

## Supplementary material

**eTable 1.** Incidence rate of VTE and association of ALS with VTE, after exclusion of ALS cases with edaravone prescription at any point in the study period.

	<b>ALS cases</b>	<b>Controls</b>
<b>All</b>	4,145	20,725
Patients with a VTE during follow-up	131 (3.2%)	244 (1.2%)
Median time to VTE (months)	10.0	17.4
Incidence rate of VTE per 1,000 person-years (95% CI)	20.0 (16.7,23.7)	6.1 (5.3,6.9)
Hazard ratio (95% CI)	3.2 (2.6,4.0)	
<b>Men</b>	2,363	11,815
Patients with a VTE during follow-up	84 (3.5%)	133 (1.1%)
Median time to VTE (months)	10.8	15.6
Incidence rate of VTE per 1,000 person-years (95% CI)	21.6 (17.3,26.8)	6.0 (5.1,7.2)
Hazard ratio (95% CI)	3.5 (2.7,4.6)	
<b>Women</b>	1,782	8,910
Patients with a VTE during follow-up	47 (2.6%)	111 (1.2%)
Median time to VTE (months)	9.7	19.1
Incidence rate of VTE per 1,000 person-years (95% CI)	17.6 (13.0,23.5)	6.1 (5.0,7.3)
Hazard ratio (95% CI)	2.9 (2.0,4.0)	
<b>Age at index date</b>		
<b>&lt;50 years</b>	461	2,305
Patients with a VTE during follow-up	16 (3.5%)	6 (0.3%)
Median time to VTE (months)	13.0	8.7
Incidence rate of VTE per 1,000 person-years (95% CI)	16.7 (9.5, 27.1)	1.6 (0.6, 3.5)
Hazard ratio (95% CI)	10.7 (4.2, 27.4)	
<b>50–59 years</b>	730	3,650
Patients with a VTE during follow-up	32 (4.4%)	27 (0.7%)
Median time to VTE (months)	10.6	15.2
Incidence rate of VTE per 1,000 person-years (95% CI)	26.5 (18.2,37.5)	4.6 (3.0,6.7)
Hazard ratio (95% CI)	5.7 (3.4,9.5)	
<b>60–69 years</b>	1,239	6,195
Patients with a VTE during follow-up	39 (3.1%)	56 (0.9%)
Median time to VTE (months)	9.9	13.4
Incidence rate of VTE per 1,000 person-years (95% CI)	21.3 (15.1,29.1)	4.9 (3.7,6.3)
Hazard ratio (95% CI)	4.1 (2.7,6.3)	
<b>≥70 years</b>	1,715	8,575
Patients with a VTE during follow-up	44 (2.6%)	155 (1.8%)
Median time to VTE (months)	9.3	19.6
Incidence rate of VTE per 1,000 person-years (95% CI)	17.3 (12.5,23.2)	8.1 (6.9,9.5)
Hazard ratio (95% CI)	2.1 (1.5,3.0)	

**eTable 2** ICD codes for motor neuron disease

VTE categories	ICD-9	ICD-10
Motor neuron disease, unspecified		G12.20
Amyotrophic lateral sclerosis	335.20	G12.21
Progressive muscular atrophy	335.21	G12.22
Progressive bulbar palsy	335.22	G12.23
Pseudobulbar palsy	335.23	G12.24
Primary lateral sclerosis	335.24	G12.25
Other motor neuron disease	335.29	G12.29

VTE = venous thromboembolism.

**eTable 3** ICD-9 and ICD-10 codes for VTE

VTE categories	ICD-9	ICD-10	Category
Phlebitis and thrombophlebitis	451.x excluding 451.0 and 451.82	I80.1x, I80.2x, I80.3, I80.8, I80.9	DVT other
Budd-Chiari syndrome	453.0	I82.0	DVT other
Thrombophlebitis migrans	453.1	I82.1	DVT other
Embolism and thrombosis of vena cava and other thoracic veins	453.2	I82.2x	DVT other
Embolism and thrombosis of renal vein	453.3	I82.3	DVT
Embolism and thrombosis of deep veins of lower extremity	453.4x	I82.4x	DVT lower extremity
Chronic embolism and thrombosis of deep veins of lower extremity	453.5x	I82.5x	DVT lower extremity
Embolism and thrombosis of veins of upper extremity (including axillary, subclavian, and internal jugular vein)	453.7x excluding 453.71; 453.8x excluding 453.81	I82.6x excluding I82.61x; I82.Ax, I82.Bx, I82.Cx, I82.70x, I82.72x	DVT upper extremity
Embolism and thrombosis of other specified veins/unspecified veins	453.9	I82.89x; I82.9x	DVT other
Pulmonary embolism	415.x excluding 415.0	I26.x	PE

DVT = deep vein thrombosis; PE = pulmonary embolism; VTE = venous thromboembolism.

