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Anticoagulation trends in adults aged 65 and over with atrial fibrillation; a cohort study.

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Abstract:	Objective: To describe patterns of anticoagulation prescription and persistence for those aged ≥65 years with atrial fibrillation (AF). Methods: Descriptive cohort study using electronic general practice records of patients in England, who attended a flu vaccination aged ≥65 and were diagnosed with AF between 2008-2018. Patients were stratified by 10-year age group and year of diagnosis. Proportion anticoagulated, type of anticoagulation (direct oral anticoagulant (DOAC) or warfarin) initiated at diagnosis and persistence with anticoagulation over time are reported. Results: 42,290 patients (49% female), aged 65-74 (n=11,722), 75-84 (n=19,055) and 85+ (n=11,513) at AF diagnosis are included. Prescription of anticoagulation at diagnosis increased over the time period from 55% to 86% in people aged 65-74, from 54% to 86% in people aged 75-84 and from 27% to 75% in people aged 85 and over. By 2018 92% of patients with newly diagnosed AF were started on a DOAC. Survivor function for 5-year persistence in patients prescribed DOAC was 0.80 (0.77:0.82) and for warfarin 0.71(0.70:0.72). Survivor function for any anticoagulation at 5 years was 0.79(0.78:0.81), 0.73(0.72:0.75), 0.58(0.59:0.64) for people aged 65-74, 75-84 and 85+ respectively. Conclusions: Rates of anticoagulation in AF in those aged ≥65 have increased from 2008 to 2018, over which time period there has been a shift from initiating anticoagulation with warfarin to DOAC. Persistence with anticoagulation is higher in people on DOACs than on warfarin and in people <85.

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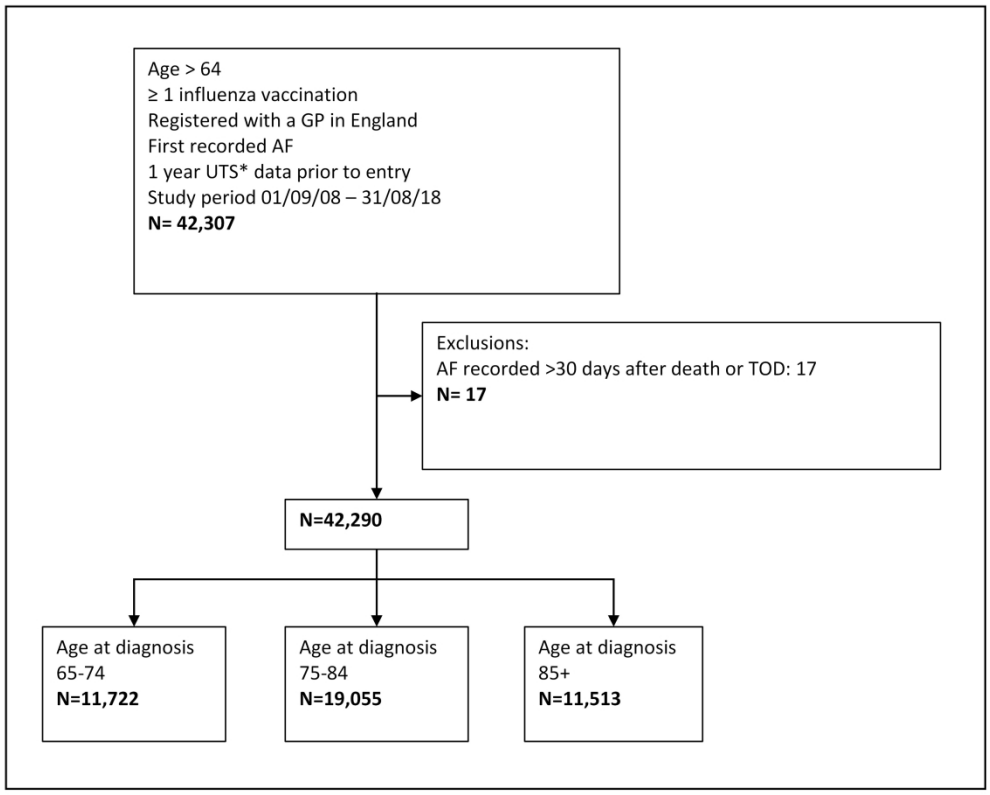
Figure 1: Patient flow diagram



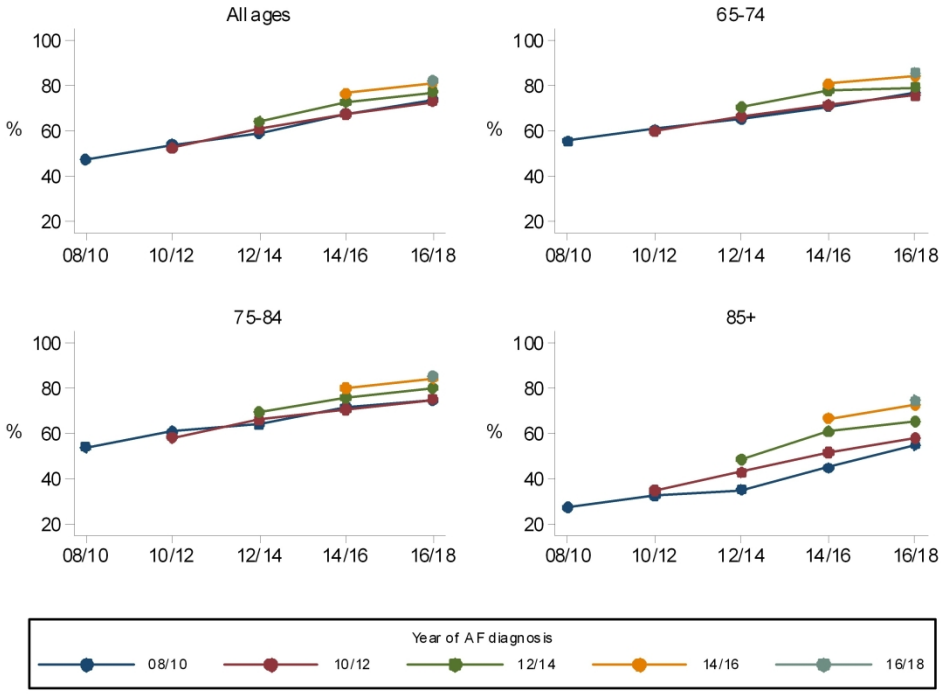
*UTS: Up to standard. CPRD defined criteria for data quality. [9]

TOD: Transfer out Date. Date at which patients transfers to another practice.

