

RESEARCH ARTICLE



## How does the Cox maze procedure compare? Cost-effectiveness analysis of alternative treatments of atrial fibrillation

Y. Tony Yang<sup>a</sup> and Jesse Ortendahl<sup>b</sup>

<sup>a</sup>Center for Health Policy and Media Engagement, George Washington University School of Nursing, and Department of Health Policy and Management, George Washington University Milken Institute School of Public Health, Washington, DC, USA; <sup>b</sup>Partnership for Health Analytic Research LLC, Beverly Hills, CA, USA

### ABSTRACT

**Objectives:** Data related to the cost effectiveness of surgical interventions and catheter ablation is sparse. This model-based analysis assessed the clinical and economic trade-offs involved in using catheter ablation or the Cox maze procedure in treating patients with atrial fibrillation.

**Methods:** A deterministic model was developed to project 1 year and lifetime health-related outcomes, costs, quality-adjusted life years (QALYs) and cost effectiveness of each treatment in patients with atrial fibrillation. Using previously unpublished Inova Heart and Vascular Institute (IHVI) data for patients undergoing either procedure, 1 year cost and clinical efficacy inputs were estimated. This data was supplemented with published literature and used to estimate costs, utilities, mortality and likelihood of patient improvement. Results were reported as cost-effectiveness ratios in \$/QALY. Sensitivity analyses were conducted to assess the robustness of results.

**Results:** Patients initially treated with a Cox maze procedure were estimated to have higher costs than those treated with catheter ablation, both after 1 year and over the lifetime. However, patients undergoing the Cox maze procedure also had lower rates of 1 year mortality than catheter ablation patients (3.5% vs. 8.5%) and the highest rate of improvement following treatment, resulting in higher QALYs (12.4 vs. 10.2). Compared to catheter ablation, the lifetime incremental cost-effectiveness ratio for the Cox maze surgical procedure was \$12,794 per QALY gained. Without quality adjustment, the ratio was \$11,315. Results were most sensitive to the likelihood of improvement following each intervention and the cost of the initial procedure.

**Conclusions:** At a societal willingness to pay of \$100,000/QALY, Cox maze procedure was found to both increase overall and quality-adjusted survival and constitute an effective use of resources in patients with atrial fibrillation.

### ARTICLE HISTORY

Received 18 June 2018  
Accepted 6 November 2018

### KEYWORDS

Atrial fibrillation; cost effectiveness; Cox maze; cardiology

### Introduction

Atrial fibrillation (AF) is a cardiac rhythm disorder that currently affects more than 2.6 million Americans<sup>1</sup>, making it the most common of all clinical sustained heart arrhythmias<sup>2</sup>. AF was found to be associated with increased risk of stroke, heart failure, decreased quality of life and death<sup>2</sup>. In 2011, more than six million adults in the United States experienced a stroke<sup>3</sup> – it is the fourth most common cause of death in the nation<sup>4</sup> – and approximately 15% of all strokes are attributable to documented AF<sup>5</sup>. The likelihood of developing AF increases with age, as 7.2% of people over 65 have the disorder, a figure that increases to 10.3% for those over 75<sup>6</sup>. Given a rapidly aging population, the number of AF patients in the US is expected to increase to over 12 million by 2050<sup>1</sup>.

Treatment for AF includes various medications and a number of different procedures<sup>7</sup>. Medications include blood thinners to reduce the risk of stroke (e.g. warfarin), rate control medications that slow heart rates and lessen weakening of heart muscles (e.g. beta blockers like metoprolol and atenol, calcium channel blockers like diltizem and verapamil, and digitalis, or digoxin), and rhythm control medications

that help patients maintain normal heart rates (e.g. amiodarone, sotalol, flecainide, propafenone). Primary procedural options include percutaneous catheter ablation<sup>3</sup> and surgical ablation, including the Cox maze procedure<sup>7</sup>.

