

# Clinical trajectory of atrial fibrillation patients: a Nationwide study of 5.6 million individuals

Rui Providencia<sup>1,2</sup>, Reecha Sofat<sup>1</sup>, Dionisio Acosta<sup>1</sup>, Julie Taylor<sup>1</sup>, Pier D Lambiase<sup>1,3</sup>, Juan P Casas<sup>4,5</sup>, Sheng-Chia Chung<sup>1</sup>

<sup>1</sup> Institute of Health Informatics Research, University College London, London, UK; <sup>2</sup> Barts Health NHS Trust, London, UK; <sup>3</sup> Institute of Cardiovascular Science, University College London, London, UK; <sup>4</sup> Massachusetts Veterans Epidemiology Research and Information Center (MAVERIC), Boston, MA, USA; <sup>5</sup> Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA.

**Background:** The detailed clinical trajectory of patients with atrial fibrillation (AF) on the Health System is not known. A clear understanding of the events pre and post AF diagnosis and the interactions with the Health System would allow the identification of groups at risk and opportunities for effective health care interventions.

**Aim:** To investigate the incidence, comorbidity, hospitalisations pre and post incident AF, mortality, cause of death, and vulnerable populations of AF on a nationwide dataset.

**Methods:** To study the AF incidence, mortality and case-fatality, we implemented a longitudinal cohort study with the linked electronic health records of a 5.6 million population nationwide dataset from 1998 to 2016. A matched case-control study was used to investigate causes of hospitalisation, GP visits and death comparing individuals with and without incident AF.

Characteristics of patients with incident atrial fibrillation at study entry

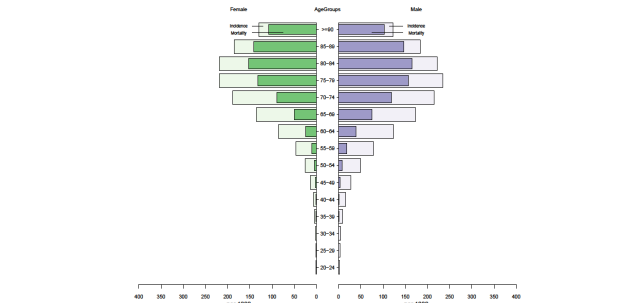
	All patients		Sex		Socioeconomic status	
	Male	Female	Quintile 1	Quintile 5	Quintile 1	Quintile 5
Age category at diagnosis (years)	(n=159 433)	(n=99 281)	(n=100 152)	(n=33 632)	(n=44 466)	
Age at diagnosis (years)	75.8 (12.7)	72.7 (13.1)	78.9 (11.5)	76.3 (12.8)	75.0 (12.8)	
Women	100152 (60.2%)	--	16797 (49.9%)	2241 (50%)		
Socioeconomic quintile						
Quintile 1 (least deprived)	33632 (16.9%)	16835 (17%)	16797 (16.8%)	--	--	
Quintile 5 (most deprived)	44666 (22.3%)	22225 (22.4%)	22241 (22.2%)	--	--	
Smoking	86207 (43.2%)	53004 (53.4%)	33026 (33.2%)	13026 (38.7%)	21902 (49.3%)	
By CHA <sub>2</sub> DS <sub>2</sub> -VASc score categories						
0	26079 (13.1%)	16797 (16.9%)	9282 (9.3%)	4867 (14.5%)	5591 (12.6%)	
1	18475 (9.3%)	11423 (11.5%)	7052 (7.0%)	3066 (9.1%)	4493 (10.1%)	
≥2	154879 (77.7%)	71061 (71.6%)	83818 (83.7%)	25699 (76.4%)	34382 (77.3%)	
Comorbidities						
Hypertension	99644 (50.6%)	46309 (46.6%)	53335 (53.3%)	16224 (48.2%)	22886 (51.5%)	
Diabetes	31099 (15.5%)	17064 (17.2%)	13945 (13.9%)	4471 (13.3%)	7704 (17.3%)	
Valvular disease	20487 (10.3%)	9870 (9.9%)	10597 (10.6%)	3656 (10.5%)	4417 (9.9%)	
Angina	37846 (19.0%)	20854 (21.0%)	16992 (17.0%)	5657 (16.8%)	9810 (22.1%)	
Ischemic heart disease	33558 (16.7%)	19897 (20.0%)	13461 (13.4%)	5289 (15.7%)	7961 (17.9%)	
Heart failure	41925 (21.0%)	20326 (20.4%)	21689 (21.4%)	6254 (18.6%)	10297 (23.2%)	
Stroke	23208 (11.6%)	10897 (11.0%)	12311 (12.3%)	3715 (11.0%)	5290 (11.9%)	
Asthma	30252 (15.2%)	14059 (14.2%)	16193 (16.2%)	4908 (14.6%)	7425 (16.7%)	
Cataract	35336 (17.7%)	13337 (13.4%)	21999 (22.0%)	5752 (17.1%)	7924 (17.8%)	
Hyperthyroidism	4825 (2.4%)	1028 (1.0%)	3797 (3.8%)	730 (2.2%)	1178 (2.6%)	
Cancer	38979 (19.5%)	20263 (20.4%)	18713 (18.7%)	6805 (20.2%)	8354 (18.8%)	
Chronic kidney disease	40362 (20.2%)	18895 (19.1%)	21377 (21.3%)	6222 (18.5%)	9750 (21.9%)	
Chronic obstructive pulmonary disease	25795 (12.9%)	14182 (14.3%)	11613 (11.6%)	3377 (10.0%)	7306 (16.4%)	
Dementia	12254 (6.1%)	4354 (4.4%)	7900 (7.9%)	2105 (6.3%)	2647 (6.0%)	
Sleep apnoea	1993 (1.0%)	1552 (1.6%)	441 (0.4%)	366 (1.1%)	489 (1.1%)	
Three or more comorbidities	83801 (42.0%)	40729 (41.0%)	43072 (43.0%)	13016 (38.7%)	20160 (45.3%)	

