Check for updates

Journal of the American Heart Association

ORIGINAL RESEARCH

Declining Incidence of Atrial Fibrillation–Associated Ischemic Stroke in Auckland, New Zealand (2012 Versus 2021)

Karim M. Mahawish, MBChB; Rita Krishnamurthi, PhD; Alan Davis, MBChB; Claudia Zagreanu, PhD; Irene Zeng, PhD; Harvey D. White, MBChB, DSc; Valery Feigin, PhD

BACKGROUND: Atrial fibrillation (AF) is a major cause of ischemic stroke (IS), and this risk can be substantially reduced with oral anticoagulants (OACs). Using the population-based ARCOS (Auckland Regional Community Stroke) study, we investigated the temporal trends in AF-associated IS.

METHODS: We analyzed ARCOS IV (March 2011–February 2012) and ARCOS V (September 2020–August 2021). AF-associated IS incidence was compared using Poisson exact methods. Regional OAC dispensing trends were also evaluated. Propensity score–weighted logistic regression estimated the marginal association between cohort and AF-associated IS after standardizing for vascular risk factors. Interaction tests were performed for ethnicity, and sex-specific differences were assessed using heterogeneity testing. OAC-associated intracerebral hemorrhage rates were also examined.

RESULTS: Among 1694 (ARCOS IV) and 1982 (ARCOS V) IS cases, the proportion of AF-associated IS declined from 32.4% to 21.5% (–10.8% [95% CI –13.7 to –8.0], $P<0.0001$). Crude AF-associated IS incidence fell from 49.0 to 32.7 per 100 000 population. A larger decline occurred in women (relative risk, 0.56) than men (relative risk, 0.76; $p=0.02$ for heterogeneity). Temporal reductions differed by ethnicity, with greater decline in the "Other" ethnicity categories, but not in Māori or Pacific peoples. During the same period, patients dispensed OACs increased from 1094 to 1928 per 100 000 ($P<0.001$). OAC-associated intracerebral hemorrhage increased from 2.1 to 3.6 per 100 000, equating to 11 IS cases prevented per excess intracerebral hemorrhage.

CONCLUSION: AF-associated IS incidence declined in Auckland between 2012 and 2021, during a period of substantially increased community OAC use. Persistent ethnic inequities and sex-specific variation highlight the need for improved AF detection, risk stratification, and prevention strategies.

Key Words: anticoagulants ■ atrial fibrillation ■ ischemic stroke ■ population-based study

Atrial fibrillation (AF) is a leading cause of ischemic stroke (IS) worldwide, and the burden has risen with time due to an aging population and trends in cardiovascular risk factors.[1] IS resulting from AF is associated with greater disability and death than non–AF-associated IS.[2] In one retrospective cohort study of 739 695 New Zealanders, AF was found to affect ≈1.7% of the population, signaling its substantial health burden.[3] Oral anticoagulants (OACs; eg, warfarin, dabigatran, and rivaroxaban) are the primary strategy for IS prevention, reducing the risk by approximately two-thirds compared with a 22% risk reduction with aspirin.[4] However, these drugs increase the risk of intracranial and systemic hemorrhage, necessitating

Correspondence to: Karim M. Mahawish, ARHOP, Level 2, Esme Green, Middlemore Hospital, 100 Hospital Road, Otahuhu, Auckland, 2025 New Zealand. Email: tyj9598@aut.ac.nz

This article was sent to Fadar O. Otite, MD, SM, Associate Editor, for review by expert referees, editorial decision, and final disposition.

Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.125.045260

For Sources of Funding and Disclosures, see page 9.

© 2026 The Author(s). Published on behalf of the American Heart Association, Inc., by Wiley. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

JAHA is available at: www.ahajournals.org/journal/jaha

Downloaded from http://ahajournals.org by on April 13, 2026

CLINICAL PERSPECTIVE

What Is New?

- In a population-based stroke registry spanning a decade in Auckland, New Zealand, the proportion and incidence of atrial fibrillation–associated ischemic stroke declined by approximately one-third, while regional oral anticoagulant use increased substantially.
- Propensity-weighted and sensitivity analyses confirmed that the decline was not explained by differences in patient risk profiles or causal classification, indicating a genuine population-level reduction.

What Are the Clinical Implications?

- Persistent ethnic disparities and sex-specific differences in temporal trends highlight the need for improved atrial fibrillation detection, risk stratification, and equitable prevention strategies.

Nonstandard Abbreviations and Acronyms

ARCOS	Auckland Community Stroke Study
CHA_2DS_2-VASc	congestive heart failure, hypertension, age ≥75 years, diabetes, previous stroke or transient ischemic attack, vascular disease, age 65 to 74 years, and sex category
DOAC	direct oral anticoagulant
ICH	intracerebral hemorrhage
IPW	inverse probability weighting
IRR	incidence rate ratio
IS	ischemic stroke
NMDS	National Minimum Dataset
OAC	oral anticoagulant
TOAST	Trial of Org 10172 in Acute Stroke Treatment
TTR	time in therapeutic range

careful patient selection to ensure a favorable risk–benefit balance. Direct OACs (DOACs; eg, dabigatran and rivaroxaban) for stroke prevention offer the advantage of a fixed dosing schedule, with less frequent blood monitoring compared with warfarin. Trials of DOACs versus warfarin have demonstrated at least noninferiority, with the added benefit of a 50% reduction in intracranial hemorrhage.[5] Further, real-world data demonstrate higher rates of adherence to DOACs.[6] Warfarin remains the preferred option in patients with mechanical heart valves or moderate to severe mitral stenosis.

Despite the rising prevalence of AF, international data demonstrate a decline in the rates of AF-associated IS. We previously reported international data demonstrating an annual 2% relative reduction in incident IS rates in patients with AF between 1992 and 2021, coinciding with increased OAC use.[7] The data showed little variance, indicating that the trend was independent of geographical location.

