

Supplementary Material

**Epidemiology and Treatment Patterns of Venous Thromboembolism: An Observational
Study of Nationwide TimeSeries Trends in Japan**

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Supplementary Tables

Table S1 ICD10 codes used to define venous thromboembolism and cancer

Disease	ICD10 code (Japanese version)
VTE	
DVT	I80.x, I81.x, I82.x
PE	I26.0, I26.9
Malignant neoplasms	
Lip, oral cavity, and pharynx	C00-C14, D00.0, D02.0, D02.3
Digestive organs	C15-C26, D00.1x, D01.x
Respiratory and intrathoracic organs	C30-C39, D02.1, D02.2
Bone and articular cartilage	C40-41
Skin and melanoma	C43-C44, D03.x
Mesothelial and soft tissue	C45-C49
Breast	C50
Female genital organs	C51-C58, D05.x, D06.x, D07.0-3
Male genital organs	C60-C63, D07.4-5
Urinary tract	C64-C68, D090
Eye, brain, and other CNS tissues	C69-C72
Thyroid and other endocrine glands	C73-C75
Ill-defined, secondary (metastatic), and unspecified sites	C76-C80
Lymphoid, hematopoietic, and related tissue	C81-C96
Others	D04.x, D09.2, D09.9

DVT deep vein thrombosis, *PE* pulmonary embolism, *VTE* venous thromboembolism

Table S2 Annual trends in the numbers of patients with deep vein thrombosis or pulmonary embolism

	Year							
	2011	2012	2013	2014	2015	2016	2017	2018
All patients with DVT	1,304	1,915	3,745	6,168	8,777	10,982	14,295	16,629
Outpatients with DVT ^a	425 (32.6)	630 (32.9)	1,194 (31.9)	1,890 (30.6)	2,926 (33.3)	3,908 (35.6)	5,288 (37.0)	6,400 (38.5)
Inpatients for DVT treatment ^a	183 (14.0)	238 (12.4)	402 (10.7)	627 (10.2)	690 (7.9)	713 (6.5)	824 (5.8)	745 (4.5)
Inpatients for conditions other than DVT ^a	696 (53.4)	1,047 (54.7)	2,149 (57.4)	3,651 (59.2)	5,161 (58.8)	6,361 (57.9)	8,183 (57.2)	9,484 (57.0)
All patients with PE	416	587	1,068	1,786	2,224	2,534	3,359	3,541
Outpatients with PE ^b	19 (4.6)	33 (5.6)	57 (5.3)	89 (5.0)	170 (7.6)	237 (9.4)	389 (11.6)	401 (11.3)
Inpatients for PE treatment ^b	210 (50.5)	285 (48.6)	478 (44.8)	803 (45.0)	970 (43.6)	1,035 (40.8)	1,277 (38.0)	1,351 (38.2)
Inpatients for conditions other than PE ^b	187 (45.0)	269 (45.8)	533 (49.9)	894 (50.1)	1,084 (48.7)	1,262 (49.8)	1,693 (50.4)	1,789 (50.5)

Data are presented as n (%).

^aPercentages relative to all patients with DVT.

^bPercentages relative to all patients with PE.

DVT deep vein thrombosis, *PE* pulmonary embolism

Table S3 Chi-square test for the association between treatment status and cancer status (2017–2018)

Items	Without active cancer	With active cancer	Total
Outpatient treatment	8,889 (31.9)	3,589 (36.2)	12,478 (33.0)
Other than outpatient treatment	19,008 (68.1)	6,338 (63.8)	25,346 (67.0)
Total	27,897 (100.0)	9,927 (100.0)	37,824 (100.0)
Chi-square test	60.96* (P<.0001)		

*Chi-square value
Significant at P<.05

Table S4 Prescription dose at initiation in patients who used direct oral anticoagulants at any point in their VTE treatment

