# My Approach to
# Multi-Vessel Disease

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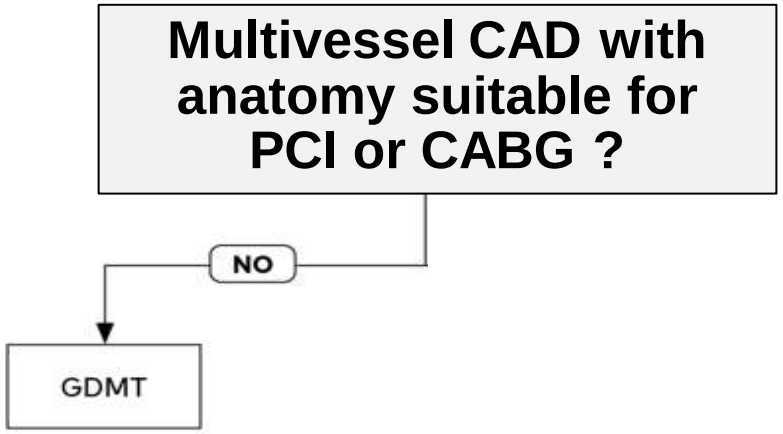
# *ESC Guidelines 2018*
# *Elective PCI for 3 Vessel Disease*

| | CABG | | PCI | |
|---|---|---|---|---|
| **3-VD without Diabetes Mellitus** | **Class** | **Level** | **Class** | **Level** |
| **3 VD with low SYNTAX score (0-22)** | **I** | **A** | **I** | **A** |
| **3 VD with intermediate of high SYNTAX score (>22)** | **I** | **A** | **III** | **A** |
| **3-VD with Diabetes Mellitus** | | | | |
| **3 VD with low SYNTAX score (0-22)** | **I** | **A** | **IIb** | **A** |
| **3 VD with intermediate of high SYNTAX score (>22)** | **I** | **A** | **III** | **A** |

# *2021* ACC/AHA/SCAI, Guideline for Coronary Artery Revascularization



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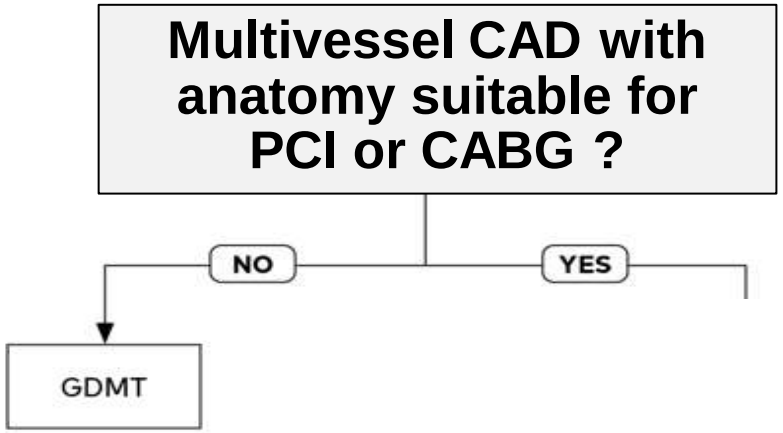

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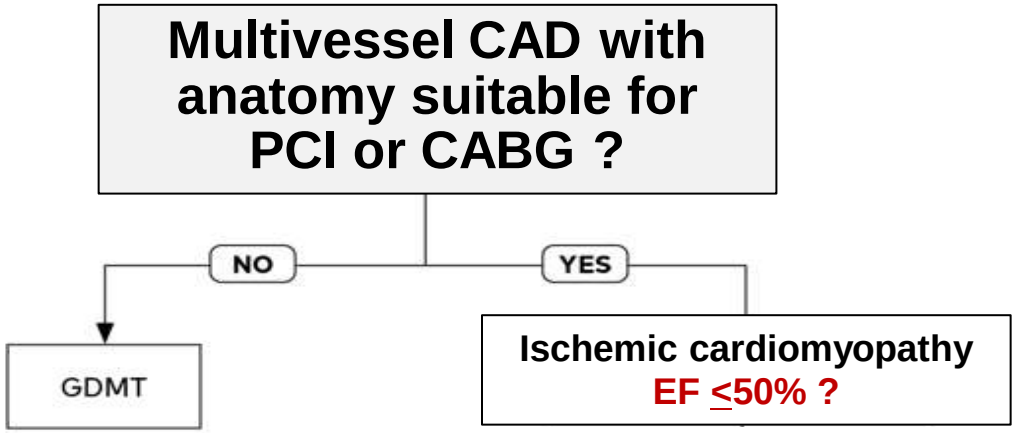

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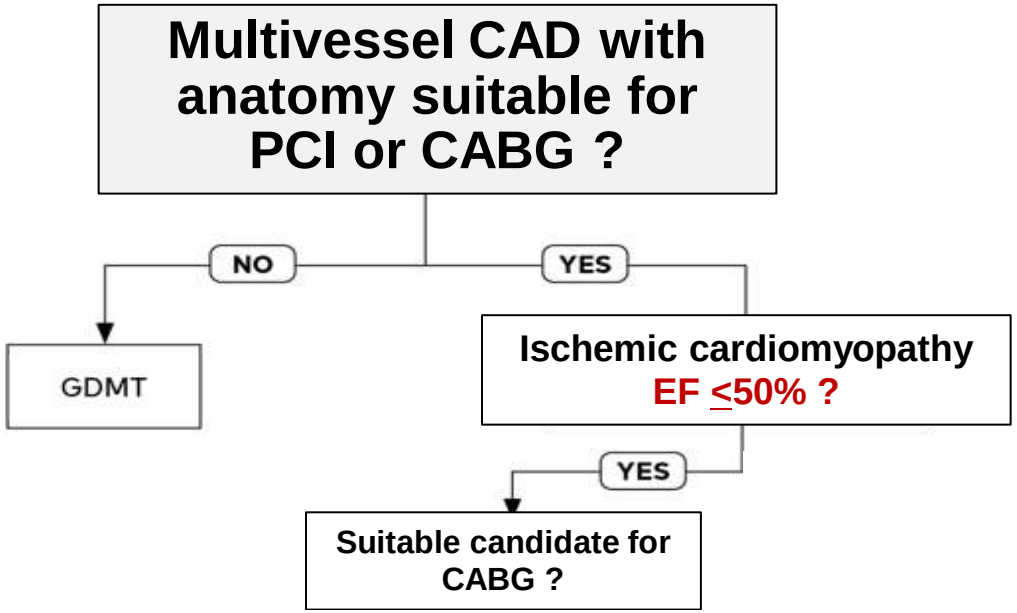

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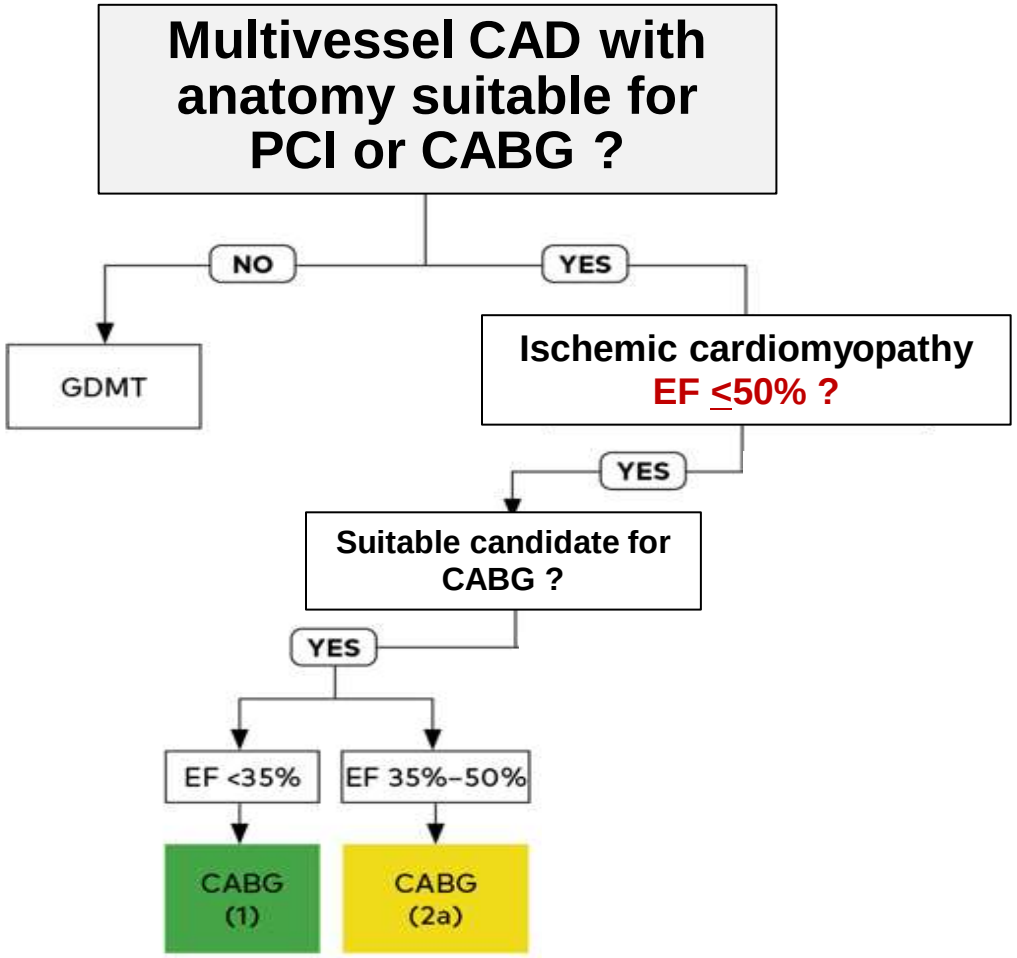

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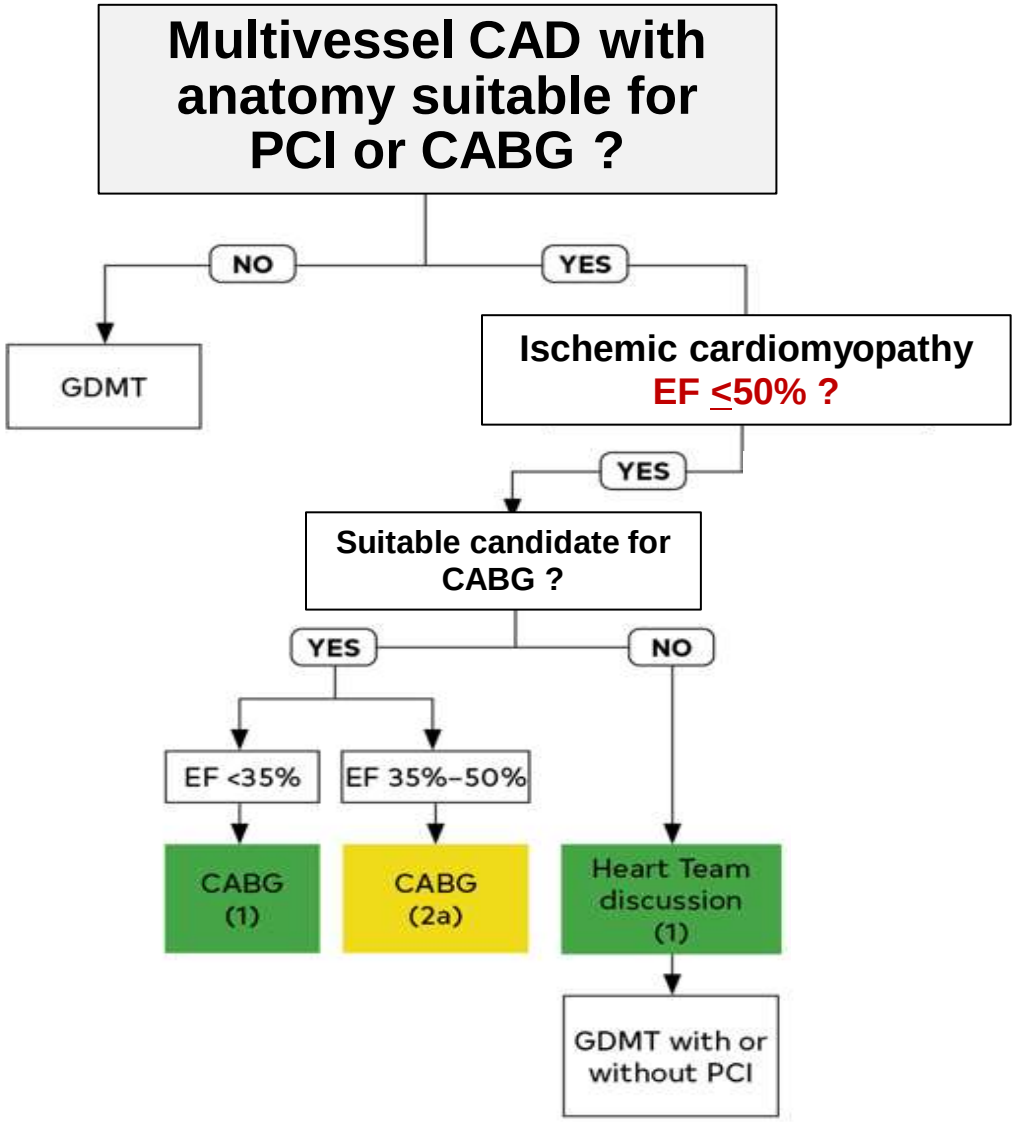

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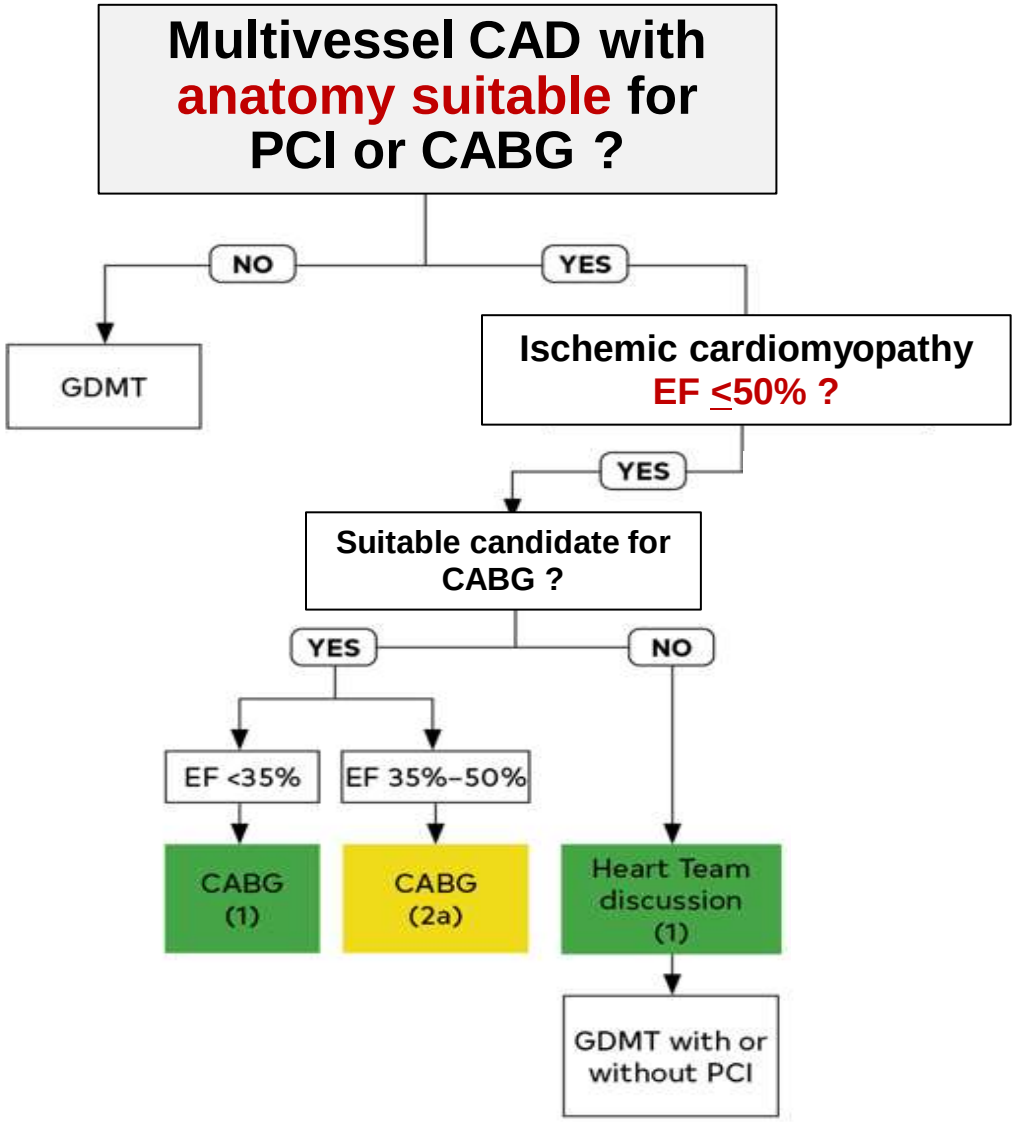


## ***Anatomy Suitable for PCI***

*All Ischemic lesions,*

*Diameter Stenosis ≥80% and RVD ≥2.25 mm*

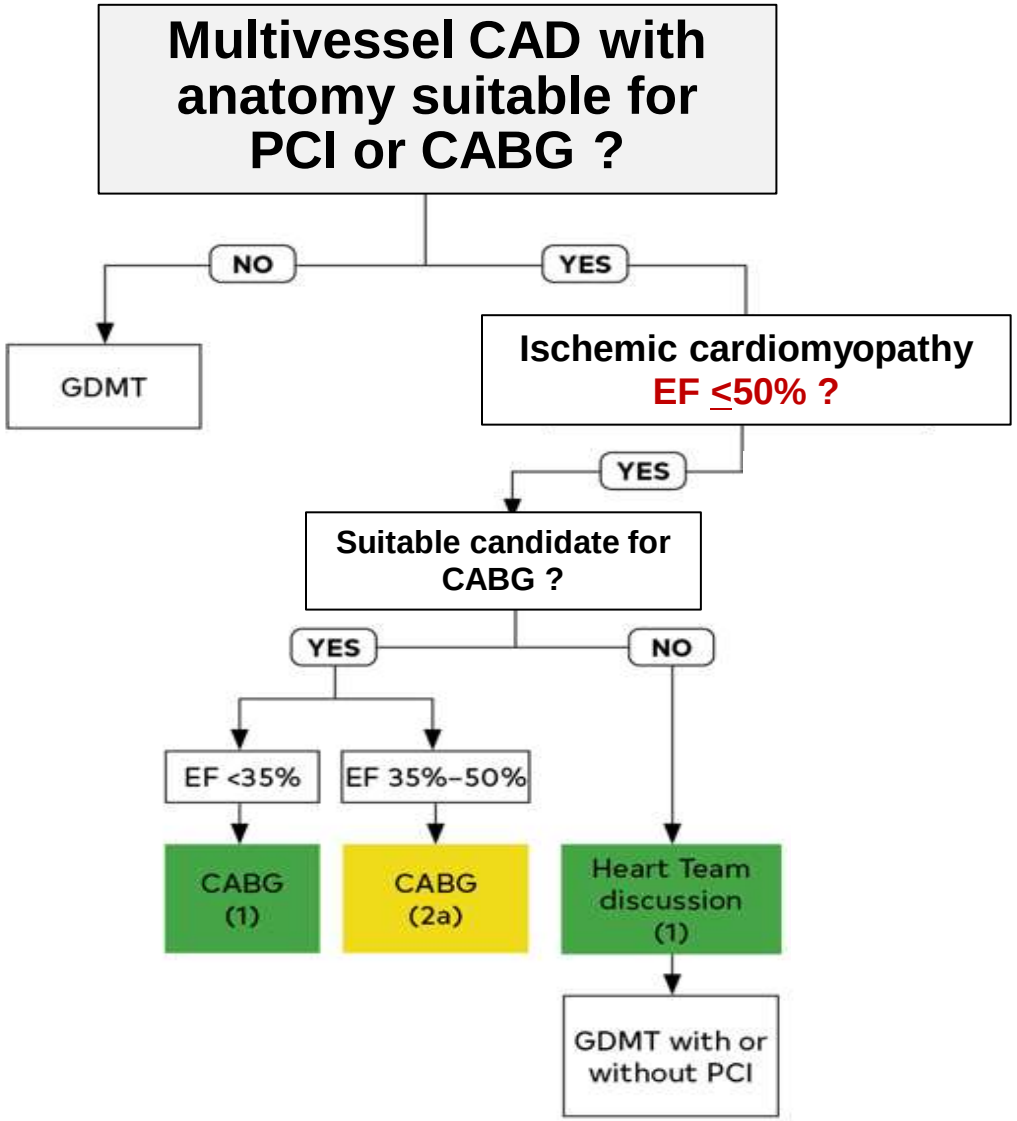
*FFR and IVUS strongly recommended*

## ***Anatomy Suitable for CABG***

*Anatomically, all coronary arteries with ≥70% stenosis and >1.5 mm in diameter should be revascularized.*

*Functionally, all ischemic myocardial areas should be grafted.*

# *2021* ACC/AHA/SCAI, Guideline for Coronary Artery Revascularization




**EF ≤50%**

*Low EF Is Only Important Index to Do CABG!*

*Guideline did Not mention about SYNTAX Score.*

# 2021 ACC/AHA/SCAI, Guideline for Coronary Artery Revascularization

***U*sefulness of SYNTAX Score Calculation in Treatment Decisions *is Less Clear***

because of the interobserver variability in its calculation and its absence of clinical variables.

