

# DANPACE: The Danish multicenter randomised trial on AAIR versus DDDR pacing in sick sinus syndrome

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*Jens Cosedis Nielsen,  
Aarhus University Hospital  
on behalf of the DANPACE investigators*

# Conflicts of interest

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- Jens Cosedis Nielsen has received speakers fees and/or consultant honoraries from Medtronic, St Jude Medical, Biotronik, Astra-Zeneca, and Sanofi-Aventis.

# DANPACE investigators

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## **Steering Committee (numbers of patients included):**

- Henning Rud Andersen (chairman) and Jens Cosedis Nielsen (co-chairman), Aarhus University Hospital, Skejby (337);
- Poul-Erik Bloch-Thomsen, Gentofte Hospital (180);
- Søren Højberg, Bispebjerg Hospital (121);
- Mogens Møller, Odense University Hospital (114);
- Thomas Vesterlund, Aalborg Hospital (111);
- Dorthe Dalsgaard, Herning Hospital (108);
- Tonny Nielsen, Esbjerg Hospital (77);
- Mogens Asklund, Kolding Hospital (72);
- Elsebeth Vibeke Friis, Haderslev Hospital (70);
- Per Dahl Christensen, Viborg Hospital (56);
- Erik Hertel Simonsen, Hillerød Hospital (47);
- Ulrik Hedegaard Eriksen, Vejle Hospital (39);
- Gunnar Vagn Hagemann Jensen, Roskilde Hospital (28);
- Jesper Hastrup Svendsen, Rigshospitalet (24).

## **From United Kingdom:**

- William D. Toff (UK coordinating investigator), J. Douglas Skehan, Kieran Brack, Glenfield Hospital, Leicester (8);
- Craig Barr, Andreas Tselios, Nicola Gordon, Russells Hall Hospital, Dudley (6);
- John Cleland, Andrew Clark, Sarah Hurren, Castle Hill Hospital, East Cottingham (3);
- David McEneaney, Andrew Moriarty, Anne Mackin, Craigavon Area Hospital, Craigavon (2);
- Arif Ahsan, Jane Burton, Ruth Oliver, Nottingham City Hospital (2),
- Barry Kneale, Lynda Huggins, Worthing Hospital (2).

## **From Canada:**

- Jeffrey S. Healey, Hamilton (8).

# Background

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- In patients with sick sinus syndrome (SSS) bradycardia can be treated with any pacemaker: AAIR, VVIR, or DDDR.
- VVIR pacing increases atrial fibrillation as compared with physiological pacing (DDDR or AAIR), and VVIR pacing was associated with increased mortality as compared with AAIR pacing in one small trial.<sup>1</sup>
- Ventricular pacing has been found to cause ventricular desynchronisation with lowering of LVEF and left atrial dilatation, resulting in heart failure and atrial fibrillation.

<sup>1</sup>: Andersen HR et al., Lancet 1997

# Aim

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- To compare AAIR and DDDR pacing in SSS.
- Primary endpoint:
  - Death from any cause.
- Secondary endpoints:
  - Paroxysmal atrial fibrillation (at planned follow-up)
  - Chronic atrial fibrillation
  - Stroke
  - Heart failure
  - Pacemaker reoperation

# Statistics

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- 1,900 patients.
- Followed for in mean 5.5 years.
- Identify a 6% absolute difference in mortality.
- Power 80%, overall  $\alpha=0.05$ .
- Intention to treat.
  
- Two planned interim analyses after 1/3 and 2/3 of the expected number of deaths.

# Methods

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- Randomised controlled trial.
- Inclusion criteria:
  - symptomatic bradycardia and documented sinus-pause >2s or sinus bradycardia <40bpm >1 minute whilst awake,
  - PR-interval  $\leq 0.22$ s (age 18-70 years) or PR-interval  $\leq 0.26$ s (age  $\geq 70$  years),
  - QRS width <0.12s.
- Exclusion criteria:
  - AV block,
  - bundle branch block,
  - persistent atrial fibrillation >12 months,
  - atrial fibrillation with QRS rate <40 bpm for  $\geq 1$  min or pauses >3s,
  - a positive test for carotid sinus hypersensitivity.

