

# Primary outcomes of DEFINE-FLAIR and iFR SwedeHeart



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**Imperial College London**

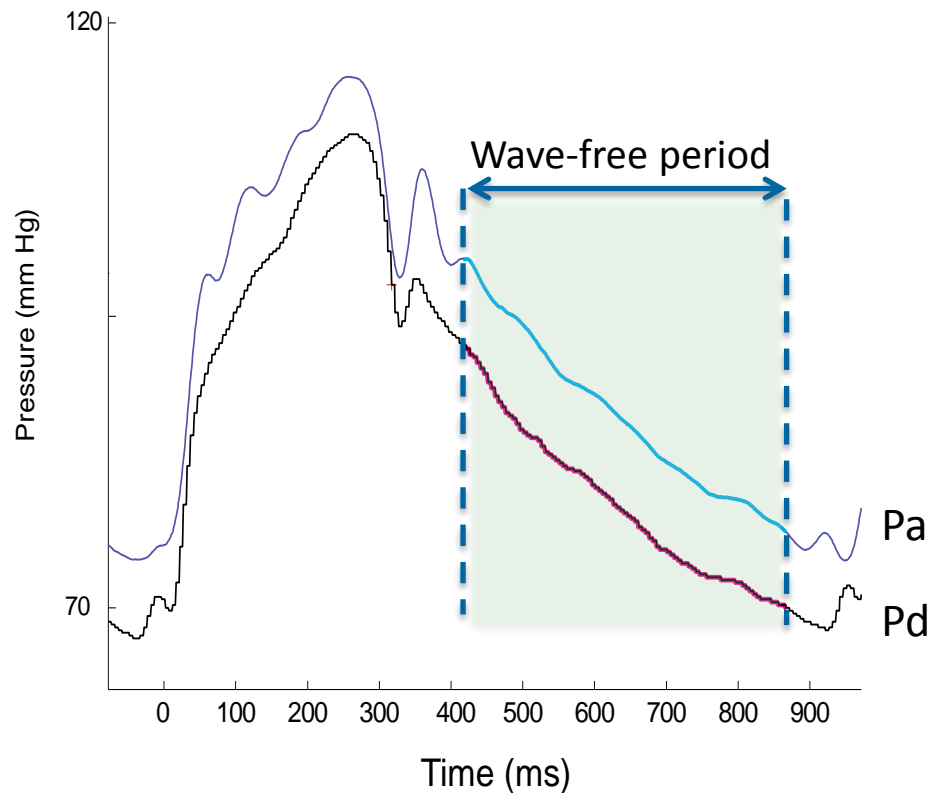
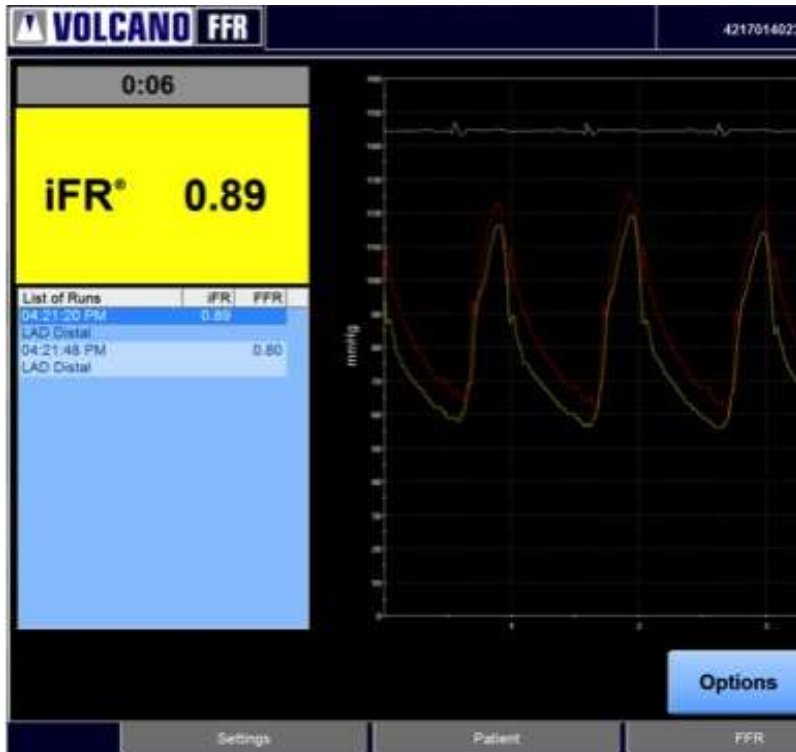


**Imperial College**  
**London**

TCTAP, 2017

# Definition of iFR:

Instant wave-free ratio across a stenosis during the wave-free period, when **resistance is naturally constant** and minimized in the cardiac cycle



# iFR compared to FFR has been well validated

Oct 2011

May 2012

Aug 2012

Oct 2012

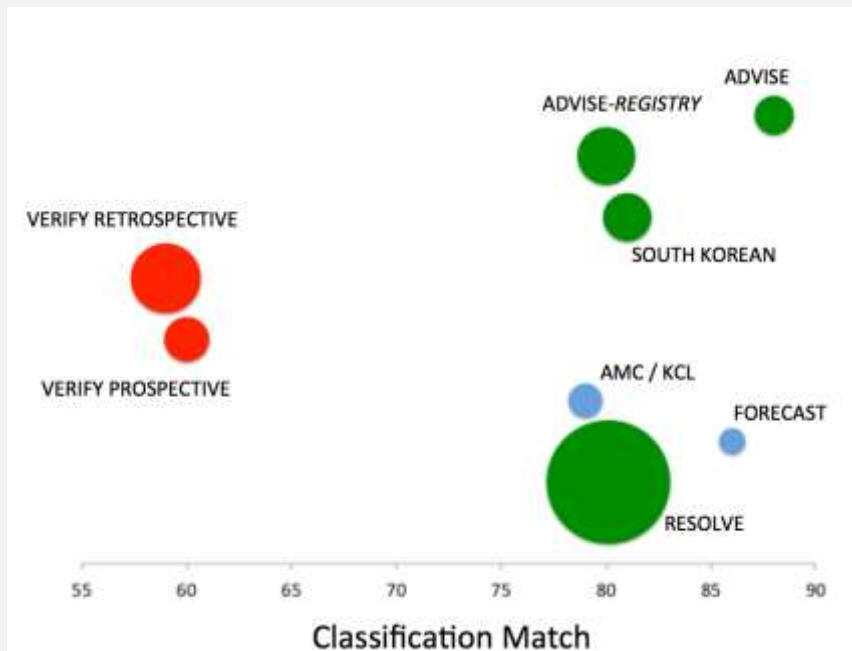
ADVISE study

ADVISE Registry

HYBRID strategy

**RESOLVE study<sup>4</sup>**

- Over 3000 stenoses evaluated, core lab analysis, using the Philips Volcano algorithm



