

# The most important late breaking clinical trials in 2017

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# Nothing to disclose

# The most important late breaking clinical trials

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## New evidences about PFO occlusion

*Søndergaard L, et al. NEJM. 2017;377(11):1033-1042.*

*Saver JL, et al. NEJM. 2017;377(11):1022-1032.*

*Meier B, et al. NEJM 2017; 377(11):1011-1021.*

## Lack of efficacy of bivalirudine administration in ACS

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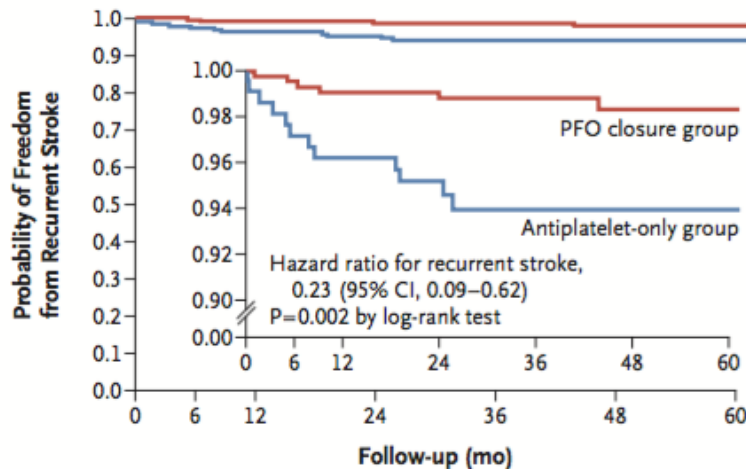
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## New evidences about PFO occlusion

*Søndergaard L, et al. NEJM. 2017;377(11):1033-1042.*

- 664 patients
- Mean age 45.2
- PFO closure plus antiplatelet vs. antiplatelet alone
- Randomization 2:1
- 20% of aneurysm in the closure group



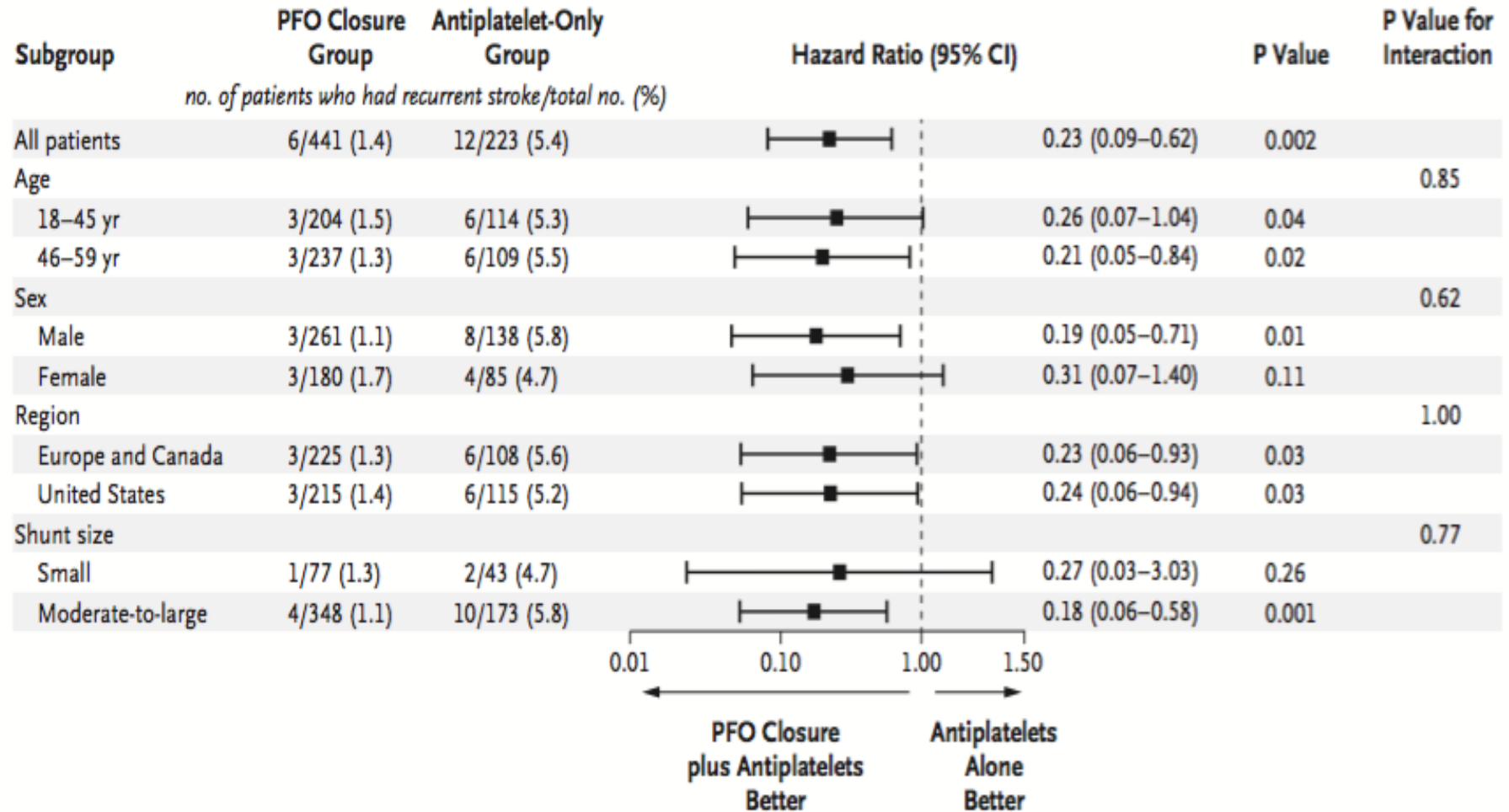
**Table 2.** Coprimary End Points of Freedom from Clinical Ischemic Stroke and Incidence of New Brain Infarction.\*

| End Point                          | PFO Closure Group             | Antiplatelet-Only Group | Effect Size       | P Value |
|------------------------------------|-------------------------------|-------------------------|-------------------|---------|
|                                    | no. of patients/total no. (%) |                         |                   |         |
| Clinical ischemic stroke†          | 6/441 (1.4)                   | 12/223 (5.4)            | 0.23 (0.09–0.62)‡ | 0.002§  |
| New brain infarction¶              | 22/383 (5.7)                  | 20/177 (11.3)           | 0.51 (0.29–0.91)  | 0.04**  |
| Recurrent clinical ischemic stroke | 5/383 (1.3)                   | 12/177 (6.8)            | 0.19 (0.07–0.54)  | 0.005** |
| Silent brain infarction only       | 17/383 (4.4)                  | 8/177 (4.5)             | 0.98 (0.43–2.23)  | 0.97**  |

|                         |     |     |     |     |     |     |     |
|-------------------------|-----|-----|-----|-----|-----|-----|-----|
| No. at Risk             |     |     |     |     |     |     |     |
| PFO closure group       | 441 | 422 | 417 | 398 | 278 | 182 | 102 |
| Antiplatelet-only group | 223 | 202 | 194 | 173 | 116 | 78  | 30  |

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# RESPECT Trial

## New evidences about PFO occlusion

*Saver JL, et al. NEJM. 2017;377(11):1022-1032.*

- **980 patients**
- **Mean age 45.9**

**Table 2. Coprimary End Points of Freedom from Clinical Ischemic Stroke and Incidence of New Brain Infarction.\***

| End Point                          | PFO Closure Group                    | Antiplatelet-Only Group | Effect Size       | P Value |
|------------------------------------|--------------------------------------|-------------------------|-------------------|---------|
|                                    | <i>no. of patients/total no. (%)</i> |                         |                   |         |
| Clinical ischemic stroke†          | 6/441 (1.4)                          | 12/223 (5.4)            | 0.23 (0.09–0.62)‡ | 0.002§  |
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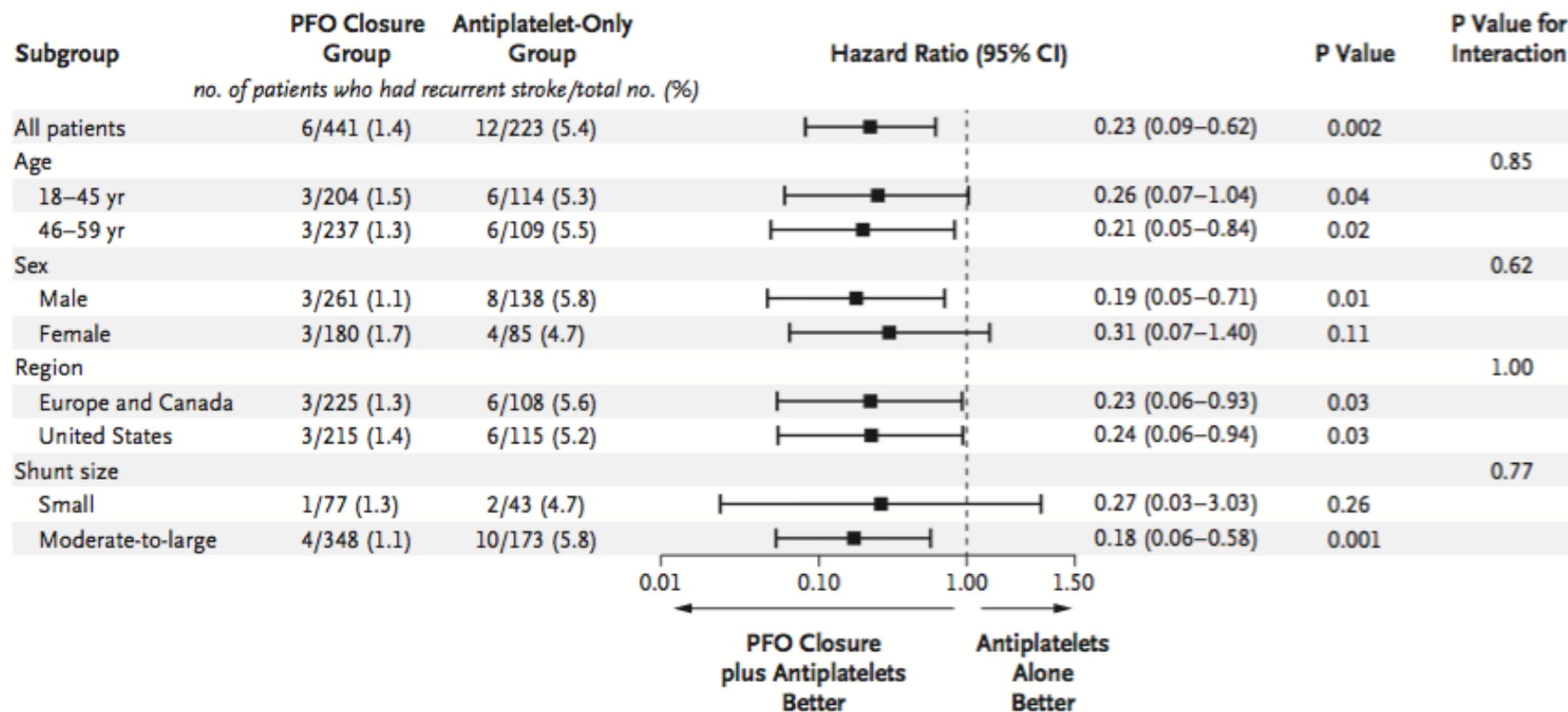
|                         |     |     |     |     |     |     |     |
|-------------------------|-----|-----|-----|-----|-----|-----|-----|
| <b>No. at Risk</b>      |     |     |     |     |     |     |     |
| PFO closure group       | 441 | 422 | 417 | 398 | 278 | 182 | 102 |
| Antiplatelet-only group | 223 | 202 | 194 | 173 | 116 | 78  | 30  |



# RESPECT Trial

## New evidences about PFO occlusion

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## New evidences about PFO occlusion

