

APPENDIX A
LITERATURE SEARCH STRATEGY

The search strategy for catheter ablation was:

Databases:

- Ovid Medline(R) 1996 to Present with Daily Update
- Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

Search:

1. atrial fibrillation.mp OR exp atrial fibrillation/
2. atrial flutter.mp OR exp atrial flutter/
3. (atrial adj (arrhythmia or tachycardia)).mp
4. OR/1-3
5. limit 4 to (english language AND humans AND yr=2000-2010)
6. limit 5 to (addresses OR bibliography OR biography OR case reports OR comment OR editorial OR lectures OR legal cases OR letter OR news OR newspaper article)
7. 5 NOT 6
8. exp catheter ablation/
9. pulmonary vein\$.mp OR exp pulmonary veins/
10. catheter ADJ2 ablat\$.mp
11. (transcatheter OR trans-catheter) ADJ2 ablat\$.mp
12. OR/8-11
13. 7 AND 12
14. remove duplicates from 13

Database:

- EMBASE

Search:

1. 'heart atrium fibrillation'/exp
2. 'atrial flutter'/exp
3. atrial NEXT/1 (tachycardia OR arrhythmia)
4. #1 OR #2 OR #3
5. #4 AND [humans]/lim AND [english]/lim AND [2000-2010]/py
6. #5 NOT (editorial:it OR letter:it OR note:it)
7. 'catheter ablation'/exp
8. 'pulmonary veins'/exp
9. catheter NEXT/2 ablat*
10. (transcatheter OR trans-catheter) NEXT/2 ablat*
11. #7 OR #8 OR #9 OR #10
12. #6 AND #11 AND [embase]/lim NOT[medline]/lim

Databases:

- EBM Reviews - Cochrane Database of Systematic Reviews 2005 to May 2010
- EBM Reviews - Database of Abstracts of Reviews of Effects 2nd Quarter 2010
- EBM Reviews - Health Technology Assessment 2nd Quarter 2010

- EBM Reviews - Cochrane Central Register of Controlled Trials 2nd Quarter 2010

Search:

1. atrial fibrillation.mp
2. atrial flutter.mp
3. (atrial adj (arrhythmia or tachycardia)).mp.
4. OR/1-3
5. limit 4 to (english language AND humans AND yr=2000-2010)
6. 'catheter ablation'.mp
7. pulmonary vein\$.mp
8. catheter ADJ2 ablat\$.mp
9. (transcatheter adj2 ablat\$).mp
10. (trans-catheter adj2 ablat\$).mp
11. OR/6-10
12. 5 AND 11
13. remove duplicates from 12

The search strategy for thorascopic, off-pump surgical ablation was:

Databases:

- Ovid Medline(R) 1996 to Present with Daily Update
- Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

Search:

1. atrial fibrillation.mp OR exp atrial fibrillation/
2. atrial flutter.mp OR exp atrial flutter/
3. (atrial adj (arrhythmia or tachycardia)).mp
4. OR/1-3
5. limit 4 to (english language AND humans AND yr=2000-2010)
6. limit 5 to (addresses OR bibliography OR biography OR case reports OR comment OR editorial OR lectures OR legal cases OR letter OR news OR newspaper article)
7. 5 NOT 6
8. surgical ADJ2 ablation.mp
9. (minimize OR mini-maze OR mini maze).mp
10. minimally ADJ invasive ADJ surg\$.mp OR exp Surgical Procedures, Minimally Invasive/
11. (intraoperative OR intra-operative) ADJ2 ablat\$.mp
12. pulmonary vein\$.mp OR exp pulmonary veins/
13. OR/8-12
14. (Cox-Maze OR Cox-Maze III OR Maze III).mp
15. 13 NOT 14
16. 7 AND 15
17. remove duplicates from 16

Database:

- EMBASE

Search:

1. 'heart atrium fibrillation'/exp
2. 'atrial flutter'/exp
3. atrial NEXT/1 (tachycardia OR arrhythmia)
4. #1 OR #2 OR #3
5. #4 AND [humans]/lim AND [english]/lim AND [2000-2010]/py
6. #5 NOT (editorial:it OR letter:it OR note:it)
7. surgical NEXT/2 ablation
8. minimize OR 'mini maze'
9. 'minimally invasive surgery'/exp
10. (intraoperative OR intra-operative) NEXT/2 ablat*
11. #7 OR #8 OR #9 OR #10
12. Cox-Maze OR 'Cox-Maze III' OR 'Maze III'
13. #11 NOT #12
14. #6 AND #13 AND [embase]/lim NOT [medline]/lim

Databases:

- EBM Reviews - Cochrane Database of Systematic Reviews 2005 to May 2010
- EBM Reviews - Database of Abstracts of Reviews of Effects 2nd Quarter 2010
- EBM Reviews - Health Technology Assessment 2nd Quarter 2010
- EBM Reviews - Cochrane Central Register of Controlled Trials 2nd Quarter 2010

Search:

1. atrial fibrillation.mp
2. atrial flutter.mp
3. (atrial adj (arrhythmia or tachycardia)).mp.
4. OR/1-3
5. limit 4 to (english language AND humans AND yr=2000-2010)
6. surgical ADJ2 ablation.mp
7. (minimize OR mini-maze OR mini maze).mp
8. minimally ADJ invasive ADJ surg\$.mp
9. (intraoperative OR intra-operative) ADJ2 ablat\$.mp
10. OR/6-9
11. (Cox-Maze OR Cox-Maze III OR Maze III).mp
12. 10 NOT 11
13. 5 AND 12
14. remove duplicates from 13

The search strategy for antiarrhythmic agents was:

Databases:

- Ovid Medline(R) 1996 to Present with Daily Update
- Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

1. atrial fibrillation.mp OR exp atrial fibrillation/
2. atrial flutter.mp OR exp atrial flutter/
3. (atrial adj (arrhythmia or tachycardia)).mp
4. OR/1-3
5. limit 4 to (english language AND humans AND yr=2000-2010)
6. limit 5 to (addresses OR bibliography OR biography OR case reports OR comment OR editorial OR lectures OR legal cases OR letter OR news OR newspaper article)
7. 5 NOT 6
8. amiodarone/ OR amiodarone.mp
9. dofetilide/ OR dofetilide.mp
10. sotalol/ OR sotalol.mp
11. flecainide/ OR flecainide.mp
12. propafenone/ OR propafenone.mp
13. dronedarone/ OR dronedarone.mp
14. OR/8-13
15. 7 AND 14
16. remove duplicates from 15

Database:

- EMBASE

1. 'heart atrium fibrillation'/exp
2. 'atrial flutter'/exp
3. atrial NEXT/1 (tachycardia OR arrhythmia)
4. #1 OR #2 OR #3
5. #4 AND [humans]/lim AND [english]/lim AND [2000-2010]/py
6. #5 NOT (editorial:it OR letter:it OR note:it)
7. amiodarone:dd OR pacerone:tn OR cordarone:tn
8. dofetilide:dd OR tikosyn:tn
9. sotalol:dd OR betapace:tn
10. flecainide:dd OR tambocor:tn
11. propafenone:dd OR rythmol:tn
12. dronedarone:dd OR multaq:tn
13. #7 OR #8 OR #9 OR #10 OR #11 OR #12
14. #6 AND #13 AND [embase]/lim NOT[medline]/lim

Databases:

- EBM Reviews - Cochrane Database of Systematic Reviews 2005 to May 2010
- EBM Reviews - Database of Abstracts of Reviews of Effects 2nd Quarter 2010

- EBM Reviews - Health Technology Assessment 2nd Quarter 2010
- EBM Reviews - Cochrane Central Register of Controlled Trials 2nd Quarter 2010

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7. dofetilide.mp
8. sotalol.mp
9. flecainide.mp
10. propafenone.mp
11. dronedarone.mp
12. OR/6-11
13. 5 AND 12
14. remove duplicates from 13

APPENDIX B

SYSTEMATIC REVIEW EVIDENCE TABLES

Table B1. Study Characteristics

Author	Year	Study Design	Study N	AF monitoring method	% PAF	% PmAF	% PeAF	Mean Age	% Male	Study specific parameters	
				Catheter ablation						Ancillary ablation sets, procedures, and/or populations	Non-catheter ablation comparators
Arentz	2003	Case Series	55	ECG, 24-hour Holter monitor	67.3	0	32.7	53	72.7	SVC, tricuspid annulus/IVC isthmus ablation	NA
Arentz	2003	Case Series	47	24-hour Holter monitor	76.6	0	23.4	55	78.1	RA, SVC, LA	NA
Atienza	2009	Case Series	50	ECG	64	0	36	52	74	CPVI + dominant frequency sites	NA
Baman	2009	Case Series	93	ECG, event monitor	56	0	44	60	77	CFAEs in LA and CS	NA
Berkowitsch	2009	Prospective Cohort Study	215	Symptoms report, 7-day Holter ECG	69.3	NR	NR	57	71.6	CFAEs, with RFCA	NA
			105		90.5	NR	NR	58	57.1	CFAEs, with cryoballoon ablation	NA
			240		NR	NR	NR	57	72.3	Segmental PV ostia isolation	NA
Bertaglia	2009	Prospective Cohort Study	107	24-hour ECG Holter or a 7-day ECG recording	NR	NR	NR	54.5	84.1	CPVI guided by 3D electroanatomical mapping	NA
			226		NR	NR	NR	57	77.3	CPVI guided by electroanatomical mapping integrated with MR/CT images of the left atrium	NA
Bunch	2010	Prospective Cohort Study	717	Event monitor	54.1	17.7	28.2	64.1	59.3	WACA, LA linear ablation, CTI; ablation in <80 year olds	NA

Author	Year	Study Design	Study N	AF monitoring method	% PAF	% PmAF	% PeAF	Mean Age	% Male	Study specific parameters	
			35		45.7	20.1	34.3	82.1	45.7	WACA, LA linear ablation, CTI; ablation in ≥80 year olds	NA
			33		64	NR	NR	52.1	79	LA roof and LA posterior wall, mitral isthmus	NA
Calvo	2010	Prospective Cohort Study	42	24- or 48-hour Holter monitor, ECG	74	NR	NR	48.5	93	LA roof and LA posterior wall, mitral isthmus; patients with lone AF who are also athletes	NA
			107		74	NR	NR	47.3	77	LA roof and LA posterior wall, mitral isthmus; patients with lone AF	NA
Cheema	2006	Case Series	64	ECG, 7-day Holter monitor, event monitor	45	25	29	59	73	CPVI	NA
Corrado	2009	RCT	160	ECG, 48-hour Holter monitor	46	28	26	57	73.4	PVI only	NA
			134		46	29	25	55	73.9	SVC	NA
Deisenhofer	2003	Case Series	75	7-day Holter monitor	92	0	8	58	73.3	PVI only	NA
Deisenhofer	2009	RCT	48	7-day Holter ECG	NR	NR	NR	58	69	PVI only	NA
			50		NR	NR	NR	55	82	CFAEs	NA
Della Bella	2009	RCT	145	7-day Holter, 24-hour ECG Holter monitor	73	0	27	56	75.8	CartoMerge™	NA
			145		70	0	30	55	69	Conventional RFCA procedure	NA
Di Biase	2009	Prospective Cohort Study	193	7-day Holter monitor	66	2	28	63	75	Posterior LA wall, CFAEs, mitral annular/LA roof lesions, CS isolation, and RA ablation; manual approach	NA

Author	Year	Study Design	Study N	AF monitoring method	% PAF	% PmAF	% PeAF	Mean Age	% Male	Study specific parameters	
			197		69	3	28	61	74	Posterior left atrial wall, CFAEs, mitral annular/LA roof lesions, CS isolation, and RA ablation; robotic approach	NA
Di Biase	2009	RCT	35	48-hour Holter monitor, event recorder	100	0	0	57	83	PVI only	NA
			34		100	0	0	59.9	76	CFAEs ablation only	NA
			34		100	0	0	58.4	88	CFAEs	NA
Essebag	2005	Case Series	85	24-hour Holter monitor, 2-week event recorder, or continuous mobile outpatient cardiac telemetry	100	0	0	53	66	Mitral isthmus line and/or posterior LA line	NA
Forleo	2009	RCT	35	ECG Holter monitor	45.7	0	0	63.2	57.1	CTI, roofline connecting superior PVs, isthmus between mitral annulus and left inferior PV	NA
			35		37.1	0	0	64.8	65.7	NA	ADT (Oral flecainide, oral propafenone, oral sotalolol, or oral amiodarone according to recommended guidelines)
Helms	2009	Case Series	73	Holter or event monitor	66	0	34	56	82	CPVI (Linear ablation - LA roof line plus a line connecting the left inferior PV to the mitral annulus)	NA
Hocini	2005	RCT	45	ECG	100	0	0	55	76	PVI only	NA

Author	Year	Study Design	Study N	AF monitoring method	% PAF	% PmAF	% PeAF	Mean Age	% Male	Study specific parameters	
			45		100	0	0	54	82	Linear ablation joining the 2 superior PVs (roofline) + CTI	NA
Hof	2009	Case Series	146	ECG with event monitoring and reporting of symptoms	55	27	18	57	83	WACA	NA
Hsieh	2005	Prospective Cohort Study	37	ECG	100	0	0	72	92	SVC, non-PV foci, and CTI	NA
			32		100			0	0	73	81
Hunter	2010	Case series	285	Ambulatory monitor	53	0	47	57	75	WACA; for persistent AF: linear ablation and CFAEs	NA
Husser	2004	Case Series	79	ECG, Holter monitor, or event monitor	68	0	32	55	65	RA isthmus	NA
			53		100	0	0	49.7	84.9	Allowed at discretion of investigator; CTI, linear lesions (LA roof), mitral isthmus	NA
Jais	2008	RCT	59	ECG, 24-hour Holter monitor	100	0	0	52.4	83.1	NA	ADT (Amiodarone, quinidine, disopyramide, flecainide, propafenone, cibenzoline, dofetilide, and sotalol). No specific regimen was mandated
Joshi	2009	Case Series	72	ECG, Holter monitor, event monitor, loop recorder for AF	67	0	33	59.8	69	Linear ablation (mitral isthmus and LA roof)	NA

Author	Year	Study Design	Study N	AF monitoring method	% PAF	% PmAF	% PeAF	Mean Age	% Male	Study specific parameters
				burden						
Kanagara tnam	2001	Case Series	71	48-hour Holter monitor, loop recorder	0	0	100	57	73.2	PVI only NA
Khaykin	2009	RCT	30	ECG, 24-hour Holter monitor	83	0	17	54	80	PVI only NA
			30		77	0	23	57	77	CPVI, CFAE (30%), mitral isthmus and LA roof lines (77%) NA
Kim	2010	Prospective Cohort Study	49	ECG or 24-hour Holter monitor	NR	NR	NR	52.3	77.6	CPVI with ablation of residual potentials NA
			53		NR	NR	NR	54.2	83	CPVI alone NA
Klemm	2006	Case Series	80	Transtelephonic ECG, Holter ECG	NR	NR	NR	59	73	Segmental PVI, RA isthmus ablation NA
Knecht	2010	Prospective Cohort Study	47	Ambulatory monitor	43.2	0	56.2	58	NR	LA and RA appendages, CFAEs, CTI using 3DATG imaging NA
			44		32	0	68.1	57	NR	LA and RA appendages, CFAEs, CTI using Carto imaging NA
Kriatselis	2009	Case series	44	24-hour Holter ECG	63.6	0	36.4	57	NR	PVI only NA
Kumagai	2005	Prospective Cohort Study	50	ECG, 24-hour Holter monitor	100	0	0	58	80	Circular catheter-guided ablation NA
			50		100	0	0	57	70	Basket catheter-guided ablation NA
Kusumoto	2009	Case Series	240	24-hour ambulatory ECG monitor, 30-day event recorder, or 21-day mobile cellular outpatient	58.7	41.3	0	66.4	72.08	Stepwise ablation: after PVI, linear ablation, CFAEs NA

Author	Year	Study Design	Study N	AF monitoring method	% PAF	% PmAF	% PeAF	Mean Age	% Male	Study specific parameters	
				telemetry							
Lakkireddy	2005	Prospective Cohort Study	86	Rhythm transmitter, 48-hour Holter monitor	59	28	13	60	60	PVI in patients with pacemakers or ICD	NA
			86		61	29	10	60	60	PVI in patients without pacemakers or ICD	NA
Lin	2009	Prospective Cohort Study	30	24-hour Holter monitor and/or cardiac event monitor	0	NR	NR	49	86.7	Linear ablation (roof line and lateral mitral line)	NA
			30		0	NR	NR	49	80	Linear ablation (roof line and lateral mitral line) + CFAEs	NA
Lo	2009	Prospective Cohort Study	49	24-hour Holter monitor and/or cardiac event monitor	0	0	100	55	79.6	Linear ablation, CFAEs; LA diameter of < 45mm	NA
			37		0	0	100	51	89.2	Linear ablation, CFAEs; LA diameter of ≥45mm	NA
Macle	2002	Case Series	136	Telephone interview	90	0	10	52	80	Bidirectional CTI block, linear ablation, lateral mitral isthmus line	NA
Macle	2007	Case Series	64	ECG, Holter monitor	76.6	0	23.4	52	79.7	Posterior LA	NA
Malmborg	2003	Case Series	40	24-hour Holter ECG	80	0	20	56.3	90	PVI only	NA

Author	Year	Study Design	Study N	AF monitoring method	% PAF	% PmAF	% PeAF	Mean Age	% Male	Study specific parameters	
Mangrum	2002	Case Series	64	ECG, Holter monitor; 24-hour Holter monitor or 30-day event recorder	100	0	0	52	71.4	CPVI; additional ablation for AFL or right AFL: tricuspid annulus/IVC linear lesion(s) and ectopy-initiating AF outside the PV	NA
Marrouche	2007	RCT	26	24-hour Holter monitor	61.5	38.5	0	53	73.1	Open-Irrigation	NA
			27		38.5	61.5	0	54	7.8	ICE-Guided Energy Delivery with a Non-Irrigated Catheter	NA
Matsuo	2009	Case series	90	ECG, 24-hour Holter monitor, 24-hour ambulatory monitor	0	0	100	56.5	84.4	CFAEs, linear ablation if AF continued (joining right and left superiorPVs), then if it still continued, a mitral isthmus line	NA
Meissner	2009	Case Series	72	24-hour Holter monitor	65.3	18.1	16.7	60.5	68	PVI only	NA
Mesas	2006	Case Series	47	Transtelephonic ECG, Holter monitor	59.6	0	40.4	56.7	74.5	CPVI	NA
Nademanee	2008	Case Series	674	Holter monitor	40	23	37	67	66.6	CFAE ablation only	NA
Neuman	2008	Prospective Cohort Study	293	7-day Holter monitor	100	0	0	59	59	CPVI in PAF patients	NA
			53		0	0	100	59	77.4	CPVI in PeAF patients	NA
O'Neill	2009	Case Series	153	Holter monitor	NR	NR	46	55.6	85	CFAEs, linear ablation (mitral isthmus and LA roof), RA, SVC, linear ablation (CTI)	NA

Author	Year	Study Design	Study N	AF monitoring method	% PAF	% PmAF	% PeAF	Mean Age	% Male	Study specific parameters	
Oral	2006	Case Series	755	Event monitors and/or serial ECGs and 24-hour Holter monitor	64.9	35.1	0	55	76.4	LA RFCA performed in 29% of patients; CPVI in 71% of patients	NA
Oral	2006	RCT	77	Event monitor	0	0	100	55	87	CPVI	NA
			69		0	0	100	58	89.9	NA	Amiodarone/car di diversion
Pappone	2001	Case Series	251	Holter monitor	71.3	0	28.7	NR	NR	CPVI	NA
			589		69	0	31	65	58	CPVI	NA
Pappone	2003	Prospective Cohort Study	582	ECG and 24-hour Holter monitor	71	0	29	65	59	NA	ADT (Amiodarone, propafenone, flecainide, sotalol, quinidine, disopyramide)
Pappone	2006	RCT	99	ECG, 24-hour Holter monitor, event monitor	100	0	0	55	69.7	CPVI	NA
			99		100	0	0	57	64.6	NA	ADT (Amiodarone, flecainide, or sotalol, either as single drugs or in combination at the maximum tolerable doses)
Patel	2010	Prospective Cohort Study	518	Transtelephonic ECG, 48-hour Holter monitor, event monitor	46	0	28	59	0	Posterior wall between PVs, anterior tissue to the right PV along the left septum, SVC, CFAEs; ablation performed in females	NA

Author	Year	Study Design	Study N	AF monitoring method	% PAF	% PmAF	% PeAF	Mean Age	% Male	Study specific parameters	
			2747		55	0	25	56	100	Posterior wall between PVs, anterior tissue to the right PV along the left septum, SVC, CFAEs; ablation performed in males	NA
Pontoppidan	2009	RCT	73	ECG, Holter monitor	52	0	48	56	74	CTI	NA
			76		55						
Rossillo	2008	Retrospective matched cohort study	85	Holter monitor	31.7	17.8	50.5	62	84	SVC	NA
			85		0						
Saliba	2008	Case Series	40	Holter monitor	72.5	0	27.5	57	NR	SVC	NA
Sawhney	2009	Case Series	71	Event monitor	100	0	0	60	77.5	CPVI and LA linear ablation	NA
Scharf	2009	Case Series	50	7-day ECG	0	0	100	58	NR	PVI only	NA
Shin	2006	Case Series	68	ECG	33	0	67	55.9	93	Non-PV triggers	NA
Siklody	2009	Case Series	30	ECG, 24-hour Holter monitor	73.3	NR	NR	57.7	84	PVI only	NA
			68		61.8	0	38.2	62.2	54.4	CPVI with CTI line	NA
Stabile	2006	RCT	69	Transtelephonic ECG recorder, standard ECG, Holter monitor	72.3	0	27.5	62.3	63.8	NA	ADT (Amiodarone, flecainide, propafenone, sotalol, disopyramide; 30% of control group treated with a drug that had previously failed)
Stabile	2009	Prospective Cohort Study	36	ECG or 24-hour ambulatory monitor	NR	NR	NR	60	80.5	LA, CTI using anatomical approach	NA
			61		NR						

Author	Year	Study Design	Study N	AF monitoring method	% PAF	% PmAF	% PeAF	Mean Age	% Male	Study specific parameters	
Steven	2010	Prospective Cohort Study	30	3-day Holter monitor	NR	NR	NR	62	66.6	Posterior LA wall, ipsilateral veins with robotic navigation of catheter	NA
			30		NR	NR	NR	61	46.7	Posterior LA wall, ipsilateral veins using a conventional approach to catheter ablation	NA
Tambore ro	2009	RCT	60	48-hour Holter monitor	62	20	18	52.5	73	Superior PVs were connected by linear lesions along the LA roof	NA
			60		58	20	22	52.9	80	LA posterior wall isolated by adding a second line connecting the inferior aspect of the 2 inferior PVs	NA
Tan	2009	Case Series	99	48-hour Holter monitor	58	0	42	54	81	PVI only	NA
Themisto clakis	2010	Prospective Cohort Study	2692	ECG, Holter monitor, transtelephonic monitor	62	22	16	57	79	Ostial or antral level PVI; linear lesions, ablation of CFAEs, and isolation of the SVC were performed per institutional preference; discontinued with OAT	NA

Author	Year	Study Design	Study N	AF monitoring method	% PAF	% PmAF	% PeAF	Mean Age	% Male	Study specific parameters	
			663		51	22	26	59	70	Ostial or antral level PVI; linear lesions, ablation of CFAEs, and isolation of the SVC were performed per institutional preference; continued with OAT	NA
Tzou	2010	Case series	123	Transtelephonic monitor, ECG	85	NR	NR	54	80	PVI only	NA
Udyavar	2008	Case Series	97	24-hour Holter monitor	84.5	0	14.5	50	77.3	CPVI with PV carina	NA
Van Belle	2008	Case Series	141	Transtelephonic ECG, 24-hour Holter ECG	NR	NR	NR	56	70.9	CPVI; CTI ablation in 7 patients with isthmus flutter	NA
Wazni	2005	RCT	33	Loop-event recorder; 24-hour Holter monitor	97	0	3	53	NR	PVI only	NA
			37		95	0	5	54	NR	NA	ADT (Flecainide, propafenone, or sotalol.)
Wazni	2009	Case Series	71	Event recorder	43.7	NR	NR	59	NR	SVC, using the Hansen ablation system	NA
Wiesfeld	2004	Case Series	25	24-hour Holter monitor, ambulatory monitor	52	0	48	46	64	LA, RA and respective appendages	NA
Wilber	2010	RCT	106	ECG, transtelephonic ECG, Holter monitor	100	0	0	55.5	68.9	Allowed at discretion of investigator; included left atrial linear lesions, CFAEs and CTI ablation	NA

Author	Year	Study Design	Study N	AF monitoring method	% PAF	% PmAF	% PeAF	Mean Age	% Male	Study specific parameters	
			61		100	0	0	56.1	62	NA	ADT (Previously unused class I or class III (dofetilide, flecainide, propafenone, sotalol, or quinidine; choice of drug at discretion of investigator))
Wokhlu	2010	Case Series	502	Holter monitor	51	35	13	55	82	Some CPVI, other WACA with additional linear lesions along the LA roof and the left inferior isthmus	NA
Wokhlu	2010	Case Series	774	ECG, 24-hour Holter monitor	55	0	34	54	81	Some PVI, some WACA	NA
Yamada	2006	Case Series	55	24-hour Holter and cardiac recordings; event monitor	100	0	0	58	85.5	CPVI	NA
Yamada	2009	Prospective Cohort Study	60	24-hour Holter recordings, event monitor	100	0	0	59	76.7	Segmental PVI with vagal nerve ablation	NA
			60		100	0	0	60	78.3	CPVI with vagal nerve ablation	NA
Yoshida	2009	Case Series	97	24-hour Holter monitor, event monitor	100	0	0	58	76.3	PVI only	NA
Antiarrhythmic agents										AAD	Maintenance Dose
AFFIRM	2003	RCT	106	ECG	NR	NR	NR	67.7	65.1	Amiodarone	200 mg per day
			116		NR	NR	NR	70.1	59.5	Class I	Various
			131		NR	NR	NR	67.9	65.6	Amiodarone	200 mg per day
			125		NR	NR	NR	70.4	63.2	Sotalol	240mg per day

