

# The Impact of Cryoballoon Versus Radiofrequency Ablation for Paroxysmal Atrial Fibrillation on Healthcare Utilization and Costs: An Economic Analysis From the FIRE AND ICE Trial

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**Background**—This study sought to assess payer costs following cryoballoon or radiofrequency current (RFC) catheter ablation of paroxysmal atrial fibrillation in the randomized FIRE AND ICE trial.

**Methods and Results**—A trial period analysis of healthcare costs evaluated the impact of ablation modality (cryoballoon versus RFC) on differences in resource use and associated payer costs. Analyses were based on repeat interventions, rehospitalizations, and cardioversions during the trial, with unit costs based on 3 national healthcare systems (Germany [€], the United Kingdom [£], and the United States [\$]). Total payer costs were calculated by applying standard unit costs to hospital stays, using *International Classification of Diseases, 10th Revision* diagnoses and procedure codes that were mapped to country-specific diagnosis-related groups. Patients (N=750) randomized 1:1 to cryoballoon (n=374) or RFC (n=376) ablation were followed for a mean of 1.5 years. Resource use was lower in the cryoballoon than the RFC group (205 hospitalizations and/or interventions in 122 patients versus 268 events in 154 patients). The cost differences per patient in mean total payer costs during follow-up were €640, £364, and \$925 in favor of cryoballoon ablation ( $P=0.012$ , 0.013, and 0.016, respectively). This resulted in trial period total cost savings of €245 000, £140 000, and \$355 000.

**Conclusions**—When compared with RFC ablation, cryoballoon ablation was associated with a reduction in resource use and payer costs. In all 3 national healthcare systems analyzed, this reduction resulted in substantial trial period cost savings, primarily attributable to fewer repeat ablations and a reduction in cardiovascular rehospitalizations with cryoballoon ablation.

**Clinical Trial Registration**—URL: <http://www.clinicaltrials.gov>. Identifier: NCT01490814. (*J Am Heart Assoc.* 2017;6:e006043. DOI: 10.1161/JAHA.117.006043.)

**Key Words:** atrial fibrillation • catheter ablation • cryoballoon • health economics • pulmonary vein isolation

Atrial fibrillation (AF) is a common and chronic cardiac arrhythmia that is a burden to patients and the healthcare system, with an estimated annual cost of €660 million to the German healthcare system,<sup>1</sup> 1% of the National Health Service budget in the United Kingdom,<sup>2</sup> and \$6 billion in the US

healthcare system.<sup>3</sup> Pulmonary vein isolation (PVI) by way of catheter ablation has been proven to be an effective treatment option for patients with symptomatic paroxysmal AF. However, despite a class I indication in guidelines,<sup>4,5</sup> only a minority of patients who are indicated receive AF ablation therapy.<sup>6</sup>

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An accompanying Appendix S1 is available at <http://jaha.ahajournals.org/content/6/8/e006043/DC1/embed/inline-supplementary-material-1.pdf>

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## Clinical Perspective

### What Is New?

- Pulmonary vein isolation using cryoballoon ablation resulted in a significant reduction in trial period healthcare payer costs and resource utilization in 3 national healthcare systems when compared with patients treated with radiofrequency current catheter ablation.
- Trial period healthcare cost savings per patient in the 3 systems analyzed were: Germany=€640, the United Kingdom=£364, and the United States=\$925, in favor of cryoballoon compared with radiofrequency current.
- Reduction in payer costs associated with pulmonary vein isolation using cryoballoon is driven by the reductions in repeat ablations and cardiovascular rehospitalizations in patients treated with cryoballoon versus radiofrequency current.

### What Are the Clinical Implications?

- Pulmonary vein isolation using cryoballoon resulted in decreased atrial fibrillation healthcare disease burden and symptoms and fewer reinterventions, with significant clinical and economic impact.
- Healthcare and resource cost savings in patients with drug-refractory paroxysmal atrial fibrillation were demonstrated across multiple diverse healthcare systems.
- The implications on daily clinical practice and healthcare costs should be an important consideration for the optimization of patient outcomes with maximum efficiency given the imperative for improving value-based health care.

