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Supplementary appendix

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Supplementary Material

50 year trends in atrial fibrillation prevalence, incidence, risk factors, and mortality in the Framingham Heart Study: a cohort study

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Supplementary Methods 1

Risk factor assessment

The diagnosis of diabetes was based on a fasting blood glucose ≥ 126 mg/dL, non-fasting blood glucose ≥ 200 mg/dL, or current use of insulin or oral hypoglycemic medications. The mean of two Framingham physician blood pressure measurements was used to define systolic and diastolic blood pressure (except for Offspring cohort examination 1 at which only a single physician reading was available for most participants). Medication use, smoking habits, and alcohol consumption were self-reported. Participants who regularly smoked at least 1 cigarette per day within the last year prior to the index examination were classified as current smokers. Alcohol consumption was classified as none, mild (1-14 drinks/week in men and 1-7 drinks/week in women), and moderate or heavy consumption (>14 drinks/week in men and >7 drinks/week in women). Electrocardiographic voltage criteria in conjunction with repolarization changes were used for diagnosis of left ventricular hypertrophy.¹ Heart failure was diagnosed based on major clinical criteria that have been used for all heart failure cases of Framingham participants.² Major criteria included paroxysmal nocturnal dyspnea or orthopnoea, rales on auscultation, third heart sound, pulmonary edema, distended neck veins, increased venous pressure, hepatjugular reflux, significant weight loss on diuretic therapy, and radiographic cardiomegaly.

A heart murmur was considered clinically significant if a systolic murmur of at least three out of six intensity, or any diastolic murmur was detected on physician auscultation at the Framingham Heart Study clinic examination. All characteristics including heart failure, myocardial infarction and stroke prevalence were assessed from index exam, which was identified for each individual for each time period. The index examination was defined as the last examination prior to AF but no more than 10 years earlier. For the analysis of atrial fibrillation on Framingham examination: If participants had a diagnosis of atrial fibrillation in the interim (between Framingham exams), but returned for follow-up at the Framingham clinic the case was counted as incident disease if atrial fibrillation was present on the clinic electrocardiogram. If a participant was missing information on valvular heart disease,

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electrocardiographic left ventricular hypertrophy, or diabetes at an examination, the risk factor information was carried over from prior examination cycles within the last four years.

The date of last follow-up was December 31, 2011.

Decades 1958-1967, 1968-1977, 1978-1987, 1988-1997, 1998-2007 were coded as 1, 2, 3, 4 and 5. For post-AF incident stroke and survival analysis, events were censored at 20 years or end of 2011 (or death in stroke analyses), whichever came first. For all other analyses, the events were censored at the end of each decade, loss to follow up or death, whichever came first.

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Supplementary Methods 2

Population Attributable Risk Calculation

- A. Continuous risk factors were categorized into 3 (drinking and body mass index) or 5 (systolic blood pressure) levels as in Table 2. For each level of these risk factors or each dichotomous risk factor, a trend test was conducted to assess whether prevalence increased or decreased over time period. We used logistic regression models with decade as predictor adjusting for age and sex. If trend is significant ($p < 0.05$), the average predicted prevalence from the model with age, sex and decade as predictors is reported is used in PAR; if trend is not significant, the average predicted prevalence from the model with age and sex only is used in PAR. These values are all reported in Table 2.
- B. To assess linear trend across decades for hazard ratios for each trait we performed Cox's proportional hazards models with time to AF as outcome, age, sex, decade, risk factor and interaction(s) between risk factor and decade as predictors. The hazard ratio estimates from these models are displayed in Table 3. If the interaction term is significant ($p < 0.05$), i.e. linear trend across decade is significant, hazard ratios estimated from models with interaction terms (App. Table 2-2) are used in PAR; otherwise hazard ratios estimated from model without interaction terms, i.e. adjusting for age, sex and decade only (App. Table 2-1) are used in PAR.
- C. We used adjusted hazard ratios to calculate population attributable risk [PAR] Equation 4,³ i.e., $PAR = 100 * (pd * [(HR - 1)]/HR$, where pd is the prevalence of the particular trait estimated in A and HR is the hazard ratio estimated in B. For multi-level risk factors PAR was calculated using Equation 5,³ i.e. $PAR = 100 * (pd(i) * [1 - (\sum pd(i) \div HR(i))]$ where $pd(i)$ is the prevalence for each level of the multinomial trait and $HR(i)$ is the corresponding hazard associated with

