Clinical Epidemiology

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Prevalence and Incidence Rates of Atrial Fibrillation in Denmark 2004–2018

Emilie R Hegelund[1,2], Lars J Kjerpeseth[3], Laust H Mortensen[1,2], Jannicke Igland[4], Trygve Berge[5], Mariam Anjum[3,5], Grethe S Tell[4], Inger Ariansen[3]

[1]Methodology and Analysis, Statistics Denmark, Copenhagen, Denmark; [2]Department of Public Health, University of Copenhagen, Copenhagen, Denmark; [3]Department of Chronic Diseases, Norwegian Institute of Public Health, Oslo, Norway; [4]Department of Global Public Health and Primary Care, University of Bergen, Bergen, Norway; [5]Department of Medical Research, Bærum Hospital, Vestre Viken Hospital Trust, Gjettum, Norway

Inger Ariansen, Department of Chronic Diseases, Norwegian Institute of Public Health, PO Box 222 Skøyen, Oslo, N-0213, Norway, Tel +47 21 07 70 00, Fax +47 22 35 36 05, Email inger.ariansen@fhi.no

Video Abstract

Point your SmartPhone at the code above. If you have a QR code reader the video abstract will appear. Or use: https://youtu.be/ov6Ab_Q65eU

Purpose: To estimate the prevalence and incidence of atrial fibrillation (AF) in Denmark during 2004–2018 and to investigate whether methodological choices influence these estimates.

Patients and Methods: A register-based cohort study was conducted of all individuals aged ≥18 years in Denmark 2004–2018. The cumulative prevalence of AF at the end of the study period was calculated as the number of AF cases alive with at least one inpatient or two outpatient diagnoses during 1994–2018 divided by the number of Danish residents in 2018. Incidence rates were calculated as the number of annual AF cases with no previous diagnosis in the past 10 years (ie, a 10-year washout period) divided by the person-time contributed by the population free of AF on 1 January in the same calendar year. Furthermore, the influence of varying case definitions was investigated.

Results: The cumulative prevalence of AF was 3.0% in 2018. The incidence rate increased from 391 to 481 per 100,000 person-years (PYs) from 2004 to 2015 (1.7% average annual increase) after which it declined to 367 per 100,000 PYs in 2018 (8.5% average annual decrease). This pattern was observed in both sexes irrespective of age. Methodological choices, particularly the case definition's strictness and the length of the washout period, had a substantial influence on the reported estimates.

Conclusion: The cumulative prevalence of AF is currently around 3.0% in the Danish population, but the incidence has declined since 2015. As these estimates are influenced by methodological choices, future studies should strive for precise reporting of study methodology.

Keywords: atrial fibrillation, prevalence, incidence, time trends, Nordic countries

Introduction

Atrial fibrillation (AF) is the most common type of cardiac arrhythmia with a lifetime risk of 37% from 55 years and onwards.[1] In the European Union, it is estimated that 8.8 million individuals aged ≥55 years had AF in 2010 and this number is projected to double by 2060.[2] As AF is associated with increased risks of serious diseases and mortality, such as stroke, heart failure, dementia, cardiovascular mortality, and all-cause mortality,[3] the forecasted AF epidemic may have serious consequences for both the individual and the society.

The reported occurrence of AF varies across time and place and it is often difficult to evaluate whether the inconsistent numbers are due to true variation between populations or due to methodological differences between studies.[4,5] A literature review and data synthesis covering studies published until 2012 reported an overall sex- and age-adjusted pooled prevalence of 2.8% (95% CI: 2.3–3.4%) among adults.[6] More recent population-based studies have reported similar prevalence estimates in European countries.[7–9] Even within the relatively homogenous Nordic countries, the prevalence estimates vary. In Denmark, the cumulative prevalence of AF was reported to be 2.0% among the whole population from 1983 to 2012.[10] In Sweden, the cumulative prevalence was reported to be 2.9% among those aged ≥20 years from 2005 to 2010.[11] In Finland, the cumulative prevalence was reported to be 4.1% among the whole population from 2004 to 2018.[12] Finally, in Norway, we reported a cumulative prevalence of 3.4% among those aged ≥18 years from

Received: 12 May 2022
Accepted: 21 August 2022
Published: 26 October 2022

1994 to 2014.[13] However, it is important to bear in mind that these observations may be influenced by the AF case definition (including the chosen age range of the population at risk), the health care systems' traditions for registration of AF diagnoses, as well as random variation.

With regard to AF incidence, the majority of previous studies have found increasing or stable incidence rates.[14–17] Thus, the incidence rate was reported to increase from 1983 to 2015 in Denmark,[10,18] while we reported stable incidence rates from 2004 to 2014 in Norway.[13] Methodological choices may have contributed to the varying time trends in these two countries, but findings from the Global Burden of Disease database suggest that time trends did vary between countries from 1990 to 2017.[19] To evaluate whether inconsistent findings are due to true variation between populations or methodological differences, there is a need for studies with more precise reporting of study methodology, including thorough descriptions of the data sources and case definition, as well as use of publicly available standard populations. Such studies are both important for research, as well as for clinical practice and policy as reliable and valid estimates of AF occurrence are crucial for planning in the health care system.

Therefore, the aim of this study was to estimate the cumulative prevalence of AF and time trends in incidence rates in the Danish population from 2004 through 2018 and to investigate how varying case definitions influence these estimates. As a secondary aim, the findings were compared to Norwegian estimates derived using the same methodology to explore the findings' generalizability to a neighboring country with a comparable health care system.

Materials and Methods

Study Design and Participants

A register-based study was conducted of all individuals aged ≥18 years who lived in Denmark at any point during the period 2004 through 2018 (N = 5,910,223). All Danish residents are registered in the Danish Civil Registration System with a unique personal identification number,[20] making it possible to link individual-level data from nationwide registers, including the Danish National Patient Register and the Danish Register of Causes of Death.

