Clinical and Demographic Characteristics Associated With Suboptimal Primary Stroke and Transient Ischemic Attack Prevention

Retrospective Analysis

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Background and Purpose—Primary prevention of stroke and transient ischemic attack (TIA) is important to reduce the burden of these conditions; however, prescribing of prevention drugs is suboptimal. We aimed to identify individual clinical and demographic characteristics associated with potential missed opportunities for prevention therapy with lipid-lowering, anticoagulant, or antihypertensive drugs before stroke/TIA.

Methods—We analyzed anonymized electronic primary care records from a UK primary care database that covers 561 family practices. Patients with first-ever stroke/TIA, ≥18 years, with diagnosis between January 1, 2009, and December 31, 2013, were included.Missed opportunities for prevention were defined as people with clinical indications for lipid-lowering, anticoagulant, or antihypertensive drugs but not prescribed these drugs before their stroke/TIA. Mixed-effect logistic regression models evaluated the relationship between missed opportunities and individual clinical/demographic characteristics.

Results—The inclusion criteria were met by 29 043 people with stroke/TIA. Patients with coronary heart disease, chronic kidney disease, peripheral arterial disease, or diabetes mellitus were at less risk of a missed opportunity for prescription of lipid-lowering and antihypertensive drugs. However, patients with a 10-year cardiovascular disease risk ≥20% but without these diagnoses had increased risk of having a missed opportunity for prescription of lipid-lowering drugs or antihypertensive drugs. Women were less likely to be prescribed anticoagulants but more likely to be prescribed antihypertensive drugs. The elderly (≥85 years of age) were less likely to be prescribed all 3 prevention drugs, compared with people aged 75 to 79 years.

Conclusions—Knowing the patient characteristics predictive of missed opportunities for stroke prevention may help primary care identify and appropriately manage these patients. Improving the management of these groups may reduce their risk and potentially prevent large number of future strokes and TIAs in the population. **(*Stroke*. 2018;49:682-687. DOI: 10.1161/STROKEAHA.117.020080.)**

Key Words: atrial fibrillation ■ hypertension ■ ischemic attack, transient ■ primary health care ■ stroke

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Stroke is a leading cause of death and disability worldwide; the Global Burden of Disease Study found stroke is the second leading cause of death[1] and disability.[2] Furthermore stroke incidence, in terms of absolute numbers, and age-adjusted prevalence rates have increased.[3] Therefore, primary prevention of stroke and transient ischemic attack (TIA)—a risk factor for stroke—is essential more than ever to reduce the burden of these conditions.

Dyslipidemia, atrial fibrillation (AF), and hypertension are modifiable risk factors for stroke, which can be targeted through pharmacotherapy to reduce stroke risk.[4–6] However, despite evidence-based guidelines, prescribing lipid-lowering, anticoagulant, and antihypertensive drugs for primary stroke/TIA prevention is suboptimal in primary care. We previously found that over half of people eligible for ≥1 of these drugs were not prescribed them before first stroke/TIA.[7] Approximately, 12 000 first-strokes could potentially be prevented annually in the United Kingdom through optimal prescribing of lipid-lowering, anticoagulant, and antihypertensive drugs.[7]

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Several studies suggest variations and inequalities in prescribing lipid-lowering, anticoagulant, and antihypertensive drugs for prevention of cardiovascular disease (CVD).[8–14] There are inconsistent findings on the association between deprivation status and prescribing of prevention drugs;[10,13] a Scottish study found that more deprived people were less likely to be prescribed statins,[11] whereas a survey of English family practices found higher prescriptions of statins in more deprived areas.[9] Sex differences have also been observed; a survey of hypertension treatment in Europe and North America found women were more likely than men to be prescribed antihypertensive drugs.[14] Conversely, French and Japanese studies reported women were less likely to be prescribed anticoagulant drugs.[8,12] However, these studies did not consider prescribing practice in the context of predicted CVD and stroke risk and clinical indications for prescribing. This is important because a treatment–risk paradox has been observed whereby there is overprescribing of prevention drugs in people without a clinical indication[13] and suboptimal prescribing in people at high risk.[15] Understanding what characteristics are associated with suboptimal prescribing of prevention drugs in eligible patients is important to improve primary prevention of stroke/TIA.

Our objective was to determine the relationship between clinical and demographic characteristics and prescription of lipid-lowering, anticoagulant, or antihypertensive drugs in patients with clinical indications before stroke/TIA.

