Supplemental Table 1. Genotype Frequencies by Race

	Genotype	Caucasians n=3261	Blacks n=152	East Asians[a] n=168
VKORC1	G/G	1220 (37.4)	128 (84.2)	2 (1.2)
	G/A	1533 (47.0)	24 (15.8)	38 (22.6)
	A/A	508 (15.6)	0	128 (76.2)
CYP2C9	*1/*1	2101 (64.4)	146 (96.1)	155 (92.3)
	*1/*2	689 (21.1)	3 (2.0)	0
	*1/*3, *2/*2, *2/*3, or *3/*3	471 (14.4)	3 (2.0)	13 (7.7)

All values are n (%)

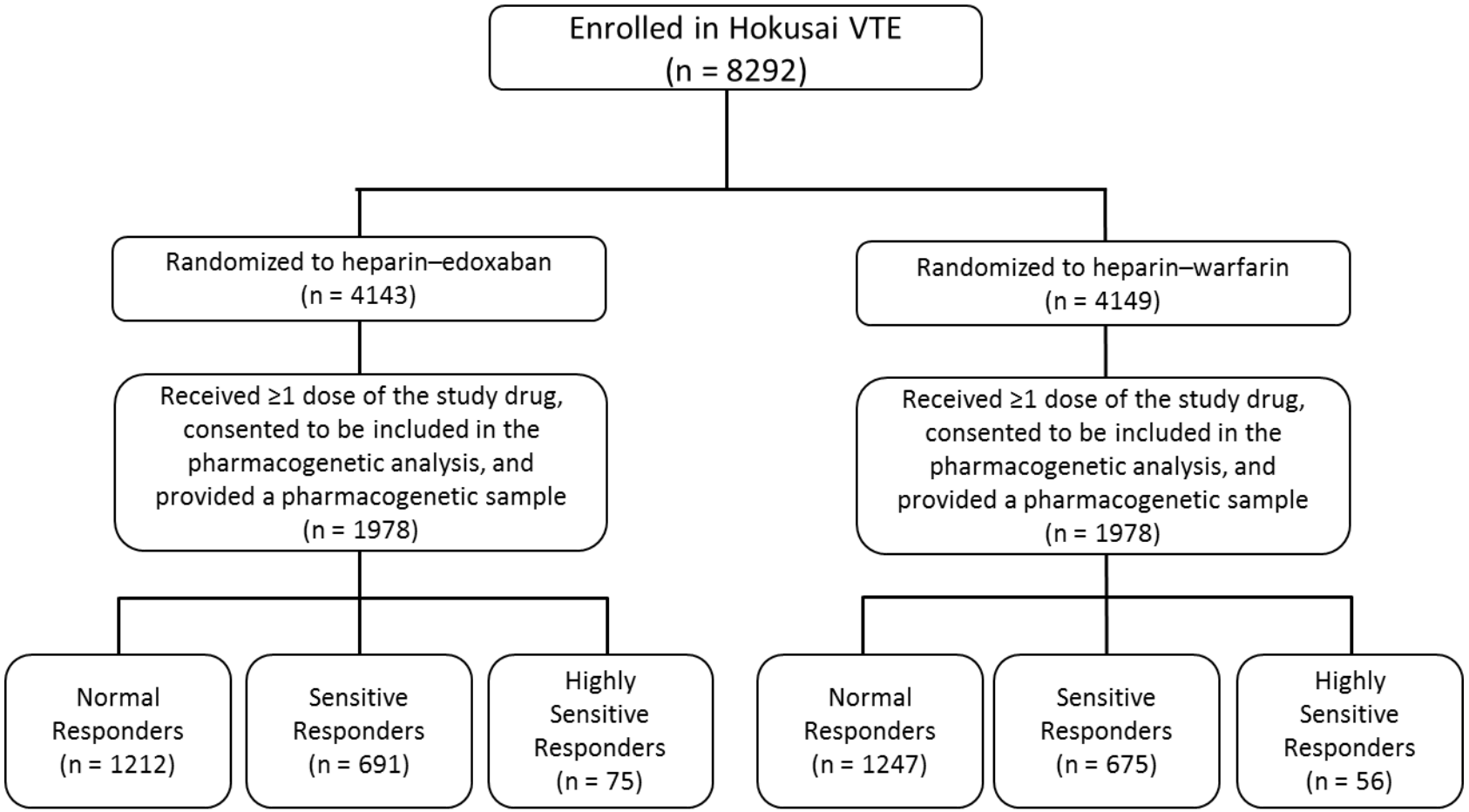
[a] Includes subjects from Japan, China, Taiwan, and Korea only