The debate over the most effective treatment method is by no means simple; rather, trade-offs exist with respect to medical effectiveness, procedural risk and relative cost of treatments. Currently there are no randomized controlled trials to compare the two methods when it comes to clinical endpoints and cost effectiveness. This model-based study aims to use primary data from a hospital database to assist decision makers in better weighing the clinical benefits and costs to ensure that care for AF patients is being conducted safely and appropriately, and that resources are being utilized efficiently across the broader healthcare system.

### Methods

Institutional databases from the Inova Heart and Vascular Institute (IHVI) related to the (minimally invasive) Cox maze procedure and percutaneous catheter ablation were used.

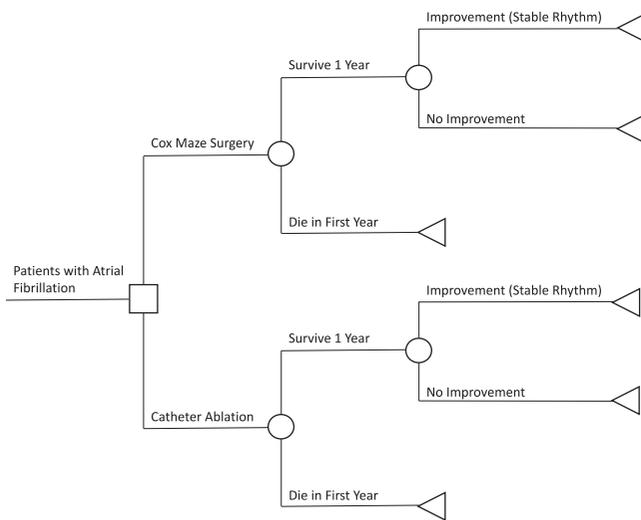


Figure 1. Decision tree depiction of treatment model.

These databases comprise data drawn from IHVI patients who underwent the Cox maze procedure for nonparoxysmal AF (alongside a full year of follow-up data) as well as IHVI patients who were treated with catheter ablation. The registries are unique in their ability to capture specific health events related to each procedure, providing Cox maze and catheter ablation specific information for each patient from the initial procedure through follow-up. In addition, the registry data can be merged with hospital and mortality records to form a complete longitudinal record for each patient<sup>8</sup>.

Given the availability of different treatment choices and the tradeoffs between them, a decision analytic approach was used to identify the relative value of each treatment option. We constructed a Markov model, populated with primary data, and supported by data from literature and other publicly available sources, that projected 1 year and lifetime outcomes, including costs, life years and quality-adjusted life years (QALYs) gained for each treatment option. These projections were used to calculate incremental cost-effectiveness ratios and allowed us to evaluate treatment options in ways that clinical trials may not, and in so doing can provide information on which options are most cost effective. Here, the deterministic cohort model incorporated all relevant characteristics of each AF treatment option (i.e. risk, clinical effectiveness and cost), allowing us to calculate the cost effectiveness of Cox maze compared with catheter ablation.

The model was developed in TreeAge Pro 2015 (TreeAge, Williamstown, MA, USA) to analyze the model strategies (i.e. initial treatment method) in patients with atrial fibrillation. During the first year, patients could alternatively: 1) achieve stable rhythm, 2) fail to improve, or 3) die. The likelihood of following each model pathway differed based on choice of initial treatment and based on registry data. At the conclusion of the first year, the annual costs and probability of each model outcome were calculated. Patients alive at the conclusion of the first year were assigned differing lengths of survival and subsequent costs for time beyond the first year, depending on whether they had achieved rhythm control (Figure 1). In the base case analysis, a lifetime time horizon

Table 1. Patient population and clinical parameters.

	Cox Maze Procedure	Catheter Ablation
Sample size	79	56
Age (mean years)	58.7	63.3
Male (%)	89.9	66.1
First year probability of stable rhythm (%)	93.4	62.8
First year mortality (%)	3.8	8.5
Life expectancy beyond first year (years)		
With stable rhythm	19.53	
No stable rhythm	11.48	

was taken, and costs and clinical benefits (i.e. life-expectancy and QALYs gained) were discounted at 3% annually.