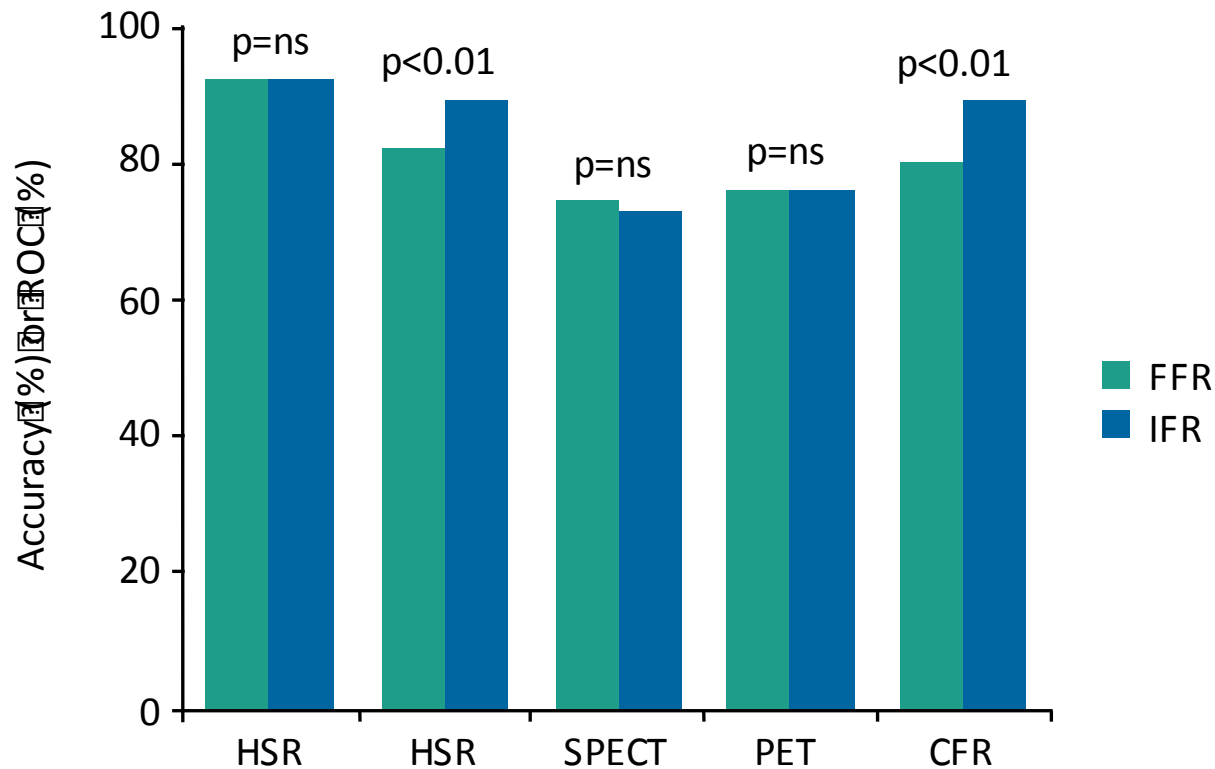
**Algorithm is critical for accurate calculation of iFR**

**Confirmed previous studies**

**VERIFY was the clear outlier**

# What we know about iFR:

*Vasodilators do not improve physiological diagnostic accuracy*



CFR, Coronary Flow Reserve; HSR, Hyperaemic Stenosis Resistance; ROC, receiver-operating characteristic; PET, positron emission tomography; SPECT, single-photon emission computed tomography

1. Van de Hoef TP et al. *Circ Cardiovasc Interv.* 2012;5:508-14; 2. Sen S et al. *J Am Coll Cardiol.* 2013;61:1409-20; 3. Van de Hoef TP et al. *EuroIntervention.* 2015;11:914-25; 4. Sen S et al. *J Am Coll Cardiol.* 2013;62:566; 5. Petraco R et al. *Circ. Int.* 2014;7:492-502; 6. de Waard G et al. *J Am Coll Cardiol.* 2014;63:A1692.

# DEFINE FLAIR



## Primary objective

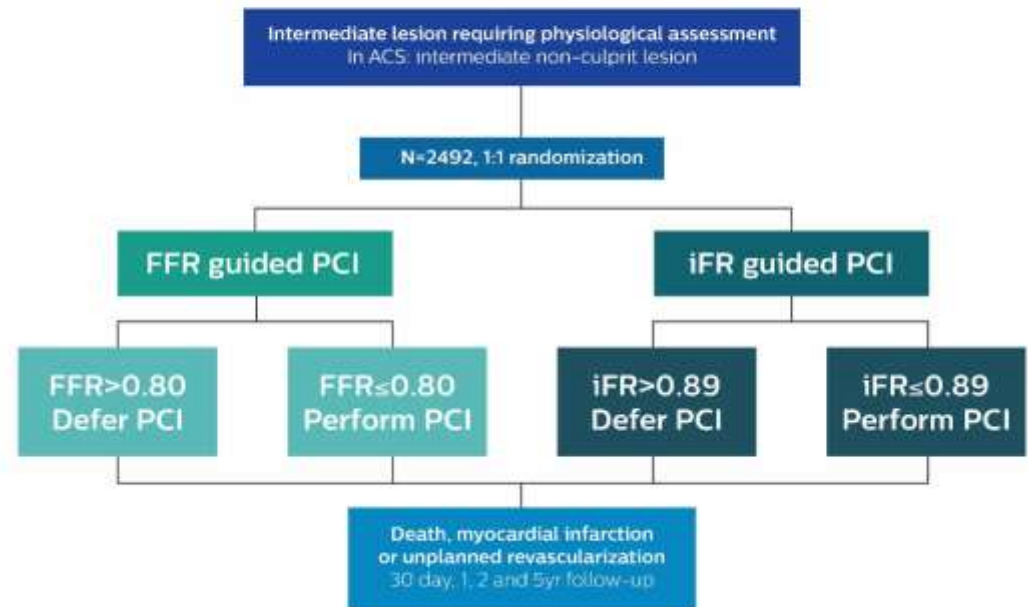
- Assess safety and efficacy of decision-making on coronary revascularisation based on iFR vs FFR
- Assess if iFR is non-inferior to FFR when used to guide treatment of coronary stenosis with PCI

## Primary endpoint

- Major adverse cardiac events (MACE) rate in the iFR and FFR groups at 30 days, 1 and 2 years.
- MACE (combined endpoint of death, non-fatal MI, or unplanned revascularisation)

