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Research Paper

Patient-related factors associated with oral anticoagulation control: a population-based cohort study

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Abstract

Objectives Time in therapeutic range (TTR) of ≥70% is a commonly used indicator of optimal anticoagulation control. This study aimed to determine the patterns and predictors of anticoagulation control in a population-based cohort of new users of warfarin.

Methods This was a retrospective cohort study. All adults (age ≥18 years) who had been newly initiated on warfarin therapy between January 2006 and March 2011 were selected from administrative health databases. TTR was calculated using the Rosendaal method. Multivariable logistic regression models were used to identify patient-related factors associated with optimal TTR. Predictors of patients spending >30% of time above and below the therapeutic international normalised ratio (INR) range were also examined.

Key findings A total of 6032 patients were included in this study. The mean TTR was 54.1 ± 18.8%, and 82.3% of patients had subthreshold TTR (<70%). Compared with New Zealand Europeans, Māori and Pacific people had decreased odds of achieving optimal TTR and increased odds of spending >30% of time below the therapeutic INR range. Patients aged 65–74 years and 75 years or older had increased odds of achieving optimal TTR but decreased odds of spending >30% of time below the therapeutic INR range than those <65 years. Compared with those living in the least socioeconomically deprived areas, those living in the most deprived areas had decreased odds of achieving optimal TTR.

Conclusions Anticoagulation control with warfarin is suboptimal in routine care in New Zealand. Age, ethnicity and deprivation index were significant predictors of TTR. It is important to ensure equitable access to appropriate, high-quality care for those living in deprived areas and those from ethnic minority groups.

Keywords: anticoagulation control; international normalised ratio; oral anticoagulant; time in therapeutic range; warfarin

Introduction

Despite the recent emergence of new oral anticoagulants (NOACs), warfarin remains in common use, particularly among patients with mechanical heart valves and with severe liver or kidney problems. Patients who are already stabilised on warfarin are also less likely to switch to NOACs. In 2015, approximately 35 000 people were taking warfarin in New Zealand (NZ).[1] Warfarin is effective for the prevention of venous thromboembolism, systemic embolism, acute myocardial infarction, stroke or death.[2] Warfarin's long-standing history of use and availability of a well-tested reversal agent offers advantages over NOACs for certain populations.[3] In patients with poor adherence to NOACs or where close monitoring or quick

reversal of anticoagulant effect is warranted, warfarin remains the anticoagulant of choice.[4]

The safety and effectiveness of warfarin are highly dependent on maintaining international normalised ratio (INR) within a therapeutic range (INR 2.0–3.0; the INR target for patients with mechanical heart valves ranges from 2.5–3.5). This range, representing moderate-intensity warfarin treatment is the range considered effective for most indications.[5, 6] Being able to maintain warfarin within this therapeutic range is key for optimal outcomes, with a large evidence base showing that patients have an increased risk of thromboembolic events when INR levels are below 2.0,[7–10] but a much high risk of bleeding complications with INR above 3.0.[10–12] These data demonstrate the importance of maintaining INR within the 2.0–3.0 target range. One way of assessing this is to use time in therapeutic range (TTR), which describes the percentage of time in which INR is within the therapeutic range. Approximately, a TTR ≥70% is needed for good anticoagulation control,[13, 14] and several studies have reported a lower risk of mortality, haemorrhagic and thromboembolic events when TTR ≥70%.[15–17] Similarly, time spent 'out-of-range' (i.e. time above range [TAR; INR >3] and time below range [TBR; INR <2]) are markers of anticoagulant control and therefore indicators of thromboembolic and haemorrhagic events, respectively.[18]

