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Disparities in the care and direct-acting oral anticoagulant (DOAC) management in atrial fibrillation (AF) and chronic kidney disease (CKD) in English primary care between 2018 and 2022: primary care sentinel network database study

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ABSTRACT

Background In England, most prescribing of direct-acting oral anticoagulants (DOACs) for patients with chronic kidney disease (CKD) and atrial fibrillation (AF) takes place in primary care. The 2024 European Society of Cardiology guidelines introduced the AF-CARE ((C) comorbidities and risk factors; (A) avoid stroke and thromboembolism by appropriate prescription of oral anticoagulants; (R) rate and rhythm control; (E) evaluation and reassessment should be individualised for every patient, with a dynamic approach) framework to address this.

Objective To describe any health disparities in CKD and AF, including anticoagulation management and correct dosing of DOACs.

Methods Using English primary care sentinel network data from 2018 to 2022, demographics of AF and CKD including anticoagulation and appropriate DOAC dosing according to creatinine clearance and other factors were assessed. The study also examined disparities in CKD and AF in relation to socioeconomic status and ethnicity. We defined socioeconomic status by Index of Multiple Deprivation (IMD), a weighted composite index combining information from the domains of deprivation including income.

Results Of 10 513 950 people registered with general practices in the sentinel network, 2.9% (n=304 678) were aged ≥18 years with a diagnosis of AF. The prevalence of CKD in AF was 26.0% (n=79 210) and 63.3% of people eligible for anticoagulation were prescribed a DOAC. Among the 54 897 people with AF and CKD 3 or 4, greater likelihood of DOAC prescribing was associated with higher socioeconomic status. Socioeconomic disparities in anticoagulation increased through the 5 years. No association was identified between ethnicity and likelihood of being anticoagulated.

In terms of correct dosing, there was no association with socioeconomic status. Overdosing was more frequent than underdosing. Incorrect dosing was associated with male sex (OR 0.80 (95% CI 0.74, 0.86)), dementia (OR 0.94 (0.83, 1.07)) and frailty (OR 0.42 (0.37, 0.48)).

Conclusions People in the most deprived IMD quintile were least likely to be anticoagulated. Incorrect DOAC dosing was associated with male sex, increasing frailty and dementia. Socioeconomic and health disparities are apparent in anticoagulation prescribing and should be addressed in line with the AF-CARE framework.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Guidelines recommend using direct-acting oral anticoagulants (DOACs) in chronic kidney disease (CKD) and non-valvular atrial fibrillation (NVAF); however, DOACs require correct dosing, which involves complex dose adjustments that vary between preparations.

⇒ If done appropriately, this can help reduce adverse events and address existing inequalities in cardiovascular care.

WHAT THIS STUDY ADDS

⇒ DOACs are being increasingly used for NVAF, surpassing vitamin K antagonists.

⇒ 63.3% of patients with CKD eligible for a DOAC were anticoagulated with DOAC.

⇒ Despite having the lowest mean age, people in the most deprived quintile have the most comorbidities and are least likely to be anticoagulated.

⇒ Overall, regardless of the quintiles, patients are more likely to be overdosed than underdosed.

⇒ Incorrect dosing was associated with male sex (OR 0.80 (95% CI 0.74, 0.86)), dementia (OR 0.94 (0.83, 1.07)) and frailty (OR 0.42 (0.37, 0.48)).

INTRODUCTION

Atrial fibrillation (AF) is the most common type of cardiac arrhythmia.[1] The prevalence of AF in CKD is about twofold to threefold higher than the estimated 2%–4% in the

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ This is the largest study to date in England on AF and CKD that evaluated if health disparities existed between Index of Multiple Deprivation quintiles and ethnicities.
- ⇒ Education, social, economic and health policies at patient and population levels can reduce health inequalities and this study shows the need for this to occur.
- ⇒ It also shows that anticoagulation and its prescribing should be addressed in line with some of the components of the AF-CARE ((C) comorbidities and risk factors; (A) avoid stroke and thromboembolism by appropriate prescription of oral anticoagulants; (R) rate and rhythm control; (E) evaluation and reassessment should be individualised for every patient, with a dynamic approach) framework.

general population. Chronic kidney disease (CKD) is defined as abnormalities of kidney structure or function lasting >3 months. There is an estimated global CKD prevalence of 13.4%. Overall, the presence of both AF and CKD causes a significant rise in the risk of thromboembolism and all-cause mortality, coupled with a paradoxical rise in bleeding events.[2,3] Therefore, the management of such patients presents a challenging scenario for physicians, especially about the use of oral anticoagulants (OACs).[4] Direct oral anticoagulants (DOACs) have been increasingly adopted over vitamin K antagonists (VKAs) such as warfarin for the management of non-valvular AF (NVAF). This is likely due to an improved efficacy/safety ratio, fewer food and drug interactions, favourable bleeding profile, simple dosing regime and less routine monitoring.[5]

To reduce the risks of bleeding and stroke, DOACs should be prescribed with an appropriate dose according to the summary of product characteristics (SPC),[6,7] which includes creatinine clearance, age and weight. There has been limited research as to whether dose reduction has occurred in renal impairment in CKD. This is important because some of these medicines are mainly excreted via the kidney and have a narrow therapeutic index.[7] Dose adjustments are mainly due to creatinine clearance, which is estimated by variables which include patient weight and estimated glomerular filtration rate. In patients with CKD, the dose adjustments are more difficult as most of the drugs are also renally excreted to a certain extent. There is little data about anticoagulation in CKD and AF and, most importantly, in primary care, where clinicians carry out most of the anticoagulant prescribing. This has been shown in the recent systematic review and meta-analysis.[6]

The European Society of Cardiology (ESC) guidelines, published in August 2024, state that anticoagulation and its prescribing should be addressed in line with the AF-CARE framework ((C) comorbidities and risk factors; (A) avoid stroke and thromboembolism by appropriate prescription of oral anticoagulants; (R) rate and rhythm control; (E) evaluation and reassessment should be individualised for every patient, with a dynamic approach). We aimed to evaluate the congruence of these components in our findings.[8]

We conducted this study to look at disparities in healthcare in AF and CKD between 2018 and 2022. We defined socioeconomic status by the Index of Multiple Deprivation (IMD), a weighted composite index combining information from the seven domains of deprivation (ie, income, employment, health, education, housing, crime and living environment) for each small, fixed geographical area of approximately 1500 residents in England.[9,10] Using IMD, we classified all areas into five quintiles, with quintile 1 (IMD 1) representing the most deprived population and quintile 5 (IMD 5) corresponding to the least deprived population.

Each person in our cohort was allocated to an IMD quintile according to their area of residence. The primary care sentinel cohort (PCSC) has previously been involved in AF research, including the development of a quality improvement dashboard.[11]

METHODS

Data source

Data were obtained from the Oxford-Royal College of General Practitioners (RCGP) Clinical Informatics Digital Hub (ORCHID).[11] ORCHID is the trusted research environment that holds RCGP Research and Surveillance Centre (RSC) data, which were collected from the PCSC,[11] a subset of 783 general practices, with 10.51 million currently registered patients at the time of this study being part of the database.

PCSC data were used to provide an accurate denominator, long-term use of computerised medical records (CMR), plus financially incentivised chronic disease management. Pseudonymised NHS numbers provided a unique identifier across the NHS, ensuring that key data flowed into the general practitioner (GP) CMR system.[12] This included all registration, de-registration and death data, pathology data and prescription data. NHS numbers also facilitate the transmission of prescriptions electronically to the patient's registered pharmacist. The variables were recorded in the primary care CMR using the systematised nomenclature of medicine clinical terms (SNOMED CT) and carefully curated.

