

Cryptogenic Stroke: Searching for a Cause Using Implantable Loop Recorders

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Disclosures

- I currently have a pen from Medtronic.
- Scrap paper for notes donated by St. Jude.
- The rep from Boston Scientific gave me a protein bar the other day after a long case.
- In all seriousness, I have received honoraria and travel expenses from Boehringer Ingelheim, Medtronic, Boston Scientific, St. Jude Medical. I have also consulted for St. Jude Medical.



Discussion Goals

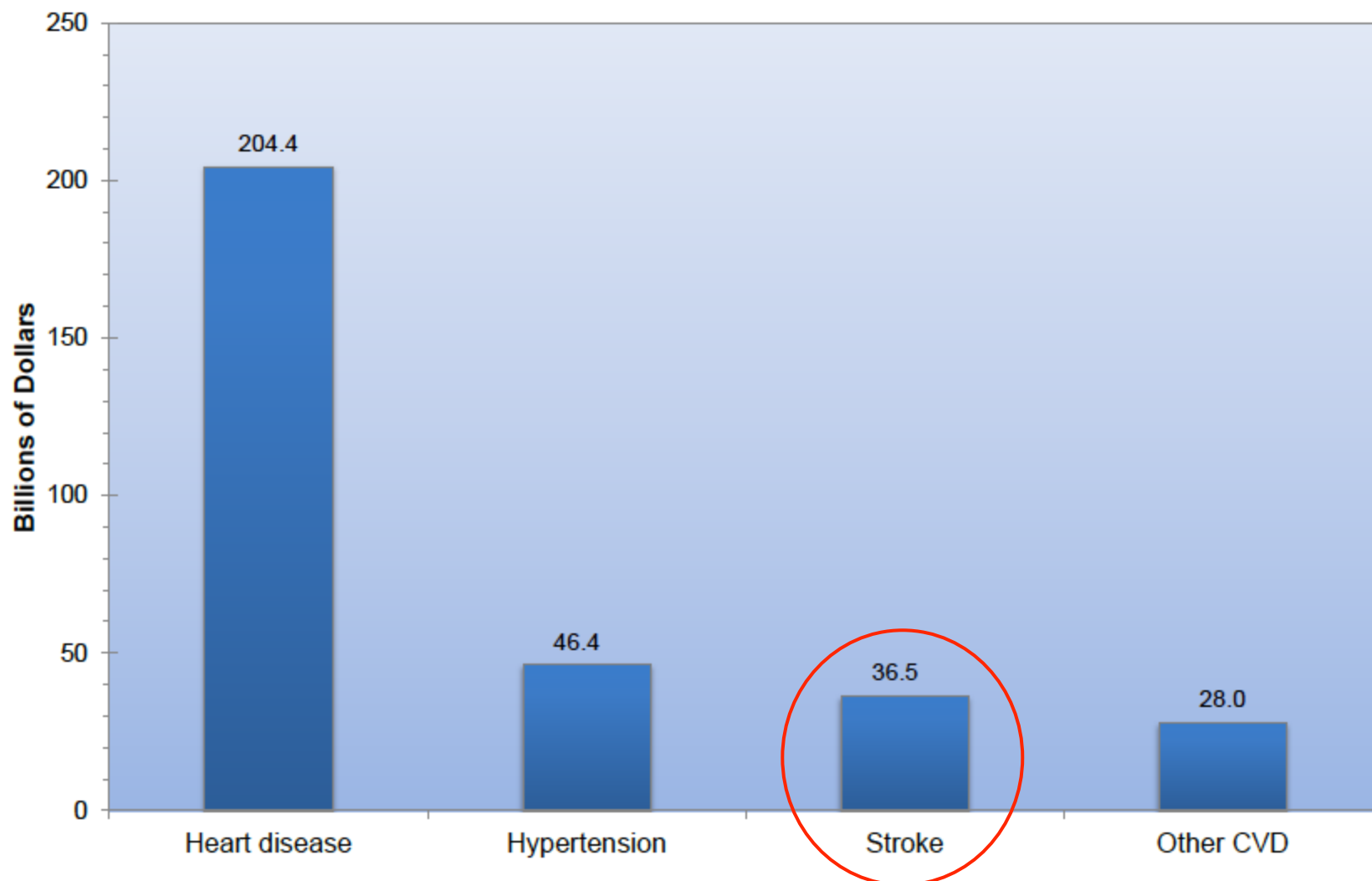
- ❖ Clinical prevalence and societal impact of cryptogenic stroke
- ❖ AF's role in ischemic strokes
- ❖ Traditional workup
- ❖ Effectiveness of implantable loop recorders in complimenting workup

US Stroke Statistics

- Kills ~130,000 people annually – 1 out of every 19 deaths!
- On average, 1 person dies from a stroke every 4 minutes
- > 795,000 people suffer a stroke
 - ~610,000 are first or new strokes
 - ~185,000 (nearly 1:4) are recurrent
- Leading cause of long-term disability

