

The Aggressive Case for PFO Closure after Cryptogenic Stroke

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**Conflicts of interest:
Research grants and speaker fees
from St. Jude - AGA**

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All PFOs

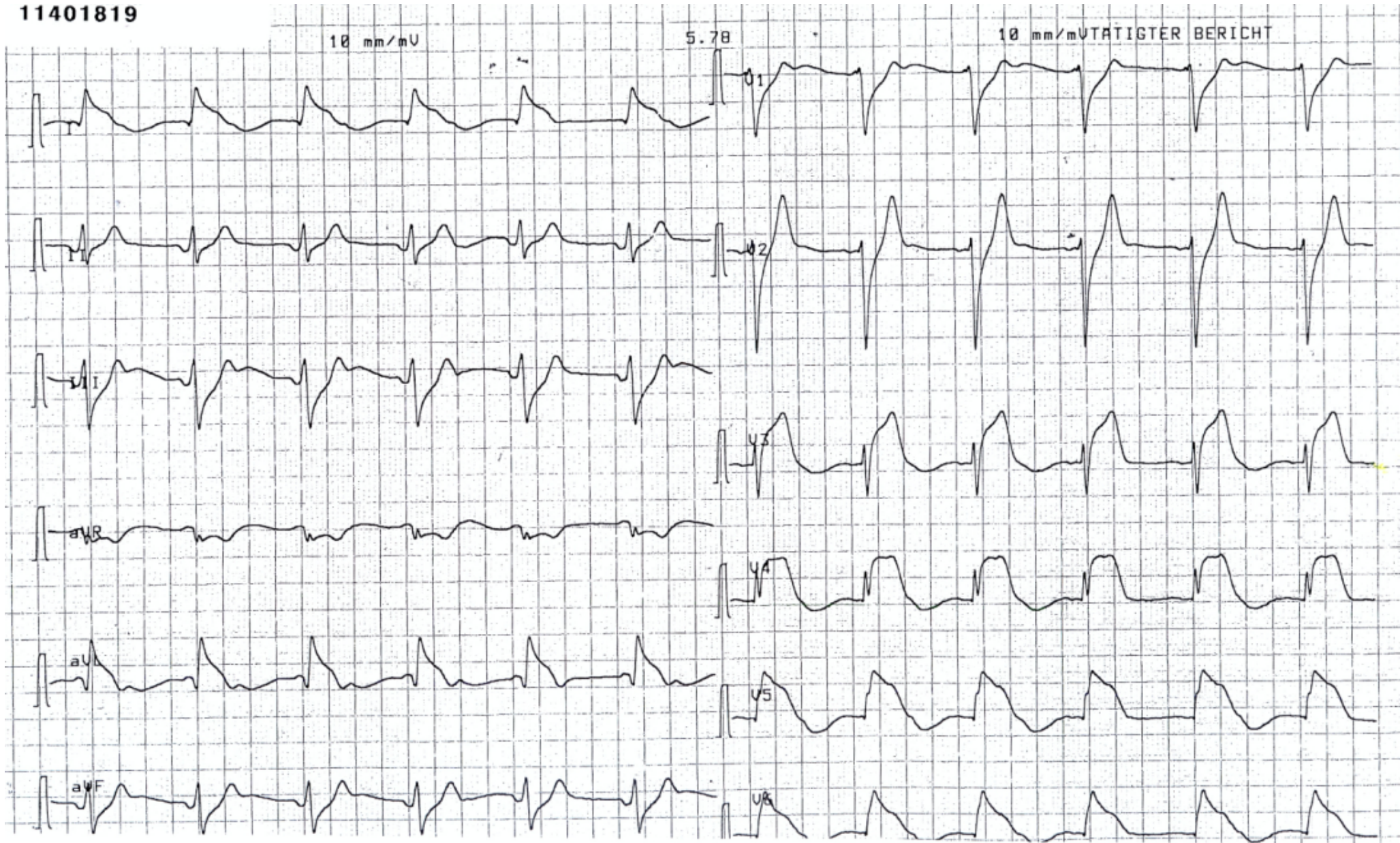
Should Be

Closed!

PFO-Death in Healthy 34-Year-Old Man, 1 Day after a Soccer Bruise to the Thigh

Sudden collapse: cardiogenic shock --> catheterization under cardiac massage Pilgrim T, J Invasive Cardiol 25:162-164, 2013

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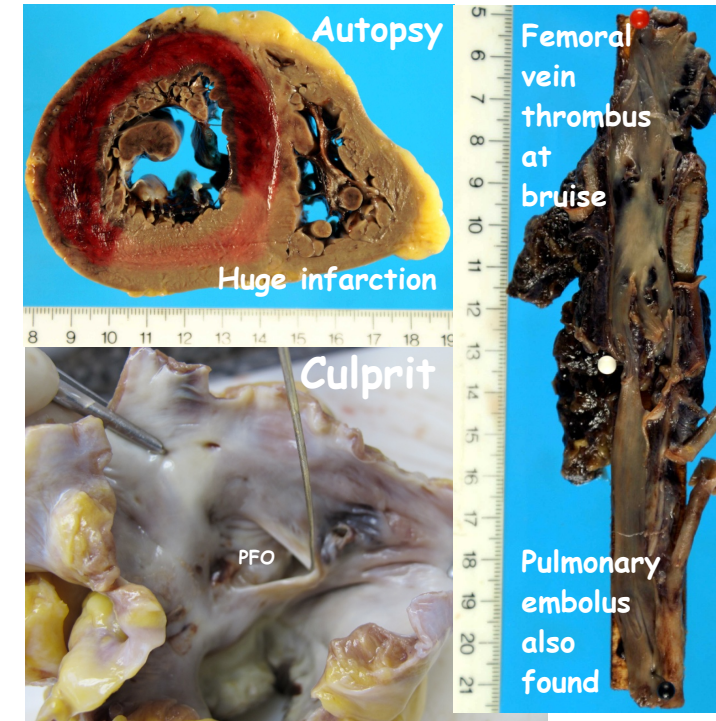
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TandemHeart stopped the next day due to brain death

