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Socioeconomic factors and mortality in patients with atrial fibrillation—a cohort study in Swedish primary care

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Background: Preventing ischaemic stroke attracts significant focus in atrial fibrillation (AF) cases. Less is known on the association between socioeconomic factors and mortality and cardiovascular outcomes in patients with AF. **Methods:** Our study population included adults (n=12 283) ≥45 years diagnosed with AF at 75 primary care centres in Sweden 2001–07. Cox regression was used to calculate hazard ratios (HRs) with 95% confidence intervals (CIs) for the association between the exposures educational level, marital status, neighbourhood socioeconomic status and the outcomes all-cause mortality, after adjustment for age, and comorbid cardiovascular conditions. **Results:** During a mean of 5.8 years (SD 2.4) of follow-up, 3954 (32.3%) patients had died; 1971 were women (35.0%) and 1983 were men (29.8%). Higher educational level was associated with a reduced mortality in fully adjusted models: HR 0.85 (95% CI 0.77–0.96) for secondary school in men, HR 0.73 (95% CI 0.60–0.88) for college/university in women, and HR 0.82 (95% CI 0.71–0.94) for college/university in men, compared to primary school. Unmarried men and divorced men had an increased risk of death, compared with married men: HR 1.25 (95% CI 1.05–1.50), and HR 1.23 (95% CI 1.07–1.42), respectively. College/university education level was also associated with lower risk of myocardial infarction in men and women, and lower risk of congestive heart failure in women. **Conclusion:** More attention could be paid to individuals of lower levels of formal education, and unmarried men, in order to provide timely management for AF and prevent its debilitating complications.

Introduction

Atrial fibrillation (AF) is the most common arrhythmia in the global population. In Sweden, the prevalence of a registered diagnosis of AF is estimated at 2%,[1] or almost 3% in individuals aged above 20 years.[1] The prevalence of AF has been estimated to be ∼2% among individuals 20 years of age or older in Europe.[2] In terms of mortality in AF patients, The Framingham Heart Study showed an excess risk with an odds ratio (OR) of 1.5 among men and 1.9 among women,[3] and this excess mortality has also been found in other studies.[4]

Sex is one of the non-modifiable risk factors for cardiovascular disease.[5] The prevalence of AF has been estimated to be 20% higher in men than that in women in Europe;[2] men typically develop AF on average 5–7 years earlier than women.[6–8] By contrast, women with AF exert a higher relative risk of both stroke and mortality than men,[9] making sex-stratified analyses of AF interesting and relevant. Other important risk factors for AF include older age, heredity, hypertension, heart disease (heart failure and coronary artery disease), being overweight and obesity, higher amount of pericardial fat, sleep apnoea, atrial dilatation and stretch, chronic kidney disease, smoking, high alcohol consumption, diabetes and thyroid dysfunction.[10] Cardiometabolic comorbidities of importance among AF patients include hypertension, congestive heart failure (CHF), cerebrovascular diseases (CVD) and diabetes,[1] as well as coronary heart disease (CHD).[11] CHD and myocardial infarction (MI) increase the risk of CHF and mortality in AF patients,[12] and CHF is also associated with increased mortality in AF patients.[13,14] Besides, psychological distress is often present among AF patients,[15] and symptoms of depression and/or anxiety are linked to greater symptom severity of AF,[16–18] and higher mortality.[19]

Social inequalities in health is a well-known fact,[20,21] and low socioeconomic status (SES) is one of the strongest predictors of morbidity and premature mortality in the world, even after taking traditional risk factors into consideration,[22] not the least for the diseases contributing most to the mortality rate, i.e. cancer and CVD.[23,24] Therefore, low SES substantially contributes to the burden of CVD.[25] Indicators used on an individual level include education, occupation and income.[26] Educational level is often used as a stable indicator of SES as it usually remains constant throughout adult life and is predictive of working opportunities and earning potential.[26] Other SES indicators are also used, such as area of residence, wealth and house condition. On an area SES level, neighbourhood SES is often used as a factor that goes beyond the individual SES level.[27]

Regarding educational level, a protective effect on mortality of high educational level among AF patients has been shown.[28] Neighbourhood SES has been found to be associated with overall health,[27] cardiovascular health[29,30] and all-cause mortality[31] and a higher relative risk of all-cause mortality among men with AF.[32]

Marital status is also an important socioeconomic factor of importance; living alone is often associated with a lower income. Compared to married men, unmarried, divorced and widowed men exert a higher mortality,[33] with married men having half the age-adjusted relative mortality risk compared to unmarried.[34]

Even if effects by socioeconomic factors in general in relation to CVD are well known and described, more data on the situation for patients with AF are warranted, especially regarding patients in primary care, and in relation to the three most important comorbid cardiovascular conditions, i.e. MI, stroke and CHF.

