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Shift work is associated with 10-year incidence of atrial fibrillation in younger but not older individuals from the general population: results from the Tromsø Study

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ABSTRACT

Objectives Shift work is associated with myocardial infarction and stroke. We studied if shift work is also associated with incident atrial fibrillation (AF) and if this association differs, depending on sex and age.

Methods We studied 22 339 participants (age 37.0±9.8 years, 49% women) with paid work from the third (1986–1987), fourth (1994–1995), fifth (2001) and sixth (2007–2008) surveys of the population-based Tromsø Study, Norway. Participants were followed up for ECG-confirmed AF through 2016. Shift work was assessed by questionnaire at each survey. We used unadjusted and multivariable-adjusted Cox regression models to study the association of shift work with 10-year incident AF and incident AF during extensive follow-up up to 31 years. Interactions with sex and age were tested in the multivariable model.

Results Shift work was reported by 21% of participants at the first attended survey. There was an interaction between shift work and age for 10-year incident AF (p=0.069). When adjusted for AF risk factors, shift work was significantly associated with 10-year incident AF in participants <40 years (HR 2.90, 95% CI 1.12 to 7.49) but not≥40 years of age (HR 0.90, 95% CI 0.53 to 1.51). Shift work was not associated with incident AF during extensive follow-up (HR 1.03, 95% CI 0.89 to 1.20). There was no interaction between shift work and sex.

Conclusions Shift work was associated with 10-year incident AF in individuals <40 years but not ≥40 years of age. Shift work was not associated with incident AF during extensive follow-up up to 31 years, and there were no sex differences.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Shift work is associated with coronary artery disease and stroke. However, comparatively little is known about the association between shift work and atrial fibrillation (AF).

⇒ One previous study found a significant association between shift work and AF but did not include younger individuals.

WHAT THIS STUDY ADDS

⇒ In a large population-based cohort, we found that shift work was associated with 10-year incident AF in individuals <40 years but not ≥40 years of age.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our findings demonstrate that future studies into shift work and AF, as well as potential preventive measures in shift workers, should also focus on younger individuals.

INTRODUCTION

Atrial fibrillation (AF) is a major cause of morbidity, mortality and reduced quality of life.[1 2] The lifetime risk of AF is estimated to be up to one in three, and its prevalence will likely increase even further due to increases in life expectancy and rising prevalence of risk factors for AF.[1 3] In order to improve prevention and early detection of AF, it is essential to identify people at risk of AF.

Shift work, which is generally defined as any type of work that is done outside of conventional daytime working schedules,[4] is becoming increasingly common due to increasing demands from the so-called '24-hour society' that has emerged in recent years.[5 6] In 2015, approximately 21% of workers in the European Union reported doing shift work, compared with 17% in 2005 and 2010.[7] Previous studies have demonstrated that shift work is associated with adverse cardiovascular outcomes, in particular coronary artery disease and stroke.[4 6 8 9] Since AF and other types of cardiovascular disease (CVD) share similar risk factors and increase the risk of each other,[10 11] it seems likely that shift work could also be associated with AF. Furthermore, shift work is associated

with reduced heart rate variability and autonomic dysfunction, which are in turn associated with AF.[12–16] Indeed, previous studies have demonstrated that unhealthy sleep patterns and long working hours, both of which may be a consequence of shift work, are associated with a higher risk of AF.[17 18]

Nevertheless, only one study has previously studied the association of shift work with AF.[19] This study demonstrated that current shift work was associated with increased risk of incident AF in individuals 40–69 years of age.[19] Furthermore, the study reported a significant association between lifetime exposure to shift work and incident AF in women but not in men.[19] Still, additional studies are needed in order to corroborate these findings. Furthermore, it remains unknown if shift work is associated with an increased risk of AF in younger individuals.

Therefore, we studied the association between shift work and incident AF as well as potential interactions with age and sex.

METHODS

Study population and procedures

The study was performed using data from the Tromsø Study, which has been described in detail previously.[20 21] In short, the Tromsø Study is an ongoing population-based cohort study conducted in the municipality of Tromsø, Norway. The study includes participants from the general population, who are invited based on birth cohorts and random cohorts. Starting in 1974, seven surveys (Tromsø1–Tromsø7) have been performed thus far, all of which have included extensive questionnaires, clinical examinations and blood sampling. At each survey, participants from previous surveys as well as new participants are included.

For the present study, we used data from the Tromsø3 (1986–1987), Tromsø4 (1994–1995), Tromsø5 (2001) and Tromsø6 (2007–2008) surveys. We included all participants with paid work who attended at least one of these four surveys (n=24 535). If participants attended multiple surveys, the first attended survey was considered the baseline visit. Tromsø3 was the first attended survey for 69% of all included participants. Tromsø4, Tromsø5 and Tromsø6 were the first attended survey for 22%, 2% and 7% of participants, respectively. We excluded participants with insufficient data on AF or in whom it was unclear whether they developed AF or not (n=1066), participants with prevalent AF at baseline (n=43) and participants without available data on shift work (n=1062), leaving a total of 22 339 participants.