Zhang YJ, Patrick SW et al. JACC 2014;64(5):423-432
J Am Coll Cardiol. Dec 09, 2021. Epublished DOI: 10.1016/j.jacc.2021.09.006

# Underlying Data, 1

***Low EF (<50%) Is***
***Only Important Index to Do CABG***
***for Multi Vessel Disease.***

# ***CABG vs. Medical Treatment***

## *for Multi-Vessel Disease*

1. CASS Trial
2. STICH

***Very Limited Data !***

# CABG vs. Medical Treatment for MVD

## 1st Randomized Study, CASS Trial

**Coronary Artery Surgery Study (CASS): a randomized trial of coronary artery bypass surgery**

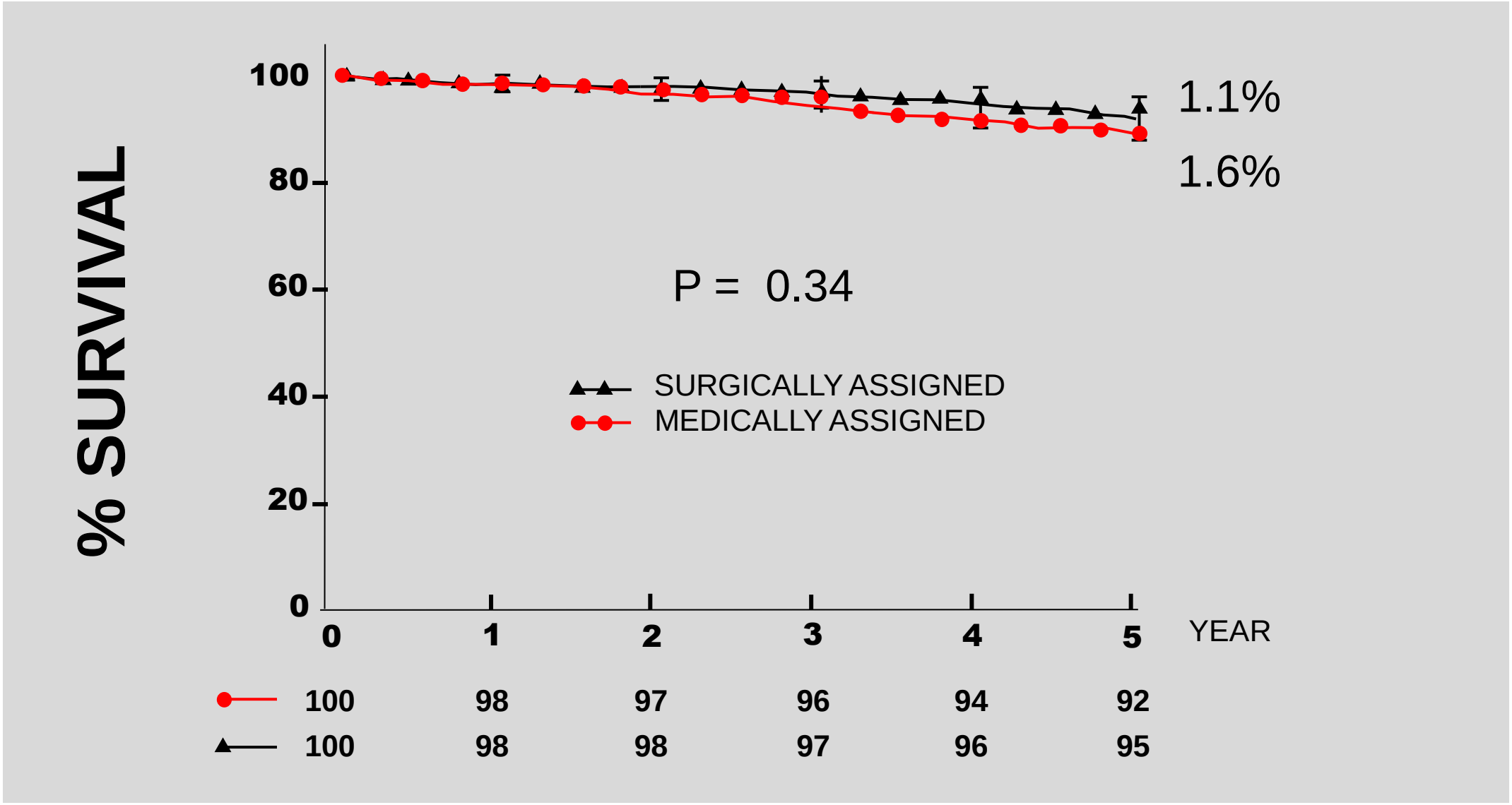
1. 780 patients,
2. Surgical (n=390) vs. Medical (n=390)
3. 70%, 1 or 2 vessel disease
4. Nitrate and Beta Blocker Available, <50%

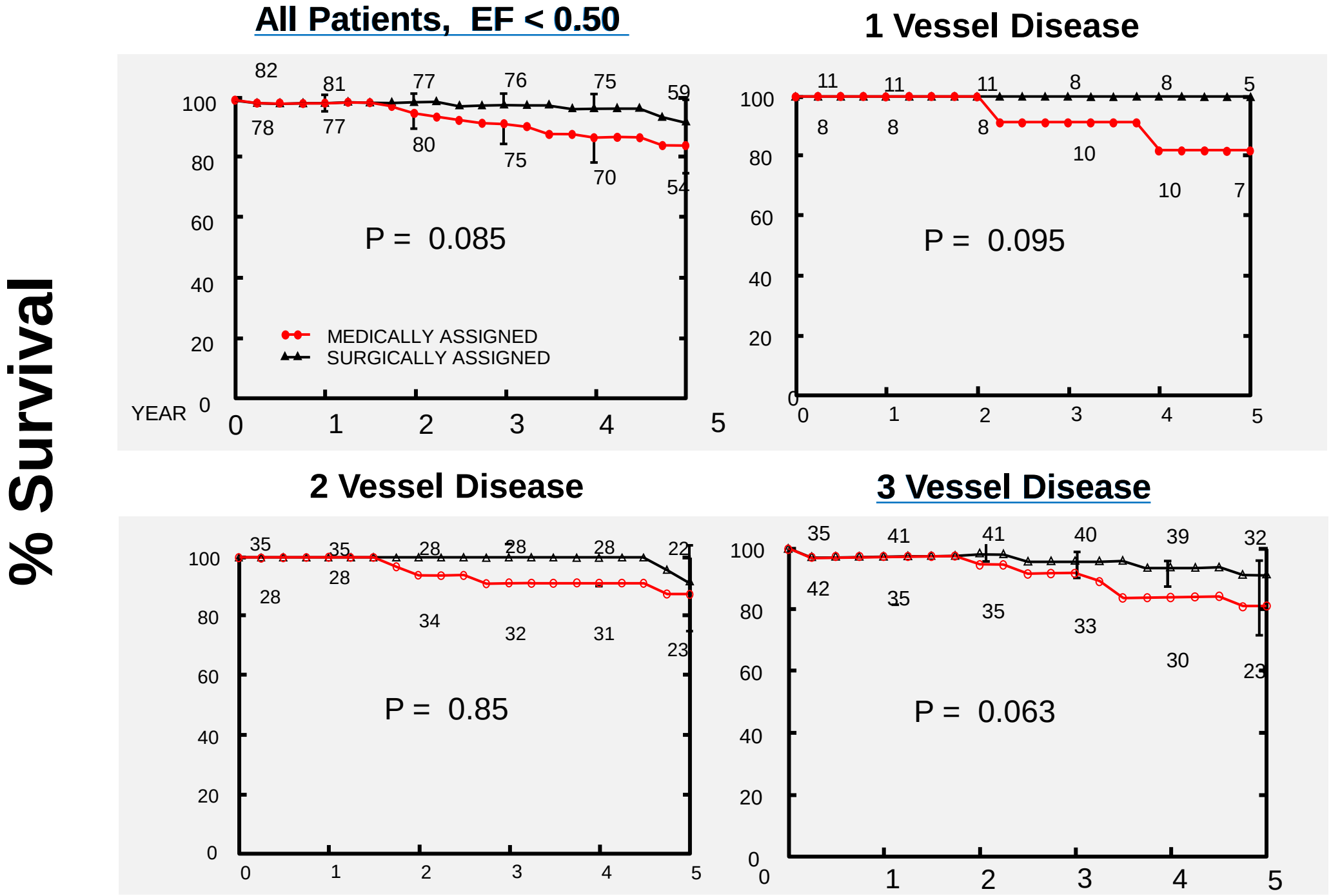
rates observed both in CASS patients assigned to receive medical and those assigned to receive surgical therapy and the similarity of survival rates in the two groups of patients in this randomized trial lead to the conclusion that patients similar to those enrolled in this trial can safely defer bypass surgery until symptoms worsen to the point that surgical palliation is required.

*Circulation 68, No. 5, 939–950, 1983.*

Circulation 1983 Nov;68(5):939-50. doi: 10.1161/01.cir.68.5.939.

# All Cause Mortality




All Patients, EF < 0.50
1 Vessel Disease
2 Vessel Disease
3 Vessel Disease
% Survival
YEAR
P = 0.085
P = 0.095
P = 0.85
P = 0.063
MEDICALLY ASSIGNED
SURGICALLY ASSIGNED

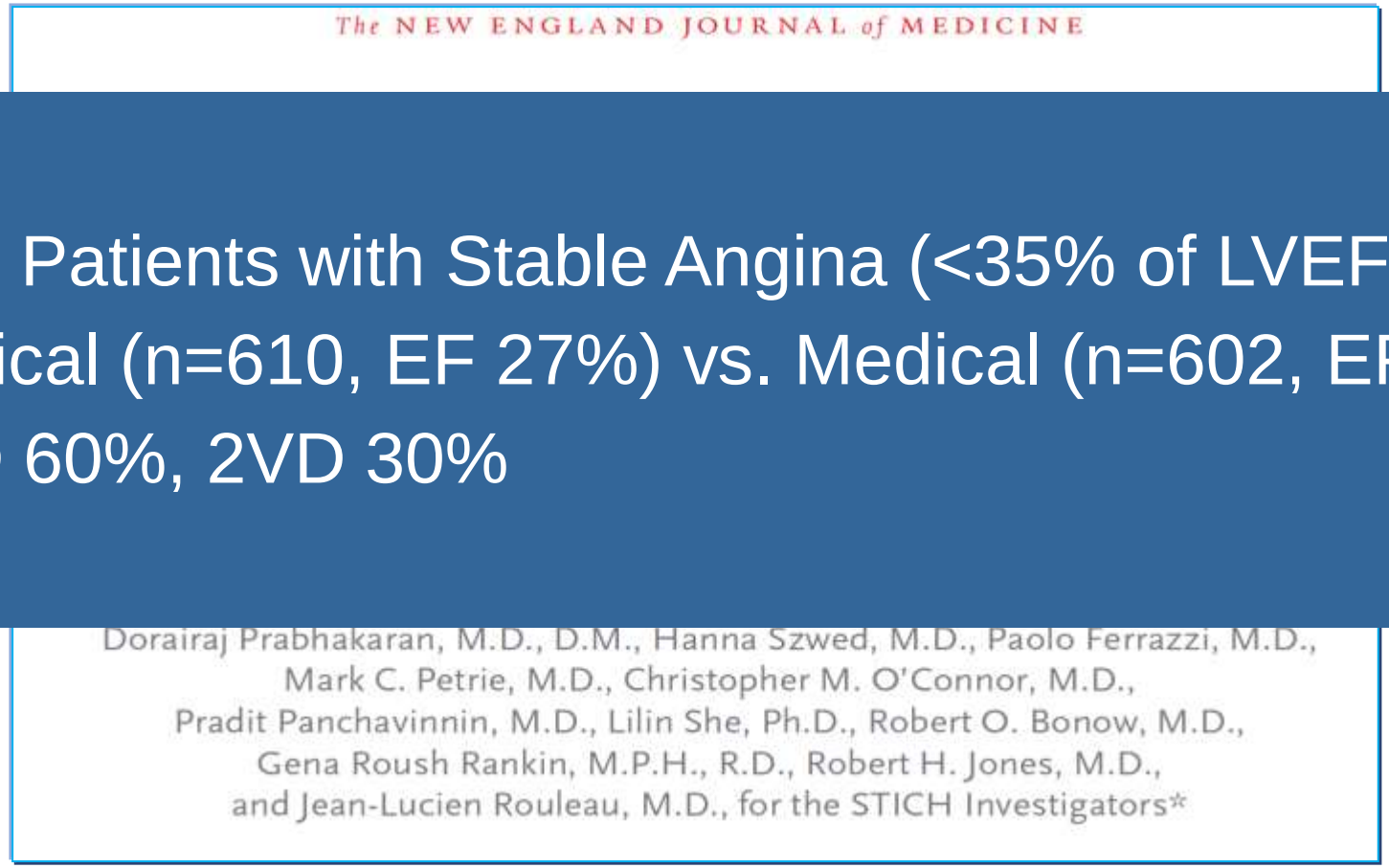
# CABG vs. Medical Treatment for MVD

From Coronary Artery Surgery (CASS) Study

***CABG Is Better Over Medication in Patients with Stable Angina (<50% of LVEF)***

# CABG vs. Medical Treatment

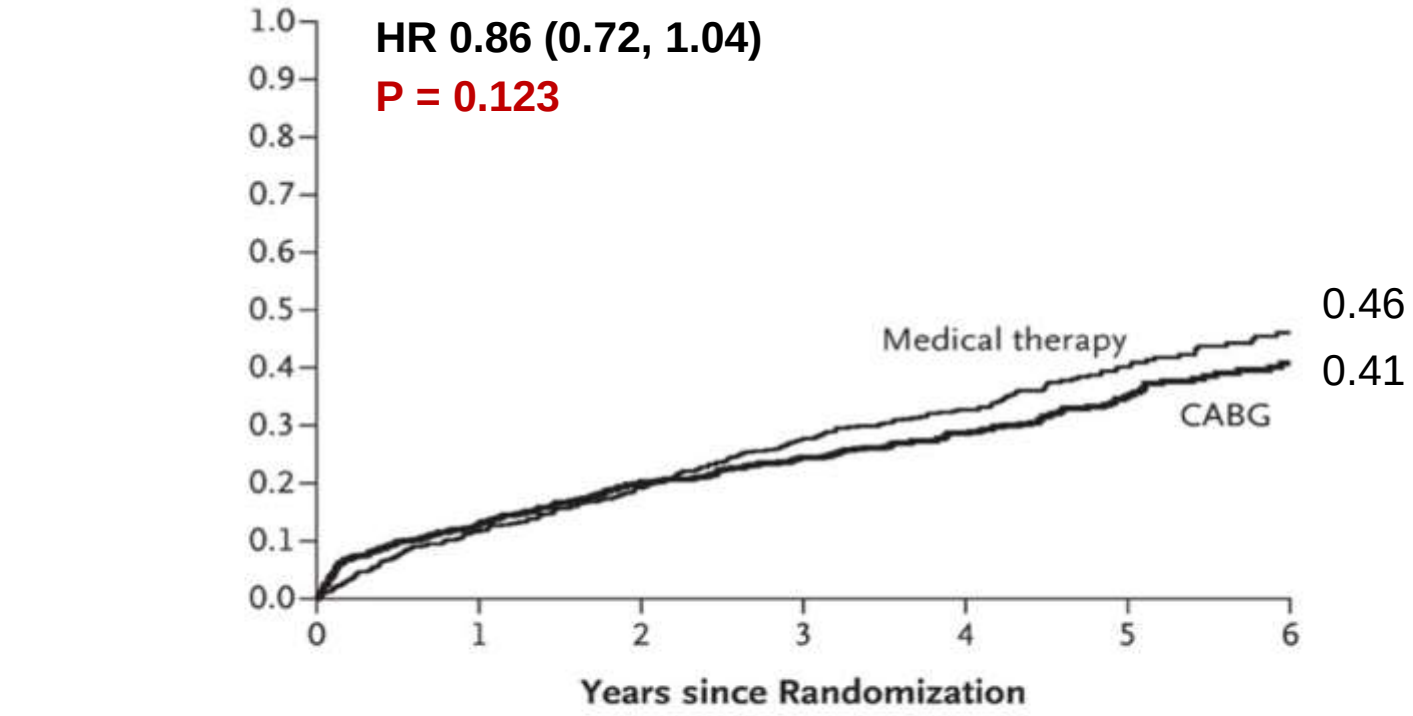
## Surgical Treatment for Ischemic Heart Failure (STICH) Trial




1. 1212 Patients with Stable Angina (<35% of LVEF),
2. Surgical (n=610, EF 27%) vs. Medical (n=602, EF 28%)
3. 3-VD 60%, 2VD 30%

Velazquez EJ, et al. N Engl J Med 2016; 374:1511-1520 DOI: 10.1056/NEJMoa1602001

# All Cause Mortality at 5 year

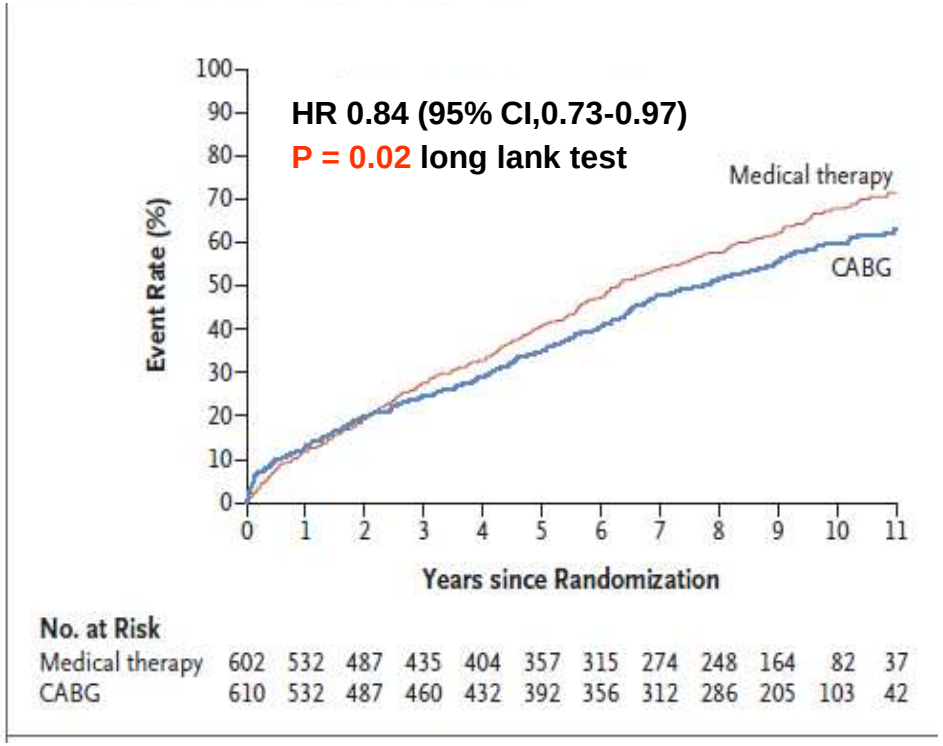



**Not Different**

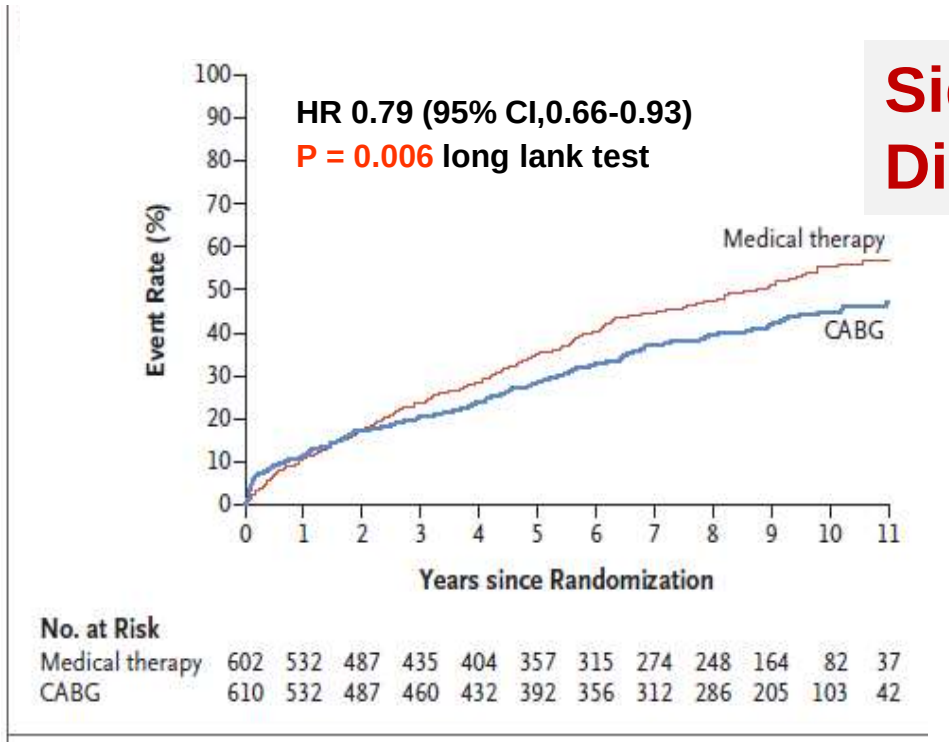
Velazquez EJ, et al. NEJM 2011;364:1607-16.

