

PFO: to Close or Not to Close

Positive signals to close

Bernhard Meier, MD

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

Swiss Cardiovascular Center Bern
University Hospital
Bern, Switzerland



All PFOs

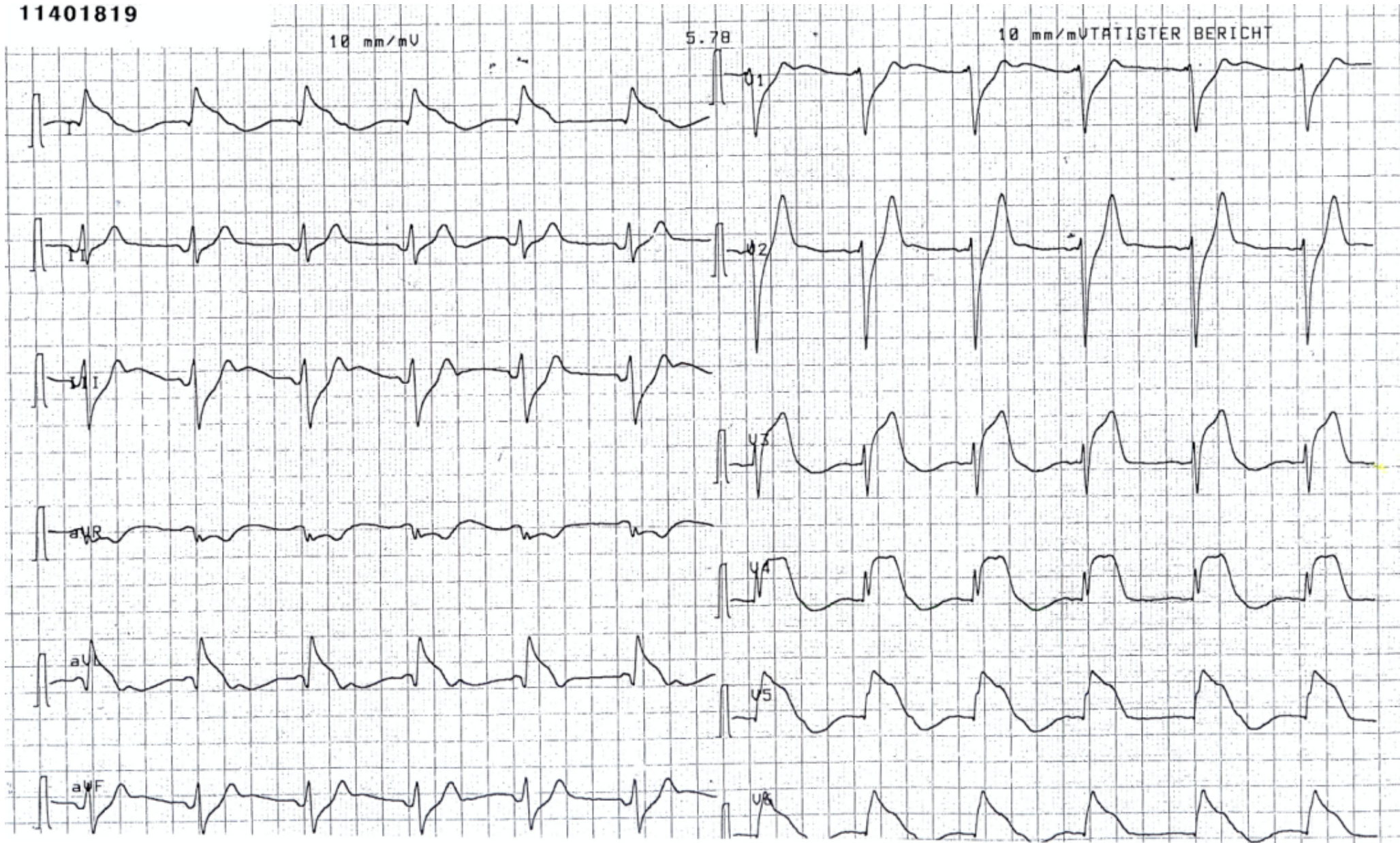
Should Be

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

11401819



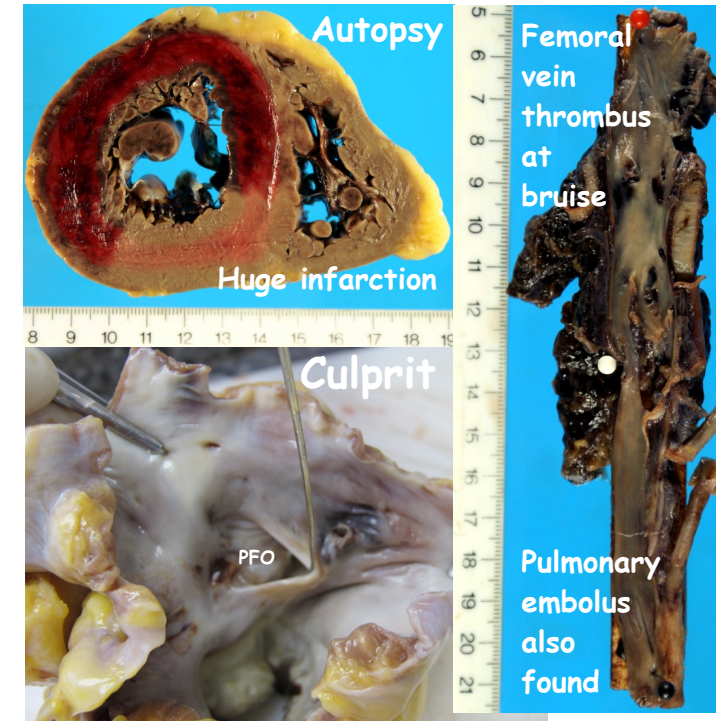
PFO-Death in Healthy 34-Year-Old Man, 1 Day after a Soccer Bruise to the Thigh

