

# Meta-analysis of iFR-SWEDEHEART and DEFINE-FLAIR

Five-year major cardiovascular events are increased when coronary revascularization is guided by instantaneous wave-free ratio compared to fractional flow reserve: a pooled analysis of iFR-SWEDEHEART and DEFINE-FLAIR trials

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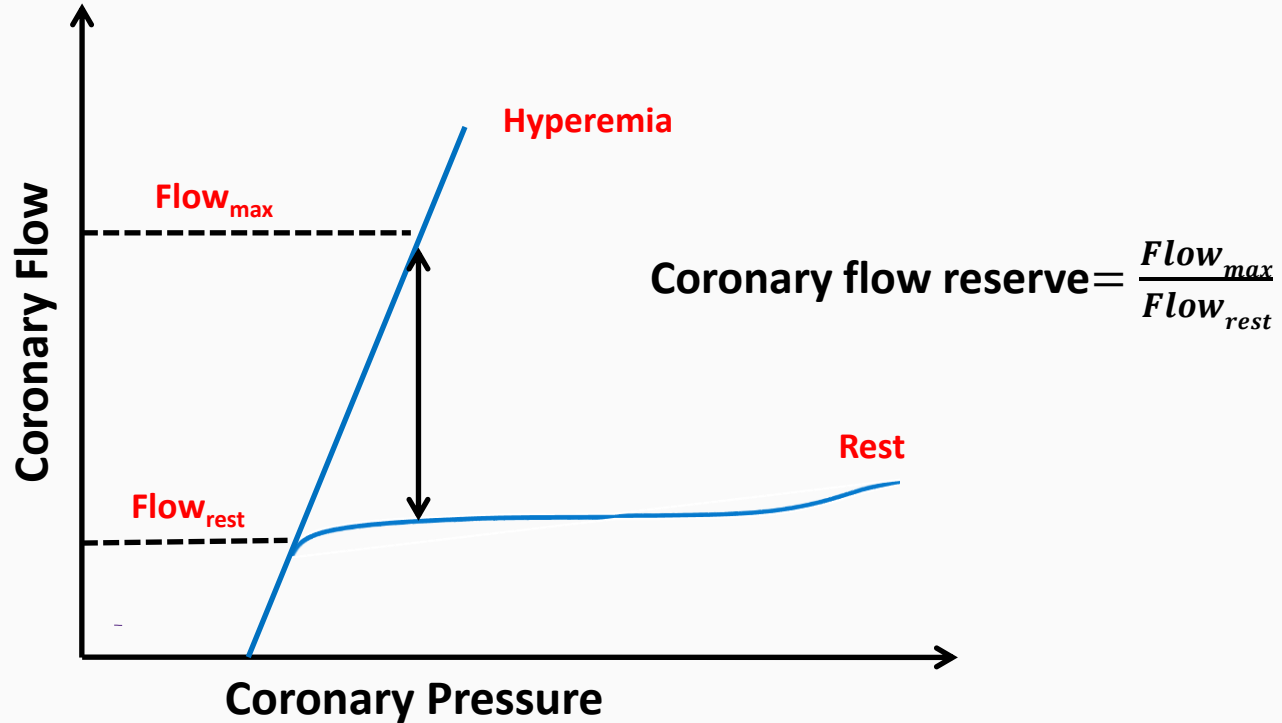
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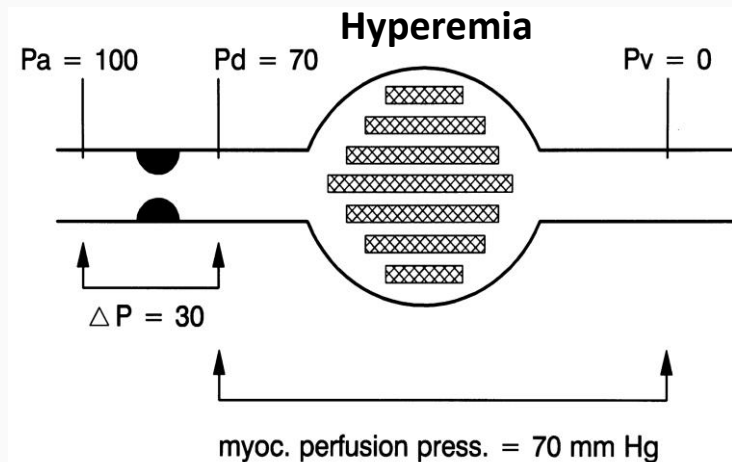
# Conflicts of interests