Author	Year	Study Design	Study N	AF monitoring method	% PAF	% PmAF	% PeAF	Mean Age	% Male	Study specific parameters	
			88		NR	NR	NR	70.6	61.4	Sotalol	240mg per day
			95		NR	NR	NR	69.5	62.1	Class I	Various
Aizawa	2010	Case series	381	ECG	100	0	0	65.1	70	ADT	NR
Banchs	2008	Case Series	80	ECG, Holter monitor, or event recorder	33	0	64	64	60	Dofetilide	405 µg BID on creatine clearance
			102		0	24.9	75.1	50	NR	Propafenone	450 mg per day if body weight was ≤60 kg; 900 mg per day if it was >60 kg
Bellandi	2001	RCT	106	ECG, 24-hour Holter monitor	0	24.3	75.7	53	NR	Sotalol	120 mg per day if body weight was ≤60 kg; 240 mg per day if it was >60 kg
			92		0	26.1	73.9	54	NR	Placebo	NR
Carlsson	2003	RCT	100	ECG	NR	NR	NR	65.3	59	ADT	NR
			100		NR	NR	NR	66.2	68	Rate control	NR
			62		NR	NR	NR	65	73	Amiodarone - short-term	400mg BID, then 200mg per day for 44 weeks
Channer	2004	RCT	63	ECG	NR	NR	NR	66	77	Amiodarone - long term	400mg BID, then 200mg per day for 52 weeks
			38		NR	NR	NR	68	79	Placebo	NR
Connolly	2009	RCT	2301	NR	NR	0	NR	72	51	Dronedarone	400 mg BID
			2327		NR	0	NR	72	55	Placebo	400 mg BID
Dogan	2004	RCT	51	ECG	0	0	27	60	42	Propafenone	600 mg
			48		0	0	69	62	48	Placebo	NR
			383	Event recorder (Tele-ECG) and had to record and transmit via telephone at least	NR	NR	NR	62	66	Sotalol	160 mg BID
Fetsch	2004	RCT	88		0	100	0	82	71	Placebo	NR

Author	Year	Study Design	Study N	AF monitoring method	% PAF	% PmAF	% PeAF	Mean Age	% Male	Study specific parameters	
				one ECG per day during follow-up; Holter ECG							
Galperin	2001	RCT	47	ECG, Holter ECG	0	100	0	61.63	63.8	Amiodarone	600 mg
			48		0	100	0	65.1	81.3	Placebo	NR
Hohnloser	2000	RCT	127	ECG	0	0	100	60	72	Amiodarone	200mg per day
			125		0	0	100	61	74	Diltiazem	90 mg 2-3x/day
Hohnloser	2009	RCT	2301	ECG, 24 h Holter monitor	NR	0	NR	71.6	50.8	Dronedarone	400 mg BID
			2327		NR	0	NR	71.7	55.4	Placebo	NR
Kilborn	2002	RCT	550	NR	NR	NR	NR	77	64.2	Amiodarone	NR
			14730		NR	NR	NR	79.1	48.7	Placebo	NR
Kochiadakis	2000	RCT	65	24-hour ambulatory ECG	64.6	35.4	0	63.2	52.3	Amiodarone	200mg per day
			61		63.9	36.1	0	62.8	52.5	Sotalol	480 mg BID
			60		66.7	33.3	0	62.8	51.7	Placebo	NR
Kochiadakis	2004	RCT	85	24-hour ambulatory ECG	58.8	0	41.2	63	50.6	Sotalol	480 mg per day
			86		60.5	0	39.5	63	48.8	Propafenone	150 mg 3x/day
			83		59	0	41	62	51.8	Placebo	3 tablets a day
Kochiadakis	2004	RCT	72	24-h ambulatory ECG	59.7	0	40.3	62	51.4	Amiodarone	200 mg per day
			74		66.2	0	33.8	64	47.3	Propafenone	150 mg per day
Kuhlkamp	2000	RCT	197	ECG	NR	NR	NR	61	71.1	Metoprolol	200 mg per day
			197		NR	NR	NR	59.9	69.5	Placebo	NR
Le Heuzey	2009	RCT	249	ECG	4.4	2	61.8	64.4	70.7	Dronedarone	400mg BID
			255		4.3	3.9	63.9	63.7	71.4	Amiodarone	200mg per day
Li	2004	Prospective Cohor Study	50	NR	0	0	100	69.4	70	ADT	Various
			100		0	0	0	71.3	64	Rate control	Various
Ogawa	2009	RCT	419	ECG	100	0	0	64.9	69	ADT	Various
			404		100	0	0	64.5	69.6	Rate control	Various
Opolski	2004	RCT	104	ECG Holter recordings	0	0	100	60.4	68.3	ADT	Various
			101		0	0	100	61.4	62.4	Rate control	Various
Patten	2004	RCT	264	Trans-telephonic ECG	100	0	0	59.6	65.1	Sotalol	320 mg
			251		100	0	0	60	65.4	Placebo	NR

Author	Year	Study Design	Study N	AF monitoring method	% PAF	% PmAF	% PeAF	Mean Age	% Male	Study specific parameters	
Plewan	2001	RCT	64	ECG, Holter ECG	0	0	100	59	59.4	Sotalol	80mg BID
			64		0	0	100	59	55.6	Bisoprolol	5 mg per day
Pritchett	2003	RCT	126	24-hour Holter ECG, transtelephonic ECG	NR	NR	NR	64	60	Propafenone	225 mg per day
			135		NR	NR	NR	63	59	Propafenone	325 mg per day
			136		NR	NR	NR	63	57	Propafenone	425 mg per day
			126		NR	NR	NR	63	60	Placebo	NR
Roy	2000	RCT	201	ECG	49	0	51	65	55	Amiodarone	200 mg per day
			202		43	0	57	65	56	Sotalol/Propafenone	Various
Roy	2008	RCT	682	ECG	33	0	67	66	78	ADT	Various
			694		30	0	70	67	85	Rate control	Various
Singh	2000	RCT	82	ECG	NR	NR	NR	66	82.9	Dofetilide	125 µg/BID
			82		NR	NR	NR	68	84.2	Dofetilide	250 µg/BID
			77		NR	NR	NR	67	81.8	Dofetilide	500 µg/BID
			84		NR	NR	NR	67	86.9	Placebo	NR
Singh	2005	RCT	267	ECG	NR	NR	NR	67.1	99.3	Amiodarone	200 mg per day
			261		NR	NR	NR	66.8	98.5	Sotalol	1600 mg BID
			137		NR	NR	NR	67.7	99.3	Placebo	NR
Singh	2007	Randomized Controlled Trial	828	Transtelephonic ECG monitor, ECG	NR	NR	NR	63.5	69.8	Dronedarone	400 mg BID
			409		NR	NR	NR	62.2	68.5	Placebo	NR
Touboul	2003	RCT	54	Transtelephonic ECG monitor, ECG	NR	NR	NR	64	57	Dronedarone	800mg BID
			54		NR	NR	NR	63	70	Dronedarone	1200mg BID
			43		NR	NR	NR	62	67	Dronedarone	1600mg BID
			48		NR	NR	NR	65	79	Placebo	NR
Tse	2003	Case Series	25	ECG, Holter monitor	NR	NR	NR	65	75	Sotalol	308mg (mean)
van Gelder	2002	RCT	266	ECG	0	0	100	68	64	ADT	Various
			256		0	0	100	68	63	Rate control	Various
Wyse	2002	RCT	2027	NR	NR	NR	NR	69.8	59.4	Rate control	Various
			2033		NR	NR	NR	69.7	62.1	ADT	Various

Thoroscopic, off-pump surgical ablation										Ablation Approach	Energy Type
Bagge	2009	Case Series	43	24-hour Holter recording, ECG	65	21	14	58	67.4	Thoracoscopic off-pump epicardial PVI and GP ablation	Bipolar RF
Beyer	2009	Case Series	100	24-hour Holter monitor	39	32	29	65	70	PVI/autonomic denervation, GP stimulation	Bipolar RF
Castella	2010	Case Series	34	24-hour Holter monitor	NR	NR	NR	54	NR	Thoracoscopic PVI	Bipolar RF
Cui	2010	Case Series	81	ECG analysis, and 24- to 48-hour Holter monitor (for patients in SR with ECG)	60.5	0	39.5	57.6	63	Bilateral PV antrum isolation and division of the LOM	Bipolar RF
Edgerton	2009	Case Series	74	ECG, 14- to 21-day auto-triggered event monitor	62.2	0	37.8	NR	NR	Bilateral PV antrum isolation	Bipolar RF
Edgerton	2009	Case Series	114	ECG and 24-hour Holter monitor OR long-term monitor (a 14 to 21-day auto trigger event monitor)	52.6	28.1	19.3	59.5	69.3	PVI/left-sided "Dallas" set	Bipolar RF
Edgerton	2009	Case Series	30	14- to 21-day event monitor	0	0	33.3	58	86.7	Bilateral PVI/GP stimulation/additional ablation post-testing	Bipolar RF
Edgerton	2010	Case Series	52	ECG, 24-hour Holter monitor, 2-3 week event monitor, or interrogation of implanted pacemaker	100	0	0	60.3	67.3	Bilateral, epicardial PVI and partial autonomic denervation	Bipolar RF
Han	2009	Case Series	45	External loop recorder	73	0	27	64	56	Bilateral PVI/GP ablation/LOM ablation	Unipolar RF

Sirak	2008	Case Series	32	ECG	0	0	100	65.6	Totally thoracoscopic PVI, extended linear ablations across critical segments of atrial substrate	Bipolar RF	
Wolf	2005	Case Series	27	ECG or telemetry monitor	66.7	18.5	14.8	57.2	81.5	Bilateral PVI	Bipolar RF
Yilmaz	2010	Case Series	30	ECG and 24-hour Holter monitor	63	10	27	55.6	77	Bilateral PVI/GP ablation	Bipolar RF
				Stroke prevention						Intervention	Dose
Connolly	2009	RCT	6015	NA	32.1	35.4	32.4	71.4	64.3	Dabigatran	110 mg
			6076		32.6	36	31.4	71.5	63.2	Dabigatran	150 mg
			6022		33.8	34.1	32	71.6	63.3	Warfarin	Adjusted-dose
Holmes	2009	RCT	463	NA	43.2	34.6	21	71.7	70.4	Watchman	NA
			244		40.6	38.1	20.5	72.7	70.1	Warfarin	Adjusted-dose

ADT, antiarrhythmic drug therapy; AF, atrial fibrillation; AFL, atrial flutter; AVN, atrioventricular junction ; BID, twice per day; CFAEs, complex fractionated atrial electrograms; CPVI, circumferential pulmonary vein isolation; CS, coronary sinus; CT, computed tomography; CTI, cavotricuspid isthmus; DC, direct-current; ECG, electrocardiogram; GP, ganglionic plexi; ICD, implantable cardioverter-defibrillators; ICE, intracardiac echocardiogram; IVC, inferior vena cava; LA, left atrium; LOM, ligament of Marshall; MR, magnetic resonance; NA, not applicable; NR, not reported; OAT, oral anti-coagulation; PAF, paroxysmal atrial fibrillation; PeAF, persistent atrial fibrillation; PmAF, permanent atrial fibrillation; PV, pulmonary vein; PVI, pulmonary vein isolation; RA, right atrium; RCT, randomized controlled trial; RF, radiofrequency; RFCA, radiofrequency catheter ablation; SVC, superior vena cava; WACA, wide-area circumferential ablation

Table B2. Annual Mortality Rates

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Deaths during follow-up period	Annual Mortality Rate
Catheter ablation							
Bunch	2010	Prospective Cohort Study	WACA, LA linear ablation, CTI; ablation in <80 year olds	717	36	0	0.0%
			WACA, LA linear ablation, CTI; ablation in ≥80 year olds	35	36	0	0.0%
Deisenhofer	2003	Case series	PVI only	75	7.6	0	0.0%
Essebag	2005	Case series	PVI + mitral isthmus line and/or posterior LA line	85	12	0	0.0%
Hsieh	2005	Prospective Cohort Study	PVI + SVC, non-PV foci, and CTI	37	52	3	1.9%
			AVN ablation	32	58	5	3.2%
Hunter	2010	Case series	WACA; for persistent AF: linear ablation and CFAEs	285	32.4	7	0.9%
Jais	2008	RCT	PVI + CTI, linear lesions (LA roof), mitral isthmus	53	12	0	0.0%
			ADT	59	12	2	3.4%
Meissner	2009	Case series	PVI only	72	6	0	0.0%
Nademanee	2008	Case series	CFAE ablation only	517	27.9	29	2.4%
Neumann	2008	Prospective Cohort Study	CPVI in paroxysmal AF patients	293	12	0	0.0%
			CPVI in persistent AF patients	31	12	0	0.0%
Oral	2006	RCT	CPVI	77	12	1	1.3%
			Amiodarone + cardioversion	69	12	NR	NR
Pappone	2003	Prospective Cohort Study	CPVI	589	28.7	38	2.7%
			ADT	582	30.4	83	5.6%
Patel	2010	Prospective Cohort Study	Posterior wall between PVs, anterior tissue to the right PV along the left septum, SVC	518	24.28	5	0.5%
			Posterior wall between PVs, anterior tissue to the right PV along the left septum, SVC, CFAEs	2747	35.57	NR	NR

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Deaths during follow-up period	Annual Mortality Rate
Stabile	2006	RCT	CPVI with CTI line	68	12	1	1.5%
			ADT	69	12	2	2.9%
Themistoclakis	2010	Prospective Cohort Study	Ostial or antral level PVI; linear lesions, ablation of CFAEs, and isolation of the SVC were performed per institutional preference; discontinued with OAT	2692	10	0	0.0%
			Ostial or antral level PVI; linear lesions, ablation of CFAEs, and isolation of the SVC were performed per institutional preference; continued with OAT	663	10	1	0.2%
Wilber	2010	RCT	PVI + left atrial linear lesions, CFAEs and CTI ablation	106	9	1	1.3%
			ADT	61	1	0	0.0%
Antiarrhythmic agents							
AFFIRM	2003	RCT	Amiodarone	106	46	10	2.5%
			Class IC	116	46	26	5.8%
			Amiodarone	131	46	15	3.0%
			Sotalol	125	46	24	5.0%
Channer	2004	RCT	Amiodarone	61	12	0	0.0%
			Amiodarone	62	12	0	0.0%
			Placebo	38	12	0	0.0%
Galperin	2001	RCT	Amiodarone	47	16.03	0	0.0%
			Placebo	48	16.03	0	0.0%
Hohnloser	2000	RCT	Amiodarone	127	12	2	1.6%
			Diltiazem	125	12	2	1.6%
Hohnloser	2009	RCT	Dronedarone	2301	21	116	2.9%
			Placebo	2327	21	139	3.4%
Kilborn	2002	Retrospective Cohort Study	Amiodarone	550	12	196	35.6%
			Placebo	14730	12	4655	31.6%
Kochiadak	2000	RCT	Amiodarone	65	24	0	0.0%

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Deaths during follow-up period	Annual Mortality Rate
is			Sotalol	61	24	0	0.0%
			Placebo	60	24	0	0.0%
Heuzey	2009	RCT	Dronedaron	249	7	2	1.4%
			Amiodarone	255	7	5	3.4%
Singh	2005	RCT	Amiodarone	267	12	13	4.9%
			Sotalol	261	12	15	5.7%
Singh	2007	RCT	Placebo	137	12	3	2.2%
			Dronedaron	828	12	8	1.0%
Touboul	2003	RCT	Placebo	409	12	3	0.7%
			Dronedaron	151	12	1	0.7%
			Placebo	48	12	0	0.0%
Thorascopic, off-pump surgical ablation							
Bagge	2009	Case Series	Thorascopic off-pump epicardial PVI and GP ablation	43	12	0	0.0%
Beyer	2009	Case Series	PVI/autonomic denervation, GP stimulation	100	13.6	0	0.0%
Castella	2010	Case Series	Thorascopic PVI	34	16	0	0.0%
Cui	2010	Case Series	Bilateral PV antrum isolation and division of the LOM	81	12.7	0	0.0%
Edgerton	2009	Case Series	PVI/left-sided "Dallas" set	114	17	1	0.6%
Edgerton	2009	Case Series	Bilateral PVI/GP stimulation/additional ablation post-testing	30	6	0	0.0%
Edgerton	2010	Case Series	Bilateral, epicardial PVI and partial autonomic denervation	52	12	0	0.0%
Han	2009	Case Series	Bilateral PVI/GP ablation/LOM ablation	45	17	0	0.0%
Wolf	2005	Case Series	Bilateral PVI	27	6	0	0.0%
Yilmaz	2010	Case Series	Bilateral PVI/GP ablation	30	11.6	0	0.0%
Stroke prevention							
Connolly	2009	RCT	Dabigatran, 110mg	6015	24	446	3.7%

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Deaths during follow-up period	Annual Mortality Rate
			Dabigatran, 150mg	6076	24	438	3.6%
			Warfarin	6022	24	487	4.0%
Holmes	2009	RCT	Watchman	463	18	21	3.0%
			Warfarin	244	18	18	4.9%

ADT, antiarrhythmic drug therapy; AVN, atrioventricular junction ; CFAEs, complex fractionated atrial electrograms; CPVI, circumferential pulmonary vein isolation; CTI, cavotricuspid isthmus; GP, ganglionic plexi; LA, left atrium; LOM, radiofrequency; LOM, ligament of Marshall; NR, not reported; OAT, oral anti-coagulation; PAF, paroxysmal atrial fibrillation; PeAF, persistent atrial fibrillation; PV, pulmonary vein; PVI, pulmonary vein isolation; RA, right atrium; RCT, randomized controlled trial; SVC, superior vena cava; WACA, wide-area circumferential ablation

Table B3. Annual Stroke Rates

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Strokes during follow-up period	Stroke Type	Annual Stroke Rate
Catheter ablation								
Bunch	2010	Prospective Cohort Study	WACA, LA linear ablation, CTI; ablation in ≥80 year olds	35	36	0	All strokes	0.0%
			WACA, LA linear ablation, CTI; ablation in <80 year olds	717	36	4		0.2%
Cheema	2006	Case Series	CPVI	64	12	0		0.0%
Corrado	2009	RCT	PVI only vs. PVI + SVC	294	12	1		0.3%
Deisenhofer	2003	Case Series	PVI only	75	7.6	0		0.0%
Della Bella	2009	RCT	CartoMerge™	145	14	0		0.0%
			Conventional RFCA procedure	145	14	0		0.0%
Essebag	2005	Case Series	PVI + mitral isthmus line and/or posterior LA line	85	12	1		1.2%
Hsieh	2005	Prospective Cohort Study	PVI + SVC, non-PV foci, and CTI	37	52	1		0.6%
			AVN ablation	32	58	0		0.0%
Hunter	2010	Case Series	WACA; for persistent AF: linear ablation and CFAEs	285	32.4	1		0.1%
Khaykin	2009	RCT	PVI only	30	25.2	0		0.0%

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Strokes during follow-up period	Stroke Type	Annual Stroke Rate
			CPVI, CFAE (30%), mitral isthmus and LA roof lines (77%)	30	25.2	0		0.0%
Lakkireddy	2005	Prospective Cohort Study	PVI in patients with pacemakers or ICD	86	12	0		0.0%
			PVI in patients without pacemakers or ICD	86	12	0		0.0%
Macle	2002	Case Series	Bidirectional CTI block, linear ablation, lateral mitral isthmus line	136	8.8	0		0.0%
Macle	2007	Case Series	Posterior LA	64	16	0		0.0%
Mangrum	2002	Case Series	CPVI; additional ablation for AFL or right AFL; tricuspid annulus/IVC linear lesion(s) and ectopy-initiating AF outside the PV	56	13	3		4.9%
Meissner	2009	Case Series	PVI only	72	6	0		0.0%
Nademanee	2008	Case Series	CFAE ablation only	517	27.9	7		0.6%
Neumann	2008	Prospective Cohort Study	CPVI in paroxysmal AF patients	293	12	0		0.0%
			CPVI in persistent AF patients	31	12	0		0.0%

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Strokes during follow-up period	Stroke Type	Annual Stroke Rate
Oral	2006	Case Series	LA RFA performed in 29% of patients; CPVI in 71% of patients	755	25	2		0.1%
Pappone	2001	Case Series	CPVI	251	10.4	0		0.0%
Pappone	2003	Prospective Cohort Study	PVI only	589	28.7	6		0.4%
			ADT	582	30.4	22		1.5%
Patel	2010	Prospective Cohort Study	Posterior wall between PVs, anterior tissue to the right PV along the left septum, SVC; ablation performed in females	518	24.28	4		0.4%
			Posterior wall between PVs, anterior tissue to the right PV along the left septum, SVC, CFAEs; ablation performed in males	2747	35.57	17		0.2%
Rossillo	2008	Retrospective matched cohort study	PVI only	85	16	0		0.0%
			DC-Shock	85	16	5		4.4%
Sawhney	2009	Case Series	CPVI and LA linear ablation	71	63	0		0.0%
Stabile	2006	RCT	CPVI with CTI line	68	12	0		0.0%
			ADT	69	12	0		0.0%

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Strokes during follow-up period	Stroke Type	Annual Stroke Rate
Steven	2010	Prospective Cohort Study	Posterior LA wall, ipsilateral veins with robotic navigation of catheter	30	12	0		0.0%
			Posterior LA wall, ipsilateral veins using a conventional approach to catheter ablation	30	12	0		0.0%
Tan	2009	Case Series	PVI only	99	6	0		0.0%
Themistoclakis	2010	Prospective Cohort Study	Ostial or antral level PVI; linear lesions, ablation of CFAEs, and isolation of the SVC were performed per institutional preference; discontinued with OAT	2692	10	1		0.0%
			Ostial or antral level PVI; linear lesions, ablation of CFAEs, and isolation of the SVC were performed per institutional preference; continued with OAT	663	10	4		0.7%

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Strokes during follow-up period	Stroke Type	Annual Stroke Rate
Wokhlu	2010	Case Series	Some CPVI, other WACA with additional linear lesions along the LA roof and the left inferior isthmus	323	36	4		0.4%
Antiarrhythmic agents								
Connolly	2009	RCT	Dronedarone	2301	30	46	Total Strokes	0.8%
			Placebo	2327	30	70		1.2%
Connolly	2009	RCT	Dronedarone	2301	30	6	Hemorrhagic	0.1%
			Placebo	2327	30	6		0.1%
Connolly	2009	RCT	Dronedarone	2301	30	33	Ischemic	0.6%
			Placebo	2327	30	49		0.8%
Connolly	2009	RCT	Dronedarone	2301	30	14	Fatal	0.2%
			Placebo	2327	30	21		0.4%
Singh	2005	RCT	Amiodarone	267	12	NR	Major strokes	1.19/100 patient-years
			Placebo	137	12	NR		0.96/100 patient-years
			Amiodarone	267	12	NR	Minor strokes	0.87/100 patient-years
			Placebo	137	12	NR		0.95/100 patient-years
Singh	2007	RCT	Dronedarone	828	12	4	All Strokes	0.5%
			Placebo	409	12	3		0.7%
Thorascopic, off-pump surgical ablation								
No strokes reported during follow-up period								
Stroke prevention								
Connolly	2009	RCT	Dabigatran, 110mg	6015	24	171	Total	1.4%
			Dabigatran, 150mg	6076	24	122		1.0%

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Strokes during follow-up period	Stroke Type	Annual Stroke Rate
			Warfarin	6022	24	185		1.5%
			Dabigatran, 110mg	6015	24	159		1.3%
Connolly	2009	RCT	Dabigatran, 150mg	6076	24	111	Ischemic	0.9%
			Warfarin	6022	24	142		1.2%
			Dabigatran, 110mg	6015	24	14		0.1%
Connolly	2009	RCT	Dabigatran, 150mg	6076	24	12	Hemorrhagic	0.1%
			Warfarin	6022	24	45		0.4%
			Watchman	463	24	16		1.7%
Holmes	2009	RCT	Warfarin	244	24	12	Total	2.5%
			Watchman	463	24	15		1.6%
Holmes	2009	RCT	Warfarin	244	24	6	Ischemic	1.2%
			Watchman	463	18	1		0.1%
Holmes	2009	RCT	Warfarin	244	18	6	Hemorrhagic	1.6%

ADT, antiarrhythmic drug therapy; AFL, atrial flutter; AVN, atrioventricular junction ; CFAEs, complex fractionated atrial electrograms; CPVI, circumferential pulmonary vein isolation; CTI, cavotricuspid isthmus; DC, direct-current; IVC, inferior vena cava; LA, left atrium; NR, not reported; OAT, oral anti-coagulation; PAF, paroxysmal atrial fibrillation; PeAF, persistent atrial fibrillation; PVI, pulmonary vein isolation; RCT, randomized controlled trial; RFCA, radiofrequency catheter ablation; SVC, superior vena cava; WACA, wide-area circumferential ablation