Methods

The full protocol for this study has been published elsewhere,[16] and methods are summarized in brief below. The data that support the findings of this study are available from the corresponding author on reasonable request.

Study Design and Data Source

We conducted a retrospective analysis of electronic medical records from 561 family practices in the United Kingdom. Anonymized data were obtained from The Health Improvement Network[17]—a large primary care database, which covers ≈6% of the UK population and is broadly generalizable in terms of age, sex, and morbidity.[18] Recording of stroke and TIA in The Health Improvement Network has a high validity.[19] Furthermore, prescribing data are comprehensive and accurate because these data are automatically retained in patients' electronic medical records from software used to print prescriptions.[20]

Analysis of The Health Improvement Network data has ethical approval from the National Health Service South-East Multicentre Research Ethics Committee, subject to independent scientific review.[21] This study had approval by a scientific review committee administered by the Intercontinental Marketing Services Health Real-World Evidence Solutions.[13–23]

Population

We defined primary stroke prevention as prevention of stroke in individuals with no history of stroke; therefore, the study population comprised patients with a diagnosis of first stroke (with or without previous TIA) and first TIA (if no prior stroke). Patients were included who had a stroke/TIA diagnosis between January 1, 2009, and December 31, 2013, and were aged ≥18 years at their diagnosis. The date of first-ever stroke or TIA was taken as the index date.

Definitions of Missed Opportunities for Primary Stroke/TIA Prevention

A potential missed opportunity for stroke/TIA prevention was defined as a person in whom a prevention drug was clinically indicated at the time of their stroke or TIA but who was not receiving treatment. This meant no prescription of a lipid-lowering or antihypertensive drug within the previous 90 days (the usual maximum prescription length in the United Kingdom) or for an anticoagulant drug within 120 days (to allow for referral to an anticoagulation clinic). Patients with a clinical code for anticoagulation monitoring were also considered to be on anticoagulant drugs.

The most recent risk factor data before the stroke/TIA were used to determine whether stroke prevention drugs were clinically indicated. Clinical indications for lipid-lowering, anticoagulant, and antihypertensive drugs were based on UK national guidelines used during the study period (online-only Data Supplement).[5,22,23]

Analysis

All analyses were conducted using STATA, version 12 (StataCorp). The relationship between clinical/demographic characteristics (online-only Data Supplement) and missed prescribing opportunities was evaluated using mixed-effects logistic regression, with family practice as a random effect and odds ratios (ORs) reported. Age and sex were forced into the models because they were preidentified as important predictors of undertreatment.[24–26] Year of stroke/TIA was included as a covariate in the regression models. Backward elimination with a P-to-eliminate value of >0.05 was used to select variables to be included in the final models. Exploratory analyses are detailed in the online-only Data Supplement. No attempt was made to impute missing data, but a missing category was created for categorical variables.

Results

The inclusion criteria were met by 29 043 people with stroke/TIA (Table). The median age was 74 years (interquartile range, 64–82), and 51% were women. The number of patients who had a clinical indication for ≥1 stroke prevention drug was 17 680, of which, 9579 were not prescribed these drugs at the time of their stroke or TIA. Missed opportunities for prescribing of prevention drugs were found in 49% (7836/16 028) of patients with a clinical indication for lipid-lowering drugs, 52% (1647/3194) for anticoagulant drugs and, 25% (1740/7008) for antihypertensive drugs.[7]

Predictors of Missed Opportunities for Prescription of Prevention Drugs

The adjusted ORs for each prevention drug are presented below and reported in Tables I through III in the online-only Data Supplement.

Sex

Women had increased odds of having a missed opportunity for prescribing anticoagulant drugs (OR, 1.37; 95% confidence interval [CI], 1.18–1.58); however, the opposite was true for antihypertensive drugs (OR, 0.85; 95% CI, 0.74–0.97), and there was no sex effect for lipid-lowering drugs.