Ascertainment of AF

The method of AF ascertainment has been described in detail previously.[22 23] In summary, participants were linked to the hospital diagnosis registry of the University Hospital of North Norway, which is the only hospital in the Tromsø municipality. This registry contains diagnoses from inpatient and outpatient visits, which are coded according to the 9th and/or 10th revision of the International Classification of Diseases (ICD-9 and ICD-10). In order to identify potential cases of AF, the registry was searched for ICD-9 code 427 (cardiac dysrhythmias) and ICD-10 codes I47 (paroxysmal tachycardia) and I48 (AF and flutter). In addition, the medical records of all participants with other cardiovascular or cerebrovascular events (based on ICD-9 codes 410–414, 428 and 430–438 and ICD-10 codes I20-I25, I46, I50 and I60–I69) were searched for notes mentioning AF. All events were adjudicated by an independent endpoint committee. The diagnosis of AF was confirmed only if AF was documented by ECG. AF that occurred within 28 days of acute myocardial infarction, acute heart failure or cardiac surgery, as well as AF occurring within the 7 days prior to death, was not classified as AF. For the present study, follow-up data for AF were available through 2016.

Exposure

Shift work was defined as self-reported shift or night work, as assessed by a single yes/no questionnaire item at each survey.

Covariates

Systolic and diastolic blood pressures, resting heart rate, body mass index (BMI) and total cholesterol were measured according to previously published methods.[23] Information regarding diabetes, use of antihypertensive drugs, history of myocardial infarction and stroke, smoking, physical activity, education level and (paid) work status was determined by questionnaire. Hypertension was defined as systolic blood pressure of ≥140 mm Hg and/or diastolic blood pressure of ≥90 mm Hg and/or use of antihypertensive drugs. Overweight and obesity were defined as BMI of 25–30 kg/m^2 and BMI of ≥30 kg/m^2, respectively. Education level was classified as <10 years (primary education only), 10–12 years (high school education) or >12 years (higher education).

Follow-up

The follow-up duration was calculated as the time from the first attended survey to the date of incident AF, censoring due to migration or death or the end of the follow-up period (31 December 2016), whichever came first. Data regarding death and migration were retrieved from the National Population Register of Norway.

Statistical analyses

Clinical characteristics were compared between participants with and without shift work. For continuous data, characteristics were compared using the independent samples t-test. For binary data, Pearson's χ^2 test was used.

We used Kaplan-Meier analyses and Cox regression models to study the association of shift work at baseline with (1) 10-year incident AF and (2) incident AF during extensive follow-up through 2016. For both outcomes,

Table 1 Clinical characteristics of participants with and without shift work: the Tromsø Study

Characteristics	Shift work		P value
	No (n=17 623)	Yes (n=4716)	
Age (years)	37.4±9.9	35.6±9.4	<0.001
Female sex	8544 (48%)	2336 (50%)	0.199
BMI (kg/m^2)	24.1±3.4	24.3±3.7	0.001
Overweight	5053 (29%)	1378 (29%)	0.471
Obesity	1023 (5.8%)	346 (7.3%)	<0.001
SBP (mmHg)	127.3±14.8	125.8±14.4	<0.001
DBP (mmHg)	75.6±10.6	74.1±10.4	<0.001
Antihypertensive drug use	389 (2.2%)	76 (1.6%)	0.011
Hypertension	3766 (21%)	830 (18%)	<0.001
Resting heart rate (beats/min)	71.5±13.2	71.5±12.7	0.970
Total cholesterol (mmol/L)	5.6±1.2	5.6±1.2	0.601
Diabetes	96 (0.5%)	21 (0.4%)	0.398
History of myocardial infarction	80 (0.5%)	21 (0.4%)	0.934
History of stroke	32 (0.2%)	5 (0.1%)	0.256
Current smoking	6860 (39%)	2220 (47%)	<0.001
Sedentary lifestyle	4234 (24%)	1255 (27%)	<0.001
Highly active lifestyle	3509 (20%)	853 (18%)	0.005
Primary education only	4326 (25%)	1314 (28%)	<0.001
Higher education	7509 (43%)	1655 (35%)	<0.001

Data presented as mean±SD or count (%). P values represent the difference between participants with and without shift work at baseline. Overweight was defined as BMI of 25–30 kg/m^2, obesity as BMI of ≥30 kg/m^2 and hypertension as SBP of ≥140 mm Hg and/or DBP of ≥90 mm Hg and/or use of antihypertensive drugs.
BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure.

we built four Cox regression models: (1) an unadjusted model including shift work only; (2) model 1, additionally adjusted for age and sex; (3) model 2, additionally adjusted for components of the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) AF risk model (weight, height, systolic blood pressure, diastolic blood pressure, use of antihypertensive drugs, diabetes, smoking and history of myocardial infarction)[24]; and (4) model 3, additionally adjusted for education level. Next, we tested for interactions with age and sex in the full multivariable model. In case of a significant interaction, the analyses were stratified by the interaction variable. For age, a cut-off of 40 years was chosen since participants <40 years of age were not included in previous studies on shift work and AF.

We performed several sensitivity analyses. For 10-year incident AF, due to the modest number of AF events in participants <40 years and the consequent risk of overfitting for models 3 and 4, we built additional Cox regression models in which we used propensity score adjustment rather than adjustment for all separate covariates. The propensity score for the presence of shift work was calculated using relevant clinical characteristics as included in table 1. Furthermore, we performed sensitivity analyses in which the follow-up duration was restricted to 62, 67 or 75 years of age (the minimum, usual and maximum retirement age in Norway, respectively). For incident AF during extensive follow-up, we performed additional Cox regression analyses in which shift work status was allowed to change over time (ie, shift work was included as a time-varying covariate). In these analyses, we additionally adjusted for paid work status at each visit in order to account for changes in employment status after baseline. Finally, we additionally performed Cox regression analyses in which we classified participants according to shift work status at the first and second attended surveys: (1) no shift work at either survey (reference category), (2) shift work at the first but not the second survey, (3) shift work at the second survey only and (4) shift work at both surveys. For these additional analyses, we included all participants with available shift work data at two or more surveys. Here, the second attended survey was considered to be the baseline, and we excluded participants in whom AF was diagnosed prior to this date.

