Revascularization in Heart Failure

D. Richter, MD, FESC, FAHA
Head of Cardiac Dept., Euroclinic Hosp.

- ***I have received research grants, consulting or speaker fees from:***

- ***AstraZeneca, Bayer, Sanofi, Pfizer, Vianex, MSD, Unilever, Boehringer, Novartis, Abbott, Galenica, Amgen, Specifar, Menarini, Merck, Pharmaswiss, Winmedica***

Joint ESC - EACTS Guidelines on Myocardial Revascularisation Special Conditions

Joint Task Force on Myocardial Revascularisation of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Developed with the special contribution of the European Association for Percutaneous Cardiovascular Interventions (EAPCI)

European Heart Journal (2010) 31, 2501–2555
European Journal of Cardio-thoracic Surgery (2010) 38, S1-S52

EACTS

EUROPEAN SOCIETY OF CARDIOLOGY®

Myocardial revascularisation in chronic heart failure (CHF)

In patients with CHF and presenting with angina

	Class	Level
CABG is recommended for : • significant LM stenosis, • LM equivalent (proximal stenosis of both LAD and LCx), • proximal LAD stenosis with 2- or 3- vessel disease.	I	B
CABG with SVR may be considered in patients with LVESV index ≥ 60 mL/m^2 and scarred LAD territory.	IIb	B
PCI may be considered if anatomy is suitable, in the presence of viable myocardium.	IIb	C

- Myocardial revascularisation should be performed in patients with CHF and systolic LV dysfunction, presenting predominantly with anginal symptoms, regardless of ventricular volumes.

SVR: surgical ventricular reconstruction.

European Heart Journal (2010) 31, 2501–2555
European Journal of Cardio-thoracic Surgery (2010) 38, S1-S52

Myocardial revascularisation in chronic heart failure (CHF)

Recommendations for patients with CHF and systolic LV dysfunction (EF < 35%), presenting predominantly with HF symptoms (no or mild angina: CCS 1-2)

	Class	Level
LV aneurysmectomy during CABG is indicated in patients with a large LV aneurysm.	I	C
CABG should be considered in the presence of viable myocardium, irrespective of LVESV.	IIa	B
CABG with SVR may be considered in patients with a scarred LAD territory.	IIb	B
PCI may be considered if anatomy is suitable, in the presence of viable myocardium.	IIb	C
Revascularisation in the absence of evidence of myocardial viability is not recommended.	III	B

SVR: surgical ventricular reconstruction.

European Heart Journal (2010) 31, 2501–2555
European Journal of Cardio-thoracic Surgery (2010) 38, S1-S52

www.escardio.org/guidelines

Joint 2010 ESC - EACTS Guidelines on Myocardial Revascularisation

EACTS

EUROPEAN SOCIETY OF CARDIOLOGY®

European Heart Journal (2013) 34, 39–47
doi:10.1093/eurheartj/ehs021

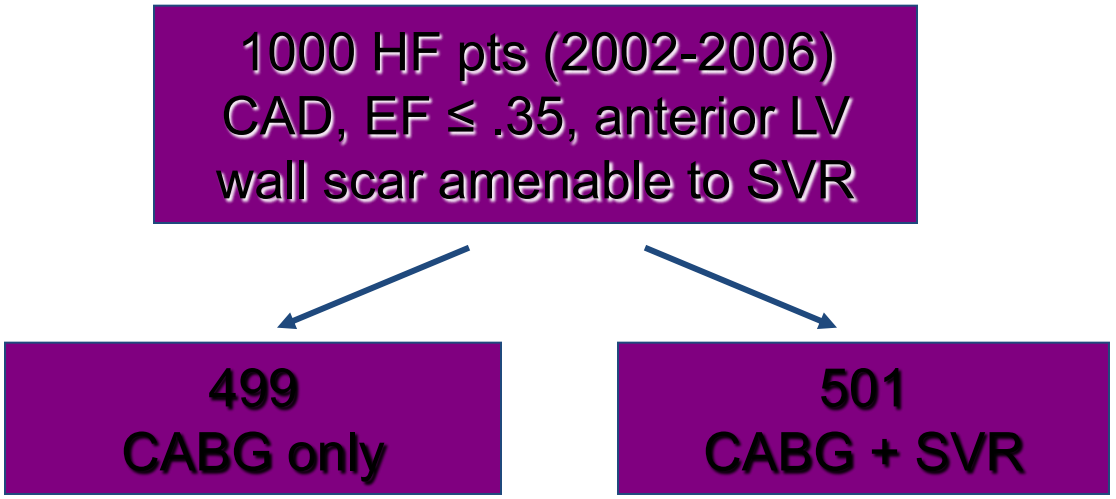
Influence of baseline left ventricular function on the clinical outcome of surgical ventricular reconstruction in patients with ischaemic cardiomyopathy

Conclusions Subgroup analyses of the STICH trial suggest that patients with less dilated LV and better LVEF may benefit from SVR, while those with larger LV and poorer LVEF may do worse.

Clinical Trial Registration #: NCT00023595.

STICH 1° Hypothesis and Design Overview

1° Hypothesis: Adding SVR to CABG in ischemic HF pts will ↓ death/ cardiac rehospitalization



Median follow-up 48 months

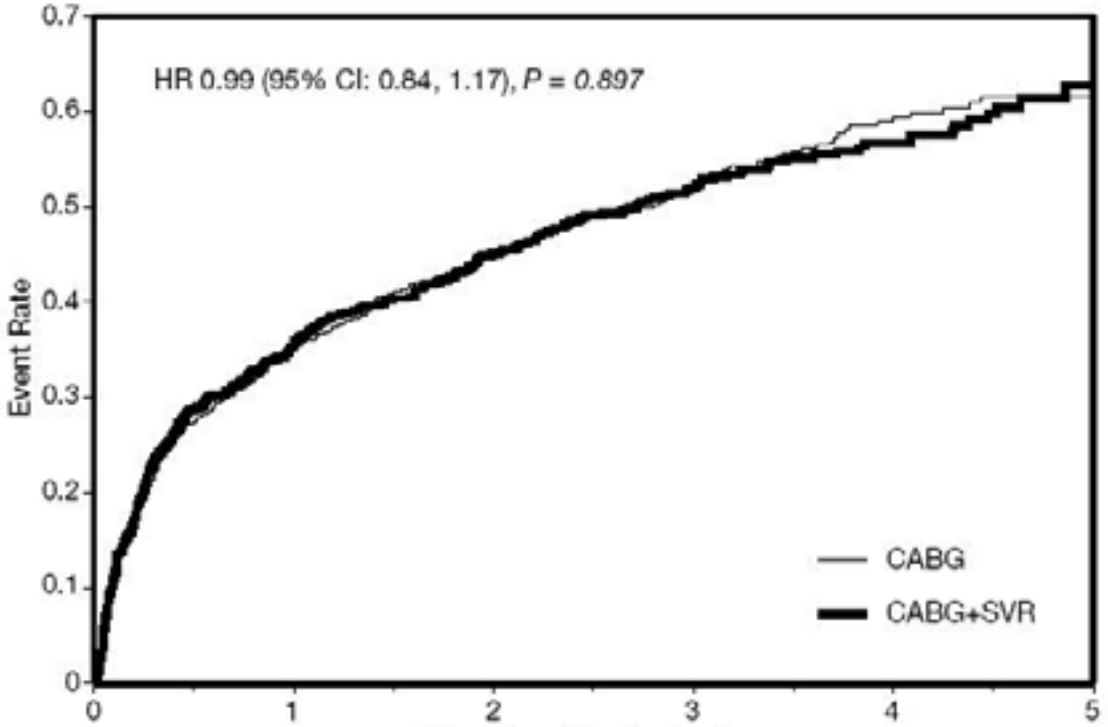
- 7% did not receive operation
- 9% did not receive operation

EQOL STICH Baseline Characteristics

	CABG only (n=499)	CABG + SVR (n=501)
Age (mean)	62	62
Female	16%	14%
Race, nonwhite	10%	8%
Current NYHA Class		
I	7%	10%
II	45%	41%
III	42%	44%
IV	6%	5%
Previous MI	87%	87%
Diabetes	35%	34%

STICH

STICH 1° Composite Endpoint: Death or Cardiac Rehospitalization



No. at Risk						
CABG	499	317	266	208	93	22
CABG+SVR	501	316	264	199	105	21

STICH

Jones RH et al.
NEJM 09

STICH Economics and Quality of Life Study: Key Questions

- **Does SVR added to CABG significantly improve functioning and well-being in ischemic heart failure?**