# All Cause Mortality at 10 year

## Any Death




## Cardiovascular Death




**Significantly Different !**

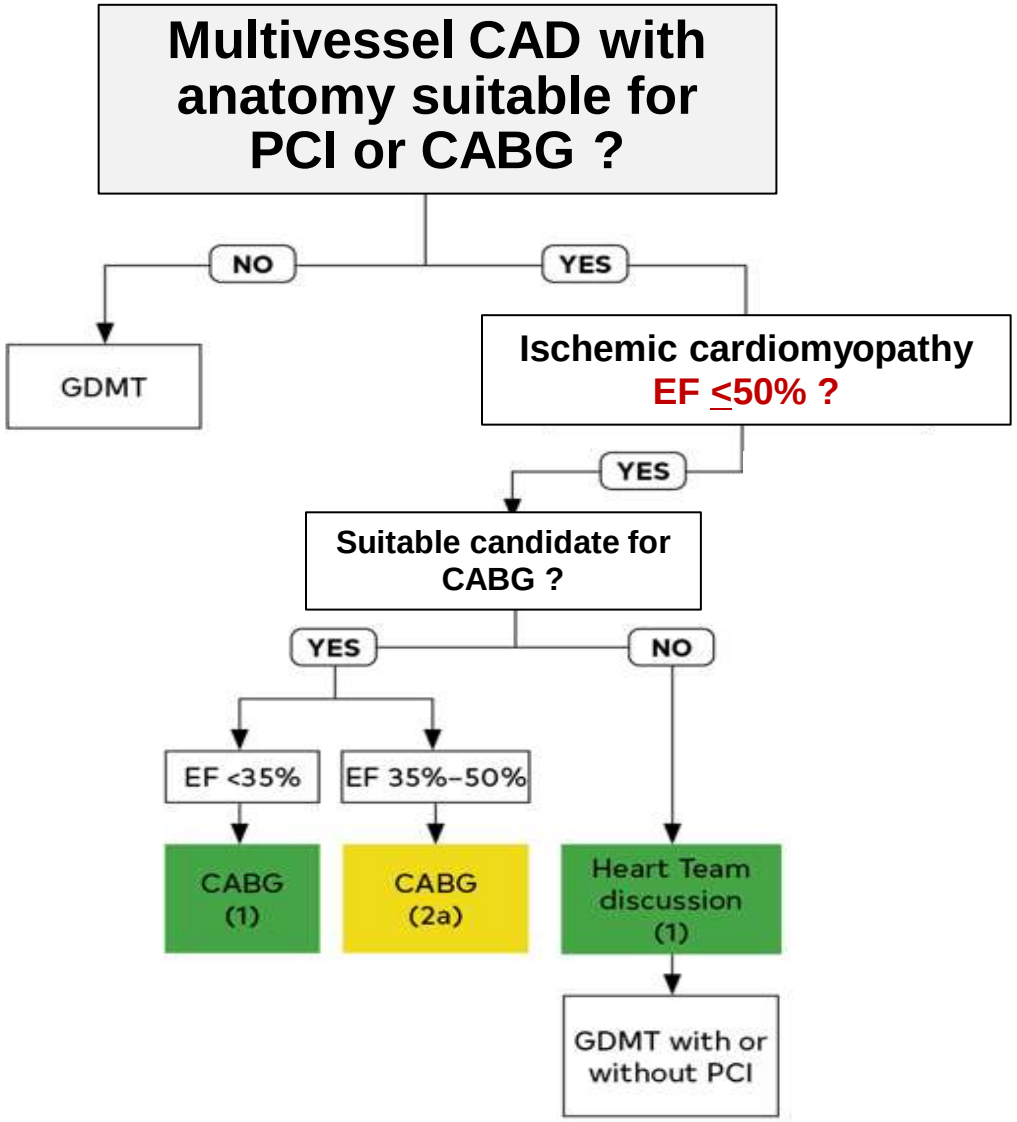
Velazquez EJ, et al. N Engl J Med 2016; 374:1511-1520 DOI: 10.1056/NEJMoa1602001

# CABG vs. Medical Treatment for MVD

Surgical Treatment for Ischemic Heart Failure (STICH) Trial

***CABG Is Better Over Medication in Patients with Stable Angina (<35% of LVEF)***

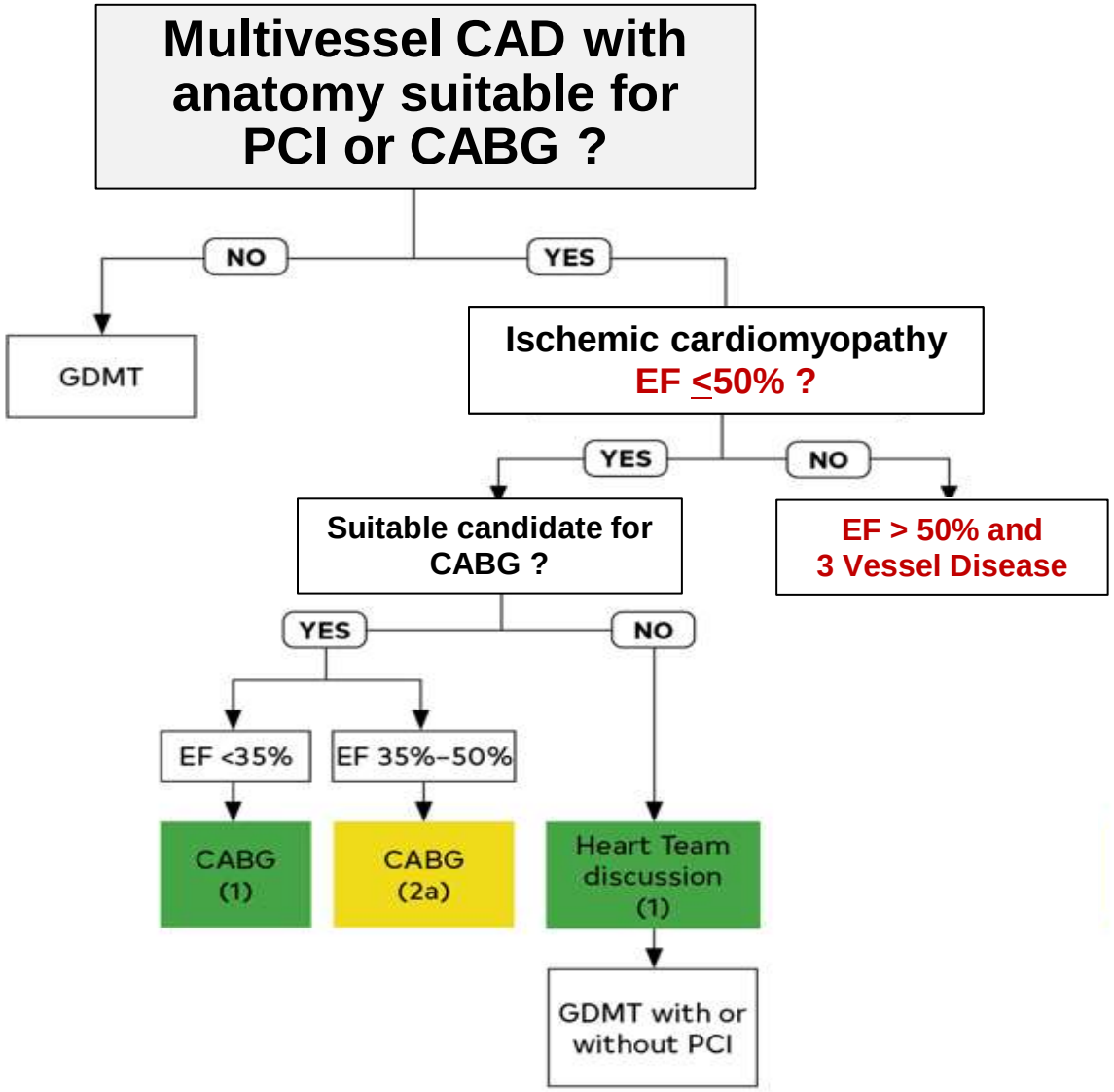
# *2021* ACC/AHA/SCAI, Guideline for Coronary Artery Revascularization




**EF ≤50% and 3 Vessel Disease**

**CABG Is Better !**

# *2021* ACC/AHA/SCAI, Guideline for Coronary Artery Revascularization



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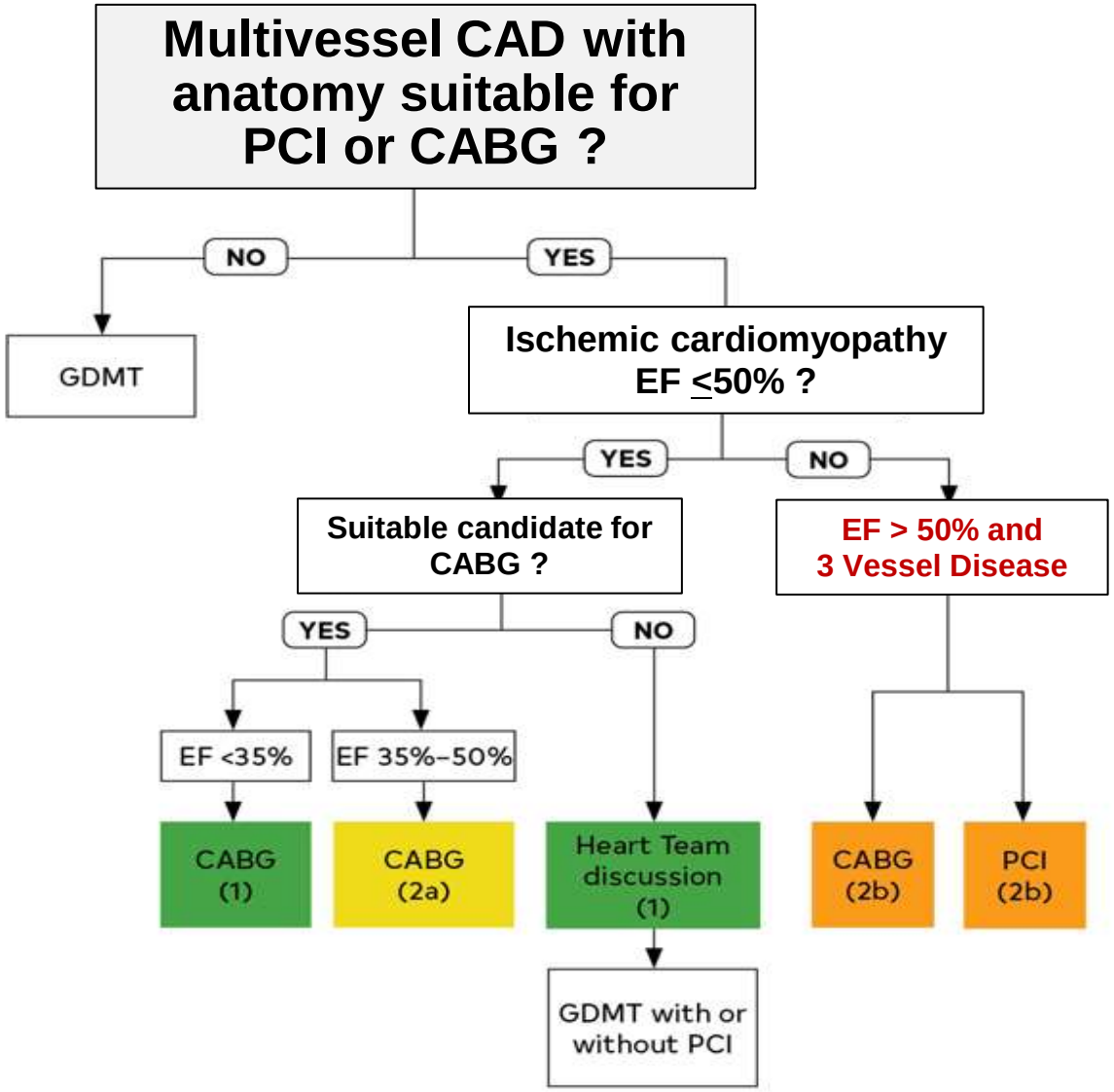



**Any Revascularizations (2b)**

# Any Revascularizations (2b)

**Class 2b (WEAK)** **Benefit ≥ Risk**

**Suggested phrases for writing recommendations:**

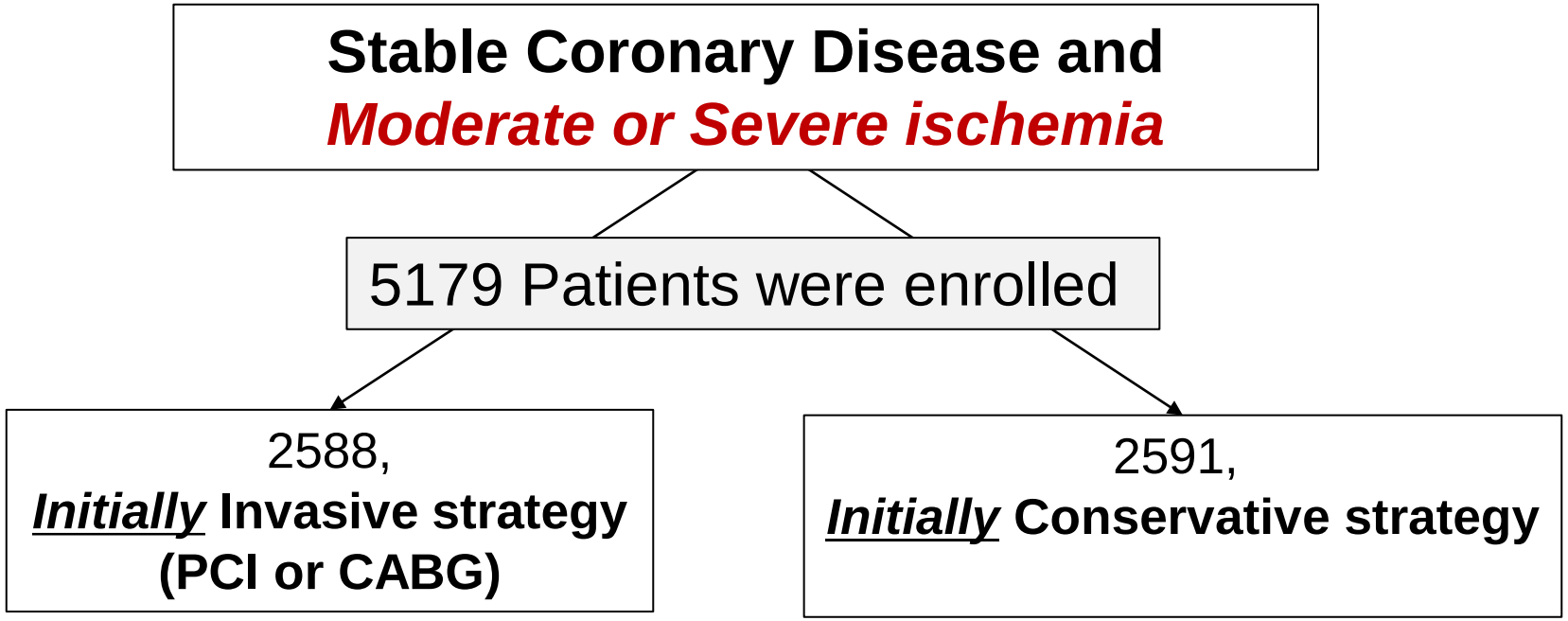
- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well-established

# Underlying Data, 2

## Any Revascularizations (2b)

***Why ?***

# ISCHEMIA Study




***The primary outcome;*** composite of death from cardiovascular causes, myocardial infarction, or hospitalization for unstable angina, heart failure, or resuscitated cardiac arrest.