Table B4. Freedom from AF/Maintenance of Sinus rhythm

Author	Year	Study Design	Intervention	Study population	Mean Follow-up, months	Outcome	AF monitoring method	Reported Crude%	Reported Kaplan%	
Catheter ablation										
Arentz	2003	Case Series	PVI + SVC, tricuspid annulus/IVC isthmus ablation	55	12	Freedom from AF	ECG, 24-hour Holter monitor	87.3%	NR	
Arentz	2003	Case Series	PVI + RA, SVC, LA	47	24	Freedom from AF	24-hour Holter monitor	76.6%	NR	
Atienza	2009	Case Series	CPVI + dominant frequency sites	50	9.3	Freedom from AF	ECG	76.0%	NR	
Baman	2009	Case Series	PVI + CFAEs in LA and CS	74	16	Freedom from AF	ECG, event monitor	29.7%	NR	
Berkowitsch	2009	Prospective Cohort Study	PVI + CFAEs, with RFCA	215	24	Freedom from AF	Symptoms report, 7-day Holter ECG	59.8%	NR	
			PVI + CFAEs, with cryoballoon ablation	105				63.1%	NR	
Bertaglia	2009	Prospective Cohort Study	Segmental PV ostia isolation	240	11.2	Freedom from AF	24 h ECG Holter or a 7-day ECG recording	44.6%	NR	
			CPVI guided by 3D electroanatomical mapping	107				12.3	41.1%	NR
			CPVI guided by electroanatomical mapping integrated with MR/CT images of the left atrium	226				11.2	22.6%	NR
Bunch	2010	Prospective Cohort Study	WACA, LA linear ablation, CTI; ablation in ≥80 year olds	35	36	Freedom from AF	Event monitor	NR	78.0%	
			WACA, LA linear ablation, CTI; ablation in <80 year olds	717				NR	75.0%	

Author	Year	Study Design	Intervention	Study population	Mean Follow-up, months	Outcome	AF monitoring method	Reported Crude%	Reported Kaplan%
Calvo	2010	Prospective Cohort Study	PVI + LA roof and LA posterior wall, mitral isthmus	33	12	Freedom from AF	24 or 48-hour Holter monitor, ECG	NR	48.0%
			PVI + LA roof and LA posterior wall, mitral isthmus; patients with lone AF who are also athletes	42				NR	59.0%
			PVI + LA roof and LA posterior wall, mitral isthmus; patients with lone AF	107				NR	47.0%
Cheema	2006	Case Series	CPVI	64	13	Freedom from AF	ECG, 7-day Holter monitor, event monitor	62.0%	NR
Corrado	2009	RCT	PVI only	160	12	Sinus rhythm	ECG, 48-hour Holter monitor	74.0%	NR
			PVI + SVC	134				81.0%	NR
Deisenhofer	2003	Case Series	PVI	75	7.6	Sinus rhythm	7-day Holter monitor	51.0%	NR
Deisenhofer	2009	RCT	PVI only	48	19	Freedom from AF	7-day Holter ECG	74.0%	73.9%
			PVI + CFAEs	50				83.0%	83.3%
Della Bella	2009	RCT	CartoMerge™	145	14	Freedom from AF	7-day Holter, 24-hour ECG Holter monitor	NR	89.0%
			Conventional RFCA procedure	145				NR	69.7%
Di Biase	2009	Prospective Cohort Study	PVI + Posterior LA wall, CFAEs, mitral annular/LA roof lesions, CS isolation, and RA ablation; manual approach	193	14.1	Freedom from AF	7-day Holter monitor	81.0%	NR

Author	Year	Study Design	Intervention	Study population	Mean Follow-up, months	Outcome	AF monitoring method	Reported Crude%	Reported Kaplan%
			PVI + Posterior left atrial wall, CFAEs, mitral annular/LA roof lesions, CS isolation, and RA ablation; robotic approach	197	14.1	Freedom from AF		85.0%	NR
Di Biase	2009	RCT	PVI only	35	12	Freedom from AF	48-hour Holter monitor, event recorder	89.0%	NR
			CFAEs ablation only	34	12	Freedom from AF		23.0%	NR
			PVI + CFAEs	34	12	Freedom from AF		91.0%	NR
Essebag	2005	Case Series	PVI + mitral isthmus line and/or posterior LA line	85	12	Freedom from AF	24-hour Holter monitor, 2-week event recorder, or continuous mobile outpatient cardiac telemetry	NR	76.0%
Forleo	2009	RCT	PVI + CTI, roofline connecting superior PVs, isthmus between mitral annulus and left inferior PV	35	12	Freedom from AF	ECG Holter monitor	NR	80.0%
			ADT	35				NR	42.9%
Helms	2009	Case Series	CPVI	73	12	Freedom from AF	Holter or event monitor	66.0%	NR
Hocini	2005	RCT	PVI + linear ablation joining the 2 superior PVs (roofline) + CTI	45	14	Freedom from AF	ECG	87.0%	87.0%
			PVI only	45	15	Freedom from AF		69.0%	69.0%
Hof	2009	Case Series	WACA	146	19	Freedom from AF	ECG with event monitoring and reporting of	66.0%	NR

Author	Year	Study Design	Intervention	Study population	Mean Follow-up, months	Outcome	AF monitoring method	Reported Crude%	Reported Kaplan%
							symptoms		
Hsieh	2005	Prospective Cohort Study	PVI + SVC, non-PV foci, and CTI	37	52	Freedom from AF	ECG	NR	81.0%
			AVN ablation	32	58				100.0%
Hunter	2010	Case Series	WACA; for persistent AF: linear ablation and CFAEs	285	32.4	Freedom from AF	Ambulatory monitor	NR	73.8%
Husser	2004	Case Series	PVI + RA isthmus	78	6	Freedom from AF	ECG, Holter monitor, or event monitor	42.0%	NR
Jais	2008	RCT	PVI + CTI, linear lesions (LA roof), mitral isthmus	53	12	Freedom from AF	ECG, 24-hour Holter monitor	NR	89.0%
			ADT	59					23.0%
Joshi	2009	Case Series	PVI + Linear ablation (mitral isthmus and LA roof)	72	12	Freedom from AF	ECG, Holter monitor, event monitor, loop recorder for AF burden	65.0%	NR
Kanagaratnam	2001	Case Series	PVI only	71	29	Sinus rhythm	48-hour Holter monitor, loop recorder	21.0%	NR
Khaykin	2009	RCT	PVI only	30	25.2	Freedom from AF	ECG, 24-hour Holter monitor	80.0%	NR
			CPVI, CFAE (30%), mitral isthmus and LA roof lines (77%)	30					60.0%
Kim	2010	Prospective Cohort Study	CPVI with ablation of residual potentials	49	23.1	Freedom from AF	ECG or 24-hour Holter monitor	79.6%	NR
			CPVI alone	53	23.4	Freedom from AF			81.1%
Klemm	2006	Case Series	Segmental PVI, RA isthmus ablation	80	6	Sinus rhythm	Transtelephonic ECG, Holter ECG	61.3%	NR

Author	Year	Study Design	Intervention	Study population	Mean Follow-up, months	Outcome	AF monitoring method	Reported Crude%	Reported Kaplan%
Knecht	2010	Prospective Cohort Study	LA and RA appendages, CFAEs, CTI using 3DATG imaging	44	10	Freedom from AF	Ambulatory monitoring	NR	80.0%
			LA and RA appendages, CFAEs, cavotricuspid isthmus using Carto imaging	47				NR	85.0%
Kriatselis	2009	Case Series	PVI only	44	6	Sinus rhythm	24-hour Holter ECG	70.0%	NR
Kumagai	2005	Prospective Cohort Study	Basket catheter-guided ablation	50	12	Freedom from AF	ECG, 24-hour Holter monitor	80.0%	NR
			Circular catheter-guided ablation	50				62.0%	NR
Kusumoto	2009	Case Series	PVI with stepwise ablation: after PVI, linear ablation, CFAEs	240	12	Sinus rhythm	24-hour ambulatory ECG monitor, 30-day event recorder, or 21 day mobile cellular outpatient telemetry	92.1%	NR
Lakkireddy	2005	Prospective Cohort Study	PVI in patients without pacemakers or ICD	86	12	Freedom from AF	Rhythm transmitter, 48-hour Holter monitor	21.0%	79.0%
			PVI in patients with pacemakers or ICD	86	12	Freedom from AF		19.0%	81.0%
Lin	2009	Prospective Cohort Study	PVI + Linear ablation (roof line and lateral mitral line) + CFAEs	30	19	Sinus rhythm	24-hour Holter monitor and/or cardiac event monitor	83.0%	NR
			PVI + Linear ablation (roof line and lateral mitral line)	30				67.0%	NR
Lo	2009	Prospective Cohort Study	PVI + Linear ablation, CFAEs; LA diameter of < 45mm	49	24	Freedom from AF	24-hour Holter monitor and/or cardiac event monitor	55.0%	NR

Author	Year	Study Design	Intervention	Study population	Mean Follow-up, months	Outcome	AF monitoring method	Reported Crude%	Reported Kaplan%
			PVI + Linear ablation, CFAEs; LA diameter of ≥ 45 mm	37				45.0%	NR
Macle	2002	Case Series	PVI + Bidirectional CTI block, linear ablation, lateral mitral isthmus line	136	8.8	Freedom from AF	Telephone interview	81.0%	NR
Macle	2007	Case Series	PVI + Posterior LA	64	16	Freedom from AF	ECG, Holter monitor	92.0%	NR
Malmborg	2003	Case Series	PVI only	40	8.9	Freedom from AF	24-hour Holter ECG	52.5%	NR
Mangrum	2002	Case Series	CPVI; additional ablation for AFL or right AFL: tricuspid annulus/IVC linear lesion(s) and ectopy-initiating AF outside the PV	56	13	Freedom from AF	ECG, Holter monitor; 24-h Holter monitor or 30-day event recorder	66.0%	NR
Marrouche	2007	RCT	Open-Irrigation	26	12	Freedom from AF	24-hour Holter monitor	80.8%	NR
			ICE-Guided Energy Delivery with a Non-Irrigated Catheter	27				77.8%	NR
Matsuo	2009	Case Series	PVI + CFAEs, linear ablation if AF continued (joining right and left superior PVs), then if it still continued, a mitral isthmus line	90	28	Freedom from AF	ECG, 24-hour Holter monitor, 24-hour ambulatory monitor	85.0%	NR
Meissner	2009	Case Series	PVI only	72	6	Freedom from AF	24-hour Holter monitor	72.2%	NR
Mesas	2006	Case Series	CPVI	47	12.7	Freedom from AF	Transtelephonic ECG, Holter monitor	58.0%	NR
Nademanee	2008	Case Series	CFAE ablation only	635	27.9	Sinus rhythm	Holter monitor	81.4%	NR

Author	Year	Study Design	Intervention	Study population	Mean Follow-up, months	Outcome	AF monitoring method	Reported Crude%	Reported Kaplan%
Neumann	2008	Prospective Cohort Study	CPVI in paroxysmal AF patients	293	12	Sinus rhythm	7-day Holter monitor	NR	74.0%
			CPVI in persistent AF patients	53	12	Sinus rhythm		NR	42.0%
O'Neill	2009	Case Series	PVI + CFAEs, linear ablation (mitral isthmus and LA roof), RA, SVC, linear ablation (CTI)	153	34	Freedom from AF	Holter monitor	NR	85.0%
Oral	2006	Case Series	PVI + LA RFCA performed in 29% of patients; CPVI in 71% of patients	755	25	Sinus rhythm	Event monitors and/or serial ECGs and 24-hour Holter monitor	69.1%	NR
Oral	2006	RCT	CPVI	77	12	Freedom from AF	Event monitor	74.0%	NR
			ADT	69	12	Freedom from AF		58.0%	NR
Pappone	2001	Case Series	CPVI	251	10.4	Freedom from AF	Holter monitor	80.1%	NR
Pappone	2003	Prospective Cohort Study	CPVI	589	28.7	Freedom from AF	ECG and 24-hour Holter monitor	NR	78.0%
			ADT	582	30.4			NR	37.0%
Pappone	2006	RCT	CPVI	99	12	Freedom from AF	ECG, 24-hour Holter monitor, event monitor	NR	86.0%
			ADT	99				NR	22.0%
Patel	2010	Prospective Cohort Study	PVI + Posterior wall between PVs, anterior tissue to the right PV along the left septum, SVC, CFAEs; ablation performed in females	518	24	Freedom from AF	Transtelephonic ECG, 48-hour Holter monitor, event monitor	NR	68.5%

Author	Year	Study Design	Intervention	Study population	Mean Follow-up, months	Outcome	AF monitoring method	Reported Crude%	Reported Kaplan%
			PVI + Posterior wall between PVs, anterior tissue to the right PV along the left septum, SVC, CFAEs; ablation performed in males	2747	35	Freedom from AF		NR	77.5%
Pontoppidan	2009	RCT	PVI only	76	12	Freedom from AF	ECG, Holter monitor	NR	32.0%
			PVI + CTI	73				NR	34.0%
Rossillo	2008	Retrospective matched cohort study	PVI + SVC	85	15	Freedom from AF	Holter monitor	82.0%	NR
			DC-Shock	85				40.0%	NR
Saliba	2008	Case Series	PVI + SVC	40	12	Freedom from AF	Holter monitor	97.5%	NR
Sawhney	2009	Case Series	CPVI and LA linear ablation	71	63	Freedom from AF	Event monitor	NR	56.0%
Scharf	2009	Case Series	PVI only	50	6.3	Freedom from AF	7-day ECG	70.0%	NR
Shin	2008	Case Series	PVI + Non-PV triggers	68	6	Freedom from AF	ECG	78.0%	NR
Siklody	2009	Case Series	PVI only	30	7.4	Freedom from AF	ECG, 24-hour Holter monitor	73.3%	NR
Stabile	2006	RCT	CPVI with CTI line	68	12	Freedom from AF	Transtelephonic ECG recorder, standard ECG, Holter monitor	55.9%	NR
			ADT	69				8.9%	NR
Stabile	2009	Prospective Cohort Study	PVI + LA, CTI, using integrated approach	61	14.9	Freedom from AF	ECG or 24-hour ambulatory monitor	56.0%	NR
			PVI + LA, CTI using anatomical approach	36	15.2	Freedom from AF		58.0%	NR
Steven	2010	Prospective Cohort Study	PVI + Posterior LA wall, ipsilateral veins with robotic navigation of catheter	30	6	Freedom from AF	3-day Holter monitor	NR	73.0%

Author	Year	Study Design	Intervention	Study population	Mean Follow-up, months	Outcome	AF monitoring method	Reported Crude%	Reported Kaplan%
			PVI + Posterior LA wall, ipsilateral veins using a conventional approach to catheter ablation	30				NR	77.0%
Tan	2009	Case Series	PVI only	99	6	Freedom from AF		NR	60.6%
Tamborero	2009	RCT	Superior PVs were connected by linear lesions along the LA roof	60	9.8	Freedom from AF	48-hour Holter monitor	NR	47.0%
			PVI + LA posterior wall isolated by adding a second line connecting the inferior aspect of the 2 inferior PVs	60			48-hour Holter monitor	NR	45.0%
Themistoclakis	2010	Prospective Cohort Study	Ostial or antral level PVI; linear lesions, ablation of CFAEs, and isolation of the SVC were performed per institutional preference; discontinued with OAT	2692	10	Freedom from AF	ECG, Holter monitor, transtelephonic monitor	97.1%	NR
			Ostial or antral level PVI; linear lesions, ablation of CFAEs, and isolation of the SVC were performed per institutional preference; continued with OAT	663				NR	NR
Tzou	2010	Case Series	PVI only	120	60	Freedom from AF	Transtelephonic monitor, ECG	NR	71.0%

Author	Year	Study Design	Intervention	Study population	Mean Follow-up, months	Outcome	AF monitoring method	Reported Crude%	Reported Kaplan%
Udyavar	2008	Case Series	CPVI with PV carina	97	12.9	Freedom from AF	24-hour Holter monitor	74.2%	NR
Van Belle	2008	Case Series	CPVI; CTI ablation in 7 patients with isthmus flutter	141	24	Freedom from AF	Transtelephonic ECG, 24-hour Holter ECG	NR	86.0%
Wazni	2005	RCT	PVI only	33	12	Freedom from AF	Loop-event recorder; 24-hour Holter monitor	NR	63.0%
			ADT	37				NR	37.0%
Wazni	2009	Case Series	SVC, using the Hansen ablation system	63	6	Freedom from AF	Event recorder	76.0%	NR
Wiesfeld	2004	Case Series	PVI + LA, RA and respective appendages	25	28	Freedom from AF	24-hour Holter monitor, ambulatory monitor	NR	32.0%
Wilber	2010	RCT	PVI - Allowed at discretion of investigator; included left atrial linear lesions, CFAEs and CTI ablation	106	9	Freedom from AF	ECG, transtelephonic ECG, Holter monitor	NR	66.0%
			ADT	61				NR	16.0%
Wokhlu	2010	Case Series	Some CPVI, other WACA with additional linear lesions along the LA roof and the left inferior isthmus	323	24	Freedom from AF	Holter monitor	87.0%	NR
Wokhlu	2010	Case Series	Some PVI, some WACA	774	36	Freedom from AF	ECG, 24-hour Holter monitor	64.2%	NR
Yamada	2006	Case Series	CPVI	55	17	Freedom from AF	24-hour Holter and cardiac recordings; event monitor	92.7%	NR
Yamada	2009	Prospective Cohort Study	CPVI with vagal nerve ablation	60	12	Freedom from AF	24-hour Holter recordings, event	66.7%	NR

Author	Year	Study Design	Intervention	Study population	Mean Follow-up, months	Outcome	AF monitoring method	Reported Crude%	Reported Kaplan%
			Segmental PVI with vagal nerve ablation	60			monitor	46.7%	NR
Yoshida	2009	Case Series	PVI only	77	12	Freedom from AF	24-hour Holter monitor, event monitor	NR	66.2%
Antiarrhythmic agents									
AFFIRM	2003	RCT	Amiodarone	106	60	Freedom from AF	ECG	NR	31.0%
			Class I	116	60	Freedom from AF		NR	21.0%
			Amiodarone	131	60	Freedom from AF		NR	37.0%
			Sotalol	125	60	Freedom from AF		NR	15.0%
Channer	2004	RCT	Amiodarone	62	12	Sinus rhythm	ECG	33.0%	NR
			Amiodarone	63	12	Sinus rhythm		49.0%	NR
			Placebo	38	12	Sinus rhythm		5.0%	NR
Galperin	2001	RCT	Amiodarone	47	16.03	Sinus rhythm	ECG, Holter ECG	62.9%	NR
			Placebo	48	16.03	Sinus rhythm		20.0%	NR
Hohnloser	2000	RCT	Amiodarone	127	12	Sinus rhythm	ECG	56.0%	NR
			Diltiazem	125	12	Sinus rhythm		10.0%	NR
Kochiadakis	2000	RCT	Amiodarone	65	24	Sinus rhythm	24 hour ambulatory ECG	NR	42.6%
			Sotalol	61	24	Sinus rhythm		NR	13.3%
			Placebo	60	24	Sinus rhythm		NR	10.0%
Kochiadakis	2004	RCT	Amiodarone	72	21	Freedom from AF	24-h ambulatory ECG	NR	59.0%
			Propafenone	74	19	Freedom from AF		NR	52.0%
Le Heuzey	2009	RCT	Dronedarone	249	7	Freedom from AF	ECG	NR	36.5%
			Amiodarone	255	7	Freedom from AF		NR	58.0%
Roy	2000	RCT	Amiodarone	201	15.6	Freedom from AF	ECG	64.7%	NR
			Sotalol/Propafenone	202	15.6	Freedom from AF		37.1%	NR

Author	Year	Study Design	Intervention	Study population	Mean Follow-up, months	Outcome	AF monitoring method	Reported Crude%	Reported Kaplan%
						AF			
Singh	2005	RCT	Amiodarone	267	12	Freedom from AF	ECG	NR	52.0%
			Sotalol	261	12	Freedom from AF		NR	32.0%
			Placebo	137	12	Freedom from AF		NR	13.0%
Singh	2007	RCT	Dronedarone	828	12	Freedom from AF	Transtelephonic ECG monitor, ECG	NR	35.9%
			Placebo	409	12	Freedom from AF		NR	24.8%
Touboul	2003	RCT	Dronedarone	151	12	Freedom from AF	Transtelephonic ECG monitor, ECG	23.2%	NR
			Placebo	48	12	Freedom from AF		10.0%	NR
Thorascopic, off-pump surgical ablation									
Bagge	2009	Case Series	Thorascopic off-pump epicardial PVI and GP ablation	43	12	Freedom from AF	24-hour Holter recording, ECG	76.0%	NR
Beyer	2009	Case Series	PVI/autonomic denervation, GP stimulation	100	13.6	Sinus rhythm	24-hour Holter monitor	NR	87.0%
Castella	2010	Case Series	Thorascopic PVI	34	16	Freedom from AF	24-hour Holter monitor	62.0%	NR
Cui	2010	Case Series	Bilateral PV antrum isolation and division of the LOM	81	12.7	Sinus rhythm	ECG analysis, and 24- to 48-hour Holter monitor (for patients in SR with ECG)	79.6%	86.0%
Edgerton	2009	Case Series	Bilateral PV antrum isolation	74	6	Freedom from AF	ECG, 14- to 21-day auto-triggered event monitor	74.2%	NR
Edgerton	2009	Case Series	PVI/left-sided "Dallas" set	114	6	Sinus rhythm	ECG and 24-hour Holter monitor OR long-term monitor (a 14 to 21-day auto	71.1%	NR

Author	Year	Study Design	Intervention	Study population	Mean Follow-up, months	Outcome	AF monitoring method	Reported Crude%	Reported Kaplan%
							trigger event monitor)		
Edgerton	2009	Case Series	Bilateral PVI/GP stimulation/additional ablation post-testing	30	6	Freedom from AF	14- to 21-day event monitoring	80.0%	NR
Edgerton	2010	Case Series	Bilateral, epicardial PVI and partial autonomic denervation	52	12	Sinus rhythm	24-hour Holter monitor, 2-3 week event monitor, or interrogation of implanted pacemaker	80.8%	NR
Han	2009	Case Series	Bilateral PVI/GP ablation/LOM ablation	43	17	Freedom from AF	External loop recorder	65.0%	NR
Sirak	2008	Case Series	Totally thoracoscopic PVI, extended linear ablations across critical segments of atrial substrate	32	13	Freedom from AF	ECG	87.5%	NR
Wolf	2005	Case Series	Cox Maze IV	23	3	Freedom from AF	ECG or telemetry monitor	91.0%	NR
Yilmaz	2010	Case Series	Minimally invasive Cryomaze	30	11.6	Freedom from AF	ECG and 24-hour Holter monitor	77.0%	NR

ADT, antiarrhythmic drug therapy; AF, atrial fibrillation; AFL, atrial flutter; AVN, atrioventricular junction ; CFAEs, complex fractionated atrial electrograms; CPVI, circumferential pulmonary vein isolation; CS, coronary sinus; CT, computed tomography; CTI, cavotricuspid isthmus; DC, direct-current; ECG, electrocardiogram; GP, ganglionic plexi; ICD, implantable cardioverter-defibrillators; ICE, intracardiac echocardiogram; IVC, inferior vena cava; LA, left atrium; LOM, ligament of Marshall; MR, magnetic resonance; NR, not reported; OAT, oral anti-coagulation; PAF, paroxysmal atrial fibrillation; PeAF, persistent atrial fibrillation; PV, pulmonary vein; PVI, pulmonary vein isolation; RA, right atrium; RCT, randomized controlled trial; RF, radiofrequency; RFCA, radiofrequency catheter ablation; SVC, superior vena cava; WACA, wide-area circumferential ablation

Table B5. Hospitalizations

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Hospitalization Type	No. Hospitalizations	% Hospitalizations
Catheter ablation								
Forleo	2009	RCT	PVI + CTI, roofline connecting superior PVs, isthmus between mitral annulus and left inferior PV	35	12	Hospitalization	3	8.6%
			ADT	35	12	Hospitalization	12	34.4%
Kusumoto	2009	Case Series	PVI with stepwise ablation: after PVI, linear ablation, CFAEs	240	12	Hospitalization	9	3.8%
Pappone	2006	RCT	CPVI	99	12	Total hospitalizations	24	NA
			ADT	99	12	Total hospitalizations	167	NA
Themistoclakis	2010	Prospective Cohort Study	Ostial or antral level PVI; linear lesions, ablation of CFAEs, and isolation of the SVC were performed per institutional preference; discontinued with OAT	2692	10	Hospitalization	1	0.0%

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Hospitalization Type	No. Hospitalizations	% Hospitalizations
			Ostial or antral level PVI; linear lesions, ablation of CFAEs, and isolation of the SVC were performed per institutional preference; continued with OAT	663	10	Hospitalization	13	2.0%
Antiarrhythmic agents								
Hohnloser	2000	RCT	Amiodarone	127	12	Hospitalization	87	68.5%
		RCT	Diltiazem	125	12	Hospitalization	30	24.0%
Connolly	2009	RCT	Dronedarone	2301	30	Stroke-related hospitalizations	38	1.7%
			Placebo	2327	30	Stroke-related hospitalizations	55	2.4%
Hohnloser	2009	RCT	Dronedarone	2301	21	Cardiovascular events-related hospitalizations	675	29.3%
			Placebo	2327	21	Cardiovascular events-related hospitalizations	859	36.9%
Hohnloser	2009	RCT	Dronedarone	2301	21	Hospitalization for Atrial fibrillation	335	14.6%
			Placebo	2327	21	Hospitalization for Atrial fibrillation	510	21.9%

Thorascopic, off-pump surgical ablation

No hospitalizations reported during follow-up period

Stroke prevention

Connolly	2009	RCT	Dabigatran, 110 mg	6015	24	Hospitalization	2311	38.4%
			Dabigatran, 150 mg	6076	24	Hospitalization	2430	40.0%
			Placebo	6022	24	Hospitalization	2458	40.8%

ADT, antiarrhythmic drug therapy; CFAEs, complex fractionated atrial electrograms; CPVI, circumferential pulmonary vein isolation; CS, coronary sinus; CTI, cavotricuspid isthmus; DC, direct-current; NR, not reported; OAT, oral anti-coagulation; PVI, pulmonary vein isolation; RCT, randomized controlled trial; SVC, superior vena cava; WACA, wide-area circumferential ablation

Table B6. Quality of Life

Author	Year	Study Design	Intervention	Study N	Measure	Mean Δ in measurement score, treatment	Mean Δ in measurement score, control	p-value
Catheter ablation								
Jais	2008	RCT	PVI + CTI, linear lesions (LA roof), mitral isthmus	53	SF-36 physical, 12 months	8	5	0.01
					SF-36 mental, 12 months	10	7	0.01
			ADT	58	Symptom frequency, 12 months	-11	-4	0.002
					Symptom severity, 12 months	-12	-8	<0.0001
Khaykin	2009	RCT	PVI only	30	SF-36 physical, 6 months	9	1	0.29
					SF-36 physical role, 6 months	25	10	0.73
					SF-36 emotional role, 6 months	12	8	0.95

