

## Supplemental Appendix

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**Table S1:** Rural NHS hospitals and their populations

Hospital	Location	Total population	Proportion Remote	Remote Population
St Mary's Hospital	Isle of Wight	138,393	1	138,393
North Devon District Hospital	Barnstaple, North Devon	169,852	0.810	137,580
Furness General Hospital	Barrow, Cumbria	111,207	0.617	68,615
Pilgrim Hospital	Boston, Lincolnshire	190,677	0.268	51,101
Hereford County Hospital	Hereford, Herefordshire	182,303	0.236	43,024
Cumberland Infirmary	Carlisle, Cumbria	178,338	0.213	37,986
Scarborough General Hospital	Scarborough, North Yorkshire	194,103	0.105	20,381
Dorset County Hospital	Dorchester, Dorset	162,271	0.042	6,815
Royal Shrewsbury Hospital	Shrewsbury, Shropshire	199,154	0.024	4,780
* Royal Cornwall Hospital	Truro, Cornwall	420,000	0.01	4,200
		<b>1,946,298</b>		<b>512,875</b>

\*Includes Isle of Scilly

**Data source:** Smyth C, Lorrimer S and Chaplin M. (2016)

**Table S2:** Remote hospitals, nearest neuroscience centre, travel distance and time, air ambulance service

Hospital	Location	Nearest neuroscience centre	Distance (miles)	Ground Emergency Medical Services Travel Time (Mins)	Helicopter Emergency Medical Service
St Mary's Hospital	Isle of Wight	Southampton	17.0	128	Hampshire & Isle of Wight
North Devon District Hospital	Barnstaple, Devon	Plymouth	59.6	113	Devon
Furness General Hospital	Barrow, Cumbria	Preston	134.0	155	North West Air Ambulance
Pilgrim Hospital	Boston, Lincolnshire	Nottingham	60.3	107	Lincolnshire & Nottinghamshire
Hereford County Hospital	Hereford, Herefordshire	Birmingham	57.8	95	Midlands
Cumberland Infirmary	Carlisle, Cumbria	Newcastle-upon-Tyne	59.7	80	Great North Air Ambulance
Scarborough General Hospital	Scarborough, Yorkshire	Hull	45.8	102	Yorkshire
Dorset County Hospital	Dorchester, Dorset	Southampton	57.3	83	Dorset & Somerset
Royal Shrewsbury Hospital	Shrewsbury, Shropshire	Stoke-on-Trent	41.5	71	Midlands
Royal Cornwall Hospital	Truro, Cornwall	Plymouth	54.7	99	Cornwall

**Data Source:** Ambulance travel distances and times calculated from Google Maps. This approach was deemed reasonable by previous research by team members that suggested that ambulances in urban areas were able to exceed general traffic speed, whereas, the opposite effect was seen in suburban and rural road networks (McMeekin *et al.* 2014).

**Table S3:** Estimated number of stroke patients and potential costs and health effects implications for air ambulance in rural England

Hospital	No. of Stroke Patients	No. of Early Presenters	Hypothetical Change in Travel Time by Air (Mins)	Mean Cost Savings (95% CI)	Mean QALYs (95% CI)
St Mary's Hospital	302	38	-90	-£30,458 (-£244,479, £167,373)	4 (0, 11)
North Devon District Hospital	425	53	-60	-£34,974 (-£247,921, £171,028)	4 (0, 12)
Furness General Hospital	219	29	-60	-£20,862 (-£213,713, £156,117)	3 (0, 8)
Pilgrim Hospital	523	66	-90	-£50,244 (-£314,467, £193,994)	6 (0, 17)
Hereford County Hospital	518	66	-60	-£36,682 (-£252,585, £167,275)	5 (0, 13)
Cumberland Infirmary	410	52	-30	-£24,750 (-£193,220, £129,426)	3 (0, 9)
Scarborough General Hospital	250	32	-60	-£22,544 (-£219,912, £157,472)	3 (0, 10)
Dorset County Hospital	407	52	-45	-£25,145 (-£211,643, £150,287)	3 (0, 11)
Royal Shrewsbury Hospital	64	8	-15	-£27,923 (-£151,294, £84,338)	2 (0, 7)
Royal Cornwall Hospital	828	105	-60	-£61,493 (-£319,867, £201,647)	7 (1, 17)

**Data source:** Number of stroke patients per rural hospital from SSNAP data. Estimated number of early presenters eligible for mechanical thrombectomy based on McMeekin *et al.* 2017. The hypothetical change in travel time is based on best possible conditions and a readily available helicopter emergency medical services at rural hospital. This does not take account of a myriad of factors that could affect ability to transport patient such as bad weather, normal working hours and medical consideration such as fear of flying or weight/size. Estimated change in travel time with resulting mean cost savings and QALYs are based on discrete event simulation available from McMeekin *et al.* 2019.