The FIRE AND ICE study is the largest randomized trial to compare the efficacy and safety of PVI in patients with drug-refractory symptomatic paroxysmal AF, using either the “single-shot” cryoballoon or the point-by-point radiofrequency current (RFC) methodology. Results for primary and secondary study end points have been previously reported.<sup>7,8</sup> The trial met the primary safety and efficacy end points and confirmed that cryoballoon ablation was noninferior to RFC ablation when assessed by the time to first documented clinical failure (recurrence of AF lasting for >30 seconds, occurrence of atrial flutter/tachycardia, use of antiarrhythmic drugs, or repeat ablation) following a 90-day blanking period.<sup>7</sup> In the secondary end point analysis, comprehensive trial period reinterventions, rehospitalizations, and quality-of-life measures were evaluated. While the average quality-of-life scores improved to a similar extent in both groups, patients who underwent PVI with the cryoballoon demonstrated: (1) a 21% reduction in all-cause rehospitalizations; (2) a 34% reduction in cardiovascular rehospitalizations; (3) a 33% reduction in repeat ablations; and (4) a 50% reduction in direct-current cardioversions.<sup>8</sup>

This reduction in clinically relevant events during follow-up after PVI not only reflects a reduced AF burden in the cryoballoon group, it may also have a significant impact on healthcare costs when the 2 technologies are compared. There is a growing need to make transparent assessments of the value of healthcare interventions, balancing costs with health outcomes.<sup>9</sup> Consequently, in this report, we present a trial period economic analysis to better understand the differential cost between cryoballoon and RFC ablation from the perspective of a payer. The analyses were performed across national reimbursement systems in 3 different countries to explore whether reductions in resource use, specifically, rehospitalizations, reinterventions, and cardioversions, result in similar cost differences in each country.

## Methods

### Study Design and Patient Population

FIRE AND ICE (ClinicalTrials.gov Identifier: NCT01490814) was a controlled, prospective, randomized, noninferiority, blinded-outcomes, parallel-group trial designed to evaluate PVI using cryoballoon or RFC catheter ablation for the treatment of symptomatic, drug-refractory, paroxysmal AF. The study was conducted in 16 centers in 8 European countries. The design, primary end points, secondary end points, secondary analyses, and procedural techniques have been previously published.<sup>7,8,10</sup> After approval from each center’s respective ethics committee, written informed consent was obtained from each patient before 1:1 randomization to either cryoballoon ablation (the Arctic Front family of cryoballoon catheters) or RFC catheter ablation (the ThermoCool family of RFC catheters). Patients aged between 18 and 75 years were required to have at least 2 episodes of symptomatic drug-refractory paroxysmal AF, 1 episode of documented paroxysmal AF in the previous 12 months, and at least one treatment failure with a membrane-active antiarrhythmic drug. Major exclusion criteria included prior left atrial ablation, a left atrial diameter >55 mm, stroke within the past 6 months, any cardiac surgery or intervention, or myocardial infarction within 3 months of enrollment.

### Economic Analysis

The primary efficacy and safety analyses for FIRE AND ICE demonstrated no significant differences between RFC and cryoballoon ablation, and no significant differences were observed in the quality-of-life data from the secondary analyses. Therefore, a trial period economic analysis from a payer perspective was selected as the most appropriate type of economic evaluation (as opposed to a cost-effectiveness analysis). The analysis was performed across healthcare

systems in Germany, the United Kingdom, and the United States. Electronic case report forms captured detailed resource utilization, hereafter referred to as healthcare utilization (HCU) data during the trial period. Specifically, all-cause rehospitalization, cardiovascular rehospitalizations (AF related and non-AF related), repeat ablations, and direct current/pharmacological cardioversions were required to be reported and are included in this analysis. The aforementioned categories analyzed were not unique outcomes/end points of the study. Repeat ablation and cardioversions were unique outcomes, but “other cardiovascular rehospitalizations” and “noncardiovascular hospitalizations” are post hoc aggregations of numerous hospitalization episodes. Treatment details for each HCU during the trial follow-up period were evaluated. Diagnosis and procedure codes from the *International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10)* were retrospectively assigned in a bottom-up assignment of 473 resource utilizations by a professional coder who was blinded to the therapy randomization but had full access to the study HCU data. ICD-10 codes were assigned to each event, independent of the treatment group, to facilitate the assignment of diagnosis-related group (DRG) payment codes for each respective country. Data were further evaluated to identify the unique hospital stays (which is of relevance to payers). For example, a cardioversion completed as part of a hospital stay is costed within a single DRG payment. The most recently available payment rate for each DRG (>80 unique DRGs assigned) was applied and the respective utilization categorized as: (1) all-cause rehospitalization; (2) cardiovascular rehospitalizations (AF related and non-AF related); (3) repeat ablations; and (4) cardioversions. Costs related to the index ablation hospital stay were not included in this utilization and cost analysis for pragmatic reasons. First, payer costs incurred for the index ablation are equivalent and analyses including index ablation procedure/hospitalization costs would not change the results of the analysis. Further supporting this approach, the trial found no significant difference between the 2 technologies with regard to serious procedure-related adverse events, which suggests no meaningful difference in payer costs specific to the treatment of adverse events.

