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Thromboprophylaxis of elderly patients with AF in the UK: an analysis using the General Practice Research Database (GPRD) 2000–2009

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ABSTRACT

Objective To assess use of thromboprophylaxis in UK general practise among patients with atrial fibrillation (AF); to investigate whether elderly patients are less likely to receive anticoagulation therapy than younger patients.

Design Retrospective cohort study

Setting UK General Practice Research Database (GPRD)

Patients Aged ≥60 years with a new diagnosis of AF (2000–2009).

Interventions None.

Main outcome measures The main outcome measure was initiation of warfarin in the first year following diagnosis. Patients were categorised by stroke risk ($CHADS_2$ score) and bleeding risk (HAS-BLED score).

Results 81 381 patients were identified (21% aged 60–69 years, 37% aged 70–79 years, 42% aged 80+ years). Patients aged 80+ years were significantly less likely to be initiated on warfarin than younger patients, adjusted for gender, practice and comorbidities; 32% of patients aged 80+ years received warfarin compared with 57% aged 60–69 years ($p<0.0001$), and 55% aged 70–79 years ($p<0.0001$). For all strata of $CHADS_2$/HASBLED scores, patients aged 80+ years were significantly less likely to be treated with warfarin than younger patients. Logistic regression showed that female sex, low Basal Metabolic Index (BMI), age over 80 years, increasing HAS-BLED score and dementia were independently associated with reduced use of warfarin. Stroke/Transient Ischaemic Attack (TIA), hypertension, heart failure and left ventricular systolic dysfunction were associated with increased use. Patients with HAS-BLED>$CHADS_2$ were less likely to be initiated on warfarin. Higher $CHADS_2$ scores were associated with increased anticoagulation use.

Conclusions Anticoagulation is being under-used in patients with AF aged 80+ years, even after taking into account increased bleeding risk in this age group.

INTRODUCTION

Atrial fibrillation (AF) is the most common cardiac arrhythmia, and is associated with high morbidity and mortality, with stroke being the most significant complication.[1] AF increases the risk of stroke 5-fold, and accounts for around 15% of all strokes.[2] While AF can affect adults of any age, the prevalence increases with age: 3.8% among people aged >60 years rising to 9.0% among those aged >80 years.[3] AF is a growing problem, projected to increase with the ageing population and the increased survival of patients with chronic cardiac disorders, such as ischaemic heart disease and congestive heart failure (CHF) that predispose to AF.[4]

Oral anticoagulation treatment with a vitamin K antagonist, traditionally warfarin, has been demonstrated to be highly effective, reducing the relative risk of stroke in patients with AF by around two-thirds, with a typical absolute annual risk reduction of 2.7%.[5] Guidelines recommend that the decision to use anticoagulation is primarily based around an assessment of stroke risk in atrial fibrillation.[6] Older age is recognised as one of the key risk factors. With regard to the two risk stratification schemes in common use, the CHA_2DS_2-VASc score recommends that all people in AF age ≥75 years should be anticoagulated, and the $CHADS_2$ score that anticoagulation is considered for all people in this age group, but is recommended in the presence of an additional risk factor.[7] However, recent studies have found that warfarin prescription was unrelated to $CHADS_2$ score.[8 9]

Recent National Institute for Health & Clinical Excellence (NICE) guidance recommends use of anticoagulation for all people aged ≥75 years in AF.[10] Despite this, less than half the patients aged over 80 years receive warfarin among both hospitalised and outpatient populations.[10–16] A UK study found that between 1994 and 2003, patients with AF aged 85 years and above were five times less likely to be treated with anticoagulants than patients aged 55–64 years.[17]

Bleeding risk is often cited as a reason for non-use of warfarin among elderly patients, in which case, aspirin is often used as an alternative.[11 14] However, the Warfarin versus Aspirin for Stroke Prevention in Octogenarians with AF (WASPO) trial showed that in patients aged 80–89 years there were significantly more adverse events including bleeding in patients treated with aspirin compared with warfarin.[18] This is consistent with the Birmingham Atrial Fibrillation Treatment of the Aged (BAFTA) study which found no significant difference in risk of major haemorrhage between warfarin and aspirin in people aged ≥75 years.[19]

In the light of the stronger evidence base for using anticoagulation in the elderly,[19] the development of scores to quantify bleeding risk in atrial fibrillation,[20] and the emergence of new anticoagulants, it is timely to examine whether the underuse of anticoagulation in the elderly persists, and the extent to which this can be explained by risk of bleeding. This study sought to examine anticoagulation treatment of elderly patients (80+ years) compared with younger

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patients (60–69 years, 70–79 years) within a cohort of patients with AF from the UK population, and to determine the extent to which any differences in treatment prescribing among different age groups might be explained by bleeding risk.

METHODS

Study design

This was a cohort study of patients from the General Practice Research Database (GPRD)[21] with a first diagnosis of AF, between 2000 and 2009. The GPRD includes approximately three million residents in the UK registered with over 600 general practitioners (GPs). The database includes demographics, medical diagnoses, referrals and prescriptions. AF diagnoses were identified using the GPRD Read codes (see appendix 1).

To be eligible, patients had to be flagged as having data of an acceptable quality (as defined by GPRD), and be registered with practices whose data quality met the criteria for an 'up-to-standard' practice. Each patient had to have at least 12 months of data between registering with the practice and their first diagnosis of AF. Patients had to be over the age of 60 years at the time of first diagnosis of AF.

From this cohort, patients who were initiated on warfarin in the year following the AF diagnosis were identified. Warfarin initiation was defined as at least one prescription for warfarin within the first year following AF diagnosis (see appendix 2 for warfarin codes).

Data analysis

Descriptive statistics were recorded at baseline for the AF cohort at first diagnosis of AF, and for the cohort of patients treated with warfarin at first prescription for warfarin (if within 12 months of diagnosis). Comorbid conditions were defined using GPRD Read codes (see Appendix 1). Patients were split into three age groups: 60–69 years, 70–79 years, and 80+ years based upon age at AF diagnosis. Differences between groups were tested using χ^2 tests, with the group of patients aged 80+ years as the reference group.

Patients were split between warfarin-treated and warfarin-untreated, based on whether they were initiated on warfarin within their first year following AF diagnosis.

Patients within the AF cohort were categorised into risk groups at baseline using two commonly used risk scores: $CHADS_2$ and CHA_2DS_2-VASc. $CHADS_2$ score allocates one point each for CHF, hypertension, age >75 years, diabetes mellitus and two points for a prior stroke/TIA. The $CHADS_2$ score was used to stratify patients within the analysis, as this method is most widely used. The CHA_2DS_2-VASc score incorporates the additional risk factors of vascular disease, age 65–74 years, and female gender, and gives two points each to age ≥75 years and prior stroke/TIA/thromboembolism, and one point each to all other factors.

