

# 2013 TCTAP

Wrap-Up Interview

## Structural Heart Disease

Moderator

Ziyad M. Hijazi

Interviewees

Saibal Kar, Bernhard Meier, Horst Sievert

# Issues Briefs

## PFO Closure for Stroke Prevention

Big debates in PFO Closure: To close or Not to close?

- Clinical studies: CLOSURE I, PC, RESPECT
- Discussion: Interpretation, Future perspective

## LAA Closure and Atrial Fibrillation

Will LAA Closure transform management of AF?

- Clinical studies: PROTECT AF, CAP, ASAP, PREVAIL
- Discussion: Interpretation, Future perspective

# Cryptogenic Stroke - PFO Trials

	CLOSURE 1	RESPECT	PC	REDUCE
Subjects	960	980 (event driven endpoint)	414	≈ 664
Randomization	1:1	1:1	1:1	2:1
Entry	Clinical Stroke or TIA	Stroke on MRI	Clinical and Radiologic Stroke/TIA	Stroke or TIA on MRI
Screening event	6 months	9 months	5 years	6 months
Medical Rx	Device Arm: <u>6</u> mos clopidogrel & <u>24</u> mos aspirin Control Arm: <u>24</u> mos aspirin/warfarin <u>or</u> both	Warfarin or aspirin ± dipyridamole	Warfarin or aspirin ± dipyridamole	Both Arms: aspirin or aspirin + dipyrid or clopidogrel
Device	StarFlex NM	Amplatzer	Amplatzer	Helex
Endpoint	Stroke or TIA	Stroke or Death	Stroke/TIA or Death	Stroke/TIA on MR or death

# CLOSURE 1 Trial using StarFlex device 909 patients

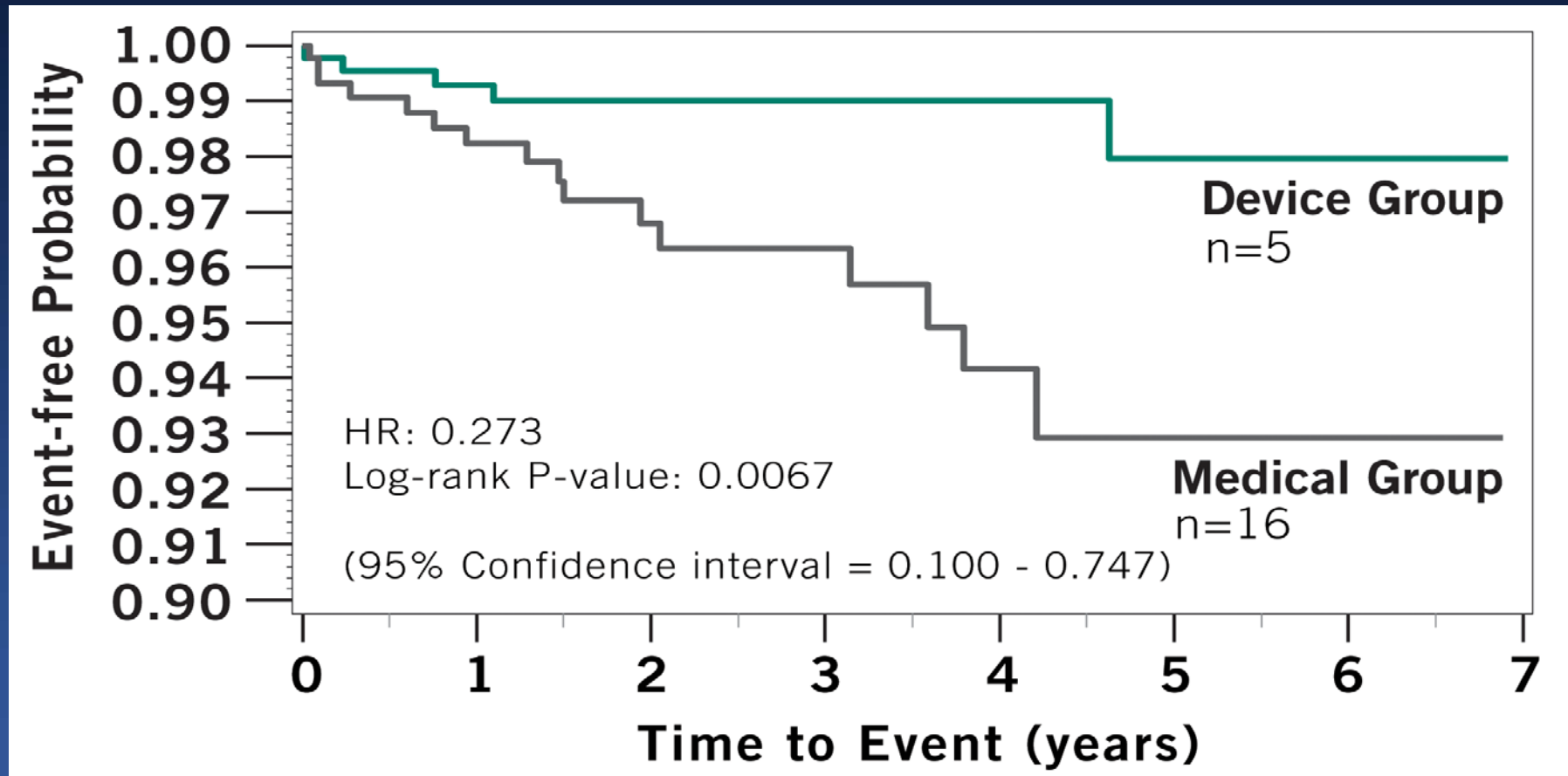
1. PFO closure with StarFlex was “equivalent to medical Rx”
2. Did not reach 1<sup>o</sup> endpoint of device superior to med Rx  
(a. warfarin b. warfarin + aspirin or c. aspirin alone)
3. “Effective Closure Rate” only 87%



