

**Supplementary Table 4.** Crude analysis of clinical outcomes in the overall and high-risk PFO population

	Overall cohort					
	Medical therapy alone (n=276)		PFO closure (n=161)		HR (95% CI) <sup>†</sup>	P
	N (%) <sup>*</sup>	Incidence rate (100 PY, 95% CI)	N (%) <sup>*</sup>	Incidence rate (100 PY, 95% CI)		
<b>Primary outcome</b>						
Ischemic stroke or TIA	50 (18.1)	3.98 (3.02–5.26)	14 (8.7)	2.24 (1.33–3.79)	0.52 (0.29–0.95)	0.034
<b>Secondary outcomes</b>						
All-cause death	24 (8.7)	1.71 (1.15–2.55)	2 (1.2)	0.30 (0.07–1.20)	0.19 (0.04–0.81)	0.025
Ischemic stroke	40 (14.5)	3.12 (2.29–4.25)	12 (7.5)	1.91 (1.09–3.37)	0.56 (0.30–1.08)	0.083
Ischemic stroke, TIA, or systemic embolization	51 (18.5)	4.08 (3.10–5.37)	15 (9.3)	2.42 (1.46–4.01)	0.55 (0.31–0.99)	0.046
Intracranial bleeding	9 (3.3)	0.65 (0.34–1.25)	2 (1.2)	0.30 (0.08–1.21)	0.40 (0.09–1.86)	0.243
Major bleeding	18 (6.5)	1.33 (0.84–2.12)	6 (3.7)	0.91 (0.41–2.03)	0.62 (0.25–1.58)	0.319
Atrial fibrillation	13 (4.7)	0.95 (0.55–1.64)	15 (9.3)	2.45 (1.48–4.06)	2.28 (1.08–4.82)	0.030
	High-risk PFO cohort					
	Medical therapy alone (n=156)		PFO closure (n=147)		HR (95% CI) <sup>†</sup>	P
	N (%) <sup>*</sup>	Incidence rate (100 PY, 95% CI)	N (%) <sup>*</sup>	Incidence rate (100 PY, 95% CI)		
<b>Primary outcome</b>						
Ischemic stroke or TIA	37 (23.7)	5.54 (4.01–7.64)	12 (8.2)	2.08 (1.18–3.66)	0.36 (0.19–0.69)	0.002
<b>Secondary outcomes</b>						
All-cause death	11 (7.1)	1.43 (0.79–2.58)	2 (1.4)	0.32 (0.08–1.30)	0.25 (0.05–1.14)	0.074
Ischemic stroke	31 (19.9)	4.48 (3.15–6.37)	10 (6.8)	1.72 (0.93–3.21)	0.36 (0.18–0.75)	0.006
Ischemic stroke, TIA, or systemic embolization	38 (24.4)	5.74 (4.18–7.89)	13 (8.8)	2.27 (1.32–3.91)	0.38 (0.20–0.72)	0.003
Intracranial bleeding	7 (4.5)	0.93 (0.45–1.96)	1 (0.7)	0.16 (0.02–1.15)	0.16 (0.02–1.30)	0.087
Major bleeding	15 (9.6)	2.06 (1.24–3.41)	4 (2.7)	0.65 (0.24–1.74)	0.29 (0.10–0.88)	0.028
Atrial fibrillation	8 (5.1)	1.08 (0.54–2.16)	15 (10.2)	2.67 (1.61–4.43)	2.20 (0.93–5.19)	0.073

PFO, patent foramen ovale; HR, hazard ratio; CI, confidence interval; TIA, transient ischemic attack.

<sup>\*</sup>Data are presented as crude number and event rates; <sup>†</sup>Hazard ratios are for the PFO closure group as compared with the medical therapy alone group.