- I do not have any potential conflict of interest to declare

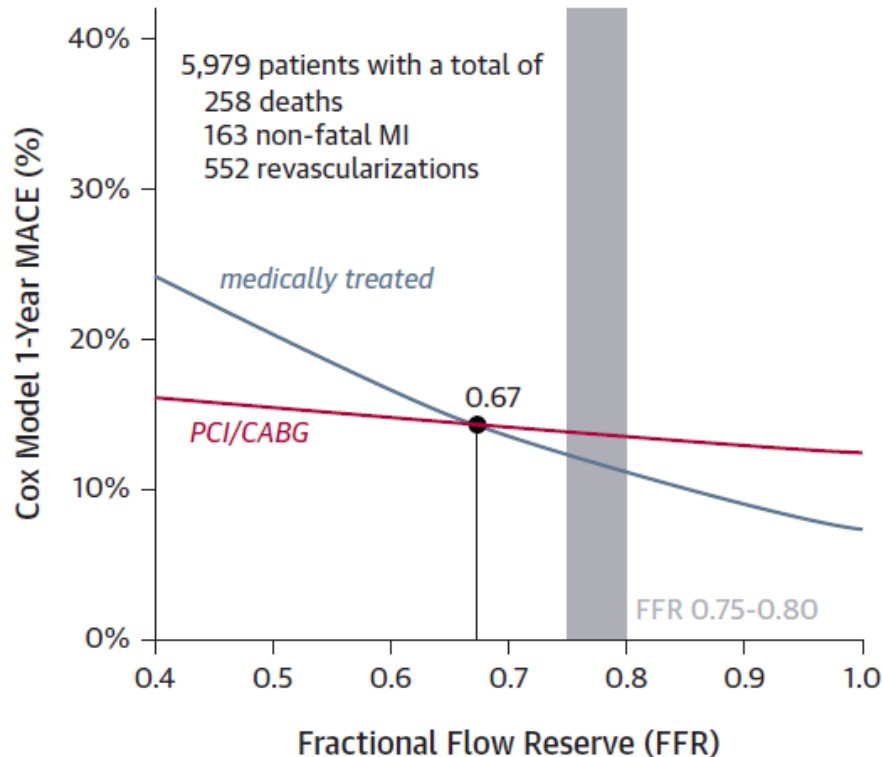
# Coronary Flow and Pressure



# Fractional flow reserve



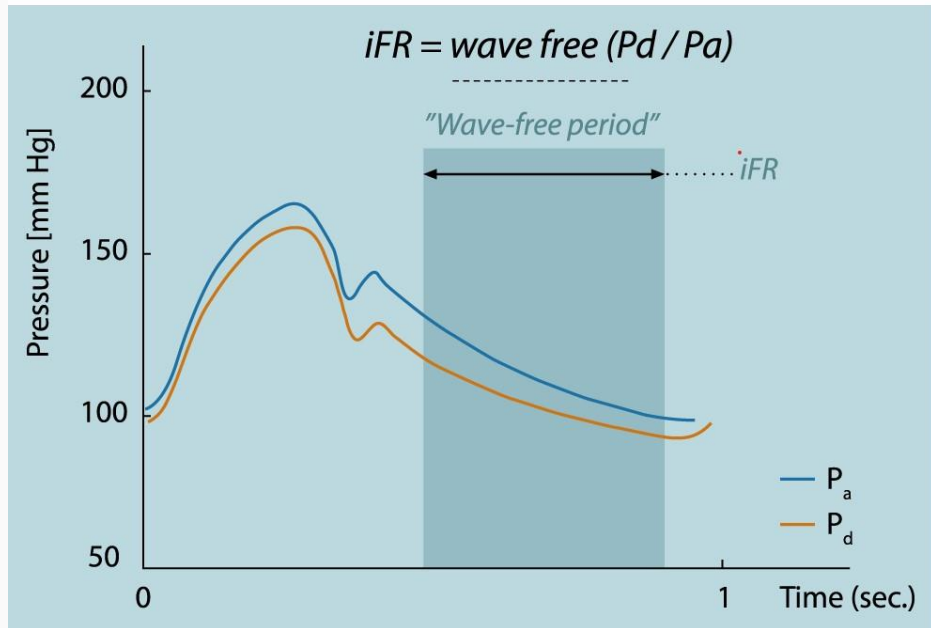
$$FFR = \frac{70 \text{ mmHg}}{100 \text{ mmHg}} = \mathbf{0.70}$$



Pijls N. et al. Circulation 1995

Johnson NP et al. JACC 2021

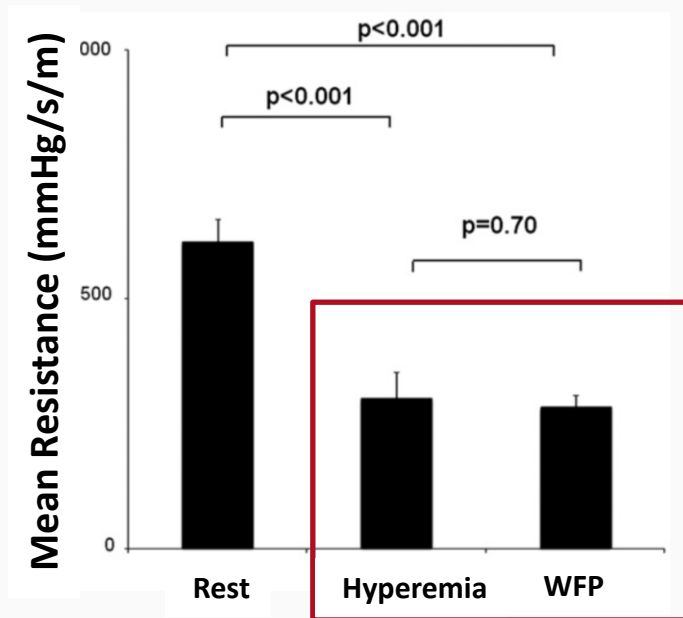
# Instantaneous wave-free ratio (iFR)



