Socioeconomic Inequalities in the Prescription of Oral Anticoagulants in Stroke Patients With Atrial Fibrillation

Maria Sjölander, PhD; Marie Eriksson, PhD; Kjell Asplund, MD, PhD; Bo Norrving, MD, PhD; Eva-Lotta Glader, MD, PhD

Background and Purpose—Oral anticoagulants (OACs) are effective against ischemic stroke in patients with atrial fibrillation. Our aim was to investigate differences in the prescribing of OACs after ischemic stroke in patients with atrial fibrillation based on age, sex, country of birth, and socioeconomic status.

Methods—Patients with first-ever ischemic stroke and atrial fibrillation without OAC treatment were included from the Swedish stroke register from 2009 to 2012. The outcome was OAC prescribed at discharge. Income, education, country of birth, and risk factors were obtained from official registers. Risk factors and health status were controlled for in multivariable logistic regression.

Results—Of 12,088 stroke patients, 36.3% were prescribed an OAC. Prescribing was less common with older age and, in patients born in other Nordic countries (odds ratio [OR], 0.82; 95% confidence interval [CI], 0.68–0.98) or countries outside of Europe (OR, 0.65; 95% CI, 0.42–0.99) compared with those born in Sweden. University education (OR, 1.20; 95% CI, 1.05–1.36) and highest income (OR, 1.19; 95% CI, 1.06–1.33) were associated with higher levels of OAC prescribing compared with those with primary school education or lowest income level.

Conclusion—Differences by age, income, education, and country of birth were found in the prescribing of OACs after stroke. Differences were not explained by common risk factors. This indicates socioeconomic inequalities in the prescribing of preventive treatment after stroke. (Stroke. 2015;46:2220-2225. DOI: 10.1161/STROKEAHA.115.009718.)

Key Words: anticoagulants — atrial fibrillation — drug prescriptions — secondary prevention — socioeconomic factors

Atrial fibrillation (AF) is an independent risk factor for ischemic stroke and increases an individual’s risk by ≤5 times.1 According to a recently published study from Sweden, 33.4% of patients who had an ischemic stroke in 2005 to 2010 had a diagnosis of AF.2 The prevalence of AF increases with age and is higher among men, but AF is a stronger relative risk factor in women.

Oral anticoagulants (OACs) have shown good preventive effects against stroke and embolism in patients with AF3,4 and are recommended for secondary prevention according to national and international guidelines.5–7 Warfarin has been the main OAC, but new drugs were introduced in 2011 to 2012, including dabigatran, rivaroxaban, and apixaban.

Antiplatelet drugs (APDs) are not recommended for prevention of ischemic stroke in patients with AF. A Cochrane review showed that OACs are better than APDs in preventing stroke in patients with AF.8 The Birmingham Atrial Fibrillation Treatment of the Aged (BAFTA) study showed that warfarin is also better than acetylsalicylic acid in preventing thromboembolic stroke in patients >75 years of age without increasing the risk of bleeding.9 According to the 2009 Swedish guidelines, patients with AF should not be treated with APDs unless there is a contraindication for OACs.5

Although the exact proportions varied in different geographical areas, patient groups, and types of data, the results from previous studies on the use of OACs in patients with AF showed that OACs are generally underused in stroke prevention.2,10–13 Reasons for not prescribing OACs in high-risk patients include previous bleeding events, patient refusal, interactions with other drugs, poor patient adherence, fall risk, and dementia.13,14

All patients should, according to Swedish law and national guidelines, be treated on equal terms. The use of OACs should, therefore, be based on individual risk and expected benefit, but previous studies have shown inequalities in the use of drugs in general5,16 and of OACs in particular.14,17

The objective of this nationwide study was to investigate differences between patient groups in the prescribing of OACs after ischemic stroke in patients with AF. Patient groups were based on age, sex, country of birth, and socioeconomic status measured as education and income level.