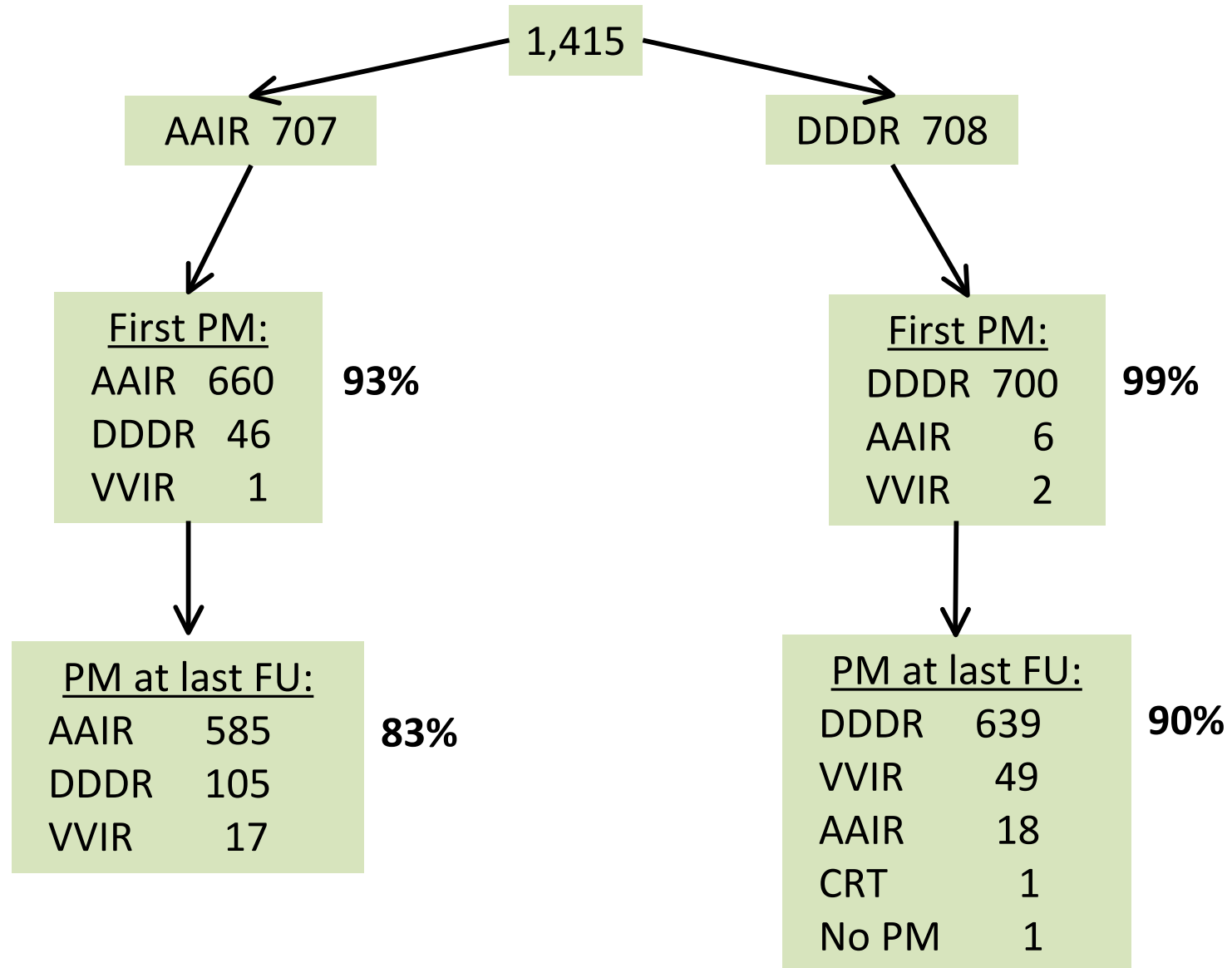
# Pacemaker programming

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- Rate adaptive function was active
- Lower rate 60 bpm
- Upper rate 130 bpm
  
- DDDR:
  - Paced AV-interval  $\leq 220$  ms
  - Sensed AV-interval  $\leq 200$  ms.
  - Rate-adaptive shortening of the AV-interval.

