prescribing of drugs as a first step in how treatment is implemented. The main outcome variable was prescribing of statins at discharge from hospital. Whether patients purchase and actually use their prescribed drugs is of course an important questions but beyond the scope of this study.

Differences in prescribing have, in some cases, been shown to relate to patients' expectations, but also to prescribers' perceptions of patients' expectations [31]. Prescribing of drugs has also correlated with patients' tendencies to seek health care [32]. Both patients' expectations of receiving a prescription and patients' tendencies to seek health care might vary between patient groups, but this is not possible to analyse with available data. In this study, all patients have, however, been treated in a hospital. Age distribution and risk-factor profile differs between different ethnic groups – those born in Sweden are older and have more risk factors (data not shown), but the differences in prescribing of statins remain after adjusting for this. To fully understand the reasons for the ethnic differences seen in this study, future studies with more targeted data collection are needed.

This study provides real-life data on statin prescribing and it includes data on approximately 85% of all stroke patients in Sweden. Patients have been included from all hospitals that treated acute stroke patients. An analysis of data quality in Riks-Stroke has shown high validity for clinical data [17]. In many studies on differences in use of drugs, aggregated data has been used as indicators of socioeconomic status, e.g. data at regional or health service level [33, 34]. In this study, the association between use of statins and socioeconomic status has been analysed on an individual level.

A national study of this size has high power to detect small differences, hence clinical relevance has to be considered in addition to statistical significance. However, this study shows results with clinical implications. For example, the chance of being prescribed statins after stroke is one third if you are older than 80 years. If you belong to a high-income group you have a 25% increased chance of receiving statins. To be able to assure a good and equal stroke care for all stroke patients, the differences have to be identified.

Health has been shown to be unequally distributed in society. Living conditions, environmental conditions as well as structures in society all affect public health. As long as there are differences in society there will be differences in health, and health care cannot solve this problem, but it should not increase the disparities. The National Guidelines for Stroke Care are based on horizontal equality: equal cases should be treated equally, but data in this study shows lower levels of prescribing in groups with lower incomes and lower levels of education, groups with higher stroke incidence and stroke mortality. Treating everyone exactly the same, irrespective of for example risk level, does not necessarily yield equity, but groups with higher risks should not receive less preventive treatment.

Study limitations

This is an analysis of prescribing patterns, not of what drugs are actually used by the patients. Patients might not start a treatment that has been prescribed or they might end a prescribed treatment. Differences in adherence to treatment between different patient groups could generate differences in the actual use of statins which are not equal to the differences in prescribing.

Whether or not a patient is prescribed preventive drugs has been shown to be related to the practice of individual prescribers [35]. Including prescribers in this analysis was not possible since the stroke register does not include data on prescribers.

Data quality in Riks-Stroke is continuously validated and has been shown high. However, those patients missing are more often elderly and affected by more severe strokes, which could have had impact on the results in this study.

The analysis have controlled for several factors including some patient characteristics and risk factors. One risk factor not included was a measurement of blood lipids. Data on cardiovascular co morbidities, e.g. previous MI, was not available.

Summary/Conclusion

Statin prescribing after ischemic stroke has increased in Sweden from 2004 to 2009. Results also show a social stratification in the dissemination of statins. Patients with higher incomes and higher levels of education were prescribed more statins compared with those on low incomes and with a low level of education, and patients born in Sweden were prescribed less statins compared with patients born in other countries.

Acknowledgments: The authors would like to thank Riks-Stroke for providing the database and Professor Rune Dahlqvist for his comments on the manuscript.

Sources of funding: Riks-Stroke, the Swedish Stroke Register, is funded by the National Board of Health and Welfare and the Swedish Association of Local Authorities and Regions. This study was supported by the VINNVÅRD research programme, the Swedish Council for Working Life and Social Research (FAS), and the Swedish Research Council.

Disclosures: The authors declare that they have no conflict of interest.

