

Supplemental Appendix

SUPPLEMENTARY METHODS

Cardiovascular Events

To accommodate multiple cardiovascular adverse events occurring to the same patient, the following simplifying assumptions were made: (1) If a patient had a non-disabling event and then experienced a second non-disabling event of the same type (i.e. two non-disabling major bleeds), the second mild event was treated the same as a major/disabling event; (2) if a patient had a major/disabling event, the assumption was made that any future events of the same type were also be considered major/disabling; and (3) if a patient experienced two major/disabling events of the same type, it was assumed that the patient would not survive the second event, moving to the dead state.

A best evidence review of published literature was performed to populate the cardiovascular event rates in the model. The search included observational studies published from 1/1/2015 through 3/31/2020 comparing an ablation strategy to any medical therapy or non-ablation strategy that reported outcomes of interest. Studies published most recently, with large, representative, matched cohorts and with longer-term follow-up were prioritized.

Ten randomized clinical trials published between 2003-2019 met the criteria for the systematic literature review. Ten studies reported freedom from recurrence at the 12-month time point,¹⁻¹⁰ three also reported it at 48 months,^{7 11 12} and one study had additional long term follow-up extending out to 144 months.¹¹ A derivative of the exponential decay formula was used to calculate quarterly transition probabilities, incorporating the cumulative probabilities of recurrence at the three time points. The transition probability for recurrence from 48-144 months was used for all time points beyond 48 months.

Comparing catheter ablation and medical therapy groups for AF recurrence using a systematic review and meta-analysis.

A systematic literature review and meta-analysis of randomized clinical trials was conducted to populate the arrhythmia recurrence parameter following standard methodology, as standardized monitoring between groups was not generally available from published real-world/observational sources. The National Library of Medicine's PubMed database, the Cochrane CENTRAL register of controlled trials, EMBASE, and manual reference checks of recent reviews were sources for the electronic search. The search was limited to the English language and covered publications dated between January 2000 to June 2019 that compared catheter ablation to medical therapy (where MT includes rhythm and/or rate control) in AF. The full results of the meta-analysis are shown in the Supplemental Appendix. Recurrence data was extracted for three distinct time-points to inform transitional probabilities for arrhythmia recurrence: 12-months, 48-

months, and 144-months. If event rates were not directly reported for a given interim time point (e.g. event rates were reported for 12-months and 144-months, but not for 48-months), the value was obtained from the published Kaplan-Meier survival curves, using the software Digitzelt (Braunscheig, Germany). A pairwise meta-analysis was performed to estimate the relative risk of arrhythmia recurrence at 12- and 48-months for patients receiving catheter ablation compared to medical therapy. Additionally, single-arm event rate values were estimated for both catheter ablation and medical therapy.

Statistical analysis was performed using SAS Software, Version 9 for Windows (SAS Institute Inc., Cary, NC, USA), as well as R Core Team 2020 (R Foundation for Statistical Computing, Vienna, Austria).

SUPPLEMENTARY TABLES

Table S1. Model Summary Table

Component	Description
Population	Patients treated for AF in the United Kingdom, including those with concomitant HF. Patients not previously treated with AADs were not modelled in the base case analysis.
Intervention	Catheter ablation using contact-force sensing radiofrequency catheter technology.
Comparator	Medical therapy (no ablation) - may include anti-arrhythmic drugs (AADs)
Outcomes	1. Incremental cost-effectiveness ratio (cost per QALY gained) 2. Average total expected costs and QALYs gained
Analysis Type	Cost-utility analysis
Model Type	Markov patient microsimulation health-state transition model
Cycle Length	3 months
Willingness to Pay	£20,000 / £30,000
Simulated Patients	250,000 (20% sample [50,000] for sensitivity analyses)
Perspective	NHS and PSS
Time horizon	Lifetime (min. age 64, max. age of 100) analysis
Data sources	1. Rapid review of published evidence using real-world data 2. Publicly available data (i.e. fee schedules, life tables, etc.) 3. Systematic literature review and meta-analysis of RCTs for AF recurrence

Table S2. Ablation Technology by Study

Author/Year	Ablation technology
AF Recurrence	
12 months	
Blomstrom-Lundqvist 2019	80% irrigated RF (20% cryoballoon)
Forleo 2009	Irrigated RF
Jais 2008	85% irrigated RF (15% non-irrigated RF)
Krittayaphong 2003	Non-irrigated RF
Mont 2014	Irrigated RF
Oral 2006	Non-irrigated RF
Packer 2019	Mixed / not specified
Pappone 2006	49.5% irrigated RF, 50.5% non-irrigated RF
Stabile 2006	75% irrigated RF (25% non-irrigated RF)
Wilber 2010	Irrigated RF
48 months	
Packer 2019	Mixed / not specified
Bertaglia 2017	75% irrigated RF (25% non-irrigated RF)
Pappone 2011	49.5% irrigated RF, 50.5% non-irrigated RF
144 months	
Bertaglia 2017	75% irrigated RF (25% non-irrigated RF)
Healthcare Utilization	
Acute ischemic stroke, Major bleeding events, and Cardiac arrest	
Noseworthy 2019	Mixed / not specified
HF Hospitalizations	
Srivatsa 2018	Mixed / not specified