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the level of the multinomial trait estimated in B. As a consequence, for a risk factor if there is no trend in prevalence, nor is there linear trend in hazard ratio, the PAR is constant. Risk factors that are not associated with incident AF (p value for constant HR >0.05) are deemed not contributing.

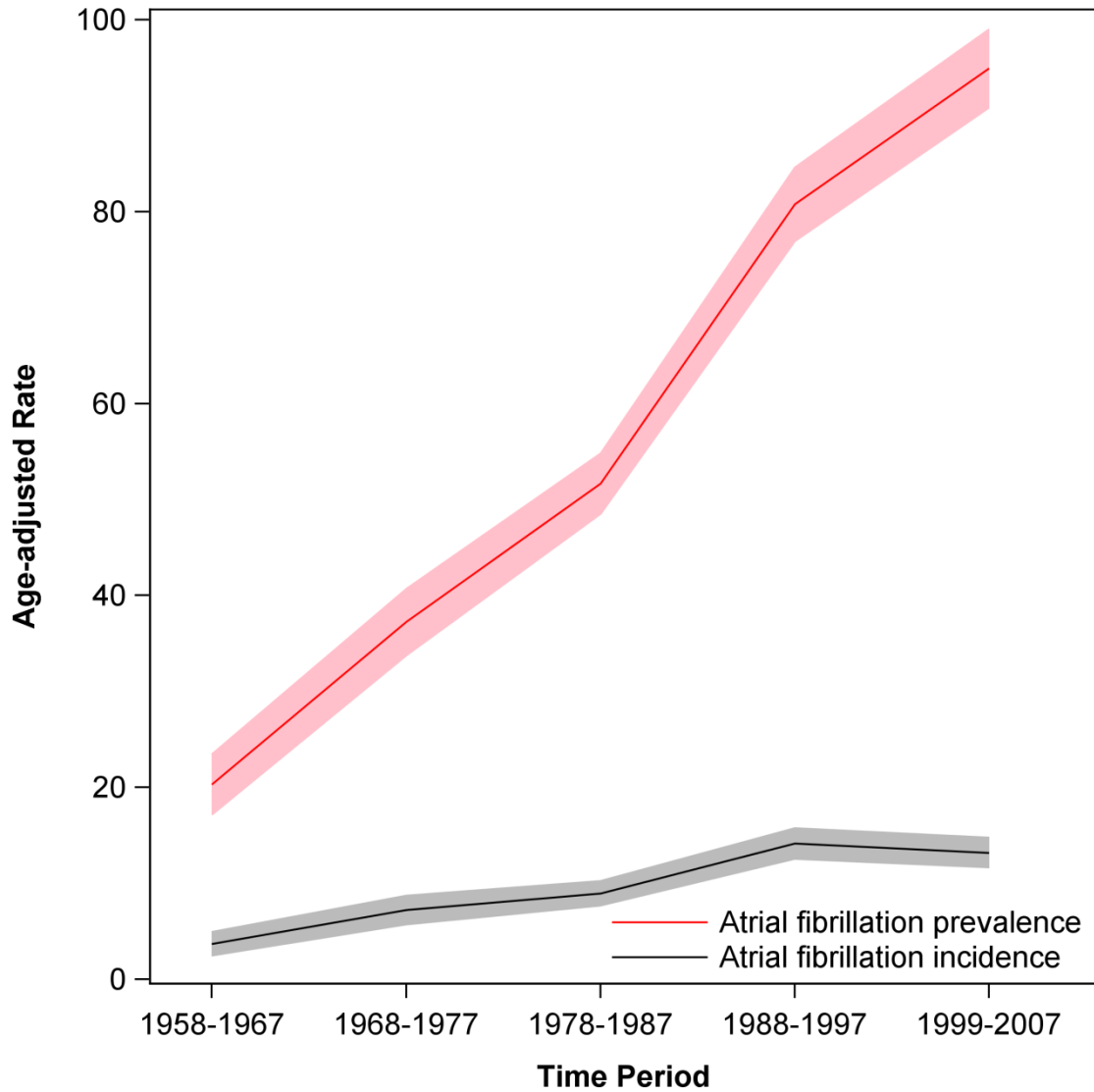
Reference List

- 1 Kannel WB, Gordon T, Offutt D. Left ventricular hypertrophy by electrocardiogram. Prevalence, incidence, and mortality in the Framingham study. *Ann Intern Med* 1969;**71**:89-105.