The HAS-BLED score (hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalised ratio (INR), elderly (>65 years), drugs/alcohol) is recommended to assess the bleeding risk of patients with AF when deciding whether to prescribe anticoagulation.[22] Hypertension was defined as a diagnosis of hypertension, or a systolic blood pressure reading of at least 160 mmHg in the last year. Abnormal renal function required a patient to have a Read code for chronic dialysis, renal transplant, chronic kidney disease stage 5, or a serum creatinine level of 200 mmol/l or above. Abnormal liver function included chronic hepatic disease, cirrhosis or significant hepatic derangement. Bleeding history or predisposition was defined as patients with a record of a serious bleed or anaemia in the previous year, and a labile INR required that the patient was prescribed warfarin in the year prior to AF diagnosis, and had a time in therapeutic range lower than 60% in that year. Drugs refer to Non-steroidal Anti-inflammatory Drugs (NSAID) or antiplatelet use, and patients were allocated one point if they had at least two prescriptions for either of these in the latest year, and another point for a diagnosis of alcoholism in the latest year.

Pisters *et al* proposed that if HAS-BLED score is greater than $CHADS_2$ score in patients with $CHADS_2$ ≥2, then anticoagulation should not be given due to risk of bleeding.[22] The percentage of patients treated with warfarin in each age group was split by HAS-BLED > $CHADS_2$ and HAS-BLED≤$CHADS_2$.

Logistic regression was used to identify the factors which affected whether patients were initiated on warfarin. Results were found to be significantly different between sexes, so men and women were modelled separately in order to produce clinically useful estimates. The results were adjusted for practice, to take into account differential prescribing practices between practices, as well as regional variation, by including dummy variables for each practice in the model. Logistic regression models were fitted using SAS software, V.9.2 (SAS Institute Inc, Cary, North Carolina, USA) using PROC LOGISTIC.

Further logistic regression models were used to investigate whether stroke risk (measured using CHADS2 score) had an effect on whether men and women were treated with warfarin, adjusted for age and practice.

RESULTS

Patients

A cohort of 81 381 patients with AF was identified, of whom 17 054 (21%) were aged 60–69 years, 30 350 (37%) were aged 70–79 years, and 33 977 (42%) were aged 80+ years. Just over half the cohort (52%; n=42 318) were women. More patients with AF were female in the older age group (≥80 years; 63% female), while patients in the youngest age group were predominantly men (60–69 years; 63% male) (table 1).

Warfarin treatment

Patients aged 80+ years were significantly less likely to be initiated on warfarin in the first year following AF diagnosis than younger patients; 32% of patients aged 80+ years received warfarin compared with 55% aged 70–79 years, $\chi^2(1, n=64\,327)=3453$ ($p<0.0001$), and 57% aged 60–69 years, $\chi^2(1, n=51\,031)=2883$ ($p<0.0001$) (table 1). This remained true in all subgroups of patients with comorbidities. Men were more likely to be initiated on warfarin than women in all age groups (table 1).

Over the 10-year study period (2000–2009), there was a trend towards increased prescribing of warfarin in patients with AF, which was consistent across the three age groups. The proportion of patients aged 80+ years initiated on warfarin following AF diagnosis increased from 25% to 37% between 2000 and 2009, but was still much lower than the proportion in younger patients (48% to 61% in patients aged 70–79 years, and 54% to 55% in patients aged 60–69 years).

Logistic regression models of whether warfarin was initiated in the year following AF diagnosis are presented (table 2). For both men and women, age was the strongest independent predictor of warfarin use. A patient aged 60–69 years, or 70–79 years, was more than twice as likely to be initiated on warfarin following a diagnosis of AF, than a patient with the same BMI, gender and comorbidities aged ≥80 years (table 2). Having adjusted for other factors, patients with BMI <20 kg/m^2 were significantly less likely to receive warfarin treatment than patients with BMI 20–25 kg/m^2. Patients with higher BMIs were

Table 1 Frequency of comorbidities in total atrial fibrillation patient population and among those treated with warfarin

		60–69 years				70–79 years				80+ years (reference group)	
Age group	All patients n (%)	Patients n (%)	Patients treated with warfarin n (%)	χ^2 Value*	p Value*	Patients n (%)	Patients treated with warfarin n (%)	χ^2 Value†	p Value†	Patients n (%)	Patients treated with warfarin n (%)
Number of patients	81 381	17 054	9648 (57)	2883	<0.0001	30 350	16 641 (55)	3453	<0.0001	33 977	10 830 (32)
Women	42 318 (52)	6300 (37)	3268 (52)	1094	<0.0001	14 315 (47)	7433 (52)	1849	<0.0001	21 300 (63)	6246 (29)
Men	39 063 (48)	10 754 (63)	6380 (59)	1254	<0.0001	16 035 (53)	9208 (57)	1283	<0.0001	12 677 (37)	4584 (36)
BMI, mean (SD)	27.1 (5.2)	29.0 (5.9)	29.5 (6.1)			27.6 (5.2)	28.0 (5.2)			25.8 (4.7)	26.5 (4.6)
% with non-missing BMI		85	87			74	87			74	82
Hypertension (diagnosed)	44 841 (55)	8362 (49)	4951 (59)	1461	<0.0001	17 328 (57)	9692 (56)	1694	<0.0001	19 151 (56)	6603 (34)
Diabetes	10 022 (12)	2233 (13)	1333 (60)	377	<0.0001	4291 (14)	2358 (55)	355	<0.0001	3498 (10)	1175 (34)
LVEF <40%	2719 (3)	723 (4)	529 (73)	109	<0.0001	1165 (4)	797 (68)	92	<0.0001	831 (2)	391 (47)
Coronary heart disease	19 860 (2)	3531 (2)	2088 (59)	588	<0.0001	8052 (27)	4592 (57)	794	<0.0001	8277 (24)	2901 (35)
Congestive heart failure	21 075 (26)	3094 (18)	2152 (70)	1277	<0.0001	7401 (24)	4490 (61)	1296	<0.0001	10 580 (31)	3549 (34)
Stroke	8142 (10)	1264 (7)	807 (64)	369	<0.0001	3084 (10)	1760 (57)	394	<0.0001	3794 (11)	1259 (33)
Stroke/TIA	10 763 (13)	1567 (9)	1029 (66)	496	<0.0001	3928 (13)	2299 (59)	543	<0.0001	5268 (16)	1797 (34)
Alzheimer's/dementia	5382 (7)	187 (1)	95 (51)	121	<0.0001	1519 (5)	617 (41)	294	<0.0001	3676 (11)	664 (18)
Thromboembolism‡	4619 (6)	803 (5)	554 (69)	132	<0.0001	1729 (6)	1109 (64)	137	<0.0001	2087 (6)	943 (45)
Vascular disease‡	12 389 (15)	2 225 (13)	1353 (61)	418	<0.0001	4997 (16)	2847 (57)	487	<0.0001	5167 (15)	1816 (35)
$CHADS_2$ score											
0	10 241 (13)	6243 (37)	3072 (49)	–	–	3998 (13)	2038 (51)	–	–	0 (0)	0 (0)
1	24 859 (31)	6701 (39)	3925 (59)	1514	<0.0001	9865 (33)	5297 (54)	1310	<0.0001	8293 (24)	2249 (27)
2+	46 281 (57)	4110 (24)	2651 (65)	1458	<0.0001	16 487 (56)	9306 (56)	2181	<0.0001	25 684 (76)	8581 (33)
CHA_2DS_2 -VASc score											
0	1620 (2)	1620 (9)	798 (49)	–	–	0 (0)	0 (0)	–	–	0 (0)	0 (0)
1	6276 (8)	4348 (25)	2292 (53)	–	–	1928 (6)	1028 (53)	–	–	0 (0)	0 (0)
2+	73 485 (90)	11 086 (65)	6 558 (59)	2625	<0.0001	28 422 (94)	15 613 (55)	3370	<0.0001	33 977 (100)	10 830 (32)
HAS-BLED											
0–1	31 522 (39)	10 337 (61)	5805 (56)	1169	<0.0001	10 445 (34)	5857 (56)	1167	<0.0001	10 740 (32)	3518 (33)
2+	49 859 (61)	6717 (39)	3843 (57)	1478	<0.0001	19 905 (66)	10 784 (54)	2271	<0.0001	23 237 (68)	7312 (31)