A high TTR can be difficult to achieve due to the complex pharmacodynamic and pharmacokinetic properties of warfarin and the correspondingly narrow therapeutic range.[6] TTR can be affected by many factors, such as dietary intake of vitamin K, interacting medications[19]; comorbidities, tobacco use and obesity, which affect the metabolism of warfarin[20]; and patient non-adherence or miscommunication between the health provider and patient. Other factors that have been shown to be associated with poor anticoagulant control include being of non-White ethnicity, female sex, having paroxysmal atrial fibrillation,[21, 22] being new to warfarin[8] and having a non-standard target INR range (i.e. patients requiring a higher intensity of anticoagulation).[12] Patients who have access to special anticoagulation clinics also spend more time in range than patients managed outside of clinic settings.[8, 9] In Auckland in the last 10 years, patients on long-term warfarin have the option of being managed by community pharmacists through the Community Pharmacy Anticoagulation Management Service (CPAMS). The use of the CPAMS has been shown to be safe and effective and has resulted in significant improvements in TTR.[23]

However, there currently remain limited data on the quality of long-term warfarin anticoagulation achieved in the Auckland Region, and the factors affecting anticoagulant control. This study aimed to determine the pattern and predictors of optimal anticoagulant control (i.e. TTR ≥70%), in patients on newly initiated warfarin therapy in Auckland, NZ. Additionally, the pattern and predictors of TBR and TAR were examined.

Methods

Study design and data source

We carried out a population-based retrospective cohort study among patients on newly initiated warfarin therapy in Auckland from 1 January 2006 to 31 March 2011 using national administrative health databases in NZ. Information on warfarin prescriptions was obtained from the Pharmaceutical Collection (Pharms) database, which contains comprehensive information on all subsidised medicines dispensed from any community pharmacy in Auckland. Warfarin is fully subsidised in Auckland and available only on prescription. Some individuals may not be eligible for subsidised health care, such as people on short-term temporary work visas, and information on warfarin dispensed for this group may not be available in the Pharms database. Warfarin prescribed to hospital in-patients is also not captured by the Pharms data. However, these situations represent a very small proportion of patients on warfarin. Details of INR monitoring test results were derived from the TestSafe database (www.careconnect.co.nz/testsafe/), which is a clinical information sharing service provided by the northern region district health boards in NZ that contains laboratory and medication dispensing data. Some patients might be self-testing their INR using a home testing device, and their INR data may not be recorded in the regional laboratory database. Again, these represent only a small proportion of patients. Demographic information and death records were obtained from the National Health Index (NHI) and the National Mortality Collection (MORT) databases, respectively.[24] The study cohort was created by anonymously linking the Pharms, MORT, TestSafe and NHI databases. These databases were linked with an encrypted NHI number, a unique patient identifier that is assigned to every individual who used publicly funded health services in NZ. The study cohort included residents of Auckland, the largest city in NZ with a population of 1.5 million. The study was approved by the Health and Disability Ethics Committee (HDEC) of NZ (Ref: 12/NTA/52).

Participant selection

The study population included all patients in Auckland who newly initiated warfarin therapy for any indication between 1 January 2006 and 31 March 2011, inclusive. National medication code corresponding to warfarin (ChemID = 2331) was used to identify warfarin prescriptions in the Pharms database. We defined the date of entry into the cohort as the date on which the first prescription for warfarin was dispensed during the study period. This analysis is intended to evaluate patients on long-term warfarin therapy, thus patients with <5 INR measurements were excluded. The study cohort included new warfarin users. Patients were considered as new warfarin users if they received their first warfarin prescription after 1 January 2006 without any warfarin use in 6 months before cohort entry date.

Follow-up

All the study participants were followed from their warfarin initiation date until a 56-day gap in consecutive INR tests occurred or end of the study period (31 March 2011), whichever came first. Patients with gaps of >56 days between INR tests were censored to ensure inclusion of only patients who continually took warfarin and had no gaps between therapies.

INR values and time in the therapeutic range

INR values during the follow-up period were included in the analysis. Each person-day of warfarin therapy was characterised as being below (INR <2.0), within (INR 2–3) or above (INR >3) the target therapeutic range of INR. All available INR values were evaluated for each patient to determine their TTR using the Rosendaal method.[25] This method uses linear interpolation to assign an INR value to each day between successive observed INR values. As has been indicated above, two consecutive INR tests could not have a gap >56 days. To calculate the percentage of TBR, TTR or TAR, the therapeutic range of INR for the study population, each person's

experience was weighted according to the total time receiving warfarin therapy during the 5-year follow-up.