- 2 Ho KK, Anderson KM, Kannel WB, Grossman W, Levy D. Survival after the onset of congestive heart failure in Framingham Heart Study subjects. *Circulation* 1993;**88**:107-15.
- 3 Rockhill B, Newman B, Weinberg C. Use and misuse of population attributable fractions. *Am J Public Health* 1998;**88**:15-9.

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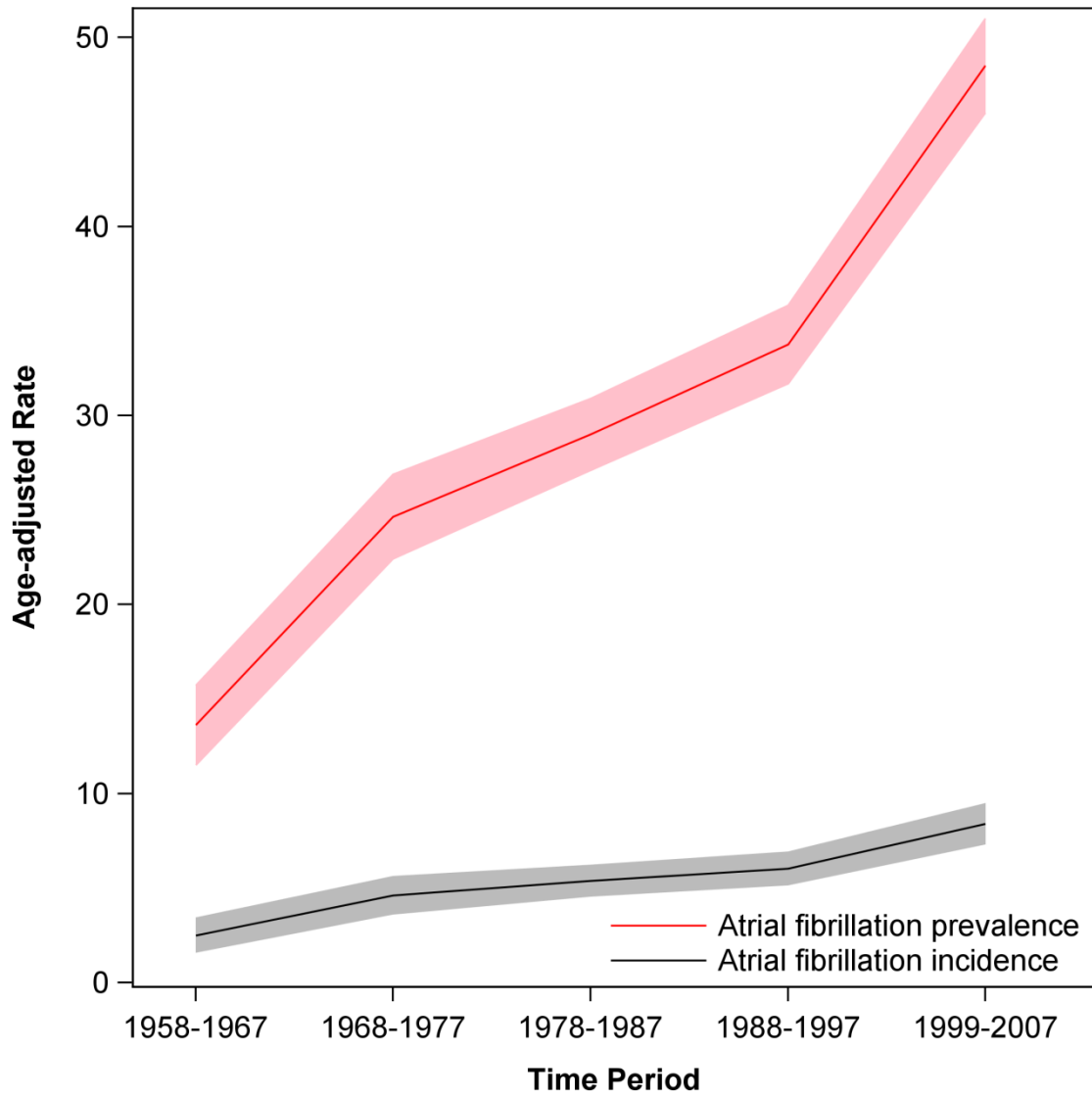
Supplementary Figure 1. Trends in total atrial fibrillation incidence rates and prevalence rates per 1000 person-years lived during each period with 95% confidence intervals shown by color bands.