David J. Maron et al, for the ISCHEMIA Research Group, N Engl J Med 2020; 382:1395-1407
https://www-nejm-org-ssl.libproxy.amc.seoul.kr/doi/10.1056/NEJMoa1915922

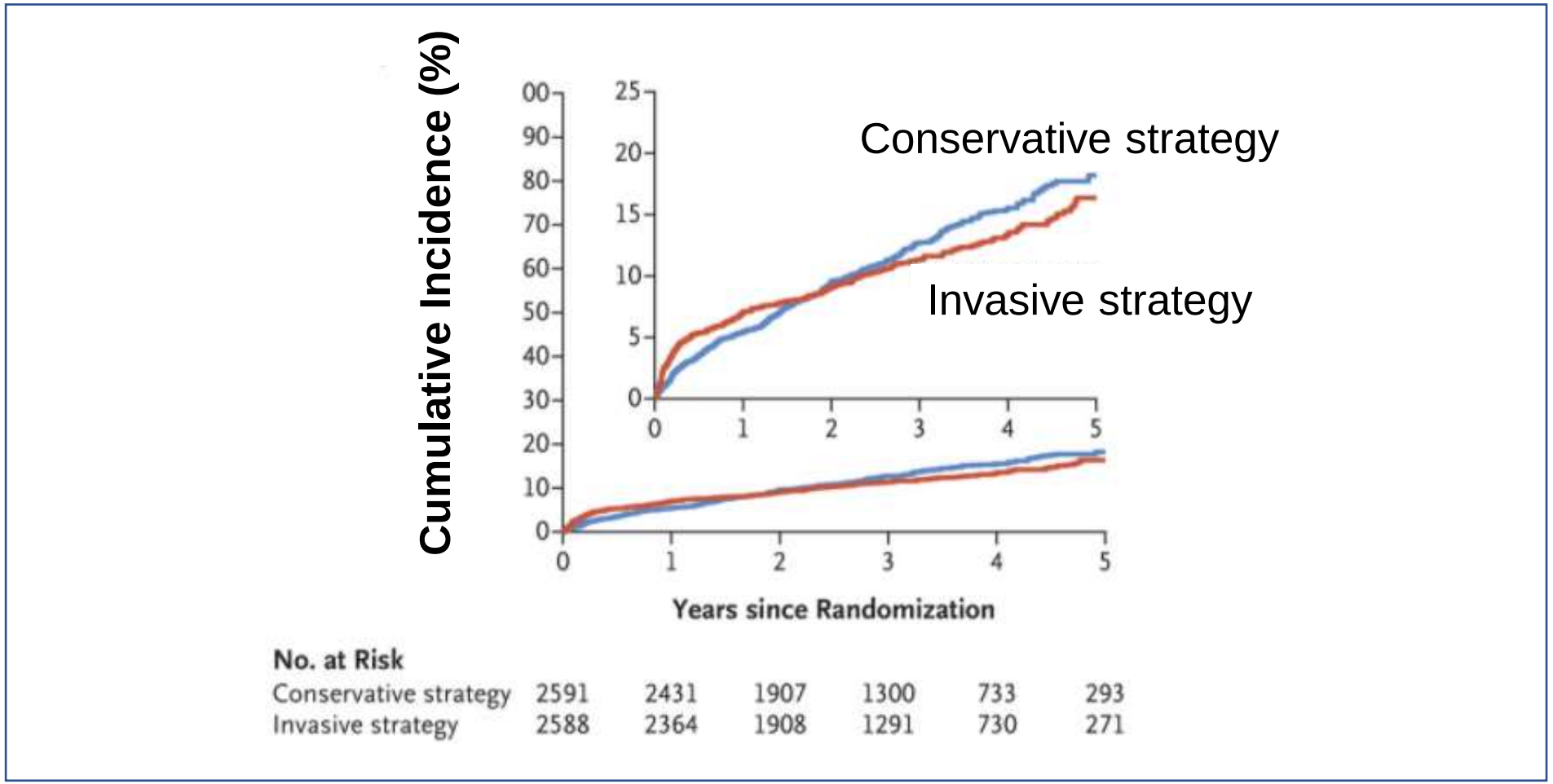
# Coronary Anatomy by CCTA (≥ 50% stenosis)

| | Total (N=5179) | INV (N=2588) | CON (N=2591) |
|---|---|---|---|
| 0 | 0.1% (4/2986) | 0.1% (2/1490) | 0.1% (2/1496) |
| 1 | 23.3% (697/2986) | 24.2% (360/1490) | 22.5% (337/1496) |
| 2 | 31.4% (938/2986) | 29.1% (434/1490) | 33.7% (504/1496) |
| 3 | 45.1% (1347/2986) | 46.6% (694/1490) | 43.6% (653/1496) |

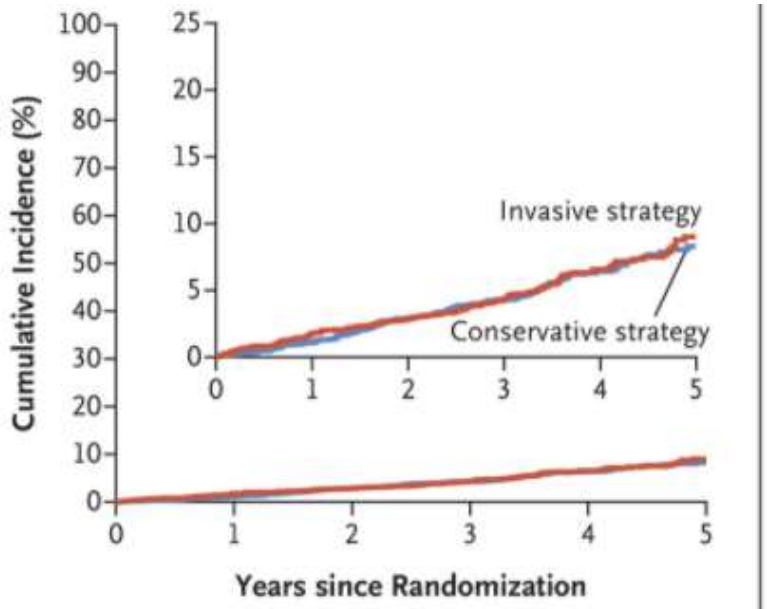
***Multivessel Disease >75%***

# Primary Composite Outcomes at 3.2 years

Death from cardiovascular causes, Myocardial infarction, or Hospitalization for unstable angina, Heart failure, or Resuscitated cardiac arrest.

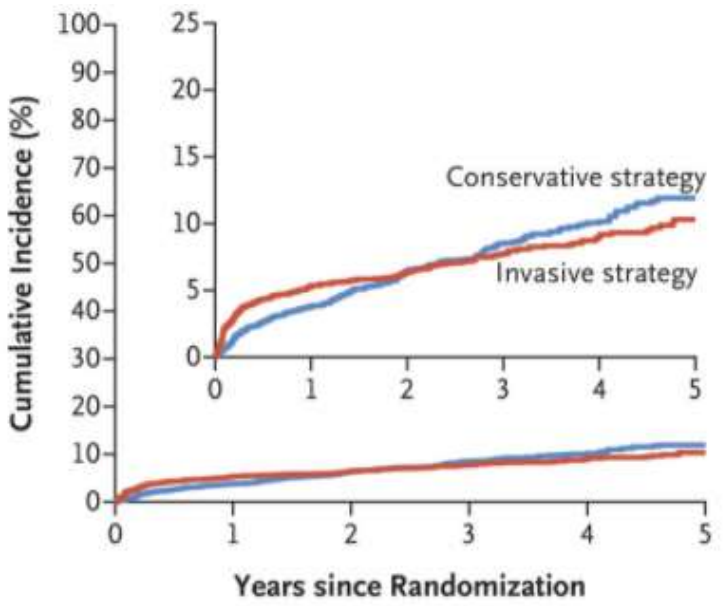


# Death from Any Cause




| No. at Risk | | | | | | |
|---|---|---|---|---|---|---|
| Conservative strategy | 2591 | 2548 | 2065 | 1445 | 844 | 349 |
| Invasive strategy | 2588 | 2518 | 2061 | 1431 | 827 | 317 |

# Myocardial Infarction

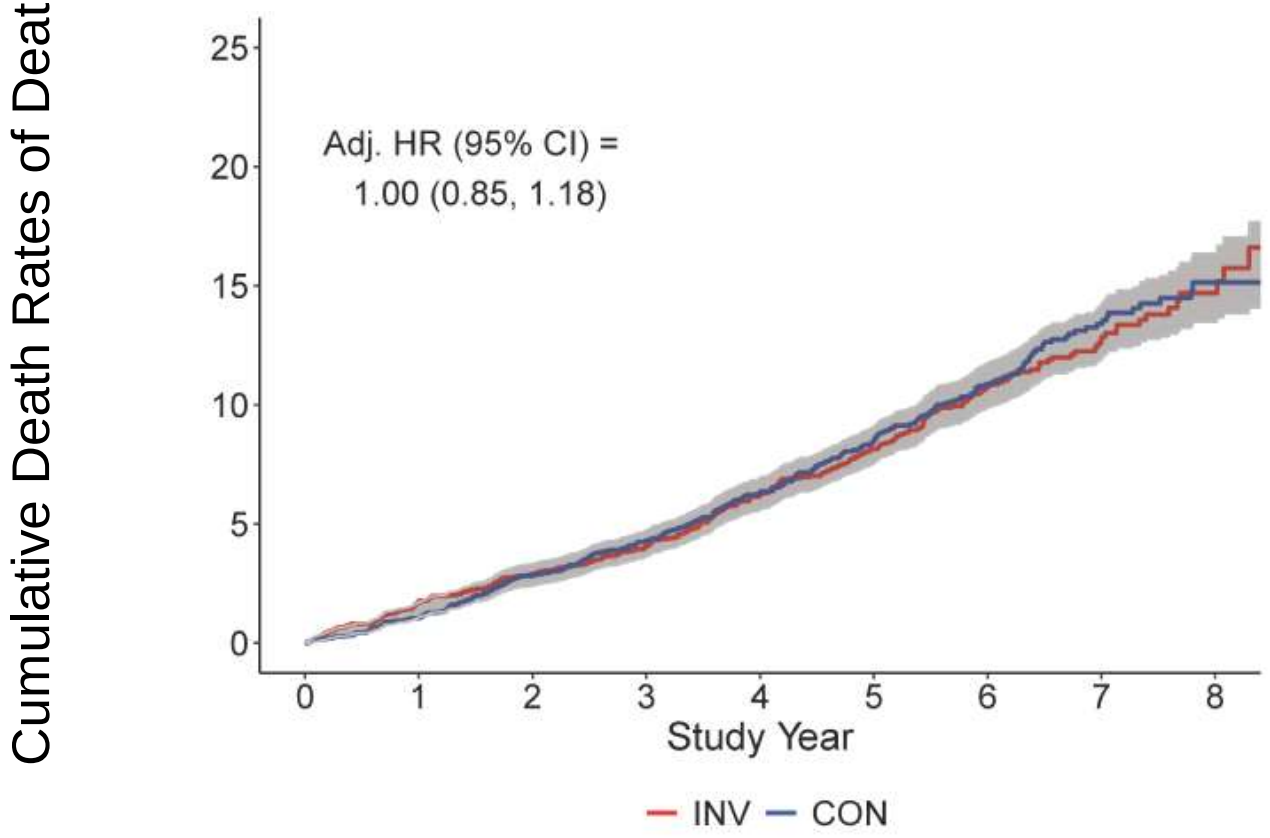



| No. at Risk | | | | | | |
|---|---|---|---|---|---|---|
| Conservative strategy | 2591 | 2452 | 1931 | 1321 | 747 | 298 |
| Invasive strategy | 2588 | 2379 | 1931 | 1313 | 742 | 283 |

# ISCHEMIA-EXTEND- ***All Death***

## Extended Follow-up 5.7 years median

## ***Main Message Doesn't Change!***




**Nearly Identical**

Judith S. Hochman et al, AHA, 2022, 10.1161/CIRCULATIONAHA.122.062714

# ISCHEMIA study

***No Survival and Ischemic Event Benefit of Invasive Strategy, as Compared With Conservative Strategy For the Patients with Moderate or Severe Ischemia. (>75% Multi-Vessel Disease included).***

Judith S. Hochman et al, AHA, 2022, 10.1161/CIRCULATIONAHA.122.062714
David J. Maron et al, for the ISCHEMIA Research Group, N Engl J Med 2020; 382:1395-1407

# ***Main Message***
# form ISCHEMIA study

***Optimal Medical Therapy Is Good Enough for Majority Patients of Stable Coronary Disease,***
***And So, We Have to Think About Unnecessary Revascularization !***

David J. Maron et al, for the ISCHEMIA Research Group, N Engl J Med 2020; 382:1395-1407

# Underlying Data, 3

***PCI vs. CABG***

***For Multi-Vessel Disease***

# ***PCI vs. CABG***

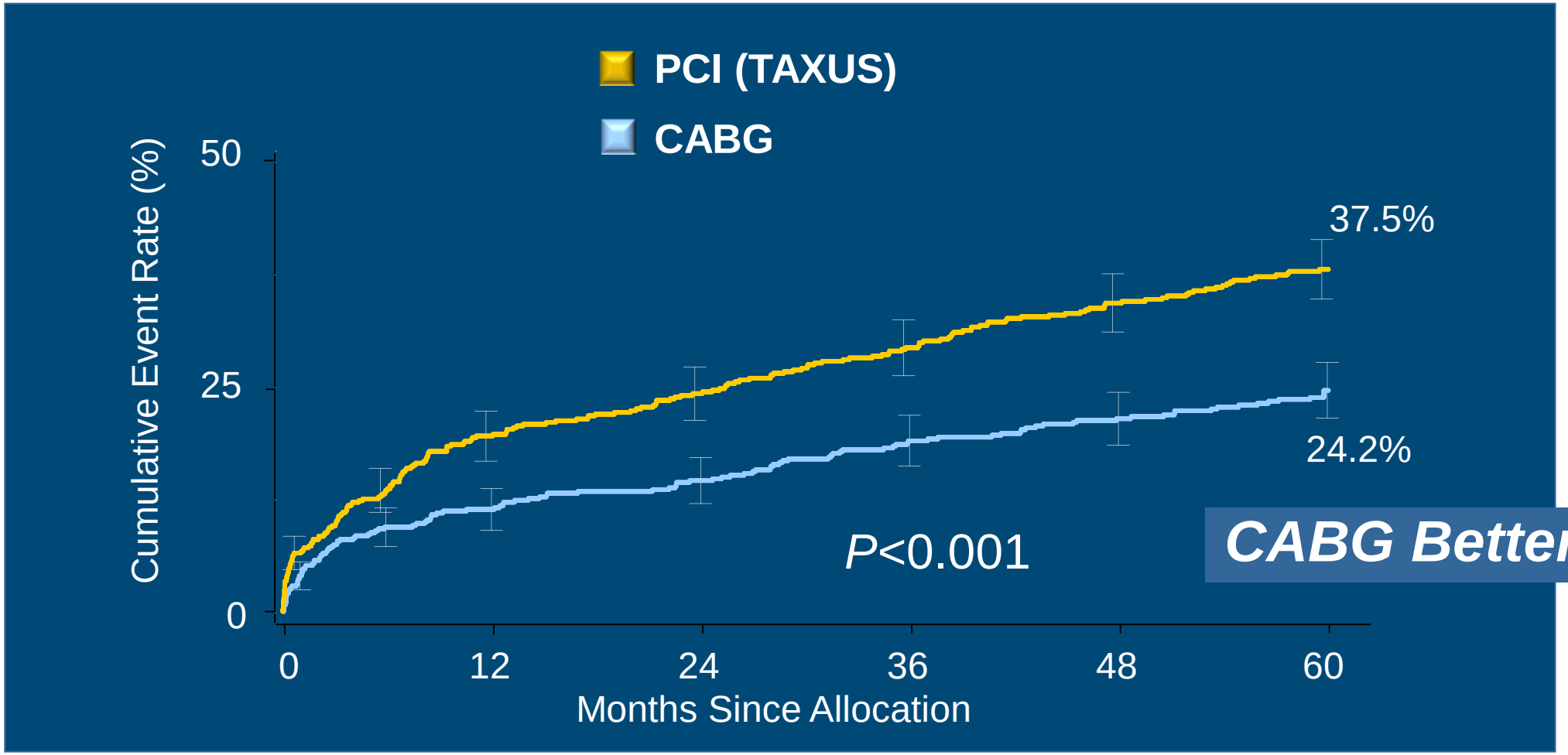
## *for Multi-vessel Disease*

1. BARI 2D
2. FREEDOM
3. SYNTAX
4. BEST

***Very Limited Data !***

# SYNTAX *(3VD Subset)*

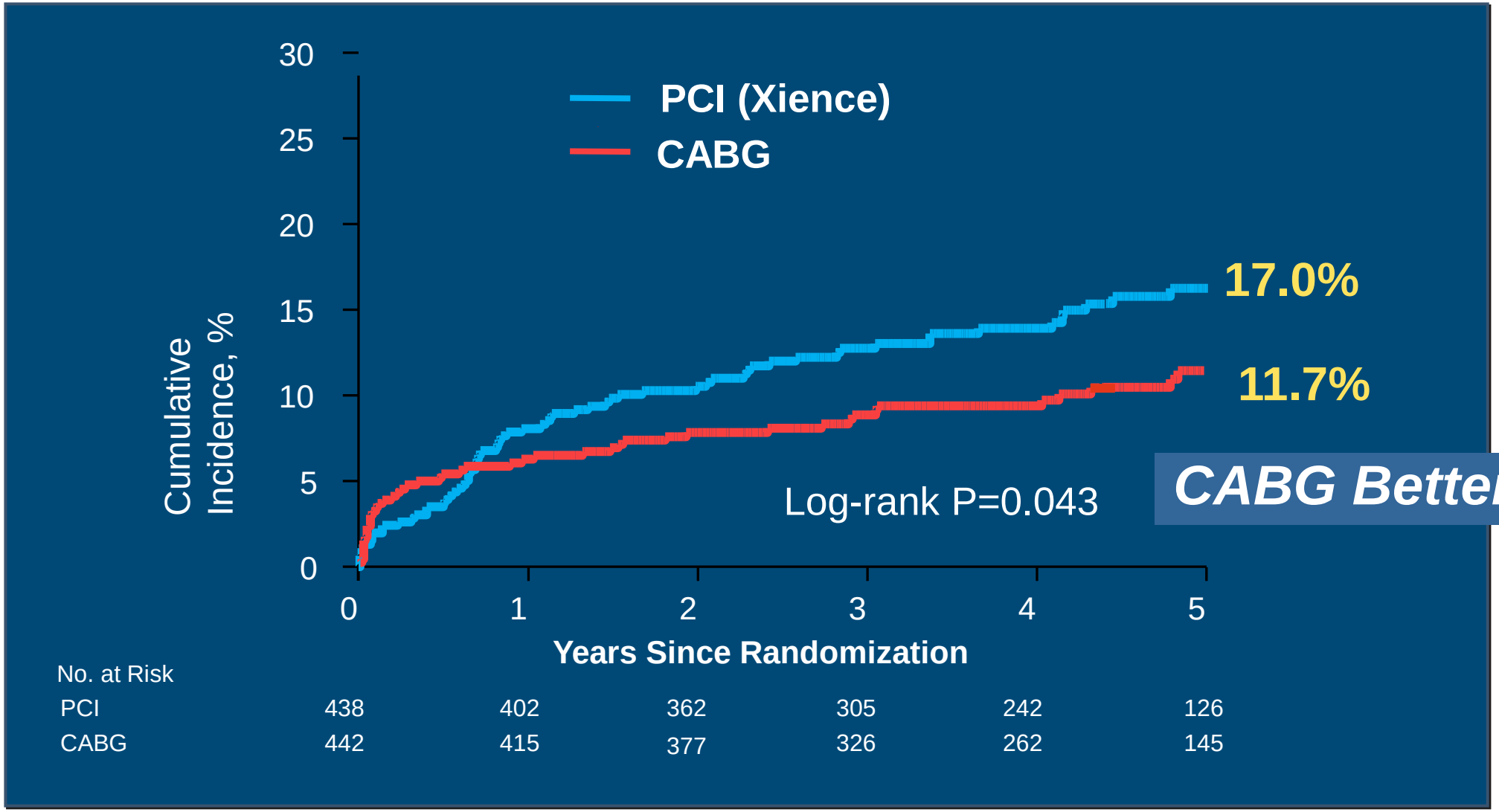
## Death, MI, Stroke or Any RR at 5 Year




