Prevalence and incidence rates of atrial fibrillation in Norway 2004–2014

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ABSTRACT

Objective To study time trends in incidence of atrial fibrillation (AF) in the entire Norwegian population from 2004 to 2014, by age and sex, and to estimate the prevalence of AF at the end of the study period.

Methods A national cohort of patients with AF (≥18 years) was identified from inpatient admissions with AF and deaths with AF as underlying cause (1994–2014), and AF outpatient visits (2008–2014) in the Cardiovascular Disease in Norway (CVDNOR) project. AF admissions or out-of-hospital death from AF, with no AF admission the previous 10 years defined incident AF. Age-standardised incidence rates (IR) and incidence rate ratios (IRR) were calculated. All AF cases identified through inpatient admissions and outpatient visits and alive as of 31 December 2014 defined AF prevalence.

Results We identified 175 797 incident AF cases (30% primary diagnosis, 69% secondary diagnosis, 0.6% out-of-hospital deaths). IRs (95% confidence intervals) per 100 000 person years were stable from 2004 (433 (426–440)) to 2014 (440 (433–447)). IRs were stable or declining across strata of sex and age with the exception of an average yearly increase of 2.4% in 18–44-year-olds: IRR 1.024 (1.014–1.034). In 2014, the prevalence of AF in the adult population was 3.4%.

Conclusions We found overall stable IRs of AF for the adult Norwegian population from 2004 to 2014. The prevalence of AF was 3.4% at the end of 2014, which is higher than reported in previous studies. Signs of an increasing incidence of early-onset AF (<45 years) are worrying and need further investigation.

INTRODUCTION

Atrial fibrillation (AF) is an important prognostic indicator for stroke, heart failure, cardiovascular and all-cause mortality. The high mortality of patients with AF highlights the importance of disease surveillance for better healthcare resource allocation and for planning of preventive public health activities.

The reported incidence and prevalence of AF have been inconsistent across studies and countries, reflecting methodological differences making comparisons difficult. However, the majority of studies provide evidence of an increasing incidence of AF in Western societies. In Olmsted County (Minnesota, USA), incidence rates of AF (inpatients and outpatients) increased from 1980 to 2000 and then stabilised. In the Framingham Heart Study, incidence rates of AF (detected by all health data sources) increased from 1958 to 2007. In Denmark, the incidence of AF causing hospitalisation increased between 1983 and 2012, while in Iceland, incidence rates of AF (inpatients and outpatients) increased among women, but not men between 1991 and 2008. A pooled estimate of age-adjusted and sex-adjusted AF prevalence reported in population studies for the period 1968–2010 suggested a prevalence of 2.8% in the adult population. However, the estimates varied from 0.6% to 6.6%, reflecting differences in the age distribution of the study populations: from 20 years and older to 65 years and older.

We aimed to study trends in incidence of AF in Norway during 2004–2014, and to estimate the prevalence of AF, by age and sex.

METHODS

Data sources and data linkages

We used nationwide data on hospital visits and causes of death from the Cardiovascular Disease in Norway (CVDNOR) project. The data included time of admission and primary and secondary discharge diagnoses for all somatic inpatient hospital stays recorded in electronic patient administrative systems at all Norwegian hospitals during 1994–2009 and in the Norwegian Patient Registry from 2008 to 2014. The data also included visits to hospital outpatient clinics and to physician specialist practices with reimbursement contracts with the public health authorities registered in the Norwegian Patient Registry (2008–2014). These data were linked with data from the Norwegian Cause of Death Registry (1994–2014) and data on vital status (alive, dead or emigrated) on 1 January each year from Statistics Norway (1994–2014). The linkage was performed by Statistics Norway, using the national personal identification number.

This research was done without patient involvement.

Identification of incident and prevalent AF cases

AF was defined by the International Classification of Diseases, 9th Revision (ICD-9) diagnosis code 427.3 or ICD-10 diagnosis code I48 (including subcategories): AF and atrial fibrillation. AF cases thus included a minor proportion of atrial flutter
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The cohort of AF cases was identified from all inpatient admissions with AF as primary or secondary diagnosis during 1994–2014 and from out-of-hospital deaths with AF as underlying cause, in the adult population ≥18 years.