Post PCI with TandemHeart

- Good flow
- No LV function

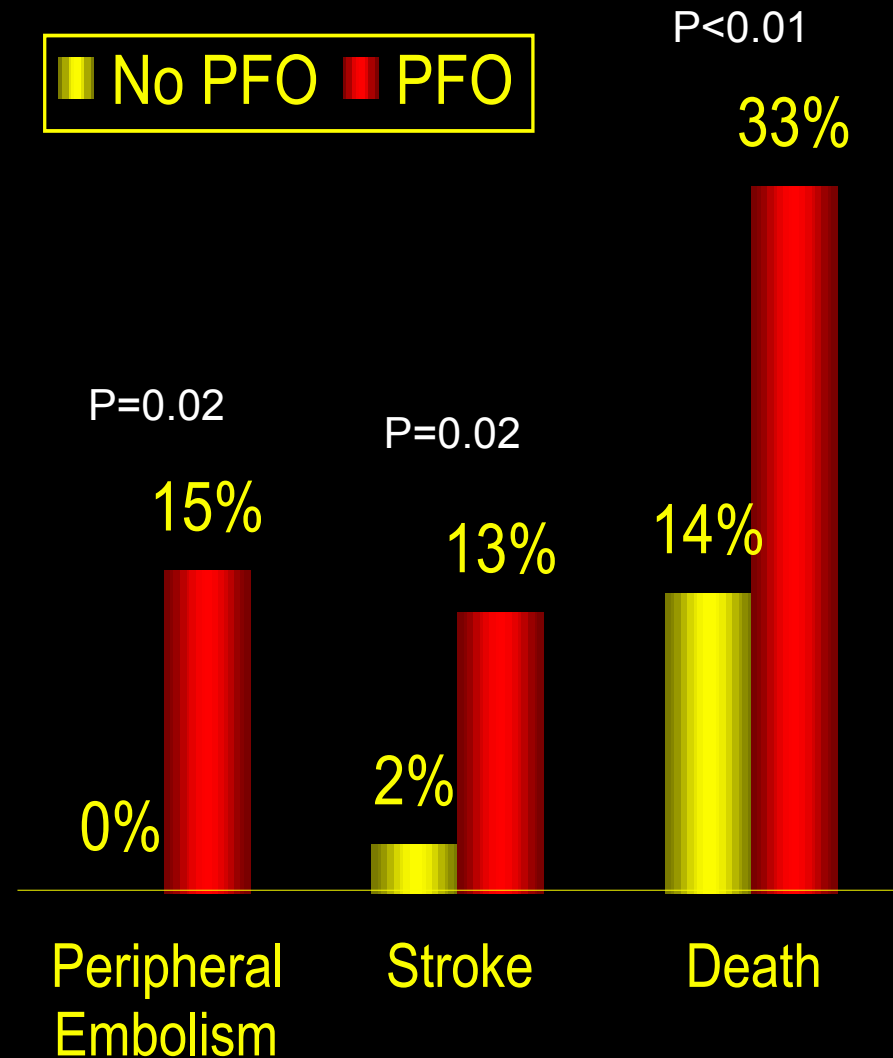


PFO as Predictor of Adverse Outcome in Patients With Major Pulmonary Embolism

Konstantinides S et al. *Circulation* 1998;97:1946

- 139 patients with major pulmonary embolism undergoing TEE
 - 35% with PFO
 - 59±17 (17 - 89) years
- Clinical endpoints
 - death
 - cerebral embolism
 - arterial thrombo-embolism
 - major bleeding

- PFO: independent predictor of mortality
- Suggested mechanism: paradoxical embolism