The present study is conducted according to the rules of the Danish Data Protection Agency. Statistics Denmark acts as the data processor. In Denmark, the use of registry data for research does not require medical ethics committee approval.

Definition of AF Cases

An AF case was defined as a registered in- or outpatient diagnosis (primary or secondary) or underlying cause of death of atrial fibrillation or flutter (ICD-10 code: I48) in the Danish National Patient Register or the Danish Register of Causes of Death. The AF cases include a minor proportion of atrial flutter cases.[21] An outpatient diagnosis had to be followed by at least one subsequent in- or outpatient diagnosis or death to be counted, and the first registered date defined the date of the event. Among individuals whose first AF diagnosis was an outpatient diagnosis, around 9% were not registered with a second AF diagnosis. For the remaining of these individuals, the median time to the second AF diagnosis was 0.4 years (IQR: 0.1–2.1 years). The Danish National Patient Register contains information on all hospital inpatients since 1977, as well as information on both hospital in- and outpatients since 1995.[22] For each observation, the date of diagnosis and primary and secondary diagnosis codes are registered. A previous study has found a high validity of in- and outpatient AF diagnoses in this register, reporting that the positive predictive value of a first-time diagnosis was 95%.[23] The Danish Register of Causes of Death contains information on all individuals dying in Denmark since 1970.

Statistical Analysis

First, the cumulative prevalence of AF at the end of the study period was calculated as the number of AF cases alive with a registered diagnosis from 1994 to 2018 divided by the number of individuals aged ≥18 years on 1 January 2019. Second, time trends in the incidence of AF were investigated by calculating annual incidence rates; that is, the number of incident AF cases with no previous diagnosis registered in the past 10 years (ie, a 10-year washout period) divided by the person-time contributed by the population free of AF on 1 January in the same calendar year. Person-time was counted as the number of days that the population was at risk of AF, that is, the population was followed until the first occurrence of

an AF diagnosis or death from any cause. Average annual changes in incidence rates were estimated by Poisson regression models including calendar year and age as covariates. Numbers were age-standardized by direct standardization to the age distribution of a Nordic standard population (the NORDCAN population in 2000).[24] Third, previously published Norwegian data available from 1994 to 2014 were reanalyzed using identical methods to explore the findings' generalizability to a neighboring country with a comparable health care system.[13] The Norwegian data are described in Supplementary Material 1. Due to the availability of the Norwegian data, Danish data were also studied from 1994.

In sensitivity analyses, the impact of different methodological choices — ie the inclusion of information from various data sources and patient types, the strictness of the case definition (that is, whether an outpatient diagnosis had to be followed by at least one subsequent in- or outpatient diagnosis to be counted as a case or not), and the length of the washout period when considering incident cases — was investigated.

The statistical analyses were carried out using R version 4.0.2 for the Danish data and Stata/SE version 16.1 for the Norwegian data.

Results

We included 5,910,223 individuals aged ≥18 years who lived in Denmark at any point during 2004–2018. Among these, 246,527 individuals were registered with one or more AF diagnoses during the study period resulting in a total of 248,256 incident AF events.

Women constituted 45.9% of the incident events and had a higher mean age at diagnosis (77.2 years, *SD* 11.9) than men (71.2 years, *SD* 12.7) (Supplementary Table S1). However, in both sexes, the mean age at diagnosis increased during the study period, corresponding to an overall increase from 73.8 to 74.8 years. About 2.5% of the individuals with incident events were younger than 45 years at the time of diagnosis, 19.5% were 45–64 years, 57.9% were 65–84 years, and 20.0% were ≥85 years. The proportion of men was higher in all age groups except in the oldest category.

Prevalence and Incidence of Atrial Fibrillation

The cumulative prevalence of AF was 3.0% (3.6% in men and 2.4% in women) in 2018, corresponding to 138,844 individuals living with AF (58.6% men and 41.4% women). The prevalence increased steadily with age, but men had a higher prevalence than women in all age groups (Table 1 and Figure 1).

Table 1 Cumulative Prevalence of Atrial Fibrillation in Denmark from 1994 to 2018 by Age,

Age Group	Men			Women			Total		
	Cases	Population	Prevalence (%)	Cases	Population	Prevalence (%)	Cases	Population	Prevalence (%)
18–24	105	269,115	0.0	41	257,583	0.0	146	526,698	0.0
25–29	222	199,185	0.1	77	191,713	0.0	299	390,898	0.1
30–34	314	176,119	0.2	108	169,200	0.1	422	345,319	0.1
35–39	542	166,929	0.3	200	164,236	0.1	742	331,165	0.2
40–44	1007	185,973	0.5	309	185,499	0.2	1316	371,472	0.4
45–49	1811	195,363	0.9	634	194,051	0.3	2445	389,414	0.6
50–54	3215	211,916	1.5	1204	208,301	0.6	4419	420,217	1.1
55–59	4750	188,389	2.5	1897	188,268	1.0	6647	376,657	1.8
60–64	7089	169,607	4.2	3122	172,890	1.8	10,211	342,497	3.0
65–69	10,462	156,241	6.7	5139	163,915	3.1	15,601	320,156	4.9
70–74	16,037	158,514	10.1	9201	169,695	5.4	25,238	328,209	7.7
75–79	14,641	103,927	14.1	10,169	119,885	8.5	24,810	223,812	11.1
80–84	11,162	61,700	18.1	10,218	80,351	12.7	21,380	142,051	15.1
85–89	6779	29,495	23.0	8255	47,420	17.4	15,034	76,915	19.5
90–94	2719	10,553	25.8	5093	24,108	21.1	7812	34,661	22.5
95–99	500	1915	26.1	1590	7057	22.5	2090	8972	23.3
≥100	44	163	27.0	188	942	20.0	232	1105	21.0
All ages	81,399	2,285,104	3.6	57,445	2,345,114	2.4	138,844	4,630,218	3.0
Age-standardised									2.7