**eTable 4** VTE related procedure codes

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**ICD codes**

**Interruption of vena cava**

02HV0DZ	Insertion of Intraluminal Device into Superior Vena Cava, Open Approach
02HV3DZ	Insertion of Intraluminal Device into Superior Vena Cava, Percutaneous Approach
02HV3DZ	Insertion of Intraluminal Device into Superior Vena Cava, Percutaneous Approach
02LV0CZ	Occlusion of Superior Vena Cava with Extraluminal Device, Open Approach
02LV0DZ	Occlusion of Superior Vena Cava with Intraluminal Device, Open Approach
02LV0ZZ	Occlusion of Superior Vena Cava, Open Approach
02LV3CZ	Occlusion of Superior Vena Cava with Extraluminal Device, Percutaneous Approach
02LV3DZ	Occlusion of Superior Vena Cava with Intraluminal Device, Percutaneous Approach
02LV3ZZ	Occlusion of Superior Vena Cava, Percutaneous Approach
02LV4CZ	Occlusion of Superior Vena Cava with Extraluminal Device, Percutaneous Endoscopic Approach
02LV4DZ	Occlusion of Superior Vena Cava with Intraluminal Device, Percutaneous Endoscopic Approach
02LV4ZZ	Occlusion of Superior Vena Cava, Percutaneous Endoscopic Approach
02VV0CZ	Restriction of Superior Vena Cava with Extraluminal Device, Open Approach
02VV0DZ	Restriction of Superior Vena Cava with Intraluminal Device, Open Approach
02VV0ZZ	Restriction of Superior Vena Cava, Open Approach
02VV3CZ	Restriction of Superior Vena Cava with Extraluminal Device, Percutaneous Approach
02VV3DZ	Restriction of Superior Vena Cava with Intraluminal Device, Percutaneous Approach
02VV3ZZ	Restriction of Superior Vena Cava, Percutaneous Approach
02VV4CZ	Restriction of Superior Vena Cava with Extraluminal Device, Percutaneous Endoscopic Approach
02VV4DZ	Restriction of Superior Vena Cava with Intraluminal Device, Percutaneous Endoscopic Approach
02VV4ZZ	Restriction of Superior Vena Cava, Percutaneous Endoscopic Approach
06H00DZ	Insertion of Intraluminal Device into Inferior Vena Cava, Open Approach
06H03DZ	Insertion of Intraluminal Device into Inferior Vena Cava, Percutaneous Approach
06H04DZ	Insertion of Intraluminal Device into Inferior Vena Cava, Percutaneous Endoscopic Approach
06L00CZ	Occlusion of Inferior Vena Cava with Extraluminal Device, Open Approach
06L00DZ	Occlusion of Inferior Vena Cava with Intraluminal Device, Open Approach
06L00ZZ	Occlusion of Inferior Vena Cava, Open Approach
06L03CZ	Occlusion of Inferior Vena Cava with Extraluminal Device, Percutaneous Approach
06L03DZ	Occlusion of Inferior Vena Cava with Intraluminal Device, Percutaneous Approach
06L03ZZ	Occlusion of Inferior Vena Cava, Percutaneous Approach
06L04CZ	Occlusion of Inferior Vena Cava with Extraluminal Device, Percutaneous Endoscopic Approach
06L04DZ	Occlusion of Inferior Vena Cava with Intraluminal Device, Percutaneous Endoscopic Approach