	All patients with DVT	Outpatients with DVT	DVT inpatients 1	DVT inpatients 2	DVT patients with active cancer	DVT patients without active cancer
Number of patients	30,924	11,688	1,569	17,667	8,147	22,777
Apixaban						
Number of patients treated with apixaban (%) ^a	3,612 (11.7)	1,303 (11.1)	364 (23.2)	1,945 (11.0)	882 (10.8)	2,730 (12.0)
Median number of days from index date to start of use	1.0	0.0	0.0	2.0	2.0	0.0
Number of patients whose starting dose was 20 mg/day (%)	1,137 (31.5)	461 (35.4)	190 (52.2)	486 (25.0)	268 (30.4)	869 (31.8)
Number of patients whose starting dose was 10 mg/day (%)	1,315 (36.4)	481 (36.9)	128 (35.2)	706 (36.3)	360 (40.8)	955 (35.0)
Number of patients whose starting dose was other (%)	1,160 (32.1)	361 (27.7)	46 (12.6)	753 (38.7)	254 (28.8)	906 (33.2)
Edoxaban						
Number of patients treated with edoxaban (%) ^a	15,274 (49.4)	6,266 (53.6)	622 (39.6)	8,386 (47.5)	3,564 (43.7)	11,710 (51.4)
Median number of days from index date to start of use	3.0	7.0	2.0	2.0	3.0	3.0
Number of patients whose starting dose was 60 mg/day (%) ^b	2,184 (14.3)	977 (15.6)	177 (28.5)	1,030 (12.3)	669 (18.8)	1,515 (12.9)
Number of patients whose starting dose was 30 mg/day (%) ^b	10,569 (69.2)	4,214 (67.3)	430 (69.1)	5,925 (70.7)	2,661 (74.7)	7,908 (67.5)
Number of patients whose starting dose was other (%) ^b	2,521 (16.5)	1,075 (17.2)	15 (2.4)	1,431 (17.1)	234 (6.6)	2,287 (19.5)
Rivaroxaban						
Number of patients treated with rivaroxaban (%) ^a	2,829 (9.1)	1,146 (9.8)	321 (20.5)	1,362 (7.7)	680 (8.3)	2,149 (9.4)
Median number of days from index date to start of use	1.0	0.0	0.0	1.0	2.0	1.0
Number of patients whose starting dose was 30 mg/day (%) ^b	1,088 (38.5)	489 (42.7)	196 (61.1)	403 (29.6)	255 (37.5)	833 (38.8)
Number of patients whose starting dose was 15 mg/day (%) ^b	1,108 (39.2)	443 (38.7)	95 (29.6)	570 (41.9)	306 (45.0)	802 (37.3)
Number of patients whose starting dose was other (%) ^b	633 (22.4)	214 (18.7)	30 (9.3)	389 (28.6)	119 (17.5)	514 (23.9)
	All patients with PE	Outpatients with PE	PE inpatients 1	PE inpatients 2	PE patients with active cancer	PE patients without active cancer
Number of patients	6,900	790	2,628	3,482	1,780	5,120
Apixaban						
Number of patients treated with apixaban (%) ^a	1,416 (20.5)	170 (21.5)	694 (26.4)	552 (15.9)	382 (21.5)	1,034 (20.2)

Median number of days from index date to start of use	1.0	0.0	0.0	1.5	1.0	0.0
Number of patients whose starting dose was 20 mg/day (%) ^b	704 (49.7)	83 (48.8)	392 (56.5)	229 (41.5)	178 (46.6)	526 (50.9)
Number of patients whose starting dose was 10 mg/day (%) ^b	504 (35.6)	61 (35.9)	236 (34.0)	207 (37.5)	154 (40.3)	350 (33.8)
Number of patients whose starting dose was other (%) ^b	208 (14.7)	26 (15.3)	66 (9.5)	116 (21.0)	50 (13.1)	158 (15.3)
Edoxaban						
Number of patients treated with edoxaban (%) ^a	2,529 (36.7)	300 (38.0)	951 (36.2)	1,278 (36.7)	724 (40.7)	1,805 (35.3)
Median number of days from index date to start of use	3.0	1.0	3.0	4.0	4.0	3.0
Number of patients whose starting dose was 60 mg/day (%) ^b	794 (31.4)	106 (35.3)	373 (39.2)	315 (24.6)	218 (30.1)	576 (31.9)
Number of patients whose starting dose was 30 mg/day (%) ^b	1,630 (64.5)	183 (61.0)	573 (60.3)	874 (68.4)	492 (68.0)	1,138 (63.0)
Number of patients whose starting dose was other (%) ^b	105 (4.2)	11 (3.7)	5 (0.5)	89 (7.0)	14 (1.9)	91 (5.0)
Rivaroxaban						
Number of patients treated with rivaroxaban (%) ^a	1,196 (17.3)	129 (16.3)	683 (26.0)	384 (11.0)	262 (14.7)	934 (18.2)
Median number of days from index date to start of use	1.0	0.0	0.0	2.0	2.0	1.0
Number of patients whose starting dose was 30 mg/day (%) ^b	706 (59.0)	76 (58.9)	460 (67.3)	170 (44.3)	150 (57.3)	556 (59.5)
Number of patients whose starting dose was 15 mg/day (%) ^b	396 (33.1)	46 (35.7)	193 (28.3)	157 (40.9)	94 (35.9)	302 (32.3)
Number of patients whose starting dose was other (%) ^b	94 (7.9)	7 (5.4)	30 (4.4)	57 (14.8)	18 (6.9)	76 (8.1)