Table S3. Summary of Clinical Inputs

Parameter	Medical Therapy	Catheter Ablation	Source
Demographics			
Starting Age	64		Noseworthy 2019 ¹³
Maximum Age	100		Assumption
Gender (% Male)	65.5%		Noseworthy 2019 ¹³
Proportion with HF	34.5%		Noseworthy 2019 ¹³
AF Recurrence			
First Recurrence			
12 months			
Odds Ratio (CA vs AAD)		0.15	Meta-analysis of 10 studies ¹⁻¹⁰
Cumulative Probability	69.2%	24.9%	Meta-analysis of 10 studies ¹⁻¹⁰
Quarterly Transition Probability	25.5%	6.9%	Calculation using derivative of the exponential decay formula
48 months			
Odds Ratio (CA vs AAD)		13.0%	
Cumulative Probability	86.1%	44.4%	Meta-analysis of Packer 2019 ⁷ , Bertaglia 2017 ¹¹ , and Pappone 2011 ¹²
Annual rate (years 2-4)	24.1%	9.5%	Calculation using derivative of exponential decay formula, incorporating cumulative prob at 12 and 48 months.
Quarterly Transition Probability	6.4%	2.5%	Calculation using derivative of the exponential decay formula
144 months			
Cumulative Probability	95.7%	72.1%	Bertaglia 2017 ¹¹
Annual rate (years 4+)	12.3%	8.2%	Calculation using derivative of the exponential decay formula
Quarterly Transition Probability	3.6%	2.1%	Calculation using derivative of the exponential decay formula
Subsequent Recurrence			
3 months	50.8%	39.0%	Mark 2019 ¹⁴
12 months	40.2%	21.2%	Mark 2019 ¹⁴
24 months	39.0%	23.1%	Mark 2019 ¹⁴
36 months	38.7%	25.4%	Mark 2019 ¹⁴
48 months	40.9%	25.4%	Mark 2019 ¹⁴

Parameter	Medical Therapy	Catheter Ablation	Source
60 months	35.2%	25.0%	Mark 2019 ¹⁴
60+ months	12.3%	8.2%	Bertaglia 2017 ¹¹
Cardiovascular Events			
Ischemic Stroke	0.9%	0.5%	Noseworthy 2019 ¹³
Proportion disabling	38.5%	38.5%	Han 2017 ¹⁵ . Proportion of stroke patients with Modified Rankin Scale (MRS) 4-5
Major Bleeding	2.0%	2.1%	Noseworthy 2019 ⁹
Proportion disabling	3.4%	3.4%	Simpson 2013 ¹⁶ . Proportion of major bleed patients with Glasgow Outcome Scale (GOS) < 5
Cardiac Arrest	0.3%	0.2%	Noseworthy 2019 ¹⁷
Proportion disabling	16.0%	16.0%	von Vopelius-Feldt 2017 ¹⁸ . Proportion of cardiac arrest patients with Cognitive Performance Capacity (CPC) 1-2
HF Hospitalizations			
3 months (3-month probability)	1.0%	1.3%	Srivatsa 2018 ¹⁹
> 3 months (annual probability)	2.1%	0.8%	Srivatsa 2018 ¹⁹
All-cause mortality			
First seven years	3.6%	2.4%	Noseworthy 2019 ¹³
Subsequent years	Dependent on age and gender		2019 UK national life tables ²⁰ , assuming no differences between CA and MT for AF. Odds ratio of 0.51 (CA vs. MT) applied to AF+HF (Chen 2019)
Stroke Prevention			
OAC Use			Arbelo 2017 ²¹
First 3 months	83.7%	100.0%	
Months 4 – 12	83.7%	83.6%	
Subsequent months	83.7%	81.9%	
% on NOAC (vs. Warfarin)	74.0%		Ho 2020 ²²

Table S4. Summary of Cost Inputs

Parameter	Cost ⁺	Assumption/Source
Common		
Oral anti-coagulation (Quarterly)	£127	Assumes 74% are on NOAC products (Pradaxa, Eliquis, Xarelto, Lixiana), with the remainder on Warfarin (with monitoring) (BNF ²³ , NHS National Tariff ²⁴ , HCHSC 2018 ²⁵)
Long-term follow-up cost (Quarterly)	£9	Annual GP visit (PSSRU 2018 ²⁶)
AF recurrence episode cost	£200	Cardiology consult and 24-hr Holter monitoring (NHS National Tariff ²⁴)
Annual ischemic stroke cost		
Mild/Moderate		
First year	£19,415	Patel 2020 ²⁷
Subsequent years	£8,285	Patel 2020 ²⁷
Severe		
First year	£27,244	Patel 2020 ²⁷
Subsequent years	£13,686	Patel 2020 ²⁷
Major bleeding event cost		
Initial event cost (Quarterly)	£4,254	Average non-elective inpatient spell costs for bleeding events (NHS National Tariff ²⁴)
Ongoing cost for disabling event (Annual)	£40,689	Simpson 2013 ¹⁶
Cardiac arrest cost		
Initial event cost (Quarterly)	£2,103	Average non-elective inpatient spell costs for cardiac arrest (NHS National Tariff ²⁸)
Ongoing cost for disabling event (Annual)	£46,497	von Vopelius-Feldt 2019 ²⁹ . Average annual costs for cardiac arrest patients with CPC 3-4
HF hospitalization cost	£2,849	NICE Guideline, No. 106 ³⁰
Rate control drug cost (Quarterly)	£33	Quarterly price of digoxin (BNF ³¹), annual GP visit, and annual cardiology visit (BNF ³² , NHS National Tariff ²⁴ , PSSRU 2018 ²⁶)

