Received: 29 July 2021 | Revised: 21 October 2021 | Accepted: 27 October 2021

DOI: 10.1111/jce.15317

ORIGINAL ARTICLE

WILEY

Cost-effectiveness of catheter ablation versus medical therapy for the treatment of atrial fibrillation in the United Kingdom

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Ryan J. Imhoff is an employee of, and Diana Frame and Peter J. Mallow are consultants of, CTI Clinical Trial and Consulting Services, which is a consultant to Biosense Webster, the study sponsor. Mark M. Gallagher has received research funding from Attune Medical and has acted as a consultant and paid speaker for Boston Scientific and Cook Medical. Lisa W. M. Leung has received research support from Attune Medical. Laura Goldstein, Tom Wei, Maria Valleca, and Hannah Taylor are employees of Johnson & Johnson, the study sponsor. Other author: No disclosure.

Funding information

Biosense Webster, Grant/Award Number: N/A

Abstract

Introduction: Research evidence has shown that catheter ablation is a safe and superior treatment for atrial fibrillation (AF) compared to medical therapy, but real-world practice has been slow to adopt an early interventional approach. This study aims to determine the cost effectiveness of catheter ablation compared to medical therapy from the perspective of the United Kingdom.

Methods: A patient-level Markov health-state transition model was used to conduct a cost-utility analysis. The population included patients previously treated for AF with medical therapy, including those with heart failure (HF), simulated over a lifetime horizon. Data sources included published literature on utilization and cardiovascular event rates in real world patients, a systematic literature review and meta-analysis of randomized controlled trials for AF recurrence, and publicly available government data/reports on costs.

Results: Catheter ablation resulted in a favorable incremental cost-effectiveness ratio (ICER) of £8614 per additional quality adjusted life years (QALY) gained when compared to medical therapy. More patients in the medical therapy group failed rhythm control at any point compared to catheter ablation (72% vs. 24%) and at a faster rate (median time to treatment failure: 3.8 vs. 10 years). Additionally, catheter ablation was estimated to be more cost-effective in patients with AF and HF (ICER = £6438) and remained cost-effective over all tested time horizons (10, 15, and 20 years), with the ICER ranging from £9047–£15 737 per QALY gained.

Conclusion: Catheter ablation is a cost-effective treatment for atrial fibrillation, compared to medical therapy, from the perspective of the UK National Health Service.

KEYWORDS

antiarrhythmic drugs, atrial fibrillation, catheter ablation, cost-effectiveness, economic evaluation

1 | INTRODUCTION

Atrial fibrillation (AF) is an increasingly common medical condition worldwide, currently affecting nearly 1.5 million people in England alone.[1] Across Europe, the prevalence is projected to increase by 70% over the next decade, leading to an additional 340 000 strokes and 4 million hospitalizations.[2] Characterized by an irregular and fast heartbeat, the treatment for symptomatic AF is primarily focused on restoring and maintaining normal sinus rhythm and preventing stroke.[3–5] Medical therapy, such as antiarrhythmic drugs, are frequently used for the treatment of AF; however, randomized trials have revealed recurring AF symptoms for many patients over time.[6] A robust evidence base has shown that for AF patients, catheter ablation is a safe and superior treatment compared to antiarrhythmic drugs, more effectively restoring and maintaining normal sinus rhythm, and preventing future AF recurrence.[3,4,7–10] Ablation can also reduce the occurrence of debilitating and expensive cardiovascular (CV) events such as stroke, while yielding significant increases in quality of life.

Moreover, roughly a third of AF patients also have heart failure (HF). In this patient population, the clinical improvements associated with catheter ablation are particularly strong, with patients experiencing even lower rates of AF recurrence, stroke, and mortality, compared to medical therapy.[11] Despite the well-established clinical advantages and rapid advances in ablation technology in the last decade, there has been a lack of research conducted to evaluate the economic impact of catheter ablation—as economic assessments in the United Kingdom (UK) have become outdated and often do not include real world data.[7,10,12,13] Recently, NICE used randomized controlled trial data in the AF clinical guideline published in April 2021, finding RF point-by-point technology to be more cost-effective over a lifetime than AAD and other ablation strategies in people that have failed one or more AADs.[14]

With the population of AF patients growing and tremendous economic burden placed on the healthcare system by AF patients, the selection of, and investment in, treatment methods will have important implications for future health care spending.

The objective of this study was to assess the cost-effectiveness of catheter ablation compared to medical therapy (MT) for the treatment of AF in the UK using real-world data, from the perspective of the National Health Service (NHS).

2 | METHODS

2.1 | Overview

A health-state transition model was developed to compare the cost-effectiveness of catheter ablation versus medical therapy in adult patients with AF (paroxysmal, persistent, or long-standing persistent) that have previously failed at least one antiarrhythmic drug and were eligible for catheter ablation (CA). The analysis was performed from the perspective of the UK NHS and Prescribed Special Services (PSS). A summary of the model is shown in the Table S1. Data sources used to populate the parameters within this model included a combination of real-world evidence studies and randomized trials. These were derived from: (1) a systematic literature review and meta-analysis of randomized controlled trials for AF recurrence; (2) targeted searches of published literature for utilization, CV event rates, and utility, focusing on real-world AF populations and long-term follow-up; and (3) publicly available data/government reports, such as the NHS National Tariffs, British National Formulary (BNF), and consumer price index (CPI) data.