Incident AF was defined as the first inpatient admission with AF or out-of-hospital death due to AF with no previous inpatient admission with AF noted in the past 10 years. For the incidence analyses, we defined inpatient admissions with a primary or secondary diagnosis of AF as hospitalised AF, and AF as underlying cause of death in the Cause of Death Registry without a registered hospitalisation for AF as out-of-hospital AF death. A 10-year washout period was applied to minimise misclassification of recurrent cases as incident cases, while still allowing for a reasonably long study period. By this definition, less than 5% of incident cases in 2014 were recurrent cases, that is, they had received an inpatient AF diagnosis before 2014, but more than 10 years ago. Corresponding numbers using 6–9 years were 2% (online supplementary figure 1). The number of prevalent AF cases at the end of 2014 was estimated, using Poisson regression analyses with calendar year as a continuous covariate, expressed as average yearly change in incidence rates. Average yearly change in proportion with comorbidity among incident AF cases were estimated by risk ratios with 95% CI using binomial regression analyses with calendar year as continuous covariate. An interaction term between calendar year and sex was introduced to test potential sex-differences in time trends. Risk of comorbidity in men relative to women was assessed as risk ratios with 95% CI using age-adjusted binomial regression with sex as exposure variable. In addition to overall results, we report results stratified by sex and by age groups (18–44, 45–64, 65–84 and ≥85 years). Stata V.15.0 (Stata, College Station, Texas, USA) software was used for all analyses.

RESULTS
Study population
We identified 175 979 cases with incident AF in Norway from 2004 to 2014 (online supplementary figure 1). Of these, 30.0% had AF as the primary diagnosis at inpatient admission, 69.4% had AF as a secondary diagnosis at inpatient admission and 0.6% were out-of-hospital AF death cases. The proportion of incident cases with AF as the primary hospital discharge diagnosis increased from 2004 (27%) to 2014 (33%) overall and across all age and sex strata (online supplementary table 2).

Women accounted for 45% of the cohort of incident AF cases and had a higher mean age ± standard deviation at diagnosis (79.1 ± 11.2) than men (72.1 ± 13.0), both for primary and secondary AF diagnosis and over time (online supplementary table 3). Only 2% of the patients were younger than 45 years of age at diagnosis, 17% were 45–64, 55% were 65–84 and 26% were 85 years of age or older. The proportion of men was higher in all age groups except for the oldest group.

Comorbidity
Among hospitalised patients with AF as the primary diagnosis, 12% had CCI score of ≥2 in contrast to 38% among those with AF as a secondary diagnosis. The most prevalent comorbid conditions at incident inpatient admission for AF were hypertension (28%), coronary heart disease (25%), heart failure (21%) and pneumonia (13%). The majority of comorbidities were more common in men, especially co-occurring malignancy, renal disease and peripheral vascular disease. The exception was thyroid disorders, autoimmune diseases, hypertension, valvular heart disease, stroke, thromboembolism, dementia and frailty, which were more often present in women (online supplementary tables 4 and 5). The proportion with a CCI score ≥2 declined from 31% in 2004 to 28% in 2014 for all incident AF cases. A similar pattern was found for myocardial infarction, heart failure and diabetes, with somewhat more favourable decline over time in women than in men. For patients with AF as primary diagnosis, the proportion with co-occurring myocardial infarction increased and the proportion with heart failure was stable over time. In contrast, the co-occurrence of these conditions declined for patients with AF as secondary diagnosis (figure 1, online supplementary table 6).

Incidence
The age-standardised incidence rate of inpatient admission (primary or secondary diagnoses) or death from AF per 100 000 person years was stable, at 433 (95% CI 426 to 440) in 2004.
and 440 (95% CI 433 to 447) in 2014 (figure 2, table 1). On average, the total yearly incidence rate did not change markedly (−0.2%, 95% CI −0.3% to 0.0%, p=0.02). Consistent rates across all strata of age group and sex were observed with the exception of those aged 18–44 years where we observed a 2.4% (95% CI 1.4% to 3.4%, p<0.001) increase in the overall yearly incidence rate (women 2.1% (95% CI −0.1% to 4.3%, p=0.06), men 2.4% (95% CI 1.1% to 3.5%, p<0.001)) (figure 3, table 2).

The age-standardised incidence rate of inpatient admission with a primary diagnosis of AF per 100 000 person years increased from 117 (95% CI 113 to 120) in 2004 to 142 (95% CI 139 to 146) in 2014 (online supplementary figure 3 and table 3). The overall trend was a mean yearly increase of 1.9% (95% CI 1.7% to 2.2%, p<0.001). The increase was consistent in women (2.1% per year, 95%CI 1.7% to 2.6%, p<0.001) and men (1.6% per year, 95%CI 1.3% to 2.0%, p<0.001) and across age groups in both sexes, although the increase was small among those aged 45–64 years (online supplementary figure 4 and table 7).

In analysis of incident cases with AF as a secondary diagnosis at inpatient admission, we observed a stable to slightly decreasing trend in the incidence rate per 100 000 person years, from 313 (95% CI 308 to 319) in 2004 to 295 (95% CI 290 to 301) in 2014 (online supplementary figure 5 and table 3). On average, the yearly decrease was 1.1% (95% CI 0.9% to 1.2%, p<0.001). This finding was consistent across sex and age groups, even though the estimates for those aged 18–45 years were imprecise (online supplementary figure 6 and table 7).