Population and study period

Retrospective repeated cross-sectional analysis was undertaken for individuals aged ≥18 years with NVAF and CKD diagnosed between January 2018 and December 2022. Patients taking an anticoagulant for other indications (eg, deep vein thrombosis, valvular AF and pulmonary embolism) were excluded, as well as those with CKD 5. The latter with advanced CKD were excluded as the numbers with CKD 5 on DOACs were very small (n=5). Follow-up was carried out between 2018 and 2022 until an outcome event, death or the patient left the practice.

AF cohort data were extracted from the ORCHID database. These were patients who had an SNOMED code of

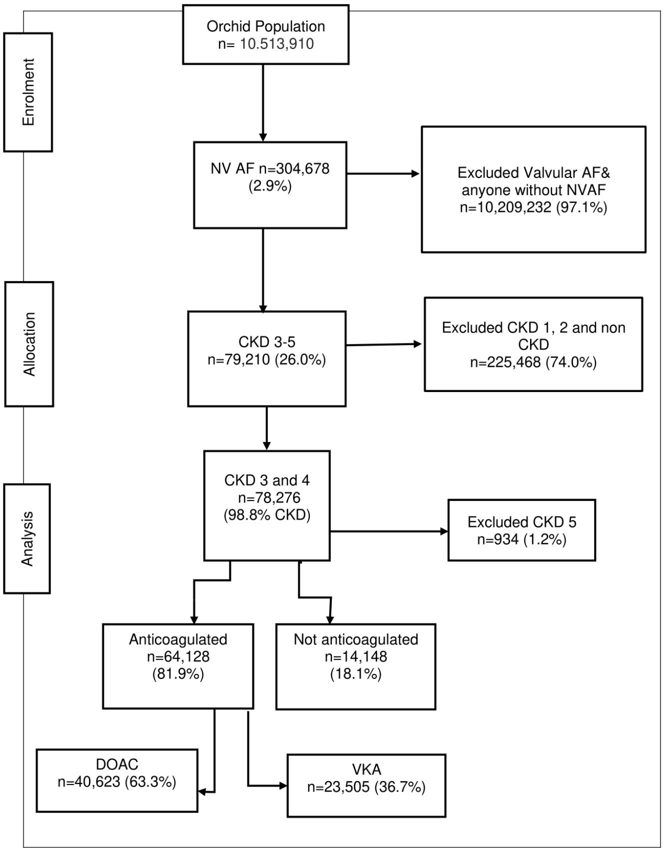

Figure 1 Consolidated Standards of Reporting Trials diagram with the study population. CKD, chronic kidney disease; DOAC, direct-acting oral anticoagulant; NVAF, non-valvular atrial fibrillation; VKA. vitamin K antagonist.

AF and were registered in the RSC period between 2018 and 2022 (figure 1).

A CKD cohort was extracted from RSC data who had a SNOMED CT for CKD with GP coding in CMR.

Study variables

The population of interest was patients with a diagnosis of AF and CKD 3 and 4. Valvular AF was excluded via terminology tight mitral stenosis and mechanical valve replacement. CKD 5 was excluded as the numbers were low and those on DOACs were minimal (n=5) and also because DOACs are not currently licensed for CKD 5. Patients with left atrial appendage occlusion were not included due to poor GP coding with this. Anticoagulant prescribing and baseline demographics were examined according to socioeconomic data in terms of IMD quintiles and ethnicities. An ontological approach was used to describe ethnicities and was categorised as white, Asian, black, mixed and other ethnicities.[12] Black, mixed and other categories were combined due to low numbers. The socioeconomic status was calculated using the IMD, which was divided into quintiles, where quintile 1 signifies the most deprived and quintile 5 is the least deprived.[9 10]

The analysis included age, gender, comorbidities and frailty. Frailty was categorised as mild, moderate and severe according to the electronic frailty index (eFI) recorded in notes. Smoking status was also recorded and classified as current, ex-smoker and non-smoker. Anticoagulants were classified as VKAs (warfarin) and DOACs (apixaban, edoxaban and rivaroxaban and dabigatran).

Outcome measures

Our primary outcome measure was to evaluate correct dosing according to DOAC SPC (table 1), and to look at any trends in pattern with socioeconomic data, and to evaluate any disparities.

Repeated cross-sectional analysis of the RSC data was employed for each year from 2018 to 2022 to explore whether there was a trend in the quality of correct DOAC dosing. Good quality prescribing was defined as dose reduction of DOACs guided by prior measurement of creatinine clearance and/or weight, age and/or creatinine according to SPC recommendations. This was identified from codes for creatinine clearance in the CMRs, or by calculating the creatinine clearance using the Cockcroft-Gault formula if its components were available within the CMR.

Two sensitivity analyses were performed in which correct DOAC dosing was based on GFR measurements only and on creatinine clearance only, without considering pharmacological interactions reflected in SPC recommendation on age, weight or creatinine.

Patients who switched DOAC were included in the outcomes if they had at least two DOAC doses done over two consecutive years.

Statistical analysis

We included data from all patients with AF during the period 2018–2022. First, patients were categorised by

Table 1 Criteria for dose reduction of DOACs according to summary of product characteristics

Dosing criteria for AF	Edoxaban	Apixaban	Dabigatran	Rivaroxaban
Normal dosing regime	60 mg once daily	5 mg two times per day	150 mg two times per day	20 mg once daily
Reduced dosing regime	30 mg once daily	2.5 mg two times per day	110 mg two times per day	15 mg once daily
Criteria for dose reduction (SmPC recommended[17])	Body weight ≤60 kg	≥2 of following: age >80 years Body weight ≤60 kg Serum creatinine 133 µmol/L		
Renal criteria for dose reduction	CrCl 15–50 mL/min	CrCl 15–29 mL/min	CrCl 30–50 mL/min	CrCl 15–50 mL/min

AF, atrial fibrillation; CrCl, creatinine clearance; DOAC, direct-acting oral anticoagulant.

Table 2 Baseline characteristics of chronic kidney disease 3 and 4 with respect to IMD quintiles