Patient flow diagram

159x148mm (600 x 600 DPI)

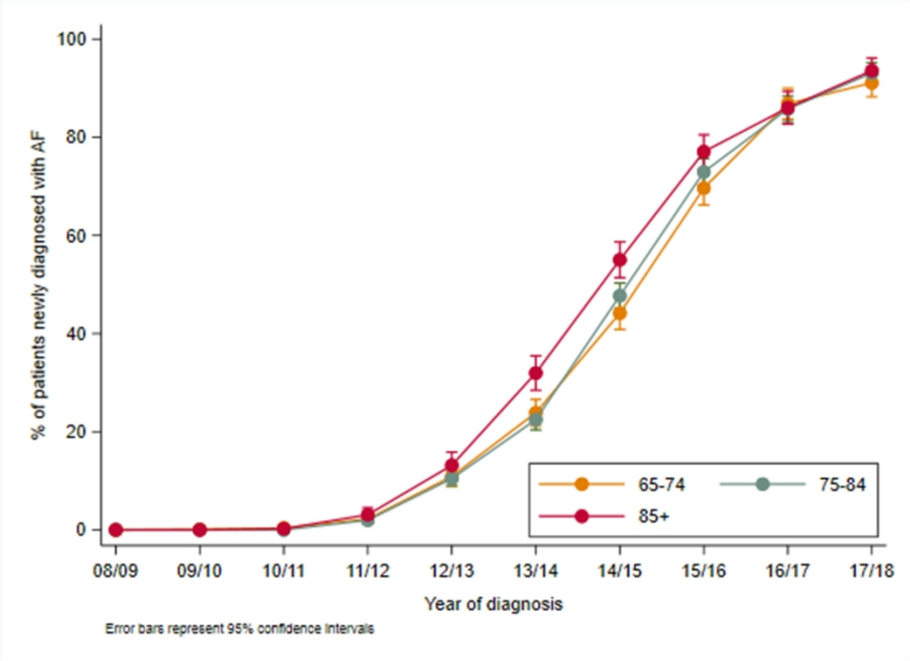
Figure 2: Anticoagulation for AF by cohort; age and year of diagnosis



Anticoagulation for AF by cohort; age and year of diagnosis

159x125mm (600 x 600 DPI)

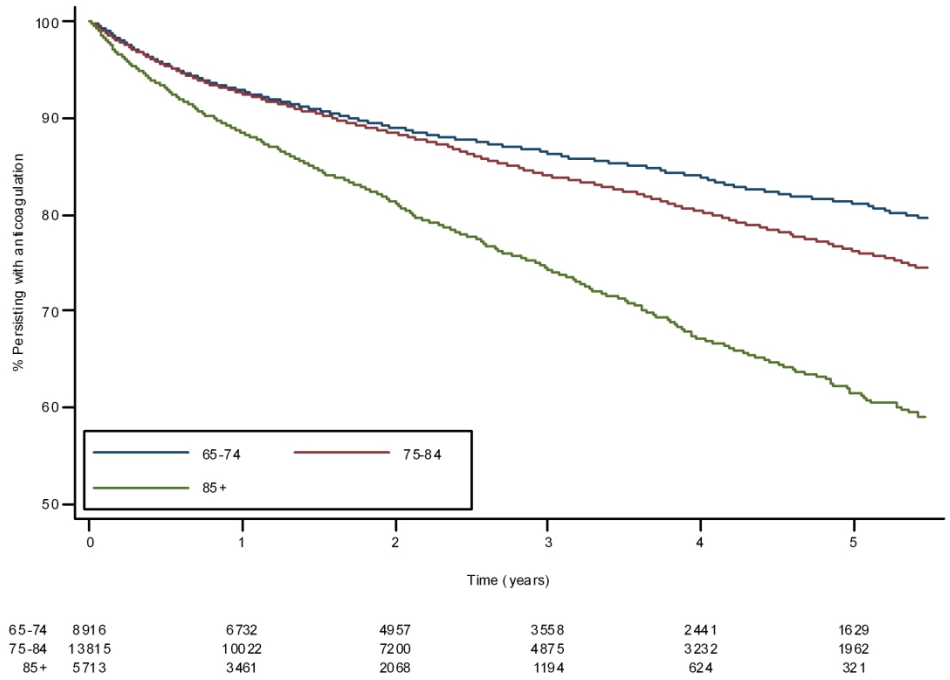
Figure 3: The proportion of first anticoagulation prescriptions for newly diagnosed AF that are for a DOAC



The proportion of first anticoagulation prescriptions for newly diagnosed AF that are for a DOAC

159x115mm (600 x 600 DPI)

Figure 4: Anticoagulation persistence by age

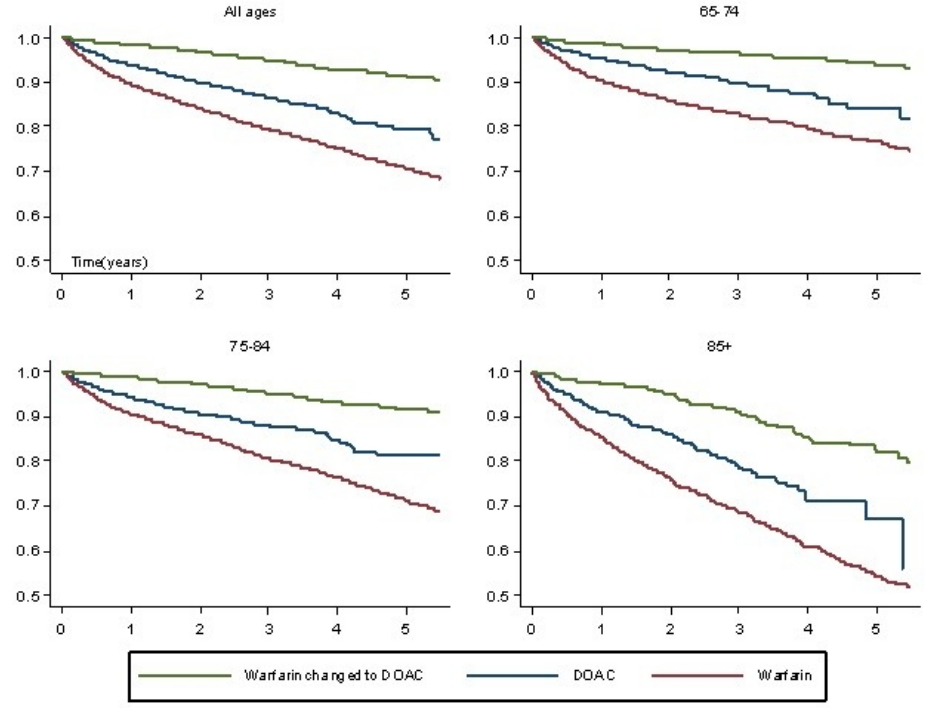


Anticoagulation persistance by age

159x124mm (600 x 600 DPI)

Figure 5: Anticoagulation persistence by age and type

**Due to small patient numbers those who have transferred from DOAC to Warfarin are not presented.*



	All ages			65-74			75-84			85+		
Time(Years)	DOAC	Warfarin	Warfarin changed to DOAC	DOAC	Warfarin	Warfarin changed to DOAC	DOAC	Warfarin	Warfarin changed to DOAC	DOAC	Warfarin	Warfarin changed to DOAC
1	4786	12210	3021	1522	4082	1050	2197	6216	1520	1070	1912	453
2	2531	8917	2650	851	3112	941	1185	4611	1343	495	1194	367
3	1136	6233	2193	401	2324	798	536	3190	1120	200	719	277
4	419	4149	1689	154	1634	636	205	2127	884	63	390	172
5	128	2539	1226	52	1073	496	62	1264	629	14	206	102

Anticoagulation persistence by age and type

119x141mm (144 x 144 DPI)

Anticoagulation trends in adults aged 65 and over with atrial fibrillation; a cohort study.

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Abstract

Objective: To describe patterns of anticoagulation prescription and persistence for those aged ≥65 years with atrial fibrillation (AF).

Methods: Descriptive cohort study using electronic general practice records of patients in England, who attended a flu vaccination aged ≥65 and were diagnosed with AF between 2008-2018. Patients were stratified by 10-year age group and year of diagnosis. Proportion anticoagulated, type of anticoagulation (direct oral anticoagulant (DOAC) or warfarin) initiated at diagnosis and persistence with anticoagulation over time are reported.

