How Should STICH Trial Results Modify Clinical Practice?

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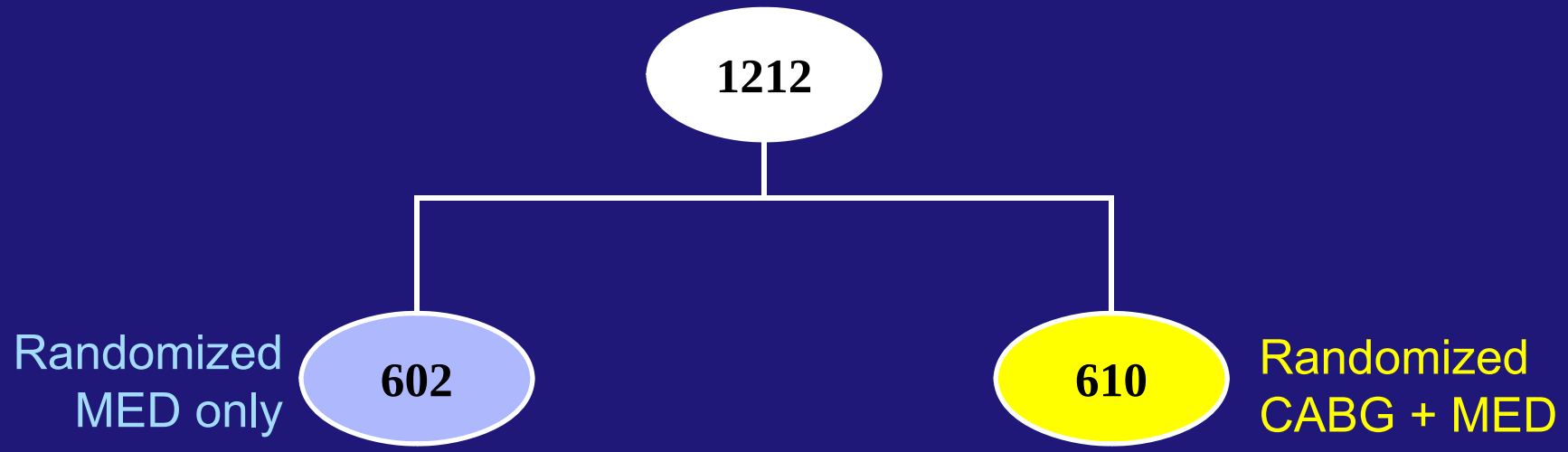
Hypothesis 1 – Key Details

- 1,212 patients
- Median duration of follow-up: 56 months
- Maximum follow-up: 8⅓ years (100 months)
- 462 deaths (38%) (primary endpoint events)

Hypothesis 1 Randomization



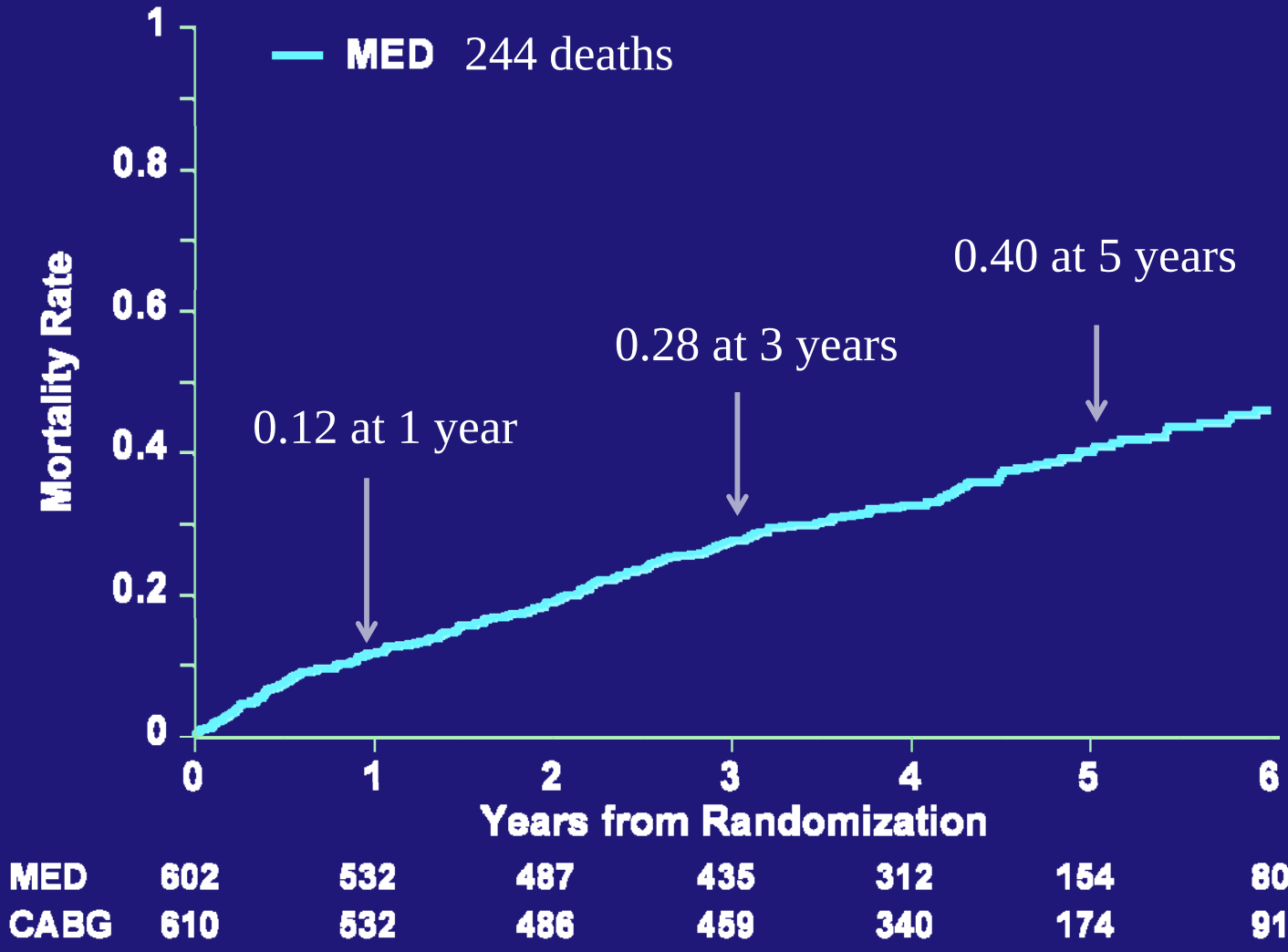
244 deaths (41%)

218 deaths (36%)

Operative Events
(During or Within 30 Days After CABG)