	Overall	IMD 1 (most deprived)	IMD 2	IMD 3	IMD 4	IMD 5 (least deprived)	P value
N	78 276	11 259	14 634	16 421	18 126	17 836	
Age (mean (SD))	80.72 (8.52)	79.44 (9.16)	80.48 (8.74)	80.93 (8.40)	81.09 (8.29)	81.17 (8.18)	<0.001
Sex, male (%)	36 301 (46.4)	4971 (44.2)	6505 (44.5)	7549 (46.0)	8565 (47.3)	8711 (48.8)	<0.001
Asian (%)	917 (1.2)	259 (2.3)	259 (1.8)	155 (0.9)	129 (0.7)	115 (0.6)	<0.001
Black/Mixed/Other (%)	999 (1.3)	362 (3.2)	267 (1.8)	171 (1.0)	100 (0.6)	99 (0.6)	<0.001
White (%)	68 137 (87.0)	9867 (87.6)	12 534 (85.6)	14 267 (86.9)	15 916 (87.8)	15 553 (87.2)	<0.001
Unknown (%)	8223 (10.5)	771 (6.8)	1574 (10.8)	1828 (11.1)	1981 (10.9)	2069 (11.6)	<0.001
Heart failure (%)	25 954 (33.2)	3959 (35.2)	5082 (34.7)	5431 (33.1)	5870 (32.4)	5612 (31.5)	<0.001
Hypertension (%)	64 906 (82.9)	9568 (85.0)	12 236 (83.6)	13 592 (82.8)	14 999 (82.7)	14 511 (81.4)	<0.001
Diabetes mellitus (%)	23 494 (30.0)	4124 (36.6)	4744 (32.4)	4896 (29.8)	5173 (28.5)	4557 (25.5)	<0.001
Haemorrhagic stroke (%)	1449 (1.9)	210 (1.9)	279 (1.9)	312 (1.9)	323 (1.8)	325 (1.8)	0.904
Ischaemic stroke (%)	4487 (5.7)	674 (6.0)	844 (5.8)	943 (5.7)	1027 (5.7)	999 (5.6)	0.718
Transient ischaemic attack (%)	9694 (12.4)	1301 (11.6)	1718 (11.7)	2061 (12.6)	2352 (13.0)	2262 (12.7)	<0.001
Vascular disease (%)	1954 (2.5)	301 (2.7)	416 (2.8)	387 (2.4)	477 (2.6)	373 (2.1)	<0.001
Ischaemic heart disease (%)	32 918 (42.1)	5067 (45.0)	6378 (43.6)	6980 (42.5)	7332 (40.5)	7161 (40.1)	<0.001
Heavy drinking (%)	2330 (3.0)	486 (4.3)	472 (3.2)	489 (3.0)	464 (2.6)	419 (2.3)	<0.001
Myocardial infarction (%)	12 144 (15.5)	1867 (16.6)	2415 (16.5)	2495 (15.2)	2728 (15.1)	2639 (14.8)	<0.001
Liver disease (%)	3790 (4.8)	660 (5.9)	740 (5.1)	778 (4.7)	830 (4.6)	782 (4.4)	<0.001
Body mass index obesity (%)	8051 (10.3)	1491 (13.2)	1951 (13.3)	1727 (10.5)	1577 (8.7)	1305 (7.3)	<0.001
Sleep apnoea (%)	7594 (9.7)	1129 (10.0)	1479 (10.1)	1555 (9.5)	1735 (9.6)	1696 (9.5)	0.183
Asthma (%)	11 495 (14.7)	1912 (17.0)	2320 (15.9)	2372 (14.4)	2496 (13.8)	2395 (13.4)	<0.001
Chronic obstructive pulmonary disease (%)	9529 (12.2)	1918 (17.0)	2085 (14.2)	1829 (11.1)	1997 (11.0)	1700 (9.5)	<0.001
Dementia (%)	9340 (11.9)	1452 (12.9)	1862 (12.7)	2006 (12.2)	2134 (11.8)	1886 (10.6)	<0.001
Smoking status (%)							<0.001
Active smoker	14 157 (18.4)	2753 (24.7)	2935 (20.3)	2911 (18.0)	2916 (16.3)	2642 (15.1)	
Ex-smoker	34 708 (45.0)	4563 (41.0)	6372 (44.2)	7360 (45.6)	8162 (45.7)	8251 (47.1)	
Non-smoker	28 211 (36.6)	3822 (34.3)	5121 (35.5)	5863 (36.3)	6786 (38.0)	6619 (37.8)	
Gastrointestinal bleeding (%)	11 131 (14.2)	1626 (14.4)	2025 (13.8)	2264 (13.8)	2558 (14.1)	2658 (14.9)	0.02
CHA_2DS_2VASc (%)							<0.001
0–1	1873 (2.8)	267 (2.8)	324 (2.6)	386 (2.8)	418 (2.7)	478 (3.1)	
	6391 (9.6)	922 (9.6)	1134 (9.1)	1317 (9.4)	1443 (9.3)	1575 (10.3)	
3–4	32 298 (48.3)	4454 (46.2)	5889 (47.2)	6784 (48.5)	7659 (49.4)	7512 (49.4)	
5–9	26 275 (39.3)	3989 (41.4)	5141 (41.2)	5504 (39.3)	5988 (38.6)	5653 (37.1)	
HASBLED_3–8 (%)	3767 (21.9)	547 (21.8)	770 (22.7)	747 (21.1)	900 (21.6)	803 (22.4)	0.517
ORBIT (%)							0.473
0–2	221 (60.9)	26 (53.1)	49 (69.0)	35 (54.7)	60 (65.2)	51 (58.6)	
3	28 (7.7)	6 (12.2)	3 (4.2)	7 (10.9)	7 (7.6)	5 (5.7)	
4–7	114 (31.4)	17 (34.7)	19 (26.8)	22 (34.4)	25 (27.2)	31 (35.6)	
Frailty (%) (eFI)							<0.001
Fit	9919(0.3)	85 (0.8)	145 (1.0)	221 (1.4)	248 (1.4)	292 (1.7)	
Mild	13 769 (18.2)	1484 (13.9)	2405 (17.1)	2954 (18.5)	3298 (18.7)	3628 (20.8)	
Moderate	27 815 (36.7)	3636 (34.0)	5034 (35.7)	5866 (36.7)	6597 (37.4)	6682 (38.4)	
Severe	33 248 (43.8)	5491 (51.3)	6508 (46.2)	6926 (43.4)	7503 (42.5)	6820 (39.1)	

Continued

Table 2 Continued

	Overall	IMD 1 (most deprived)	IMD 2	IMD 3	IMD 4	IMD 5 (least deprived)	P value
							0.022
Anticoagulated DOAC	40 623 (51.9)	5684 (50.5)	7578 (51.8)	8498 (51.8)	9455 (52.2)	9408 (52.7)	
Anticoagulated VKA	23 505 (30.0)	3463 (30.8)	4381 (29.9)	4925 (30.0)	5480 (30.2)	5256 (29.5)	
Not anticoagulated	14 148 (18.1)	2112 (18.8)	2675 (18.3)	2998 (18.3)	3191 (17.6)	3172 (17.8)	

CHA_2DS_2VASc, Congenital Heart Failure, Hypertension, Age ≥75, Diabetes, Stroke, Vascular Disease, Age 65–75, Sex, Age Category; DOAC, direct-acting oral anticoagulant; eFI, electronic frailty index; HASBLED, hypertension, abnormal kidney and liver function, stroke and bleeding; IMD, Index of Multiple Deprivation; ORBIT, Outcome Registry Better Informed Treatment; VKA, vitamin K antagonist.

their CKD stage classification, according to the documented GP diagnosis each year. All main analyses were then performed on those classified as CKD stage 3 and 4.

Baseline characteristics were summarised and stratified by IMD quintiles and ethnicities (white, black/mixed/other, Asian and unknown). Means and SD are presented for continuous baseline variables and percentages for categorical variables.

We investigated the effect of IMD class and ethnicity on the outcome of correct/incorrect dosing (either overdosing or underdosing). These investigations were performed through two separate simple multilevel logistic regression models. Correct dosing was evaluated every time a patient started a new DOAC prescription. The year of the start of the prescription is included in these models as a random intercept to adjust for the clustering of outcomes within each patient. The same modelling results were additionally transformed into percentages and presented graphically with error bars (representing 95% CI) by year and by social class and ethnicity. A third multiple logistic regression model was fitted that included IMD class, ethnicity and other baseline characteristics to investigate the adjusted impact of these variables.

All statistical analyses were performed using the R statistical programming language V.4.3.2. All outcome measures and measures of association are reported with 95% CIs.

