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The Relationship Between Daily Atrial Tachyarrhythmia Burden From Implantable Device Diagnostics and Stroke Risk: The TRENDS Study

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Circ Arrhythmia Electrophysiol. 2009; 2:474-480.

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/ Financial Relationship	Company
• Grant/Research Support	• Medtronic
• Consulting Fees/Honoraria	• Medtronic, St. Jude

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Study Aims

- To assess the relationship between device-detected AT/AF and risk of Thromboembolic Events (TE)
- To determine if there is a threshold value of AT/AF burden which increases TE risk

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TRENDS Methods
Patient Selection

- 2814 pts
- Class I/II indication for implantation of a dual chamber pacemaker, ICD, or CRT device

- ≥ 1 stroke risk factor:
  - Diabetes
  - HTN
  - CHF
  - Prior stroke/TIA
  - Age ≥ 65

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Methods
Follow Up & Outcome

- Device diagnostics downloaded at 3 month intervals
- Clinical evaluation at 6 month intervals
- Antithrombotic therapy was directed by patients' MDs
- TEs were adjudicated by 3 neurologists

- **Primary outcome: Thromboembolic event (TE)**
  - Ischemic stroke
  - TIA
  - Systemic embolism

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Methods
AT/AF Detection

- All devices were programmed to dual chamber operation with active mode switching

- Threshold for AT/AF episode detection was:
  - Atrial rate >175 beats per minute
  - Lasting at least 20 seconds

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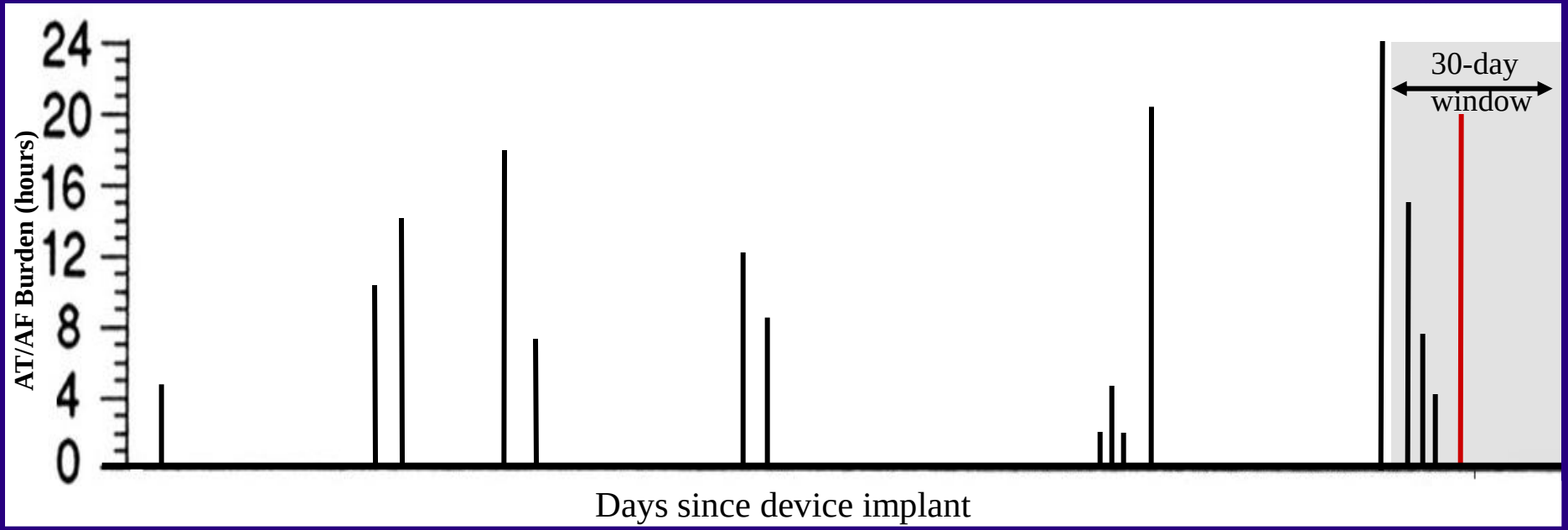
TRENDS Methods
AT/AF Burden

- AT/AF burden was defined as the longest total duration of AT/AF in hours (h) on any given day during a 30-day rolling window