Results: 42,290 patients (49% female), aged 65-74 (n=11,722), 75-84 (n=19,055) and 85+ (n=11,513) at AF diagnosis are included. Prescription of anticoagulation at diagnosis increased over the time period from 55% to 86% in people aged 65-74, from 54% to 86% in people aged 75-84 and from 27% to 75% in people aged 85 and over. By 2018 92% of patients with newly diagnosed AF were started on a DOAC. Survivor function for 5-year persistence in patients prescribed DOAC was 0.80 (0.77:0.82) and for warfarin 0.71(0.70:0.72). Survivor function for any anticoagulation at 5 years was 0.79(0.78:0.81), 0.73(0.72:0.75), 0.58(0.59:0.64) for people aged 65-74, 75-84 and 85+ respectively.

Conclusions: Rates of anticoagulation in AF in those aged ≥65 have increased from 2008 to 2018, over which time period there has been a shift from initiating anticoagulation with warfarin to DOAC. Persistence with anticoagulation is higher in people on DOACs than on warfarin and in people <85.

Key Messages

What is already known?

Anticoagulation is a highly effective way of reducing the risk of stroke associated with AF, but is underused, particularly in older people. The introduction of DOACs has been associated with increasing use of anticoagulation in AF.

The UK national screening committee has stated that insufficient evidence about anticoagulation prescribing patterns, compliance and persistence is one of the barriers to a national screening programme for AF.

What does this study add?

Our study provides up to date information on anticoagulation for AF in older people who are most at risk of AF related stroke and highlights particular increases in use of anticoagulation in people aged 85 and over.

DOACs are now the major class of anticoagulant prescribed to patients with new AF in UK general practice.

Long term persistence with anticoagulation is higher with DOACs than warfarin, but drops in all age groups over 5 years.

How might this impact on clinical practice?

Improved uptake of anticoagulation at all ages removes one of the potential barriers to screening for atrial fibrillation, but new strategies may be needed to enhance longer term persistence with treatment.

Introduction

Atrial Fibrillation (AF) is an independent risk factor for stroke. Incidence of AF increases from 6 per 1000 in those aged 60-69 to 39 per 1000 in those aged 80-89. 31% of strokes in those aged 80-89 may be attributed to AF, compared with 7.3% in those aged 60-69.[1]

Oral anticoagulation reduces the risk of stroke by 65%. Though use is increasing, it is still under used in the UK, with 22% of eligible patients not receiving treatment in 2018.[2 3]

Warfarin, a vitamin K antagonist, was the first oral anticoagulant available and was licenced in the USA in 1954. Dabigatran was the first of the Direct Oral Anticoagulation (DOAC) medications licensed for use in the UK in 2008. This has been followed by others in this group, including rivaroxaban, apixaban and edoxaban. Their arrival has been associated with an increase in prescribing of anticoagulation in non-valvular AF for all age groups.[4]

Since risk of stroke in AF rises with age, the potential benefit from anticoagulation also rises with age, though so do risk of bleeding complications.[5] NICE guidance recommends the use of anticoagulation in all those with a CHA_2DS_2VASC2 score of 2 or more and the consideration of anticoagulation in those with a score of 1 where this is not due to gender, which means all patients aged ≥65 years with AF are potential candidates for anticoagulation, and all patients aged ≥75 years should be offered such treatment. Historically, older people have been less likely to receive anticoagulation despite evidence that the potential benefit is greater than the risk. [6]

AF has been considered as a candidate for a national screening programme in the UK. One of the criteria for adopting screening is that the clinical management of the condition should be optimised prior to implementation of screening.[7] The UK NSC (national screening committee) reviewed patterns of anticoagulation prescribing for AF in 2019. It concluded that there was insufficient evidence of optimised compliance, and around prescribing patterns of anticoagulation in AF, in part because of lack of evidence about anticoagulation persistence over time.[8]

The objective of this study is therefore to provide this evidence of patterns of anticoagulation prescribing and persistence by 10-year age group over the age of 65.

We answered three research questions using an electronic primary care database study;

1. How has the proportion of people with AF aged over 65 who are anticoagulated changed between 2008/2018?
2. How has the type of anticoagulant prescribed changed for people with incident AF?
3. How is anticoagulation persistence over the age of 65 affected by age and type of anticoagulation?

Method

Data and Population

Data were extracted from the Clinical Practice Research Datalink (CPRD), a primary care research database of anonymised, electronic coded records from the Vision computer system.[9] All clinical activity (including diagnoses and prescribing) in primary care are recorded using clinical codes. The dataset upon which these analyses were performed was originally extracted to explore the impact of case finding for atrial fibrillation at the time of influenza vaccination. Influenza vaccination is offered to everyone over the age of 65 in the UK, and uptake in this age group over the time period of the study was 71-75%[10].

Patients included in this study were registered with a GP in England, had records which fulfilled CPRD data quality standards[9], had a first diagnosis of AF between 01/09/2008 and 31/08/2018, and attended at least one influenza vaccine after the age of 65 and during the study period, with at least one year's registration before their first eligible flu vaccination. For each patient follow up started at the date of first recorded AF diagnosis and ended when the patient left the GP practice or died, the practice stopped contributing data to CPRD, or 31/08/2018, whichever was

earliest. Further limited exclusions for data quality were made; patients with an AF diagnosis recorded more than 30 days after the end of follow up were excluded. Details of patient selection, inclusion and exclusion criteria are given in figure 1.

Definitions of AF and anticoagulation

We analysed cases of AF diagnosed each year from 2008/09 to 2017/18 (1st September – 31 August).

The date and type of first anticoagulation are defined at the first record of an oral anticoagulant prescription. For all analyses we defined an anticoagulation prescription as a medication from the prespecified list (appendix 1) with a tablet quantity greater than zero.

Lists of codes which record AF diagnoses and anticoagulation prescribing available in supplementary data, appendix 1.

Demographic and clinical characteristics

We defined three age groups, 65-74, 75-84 and 85+. People aged 85 and over were grouped because of small numbers and the risk of statistical disclosure. We described the clinical characteristics of the study population on the day before AF diagnosis as the count of long term conditions (out of the 20 included in the Cambridge multi morbidity score).[11] Deprivation was defined as the index of multiple deprivation (IMD) score of the GP practice attended by each cohort member, linked and provided by CPRD. IMD score is a small area measure of deprivation, measured across seven domains and reported for 32,844 small areas in England.[12]

Analyses

In our first analysis we explored changes in the proportion of people with AF prescribed anticoagulation by age and year. Each cohort was defined by age group at diagnosis and 2-year diagnosis interval. Patients were included in the denominator of each 2-year time point analysis if they had contributed data at any point during the 2 year time interval and were defined as anticoagulated if they had received any prescription of anticoagulation in this time.

For our second analysis we included incident AF cases who received anticoagulation within 365 days of diagnosis and calculated the proportion, with 95% confidence intervals, of these, stratified by age group, who received a DOAC as the first prescription after AF diagnosis. For this analysis patients contributed to both the numerator and denominator of any year if they had a minimum of 365 days of follow up after AF diagnosis.

