SUPPLEMENTAL MATERIAL

Table I: model parameters and range of values for sensitivity analysis

Probabilities in the decision tree				
Model input Probability that/of	Base-case value	Distribution	Distribution parameters	Reference(s) and comments
a suspected stroke patient of the emergency setting has an ischemic stroke	69.7%	Dirichlet	0-1	SSNAP Sentinel Stroke National Audit Programme (1)
a suspected stroke patient of the emergency setting has an hemorrhagic stroke	10.2%	Dirichlet	0-1	
a suspected stroke patient of the emergency setting has a non-stroke	20.1%	Dirichlet	0-1	Watkins (2)
an ischemic patient is imaged (CT or AdvImg) within 4.5 hours after symptom onset	24%	Beta	$\alpha = 24$ $\beta = 76$ *	Multiple sources, see calculation methods in Appendix
an ischemic patient is imaged (CT or AdvImg) beyond 4.5 hours or that the time from symptom onset is unknown	76%	Beta	NA*	
an ischemic patient imaged (CT or AdvImg) beyond 4.5 hours is assessed within 6 hours after symptom onset	3.4%	Beta	$\alpha = 3$ $\beta = 97$ *	Multiple sources, see calculation methods in Appendix
an ischemic patient imaged (CT+CTA or AdvImg) between 4.5 and 6 hours receives MT within 6 hours	8.1%	Dirichlet	0-1	Multiple sources, see calculation methods in Appendix
an ischemic patient fully imaged (CT+CTA) between 4.5 and 6 hours does not receive MT within 6 hours	27.6%	Dirichlet		CCEMT strategy: 30% of the patients imaged between 4.5 and 6 hours and not receiving MT were assumed to have received a CTA
an ischemic patient imaged (CT) between 4.5 and 6 hours receives neither CTA nor MT within 6 hours	64.3%	Dirichlet		
an ischemic patient who received IV-tPA receives MT (following CTA for the CCEMT path) within 6 hours	3.4%	Dirichlet	0-1	Multiple sources, see calculation methods in Appendix.
an ischemic patient who received IV-tPA receives CTA but no MT within 6 hours	29%	Dirichlet		CCEMT strategy: 30% of the patients who received IV-tPA and are not receiving MT were assumed to have received a CTA
an ischemic patient who received IV-tPA receives neither CTA nor MT within 6 hours	67.6%	Dirichlet		
an ischemic patient imaged (CT or AdvImg) within 4.5 hours receives IV-tPA	61%	Dirichlet	0-1	SSNAP Sentinel Stroke National Audit Programme (1) See calculation in Appendix
an ischemic patient imaged (CT or AdvImg) within 4.5 hours receives MT alone (without IV-tPA) (following CTA for the CCEMT path) within 4.5 hours	0.3%	Dirichlet		Multiple sources, see calculation methods in Appendix
an ischemic patient imaged within 4.5 hours receives CTA but no treatment within 4.5 hours (CCEMT strategy)	11.7%	Dirichlet		CCEMT strategy: 30% of the patients who did not receive IV-tPA and are not receiving MT were assumed to have received a CTA
an ischemic patient imaged (CT or AdvImg) within 4.5 hours receives no CTA and no treatment within 4.5 hours (CCEMT strategy)	27%	Dirichlet		
*: given the different sources used and hypothesis made in calculating the base-case value, we considered a conservative sample size of 100 to calculate the α and β				

Health outcomes at 90 days in the decision tree			Range		Comments
mRS 0 after MT beyond 4,5 and up to 6 hours from onset	7.9%	Dirichlet	0-1	Minnerup (3)	Germany, REVASK registry