AF patients with, and without, concomitant HF were included in the analysis, as HF patients represent a considerable portion of the AF population.[15] The model structure and design was the same for both groups of patients; however, for patients with HF, unique estimates for AF recurrence, acute ischemic stroke, and all-cause mortality were applied based on a published systematic review and meta-analysis in an AF and HF population.[11] Values for all other variables were the same as non-HF patients. The medical therapy arm of this model evaluated a rhythm control strategy, and thus the assumption was made that all medical therapy patients were on AADs at index.

An individual patient-level microsimulation approach was taken to estimate the total expected costs, in pound sterling (£), and expected benefits, measured in terms of quality-adjusted life years (QALYs) incurred over the lifetime of a patient. These outcomes were used to determine the incremental cost-effectiveness ratio (ICER), expressed in terms of the added cost required to gain one additional QALY. The ICER was compared to a willingness-to-pay (WTP) threshold of £20 000 per QALY to determine cost-effectiveness for reimbursement decisions; this WTP threshold was chosen as it is frequently used by the National Institute of Clinical Excellence (NICE) for treatment allocation.

The model simulated a hypothetical cohort of 250 000 patients over the remainder of their life, with a maximum age of 100 years old.

The relevant demographic make-up of these patients was derived from published estimates in the literature and are shown in Table 2. Patients were simulated individually through the treatment arms to estimate the expected costs and benefits. The results of all patients were pooled and analyzed to estimate the average results per patient in each treatment arm.

This analysis followed the recommendations and guidelines from the NICE Reference Case. A lifetime horizon was chosen to evaluate the long-term benefits of catheter ablation treatment (maximum age of 100). The model cycle length for health state transitions was three months, with costs and QALYs discounted at an annual rate of 3.5%. Only costs relevant to the NHS and PSS, and clinical events shown to be different across both treatment cohorts, were included in this analysis. All economic simulation modeling was performed and validated in TreeAge Pro Healthcare 2020 (TreeAge Software, Inc.).

3 | MODEL STRUCTURE

The simulated clinical pathway and assumptions were informed by current clinical practice and aligned with the NICE clinical guidelines for the treatment and management of AF.[3,4] A starting age of 64 was chosen for patients entering the model based on real-world database analysis (Table 1). A lifetime analysis was performed to observe potential long-term costs and QALYs accrued. The model accounted for AF recurrence, cost of resource utilization incurred through follow-up visits, and any clinical major adverse events or major adverse CV events, including acute ischemic stroke, major bleeding event, cardiac arrest, and HF hospitalizations), and all-cause mortality.

Upon entering the model, all patients began in the treatment state. Patients incurred expenses related to both the pretreatment work-up (imaging, lab tests, etc.), as well as the treatment itself, either catheter ablation or medical therapy. It was assumed that patients in both treatment groups did not receive a benefit from the therapy whilst in the treatment state and had the AF disutility applied. From the treatment state, patients either moved into the normal sinus rhythm state, experienced a recurrence of their AF, moving back into the AF state, or died. Patients incurred costs related to routine follow-up/maintenance care according to best practice guidelines in the UK.[3,4] Figure 1 depicts the patient flow within the model through this process, where patients continue to cycle between various health states until either death or reaching an age of 100 years.

3.1 | Cardiovascular events

In each health state (except treatment and death), patients were at risk of experiencing one of four possible CV adverse events (acute ischemic stroke, major bleed, cardiac arrest, HF hospitalization). The assumption was made that a patient could only experience one CV adverse-related event per cycle. If one of these events occurred, it led to an increased cost and decreased health utility for that cycle. A difference in the CV event rates between treatment arms was assumed for the first seven years.[15] After that, the average of both groups was applied for the remainder of the model. For acute ischemic stroke, major bleed, and cardiac arrest, the event was categorized as "severe/disabling" or as "mild/not disabling." If the event was not disabling, the patient resumed rhythm control efforts as usual after the cycle ended, but with a disutility applied in future cycles (and in the case of acute ischemic stroke, an ongoing cost as well). If the event was considered severe/disabling, the patient moved to a post-disabling event state corresponding to the event that occurred (i.e., post-disabling acute ischemic stroke) and stay there for the remainder of the model until death. While in the post-disabling CV event states, additional adverse events may occur. A summary of the clinical data used is shown in Table 1. Additional details regarding the handling of multiple/sequencing of events, along with the full data used and sources, can be found in the Appendix.

3.2 | AF recurrence

A major driver of health utility in our model was freedom from versus recurrence of AF. The treatment protocol for AF recurrence (Figure 1) was adapted from Reynolds et al.[13] and reasonably reflected current long-term standard care in both groups. Patients assigned to medical therapy (antiarrhythmic treatment) could have had a maximum of three switches (or received four different types of antiarrhythmic drugs in total) of pharmacological therapy before a patient is deemed to have failed rhythm control strategy. In the ablation treatment pathway, after ablation treatment, a patient may receive one additional procedure, either as the next step or in between periods of antiarrhythmic drug therapy. After failing rhythm control treatment, patients entered the *cease rhythm control efforts* state, where only rate control drugs were administered, and were assumed to have a quality of life similar to someone in AF/uncontrolled AF.