Minimum resistance during wave free period

$$iFR = \frac{Pd_{\text{wave free}}}{Pa_{\text{wave free}}}$$

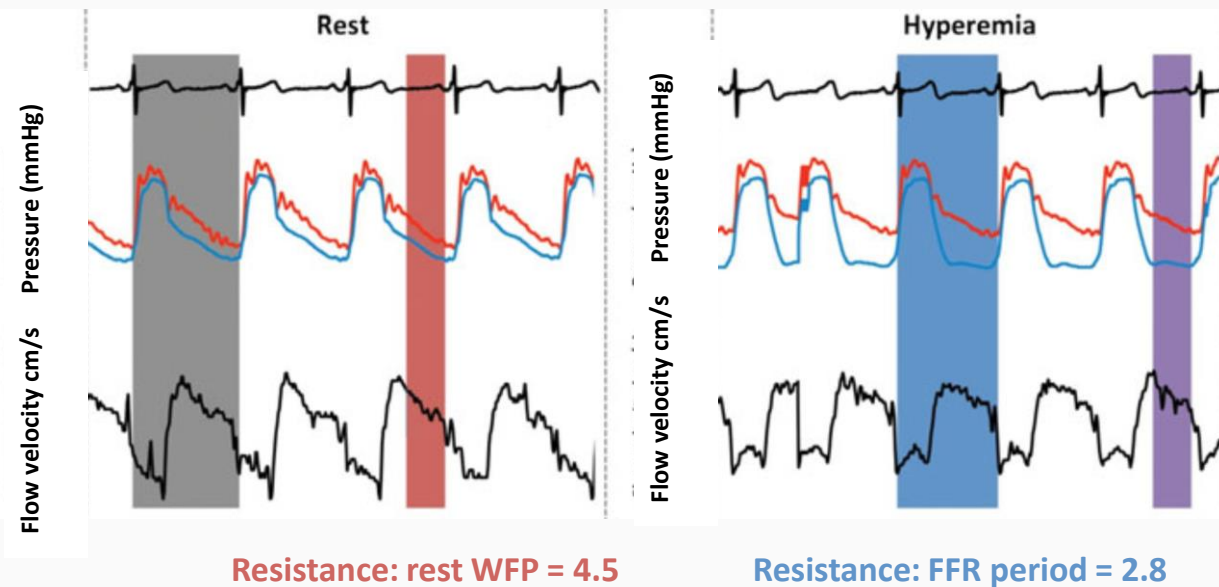
# Resistance during the wave-free period (WFP)



**"In the first part of this study, we identified the existence of a diastolic interval in which intracoronary resistance rest is equivalent to time-averaged resistance during FFR measurements."**

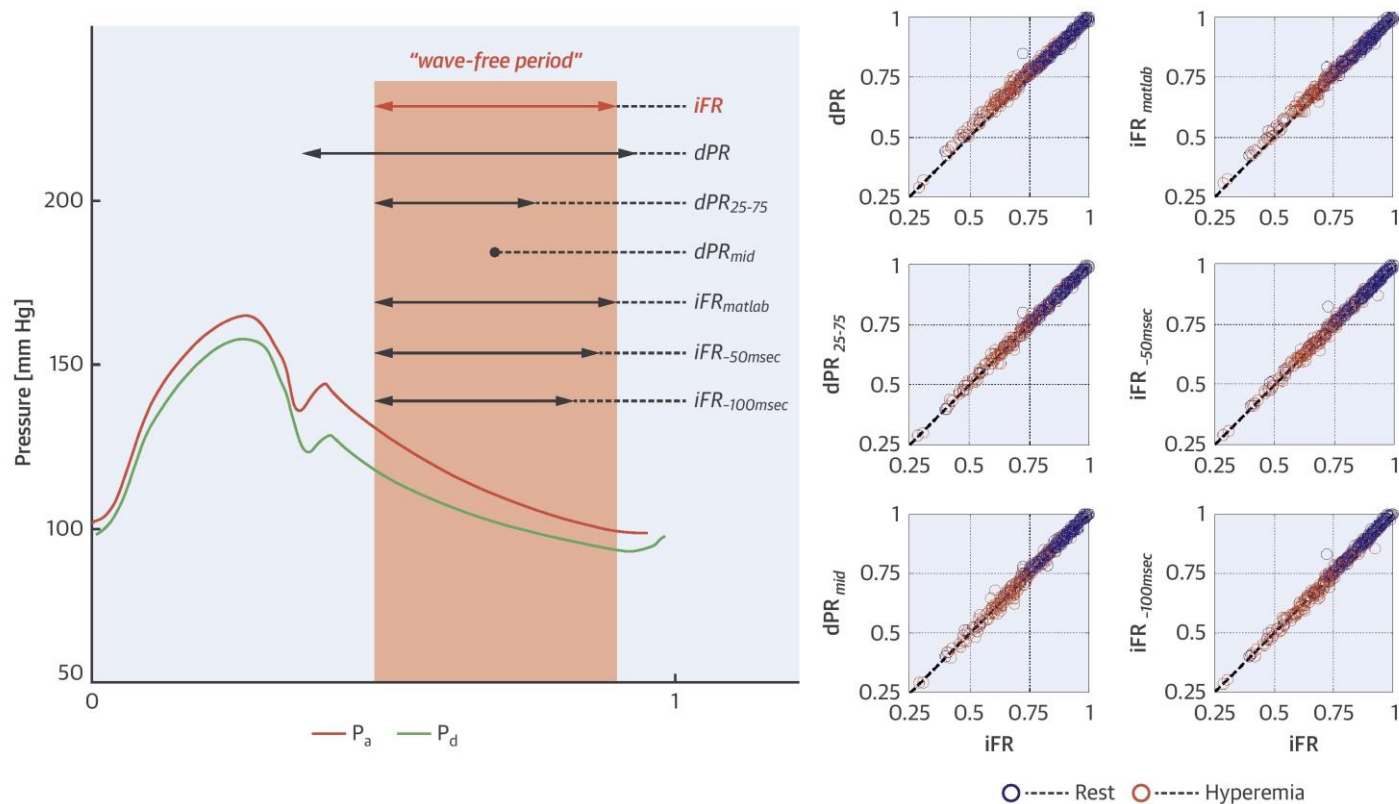
Sen S, JACC. 2012 Apr 10;59(15):1392-402. (Figure 5A and Methods text with *emphasis*)

