

# COST-EFFECTIVENESS OF ANTIARRHYTHMIC DRUGS FOR TREATING PAROXYSMAL OR PERSISTENT ATRIAL FIBRILLATION IN CHINA

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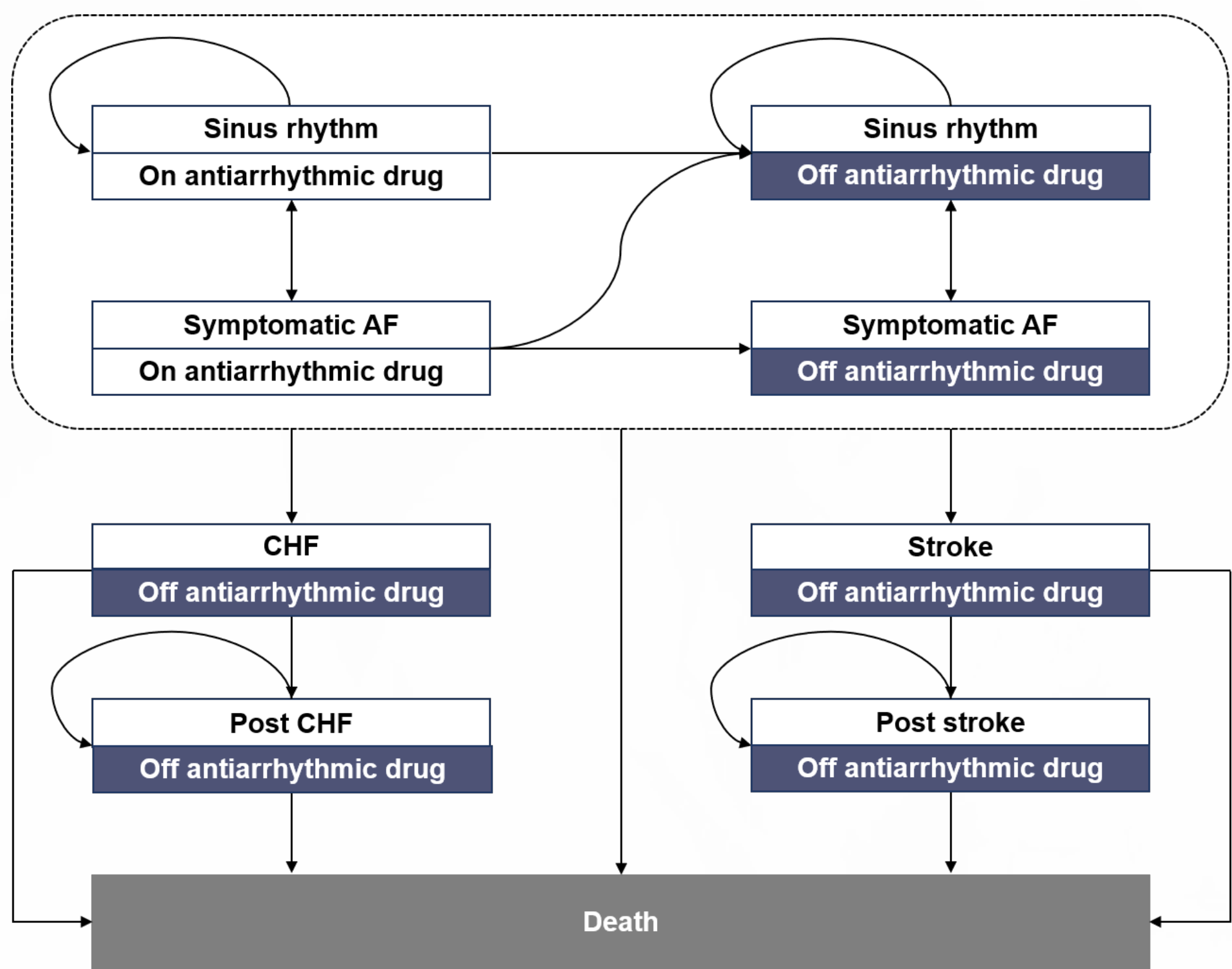
## INTRODUCTION & OBJECTIVES

