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Association Between Newly Diagnosed Atrial Fibrillation and Work Disability (from a Nationwide Danish Cohort Study)

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It is previously shown that cardiovascular conditions have a negative effect on the ability to work. However, it is unknown if incident atrial fibrillation (AF) influences the ability to work. We examined the association between AF and the risk of work disability and the influence of socioeconomic factors. All Danish residents with a hospital diagnosis of AF and aged ≥30 and ≤63 years in the period January 1, 2000, to September 31, 2014, were included and matched 1:10 with an AF-free gender and age-matched random person from the general population. Permanent social security benefit was used as a marker of work disability. Risk difference (RD) and 95% confidence interval (95% CI) of work disability were calculated over 15 months. The analyses were furthermore stratified in low, medium, and high levels of socioeconomic factors. In total, 28,059 patients with AF and 312,667 matched reference persons were included. The risk of receiving permanent social security benefits within 15 months was 4.5% (4.3% to 4.8%) for the AF cohort and 1.3% (95% CI 1.3% to 1.4%) for the matched reference cohort. Adjusted RD (95% CI) was 2.3% (2.0% to 2.5%). Stratified on income, RDs were higher in low-income groups (adjusted RD 3.7% [95% CI 3.1% to 4.3%]) versus high-income groups (RD 1.3% [1.0% to 1.5%]). In conclusion, the risk of work disability within 15 months after incident AF was more than 3 times as high in patients with AF compared with the general population, especially when comparing individuals in lower socioeconomic strata. **(Am J Cardiol 2022;169:64−70)**

Atrial fibrillation (AF) was for many years considered a trivial condition, but it is now recognized as a contributor to mortality and morbidity[1] such as heart failure (HF) and stroke.[2] Nevertheless, although the fatal consequences of AF are being increasingly recognized, the social consequences after AF are less examined. It is previously shown that cardiovascular conditions such as congenital heart disease,[3] myocardial infarction,[4] HF,[5] or cardiac arrest[6] have a negative effect on the ability to work. Some of the mentioned studies[4−6] also reported that high levels of socioeconomic factors (SEFs) were associated with a higher likelihood of returning to work after incident myocardial infarction, HF, or cardiac arrest, respectively. To our knowledge, no study has examined the association between AF and the risk of permanent work disability and the influence of SEFs. The study aimed to examine the association between incident AF and the risk of work disability and if SEFs have an influence.

Methods

The study was designed as a register-based cohort study using individual-level data from nationwide Danish registers accessed at Statistics Denmark.[7] The Danish National Patient Registry has information about diagnoses and procedures where diagnoses are coded according to the International Classification of Diseases (ICD), version 8 before 1994 and ICD-10 afterwards.[8,9]

The Danish National Prescription Registry keeps information on dispensed prescriptions from Danish pharmacies since the year 1994. Prescriptions are coded using the Anatomical Therapeutic Chemical system.[10] Income register and educational registers are also available through Statistics Denmark.[11,12]

The Danish Civil Registration system keeps information such as vital status, gender, and place of residence on all residents living in Denmark.[13]

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Information about social security benefits transfer was obtained from the DREAM database which keeps the information about public transfer payments for Danish citizens each week.[14] All persons living in Denmark have a personal identification number that can be used to link data across registers at an individual level.[7,13]

We included all patients ≥30 and ≤63 years old with incident AF and/or atrial flutter (ICD-10 Code I48) and followed them from January 1, 2000 to December 31, 2015. To have a complete follow-up on all patients, inclusion ended September 30, 2014. The combined diagnosis of AF and atrial flutter had a high validity (positive predictive value 92.6%).[15] Information about symptoms was not available in the registers. To obtain a reference cohort from the general population, patients with AF were matched on gender and date of birth in ratio 1:10 with random unexposed (at the date of matching) persons from the general population using the Danish Civil Registration System. The date of discharge for incident AF was used as the date of matching (index date).[3] We excluded patients who received permanent social security benefits defined as disability pension, flexi-job (can be awarded if the ability to work of a person is permanently and significantly reduced), or early retirement in the 4 weeks before incident AF.[3,14] Additionally, we excluded patients with missing data on SEFs.