The Cox proportional hazards assumption was assessed graphically using Kaplan-Meier curves,[25] which revealed no violations of the proportional hazards assumption. Analyses were performed using IBM SPSS V.25. P values of <0.05 or interaction p values of <0.10 were considered statistically significant.

RESULTS

Participant characteristics

Mean age was 37.0±9.8 years, and 49% were women. Current shift work was reported by 4716 (21%) participants at the first attended survey. Shift workers were younger (35.6±9.4 vs 37.4±9.9) and less physically active (27% vs 24% with sedentary lifestyle and 18% vs 20% with highly active lifestyle), and had lower education levels (35% vs 43% higher education), lower prevalence of hypertension (18% vs 21%), higher BMI (24.3±3.7 vs 24.1±3.4) and higher prevalence of smoking (47% vs 39%) compared with those without shift work (table 1).

Shift work and 10-year incident AF

During 10 years of follow-up, 129 participants (0.6%) developed incident AF. Of all 10-year incident AF cases, 25 occurred in participants with shift work (incidence rate 0.59 per 1000 person-years) and 104 in participants without shift work (incidence rate 0.65 per 1000 person-years).

In the total study population, shift work was not significantly associated with 10-year incident AF (online supplemental table S1). However, there was a significant interaction between shift work and age (p for interaction=0.069) for 10-year incident AF. Age-stratified Kaplan-Meier plots demonstrated that shift work was significantly associated with 10-year incident AF in participants <40 years (p=0.033) but not ≥40 years of age (p=0.601) (figure 1A,B, and online supplemental figure S1A,B). Age-stratified participant characteristics are shown in online supplemental table S2A,B. Further stratification of the older age group revealed no significant associations between shift work and incident AF in participants 40–49 years, 50–59 years or 60–69 years of age (online supplemental table S3).

Age-stratified Cox regression showed that, after adjustment for age, sex and risk factors, shift work was significantly associated with 10-year incident AF in participants <40 years (HR 2.90, 95% CI 1.12 to 7.49, p=0.028) but not ≥40 years of age (HR 0.90, 95% CI 0.53 to 1.51, p=0.677) (table 2). The association of shift work with 10-year incident AF in participants <40 years of age was slightly attenuated after additional adjustment for education level and physical activity (HR 2.64, 95% CI 0.99 to 7.00, p=0.051) (table 2). Propensity score-adjusted Cox regression models produced virtually identical results (online supplemental table S4). Classifying participants according to shift work status at the first and second attended surveys also produced largely similar results (online supplemental table S5). There was no significant interaction between shift work and sex (p for interaction=0.743).

Shift work and incident AF during extensive follow-up of up to 31 years

During extensive follow-up with a median duration of 24 (15–30) years, 1244 participants (5.6%) developed AF. Of all incident AF cases, 221 occurred in participants with shift work (incidence rate 2.3 per 1000 person-years) and 1023 in participants without shift work (incidence rate 2.7 per 1000 person-years).

During the extensive follow-up, shift work was not significantly associated with incident AF in any of the models (HR 0.88, 95% CI 0.76 to 1.02, p=0.083 for model 1; HR 1.02, 95% CI 0.88 to 1.19, p=0.773 for model 4) (table 3), and none of the interaction terms with age (p for interaction=0.170) or sex (p for interaction=0.511) were significant. Sensitivity analyses in which the follow-up was restricted to 62, 67 or 75 years of age (results not shown), in which shift work was included as a time-varying covariate (online supplemental table S6), or in which participants were classified according to shift work status at the first and second attended surveys (online supplemental table S7), did not yield materially different results.

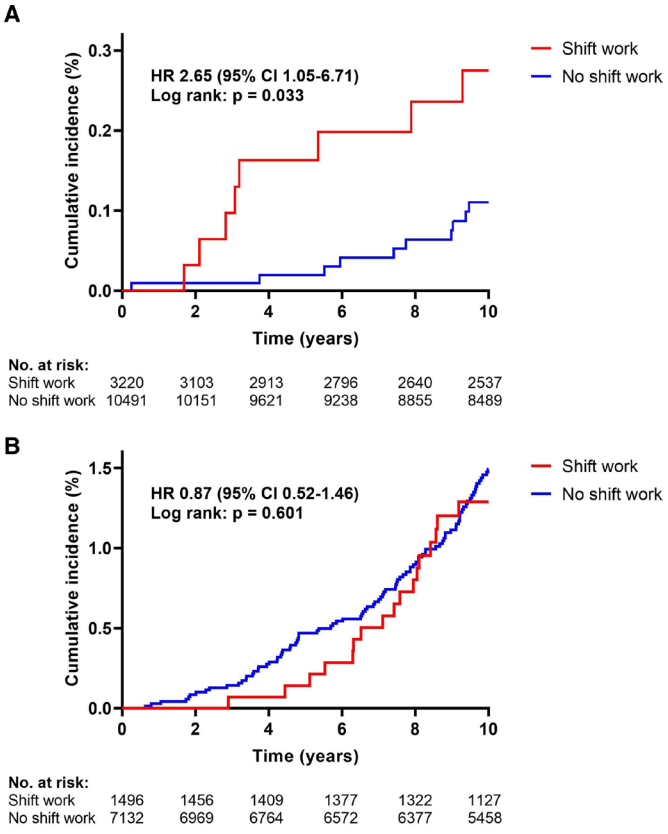

Figure 1 (A) Kaplan-Meier cumulative incidence plot for incident AF in participants <40 years with and without shift work: the Tromsø Study. (B) Kaplan-Meier cumulative incidence plot for incident AF in participants ≥40 years with and without shift work:The Tromsø Study. AF, atrial fibrillation.