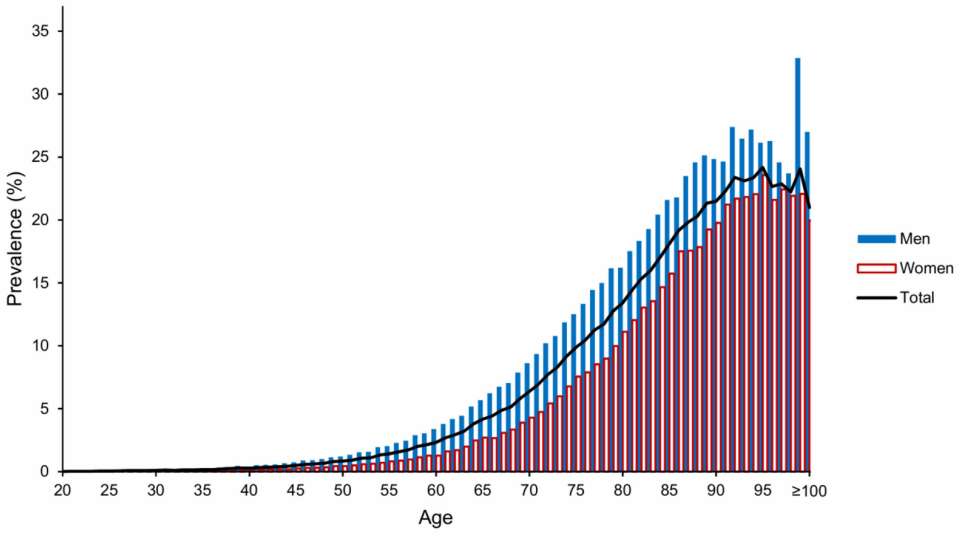

Figure 1 Cumulative prevalence of atrial fibrillation in Denmark from 1994 to 2018 by age.

The age-standardized incidence rate of AF increased from 391 per 100,000 person-years in 2004 to 481 per 100,000 person-years in 2015 (1.7% average annual increase), after which it declined to 367 per 100,000 person-years in 2018 (8.5% average annual decrease) (Tables 2 and 3 and Figure 2). Although the incidence rates generally were higher among men and older individuals, a similar time trend was observed in both men and women irrespective of age (Figure 3).

Comparison of Atrial Fibrillation Occurrence in Denmark and Norway

Focusing on the period before 2015, when comparable Danish and Norwegian data were available, the age-standardized cumulative prevalence of AF was 2.7% in the Danish population and 3.1% in the Norwegian population in 2014.

With regard to time trends in AF incidence, the Norwegian data were only available for inpatient diagnoses and deaths. However, the Danish data suggested that 98.5% of all incident events were eventually captured when only inpatient diagnoses and deaths were included and general descriptive statistics, such as the sex distribution, the mean age at diagnosis, and the proportion of inpatient diagnoses and deaths (Supplementary Table S2), did not differ from that of the total sample.

Thus, in 2004 the age-standardized incidence rate of AF inpatient diagnoses and deaths was 370 (95% CI: 362–378) per 100,000 person-years in Denmark and 483 (95% CI: 473–493) per 100,000 person-years in Norway. However, while the Danish incidence rate increased from 2004 to 2014 to 460 (95% CI: 452–469) per 100,000 person-years corresponding to an average annual increase of 2.0% (IRR: 1.020 (95% CI: 1.019–1.022); $p < 0.001$), the corresponding Norwegian incidence rate remained stable at 487 (95% CI: 478–496) per 100,000 person-years (IRR: 0.998 (0.996–0.999); $p < 0.01$) (Figure 4). The Danish incidence rates based on AF inpatient diagnoses and deaths were slightly lower than those based on both in- and outpatient diagnoses and deaths.

Sensitivity Analyses

The vast majority of AF cases in Denmark and Norway were registered in the public hospitals' somatic departments (Supplementary Table S3). Inclusion of information from private hospitals and specialists with reimbursement contracts, as well as information on psychiatric patients, did not influence the prevalence estimates. Yet, the strictness of the case definition did; that is, whether an outpatient diagnosis was not counted as a case unless it was followed by at least one subsequent diagnosis or death (referred to as a "strict" case definition), or whether all in- and outpatient diagnoses were counted as cases (referred to as a "wide" case definition). For instance, the age-standardized cumulative prevalence in Denmark increased from 2.7% using the strict definition to 3.1% using the wide case

Table 2 Age-Standardized Incidence Rates of Atrial Fibrillation per100,000 Person-Years in Denmark 2004–2018 by Calendar Year, Sex, and Age Group

	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Men															
18–44 years															
Incidence rate	30	36	37	35	36	37	37	38	39	36	34	38	32	31	26
Cases	302	367	375	350	363	367	357	364	364	330	315	346	287	276	222
45–64 years															
Incidence rate	286	310	302	300	318	312	327	335	325	326	328	317	315	288	260
Cases	2076	2296	2272	2297	2428	2419	2494	2552	2440	2422	2415	2344	2323	2137	1931
65–84 years															
Incidence rate	1662	1636	1591	1648	1602	1657	1763	1808	1870	1950	1837	1922	1804	1614	1402
Cases	4327	4316	4250	4431	4441	4648	5104	5406	5729	6141	5967	6383	6197	5725	5096
≥85 years															
Incidence rate	3506	3779	3918	3856	4527	4083	4826	4333	5142	5086	6209	5710	5491	4921	4384
Cases	848	859	874	913	937	921	1021	1073	1162	1188	1311	1370	1318	1284	1138
All ages															
Incidence rate	489	502	495	502	517	514	556	555	583	595	602	603	573	516	454
Cases	7553	7838	7771	7991	8169	8355	8976	9395	9695	10,081	10,008	10,443	10,125	9422	8387
Women															
18–44 years															
Incidence rate	11	10	12	14	13	12	14	15	13	13	13	12	12	10	7
Cases	107	100	120	135	126	119	130	140	122	117	118	111	106	86	60
45–64 years															
Incidence rate	128	122	137	141	144	148	140	144	153	154	143	140	134	123	104
Cases	952	927	1066	1099	1136	1175	1122	1130	1192	1180	1091	1073	1037	958	806
65–84 years															
Incidence rate	1109	1117	1111	1134	1138	1147	1222	1250	1254	1246	1237	1258	1165	1091	926
Cases	3997	4028	3983	4051	4076	4139	4439	4628	4739	4815	4863	5077	4826	4653	4059
≥85 years															
Incidence rate	2886	3233	3218	3129	3173	3402	3478	3935	4010	3797	4136	4533	3970	4056	3760
Cases	1685	1772	1831	1895	1775	1945	2033	2168	2186	2148	2182	2319	2150	2107	1837
All ages															
Incidence rate	315	323	327	331	333	341	355	373	378	371	374	386	354	338	294
Cases	6741	6827	7000	7180	7113	7378	7724	8066	8239	8260	8254	8580	8119	7804	6762