*χ^2 tests comparing the proportion of patients treated with warfarin in the 60–69 years age group compared with the 80+ years age group.
†χ^2 tests comparing the proportion of patients treated with warfarin in the 70–79 years age group compared with the 80+ years age group.
‡Diagnostic codes used to define are shown in appendix S1.
BMI, body mass index; LVEF, left ventricular ejection fraction; TIA, transient ischemic attack.

increasingly likely to be treated with warfarin than patients with BMI 20–25 kg/m^2. Increasing bleeding risk, as measured using HAS-BLED score, reduced the probability that a patient was treated with warfarin.

In men and women, hypertension, heart failure, reduced left ventricular ejection fraction, thromboembolism and a history of stroke or TIA, all independently increased the likelihood that a patient received warfarin. Paradoxically, men with diabetes were less likely to be anticoagulated, and presence of diabetes was not associated with use of anticoagulation in women. In both sexes, dementia halved the chance that warfarin was used.

Stroke and bleeding risk analysis

As would be anticipated, $CHADS_2$ scores rise with age, with 76% of patients aged 80+ years having a $CHADS_2$ score of 2 or above compared with 56% of patients aged 70–79 years, and 24% of patients aged 60–69 years.

Patients in the 80+ years age group had higher HAS-BLED scores than patients aged 60–69 years; 68% of patients aged 80+ years had a HAS-BLED score ≥2 compared with 39% of patients aged 60–69 years (and 66% patients aged 70–79 years) (table 1).

Patients with HAS-BLED>$CHADS_2$ were slightly less likely to be initiated on warfarin. This effect was greater in patients with $CHADS_2$ ≥2, and in patients aged 60–69 years (table 3). For all strata of $CHADS_2$/HAS-BLED scores in table 3 (bar one, due to small numbers), patients in the 80+ years age group were significantly less likely to be treated with warfarin than those of younger ages.

Logistic regression models investigating $CHADS_2$ (table 4) found evidence in both men and women of a significant increase in the chance of being prescribed warfarin as $CHADS_2$ score increased, when adjusted for age group and practice.

DISCUSSION

Patients with AF, aged 80 years or over, are much less likely to be treated with warfarin than younger patients. This holds true if the data are adjusted to take into account factors that might deter a clinician from prescribing warfarin, such as frailty (indicated by low BMI), bleeding risk and Alzheimer's disease. While the proportion of people over 80 years treated with warfarin has increased moderately over the study period (2000–2009), it remains substantially lower than the proportion treated in the younger age groups. Logistic regression analysis demonstrated that a patient aged 60–79 years is more than twice as likely to be initiated on warfarin following a diagnosis of AF, than a patient with the same gender, BMI, comorbidities and bleeding risk aged over 80 years (table 2).

Our finding of low warfarin use among elderly patients in the UK is consistent with findings of US studies in hospitals and in primary care, which found warfarin prescribed in only

Table 2 Logistic regression models

Variable	Unadjusted OR§	95% CI	p Value	Adjusted OR§	95% CI	p Value
Men						
Age 60–69*	2.55	2.4 to 2.72	<0.0001	2.15	2.01 to 2.29	<0.0001
Age 70–79*	2.32	2.19 to 2.45	<0.0001	2.20	2.08 to 2.33	<0.0001
BMI <20†	0.56	0.49 to 0.65	<0.0001	0.60	0.52 to 0.70	<0.0001
BMI 25-<30†	1.43	1.35 to 1.51	<0.0001	1.30	1.23 to 1.38	<0.0001
BMI 30-<35†	1.75	1.63 to 1.87	<0.0001	1.46	1.36 to 1.57	<0.0001
BMI 35+†	2.30	2.07 to 2.55	<0.0001	1.73	1.55 to 1.93	<0.0001
Hypertension	1.17	1.11 to 1.22	<0.0001	1.24	1.18 to 1.3	<0.0001
Heart Failure	1.34	1.27 to 1.41	<0.0001	1.41	1.33 to 1.49	<0.0001
LVEF	2.09	1.86 to 2.35	<0.0001	1.72	1.52 to 1.94	<0.0001
Diabetes	1.08	1.01 to 1.15	<0.0001	0.94	0.88 to 1.00	0.05650
Stroke/TIA	1.15	1.07 to 1.23	<0.0001	1.56	1.44 to 1.68	<0.0001
Dementia	0.47	0.42 to 0.53	<0.0001	0.59	0.52 to 0.66	<0.0001
Vascular Disease	1.10	1.04 to 1.17	0.0006	1.10	1.03 to 1.16	0.00260
Thromboembolism	1.59	1.44 to 1.76	<0.0001	1.59	1.44 to 1.77	<0.0001
HAS-BLED 2	0.82	0.78 to 0.87	<0.0001	0.8	0.76 to 0.85	<0.0001
HAS-BLED 3	0.69	0.65 to 0.74	<0.0001	0.612	0.57 to 0.66	<0.0001
HAS-BLED 4	0.55	0.5 to 0.61	<0.0001	0.432	0.38 to 0.49	<0.0001
	p					
Goodness-of-fit‡	0.79					
Women						
Age 60–69*	2.29	2.14 to 2.44	<0.0001	1.95	1.82 to 2.10	<0.0001
Age 70–79*	2.43	2.31 to 2.55	<0.0001	2.29	2.17 to 2.41	<0.0001
BMI <20†	0.63	0.58 to 0.70	<0.0001	0.69	0.62 to 0.76	<0.0001
BMI 25-<30†	1.35	1.28 to 1.43	<0.0001	1.25	1.18 to 1.32	<0.0001
BMI 30-<35†	1.55	1.45 to 1.66	<0.0001	1.33	1.24 to 1.42	<0.0001
BMI 35+†	1.96	1.81 to 2.13	<0.0001	1.46	1.34 to 1.59	<0.0001
Hypertension	1.14	1.09 to 1.19	<0.0001	1.23	1.17 to 1.3	<0.0001
Heart Failure	1.18	1.12 to 1.24	<0.0001	1.28	1.21 to 1.35	<0.0001
LVEF	1.82	1.58 to 2.11	<0.0001	1.55	1.33 to 1.80	<0.0001
Diabetes	1.00	0.94 to 1.07	0.93	Not included in final model		
Stroke/TIA	1.16	1.08 to 1.24	<0.0001	1.49	1.38 to 1.60	<0.0001
Dementia	0.41	0.37 to 0.46	<0.0001	0.51	0.46 to 0.57	<0.0001
Vascular disease	0.96	0.89 to 1.03	0.22	Not included in final model		
Thromboembolism	1.74	1.58 to 1.91	<0.0001	1.72	1.56 to 1.90	<0.0001
HAS-BLED 2	0.85	0.81 to 0.9	<0.0001	0.83	0.79 to 0.88	<0.0001
HAS-BLED 3	0.78	0.73 to 0.83	<0.0001	0.71	0.66 to 0.76	<0.0001
HAS-BLED 4	0.61	0.55 to 0.68	<0.0001	0.51	0.45 to 0.57	<0.0001
	p					
Goodness-of-fit‡	0.43					

