



INSTITUTE FOR CLINICAL
AND ECONOMIC REVIEW

***Management Options for
Atrial Fibrillation***

**Evidence Review Group Meeting
Massachusetts General Hospital
Boston, MA**

July 16, 2010

Agenda for the Day

- Introductions and potential influences on judgment
- Systematic review on comparative clinical effectiveness
- Decision modeling on comparative clinical effectiveness and comparative value
- Introduction to ICER rating system
- Discussion of potential evidence ratings
- Close

Institute for Clinical and Economic Review (ICER)

- Independent, academic base within the Mass. General Hospital
- Diverse funding
- Broad stakeholder engagement
- Mission:
 - Catalyze the application of evidence on effectiveness and value to guide health care decisions

Appraisal of Management Options for Atrial Fibrillation

Dan Ollendorf, MPH

Scope

- Patients: adults with non-valvular AF, w/o concomitant indications for open-heart surgery
- Interventions and Comparators:
 - AF Management
 - Rhythm control (focus on amiodarone & dronedarone)
 - Catheter ablation (PVI w/ or w/o additional lesion sets)
 - Minimally-invasive surgical ablation (MISA)
 - Stroke Prevention
 - Dabigatran extexilate
 - WATCHMAN™ occlusive device
 - Warfarin

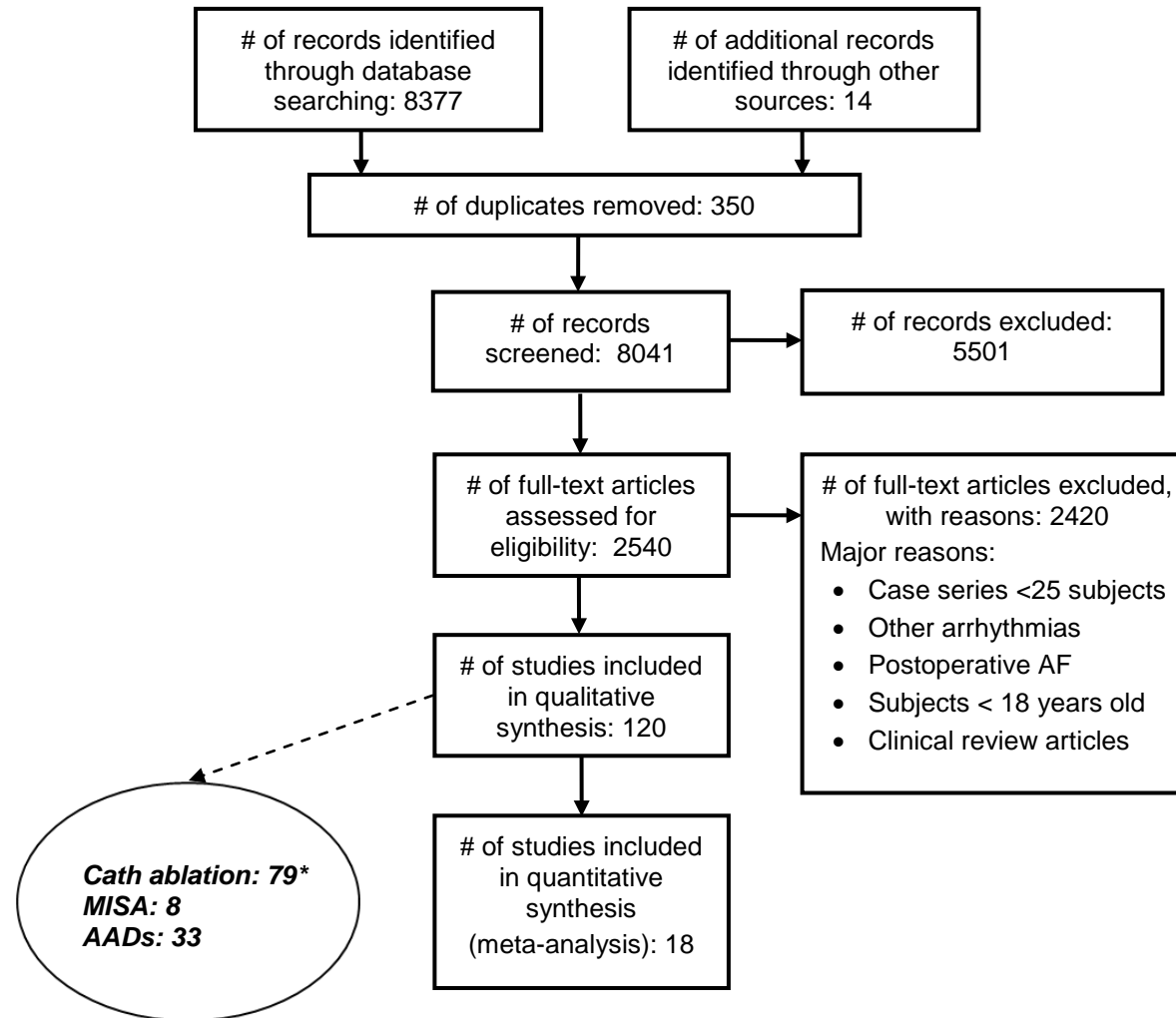
Populations of Particular Interest

- Younger patients with paroxysmal AF and limited/no comorbidities
 - “60 y.o. paroxysmal”
- Patients with symptomatic left ventricular dysfunction in whom return to sinus rhythm may improve cardiac function, quality of life, and length of life
 - “65 y.o. CHF”
- Older patients with persistent/long-standing persistent AF and moderate comorbidity
 - “75 y.o. comorbidity”
- *Additional interest in exploring differential effects of treatment by sex, race/ethnicity, AF type*

Literature Search

- 2009 AHRQ review of catheter ablation used as starting point
 - Additional RCTs, cohorts, and case series abstracted through May 2010
- Major exclusions:
 - Other arrhythmias or atrial flutter
 - Other types of AF (e.g., temporary AF following major surgery)
 - Specific cardiovascular conditions posing independent risks downstream (e.g., congenital heart disease, hypertrophic cardiomyopathy)

Search Results



*Data included on 12 studies from AHRQ review; 67 studies newly-abstracted
MISA: Minimally-invasive surgical ablation; AADs: Antiarrhythmic drugs

Use of Evidence

- Focus on RCT/comparative cohort data for comparisons of effectiveness/harms by management option
 - Meta-analyses conducted when (a) 3 or more fair/good RCTs available; and (b) uniform reporting methods used for outcome
- Case series data summarized descriptively for all outcomes
 - Series exhibiting certain characteristics (e.g., long-term follow-up, large sample size) highlighted

Evidence Quality

- RCT data
 - AADs = 28 (22 good/fair)
 - Catheter ablation = 16 (8 good/fair)
 - MISA = 0
 - Dabigatran = 1
 - WATCHMAN = 1
- Notable heterogeneity in technique, approach, patient populations, follow-up in catheter ablation RCTs

**AADs vs.
Catheter Ablation vs.
MISA**

Patient Population Heterogeneity Across Interventions

Estimate (unweighted average across studies)

Intervention	% Paroxysmal AF	% Male	Age (y)
Catheter Ablation	66.0	76.3	57.0
MISA	55.8	70.7	60.6
AADs	30.0	64.2	65.0

AF: Atrial fibrillation; MISA: Minimally-invasive surgical ablation; AADs: Antiarrhythmic drugs

Benefits: Mortality (all-cause)

- Did not differ between catheter ablation and AADs in RCTs
- Mortality benefit of 50% observed for ablation vs. AADs only in single retrospective cohort study
- Meta-analysis shown in report: no significant mortality effect for ablation vs. AADs
- Literature on MISA too limited to make comparisons with catheter ablation