RESULTS

Demographics and anticoagulation status

Of the 10 513 950 people registered with general practices that are part of ORCHID, 2.9% (n=304 678) were

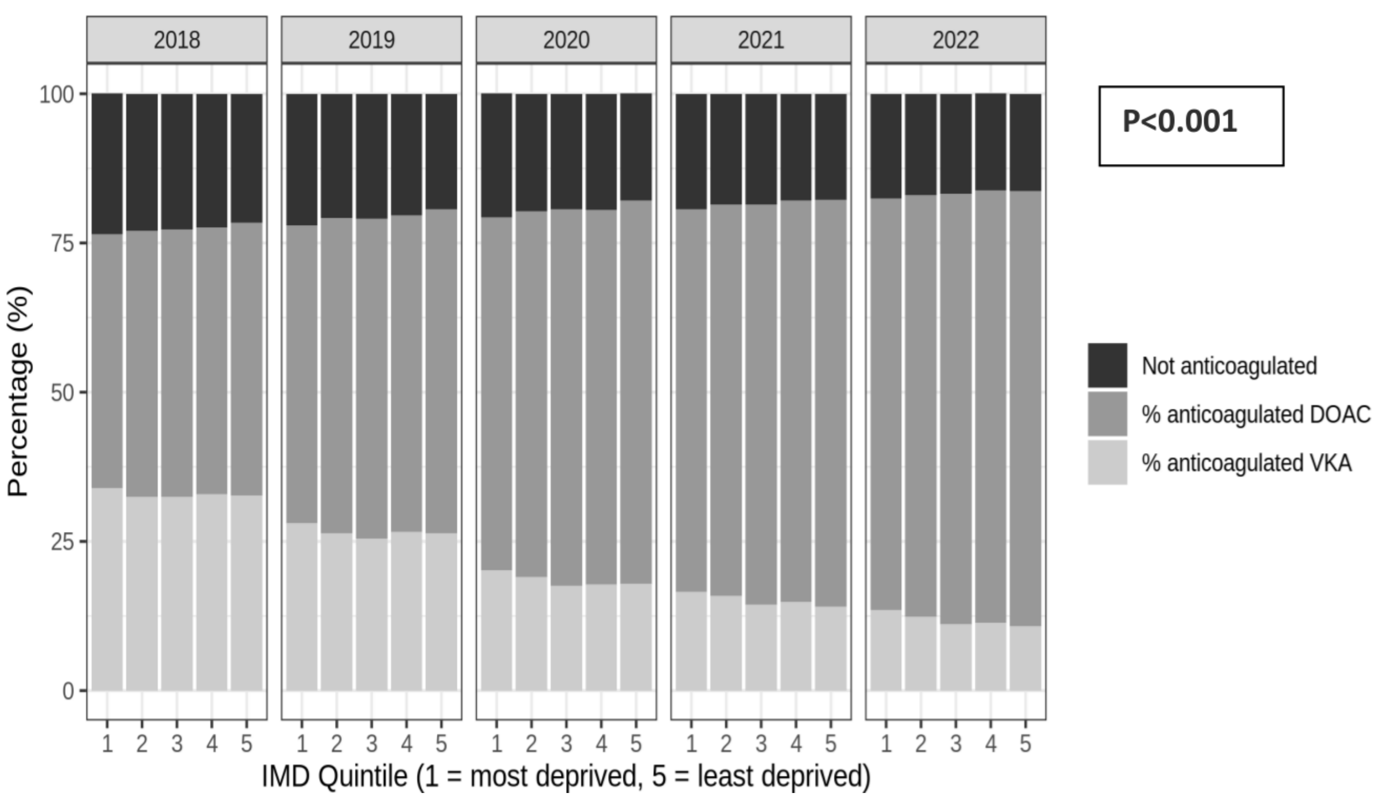

Figure 2 Improving anticoagulation status across the quintiles 2018–2022. DOAC, direct-acting oral anticoagulant; IMD, Index of Multiple Deprivation; VKA. vitamin K antagonist.

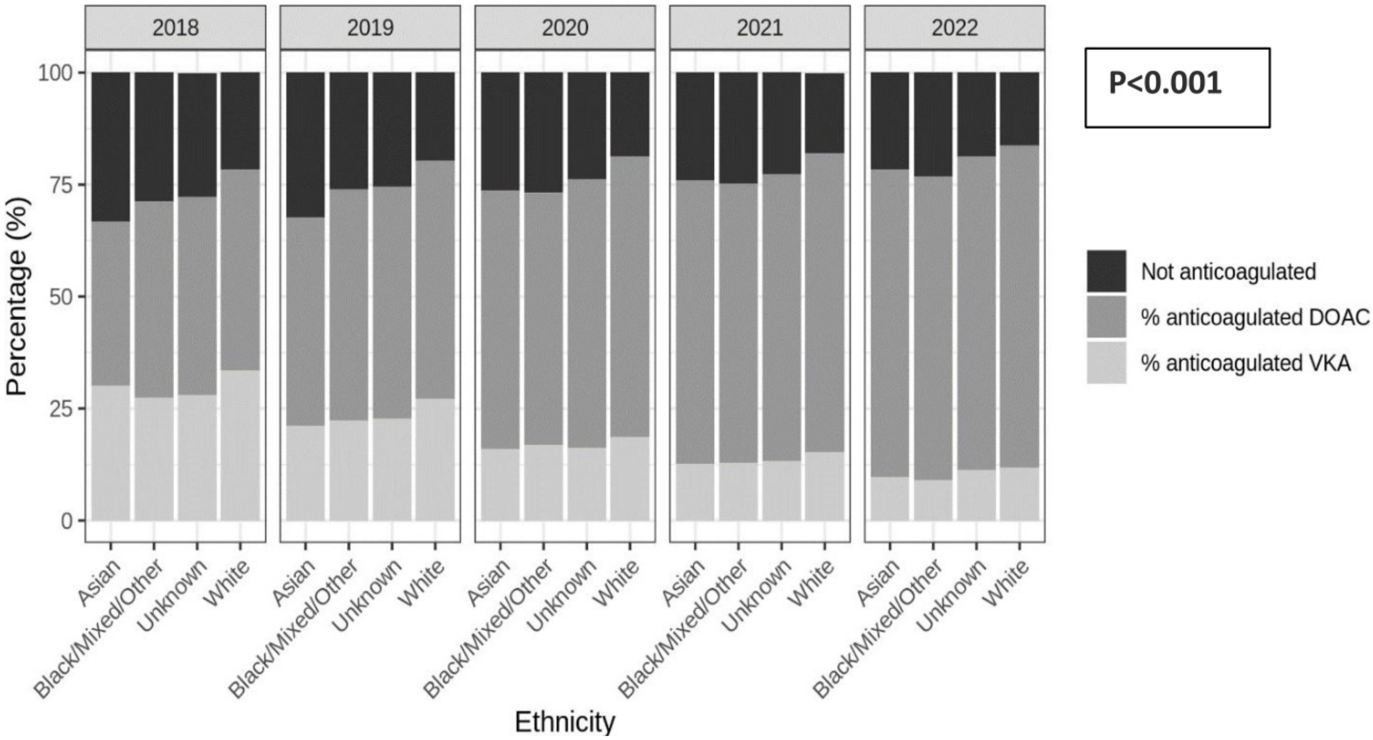

Figure 3 Improving anticoagulation status across the ethnicities 2018–2022. DOAC, direct-acting oral anticoagulant; VKA. vitamin K antagonist.

≥18 years of age with a diagnosis of AF. The prevalence of CKD in AF was 26.0% (n=79 210) (figure 1).

The mean age of our AF and CKD cohort with CKD 3 and 4 was 81.9 (SD 7.9), but there was a steady increase in age on going from IMD quintile 1 to 5: 80.6 (SD 8.6), 81.5 (SD 8.1), 82.0 (SD 7.8), 82.2 (SD 7.7) and 82.4 (SD 7.6). The proportions with severe frailty in quintiles 1–5 were as follows: 47.6%, 41.8%, 40.6%, 38.8% and 36.4%. The percentages of patients who were fit and had mild frailty were higher in IMD quintile 5 compared with quintile 1, and this proportion increased progressively from IMD 1 to IMD 5 (table 2).

Of the 78 276 people with CKD 3 and 4 eligible for a DOAC only, 51.9% of people (n=40 623) were prescribed this. However, 81.9% (n=64 128) of people were anticoagulated with DOAC or VKA (figure 1, table 2).

Of the 17 836 people with CKD 3 and 4 with AF in the least deprived quintile, more patients were anticoagulated with DOACs compared with VKA (52.7%, n=9408) than in other IMD quintiles (table 2).