Parameter	Cost ⁺	Assumption/Source
Catheter Ablation		
Pre-operative workup cost	£278	Cardiology consult, INR test, TTE, cardiac CT scan (NHS National Tariff ³³)
Procedural costs (including catheters)	£6,632	Average ordinary, inpatient, elective spell costs for HRGs EY30A, EY30B, EY31A and EY31B (NHS National Tariff ²). List price of Pentaray mapping catheter and Thermocool SmartTouch ablation catheter, provided by manufacturer (Biosense Webster, Inc.)
First year follow-up		
3-month post-op visit	£395	Cardiology consult, TTE, and 24-hr Holter monitoring (NHS National Tariff ²⁴)
12-month post-op visit	£200	Cardiology consult and 24-hr Holter monitoring (NHS National Tariff ²⁴)
Medical Therapy		
Pre-treatment workup costs	£171	Cardiology consult and 12-lead ECG (NHS National Tariff ²⁴) plus serum potassium and liver function tests and thyroid function test (NHS Reference Costs)
Drug cost (Quarterly)	£31	Average price of Amiodarone, Sotalol, Flecainide, Bisoprolol, Diltiazem, and Verapamil (BNF ²³)
Follow-up monitoring cost (Quarterly)	£35	Quarterly GP visit (PSSRU 2018 ²⁶), thyroid and liver function tests (NHS Reference Costs); annual ophthalmic exam and chest x-ray (NHS National Tariff ²⁴)
+ Costs are presented in 2019 GBP. Costs published from previous years were converted to 2019 using the UK CPI (Detailed goods and services breakdown: 2008 to 2019. Table 29, DKC3 - Medical services)		

Table S5. Heart Failure Parameter Values

Parameter	Medical Therapy	Catheter Ablation	Source
AF Recurrence			
First Recurrence			
12 months			
Cumulative Probability	69.2%	8.2%	CA calculated from odds ratio and AAD estimate (Chen 2019)
48 months			
Cumulative Probability	24.1%	4.4%	CA calculated from odds ratio and AAD estimate (Chen 2019)
Cardiovascular Events			
Ischemic Stroke	0.9%	0.6%	CA calculated from odds ratio and AAD estimate (Chen 2019)
All-cause mortality			
First seven years	3.6%	1.9%	CA calculated from odds ratio and AAD estimate (Chen 2019)

Table S6. Summary of Health Utility

Parameter	Estimate	Source / Assumption
NSR State (adjusted for controlled AF)		Sharma 2015 ³⁴
35-44	0.87	
45-54	0.81	
55-64	0.76	
65-74	0.74	
≥ 75	0.69	
AF	-0.05	Steg 2011 ³⁵ , difference in EQ-5D utility score between controlled and uncontrolled AF patients
Adverse Events		
Ischemic Stroke without Disability	0.82	Simpson 2013 ¹⁶ . Utility multiplier for patients with MRS 1-2
Ischemic Stroke with Disability	0.48	Simpson 2013 ¹⁶ . Utility multiplier for patients with MRS 3-5
Major Bleeding without Disability	0.99	Simpson 2013 ¹⁶ . Utility multiplier for patients with GOS 5, weighted average for GI bleed and ICH
Major Bleeding with Disability	0.24	Simpson 2013 ¹⁶ . Utility multiplier for patients with GOS 1-4
Cardiac Arrest without Disability	0.03	von Vopelius-Feldt 2019 ²⁹ . Disutility for patients with CPC 3-5 (disutility calculated as difference between average utility after event and general UK population average)
Cardiac Arrest with Disability	0.31	von Vopelius-Feldt 2019 ²⁹ . Disutility for patients with CPC 1-2 (disutility calculated as difference between average utility after event and general UK population average)
HF Hospitalization	0.19	NICE Guidance, no. 106 ³⁰ , applied for 7 days (average LOS)

Table S7. Base Case Model – Cease Rhythm Control (CRC) State

Outcome	MT	CA	Difference	% Difference
Percent entering CRC state at any point	72%	24%	-48%	-67%
Time-to-CRC state (years)				
Median	3.8	10.0	6.3	167%
Mean	5.1	12.1	7.1	140%

Table S8. Heart Failure Scenario Analysis Results

Strategy	Cost	Δ Cost	QALYs	Δ QALYs	ICER (\$/QALY)
MT	£16,678		7.93		
Catheter Ablation	£24,462	£7,784	9.14	1.21	£6,438

Table S9. Sensitivity Analysis of Model Time Horizon

Strategy	Cost	Δ Cost	QALYs	Δ QALYs	ICER (\$/QALY)
10 years					
MT	£9,178		5.05		
Catheter Ablation	£16,834	£7,656	5.54	0.49	£15,737
15 years					
MT	£12,250		6.38		
Catheter Ablation	£20,217	£7,966	7.12	0.73	£10,868
20 years					
MT	£14,253		7.19		
Catheter Ablation	£22,451	£8,198	8.10	0.91	£9,047
Lifetime (Base Case)					
Medical Therapy	£15,645		7.83		
Catheter Ablation	£24,387	£8,742	8.85	1.01	£8,614