*B. Meier, et al. NEJM 2017; 377(11):1011-1021*

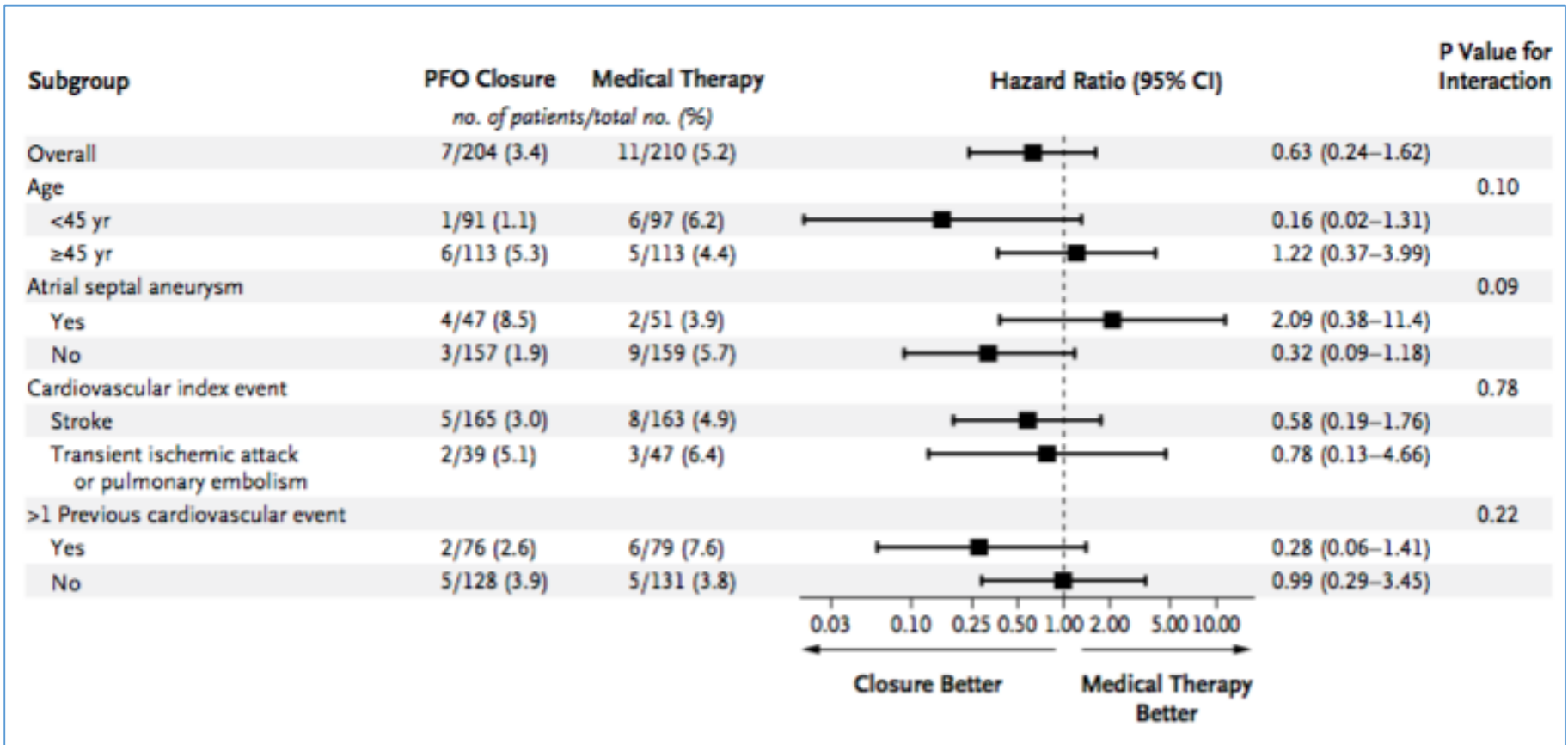
- 404 patients

**Table 2. Clinical Outcomes.\***

| Outcome                                                                 | PFO Closure<br>(N = 204)   | Medical Therapy<br>(N = 210) | Hazard Ratio or Relative<br>Risk (95% CI)† | P Value |
|-------------------------------------------------------------------------|----------------------------|------------------------------|--------------------------------------------|---------|
|                                                                         | <i>no. of patients (%)</i> |                              |                                            |         |
| Primary composite outcome of death, stroke, TIA, or peripheral embolism | 7 (3.4)                    | 11 (5.2)                     | 0.63 (0.24–1.62)                           | 0.34    |
| Death‡                                                                  | 2 (1.0)                    | 0                            | 5.20 (0.25–107.61)                         | 0.24    |
| Cardiovascular                                                          | 0                          | 0                            | NA                                         |         |
| Noncardiovascular                                                       | 2 (1.0)                    | 0                            | 5.20 (0.25–107.61)                         | 0.24    |
| Thromboembolic event                                                    |                            |                              |                                            |         |
| Stroke§                                                                 | 1 (0.5)                    | 5 (2.4)                      | 0.20 (0.02–1.72)                           | 0.14    |
| TIA                                                                     | 5 (2.5)                    | 7 (3.3)                      | 0.71 (0.23–2.24)                           | 0.56    |
| Peripheral embolism                                                     | 0                          | 0                            | NA                                         |         |
| Secondary composite outcome of stroke, TIA, or peripheral embolism      | 5 (2.5)                    | 11 (5.2)                     | 0.45 (0.16–1.29)                           | 0.14    |

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**Table 1. Baseline Characteristics of the Patients.\***

| Characteristic                                                                           | Bivalirudin Group (N=3004) | Heparin Group (N=3002) | All Patients Enrolled in the Trial (N=6006) | Screened Patients Not Enrolled in the Trial (N=6555) |
|------------------------------------------------------------------------------------------|----------------------------|------------------------|---------------------------------------------|------------------------------------------------------|
| STEMI — no. (%)                                                                          | 1501 (50.0)                | 1504 (50.1)            | 3005 (50.0)                                 | 2318 (35.4)                                          |
| Male sex — no. (%)                                                                       | 2229 (74.2)                | 2177 (72.5)            | 4406 (73.4)                                 | 4555 (69.5)                                          |
| Age                                                                                      |                            |                        |                                             |                                                      |
| Median — yr                                                                              | 68.0                       | 68.0                   | 68.0                                        | 71.0                                                 |
| Interquartile range — yr                                                                 | 59.0–75.0                  | 60.0–75.0              | 60.0–75.0                                   | 62.0–79.0                                            |
| ≥65 yr — no. (%)                                                                         | 1819 (60.6)                | 1852 (61.7)            | 3671 (61.1)                                 | 4528 (69.1)                                          |
| Body-mass index†                                                                         |                            |                        |                                             |                                                      |
| Median                                                                                   | 26.8                       | 26.9                   | 26.9                                        | 26.9                                                 |
| Interquartile range                                                                      | 24.5–29.7                  | 24.5–29.7              | 24.5–29.7                                   | 24.2–30.1                                            |
| Weight <60 kg — no. (%)                                                                  | 139 (4.6)                  | 156 (5.2)              | 295 (4.9)                                   | 469 (7.2)                                            |
| Previous smoker — no. (%)                                                                | 1027 (34.2)                | 1020 (34.0)            | 2047 (34.1)                                 | 2314 (35.3)                                          |
| Current smoker — no. (%)                                                                 | 716 (23.8)                 | 710 (23.7)             | 1426 (23.7)                                 | 1361 (20.8)                                          |
| Diabetes — no. (%)                                                                       | 491 (16.3)                 | 508 (16.9)             | 999 (16.6)                                  | 1631 (24.9)                                          |
| Hypertension — no. (%)                                                                   | 1557 (51.8)                | 1548 (51.6)            | 3105 (51.7)                                 | 4080 (62.2)                                          |
| Hyperlipidemia — no. (%)                                                                 | 953 (31.7)                 | 936 (31.2)             | 1889 (31.5)                                 | 2893 (44.1)                                          |
| Previous myocardial infarction — no. (%)                                                 | 490 (16.3)                 | 484 (16.1)             | 974 (16.2)                                  | 1831 (27.9)                                          |
| Previous percutaneous coronary intervention — no. (%)                                    | 456 (15.2)                 | 426 (14.2)             | 882 (14.7)                                  | 1436 (21.9)                                          |
| Previous coronary-artery bypass grafting — no. (%)                                       | 152 (5.1)                  | 141 (4.7)              | 293 (4.9)                                   | 653 (10.0)                                           |
| Previous stroke — no. (%)                                                                | 115 (3.8)                  | 125 (4.2)              | 240 (4.0)                                   | 467 (7.1)                                            |
| Cardiopulmonary resuscitation before arrival at the catheterization laboratory — no. (%) | 26 (0.9)                   | 20 (0.7)               | 46 (0.8)                                    | 83 (1.3)                                             |
| Killip class II, III, or IV — no. (%)‡                                                   | 108 (3.6)                  | 86 (2.9)               | 194 (3.2)                                   | 519 (7.9)                                            |

**Table 3. Clinical Outcomes at 180 Days.**

| Outcome                                                                           | Bivalirudin<br>Group<br>(N=3004) | Heparin<br>Group<br>(N=3002) | Hazard Ratio<br>(95% CI) | P Value |
|-----------------------------------------------------------------------------------|----------------------------------|------------------------------|--------------------------|---------|
|                                                                                   | no. (%)                          |                              |                          |         |
| Primary end point: death from any cause, myocardial infarction, or major bleeding | 369 (12.3)                       | 383 (12.8)                   | 0.96 (0.83–1.10)         | 0.54    |
| Death from any cause                                                              | 88 (2.9)                         | 84 (2.8)                     | 1.05 (0.78–1.41)         | 0.76    |
| Death from cardiovascular causes                                                  | 73 (2.4)                         | 70 (2.3)                     | 1.04 (0.75–1.45)         | 0.80    |
| Myocardial infarction                                                             | 60 (2.0)                         | 71 (2.4)                     | 0.84 (0.60–1.19)         | 0.33    |
| Periprocedural type 4a myocardial infarction                                      | 5 (0.2)                          | 2 (0.1)                      |                          |         |
| Major bleeding                                                                    | 259 (8.6)                        | 257 (8.6)                    | 1.00 (0.84–1.19)         | 0.98    |
| BARC type 2                                                                       | 170 (5.7)                        | 180 (6.0)                    |                          |         |
| BARC type 3                                                                       | 94 (3.1)                         | 87 (2.9)                     |                          |         |
| BARC type 5                                                                       | 6 (0.2)                          | 3 (0.1)                      |                          |         |
| Bleeding at the access site                                                       | 68 (2.3)                         | 86 (2.9)                     |                          |         |
| Stent thrombosis†                                                                 | 56 (1.9)                         | 59 (2.0)                     | 0.95 (0.66–1.37)         | 0.78    |
| Definite                                                                          | 12 (0.4)                         | 22 (0.7)                     | 0.54 (0.27–1.10)         | 0.09    |
| Probable                                                                          | 11 (0.4)                         | 11 (0.4)                     |                          |         |
| Possible                                                                          | 3 (0.1)                          | 4 (0.1)                      |                          |         |
| Intraprocedural                                                                   | 31 (1.0)                         | 24 (0.8)                     | 1.30 (0.76–2.21)*        | 0.34    |
| Stroke                                                                            | 25 (0.8)                         | 25 (0.8)                     | 1.00 (0.57–1.74)         | 1.00    |
| Primary hemorrhagic stroke                                                        | 5 (0.2)                          | 0                            |                          |         |
| Death, myocardial infarction, major bleeding, or stroke                           | 379 (12.6)                       | 398 (13.3)                   | 0.94 (0.82–1.09)         | 0.42    |
| Death, myocardial infarction, or BARC type 3 or 5 bleeding                        | 221 (7.4)                        | 226 (7.5)                    | 0.97 (0.81–1.17)         | 0.78    |

Bivalirudin 3004 2893 2879 2869 2851 2838 2827  
Heparin 3002 2891 2873 2859 2846 2831 2820

Bivalirudin 3004 2775 2748 2717 2688 2664 2644  
Heparin 3002 2759 2727 2699 2676 2653 2638

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**Table 1. Characteristics of the Patients at Baseline\***

| Characteristic                                 | Scaffold Group<br>(N = 924) | Stent Group<br>(N = 921) |
|------------------------------------------------|-----------------------------|--------------------------|
| Age — yr                                       | 64.3±10.6                   | 64.0±10.5                |
| Male sex — no. (%)                             | 670 (72.5)                  | 700 (76.0)               |
| Risk factors — no./total no. (%)               |                             |                          |
| Diabetes mellitus                              | 171/924 (18.5)              | 153/921 (16.6)           |
| Treated with oral medication                   | 95/171 (55.6)               | 97/153 (63.4)            |
| Treated with insulin                           | 65/171 (38.0)               | 45/153 (29.4)            |
| Hypertension                                   | 468/920 (50.9)              | 464/919 (50.5)           |
| Hypercholesterolemia                           | 344/915 (37.6)              | 350/914 (38.3)           |
| Family history of coronary artery disease      | 451/886 (50.9)              | 469/886 (52.9)           |
| Current smoker                                 | 248/867 (28.6)              | 273/861 (31.7)           |
| History — no./total no. (%)                    |                             |                          |
| Chronic renal failure                          | 70/924 (7.6)                | 91/921 (9.9)             |
| Ejection fraction <30%                         | 22/910 (2.4)                | 17/900 (1.9)             |
| Previous stroke or transient ischemic attack   | 46/923 (5.0)                | 58/921 (6.3)             |
| Peripheral vascular disease                    | 65/924 (7.0)                | 56/918 (6.1)             |
| Previous myocardial infarction                 | 166/924 (18.0)              | 172/921 (18.7)           |
| Previous percutaneous coronary intervention    | 202/924 (21.9)              | 184/921 (20.0)           |
| Previous bypass surgery                        | 38/924 (4.1)                | 26/921 (2.8)             |
| Clinical presentation — no. (%)                |                             |                          |
| ST-segment elevation myocardial infarction     | 240 (26.0)                  | 225 (24.4)               |
| Non-ST-segment elevation myocardial infarction | 185 (20.0)                  | 192 (20.8)               |
| Unstable angina                                | 70 (7.6)                    | 87 (9.4)                 |
| Stable angina, documented ischemia, or both    | 361 (39.1)                  | 370 (40.2)               |
| Angiographically driven indication for PCI†    | 51 (5.5)                    | 36 (3.9)                 |
| Other                                          | 17 (1.8)                    | 11 (1.2)                 |
| SYNTAX score‡                                  |                             |                          |
| Mean                                           | 13.2±8.6                    | 12.6±8.4                 |
| Median (interquartile range)                   | 11 (7–18)                   | 11 (7–17)                |