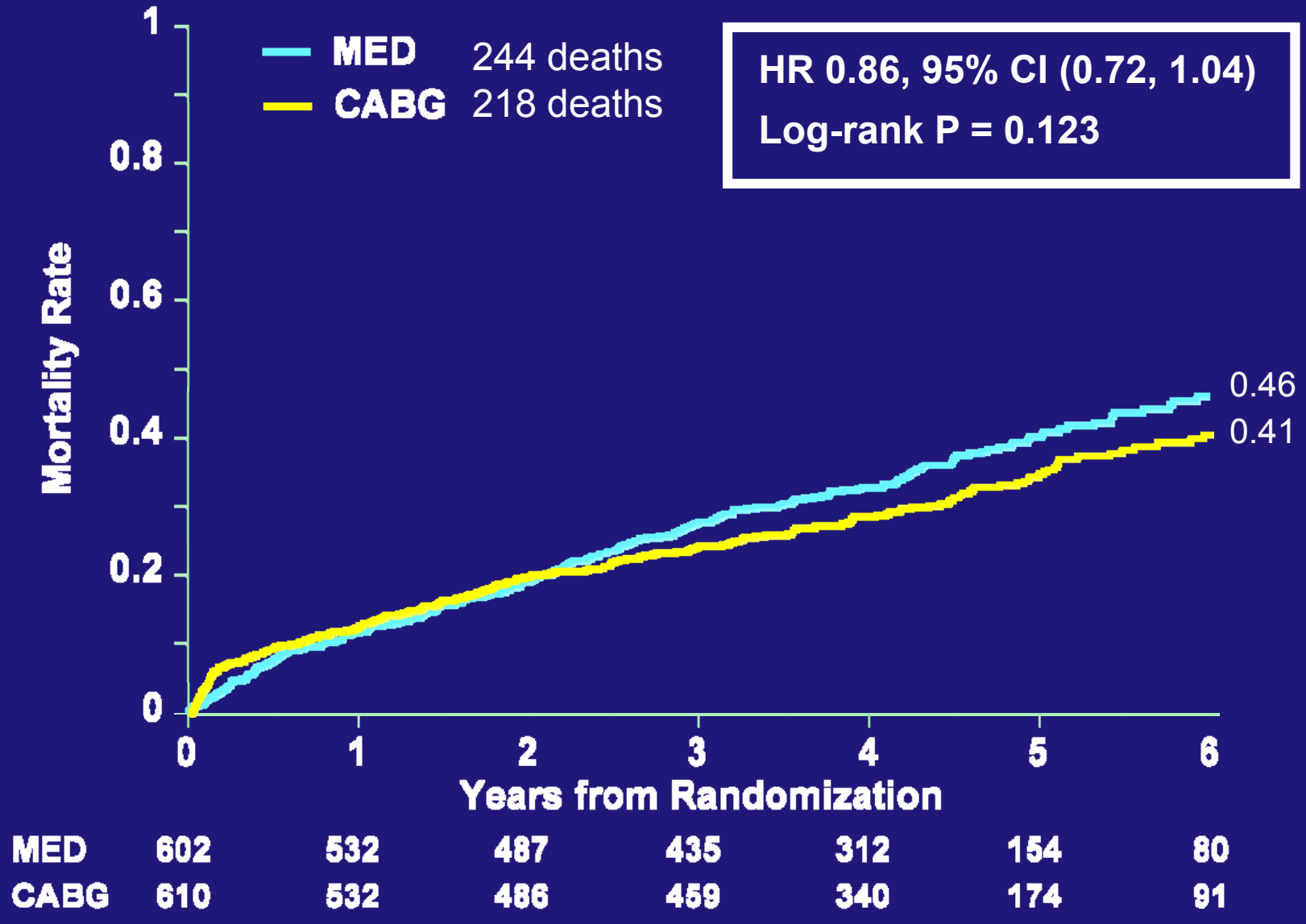
Randomized to CABG and received CABG	555
Death	26 (4.7%)

Primary Endpoint – All-Cause Mortality
Kaplan-Meier Estimates – As Randomized



MED	602	532	487	435	312	154	80
CABG	610	532	486	459	340	174	91

Primary Endpoint – All-Cause Mortality
Kaplan-Meier Estimates – As Randomized



Pattern of Deaths

(Treatments as Randomized)

	CABG (N=610)	MED (N=602)
0 – 30 days	22	7
31 – 365 days	56	63
366 – 2 years	45	45
>2 years	95	129
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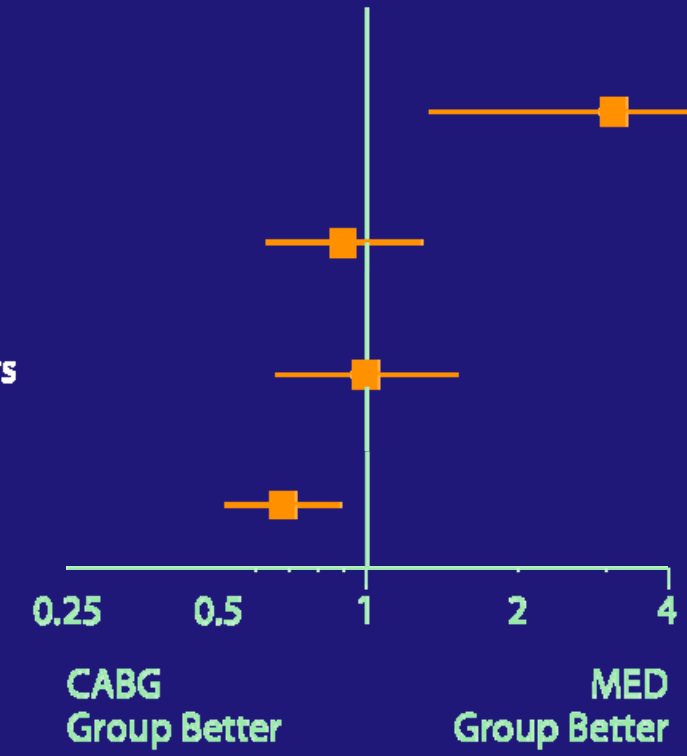
	218	244

Time-varying Hazard Ratios

CABG vs. MED as Randomized



Time Periods	Hazard Ratio (95% CI)	P-Value
≤ 30 days	3.12 (1.33, 7.31)	0.009
31–365 days	0.90 (0.63, 1.29)	0.568
366 days–2 years	1.00 (0.66, 1.52)	0.982
≥ 2 years	0.68 (0.52, 0.89)	0.004

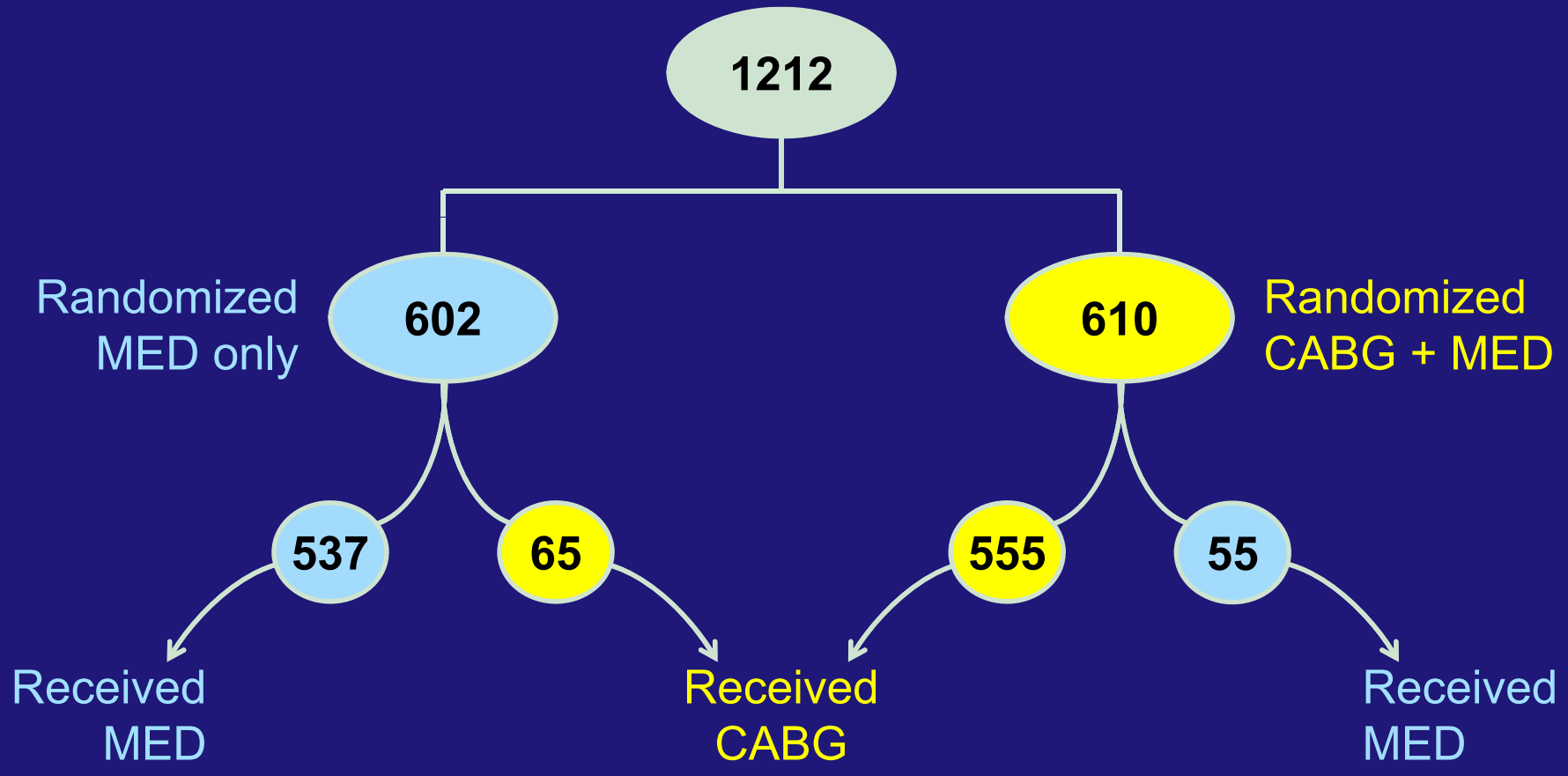
CABG vs. MED Hazard Ratio Varies over Time in STICH