End Point after 2 years	Device (%)	Medical Therapy (%)	p
Composite end point	5.9	7.7	0.30
Stroke	3.1	3.4	0.77
TIA	3.3	4.6	0.39
Major vascular complications	3.2	0.0	<0.001
Atrial fibrillation	5.7	0.7	<0.001

# RESPECT

## Primary Endpoint Analysis – As Treated Cohort



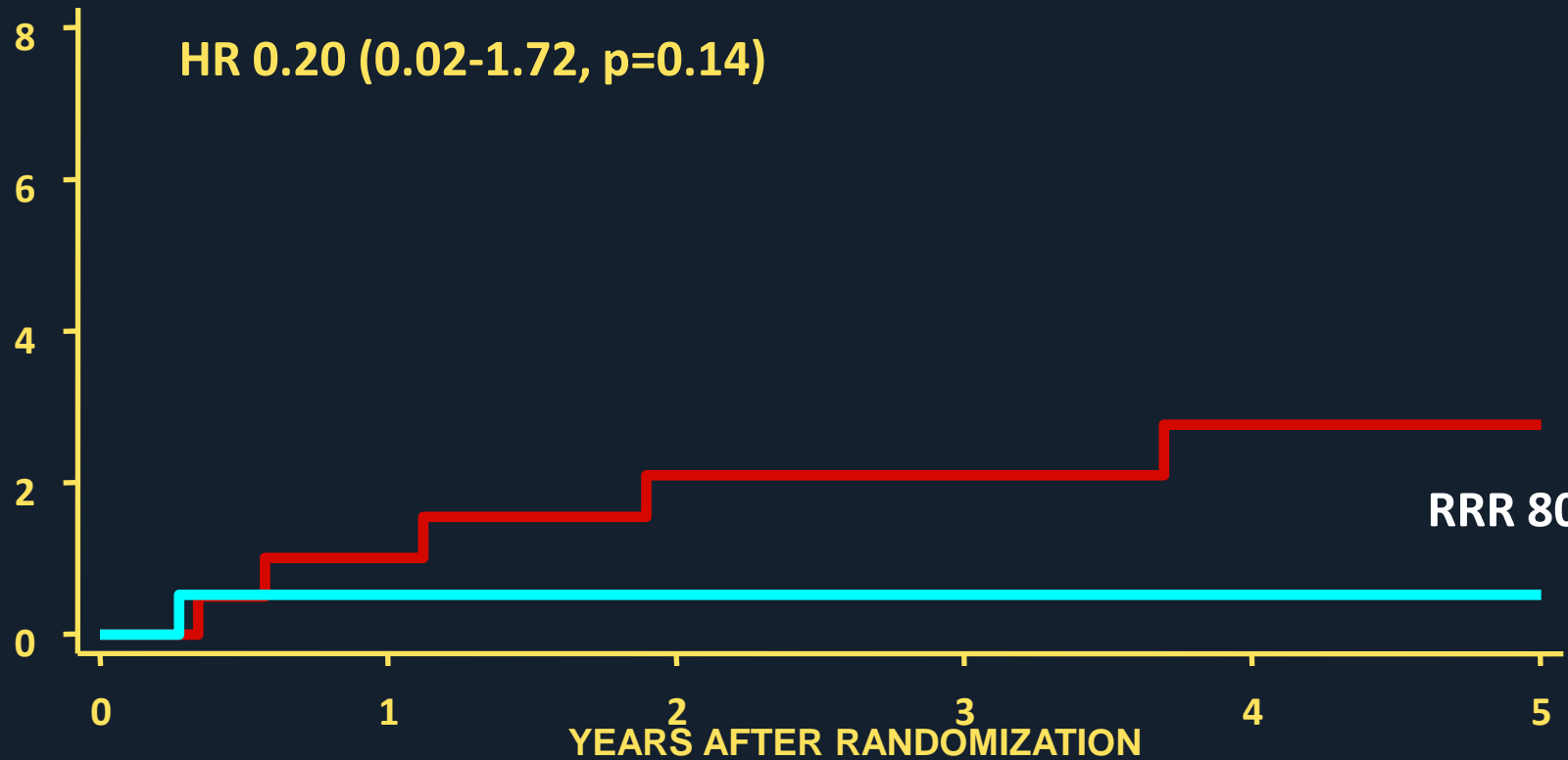
72.7% risk reduction of stroke in favor of device

