Online Supplementary Appendix

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Appendix S1 –

Event rates per patient-year were computed to account for differences in observable time among INR ranges. A Poisson model with offset equal to the log INR years, as determined by the natural log of the time spent in INR range, was used to develop estimates, confidence intervals, and compare ranges. No overdispersion was identified. Poisson models were developed using generalized estimating equations to account for correlated data corresponding to patients providing data towards multiple INR ranges.

Table S1 –

	Internal data deaths/patient month	Literature Review deaths/patient month	Value utilized in weighing scheme
Pump Thrombosis	0.142	0.18(1)	0.16
GI Bleed	0.008	0.01 (9)	0.01
Ischemic Stroke	0.113	0.10 (4,5)	0.11
Hemorrhagic Stroke	0.58	0.40 (6)	0.49

GI = gastrointestinal

Table S2 –

INR range	Patient years	Events Per INR range			Event rate per 10 patient-years		
		ICH	GIB	Total	ICH	GIB	Total
0 – 1.49	40.32	0	3	3	0	0.7	0.7
1.50 – 1.99	110.74	1	10	11	0.1	0.9	1.0
2.00 – 2.49	101.26	1	20	21	0.1	2.0	2.1
2.50 – 2.99	47.53	2	5	7	0.4	1.1	1.5
3.00 – 3.49	15.04	2	4	6	1.3	2.7	4.0
≥ 3.5	9.86	3	11	14	3.0	11.2	14.2

ICH = intracranial hemorrhage; GIB = gastrointestinal bleeding.

Table S3 –

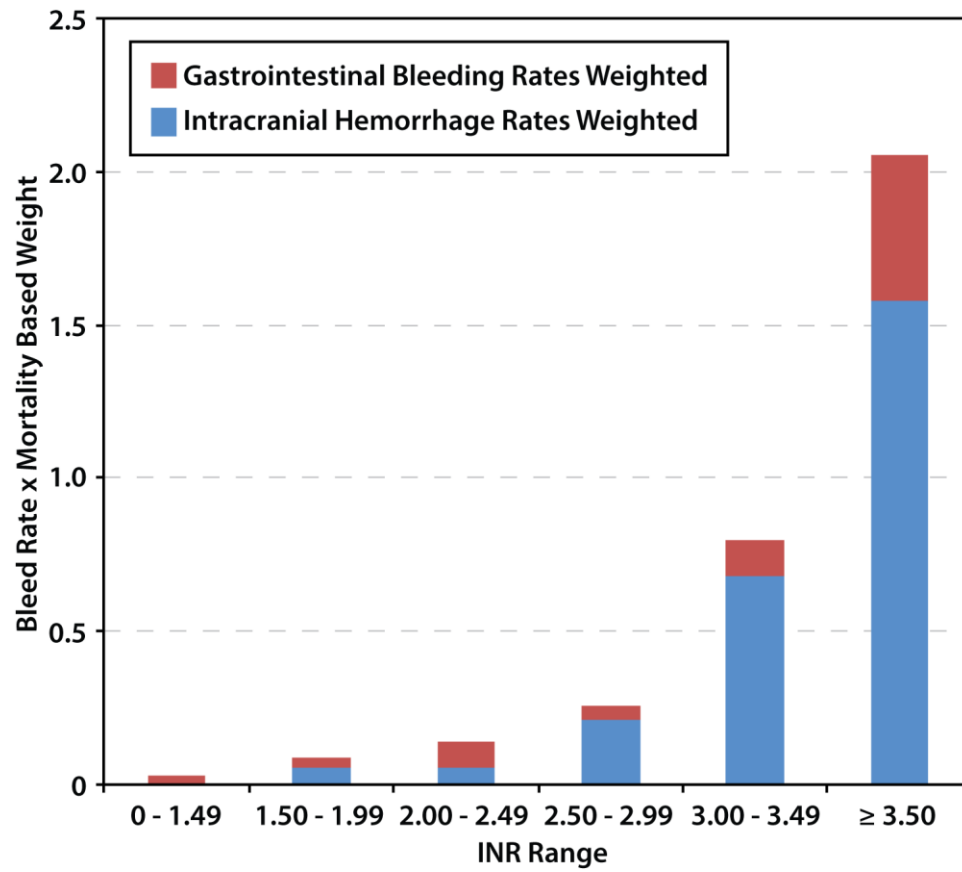| INR range	Patient years	Event Per INR range			Event rate per 10 patient-years		
		PT	**Isc St**	**Total**	**PT**	**Isc St**	**Total**
0 – 1.49	40.31	9	7	16	2.2	1.7	4.0
1.50 – 1.99	111.39	13	4	17	1.2	0.4	1.5
2.00 – 2.49	101.76	9	3	12	0.9	0.3	1.2
2.50 – 2.99	47.80	0	0	0	0	0	0
3.00 – 3.49	15.22	1	0	1	0.7	0	0.7
≥ 3.5	9.95	0	0	0	0	0	0

PT = pump thrombosis; Isc St = ischemic stroke.