## DEFINE FLAIR

Functional Lesion Assessment of Intermediate stenosis to guide Revascularisation



# iFR-Swedeheart



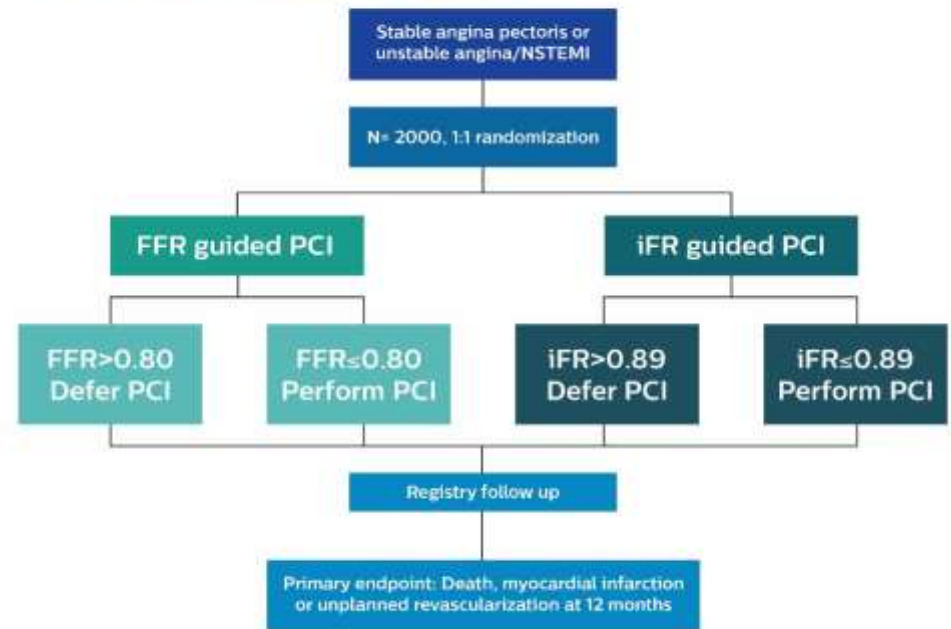
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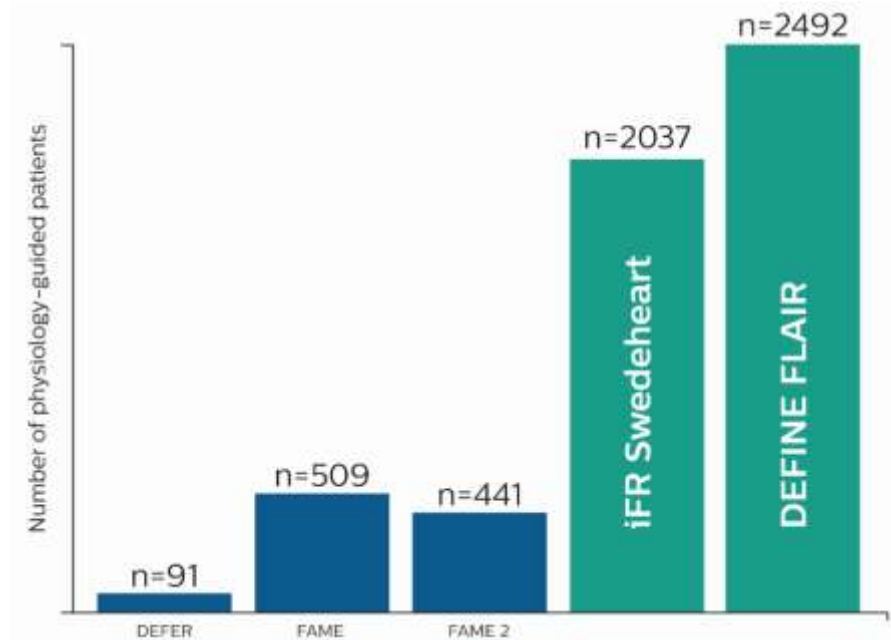
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## iFR Swedeheart

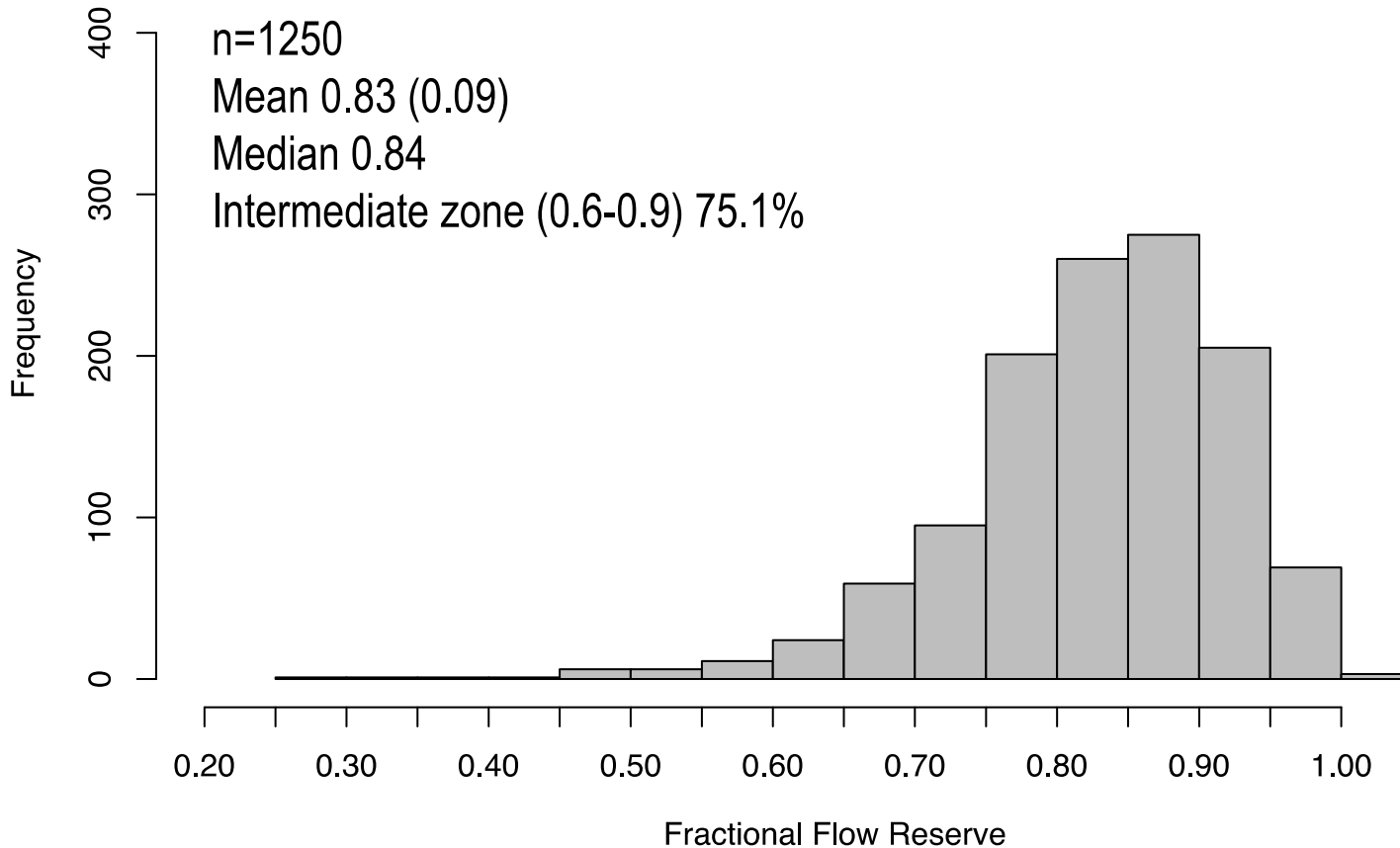


# DEFINE-FLAIR and iFR SwedeHeart: The largest global physiology outcome trials

- DEFINE FLAIR and iFR Swedeheart are the new landmark physiology studies
- **4500+** patients, more than twice the combined patient population of previous landmark physiology studies
  - DEFINE FLAIR: n = 2492 patients
  - iFR Swedeheart: n = 2037 patients
- **2** prospective, randomized, controlled trials