**Table S4:** Model parameters for decision-tree and range of values for sensitivity analysis

Parameter	Point Estimate	Probability Distribution Function	Source
<b>Decision tree</b>			
Eligibility for MT after advanced imaging	0.95	Beta	McMeekin et al. 2017
Received MT after transfer	0.95	Beta	McMeekin et al. 2017
Cost of HEMS	£2,900	Gamma	Great North Air Ambulance (GNAA)
Cost of GEMS	£252	Gamma	NHS Reference Costs 2017-18 (Code: ASS02)
<b>MT by HEMS:</b>			
mRS 0-2 (IV-tPA + MT)	0.57	Conditional beta	Extrapolated Saver et al. 2016
mRS 3-5 (IV-tPA + MT)	0.36	Conditional beta	Extrapolated Saver et al. 2016
mRS 6 (IV-tPA + MT)	0.08	Conditional beta	Extrapolated Saver et al. 2016
<b>MT by GEMS:</b>			
mRS 0-2 (IV-tPA + MT)	0.53	Conditional beta	Extrapolated Saver et al. 2016
mRS 3-5 (IV-tPA + MT)	0.39	Conditional beta	Extrapolated Saver et al. 2016
mRS 6 (IV-tPA + MT)	0.10	Conditional beta	Extrapolated Saver et al. 2016
<b>IV-tPA only:</b>			
mRS 0-2 (IV-tPA only)	0.26	Conditional beta	Ganesalingam et al. 2015
mRS 3-5 (IV-tPA only)	0.55	Conditional beta	Ganesalingam et al. 2015
mRS 6 (IV-tPA only)	0.19	Conditional beta	Ganesalingam et al. 2015

**Table S5:** Model parameters for Markov model and range of values for sensitivity analysis

Parameter	Point Estimate	Probability Distribution Function	Source
<b>Year 1</b>			
From independent (mRS 0-2) to:			
mRS 0-2	0.955	Conditional beta	Davis et al. 2012
mRS 3-5	0.024	Conditional beta	Davis et al. 2012
Recurrent stroke	0.013	Conditional beta	Davis et al. 2012
Dead	0.008	Conditional beta	Davis et al. 2012
From dependent (mRS 3-5) to:			
mRS 0-2	0.029	Conditional beta	Davis et al. 2012
mRS 3-5	0.919	Conditional beta	Davis et al. 2012
Recurrent stroke	0.013	Conditional beta	Davis et al. 2012
Dead	0.039	Conditional beta	Davis et al. 2012
<b>After Year 1</b>			
From independent (mRS 0-2) to:			
mRS 0-2	0.979	Conditional beta	Davis et al. 2012
mRS 3-5	0	Conditional beta	Davis et al. 2012
Recurrent stroke	0.013	Conditional beta	Davis et al. 2012
Dead	0.008	Conditional beta	Davis et al. 2012
From dependent (mRS 3-5) to:			
mRS 0-2	0	Conditional beta	Davis et al. 2012
mRS 3-5	0.948	Conditional beta	Davis et al. 2012
Recurrent stroke	0.013	Conditional beta	Davis et al. 2012
Dead	0.039	Conditional beta	Davis et al. 2012
<b>Recurrent stroke to:</b>			
(IV-tPA + Throm) mRS 0-2	0.867	Conditional beta	Davis et al. 2012
(IV-tPA + Throm) mRS 3-5	0.104	Conditional beta	Davis et al. 2012
(IV-tPA + Throm) recurrent stroke	0	Conditional beta	Davis et al. 2012
(IV-tPA + Throm) dead	0.029	Conditional beta	Davis et al. 2012
(IV-tPA alone) mRS 0-2	0.834	Conditional beta	Davis et al. 2012
(IV-tPA alone) mRS 3-5	0.137	Conditional beta	Davis et al. 2012
(IV-tPA alone) recurrent stroke	0	Conditional beta	Davis et al. 2012
(IV-tPA alone) dead	0.029	Conditional beta	Davis et al. 2012
<b>Health Utilities</b>			
Independent	0.74	Beta	Sandercock et al. 2002
Dependent	0.38	Beta	Sandercock et al. 2002