DISCUSSION

In this study, we demonstrated that shift work was associated with 10-year incident AF in working participants <40 years but not ≥40 years of age from the population-based Tromsø Study. Shift work was not associated with incident AF during extensive follow-up of up to 31 years, and we

Table 2 HRs for the association between shift work and 10-year incidence of AF, stratified by age: the Tromsø Study

Determinant and age group	HR (95% CI)	P value
Model 1: unadjusted		
Shift work (age <40 years)	2.65 (1.05 to 6.71)	0.040
Shift work (age ≥40 years)	0.87 (0.52 to 1.46)	0.601
Model 2: adjusted for age and sex		
Shift work (age <40 years)	2.90 (1.14 to 7.34)	0.025
Shift work (age ≥40 years)	0.93 (0.55 to 1.56)	0.778
Model 3: adjusted for age, sex and CHARGE-AF risk model		
Shift work (age <40 years)	2.90 (1.12 to 7.49)	0.028
Shift work (age ≥40 years)	0.90 (0.53 to 1.51)	0.677
Model 4: adjusted for age, sex, CHARGE-AF risk model, education level and physical activity		
Shift work (age <40 years)	2.64 (0.99 to 7.00)	0.051
Shift work (age ≥40 years)	0.92 (0.54 to 1.55)	0.744

HRs and p values represent the association between shift work and 10-year AF in participants aged <40 years (n=13 711, number of AF cases=18, crude incidence=0.1%) or participants aged ≥40 years (n=8628, number of AF cases=111, crude incidence=1.3%). Components of the CHARGE-AF risk model were weight, height, systolic and diastolic blood pressures, antihypertensive drug use, diabetes, smoking and history of myocardial infarction.
AF, atrial fibrillation.

did not find sex differences in the association between shift work and AF.

Only one study has previously studied the relationship between shift work and AF: in working individuals from the UK Biobank, during a median follow-up of 10.4 years, current night shift work and lifetime exposure to night shift work were associated with incident AF.[19] Our finding that shift work was associated with 10-year incident AF in participants aged 40 years is seemingly in line with these previous results. However, in contrast to the Tromsø Study, only participants 40–69 years of age were included in the UK Biobank. Furthermore, the study on UK Biobank participants did not report on possible interactions between shift work and age. Therefore, our study provides novel and important insights regarding the association between shift work and AF in different age groups.

Table 3 HRs for the association between shift work and incident AF during extensive follow-up of up to 31 years: the Tromsø Study

HR (95% CI)	P value
Model 1: unadjusted	
0.88 (0.76 to 1.02)	0.083
Model 2: adjusted for age and sex	
1.07 (0.92 to 1.23)	0.385
Model 3: adjusted for age, sex and CHARGE-AF risk model	
1.03 (0.89 to 1.20)	0.675
Model 4: adjusted for age, sex, CHARGE-AF risk model, education level and physical activity	
1.02 (0.88 to 1.19)	0.773

HRs and p values represent the association between shift work and incident AF during extensive follow-up (number of AF cases=1244) in the total study population (n=22 339). Components of the CHARGE-AF risk model were weight, height, systolic and diastolic blood pressures, antihypertensive drug use, diabetes, smoking and history of myocardial infarction.
AF, atrial fibrillation.

In contrast to the results from the UK Biobank, we did not find a significant association between shift work and 10-year incident AF in participants aged ≥40 years, nor did we find a significant interaction between shift work and sex. Potential explanations for these contrasting findings may be regional differences (Northern Norway vs UK) or differences in the time period during which participants were included (1986–2008 for the Tromsø Study vs 2006–2010 for the UK Biobank). Such contrasts in time and region may in turn be associated with differences in lifestyle and the type of (shift) work, as well as healthcare differences. Furthermore, different definitions were used between the UK Biobank (night shift work) and the Tromsø Study (shift work in general).

Our finding that shift work was associated with 10-year incident AF in younger, but not older, participants seems consistent with previous studies which have demonstrated that risk factors generally confer a larger *relative* risk of CVD in younger age groups, despite lower *absolute* risk.[26–28] This may be explained by the fact that multiple risk factors (including age itself) accumulate with advancing age.[29] As a consequence of these competing risk factors, the role of shift work may become comparatively small in older individuals. In general, estimates of relative risk are dependent on baseline risk.[30] Although the relative risk of AF associated with shift work was higher in younger compared with older participants, the absolute risk of AF was substantially lower in younger participants.

Another factor that may have affected our results is the so-called 'healthy worker effect': individuals with existing health issues may opt for jobs with conventional working schedules, and shift workers who develop new health issues (potentially as a consequence of shift work) may stop doing shift work as a result.[5 8] Because shift workers are less at risk to begin with, the risk associated with shift work may be underestimated.[29] In our study, shift workers less often had hypertension (despite higher prevalence of obesity and smoking) compared with non-shift workers, which could be indicative of the healthy worker effect. Furthermore, in participants ≥40 years of age, the risk of AF in shift work was lower during the first years of follow-up (possibly due to the healthy worker effect), but caught up with non-shift workers after roughly 8 years of follow-up (potentially due to competing risk factors).