Age

The elderly (≥85 years) had increased odds of not being prescribed lipid-lowering, anticoagulant, and antihypertensive drugs when clinically indicated (Tables I through III in the online-only Data Supplement). For lipid-lowering and antihypertensive drugs, there was a J-shaped relationship between age and missed prescribing opportunities where younger age categories (50–69 years) also had increased odds of missed opportunities (reference category, 75–79 years; Tables I and

Table. Characteristics of the Study Population

Diagnosis, n (%)	Stroke only	16 245 (55.9)
	TIA only	10 446 (36.0)
	Stroke with previous TIA	2352 (8.1)
Age, median (IQR)	Years	74 (64–82)
Sex, n (%)	Men	14 204 (48.9)
	Women	14 839 (51.1)
Comorbidity, n (%)	Atrial fibrillation	3544 (12.2)
	Asthma	3062 (10.5)
	Cancer	3239 (11.2)
	CHD	5543 (19.1)
	CKD	5774 (19.9)
	COPD	2198 (7.6)
	Dementia	1270 (4.4)
	Depression	6174 (21.3)
	Diabetes mellitus	4512 (15.5)
	Epilepsy	614 (2.1)
	Heart failure	1625 (5.6)
	Hypertension	14 646 (50.4)
	Hypothyroidism	2890 (10.0)
	Learning disability	130 (0.5)
	Osteoporosis	2318 (8.0)
	PAD	1431 (4.9)
	Palliative care	359 (1.2)
	Psychosis	439 (1.5)
	Rheumatoid arthritis	655 (2.3)

CHD indicates coronary heart disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; IQR, interquartile range; PAD, peripheral artery disease; and TIA, transient ischemic attack.

III in the online-only Data Supplement). However, for anticoagulant drugs, patients between 55 and 59 years of age had reduced odds of having a missed opportunity (Table II in the online-only Data Supplement).

Comorbidities

The odds of missed opportunities for lipid-lowering drug prescribing were less than a third in stroke/TIA patients with a diagnosis of coronary heart disease (CHD; OR, 0.21; 95% CI, 0.19–0.22) or diabetes mellitus (OR, 0.31; 95% CI, 0.28–0.33) and significantly reduced in patients with a diagnosis of peripheral arterial disease (PAD; OR, 0.52; 95% CI, 0.45–0.60), hypertension (OR, 0.69; 95% CI, 0.64–0.75), or chronic kidney disease (CKD; OR, 0.86; 95% CI, 0.79–0.94).

For antihypertensive drugs, odds of having a missed opportunity were substantially lower in patients with a diagnosis of hypertension (OR, 0.09; 95% CI, 0.07–0.11), CHD (OR, 0.26; 95% CI, 0.21–0.33), AF (OR, 0.35; 95% CI, 0.27–0.47), diabetes mellitus (OR, 0.43; 95% CI, 0.35–0.52), heart failure (OR, 0.49; 95% CI, 0.33–0.73), and CKD (OR, 0.50; 95% CI, 0.41–0.60). In addition, significantly reduced odds of having a missed opportunity for a prescription for antihypertensive drugs was found for patients with a diagnosis of PAD (OR, 0.62; 95% CI, 0.47–0.81), cancer (OR, 0.78; 95% CI, 0.62–0.98), hypothyroidism (OR, 0.79; 95% CI, 0.63–1.00), or asthma (OR, 0.79; 95% CI, 0.62–1.00). For anticoagulant drugs, a diagnosis of heart failure (OR, 0.53; 95% CI, 0.44–0.63) or diabetes mellitus (OR, 0.82; 95% CI, 0.69–0.98) was associated with reduced odds of having a missed opportunity for prescribing these drugs.

Increased odds of having a missed opportunity were associated with a diagnosis of dementia for anticoagulant (OR, 1.51; 95% CI, 1.11–2.06) and antihypertensive drugs (OR, 1.78; 95% CI, 1.26–2.51); palliative care (OR, 2.48; 95% CI, 1.83–3.34) for lipid-lowering drugs; and number of comorbidities (OR, 1.28 per unit increase; 95% CI, 1.16–1.42) for antihypertensive drugs. There was no association between the number of comorbidities and prescription of lipid-lowering or anticoagulant drugs.

CVD Risk

Exploratory analyses (online-only Data Supplement) found that people with a 10-year CVD risk ≥20% but without high-risk comorbidities (CHD, CKD, PAD, diabetes mellitus, or familial hypercholesterolemia) had a 3-fold increased odds having a missed opportunity for lipid-lowering drug prescription (OR, 2.81; 95% CI, 2.47–3.21). There were 2780 patients with a clinical indication for lipid-lowering drugs who had a 10-year CVD risk ≥20% but no high-risk comorbidities; 81% (2238/2780) of these were not prescribed these drugs. Similarly, patients with a clinical indication for antihypertensive drugs who had a 10-year CVD risk ≥20% but no high-risk comorbidities had increased odds of having a missed opportunity for these drugs (OR, 1.43; 95% CI, 1.17–1.75). There were 1076 of these patients eligible for antihypertensive drugs because of a 10-year CVD risk ≥20% but no high-risk comorbidities; 45% (479/1076) were not prescribed these drugs.