### HCU Payments in Germany

The utilization and cost analysis for Germany used G-DRG Version 2016. The online DRG grouper software was used to select the appropriate DRG for each hospital stay. In the cases where the appropriate DRG codes were subdivided according to comorbidities and complications (eg, with and without major comorbidities and complications), the number of hospitalizations per category per year were obtained and the weighted average costs were calculated for each DRG.

Electrical cardioversions without an overnight hospital stay were assigned a day-case tariff of €655 for DRG F71B (nonsevere cardiac arrhythmia and conduction disturbances without extremely severe comorbidity or complications, without catheter-based electrophysiologic study of the heart). Similarly, pharmacological cardioversions were assigned an emergency department visit with a cost of €90.89, based on fees established in the Einheitlicher Bewertungsmaßstab catalogue of physician fees.

### HCU Payments in the United Kingdom

The utilization and cost analysis for the United Kingdom used the National Schedule of Reference Costs (year 2014–2015, spell level data). This source was preferred to the most recent “Payment-by-Results” tariffs, because reference costs provide average costs per Healthcare Resource Group (HRG), including all categories of hospitalizations (eg, day case and short and long stay). Reference cost data are recommended for use in economic evaluations by the National Institute for Health and Care Excellence. Commercially available HRG Grouper software was used to select the appropriate HRG for each hospital stay. Reference cost data are reported for various levels of complications and comorbidities, with the number of hospitalizations per category per year, and the weighted average cost was calculated for each HRG. Electrical and pharmacological cardioversions without an overnight stay were assigned a cost of £678 using a day-case cost for HRG EB07 (arrhythmia or conduction disorder).

### HCU Payments in the United States

For the United States, payments for trial HCUs represent the national Medicare payment levels for the year 2016. In the case where there was ambiguity in the data (eg, whether additional procedures were performed or comorbidities were present based on secondary diagnoses), the lowest acuity codes were selected. Since billing information was not collected as part of the original trial, it was imputed using HCU data from the case report forms. This imputation was performed using Centers for Medicare & Medicaid Services DRG (MS-DRG). ICD-10 principal diagnosis and procedure codes were used to create an MS-DRG assignment and mapped to the associated national Medicare payments. Patients with AF are ablated in both inpatient and outpatient settings. To be conservative, this analysis uses the lower of the 2 payments, which is associated with the inpatient setting.

### Statistical Analyses

The number of HCUs and patients who had HCU events were calculated within the treatment groups and subclassified by

event type for the entire trial period (1.54±0.80 years for patients randomized to cryoballoon ablation and 1.54±0.79 years for patients randomized to RFC ablation). Costs for each HCU event were drawn from the DRG/HRG payment assignments. Total trial period costs per patient were calculated by summing all HCU costs across the duration of the trial. Because costs did not have a normal distribution (they exhibited a right skew along with a large spike at zero), 2-sided Wilcoxon rank-sum tests with  $\alpha=0.05$  were used to determine whether HCU costs differed between treatment groups. Total trial period costs are presented at the study level and patient level, total trial costs per randomization group, and average total trial costs per patient.

Bootstrapping statistical methods were used for the resampling analysis to estimate the distribution of cost difference between the 2 treatment groups. In the bootstrap, the sample data are treated as the population. Data are then randomly generated from the sample data to obtain a distribution.<sup>11</sup> Bootstrapping takes repeated samples from the data to calculate the accuracy of estimates for the entire population. The bootstrap method was applied by taking 1000 random resamplings with replacement from the FIRE AND ICE data set, and the result is a random variance from the original sample. The cryoballoon and RFC groups were replicated (1000 iterations) by resampling from the individual patient data. This was performed for all-cause rehospitalizations and repeated for cardiovascular rehospitalizations.