In July 2011, dabigatran became funded in New Zealand for stroke prevention in patients with AF, followed by rivaroxaban in August 2018.[8] Subsequently, the number of people taking OACs in New Zealand increased from 46 000 in 2011 to 105 000 by 2021, driven by the increased use of DOACs, while warfarin use decreased by 50%.[8]

Ethnicity is an important social determinant of health in New Zealand, with well-documented disparities in stroke incidence and outcomes. Including ethnicity in risk adjustment is critical to evaluate and address these disparities in AF-associated IS.[9] Auckland's population is ethnically diverse, comprising ≈12% Māori, 14% Pacific peoples, 37% Asian, and 38% and European or "Other" (eg, Indian and Chinese) ethnicities.[10]

The ARCOS (Auckland Regional Community Stroke) study is a 4-decade study that identifies all stroke and transient ischemic attack (TIA) events occurring during a 12-month period once every decade. It is internationally recognized as an ideal registry containing comprehensive data on patient demographics, comorbidities, and outcomes. The target population covers the well-defined geographical area of the Auckland region.[11,12] Complete case ascertainment is ensured through multiple overlapping sources of information on all new hospitalized or nonhospitalized cases (eg, private hospitals, general practice, and coroner/autopsy reports). All residents meeting the inclusion criteria are included, even if their stroke occurs outside the Auckland region, while those whose strokes or TIAs occur in Auckland but reside outside the region are excluded.

This study used data from ARCOS IV (March 1, 2011–February 29, 2012) and ARCOS V (September 1, 2020–August 31, 2021) to examine trends in AF-associated IS in Auckland, stratified by age, sex, and ethnicity. We also determined rates of OAC-associated intracerebral hemorrhage (ICH) in patients with AF. Population estimates for Auckland, 1 119 192 (ARCOS IV) and 1 346 900 (ARCOS V), were applied, as previously reported.[11]

METHODS

This study has been approved by the Health and Disability ethics committee (reference: 2023 AM 9094)

Downloaded from http://ahajournals.org by on April 13, 2026

and the Auckland University of Technology ethics committee (24/4) and granted an exemption from obtaining informed consent. Anonymized data from this study will be made available from the corresponding author on reasonable request and subject to institutional and ethical approval. All methods used in the analysis are described in the article.

We included data from ARCOS IV and ARCOS V of patients with IS and ICH. We collected data on demographics, including prioritized self-identified ethnicity (ie, Māori, Pacific peoples, "Other," eg, Indian and Chinese, and European). Comorbidities (including AF and stroke subtype) and antithrombotic medication were extracted from the ARCOS data set for this study. The interval between AF diagnosis and incident IS was not available for all patients. "AF-associated IS" was defined pragmatically as any incident stroke occurring in a patient with a documented diagnosis of AF before or during the index stroke admission, regardless of presumed mechanism. This approach aligns with prior ARCOS analyses and enables direct comparison between ARCOS IV and ARCOS V. All suspected strokes were adjudicated by stroke physicians in the ARCOS Stroke Adjudication Committee, using standardized criteria to confirm stroke diagnosis and clinical subtype where possible, as per the methods detailed in the ARCOS V paper.[11] For context, we also obtained data from the Ministry of Health's National Minimum Dataset (NMDS) on the number of Auckland patients hospitalized with AF in 2011 and 2020, as well as data from the Pharmaceutical Collection on the number of patients dispensed at least three anticoagulant prescriptions during each respective calendar year.

DOAC adherence was measured using the proportion of days covered and, for warfarin users, time in therapeutic range (TTR). The proportion of days covered was calculated by dividing the total days covered by medication within a given timeframe by the number of days in that timeframe; a proportion of days covered rate of ≥80% is considered good adherence.[13] TTR represents the proportion of international normalized ratio values within the therapeutic range, using Rosendaal linear interpolation method. This method estimates the time spent within the target international normalized ratio range by interpolating between observed values.[5,14] According to European Society of Cardiology guidelines, ≥70% defines good TTR.[5]

Outcomes

The primary outcome was the incidence of AF-associated IS, comparing the ARCOS IV and ARCOS V cohorts. Secondary outcomes included the incidence of OAC-associated ICH in patients with AF and the ethnic-specific adjusted odds of AF-associated IS.

Statistical Analysis

Continuous variables are summarized as means (SDs) for normally distributed data and as medians (interquartile ranges [IQRs]) for nonnormal data, and compared using *t* test or Wilcoxon rank sum tests, respectively. Categorical variables are displayed as frequencies (percentages) and differences between cohorts were compared using χ^2 or Fisher exact tests as appropriate.

Logistic regression was used to assess associations between cohort (ARCOS IV versus ARCOS V) and AF-associated IS, adjusting for age, sex, ethnicity, and comorbidities (congestive heart failure, hypertension, age, diabetes, previous IS or TIA, and vascular disease). The linearity assumption for age was evaluated with both the Box-Tidwell approach and graphical assessment of the relationship between age and the logit of the outcome (lowess-smoothed plot). Model assumptions were assessed by examining residual plots, influential observations, and variance inflation factors (<2). Prestroke OAC use was excluded because it was collinear with cohort and lies on the causal pathway, making it inappropriate for adjustment in these models. Since each cohort represented a complete 1-year ascertainment period, time to event adjustment was unnecessary.

In addition, we conducted a post hoc analysis to estimate the association between cohort period (ARCOS V versus ARCOS IV) and AF-associated IS. Patients in ARCOS V had a lower overall vascular risk profile compared with patients in ARCOS IV, which may confound the association between cohort and AF-associated IS. Hence, we applied inverse probability weighting (IPW) using propensity scores derived from age, sex, and vascular risk factors (cardiac failure, hypertension, diabetes, previous IS/TIA, vascular disease) to balance baseline vascular risk between cohorts. Weighted logistic regression model was then applied to estimate the association between cohort period (ARCOS IV versus ARCOS V) and AF-associated IS. The resultant odds ratio (OR) represents the marginal association (the population-average effect on the outcome), between cohort period and AF-associated IS after standardizing for baseline vascular risk factors. Because OAC use was not modeled as an exposure, the analysis does not quantify the effect of anticoagulation, and causal inference regarding the contribution of OAC to the temporal decline is not possible.

