STICH: Physician

Angioplasty Summit – TCTAP 2012

Seoul, Korea

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Presenter Disclosure Information

David R. Holmes, Jr., M.D.

"STICH: Physician"

The following relationships exist related to this presentation:

Immediate Past President ACC

What do Interventional Cardiologists Think?

- Interventional cardiologists actually do think (contrary to what surgeons may believe)
- Ischemic burden is important for treatment strategies
- Myocardial viability is important for outcome
- LV dysfunction and extensive complex MVD is best treated by CABG

CABG with or without Surgical Ventricular Reconstruction – STICH Trial

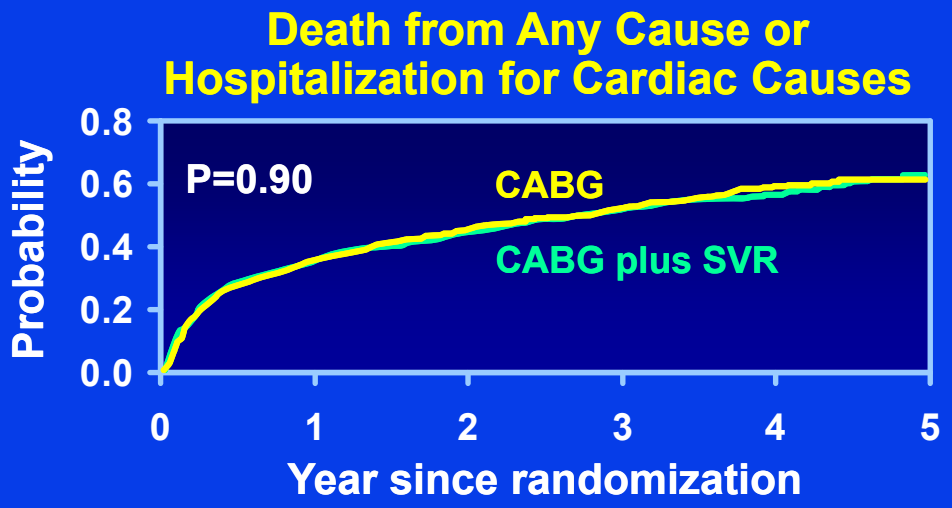
1,000 pt

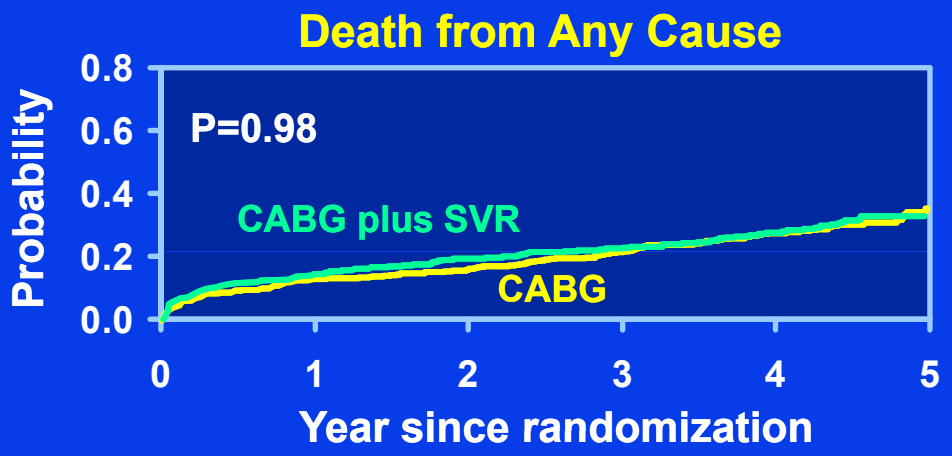
EF ≤0.35

CAD

Dominant anterior LV dysfunction

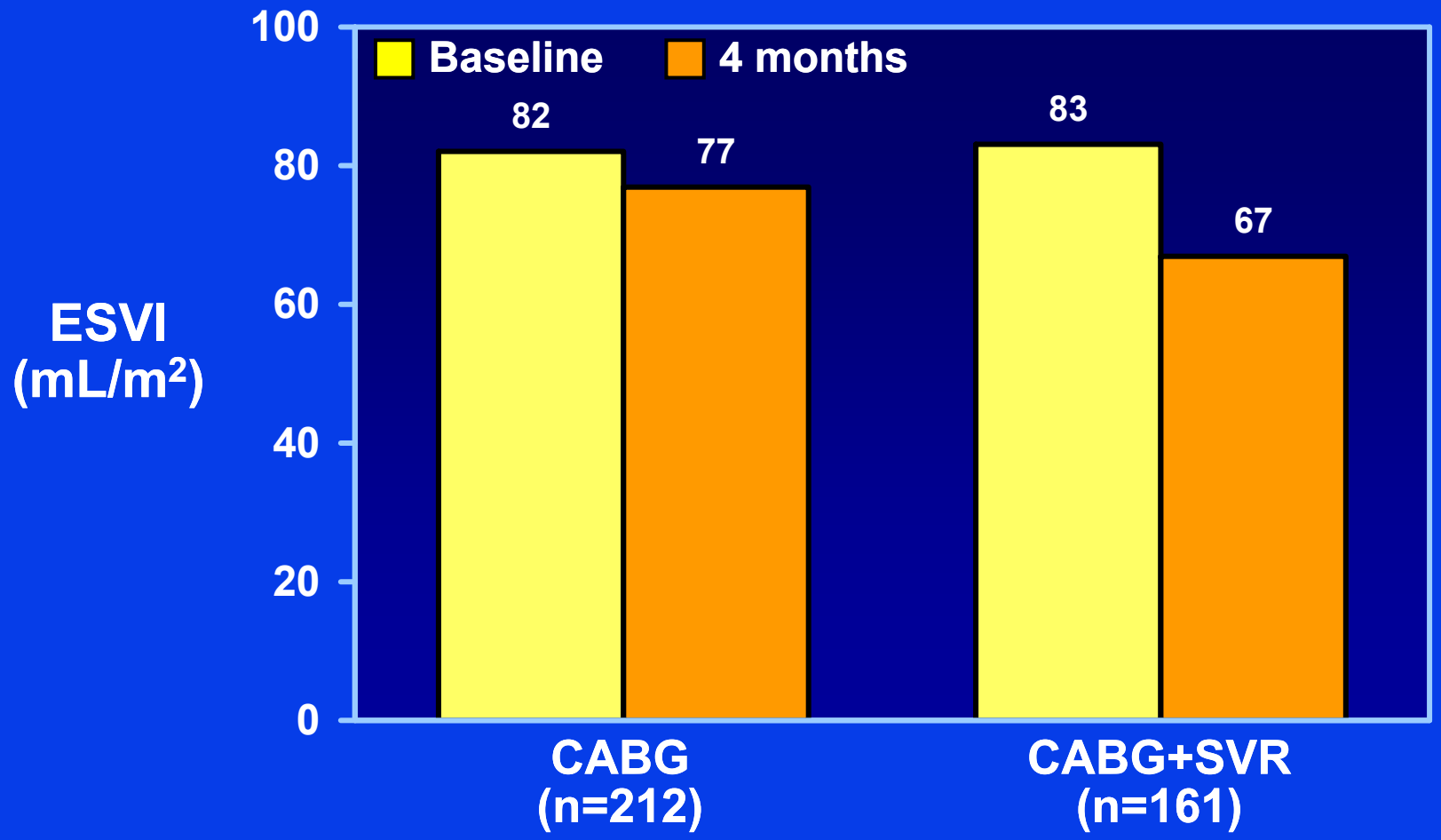
- CABG alone
- CABG + surg ventricular reconstruction