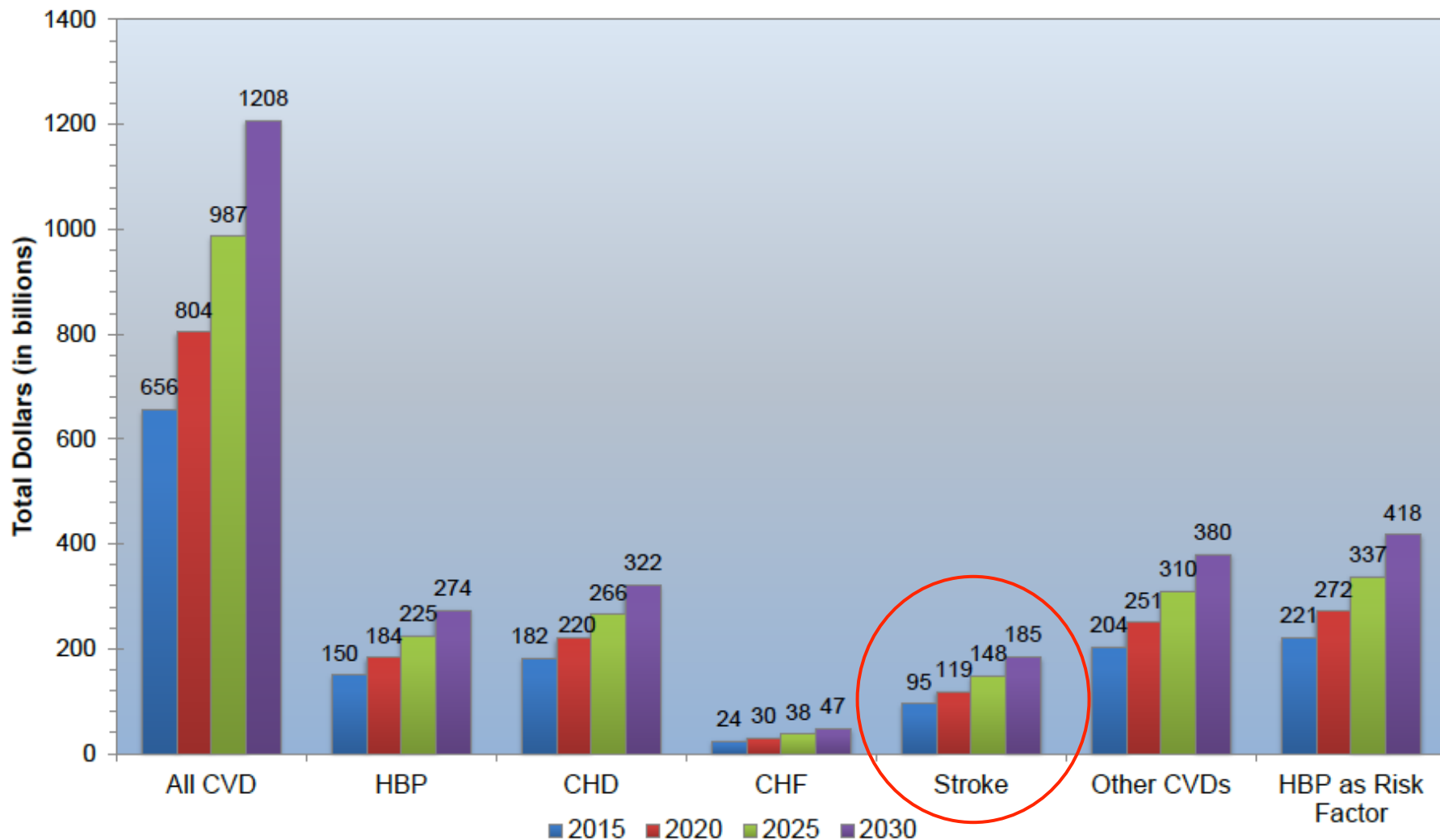


Direct and indirect costs (in billions of dollars) of major cardiovascular diseases and stroke (United States: 2010)



Source: National Heart, Lung, and Blood Institute.

Projected Total Costs of CVD, 2015–2030 (in Billions 2012\$) in the United States

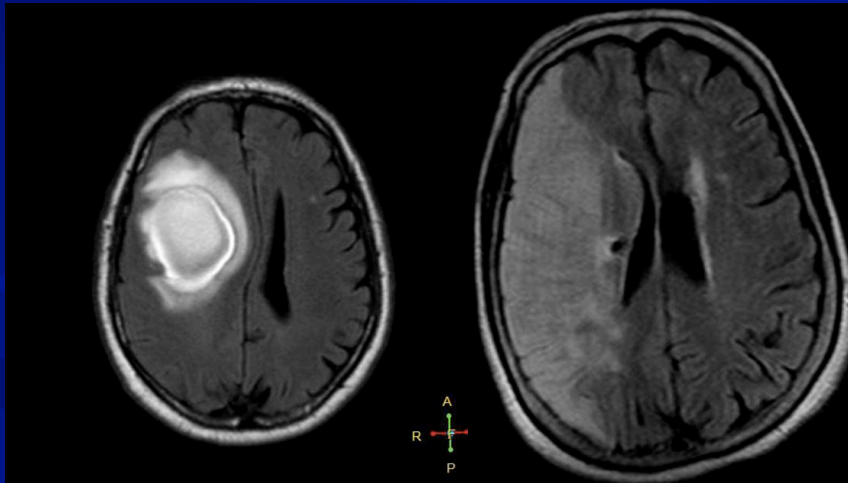


Unpublished data tabulated by AHA using methods described in *Circulation*. 2011;123:933–944.

Stroke Etiologies

Haemorrhage
from Vessel
Rupture (15%)

Arterial
Occlusion (85%)



Subtypes of Ischemic Stroke

- **Large artery atherosclerosis (15-20%)**
- **Cardioembolic (20-25%)**
- **Small artery occlusion (20-25%)**
- **Other/Uncommon (2-4%)**
- **Cryptogenic (30-40%)**



Cryptogenic Stroke

An ischemic stroke that cannot be attributed to large vessel atherosclerosis, small artery occlusion, cardioembolic origin, or other/uncommon causes despite an extensive evaluation.