**Table 1.** HCUs by Ablation Group

HCU Type	Cryoballoon HCUs (No. of Patients) (n=374)	RFC HCUs (No. of Patients) (n=376)
Subtotal cardiovascular-related rehospitalization	139 (88)	212 (132)
Repeat ablation	49 (44)	70 (66)
Cardiovascular rehospitalization	74 (53)	109 (80)
AF related	34 (25)	55 (48)
Non-AF related	40 (33)	54 (40)
Cardioversion	16 (13)	33 (28)
Subtotal noncardiovascular rehospitalization	66 (49)	56 (42)
Total <sup>†</sup>	205 (122)	268 (154)

AF indicates atrial fibrillation; HCU, healthcare utilization; RFC, radiofrequency current. <sup>†</sup>Total=subtotal cardiovascular-related rehospitalization+subtotal noncardiovascular rehospitalization.

One-way sensitivity analysis was conducted using ±20% payment variance for the 4 most commonly used payment codes, which collectively represented 61% of all hospital stays (repeat ablation, arrhythmia-related rehospitalization, electrical cardioversion, and pharmacological cardioversion).

All statistical analyses were completed using SAS 9.4 software (SAS Institute Inc).

**Table 2.** Tariff/Payment Levels for the Most Common Healthcare Utilizations

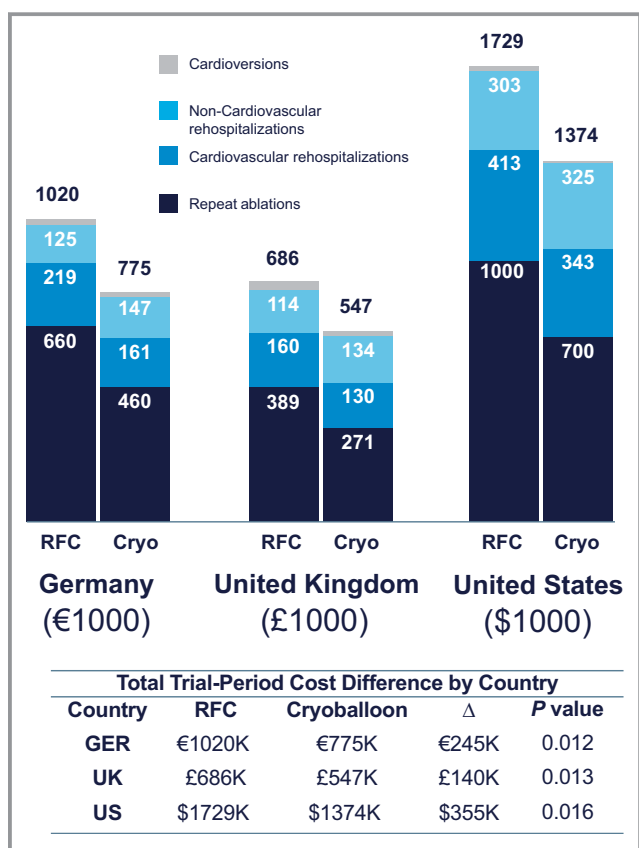
List of DRGs With >5 Occurrences	Germany	United Kingdom	United States
Arrhythmia ablation—percutaneous intracardiac procedures without MCC	€9505	£5622	\$14 291
AF hospitalization—cardiac arrhythmia & conduction disorders without MCC	€1796	£1195	\$3312
Electrical cardioversion	€655	£679	\$467
Pharmacological cardioversion	€91	£679	\$173
Esophagitis, gastrointestinal, and digestive disorders without MCC	€1662	£2056	\$4371
Respiratory signs and symptoms	€1550	£1033	\$4306
Peripheral vascular disorders without CC/MCC	€2548	£2092	\$4148
Syncope and collapse	€1722	£1141	\$4506
Simple pneumonia and pleurisy without CC/MCC	€2527	£3430	\$4200
Medical back problems without MCC	€1971	£3732	\$5108
Signs and symptoms of musculoskeletal system and connective tissue without MCC	€1792	£829	\$4394
Disequilibrium	€1832	£1627	\$3961
Bone diseases and arthropathies without MCC	€2272	£1207	\$4333
Atherosclerosis without MCC	€1822	£2134	\$3796
Hypertension without MCC	€1666	£939	\$3913

AF indicates atrial fibrillation; CC, complication or comorbidity; DRG, diagnosis-related group; MCC, major complications and comorbid condition.