Behavioral and Other Demographic Characteristics

After adjustment for clinical and other patient factors, current smokers and people with a missing smoking status were more likely to have a missed opportunity for prescription of lipid-lowering and anticoagulant drugs, compared with nonsmokers (Tables I and II in the online-only Data Supplement). Patients with stroke/TIA who were underweight (body mass index [BMI], <18.5 kg/m^2) or missing BMI had increased odds of not being prescribed lipid-lowering and anticoagulant drugs, compared with people with a healthy BMI (18.5–25.9 kg/m^2; Tables I and II in the online-only Data Supplement). Being overweight (BMI, 26.0–30.0 kg/m^2) or obese (BMI, >30.0 kg/m^2) was associated with increased odds of having a missed opportunity for anticoagulant drugs but reduced odds for lipid-lowering drugs (Tables I and II in the online-only Data Supplement). There was no association between BMI or smoking and antihypertensive prescribing.

Provision of lifestyle advice was associated with reduced odds of missed opportunities for prescribing lipid-lowering drugs (advice on smoking and weight) and antihypertensive

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drugs (advice on weight; Tables I and III in the online-only Data Supplement). There were statistically significant regional differences for prescribing of lipid-lowering drugs with stroke/TIA patients in Wales (OR, 0.72; 95% CI, 0.59–0.89) and Northern Ireland (OR, 0.72; 95% CI, 0.59–0.88) more likely to be prescribed these drugs (West Midlands region of England as reference).

Deprivation and rurality (urban/rural) status had no effect on missed prescribing opportunities for any of the 3 prevention drugs.

Discussion

Principal Findings

We identified population subgroups where there are potential missed opportunities for prevention of stroke/TIA. Women were less likely to be prescribed anticoagulants but more likely to be prescribed antihypertensive drugs; however, there was no sex effect for lipid-lowering drugs. Compared with patients aged 75 to 79 years, the elderly (≥85 years) and patients aged 50 to 69 years were less likely to be prescribed preventative drugs. Patients on a disease register for CHD, CKD, PAD, or diabetes mellitus were markedly more likely to be prescribed lipid-lowering and antihypertensive drugs. In contrast, patients at high risk (ie, with a 10-year CVD risk ≥20%) but not on these disease registers were much less likely to be prescribed these drugs. Deprivation and urban/rural status had no effect on prescribing.

Strengths and Weaknesses of the Study

The strengths of this study are that the data source is generalizable to UK family practices and reflects routine clinical practice. Prescribing data are accurate and comprehensively recorded,[27] and the sample size is large. Stroke and the main comorbidities are likely to be accurately recorded because they are clinically significant; diagnoses have been validated within The Health Improvement Network;[19] and, in the UK, general practitioners are incentivized through the Quality and Outcomes Framework to keep a register of patients with these conditions.

This was an epidemiological, descriptive study; therefore, an important limitation is that the reasons for nonprescribing are unclear. There may be legitimate reasons why patients were not prescribed preventative medication, which is not routinely coded in electronic patient records, such as patients' preference, limited life expectancy, or increased bleeding risk (when prescribing anticoagulant drugs). Clinical judgment should be used in combination with patient preference when considering prescribing preventative medication. Therefore, nonprescribing of these drugs should not be considered a missed opportunity if the doctor and patient have engaged in a shared decision-making process incorporating the best available evidence. Patients with clinical codes indicating prevention drugs were declined, contraindicated, or an adverse reaction were not excluded from the analysis because it is unclear whether these were relevant at the time of index stroke/TIA. The number of patients in our sample with these codes was small (5%, 7%, and 0.7% for lipid-lowering, anticoagulant, and antihypertensive drugs, respectively), suggesting that this information would not have altered our conclusions. Lastly, prevention of stroke/TIA is complex, and our definition of missed prescribing opportunities does not address patients' adherence to medication, appropriate prescribing of drug combinations, or medication targets, such as blood pressure levels.