- **What are the economic implications of adding SVR to CABG in patients with ischemic heart failure?**

STICH

EQOL STICH:
Selected QOL Assessment Instruments

Instrument	QOL Domain
Kansas City Cardiomyopathy Questionnaire (KCCQ)	Heart Failure-specific health status
Seattle Angina Questionnaire	Angina symptoms
SF-36 scales, SF-12	Psychological well-being (MHI-5), role function, social function, vitality, overall health status
Center for Epidemiologic Studies -Depression (CES-D) Scale	Depressive symptoms
Euro-QoL 5D	Patient utilities

STICH

European Heart Journal (2012) 33, 1787-1847
doi:10.1093/eurheartj/ehs104

ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012

The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC

Authors/Task Force Members: John J.V. McMurray (Chairperson) (UK), Stamatis Adamopoulos (Greece), Stefan D. Anker (Germany), Angelo Auricchio (Switzerland), Michael Böhm (Germany), Kenneth Dickstein (Norway), Volkmar Falk (Switzerland), Gerasimos Filippatos (Greece), Cândida Fonseca (Portugal), Miguel Angel Gomez-Sanchez (Spain), Tiny Jaarsma (Sweden), Lars Køber (Denmark), Gregory Y.H. Lip (UK), Aldo Pietro Maggioni (Italy), Alexander Parkhomenko (Ukraine), Burkert M. Pieske (Austria), Bogdan A. Popescu (Romania), Per K. Rønnevik (Norway), Frans H. Rutten (The Netherlands), Juerg Schwitter (Switzerland), Petar Seferovic (Serbia), Janina Stepinska (Poland), Pedro T. Trindade (Switzerland), Adriaan A. Voors (The Netherlands), Faiez Zannad (France), Andreas Zeiher (Germany).

European Heart Journal (2012) 33, 1787–1847
European Journal of Heart Failure (2012) 14, 803–869

What's new in treatment Surgery/surgical devices?

Treatment	Trial	Question
VAD	Heart Mate II trial	Continuous vs. pulsatile flow.
CABG	STICH	Role in patients with systolic HF.

European Heart Journal (2012) 33, 1787–1847
European Journal of Heart Failure (2012) 14, 803–869

Main changes from 2008 guidelines

1. An expanded indication for mineralocorticoid (aldosterone) receptor antagonists (MRAs).
2. A new indication for the sinus node inhibitor ivabradine.
3. An expanded indication for cardiac resynchronization therapy (CRT).
4. New information on the role of coronary revascularization in systolic HF.
5. Recognition of the growing use of ventricular assist devices (VADs).
6. The emergence of transcatheter valve interventions.

European Heart Journal (2012) 33, 1787–1847
European Journal of Heart Failure (2012) 14, 803–869

Indications for myocardial revascularization

- CABG indicated in symptomatic patients with left main or multivessel disease.
- No indication for revascularization in asymptomatic patients without viable myocardium (scar).

Recommendations	Class	Level
CABG is recommended for patients with angina and significant left main stenosis, who are otherwise suitable for surgery and expected to survive >1 year with good functional status, to reduce the risk of premature death.	I	C
CABG is recommended for patients with angina and two- or three-vessel coronary disease, including a left anterior descending stenosis, who are otherwise suitable for surgery and expected to survive >1 year with good functional status, to reduce the risk of hospitalization for cardiovascular causes and the risk of premature death from cardiovascular causes.	I	B
Alternative to CABG: PCI may be considered as an alternative to CABG in the above categories of patients unsuitable for surgery.	IIb	C
CABG and PCI are NOT recommended in patients without angina AND without viable myocardium.	III	C

www.escardio.org/guidelines

European Heart Journal (2012) 33, 1787–1847
European Journal of Heart Failure (2012) 14, 803–869

EUROPEAN SOCIETY OF CARDIOLOGY®

Table 7 Possible applications of various imaging techniques in the diagnosis of HF

		Echo	CMR	Cath	SPECT	MDCT	PET
CAD:	Ischaemia	+++[a]	+++	+++[b]	+++	-	+++
	Hibernation	+++[a]	+++[a]	-	+++	-	+++
	Scar	++	+++	-	++	-	++
	Coronary anatomy	-	-	+++	-	+++	-

Coronary Artery Bypass Graft Surgery in Patients with Ischemic Heart Failure

Eric J. Velazquez, MD
on behalf of the STICH Investigators

April 4, 2011

Background — II

- In the 1970s, RCTs of CABG vs. medical therapy for chronic stable angina excluded patients with LVD (LVEF < 35%)
  - Only 4.0% symptomatic with HF
- Major advances in surgical care and medical therapy (MED) for CAD, HF and LVD render previous limited data obsolete for clinical decision making
- Recent observational analyses suggest a role for CABG for HF which is increasingly utilized, yet substantial clinical uncertainty remains

STICH

Surgical Treatment for Ischemic Heart Failure Trial (STICH)

Surgical Revascularization Hypothesis

In patients with HF, LVD and CAD amenable to surgical revascularization, CABG added to intensive medical therapy (MED) will decrease all-cause mortality compared to MED alone.

STICH

Endpoints

Primary Endpoint

- All-cause mortality

Major Secondary Endpoints

- Cardiovascular mortality
- Death (all-cause) + cardiovascular hospitalization

STICH

Statistical Assumptions and Analyses

Statistical Assumptions

- MED mortality of 25% at 3 years
- CABG would reduce mortality by 25%
- 20% or fewer crossovers from MED to CABG
- 400 or more deaths
- 90% power

Planned Analyses

- Intention to treat (as randomized)
- Covariate-adjusted
- As treated
  - Time-dependent
- Per protocol

STICH

Important Inclusion Criteria

- LVEF ≤ 0.35 within 3 months of trial entry
- CAD suitable for CABG
- MED eligible
  - Absence of left main CAD as defined by an intraluminal stenosis of ≥ 50%
  - Absence of CCS III angina or greater (angina markedly limiting ordinary activity)

STICH

Major Exclusion Criteria

- Recent acute MI (within 30 days)
- Cardiogenic shock (within 72 hours of randomization)
- Plan for percutaneous intervention
- Aortic valve disease requiring valve repair or replacement
- History of more than 1 prior CABG
- Non-cardiac illness with a life expectancy of less than 3 years or imposing substantial operative mortality

STICH

Selected Baseline Characteristics

Variable	MED (N=602)	CABG (N=610)
Age, median (IQR), yrs	59 (53, 67)	60 (54, 68)
Female, %	12	12
Black or other, %	30	33
Myocardial infarction, %	78	76
Diabetes, %	40	39
Previous PCI or CABG, %	15	16
NYHA HF Class I/II, %	63	63
NYHA HF Class III/IV, %	37	37
No angina or CCS Class I, %	52	52
CCS Angina Class II–IV, %	48	48