Study variables

The outcomes of interest were TBR, TTR and TAR during the study period. We examined the association between patient-related factors (sex, age, ethnicity and socioeconomic deprivation) and target outcomes. The New Zealand Index of Socioeconomic Deprivation 2006 version was used to determine socioeconomic position.[26]

Data analysis

Data aggregation, storage and cleaning were performed in Microsoft SQL Server, and statistical analyses were performed using SPSS version 25. The study cohort was summarised using mean (SD) and median (interquartile range [IQR]). Categorical variables were summarised using frequency and percentages.

The primary outcome measure was quality of anticoagulation control, defined as the percentage of time that INR values were within their target ranges (i.e. TTR; INR 2–3). A TTR level <70% was defined as suboptimal anticoagulation control, whereas a TTR level ≥70% was considered as optimal anticoagulation control.[13, 14] The patterns of poor anticoagulation control for all patients in the cohort were explored using two additional metrics: percentage time spent below therapeutic range (TBR; INR <2) and percentage time spent above therapeutic range (TAR; INR >3). Based on previous research, we defined cut-offs of TBR >30% and TAR >30%.[18] We used multivariable logistic regression models to test the ability of patient-related factors to predict optimal anticoagulation control (TTR ≥70%). The secondary outcomes were (1) >30% of time spent below therapeutic range (TBR >30%) and (2) >30% of time spent above therapeutic range (TAR >30%). Separate multivariable logistic regression models were used to examine the predictors of TBR >30% and TAR >30%. Statistical significance was determined using significance thresholds value of $\alpha = 0.05$ and 95% confidence intervals (CI).

Results

There were in total 25 162 incident warfarin users during the study period in Auckland. Of these, 6032 patients were included in the final analysis for this study. Patients (N = 19 130) were excluded because (i) they had <5 INR tests; (ii) their INR measurements were missing/unretrievable; or (iii) their warfarin dispensing and INR records could not be matched. Excluded patients had similar age (mean age for both cohorts is 66.6 years) and gender (57% and 58.9% of included and excluded patients were males, respectively) distribution compared with patients included in the study. However, a lower proportion of New Zealand Europeans (54.0% versus 62.6%), but higher proportions of Māori (15.3% versus 8.1%) and Pacific people (14.4% versus 6.5%) were included in this study compared with excluded cohort. Additionally, a higher proportion of included patients were living in the most deprived areas of Auckland compared with excluded patients (29.6% versus 17.4%). The main characteristics of the study participants are summarised in Table 1. The mean ± SD age of included patients was 66.7 ± 12.7 years, and 58.9% of them were males. More than half of the patients (54%) were NZ Europeans, and 29.6% were living in the most deprived areas (quintile 5) of Auckland.

On average each patient had 67.4 INR tests during the study period. The mean TTR was 54.1 ± 18.8%, and 82.3% of patients had suboptimal TTR (<70%). The average percentage of time that

Table 1 Participants characteristics according to proportion of time in therapeutic range