Author	Year	Study Design	Intervention	Study N	Measure	Mean Δ in measurement score, treatment	Mean Δ in measurement score, control	p-value
					SF-36 social functioning, 6 months	15	-4	0.32
					SF-36 bodily pain, 6 months	1	3	0.48
			CPVI, CFAE (30%), mitral isthmus and LA roof lines (77%)	30	SF-36 general health, 6 months	-5	-2	0.79
					Energy, 6 months	15	1	0.07
					Emotional well-being, 6 months	0	2	0.83
Pappone	2003	Prospective Cohort Study	CPVI	589	SF-36 physical, 12 months	10	1	ND
			ADT	582	SF-36 mental, 12 months	8	1	ND
Wazni	2005	Randomized Controlled Trial	PVI only	33	SF-36 general health, 6 months	22	11	<0.001
			ADT		SF-36 physical, 6 months	26	6	0.001

Author	Year	Study Design	Intervention	Study N	Measure	Mean Δ in measurement score, treatment	Mean Δ in measurement score, control	p-value
				37	SF-36 mental, 6 months	0	4	0.62
Wilber	2010	Randomized Controlled Trial	PVI - Allowed at discretion of investigator; included left atrial linear lesions, CFAEs and CTI ablation	106	SF-36 mental, 3 months	8.5	1.6	<0.001
					SF-36 physical, 3 months	6.9	0.4	<0.001
			ADT	61	Symptom frequency	-11.1	0.7	<0.001
					Symptom severity	-9.4	0	<0.001
Author	Year	Study Design	Intervention	Study N	Measure	Baseline Value (sd)	Post-ablation value (sd)	p-value
Wokhlu	2010	Case Series	Some CPVI, other WACA with additional linear lesions along the LA roof and the left inferior isthmus	323	SF-36 total score, 3 months	63.9 ± 19.2	80.8 ± 15.6	<0.001
					SF-36 total score, 12 months		80.6 ± 15.7	<0.001
					SF-36 total score, 24 months		80.5 ± 16.5	<0.001
					SF-36 physical score, 24 months	58.8 ± 20.1	76.2 ± 19.2	<0.001
					SF-36 mental score, 24 months	65.3 ± 18.6	79.8 ± 15.8	<0.001
Antiarrhythmic agents								
Hohnloser	2000	RCT	Amiodarone	127	SF-36 physical, 12 months	8	7	0.76
					SF-36 physical role, 12 months	17	20	0.66

Author	Year	Study Design	Intervention	Study N	Measure	Mean Δ in measurement score, treatment	Mean Δ in measurement score, control	p-value
					SF-36 bodily pain, 12 months	8	10	0.64
					SF-36 vitality, 12 months	7	10	0.24
			Diltiazem	125	SF-36 social functioning, 12 months	10	8	0.58
					SF-36 emotional role, 12 months	0	3	0.62
					SF-36 mental, 12 months	4	5	0.67
					SF-36 general health, 12 months	3	3	0.99
Thorascopic, off-pump surgical ablation								
Author	Year	Study Design	Intervention	Study N	Measure	Baseline Value (95% CI)	Post-ablation value (95% CI)	p-value
Bagge	2009	Case Series	Thorascopic off-pump epicardial PVI and GP ablation	43	SF-36 bodily pain, 12 months	72 (60-80)	74 (62-81)	0.39
					SF-36 general health, 12 months	52 (44-60)	64 (59-77)	0.007
					SF-36 vitality, 12 months	42 (36-46)	60 (48-70)	<0.001
					SF-36 social function, 12 months	63 (57-76)	82 (77-91)	<0.001
					SF-36 role function limited due to emotional problems, 12 months	45 (37-59)	78 (62-89)	<0.001
					SF-36 mental health, 12 months	64 (60-78)	78 (74-84)	<0.001

Author	Year	Study Design	Intervention	Study N	Measure	Mean Δ in measurement score, treatment	Mean Δ in measurement score, control	p-value
					SF-36 physical functioning, 12 months	67 (60-72)	80 (78-88)	0.0019
					SF-36 role function limited due to physical problems, 12 months	33 (20-42)	58 (44-75)	0.0078
					Symptoms-palpitation, 6 months	2.6 (2.1-3.1)	1.8 (1.1-2.4)	0.09
					Symptoms- fatigue, 6 months	3.6 (3.2-4.1)	2.2 (1.5-3.0)	0.018
					Symptoms- dizziness, 6 months	2.1 (1.7-2.5)	1.9 (1.2-2.7)	0.35
					Symptoms- lack of energy, 6 months	3.9 (3.5-4.3)	2.5 (1.6-3.4)	0.07
					Symptoms- dyspnea, 6 months	2.9 (2.5-3.4)	1.9 (1.2-2.7)	0.07
					Symptoms-palpitation, 12 months	2.6 (2.1-3.1)	2.2 (1.7-2.6)	0.28
					Symptoms- fatigue, 12 months	3.6 (3.2-4.1)	2.2 (1.7-2.7)	0.004
					Symptoms- dizziness, 12 months	2.1 (1.7-2.5)	1.8 (1.4-2.3)	0.67
					Symptoms- lack of energy, 12 months	3.9 (3.5-4.3)	2.5 (2.0-3.0)	0.006
					Symptoms- dyspnea, 12 months	2.9 (2.5-3.4)	2.0 (1.5-2.4)	<0.001

ADT, antiarrhythmic drug therapy; CFAEs, complex fractionated atrial electrograms; CPVI, circumferential pulmonary vein isolation; CTI, cavotricuspid isthmus; LA, left atrium; PVI, pulmonary vein isolation; RCT, randomized controlled trial; RFCA, radiofrequency catheter ablation; WACA, wide-area circumferential ablation

Table B7. Cessation of Anticoagulation

Author	Year	Study Design	Intervention	Study population	No. discontinuations	%Discontinued OAT	CVAs during follow-up
Jais	2008	RCT	PVI + CTI, linear lesions (LA roof), mitral isthmus	52	31	59.6%	NR
			ADT	53	18	34.0%	NR
Nademanee	2008	Case Series	CFAE ablation only	517	434	83.9%	5
Oral	2006	Case Series	CPVI	755	383	50.7%	0
Pappone	2006	RCT	CPVI	85	82	96.5%	NR
			ADT	NR	NR	NR	NR
Rossillo	2008	Retrospective matched cohort study	PVI + SVC	85	77	90.6%	0
			DC-Shock	85	29	34.1%	5
Themistoclakis	2008	Prospective Cohort Study	Ostial or antral level PVI; linear lesions, ablation of CFAEs, and isolation of the SVC were performed per institutional preference; discontinued with OAT	2692	2692	100.0%	2

Author	Year	Study Design	Intervention	Study population	No. discontinuations	%Discontinued OAT	CVAs during follow-up
			Ostial or antral level PVI; linear lesions, ablation of CFAEs, and isolation of the SVC were performed per institutional preference; continued with OAT	663	0	0.0%	3
Wokhlu	2010	Case Series	Some CPVI, other WACA with additional linear lesions along the LA roof and the left inferior isthmus	306	210	68.6%	NR

ADT, antiarrhythmic drug therapy; AF, atrial fibrillation; CFAEs, complex fractionated atrial electrograms; CPVI, circumferential pulmonary vein isolation; CTI, cavotricuspid isthmus; DC, direct-current; NR, not reported; OAT, oral anti-coagulation; PVI, pulmonary vein isolation; RA, right atrium; RCT, randomized controlled trial; SVC, superior vena cava; WACA, wide-area circumferential ablation

Table B8. Repeat Ablations

Author	Year	Study Design	Intervention	Study N	# with Repeat ablation	Total # ablations	No. procedures per patient	% with repeat ablations	Blanking Period	Ablations during BP/Early ablations	Ablations Post-BP/Late ablations
Arentz	2003	Case Series	PVI + SVC, tricuspid annulus/IVC isthmus ablation	55	15	NR	1.27	27.3%	NR	NR	NR
Arentz	2003	Case Series	PVI + RA, SVC, LA	47	5	NR	1.6	10.6%	NR	NR	NR
Atienza	2009	Case Series	CPVI + dominant frequency sites	50	9	60	1.2	18.0%	2	NR	NR
Bunch	2010	Prospective Cohort Study	WACA, LA linear ablation, CTI; ablation in <80 year olds	717	559	NR	NR	78.0%	3	NR	NR
Bunch	2010	Prospective Cohort Study	WACA, LA linear ablation, CTI; ablation in ≥80 year olds	35	28	NR	NR	80.0%	3	NR	NR
Calvo	2010	Case Series	PVI + LA roof and LA posterior wall, mitral isthmus	182	67	NR	NR	36.8%	NR	NR	NR
Cheema	2006	Case Series	CPVI	64	19	NR	NR	29.7%	3	NR	NR
Corrado	2009	RCT (both arms)	PVI only // PVI + SVC	294	11	NR	NR	3.7%	2	NR	NR
Deisenhofer	2003	Case Series	PVI	75	34	109	1.5	45.3%	NR	23	11
Deisenhofer	2009	RCT	PVI only	48	15	NR	1.3	31.3%	1	0	15
Deisenhofer	2009	RCT	PVI + CFAEs	50	17	NR	1.4	34.0%	1	0	17
Essebag	2005	Case Series	PVI + mitral isthmus line and/or posterior LA line	85	5	NR	NR	5.9%	NR	NR	NR
Helms	2009	Case Series	CPVI	73	9	NR	NR	12.3%	1	NR	NR
Hof	2009	Case Series	WACA	146	15	NR	NR	10.3%	3	NR	NR

Author	Year	Study Design	Intervention	Study N	# with Repeat ablation	Total # ablations	No. procedures per patient	% with repeat ablations	Blanking Period	Ablations during BP/Early ablations	Ablations Post-BP/Late ablations
Hunter	2010	Case Series	WACA; for persistent AF: linear ablation and CFAEs	285	163	530	1.9	NA	3	0	530
Jais	2008	RCT	PVI + CTI, linear lesions (LA roof), mitral isthmus	53	23	155	1.8	43.4%	3	0	23
Joshi	2009	Case Series	PVI + Linear ablation (mitral isthmus and LA roof)	72	7	NR	NR	9.7%	3	NR	NR
Klemm	2006	Case Series	Segmental PVI, RA isthmus ablation	80	18	NR	NR	22.5%	NR	NR	NR
Kumagai	2005	Prospective Cohort Study (both arms)	Basket catheter-guided ablation//Circular catheter-guided ablation	50	34	100	2.0	68.0%	NR	NR	NR
Kusumoto	2009	Case Series	PVI with stepwise ablation: after PVI, linear ablation, CFAEs	240	38	NR	NR	15.8%	3	NR	NR
Lin	2009	Prospective Cohort Study	PVI + Linear ablation (roof line and lateral mitral line)	30	18	NR	NR	60.0%	2	0	18
Lin	2009	Prospective Cohort Study	PVI + Linear ablation (roof line and lateral mitral line) + CFAEs	30	6	NR	NR	20.0%	2	0	6

Author	Year	Study Design	Intervention	Study N	# with Repeat ablation	Total # ablations	No. procedures per patient	% with repeat ablations	Blanking Period	Ablations during BP/Early ablations	Ablations Post-BP/Late ablations
Lo	2009	Prospective Cohort Study	PVI + Linear ablation, CFAEs; LA diameter of < 45mm	49	14	NR	NR	28.6%	NR	NR	NR
Lo	2009	Prospective Cohort Study	PVI + Linear ablation, CFAEs; LA diameter of ≥45mm	37	7	NR	NR	18.9%	NR	NR	NR
Macle	2002	Case Series	PVI + Bidirectional CTI block, linear ablation, lateral mitral isthmus line	136	67	NR	NR	49.3%	NR	NR	NR
Macle	2007	Case Series	PVI + Posterior LA CPVI; additional ablation for AFL or right AFL: tricuspid annulus/IVC linear lesion(s) and ectopy-initiating AF outside the PV	64	38	100	1.6	59.4%	NR	NR	NR
Mangrum	2002	Case Series	Open-Irrigation	64	7	NR	NR	10.9%	NR	NR	NR
Marrouche	2007	RCT	ICE-Guided Energy Delivery with a Non-Irrigated Catheter	26	2	NR	NR	7.7%	NR	NR	NR
Marrouche	2007	RCT	CPVI	27	2	NR	NR	7.4%	NR	NR	NR
Mesas	2006	Case Series	PVI + CFAEs, linear ablation (mitral isthmus and LA roof), RA, SVC, linear ablation (CTI)	47	47	NR	NR	100.0%	NR	NR	NR
O'Neill	2009	Case Series		153	79	NR	NR	51.6%	1	0	79

Author	Year	Study Design	Intervention	Study N	# with Repeat ablation	Total # ablations	No. procedures per patient	% with repeat ablations	Blanking Period	Ablations during BP/Early ablations	Ablations Post-BP/Late ablations
Oral	2006	RCT	PVI + LA RFCA performed in 29% of patients; CPVI in 71% of patients	755	25	929	1.2	3.3%	2	0	25
Pappone	2006	RCT	CPVI	99	6	NR	NR	6.1%	1.75	0	6
Sawhney	2009	Case Series	CPVI and LA linear ablation	71	31	114	1.6	43.7%	1.5	0	31
Scharf	2009	Case Series	PVI only	50	25	NR	NR	50.0%	NR	NR	NR
Shin	2008	Case Series	PVI + Non-PV triggers	15	3	NR	NR	20.0%	NR	NR	NR
Tan	2009	Case Series	PVI only	99	41	NR	NR	41.4%	NR	NR	NR
Tzou	2010	Case Series	PVI only	123	15	NR	1.3	12.2%	NR	NR	NR
Van Belle	2008	Case Series	CPVI; CTI ablation in 7 patients with isthmus flutter	141	24	NR	NR	17.0%	3	NR	NR
Wazni	2005	RCT	PVI only	33	0	NR	NR	0.0%	2	NA	NA
Wazni	2009	Case Series	SVC, using the Hansen ablation system	71	5	NR	NR	7.0%	2	NR	NR
Wilber	2010	RCT	PVI - Allowed at discretion of investigator; included left atrial linear lesions, CFAEs and CTI ablation	106	13	NR	NR	12.3%	3	NR	NR
Yamada	2006	Case Series	CPVI	55	7	NR	NR	12.7%	NR	NR	NR
Yamada	2009	Prospective Cohort Study	Segmental PVI with vagal nerve ablation	60	15	NR	NR	25.0%	NR	NR	NR
Yamada	2009	Prospective Cohort	CPVI with vagal nerve ablation	60	8	NR	NR	13.3%	NR	NR	NR

Author	Year	Study Design	Intervention	Study N	# with Repeat ablation	Total # ablations	No. procedures per patient	% with repeat ablations	Blanking Period	Ablations during BP/Early ablations	Ablations Post-BP/Late ablations
Yoshida	2009	Case Series	PVI only	97	18	NR	NR	18.6%	NR	NR	NR

AFL, atrial flutter; BP: blanking period; CFAEs, complex fractionated atrial electrograms; CPVI, circumferential pulmonary vein isolation; CTI, cavotricuspid isthmus; ICD, implantable cardioverter-defibrillators; ICE, intracardiac echocardiogram; IVC, inferior vena cava; LA, left atrium; NA, not applicable; NR, not reported; PeAF, persistent atrial fibrillation; PV, pulmonary vein; PVI, pulmonary vein isolation; RA, right atrium; RCT, randomized controlled trial; RFCA, radiofrequency catheter ablation; SVC, superior vena cava; WACA, wide-area circumferential ablation

Table B9. Harms

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Intervention-specific harms			
						Periop. Mort.	Periop. Stroke	%Major compl.	%Minor compl.
			Catheter ablation						
Arentz	2003	Case Series	PVI + SVC, tricuspid annulus/IVC isthmus ablation	55	12	NR	NR	3.6%	1.8%
Arentz	2003	Case Series	PVI + RA, SVC, LA	47	24	NR	NR	2.1%	27.7%
Atienza	2009	Case Series	CPVI + dominant frequency sites	50	9.3	NR	NR	0.0%	8.0%
Baman	2009	Case Series	PVI + CFAEs in LA and CS	93	16	NR	NR	0.0%	0.0%
Berkowitsch	2009	Prospective Cohort Study	PVI + CFAEs, with RFCA	215	24	NR	NR	0.0%	0.0%
Berkowitsch	2009	Prospective Cohort Study	PVI + CFAEs, with cryoballoon ablation	105	24	NR	NR	0.0%	0.0%
Bertaglia	2009	Prospective Cohort Study	Segmental PV ostia isolation	240	11.6	NR	NR	2.5%	5.4%
Bunch	2010	Prospective Cohort Study	WACA, LA linear ablation, CTI; ablation in <80 year olds	717	36	0.7%	NR	1.5%	1.3%
Bunch	2010	Prospective Cohort Study	WACA, LA linear ablation, CTI; ablation in ≥80 year olds	35	36	0.0%	NR	5.7%	2.9%

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Intervention-specific harms			
Calvo	2010	Prospective Cohort Study	PVI + LA roof and LA posterior wall, mitral isthmus	182	18.69	NR	NR	1.6%	1.1%
Cheema	2006	Case Series	CPVI	64	13	0.0%	0.0%	3.1%	3.1%
Corrado	2009	RCT	PVI only	160	12	NR	NR	1.3%	0.0%
Corrado	2009	RCT	PVI + SVC	134	12.0	NR	NR	0.0%	1.5%
Deisenhofer	2003	Case Series	PVI	75	19.2	0.0%	0.0%	10.7%	14.7%
Deisenhofer	2009	RCT	PVI only	48	19	NR	NR	0.0%	2.1%
Deisenhofer	2009	RCT	PVI + CFAEs	50	19	NR	NR	0.0%	4.0%
Della Bella	2009	RCT	CartoMerge™	145	14	NR	0.0%	1.4%	0.7%
Della Bella	2009	RCT	Conventional RFCA procedure	145	14	NR	0.0%	0.0%	0.7%
Di Biase	2009	Prospective Cohort Study	PVI + Posterior left atrial wall, CFAEs, mitral annular/LA roof lesions, CS isolation, and RA ablation; robotic approach	197	13.7	NR	NR	0.5%	0.5%
Di Biase	2009	Prospective Cohort Study	PVI + Posterior LA wall, CFAEs, mitral annular/LA roof lesions, CS isolation, and RA ablation; manual approach	193	14.6	NR	NR	1.0%	0.5%
Di Biase	2009	RCT	PVI only	35	13.7	NR	NR	0.0%	0.0%
Di Biase	2009	RCT	CFAEs ablation	34	13.7	NR	NR	0.0%	0.0%

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Intervention-specific harms			
			only						
Di Biase	2009	RCT	PVI + CFAEs	34	13.7	NR	NR	0.0%	0.0%
Essebag	2005	Case Series	PVI + mitral isthmus line and/or posterior LA line	85	15.8	0.0%	NR	2.4%	1.2%
Forleo	2009	RCT	PVI + CTI, roofline connecting superior PVs, isthmus between mitral annulus and left inferior PV	35	12	NR	NR	5.7%	5.7%
Helms	2009	Case Series	CPVI	73	12	NR	NR	0.0%	0.0%
Hocini	2005	Prospective Cohort Study	PVI + linear ablation joining the 2 superior PVs (roofline) + CTI//PVI only	90	14.5	NR	NR	2.2%	1.1%
Hof	2009	Case Series	WACA	146	19	NR	NR	0.0%	0.0%
Hsieh	2005	Prospective Cohort Study	PVI + SVC, non-PV foci, and CTI	37	58	0.0%	NR	0.0%	0.0%
Hsieh	2005	Prospective Cohort Study	AVN ablation	32	52	0.0%	NR	0.0%	0.0%
Hunter	2010	Case series	WACA; for persistent AF: linear ablation and CFAEs	285	32.4	0.0%	1.1%	3.2%	27.4%

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Intervention-specific harms			
Husser	2004	Case Series	PVI + RA isthmus	79	60.84	NR	NR	1.3%	2.5%
Jais	2008	RCT	PVI + CTI, linear lesions (LA roof), mitral isthmus	53	12	NR	NR	1.9%	3.8%
Joshi	2009	Case Series	PVI + Linear ablation (mitral isthmus and LA roof)	72	12	NR	NR	0.0%	0.0%
Kanagaratnam	2001	Case Series	PVI only	71	29	NR	NR	7.0%	19.7%
Khaykin	2009	RCT	PVI only	30	25.2	0.0%	0.0%	0.0%	3.3%
Khaykin	2009	RCT	CPVI, CFAE (30%), mitral isthmus and LA roof lines (77%)	30	25.2	0.0%	0.0%	0.0%	0.0%
Kim	2010	Prospective Cohort Study	CPVI with ablation of residual potentials	49	23.1	NR	NR	0.0%	0.0%
Kim	2010	Prospective Cohort Study	CPVI alone	53	23.4	NR	NR	0.0%	0.0%
Klemm	2006	Case Series	Segmental PVI, RA isthmus ablation	80	6	NR	NR	0.0%	0.0%
Knecht	2010	Prospective Cohort Study	LA and RA appendages, CFAEs, CTI using Carto imaging	47	10	NR	NR	0.0%	0.0%
Knecht	2010	Prospective Cohort Study	LA and RA appendages, CFAEs, CTI using 3DATG imaging	44	10	NR	NR	0.0%	0.0%

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Intervention-specific harms			
Kriatselis	2009	Case series	PVI only	44	6	NR	NR	0.0%	4.5%
Kumagai	2005	Prospective Cohort Study	Circular catheter-guided ablation	50	12	NR	NR	0.0%	28.0%
Kumagai	2005	Prospective Cohort Study	Basket catheter-guided ablation	50	12	NR	NR	0.0%	12.0%
Kusumoto	2009	Case Series	PVI with stepwise ablation: after PVI, linear ablation, CFAEs	240	12	NR	NR	0.0%	0.8%
Lakkireddy	2005	Prospective Cohort Study	PVI in patients with pacemakers or ICD	86	12	NR	1.2%	2.3%	1.2%
Lakkireddy	2005	Prospective Cohort Study	PVI in patients without pacemakers or ICD	86	12	NR	1.2%	1.2%	0.0%
Lin	2009	Prospective Cohort Study	PVI + Linear ablation (roof line and lateral mitral line) + CFAEs	30	19	NR	NR	0.0%	0.0%
Lin	2009	Prospective Cohort Study	PVI + Linear ablation (roof line and lateral mitral line)	30	19	NR	NR	0.0%	0.0%
Lo	2009	Prospective Cohort Study	PVI + Linear ablation, CFAEs; LA diameter of < 45mm	49	21	NR	NR	0.0%	2.0%

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Intervention-specific harms			
Lo	2009	Prospective Cohort Study	PVI + Linear ablation, CFAEs; LA diameter of ≥ 45 mm	37	21	NR	NR	0.0%	0.0%
Macle	2002	Case Series	PVI + Bidirectional CTI block, linear ablation, lateral mitral isthmus line	136	8.8	NR	0.0%	0.0%	1.5%
Macle	2007	Case Series	PVI + Posterior LA	64	16	NR	0.0%	3.1%	0.0%
Malmborg	2003	Case Series	PVI only	40	8.9	NR	NR	0.0%	20.0%
Mangrum	2002	Case Series	CPVI; additional ablation for AFL or right AFL: tricuspid annulus/IVC linear lesion(s) and ectopy-initiating AF outside the PV	64	13	NR	NR	1.6%	4.7%
Marrouche	2007	RCT	Open-Irrigation	26	14	NR	NR	0.0%	19.2%
Marrouche	2007	RCT	ICE-Guided Energy Delivery with a Non-Irrigated Catheter	27	14	NR	NR	0.0%	29.6%
Matsuo	2009	Case series	PVI + CFAEs, linear ablation if AF continued (joining right and left superior PVs), then if it still continued, a mitral	90	28	NR	NR	0.0%	0.0%

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Intervention-specific harms			
			isthmus line						
Meissner	2009	Case Series	PVI only	72	6	0.0%	0.0%	0.0%	4.2%
Mesas	2006	Case Series	CPVI	72	12.7	NR	NR	0.0%	0.0%
Nademanee	2008	Case Series	CFAE ablation only	517	27.9	0.2%	0.4%	2.9%	2.3%
Neumann	2008	Prospective Cohort Study	CPVI in paroxysmal and persistent AF patients	346	12	0.0%	0.0%	0.6%	2.0%
O'Neill	2009	Case Series	PVI + CFAEs, linear ablation (mitral isthmus and LA roof), RA, SVC, linear ablation (CTI)	153	32	NR	NR	1.3%	2.6%
Oral	2006	Case series	PVI + LA RFCA performed in 29% of patients; CPVI in 71% of patients	755	25	NR	0.9%	0.0%	0.0%
Oral	2006	RCT	CPVI	77	12	0.0%	NR	1.3%	0.0%
Pappone	2001	Case Series	CPVI	251	10.4	NR	0.0%	0.8%	0.8%
Pappone	2003	Prospective Cohort Study	CPVI	589	28.7	NR	0.0%	5.6%	0.2%

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Intervention-specific harms			
Pappone	2006	RCT	CPVI	99	12	NR	NR	0.0%	0.0%
Patel	2010	Prospective Cohort Study	PVI + Posterior wall between PVs, anterior tissue to the right PV along the left septum, SVC, CFAEs; ablation performed in females	518	24.28	NR	NR	0.0%	4.2%
Patel	2010	Prospective Cohort Study	PVI + Posterior wall between PVs, anterior tissue to the right PV along the left septum, SVC, CFAEs; ablation performed in males	2747	35.57	NR	NR	0.0%	3.2%
Pontoppidan	2009	RCT	PVI + CTI	73	31	NR	1.5%	5.5%	0.0%
Pontoppidan	2009	RCT	PVI only	76	37	NR	0.0%	2.6%	1.3%
Rossillo	2008	Retrospective matched cohort study	PVI + SVC//DC-Shock	170		NR	0.0%	0.0%	3.5%
Saliba	2008	Case Series	PVI + SVC	40	12	NR	NR	5.0%	0.0%
Sawhney	2009	Case Series	CPVI and LA linear ablation	71	42.2	NR	0.0%	0.0%	4.2%
Scharf	2009	Case	PVI only	50	20	NR	NR	4.0%	8.0%