**Table 3.** Healthcare Cost Savings per Patient

Healthcare Utilization	Germany			United Kingdom			United States		
	Cryoballoon	RFC	Δ	Cryoballoon	RFC	Δ	Cryoballoon	RFC	Δ
Subtotal cardiovascular-related rehospitalization	€1680	€2379	€700 <sup>†</sup>	£1103	£1523	£419 <sup>†</sup>	\$2804	\$3792	\$988 <sup>†</sup>
Repeat ablation	€1233	€1757	€524 <sup>†</sup>	£726	£1036	£310 <sup>†</sup>	\$1872	\$2661	\$788 <sup>†</sup>
AF-related cardiovascular rehospitalization	€196	€287	€91 <sup>†</sup>	£140	£195	£55 <sup>†</sup>	\$410	\$513	\$103 <sup>†</sup>
Non-AF-related cardiovascular rehospitalization	€235	€298	€63	£209	£233	£24	\$508	\$588	\$80
Cardioversion	€16	€38	€22 <sup>†</sup>	£29	£60	£31 <sup>†</sup>	\$14	\$31	\$17 <sup>†</sup>
Subtotal noncardiovascular rehospitalization	€395	€335	€-60	£360	£304	£-56	\$870	\$807	\$-63
<b>Total</b>	<b>€2075</b>	<b>€2714</b>	<b>€639.51<sup>†</sup></b>	<b>£1464</b>	<b>£1827</b>	<b>£363.50<sup>†</sup></b>	<b>\$3674</b>	<b>\$4599</b>	<b>\$924.62<sup>†</sup></b>

AF indicates atrial fibrillation; RFC, radiofrequency current. Total=subtotal cardiovascular-related rehospitalization+subtotal noncardiovascular rehospitalization. <sup>†</sup>P<0.05.



**Figure 1.** Healthcare cost savings: Total trial period payer costs of healthcare utilizations (HCU) for the cryoballoon and radiofrequency current (RFC) groups calculated by multiplying the number of HCUs by the specific payer cost per HCU across 3 national healthcare systems. The cryoballoon group demonstrated a statistically significant cost reduction in all 3 systems when compared with RFC, with the largest cost reductions in repeat ablations and cardiovascular rehospitalizations. Cryo indicates cryoballoon.