In our final analyses we described the time to end of anticoagulation use, stratified by age group at diagnosis and by age and type of anticoagulation. Analysis entry point was defined as the later of AF diagnosis date or first anticoagulation prescription date. The date of end of anticoagulation is defined as the date of the last anticoagulation prescription if this is greater than 90 days before leaving the sample. If the patient left the sample for any reason within 90 days of anticoagulation prescription they were censored at the leaving date. For this analysis type of anticoagulation was defined as one of four categories; Warfarin only, DOAC only, Warfarin changed to DOAC during follow up and DOAC changed to Warfarin. Patients with a prescription for a vitamin K antagonist other than Warfarin were excluded due to small numbers. The survivor function was calculated, with 95% confidence intervals, at the 5-year time point for all age and medication cohorts.

All data analysis was completed using STATA software v.16. [13] There was no patient or public involvement in this project.

Results

There were 42,290 patients with newly recorded AF during the study. Respectively 28% (11,722)), 45% (19055) and 27% (11,513) of patients were aged 65-74, 75-84 and 85+ at diagnosis. 49% (20,850) of patients in the total sample were female. The proportion of new cases diagnosed in female patients rose from 39% (4583) in the 65-74 age group to 61% (6994) in the over 85s. 35% (14861) of cases were diagnosed in those with 4 or more pre-existing

comorbidities, falling to 6% (2492) in those with no other comorbidities with no systematic variation by deprivation. Across all age groups there were falling numbers of cases in the later years of the study, this represents the falling number of practices contributing to CPRD using the Vision computer software over this time period. (Table 1)

Both cohort and period effects are seen in the prescription of anticoagulation over the 10 years of the study. For all age groups the proportion of patients anticoagulated at the time of diagnosis increased between 2008 and 2018 (Figure 2, Table 2). This change is most marked in those aged 85+, where there was a rise from 27% (679) in 2008-2010 to 74% (865) in 2016-2018. During the same time period anticoagulation for the 65-74 age group rose from the higher baseline of 55% (1482) to 86% (937), and for the 75-84 age group from 54% (2339) to 86% (1430). The difference in the proportion of those anticoagulated between the oldest and youngest age groups narrows considerably over the 10-year period, from 28% to 11%. Within each age and year of diagnosis cohort there is also a consistent upward trend in the proportion who are anticoagulated over time. For example, in those aged 85+ during 2008-2010 the proportion anticoagulated at diagnosis is 27% (679). By 2016-2018, of those who remain in this cohort, now aged 95+, 55% (56) are receiving treatment.

No patients diagnosed with AF in 2008/2009 were prescribed a DOAC, but by 2017/2018, 70% (1222) received a DOAC within 1 year of diagnosis (figure 3). DOACs represented 92% (1222/1319) of first anticoagulant prescriptions for AF in 2017/18. The use of DOACs increased rapidly in all age groups, with the largest increases seen between 2012 and 2016. The rate of increase was initially highest in the 85+ age group. There was no significant difference between age groups in the proportion given a DOAC from 2016 onwards. (Figure 3).

29,644 patients received a prescription for oral anticoagulation at any timepoint following AF diagnosis. Of these 60% (17,753) received only warfarin, 28% (8351) only DOAC, 11% (3298) switched from warfarin to DOAC during the study period and 1% (246) changed from DOAC to warfarin. Due to the small number of patients who changed from DOAC to Warfarin these patients were excluded from further analysis (Table 3).

Persistence with anticoagulation was high across all age groups, with the greatest rate of decrease in the first year. (Figure 4) Anticoagulation persistence was higher in the younger age groups at all time points. At 5 years the survivor function for anticoagulation was 0.79 (0.78:0.81) in those aged 65-74, 0.73(0.72:0.75) in those aged 75-84 and 0.58 (0.54:0.61) in those aged 85+.

Of those who received a single type of anticoagulation, persistence was highest in those prescribed a DOAC (Figure 5). At 5 years the probability of continuing anticoagulation for those only prescribed a DOAC was 0.790.77:0.82) compared to 0.71(0.71:0.76) in those only prescribed Warfarin. If all patients initially prescribed warfarin are considered, including those who subsequently switched to a DOAC, then five year probability of continuing anticoagulation was 0.75 (0.74:0.76).

Discussion

Summary

Anticoagulation has increased across all age groups from 2008-2018 with the greatest rise in those aged over 85. There have been both cohort and period effects with regard to prescription of anticoagulation. Increases are greatest in those with newly diagnosed AF. DOACs now represent the vast majority of anticoagulant prescriptions offered to all patients aged over 65 with newly diagnosed AF. Anticoagulation persistence decreases with age, being lowest in those aged over 85. Persistence is higher in those prescribed DOACs as compared to warfarin.

Strengths and Limitations

The major strength of this study is the large sample size and generalisability to the UK population. Ours is the first study to tease out period from cohort effects in anticoagulation prescribing in this age group. As with all electronic record studies a major limitation is the reliance on recorded, coded, diagnoses. It is possible that patients receiving anticoagulation are more likely to have a coded diagnosis of atrial fibrillation and therefore the incidence of anticoagulation seen in this paper may be artificially elevated.

Inclusion of only patients who have had an influenza vaccination may mean that the cohort of patients described in this study are those more likely to attend for healthcare and therefore more likely to receive anticoagulation. However, the AF incidence seen is comparable to that reported using all CPRD records.[14] These potential biases are unlikely to have had any major effect on the observed trends, since their magnitude will not have changed substantially over the time period of the study.

A further limitation is the use of anticoagulant prescription issues as a marker for persistence with medication. It is possible that prescriptions are issued without medication being taken, particularly considering the move toward electronic repeat dispensing in the UK.

We have shown that anticoagulation goes up over time in all age groups. This is likely in part due to increased use of anticoagulation but may also represent differential survival in those who are anticoagulated.

Comparison with existing literature

The trends in overall anticoagulation and the use of DOAC as the anticoagulant of choice we present are consistent with previous UK studies.[4 15] Our work brings these results up to date and presents new data with regard to age stratification for those aged over 65.

We show that people who were started on a DOAC tend to persist longer than those on warfarin, however there may be both patient selection and time effects. DOACs were initiated in later years than warfarin and there has been, over the period of the study, increased knowledge and awareness of the importance of persisting with anticoagulation. What we have observed is similar to the persistence seen in a recent meta-analysis where pooled persistence with DOACs was higher than vitamin K antagonists (OR 1.44),[16] although many of the studies included within this have a significantly shorter period of follow up. Anticoagulation persistence is known to be lower in younger age groups[17 18], our patients were older, mean age 80 years, than in any of the studies included in the systematic review and this may partially explain the high overall persistence seen. In clinical trials where randomisation eliminates patient selection bias there was no clear pattern of superiority of DOAC over Warfarin.[19-21] Our study is observational and therefore we cannot be sure of the effects of patient selection bias. The choice of anticoagulant is largely an individual decision made between clinician and patient and there may be an unmeasured characteristic that affects the choice of medication and the likelihood of persistence.

Implications for research policy and practice

Our results show there has been a major shift in the use of anticoagulation in the UK. DOACs have become the first line anticoagulant for those with AF and are being used in ever increasing numbers of patients, including large numbers aged over 85. We provide some circumstantial evidence to support the success of initiatives to increase uptake of anticoagulation.[22] This suggests that poor uptake of anticoagulation may no longer a barrier to screening for atrial fibrillation.