Supplemental Table 2. Bleeding Events During the First 28 Days of Treatment Across Genotype Categories

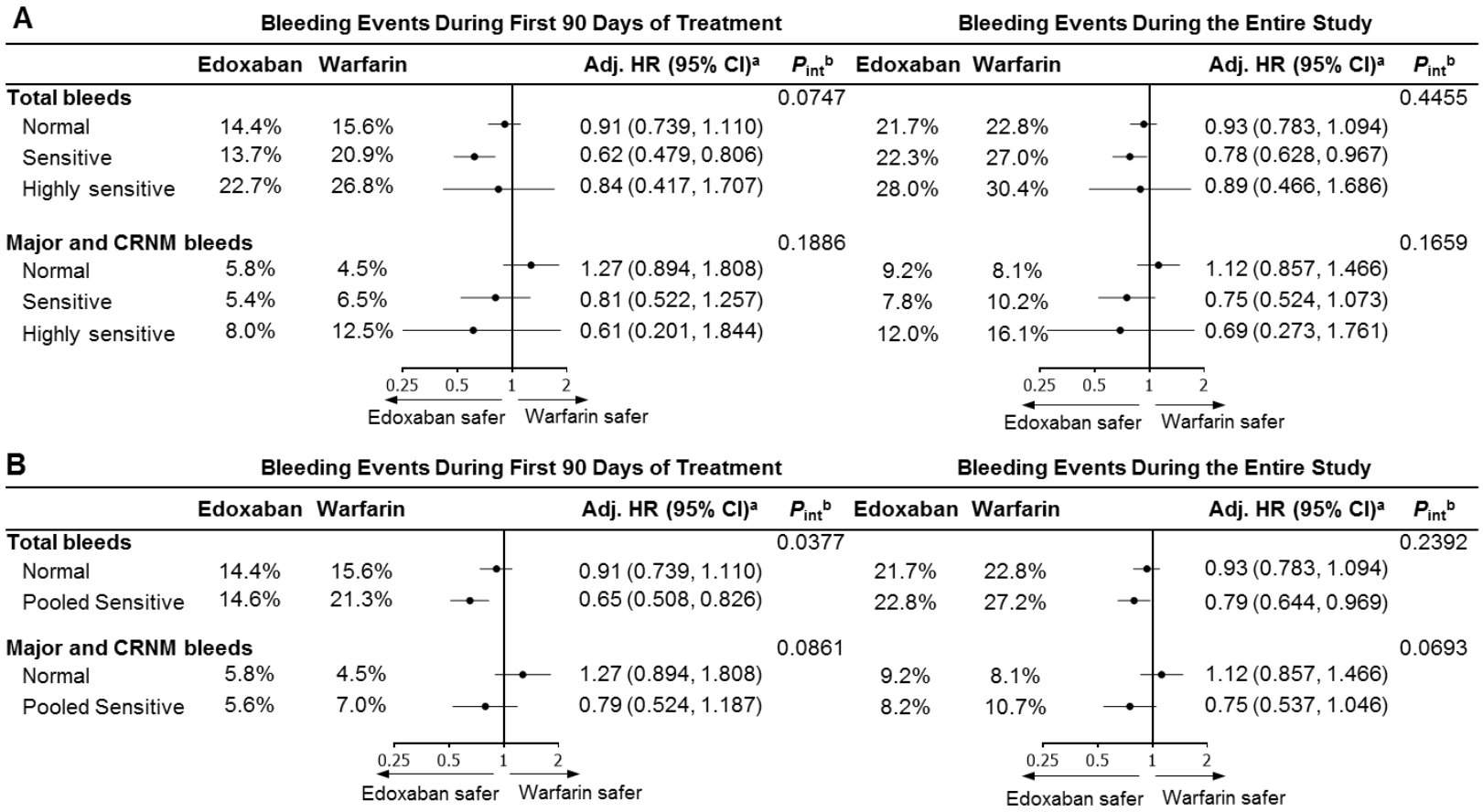
	Normal Responder		Sensitive Responder		Highly Sensitive Responder		Overall	
Bleeding Events	Edoxaban (n=1212)	Warfarin (n=1247)	Edoxaban (n=691)	Warfarin (n=675)	Edoxaban (n=75)	Warfarin (n=56)	Edoxaban (n=1978)	Warfarin (n=1978)
Major	7 (0.6%)	3 (0.2%)	3 (0.4%)	1 (0.2%)	2 (2.7%)	0 (0.0%)	12 (0.6%)	4 (0.2%)
Major or CRNM	22 (1.8%)	33 (2.7%)	18 (2.6%)	28 (4.2%)	3 (4.0%)	3 (5.4%)	43 (2.2%)	64 (3.2%)
All	96 (7.9%)	121 (9.7%)	61 (8.8%)	101 (15.0%)	11 (14.7%)	9 (16.1%)	168 (8.5%)	231 (11.7%)