# FFR value distribution reflecting real world practice of physiology

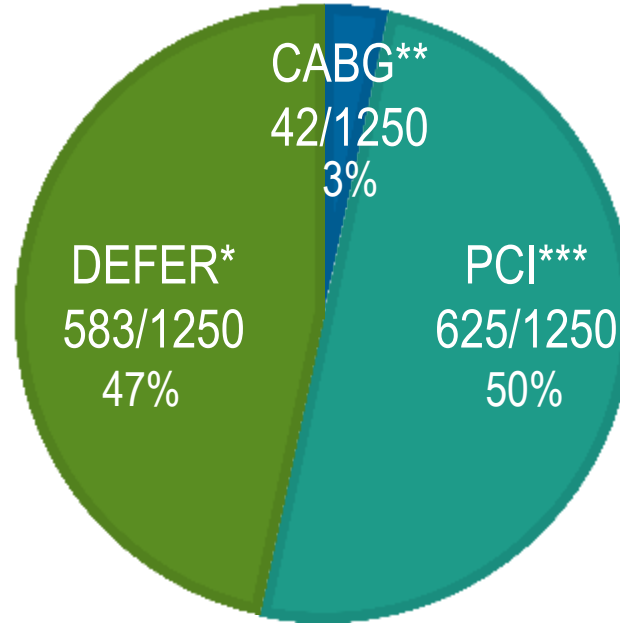
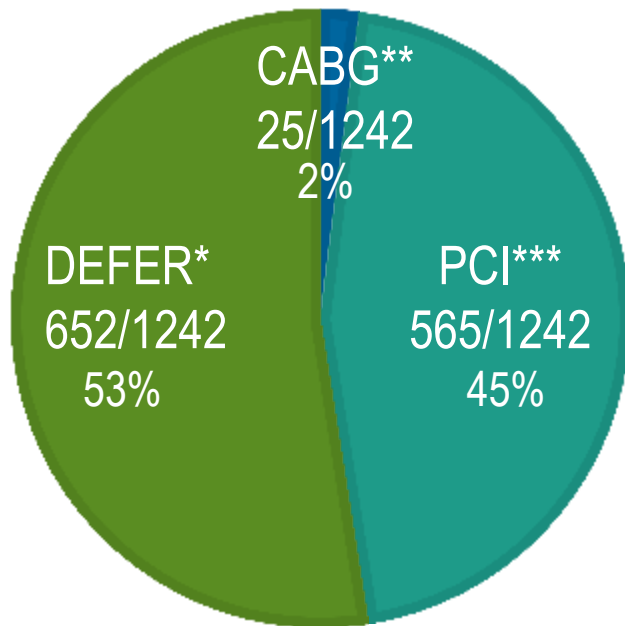




# Treatment allocation with iFR and FFR

## iFR

## FFR



p for comparison between patients randomized to iFR and FFR

DEFER\* p=0.003

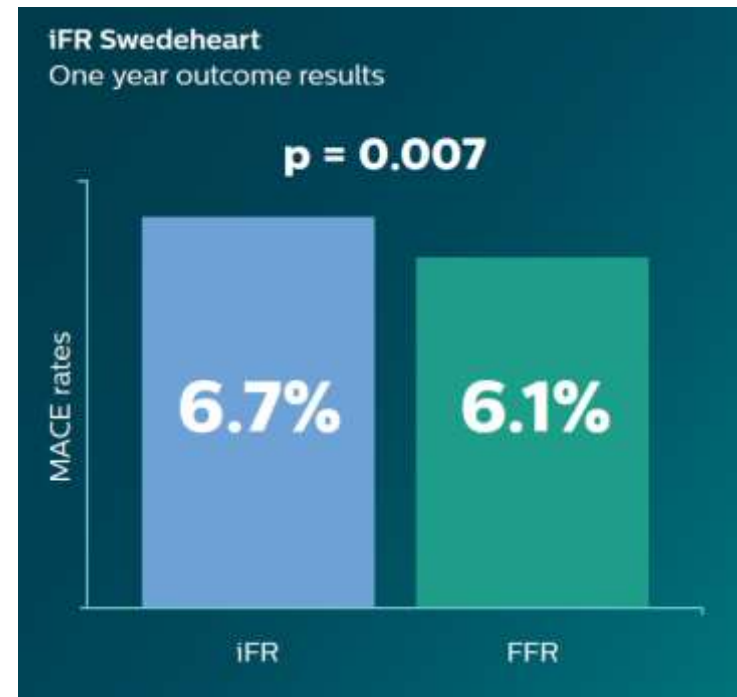
CABG\*\* p=0.04

PCI\*\*\* p=0.02

Significantly less revascularization based on iFR interrogation

# Consistent patient outcome

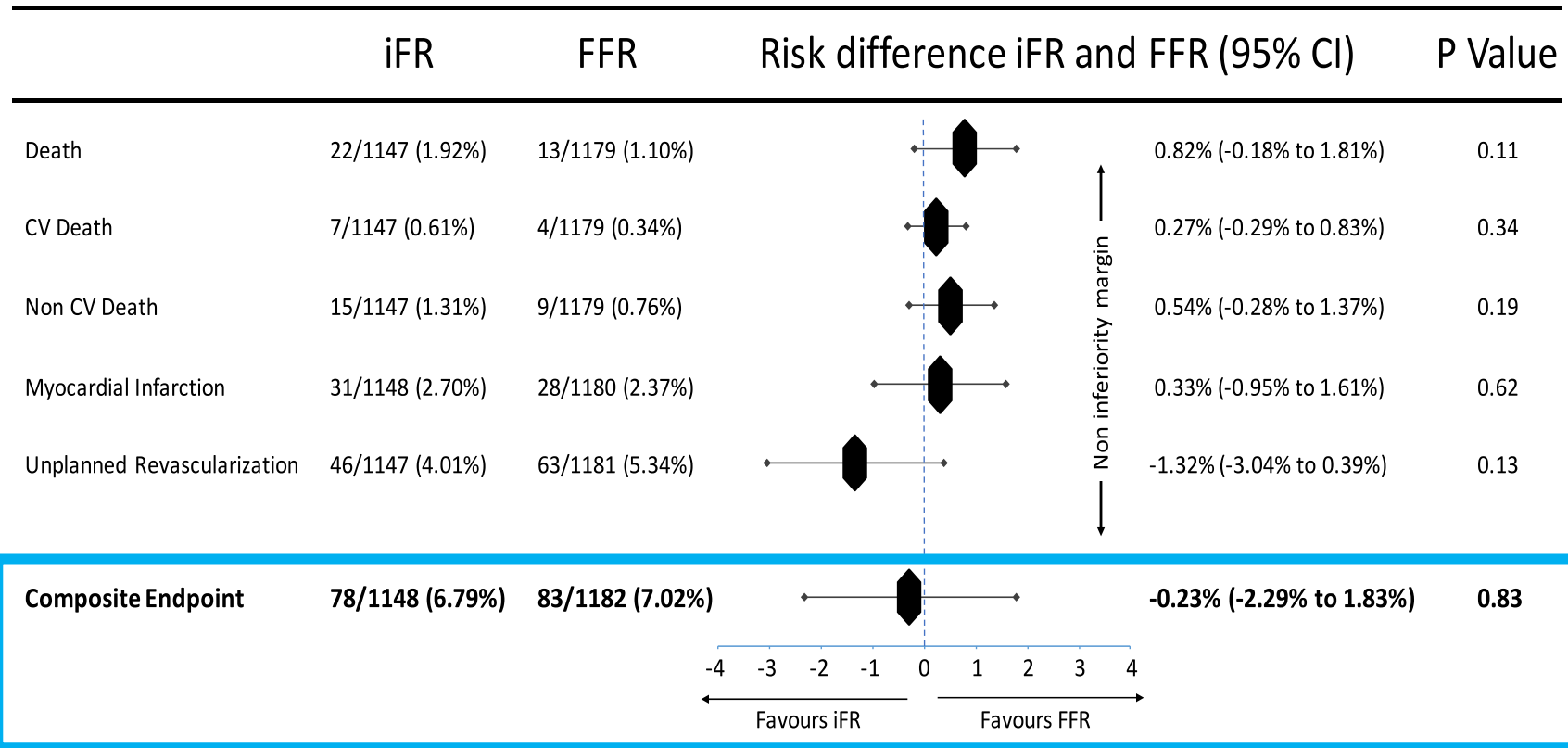
- An iFR guided strategy is statistically comparable to an FFR-Guided Strategy for patient outcome\*
  - Primary endpoint: major cardiovascular adverse event rates, assessed at 1-year



