

No More Device, Lack of Evidence

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Disclosure Information

The following relationships exist:

Grant support: Abbott, BSC,
Edwards, St Jude, WL Gore

Consultant: Abbott, BSC, Coherex, Edwards, Intervale,
Diiachi Sankyo-Lilly, WL Gore

Speaker: Boston Scientific

*Off label use of products and investigational devices
will be discussed in this presentation*

Evidence Base for PFO Closure

- Observational
- Retrospective
- Meta-analysis
- Prospective RCT

Paradoxical Embolism

The condition known as *crossed* or *paradoxical embolism* is defined.

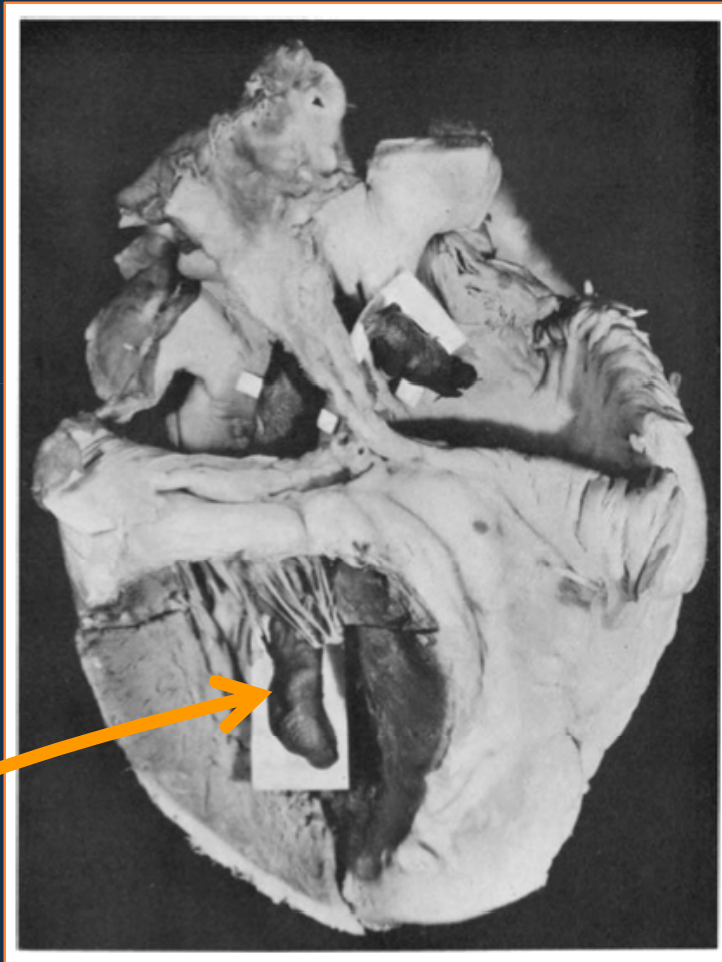
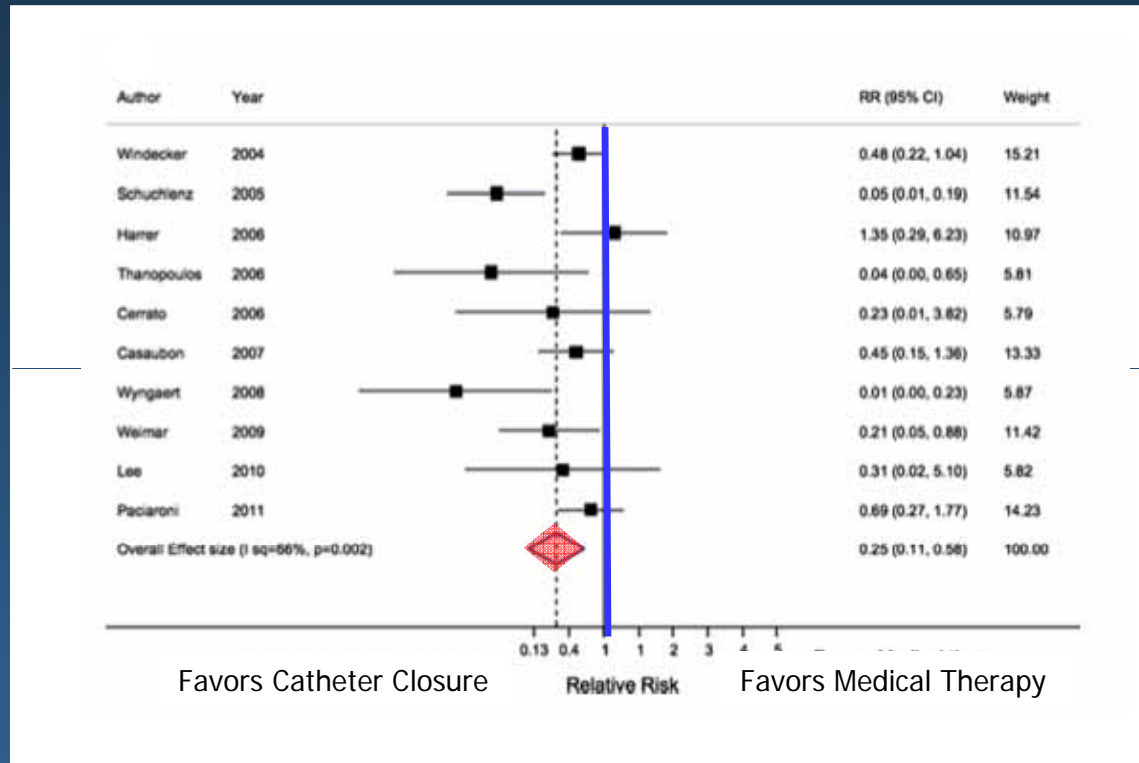