## Temporary Twilight of the ABSORB

*Wykrzykowska JJ, et al NEJM. 2017;376(24):2319-2328.*

**Table 2. Procedural Characteristics.\***

| Outcome                                                      | Scaffold Group | Stent Group   | P Value |
|--------------------------------------------------------------|----------------|---------------|---------|
| <b>Patients</b>                                              |                |               |         |
| Total no.                                                    | 924            | 921           |         |
| Treated lesions per patient                                  | 1.34±0.63      | 1.31±0.59     | 0.36    |
| No. of devices per patient                                   | 1.54±0.84      | 1.45±0.79     | 0.01    |
| Total device length per patient — mm                         | 31.1±19.6      | 29.7±19.2     | 0.11    |
| Minimum device diameter per patient — mm                     | 2.73±0.27      | 2.88±0.35     | 0.05    |
| <b>Device implantation — no. (%)</b>                         |                |               |         |
| Any assigned study device                                    | 895 (96.9)     | 919 (99.8)    | <0.001  |
| Only assigned study devices                                  | 859 (93.0)     | 910 (98.8)    | <0.001  |
| Any unassigned device                                        | 65 (7.0)       | 11 (1.2)      | <0.001  |
| Only unassigned devices                                      | 29 (3.1)       | 2 (0.2)       | <0.001  |
| After failure of assigned device                             | 20             | 1             |         |
| Unassigned device first choice                               | 9              | 1             |         |
| Procedure time — min†                                        | 49±26          | 44±23         | <0.001  |
| Contrast material used — ml‡                                 | 160±74         | 151±72        | 0.02    |
| Predilation of first treated lesion — no. (%)                | 911 (98.6)     | 892 (96.9)    | 0.01    |
| Procedural success — no. (%)§                                | 833 (90.2)     | 887 (96.3)    | <0.001  |
| <b>Treated lesions¶</b>                                      |                |               |         |
| Total no.                                                    | 1237           | 1209          |         |
| Rotational atherectomy — no./total no. of target lesions (%) | 24/1232 (1.9)  | 26/1208 (2.2) | 0.78    |
| Predilation performed — no. (%)                              | 1199 (96.9)    | 1103 (91.2)   | <0.001  |
| Total number of devices implanted                            | 1425           | 1336          |         |
| Number of devices per lesion                                 | 1.15±0.40      | 1.11±0.34     | 0.001   |
| Postdilation performed — no. (%)                             | 915 (74.0)     | 594 (49.1)    | <0.001  |

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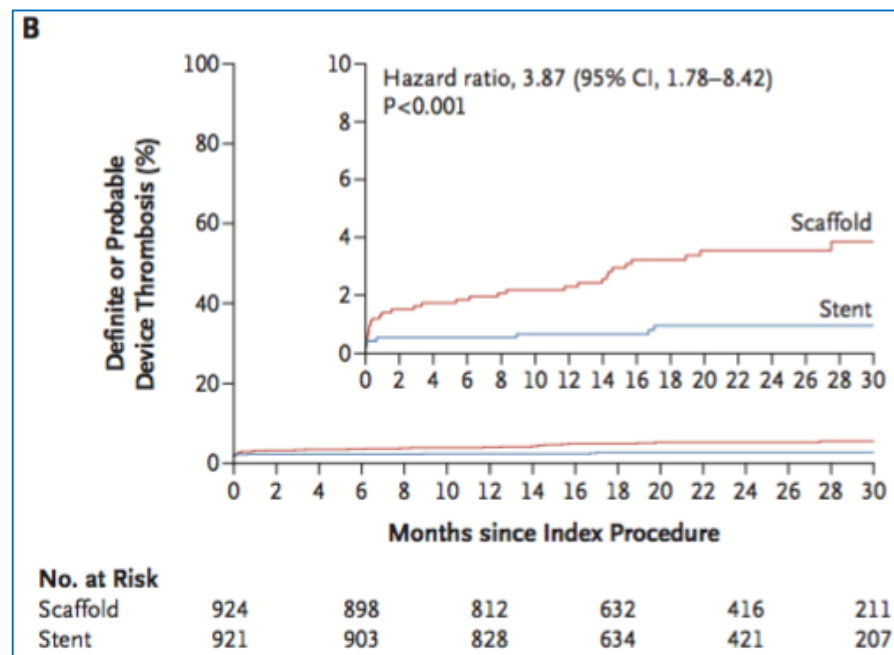
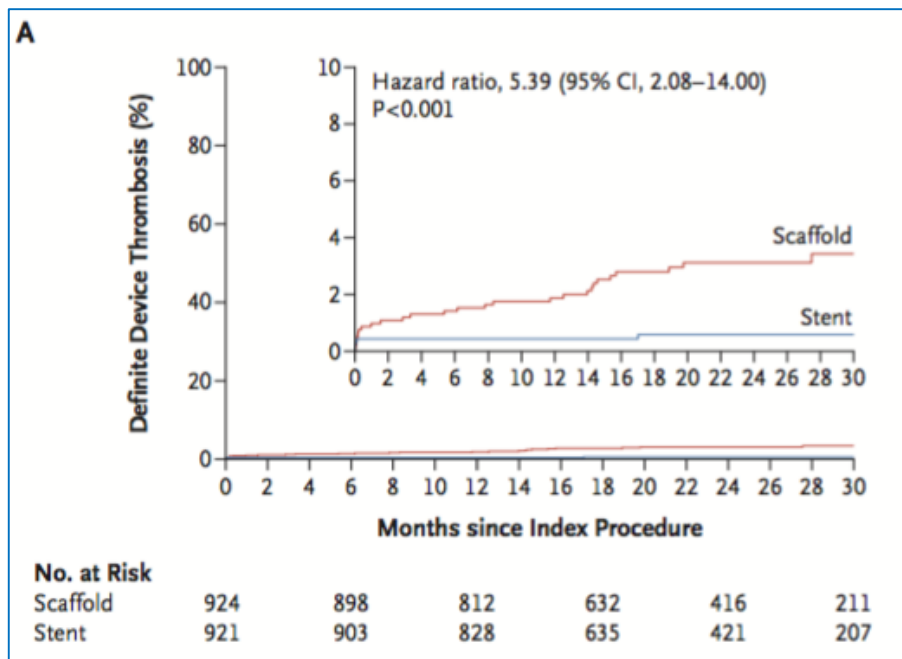


Table 3. Safety and Efficacy Outcomes.

| Outcome                        | Patients with an Event    |                        | 2-Year Cumulative Event Rate <sup>a</sup> |                        | Hazard Ratio<br>(95% CI) | P Value <sup>†</sup> |
|--------------------------------|---------------------------|------------------------|-------------------------------------------|------------------------|--------------------------|----------------------|
|                                | Scaffold Group<br>(N=924) | Stent Group<br>(N=921) | Scaffold Group<br>(N=924)                 | Stent Group<br>(N=921) |                          |                      |
|                                | <i>number</i>             |                        | <i>percent</i>                            |                        |                          |                      |
| Clinical events                |                           |                        |                                           |                        |                          |                      |
| Death from any cause           | 32                        | 43                     | 3.5                                       | 4.3                    | 0.74 (0.47–1.17)         | 0.19                 |
| Cardiac                        | 18                        | 23                     | 2.0                                       | 2.7                    | 0.78 (0.42–1.44)         | 0.43                 |
| Cardiovascular                 | 22                        | 25                     | 2.6                                       | 2.9                    | 0.88 (0.49–1.55)         | 0.65                 |
| Noncardiovascular              | 10                        | 18                     | 0.9                                       | 1.5                    | 0.55 (0.25–1.19)         | 0.13                 |
| All myocardial infarction      | 62                        | 41                     | 7.1                                       | 4.2                    | 1.52 (1.02–2.25)         | 0.04                 |
| Target vessel                  | 48                        | 30                     | 5.5                                       | 3.2                    | 1.60 (1.01–2.53)         | 0.04                 |
| During index procedure         | 9                         | 6                      | 1.0                                       | 0.7                    | 1.50 (0.53–4.20)         | 0.44                 |
| Not during index procedure     | 39                        | 24                     | 4.5                                       | 2.6                    | 1.62 (0.98–2.70)         | 0.06                 |
| Nontarget vessel               | 15                        | 11                     | 1.7                                       | 1.0                    | 1.36 (0.62–2.96)         | 0.44                 |
| Death or myocardial infarction | 88                        | 80                     | 9.6                                       | 8.1                    | 1.10 (0.82–1.49)         | 0.52                 |
| Any revascularization          | 115                       | 103                    | 13.2                                      | 11.6                   | 1.11 (0.85–1.45)         | 0.43                 |
| Target vessel                  | 76                        | 65                     | 8.7                                       | 7.5                    | 1.16 (0.84–1.62)         | 0.37                 |
| Target lesion                  | 60                        | 45                     | 7.0                                       | 5.2                    | 1.33 (0.90–1.96)         | 0.15                 |
| Device thrombosis–related      | 26                        | 5                      | 3.0                                       | 0.6                    | 5.19 (1.99–13.50)        | <0.001               |
| Device stenosis–related        | 35                        | 40                     | 4.1                                       | 4.6                    | 0.87 (0.55–1.36)         | 0.53                 |
| Nontarget lesion               | 21                        | 22                     | 2.5                                       | 2.5                    | 0.94 (0.52–1.71)         | 0.84                 |
| Nontarget vessel               | 55                        | 50                     | 6.8                                       | 5.5                    | 1.09 (0.74–1.60)         | 0.66                 |
| Composite end points           |                           |                        |                                           |                        |                          |                      |
| Target-vessel failure‡         | 105                       | 94                     | 11.7                                      | 10.7                   | 1.12 (0.85–1.48)         | 0.43                 |
| Target-lesion failure§         | 91                        | 78                     | 10.3                                      | 8.9                    | 1.17 (0.86–1.58)         | 0.31                 |
| Patient-oriented end point¶    | 161                       | 149                    | 17.8                                      | 16.1                   | 1.08 (0.87–1.35)         | 0.49                 |
| Device thrombosis              |                           |                        |                                           |                        |                          |                      |
| Definite                       | 27                        | 5                      | 3.1                                       | 0.6                    | 5.39 (2.08–14.00)        | <0.001               |
| Probable                       | 4                         | 3                      | 0.4                                       | 0.4                    | 1.32 (0.30–5.91)         | 0.71                 |
| Possible                       | 6                         | 12                     | 0.6                                       | 1.5                    | 0.50 (0.19–1.33)         | 0.15                 |
| Definite or probable           | 31                        | 8                      | 3.5                                       | 0.9                    | 3.87 (1.78–8.42)         | <0.001               |
| Acute (≤24 hr)                 | 3                         | 3                      |                                           |                        |                          |                      |
| Subacute (>24 hr to 30 days)   | 10                        | 2                      |                                           |                        |                          |                      |
| Late (31 days to 1 yr)         | 8                         | 1                      |                                           |                        |                          |                      |
| Very late (>1 to 2 yr)         | 9                         | 2                      |                                           |                        |                          |                      |
| Very late (>2 to 3 yr)         | 1                         | 0                      |                                           |                        |                          |                      |
| Any device thrombosis          | 37                        | 20                     | 4.1                                       | 2.5                    | 1.85 (1.08–3.19)         | 0.02                 |

# The most important late breaking clinical trials

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## New evidences about PFO occlusion

*Søndergaard L, et al. NEJM. 2017;377(11):1033-1042.*

*Saver JL, et al. NEJM. 2017;377(11):1022-1032.*

*Meier B, et al. NEJM 2017; 377(11):1011-1021.*

## Lack of efficacy of bivalirudine administration in ACS

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$$iFR = \frac{\text{distal coronary pressure}_{\text{wave-free period}}}{\text{proximal coronary pressure}_{\text{wave-free period}}}$$