Permanent social security benefits, including disability pension and flexi-job (a job created for persons with limited and permanently reduced work capacity),[3] was used as a marker of work disability. The time to being on permanent social security benefits was in this study defined as the first date of the first 4 weeks receiving transfer payments for disability pension, flexi-job, or unemployment benefit concerning flexi-job[3,14] within 15 months. In addition to permanent social security benefits, we used the work participation score (WPS) as an outcome measure for job retention. WPS was calculated in a 3-month period starting 12 months after incident AF. We chose 1 year after incident AF as we wanted to look at the working ability after the acute phase, and not in relation to AF hospitalization. Work status was defined as WPS from 0% to 100% where the number of weeks being self-supported (defined as no public transfer payment, State Education Fund Grant, maternity leave or leave-of-absence scheme[6,14]) were placed in the numerator and the number of weeks receiving social security benefits and the number of weeks being self-supported in the denominator (13 weeks in total).[16] In this analysis we only included those in the study population being alive at the end of 15 months and not receiving permanent social security benefits during the time.

Income, education, and cohabiting status were defined as previously described.[17] In brief, income was defined as the equivalized family income divided into year-specific (2-year intervals) and age-specific (5-year intervals) tertiles.[17] Education was divided into 3 categories: low (no registered education, lower secondary education, or less), medium (short-cycle tertiary education or less if date of birth was ≤1965 and bachelor's degree or less if date of birth was >1965), and high (bachelor's degree and more if date of birth was ≤1965 and ≥master's degree if date of birth was >1965).[17] Cohabiting status was categorized into living alone or living together with someone.[17] Furthermore, residence was divided as previously described[17,18] into 4 categories of municipalities: urban, intermediate, rural, and peripheral.[19] The diseases evaluated as potential confounders were chronic pulmonary disease, ulcer disease, peripheral vascular disease, liver disease, dementia, connective tissue disease, renal disease, any cancer, diabetes mellitus, HF, ischemic heart disease, alcoholism, anxiety, depression, mood disorders, abuse, schizophrenia, and back pain. The ICD/Anatomical Therapeutic Chemical-codes used in this study are presented in Supplementary Material S1.

Baseline characteristics were presented for patients with AF and matched individuals with counts and percentages for the categorical variables and means and SDs for the continuous variable (age and baseline WPS). Baseline WPS were calculated in a 3-month period 1 year before incident AF (-15 to -12 months prior to AF).

First, to obtain an unadjusted description of work disability in AF cohort and matched reference cohort, we assessed their status in the period 0 to 3 years after the index date (incident AF) classified into "permanent social security benefit", "early retirement", "state pension," or "dead". The patients were classified according to their first observed end point. The cumulated total mortality included deaths occurring after other end points as well, in line with Fenger-Grøn et al.[20] Second, in a timeframe of 15 months, we calculated absolute risk of receiving permanent social security benefits in different models. For some persons, 15 months might not be long enough to be granted permanent social security benefits because their workability must be assessed first. However, if we looked longer than 15 months, other diseases occurring with time might be more likely causes of receiving permanent social security benefits. Hence, we chose 15 months to calculate absolute risk and risk difference (RD) of receiving permanent social security benefits because it is still assumed to be related to AF and it might also be long enough for some patients to be granted permanent social security benefits. The absolute RDs were calculated using a generalized linear model[21] with an identity link and robust standard errors to account for a binary response variable that was not normally distributed. Death, emigration, state pension, and early retirement were considered as competing risks. We adjusted for potential confounders and the models were decided before data analysis.

First, we adjusted for sociodemographic variables in model 1; age, gender, income, education, cohabiting status, residence, and baseline WPS. Second, we adjusted for several potential confounders in model 2; hypertension, ischemic heart disease, peripheral vascular disease, chronic pulmonary disease, diabetes mellitus, alcoholism, cancer, chronic kidney disease, back pain, and HF. Note, HF might be a mediator or confounder in the relationship between AF and permanent social security benefits. Third, we supplied a model 3 and adjusted for stroke, dementia, and anxiety/depression which are all strong risk factors for permanent work disability. They are also potential consequences of AF, however, only weakly associated with increasing the risk of AF through shared risk factors. We considered model 2 as the main model of interpretation. See Supplementary Material S2 for further explanation of the choice of models. Subsequently, all results were stratified on SEFs. We used the Wald test to test for effect modification for SEFs. Finally, we also investigated the risk of permanent work disability stratified on age groups (30 to 40 years, 41 to 50 years, and 51 to 63 years. In a subcohort of the population, still alive and able