- Atrial fibrillation (AF) is an increasingly prevalent cardiac arrhythmia worldwide that is closely associated with an increased risk of stroke and heart failure, and further contributing to hospitalization and increased mortality [1].
- Over the past few years, antiarrhythmic drug (AAD) therapies have become the foundation of long-term AF clinical management, yet there remains uncertainty in clinical and reimbursement decisions in China.
- This study aims to develop a cost-effectiveness model based on the ATHENA clinical trial to estimate the lifetime cost-effectiveness of dronedarone, in addition to standard of care, compare to amiodarone and sotalol for the treatment of paroxysmal or persistent AF in China from the health system perspective.

## METHODS

- Model structure**
  - A Markov decision model with nine health states (including on/off antiarrhythmic drug, symptomatic AF recurrence, CHF, stroke, and death) was developed based on literature review and expert consultation, with a chosen cycle length of one year.
  - The model adopted a lifetime perspective as its baseline time horizon, extending until the death state was reached by 99% of patients.
  - Adverse events (AEs) due to AAD taken by patients were considered in each cycle.
- Target population and treatment regimen**
  - Baseline characteristics of the patients were obtained from the CCC-AF program [2], with an initial age of 68.6 years, 45.4% being female, and may accompanied by disease history. 16.6% patients with permanent AF were assumed to have discontinued AAD and were not included in the model.
  - Patients would receive long-term oral AAD treatment alone with dronedarone (400 mg/tablet, 2 tablets/day) in the study group and amiodarone (200 mg/tablet, 1 tablet/day) and sotalol (80 mg/tablet, 2 tablets/day) in the control group.

Figure 1 Model structure



- Model parameters**
  - Transition probabilities were calculated using data from the ATHENA trial results for the dronedarone arm [3].
  - The probability of transitioning from the state On AAD to the state Off AAD was derived from the ATHENA study's patient discontinuation rates, while transition probabilities to stroke, CHF, and symptomatic AF states were calculated using ATHENA-reported incidence rates for these conditions. The transformation of the trial results to transition probabilities was referenced to Åkerborg et al [4] and Nilsson et al [5].
  - The relative efficacy estimates for the amiodarone and sotalol comparators from a mixed treatment comparison by Freemantle et al. [6] were applied as relative risks to adjust the transition probabilities calculated for dronedarone.
  - Treatment related costs (including drug acquisition, routine clinical monitoring and administration costs including the management of adverse effect) and utilities for health states were derived from real-world data and supplemented by expert opinion and literature review.
- Key assumptions:** Patients with a history of CHF or stroke at baseline have treatment costs and a utility reduction applied when moving to the post state.
- The incremental cost-effectiveness ratio (ICER) was calculated as the cost per quality-adjusted life year (QALY) gained. All costs were expressed in 2023 US dollars (US\$1 = 7.08 CNY), and costs and QALYs were discounted at an annual rate of 5%.

## Sensitivity analyses

- One-way sensitivity analyses (OWSA) were conducted to assess the impact of individual parameters on the base-case ICER. Probability sensitivity analyses (PSA) were performed using 5,000 Monte Carlo simulations to evaluate the effect of parameter uncertainty on model outcomes.

## RESULTS

### Base-case results

- Compared to amiodarone and sotalol, dronedarone was expected to gain additional 1.28 QALYs (5.15 vs. 3.87) and 1.78 QALYs (5.15 vs. 3.37), with higher costs of \$6,632 (\$11,025 vs. \$4,393) and \$6,278 (\$11,025 vs. \$4,748) over a lifetime horizon, leading to ICERs of \$5,166 and \$3,524 per QALY, respectively.
- For gender-specific subgroups, the cumulative QALY benefits potentially being greater for females than males in any AAD (4.64 vs. 4.16). However, compared to amiodarone, males treated with dronedarone produced more QALY gains (1.33 vs. 1.23) and incurred lower costs (\$6,462 vs. \$6,835) than females, with ICERs of \$4,869 per QALY gained for males and \$5,552 per QALY gained for females.
- A similar trend was observed for sotalol (ICER: \$3,393 per QALY gained and \$3,695 per QALY gained, respectively).