As standardized monitoring for AF recurrence between groups is not generally available from real-world/observational sources. A systematic literature review and meta-analysis of randomized trials was conducted to populate the AF recurrence parameter. Details on the methodology, results of the meta-analysis, and the estimates of recurrence rates over time are shown in Figures S1–S4. A total of 10 randomized clinical trials published between 2003 and 2019 met the criteria with data at the 12-month time point,[17,28–36] three that reported it at 48 months,[34,37,38] and one study had additional long-term follow-up extending out to 144 months.[37] The type of ablation technology used in the studies is detailed in Table S2, the majority of studies reported the use of radiofrequency technology. The estimated probability of a patient in the model experiencing their first episode of recurrence is shown in Figure 2. Transition probabilities within the model were estimated using this freedom from recurrence data.

All ablation patients were assumed to use oral anticoagulation (OAC) therapy for three months postablation, after which it was assumed a portion of patients with a CHADs-VASC score of <2 would be able to stop OAC usage over time. The proportion of patients utilizing OACs are based on a study published in 2017 by Arbelo et al.,

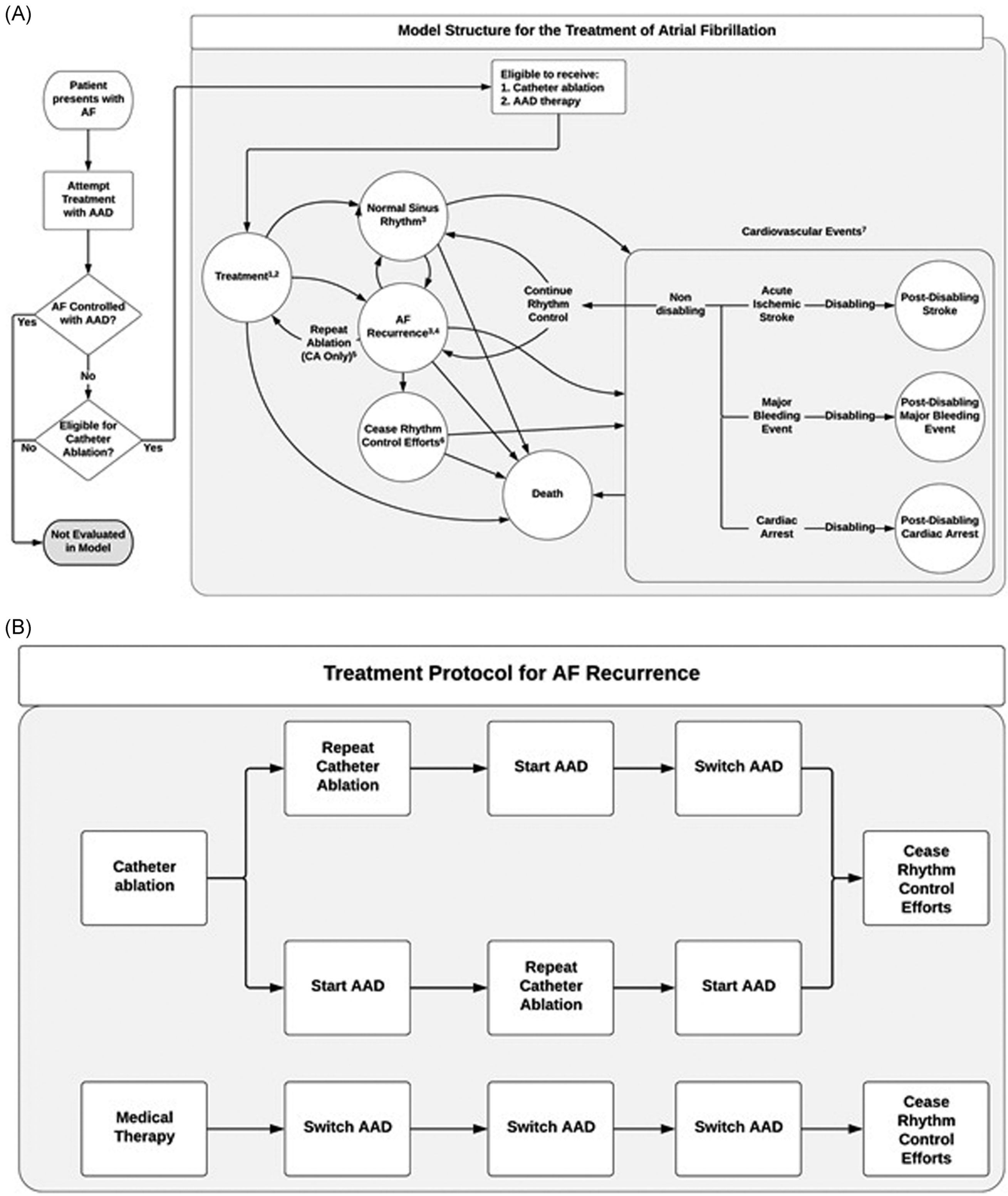

FIGURE 1 (See caption on next page)

evaluating the experience of patients after ablation in a UK population.[22] Non-vitamin K antagonist products (e.g. Pradaxa, Eliquis, Xarelto, and Lixiana) were assumed to account for 74% of patients on OACs, with the remainder on Warfarin (with monitoring).[23]