Finally, during extensive follow-up of up to 31 years, we found no significant association between shift work and incident AF, and the interaction with age became non-significant. This could be due to competing risk factors,

retirement of older participants, changes in employment or changes in shift work status, all of which may have diluted the long-term results. In order to account for retirement, we performed sensitivity analyses in which we limited the follow-up duration to the minimum, usual and maximum retirement ages in Norway. In order to account for changes in employment and shift work status, we additionally performed sensitivity analyses with time-varying covariates for shift work and paid work status. None of the sensitivity analyses materially altered the results. Still, since not all participants attended multiple surveys, unknown changes in employment and shift work status may have influenced the long-term results.

Strengths and limitations

Our study was performed in a large population-based cohort with prospective data collection, long-term follow-up and solid validation of incident AF.

Limitations include the lack of information regarding the frequency or lifetime exposure to shift work, both of which were previously shown to be associated with incident AF.[19] Furthermore, no distinction was made between different types of shift work (eg, evening or night work, rotational shifts), which may have different effects on the risk of AF and should be taken into account in future studies. The incidence of AF in our study was fairly low, which may be explained by the inclusion of mainly young and healthy participants (healthy volunteer selection bias), a known issue to population-based cohort studies.[19] Given the modest number of incident AF events, particularly in younger participants, our findings should be interpreted with some caution. Despite the thorough adjudication of hospital records for possible AF events, cases of unrecognised AF as well as cases treated exclusively in primary care may have been missed. Although we extensively adjusted for components of the CHARGE-AF risk model, residual confounding by unknown factors may play a role in the association between shift work and AF. Since the majority of participants were first included in Tromsø3 (1986–1987), results for 10-year incident AF might be different in a more contemporary setting due to changes in (the type of) shift work and lifestyle, as well as advances in risk factor management and AF screening. Finally, the population from Tromsø is predominantly Caucasian, which may limit the generalisability of our results.

CONCLUSIONS

In a large, population-based cohort, shift work at baseline was associated with 10-year risk of AF in individuals <40 years but not ≥40 years of age. During extensive follow-up of up to 31 years, shift work was not associated with incident AF. We did not find sex differences in the association between shift work and AF. Additional studies are needed to further clarify the relationship between shift work and AF, and such studies should take into account frequency, lifetime exposure and type of shift work. Our findings highlight that future studies, as well as potential preventive measures in shift workers, should also focus on younger individuals.

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Contributors VWZ, ES, MLL and MR contributed to the conception, design and acquisition of the work, data analysis and interpretation. VWZ and MR drafted the manuscript and are responsible for the overall content of the work as guarantors. All authors contributed to the critical revision of the manuscript, gave final approval of the version to be published and agreed to be accountable for all aspects of the work.

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Patient consent for publication Not applicable.

Ethics approval The Tromsø Study as well as the present study were approved by the Regional Committee for Medical and Health Research Ethics, North Norway (reference number for the present study: 138884). The Tromsø Study was performed in accordance with the Declaration of Helsinki. From Tromsø4 and onwards, participants provided written informed consent, and living participants from prior surveys were provided the opportunity to withdraw from the study.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. Data may be obtained by submitting an application to the Tromsø Study. For more information, please visit: https://uit.no/research/tromsostudy.

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Supplementary data

Shift work is associated with 10-year incidence of atrial fibrillation in younger but not older individuals from the general population: results from the Tromsø Study

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Contents

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Table S1: Hazard ratios for the association between shift work and 10-year incidence of atrial fibrillation in the total study population. The Tromsø Study

Hazard ratio (95% confidence interval)	p-value
Model 1: unadjusted	
0.91 (0.59-1.42)	0.688
Model 2: adjusted for age and sex	
1.17 (0.76-1.81)	0.480
Model 3: adjusted for age, sex, and CHARGE-AF risk model	
1.13 (0.72-1.75)	0.597
Model 4: adjusted for age, sex, CHARGE-AF risk model, education level, and physical activity	
1.13 (0.72-1.77)	0.590

Hazard ratios and p-values represent the association between shift work and 10-year incident AF (number of AF cases = 129) in the total study population (n = 22 339). Components of the CHARGE-AF risk model were weight, height, systolic and diastolic blood pressure, antihypertensive drug use, diabetes, smoking, and history of myocardial infarction. AF, atrial fibrillation.

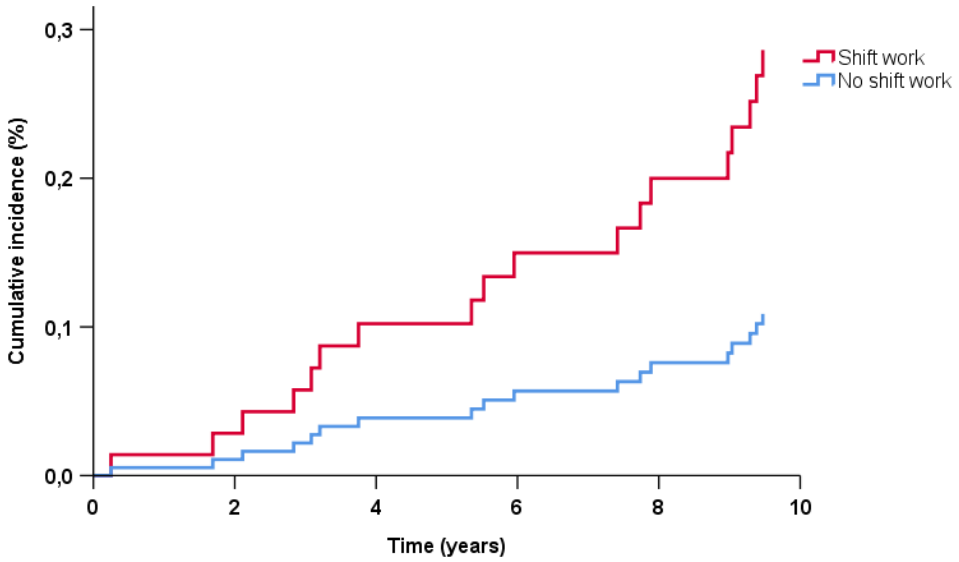

Figure S1a: Propensity score-adjusted Kaplan-Meier cumulative incidence plot for incident atrial fibrillation in participants <40 years with and without shift work