Table S10. Sensitivity Analysis Parameter Ranges

Parameter	Base Case	Low	High
CA Procedure Cost	£6,632	£4,974	£8,290
Starting Age	64	58	70
Annual Mortality Rate (MT)	3.58%	3.22%	3.94%
Annual Mortality Rate (CA)	2.38%	2.14%	2.62%
Acute Ischemic Stroke Rate (MT)	0.94%	0.85%	1.0%
Major Bleeding Event Rate (CA)	2.07%	1.86%	2.3%
Non-disabling Stroke Cost (Years 2+)	£8,285	£6,214	£10,356
AF Disutility	-0.013	-0.014	-0.011
Mortality Odds Ratio – HF	0.51	0.46	0.56
CA Complication Rate	3.0%	0.7%	6.8%
Acute Ischemic Stroke Rate (CA)	0.54%	0.49%	0.6%
AF Trans Prob for 48+ mo (CA)	2.1%	1.9%	2.3%
AF Trans Prob for first 12 mo (CA)	6.9%	6.2%	7.6%
Major Bleeding Event Rate (MT)	2.02%	1.82%	2.2%
Cost of AF Recurrence Episode	£200	£150	£250
3-mo Follow-up Cost (CA)	£395	£296	£494
Cease Rhythm Control FU Costs	£29	£21	£36
Probability of HF	34.5%	31.1%	38.0%
AF Trans Prob for 12-48 mo (CA)	2.5%	2.2%	2.7%
MT Monitoring Cost	£35	£26	£44
CA Workup Cost	£278	£209	£348
Acute ischemic stroke rate (CA) - HF	0.56%	0.50%	0.6%
Acute ischemic stroke odds ratio - HF	0.59	0.53	0.65
Major Bleeding w/o Disability Disutility Multiplier	0.987	0.888	1.000
MT Drug Cost	£31	£23	£39

Table S11. PSA Cost-Effectiveness Results

Strategy	Cost	Δ Cost	QALYs	Δ QALYs	ICER (\$/QALY)	95% Confidence Range
MT	£14,015		7.74			
Catheter Ablation	£22,634	£8,619	8.75	1.00	£8,583	£2,410 to £14,597

Supplemental Figures

Figure S1. Meta-Analysis Results – Arrhythmia Recurrence – Odds Ratio at 12 months

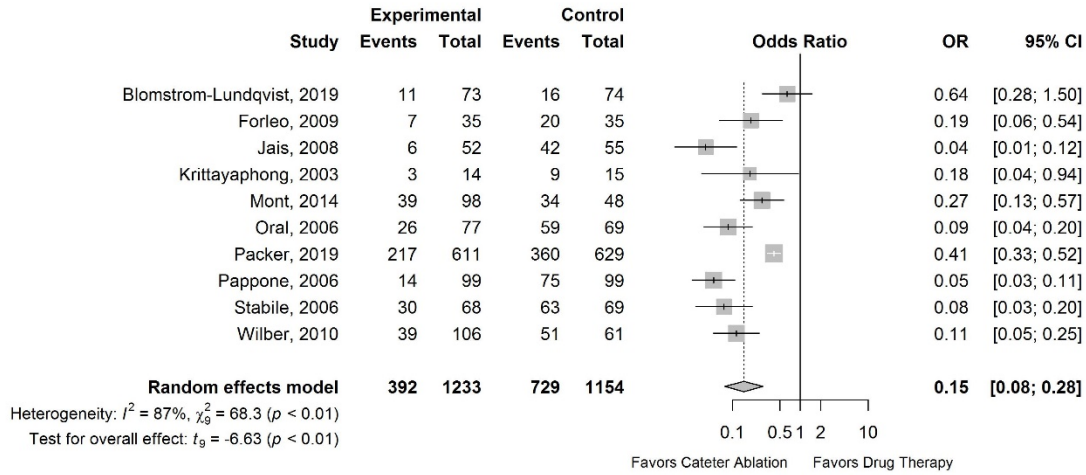


Figure S2. Meta-Analysis Results – Arrhythmia Recurrence – Odds Ratio at 48 months

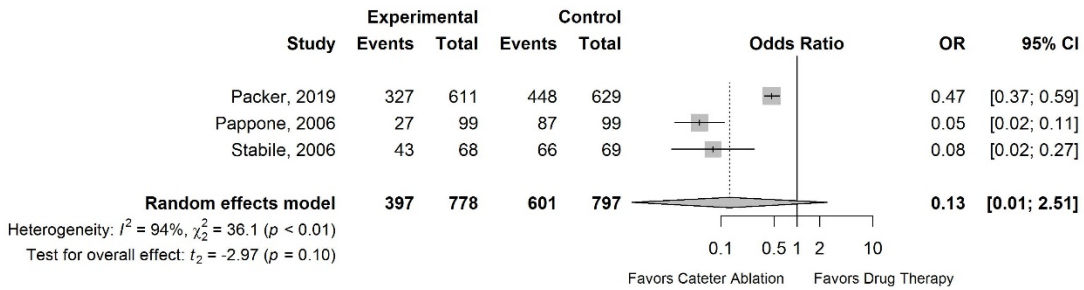


Figure S3. Meta-Analysis Results – Arrhythmia Recurrence – Catheter Ablation at 12 months