Top 10 reasons for hospitalisation in atrial fibrillation patients, compared to controls, within 5 years pre and post incident AF diagnosis\*

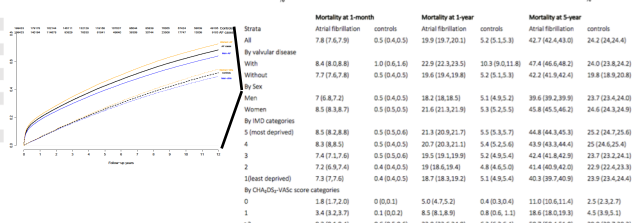
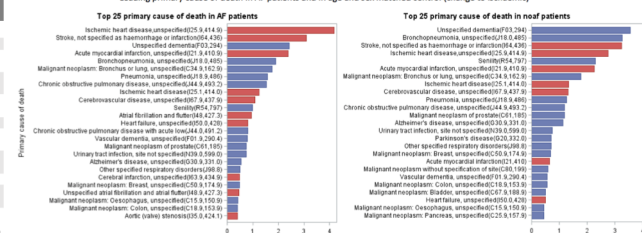
Rank	Term	Before			Incident Atrial Fibrillation			After				
		Cases	Ctrls	Ratio	Term	Cases	Ctrls	Ratio	Term	Cases	Ctrls	Ratio
1	Cataracts(I26.9/I25.1/I25.9)	8.5	8.8	0.97	Atrial fibrillation and flutter(I48)	8.4	N/A	N/A	Cataracts(I26.9/I25.1/I25.9)	5.16	8.07	0.64
2	Ischemic heart disease, incl. UA/AMI(I21/I20/I219)	3.66	2.34	1.56	Lower respiratory tract infection(I22/I18.1/I18.9)	4.78	3.08	1.55	Ischemic heart disease, incl. UA/AMI(I21/I20/I219)	3.22	2.53	1.27
3	Low respiratory tract infection(I22/I18.1/I18.9)	2.54	2.14	1.19	Stroke, not specified(I69)	2.26	2.56	0.88	Stroke, not specified(I69)	1.15	1.51	0.76
4	Urinary tract infection, site not specified(N59.0)	1.54	1.32	1.16	Heart failure(I50.0/I50.1)	1.32	0.79	1.68	Heart failure(I50.0/I50.1)	1.14	0.89	1.29
5	Chest pain, unspecified(R07.4)	1.49	0.87	1.72	Chronic obstructive pulmonary disease with acute low(I44.0)	1.20	0.66	1.82	Chronic obstructive pulmonary disease with acute low(I44.0)	1.11	0.86	1.3
6	Stroke, not specified(I69)	1.37	1.41	0.97	Unknown or unspecified causes of morbidity(R69)	1.00	1.97	0.51	Unknown or unspecified causes of morbidity(R69)	1.1	1.7	0.64
7	Unknown and unspecified causes of morbidity(R69)	1.15	1.51	0.76								
8	Heart failure(I50.0/I50.1)	1.14	0.89	1.29								
9	Syncope and collapse(R55)	1.11	0.86	1.3								
10	Unilateral or unspecified inguinal hernia (K40.9)	1.1	1.7	0.64								