# Randomisation and pacing mode

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Baseline Characteristic	AAIR (N=707)	DDDR (N=708)	p-value
Female gender no. (%)	472 (66.8)	441 (62.3)	0.08
Age (years, mean±SD)	73.5 ±11.2	72.4 ±11.4	0.054
Brady-tachy syndrome no. (%)	303 (42.9)	318 (44.9)	0.44
Hypertension	241 (34.1)	239 (33.8)	0.90
Previous myocardial infarction no. (%)	94 (13.3)	90(12.7)	0.74
Diabetes no. (%)	68 (9.6)	72 (10.2)	0.73
Previous transient cerebral ischemia no. (%)	35 (5.0)	37 (5.2)	0.81
Previous stroke no. (%)	61 (8.6)	53 (7.5)	0.43
Left ventricular ejection fraction reduced (< 50%) no. (%)	59 (10.6)	54 (9.5)	0.55
Left ventricular end-diastolic diameter (mm, mean±SD)	47.7 ± 7.3	47.8 ± 7.3	0.45
Left atrial diameter (mm, mean±SD)	39.3 ± 6.5	38.8 ± 6.4	0.23
Symptoms before pacemaker no. (%)			
Syncope	359 (50.8)	349 (49.3)	0.58
Dizzy spells	597 (84.4)	587 (82.9)	0.44
Heart failure	86 (12.2)	79 (11.2)	0.56
≥2 of the above three symptoms	317 (44.8)	291 (41.1)	0.16
Medication at randomization no. (%)			
Anticoagulation	108 (15.3)	89 (12.6)	0.14
Aspirin	369 (52.2)	361 (51.1)	0.67
Sotalol	43 (6.1)	44 (6.2)	0.91
Beta-blocker other than sotalol	159 (22.5)	132 (18.7)	0.08
Calcium-channel blocker	137 (19.4)	142 (20.1)	0.75
Digoxin	73 (10.3)	62 (8.8)	0.32
Amiodarone	25 (3.5)	24 (3.4)	0.88
Class I Antiarrhythmics	14 (2.0)	20 (2.8)	0.30
Angiotensin-converting-enzyme inhibitors	160 (22.6)	170 (24.0)	0.53
Diuretics	304 (43.0)	263 (37.2)	0.03
New York Heart Association functional class no. (%)			0.33
I	503 (71.4)	522 (73.9)	
II	172 (24.4)	158 (22.4)	
III	29 (4.1)	24 (3.4)	
IV	0	2 (0.3)	
Wenckebach block point (≥100 bpm, %)	611 (94.1)	581 (91.6)	0.08
Treated as randomized	660 (93.4)	700 (98.9)	<0.001