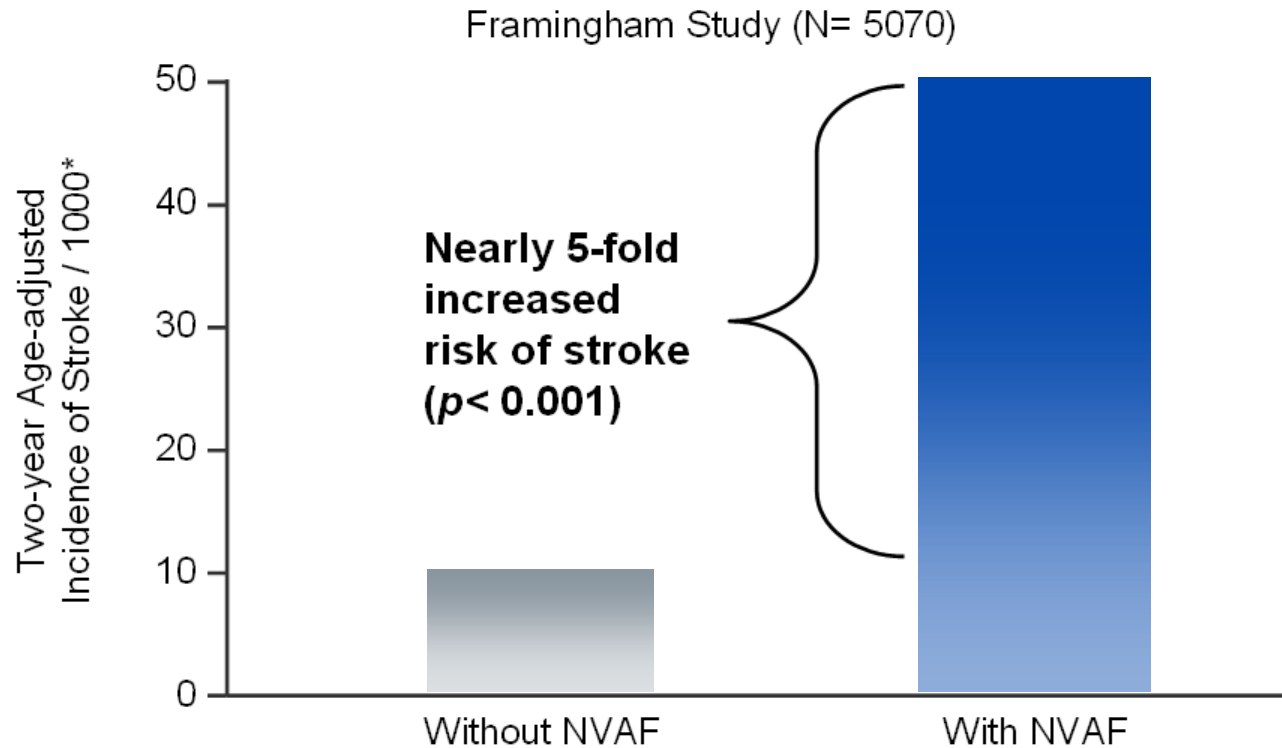
Typical Workup

Large Vessel Atheroma	Small Vessel Disease	Cardioembolic	Other/ Uncommon
CT-angiogram MRA Transcranial Doppler Carotid duplex	CT-angiogram MRA	TTE TEE EKG Holter MCOT ZioPatch	Hypercoagulable workup including blood work and genetic testing Basic blood work ESR Syphilis (RPR)