Thus, the objectives of this study are 2-fold: (i) to explore the effects of socioeconomic factors on mortality in patients with AF in Swedish primary care after adjustment for relevant confounders; and (ii) to explore the effects of socioeconomic factors on MI, ischaemic stroke (IS) and CHF in patients with AF.

Methods

Design

We used individual-level patient data from 75 primary health care centres (PHCCs), with 48 located in Stockholm County. Individuals attending any of the participating PHCCs between 2001 and 2007 were included. We used *Extractor* software (http://www.slso.sll.se/SLPOtemplates/SLPOPage1____10400.aspx; accessed September 19, 2010) to extract individual electronic patient records. National identification numbers were replaced with new unique serial numbers. The files were linked to a database constructed using the Total Population Register, the Inpatient Register and the Swedish Cause of Death Register, with individual-level data on age, gender, education and hospital admissions for all residents registered in Sweden. Data from the Cause of Death Register were used for follow-up.

Ethical approvals were obtained from the regional ethics committees at Karolinska Institutet and the University of Lund.

Study population

The study included all patients with AF, identified by the presence of the ICD-10 code (10th version of the WHO's International Classification of Diseases) for AF (I48) in patients' medical records. The study included a total of 12 283 individuals (6646 men and 5637 women), aged 45 years or older at the time of their first recorded AF diagnosis with a recorded visit from 1 January 2001, until 31 December 2007, and with data on neighbourhood SES from 1990 to 2006. The individuals in this cohort study were thus both prevalent and incident cases with AF treated in primary care.

Exposure

Educational level was categorized as $\leq$9 years (partial or complete basic schooling), 10–12 years (partial or complete secondary schooling) and >12 years (college and/or university studies), using data from 2001 to 2007.

Marital status was classified as married, unmarried, divorced or widowed, using data from 2001 to 2007.

The neighbourhood SES areas were categorized into three groups according to the neighbourhood index: more than one SD below the mean (high SES or low deprivation level), more than one SD above the mean (low SES or high deprivation level) and within one SD of the mean (for more information see Supplementary material).[35]

Outcome variable

The primary outcome was time from first AF diagnosis to mortality (until 31 December 2010).

The secondary outcome included time from first AF diagnosis until a registered hospital diagnosis of MI, IS or CHF.

Comorbidities

We identified the following cardiovascular and psychiatric comorbidities from the electronic patient records: hypertension; CHD, also including registered hospitalizations for incident MI; CHF, also including hospitalizations for CHF; non-rheumatic valvular diseases; cardiomyopathy; CVD, including registered hospitalizations for ischaemic or haemorrhagic stroke; diabetes mellitus; depression or anxiety disorders (for ICD-10 codes see Supplementary material).

Statistical analyses

Means of age and distributions of socioeconomic groups and comorbidities were analysed.

For follow-up analyses we used Cox regression with hazard ratios (HRs) and 95% confidence interval (95% CI), with death as outcome, and time to death. Secondly, Laplace regression was used to calculate the difference in years until death for the first 25% of the participants (as over 30% actually had died).[36] As different distributions and mathematical calculations are used in Cox and Laplace regression, we consider results to be more robust with findings verified with both methods. The regression models included interaction terms when relevant. Three regression models were used for both Cox and Laplace regression: Model 1 univariable with age-adjustment; Model 2 additionally adjusted for socioeconomic factors (educational level, marital status and neighbourhood SES) and Model 3 also for comorbidity (depression, hypertension, CHD, CHF, diabetes, CVD, valvular heart disease and cardiomyopathy). We excluded anxiety disorders as not being statistically significant. For the secondary analyses regarding hospital-registered events of incident MI (n = 11 699; 5398 women and 6301 men), IS (n = 11 517; 5248 women and 6269 men) or CHF (n = 9424; 4213 women and 5211 men) patients with an earlier recorded diagnosis of MI (n = 584), IS (n = 766) and CHF (n = 2859), respectively, were excluded. For secondary outcomes, we performed analyses in a similar way but excluding comorbid events occurring after the respective outcome (hospital diagnoses of MI, IS or CHF). All analyses were stratified by sex.