Rank	Term	Before			After			
		Cases	Ctrls	Ratio	Term	Cases	Ctrls	Ratio
1	Essential hypertension	3.61	3.21	1.1	Atrial fibrillation	21.7	4.41	4.92
2	Chest infection	3.5	4.01	0.9	Atrial fibrillation and flutter	4.41	2.97	1.48
3	Chest infection NOS	1.84	0.37	5.0	Chest infection	2.97	3.99	0.7
4	Hypertensive disease	1.83	3.32	0.6	Paroxysmal atrial fibrillation	2.53	2.31	1.09
5	Shoulder pain	1.8	1.06	1.7	Essential hypertension	2.31	3.85	0.6
6	Low back pain	1.68	1.08	1.5	Chest infection NOS	1.57	0.96	1.6
7	Cervicgia/l pain in neck	1.62	1.08	1.5	Type 2 diabetes mellitus	1.45	0.64	2.3
8	Type 2 diabetes mellitus	1.47	0.53	2.7	Urinary tract infection, site not specified	1.4	0.97	1.4
9	Hip pain	1.34	0.56	2.4	Ischaemic heart disease	1.34	1.15	1.2
10	Angina pectoris	1.23	1.31	0.9	Shoulder pain	1.32	1.19	1.1

The highest three ratios comparing AF patients to controls are in bold.



Leading primary cause of death in AF patients and in age and sex matched control (change to ischaemic)



**Results:** Population AF incidence rates at 1st year, 5th year and 10th year of follow-up were 0.23% (95% confidence interval: 0.22%, 0.23%), 1.28% (95% CI: 1.27%, 1.29%), and 3.12% (95% CI: 3.11%, 3.14%). Increased risk of hospitalisation for ischaemic heart disease or heart failure was present among patients who later develop AF. Following an AF diagnosis, patients were frequently admitted to the hospital for ischaemic heart disease, heart failure, lower respiratory tract infection and chronic obstructive pulmonary disease. In one in 5 AF patients died during the first year after diagnosis, and the mortality increased to 42.7% at the 5th year. The excess deaths compared AF cases to controls may be resulting from cardiovascular diseases, infection and metabolic disorders. Novel associations (e.g. cataracts and fracture of the head of the femur both significantly less frequent in AF patients) suggest novel pathways worth exploring for better understanding of this arrhythmia. Individuals from areas with higher deprivation in socioeconomic and living status had both higher AF incidence and fatality.

**Conclusions:** We report a significant heterogeneity in AF predisposition, progression and disease burden in the population. Focused interventions are recommended for early diagnosis, comorbidity management, and strengthening AF prevention and care for individuals who are vulnerable or living in high deprivation areas.