- Window is "rolled" in 1-day increments

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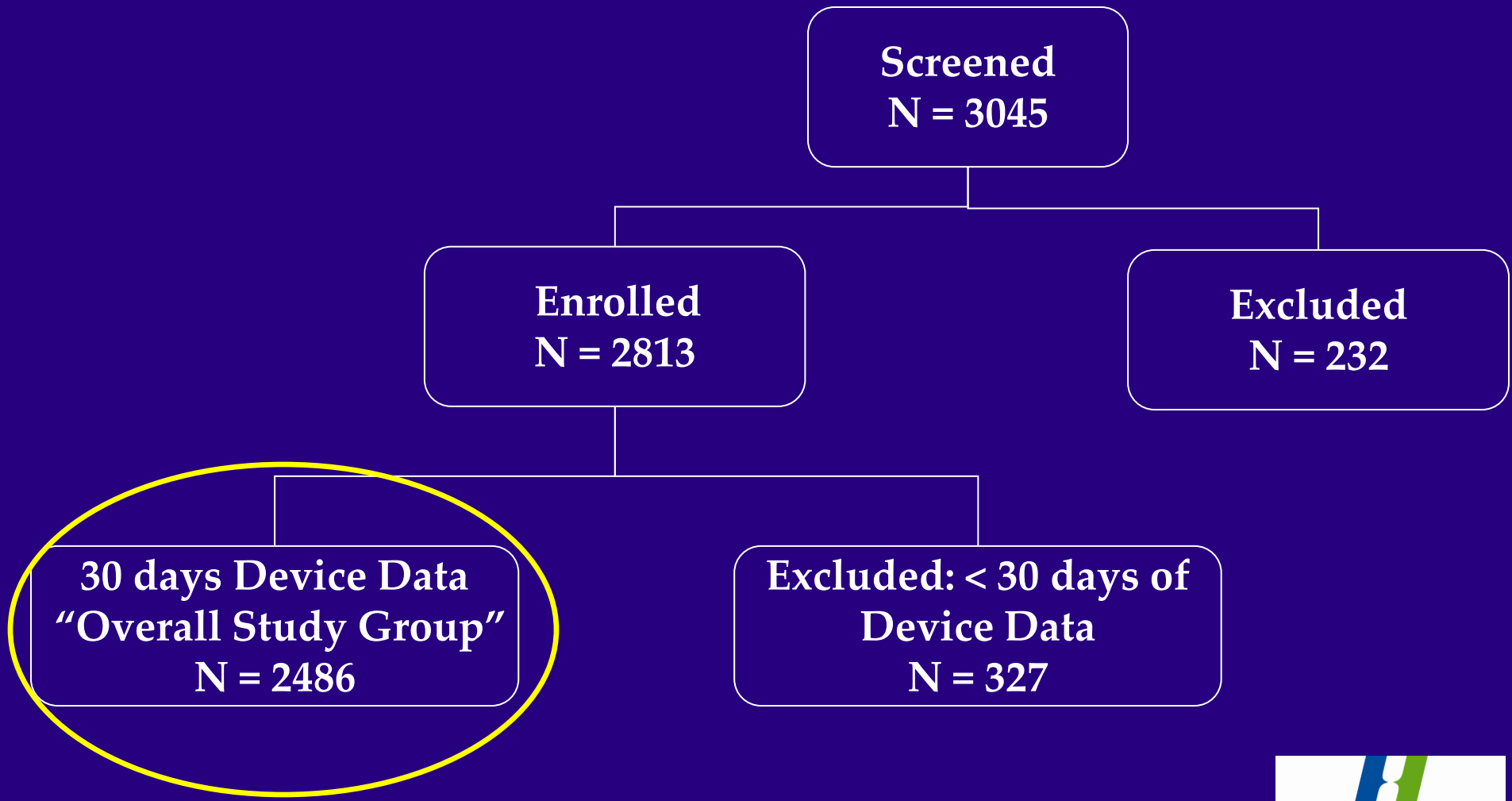
Results
Assembly of the Cohort



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Results
Baseline Clinical Features - 1

Variable	Value
Age	70.9 ± 11.1 yrs
Male	1650 (66.4%)
$CHADS_2$	2.2 ± 1.2
CHF	1479 (59.5%)
Hypertension	1887 (75.9%)
Diabetes	783 (31.5%)
Prior Stroke/TIA	333 (13.4%)
Systolic BP	133.3 ± 22.5 mmHg

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Results
Baseline Clinical Features - 2

Variable	Value
IPG	1234 (49.6%)
ICD	781 (31.4%)
CRT	471 (18.9%)
Warfarin	517 (20.8%)
Aspirin	1547 (62.2%)
Documented AT/AF History	498 (20.0%)

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Results

- Average follow-up was 1.4 years (3382 patient-years)
- 40 TE events
  - 20 ischemic strokes
  - 17 TIAs
  - 3 systemic emboli
- Annualized TE event rate was *1.2% [0.8, 1.6%]*