Men



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Women



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Supplementary Table 1. Sources of First Detected Atrial Fibrillation

Source of ECG		Decade					Total N
		1958-1967	1968-1977	1978-1987	1988-1997	1998-2007	
Hospital or emergency room	N	35	106	242	326	342	1051
	%	46.7	55.5	74.0	70.9	69.7	
Outside physician	N	0	2	4	48	90	144
	%	0.0	1.1	1.2	10.4	18.3	
Framingham Heart Study exam	N	28	56	59	38	21	202
	%	37.3	29.3	18.0	8.3	4.3	
Outside Holter electrocardiogram	N	0	0	1	6	12	19
	%	0.0	0.0	0.3	1.3	2.4	
Framingham Heart Study electrocardiogram	N	0	0	6	1	0	7
	%	0.0	0.0	1.8	0.2	0.0	
By history, electrocardiographic report*	N	12	27	15	41	24	119
	%	16.0	14.1	4.6	8.9	4.9	
Implantable cardiac device interrogation	N	0	0	0	0	2	2
	%	0.0	0.0	0.0	0.0	0.4	
Total	N	75	191	327	460	491	1544

Provided are number and column %.

*Close to 100% of individuals with first diagnosis of atrial fibrillation based on history or electrocardiographic report only had a subsequent electrocardiographic tracing with atrial fibrillation.

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Supplementary Table 2. Clinical Characteristics for Participants with Incident Atrial Fibrillation by Sex*