Jones: NEJM, 2009

Baseline and 4 Month ESVI: STICH Trial



P<0.001

Jones: NEJM, 2009

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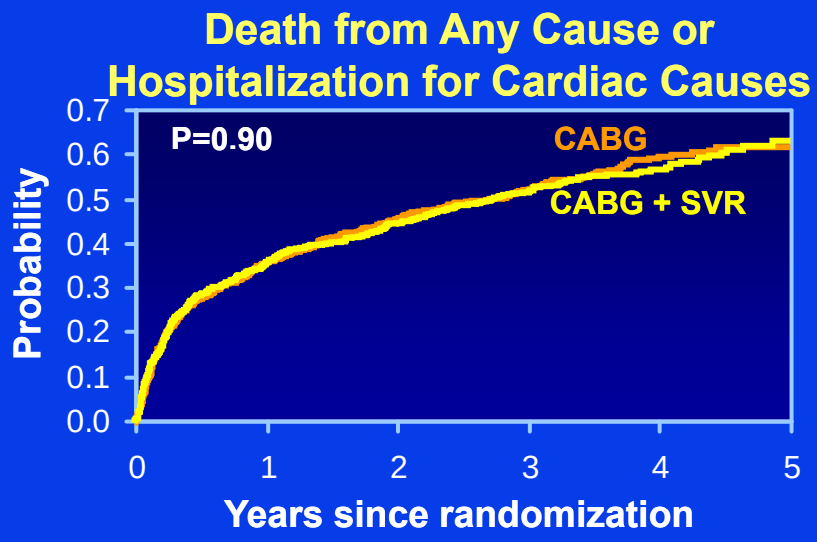
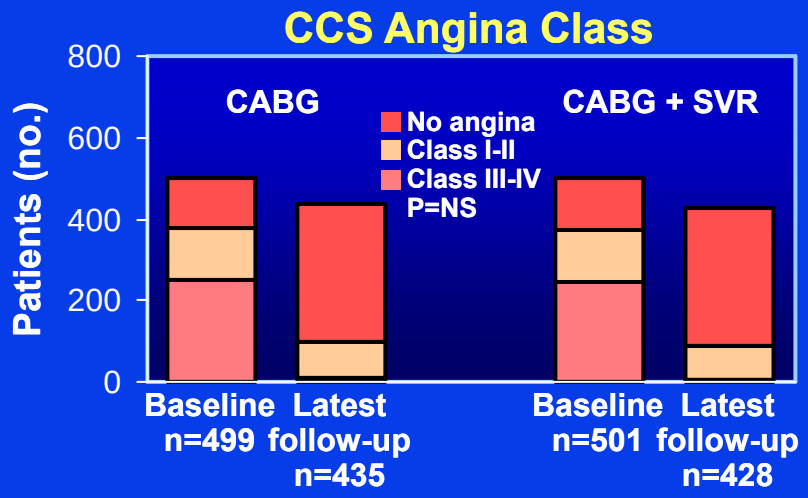
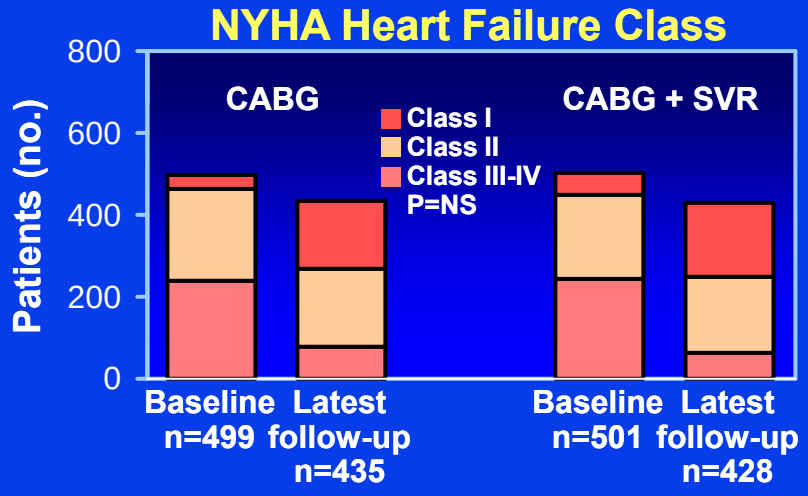
STICH Trial: CABG With or Without Surgical Ventricular Reconstruction

- 2002-2006
- 1000 patients
- EF <0.35







Jones: NEJM, 2009

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STICH Trial
Observations

- Population: 1000 pts with EF ≤35%, CAD amenable to CABG, dominant anterior LV dysfunction amenable to reconstruction
  - 64% - 3VD, 14% LMCA, EF 28%
  - 50% CCS III or IV angina
  - 48% NYHA CHF Class III or IV
- "The findings of this study do not support the use of surgical ventricular reconstruction in this population"

Jones et al: N Engl J Med 360:1705-17, 2009

STICH Trial
Issues

- Negative trial: “No significant difference in primary outcome which occurred in 59% of patients assigned to CABG alone and 58% assigned to CABG and surgical ventricular reconstruction (HR 0.99, 95% CI, 0.84-1.17 p=0.90)