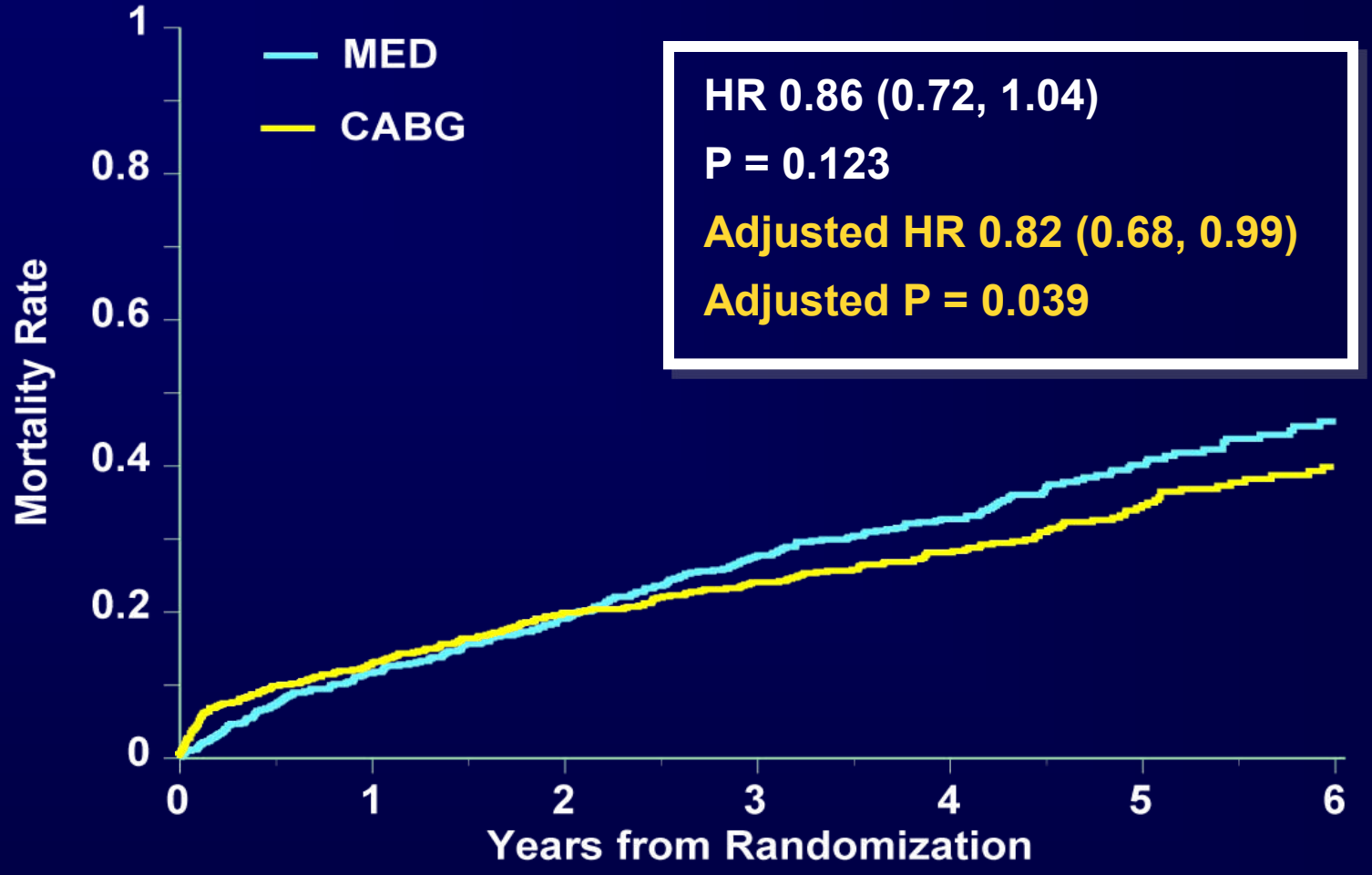
STICH

Medication Use

	MED (N=602)		CABG (N=610)	
Medication, %	**Baseline**	**Latest Follow-up**	**Baseline**	**Latest Follow-up**
Aspirin	85	84	80	84
Aspirin or warfarin	91	93	84	92
ACE inhibitor or ARB	88	89	91	89
Beta-blocker	88	90	83	90
Statin	83	87	79	90

STICH

All-Cause Mortality — As Randomized



HR 0.86 (0.72, 1.04)

P = 0.123

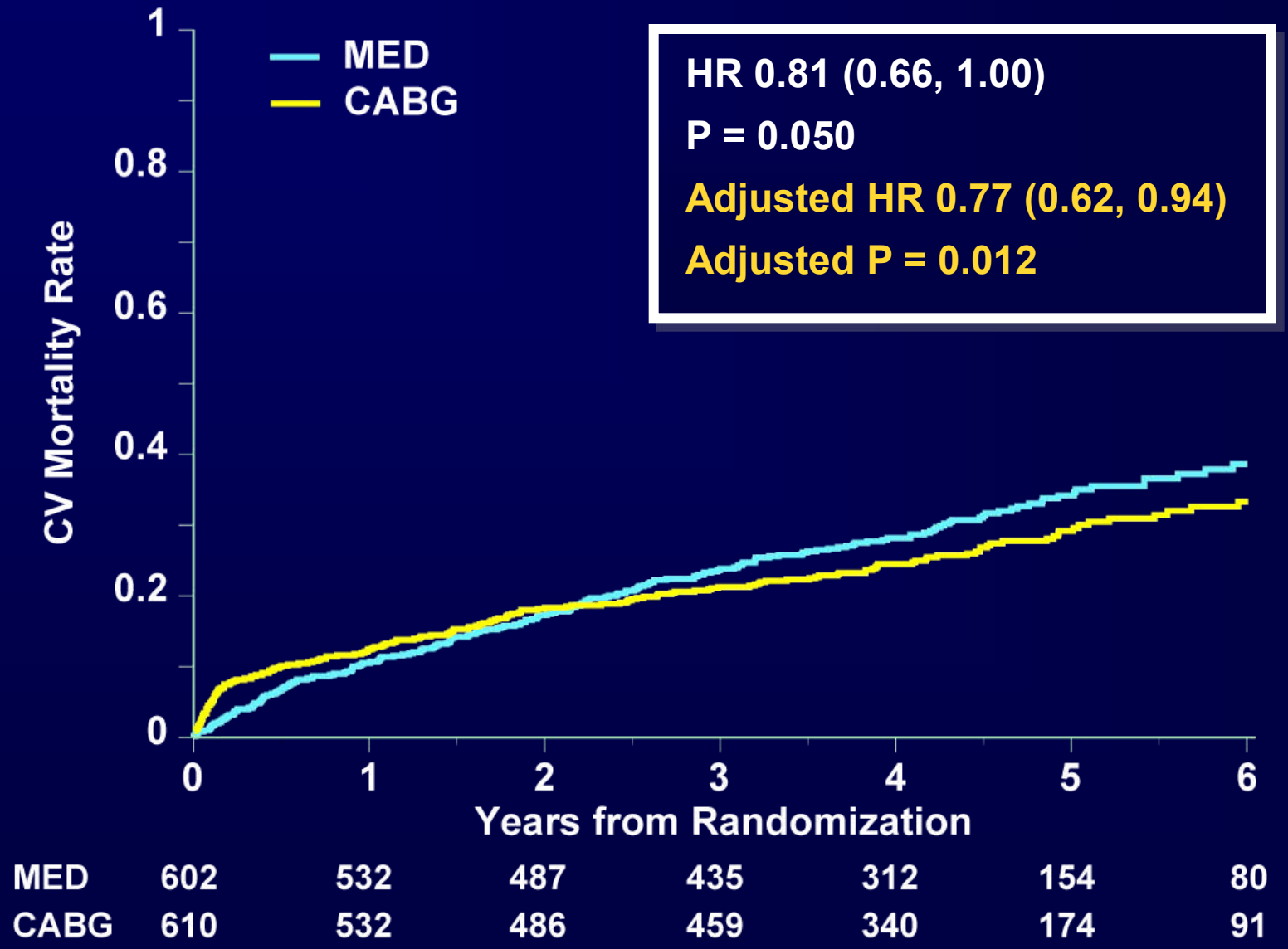
Adjusted HR 0.82 (0.68, 0.99)

Adjusted P = 0.039

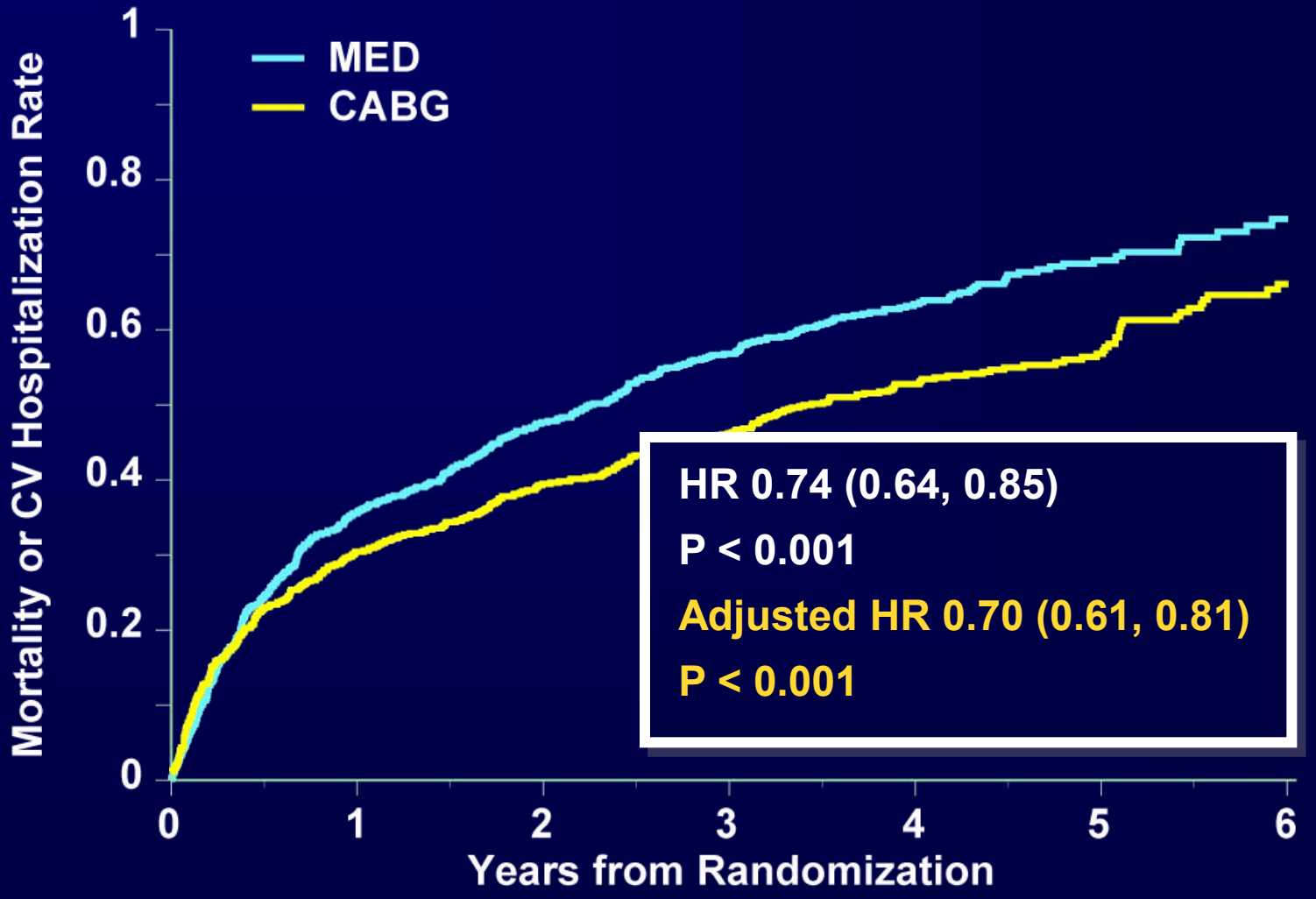
MED	602	532	487	435	312	154	80
CABG	610	532	486	459	340	174	91