**Cumulative prevalence**

Since 1994, AF had been diagnosed during an inpatient admission or outpatient visit in 136 828 individuals (women: 55 440 (41%); men: 81 388 (59%)) in Norway as of 31 December 2014. This corresponds to a cumulative prevalence of 3.4% of the total Norwegian population ≥18 years (2.8% in women and 4.0% in men) at the end of 2014. Figure 4 and table 3 show the prevalence by age for men and women.

**Sensitivity analysis of outpatient visits**

In total, 77 494 patients were registered with an AF diagnosis at one or more visits to a hospital outpatient clinic during 2008–2014. The number of outpatients with no inpatient admission for AF in the preceding 10 years totalled 30 185, increasing from 4041 in 2008 to 4895 in 2014, corresponding to 20% and 23% of all incident AF cases.

**DISCUSSION**

We observed stable age-standardised incidence rates of AF from 2004 to 2014. The findings were generally consistent across sex and age groups except for a mean yearly increase of 2.4% in the youngest age group (18–44 years), which was most prominent among men. The cumulative prevalence of AF was 3.4% in the adult Norwegian population. Temporal changes in coding practice, reimbursement rates, clinical guidelines, treatment strategies and handling of patients have to be taken into account when interpreting registry data from patient administrative systems. These changes may influence the preference of AF as primary or secondary diagnosis and could partly explain the decreased incidence of hospitalisations with AF as a secondary diagnosis. Alternatively, the apparent decrease reflects the declining incidence rates of associated conditions such as acute myocardial infarction and heart failure in Norway.14 15 Comorbidity burden and proportions with co-occurring myocardial infarction and heart failure for all incident AF cases in our study decreased over time, as previously shown.4–6 16–18 However, two population-based health examination surveys found stable rates of comorbid myocardial infarction,
more in agreement with the novel finding from our study of increasing proportions of co-occurring myocardial infarction for admissions with AF as primary diagnosis. 4 5 In contrast to our study, a Danish registry study reported lower, but increasing levels of comorbidity burden over time.6 Of interest, we found higher comorbidity in men with more co-occurring malignancy, renal disease and peripheral vascular disease, whereas women who were older had more often dementia, frailty and autoimmune disease. We also found that men had more co-occurring coronary heart disease and women more hypertension, thyroid disorders and stroke, similar to previous reports.5 16

Detection of AF has possibly increased during the study period due to increased awareness of AF and its complications among clinicians and in the population.1 5 Furthermore, it has been

| Year | Incidence rate | Cases |
|------|---------------|-------|
| 2004 | 576           | 1192  |
| 2005 | 601           | 1458  |
| 2006 | 1241          | 3996  |
| 2007 | 1244          | 3975  |
| 2008 | 1248          | 3908  |
| 2009 | 1226          | 3772  |
| 2010 | 1235          | 3750  |
| 2011 | 1205          | 3633  |
| 2012 | 1204          | 3613  |
| 2013 | 1220          | 3681  |
| 2014 | 1280          | 3915  |

Table 1  Age-standardised incidence rates of inpatient admission or death from atrial fibrillation per 100 000 person years in Norway 2004–2014 by year, sex and age group

Incidence rates including 95% CIs are illustrated in figures 2 and 3.
suggested that increased incidence rates may partly arise due to improvements in surveillance methods (new modalities for short-term and long-term ECG monitoring) and their increased use in different patient groups (eg, poststroke ECG screening). In the population-based Framingham Heart Study, incidence rates of AF detected by all health data sources increased from 1958 to 2007, yet the rate of AF detected by ECG at repeated study visits did not increase during this period.

Our results suggested a shift over time in referral practice to more outpatient treatment for new patients with AF, similar to reports from a Danish registry study. The described stable incidence rates of AF may therefore have been increasingly underestimated and likely reflect an unbiased upward trend which supports the observation that incidence rates have not decreased.

Changes in AF incidence over time are of clinical interest and need surveillance. Our observed increased incidence rate of AF in young adults is worrisome and requires further study of changes in underlying risk factors, primarily factors that impact younger birth cohorts born after the 1950s–1960s differently than older cohorts. In Norway, prevalence of obesity has increased over time, especially in the young adult population. In addition, the non-declining incidence rates of acute myocardial infarction in those below 45 years during 2001–2014 in Norway, could add to AF risk. Nevertheless, declining blood pressure has been observed in younger cohorts, which may lower the AF risk. Increased awareness of obesity as an important modifiable risk factor in younger cohorts, as well as preventive measures that promote a stable or reduced body mass index over time, may reduce AF incidence.