The disparities with anticoagulation throughout the quintiles did exist in 2018 but increased through the 5 years (figure 2).

Using logistic regression and adjusting for other factors, it was found that there was an association with people in IMD quintile 5 being more likely to be anticoagulated and to receive a DOAC than those with IMD quintile 1. People in IMD quintile 2 were also more likely to receive a DOAC compared with IMD quintile 1, but there were not many differences between other IMD quintiles with statistical significance once adjusted for other factors (online supplemental table 1).

In terms of ethnicity (online supplemental table 2), the numbers of Asians (n=917) and black and mixed-race people (n=999) were small compared with white people (n=68 137) in our population, but the non-white groups were from mainly IMD quintiles 1 and 2 as opposed to white people, which were more equally distributed across the IMD quintiles. Although the average age of our cohort was 81.9 (SD 7.9) years, Asians (77.4 years; SD 9.5) and patients from black and mixed-race ethnicities (78.2 years; SD 9.8) were much younger than white people.

In terms of ethnicities and baseline characteristics (online supplemental table 2), 82.8% (n=56 391) of white people were anticoagulated, and of those anticoagulated 52.4% (n=35 675) received a DOAC. 77.2% (n=708) of Asians were anticoagulated and of these, 63.3% overall received a DOAC. Overall, there was an increase in all groups receiving anticoagulation and receiving a DOAC over the years, which was statistically significant (figure 3).

However, using logistic regression and adjusting for other factors, no significant differences were found between ethnic groups in the likelihood of being anticoagulated or receiving a DOAC (online supplemental table 1).

Dosing trends

The proportion of people with AF who have been underdosed with DOAC for AF in CKD was 31.9% (95% CI 15.5 to 37.7) in quintile 1 and 29.0% (95% CI 15.8 to 30.6) in 2018. However, in 2020, following COVID-19,

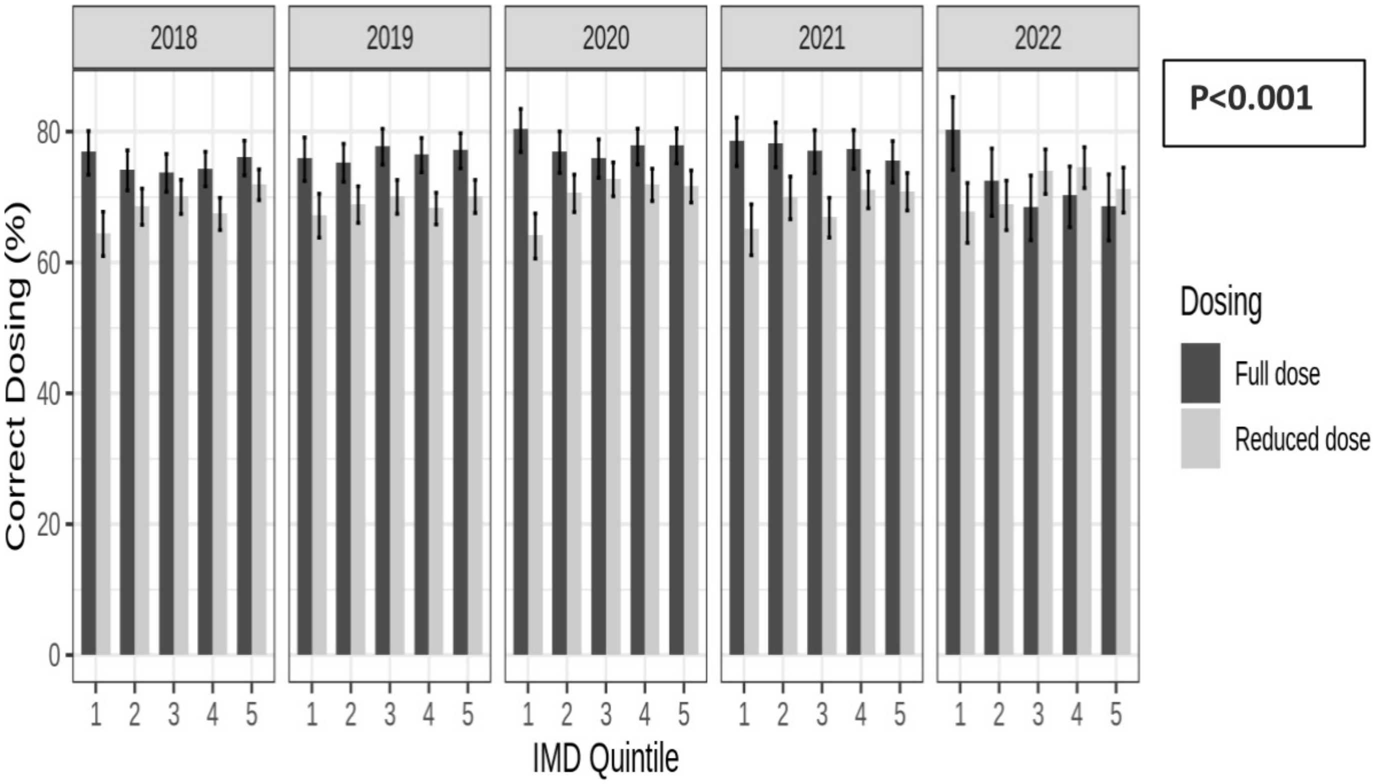

Figure 4 Correct dosing by IMD quintiles according to the summary of product recommendations. IMD, Index of Multiple Deprivation.

this reduced in all quintiles. It was 19.7% (95% CI 14.7 to 25.8) in most deprived quintile (IMD quintile 1) with the least deprived quintile (IMD quintile 5) being significantly reduced to 31.4% (95% CI 26.5 to 36.6) (figure 4).

With respect to overdosing, this increased across all quintiles, being 42.6% (95% CI 39.1% to 46.1%) in quintile 1 and 36.8% (95% CI 34.5% to 39.5%) in quintile 5 in 2018. Correct dosing in quintile 1 has increased over time, despite a slight reduction during the COVID-19 year (2020), with correct dosing reaching 59.4% in 2022 (95% CI 54.5 to 64.1%). In all other quintiles apart from quintile 5, there has been a steady increase from 2018 to 2022. In contrast, rates in quintile 5 have remained stable over this period (figure 4).

With respect to ethnicity (online supplemental figure 1), certain trends were seen: black patients overall had the least underdosing and overdosing through most of the years. However, in 2020, Asians patients recorded the lowest rate of underdosing and overdosing during the 5-year period, at 15.4%. White people, the largest cohort, had the least underdosing and overdosing in 2020, at 22.1%. Black and mixed-race patients had the highest overdosing and underdosing during 2019 to 2020 (the COVID-19 period), However, by 2022, rates had significantly decreased among black patients, with underdosing and overdosing falling to 16.2%, compared with other ethnicities.

Using logistic regression and adjusting for other factors, male sex, dementia and frailty were associated with both overdosing and underdosing, the likelihood of dosing errors increasing with the severity of frailty. However, after adjusting for other factors, no association was found between underdosing or overdosing and IMD quintiles or ethnicities. Being anticoagulated with edoxaban was more strongly associated with correct DOAC dosing compared with apixaban, which in turn was associated with more correct dosing than rivaroxaban and dabigatran (table 3).

Our sensitivity analysis on substituting eGFR and creatinine clearance for dosing according to SPC recommendations showed significant changes, particularly when eGFR was used at reduced doses, as seen in 2018 when the highest overdosing occurred in quintile 1 (figure 5).

This has been further seen in 2022 when the lowest overdosing occurred (figure 5, online supplemental figure 2). With underdosing, the sensitivity analysis did not show as many changes as with overdosing using eGFR.