to work 15 months after the index date, we calculated the WPS over a 3-month period starting 12 months after the index date. More specifically, those who died, received permanent social security benefits, state pension, or early voluntary state pension within 15 months of the index date, were not included in this analysis. We used linear regression to calculate the difference in WPS between the matched reference cohort versus the AF cohort. To address the non-normal distribution issue of WPS (floor and ceiling effect), we used bootstrapping with 1,000 replications to correctly estimate standard errors. Subsequently, we stratified the analysis on income, education, and cohabiting status. Also, we adjusted for age, gender, and baseline WPS because the age- and gender-matched cohort were violated after excluding relevant individuals and stratifying on SEFs. We used STATA/MP version 16.1 (StataCorp LLC., College Station, Texas) for statistical analyses. A p value <0.05 was considered statistically significant.

Results

In total, 41,856 patients with AF and corresponding 418,560 AF-free matched individuals aged ≥30 to ≤63 years old were included in the period January 1, 2000 to September 31, 2014. After excluding patients with missing variables on SEFs and baseline permanent social security benefits or early retirement, 28,059 patients with AF and 312,667 matched individuals were included in the final study population. Also, 24,113 patients with AF and 287,738 individuals in the matched reference cohort were used to analyze WPS in the subcohort (Figure 1). Baseline characteristics are listed in Table 1. In the matched reference cohort, 71% were men whereas 73% in the AF cohort were men. Mean age was 54.5 and 54.4 years for the matched reference cohort and the AF cohort, respectively. Note, income tertiles were defined based on the average income of the age of the general population before exclusions and are therefore not distributed as tertiles in this study population. All diseases were more common in the AF cohort than in the matched reference cohort, especially cardiovascular diseases. Patients with AF received more permanent social security benefits and had higher mortality (rates) than the matched reference cohort during both the 15-month and 3-year period, whereas the matched reference cohort and the AF cohort received approximately the same amount of early retirement and state pension (Figure 2).

Overall, the risk of receiving permanent social security benefits was 4.5% (95% CI 4.3% to 4.8%) in the AF cohort,