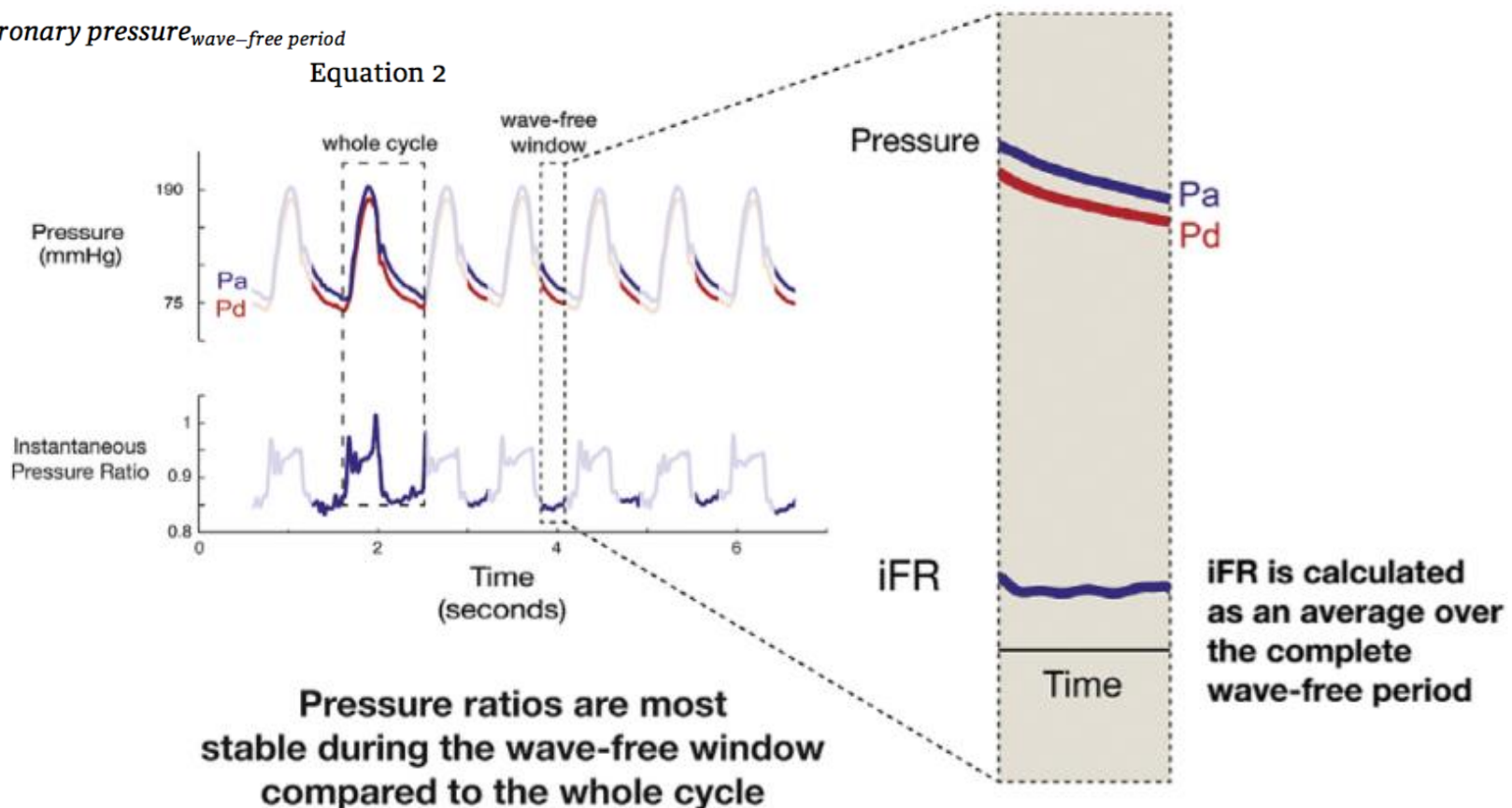
Equation 1

iFR gradient =

$$\text{proximal coronary pressure}_{\text{wave-free period}}$$

$$- \text{distal coronary pressure}_{\text{wave-free period}}$$

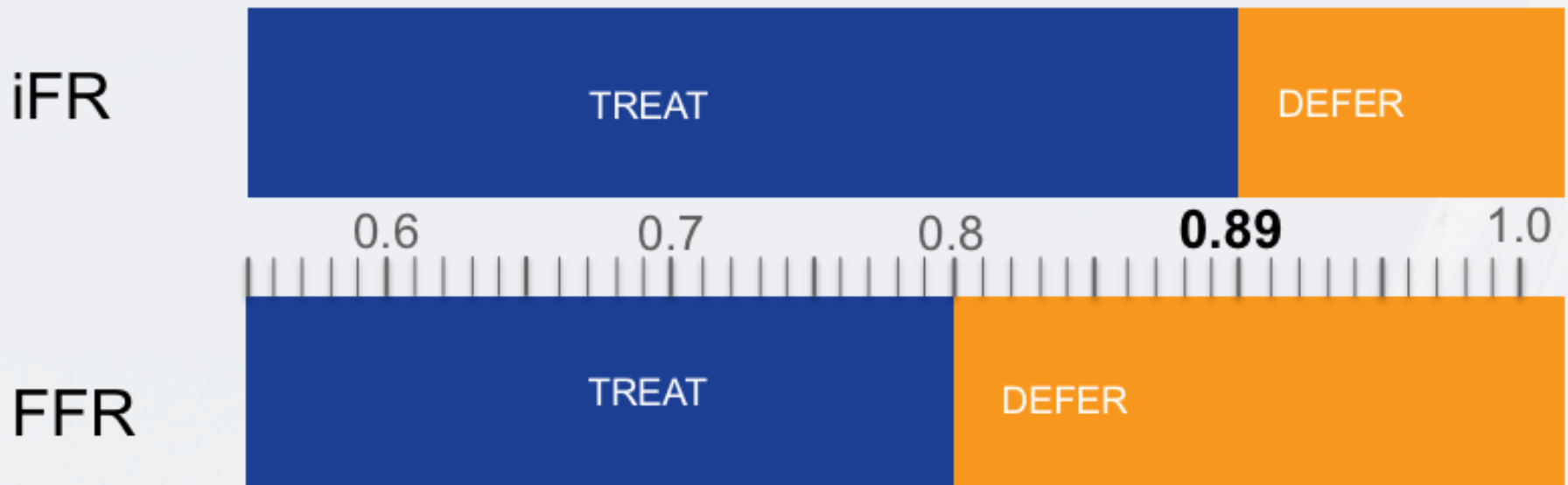
Equation 2



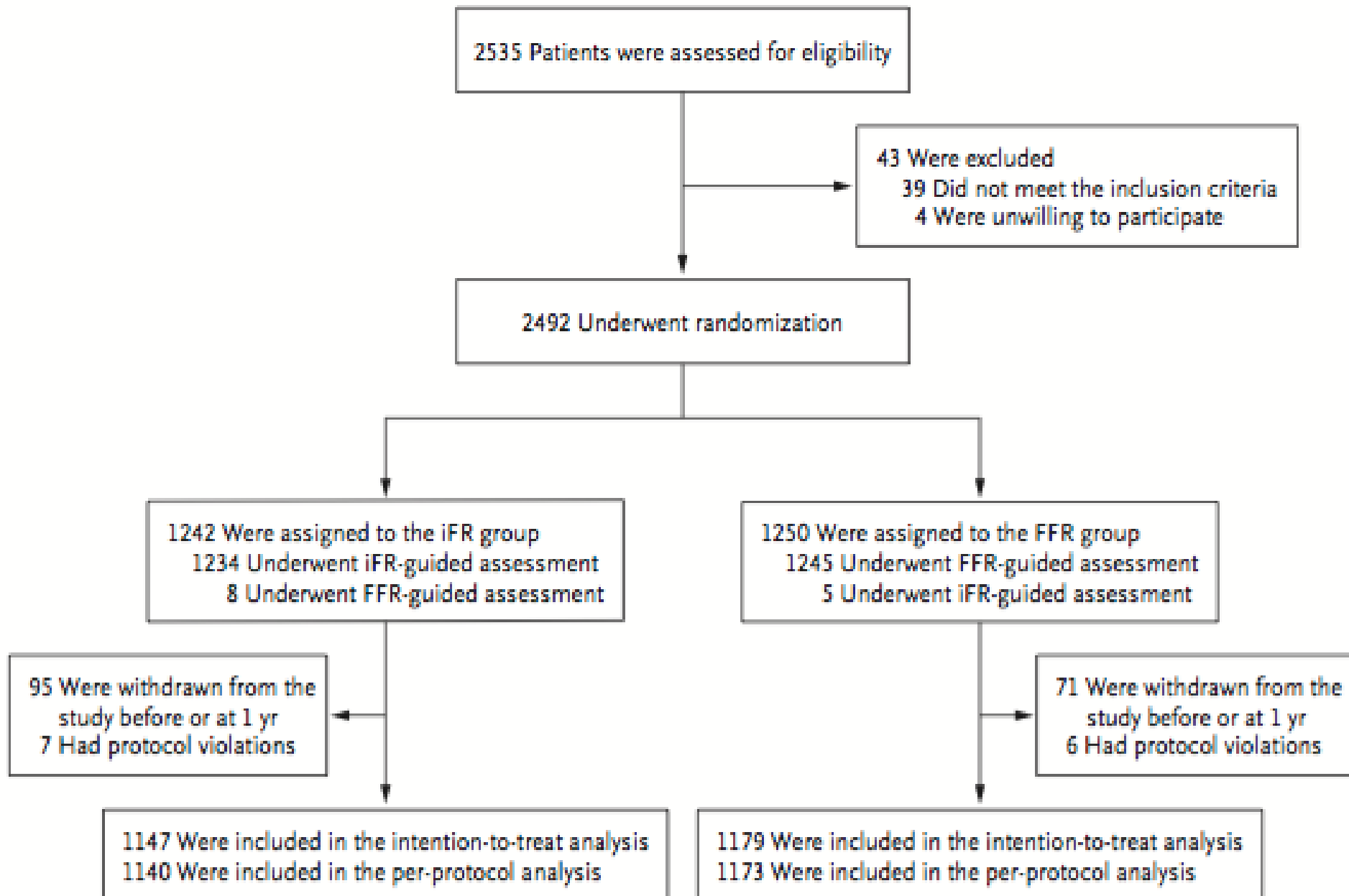
# iFR: a new diagnostic tool for the interventional cardiologist