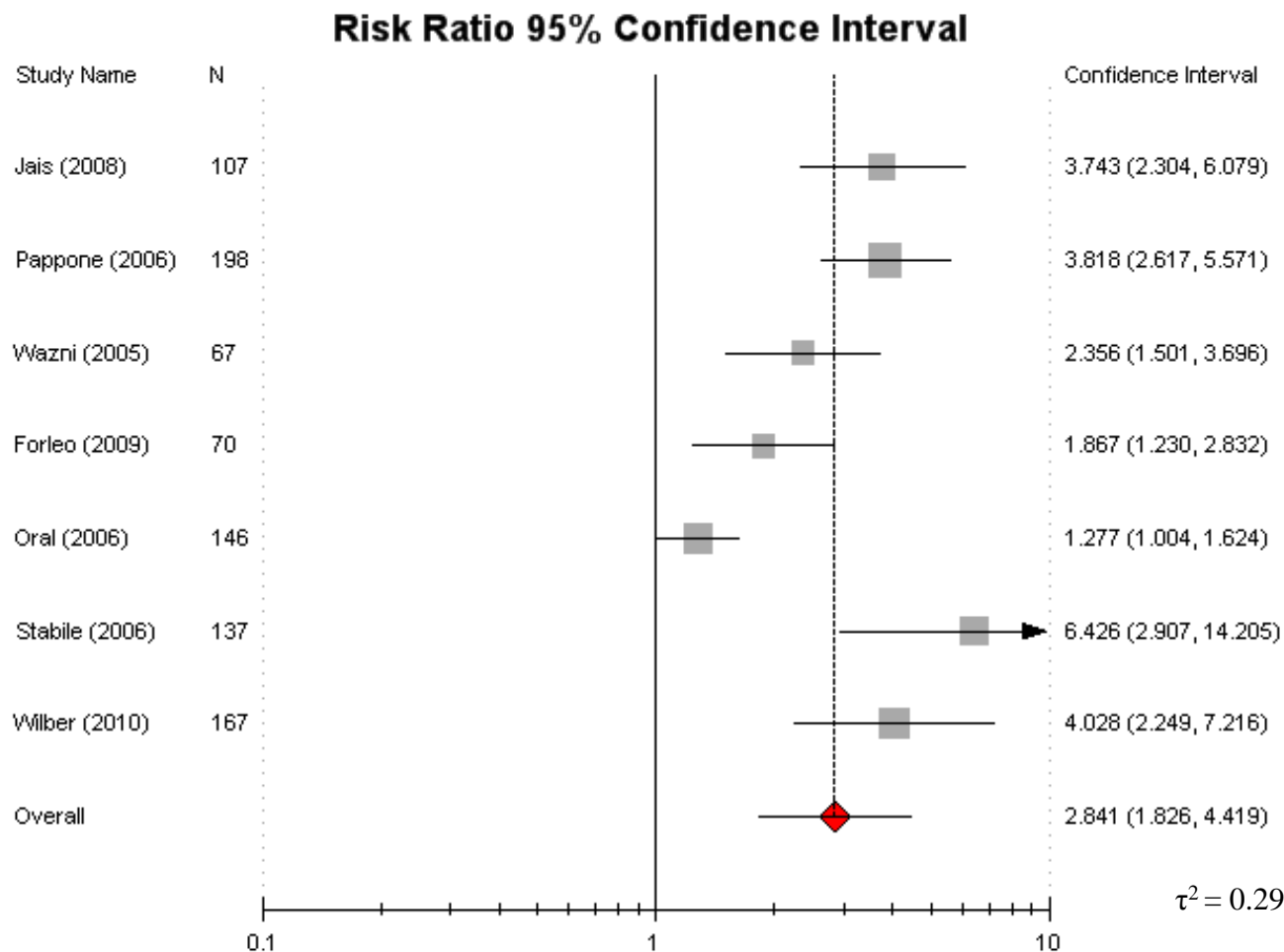
Benefits: Stroke

- Data available only in case series/cohort studies and too limited to be able to make comparisons with any degree of confidence

Benefits: Freedom from AF

- 3-fold greater chance of freedom from AF for catheter ablation vs. AADs at 6-12 months (see next slide)
- Effect more pronounced in studies w/ $\geq 65\%$ paroxysmal patients (RR=3.4) vs. those with “mixed” AF types (RR=2.2)
- MISA data only from case series, but range comparable to that seen for catheter ablation (65-87% at 6-12 mos)

Freedom from AF at 6-12 Months: Catheter Ablation vs. AADs



Benefits: “Late” AF Recurrence

- Short follow-up from most RCTs provides limited view into AF recurrence after 1 year
- Case series data:
 - 40-60% cumulative rates at 2-3 years of follow-up (12-20% after 1 yr)
 - Higher rates seen with persistent vs. paroxysmal AF
 - Diabetes also independent predictor
- CABANA pilot data showed high recurrence rates at 1+ yrs for both catheter ablation (55%) and AADs (69%)

Benefits: Hospitalization

- Evidence from 2 RCTs suggests reductions in rehospitalization rates for catheter ablation vs. AADs (8-9% vs. 34-54%, $p < 0.01$ in both studies)
- Treatment goals make comparisons problematic (e.g., hospitalization for cardioversion/medication change in AAD arms)

Benefits: Quality of Life

- Quality of Life

- Limited evidence from RCTs suggests significant improvement on SF-36 and AF Symptom Frequency and Severity Checklist for catheter ablation vs. AADs at 3-12 months
- Long-term data from recent series suggests effect is independent of ablation outcome (i.e., in NSR, in NSR w/AADs, w/AF recurrence) (Wokhlu, 2010)

- Cessation of Anticoagulation

- No RCT data on impact of stopping oral anticoagulation after catheter ablation on stroke rates
- Cohort data from 5 institutions on 2,700 patients suggest no detrimental effect of stopping OAT, but data are limited by restriction to very low-risk populations and observational nature (Themistoclakis, 2010)

Harms: Repeat Ablation

- Wide range of % of patients requiring repeat catheter ablations in RCTs (10-70%); patients on average required 1.5 ablation procedures
- National payer data suggests ~20% require repeat ablations over 1-3 years of follow-up, with most repeats occurring 12-18 months following initial procedure
- Requirements for retreatment (typically catheter ablation) following MISA seen in 7-18% of patients in case series

Harms: Peri-operative Complications

- Peri-operative mortality and stroke appear to be very rare, with rates $<1\%$ in most circumstances for both catheter ablation and MISA
- Major complications
 - Catheter ablation (range: 0-6% across studies)
 - Major bleeding, cardiac tamponade, worsening heart failure, and moderate-to-severe PV stenosis
 - AE fistula relatively rare (0-2% across studies)
 - MISA (range: 0-13% across studies)
 - Major bleeding or pleural adhesions
- Minor complications
 - Ranges 0-30% for catheter ablation, 6-17% for MISA
 - Most commonly PV stenosis, pericardial effusion, phrenic nerve injury, pacemaker implant

Harms: Training/Learning Curve

- No observational data in the published literature on thresholds for training or the impact of a learning curve for catheter ablation or MISA techniques
 - Findings from 2005 survey suggest better outcomes at centers performing >100 procedures annually (Cappato, 2005)

Primary Catheter Ablation

- Single RCT of primary catheter ablation vs. AADs (Wazni, 2005):
 - 67 patients
 - Limited to younger, paroxysmal only
 - Freedom from AF at 1 year was 87% in PVI group vs. 37% in AAD group ($p < .001$)

Amiodarone vs. Dronedarone

Benefits: Mortality

- Did not differ in head-to-head DIONYSOS trial
- ICER mixed treatment comparison (MTC) meta-analysis found no statistically significant difference between amiodarone and dronedarone in all-cause mortality (OR=1.80; 95% CI=0.68, 4.78)

Benefits: Stroke

- No head-to-head data available
- Stroke rates do not differ between active treatment and placebo/control in all primary RCT analyses
- Post hoc analysis of ATHENA suggests reduced rate with dronedarone (1.2% vs. 1.8%, $p=.027$)

Benefits: Freedom from AF

- Amiodarone ~60% more likely to result in freedom from AF at 12 months in DIONYSOS (58% vs. 37% for dronedarone, $p < .001$)
- ICER MTC meta-analysis found significantly reduced likelihood of freedom from AF for dronedarone and sotalol vs. amiodarone:

	Amiodarone	Sotalol	Dronedarone
	Odds Ratio (95% CI)		
Control	5.68 (3.23, 9.66)	2.16 (0.96, 4.20)	1.67 (0.68, 3.66)
Amiodarone		0.39 (0.18, 0.74)	0.31 (0.12, 0.68)
Sotalol			0.88 (0.27, 2.27)