In developing the model, rates of rhythm improvement and all-cause mortality were required for each of the treatment options. To inform these parameters, we used data from the IHVI Cox maze database that tracks and records hospital and long-term outcomes from surgical ablations and the IHVI Percutaneous Coronary Intervention (PCI) Registry that tracks non-surgical treatments for atrial fibrillation. Supplementary data was also obtained as needed from hospital charts and physician offices. Estimates of treatment efficacy were derived from 79 patients undergoing the stand-alone Cox maze procedure for non-paroxysmal AF from 2010 to 2015, and 56 patients undergoing catheter ablation in 2010. Data availability limited the inclusion of those undergoing catheter ablation to the single year. Characteristics of the patient population, as well as clinical parameters used in the model to inform the efficacy of treatment options, are shown in Table 1. To supplement registry data, we extracted survival estimates after the first year from the published literature<sup>9,10</sup>. IRB approval was obtained from the Inova Institutional Review Board and written informed consent was waived. The funding source had no involvement in study design, collection, analysis and interpretation of data, or in the writing of this paper.

Costs were reported in 2016 US dollars, with costs from different sources converted to year 2016 using the medical component of the consumer price index<sup>11</sup>. For each of the treatments, first-year costs were obtained from the registries. Direct costs included clinician salaries, equipment, medications and disposable supplies. Costs were calculated inclusive of all such resources utilized throughout the entire year following treatment, including follow-up visits and treating any resultant complications, including pacemaker implantation. From the registry, we found that 7% of patients had a pacemaker implanted. After the first year, costs were applied differentially depending on whether the patient had achieved rhythm control. These costs were derived from a retrospective analysis of MarketScan data and showed higher costs in individuals with active atrial fibrillation<sup>12</sup>. Costs are set forth in Table 2.

The impact of the interventions on quality of life was incorporated into the model through the use of utility weights. Utility weights range from 0 to 1, with 0 representing death, 1 representing perfect health and values in between reflecting the decreased quality of life for patients with a given condition. Utility weights for patients with ongoing atrial fibrillation as well as values for those whose

**Table 2.** Treatment costs and utility weights.

Parameter	Value <sup>a</sup>
First year treatment costs (per patient)	
Cox maze procedure <sup>b</sup>	\$30,532
Catheter ablation	\$8837
Treatment costs beyond first year (per person)	
With stable rhythm	\$14,214
No stable rhythm	\$24,555
Health-related quality of life (utility weight)	
With stable rhythm	0.823
No stable rhythm	0.774

<sup>a</sup>All costs reported in 2016 \$US.

<sup>b</sup>Includes the costs of prior catheter ablation for 72% of patients.

condition improved were based on estimated EQ-5D data from published literature<sup>13</sup> (Table 2).

In the base case, the strategies were compared at both year one and over a patient's lifetime. The 1 year results reflect the real-world data available from the registry without extrapolation. The lifetime results required additional assumptions, but were conducted to adhere to published guidelines on best practices in cost-effectiveness analyses<sup>14</sup>. Model outputs included costs and quality-adjusted life expectancy for each strategy, which were used to calculate the incremental cost-effectiveness ratio. To assess the impact of uncertainty in model parameters, one-way sensitivity analyses were conducted in which each model input was varied  $\pm 10\%$  of the base case value. Results of one-way sensitivity analyses are depicted in a tornado diagram (Figure 2a). Additionally, a probabilistic sensitivity analysis (PSA) was conducted in which all parameters were varied simultaneously. In PSA, the Cox maze procedure was compared to catheter ablation across 1000 iterations, with results shown in a cost-effectiveness scatterplot (Figure 2b).