*Age: reference group=Age 80+ years;
†BMI: reference group=BMI 20-<25;
‡Hosmer and Lemeshow goodness-of-fit test.
§ OR, unadjusted is crude OR adjusted for practice only, adjusted is OR from multivariable model adjusted for practice and all other variables included in the final model.

40%–45% of patients with AF, with age increasing the risk of not being treated.[11–14] Our findings are also consistent with an earlier analysis of patients with AF from the GPRD database in 1996 that found among potential candidates for anticoagulation, only 22% of those aged 70+ years were prescribed warfarin compared with 49% among patients aged 40–60 years.[23] While a trend towards increasing warfarin prescribing practice in recent years has been demonstrated in our study, the results show that current prescribing practice is not in step with the current evidence base, and that anticoagulation therapy is particularly under-used in elderly patients. This is important, since there is now a clear evidence base that anticoagulation is effective for stroke prevention in elderly people in atrial fibrillation.[19] Indeed, a recent non-randomised study found that warfarin use in this age group not only was associated with reduced stroke risk, but also with improved life expectancy.[9]

This study found that in the UK, women with AF are less likely to be prescribed warfarin than men with the same risk factors for stroke, even though female sex has been associated with increased risk of stroke in AF.[4] This is consistent with findings in Scotland that women with AF were 25% less likely to receive warfarin than men,[24] and a Canadian study which showed that women were 54% less likely to receive warfarin, but only in the subgroup of patients aged ≥75 years.[25] However, a more recent Canadian study found no evidence of reduced usage of warfarin in women compared with men.[26]

It is difficult to explain the disparity of use of anticoagulation in women as compared with men. Gender inequalities have been

Table 3 Warfarin treatment by HAS-BLED and CHADS2 score

$CHADS_2$	Age group	60–69 years				70–79 years				80+ years (reference group)	
		Patients n	Patients treated with warfarin (%)	χ^2 Value*	p Value*	Patients n	Patients treated with warfarin (%)	χ^2 Value†	p Value†	Patients n	Patients treated with warfarin (%)
0	HAS-BLED > $CHADS_2$	4265	49	–	–	3998	51	–	–	0	–
	HAS-BLED≤$CHADS_2$	1978	49	–	–	0	–	–	–	0	–
1	HAS-BLED>$CHADS_2$	2880	56	692	<0.0001	5556	52	697	<0.0001	3801	25
	HAS-BLED≤$CHADS_2$	3821	60	814	<0.0001	4309	56	640	<0.0001	4492	29
2	HAS-BLED>$CHADS_2$	512	55	130	<0.0001	2296	52	266	<0.0001	3286	30
	HAS-BLED≤$CHADS_2$	2137	65	772	<0.0001	6997	58	1022	<0.0001	10596	33
3	HAS-BLED>$CHADS_2$	128	52	31	<0.0001	419	53	71	<0.0001	526	26
	HAS-BLED≤$CHADS_2$	965	69	419	<0.0001	4157	58	554	<0.0001	6524	34
4+	HAS-BLED>$CHADS_2$	7	57	3	0.0762	62	53	13	0.0004	111	26
	HAS-BLED≤$CHADS_2$	361	66	129	<0.0001	2556	57	286	<0.0001	4641	36

*χ^2 tests comparing the proportion of patients treated with warfarin in the 60–69 years age group compared with the 80+ years age group.
†χ^2 tests comparing the proportion of patients treated with warfarin in the 70–79 years age group compared with the 80+ years age group.

observed in use of therapies in other areas of cardiovascular medicine.[27] These have been attributed to a possible perceived lower risk of cardiovascular disease in women compared with men, leading to under-recording of risk factors and lower rates of prophylactic treatment in women. It may be that the same factors apply in the use of anticoagulation in patients with AF.

The factors that determine whether warfarin is prescribed in clinical practice are complex, and our study was not designed to investigate the reasons behind clinical decision making. Physicians often avoid anticoagulation in elderly patients due to fear of bleeding, fall risk, non-adherence and monitoring concerns.[13–15] While the efficacy of warfarin in stroke prevention is established, warfarin has many limitations, including a narrow therapeutic index, slow onset and offset of action, multiple drug and food interactions, and a requirement for close laboratory monitoring of coagulation via the International Normalised Ratio (INR) and subsequent dose adjustments.[28] Close monitoring necessitates regular clinic visits with increased financial burden and inconvenience to patients; thus, many eligible patients choose not to use warfarin.[29] However, patient education and self-monitoring may promote better compliance and INR control among elderly patients with AF.[30]

Unlike recent Swedish and Canadian studies, in this study, $CHADS_2$ scores predicted anticoagulation use in a British population.[8 9] The difference between these findings may reflect international variation in practice, or may be related to issues of study design: for instance, the present study was restricted to patients aged 60 years and over; and the Swedish study was smaller, so it cannot exclude associations of a similar magnitude to the present study.

The recent development of new anticoagulants, such as dabigatran, rivaroxaban and apixaban, represent potential new therapies for patients with AF that may circumvent many of the inconveniences of warfarin, such as regular INR checks, dietary restrictions and drug interactions. How new agents will be used in the management of elderly patients with AF in everyday practice remains to be established; however, recent NICE guidance recommends the use of dabigatran in atrial fibrillation under the licensed indication, which includes patients aged >75 years, and those aged >65 years with an additional risk factor.[10]

Study limitations

In this study, patients with at least one prescription for warfarin in their GP record were assumed to have been initiated on warfarin. The GPRD records prescriptions issued rather than dispensed, thus, it would not be possible to confirm whether a patient was taking the medication from an initial prescription alone. However, as this study aimed to investigate the

Table 4 Logistic regression models- CHADS2

Variable	Unadjusted OR*	95% CI	p Value	Adjusted OR*	95% CI	p Value
Men						
$CHADS_2$=2†	0.98	0.93 to 1.03	0.47	1.30	1.23 to 1.38	<0.0001
$CHADS_2$=3†	0.98	0.92 to 1.05	0.62	1.35	1.26 to 1.45	<0.0001
$CHADS_2$=4+†	0.97	0.90 to 1.06	0.53	1.44	1.32 to 1.57	<0.0001
Goodness-of-fit‡						0.952
Women						
$CHADS_2$=2†	0.88	0.83 to 0.92	<0.0001	1.21	1.14 to 1.28	<0.0001
$CHADS_2$=3†	0.93	0.87 to 0.99	0.03	1.32	1.23 to 1.42	<0.0001
$CHADS_2$=4+†	0.89	0.82 to 0.96	0.004	1.34	1.23 to 1.46	<0.0001
Goodness-of-fit‡						0.575

*OR, unadjusted is crude OR adjusted for practise only, adjusted is OR from multivariable model adjusted for practise and age.
†$CHADS_2$: Reference group $CHADS_2$=0/1.
‡Hosmer and Lemeshow goodness-of-fit test.

prescribing decision rather than the treatment, this will not have introduced major misclassification.