Recurrent stroke	0.34	Beta	Sandercock et al. 2002
<b>Costs</b>			
IV-tPA (Drug & 24-hr care)	£2,339.34	Gamma	BNF 2018 & Davis et al. 2012
Thrombectomy (24-hour)	£8,479.27	Gamma	Balami et al. 2018
<b>First 3 months:</b>			
Independent	£7,773.00	Gamma	Ganesalingam et al. 2015
Dependent	£16,632.70	Gamma	Ganesalingam et al. 2015
Fatal	£10,658.07	Gamma	Ganesalingam et al. 2015
<b>Ongoing per 3 months:</b>			
Independent	£748.53	Gamma	Youman et al 2003
Dependent	£2,014.12	Gamma	Youman et al 2003
<b>Recurrent Stroke</b>			
Average NHS stroke patient	£13,935.53	Gamma	Xu et al.2017
<b>Mortality Factor</b>			
Independent	1.16	-	Davis et al. 2012, Ganesalingam et al. 2015
Dependent	5.65	-	Davis et al. 2012, Ganesalingam et al. 2015

**Note:** NHS costs were valued at 2017-2018 prices using a Bank of England inflation calculator.



**Table S6:** Time horizons probabilistic sensitivity analysis for early presenters

Time Horizon	Helicopter Emergency Medical Service		Ground Emergency Medical Services		Incremental Cost (95% CI)	Incremental QALYs gained (95% CI)	Incremental Cost/QALY gained (ICER)	% CE at £20K/QALY	% CE at £30K/QALY
	Mean Cost (SE)	Mean QALYs gained (SE)	Mean Cost (SE)	Mean QALYs gained (SE)					
1-year	£26,765 (£41)	0.64 (0.00)	£24,325 (£41)	0.63 (0.00)	£2,440 (£2,380, £2,500)	0.02 (0.02, 0.02)	£139,306	0.0	0.0
3-year	£35,433 (£53)	1.53 (0.00)	£32,679 (£53)	1.49 (0.00)	£2,743 (£2,680, £2,800)	0.04 (0.04, 0.04)	£65,803	0.1	2.8
5-year	£42,375 (£79)	2.27 (0.01)	£39,374 (£78)	2.21 (0.01)	£3,000 (£2,940, £3,060)	0.06 (0.06, 0.07)	£47,910	1.2	11.1
10-year	£53,580 (£175)	3.51 (0.00)	£50,130 (£170)	3.40 (0.01)	£3,450 (£3,380, £3,520)	0.10 (0.09, 0.11)	£34,066	7.9	34.4
15-year	£58,547 (£256)	4.10 (0.02)	£54,873 (£248)	3.98 (0.02)	£3,674 (£3,590, £3,760)	0.12 (0.11, 0.13)	£29,961	12.2	54.4
20-year	£60,242 (£300)	4.33 (0.03)	£56,484 (£289)	4.20 (0.03)	£3,758 (£3,670, £3,840)	0.13 (0.12, 0.14)	£28,533	14.1	61.3

**Table S7:** Scenario analysis for early presenters

Travel Time (Mins)	30 minutes difference				
<i>HEMS vs GEMS</i>	<i>HEMS (pInd; pDep; pDead)</i>	<i>GEMS (pInd; pDep; pDead)</i>	<i>ICER</i>	<i>% CE at £20k/QALY</i>	<i>% CE at £30k/QALY</i>
330 vs 360	0.55;0.37;0.08	0.53;0.39;0.08	£70,876	5.0	12.8
300 vs 330	0.57;0.36;0.07	0.55;0.37;0.08	£52,939	6.2	15.5
270 vs 300	0.59;0.35;0.06	0.57;0.36;0.07	£52,629	7.1	16.1
210 vs 240	0.62;0.32;0.06	0.61;0.33;0.06	£151,866	6.7	12.4

