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Is "Detection of Diagnosis" a Useful Quality Indicator in Primary Care?

- A Registry Based Prospective Cohort Study

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ABSTRACT

Objectives The aim of this study was to explore whether detection of diagnosis could be used as a quality indicator in primary care. The indicator measures whether patients that transition between different levels of care – from hospital inpatient care to primary care – are diagnosed with their hospital diagnosis, or a corresponding follow-up diagnosis, in primary care.

We hypothesized that detection of diagnosis in primary care was associated with increased patient utilization of recommended medications in the long term.

Design Registry based prospective cohort study.

Setting and participants 20 024 patients with a hospital discharge diagnosis of transient ischemic attack (TIA), stroke or acute coronary syndrome from hospitals in Stockholm County between 1st January 2010 and 31st December 2013 were included in the study.

Main outcome measure The outcome of the study was adherence to recommended medications. Data on dispensation of medications in the entire patient cohort was extracted as a marker of adherence. Patients were considered adherent if they had at least two filled prescriptions in the second year following their hospital discharge.

Results: With the exception for antihypertensives, detection of diagnosis was associated with higher utilization of recommended medications for all studied diagnosis groups.

Conclusion: The results show that patients who are diagnosed with their hospital diagnosis in primary care receive recommended treatment to a higher extent than patients without such diagnosis in primary care. The results imply that detection of diagnosis could serve as a useful quality indicator in primary care. However, further study is necessary in order to determine the optimal way to construct the indicator.

Strengths and limitations of this study

- Whether or not registering a primary care diagnosis is associated with greater adherence to recommended treatment is something that, to our knowledge, has not been investigated before.
- The study is based on data from a registry which includes all residents in Stockholm County and not just a sample.
- In stroke and acute coronary syndrome the validity of discharge diagnosing in hospitals is higher than for TIA where there may be greater uncertainty and variation in accuracy of diagnosing due to the diagnosis defining lack of objective symptoms.
- The included diagnoses were chosen in order to select patients where secondary preventive pharmacologic treatment was indicated and clearly defined which limits the possibility to generalize the results to a more diverse primary care population.

INTRODUCTION

Healthcare in Sweden has traditionally been organized by non-market principles with public funding and public provision. During the last decades the use of market mechanisms, within the publicly financed healthcare system, has been introduced. The tax-based financing has remained, but the provider side of the system, especially in primary care, has gone through large changes in terms of introduction of competition and freedom of choice for patients.[1]

The changes to the healthcare market have increased the need for objective indicators to monitor the quality of healthcare provided. Quality indicators are needed in order to both give patients support in their choice of provider, and to evaluate the performance of different providers. Sweden has a long history of producing quality indicators in specialized care. In primary care the number of available indicators is more limited[2, 3] even though primary care is the level of care most patients with chronic disease will depend upon for their long term care[4] and primary care is a prioritized area in Swedish health care.[5]

In this study we explore ”detection of diagnosis” as a potential new quality indicator in primary care. Detection of diagnosis is an indicator that targets a well-known problem in most healthcare systems – the fragmentation of the system and the lack of communication between different segments of the system.[5-10] The indicator measures whether patients that transition between different levels of care – from hospital inpatient care to primary care – are diagnosed with their hospital diagnosis, or a corresponding follow-up diagnosis, in primary care. A diagnosis that is not being recognized, ”detected”, in primary care could be an indication of lack of communication between the different health care providers which could affect the quality of the subsequent care and treatment. To our knowledge, the association between follow-up diagnosis and the quality of the long term care has not been investigated before.

To investigate whether ”detection of diagnosis” is associated with increased quality in the long term care, four common groups of diagnoses with clear and evidence based clinical guidelines with regard to medical treatment were chosen: acute coronary syndromes, ischemic and hemorrhagic stroke, and transient ischemic attack (TIA). The clear clinical recommendations for these diagnoses,[11-13] and the possibility to track dispensed prescriptions through registry data, allow us to investigate the association between detection and recommended treatment. If such an association is found there is reason to believe that

detection of diagnosis could be important, even for other conditions where recommended treatments are more diverse and not as easily captured with registry data.

Objective

The aim of this study was to explore whether detection of diagnosis could be used as a quality indicator in primary care. We hypothesized that detection of diagnosis in primary care was associated with increased patient utilization of recommended medications in the long term.

METHODS

Setting

Stockholm County Council provides health care to 2.2 million inhabitants at three levels: inpatient acute care at 7 hospitals, outpatient secondary specialist care at hospitals or contracted specialist units, and primary care in 208 centers. Approximately 94 % of the population chooses to list at a primary care practice (private or public) for their basic care. ”Listing” means a patient choosing a specific center to be their provider of primary care, with complete freedom to change provider at any point in time. The remaining part will be living in special accommodation or be unlisted. As an alternative to primary care practices, people may also visit some hundred private specialists working on the basis of the National tariff system (*nationella taxan*).

Study Design and Participants

For this registry based prospective cohort study, data from the Stockholm County Council regional healthcare database, VAL, was used. The VAL database contains anonymized and encrypted data on the health care consumption, including dispensed medications, for the 2.2 million individuals residing in Stockholm County. The data include detailed information from both inpatient and outpatient care including primary care. Diagnoses from inpatient care and secondary care are registered from 1993 and diagnoses from primary care are available from 2003. More than 95 % of visits to primary care physicians are coded with one or more diagnoses according to the ICD-system. The database also contains information on age, sex, migration, and mortality for all residents.[14]

Unique patients living in Stockholm County who received a discharge diagnosis of stroke, TIA, and/or acute coronary syndrome from hospitals in Stockholm County between 1st January 2010 and 31st December 2013 (see appendix 1 for specific ICD-10 codes) were selected using the VAL-database. The year in which a patient received a diagnosis is referred to as *index year*. Patients receiving one of the pre-specified discharge diagnoses more than once during the period (”multiple diagnoses” in Figure 1) or dying before the end of their follow-up period were excluded. Patients living in nursing homes and individuals that were not listed at a primary healthcare center were also excluded.

Out of the total 36 646 patients initially selected, 20 024 were finally included in the study population. Out of these, 41 percent were women (see Figure 1).

Registration of diagnosis in primary care

Detection of diagnosis in primary care was the pre-defined *exposure* within the cohort. Being detected was defined as receiving a primary care diagnosis related to, but not necessarily identical with, the initial hospital diagnosis during the two years following the index year (irrespective of month). This period was defined as the *detection period*. Patients with a hospital diagnosis in 2010 were thus analyzed with regards to primary care detection in 2011-2012 and those with hospital diagnosis 2011 were analyzed 2012-2013 etc. Patients not receiving any of the pre-specified diagnoses (see appendix 1) were defined as *not detected.*

Medication adherence and dispensation

The *outcome* of the study was medication adherence. Data on dispensation of medications in the entire patient cohort was extracted as a marker of adherence. Patients were considered adherent if they had at least two filled prescriptions in the second year following their index event, henceforth referred to as *dispensation period* (see Figure 2). The second year following their index year was chosen because in many cases the hospital will be in charge of prescriptions for the first period following the index event. However, these prescriptions will last for up to a maximum of one year and if the prescribed therapy is to continue it is up to the primary care physician to take over prescriptions.

Recommended medications in ischemic stroke and TIA include antihypertensives and statins.[11] Antiplatelet agents are recommended in non-embolic stroke/TIA, while anticoagulants are recommended in embolic stroke/TIA.[11] For hemorrhagic stroke, antihypertensives are recommended.[13] In patients with acute coronary syndromes without

persistent ST-segment elevation guidelines recommend statins, antiplatelet agents, and that patients are kept normotensive.[12] Additionally, regional guidelines in Stockholm[15, 16] have recommended beta-blockers to all patients discharged from hospitals with acute coronary syndrome during the entire time period of our study.

Medications were divided into four groups: antithrombotics (antiplatelet agents and anticoagulants including new oral anticoagulants), antihypertensives, statins, and beta-blockers. Medications studied for TIA, ischemic stroke, and acute coronary syndrome were antihypertensives, antithrombotics, and statins. Additionally, in acute coronary syndromes beta-blockers were studied. For hemorrhagic stroke only data on dispensation of antihypertensives was collected. The specific ATC-codes used can be seen in appendix 2. Medication adherence was compared between detected and undetected patients during all detection periods (2011-2015).

Potential confounders

Sex, age, visits to private specialists, and index year were identified as potential confounders. There may be differences between men and women both when it comes to the exposure, likelihood of detection in primary care, and the outcome, likelihood of receiving certain medications.[17] Age is also a factor that may be associated with both the exposure and the outcome. Elderly patients have greater comorbidity and it may be argued that this increases the number of diagnoses from which the primary care physician can choose. Also, this comorbidity implies that patients may have an indication for several different medications potentially influencing prescription behavior.

As private specialists linked to the National tariff system often serve as a substitute to primary care physicians, their patients are less likely to receive a primary care diagnosis. In addition, these visits affect the outcome as private specialists also prescribe medications. Lastly, index year may influence the results should diagnosing behavior and/or medication prescription patterns change over time. Appendix 3 shows descriptive statistics for age and for visits o private specialists.

Statistical analysis

Standard descriptive statistics were used and data are presented as proportions. Logistic regression was used in the analyses to calculate adjusted odds ratios with 95 percent confidence intervals for drug adherence for detected vs undetected patients (reference group).

Adjustments were made for age, index year, and for health care consumption in the form of physician visits to private specialists that may function as a substitute to some patients' primary care provider. The results were stratified by sex. All statistical analyses were performed using SAS software, version 9.4 (SAS Institute Inc., Cary, NC).

Ethical permit

The study was approved by the regional ethics review board in Stockholm, Dnr 2015/803-31/5 and DNR 2016/1547-32.

RESULTS

Table 1 shows the absolute number and proportion of men and women detected by diagnosis. The lowest proportion of detected patients in primary care was found in the group of patients with TIA whereas patients with acute coronary syndromes had the highest detection rate. In all studied diagnoses, except for TIA, a lower percentage of women were detected compared to men.

Table 1. Absolute number and proportion of men and women detected and undetected by diagnosis.

	Detected		**Undetected**	
	Women	*Men*	*Women*	*Men*
TIA	353 (16%)	318 (15%)	1 892 (84%)	1 817 (85%)
Ischemic stroke	1 248 (41%)	1 649 (45%)	1 794 (59%)	1 976 (55%)
Hemorrhagic stroke	107 (35%)	184 (42%)	203 (65%)	253 (58%)
Acute Coronary Syndrome	1 128 (44%)	2 655 (47%)	1 450 (56%)	2 997 (53%)

Table 2 shows medication adherence by detection status for all diagnosis groups in both men and women. Detected patients were more likely to be adherent to both statin- and antithrombotic therapy across all diagnoses; a difference which remained after adjustment for age, visits to private specialist, and index year (table 3).

Table 2. Absolute number and proportion of men and women adherent to medications by medication class, detection status, and diagnosis.

			Statins	Antithrombotics	Antihypertensives	Beta-blockers
TIA	Women	Undetected	902 (48%)	1 524 (81%)	1 325 (70%)	
		Detected	208 (59%)	320 (91%)	215 (61%)	
	Men	Undetected	1 061 (58%)	1 526 (84%)	1 283 (71%)	
		Detected	210 (66%)	298 (94%)	218 (69%)	
Ischemic stroke	Women	Undetected	894 (50%)	1 502 (84%)	1 379 (77%)	
		Detected	817 (65%)	1 157 (93%)	939 (75%)	
	Men	Undetected	1 196 (61%)	1 726 (87%)	1 477 (75%)	
		Detected	1 171 (71%)	1 540 (93%)	1 243 (75%)	
Hemorrhagic stroke	Women	Undetected			1 31 (65%)	
		Detected			76 (71%)	
	Men	Undetected			159 (63%)	
		Detected			153 (83%)	
Acute coronary syndrome	Women	Undetected	874 (60%)	1 239 (85%)	1 320 (91%)	1 120 (77%)
		Detected	838 (74%)	1 060 (94%)	1 075 (95%)	957 (85%)
	Men	Undetected	2 307 (77%)	2 706 (90%)	2 705 (90%)	2 359 (79%)
		Detected	2 257 (85%)	2 515 (95%)	2 515 (95%)	2 231 (84%)

Table 3. Crude and adjusted odds ratios for medication adherence according to detection status by sex and diagnosis. Undetected patients are the reference group. OR >1 means detected patients are more adherent. Adjustments made for age, visit to private specialist, and index year.