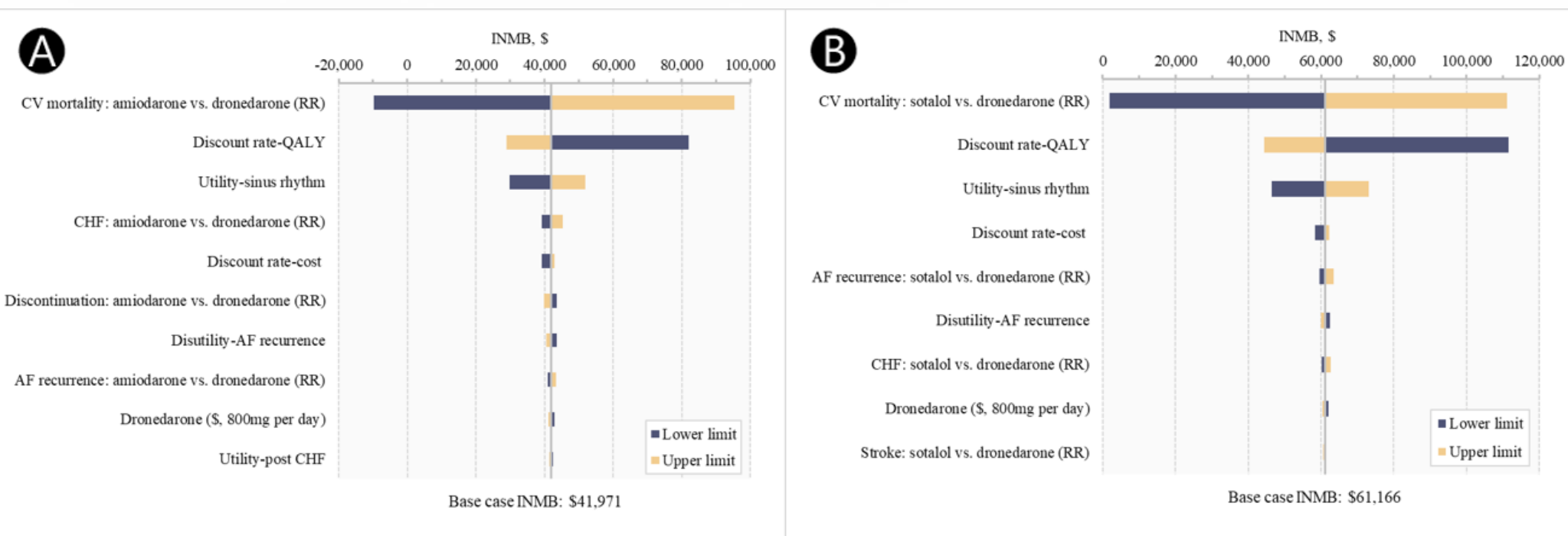
Table 1 Cost-effectiveness of base-case analysis results

Strategy	Dronedarone			Amiodarone			Sotalol		
	Male	Female	Overall	Male	Female	Overall	Male	Female	Overall
Total costs (\$)	5,688	5,337	11,025	2,159	2,234	4,393	2,272	2,475	4,748
Total QALYs	2.63	2.52	5.15	1.90	1.96	3.87	1.62	1.75	3.37
Dronedarone vs. Amiodarone									
Incremental cost (\$)	-	-	-	3,528	3,103	6,632	3,415	2,862	6,278
Incremental QALY	-	-	-	0.72	0.56	1.28	1.01	0.77	1.78
ICER (\$ per QALY gained)	-	-	-	4,869	5,552	5,166	3,393	3,695	3,524