Venous Thromboembolism (VTE) and Stroke/MI

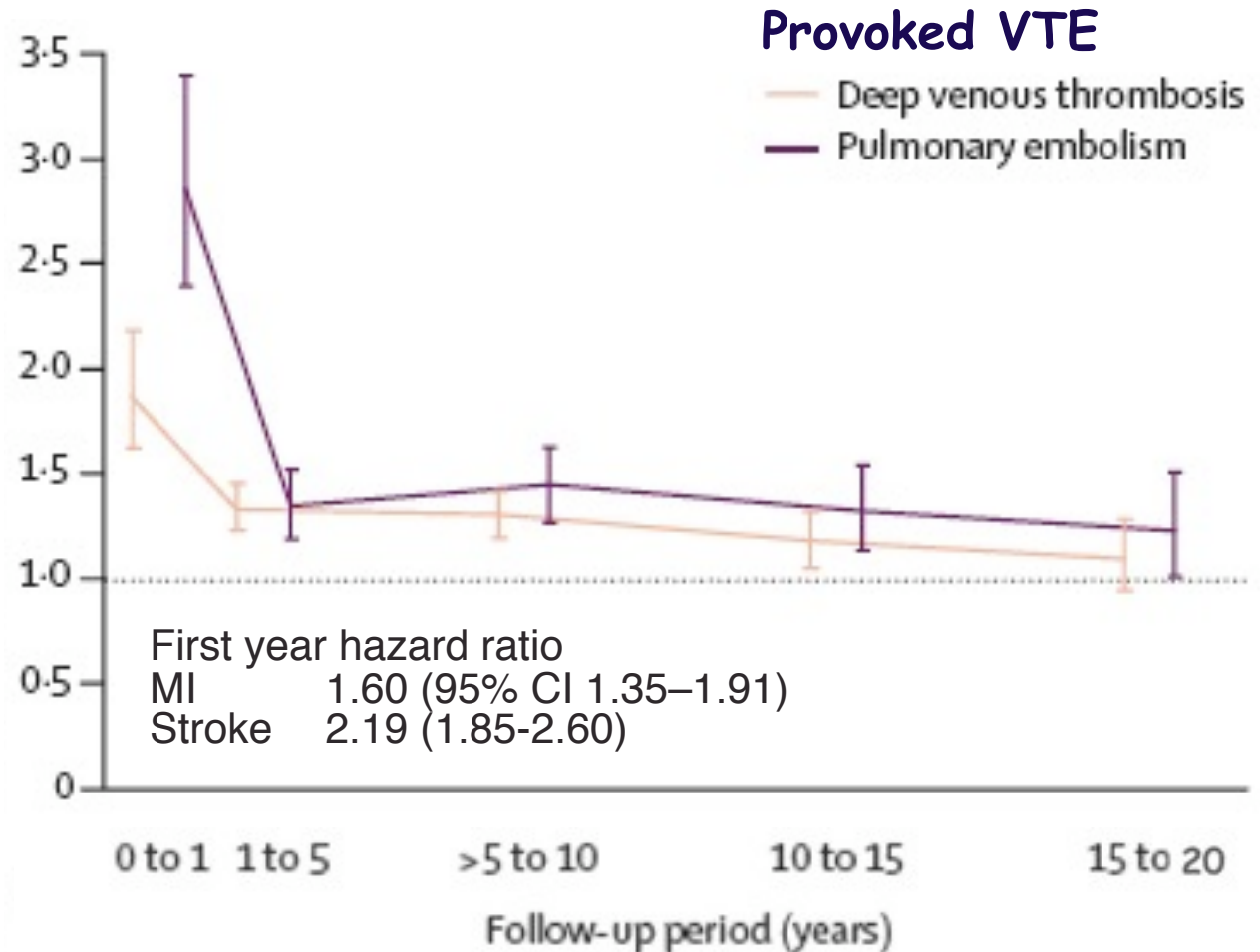
- 20-year population-based cohort study
- Danish medical databases
- No known cardiovascular disease
- 25 199 patients with deep venous thrombosis