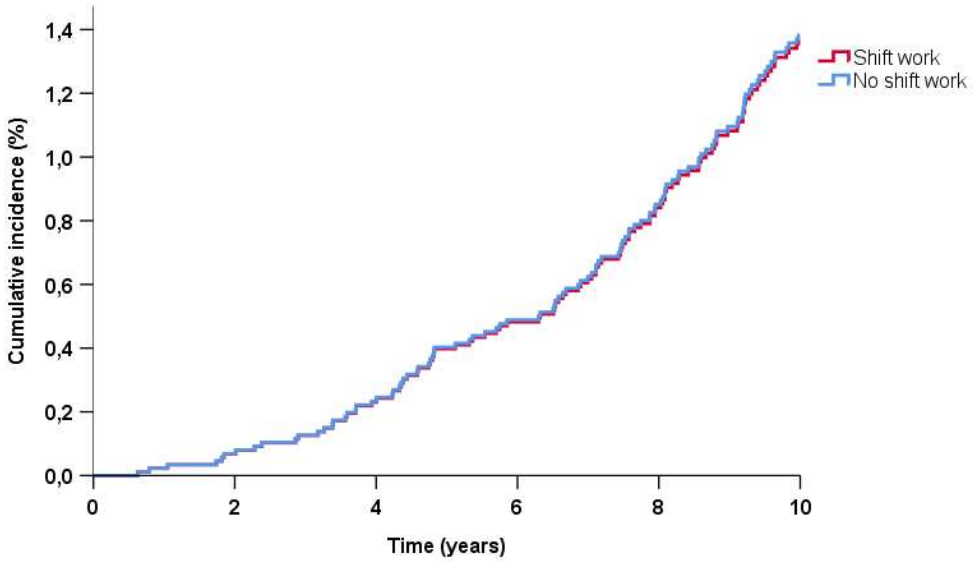

Figure S1b: Propensity score-adjusted Kaplan-Meier cumulative incidence plot for incident atrial fibrillation in participants ≥40 years with and without shift work

Table S2a: Clinical characteristics of participants <40 years with and without shift work. The Tromsø Study

Characteristic	Shift work		p-value
	No (n = 10 491)	Yes (n = 3220)	
Age (years)	30.7 ± 5.3	30.3 ± 5.0	<0.001
Female sex	5271 (50%)	1680 (52%)	0.055
BMI (kg/m^2)	23.5 ± 3.2	23.8 ± 3.5	<0.001
Overweight	2393 (23%)	779 (24%)	0.106
Obesity	434 (4%)	186 (6%)	<0.001
SBP (mmHg)	125.0 ± 12.9	123.8 ± 12.7	<0.001
DBP (mmHg)	72.6 ± 9.4	71.6 ± 9.3	<0.001
Antihypertensive drug use	52 (0.5%)	10 (0.3%)	0.171
Hypertension	1499 (14%)	369 (11%)	<0.001
Resting heart rate (bpm)	71.7 ± 13.1	71.5 ± 12.6	0.334
Total cholesterol (mmol/L)	5.3 ± 1.0	5.3 ± 1.1	0.035
Diabetes	31 (0.3%)	9 (0.3%)	0.882
History of MI	3 (0.0%)	4 (0.1%)	0.057
History of stroke	11 (0.1%)	4 (0.1%)	0.763
Current smoking	4300 (41%)	1541 (48%)	<0.001
Sedentary lifestyle	2536 (24%)	840 (26%)	0.025
Highly active lifestyle	2277 (22%)	613 (19%)	0.001
Primary education only	1705 (16%)	640 (20%)	<0.001
Higher education	4929 (47%)	1299 (40%)	<0.001

Data presented as mean ± standard deviation or count (%). P-values represent the difference between participants with and without shift work at baseline. Overweight was defined as BMI 25-30 kg/m^2, obesity as BMI ≥ 30 kg/m^2, and hypertension as SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg and/or use of antihypertensive drugs. BMI, body mass index; bpm, beats per minute; DBP, diastolic blood pressure; MI, myocardial infarction; SBP, systolic blood pressure.