## Results

In the base case when considering 1 year results, the Cox maze procedure cost was \$30,532 per patient, compared to \$8837 per catheter ablation patient. The Cox maze procedure also provided greater benefit in terms of reduced mortality and achievement of stable rhythm, with 1 year QALYs of 0.759 compared to 0.741 for catheter ablation. Combining these results, the Cox maze procedure had a cost-effectiveness ratio of \$1,192,023/QALY, compared to the catheter ablation strategy (Table 3).

Over a lifetime, the Cox maze procedure cost \$232,162 per patient, compared to \$208,371 per patient for catheter ablation. Patients undergoing the Cox maze procedure were estimated to live an average of 14.72 years following the procedure, which equated to 12.04 QALYs. The corresponding estimates for catheter ablation were 12.62 years and 10.18 QALYs. Based on these results, the Cox maze procedure had a cost-effectiveness ratio of \$12,794/QALY when compared to catheter ablation. Without quality adjustment, this ratio decreased to \$11,315/QALY (Table 3).

In one-way sensitivity analyses, varying the likelihood of improvement had the largest impact on results. When the probability of improvement for patients undergoing the Cox maze procedure was varied by  $\pm 10\%$ , the ratio for Cox maze

ranged from \$11,993/QALY to \$18,181/QALY. When the probability of improvement for patients undergoing catheter ablation was varied  $\pm 10\%$ , the resulting cost-effectiveness ratio ranged from \$10,451 to \$15,917/QALY. Results were less sensitive to variations in the assumptions regarding costs and survival after the first year, and procedure-related mortality. One-way sensitivity analysis results are shown in the tornado diagram (Figure 2a).

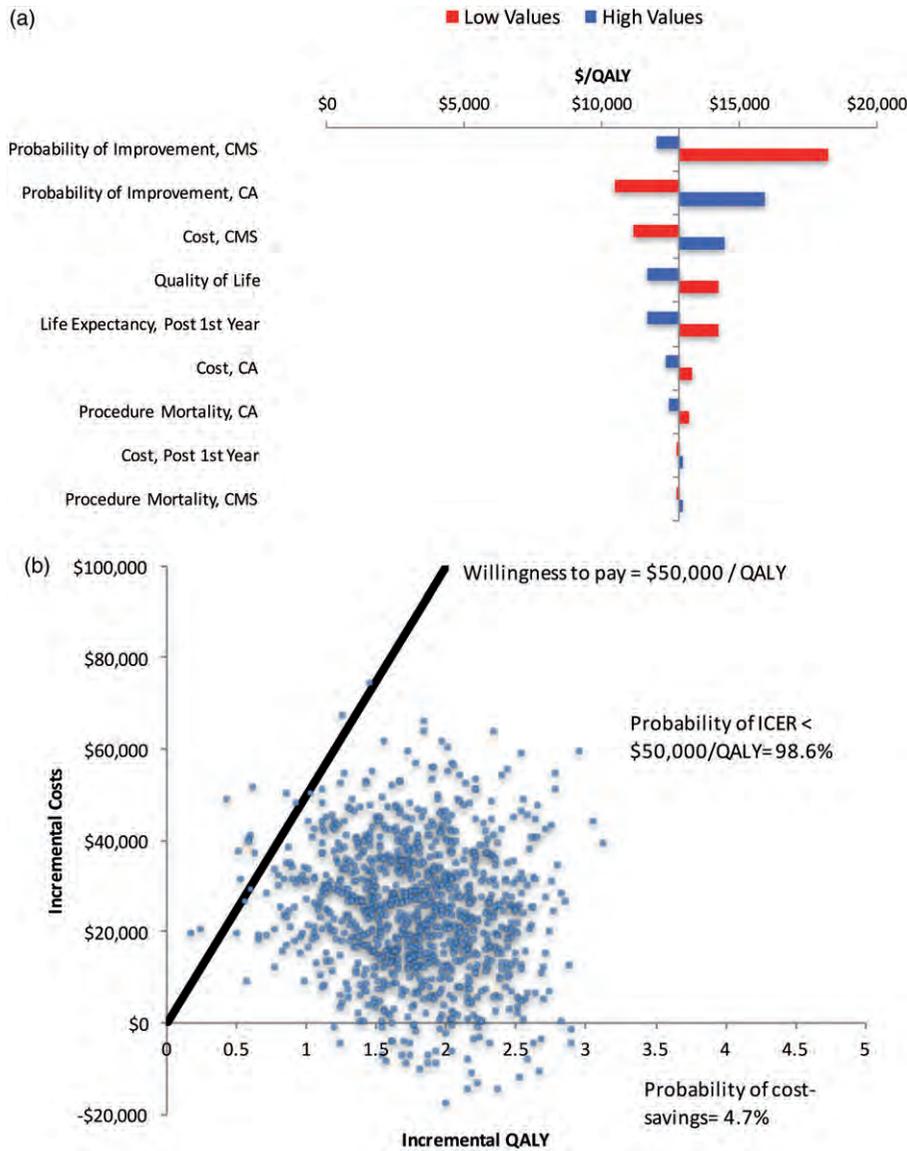
In probabilistic sensitivity analyses, Cox maze surgery had higher quality-adjusted life expectancy in all 1000 iterations. It was the dominant strategy (i.e. higher clinical benefits and lower costs) in 4.7% of iterations, and had a cost-effectiveness ratio below \$50,000 in 98.6% (Figure 2b).