Jones et al: N Engl J Med 360:1705-17, 2009

STYNTAX Trial

- Negative Trial: “Since noninferiority was not proven in this cohort, specific information for each subgroup is of an observational nature and is (only) hypothesis generating”

Serruys et al: N Engl J Med 360:1961-73, 2009

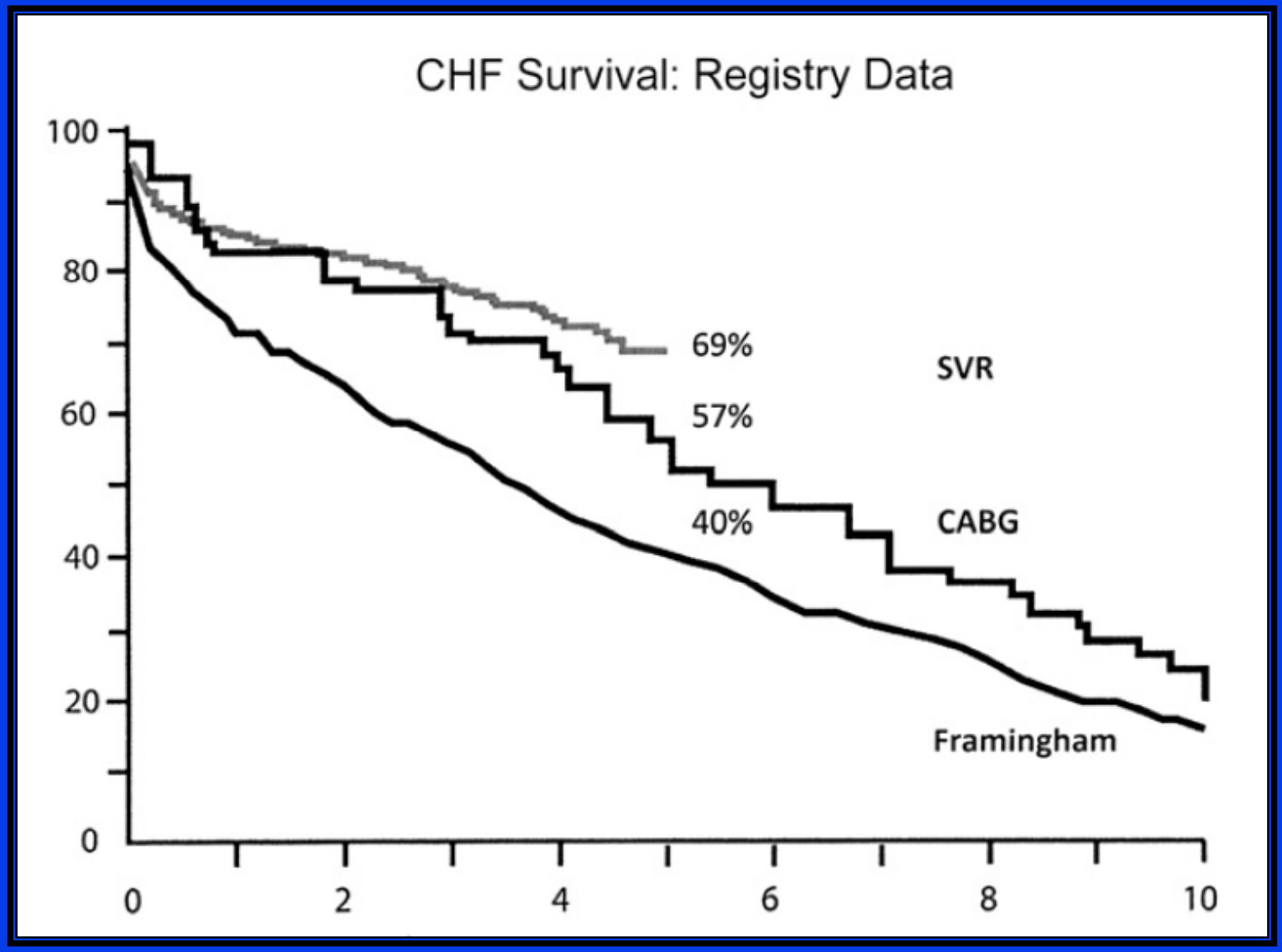
STICH Trial
Why Didn't Surgical Reconstruction Work?

- Maybe it just doesn't (diastolic distensibility)
- Maybe the surgeons did not know how to do it
- Wrong patient group (inclusion criteria liberalized)
- Selective patient enrollment

Acrimony

- "We conclude the editorial by….is misleading"
- "To suggest otherwise is inaccurate"
- "The STICH trial unraveled"
- 'The STICH trial: misguided conclusions"
- "Statisticians can defy nature from a flawed database"
- "Costly, flawed, inaccurate"