mRS 1-2 after MT beyond 4,5 and up to 6 hours from onset	33.2%	Dirichlet	0-1		
mRS 3-5 after MT beyond 4,5 and up to 6 hours from onset	33.9%	Dirichlet	0-1		
mRS 6 after MT beyond 4,5 and up to 6 hours from onset	25%	Dirichlet	0-1		
mRS 0 after no IV-tPA nor MT beyond 4,5 and up to 6 hours from onset	18%	Dirichlet	0-1	Hacke (4)	14 European countries Australia and New-Zealand. ECASS II trial. Outcome for the placebo-group patients (against iv-TPA).
mRS 1-2 when no IV-tPA nor MT beyond 4,5 and up to 6 hours from onset	28.3%	Dirichlet	0-1		
mRS 3-5 when no IV-tPA nor MT beyond 4,5 and up to 6 hours from onset	43.5%	Dirichlet	0-1		
mRS 6 when no IV-tPA nor MT beyond 4,5 and up to 6 hours from onset	10.4%	Dirichlet	0-1		
Health outcomes for patients with onset above 6 hours					
TP (AIELMT strategy)					
mRS 0 after LVO and MT alone beyond 6 hours from onset	9.3%	Dirichlet	0-1	Nogueira (5)	DAWN trial, MT arm, 5% of the patients in the arm received IV-tPA
mRS 1-2 after LVO and MT alone beyond 6 hours from onset	39.3%	Dirichlet	0-1		
mRS 3-5 after LVO and MT alone beyond 6 hours from onset	26.3%	Dirichlet	0-1		
mRS 6 after LVO and MT alone beyond 6 hours from onset	25.3%	Dirichlet	0-1		
FN and MT would benefit (respectively AIELMT and CCEMT strategies)					
mRS 0 after LVO and no MT beyond 6 hours from onset	4.3%	Dirichlet	0-1	Nogueira (5)	DAWN trial, control arm, 13% of the patients in the arm received IV-tPA
mRS 1-2 after LVO and no MT beyond 6 hours from onset	9.3%	Dirichlet	0-1		
mRS 3-5 after LVO and no MT beyond 6 hours from onset	50.3%	Dirichlet	0-1		
mRS 6 after LVO and no MT beyond 6 hours from onset	36.3%	Dirichlet	0-1		
TN and MT would not benefit (respectively AIELMT and CCEMT strategies)					
mRS 0 after mild stroke and no MT beyond 6 hours from onset	18.3%	Dirichlet	0-1	Lees (6)	Pooled analysis from 9 randomized trials, patients with mild stroke (NIHSS 5 to 10, mean NIHSS 7.4, control arm against IV-tPA (supplementary material)
mRS 1-2 after mild stroke and no MT beyond 6 hours from onset	42.5%	Dirichlet	0-1		
mRS 3-5 after mild stroke and no MT beyond 6 hours from onset	30.2%	Dirichlet	0-1		
mRS 6 after mild stroke and no MT beyond 6 hours from onset	9%	Dirichlet	0-1		
FP (AIELMT strategy)					
mRS 0 after mild stroke and no MT beyond 6 hours from onset	16.5%	Dirichlet	0-1	Lees (6) and Gascou (7)	Outcomes after correction of TN for procedural complications
mRS 1-2 after mild stroke and no MT beyond 6 hours from onset	40.7%	Dirichlet	0-1		
mRS 3-5 after mild stroke and no MT beyond 6 hours from onset	28.4%	Dirichlet	0-1		
mRS 6 after mild stroke and no MT beyond 6 hours from onset	14.4%	Dirichlet	0-1		
Health outcomes (AIELMT and CCEMT strategies)					
mRS 0 after IV-tPA and MT within 4.5 hours from onset	3%	Dirichlet	0-1	Berkhemer (8)	Netherlands, MR CLEAN trial, IV-tPA and MT arm, iv-TPA until 4.5 hours but MT until 6 hours
mRS 1-2 after IV-tPA and MT within 4.5 hours from onset	30%	Dirichlet	0-1		
mRS 3-5 after IV-tPA and MT within 4.5 hours from onset	46%	Dirichlet	0-1		
mRS 6 after IV-tPA and MT within 4.5 hours from onset	21%	Dirichlet	0-1		
mRS 0 after IV-tPA alone within 4.5 hours from onset	6.25%	Dirichlet	0-1	Berkhemer (8)	Netherlands, MR CLEAN trial, IV-tPA and MT arm
mRS 1-2 after IV-tPA alone within 4.5 hours from onset	29.25%	Dirichlet	0-1		