A P value for two-sided tests of <0.01 was considered statistically significant due to the multiple comparisons between men and women. A two-sided P value of <0.05 was considered statistically significant for variables in the Cox regression and Laplace regression analyses. All analyses were performed in STATA 14.1, with an amendment for Laplace regression provided by Professor Bottai.[36]

Results

Characteristics of the study population (n = 12 283 individuals) are shown separately for men (n = 6646) and women (n = 5637), and also divided into survivors or deceased (table 1). As seen in table 1, most variables were markedly different between survivors and deceased, with few exceptions.

Table 1 Characteristics for patients aged ≥45 years with diagnoses of AF, categorized into all including men and women and also deceased men and women, at baseline (*n* = 12 283) in primary care attending the 75 PHCCs between 1 January 2001 and 31 December 2007

Number of patients	All men and women *N* = 12 283	All men *N* = 6646	All women *N* = 5637	Deceased men *N* = 1983	Deceased women *N* = 1971
Age (years), mean (SD)	74.4 (10.1)	72.1 (10.2)	77.1 (9.3)	78.3 (8.3)	82.3 (7.1)
Age groups (years),					
45–54	475 (3.9)	370 (5.6)	105 (1.9)	24 (1.2)	5 (0.3)
55–64	1743 (14.2)	1222 (18.4)	521 (9.2)	119 (6.0)	38 (1.9)
65–74	3308 (26.9)	2042 (30.7)	1266 (22.5)	399 (20.1)	188 (9.5)
75–79	2427 (19.8)	1257 (18.9)	1170 (20.8)	459 (23.2)	334 (17.0)
80–84	2447 (19.9)	1.083 (16.3)	1364 (24.2)	525 (26.5)	603 (30.6)
≥85	1883 (15.3)	672 (10.1)	1211 (21.5)	457 (23.1)	803 (40.7)
Deceased	3954 (32.2)	1983 (29.8)	1971 (35.0)	1983	1971
Educational level	(*n* = 11 241)	(*n* = 6290)	(*n* = 4951)	(*n* = 1738)	(*n* = 1499)
Basic schooling	5085 (45.2)	2486 (39.5)	2599 (52.5)	853 (49.1)	942 (62.8)
Secondary schooling	3995 (35.5)	2.367 (37.6)	1628 (32.9)	587 (33.8)	429 (28.6)
College and/or university studies	2161 (19.2)	1437 (22.9)	724 (14.6)	298 (17.2)	128 (8.5)
Marital status	(*n* = 12 232)	(*n* = 6621)	(*n* = 5611)	(*n* = 1969)	(*n* = 1953)
Married	5613 (45.9)	3950 (59.7)	1663 (29.6)	1026 (52.1)	373 (19.1)
Unmarried	1029 (8.4)	630 (9.5)	399 (7.1)	168 (8.5)	127 (6.5)
Divorced	1813 (14.8)	1021 (15.4)	792 (14.1)	268 (13.6)	240 (12.3)
Widowed	3777 (30.9)	1020 (15.4)	2757 (49.1)	507 (25.8)	1213 (62.1)
Neighbourhood SES					
High	4604 (37.5)	2956 (40.0)	1948 (35.6)	697 (35.2)	635 (32.2)
Middle	5807 (47.3)	3030 (45.6)	2777 (49.3)	986 (49.7)	1013 (51.4)
Low	1872 (15.2)	960 (14.4)	912 (16.2)	300 (15.1)	323 (16.4)
Diagnosis					
Hypertension	5586 (45.5)	2799 (42.1)	2787 (49.4)	779 (39.3)	853 (43.3)
Coronary heart disease	3234 (26.3)	1722 (25.9)	1512 (26.8)	688 (34.7)	684 (34.7)
Congestive heart failure	2308 (18.8)	1155 (17.4)	1153 (20.5)	1296 (65.4)	1371 (69.6)
Valvular disease	571 (4.7)	294 (4.4)	277 (4.9)	112 (5.7)	119 (6.0)
Cardiomyopathy	90 (0.7)	60 (0.9)	30 (0.5)	20 (1.0)	7 (0.4)
Cerebro-vascular diseases	2566 (20.9)	1277 (19.2)	1289 (22.9)	554 (27.9)	641 (32.5)
Diabetes mellitus	2405 (19.6)	1312 (19.7)	1093 (19.4)	428 (21.6)	411 (20.9)
Depression	1039 (8.5)	412 (6.2)	627 (11.1)	159 (8.0)	228 (11.6)
Anxiety disorders	496 (4.0)	183 (2.8)	313 (5.6)	62 (3.1)	102 (5.2)

