

SUPPLEMENTAL MATERIAL

Cost effectiveness of left atrial appendage closure with the Watchman Device compared to warfarin or NOACs for secondary prevention in NVAF

Abbreviations list

AF=Atrial fibrillation

GI=gastrointestinal

ICER=Incremental cost-effectiveness ratio

LAAC=Left atrial appendage closure

MRS=modified Rankin score

NOACs=non-warfarin oral anticoagulants

OACs=Oral anticoagulants

PSA=Probabilistic sensitivity analysis

QoL=Quality of life

QALYs=Quality-adjusted life years

TEE=Transesophageal echocardiogram

TIA=Transient ischemic attack

Supplemental Methods

Health State Utilities and Stroke Outcomes

Health state utilities and stroke outcomes are reported in Table II. Warfarin stroke outcomes were estimated using a weighted average of outcomes from four warfarin trials and reflect the results from all patients due to the fact that warfarin secondary prevention stroke outcomes varied widely across studies.^{1,2,3,4} To remain consistent, NOAC stroke outcomes were also taken from the overall stroke prevention populations from each of the respective trials, as available.^{5,6,7} Rates of nondisabling strokes were obtained for all three NOACs, and the rate of fatal strokes was available for apixaban and rivaroxaban. For dabigatran, the rate of fatal strokes was calculated as the average of the ratio of fatal stroke to nondisabling strokes for apixaban and rivaroxaban. The inverse of nondisabling and fatal strokes was assumed to represent disabling strokes for each of the NOACs and was evenly distributed across the moderately disabling and severely disabling stroke outcomes.

Supplemental Tables

Table I. Clinical inputs

	Value	Range	Distribution	Source
LAAC – Post-procedural Events				
RR of ischemic stroke*	1.08	0.86-1.30	Lognormal	Boston Scientific, unpublished data, 2017
RR of major bleeding*	0.68	0.54-0.82	Lognormal	8
Percentage of major bleeding that is hemorrhagic stroke [†]	33.00%	26.40-39.60%	Beta	9
Annual risk of systemic embolism [‡]	0.22%	0.18-0.26%	Beta	Boston Scientific, unpublished data, 2017,9
Annual risk of myocardial infarction	1.01%	0.81-1.21%	Beta	9
Annual risk of minor bleeding	Based on concomitant drug therapy			
Warfarin				
RR of ischemic stroke (relative to no therapy)	0.35	0.20-0.57	Lognormal	9
RR of major bleeding (relative to HAS-BLED)	1.00	0.80-1.20	Lognormal	8
Percentage of major bleeding that is hemorrhagic stroke [†]	21.75%	17.40-26.10%	Beta	10
Annual risk of systemic embolism	0.20%	0.16-0.24%	Beta	9
Annual risk of myocardial infarction	0.64%	0.51-0.77%	Beta	5,6,7,9
Annual risk of minor bleeding	18.0%	14.4-21.6%	Beta	5,6,7,9

Dabigatran				
RR of ischemic stroke*	1.00	0.65-1.54*	Lognormal	5
RR of major bleeding*	1.00	0.77-1.34*	Lognormal	5
Percentage of major bleeding that is hemorrhagic stroke [†]	12.75%	10.40-15.60%	Beta	5
Annual risk of systemic embolism	0.16%	0.13-0.19%	Beta	5
Annual risk of myocardial infarction	1.02%	0.82-1.22%	Beta	5
Annual risk of minor bleeding	12.75%	10.2-15.3%	Beta	5
Apixaban				
RR of ischemic stroke*	0.86	0.60-1.22	Lognormal	7
RR of major bleeding*	0.73	0.55-0.98	Lognormal	7
Percentage of major bleeding that is hemorrhagic stroke [†]	19.48%	15.58-23.38%	Beta	7
Annual risk of systemic embolism	0.21%	0.16-0.24%	Beta	7
Annual risk of myocardial infarction	0.56%	0.45-0.68%	Beta	11
Annual risk of minor bleeding	16.51%	13.21-19.81%	Beta	7
Rivaroxaban				
RR of ischemic stroke*	1.03	0.82-1.30	Lognormal	6
RR of major bleeding*	0.97	0.79-1.19	Lognormal	6
Percentage of major bleeding that is	19.10%	15.28-22.92%	Beta	6