- Mortality curves cross (hazards are not proportional)
  - Early risk with CABG, reduced mortality later
- One single hazard ratio not adequate to fully characterize the treatment effect

Other Study Outcomes (as randomized)

Outcome	MED (n = 602)	CABG (n = 610)	HR	95% CI	P
All-cause mortality	244 (41%)	218 (36%)	0.86	(0.72, 1.04)	0.12
Death within 30 days after randomization	7 (1%)	22 (4%)	3.12	(1.33, 7.31)	0.006
CV death	201 (33%)	168 (28%)	0.81	(0.66, 1.00)	0.050
Death or CV hospitalization	411 (68%)	351 (58%)	0.74	(0.64, 0.85)	< 0.001
Death or HF hospitalization	324 (54%)	290 (48%)	0.84	(0.71, 0.98)	0.030
Death or any hospitalization	442 (73%)	399 (65%)	0.81	(0.71, 0.93)	0.003
Death or revascularization	333 (55%)	237 (39%)	0.60	(0.51, 0.71)	< 0.001

Hypothesis 1
Treatment Received

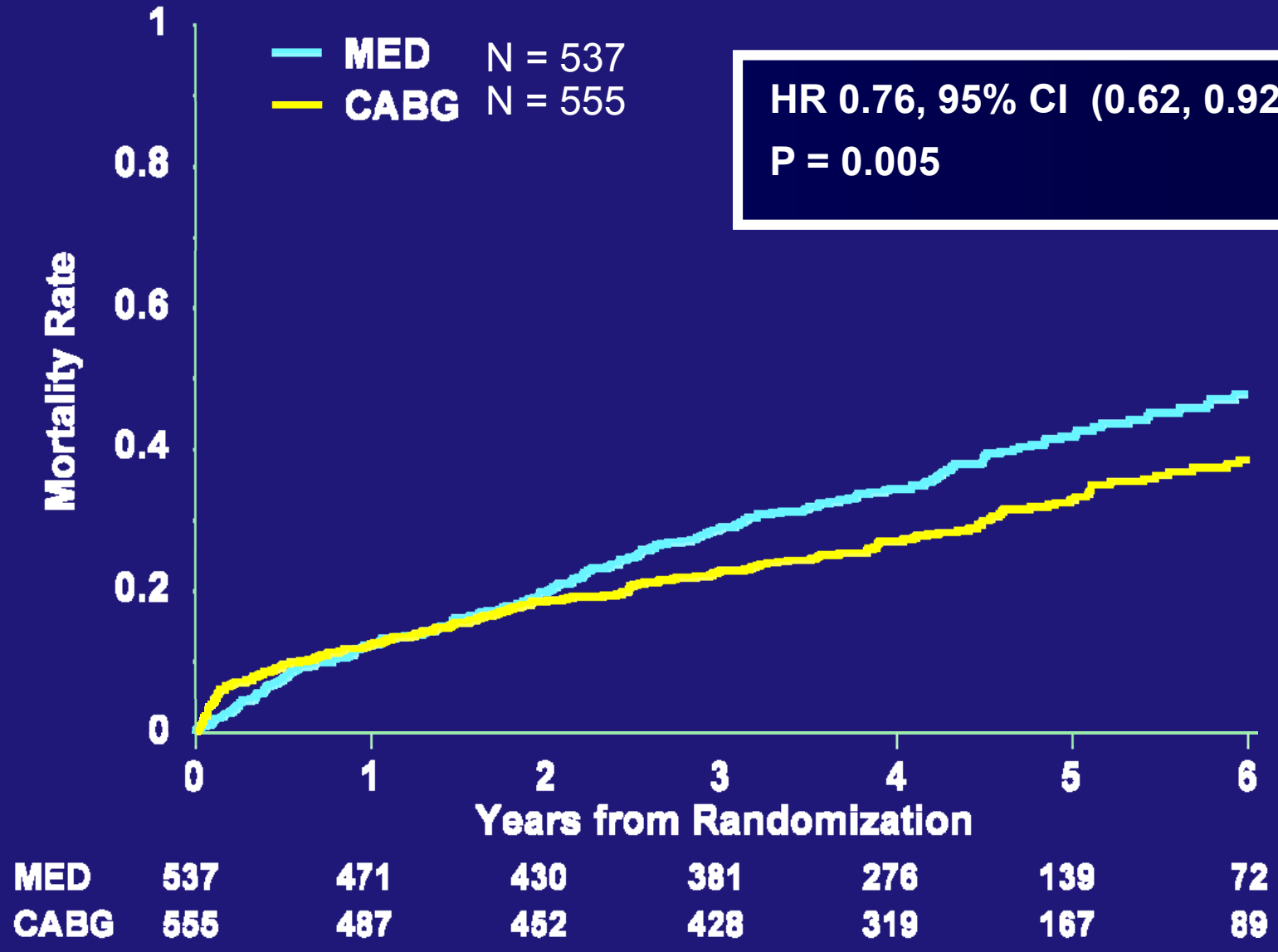


Per protocol: MED (537) vs. CABG (555)

As treated: MED (592) vs. CABG (620)

All-Cause Mortality

Per Protocol (Patients Who Received Their Randomized Treatment)



STICH Viability Hypothesis

Criteria for myocardial viability were ***prospective*** and ***pre-specified***

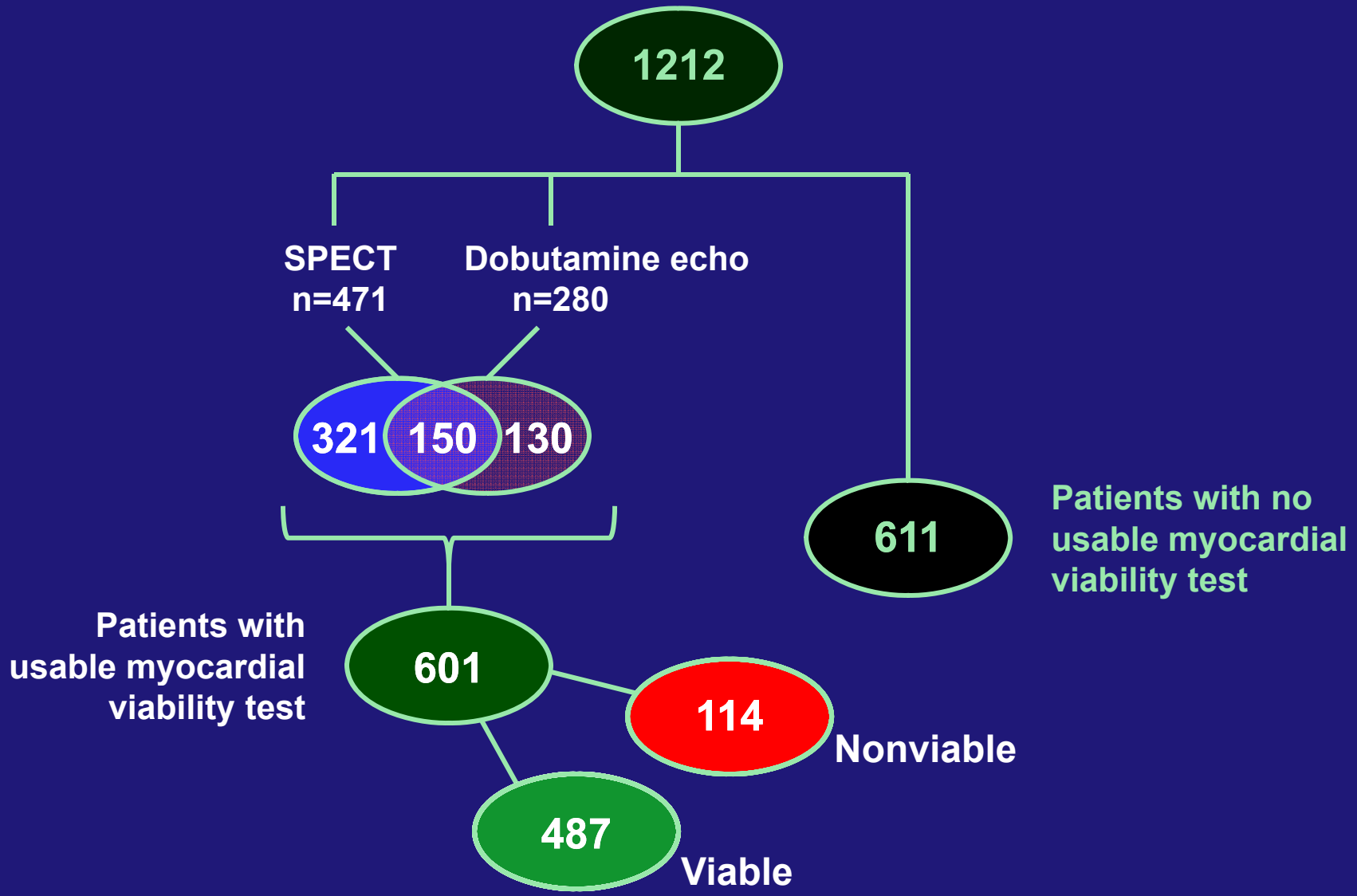
SPECT:

- 17 segment model
- ≥11 segments manifesting viability based on relative tracer activity

Dobutamine echo:

- 16 segment model
- ≥5 segments with dysfunction at rest manifesting contractile reserve with dobutamine

Patients Randomized in STICH Revascularization Hypothesis



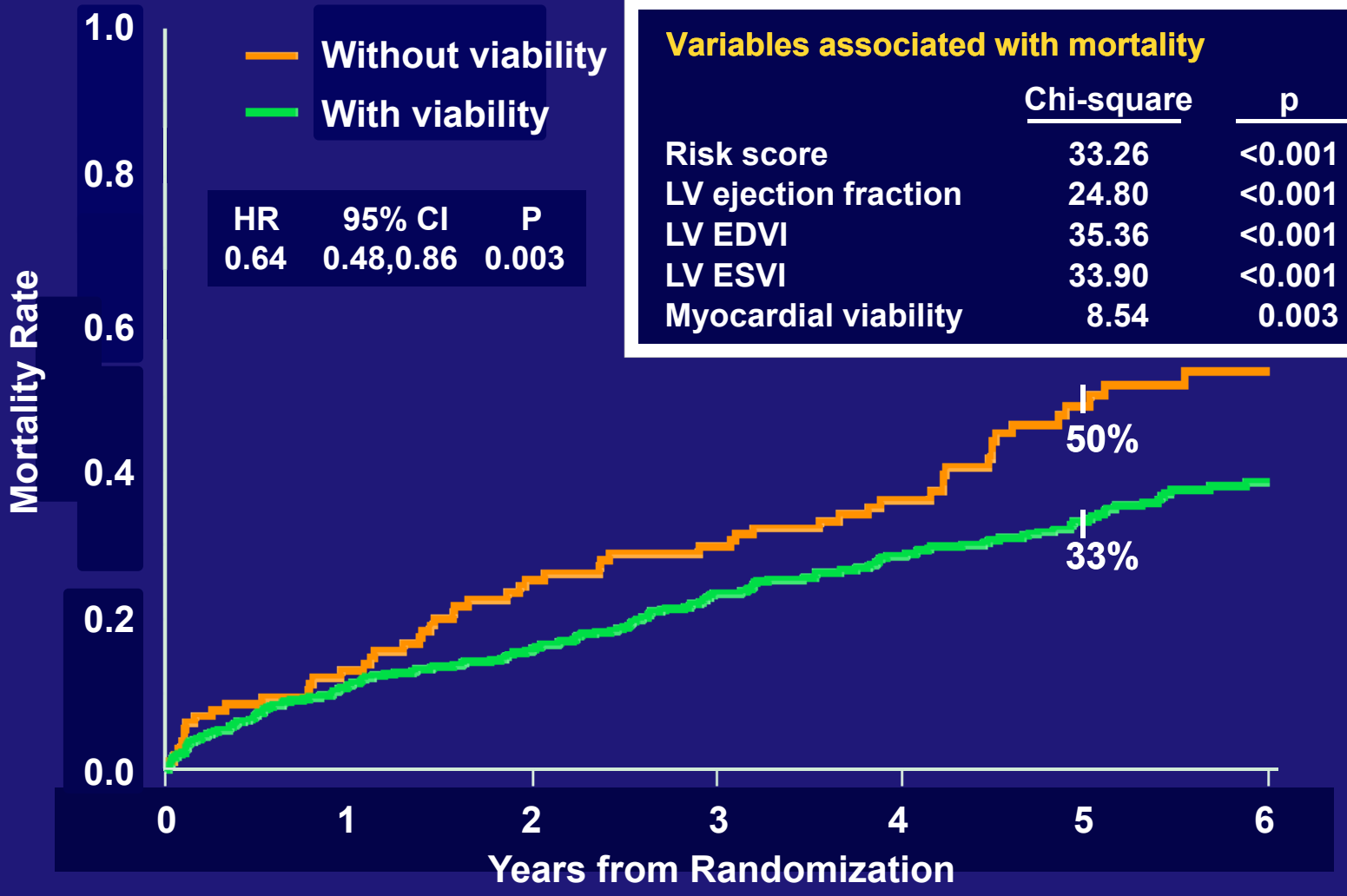
Baseline Characteristics

Variable	Viable (n=487)		P value	Non-Viable (n=114)		P value
	MED (n=243)	CABG (n=244)		MED (n=60)	CABG (n=54)	
Age	60 ± 10	62 ± 9	NS	62 ± 9	60 ± 9	NS
Gender (% male)	84%	86%	NS	92%	93%	NS
Previous MI	78%	75%	NS	93%	96%	NS
Multivessel CAD	72%	73%	NS	68%	78%	NS
Proximal LAD	65%	63%	NS	70%	70%	NS
Risk score*	11.9 ± 8.4	12.8 ± 903	NS	13.7 ± 9.8	12.9 ± 9.3	NS
LV EF (percent)	28 ± 8	27± 8	NS	23 ± 9	23 ± 9	NS
LV EDVI (ml/m^2)	118 ± 38	116 ± 35	NS	151 ± 51	140 ± 54	NS
LV ESVI (ml/m^2)	86 ± 34	86 ± 32	NS	121 ± 50	111 ± 51	NS

* Significant covariates in risk model: Age, renal function, heart failure, ejection fraction, CAD index, MR, stroke