Methods

Data from 3 national registers were used. Information from Riksstroke, the Swedish stroke register, was through the Swedish personal identification number linked to data from the Longitudinal

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2220
Integration Database for Health Insurance and Labor Market Studies (LISA) and the Swedish National Inpatient Register (IPR).18–20

Registers
Riksstroke is based on voluntary participation of stroke patients treated in all Swedish hospitals that admit patients with acute stroke. According to the Riksstroke annual reports of 2009 to 2012, the estimated coverage during this time period was >90%. Riksstroke contains information about stroke events, and information is collected from before the event, from the hospital stay (including discharge), and from follow-up questionnaires. Clinical data in Riksstroke have shown high consistency with medical records.21

The LISA database at Statistics Sweden contains individualized information on all Swedish citizens from 16 years of age. Information includes, for example, education, income, and country of birth, and the database is updated yearly.

The IPR includes information on primary and additional diagnoses for all admissions to inpatient care in Sweden from 1987. More than 99% of all hospital discharges are included in the IPR.18

Study Population
Included patients had an ischemic stroke (first-ever stroke) between 1 January 2009 and 31 December 2012, had AF according to the stroke register, and were not treated with OACs at the onset of stroke.

Variables
The outcome variable was prescription of any OAC at discharge from the hospital according to the stroke register. For 2009 to 2010, warfarin was the only OAC registered in the stroke register. New oral anticoagulants (NOACs) were introduced in 2011 to 2012. Information about prescribed OACs was dichotomized to Yes or No.

Highest level of education and family disposable income in the year before the stroke were used as indicators of socioeconomic status. Disposable income was adjusted to the consumer price index for 2012 and divided into tertiles classified as low, medium, and high income. Level of education was categorized as primary school (<9 years in compulsory school), secondary school (the upper levels of comprehensive school), and university level. Country of birth was grouped into Sweden, Nordic countries (other than Sweden), Europe (other than Nordic countries), and other countries.

Other variables included from the stroke register were whether living alone before stroke, dependency in activities of daily living, discharge disposition, level of consciousness at admission to the hospital, and smoking. Information about diabetes mellitus and hypertension was included from both the stroke register and the IPR, and patients were classified as having diabetes mellitus or hypertension if information in either register indicated diabetes mellitus or hypertension. Information about congestive heart failure and vascular disease was retrieved from the IPR. Data on comorbidities from the IPR were included from 1997 onwards (for International Classification of Diseases codes, please see Table I in the online-only Data Supplement).

Age was categorized as 18 to 69, 70 to 79, 80 to 89, or 90+ years. The variables of cohabitation, dependency in activities of daily living, congestive heart failure, history of diabetes mellitus, hypertension or antihypertensive medication, vascular disease, and smoking were coded as Yes or No. The level of consciousness at admission was coded as Alert or Drowsy/unconscious, and discharge disposition as Own home or Other.

The project has been approved by the Ethical Review Board in Umeå (nr. 2012-321-31M and 2013-176-32M).

Statistical Analysis
The frequencies and proportions of prescribing OACs were calculated. The associations between patient characteristics and drug prescribing were analyzed by multivariable logistic regression models, the first adjusting for age and the second controlling for year of stroke onset, sex, age group, country of birth, education, income, living alone, dependency in activities of daily living, discharge disposition, level of consciousness at admission, congestive heart failure, history of diabetes mellitus, hypertension or antihypertensive medication, vascular disease, and smoking. The results are presented as odds ratios with 95% confidence intervals. All the analyses were performed with SPSS 22.0.

Results
Out of the 100,926 cases of stroke that were registered in Riksstroke during 2009 to 2012, 12,088 (12.0%) were ≥18 years of age and discharged from the hospital alive, had an ischemic stroke (first-ever stroke), had AF, and were without OAC treatment. Of these, 6640 (54.9%) were women and 7380 (61.1%) were ≥80 years of age. Characteristics of the study population are presented in Table 1.