To assess ethnic differences while accounting for differences in baseline vascular risk, IPW were constructed using a multinomial logistic regression with ethnicity as the dependent variable and the CHA_2DS_2-VASc covariates (age, sex, and comorbidities) as predictors following standard methods.[15] Stabilized weights were calculated as the overall proportion of

Downloaded from http://ahajournals.org by on April 13, 2026

each ethnic group divided by its predicted probability from the model. Weighted logistic regression was then used to estimate marginal (population-average) associations between ethnicity and AF-associated IS. Covariate balance among ethnic groups was assessed using IPW means and standardized mean differences.

Given the observed sex difference in the reduction of AF-associated IS, we conducted a post hoc population-level analysis comparing incidence ratios between men and women among ARCOS IV and ARCOS V. Using sex-specific numerator and denominator data, we calculated incidence ratios for each sex and formally tested for heterogeneity in the magnitude of decline. This analysis quantifies sex-specific differences in population incidence trends but cannot address individual-level causal mechanisms.

To account for the possibility that patients with AF may experience stroke from competing mechanisms, we conducted a sensitivity analysis restricted to cardioembolic and AF-associated IS using the ARCOS data sets and Auckland population data. We examined the proportion of all IS classified as cardioembolic according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification, a standardized system for categorizing ischemic stroke subtypes based on presumed cause (eg, large-artery atherosclerosis, cardioembolism, small-vessel occlusion, other determined, or undetermined causes).[16] We also determined the proportion of AF-associated IS cases adjudicated as cardioembolic. This allowed us to assess whether temporal trends were influenced by changes in causal classification.

We calculated crude incidence per 100 000 population for each 12-month period and derived exact Poisson 95% CIs using standard methods for small event counts; cohort differences were compared using incidence rate ratios (IRRs).[17] Proportions within the stroke case series (eg, the percentage of all cases classified as cardioembolic) are presented descriptively.

We assessed the distribution of baseline CHA_2DS_2-VASc scores among patients with AF-associated IS in ARCOS IV and ARCOS V to examine potential differences among ethnic groups. Scores were calculated using standard criteria, assigning 1 point for age 65 to 74 years and 2 points for age ≥75 years.[18] Ethnicity was included as a covariate in our risk-adjustment models to account for its role as a social determinant of health, reflecting disparities in access to care, diagnosis, and management of comorbidities that may contribute to stroke risk in AF. To explore the impact of earlier vascular risk onset in Māori and Pacific populations, we also recalculated CHA_2DS_2-VASc scores using a modified age threshold, assigning 1 point for age 55 to 74 years, while retaining 2 points for age ≥75 years. Distributions of standard and modified scores were compared among ethnic groups using histograms and distribution plots to assess whether the modified age threshold aligned score distributions reflective of the risk of AF-associated IS.

This study used data routinely collected as part of clinical care, with minimal missing values. A complete case analysis approach was used. All statistical analyses were performed using Stata BE version 17 (StataCorp). A 2-sided *P* value <0.05 was considered statistically significant.

The study was conducted and reported in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.[19]

RESULTS

Study Population

We identified 1694 and 1982 patients with IS in ARCOS IV and ARCOS V, respectively, including 548 and 427 AF-associated IS cases. A flow diagram of study participants is presented in Figure 1.

The median age in of patients with AF-associated IS remained static (*P*=0.82). The proportion of AF-associated IS declined between the 2 cohorts: 32.4% to 21.5% (–10.8% [95% CI, –13.7 to –8.0], *P*<0.0001). There was no significant difference between ethnic groups in the 2 cohorts (*P*=0.11). Data on patients with AF are summarized in Table 1.

Predictors of AF-Associated IS

In univariate analyses (Table 2), older age, female sex, cardiac failure, hypertension, prior IS or TIA, and vascular disease were associated with increased odds of AF-associated IS within the stroke cohort. Model diagnostics supported the adequacy of the logistic model: the Box-Tidwell test showed no violation of the linearity assumption for age (*P*=0.56), and a lowess plot confirmed an approximately linear relationship with the logit. No evidence of multicollinearity was detected (mean VIF, 1.07; all <1.5). Pearson residuals were symmetrically distributed, leverage values were uniformly low (<0.01), and no influential observations were identified, indicating good model fit.

In multivariable analyses adjusting for age, sex, ethnicity, and comorbidities, older age remained significantly associated with higher odds of AF-associated IS (adjusted OR [aOR], 1.05 per year [95% CI 1.04–1.06], *P*<0.001). The association with female sex was attenuated and no longer significant (aOR, 1.06 [95% CI, 0.91–1.25], *P*=0.46). Compared with Europeans, Māori and Pacific peoples had significantly higher adjusted odds (aOR 2.07 [95% CI 1.52–2.84], *P*<0.001; and aOR, 1.68 [95% CI, 1.29–2.18], *P*<0.001, respectively), while the "Other" ethnic group remained lower (aOR, 0.54 [95% CI, 0.42–0.7], *P*<0.001). The reversal of direction for Māori and Pacific peoples between the unadjusted and adjusted models likely reflects