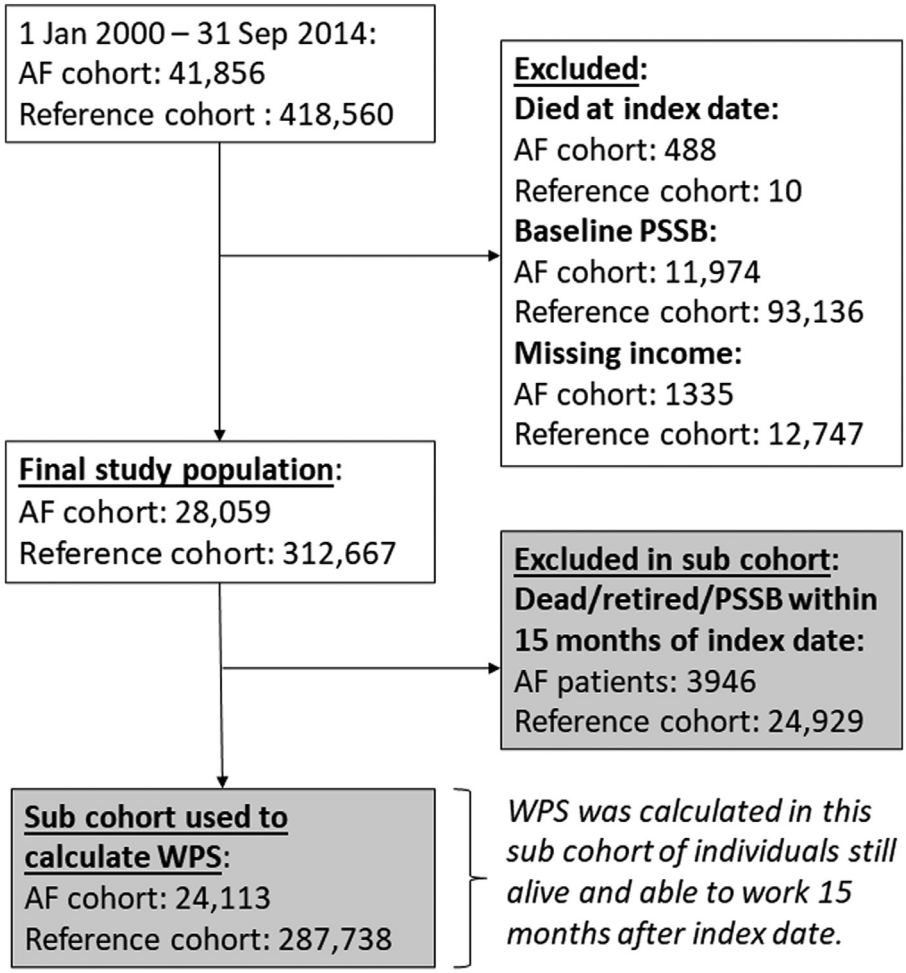

Figure 1. Flowchart of the final study population. PSSB = permanent social security benefit.

whereas it was 1.3% (95% CI 1.3% to 1.4%) in the matched reference cohort. After adjusting for potential confounders, the RDs were slightly attenuated. When stratifying the results on education, income, and cohabiting status, RDs for the AF cohort (reference matches) were highest in the cohorts with low education, low income, and living alone, and lowest in groups with high education, high income, and not living alone (Table 2). The risk of permanent work disability was present in all the age-stratified cohorts (30 to 40 years, 41 to 50 years, and 51 to 63 years), however, the association was strongest in the eldest cohort (Supplementary Material S3).

Of individuals alive and still able to work 15 months after incidence AF, the AF cohort had a lower WPS than the matched reference cohort: WPS for the matched reference cohort was 90% whereas it was 83% for the AF cohort and adjusted RD for the patients with AF was −5.9% (95% CI −6.3% to −5.5%). The same pattern with education, income and cohabiting status as seen for permanent work disability was seen for WPS. WPS and differences for the matched reference cohort and the AF cohort are listed in Table 3. Formal tests for effect modification for SEFs revealed that effect modification was strongly statistically significant for income and education, however, weaker for cohabiting status (Tables 2 and 3).

Discussion

Our principal findings were (1) individuals with AF aged between ≥30 and ≤63 years old had a higher risk of permanent work disability than the matched reference cohort, (2) patients with AF and a part of the workforce 15 months