3.3 | Health utility data

To estimate the QALYs gained for each cohort, health utility data were used to assess the impact on quality of life associated with

AF recurrence, procedural complications, and CV adverse events. The health utility for each state was multiplied by the duration spent in that health state. In the case of some adverse events (acute ischemic stroke, major bleeding, and cardiac arrest), a disutility was applied in all future cycles after the event, in addition to the cycle during which the event occurred. The search conducted for utility data looked at studies published within the last ten years, prioritizing studies cited in past NICE health technology assessments or data published in NICE guidance documents. Studies using the EQ-5D quality of life scale to estimate utility were prioritized, as were those using patients from the UK. Table S6 shows the health state utilities applied.

3.3.1 | Cost data

The cost of ablation was comprised of costs related to the work-up for ablation (pre-operation consultations and tests) as well as procedural costs (including the cost of state-of-the-art radiofrequency ablation and mapping catheters). The cost of re-ablation is assumed to be the same as for the initial ablation.

Utilization and resource use after initial treatment were based on best practices in the UK, informed by a combination of the NICE guidelines and the real-world experience and expert opinion of practicing clinicians. Unit costs for ablation and medical therapy were primarily extracted from the British National Formulary,[24] NHS National Tariffs/Reference Costs,[25] and past NICE health technology assessments. These were supplemented by a best-evidence review of studies published in the UK within the last 5 years, reporting relevant costs from the NHS/PSS perspective (Table 2). Costs are presented in 2019 GBP. Costs published from previous years were converted to 2019 using the UK CPI.[39]

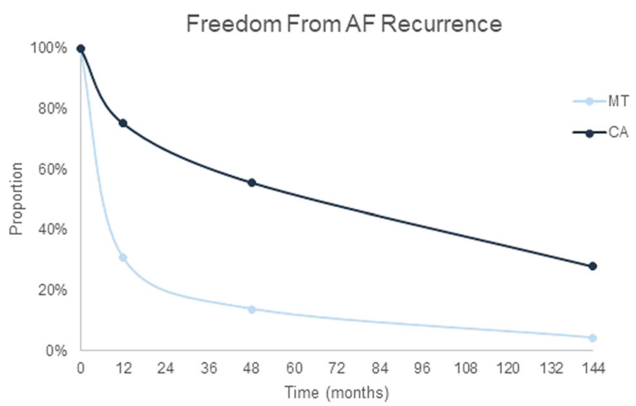

FIGURE 2 Estimated Freedom from AF Recurrence from Meta-Analysis (Model Inputs/Transition Probabilities). A systematic literature review and meta-analysis was performed to estimate the probability of a patient experiencing recurrence at 12-, 48-, and 144-months after beginning treatment. These estimates were used, assuming an exponential decay over time, to develop the model inputs for the chance of a patient having a recurrence over time. The figure above depicts the probabilities over time, interpolated from the estimates at the three time points.
CA: Catheter ablation; MT: Medical therapy

3.3.2 | Heart failure scenario analysis

While the base case analysis included a subset of patients with concomitant HF, a scenario analysis was conducted to specifically look at the cost-effectiveness of AF patients with HF. This scenario utilized the same model structure and framework as the base case analysis. The only changes were the estimated treatment effects for AF recurrence, acute ischemic stroke, and all-cause mortality, which were specific to each group. Their values can be found in Table S5.

3.3.3 | Sensitivity analyses

A one-way deterministic sensitivity analysis was conducted to assess the impact of the model parameters. Base case values were varied by ±10% for clinical/utility variables and by ±25% for costs, allowing for greater variation in cost values to account for difference in pricing/discounting practices (Table S10). Scenario analyses were performed to assess alternative time horizons (10, 15, and 20 years). Finally, a Monte Carlo probabilistic sensitivity analysis was performed to estimate the proportion of simulations for which ablation was cost-effective. Transition probabilities and costs were varied over their reported confidence intervals, to assess their impact on results. In the absence of confidence interval/distribution data, a triangular