As discussed above, clinical practice is driven by other factors than are in the clinical guidelines such as patient preference, that may affect the decision as to whether warfarin is initiated, which are not recorded in GPRD. It might be that these factors have confounded the associations that we observed between age and sex and use of warfarin. Socioeconomic factors were not taken into account in our analysis, however, an earlier analysis of anticoagulation use in AF using general practice data suggests that these were not significant confounders of any association with anticoagulation use.[17]

While this study was able to look at the extent to which warfarin use was influenced by bleeding risk, as assessed using the HAS-BLED score, this tool does have limitations in terms of accuracy.[20] Therefore, it is possible that we have not fully accounted for bleeding risk in our models. Nevertheless, we did find that higher HAS-BLED scores were associated with lower use of warfarin, suggesting that this tool does have reasonable utility as a means of adjusting for bleeding risk in this analysis.

CONCLUSIONS

Our analysis has demonstrated that age is much the strongest single predictor of whether or not anticoagulation is used in AF. The low use of warfarin in people aged 80 years is not explained by increased comorbidity or increased bleeding risk, since marked differences in use of warfarin were observed when we compared use in people aged 80+ years with other ages, after we stratified by these factors, or adjusted for them. This suggests that there is genuine under-use of anticoagulation in the elderly. Strategies need to be developed to improve the uptake of anticoagulation in this age group.

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Appendix 1 – GPRD Clinical Codes

Atrial Fibrillation

Pegasus Code	Read Code	Read Term
1664	G573000	Atrial fibrillation
2212	G573.00	Atrial fibrillation and flutter
1268	G573200	Paroxysmal atrial fibrillation
18746	662S.00	Atrial fibrillation monitoring
6345	14AN.00	H/O: atrial fibrillation
3757	3272	ECG: atrial fibrillation
57832	9Os..00	Atrial fibrillation monitoring administration
45773	6A9..00	Atrial fibrillation annual review
39114	9hF1.00	Excepted from atrial fibrillation qual indic: Inform dissent
23437	G573z00	Atrial fibrillation and flutter NOS
90187	9Os0.00	Atrial fibrillation monitoring first letter
63350	9hF..00	Exception reporting: atrial fibrillation quality indicators
96076	G573500	Persistent atrial fibrillation
9479	7936A00	Implant intravenous pacemaker for atrial fibrillation
90188	9Os1.00	Atrial fibrillation monitoring second letter
35127	G573300	Non-rheumatic atrial fibrillation
90189	9Os2.00	Atrial fibrillation monitoring third letter
96277	G573400	Permanent atrial fibrillation
90190	9Os3.00	Atrial fibrillation monitoring verbal invite
90191	9Os4.00	Atrial fibrillation monitoring telephone invite

Stroke

Pegasus Code	Read Code	Read Term
1469	G66..00	Stroke and cerebrovascular accident unspecified
1298	G66..11	CVA unspecified
3149	G64z.00	Cerebral infarction NOS
5363	G64..11	CVA - cerebral artery occlusion
6116	G66..13	CVA - Cerebrovascular accident unspecified
6960	G61..11	CVA - cerebrovascular accid due to intracerebral haemorrhage
569	G64..12	Infarction - cerebral
7780	G667.00	Left sided CVA
12833	G668.00	Right sided CVA
6155	G64..13	Stroke due to cerebral arterial occlusion
6253	G66..12	Stroke unspecified
18604	G61..12	Stroke due to intracerebral haemorrhage
17322	G664.00	Cerebellar stroke syndrome
8443	G663.00	Brain stem stroke syndrome
9985	G64z200	Left sided cerebral infarction
10504	G64z300	Right sided cerebral infarction
36717	G640000	Cerebral infarction due to thrombosis of cerebral arteries
23671	G63y000	Cerebral infarct due to thrombosis of precerebral arteries
6228	G68X.00	Sequelae of stroke,not specfd as h'morrhage or infarction
24446	G63y100	Cerebral infarction due to embolism of precerebral arteries
39344	G676000	Cereb infarct due cerebral venous thrombosis, nonpyogenic
27975	G641000	Cerebral infarction due to embolism of cerebral arteries
53745	Gyu6400	[X]Other cerebral infarction
39403	G683.00	Sequelae of cerebral infarction
47607	L440.11	CVA - cerebrovascular accident in the puerperium
51759	G677000	Occlusion and stenosis of middle cerebral artery
31704	G677.00	Occlusion/stenosis cerebral arts not result cerebral infarct
65770	G677200	Occlusion and stenosis of posterior cerebral artery
57527	G677100	Occlusion and stenosis of anterior cerebral artery
56279	L440.12	Stroke in the puerperium

History of Stroke (Additional to Stroke Codes)

Pegasus Code	Read Code	Read Term
10792	662M.00	Stroke monitoring
11039	9h21.00	Excepted from stroke quality indicators: Patient unsuitable
18686	662e.00	Stroke/CVA annual review
28753	9Om0.00	Stroke/transient ischaemic attack monitoring first letter
6305	14A7.11	H/O: CVA
5871	14A7.12	H/O: stroke
34245	9Om1.00	Stroke/transient ischaemic attack monitoring second letter
34135	14A7.00	H/O: CVA/stroke
31218	9Om..00	Stroke/transient ischaemic attack monitoring administration
34375	9Om2.00	Stroke/transient ischaemic attack monitoring third letter
7138	ZV12512	[V]Personal history of cerebrovascular accident (CVA)
19348	ZV12511	[V]Personal history of stroke
89913	9Om4.00	Stroke/transient ischaemic attack monitoring telephone invte
28914	662o.00	Haemorrhagic stroke monitoring
66873	14AK.00	H/O: Stroke in last year
56458	8HHM.00	Ref to multidisciplinary stroke function improvement service
55351	7P24200	Delivery of rehabilitation for stroke