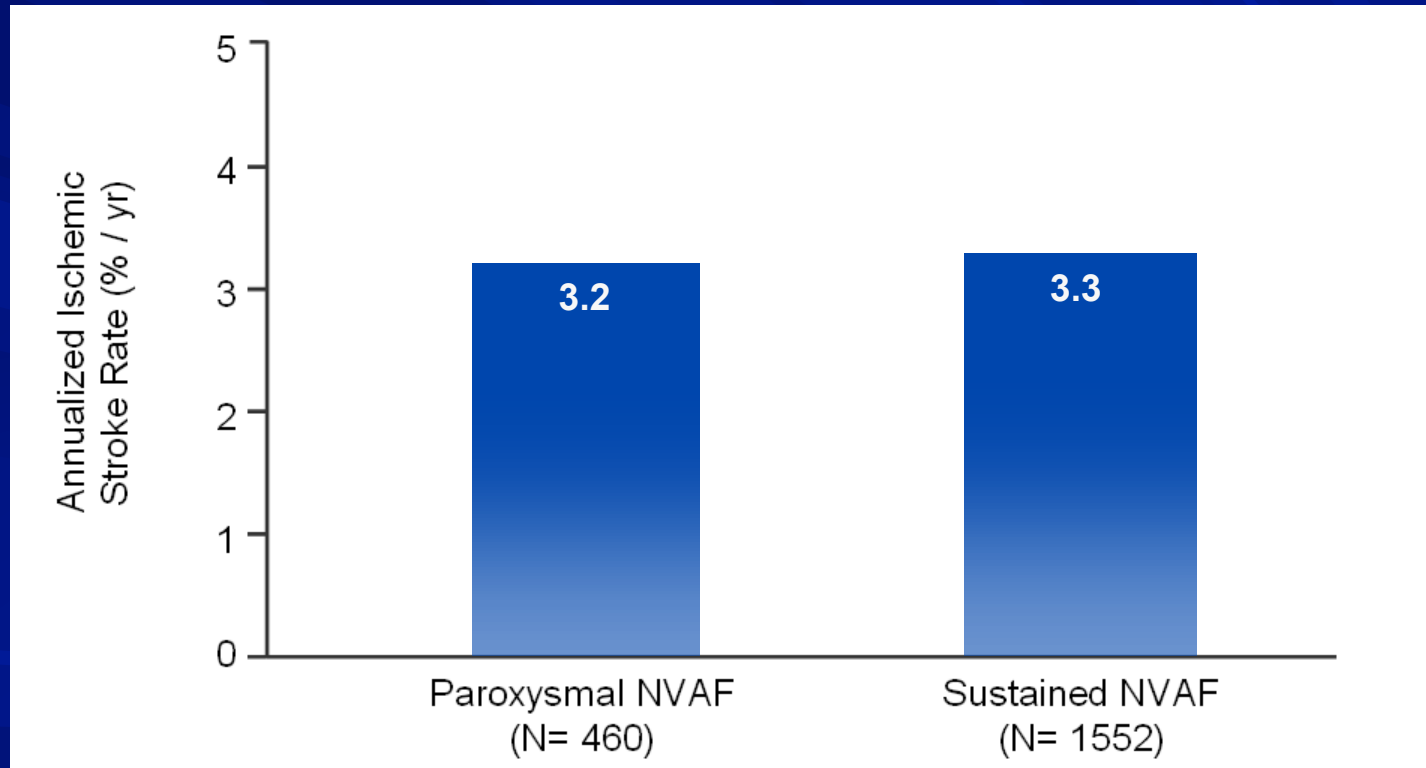
ATRIAL FIBRILLATION AS A SOURCE FOR STROKE



Risk of Stroke with AF

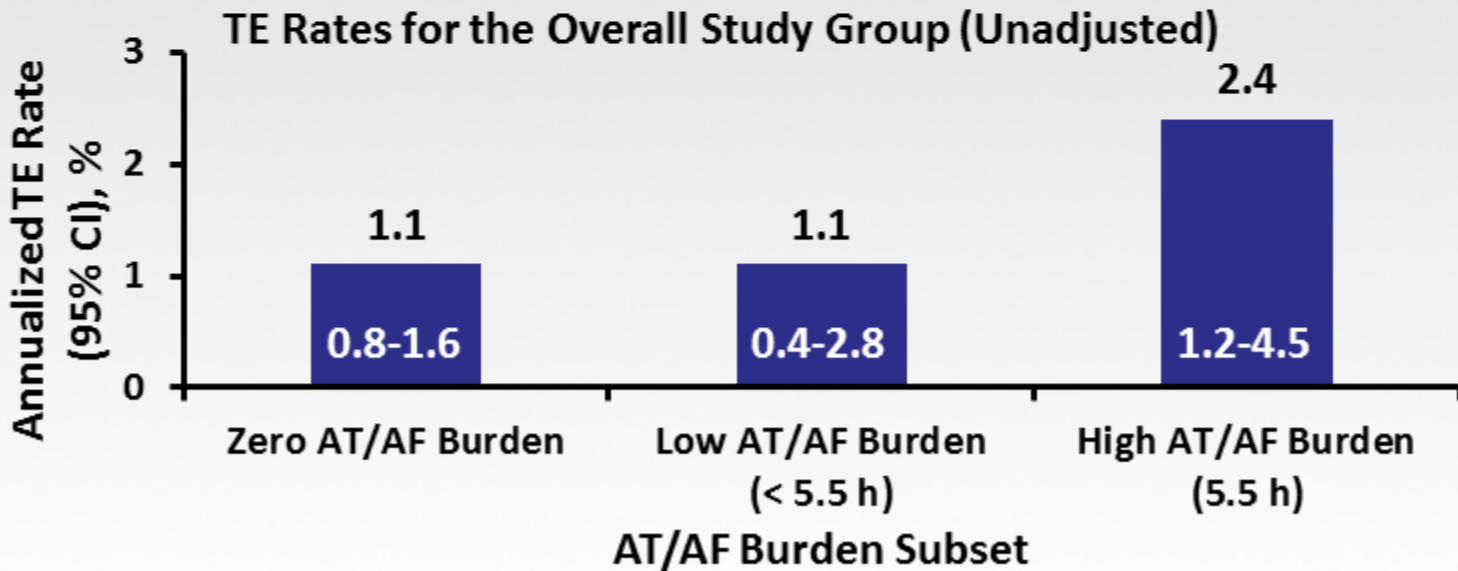


AF Classification - Stroke Risk



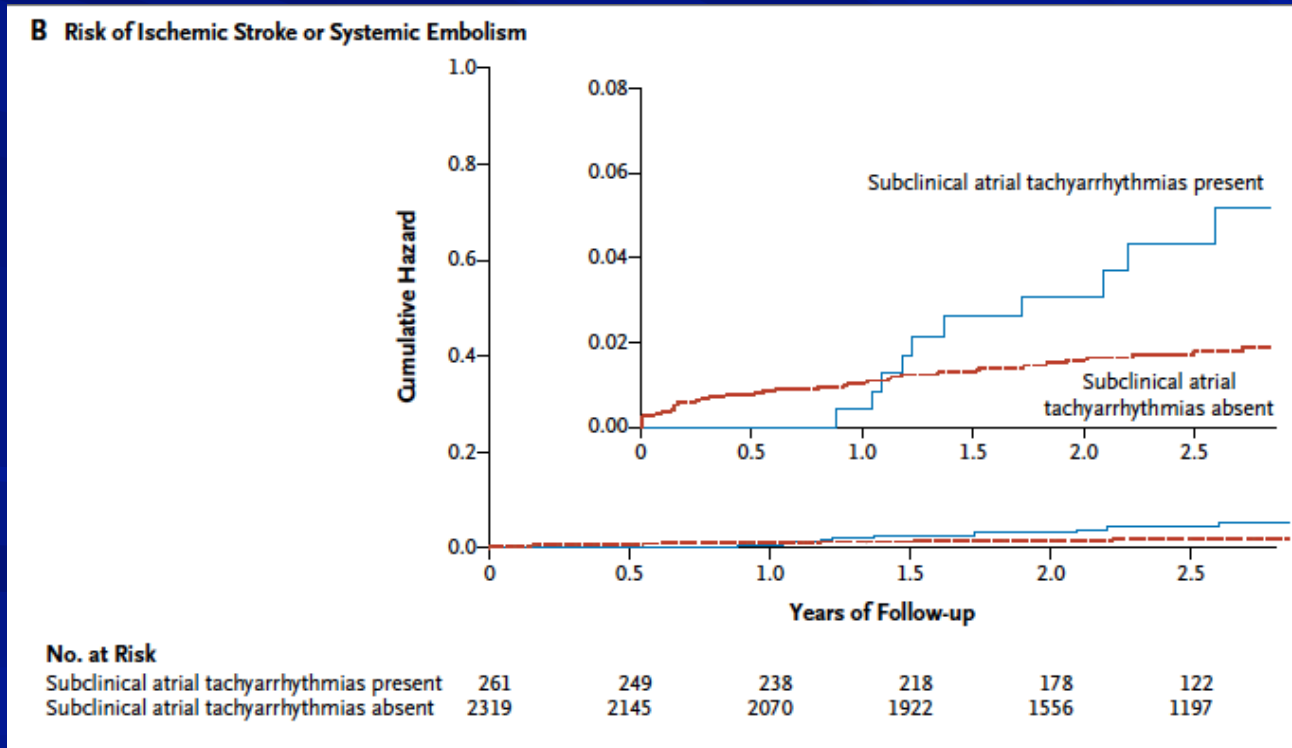
TRENDS

AF burden ≥ 5.5 hrs of AF on any day in the last 30 days was associated with a doubling of risk for a thromboembolic event.



ASSERT Trial

- 2580 pts recently implanted with a pacemaker or ICD and no prior h/o AF
- All patients > 65yo and h/o HTN
- Monitored for occurrence of AT or AF >190 bpm and > 6 min in the first 3 months after implantation
- Followed patients for 2.5yrs for ischemic stroke or embolism



ASSERT Trial

Table 3. Risk of Ischemic Stroke or Systemic Embolism after the 3-Month Visit, According to Baseline CHADS₂ Score and According to Whether Subclinical Atrial Tachyarrhythmias Were or Were Not Detected between Enrollment and the 3-Month Visit.