Implications for Clinical Practice

The relationship we identified between sex and prescription of preventative drugs has important clinical implications, particularly for anticoagulant drugs. Female sex is an independent risk factor for stroke in patients with AF, and strokes in women with AF are associated with increased mortality and disability compared with men.[28,29] Therefore, suboptimal prescribing of anticoagulants in women is likely to have a large impact on the burden of stroke. Bleeding risk has been cited as the most common reason for physicians not prescribing anticoagulants,[30] and some evidence suggests that bleeding risk is greater in women.[31] However, a recent systematic review found no difference in risk of bleeding between men and women.[32] Anticoagulation in AF patients with the highest stroke risk is likely to provide the greatest benefit; therefore, raising clinicians' awareness of suboptimal prescribing of anticoagulants in women, and the associated burden has potential to improve stroke prevention in these high-risk patients.

Missed opportunities for stroke prevention in patients with a high 10-year CVD risk may suggest that absolute risk is not considered. This is supported by our finding that patients with a diagnosis of CHD, CKD, PAD, or diabetes mellitus were more likely to be prescribed lipid-lowering and antihypertensive drugs, whereas those without these diagnoses but with a high 10-year CVD risk were less likely to be prescribed these drugs. Our study calculated patients' CVD risk scores post hoc; however, many of the patients may not have had their CVD risk calculated by general practitioners. A survey of physicians from 6 European countries found that only 38% used risk scores to estimate CVD risk.[33] This has important implications because evidence suggests that both patients[34] and clinicians[35,36] underestimate CVD risk. This is particularly relevant following the most recent guideline recommendations for lipid-lowering drug prescribing, which decrease the 10-year CVD risk cutoff from ≥20% to ≥10%.[4] Furthermore, perception of risk is influenced by social context, such as the media.[37] A study of UK primary care found that a period of intense media coverage on statins was associated with a decrease in recording of CVD risk scores and increase in the number of people who stopped taking statins.[38] The responsibility of general practitioners to accurately assess absolute CVD risk and effectively communicate this risk is essential to inform the shared decision-making process and prevent patients missing out on preventative medication that they may benefit from and wish to take.[39]

Presence of a single comorbidity was associated with with reduced odds of having a missed opportunity for prescribing antihypertensives; however, an increased number of comorbidities increased the odds of having a missed opportunity for these drugs (Table III in the online-only Data Supplement). Prescribing of antihypertensives in patients with a single comorbidity may be higher because in UK primary care, general practices are incentivized to include these patients on a disease register and regularly follow them up. This increases

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the opportunities for detection and treatment of hypertension. The reason for underprescribing of antihypertensive drugs in people with multimorbidity is unclear; however, it could be reflective of documented barriers to antihypertensive drug, which include hypertension not considered a clinical priority,[40] competing medical problems,[41] polypharmacy,[25] and physicians lack of belief of the benefit of these drugs.[25] Inadequate blood pressure control in people with multimorbidity has been observed in the literature.[42]

Missed opportunities to prescribing prevention drugs to the elderly has important implications because age is one of the most important risk factors for stroke/TIA, and the population is aging.[43] In particular, this is relevant for anticoagulant prescribing where 39% (1240/3194) of stroke/TIA patients with these drugs clinically indicated were aged ≥85 years, compared with 21% (3368/16 028) and 22% (1538/7008) for lipid-lowering and antihypertensive drugs, respectively. There is a lot of potential gain in this elderly patient group; the net benefit of anticoagulation is greatest in the elderly and the benefits of anticoagulation in the elderly have been shown to outweigh the risk.[44]

Current lipid-lowering guidelines recommend all patients aged ≥85 years are considered high risk,[4] and hypertension guidelines recommend people aged >80 years are prescribed the same antihypertensives as patients aged 55 to 80 years.[5] However, the guidelines acknowledge that there is a lack of evidence to support these recommendations,[4,5] particularly for stroke prevention. Furthermore, there are greater risks for prescribing prevention drugs to the elderly in the context of multimorbidity and polypharmacy. The benefit of preventative medication may be redundant if a patient has reduced life expectancy, frailty, or the treatment burden is greater than the added length or quality of life.[45] Multimorbidity guidelines recommend that prescribing of preventative medication should take a personalized approach and include patients' preferences and health priorities.[45] Therefore, age alone should not preclude prescribing of prevention drugs, but prescribing of these drugs should be undertaken using shared decision making in consideration of the best available evidence, treatment burden, and patients' preference.