# Resistance in WFP higher than hyperemic resistance

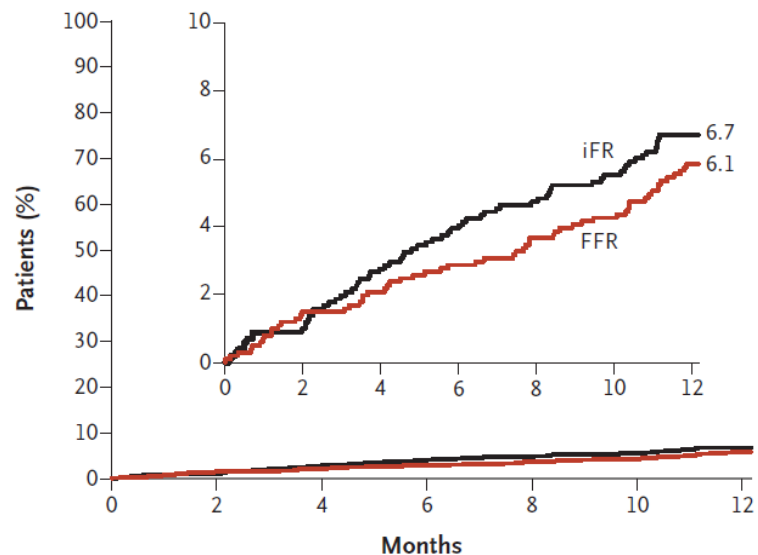


“A *natural incremental hierarchy exists* between the physiological states assessed: resting whole cycle, *resting wave-free period*, *hyperaemic whole cycle* and hyperaemic wave-free period physiology.”

# **CENTRAL ILLUSTRATION: Correlations and AUC Values >0.99 for All Resting Pd/Pa Ratios Over Different Periods in Diastole Compared With iFR as the Reference Standard**

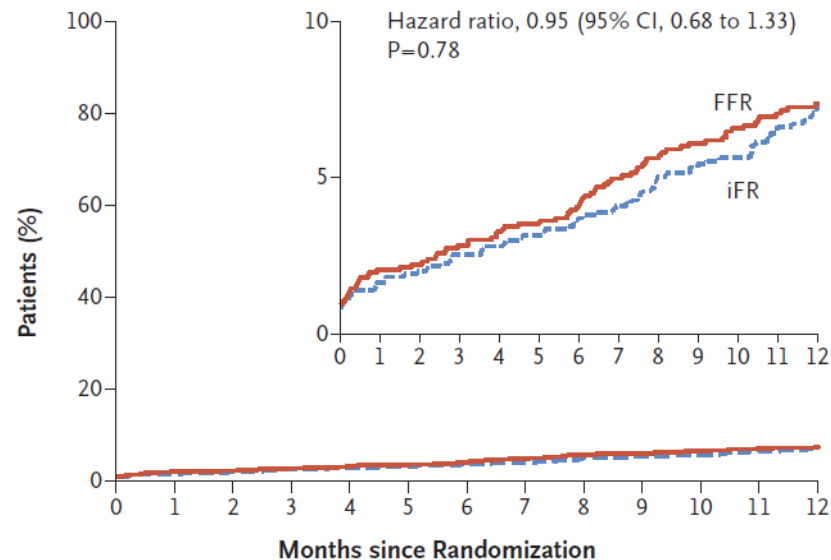


# DEFINE-FLAIR and iFR-SWEDEHEART – MACE 12 months



No. at Risk

|     |      |      |     |     |     |     |     |
|-----|------|------|-----|-----|-----|-----|-----|
| iFR | 1012 | 1002 | 984 | 971 | 963 | 956 | 944 |
| FFR | 1007 | 990  | 984 | 976 | 968 | 961 | 946 |