Downloaded from http://ahajournals.org by on April 13, 2026

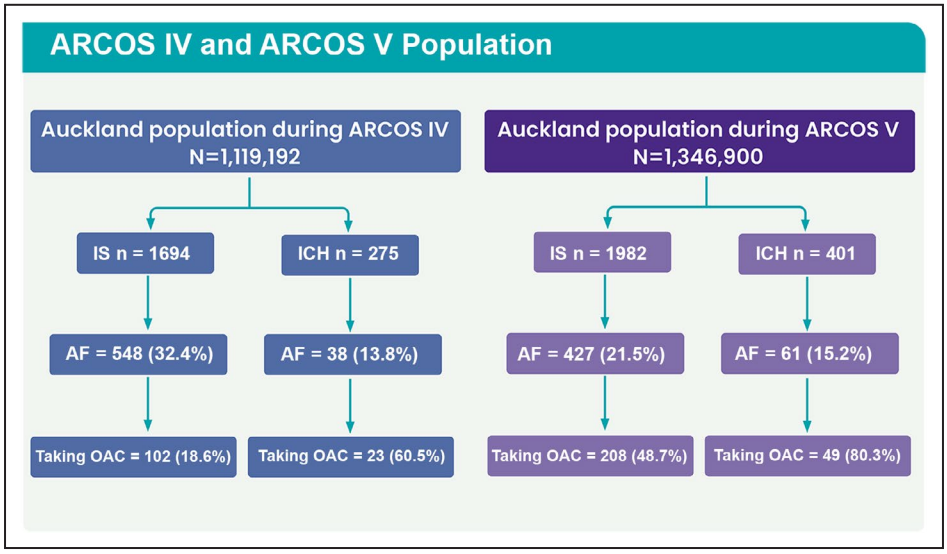

Figure 1. Flow diagram of study participants in ARCOS IV and ARCOS V.
AF indicates atrial fibrillation; ARCOS, Auckland Regional Community Stroke; and OAC, oral anticoagulant.

differences in baseline vascular risk, as well as unmeasured confounders that contribute to the ethnic disparities described above. Cardiac failure and vascular disease remained significant predictors in the adjusted models (aOR, 2.6 [95% CI, 2.13–3.33], *P*<0.001; and aOR, 1.26 [95% CI, 1.06–1.15], *P*<0.001, respectively). Hypertension,

Table 1. Baseline Characteristics of Patients With AF in ARCOS IV and ARCOS V

Variable	ARCOS IV (n=1694)	ARCOS V (n=1982)	Mean change (95% CI), *P* value
AF, n (%)	548 (32.4)	427 (21.5)	−10.8% (−13.7 to −8.0), *P*<0.0001
Women	313 (37.1)	206 (22.1)	−15.1% (−19.3 to −10.9), *P*<0.0001
Men	235 (27.6)	221 (21.1)	−6.5% (−10.4 to −2.6), *P*<0.001
Ethnic group, n (%)			*P*=0.11
European	402 (73.4)	294 (68.9)	
Māori	34 (6.2)	44 (10.3)	
Pacific peoples	65 (11.9)	55 (12.9)	
"Other" (eg, Chinese and Indian)	47 (8.6)	34 (8.0)	
Age, median (IQR), y	80 (71–86)	80 (70–87)	*P*=0.82
Comorbidities, n (%)			
Cardiac failure	137 (25.0)	37 (8.7)	*P*<0.001
Hypertension	390 (71.2)	252 (59.0)	*P*<0.001
Diabetes	120 (21.9)	107 (25.1)	*P*=0.25
Previous IS/TIA	202 (36.9)	122 (28.6)	*P*=0.0064
Vascular disease (eg, heart/peripheral arterial disease)	194 (35.4)	130 (30.4)	*P*=0.1
CHA_2DS_2-VASc, mean (SD)	4.4 (1.8)	3.8 (1.7)	*P*<0.0001
Prestroke OAC, n (%)	102 (18.6)	208 (48.7)	30.1% (24.4–35.9), *P*<0.0001
Women	54 (17.3)	95 (46.1)	28.9% (20.8–36.9), *P*<0.0001
Men	48 (20.4)	113 (51.1)	30.7% (22.3–39.1), *P*<0.0001
Antiplatelet use, n (%)	293 (53.5)	96 (22.5)	−31.0% (−36.7 to −25.2), *P*<0.0001
Good OAC control, n (%)	36/91 (39.6)	73/105 (69.5)	30.0% (16.6–43.3), *P*<0.0001

Good OAC control is defined as the proportion of days covered ≥80% for those taking DOACs or time in therapeutic range ≥70% for those taking warfarin. AF indicates atrial fibrillation; ARCOS, Auckland Regional Community Stroke; CHA_2DS_2-VASc, congestive heart failure, hypertension, age ≥75 years, diabetes, previous stroke or transient ischemic attack, vascular disease, age 65 to 74 years, and sex category; IQR, interquartile range; OAC, oral anticoagulant; IS, ischemic stroke; and TIA, transient ischemic attack.

Downloaded from http://ahajournals.org by on April 13, 2026

Table 2. Univariate and Multivariable Logistic Regression Analyses of Predictors of AF-Associated IS

Covariate	Crude OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value
ARCOS V (logistic regression)	0.57 (0.50–0.67)	<0.001	0.63 (0.54–0.74)	<0.001
ARCOS V (IPW)	As above	…	0.66 (0.56–0.77)	<0.001
Ethnic group (logistic regression)				
Europeans	(ref)		(reference)	
Māori	0.97 (0.74–1.28)	0.84	2.07 (1.52–2.84)	<0.001
Pacific	0.85 (0.68–1.06)	0.15	1.68 (1.29–2.18)	<0.001
"Other"	0.4 (0.32–0.51)	<0.001	0.54 (0.42–0.70)	<0.001
Ethnic group (IPW)	As above	…		
Europeans			(reference)	…
Māori			1.52 (1.08–2.14)	0.017
Pacific			1.31 (0.96–1.80)	0.09
"Other"			0.53 (0.32–0.68)	<0.001
Age	1.05 (1.04–1.05)	<0.001	1.05 (1.04–1.06)	<0.001
Women	1.31 (1.13–1.51)	<0.001	1.06 (0.91–1.25)	0.46
Comorbidities				
Cardiac failure	3.62 (2.87–4.56)	<0.001	2.6 (2.03–3.33)	<0.001
Hypertension	1.22 (1.05–1.42)	0.011	0.92 (0.79–1.09)	0.35
Diabetes	0.82 (0.69–0.97)	0.019	0.87 (0.72–1.05)	0.15
Previous IS/TIA	1.43 (1.22–1.68)	<0.001	1.12 (0.95–1.34)	0.17
Vascular disease (eg, ischemic heart/ peripheral arterial disease)	1.74 (1.48–2.04)	<0.001	1.26 (1.06–1.50)	<0.001
Prestroke OAC use in AF	15.8 (12.3–20.4)	<0.001	…	…
Antiplatelet use	0.98 (0.85–1.14)	0.82	…	…