\* p-values are for non-inferiority of an iFR-guided strategy versus an FFR-guided strategy with respect to 1-year MACE rates; pre-specified non-inferiority margins were 3.4% and 3.2% in DEFINE FLAIR and iFR Swedeheart, respectively

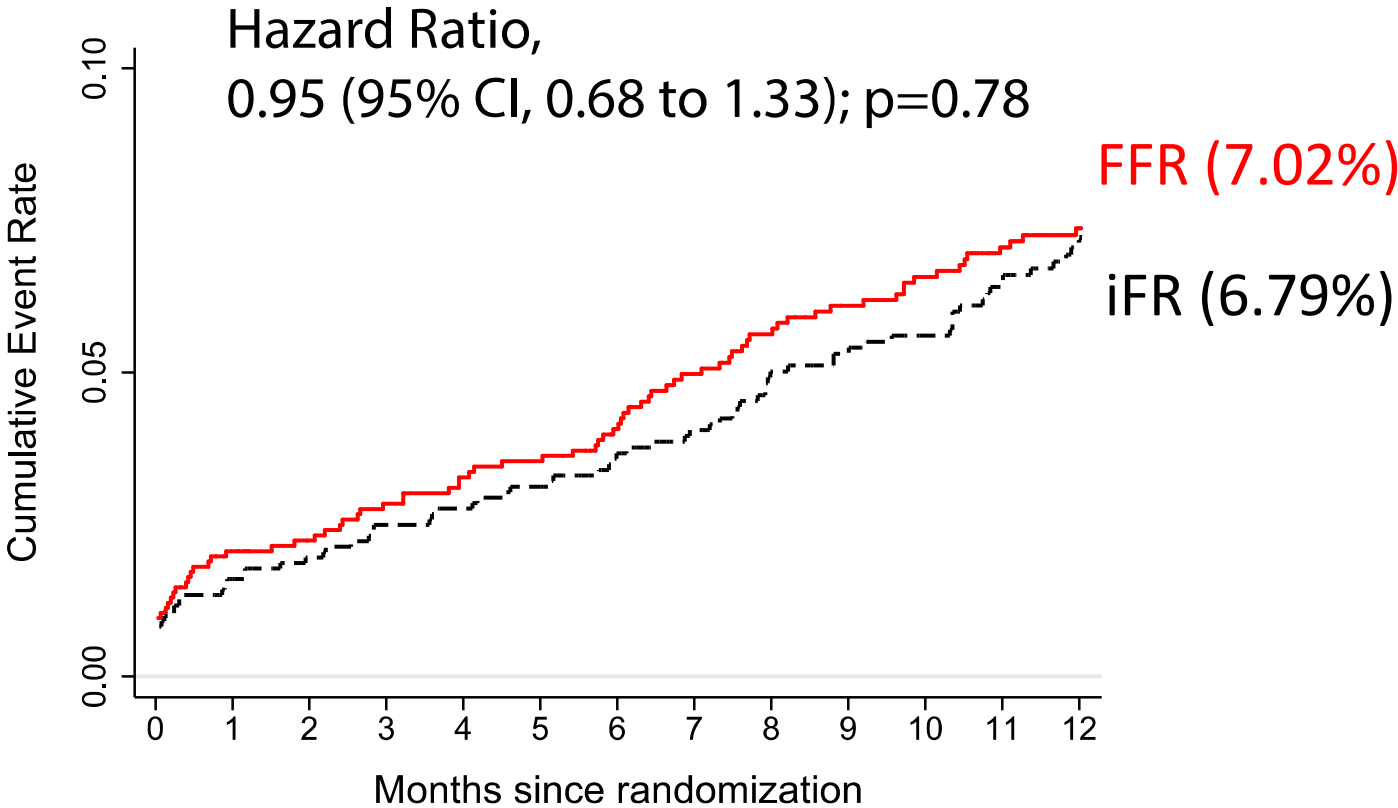
# Consistent patient outcome

- In DEFINE FLAIR, the hazard ratio was 0.95 in favour of iFR, with a risk difference of minus 0.23% and 95% confidence intervals within the pre-specified non-inferiority margin, thus confirming non-inferiority of iFR.