Benefits: Hospitalization

- There are no data from published studies with which to compare hospitalization rates for patients on amiodarone vs. dronedarone

Benefits: Quality of Life

- Data from 1 amiodarone RCT suggests no difference in QoL improvement vs. rate control
- No published QoL data on dronedarone

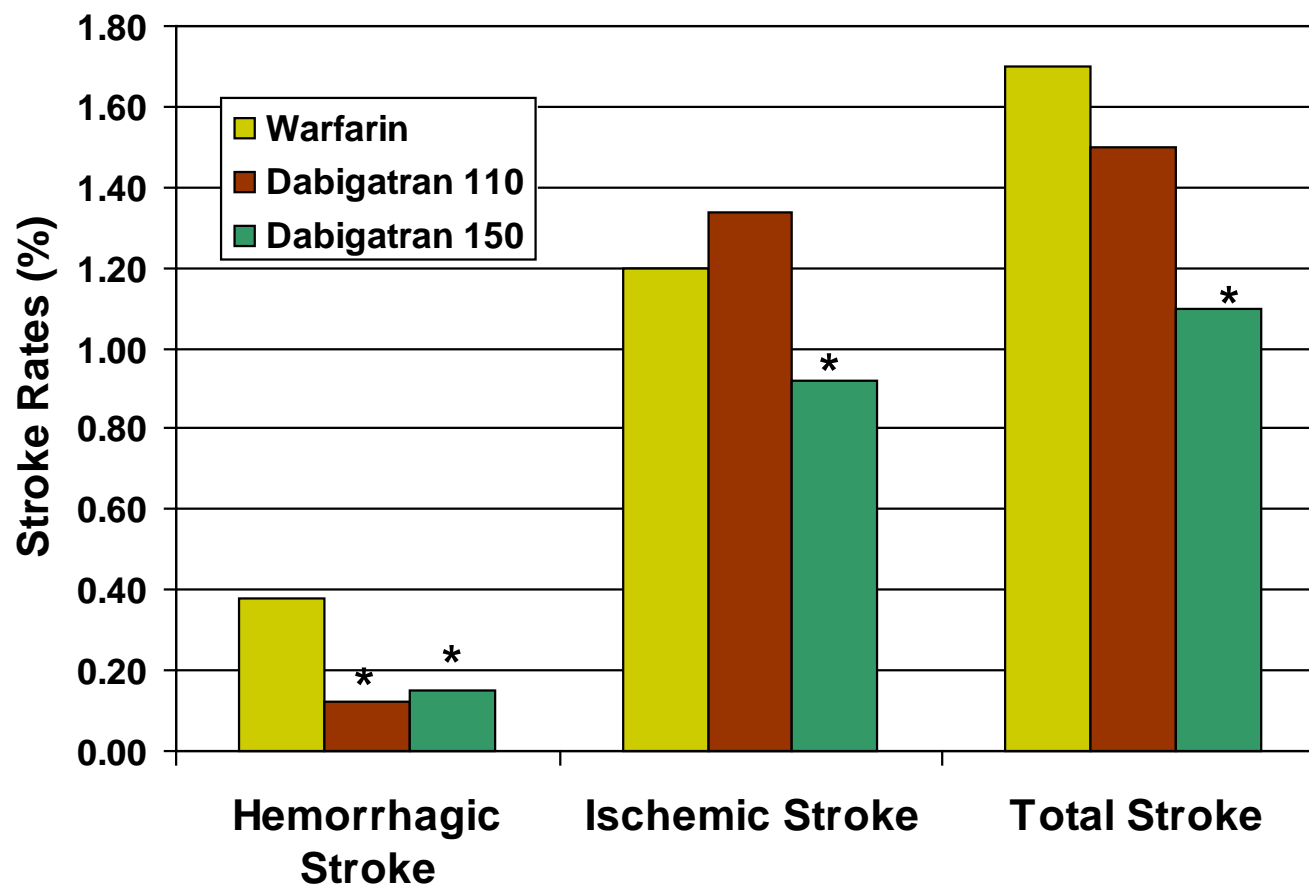
Harms: Drug Toxicities

- Pulmonary toxicity
 - No pulmonary events in either arm in DIONYSOS
 - Wide reported range for amiodarone in past (1-17%) appears to have narrowed with advent of 200 mg maintenance dose (1-2%); rates in RCTs in our review ranged from 0-1.6%
 - Pulmonary toxicity events reported in only one dronedarone RCT, ATHENA (0.1%)
- Thyroid toxicity
 - Higher rate observed for amiodarone in DIONYSOS (10.1% vs. 1.4%, not significance-tested), due primarily to hypothyroidism
 - Rates vary across studies for both agents (0-13%) due to definitional differences

**Dabigatran vs.
WATCHMAN vs.
Warfarin**

Benefits: Stroke Prevention

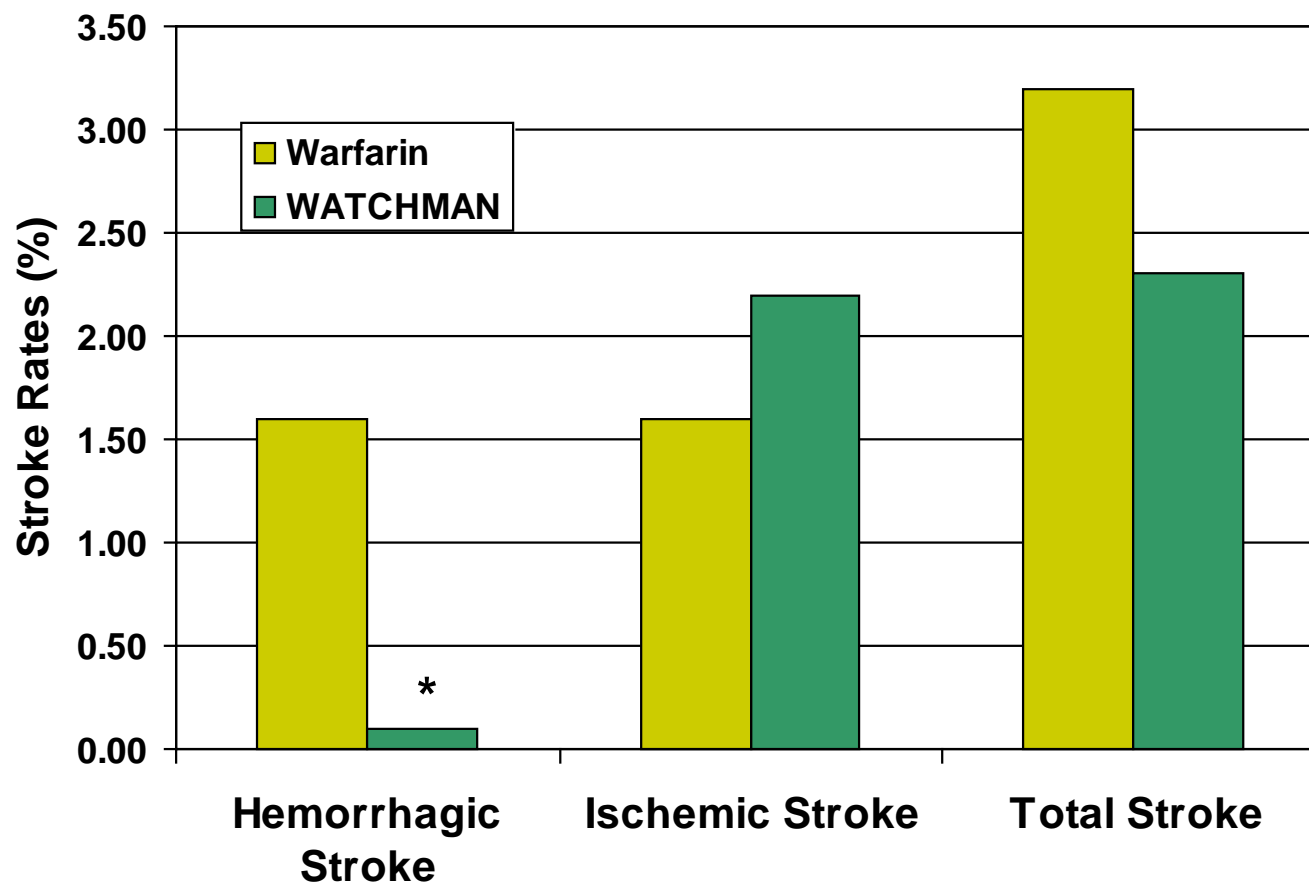
- Annual stroke rates in RE-LY:



*p<.05 vs. warfarin

Benefits: Stroke Prevention

- Annual stroke rates in PROTECT-AF:



*probability of superiority=99.8%

Benefits: Mortality

- Did not significantly differ in either dabigatran or WATCHMAN RCTs
- Comparison of dabigatran 150 mg to warfarin very nearly significant in RE-LY study (3.6% vs. 4.1% for warfarin, $p=.051$)

Benefits: Hospitalization

- Evaluated only in RE-LY
- All-cause annual hospitalization rate significantly reduced for dabigatran 110 mg vs. warfarin (19.4% vs. 20.8%, $p=.003$)
- Rate did not differ for higher dose of dabigatran vs. warfarin

Harms: Bleeding

- Major Bleeding (other than ICH)
 - Annual rate significantly lower for dabigatran 110 mg vs. warfarin (2.7% vs. 3.4%, $p=.003$), comparable in 150 mg comparison (3.1% vs. 3.4%, $p=.31$) in RE-LY
 - Annual rate did not differ for WATCHMAN vs. warfarin in PROTECT-AF (3.5% vs. 4.1%)
- Other Harms
 - Primary safety events occurred more frequently with WATCHMAN in PROTECT-AF (7.4 vs. 4.4 per 100 patient-years), due primarily to serious pericardial effusion and major bleeding

Other Patient Subgroups

- Data generally quite limited
 - No differences in mortality or stroke observed by age or sex
 - Freedom from AF significantly greater among males in 1 catheter ablation cohort study (77.5% vs. 68.5% for females at 24 months, $p < .001$) (Patel, 2010)
 - Dronedarone appears to reduce AF recurrence to a greater extent in patients with heart failure (HR=0.59 vs. 0.81 for those without heart failure) (EURIDIS/ADONIS study)
 - Overall, WATCHMAN was found to be comparable to warfarin on primary outcome; significant reductions in risk were observed among males and those with persistent AF, however

Clinical & Economic Model of Atrial Fibrillation Management Options

Marc D. Silverstein, MD, FACP

Overview

- Key Comparisons
- Model approach, structure, data & analysis
- Patients
- Key Assumptions
- Key Comparisons
 - Results
 - Sensitivity Analyses
 - Findings & Interpretation
- Discussion

Key Comparisons

- Catheter ablation
- Minimally invasive surgical ablation
- Dronedarone for rhythm control
- Dabigatran for stroke prevention
- WATCHMAN procedure for stroke prevention

Model Approach

Approach, 1

- Decision Analysis model
 - Each alternative strategy is represented graphically in a decision tree
- Markov Models
 - Each management strategy has a cardiovascular management component and a stroke prevention component
 - Each management strategy is represented as discrete clinical states, and patients transition between the clinical states over time

Approach, 2

- Perspective
 - Health care system payers perspective with Medicare costs
- 3 Month Markov stage or cycle
 - Lifetime horizon from onset of symptomatic AF
- Discount future costs and QALYs to estimate net present value
 - Discount rate 3% (range 0 to 5%)

Key Strategy Assumptions

Key Strategy Assumptions

- LACA
- MISA
- Dronedarone
- Dabigatran
- WATCHMAN

Patients



Patient Types

- 60 yrs, Paroxysmal AF, ($CHADS_2=0$)
- 65 yrs, CHF, Persistent AF ($CHADS_2=1$)
- 75 yrs, DM, HTN, Persistent AF ($CHADS_2=3$)

Model Data

Model Data

- Probabilities
 - Published data & vital statistics
 - ICER systematic review
- Costs
 - Medicare fee schedule
- Utilities - Quality of Life (QoL)
 - Published CEAs - AF patients
 - EuroQol (EQ-5D) for US non-institutionalized population, US norms

Atrial Fibrillation Alternative Scenarios

Four Alternative Scenarios for Sensitivity Analysis

- Impact of atrial fibrillation on quality of life
- Stroke risk in normal sinus rhythm after ablation
- Stopping warfarin in normal sinus rhythm after ablation
- Impact of warfarin on quality of life

#1 Catheter Ablation Strategies

Rhythm vs. Rate Control

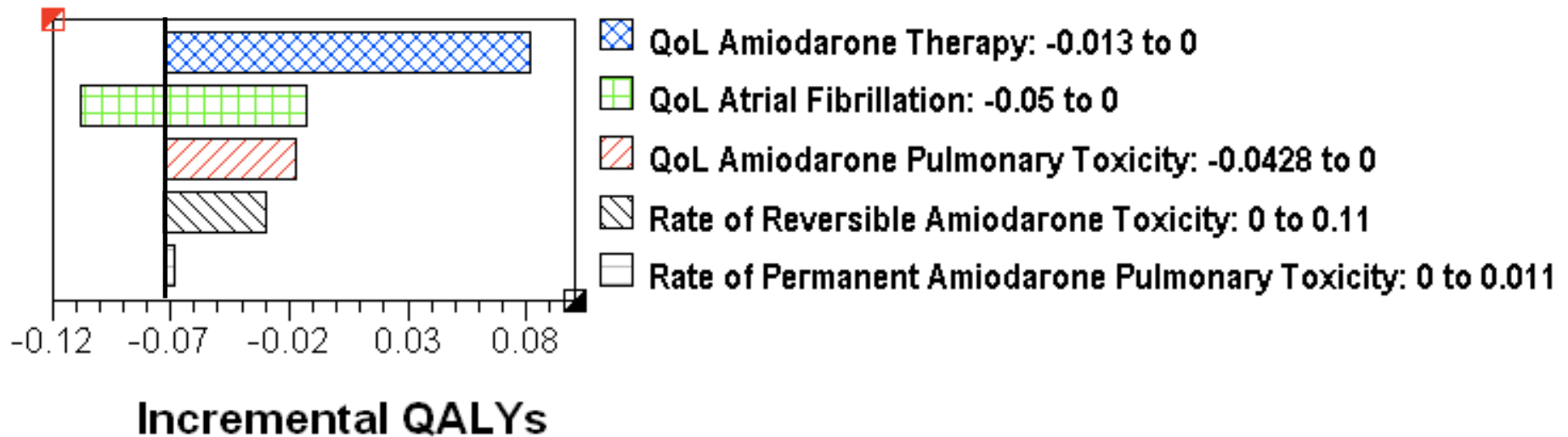
Strategy	Cost	Incremental Cost	QALYs	Incremental QALYs	ICER (\$/QALYs)
60 yrs, Paroxysmal AF					
Rate Control	\$16,985		12.025		
Rhythm Control	\$27,315	\$10,330	11.922	-0.104	Dominated
65 yrs, CHF, Persistent AF					
Rate Control	\$17,722		9.454		
Rhythm Control	\$26,293	\$8,570	9.383	-0.072	Dominated
75 yrs, DM, HTN, Persistent AF					
Rate Control	\$16,059		6.522		
Rhythm Control	\$22,088	\$6,028	6.485	-0.038	Dominated

Sensitivity Analysis

Rhythm vs. Rate Control

Sensitivity Analysis, 65 yrs, CHF Persistent AF

Rhythm Control vs. Rate Control



Rhythm Control vs. Rate Control

Summary

- Rhythm control has lower QoL and higher costs than rate control across all three patient scenarios.
- The lower QoL of rhythm control results from the decreased quality of life associated with amiodarone toxicity.