(*Continued*)

https://doi.org/10.2147/CLEP.S374468

Table 2 (Continued).

	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Total															
18–44 years															
Incidence rate	20	23	25	24	25	25	25	26	26	25	24	25	22	20	16
Cases	409	467	495	485	489	486	487	504	486	447	433	457	393	362	282
45–64 years															
Incidence rate	207	216	219	220	230	229	232	238	238	238	234	227	223	204	180
Cases	3028	3223	3338	3396	3564	3594	3616	3682	3632	3602	3506	3417	3360	3095	2737
65–84 years															
Incidence rate	1342	1338	1319	1355	1341	1371	1461	1497	1526	1557	1504	1553	1450	1324	1139
Cases	8324	8344	8233	8482	8517	8787	9543	10,034	10,468	10,956	10,830	11,460	11,023	10,378	9155
≥85 years															
Incidence rate	3049	3387	3386	3296	3465	3548	3779	4060	4279	4092	4585	4857	4352	4314	3981
Cases	2533	2631	2705	2808	2712	2866	3054	3241	3348	3336	3493	3689	3468	3391	2975
All ages															
Incidence rate	391	403	401	405	410	417	440	456	467	467	467	481	448	418	367
Cases	14,294	14,665	14,771	15,171	15,282	15,733	16,700	17,461	17,934	18,341	18,262	19,023	18,244	17,226	15,149

Notes: Incidence rates including 95% CIs are illustrated in Figures 2 and 3.

https://doi.org/10.2147/CLEP.S374468 DovePress

Table 3 Average Annual Change in Incidence Rates of Atrial Fibrillation in Denmark 2004–2015 and 2015–2018, Respectively, by Sex and Age Group

	Cases	2004–2015	*p*	Cases	2015–2018	*p*
		Incidence Rate Ratio (95% CI)			Incidence Rate Ratio (95% CI)	
Men						
18–44 years	4200	1.010 (1.001–1.019)	0.02	1131	0.880 (0.835–0.927)	<0.001
45–64 years	28,455	1.009 (1.006–1.013)	<0.001	8735	0.933 (0.916–0.951)	<0.001
65–84 years	61,143	1.017 (1.015–1.019)	<0.001	23,401	0.902 (0.892–0.913)	<0.001
≥85 years	12,477	1.028 (1.023–1.034)	<0.001	5110	0.935 (0.912–0.958)	<0.001
All ages	106,275	1.017 (1.015–1.019)	<0.001	38,377	0.913 (0.905–0.921)	<0.001
Women						
18–44 years	1445	1.016 (1.001–1.031)	0.04	363	0.836 (0.762–0.918)	<0.001
45–64 years	13,143	1.011 (1.006–1.016)	<0.001	3874	0.909 (0.883–0.935)	<0.001
65–84 years	52,835	1.013 (1.011–1.016)	<0.001	18,615	0.909 (0.897–0.920)	<0.001
≥85 years	23,939	1.023 (1.020–1.027)	<0.001	8413	0.936 (0.918–0.954)	<0.001
All ages	91,362	1.016 (1.014–1.018)	<0.001	31,265	0.916 (0.907–0.926)	<0.001
Total						
18–44 years	5645	1.011 (1.003–1.019)	<0.01	1494	0.869 (0.830–0.910)	<0.001
45–64 years	41,598	1.009 (1.007–1.012)	<0.001	12,609	0.925 (0.911–0.940)	<0.001
65–84 years	113,978	1.016 (1.014–1.018)	<0.001	42,016	0.905 (0.898–0.913)	<0.001
≥85 years	36,416	1.026 (1.023–1.029)	<0.001	13,523	0.936 (0.922–0.950)	<0.001
All ages	197,637	1.017 (1.016–1.018)	<0.001	69,642	0.915 (0.909–0.921)	<0.001

definition. The age-standardization in itself also influenced the findings. Thus, when using the Nordic standard population, the cumulative prevalence decreased from 3.0% (crude) to 2.7% (age-standardized) in Denmark while remaining the same in Norway.

Likewise, the length of the washout period when considering incident cases influenced the reported findings such that the longer the washout period, the smaller the proportion of recurrent individuals among the incident cases (Supplementary Table S4). Using an 8-year washout period, 11.4% of the cases defined as incident had been registered with AF >8 years ago and were, in fact, recurrent in 2018. This number decreased to 7.0% when using a 10-year washout