- 16 925 patients with pulmonary embolism
- 163 566 population controls

No consideration of PFO !!

Paper
Sørensen HT, Lancet 2007; 370: 1773–9
(Denmark, Italy, US)

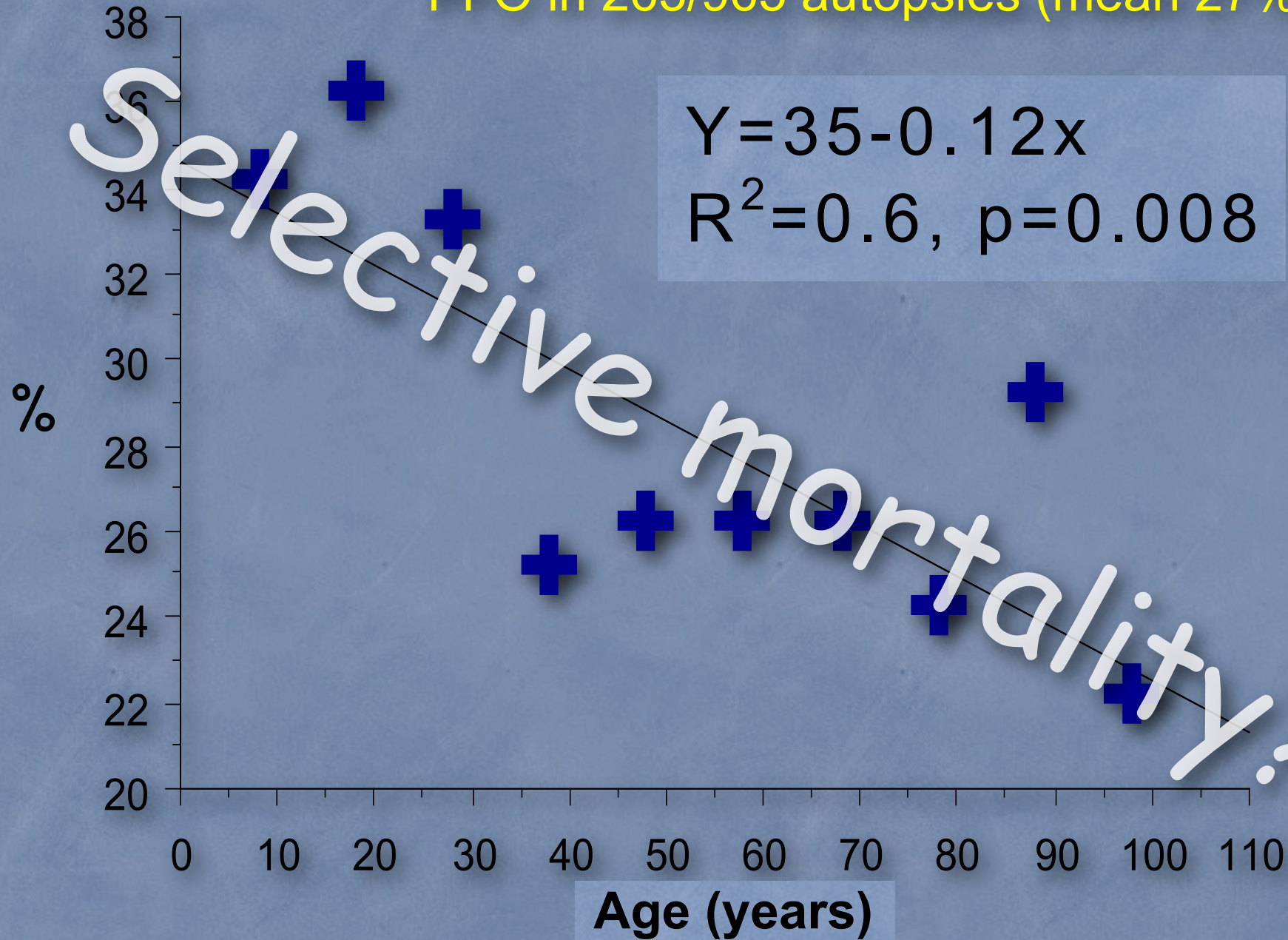
Editorial
Lowe GDO, Lancet 2007; 370: 1743-4
(Glasgow)