Multivariable model adjusted for age, sex, ethnicity, cardiac failure, hypertension, diabetes, prior IS/TIA, and vascular disease. Prestroke OAC use was excluded from the adjusted model due to collinearity and causal pathway considerations. AF indicates atrial fibrillation; ARCOS, Auckland Regional Community Stroke; IPW, inverse probability weighting; IS, ischemic stroke; OAC, oral anticoagulant; and TIA, transient ischemic attack.

diabetes, and prior IS or TIA were not significantly associated with AF-associated IS after adjustment. Detailed findings are presented in Table 2.

Importantly, the 2020 to 2021 cohort (ARCOS V) was associated with a significantly lower risk of AF-associated IS compared with the 2011 to 2012 cohort, independent of age, sex, ethnicity, and vascular risk factors (aOR, 0.63 [95% CI, 0.54–0.74], *P*<0.001).

IPW Analysis

The unadjusted OR for AF-associated IS in ARCOS V versus ARCOS IV was 0.57 (95% CI, 0.5–0.67; *P*<0.001). In the IPW analysis, the distribution of stabilized weights was well-behaved (range, 0.29–2.27; mean, 1.20 [SD, 0.99]), suggesting minimal influence from extreme weights; therefore, no trimming was required. After propensity score weighting, baseline characteristics were well balanced between the 2 cohorts (Table S1). All standardized mean differences were <10%, and variance ratios for continuous variables were close to 1, indicating effective minimization of confounding.

The IPW analysis, the weighted odds of AF-associated IS remained significantly lower in ARCOS V compared with ARCOS IV (OR, 0.66 [95% CI, 0.56–0.77], *P*<0.001). The attenuation of the effect after weighting (OR from 0.57 to 0.66) suggests that part of the observed reduction in AF-associated IS was attributable to lower baseline vascular risk in ARCOS V. Since OAC use was not included as an exposure in the weighting model, this analysis does not quantify the impact of anticoagulation on AF-associated IS and cannot be used to draw causal conclusions.

IPW analysis was used to estimate the marginal (population-average) association between ethnicity and AF-associated IS, standardizing for age, sex, and vascular comorbidities. After weighting, the associations were attenuated but remained elevated for Māori (OR, 1.52 [95% CI, 1.08–2.14]), and borderline for Pacific peoples (OR, 1.31 [95% CI, 0.96–1.79]), while the "Other" group showed lower odds (OR, 0.53 [95% CI, 0.41–0.69]) compared with Europeans (Table 2, Figure S1). The stabilized weight distribution was well-behaved (mean±SD, 1.00±0.61; range, 0.19–7.46), indicating good model performance and overlap among ethnic groups, with no trimming required.

Downloaded from http://ahajournals.org by on April 13, 2026

Sensitivity Analysis: Role of Cardioembolism

We found no significant differences in the proportions of all patients with IS attributed to cardioembolism among ARCOS IV and ARCOS V. The proportions of AF-associated IS cases adjudicated as cardioembolic were also similar between cohorts (72.4% versus 72.3%; OR, 1.0 [95% CI, 0.92–1.08], *P*=0.97), indicating no change in the relative contribution of cardioembolism among patients with AF-associated IS. However, because the overall number of AF-associated IS cases declined, the population incidence of cardioembolic AF-associated IS also fell significantly (IRR, 0.65 [95% CI, 0.56–0.75], *P*<0.0001). Data are summarized in Table 3.

Anticoagulant Medication

Warfarin was the only anticoagulant used in the ARCOS IV cohort. TTR was available for 91 patients in ARCOS IV for the 6 months prior and was 61.1% (SD, 20.4). Only 36 (39.6%) had good control (ie, TTR ≥70%).

A total of 166 patients with AF from ARCOS V were randomly selected for subgroup analysis of OAC adherence. Of these, 105 (63.3%) were taking an OAC; dabigatran 64 (61%), rivaroxaban 22 (21%), warfarin 19 (18%). Although apixaban is available in New Zealand, it is not publicly funded. Of patients with AF taking warfarin in ARCOS V, 6 (31.6%) patients had good control, a similar proportion to the ARCOS IV cohort (*P*=0.61), while 67 of 86 (77.9%) of patients taking a DOAC had good control (ie, proportion of days covered ≥80%) in the months before IS. In ARCOS V, use of DOACs was associated with a 2.5-fold higher likelihood of achieving good control than warfarin (relative risk [RR], 2.47 [95% CI, 1.26–4.83], *P*=0.0001).

Sex- and Ethnic-Specific Differences With Anticoagulant Use

Using sex-specific population denominators for each cohort, women showed a larger decline in AF-associated IS incidence between ARCOS IV and ARCOS V (RR, 0.56) than men (RR, 0.76). A formal heterogeneity test confirmed that the magnitude of reduction differed significantly by sex (*P*=0.02).

The higher likelihood (odds) of AF-associated stroke in Māori and Pacific peoples, despite similar anticoagulation rates (Figure S2), suggests that current risk stratification tools may underestimate stroke risk in these populations. To assess whether temporal trends differed by ethnicity, we performed a subgroup analysis testing for interaction between the ARCOS cohort and ethnicity on AF-associated IS. No significant interaction was observed for Māori or Pacific peoples. In the "Other" ethnicity group, however, the reduction in AF-associated IS between cohorts was greater (OR, 0.55 [95% CI, 0.34–0.92], *P*=0.02), indicating heterogeneity in temporal trends among ethnic groups.