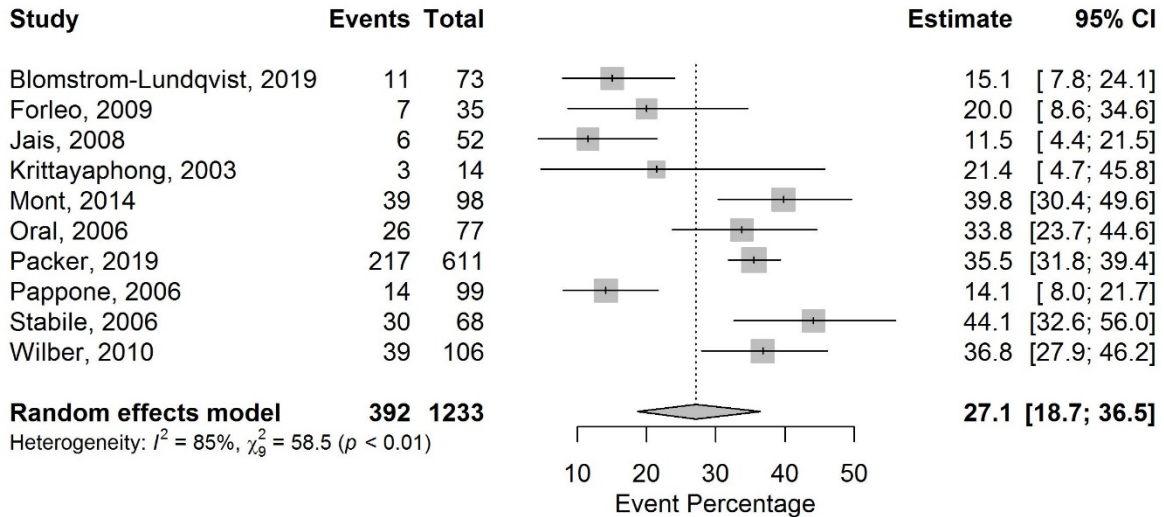


Figure S4. Meta-Analysis Results – Arrhythmia Recurrence – Medical Therapy at 12 months