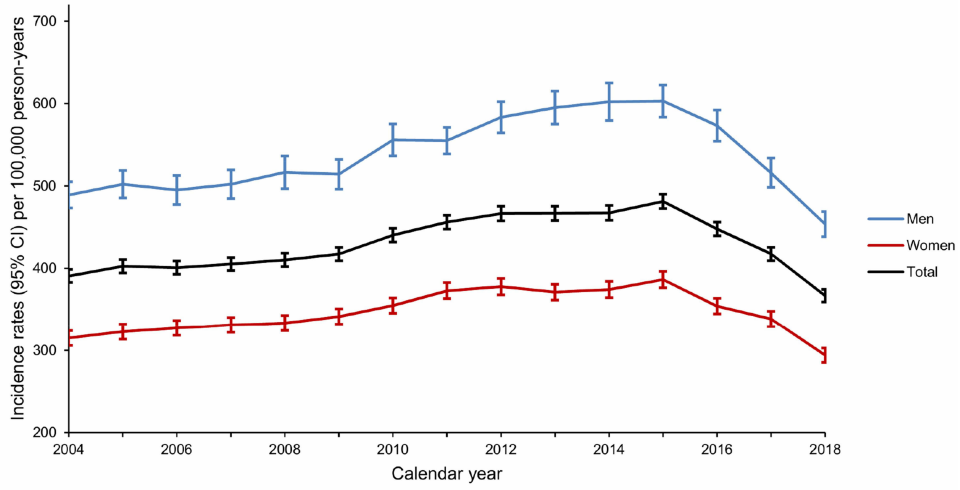

Figure 2 Age-standardized incidence rates with 95% CI of atrial fibrillation per100,000 person-years in Denmark from 2004 to 2018 by calendar year and sex.

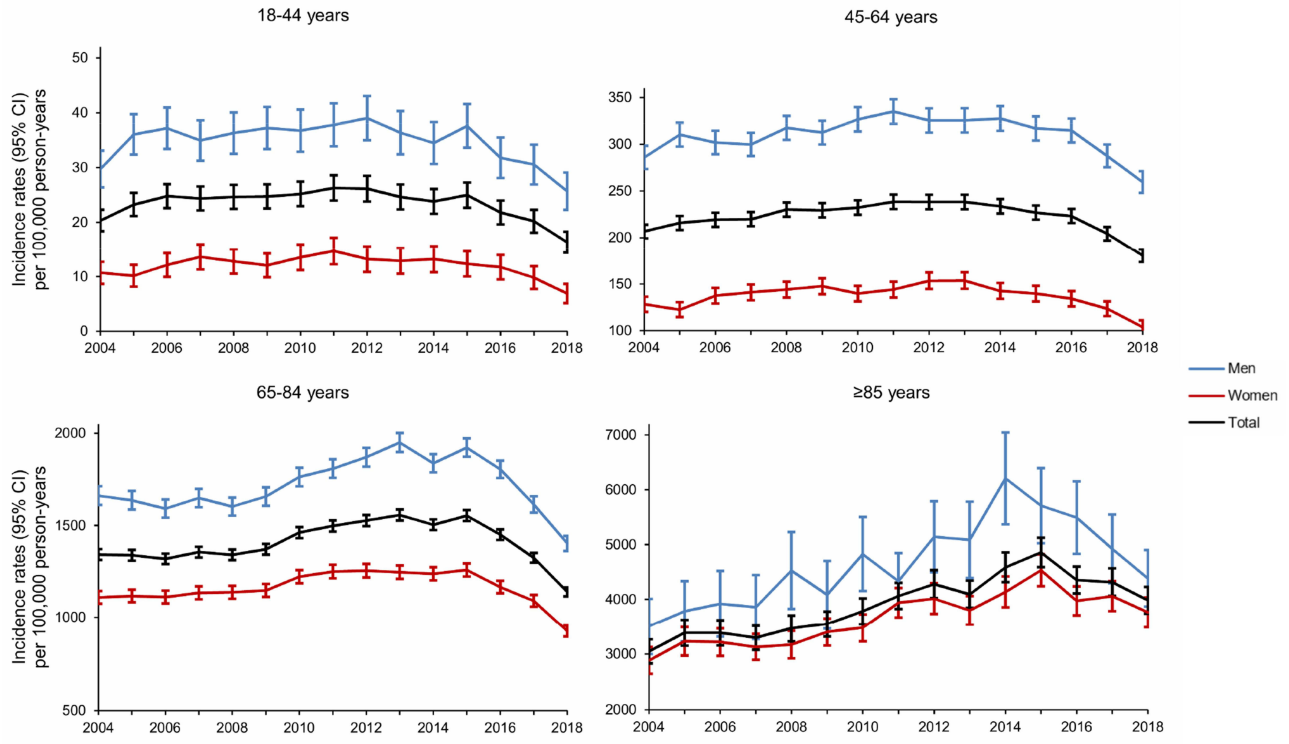

Figure 3 Age-standardized incidence rates with 95% CI of atrial fibrillation per 100,000 person-years in Denmark from 2004 to 2018 by calendar year, sex, and age group.

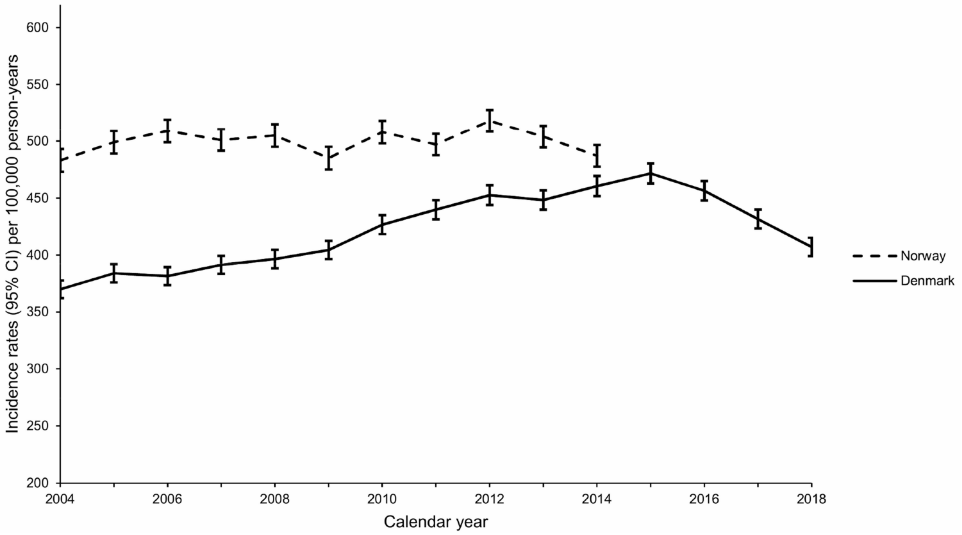

Figure 4 Age-standardized incidence rates with 95% CI of atrial fibrillation inpatient diagnoses and deaths per 100,000 person-years in Norway 2004–2014 and Denmark 2004–2018 by calendar year.