mRS 3-5 after IV-tPA alone within 4.5 hours from onset	42.25%	Dirichlet	0-1		
mRS 6 after IV-tPA alone within 4.5 hours from onset	22.25%	Dirichlet	0-1		
mRS 0 after MT alone within 4.5 hours from onset	7.9%	Dirichlet	0-1	Minnerup (3)	Germany, REVASK registry
mRS 1-2 after MT alone within 4.5 hours from onset	33.2%	Dirichlet	0-1		
mRS 3-5 after MT alone within 4.5 hours from onset	33.9%	Dirichlet	0-1		
mRS 6 after MT alone within 4.5 hours from onset	25%	Dirichlet	0-1		
mRS 0 after no IV-tPA nor MT within 4.5 hours from onset	17.95%	Dirichlet	0-1	Hacke (4)	14 European countries Australia and New-Zealand. ECASS II trial. Outcome for the placebo-group patients (against IV-tPA).
mRS 1-2 after no IV-tPA nor MT within 4.5 hours from onset	28.3%	Dirichlet	0-1		
mRS 3-5 after no IV-tPA nor MT within 4.5 hours from onset	43.4%	Dirichlet	0-1		
mRS 6 after no IV-tPA nor MT within 4.5 hours from onset	10.35%	Dirichlet	0-1		

TP: true positive; FP: false positive; FN: false negative; TN: true negative; IV-tPA: intravenous tissue-type plasminogen activator

MT: mechanical thrombectomy

Table I continued

Transition probabilities in the Markov model					
		State at end of cycle			
		mRS 0-2	**mRS 3-5**	**recurrent stroke**	**mRS 6**
State at start of cycle	**Year 1 (month 3 to 12)**				
	mRS 0-2	0.955*	0.024*	0.013*	0.008*
	Distribution	Dirichlet (range 0-1)			
	mRS 3-5	0.029*	0.919*	0.013*	0.039*
	Distribution	Dirichlet (range 0-1)			
	Year 2 and onward				
	mRS 0-2	Varied based on mortality risk	0 (assumed)	0.013	UK life table (9) + hazard ratio: 1.29 (10)
	Distribution	Based on mortality risk	NA	Beta ($\alpha = 1.3$; $\beta = 98.7$)	Log-normal for hazard ratio (SE=0.22)

	mRS 3-5	0 (assumed)	Varied based on mortality risk	0.013	UK life table (9) + hazard ratio: 3.33 (10)
	Distribution	NA	Varied based on mortality risk	Beta ($\alpha = 1.3$; $\beta = 98.7$)	Log-normal for hazard ratio (SE=0.75)

*Ganesalingam (11)

Transition probabilities after recurrence
(base-case ranges for the 9 scenarios according to the results of the short-run 90-day decision-tree)

CCEMT strategy		**State after recurrence**		
State before recurrence		**mRS 0-2**	**mRS 3-5**	**mRS 6**
	mRS 0-2	0.45 to 0.52	0.35 to 0.38	0.13 to 0.17
	mRS 3-5	0 **	0.83 to 0.87	0.13 to 0.17***

AIELMT strategy				
State before recurrence		**mRS 0-2**	**mRS 3-5**	**mRS 6**
	mRS 0-2	0.51 to 0.54	0.32 to 0.34	0.12 to 0.16
	mRS 3-5	0 **	0.84 to 0.88	0.12 to 0.16***

Distributions: No independent distribution was defined for these probabilities. Probabilities are varying based on the 3000 PSA results (expected value of probabilities) of the decision tree.

** assumed according to natural evolution of stroke
*** assumed to be equal to the transition from recurrence to death of patients initially in mRS 0-2

Costs and resource use

Item	Base-Case value	Distribution	Range	Source
Costs and resource use in the decision tree				
CT scan	$117 (£88)	Beta Pert	$113-$121 (£85-£91)	(RD20A) in the 2017/2018 National Schedule of Reference Costs (12)
CTA scan	$141 (£106)	Beta Pert	$135-$146 (£102-£110)	(RD21A) in the 2017/2018 National Schedule of Reference Costs (12)
Advanced-Imaging scan	$213 (£160)	Beta Pert	$186-$239 (£140-£180)	Assumed
IV-tPA (acquisition + administration)	$2,318 (£1743)	Beta Pert	$2,088-$2,548 (£1,570-£1,916)	Multiple sources, see calculation methods in Appendix
MT (including stent, material and surgery)	$11,784 (£8860)	Beta Pert	$8,261-$15,320 (£6,212-£11,519)	Ganesalingam (11), clinical expert feedback
Acute first 3-month costs mRS 0-2	 $5,095 (£3,831)	Beta Pert	 $2,100-$8,090 (£1,579-£6,083)	Luengo-Fernandez (13)