Relative Risk of MI or Stroke



Prevalence of PFO According to Age

PFO in 263/965 autopsies (mean 27%)



PFO and Migraine

MIST Serious Adverse Events

74 patients

implant group

tamponade

pericardial effusion

retroperitoneal bleed

atrial fibrillation

chest pain

73 patients

sham group

incision site bleed

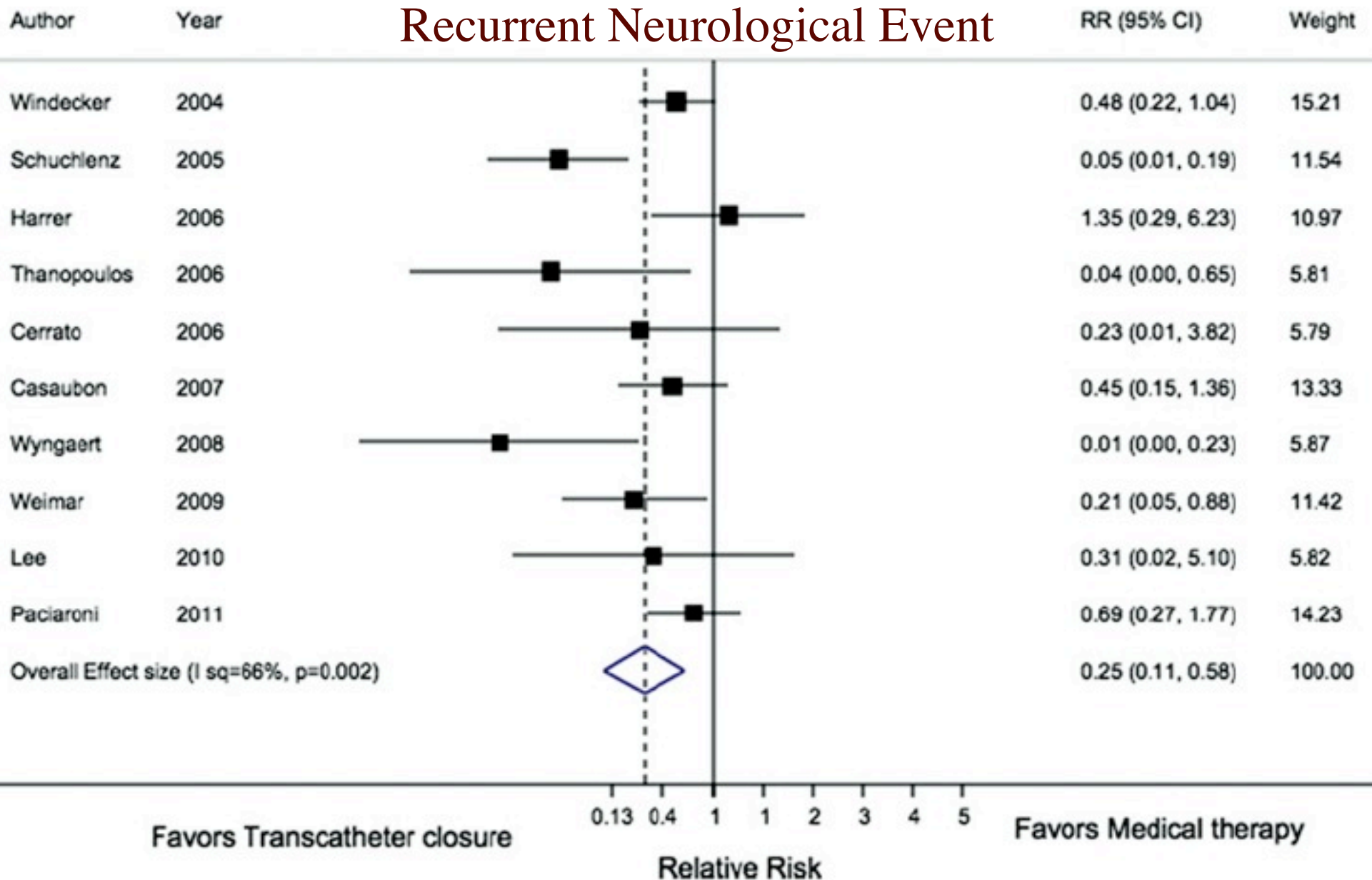
anemia

nose bleed