Friedrich W Mohr et al. LANCET 2013, 381; 629-638

# *BEST*

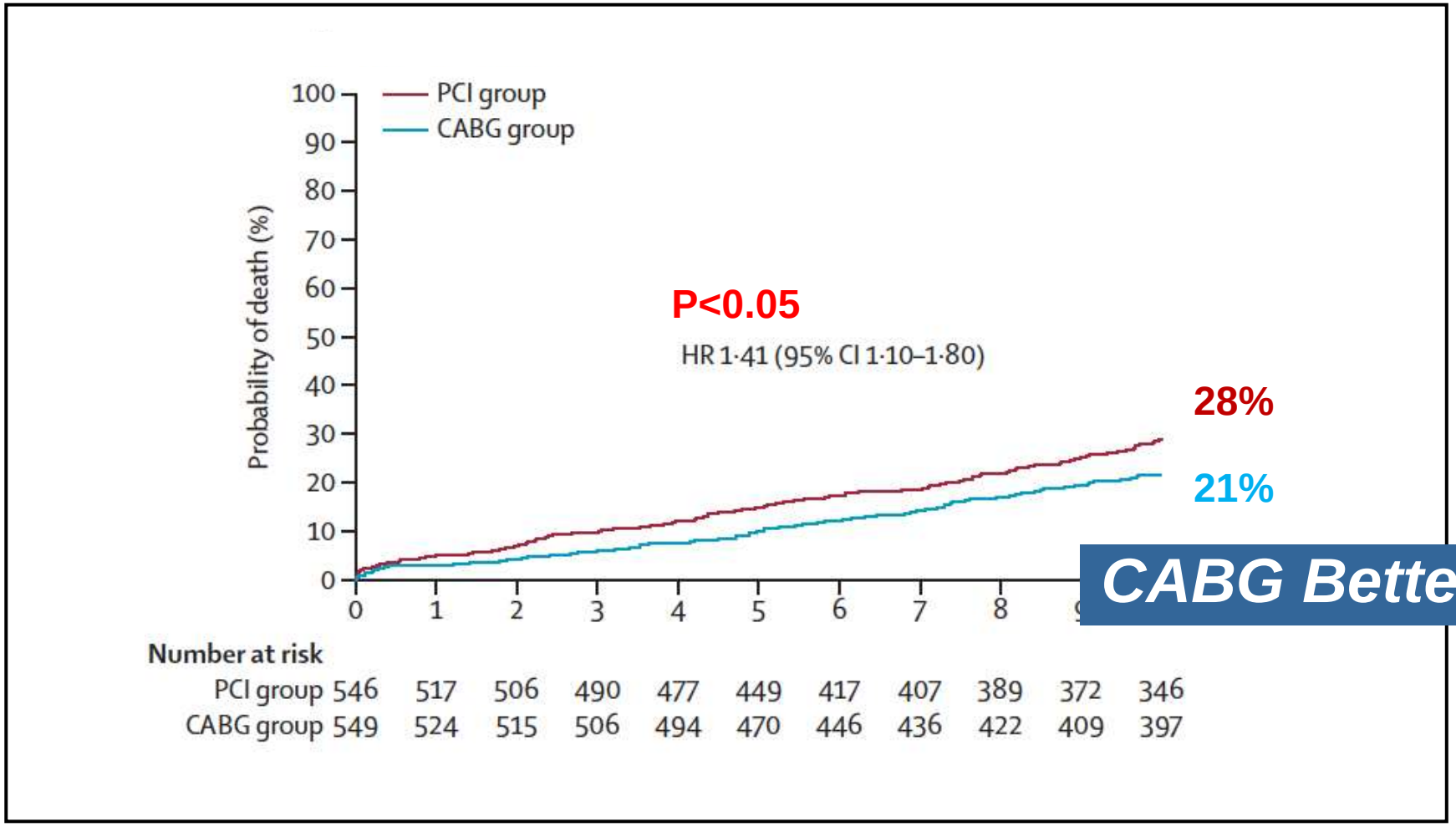
## Death, MI or TVR at 5 Year




Park SJ et al, NEJM. 2015; 372: 1204-1212

# SYNTAX *(3VD Subset)*

## *All Death at 10 Year*



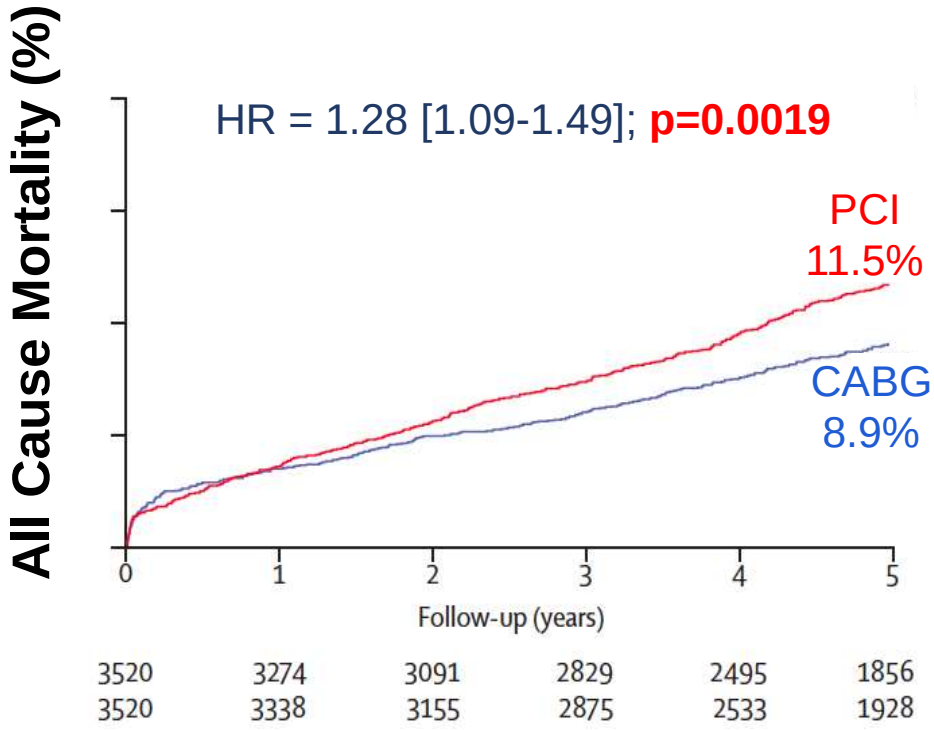

Lancet 2019; 394: 1325–34

# All Death

## *IPD Meta-analysis:*

*11,518 Patients From 11 Randomized Trials*

### Multivessel Disease (n=7040)

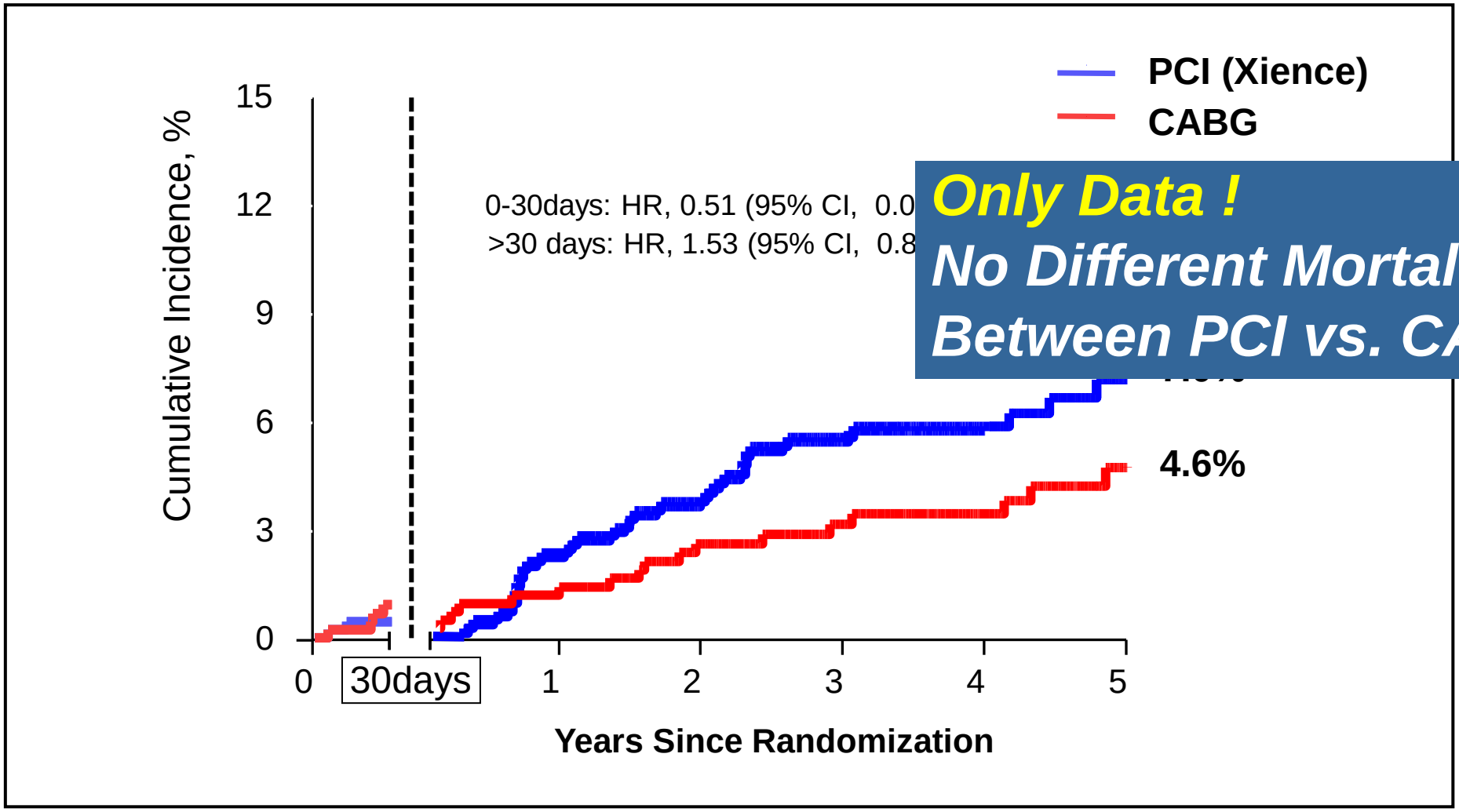



***CABG Better !***

Head SJ et al. Lancet 2018; 391: 939-48

# BEST

## All Death at 5 Year




***Only Data !***
***No Different Mortality, Between PCI vs. CABG***

Park SJ et al, NEJM. 2015; 372: 1204-1212

# PCI vs. CABG
## *for Multi-Vessel Disease*

***CABG was superior*** to PCI with DESs in patients with advanced CAD (predominantly, 3 VD).

# 2021 ACC/AHA/SCAI, Guideline Revascularization for *3 Vessel Disease (>50% EF)*

| COR | LOE | Recommendations |
|---|---|---|
| 2b | B-R | 1. In patients with SIHD, normal ejection fraction, significant stenosis in 3 major coronary arteries (with or without proximal LAD), and anatomy suitable for CABG, CABG may be reasonable to improve survival.[37,40,50,51] |
| 2b | B-R | 2. In patients with SIHD, normal ejection fraction, significant stenosis in 3 major coronary arteries (with or without proximal LAD), and anatomy suitable for PCI, the usefulness of PCI to improve survival is uncertain.[59,60] |

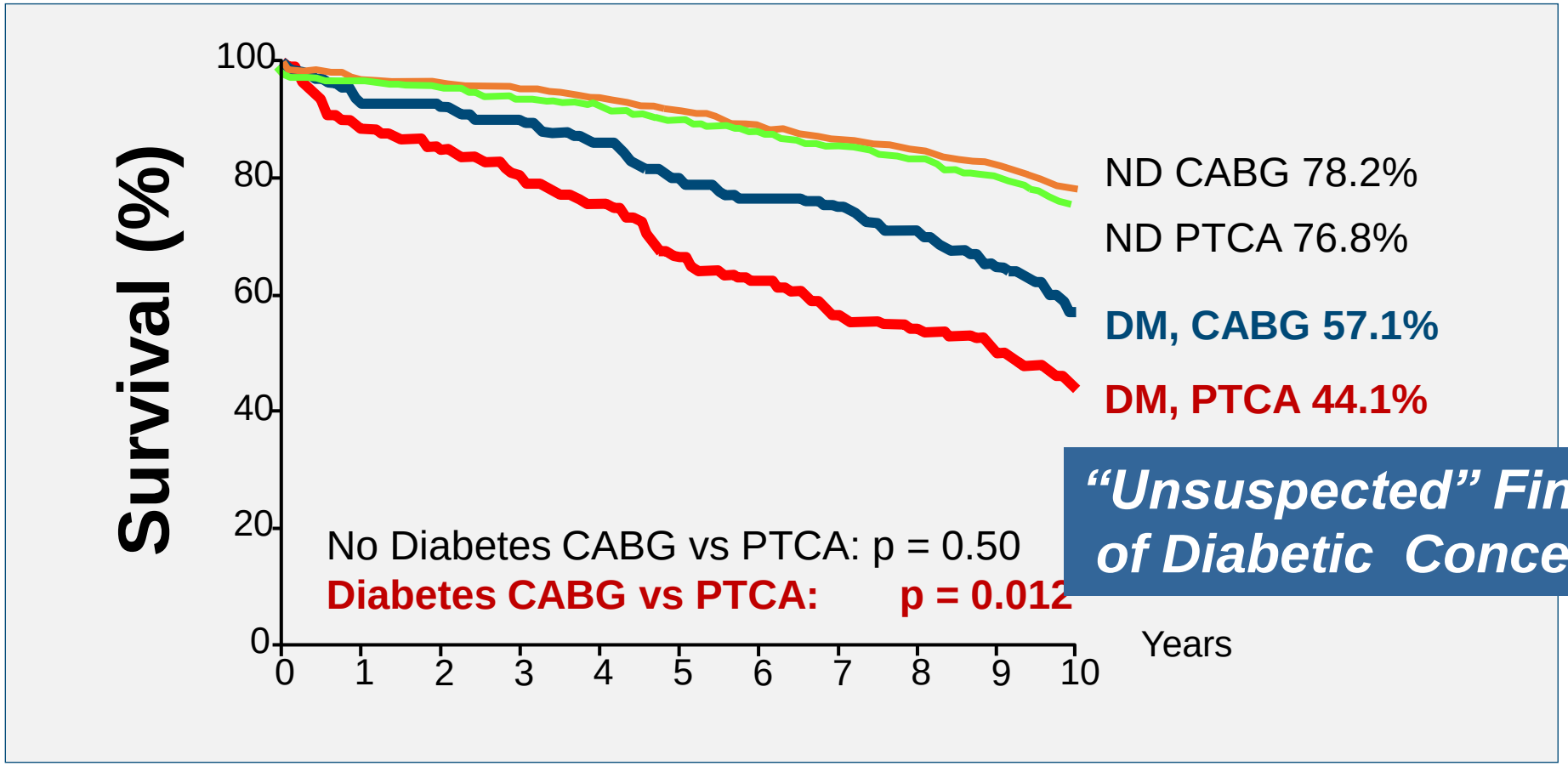
# Underlying Data, 3

***Issue of Diabetes***

# BARI 10-Year Survival

## *PTCA vs. CABG in Multi-Vessel Disease*

*From 1988 to 1991 (n=1,829)*

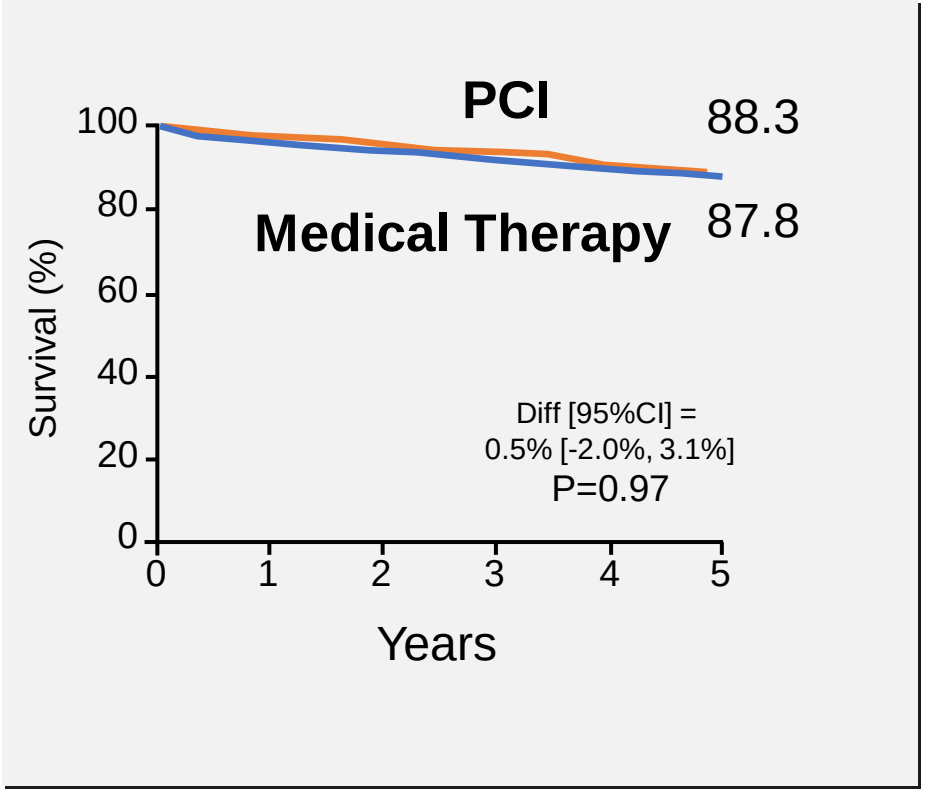



***"Unsuspected" Finding of Diabetic Concerns***

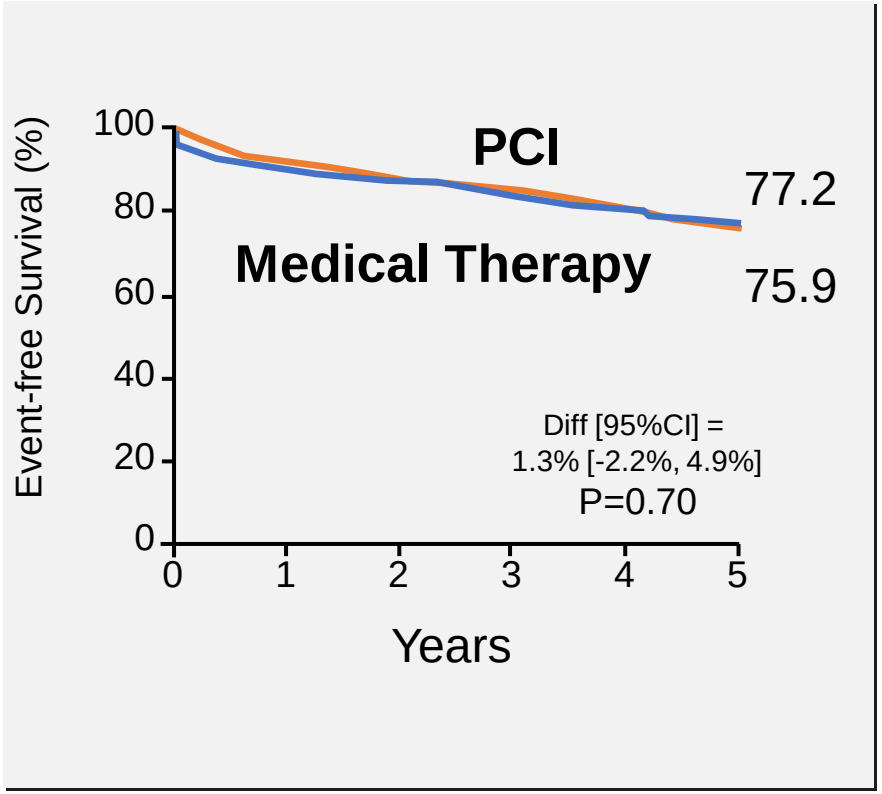
JACC. 2007 Apr 7;49(15):1600-6.