STICH

Myocardial Viability and Mortality

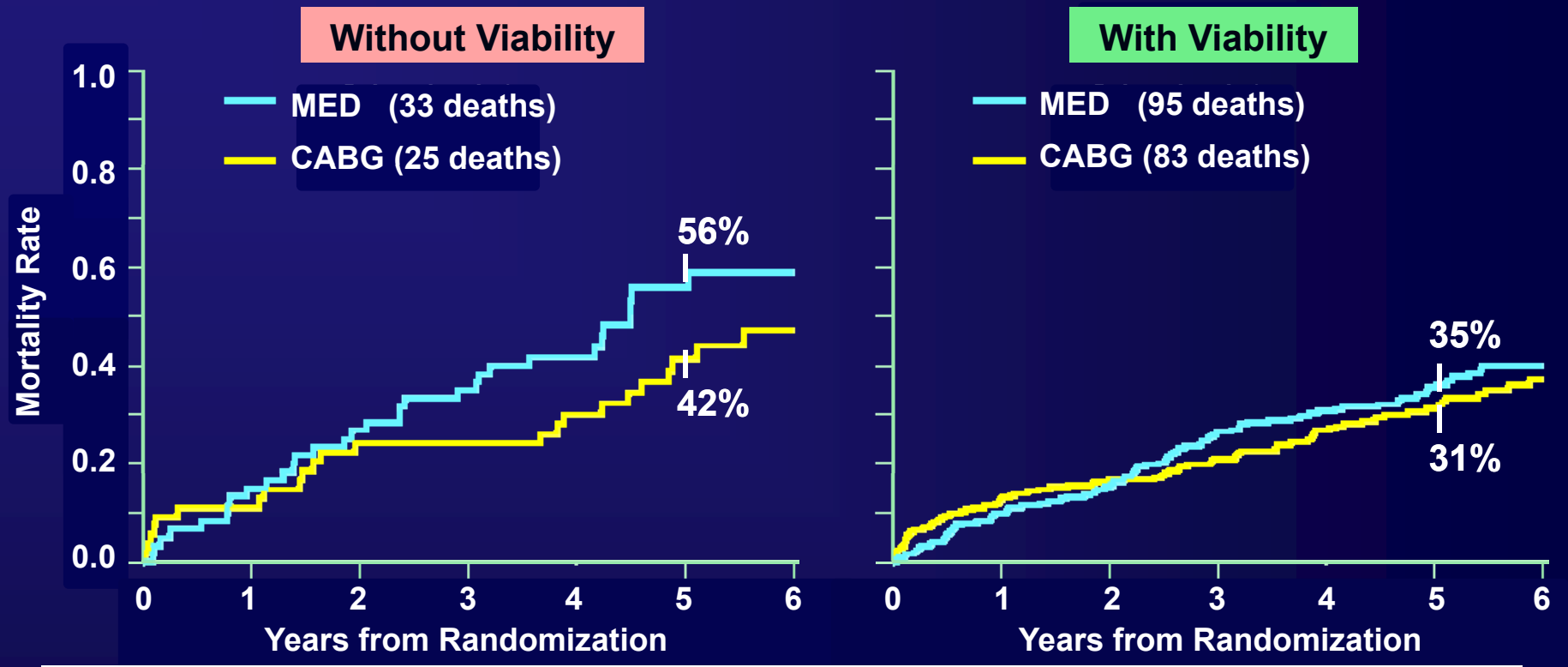


Variables associated with mortality

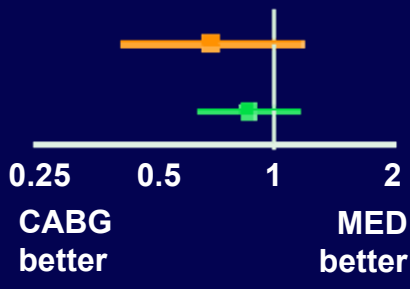
	Chi-square	p
Risk score	33.26	<0.001
LV ejection fraction	24.80	<0.001
LV EDVI	35.36	<0.001
LV ESVI	33.90	<0.001
Myocardial viability	8.54	0.003

Without viability	114	99	85	80	63	36	16
With viability	487	432	409	371	294	188	102

Myocardial Viability and Mortality



Subgroup	N	Deaths	HR	95% CI
Without viability	114	58	0.70	0.41, 1.18
With viability	487	178	0.86	0.64, 1.16



Interaction P value

0.528

Viability Prediction of Death in 601 Patients with Viability Test

	Viability	No Viability	Total Cohort
CABG	83/244 = 34%	25/54 = 46%	108/298 = 36%
MED	95/243 = 39%	33/60 = 55%	128/303 = 42%
Total	178/487 = 36%	58/114 = 51%	236/601 = 39%

Deaths/Patients = Mortality

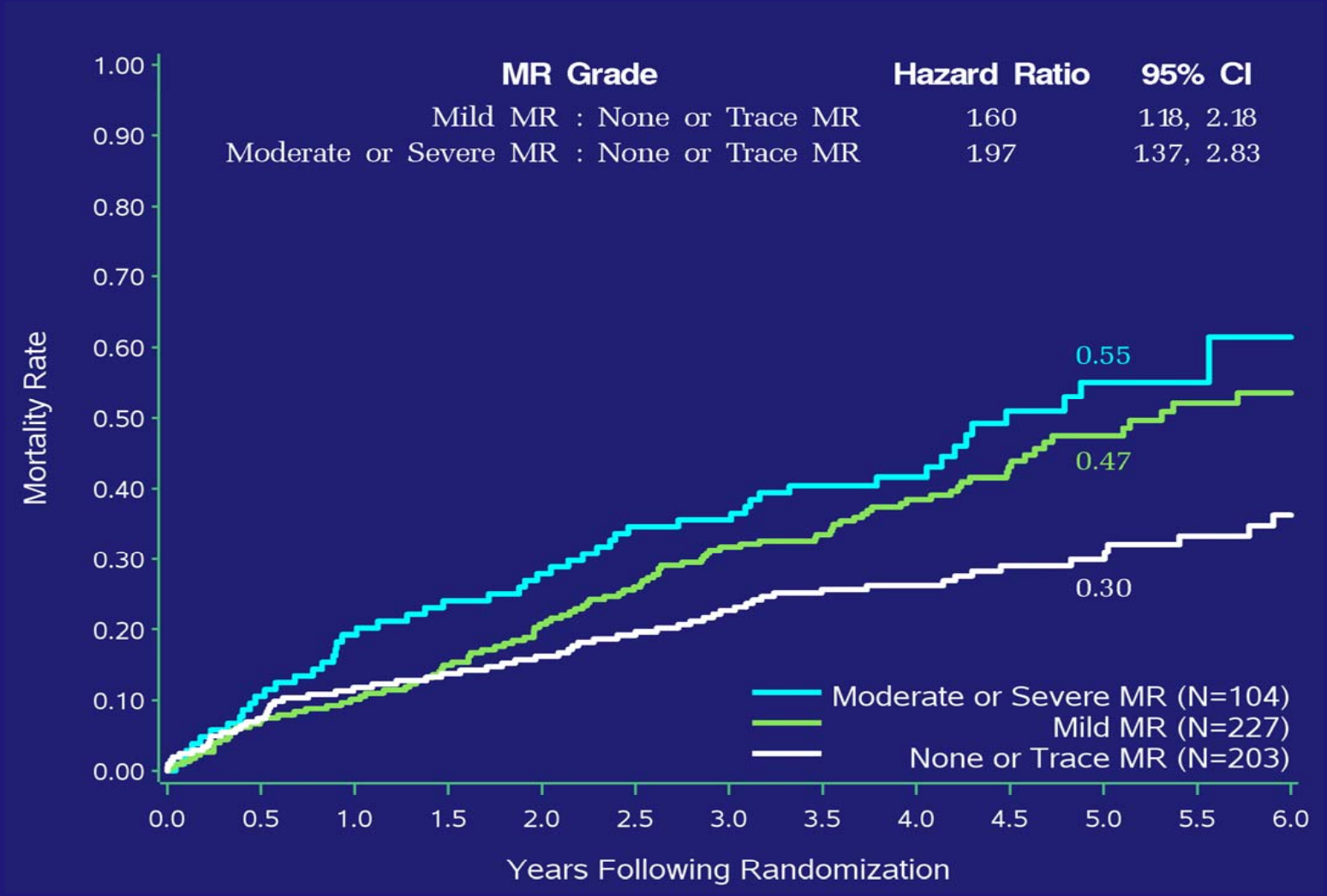
STICH Viability Hypothesis

Implications:

In patients with CAD and LV dysfunction, assessment of myocardial viability does not identify patients who will have the greatest survival benefit from adding CABG to aggressive medical therapy