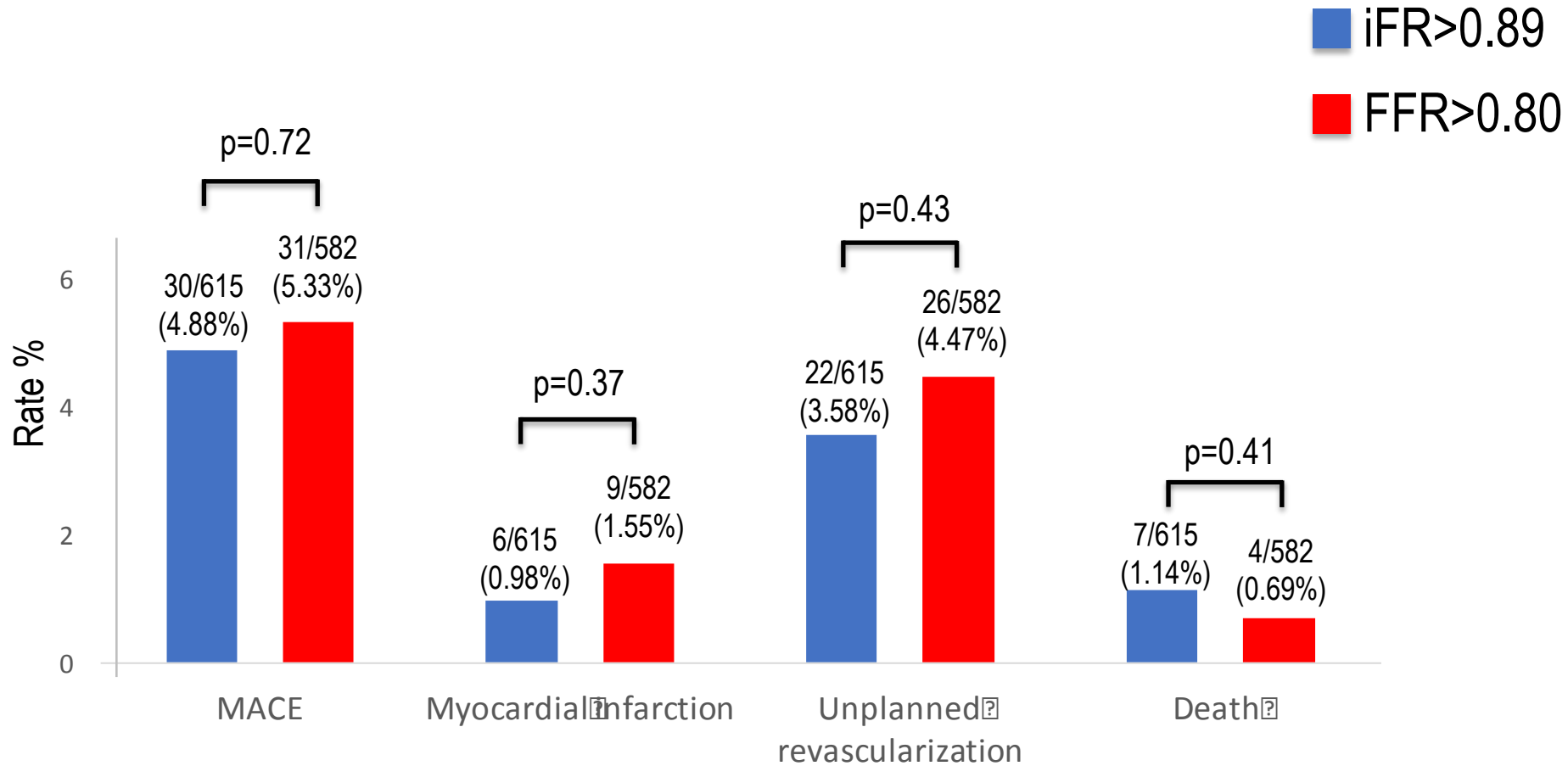
# Primary endpoint (MACE)

## iFR equivalent to FFR with less PCI and CABG



Davies JE et al. NEJM 2017

# Event rates in deferred patients at 12 months



# Published online NEJM



The NEW ENGLAND  
JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Use of the Instantaneous Wave-free Ratio or Fractional Flow Reserve in PCI

J.E. Davies, S. Sen, H.-M. Dehbi, R. Al-Lamee, R. Petraco, S.S. Nijjer, R. Bhindi, S.J. Lehman, D. Walters, J. Sapontis, L. Janssens, C.J. Vrints, A. Khashaba, M. Laine, E. Van Belle, F. Krackhardt, W. Bojara, O. Goling, T. Härtle, C. Indolfi, G. Niccoli, F. Ribichini, N. Tanaka, H. Yokoi, H. Takashima, Y. Kikuta, A. Erglis, H. Vinhas, P. Canas Silva, S.B. Baptista, A. Alghamdi, F. Hellig, B.-K. Koo, C.-W. Nam, E.-S. Shin, J.-H. Doh, S. Brugaletta, E. Alegria-Barrero, M. Meuwissen, J.J. Plek, N. van Royen, M. Sozer, C. Di Mario, R.T. Gerber, I.S. Malik, A.S.P. Sharp, S. Talwar, K. Tang, H. Samady, J. Altman, A.H. Seto, J. Singh, A. Jeremias, H. Matsuo, R.K. Kharbada, M.R. Patel, P. Serruys, and J. Escaned



The NEW ENGLAND  
JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Instantaneous Wave-free Ratio versus Fractional Flow Reserve to Guide PCI

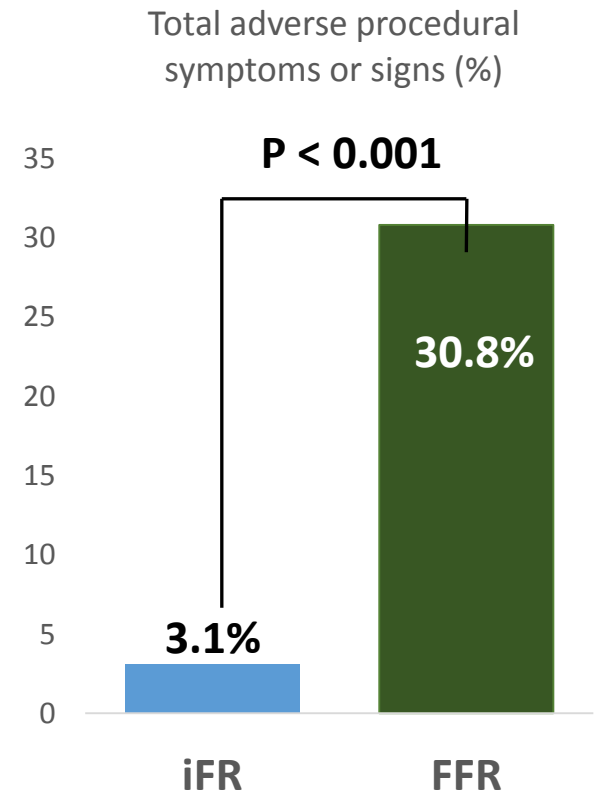
M. Götzberg, E.H. Christiansen, I.J. Gudmundsdottir, L. Sandhall, M. Danielewicz, L. Jakobsen, S.-E. Olsson, P. Öhagen, H. Olsson, E. Omerovic, F. Calais, P. Lindroos, M. Maeng, T. Tödt, D. Venetsanos, S.K. James, A. Käregren, M. Nilsson, J. Carlsson, D. Hauer, J. Jensen, A.-C. Karlsson, G. Panayi, D. Erlinge, and O. Fröbert, for the IFR-SWEDEHEART Investigators\*

Online now at [nejm.org](http://nejm.org)

# An iFR-guided strategy significantly reduces patient discomfort

- DEFINE FLAIR reported that without the need of hyperemia, you can achieve a 90% reduction of patient discomfort during procedures

	iFR (n = 1242)	FFR (n=1250)
Patient reported adverse symptoms		
Dyspnoea	13	250
Chest pain	19	90
Patient reported adverse signs		
Rhythm disturbance	2	60
Significant Hypotension	4	13
Vomiting or nausea	1	11
Serious symptoms or bronchospasm	1	8
other	4	38
<b>Total adverse procedural symptoms or signs</b>	<b>39</b>	<b>385</b>