FIGURE 1 Model Structure for the Treatment of Atrial Fibrillation & Treatment Protocol for AF Recurrence. The structure and flow of patients through the model are depicted in the diagrams above. Figure 1A shows the general flow of patients through the various health states in the model, while Figure 1B depicts the protocol for patients that experience recurrence in the model. 1) All patients will begin in the "Treatment" state, incurring expenses related to the both the pretreatment work-up and treatment itself. 2) Patients who undergo ablation are assumed to have initial procedural success. 3) In the "Normal Sinus Rhythm" and "AF Recurrence" health states, patients incur costs related to follow-up/maintenance care. 4) All patients in the ablation arm that restore normal sinus rhythm from AF recurrence do so because of 1) starting AADs or 2) receiving a repeat ablation. In the AAD arm, it is assumed that all patients do so because of changing AADs. 5) In the catheter ablation arm, a subset of patients with AF recurrence will receive a single repeat ablation procedure. 6) After attempting 4 treatments, as outlined in the Recurrence Treatment Protocol, patients will cease rhythm control efforts, going on rate control drugs for remainder of model. 7) Patients may experience CV events (ischemic stroke, major bleeding event, or cardiac arrest) during the model time horizon. After a CV event, patients can recover without disability and continue rhythm control efforts moving to either the normal sinus rhythm or AF recurrence states, become disabled and move into a post-AE state, or die.
AAD: Antiarrhythmic drug; AF: Atrial fibrillation; CA: Catheter ablation; MT: Medical therapy

TABLE 3 Base case results

Strategy	Cost	Δ Cost	QALYs	Δ QALYs	ICER ($/QALY)
Medical therapy	£15 645		7.83		
Catheter ablation	£24 387	**£8742**	8.85	**1.01**	**£8614**

TABLE 4 Base case model—CV events

Outcome	Medical therapy	Catheter ablation	Difference	Percent change
Total CV events	0.78	0.74	−0.04	−6%
HF hospitalization	0.28	0.23	−0.06	−20%
Acute ischemic stroke	0.13	0.12	−0.01	−11%
Cardiac arrest	0.04	0.04	−0.01	−14%
Major bleeding event	0.33	0.36	0.03	10%

distribution was assumed with ±10% for clinical/utility variables and ±25% for costs. The analysis consisted of 10,000 different model simulations with 25 000 patients each.

4 | RESULTS

Two-hundred and fifty thousand hypothetical patients were simulated over their lifetime, estimating the costs and benefits associated with each treatment arm. The mean age at treatment was 64 years old, 65.5% were male, and 34.5% had heart failure.

4.1 | Base case

From the perspective of the NHS, catheter ablation was calculated to lead to an additional cost of £8742 and result in an increase of 1.01 QALYs over a patient's lifetime (Table 3). This corresponds to an ICER of £8614 per additional QALY gained.

On average, ablation patients experienced a 20% decrease in HF hospitalizations, 11% decrease in acute ischemic stroke, 14% decrease in cardiac arrest, and 10% increase in major bleeding events, over their lifetime compared to medical therapy patients (Table 4). Driven by the lower rate of AF recurrence, only 24% of ablation patients entered the *Cease Rhythm Control Efforts* state at any point in their lifetime and discontinued rhythm control efforts, compared to 72% in the medical therapy group. The median time-to-cease rhythm control state was 10 years for catheter ablation versus 3.8 years for medical therapy (Table S7).

4.2 | Heart failure scenario analysis

For the cohort consisting solely of HF patients, catheter ablation led to an additional cost of £7784 over a patient's lifetime and resulted in an increase of 1.21 QALYs (Table S8). This represented a slight decrease in cost incurred, and an increase in QALYs gained, compared with the base case. The corresponding ICER was determined to be £6438 per additional QALY gained—well below the assumed WTP threshold and indicative of greater cost-effectiveness compared to the base case analysis.

4.3 | Sensitivity analyses

Cost-effectiveness of catheter ablation was retained across all tested parameter values. The model was most sensitive to ablation procedure cost, starting age, and the annual mortality rate for each cohort. The full results of the one-way sensitivity analysis are shown as a tornado diagram in Figure S5. As expected, shortening the duration of the model time horizon led to increases in the ICER (more upfront cost in the ablation group, with less time to recoup this cost in terms of improved quality of life). Despite this, in addition to being cost-effective over a lifetime horizon, ablation remained cost-effective over all tested time horizons (10, 15, and 20 years), with the ICER ranging from £9047–15 737 per QALY (Table S9).

Catheter ablation was cost-effective compared to medical therapy in 99% of simulations run at the £20 000 WTP threshold (Figure 3). The average ICER across all model runs was determined to be £8,583 per QALY, with a 95% pseudo-confidence range of the ICER (estimated as the average ±1.96*SD*) of £2410–£14 597 (Table S11). Figure S6 shows the cost-effectiveness acceptability curve, displaying the probability of being cost-effective at various WTP thresholds.

5 | DISCUSSION

5.1 | Overview of findings

The current study presents a cost-effectiveness analysis conducted to determine if ablation is more cost-effective than medical therapy for the treatment of AF. The base case analysis considered the cost of state-of-the-art radiofrequency ablation and followed patients over the remainder of their life.