Men	Decade					P for Trend†	Trend
	1958-1967	1968-1977	1978-1987	1988-1997	1998-2007		
Total no. atrial fibrillation in period	40	101	166	266	248		Direction
No. atrial fibrillation with index exam	38 (95%)	99 (98%)	146 (88%)	235 (88%)	223 (90%)		
<i>Age, years</i>	62.6±6.5	68.1±7.6	69.7±9.2	71.0±9.5	71.5±9.6	<0.0001	↑
50-59	10(26.3)	12(12.1)	20(13.7)	36(15.3)	31(13.9)		
60-69	22(57.9)	42(42.4)	58(39.7)	51(21.7)	62(27.8)		
70-79	6(15.8)	40(40.4)	43(29.5)	100(42.6)	75(33.6)		
80-89	0 (0.0)	5(5.1)	25(17.1)	48(20.4)	55(24.7)		
Current smoking — no. (%)	17(48.6)	20(24.1)	36(25.4)	39(16.7)	25(11.2)	<0.0001	↓
<i>Alcohol consumption</i>							
None — no. (%)	9(29.0)	27(28.7)	49(34.3)	82(35.2)	77(35.0)	0.77	—
Mild — no. (%)	19(61.3)	51(54.3)	76(53.1)	140(60.1)	135(61.4)	0.06	?
Moderate or heavy — no. (%)	3(9.7)	16(17)	18(12.6)	11(4.7)	8(3.6)	<0.0001	↓
<i>Body mass index, kg/m²</i>	26.7±3.4	27.0±4.0	26.8±3.7	27.6±3.9	29.3±4.8	<0.0001	↑
Normal, <25	9(25)	28(31.8)	47(32.9)	60(26)	44(21.6)	0.001	↓
Overweight, 25 to <30	19(52.8)	46(52.3)	62(43.4)	121(52.4)	81(39.7)	0.20	-
Obese, ≥30	8(22.2)	14(15.9)	34(23.8)	50(21.6)	79(38.7)	<0.0001	↑

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Men	Decade					P for Trend†	Trend
	1958-1967	1968-1977	1978-1987	1988-1997	1998-2007		
Total no. atrial fibrillation in period	40	101	166	266	248		Direction
No. atrial fibrillation with index exam	38 (95%)	99 (98%)	146 (88%)	235 (88%)	223 (90%)		
<i>Systolic blood pressure, mm Hg</i>	154±29	146±23	142±22	141±22	135±19	<0•0001	↓
Optimal, <120	3(7•9)	14(14•1)	21(14•4)	38(16•2)	49(22)	0•001	↑
Normal, 120-129	7(18•4)	10(10•1)	16(11)	37(15•7)	40(17•9)	0•09	?
High-normal 130-139	2(5•3)	12(12•1)	29(19•9)	43(18•3)	52(23•3)	0•004	↑
Stage I Hypertension, 140-159	12(31•6)	38(38•4)	54(37)	79(33•6)	58(26)	0•008	↓
Stage II-IV Hypertension ≥160	14(36•8)	25(25•3)	26(17•8)	38(16•2)	24(10•8)	<0•0001	↓
Hypertension treatment — no. (%)	5(13•9)	29(30•5)	58(39•7)	122(52•4)	126(56•8)	<0•0001	↑
Diabetes — no. (%)	1(2•6)	16(16•2)	21(14•6)	48(20•6)	51(23•7)	0•002	↑
Electrocardiographic left ventricular hypertrophy — no. (%)	6(15•8)	13(13•1)	5(3•4)	15(6•9)	7(3•3)	<0•0001	↓
Significant heart murmur — no. (%)	6(15•8)	15(15•8)	17(12•1)	20(8•5)	21(10•1)	0•045	↓
Prevalent heart failure — no. (%)	2(5•3)	10(10•1)	6(4•1)	11(4•7)	9(4)	0•054	?
Prevalent myocardial infarction — no. (%)	5(13•2)	14(14•1)	20(13•7)	37(15•7)	35(15•7)	0•45	-
Prevalent stroke — no. (%)	1(2•6)	5(5•1)	6(4•1)	13(5•5)	15(6•7)	0•64	-