We note that the high levels of anticoagulant prescribing that we observed are against a background of multi-morbidity, which would be expected to increase the potential iatrogenic effects of anticoagulation prescribing, as multi-morbidity increases risk of haemorrhage.[23]

Those prescribed warfarin require frequent monitoring and dose adjustment. Currently there are multiple models of care as to how this service is provided, across both primary and secondary care. As the number of patients receiving warfarin continues to decline consideration will need to be given to the best model of care for continuation of specialist warfarin services for the small number of patients who continue to use it. This will need to account for the likely older age profile of these patients.

A final consideration is that the current data are all drawn prior to the COVID-19 pandemic. As a result of the pandemic, UK guidance, endorsed by the Royal College of General Practitioners, has encouraged the accelerated switching of warfarin to DOAC for patients with AF to avoid unnecessary trips to health care settings for monitoring.[24] Pandemic guidance from NHS England explicitly recommends that patients newly diagnosed with AF

are offered a DOAC in preference to Warfarin. Therefore the trends seen in this paper may well have accelerated in 2020.

Conclusion

The use of anticoagulation for AF has increased over the period 2008-2018, with the greatest increases seen in those aged over 85, both in terms of initiation and persistence than previously reported. DOACs now represent the vast majority of anticoagulation prescriptions for newly diagnosed AF. This study provides some evidence that DOACs are associated with higher long term persistence in older adults than warfarin.

Data availability statement:

Deidentified data used for this study is available from CPRD. https://cprd.com/Data-access.

Access to CPRD data is subject to protocol approval by an Independent Scientific Advisory Committee (ISAC). ISAC is a non-statutory expert advisory body established in 2006 by the Secretary of State for Health to provide scientific advice on research requests to access data provided by CPRD.

Contributors:

JL Wrote the protocol and statistical analysis plan, cleaned and analysed the data, drafted and revised the paper. CS wrote the statistical analysis plan, drafted and revised the paper. DE wrote the protocol and revised the draft paper. JM wrote the protocol and revised the draft paper.

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Jonathan Mant is an NIHR Senior Investigator.

Competing interests:

No competing interests are declared.

Ethical approval:

Permission for the CPRD to receive and supply anonymous patient data for generic public health research is granted directly to the CPRD by the national Research Ethics Service of the UK Health Research Authority. Regulatory approvals to use CPRD data for the current project were granted by the CPRD Independent Scientific Advisory Committee (ISAC protocol 17_141RMn).

Figure legends:

Figure 1: Patient Flow diagram

Figure 2: Anticoagulation for AF by cohort; age and year of diagnosis

Figure 3: The proportion of first anticoagulation prescriptions for newly diagnosed AF that are for a DOAC

Figure 4: Anticoagulation persistence by age

Figure 5: Anticoagulation persistence by age and type. Due to small patient numbers those who have transferred from DOAC to Warfarin are not presented.

References

1. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation: a major contributor to stroke in the elderly. The Framingham Study. *Arch Intern Med* 1987;147(9):1561-4. [published Online First: 1987/09/01]
2. Lane DA, Wolff A, Shantsila E, et al. Optimising stroke prevention in patients with atrial fibrillation. *Br J Gen Pract* 2015;65(632):117. doi: 10.3399/bjgp15X683905 [published Online First: 2015/03/04]
3. Robson J, Homer K, Ahmed Z, et al. Variation in anticoagulation for atrial fibrillation between English clinical commissioning groups: an observational study. *Br J Gen Pract* 2018;68(673):e551-e58. doi: 10.3399/bjgp18X697913 [published Online First: 2018/07/05]
4. Loo SY, Dell'Aniello S, Huiart L, et al. Trends in the prescription of novel oral anticoagulants in UK primary care. *Br J Clin Pharmacol* 2017;83(9):2096-106. doi: 10.1111/bcp.13299 [published Online First: 2017/04/09]
5. Torn M, Bollen WL, van der Meer FJ, et al. Risks of oral anticoagulant therapy with increasing age. *Arch Intern Med* 2005;165(13):1527-32. doi: 10.1001/archinte.165.13.1527 [published Online First: 2005/07/13]
6. Zathar Z, Karunatilleke A, Fawzy AM, et al. Atrial Fibrillation in Older People: Concepts and Controversies. *Front Med (Lausanne)* 2019;6:175. doi: 10.3389/fmed.2019.00175 [published Online First: 2019/08/24]
7. Criteria for appraising the viability, effectiveness and appropriateness of a screening programme: Public Health England; [updated October 2015. Available from: https://www.gov.uk/government/publications/evidence-review-criteria-national-screening-programmes/criteria-for-appraising-the-viability-effectiveness-and-appropriateness-of-a-screening-programme accessed 5/10/2020.
8. King S, et al. Evidence Summary for Screening for Atrial Fibrillation in Adults. External review against programme appraisal criteria for the UK National Screening Committee, 2019.
9. Herrett E, Gallagher AM, Bhaskaran K, et al. Data Resource Profile: Clinical Practice Research Datalink (CPRD). *Int J Epidemiol* 2015;44(3):827-36. doi: 10.1093/ije/dyv098
10. Adult flu vaccination coverage: Nuffield Trust; 2020 [Available from: https://www.nuffieldtrust.org.uk/resource/adult-flu-vaccination-coverage accessed 17/11/2020.
11. Payne RA, Mendonca SC, Elliott MN, et al. Development and validation of the Cambridge Multimorbidity Score. *CMAJ* 2020;192(5):E107-E14. doi: 10.1503/cmaj.190757
12. English indices of deprivation 2019: Ministry of Housing, Communities and Local Government; 2019 [Available from: https://www.gov.uk/government/statistics/english-indices-of-deprivation-2019 accessed 25/05/2021.
13. StataCorp. Stata Statistical Software:Release 16. College Station, TX: StataCorp LLC, 2019.
14. Mendonca SC, Saunders CL, Lund J, et al. Temporal trends in incidence of atrial fibrillation in primary care records: a population-based cohort study. *BMJ Open* 2020;10(12):e042518. doi: 10.1136/bmjopen-2020-042518 [published Online First: 2020/12/29]
15. Adderley N, Ryan R, Marshall T. The role of contraindications in prescribing anticoagulants to patients with atrial fibrillation: a cross-sectional analysis of primary care data in the UK. *Br J Gen Pract* 2017;67(662):e588-e97. doi: 10.3399/bjgp17X691685 [published Online First: 2017/06/21]
16. Ozaki AF, Choi AS, Le QT, et al. Real-World Adherence and Persistence to Direct Oral Anticoagulants in Patients With Atrial Fibrillation: A Systematic Review and Meta-Analysis. *Circ Cardiovasc Qual Outcomes* 2020;13(3):e005969. doi: 10.1161/CIRCOUTCOMES.119.005969 [published Online First: 2020/03/10]
17. Banerjee A, Benedetto V, Gichuru P, et al. Adherence and persistence to direct oral anticoagulants in atrial fibrillation: a population-based study. *Heart* 2020;106(2):119-26. doi: 10.1136/heartjnl-2019-315307 [published Online First: 2019/10/12]
18. Zielinski GD, van Rein N, Teichert M, et al. Persistence of oral anticoagulant treatment for atrial fibrillation in the Netherlands: A surveillance study. *Res Pract Thromb Haemost* 2020;4(1):141-53. doi: 10.1002/rth2.12261 [published Online First: 2020/01/29]
19. Granger CB, Alexander JH, McMurray JJ, et al. Apixaban versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2011;365(11):981-92. doi: 10.1056/NEJMoa1107039 [published Online First: 2011/08/30]
20. Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med* 2011;365(10):883-91. doi: 10.1056/NEJMoa1009638 [published Online First: 2011/08/13]
21. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2009;361(12):1139-51. doi: 10.1056/NEJMoa0905561 [published Online First: 2009/09/01]