period and 4.5% when using a 12-year washout period. Yet, irrespective of the length of the washout period, the proportion of recurrent individuals among the incident cases was found to increase over time. This could not solely be explained by the extended length of the observation period since using a fixed time window of observation of recurrent cases pointed to the same finding (eg when using a 10-year washout period with a fixed 5 extra years of observation to check for events before the 10-year time window, the proportion of recurrent individuals among the incident cases

increased from 3.1% in 2010 to 5.0% in 2018). The length of the washout period also influenced the incidence rates. More specifically, the incidence rate ratios suggested smaller average annual changes in incidence rates with increasing length of washout period during 2004–2015 when the incidence rates were increasing, but numerically larger average annual changes with increasing length of washout period during 2015–2018 when the incidence rates were declining (Supplementary Figure S1).

Discussion

Main Findings

In Denmark, the cumulative prevalence of AF was 3.0% in 2018. The incidence rate increased from 2004 to 2015 after which it declined steeply until the end of follow-up in 2018. Comparing the reported prevalence and incidence to corresponding Norwegian estimates before 2015 using the same approach, the Norwegian prevalence was higher, and the incidence rate remained stable over time and was likewise at a higher level. Both prevalence and incidence rate estimates varied according to the AF case definition and length of washout period, highlighting the need for transparent and thorough descriptions of study methodology in order to compare results across studies.

Comparison with the Existing Literature

The finding of a cumulative prevalence of AF of 3.0% in Denmark in 2018 is consistent with a large data synthesis covering 182 studies reporting an overall sex- and age-adjusted prevalence of 2.8% (95% CI: 2.3–3.4%) among adults.[6] However, both in Denmark and Norway, the cumulative prevalence varied with changing case definitions. When using a wide definition, where all in- and outpatient diagnoses were counted as cases, the prevalence estimates were 0.3–0.4% percentage points higher than when using a stricter definition, in which an outpatient diagnosis was not counted as a case unless it was followed by at least one subsequent diagnosis or death. Furthermore, findings from a previous study suggest that the cumulative prevalence increases with increasing retrospective time window for up to 10 years.[25] Yet, we found that the cumulative prevalence remained stable irrespective of whether it was based on a 20- or 25-year retrospective time window, suggesting that time windows of such length may not be of major importance. Age-standardizing the cumulative prevalence to the age distribution of the Nordic standard population, on the other hand, resulted in a lower estimate in Denmark compared to the crude number, while the Norwegian estimate was not affected. Overall, these findings highlight the need for the use of the exact same case definitions and standard populations when comparing prevalence estimates across countries.

With regard to AF incidence, our finding of increasing incidence rates in Denmark during 2004–2015 is in line with previously reported time trends in Denmark during 1983–2015,[10,18] while corresponding incidence rates in Norway remained stable Generally, varying time trends may be explained by factors such as populations' different risk factor profiles and health care systems. However, although the Danish and Norwegian populations do not have the same prevalence of risk factors, as smoking and alcohol consumption are at somewhat higher levels in Denmark,[26] we are not aware of any particular differences between the two populations that can explain their varying time trends. Furthermore, we are not aware of any changing trends in risk factors preceding the decline in incidence rate in Demark from 2015 to 2018, as estimates have shown steady declining trends in prevalence of raised blood pressure and increase in obesity since 1975.[27,28] Still, the finding is consistent with estimates from the Global Burden of Disease database pointing to varying time trends between European countries during 1990–2017.[10,18,19] Thus, in Denmark and Sweden, the incidence rates showed an initial increase followed by a subsequent decline, consistent with our study, while there was no evidence of a general increase in incidence rates for other countries.

The observed time trend may be partly explained by changes in clinical practice and policy initiatives, such as the introduction of direct oral anticoagulants and new guidelines increasing eligibility and tolerability for anticoagulation, new and more available ablation procedures, as well as an increased focus on AF.[29,30] However, such mechanisms can most likely not explain the sudden change in the direction of the time trend although policy initiatives in some circumstances may have extreme impacts, as suggested by a Danish study reporting a 47% decline in AF incidence following a national lockdown due to COVID-19.[31] Another possible explanation of the observed time trend is an

increased case detection rate. For instance, in the Framingham Heart Study, US, incidence rates were found to increase when cases were identified by all available health data sources but remained stable when cases were identified by ECG at routine study visits.[17] In other words, the observed initial increase in incidence rates may be linked to an increased case detection rate due to enhanced surveillance, such as increased use of standard ECG.[32] After some time with enhanced surveillance, the pool of undetected AF cases may diminish, which may eventually shift the number of identified cases downwards resulting in an inverse U-shaped trend.

Finally, it is important to mention that our study's methodological choices also influenced the time trends. Previously, we have shown how the length of the washout period influenced incidence rates of AF inpatient contacts in Norway.[13] Using a 10-year washout period, less than 5% of the cases defined as incident were recurrent, but this number increased substantially with shorter washout periods. Interestingly, in our current study, we found that the proportion of recurrent cases classified as incident (that is, individuals who had previously been diagnosed with AF, but had not had any AF events during the entire washout period) increased over time, even when we used a fixed washout period. This suggests that we would have to use a dynamic washout period with increasing size over time to keep the misclassification rate below 5%. The increasing misclassification over time may have biased the observed time trend upwards, suggesting that the initial increase is somewhat overestimated, while the subsequent decline is underestimated. Therefore, we chose to demonstrate how varying washout periods influenced the reported time trends. Our findings are in line with a previous study that reported incidence rates to be influenced by both the case definition algorithm and the length of the washout period.[25]

Strengths and Limitations

The major strength of this study is its nationwide study design, including the entire Danish population ≥18 years during 2004–2018. Moreover, the use of individual-level information from national administrative registers guaranteed a continuous and complete follow-up of the study population, as well as reliable and valid information on AF. Another strength is that we were able to compare AF prevalence and incidence rates using identical case definitions and analyses in two countries with comparable healthcare systems and health registries.