TIA

Pegasus Code	Read Code	Read Term
1433	G65..12	Transient ischaemic attack

Bleed Codes

Intracranial Bleeds

Pegasus Code	Read Code	Read Term
1786	G60..00	Subarachnoid haemorrhage
5051	G61..00	Intracerebral haemorrhage
6960	G61..11	CVA - cerebrovascular accid due to intracerebral haemorrhage
4273	G621.00	Subdural haemorrhage - nontraumatic
3535	G61z.00	Intracerebral haemorrhage NOS
18604	G61..12	Stroke due to intracerebral haemorrhage
18912	G623.00	Subdural haemorrhage NOS
13564	G613.00	Cerebellar haemorrhage
23580	G60z.00	Subarachnoid haemorrhage NOS
30202	G617.00	Intracerebral haemorrhage, intraventricular
19412	G602.00	Subarachnoid haemorrhage from middle cerebral artery
7912	G614.00	Pontine haemorrhage
40338	G611.00	Internal capsule haemorrhage
36178	G620.00	Extradural haemorrhage - nontraumatic
28314	G61X000	Left sided intracerebral haemorrhage, unspecified
19201	G61X100	Right sided intracerebral haemorrhage, unspecified
42331	G603.00	Subarachnoid haemorrhage from anterior communicating artery
43451	G682.00	Sequelae of other nontraumatic intracranial haemorrhage
31805	G62..00	Other and unspecified intracranial haemorrhage
31595	G610.00	Cortical haemorrhage
46316	G612.00	Basal nucleus haemorrhage

9696	G604.00	Subarachnoid haemorrhage from posterior communicating artery
41910	G605.00	Subarachnoid haemorrhage from basilar artery
44740	G680.00	Sequelae of subarachnoid haemorrhage
48149	G681.00	Sequelae of intracerebral haemorrhage
57315	G618.00	Intracerebral haemorrhage, multiple localized
53810	Gyu6200	[X]Other intracerebral haemorrhage
65745	Gyu6100	[X]Other subarachnoid haemorrhage
60692	G606.00	Subarachnoid haemorrhage from vertebral artery
63806	Q200y00	Subdural or cerebral haemorrhage due to birth trauma OS
56007	G601.00	Subarachnoid haemorrhage from carotid siphon and bifurcation
96630	Gyu6F00	[X]Intracerebral haemorrhage in hemisphere, unspecified
2883	S622.00	Closed traumatic subdural haemorrhage
5682	S62..00	Cerebral haemorrhage following injury
20284	G62z.00	Intracranial haemorrhage NOS
27661	S62..11	Extradural haemorrhage following injury
31060	G61X.00	Intracerebral haemorrhage in hemisphere, unspecified
8181	S628.00	Traumatic subdural haemorrhage
46545	S62z.00	Cerebral haemorrhage following injury NOS
38304	S620.00	Closed traumatic subarachnoid haemorrhage
45421	S624.00	Closed traumatic extradural haemorrhage
28077	S62..14	Traumatic cerebral haemorrhage
58545	S627.00	Traumatic subarachnoid haemorrhage
30045	G616.00	External capsule haemorrhage
62342	G615.00	Bulbar haemorrhage
73471	S625.00	Open traumatic extradural haemorrhage
94351	S623.00	Open traumatic subdural haemorrhage
96717	S621.00	Open traumatic subarachnoid haemorrhage
6569	S62..13	Subdural haemorrhage following injury

GI Bleeds

Pegasus Code	Read Code	Read Term
1642	J68z.11	GIB - Gastrointestinal bleeding
3097	J68..00	Gastrointestinal haemorrhage
4354	J68z200	Upper gastrointestinal haemorrhage
2814	J12y100	Unspecified duodenal ulcer with haemorrhage
4636	J68zz00	Gastrointestinal tract haemorrhage NOS
15517	J68z000	Gastric haemorrhage NOS
18001	J120100	Acute duodenal ulcer with haemorrhage
2150	J68z100	Intestinal haemorrhage NOS
12471	J68z.00	Gastrointestinal haemorrhage unspecified
11124	J110111	Bleeding acute gastric ulcer
30054	J110100	Acute gastric ulcer with haemorrhage
48951	J121100	Chronic duodenal ulcer with haemorrhage
44637	J130100	Acute peptic ulcer with haemorrhage
63582	J111100	Chronic gastric ulcer with haemorrhage
36583	J111111	Bleeding chronic gastric ulcer
48730	J120300	Acute duodenal ulcer with haemorrhage and perforation
57958	J11y100	Unspecified gastric ulcer with haemorrhage

53126	J131100	Chronic peptic ulcer with haemorrhage
94397	J11yy00	Unspec gastric ulcer; unspec haemorrhage and/or perforation
70456	J13y100	Unspecified peptic ulcer with haemorrhage
71403	J110300	Acute gastric ulcer with haemorrhage and perforation
71897	J111300	Chronic gastric ulcer with haemorrhage and perforation
28366	J12yy00	Unspec duodenal ulcer; unspec haemorrhage and/or perforation
71881	J121300	Chronic duodenal ulcer with haemorrhage and perforation
45304	J130300	Acute peptic ulcer with haemorrhage and perforation
60346	J14y100	Unspecified gastrojejunal ulcer with haemorrhage
93436	J12y300	Unspecified duodenal ulcer with haemorrhage and perforation
96622	J13y300	Unspecified peptic ulcer with haemorrhage and perforation
96628	J140100	Acute gastrojejunal ulcer with haemorrhage

Coronary Heart Disease

Pegasus Code	Read Code	Read Term
241	G30..00	Acute myocardial infarction
14658	G30z.00	Acute myocardial infarction NOS
1677	G30..15	MI - acute myocardial infarction
10562	G307100	Acute non-ST segment elevation myocardial infarction
5904	792..00	Coronary artery operations
1678	G308.00	Inferior myocardial infarction NOS
1204	G30..14	Heart attack
12229	G30X000	Acute ST segment elevation myocardial infarction
2491	G30..12	Coronary thrombosis
14897	G301z00	Anterior myocardial infarction NOS
7442	7920200	Saphenous vein graft replacement of three coronary arteries
5387	G301.00	Other specified anterior myocardial infarction
12139	G300.00	Acute anterolateral infarction
8935	G302.00	Acute inferolateral infarction
11610	7920300	Saphenous vein graft replacement of four+ coronary arteries
17872	G301100	Acute anteroseptal infarction
7634	7920100	Saphenous vein graft replacement of two coronary arteries
9507	G307000	Acute non-Q wave infarction
10603	792z.00	Coronary artery operations NOS
23892	G304.00	Posterior myocardial infarction NOS
7783	323..00	ECG: myocardial infarction
16408	G32..11	Healed myocardial infarction
14898	G305.00	Lateral myocardial infarction NOS
13571	G30..16	Thrombosis - coronary
29643	G303.00	Acute inferoposterior infarction
17689	G30..17	Silent myocardial infarction
46017	G30yz00	Other acute myocardial infarction NOS
18842	G35..00	Subsequent myocardial infarction
13566	G30..11	Attack - heart
47788	7927	Other open operations on coronary artery
32272	G38..00	Postoperative myocardial infarction
9555	G33z500	Post infarct angina
34803	G30y.00	Other acute myocardial infarction
29758	G30X.00	Acute transmural myocardial infarction of unspecif site
41221	G30y200	Acute septal infarction
10209	7921200	Autograft replacement of three coronary arteries NEC
23579	G310.00	Postmyocardial infarction syndrome
42708	7921300	Autograft replacement of four of more coronary arteries NEC
19413	7921100	Autograft replacement of two coronary arteries NEC