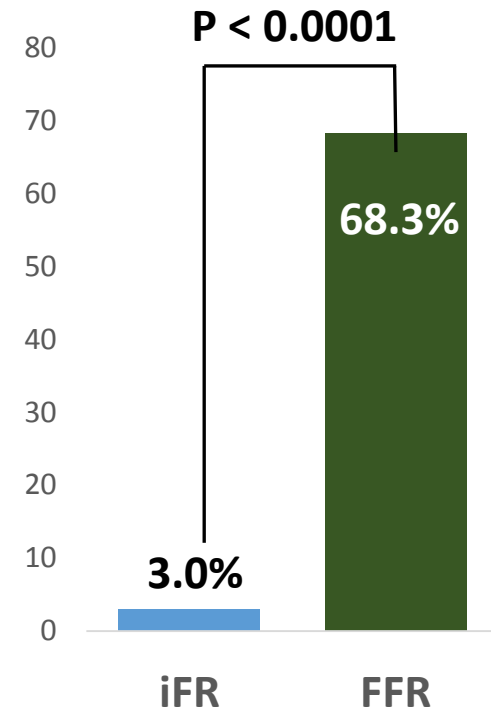
# An iFR-guided strategy significantly reduces patient discomfort

- iFR Swedeheart reported a 95.7% reduction in patient discomfort

	iFR (n = 1012)	FFR (n=1007)
Discomfort during procedure		
None	982	319
Mild	26	316
Moderate	2	285
Severe	2	87

- Using an iFR-guided strategy, you can almost completely eliminate moderate to severe patient discomfort during PCI procedures
  - 4 patients in iFR arm vs 372 patients in FFR arm reported moderate to severe discomfort

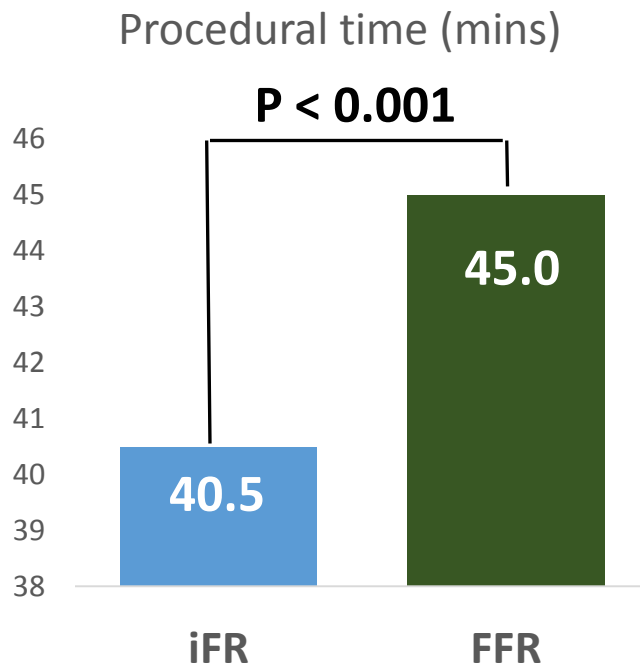
Total adverse procedural symptoms or signs (%)





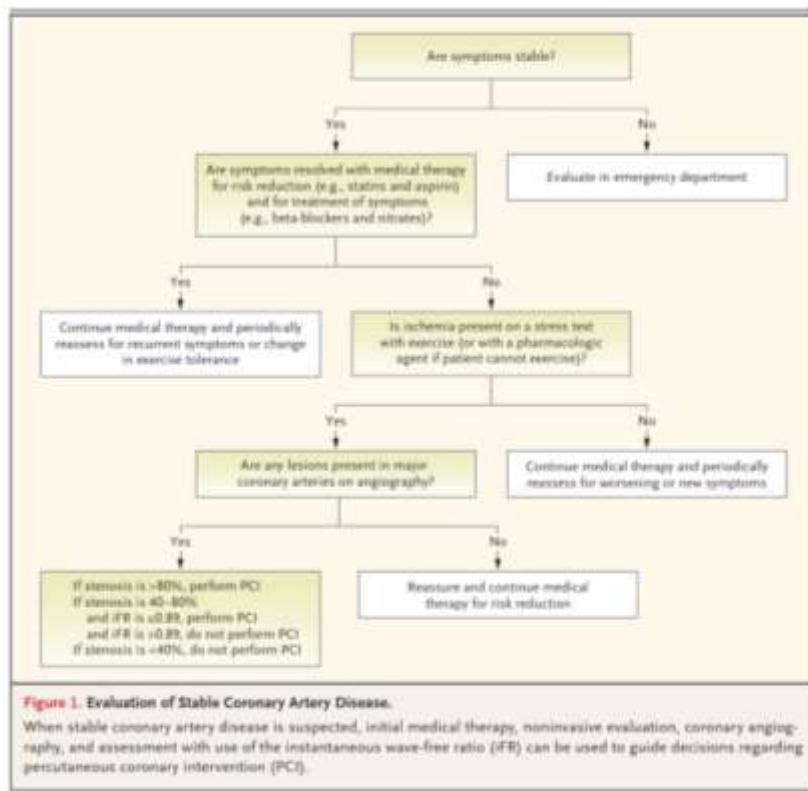
# An iFR-guided strategy significantly reduces procedural time and cost

- DEFINE FLAIR reported an average procedural time of 40.5 minutes in the iFR arm, vs. 45.0 minutes in the FFR arm ( $p < 0.001$ )
- This means a 10% reduction in procedural time