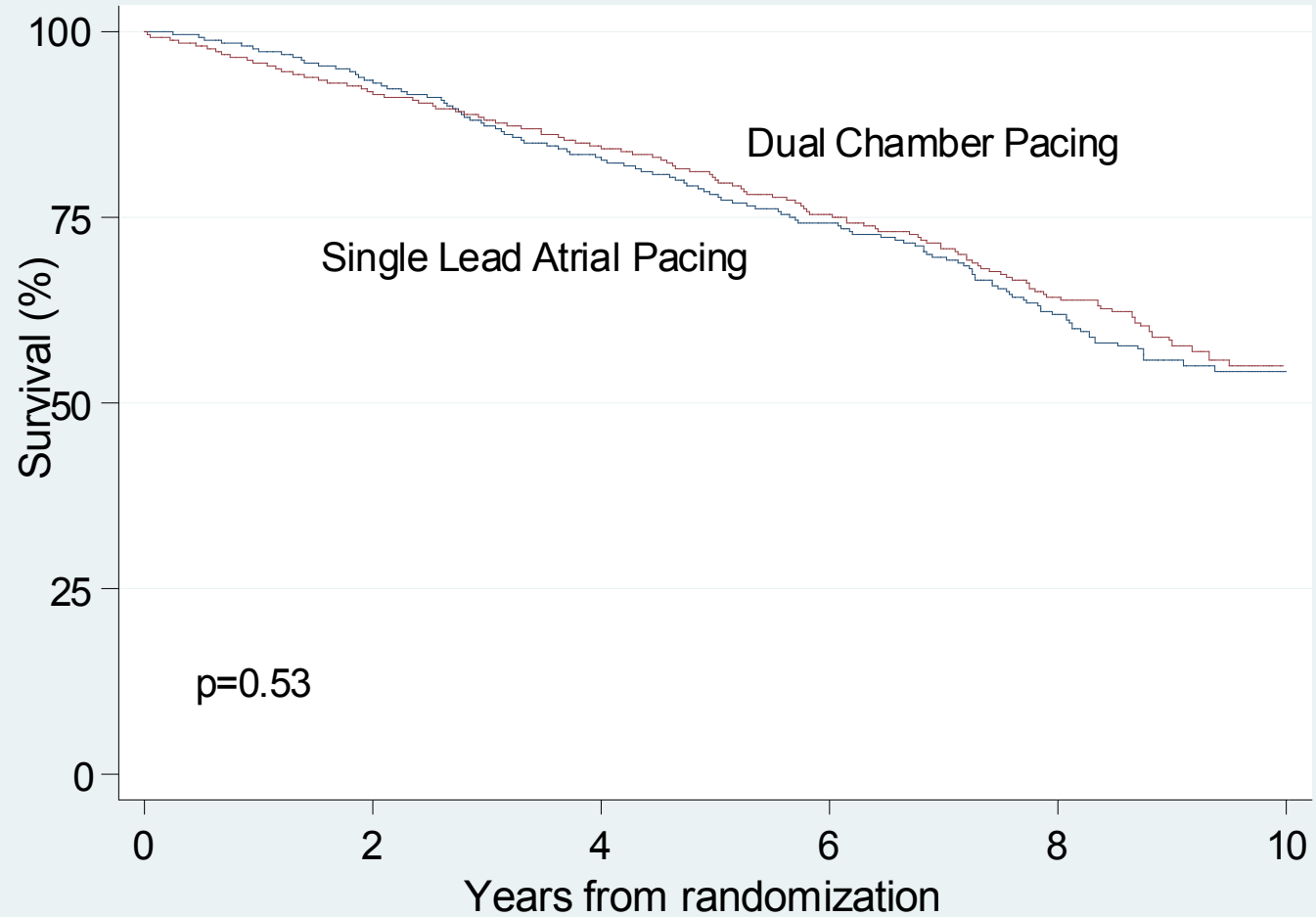
# Results

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- Follow-up  $5.4 \pm 2.6$  years
- No patients lost for follow-up
- Pacing in the atrium:
  - AAIR group:  $58 \pm 29\%$
  - DDDR group:  $59 \pm 31\%$