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

TandemHeart stopped the next day due to brain death

Post PCI with TandemHeart

- Good flow
- No LV function

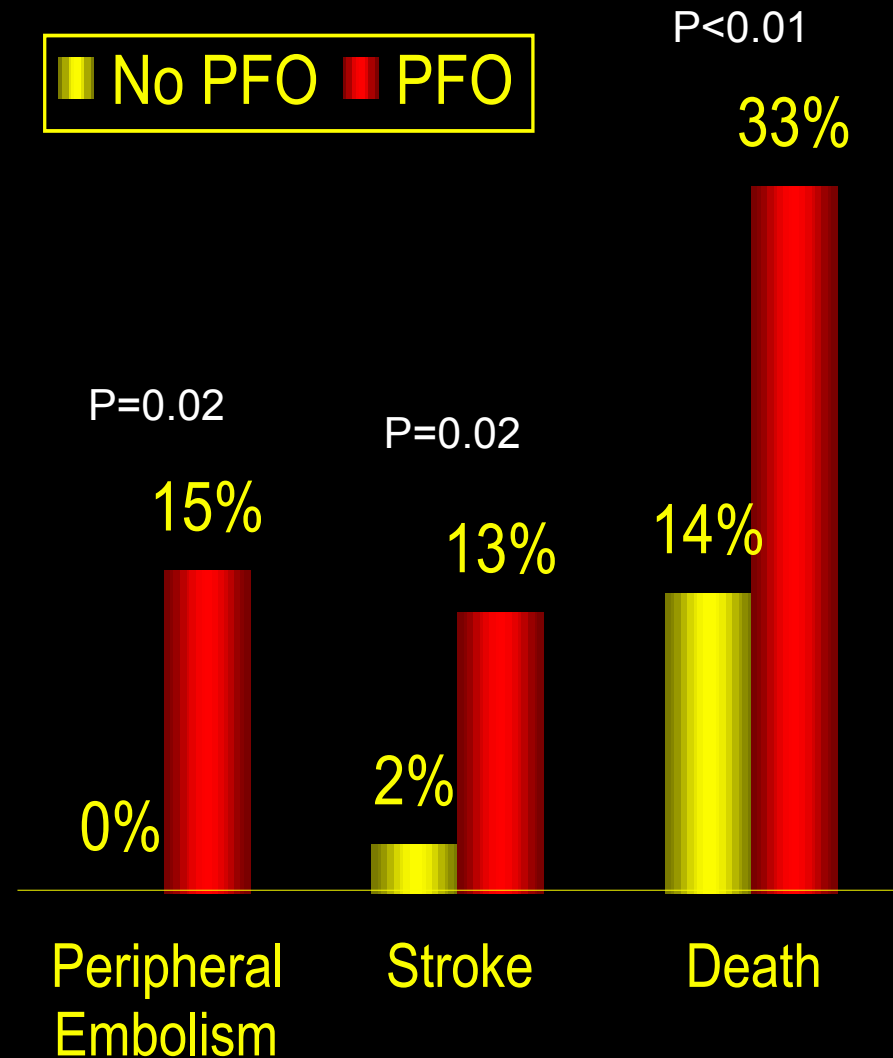


PFO as Predictor of Adverse Outcome in Patients With Major Pulmonary Embolism