CHADS ₂ Score	No. of Patients	Subclinical Atrial Tachyarrhythmias between Enrollment and 3 Months						Hazard Ratio for Ischemic Stroke or Systemic Embolism with Subclinical Atrial Tachyarrhythmias (95% CI)*
		Present			Absent			
		<i>no. of patients</i>	<i>no. of events</i>	<i>%/yr</i>	<i>no. of patients</i>	<i>no. of events</i>	<i>%/yr</i>	
1	600	68	1	0.56	532	4	0.28	2.11 (0.23–18.9)
2	1129	119	4	1.29	1010	18	0.70	1.83 (0.62–5.40)
>2	848	72	6	3.78	776	18	0.97	3.93 (1.55–9.95)

* The P value for trend is 0.35.

Risk of stroke ~4%/yr if CHADS₂ > 2



AF Morbidity & Mortality

Morbidity:

- Increases risk of embolic CVA 3-5X;
- Constitutes 1/3 of all embolic strokes > 60 yr (15% of all strokes nationally)¹

Mortality:

- Increases mortality independent of preexisting risk factors:
Odds ratio: 1.5 in men and 1.9-2.1 in women^{2, 3}

¹ Arch Internal Med 1994;154: 1449-1457.

² Benjamin E. Circulation 1996;98: 946-952.

³ Conen D. JAMA 2011; 305:2080-7.