	Women		**Men**	
	Crude Odds Ratios (95% CI)	*Adjusted Odds Ratios (95% CI)*	*Crude Odds Ratios (95% CI)*	*Adjusted Odds Ratios (95% CI)*
TIA				
Statins	1.57 (1.25-1.98)	1.58 (1.25-1.98)	1.39 (1.08-1.78)	1.41 (1.09-1.81)
Antithrombotics	2.34 (1.61-3.41)	2.50 (1.70-3.67)	2.84 (1.78-4.54)	2.89 (1.79-4.65)
Antihypertensives	0.67 (0.53-0.84)	0.67 (0.52-0.86)	0.91 (0.70-1.17)	0.90 (0.69-1.17)
Ischemic stroke				
Statins	1.91 (1.64-2.22)	1.92 (1.65-2.23)	1.60 (1.39-1.84)	1.66 (1.44-1.91)

Antithrombotics	2.47 (1.93-3.17)	2.78(2.15-3.58)	2.05 (1.62-2.59)	2.23 (1.76-2.84)
Antihypertensives	0.92 (0.77-1.08)	1.05 (0.87-1.25)	1.03 (0.89-1.20)	1.12 (0.960-1.31)
Hemorrhagic stroke				
Antihypertensives	1.35 (0.81-2.24)	1.57 (0.87-2.81)	2.92 (1.84-4.63)	3.17 (1.95-5.17)
Acute coronary syndrome				
Statins	1.90 (1.61-2.26)	1.97 (1.65-2.34)	1.70 (1.48-1.94)	1.84 (1.60-2.12)
Antithrombotics	2.66 (2.00-3.53)	2.66 (2.00-3.54)	1.93 (1.57-2.38)	2.06 (1.67-2.54)
Antihypertensives	2.00 (1.44-2.78)	1.99 (1.43-2.77)	1.94 (1.57-2.39)	1.98 (1.60-2.44)
Beta-blockers	1.65 (1.35-2.02)	1.63 (1.33-2.00)	1.42 (1.24-1.63)	1.424(1.24-1.63)

For antihypertensives however, there was no significant difference in medication adherence between detected/undetected in ischemic stroke and TIA, and in women with TIA undetected patients were more adherent to antihypertensive therapy (table 3). In hemorrhagic stroke detected men but not detected women were more adherent to antihypertensive therapy. For acute coronary syndrome, detection was associated with greater adherence to both antihypertensive- and beta-blocker therapy in both sexes.

DISCUSSION

Key results

With the exception for antihypertensives, detection of diagnosis was associated with higher utilization of recommended medications for all studied diagnosis groups.

Potential explanations

Several factors could explain the association between detection and utilization of recommended medications. Previous studies have shown that the transfer of information, when patients move between different parts of the health care system, frequently is insufficient and that this lack of communication may affect subsequent patient care.[18, 19] A diagnosis is chosen by the primary care physician *after* a patient visit has been completed, when potential medication prescriptions have already been communicated with the patient. The act of selecting a diagnosis cannot therefore, in itself, have any effect on a doctor choosing to prescribe a certain drug as they are not temporally related. However, some of the

factors influencing physician likelihood of detecting patients may be closely related to those influencing prescription and consequentially dispensation.

Knowledge of a patients' past medical history is most likely an important factor when it comes to both registering a certain diagnosis and prescribing recommended medications. In this respect, the interaction and communication between hospitals and primary healthcare centers are important. Discharge summaries from hospitals may be lacking or may not reach the responsible primary care physician leading to an inadequate transfer of information.[18-19] When a patient chooses to re-list from one primary health care provider to another there may also be a risk of patient data not being transferred which could affect knowledge of patients' medical history and reduce the likelihood of both detection and prescription.

Knowledge of the condition in question including awareness of current guidelines is also a factor that could influence both choice of diagnosis and dispensation. The level of knowledge may affect the likelihood of the physician focusing on the condition during visits and in continuation registering the diagnosis as well as the likelihood of prescribing medications according to guidelines and also motivating the patient to continue using the preventive medications.

There may also be important differences in *patient factors* between the detected and undetected groups which may lead to both a higher level of detection and increased dispensation in the detected group. It is possible that detected patients are more knowledgeable about their diagnoses and more assertive in their communication toward physicians which may lead to an increased level of physician prescribing. As this is a registry study it is difficult to ascertain whether or not this is the case.

A potential explanation for the lack of association between adherence to antihypertensive therapy and detection for most groups could stem from the fact that treatment of hypertension is well established. As many patients with stroke and/or ischemic heart disease have established hypertension[20, 21] they would be treated regardless of other diagnoses. This is not the case for antithrombotics and statins. Hypertension is also a common condition with a high prevalence of treatment and this diagnosis may be chosen instead of a diagnosis of cardio/cerebrovascular disease.

Policy implications

The results show that detection of diagnosis is associated with higher utilization of recommended medications. Does this mean that detection of diagnosis could be used as a quality indicator? Requirements for indicators are acceptability, feasibility, reliability, sensitivity to change, and validity.[22] Adjustments to the indicator may be necessary in order to meet all the requirements. Nevertheless, in the future, detection of diagnosis could potentially be used as an indicator of both physician adherence to recommended treatment, and the quality of the chain of care from hospital to primary care. Information about detection degree at each primary health care center could also be useful from the health care center's perspective as it provides information about their patient population which could be used to improve the provided care. However, if detection of diagnosis is to be used as a quality indicator it is important to take into consideration that detection can be influenced by factors out of the control for the primary health care center such as patient factors and hospital behavior.

Strengths and limitations

A strength of the study is the use of registry data which has allowed for an unbiased inclusion of a large number of patients based on all residents in Stockholm County and not just a sample. However, using hospital registries is fraught with the risk of misdiagnosing which could lead to potential inclusion errors. In the case of our chosen diagnoses there are however quality registries[23-26] where 84-90% of hospital discharge diagnoses are registered. Diagnoses are generally better verified when reported to quality registries. Thus if a high proportion of discharge diagnoses are captured by the registries it is an indication of the high validity of the discharge diagnosing in stroke and ischemic heart disease in hospital. For TIA there may be greater uncertainty and variation in accuracy of diagnosing due to the diagnosis-defining lack of objective symptoms. There are different definitions of medication adherence in use. We have defined medication adherence as two dispensations in one year. However, our results may have been different if we had chosen another definition of medication adherence.

Generalizability

The generalizability of the results depends on the definition of the study population and the included diagnoses. In the present study the aim was to investigate the association between diagnosis detection and recommended treatment and it was necessary to include only

diagnoses with clear recommendations regarding medical treatment. The initial choice of ICD-codes in the index year, where unspecific diagnoses (I64.9 - Stroke, not specified as hemorrhage or infarction for example) were not included, allowed a selection of patients with diagnoses for which secondary preventive pharmacologic treatment was indicated.

In order to utilize detection of diagnosis in a diverse primary care population with a wide range of diagnoses, many of which are received in primary care only, the model used for detection would have to be altered and further studied. One potential way could be to search all levels of health care for a pre-defined diagnosis over a five year period retrospectively and choose this as the index period. The last two years of the period could then be selected as detection period and dispensation period.

CONCLUSION

The results show that physicians detecting diagnoses in primary care seems beneficial for patient utilization of recommended medications in TIA, stroke, and acute coronary syndrome. Patients who are diagnosed with their hospital diagnosis in primary care receive recommended treatment to a higher extent than patients without such diagnosis in primary care. The results imply that detection of diagnosis could serve as a useful quality indicator in primary care. However, further study is necessary in order to determine the optimal way to construct the indicator.

AUTHOR CONTRIBUTIONS

Cecilia Dahlgren: Contributed to the study design, researched data, contributed to analysis and interpretation of data, and drafted the manuscript.

Lukas Geary: Contributed to the study design, researched the literature, contributed to analysis and interpretation of data, and drafted the manuscript.

Clas Rehnberg, Karin Schenck-Gustafsson, and Per Wändell: Contributed to the study design, contributed to analysis and interpretation of data, and critically revised the manuscript.

Jan Hasselström and Mia von Euler: Came up with the original idea, contributed to the study design, contributed to analysis and interpretation of data, and critically revised the manuscript.

All authors approved the final manuscript.

COMPETING INTERESTS

None declared.

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DATA SHARING

Additional aggregate level data could be made available by emailing cecilia.dahlgren@ki.se

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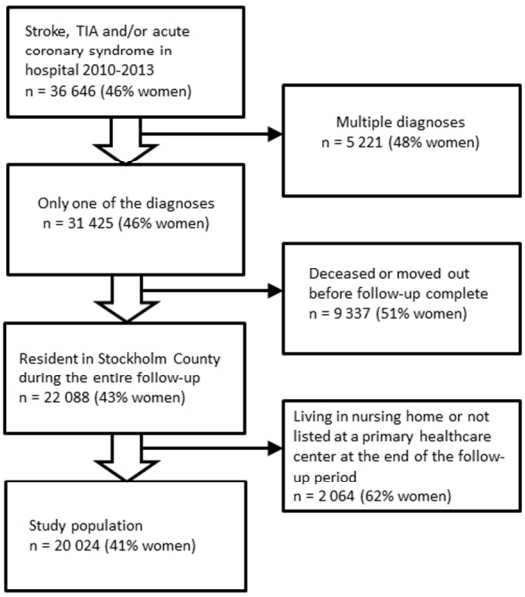
Figure 1. Selection of study population

Figure 2. Illustration of index year, detection period and dispensation period



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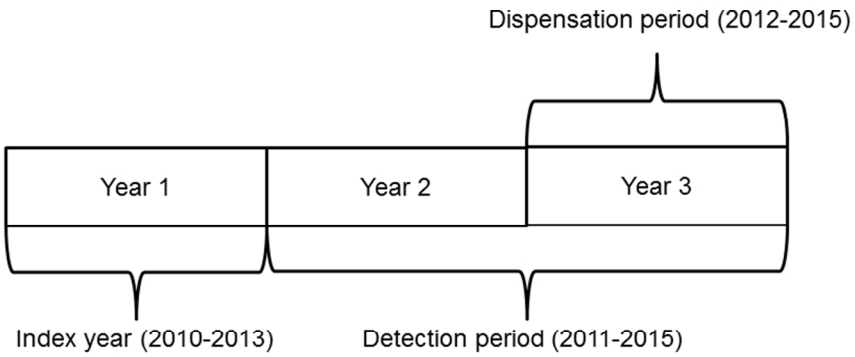

254x190mm (96 x 96 DPI)

APPENDIX 1: ICD10-codes

Ischemic stroke

Index year diagnosis

I63.0, I63.1, I63.2, I63.3, I63.4, I63.5, I63.6, I63.8, I63.9

Detection period diagnosis

I63.0, I63.1, I63.2, I63.3, I63.4, I63.5, I63.6, I63.8, I63.9, I64.9, I69.3, I69.4, I69.8, Z86.6B, Z86.7C

ICD10P: I63.-, I64.-, I67.-P, I69.-

Transient ischemic attack (TIA)

Index year diagnosis

G45.0, G45.1, G45.3, G45.8, G45.9

Detection period diagnosis

G45.0, G45.1, G45.3, G45.8, G45.9, Z86.6A, Z86.6B

ICD10P: G45.-P , I69.-

Hemorrhagic stroke

Index year diagnosis

I61.0, I61.1, I61.2, I61.3, I61.4, I61.5, I61.6, I61.8, I61.9

Detection period diagnosis

I61.0, I61.1, I61.2, I61.3, I61.4, I61.5, I61.6, I61.8, I61.9, I64.9, I69.1, I69.2, I69.4, I69.8, Z86.7C

ICD-10P: I61.-P, I62, I64.-, I67.-P, I69.-

Acute coronary syndrome

Index year diagnosis

I20.0, I21.0, I21.1, I21.2, I21.3, I21.4, I21.4A, I21.4B, I21.4W, I21.4X, I21.9, I22.0, I22.1, I22.8, I22.9, I23.0, I23.1, I23.2, I23.3, I23.4, I23.5, I23.6, I23.8

Detection period diagnosis

I20.0, I20.1, I20.8, I20.9, I21.0, I21.1, I21.2, I21.3, I21.4, I21.4A, I21.4B, I21.4W, I21.4X, I21.9, I22.0, I22.1, I22.8, I22.9, I23.0, I23.1, I23.2, I23.3, I23.4, I23.5, I23.6, I23.8, I24.0, I24.1, I24.8, I24.9, I25.0, I25.1, I25.2, I25.5, I25.6, I25.8, I25.9

ICD 10P: I20.0, I21.-P, I22, I23, I24, I25.-P

APPENDIX 2: ATC-codes

Statins

C10AA

Antithrombotics

B01AC04, B01AC06, B01AC07, B01AC22, B01AC24, B01AC30, B01AA, B01AE07, B01AF

Antihypertensives

C03A, C03B, C03C, C03D, C03E, C07, C08, C09

Beta-blockers

C07

APPENDIX 3

Table 4. Mean age of men and women by detection status and diagnosis. Also proportion of men and women with at least one visit to a private specialist during the detection period, by detection status and diagnosis.

		Detected		Undetected	
		Women	*Men*	*Women*	*Men*
TIA	*Mean age*	73.2	71.4	74.0	70.8
	At least one visit to private specialist	20%	17%	21%	23%
Ischemic stroke	*Mean age*	72.3	69.3	74.9	71.0
	At least one visit to private specialist	16%	14%	18%	20%
Hemorrhagic stroke	*Mean age*	67.3	63.2	67.8	64.2
	At least one visit to private specialist	19%	15%	9%	13%
Acute Coronary Syndrome	*Mean age*	74.4	68.2	74.3	67.4
	At least one visit to private specialist	22%	20%	25%	32%

BMJ Open

Recording a Diagnosis of Stroke, TIA, or Myocardial Infarction in Primary Health Care and the Association with Dispensation of Secondary Preventive Medication – a Registry Based Prospective Cohort Study

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Recording a Diagnosis of Stroke, TIA, or Myocardial Infarction in Primary Health Care and the Association with Dispensation of Secondary Preventive Medication – a Registry Based Prospective Cohort Study

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ABSTRACT

Objectives The aim of this study was to explore whether recording in primary care of a previously recorded hospital diagnosis was associated with increased patient utilization of recommended medications.

Design Registry based prospective cohort study.

Setting and participants 19 072 patients with a hospital discharge diagnosis of transient ischemic attack (TIA), stroke or acute coronary syndrome (ACS) from hospitals in Stockholm County 2010- 2013 were included in the study.