Note: Information on educational level and marital status is missing for some individuals, why number of individuals with data on this are shown in the table.

A total of 1983 men (29.8%) and 1971 women (35.0%) died during follow-up. The mean follow-up time was 5.8 years (SD 2.4), and HRs for mortality were calculated based on 71 602 person-years at risk (39 154 among men and 32 448 among women). Incidence rates for mortality per 100 person-years were 6.07 (95% CI 5.81–6.35) for women, and 5.06 (95% CI 4.85–5.29) for men. Cox regression models for subjects stratified by sex are shown in table 2, and Laplace regression models in table 3. In fully adjusted models, higher educational level was associated with significantly lower relative mortality risks among both men and women, and marital status was associated with higher relative mortality risks only among unmarried and divorced men but not for women. The corresponding Laplace regression models showed higher educational level to be associated with a longer survival until mortality of the first 25% of both men and women. In contrast, a shorter survival was found for unmarried and divorced men, but not among women.

Table 4 presents the CVD outcomes, with hospital diagnoses of incident MI, IS and CHF as outcomes in patients with AF. For MI, the highest educational level, i.e. college or university, was associated with lower risk estimates in Cox regression models in men and women, and longer survival until the first 25% events among both men and women. Furthermore, men living in neighbourhoods with low SES were associated with a higher mortality rate and a shorter time to event until the first 25% had died. For IS, secondary school was associated with a higher relative risk and a shorter survival among men, and, among women, the highest educational level was associated with a longer survival. For CHF, unmarried and divorced men had higher relative risks, and divorced men a shorter survival until the first 25% had died.

Discussion

The main finding of this study was that a higher educational level was associated with lower mortality risks in both men and women. Moreover, unmarried or divorced men had higher mortality risks than married men. For the CVD outcomes, different patterns were found. For MI, lower associated risk was found in the highest educational level for men and women, and higher risk was associated with men living in low SES neighbourhoods. For IS, a higher associated risk was found among men with middle educational level, i.e. secondary school. For CHF, higher associated risks were found among unmarried and divorced men. Furthermore, among women, both the higher educational levels were associated with lower risk.

Our results concerning the association between lower educational level and increased mortality among patients with AF are in congruence with a Norwegian study.[28] A higher educational level was protective of MI among both men and women, and of CHF among women.

For neighbourhood SES, low neighbourhood SES was not associated with mortality when adjusting for comorbidities in the Cox regression, even if the survival time until the first 25% had died in the Laplace regression was longer. However, as regards the risk of MI was increased among men living in low SES neighbourhoods. Previously published studies have shown an association between neighbourhood SES and lower cardiovascular health,[29,30] as well as with increased all-cause mortality.[29,31]

Regarding marital status, one earlier study found a similar result as ours, with unmarried men exhibiting an overall increased mortality risk compared to married men.[34] However, our findings were true only for men, in contrast to another study, where both

Table 2 Cox regression models [with hazard ratios (HRs) and 95% confidence interval (CI)] for mortality among patients aged ≥45 years with diagnoses of AF (*n* = 12 283) in primary care attending the 75 PHCCs between 1 January 2001 and 31 December 2007