## Results

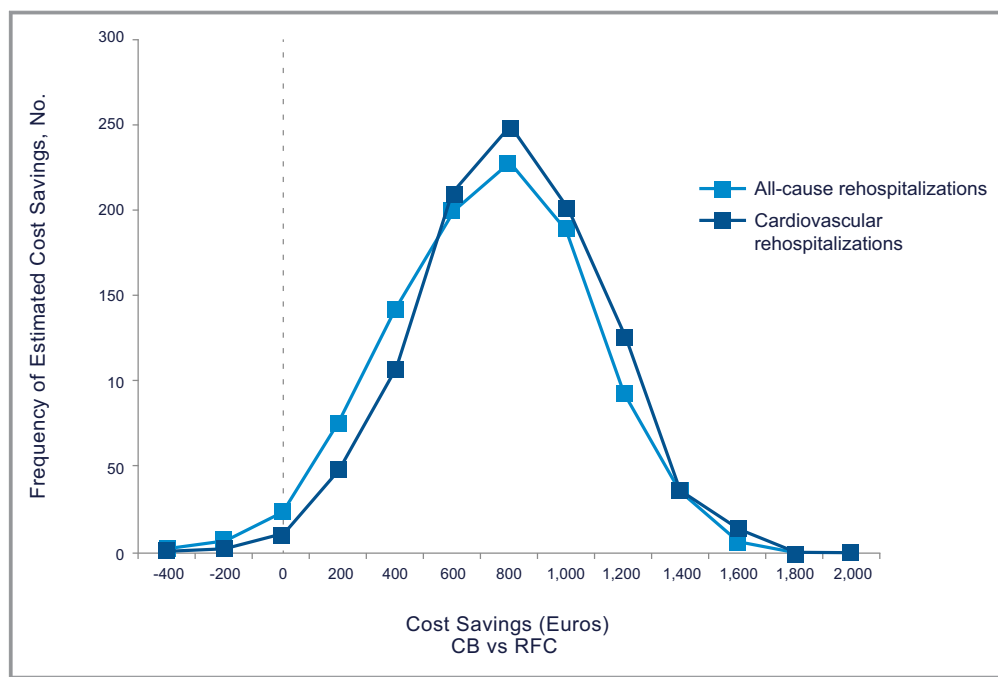
### Trial Period HCU and Costs

Patients (N=750) randomized 1:1 to cryoballoon (n=374) or RFC (n=376) ablation were followed for a mean of 1.5 years. As detailed in Table 1, a total of 205 HCUs were observed in 122 of the 374 patients randomized to cryoballoon ablation and 268 HCUs were observed in 154 of the 376 patients randomized to RFC ablation. The trial period incidence of repeat ablations, AF-related cardiovascular rehospitalizations, non-AF-related cardiovascular rehospitalizations, and cardioversions were all lower in the cryoballoon group when compared with RFC (49 versus 70 HCUs, 34 versus 55 HCUs, 40 versus 54 HCUs, and 16 versus 33 HCUs, respectively). A marginally higher incidence of noncardiovascular hospitalizations was observed in the cryoballoon group. The unique healthcare system-related costs assigned to DRGs with at least 5 occurrences during the trial period are summarized in Table 2.

### Trial Period Cost Differences

Table 3 depicts the total cost differences per patient during the FIRE AND ICE trial period in the 3 healthcare systems included in this analysis. Trial period costs per patient were lower in the cryoballoon group, resulting in cost differences of €640 (P=0.012) in Germany, £364 (P=0.013) in the United Kingdom, and \$925 (P=0.016) in the United States. These cost differences were driven by significantly reduced costs associated with repeat ablations and AF-related and non-AF-related cardiovascular rehospitalizations. Figure 1 summarizes the cost differentials across the 3 national healthcare systems within the respective treatment cohorts. These per-





**Figure 2.** Cost-savings distribution: German healthcare system results of bootstrap modeling of 1000 healthcare utilization (HCU) iterations in the German healthcare system, with the y axis demonstrating the frequency of cost savings and the x axis demonstrating the amount of cost savings. As demonstrated by the distributions to the right of the dotted line, the cryoballoon (CB) group demonstrated cost savings compared with the radiofrequency current (RFC) group, with 97% and 98% probability in the all-cause rehospitalization and cardiovascular-only rehospitalization analyses, respectively.

patient cost differences translated to a significant reduction in total costs between the 2 treatment groups: €245 000 in Germany, £140 000 in the United Kingdom, and \$355 000 in the United States. The largest payer cost reductions were observed for repeat ablations and cardiovascular rehospitalizations.

### Sensitivity Analysis

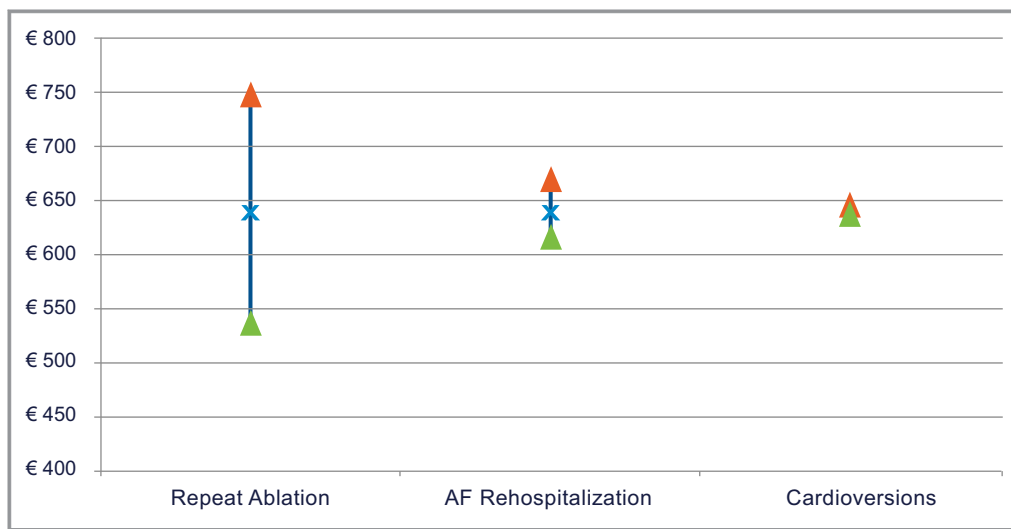
The results of the bootstrapping analysis are presented in Figure 2. The distribution of estimated cost savings indicates an extremely high likelihood of cryoballoon being cost saving compared with RFC, with a 97% and 98% probability of cost savings in the all-cause rehospitalization and cardiovascular rehospitalization analyses. The results of the 1-way sensitivity analyses are presented in Figure 3. The size of the cost savings was most dependent on the payment level for a repeat ablation (higher payment associated with higher cost savings) and largely insensitive to changes in the individual payment levels for other types of HCU.