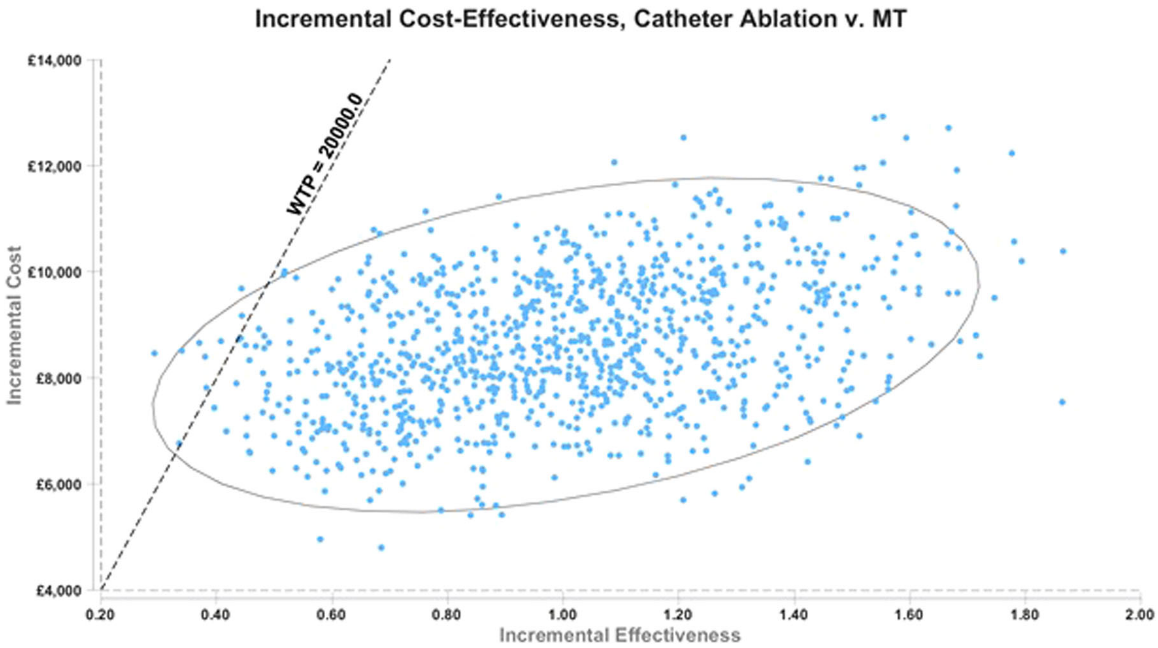

FIGURE 3 Scatterplot of ICER values. To test uncertainty in the model input values, a Monte Carlo probabilistic sensitivity analysis was conducted – running the analysis 10,000 times with different sets of model inputs. The ICER (incremental cost per QALY gained) from each of the 10,000 simulations are shown in the scatter plot above. The willingness-to-pay (WTP) line shows the threshold for which catheter ablation is considered to be cost effective – with each data point that is below the line representing a simulation that was cost-effective. The analysis found ablation to be cost-effective in 99% of the simulations that were run. ICER: Incremental cost-effectiveness ratio; MT: Medical therapy; QALY: Quality-adjusted life year; WTP: Willingness to pay

The findings of this study support catheter ablation as a highly cost-effective strategy for patients suffering from AF, compared to medical therapy. Despite a higher up-front cost for the ablation procedure, a highly significant decrease in CV adverse events and AF recurrence during follow-up led to an ICER of £8614, which is well below the current WTP threshold of £20 000. Not only was ablation highly cost-effective when evaluating patients over their lifetime—catheter ablation also remained cost-effective at time horizons of 10, 15, and 20 years.

With ablation having an improved efficacy in patients with concomitant AF and HF, the scenario analysis performed on this population showed catheter ablation treatment to be more cost-effective than in both the base case analysis and the scenario evaluating non-HF patients.

5.1.1 | AF subtypes and first line treatment

There is public interest and debate over the potential benefits and cost-effectiveness of catheter ablation versus medical therapy, particularly in patients with persistent AF. This study examined patients with all types of AF and did not specifically break out or model patients with paroxysmal versus persistent AF, using population level treatment effects that were applicable to all AF subtypes. This was done for two reasons—first, by evaluating all AF patients, it gives a more comprehensive view of the real-world cost-effectiveness of ablation to inform policy and reimbursement decisions. Second, there is a lack of direct published evidence, particularly in real-world studies, comparing catheter ablation to medical therapy in persistent AF. As more evidence becomes available, it will be important to conduct future health economic research on the sub-types of AF. The same limitations apply to questions surrounding the health and economic benefits associated with first line treatment of AF.

5.1.2 | Comparison with existing literature

In April 2021, NICE published the results of their cost-effectiveness analysis comparing AADs to seven different types of ablation technology including RF point by point (PP) and cryoballoon ablation over a lifetime horizon.[14] In that analysis, RF PP ablation was found to be the most cost-effective option, with an ICER of £9764 per QALY gained. The study by NICE only utilized data published from clinical trials to populate utilization parameters and drive the analysis. In contrast, the current study presented here used real-world data with large sample sizes to estimate utilization. Our findings confirm the those of NICE in a real-world setting, providing support for the conclusion that RF ablation is a more cost-effective treatment option than medical therapy.