38609	G351.00	Subsequent myocardial infarction of inferior wall
63467	G306.00	True posterior myocardial infarction
32854	G30B.00	Acute posterolateral myocardial infarction
41835	G384.00	Postoperative subendocardial myocardial infarction
45370	7922300	Allograft replacement of four or more coronary arteries
45886	7922200	Allograft replacement of three coronary arteries
31540	7924200	Revision of bypass for three coronary arteries
26972	3234	ECG:posterior/inferior infarct
67761	7923300	Prosthetic replacement of four or more coronary arteries
46276	G381.00	Postoperative transmural myocardial infarction inferior wall
55092	792C000	Replacement of coronary arteries using multiple methods
66236	7923200	Prosthetic replacement of three coronary arteries
57241	7922100	Allograft replacement of two coronary arteries
67554	7924100	Revision of bypass for two coronary arteries
68748	G38z.00	Postoperative myocardial infarction, unspecified
31519	7925100	Double implant of mammary arteries into coronary arteries
46112	G380.00	Postoperative transmural myocardial infarction anterior wall
46166	G35X.00	Subsequent myocardial infarction of unspecified site
62608	7926000	Double anastom thoracic arteries to coronary arteries NEC
62626	G30y100	Acute papillary muscle infarction
66664	7923100	Prosthetic replacement of two coronary arteries
72562	G353.00	Subsequent myocardial infarction of other sites
96838	Gyu3400	[X]Acute transmural myocardial infarction of unspecif site
1430	G33..00	Angina pectoris
19542	662K000	Angina control - good
1431	G311.13	Unstable angina
13185	662K.00	Angina control
1344	G340.12	Coronary artery disease
7347	G311100	Unstable angina
8942	7929400	Insertion of coronary artery stent
28554	G33zz00	Angina pectoris NOS
7137	7920y00	Saphenous vein graft replacement of coronary artery OS
1414	G33z300	Angina on effort
4656	G311.11	Crescendo angina
12804	G33z700	Stable angina
25842	G33z.00	Angina pectoris NOS
15373	662K100	Angina control - poor
18118	G311400	Worsening angina
17054	7N41300	[SO]Coronary artery
18249	7920	Saphenous vein graft replacement of coronary artery
14782	662K200	Angina control - improving
15349	662Kz00	Angina control NOS
17307	G311200	Angina at rest
18889	G34z000	Asymptomatic coronary heart disease
19655	G311.14	Angina at rest
36854	G332.00	Coronary artery spasm
12986	G331.00	Prinzmetal's angina
22020	792B000	Endarterectomy of coronary artery NEC
42304	7929500	Insertion of drug-eluting coronary artery stent
8679	7920000	Saphenous vein graft replacement of one coronary artery
17133	G30A.00	Mural thrombosis
51515	7920z00	Saphenous vein graft replacement coronary artery NOS
9414	7921	Other autograft replacement of coronary artery
24888	7929	Other therapeutic transluminal operations on coronary artery

18125	G330000	Nocturnal angina
26863	G33z600	New onset angina
11048	G331.11	Variant angina pectoris
30421	G30..13	Cardiac rupture following myocardial infarction (MI)
34328	G311300	Refractory angina
31571	792y.00	Other specified operations on coronary artery
45960	8B27.00	Antianginal therapy
34965	792A.00	Diagnostic transluminal operations on coronary artery
28736	G30y000	Acute atrial infarction
40429	G301000	Acute anteroapical infarction
39449	G312.00	Coronary thrombosis not resulting in myocardial infarction
44561	7921000	Autograft replacement of one coronary artery NEC
44585	792Bz00	Repair of coronary artery NOS
31556	7922	Allograft replacement of coronary artery
45809	G350.00	Subsequent myocardial infarction of anterior wall
55137	G311011	MI - myocardial infarction aborted
33620	792B.00	Repair of coronary artery NEC
61072	G311000	Myocardial infarction aborted
51043	ZRBN.00	Duke's coronary artery disease score
6182	7929y00	Other therapeutic transluminal op on coronary artery OS
29902	G330z00	Angina decubitus NOS
19402	7923	Prosthetic replacement of coronary artery
51702	7927400	Exploration of coronary artery
51507	7925300	Single anastomosis of mammary artery to coronary artery NEC
33718	7925000	Double anastomosis of mammary arteries to coronary arteries
55598	792C.00	Other replacement of coronary artery
41757	7927z00	Other open operation on coronary artery NOS
7609	7921z00	Other autograft replacement of coronary artery NOS
37719	7925y00	Connection of mammary artery to coronary artery OS
48767	7922z00	Allograft replacement of coronary artery NOS
61248	792Az00	Diagnostic transluminal operation on coronary artery NOS
66583	7929200	Percut translum inject therap subst to coronary artery NEC
93618	7929600	Percutaneous transluminal atherectomy of coronary artery
56905	792Ay00	Diagnostic transluminal operation on coronary artery OS
68139	7925400	Single implantation of mammary artery into coronary artery
61310	7921y00	Other autograft replacement of coronary artery OS
69247	792By00	Other specified repair of coronary artery
70755	792Cz00	Replacement of coronary artery NOS
52615	P6y7.00	Myocardial bridge of coronary artery
59423	7922y00	Other specified allograft replacement of coronary artery
60753	7926300	Single implantation thoracic artery into coronary artery NEC
67591	7926200	Single anastomosis of thoracic artery to coronary artery NEC
70111	7922000	Allograft replacement of one coronary artery
19193	7923z00	Prosthetic replacement of coronary artery NOS
39546	Gyu3000	[X]Other forms of angina pectoris
61592	7927200	Transection of muscle bridge of coronary artery
72780	7926z00	Connection of other thoracic artery to coronary artery NOS
92419	7923000	Prosthetic replacement of one coronary artery
93828	792Cy00	Other specified replacement of coronary artery
94783	792B100	Repair of rupture of coronary artery
95382	7927y00	Other specified other open operation on coronary artery
96804	7926	Connection of other thoracic artery to coronary artery