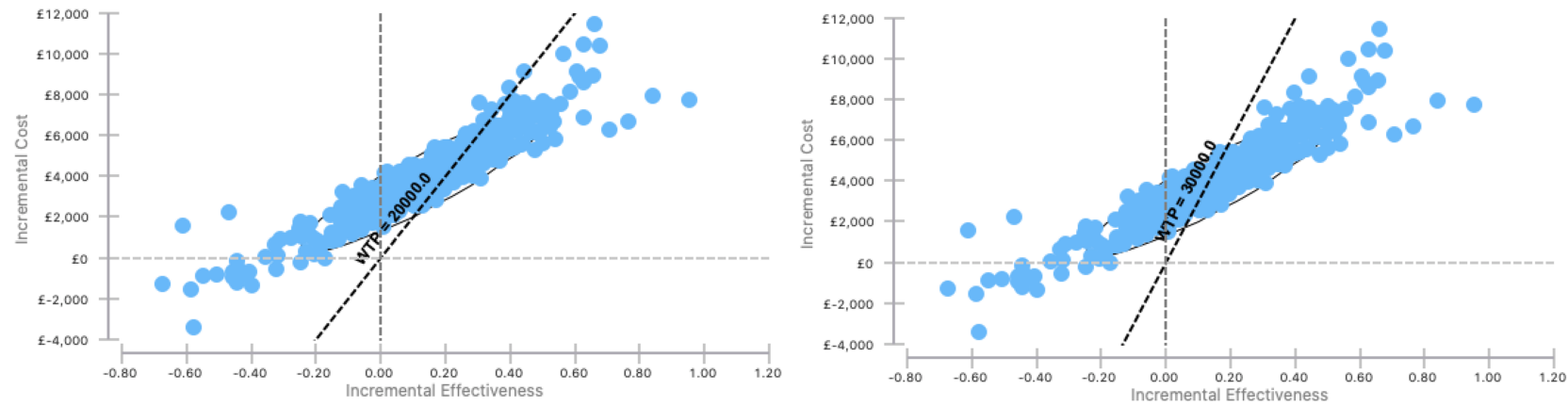
Travel Time (Mins)	15 minutes difference				
<i>HEMS vs GEMS</i>	<i>HEMS (pInd; pDep; pDead)</i>	<i>GEMS (pInd; pDep; pDead)</i>	<i>ICER</i>	<i>% CE at £20k/QALY</i>	<i>% CE at £30k/QALY</i>
345 vs 360	0.54;0.38;0.08	0.53;0.39;0.08	£158,896	2.9	8.4
315 vs 330	0.56;0.37;0.07	0.55;0.37;0.08	£85,862	4.2	10.4
285 vs 300	0.58;0.35;0.07	0.57;0.36;0.07	£155,374	4.8	10.8
225 vs 240	0.62;0.33;0.05	0.61;0.33;0.06	£83,744	6.7	14.0