Variables	TTR <70%	TTR ≥70%	Total
	N (%) = 4967 (82.3)	*N* (%) = 1065 (17.7)	*N* (%) = 6032 (100)
Sex			
Female	2049 (41.3%)	429 (40.3%)	2478 (41.1%)
Male	2918 (58.7%)	635 (59.7%)	3553 (58.9%)
Missing	–	–	1 (0.02%)
Age in years			
<65	2110 (42.5%)	312 (29.3%)	2422 (40.2%)
65–74	1432 (28.8%)	335 (31.5%)	1767 (29.3%)
75 or over	1425 (28.7%)	418 (39.2%)	1843 (30.6%)
Ethnicity			
New Zealand European	2562 (51.6%)	695 (65.3%)	3257 (54.0%)
Māori	840 (16.9%)	81 (7.6%)	921 (15.3%)
Pacific people	774 (15.6%)	92 (8.6%)	866 (14.4%)
Asian	167 (3.4%)	30 (2.8%)	197 (3.3%)
Other	624 (12.6%)	166 (15.6%)	790 (13.1%)
Missing	–	–	1 (0.02%)
Socioeconomic deprivation quintile[1]			
Quintile 1 (least deprived)	765 (15.4%)	219 (20.6%)	984 (16.3%)
Quintile 2	778 (15.7%)	208 (19.5%)	986 (16.3%)
Quintile 3	968 (19.5%)	235 (22.1%)	1203 (19.9%)
Quintile 4	873 (17.6%)	193 (18.1%)	1066 (17.7%)
Quintile 5 (most deprived)	1577 (31.8%)	209 (19.6%)	1786 (29.6%)
Missing	–	–	7 (0.1%)

Abbreviation: TTR, time within the therapeutic range.

[1]Socioeconomic deprivation is measured using the New Zealand deprivation (NZDep) index 2006 version. NZDep2006 is based on nine Census variables. The NZDep2006 index ranges from 1 to 10, where 1 represents the areas with the least deprived scores and 10 the areas with the most deprived scores.

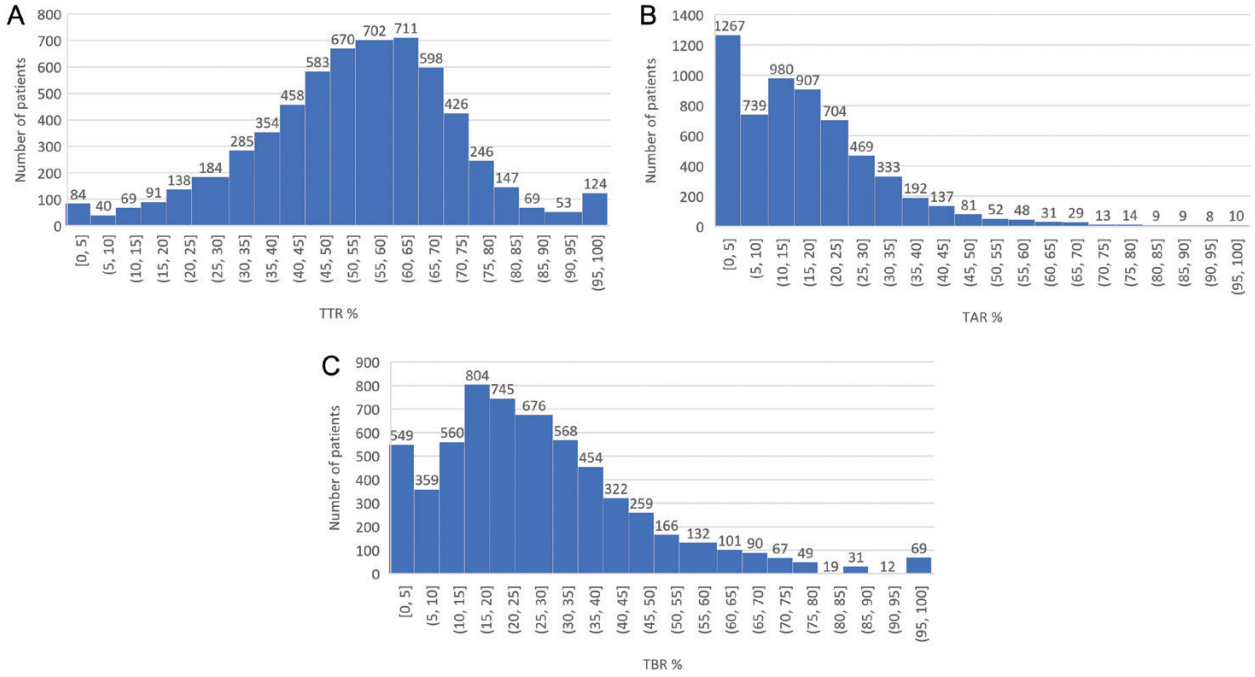

Figure 1 Time spent in the therapeutic range (TTR), time spent above therapeutic range (TAR) and time spent below therapeutic range (TBR) over the study period for patients treated with warfarin ($N = 6032$).