# PC trial : STROKE

CUMULATIVE INCIDENCE (%)

HR 0.20 (0.02-1.72, p=0.14)

RRR 80%



MEDICAL THERAPY 210  
PFO CLOSURE 204

187  
188

175  
183

164  
167

134  
146

92  
112

# Discussion

- Debating Issues
  - Follow up duration: Too short or enough
  - Devices: Amplatzer or an alternative
  - Other indication for PFO closure besides stroke?

# Novel Oral Anticoagulants

	Dabigatran	Rivaroxaban	Apixaban
<b>Mechanism</b>	direct thrombin inhibitor (both free and clot-bound)	direct factor Xa inhibitor	direct factor Xa inhibitor
<b>Half life</b>	14-17hrs	4-9hrs (up to 12hrs in patients >75yo)	10-14hrs
<b>Metabolism</b>	activated by liver up to 80% excreted by kidney	66% excreted by kidney	Partially by CYP3A4 25% excreted by kidney
<b>Study</b>	RELY	ROCKET-AF	ARISTOTLE
<b>Stroke or Systemic Embol: Non-Inferiority</b>	110mg: 1.53%/yr, 0.91(HR), P<0.001 150mg: 1.11%/yr, 0.66(HR), P<0.001 Warfarin: 1.69%	20mg: 1.7%/yr, 0.79(HR), P<0.001 Warfarin: 2.2%/yr	5mg: 1.27%/yr, 0.79(HR), P<0.001 Warfarin: 1.6%/yr