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Intervention-specific harms			
		Series							
Shin	2006	Case Series	PVI + Non-PV triggers	68	6	NR	NR	0.0%	0.0%
Siklody	2009	Case Series	PVI only	30	7.4	NR	NR	0.0%	20.0%
Stabile	2006	RCT	CPVI with CTI line	68	12	NR	1.5%	0.0%	4.4%
Stabile	2009	Prospective Cohort Study	PVI + LA, CTI, using integrated approach	36	15.2	NR	NR	0.0%	2.8%
Stabile	2009	Prospective Cohort Study	PVI + LA, CTI using anatomical approach	61	14.9	NR	NR	0.0%	0.0%
Steven	2010	Prospective Cohort Study	PVI + Posterior LA wall, ipsilateral veins with robotic navigation of catheter	30	15.2	NR	0.0%	0.0%	0.0%
Steven	2010	Prospective Cohort Study	PVI + Posterior LA wall, ipsilateral veins using a conventional approach to catheter ablation	30	15.2	NR	0.0%	0.0%	0.0%
Tamborero	2009	RCT	Superior PVs were connected by linear lesions along the LA roof	60	9.8	NR	NR	0.0%	1.7%
Tamborero	2009	RCT	LA posterior wall isolated by adding a second line connecting the inferior aspect of	60	9.8	NR	NR	0.0%	3.3%

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Intervention-specific harms			
			the 2 inferior PVs						
Tan	2009	Case Series	Catheter ablation	99	6	NR	1.0%	1.0%	5.1%
Themistoclakis	2010	Prospective Cohort Study	No-OAT/Catheter ablation	2692	10	NR	0.2%	0.0%	0.0%
Themistoclakis	2010	Prospective Cohort Study	OAT/Catheter ablation	663	10	NR	0.0%	0.0%	0.0%
Tzou	2010	Case series	PVI only	123	70.8	NR	NR	0.0%	0.0%
Udyavar	2008	Case Series	CPVI with PV carina	97	12.9	NR	NR	0.0%	0.0%
Van Belle	2008	Case Series	CPVI; CTI ablation in 7 patients with isthmus flutter	141	24	NR	NR	1.4%	5.7%
Wazni	2005	RCT	PVI only	32	12	NR	NR	6.3%	6.3%
Wazni	2009	Case Series	SVC, using the Hansen ablation system	71	6	0.0%	NR	9.9%	8.5%
Wiesfeld	2004	Case Series	PVI + LA, RA and respective appendages	25	28	NR	NR	8.0%	12.0%
Wilber	2010	RCT	PVI - Allowed at discretion of investigator; included left atrial linear lesions, CFAEs and CTI	106	9	0.0%	NR	1.9%	2.8%

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Intervention-specific harms			
ablation									
Wokhlu	2010	Case Series	Some CPVI, other WACA with additional linear lesions along the LA roof and the left inferior isthmus	502	36	NR	1.2%	3.4%	7.4%
Wokhlu	2010	Case Series	Some PVI, some WACA	774	36	NR	NR	0.0%	0.0%
Yamada	2006	Case Series	CPVI	55	11	NR	NR	0.0%	0.0%
Yamada	2009	Prospective Cohort Study	CPVI with vagal nerve ablation	60	12	NR	NR	0.0%	0.0%
Yamada	2009	Prospective Cohort Study	Segmental PVI with vagal nerve ablation	60	12	NR	NR	0.0%	0.0%
Yoshida	2009	Case Series	PVI only	77	12	NR	NR	0.0%	0.0%
Antiarrhythmic agents						Annual Rate - Pulm. toxicity	Annual Rate - Thyroid toxicity	Annual Rate - Premature discount.	
AFFIRM	2003	RCT	Amiodarone	154	46	0.5%	NR	NR	
AFFIRM	2003		Placebo	135	46	0.1%	NR	NR	
Channer	2004	RCT	Amiodarone	62	12	1.6%	0.0%	8.1%	

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Intervention-specific harms		
Channer	2004		Amiodarone	63	12	0.0%	6.3%	17.5%
Channer	2004		Placebo	38	12	2.6%	0.0%	2.6%
Connolly	2009	RCT	Dronedarone	2301	30	NR	NR	NR
Connolly	2009		Placebo	2327	30	NR	NR	NR
Galperin	2001	RCT	Amiodarone	47	16.03	NR	1.6%	1.6%
Galperin	2001		Placebo	48	16.03	NR	0.0%	0.0%
Hohnloser	2000	RCT	Amiodarone	127	12	NR	5.5%	24.4%
Hohnloser	2000		Diltiazem	125	12	NR	0.0%	13.6%
Hohnloser	2009	RCT	Dronedarone	2301	21	0.1%	0.4%	7.2%
Hohnloser	2009		Placebo	2327	21	0.1%	0.3%	4.6%
Killborn	2002	Prospective Cohort Study	Amiodarone	550	12	NR	NR	NR
Killborn	2002		Placebo	14730	12	NR	NR	NR
Kochiadakis	2000	RCT	Amiodarone	65	24	NR	6.2%	11.5%
Kochiadakis	2000		Sotalol	61	24	NR	0.0%	1.6%
Kochiadakis	2000		Placebo	60	24	0.0%	0.0%	0.0%
Kochiadakis	2004	RCT	Amiodarone	72	19	NR	12.3%	10.5%
Kochiadakis	2004		Propafenone	72	21	NR	NR	1.6%
Le Heuzey	2009	RCT	Dronedarone	249	7	0.0%	2.8%	9.0%
Le Heuzey	2009		Amiodarone	255	7	0.0%	10.1%	18.8%
Roy	2000	RCT	Amiodarone	201	15.6	1.5%	1.1%	26.0%
Roy	2000		Sotalol/Propafenone	202	15.6	0.0%	0.0%	35.4%
Singh	2005	RCT	Amiodarone	267	12	0.7%	NR	NR
Singh	2005		Sotalol	261	12	0.0%	NR	NR

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Intervention-specific harms			
Singh	2005	RCT	Placebo	137	12	0.7%	NR	NR	
Singh	2007		Dronedarone	828	12	NR	13.4%	17.9%	
Singh	2007		Placebo	409	12	NR	17.1%	14.9%	
Touboul	2003	RCT	Dronedarone	54	12	NR	NR	0.0%	
Touboul	2003		Dronedarone	54	12	NR	NR	5.6%	
Touboul	2003		Dronedarone	43	12	NR	NR	11.6%	
Touboul	2003		Placebo	48	12	NR	NR	29.2%	
Thorascopic, off-pump surgical ablation						Periop. Mort.	Periop. Stroke	%Major compl.	%Minor compl.
Bagge	2009	Case Series	Thorascopic off-pump epicardial PVI and GP ablation	43	12	0.0%	2.3%	14.0%	23.3%
Beyer	2009	Case Series	PVI/autonomic denervation, GP stimulation	100	13.6	0.0%	NR	4.0%	8.0%
Castella	2010	Case Series	Thorascopic PVI	34	16	0.0%	2.9%	8.8%	2.9%
Cui	2010	Case Series	Bilateral PV antrum isolation and division of the LOM	81	12.7	1.2%	1.2%	3.7%	4.9%
Edgerton	2009	Case Series	Bilateral PV antrum isolation	74	6	NR	NR	0.0%	0.0%
Edgerton	2009	Case Series	PVI/left-sided "Dallas" set	114	17	1.8%	NR	4.4%	6.1%

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Intervention-specific harms				
Edgerton	2009	Case Series	Bilateral PVI/GP stimulation/additional ablation post-testing	30	6	0.0%	0.0%	0.0%	16.7%	
Edgerton	2010	Case series	Bilateral, epicardial PVI and partial autonomic denervation	52	12	0.0%	0.0%	0.0%	7.7%	
Han	2009	Case Series	Bilateral PVI/GP ablation/LOM ablation	45	17	0.0%	NR	0.0%	11.1%	
Sirak	2008	Case Series	Totally thoracoscopic PVI, extended linear ablations across critical segments of atrial substrate	32	13	0.0%	0.0%	3.1%	0.0%	
Wolf	2005	Case Series	Cox Maze IV	27	14.5	0.0%	0.0%	3.7%	11.1%	
Yilmaz	2010	Case Series	Minimally invasive Cryomaze	30	11.6	0.0%	0.0%	3.3%	6.7%	
Stroke prevention - Dabigatran						Annual Rate - Major bleeding	Annual Rate - Minor bleeding	Annual Rate - Intracranial bleeding	Annual Rate - Extracranial bleeding	Annual Rate - Discontinuation
Connolly	2009	RCT	Dabigatran, 110 mg	6015	24	2.71	13.16	0.23	2.51	9.7%
			Dabigatran, 150 mg	6076	24	3.11	14.84	0.3	2.84	10.0%
			Warfarin	6022	24	3.36	16.37	0.74	2.67	7.5%

Author	Year	Study Design	Intervention	Study N	Mean Follow-up, months	Intervention-specific harms		
						Periop. Mort.	Periop. Stroke	Procedural Compl.
Stroke prevention - Watchman								
Holmes	2009	RCT	Watchman	463	18	0	1.1%	6.50%
			Warfarin	244	18	NR	0	NR

ADT, antiarrhythmic drug therapy; AFL, atrial flutter; AVN, atrioventricular junction ; CFAEs, complex fractionated atrial electrograms; Compl., complications; CPVI, circumferential pulmonary vein isolation; CS, coronary sinus; CT, computed tomography; CTI, cavotricuspid isthmus; DC, direct-current; ECG, electrocardiogram; GP, ganglionic plexi; ICD, implantable cardioverter-defibrillators; ICE, intracardiac echocardiogram; IVC, inferior vena cava; LA, left atrium; LOM, ligament of Marshall; MR, magnetic resonance; Mort., mortality; NR, not reported; OAT, oral anti-coagulation; periop., perioperative; PeAF, persistent atrial fibrillation; PV, pulmonary vein; PVI, pulmonary vein isolation; RA, right atrium; RCT, randomized controlled trial; RFCA, radiofrequency catheter ablation; SVC, superior vena cava; WACA, wide-area circumferential ablation

APPENDIX C
META-ANALYSES

Figure C1. Meta-analysis of all-cause mortality for catheter ablation vs. AADs.

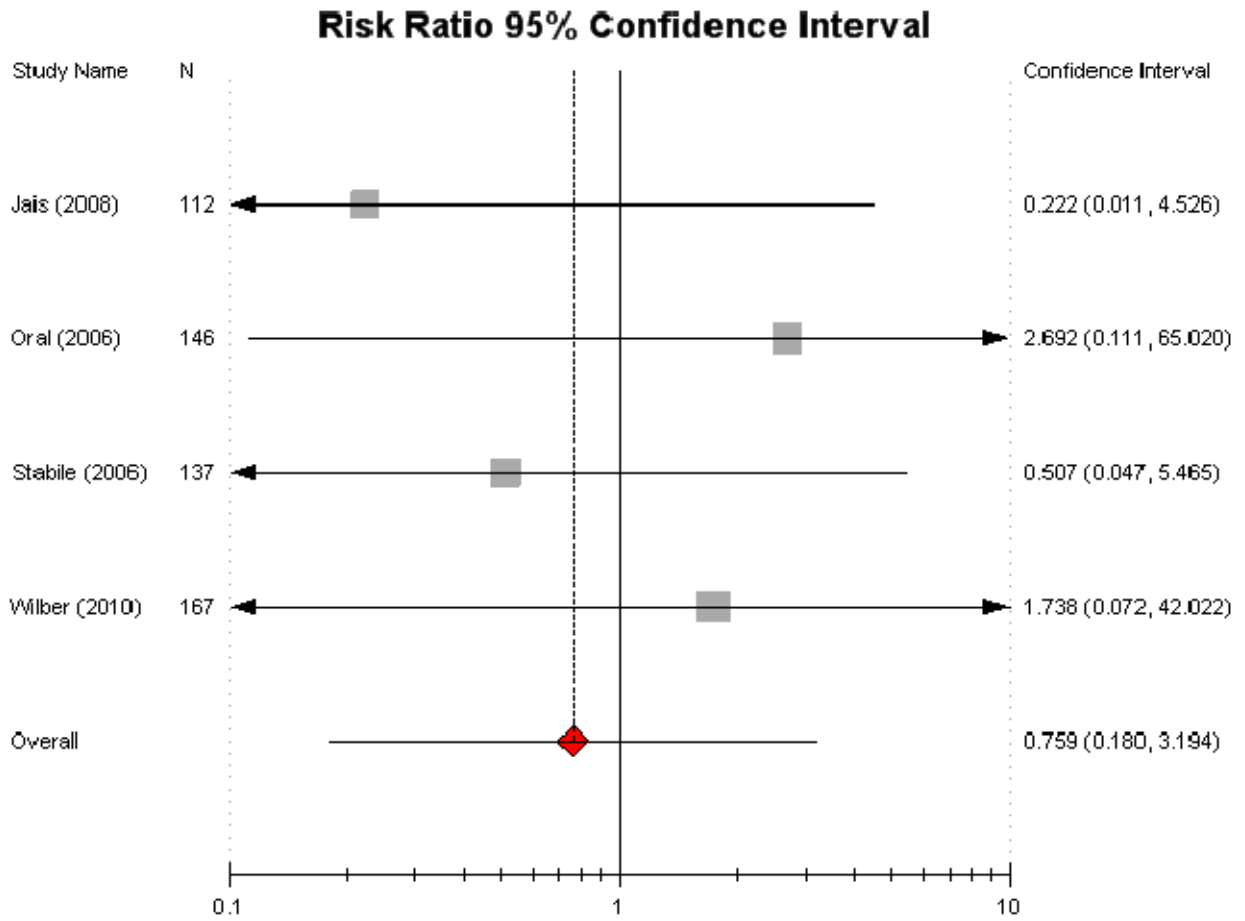


Figure C2. Meta-analysis of short-term freedom from AF for catheter ablation vs. AADs.

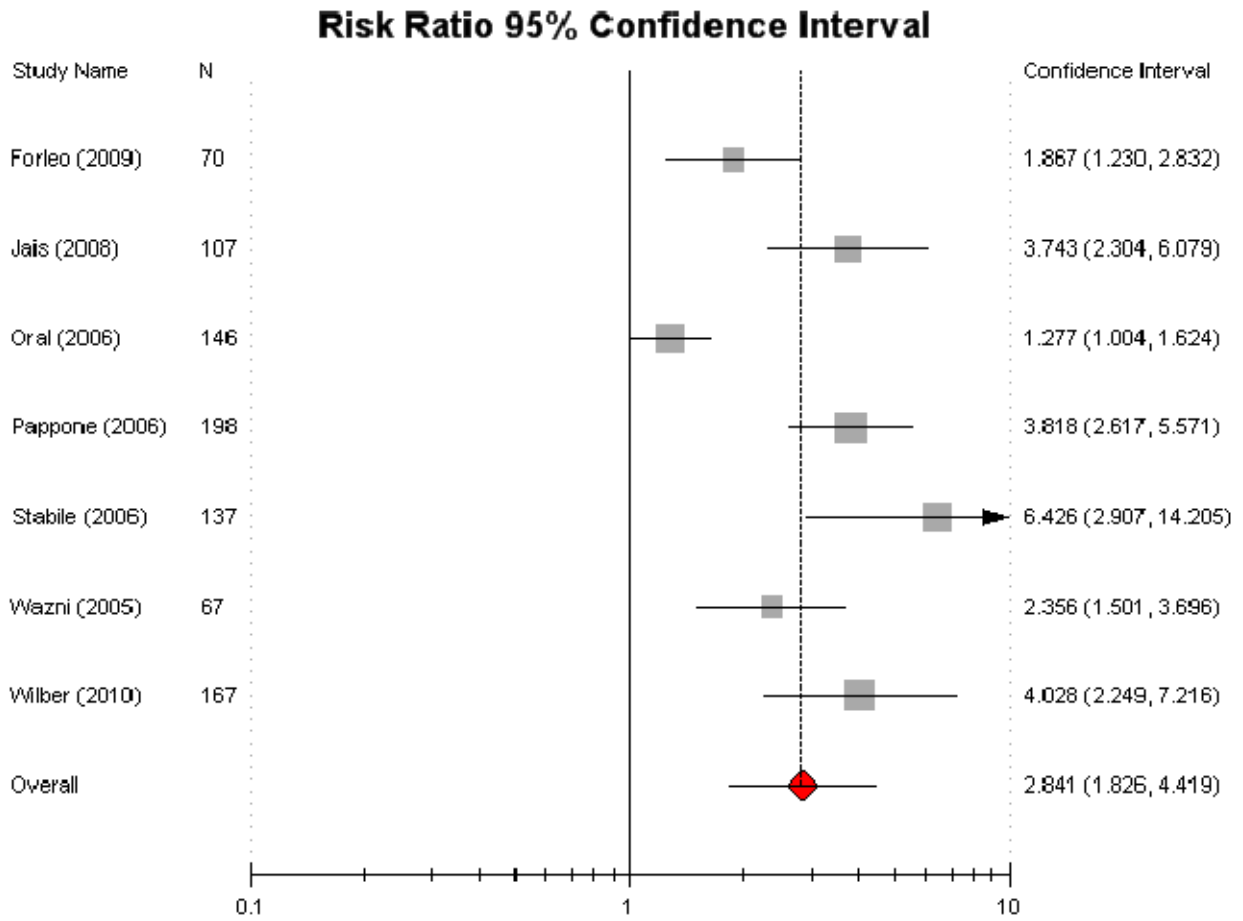


Figure C3. Meta-analysis of short-term freedom from AF for catheter ablation vs. AADs; predominantly paroxysmal AF populations.

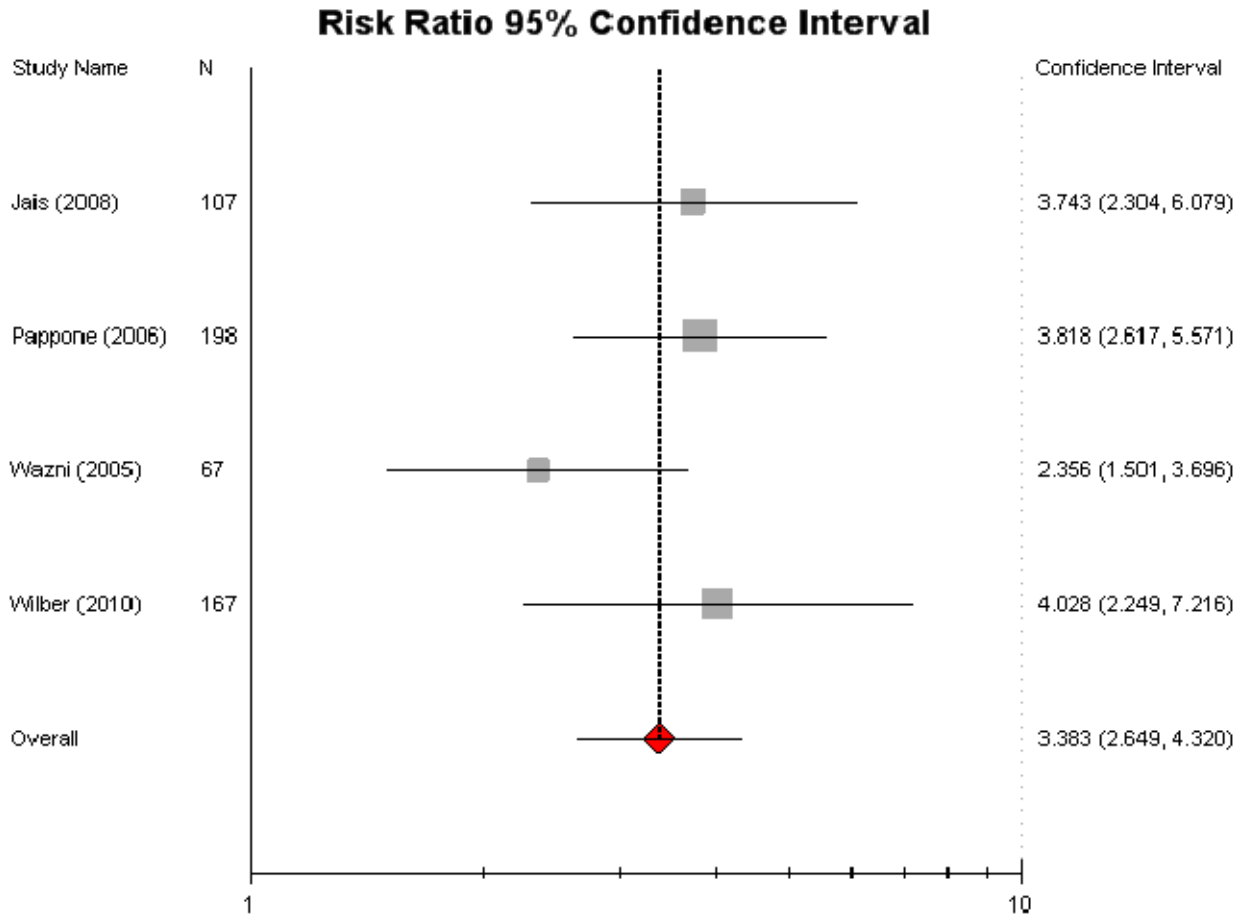


Figure C4. Meta-analysis of short-term freedom from AF for catheter ablation vs. AADs; mixed AF populations.

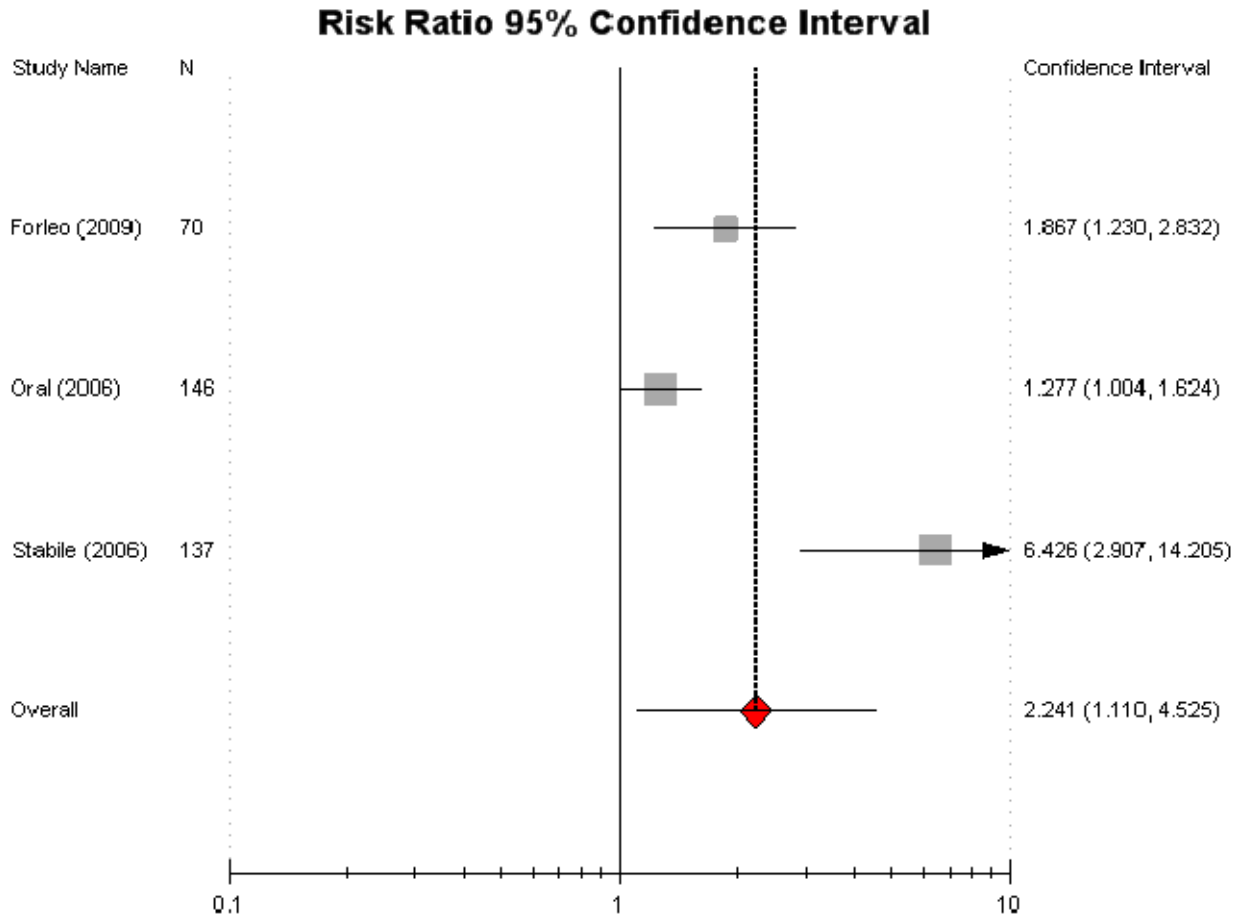


Figure C5. Pooled estimate of impact of amiodarone on all-cause mortality.

