Supplementary Appendix Table S1: Baseline characteristics of ENCHANTED trial participants in England and Wales compared to the overall ENCHANTED trial

	UK Sites Total (n=770)	Non-UK Sites Total (n=2527)	P value[4]
Time from stroke onset to randomisation (hrs), median (Q1 Q3)	2.3 (1.8 - 2.9)	2.8 (2.1 - 3.6)	<0.0001
Age (years), mean (SD)	72.1 (13.6)	64.9 (12.1)	<0.0001
>=80, n(%)	252/ 770 (32.7)	220/2527 (8.7)	<0.0001
Female, n(%)	317/ 770 (41.2)	931/2527 (36.8)	0.03
Ethnicity			
Non-Asian	753/ 770 (97.8)	459/2521 (18.2)	<0.0001
Asian	17/ 770 (2.2)	2062/2521 (81.8)	<0.0001
Clinical features			
Systolic BP (mmHg), mean (SD)	151.4 (19.5)	148.6 (19.9)	0.0009
Diastolic BP (mmHg), mean (SD)	81.4 (13.2)	85.7 (12.7)	<0.0001
Heart rate (beats per minute), mean (SD)	80.2 (17.6)	78.7 (14.6)	0.15
NIHSS score			
Median (Q1 Q3)	7.0 (5.0 - 13.0)	9.0 (5.0 - 14.0)	0.013
>=14, n(%)	175/ 770 (22.7)	678/2527 (26.8)	0.023
GCS score			
Median (Q1 Q3)	15.0 (14.0 - 15.0)	15.0 (13.0 - 15.0)	<0.0001
Severe (3-8), n(%)	10/ 770 (1.3)	126/2527 (5.0)	<0.0001
Medical History			
Hypertension, n(%)	471/ 770 (61.2)	1594/2518 (63.3)	0.28
Previous stroke	109/ 770 (14.2)	480/2527 (19.0)	0.002
Coronary artery disease, n(%)	111/ 770 (14.4)	368/2518 (14.6)	0.89
Other heart disease (valvular or other), n(%)	74/ 770 (9.6)	161/2518 (6.4)	0.002
Diabetes Mellitus	134/ 770 (17.4)	512/2518 (20.3)	0.07
Atrial fibrillation confirmed on ECG, n(%)	187/ 768 (24.3)	449/2517 (17.8)	<0.0001
Hypercholesterolaemia, n(%)	259/ 770 (33.6)	296/2518 (11.8)	<0.0001
Current smoker, n(%)	123/ 766 (16.1)	647/2518 (25.7)	<0.0001
Pre-stroke function (mRS)			
No symptoms, n(%)	531/ 769 (69.1)	2143/2517 (85.1)	<0.0001
No significant disability, n(%)	238/ 769 (30.9)	374/2517 (14.9)	
Medication at time of admission			
Antihypertensive agents, n(%)	428/ 770 (55.6)	1070/2518 (42.5)	<0.0001
Warfarin anticoagulation, n(%)	23/ 769 (3.0)	59/2516 (2.3)	0.32
Aspirin or other anti-platelet agent, n(%)	272/ 769 (35.4)	480/2516 (19.1)	<0.0001
Statin or other lipid lowering agent, n(%)	103/ 769 (13.4)	313/2516 (12.4)	0.49
Brain imaging features			
CT scan used, n(%)	765/ 770 (99.4)	2421/2518 (96.1)	<0.0001

MRI scan used, n(%)	8/ 770 (1.0)	426/2518 (16.9)	<0.0001
Visible early ischaemic changes, n(%)	229/ 770 (29.7)	542/2518 (21.5)	<0.0001
Visible cerebral infarction, n(%)	144/ 770 (18.7)	599/2518 (23.8)	0.003
Visible cerebral infarction with mass effect, n(%)	8/ 770 (1.0)	39/2518 (1.5)	0.30
CT or MR angiogram show proximal occlusion, n(%)	111/ 731 (15.2)	394/2515 (15.7)	0.752
Final diagnosis at time of hospital separation			
Non-stroke, n(%)	50/ 764 (6.5)	47/2472 (1.9)	<0.0001
Presumed stroke pathology, n(%)			
Large artery occlusion due to significant atheroma	170/ 763 (22.3)	1100/2471 (44.5)	
Small vessel or perforating vessel lacunar disease	137/ 763 (18.0)	536/2471 (21.7)	
Cardio-emboli	181/ 763 (23.7)	460/2471 (18.6)	
Other or uncertain aetiology	225/ 763 (29.5)	328/2471 (13.3)	

Data are mean (standard deviation), median (interquartile range), n (%), as stated.
BP: blood pressure; NIHSS: national institutes of health stroke scale; GCS: Glasgow coma score; ECG: electrocardiogram; CT: computerized tomography; MRI: magnetic resonance imaging.