# Efficacy vs Warfarin: All Stroke

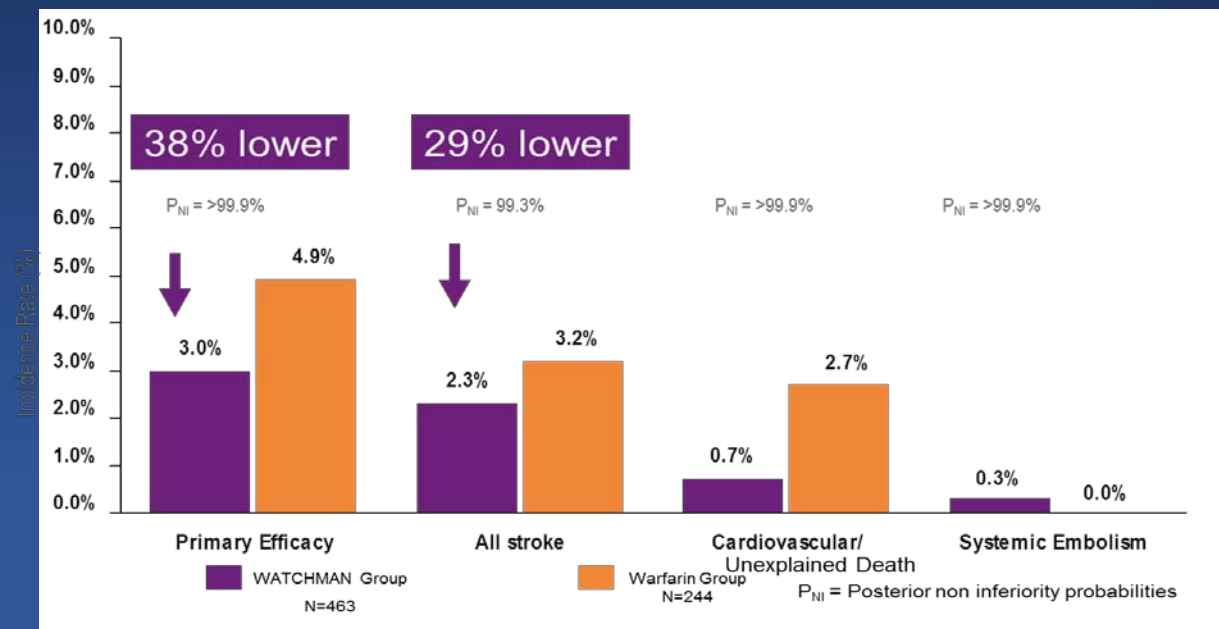
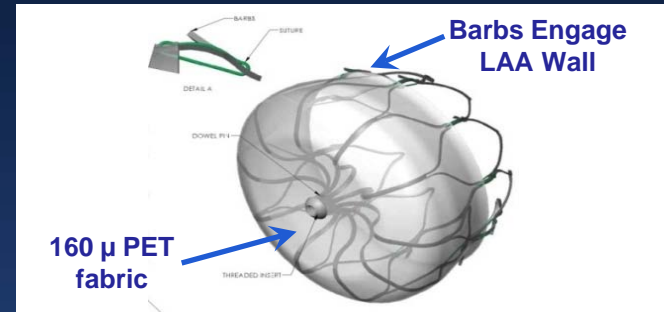
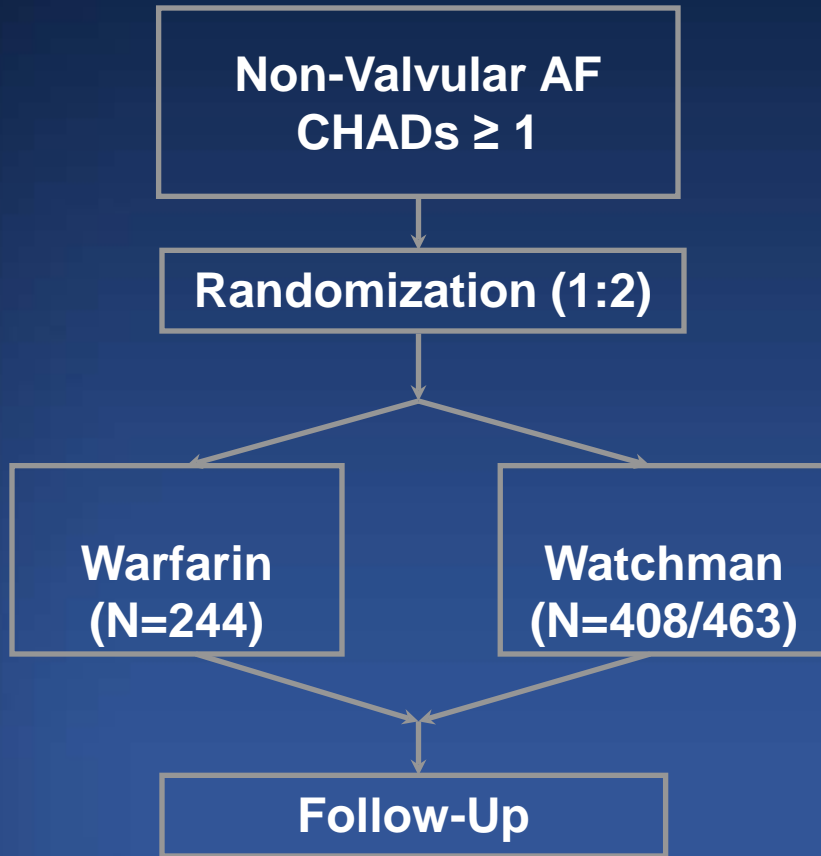
Treatment	Number	Follow Up	RR	95% CI
Dabigatran-110	12,000*	2.0 yrs	0.91	0.74 -1.11
Dabigatran-150	12,000*	2.0 yrs	0.66	0.53 – 0.82
Rivaroxaban	14,264	1-2 yrs	0.88	0.74 – 1.03
Apixaban	18,201	1.8 yrs	0.79	0.66 – 0.95
Watchman	707	2.3 yrs	0.58	0.35 – 1.09

# WATCHMAN: Clinical Studies

STUDY	PATIENTS	SITES	COMMENTS
PROTECT AF	800	59	<ul style="list-style-type: none"> <li>1,500 patient years of follow-up</li> <li>27 months average follow-up per patient</li> </ul>
Continued Access Registry (CAP)	566	26	<ul style="list-style-type: none"> <li>Significantly improved safety results</li> </ul>
ASAP	150	4	<ul style="list-style-type: none"> <li>Treat patients contra-indicated for warfarin</li> </ul>
PREVAIL	400	≤50	<ul style="list-style-type: none"> <li>Same endpoints as PROTECT AF</li> <li>Revised inclusion/exclusion criteria</li> <li>Initiate enrollment October 2010</li> </ul>