However, since the Norwegian data were only available for the first part of the study period, we do not know whether the recent steep decline in incidence rates observed in Denmark may be similar in Norway. Moreover, the use of administrative register data makes it hard to distinguish time trends in biological disease from time trends in the use of and access to health care services. As the reported time trends depend on the length of the washout period when considering incident cases, the choice of the washout period is important. To determine what constitutes a sensible length of washout period, we would need to disentangle the impact of longer survival and better treatment for comorbid cardiovascular diseases from the impact of increased access to health care services over time, which unfortunately is not possible. It is also important to bear in mind that the use of hospital administrative register data likely has resulted in an underestimation of the "true" occurrence of AF as some individuals with diagnosed AF may only be seen in primary care practices,[11] Linkage to national prescription data was not available. Prescription data would have refined our assessment of individuals with only one registered outpatient AF diagnosis. Moreover, it is estimated that 15–25% of all individuals with AF remain undiagnosed.[33,34] Finally, the generalizability of register-based studies may be compromised by variation in coding practices across time and place.

Conclusion

The cumulative prevalence of AF is currently around 3.0% in Denmark, while the incidence rate has declined since 2015. Compared to Norway, the Danish incidence rates are lower, and the shape of the time trends differ between these neighboring nations with comparable health care systems. Lastly, estimated prevalence and incidence rates are influenced by AF case definition and lengths of washout periods, which need to be precisely reported in order to compare findings from various studies and over time.

Abbreviations

AF, atrial fibrillation; CI, confidence interval; ICD, International Classification of Diseases; IRR, incidence rate ratio; PY, person-year.

Data Sharing Statement

The authors are not allowed to make the used register data available to others but interested readers can apply to the Danish Health Data Authority and Statistics Denmark to obtain access to the registers. The analytic code will be shared immediately following publication with anyone who wishes to access this document for any purpose. Requests should be directed to emhe@sund.ku.dk.

Acknowledgments

The authors thank Tomislav Dimoski at The Norwegian Institute of Public Health for his contribution by developing the software necessary for obtaining data from Norwegian hospitals, conducting the data collection and quality assurance of data in this project.

Funding

This work was partly supported by the Novo Nordisk Foundation Challenge Programme: Harnessing the Power of Big Data to Address the Societal Challenge of Aging [NNF17OC0027812]. LJK was supported by the Research Council of Norway as part of the International Pregnancy Drug Safety Studies (InPreSS, project no. 273366) and NordForsk as part of the Nordic Pregnancy Drug Safety Studies (NorPreSS, project no. 83539). The sponsors had no involvement in any of the stages from study design to submission of the paper for publication.

Disclosure

Trygve Berge reports speaking fees from Boehringer-Ingelheim, Bayer and Pfizer/Bristol-Myers Squibb, outside the submitted work. The authors report no other potential conflicts of interest in this work.

References

1. Staerk L, Wang B, Preis SR, et al. Lifetime risk of atrial fibrillation according to optimal, borderline, or elevated levels of risk factors: cohort study based on longitudinal data from the Framingham Heart Study. *BMJ*. 2018;361:k1453. doi:10.1136/bmj.k1453
2. Krijthe BP, Kunst A, Benjamin EJ, et al. Projections on the number of individuals with atrial fibrillation in the European Union, from 2000 to 2060. *Eur Heart J*. 2013;34:2746–2751. doi:10.1093/eurheartj/eht280
3. Hindricks G, Potpara T, Dagres N, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS). *Eur Heart J*. 2020;42(5):373–498.
4. Rienstra M, Van Gelder IC. Incidence and outcome of atrial fibrillation: diversity throughout Europe. *Eur Heart J*. 2021;42:858–860. doi:10.1093/eurheartj/ehaa1078
5. Yang PS, Ryu S, Kim D, et al. Variations of prevalence and incidence of atrial fibrillation and oral anticoagulation rate according to different analysis approaches. *Sci Rep*. 2018;8:6856. doi:10.1038/s41598-018-25111-6
6. Ball J, Carrington MJ, McMurray JJ, Stewart S. Atrial fibrillation: profile and burden of an evolving epidemic in the 21st century. *Int J Cardiol*. 2013;167:1807–1824. doi:10.1016/j.ijcard.2012.12.093
7. Adderley NJ, Ryan R, Nirantharakumar K, Marshall T. Prevalence and treatment of atrial fibrillation in UK general practice from 2000 to 2016. *Heart*. 2019;105:27–33. doi:10.1136/heartjnl-2018-312977
8. Rodriguez-Manero M, Lopez-Pardo E, Cordero-Fort A, et al. Prevalence and outcomes of atrial fibrillation in a European healthcare area gained through the processing of a health information technology system. *Rev Port Cardiol*. 2019;38:21–29. doi:10.1016/j.repc.2018.06.008
9. Marzona I, Proietti M, Vannini T, et al. Sex-related differences in prevalence, treatment and outcomes in patients with atrial fibrillation. *Intern Emerg Med*. 2020;15:231–240. doi:10.1007/s11739-019-02134-z
10. Schmidt M, Ulrichsen SP, Pedersen L, Botker HE, Nielsen JC, Sorensen HT. 30-year nationwide trends in incidence of atrial fibrillation in Denmark and associated 5-year risk of heart failure, stroke, and death. *Int J Cardiol*. 2016;225:30–36. doi:10.1016/j.ijcard.2016.09.071
11. Friberg L, Bergfeldt L. Atrial fibrillation prevalence revisited. *J Intern Med*. 2013;274:461–468. doi:10.1111/joim.12114
12. Lehto M, Halminen O, Mustonen P, et al. The nationwide Finnish anticoagulation in atrial fibrillation (FinACAF): study rationale, design, and patient characteristics. *Eur J Epidemiol*. 2022;37:95–102. doi:10.1007/s10654-021-00812-x
13. Kjerpeseth LJ, Igland J, Selmer R, et al. Prevalence and incidence rates of atrial fibrillation in Norway 2004–2014. *Heart*. 2020;107(3):201–207. doi:10.1136/heartjnl-2020-316624
14. Miyasaka Y, Barnes ME, Gersh BJ, et al. Secular trends in incidence of atrial fibrillation in Olmsted County, Minnesota, 1980 to 2000, and implications on the projections for future prevalence. *Circulation*. 2006;114:119–125. doi:10.1161/CIRCULATIONAHA.105.595140
15. Chamberlain AM, Gersh BJ, Alonso A, et al. Decade-long trends in atrial fibrillation incidence and survival: a community study. *Am J Med*. 2015;128:260–267. doi:10.1016/j.amjmed.2014.10.030
16. Stefansdottir H, Aspelund T, Gudnason V, Arnar DO. Trends in the incidence and prevalence of atrial fibrillation in Iceland and future projections. Europace: European pacing, arrhythmias, and cardiac electrophysiology: journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the. *Eur Soc Cardiol*. 2011;13:1110–1117.