brainstem stroke

PFO Closure Versus Medical Treatment for Stroke Prevention Meta-Analysis

Recurrent Neurological Event



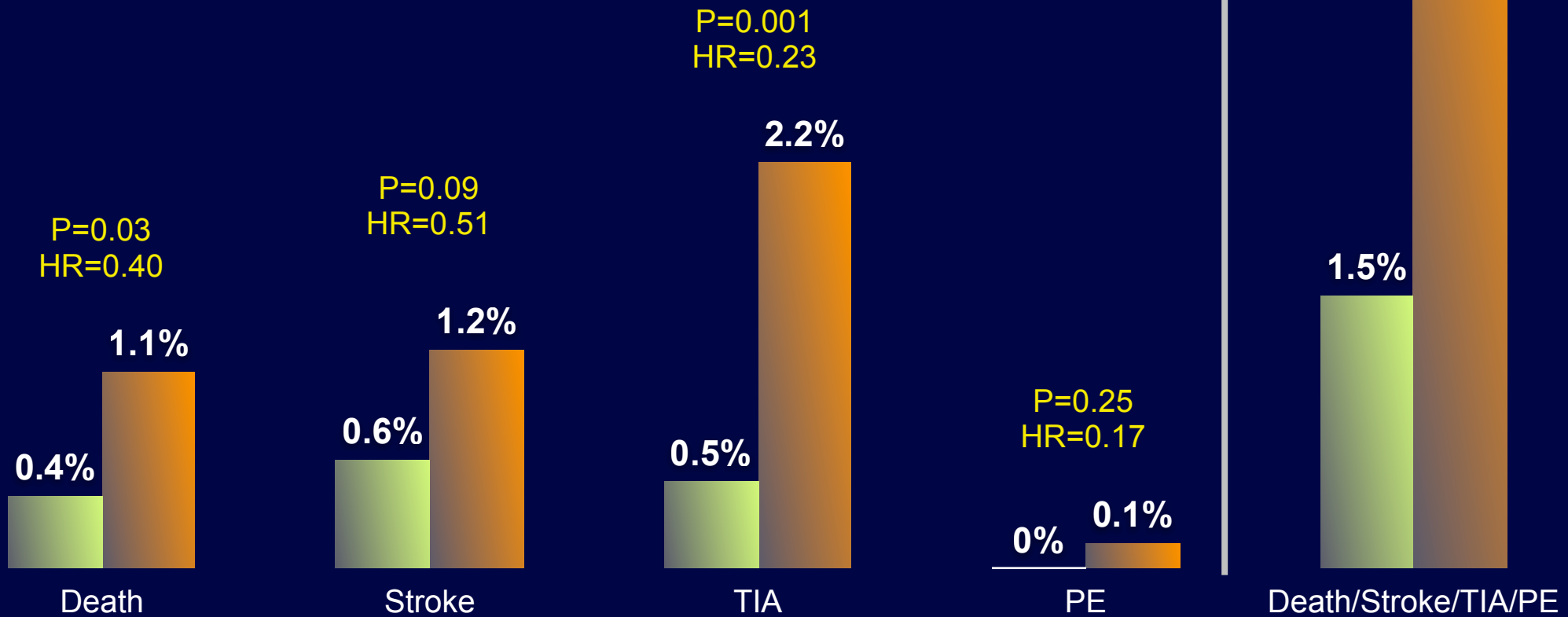
Event Rates per Year

P<0.001
HR=0.34

308 **PFO** patients after index event
10-year median follow-up

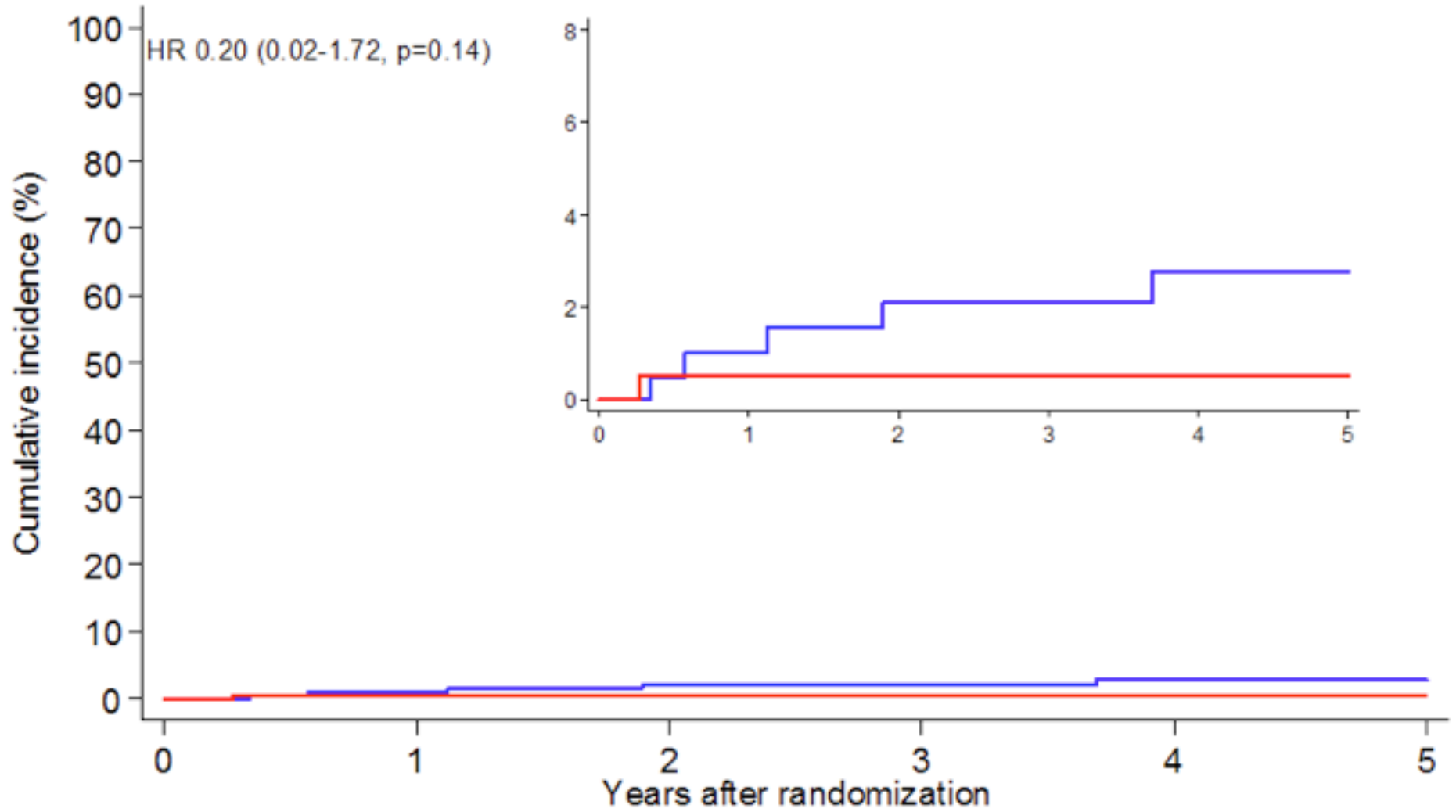
After Closure
(1,872 patient-years)

Without/Before Closure
(1,394 patient-years)