22. TheAHSNNetwork. Atrial Fibrillation. Detect, Protect, Perfect. 2019 [accessed 17th August 2020.
23. Proietti M, Marzona I, Vannini T, et al. Long-Term Relationship Between Atrial Fibrillation, Multimorbidity and Oral Anticoagulant Drug Use. *Mayo Clin Proc* 2019;94(12):2427-36. doi: 10.1016/j.mayocp.2019.06.012 [published Online First: 2019/11/02]
24. Williams H. Guidance for the safe switching of warfarin to direct oral anticoagulants (DOACs) for patients with non-valvular AF and venous thromboembolism (DVT / PE) during the coronavirus pandemic: Royal Pharmaceutical Society; 2020 [Available from: https://www.rpharms.com/Portals/0/RPS%20document%20library/Open%20access/Coronavirus/FINAL%20Guidance%20on%20safe%20switching%20of%20warfarin%20to%20DOAC%20COVID-19%20Mar%202020.pdf?ver=2020-03-26-180945-627 accessed 06th July 2020.

Table 1: Patient Characteristics

		08/09	09/10	10/11	11/12	12/13	13/14	14/15	15/16	16/17	17/18	All years
Incident AF* cases		4376	5164	5255	5576	5528	4907	4391	3172	2170	1751	42290
By age(%)	65	1204 (27.5)	1469 (28.5)	1410 (26.8)	1589 (28.5)	1548 (28.0)	1321 (26.9)	1192 (27.2)	899 (28.3)	596 (27.5)	494 (28.2)	11722 (27.7)
	75	2001 (45.7)	2338 (45.3)	2430 (46.2)	2510 (45.0)	2485 (45.0)	2251 (45.9)	1997 (45.5)	1371 (43.2)	920 (42.4)	752 (43.0)	19055 (45.1)
	85	1171 (26.8)	1357 (26.3)	1415 (26.9)	1477 (26.5)	1495 (27.0)	1335 (27.2)	1202 (27.4)	902 (28.4)	654 (30.1)	505 (28.8)	11513 (27.2)
Female(%)	65	477 (39.6)	564 (38.4)	578 (41.0)	627 (39.5)	624 (40.3)	490 (37.1)	455 (38.2)	355 (39.5)	236 (39.6)	177 (35.8)	4583 (39.1)
	75	977 (48.8)	1174 (50.2)	1166 (48.0)	1245 (49.6)	1180 (47.5)	1084 (48.2)	1005 (50.3)	677 (49.4)	425 (46.2)	340 (45.2)	9273 (48.7)
	85	737 (62.9)	827 (60.9)	856 (60.5)	916 (62.0)	895 (59.9)	831 (62.2)	686 (57.1)	557 (61.8)	405 (61.9)	284 (56.2)	6994 (60.7)
IMD quintile(%)*	1	864 (19.7)	1000 (19.4)	1023 (19.5)	1115 (20.0)	1019 (18.4)	848 (17.3)	779 (17.7)	532 (16.8)	410 (18.9)	338 (19.3)	7928 (18.8)
	2	773 (17.7)	895 (17.3)	1030 (19.6)	1065 (19.1)	1037 (18.8)	944 (19.2)	840 (19.1)	543 (17.1)	365 (16.8)	278 (15.9)	7770 (18.4)
	3	920 (21.0)	1073 (20.8)	1143 (21.8)	1193 (21.4)	1211 (21.9)	1157 (23.6)	919 (20.9)	603 (19.0)	415 (19.1)	319 (18.2)	8953 (21.2)
	4	873 (20.0)	1012 (19.6)	966 (18.4)	949 (17.0)	985 (17.8)	885 (18.0)	795 (18.1)	579 (18.3)	362 (16.7)	239 (13.7)	7645 (18.1)
	5	884 (20.2)	1095 (21.2)	989 (18.8)	1160 (20.8)	1165 (21.1)	935 (19.1)	933 (21.3)	784 (24.7)	495 (22.8)	413 (23.6)	8853 (20.9)
Morbidity count(%)	0	283 (6.5)	336 (6.5)	307 (5.8)	360 (6.5)	318 (5.8)	250 (5.1)	246 (5.6)	169 (5.3)	113 (5.2)	110 (6.3)	2492 (5.9)
	1	767 (17.5)	826 (16.0)	848 (16.1)	903 (16.2)	875 (15.8)	757 (15.4)	665 (15.1)	470 (14.8)	300 (13.8)	270 (15.4)	6681 (15.8)
	2	992 (22.7)	1172 (22.7)	1200 (22.8)	1294 (23.2)	1185 (21.4)	1052 (21.4)	861 (19.6)	627 (19.8)	483 (22.3)	367 (21.0)	9233 (21.8)
	3	935 (21.4)	1129 (21.9)	1146 (21.8)	1200 (21.5)	1164 (21.1)	1030 (21.0)	920 (21.0)	693 (21.9)	445 (20.5)	361 (20.6)	9023 (21.3)
	4+	1399 (32.0)	1701 (32.9)	1754 (33.4)	1819 (32.6)	1986 (35.9)	1818 (37.1)	1699 (38.7)	1213 (38.2)	829 (38.2)	643 (36.7)	14861 (35.1)
Ever prescribed anticoagulation(%)	65	979 (81.3)	1243 (84.6)	1213 (86.0)	1369 (86.2)	1393 (90.0)	1280 (96.9)	1153 (96.7)	866 (96.3)	573 (96.1)	475 (96.2)	10609 (90.5)
	75	1483 (74.1)	1723 (73.7)	1914 (78.8)	2102 (83.7)	2173 (87.4)	2101 (93.3)	1927 (96.5)	1319 (96.2)	900 (97.8)	708 (94.1)	16425 (86.2)
	85	413 (35.3)	529 (39.0)	617 (43.6)	777 (52.6)	879 (58.8)	921 (69.0)	947 (78.8)	735 (81.5)	553 (84.6)	432 (85.5)	6888 (59.8)
Ever prescribed DOAC(%)**	65	125 (10.4)	217 (14.8)	196 (13.9)	255 (16.0)	343 (22.2)	443 (33.5)	546 (45.8)	588 (65.4)	468 (78.5)	414 (83.8)	3660 (31.2)
	75	153 (7.6)	224 (9.6)	327 (13.5)	404 (16.1)	519 (20.9)	687 (30.5)	965 (48.3)	929 (67.8)	722 (78.5)	628 (83.5)	5633 (29.6)
	85	40 (3.4)	54 (4.0)	92 (6.5)	132 (8.9)	240 (16.1)	359 (26.9)	523 (43.5)	538 (59.6)	440 (67.3)	381 (75.4)	2884 (25.0)
Anticoagulation within 365 days (%)	65	658 (54.7)	773 (52.6)	805 (57.1)	931 (58.6)	954 (61.6)	951 (72.0)	856 (71.8)	685 (76.2)	456 (76.5)	382 (77.3)	7516 (64.1)
	75	1075 (53.7)	1208 (51.7)	1301 (53.5)	1470 (58.6)	1576 (63.4)	1531 (68.0)	1432 (71.7)	1031 (75.2)	710 (77.2)	579 (77.0)	11988 (62.9)
	85	287 (24.5)	359 (26.5)	419 (29.6)	550 (37.2)	608 (40.7)	682 (51.1)	716 (59.6)	571 (63.3)	422 (64.5)	358 (70.9)	5057 (43.9)
DOAC within 365 days(%)	65	0 (0.0)	<10 (0.0)	<10(0.0)	21 (1.3)	104 (6.7)	227 (17.2)	378 (31.7)	477 (53.1)	396 (66.4)	348 (70.4)	2020 (17.2)
	75	0 (0.0)	0 (0.0)	0 (0.0)	29 (1.2)	165 (6.6)	344 (15.3)	683 (34.2)	752 (54.9)	609 (66.2)	539 (71.7)	3196 (16.8)
	85	0 (0.0)	0 (0.0)	<10 (0.0)	17 (1.2)	80 (5.4)	218 (16.3)	394 (32.8)	440 (48.8)	363 (55.5)	335 (66.3)	1933 (16.8)