17. Schnabel RB, Yin X, Gona P, et al. 50 year trends in atrial fibrillation prevalence, incidence, risk factors, and mortality in the Framingham Heart Study: a cohort study. *Lancet*. 2015;386:154–162. doi:10.1016/S0140-6736(14)61774-8
18. Wodschow K, Bihrmann K, Larsen ML, Gislason G, Ersboll AK. Geographical variation and clustering are found in atrial fibrillation beyond socioeconomic differences: a Danish cohort study, 1987–2015. *Int J Health Geogr*. 2021;20:11. doi:10.1186/s12942-021-00264-2
19. Al-Khayatt BM, Salciccioli JD, Marshall DC, Krahn AD, Shalhoub J, Sikkel MB. Paradoxical impact of socioeconomic factors on outcome of atrial fibrillation in Europe: trends in incidence and mortality from atrial fibrillation. *Eur Heart J*. 2021;42:847–857. doi:10.1093/eurheartj/ehaa1077
20. Copenhagen Healthtech Cluster. The central person registry [Internet]; 2020.
21. Rix TA, Riahi S, Overvad K, Lundbye-Christensen S, Schmidt EB, Joensen AM. Validity of the diagnoses atrial fibrillation and atrial flutter in a Danish patient registry. *Scand Cardiovasc J*. 2012;46:149–153. doi:10.3109/14017431.2012.673728
22. Lynge E, Sandegaard JL, Rebolj M. The Danish National patient register. *Scand J Public Health*. 2011;39:30–33. doi:10.1177/1403494811401482
23. Sundboll J, Adelborg K, Munch T, et al. Positive predictive value of cardiovascular diagnoses in the Danish National Patient Registry: a validation study. *BMJ open*. 2016;6:e012832. doi:10.1136/bmjopen-2016-012832
24. Engholm G, Ferlay J, Christensen N, et al. NORDCAN–a Nordic tool for cancer information, planning, quality control and research. *Acta oncologica*. 2010;49:725–736. doi:10.3109/02841861003782017
25. Hawkins NM, Daniele PR, Humphries KH, et al. Empirical insights when defining the population burden of atrial fibrillation and oral anticoagulation utilization using administrative data. *Can J Cardiol*. 2019;35:1412–1415. doi:10.1016/j.cjca.2019.05.009
26. Ásgeirsdóttir TL, Gerdtham UG. Health behavior in the Nordic countries. *Nord J Health Econ*. 2016;4:28–40. doi:10.5617/njhe.2717
27. Collaboration NCDRF. Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19.1 million participants. *Lancet*. 2017;389:37–55. doi:10.1016/S0140-6736(16)31919-5
28. Collaboration NCDRF. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. *Lancet*. 2017;390:2627–2642. doi:10.1016/S0140-6736(17)32129-3
29. Weber C, Hung J, Hickling S, Li I, McQuillan B, Briffa T. Drivers of hospitalisation trends for non-valvular atrial fibrillation in Western Australia, 2000–2013. *Int J Cardiol*. 2019;276:273–277. doi:10.1016/j.ijcard.2018.09.047
30. Mendonca SC, Saunders CL, Lund J, Mant J, Edwards D. Temporal trends in incidence of atrial fibrillation in primary care records: a population-based cohort study. *BMJ Open*. 2020;10:e042518. doi:10.1136/bmjopen-2020-042518
31. Holt A, Gislason GH, Schou M, et al. New-onset atrial fibrillation: incidence, characteristics, and related events following a national COVID-19 lockdown of 5.6 million people. *Eur Heart J*. 2020;41:3072–3079. doi:10.1093/eurheartj/ehaa494
32. Williams BA, Chamberlain AM, Blankenship JC, Hylek EM, Voyce S. Trends in atrial fibrillation incidence rates within an integrated health care delivery system, 2006 to 2018. *JAMA Netw Open*. 2020;3:e2014874. doi:10.1001/jamanetworkopen.2020.14874
33. Jones NR, Taylor CJ, Hobbs FDR, Bowman L, Casadei B. Screening for atrial fibrillation: a call for evidence. *Eur Heart J*. 2020;41:1075–1085. doi:10.1093/eurheartj/ehz834
34. Yao RJR, Andrade JG, Deyell MW, Jackson H, McAlister FA, Hawkins NM. Sensitivity, specificity, positive and negative predictive values of identifying atrial fibrillation using administrative data: a systematic review and meta-analysis. *Clin Epidemiol*. 2019;11:753–767. doi:10.2147/CLEP.S206267