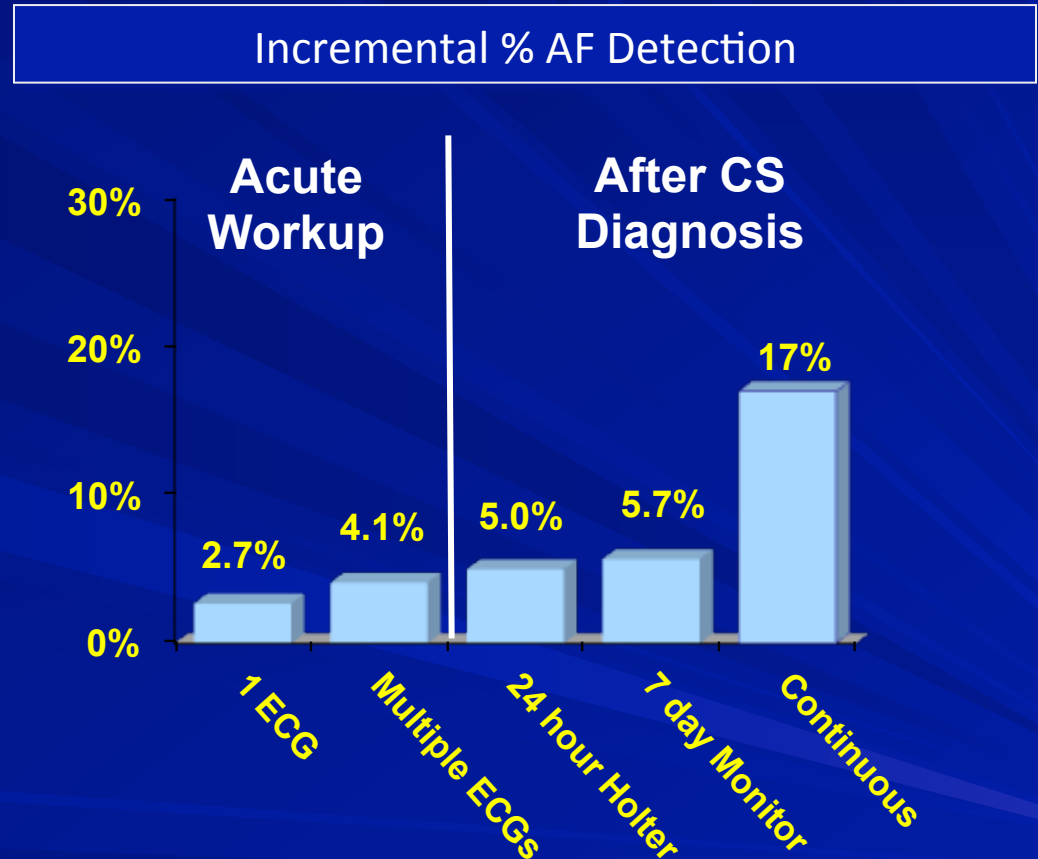


ROLE FOR IMPLANTABLE LOOP RECORDERS



Seek and Ye Shall Find...

- N = 149¹
- Acute stroke or TIA and no history of AF
- ECG monitoring in Hospital
- 24-hour Holter recording if normal ECG
- 7-day event monitor if normal Holter



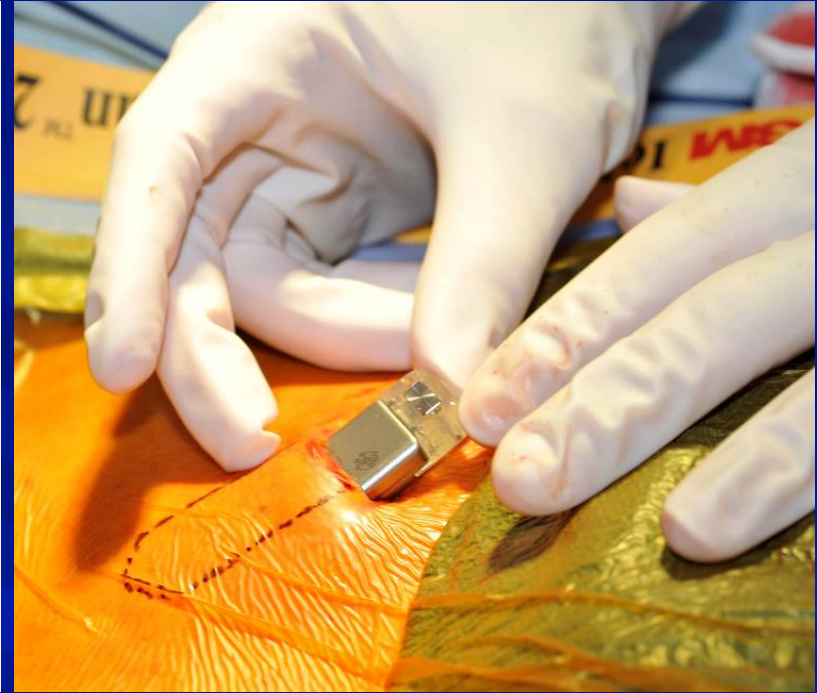
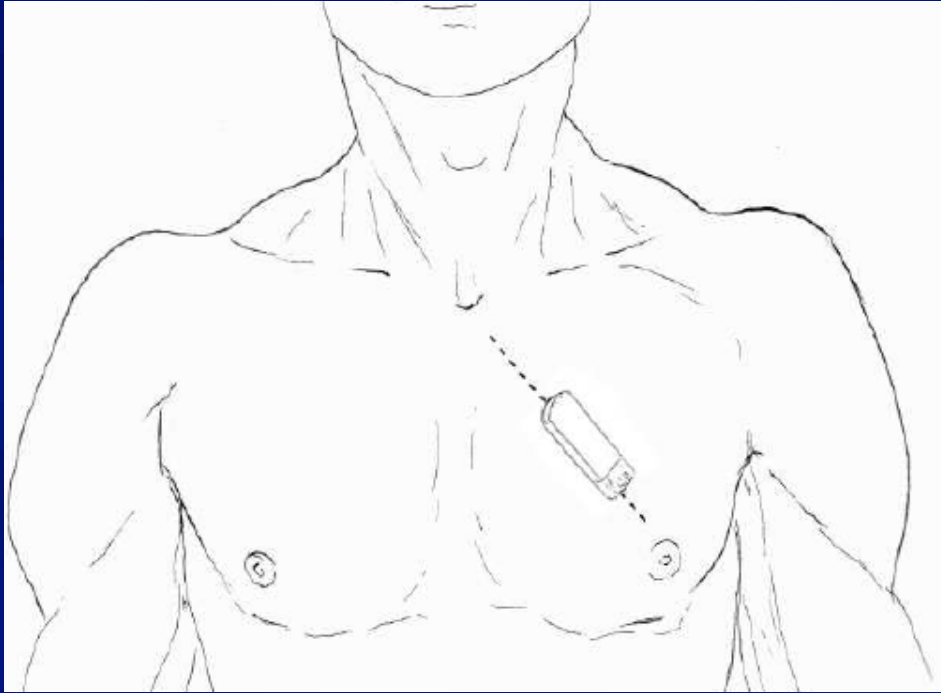
1. Jabaudon D. Et al. Stroke 2004;35:1647-1651.
2. Cotter, P.E., et al. Neurology, 2013 Apr 23;80(17):1546-50
3. Ritter, M.A., et al. Stroke, 2013 May;44(5):1449-52.