During this time period, 4389 (36.3%) patients were prescribed an OAC at discharge, 6955 (57.5%) were prescribed an APD, 384 (3.2%) were prescribed both an OAC and an APD, and 1083 (9.0%) were not prescribed an OAC or an APD. At stroke onset, 7103 (58.8%) were using some type of APD.

The prescribing of OACs has increased over time. NOACs were introduced in 2011, and 3.8% and 6.2% of patients were prescribed NOACs in 2011 and 2012, respectively. Excluding NOACs still showed an increase in the prescribing of warfarin in 2011 to 2012 (Figure). Age was strongly related to OAC prescribing with younger age groups being more likely to receive OACs (Table 1). Our results also showed socioeconomic differences in the prescribing of preventive treatment. Patients with lower socioeconomic status were prescribed the recommended treatment to a lower extent than patients with higher socioeconomic status. A smaller proportion of patients born in the Nordic countries (odds ratio, 0.82; 95% confidence interval, 0.68–0.98) and in countries outside of Europe (odds ratio, 0.65; 95% confidence interval, 0.42–0.99) were prescribed OACs compared with patients born in Sweden (Table 2). University education (compared with primary school) and the highest income (compared with the lowest) were associated with higher levels of OAC prescribing (Table 2).

In most cases, risk factors for stroke were negatively associated with the prescribing of OACs (Table 2). Patients with congestive heart failure, diabetes mellitus, or vascular disease were less likely to be prescribed OACs compared with patients without these risk factors.

OAC prescribing was less common in patients living alone compared with those who were cohabiting. Patients who were dependent in activities of daily living or not discharged to their own home were prescribed OACs to a lower extent. A lower level of consciousness at admission to hospital (drowsy or unconscious) was also associated with lower levels of OAC prescriptions.

Discussion
Of patients with ischemic stroke and AF, 36.3% were prescribed OACs. Differences based on age and socioeconomic status were found, and patients in older age groups, patients born in Nordic countries or outside of Europe, and patients with a low level of education or income were less likely to be prescribed the recommended treatment. The differences...
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in prescribing were not explained by demography, health status, or common risk factors. In this sample, 57.5% of patients received APDs even though APDs were not recommended. Our results showed that the use of OACs has been increasing in recent years and that the increase was not just because of the addition of newer drugs but also because of an increase in the use of warfarin.

The overall level of 36.3% of patients being prescribed an OAC is low compared with other studies but could possibly be explained by the old age in this sample. A large proportion (61.1%) was ≥80 years old. The prescribing of OACs was significantly lower in the oldest age groups, and this is consistent with results from other studies.2,10,23 It is reasonable to think that contraindications for warfarin and the risks associated with comorbidities, frailty, and polypharmacy might increase and that the expected benefit might decrease with age. However, age alone is not a contraindication for OACs.7 This analysis only includes prescribing of OACs to patients not already using OACs, and this might be less common in the oldest patients. NOACs might be important in older age groups because of the problems with warfarin.

A study from Scotland showed that stroke survivors with AF living in areas with high deprivation scores were prescribed vitamin K antagonists to a lower extent compared with less deprived areas.24 An Italian study comparing the prescribing of OACs divided the country into the North, Central, and South regions (both education level and income decrease from north to south) and found that OACs were significantly less prescribed to high-risk patients in the south.25

Table 1. Baseline Characteristics, Prescribing Frequencies, and Proportions for Oral Anticoagulants in Subgroups of Ischemic Stroke Patients With Atrial Fibrillation and Without Anticoagulant Treatment at Stroke Onset