Conclusions

Stroke can be preventable; however, opportunities for prevention may be missed. We identified characteristics that are associated with missed prescribing opportunities for lipid-lowering, anticoagulant, and antihypertensive drugs. Patients with a high calculated CVD risk but who did not have high-risk comorbidities were markedly less likely to be prescribed lipid-lowering and antihypertensive drugs. In addition, female patients with AF were less likely to be prescribed anticoagulant drugs, and people aged ≥85 years were less likely to be prescribed all 3 prevention drugs. Despite evidence-based guidelines, prevention of stroke and TIA with pharmacotherapy remains suboptimal in primary care. Knowledge of patient characteristics associated with missed opportunities for prescribing of prevention drugs provides an opportunity to raise awareness among clinicians and improve primary prevention of stroke/TIA.

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SUPPLEMENTAL MATERIAL

Clinical and Demographic Characteristics Associated with Sub-optimal Primary Stroke and TIA Prevention: Retrospective Analysis

Grace M Turner, Melanie Calvert, Max G Feltham, Ronan Ryan, Samuel Finnikin, Tom Marshall

eTable I: Adjusted* odds ratios for effects of patient and demographic characteristics on having a missed opportunity for prescription of lipid-lowering drugs in eligible patients prior to stroke or TIA.

		Odds Ratio	95% CI	P value
Age (years)	<45	2.34	1.46,3.74	<0.01
	45-49	1.11	0.83,1.47	0.48
	50-54	1.50	1.21,1.86	<0.01
	55-59	1.36	1.13,1.64	<0.01
	60-64	1.28	1.10,1.50	<0.01
	65-69	1.27	1.10,1.47	<0.01
	70-74	1.08	0.94,1.24	0.26
	75-79	1.00		
	80-84	1.30	1.13,1.48	<0.01
	85-89	1.63	1.42,1.86	<0.01
	90-94	3.14	2.61,3.78	<0.01
	≥95	7.11	4.93,10.26	<0.01
Sex	Male	1.00		
	Female	0.96	0.89,1.04	0.28
Comorbidity	CHD	0.21	0.19,0.22	<0.01
	CKD	0.86	0.79,0.94	<0.01
	PAD	0.52	0.45,0.60	<0.01
	Diabetes	0.31	0.28,0.33	<0.01
	Hypertension	0.69	0.64,0.75	<0.01
	Palliative care	2.48	1.83,3.34	<0.01
BMI	Healthy (18.5-25.9 kg/m^2)	1.00		
	Underweight (<18.5 kg/m^2)	1.93	1.45,2.57	<0.01
	Overweight (26-30 kg/m^2)	0.89	0.81,0.97	0.01
	Obese (>30 kg/m^2)	0.79	0.72,0.88	<0.01
	Missing	1.58	1.32,1.88	<0.01
Smoking	Non-smoker	1.00		
	Current	1.40	1.21,1.61	<0.01
	Ex	1.08	0.98,1.19	0.12
	Missing	1.65	1.31,2.07	<0.01
Region	West Midlands	1.00		
	Yorkshire & Humber	0.95	0.72,1.25	0.72
	North West	0.85	0.70,1.05	0.13
	East Midlands	1.01	0.81,1.25	0.93
	North East	0.85	0.65,1.13	0.26
	East of England	0.94	0.75,1.18	0.59
	London	0.84	0.70,1.02	0.07

	South East Coast	0.87	0.73,1.05	0.16
	South Central	1.01	0.86,1.20	0.87
	South West	1.00	0.96,1.18	0.96
	Northern Ireland	0.72	0.59,0.88	<0.01
	Scotland	0.92	0.78,1.09	0.34
	Wales	0.72	0.59,0.89	<0.01
	Missing	0.80	0.47,1.37	0.42
Lifestyle	Smoking	0.76	0.68,0.84	<0.01
intervention	Weight	0.78	0.67,0.91	<0.01

*Each odds ratio is adjusted for the other variables in the table.

BMI: Body Mass Index, CHD: Coronary Heart Disease, CI: Confidence Intervals, CKD: Chronic Kidney Disease, PAD: Peripheral Artery Disease

eTable II: Adjusted* odds ratios for effects of patient and demographic characteristics on having a missed opportunity for prescription of anticoagulant drugs in eligible patients prior to stroke or TIA.