SVR Outcomes



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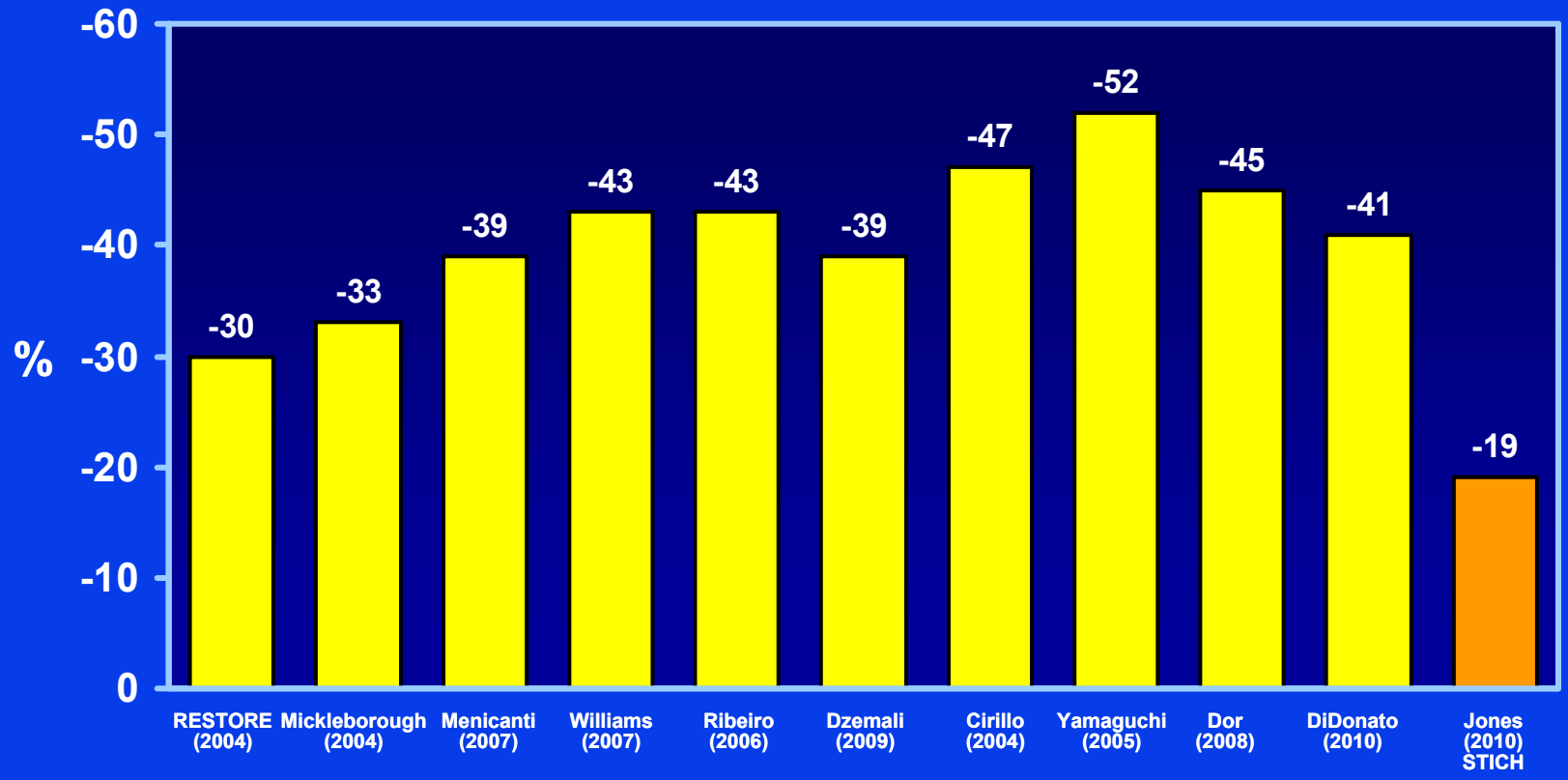
Buckberg GD et al: J Thorac Cardiovasc Surg 138:1060-4, 2009

LVESV and SVR

Author (yr)	# Pts.	Preop	Postop	Reduction (%)
Di Donato (2009)				
Type 1	56	83	35	48 (58)
Type 2	55	87	39	48 (55)
Type 3	67	96	57	39 (41)
Suma (2009)	76	123	74	49 (40)
Dor (2008)	104	93	51	42 (45)
Menicanti (2007)	301	173	100	73 (42)
O'Neill (2006)	135	120	77	43 (36)
Adams (2006)	8	92	59	33 (36)
Schreuder (2005)	9	92	45	47 (51)
Tulner (2006)	21	186	101	85 (46)
Yamaguchi (2005)	20	137	65	72 (53)
Mickleborough (2004)	41	97	65	32 (33)
Athanasuleas (2004)	671	80	57	24 (30)
Jones (STICH 2009)	161	83	67	16 (19)

Buckberg GD et al: J Thorac Cardiovasc Surg 138:1060-4, 2009

Extent of LVESV Reduction Following SVR
11 Published Series



Menicanti LA & Wechsler A

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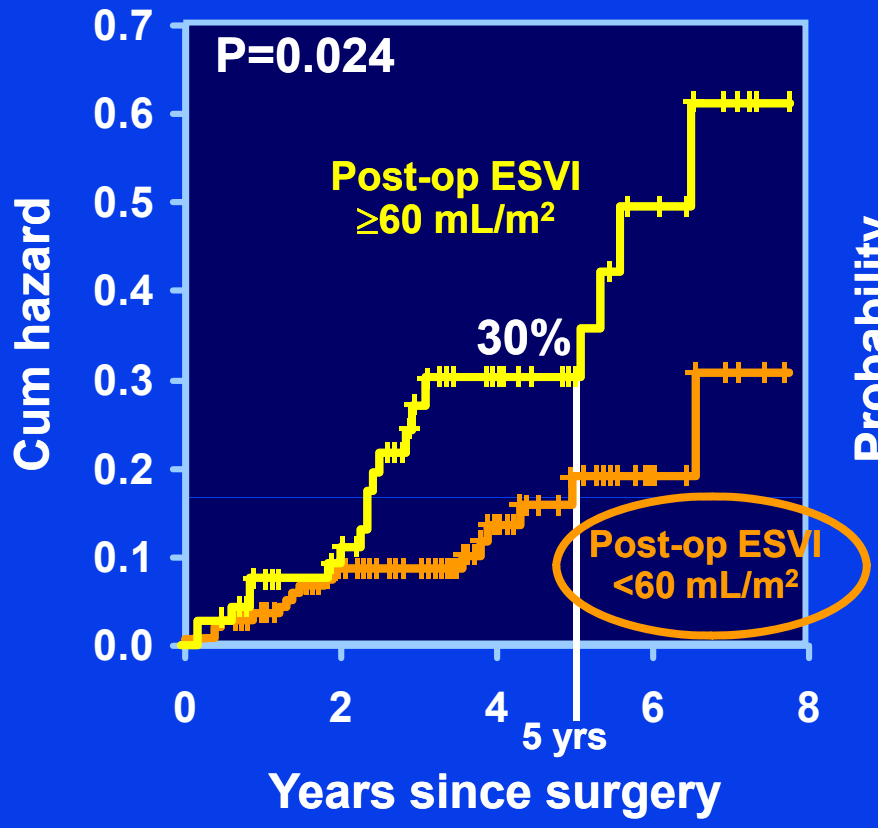
San Donato, Milan Hospital Experience