Commercially Available ILRs



Basic Implantation of ILR



- Minimally invasive
- No leads or fluoroscopy required
- Well-tolerated
- Monitoring can last up to 3 years
- Now with wireless transmission of data

Cardiac Compass® Report

Trended Diagnostics

Cardiac Compass Report

Device: REVEAL XT 9529

Serial Number:

Date of Visit:

Patient:

ID:

Physician:

Mar May Jul Sep Nov Jan Mar

P = Program
I = Interrogate
_ = Remote

P

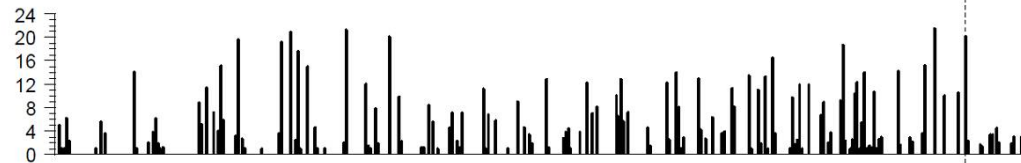
I

P

Daily AF Burden



AT/AF total hours/day



Ventricular Rate During AF



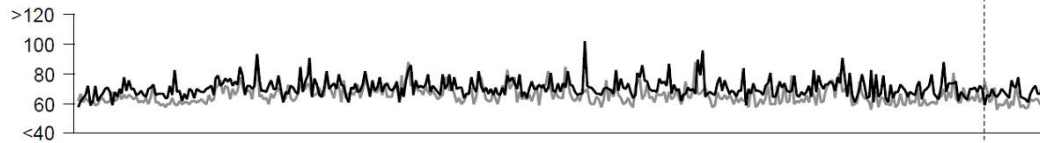
V. rate during AT/AF (bpm)
max/day
avg/day



Day/Night HR



Avg V. rate (bpm)
Day
Night



Patient Activity



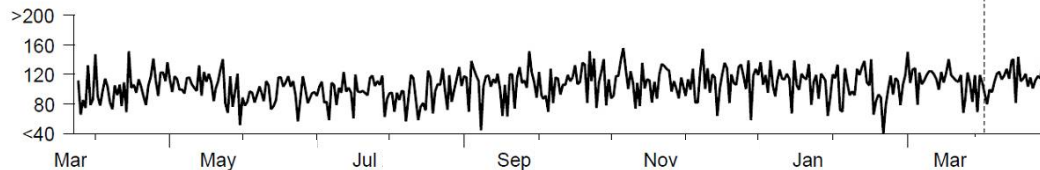
Patient activity hours/day



Heart Rate Variability

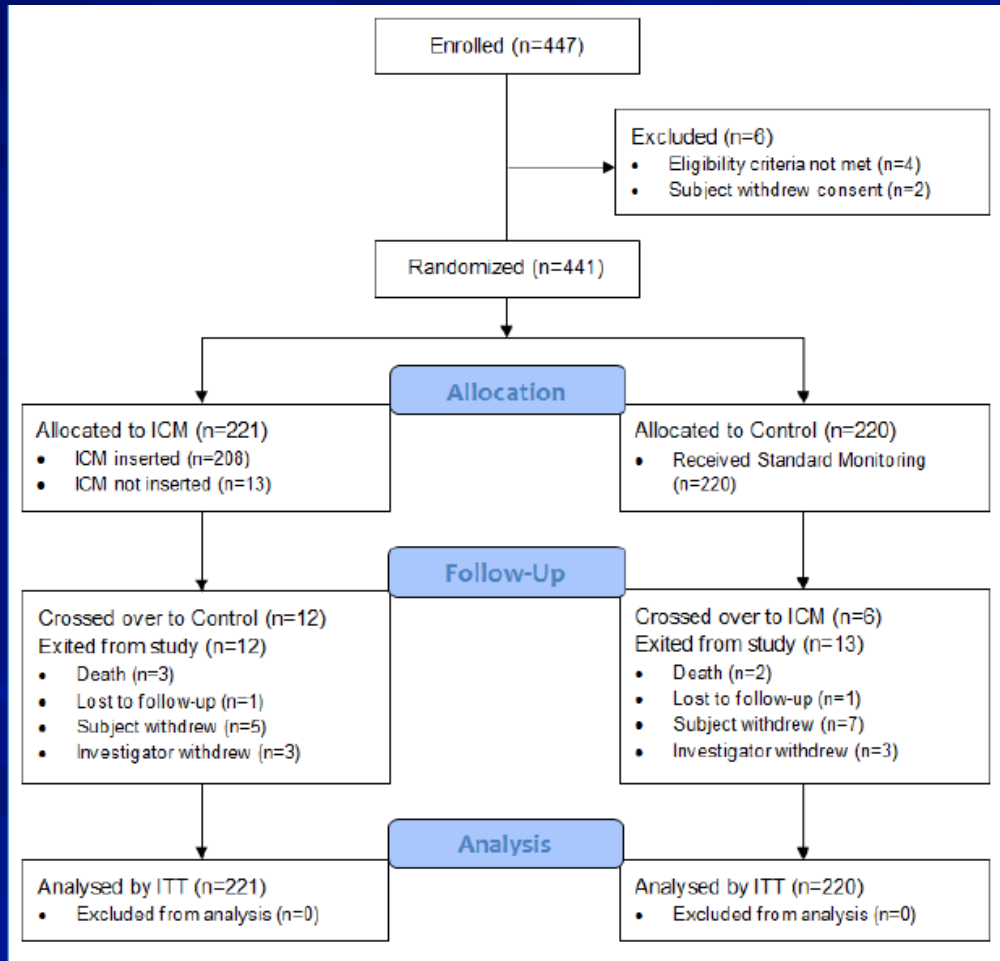


Heart rate variability (ms)