Hypertension

Pegasus Code	Read Code	Read Term
799	G20..00	Essential hypertension
4444	662..12	Hypertension monitoring
204	G2...00	Hypertensive disease
13186	662P.00	Hypertension monitoring
351	G20..11	High blood pressure
10818	G20z.00	Essential hypertension NOS
19070	662d.00	Hypertension annual review
3712	G20z.11	Hypertension NOS
18482	662c.00	Hypertension six month review
11056	8BL0.00	Patient on maximal tolerated antihypertensive therapy
3425	662O.00	On treatment for hypertension
16565	6627	Good hypertension control
7057	G2z..00	Hypertensive disease NOS
27511	6628	Poor hypertension control
13188	662G.00	Hypertensive treatm.changed
1894	G201.00	Benign essential hypertension
8732	G2...11	BP - hypertensive disease
4372	G202.00	Systolic hypertension
27634	9N1y200	Seen in hypertension clinic
18057	8B26.00	Antihypertensive therapy
21826	662F.00	Hypertension treatm. started
24127	9OIA.11	Hypertension monitored
6702	F421300	Hypertensive retinopathy
16292	G21..00	Hypertensive heart disease
15377	G200.00	Malignant essential hypertension
18590	662b.00	Moderate hypertension control
22356	1JD..00	Suspected hypertension
7329	G24..00	Secondary hypertension
12680	8CR4.00	Hypertension clinical management plan
4668	G22..00	Hypertensive renal disease
8857	G21z011	Cardiomegaly - hypertensive
30776	6629	Hypertension:follow-up default
29310	G22z.11	Renal hypertension
16059	G24z.00	Secondary hypertension NOS
18765	G2y..00	Other specified hypertensive disease
16173	G21zz00	Hypertensive heart disease NOS
3979	G672.00	Hypertensive encephalopathy
21660	TJC7.00	Adverse reaction to other antihypertensives
31341	G24z100	Hypertension secondary to drug
20497	TJC7z00	Adverse reaction to antihypertensives NOS
22333	8I3N.00	Hypertension treatment refused
32976	6146200	Hypertension induced by oral contraceptive pill
15106	G22z.00	Hypertensive renal disease NOS
83473	G203.00	Diastolic hypertension
31387	G24z000	Secondary renovascular hypertension NOS
42229	G24zz00	Secondary hypertension NOS
39649	G220.00	Malignant hypertensive renal disease
31816	G672.11	Hypertensive crisis
34744	G244.00	Hypertension secondary to endocrine disorders
25371	G241000	Secondary benign renovascular hypertension
31464	G21z.00	Hypertensive heart disease NOS
32423	G222.00	Hypertensive renal disease with renal failure

57288	G241.00	Secondary benign hypertension
28684	G233.00	Hypertensive heart and renal disease with renal failure
51635	G241z00	Secondary benign hypertension NOS
31755	G240.00	Secondary malignant hypertension
37086	F404200	Blind hypertensive eye
30770	U60C511	[X] Adverse reaction to other antihypertensives
21837	G232.00	Hypertensive heart&renal dis wth (congestive) heart failure
43935	G221.00	Benign hypertensive renal disease
69753	Gyu2.00	[X]Hypertensive diseases
52427	G211.00	Benign hypertensive heart disease
61166	G21z000	Hypertensive heart disease NOS without CCF
63466	G23..00	Hypertensive heart and renal disease
62718	G21z100	Hypertensive heart disease NOS with CCF
50157	G210.00	Malignant hypertensive heart disease
44350	U60C51A	[X] Adverse reaction to antihypertensives NOS
52127	G211100	Benign hypertensive heart disease with CCF
59383	G240000	Secondary malignant renovascular hypertension
68659	G23z.00	Hypertensive heart and renal disease NOS
61660	G211000	Benign hypertensive heart disease without CCF
73293	G240z00	Secondary malignant hypertension NOS
67232	G230.00	Malignant hypertensive heart and renal disease
85944	7Q01.00	High cost hypertension drugs
63000	G231.00	Benign hypertensive heart and renal disease
63260	SLC6z00	Hypertensive agent poisoning NOS
95334	G210000	Malignant hypertensive heart disease without CCF
72226	SLC6.00	Other hypertensive agent poisoning
72668	G210100	Malignant hypertensive heart disease with CCF
97533	Gyu2100	[X]Hypertension secondary to other renal disorders

Appendix 2

Warfarin Codes

Product Code	Product Name	Drug substance
45	warfarin sodium tablets 1mg	warfarin sodium
61	warfarin sodium tablets 3mg	warfarin sodium
1781	warfarin sodium tablets 5mg	warfarin sodium
6262	warfarin sodium tablets 500 micrograms	warfarin sodium
8466	MAREVAN tablets 1mg [GOLDSHIELD]	warfarin sodium
8467	MAREVAN tablets 3mg [GOLDSHIELD]	warfarin sodium
13348	MAREVAN tablets 5mg [GOLDSHIELD]	warfarin sodium
23078	WARFARIN tablets 1mg [WB]	warfarin sodium
31511	WARFARIN tablets 3mg [WB]	warfarin sodium
17965	MAREVAN tablets 500 micrograms [GOLDSHIELD]	warfarin sodium
33711	WARFARIN tablets 5mg [WB]	warfarin sodium
31937	WARFARIN tablets 5mg [TEVA]	warfarin sodium
34019	WARFARIN tablets 1mg [IVAX]	warfarin sodium
34758	WARFARIN tablets 3mg [IVAX]	warfarin sodium
34864	WARFARIN tablets 5mg [IVAX]	warfarin sodium
34299	WARFARIN tablets 1mg [TEVA]	warfarin sodium
30202	WARFARIN WBP tablets 1mg [BOEH I HSP]	warfarin sodium
43408	WARFARIN tablets 1mg [HILLCROSS]	warfarin sodium
30203	WARFARIN WBP tablets 3mg [BOEH I HSP]	warfarin sodium
34087	WARFARIN tablets 1mg [CELLTECH]	warfarin sodium
43407	WARFARIN tablets 3mg [HILLCROSS]	warfarin sodium
34417	WARFARIN tablets 3mg [TEVA]	warfarin sodium
34095	WARFARIN WBP tablets 5mg [BOEH I HSP]	warfarin sodium
43409	WARFARIN tablets 5mg [HILLCROSS]	warfarin sodium
34086	WARFARIN tablets 3mg [CELLTECH]	warfarin sodium
833	warfarin sodium oral liquid 3mg/5ml	warfarin sodium
36099	warfarin sodium oral suspension 1mg/5ml	warfarin sodium
40143	WARFARIN tablets 500 micrograms [HILLCROSS]	warfarin sodium
34088	WARFARIN tablets 5mg [CELLTECH]	warfarin sodium
34526	WARFARIN tablets 3mg [GEN (UK)]	warfarin sodium
34418	WARFARIN tablets 5mg [GEN (UK)]	warfarin sodium
34517	WARFARIN tablets 1mg [GEN (UK)]	warfarin sodium
34416	WARFARIN tablets 1mg [KENT]	warfarin sodium
38041	warfarin sodium oral suspension 5mg/5ml	warfarin sodium
34576	WARFARIN tablets 1mg [LAGAP]	warfarin sodium
38044	warfarin sodium oral solution 5mg/5ml	warfarin sodium
10560	WARFARIN 10 MG TAB	
39866	WARFARIN tablets 1mg [ALMUS]	warfarin sodium
34918	WARFARIN tablets 5mg [ACTAVIS]	warfarin sodium
34691	WARFARIN tablets 5mg [REGENT]	warfarin sodium
20754	WARFARIN	
43655	warfarin sodium oral liquid	warfarin sodium