06L04ZZ Occlusion of Inferior Vena Cava, Percutaneous Endoscopic Approach  
06V00CZ Restriction of Inferior Vena Cava with Extraluminal Device, Open Approach  
06V00DZ Restriction of Inferior Vena Cava with Intraluminal Device, Open Approach  
06V00ZZ Restriction of Inferior Vena Cava, Open Approach  
06V03CZ Restriction of Inferior Vena Cava with Extraluminal Device, Percutaneous Approach  
06V03DZ Restriction of Inferior Vena Cava with Intraluminal Device, Percutaneous Approach  
06V03ZZ Restriction of Inferior Vena Cava, Percutaneous Approach  
06V04CZ Restriction of Inferior Vena Cava with Extraluminal Device, Percutaneous Endoscopic Approach  
06V04DZ Restriction of Inferior Vena Cava with Intraluminal Device, Percutaneous Endoscopic Approach  
06V04ZZ Restriction of Inferior Vena Cava, Percutaneous Endoscopic Approach

#### **Thrombolytic agent**

3E03017 Introduction of Other Thrombolytic into Peripheral Vein, Open Approach  
3E03317 Introduction of Other Thrombolytic into Peripheral Vein, Percutaneous Approach  
3E04017 Introduction of Other Thrombolytic into Central Vein, Open Approach  
3E04317 Introduction of Other Thrombolytic into Central Vein, Percutaneous Approach  
3E05317 Introduction of Other Thrombolytic into Peripheral Artery, Percutaneous Approach  
3E06317 Introduction of Other Thrombolytic into Central Artery, Percutaneous Approach  
3E08317 Introduction of Other Thrombolytic into Heart, Percutaneous Approach

#### **Platelet inhibitor**

3E030PZ Introduction of Platelet Inhibitor into Peripheral Vein, Open Approach  
3E033PZ Introduction of Platelet Inhibitor into Peripheral Vein, Percutaneous Approach  
3E040PZ Introduction of Platelet Inhibitor into Central Vein, Open Approach  
3E043PZ Introduction of Platelet Inhibitor into Central Vein, Percutaneous Approach  
3E050PZ Introduction of Platelet Inhibitor into Peripheral Artery, Open Approach  
3E053PZ Introduction of Platelet Inhibitor into Peripheral Artery, Percutaneous Approach  
3E060PZ Introduction of Platelet Inhibitor into Central Artery, Open Approach  
3E063PZ Introduction of Platelet Inhibitor into Central Artery, Percutaneous Approach

#### **HCPCS codes**

C1880 Vena cava filter  
C1757 Catheter, thrombectomy/embolectomy

#### **CPT codes**

37184 PRIM ART M-THRMBC 1ST VSL  
37185 PRIM ART M-THRMBC SBSQ VSL  
37186 SEC ART THROMBECTOMY ADD-ON

37187	VENOUS MECH THROMBECTOMY
37188	VENOUS M-THROMBECTOMY ADD-ON
37191	INS ENDOVAS VENA CAVA FILTR
37192	REDO ENDOVAS VENA CAVA FILTR
37193	REM ENDOVAS VENA CAVA FILTER
37211	THROMBOLYTIC ART THERAPY
37212	THROMBOLYTIC VENOUS THERAPY
37213	THROMBLYTIC ART/VEN THERAPY

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VTE = venous thromboembolism.

**eTable 5** Incidence of VTE using an expanded definition of VTE: two or more VTE diagnostic codes where one or more of the diagnostic codes was the primary diagnosis at discharge

	<b>ALS cases</b>	<b>Controls</b>
<b><u>Incidence of VTE</u></b>		
<b>All</b>	4,205	21,025
Patients with a VTE during follow-up	141 (3.4%)	257 (1.2%)
Median time to VTE (months)	9.9	17.7
Incidence rate of VTE per 1,000 person-years (95% CI)	21.3 (17.9, 25.1)	6.3 (5.6, 7.1)
Unadjusted hazard ratio (95% CI)	3.3 (2.7, 4.1)	
<b>Men</b>	2,391	11,955
Patients with a VTE during follow-up	90 (3.8%)	137 (1.1%)
Median time to VTE (months)	10.2	15.8
Incidence rate of VTE per 1,000 person-years (95% CI)	23.0 (18.5, 28.3)	6.2 (5.2, 7.3)
Unadjusted hazard ratio (95% CI)	3.7 (2.8, 4.8)	
<b>Women</b>	1,814	9,070
Patients with a VTE during follow-up	51 (2.8%)	120 (1.3%)
Median time to VTE (months)	8.8	19.8
Incidence rate of VTE per 1,000 person-years (95% CI)	18.9 (14.0, 24.8)	6.5 (5.4, 7.8)
Unadjusted hazard ratio (95% CI)	2.9 (2.1, 4.0)	
<b>Age at index date</b>		
<b>Age &lt;50 years</b>	461	2,305
Patients with a VTE during follow-up	17 (3.7%)	6 (0.3%)
Median time to VTE (months)	12.2	8.7
Incidence rate of VTE per 1,000 person-years (95% CI)	17.7 (10.3, 28.4)	1.6 (0.6, 3.5)
Unadjusted hazard ratio (95% CI)	11.4 (4.5, 28.8)	
<b>Age 50–59 years</b>	732	3,660
Patients with a VTE during follow-up	32 (4.4%)	28 (0.8%)
Median time to VTE (months)	10.6	14.5
Incidence rate of VTE per 1,000 person-years (95% CI)	26.5 (18.1, 37.5)	4.7 (3.1, 6.8)
Unadjusted hazard ratio (95% CI)	5.5 (3.3, 9.1)	