mRS 3-5	$29.274 (£22,011)		$22,934-$35,613 (£17,244-£26,777)	
mRS 6	$4.570 (£3,436)		$2,530-$6,611 (£1,902-£4,971)	
Costs and resource use in the Markov model				
3-monthly long-term healthcare costs (day 90 onwards)		Beta Pert		Luengo-Fernandez (13)
mRS 0-2	$818 (£615)		$479-1,158 (£360-£871)	
mRS 3-5	$1738 (£1,307)		$912-2564 (£686-£1,928)	
Cost of recurrent stroke (90 days following stroke recurrence)		No independent distribution was defined. Costs are varying based on the 3000 PSA results (expected value of costs) of the decision tree.		From short-run 90-day decision-tree
In the CCEMT strategy	$9,827 (£7,389) to $10,307 (£7,750)			
In the AIELMT strategy	$10,161 (£7,640) to $12,534 (£9,424)			
Utilities				
Independent mRS 0-1-2	0.71	Beta	0.7-0.72	Wardlaw, analysis of CLOTS (14)
Dependent mRS 3-4-5	0.20	Beta	0.19-0.21	
Dead mRS 6	0	-	-	-
Recurrent stroke (90 days following stroke recurrence)		No independent distribution was defined. Utilities are varying based on the 3000 PSA results (expected value of stroke recurrence) of the decision tree.		From short-run 90-day decision-tree
In the CCEMT strategy	0.28 to 0.31			
In the AIELMT strategy	0.30 to 0.32			

Table II: Hazard ratios for mortality
Table from Slot et al. study (10)**.**

mRS	Lothian (N=2054)
0	1; N=283
1	0.98 (0.63, 1.54); N=404
2	1.74 (1.16, 2.61); N=455
3	2.58 (1.73, 3.87); N=360
4	3.89 (2.48, 6.12); N=122
5	4.98 (3.15, 7.88); N=122
6	0

A weighted average of these values gives 1.29 for mRS012 and 3.33 for mRS345.

Table III: Intermediate outcomes of late MT according to advanced imaging accuracy (as modelled in the AIELMT strategy of the decision tree)

	Truth (late MT will be beneficial)	Truth (late MT will not be beneficial)
Positive test (AdvImg informs that late MT will be beneficial)	**TP rate** (patients with LAO moderate or severe receiving late MT) = prior probability * sensitivity	**FP rate** (patients with LAO mild or small occlusions receiving late MT) = 1 – TP – FN – TN
Negative test (AdvImg informs that late MT will not be beneficial)	**FN rate** (patients with LAO moderate or severe not receiving late MT) = prior probability - TP	**TN rate** (patients with LAO mild or small occlusions not receiving late MT) = (1 – prior probability) * specificity
	Sensitivity = **TP/(TP+FN)**	**Specificity** = **TN/(FP+TN)**

TP: true positive; FP: false positive; FN: false negative; TN: true negative

MT: mechanical thrombectomy

Table IV: Outcomes for FP AIS patients after correction for embolic and hemorrhagic complications after standalone MT (AIELMT strategy)

a) Rates of periprocedural complications and deaths after complications after MT

	Standalone MT	MT combined to IV-tPA	Death after complications	Death after embolic and hemorrhagic complications after standalone MT
Total patients	50	94	-	
Embolic complications	8 (16%)	10 (10.6%)	38.9%	16% * 38.9% = 6.2%
Hemorrhagic complications	9 (18%)	20 (21.3%)	45.5%	45.5% * 18% = 8.2%
				6.22% + 8.19% = 14.4%

b) Outcomes for FP AIS patients after correction for periprocedural complications