In AF-associated IS, European patients exhibited an approximately normal distribution of CHA_2DS_2-VASc scores using standard criteria, with scores spanning the full range (Figure S3A). In contrast, Māori and Pacific patients demonstrated skewed distributions with clustering at lower scores, reflecting younger age at stroke despite the presence of other vascular risk factors. When applying the modified age threshold of 55 to 74 years, the distributions of CHA_2DS_2-VASc scores in Māori and Pacific patients shifted toward a more normal distribution, aligning more closely with the European pattern (Figure S3B).

Population-Level Trends

Auckland data from the Ministry of Health's NMDS and Pharmaceutical Collection demonstrate a relative reduction in the incidence of AF hospitalizations per 100 000 population between 2011 and 2020 (IRR, 0.95 [95% CI, 0.92–0.98], *P*=0.002), despite an increase in absolute admissions from 6528 to 7454 due to population growth. During the same period, community dispensing data show that the number of patients receiving anticoagulants increased from 12 238 to 25 967, a 76% increase (IRR, 1.76 [95% CI, 1.73–1.80] *P*<0.001).

Table 3. Sensitivity Analysis of the Role of Cardioembolism as the Mechanism of IS

Variable	ARCOS IV, n=1694	ARCOS V, n=1982	Proportion ratio (95% CI, *P* value)	ARCOS IV Incidence/100 000 (95% CI)	ARCOS V Incidence/100 000 (95% CI)	IRR (95% CI, *P* value)
TOAST criteria: Cardioembolism	500 (27.4%)	544 (25.5%)	0.93 (0.84–1.03) *P*=0.17	44.7 (40.8–48.6)	40.4 (37.0–43.8)	0.90 (0.80–1.02) *P*=0.11
AF-associated IS	548 (32.4%)	427 (21.5%)	0.67 (0.60–0.74) *P*<0.0001	49.0 (44.9–53.1)	31.7 (28.7–34.7)	0.65 (0.57–0.73) *P*<0.0001
AF-associated IS: TOAST criteria - cardioembolism	396/548 (72.4%)	309/427 (72.3%)	1.0 (0.92–1.08) *P*=0.97	35.4 (31.9–38.9)	22.9 (20.4–25.5)	0.65 (0.56–0.75) *P*<0.0001

Incidence calculated per 100 000 population for each 12-month cohort and IRR estimated by Poisson regression. TOAST classification: a standardized system for categorizing ischemic stroke subtypes taken from the Trial of Org 10172 in Acute stroke Treatment. AF indicates atrial fibrillation; ARCOS, Auckland Regional Community Stroke; IRR, incidence rate ratio; IS, ischemic stroke; and TOAST, Trial of Org 10172 in Acute Stroke Treatment.

Downloaded from http://ahajournals.org by on April 13, 2026

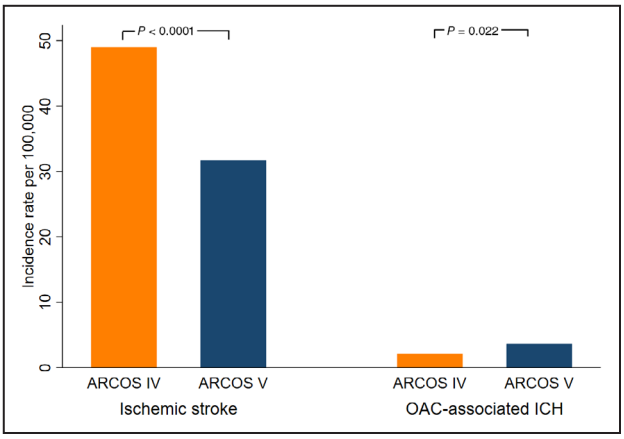

Figure 2. Population-level change in IS and OAC-associated ICH incidence among patients with atrial fibrillation.
ARCOS indicates Auckland Regional Community Stroke; ICH, intracerebral hemorrhage; IS, ischemic stroke; and OAC, oral anticoagulant.

Using Auckland population estimates, the crude incidence of IS remained stable between the 2 periods, 147 per 100 000 and 151 per 100 000, in ARCOS V and ARCOS IV, respectively (IRR, 1.03 [95% CI, 0.81–1.3], *P*=0.34), while AF-associated IS fell from 49.0 to 31.7 per 100 000 (IRR, 0.65 [95% CI, 0.57–0.73], *P*<0.0001). Among patients with AF receiving OACs, we identified 23 incident ICH cases in ARCOS IV and 49 in ARCOS V. Thus, at the population level, in OAC-treated patients with AF, ICH rose from 2.1 to 3.6 per 100 000 (IRR, 1.77 [95% CI, 1.09–2.91], *P*=0.022), with a net 11 IS cases prevented per excess hemorrhage (Figure 2). Among patients with ICH and AF treated with OACs, patients taking warfarin had significantly higher odds of ICH compared with those taking DOACs (OR, 2.11 [95% CI, 1.10–4.06], *P*<0.05).

DISCUSSION

Between ARCOS IV and ARCOS V, AF-associated IS declined markedly at the population level. Propensity score weighting showed that this reduction was not attributable to differences in age, sex, or comorbidity burden, as weighted and adjusted estimates remained highly consistent. The decline occurred alongside a substantial increase in OAC use regionally, and although causality cannot be established, the pattern is consistent with extensive evidence supporting anticoagulation for AF-related stroke prevention. Notably, the modest rise in OAC-associated ICH was greatly outweighed by the reduction in AF-associated and cardioembolic IS.

The observed greater stroke risk reduction in women may reflect higher baseline risk of AF-associated IS, resulting in a greater absolute benefit from OAC therapy. Biological differences in thromboembolic susceptibility, recent trends in reduced overall vascular risk, and residual confounding may also contribute. These findings align with prior evidence supporting sex-specific variation in AF-related stroke risk and treatment response.[20,21]

Other findings in this study included the lower ICH risk with DOACs compared with warfarin. While this study reassuringly provides evidence of increased application of guideline-directed antithrombotic therapy for AF, it also identifies that more than half of people who have known AF and subsequent IS are not receiving OACs before their stroke event. This suggests there is room for further gain.