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

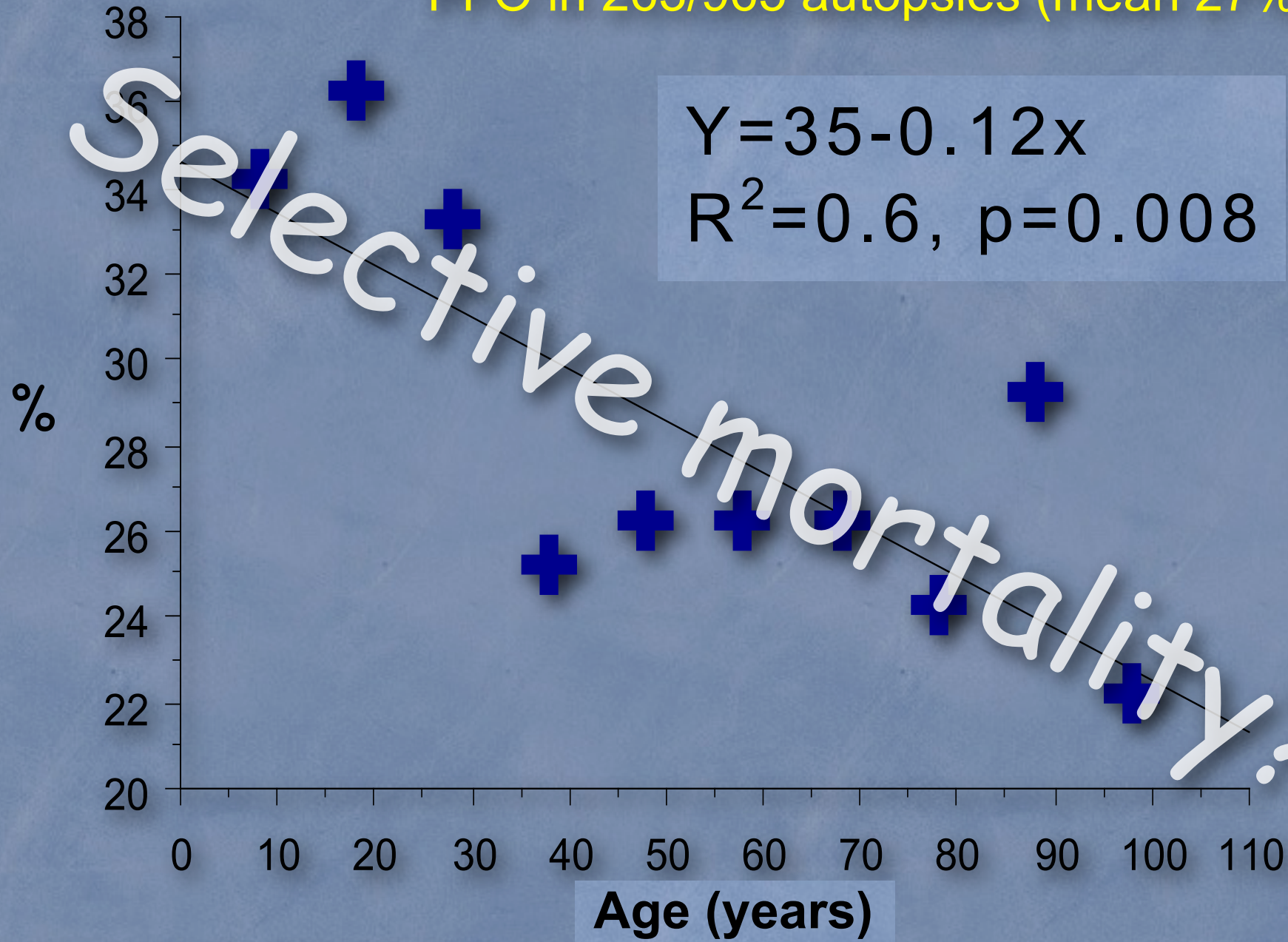
- 139 patients with major pulmonary embolism undergoing TEE
 - 35% with PFO
 - 59±17 (17 - 89) years
- Clinical endpoints
 - death
 - cerebral embolism
 - arterial thrombo-embolism
 - major bleeding