FIG. 2. Showing the heart in Mr. Ferguson Wilson's case. The auricles and left ventricle are viewed from behind. The embolus extends from the right auricle to the apex of the left ventricle and is seen passing through a patent foramen ovale into the left auricle and finally through the mitral valve into the left ventricle.

It is clear that paradoxical embolism can cause stroke- does that mean that PFO should always be closed when associated with stroke?

Meta-Analysis of Transcatheter Closure Versus Medical Therapy for PFO After Presumed Paradoxical Embolism

Rate of recurrent neurological events



a meta-analysis of observational studies was performed to compare the rate of recurrent neurological events of patients with cryptogenic stroke/TIA and PFO

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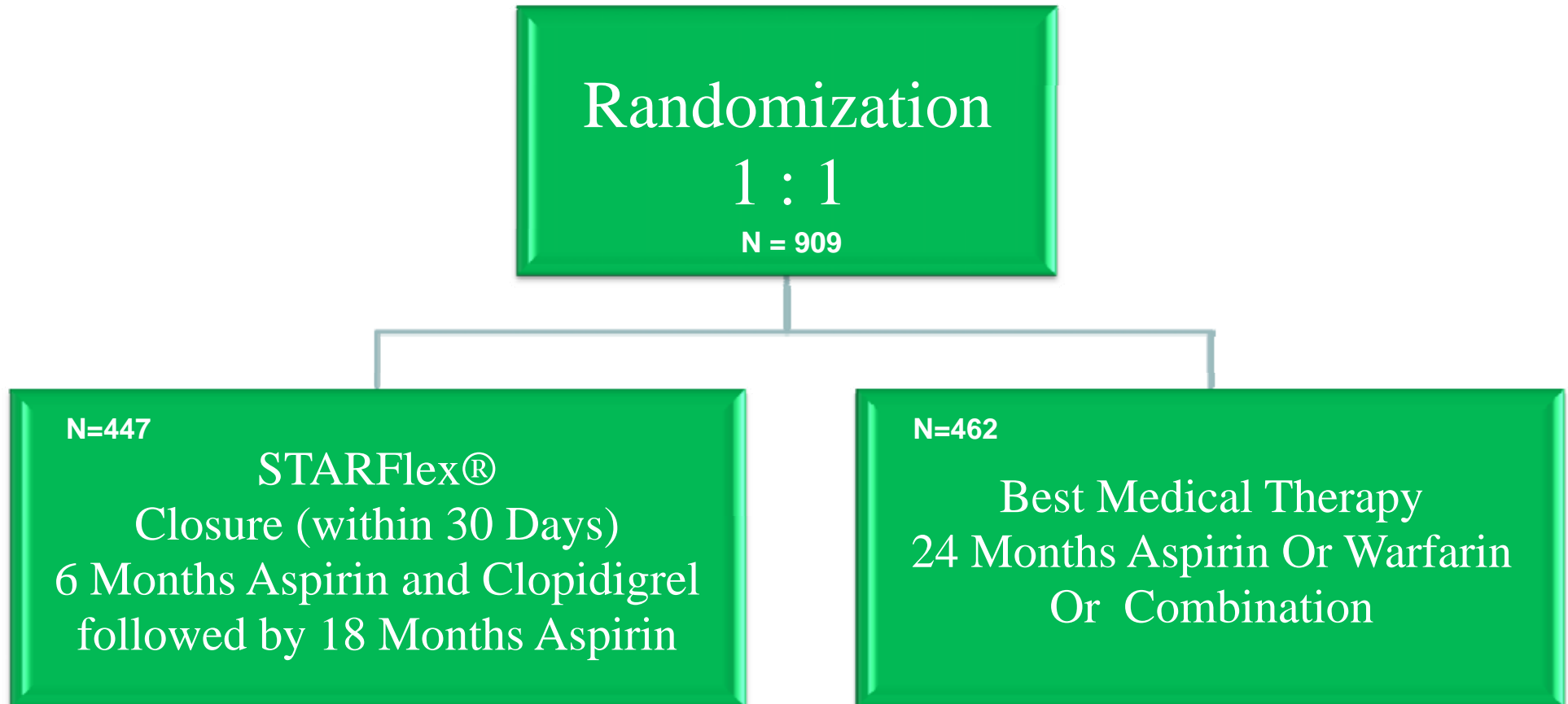
- Stroke
- TIA
- Migraine
- Anxiety
- Other...