<table>
<thead>
<tr>
<th>Year of stroke onset</th>
<th>Valid Observations</th>
<th>Prescribing Frequency</th>
<th>Proportion, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>2939</td>
<td>907</td>
<td>30.9</td>
</tr>
<tr>
<td>2010</td>
<td>3131</td>
<td>973</td>
<td>31.1</td>
</tr>
<tr>
<td>2011</td>
<td>3065</td>
<td>1254</td>
<td>40.9</td>
</tr>
<tr>
<td>2012</td>
<td>2898</td>
<td>1255</td>
<td>43.3</td>
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<table>
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<th>Valid Observations</th>
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<th>Proportion, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>5423</td>
<td>2292</td>
<td>42.3</td>
</tr>
<tr>
<td>Women</td>
<td>6610</td>
<td>2097</td>
<td>31.7</td>
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<table>
<thead>
<tr>
<th>Age group</th>
<th>Valid Observations</th>
<th>Prescribing Frequency</th>
<th>Proportion, %</th>
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<tbody>
<tr>
<td>18–69</td>
<td>1789</td>
<td>1098</td>
<td>61.4</td>
</tr>
<tr>
<td>70–79</td>
<td>2909</td>
<td>1531</td>
<td>52.6</td>
</tr>
<tr>
<td>80–89</td>
<td>5342</td>
<td>1551</td>
<td>29.0</td>
</tr>
<tr>
<td>90+</td>
<td>1993</td>
<td>209</td>
<td>10.5</td>
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<table>
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<th>Country of birth</th>
<th>Valid Observations</th>
<th>Prescribing Frequency</th>
<th>Proportion, %</th>
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<tbody>
<tr>
<td>Sweden</td>
<td>10718</td>
<td>3898</td>
<td>36.4</td>
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<tr>
<td>Nordic countries*</td>
<td>658</td>
<td>237</td>
<td>36.0</td>
</tr>
<tr>
<td>Europe†</td>
<td>466</td>
<td>192</td>
<td>41.2</td>
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<tr>
<td>Other countries</td>
<td>131</td>
<td>37</td>
<td>28.2</td>
</tr>
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<table>
<thead>
<tr>
<th>Education‡</th>
<th>Valid Observations</th>
<th>Prescribing Frequency</th>
<th>Proportion, %</th>
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<tr>
<td>Primary school</td>
<td>6343</td>
<td>1993</td>
<td>31.4</td>
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<tr>
<td>Secondary school</td>
<td>3683</td>
<td>1501</td>
<td>40.8</td>
</tr>
<tr>
<td>University</td>
<td>1710</td>
<td>816</td>
<td>47.7</td>
</tr>
<tr>
<td>Unknown</td>
<td>297</td>
<td>79</td>
<td>26.6</td>
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<table>
<thead>
<tr>
<th>Income</th>
<th>Valid Observations</th>
<th>Prescribing Frequency</th>
<th>Proportion, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>3988</td>
<td>1265</td>
<td>31.7</td>
</tr>
<tr>
<td>Medium</td>
<td>3993</td>
<td>1280</td>
<td>32.1</td>
</tr>
<tr>
<td>High</td>
<td>3992</td>
<td>1819</td>
<td>45.6</td>
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<tr>
<th>Living alone</th>
<th>Valid Observations</th>
<th>Prescribing Frequency</th>
<th>Proportion, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>5074</td>
<td>2416</td>
<td>47.6</td>
</tr>
<tr>
<td>Yes</td>
<td>6907</td>
<td>1959</td>
<td>28.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dependent in ADL</th>
<th>Valid Observations</th>
<th>Prescribing Frequency</th>
<th>Proportion, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>10596</td>
<td>4246</td>
<td>40.1</td>
</tr>
<tr>
<td>Yes</td>
<td>1245</td>
<td>125</td>
<td>10.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Discharged to</th>
<th>Valid Observations</th>
<th>Prescribing Frequency</th>
<th>Proportion, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Own home</td>
<td>7466</td>
<td>3644</td>
<td>48.8</td>
</tr>
<tr>
<td>Other</td>
<td>4544</td>
<td>737</td>
<td>16.2</td>
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<table>
<thead>
<tr>
<th>Level of consciousness at admission</th>
<th>Valid Observations</th>
<th>Prescribing Frequency</th>
<th>Proportion, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alert</td>
<td>10135</td>
<td>3990</td>
<td>39.4</td>
</tr>
<tr>
<td>Drowsy/unconscious</td>
<td>1789</td>
<td>371</td>
<td>20.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Congestive heart failure</th>
<th>Valid Observations</th>
<th>Prescribing Frequency</th>
<th>Proportion, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>10577</td>
<td>4062</td>
<td>38.4</td>
</tr>
<tr>
<td>Yes</td>
<td>1456</td>
<td>327</td>
<td>22.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>History of diabetes mellitus</th>
<th>Valid Observations</th>
<th>Prescribing Frequency</th>
<th>Proportion, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>9627</td>
<td>3610</td>
<td>37.5</td>
</tr>
<tr>
<td>Yes</td>
<td>2406</td>
<td>779</td>
<td>32.4</td>
</tr>
</tbody>
</table>
hypertension, heart failure, or vascular disease were more likely to be initiated on warfarin treatment.23

