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ORIGINAL ARTICLE

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Geographical variation in persistence to oral anticoagulation therapy and clinical outcomes among patients with atrial fibrillation initiating therapy in Denmark, Sweden, Norway and Finland

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Abstract

Aim: To examine inter-national and regional variations in persistence of oral anticoagulation (OAC) therapy and incidence of clinical outcomes and mortality, among patients with incident atrial fibrillation (AF) in the Nordic countries.

Methods: We conducted a registry-based multinational cohort study of OAC-naïve patients diagnosed with AF that redeemed at least one prescription of OAC after AF in Denmark ($N = 25\,585$), Sweden ($N = 59\,455$), Norway ($N = 40\,046$) and Finland ($N = 22\,415$). Persistence was dispensing at least one prescription of OAC from Day 365 after the first prescription and 90 days forward.

Results: Persistence was 73.6% (95% confidence interval 73.0–74.1) in Denmark, 71.1% (70.7–71.4) in Sweden, 89.3% (88.2–90.1) in Norway and 68.6% (68.0–69.3) in Finland. One-year risk of ischemic stroke varied between

2.0% (1.8–2.1) in Norway and 1.5% (1.4–1.6) in Sweden and 1.5% (1.3–1.6) in Finland. One-year risk of major bleeding other than intracranial bleeding varied between 2.1% (1.9–2.2) in Norway and 5.9% (5.6–6.2) in Denmark. One-year mortality risk varied between 9.3% (8.9–9.6) in Denmark and 4.2% (4.0–4.4) in Norway.

Conclusion: In OAC-naïve patients with incident AF, persistence of OAC therapy and clinical outcomes vary across Denmark, Sweden, Norway and Finland. Initiation of real-time efforts are warranted to ensure uniform high-quality care across nations and regions.

KEYWORDS
atrial fibrillation, mortality, oral anticoagulation, stroke, variation

1 | INTRODUCTION

Atrial fibrillation (AF) is the most common sustained arrhythmia worldwide, with ~38 million patients in 2017.[1] The combination of aging of the general population and intensified screening for undiagnosed AF has increased the prevalence and incidence during the last 50 years.[2] The current lifetime risk is one in three individuals of European ancestry.[3] A projection study suggests that the prevalence in Europe will double to 17.9 million people in 2060.[4]

Clinically manifested AF is associated with an average five-fold increased risk of stroke,[5] and AF-related strokes are associated with high mortality and morbidity.[6] The current European guidelines from 2020 recommend consideration of oral anticoagulation (OAC) therapy among male patients with a CHA_2DS_2-VASc (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism, vascular disease, age 65 to 74 years, sex category) score of ≥1, and among female patients, a CHA_2DS_2-VASc score of ≥2.[7] Both vitamin K antagonists (VKAs) and direct oral anticoagulant (DOACs) reduce the risk of stroke and mortality markedly.[8]

Effective implementation of clinical guidelines recommendations on OAC therapy has been proven challenging. It is well-known that the use of OAC therapy and clinical outcomes in AF populations, such as mortality and stroke, vary substantially globally.[9–11] However, direct comparisons between countries and/or regions are typically unfeasible because most patient cohorts are not population-based, which questions the comparability and generalisability of the findings. We have recently published detailed data on the use of OAC and clinical outcomes according to the place of residence in Danish patients with AF.[12] The study demonstrated substantial geographical variation in OAC use and clinical outcomes at a regional and municipal level in Denmark, even though Denmark has a tax-funded healthcare system with universal coverage. It is currently unknown whether similar patterns of variation exist in other countries, including countries with comparable healthcare systems.

Data on contemporary nationwide studies examining the persistence of OAC and clinical outcomes among patients with AF in a real-world multinational setting are sparse. Such data provide valuable insights into AF care and may further enhance the focus on improvement in the quality of AF care. As the Nordic countries are among the members of the exclusive list of countries with access to such data,[13] it seems reasonable that the nations use this unique opportunity. The aims of the present study were to examine the variation and trend in persistence to OAC and the variation and temporal trend in the incidence of clinical outcomes and mortality internationally and inter-regionally in Nordic countries.

2 | METHODS

The study was conducted in accordance with the Basic & Clinical Pharmacology & Toxicology policy for experimental and clinical studies.[14]

2.1 | Settings and data sources

The populations of Denmark (5.8 million), Sweden (10.0 million), Norway (5.3 million) and Finland (5.5 million) sum up to about 26.5 million inhabitants. The healthcare systems in the countries have many similarities including taxpaid healthcare, with only a very small amount of user payment per visit for medical care in Sweden, Norway and Finland, but none in Denmark. In all countries, there is a partial reimbursement of consumer costs of

medical treatment. All countries have complete and continuously updated information on the citizens' vital and emigration status, and all hold hospital registries with information on hospitalizations and registries with pharmacy-dispensed medication. A unique civil registration number allocated to each individual enables linkage between nationwide registries within each country.