hemorrhagic stroke [†]				
Annual risk of systemic embolism	0.17%	0.14-0.20%	Beta	6
Annual risk of myocardial infarction	0.72%	0.58-0.87%	Beta	6
Annual risk of minor bleeding	10.78%	8.62-12.94%	Beta	6
No Therapy				
RR of ischemic stroke*	1.00	0.80 – 1.20	Lognormal	Based on CHADS2
RR of major bleeding*	0.24	0.19 – 0.29	Lognormal	9
Percentage of major bleeding that is hemorrhagic stroke [†]	25.00%	20.00 – 30.00%	Beta	9
Annual risk of systemic embolism	1.25%	1.00 – 1.50%	Beta	9
Annual risk of myocardial infarction	1.10%	0.88 – 1.32%	Beta	9
Annual risk of minor bleeding	5.60%	4.48% - 6.72%	Beta	9
Aspirin				
RR of ischemic stroke (relative to no therapy)	0.76	0.61 – 0.91	Lognormal	9
RR of major bleeding*	0.68	0.54 – 0.82	Lognormal	12
Percentage of major bleeding that is hemorrhagic stroke [†]	33.00%	26.40 – 39.60%	Beta	9
Annual risk of systemic embolism	0.71%	0.57 – 0.85%	Beta	9

Annual risk of myocardial infarction	0.95%	0.76 – 1.14%	Beta	9
Annual risk of minor bleeding	7.00%	5.60 – 8.40%	Beta	9

RR = relative risk

* All relative risks are relative to warfarin unless otherwise stated.

† Hemorrhagic stroke is calculated as a percent of major bleeding events.

‡ No systemic emboli were observed in the secondary prevention sub-group analysis of PROTECT AF. To adjust for this, the ongoing risk of systemic embolism was calculated using the risk of systemic embolism from the warfarin arm of the secondary prevention analysis of the European Atrial Fibrillation Trial multiplied by the relative risk of ischemic stroke from PROTECT AF. (Boston Scientific, unpublished data, 2017,⁹)

Table II. Stroke outcomes and health state utilities

	LAAC	Warfarin	Dabigatran	Apixaban	Rivaroxaban	Utility Value
Nondisabling stroke (MRS 0-2)	75% (Boston Scientific, unpublished data, 2017)	24% (1-4)	36%(13)	58%(11)	48%(14)	0.76(15)
Moderately disabling stroke (MRS 3)	5% (Boston Scientific, unpublished data, 2017)	29% (1-4)	24%*	11%*	13%*	0.39(15)
Severely disabling stroke (MRS 4-5)	10% (Boston Scientific, unpublished data, 2017)	35% (1-4)	24%*	10%*	13%*	0.11(15)
Fatal stroke (MRS 6)	10% (Boston Scientific, unpublished data, 2017)	12% (1-4)	16%*	21%(11)	26%(14)	0.000

* Dabigatran fatal strokes was calculated as the average ratio of fatal strokes to nondisabling strokes for apixaban and rivaroxaban; the inverse of nondisabling and fatal strokes was assumed to represent disabling strokes for each of the NOACs and was evenly distributed across the moderately disabling and severely disabling stroke outcomes.

Table III. Cost inputs

Event	Costs	Code (Source)
LAAC procedure and 2 TEEs*	\$16,109	DRG 273/274 (16,17)
Fatal ischemic stroke	\$11,171	DRG 063 (16)
Severe ischemic stroke	\$47,886	DRG 061/CMG 108-110 (16,18)
Moderate ischemic stroke	\$33,034	DRG 062/CMG 105-107 (16,18)
Nondisabling ischemic stroke	\$23,128	DRG 063/CMG 101-104 (16,18)
TIA	\$4,267	DRG 069 (16)
Systemic embolism (non-fatal)	\$5,155	DRG 068 (16)
Systemic embolism (fatal)	\$8,466	DRG 067 (16)
Fatal hemorrhagic stroke	\$10,231	DRG 064 (16)
Severe hemorrhagic stroke	\$42,267	DRG 064/CMG 108-110 (16,18)
Moderate hemorrhagic stroke	\$28,118	DRG 065/CMG 105-107 (16,18)
Nondisabling hemorrhagic stroke	\$18,603	DRG 066/CMG 101-104 (16,18)
Major extracranial hemorrhage (non-fatal)	\$5,875	DRG 377 (16)
Major extracranial hemorrhage (fatal)	\$10,339	DRG 378 (16)
Minor bleeding	\$420	CPT 42970 (17)
Myocardial infarction (non-fatal)	\$6,042	DRG 280,281,282 (16)
Myocardial infarction (fatal)	\$5,829	DRG 283,284,285 (16)
Quarterly Costs		
Warfarin + INR monitoring	\$109	CPT 85610, 99211 (17,19)
NOAC	\$969	19
Independent post-stroke	\$108	20,21,22
Moderately disabled post-stroke	\$9,381	20,21,22
Severely disabled post-stroke	\$15,274	20,21,22