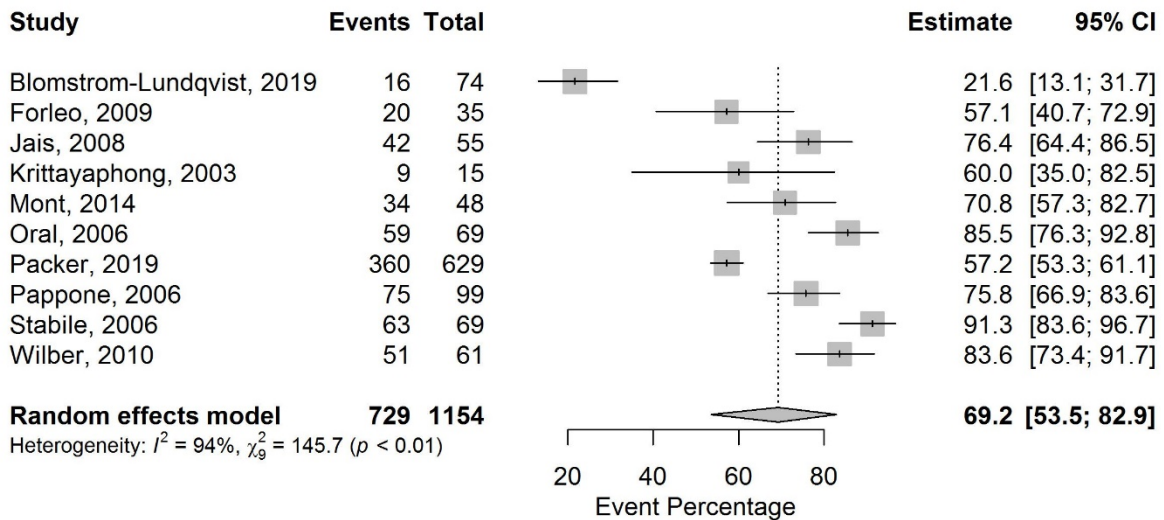


Figure S5. One-Way Sensitivity Analysis Tornado Diagram

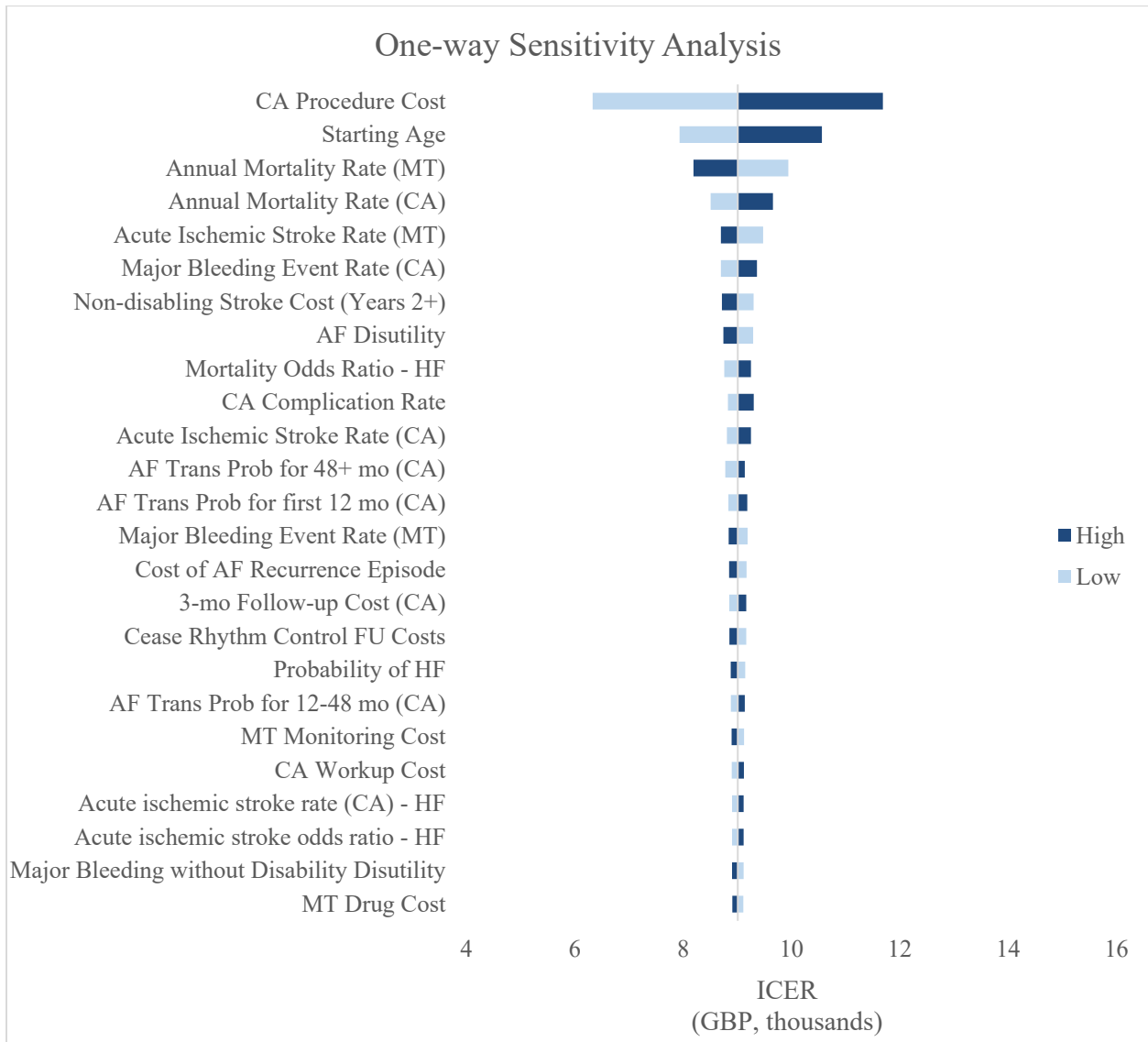
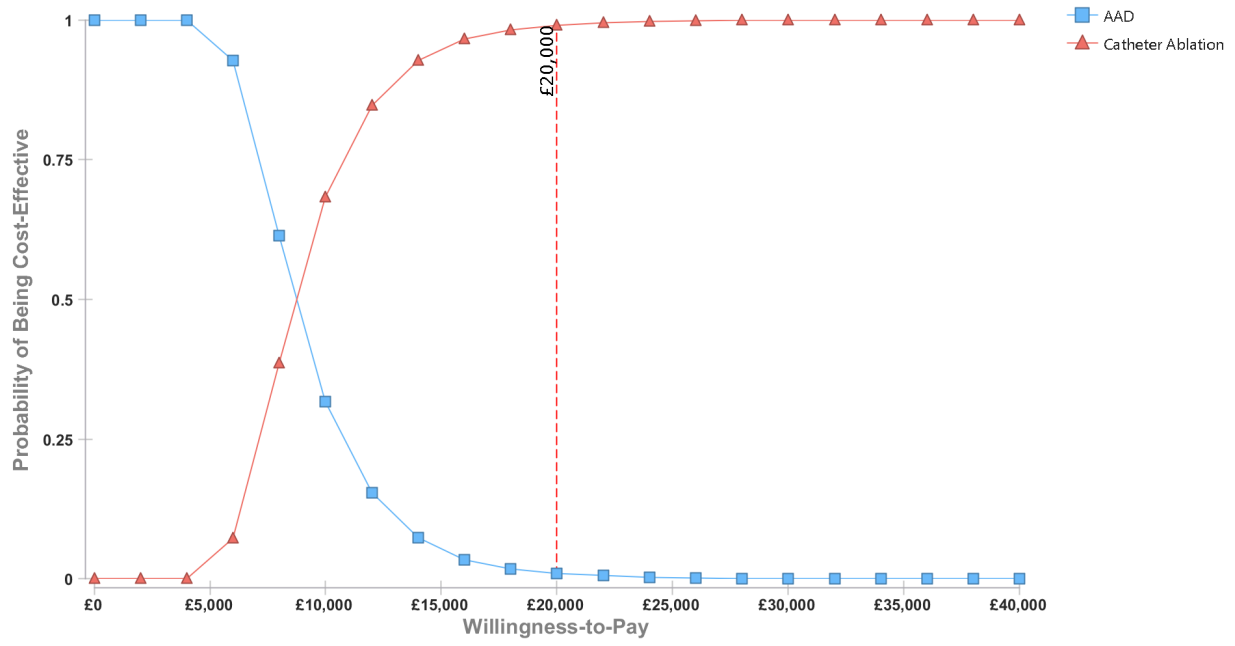