Each country retrieved data from nationwide patient registries, prescription registries and civil registration systems. National Patient Registries were established in Denmark in 1977, Sweden in 1987, Norway in 2009 and Finland in 1967. The registries contain prospectively registered data on inpatients and outpatients. Data include individual-level information on dates of admission and discharge, surgical procedures performed, and one primary and multiple secondary diagnoses per discharge. The coding of diagnoses followed the International Classification of Diseases 10th revision (ICD-10). ICD-10 was used from 1994 in Denmark, from 1997 in Sweden, from 1997 in Norway and from 1996 in Finland. The physician who discharged a patient coded all diagnoses for that patient. The registries provided information on AF and comorbidities.

The nationwide prescription registries were established in Denmark in 1995, Sweden in 2005, Norway in 2003 and Finland in 1994. They contain individual-level data on all dispensed prescriptions, and the coding follows the Anatomical Therapeutic Chemical (ATC) Classification System. We used prescription data to define persistence and to define comorbidities.

Each nation-specific civil registration system contains daily updated individual-level information on sex, date of birth, migration status and dates, and vital status and date of death.

2.2 | Design and national populations

We conducted a nationwide registry-based cohort study in each of the Nordic countries: Denmark, Sweden, Norway and Finland, and analysed and compared findings within and between the countries. Baseline was the day the patients redeemed the first prescription for an OAC after a first-time diagnosis of AF. Patients were followed for persistence and clinical outcome after baseline (Figure S1).

We included all patients aged ≥40 and <90 years with a first-time diagnosis of AF reported from a hospital or an outpatient clinic to the respective national patient registries who redeemed a prescription of OAC between diagnosis of AF and up to 90 days after (codes given Table S1, Figure S1). The corresponding baseline year was between 1 January 2012 and 31 December 2016. A diagnosis of AF (primary or secondary diagnoses, including "open" hospital contacts, i.e., typically patients seen regularly in hospital outpatient clinics) was identified using ICD-10 I48. The date of diagnosis was on the discharge day for inpatients or the date of diagnosis for outpatients.

Exclusion criteria included patients whose first-time diagnosis of AF was valvular AF (AF with mitral stenosis or mechanical prosthetic heart valves, Table S2)[15]; patients with less than 5 years complete look-back history in the national registers; male patients with a CHA_2DS_2-VASc of 0 and female patients with a CHA_2DS_2-VASc score of 1 (definition given in Table S3); patients with civil registration status classified as inactive or disappeared in all or part of the study period, patients who redeemed at least one prescription for OAC in the period from 1 year before baseline; and patients with a history of ischemic stroke defined as a diagnosis on the baseline date or before (Table S3, Figure S1). We excluded patients with a history of ischemic stroke because it is our experience that registration of the diagnosis may be repeated in consecutive hospital contacts related to the same course of the disease. Such repeated registration of an identical clinical event increases the risk of misclassifying an index ischemic stroke as a recurrent ischemic stroke event.

2.3 | Regions/counties in each country

Information on residential municipalities and regions/counties was identified in the national civil registration systems. Denmark has five regions, Sweden has 21 counties, Norway has four regions, and Finland has five university hospital regions.

2.4 | Ascertainment of OAC persistence

Persistence was assessed among all patients who were still alive and had not emigrated on Day 365 after baseline. We defined persistence as dispensing at least one prescription of OAC from Day 365 after baseline and 90 days forward in this cohort. Table S1 shows the definition of OAC.

2.5 | Ascertainment of clinical outcomes and mortality

Outcomes of interest included ischemic stroke, intracerebral haemorrhage, intracranial bleeding, other major

bleeding and all-cause mortality (definitions given in Table S4). Information on vital status was retrieved from the civil registration systems. We examined the risks of clinical outcomes and all-cause mortality at 1 year. The 1-year period was a pragmatic decision that reflected our aim of having a standardized time window allowing for valid comparisons between geographical areas and over time. The time window was inspired by the European quality indicators for outcomes among adults with AF.[16]

2.6 | Covariates

Covariates included comorbidities and concomitant medication. We included the following comorbidities with ascertainment at baseline: abnormal liver function, abnormal renal function, alcohol-related disease, bleeding, congestive heart failure, diabetes, hypertension, thromboembolism, stroke and vascular disease. For each patient, we computed the CHA_2DS_2-VASc score (Table S3) and a modified HAS-BLED score (Table S5). The HAS-BLED was "modified" because information on the international normalized ratio was unavailable. The national patient registries and prescription registries provided information on comorbidities, which we identified using ICD-10 and ATC codes. We only considered medication prescribed in a window of 1 year before or at baseline. We considered both primary (A) and secondary (B) diagnoses and operation codes reported in a window of 5 years before or at baseline.