Table S2b: Clinical characteristics of participants ≥40 years with and without shift work. The Tromsø Study

Characteristic	Shift work		p-value
	No (n = 7132)	Yes (n = 1496)	
Age (years)	47.3 ± 6.1	46.9 ± 5.9	0.019
Female sex	3273 (46%)	656 (44%)	0.149
BMI (kg/m^2)	25.0 ± 3.5	25.4 ± 3.8	<0.001
Overweight	2660 (37%)	599 (40%)	0.049
Obesity	589 (8%)	160 (11%)	0.002
SBP (mmHg)	130.5 ± 16.8	130.1 ± 16.7	0.422
DBP (mmHg)	80.0 ± 10.7	79.4 ± 10.7	0.096
Antihypertensive drug use	337 (5%)	66 (4%)	0.599
Hypertension	2267 (32%)	461 (31%)	0.437
Resting heart rate (bpm)	71.1 ± 13.4	71.4 ± 12.9	0.314
Total cholesterol (mmol/L)	6.1 ± 1.2	6.3 ± 1.3	<0.001
Diabetes	65 (1%)	12 (1%)	0.678
History of MI	77 (1%)	17 (1%)	0.854
History of stroke	21 (0.3%)	1 (0.1%)	0.157
Current smoking	2560 (36%)	679 (45%)	<0.001
Sedentary lifestyle	1698 (24%)	415 (28%)	0.001
Highly active lifestyle	1232 (17%)	240 (16%)	0.255
Primary education only	2621 (37%)	674 (45%)	<0.001
Higher education	1580 (36%)	356 (24%)	<0.001

Data presented as mean ± standard deviation or count (%). P-values represent the difference between participants with and without shift work at baseline. Overweight was defined as BMI 25-30 kg/m^2, obesity as BMI ≥ 30 kg/m^2, and hypertension as SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg and/or use of antihypertensive drugs. BMI, body mass index; bpm, beats per minute; DBP, diastolic blood pressure; MI, myocardial infarction; SBP, systolic blood pressure.

Table S3: Hazard ratios for the association between shift work and 10-year incidence of atrial fibrillation, stratified by age category. The Tromsø Study

Determinant and age group	HR (95% CI)	p-value
Model 1: unadjusted		
Age < 40 years	2.65 (1.05-6.71)	0.040
Age 40-49 years	1.07 (0.50-2.30)	0.860
Age 50-59 years	0.98 (0.46-2.10)	0.956
Age 60-69 years	0.33 (0.04-2.44)	0.277
Model 2: adjusted for age and sex		
Age < 40 years	2.90 (1.14-7.34)	0.025
Age 40-49 years	1.03 (0.48-2.22)	0.940
Age 50-59 years	1.06 (0.50-2.28)	0.874
Age 60-69 years	0.36 (0.05-2.70)	0.321
Model 3: adjusted for age, sex, and CHARGE-AF risk model		
Age < 40 years	2.90 (1.12-7.49)	0.028
Age 40-49 years	0.99 (0.45-2.14)	0.971
Age 50-59 years	1.01 (0.47-2.19)	0.973
Age 60-69 years	0.43 (0.06-3.24)	0.411
Model 4: adjusted for age, sex, CHARGE-AF risk model, education level, and physical activity		
Age < 40 years	2.64 (0.99-7.00)	0.051
Age 40-49 years	0.97 (0.44-2.13)	0.943
Age 50-59 years	1.07 (0.49-2.34)	0.873
Age 60-69 years	0.44 (0.06-3.39)	0.432

Hazard ratios and p-values represent the association between shift work and 10-year AF in participants aged <40 years (n = 13 711, number of AF cases = 18, crude incidence = 0.1%), 40-49 years (n = 5818, number of AF cases = 44, crude incidence = 0.8%), 50-59 years (n = 2429, number of AF cases = 46, crude incidence = 1.9%), and 60-69 years (n = 378, number of AF cases = 21, crude incidence = 5.6%). Components of the CHARGE-AF risk model were weight, height, systolic and diastolic blood pressure, antihypertensive drug use, diabetes, smoking, and history of myocardial infarction. AF, atrial fibrillation; CI, confidence interval; HR, hazard ratio.

Table S4: Propensity score-adjusted hazard ratios for the association between shift work and 10-year incidence of atrial fibrillation, stratified by age. The Tromsø Study

Determinant and age group	HR (95% CI)	p-value
Model 1: unadjusted		
Shift work (age < 40 years)	2.65 (1.05-6.71)	0.040
Shift work (age ≥ 40 years)	0.87 (0.52-1.46)	0.601
Model 2: adjusted for propensity score		
Shift work (age < 40 years)	2.64 (1.03-6.74)	0.043
Shift work (age ≥ 40 years)	0.99 (0.57-1.66)	0.962
Model 3: adjusted for propensity score and additionally adjusted for age and sex		
Shift work (age < 40 years)	2.59 (1.00-6.73)	0.050
Shift work (age ≥ 40 years)	0.92 (0.54-1.55)	0.754

Hazard ratios and p-values represent the association between shift work and 10-year AF in participants aged <40 years (n = 13 711, number of AF cases = 18, crude incidence = 0.1%) or participants aged ≥40 years (n = 8628, number of AF cases = 111, crude incidence = 1.3%). The propensity score was calculated using relevant clinical characteristics as included in Table 1 (age, sex, weight, height, systolic and diastolic blood pressure, antihypertensive drug use, resting heart rate, total cholesterol, diabetes, history of myocardial infarction, history of stroke, smoking, physical activity, and education level). AF, atrial fibrillation; CI, confidence interval; HR, hazard ratio.