Figure S6. Cost-Effectiveness Acceptability Curve



REFERENCES

1. Blomstrom-Lundqvist C, Gizurarson S, Schwieler J, et al. Effect of catheter ablation vs antiarrhythmic medication on quality of life in patients with atrial fibrillation: the CAPTAF randomized clinical trial. *Jama* 2019;321(11):1059-68. doi: 10.1001/jama.2019.0335 [published Online First: 2019/03/16]
2. Forleo GB, Mantica M, De Luca L, et al. Catheter ablation of atrial fibrillation in patients with diabetes mellitus type 2: results from a randomized study comparing pulmonary vein isolation versus antiarrhythmic drug therapy. *Journal of cardiovascular electrophysiology* 2009;20(1):22-8. doi: 10.1111/j.1540-8167.2008.01275.x [published Online First: 2008/09/09]
3. Jais P, Cauchemez B, Macle L, et al. Catheter ablation versus antiarrhythmic drugs for atrial fibrillation: the A4 study. *Circulation* 2008;118(24):2498-505. doi: 10.1161/circulationaha.108.772582 [published Online First: 2008/11/26]
4. Krittayaphong R, Raungrattanaamporn O, Bhuripanyo K, et al. A randomized clinical trial of the efficacy of radiofrequency catheter ablation and amiodarone in the treatment of symptomatic atrial fibrillation. *Journal of the Medical Association of Thailand = Chotmaihet thangphaet* 2003;86 Suppl 1:S8-16. [published Online First: 2003/07/19]
5. Mont L, Bisbal F, Hernandez-Madrid A, et al. Catheter ablation vs. antiarrhythmic drug treatment of persistent atrial fibrillation: a multicentre, randomized, controlled trial (SARA study). *European heart journal* 2014;35(8):501-7. doi: 10.1093/eurheartj/ehf457 [published Online First: 2013/10/19]
6. Oral H, Pappone C, Chugh A, et al. Circumferential pulmonary-vein ablation for chronic atrial fibrillation. *The New England journal of medicine* 2006;354(9):934-41. doi: 10.1056/NEJMoa050955 [published Online First: 2006/03/03]
7. Packer DL, Mark DB, Robb RA, et al. Effect of catheter ablation vs antiarrhythmic drug therapy on mortality, stroke, bleeding, and cardiac arrest among patients with atrial fibrillation: the CABANA randomized clinical trial. *Jama* 2019;321(13):1261-74. doi: 10.1001/jama.2019.0693 [published Online First: 2019/03/16]
8. Pappone C, Augello G, Sala S, et al. A randomized trial of circumferential pulmonary vein ablation versus antiarrhythmic drug therapy in paroxysmal atrial fibrillation: the APAF Study. *Journal of the American College of Cardiology* 2006;48(11):2340-7. doi: 10.1016/j.jacc.2006.08.037 [published Online First: 2006/12/13]
9. Stabile G, Bertaglia E, Senatore G, et al. Catheter ablation treatment in patients with drug-refractory atrial fibrillation: a prospective, multi-centre, randomized, controlled study (Catheter Ablation For The Cure Of Atrial Fibrillation Study). *European heart journal* 2006;27(2):216-21. doi: 10.1093/eurheartj/ehi583 [published Online First: 2005/10/11]
10. Wilber DJ, Pappone C, Neuzil P, et al. Comparison of antiarrhythmic drug therapy and radiofrequency catheter ablation in patients with paroxysmal atrial fibrillation: a randomized controlled trial. *Jama* 2010;303(4):333-40. doi: 10.1001/jama.2009.2029 [published Online First: 2010/01/28]
11. Bertaglia E, Senatore G, De Michieli L, et al. Twelve-year follow-up of catheter ablation for atrial fibrillation: A prospective, multicenter, randomized study. *Heart rhythm* 2017;14(4):486-92. doi: 10.1016/j.hrthm.2016.12.023 [published Online First: 2016/12/19]
12. Pappone C, Vicedomini G, Augello G, et al. Radiofrequency catheter ablation and antiarrhythmic drug therapy: a prospective, randomized, 4-year follow-up trial: the APAF study. *Circulation Arrhythmia and electrophysiology* 2011;4(6):808-14. doi: 10.1161/circep.111.966408 [published Online First: 2011/09/29]