A challenge with both our model and the NICE ablation cost-effectiveness analysis is that the clinical evidence includes ablation technology that is no longer considered standard of care. The AF

TABLE 1 Summary of clinical inputs

Parameter	Medical therapy	Catheter ablation	Source/assumption
Demographics			
Starting age	64		[15]
Maximum age	100		Assumption
Gender (% male)	65.5%		[15]
Proportion with HF	34.5%		[15]
Cardiovascular events			
Ischemic stroke	0.9%	0.5%	[15]
Proportion disabling	38.5%	38.5%	Proportion of stroke patients with Modified Rankin Scale 4–5[16]
Major bleeding	2.0%	2.1%	[17]
Proportion disabling	3.4%	3.4%	Proportion of major bleed patients with GOS < 5[18]
Cardiac arrest	0.3%	0.2%	[10]
Proportion disabling	16.0%	16.0%	Proportion of cardiac arrest patients with CPC 1-2[19]
HF hospitalizations			
3 months (3-month probability)	1.0%	1.3%	[20]
>3 months (annual probability)	2.1%	0.8%	[20]
All-cause mortality			
First 7 years	3.6%	2.4%	[15]
Subsequent years	Dependent on age and gender		Assumed no differences between CA and MT for AF[21]
Stroke prevention			
OAC Use			
First 3 months	83.7%	100.0%	[22]
Months 4–12	83.7%	83.6%	[22]
Subsequent months	83.7%	81.9%	[22]
% on NOAC (vs. Warfarin)	74.0%		[23]

Note: See Table S3 for full listing of inputs.

Abbreviations: AF, atrial fibrillation; CA, catheter ablation; CPC, cognitive performance capacity; GOS, Glasgow Outcome Scale; HF, heart failure; NOAC, non-vitamin K oral anti-coagulation; OAC, oral anticoagulation.

recurrence network meta-analysis NICE performed identified 16 studies that included RF PP technology; however, only 4/16 studies included contact force sensing technology. Contact force sensing technology is considered to be a significant improvement upon older technology.[40–44] A recent network meta-analysis (Gupta 2020) found increased freedom from AF in the latest generations of RF technology compared to noncontact force sensing. Our model included the costs of state-of-the-art radiofrequency ablation, but not the clinical outcomes, thus in reality, the cost-effectiveness of ablation may be further improved.

Beyond the NICE analysis, a 2014 study by Reynolds et al.[13] compared the cost-effectiveness of cryoballoon ablation to antiarrhythmic drugs in the UK found an ICER of £21 957, which was above the WTP threshold. The Reynolds study only looked at a time-horizon of 5 years and did not consider events such as HF hospitalizations, which may explain the higher ICER. Additionally, the catheter costs used in this current study are reflective of state-of-the-art radiofrequency catheters, as opposed to older generation cryoballoon catheters. The AF recurrence data in this study are predominantly from radiofrequency ablation studies although it was not possible to determine the technology used in the CABANA study which has the heaviest weighting in the meta-analysis.

A study performed in Australia by Gao and Moodie[27] looked at the cost-effectiveness of catheter ablation versus medical therapy in patients with both AF and HF, yielding an ICER that was above the WTP threshold. However, the study outcome was only evaluated on the impact of reduced mortality. Therefore, healthcare facility utilization and other clinical events were not accounted for, which are important variables with significant impact on cost and quality of life.

Another important distinction between this study and many of the previously published cost-effectiveness studies was the use of real-world evidence.[10,13,27] Clinical trials often have protocols that

TABLE 2 Summary of cost inputs

Parameter	Cost[a]	Assumption/source
Common		
Oral anticoagulation (quarterly)	£127	Assumes 74% are on NOAC products (Pradaxa, Eliquis, Xarelto, Lixiana), with the remainder on Warfarin (with monitoring) (BNF,[24] NHS National Tariff,[25] HCHSC 2018[4])
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[25])
Rate control drug cost (Quarterly)	£33	Quarterly price of digoxin (BNF[3]), annual GP visit, and annual cardiology visit (BNF,[1] NHS National Tariff,[25] PSSRU 2018[26])
Catheter ablation		
Preoperative workup cost	£278	Cardiology consult, INR test, TTE, cardiac CT scan (NHS National Tariff[27])
Procedural costs (including catheters)	£6,632	Average ordinary, inpatient, elective spell costs for HRGs EY30A, EY30B, EY31A and EY31B (NHS National Tariff[28]). 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[25])
12-month post-op visit	£200	Cardiology consult and 24-hr Holter monitoring (NHS National Tariff[25])
Medical therapy		
Pretreatment workup costs	£171	Cardiology consult and 12-lead ECG (NHS National Tariff[25]) 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[24])
Follow-up monitoring cost (quarterly)[a]	£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[25])

Note: See Table S4 for full listing of inputs.

Abbreviations: AF, atrial fibrillation; BNF, British National Formulary; GP, general practice; HF, heart failure; NHS, National Health System; NOAC, non-vitamin K oral anticoagulation; PSSRU, Personal Social Services Research Unit.

[a]Costs are presented in 2019 GBP. Costs published from previous years were converted to 2019 using the UK CPI.[29]

influence utilization, are performed at the top-performing high-volume clinical sites, and generally have relatively small sample sizes. By using large real-world populations to derive many of the estimates used in this model, the results become more generalizable and can capture benefits that may not be seen in smaller, randomized trials. This approach may become more widespread due to NICE announcing more routine use of real-world data as part of their 5-year strategy launched April 2021.