# BARI 2D (DM) *at 5 year*
## *PCI Had No Benefit Over Medical Treatment in Low Risk Patients*

### Survival



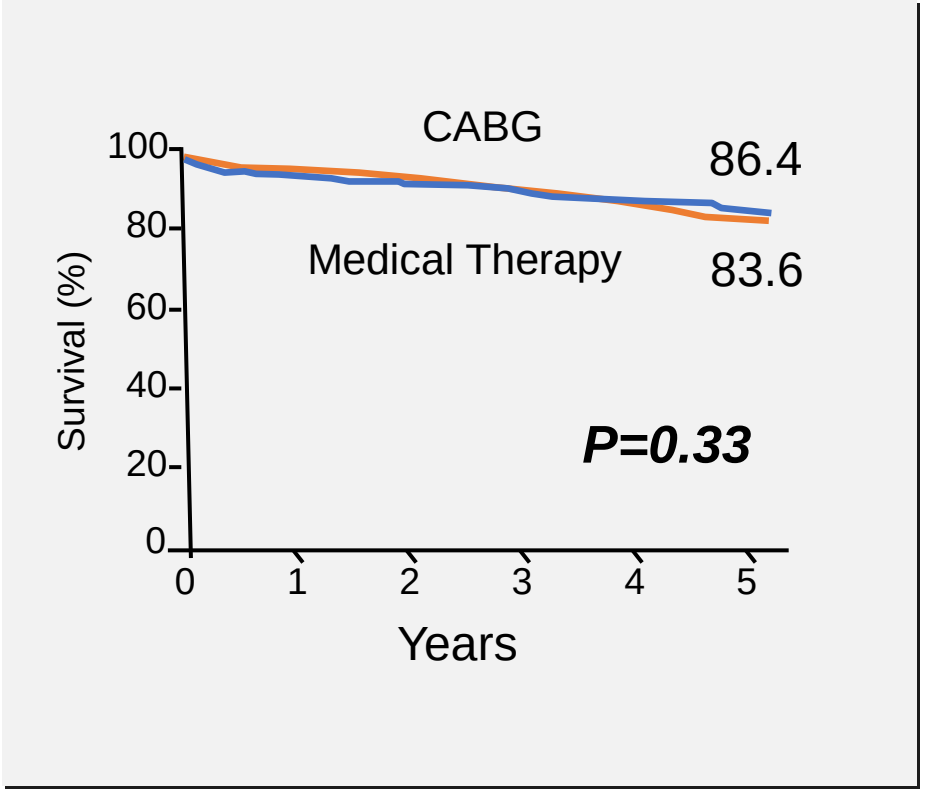

### Freedom from MACE (Death, MI, or Stroke)



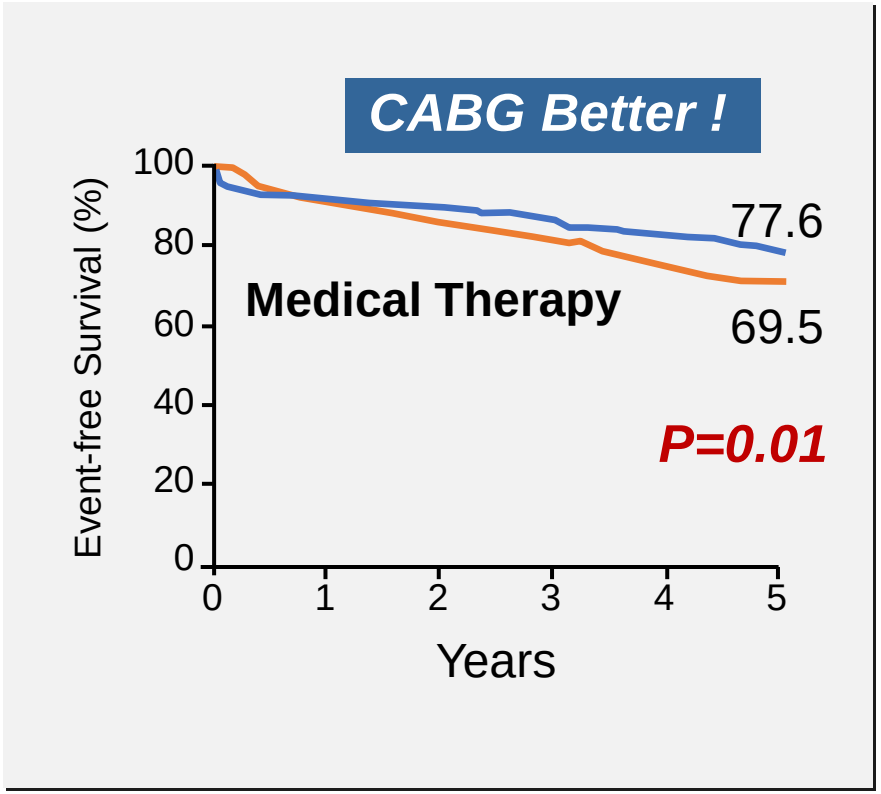

The BARI 2D Study Group.*NEJM* 2009;360:2503-15

# BARI 2D (DM) *at 5 year*
## *CABG Is Better Over Medical Treatment in High Risk Patients*

### Survival

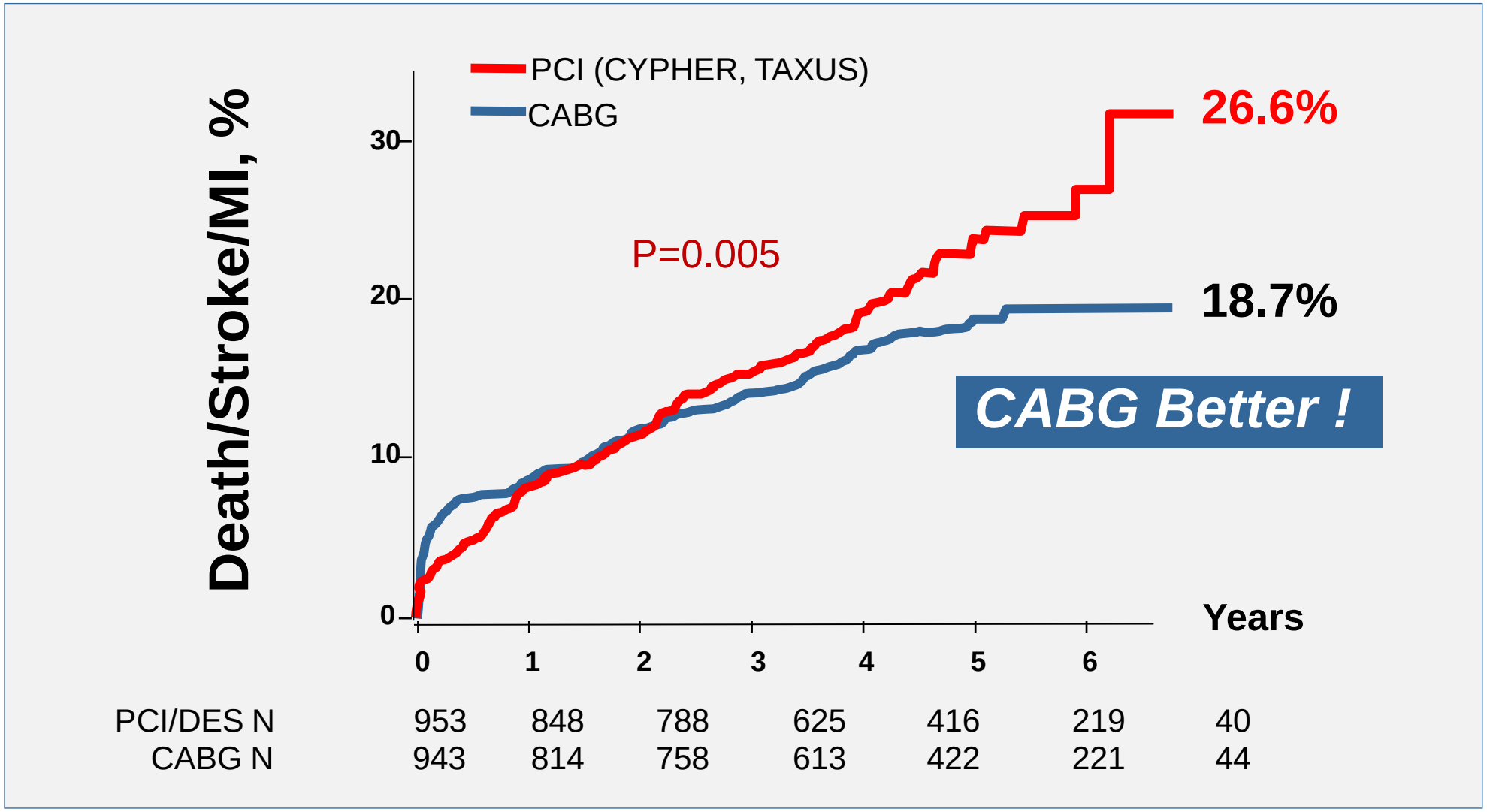



### Freedom from MACE (Death, MI, or Stroke)



# FREEDOM *(DM and MVD)*

## Death / MI / Stroke at 5 Year

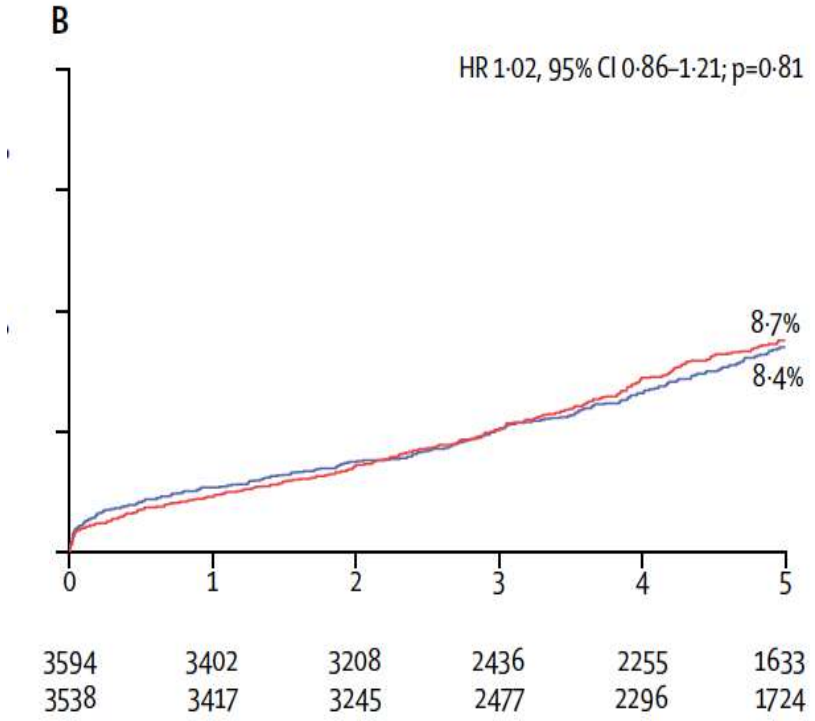



Farkouh et al, *NEJM* 2012 November 4

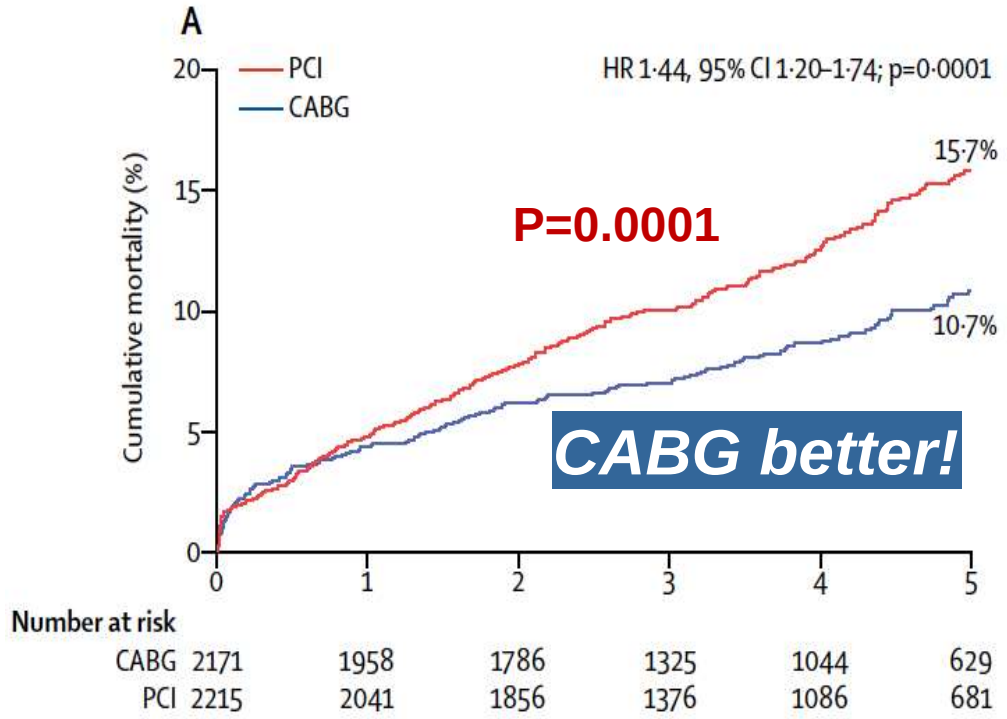
# All Death

Individual Patient-Data Pooled Analysis
of 11,518 Patients From 11 Randomized Trials

## Non-DM




## DM




Head SJ et al. Lancet 2018; 391: 939-48,

# *2021 ACC/AHA/SCAI, Guideline for Diabetic Multivessel Disease*

1. **Patients with Diabetes who Have 3 VD *Should Undergo CABG (1A).***
2. ***If they are Poor Candidates for CABG, PCI May be Considered (2a, B-NR).***

J Am Coll Cardiol. Dec 09, 2021. Epublished DOI: 10.1016/j.jacc.2021.09.006

# *Limited Data Interpretation*

1. **All Studies Used 1st Generation DES**

   **BARI 2D:** DES 35% BMS 56%,
   **FREEDOM:** Cypher 49%, TAXUS 41%,
   **SYNTAX:** TAXUS 100%

2. **Lack of Concept of Physiology and Imaging of PCI**
3. **Issue of Complete Revascularization**

# ***BEST study***

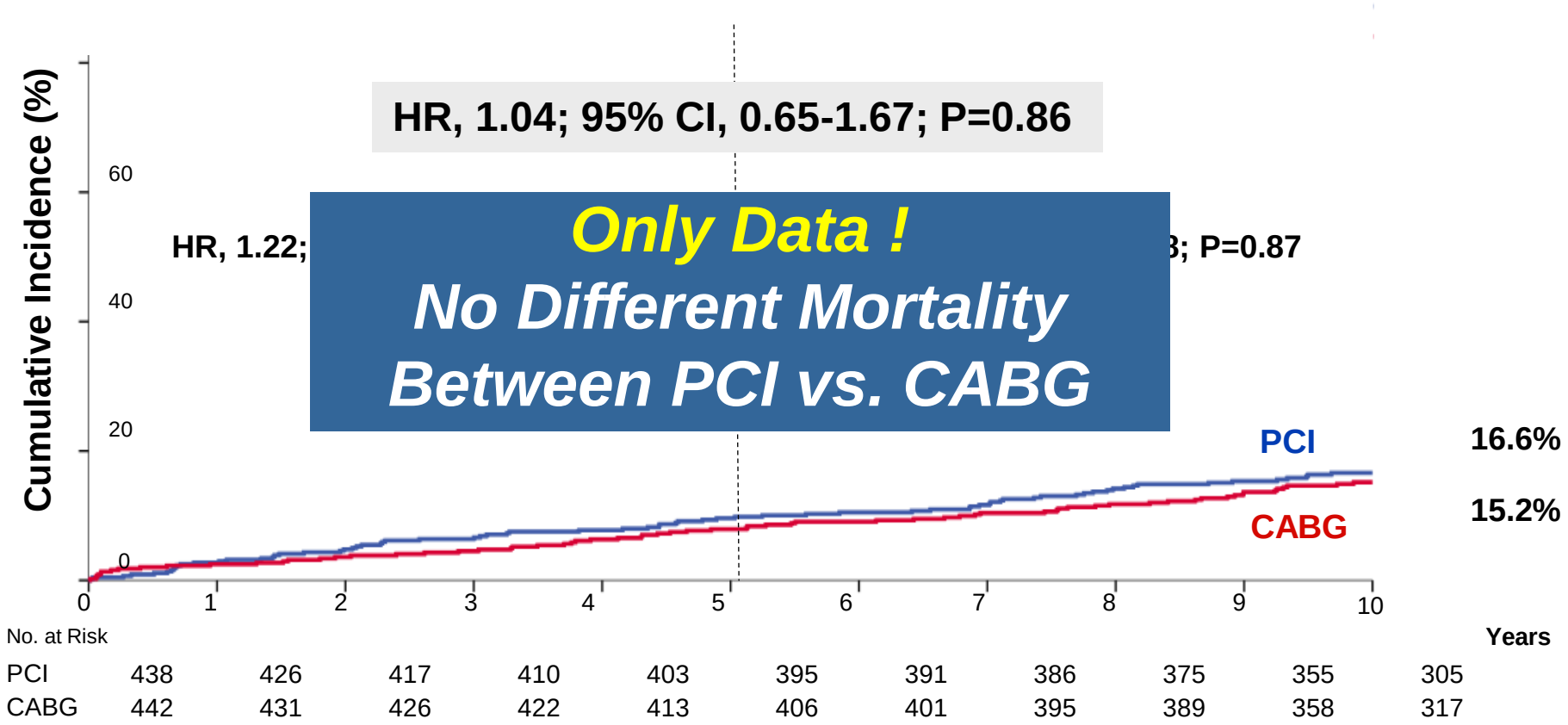
## ***PCI vs. CABG for MVD***

- ***All XIENCE (2nd Generation) DES Used***
- ***IVUS Used 70%***

Park SJ et al, NEJM. 2015; 372: 1204-1212

# BEST

# All Death at 10 Year




Ahn JM, Park SJ et al, Circulation 2022, Sep 19

***What Does It Mean ?***

**Contemporary PCI,**

***(Physiology and Image Supported)***

**Is Totally Different !**

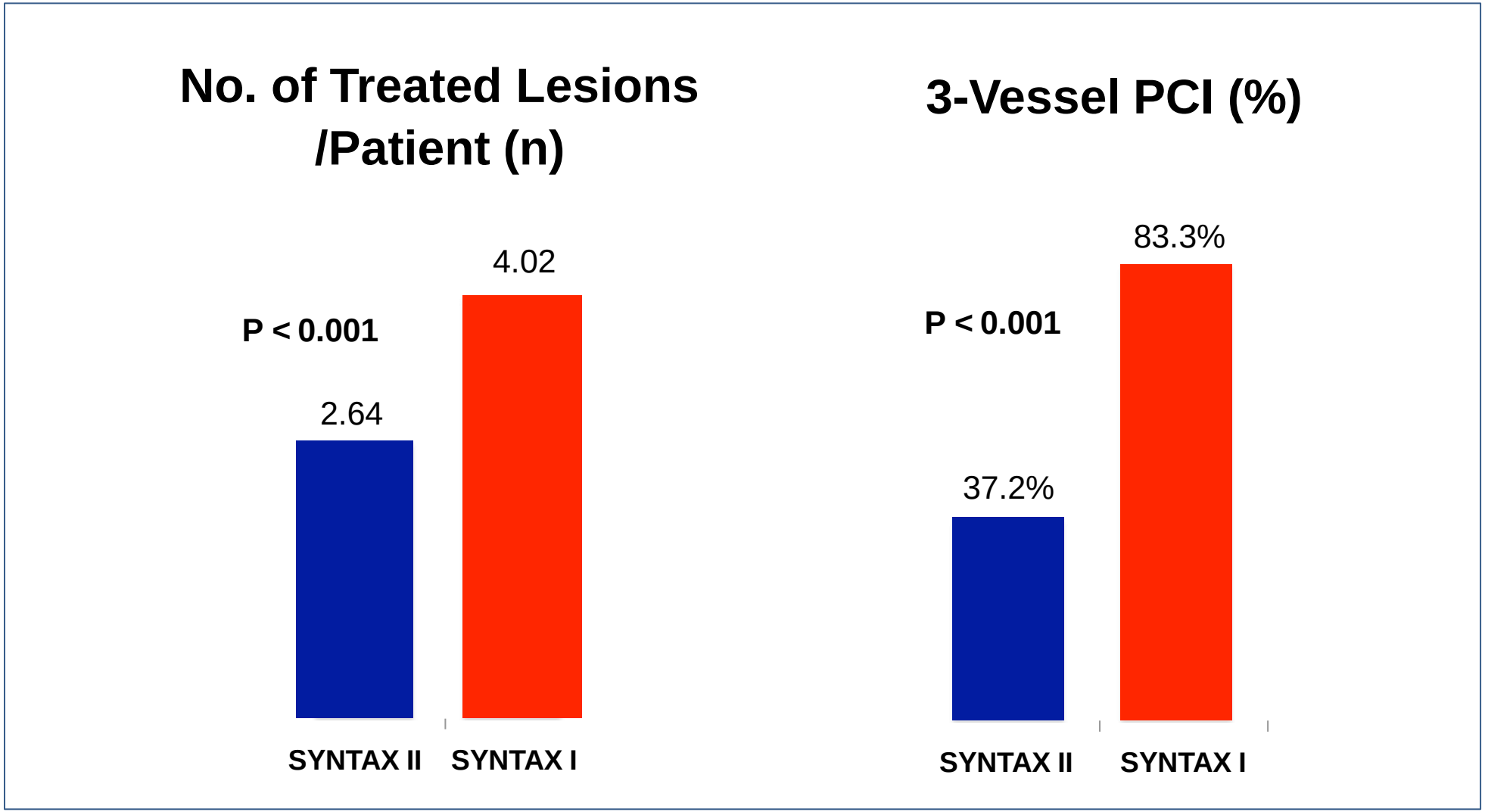
# ***Impact of Physiology and Imaging on Revascularization Outcome for Multi-Vessel Disease (SYNTAX II)***

- iFR/FFR Measured Lesions (n=1177),
- 84.1% of IVUS Used
- MACE (all-cause death, stroke, any myocardial infarction, or any revascularization)

Escaned J, Banning A, Serruys PW. Eur Heart J. 2017 Nov 7;38(42):3124-3134.