Full report available at www.NEJM.org

All-Cause Mortality Estimates for 534 MED Patients by MR Severity



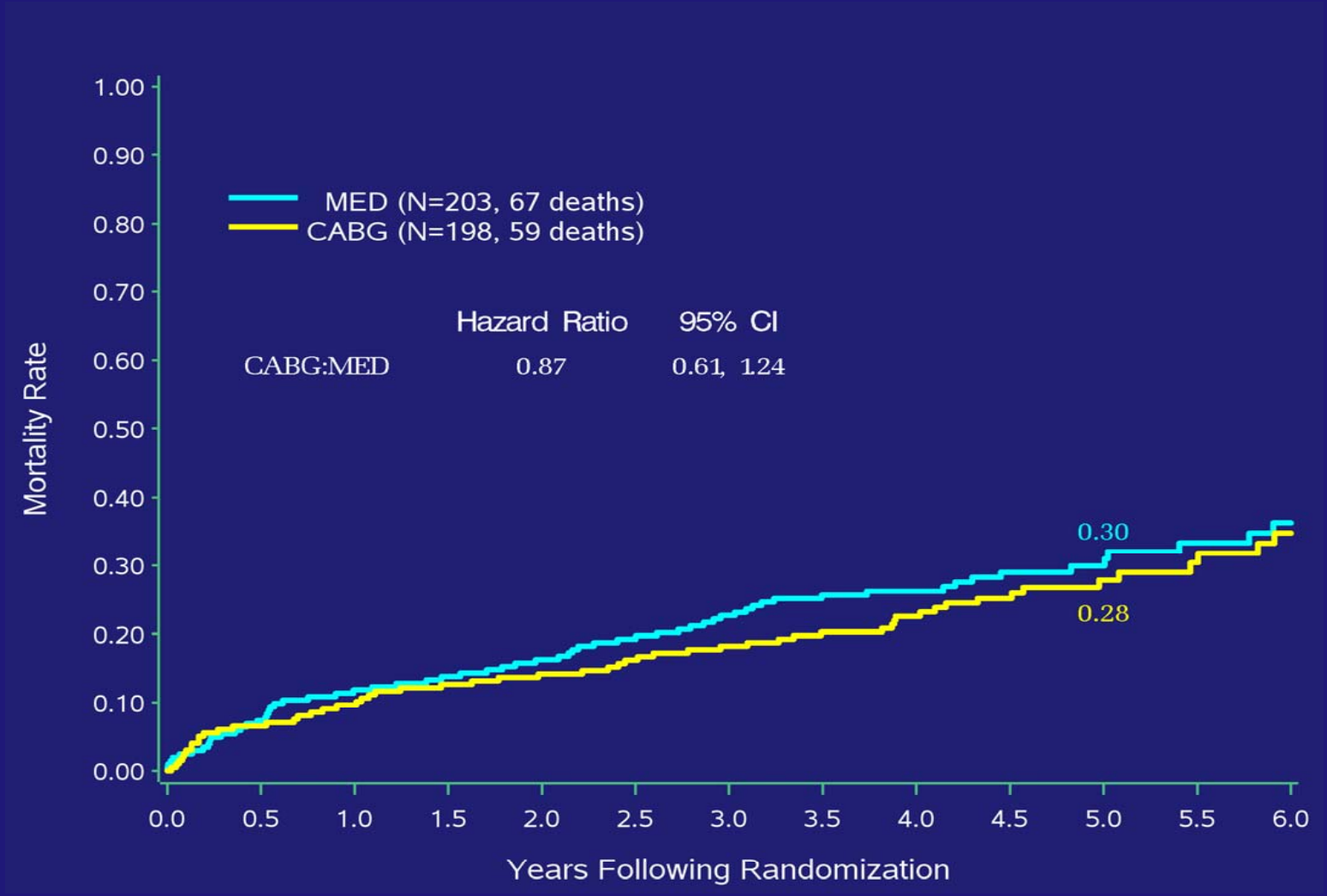
Operative Conduct by MR Grade

Surgical data	None/trace MR (N=198)	Mild MR (N=266)	Moderate/severe MR (N=91)	p
No of distal anastomoses	3 (2, 3)	3 (2, 3)	3 (2, 4)	0.019
Arterial conduits ≥1	93%	91%	88%	0.366
Procedures on MV				<0.001
None	99%	95%	46%	
Repair/Replacement	1% / 0	5% / 0	53% / 1%	
Off pump	23%	20%	19%	0.695
Cardioplegia				0.309
None	28%	27%	26%	
Crystalloid	22%	25%	14%	
Blood	47%	45%	58%	
X-clamp time, min	48 (35, 64)	51 (34, 70)	79 (56, 110)	<0.001
CPB time, min	81 (63, 105)	88 (67, 116)	123 (95, 161)	<0,001

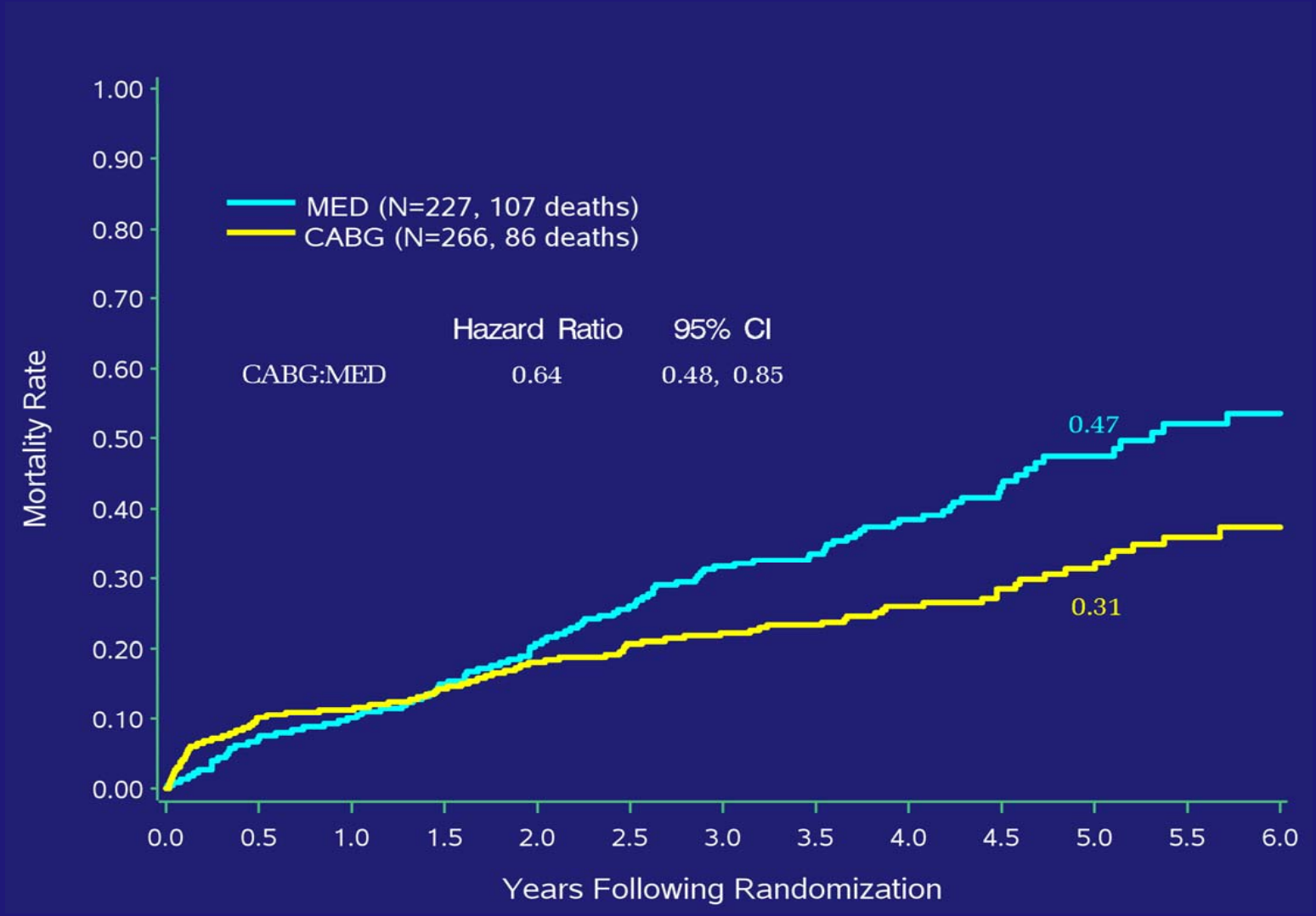
Perioperative Outcome by MR Grade

Outcome	None/trace MR (N=198)	Mild MR (N=266)	Moderate/severe MR (N=91)	p
Time intubated, hrs	17 (11, 22)	15 (11, 22)	21 (14, 24)	<0.001
Time in ICU, hrs	49 (40, 92)	47 (38, 90)	91 (54, 155)	<0.001
Time in hospital, days	8 (7, 11)	9 (7, 13)	9 (7, 14)	0.024
Hospital stay >30 days	3%	5%	7%	0.331
Inotropes for low CO	34%	38%	52%	0.015
IABP for low CO	13%	15%	26%	0.010
Death within 30 days	3%	5%	8%	0.214