Supplementary Appendix Table S2: Use of alteplase and other management details during the first 7 days of hospital admission in ENCHANTED trial participants in England and Wales compared to the overall ENCHANTED trial

	UK Sites Total (n=770)	Non-UK Sites Total (n=2527)	P value
Thrombolysis treatment			
Body Weight			
Patients with estimated body weight prior to alteplase, n(%)	770/ 770 (100)	2527/2527 (100)	0.95
Estimated measurement prior to alteplase use (kg), mean (SD)	77.4 (17.1)	67.4 (12.6)	<0.0001
Patients with direct measured body weight after alteplase use, n(%)	661/ 770 (85.8)	2309/2527 (91.4)	<0.0001
Direct measured body weight after alteplase use (kg), mean (SD)	76.4 (18.1)	67.2 (12.5)	<0.0001
Alteplase given			
Any given, n(%)	761/ 770 (98.8)	2484/2521 (98.5)	0.54
Bolus dose (mg), mean (SD)	6.9 (1.3)	6.1 (1.8)	<0.0001
Infusion over 60 mins dose (mg), mean (SD)	50.3 (15.1)	44.3 (13.3)	<0.0001
Time from randomisation to treatment (mins), median (Q1 Q3)	2.8 (0.2 - 5.4)	7.1 (3.0 - 13.6)	<0.0001
Time from stroke onset to treatment (mins), median (Q1 Q3)	139.0 (110.0 - 177.0)	180.0 (140.0 - 225.0)	<0.0001
Management			
Cerebral angiogram undertaken, n(%)	22/ 770 (2.9)	149/2518 (5.9)	0.0008
Occluded cerebral vessel identified, n(%)	18/ 22 (81.8)	133/ 148 (89.9)	0.26
Endovascular clot retrieval used, n(%)	16/ 22 (72.7)	108/ 149 (72.5)	0.98

	UK Sites Total (n=770)	Non-UK Sites Total (n=2527)	P value
Any intravenous BP lowering treatment in first 24 hours, n(%)	110/ 768 (14.3)	683/2503 (27.3)	<0.0001
Any intravenous BP lowering treatment in days 2-7, n(%)	54/ 764 (7.1)	558/2470 (22.6)	<0.0001
Systolic BP at 24 hours (mmHg), mean (SD)	136.7 (21.0)	136.7 (19.3)	0.58
Intubation and ventilation, n(%)	12/ 763 (1.6)	158/2471 (6.4)	<0.0001
Fever occurrence, n(%)	115/ 763 (15.1)	504/2470 (20.4)	0.0011
Fever treated, n(%)	85/ 636 (13.4)	433/2228 (19.4)	0.0005
Nasogastric feeding given, n(%)	103/ 763 (13.5)	480/2470 (19.4)	0.0002
Patient mobilized by therapist, n(%)	615/ 763 (80.6)	839/2470 (34.0)	<0.0001
Compression stockings used, n(%)	80/ 763 (10.5)	203/2469 (8.2)	0.053
Subcutaneous heparin used, n(%)	70/ 770 (9.1)	557/2527 (22.0)	<0.0001
Any antithrombotic agent (antiplatelet or heparin) used in first 24 hours, n(%)	148/ 770 (19.2)	424/2512 (16.9)	0.13
Intravenous steroids administered, n(%)	11/ 763 (1.4)	66/2470 (2.7)	0.051
Hemicraniectomy performed, n(%)	./ . (.)	35/2471 (1.4)	0.0009
Any neurosurgery performed, n(%)	41/ 770 (5.3)	73/2527 (2.9)	0.0012
Any stroke unit admission, n(%)	680/ 763 (89.1)	1297/2471 (52.5)	<0.0001
Any intensive care unit admission, n(%)	20/ 762 (2.6)	752/2471 (30.4)	<0.0001
Any rehabilitation given, n(%)	517/ 763 (67.8)	1124/2471 (45.5)	<0.0001
Decision to withdrawal active care, n(%)	21/ 764 (2.7)	64/2471 (2.6)	0.81

Data are mean (standard deviation), median (interquartile range), n (%), as stated.
BP: blood pressure.

Table S3: Selected baseline and management characteristics of ENCHANTED participants treated with standard-dose alteplase compared to eligible and treated patients at ENCHANTED SSNAP sites in England and Wales.

	SSNAP sites participating in ENCHANTED		
	Trial participants treated with standard-dose (n=383)	SSNAP Eligible/ treated patients (n=3,957)	P value
Age, years	72 (14)	70 (14)	0.008
>80	130/383 (33.9)	1143/3957 (28.9)	
Female	155/383 (59.5)	1716/2957 (43.4)	0.038
Non-Asian ethnicity	374/383 (97.7)	3811/3957 (96.3)	0.275
NIHSS score	7.0 (5.0-13.0)	10.0 (6.0-16.0)	
Onset to treatment, mins	137 (107-171)	137 (107-180)	
Medical history			
Hypertension	232/282 (60.6)	2109/3957 (53.3)	0.006
Atrial fibrillation	98/383 (25.6)	679/3957 (17.2)	<0.001
Diabetes	57/383 (14.9)	633/3957 (16.0)	0.57
Antiplatelet therapy	39/98 (39.8)	299/679 (44.0)	0.43
Anticoagulation	5/98 (5.1)	125/679 (18.4)	0.001
Pre-morbid symptoms	119/382 (31.2)	750/3957 (19.0)	<0.001
Management			
Stroke unit	336/378 (88.9)	3926/3957 (99.2)	<0.001
ICU	9/377 (2.4)	95/3957 (2.4)	0.99
Withdrawal care	14/379 (3.7)	80/3957 (2.0)	0.033

Data are presented as n/N (%), mean (SD), median (IQR)
ENCHANTED denotes the Enhanced Control of Hypertension and Thrombolysis Stroke study, ICU intensive care unit, mRS modified Rankin, NIHSS National Institutes of Health Stroke Scale, SSNAP Sentinel Stroke National Audit Programme.

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