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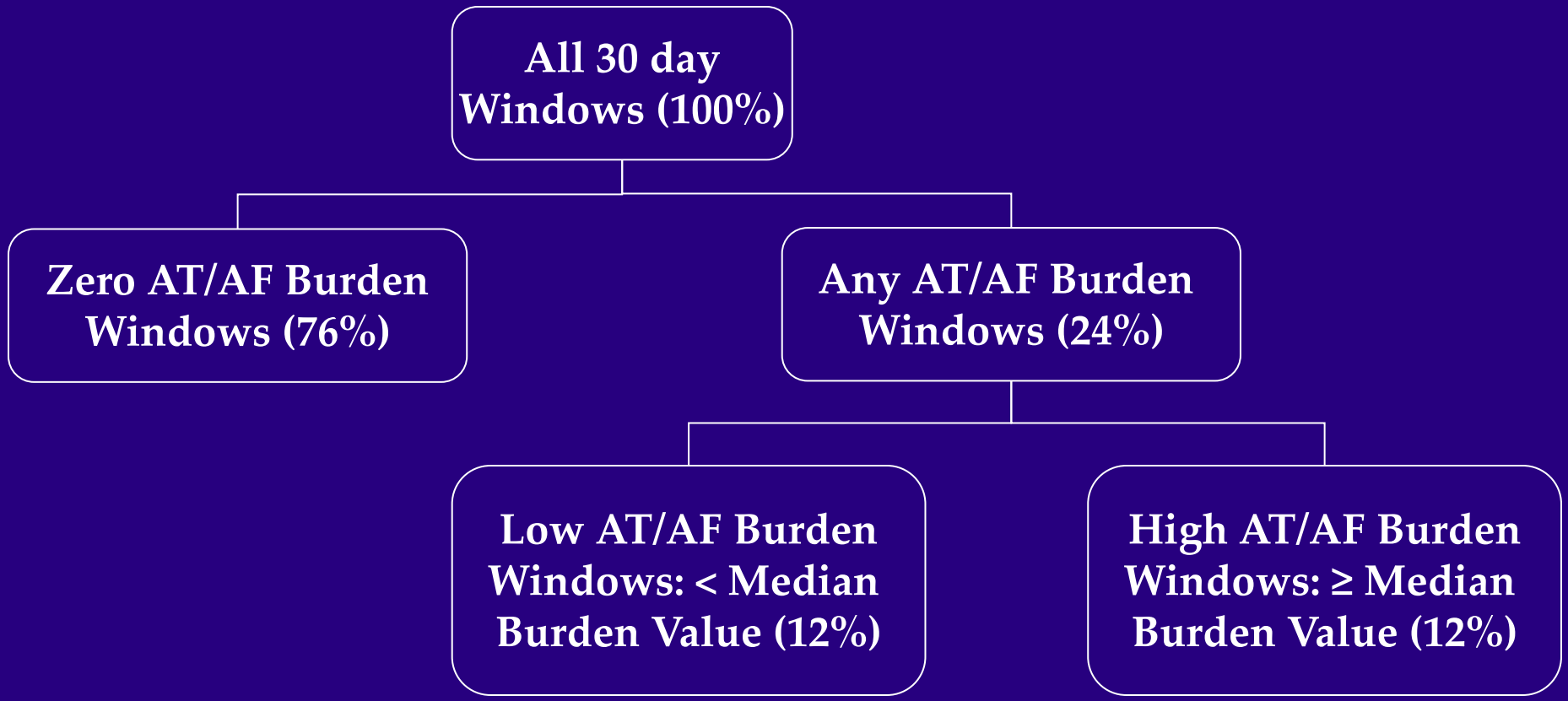
Results



- The median value for maximum daily burden in all 30-day windows with non-zero AT/AF was 5.5 h

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TRENDS Results
Annualized TE Event Rates

	Annualized Rate	Annualized Rate (Excluding TIAs)
Zero Burden	1.1%/Year	0.5%/Year
Low Burden < 5.5 hours	1.1%/Year	1.1%/Year
High Burden ≥ 5.5 hours	2.4%/Year	1.8%/Year

Glotzer et al. Circ Arrhythmia Electrophysiol. 2009; 2:474-480.

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TRENDS Results

Cox proportional hazard model adjusting for baseline stroke risk factors & time dependent AT/AF burden & antithrombotic therapy

Variable	Hazard Ratio*	95% Confidence Interval	p-value
Low Burden < 5.5 hours	**0.98**	**0.34 to 2.82**	**0.97**
High Burden ≥ 5.5 hours	**2.20**	**0.96 to 5.05**	**0.06**

**compared to no AT/AF burden*

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Summary

- The observed stroke rate in this study was very low compared to prior studies of AF patients with similar risk profiles

- Our results suggest that device-detected AT/AF burden ≥5.5 h on any day during a 30 day window doubles the risk for TE, independent of known risk factors and antithrombotic therapy