*iFR Swedheart, Götberg M, et al NEJM. 2017; 376(19):1813-1823*

*Davies JE et al. NEJM. 2017; 376(19):1824-1834.*



# DEFINE FLAIR trial

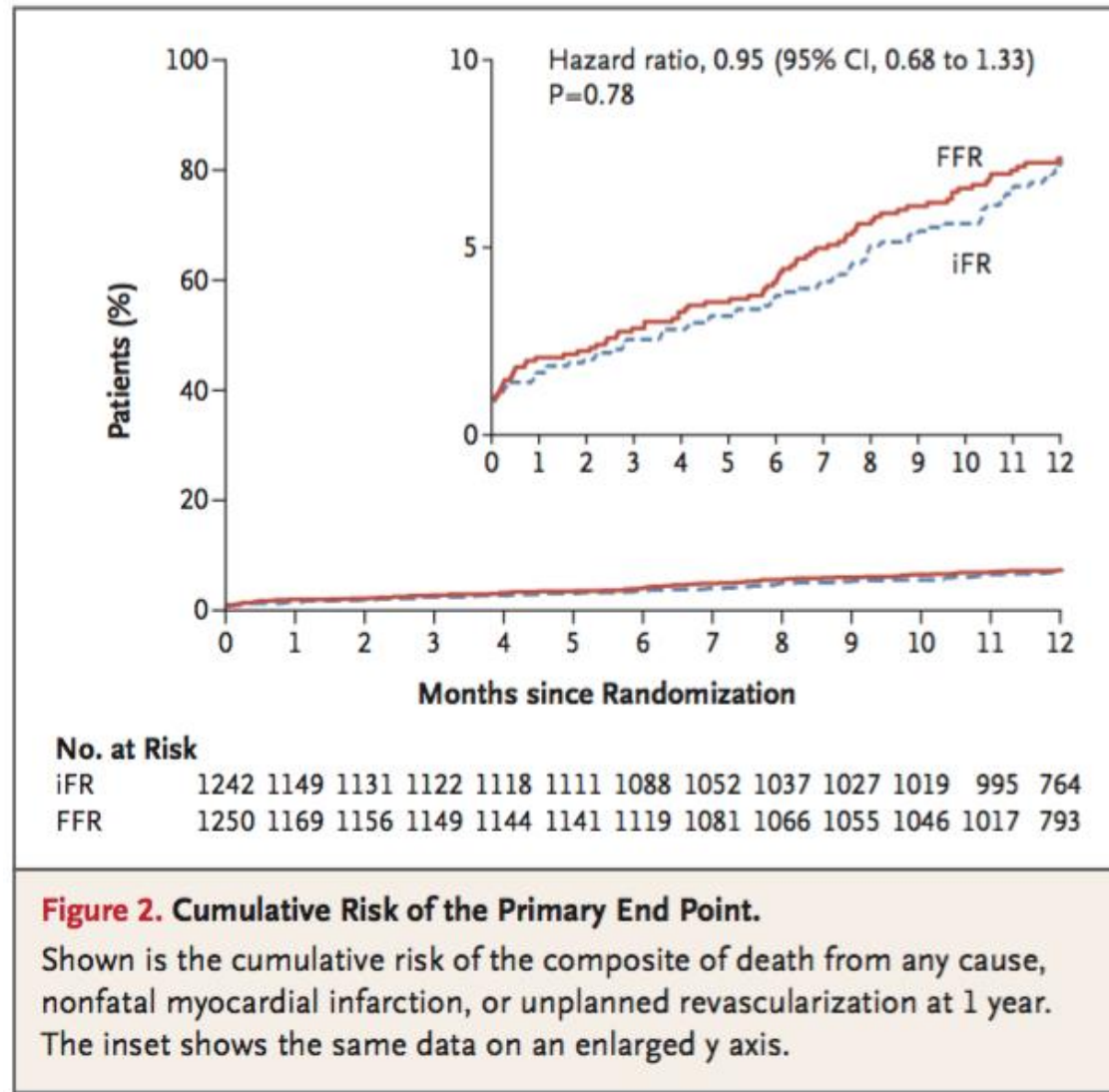


**Table 1. Baseline Characteristics of the Patients.\***

| Characteristic                                        | iFR Group<br>(N = 1242) | FFR Group<br>(N = 1250) |
|-------------------------------------------------------|-------------------------|-------------------------|
| Age — yr                                              | 65.5±10.8               | 65.2±10.6               |
| Sex — no. (%)                                         |                         |                         |
| Female                                                | 280 (22.5)              | 321 (25.7)              |
| Male                                                  | 962 (77.5)              | 929 (74.3)              |
| Disease type — no. (%)†                               |                         |                         |
| STEMI                                                 | 49 (3.9)                | 42 (3.4)                |
| Acute coronary syndrome                               | 186 (15.0)              | 184 (14.7)              |
| Stable disease                                        | 986 (79.4)              | 1012 (81.0)             |
| Diabetes — no. (%)                                    |                         |                         |
| Non-insulin dependent                                 | 288 (23.2)              | 282 (22.6)              |
| Insulin dependent                                     | 94 (7.6)                | 94 (7.5)                |
| Smoking status — no. (%)                              |                         |                         |
| Former smoker                                         | 461 (37.1)              | 443 (35.4)              |
| Current smoker                                        | 243 (19.6)              | 262 (21.0)              |
| Hypertension — no. (%)                                | 873 (70.3)              | 884 (70.7)              |
| Hypercholesterolemia — no. (%)                        | 794 (63.9)              | 792 (63.4)              |
| Previous myocardial infarction — no. (%)              | 358 (28.8)              | 376 (30.1)              |
| Previous percutaneous coronary intervention — no. (%) | 489 (39.4)              | 527 (42.2)              |
| Previous heart condition — no. (%)                    | 489 (39.4)              | 530 (42.4)              |
| Congestive heart failure — no. (%)                    | 77 (6.2)                | 67 (5.4)                |
| NYHA class — no. (%)‡                                 |                         |                         |
| I                                                     | 21 (1.7)                | 13 (1.0)                |
| II                                                    | 28 (2.3)                | 32 (2.6)                |
| III                                                   | 16 (1.3)                | 14 (1.1)                |
| IV                                                    | 1 (0.1)                 | 3 (0.2)                 |
| Impairment of left ventricular function — no. (%)     |                         |                         |
| Mild                                                  | 147 (11.8)              | 150 (12.0)              |
| Moderate                                              | 65 (5.2)                | 58 (4.6)                |
| Severe                                                | 23 (1.9)                | 27 (2.2)                |
| CCS angina class — no. (%)§                           |                         |                         |
| I                                                     | 347 (27.9)              | 305 (24.4)              |
| II                                                    | 374 (30.1)              | 370 (29.6)              |
| III                                                   | 127 (10.2)              | 154 (12.3)              |
| IV                                                    | 81 (6.5)                | 72 (5.8)                |
| Systolic blood pressure — mm Hg                       | 133.9±20.3              | 134.3±20.1              |
| Diastolic blood pressure — mm Hg                      | 74.9±11.9               | 75.0±11.8               |
| Heart rate — beats/min                                | 68.9±12.6               | 69.1±12.8               |
| Body-mass index¶                                      | 27.8±5.0                | 27.5±5.0                |
| Total cholesterol — mmol/liter                        | 4.1±1.0                 | 4.1±0.9                 |
| Hemoglobin — mg/dl                                    | 13.9±1.6                | 13.8±1.6                |
| Creatinine — mmol/liter                               | 90.2±62.0               | 93.2±81.1               |

## iFR: a new diagnostic tool for the interventional cardiologist

*Davies JE et al. NEJM. 2017; 376(19):1824-1834.*



**Table 2. (Continued.)**

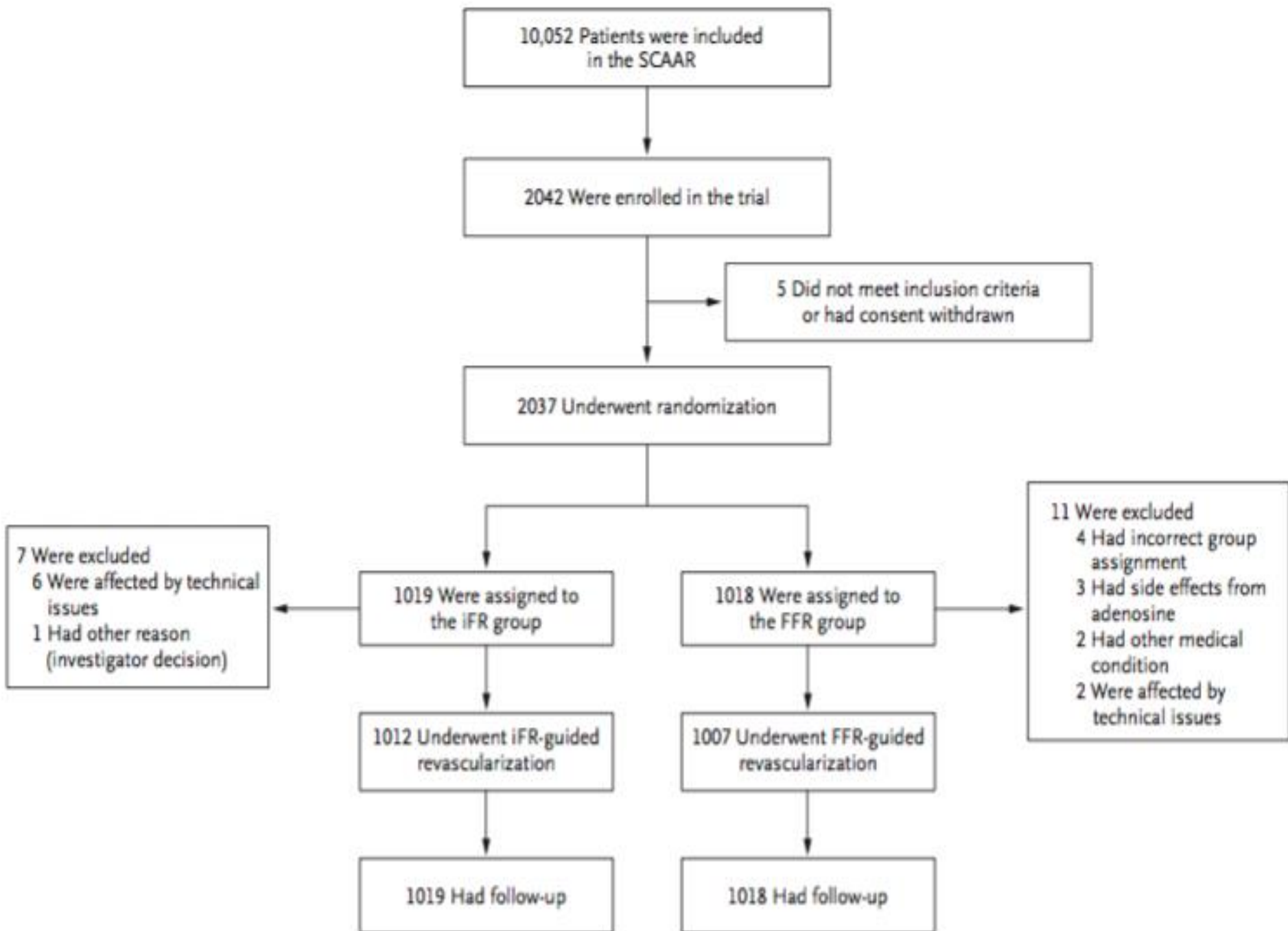
| Variable                                                                     | iFR Group<br>(N = 1242) | FFR Group<br>(N = 1250) | P Value† |
|------------------------------------------------------------------------------|-------------------------|-------------------------|----------|
| Stent diameter — mm                                                          |                         |                         |          |
| Median                                                                       | 3.00                    | 3.00                    | 0.44     |
| Interquartile range                                                          | 2.67–3.25               | 2.75–3.25               |          |
| Stents placed with postdilation — no. (% of total stents placed)             | 407 (49.5)              | 425 (46.9)              | 0.28     |
| PCI procedures performed with pressure wire — no. (% of total stents placed) | 261 (31.8)              | 278 (30.7)              | 0.63     |
| Patient-reported adverse procedural symptoms or signs — no. of patients (%)  | 39 (3.1)                | 385 (30.8)              | <0.001   |
| Patient-reported dyspnea — no. of patients (%)                               | 13 (1.0)                | 250 (20.0)              |          |
| Patient-reported chest pain — no. of patients (%)                            | 19 (1.5)                | 90 (7.2)                |          |
| Physician-reported adverse procedural signs — no. of patients (%)            |                         |                         |          |
| Heart-rhythm disturbance                                                     | 2 (0.2)                 | 60 (4.8)                |          |
| Significant hypotension                                                      | 4 (0.3)                 | 13 (1.0)                |          |
| Vomiting or nausea                                                           | 1 (0.1)                 | 11 (0.9)                |          |
| Ventricular arrhythmia or bronchospasm¶                                      | 1 (0.1)                 | 8 (0.6)                 |          |
| Other                                                                        | 4 (0.3)                 | 38 (3.0)                |          |

## iFR: a new diagnostic tool for the interventional cardiologist

*Davies JE et al. NEJM. 2017; 376(19):1824-1834.*

**Table 3. Outcomes for Difference in Risk at 1 Year.\***

| Outcome                                                                                                 | iFR Group<br><br>no./total no. (%) | FFR Group<br><br>no./total no. (%) | Difference in Risk            |                               | P Value |
|---------------------------------------------------------------------------------------------------------|------------------------------------|------------------------------------|-------------------------------|-------------------------------|---------|
|                                                                                                         |                                    |                                    | percentage points<br>(95% CI) | percentage points<br>(99% CI) |         |
| Primary end point: death from any cause, nonfatal myocardial infarction, or unplanned revascularization | 78/1148 (6.8)                      | 83/1182 (7.0)                      | -0.2 (-2.3 to 1.8)†           | -0.2 (-2.9 to 2.5)            | 0.83    |
| Unplanned revascularization                                                                             | 46/1147 (4.0)                      | 63/1181 (5.3)                      | -1.3 (-3.0 to 0.4)            | -1.3 (-3.1 to 1.9)            | 0.13    |
| Nonfatal myocardial infarction                                                                          | 31/1148 (2.7)                      | 28/1180 (2.4)                      | 0.3 (-1.0 to 1.6)             | 0.3 (-1.4 to 2.0)             | 0.62    |
| Death from cardiovascular causes                                                                        | 7/1147 (0.6)                       | 4/1179 (0.3)                       | 0.3 (-0.3 to 0.8)             | 0.3 (-0.5 to 1.0)             | 0.34    |
| Death from noncardiovascular causes                                                                     | 15/1147 (1.3)                      | 9/1179 (0.8)                       | 0.5 (-0.3 to 1.4)             | 0.5 (-0.5 to 1.6)             | 0.19    |
| Death from any cause                                                                                    | 22/1147 (1.9)                      | 13/1179 (1.1)                      | 0.8 (-0.2 to 1.8)             | 0.8 (-0.5 to 2.1)             | 0.11    |



**Table 1. Baseline Characteristics of the Patients.\***

| Characteristic                                        | iFR Group<br>(N = 1019) | FFR Group<br>(N = 1018) |
|-------------------------------------------------------|-------------------------|-------------------------|
| Age — yr                                              | 67.6±9.6                | 67.4±9.2                |
| Male sex — no. (%)                                    | 756 (74.2)              | 766 (75.2)              |
| Body-mass index†                                      | 27.6±4.3                | 27.6±4.3                |
| Indication for angiography — no. (%)                  |                         |                         |
| Stable angina                                         | 632 (62.0)              | 632 (62.1)              |
| Unstable angina                                       | 211 (20.7)              | 208 (20.4)              |
| NSTEMI                                                | 176 (17.3)              | 178 (17.5)              |
| Angina class — no./total no. with stable angina (%)‡  |                         |                         |
| I                                                     | 153/632 (24.2)          | 121/632 (19.1)          |
| II                                                    | 355/632 (56.2)          | 343/632 (54.3)          |
| III                                                   | 49/632 (7.8)            | 74/632 (11.7)           |
| IV                                                    | 0                       | 3/632 (0.5)             |
| Missing data                                          | 75/632 (11.9)           | 91/632 (14.4)           |
| Diabetes mellitus — no. (%)                           | 232 (22.8)              | 213 (20.9)              |
| Hypertension — no. (%)                                | 730 (71.6)              | 710 (69.7)              |
| Hyperlipidemia — no. (%)                              | 733 (71.9)              | 704 (69.2)              |
| Smoking status — no. (%)                              |                         |                         |
| Never smoked                                          | 351 (34.4)              | 368 (36.1)              |
| Former smoker                                         | 501 (49.2)              | 467 (45.9)              |
| Current smoker                                        | 159 (15.6)              | 167 (16.3)              |
| Missing data                                          | 8 (0.8)                 | 16 (1.6)                |
| Previous myocardial infarction — no. (%)              | 337 (33.1)              | 335 (32.9)              |
| Previous percutaneous coronary intervention — no. (%) | 429 (42.1)              | 425 (41.7)              |
| Previous coronary-artery bypass grafting — no. (%)    | 49 (4.8)                | 43 (4.2)                |
| Angiographic findings — no. (%)§                      |                         |                         |
| Nonsignificant coronary artery disease                | 203 (20.0)              | 198 (19.4)              |
| One-vessel disease                                    | 452 (44.3)              | 453 (44.5)              |
| Two-vessel disease                                    | 256 (25.1)              | 267 (26.2)              |
| Three-vessel disease                                  | 108 (10.6)              | 101 (9.9)               |

