## 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

Victor W. Zwartkruis, Ekaterina Sharashova, Tom Wilsgaard, Rudolf A. De Boer, Maja-Lisa Løchen, Michiel Rienstra

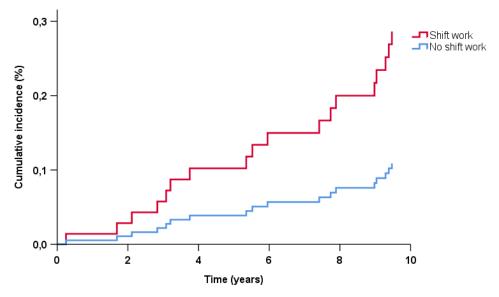
## **Contents**

Table S1	2
Figure S1a	
Figure S1b	
Table S2a	4
Table S2b	
Table S3	6
Table S4	7
Table S5	8
Table S6	9
Table \$7	10

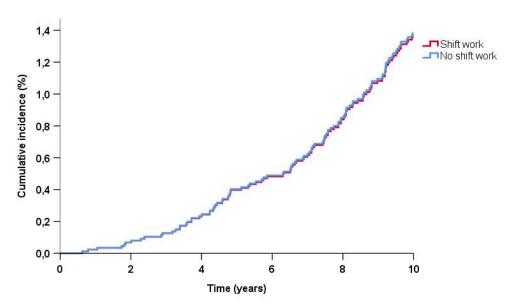
Table S1: Hazard ratios for the association between shift work and 10-year incidence of atrial fibrillation in the total study population. The Tromsø Study

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	Shift work	
	No (n = 10 491)	Yes (n = 3220)	1
Age (years)	30.7 ± 5.3	30.3 ± 5.0	<0.001
Female sex	5271 (50%)	1680 (52%)	0.055
BMI (kg/m²)	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  $\pm$  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/m², obesity as BMI  $\ge$  30 kg/m², and hypertension as SBP  $\ge$  140 mmHg and/or DBP  $\ge$  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	Shif	Shift work	
	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/m²)	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  $\pm$  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/m², obesity as BMI  $\ge$  30 kg/m², and hypertension as SBP  $\ge$  140 mmHg and/or DBP  $\ge$  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 CH,	ARGE-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, CHARG	E-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 an	nd 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  $\geq$ 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 1<sup>st</sup> and 2<sup>nd</sup> 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 1 <sup>st</sup> survey only	0.81 (0.41-1.60)	0.550	
Shift work at 2 <sup>nd</sup> 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 1 <sup>st</sup> survey only	1.18 (0.60-2.33)	0.627	
Shift work at 2 <sup>nd</sup> 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 1 <sup>st</sup> survey only	1.10 (0.56-2.18)	0.780	
Shift work at 2 <sup>nd</sup> 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 ı	model, education level, and physica	al activity	
No shift work at either survey	Ref.	Ref.	
Shift work at 1 <sup>st</sup> survey only	1.10 (0.56-2.19)	0.780	
Shift work at 2 <sup>nd</sup> 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 1 <sup>st</sup> survey only	1.11 (0.56-2.19)	0.764	
Shift work at 2 <sup>nd</sup> 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  $2^{nd}$  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  $1^{st}$  survey only (n = 670, number of AF cases = 9, crude incidence = 1.3%), with shift work at the  $2^{nd}$  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 1<sup>st</sup> and 2<sup>nd</sup> 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 1 <sup>st</sup> survey only	0.74 (0.49-1.10)	0.138
Shift work at 2 <sup>nd</sup> 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 1 <sup>st</sup> survey only	1.07 (0.71-1.60)	0.755
Shift work at 2 <sup>nd</sup> 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	E-AF risk model	
No shift work at either survey	Ref.	Ref.
Shift work at 1 <sup>st</sup> survey only	0.95 (0.63-1.44)	0.807
Shift work at 2 <sup>nd</sup> 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 1 <sup>st</sup> survey only	0.94 (0.62-1.42)	0.752
Shift work at 2 <sup>nd</sup> 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 1 <sup>st</sup> survey only	0.89 (0.59-1.34)	0.567
Shift work at 2 <sup>nd</sup> 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  $2^{nd}$  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  $1^{st}$  survey only (n = 670, number of AF cases = 25, crude incidence = 3.7%), with shift work at the  $2^{nd}$  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.