* AF: Atrial Fibrillation **Practice level IMD (index of multiple deprivation) data is missing for 1141 patients. *** DOAC: direct oral anticoagulant.

Table 2: Incident cases and anticoagulation by age and year of diagnosis.

		Year and and age at diagnosis														
		2008/10			2010/12			2012/14			2014/16			2016/18		
		65-74	75-84	85+	65-74	75-84	85+	65-74	75-84	85+	65-74	75-84	85+	65-74	75-84	85+
No. patients in cohort (no. anticoagulated)	2008/10	2673 (1482)	4339 (2339)	2528 (679)	-	-	-	-	-	-	-	-	-	-	-	-
	2010/12	2410 (1461)	3749 (2279)	1858 (601)	2999 (1796)	4940 (2872)	2892 (1001)	-	-	-	-	-	-	-	-	-
	2012/14	1967 (1284)	2811 (1797)	1073 (374)	2712 (1806)	4243 (2800)	2128 (904)	2869 (2027)	4736 (3290)	2830 (1370)	-	-	-	-	-	-
	2014/16	1322 (940)	1671 (1201)	462 (206)	1829 (1309)	2604 (1842)	981 (504)	2275 (1778)	3589 (2727)	1807 (1098)	2091 (1691)	3368 (2696)	2104 (1407)	-	-	-
	2016/18	565 (437)	667 (498)	102 (56)	833 (631)	1002 (755)	280 (162)	1055 (840)	1502 (1206)	541 (354)	1331 (1125)	1991 (1686)	1041 (757)	1090 (937)	1672 (1430)	1159 (865)

Table 3: Type of anticoagulation by age

Age at diagnosis	65-74	75-84	85+	All ages
DOAC only	2,379	3,761	2,211	8,351
Warfarin only	5,653	8,831	3,269	17,753
Warfarin changed to DOAC	1,125	1,646	527	3,298
DOAC changed to Warfarin	78	125	43	246

Appendicies

Appendix 1: CPRD codes defining exposure and outcomes

1a: Atrial Fibrillation

CPRD medcode	Readcode	Description
1268	G573200	Paroxysmal atrial fibrillation
1664	G573000	Atrial fibrillation
1757	G573100	Atrial flutter
2212	G573.00	Atrial fibrillation and flutter
23437	G573z00	Atrial fibrillation and flutter NOS
35127	G573300	Non-rheumatic atrial fibrillation
96076	G573500	Persistent atrial fibrillation
96277	G573400	Permanent atrial fibrillation
107472	G573600	Paroxysmal atrial flutter

1b: Anticoagulation

CPRD prodcode	Product Name	Drug substance	Dose	Anticoagulant Type
39119	Rivaroxaban 10mg tablets	Rivaroxaban	10mg	DOAC
39444	Dabigatran etexilate 110mg capsules	Dabigatran etexilate mesilate	110mg	DOAC
39503	Dabigatran etexilate 75mg capsules	Dabigatran etexilate mesilate	75mg	DOAC
39639	Xarelto 10mg tablets (Bayer Plc)	Rivaroxaban	10mg	DOAC
39755	Pradaxa 110mg capsules (Boehringer Ingelheim Ltd)	Dabigatran etexilate mesilate	110mg	DOAC
42474	Pradaxa 75mg capsules (Boehringer Ingelheim Ltd)	Dabigatran etexilate mesilate	75mg	DOAC
46632	Dabigatran etexilate 150mg capsules	Dabigatran etexilate mesilate	150mg	DOAC
46678	Pradaxa 150mg capsules (Boehringer Ingelheim Ltd)	Dabigatran etexilate mesilate	150mg	DOAC
47207	Rivaroxaban 20mg tablets	Rivaroxaban	20mg	DOAC
47353	Rivaroxaban 15mg tablets	Rivaroxaban	15mg	DOAC
47566	Apixaban 2.5mg tablets	Apixaban	2.5mg	DOAC
47925	Xarelto 20mg tablets (Bayer Plc)	Rivaroxaban	20mg	DOAC
48134	Xarelto 15mg tablets (Bayer Plc)	Rivaroxaban	15mg	DOAC

48966	Rivaroxaban 15mg tablets	Rivaroxaban	15mg	DOAC
53740	Eliquis 2.5mg tablets (Bristol-Myers Squibb Pharmaceuticals Ltd)	Apixaban	2.5mg	DOAC
54066	Apixaban 5mg tablets	Apixaban	5mg	DOAC
54451	Rivaroxaban 20mg tablets	Rivaroxaban	20mg	DOAC
56289	Xarelto 20mg tablets (Bayer Plc)	Rivaroxaban	20mg	DOAC
56640	Xarelto 15mg tablets (Bayer Plc)	Rivaroxaban	15mg	DOAC
58594	Eliquis 5mg tablets (Bristol-Myers Squibb Pharmaceuticals Ltd)	Apixaban	5mg	DOAC
62150	Rivaroxaban 2.5mg tablets	Rivaroxaban	2.5mg	DOAC
64500	Xarelto 2.5mg tablets (Bayer Plc)	Rivaroxaban	2.5mg	DOAC
64678	Edoxaban 60mg tablets	Edoxaban tosilate	60mg	DOAC
65247	Edoxaban 30mg tablets	Edoxaban tosilate	30mg	DOAC
65850	Lixiana 60mg tablets (Daiichi Sankyo UK Ltd)	Edoxaban tosilate	60mg	DOAC
65876	Edoxaban 15mg tablets	Edoxaban tosilate	15mg	DOAC
45	Warfarin 1mg tablets	Warfarin sodium	1mg	Warfarin
61	Warfarin 3mg tablets	Warfarin sodium	3mg	Warfarin
833	Warfarin 3mg/5ml oral solution	Warfarin sodium	600microgram/1ml	Warfarin
1781	Warfarin 5mg tablets	Warfarin sodium	5mg	Warfarin
6262	Warfarin 500microgram tablets	Warfarin sodium	500microgram	Warfarin
8466	Marevan 1mg tablets (AMCo)	Warfarin sodium	1mg	Warfarin
8467	Marevan 3mg tablets (AMCo)	Warfarin sodium	3mg	Warfarin
10560	WARFARIN 10 MG TAB			Warfarin
13348	Marevan 5mg tablets (AMCo)	Warfarin sodium	5mg	Warfarin
17965	Marevan 500microgram tablets (AMCo)	Warfarin sodium	500microgram	Warfarin
20754	WARFARIN			Warfarin
23078	Warfarin 1mg Tablet (WB Pharmaceuticals Ltd)	Warfarin sodium	1mg	Warfarin
30202	Warfarin wbp 1mg Tablet (Boehringer Ingelheim Ltd)	Warfarin sodium	1mg	Warfarin
30203	Warfarin wbp 3mg Tablet (Boehringer Ingelheim Ltd)	Warfarin sodium	3mg	Warfarin
31511	Warfarin 3mg Tablet (WB Pharmaceuticals Ltd)	Warfarin sodium	3mg	Warfarin