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



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

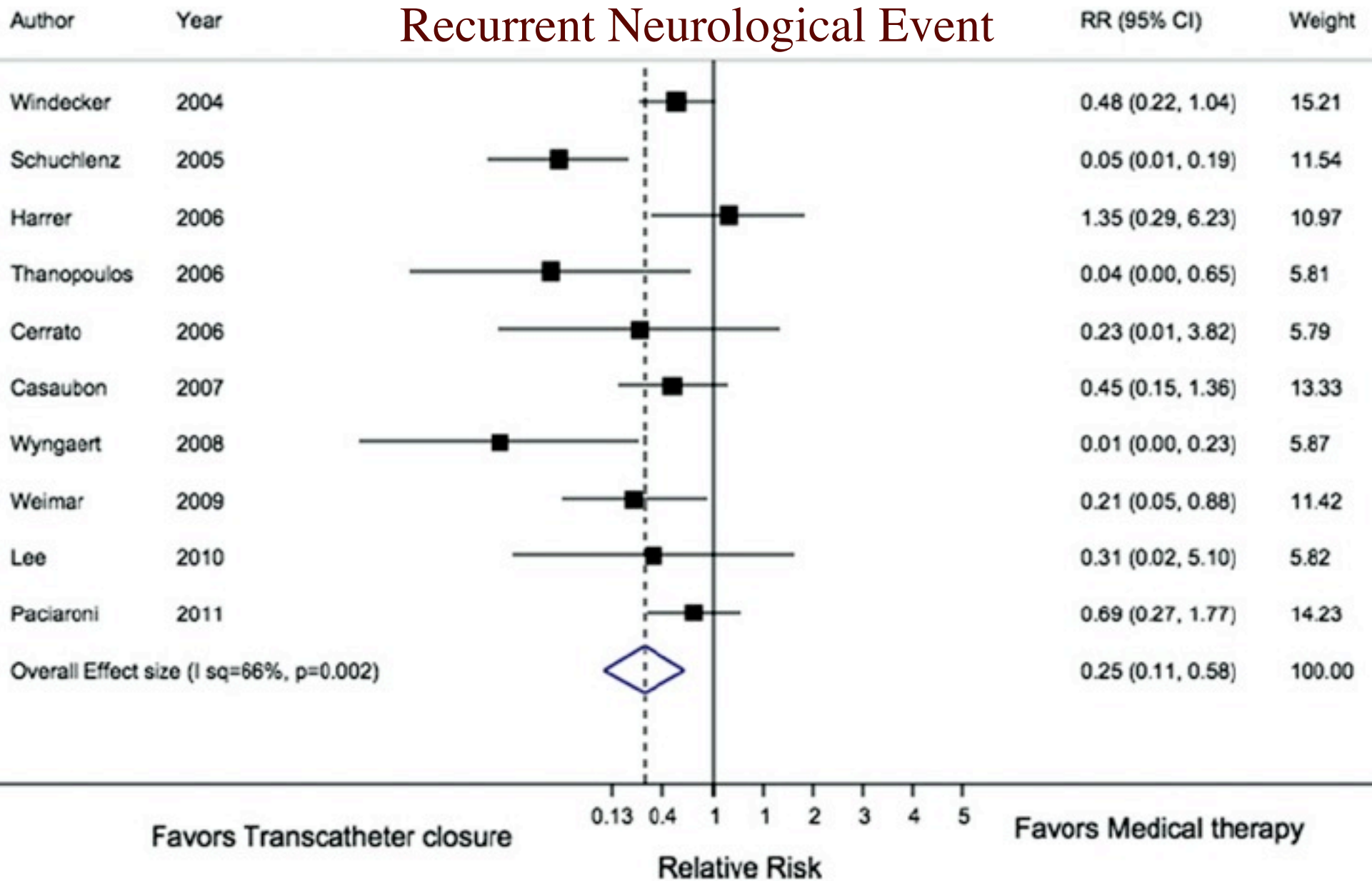
anemia

nose bleed

