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

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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...
1994 to 2014. 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. Thus, the incidence rate was reported to increase from 1983 to 2015 in Denmark, while we reported stable incidence rates from 2004 to 2014 in Norway. 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. 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, 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. 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. 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%. 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). 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. 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, Sex, and Total

| 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
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 per 100,000 Person-Years in Denmark 2004–2018 by Calendar Year, Sex, and Age Group

| 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  | 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 | 1657 | 1763 | 1808 | 1870 | 1950 | 1837 | 1922 | 1804 | 1614 | 1402 | 1380 |
| Cases     | 4327 | 4316 | 4250 | 4411 | 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  | 12  | 14  | 14  | 12  | 14  | 15  | 13  | 13  | 13  | 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 | 1122 | 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 |
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   | 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  | 234  | 238  | 234  | 223  | 204  | 180  |
| Cases                | 3028 | 3223 | 3338 | 3396 | 3564 | 3616 | 3682 | 3632 | 3602 | 3417 | 3360 | 3095 | 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 | 11,032 | 10,378 | 9,155 |
| ≥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.
Table 3  Average Annual Change in Incidence Rates of Atrial Fibrillation in Denmark 2004–2015 and 2015–2018, Respectively, by Sex and Age Group

|       | 2004–2015 |       |       | 2015–2018 |       |       |
|-------|-----------|-------|-------|-----------|-------|-------|
|       | Cases     | Incidence Rate Ratio (95% CI) | p      | Cases     | Incidence Rate Ratio (95% CI) | p      |
| 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 period.
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 (e.g., 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

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.
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. 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. 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, 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, 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 Denmark from 2015 to 2018, as estimates have shown steady declining trends in prevalence of raised blood pressure and increase in obesity since 1975. 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. 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. 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. 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. 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. 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. 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.

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. 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. 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.

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Disclosure
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