Table 1
Baseline characteristics of the study population

	AF patients	Matches	P-value*	All
All	n=28,059	n=312,667		N=340,726
Men	20,403 (73%)	221,786 (71%)	0.000	242,189 (71%)
Age, mean ± SD	54.4 ± 6.2	54.5 ± 6.1	0.001	54.5 ± 6.1
Education				
Low education	6,858 (24%)	75,291 (24%)	0.233	82,149 (24%)
Medium education	14,397 (51%)	160,366 (51%)		174,763 (51%)
High education	6,804 (24%)	77,010 (25%)		83,814 (25%)
Income				
Low income	7,328 (26%)	75,955 (24%)		83,283 (24%)
Medium income	9,736 (35%)	110,109 (35%)	0.000	119,845 (35%)
High income	10,995 (39%)	126,603 (41%)		137,598 (40%)
Cohabiting status				
Living alone	6,178 (22%)	65,451 (21%)	0.000	71,629 (21%)
Not alone	21,881 (78%)	247,216 (79%)		269,097 (79%)
Residence				
Peripheral	2,657 (10%)	30,263 (10%)	0.515	32,920 (10%)
Rural	8,087 (29%)	89,972 (29%)		98,059 (29%)
Intermediate	4,594 (16%)	50,386 (16%)		54,980 (16%)
Urban	12,635 (45%)	141,050 (45%)		153,685 (45%)
Baseline WPS† mean±SD	87.9 ± 29.7	90.7 ± 26.4	0.000	90.5 ± 26.7
Morbidity				
Hypertension	8405 (30%)	39,173 (13%)	0.000	47,578 (14%)
Heart failure	612 (2%)	400 (0%)	0.000	1012 (0%)
Chronic pulmonary disease	1032 (4%)	6145 (2%)	0.000	7177 (2%)
Diabetes mellitus	1886 (7%)	11914 (4%)	0.000	13800 (4%)
Ischemic heart disease	3236 (12%)	11027 (4%)	0.000	14263 (4%)
Peripheral vascular disease	638 (2%)	2507 (1%)	0.000	3145 (1%)
Cancer	1305 (5%)	8604 (3%)	0.000	9909 (3%)
Connective tissue disease	347 (1%)	2167 (1%)	0.000	2514 (1%)
Dementia	16 (0%)	75 (0%)	0.001	91 (0%)
Liver disease	297 (1%)	1533 (1%)	0.000	1830 (1%)
Renal disease	384 (1%)	1109 (0%)	0.000	1493 (0%)
Stroke	867 (3%)	3194 (1%)	0.000	4061 (1%)
Anxiety/depression/mood	229 (1%)	1410 (1%)	0.000	1639 (1%)
Schizophrenia	18 (1%)	86 (0%)	0.001	104 (0%)
Alcoholism or abuse	875 (3%)	4790 (2%)	0.000	5665 (2%)
Back pain	1117 (4%)	9872 (3%)	0.000	10989 (3%)
CHA_2DS_2VASc-score, mean ± SD	0.8 ± 1.0	0.5 ± 0.7	0.000	0.5 ± 0.7

* P-value indicates if there is statistically significant difference in distribution of the variables in the table between AF cohort and matched reference cohort.
†Calculated in the period -12 to -15 months prior to index date.
Abbreviations: CHA_2DS_2VASc = Congestive heart failure (1 point); SD = standard deviation.
Hypertension (1 point), Age ≥75 years old, Diabetes Mellitus (1 point), Stroke (2 point), Vascular disease (1 point), age 65-75 years old and Sex category (female sex 1 point).

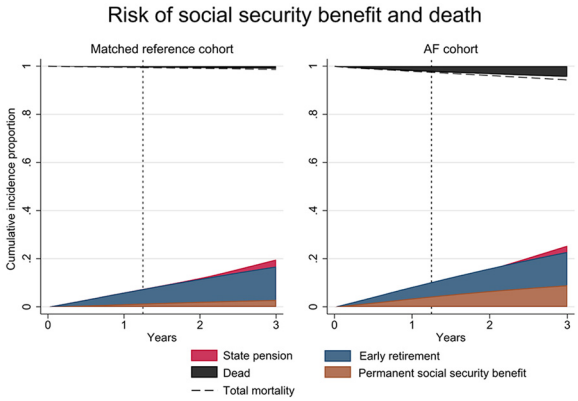

Figure 2. Status for patients with AF and matched reference cohort 0 −3 years after index date (incident AF) classified into "permanent social security benefit" *(brown color)*, "early retirement" *(blue color)*, "state pension" *(red color)*, or "dead" *(black color)* according to their first observed end point. The cumulated total mortality *(dashed black line)* included mortality occurring after other end points. The *dotted vertical lines* indicate 15 months. The matched reference cohort was matched on age and gender.

after incident AF had a lower WPS than the matched reference cohort, (3) there was effect modification by SEFs; the difference in permanent social security benefits and WPS was largest in strata including persons with lower education, lower income and living alone, whereas the absolute risk and difference were smaller in strata including persons with higher education, higher income and not living alone.