		Odds Ratio	95% CI	P value
Age (years)	<55	0.72	0.33,1.57	0.41
	55-59	0.36	0.17,0.77	0.01
	60-64	1.01	0.62,1.66	0.97
	65-69	0.98	0.68,1.40	0.90
	70-74	0.89	0.66,1.20	0.43
	75-79	1.00		
	80-84	1.01	0.81,1.26	0.94
	85-89	1.27	1.02,1.57	0.03
	90-94	1.74	1.32,2.30	<0.01
	≥95	4.54	2.60,7.94	<0.01
Sex	Male	1.00		
	Female	1.37	1.18,1.58	<0.01
Comorbidity	Heart failure	0.53	0.44,0.63	<0.01
	Diabetes	0.82	0.69,0.98	0.03
	Dementia	1.51	1.11,2.06	0.01
Smoking	Non	1.00		
	Current	1.41	1.08,1.84	0.01
	Ex	1.08	0.91,1.29	0.36
	Missing	1.67	1.07,2.62	0.03
BMI	Healthy (18.5-25.9 kg/m^2)	1.00		
	Underweight (<18.5 kg/m^2)	1.51	1.01,2.26	0.04
	Overweight (26-30 kg/m^2)	1.24	1.04,1.48	0.02
	Obese (>30 kg/m^2)	1.23	1.01,1.51	0.04
	Missing	1.60	1.13,2.27	0.01
Year of event	2009	1.00		
	2010	0.95	0.73,1.22	0.67
	2011	0.78	0.61,0.99	0.04
	2012	0.70	0.55,0.89	<0.01
	2013	0.59	0.47,0.75	<0.01

*Each odds ratio is adjusted for the other variables in the table.
BMI: Body Mass Index, CI: Confidence Intervals

eTable III: Adjusted* odds ratios for effects of patient and demographic characteristics on having a missed opportunity for prescription of antihypertensive drugs in eligible patients prior to stroke or TIA.

		Odds Ratio	95% CI	P value
Age (years)	<45	1.64	0.87,3.10	0.13
	45-49	1.50	0.93,2.40	0.10
	50-54	1.55	1.07,2.24	0.02
	55-59	1.54	1.11,2.12	0.01
	60-64	1.12	0.84,1.49	0.45
	65-69	1.30	1.00,1.68	0.05
	70-74	1.16	0.92,1.46	0.21
	75-79	1.00		
	80-84	0.96	0.76,1.22	0.74
	85-89	1.26	0.98,1.62	0.08
	90-94	1.70	1.26,2.29	<0.01
	≥95	3.61	2.18,5.99	<0.01
Sex	Male	1.00		
	Female	0.85	0.74,0.97	0.02
Comorbidity	Hypertension	0.09	0.07,0.11	<0.01
	CHD	0.26	0.21,0.33	<0.01
	AF	0.35	0.27,0.47	<0.01
	Diabetes	0.43	0.35,0.52	<0.01
	Heart failure	0.49	0.33,0.73	<0.01
	CKD	0.50	0.41,0.60	<0.01
	PAD	0.62	0.47,0.81	<0.01
	Cancer	0.78	0.62,0.98	0.03
	Hypothyroidism	0.79	0.63,1.00	0.05
	Asthma	0.79	0.62,1.00	0.05
	Dementia	1.78	1.26,2.51	<0.01
Number of comorbidities	One unit increase	1.28	1.16,1.42	<0.01
Lifestyle intervention	Weight	0.63	0.48,0.83	<0.01

*Each odds ratio is adjusted for the other variables in the table.
CHD: Coronary Heart Disease, CI: Confidence Intervals, CKD: Chronic Kidney Disease: PAD: Peripheral Artery Disease

eTable IV: Clinical and demographic characteristics entered into the logistic regression model.

Predictor variable	
Age	<45
	45-49
	50-54
	55-59
	60-64
	65-69
	70-74
	75-79
	80-84
	85-89
	90-94
	≥95
Sex	Male
	Female
Deprivation	1 (least deprived)
	2
	3
	4
	5 (most deprived)
	Missing
Rurality	Rural
	Urban
	Missing
BMI	Healthy
	Underweight
	Overweight
	Obese
	Missing
Smoking	Non
	Ex
	Current
	Missing
Alcohol	Never
	Light
	Moderate
	High
	Missing
Lifestyle intervention: Any	N
	Y
Lifestyle intervention: Alcohol	N
	Y
Lifestyle intervention: Diet	N
	Y
Lifestyle intervention: Exercise	N
	Y

Lifestyle intervention: Smoking	N Y
Lifestyle intervention: Weight	N Y
Year of event†	2009 2010 2011 2012 2013
Health authority/ Country	West Midlands East Midlands East of England London North East North West South Central South East Coast South West Yorkshire & Humber Northern Ireland Scotland Wales Missing
Number of comorbidities†	0 1 2 3 4 5 6 7 ≥8
Atrial fibrillation	N Y
Asthma	N Y
Cancer	N Y
CHD	N Y
CKD	N Y
COPD	N Y
Dementia	N Y
Depression	N Y
Diabetes	N Y