	Outcome for TN (no MT)	Outcome for FP (MT) in the AIELMT strategy after correction for complications after MT
mRS 0 after mild stroke and beyond 6 hours from onset	18.3%	16.5%

mRS 1-2 after mild stroke and beyond 6 hours from onset	42.5%	40.7%
mRS 3-5 after mild stroke and beyond 6 hours from onset	30.2%	28.4%
mRS 6 after mild stroke and beyond 6 hours from onset	9%	**14.4%**

Table Va: Inflated 2016/17 resource use costs for administration of IV-tPA from Sandercock et al. (15)

Extra staffing requirements	Comments	PSSRU 2017 definitions	2016/2017 cost per hour	2018 inflated cost per hour	2018 cost
5 min additional nurse time	PSSRU 2011 (staff nurse 24hr ward)	Nurse (Band 5) (Section 14 of PSSRU 2017) Cost per hour of patient contact	£89 (Cost per working hour is £37)	£90.59	£7.55
190 min registrar time	PSSRU 2011 (registrar group)	Registrar (Section 15 of PSSRU 2017). Cost per working hour	£43	£43.77	£138.60
50 min consultant time	PSSRU 2011 (medical consultant costs)	Medical consultant (Section 15 of PSSRU 2017) Cost per working hour	£106	£107.89	£89.91
5 min routine observation by senior nurse in place of more junior nurse	It has been assumed that observations are carried out by a senior nurse, and that each observation takes 5 minutes PSSRU 2011 (ward manager 24hr ward and staff nurse 24hr ward)	Nurse advanced (band 7) (Section 14 of PSSRU 2017) Cost per hour of patient contact	£131 (Cost per working hour is £54)	£133.34	£11.11
12 additional sets of observations at 5 min each	It has been assumed that routine observations take 5 minutes to be carried out PSSRU 2011 (ward manager 24hr ward)	Nurse advanced (band 7) (Section 14 of PSSRU 2017) Cost per hour of patient contact	£131 (Cost per working hour is £54)	£133.34	£133.34
5 hours 1:1 senior nurse care	PSSRU 2011 (ward manager 24hr ward)	Nurse advanced (band 7) (Section 14 of PSSRU 2017) Cost per hour of patient contact	£131 (Cost per working hour is £54)	£133.34	£666.69
10 min overnight junior staff review	PSSRU 2011 (foundation house officer 1)	Foundation doctor (FY1) (Section 15 of PSSRU 2017) Cost per working hour	£26	£26.46	£4.41
				TOTAL	£1052

Table Vb: breakdown of cost of IV-tPA

IV-tPA	£1743
Drug acquisition	£691.20
	900 micrograms required per kg (16);
	75kg/patient; 67.5mg per patient
	£259.20 for 20mg pack + £432 for 50mg pack =>£691.20 per patient
	Lower
	60kg/patient; 54mg per patient
	£172.80 for 10mg pack + £432 for 50mg pack => £604.80
	Upper
	85kg/patient; 76.5mg per patient
	£172.80 for 10mg pack + £259.20 for 20mg pack + £432 for 50mg pack => £864
Administration	
	£1,052
	Lower: £965
	Upper: £1,052
Drug acquisition + administration	
	Average: 691.2 + 1052 = £1,743.2
	Lower: 604.8 + 965 = £1,569.8
	Upper: 864 + 1052 = £1,916

Assuming an average patient weight of 75kg, based on an indication of 900 micrograms per kg (17), the average drug acquisition cost was estimated to be £691.20. Assuming alternative weights of 60kg and 85kg led to required doses of 54mg and 76.5mg, respectively. We then assumed a lower estimate of drug acquisition costs to be £604.80 (assuming between 50mg and 60mg are required per patient), and £864 (assuming between 70mg and 80mg are required per patient).

The administration costs, that were based on those from Sandercock et al. study (2004) (15) and inflated for 2018, amount for £1,051.6. Discussion with a clinical expert regarding general changes in the care of stroke patients over time suggests that the difference in care between patients receiving IV-tPA and those not receiving IV-tPA may not anymore be as important as the estimates that Sandercock suggested for the year 2004. In particular, less administrative (145 minutes) and consultant (20 minutes) time should be assumed for patients receiving IV-tPA compared to 2004. Based on this, we estimated a lower estimate of the costs of administration of patients receiving IV-tPA of £965.