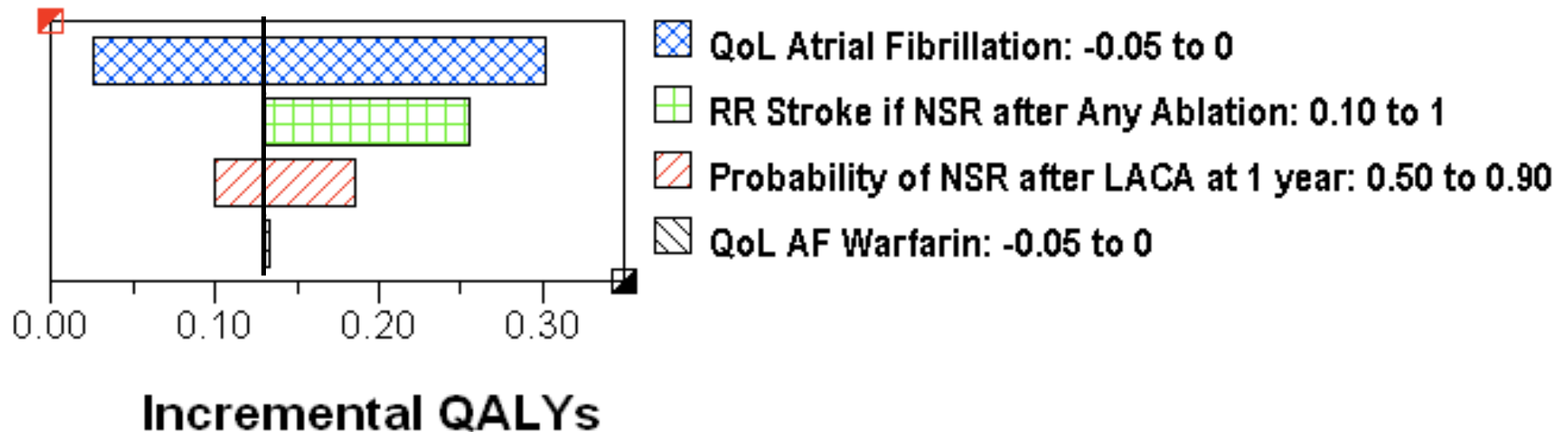
Secondary LACA vs. Rhythm Control

Strategy	Cost	Incremental Cost	QALYs	Incremental QALYs	ICER (\$/QALYs)
60 yrs, Paroxysmal AF					
Rhythm Control	\$27,315		11.922		
Secondary LACA	\$39,064	\$11,748	12.134	0.213	\$55,226
65 yrs, CHF, Persistent AF					
Rhythm Control	\$26,293		9.383		
Secondary LACA	\$41,206	\$14,913	9.514	0.131	\$114,111
75 yrs, DM, HTN, Persistent AF					
Rhythm Control	\$22,088		6.485		
Secondary LACA	\$36,317	\$14,229	6.582	0.098	\$145,604

Sensitivity Analysis

Secondary LACA vs. Rhythm Control

Sensitivity Analysis, 65 yrs, CHF Persistent AF Secondary LACA vs Rhythm Control



Secondary LACA vs. Rhythm Control Summary

- Secondary LACA has higher QoL than rhythm control across all patient scenarios but the incremental benefit diminishes with increasing age and comorbidity.
- Secondary LACA has higher incremental costs than rhythm control across all patient scenarios.
- The increased QoL results from substantial reduction in time in AF and decreased drug toxicity.
- The ICER for secondary LACA compared to rate control range from approximately \$50,000 per QALY in the younger patient with paroxysmal AF to approximately \$145,000 in the older patients with comorbidity.

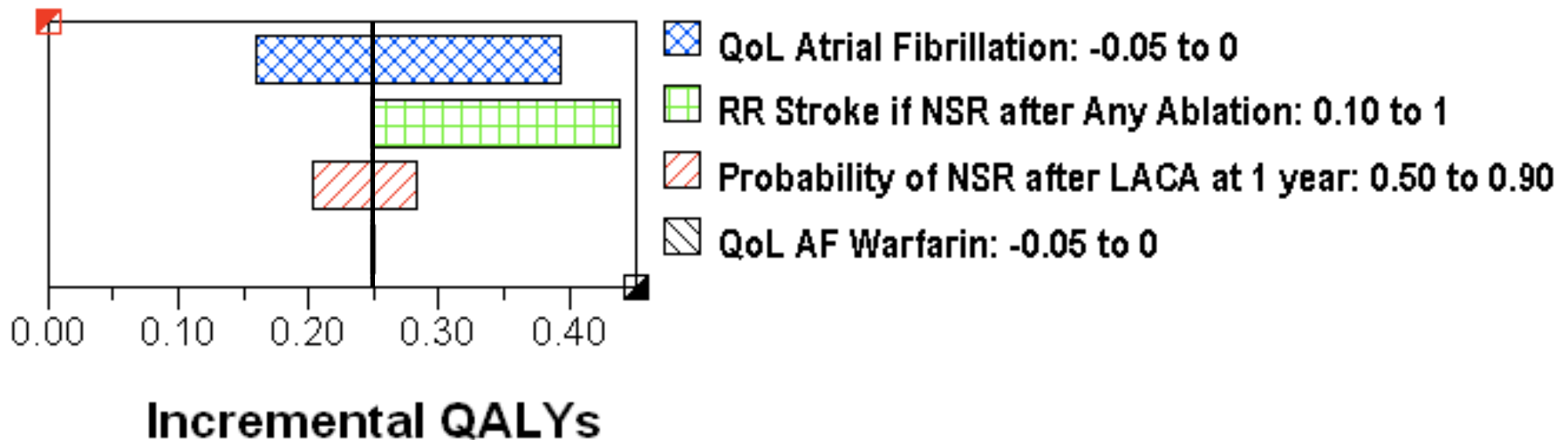
Primary LACA vs. Rhythm Control

Strategy	Cost	Incremental Cost	QALYs	Incremental QALYs	ICER (\$/QALYs)
60 yrs, Paroxysmal AF					
Rhythm Control	\$27,315		11.922		
Primary LACA	\$35,089	\$7,773	12.304	0.383	\$20,319
65 yrs, CHF, Persistent AF					
Rhythm Control	\$26,293		9.383		
Primary LACA	\$39,648	\$13,356	9.631	0.248	\$53,779
75 yrs, DM, HTN, Persistent AF					
Rhythm Control	\$22,088		6.485		
Primary LACA	\$36,408	\$14,320	6.671	0.186	\$130,618

Sensitivity Analysis

Primary LACA vs. Rhythm Control

Sensitivity Analysis, 65 yrs, CHF Persistent AF
Primary LACA vs. Rhythm



Primary LACA vs. Rhythm Control Summary

- Primary LACA compared to rhythm control has higher QoL across all patient groups, but the difference diminishes with increasing age and comorbidity.
- Primary LACA has higher costs than rhythm control.
- The higher QoL is due to the large reduction in AF time and drug toxicity; the higher QoL persists even if there were not decreased QoL with AF compared to NSR.
- The ICER of primary LACA compared to rhythm control ranges from \$20,000 in younger patients with paroxysmal AF to \$130,000 in older patients with comorbidity.

Alternative Catheter Ablation Scenarios

RR Stroke after Ablation (NSR) = 0.20

Stop warfarin for CHADS₂ = 0, 1 or 2

Alternative Scenario Summary

Stroke Risk in NSR after Ablation

- The scenario assumes
 - RR of stroke in NSR after ablation = 0.20, compared to risk predicted based on CHADS₂ adjusted for secular trends
 - Stopping warfarin for patients with CHADS₂ ≤ 2
- There is increased in QoL across all patient scenarios for both primary and secondary LACA compared to rhythm control.
- ICERs compared to rhythm control range from
 - \$4,000 to \$36,000 for Primary LACA
 - \$23,000 to \$70,000 for Secondary LACA