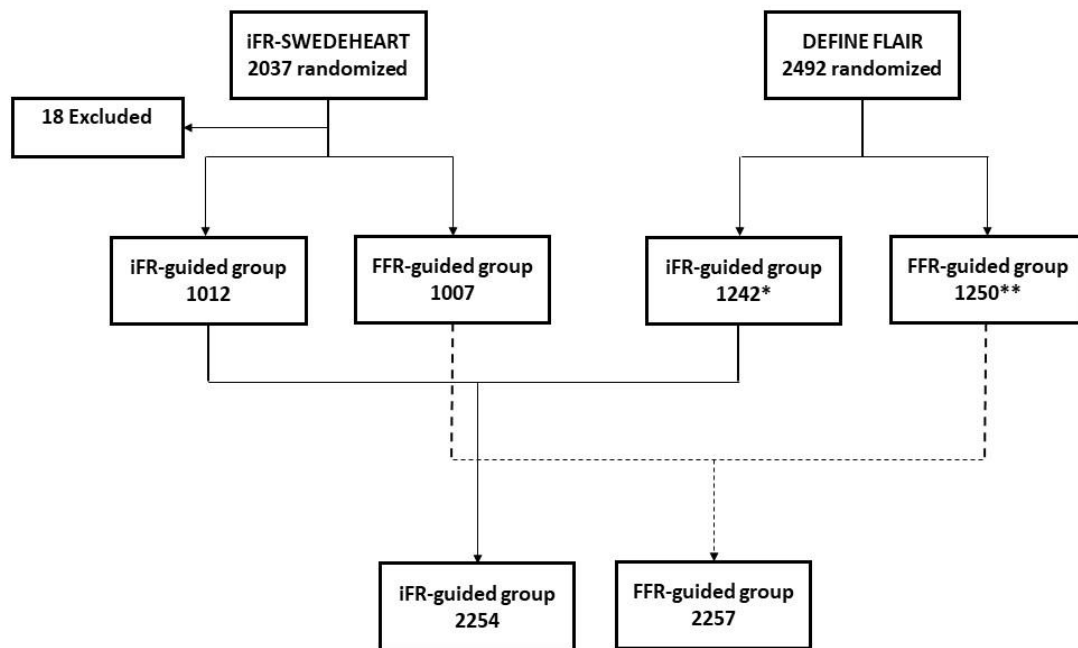
No. at Risk

|     |      |      |      |      |      |      |      |      |      |      |      |      |     |
|-----|------|------|------|------|------|------|------|------|------|------|------|------|-----|
| iFR | 1242 | 1149 | 1131 | 1122 | 1118 | 1111 | 1088 | 1052 | 1037 | 1027 | 1019 | 995  | 764 |
| FFR | 1250 | 1169 | 1156 | 1149 | 1144 | 1141 | 1119 | 1081 | 1066 | 1055 | 1046 | 1017 | 793 |

Göteborg M. et al. N Engl Med. 2017 May 11;376:1813-1823

Davies J. et al. N Engl Med. 2017 May 11;376:1824-1834

## Pooling of 5-year outcome data from iFR-SWEDEHEART and DEFINE-FLAIR



**Digitalizing 5-year KM-curves  
(Wei and Royston, Stata J 2017)**

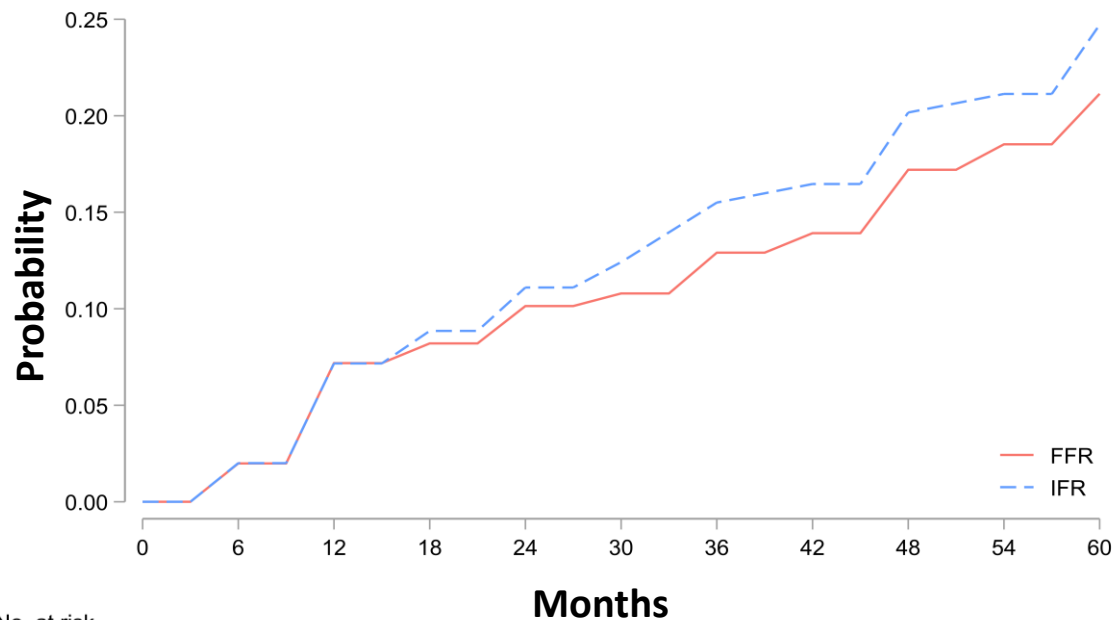
|                           | iFR Group<br>N = 2254 | FFR Group<br>N = 2257 |
|---------------------------|-----------------------|-----------------------|
| Age                       | 67.1±10               | 66.2±10               |
| Male gender               | 1718 (76)             | 1695 (75)             |
| Acute coronary syndrome   | 622 (28)              | 612 (27)              |
| Chronic coronary syndrome | 1618 (72)             | 1644 (73)             |
| CCS class                 |                       |                       |
| I                         | 500 (22)              | 426 (19)              |
| II                        | 729 (32)              | 713 (32)              |
| III                       | 176 (8)               | 228 (10)              |
| IV                        | 81 (4)                | 75 (3)                |
| Multivessel disease       | 869 (39)              | 887 (39)              |
| Diabetes                  | 614 (27)              | 589 (26)              |
| Hypertension              | 1603 (71)             | 1594 (71)             |
| Previous PCI              | 1008 (45)             | 1081 (48)             |
| Previous MI               | 695 (31)              | 711 (32)              |