31937	Warfarin 5mg tablets (Teva UK Ltd)	Warfarin sodium	5mg	Warfarin
33711	Warfarin 5mg Tablet (WB Pharmaceuticals Ltd)	Warfarin sodium	5mg	Warfarin
34019	Warfarin 1mg tablets (IVAX Pharmaceuticals UK Ltd)	Warfarin sodium	1mg	Warfarin
34086	Warfarin 3mg Tablet (Celltech Pharma Europe Ltd)	Warfarin sodium	3mg	Warfarin
34087	Warfarin 1mg Tablet (Celltech Pharma Europe Ltd)	Warfarin sodium	1mg	Warfarin
34088	Warfarin 5mg Tablet (Celltech Pharma Europe Ltd)	Warfarin sodium	5mg	Warfarin
34095	Warfarin wbp 5mg Tablet (Boehringer Ingelheim Ltd)	Warfarin sodium	5mg	Warfarin
34299	Warfarin 1mg tablets (Teva UK Ltd)	Warfarin sodium	1mg	Warfarin
34416	Warfarin 1mg tablets (Kent Pharmaceuticals Ltd)	Warfarin sodium	1mg	Warfarin
34417	Warfarin 3mg tablets (Teva UK Ltd)	Warfarin sodium	3mg	Warfarin
34418	Warfarin 5mg tablets (Mylan)	Warfarin sodium	5mg	Warfarin
34517	Warfarin 1mg tablets (Mylan)	Warfarin sodium	1mg	Warfarin
34526	Warfarin 3mg tablets (Mylan)	Warfarin sodium	3mg	Warfarin
34576	Warfarin 1mg Tablet (Lagap)	Warfarin sodium	1mg	Warfarin
34691	Warfarin 5mg Tablet (Regent Laboratories Ltd)	Warfarin sodium	5mg	Warfarin
34758	Warfarin 3mg tablets (IVAX Pharmaceuticals UK Ltd)	Warfarin sodium	3mg	Warfarin
34864	Warfarin 5mg tablets (IVAX Pharmaceuticals UK Ltd)	Warfarin sodium	5mg	Warfarin
34918	Warfarin 5mg tablets (Actavis UK Ltd)	Warfarin sodium	5mg	Warfarin
36099	Warfarin 1mg/5ml oral suspension	Warfarin sodium	200microgram/1ml	Warfarin
38041	Warfarin sodium 5mg/ml oral suspension	Warfarin Sodium	5mg/5ml	Warfarin
38044	Warfarin 5mg/5ml oral solution	Warfarin sodium	1mg/1ml	Warfarin
39866	Warfarin 1mg tablets (Almus Pharmaceuticals Ltd)	Warfarin sodium	1mg	Warfarin
40143	Warfarin 500microgram tablets (A A H Pharmaceuticals Ltd)	Warfarin sodium	500microgram	Warfarin

43407	Warfarin 3mg tablets (A A H Pharmaceuticals Ltd)	Warfarin sodium	3mg	Warfarin
43408	Warfarin 1mg tablets (A A H Pharmaceuticals Ltd)	Warfarin sodium	1mg	Warfarin
43409	Warfarin 5mg tablets (A A H Pharmaceuticals Ltd)	Warfarin sodium	5mg	Warfarin
43655	Warfarin sodium oral solution	Warfarin Sodium		Warfarin
44866	Warfarin sodium 1mg/ml oral supension SF	Warfarin Sodium	1mg/ml	Warfarin
47944	Warfarin 1mg tablets (Actavis UK Ltd)	Warfarin sodium	1mg	Warfarin
48070	Warfarin sodium tablets	Warfarin Sodium		Warfarin
48869	Warfarin 1mg/ml oral suspension sugar free	Warfarin sodium	1mg/1ml	Warfarin
50000	Warfarin 1mg/ml oral suspension sugar free (A A H Pharmaceuticals Ltd)	Warfarin sodium	1mg/1ml	Warfarin
51484	Warfarin 1mg tablets (Bristol Laboratories Ltd)	Warfarin sodium	1mg	Warfarin
51496	Warfarin 1mg tablets (Phoenix Healthcare Distribution Ltd)	Warfarin sodium	1mg	Warfarin
51509	Warfarin 1mg tablets (APC Pharmaceuticals & Chemicals (Europe) Ltd)	Warfarin sodium	1mg	Warfarin
53745	Warfarin 3mg tablets (Bristol Laboratories Ltd)	Warfarin sodium	3mg	Warfarin
53752	Warfarin 1mg tablets (Alliance Healthcare (Distribution) Ltd)	Warfarin sodium	1mg	Warfarin
54892	Warfarin 1mg/ml oral suspension sugar free (Alliance Healthcare (Distribution) Ltd)	Warfarin sodium	1mg/1ml	Warfarin
54946	Warfarin 3mg tablets (Actavis UK Ltd)	Warfarin sodium	3mg	Warfarin
55316	Warfarin 3mg/5ml oral suspension	Warfarin sodium	600microgram/1ml	Warfarin
56314	Warfarin 3mg tablets (Kent Pharmaceuticals Ltd)	Warfarin sodium	3mg	Warfarin
57032	Warfarin 1mg/ml oral suspension sugar free (Rosemont Pharmaceuticals Ltd)	Warfarin sodium	1mg/1ml	Warfarin

58519	Warfarin 1mg tablets (DE Pharmaceuticals)	Warfarin sodium	1mg	Warfarin
58787	Warfarin 5mg tablets (Alliance Healthcare (Distribution) Ltd)	Warfarin sodium	5mg	Warfarin
58962	Warfarin 3mg tablets (DE Pharmaceuticals)	Warfarin sodium	3mg	Warfarin
59400	Warfarin 500microgram tablets (Sigma Pharmaceuticals Plc)	Warfarin sodium	500microgram	Warfarin
59578	Warfarin 3mg tablets (Phoenix Healthcare Distribution Ltd)	Warfarin sodium	3mg	Warfarin
60589	Warfarin 500microgram tablets (Actavis UK Ltd)	Warfarin sodium	500microgram	Warfarin
60949	Warfarin 5mg/5ml oral suspension	Warfarin sodium	1mg/1ml	Warfarin
62309	Warfarin 500microgram tablets (Kent Pharmaceuticals Ltd)	Warfarin sodium	500microgram	Warfarin
62310	Warfarin 500microgram tablets (AMCo)	Warfarin sodium	500microgram	Warfarin
63071	Warfarin 4mg tablets	Warfarin sodium	4mg	Warfarin
65285	Warfarin 1mg tablets (Crescent Pharma Ltd)	Warfarin sodium	1mg	Warfarin
65496	Warfarin 500microgram tablets (Phoenix Healthcare Distribution Ltd)	Warfarin sodium	500microgram	Warfarin
65746	Warfarin 500microgram tablets (DE Pharmaceuticals)	Warfarin sodium	500microgram	Warfarin