DISCUSSION

This is one of the largest contemporary studies of DOAC prescribing in England with respect to AF and CKD, particularly one that evaluates inequalities in healthcare, concerning DOAC dosing.

The IMD is unique in its inclusion of a measure of geographical access as an element of deprivation and in its direct measure of poverty (through data on benefit receipts). This has the potential to provide a missing dimension of deprivation in rural areas.[9 10]

Table 3 Factors associated with correct dosing

	Multivariable OR (95% CI)	P value
DOAC (ref=apixaban)		
Dabigatran	0.90 (0.85, 0.97)	<0.001
Edoxaban	1.11 (1.06, 1.116)	<0.001
Rivaroxaban	0.98 (0.95, 1.01)	<0.001
CHA_2DS_2VASc (ref=0–1)		
2	0.55 (0.41, 0.73)	0.081
3–4	0.44 (0.33, 0.59)	0.011
5–9	0.43 (0.32, 0.58)	0.071
IMD quintile (ref=1)		
2	1.05 (0.93, 1.19)	0.411
3	1.16 (0.03, 1.31)	0.017
4	1.09 (0.97, 1.22)	0.166
5	1.09 (0.97, 1.23)	0.165
Age (years)	1.00 (0.98, 1.02)	0.273
Sex (ref=female)	0.80 (0.74, 0.86)	<0.001
Ethnicity (ref=Asian)		
White	1.03 (0.77, 1.37)	0.821
Black/Mixed/Other	1.12 (0.75, 1.69)	0.572
Unknown	1.05 (0.77, 1.43)	0.757
Smoking status (ref=current smoker)		
Ex-smoker	0.97 (0.88, 1.07)	0.564
Non-smoker	1.04 (0.94, 1.15)	0.471
Heart failure	1.05 (0.97, 1.13)	0.184
Hypertension	1.07 (0.97, 1.18)	0.196
Diabetes mellitus	0.99 (0.91, 1.08)	0.011
Vascular disease	1.16 (0.92, 1.47)	0.209
Alcohol misuse	1.02 (0.84, 1.26)	0.817
Liver disease	0.86 (0.72, 1.01)	0.065
COPD	0.98 (0.88, 1.10)	0.770
Dementia	0.94 (0.83, 1.07)	<0.001
Cerebrovascular accident—haemorrhagic	0.61 (0.46, 0.81)	0.766
Cerebrovascular accident—ischaemic	1.01 (0.88, 1.18)	0.848
Sleep apnoea	1.04 (0.92, 1.18)	0.499
Body mass index/obesity	0.93 (0.82, 1.05)	0.224
Myocardial infarction	1.01 (0.91, 1.12)	0.914
Frailty—mild	0.82 (0.72, 0.93)	<0.001
Frailty—moderate	0.61 (0.52, 0.69)	<0.001
Frailty—severe	0.42 (0.37, 0.48)	<0.001

CHA_2DS_2VASc, Congenital Heart Failure, Hypertension, Age ≥75, Diabetes, Stroke, Vascular Disease, Age 65–75, Sex, Age Category; COPD, chronic obstructive pulmonary disease; DOAC, direct-acting oral anticoagulant; IMD, Index of Multiple Deprivation.

The mean age of our cohort was 81.9, but the youngest cohort was in the most deprived quintile, with a stepwise increase in age going from IMD class 1 (most deprived) to IMD 5 (least deprived). This is consistent with recent literature[12 13] that people living in poorer areas have greater levels of multimorbidity including AF and early mortality, as it has been shown that disparities in health start at an early age, with higher rates of diagnosed mental health conditions, chronic pain, smoking, alcohol problems and financial burden starting to develop as early as the late teens and early 20s and continue to grow and change across the life cycle, through working age, and into old age.[14] This will need to be addressed at a national level with a modifiable target for healthcare policy. Individuals with AF even without CKD residing in socioeconomically deprived areas often present with more comorbidities and are less likely to receive anticoagulation therapy, particularly DOACs.[15–17]

These findings highlight the need for targeted interventions to address healthcare disparities in AF management, ensuring equitable access to appropriate therapies across different socioeconomic groups.

The trend in increased diagnosis of AF with commensurate prescription of DOACs over recent years has been reported elsewhere.[14] Overall, anticoagulant prescribing increased between 2018 and the end of 2022 with a slight decline in 2021. The decline seen may be related to post-COVID-19 coagulopathy or an increase in the ageing population with progressively ill health and with a lack of awareness of the benefits of anticoagulation. The increased workload for primary care clinicians post-COVID-19 may have also meant they had reduced confidence or reduced time with anticoagulation in patients with CKD. These observations offer significant public health implications and may highlight a need to increase anticoagulant awareness in CKD and the need for further research.

A significant proportion of the cohort with CKD and AF were not anticoagulated, and a considerable proportion was also not receiving DOAC treatment as stratified by the National Institute for Health and Care Excellence and ESC guidelines. This may be due to underlying comorbidities, as some debates exist over various options in CKD for optimised management of comorbidities to improve clinical outcomes.[8]

Of the 54 897 patients with CKD 3 and 4 and AF who were eligible for DOACs, a higher proportion of patients in the least deprived IMD quintile were anticoagulated compared with those in the more deprived quintiles. Furthermore, the patients in the least deprived IMD quintiles were more likely to be anticoagulated DOACs rather than VKAs, in contrast to those in the most deprived quintile. This has been seen in other studies and likely reflects underlying population characteristics.[17 18] High-risk patients with AF, particularly those with lower levels of education and income in the most deprived quintile, appeared to be undertreated with OACs (DOACs or VKAs). Health disparities