5.1.3 | Implications for healthcare providers and resource allocation

This is the first comprehensive economic evaluation of catheter ablation compared with medical therapy for the treatment of AF in the UK that utilizes real world data. This study now confirms that in addition to clinical effectiveness, ablation is expected to be cost effective in the long-term even with the inclusion of cost data associated with state-of-the-art radiofrequency technology. As shown in other studies, our systematic review and meta-analysis confirmed that ablation is safe with low rates of complications with reduction in CV adverse events. This evidence, when taken together, suggests that healthcare providers should prioritize investment in arrhythmia services where catheter ablation treatment is available. This investment should ideally allow easier access to newly diagnosed AF patients to specialist AF services for early screening of appropriateness of ablation treatment, resulting in improved availability of AF ablation to those in need. Regular review of the clinical and economic evidence supporting AF ablation treatment is required by committees of national frameworks, guidelines and policies to enable improvement in standard of care, particularly as studies with new generation catheters or first line approaches are published.

5.2 | Limitations

There are several limitations that should be considered when evaluating the results and interpretation of this study. While the cost of ablation was based on state-of-the-art catheters, much of the clinical evidence evaluated ablation procedures that were performed before the availability of this technology. Therefore, the clinical benefit and cost-effectiveness may be underestimated in this study.

Clinical events data were derived from a US-based population, rather than a UK population. We selected the Noseworthy et al. study for its large, well-matched, and generalizable patient population, and reporting of endpoints modeled on the CABANA trial. Likewise, AF recurrence data were extracted from randomized trials, not limited to those conducted in the UK. We do not expect that clinical endpoints should vary dramatically by region. Regardless, there may be elements of clinical practice and patient selection in other countries, which are not directly comparable to those of the UK. Additionally, while the medical therapy arm of this analysis assumes all patients were on rhythm control drugs at baseline, some of the studies used to populate the data included a relatively small portion of patients that were on rate-control drugs only. Given there was only a small number of these patients, this is unlikely to have an impact on the study results.

Another important limitation was the modeled life-time horizon. There was no direct clinical evidence evaluating the treatment effect over a patient's lifetime, as the longest follow-up time was 12 years. To mitigate any bias in extrapolation of the data, no difference in CV adverse event rates or mortality were modeled between the two groups after the first 7 years. Also, the treatment protocol for AF recurrence limited the length of time that the treatment effect was extrapolated by directing patients through a pathway of attempting other treatments, such as starting/switching antiarrhythmic drugs or receiving a repeat ablation, and limits the duration of follow-up for many patients by eventually funneling them to the cease rhythm control health state. Also, as a function of the long-term follow-up and treatment protocol, patients in the model that experienced recurrence were are all managed the same regardless of their age when AF recurrence occurs. In clinical practice, it is possible that patients may be managed differently depending on their age and other comorbid conditions.

This model did not account for inevitable crossover from medical therapy to catheter ablation, which is common in clinical practice (i.e., 27.5% of patients crossed over from medical therapy to ablation in the CABANA study),[34] but this was done to ensure a clear comparison of the ablation and medical therapy treatment strategies to assess cost-effectiveness. It is important to note that in the current environment, worsened by the coronavirus pandemic, it is not unusual to find patients deemed suitable for catheter ablation to remain on the waiting list for the procedure over a prolonged period, over three cycles (9 months) duration as per model. In this period, antiarrhythmic drug therapy may be used as a bridging measure. This period is akin to a treatment crossover despite original intentions by both patient and specialist opinion and only adds further to healthcare provider costs in addition to reduced patient quality of life.

Only one repeat ablation was modeled. In clinical practice, it is possible that patients may experience multiple repeat ablations and the cost of these procedures may vary from the index ablation; however, there is a lack of published data on the costs and utilization of multiple ablation attempts.

Finally, this model only considers direct costs to the health provider- NHS and PSS. The model does not capture out-of-pocket expenses for patients, nor does it consider burdens such as missed time from work, reduced productivity, or the burden on caregivers, particularly for those suffering a disabling CV adverse event.

AF subsets and for first line treatment of AF were not analyzed in this model due to data limitation on sub-sets such as longstanding persistent AFs, who are not as widely studied and their treatment needs differ markedly from those with paroxysmal or early to intermediate persistent AF. These groups will become the focus of future study as more data becomes available especially for those receiving first line treatment with either catheter ablation or medical therapy, where three randomized trials have recently become available.[45–47]

6 | CONCLUSIONS

Catheter ablation is a cost-effective treatment compared to medical therapy for patients with AF, driven by substantial improvements in freedom from recurrence and cardiovascular events. This was true both over a lifetime horizon and over time horizons as short as 10 years. Catheter ablation treatment was most cost-effective in the cohort with concomitant heart failure.

ACKNOWLEDGMENTS

This study was funded by Biosense Webster. The authors wish to thank Amanda Coleman and William Thatcher for their efforts in execution of the study, model creation and analysis, and medical writing.

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How to cite this article: Leung LWM, Imhoff RJ, Marshall HJ, et al. Cost-effectiveness of catheter ablation versus medical therapy for the treatment of atrial fibrillation in the United Kingdom. *J Cardiovasc Electrophysiol*. 2021;1-12. doi:10.1111/jce.15317