	Men			**Women**		
	Model 1 HR (95% CI)	**Model 2 HR (95% CI)**	**Model 3 HR (95% CI)**	**Model 1 HR (95% CI)**	**Model 2 HR (95% CI)**	**Model 3 HR (95% CI)**
Educational level						
Basic schooling	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	
Secondary schooling	**0.80 (0.72; 0.89)**	**0.86 (0.77; 0.96)**	**0.85 (0.76; 0.95)**	**0.88 (0.78; 0.98)**	**0.89 (0.79; 0.99)**	0.91 (0.81; 1.02)
College and/or university studies	**0.72 (0.63; 0.81)**	**0.79 (0.69; 0.91)**	**0.82 (0.71; 0.94)**	**0.70 (0.58; 0.84)**	**0.70 (0.58; 0.85)**	**0.73 (0.60; 0.88)**
Marital status						
Married	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	
Unmarried	**1.50 (1.27; 1.77)**	**1.36 (1.15; 1.62)**	**1.25 (1.05; 1.50)**	1.00 (0.82; 1.23)	1.02 (0.82; 1.28)	0.99 (0.79; 1.24)
Divorced	**1.34 (1.17; 1.54)**	**1.33 (1.16; 1.53)**	**1.23 (1.07; 1.42)**	1.15 (0.98; 1.36)	1.14 (0.95; 1.36)	1.05 (0.88; 1.26)
Widowed	1.08 (0.97; 1.21)	1.09 (0.96; 1.23)	1.04 (0.91; 1.17)	1.01 (0.89; 1.14)	0.97 (0.85; 1.11)	0.92 (0.80; 1.05)
Neighbourhood SES						
High	**0.80 (0.72; 0.89)**	**0.84 (0.75; 0.94)**	**0.85 (0.76; 0.95)**	0.91 (0.82; 1.01)	0.95 (0.84; 1.07)	0.93 (0.83; 1.06)
Middle	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Low	**1.26 (1.09; 1.45)**	**1.18 (1.01; 1.38)**	1.15 (0.98; 1.35)	1.14 (1.00; 1.31)	1.06 (0.90; 1.26)	1.07 (0.90; 1.26)

Bold values are statistically significant.

Notes: Information on educational level and marital status is missing for some individuals.

Models are harmonized to include the same variables among men and women, otherwise are non-significant variables excluded. Model 1 is age-adjusted, Model 2 age-adjusted and including all socioeconomic factors (educational level, marital status and neighbourhood socioeconomic status), Model 3 as Model 2 but also including depression and somatic comorbidity (i.e. cardiovascular disease and diabetes). (Model check revealed a significant interaction between age and CHF).

men and women being unmarried, divorced and widowed, were shown to exert a higher mortality rate than their married counterparts.[33] Besides, among men, marital status was also associated with a new hospital diagnosis of CHF.

There is a consistent and continuous gradient in western societies, including Sweden, between cardiovascular morbidity and mortality and SES, with lower SES on the individual or area level being more harmful.[37] Most of the cardiometabolic comorbidities in AF patients, i.e. hypertension, CHD, CHF and diabetes, increase with lower neighbourhood SES.[32] For lifestyle factors, there is a strong SES gradient for smoking, paralleling the gradient in morbidity and mortality, which together with central obesity, physical inactivity and poor dietary habits may also be a contributory factor to poor health.[37] Attitudes and beliefs about lifestyle habits differ across SES levels, with individuals living in low SES neighbourhoods showing less knowledge about health factors as well as lower probability of positive behaviour changes.[38] Furthermore, individuals residing in low SES neighbourhoods may also experience feelings of inferiority and self-doubt as a consequence of their lower social status.[39] Access to health care and differences in prescription of pharmacotherapy could also be of importance. However, Sweden has a compulsory public health insurance system that covers all Swedish citizens and as a consequence access to health care should be relatively equal. Despite the universal health care access, irrespective of individual income, Sweden also has social inequalities in health, which shows that health care reforms alone are not sufficient to contradict such inequalities. Women in general seek care more often, and the higher mortality risk among unmarried men may reflect unmet health care needs,[40] as single-living men in late adulthood have been found to be at special risk in earlier studies, which is in contrast to women.[41] Among AF patients, differences in prescription of anticoagulants and statins among both men and women have been shown with higher rates among patients in high SES neighbourhoods.[42] Another factor is the financial stress,[41] which more often affects low SES than high SES individuals, as a part of the general psychosocial stress.[43] Allostatic load is a concept related to stress, with allostasis being the physiological stress response to acute stress.[44] The allostatic load is also connected with the development of cardiovascular risk factors.[45]

In the fully adjusted model, we also adjusted for comorbidity, which could be seen as mediators of the socioeconomic factors on mortality. Thus, interpreting results from these models may have underestimated the effects of the socioeconomic factors.