brainstem stroke

PFO Closure Versus Medical Treatment for Stroke Prevention Meta-Analysis

Recurrent Neurological Event



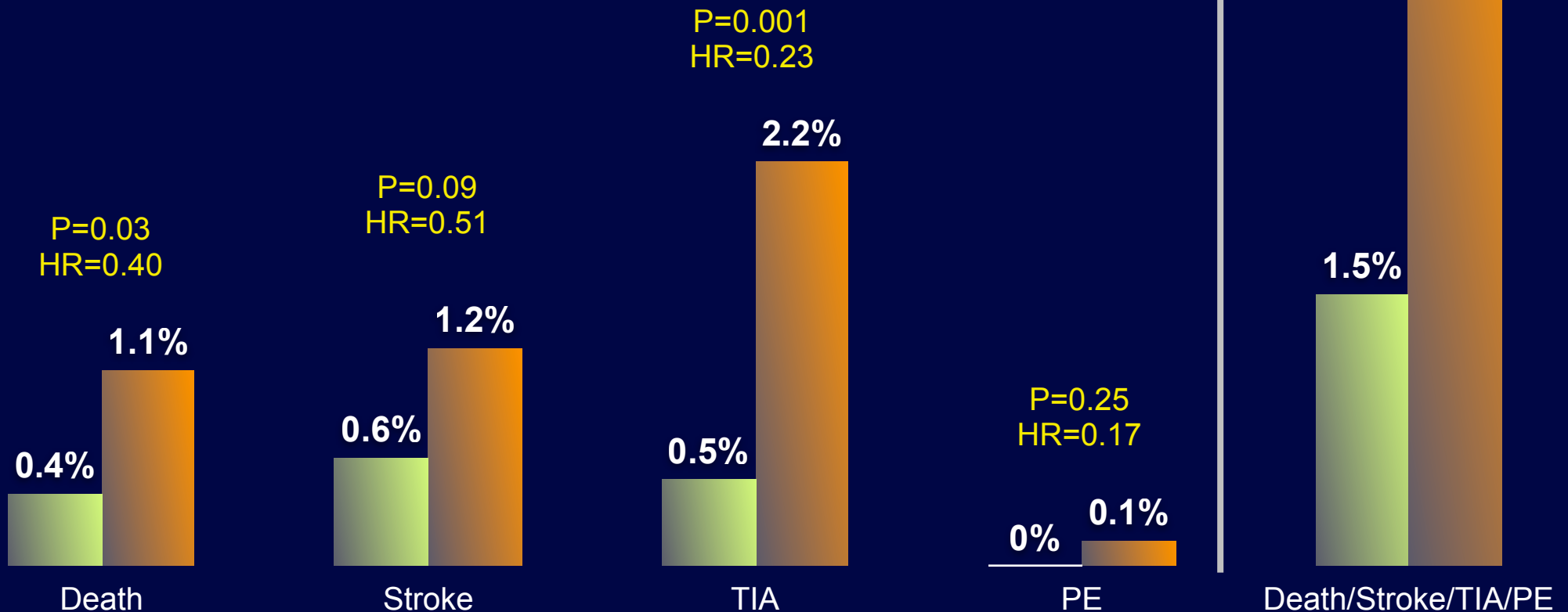