Concomitant medication at baseline included antiplatelet drugs, non-steroidal anti-inflammatory drugs (NSAIDs) and statins. The national prescription registries provided the information (Table S6). We only considered medication redeemed in a window between baseline and 1 year before.

2.7 | Statistical analyses

Each nation held its own nationwide data, and only proportions and rates with confidence intervals (CIs) were transferred between countries. We used a common data structure, and a detailed analysis plan ensured that all the definitions of variables and the syntax for all analysis were the same across countries.

The Aalen-Johansen estimator with death as a competing event was used to compute the cumulative incidence of OAC persistence with a 95% CI in the time window from baseline +365 days and 90 days forward (i.e., Day 366–456). The Aalen–Johansen estimator was also used to compute the cumulative incidence of non-fatal clinical outcomes with 95% CIs. The Kaplan–Meier estimator was used to compute the cumulative mortality (95% CI) 1 year after baseline. We used the pseudo-value approach to estimate risk ratios (95% CI) for persistence, clinical outcomes and mortality on a national and regional level by country.[17–19] To quantify the within-nation variation, we used multilevel mixed-effects linear regression to estimate nation-specific intraclass correlation coefficients (ICCs) based on the cumulative incidences for each outcome of interest. When considering the regions as clusters, an ICC of 1 would indicate that all variation was explained by differences between clusters and there was no variation within clusters.

We examined the annual change in absolute measures of persistence, clinical outcomes and mortality from 2012 to 2017 at a national level.

For all statistical analyses, we used Stata version 16.1, StataCorp LLC in Denmark; R version 4.1.1 in Sweden; Stata version 16.1, StataCorp LLC in Norway; and IBM SPSS Statistics Version 27 for descriptive statistics and Stata version 17, StataCorp LLC for statistical analyses in Finland.

2.8 | Ethics

In Denmark, registry-based studies do not need an ethics approval. In Sweden, the study has been approved by the Regional Ethical Review Board in Stockholm (dnr: 3510/2019). In Norway, registration of data into the National Patient Registry and the Norwegian Prescription Database is legally exempt from obtainment of patient consent. The study of Norwegian data is based on the approval from the Regional Ethics Committee (2017/410/REK North). Only aggregated anonymous data were exported. In Finland, no patient consents are needed according to Finnish legislation. The study has been approved by the Ethics Committee of the Medical Faculty of Helsinki University, Helsinki, Finland and granted research permission from the Helsinki University Hospital.

3 | RESULTS

3.1 | Patient characteristics

We included 25 585 patients from Denmark, 59 455 from Sweden, 40 046 from Norway and 22 415 from Finland (Table 1, Figures S2–5). The median age ranged from 73 years in Norway to 75 years in Sweden and Finland, and the proportion of male patients ranged from 44.5% in Finland to 58.5% in Norway. No data were available for Norway in 2012.

TABLE 1 Baseline characteristics of atrial fibrillation patients by nation.