Main outcome measure The outcome of the study was medication dispensation as a marker of adherence to recommended medications. Adherence was defined as having had at least two filled prescriptions in the third year following hospital discharge.

Results Recording a diagnosis was associated with higher utilization of recommended medications with the exception of antihypertensives in men and women with TIA/ischemic stroke and women with hemorrhagic stroke.

Dispensation of antithrombotics was high overall, 80-90% in patients without a recorded diagnosis and 90-94% for those with a diagnosis. Statins were dispensed less, 46-59% of women and 57-77% of men without and 56-71% of women and 68-83% of men, respectively, with a recorded diagnosis of ischemic stroke/TIA/ACS.

The difference between the groups with and without a recorded diagnosis remained after adjusting for age, index year, visit to private practitioners and clustering within providers.

The rate of diagnosis recording spanned from 15-47% and was especially low in TIA (men 15%, women 16%).

Conclusion Recording a diagnosis of TIA/stroke or acute coronary syndrome in primary care was found to be beneficial for patient dispensation of recommended medications. Potentially, recording of diagnosis could serve as a useful quality indicator in primary care. However, further study is necessary in order to determine the optimal way to construct the indicator.

Strengths and limitations of this study

- Whether or not recording a primary care diagnosis is associated with greater dispensation of recommended medication is something that, to our knowledge, has not been investigated before.
- The study is based on data from a registry which includes all residents in Stockholm County and not just a sample.
- In stroke and acute coronary syndrome the validity of discharge diagnosing in hospitals is higher than for TIA where there may be greater uncertainty and variation in accuracy of diagnosing due to the diagnosis defining lack of objective symptoms.
- The included diagnoses were chosen in order to select patients where secondary preventive pharmacologic treatment was indicated and clearly defined which limits the possibility to generalize the results to a more diverse primary care population.

INTRODUCTION

Fragmentation of health care and the lack of communication between different segments of the health care system are well known problems affecting many countries world-wide, including Sweden.[1-6] Previous studies have shown that the transfer of information between hospitals and primary care including information on discharge medication, frequently is insufficient and that this lack of communication may affect subsequent patient care.[7, 8] Primary care is the level of care most patients with chronic disease will depend upon for their long term care in Sweden.[9] It is mandatory in Stockholm for a primary care physician to record at least one diagnosis after every consultation. To our knowledge it has not been studied whether the choice of diagnosis influences patient related outcomes such as medication utilization. For several acute conditions initially treated in hospital an important part of chronic care is patients taking secondary preventive medications. It is however well known that adherence to recommended medications declines after discharge and is often sub-optimal in the long term.[10-13]

In this study we explore if "recording a diagnosis" could be a marker for good communication between hospital and primary care and thus improve utilization of recommended medications. In our study, if a primary care physician "records a diagnosis" it means that a patient discharged from hospital care to primary care is diagnosed with their hospital diagnosis, or a corresponding follow-up diagnosis, in primary care at some point. A diagnosis that is not being recorded in primary care could be an indication of lack of communication between the different health care providers which could affect the quality of the subsequent treatment. If there is an association between recording of diagnosis and utilization of recommended medications then "recording a diagnosis" could potentially be used as a quality indicator in primary care.

To investigate whether recording a diagnosis in primary care is associated with increased dispensation of recommended medication in the long term care, four common groups of diagnoses with clear and evidence based clinical guidelines,[14-16] with regard to medical treatment were chosen: acute coronary syndromes, ischemic and hemorrhagic stroke, and transient ischemic attack (TIA).

Objective

The aim of this study was to explore whether recording a diagnosis in primary care was associated with patient utilization of recommended medications in the long term. We hypothesized that patients with a recorded diagnoses were more likely to be dispensed recommended medications.

METHODS

Setting

Stockholm County Council provides health care to 2.2 million inhabitants at three levels: inpatient acute care at 7 hospitals, outpatient secondary specialist care at hospitals or contracted specialist units, and primary care in 208 centers. Approximately 90 percent of the population chooses to list at a primary care practice (private or public) for their basic care. [17] "Listing" means a patient choosing a specific center to be their provider of primary care, with complete freedom to change provider at any point in time. The remaining part will be living in nursing homes or be unlisted. As an alternative to primary care practices, people may also visit some hundred private specialists working on the basis of the National tariff system (*nationella taxan*).

Study Design and Participants

For this registry based prospective cohort study, data from the Stockholm County Council regional healthcare database, VAL, was used. The VAL database contains anonymized and encrypted data on the health care consumption, including dispensed medications, for the 2.2 million individuals residing in Stockholm County. The data include detailed information from both inpatient and outpatient care including primary care. Diagnoses from inpatient care and secondary care are registered from 1993 and diagnoses from primary care are available from 2003. More than 95 percent of visits to primary care physicians are coded with one or more diagnoses according to the ICD-system. The database also contains information on age, sex, migration, and mortality for all residents.[18]

Unique patients living in Stockholm County who received a discharge diagnosis of stroke, TIA, and/or acute coronary syndrome from hospitals in Stockholm County between 1st

January 2010 and 31st December 2013 (see appendix 1 for specific ICD-10 codes) were selected using the VAL-database. The year in which a patient received a diagnosis is referred to as the *index year*. Patients receiving different pre-specified discharge diagnoses during the study period or the same discharge diagnoses during more than one year were excluded from the study (”multiple diagnoses” in Figure 1). By excluding patients with more than one of the diagnoses (e.g. ACS and hemorrhagic stroke) we were able to be more certain of which medications were recommended as secondary prevention for each patient. Patients discharged with the same diagnosis multiple times during the study period (e.g. ischemic stroke during the index year and the year after) were excluded since, in those cases, it would have been difficult to determine if a hospital or a primary care center was in charge of the patients' long term care during the study. As a sensitivity analysis we have followed the excluded patients with multiple diagnoses in the same way as the included patients. These results are presented in appendix 2.

We also excluded patients dying before the end of their follow-up period, patients living in nursing homes, and individuals that were not listed at a primary healthcare center.

Out of the total 36 646 patients initially selected, 19 072 were finally included in the study population. Out of these, 41 percent were women (see Figure 1).

Recording a diagnosis in primary care

The recording of a diagnosis in primary care was the pre-defined *exposure* within the cohort. Recording a diagnosis was defined as the recording of a primary care diagnosis related to, but not necessarily identical with, the initial hospital diagnosis during the two years following the index year (irrespective of month). This period was defined as the *recording period*. Patients with a hospital diagnosis in 2010 were thus analyzed with regards to recording of a diagnosis in primary care in 2011-2012 and those with hospital diagnosis 2011 were analyzed 2012-2013 etc. Patients not receiving any of the pre-specified diagnoses (see appendix 1) were defined as *not recorded.*

Medication adherence and dispensation

The *outcome* of the study was medication dispensation. Data on dispensation of medications in the entire patient cohort was extracted as a marker of adherence. Patients were considered adherent if they had at least two filled prescriptions in the third year following their index event, henceforth referred to as *dispensation period* (see Figure 2). In Sweden, every filled

prescription for chronic conditions will last for three months and thus two dispensations in one year will last for 180 days. We chose two and not one dispensation as two dispensations more strongly implies use of the medication. The third year following their index year was chosen because in many cases the hospital will be in charge of prescriptions for the first period following the index event. However, these prescriptions will last for up to a maximum of one year and if the prescribed therapy is to continue it is up to the primary care physician to take over prescriptions. Also, the third year was chosen to make certain that there was no overlap between the outcome and the exposure.

Recommended medications in ischemic stroke and TIA include antihypertensives and statins.[14] Antiplatelet agents are recommended in non-embolic stroke/TIA, while anticoagulants are recommended in embolic stroke/TIA.[14] For hemorrhagic stroke, antihypertensives are recommended.[16] In patients with acute coronary syndromes without persistent ST-segment elevation guidelines recommend statins, antiplatelet agents, and that patients are kept normotensive.[15] Additionally, regional guidelines in Stockholm[19, 20] have recommended beta-blockers to all patients discharged from hospitals with acute coronary syndrome during the entire time period of our study.

Medications were divided into four groups: antithrombotics (antiplatelet agents and anticoagulants including new oral anticoagulants), antihypertensives, statins, and beta-blockers. Medications studied for TIA, ischemic stroke, and acute coronary syndrome were antihypertensives, antithrombotics, and statins. Additionally, in acute coronary syndromes beta-blockers were studied. For hemorrhagic stroke only data on dispensation of antihypertensives was collected. The specific ATC-codes used can be seen in appendix 3. Medication dispensation was compared between recorded and not recorded patients during all recording periods (2011-2016).

Potential confounders

Sex, age, visits to private specialists, clustering of results by provider, and index year were identified as potential confounders. There may be differences between men and women both when it comes to the exposure, likelihood of recording a diagnosis in primary care, and the outcome, likelihood of receiving certain medications.[10] Age is also a factor that may be associated with both the exposure and the outcome. Elderly patients have greater comorbidity and it may be argued that this increases the number of diagnoses from which the primary care

physician can choose. Also, this comorbidity implies that patients may have an indication for several different medications potentially influencing prescription behavior.

As private specialists linked to the National tariff system often serve as a substitute to primary care physicians, their patients are less likely to receive a primary care diagnosis. In addition, these visits affect the outcome as private specialists also prescribe medications.

Clustering of results by providers may also be a confounder. Some providers may be better than others at prescribing recommended medications and there is most likely also a provider effect in the likelihood of recording a diagnosis.

Lastly, index year may influence the results should diagnosis-recording behavior and/or medication prescription patterns change over time. Appendix 4 shows descriptive statistics for age and for visits to private specialists.

Statistical analysis

Standard descriptive statistics were used and data are presented as proportions. Logistic regression was used in the analyses to calculate adjusted odds ratios with 95 percent confidence intervals for drug dispensation for recorded vs not recorded patients (reference group). Adjustments were made for age (as a continuous variable), index year, for health care consumption in the form of physician visits to private specialists that may function as a substitute to some patients' primary care provider, and for clustering within providers. To adjust for clustering within providers, a categorical variable for provider was included in the model with the provider effect as a fixed effect to avoid controlling for the association of interest. The results were stratified by sex. All statistical analyses were performed using SAS software, version 9.4 (SAS Institute Inc., Cary, NC).

Ethical permit

The study was approved by the regional ethics review board in Stockholm, Dnr 2015/803-31/5 and DNR 2016/1547-32.

RESULTS

Table 1 shows the absolute number and proportion of men and women with a recorded diagnosis in primary care, by diagnosis. The lowest proportion of recorded patients in primary care was found in the group of patients with TIA whereas patients with acute coronary

syndromes had the highest rate of recording. In all studied diagnoses, except for TIA, a lower percentage of women were recorded compared to men.

Table 1. Absolute number and proportion of men and women with and without a recorded diagnosis in primary care, by diagnosis.

	Recorded		Not recorded	
	Women	*Men*	*Women*	*Men*
TIA	347 (16%)	308 (15%)	1 813 (84%)	1 746 (85%)
Ischemic stroke	1 189 (41%)	1 579 (46%)	1 683 (59%)	1 844 (54%)
Hemorrhagic stroke	105 (35%)	177 (43%)	193 (65%)	237 (57%)
Acute coronary syndrome	1 076 (44%)	2 580 (47%)	1 343 (56%)	2 852 (53%)

Table 2 shows medication dispensation for recorded and not recorded patients for all diagnosis groups in both men and women. Patients with a recorded diagnosis were more likely to be dispensed two prescriptions of both statins and antithrombotics in the dispensation period across all diagnoses. The difference remained after adjusting for age, visits to private specialist, index year, and clustering within providers (table 3).

For antihypertensives however, there was no significant difference in medication dispensation between the recorded and not recorded groups in ischemic stroke (all) and TIA (men). In hemorrhagic stroke recorded men but not recorded women had a significantly higher likelihood of having two prescriptions of antihypertensives dispensed. For acute coronary syndrome, recording was associated with greater dispensation of both antihypertensive- and beta-blocker therapy in both sexes.

In contrast to the other medications and diagnoses, recorded women with TIA were dispensed less antihypertensives (64%) than those not recorded (70%), a difference which remained significant after adjusting for confounders.

Adjusting for clustering within primary health care providers with the provider effect as a fixed effect (model 3 in table 3) was found to strengthen the association between recorded primary care diagnosis and dispensed medications. However, model 3 should be interpreted with caution, especially for the smaller patients groups, since the provider variable contains a large number of categories.

Table 2. Absolute number and proportion of men and women dispensed two prescriptions in the dispensation period, by medication class, recorded/not recorded status, and diagnosis.

			Statins	Antithrombotics	Antihypertensives	Beta-blockers
TIA	Women	Not recorded	827 (46%)	1 442 (80%)	1 271 (70%)	
		Recorded	195 (56%)	313 (90%)	221 (64%)	
	Men	Not recorded	992 (57%)	1 451 (83%)	1 222 (70%)	
		Recorded	210 (68%)	283 (92%)	211 (69%)	
Ischemic stroke	Women	Not recorded	838 (50%)	1 401 (83%)	1 276 (76%)	
		Recorded	736 (62%)	1 074 (90%)	893 (75%)	
	Men	Not recorded	1 122 (61%)	1 591 (86%)	1 373 (74%)	
		Recorded	1 106 (70%)	1 441 (91%)	1 212 (77%)	
Hemorrhagic stroke	Women	Not recorded			120 (62%)	
		Recorded			72 (69%)	
	Men	Not recorded			147 (62%)	
		Recorded			149 (84%)	
Acute coronary syndrome	Women	Not recorded	799 (59%)	1 136 (85%)	1 210 (90%)	1 015 (76%)
		Recorded	767 (71%)	1 008 (94%)	1 022 (95%)	896 (83%)
	Men	Not recorded	2 187 (77%)	2 561 (90%)	2 580 (90%)	2 208 (77%)
		Recorded	2 143 (83%)	2 414 (94%)	2 423 (94%)	2 149 (83%)

Table 3. Crude and adjusted odds ratios for being dispensed two prescriptions in the dispensation period according to recorded/not recorded status, by sex and diagnosis. Not recorded patients are the reference group. OR >1 means recorded patients are more likely to have two dispensations in the dispensation period.