^aPercentages of patients were calculated using the total number in each category as the denominator.

^bPercentages of patients were calculated using as the denominator the number of patients who were treated with each direct anticoagulant.

DVT inpatients 1 patients with DVT hospitalized for DVT treatment, *DVT inpatients 2* patients with DVT hospitalized for purposes other than DVT treatment, *PE inpatients 1* patients with PE hospitalized for PE treatment, *PE inpatients 2* patients with PE hospitalized for purposes other than PE treatment.
DVT deep vein thrombosis, *PE* pulmonary embolism

Supplementary Figures

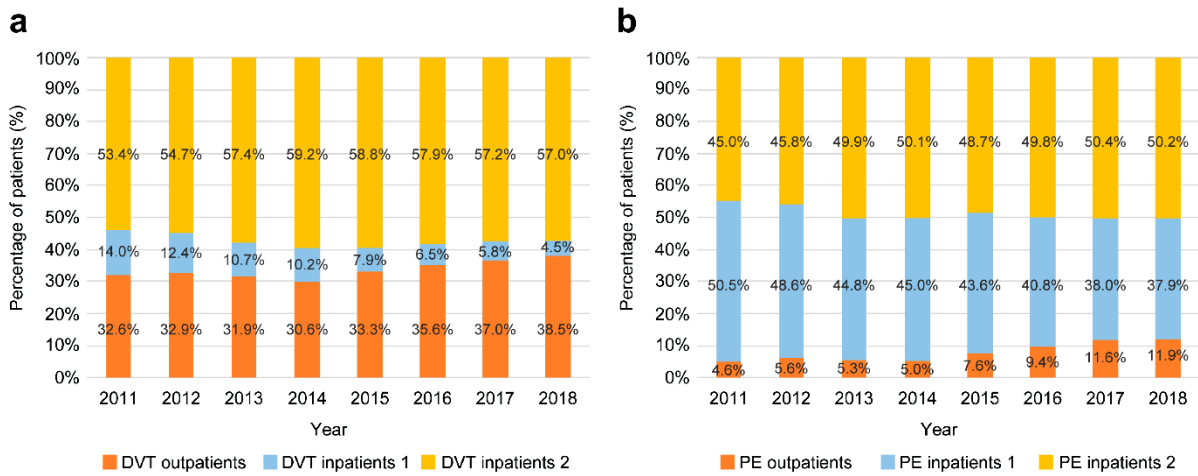


Fig. S1 Inpatient and outpatient proportions by DVT and PE (2011–2018). The percentages of inpatients and outpatients in the DVT (**a**) and PE (**b**) groups in each year (2011–2018). *Outpatients* These patients were outpatients at the time of diagnosis of DVT or PE and were subsequently treated for DVT/PE on an outpatient basis. *DVT/PE inpatients 1* These patients were outpatients at the time of VTE diagnosis and were subsequently hospitalized for VTE treatment. *DVT/PE inpatients 2* These patients were already hospitalized for other reasons at the time of VTE diagnosis (the principal diagnosis of hospitalization was not DVT or PE). *DVT* deep vein thrombosis, *PE* pulmonary embolism, *VTE* venous thromboembolism