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Women	Decade					P for Trend†	Trend Direction
	1958-1967	1968-1977	1978-1987	1988-1997	1998-2007		
Total no. atrial fibrillation in period	35	91	160	192	243		
No. atrial fibrillation with index exam	32 (91%)	79 (87%)	138 (86%)	164 (85%)	211 (87%)		
<i>Age, years</i>	64.5±6.1	71.1±7.7	73.8±9.3	74.7±8.0	74.3±9.0	<0.0001	↑
50-59	6(18.8)	5(6.3)	10(7.2)	8(4.9)	18(8.5)		
60-69	20(62.5)	27(34.2)	31(22.5)	29(17.7)	37(17.5)		
70-79	6(18.8)	33(41.8)	52(37.7)	70(42.7)	87(41.2)		
80-89	0 (0.0)	14(17.7)	45(32.6)	57(34.8)	69(32.7)		
Current smoking — number (%)	10(32.3)	15(20.3)	24(17.8)	23(14.1)	30(14.2)	0.24	-
<i>Alcohol consumption</i>							
None — no. (%)	16(57.1)	26(35.6)	78(60.5)	86(53.8)	109(53.7)	0.69	-
Mild — no. (%)	9(32.1)	41(56.2)	46(35.7)	60(37.5)	79(38.9)	0.64	-
Moderate or heavy — number (%)	3(10.7)	6(8.2)	5(3.9)	14(8.8)	15(7.4)	0.92	-
<i>Body mass index, kg/m²</i>	27.9±6.2	27.1±5.5	26.3±5.5	27.4±6.1	27.9±6.2	0.03	↑
Normal, <25	11(36.7)	28(40.6)	60(48.0)	55(37.4)	61(34.9)	0.12	-
Overweight, 25 to <30	9(30.0)	22(31.9)	39(31.2)	52(35.4)	59(33.7)	0.84	-
Obese, ≥30	10(33.3)	19(27.5)	26(20.8)	40(27.2)	55(31.4)	0.15	-
<i>Systolic blood pressure, mm Hg</i>	156±27	159±27	147±22	147±22	141±25	<0.0001	↓
Optimal, <120	2(6.3)	5(6.3)	15(10.9)	15(9.1)	39(18.6)	<0.0001	↑
Normal, 120-129	2(6.3)	3(3.8)	16(11.7)	20(12.2)	33(15.7)	0.003	↑
High-normal 130-139	6(18.8)	11(13.9)	22(16.1)	32(19.5)	39(18.6)	0.50	-

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Women	Decade					P for Trend†	Trend Direction
	1958-1967	1968-1977	1978-1987	1988-1997	1998-2007		
Total no. atrial fibrillation in period	35	91	160	192	243		
No. atrial fibrillation with index exam	32 (91%)	79 (87%)	138 (86%)	164 (85%)	211 (87%)		
Stage I Hypertension, 140-159	9(28•1)	26(32•9)	45(32•8)	55(33•5)	50(23•8)	0•07	?
Stage II-IV Hypertension ≥160	13(40•6)	34(43•0)	39(28•5)	42(25•6)	49(23•3)	<0•0001	↓
Hypertension treatment — no. (%)	10(31•3)	26(36•1)	77(56•2)	97(59•9)	131(63•0)	<0•0001	↑
Diabetes — no. (%)	3(9•4)	9(11•4)	23(16•8)	18(11•0)	29(15•0)	0•51	-
ECG left ventricular hypertrophy — no. (%)	3(9•4)	8(10•1)	14(10•6)	8(5•2)	5(2•4)	<0•0001	↓
Significant heart murmur — no. (%)	8(25•0)	17(23•0)	35(26•7)	22(14•0)	10(5•7)	<0•0001	↓
Prevalent heart failure — no. (%)	2(6•3)	5(6•3)	11(8•0)	12(7•3)	6(2•8)	0•08	?
Prevalent myocardial infarction — no. (%)	1(3•1)	2(2•5)	7(5•1)	8(4•9)	12(5•7)	0•36	-
Prevalent stroke —no. (%)	0(0•0)	6(7•6)	11(8•0)	7(4•3)	13(6•2)	0•54	-

All characteristics including heart failure, myocardial infarction and stroke prevalence were assessed from index exam, which was identified for each individual for each time period. The index examination was defined as the last examination prior to AF but no more than 10 years earlier.

*Data are mean ± standard deviation or N (%).

†P values are obtained from linear or logistic models adjusting for age.