Table S4 - Anticoagulation and Antiplatelet Protocols

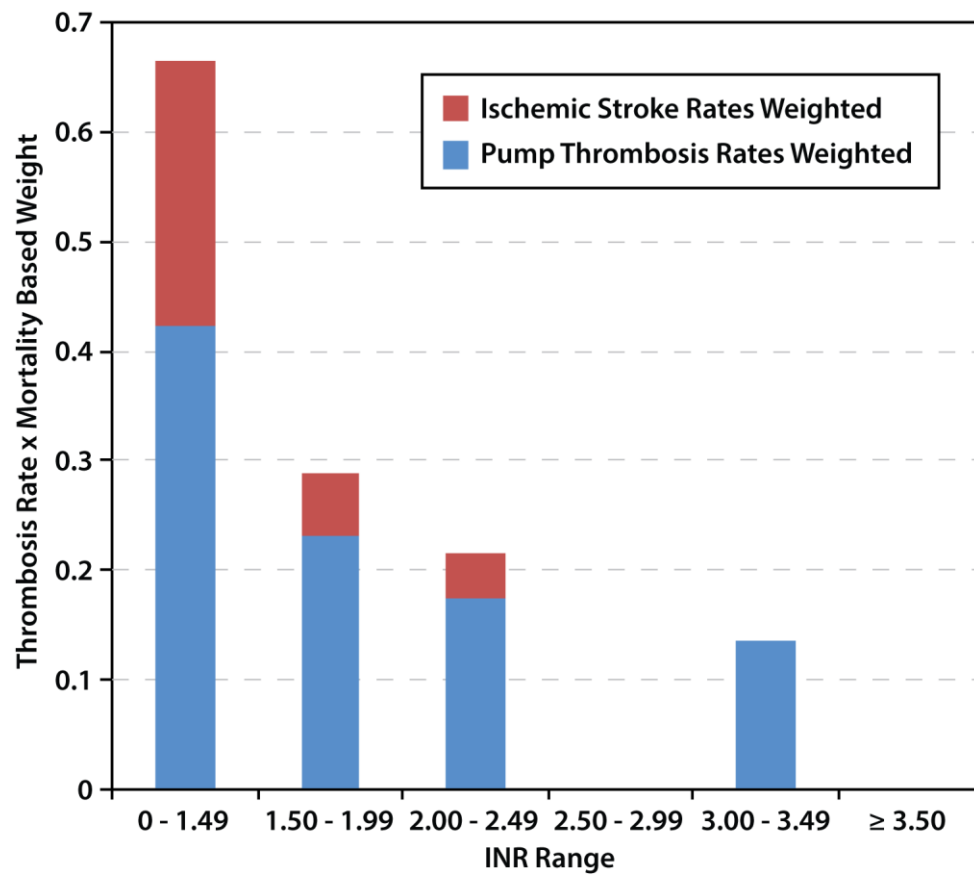|	2004 through 2008	2009 through 2011	2012 through Current
Intravenous anticoagulation – bridge to warfarin	Yes	Occasional	Yes
INR goal	2.0-2.5	1.5-2.0	2.0-3.0
Aspirin dose (mg)	81 or 325	81 or 325	325
Bivalirudin	Yes	Yes	Selective (HIT)

INR = international normalized ratio; HIT = heparin induced thrombocytopenia
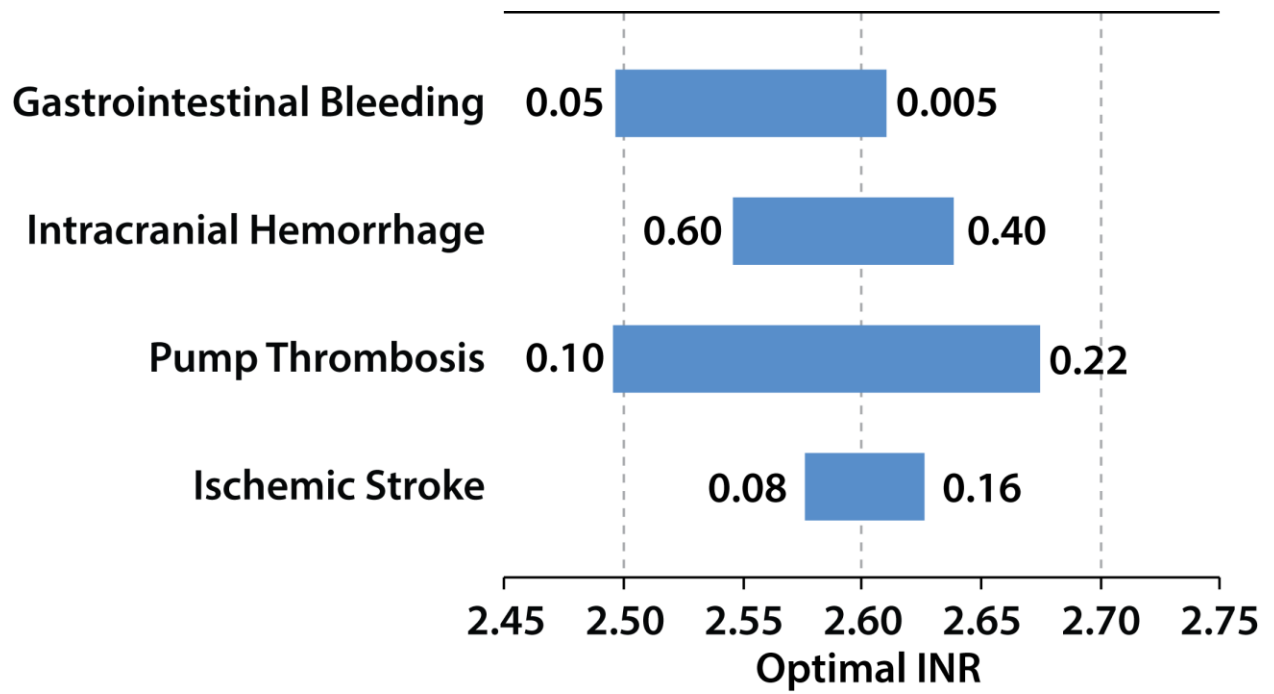
Figure S1 –

Hemorrhagic event rates per INR range multiplied by expected 30 day mortality rates for each adverse event

Figure S2 –

Thrombotic event rates per INR range multiplied by expected 30 day mortality rates for each adverse event

Figure S3-

Optimal INR ranges with varying weights of thrombotic and hemorrhagic events