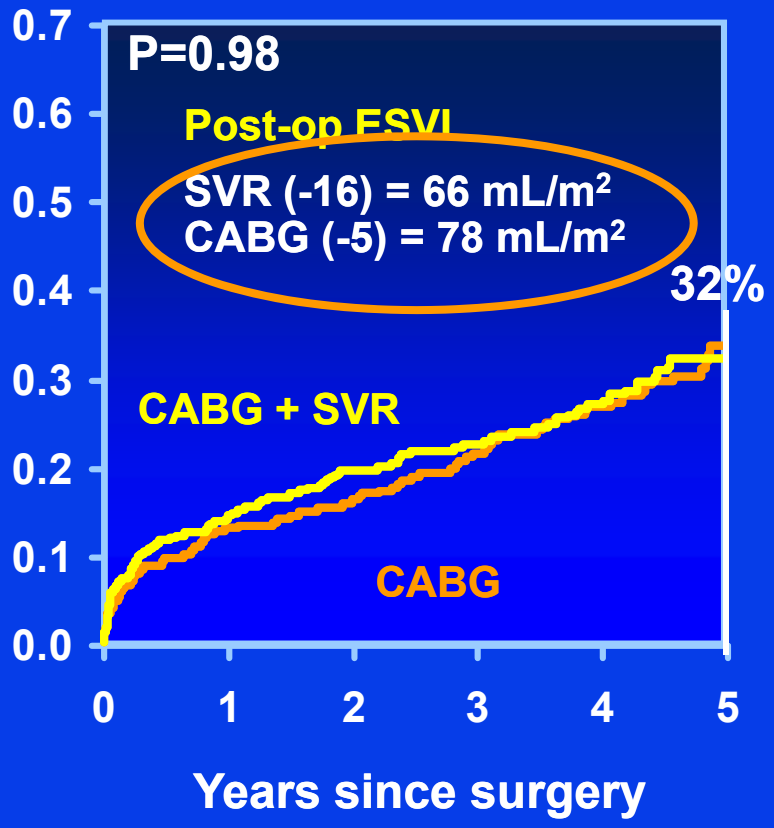
Death from any cause following SVR



Menicanti: EJHF, 2010

STICH Trial

Death from any cause



Adapted from NEJM 360:1705-17, 2009

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Joint ESC-EACTS Guidelines on Revascularization

Myocardial Revascularization in CHF

In patients with CHF and presenting with angina

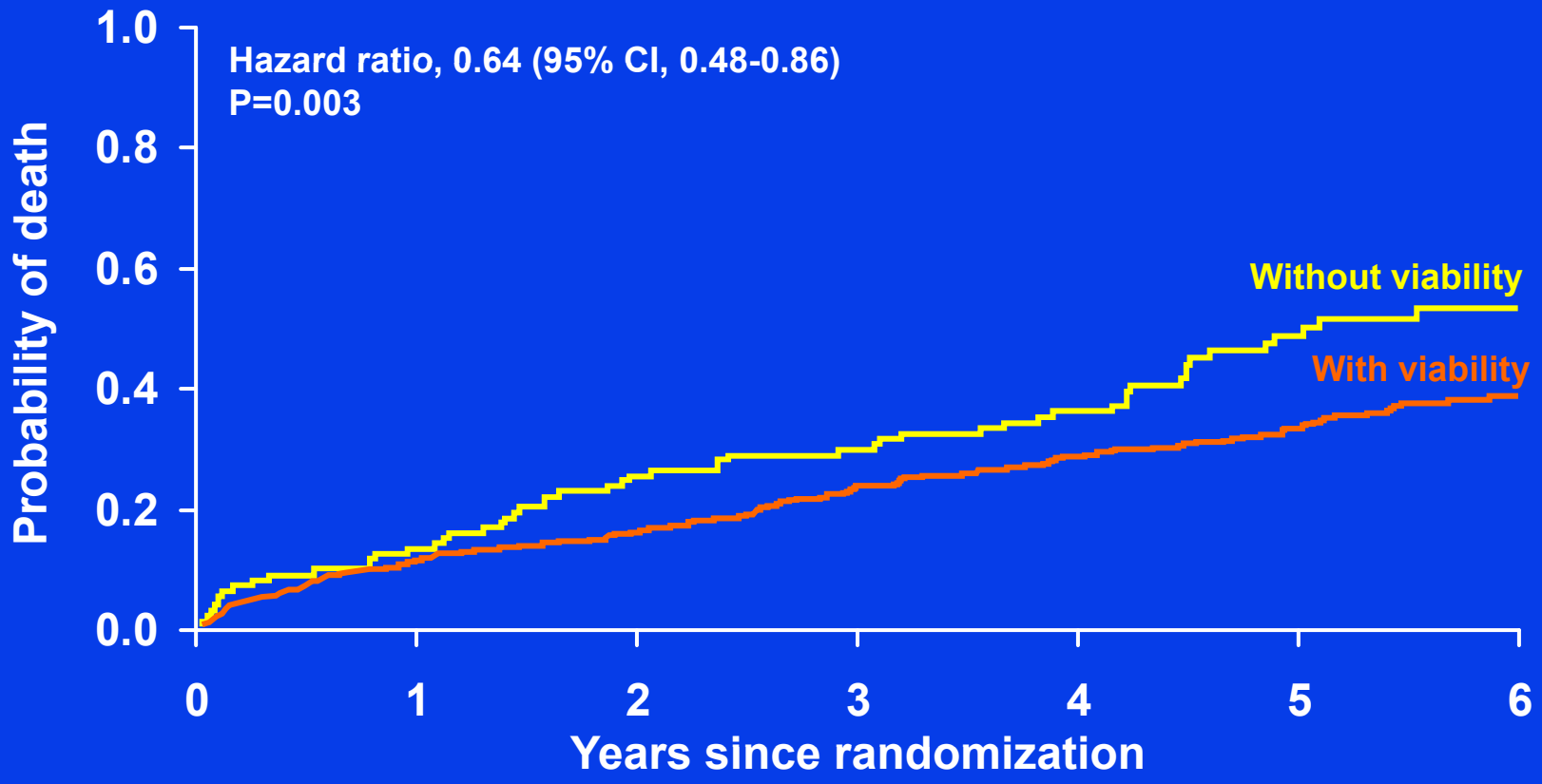
	Class	Level
CABG is recommended for: • Significant LM stenosis • LM equivalent (proximal stenosis of both LAD & LCx) • Proximal LAD stenosis with 2- or 3-vessel disease	I	B
CABG with SVR may be considered in patients with LVESV index ≥60 mL/m^2 and scarred LAD territory	IIb	B
PCI may be considered if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

Myocardial Viability and Survival
STICH Trial Substudy

- Substudy of a negative study
- Of 1,212 initially enrolled only 601 (49%) had assessment of myocardial viability and only 487 had viability (40%)
- Of 601 patients – random assignment to medical therapy + CABG or medical therapy alone

Bonow RO et al: N Engl J Med 364:1617-25, 2011

Probability of Death and Myocardial Viability



No. at risk							
Without viability	114	99	85	80	63	36	16
With viability	487	432	409	371	294	188	102