Table VI: distribution of ischemic patients across the mRS scale at three months per prior probability and AdvImg accuracy (results of the model)

	Advanced imaging accuracy	Prior probability	Ischemic patients in mRS 0	Ischemic patients in mRS 1-2	Ischemic patients in mRS 3-4-5	Ischemic patients in mRS 6
CT-CTA and no late MT strategy	NA	10%	15%	36%	35%	13%
	NA	20%	14%	34%	36%	15%
	NA	30%	13%	32%	38%	17%
AdvImg followed by late MT strategy (9 scenarios)	**perfect advanced-imaging test**	10%	16%	39%	33%	12%
		20%	15%	38%	33%	14%
		30%	14%	38%	32%	16%
	sensitivity: 80% specificity: 100%	10%	16%	38%	34%	12%
		20%	15%	38%	34%	14%
		30%	14%	37%	34%	15%
	sensitivity: 100% specificity: 70%	10%	15%	38%	33%	13%
		20%	15%	38%	33%	14%
		30%	14%	38%	33%	15%

NA: not applicable

Table VII: Lifetime costs, LYs and QALYs for the nine investigated scenarios (results of the model)

	pre-test probability	COSTS			LYs			QALYs		
		CCEMT	AIELMT	INCREM.	CCEMT	AIELMT	INCREM.	CCEMT	AIELMT	INCREM.
perfect test	10%	$55.985	$57.245	$1.260	7,186	7,339	0,153	3,732	3,886	0,154
	20%	$55.727	$58.020	$2.293	6,907	7,209	0,302	3,510	3,813	0,303
	30%	$55.474	$58.793	$3.319	6,634	7,081	0,447	3,293	3,741	0,448
se=0,8 sp=1	10%	$55.985	$57.036	$1.051	7,186	7,308	0,122	3,732	3,855	0,123
	20%	$55.727	$57.604	$1.876	6,907	7,148	0,241	3,510	3,752	0,242
	30%	$55.474	$58.169	$2.695	6,634	6,990	0,356	3,293	3,649	0,357
se=1 sp=0,7	10%	$55.985	$60.621	$4.637	7,186	7,226	0,040	3,732	3,826	0,094
	20%	$55.727	$61.014	$5.287	6,907	7,110	0,202	3,510	3,760	0,250
	30%	$55.474	$61.407	$5.932	6,634	6,994	0,360	3,293	3,695	0,402

Table VIII: ICERS at 90 days and lifetime horizon for the nine investigated scenarios (results of the model)

	ICER (cost per LY gained) lifetime			ICER (cost per QALY gained) lifetime		
	se=1 sp=1	se=0,8 sp=1	se=1 sp=0,7	se=1 sp=1	se=0,8 sp=1	se=1 sp=0,7
pre-test proba = 30%	3 months $240.245	3 months $245.411	3 months $805.037	3 months $131.805	3 months $134.640	3 months $322.752
	lifetime $7.424	lifetime $7.565	lifetime $16.465	lifetime $7.410	lifetime $7.557	lifetime $14.765
pre-test proba = 20%	3 months $250.578	3 months $258.328	3 months $1.811.967	3 months $137.474	3 months $141.726	3 monhts $494.846
	lifetime $7.586	lifetime $7.780	lifetime $26.113	lifetime $7.569	lifetime $7.767	lifetime $21.156
pre-test proba = 10%	3 months $281.579	3 months $297.079	3 months -$4.280.241	3 months $154.482	3 months $162.986	3 months $1.258.398
	lifetime $8.221	lifetime $8.586	lifetime $115.077	lifetime $8.199	lifetime $8.566	lifetime $49.515