iFR: a ne

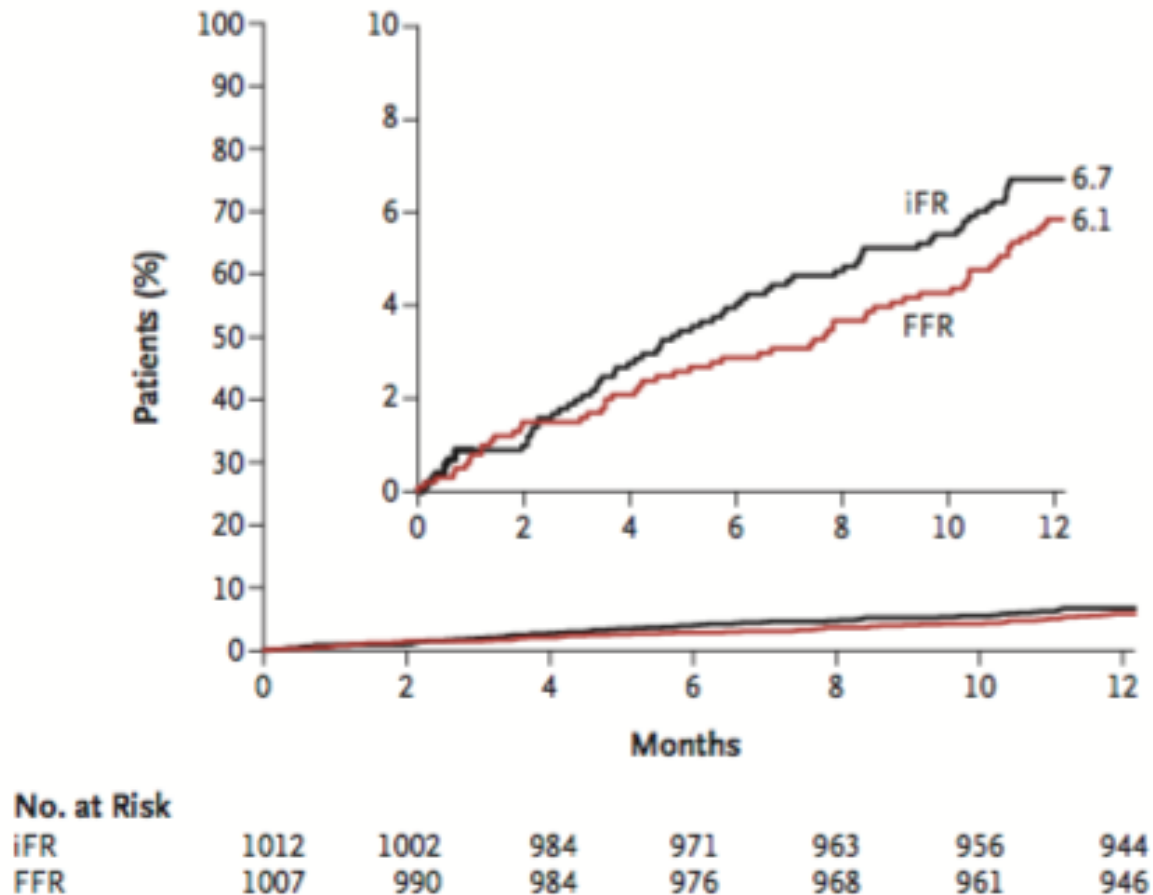
| Characteristic                                                                            | iFR Group<br>(N = 1012) | FFR Group<br>(N = 1007) | P Value |
|-------------------------------------------------------------------------------------------|-------------------------|-------------------------|---------|
| Radial-artery approach — no. of patients (%)                                              | 841 (83.1)              | 811 (80.5)              | 0.13    |
| Contrast material used per patient — ml                                                   |                         |                         | 0.10    |
| Median                                                                                    | 110                     | 115                     |         |
| Interquartile range                                                                       | 80–155                  | 80–160                  |         |
| Procedure time — min†                                                                     |                         |                         | 0.09    |
| Median                                                                                    | 50.8                    | 53.1                    |         |
| Interquartile range                                                                       | 13.8–87.8               | 18.1–88.1               |         |
| Fluoroscopy time — min                                                                    |                         |                         | 0.57    |
| Median                                                                                    | 10.5                    | 10.2                    |         |
| Interquartile range                                                                       | 6.3–16.8                | 6.5–16.0                |         |
| Intravenous adenosine administered — no. of patients (%)                                  | NA                      | 695 (69.0)              |         |
| Total no. of lesions evaluated                                                            | 1568                    | 1436                    |         |
| No. of lesions evaluated per patient                                                      | 1.55±0.86               | 1.43±0.70               | 0.002   |
| Hemodynamically important lesions — no. (% of total lesions evaluated)‡                   | 457 (29.1)              | 528 (36.8)              | <0.001  |
| No. of hemodynamically important lesions per patient‡                                     | 0.45±0.71               | 0.52±0.68               | 0.05    |
| Mean iFR                                                                                  | 0.91±0.10               | NA                      |         |
| Mean iFR in hemodynamically important lesions‡                                            | 0.80±0.13               | NA                      |         |
| Mean FFR                                                                                  | NA                      | 0.82±0.10               |         |
| Mean FFR in hemodynamically important lesions‡                                            | NA                      | 0.72±0.08               |         |
| Lesion complexity according to the ACC–AHA class — no./total no. of treated lesions (%)§¶ |                         |                         | 0.73    |
| A                                                                                         | 61/915 (6.7)            | 73/980 (7.4)            |         |
| B1                                                                                        | 304/915 (33.2)          | 320/980 (32.7)          |         |
| B2                                                                                        | 284/915 (31.0)          | 300/980 (30.6)          |         |
| C                                                                                         | 139/915 (15.2)          | 165/980 (16.8)          |         |
| Missing data                                                                              | 127/915 (13.9)          | 122/980 (12.4)          |         |
| Lesions treated in the vessel — no./total no. of treated lesions (%)¶                     |                         |                         | 0.68    |
| Left main coronary artery                                                                 | 14/915 (1.5)            | 16/980 (1.6)            |         |
| Left anterior descending artery                                                           | 434/915 (47.4)          | 469/980 (47.9)          |         |
| Left circumflex artery                                                                    | 176/915 (19.2)          | 179/980 (18.3)          |         |
| Right coronary artery                                                                     | 164/915 (17.9)          | 196/980 (20.0)          |         |
| Missing data                                                                              | 127/915 (13.9)          | 120/980 (12.2)          |         |
| Total no. of stents placed                                                                | 698                     | 787                     |         |
| No. of stents placed per patient undergoing PCI                                           | 1.58±1.08               | 1.73±1.19               | 0.05    |
| Stent length per patient — mm                                                             | 34.2±21.9               | 36.8±24.5               | 0.10    |
| Stent diameter — mm                                                                       | 2.97±0.47               | 3.01±0.49               | 0.27    |
| Drug-eluting stents placed — no. (% of total stents placed)                               | 696 (99.7)              | 770 (97.8)              | 0.50    |
| PCI as primary revascularization procedure — no. of patients (%)                          | 443 (43.8)              | 456 (45.3)              | 0.50    |
| CABG as primary revascularization procedure — no. of patients (%)                         | 93 (9.2)                | 113 (11.2)              | 0.13    |
| Revascularization performed — no. of patients (%)                                         | 536 (53.0)              | 569 (56.5)              | 0.11    |

**DEHEART**  
cardiologist

; 376(19):1813-1823

## iFR: a new diagnostic tool for the interventional cardiologist

*Göteborg M, et al NEJM. 2017; 376(19):1813-1823*



**Table 3. End Points at 12 Months in the Per-Protocol Population.**

| End Point                                                                                               | iFR Group<br>(N=1012)<br><br>no. (%) | FFR Group<br>(N=1007)<br><br>no. (%) | Hazard Ratio<br>(95% CI) | P Value |
|---------------------------------------------------------------------------------------------------------|--------------------------------------|--------------------------------------|--------------------------|---------|
| Primary end point: death from any cause, nonfatal myocardial infarction, or unplanned revascularization | 68 (6.7)                             | 61 (6.1)                             | 1.12 (0.79–1.58)         | 0.53    |
| Death from any cause                                                                                    | 15 (1.5)                             | 12 (1.2)                             | 1.25 (0.58–2.66)         | 0.57    |
| Nonfatal myocardial infarction                                                                          | 22 (2.2)                             | 17 (1.7)                             | 1.29 (0.68–2.44)         | 0.42    |
| Unplanned revascularization                                                                             | 47 (4.6)                             | 46 (4.6)                             | 1.04 (0.69–1.57)         | 0.84    |
| Target-lesion revascularization                                                                         | 29 (2.9)                             | 27 (2.7)                             | 1.21 (0.70–2.07)         | 0.49    |
| Restenosis                                                                                              | 19 (1.9)                             | 18 (1.8)                             | 1.05 (0.55–2.01)         | 0.87    |
| Stent thrombosis*                                                                                       | 1 (0.1)                              | 2 (0.2)                              |                          |         |
| Chest discomfort during procedure                                                                       |                                      |                                      |                          | <0.001† |
| None                                                                                                    | 982 (97.0)                           | 319 (31.7)                           |                          |         |
| Mild                                                                                                    | 26 (2.6)                             | 316 (31.4)                           |                          |         |
| Moderate                                                                                                | 2 (0.2)                              | 285 (28.3)                           |                          |         |
| Severe                                                                                                  | 2 (0.2)                              | 87 (8.6)                             |                          |         |

\* Stent thrombosis was defined as the presence of stent occlusion on angiography and an acute clinical presentation.

† P value was calculated by means of the Wilcoxon rank-sum test.

# The most important late breaking clinical trials

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## New evidences about PFO occlusion

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*Saver JL, et al. NEJM. 2017;377(11):1022-1032.*

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## Management of triple therapy in ischemic cardiomyopathy

*RE-DUAL PCI, Cannon CP NEJM. 2017.*

## First evidence of anti-inflammatory therapy in CAD

*CANTOS, Ridker PM, NEJM, 2017 21;377(12):1119-1131.*

**Table 1. Baseline Characteristics of the Patients.\***

| Characteristic                                 | Dual Therapy<br>with Dabigatran,<br>110 mg<br>(N = 981) | Triple Therapy<br>with Warfarin<br>(N = 981) | Dual Therapy<br>with Dabigatran,<br>150 mg<br>(N = 763) | Corresponding<br>Triple Therapy<br>with Warfarin†<br>(N = 764) |
|------------------------------------------------|---------------------------------------------------------|----------------------------------------------|---------------------------------------------------------|----------------------------------------------------------------|
| Age — yr                                       | 71.5±8.9                                                | 71.7±8.9                                     | 68.6±7.7                                                | 68.8±7.7                                                       |
| Elderly age group — no. (%)‡                   | 225 (22.9)                                              | 225 (22.9)                                   | 8 (1.0)                                                 | 8 (1.0)                                                        |
| Male sex — no. (%)                             | 728 (74.2)                                              | 750 (76.5)                                   | 592 (77.6)                                              | 594 (77.7)                                                     |
| Diabetes mellitus — no./total no. (%)          | 362/981 (36.9)                                          | 371/980 (37.9)                               | 260/763 (34.1)                                          | 303/763 (39.7)                                                 |
| Previous stroke — no./total no. (%)            | 74/981 (7.5)                                            | 100/980 (10.2)                               | 52/763 (6.8)                                            | 77/763 (10.1)                                                  |
| CHA <sub>2</sub> DS <sub>2</sub> -VASc score§  | 3.7±1.6                                                 | 3.8±1.5                                      | 3.3±1.5                                                 | 3.6±1.5                                                        |
| HAS-BLED score¶                                | 2.7±0.7                                                 | 2.8±0.8                                      | 2.6±0.7                                                 | 2.7±0.8                                                        |
| Creatinine clearance — ml/min                  | 76.3±28.9                                               | 75.4±29.1                                    | 83.7±31.0                                               | 81.3±29.6                                                      |
| Previous myocardial infarction — no. (%)       | 237 (24.2)                                              | 268 (27.3)                                   | 194 (25.4)                                              | 211 (27.6)                                                     |
| Previous PCI — no./total no. (%)               | 326/981 (33.2)                                          | 347/980 (35.4)                               | 239/763 (31.3)                                          | 272/763 (35.6)                                                 |
| Previous CABG — no./total no. (%)              | 97/981 (9.9)                                            | 111/980 (11.3)                               | 79/763 (10.4)                                           | 87/763 (11.4)                                                  |
| Type of atrial fibrillation — no./total no (%) |                                                         |                                              |                                                         |                                                                |
| Persistent                                     | 174/981 (17.7)                                          | 178/980 (18.2)                               | 132/763 (17.3)                                          | 149/763 (19.5)                                                 |
| Permanent                                      | 320/981 (32.6)                                          | 318/980 (32.4)                               | 250/763 (32.8)                                          | 238/763 (31.2)                                                 |
| Paroxysmal                                     | 487/981 (49.6)                                          | 484/980 (49.4)                               | 380/763 (49.8)                                          | 376/763 (49.3)                                                 |
| Indication for PCI — no. (%)                   |                                                         |                                              |                                                         |                                                                |
| Stable angina or positive stress test          | 433 (44.1)                                              | 429 (43.7)                                   | 320 (41.9)                                              | 339 (44.4)                                                     |
| Acute coronary syndrome                        | 509 (51.9)                                              | 475 (48.4)                                   | 391 (51.2)                                              | 369 (48.3)                                                     |
| Staged procedure                               | 156 (15.9)                                              | 168 (17.1)                                   | 138 (18.1)                                              | 134 (17.5)                                                     |
| Other                                          | 43 (4.4)                                                | 62 (6.3)                                     | 65 (8.5)                                                | 50 (6.5)                                                       |
| Type of stent — no./total no. (%)              |                                                         |                                              |                                                         |                                                                |
| Drug-eluting                                   | 804/979 (82.1)                                          | 826/976 (84.6)                               | 621/762 (81.5)                                          | 638/759 (84.1)                                                 |
| Bare-metal                                     | 148/979 (15.1)                                          | 133/976 (13.6)                               | 123/762 (16.1)                                          | 107/759 (14.1)                                                 |
| Drug-eluting and bare-metal                    | 19/979 (1.9)                                            | 12/976 (1.2)                                 | 10/762 (1.3)                                            | 9/759 (1.2)                                                    |
| Other                                          | 8/979 (0.8)                                             | 5/976 (0.5)                                  | 8/762 (1.0)                                             | 5/759 (0.7)                                                    |