## Discussion

Using the data collected from IHVI registries to populate the model and compare strategies for the treatment of AF, we found that the Cox maze procedure increased survival and quality adjusted life expectancy. Although this type of analysis has previously been conducted in order to assess treatment options for AF, prior researchers were not privy to the type of data contained in the aforementioned registries<sup>15–18</sup>. Considering the increased cost of the procedure, the lifetime incremental cost-effectiveness ratio was \$12,794/QALY. This estimate is far below commonly cited willingness to pay thresholds in the US of \$50,000–\$100,000/QALY, indicating that use of the Cox maze procedure in this patient population would be an efficient use of resources.

When considering the results over the first year, the cost-effectiveness ratio of over \$900,000 was far beyond the range that is typically considered to be good value. This finding is driven by the high upfront cost of the Cox maze procedure compared to catheter ablation, and the exclusion of survival benefits for those who achieve rhythm control and survive beyond the data collection period. In following best practices in modeling<sup>19</sup>, the lifetime horizon was considered more appropriate to use when assessing the value of the interventions, as the benefits of these strategies clearly extend beyond the first year.

While this study relied on primary data from an established patient registry, results should be considered in combination with previously published analyses. A number of decision analyses have attempted to evaluate the cost-effectiveness of AF treatments<sup>9</sup>. Lamotte *et al.*<sup>20</sup> used the Markov model to predict the cost-effectiveness among three interventional approaches, which were: (1) high-intensity focused ultrasound, (2) the classic "cut and sew" Cox maze procedure, and (3) percutaneous catheter ablation. They concluded that all interventional treatments showed good incremental cost-effectiveness ratios, compared to drug treatment. Although this study was the first to assess the health economic consequences of concomitant surgical ablation for the treatment of AF, limited data was used to generate the study results. Reynolds *et al.*<sup>21</sup> constructed a Markov disease simulation model for a hypothetical cohort of patients with drug-refractory paroxysmal AF, treated either with radiofrequency catheter ablation (RFA), with/without antiarrhythmic drug



**Figure 2.** Sensitivity analyses. a. One-way sensitivity analysis results – tornado diagram. b. Probabilistic sensitivity analysis results – CE scatterplot. Abbreviations. QALY, quality-adjusted life-year; CMS, Cox maze surgery; CA, catheter ablation; ICER, incremental cost-effectiveness ratio.