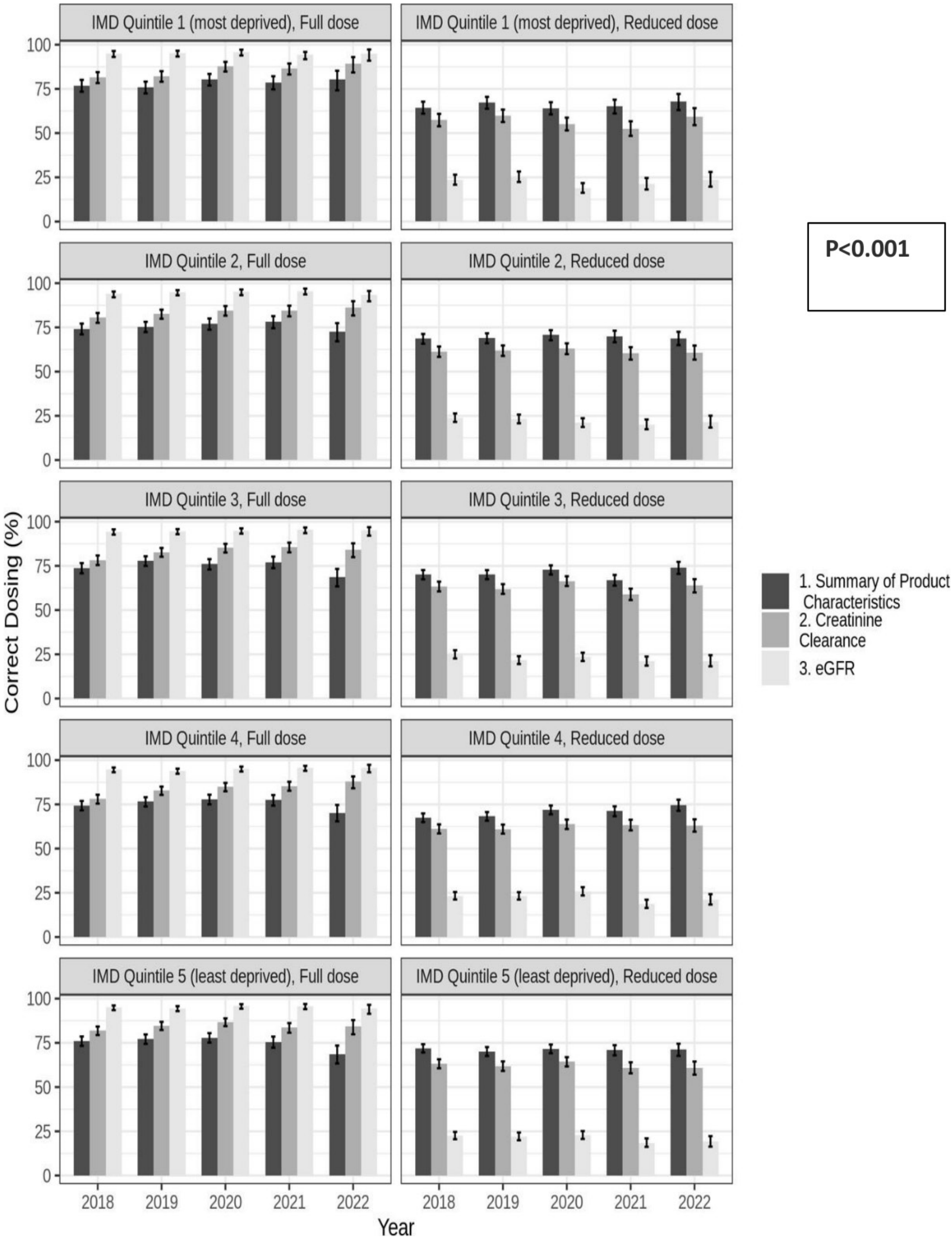

Figure 5 Sensitivity analysis comparing DOAC correct dosing in IMD quintiles according to summary of product characteristics recommendations with creatinine clearance alone and with eGFR. DOAC, direct-acting oral anticoagulant; eGFR, estimated glomerular filtration rate; IMD, Index of Multiple Deprivation.

carry significant social and economic costs for both individuals and society as a whole. These disparities may be linked to factors associated with low income, such as limited understanding of treatment options, rather than the cost of prescriptions. In England, patients over the age of 60 are exempt from prescription charges regardless of financial status, and individuals under 60 with low income are also eligible for exemption from prescription payments.[18] In our study, over 90% of individuals with AF and CKD who were prescribed DOACs were older than 60 years.

More women were treated than men and this has also been seen in other notable papers.[19–22] Our study had a larger proportion of women than in previous studies. It has been shown that the female sex is a risk modifier rather than a risk factor.[21 22] Our study showed that women are more likely to be anticoagulated than men.[21 22] This seems to agree with recent 2024 ESC guidelines, where a non-sex CHA_2DS_2VASc (ie, CHA_2DS_2-VA) is recommended.[8]

There was no statistically significant difference in anticoagulation rates between ethnic groups in our study, unlike previous studies that have shown that whites are more anticoagulated than non-white races.[22]

In terms of underdosing, the difference between the quintiles did not follow a pattern and did not show any significant disparities. The levels of correct dosing were overall much higher than the 68% previously noted.[7] This may be due to recent guidelines that emphasise education for both healthcare professionals and patients at both local and national levels, as well as financial incentives linked to pay-for-performance schemes in primary care.[23–25]

Overdosing was more common than underdosing. This is in keeping with published literature from a US cohort.[26] Failure to reduce DOAC doses may increase bleeding without additional efficacy. Inappropriate dose reductions are often carried out to mitigate bleeding risks but are associated with overall worse outcomes.[26] Our study provides the most up-to-date analysis of DOAC dosing, including the impact of COVID-19, which greatly affected those of black ethnicity. Correct dosing was more frequently associated with edoxaban compared with apixaban—a pattern not seen with other DOACs. This may be due to edoxaban being the most recently introduced DOAC, prompting greater caution among clinicians. Additionally, it is possible that edoxaban was more commonly prescribed to younger, less frail patients with fewer comorbidities. There was no association with once-daily DOACs having any advantage over twice-daily DOACs. There was also an association between dementia and frailty with incorrect DOAC. This highlights the need for closer monitoring and evaluation of these patient groups, as DOAC dosing may be a more complex procedure in such cases. Factors such as clinicians being more aware of vulnerability to adverse events and using more complex dosing patterns of certain drugs may contribute to this complexity.[25 26]

Our sensitivity analysis showed that overdosing is more likely to occur when estimated eGFR is used instead of creatinine clearance, as specified in the SPC recommendations. It has been shown that this occurs at extremes of age and weight with reduced renal function.[25 26] Awareness of these factors is crucial to ensure appropriate dosing and to prevent adverse events such as bleeding.[26] There was an association with more correct dosing with edoxaban compared with apixaban. This was not seen with other DOACs. This may be due to edoxaban being the last DOAC to be introduced and hence clinicians are more careful and also because the younger, less frail patients with less comorbidities were on edoxaban. There was no association with once-daily DOACs having any advantage over twice-daily DOACs, particularly in IMD quintile 5. The decline in correct dosing may be due to more complex dosing patterns, increased frailty and a higher burden of comorbidities.[27 28]

To tackle these disparities in anticoagulation management and increased comorbidities in the most deprived population, action should be taken at the individual, organisational and policy levels. A personalised care plan with the use of recent ESC 2024 guidelines needs to be carried out, including using the AF-CARE pathway to evaluate comorbidities alone as well as those that lead to frailty. Evaluation and dynamic reassessment need to be conducted.[8 29]

Limitations and strengths

There is a high level of congruence between our findings and those reported in the existing literature. We assumed that GP coding was accurate, as the data extraction method provided only one eGFR value per year. This single annual eGFR value aligned with GP coding in over 90% of cases, a level of agreement consistent with prevalence rates reported in other studies.[18]

We did not exclude patients with left atrial appendage occlusion from our study, as the number of such cases was minimal and there appeared to be substantial missing data. We used only creatinine clearance, along with weight, age and other relevant factors, in accordance with the dosing recommendations for apixaban and edoxaban. We did not account for other factors that can influence dosing, such as drugs like ketoconazole, or clinical conditions like reflux, due to the transient nature of some drug interactions and the difficulty in accurately capturing this information within the constraints of our study design.

We used the eFI to measure frailty, which may overestimate frailty compared with other scales,[28] but it provided the most consistently recorded by primary care clinicians in our study.

Another limitation of the study is its cross-sectional design, which precluded the evaluation of causal relationships between anticoagulation and DOAC dosing; only associations could be assessed. Patients with CKD 5 were excluded from the study due to small numbers and because DOACs are not licensed for use in individuals with a creatinine clearance <15 mL/min—a threshold that applies to majority of patients with CKD 5. As a result, we were unable to evaluate reasons for off-license prescribing in this group. Pharmacological interactions were excluded from the analysis, as interactions affecting DOAC dosing—such as those with clarithromycin—were often transient and difficult to reliably capture given the cross-sectional nature of the study design.

CONCLUSION

This is one of the largest studies in England on AF and CKD. Despite having the lowest mean age, people in the most deprived quintile had the most comorbidities and were least likely to be anticoagulated and least likely to be prescribed DOAC. However, with correct dosing, there were little disparities in health, although overdosing is more frequent than underdosing. Incorrect dosing was associated with male sex, dementia and frailty. There needs to be better education for clinicians and patients alike on correct DOAC dosing, if a reduced dose is indicated by SPC recommendations. These healthcare disparities highlight the need for improved patient engagement and coordinated multi-agency action to address the social determinants of health, in alignment with some components of the ESC guidelines' AF-CARE framework.

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Patient consent for publication Not applicable.