Different risk stratification schemes are available to aid decisions about OAC treatment. However, all patients included in this analysis had an ischemic stroke and would be classified as high-risk patients. An ischemic stroke in an AF patient is an indication for treatment with warfarin in both the 2005 and 2009 national guidelines.5,27 Still, all patients should not be treated with OACs because of an increased risk of bleeding. There are several contraindications for OAC, and in cases where patient adherence has previously been or is expected to be a problem, warfarin is not recommended. In this analysis, we did not have enough information about contraindications and previous treatment attempts to be able to estimate who and how many were not eligible for OAC treatment. An international observational study (n=10614) on the use of antithrombotic treatment in AF reported contraindications to anticoagulants in 7.8% of patients.13 Determinants for nonprescription of OACs in other studies have been bleeding risk, patient refusal, risk of drug interactions, fall risk, worsening disability, and dementia.13,14

Prescribing of warfarin increased significantly from 2010 to 2011. The introduction of NOACs highlighted the risk of ischemic stroke in patients with AF and the use of drug treatment in prevention. Newer guidelines recommend that most AF patients without contraindications should be treated with OACs,28 and NOACs provide the opportunity to treat previously excluded patients.

One reason for differences between patient groups is that they are treated in healthcare facilities with different adherence to clinical guidelines.29 In addition, the following 3 mechanisms in the patient encounter with healthcare services have been suggested to affect differences between patient groups:29:

Insufficient adaptation to varying patient characteristics or conditions, for example, treatment is influenced by patient’s knowledge or demands.
Information about patients at the group level is used for making decisions about individual patients (generalizations).
Unconscious behavior because of norms and values of the healthcare staff.

A review of cultural differences in doctor–patient communication found that doctors communicate differently with

<table>
<thead>
<tr>
<th>Year of stroke onset</th>
<th>Age-Adjusted Odds Ratio (95% CI)</th>
<th>Multiple Logistic Regression* Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2010</td>
<td>1.07 (0.95–1.20)</td>
<td>1.05 (0.93–1.19)</td>
</tr>
<tr>
<td>2011</td>
<td>1.77 (1.58–1.99)</td>
<td>1.74 (1.54–1.97)</td>
</tr>
<tr>
<td>2012</td>
<td>1.95 (1.74–2.19)</td>
<td>2.01 (1.78–2.27)</td>
</tr>
</tbody>
</table>

Sex

- **Men**: 1
- **Women**: 0.92 (0.84–0.99) 1.09 (0.99–1.20)

Age group

- **18–69**: 1
- **70–79**: 0.84 (0.73–0.96)
- **80–89**: 0.39 (0.34–0.44)
- **90+**: 0.13 (0.10–0.15)

Country of birth

- **Sweden**: 1
- **Nordic countries†**: 0.76 (0.64–0.91) 0.80 (0.66–0.96)
- **Europe‡**: 0.98 (0.80–1.20) 1.00 (0.80–1.24)
- **Other countries**: 0.57 (0.38–0.85) 0.62 (0.40–0.95)