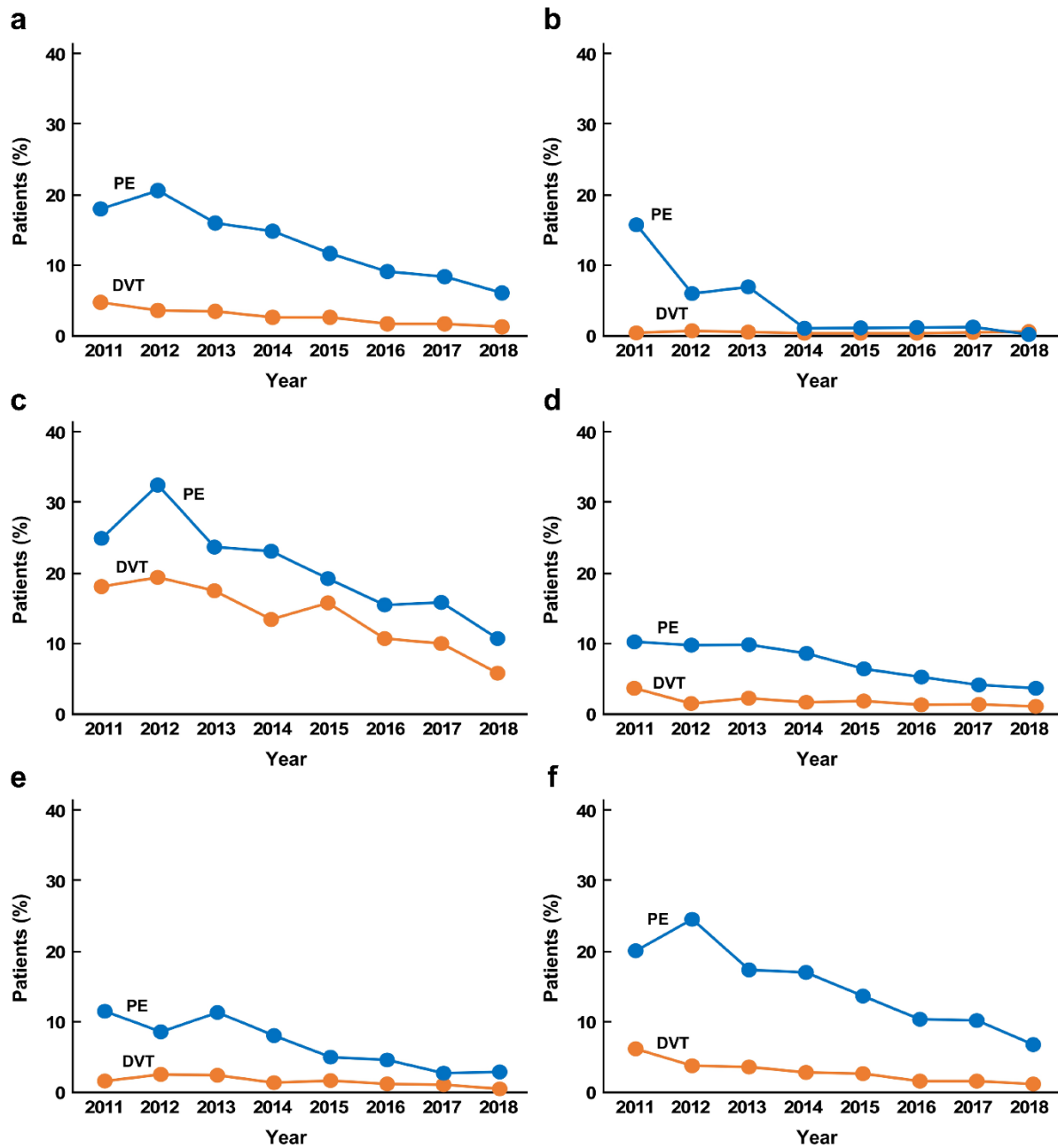


Fig. S2 Proportions of urokinase or tPA use in the treatment of venous thromboembolism in realworld settings. The percentages of patients treated with urokinase or tPA in each year (2011–2018) are shown for the DVT and PE groups. **(a)** All patients, **(b)** outpatients, **(c)** patients hospitalized for the treatment of DVT or PE, **(d)** patients hospitalized for purposes other than DVT or PE treatment, **(e)** patients with active cancer, and **(f)** patients without active cancer. *DVT* deep vein thrombosis, *PE* pulmonary embolism, *tPA* tissue plasminogen activator