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Supplementary Table 3-1 Constant Hazards Ratios Used in Population Attributable Risk Calculation

Variable	Constant Hazards Ratio	P for Constant Hazards Ratio
<i>Age, years</i>		
50-59 (referent)	1•00	
60-69	4•2	<0•0001
70-79	6•6	<0•0001
80-89	9•0	<0•0001
Current smoking	0•94	0•38
<i>Alcohol consumption, %</i>		
None (referent)	1•00	
Mild	1•04	0•54
Moderate or heavy	1•17	0•18
<i>Body mass index, kg/m²</i>		
Normal, <25 (referent)	1•00	
Overweight, 25 to <30	1•17	0•02
Obese, ≥30	1•52	<0•0001
<i>Systolic blood pressure, mm Hg</i>		
Optimal, <120 (referent)	1•00	
Normal, 120-129	0•92	0•41
High-normal 130-139	1•13	0•20
Hypertension treatment	1•47	<0•0001
Diabetes	1•44	<0•0001
Electrocardiographic left ventricular hypertrophy	2•39	<0•0001
Myocardial infarction	1•58	<0•0001

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Supplementary Table 3-2 Varying Hazards Ratios Used in Population Attributable Risk Calculation

	Decade				
	1958-1967	1968-1977	1978-1987	1988-1997	1998-2007
<i>Systolic blood pressure, mm Hg</i>					
Stage I Hypertension, 140-159	2•23	1•79	1•42	1•14	0•91
Stage II-IV Hypertension \geq 160	2•39	1•91	1•53	1•22	0•98
Significant heart murmur	5•06	3•77	2•81	2•09	1•56
Heart failure	4•32	3•35	2•60	2•02	1•56

Derivation of hazards ratios used in **Table 4** of the main manuscript. For risk factors without trend in prevalence, the average predicted prevalence from logistic models with age and sex as predictors (**Table 2** main manuscript) were used in population attributable risk calculation; for factors with trend in prevalence, the average predicted prevalence from logistics models with age, sex and period as predictors were used in population attributable risk.

For risk factors without trend in hazards ratio, the constant hazards ratio estimated from Cox models with age, sex, period and risk factors as predictors (**Supplementary Table 3-1**) were used in population attributable risk calculation; for factors with trend in hazards ratio, the hazards ratios from Cox models with age, sex, period, risk factors, and period and risk factor interaction as predictors (**Supplementary Table 3-2**) were used in population attributable risk.

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Supplementary Table 4. Adjusted Hazards Ratios for Mortality in 20 Years after Atrial Fibrillation Onset According to Time Period of Atrial

Fibrillation Onset

	Decade of Atrial Fibrillation Onset Adjusted Hazards Ratios (95% Confidence Interval)				1998-2007 Referent	Trend	
	1958-1967	1968-1977	1978-1987	1988-1997		Direction	P value
Number of atrial fibrillation	70	178	284	399	434		
Number of deaths	61 (87%)	162 (91%)	263 (93%)	355 (89%)	263 (61%)		
Total (n=1365)							
Age-sex-adjusted	1.53 (1.14-2.05)	1.38 (1.12-1.69)	1.49 (1.25-1.77)	1.14 (0.97-1.35)	1.00	↓	<0.0001
Multivariable-adjusted	1.34 (0.97-1.86)	1.34 (1.06-1.69)	1.36 (1.12-1.66)	1.13 (0.95-1.35)	1.00	↓	0.003
Men (N=741)							
Age-adjusted	1.80 (1.21-2.67)	1.15 (0.87-1.52)	1.35 (1.06-1.73)	1.00 (0.81-1.25)	1.00	↓	0.005
Multivariable-adjusted	1.67 (1.06-2.63)	1.15 (0.83-1.58)	1.29 (0.98-1.70)	0.99 (0.78-1.25)	1.00	↓	0.03
Women (N=624)							
Age-adjusted	1.27 (0.81-1.98)	1.72 (1.28-2.31)	1.62 (1.26-2.08)	1.33 (1.05-1.70)	1.00	↓	0.0007
Multivariable-adjusted	1.10 (0.69-1.76)	1.58 (1.13-2.2)	1.42 (1.06-1.88)	1.34 (1.02-1.75)	1.00	↓	0.057

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Multivariable models were adjusted for age, current smoking, systolic blood pressure, hypertension treatment, electrocardiographic left ventricular hypertrophy, diabetes, heart failure, significant heart murmur, and myocardial infarction. For trend test, time periods were coded 1(1958-1967), 2(1968-1977), 3(1978-1987), 4(1988-1997) and 5(1998-2007).