There are several limitations of this study, which must be kept in mind when interpreting the results. The cohort included patients with AF and concomitant diseases in primary health care. Both prevalent and incident cases with AF were included to obtain sufficient statistical power. The results could differ if including only incident cases, but this would demand a wash-out period of optimally five years. In another study, it was found that 64% of all registered AF patients in Stockholm County were registered with a diagnosis in primary health care.[1] Besides, we do not know the validity of registered diagnoses in primary health care, and there might be both over- and under-estimation of the various diagnoses. Results may not be generalized to AF patients in general or to patients in other settings. The findings may have been subject to survival treatment selection bias;[46] all these mentioned factors could have affected the results. Severity of CHF and CHD was not classified, and as severity of CHF is an important factor for mortality, this is also a major limitation of the study. Besides, data on ejection fraction and the criteria for diagnosis of CHF were not available. Moreover, AF could not be classified as paroxysmal, persistent or permanent and heart rhythm could not be classified as sinus rhythm or fibrillation rhythm. Additionally, we had no information about renal function. As warfarin was the anticoagulant during the study the results could be different nowadays, as the rate of anticoagulant treated patients has increased after introduction of the non-vitamin K oral anticoagulants.[47] Furthermore, we did not have access to lifestyle factors such as smoking habits or obesity.

A major strength of this study was that we were able to link clinical data from individual electronic patient records to data from national demographic and socioeconomic registers with less than 1% of information missing. While many previous follow-up studies of AF have used hospital data, this study used data from primary care, which may better reflect the risks associated with AF in the general population. Moreover, randomized controlled trials often exclude individuals with comorbidities such as AF patients with concomitant diabetes and CHF. In this study, we had the possibility to include these patients in the analyses, which means that the findings are more representative of the variety of patients

Table 3 Laplace regression models (with years gained or lost until first 25% deaths, and 95% CI) for mortality among patients aged ≥45 years with diagnoses of AF (*n* = 12 283) in primary care attending the 75 PHCCs between 1 January 2001 and 31 December 2007

	Men			**Women**		
	Model 1 Years (95% CI)	**Model 2 Years (95% CI)**	**Model 3 Years (95% CI)**	**Model 1 Years (95% CI)**	**Model 2 Years (95% CI)**	**Model 3 Years (95% CI)**
Educational level						
Basic schooling	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)
Secondary schooling	**0.83 (0.52; 1.14)**	0.36 (−0.03; 0.75)	**0.45 (0.06; 0.84)**	0.21 (−0.12; 0.54)	0.23 (−0.13; 0.58)	0.31 (−0.08; 0.71)
College and/or university studies	**1.00 (0.66; 1.34)**	**0.75 (0.33; 1.17)**	**0.60 (0.09; 1.10)**	**0.83 (0.25; 1.42)**	**1.01 (0.46; 1.57)**	**0.93 (0.12; 1.75)**
Marital status						
Married	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)
Unmarried	**−0.93 (−1.28; −0.58)**	**−0.97 (−1.54; −0.40)**	**−0.67 (−1.28; −0.07)**	−0.14 (−0.87; 0.59)	−0.25 (−1.07; 0.57)	−0.24 (−0.98; 0.51)
Divorced	**−0.92 (−1.21; −0.63)**	**−0.73 (−1.25; −0.22)**	**−0.74 (−1.24; −0.24)**	−0.47 (−1.31; 0.37)	−0.67 (−1.21; −0.13)	−0.24 (−0.90; 0.41)
Widowed	0.00 (−0.27; 0.27)	0.03 (−0.45; 0.50)	0.23 (−0.28; 0.73)	0.04 (−0.32; 0.39)	0.18 (−0.22; 0.58)	0.38 (−0.08; 0.84)
Neighbourhood SES						
High	**0.63 (0.19; 1.06)**	**0.46 (0.06; 0.86)**	**0.46 (0.03; 0.89)**	−0.09 (−0.18; 0.37)	0.08 (−0.24; 0.40)	0.20 (−0.20; 0.61)
Middle	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)
Low	**−0.71 (−1.20; −0.21)**	**−0.64 (−1.15; −0.13)**	**−0.68 (−1.23; −0.12)**	−0.53 (−1.25; 0.19)	−0.04 (−0.52; 0.43)	0.05 (−0.53; 0.62)