Characteristics	Denmark $n = 25\,585$	Sweden $n = 59\,455$	Norway $n = 40\,046$	Finland $n = 22\,415$
Men, % (n)	53.9 (13783)	53.7 (31936)	58.5 (23427)	44.5 (9973)
Age, median (IQR), year	74 (68–81)	75 (69–81)	73 (67–80)	75 (68–82)
Baseline year, % (n)				
2012	15.9 (4057)	16.6 (9890)	[a]	17.3 (3887)
2013	18.8 (4816)	18.4 (10958)	21.4 (10516)	18.7 (4196)
2014	20.6 (5272)	20.5 (12160)	20.2 (9933)	19.2 (4296)
2015	22.2 (5691)	21.8 (12963)	19.8 (9762)	20.2 (4519)
2016	22.5 (5749)	22.7 (13484)	20.0 (9835)	24.6 (5517)
Comorbidity, % (n)				
Abnormal liver function	1.3 (329)	1.3 (759)	1.0 (400)	0.7 (159)
Abnormal renal function	4.9 (1261)	4.9 (2896)	7.6 (3043)	1.9 (434)
Alcohol-related disease	3.0 (762)	4.9 (2929)	0.5 (161)	1.6 (358)
Bleeding	11.1 (2829)	11.4 (6791)	12.5 (5006)	4.6 (1041)
Congestive heart failure	15.8 (4045)	20.4 (12145)	26.4 (10572)	8.3 (1871)
Diabetes mellitus	21.2 (5,22)	19.5 (11585)	15.9 (6367)	22.7 (5084)
Hypertension	85.0 (21756)	72.2 (42922)	71.0 (28432)	72.9 (16336)
Thromboembolism	4.2 (1077)	6.0 (3563)	4.4 (1762)	3.4 (768)
Systemic embolism	0.5 (137)	1.0 (590)	0.6 (240)	0.4 (91)
Transient ischemic attack	3.7 (948)	5.1 (3005)	4.3 (1722)	3.1 (685)
Vascular disease	14.8 (3797)	17.7 (10546)	20.4 (8169)	16.3 (3660)
Acute myocardial infarction	8.8 (2241)	11.4 (6754)	11.1 (4445)	5.3 (1184)
Coronary procedure	9.4 (2396)	10.8 (6439)	No data	12.3 (2749)
Peripheral artery disease	3.6 (916)	3.6 (2128)	10.0 (4003)	3.4 (770)
Concomitant medication,[b] % (n)				
Antiplatelet drugs	41.5 (10624)	53,6 (31868)	51.1 (20423)	9.1 (2040)[c]
NSAID	41.0 (10.497)	18,7 (11134)	22.9 (9171)	26.6 (5964)
Statins	50.9 (13030)	36,6 (21774)	42.9 (18180)	45 (10095)
CHA_2DS_2-VASc, mean (SD)	2.6 (0.65)	3.1 (1.28)	3.0 (1.35)	3.2 (1.3)
CHA_2DS_2-VASc, % (n)				
1	9.1 (2332)	10.6 (6312)	13.3 (5326)	9.2 (2058)
2	21.2 (5414)	23.8 (14127)	24.5 (9811)	22.2 (4983)
≥3	69.7 (17839)	65.6 (39016)	62.2 (24909)	68.6 (5964)
HAS-BLED,[d] mean (SD)	2.1 (0.76)	2.4 (0.96)	2.0 (0.97)	2.0 (0.8)
HAS-BLED,[d] % (n)				
0	3.0 (769)	0.6 (331)	1.4 (561)	0.7 (147)
1	22.3 (5713)	19.1 (11370)	16.8 (6728)	24.4 (5459)
2	38.9 (9950)	33.4 (19829)	33.7 (13495)	49.8 (11153)
≥3	35.8 (9154)	47.0 (27925)	48.1 (19262)	25.1 (15374)

Abbreviations: IQR, interquartile range; NSAID, non-steroidal anti-inflammatory drug; OAC, oral anticoagulation; SD, standard deviation; VKA, vitamin K antagonists.

[a]Data unavailable for Norway in 2012.

[b]Concomitant medical therapy within 1 year before baseline.

[c]In Finland acetylsalicylic acid (ASA) is dispensed as over the counter-drug from pharmacy and not registered.

[d]Modified HASBLED-score without labile international normalized ratio.