**Table 3.** Base case results.

Strategy	Total Cost	Delta Cost	Total LE	Delta LE	Total QALYs	Delta QALYs	\$/LY	\$/QALY
1 year results								
Catheter ablation	\$8837		0.958		0.741			
Cox maze procedure	\$30,532	\$23,791	0.981	0.024	0.759	0.018	\$923,183	\$1,192,023
Lifetime results								
Catheter ablation	\$208,371		12.62		10.18			
Cox maze procedure	\$232,162	\$23,791	14.72	2.10	12.04	1.86	\$11,315	\$12,794

Abbreviations. LY, life-year; QALY, quality-adjusted life year; LE, life expectancy.

(AAD), or AAD alone. They found RFA was reasonably cost-effective compared with AAD therapy alone. The results of their model, however, cannot be directly applied to other subsets of the AF population due to the baseline characteristics of those patients. Moreover, they did not model all possible treatment strategies for patients with paroxysmal AF. Chan *et al.*<sup>22</sup> constructed a Markov decision analysis model to assess the cost-effectiveness of rhythm control with left atrial catheter ablation (LACA) versus two more standard approaches: rhythm control with amiodarone and medical rate control therapy. The model shows that the use of LACA

may be cost effective in patients with AF at moderate risk for stroke, but is not cost effective in low-risk patients. Their model was developed only in 55 and 65 year old cohorts and as such the findings may not apply to younger or older patients. Despite the growing significance of comparative effectiveness research, the existing decision analyses to provide evidence of the cost-effectiveness of various AF treatments are limited at best. With the limitations of the current literature, our study was warranted. Our project contributes to the literature by: (1) being one of the first studies comparing the Cox maze procedure to other AF treatments, (2)

using rich primary data from a leading heart surgery center in the nation and their local surgical registries, and (3) assessing all of the key approaches in one analysis.

While cost-effectiveness analysis is one method of assessing the value of an intervention, it is not the only factor that should be considered when selecting an appropriate therapy. Other aspects such as patient preference and patient eligibility should be considered as well. Additionally, this study was based on data from a single center; therefore, results may only be generalizable to the extent that included patients are reflective of the general population. Moreover, there were some slight differences between the two groups being considered, despite the patients included being limited to those with nonparoxysmal AF, therefore results from this analysis must be considered in light of the data limitations. To consider the cost-effectiveness of the treatments in clinical practice, an emphasis was put on incorporating data from the IHVI registries. However, this data only included patient follow-up at 1 year post-treatment, requiring estimates from the literature for survival and costs beyond this point. In incorporating this data, an assumption was made that patients who had improved after the first year were thereafter relieved of their AF symptoms, and all those who did not improve within that time-frame showed no subsequent improvement.

## Conclusion

Although Cox maze procedure is a more invasive and aggressive strategy to address AF, at a societal willingness to pay of \$100,000/QALY, our model-based analysis using real-world data found that it would improve clinical outcomes and be an efficient use of healthcare resources.

## Transparency

### Declaration of funding

This research was supported by the Mason Inova Life Sciences Research Collaboration Fund.

### Declaration of financial/other relationships

Y.T.Y. and J.O. have disclosed that they have no significant relationships with or financial interests in any commercial companies related to this study or article.

CMRO peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

## Acknowledgements

The authors thank Niv Ad, MD, and Sari D. Holmes, PhD, for their thoughtful comments.