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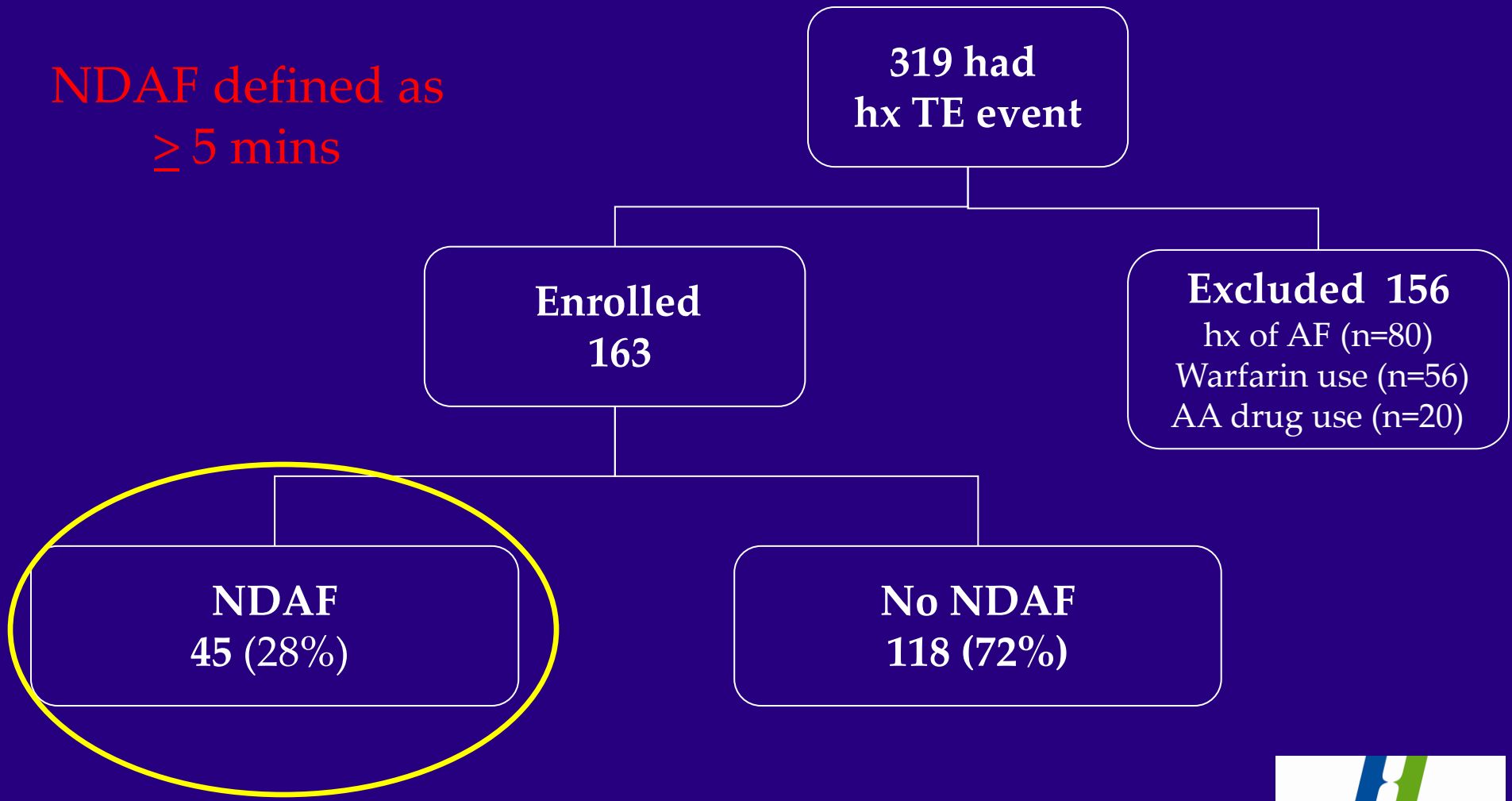
Newly Detected AF in Patients with a History of TE Event

NDAF defined as ≥ 5 mins



Zeigler et al. *Stroke*. 2010;41:256-260

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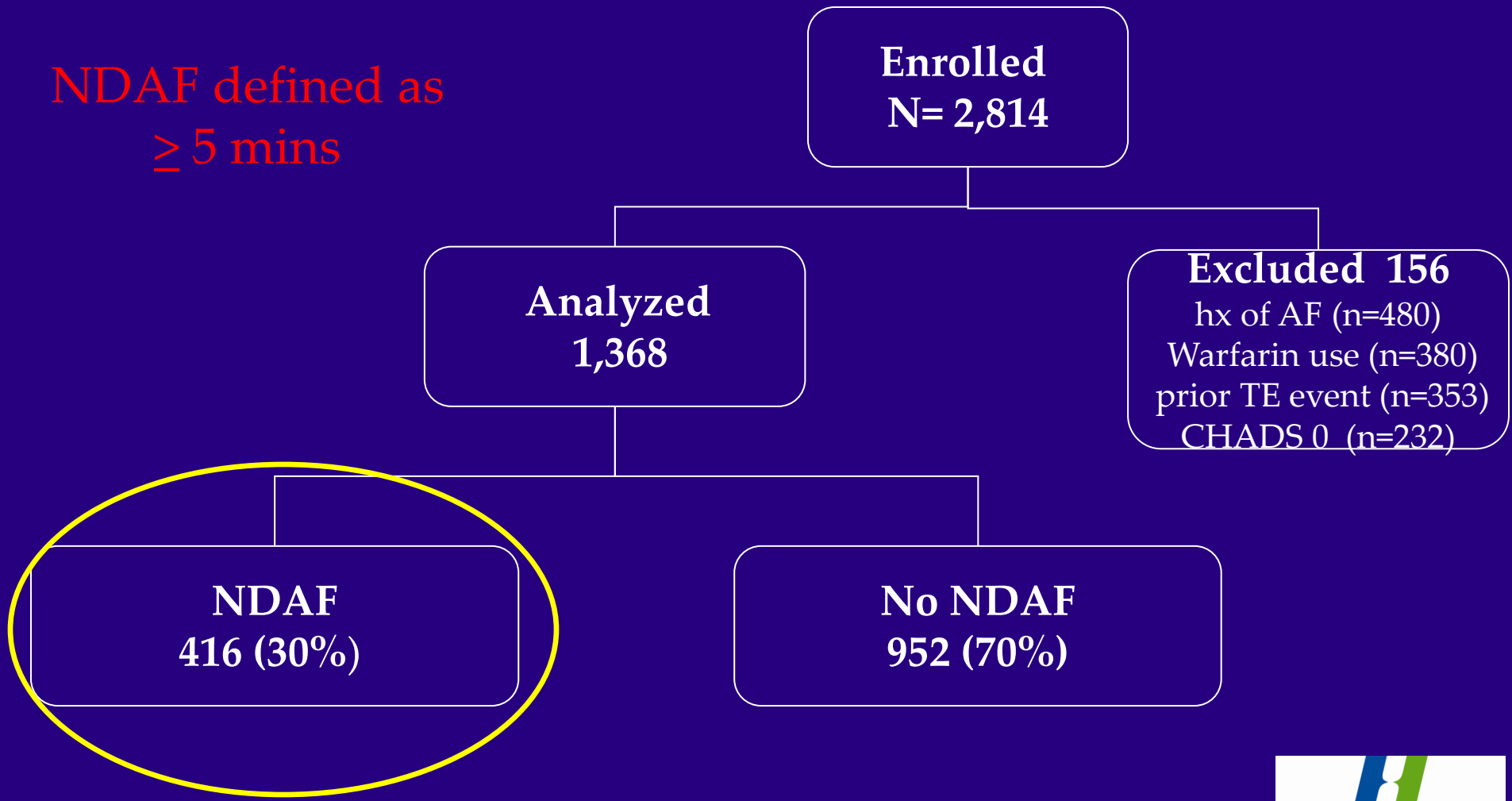
Newly Detected AF in Patients with TE Risk Factors