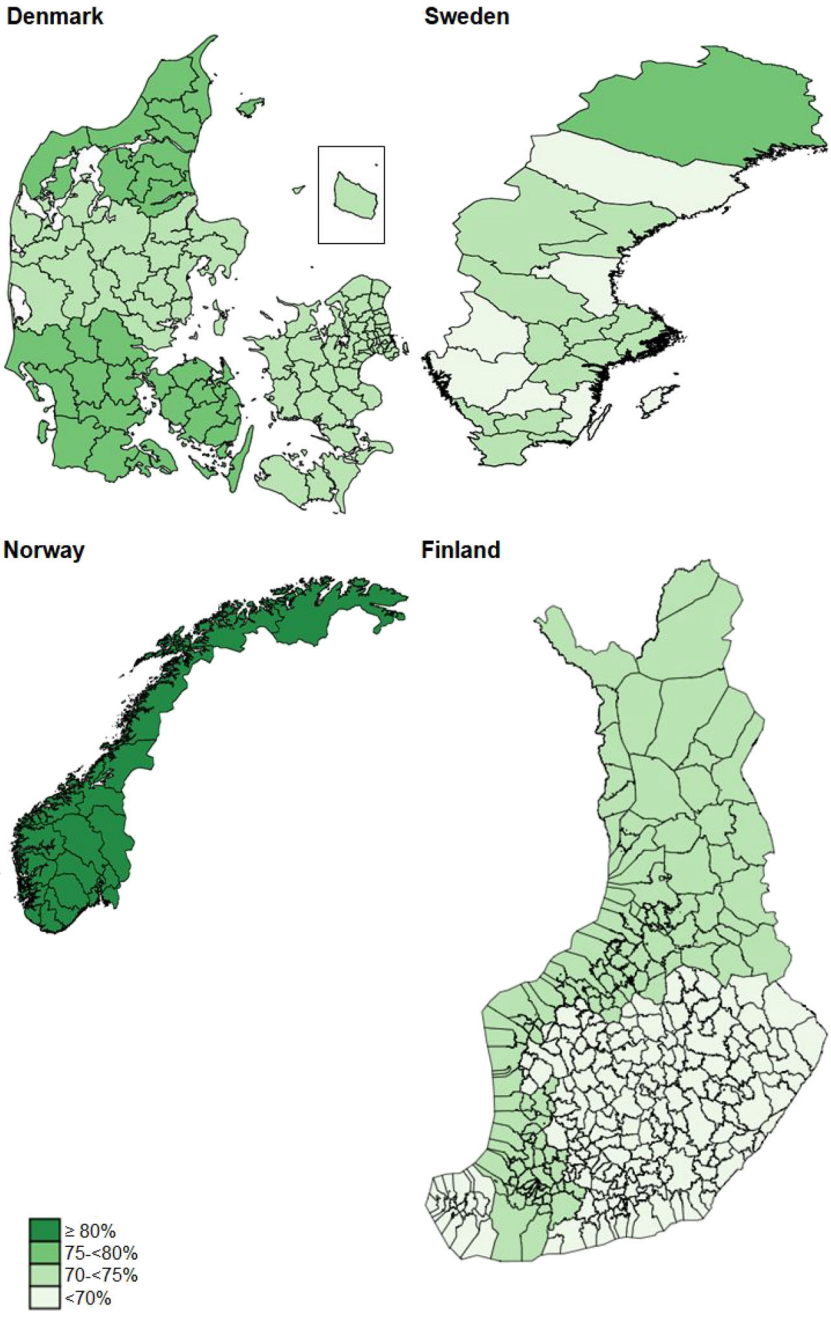

FIGURE 1 National maps showing persistence for regions and municipalities in each Nordic country. Cumulative incidence of oral anticoagulation (OAC) persistence from Day 365 and 90 days forward for regions, with death considered a competing event.

3.2 | Persistence

The OAC persistence was 73.6% (95% CI 73.0–74.1) in Denmark, 71.1% (70.7–71.4) in Sweden, 89.3% (88.2–90.1) in Norway and 68.6% (68.0–69.3) in Finland. In general, the persistence in Denmark, Sweden and Finland was low compared to the persistence in Norway.

Data at the regional level are shown in Figure 1 and Tables S7–14. In Denmark, the persistence ranged from 71% to 76% (Table S7), and we noted no statistical evidence of variation across regions (ICC < 0.01), although there were examples of individual regions that differed significantly. In Sweden, persistence ranged between 69% and 75% and the ICC of <0.01 indicated no variation (Table S9). The Norwegian persistence was similar across geographical regions, ranging from 88% to 89%, and the ICC was <0.01 (Table S11). In Finland, the persistence ranged between 67% and 71% and we noted no variation between regions (ICC < 0.01) (Table S13).

We noted an increasing temporal trend in persistence over the study period for all countries (Figure 2, left). The use of VKA declined markedly over the years whereas the use of DOACs, in particular, apixaban and rivaroxaban, increased (Figure 2, right).