CRNM = clinically relevant nonmajor

Supplemental Figure 1. Participant Disposition Flow Diagram



Supplemental Figure 2. The incidence and hazard ratios for bleeding events for edoxaban vs warfarin during the first 90 days of treatment and during the entire the duration of the study across the 3-bin warfarin sensitivity groups (A) and 2-bin warfarin sensitivity groups (B)

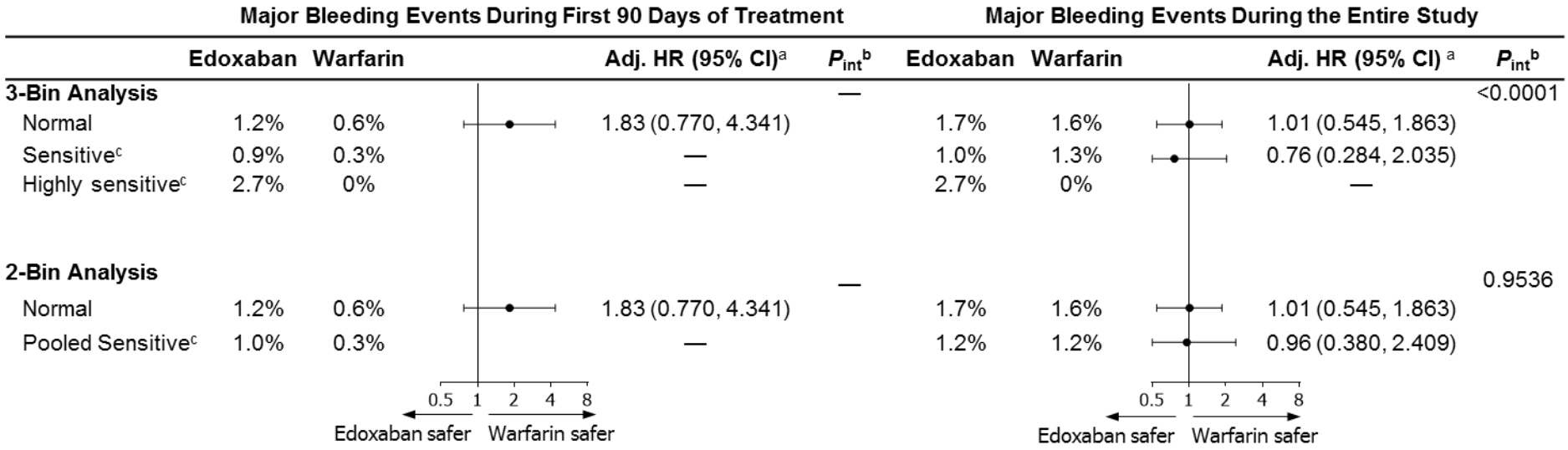


[a]Covariates used in the Cox proportional hazards model included presenting diagnosis (PE with or without DVT vs DVT only), baseline risk factors (temporary risk vs other), and the need for edoxaban dose adjustment

[b]P-values for interactions are based on the Cox proportional hazards model with additional interaction terms for applicable genotype and treatment

CI = confidence intervals; CRNM = clinically relevant non-major; DVT = deep vein thrombosis; HR = hazard ratios; PE = pulmonary embolism

