

Clinical and Economic Outcomes Associated with Use of Anti-Arrhythmic Drugs Versus Ablation in Atrial Fibrillation (AFib)

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BACKGROUND AND OBJECTIVES

- AFib is associated with considerable morbidity and mortality and is characterized by arrhythmia, tachycardia, and/or bradycardia, and symptoms often include heart palpitations, shortness of breath, and weakness.¹
- The estimated prevalence of AFib among adults ranges between 2% and 4%, with 46.3 million individuals globally having AFib/atrial flutter in 2016.²
- Guidelines recommend stroke thromboprophylaxis, rate control, and rhythm control strategies (AADs, ablation, and cardioversion).^{3,4}
- Catheter ablation is increasingly being utilized earlier in the AFib treatment pathway.³
- EAST-AFNET4 demonstrated reduction of cardiovascular events with earlier use of rhythm control.⁵
- The objective of this study was to evaluate the economic benefits of AADs compared to ablation, both as individual treatments and as combination therapy with/ without considering the order of treatment.

METHODS

- The economic impact of rhythm control treatments was calculated using a model developed in Microsoft Excel 2010 (Microsoft Corp, Redmond, WA).
- Different treatment scenarios (Figure 1) were compared to assess the economic benefits of AADs (dronedronone, amiodarone, sotalol, flecainide, propafenone, dofetilide, and AADs as a group) vs. ablation.
- The target population included US adult AFib patients. Across scenarios, total healthcare costs were calculated over one year, including costs for treatment, outpatient administration, AEs, and ablation procedural complications, reported in 2021 USD. Coinsurance and copayments were included to estimate the annual medication costs of treatment. A discount rate of 20% was included for dronedronone.
- The expected budget impact of AADs was calculated as the difference in total annual costs of AADs (individually, or in combination with ablation) with the cost of ablation among the different scenarios.
- The model considered only direct medical costs to the payer.
- OWSA evaluated the impact of individual parameters on model results.

ASSUMPTIONS

Ablation assumptions

- The model did not differentiate between different techniques used for catheter ablation such as cryoballoon and radio-frequency ablation.
- Patients could undergo at most two ablation procedures (i.e., one index ablation and one reablation) within a year.
- An index ablation with a 30% incidence rate of reablation was assumed.

AE / procedural complication assumptions

- AEs included risks from withdrawal due to AE, proarrhythmia, stroke, and AFib recurrence.
- Procedural complications of ablation included pericardial effusion, cardiac tamponade, intra-/ post-operative hemorrhage/ hematoma requiring transfusion (excluding ESRD / chronic anemia), vascular injury/ aneurysm /AV fistula (excluding ESRD patient), Intubation (96 hours in duration), and vascular injury requiring surgical intervention. These complications were selected because they have an incidence of $\geq 0.5\%$.⁷

Cost assumptions

- Procedure costs of index ablation and reablation were assumed to be the same at \$22,640,⁸ adjusted to 2021 USD. Costs of AADs were WAC⁹⁻¹⁴ (Table 1).
- Patient cost-sharing (copay/coinsurance) was paid once per refill frequency. The model did not include monitoring costs.
- Based on dosing and administration guidelines in package inserts,¹⁵⁻²⁰ the proportions of treatment received inpatient were: dofetilide and sotalol = 100%; dronedronone = 0%; other AADs = 50%.
- Cost of ablation procedural complications was based on DRG codes²¹ and converted to commercial costs using a factor of 2.24, as suggested by a 2021 report by the RAND Corporation.²²
- Due to the limited availability of data, there was no distinction between individual AADs in the temporal scenarios.

Risk assumptions

- The risks of AEs and procedural complications for reablation, for which no data were available, were assumed to be the same as for ablation (Table 2). Data for AE risks in reablation were present only for stroke and AFib recurrence.
- Direct comparison scenario: treated risk was calculated by risk ratios (Cochrane review of AADs²³) multiplied by observed risk in a comparison population of adult patients having AFib with or without structural heart disease (based on analysis of Truven MarketScan data) (Table 3).
 - Treated risks greater than 1 were assumed to have a value of 0.99 as risk ratios from the literature were unreliable due to low event rates.²³
- For non-temporal and temporal combination scenarios, the risk of AEs for AADs in combination with ablation was the same as the risk of incidence of AEs for AADs in combination with ablation and reablation (Table 4).