Criteria for judgment of causal associations

- **Temporal sequence:** Did exposure precede outcome?
- **Strength of association:** How strong is the effect, measured as relative risk or odds ratio?
- **Consistency of association:** Has effect been seen by others?
- **Biological gradient (dose-response relation):** Does increased exposure result in more of the outcome?
- **Specificity of association:** Does exposure lead only to outcome?
- **Biological plausibility:** Does the association make sense?
- **Coherence with existing knowledge:** Is the association consistent with available evidence?
- **Experimental evidence:** Has a randomised controlled trial been done?
- **Analogy:** Is the association similar to others?

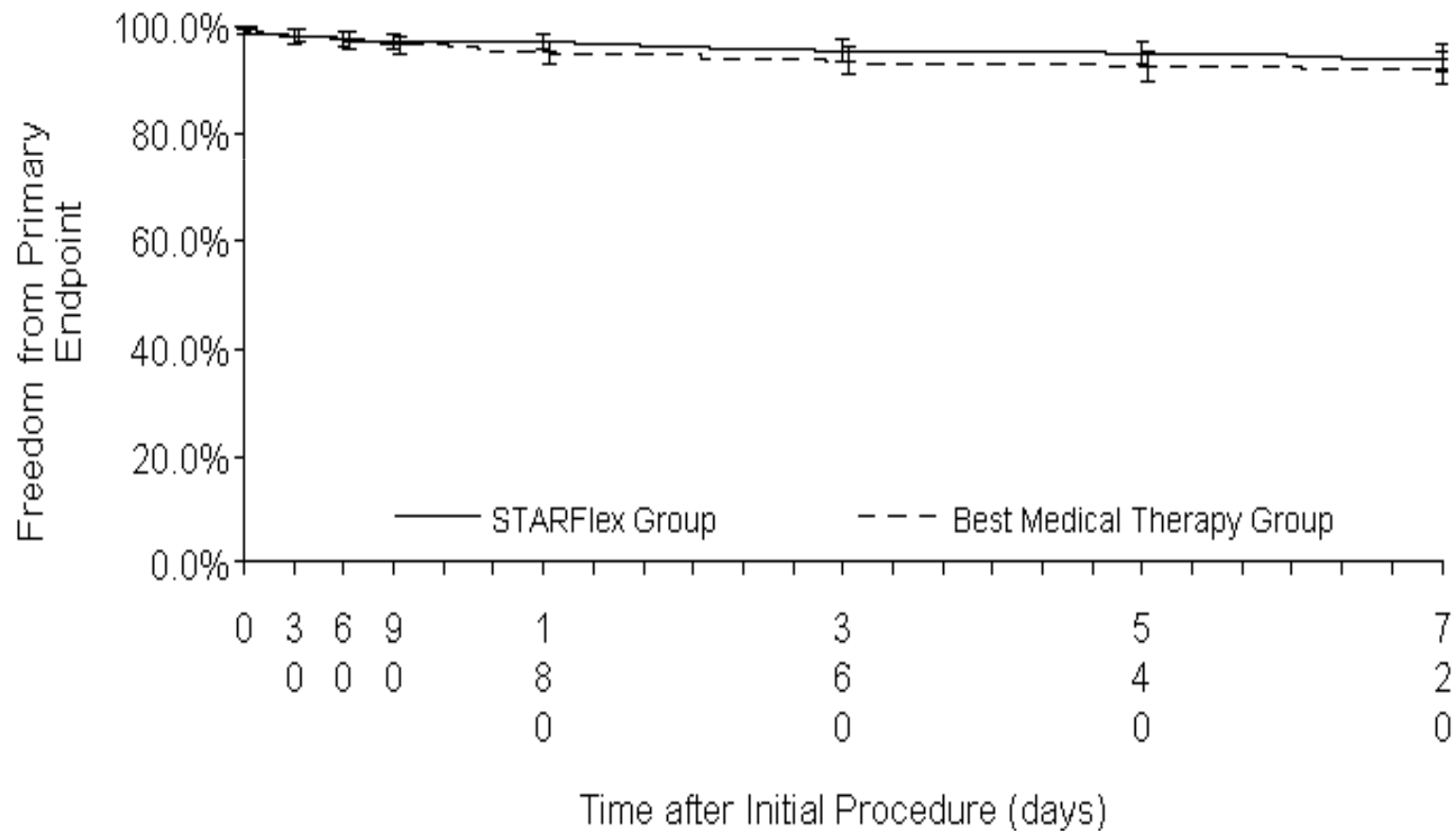


Randomization



Between June 2003 and October 2008, 909 patients randomized at 87 sites in the US and Canada. Block randomization with stratification by study site and by the presence or absence of an ASA viewed by TEE.

Kaplan-Meier for Primary Endpoint ITT



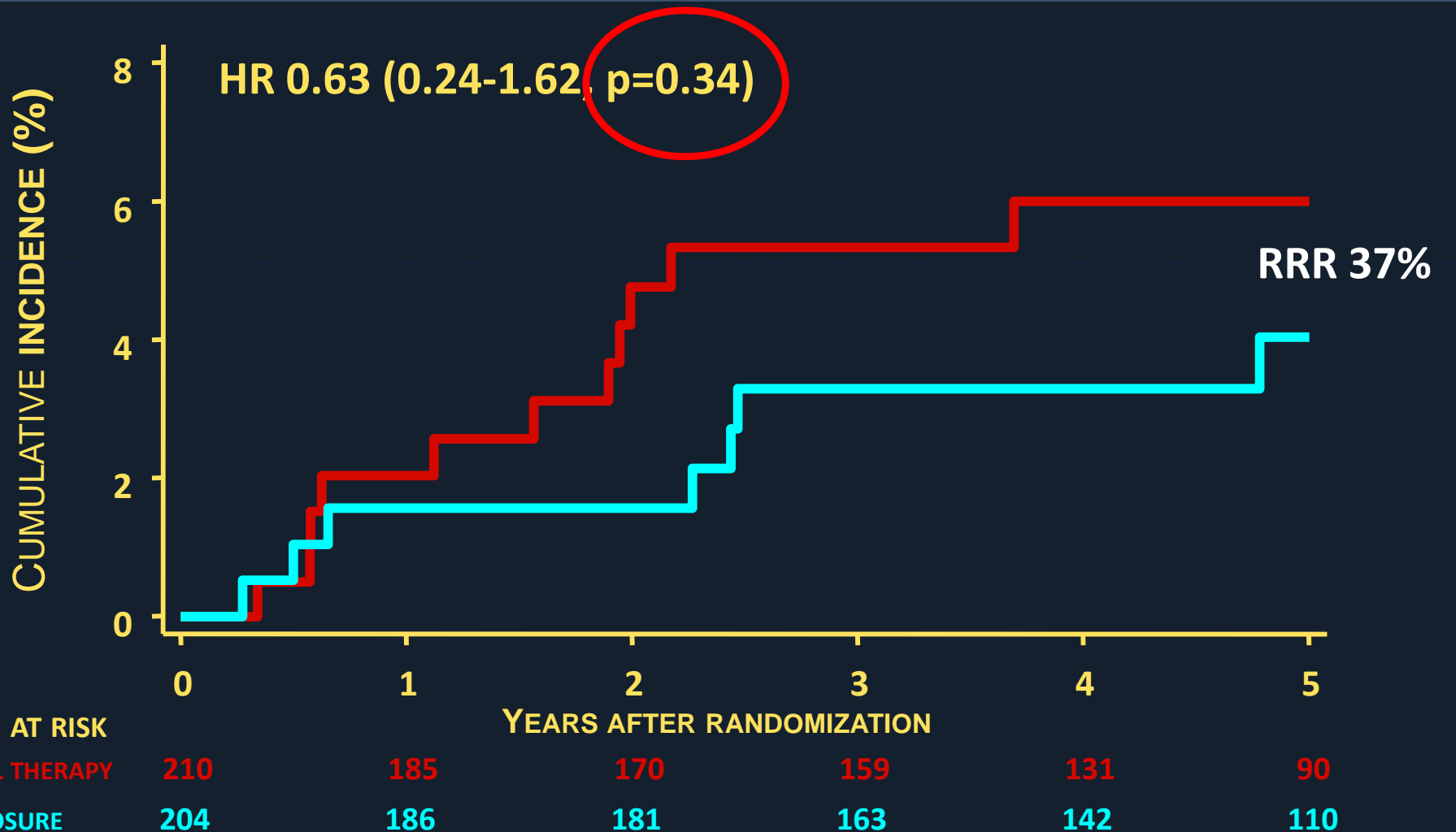
PERCUTANEOUS CLOSURE OF
PATENT FORAMEN OVALE
VERSUS MEDICAL TREATMENT IN
PATIENTS WITH CRYPTOGENIC EMBOLISM:
THE PC TRIAL