patients remained above (INR >3.0) and below the target INR (INR <2.0) was 17.6 ± 15.1% and 28.3 ± 19.6%, respectively. The mean and median follow-up time were 2.62 ± 1.8 and 2.5 (IQR 0.8–4.6) years, respectively. Figure 1 presents the overall percentage time spent below, within and above the therapeutic range over the study period.

Compared with the group that had optimal (TTR ≥70%), the group that had suboptimal TTR (<70%) had a higher proportion of females, younger patients (<65 years), Māori, Pacific people, Asians (includes both South and East Asians), and patients living in most deprived areas of Auckland (see Table 1). As shown in Table 2, in multivariable logistic regression analysis, compared with New Zealand Europeans, Māori (adjusted odds ratio [AOR] = 0.474; 95% CI, 0.365 to 0.615; $P < 0.001$) and Pacific people (AOR = 0.608; 95% CI, 0.471 to 0.785; $P < 0.001$) had decreased odds of achieving optimal TTR. Similarly, patients that were living in areas with deprivation quintile 5 (AOR = 0.694; 95% CI, 0.553 to 0.871; $P = 0.002$) had decreased odds of achieving optimal TTR compared with those living in the least deprived areas. Conversely, patients aged 65–74 years (AOR = 1.343; 95% CI, 1.128 to 1.599; $P = 0.001$) and 75 years or older (AOR = 1.556; 95% CI, 1.304 to 1.857; $P < 0.001$) had increased odds of achieving optimal TTR than patients aged <65 years.

As shown in Table 3, the mean TBR value was lower among 65–74 and ≥75 years age groups than those under 65 years age. Individuals of Māori, Pacific people or Asian ethnicity had higher mean TBR and TAR values than NZ Europeans. Those living in areas with greater socioeconomic deprivation had also higher mean TBR and TAR scores than those living in the least deprived areas. In multivariable logistic regression analysis (see Table 2), those aged 65–74 years (AOR = 0.734; 95% CI, 0.642 to 0.839; $P < 0.001$) and over 75 years (AOR = 0.703; 95% CI, 0.610 to 0.810; $P < 0.001$) had decreased odds of spending >30% of time below therapeutic INR range compared with those <65 years. On the other hand, Māori (AOR = 1.407; 95% CI, 1.189 to 1.666; $P < 0.001$) and Pacific people (AOR = 1.399; 95% CI, 1.174 to 1.667; $P < 0.001$) had increased odds of spending >30% of time below therapeutic INR range than New Zealand Europeans.

Discussion

In this study, only a small proportion of patients (17.7%) achieved optimal anticoagulation control with warfarin. Poor anticoagulation control was observed in younger patients (<65 years), ethnic minorities and patients living in areas with greatest socioeconomic deprivation. Although other studies have examined the quality of anticoagulation,[23, 27] to our knowledge, our study is the first to evaluate a large number of warfarin users to identify predictors of anticoagulation control in Auckland.

This study has some limitations. Other factors that may contribute to suboptimal TTR, including comorbidities, medicines concurrently taken with warfarin, adherence to warfarin therapy, dietary vitamin K intake and genetic factors[28, 29] were not evaluated. Thus, the results of our study might have been confounded by these factors. Lack of information on the indications for warfarin prescribing is the other limitation of the study. It is difficult to determine the precise indications for warfarin using information from national databases. Some patients might be taking warfarin for more than one indication. Hence, rather than analysing subgroups based on differing indications and target ranges, our analysis exploring the quality of warfarin control included all warfarin patients (regardless of indication); an INR target range (2–3) that spanned most indications was correspondingly used for analysis. We used data obtained from the time period before novel oral anticoagulants (NOAC) became available and utilisation patterns may have changed over time. This was a necessary choice in study design to avoid potential bias from NOAC prescribing and switching between NOAC and warfarin. Our study participants were also mostly male and older. It