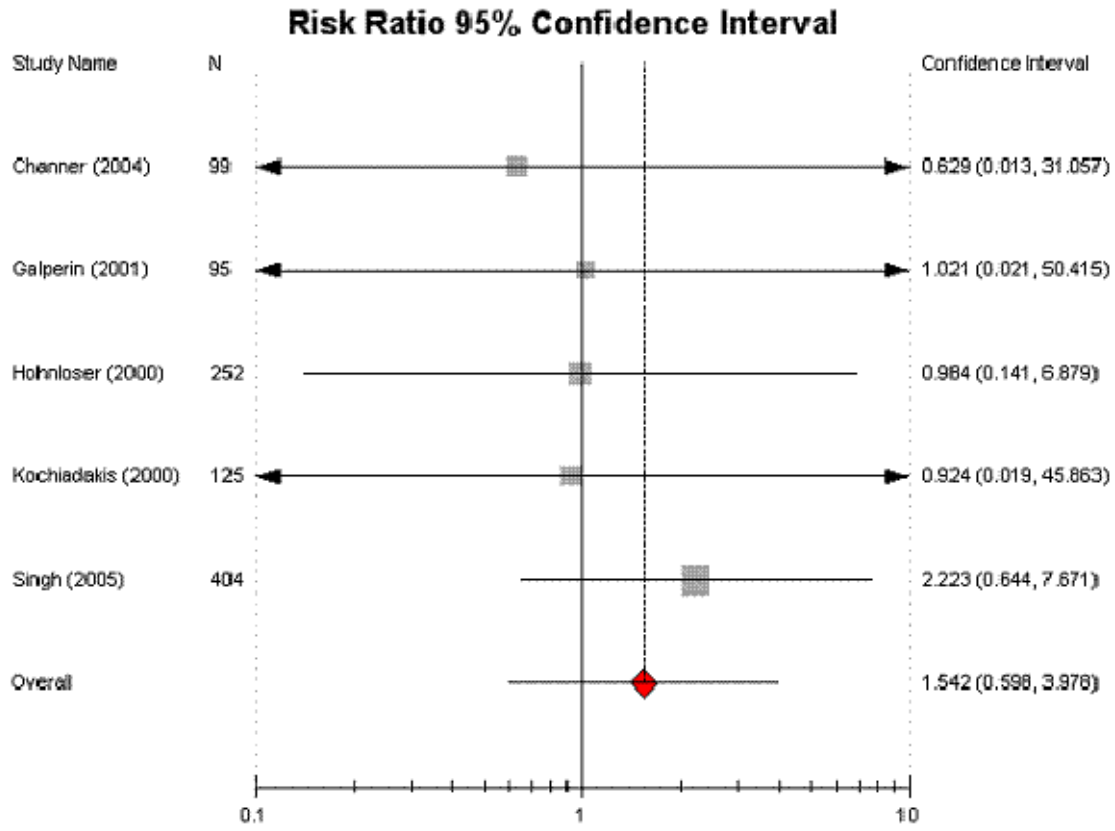


Figure C6. Pooled estimate of impact of dronedarone on all-cause mortality.

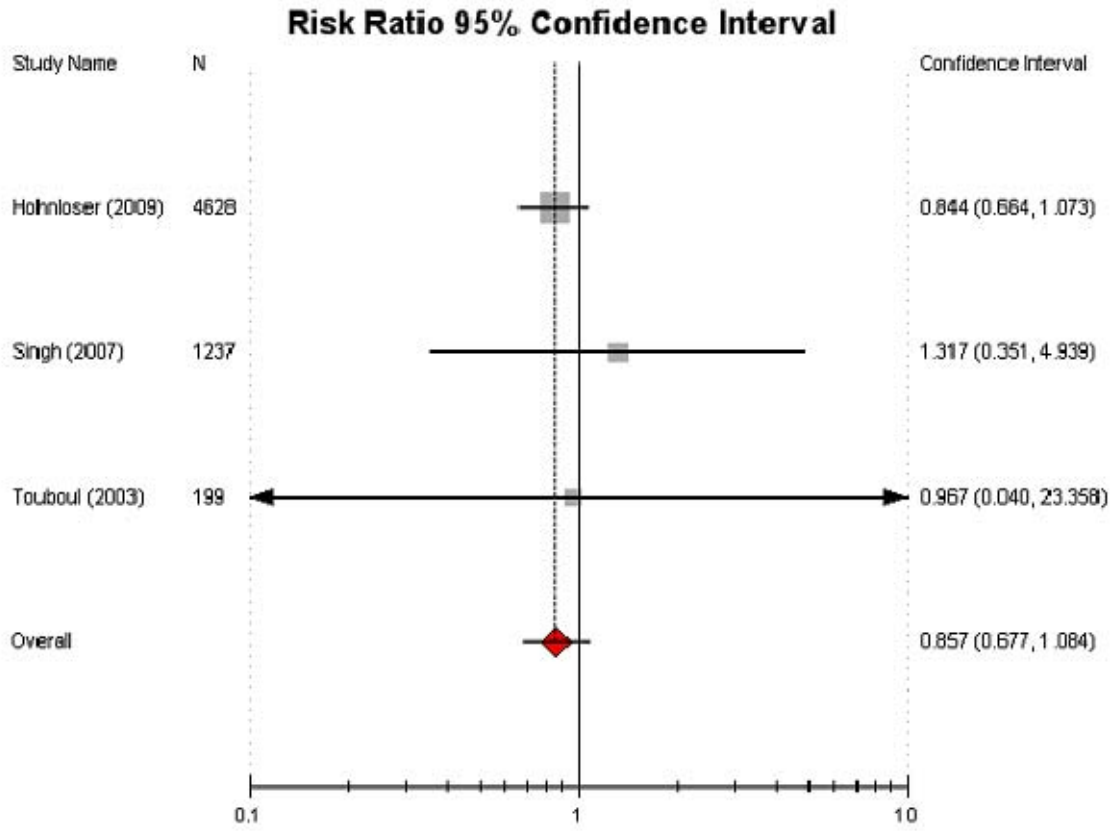


Table C1. Results of mixed treatment comparison of likelihood of freedom from AF at 6-12 months, by agent and comparison.

	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)

Note: Results are presented as agent in column vs. agent in row
 CI: Confidence interval

Table C2. Results of mixed treatment comparison of likelihood of drug discontinuation due to adverse effects, by agent and comparison.

	Amiodarone	Sotalol	Dronedarone
	Odds Ratio (95% CI)		
Control	5.82 (1.14, 20.01)	2.23 (0.13, 11.16)	8.89 (0.71, 43.41)
Amiodarone		0.46 (0.03, 2.20)	2.02 (0.14, 9.62)
Sotalol			12.86 (0.26, 74.58)

Note: Results are presented as agent in column vs. agent in row
 CI: Confidence interval

APPENDIX D

COMPARATIVE VALUE EVIDENCE TABLES

Table D1. Estimated lifetime clinical outcomes for cardiovascular management

Outcome	Rate Control	CA (Primary)	CA (Secondary)	TOP (Secondary)	Rhythm Control (Amiodarone)	Rhythm Control (Dronedarone)	Rhythm Control (Dronedarone First)
Age 60 Paroxysmal AF							
Life Years	20.484	20.407	20.216	19.92	20.28	20.28	20.28
AF Time	16.42	3.364	2.475	2.342	12.569	14.557	10.858
QALYs	11.032	11.629	11.507	11.463	11.116	11.022	11.217
<u>Microsimulation</u>							
Procedures		2.216	1.876	1.879	0	0	0
LACAs	0	2.216	1.861	0.988	0	0	0
Major complications	0	0.026	0.024	0.046	0	0	0
Minor complications	0	0.081	0.069	0.108	0	0	0
Stroke peri-procedure	0	0.009	0.007	0.009	0	0	0
Drug toxicity episodes	0.251	0.000	0.406	0.406	0.605	0.467	0.666
Strokes, Total	0.093	0.105	0.103	0.085	0.094	0.097	0.096
Intracranial hemorrhage	0.054	0.055	0.080	0.040	0.057	0.057	0.057
Deaths AF or AF related	0.026	0.017	0.029	0.024	0.038	0.039	0.037
Deaths peri-procedure	0.000	0.004	0.004	0.007	0.000	0	0.000
Death from all causes	0.962	0.957	0.948	0.954	0.949	0.948	0.951
Age 65 Persistent AF w/CHF							
Life Years	16.786	16.718	16.562	16.348	16.619	16.619	16.619
AF Time	13.013	5.011	3.554	3.405	9.602	11.335	8.091
QALYs	8.574	8.964	8.902	8.882	8.67	8.585	8.762
<u>Microsimulation</u>							
Procedures	0	2.416	1.975	1.981	0	0	0
LACAs	0	2.416	1.948	1.116	0	0	0
Major complications	0	0.028	0.025	0.046	0	0	0

Outcome	Rate Control	CA (Primary)	CA (Secondary)	TOP (Secondary)	Rhythm Control (Amiodarone)	Rhythm Control (Dronedarone)	Rhythm Control (Dronedarone First)
Minor complications	0	0.091	0.078	0.11	0	0	0
Stroke peri-procedure	0	0.008	0.006	0.009	0	0	0
Drug toxicity episodes	0.198	0	0.394	0.394	0.550	0.414	0.603
Strokes, Total	0.122	0.125	0.129	0.099	0.119	0.120	0.119
Intracranial hemorrhage	0.052	0.051	0.100	0.053	0.051	0.052	0.050
Deaths AF or AF related	0.027	0.017	0.029	0.027	0.040	0.040	0.039
Deaths peri-procedure	0	0.003	0.003	0.006	0	0	0
Death from all causes	0.961	0.957	0.949	0.952	0.948	0.948	0.949
Age 75 DM/HTN/ Persistent AF							
Life Years	10.525	10.492	10.393	10.014	10.42	10.42	10.42
AF Time	7.747	2.11	1.405	1.258	5.206	6.424	4.119
QALYs	5.703	6.003	5.944	5.828	5.797	5.733	5.87
Microsimulation							
Procedures	0	2.117	1.535	1.516	0	0	0
LACAs	0	2.117	1.515	0.754	0	0	0
Major complications	0	0.024	0.017	0.035	0	0	0
Minor complications	0	0.079	0.054	0.085	0	0	0
Stroke peri-procedure	0	0.008	0.006	0.008	0	0	0
Drug toxicity episodes	0.124	0	0.343	0.343	0.427	0.314	0.466
Strokes, Total	0.101	0.111	0.106	0.114	0.100	0.102	0.102
Intracranial hemorrhage	0.049	0.045	0.084	0.043	0.044	0.047	0.049
Deaths AF or AF related	0.020	0.013	0.024	0.025	0.028	0.029	0.029
Deaths peri-procedure	0	0.003	0.002	0.005	0	0	0
Death from all causes	0.966	0.961	0.953	0.951	0.956	0.954	0.956

Table D2. Estimated lifetime clinical outcomes for stroke prevention

Outcome	Warfarin/Aspirin	Dabigatran 110 mg	Dabigatran 150 mg	WATCHMAN
Age 60 Paroxysmal AF				
Life Years	20.484	20.783	20.814	20.221
AF Time	16.42	13.416	13.481	16.549
QALYs	11.032	11.401	11.417	11.011
<u>Microsimulation</u>				
Procedures		0	0	0.997
LACAs	0	0	0	0
Major complications	0	0	0	0.030
Minor complications	0	0	0	0.052
Stroke peri-procedure	0	0	0	0.010
Drug toxicity episodes	0.251	0.624	0.625	0.259
Strokes, Total	0.093	0.059	0.039	0.069
Intracranial hemorrhage	0.054	0.019	0.028	0.030
Deaths AF or AF related	0.026	0.026	0.023	0.018
Deaths peri-procedure	0.000	0.000	0.000	0.000
Death from all causes	0.962	0.960	0.963	0.975
Age 65 Persistent AF w/CHF				
Life Years	16.786	17.049	17.101	16.535
AF Time	13.013	10.305	10.406	13.147
QALYs	8.574	8.935	8.962	8.564
<u>Microsimulation</u>				
Procedures	0	0	0	1.00
LACAs	0	0	0	0
Major complications	0	0	0	0.033
Minor complications	0	0	0	0.054
Stroke peri-procedure	0	0	0	0.010
Drug toxicity episodes	0.198	0.571	0.571	0.212
Strokes, Total	0.122	0.076	0.051	0.088
Intracranial hemorrhage	0.052	0.015	0.024	0.024
Deaths AF or AF related	0.027	0.029	0.026	0.020
Deaths peri-procedure	0	0	0	0
Death from all causes	0.961	0.958	0.960	0.971
Age 75 DM/HTN/ Persistent AF				
Life Years	10.525	10.493	10.554	10.109
AF Time	7.747	5.391	5.488	7.565
QALYs	5.703	5.934	5.97	5.602

Outcome	Warfarin/Aspirin	Dabigatran 110 mg	Dabigatran 150 mg	WATCHMAN
<u>Microsimulation</u>				
Procedures	0	0	0	0.988
LACAs	0	0	0	0
Major complications	0	0	0	0.029
Minor complications	0	0	0	0.053
Stroke peri-procedure	0	0	0	0.010
Drug toxicity episodes	0.124	0.432	0.438	0.125
Strokes, Total	0.101	0.096	0.068	0.094
Intracranial hemorrhage	0.049	0.013	0.019	0.017
Deaths AF or AF related	0.020	0.031	0.027	0.018
Deaths peri-procedure	0	0	0	0
Death from all causes	0.966	0.953	0.956	0.969

Table D3. Estimated lifetime costs for cardiovascular management

Outcome	Rate Control	CA (Primary)	CA (Secondary)	TOP (Secondary)	Rhythm Control (Amiodarone)	Rhythm Control (Dronedarone)	Rhythm Control (Dronedarone First)
Age 60 Paroxysmal AF							
Total Costs	\$ 15,299	\$ 34,044	\$ 35,038	\$ 43,976	\$ 20,265	\$ 27,749	\$ 30,700
Procedure Costs	\$ -	\$ 22,172	\$ 17,285	\$ 29,715	\$ -	\$ -	\$ -
Complication Costs	\$ -	\$ 324	\$ 249	\$ 503	\$ -	\$ -	\$ -
Drug Costs	\$ 7,042	\$ 2,766	\$ 5,273	\$ 4,139	\$ 9,267	\$ 11,116	\$ 17,924
Adverse Event Costs	\$ 8,192	\$ 8,376	\$ 8,218	\$ 5,895	\$ 8,182	\$ 6,066	\$ 8,182
Age 65 Persistent AF w/CHF							
Total Costs	\$ 15,721	\$ 38,245	\$ 37,522	\$ 46,163	\$ 20,332	\$ 27,829	\$ 30,536
Procedure Costs	\$ -	\$ 24,868	\$ 18,837	\$ 30,918	\$ -	\$ -	\$ -
Complication Costs	\$ -	\$ 361	\$ 268	\$ 521	\$ -	\$ -	\$ -
Drug Costs	\$ 6,675	\$ 3,605	\$ 5,515	\$ 4,413	\$ 8,554	\$ 10,588	\$ 17,019
Adverse Event Costs	\$ 8,984	\$ 9,051	\$ 8,943	\$ 6,580	\$ 8,965	\$ 6,520	\$ 8,965
Age 75 DM/HTN/ Persistent AF							
Total Costs	\$ 13,792	\$ 34,410	\$ 32,081	\$ 39,744	\$ 17,759	\$ 24,334	\$ 26,560
Procedure Costs	\$ -	\$ 22,527	\$ 15,469	\$ 26,146	\$ -	\$ -	\$ -
Complication Costs	\$ -	\$ 311	\$ 211	\$ 477	\$ -	\$ -	\$ -
Drug Costs	\$ 6,708	\$ 3,756	\$ 4,877	\$ 3,174	\$ 7,939	\$ 9,014	\$ 15,120
Adverse Event Costs	\$ 7,014	\$ 6,877	\$ 6,889	\$ 5,753	\$ 7,024	\$ 5,306	\$ 7,024

Table D4. Estimated lifetime costs for stroke prevention

Outcome	Warfarin/Aspirin	Dabigatran 110	Dabigatran 150	WATCHMAN
Age 60 Paroxysmal AF				
Total Costs	\$ 15,299	\$ 83,015	\$ 82,780	\$ 23,053
Procedure Costs	\$ -	\$ -	\$ -	\$ 11,306
Complication Costs	\$ -	\$ -	\$ -	\$ 98
Drug Costs	\$ 7,042	\$ 76,046	\$ 76,232	\$ 6,423
Adverse Event Costs	\$ 8,192	\$ 4,153	\$ 3,731	\$ 5,001
Age 65 Persistent AF w/CHF				
Total Costs	\$ 15,721	\$ 72,795	\$ 72,451	\$ 22,659
Procedure Costs	\$ -	\$ -	\$ -	\$ 11,290
Complication Costs	\$ -	\$ -	\$ -	\$ 98
Drug Costs	\$ 6,675	\$ 65,255	\$ 65,613	\$ 5,764
Adverse Event Costs	\$ 8,984	\$ 4,726	\$ 4,025	\$ 5,287
Age 75 DM/HTN/ Persistent AF				
Total Costs	\$ 13,792	\$ 51,351	\$ 50,944	\$ 20,625
Procedure Costs	\$ -	\$ -	\$ -	\$ 11,215
Complication Costs	\$ -	\$ -	\$ -	\$ 97
Drug Costs	\$ 6,708	\$ 43,597	\$ 44,078	\$ 4,555
Adverse Event Costs	\$ 7,014	\$ 4,957	\$ 4,069	\$ 4,543

Table D5. Estimated 5-year clinical outcomes for cardiovascular management

Outcome	Rate Control	CA (Primary)	CA (Secondary)	TOP (Secondary)	Rhythm Control	Rhythm Control (Dronedaron)	Rhythm Control (Dronedaron First)
Age 60 Paroxysmal AF							
Life Years	4.83	4.821	4.778	4.772	4.783	4.783	4.783
AF Time	3.348	0.207	0.223	0.218	1.728	2.354	1.15
QALYs	3.548	3.739	3.675	3.672	3.627	3,589	3.675
<u>Microsimulation</u>							
Procedures	0	1.502	0.920	0.917	0	0	0
LACAs	0	1.502	0.910	0.252	0	0	0
Major complications	0	0.019	0.013	0.028	0	0	0
Minor complications	0	0.055	0.033	0.062	0	0	0
Stroke peri-procedure	0	0.006	0.003	0.005	0	0	0
Drug toxicity episodes	0	0.316	0.290	0.290	0.061	0.226	0.327
Strokes, Total	0.020	0.024	0.023	0.023	0.021	0.021	0.021
Intracranial hemorrhage	0.008	0.008	0.027	0.015	0.008	0.008	0.008
Deaths AF or AF related	0.006	0.002	0.015	0.015	0.017	0.017	0.017
Deaths peri-procedure	0.000	0.002	0.002	0.003	0.000	0	0
Death from all causes	0.063	0.063	0.062	0.063	0.061	0.061	0.058
Age 65 Persistent AF w/CHF							
Life Years	4.754	4.743	4.701	4.696	4.708	4.708	4.708
AF Time	3.275	0.38	0.289	0.274	1.689	2.3	1.125
QALYs	3.205	3.38	3.327	3.325	3.286	3.249	3.334

Outcome	Rate Control	CA (Primary)	CA (Secondary)	TOP (Secondary)	Rhythm Control	Rhythm Control (Dronedaron)	Rhythm Control (Dronedaron First)
<u>Microsimulation</u>							
Procedures	0	1.801	1.066	1.06	0	0	0
LACAs	0	1.801	1.049	0.398	0	0	0
Major complications	0	0.021	0.014	0.029	0	0	0
Minor complications	0	0.069	0.04	0.066	0	0	0
Stroke peri-procedure	0	0.006	0.003	0.005	0	0	0
Drug toxicity episodes	0.059	0	0.279	0.279	0.305	0.215	0.321
Strokes, Total	0.038	0.037	0.039	0.035	0.035	0.036	0.037
Intracranial hemorrhage	0.008	0.007	0.044	0.023	0.010	0.009	0.007
Deaths AF or AF related	0.009	0.004	0.014	0.014	0.017	0.017	0.017
Deaths peri-procedure	0.000	0.002	0.002	0.004	0.000	0	0
Death from all causes	0.094	0.093	0.093	0.096	0.093	0.094	0.094
Age 75 DM/HTN/ Persistent AF							
Life Years	4.452	4.445	4.404	4.378	4.409	4.409	4.409
AF Time	3.036	0.356	0.275	0.262	1.558	2.122	1.041
QALYs	2.817	2.982	2.931	2.935	2.896	2.861	2.94
<u>Microsimulation</u>							
Procedures	0	1.744	1.001	0.998	0	0	0
LACAs	0	1.744	0.984	0.367	0	0	0
Major complications	0	0.02	0.012	0.03	0	0	0
Minor complications	0	0.065	0.035	0.06	0	0	0
Stroke peri-procedure	0	0.007	0.003	0.004	0	0	0

Outcome	Rate Control	CA (Primary)	CA (Secondary)	TOP (Secondary)	Rhythm Control	Rhythm Control (Dronedaron)	Rhythm Control (Dronedaron First)
Drug toxicity episodes	0.054	0	0.267	0.267	0.292	0.211	0.307
Strokes, Total	0.039	0.046	0.043	0.046	0.037	0.039	0.040
Intracranial hemorrhage	0.021	0.016	0.053	0.028	0.022	0.022	0.022
Deaths AF or AF related	0.007	0.004	0.016	0.016	0.018	0.018	0.019
Deaths peri-procedure	0	0.002	0.002	0.003	0	0	0
Death from all causes	0.228	0.226	0.222	0.231	0.221	0.224	0.220

Table D6. Estimated 5-year clinical outcomes for stroke prevention

Outcome	Warfarin/Aspirin	Dabigatran 110 mg	Dabigatran 150 mg	WATCHMAN
Age 60 Paroxysmal AF				
Life Years	4.83	4.798	4.799	4.824
AF Time	3.348	1.746	1.746	3.343
QALYs	3.548	3.641	3.642	3.545
<u>Microsimulation</u>				
Procedures	0	0	0	0.997
LACAs	0	0	0	0
Major complications	0	0	0	0.035
Minor complications	0	0	0	0.052
Stroke peri-procedure	0	0	0	0.011
Drug toxicity episodes	0	0.318	0.318	0.062
Strokes, Total	0.020	0.008	0.005	0.019
Intracranial hemorrhage	0.008	0.004	0.006	0.006
Deaths AF or AF related	0.006	0.014	0.014	0.004
Deaths peri-procedure	0.000	0	0	0
Death from all causes	0.063	0.059	0.059	0.064
Age 65 Persistent AF w/CHF				
Life Years	4.754	4.73	4.731	4.748
AF Time	3.275	1.715	1.717	3.282
QALYs	3.205	3.307	3.308	3.206
<u>Microsimulation</u>				
Procedures	0	0	0	0.995
LACAs	0	0	0	0
Major complications	0	0	0	0.032
Minor complications	0	0	0	0.055
Stroke peri-procedure	0	0	0	0.008
Drug toxicity episodes	0.059	0.308	0.308	0.060
Strokes, Total	0.038	0.014	0.009	0.024
Intracranial hemorrhage	0.008	0.004	0.005	0.006
Deaths AF or AF related	0.009	0.013	0.012	0.005
Deaths peri-procedure	0.000	0	0	0
Death from all causes	0.094	0.089	0.089	0.096
Age 75 DM/HTN/ Persistent AF				
Life Years	4.452	4.411	4.415	4.407
AF Time	3.036	1.574	1.58	3.019
QALYs	2.817	2.946	2.951	2.828

Outcome	Warfarin/Aspirin	Dabigatran 110 mg	Dabigatran 150 mg	WATCHMAN
<u>Microsimulation</u>				
Procedures	0	0	0	0.988
LACAs	0	0	0	0
Major complications	0	0	0	0.030
Minor complications	0	0	0	0.052
Stroke peri-procedure	0	0	0	0.010
Drug toxicity episodes	0.054	0.293	0.294	0.058
Strokes, Total	0.039	0.038	0.027	0.041
Intracranial hemorrhage	0.021	0.005	0.007	0.007
Deaths AF or AF related	0.007	0.018	0.016	0.008
Deaths peri-procedure	0	0	0	0
Death from all causes	0.228	0.221	0.220	0.241

Table D7. Estimated 5-year costs for cardiovascular management

Outcome	Rate Control	CA (Primary)	CA (Secondary)	TOP (Secondary)	Rhythm Control (Amiodarone)	Rhythm Control (Dronedarone)	Rhythm Control (Dronedarone First)
Age 60 Paroxysmal AF							
Total Costs	\$ 2,631	\$ 17,925	\$ 15,337	\$ 25,207	\$ 6,062	\$ 11,160	\$ 12,941
Procedure Costs	\$ -	\$ 16,531	\$ 9,741	\$ 19,520	\$ -	\$ -	\$ -
Complication Costs	\$ -	\$ 205	\$ 118	\$ 348	\$ -	\$ -	\$ -
Drug Costs	\$ 1,663	\$ 135	\$ 1,088	\$ 1,066	\$ 2,285	\$ 3,082	\$ 7,634
Adverse Event Costs	\$ 953	\$ 908	\$ 917	\$ 841	\$ 960	\$ 786	\$ 960
Age 65 Persistent AF w/CHF							
Total Costs	\$ 3,052	\$ 21,657	\$ 17,340	\$ 27,009	\$ 6,464	\$ 11,541	\$ 13,299
Procedure Costs	\$ -	\$ 19,750	\$ 11,302	\$ 20,944	\$ -	\$ -	\$ -
Complication Costs	\$ -	\$ 257	\$ 142	\$ 367	\$ -	\$ -	\$ -
Drug Costs	\$ 1,647	\$ 214	\$ 1,111	\$ 1,104	\$ 2,258	\$ 3,108	\$ 7,579
Adverse Event Costs	\$ 1,391	\$ 1,265	\$ 1,299	\$ 1,154	\$ 1,393	\$ 1,101	\$ 1,393
Age 75 DM/HTN/ Persistent AF							
Total Costs	\$ 5,377	\$ 23,495	\$ 18,988	\$ 27,383	\$ 8,710	\$ 13,605	\$ 15,286
Procedure Costs	\$ -	\$ 19,219	\$ 10,657	\$ 19,812	\$ -	\$ -	\$ -
Complication Costs	\$ -	\$ 244	\$ 132	\$ 362	\$ -	\$ -	\$ -
Drug Costs	\$ 3,246	\$ 1,433	\$ 2,088	\$ 1,523	\$ 3,799	\$ 4,182	\$ 8,919
Adverse Event Costs	\$ 2,096	\$ 1,926	\$ 2,024	\$ 1,828	\$ 2,114	\$ 1,712	\$ 2,114