Adjusted for: age, sex, race, NYHA class, MI history, previous revascularization, ejection fraction; number of diseased vessels, CKD, mitral regurgitation grade, stroke history, AF

Cardiovascular Mortality — As Randomized



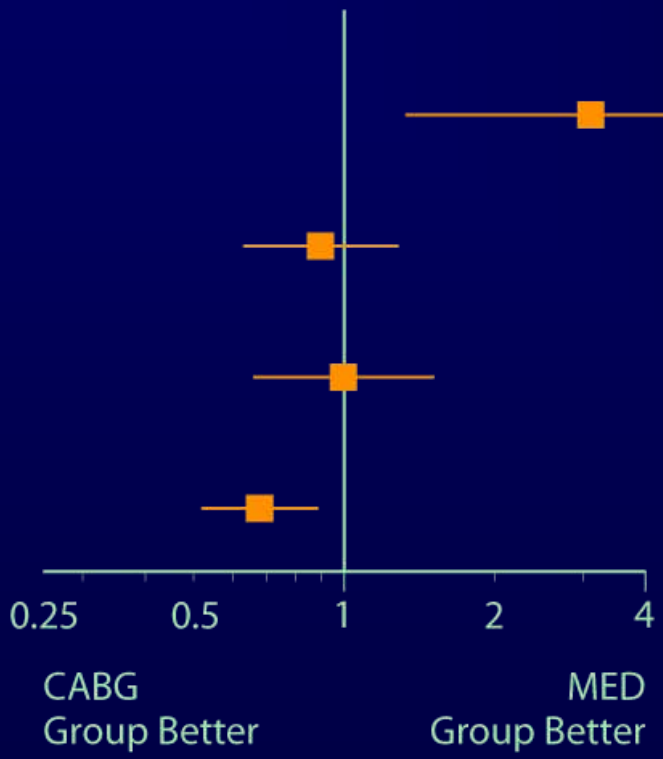
Death or Cardiovascular Hospitalization — As Randomized



MED	602	387	315	260	158	65	28
CABG	610	431	375	334	221	100	43

Time-varying Hazard Ratios — As Randomized

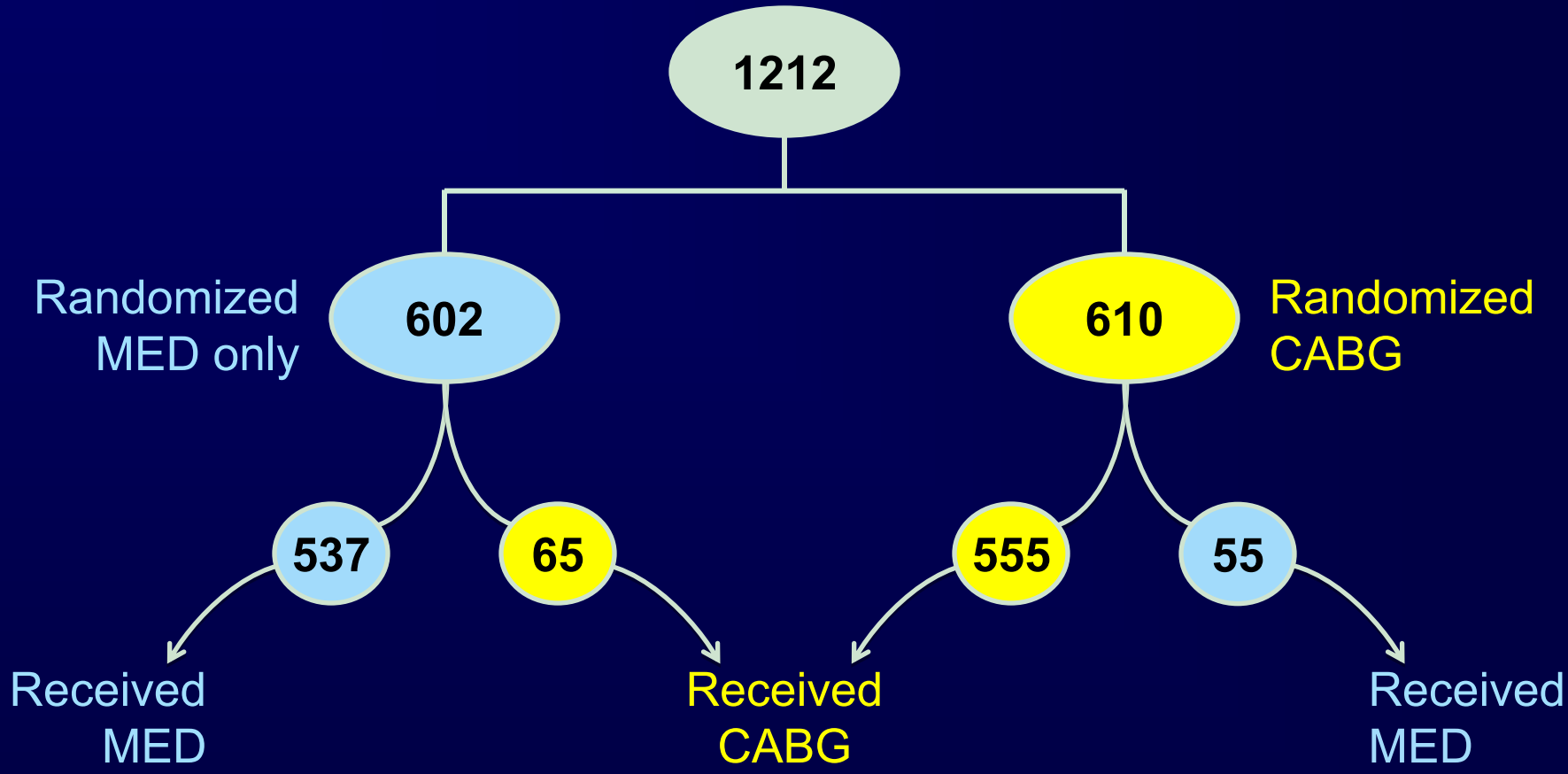
Time Periods	Hazard Ratio (95% CI)	P-Value
≤ 30 days	3.12 (1.33, 7.31)	0.009
31–365 days	0.90 (0.63, 1.29)	0.568
366 days–2 years	1.00 (0.66, 1.52)	0.982
≥ 2 years	0.68 (0.52, 0.89)	0.004