	Women			**Men**		
	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
TIA						
Statins	1.53 (1.21-1.93)	1.53 (1.21-1.93)	1.57 (1.20-2.04)	1.63 (1.26-2.11)	1.65 (1.27-2.14)	1.77 (1.32-2.37)
Antithrombotics	2.37 (1.63-3.44)	2.51 (1.72-3.67)	2.95 (1.93-4.52)	2.30 (1.50-3.53)	2.30 (1.49-3.56)	2.38 (1.48-3.84)
Antihypertensives	0.75 (0.59-0.95)	0.74 (0.58-0.96)	0.68 (0.51-0.91)	0.93 (0.72-1.21)	0.92 (0.70-1.21)	0.98 (0.72-1.33)
Ischemic stroke						
Statins	1.64 (1.41-1.91)	1.65 (1.42-1.92)	1.74 (1.47-2.06)	1.50 (1.30-1.74)	1.56 (1.35-1.81)	1.58 (1.35-1.85)
Antithrombotics	1.88 (1.49-2.37)	2.09 (1.65-2.65)	2.51 (1.92-3.29)	1.66 (1.33-2.07)	1.79 (1.43-2.24)	1.91 (1.50-2.42)
Antihypertensives	0.96 (0.81-1.14)	1.10 (0.92-1.33)	1.11 (0.90-1.37)	1.13 (0.97-1.33)	1.23 (1.05-1.45)	1.25 (1.05-1.49)
Hemorrhagic stroke						
Antihypertensives	1.33 (0.80-2.20)	1.44 (0.82-2.53)	2.54 (0.75-8.65)	3.26 (2.01-5.27)	3.63 (2.18-6.07)	13.50 (4.93-37.02)
Acute coronary syndrome						
Statins	1.69 (1.42-2.01)	1.76 (1.47-2.09)	1.84 (1.51-2.23)	1.49 (1.30-1.71)	1.59 (1.38-1.82)	1.63 (1.40-1.88)
Antithrombotics	2.70 (2.03-3.60)	2.71 (2.03-3.61)	3.22 (2.33-4.45)	1.65 (1.35-2.02)	1.76 (1.44-2.15)	1.79 (1.45-2.22)
Antihypertensives	2.08 (1.50-2.89)	2.07 (1.49-2.87)	2.10 (2.08-2.11)	1.63 (1.33-2.00)	1.64 (1.34-2.02)	1.70 (1.37-2.12)
Beta-blockers	1.61 (1.31-1.97)	1.59 (1.29-1.95)	1.58 (1.26-1.99)	1.45 (1.27-1.67)	1.45 (1.26-1.66)	1.47 (1.27-1.70)

Model 1: No adjustments

Model2: Adjustments made for age, visit to private specialist, and index year.

Model 3: Adjustments made for age, visit to private specialist, index year, and clustering within providers.

DISCUSSION

Key results

With the exception for antihypertensives, recording a diagnosis was associated with higher utilization of recommended medications for all studied diagnosis groups. The rate of diagnosis recording spanned from 15-47% and was especially low in TIA (men 15%, women 16% recorded).

Potential explanations

Several factors could explain the association between recording a diagnosis and dispensation of recommended medications. Previous studies have shown that the *transfer of information*, when patients move between different parts of the health care system, frequently is insufficient and that this lack of communication may affect subsequent patient care. Discharge summaries from hospitals may be lacking or may not reach the responsible primary care physician leading to an inadequate transfer of information.[7, 8]

There are several different electronic medical record systems used by primary care centers in Stockholm County. Some of them share systems with the hospitals enabling electronic transfer of information within the system. In these cases the primary care physician often has electronic access to detailed information on a patient's medical history including discharge medication. Theoretically this access could facilitate prescription, thus influencing dispensation. Other centers need to rely on old fashion mailing of patient information and referral notes. However, even those care givers who share the same electronic medical record system are not automatically able to read another care giver's information as informed consent from the patient is needed if a referral note has not been sent. Our registries do not allow us to know which centers use which electronic medical record systems. Thus we have not been able to determine if use of certain systems increases or decreases the likelihood of recording of a diagnosis. This could be a confounding factor.

When a patient chooses to re-list from one primary health care provider to another there may also be a risk of patient data not being transferred which could affect knowledge of patients' medical history and reduce the likelihood of both recording a diagnosis and prescription.

Knowledge of the condition in question including awareness of current guidelines is another factor that could influence both choice of diagnosis and dispensation. The level of knowledge may affect the likelihood of the physician focusing on the condition during visits and in continuation recording the diagnosis as well as the likelihood of prescribing medications according to guidelines and also motivating the patient to continue using the preventive medications.

There may also be important differences in *patient factors* between the recorded and not recorded groups which may lead to both a higher level of recorded diagnoses and increased dispensation in the recorded group. It is possible that patients who have a recorded diagnosis are more knowledgeable about their diagnoses and more assertive in their communication toward physicians which may lead to an increased level of physician prescribing. As this is a registry study it is difficult to ascertain whether or not this is the case.

A potential explanation for the lack of association between dispensation to antihypertensive therapy and recording of a diagnosis for most groups could stem from the fact that treatment of hypertension is well established. As many patients with stroke and/or ischemic heart disease have established hypertension[21, 22] they would be treated regardless of other diagnoses. This is not the case for antithrombotics and statins. Hypertension is also a common condition with a high prevalence of treatment and this diagnosis may be chosen instead of a diagnosis of cardio/cerebrovascular disease.

The strikingly low rate of recording of a diagnosis in TIA may partially be explained by the lack of remaining objective symptoms. Primary care physicians caring for a patient with chronic symptoms from a stroke will be reminded of the patient's previous disease and this may influence the likelihood of recording a stroke diagnosis. The same reminder is not provided when physicians see patients with a previous TIA in which case the diagnosis might not be recorded.

Policy implications

The results show that recording a diagnosis is associated with higher utilization of recommended medications. What does this mean for clinical practice? Could recording of a diagnosis be used as a quality indicator? We do not know of any other established quality indicators which target the lack of communication between hospitals and primary care. Previously published requirements for quality indicators are acceptability, feasibility,

reliability, sensitivity to change, and validity.[23] Future research would need to confirm that these requirements are met in which case "recording a diagnosis" could potentially be used as an indicator of both physician adherence to recommended treatment, and the quality of the chain of care from hospital to primary care. Information about degree of recording of diagnosis at each primary health care center could also be useful from the health care center's perspective as it provides information about their patient population which could be used to improve the provided care.

Strengths and limitations

A strength of the study is the use of registry data which has allowed for an unbiased inclusion of a large number of patients based on all residents in Stockholm County and not just a sample. However, using hospital registries is fraught with the risk of misdiagnosing which could lead to potential inclusion errors. In the case of our chosen diagnoses there are however quality registries [24-27] where 84-90% of hospital discharge diagnoses are registered. Diagnoses are generally better verified when reported to quality registries. Thus if a high proportion of discharge diagnoses are captured by the registries it is an indication of the high validity of the discharge diagnosing in stroke and ischemic heart disease in hospital. For TIA there may be greater uncertainty and variation in accuracy of diagnosing due to the diagnosis-defining lack of objective symptoms. Furthermore, we only included patients where there was an initial hospital diagnosis recorded since the main focus of our study was communication between hospitals and primary care. However it should be noted that in some cases a cardiovascular event may only be recorded in primary care and not in hospital.[28, 29] This means that we will not have included all patients with a stroke/TIA or acute coronary syndrome in the population during the study period.

There are different definitions of medication adherence. We have defined medication adherence as two dispensations in one year. However, our results may have been different if we had chosen another definition of medication adherence.

The absolute clinical benefits of our results are difficult to approximate in the present study since we have only studied dispensation of recommended secondary preventive medication and not actual clinical outcomes. Improved adherence to recommendations may be seen as a surrogate marker for clinical benefit since the clinical benefits of good adherence to medical therapy in cardiovascular conditions has been shown in multiple studies.[30-36] Further study is needed to determine if recording of diagnosis is associated with any improvements in

patient outcomes such as mortality, recurrence of disease etc. In table 3 when results are corrected for clustering within providers (model 3), the association between recorded primary care diagnosis and dispensed medications is strengthened. However, as some diagnostic groups are small (i.e. hemorrhagic stroke) some confidence intervals become wide and these results must be interpreted with caution.

Generalizability

The generalizability of the results depends on the definition of the study population, the included diagnoses, and the organization of the health care system. In the present study the aim was to investigate the association between recording a diagnosis and recommended treatment and it was necessary to include only diagnoses with clear recommendations regarding medical treatment. The initial choice of ICD-codes in the index year, where unspecific diagnoses (I64.9 - Stroke, not specified as hemorrhage or infarction for example) were not included, allowed a selection of patients with diagnoses for which secondary preventive pharmacologic treatment was indicated.

In order to utilize recording of a diagnosis in a diverse primary care population with a wide range of diagnoses, many of which are recorded in primary care only, the model used for recording of diagnosis would have to be altered and further studied. The generalizability is also limited to the record system and possible incentive structures used to stimulate recording of diagnoses as well as recall systems, the use of chronic diagnoses, and such factors. Different health care systems are organized differently. In systems where the diagnosis dictates which medications are subsidized, recording of a diagnosis may have a different impact and would need to be interpreted in light of this. If recording of a diagnosis were to be used as a quality indicator it would need to be used with caution and adapted to the health care system in question.

CONCLUSION

The results show that a physician recording a diagnosis in primary care seems beneficial for patient utilization of recommended medications in TIA, stroke, and acute coronary syndrome. Patients who are diagnosed with their hospital diagnosis in primary care receive recommended treatment to a higher extent than patients without such a diagnosis in primary care. Further study is necessary in order to determine if "recording a diagnosis" may be used as a quality indicator.

AUTHOR CONTRIBUTIONS

Cecilia Dahlgren: Contributed to the study design, researched data, contributed to analysis and interpretation of data, and drafted the manuscript.

Lukas Geary: Contributed to the study design, researched the literature, contributed to analysis and interpretation of data, and drafted the manuscript.

Clas Rehnberg, Karin Schenck-Gustafsson, and Per Wändell: Contributed to the study design, contributed to analysis and interpretation of data, and critically revised the manuscript.

Jan Hasselström and Mia von Euler: Came up with the original idea, contributed to the study design, contributed to analysis and interpretation of data, and critically revised the manuscript.

All authors approved the final manuscript.

COMPETING INTERESTS

None declared.

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DATA SHARING

Additional aggregate level data can be made available by emailing cecilia.dahlgren@ki.se

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Figure 1. Selection of study population

Figure 2. Illustration of index year, recording period and dispensation period

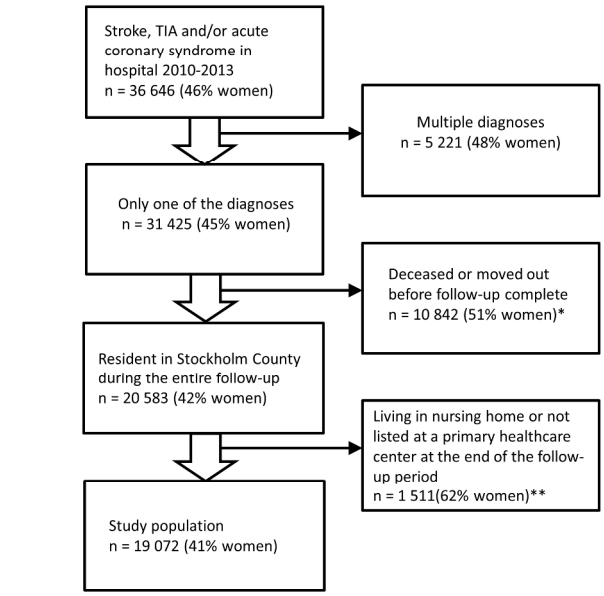

Figure 1. Selection of study population

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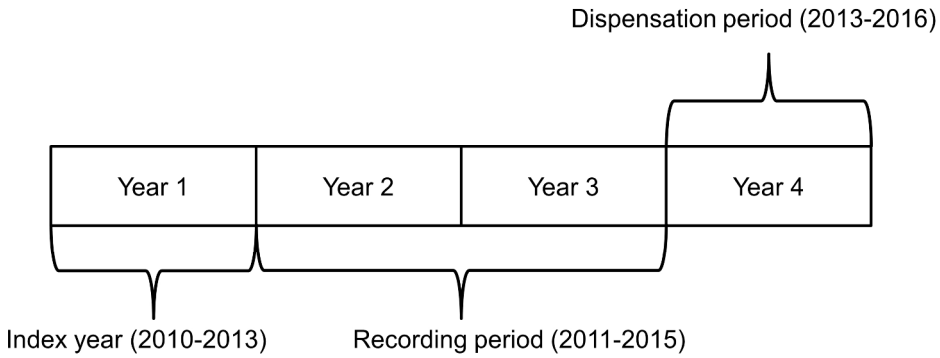