### Discussion

The primary analysis of FIRE AND ICE demonstrated noninferiority, while the secondary end point analysis of

FIRE AND ICE, which included all events (both within the blanking period and beyond a primary event) through study exit, established that using cryoballoon for PVI results in fewer HCUs than does RFC. The present economic analysis demonstrates that this reduction in HCUs is robust enough to manifest in significantly lower patient care costs from the payer perspective, and this cost reduction persists across all 3 healthcare systems analyzed. Our analysis demonstrated significant total cost savings during the trial period of €640 ( $P=0.012$ ) in Germany, £364 ( $P=0.013$ ) in the United Kingdom, and \$925 ( $P=0.016$ ) in the United States. The primary cost difference between cryoballoon and RFC was the lower incidence of repeat ablation procedures in the cryoballoon group, accounting for most of the total cost difference between therapies. These cost savings are strongly impacted by both a reduction in the probability of repeat ablation procedures (33%) and by the high payer cost of this HCU. The reduction in repeat ablations has been observed in a prior study<sup>12</sup> and is now confirmed in a large randomized trial.

The annual number of AF ablation procedures for all AF in the 3 countries evaluated is reported to be: 33 628 procedures in Germany, 6 390 procedures in the United Kingdom,<sup>13</sup> and 75 000 procedures in the United States.<sup>14</sup> Given the lower payer costs estimated in this study, if cryoballoon



**Figure 3.** Sensitivity analysis on payment levels: German healthcare system. One-way sensitivity analysis after varying the payment level for the most commonly used payment codes. The blue “x” indicates the mean cost savings per patient from the analysis. The green and red arrows illustrate how the cost savings change when the individual cost input is decreased or increased by 20%, respectively. The analysis demonstrates that cost savings was most dependent on the payment for a repeat ablation and largely insensitive to changes in the individual payment levels for other types of healthcare utilization. AF indicates atrial fibrillation.

was used instead of RFC, significant payer cost savings would be realized following index ablation. Exact savings calculations would need to be performed by each payer organization, incorporating the size of their respective paroxysmal AF population and the current ratio of treatment by cryoballoon versus RFC.

The reduction in repeat ablations and cardiovascular rehospitalizations is important, from a clinical, biophysical, and economic perspective. It indirectly reflects a decrease in AF “burden” (the fewer AF recurrences, the fewer interventions required). Thus, even though the AF burden cannot be precisely determined in FIRE AND ICE (continuous AF burden data were not collected), the number of repeat ablations and direct-current cardioversions are a valid surrogate for AF burden. The difference in repeat ablations and cardioversions following cryoballoon or RFC ablation can be explained by the different modes of lesion formation associated with either technique. In brief, during cryoballoon ablation, anatomical circumferential PVI is achieved in a uniform “single shot” of coolant delivered to the pulmonary vein antra by the cryoballoon. However, during RF catheter ablation, PVI is achieved using a “point-by-point” application of heat during serial focal ablations. Previous evaluations of PVI at repeat procedures have shown that the rate of pulmonary vein reconnection is significantly lower following cryoballoon ablation (20.4%) than following RFC ablation with contact-force sensing catheters (36.1%).<sup>15</sup> These data, when evaluated with other

published lesion durability studies reporting 37% of patients with conduction gaps post RFC ablation<sup>16</sup> and 22% of patients with gaps post cryoballoon ablation,<sup>17</sup> suggest that the cryoballoon may be more effective in creating durable transmural lesions.

The reduction in repeat ablations takes on additional importance when considering the programs that payers have implemented and plan to implement to deliver appropriate care to their members with maximum efficiency. Several European countries have implemented “budget envelopes,” under which large increases in the spending associated with a medical technology from year to year are not fully covered. If the cost or number of procedures exceeds predefined levels, payment rates are reduced for the additional procedures. Other forms of risk sharing between payers and providers (such as bundled payment for a year of care) are at various stages of implementation but are intended to have a similar effect. A health technology that can appropriately treat the same number of patients with fewer overall claims could help avoid negative economic consequences for patients, providers, and payers.