STICH

STICH Revascularization Hypothesis

Treatment Received

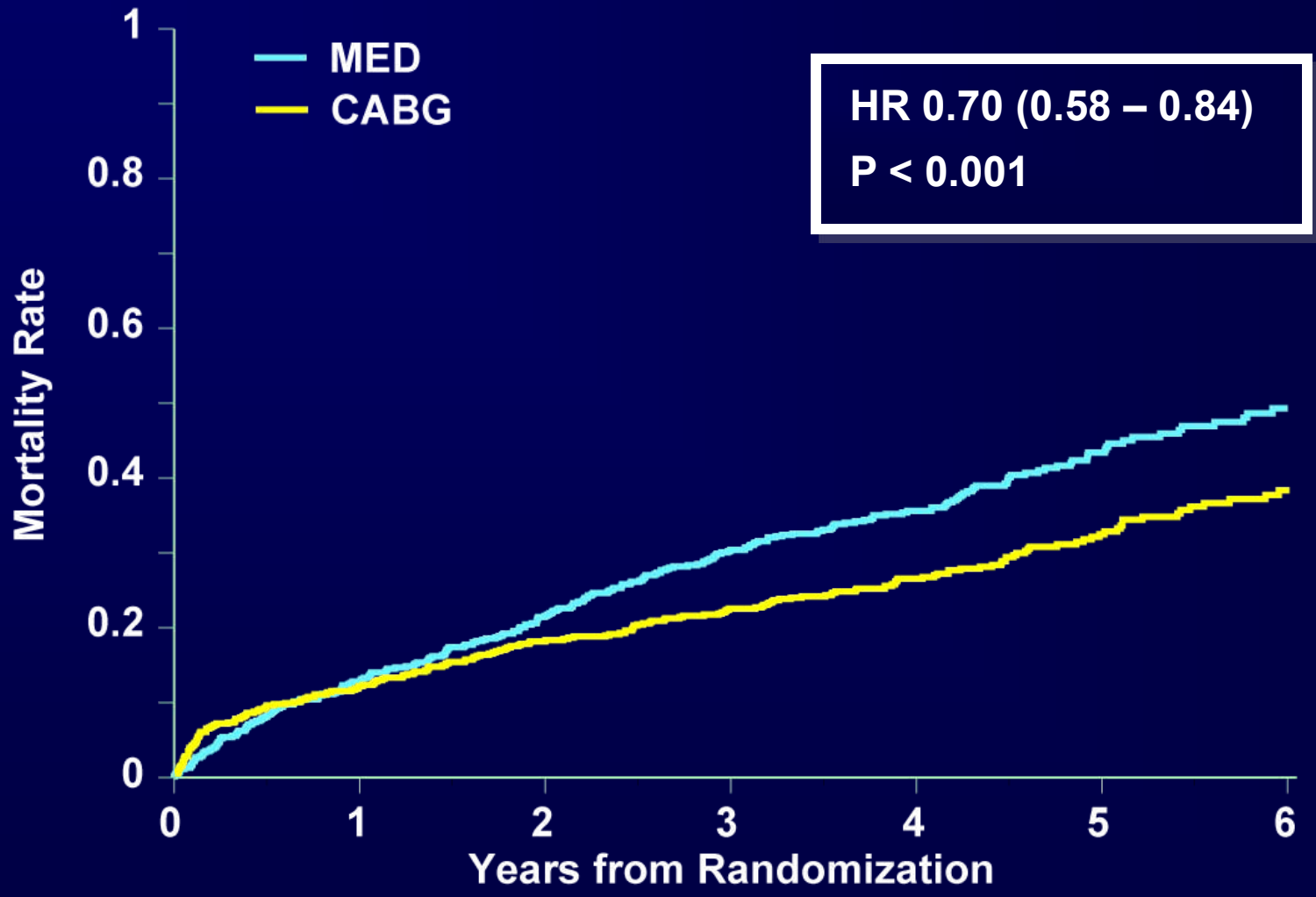


Per protocol: MED (537) vs. CABG (555)

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

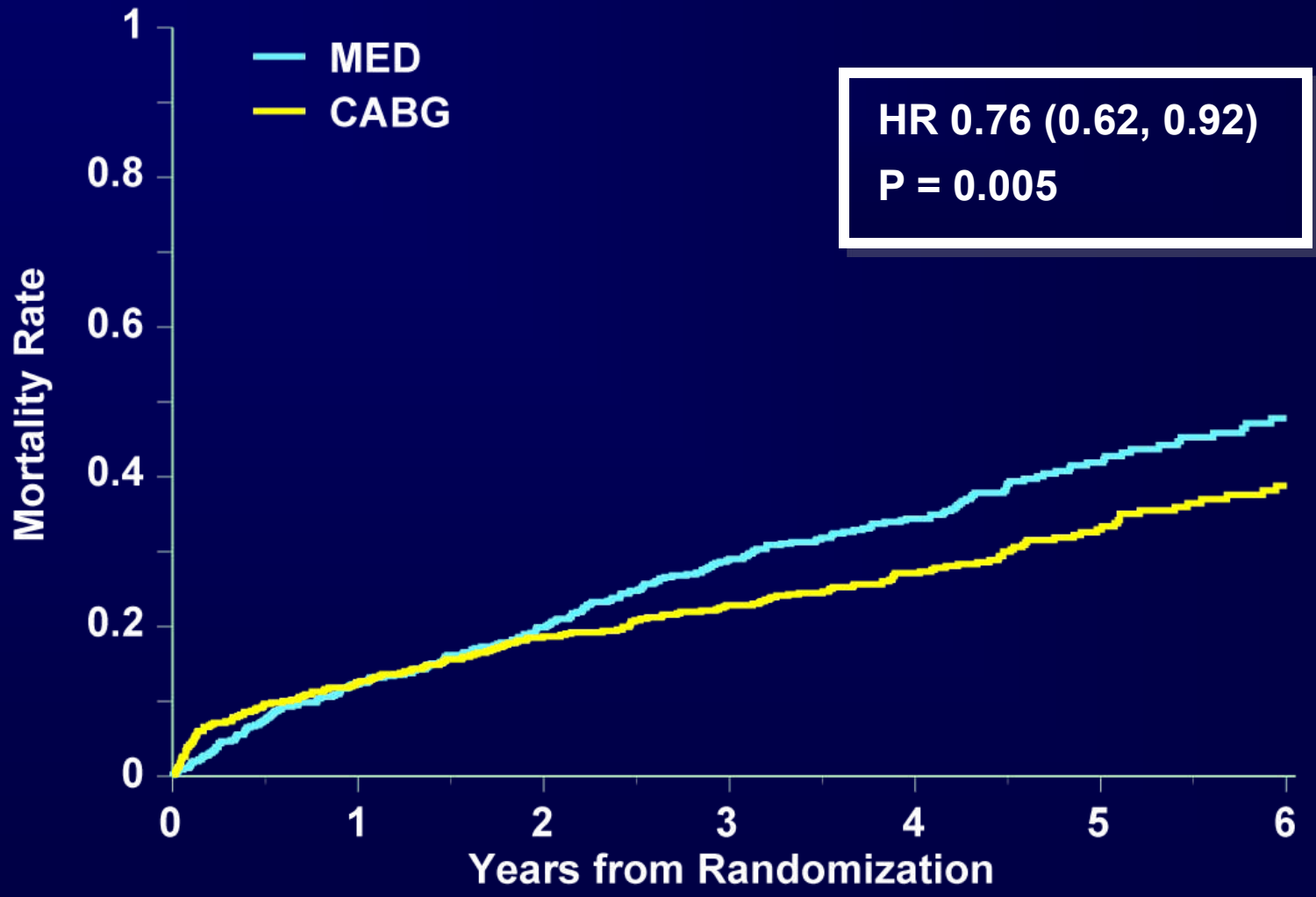
STICH

All-Cause Mortality — As Treated



MED	592	516	464	412	297	146	74
CABG	620	548	509	482	355	182	97

All-Cause Mortality — Per Protocol



MED	537	471	430	381	276	139	72
CABG	555	487	452	428	319	167	89

Summary

- We compared CABG with contemporary evidence-based MED alone among high-risk patients with CAD, HF and LVD
- Despite the excellent medical adherence and operative results achieved, STICH-like patients remain at substantial risk
  - -40% 5-year mortality risk with medical therapy only

Conclusions

- As randomized, CABG led to a 14% RRR in all-cause mortality compared to MED.
- CABG compared to MED led to statistically significant lower rates —
  - cardiovascular death: 19% RRR
  - death or cardiovascular hospitalization: 24% RRR
- When receiving CABG, patients are exposed to an early risk for 2 years.