Table D8. Estimated 5-year costs for stroke prevention

Outcome	Warfarin/Aspirin	Rhythm Control (Dabigatran 110)	Rhythm Control (Dabigatran 150)	WATCHMAN
Age 60 Paroxysmal AF				
Total Costs	\$ 2,631	\$ 26,586	\$ 26,581	\$ 14,756
Procedure Costs	\$ -	\$ -	\$ -	\$ 11,306
Complication Costs	\$ -	\$ -	\$ -	\$ 98
Drug Costs	\$ 1,663	\$ 23,243	\$ 23,248	\$ 2,329
Adverse Event Costs	\$ 953	\$ 526	\$ 515	\$ 819
Age 65 Persistent AF w/CHF				
Total Costs	\$ 3,052	\$ 26,385	\$ 26,343	\$ 14,894
Procedure Costs	\$ -	\$ -	\$ -	\$ 11,290
Complication Costs	\$ -	\$ -	\$ -	\$ 98
Drug Costs	\$ 1,647	\$ 22,883	\$ 22,904	\$ 2,307
Adverse Event Costs	\$ 1,391	\$ 688	\$ 626	\$ 996
Age 75 DM/HTN/ Persistent AF				
Total Costs	\$ 5,377	\$ 25,536	\$ 25,386	\$ 15,549
Procedure Costs	\$ -	\$ -	\$ -	\$ 11,215
Complication Costs	\$ -	\$ -	\$ -	\$ 97
Drug Costs	\$ 3,246	\$ 21,222	\$ 21,292	\$ 2,551
Adverse Event Costs	\$ 2,096	\$ 1,517	\$ 1,297	\$ 1,481

Table D9. Lifetime costs and effectiveness of rate control with digoxin/atenolol vs. amiodarone with secondary rate control for AAD failure, by patient cohort

Strategy	Cost	Incremental Cost	Effectiveness (QALYs)	Incremental Effectiveness (QALYs)	ICER (\$/QALYs)
60 M Paroxysmal AF					
Rate Control	\$ 15,299		11.032		
Rhythm Control	\$ 20,265	\$ 4,967	11.116	0.084	\$ 59,179
65 M CHF and Persistent AF					
Rate Control	\$ 15,721		8.574		
Rhythm Control	\$ 20,332	\$ 4,611	8.670	0.095	\$ 48,384
75 M DM HTN Persistent AF					
Rate Control	\$ 13,792		5.703		
Rhythm Control	\$ 17,759	\$ 3,967	5.797	0.093	\$ 42,606

D10. Lifetime costs and effectiveness of amiodarone with secondary rate control for AAD failure vs. amiodarone with LACA for AAD failure, by patient cohort

Strategy	Cost	Incremental Cost	Effectiveness (QALYs)	Incremental Effectiveness (QALYs)	ICER (\$/QALYs)
60 M Paroxysmal AF					
Rhythm Control	\$ 20,265		11.116		
Secondary LA Catheter Ablation	\$ 35,038	\$ 14,773	11.507	0.391	\$ 37,808
65 M CHF and Persistent AF					
Rhythm Control	\$ 20,332		8.670		
Secondary LA Catheter Ablation	\$ 37,522	\$ 17,190	8.902	0.232	\$ 73,947
75 M DM HTN Persistent AF					
Rhythm Control	\$ 17,759		5.797		
Secondary LA Catheter Ablation	\$ 32,081	\$ 14,322	5.944	0.148	\$ 96,846

Table D11. Lifetime costs and effectiveness of primary LA catheter ablation vs. rhythm control with amiodarone, by patient cohort

Strategy	Cost	Incremental Cost	Effectiveness (QALYs)	Incremental Effectiveness (QALYs)	ICER (\$/QALYs)
60 M Paroxysmal AF					
Rhythm Control	\$ 20,265		11.116		
Primary LA Catheter Ablation	\$ 34,044	\$ 13,779	11.629	0.512	\$ 22,172
65 M CHF and Persistent AF					
Rhythm Control	\$ 20,332		8.67		
Primary LA Catheter Ablation	\$ 38,245	\$ 17,913	8.964	0.295	\$ 60,804
75 M DM HTN Persistent AF					
Rhythm Control	\$ 17,759		5.797		
Primary LA Catheter Ablation	\$ 34,410	\$ 16,651	6.003	0.207	\$ 80,615

Table D12. Lifetime costs and effectiveness of thorascopic, off-pump surgical ablation vs. secondary LA catheter ablation, by patient cohort

Strategy	Cost	Incremental Cost	Effectiveness (QALYs)	Incremental Effectiveness (QALYs)	ICER (\$/QALYs)
60 M Paroxysmal AF					
Secondary LA Catheter Ablation	\$ 35,038		11.507		
Thorascopic, Off-Pump Surgical Ablation	\$ 43,978	\$ 8,937	11.463	-0.043	Dominated
65 M CHF and Persistent AF					
Secondary LA Catheter Ablation	\$ 37,522		8.902		
T Surgical Ablation	\$ 46,163	\$ 8,641	8.882	-0.02	Dominated
75 M DM HTN Persistent AF					
Secondary LA Catheter Ablation	\$ 32,081		5.944		
Thorascopic, Off-Pump Surgical Ablation	\$ 39,744	\$ 7,663	5.828	-0.117	Dominated

Table D13. Lifetime costs and effectiveness of amiodarone, dronedarone alone, and dronedarone first with amiodarone for recurrent AF, by patient cohort

Strategy	Cost	Incremental Cost	Effectiveness (QALYs)	Incremental Effectiveness (QALYs)	ICER (\$/QALYs)
60 M Paroxysmal AF					
Amiodarone	\$ 20,265		11.116		
Dronedarone	\$ 27,749	\$ 7,484	11.022	-0.094	Dominated
Dronedarone First	\$ 30,700	\$ 10,435	11.217	0.1	\$ 103,892
65 M CHF and Persistent AF					
Amiodarone	\$ 20,332		8.670		
Dronedarone	\$ 27,829	\$ 7,497	8.585	-0.085	Dominated
Dronedarone First	\$ 30,536	\$ 10,204	8.762	0.092	\$ 110,440
75 M DM HTN Persistent AF					
Amiodarone	\$ 17,759		5.797		
Dronedarone	\$ 24,334	\$ 6,575	5.733	-0.064	Dominated
Dronedarone First	\$ 26,560	\$ 8,801	5.870	0.073	\$ 120,398

Dronedarone strategies compared to Amiodarone.

Table D14. Lifetime costs and effectiveness of dabigatran (110 mg and 150 mg doses) vs. warfarin, by patient cohort

Strategy	Cost	Incremental Cost	Effectiveness (QALYs)	Incremental Effectiveness (QALYs)	ICER (\$/QALYs)
60 M Paroxysmal AF					
Rhythm Control (Warfarin)	\$ 20,265		11.116		
Rhythm Control (Dabigatran 150 mg)	\$ 82,780	\$ 62,514	11.417	0.301	\$ 207,760
Rhythm Control (Dabigatran 110 mg)	\$ 83,015	\$ 62,750	11.401	0.285	\$ 220,212
65 M CHF and Persistent AF					
Rhythm Control (Warfarin)	\$ 20,332		8.670		
Rhythm Control (Dabigatran 150 mg)	\$ 72,451	\$ 52,119	8.962	0.292	\$ 178,483
Rhythm Control (Dabigatran 110 mg)	\$ 72,795	\$ 52,463	8.935	0.266	\$ 197,321
75 M DM HTN Persistent AF					
Rhythm Control (Warfarin)	\$ 17,759		5.797		
Rhythm Control (Dabigatran 150 mg)	\$ 50,944	\$ 33,184	5.970	0.173	\$ 191,757
Rhythm Control (Dabigatran 110 mg)	\$ 51,351	\$ 33,592	5.934	0.138	\$ 244,121

All strategies compared to common baseline Rhythm Control.

Table D15. Lifetime costs and effectiveness of WATCHMAN vs. warfarin, by patient cohort

Strategy	Cost	Incremental Cost	Effectiveness (QALYs)	Incremental Effectiveness (QALYs)	ICER (\$/QALYs)
60 M Paroxysmal AF					
Rate Control (Digoxin/ Atenolol)	\$ 15,299		11.032		
Rate Control - WATCHMAN	\$ 23,053	\$7,754	11.011	-0.021	Dominated
65 M CHF and Persistent AF					
Rate Control (Digoxin/ Atenolol)	\$ 15,721		8.574		
Rate Control - WATCHMAN	\$ 22,659	\$6,938	8.564	-0.01	Dominated
75 M DM HTN Persistent AF					
Rate Control (Digoxin/ Atenolol)	\$ 13,792		5.703		
Rate Control - WATCHMAN	\$ 20,625	\$6,833	5.602	-0.10	Dominated

All strategies compared to Rate Control.

Table D16. 5-year costs and effectiveness of rate control with digoxin/atenolol vs. amiodarone with secondary rate control for AAD failure, by patient cohort

Strategy	Cost	Incremental Cost	Effectiveness (QALYs)	Incremental Effectiveness (QALYs)	ICER (\$/QALYs)
60 M Paroxysmal AF					
Rate Control	\$ 2,631		3.548		
Rhythm Control	\$ 6,062	\$ 3,431	3.627	0.079	\$ 43,354
65 M CHF and Persistent AF					
Rate Control	\$ 3,052		3.205		
Rhythm Control	\$ 6,464	\$ 3,412	3.286	0.081	\$ 42,323
75 M DM HTN Persistent AF					
Rate Control	\$ 5,377		2.817		
Rhythm Control	\$ 8,710	\$ 3,333	2.896	0.078	\$ 42,511

Table D17. 5-year costs and effectiveness of amiodarone with secondary rate control for AAD failure vs. amiodarone with LACA for AAD failure, by patient cohort

Strategy	Cost	Incremental Cost	Effectiveness (QALYs)	Incremental Effectiveness (QALYs)	ICER (\$/QALYs)
60 M Paroxysmal AF					
Rhythm Control	\$ 6,062		3.627		
Secondary LA Catheter Ablation	\$ 15,337	\$ 9,275	3.675	0.048	\$ 193,272
65 M CHF and Persistent AF					
Rhythm Control	\$ 6,464		3.286		
Secondary LA Catheter Ablation	\$ 17,340	\$ 10,876	3.327	0.041	\$ 267,261
75 M DM HTN Persistent AF					
Rhythm Control	\$ 8,710		2.896		
Secondary LA Catheter Ablation	\$ 18,988	\$ 10,278	2.931	0.035	\$ 294,599

Table D18. 5-year costs and effectiveness of primary LA catheter ablation vs. rhythm control with amiodarone, by patient cohort

Strategy	Cost	Incremental Cost	Effectiveness (QALYs)	Incremental Effectiveness (QALYs)	ICER (\$/QALYs)
60 M Paroxysmal AF					
Rhythm Control	\$ 6,062		3.627		
Primary LA Catheter Ablation	\$ 17,925	\$ 11,863	3.739	0.112	\$ 105,907
65 M CHF and Persistent AF					
Rhythm Control	\$ 6,464		3.286		
Primary LA Catheter Ablation	\$ 21,657	\$ 15,193	3.38	0.094	\$ 161,090
75 M DM HTN Persistent AF					
Rhythm Control	\$ 8,710		2.896		
Primary LA Catheter Ablation	\$ 23,495	\$ 14,785	2.982	0.086	\$ 171,729

Table D19. 5-year costs and effectiveness of thoroscopic, off-pump surgical ablation vs. secondary LA catheter ablation, by patient cohort

Strategy	Cost	Incremental Cost	Effectiveness (QALYs)	Incremental Effectiveness (QALYs)	ICER (\$/QALYs)
60 M Paroxysmal AF					
Secondary LA Catheter Ablation	\$ 15,337		3.675		
Thoroscopic, Off-Pump Surgical Ablation	\$ 25,207	\$ 9,870	3.672	-0.003	Dominated
65 M CHF and Persistent AF					
Secondary LA Catheter Ablation	\$ 17,340		3.327		
Thoroscopic, Off-Pump Surgical Ablation	\$ 27,009	\$ 9,669	3.325	-0.002	Dominated
75 M DM HTN Persistent AF					
Secondary LA Catheter Ablation	\$ 18,988		2.931		
Thoroscopic, Off-Pump Surgical Ablation	\$ 27,383	\$ 8,395	2.935	0.004	\$ 1,935,135

Table D20. 5-year costs and effectiveness of amiodarone, dronedarone alone, and dronedarone first with amiodarone for recurrent AF, by patient cohort

Strategy	Cost	Incremental Cost	Effectiveness (QALYs)	Incremental Effectiveness (QALYs)	ICER (\$/QALYs)
60 M Paroxysmal AF					
Amiodarone	\$ 6,062		3.627		
Dronedarone	\$ 11,160	\$ 5,098	3.589	-0.038	Dominated
Dronedarone First	\$ 12,941	\$ 6,879	3.675	0.049	\$ 141,458
65 M CHF and Persistent AF					
Amiodarone	\$ 6,464		3.286		
Dronedarone	\$ 11,541	\$ 5,077	3.249	-0.037	Dominated
Dronedarone First	\$ 13,299	\$ 6,835	3.334	0.048	\$ 143,441
75 M DM HTN Persistent AF					
Amiodarone	\$ 8,710		2.896		
Dronedarone	\$ 13,605	\$ 4,896	2.861	-0.034	Dominated
Dronedarone First	\$ 15,286	\$ 6,576	2.940	0.044	\$ 148,128

Dronedarone strategies compared to Amiodarone.

Table D21. 5-year costs and effectiveness of dabigatran (110 mg and 150 mg doses) vs. warfarin, by patient cohort

Strategy	Cost	Incremental Cost	Effectiveness (QALYs)	Incremental Effectiveness (QALYs)	ICER (\$/QALYs)
60 M Paroxysmal AF					
Rhythm Control (Warfarin)	\$ 6,062		3.627		
Rhythm Control (Dabigatran 150 mg)	\$ 26,581	\$ 20,519	3.642	0.015	\$ 1,359,423
Rhythm Control (Dabigatran 110 mg)	\$ 26,586	\$ 20,524	3.641	0.015	\$ 1,405,036
65 M CHF and Persistent AF					
Rhythm Control (Warfarin)	\$ 6,464		3.286		
Rhythm Control (Dabigatran 150 mg)	\$ 26,343	\$ 19,879	3.308	0.022	\$ 896,653
Rhythm Control (Dabigatran 110 mg)	\$ 26,385	\$ 19,921	3.307	0.021	\$ 958,922
75 M DM HTN Persistent AF					
Rhythm Control (Warfarin)	\$ 8,710		2.896		
Rhythm Control (Dabigatran 150 mg)	\$ 25,386	\$ 16,676	2.951	0.055	\$ 303,755
Rhythm Control (Dabigatran 110 mg)	\$ 25,536	\$ 16,827	2.946	0.05	\$ 334,567

All strategies compared to common baseline Rhythm Control.

Table D22. 5-year costs and effectiveness of WATCHMAN vs. warfarin, by patient cohort

Strategy	Cost	Incremental Cost	Effectiveness (QALYs)	Incremental Effectiveness (QALYs)	ICER (\$/QALYs)
60 M Paroxysmal AF					
Rate Control (Digoxin/ Atenolol)	\$ 2,631		3.548		
Rate Control - WATCHMAN	\$ 14,756	\$ 12,125	3.545	-0.003	Dominated
65 M CHF and Persistent AF					
Rate Control (Digoxin/ Atenolol)	\$ 3,052		3.205		
Rate Control - WATCHMAN	\$ 14,894	\$ 11,842	3.206	0	\$77,657,857
75 M DM HTN Persistent AF					
Rate Control (Digoxin/ Atenolol)	\$ 5,377		2.817		
Rate Control - WATCHMAN	\$ 15,549	\$ 10,172	2.828	0.011	\$ 953,220

All strategies compared to Rate Control.

APPENDIX E

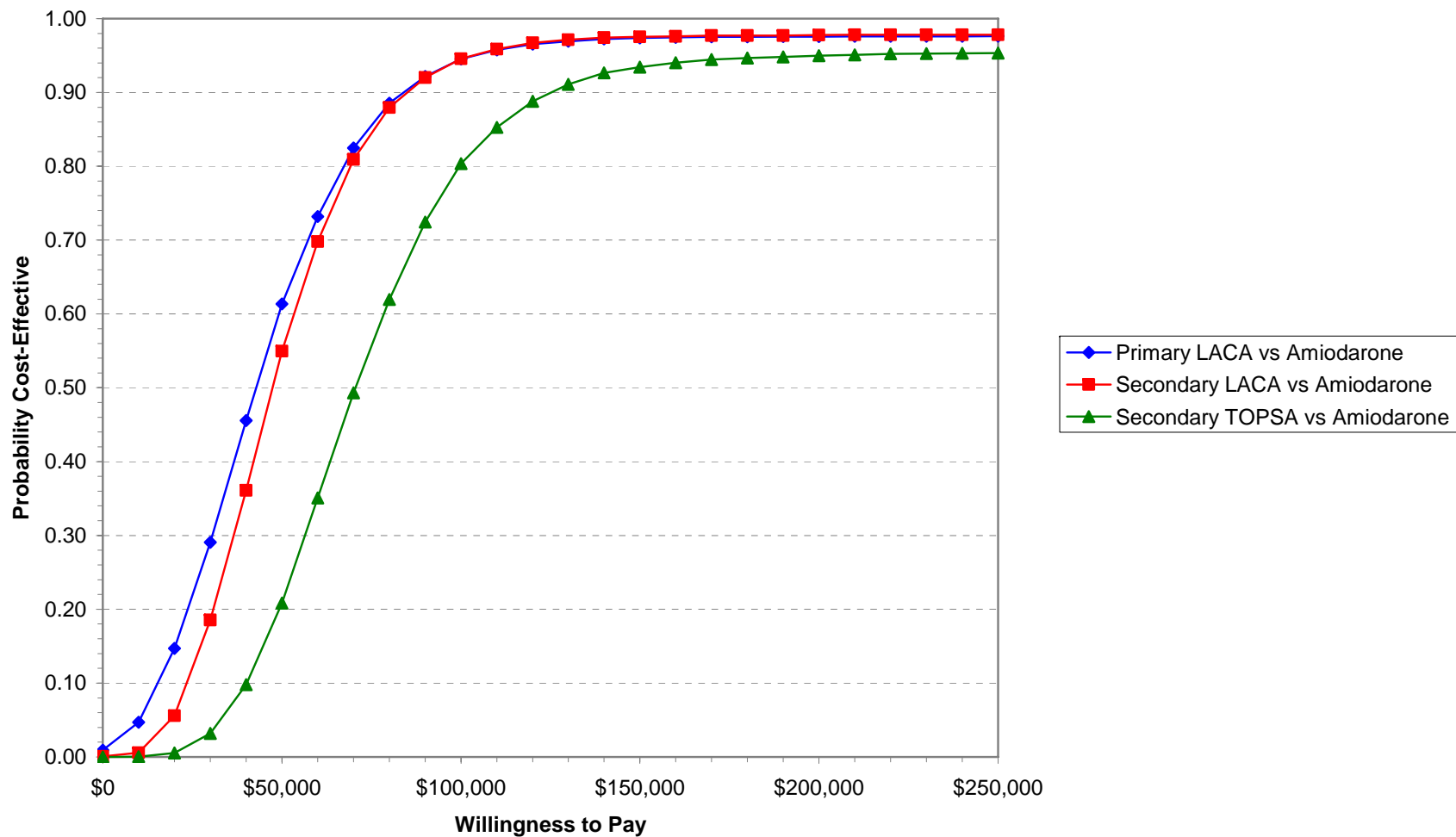
PARAMETERS FOR PROBABILISTIC SENSITIVITY ANALYSES & COST-EFFECTIVENESS ACCEPTABILITY CURVES

Variable	Value	Lower 95% CI	Upper 95% CI	Distribution	Parameter Estimation Input		Distribution Parameters		Comments
					Mean *	SD *	Parameter 1 *	Parameter 2 *	
Costs									
LACA									
Cost of LACA	\$11,231	\$5,616	\$22,462	Gamma	\$11,231	\$4,298	6.8295	0.0006	
Cost of LACA, with CO/CC	\$17,024	\$8,512	\$34,048	Gamma	\$17,024	\$6,514	6.8295	0.0004	
Thorascopic, Off-Pump (TOP) Surgical Ablation									
Top Surgical Ablation	\$26,818	\$13,409	\$53,636	Gamma	\$26,818	\$10,262	6.8295	0.0003	
Top Surgical Ablation w/minor complication	\$32,270	\$16,135	\$64,540	Gamma	\$32,270	\$12,348	6.8295	0.0002	
Top Surgical Ablation w/major complication or comorbidity	\$46,358	\$23,179	\$92,716	Gamma	\$46,358	\$17,739	6.8295	0.0001	
WATCHMAN									
WATCHMAN Implantation Procedure	\$11,340	\$5,670	\$22,680	Gamma	\$11,340	\$4,339	6.8295	0.0006	
WATCHMAN w/comorbidity or complications	\$17,133	\$8,567	\$34,266	Gamma	\$17,133	\$6,556	6.8295	0.0004	
Annual Drug Costs									
Aspirin	\$23	\$12	\$46	Gamma	\$23	\$9	6.8295	0.2969	
Amiodarone	\$4,434	\$2,217	\$8,868	Gamma	\$4,434	\$1,697	6.8295	0.0015	
Atenolol	\$80	\$40	\$160	Gamma	\$80	\$31	6.8295	0.0854	
Clopidogril	\$3,192	\$1,596	\$6,384	Gamma	\$3,192	\$1,221	6.8295	0.0021	
Dabigatran	\$4,734	\$2,367	\$9,468	Gamma	\$4,734	\$1,811	6.8295	0.0014	
Digoxin	\$263	\$132	\$526	Gamma	\$263	\$101	6.8295	0.0260	
Dronedarone	\$3,120	\$1,560	\$6,240	Gamma	\$3,120	\$1,194	6.8295	0.0022	
Warfarin	\$440	\$220	\$880	Gamma	\$440	\$168	6.8295	0.0155	
Drug Toxicity Costs									
Reversible (Thyroid) Drug toxicity	\$100	\$50	\$200	Gamma	\$100	\$38	6.8295	0.0683	
Acute Amiodarone Pulmonary Toxicity	\$4,250	\$2,125	\$8,500	Gamma	\$4,250	\$1,626	6.8295	0.0016	
Chronic Amiodarone Pulmonary Toxicity	\$4,025	\$2,013	\$8,050	Gamma	\$4,025	\$1,540	6.8295	0.0017	
Rates									
Drug Toxicity Rates									
Rate of reversible (thyroid) toxicity	0.101	0.052	0.150	Gamma	0.1010	0.0250	16.3216	161.6000	Assume sd=0.025
Rate of permanent amiodarone pulmonary toxicity	0.011	0.006	0.016	Gamma	0.0110	0.0025	19.3600	1760.0000	Assume sd=0.0025
Probabilities									
LACA Complications									
No Complications	0.945			Dirichlet	0.9450		0.9450	1.0000	
Major Complications	0.037			Gamma	0.0370		0.0370	1.0000	
Minor Complications	0.013			Gamma	0.0130		0.0130	1.0000	
Stroke	0.004			Gamma	0.0040		0.0040	1.0000	
Death	0.001			Gamma	0.0010		0.0010	1.0000	
TOP Surgical Ablation Complications									
No Complications	0.945			Dirichlet	0.9450		0.9450	1.0000	
Major Complications	0.037			Gamma	0.0370		0.0370	1.0000	
Minor Complications	0.013			Gamma	0.0130		0.0130	1.0000	
Stroke	0.004			Gamma	0.0040		0.0040	1.0000	
Death	0.001			Gamma	0.0010		0.0010	1.0000	
WATCHMAN Complications									
No Complications	0.897			Dirichlet	0.8970		0.8970	1.0000	
Major Complications	0.035			Gamma	0.0350		0.0350	2.0000	
Minor Complications	0.058			Gamma	0.0580		0.0580	3.0000	
Stroke (peri-procedure)	0.01			Gamma	0.0100		0.0100	4.0000	