Table 1. WAC costs of AADs

Treatment	WAC, \$
Dronedronone (400mg) ⁹	\$12.19
Amiodarone (200mg) ¹⁰	\$0.31
Sotalol (120mg) ¹¹	\$0.27
Flecainide (100mg) ¹²	\$0.57
Propafenone (225mg) ¹³	\$0.71
Dofetilide (125mg) ¹⁴	\$3.99

Table 2: Risk and costs: AEs and ablation procedural complications

AE / ablation procedural complication ^{6,8,24-26}	Ablation	Reablation	Cost of AEs / ablation procedural costs
Withdrawal due to AE	-	-	\$6,496
Proarrhythmia	0.079	0.079	\$10,952
Stroke	0.020	0.005	\$28,008
AFib recurrence	0.391	0.062	\$10,288
Pericardial effusion	0.022	0.022	\$30,793
Cardiac tamponade	0.013	0.013	\$30,793
Intra-/ Post-operative hemorrhage/ hematoma requiring transfusion	0.019	0.019	\$27,239
Vascular injury/ aneurysm / AV fistula	0.011	0.011	\$24,179
Intubation (96 hours in duration)	0.015	0.015	\$24,886
Vascular injury requiring surgical intervention	0.007	0.007	\$62,662

Figure 1. Framework of the rhythm control economic model

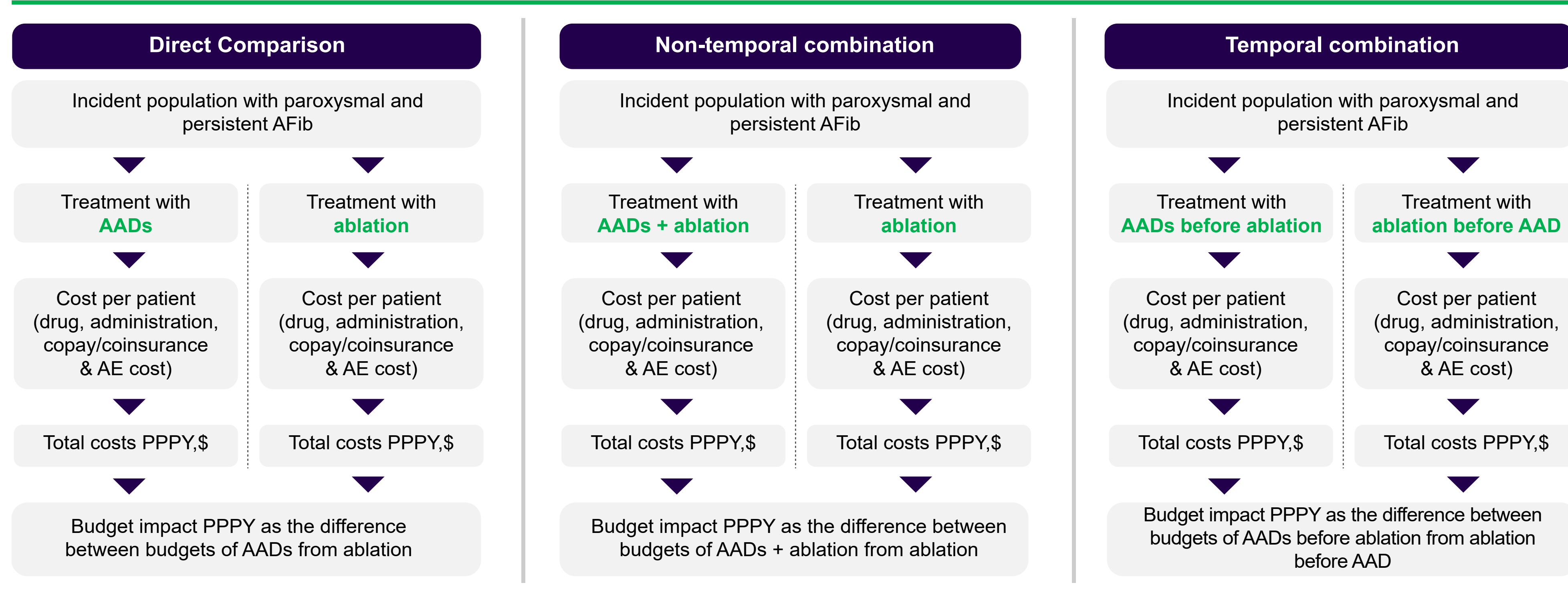


Table 3. AE risk of treatments used in direct comparison scenario and cost savings when compared with ablation

Treatment	Withdrawal due to AE	Proarrhythmia	Stroke	AFib recurrence	Cost savings PPPY, \$
Dronedronone	0.118	0.356	0.039	0.454	-\$22,505
Amiodarone	0.502	0.405	0.068	0.278	-\$24,392
Sotalol	0.146	0.648	0.087	0.443	-\$19,799
Flecainide	0.99	0.876	0.120	0.347	-\$13,853
Propafenone	0.121	0.241	0.020	0.358	-\$28,658
Dofetilide	0.133	0.990	0.064	0.384	-\$14,258
AADs (group)	0.623	0.776	0.067	0.380	-\$16,581