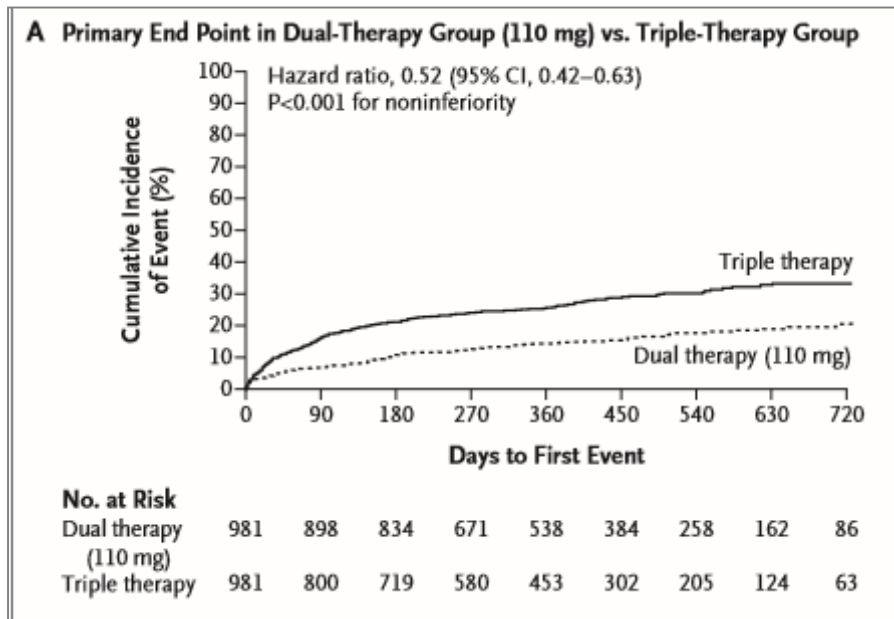
# RE-DUAL PCI trial

## Management of triple therapy in ischemic cardiomyopathy

*Dual Antithrombotic Therapy with Dabigatran after PCI in Atrial Fibrillation,*

*Cannon C.P. et al, NEJM. 2017*

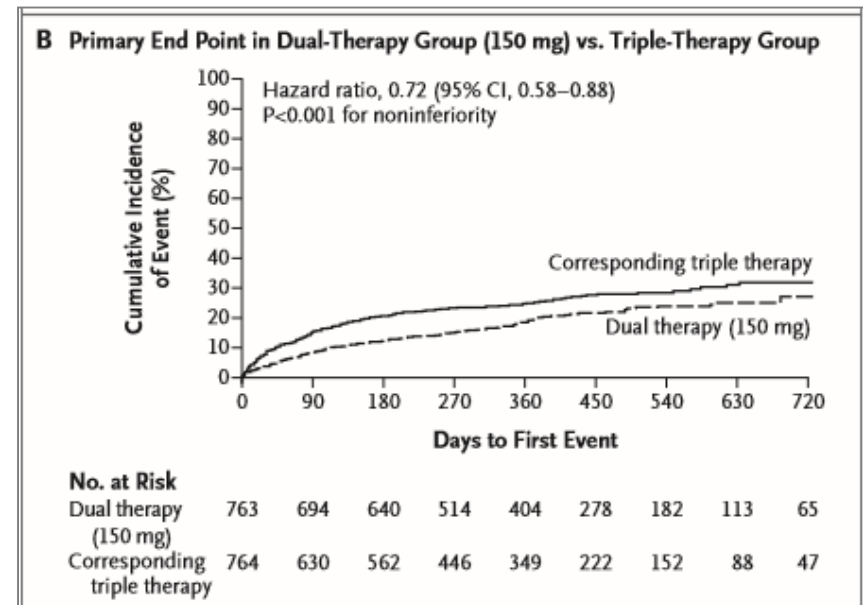
**Primary end point: major or clinically relevant nonmajor bleeding event**



**DUAL (110 mg) vs TRIPLE THERAPY**

**15.4% vs 26.9%**

**SUPERIORITY**



**DUAL (150 mg) vs TRIPLE THERAPY**

**20.2% vs 25.7%**

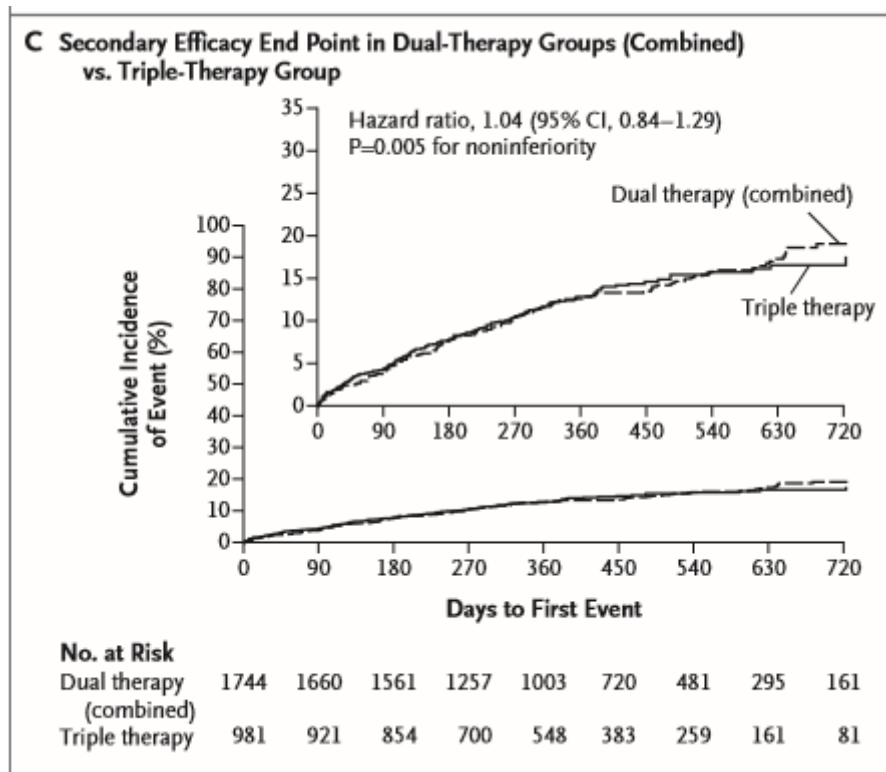
**NONINFERIORITY**

## Management of triple therapy in ischemic cardiomyopathy

*Dual Antithrombotic Therapy with Dabigatran after PCI in Atrial Fibrillation,*

*Cannon C.P. et al, NEJM. 2017*

**Secondary Efficacy end-point:** composite of thromboembolic events, death, revascularization



### SIMILAR RATE OF SERIOUS ADVERSE EVENTS

42.7% 110-mg dual-therapy group (3.9% fatal)  
39.6% 150-mg dual-therapy group (3.2% fatal)  
41.8% triple-therapy group (4.3% fatal)

**DUAL (110 and 150 mg) vs TRIPLE THERAPY**

**13.7% vs 13.4%**

**NONINFERIORITY**

# RE-DUAL PCI trial

**Table 3. Efficacy End Points.\***

| End Point                                                                                  | Dual Therapy with Dabigatran (Combined) vs. Triple Therapy with Warfarin |                              |                       |                                 | Dual Therapy with Dabigatran (110 mg) vs. Triple Therapy with Warfarin |                              |                       |          | Dual Therapy with Dabigatran (150 mg) vs. Triple Therapy with Warfarin |                                            |                       |          |
|--------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|------------------------------|-----------------------|---------------------------------|------------------------------------------------------------------------|------------------------------|-----------------------|----------|------------------------------------------------------------------------|--------------------------------------------|-----------------------|----------|
|                                                                                            | Combined Dual-Therapy Groups (N=1744)                                    | Triple-Therapy Group (N=981) | Hazard Ratio (95% CI) | P Value†                        | 110-mg Dual-Therapy Group (N=981)                                      | Triple-Therapy Group (N=981) | Hazard Ratio (95% CI) | P Value† | 150-mg Dual-Therapy Group (N=763)                                      | Corresponding Triple-Therapy Group (N=764) | Hazard Ratio (95% CI) | P Value† |
|                                                                                            | no. (%)                                                                  |                              |                       |                                 | no. (%)                                                                |                              |                       |          | no. (%)                                                                |                                            |                       |          |
| Composite efficacy end point: thromboembolic events, death, or unplanned revascularization | 239 (13.7)                                                               | 131 (13.4)                   | 1.04 (0.84–1.29)      | 0.74 (0.005 for noninferiority) | 149 (15.2)                                                             | 131 (13.4)                   | 1.13 (0.90–1.43)      | 0.30     | 90 (11.8)                                                              | 98 (12.8)                                  | 0.89 (0.67–1.19)      | 0.44     |
| Thromboembolic events or death                                                             | 168 (9.6)                                                                | 83 (8.5)                     | 1.17 (0.90–1.53)      | 0.25 (0.11 for noninferiority)  | 108 (11.0)                                                             | 83 (8.5)                     | 1.30 (0.98–1.73)      | 0.07     | 60 (7.9)                                                               | 60 (7.9)                                   | 0.97 (0.68–1.39)      | 0.88     |
| Death                                                                                      |                                                                          |                              |                       |                                 | 55 (5.6)                                                               | 48 (4.9)                     | 1.12 (0.76–1.65)      | 0.56     | 30 (3.9)                                                               | 35 (4.6)                                   | 0.83 (0.51–1.34)      | 0.44     |
| Myocardial infarction                                                                      |                                                                          |                              |                       |                                 | 44 (4.5)                                                               | 29 (3.0)                     | 1.51 (0.94–2.41)      | 0.09     | 26 (3.4)                                                               | 22 (2.9)                                   | 1.16 (0.66–2.04)      | 0.61     |
| Stroke                                                                                     |                                                                          |                              |                       |                                 | 17 (1.7)                                                               | 13 (1.3)                     | 1.30 (0.63–2.67)      | 0.48     | 9 (1.2)                                                                | 8 (1.0)                                    | 1.09 (0.42–2.83)      | 0.85     |
| Definite stent thrombosis                                                                  |                                                                          |                              |                       |                                 | 15 (1.5)                                                               | 8 (0.8)                      | 1.86 (0.79–4.40)      | 0.15     | 7 (0.9)                                                                | 7 (0.9)                                    | 0.99 (0.35–2.81)      | 0.98     |

# The most important late breaking clinical trials

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## New evidences about PFO occlusion

*Søndergaard L, et al. NEJM. 2017;377(11):1033-1042.*

*Saver JL, et al. NEJM. 2017;377(11):1022-1032.*

*Meier B, et al. NEJM 2017; 377(11):1011-1021.*

## Lack of efficacy of bivalirudine administration in ACS

*Erlinge D, et al. NEJM 2017 ;377(12):1132-1142*

## Temporary Twilight of the ABSORB

*AIDA Trial Wykrzykowska JJ, et al NEJM. 2017;376(24):2319-2328.*

## iFR: a new diagnostic tool for the interventional cardiologist

*iFR Swedheart, Götberg M, et al NEJM. 2017; 376(19):1813-1823*

*Davies JE et al. NEJM. 2017; 376(19):1824-1834.*

## Management of triple therapy in ischemic cardiomyopathy

*RE-DUAL PCI, Cannon CP NEJM. 2017.*

## First evidence of anti-inflammatory therapy in CAD

*CANTOS, Ridker PM, NEJM, 2017 21;377(12):1119-1131.*

## First evidence of anti-inflammatory therapy in CAD

*Antiinflammatory Therapy with Canakinumab for Atherosclerotic Disease,  
Ridker P.M. et al NEJM. 2017; 377(12):1119-1131*

**10061 patients**

with previous MI and a high-sensitivity C-reactive protein level of ( $> 2$  mg/l)