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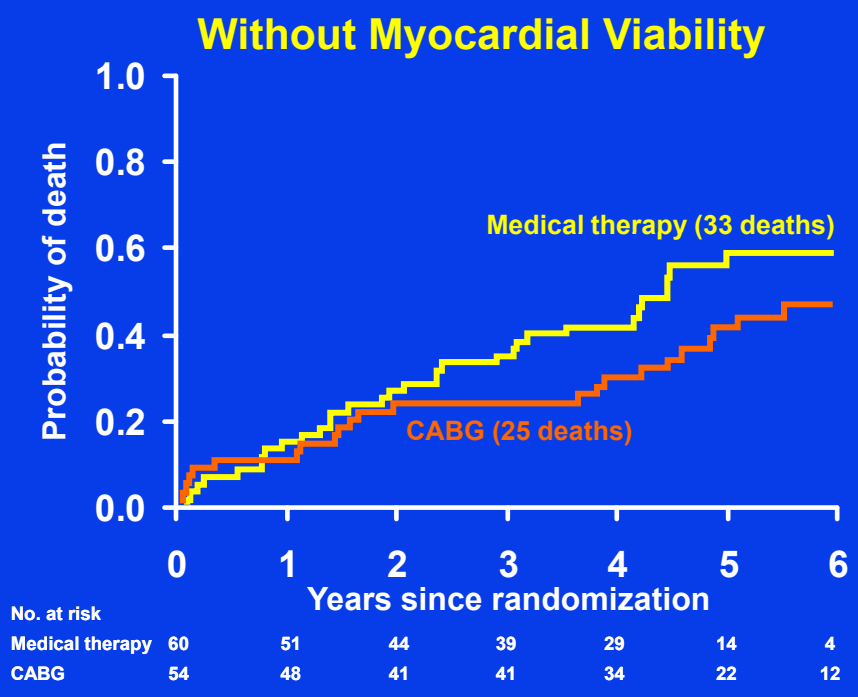
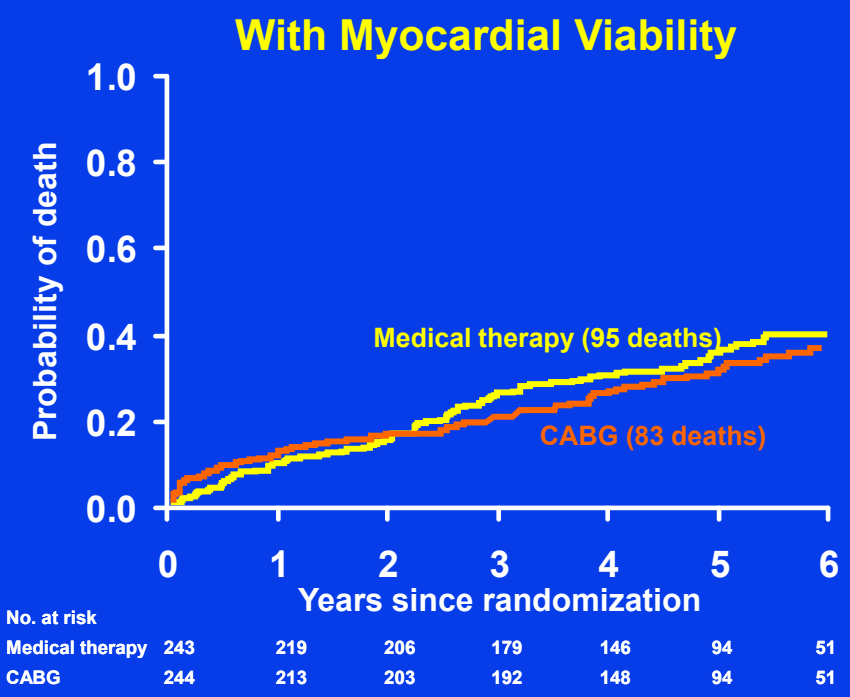
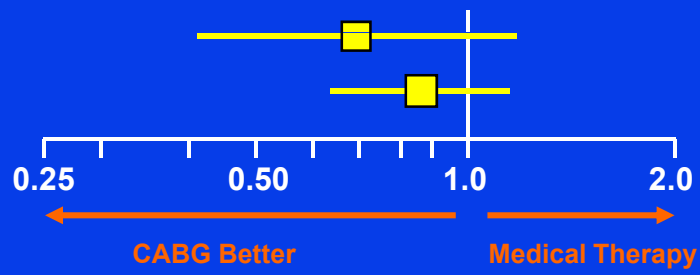
Bonow RO et al: N Engl J Med 364:1617-25, 2011

Death and Viability





Subgroup	No.	Deaths
Without viability	114	58
With viability	487	178



0.70 (0.41-1.18)
0.86 (0.64-1.16)

P
0.53

Bonow RO et al: N Engl J Med 364:1617-25, 2011

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Myocardial Viability and Survival
STICH Trial Substudy

	Viable Myocardium (n=487)	No Viable Myocardium (n=114)
Death	37%	51%

- After adjustment for baseline variables, association with mortality NS p=0.21
- No significant difference between myocardial viability and medical versus surgical therapy

Bonow RO et al: N Engl J Med 364:1617-25, 2011

Myocardial Viability and Survival
STICH Trial Substudy – Issues

- Substudy of a negative study
- Substudy represents ~ 50% of randomized study
- Small number of patients without viability
- Investigator bias
- Variable assessment of viability
- Low rates of death on maximal medical therapy

Bonow RO et al: N Engl J Med 364:1617-25, 2011

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Myocardial Viability and Survival in Ischemic Left Ventricular Dysfunction

Robert O. Bonow, M.D., Gerald Maurer, M.D., Kerry L. Lee, Ph.D., Thomas A. Holly, M.D., Philip F. Binkley, M.D., Patrice Desvigne-Nickens, M.D., Jaroslaw Drozdz, M.D., Ph.D., Pedro S. Farsky, M.D., Arthur M. Feldman, M.D., Torsten Doenst, M.D., Ph.D., Robert E. Michler, M.D., Daniel S. Berman, M.D., Jose C. Nicolau, M.D., Ph.D., Patricia A. Pellikka, M.D., Krzysztof Wrobel, M.D.,

Conclusions: The presence of viable myocardium was associated with a greater likelihood of survival in patients with coronary artery disease and left ventricular dysfunction, but this relationship was not significant after adjustment for other baseline variables. The assessment of myocardial viability did not identify patients with a differential survival benefit from CABG, as compared with medical therapy alone.

ment of myocardial viability. Of these patients, we randomly assigned 298 to receive medical therapy plus CABG and 303 to receive medical therapy alone. A total of 178 of 487 patients with viable myocardium (37%) and 58 of 114 patients without viable myocardium (51%) died (hazard ratio for death among patients with viable myocardium, 0.64; 95% confidence interval [CI], 0.48 to 0.86; P=0.003). However, after adjustment for other baseline variables, this association with mortality was not significant (P=0.21). There was no significant interaction between viability status and treatment assignment with respect to mortality (P=0.53).