Cardiovascular rehospitalizations (not inclusive of repeat ablation procedures) are also a meaningful driver of the cost difference observed in this analysis. These rehospitalizations are likely to have been driven by patients experiencing recurring AF symptoms and seeking medical care. Noncardiovascular rehospitalizations are not a cost driver, and this is likely because of the relative youth and health of the

paroxysmal AF population receiving ablations compared with other cardiovascular disease. Cardioversions were not a strong driver of costs in this analysis (because the event rate was low compared with the other HCU types), but their impact on hospital resource burden and patient experience cannot be ignored. There was no difference in payer costs for the index ablation procedure and associated hospitalization as payers do not have a cost difference because reimbursement between the 2 therapies is the same.

Although the present analysis was evaluated from the payer perspective, it is important to consider implications for other healthcare stakeholders. It should be acknowledged that from the perspective of individual hospitals, costs to perform catheter ablation, rehospitalizations, and reinterventions may vary, based on factors such as total materials used, pricing negotiations, electrophysiology laboratory staffing, efficiency in electrophysiology laboratory utilization, and length of stay.

From a hospital perspective under a fee-for-service payment model, repeat ablations and other rehospitalizations are reimbursed activities, reducing incentives to minimize their occurrence. Healthcare payment reform is happening in many countries around the world—for example, in the United States, the Department of Health and Human Services has set a goal of tying 50% of Medicare fee-for-service payments to quality or value through alternative payment models by 2018. These changes are intended to cause hospitals and payers to share incentives to improve the quality and reduce the cost of health care, including reducing the occurrence of HCUs. From a patient perspective, depending on the insurance arrangement, there may be a desire to reduce out-of-pocket expenses associated with additional healthcare use.

## Study Limitations

This economic analysis was a supplementary analysis not prespecified in the FIRE AND ICE study protocol. It represents differences in cost for hospital stays during follow-up after an index AF catheter ablation procedure. Diagnosis and procedure coding were imputed from the trial data rather than being directly collected in the study; however, this was based on information that was adjudicated by an independent adverse event committee composed of physician investigators. It is possible that information that could have impacted cost assignments was underreported. It was not possible to include all types of resource use in this analysis because of the missing data in the study, eg, medications and primary care visits. Payment levels represent national tariffs/payments rather than what an individual hospital would receive. The specific care given to patients could vary between different healthcare systems, impacting outcomes and costs.

## Conclusions

In symptomatic patients with drug-refractory paroxysmal AF, de novo PVI using cryoballoon ablation was associated with a reduction in HCU compared with RFC ablation. This reduction resulted in substantial trial period cost savings to the payer, which was attributable to the reduced need with cryoballoon for repeat ablations and a reduction in cardiovascular rehospitalizations. These cost savings persisted over multiple healthcare systems.

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# **Supplemental Material**

## Appendix

### List of FIRE AND ICE Trial Investigators

Investigator	Center	Country
Karl-Heinz Kuck Andreas Metzner Feifan Ouyang	Asklepios Klinik St. Georg, Hamburg	Germany
Julian Chun Alexander Fürnkranz	Cardioangiologisches Centrum Bethanien, Frankfurt	Germany
Arif Elvan	Isala Klinieken Zwolle	The Netherlands
Thomas Arentz	Herz-Zentrum Bad Krozingen	Germany
Michael Kühne Christian Sticherling	Universitätsspital Basel	Switzerland
Laszlo Gellér	Semmelweis Egyetem Budapest	Hungary
Matthias Busch	Uniklinik Greifswald	Germany
Josep Brugada Lluís Mont	Hospital Clinic de Barcelona	Spain
Alberto Barrera	Hospital Clínico Universitario "Virgen de la Victoria" Malaga	Spain
Thomas Deneke	Klinikum Bad Neustadt	Germany
Jean-Paul Albenque	Clinique Pasteur Toulouse	France
Volker Kühlkamp	Herz-Zentrum Bodensee	Germany
Claudio Tondo	Centro Cardiologico Monzino, University of Milan	Italy
Ricardo Ruiz-Granell	Hospital Clinico Universitario Valencia	Spain
Petr Neuzil	NA Homolce Hospital Prague	Czech Republic
Nicasio Pérez-Castellano	Hospital Clinico San Carlos, Madrid	Spain