Previous studies have shown an association between detachment from employment related to, for example, myocardial infarction[4] and HF.[5] Also, a United States study found that AF and other heart arrhythmias represented a severe burden to the United States workforce because of significant prevalence in the working population and additional costs because of drugs and absence from work.[22] Hence, we did expect to find an association between AF and permanent work disability. Our results supported this assumption. It is very likely that work disability partly was caused by consequences of AF such as stroke, especially if they were granted permanent social security benefit within only 15 months. More specifically, if a person was severely physically handicapped because of an AF-related stroke, one might quickly ascertain that the ability to work cannot be improved very much and grant the person some sort of permanent social security benefit within 15 months. Although effective treatment strategies exist, such as oral anticoagulation therapy for stroke prevention to patients with AF and with a high risk of stroke, studies have shown that this is underused, especially in patients with low socioeconomic positions.[17] In other words, work disability in patients with AF might be mediated through the consequences of AF such as stroke, and it might also partly explain why the difference was larger in lower socioeconomic groups. Also, psychological consequences of AF may play an important role in the causal pathway between AF and work disability; a previous study reported that 1 of 3 patients with AF had signs of anxiety and depression.[23] Anxiety and depression are some of the most common causes of disability pension and sick days in Denmark.[24] Hence, AF might contribute to triggering symptoms of anxiety and/or depression which eventually cause work disabilities and low work participation. Future studies should look more into the role of anxiety/depression in patients with AF with work disabilities and low work participation. Potentially, public health authorities might suggest incorporating screening for depression and accompanying treatment to the standard care program for AF management. In the long term, this might reduce the economic and health burden related to AF.

We also observed that the risk of work disability in the AF cohort versus matched reference cohort was more

Table 2
Risk difference of permanent social security benefit for patients with AF versus matched individuals stratified on groups of socioeconomic factors.

	Risk for AF cohort	Risk for reference cohort	RD and 95% CI (**Model 1**)	RD and 95% CI (**Model 2**)	RD and 95% CI (**Model 3**)
All	4.5 (4.3 to 4.8)	1.3 (1.3 to 1.4)	3.1 (2.9 to 3.4)	2.3 (2.0 to 2.5)	2.1 (1.9 to 2.4)
Education					
Low	6.9 (6.3 to 7.5)	2.1 (2.0 to 2.2)	4.7 (4.1 to 5.3)	3.5 (2.9 to 4.1)	3.4 (2.8 to 4.0)
Medium	4.4 (4.1 to 4.7)	1.3 (1.2 to 1.3)	3.1 (2.8 to 3.4)	2.2 (1.9 to 2.5)	2.1 (1.8 to 2.4)
High	2.4 (2.0 to 2.7)	0.8 (0.7 to 0.8)	1.6 (1.2 to 2.0)	1.1 (0.8 to 1.5)	1.1 (0.7 to 1.4)
P-value	-	-	0.0000	0.0000	0.0000
Income					
Low	8.5 (7.9 to 9.2)	3.1 (2.9 to 3.2)	5.5 (4.8 to 6.1)	3.7 (3.1 to 4.3)	3.5 (2.9 to 4.2)
Medium	4.1 (3.7 to 4.5)	1.1 (1.0 to 1.1)	3.1 (2.7 to 3.5)	2.3 (1.9 to 2.7)	2.2 (1.8 to 2.6)
High	2.2 (1.9 to 2.5)	0.5 (0.5 to 0.6)	1.7 (1.4 to 1.9)	1.3 (1.0 to 1.5)	1.2 (0.9 to 1.5)
P-value	-	-	0.0000	0.0000	0.0000
Cohabiting status					
Alone	5.7 (5.2 to 6.3)	1.8 (1.7 to 1.9)	3.8 (3.3 to 4.4)	2.6 (2.0 to 3.2)	2.4 (1.8 to 3.0)
Not alone	4.2 (3.9 to 4.4)	1.2 (1.2 to 1.2)	2.9 (2.7 to 3.2)	2.2 (1.9 to 2.4)	2.1 (1.8 to 2.3)
P-value			0.0051	0.1898	0.2908

Model 1: Age, gender, residence, income, education and cohabiting status.

Model 2: Model 1 and CAD, HF, DM, hypertension, peripheral vascular disease, liver disease, renal disease, alcoholism, abuse, connective tissue disease, chronic pulmonary disease, cancer, schizophrenia and backpain.

Model 3: Model 2 and stroke, dementia, and anxiety/depression.

AF = atrial fibrillation; CI = confidence interval; CAD = coronary artery disease; HF = heart failure; DM = diabetes mellitus; RD = risk difference.

P-value: Indicates if effect modification by education, income and cohabiting status was statistically significant.