Although OAC use increased similarly among all ethnic groups between ARCOS IV and ARCOS V, Māori and Pacific peoples continued to have higher adjusted odds of AF-associated IS after accounting for age, sex, and comorbidities, suggesting that factors beyond anticoagulation contribute to persistent inequities. We acknowledge that ethnicity is a social construct and, to our knowledge, no ethnicity-based biological mechanisms explain the increased risk of stroke in AF. However, ethnic differences in outcomes and treatment disparities in New Zealand stem from health inequities in healthcare delivery and are critical social determinants of health, with comorbidities such as heart failure, diabetes, and hypertension potentially being undetected for longer or suboptimally managed. The significant interaction in the "Other" ethnicity group, but not for Māori and Pacific peoples, supports this interpretation, but should be interpreted cautiously due to small group size and potential instability of the estimates.

We also found that Māori and Pacific patients with AF-associated IS tend to have lower CHA_2DS_2-VASc scores driven by younger age at presentation. Reclassifying age ≥55 years as meeting age criterion resulted in a more uniform score distribution among ethnic groups. These findings are consistent with findings in a Taiwanese cohort, where lowering the CHA_2DS_2-VASc age threshold to ≥50 years led to an improved risk classification and was associated with a 30% reduction in IS risk.[22] Although this stroke-only cohort cannot evaluate CHA_2DS_2-VASc predictive performance, these observations support the hypothesis that the score may underestimate stroke risk in younger high-risk Māori and Pacific patients. Local recalibration or ethnic-specific adaptation of existing risk scores may improve stratification and reduce inequities in AF-related stroke prevention.

Strengths of this study include the use of a large, ethnically diverse, population-based stroke registry with rigorous case ascertainment, enabling accurate assessment of AF-associated stroke trends over time.

Downloaded from http://ahajournals.org by on April 13, 2026

We applied IPW to adjust for vascular risk factor differences between cohorts, enhancing internal validity. We also examined temporal trends in OAC prescribing in parallel with changes in AF-associated and cardioembolic stroke incidence, providing population-level context for the observed decline without implying causal effects.

A major limitation of this study is its observational, post hoc design, which may result in inaccurate estimates due to unmeasured or unknown confounders, despite propensity weighting. These factors limit the ability to establish causality. In addition, the absence of a stroke-free AF cohort precluded estimation of absolute stroke risks and numbers needed to treat with OAC. The classification of AF-associated IS relied on clinical adjudication and available documentation, introducing potential misclassification bias. In New Zealand, individuals may identify with multiple ethnicities. For this analysis, we used the convention of prioritized ethnicity to align with national data reporting; however, this approach may mask multiethnic identities. Finally, the generalizability of our findings may be limited to the New Zealand/Auckland context, necessitating validation in other regions to assess broader applicability. Nonetheless, integrating population-level stroke trends with contemporaneous prescribing patterns offers valuable epidemiological insight into how anticoagulation practices and AF-related stroke burden have evolved over time.

CONCLUSIONS

AF-associated IS incidence in Auckland declined between the 2 periods, coinciding with increased OAC use at the population level. Persistent ethnic disparities in AF-associated IS risk underscore the need for tailored AF detection, risk stratification, and management to achieve equity. Future work linking individual-level AF prevalence, comorbidities, and anticoagulation data will be essential to determine the drivers of temporal change and to identify opportunities for targeted prevention, particularly among Māori and Pacific peoples.

ARTICLE INFORMATION

Received July 21, 2025; accepted January 6, 2026.

Affiliations

Stroke Department, Adult Rehabilitation & Health of Older People (ARHOP), Health New Zealand - Te Whatu Ora Counties Health, Auckland, New Zealand (K.M.M.); National Institute for Stroke and Applied Neurosciences, School of Community and Public Health, Auckland University of Technology, Auckland, New Zealand (K.M.M., R.K., V.F.); National Stroke Network, Te Whatu Ora, New Zealand (A.D.); Department of Oral Health, Faculty of Health and Environmental Sciences (C.Z.) and Biostatistics, School of Nursing, Clinical Sciences Management, Auckland University of Technology, Auckland, New Zealand (I.Z.) and Health New Zealand - Te Whatu Ora, Te Toka Tumai, Green Lane Cardiovascular Service, Auckland City Hospital, Auckland, New Zealand (H.D.W.).

Acknowledgments

Author contributions: KMM designed the study and drafted this manuscript. VF, HW, IZ, AD, and RK reviewed the manuscript and provided valuable insights. CZ provided ARCOS IV data and reviewed the manuscript. RK assisted with obtaining approvals for this study. Everyone listed has agreed to authorship. Chat-GPT was used only to assist with language editing and did not influence study design, analysis, interpretation or conclusions.

Sources of Funding

This work was supported by the Health Research Council, New Zealand. The funder had no role in the design, data collection, data analysis, and reporting of this study (HRC grant number 20-680).

Disclosures

KMM received a Health Research Council of New Zealand grant as part of his doctoral studies for this research. The other authors did not receive any financial support for the research, authorship, and/or publication of this article. HDW reports grant support paid to the institution and fees for serving on Steering Committees of the ODYSSEY (Evaluation of Cardiovascular Outcomes After an Acute Coronary Syndrome During Treatment With Alirocumab) trial from Sanofi and Regeneron Pharmaceuticals, the ISCHAEMIA (International Study of Comparative Health Effectiveness With Medical and Invasive Approaches) and MINT (Myocardial Ischemia and Transfusion) study from the National Institutes of Health, the Librexia and AF and ACS studies from Janssen Research and Development LLC and the MK0616 Study from Merck Sharp & Dolme Ltd. Funding Sources.