NCT00166257

*Bernhard Meier, Bindu Kalesan, Ahmed A. Khattab,
David Hildick-Smith, Dariusz Dudek, Grethe Andersen,
Reda Ibrahim, Gerhard Schuler, Antony S. Walton,
Andreas Wahl, Stephan Windecker, Heinrich P. Mattle,
and Peter Jüni*

PRIMARY COMPOSITE ENDPOINT

*DEATH FROM ANY CAUSE, NON-FATAL STROKE,
TIA AND PERIPHERAL EMBOLISM*



PERCUTANEOUS CLOSURE OF
PATENT FORAMEN OVALE
VERSUS MEDICAL TREATMENT IN
PATIENTS WITH CRYPTOGENIC EMBOLISM:

THE
NEGATIVE
PC TRIAL

NCT00166257

***Bernhard Meier**, Bindu Kalesan, Ahmed A. Khattab,
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The Final Results with Primary End Point Analyses



RESPECT

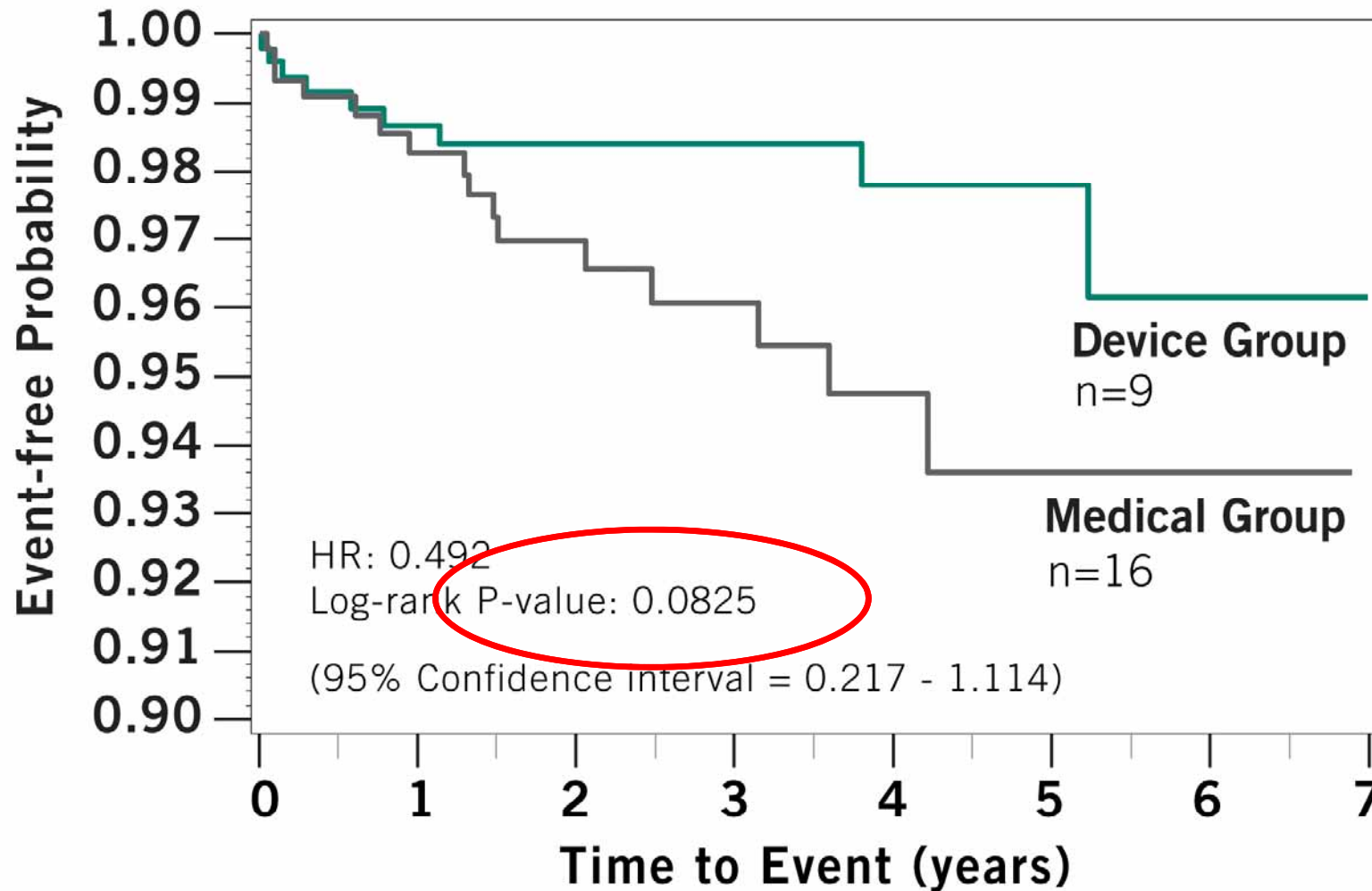
CLINICAL TRIAL

RANDOMIZED EVALUATION OF RECURRENT STROKE
COMPARING PF_O CLOSURE TO ESTABLISHED CURRENT
STANDARD OF CARE TR_EATMENT

JOHN D. CARROLL, MD, JEFFREY L. SAVER, MD, DAVID E. THALER, MD, PHD,
RICHARD W. SMALLING, MD, PHD, SCOTT BERRY, PHD, LEE A. MACDONALD, MD,
DAVID S. MARKS, MD, MBA, DAVID L. TIRSCHWELL, MD
FOR THE RESPECT INVESTIGATORS