Event Rates per Year

P<0.001
HR=0.34

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

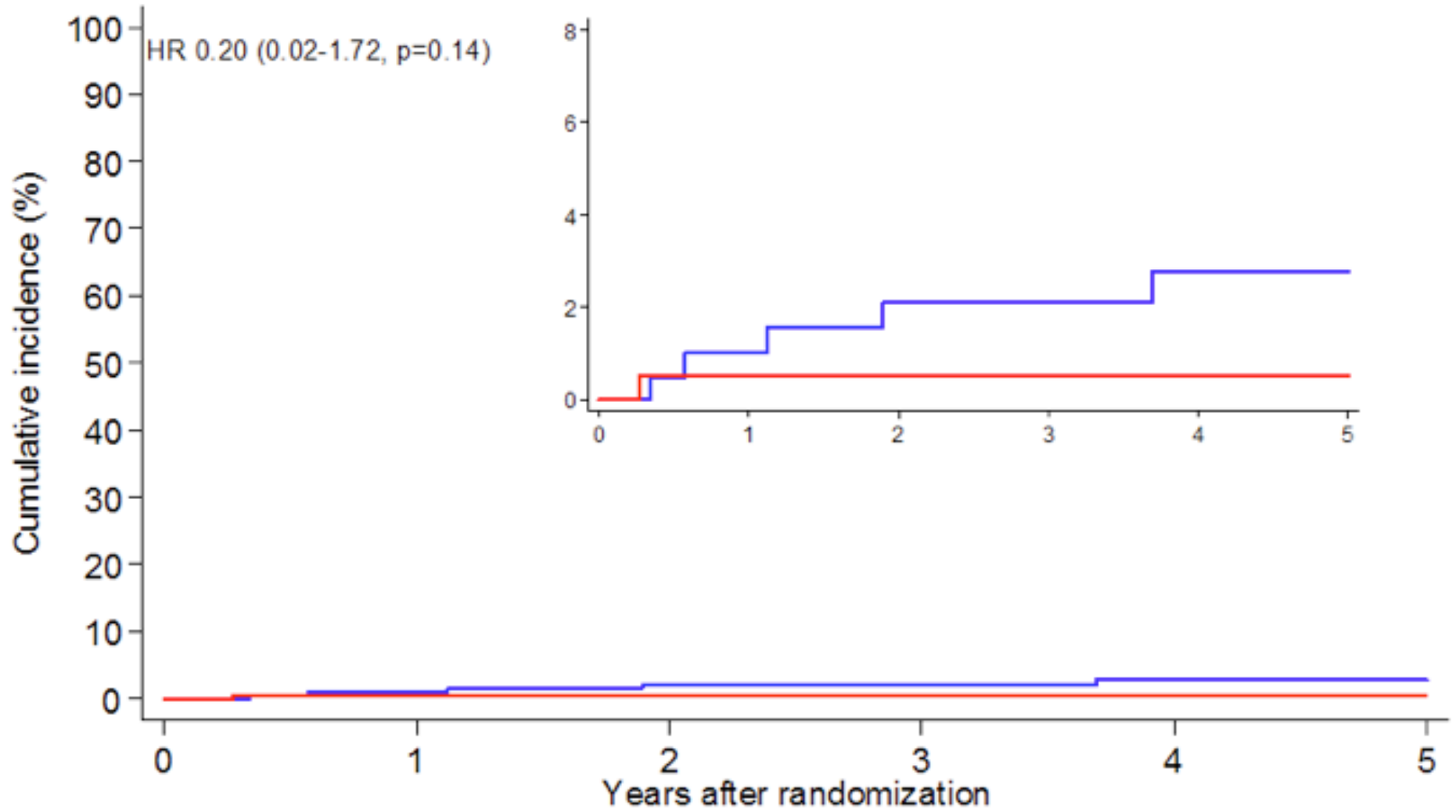
After Closure
(1,872 patient-years)