TIA: Transient Ischemic Attack, PE: Peripheral Embolism

Stroke

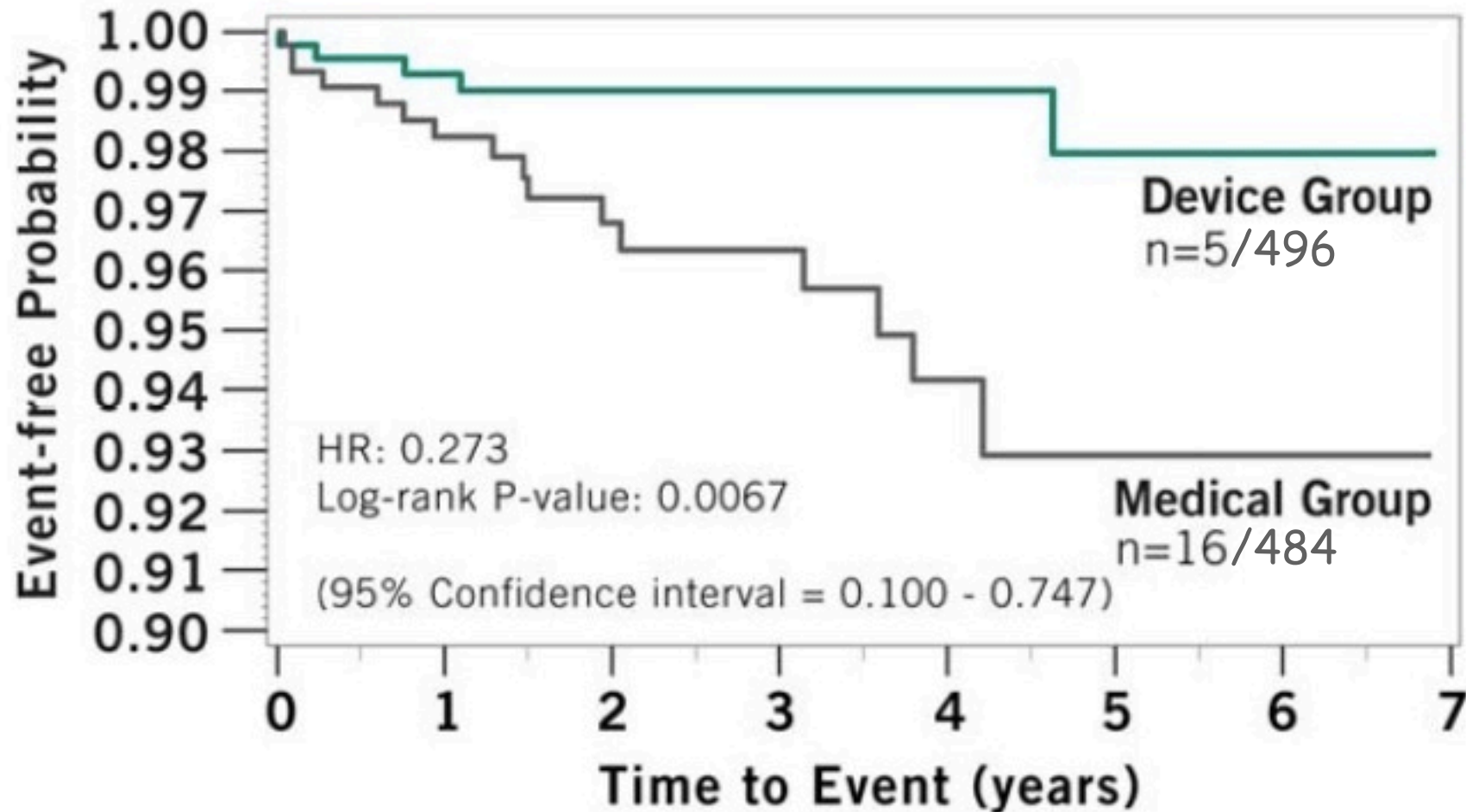


No. at risk

Medical therapy	210	187	175	164	134	92
PFO Closure	204	188	183	167	146	112

Primary Endpoint Analysis – As Treated Cohort

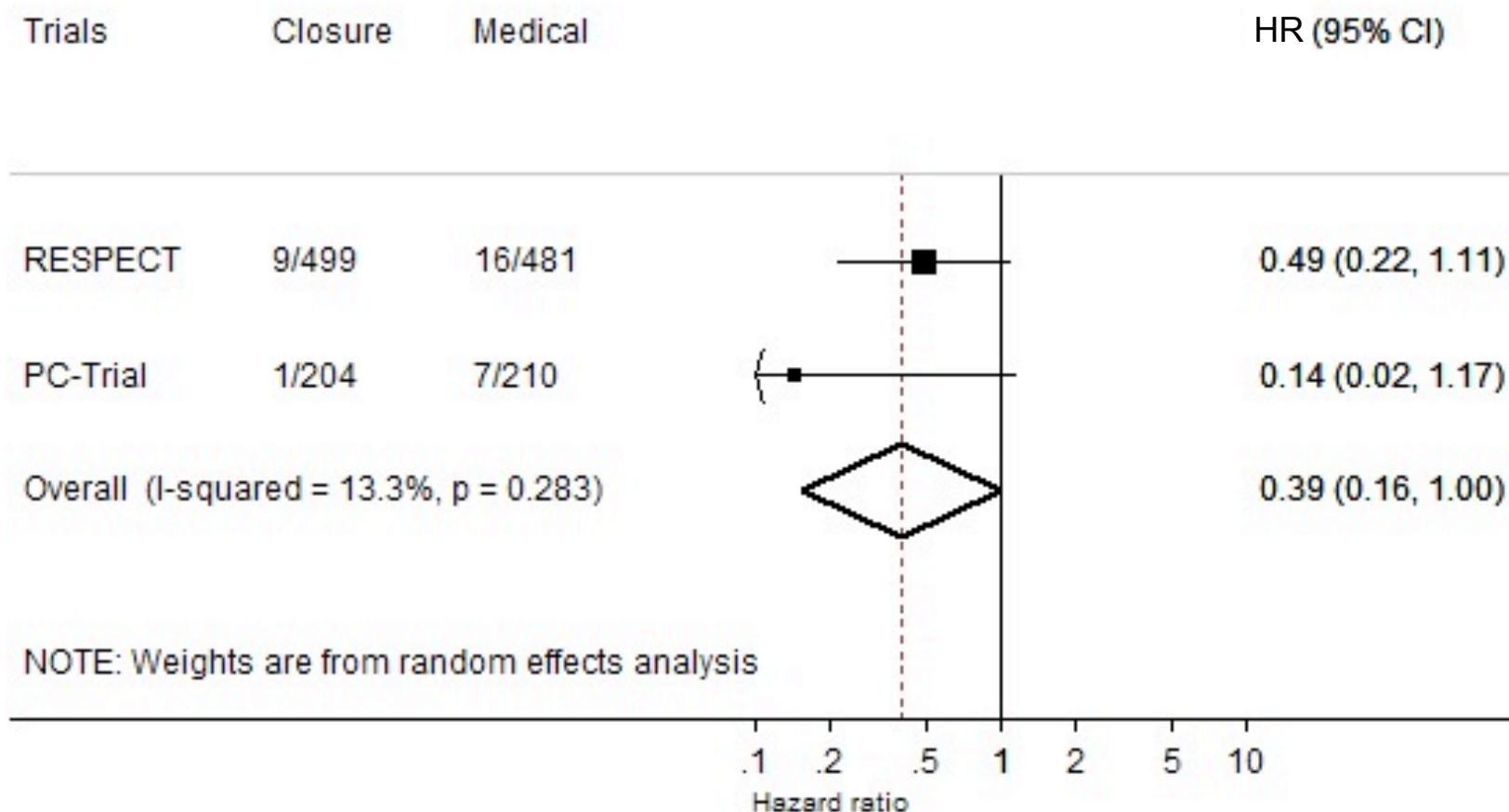
72.7% risk reduction of stroke in favor of device



- The As Treated (AT) cohort demonstrates the treatment effect by classifying subjects into treatment groups according to the treatment actually received, regardless of the randomization assignment