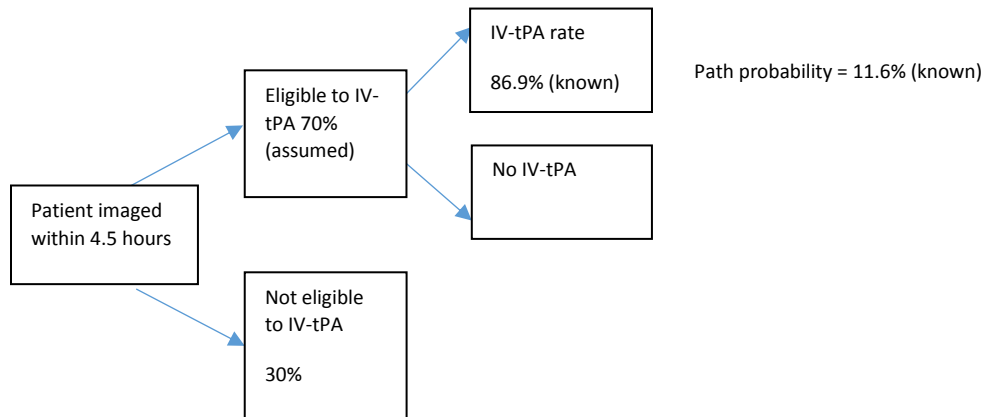**Methods and sources used to calculate the probabilities of the decision tree**

Calculation of the probability that the ischemic patient imaged within 4,5 hours receives IV-tPA:
We assumed that 70% of the ischemic stroke patients managed within 4,5 hours were eligible to IV-tPA (in reference to the fact that 80+ patients should be considered on individual basis).
The percentage of all stroke patients (all stroke types) given thrombolysis (April 2016-March 2017) is 11.6%.
The percentage of eligible patients (according to the Royal College of Physicians guideline minimum threshold) given thrombolysis (April 2016-March 2017) is 86.9%.
Based on these proportions, we calculated the probability that the ischemic patient imaged within 4,5 hours receives IV-tPA.

Based on the above data:
Probability that the ischemic patient imaged within 4,5 hours receives IV-tPA
= (86.9*70/100)/100
= 0.608

This appeared to be consistent with the study by Mc Meekin et al. (18). They reported that:
- the early presenters (within 4 hours) were 15350.
- those who received IV-tPA if eligible were 10130
This lead to a probability to receive IV-tPA of 10130/15350= 65.9%.

Calculation of the probability that the ischemic patient is being imaged within 4.5 hours after symptom onset and calculation of the probability that the ischemic patient is being imaged between 4.5 and 6 hours after symptom onset

1. The distribution of onset to hospital times is known (figure below)
2. The probability to receive a scan within 1 hour once the patient is in the hospital is known (51.3%) based on these, we estimated the distribution from onset to CT times
3. Assumptions:
3a. the distribution of patients with known and unknown onset time is the same among ischemic and hemorrhagic patients.
3b. we found in the literature the proportion of patients per hour range from onset to hospital arrival (for patients with known onset). In each hour range, we assumed that the proportion of patients in the first half hour equals the proportion of patients in the second half hour.
3c. finally, we assumed that the probability for a patient to receive a scan within 1 hour is related to the time from symptom onset to arrival at hospital. Patients that have a shorter time since onset are more likely to receive a scan within 1 hour than those who had their onset a longer time ago. Therefore, we assumed that the probability to receive a scan within 1 hour when the time from onset is below 3.5 hours was 60%.

Values	Reference
Percentage of patients scanned within 1 hour of arrival at hospital: 2016/2017: 51.3%	The Fourth SSNAP Annual Report https://www.strokeaudit.org/Documents/AnnualReport/2016-17-SSNAP-Annual-Report.aspx
32% of patients had an unknown stroke onset 68% had a precise or best estimate of the stroke onset time	https://www.strokeaudit.org/getattachment/AnnualReport/Historical-Guideline/Apr2014Mar2015-AnnualReport.pdf.aspx
Distribution of onset to arrival at hospital time Time from onset to arrival < 3.5 hours: 59% Time from from onset to arrival known and >3.5 hours: 41% Time from onset to arrival between 3.5 and 5 hours: 8.5%	https://www.strokeaudit.org/AnnualReport/Historical.aspx figure 4: Symptom onset time to arrival at hospital, for patients with known or estimated onset time

Calculation:

probability that the ischemic patient is being imaged within 4.5 hours after symptom onset

= probability that the time from onset is known * probability that the time from onset is less than 3.5 hours * probability that the patient receives a scan within 1 hour of hospital admission

= 0.68 * 0.59 *0.6

= 0.24

probability that the ischemic patient is being imaged between 4.5 and 6 hours after symptom onset

= 0.68 * 0.085 * 0.6

= 0.034

Calculation of the conditional probabilities that the ischemic patient receives MT

The calculation of the probabilities to have a trombectomy within and beyond 4.5 hours and with or without IV-tPA (among all thrombectomies) was based on some known proportions and complemented by assumptions.