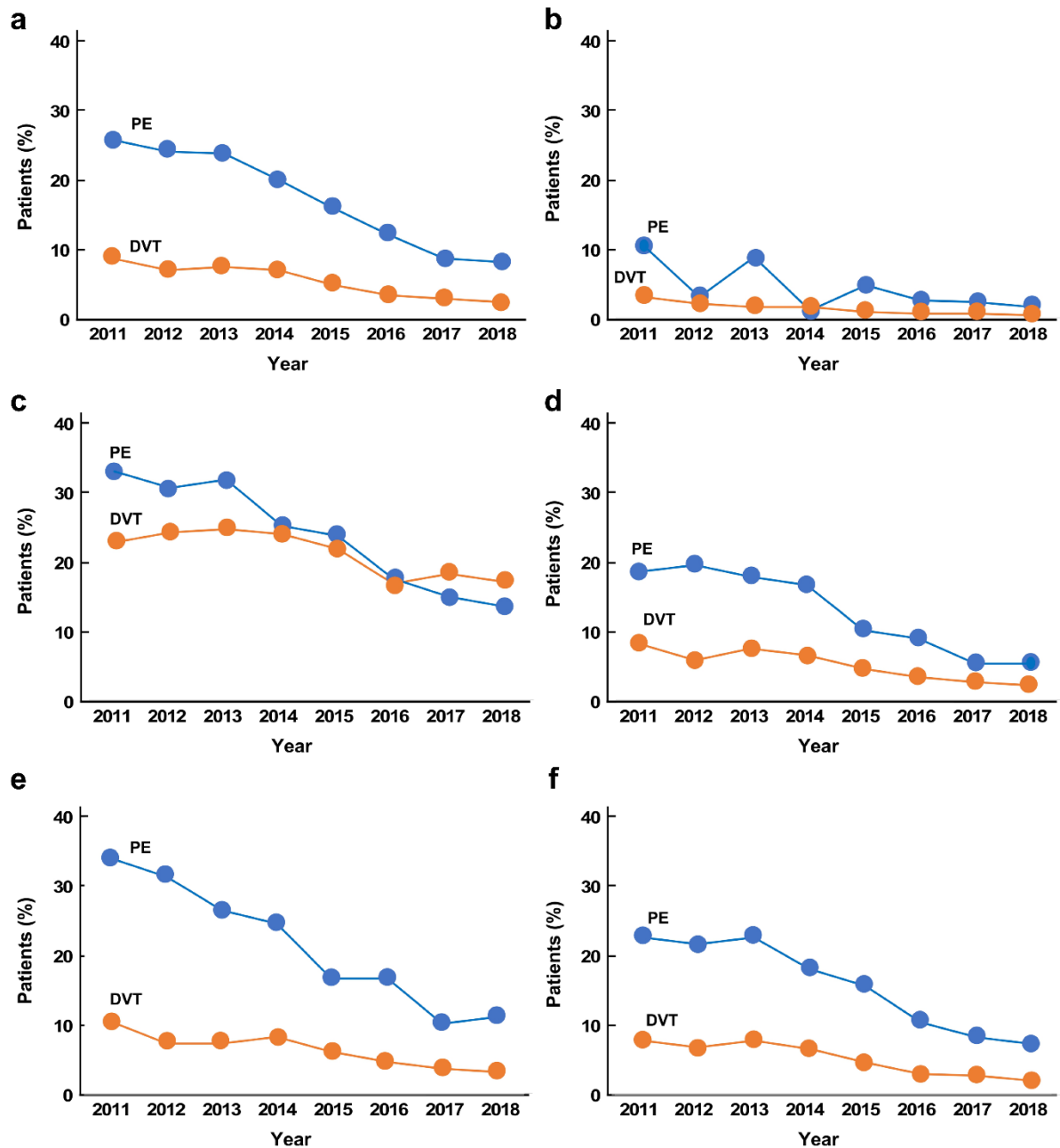


Fig. S3 Proportion of IVC filter use in the treatment of venous thromboembolism in realworld settings. The percentages of patients undergoing IVC filter placement in each year (2011–2018) are shown for the DVT and PE groups. **(a)** All patients, **(b)** outpatients, **(c)** patients hospitalized for the treatment of DVT or PE, **(d)** patients hospitalized for purposes other than DVT or PE treatment, **(e)** patients with active cancer, and **(f)** patients without active cancer. *DVT* deep vein thrombosis, *IVC* inferior vena cava, *PE* pulmonary embolism