Table 2 Multivariable logistic regression models examining the predictors of percentage time spent below, within and above therapeutic INR range (TTR) (*N* = 6025)

	TTR <70[1] versus TTR ≥70%		TAR ≤30[1] versus TAR >30%		TBR ≤30[1] versus TBR >30%	
	Adjusted odds ratio (95% CI)	*P*-value	Adjusted odds ratio (95% CI)	*P*-value	Adjusted odds ratio (95% CI)	*P*-value
Gender						
Male[1]	1		1		1	
Female	0.971 (0.845–1.116)	0.676	1.071 (0.930–1.233)	0.343	0.984 (0.882–1.099)	0.781
Age group						
Age <65 years[1]	1		1		1	
Age 65–74 years	**1.343 (1.128–1.599)**	**0.001**	0.919 (0.771–1.096)	0.349	**0.734 (0.642–0.839)**	**<0.001**
Age ≥75 years	**1.556 (1.304–1.857)**	**<0.001**	1.119 (0.934–1.339)	0.223	**0.703 (0.610–0.810)**	**<0.001**
Ethnicity						
New Zealand European[1]	1		1		1	
Māori	**0.474 (0.365–0.615)**	**<0.001**	1.180 (0.950–1.467)	0.135	**1.407 (1.189–1.666)**	**<0.001**
Pacific people	**0.608 (0.471–0.785)**	**<0.001**	1.030 (0.816–1.302)	0.802	**1.399 (1.174–1.667)**	**<0.001**
Asian	0.778 (0.518–1.167)	0.225	1.211 (0.826–1.776)	0.326	1.324 (0.977–1.796)	0.071
Other	0.977 (0.806–1.185)	0.813	0.894 (0.718–1.113)	0.316	1.072 (0.907–1.267)	0.412
Socioeconomic deprivation quintile[2]						
Quintile 1 (least deprived)[1]	1		1		1	
Quintile 2	0.940 (0.756–1.168)	0.574	1.062 (0.837–1.348)	0.619	1.040 (0.860–1.258)	0.685
Quintile 3	0.905 (0.733–1.117)	0.352	1.005 (0.799–1.264)	0.969	0.983 (0.819–1.178)	0.849
Quintile 4	0.904 (0.723–1.128)	0.371	1.007 (0.793–1.278)	0.957	1.036 (0.858–1.251)	0.716
Quintile 5 (most deprived)	**0.694 (0.553–0.871)**	**0.002**	0.870 (0.689–1.100)	0.244	1.121 (0.936–1.343)	0.215

The multivariable logistic regression models were adjusted for follow-up time

Abbreviations: INR, international normalised ratio; TAR, percentage time spent above therapeutic range; TBR, percentage time spent below therapeutic range; TTR, percentage time within the therapeutic range.

[1]Reference group.

[2]Socioeconomic deprivation is measured using the New Zealand deprivation (NZDep) index 2006 version. NZDep2006 is based on nine Census variables. The NZDep2006 index ranges from 1 to 10, where 1 represents the areas with the least deprived scores and 10 the areas with the most deprived scores.

Bold values indicate statistically significant association ($P < 0.05$).

is not known how our findings might have differed if the sample comprised more females and younger patients. We also excluded patients with <5 INR measurements and with >56 days gap between INR tests; these subgroups of patients are likely to have poor anticoagulation control. As such, we might have underestimated the prevalence of suboptimal TTR. In general, our findings are more applicable to patients who remain on warfarin for longer periods of time than those who may stop taking warfarin after shorter period or poorly adhere to warfarin therapy. As the outcome measures are not amendable to survival modelling, we used logistic regression models. Although the Rosandaal's approach used to calculate the outcome event (i.e. average TTR) considers follow-up time for individual patient, unequal follow-up time for patients in this study could affect the logistic regression model's predictive efficiency.