# Management of CAD

TS: NEW ENGLAND JOURNAL of MEDICINE



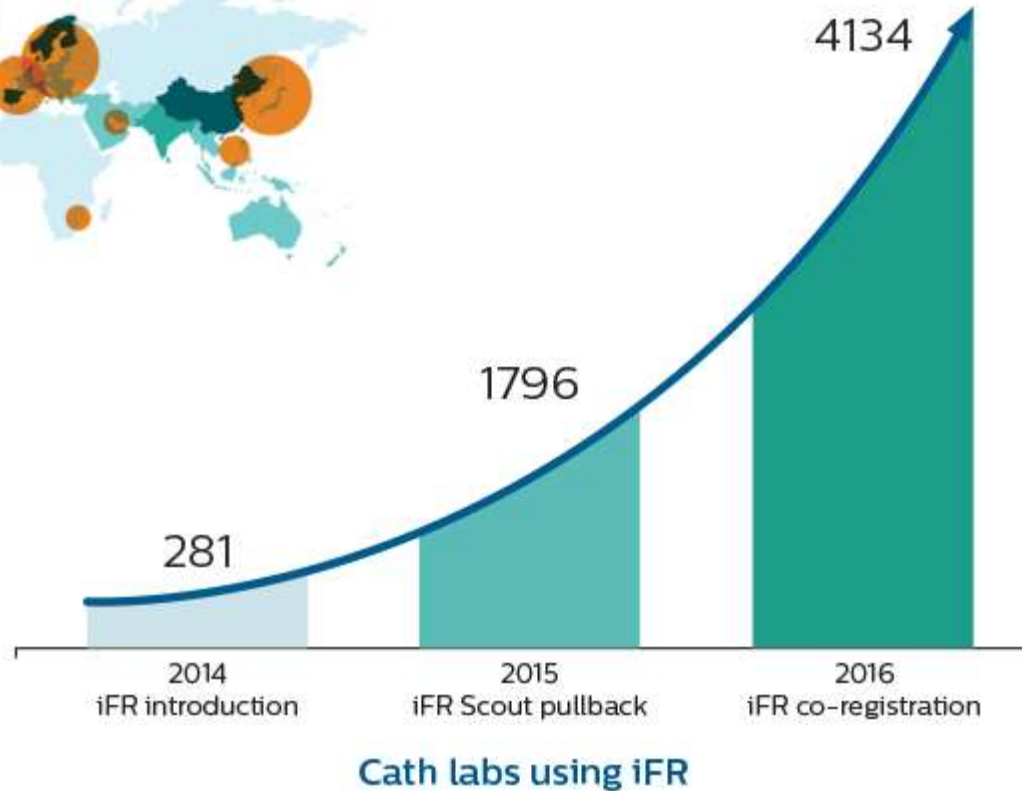
“ FFR has been the evidence-based standard for invasive evaluation of such lesions, but it now appears that iFR may be the new standard.

Deepak Bhatt, NEJM 2017



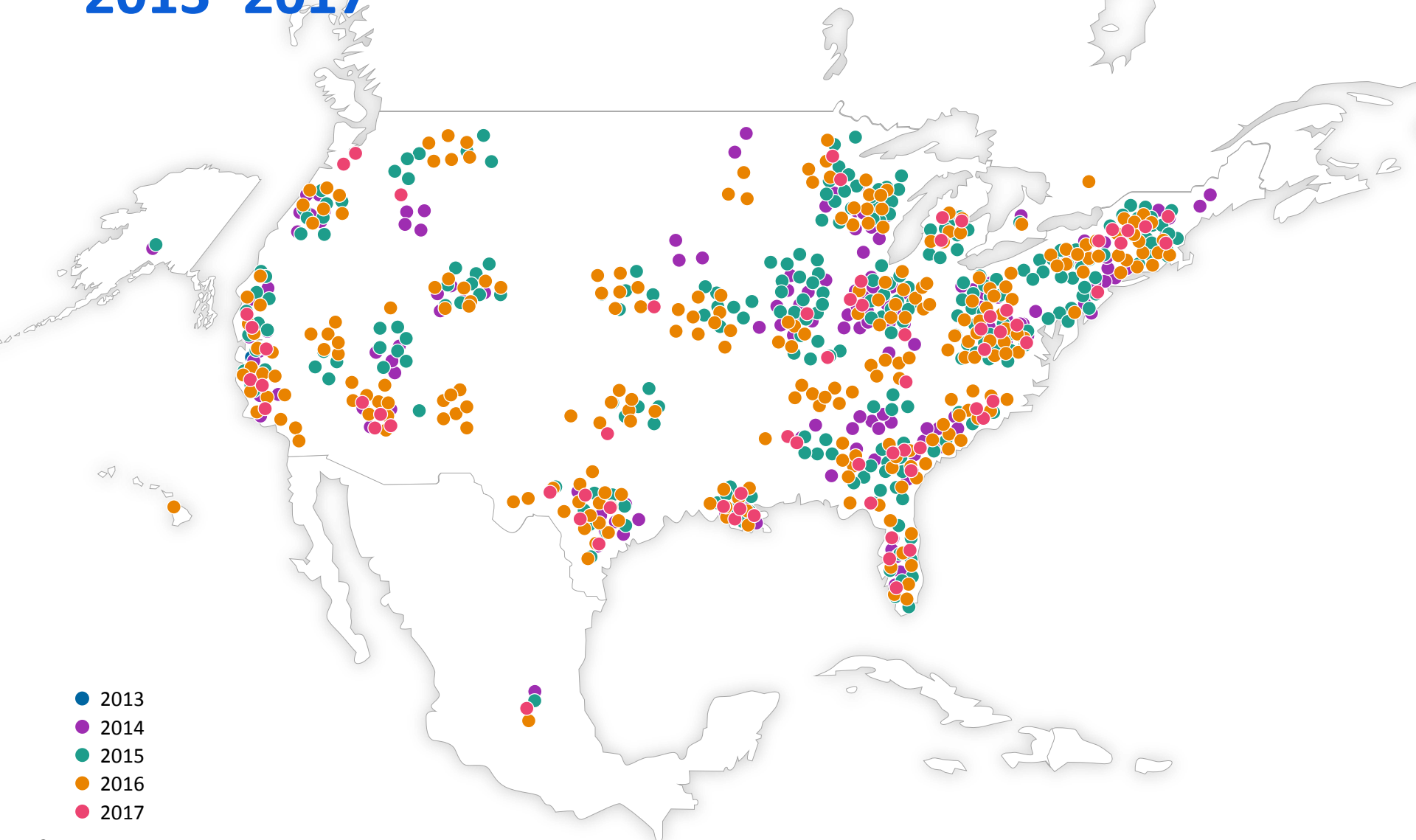
# iFR has been adopted in +4000 cath labs world wide

## iFR adoption worldwide



# iFR North America

## 2013–2017



- 2013
- 2014
- 2015
- 2016
- 2017



  **TUESDAY 16 MAY 2017**  **11:30 -12:50**  **MAIN ARENA**

## Late-breaking trials and trial update ▶



### Chairpersons:

D. Capodanno , W. Wijns

### Panellists:

V. Bapat , R. Byrne , R. Gao , P. Juni , U. Kaul , C. Lotan

### Speakers:

T. Cuisset , R.J. De Winter , J. Escaned , T. Feldman

### Theme / Topic:

Coronary Interventions, Interventions for Valvular Disease

### Session format:

Hot Line / LBT

12:10

**Safety of coronary revascularisation deferral based on iFR and FFR measurements in stable angina and acute coronary syndromes. A pooled patient-level analysis of DEFINE FLAIR and IFR SWEDEHEART trials**

*J. Escaned*

# Take homes from DEFINE-FLAIR and iFR SwedeHeart

- iFR is as safe as FFR to guide coronary revascularization decision-making
- iFR has fewer adverse side effects and symptoms
- iFR is quicker to perform

# Building evidence, and expanding choice in intracoronary physiology assessment



Morton Kern

## **“The iFR concept has great appeal.**

It would make lesion assessment quicker, easier, less expensive, and more widely used, but it must be carefully vetted before wholesale implementation. Each new paradigm rewrites the history of its predecessor. Old theories are discarded and then reconstructed, emerging under a new paradigm. Such was the case with FFR compared with earlier physiology methods. Should large-scale validation studies meet positive expectations, iFR may take its place among catheter lab lesion assessment methods, providing critical information for the treatment of our PCI patients.”

Kern M. JACC 2012