Ethics approval Ethical approval was obtained from the Primary Care Hosted Research Datasets Independent Scientific Committee (PrimDISC) on 23 February 2023 (reference number PD-0009-2022; https://www.phc.ox.ac.uk/intranet/better-workplace-groups-committees-open-meetings/primdisc-committee-1). The study was also approved by the University-Royal College of General Practitioners (RCGP) Joint Research and Surveillance Centre Committee (JRSCC). This is a retrospective, cross-sectional study with no direct patient involvement. All practices participating in the RCGP Research and Surveillance Centre (RSC) have obtained consent from their patients for data to be used in research. Pseudonymised data from the RSC were used for analysis within the Oxford–RCGP Clinical Informatics Digital Hub (ORCHID), a secure Trusted Research Environment (TRE). This TRE meets the requirements of NHS Digital's Data Security and Protection (DSP) Toolkit and is registered under Organisational Data Service (ODS) number EE133863-MSD-NDPCHS.

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REFERENCES

1 Roth GA, Mensah GA, Johnson CO, *et al*. Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019. *J Am Coll Cardiol* 2020;76:2982–3021.
2 Olesen JB, Lip GYH, Kamper A-L, *et al*. Stroke and bleeding in atrial fibrillation with chronic kidney disease. *N Engl J Med* 2012;367:625–35.
3 Laupacis A, Boysen G, Connolly S, *et al*. Risk Factors for Stroke and Efficacy of Antithrombotic Therapy in Atrial Fibrillation. *Arch Intern Med* 1994;154:1449.
4 Potpara TS, Ferro CJ, Lip GYH. Use of oral anticoagulants in patients with atrial fibrillation and renal dysfunction. *Nat Rev Nephrol* 2018;14:337–51.
5 Shen N-N, Zhang C, Wang N, *et al*. Effectiveness and Safety of Under or Over-dosing of Direct Oral Anticoagulants in Atrial Fibrillation: A Systematic Review and Meta-analysis of 148909 Patients From 10 Real-World Studies. *Front Pharmacol* 2021;12:645479.
6 Emanuel S, Kaba RA, Delanerolle G, *et al*. Correct dosing, adherence and persistence of DOACs in atrial fibrillation and chronic kidney disease: a systematic review and meta-analysis. *Open Heart* 2023;10:e002340.
7 Joy M, Williams J, Emanuel S, *et al*. Trends in direct oral anticoagulant (DOAC) prescribing in English primary care (2014-2019). *Heart* 2023;109:195–201.
8 Van Gelder IC, Rienstra M, Bunting KV, *et al*. 2024 ESC Guidelines for the management of atrial fibrillation developed in collaboration

with the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2024;45:3314–414.

9 Jordan H, Roderick P, Martin D. The Index of Multiple Deprivation 2000 and accessibility effects on health. *Journal of Epidemiology & Community Health* 2004;58:250–7.

10 Lloyd CD, Norman PD, McLennan D. Deprivation in England, 1971-2020. *Appl Spat Anal Policy* 2023;16:461–84.

11 Leston M, Elson WH, Watson C, *et al*. Representativeness, Vaccination Uptake, and COVID-19 Clinical Outcomes 2020-2021 in the UK Oxford-Royal College of General Practitioners Research and Surveillance Network: Cohort Profile Summary. *JMIR Public Health Surveill* 2022;8:e39141.

12 Kraftman L, Hardelid P, Banks J. Age specific trends in mortality disparities by socio-economic deprivation in small geographical areas of England, 2002-2018: A retrospective registry study. *The Lancet Regional Health - Europe* 2021;7:100136.

13 Wu J, Nadarajah R, Nakao YM, *et al*. Temporal trends and patterns in atrial fibrillation incidence: A population-based study of 3·4 million individuals. *The Lancet Regional Health - Europe* 2022;17:100386.

14 Lunde ED, Joensen AM, Fonager K, *et al*. Socioeconomic inequality in oral anticoagulation therapy initiation in patients with atrial fibrillation with high risk of stroke: a register-based observational study. *BMJ Open* 2021;11:e048839.

15 Essien UR, Kornej J, Johnson AE, *et al*. Social determinants of atrial fibrillation. *Nat Rev Cardiol* 2021;18:763–73.

16 Gurusamy VK, Brobert G, Vora P, *et al*. Sociodemographic factors and choice of oral anticoagulant in patients with non-valvular atrial fibrillation in Sweden: a population-based cross-sectional study using data from national registers. *BMC Cardiovasc Disord* 2019;19:43.

17 Jilani MH, Javed Z, Yahya T, *et al*. Social Determinants of Health and Cardiovascular Disease: Current State and Future Directions Towards Healthcare Equity. *Curr Atheroscler Rep* 2021;23:55.

18 Dalmau Llorca MR, Aguilar Martín C, Carrasco-Querol N, *et al*. Gender and Socioeconomic Inequality in the Prescription of Direct Oral Anticoagulants in Patients with Non-Valvular Atrial Fibrillation in Primary Care in Catalonia (Fantas-TIC Study). *Int J Environ Res Public Health* 2021;18:10993.

19 Law SWY, Lau WCY, Wong ICK, *et al*. Sex-Based Differences in Outcomes of Oral Anticoagulation in Patients With Atrial Fibrillation. *J Am Coll Cardiol* 2018;72:S0735-1097(18)34830-7:271–82:.

20 Lip GYH, Teppo K, Nielsen PB. CHA2DS2-VASc or a non-sex score (CHA2DS2-VA) for stroke risk prediction in atrial fibrillation: contemporary insights and clinical implications. *Eur Heart J* 2024;45:3718–20.

21 Nielsen PB, Overvad TF. Female Sex as a Risk Modifier for Stroke Risk in Atrial Fibrillation: Using CHA2DS2-VASc versus CHA2DS2-VA for Stroke Risk Stratification in Atrial Fibrillation: A Note of Caution. *Thromb Haemost* 2020;120:894–8.

22 Wilson LE, Luo X, Li X, *et al*. Clinical outcomes and treatment patterns among Medicare patients with nonvalvular atrial fibrillation (NVAF) and chronic kidney disease. *PLoS One* 2019;14:e0225052.

23 Chung S-C, Sofat R, Acosta-Mena D, *et al*. Atrial fibrillation epidemiology, disparity and healthcare contacts: a population-wide study of 5.6 million individuals. *The Lancet Regional Health - Europe* 2021;7:100157.

24 Medlinskiene K, Richardson S, Petty D, *et al*. Barriers and enablers to healthcare system uptake of direct oral anticoagulants for stroke prevention in atrial fibrillation: a qualitative interview study with healthcare professionals and policy makers in England. *BMJ Open* 2023;13:e069575.

25 Jackson LR 2nd, Schrader P, Thomas L, *et al*. Dosing of Direct Oral Anticoagulants in Patients with Moderate Chronic Kidney Disease in US Clinical Practice: Results from the Outcomes Registry for Better Informed Treatment of AF (ORBIT-AF II). *Am J Cardiovasc Drugs* 2021;21:553–61.

26 Kim DH, Pawar A, Gagne JJ, *et al*. Frailty and Clinical Outcomes of Direct Oral Anticoagulants Versus Warfarin in Older Adults With Atrial Fibrillation : A Cohort Study. *Ann Intern Med* 2021;174:1214–23.

27 Broad A, Carter B, Mckelvie S, *et al*. The Convergent Validity of the electronic Frailty Index (eFI) with the Clinical Frailty Scale (CFS). *Geriatrics (Basel)* 2020;5:88.

28 Arbelo E, Aktaa S, Bollmann A, *et al*. Quality indicators for the care and outcomes of adults with atrial fibrillation. *Europace* 2021;23:494–5.

29 Linz D, Andrade JG, Arbelo E, *et al*. Longer and better lives for patients with atrial fibrillation: the 9th AFNET/EHRA consensus conference. *Europace* 2024;26:euae070.