Table 4: AE risk of treatments (non-temporal and temporal scenarios) and cost savings vs. ablation

Scenarios	Treatment	Withdrawal due to AE	Proarrhythmia	Stroke	AFib recurrence	Cost savings PPPY, \$
Non-temporal	Dronedronone + Ablation	0.124	0.095	0.012	0.496	-\$19,213
	Amiodarone + Ablation	0.123	0.098	0.028	0.420	-\$24,402
	Sotalol + Ablation	0.109	0.119	0.025	0.455	-\$21,772
	Flecainide + Ablation	0.064	0.057	0.014	0.453	-\$24,466
	Propafenone + Ablation	0.081	0.081	0.014	0.514	-\$23,945
	Dofetilide + Ablation	0.130	0.099	0.015	0.527	-\$17,190
Temporal	AADs (group) + Ablation	0.099	0.086	0.019	0.458	-\$22,102
	AADs before ablation	0.082	0.082	0.011	0.422	-\$22,859
	Ablation before AADs	0.112	0.394	0.028	0.307	-\$19,958

RESULTS

Direct comparison of individual therapies

- Base case scenario: comparison of AADs with ablation resulted in PPPY cost savings of \$22,505 for dronedronone, \$24,392 for amiodarone, \$19,799 for sotalol, \$13,853 for flecainide, \$28,658 for propafenone, \$14,258 for dofetilide, and \$16,581 for AADs (group).
- Greater cost savings of AADs were mainly driven by higher procedural costs of ablation.
- AE costs (including procedural complication costs for ablation) were comparable between ablation (\$9,948) and AADs (\$7,678-\$22,964).

Non-temporal comparison of combination therapies

- The combination of AADs with ablation resulted in PPPY cost savings when compared to ablation due to higher procedural costs associated with ablation (\$29,432). AE costs (including procedural complications for ablation) were comparable between ablation (\$9,948) and the combination therapies (\$10,079-\$11,780).

Temporal comparison of combination therapies

- AADs before ablation resulted in PPPY cost savings of \$2,900 compared to ablation before AADs.
- AE costs were the driving factor for cost savings (\$10,080 for AADs before ablation and \$12,981 for ablation before AADs).
- Compared to ablation, PPPY cost savings were \$22,858 for AADs before ablation and \$19,958 for ablation before AADs.

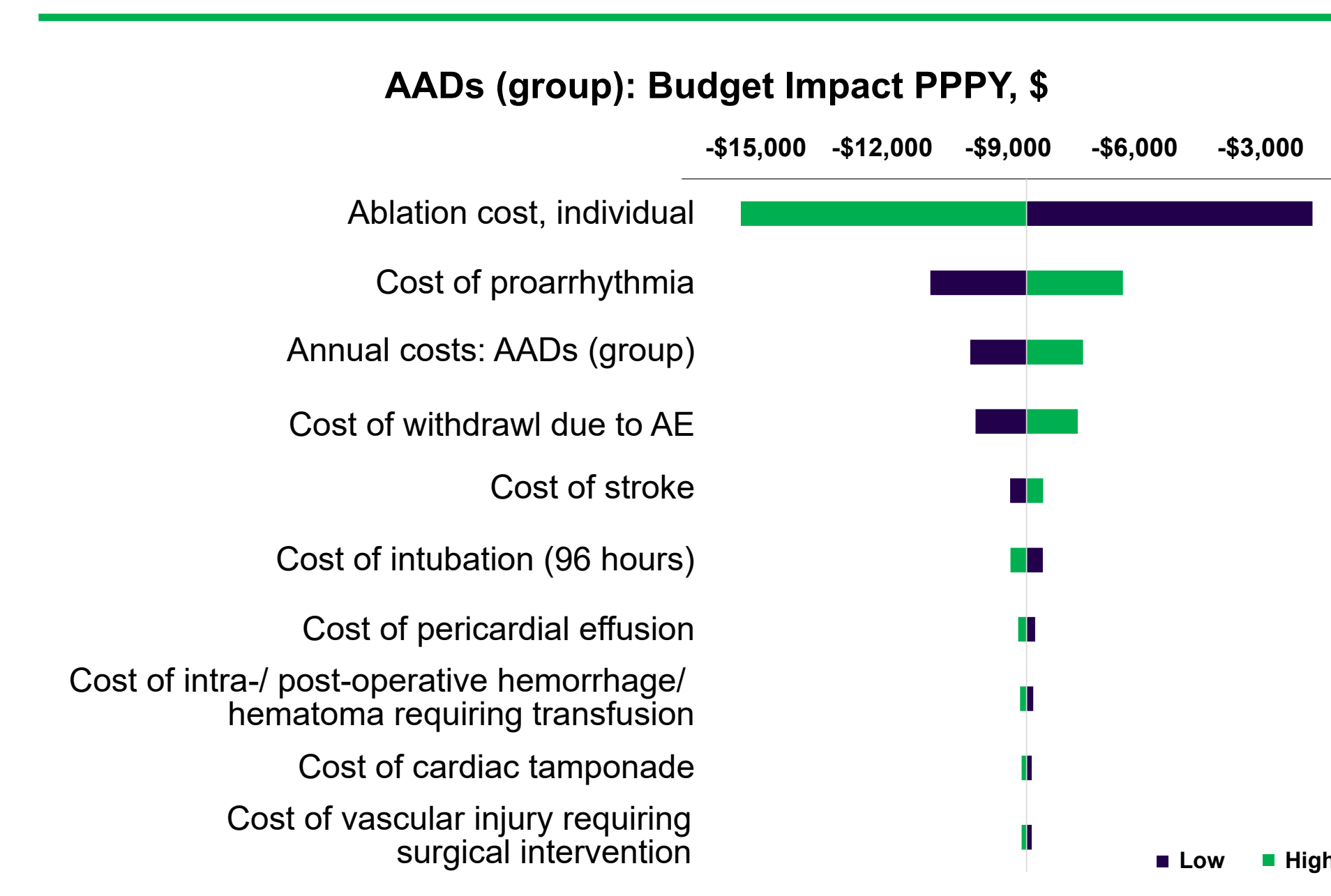
Sensitivity analysis (direct comparison of individual therapies)