## References

- Centers for Disease Control and Prevention. Atrial Fibrillation Fact Sheet. Available at: [http://www.cdc.gov/dhdsdp/data\\_statistics/factsheets/fs\\_atrial\\_fibrillation.htm](http://www.cdc.gov/dhdsdp/data_statistics/factsheets/fs_atrial_fibrillation.htm) [Last accessed 23 May 2018]
- Lip G, Tse HF. Management of atrial fibrillation. *Lancet* 2007;370:604–18
- Centers for Disease Control and Prevention. Summary Health Statistics for U.S. Adults: National Health Interview Survey (Series 10, No. 256, December 2012). Available at: [http://www.cdc.gov/nchs/data/series/sr\\_10/sr10\\_256.pdf](http://www.cdc.gov/nchs/data/series/sr_10/sr10_256.pdf) [Last accessed 23 May 2018]
- Murphy SL, Xu J, Kochanek KD. Deaths: final data for 2010. *Natl Vital Stat Rep* 2013;61:4
- Healey JS, Connolly SJ, Gold MR, et al. Subclinical atrial fibrillation and the risk of stroke. *N Engl J Med* 2012;366:120–9
- Hobbs FD, Fitzmaurice DA, Mant J, et al. A randomised controlled trial and cost-effectiveness study of systematic screening (targeted and total population screening) versus routine practice for the detection of atrial fibrillation in people aged 65 and over. The SAFE study. *Health Technol Assess* 2005;9:iii-iv, ix-x, 1–74
- NIH National Heart, Lung & Blood Inst. How Is Atrial Fibrillation Treated? Available at: <http://www.nhlbi.nih.gov/health/health-topics/topics/af/treatment.html> [Last accessed 23 May 2018]
- Inova Heart and Vascular Inst. Cardiac and Thoracic Surgery: 2010 Outcomes Report. Available at: <http://www.inovaheart.org/upload/docs/IHVI/Outcomes-Report-Cardiac-and-Thoracic-Surgery-2010.pdf> [Last accessed 23 May 2018]
- Nieuwlaat R, Prins M, Le Heuzey J, et al. Prognosis, disease progression, and treatment of atrial fibrillation patients during 1 year: follow-up of the Euro Heart Survey on Atrial Fibrillation. *Eur Heart J* 2008;29:1181–9
- Benjamin E, Wolf P, D'Agostino R, et al. Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. *Circulation* 1998;98:946–52
- US Bureau of Labor Statistics. Databases, Tables & Calculators by Subject. Available at: [https://data.bls.gov/timeseries/CUUR0000SAM?output\\_view=pct\\_12mths](https://data.bls.gov/timeseries/CUUR0000SAM?output_view=pct_12mths) [Last accessed 23 May 2018]
- Kim M, Johnston S, Chu B, et al. Estimation of total incremental health care costs in patients with atrial fibrillation in the United States. *Circ Cardiovasc Qual Outcomes* 2011;4:313–20
- Sullivan P, Ghushchyan V. Preference-based EQ-5D Index Scores for Chronic Conditions in the United States. *Med Decis Making* 2006;26:410–20
- World Health Organization. WHO guide to cost-effectiveness analysis. 2003. Available at: [http://www.who.int/choice/publications/p\\_2003\\_generalised\\_cea.pdf](http://www.who.int/choice/publications/p_2003_generalised_cea.pdf) [Last accessed 23 May 2018]
- Quenneville SP, Xie X, Brophy JM. The cost-effectiveness of maze procedures using ablation techniques at the time of mitral valve surgery. *Int J Tech Assess Health Care* 2009;25:485–96
- Fonteneau A, Petit A, Piccardo A, et al. Medical and economic interest of the use of cryosurgery in the instrumental treatment of atrial fibrillation. *Pharmacology* 2011;87:28–35
- Andrikopoulos G, Tzeis S, Maniadakis N, et al. Cost-effectiveness of atrial fibrillation catheter ablation. *Europace* 2009;11:147–51
- Wyse DG, Waldo AL, DiMarco JP, et al. A comparison of rate control and rhythm control in patients with atrial fibrillation. *N Engl J Med* 2002;347:1825–33
- Caro J, Briggs A, Siebert U, et al. Modeling good research practices – overview: a report of the ISPOR–SMDM Modeling Good Research Practices Task Force – 1. *Value Health* 2012;15:796–803
- Lamotte M, Annemans L, Bridgewater B, et al. A health economic evaluation of concomitant surgical ablation for atrial fibrillation. *Eur J Cardiothorac Surg* 2007;32:702–10
- 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 Electrophysiol* 2009;2:362–9
- Chan PS, Vijac S, Morady F, Oral H. Cost-effectiveness of radiofrequency catheter ablation for atrial fibrillation. *J Am Coll Cardiol* 2006;47:2513–20