Despite the above limitations, population-based design, inclusion of a large number of ethnic minority patients in whom there is little published research data, and the large sample size are particular strengths of this study.

Our findings demonstrate that there is a lack of adequate anticoagulation control in warfarin users, with a mean TTR of 54.1%, and 82.3% of patients had suboptimal TTR (<70%). The low TTR results observed in this study are generally consistent with TTR results previously reported in meta-analysis of routine clinical practices in other countries.[30] In a meta-analysis of retrospective studies, a 6.9% improvement in the TTR significantly reduced major bleeding by 1 event per 100 patient-years of treatment, and an 11.9% increase in TTR reduced thromboembolic events by 1 event per 100 patient-years.[9] Thus, a large proportion of our study cohort were either at high risk of adverse events or not benefiting at all from warfarin therapy. The quality of patient care might have contributed for low TTR. Further investigations are required to understand factors related to patient care, prescribing practices and patient behaviour that might influence anticoagulation control with warfarin.

In our study, evaluation of warfarin control across age groups showed that patients within (65–74 years) and (≥75 years) age groups have better warfarin control than younger patients (<65 years), and positive association was evident between age and TTR level in multivariable logistic regression. In the literature, there have been conflicting reports on the association between age and TTR. In a US study of 124 619 veteran patients, age <55 years predicted suboptimal anticoagulation control,[22] and retrospective cohort studies in Sweden[31] and Turkey[32] found older age to be a significant predictor of suboptimal TTR. Whereas, other studies did not find any significant association between age and TTR after controlling for other factors.[33, 34] As noted by Nelson et al. 'younger patients tend to perceive themselves as healthier and thus may be less likely to adhere to warfarin therapy',[33] which may explain why young warfarin users in our study had poorer anticoagulation control. An alternative explanation is that younger patients might not have time for the frequent follow-up appointments and monitoring that is required for patients on warfarin therapy due to the demands of a full-time job and busy lifestyle.[22] Further studies with a larger sample size and diverse population are required to further establish the relationship between age and TTR.

Table 3 Mean TTR, TBR and TAR of patients taking warfarin, who had >5 INR measurements during 2006–2011

	N	TTR	TAR	TBR
		Mean (SD)	Mean (SD)	Mean (SD)
Sex				
Female	2478	54.1 (18.7)	17.7 (15.1)	28.2 (19.5)
Male	3553	54.2 (18.8)	17.5 (15.1)	28.4 (19.6)
Age in years				
<65	2422	51.3 (17.7)	18.0 (14.9)	30.7 (19.6)
65–74	1767	55.4 (18)	17.3 (14)	27.3 (18.8)
75 or over	1843	56.6 (20.3)	17.3 (16.4)	26.1 (20.1)
Ethnicity				
NZ European	3257	56.5 (18.9)	17.1 (15.9)	26.4 (19.5)
Māori	921	49.4 (16.8)	19.2 (13.2)	31.4 (18.3)
Pacific people	866	48.9 (18.3)	18.1 (13.7)	32.9 (20.6)
Asian	197	49.6 (19.4)	18.1 (16.5)	32.3 (21.4)
Other	790	56.9 (18.2)	16.9 (14.8)	26.3 (18.6)
Socioeconomic deprivation quintile[1]				
Quintile 1 (least deprived)	984	56.8 (19.1)	16.9 (16.9)	26.3 (19.4)
Quintile 2	986	55.5 (19.0)	17.8 (15.9)	26.7 (19.6)
Quintile 3	1203	55.2 (18.6)	17.5 (15.7)	27.3 (19.1)
Quintile 4	1066	54.2 (18.8)	17.5 (14.7)	28.3 (19.6)
Quintile 5 (most deprived)	1786	51.1 (18.1)	17.9 (13.4)	31.0 (19.8)
All patients	6032	54.1 (18.8)	17.6 (15.1)	28.3 (19.6)

Abbreviations: INR, international normalised ratio; NZDep2006 index, New Zealand Deprivation Index 2006 version; SD, standard deviation; TAR, percentage time spent above therapeutic range; TBR, percentage time spent below therapeutic range; TTR, percentage time within the therapeutic range.