Crystal AF – ISC 2014

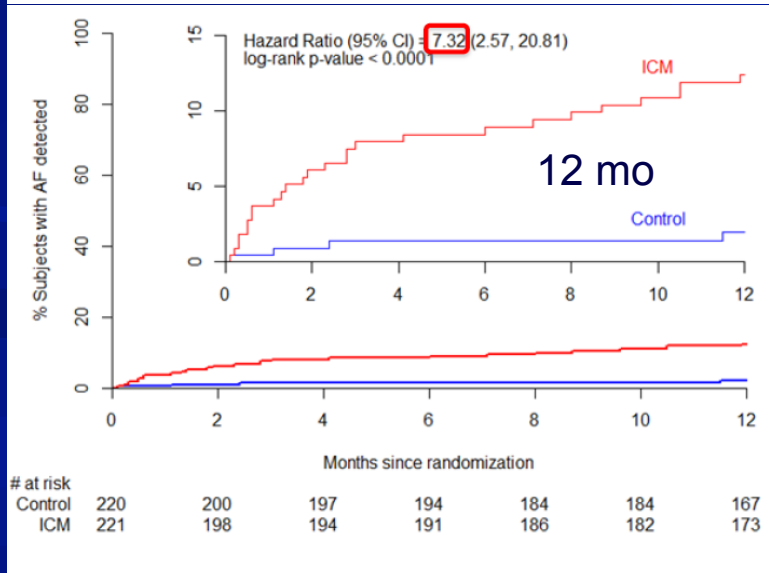
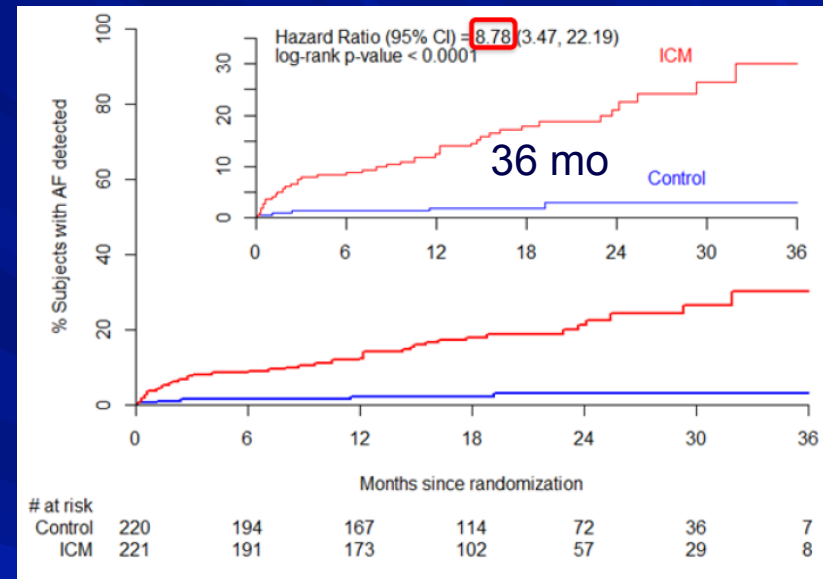
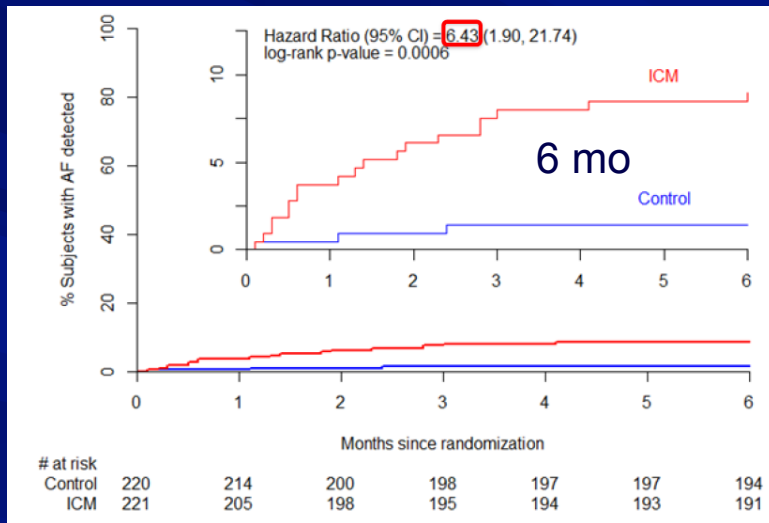
Late Breaking Abstract



- 441 patients randomized
- Primary Endpoint – AF detection @ 6 months
- Follow-up 1, 6, 12, and every 6 months thereafter till study end
- AF defined as any episode lasting > 30 seconds

Crystal AF – ISC 2014

Late Breaking Abstract



ILR superior to standard monitoring in detecting AF

Monitoring to Detect AF

	ICM	Control
Median Time from Randomization to AF Detection	41 days	32 days
Patients found to have AF	19	3
% Asymptomatic Episodes	74%	33%
Oral Anticoagulation Usage, overall	10.1%	4.6%
OAC use in patients with detected AF	94.7%	66.7%
Testing required to detect AF	Automatic AF detection	88 ECGs 20 24-hour Holters 1 event recorder

6 months

12 months

	ICM	Control
Median Time from Randomization to AF Detection	84 days	52.5 days
Patients found to have AF	29	4
% Asymptomatic Episodes	79%	50%
Oral Anticoagulation Usage, overall	14.7%	6.0%
OAC use in AF patients	96.6%	100%
Tests required to find AF	Automatic AF detection	121 ECGs 32 24-hour Holters 1 Event Recorder
Complications	5 (2.4%) ICMs removed due to insertion site infection or pocket erosion	None



Summary

- ◆ Cryptogenic stroke accounts for 30-40% of all ischemic strokes
- ◆ Asymptomatic AF may be detected in up to 25-30% of patients with cryptogenic stroke
- ◆ Thoroughly investigating for AF is paramount since detection will impact treatment and potentially prevent recurrent stroke
- ◆ Implantable loop recorders offer a powerful solution for long term monitoring