Figure 2. Illustration of index year, recording period, and dispensation period

254x190mm (300 x 300 DPI)

APPENDIX 1: ICD10-codes

Ischemic stroke

Index year diagnosis
I63.0, I63.1, I63.2, I63.3, I63.4, I63.5, I63.6, I63.8, I63.9

Recording period diagnosis
I63.0, I63.1, I63.2, I63.3, I63.4, I63.5, I63.6, I63.8, I63.9, I64.9, I69.3, I69.4, I69.8, Z86.6B, Z86.7C

ICD10P: I63.-, I64.-, I67.-P, I69.-

Transient ischemic attack (TIA)

Index year diagnosis
G45.0, G45.1, G45.3, G45.8, G45.9

Recording period diagnosis
G45.0, G45.1, G45.3, G45.8, G45.9, Z86.6A, Z86.6B

ICD10P: G45.-P , I69.-

Hemorrhagic stroke

Index year diagnosis
I61.0, I61.1, I61.2, I61.3, I61.4, I61.5, I61.6, I61.8, I61.9

Recording period diagnosis
I61.0, I61.1, I61.2, I61.3, I61.4, I61.5, I61.6, I61.8, I61.9, I64.9, I69.1, I69.2, I69.4, I69.8, Z86.7C
ICD-10P: I61.-P, I62, I64.-, I67.-P, I69.-

Acute coronary syndrome

Index year diagnosis
I20.0, I21.0, I21.1, I21.2, I21.3, I21.4, I21.4A, I21.4B, I21.4W, I21.4X, I21.9, I22.0, I22.1, I22.8, I22.9, I23.0, I23.1, I23.2, I23.3, I23.4, I23.5, I23.6, I23.8

Recording period diagnosis
I20.0, I20.1, I20.8, I20.9, I21.0, I21.1, I21.2, I21.3, I21.4, I21.4A, I21.4B, I21.4W, I21.4X, I21.9, I22.0, I22.1, I22.8, I22.9, I23.0, I23.1, I23.2, I23.3, I23.4, I23.5, I23.6, I23.8, I24.0, I24.1, I24.8, I24.9, I25.0, I25.1, I25.2, I25.5, I25.6, I25.8, I25.9

ICD 10P: I20.0, I21.-P, I22, I23, I24, I25.-P

APPENDIX 2: ANALYSIS OF PATIENTS WITH MORE THAN ONE EVENT

In the main analysis of this paper, 5 221 patients were excluded from the study population because they had had hospital admissions with more than one of the studied diagnoses or because they had had hospital admissions with the same diagnosis in more than one index year. In the following sensitivity analysis, we analyze this sub-group of patients. It should be noted that patients with several hospital admission with the same diagnosis within the same index year were not excluded from the main analysis.

The 5 221 patients in the sub-group had a total of 11 458 events during the period 2010-2013. An event is defined as all discharge diagnoses in one diagnosis group in one index year for an individual. A patient with two ischemic strokes in one year is counted as only one event. A patient who has an ischemic stroke and a TIA in the same year is counted as two events. Likewise, a patient that has a TIA one year and another TIA the year after is also counted as two events.

In order to keep as much information as possible, we allowed patients to occur more than once in the analysis. A patient with two events, e.g. a TIA in 2010 and another TIA in 2011 were included twice in the material. Apart from that, the same exclusion criteria were applied as in the main analysis, see *Figure A2-1*, and a total of 5 885 events were finally included in the analysis.

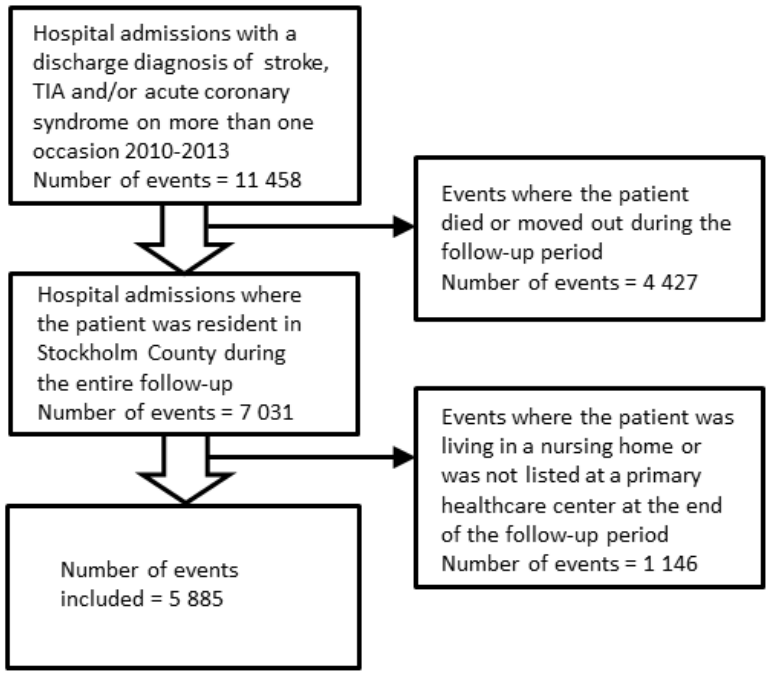

Figure A2-1 Selection of events included in analysis of strata of patients with multiple events.

Table A2-1 shows the absolute number and proportion of patients with and without a recorded diagnosis in primary care. The results are very similar to the results of the groups in the main analysis when it comes to proportion of recorded patients. However, patients in the strata with multiple events had a recorded diagnosis in primary care to a slightly higher extent than those with only one event. The only exception was men with hemorrhagic stroke where 42 percent were recorded in the strata with multiple events and 43 percent were recorded in the main analysis.

Table A2-1. Absolute number and proportion in strata with multiple events, with and without a recorded diagnosis in primary care, by diagnosis (the same individual can occur more than once in the material).

	Recorded		**Not recorded**	
	Women	*Men*	*Women*	*Men*
TIA	136 (23%)	113 (16%)	465 (77%)	602 (84%)
Ischemic stroke	478 (46%)	672 (52%)	564 (54%)	622 (48%)
Hemorrhagic stroke	55 (40%)	78 (42%)	83 (60%)	107 (58%)
Acute coronary syndrome	305 (44%)	588 (48%)	382 (56%)	632 (52%)

Table A2-2 shows the absolute number and proportion of patients in strata with multiple events that were dispensed two prescriptions in the dispensation period, by medication class,

recorded/not recorded status, and diagnosis. In 18 out of 22 groups, the results point in the same direction as in the main analysis, that recorded patients are dispensed two medications to a higher extent than not recorded patients in most groups.

Table A2-2. Absolute number and proportion in strata with multiple events that were dispensed two prescriptions in the dispensation period, by medication class, recorded/not recorded status, and diagnosis (the same individual can occur more than once in the material).

			Statins	Antithrombotics	Antihypertensives	Beta-blockers
TIA	Women	Not recorded	244 (52 %)	418 (90 %)	398 (86 %)	
		Recorded	69 (51 %)	127 (93 %)	104 (76 %)	
	Men	Not recorded	410 (68 %)	527 (88 %)	481 (80 %)	
		Recorded	94 (81 %)	113 (97 %)	96 (83 %)	
Ischemic stroke	Women	Not recorded	290 (51 %)	480 (85 %)	483 (86 %)	
		Recorded	293 (61 %)	417 (87 %)	394 (82 %)	
	Men	Not recorded	410 (66 %)	518 (83 %)	507 (82 %)	
		Recorded	477 (71 %)	604 (90 %)	552 (82 %)	
Hemorrhagic stroke	Women	Not recorded			49 (59 %)	
		Recorded			40 (73 %)	
	Men	Not recorded			85 (79 %)	
		Recorded			69 (88 %)	
Acute coronary syndrome	Women	Not recorded	205 (54 %)	331 (87 %)	352 (92 %)	304 (80 %)
		Recorded	205 (67 %)	287 (94 %)	293 (96 %)	256 (84 %)
	Men	Not recorded	467 (74 %)	556 (88 %)	574 (91 %)	498 (79 %)
		Recorded	468 (80 %)	525 (89 %)	551 (94 %)	491 (84 %)

When adjusting for confounders (Table A2-3), the confidence intervals are wider for the strata with multiple events because of the lower number of included observations. The differences between the recorded and not recorded group are statistically significant to a lesser extent than in the main analysis. Model 3 is included for comparative purposes but should be interpreted with caution. For hemorrhagic stroke, model 3 is not specified because of the few observations in the group and the large number of categories in the provider variable.

Table A2-3. Crude and adjusted odds ratios for being dispensed two prescriptions in the dispensation period according to recorded/not recorded status, by sex and diagnosis. Patients that are not recorded are the reference group. OR >1 means recorded patients are more likely to have two dispensations in the dispensation period (the same individual can occur more than once in the material).

	Women			**Men**		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
TIA						
Statins	0.90 (0.60-1.34)	0.85 (0.56-1.29)	0.77 (0.41-1.45)	1.63 (0.99-2.69)	1.64 (0.99-2.72)	1.96 (1.03-3.74)
Antithrombotics	2.04 (0.78-5.34)	2.07 (0.79-5.43)	1.80 (0.49-6.60)	3.30 (1.01-10.81)	3.29 (0.99-10.88)	3.21 (3.14-3.28)
Antihypertensives	0.48 (0.30-0.79)	0.50 (0.30-0.83)	0.39 (0.17-0.88)	0.96 (0.56-1.63)	0.93 (0.54-1.59)	1.20 (0.58-2.50)
Ischemic stroke						
Statins	1.33 (1.02-1.73)	1.37 (1.05-1.78)	1.57 (1.10-2.24)	1.30 (1.01-1.68)	1.32 (1.02-1.70)	1.31 (0.95-1.80)
Antithrombotics	1.03 (0.69-1.54)	1.15 (0.77-1.74)	0.90 (0.53-1.53)	2.14 (1.45-3.17)	2.31 (1.54-3.46)	3.15 (3.12-3.18)
Antihypertensives	0.75 (0.52-1.08)	0.95 (0.64-1.41)	1.22 (0.71-2.09)	0.98 (0.72-1.33)	1.02 (0.74-1.40)	1.17 (0.77-1.78)
Hemorrhagic stroke						
Antihypertensives	1.73 (0.81-3.72)	1.53 (0.62-3.78)	*	1.77 (0.72-4.34)	2.02 (0.78-5.20)	*
Acute coronary syndrome						
Statins	1.68 (1.20-2.34)	2.16 (1.51-3.11)	1.77 (1.04-3.01)	1.30 (0.96-1.76)	1.39 (1.03-1.89)	1.48 (0.99-2.21)
Antithrombotics	4.57 (2.00-10.44)	5.05 (2.19-11.65)	9.61 (2.74-33.69)	1.10 (0.71-1.72)	1.17 (0.75-1.82)	1.06 (0.60-1.88)
Antihypertensives	2.28 (0.95-5.52)	2.23 (0.91-5.46)	0.83 (0.81-0.85)	1.23 (0.75-2.03)	1.28 (0.77-2.13)	1.46 (1.44-1.47)
Beta-blockers	1.44 (0.94-2.23)	1.45 (0.94-2.26)	1.13 (0.60-2.10)	1.28 (0.93-1.77)	1.31 (0.95-1.82)	1.37 (0.88-2.12)

Model 1: No adjustments

Model2: Adjustments made for age, visit to private specialist, and index year.

Model 3: Adjustments made for age, visit to private specialist, index year, and clustering within providers (model 3 is not specified for hemorrhagic stroke because of the small number of individuals in the group and the large number of categories in the provider variable)

APPENDIX 3: ATC-codes

Statins

C10AA

Antithrombotics

B01AC04, B01AC06, B01AC07, B01AC22, B01AC24, B01AC30, B01AA, B01AE07, B01AF

Antihypertensives

C03A, C03B, C03C, C03D, C03E, C07, C08, C09

Beta-blockers

C07

APPENDIX 4: DESCRIPTIVE STATISTICS

Table A4-1. Mean age of men and women by recorded/not recorded status and diagnosis. Also proportion of men and women with at least one visit to a private specialist during the recording period, by recorded/not recorded status and diagnosis.

		Recorded		Not recorded	
		Women	*Men*	*Women*	*Men*
TIA	*Mean age*	73.1	71.4	73.7	70.5
	At least one visit to private specialist	20%	17%	21%	23%
Ischemic stroke	*Mean age*	71.9	69.9	74.3	70.5
	At least one visit to private specialist	16%	14%	18%	20%
Hemorrhagic stroke	*Mean age*	67.4	62.9	67.6	63.7
	At least one visit to private specialist	19%	15%	9%	14%
Acute coronary syndrome	*Mean age*	74.0	67.9	73.7	67.0
	At least one visit to private specialist	22%	21%	26%	33%

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5-6
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7
Bias	9	Describe any efforts to address potential sources of bias	7-8
Study size	10	Explain how the study size was arrived at	5 -6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	Appendix 2
		(*c*) Explain how missing data were addressed	n/a
		(*d*) If applicable, explain how loss to follow-up was addressed	6
		(*e*) Describe any sensitivity analyses	6, Appendix 2
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	figure 1, pages 5-6
		(b) Give reasons for non-participation at each stage	figure 1
		(c) Consider use of a flow diagram	figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1, table appendix 4
		(b) Indicate number of participants with missing data for each variable of interest	n/a
		(c) Summarise follow-up time (eg, average and total amount)	n/a
Outcome data	15*	Report numbers of outcome events or summary measures over time	table 2
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Tables 2 and 3, pages7-8
		(*b*) Report category boundaries when continuous variables were categorized	n/a
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Appendix 2
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

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

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Recording a Diagnosis of Stroke, TIA, or Myocardial Infarction in Primary Health Care and the Association with Dispensation of Secondary Preventive Medication – a Registry Based Prospective Cohort Study

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Recording a Diagnosis of Stroke, TIA, or Myocardial Infarction in Primary Health Care and the Association with Dispensation of Secondary Preventive Medication – a Registry Based Prospective Cohort Study

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ABSTRACT

Objectives: The aim of this study was to explore whether recording in primary care of a previously recorded hospital diagnosis was associated with increased patient utilization of recommended medications.