The reported incidence of AF has been inconsistent across published studies, depending on approaches used. In different US health registry databases, AF incidence rates increased from 2001 to 2008 and from 2004 to 2016. In line with our finding of a stable incidence from 2004 to 2014, AF incidence rates increased from 1998 up to 2007 and then plateaued from 2007 to 2010 in a UK primary care database linked with hospitalisation data. Incidence rates of AF in the Korean National Health Insurance database were stable from 2006 to 2015. In a Western Australian population, incidence rates of hospitalisations with AF as the primary diagnosis increased, whereas incidence rates of hospitalisations with AF as any diagnosis decreased from 1995 to 2010, using a hospital admission database, in line with our findings.

In a systematic review, Ball et al estimated a pooled prevalence of 2.8% (95% CI 2.3% to 3.4%) in adults, 2.4% (95% CI 1.9% to 2.9%) in females and 3.3% (95% CI 2.7% to 4.0%) in males. Interestingly, we found a prevalence in Norway at the upper limit of these CIs, namely 3.4% in adults, 2.8% in women and 4.0% in men. To our knowledge, this is the highest nationwide prevalence reported to date. Based on inpatient and outpatient hospital records, the prevalence was 2.9% in the Swedish adult population in 2010. A similar prevalence, 3.0%, was found in a smaller cohort in Northern Sweden in 2010, using hospital records and a regional ECG database.

A major strength of our study is the use of nationwide data, and a long observation period, which in turn allow for an adequate washout period and enabled calculations of temporal trends of incidence. Our analysis of AF incidence is limited to inpatient admissions only as data from outpatient visits did not allow for an adequate washout period to define incident cases and were further limited by poor reporting: the proportion of

Table 2  Average yearly change in incidence rates of inpatient admission or death from atrial fibrillation in Norway 2004–2014 by sex and age group

| Cases | Incidence rate ratio (95% CI) | P value |
|-------|------------------------------|---------|
| Men   |                              |         |
| 18–44 years | 3258 | 1.024 (1.013 to 1.035) | <0.001 |
| 45–64 years | 21729 | 0.996 (0.992 to 1.000) | 0.062 |
| 65–84 years | 55352 | 0.998 (0.995 to 1.001) | 0.117 |
| ≥85 years | 16750 | 1.000 (0.995 to 1.005) | 0.987 |
| All ages | 97089 | 0.999 (0.997 to 1.001) | 0.486 |
| Women  |                              |         |
| 18–44 years | 846 | 1.021 (0.999 to 1.043) | 0.060 |
| 45–64 years | 7609 | 0.991 (0.984 to 0.998) | 0.016 |
| 65–84 years | 41842 | 0.999 (0.996 to 1.002) | 0.439 |
| ≥85 years | 28593 | 0.995 (0.991 to 0.998) | 0.004 |
| All ages | 78890 | 0.994 (0.992 to 0.997) | <0.001 |
| Total  |                              |         |
| 18–44 years | 4104 | 1.024 (1.014 to 1.034) | <0.001 |
| 45–64 years | 29338 | 0.995 (0.991 to 0.999) | 0.009 |
| 65–84 years | 97194 | 0.999 (0.998 to 1.001) | 0.611 |
| ≥85 years | 45343 | 0.998 (0.995 to 1.001) | 0.132 |
| All ages | 175979 | 0.998 (0.997 to 1.000) | 0.020 |
specialists that reported their activity to the Norwegian Patient Registry was 56% in 2009. In addition, our definition of AF cases was based on inpatient hospital registry data and not verified by ECG or additional medical records. However, the validity of AF reported in Scandinavian studies has been high. Among patients with a hospital register-based AF diagnosis code, AF was confirmed by medical records or ECG from hospitals or primary care in 89%–97%. Another limitation is that we lacked data from primary care physicians and nursing homes to better estimate the true prevalence of AF. While we do not know the proportion of patients with AF in Norway that are treated only out-of-hospital, a study by Friberg et al suggested that 22% of Swedish patients with AF were seen only in primary care practices. If we extrapolate this to our results, the prevalence of AF in the adult Norwegian population would be as high as 4.1%.

**CONCLUSION**

For the adult population in Norway, we found overall stable incidence rates of AF from 2004 to 2014 and an AF prevalence of at least 3.4% at the end of 2014. Signs of increased incidence rates of early-onset AF (<45 years) are of concern and need further investigation.

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**Contributors** GST, IA, JI and RS planned the work. LJK, JI and IA had access to the data and contributed to the statistical analyses. LJK drafted the manuscript. All authors contributed to the design of the study, have critically revised the draft and have approved the final version of the submitted manuscript. LJK and IA are responsible for the overall content as guarantors.

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