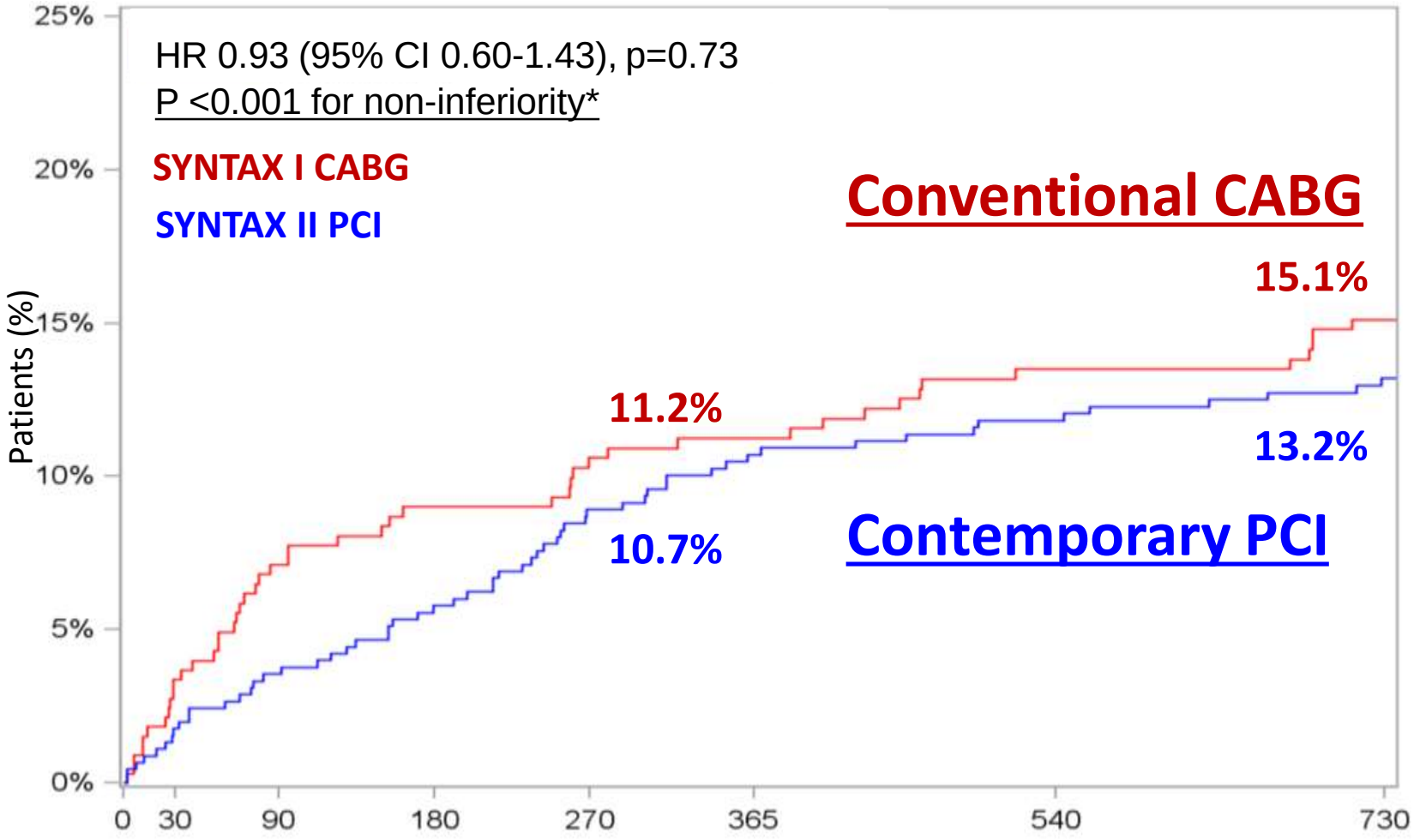
# Impact of Physiology on PCI

## *31% of PCI Was Deferred After iFR/FFR*



# *PCI vs. CABG at 2 years*

## MACCE




**Not Different**

# *Message From SYNTAX II*

1. ***Integrated Use of FFR and IVUS Decrease MACCE***
2. ***Outcomes of Physiology Guided PCI Are Comparable with Conventional CABG for Patients with 3 Vessel Disease.***
3. ***PCI Outcomes Are Not Related with Syntax Score***

# *Message From SYNTAX II*

**Contemporary PCI (physiology and Image supported) Is *Totally Different Strategy and Has Totally Different Clinical Outcomes* Compared to Conventional Angio-Guided PCI.**

# *MisUnderstanding about FFR*

# FAME 3

**Patients with *Angiographically 3 Vessel Disease (n=1500)***

R

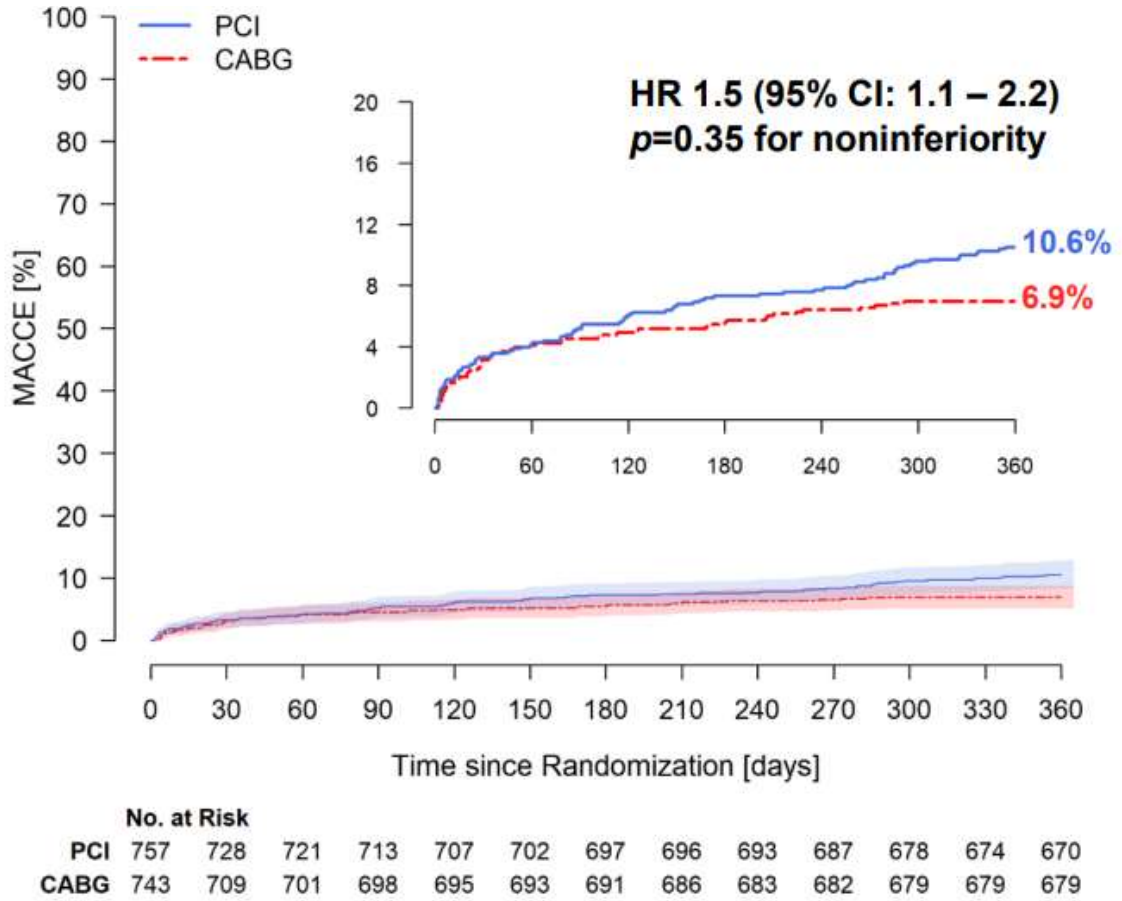
**FFR Guided PCI + OMT (n=757)**

**CABG (n=743)**

**Primary Endpoint at 1 year :**
Death, MI, Stroke or Repeat Revascularization

# Primary Endpoint

## Death, MI, Stroke or Repeat Revascularization




William F. Fearon, et al, N Engl J Med 2022; 386:128-137

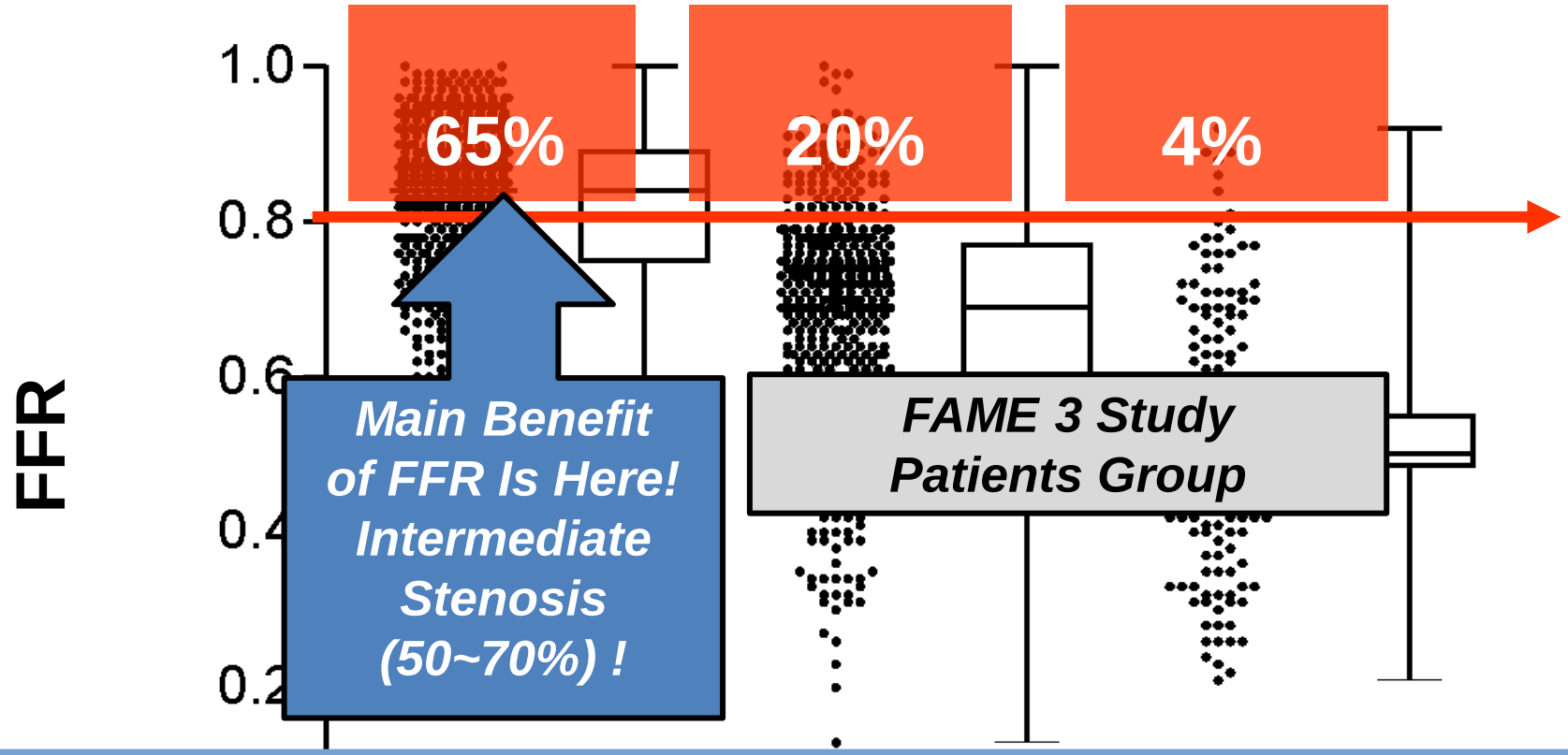
# Procedural Characteristics

| Variable | PCI (n=757) |
|---|---|
| % Lesions FFR measured | 82% |
| FFR>0.80 | 24% |
| Staged procedure | 22% |
| Number of stents | 3.7±1.9 |
| Total stent length | 80 mm |
| Intravascular imaging | 12% |
| FFR measured after PCI | 60% |

| Variable | CABG (n=743) |
|---|---|
| FFR measured prior to CABG | 10% |
| # of distal anastomoses | 3.4±1.0 |
| Multiple arterial grafts | 25% |
| LIMA | 97% |
| Off-Pump surgery | 24% |

## Too Tough Lesion Subset ?

# ***FFR-guided Arm from FAME Study (1329 lesions)***

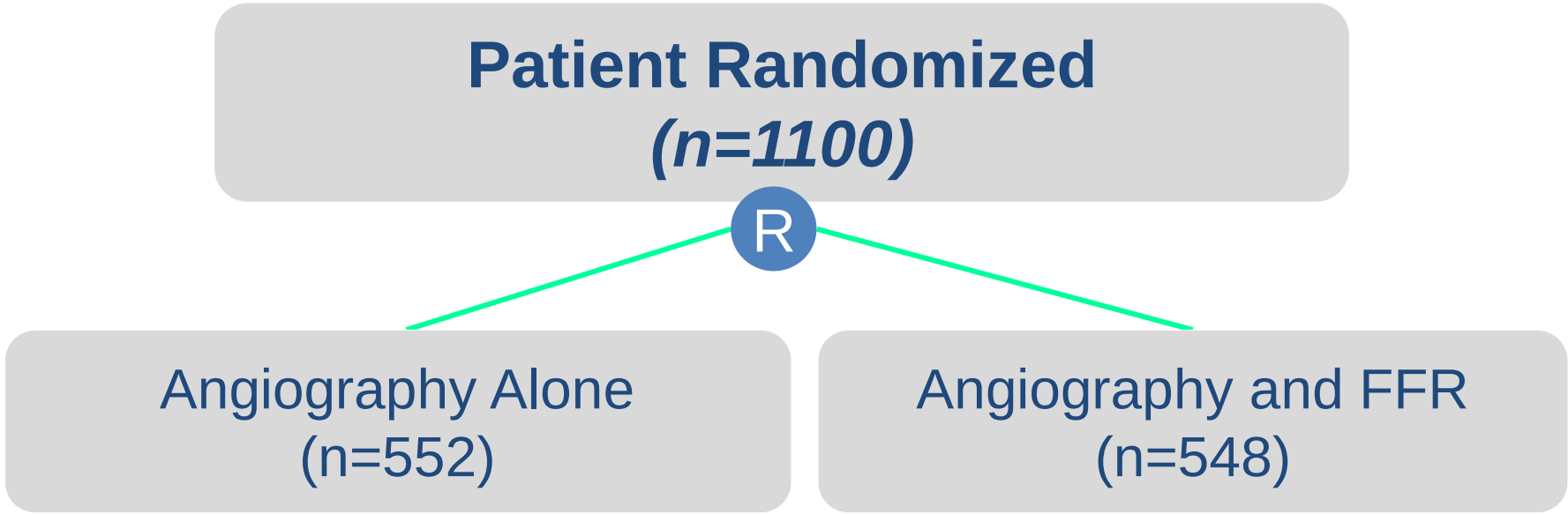



**FAME 3 Dealt with Too Tight Lesion Subset,**
**It Could Not Show the BENEFIT of FFR !**

JACC 2010;55:2816–21

# *Difference Between Misunderstanding and Ignorance*

# RIPCORD 2




**Primary Endpoint at 1 year :**

The coprimary outcomes assessed at 1 year were

**Hospital Costs and Quality of Life.**

# RIPCORD 2

***A strategy of systematic FFR assessment did not result in a significant reduction in cost or improvement in quality of life* compared with angiography alone**

Rodney H. Stables et al, Circulation. 2022;146:687–698

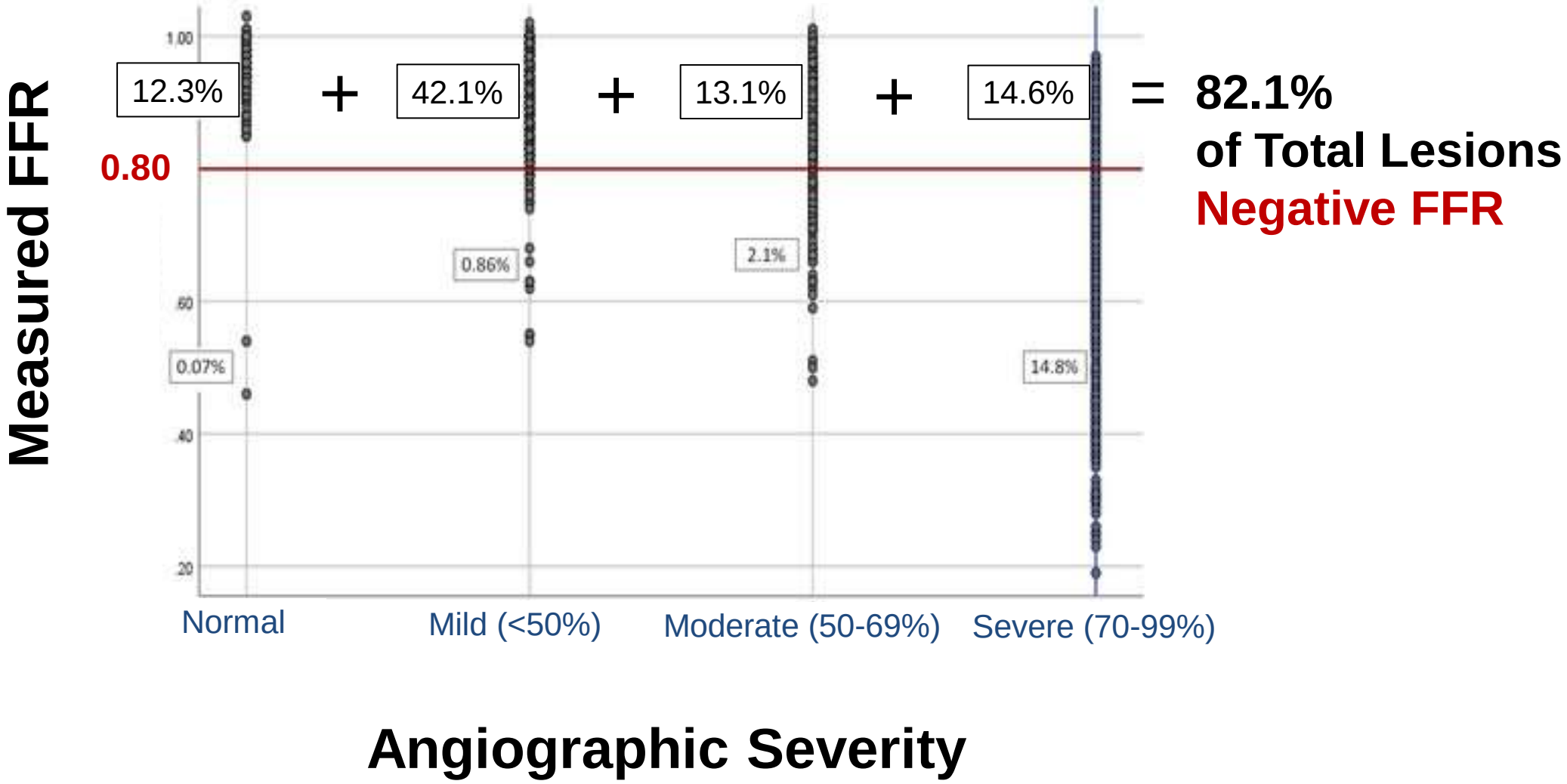
# RIPCORD 2

**Since FFR was done for people without disease, *the Cost will* of course *Increase in FFR arm,***

| | | |
|---|---|---|
| 0-vessel disease ? | 26 | 28 |
| 1-vessel disease | 48 | 40 |
| 2-vessel disease | 19.6 | 20.4 |
| 3-vessel disease | 6.5 | 11.3 |
| Final Management (%) | | |
| Medical therapy | 30 | 32 |
| PCI | 61 | 56 |
| CABG | 9.2 | 12 |

**70%**

# RIPCORD 2


Measured FFR
1.00
.80
.60
.40
.20
0.80
12.3%
+
42.1%
+
13.1%
+
14.6%
= 82.1%
of Total Lesions
Negative FFR
0.07%
0.86%
2.1%
14.8%
Normal
Mild (<50%)
Moderate (50-69%)
Severe (70-99%)
Angiographic Severity

# RIPCORD 2

***82.1% negative FFR did not have any Influence on treatment,* How Would you explain that ? And then, *Why FFR ?***

| | | |
|---|---|---|
| 1-vessel disease | 48 | 40 |
| 2-vessel disease | 19.6 | 20.4 |
| 3-vessel disease | 6.5 | 11.3 |
| Final Management (%) | | |
| Medical thera | | 32 |
| PCI | | 56 |
| CABG | | 12 |
| Coronary Segment for PCI (%) | | |
| 1 | 76 | 71 |
| 2 | 18.8 | 21.8 |
| 3 | 4.8 | 6.8 |
| 4 | 0.6 | 1.0 |