Education§

- **Primary school**: 1
- **Secondary school**: 1.16 (1.05–1.27) 1.10 (0.99–1.21)
- **University**: 1.43 (1.27–1.61) 1.18 (1.04–1.35)
- **Unknown**: 0.72 (0.55–0.96) 0.85 (0.60–1.23)

Income

- **Low**: 1
- **Medium**: 1.05 (0.95–1.16) 1.04 (0.93–1.16)
- **High**: 1.35 (1.22–1.49) 1.16 (1.04–1.30)

Living alone

- **No**: 1
- **Yes**: 0.65 (0.60–0.70) 0.79 (0.72–0.87)

Dependent in ADL

- **No**: 1
- **Yes**: 0.25 (0.20–0.30) 0.39 (0.32–0.48)

Discharged to

- **Own home**: 1
- **Other**: 0.28 (0.25–0.31) 0.36 (0.33–0.40)

Level of consciousness at admission

- **Alert**: 1
- **Drowsy/unconscious**: 0.45 (0.39–0.51) 0.68 (0.59–0.78)

Congestive heart failure

- **No**: 1
- **Yes**: 0.57 (0.50–0.66) 0.67 (0.58–0.78)

History of diabetes mellitus

- **No**: 1
- **Yes**: 0.70 (0.63–0.77) 0.79 (0.71–0.88)

(Continued)
different groups of patients, but little information was found on reasons for or effects of differences in communication.\(^3\)

In the case of warfarin, it is possible that poor language skills is seen as a problem because of the rather complicated treatment regimen. Thus, the effects of language difficulties and cultural differences should be included in future research into the reasons behind differences in prescribing between patient groups.

The majority of patients in this study were born in Sweden (89%), and only 1% were born outside of Europe. Thus, the results from country of birth were less stable compared with other socioeconomic factors and need confirmation.

**Strengths and Weaknesses**

Strengths of this study are the real-life data with national coverage over several years. Linking data from 3 registers gave an impression of the socioeconomic differences found in the prescribing of OACs. The results on country of birth and to explain the reasons for the socioeconomic differences found in the prescribing of OACs.

We have not investigated contraindications for use of OACs. Risk of bleeding would have been valuable information, but too much information was missing to calculate a HAS-BLED (Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly) score. Contraindications are rarely clear-cut. Different factors interact, and this is particularly the case with warfarin. If the extent of contraindications differs between patient groups, this could affect the analysis.

**Conclusions**

This study showed that although OACs were highly recommended among stroke patients with AF, there were socioeconomic differences in the prescription of OACs to patients with a first-ever ischemic stroke who were not treated with OACs at stroke onset. Patients in older age groups, those born in Nordic countries or outside of Europe, and those with low levels of education or income were less likely to be prescribed the recommended treatment. Further studies are needed to confirm the results on country of birth and to explain the reasons for the socioeconomic differences found in the prescribing of OACs.

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**Disclosures**

None.

**References**

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http://stroke.ahajournals.org/content/suppl/2015/06/16/STROKEAHA.115.009718.DC1

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Article title: Socioeconomic inequalities in the prescription of oral anticoagulants in stroke patients with atrial fibrillation.

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Table I: ICD-10 codes for identification of comorbidities/risk factors in the Swedish National Inpatient Register (IPR)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Hospital admission (IPR) ICD-10 codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>E10-14</td>
</tr>
<tr>
<td>Hypertension</td>
<td>I10-15</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>150</td>
</tr>
<tr>
<td>Vascular disease</td>
<td>I20 (except I20.1) I21 I22 I23 I24 I25.2 I65 I74 K55.0 N28.0 D73.5 E27.4 E07.8 I70-73 (except I71.1, I71.2, I73.0, I73.1, I73.8, I73.8A, I73.8B, I73.8C, I73.8D, I73.8W and I73.9A)</td>
</tr>
</tbody>
</table>