CONCLUSIONS

The presence of viable myocardium was associated with a greater likelihood of survival in patients with coronary artery disease and left ventricular dysfunction, but this relationship was not significant after adjustment for other baseline variables. The assessment of myocardial viability did not identify patients with a differential survival benefit from CABG, as compared with medical therapy alone. (Funded by the National Heart, Lung, and Blood Institute; STICH ClinicalTrials.gov number, NCT00023595.)

Myocardial Viability and Survival
STICH Trial Substudy

"The findings of this multivariable analysis do not necessarily indicate that myocardial viability does not have pathophysiological importance in patients with CAD and LV dysfunction."

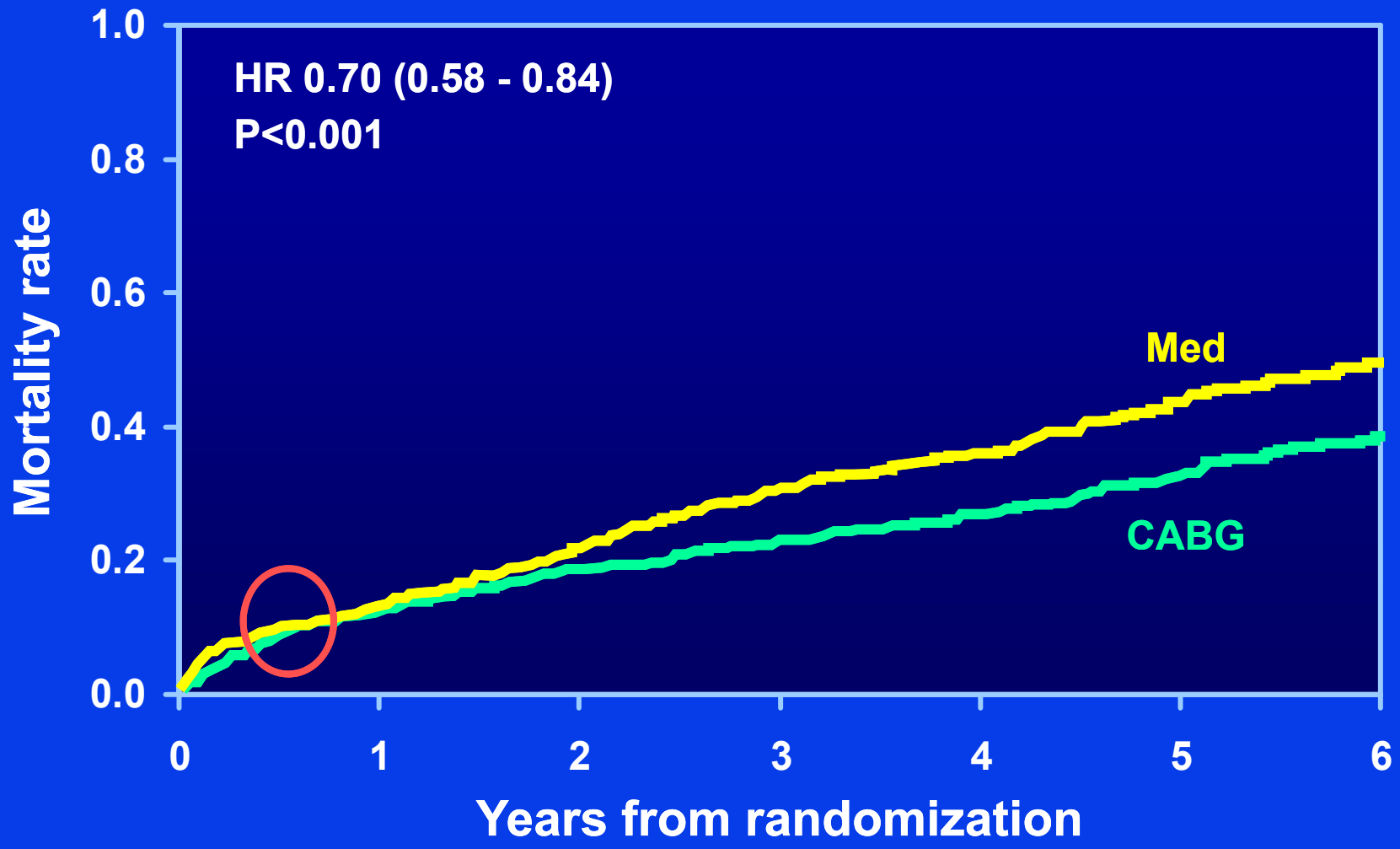
Bonow RO et al: N Engl J Med 364:1617-25, 2011

CABG in Patients with LV Dysfunction
STICH Substudy

- 1,212 patients with EF of ≤35% and CAD amenable to CABG
- Random assignment to medical therapy or medical therapy plus CABG
- Primary outcome death from any cause