Table 3
Work participation score (WPS) difference for patients with AF the subcohort stratified on groups of socioeconomic factors.

	Mean WPS for AF cohort	Mean WPS for reference cohort	Crude difference	Adjusted difference*
WPS	83.1	89.9	-6.8 (-7.3 to -6.4)	-5.9 (-6.3 to -5.5)
Education				
Low	74.9	84.5	-9.6 (-10.7 to -8.6)	-7.7 (-8.7 to -6.7)
Medium	83.1	90.2	-7.0 (-7.7 to -6.4)	-6.2 (-6.8 to -5.6)
High	90.5	94.5	-4.1 (-4.8 to -3.4)	-3.7 (-4.3 to -3.0)
P-value			0.0000	0.0000
Income				
Low	67.7	78.3	-10.7 (-11.8 to -9.5)	-8.7 (-9.6 to -7.7)
Medium	84.3	91.5	-7.2 (-7.9 to -6.5)	-6.7 (-7.3 to -6.0)
High	91.6	95.4	-3.8 (-4.4 to -3.3)	-3.6 (-4.1 to -3.1)
P-value			0.0000	0.0000
Cohabiting status				
Alone	78.4	86.4	-8.0 (-9.1 to -6.9)	-6.7 (-7.6 to -5.7)
Not alone	84.4	90.9	-6.5 (-7.0 to -6.0)	-5.6 (-6.1 to -5.2)
P-value			0.0000	0.0540

AF = atrial fibrillation; CI = confidence interval; ref = reference; WPS = work participation score.
*Adjusted for age, baseline WPS and gender.
P-value: Indicates if effect modification by education, income and cohabiting status was statistically significant.

prominent in individuals with lower education, lower income, and living alone than in those with higher education, higher income, and not living alone. This indicates that SEFs play an important role in lower ability to work for patients with AF.

Some limitations must be mentioned. First, because of the observational design of this study, no causal associations can be made. By extension, residual confounding is an issue, both by unknown factors and by known factors which we cannot measure. For example, we have information on patients diagnosed with anxiety or depression at the hospital, however, most patients with anxiety/depression are treated by their general practitioner from whom we do not have information. Hence, the baseline results in Table 1 demonstrating that 1% of the matched reference cohort and patients with AF had anxiety/depression is probably severely underestimated. The same problem applies to, for example, back pain. Also, it could have been interesting to see how many patients developed anxiety/depression after a diagnosis of AF and consequently were potential mediators. Second, we did not have information on important factors related to work and long-term outcomes such as type of job, job satisfaction and, physical capacity.[4] Neither did we have information on the actual cause(s) of why people received permanent social security benefits. For example, we do not know if it was because they were symptomatic or because complications (e.g., stroke) occurred. Third, although Denmark is a welfare state with equal social rights to all citizens, some factors might vary with income and insurance. Finally, WPS for the AF cohort and the matched reference cohort probably does not reflect the "true" WPS in an unselected population with AF or the general population because we excluded all persons who died in the period or received permanent social security. Consequently, these results must be interpreted with caution.

Some strengths must be mentioned. First, AF, in general, is rare in the younger population; however, using nationwide registers we were able to obtain a very large population of working-age patients with AF. Second, Danish nationwide registers are of high quality with almost complete follow-up.[9] Third, using nationwide registers, the risk of recall bias and selection bias was minimized. Fourth, in Denmark, all citizens have the same right to be entitled to social security benefits if they are not capable of maintaining a full-time job because of their physical or psychological health. Consequently, receiving a permanent social security benefit must be assumed to be a reliable marker of work disability.

In conclusion, incident AF is associated with a higher risk of work disability. Also, patients with AF still alive and working actively 1 year after the incident AF had lower work participation than the general population. Future studies should explore the mechanism behind these findings. Holistic management of patients with AF might be beneficial to keep patients with AF in the labor market, for example, stroke prevention, symptom control, optimizing cardiovascular risk factors, patient education, and handling of psychosocial side effects.

Disclosures

The authors have no conflicts of interest to declare.

Data Availability

Access to data is only given to researchers who are responsible for the specific study. Hence, according to Danish law, data from this article cannot be shared publicly.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2021.12.039.

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