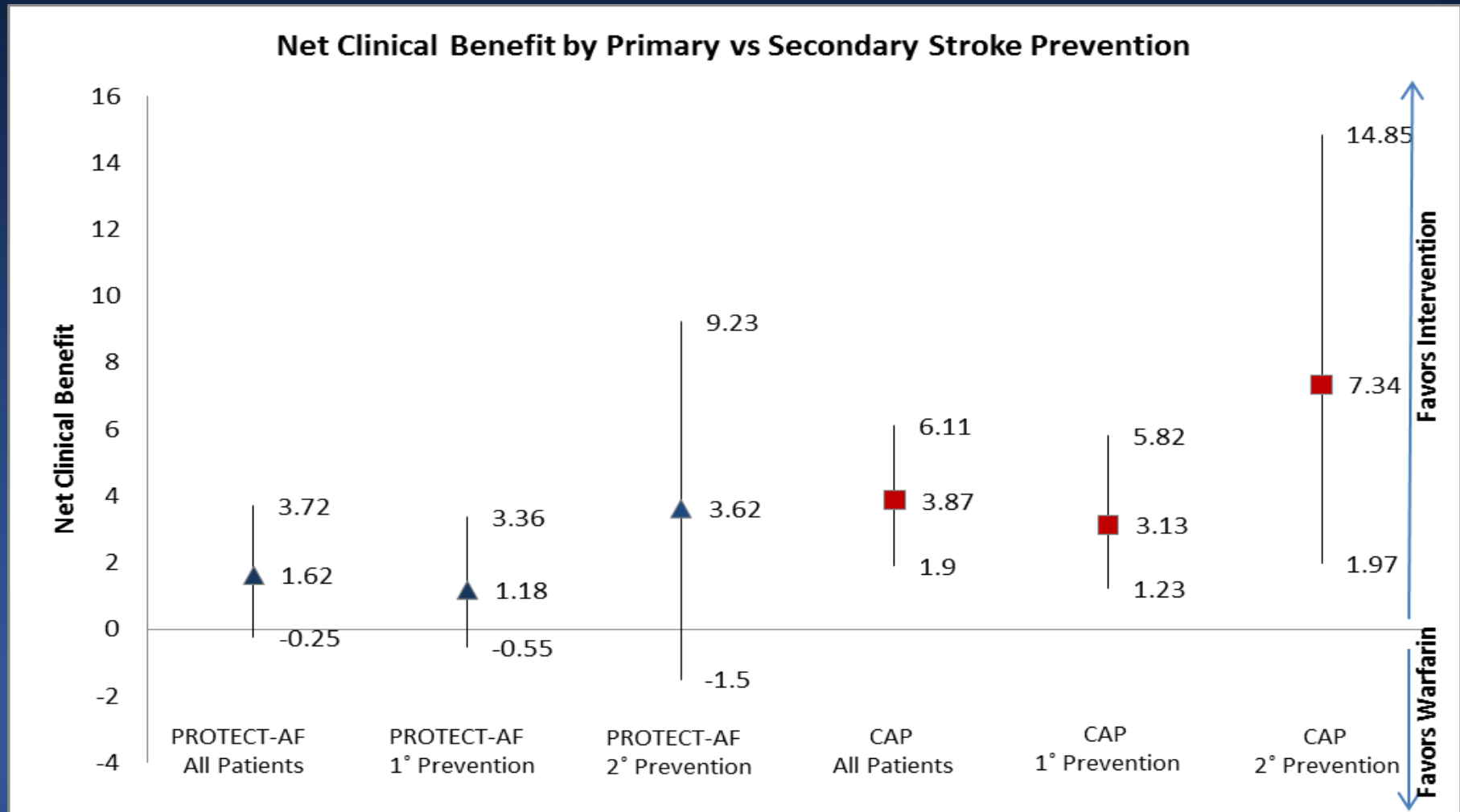
# PROTECT AF Trial

## LAA Closure with Watchman



DR.Holmes, VR.Reddy, ZG.Turi, et al. Lancet 2009; 374:534.

# Net Clinical Benefit for Stroke Prevention



# Discussion

- Transcatheter LAA Closure
  - Beyond Oral Anticoagulants?
  - What populations to be considered?
  - Device selection:  
Watchman vs. Cardiac Plug