1. The total number of thrombectomies from April 2016 to March 2017 was 580. The number of thrombectomies with IV t-PA is known (369 per year, 63.6% of all thrombectomies). It was assumed that thrombectomies performed after IV t-PA were administered either right after thrombolysis or in a delay of maximum 6 hours.

2. It was assumed that 75% of the thrombectomies performed without IV t-PA happened between 4.5 and 6 hours from symptom onset. The remaining 25% of the thrombectomies performed without IV t-PA happened within 4.5 hours from onset.

	Total	Probabilities among all thrombectomies	References
Thrombectomies	580	100%	https://www.strokeaudit.org/results/Clinical-audit/National-Results.aspx
Thrombectomies after IV t-PA	369	63.6%	Thrombectomy Report for April 2016 - March 2017
Thrombectomies without IV t-PA	211	36.4%	
Thrombectomies without IV t-PA beyond 4.5 hours (and within 6 hours)	158	27.3%	Assumed
Thrombectomies without IV t-PA within 4.5 hours	53	9.1%	Assumed

	Thrombectomies after IV t-PA	Thrombectomies without IV t-PA	Total thrombectomies with and without IV t-PA
Thrombectomies within 4.5 hours		53 (25%*36.4% = 9.1%)	-
Thrombectomies between 4.5 and 6 hours	369 (63.6%)	158 (75%*36.4% = 27.3%)	-
Total thrombectomies within and after 4.5 hours	369 (63.6%)	211 (36.4%)	580 (100%)

	Probability among all thrombectomies

Thrombectomies without IV t-PA within 4.5 hours	9.1%
Thrombectomies without IV t-PA between 4.5 and 6 hours	27.3%
Thrombectomies after IV t-PA	63.6%

all strokes (England, Wales, Northern Island)	85122
ischemic stroke patients	74216
hemorrhagic stroke patients	10906

3. The 3 conditional probabilities of interest used in the decision tree were back-calculated using the conditional probabilities in the related branches.

3a. Probability that the ischemic patient imaged within 4.5 hours receives MT any time after IV t-PA:
Probability to be imaged within 4.5 hours * Probability to receive IV t-PA * Probability to have a MT after IV t-PA = percentage of ischemic stroke patients receiving MT after IV t-PA
Hence:
Probability to have a MT after IV t-PA
= percentage of ischemic stroke patients receiving MT after IV t-PA / (Probability to be imaged within 4.5 hours * Probability to receive IV t-PA)
= (369/74216)/(0.24*0.60)
= 0.034

3b. Probability that the ischemic patient imaged within 4.5 hours receives MT alone (without IV t-PA):

Probability to be imaged within 4.5 hours * Probability to receive MT within 4.5 hours = percentage of ischemic stroke patients receiving MT within 4.5 hours without IV-tPA
Hence:
Probability to have a MT within 4.5 hours from onset (without IV t-PA)
= percentage of ischemic stroke patients receiving MT within 4.5 hours without IV-tPA /
Probability to be imaged within 4.5 hours
= (53/74216)/0.24
= 0.0029

3c. Probability that the ischemic patient imaged beyond 4.5 hours receives MT between 4.5 and 6 hours from symptom onset (without IV t-PA):

Probability to be imaged beyond 4.5 hours * Probability to receive care between 4.5 and 6 hours * Probability to receive MT between 4.5 and 6 hours = percentage of ischemic stroke patients receiving MT beyond 4.5 hours without IV t-PA
Hence:
Probability to have a MT between 4.5 and 6 hours from onset (without IV t-PA)
= percentage of ischemic stroke patients receiving MT beyond 4.5 hours without IV t-PA/
(Probability to be imaged beyond 4.5 hours* Probability to receive care between 4.5 and 6 hours)
= (158/74216)/(0.76*0.034)
=0.08

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