Table S5: Hazard ratios for the association between shift work status at the 1st and 2nd attended survey and 10-year incidence of atrial fibrillation. The Tromsø Study

Determinant	HR (95% CI)	p-value
Model 1: unadjusted		
No shift work at either survey	Ref.	Ref.
Shift work at 1st survey only	0.81 (0.41-1.60)	0.550
Shift work at 2nd survey only	0.45 (0.21-0.96)	0.039
Shift work at both surveys	0.65 (0.38-1.11)	0.111
Model 2: adjusted for age and sex		
No shift work at either survey	Ref.	Ref.
Shift work at 1st survey only	1.18 (0.60-2.33)	0.627
Shift work at 2nd survey only	0.67 (0.31-1.44)	0.307
Shift work at both surveys	0.77 (0.45-1.31)	0.327
Model 3: adjusted for age, sex, and CHARGE-AF risk model		
No shift work at either survey	Ref.	Ref.
Shift work at 1st survey only	1.10 (0.56-2.18)	0.780
Shift work at 2nd survey only	0.69 (0.32-1.48)	0.344
Shift work at both surveys	0.76 (0.44-1.33)	0.342
Model 4: adjusted for age, sex, CHARGE-AF risk model, education level, and physical activity		
No shift work at either survey	Ref.	Ref.
Shift work at 1st survey only	1.10 (0.56-2.19)	0.780
Shift work at 2nd survey only	0.72 (0.34-1.55)	0.404
Shift work at both surveys	0.81 (0.47-1.42)	0.468
Model 5: adjusted for propensity score		
No shift work at either survey	Ref.	Ref.
Shift work at 1st survey only	1.11 (0.56-2.19)	0.764
Shift work at 2nd survey only	0.52 (0.23-1.18)	0.116
Shift work at both surveys	0.90 (0.53-1.55)	0.706

Hazard ratios and p-values represent the association between shift work status and 10-year incident AF (starting from the 2nd attended survey). Results are shown for participants with no shift work at either survey (reference group, n = 7731, number of AF cases = 135, crude incidence = 1.7%), with shift work at the 1st survey only (n = 670, number of AF cases = 9, crude incidence = 1.3%), with shift work at the 2nd survey only (n = 885, number of AF cases = 7, crude incidence = 0.8%), and with shift work at both surveys (n = 1306, number of AF cases = 15, crude incidence = 1.1%). Components of the CHARGE-AF risk model were weight, height, systolic and diastolic blood pressure, antihypertensive drug use, diabetes, smoking, and history of myocardial infarction. AF, atrial fibrillation; CI, confidence interval; HR, hazard ratio.

Table S6: Hazard ratios for the association of shift work with incident atrial fibrillation during extensive follow-up, with shift work included as a time-varying covariate. The Tromsø Study

Hazard ratio (95% confidence interval)	p-value
Model 1: unadjusted	
0.70 (0.59-0.84)	<0.001
Model 2: adjusted for age and sex	
0.98 (0.82-1.16)	0.779
Model 3: adjusted for age, sex, and CHARGE-AF risk model	
0.94 (0.79-1.12)	0.482
Model 4: adjusted for age, sex, CHARGE-AF risk model, education level, and physical activity	
0.93 (0.78-1.12)	0.455

Hazard ratios and p-values represent the association of shift work (included as time-varying covariate) with incident AF during extensive follow-up (n = 1244) in the total study population (n = 22 339). In order to account for changes in paid work status after baseline, paid work (included as time-varying covariate) was included in all models. Components of the CHARGE-AF risk model were weight, height, systolic and diastolic blood pressure, antihypertensive drug use, diabetes, smoking, and history of myocardial infarction. AF, atrial fibrillation.

Table S7: Hazard ratios for the association between shift work status at the 1st and 2nd attended survey and incident atrial fibrillation during extensive follow-up. The Tromsø Study

Determinant	HR (95% CI)	p-value
Model 1: unadjusted		
No shift work at either survey	Ref.	Ref.
Shift work at 1st survey only	0.74 (0.49-1.10)	0.138
Shift work at 2nd survey only	0.60 (0.42-0.84)	0.003
Shift work at both surveys	0.94 (0.74-1.20)	0.623
Model 2: adjusted for age and sex		
No shift work at either survey	Ref.	Ref.
Shift work at 1st survey only	1.07 (0.71-1.60)	0.755
Shift work at 2nd survey only	0.83 (0.59-1.17)	0.294
Shift work at both surveys	1.07 (0.84-1.35)	0.604
Model 3: adjusted for age, sex, and CHARGE-AF risk model		
No shift work at either survey	Ref.	Ref.
Shift work at 1st survey only	0.95 (0.63-1.44)	0.807
Shift work at 2nd survey only	0.80 (0.56-1.14)	0.223
Shift work at both surveys	1.07 (0.84-1.37)	0.570
Model 4: adjusted for age, sex, CHARGE-AF risk model, education level, and physical activity		
No shift work at either survey	Ref.	Ref.
Shift work at 1st survey only	0.94 (0.62-1.42)	0.752
Shift work at 2nd survey only	0.81 (0.57-1.16)	0.248
Shift work at both surveys	1.08 (0.85-1.38)	0.538
Model 5: adjusted for propensity score		
No shift work at either survey	Ref.	Ref.
Shift work at 1st survey only	0.89 (0.59-1.34)	0.567
Shift work at 2nd survey only	0.72 (0.51-1.02)	0.063
Shift work at both surveys	1.18 (0.93-1.50)	0.180

Hazard ratios and p-values represent the association between shift work status and incident AF during extensive follow-up (starting from the 2nd attended survey). Results are shown for participants with no shift work at either survey (reference group, n = 7731, number of AF cases = 482, crude incidence = 6.2%), with shift work at the 1st survey only (n = 670, number of AF cases = 25, crude incidence = 3.7%), with shift work at the 2nd survey only (n = 885, number of AF cases = 35, crude incidence = 4.0%) and with shift work at both surveys (n = 1306, number of AF cases = 79, crude incidence = 6.0%). Components of the CHARGE-AF risk model were weight, height, systolic and diastolic blood pressure, antihypertensive drug use, diabetes, smoking, and history of myocardial infarction. AF, atrial fibrillation; CI, confidence interval; HR, hazard ratio.