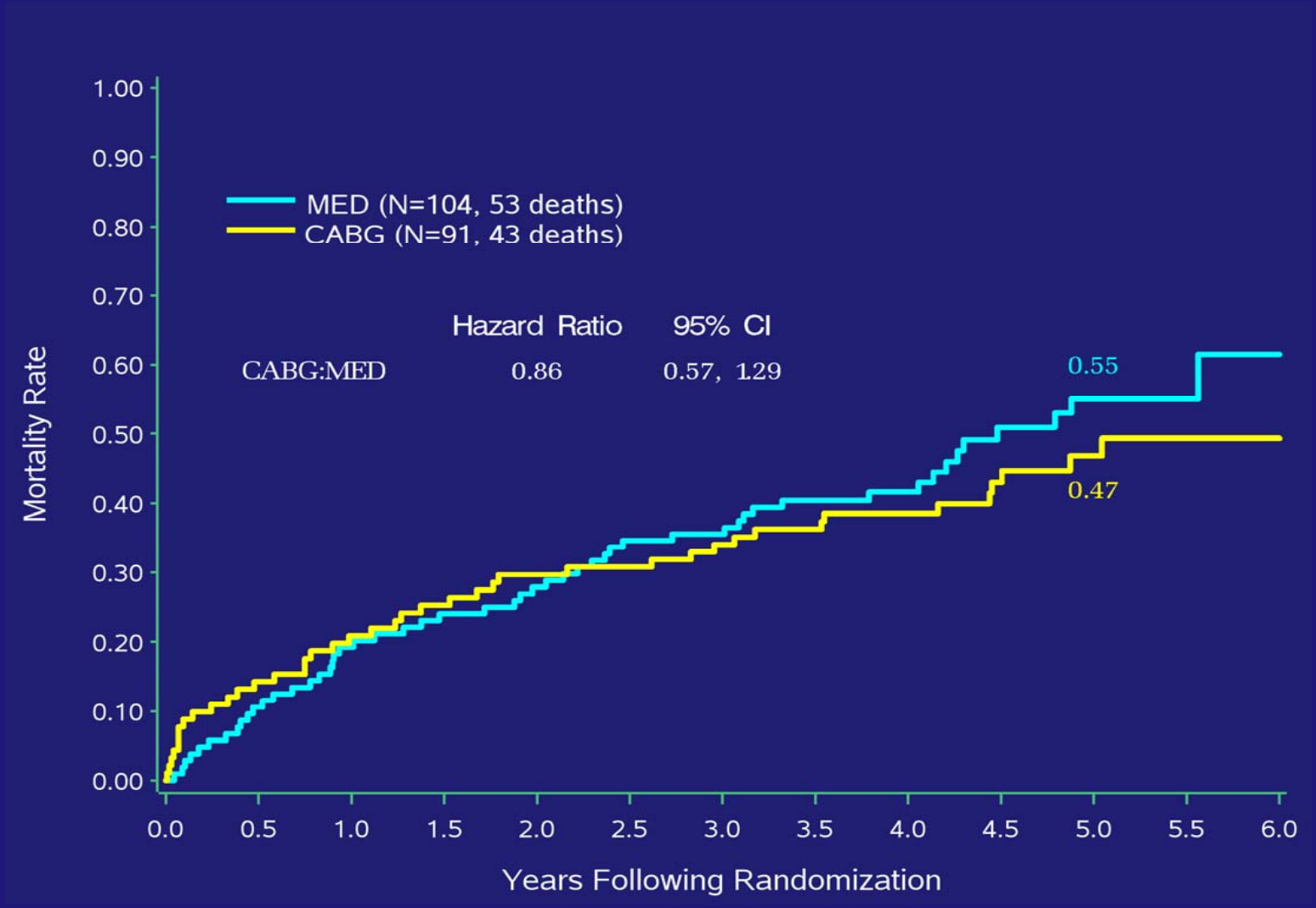
All-Cause Mortality Estimates for 401 Patients with None or Trace MR



All-Cause Mortality Estimates for 493 Patients with Mild MR



All-Cause Mortality Estimates for 195 Patients with Moderate/Severe MR



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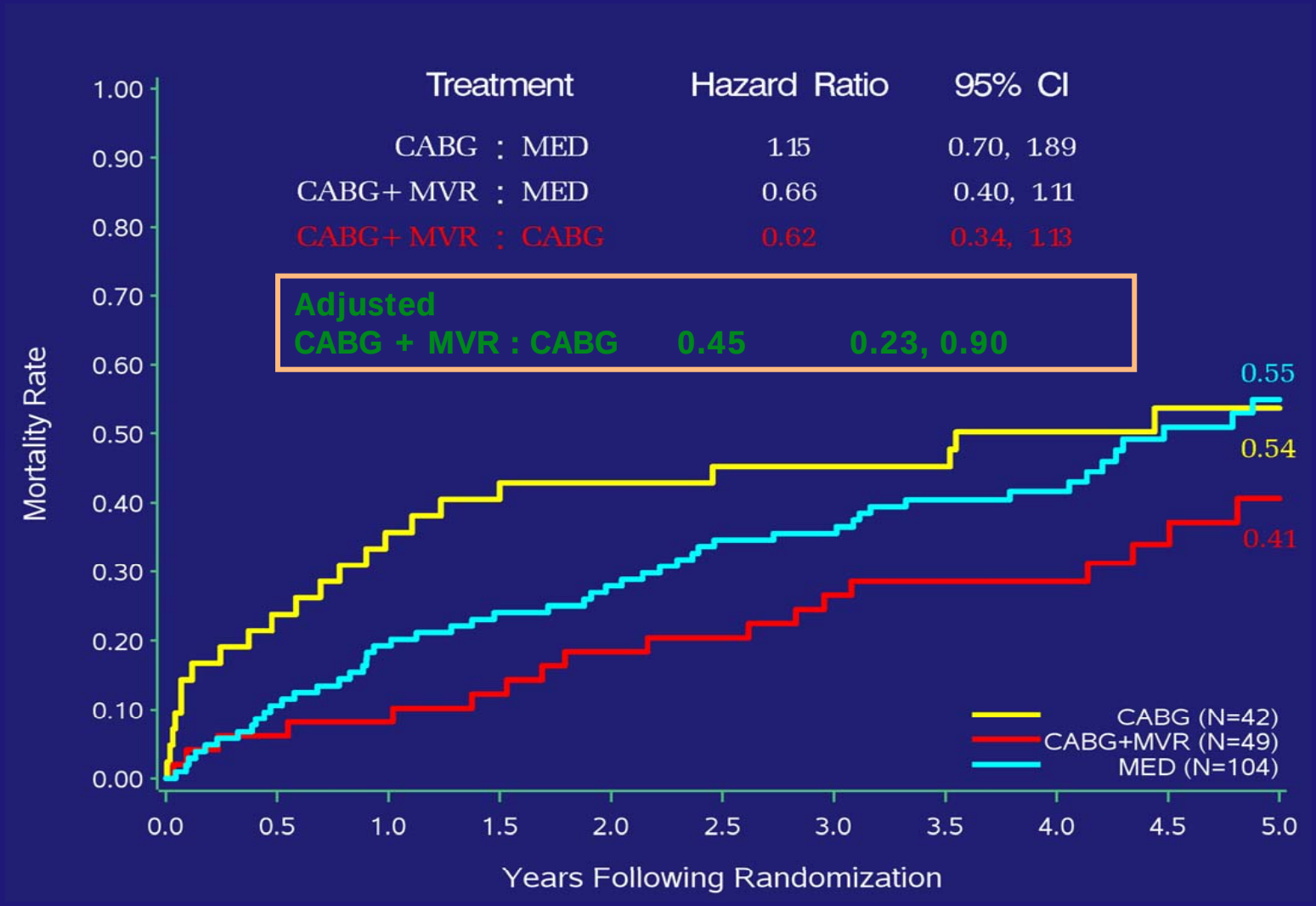
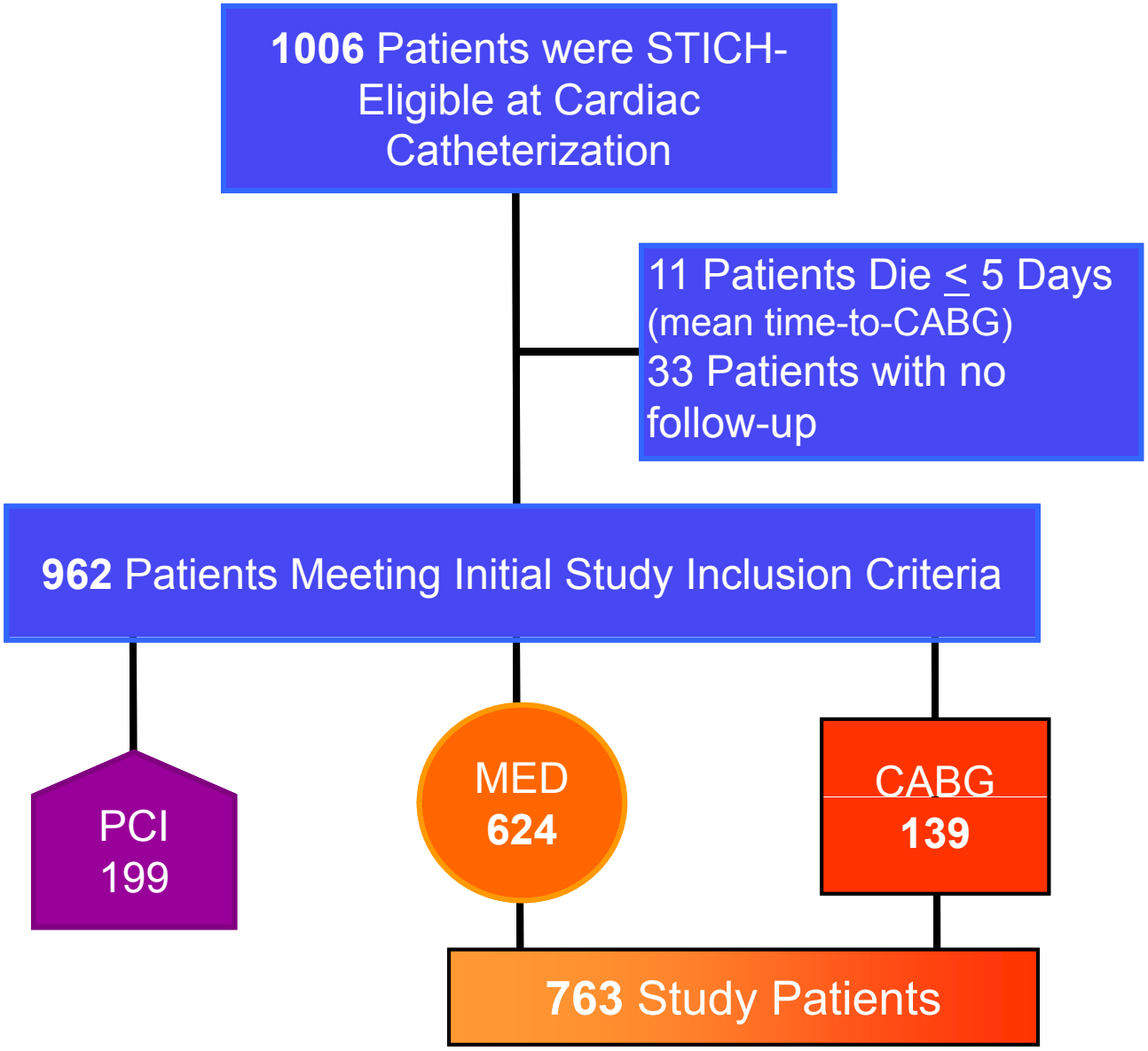