*What a Absurd !*

**82.1%**
**of Total Lesions**
**Negative FFR**

↓

**Not Different**
**Management**
**Pattern**

# RIPCORD 2

## Clinical Characteristics of Study Patients

| | Angiography | Angiography + FFR |
|---|---|---|
| Age, y | 64.2 | 64.2 |
| History o | | |
| History if | | |

**Mean Age 64-year With Normal EF, 70% of 0VD and 1VD, 2 Groups of Healthy People were Compared, so of course *There is No Difference in QOL* At 1 year.**

*What a Dumbfounded !*

Rodney H. Stables et al, Circulation. 2022;146:687–698


# Circulation Magazine ?

***Several Shapeless Studies***

***Can Not Break Up Basic Concept of FFR !***

***Clinical Benefit of FFR measurement Is Mainly for Intermediate Stenosis 50~80% !***

# *Limited Data Interpretation*

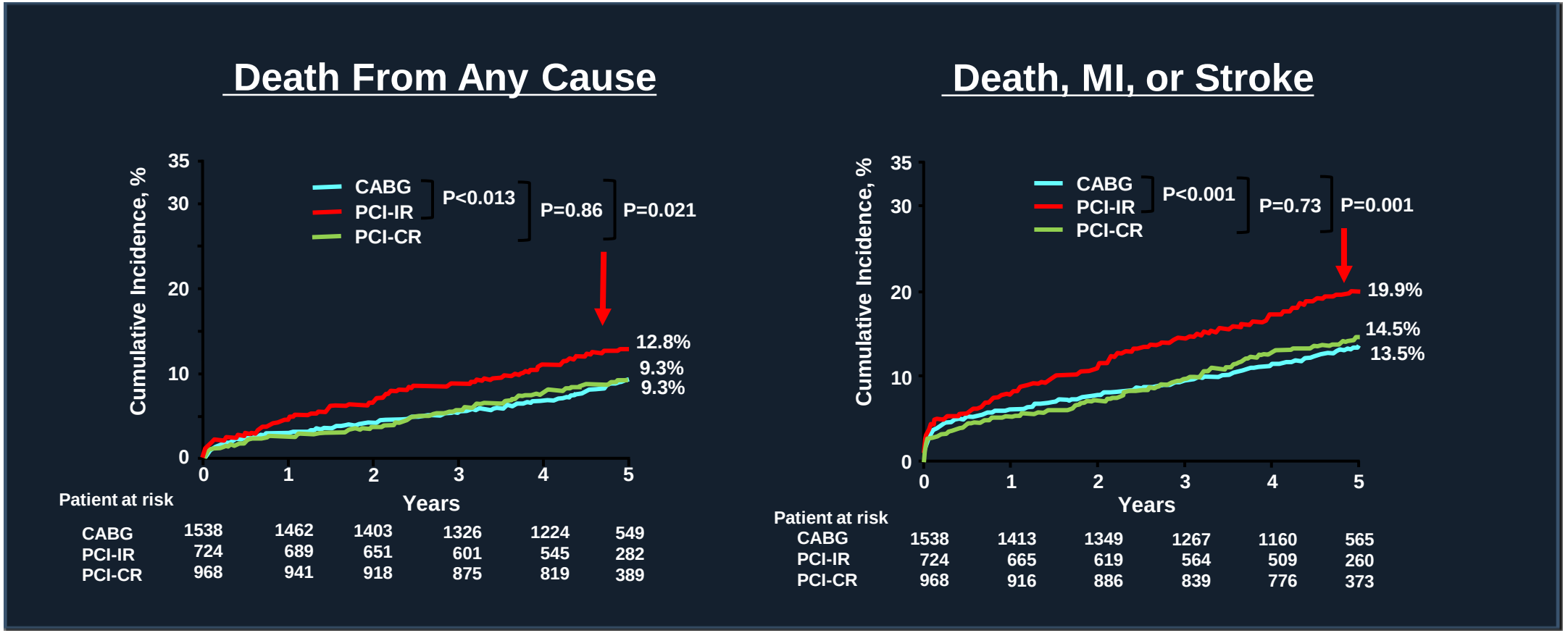
1. **All Studies Used 1st Generation DES**

   **BARI 2D:** DES 35% BMS 56%,
   **FREEDOM:** Cypher 49%, TAXUS 41%,
   **SYNTAX:** TAXUS 100%

2. **Lack of Concept of Physiology and Imaging of PCI**
3. **Issue of Complete Revascularization**

# Complete vs Incomplete

## *PCI with Incomplete Revascularization Is the Worst !*




Ahn JM, et al. JACC Cardiovasc Interv. 2017 Jul 24;10(14):1415-1424. doi: 10.1016/j.jcin.2017.04.037.
Patient-Level Meta-Analysis (n=3,280) from SYNTAX, BEST and PRECOMBAT

# ***Message from These Data***

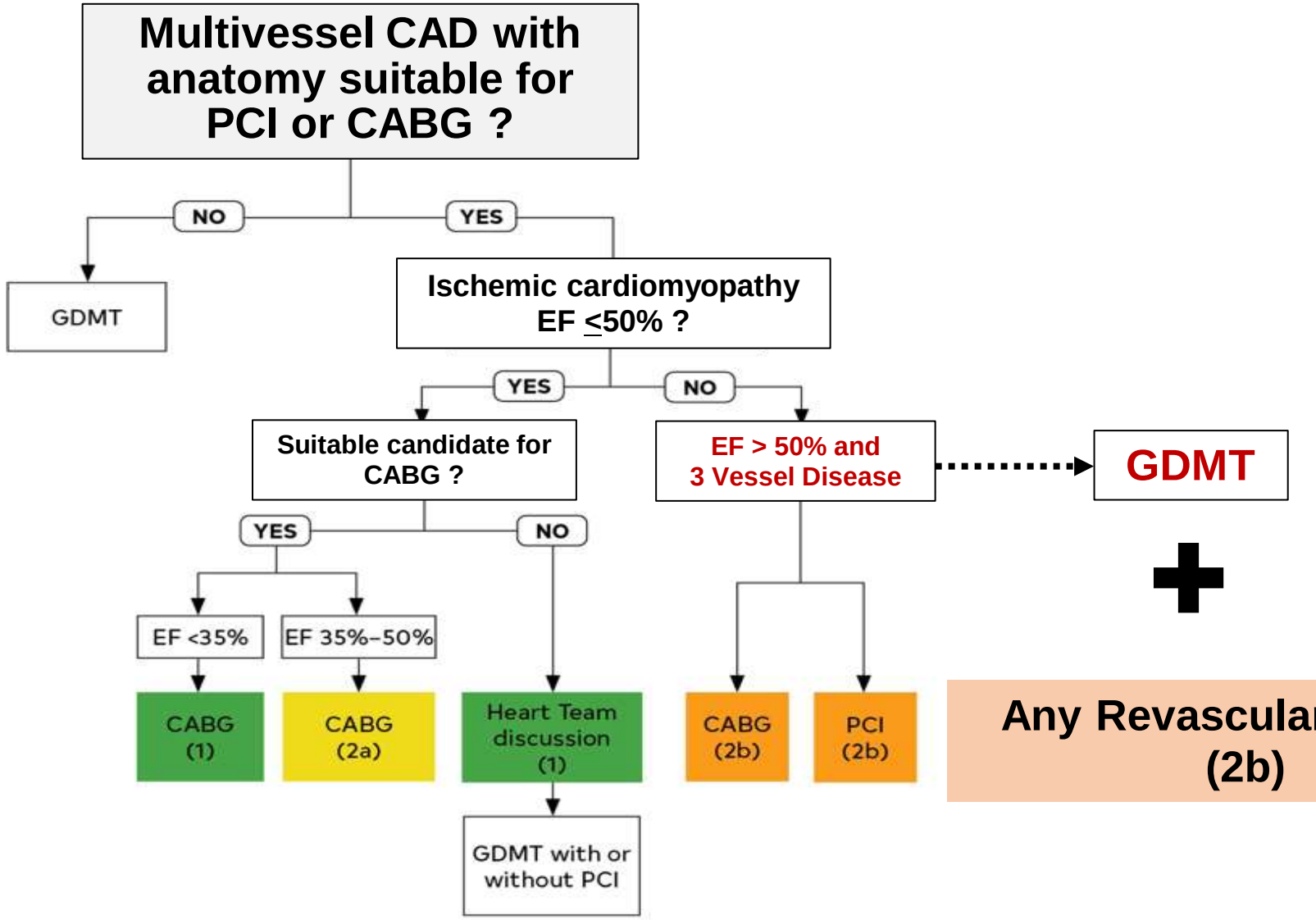
***Complete Revascularization***
***Is One of the Important Practical Issues !***

# *W*hat is

# the *Best Revascularization Strategy*

# for Multivessel Disease Treatment ?

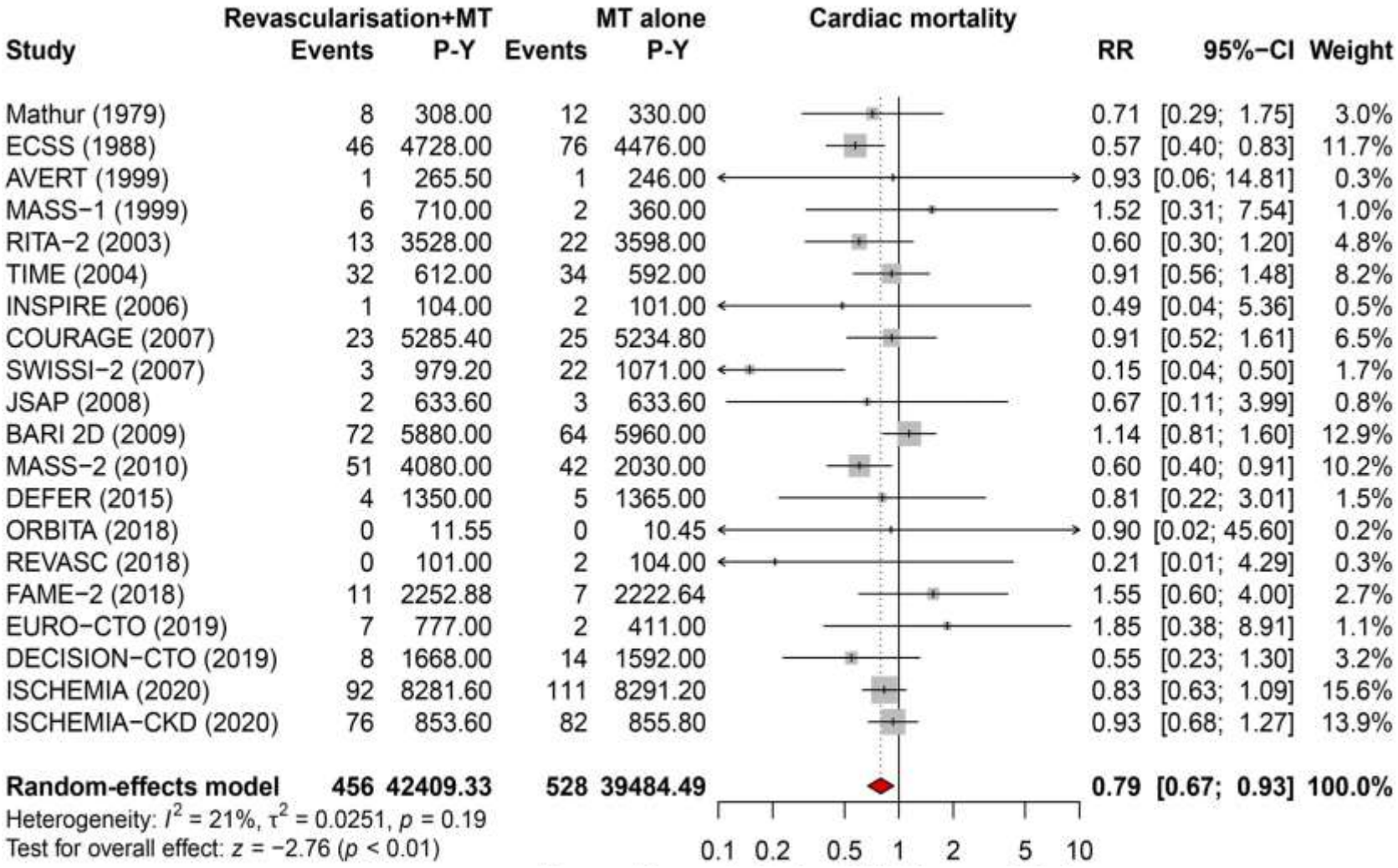
# *2021* ACC/AHA/SCAI, Guideline for Coronary Artery Revascularization



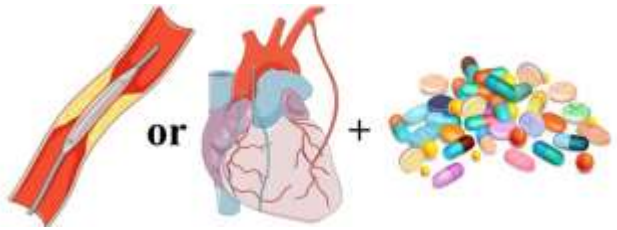

**Any Revascularizations (2b)**

# A Systematic Review and Meta-analysis

25 trials, 19,806 Patients




Eliano P Navarese, et al, Eur Heart J, Volume 42, Issue 45, 1 December 2021, Pages 4638–4651



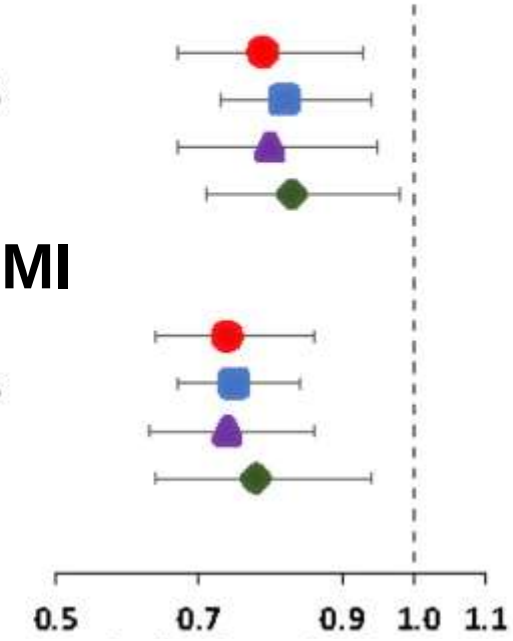

**25 randomised trials**
**N = 19,806**

## Cardiac Death

| | RR [95% CI] | p value |
|---|---|---|
| Overall | 0.79 [0.67;0.93] | <0.01 |
| without post-ACS | 0.82 [0.73;0.94] | <0.01 |
| without CTO | 0.80 [0.67;0.95] | <0.01 |
| without CABG | 0.83 [0.71;0.98] | 0.03 |

## Spontaneous MI

| | | |
|---|---|---|
| Overall | 0.74 [0.64;0.86] | <0.01 |
| without post-ACS | 0.75 [0.67;0.84] | <0.01 |
| without CTO | 0.74 [0.63;0.86] | <0.01 |
| without CABG | 0.78 [0.64;0.94] | 0.01 |



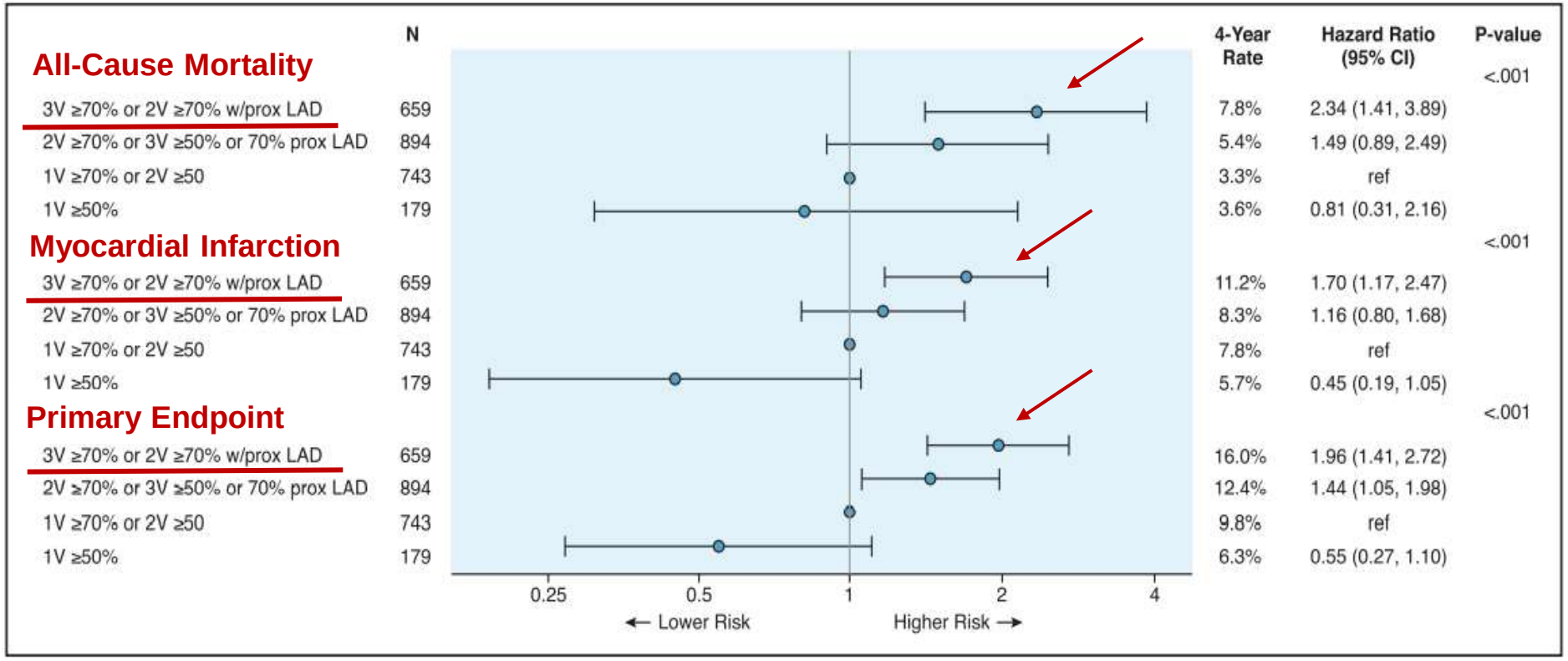

**Revascularization + MT** **>** **MT alone**

Eliano P Navarese, et al, Eur Heart J, Volume 42, Issue 45, 1 December 2021, Pages 4638–4651

***We Have to Consider***
***Individualized Treatment Strategy !***

*According to*
*the different CAD severity, ischemic severity, different anatomic complexity or suitability for CABG or PCI, LV dysfunction and different clinical comorbidity status.*

# Coronary Artery Disease Severity and Clinical Outcomes




ISCHEMIA Study, Circulation. 2021;144:1024–1038. DOI: 10.1161/CIRCULATIONAHA.120.04975

# Coronary Artery Disease Severity
## and Clinical Outcomes

***High Risk,***
***3VD >70% or***
***2VD >70% with pLAD,***

***Intermediate Risk,***
***2VD >70% or 3VD >50%***
***or >70% pLAD,***

***Low Risk,***
***1VD >70% or 2 D >50%***
***Any 1VD >50%***

***Revascularization***
**+** ***Medical Therapy***

***Medical Therapy Alone***

# ***My Approach 1.***

## for Multivessel Disease Treatment

***All Ischemic Lesions,***

**RVD >2.5 mm and/or**

**Lesion Length < 50 mm and**

**Favourable Anatomy for PCI,**

***I Would Try, Complete Ischemic Revascularization with DES !***

# *My Approach 2.*
# for Multivessel Disease Treatment

***Unfavourable Anatomy for PCI,***
**I would Consider *DES for Proximal LAD with Optimal Medical Therapy*.**
***Unfavourable Anantomy of pLAD and Other Proximal lesions for PCI (<50% EF),***
**I would Consider *CABG.***

# *My Approach 3.*
# for Multivessel Disease Treatment

***Diabetic Patients with Low EF (<50%),***
**I would *Consider CABG First,***
**but In Case of Favourable Anatomy for PCI,**
***Multiple DES* Would be Also Considered.**

# *In Fact,* We Have No data Yet

1. ***Contemporary PCI*** **vs. CABG for Multivessel Disease Patients with *Ischemic Cardiomyopathy (<50% EF).***
2. ***Contemporary PCI*** **vs. CABG for for Multivessel Disease Patients with *Diabetes.***

***We Need More Data!***