Bold values are statistically significant.
Notes: Information on educational level and marital status is missing for some individuals.
Models are harmonized to include the same variables among men and women, otherwise are non-significant variables excluded. Model 1 is age-adjusted, Model 2 age-adjusted and including all socioeconomic factors (educational level, marital status and neighbourhood socioeconomic status), Model 3 as Model 2 but also including depression and somatic comorbidity (i.e. cardiovascular disease and diabetes).

Table 4 Cox regression models (with HRs and 95% CI) and Laplace regression models (with time in years until first 25% event with 95% CI) for newly diagnosed myocardial infarction (MI), ischaemic stroke (IS) or congestive heart failure (CHF) among patients aged ≥45 years with a diagnosis of AF (*n* = 12 283) in primary care attending the 75 PHCCs between 1 January 2001 and 31 December 2007

	Men			**Women**		
	MI	**IS**	**CHF**	**MI**	**IS**	**CHF**
Cox regression:	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Educational level						
Basic schooling	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Secondary schooling	0.85 (0.69; 1.04)	**1.20 (1.01; 1.44)**	1.00 (0.87; 1.15)	0.96 (0.76; 1.19)	0.87 (0.73; 1.04)	**0.83 (0.71; 0.96)**
College and/or university studies	**0.72 (0.55; 0.93)**	1.10 (0.88; 1.36)	0.91 (0.76; 1.08)	**0.66 (0.45; 0.96)**	0.78 (0.60; 1.01)	**0.78 (0.63; 0.96)**
Marital status						
Married	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Unmarried	1.00 (0.71; 1.40)	1.06 (0.79; 1.42)	**1.49 (1.20; 1.85)**	0.90 (0.57; 1.41)	1.08 (0.77; 1.52)	1.11 (0.85; 1.46)
Divorced	1.13 (0.87; 1.46)	1.09 (0.87; 1.37)	**1.40 (1.17; 1.66)**	1.07 (0.76; 1.49)	1.10 (0.84; 1.43)	1.19 (0.96; 1.48)
Widowed	1.20 (0.95; 1.52)	1.22 (0.99; 1.51)	1.13 (0.95; 1.33)	1.02 (0.79; 1.31)	1.15 (0.94; 1.39)	1.04 (0.88; 1.21)
Neighbourhood SES						
High	1.02 (0.82; 1.26)	0.99 (0.83; 1.18)	0.92 (0.80; 1.07)	0.87 (0.69; 1.12)	1.06 (0.88; 1.28)	1.03 (0.89; 1.20)
Middle	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Low	**1.48 (1.11; 1.97)**	1.03 (0.79; 1.35)	1.03 (0.83; 1.27)	1.33 (0.98; 1.80)	0.81 (0.62; 1.06)	1.11 (0.90; 1.36)
Laplace regression models, 25%	Years (95% CI)	Years (95% CI)	Years (95% CI)	Years (95% CI)	Years (95% CI)	Years (95% CI)
Educational level						
Basic schooling	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)
Secondary schooling	0.79 (−0.13; 1.70)	**−0.93 (−1.79; −0.06)**	−0.03 (−0.58; 0.52)	0.22 (−0.69; 1.12)	0.70 (−0.11; 1.51)	**0.85 (0.27; 1.43)**
College and/or university studies	**1.41 (0.28; 2.54)**	−0.35 (−1.43; 0.72)	0.24 (−0.40; 0.89)	**1.63 (0.09; 3.17)**	**1.19 (0.09; 2.30)**	**1.00 (0.20; 1.79)**
Marital status						
Married	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)
Unmarried	−0.11 (−1.61; 1.39)	−0.19 (−1.52; 1.14)	−1.04 (−2.14; 0.06)	0.60 (−1.21; 2.41)	−0.28 (−1.87; 1.31)	−0.66 (−2.25; 0.94)
Divorced	−0.67 (−1.87; 0.53)	−0.50 (−1.60; 0.60)	**−1.21 (−2.04; −0.37)**	−0.36 (−1.73; 1.02)	−0.42 (−1.69; 0.86)	**−0.86 (−1.68; -0.04)**
Widowed	−0.66 (−1.78; 0.46)	−0.89 (−1.98; 0.20)	−0.24 (−0.81; 0.32)	0.05 (−0.97; 1.07)	−0.37 (−1.84; 0.63)	−0.30 (−0.94; 0.35)
Neighbourhood SES						
High	−0.09 (−0.99; 0.81)	0.18 (−0.67; 1.02)	0.14 (−0.42; 0.70)	0.50 (−0.45; 1.45)	−0.14 (−0.97; 0.687)	−0.19 (−0.80; 0.43)
Middle	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)	0 (ref)
Low	**−1.76 (−3.03; −0.50)**	0.04 (−1.28; 1.36)	−0.50 (−1.39; 0.39)	−1.31 (−2.66; 0.05)	0.96 (−0.12; 2.05)	−0.44 (−1.25; 0.37)