# MACE

iFR 21.5 %

FFR 18.6 %

HR 1.18 95% CI[1.04; 1.34]



No. at risk

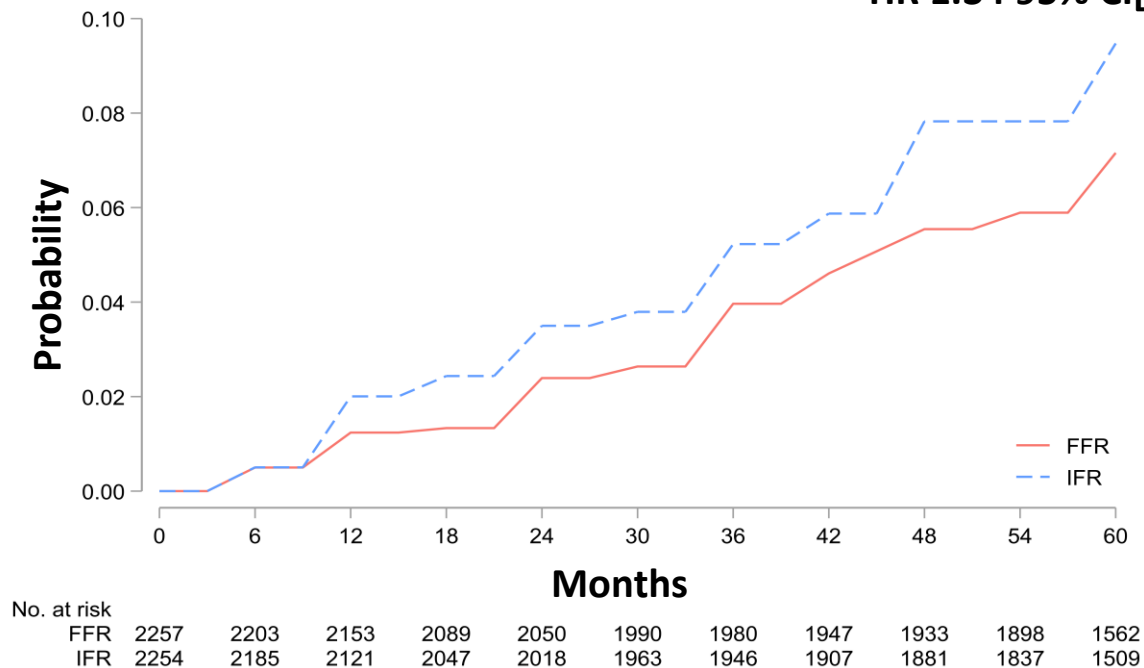
|     |      |      |      |      |      |      |      |      |      |      |      |
|-----|------|------|------|------|------|------|------|------|------|------|------|
| FFR | 2257 | 2164 | 2037 | 1910 | 1849 | 1789 | 1773 | 1726 | 1703 | 1631 | 1339 |
| iFR | 2254 | 2149 | 2011 | 1873 | 1824 | 1757 | 1731 | 1670 | 1647 | 1574 | 1275 |

# All-cause mortality

iFR 8.3 %

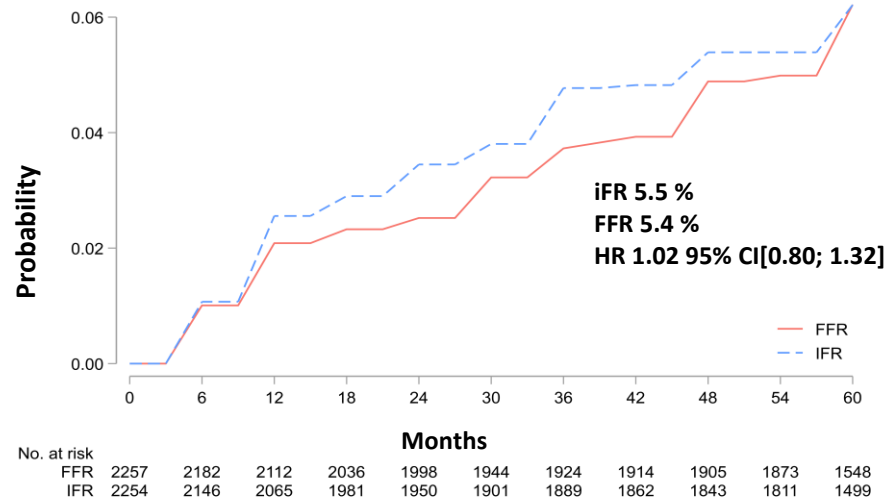
FFR 6.3 %

HR 1.34 95% CI[1.08; 1.67]