*Costs for the LAAC procedure reflect 2016 CMS reimbursement rates. Weighting reflects an 18%/82% split across DRG 273 and 274.²³

Table IV. Total costs and QALYs over 20 years for warfarin, dabigatran, and apixaban using base case inputs. Incremental costs, incremental QALYs, and ICERs were calculated relative to warfarin.

	Total Costs	Total QALYs	Incremental Costs (NOAC minus warfarin)	Incremental QALYs (NOAC minus warfarin)	ICER (NOAC versus warfarin)
20 Years					
Warfarin	\$85,577	5.662	--	--	--
Dabigatran	\$87,636	5.841	\$2,059	0.178	\$11,555
Apixaban	\$85,426	5.821	-\$151	0.159	Dominant*

*Dominant indicates a therapy is more effective and less expensive than comparators

Figure I. One-way sensitivity analyses at 20 years of LAAC versus warfarin, LAAC versus dabigatran, and LAAC versus apixaban

Figure Ia. LAAC versus warfarin

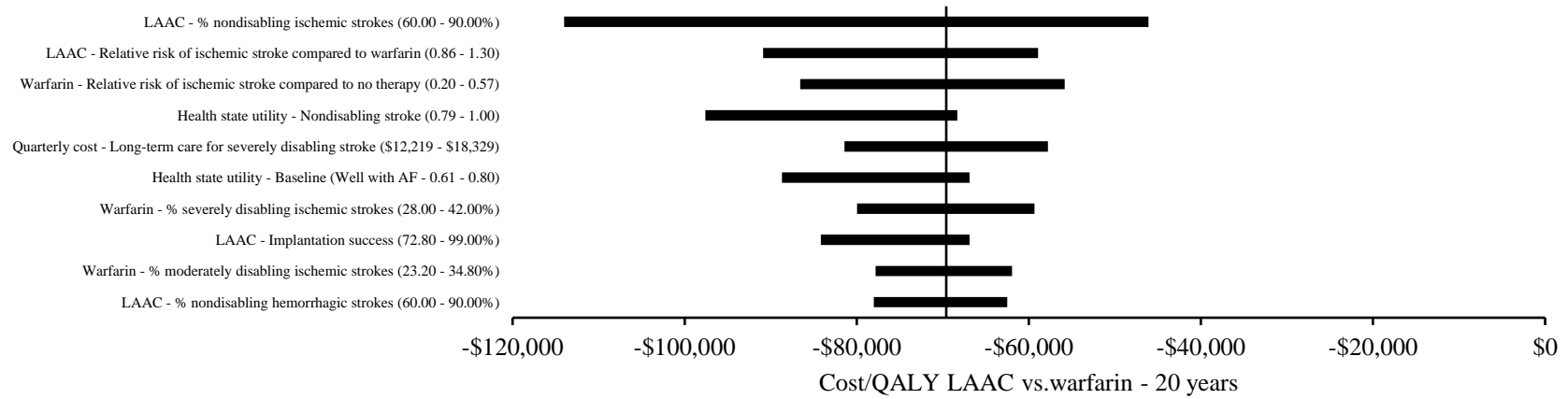