Design: Registry based prospective cohort study.

Setting and participants: 19 072 patients with a hospital discharge diagnosis of transient ischemic attack (TIA), stroke or acute coronary syndrome from hospitals in Stockholm County 2010- 2013 were included in the study.

Main outcome measure: The outcome of the study was medication dispensation as a marker of adherence to recommended medications. Adherence was defined as having had at least two filled prescriptions in the third year following hospital discharge.

Results: Recording a diagnosis was associated with higher utilization of all recommended medications with the exception of antihypertensives in patients with TIA. The differences between the groups with and without a recorded diagnosis remained after adjusting for age, sex, index year, and visits to private practitioners.

Dispensation of antithrombotics was high overall, 80-90% in patients without a recorded diagnosis and 90-94% for those with a diagnosis. Women with recorded ischemic stroke/TIA/acute coronary syndrome (56-71%) were dispensed more statins than those with no recorded diagnosis (46-59%). Similarly 68-83% of men with a recorded diagnosis were dispensed statins (57-77% in men with no recorded diagnosis).

The rate of diagnosis recording spanned from 15-47% and was especially low in TIA (men 15%, women 16%).

Conclusion: Recording a diagnosis of TIA/stroke or acute coronary syndrome in primary care was found to be associated with higher dispensation of recommended secondary preventive medications. Further study is necessary in order to determine the mechanisms underlying our results and to establish the utility of our findings.

Strengths and limitations of this study

- Whether or not recording a primary care diagnosis is associated with greater dispensation of recommended medication is something that, to our knowledge, has not been investigated before.
- The study is based on data from a registry, which includes all residents in Stockholm County and not just a sample.
- In stroke and acute coronary syndrome the validity of discharge diagnosing in hospitals is higher than for TIA where there may be greater uncertainty and variation in accuracy of diagnosing due to the diagnosis defining lack of objective symptoms.
- The included diagnoses were chosen in order to select patients where secondary preventive pharmacologic treatment was indicated and clearly defined which limits the possibility to generalize the results to a more diverse primary care population.

INTRODUCTION

Fragmentation of health care and the lack of communication between different segments of the health care system are well known problems affecting many countries world-wide, including Sweden.[1-6] Previous studies have shown that the transfer of information between hospitals and primary care including information on discharge medication, frequently is insufficient and that this lack of communication may affect subsequent patient care.[7, 8] Primary care is the level of care most patients with chronic disease will depend upon for their long term care in Sweden.[9] It is mandatory in Stockholm for a primary care physician to record at least one diagnosis after every consultation. To our knowledge it has not been studied whether the choice of diagnosis influences patient related outcomes such as medication utilization. For several acute conditions initially treated in hospital, an important part of chronic care is patients taking secondary preventive medications. It is however well known that adherence to recommended medications declines after discharge and is often sub-optimal in the long term.[10-13]

In this study, we explore if "recording a diagnosis" has an impact on the utilization of recommended medications. In our study, if a primary care physician "records a diagnosis" it means that a patient discharged from hospital care to primary care is diagnosed with their hospital diagnosis, or a corresponding follow-up diagnosis, in primary care at some point. A diagnosis that is not being recorded in primary care could be an indication of lack of communication between the different health care providers, which could affect the quality of the subsequent treatment. If there is an association between recording of diagnosis and utilization of recommended medications, then "recording a diagnosis" could potentially be used as a quality indicator in primary care.

To investigate whether recording a diagnosis in primary care is associated with increased dispensation of recommended medication in the long term care, four common groups of diagnoses with clear and evidence based clinical guidelines,[14-16] with regard to medical treatment were chosen: acute coronary syndromes, ischemic and hemorrhagic stroke, and transient ischemic attack (TIA).

Objective

The aim of this study was to explore whether recording a diagnosis in primary care was associated with patient utilization of recommended medications in the long term. We hypothesized that patients with a recorded diagnosis were more likely to be dispensed recommended medications.

METHODS

Setting

Stockholm County Council provides health care to 2.2 million inhabitants at three levels: inpatient acute care at 7 hospitals, outpatient secondary specialist care at hospitals or contracted specialist units, and primary care in 208 centers. Approximately 90 percent of the population chooses to list at a primary care practice (private or public) for their basic care. [17] "Listing" means a patient choosing a specific center to be their provider of primary care, with complete freedom to change provider at any point in time. The remaining part will be living in nursing homes or be unlisted. As an alternative to primary care practices, people may also visit some hundred private specialists working on the basis of the National tariff system (*nationella taxan*).

Study Design and Participants

For this registry based prospective cohort study, data from the Stockholm County Council regional healthcare database, VAL, was used. The VAL database contains anonymized and encrypted data on the health care consumption, including dispensed medications, for the 2.2 million individuals residing in Stockholm County. The data include detailed information from both inpatient and outpatient care including primary care. Diagnoses from inpatient care and secondary care are registered from 1993 and diagnoses from primary care are available from 2003. More than 95 percent of visits to primary care physicians are coded with one or more diagnoses according to the ICD-system. The database also contains information on age, sex, migration, and mortality for all residents.[18]

Unique patients living in Stockholm County who received a discharge diagnosis of stroke, TIA, and/or acute coronary syndrome from hospitals in Stockholm County between 1st

January 2010 and 31st December 2013 (see supplementary file table S1 for specific ICD-10 codes) were selected using the VAL-database. The year in which a patient received a diagnosis is referred to as the *index year*. Patients receiving different pre-specified discharge diagnoses during the study period or the same discharge diagnoses during more than one year were excluded from the study ("multiple diagnoses" in Figure 1). By excluding patients with more than one of the diagnoses (e.g. acute coronary syndrome and hemorrhagic stroke) we were able to be more certain of which medications were recommended as secondary prevention for each patient. Patients discharged with the same diagnosis multiple times during the study period (e.g. ischemic stroke during the index year and the year after) were excluded since, in those cases, it would have been difficult to determine if a hospital or a primary care center was in charge of the patients' long term care during the study. As a sensitivity analysis we have followed the excluded patients with multiple diagnoses in the same way as the included patients. These results are presented in the supplementary file.

We also excluded patients who died before the end of their follow-up period, patients living in nursing homes, and individuals that were not listed at a primary healthcare center.

Out of the total 36 646 patients initially selected, 19 072 were finally included in the study population. Out of these, 41 percent were women (see Figure 1).

Recording a diagnosis in primary care

The recording of a diagnosis in primary care was the pre-defined *exposure* within the cohort. Recording a diagnosis was defined as the recording of a primary care diagnosis related to, but not necessarily identical with, the initial hospital diagnosis during the two years following the index year (irrespective of month). This period was defined as the *recording period*. Patients with a hospital diagnosis in 2010 were thus analyzed with regards to recording of a diagnosis in primary care in 2011-2012 and those with hospital diagnosis 2011 were analyzed 2012-2013 etc. Patients not receiving any of the pre-specified diagnoses (see supplementary file, table S1) were defined as *not recorded.*

Medication adherence and dispensation

The *outcome* of the study was medication dispensation. Data on dispensation of medications in the entire patient cohort was extracted as a marker of adherence. Patients were considered adherent if they had at least two filled prescriptions in the third year following their index event, henceforth referred to as *dispensation period* (see Figure 2). In Sweden, every filled

prescription for chronic conditions will last for three months and thus two dispensations in one year will last for 180 days. We chose two and not one dispensation as two dispensations more strongly implies use of the medication. The third year following their index year was chosen because in many cases the hospital will be in charge of prescriptions for the first period following the index event. However, these prescriptions will last for up to a maximum of one year and if the prescribed therapy is to continue it is up to the primary care physician to take over prescriptions. Also, the third year was chosen to make certain that there was no overlap between the outcome and the exposure.

Recommended medications in ischemic stroke and TIA include antihypertensives and statins.[14] Antiplatelet agents are recommended in non-embolic stroke/TIA, while anticoagulants are recommended in embolic stroke/TIA.[14] For hemorrhagic stroke, antihypertensives are recommended.[16] In patients with acute coronary syndromes without persistent ST-segment elevation guidelines recommend statins, antiplatelet agents, and that patients are kept normotensive.[15] Additionally, regional guidelines in Stockholm[19, 20] have recommended beta-blockers to all patients discharged from hospitals with acute coronary syndrome during the entire time period of our study.

Medications were divided into four groups: antithrombotics (antiplatelet agents and anticoagulants including new oral anticoagulants), antihypertensives, statins, and beta-blockers. Medications studied for TIA, ischemic stroke, and acute coronary syndrome were antihypertensives, antithrombotics, and statins. Additionally, in acute coronary syndrome beta-blockers were studied. For hemorrhagic stroke only data on dispensation of antihypertensives were collected. The specific ATC-codes used can be seen in the supplementary file, table S2. Medication dispensation was compared between recorded and not recorded patients during all recording periods (2011-2016).

Potential confounders

Sex, age, index year, and visits to private specialists were identified as potential confounders. There may be differences between men and women both when it comes to the exposure, likelihood of recording a diagnosis in primary care, and the outcome, likelihood of receiving certain medications.[10] Age is also a factor that may be associated with both the exposure and the outcome. Elderly patients have greater comorbidity and it may be argued that this increases the number of diagnoses from which the primary care physician can choose. Also,

this comorbidity implies that patients may have an indication for several different medications potentially influencing prescription behavior.

Index year may influence the results should diagnosis-recording behavior and/or medication prescription patterns change over time. Table S6 in the supplementary file shows descriptive statistics for age and for visits to private specialists.

Lastly, as private specialists linked to the National tariff system often serve as a substitute to primary care physicians, their patients are less likely to receive a primary care diagnosis. In addition, these visits affect the outcome as private specialists also prescribe medications.

Statistical analysis

Standard descriptive statistics were used and data are presented as proportions. Logistic regression was used in the analyses to calculate adjusted odds ratios with 95 percent confidence intervals for drug dispensation for recorded vs not recorded patients (reference group). Adjustments were made for age (age categories <51, 51-65, 66-75, and >75), sex, index year, and for health care consumption in the form of visits to private specialists that may function as a substitute to some patients' primary care provider. The patients in our dataset are grouped within different primary health care centers. This implies a risk that the data are cluster-correlated and that the estimated standard errors are not independent. In order to adjust for this, without adjusting for the provider effect, which could be a mediator in the casual pathway, we have based standard errors on the "sandwich" variance estimator. All statistical analyses were performed using SAS software, version 9.4 (SAS Institute Inc., Cary, NC).

Ethical permit

The study was approved by the regional ethics review board in Stockholm, Dnr 2015/803-31/5 and Dnr 2016/1547-32.

RESULTS

Table 1 shows the absolute number and proportion of men and women with a recorded diagnosis in primary care, by diagnosis. The lowest proportion of recorded patients in primary care was found in the group of patients with TIA whereas patients with acute coronary syndromes had the highest rate of recording. In all studied diagnoses, except for TIA, a lower percentage of women were recorded compared to men.

Table 1. Absolute number and proportion of men and women with and without a recorded diagnosis in primary care, by diagnosis.

	Recorded		Not recorded	
	Women	*Men*	*Women*	*Men*
TIA	347 (16%)	308 (15%)	1 813 (84%)	1 746 (85%)
Ischemic stroke	1 189 (41%)	1 579 (46%)	1 683 (59%)	1 844 (54%)
Hemorrhagic stroke	105 (35%)	177 (43%)	193 (65%)	237 (57%)
Acute coronary syndrome	1 076 (44%)	2 580 (47%)	1 343 (56%)	2 852 (53%)

Table 2 shows medication dispensation for recorded and not recorded patients for all diagnosis groups in both men and women. Patients with a recorded diagnosis were more likely to be dispensed two prescriptions of statins, antithrombotics, and beta-blockers in the dispensation period across all studied diagnoses. The difference remained after adjusting for age, sex, index year, and visits to private specialists (table 3 and table S7 in the supplementary file where results are stratified by sex).

For antihypertensives, the adjusted results show that recorded patients with stroke and acute coronary syndrome were more likely to be dispensed two prescriptions. However, recorded patients with TIA were less likely to be dispensed antihypertensives than the not recorded group.

Adjusting for clustering with the "sandwich" variance estimator only marginally affected the confidence intervals, which implies that the data are not clustered to a high extent.

Table 2. Absolute number and proportion of men and women dispensed two prescriptions in the dispensation period, by medication class, recorded/not recorded status, and diagnosis.