PFO CLOSURE **VERSUS** MEDICAL THERAPY PC **AND** RESPECT **TRIALS**

STROKE



Closure of Patent Foramen Ovale (PFO) for Cryptogenic Cerebral Embolism

Randomized Trials

Acronym	Place	Device	Patients	Status
• CLOSURE I	US	STARFlex	910/800	published ¹ (2012)
• PC	global	Amplatzer	414	published ² (2013)
• RESPECT	US	Amplatzer	980*	published ³ (2013)
• CLOSE	France	Multiple	??*/900	recruiting (2012)
• DEFENCE-PFO	South Korea	Amplatzer	??*/210	recruiting (2017)
• REDUCE**	global	HELEX	??*/664	recruiting (2018)

*Endpoint driven; **Aspirin permanently in both groups

¹Furlan AJ, N Engl J Med 2012;366:991-9

²Meier B, N Engl J Med 2013;368:1083-91

³Carrol JD, N Engl J Med 2013;368:1092-100

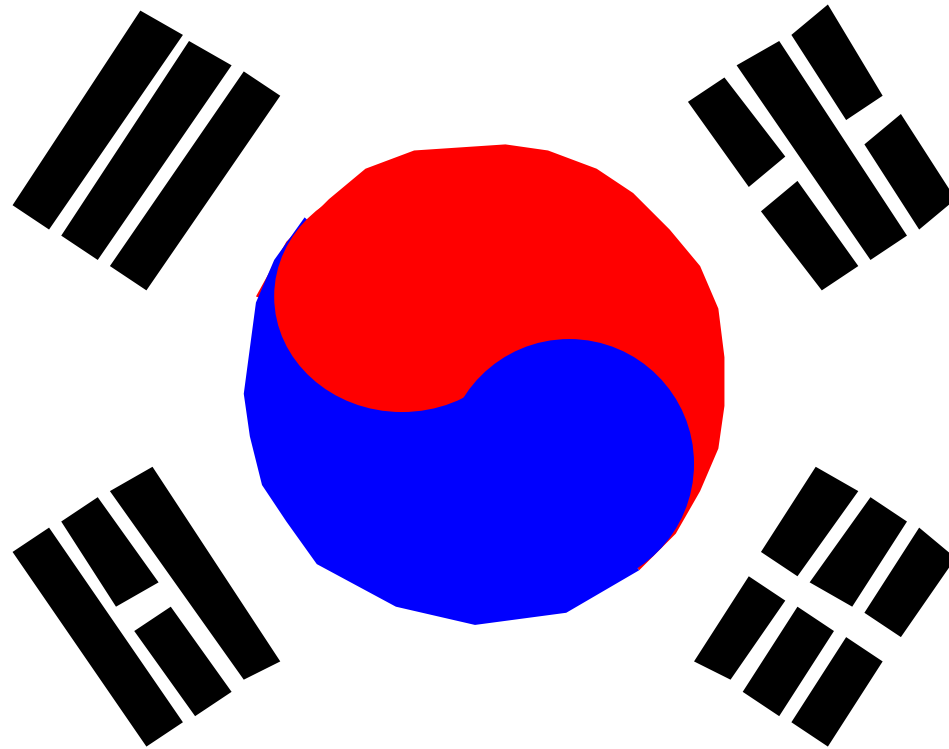
Ongoing Randomized PFO Closure Trials

DEFENSE-PFO (South Korea)

Device Closure Versus Medical Therapy for Secondary Prevention in Cryptogenic Stroke Patients With High-Risk Patent Foramen Ovale

- **Single-blind randomization: Medication (antiplatelet or oral anticoagulation) vs. Amplatzer PFO Occluder**
- **Inclusion criteria**
 - **Cryptogenic stroke within the previous 3 months, radiologically verified**
 - **High-risk PFO (PFO size \geq 2 mm or atrial septal aneurysm or hypermobility by TEE)**
 - **Age: 18 - 80 years**
- **Estimated enrollment: 210**
- **Primary endpoint: Nonfatal stroke / vascular death / TIMI-major bleeding**
- **Study start date: February 2012**
- **Follow-up: \geq 2 years**
- **Estimated completion: February 2017 (Final data collection date for primary outcome measure)**

Potential Indications for PFO Closure (North Korea)



PFO with Severe Atrial Septal Aneurysm or Eustachian Valve

- **3%** of population
 - 1.5 mio to start with
 - 18,000 annual accrual

PFO with Bad Migraine

- **6%** of population
 - 3.0 mio to start with
 - 35,000 annual accrual

PFO

- **25%** of population
 - 12.5 mio to start with
 - 147,000 annual accrual

(Potential) Indications for PFO Closure

- **Secondary prevention**

- Stroke
- Transient ischemic attack
- Embolic myocardial infarction
- Peripheral embolism
- Decompression incident
- High altitude pulmonary edema

- **Primary prevention**

- Aggravating PFO attributes
 - Atrial septal aneurysm
 - Eustachian valve
 - Chiari network
- Prothrombotic state
- Deep vein thrombosis
- Pulmonary embolism
- Pacemaker/defibrillator electrodes
- Embolism-prone surgery
 - Major orthopedic
 - Cerebral in sitting position
- Planned pregnancy
- Carcinoid tumor
- Special congenital situations

- **Therapeutic**

- Migraine (with aura)
- Platypnea orthodeoxia
- Sleep apnea
- Provoked exercise desaturation

- **Vocational or recreational**

- Deep sea diver
- Mountain climber, highlander
- Brass musician
- Glass blower
- Tile setter
- Military jet / acrobat pilot
- Astronaut
- Commercial driver or pilot