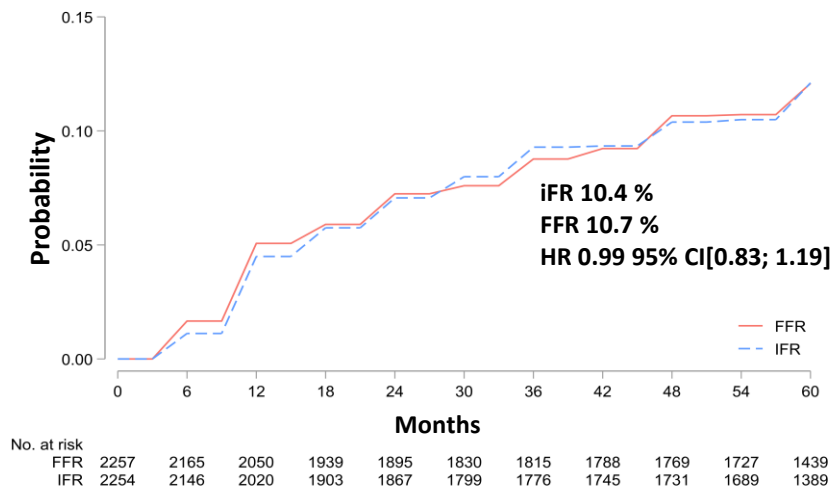


# Myocardial infarction and unplanned revascularization

## Myocardial infarction



## Unplanned revascularization



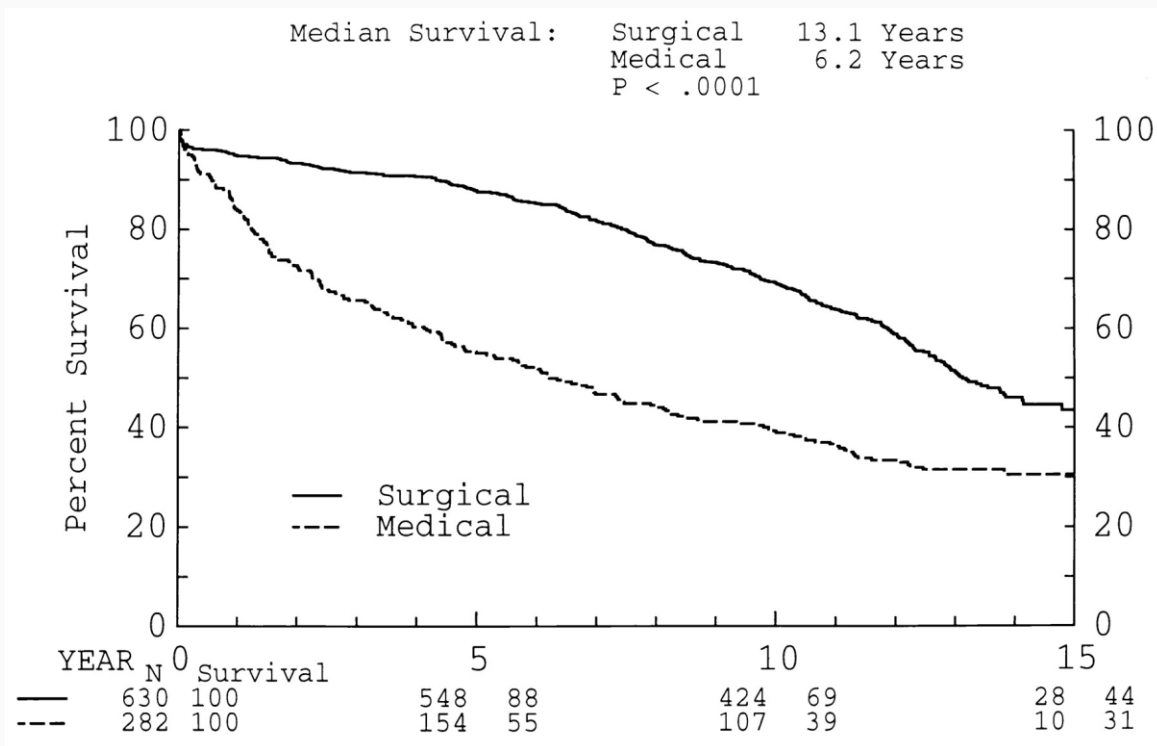
## Procedural data

|                   | iFR Group<br>N = 2254 | FFR Group<br>N = 2257 | RR<br>95% [CI]    |
|-------------------|-----------------------|-----------------------|-------------------|
| Mean FFR          | NA                    | 0.83±0.1              |                   |
| Mean iFR          | 0.91±0.1              | NA                    |                   |
| Revascularization | 1126 (50)             | 1236 (55)             | 0.91 [0.86; 0.96] |
| PCI               | 1008 (45)             | 1081 (48)             | 0.94 [0.75; 0.99] |
| Total stents      | 1520                  | 1693                  | 0.90 [0.84; 0.96] |
| CABG              | 118 (5)               | 155 (7)               | 0.86 [0.75; 0.99] |