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Figure Captions

Fig. 1 Proportion of patients treated with statins after ischemic stroke in different age groups, data from 2004 to 2009

Fig. 2 Proportion of men and women treated with statins after ischemic stroke, data from 2004 to 2009, and patients 18–79 and 80+ years old in separate panels

Fig. 3 Proportion of patients treated with statins after ischemic stroke in groups with different levels of education, data from 2004 to 2009, and patients 18–79 and 80+ years old in separate panels

Fig. 4 Proportion of patients treated with statins after ischemic stroke in groups with different income levels, data from 2004 to 2009, and patients 18–79 and 80+ years old in separate panels

Fig. 5 Proportion of patients treated with statins after ischemic stroke in groups born in different countries, data from 2004 to 2009, and patients 18–79 and 80+ years old in separate panels

Tables

	Statin treatment				
				Multiple logistic	
	Valid			Age adjusted	regression
	observa		Proportion	odds ratios	odds ratios
	tions	Frequency	(%)	(95% CI)	(95% CI)
Year of stroke onset					
2004	13 706	4 503	32.9	Ref	Ref
2005	19 256	7 259	37.7	1.28 (1.22–1.34)	1.25 (1.18–1.31)
2006	18 503	7 826	42.3	1.60 (1.53–1.68)	1.54 (1.46–1.62)
2007	18 536	8 947	48.3	2.13 (2.03–2.24)	2.04 (1.94–2.15)
2008	18 819	10 145	53.9	2.68 (2.55–2.81)	2.52 (2.40–2.66)
2009	19 195	11 529	60.1	3.58 (3.41–3.76)	3.13 (2.97–3.30)
Age group					
18–59	10 663	6 519	61.1		Ref
60–69	18 952	12 716	67.1		1.26 (1.20–1.33)
70–79	32 357	18 448	57.0		0.93 (0.88–0.98)
80+	46 043	12 526	27.2		0.35 (0.33–0.37)
Sex					
Men	55 472	28 907	52.1	Ref	Ref
Women	52 543	21 302	40.5	0.80 (0.78–0.82)	0.88 (0.85–0.90)
Education					
Primary school	47 263	22 685	48.0	Ref	Ref
Secondary school	31 786	17 714	55.7	1.14 (1.11–1.18)	1.07 (1.04–1.11)
University	12 550	7 194	57.3	1.17 (1.12–1.22)	1.05 (1.01–1.10)

Income

Low	35 764	14 341	40.1	Ref	Ref
Medium	35 806	15 290	42.7	1.12 (1.09–1.16)	1.02 (0.99–1.06)
High	35 850	20 290	56.6	1.50 (1.46–1.55)	1.24 (1.19–1.28)

Country of birth

Sweden	95 706	43 609	45.6	Ref	Ref
Nordic countries*	5 720	3 013	52.7	1.07 (1.01–1.13)	1.07 (1.01–1.14)
Europe†	4 399	2 417	54.9	1.20 (1.12–1.28)	1.31 (1.22–1.40)
Other countries	1 800	987	54.8	1.04 (0.94–1.15)	1.20 (1.08–1.34)

Smoking

No	81 957	37 054	45.2	Ref	Ref
Yes	15 242	9 029	59.2	1.07 (1.03–1.11)	1.09 (1.05–1.13)

Dependent in ADL

No	96 566	47 434	49.1	Ref	Ref
Yes	10 323	2 493	24.1	0.45 (0.43–0.48)	0.45 (0.42–0.47)

History of stroke

No	78 930	36 920	46.8	Ref	Ref
Yes	28 188	12 941	45.9	1.11 (1.08–1.15)	1.19 (1.16–1.23)

Atrial fibrillation

No	77 414	39 399	50.9	Ref	Ref
Yes	29 592	10 331	34.9	0.70 (0.68–0.72)	0.68 (0.66–0.71)

History of diabetes

No	85 151	37 923	44.5	Ref	Ref
Yes	22 366	12 033	53.8	1.38 (1.34–1.42)	1.35 (1.31–1.40)

Antihypertensive

medication					
No	54 324	19 397	42.8	Ref	Ref
Yes	61 553	30 331	49.3	1.52 (1.48–1.56)	1.47 (1.42–1.51)
Level of consciousness					
at admission					
Alert	96 083	46 675	48.6	Ref	Ref
Drowsy	9 394	2 861	30.5	0.53 (0.51–0.56)	0.61 (0.58–0.64)
Unconscious	1 682	352	20.9	0.31 (0.27–0.35)	0.34 (0.30–0.39)

*Nordic countries (except Sweden)

†Europe (except the Nordic countries)

Table. Frequencies and proportions of statin prescribing in subgroups of ischemic stroke patients

Figures

Figure 1

Figure 2

Figure 3

Figure 4

Figure 5