Appendix 6: Association between anticoagulation intensity and risk of events in studies recording intracranial or fatal hemorrhages alone\*

International normalized ratio	Hemorrhagic events (n = 356 546)				Combined events (n = 214 095)†		
	Relative risk (95% CI)		Absolute risk (95% CI)		Relative risk (95% CI)		Absolute risk (95% CI)
< 2	1.4	(0.8–2.5)	0.5	(0.3–0.9)	3.1	(2.6–3.6)	4.1 (2.7–6.2)
2–3	1.0	(Ref)	0.3	(0.3–0.4)	1.0	(Ref)	1.3 (0.7–2.3)
3–5	3.1	(2.0-4.6)	1.0	(0.7–1.7)	2.0	(1.6–2.4)	2.6 (1.2–5.5)
> 5	28.8	(12.6–66.0)	9.9	(4.0–24.7)	16.7	(12.3–22.6)	22.0 (9.0–52.8)

## References

- ESPRIT Study Group; Algra A. Medium intensity oral anticoagulants versus aspirin after cerebral ischaemia of arterial origin (ESPRIT): a randomised controlled trial. Lancet Neurol 2007;6:115-24.
- Hylek EM, Go AS, Chang Y, et al. Effect of intensity of oral anticoagulation on stroke severity and mortality in atrial fibrillation. N Engl J Med 2003;349:1019-26.
- 3. Oden A, Fahlen M. Oral anticoagulation and risk of death: a medical record linkage study. BMJ 2002;325:1073-5.

Note: CI = confidence interval.
\*Studies by the ESPRIT group, ¹ Hylek² and Oden.³
†Oden did not report thromboembolic events and we excluded this study from our analysis of combined events.