} P=0.52
- Pacing in the ventricle:
  - DDDR group:  $65 \pm 33\%$

# Survival

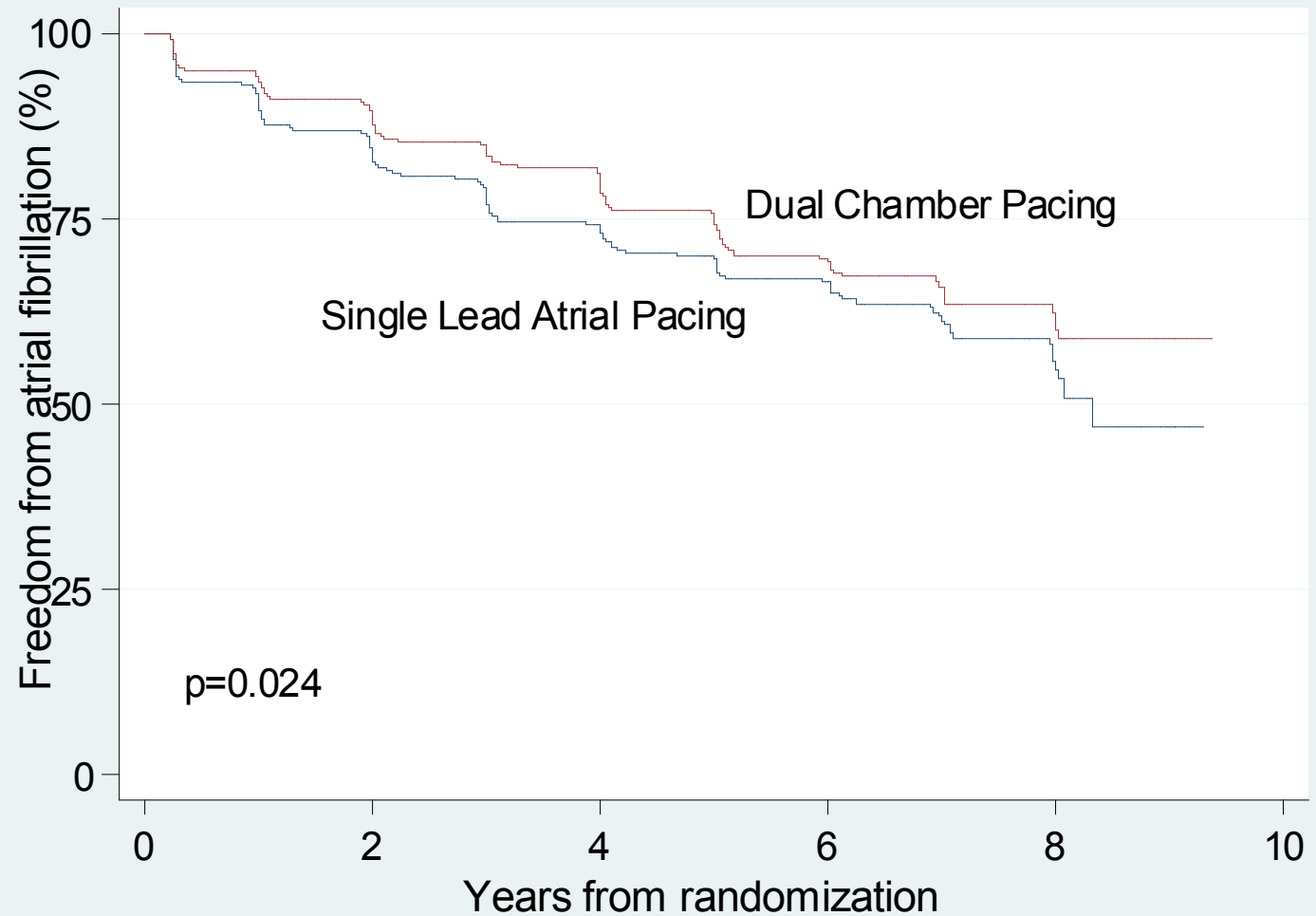


No. at Risk

Single Lead	707	648	466	298	147	25