	<b>ALS cases</b>	<b>Controls</b>
<b>Age 60–69 years</b>	1,260	6,300
Patients with a VTE during follow-up	40 (3.2%)	58 (0.9%)
Median time to VTE (months)	10.0	11.2
Incidence rate of VTE per 1,000 person-years (95% CI)	21.6 (15.4, 29.4)	5.0 (3.8, 6.5)
Unadjusted hazard ratio (95% CI)	4.1 (2.7, 6.2)	
<b>Age ≥70 years</b>	1,752	8,760
Patients with a VTE during follow-up	52 (3.0%)	165 (1.9%)
Median time to VTE (months)	7.4	21.9
Incidence rate of VTE per 1,000 person-years (95% CI)	20.0 (14.9, 26.2)	8.5 (7.3, 9.9)
Unadjusted hazard ratio (95% CI)	2.3 (1.7, 3.2)	
<b><u>Incidence of PE</u></b>		
<b>All</b>	4,205	21,025
Patients with a PE during follow-up	56 (1.3%)	93 (0.4%)
Median time to PE (months)	10.3	19.6
Incidence rate of PE per 1,000 person-years (95% CI)	8.3 (6.3, 10.8)	2.3 (1.8, 2.8)
Unadjusted hazard ratio (95% CI)	3.6 (2.6, 5.1)	
<b>Men</b>	2,391	11,955
Patients with a PE during follow-up	38 (1.6%)	45 (0.4%)
Median time to PE (months)	10.3	19.6
Incidence rate of PE per 1,000 person-years (95% CI)	9.6 (6.8, 13.1)	2.0 (1.5, 2.7)
Unadjusted hazard ratio (95% CI)	4.7 (3.1, 7.3)	
<b>Women</b>	1,814	9,070
Patients with a PE during follow-up	18 (1.0%)	48 (0.5%)
Median time to PE (months)	10.6	20.2
Incidence rate of PE per 1,000 person-years (95% CI)	6.6 (3.9, 10.4)	2.6 (1.9, 3.4)
Unadjusted hazard ratio (95% CI)	2.5 (1.5, 4.4)	
<b><u>Incidence of DVT</u></b>		
<b>All</b>	4,205	21,025
Patients with a PE during follow-up	96 (2.3%)	180 (0.9%)

	<b>ALS cases</b>	<b>Controls</b>
Median time to PE (months)	10.1	17
Incidence rate of PE per 1,000 person-years (95% CI)	14.4 (11.7, 17.6)	4.4 (3.8, 5.1)
Unadjusted hazard ratio (95% CI)	3.2 (2.5, 4.1)	
<b>Men</b>	2,391	11,955
Patients with a PE during follow-up	58 (2.4%)	100 (0.8%)
Median time to PE (months)	10.8	14.6
Incidence rate of PE per 1,000 person-years (95% CI)	14.7 (11.2, 19.0)	4.5 (3.7, 5.5)
Unadjusted hazard ratio (95% CI)	3.2 (2.3, 4.5)	
<b>Women</b>	1,814	9,070
Patients with a PE during follow-up	38 (2.1%)	80 (0.9%)
Median time to PE (months)	9.8	20.7
Incidence rate of PE per 1,000 person-years (95% CI)	13.9 (9.9, 19.1)	4.3 (3.4, 5.4)
Unadjusted hazard ratio (95% CI)	3.2 (2.2, 4.7)	

CI = confidence interval; DVT = deep vein thrombosis; PE = pulmonary embolism; VTE = venous thromboembolism.