**Table S8a:** Scenario analysis for late presenters based on DAWN trial eligibility

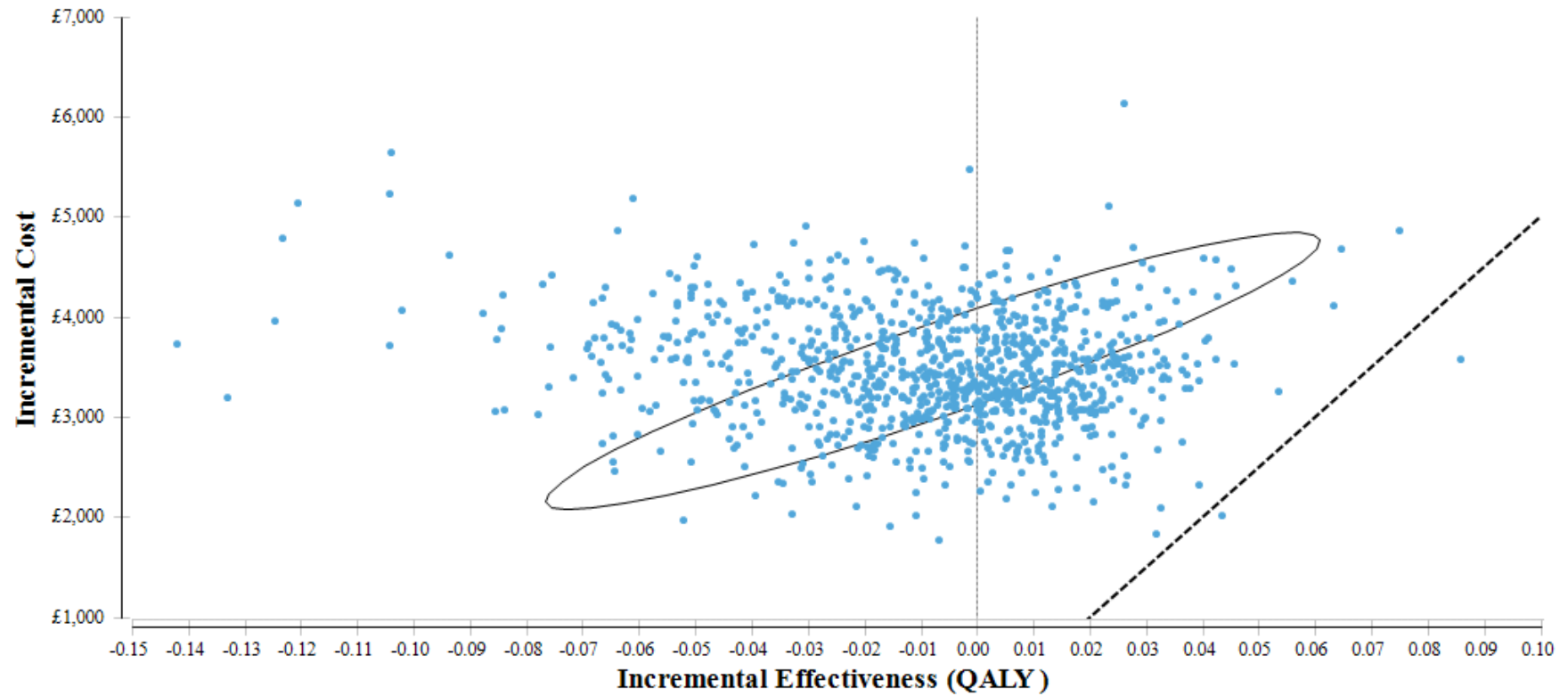
	HEMS		GEMS		Incremental Cost (95% CI)	Incremental QALYs gained (95% CI)	Incremental Cost /QALY gained (ICER)	Incremental Net Monetary Benefit
	Mean Cost (SE)	Mean QALYs gained (SE)	Mean Cost (SE)	Mean QALYs gained (SE)				
<b>Deterministic Analysis</b>	£54,632 (£6)	3.41 (0.00)	£51,217 (£5)	3.42 (0.00)	£3,416 (£3,411, £3,421)	-0.01 (-0.01, -0.01)	Dominated	-
<b>Probabilistic Analysis</b>	£55,000 (£316)	3.41 (0.03)	£51,536 (£310)	3.42 (0.03)	£3,463 (£3,378, £3,548)	-0.01 (-0.01, -0.01)	Dominated	-

**Table 8b:** Parameters' point estimate for late presenters

Parameter	Point Estimate	Probability Distribution Function	Source
Eligibility for MT after advanced imaging	0.50	Beta	Expert opinion
Received MT after transfer	0.50	Beta	Expert opinion
<b>MT by HEMS:</b>			
mRS 0-2 (IV-tPA + MT)	0.40	Conditional beta	Albers et al. 2018 (DAWN trial)
mRS 3-5 (IV-tPA + MT)	0.46	Conditional beta	Albers et al. 2018 (DAWN trial)
<b>MT by GEMS:</b>			
mRS 0-2 (IV-tPA + MT)	0.38	Conditional beta	Albers et al. 2018 (DAWN trial)
mRS 3-5 (IV-tPA + MT)	0.48	Conditional beta	Albers et al. 2018 (DAWN trial)



**Figure S1:** Monte Carlo simulations of incremental cost per QALY gained from mechanical thrombectomy within a cohort of 1,000 patients using a Willingness-To-Pay (WTP) threshold of A) £ 20,000 per QALY gained and B) £30,000 per QALY gained for early-presenters. Also included is the 95% credible region of the ICER using the confidence ellipse method.