NDAF defined as
≥ 5 mins



Zeigler et al, Am J Cardiol 2012; 110:1309-1314

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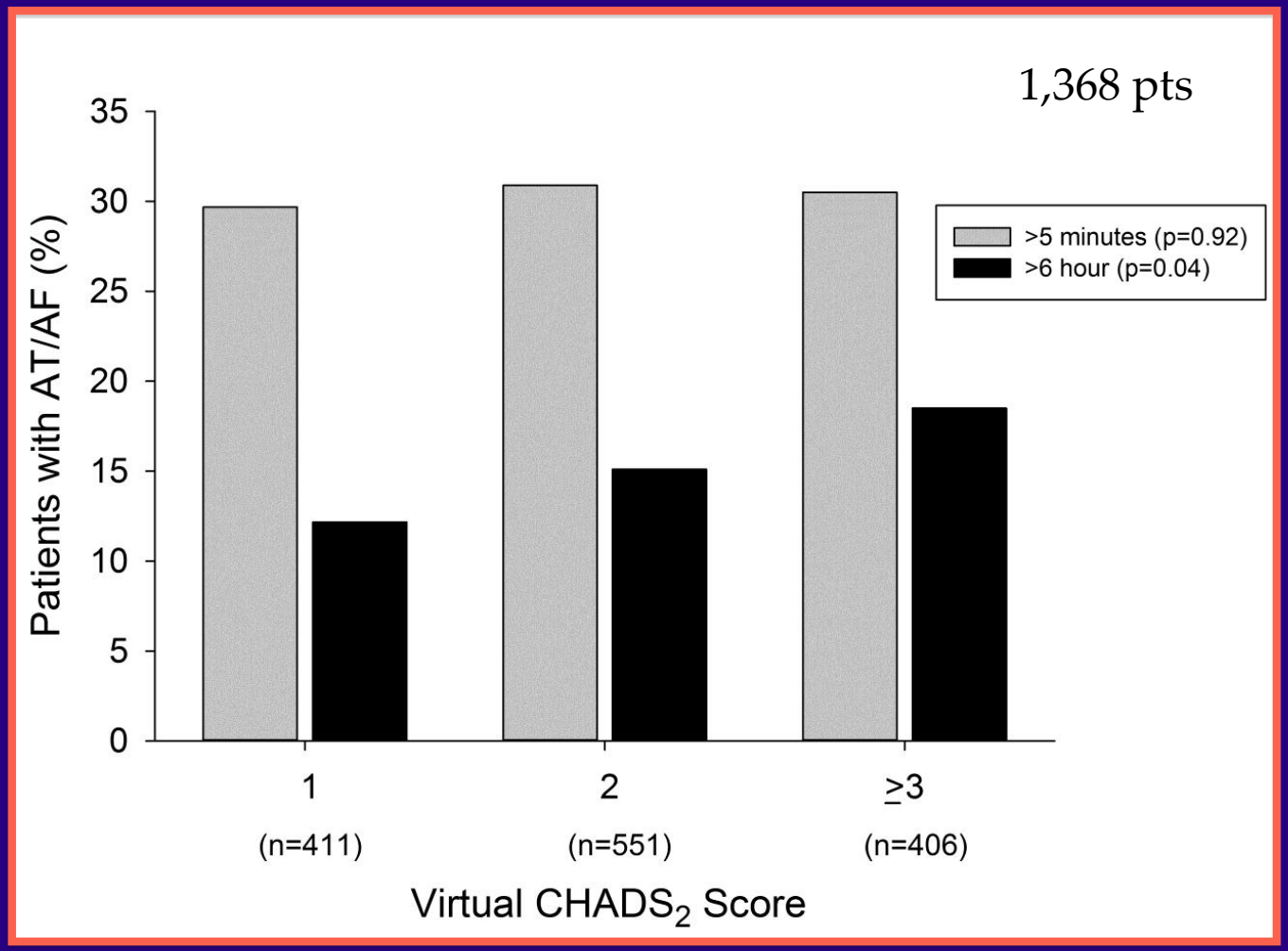
What Percent of Patients have NDAF?