## Sensitivity Analyses results

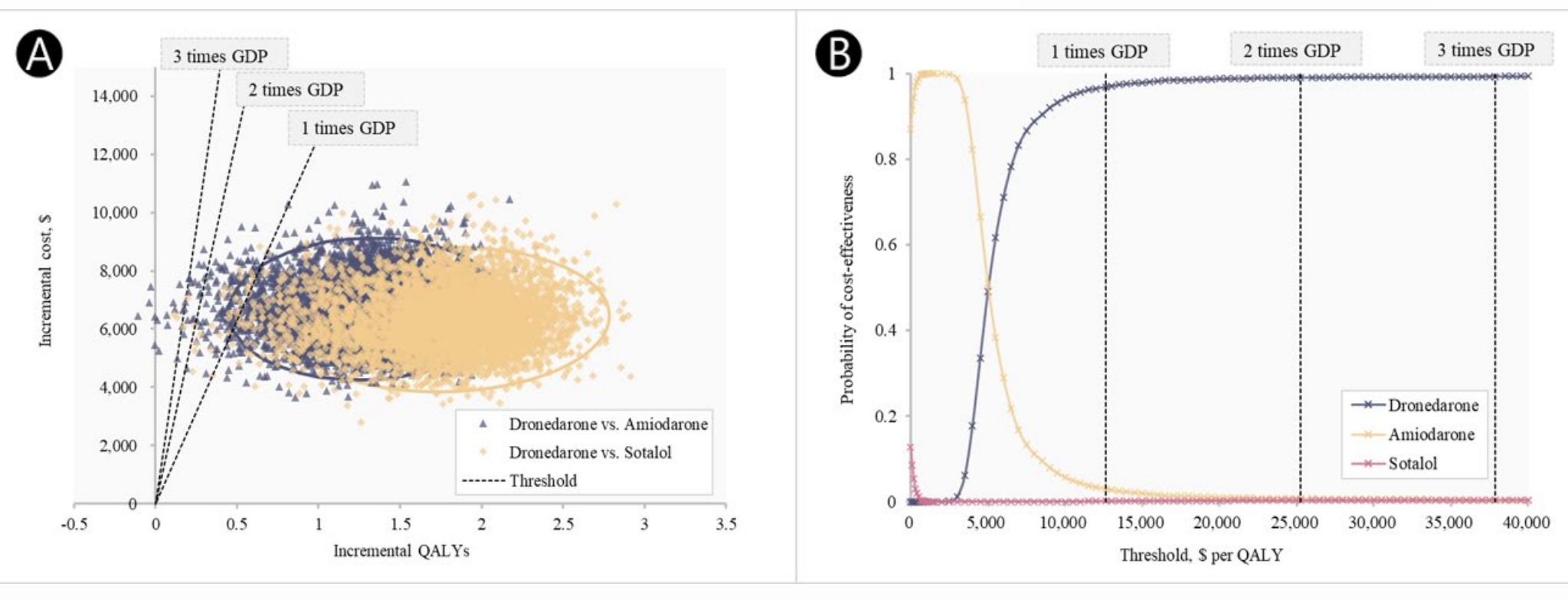
- The OWSA demonstrated similar results between the two comparisons, with the RR of CV mortality, the discount rate of QALYs and the utility for sinus rhythm were most associated with model outcomes.

Figure 2 Tornado diagrams of one-way sensitivity analyses. (A) Dronedarone vs. Amiodarone. (B) Dronedarone vs. Sotalol.



- The scatter plot indicated that dronedarone maintained cost-effectiveness even when the threshold was set at one time the per capita GDP per QALY gained compared to amiodarone or sotalol.
- If we set a threshold of one to three times per capita GDP per QALY gained, the probability of cost-effectiveness for dronedarone ranged from 97.0% to 99.4%, whereas the probability for amiodarone ranged from 3.0% to <1%, and for sotalol was always <1%.

Figure 3 . Results of the probabilistic sensitivity analysis. (A) Scatter plot. (B) Cost-effectiveness acceptability curves.



## CONCLUSIONS

Our analysis suggests that dronedarone is a cost-effective AAD compared to amiodarone and sotalol for patients with paroxysmal or persistent AF in China, offering improvements in life expectancy and QALY in the long-term rhythm control.

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