Figure Ib. LAAC versus dabigatran

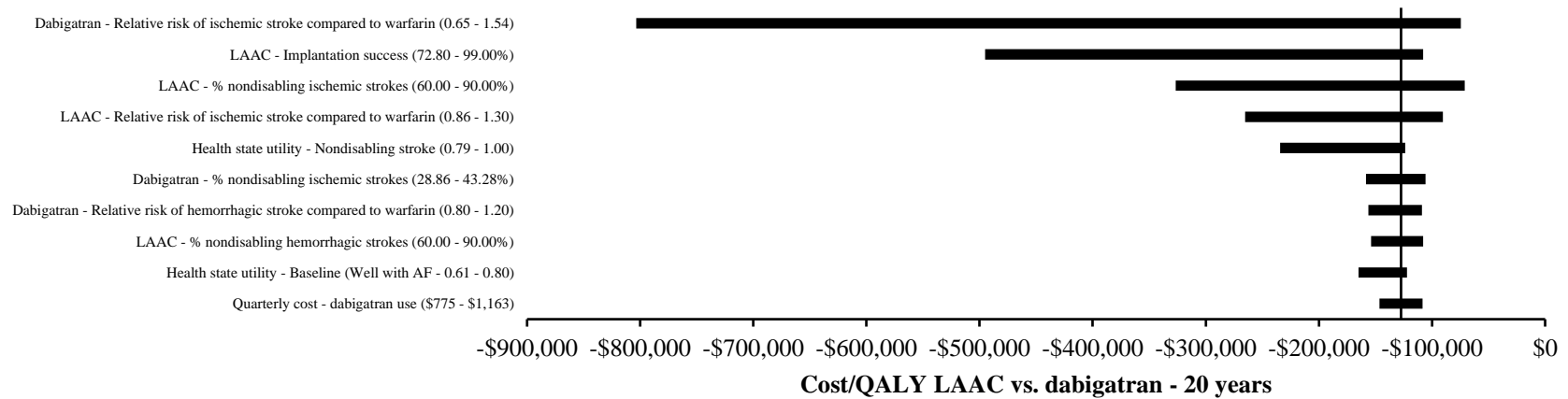


Figure Ic. LAAC versus apixaban

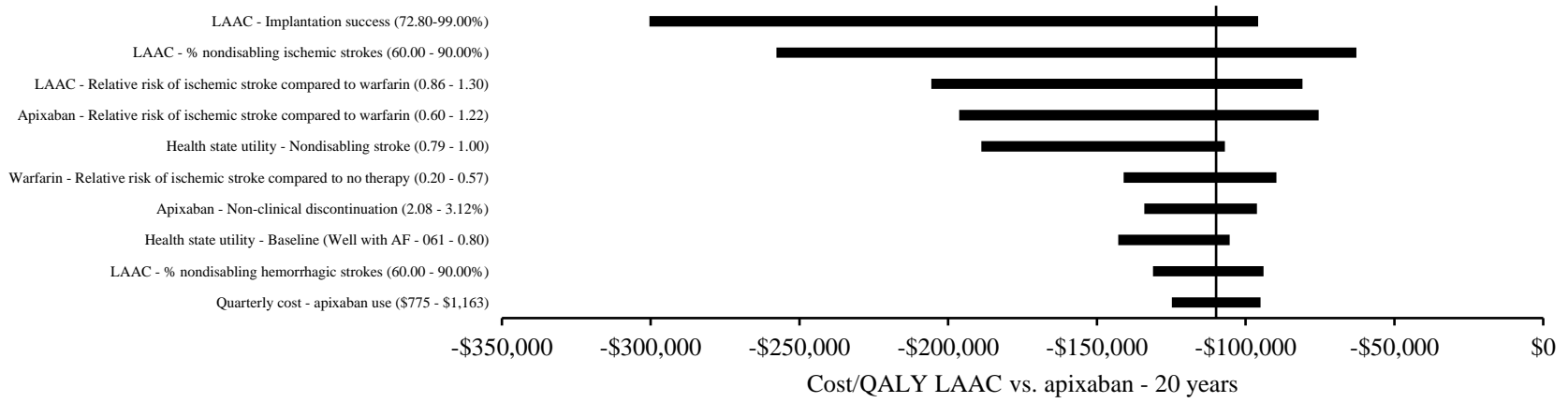


Table V. Total costs and QALYs over 20 years for LAAC, warfarin, dabigatran, and apixaban using Kamel stroke outcomes data. Incremental costs, incremental QALYs, and ICERs were calculated relative to warfarin.

	Total Costs	Total QALYs	Incremental Costs*	Incremental QALYs*	ICER versus warfarin
20 Years					
LAAC	\$59,675	6.066	--	--	--
Warfarin	\$107,394	5.531	-\$47,720	0.535	Dominant†
Dabigatran	\$116,896	5.670	\$9,501	0.139	\$68,195
Apixaban	\$104,141	5.708	-\$3,253	0.178	Dominant†

*Incremental costs and incremental QALYs were calculated as LAAC minus warfarin and NOACs minus warfarin, respectively

† Dominant indicates a therapy is more effective and less expensive than comparators

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