- Index ablation costs, the proportion of patients undergoing reablation, the cost of proarrhythmia, and the annual cost of AADs (group) had the greatest influence on OWSA results. Other key variables influencing OWSA results are depicted in Figure 2.
- A 30% increase in index ablation costs increased PPPY savings for AADs by \$8,830 from its base case value (\$16,581).

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Figure 2. Tornado diagram - Sensitivity analysis results (direct comparison scenario)



Sensitivity analysis (non-temporal comparison of combination therapies)

- Index ablation costs, the proportion of patients undergoing reablation, the annual cost of AADs (group), and the ablation cost associated with AADs (group) had the greatest influence on OWSA results.
- A 30% increase in index ablation costs increased PPPY savings for AADs (group) in combination with ablation by \$8,830 from its base case value (\$22,102).
- Similarly, a 30% change in the proportion of patients undergoing reablation, the annual cost of AADs (group), and ablation cost associated with AADs (group) resulted in PPPY savings of \$2,048, \$1,340, and \$592, from base case, respectively.

Sensitivity analysis (temporal comparison of combination therapies)

- Costs of AEs influenced OWSA results.
- A 30% increase in proarrhythmia costs increased PPPY savings for AADs (group) before ablation by \$1,026 from its base case value (\$22,859).
- Similarly, a 30% change in cost of AFib recurrence, stroke, and withdrawal due to AE resulted in PPPY savings of \$4,280, \$1713, and \$697, from base case, respectively.

CONCLUSIONS

- Use of AADs, individual or in combination with ablation, resulted in comparable clinical outcomes and overall cost savings due to high procedural costs of ablation.
- AADs placed before ablation resulted in cost savings compared to ablation before AADs.
- Findings from this model can help decision-makers define best treatment strategies to minimize costs.

List of Abbreviations

Abbreviation	Full form
AAD	Antiarrhythmic drug
AE	Adverse event
AFib	Atrial fibrillation
AV	Atrioventricular
ESRD	End-stage renal disease
Mg	Milligram
OWSA	One-way sensitivity analysis
PPPM	Per patient per month
PPPY	Per patient per year
USD	United States dollar
WAC	Wholesale acquisition cost

ACKNOWLEDGMENTS:

Writing and editorial support was provided by JKO and SSSS of Atria (Berkeley Heights, NJ, USA) and was funded by Sanofi.

DISCLOSURES:

JKO and SSSS are employees of Atria, which received funding from Sanofi for this analysis. LF and PV were employees of Atria during the conduct of this study. RP, SP, SC, and AR are employees of Sanofi and are stockholders of Sanofi stock.

ISPOR Europe 2022
6-9 November, Vienna,
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