STICH

Limitations

- Secondary analyses although informative should be considered provisional
- The STICH trial was not blinded and non-fatal outcomes could have been influenced by the knowledge of the treatment received

STICH

Outcomes — ITT

Variable	MED (N=602)	CABG (N=610)	Hazard Ratio (95% CI)	P Value
Death from any cause, ITT—no.	244	218	0.86 (0.72, 1.04)	0.123
Baseline-covariate adjusted				
Model 2			0.84 (0.70, 1.00)	0.056
Model 3			0.82 (0.68, 0.99)	0.039
Analyses with CABG as a time-dependent covariate				
Analysis 1			0.77 (0.64, 0.92)	0.005
Analysis 2			0.74 (0.61, 0.89)	0.001
Analysis 3			0.83 (0.69, 0.99)	0.044

STICH

Myocardial Viability and Survival in Ischemic Left Ventricular Dysfunction

Robert O. Bonow, MD

On behalf of the STICH Trial Investigators

Background

- LV dysfunction in patients with CAD is not always an irreversible process, as LV function may improve substantially after CABG
- Assessment of myocardial viability is often used to predict improvement in LV function after CABG and thus select patients for CABG
- Numerous studies have suggested that identification of viable myocardium also predicts **improved survival** after CABG

STICH

STICH Viability Hypothesis

In this prospective substudy, we tested the hypothesis that assessment of myocardial viability identifies patients with CAD and LV dysfunction who have the greatest survival benefit with CABG compared to aggressive medical therapy

STICH

STICH Viability Hypothesis

- All randomized patients were eligible for viability testing with SPECT myocardial perfusion imaging or dobutamine echo.
- Viability testing was optional at enrolling sites and was not a prerequisite for enrollment.

STICH

STICH Viability Hypothesis

SPECT protocols:

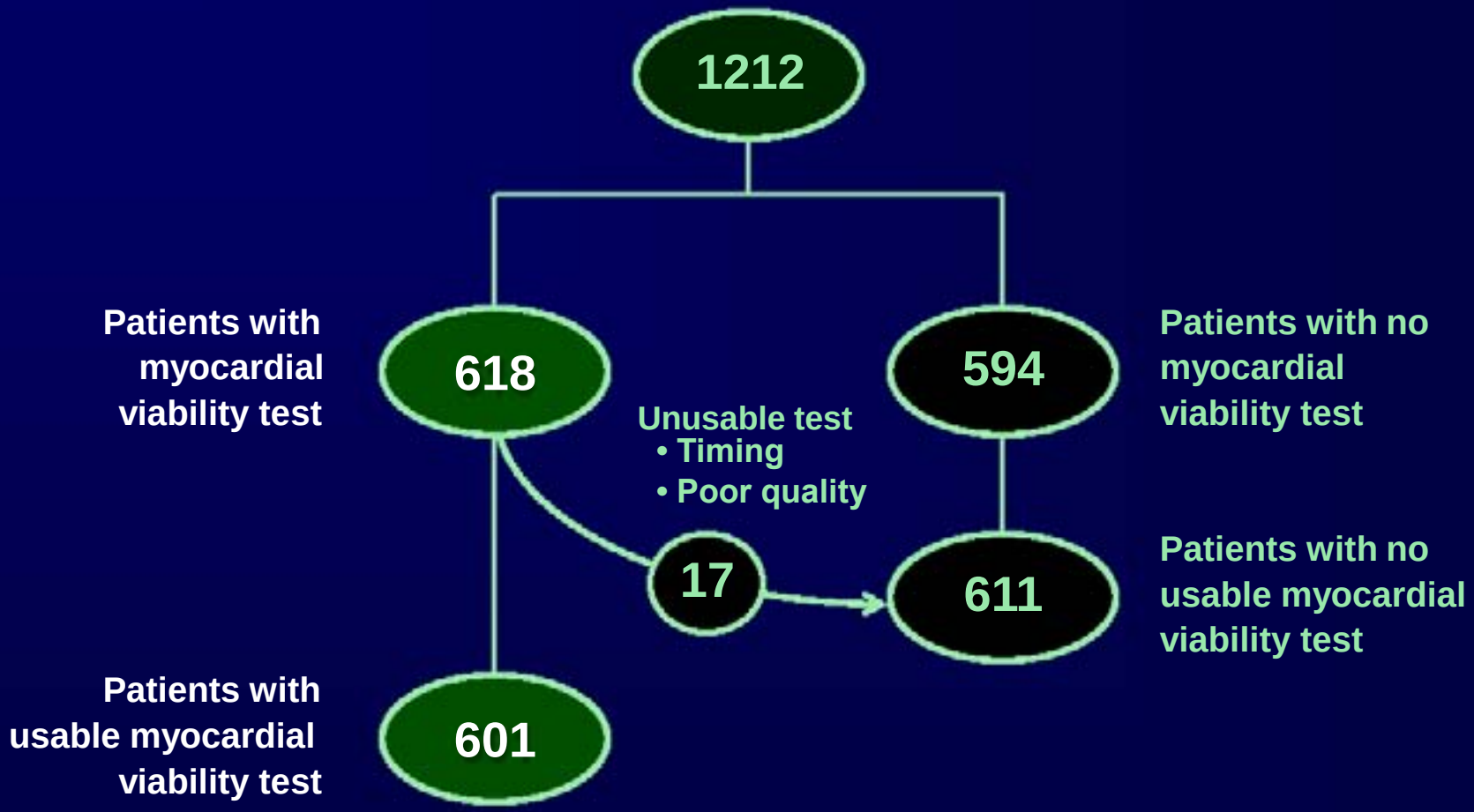
- Thallium-201 stress-redistribution-reinjection
- Thallium-201 rest-redistribution
- Nitrate-enhanced Tc-99m perfusion imaging

Dobutamine echo protocols:

- Staged increase in dobutamine starting at 5 µg/kg/min

STICH

Patients randomized in STICH Revascularization Hypothesis



Baseline Characteristics

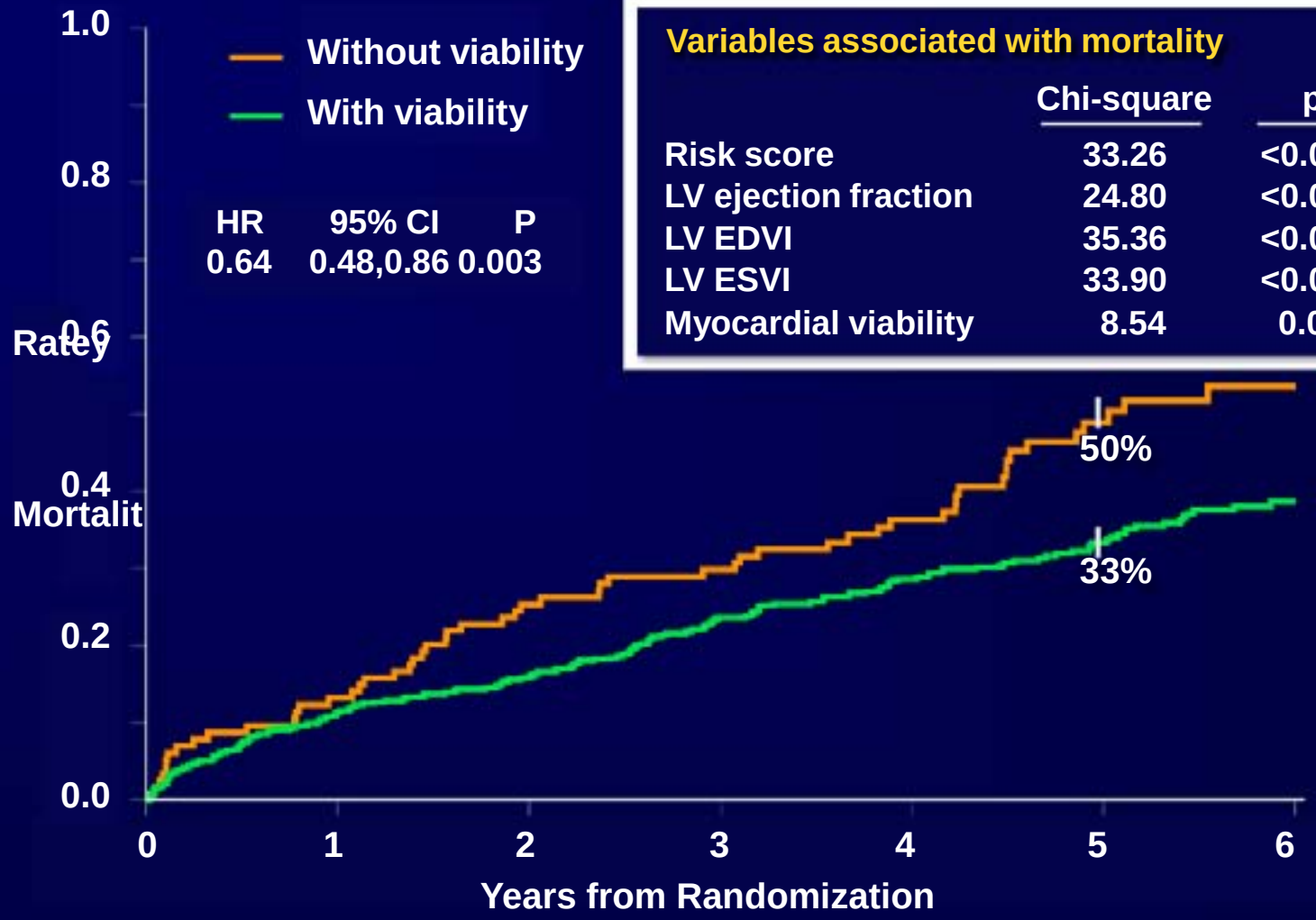
Patients With and Without Myocardial Viability