Inclusion Criteria

- Between January 1, 1995 and July 31, 2009, 86,958 patients underwent cardiac catheterization for the clinical indication of CAD and were evaluated for inclusion in the analysis

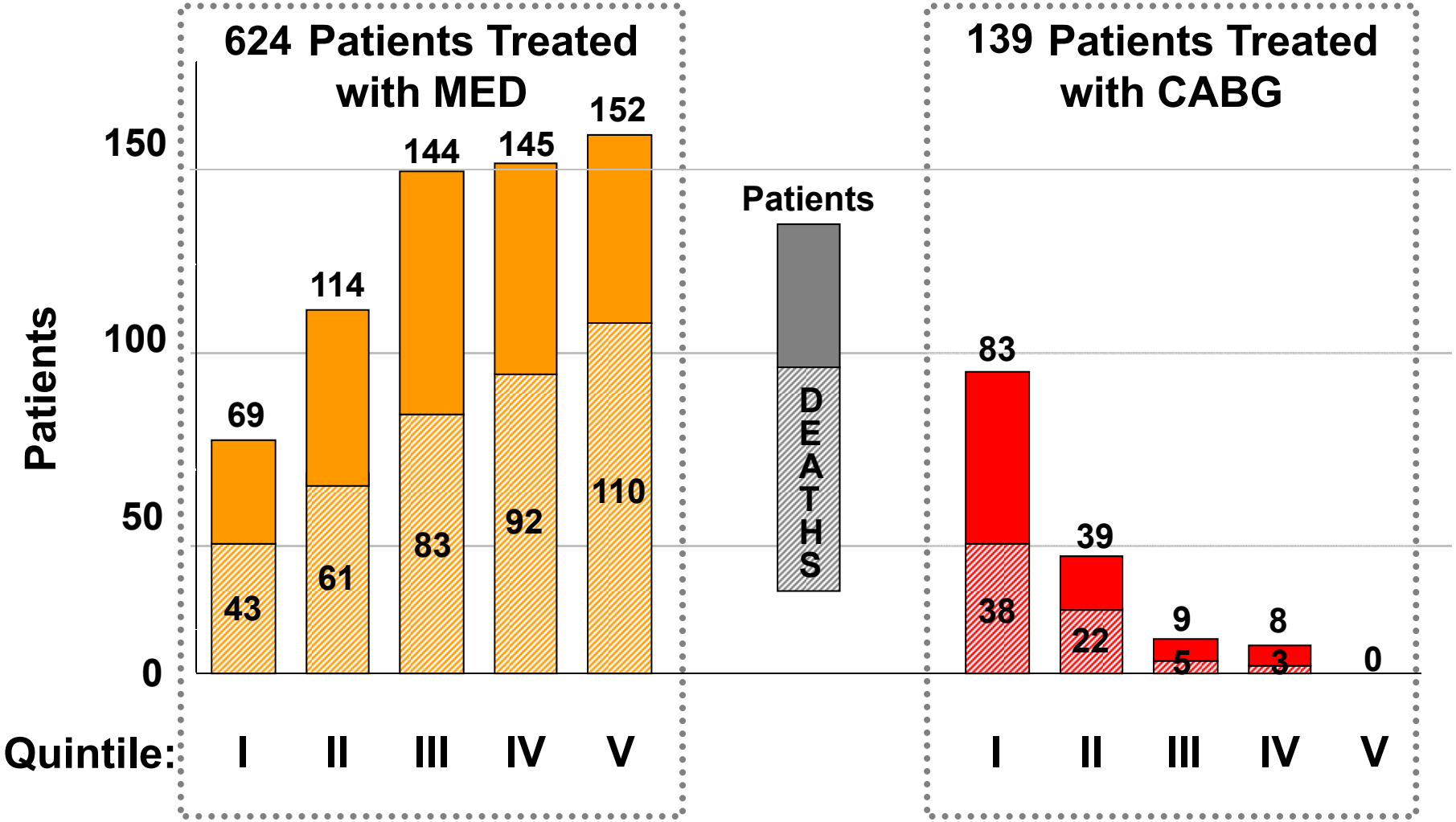
- Applying STICH trial criteria to the Duke Databank, criteria for inclusion consisted of:
  - LVEF ≤ 0.35 within 3 months
  - CAD suitable for CABG
  - No left main disease ≥ 50%
  - No angina markedly limiting ordinary activity (CCS III angina or greater)
  - No non-cardiac illness with a life expectancy of less than 3 years

Identification of Study Cohort



Propensity Model

(N=763)



Kaplan Meier Curves for Time to Death
For STICH and Duke Database (DDCD) Patients