			Statins	Antithrombotics	Antihypertensives	Beta-blockers
TIA	Women	Not recorded	827 (46%)	1 442 (80%)	1 271 (70%)	
		Recorded	195 (56%)	313 (90%)	221 (64%)	
	Men	Not recorded	992 (57%)	1 451 (83%)	1 222 (70%)	
		Recorded	210 (68%)	283 (92%)	211 (69%)	
Ischemic stroke	Women	Not recorded	838 (50%)	1 401 (83%)	1 276 (76%)	
		Recorded	736 (62%)	1 074 (90%)	893 (75%)	
	Men	Not recorded	1 122 (61%)	1 591 (86%)	1 373 (74%)	
		Recorded	1 106 (70%)	1 441 (91%)	1 212 (77%)	
Hemorrhagic stroke	Women	Not recorded			120 (62%)	
		Recorded			72 (69%)	
	Men	Not recorded			147 (62%)	
		Recorded			149 (84%)	
Acute coronary syndrome	Women	Not recorded	799 (59%)	1 136 (85%)	1 210 (90%)	1 015 (76%)
		Recorded	767 (71%)	1 008 (94%)	1 022 (95%)	896 (83%)
	Men	Not recorded	2 187 (77%)	2 561 (90%)	2 580 (90%)	2 208 (77%)
		Recorded	2 143 (83%)	2 414 (94%)	2 423 (94%)	2 149 (83%)

Table 3. Crude and adjusted odds ratios for being dispensed two prescriptions in the dispensation period according to recorded/not recorded status, by diagnosis. Not recorded patients are the reference group. Odds Ratios >1 mean recorded patients are more likely to have two dispensations in the dispensation period.

	Crude Odds Ratios (95% Confidence Intervals)	Adjusted Odds Ratios* (95% Confidence Intervals)
TIA		
Statins	1.55 (1.31-1.84)	1.53 (1.28-1.82)
Antithrombotics	2.33 (1.76-3.08)	2.33 (1.74-3.11)
Antihypertensives	0.83 (0.69-0.99)	0.80 (0.66-0.96)
Ischemic stroke		
Statins	1.59 (1.43-1.76)	1.58 (1.42-1.76)
Antithrombotics	1.78 (1.52-2.08)	1.92 (1.63-2.27)
Antihypertensives	1.05 (0.94-1.18)	1.16 (1.03-1.31)
Hemorrhagic stroke		
Antihypertensives	2.21 (1.57-3.12)	2.54 (1.72-3.76)
Acute coronary syndrome		
Statins	1.58 (1.42-1.75)	1.64 (1.47-1.83)
Antithrombotics	1.97 (1.68-2.32)	2.02 (1.72-2.38)
Antihypertensives	1.74 (1.47-2.07)	1.76 (1.48-2.10)
Beta-blockers	1.50 (1.34-1.68)	1.48 (1.32-1.66)

* *Adjustments made for age, sex, index year, and visits to private specialists. To adjust for clustering, standard errors are based on the "sandwich" variance estimator.*

DISCUSSION

Key results

Recording a diagnosis was associated with higher utilization of recommended medications for all studied diagnosis groups, except for antihypertensives in TIA patients. The rate of diagnosis recording spanned from 15-47% and was especially low in TIA (men 15%, women 16% recorded).

Potential explanations

Several factors could explain the association between recording a diagnosis and dispensation of recommended medications. Previous studies have shown that the *transfer of information*, when patients move between different parts of the health care system, frequently is insufficient and that this lack of communication may affect subsequent patient care. Discharge summaries from hospitals may be lacking or may not reach the responsible primary care physician leading to an inadequate transfer of information.[7, 8]

There are several different electronic medical record systems used by primary care centers in Stockholm County. Some of them share systems with the hospitals enabling electronic transfer of information within the system. In these cases, the primary care physician often has electronic access to detailed information on a patient's medical history including discharge medication. Theoretically, this access could facilitate prescription, thus influencing dispensation. Other centers need to rely on old fashion mailing of patient information and referral notes. However, even those caregivers who share the same electronic medical record system are not automatically able to read another care giver's information as informed consent from the patient is needed if a referral note has not been sent. Our registries do not allow us to know which centers use which electronic medical record systems. Thus, we have not been able to determine if use of certain systems increases or decreases the likelihood of recording of a diagnosis. This could be a confounding factor.

When a patient chooses to re-list from one primary health care provider to another there may also be a risk of patient data not being transferred which could affect knowledge of patients' medical history and reduce the likelihood of both recording a diagnosis and prescription.

Knowledge of the condition in question including awareness of current guidelines is another factor that could influence both choice of diagnosis and dispensation. The level of knowledge

may affect the likelihood of the physician focusing on the condition during visits and in continuation recording the diagnosis as well as the likelihood of prescribing medications according to guidelines and motivating the patient to continue using the preventive medications.

There may also be important differences in *patient factors* between the recorded and not recorded groups, which may lead to both a higher level of recorded diagnoses and increased dispensation in the recorded group. It is possible that patients who have a recorded diagnosis are more knowledgeable about their diagnoses and more assertive in their communication toward physicians, which may lead to an increased level of physician prescribing. As this is a registry study, it is difficult to ascertain whether this is the case.

In contrast to the overall pattern, TIA patients with a recorded diagnosis were dispensed less antihypertensives than those with no recorded diagnosis. A potential explanation for the varying associations between dispensation of antihypertensive therapy and recording of the different diagnoses could stem from the fact that treatment of hypertension is well established. As many patients with stroke/TIA and/or ischemic heart disease have established hypertension [21, 22] they would be treated regardless of other diagnoses. This is not the case for antithrombotics and statins. Hypertension is also a common condition with a high prevalence of treatment and this diagnosis may be chosen instead of a diagnosis of cardio/cerebrovascular disease. However, it should be noted that the proportion of recorded TIA patients is small and the data concerning this group should be interpreted with caution.

The strikingly low rate of recording of a diagnosis in TIA may partially be explained by the lack of remaining objective symptoms. Primary care physicians caring for a patient with chronic symptoms from a stroke will be reminded of the patient's previous disease and this may influence the likelihood of recording a stroke diagnosis. The same reminder is not provided when physicians see patients with a previous TIA in which case the diagnosis might not be recorded. However the low rate of recording in TIA needs further research as the causes are, is in all likelihood, multifactorial. Acute coronary syndrome patients also lack symptoms at follow up in many cases, and still those patients are recorded to a high degree.

Policy implications

The results show that recording a diagnosis is associated with higher utilization of recommended medications. Diagnosis recording is potentially an indicator of physician

adherence to recommended treatment and a marker of an intact chain of care from hospital to primary care. What does this mean for clinical practice? Could recording of a diagnosis be used as a quality indicator? Previously published requirements for quality indicators are acceptability, feasibility, reliability, sensitivity to change, and validity.[23] Future research needs to confirm that these requirements are met for "recording a diagnosis" before its utility as a quality indicator can be considered. Information about degree of recording of diagnosis at each primary health care center could also be useful from the health care center's perspective as it provides information about their patient population, which could be used to improve the provided care.

Strengths and limitations

A strength of the study is the use of registry data, which has allowed for an unbiased inclusion of a large number of patients based on all residents in Stockholm County and not just a sample. Using hospital registries is fraught with the risk of misdiagnosing which could lead to potential inclusion errors. However, in the case of our chosen diagnoses, there are quality registries [24-27] where 84-90% of hospital discharge diagnoses are registered. Diagnoses are generally better verified when reported to quality registries. Thus if a high proportion of discharge diagnoses are captured by the registries it is an indication of the high validity of the discharge diagnosing in stroke and ischemic heart disease in hospital. For TIA there may be greater uncertainty and variation in accuracy of diagnosing due to the diagnosis-defining lack of objective symptoms. Furthermore, we only included patients where there was an initial hospital diagnosis recorded since the focus of our study was communication between hospitals and primary care. However it should be noted that in some cases a cardiovascular event may only be recorded in primary care and not in hospital.[28, 29] This means that we will not have included all patients with a stroke/TIA or acute coronary syndrome in the population during the study period.

There are different definitions of medication adherence. We have defined medication adherence as two dispensations in one year. However, our results may have been different if we had chosen another definition of medication adherence.

The absolute clinical benefits of our results are difficult to approximate in the present study since we have only studied dispensation of recommended secondary preventive medication and not actual clinical outcomes. Improved adherence to recommendations may be seen as a surrogate marker for clinical benefit since the clinical benefits of good adherence to medical

therapy in cardiovascular conditions has been shown in multiple studies.[30-36] Further study is needed to determine if recording of diagnosis is associated with any improvements in patient outcomes such as mortality, recurrence of disease etc.

Generalizability

The generalizability of the results depends on the definition of the study population, the included diagnoses, and the organization of the health care system. In the present study, the aim was to investigate the association between recording a diagnosis and recommended treatment and it was necessary to include only diagnoses with clear recommendations regarding medical treatment. The initial choice of ICD-codes in the index year, where unspecific diagnoses (I64.9 - Stroke, not specified as hemorrhage or infarction for example) were not included, allowed a selection of patients with diagnoses for which secondary preventive pharmacologic treatment was indicated.

In order to utilize recording of a diagnosis in a diverse primary care population with a wide range of diagnoses, many of which are recorded in primary care only, the model used for recording of diagnosis would have to be altered and further studied. The generalizability is also limited to the record system and possible incentive structures used to stimulate recording of diagnoses as well as recall systems, the use of chronic diagnoses, and such factors. Different health care systems are organized differently. In systems where the diagnosis dictates which medications are subsidized, recording of a diagnosis may have a different impact and would need to be interpreted in light of this. If recording of a diagnosis were to be used as a quality indicator it would need to be used with caution and adapted to the health care system in question.

CONCLUSION

The results show that a physician recording a diagnosis in primary care seems beneficial for patient utilization of recommended medications in TIA, stroke, and acute coronary syndrome. Patients who are diagnosed with their hospital diagnosis in primary care receive recommended treatment to a higher extent than patients without such a diagnosis in primary care. Further study is necessary in order to determine if “recording a diagnosis” may be used as a quality indicator.

AUTHOR CONTRIBUTIONS

Cecilia Dahlgren: Contributed to the study design, researched data, contributed to analysis and interpretation of data, and drafted the manuscript.

Lukas Geary: Contributed to the study design, researched the literature, contributed to analysis and interpretation of data, and drafted the manuscript.

Clas Rehnberg, Karin Schenck-Gustafsson, and Per Wändell: Contributed to the study design, contributed to analysis and interpretation of data, and critically revised the manuscript.

Jan Hasselström and Mia von Euler: Came up with the original idea, contributed to the study design, contributed to analysis and interpretation of data, and critically revised the manuscript.

All authors approved the final manuscript.

COMPETING INTERESTS

None declared.

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DATA SHARING

Additional aggregate level data can be made available by emailing cecilia.dahlgren@ki.se

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Figure 1. Selection of study population

Figure 2. Illustration of index year, recording period and dispensation period

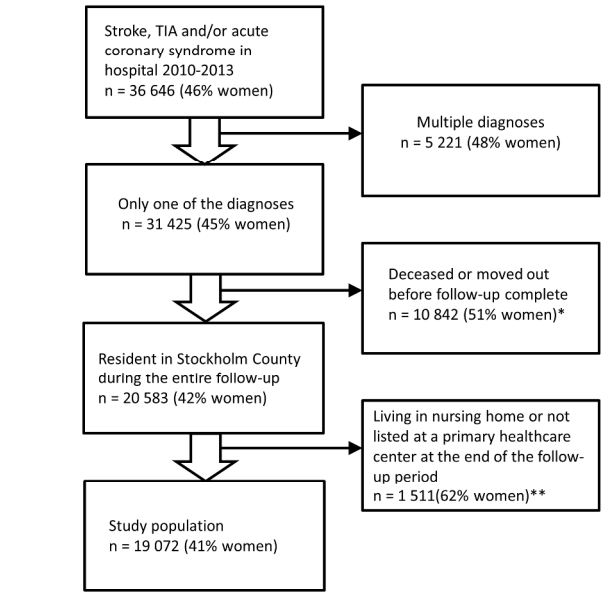

Figure 1. Selection of study population

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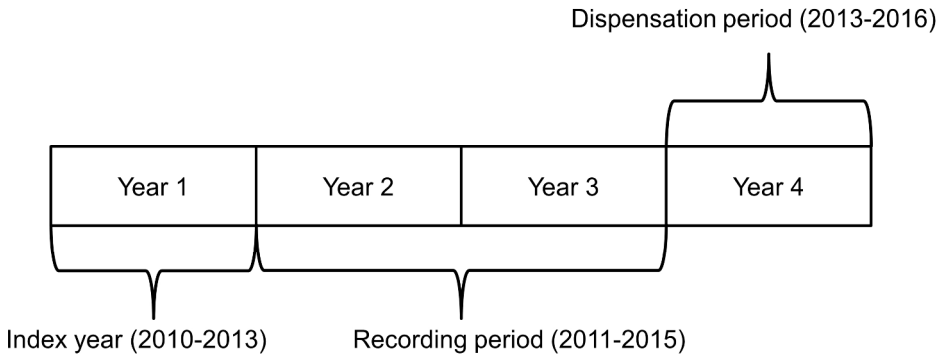

Figure 2. Illustration of index year, recording period, and dispensation period

254x190mm (300 x 300 DPI)