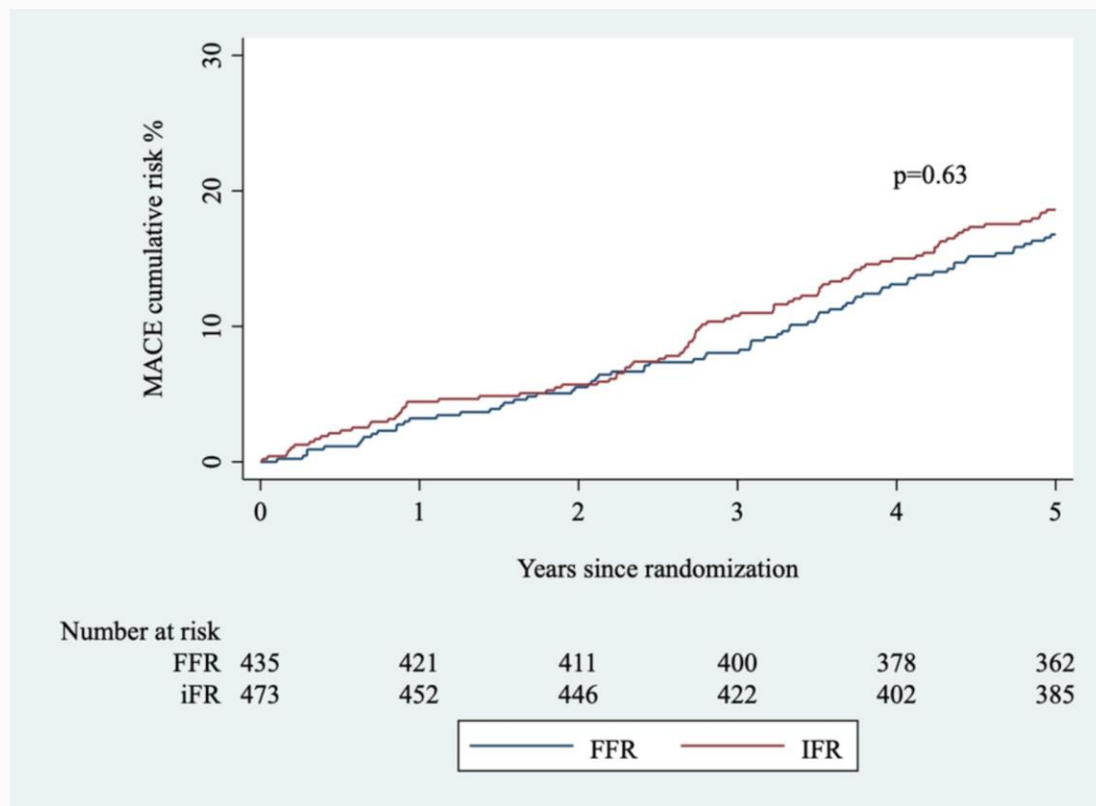
## Angio vs. physiology guided strategy

|                          | Physiology-guided strategy | Angio-guided strategy | Total treated vessels/patients |
|--------------------------|----------------------------|-----------------------|--------------------------------|
| iFR-SWEDEHEART (vessels) | 958 (50.6)                 | 937 (49.4)            | 1895 (100)                     |
| DEFINE-FLAIR (patients)  | 912 (72.6)                 | 345 (27.4)            | 1257 (100)                     |

# Prognostic value of LM/LAD-lesions



# Deferred cases – iFR-SWEDEHEART



# Summary and conclusion

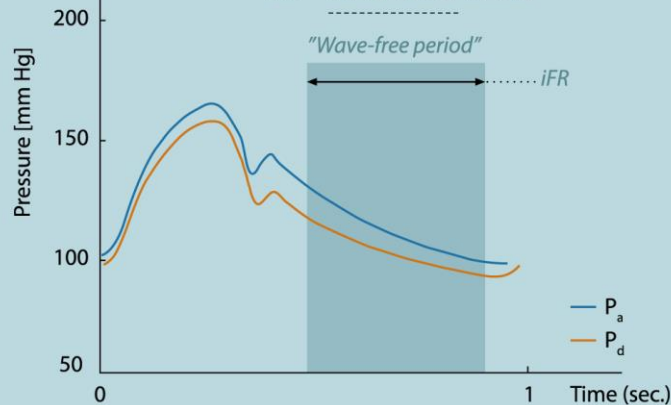
## PURPOSE

Evaluate clinical outcome of iFR vs. FFR guided PCI

Theoretical calculation of FFR and iFR

$$FFR = \text{hyperemic } (P_d / P_a)$$

$$iFR = \text{wave free } (P_d / P_a)$$



## METHODS

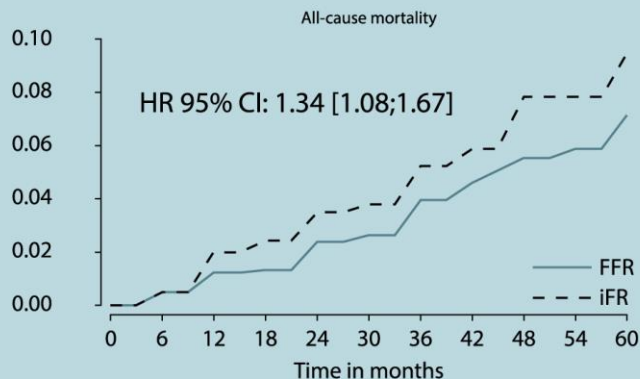
Study-level meta-analysis of DEFINE FLAIR and iFR SWEDEHEART at 5-years

## FINDINGS

FFR  
N = 2257

iFR  
N = 2254

### Increased all-cause mortality in iFR-arm



No. at risk

|     |      |      |      |      |      |      |      |      |      |      |      |
|-----|------|------|------|------|------|------|------|------|------|------|------|
| FFR | 2257 | 2203 | 2153 | 2089 | 2050 | 1990 | 1980 | 1947 | 1933 | 1898 | 1562 |
| iFR | 2254 | 2185 | 2121 | 2047 | 2018 | 1963 | 1946 | 1907 | 1881 | 1837 | 1509 |

Eftekhari A et al. Eur Heart J. 2023, in press