Bold values are statistically significant.
Notes: Information on educational level and marital status is missing for some individuals.
Fully adjusted models shown, i.e. adjusted for: age, socioeconomic factors (educational level, marital status and neighbourhood socioeconomic status) and comorbidity. (Model check did not reveal any significant interactions).

encountered in clinical practice today, especially in primary care settings.

Clinical implications for health care professionals are to pay attention to socioeconomic risk groups. To address socioeconomic inequalities in pharmacotherapy in AF patients, more efforts and resources should be allocated within primary care in deprived neighbourhoods. Furthermore, men living under poor social conditions could need more attention to ensure their health care needs are met.

In conclusion, our findings suggest that adverse outcomes among AF patients are more common in men and women with lower education level. Thus, more attention should be paid to patients with AF of lower levels of formal education, and to unmarried men, in order to provide timely management for AF and to prevent its debilitating complications. Further studies are warranted investigating the preventive treatment of stroke, CHF and MI in AF patients with lower education, and in unmarried or divorced men, and how to monitor these groups of patients in primary care.

Supplementary data

Supplementary data are available at *EURPUB* online.

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Key points

- Our findings suggest that adverse outcomes among patients with AF are more common in men and women with lower education level.
- Furthermore, unmarried or divorced men had higher mortality risks, and shorter survival than married men.
- Another finding was a higher risk of MI in AF patients, and shorter time to event, among men living in low SES neighbourhoods.

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Socioeconomic predictors of referral to a diagnostic centre on suspected adverse events following HPV vaccination

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Background: In Denmark, the human papillomavirus (HPV) vaccines have been suspected of adverse events since 2014. However, as no causal associations between the HPV vaccines and numerous diseases have been demonstrated, factors prior to vaccination may influence the risk of suspecting the HPV vaccines of causing symptoms. We studied the associations between individual and parental socioeconomic characteristics and the risk of referral to a diagnostic centre in a female population aged 11–29 years with a first HPV vaccination in January 2008 to June 2015. **Methods:** Individual and parental data from national registries were linked using the unique personal identification number. Logistic regression analyses were used to estimate crude and adjusted odds ratio's according to each individual and parental socioeconomic factor with two-sided 95% 95% CI. **Results:** The cohort consisted of 453 216 individuals of which 1316 (0.29%) were referred to a diagnostic centre in 2015. Having a mother outside the workforce or an unemployed mother was associated with an increased risk of referral, while girls and women who had fathers with a higher educational level were less likely to be referred. In addition, women aged 20–29 years who were unemployed or outside the workforce prior to vaccination had increased odds of being referred to a diagnostic centre. **Conclusion:** We found social inequality in the referral to a diagnostic centre following HPV vaccination. This might be explained by an increased morbidity in girls and women of lower socioeconomic status.