Appendix A

Impact of gender on event rates at 1 year in patients with newly diagnosed non-valvular atrial fibrillation: contemporary perspective from the GARFIELD-AF registry

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Supplementary Table 1. Hazard ratios for stroke/SE after multiple imputation. Model 3 only contains "significant interactions between gender and risk" defined as $p < 0.20$.

STROKE/SE	Model 1 without interaction			Model 2 with interactions						p-value interaction with gender	Model 3 with important interactions			
	HR	95% CI		HR	95% CI		HR	95% CI			HR	95% CI		
	MEN AND WOMEN			MEN			WOMEN							
Female (ref: male)	1.30	1.04	1.63	-	-	-	-	-	-	-				
Age 65-69 years (ref: <65)	1.67	1.15	2.41	2.39	1.50	3.81	0.93	0.50	1.75	0.17	2.37	1.49	3.76	Men
											0.93	0.50	1.75	Women
Age 70-74 years (ref: <65)	1.91	1.35	2.69	2.45	1.55	3.87	1.38	0.82	2.33	-	2.41	1.53	3.79	Men
											1.38	0.82	2.33	Women
Age >= 75 years (ref: <65)	2.09	1.54	2.85	2.05	1.34	3.16	1.89	1.21	2.94	-	1.98	1.30	3.03	Men
											1.89	1.21	2.94	Women
Diabetes mellitus (ref: no)	1.09	0.86	1.39	1.18	0.83	1.66	1.04	0.74	1.46	0.63	1.10	0.87	1.41	
Hypertension as in CHA2DS2-Vasc (ref: no)	1.17	0.87	1.57	1.15	0.77	1.70	1.19	0.76	1.85	0.90	1.16	0.87	1.56	
Stroke/TIA/SE as in CHA2DS2-Vasc (ref: no)	2.14	1.68	2.72	2.69	1.92	3.77	1.69	1.20	2.38	0.06	2.64	1.89	3.69	Men
											1.69	1.20	2.38	Women
Congestive cardiac failure as in CHA2DS2-Vasc (ref: no)	1.25	1.00	1.57	1.34	0.97	1.86	1.18	0.86	1.61	0.57	1.25	1.00	1.57	
History of bleeding (ref: no)	1.54	0.97	2.43	1.25	0.63	2.46	1.85	1.00	3.44	0.40	1.53	0.97	2.42	
Vascular disease (ref: no)	1.15	0.89	1.50	1.01	0.70	1.46	1.33	0.92	1.95	0.30	1.15	0.89	1.50	
AC Treatment (ref: no)	0.59	0.48	0.73	0.45	0.33	0.61	0.77	0.57	1.03	0.01	0.46	0.34	0.62	Men
											0.77	0.57	1.03	Women
Race: Asian/Chinese (ref: Caucasian/Hisp/Latino)	0.97	0.75	1.24	0.93	0.65	1.32	0.99	0.69	1.42	0.89	0.96	0.74	1.23	

Ex-smoker (ref: no)	0.95	0.71	1.27	0.96	0.67	1.37	0.92	0.54	1.58	0.98	0.95	0.71	1.27
Current smoker (ref: no)	1.56	1.11	2.19	1.51	0.99	2.31	1.60	0.85	3.03	-	1.53	1.09	2.15
Permanent AF (ref: Paroxysmal)	1.21	0.86	1.70	1.22	0.74	2.02	1.19	0.74	1.91	0.96	1.20	0.85	1.69
Persistent AF (ref: Paroxysmal)	1.34	0.97	1.86	1.25	0.77	2.02	1.44	0.92	2.23	-	1.34	0.97	1.85
New AF (ref: Paroxysmal)	1.06	0.82	1.38	1.07	0.73	1.56	1.05	0.73	1.49	-	1.05	0.81	1.37
Severe Renal disease III-IV-V (ref: I, II, Unknown, no)	1.53	1.16	2.02	1.30	0.83	2.04	1.70	1.19	2.42	0.36	1.53	1.16	2.02

Supplementary Table 2. Hazard ratios for Mortality after multiple imputation. Model 3 only contains "significant interactions between gender and risk" defined as $p < 0.20$.