Supplemental Figure 3. The incidence and hazard ratios for major bleeding events for edoxaban vs warfarin during the first 90 days of treatment and during the entire the duration of the study across the 3-bin warfarin sensitivity groups (A) and 2-bin warfarin sensitivity groups (B)



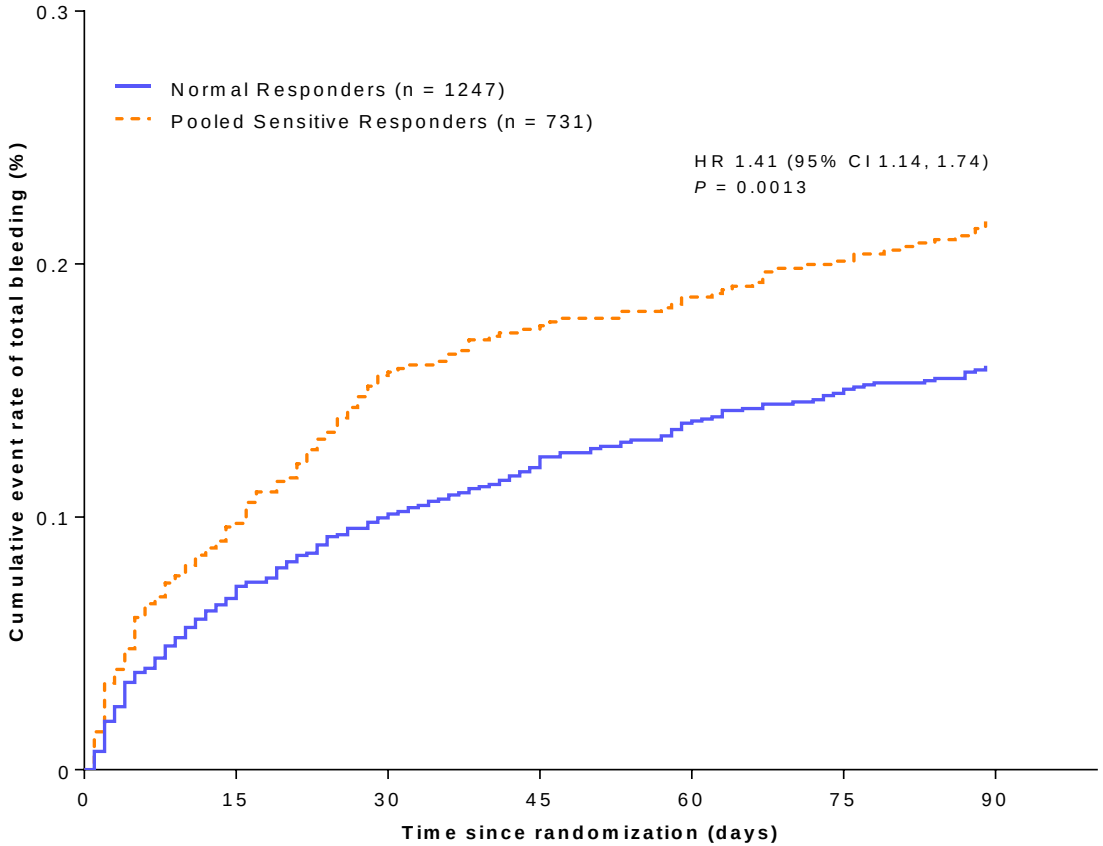
[a] Covariates used in the Cox proportional hazards model included presenting diagnosis (PE with or without DVT vs DVT only), baseline risk factors (temporary risk vs other), and the need for edoxaban dose adjustment

[b]P-values for interactions are based on the Cox proportional hazards model with additional interaction terms for applicable genotype and treatment

[c] There were too few major bleeding events to reliably establish estimates of the risk of major bleeding or to estimate the P_{int} values

CI = confidence intervals; DVT = deep vein thrombosis; HR = hazard ratios; PE = pulmonary embolism

Supplemental Figure 4. Kaplan-Meier curve for the incidence of bleeding events in warfarin treated patients across 2-bin warfarin sensitivity genotypes



Patients at risk (n)

Normal Responders	1247	1147	1091	1055	1030	1010	989
Pooled Sensitive Responders	731	653	601	585	573	561	546

CI = confidence intervals; HR = hazard ratio