**Figure S2:** Monte Carlo simulations of incremental cost per QALY gained from mechanical thrombectomy within a cohort of 1,000 patients using a Willingness-To-Pay (WTP) threshold of £50,000 per QALY gained for late-presenters. Also included is the 95% credible region of the ICER using the confidence ellipse method.

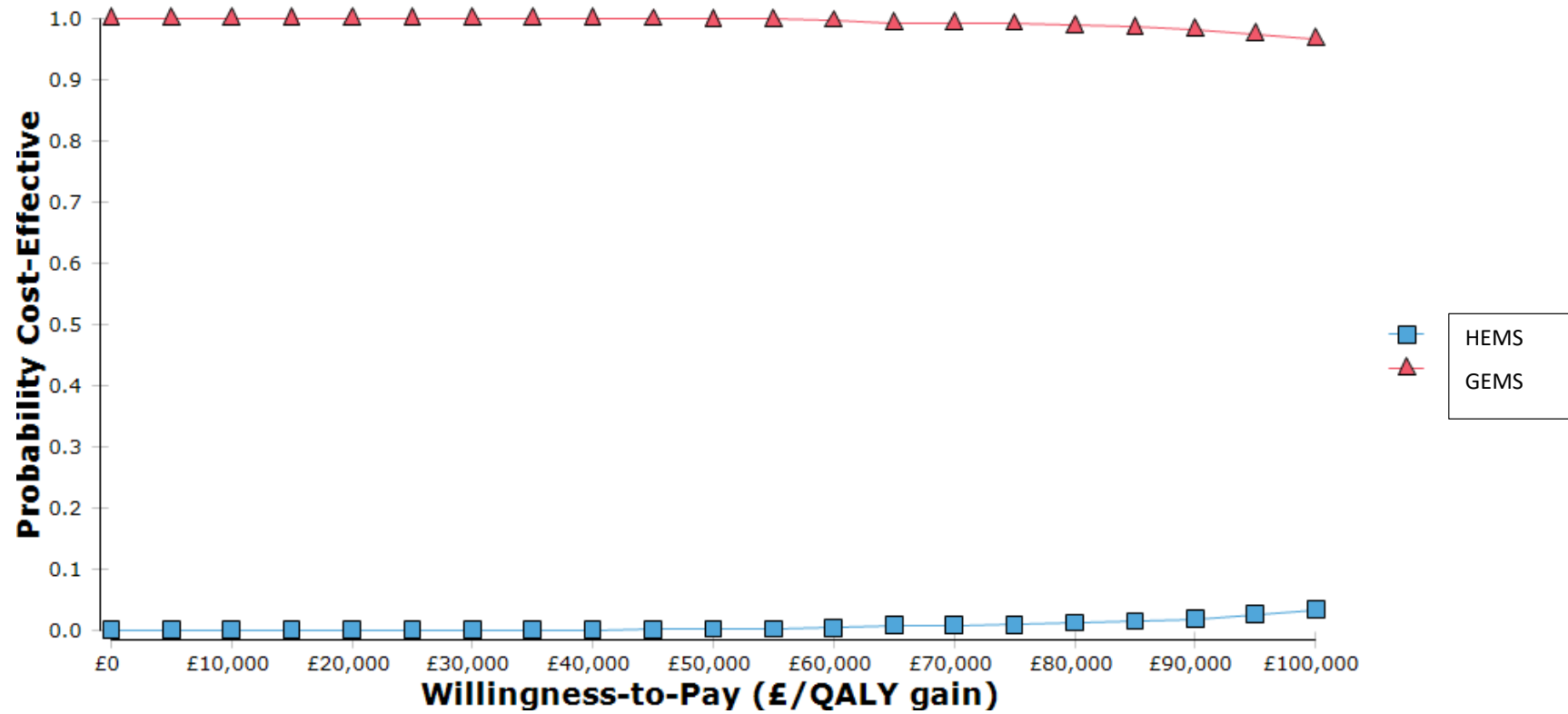


Figure S3: Cost-effectiveness acceptability curve for late presenters by transportation strategy

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