Figure 2



Zeigler et al, Am J Cardiol 2012; 110:1309-1314

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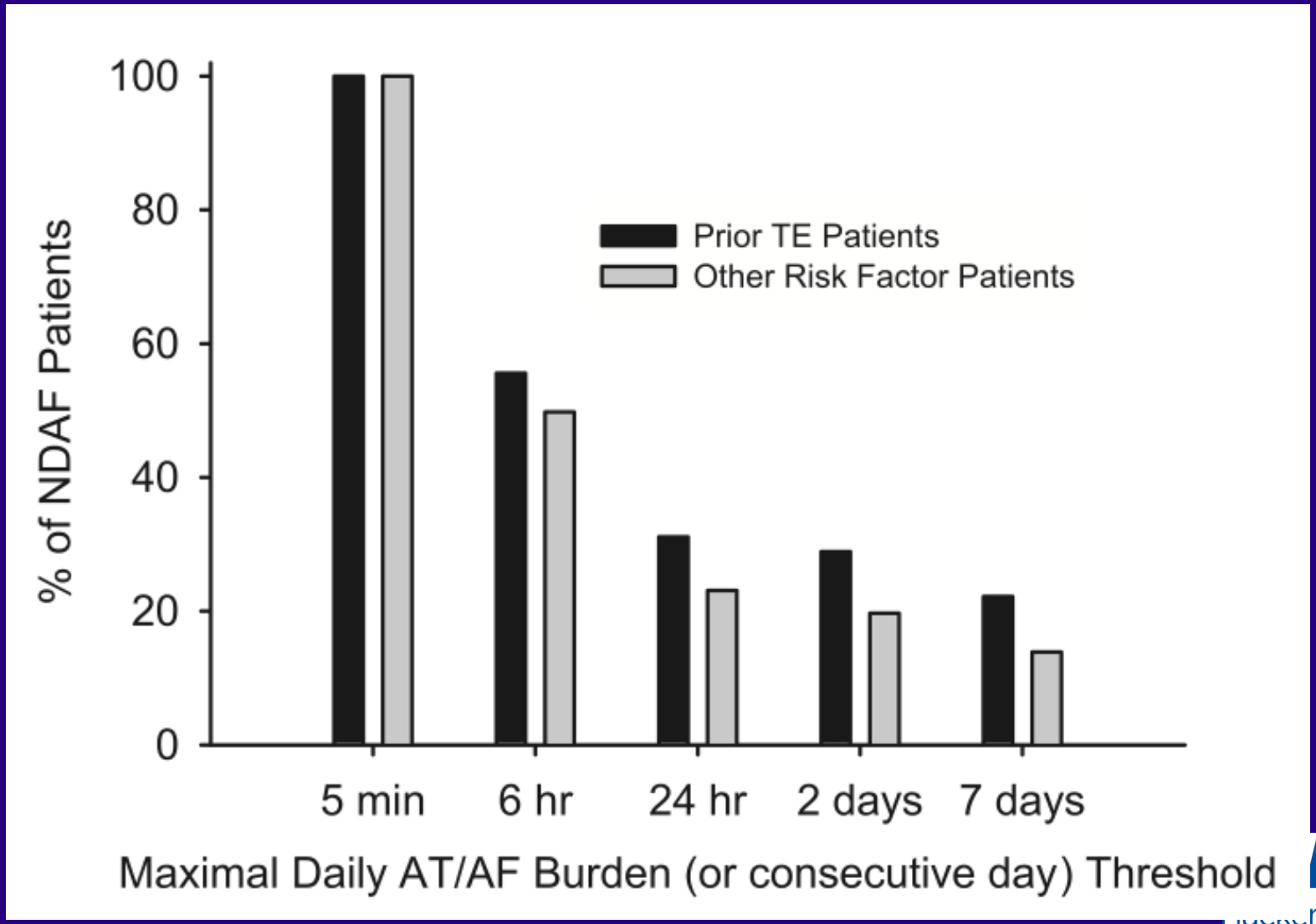
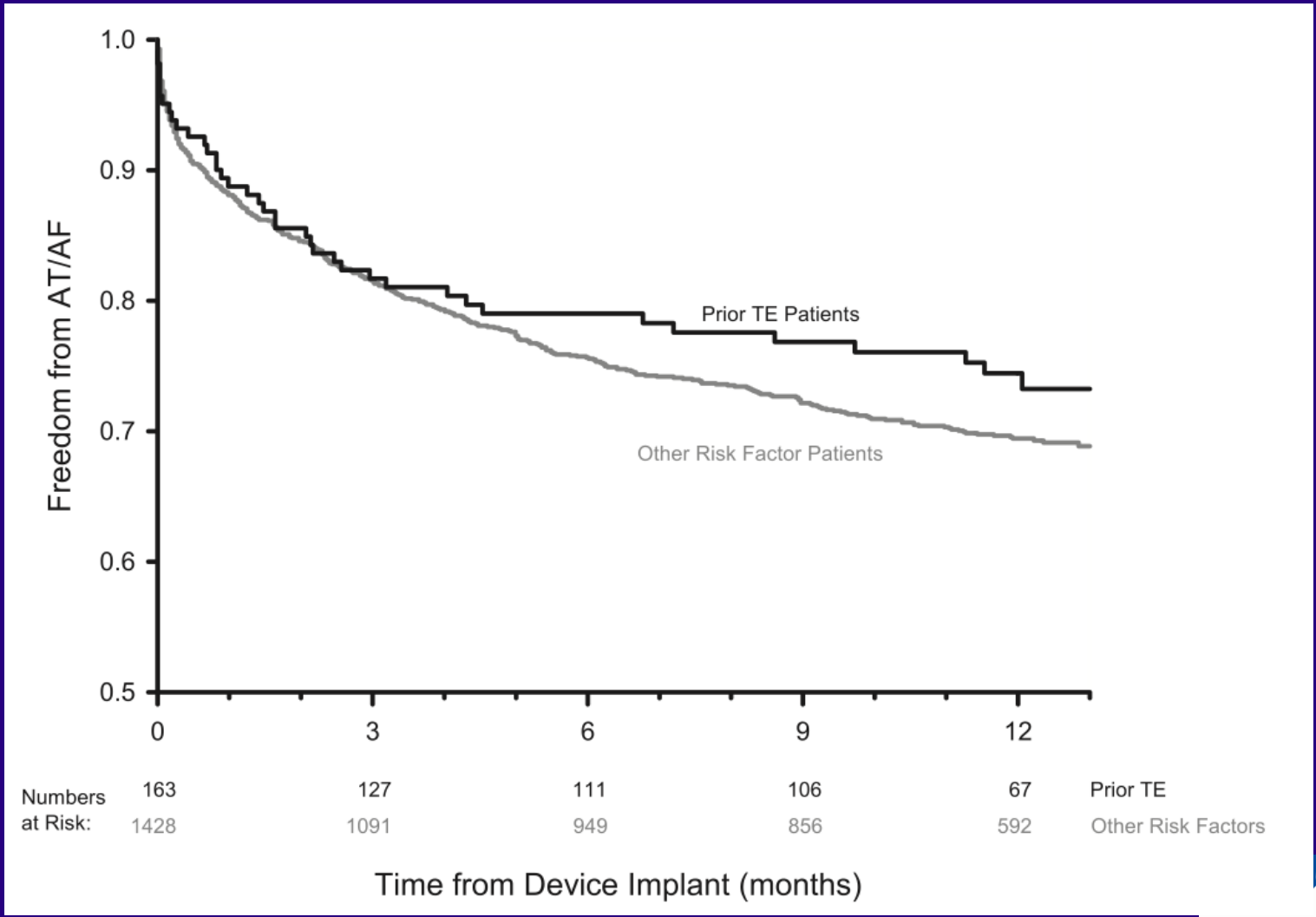
Percentage of NDAF pts exceeding different AF burden thresholds