Primary Endpoint Analysis – ITT Cohort

50.8% risk reduction of stroke in favor of device



- **3/9** device group patients did not have a device at time of endpoint stroke

3 Negative Randomized Trials



Still No Closure on the Question of PFO Closure

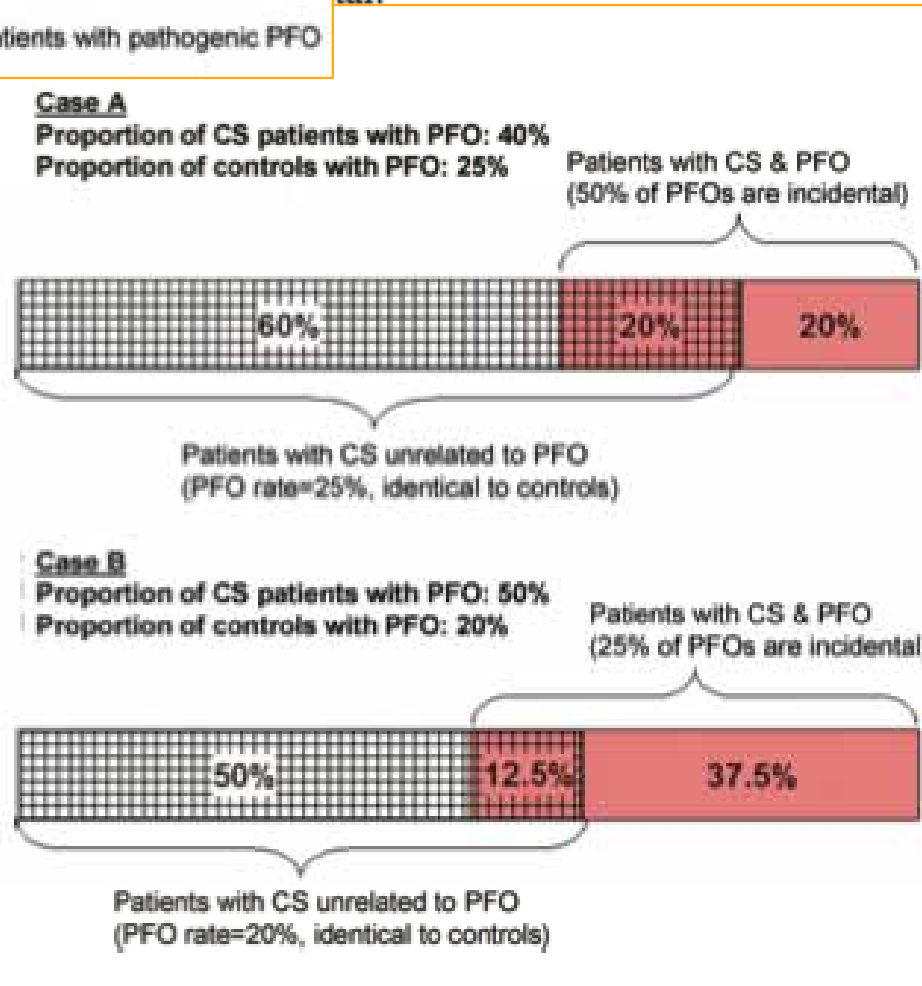
- failure of trials to show superiority of closure over medical therapy
- enormous potential for overuse of percutaneous closure
- low risk of stroke in patients who are treated medically
- routine use of this therapy seems unwise without a clearer view of who, if anyone, is likely to benefit

PFO in Cryptogenic Stroke Incidental or Pathogenic?

- Patients without PFO
- ▨ Patients with incidental PFO
- Patients with pathogenic PFO

Patent foramen ovale (PFO) is significantly associated with cryptogenic stroke (CS). However, a PFO can be an incidental finding. We sought to estimate the probability that a PFO in a patient with CS is incidental.

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examining the prevalence of PFO in patients with CS. Under simple assumptions and Bayes' theorem, we calculated the effects meta-analyses estimated the odds ratio (OR) of a PFO with or without atrial septal aneurysms, and were used to estimate the probability that a PFO in a patient with CS is incidental.

The corresponding OR for control subjects was 2.9 (CI, 2.1 to 4.0). The corresponding OR for patients with CS was 3.3 (3.3 to 7.8) and 2.0 (>1.0 to 3.7), respectively. The proportion of incidental PFOs were 33% (28% to 39%) in age-inclusive studies, and 33% in older patients. These probabilities were much lower than those in younger patients.

One-third of discovered PFOs are likely to be incidental and hence not benefit from closure. Patient characteristics such as age and the presence of atrial septal aneurysms are important in selection in therapeutic decision-making. (*Stroke. 2009;*

approximately one third of PFOs are likely to be incidental and hence not benefit from closure

The GORE REDUCE Clinical Study

- Patient has presence of cryptogenic, ischemic stroke or transient ischemic attack (TIA) with MRI (or CT) evidence of a presumably embolic infarction verified by a neurologist within 180 days prior to randomization
- 2:1 randomization
- Antiplatelet regimens for **all subjects**:
 - Aspirin alone or
 - Aggrenox or generic equivalent (aspirin and dipyridamole) or
 - Clopidogrel (Plavix®)
- Warfarin NOT allowed after randomization

World's Most Accurate Chart



- Pie I have eaten
- Pie I have not yet eaten

The way to a man's head is through his heart.