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Supplementary Table 5. Age-adjusted Survival Rates After Atrial Fibrillation Onset for 5-Year Intervals by Sex and Decade

Time (years)		1958-1967	1968-1977	1978-1987	1988-1997	1998-2007
Men	5	0•47(0•39-0•55)	0•51(0•46-0•56)	0•50(0•45-0•55)	0•58(0•54-0•62)	0•63(0•59-0•67)
	10	0•25(0•18-0•32)	0•29(0•24-0•34)	0•28(0•24-0•32)	0•35(0•31-0•39)	0•41(0•36-0•46)
	15	0•14(0•09-0•19)	0•17(0•13-0•21)	0•16(0•13-0•19)	0•22(0•19-0•25)	
Women	5	0•45(0•36-0•54)	0•49(0•43-0•55)	0•48(0•43-0•53)	0•56(0•52-0•60)	0•61(0•57-0•65)
	10	0•22(0•15-0•29)	0•25(0•20-0•30)	0•25(0•21-0•29)	0•32(0•28-0•36)	0•38(0•33-0•43)
	15	0•11(0•07-0•15)	0•13(0•09-0•17)	0•12(0•09-0•15)	0•17(0•14-0•20)	

Provided are survival rates for new onset atrial fibrillation after 5, 10 and 15 years by decade of atrial fibrillation onset.

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Supplementary Table 6. Adjusted Hazards Ratios for Incident Stroke in 20 Years after Atrial Fibrillation Onset According to Time Period of Atrial Fibrillation Onset

	Decade of Atrial Fibrillation Onset Adjusted Hazards Ratios (95% Confidence Interval)				1998-2007 Referent	Trend	
	1958-1967	1968-1977	1978-1987	1988-1997		Direction	P value
Number of atrial fibrillation	64	157	249	363	384		
Number of strokes	20 (31%)	33 (21%)	46 (18%)	66 (18%)	36 (9%)		
Total (n=1217)							
Age- and sex-adjusted	3.19(1.79-5.69)	2.07(1.27-3.36)	1.94(1.25-3.03)	1.59(1.06-2.41)	1.00	↓	<0.0001
Multivariable-adjusted	3.77(1.98-7.20)	2.20(1.26-3.83)	2.11(1.28-3.47)	1.80(1.14-2.85)	1.00	↓	0.0001
Men (N=669)							
Age-adjusted	2.72(0.98-7.55)	1.84(0.82-4.13)	1.86(0.88-3.94)	1.73(0.88-3.39)	1.00	↓	0.07
Multivariable-adjusted	3.32(0.99-11.1)	2.26(0.91-5.61)	2.15(0.94-4.93)	1.80(0.86-3.78)	1.00	↓	0.04
Women (N=548)							
Age-adjusted	3.48(1.72-7.05)	2.23(1.22-4.09)	1.98(1.14-3.44)	1.48(0.87-2.52)	1.00	↓	0.0002
Multivariable-adjusted	3.95(1.82-8.56)	2.05(1.01-4.16)	2.01(1.07-3.8)	1.82(1.01-3.28)	1.00	↓	0.0016

Strokes developed before atrial fibrillation were excluded from this analysis. Multivariable models adjusted for age, (sex for total), current smoking, systolic blood pressure, hypertension treatment, electrocardiographic left ventricular hypertrophy, diabetes, heart failure, significant heart murmur, and myocardial infarction. For trend test, time periods were coded 1(1958-1977), 2(1968-1977), 3(1978-1987), 4(1988-1997) and 5(1998-2007).