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Dual Chamber	708	629	462	287	136	24
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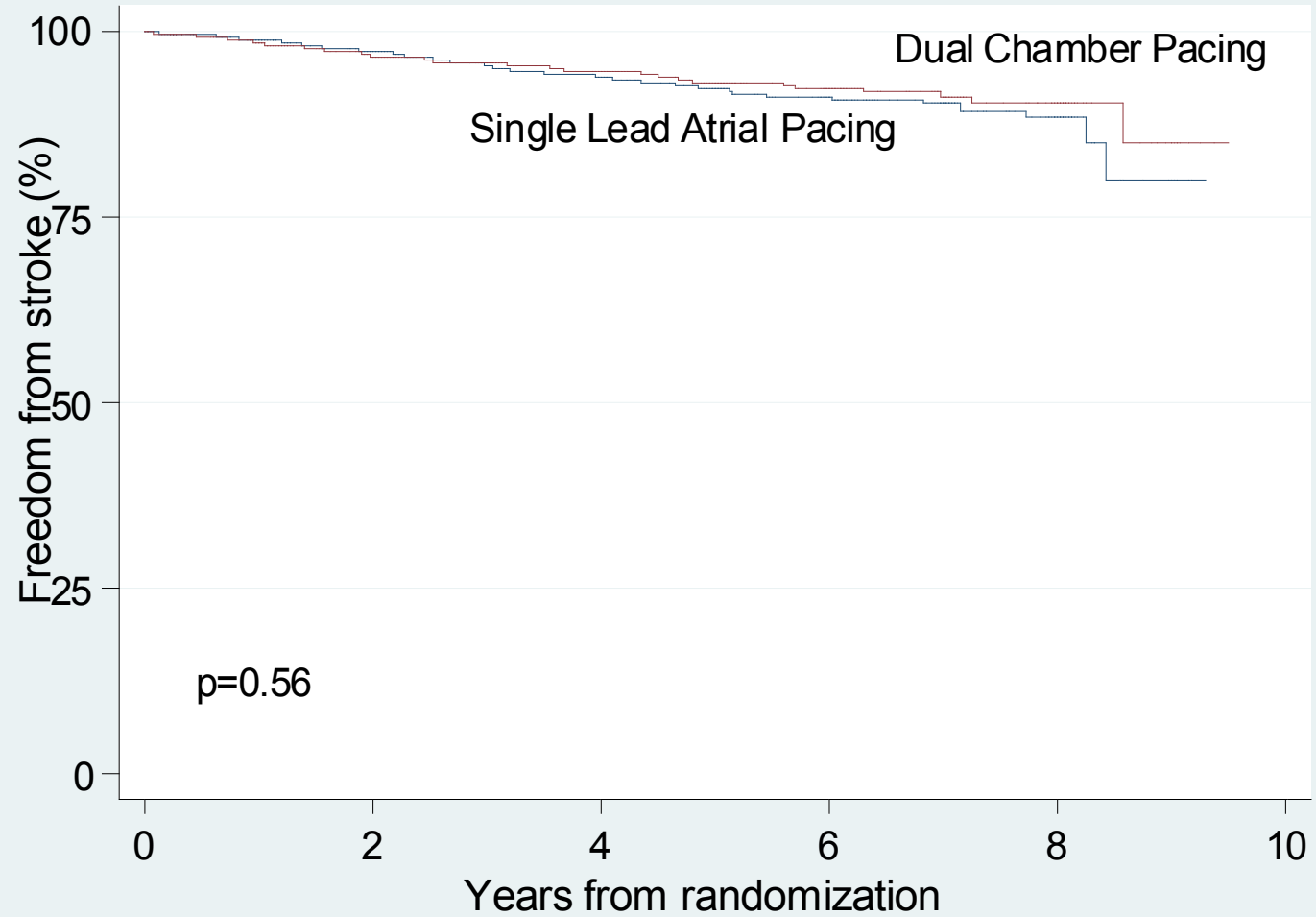
# Atrial fibrillation