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



TIA: Transient Ischemic Attack, PE: Peripheral Embolism

Stroke



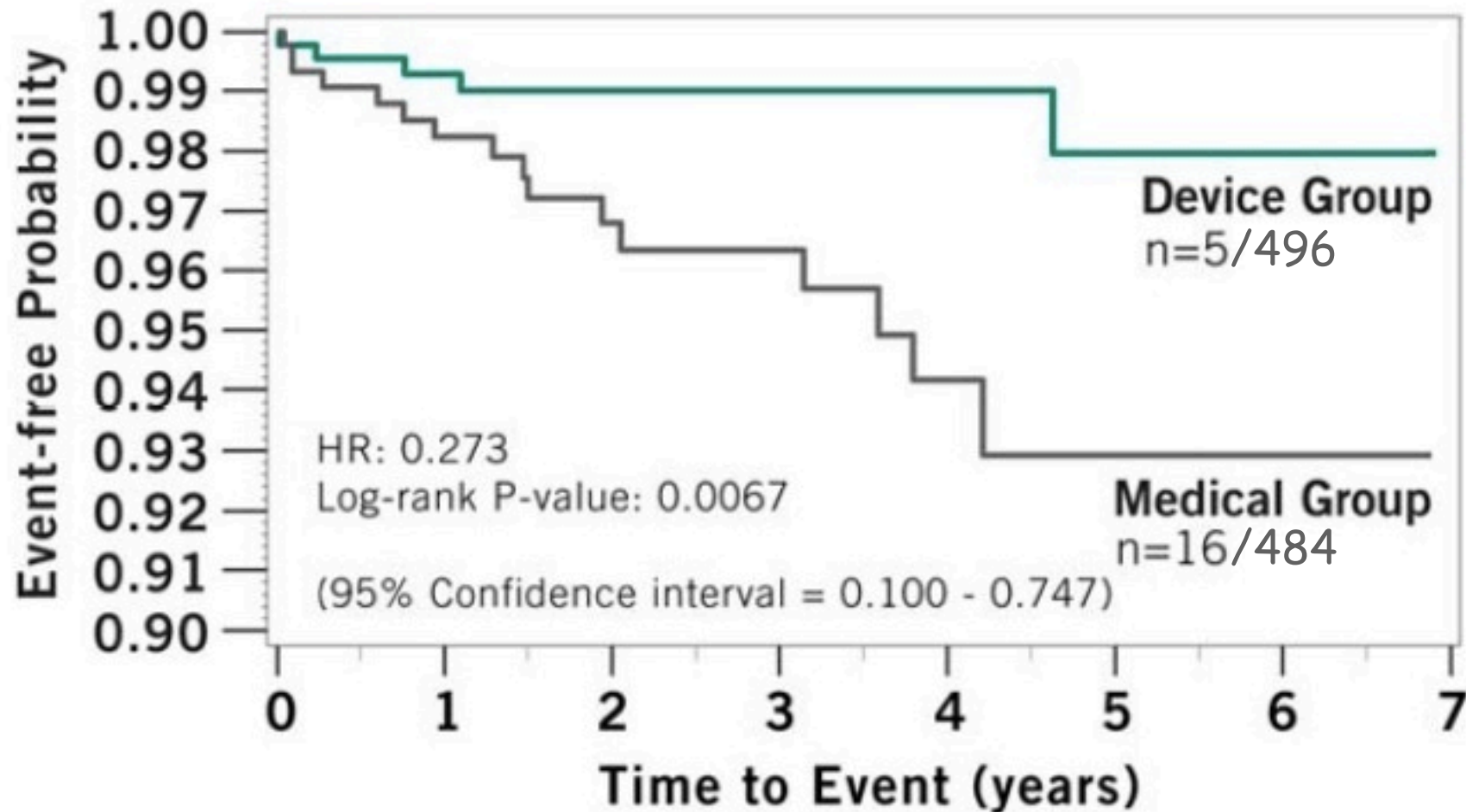
No. at risk

| | | | | | | |
|-----------------|-----|-----|-----|-----|-----|-----|
| 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