[1]Socioeconomic deprivation is measured using the New Zealand deprivation (NZDep) index 2006 version. NZDep2006 is based on nine Census variables. The NZDep2006 index ranges from 1 to 10, where 1 represents the areas with the least deprived scores and 10 the areas with the most deprived scores.

Although ethnic minorities experience a disproportionate burden of cardiovascular disorders,[35] they were under-represented in landmark anticoagulation trials.[36–38] Therefore, racial and ethnic differences in warfarin response could not be assessed from clinical trial data. Several studies have reported suboptimal anticoagulation control among non-Caucasian patients.[22, 39–45] In our study of real-world warfarin use, Māori and Pasifika patients had poorer warfarin control than NZ Europeans (a mean TTR difference of 7.1% and 7.6%, respectively). Māori and Pasifika had also decreased odds of achieving optimal TTR (≥70%) and increased odds of spending >30% of time below or above target INR range than NZ Europeans. These findings are significant as there are limited reported data on outcomes of ethnic minorities and of indigenous populations on warfarin treatment. Ethnic disparities in response to warfarin might be impacted by other factors, including patient, healthcare and provider variables. Māori and Pacific people have a higher burden of cardiovascular risk factors, including smoking, diabetes and limited access to healthy foods.[46, 47] Moreover, cultural factors, low health literacy rates,[48] mistrust in care providers and the healthcare system,[49, 50] and low adherence to warfarin therapy[51] may perpetuate disparities in warfarin response. Multifactorial, culturally tailored interventions that target underlying causes of ethnic disparities are likely to be effective,[52] but more studies are required to explore potential solutions.

In a large US study of veteran patients, living in poorer suburbs predicted suboptimal warfarin control, with residents of the poorest suburbs having TTR 2.7% lower than the wealthiest.[22] Similarly, in our study, patients living in most socioeconomically deprived areas had worse anticoagulation control than those living in the least deprived areas. Patients with lower socioeconomic status may have poorer health literacy and poorer understanding of warfarin management.[53, 54] Hence, integrating our findings into warfarin monitoring practices may help alleviate socioeconomic-related disparities and associated poorer outcomes.

Overall, the poor TTR observed in our study demonstrates the need for better warfarin management in Auckland, NZ. As frequent INR monitoring is not needed for NOACs, these treatments could be considered as alternatives to warfarin. Disadvantaged groups receiving warfarin therapy, including those living in more deprived areas and individuals of Māori and Pacific people ethnicity, should always be given the utmost care and attention to enhance their knowledge and awareness on anticoagulation control. Besides healthcare-related factors, social factors can influence anticoagulation control among disadvantaged groups. Thus, special attention to social factors may help to address ethnic disparities in warfarin control.

Conclusions

Our study provides useful information about warfarin control in routine clinical practice. Overall, the study population had suboptimal anticoagulation control. As such, they are at higher risk for cardiovascular complications, such as bleeding, stroke, heart attack or death. We found evidence of anticoagulation disparities between NZ Europeans and ethnic minorities as well as socioeconomic groups in Auckland. These disparities suggest that developing culturally and socioeconomically appropriate strategies to improve anticoagulation management among poorer and ethnic minority patients is a critical public health importance. Our findings can guide future research and intervention strategies that aim to reduce disparities in warfarin use and outcomes.

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Author Contributions

PN and JH contributed to the study concept and design. KB took the lead in data analysis, in results interpretation, and drafting the first manuscript. PN and JH contributed to data collection and analysis. AHYC, PN, and JH contributed to writing, results interpretation, and revising the manuscript for publication. The final manuscript was read and approved by all authors.

Conflict of Interest

None declared.

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