No. at Risk

Single Lead	707	498	301	157	47	0
Dual Chamber	708	504	330	158	52	0

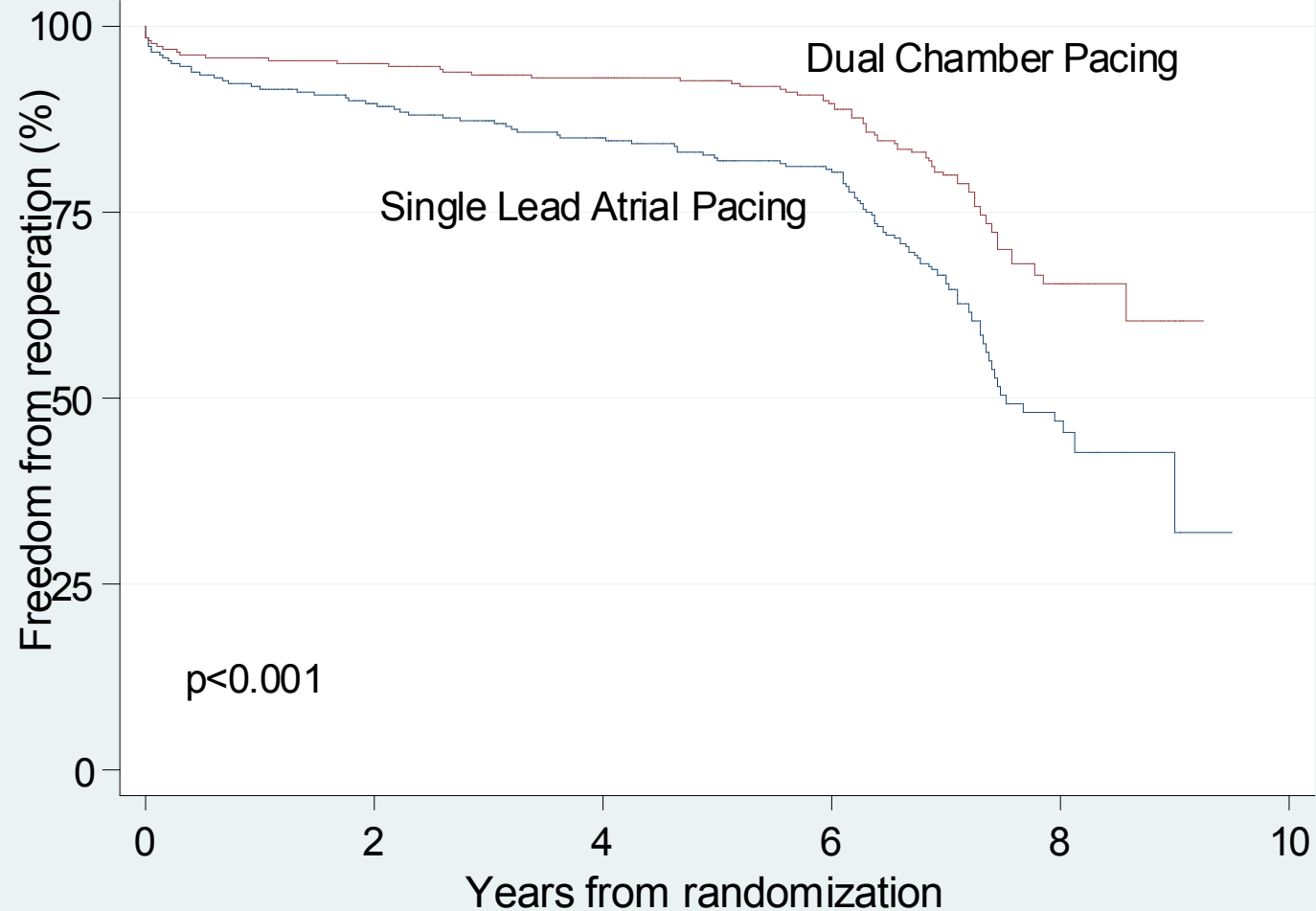
# Stroke



No. at Risk

Single Lead	707	571	383	225	68	0
Dual Chamber	708	550	391	215	73	0

# Reoperation



No. at Risk		0	2	4	6	8	10
Single Lead	707	527	340	196	33	0	0
Dual Chamber	708	534	377	198	44	0	0

# Heart failure

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- NYHA class at last FU:  $p=0.43$ .
- Diuretics at last follow-up:  
 $p=0.89$ .
- Hospitalization for heart failure:  $p=0.90$ .

# Clinical Outcomes – Multivariate analysis

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	Adjusted HR	95% CI	P-value
Death	0.94	0.77-1.14	0.52
Paroxysmal AF	1.24	1.01-1.52	0.042
Chronic AF	1.01	0.74-1.39	0.93
Stroke	1.05	0.70-1.59	0.80
Reoperation	2.00	1.54-2.61	<0.001

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# Conclusions

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- No difference in survival between AAIR and DDDR pacing in SSS.
- Risk of reoperation is doubled with AAIR pacing.
- Paroxysmal atrial fibrillation is more common in AAIR pacing.
- DDDR pacing with an AV interval  $\leq 220$ ms is the preferred pacing mode for SSS.
- AAIR pacing should no longer be used.

# Financial support

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