**1 : 1 : 1 : 1,5 randomization**

**CANAKINUMAB**

*(therapeutic monoclonal antibody targeting IL-1 $\beta$ )*

- 50 mg
  - 150 mg
  - 300 mg
- } administered subcutaneously every 3 months

**versus PLACEBO**

**Table 1. Characteristics of the Trial Participants.\***

| Characteristic                                            | Placebo Group<br>(N = 3344) | Canakinumab             |
|-----------------------------------------------------------|-----------------------------|-------------------------|
|                                                           |                             | All Doses<br>(N = 6717) |
| Age — yr                                                  | 61.1±10.0                   | 61.1±10.1               |
| Female sex — no. (%)                                      | 865 (25.9)                  | 1722 (25.6)             |
| Current smoking — no. (%)                                 | 765 (22.9)                  | 1601 (23.8)             |
| Median body-mass index (IQR)                              | 29.7 (26.6–33.8)            | 29.9 (26.6–33.8)        |
| Hypertension — no. (%)                                    | 2644 (79.1)                 | 5364 (79.9)             |
| Diabetes — no. (%)                                        | 1333 (39.9)                 | 2696 (40.1)             |
| Qualifying myocardial infarction — no. (%)                |                             |                         |
| STEMI                                                     | 1807 (54.0)                 | 3675 (54.7)             |
| Non-STEMI                                                 | 1132 (33.9)                 | 2252 (33.5)             |
| Unknown type or missing data                              | 405 (12.1)                  | 790 (11.8)              |
| History of PCI — no. (%)                                  | 2192 (65.6)                 | 4518 (67.3)             |
| History of CABG — no. (%)                                 | 469 (14.0)                  | 942 (14.0)              |
| History of congestive heart failure — no. (%)             | 721 (21.6)                  | 1452 (21.6)             |
| Lipid-lowering therapy — no./total no. (%)                | 3132/3344 (93.7)            | 6265/6708 (93.4)        |
| Statin — no./total no. (%)                                | 3045/3344 (91.1)            | 6112/6708 (91.1)        |
| Renin-angiotensin inhibitor — no./total no. (%)           | 2665/3338 (79.8)            | 5327/6693 (79.6)        |
| Anti-ischemia agent — no./total no. (%):‡                 | 3080/3344 (92.1)            | 6111/6708 (91.1)        |
| Antithrombotic agent or anticoagulant — no./total no. (%) | 3188/3344 (95.3)            | 6365/6708 (94.9)        |
| Median high-sensitivity CRP level (IQR) — mg/liter        | 4.10 (2.75–6.85)            | 4.20 (2.80–7.10)        |
| Median interleukin-6 level (IQR) — ng/liter               | 2.61 (1.80–4.06)            | 2.56 (1.77–4.13)        |
| Median total cholesterol level (IQR) — mg/dl              | 161 (137–190)               | 160 (136–189)           |
| Median LDL cholesterol level (IQR) — mg/dl                | 82.8 (64.2–107.5)           | 82.0 (63.0–106.7)       |
| Median HDL cholesterol level (IQR) — mg/dl                | 44.5 (37.1–52.6)            | 43.7 (36.7–52.2) †      |
| Median triglyceride level (IQR) — mg/dl                   | 139 (100–194)               | 139 (102–196)           |
| Median estimated GFR (IQR) — ml/min/1.73 m <sup>2</sup>   | 79.0 (65.0–93.0)            | 78.5 (64.0–93.0)        |
| Lost to follow-up — no. (%)                               | 9 (0.3)                     | 18 (0.3)                |

## First evidence of anti-inflammatory therapy in CAD

*Antiinflammatory Therapy with Canakinumab for Atherosclerotic Disease, Ridker P.M. et al NEJM. 2017; 377(12):1119-1131*

### EFFECTS of CANAKINUMAB at 48 months

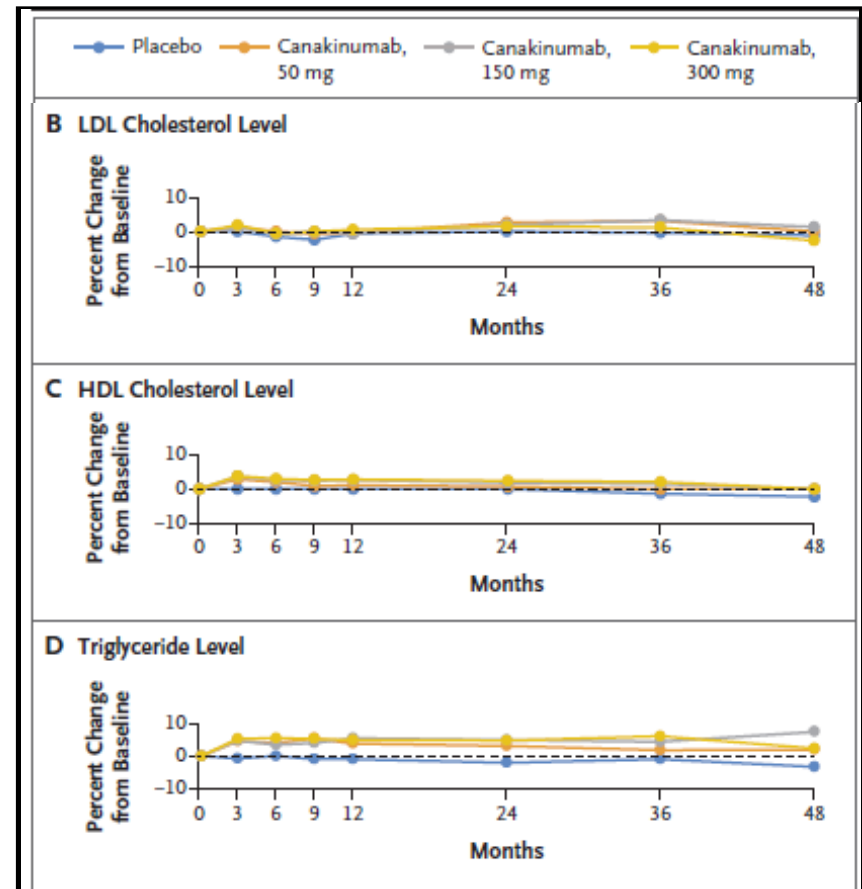
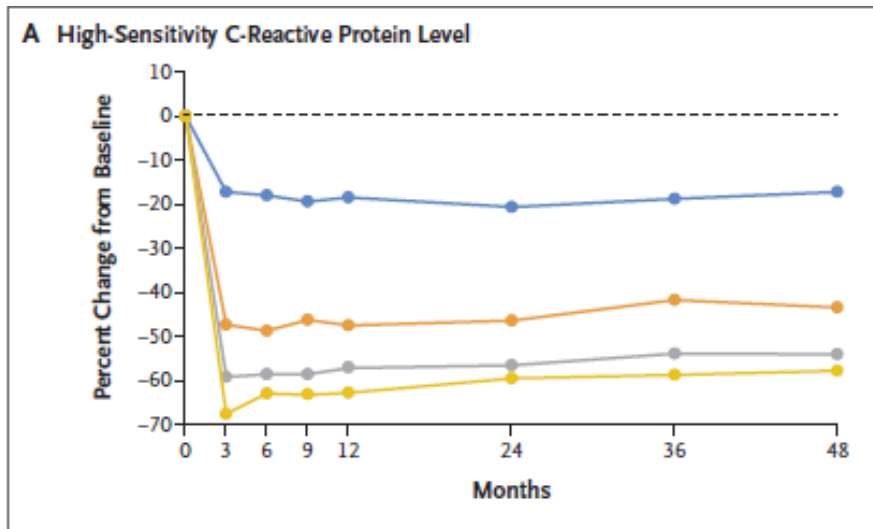
#### Reduction from baseline CPR

26% 50-mg dose group

37% 150-mg dose group

41% 300-mg dose group

#### No effects on cholesterol levels

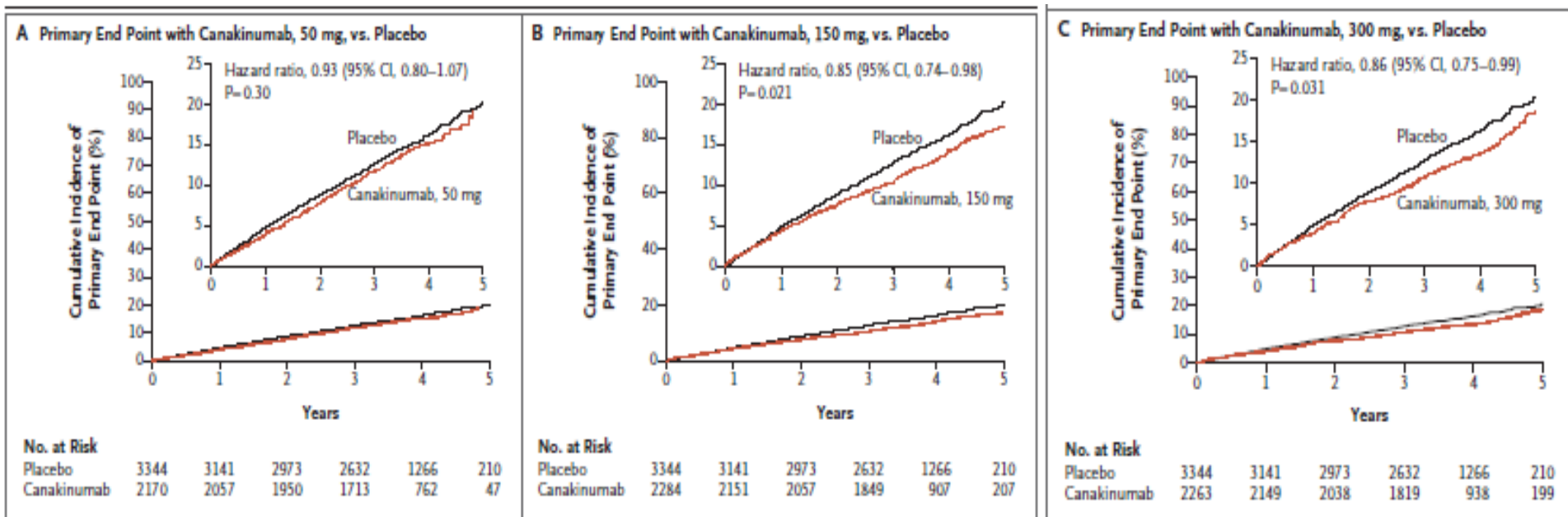


# CANTOS trial

## First evidence of anti-inflammatory therapy in CAD

*Antiinflammatory Therapy with Canakinumab for Atherosclerotic Disease, Ridker P.M. et al NEJM. 2017; 377(12):1119-1131*

**Primary Efficacy End Point:** nonfatal myocardial infarction, nonfatal stroke, or CV death



50 mg  
NOT SIGNIFICANT

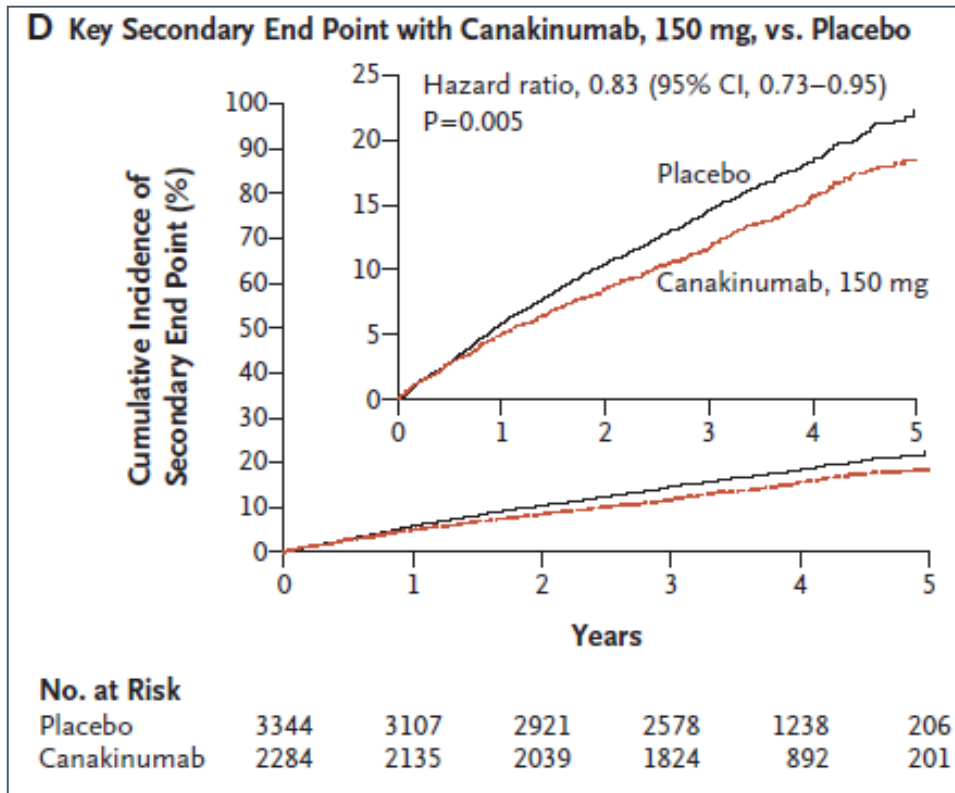
150 mg  
NOT SIGNIFICANT

300 mg  
P=0,031

## First evidence of anti-inflammatory therapy in CAD

*Antiinflammatory Therapy with Canakinumab for Atherosclerotic Disease, Ridker P.M. et al NEJM. 2017; 377(12):1119-1131*

Secondary end point: nonfatal myocardial infarction, nonfatal stroke, or CV death + hospitalization for unstable angina that led to urgent revascularization



Canakinumab was associated with a higher incidence of fatal infection than placebo (p=0,02)

No significant difference in all-cause mortality