Epilepsy	N
	Y
Heart failure	N
	Y
Hypertension	N
	Y
Hypothyroidism	N
	Y
Learning disability	N
	Y
Osteoporosis	N
	Y
PAD	N
	Y
Palliative care	N
	Y
Psychosis	N
	Y
Rheumatoid arthritis	N
	Y

† Continuous variable
BMI: Body Mass Index, CHD: Coronary Heart Disease, CKD: Chronic Kidney Disease, COPD: Chronic Obstructive Pulmonary Disease, N: No, PAD: Peripheral Artery Disease, Ref: Reference category, Y: Yes

Methods

Lipid-lowering drugs were clinically indicated if patients had coronary heart disease (CHD), chronic kidney disease (CKD) stages 3-5, peripheral arterial disease (PAD), TIA (in stroke patients with prior TIA), diabetes mellitus (type 1 and 2) and aged over 40 years, familial hypercholesterolaemia, or a 10-year CVD risk of ≥20%.[1] Familial hypercholesterolaemia was defined as having a clinical code for the diagnosis or a total cholesterol ≥9 mmol/l.[2] Ten-year CVD risk was estimated using the adjusted Framingham CVD risk score, which, for consistency, was calculated 1 day prior to the index date.

Anticoagulant drugs were clinically indicated if patients had a diagnosis of AF and were at high risk of stroke (CHADS2 score ≥1).[3] Similar to the Framingham CVD risk score, CHADS2 scores were calculated 1 day prior to the index date.

Antihypertensive drugs were clinically indicated if patients had high blood pressure (≥160/100 mm Hg) or if patients had moderately high blood pressure (≥140/90 mm Hg) and CHD, CKD, PAD, TIA (in stroke patients with prior TIA), diabetes mellitus (type 1 and 2) and age over 40 years, or a 10-year CVD risk of ≥20%. The guidelines refer to a "sustained" blood pressure ≥160/100 mm Hg or ≥140/90 mm Hg; therefore, blood pressure was the mean of the three most recent systolic and diastolic blood pressure recordings within 3 years prior to stroke/TIA.[4] People without three blood pressure recordings within 3 years were excluded from this analysis.

Demographic, clinical and prescribing data

A comprehensive list of clinical codes (Read codes)[5] for stroke and TIA was used to identify the study cohort. Patients with a clinical code indicating history of stroke or TIA recorded before the index stroke or TIA were excluded as their true index date could not be identified. Diagnoses of AF, diabetes, CVD, and other comorbidities were based on the standard list of clinical codes used to identify chronic diseases for the UK chronic disease monitoring programme (Quality and Outcomes Framework [QOF] business rules version 27)[6]. Drug prescriptions were identified using prescriptions issued for lipid-lowering, anticoagulant, and antihypertensive drugs and clinical codes in electronic patient records indicating that the patient was on these drugs.[7] Clinical codes indicating that prevention drugs were declined or contraindicated, that a patient had white coat hypertension (for patients in whom antihypertensive drugs were clinically indicated), or that there was an adverse reaction were extracted. Clinical codes indicating provision of lifestyle advice were also extracted. Rurality (urban/rural), Townsend deprivation quintiles, sub-national region or country within the UK, height, weight, smoking status and alcohol intake were extracted for each patient.[8]

Population

To ensure data quality and that important patient outcomes were being recorded consistently, the index dates had to occur at least 1 year after the practice began using Vision patient record software and after the practice date of acceptable mortality recording.[9] Only patients

registered at a practice for at least 1 year were included, to allow sufficient time for risk factor data to be recorded.

Exploratory analyses

High cardiovascular disease risk was defined as patients with coronary heart disease (CHD), chronic kidney disease (CKD) stages 3-5, peripheral arterial disease (PAD), TIA (in stroke patients with prior TIA), diabetes mellitus (type 1 and 2) and aged over 40 years, familial hypercholesterolaemia, or a 10-year CVD risk of ≥20%. Given that CHD, CKD, PAD and diabetes mellitus were associated with decreased odds of having a missing opportunity for lipid lowering and antihypertensive drugs, exploratory analysis investigated the effect of including in the regression model a variable for patients with a 10-year CVD risk ≥20% but without 'high risk comorbidities' (CHD, CKD, PAD, diabetes or familial hypercholesterolaemia).

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