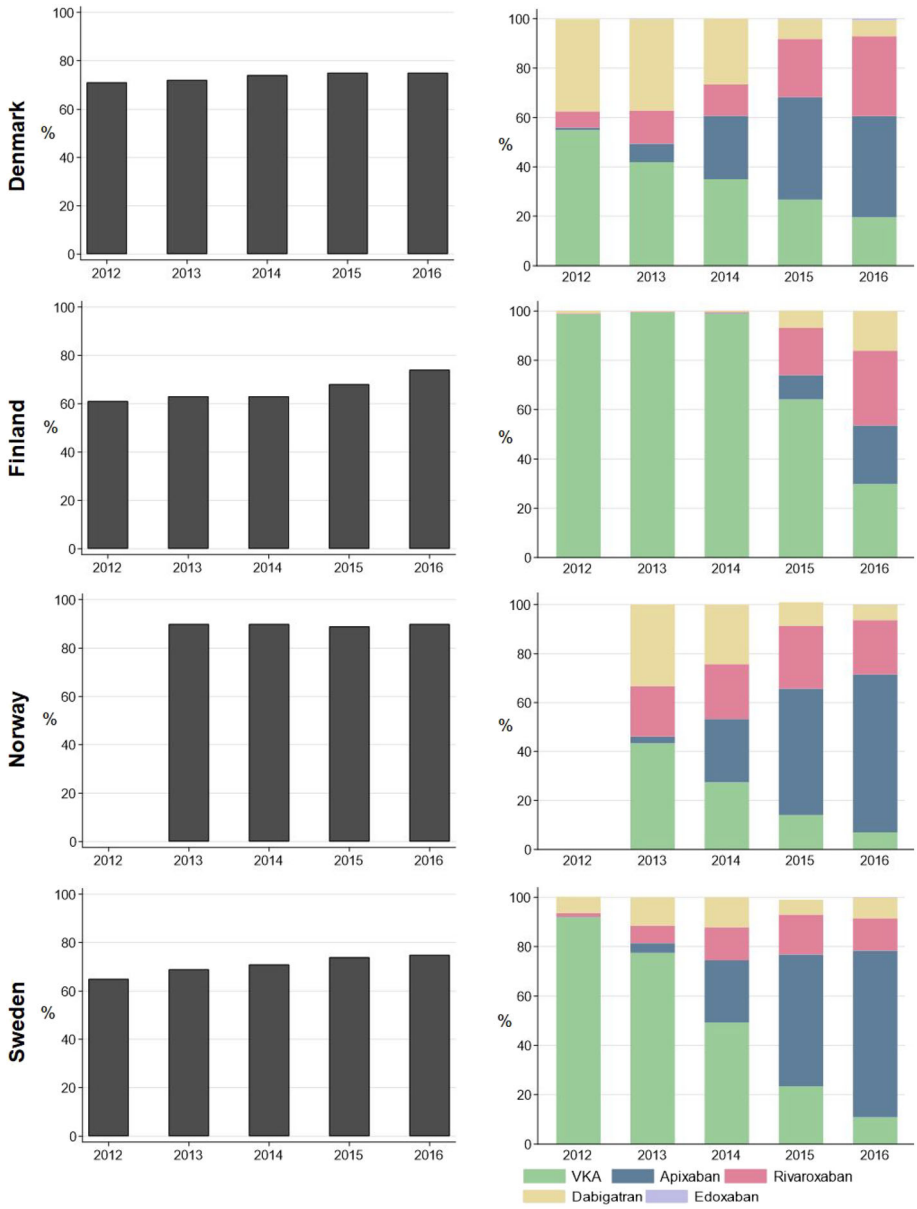

FIGURE 2 Nation-specific temporal development in oral anticoagulation (OAC) persistence (left) and relative distribution of OAC use (right), by baseline year. Abbreviation: VKA = vitamin K antagonist. Annual stacked cumulative incidence of persistence after 1 year for the four nations, with death considered a competing event.

3.3 | Clinical outcomes and mortality

Table 2 shows the clinical outcomes and mortality over 1-year follow-up by countries. The 1-year risk of ischaemic stroke was lowest in Sweden (1.5%, 1.3–1.4) and Finland (1.5%, 1.3–1.6) and appeared to be highest in Norway (2.0%, 1.8–2.1). We noted no differences in risks of intracerebral haemorrhage and intracranial bleeding across the nations. The risk of other major bleeding varied between 5.9% (5.6–6.2) in Denmark and 2.1% (1.9–2.2) in Norway, and all-cause mortality risk was highest in Denmark (9.3%, 8.9–9.6) and lowest in Norway (4.2%, 4.0–4.4). When examining temporal trends, we noted that the risk of all-cause mortality was increasing in Denmark (Figure 3) but not in the other countries.

The region-specific absolute risk and risk ratios for each country are shown in Tables S15–22. Overall, no statistically significant regional variation within the individual countries was observed for the examined outcomes, that is, all ICCs were <0.01. However, some examples of variation were observed between individual regions. Hence, in Denmark, the absolute risk of ischaemic stroke ranged between 1.2% and 2.0%, and all-cause mortality ranged between 7.9% and 10.9% (Table S15). In Sweden, the risk of ischaemic stroke varied between 0.9% and 2.0%, whereas the risk of other major bleeding varied between 2.2% and 3.9%, and all-cause mortality varied between 4.3% and 7.2%. In Norway, the risk of ischaemic stroke ranged between 1.8% and 2.3%, other major bleeding ranged between 1.9% and 2.4% and mortality risk

TABLE 2 Cumulative incidences of the outcomes by nation over 1 year of follow-up expressed as percentages (%) with 95% confidence intervals (CIs).

	Denmark	Sweden	Norway	Finland
Ischemic stroke	1.6 (1.5–1.8)	1.5 (1.4–1.6)	2.0 (1.8–2.1)	1.5 (1.3–1.6)
Intracerebral haemorrhage	0.4 (0.3–0.5)	0.4 (0.3–0.4)	-[a]	0.4 (0.3–0.4)
Intracranial bleeding	0.5 (0.4–0.6)	0.6 (0.5–0.7)	0.5 (0.4–0.6)	0.5 (0.4–0.6)
Other major bleeding	5.9 (5.6–6.2)	2.9 (2.8–3.1)	2.1 (1.9–2.2)	3.6 (3.3–3.8)
All-cause mortality	9.3 (8.9–9.6)	5.6 (5.5–5.8)	4.2 (4.0–4.4)	5.6 (5.3–5.9)

Note: Cumulative incidence of clinical outcomes 1 year after the diagnosis of atrial fibrillation (AF), with death considered a competing event except for all-cause mortality.
[a]Data unavailable.