#2 Surgical Ablation Strategies

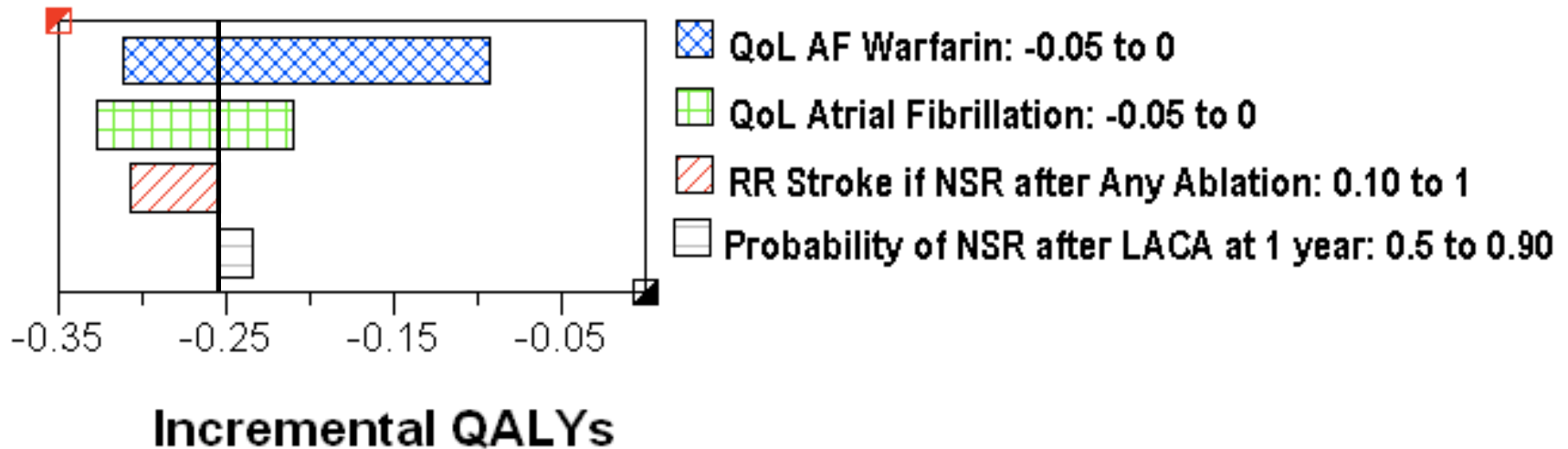
MISA vs. Secondary LACA

Strategy	Cost	Incremental Cost	QALYs	Incremental QALYs	ICER (\$/QALYs)
60 yrs, Paroxysmal AF					
Secondary LACA	\$39,064		12.134		
MISA	\$45,653	\$6,589	11.837	-0.297	Dominated
65 yrs, CHF, Persistent AF					
Secondary LACA	\$41,206		9.514		
MISA	\$45,902	\$4,696	9.259	-0.254	Dominated
75 yrs, DM, HTN, Persistent AF					
Secondary LACA	\$36,317		6.582		
MISA	\$41,677	\$5,360	6.296	-0.287	Dominated

Sensitivity Analysis

MISA vs. Secondary LACA

Sensitivity Analysis, 65 yrs, CHF Persistent AF
MISA vs. Secondary LACA



MISA vs. Secondary LACA Summary

- MISA has lower QoL than secondary LACA for all patient groups and higher incremental costs for all patient groups.
- The lower QoL results from more time in AF and the higher risk of complications.
- The analysis assumes similar 1 year NSR response rates and rates of recurrent AF, and lower AF time in primary reflects increased use of repeat LACA procedures for recurrent AF in the AF strategy.

#3 Dronedarone for Rhythm Control

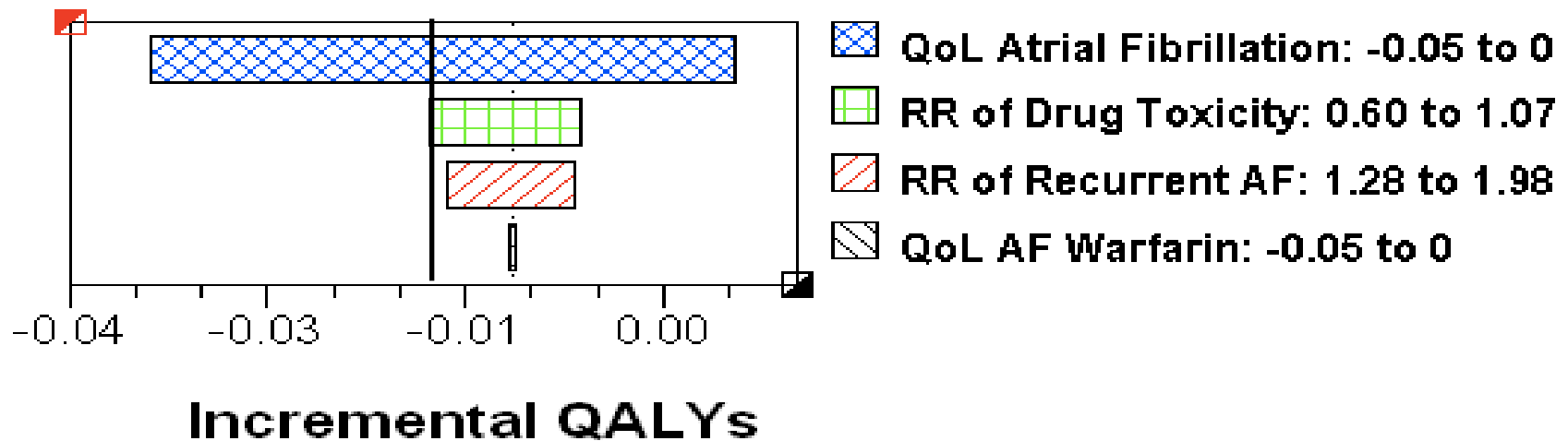
Dronedarone vs. Amiodarone

Strategy	Cost	Incremental Cost	QALYs	Incremental QALYs	ICER (\$/QALYs)
60 yrs, Paroxysmal AF					
Amiodarone	\$27,315		11.922		
Dronedarone	\$62,941	\$35,626	11.911	-0.011	Dominated
65 yrs, CHF, Persistent AF					
Amiodarone	\$26,293		9.383		
Dronedarone	\$57,802	\$31,510	9.371	-0.011	Dominated
75 yrs, DM, HTN, Persistent AF					
Amiodarone	\$22,088		6.485		
Dronedarone	\$45,174	\$23,086	6.475	-0.010	Dominated

Sensitivity Analysis

Dronedarone vs. Amiodarone

Sensitivity Analysis, 65 yrs, CHF Persistent AF Dronedarone vs Amiodarone



Dronedarone vs. Amiodarone

Summary

- Dronedarone has lower QoL than amiodarone and higher costs across all patient scenarios.
- The lower QoL of dronedarone results from the higher risk of recurrent AF and the QoL associated with AF, which have a greater impact than the decreased drug toxicity.

#4 Dabigatran for Stroke Prevention

Dabigatran vs. Warfarin

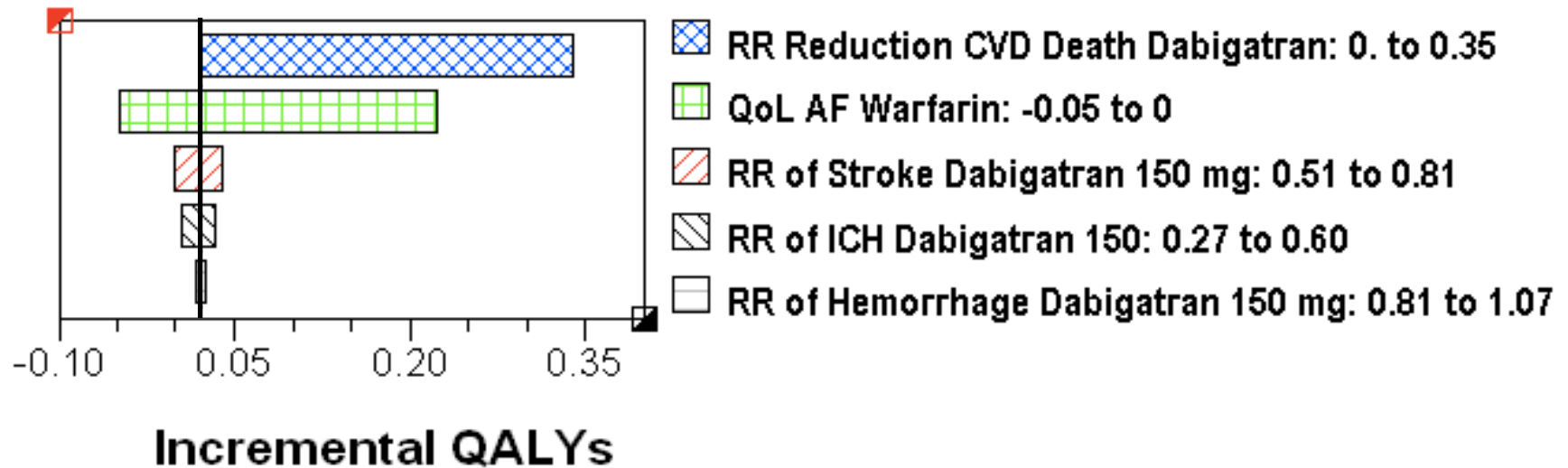
Strategy	Cost	Incremental Cost	QALYs	Incremental QALYs	ICER (\$/QALYs)
60 yrs, Paroxysmal AF					
Warfarin (Rhythm)	\$27,315		11.922		
Dabigatran 110	\$91,287	\$63,972	11.912	-0.010	Dominated
Dabigatran 150	\$91,038	\$63,722	11.927	0.005	\$11,988,467
65 yrs, CHF, Persistent AF					
Warfarin (Rhythm)	\$26,293		9.383		
Dabigatran 110	\$79,759	\$53,466	9.379	-0.004	Dominated
Dabigatran 150	\$79,388	\$53,095	9.405	0.022	\$2,402,159
75 yrs, DM, HTN, Persistent AF					
Warfarin (Rhythm)	\$22,088		6.485		
Dabigatran 110	\$56,577	\$34,489	6.344	-0.140	Dominated
Dabigatran 150	\$56,096	\$34,008	6.381	-0.104	Dominated