Supplemental Material

Table S1
Figures S1–S3

REFERENCES

1. Lippi G, Sanchis-Gomar F, Cervellin G. Global epidemiology of atrial fibrillation: an increasing epidemic and public health challenge. *Int J Stroke*. 2021;16:217–221. doi: 10.1177/1747493019897870
2. Goulart AC, Olmos RD, Santos IS, Tunes G, Alencar AP, Thomas N, Lip GY, Lotufo PA, Benseñor IM. The impact of atrial fibrillation and long-term oral anticoagulant use on all-cause and cardiovascular mortality: a 12-year evaluation of the prospective Brazilian study of stroke mortality and morbidity. *Int J Stroke*. 2022;17:48–58. doi: 10.1177/1747493021995592
3. Tomlin AM, Lloyd HS, Tilyard MW. Atrial fibrillation in New Zealand primary care: prevalence, risk factors for stroke and the management of thromboembolic risk. *Eur J Prev Cardiol*. 2017;24:311–319. doi: 10.1177/2047487316674830
4. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. *Ann Intern Med*. 2007;146:857–867. doi: 10.7326/0003-4819-146-12-200706190-00007
5. van Gelder IC, Rienstra M, Bunting KV, Casado-Arroyo R, Caso V, Crijns HJGM, 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;45:3314–3414. doi: 10.1093/eurheartj/ehae176
6. Deitelzweig S, Di Fusco M, Kang A, Savone M, Mokgokong R, Keshishian A, et al. Real-world persistence to direct oral anticoagulants in patients with atrial fibrillation: a systematic review and network meta-analysis. *Curr Med Res Opin*. 2021;37:891–902. doi: 10.1080/03007995.2021.1897555
7. Mahawish KM, Zeng I, White H, Feigin V, Krishnamurthi R. Methods article for a study protocol: refining stroke prediction in atrial fibrillation patients in an ethnically diverse population—a study protocol. *Neuroepidemiology*. 2025;5:1–19. doi: 10.1159/000546212
8. Harper P, Chang A, Stephens M. The changing use of anticoagulants in New Zealand. *N Z Med J*. 2022;135:35–43.
9. Mahawish K, White H, Feigin V, Krishnamurthi R. Refining predictive risk models for stroke in atrial fibrillation: a scoping review and meta-analysis for Aotearoa New Zealand, Māori and Pacific peoples. *N Z Med J*. 2025;138:102–113. doi: 10.26635/6965.6846

Downloaded from http://ahajournals.org by on April 13, 2026

10. Stats NZ. *Census Population Counts (by Ethnic Group, Age, and Māori Descent) and Dwelling Counts*. 2023. https://www.stats.govt.nz/information-releases/2023-census-population-counts-by-ethnic-group-age-and-maori-descent-and-dwelling-counts/.
11. Feigin VL, Krishnamurthi R, Nair B, Rautalin I, Parag V, Anderson CS, Arroll B, Barber PA, Barker-Collo S, Bennett D, et al. Trends in stroke incidence, death, and disability outcomes in a multi-ethnic population: Auckland regional community stroke studies (1981–2022). *Lancet Reg Health - West Pac*. 2025;56:101508. doi: 10.1016/j.lanwpc.2025.101508
12. Feigin VL, Krishnamurthi R, Barker-Collo S, Barber PA, Rathnasabapathy Y, Te Ao B, et al. Measuring stroke and transient ischemic attack burden in New Zealand: protocol for the fifth Auckland regional community stroke study (ARCOS V). *Int J Stroke*. 2020;15:573–583. doi: 10.1177/1747493019884528
13. Ozaki AF, Choi AS, Le QT, Ko DT, Han JK, Park SS, 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:e005969. doi: 10.1161/CIRCOUTCOMES.119.005969
14. Rosendaal FR, Cannegieter SC, van der Meer FJM, Briët E. A method to determine the optimal intensity of Oral anticoagulant therapy. *Thromb Haemost*. 1993;69:236–239.
15. Austin PC, Stuart EA. Moving towards best practice when using inverse probability of treatment weighting (IPTW) using the propensity score to estimate causal treatment effects in observational studies. *Stat Med*. 2015;34:3661–3679. doi: 10.1002/sim.6607
16. Adams HP, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of org 10172 in acute stroke treatment. *Stroke*. 1993;24:35–41. doi: 10.1161/01.STR.24.1.35
17. Dobson AJ, Kuulasmaa K, Eberle E, Scherer J. Confidence intervals for weighted sums of poisson parameters. *Stat Med*. 1991;10:457–462. doi: 10.1002/sim.4780100317
18. Lip GYH, Nieuwlaat R, Pisters R, Lane DA, Crijns HJGM. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach. *Chest*. 2010;137:263–272. doi: 10.1378/chest.09-1584
19. Vandenbroucke JP, Pocock SJ, Poole C, Schlesselman JJ, Egger M. Strengthening the reporting of observational studies in epidemiology (STROBE): explanation and elaboration. *Ann Intern Med*. 2007;147:W163–W194. doi: 10.7326/0003-4819-147-8-200710160-00010-w1
20. Nielsen PB, Skjøth F, Overvad TF, Larsen TB, Lip GYH. Female sex is a risk modifier rather than a risk factor for stroke in atrial fibrillation: should we use a CHA $_2$DS $_2$ VA score rather than CHA_2DS_2 VASc? *Circulation*. 2018;137:832–840. doi: 10.1161/CIRCULATIONAHA.117.029081
21. Teppo K, Airaksinen KEJ, Jaakkola J, Halminen O, Salmela B, Kouki E, Haukka J, Putaala J, Linna M, Aro AL, et al. Ischaemic stroke in women with atrial fibrillation: temporal trends and clinical implications. *Eur Heart J*. 2024;45:1819–1827. doi: 10.1093/eurheartj/ehae198
22. Chao TF, Lip GYH, Liu CJ, Tuan TC, Chen SJ, Wang KL, Lin Y-J, Chang S-L, Lo L-W, Hu Y-F, et al. Validation of a modified CHA_2 DS_2-VASc score for stroke risk stratification in Asian patients with atrial fibrillation: a nationwide cohort study. *Stroke*. 2016;47:2462–2469. doi: 10.1161/STROKEAHA.116.013880

Downloaded from http://ahajournals.org by on April 13, 2026