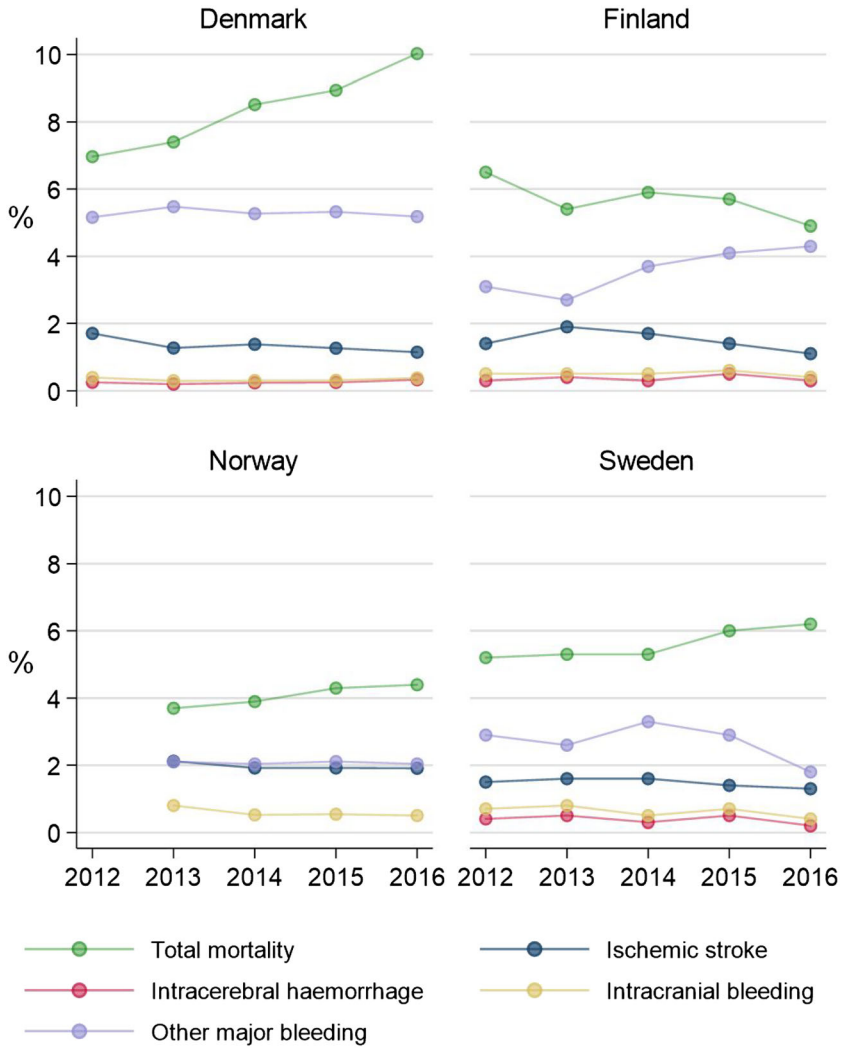

FIGURE 3 Temporal development of clinical outcomes, by baseline year.

ranged between 3.9% and 4.6%. In Finland, all-cause mortality ranged between 5.3% and 6.2%.

In all countries, at least a trend of decreasing incidence of ischaemic stroke was noticed during 2012–2016; Figure 3.

4 | DISCUSSION

In this multinational cohort study of OAC-naïve patients with incident AF, we found substantial geographical variation across Denmark, Finland, Norway and Sweden in

persistence of OAC and clinical outcomes and all-cause mortality. The persistence varied by about 20 percentage points between countries and was very high in Norway. The proportion of Norwegian patients using DOAC was very high, which suggests that the Norwegian healthcare system ensured a fast and effective uptake of DOAC. In Denmark, the absolute risks of other major bleeding and all-cause mortality were about twice as high as in the other countries. Additionally, we noted an increasing trend in all-cause mortality among Danish patients over the study period. The four countries have comparable healthcare systems, but differences in organizations and/or prioritization of resources may still contribute to the observed differences in persistence, clinical outcomes and mortality.

More patients with newly diagnosed AF were included in Norway compared to Denmark and Finland despite the population size of each of the three countries being comparable between five and six million. All Norwegian patients redeemed an OAC prescription within 90 days after the diagnosis of AF. Accordingly, a possible reason for the higher number of patients in Norway was the more effective initiation of OAC after an incident hospital diagnosis of AF.