All strategies compared within rhythm control

Sensitivity Analysis

Dabigatran 150 mg vs. Warfarin

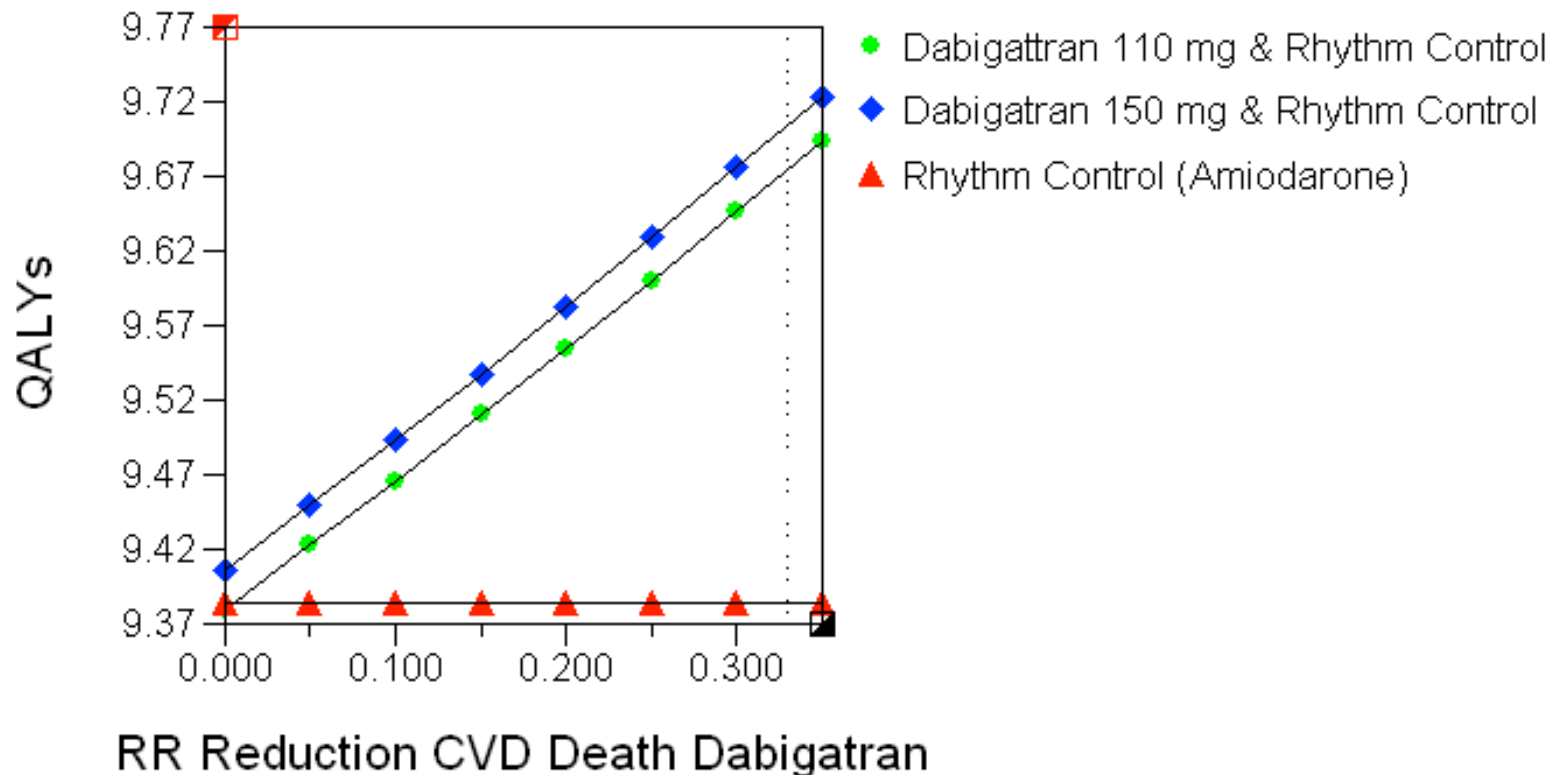
Sensitivity Analysis, 65 yrs, CHF Persistent AF
Dabigatran 150 vs Warfarin



Dabigatran Sensitivity Analysis

RRR for CVD Death

**Sensitivity Analysis on RR Reduction CVD Death Dabigatran
65 M CHF, Persistent AF**



Dabigatran vs. Warfarin Summary

- In our base case, with none of warfarin's cardio-protective effects attributed to dabigatran, warfarin produces more QALYs for most patients.
- If dabigatran were assumed to have the same reduction in cardiovascular death as warfarin, both doses of dabigatran would produce higher QALYs than warfarin.

#5 WATCHMAN for Stroke Prevention

WATCHMAN vs. Warfarin

Strategy	Cost	Incremental Cost	QALYs	Incremental QALYs	ICER (\$/QALYs)
60 yrs, Paroxysmal AF					
Warfarin	\$16,985		12.025		
WATCHMAN	\$26,475	\$9,490	12.027	0.002	\$4,544,408
65 yrs, CHF, Persistent AF					
Warfarin	\$17,722		9.454		
WATCHMAN	\$26,254	\$8,532	9.469	0.014	\$593,974
75 yrs, DM, HTN, Persistent AF					
Warfarin	\$16,059		6.522		
WATCHMAN	\$24,427	\$8,368	6.433	-0.089	Dominated

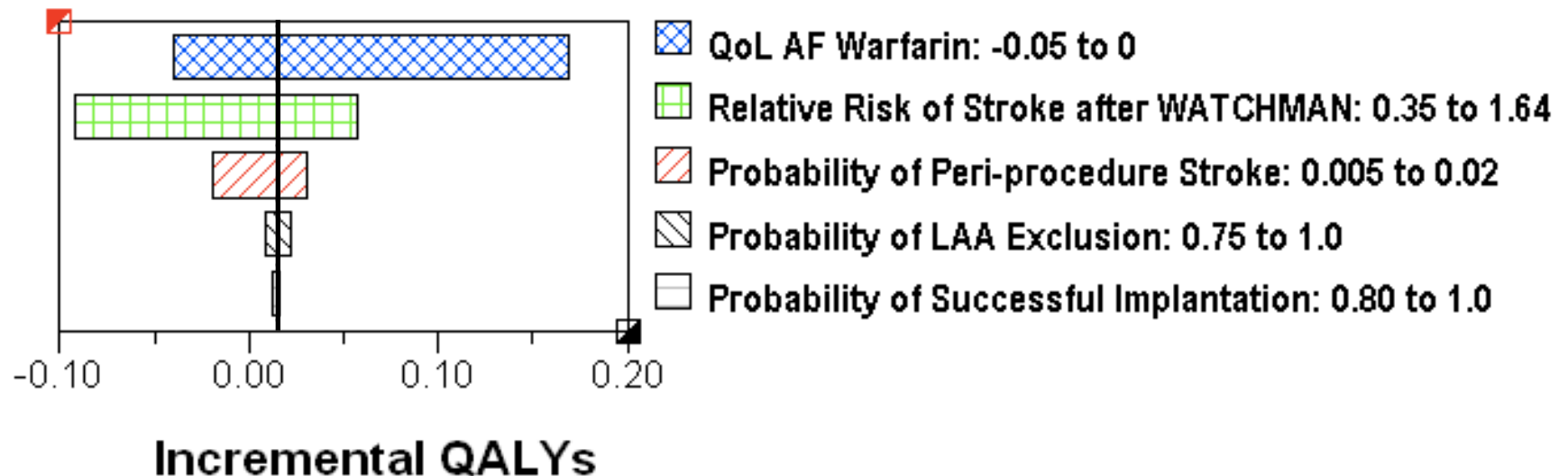
Strategies compared within rate control.