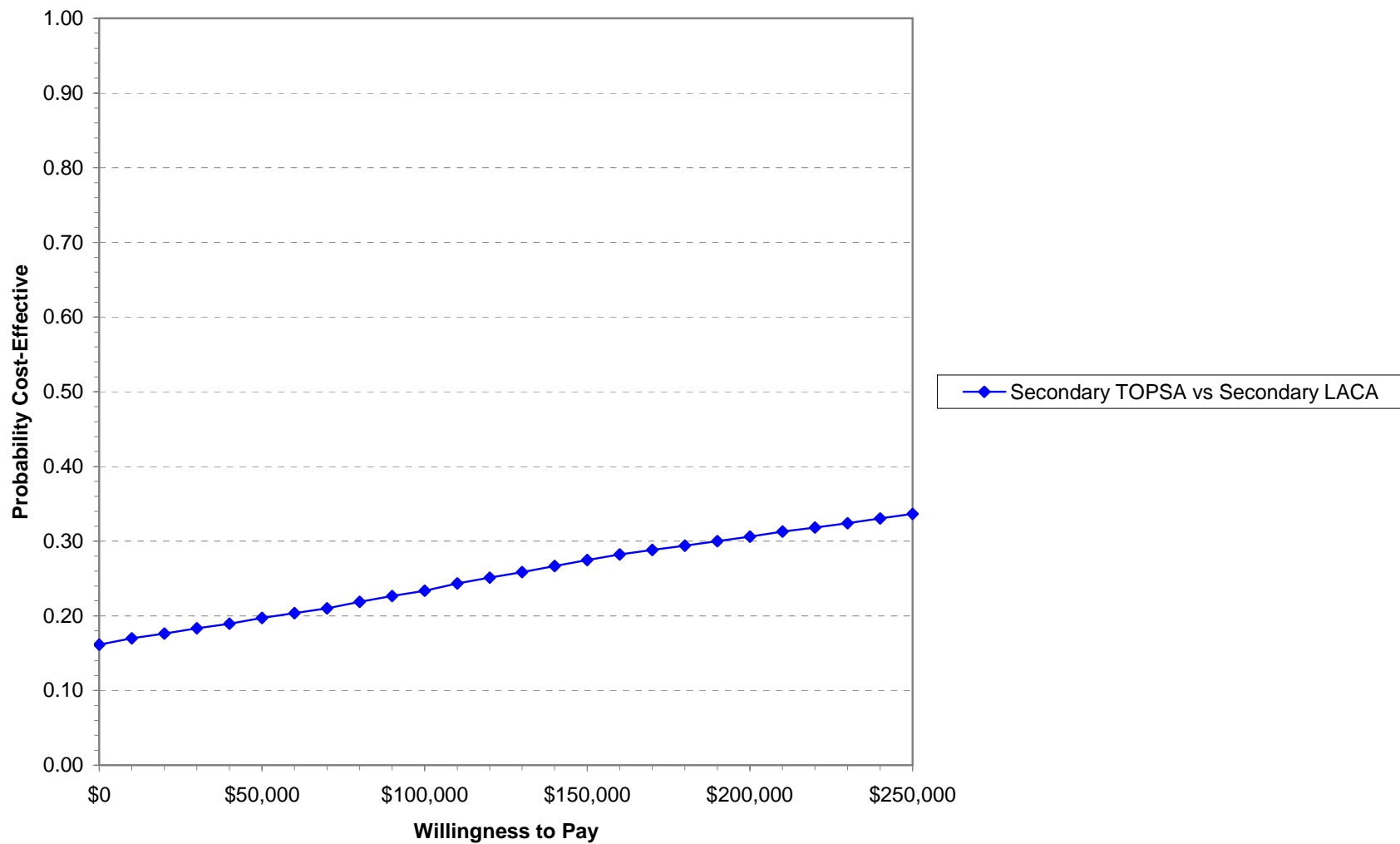
Variable	Value	Lower 95% CI	Upper 95% CI	Distribution	Parameter Estimation Input		Distribution Parameters		Comments
					Mean *	SD *	Parameter 1 *	Parameter 2 *	
LACA Cardiac Rhythm Outcomes									
Probability of NSR after LACA 1 year, paroxysmal	0.821	0.771	0.871	Beta (Real Parameters)	0.8210	0.0255	185.4007	40.4223	
Probability of NSR after LACA 1 year, persistent	0.698	0.648	0.748	Beta (Real Parameters)	0.6980	0.0255	226.0945	97.8231	
TOP Surgical Ablation Cardiac Rhythm Outcomes									
Probability of NSR after LACA 1 year, paroxysmal	0.821	0.771	0.871	Beta (Real Parameters)	0.8210	0.0255	185.4007	40.4223	Same as LACA
Probability of NSR after LACA 1 year, persistent	0.698	0.648	0.748	Beta (Real Parameters)	0.6980	0.0255	226.0945	97.8231	
RR Stroke	0.6			Beta (Real Parameters)	0.6000	0.0500	57.6000	38.4000	
WATCHMAN									
Probability of Successful LA Implantation	0.91			Beta (Real Parameters)	0.9100	0.0130	441.0000	43.6154	
Probability of LAA exclusion	0.86			Beta (Real Parameters)	0.8600	0.0160	404.4688	65.8438	
Amiodarone									
Probability of NSR after recurrent AF with dronedarone	0.777	0.731	0.833	Beta (Real Parameters)	0.7770	0.0160	525.9046	150.9353	
Relative Risks									
WATCHMAN									
RR of Stroke after WATCHMAN	0.71	0.34	1.24	LogNormal	-0.342	0.330	-0.342	0.330	
Dronedarone									
RR Recurrent AF Dronedarone vs Amiodarone	1.59	1.28	1.98	LogNormal	0.464	0.111	0.464	0.111	
RR Drug Toxicity Dronedarone vs Amiodarone	0.80	0.60	1.07	LogNormal	-0.223	0.148	-0.223	0.148	
Dabigatran									
RR Hemorrhage Dabigatran 110 mg vs warfarin	0.80	0.69	0.93	LogNormal	-0.223	0.076	-0.223	0.076	
RR Hemorrhage Dabigatran 150 mg vs warfarin	0.93	0.81	1.07	LogNormal	-0.073	0.071	-0.073	0.071	
RR ICH Dabigatran 110 mg vs warfarin	0.31	0.69	0.93	LogNormal	-1.171	0.076	-1.171	0.076	
RR ICH Dabigatran 150 mg vs warfarin	0.40	0.27	0.60	LogNormal	-0.916	0.204	-0.916	0.204	
RR Stroke Dabigatran 110 mg vs warfarin	0.92	0.74	1.13	LogNormal	-0.083	0.108	-0.083	0.108	
RR Stroke Dabigatran 150 mg vs warfarin	0.64	0.51	0.81	LogNormal	-0.446	0.118	-0.446	0.118	
Amiodarone									
Probability of Initial NSR	0.73			Beta (Integer Parameters)	182	249	0.731	0.028	
Dronedarone									
Probability of Initial NSR	0.82			Beta (Integer Parameters)	210	255	0.824	0.024	
Quality of Life									
Quality of Life (Disutility)									
Atrial Fibrillation	0.065			Beta (Real Parameters)	0.0650	0.0100	39.5038	568.2463	Assume sd=0.01
Warfarin	0.013			Beta (Real Parameters)	0.0130	0.0118	1.1980	90.9523	sd=0.0118
Procedure Morbidity	0.5			Beta (Real Parameters)	0.5000	0.0250	200.0000	200.0000	Assume SD=0.025

* Distribution Parameters for TreeAge Software, 2009
Beta Distribution (alpha, beta) for probabilities and QoL with parameters estimated from mean value & 95% CIs
Gamma Distribution (alpha, lambda) with parameters estimated from mean and 95% CIs
LogNormal Distribution for relative risks with parameters estimated from ln(mean), sd of ln(95% CIs)
Dirichlet Distribution for nodes with multiple branches estimated from mean branch probabilities, equivalent to Gamma (mean probability, 1) for each branch probability
SD directly estimated if 95% CIs not available

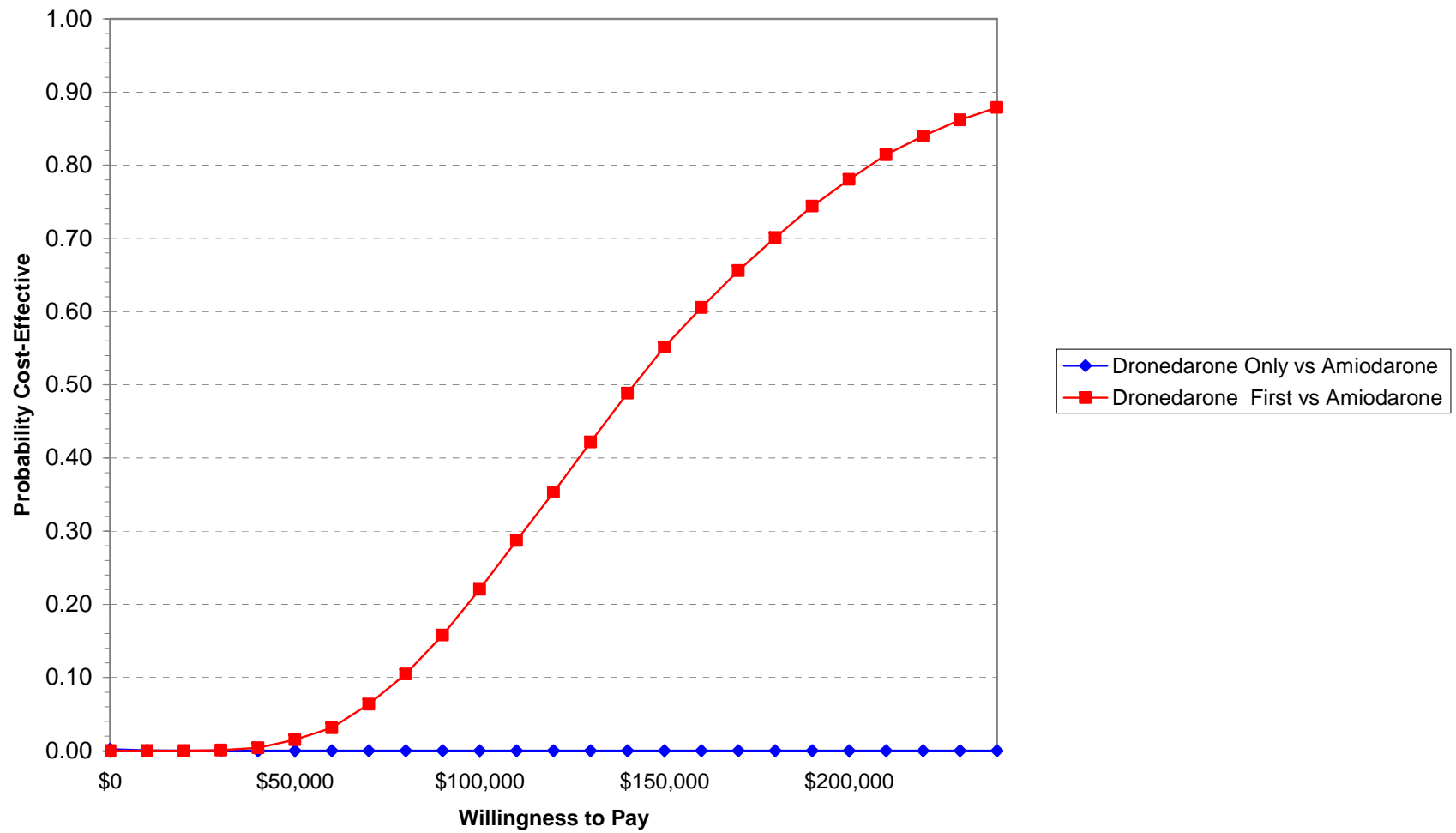
Acceptability Curve, Ablation Strategies 65 M CHF and Persistent AF



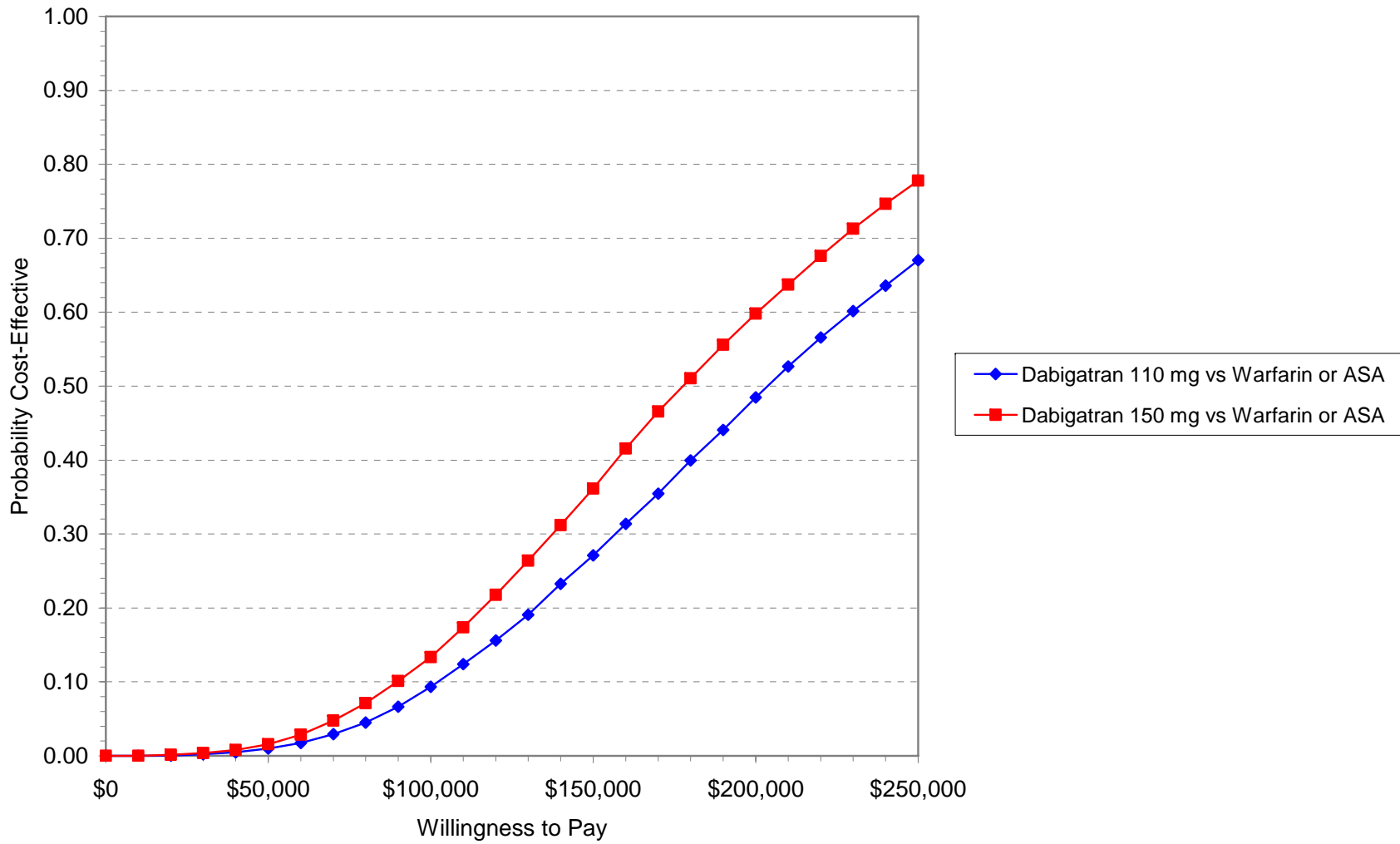
Acceptability Curve, Secondary TOP Surgical Ablation vs Secondary LACA Strategy 65 M CHF and Persistent AF



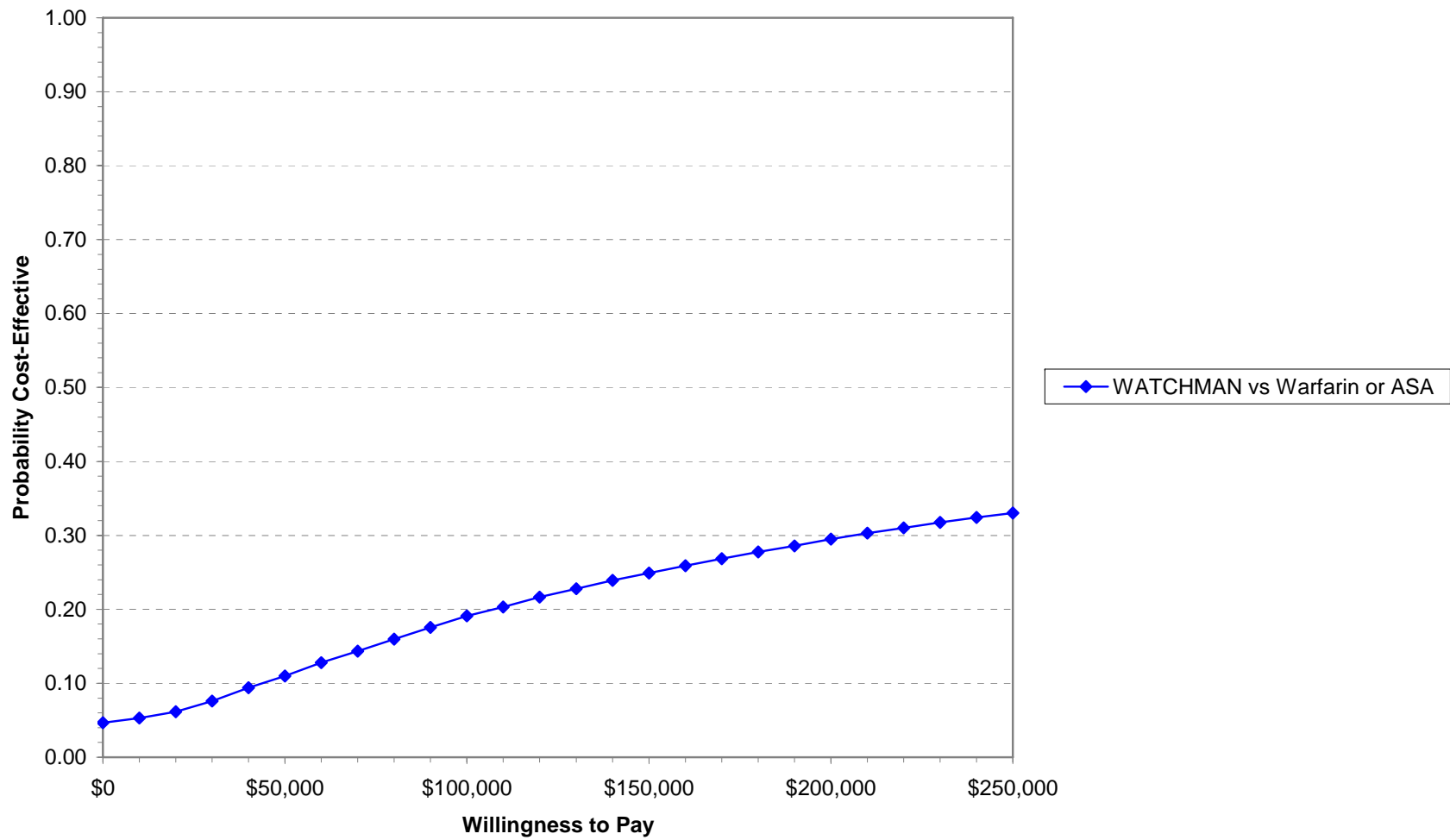
Acceptability Curve, Dronedarone Strategies 65 M CHF and Persistent AF



Acceptability Curve, Dabigatran Strategies 65 M CHF and Persistent AF



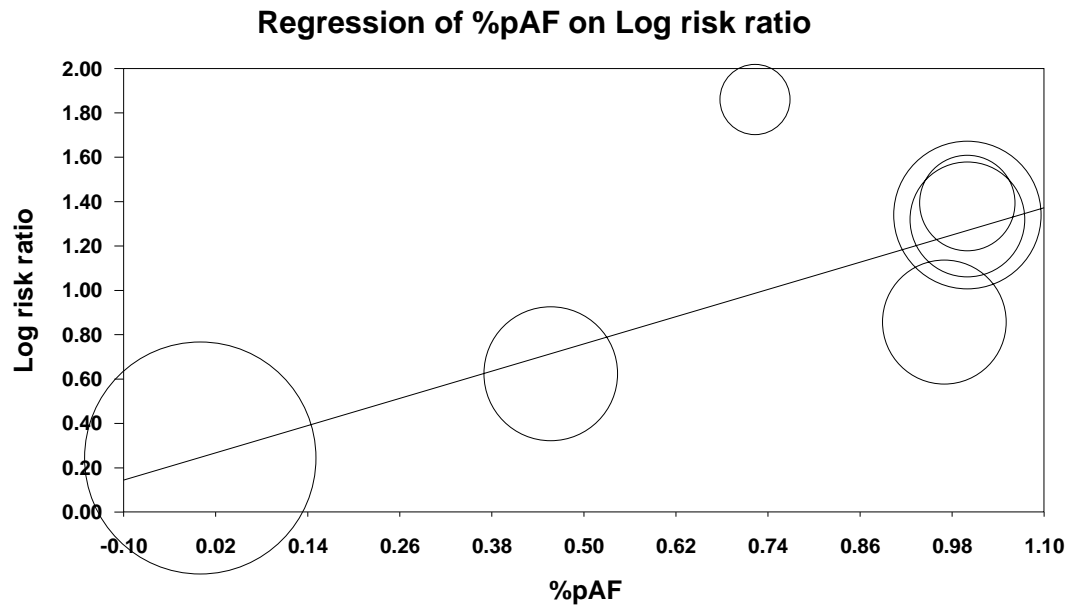
**Acceptability Curve, WATCHMAN Device Strategy
65 M CHF and Persistent AF**



APPENDIX F

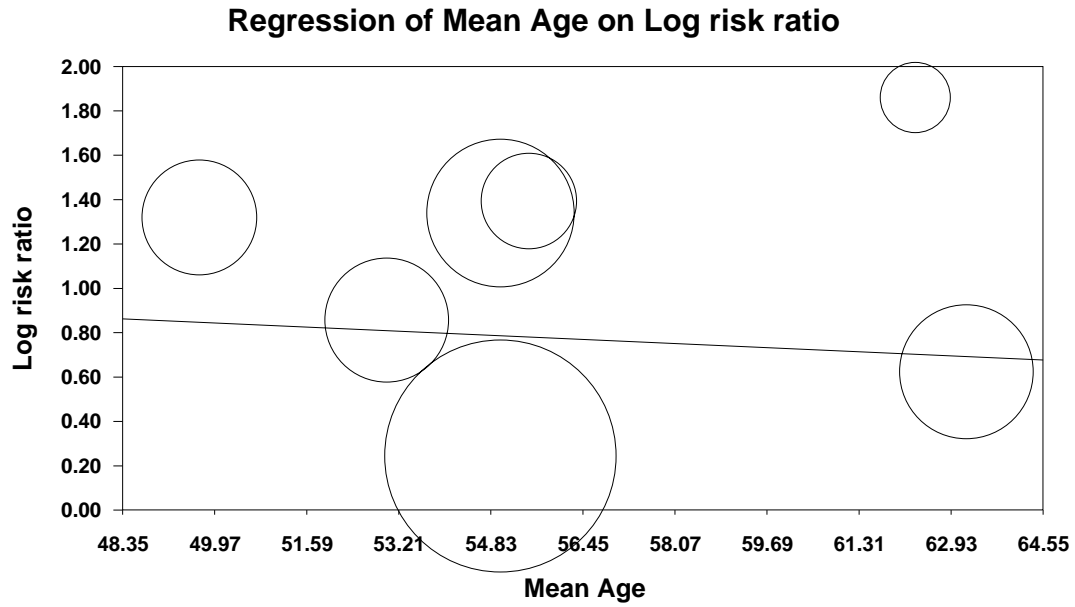
META-REGRESSION & PUBLICATION BIAS ANALYSES

Meta-Regression
Dependent Variable: Rate ratio of freedom from AF
Independent Variable: % of study participants w/paroxysmal AF



Mixed effects regression
Q: 44.25654
df: 6
p: <.0001

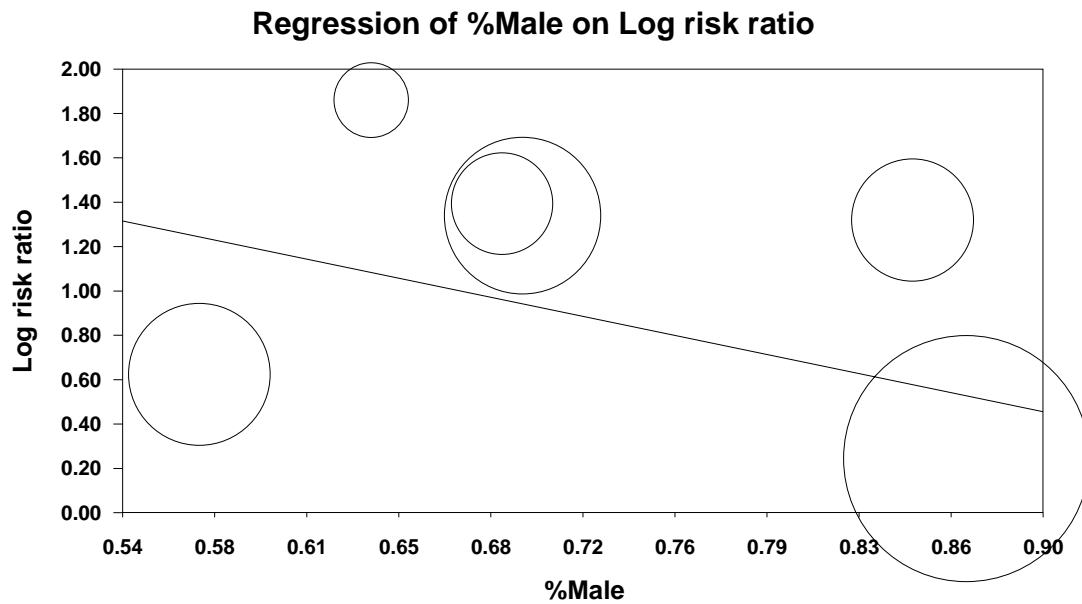
Meta-Regression
Dependent Variable: Rate ratio of freedom from AF
Independent Variable: Mean age of study participants



Mixed effects regression
Q: 6.91780
df: 6

p: 0.3285

Meta-Regression
Dependent Variable: Rate ratio of freedom from AF
Independent Variable: % of male study participants



Mixed effects regression
Q: 6.49291
df: 6
p: 0.2612

EVIDENCE DISSEMINATION BIAS

Current outcome measure	RR
Current weighting method	DL
Current model	Random effects
Original meta-analysis outcome	2.841
95% CI lower limit	1.8263
95% CI upper limit	4.4194

Effect assessment

Rank correlation tau-b (continuity corrected)	0.2857
Ties	0
P-Q (se)	7 (6.6583)
z	0.9011
p-value (two-tailed)	0.3675

Regression method	Egger
Regressor weighting	None
Intercept	6.2944
95% CI lower limit	1.811
95% CI upper limit	10.7779
p-value (two-tailed)	0.0154

Sensitivity analysis

Fail-safe N	231
Tolerance level	45

Trim-and-fill method (automatic)	L0
Number of imputed studies	2
Resulting meta-analysis outcome	2.3683
95% CI lower limit	1.6
95% CI upper limit	3.5056

RR: Rate ratio; DL: Dersimonial-Laird; CI: Confidence interval