The proportion of men was lower in Finland (44.5%) compared to 53.9% in Denmark, 53.7% in Sweden and 58.5% in Norway. In a nationwide Finnish study with less restrictive exclusion criteria, the percentage of men was 50.8%.[20] Additionally, the Finnish cohort also had the highest median age (together with Sweden), which may also have contributed to a lower proportion of men. The life expectancy is 5–6 years longer among women in Finland, and the incidence of newly diagnosed AF is accordingly higher in older age groups among women despite the individual risk of AF being higher among men. The FibStroke study demonstrated reluctance to start OAC in old and fragile women.[21] In addition, the sex difference in initiation OAC disappeared when adjusting for age group, which supports the view that the high proportion of older women is mainly responsible for this finding.

The underlying reasons for the high mortality, high risk of major bleeding and increased mortality over time in Denmark are unknown. We had no data on the underlying mechanisms, and can therefore merely speculate on the reasons. One possible explanation is the trend over time to prescribe OAC to more frail patients. Danish nationwide data from 2005–2015 demonstrated that prescription of OAC increased over time to patients with a high risk of stroke and among older patients.[22] Another possible explanation could be differences in baseline characteristics. When comparing the Danish patients with the Norwegian patients, who had the lowest mortality, we noted a slightly higher proportion of men in Norway (58.5% vs. 53.9%). The prevalence proportions of hypertension (85% vs. 71%) and diabetes (21% vs. 16%) were higher in Denmark, whereas the prevalence proportions of heart failure (26% vs. 16%) and vascular disease (20% vs. 15%) were higher in Norway. Such differences may have contributed to the differences in incidence of outcomes. Further studies are warranted to examine the underlying reasons for the observed discrepancy across the four Nordic countries.

Recently, a multinational study by Komen et al. that included data from Sweden, Denmark, Scotland, Norway and Germany examined adherence and persistence to DOACs.[23] Even though the definition of persistence was slightly different from ours, Komen et al. reported an overall persistence of 82% after 1 year across the five countries and variation from 75%–85%.[23] The result is comparable with ours and underscores the existence of a gap between clinical guideline recommendations and clinical practice. The study by Komen et al. did not examine variation within the countries or include data on clinical outcomes.

Our present work was inspired by the EuroHeart, an initiative by the European Society of Cardiology (ESC).[24] By using data from national registries, the objective is to improve healthcare by monitoring the quality of care at a national and local level. The EURObservational Research Programme Atrial Fibrillation (EORP-AF) Pilot General Registry reported in 2015 regional differences in patient characteristics, treatment options and management options among European cardiologists.[25] However, the study included no data on follow-up. To our knowledge, no surveys associated with the ESC have examined geographical variation based on follow-up data.

4.1 | Perspectives

Even though regulations of ethics prohibit sharing of individual-level data between countries, our present study is an example of a multinational collaboration with a universal protocol and data model that enables such an analysis. We hope that our study may motivate other countries to use a similar approach and conduct analyses of geographical variation within and across countries. Real-time multinational and regional monitoring have a great potential to improve care for patients with AF. First, multinational monitoring may ensure fast and more effective implementation of clinical guidelines. Second, the provision of real-time nationwide data enables international comparisons. Third, multinational initiatives may facilitate the application of future treatment options. Finally, it may lead to improved public health and cost savings in healthcare.

4.2 | Limitations

The national registries provided information on incident AF, and we may have missed patients whose AF diagnosis was not recorded or not recognized in the registries. Furthermore, we were unable to clinically evaluate the patients for undiagnosed AF, use systematic ECG- or Holter-based screening, or examine electrocardiograms to validate the diagnosis. Differences in coding practice across countries may exist. The national prescription registries provided medication information; however, information on non-reimbursed medication is incomplete in the registries, and we had no information on whether the patients took the redeemed medicine. In addition, we included no information on medication dosage. We adjusted for several relevant covariates but cannot rule out residual confounding from unmeasured variables, such as socioeconomic factors and patient preferences. We were unable to adjust estimates when comparing across countries. The organization and structure of the healthcare systems in the Nordic countries are similar and characterized by free access to tax-financed hospital care, but the results may not be generalized to different healthcare systems.

5 | CONCLUSIONS

In OAC-naïve patients with incident AF, persistence of OAC therapy and clinical outcomes vary across Denmark, Sweden, Norway and Finland. As the four countries have similar healthcare systems, major differences in organizations or resources are unlikely to explain the observed variation. However, differences in the prioritization of resources and effectiveness of implementation of guidelines recommendations may be contributing factors. Our findings underline the need to initiate additional efforts in a real-time environment that ensure uniform high-quality care for AF patients and facilitate timely monitoring of the implementation of clinical guidelines within and across healthcare systems.

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CONFLICT OF INTEREST STATEMENT

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DATA AVAILABILITY STATEMENT

Individual level data cannot be shared publicly due to national legislation. Data from the individual countries can be accessed through application to the relevant public authorities. The authors did not have special access privileges to these data.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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