Sensitivity Analysis

WATCHMAN vs. Warfarin

Sensitivity Analysis, 65 yrs, CHF Persistent AF

WATCHMAN vs. Warfarin



WATCHMAN vs. Warfarin Summary

- The WATCHMAN strategy compared to warfarin produces minimal to no QALY difference. The WATCHMAN strategy is more expensive.
- For patients with more severe disutility from taking warfarin, WATCHMAN produces modestly higher QALYs.
- The incremental cost-effectiveness ratios for WATCHMAN are very high due to the increased costs and small increased QoL.

Discussion

ERG Deliberation: Integrated Evidence Ratings

ICER Integrated Evidence Rating

Comparative Clinical Effectiveness

Superior: A	Aa	Ab	Ac
Incremental: B	Ba	Bb	Bc
Comparable: C	Ca	Cb	Cc
Inferior: D	Da	Db	Dc
Unproven/Potential: U/P	Ua	Ub	Uc
Insufficient: I	I	I	I

a
High

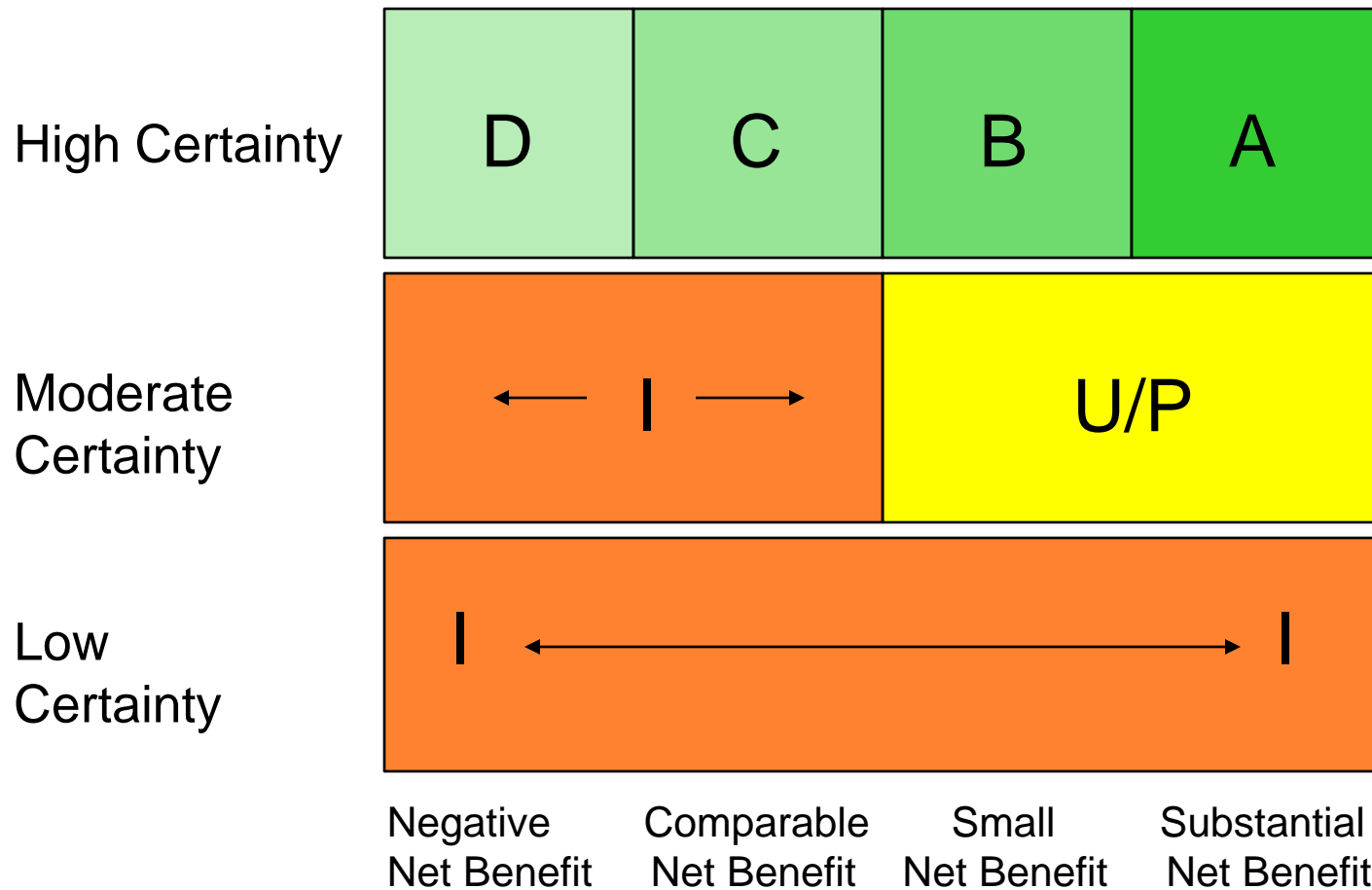
b
Reasonable/Comp

c
Low

Comparative Value

EBM Matrix

Comparative Clinical Effectiveness



Secondary LACA vs. Rhythm Control

Comparative Clinical Effectiveness

Superior: A	Aa	Ab	Ac
Incremental: B	Ba	Bb	Bc
Comparable: C	Ca	Cb	Cc
Inferior: D	Da	Db	Dc
Unproven/Potential: U/P	Ua	Ub	Uc
Insufficient: I	I	I	I
	a	b	c
	High	Reasonable/Comp	Low
	<i>Comparative Value</i>		

Primary LACA vs. Rhythm Control

Comparative Clinical Effectiveness

Superior: A	Aa	Ab	Ac
Incremental: B	Ba	Bb	Bc
Comparable: C	Ca	Cb	Cc
Inferior: D	Da	Db	Dc
Unproven/Potential: U/P	Ua	Ub	Uc
Insufficient: I	I	I	I

a
High

b
Reasonable/Comp

c
Low

Comparative Value

MISA vs. LACA

Comparative Clinical Effectiveness

Superior: A	Aa	Ab	Ac
Incremental: B	Ba	Bb	Bc
Comparable: C	Ca	Cb	Cc
Inferior: D	Da	Db	Dc
Unproven/Potential: U/P	Ua	Ub	Uc
Insufficient: I	I	I	I

a
High

b
Reasonable/Comp

c
Low

Comparative Value

Dabigatran vs. Warfarin

Comparative Clinical Effectiveness

Superior: A	Aa	Ab	Ac
Incremental: B	Ba	Bb	Bc
Comparable: C	Ca	Cb	Cc
Inferior: D	Da	Db	Dc
Unproven/Potential: U/P	Ua	Ub	Uc
Insufficient: I	I	I	I

a
High

b
Reasonable/Comp

c
Low

Comparative Value

WATCHMAN™ vs. Warfarin

Comparative Clinical Effectiveness

Superior: A	Aa	Ab	Ac
Incremental: B	Ba	Bb	Bc
Comparable: C	Ca	Cb	Cc
Inferior: D	Da	Db	Dc
Unproven/Potential: U/P	Ua	Ub	Uc
Insufficient: I	I	I	I

a

High

b

Reasonable/Comp

c

Low

Comparative Value

Close

- Next steps
- ERG Feedback
 - What information did you not find useful?
 - Process of ERG input throughout the appraisal
 - Best role for patients, clinical experts, and manufacturers?
 - Other?

Thank you!