MORTALITY	Model 1 without interaction			Model 2 with interactions						p-value interaction with gender	Model 3 with important interactions			
	HR	95% CI		HR	95% CI		HR	95% CI			HR	95% CI		
	MEN AND WOMEN			MEN			WOMEN							
Female (ref: male)	1.05	0.92	1.19	-	-	-	-	-	-	-				
Age 65-69 years (ref: <65)	1.67	1.30	2.16	1.96	1.44	2.67	1.23	0.78	1.93	0.71	1.68	1.30	2.16	
Age 70-74 years (ref: <65)	2.13	1.69	2.69	2.28	1.71	3.05	1.86	1.27	2.74	-	2.13	1.69	2.69	
Age >= 75 years (ref: <65)	4.06	3.34	4.93	4.17	3.27	5.32	3.72	2.69	5.15	-	4.07	3.35	4.94	
Diabetes mellitus (ref: no)	1.23	1.08	1.40	1.21	1.01	1.46	1.24	1.02	1.51	0.86	1.22	1.07	1.40	
Hypertension as in CHA2DS2-Vasc (ref: no)	0.78	0.67	0.90	0.79	0.65	0.97	0.75	0.60	0.95	0.73	0.78	0.67	0.90	
Stroke/TIA/SE as in CHA2DS2-Vasc (ref: no)	1.38	1.19	1.60	1.38	1.13	1.70	1.35	1.09	1.68	0.88	1.37	1.18	1.59	
Congestive cardiac failure as in CHA2DS2-Vasc (ref: no)	2.30	2.04	2.59	2.35	2.00	2.77	2.25	1.89	2.68	0.72	2.30	2.05	2.59	
History of bleeding (ref: no)	1.74	1.38	2.21	1.37	0.98	1.91	2.28	1.64	3.17	0.03	1.39	1.00	1.95	Men
											2.27	1.64	3.13	Women
Vascular disease (ref: no)	1.38	1.20	1.58	1.29	1.08	1.55	1.50	1.21	1.85	0.29	1.37	1.20	1.58	
AC Treatment (ref: no)	0.60	0.53	0.68	0.57	0.48	0.67	0.65	0.54	0.77	0.28	0.60	0.53	0.68	
Race: Asian/Chinese (ref: Caucasian/Hisp/Latino)	0.77	0.66	0.91	0.70	0.56	0.88	0.87	0.69	1.10	0.33	0.77	0.66	0.91	
Ex-smoker (ref: no)	1.29	1.12	1.50	1.24	1.04	1.48	1.42	1.11	1.84	0.61	1.29	1.12	1.50	
Current smoker (ref: no)	1.43	1.15	1.78	1.37	1.06	1.78	1.59	1.06	2.40	-	1.43	1.15	1.78	

Permanent AF (ref: Paroxysmal)	1.27	1.03	1.56	1.22	0.91	1.62	1.32	0.98	1.78	0.49	1.27	1.03	1.56
Persistent AF (ref: Paroxysmal)	1.27	1.04	1.57	1.11	0.83	1.49	1.47	1.10	1.97	-	1.28	1.04	1.57
New AF (ref: Paroxysmal)	1.50	1.29	1.76	1.49	1.20	1.86	1.51	1.20	1.89	-	1.51	1.29	1.77
Severe Renal disease III-IV-V (ref: I, II, Unknown, no)	1.84	1.60	2.12	1.99	1.64	2.42	1.69	1.38	2.07	0.25	1.84	1.60	2.11

Supplementary Table 3. Hazard ratios for Major Bleeding after multiple imputation