KM Curve for Time to Detection of NDAF



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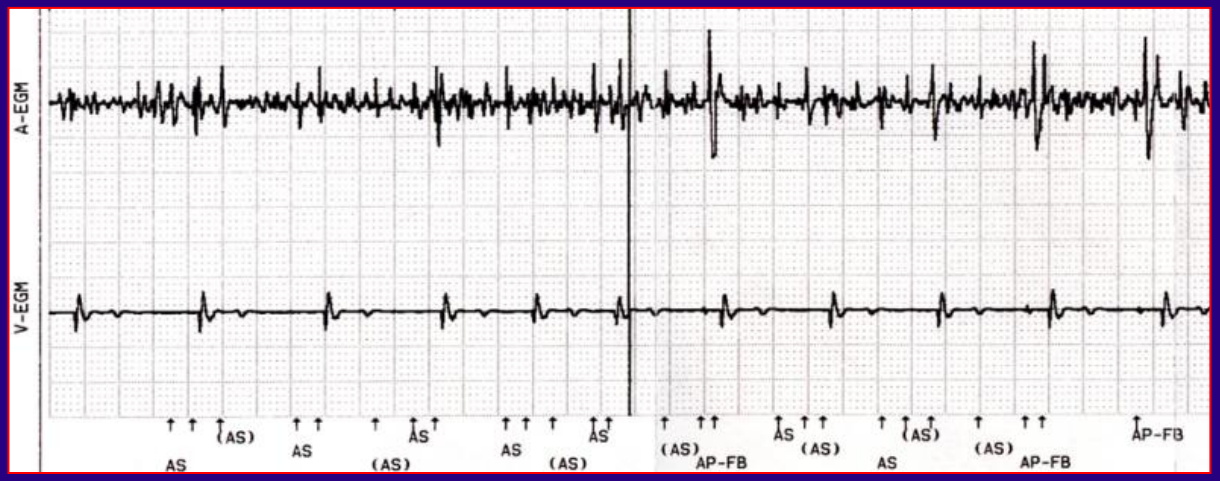
Is the AF detected by CIEDs directly responsible for Strokes?