13. Noseworthy PA, Gersh BJ, Kent DM, et al. Atrial fibrillation ablation in practice: assessing CABANA generalizability. *European heart journal* 2019;40(16):1257-64. doi: 10.1093/eurheartj/ehz085 [published Online First: 2019/03/16]
14. Mark DB, Anstrom KJ, Sheng S, et al. Effect of catheter ablation vs medical therapy on quality of life among patients with atrial fibrillation: the CABANA randomized clinical trial. *Jama* 2019;321(13):1275-85. doi: 10.1001/jama.2019.0692 [published Online First: 2019/03/16]
15. Han TS, Fry CH, Fluck D, et al. Evaluation of anticoagulation status for atrial fibrillation on early ischaemic stroke outcomes: a registry-based, prospective cohort study of acute stroke care in Surrey, UK. *BMJ open* 2017;7(12):e019122. doi: 10.1136/bmjopen-2017-019122 [published Online First: 2017/12/17]
16. Simpson E, Stevenson M, Scope A, et al. Echocardiography in newly diagnosed atrial fibrillation patients: a systematic review and economic evaluation. *Health Technol Assess* 2013;17(36):1-263, v-vi. doi: 10.3310/hta17360 [published Online First: 2013/08/30]
17. Reynolds MR, Zimetbaum P, Josephson ME, et al. Cost-effectiveness of radiofrequency catheter ablation compared with antiarrhythmic drug therapy for paroxysmal atrial fibrillation. *Circulation Arrhythmia and electrophysiology* 2009;2(4):362-9. doi: 10.1161/circep.108.837294 [published Online First: 2009/10/08]
18. von Vopelius-Feldt J, Brandling J, Bengler J. Systematic review of the effectiveness of prehospital critical care following out-of-hospital cardiac arrest. *Resuscitation* 2017;114:40-46. doi: 10.1016/j.resuscitation.2017.02.018 [published Online First: 2017/03/03]
19. Srivatsa UN, Xing G, Amsterdam E, et al. California Study of Ablation for Atrial Fibrillation: Re-hospitalization for Cardiac Events (CAABL-CE). *Journal of atrial fibrillation* 2018;11(1):2036. doi: 10.4022/jafib.2036 [published Online First: 2018/11/21]
20. UK Office for National Statistics. National life tables - life expectancy in the UK. 2019
21. Arbelo E, Brugada J, Blomström-Lundqvist C, et al. Contemporary management of patients undergoing atrial fibrillation ablation: in-hospital and 1-year follow-up findings from the ESC-EHRA atrial fibrillation ablation long-term registry. *European heart journal* 2017;38(17):1303-16. doi: 10.1093/eurheartj/ehw564 [published Online First: 2017/01/21]
22. Ho KH, van Hove M, Leng G. Trends in anticoagulant prescribing: a review of local policies in English primary care. *BMC Health Serv Res* 2020;20(1):279. doi: 10.1186/s12913-020-5058-1 [published Online First: 2020/04/05]
23. Committee JF. British National Formulary 2020 [Available from: <https://bnf.nice.org.uk/> accessed Mar 13 2020.
24. England N. 2019/20 National Tariff Payment System 2020 [Available from: <https://www.england.nhs.uk/pay-syst/national-tariff/2019-20-payment-reform-proposals/> accessed Mar 03 2020.
25. January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society in Collaboration With the Society of Thoracic Surgeons. *Circulation* 2019;140(2):e125-e51. doi: 10.1161/cir.0000000000000665 [published Online First: 2019/01/29]
26. Curtis L, Burns A. Unit Costs of Health and Social Care 2019, Personal Social Services Research Unit, University of Kent, Canterbury. 2019
27. Patel A, King D, Zahidul Q, et al. Current, future and avoidable costs of stroke in the UK. Technical Report. London: Stroke Association 2020 [Available from:

https://www.stroke.org.uk/sites/default/files/economic_impact_of_stroke_report_final_feb_2020_0.pdf.

28. Reynolds MR, Lamotte M, Todd D, et al. Cost-effectiveness of cryoballoon ablation for the management of paroxysmal atrial fibrillation. *Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology* 2014;16(5):652-9. doi: 10.1093/europace/eut380 [published Online First: 2014/01/07]
29. von Vopelius-Feldt J, Powell J, Bengner JR. Cost-effectiveness of advanced life support and prehospital critical care for out-of-hospital cardiac arrest in England: a decision analysis model. *BMJ open* 2019;9(7):e028574. doi: 10.1136/bmjopen-2018-028574 [published Online First: 2019/07/28]
30. National Guideline C. National Institute for Health and Care Excellence: Clinical Guidelines. Chronic Heart Failure in Adults: Diagnosis and Management. London: National Institute for Health and Care Excellence (UK)

Copyright © NICE 2018. 2018.

31. National Institute for Health and Care Excellence: Clinical Guidelines. Atrial fibrillation: management. London: National Institute for Health and Care Excellence (UK)

Copyright © NICE 2020. 2014.

32. Public Health England. Atrial fibrillation prevalence estimates 2015 [updated Apr 15 2020]. Available from: <https://www.gov.uk/government/publications/atrial-fibrillation-prevalence-estimates-for-local-populations> accessed Feb 9 2021.
33. Gao L, Moodie M. Modelling the lifetime cost-effectiveness of catheter ablation for atrial fibrillation with heart failure. *BMJ open* 2019;9(9):e031033. doi: 10.1136/bmjopen-2019-031033 [published Online First: 2019/09/08]
34. Sharma P, Scotland G, Cruickshank M, et al. The clinical effectiveness and cost-effectiveness of point-of-care tests (CoaguChek system, INRatio2 PT/INR monitor and ProTime Microcoagulation system) for the self-monitoring of the coagulation status of people receiving long-term vitamin K antagonist therapy, compared with standard UK practice: systematic review and economic evaluation. *Health Technol Assess* 2015;19(48):1-172. doi: 10.3310/hta19480 [published Online First: 2015/07/04]
35. Steg PG, Alam S, Chiang CE, et al. Symptoms, functional status and quality of life in patients with controlled and uncontrolled atrial fibrillation: data from the RealiseAF cross-sectional international registry. *Heart (British Cardiac Society)* 2012;98(3):195-201. doi: 10.1136/heartjnl-2011-300550 [published Online First: 2011/09/29]