SUPPLEMENTARY FILE

Table of contents

INCLUDED DIAGNOSES AND MEDICATIONS

Table S1. ICD10-codes and ICD 10P-codes for diagnoses included in the study

Ischemic stroke Index year diagnosis I63.0, I63.1, I63.2, I63.3, I63.4, I63.5, I63.6, I63.8, I63.9 Recording period diagnosis I63.0, I63.1, I63.2, I63.3, I63.4, I63.5, I63.6, I63.8, I63.9, I64.9, I69.3, I69.4, I69.8, Z86.6B, Z86.7C ICD10P: I63.-, I64.-, I67.-P, I69.-
Transient ischemic attack (TIA) Index year diagnosis G45.0, G45.1, G45.3, G45.8, G45.9 Recording period diagnosis G45.0, G45.1, G45.3, G45.8, G45.9, Z86.6A, Z86.6B ICD10P: G45.-P , I69.-
Hemorrhagic stroke Index year diagnosis I61.0, I61.1, I61.2, I61.3, I61.4, I61.5, I61.6, I61.8, I61.9 Recording period diagnosis I61.0, I61.1, I61.2, I61.3, I61.4, I61.5, I61.6, I61.8, I61.9, I64.9, I69.1, I69.2, I69.4, I69.8, Z86.7C ICD-10P: I61.-P, I62, I64.-, I67.-P, I69.-
Acute coronary syndrome Index year diagnosis I20.0, I21.0, I21.1, I21.2, I21.3, I21.4, I21.4A, I21.4B, I21.4W, I21.4X, I21.9, I22.0, I22.1, I22.8, I22.9, I23.0, I23.1, I23.2, I23.3, I23.4, I23.5, I23.6, I23.8 Recording period diagnosis I20.0, I20.1, I20.8, I20.9, I21.0, I21.1, I21.2, I21.3, I21.4, I21.4A, I21.4B, I21.4W, I21.4X, I21.9, I22.0, I22.1, I22.8, I22.9, I23.0, I23.1, I23.2, I23.3, I23.4, I23.5, I23.6, I23.8, I24.0, I24.1, I24.8, I24.9, I25.0, I25.1, I25.2, I25.5, I25.6, I25.8, I25.9 ICD 10P: I20.0, I21.-P, I22, I23, I24, I25.-P

Table S2. ATC-codes for medications included in the study

Statins C10AA
Antithrombotics B01AC04, B01AC06, B01AC07, B01AC22, B01AC24, B01AC30, B01AA, B01AE07, B01AF
Antihypertensives C03A, C03B, C03C, C03D, C03E, C07, C08, C09
Beta-blockers C07

SENSITIVITY ANALYSIS - PATIENTS WITH MORE THAN ONE EVENT

In the main analysis of this paper, 5 221 patients were excluded from the study population because they had had hospital admissions with more than one of the studied diagnoses or because they had had hospital admissions with the same diagnosis in more than one index year. In the following sensitivity analysis, we analyze this sub-group of patients. It should be noted that patients with several hospital admission with the same diagnosis within the same index year were not excluded from the main analysis.

The 5 221 patients in the sub-group had a total of 11 458 events during the period 2010-2013. An event is defined as all discharge diagnoses in one diagnosis group in one index year for an individual. A patient with two ischemic strokes in one year is counted as only one event. A patient who has an ischemic stroke and a TIA in the same year is counted as two events. Likewise, a patient that has a TIA one year and another TIA the year after is also counted as two events.

In order to keep as much information as possible, we allowed patients to occur more than once in the analysis. A patient with two events, e.g. a TIA in 2010 and another TIA in 2011, was included twice in the material. Apart from that, the same exclusion criteria were applied as in the main analysis, see *Figure S1*, and 5 885 events were finally included in the analysis.

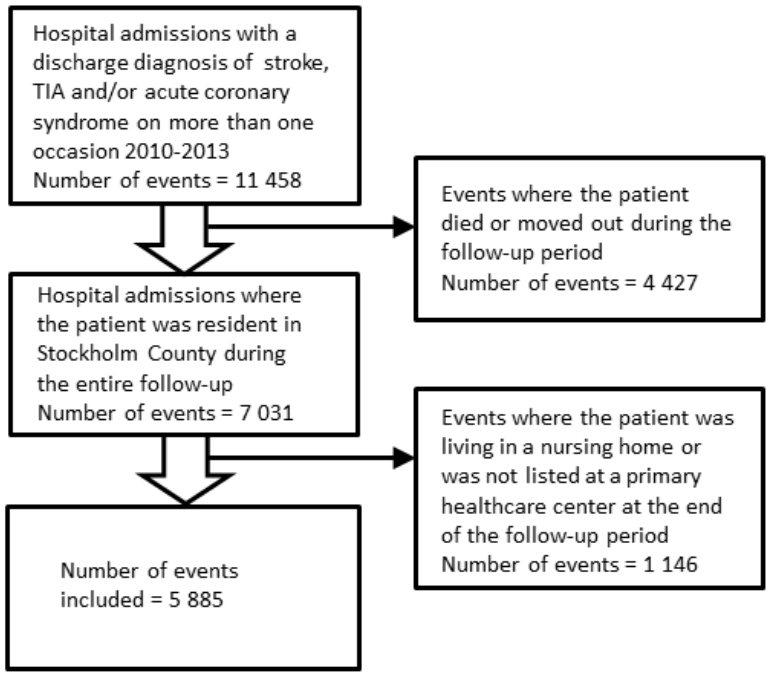

Figure S1 Selection of events included in analysis of strata of patients with multiple events.

Table S3 shows the absolute number and proportion of patients with and without a recorded diagnosis in primary care. The results are similar to the results of the groups in the main analysis when it comes to proportion of recorded patients. However, patients in the strata with multiple events had a recorded diagnosis in primary care to a slightly higher extent than those with only one event. The only exception was men with hemorrhagic stroke where 42 percent were recorded in the strata with multiple events and 43 percent were recorded in the main analysis.

Table S3. Absolute number and proportion in strata with multiple events, with and without a recorded diagnosis in primary care, by diagnosis (the same individual can occur more than once in the material).

	Recorded		**Not recorded**	
	Women	*Men*	*Women*	*Men*
TIA	136 (23%)	113 (16%)	465 (77%)	602 (84%)
Ischemic stroke	478 (46%)	672 (52%)	564 (54%)	622 (48%)
Hemorrhagic stroke	55 (40%)	78 (42%)	83 (60%)	107 (58%)
Acute coronary syndrome	305 (44%)	588 (48%)	382 (56%)	632 (52%)

Table S4 shows the absolute number and proportion of patients in strata with multiple events that were dispensed two prescriptions in the dispensation period, by sex, medication class, recorded/not recorded status, and diagnosis. In 18 out of 22 groups, the results point in the same direction as in the main analysis, that recorded patients are dispensed two medications to a higher extent than not recorded patients in most groups.

Table S4. Absolute number and proportion in strata with multiple events that were dispensed two prescriptions in the dispensation period, by sex, medication class, recorded/not recorded status, and diagnosis (the same individual can occur more than once in the material).

			Statins	Antithrombotics	Antihypertensives	Beta-blockers
TIA	Women	Not recorded	244 (52 %)	418 (90 %)	398 (86 %)	
		Recorded	69 (51 %)	127 (93 %)	104 (76 %)	
	Men	Not recorded	410 (68 %)	527 (88 %)	481 (80 %)	
		Recorded	94 (81 %)	113 (97 %)	96 (83 %)	
Ischemic stroke	Women	Not recorded	290 (51 %)	480 (85 %)	483 (86 %)	
		Recorded	293 (61 %)	417 (87 %)	394 (82 %)	
	Men	Not recorded	410 (66 %)	518 (83 %)	507 (82 %)	
		Recorded	477 (71 %)	604 (90 %)	552 (82 %)	
Hemorrhagic stroke	Women	Not recorded			49 (59 %)	
		Recorded			40 (73 %)	
	Men	Not recorded			85 (79 %)	
		Recorded			69 (88 %)	
Acute coronary syndrome	Women	Not recorded	205 (54 %)	331 (87 %)	352 (92 %)	304 (80 %)
		Recorded	205 (67 %)	287 (94 %)	293 (96 %)	256 (84 %)
	Men	Not recorded	467 (74 %)	556 (88 %)	574 (91 %)	498 (79 %)
		Recorded	468 (80 %)	525 (89 %)	551 (94 %)	491 (84 %)

When adjusting for confounders (Table S5), the confidence intervals are wider for the strata with multiple events because of the lower number of included observations. The differences between the recorded and not recorded group are statistically significant to a lesser extent than in the main analysis.

Table S5. Crude and adjusted odds ratios for being dispensed two prescriptions in the dispensation period according to recorded/not recorded status, by diagnosis. Patients that are not recorded are the reference group. Odds Ratios >1 mean recorded patients are more likely to have two dispensations in the dispensation period (the same individual can occur more than once in the material).

	Crude Odds Ratios (95% Confidence Intervals)	Adjusted Odds Ratios* (95% Confidence Intervals)
TIA		
Statins	1.06 (0.79-1.43)	1.15 (0.85-1.56)
Antithrombotics	2.53 (1.20-5.30)	2.54 (1.19-5.40)
Antihypertensives	0.68 (0.48-0.97)	0.67 (0.47-0.97)
Ischemic stroke		
Statins	1.35 (1.13-1.61)	1.32 (1.09-1.59)
Antithrombotics	1.52 (1.15-2.01)	1.68 (1.25-2.25)
Antihypertensives	0.87 (0.69-1.10)	0.97 (0.75-1.25)
Hemorrhagic stroke		
Antihypertensives	1.74 (0.98-3.06)	1.70 (0.89-3.24)
Acute coronary syndrome		
Statins	1.48 (1.19-1.85)	1.57 (1.25-1.98)
Antithrombotics	1.63 (1.12-2.36)	1.71 (1.18-2.49)
Antihypertensives	1.43 (0.93-2.19)	1.48 (0.96-2.29)
Beta-blockers	1.34 (1.04-1.73)	1.35 (1.04-1.75)

** Adjustments made for age, sex, index year, and visits to private specialists. To adjust for clustering, standard errors are based on the "sandwich" variance estimator.*

DESCRIPTIVE STATISTICS

Table S6. Mean age of men and women by recorded/not recorded status and diagnosis. Also proportion of men and women with at least one visit to a private specialist during the recording period, by recorded/not recorded status and diagnosis.

		Recorded		Not recorded	
		Women	*Men*	*Women*	*Men*
TIA	*Mean age*	73.1	71.4	73.7	70.5
	At least one visit to private specialist	20%	17%	21%	23%
Ischemic stroke	*Mean age*	71.9	69.9	74.3	70.5
	At least one visit to private specialist	16%	14%	18%	20%
Hemorrhagic stroke	*Mean age*	67.4	62.9	67.6	63.7
	At least one visit to private specialist	19%	15%	9%	14%
Acute coronary syndrome	*Mean age*	74.0	67.9	73.7	67.0
	At least one visit to private specialist	22%	21%	26%	33%

RESULTS STRATIFIED BY SEX

Table S7. Crude and adjusted odds ratios for being dispensed two prescriptions in the dispensation period according to recorded/not recorded status, by diagnosis and sex. Not recorded patients are the reference group. Odds Ratios >1 means recorded patients are more likely to have two dispensations in the dispensation period.

	Women		**Men**	
	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)
TIA				
Statins	1.53 (1.21-1.93)	1.48 (1.17-1.88)	1.63 (1.26-2.11)	1.59 (1.23-2.06)
Antithrombotics	2.37 (1.63-3.44)	2.49 (1.69-3.68)	2.30 (1.50-3.53)	2.19 (1.43-3.37)
Antihypertensives	0.75 (0.59-0.95)	0.73 (0.57-0.94)	0.93 (0.72-1.21)	0.88 (0.67-1.16)
Ischemic stroke				
Statins	1.64 (1.41-1.91)	1.63 (1.40-1.90)	1.50 (1.30-1.74)	1.54 (1.33-1.79)
Antithrombotics	1.88 (1.49-2.37)	2.13 (1.66-2.71)	1.66 (1.33-2.07)	1.79 (1.43-2.24)
Antihypertensives	0.96 (0.81-1.14)	1.11 (0.92-1.34)	1.13 (0.97-1.33)	1.22 (1.04-1.44)
Hemorrhagic stroke				
Antihypertensives	1.33 (0.80-2.20)	1.48 (0.82-2.67)	3.26 (2.01-5.27)	3.88 (2.25-6.70)
Acute coronary syndrome				
Statins	1.69 (1.42-2.01)	1.75 (1.47-2.09)	1.49 (1.30-1.71)	1.58 (1.38-1.82)
Antithrombotics	2.70 (2.03-3.60)	2.69 (2.02-3.59)	1.65 (1.35-2.02)	1.75 (1.43-2.15)
Antihypertensives	2.08 (1.50-2.89)	2.04 (1.47-2.85)	1.63 (1.33-2.00)	1.66 (1.35-2.04)
Beta-blockers	1.61 (1.31-1.97)	1.57 (1.28-1.93)	1.45 (1.27-1.67)	1.45 (1.26-1.66)

** Adjustments made for age, index year, and visits to private specialists. To adjust for clustering, standard errors are based on the "sandwich" variance estimator.*

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5-6
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7
Bias	9	Describe any efforts to address potential sources of bias	7-8
Study size	10	Explain how the study size was arrived at	5 -6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	Supplementary file tables S3-S5, figure S1
		(*c*) Explain how missing data were addressed	n/a
		(*d*) If applicable, explain how loss to follow-up was addressed	6

		(*e*) Describe any sensitivity analyses	6, Supplementary file tables S3-S5, figure S1
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	figure 1, pages 5-6
		(b) Give reasons for non-participation at each stage	figure 1
		(c) Consider use of a flow diagram	figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1, Supplementary file table S6
		(b) Indicate number of participants with missing data for each variable of interest	n/a
		(c) Summarise follow-up time (eg, average and total amount)	n/a
Outcome data	15*	Report numbers of outcome events or summary measures over time	table 2
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Tables 2 and 3, pages7-8
		(*b*) Report category boundaries when continuous variables were categorized	n/a
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Supplementary file tables S3-S5, figure S1
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

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