Variable	Viable (n=487)	Non-Viable (n=114)	P value
Age	61 ± 10	61 ± 9	NS
Multivessel CAD	73%	73%	NS
Proximal LAD stenosis	64%	70%	NS
Risk score *	12.4 ± 8.7	12.9 ± 9.3	NS
Previous MI	76.6%	94.7%	<0.001
LV ejection fraction (percent)	28 ± 8	23 ± 9	<0.001
LV end-diastolic volume index (ml/m^2)	117 ± 37	147 ± 53	<0.001
LV end-systolic volume index (ml/m^2)	86 ± 33	116 ± 50	<0.001

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

STICH

Myocardial Viability and Mortality



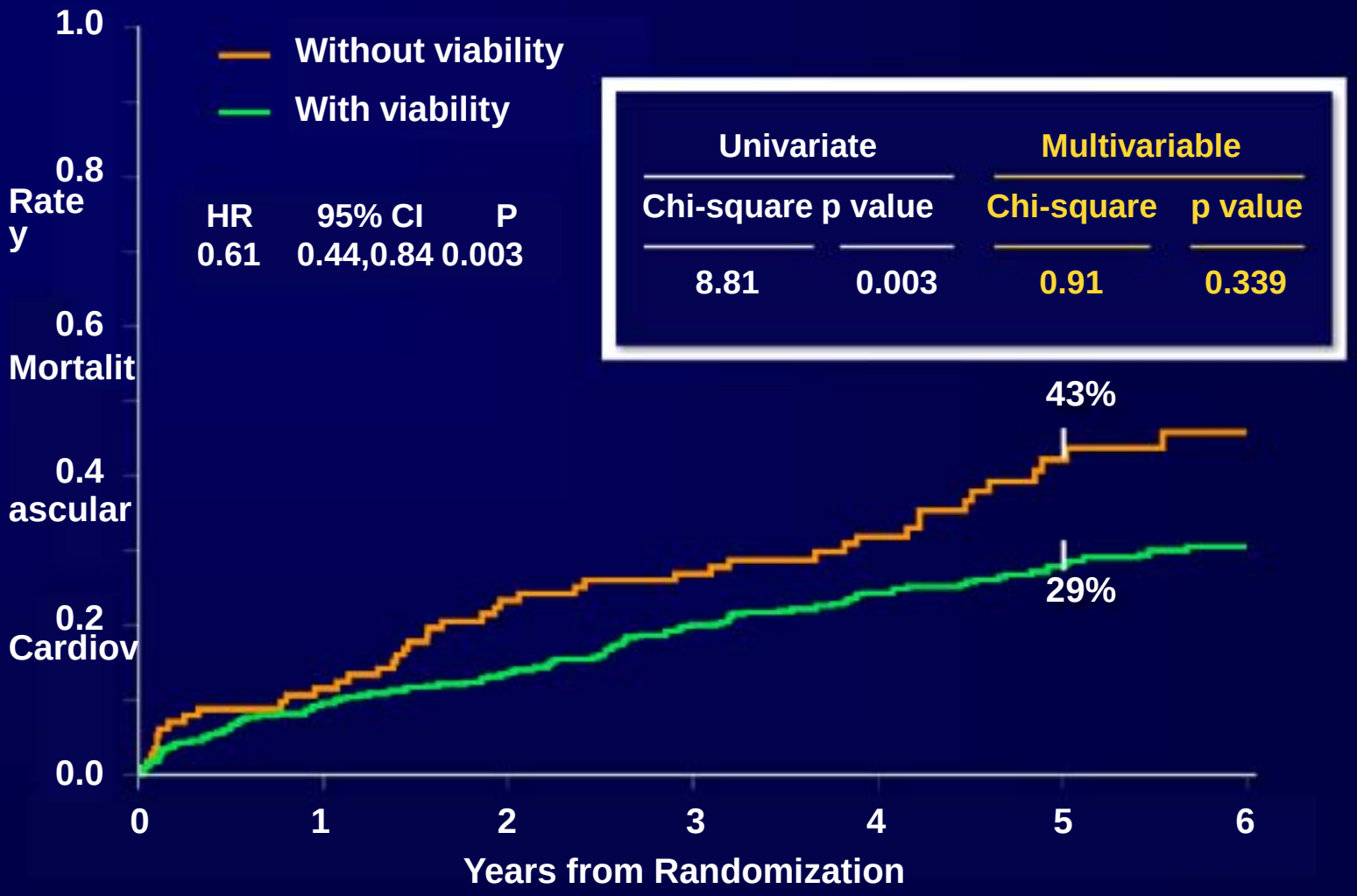
Variables associated with mortality

	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

STICH

Myocardial Viability and Cardiovascular Mortality

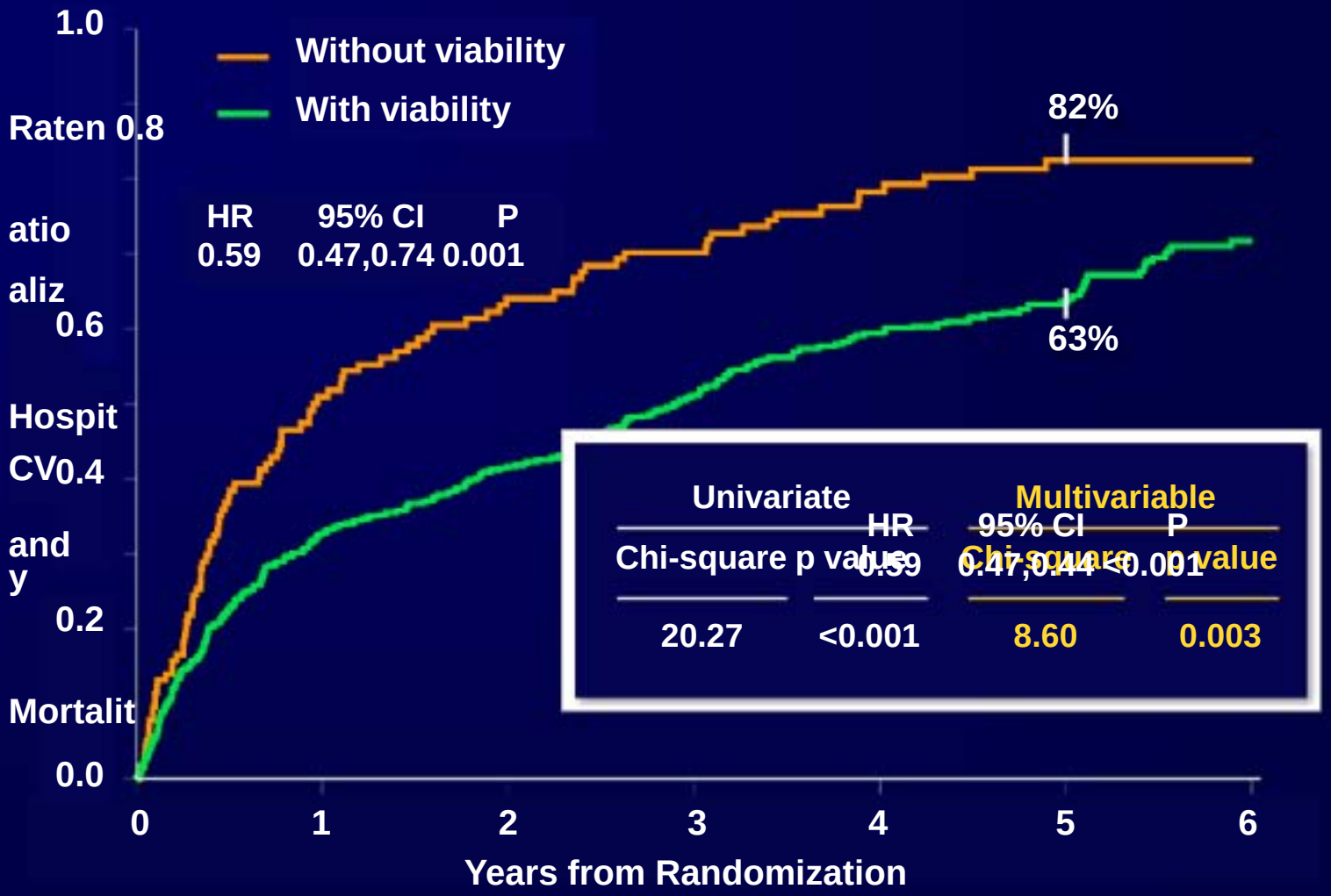


	Univariate		Multivariable	
	Chi-square	p value	Chi-square	p value
	8.81	0.003	0.91	0.339