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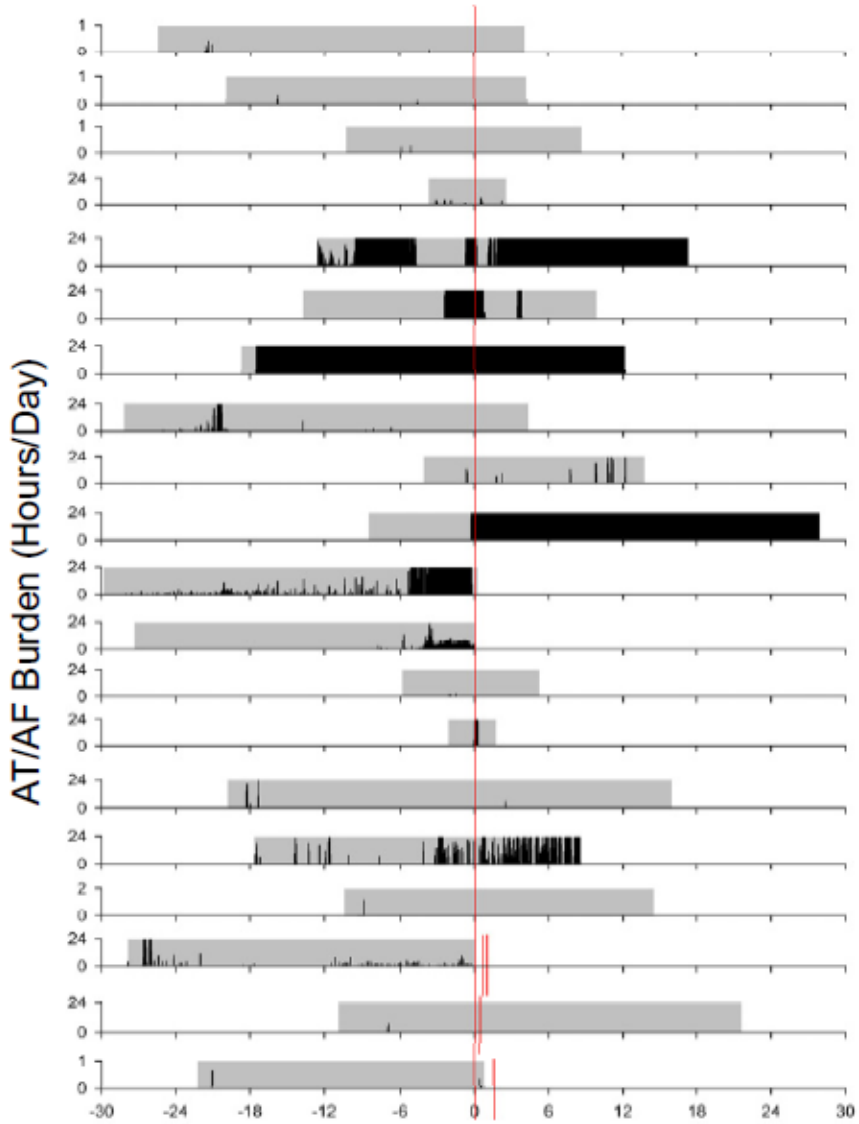
Patients with pre-stroke AT/AF burden



Patient #	$CHADS_2$ Score	Baseline Antithrombotic Therapy
1	2	None
2	3	ASA
3	6	None
4	5	ASA
5	1	OAC
6	4	ASA
7	2	ASA
8	1	OAC/ASA
9	1	OAC
10	3	ASA
11	4	OAC/ASA
12	5	ASA
13	2	None
14	2	None
15	3	ASA
16	3	None
17	3	OAC/ASA
18	4	OAC/ASA
19	2	ASA
20	2	None

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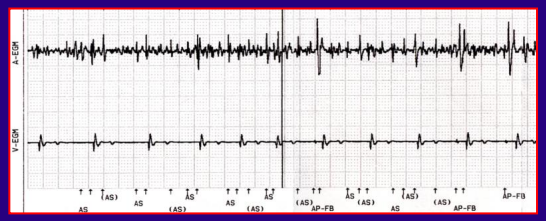
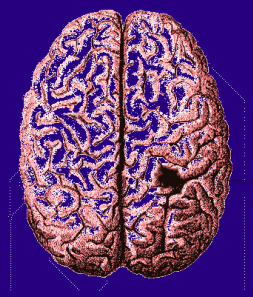
Temporal Relationship of Device-Detected AF to Thromboembolic Events

Year	Trial	Number of patients with TE Event	Definition of AF episode	Any AF Detected Prior to TE Event	AF Detected only after TE Event	No AF in 30 Days Prior to TE Event	Any AF in 30 Days Prior to TE Event
2011	TRENDS[53]	40	5 minutes	20/40 (50%)	6/40 (15%)	29/40 (73%)	11/40 (27%)
2014	ASSERT[54]	51	6 minutes	18/51 (35%)	8/51 (16%)	47/51 (92%)	4/51 (8%)
2014	IMPACT[55]	69	36/48 atrial beats ≥200bpm	20/69 (29%)	9/69 (13%)	65/69 (94%)	4/69 (6%)





Glotzer et al. . Heart Rhythm 2015;12:234–241

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Year	Study	AF Burden Measure	Hazard ratio for stroke event	
2003	MOST	5 min	6.7	p = 0.020
2005	Capucci	> 24hrs AF	3.1	p = 0.044
2009	Botto	$CHADS_2$ + AF burden	.8% vs. 5% (6.25)	
2009	TRENDS	5.5 hours	2.4	p = 0.060
2012	Home monitor CRT	3.8 hours	9.4	p = 0.006
2012	ASSERT	6 min	2.5	p = 0.008

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