MAJOR BLEEDING	Model without interaction			Model with interactions						p-value interaction with gender
	HR	95% CI		HR	95% CI		HR	95% CI		
	MEN AND WOMEN			MEN			WOMEN			
Female (ref: male)	1.13	0.85	1.50				-	-	-	-
Age 65-69 years (ref: <65)	1.34	0.80	2.27	1.48	0.77	2.84	1.13	0.47	2.73	0.64
Age 70-74 years (ref: <65)	2.13	1.35	3.36	2.39	1.35	4.24	1.78	0.84	3.78	-
Age >= 75 years (ref: <65)	2.47	1.64	3.71	2.37	1.40	4.01	2.44	1.26	4.72	-
Diabetes mellitus (ref: no)	1.00	0.74	1.37	1.20	0.80	1.81	0.80	0.50	1.30	0.21
Hypertension as in CHA2DS2-Vasc (ref: no)	0.92	0.64	1.30	0.77	0.50	1.20	1.22	0.66	2.24	0.23
Stroke/TIA/SE as in CHA2DS2-Vasc (ref: no)	1.14	0.80	1.62	0.92	0.54	1.57	1.38	0.86	2.22	0.27
Congestive cardiac failure as in CHA2DS2-Vasc (ref: no)	0.97	0.71	1.30	1.03	0.69	1.55	0.91	0.58	1.42	0.68
History of bleeding (ref: no)	1.47	0.78	2.80	1.61	0.70	3.69	1.26	0.46	3.47	0.72
Vascular disease (ref: no)	1.24	0.89	1.72	1.17	0.76	1.80	1.33	0.80	2.21	0.70
AC Treatment (ref: no)	2.10	1.49	2.95	2.33	1.41	3.84	1.86	1.16	2.99	0.53
Race: Asian/Chinese (ref: Caucasian/Hisp/Latino)	0.60	0.40	0.90	0.69	0.41	1.17	0.52	0.27	0.99	0.51
Ex-smoker (ref: no)	1.26	0.91	1.73	1.30	0.86	1.97	1.13	0.63	2.01	0.76
Current smoker (ref: no)	1.65	1.06	2.57	1.51	0.84	2.70	1.96	0.93	4.12	-
Permanent AF (ref: Paroxysmal)	1.00	0.63	1.58	1.57	0.84	2.96	0.60	0.29	1.23	0.27
Persistent AF (ref: Paroxysmal)	1.09	0.70	1.70	1.33	0.70	2.51	0.93	0.49	1.76	-
New AF (ref: Paroxysmal)	1.27	0.91	1.78	1.51	0.89	2.54	1.11	0.71	1.73	-
Severe Renal disease III-IV-V (ref: I, II, Unknown, no)	2.04	1.48	2.80	2.10	1.33	3.30	1.97	1.27	3.07	-

Supplementary Table 4. The extent of missing data from the multiple imputation approach

Variable	Missing values	Non-missing values
Age	0	28624
Gender	0	28624
Body mass index	6089	22535
Indicator of death	150	28474
Indicator of stroke/SE	150	28474
Indicator of bleed	150	28474
Type of AF	2	28622
Race	828	27796
Diabetes	2	28622
Hypertension	2	28622
Previous stroke	2	28622
Congestive heart failure	2	28622
Vascular disease	2	28622
Chronic kidney disease	3	28,621
AC treatment	408	28216
History of bleeding	75	28549
Hypercholesterolemia	548	28076
HAS-BLED	9177	19447
CHA_2DS_2 -VASc	673	27951
Smoking	2581	26043

Note: CHA_2DS_2-VASc, HAS-BLED, BMI, and Hypercholesterolemia were not used in models presented in Table 2.

Supplementary Table 5. Analysis of on international normalised ratio (INR) control based on time in therapeutic range (TTR) by gender. Based on an international guideline-defined INR range of between 2.0 and 3.0*

	n	Mean TTR	Standard deviation
Female	3538	55.2	26.9
Male	4385	55.6	27.1
Total	7923	55.4	27.0

*Notes: TTR was estimated between two consecutive INR readings only if the interval did not exceed 90 days. Implausible INR values of less than 0.8 or greater than 20 were excluded. Patients on VKA treatment at enrolment, but with fewer than three readings during the follow-up, were excluded from the analysis. Patient-level TTR was estimated by linear interpolation (according to Rosendaal et al. *Thromb Haemost* 1993;69(3):236-9) using 2.0–3.0 as the target INR range.

Supplementary Figure 1. **One year event rates (per 100 person-years) and adjusted hazard ratios according to gender.**