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

STICH

Myocardial Viability and Mortality + CV Hospitalization



Without viability	114	56	41	34	22	14	5
With viability	487	327	284	238	166	94	41

STICH

STICH Viability Hypothesis

Limitations:

- Analysis limited to SPECT and dobutamine echo, not PET or cardiac MRI
- Lack of viability data in all patients; patients represent a subpopulation of STICH

STICH

STICH Viability Hypothesis

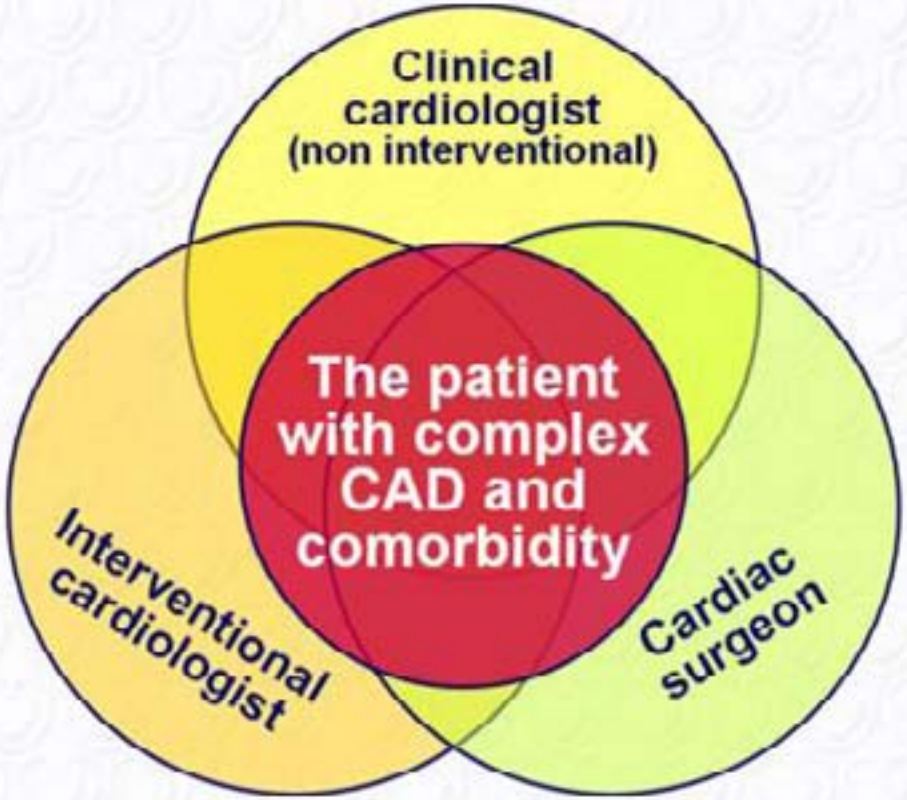
STICH results:

…demonstrate a significant association between myocardial viability and outcome, but this association is rendered non-significant when subjected to a multivariable analysis that includes other prognostic variables.

…fail to demonstrate a significant interaction between myocardial viability and medical versus surgical treatment with respect to mortality, whether assessed according to treatment assigned (intention to treat) or to the treatment actually received.

STICH

The Expanded Heart Team



European Heart Journal (2010) 31, 2501-2555
European Journal of Cardio-thoracic Surgery (2010) 38, S1-S52

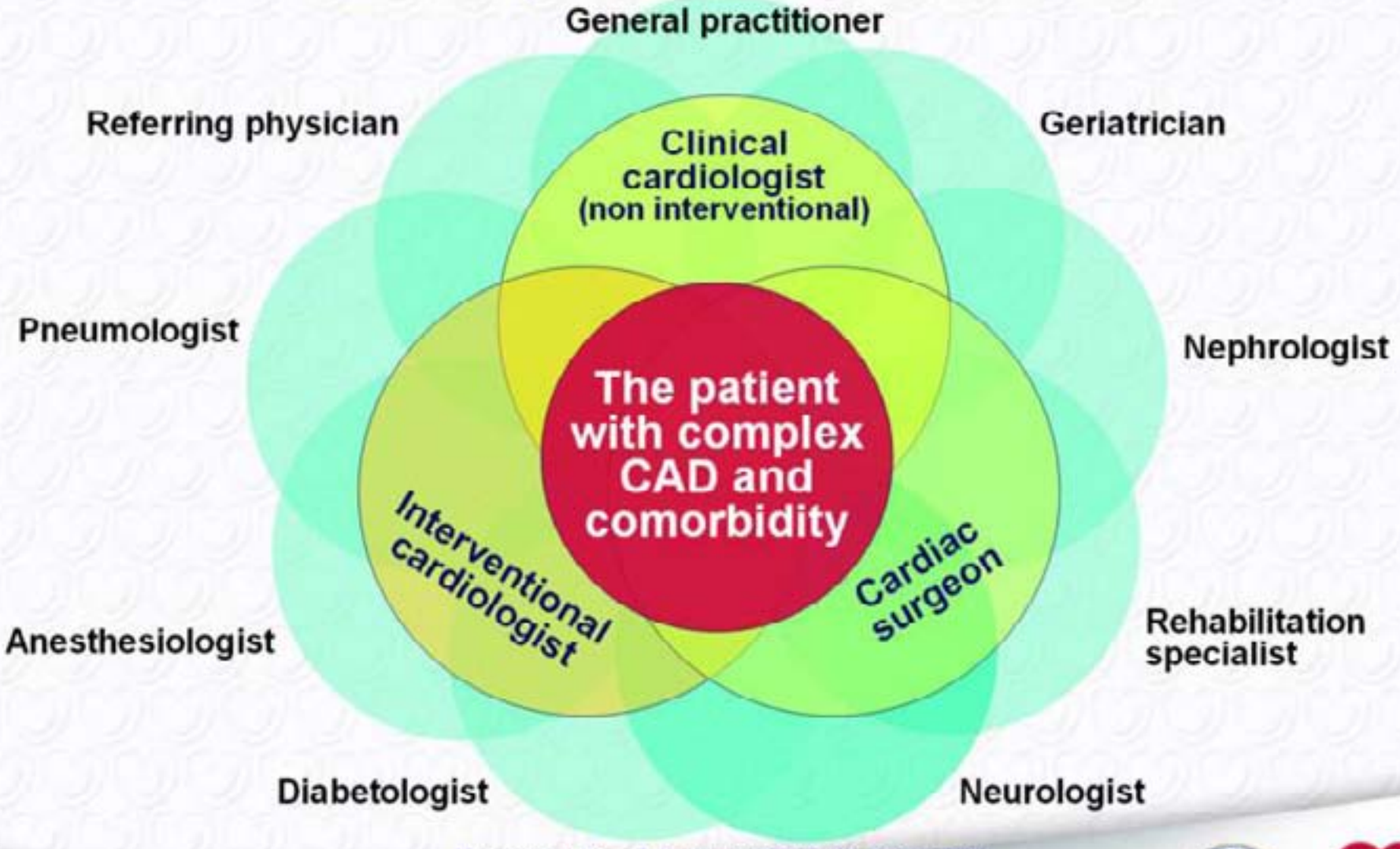
www.escardio.org/guidelines

Joint 2010 ESC - EACTS Guidelines on Myocardial Revascularisation

EACTS

EUROPEAN SOCIETY OF CARDIOLOGY®

The Expanded Heart Team



European Heart Journal (2010) 31, 2501-2555
European Journal of Cardio-thoracic Surgery (2010) 38, S1-S52

www.escardio.org/guidelines

Joint 2010 ESC - EACTS Guidelines on Myocardial Revascularisation

EACTS

EUROPEAN SOCIETY OF CARDIOLOGY®