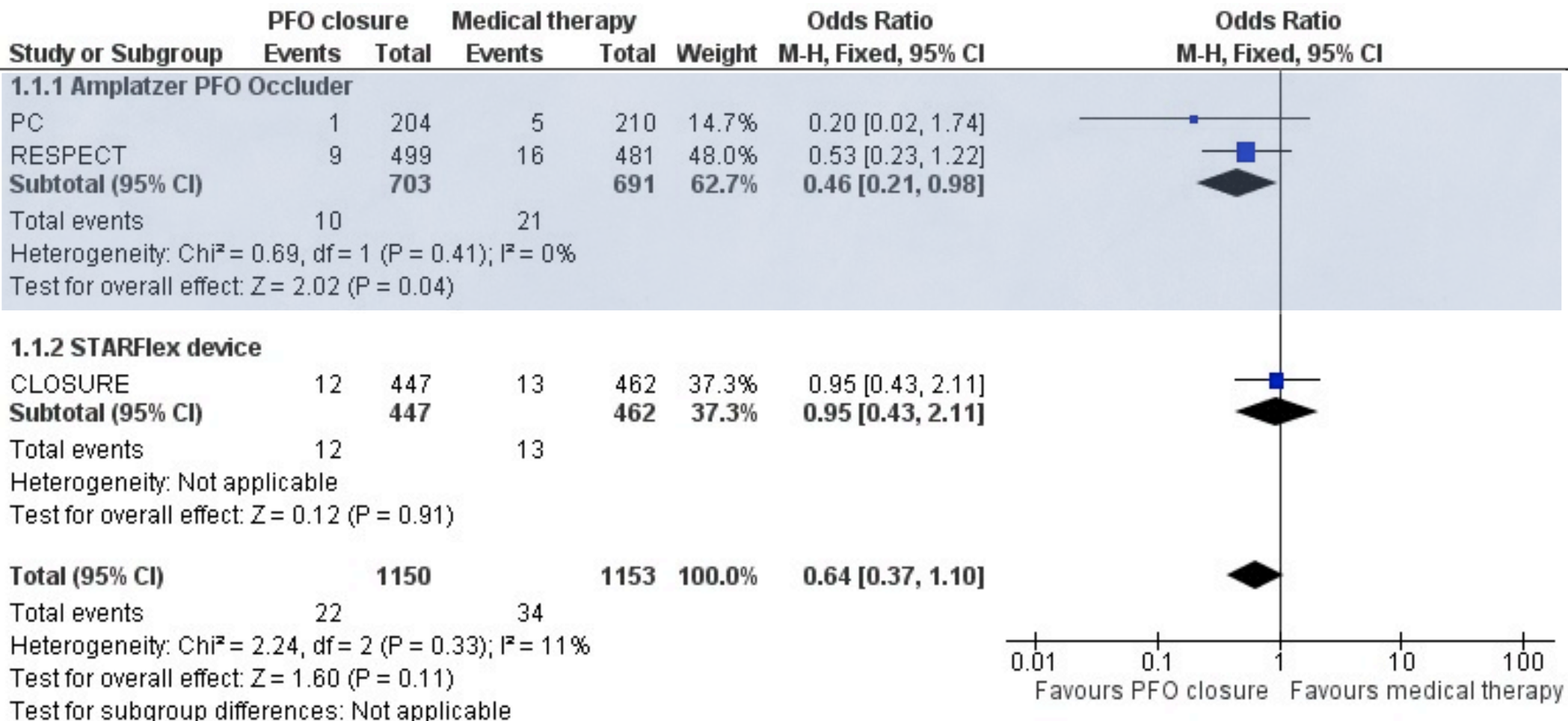


- The As Treated (AT) cohort demonstrates the treatment effect by classifying subjects into treatment groups according to the treatment actually received, regardless of the randomization assignment

Meta-Analysis of Randomized PFO Closure Trials

Ntaios G, Michel P, 2013 in print

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

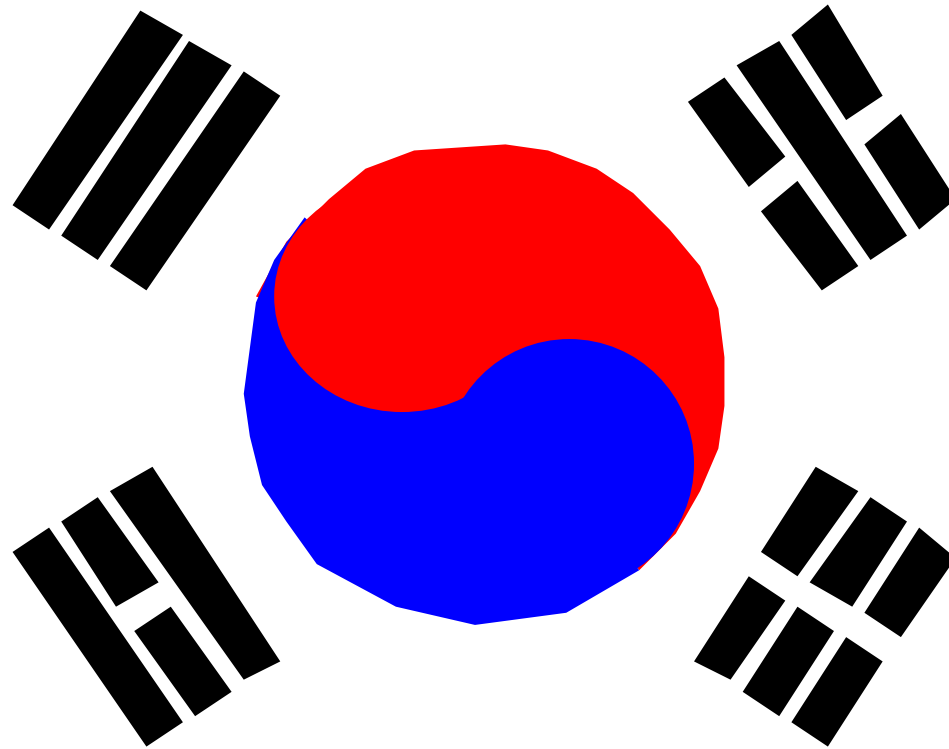
Ongoing Randomized PFO Closure Trials

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