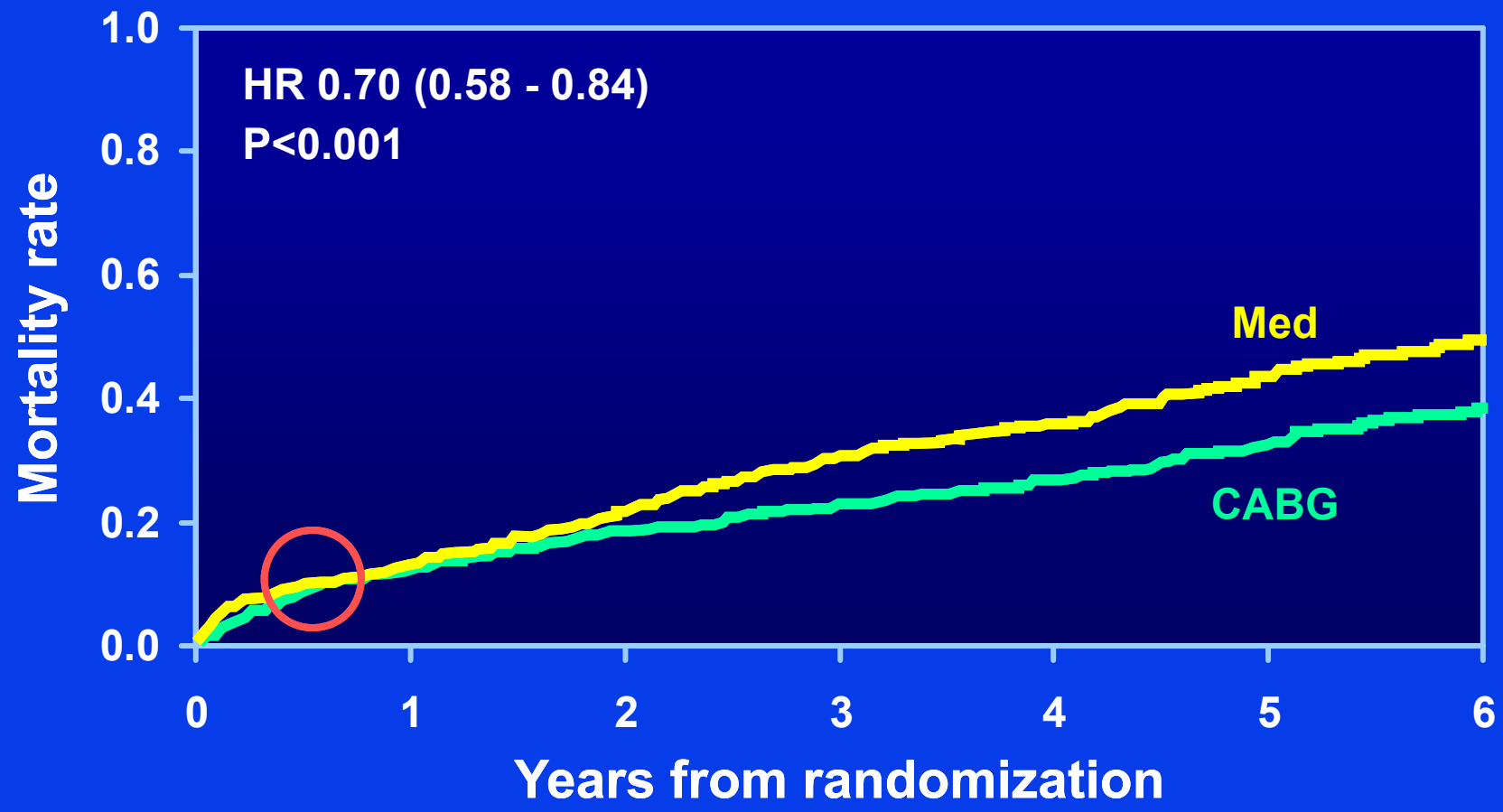
Velazquez et al. N Engl J Med 2011;364;1607-16

All-Cause Mortality – As Treated



NEJM 2011

All-Cause Mortality – As Treated

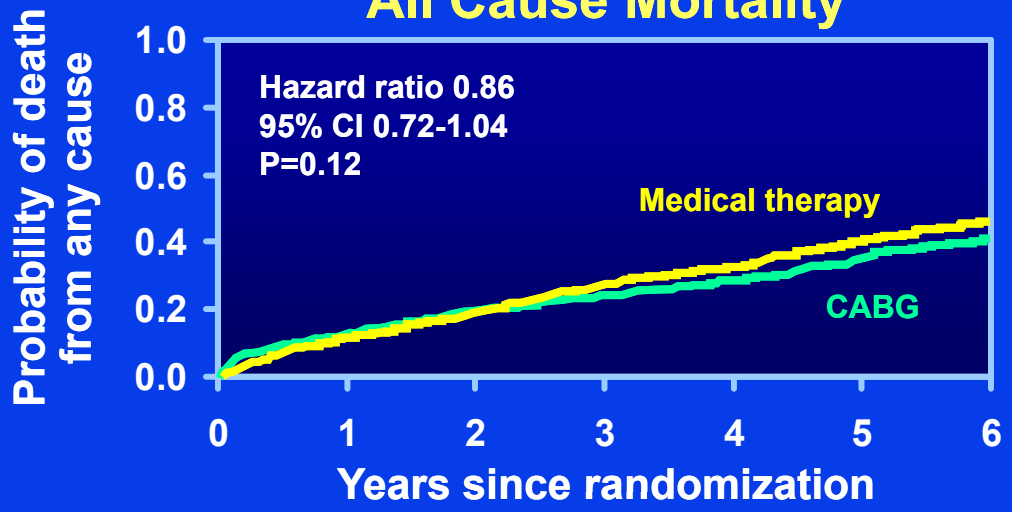


Velasquez: NEJM, 2011

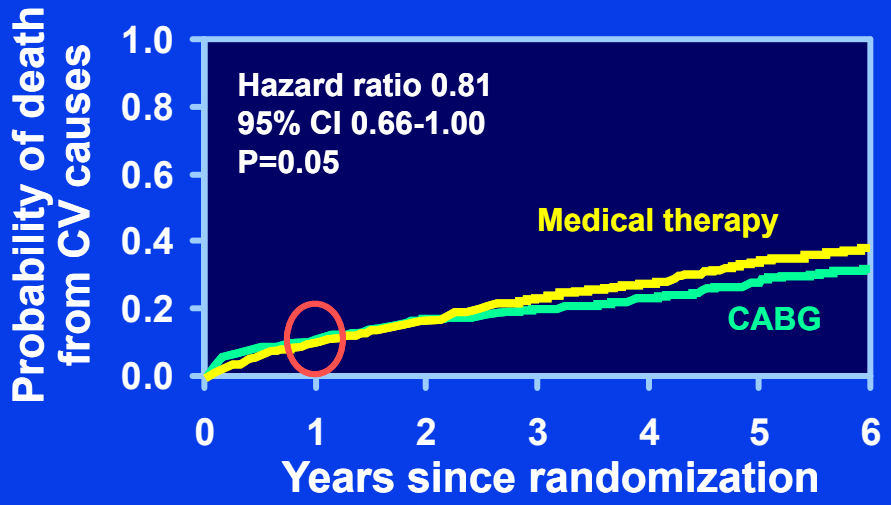
STICH Trial – Outcomes

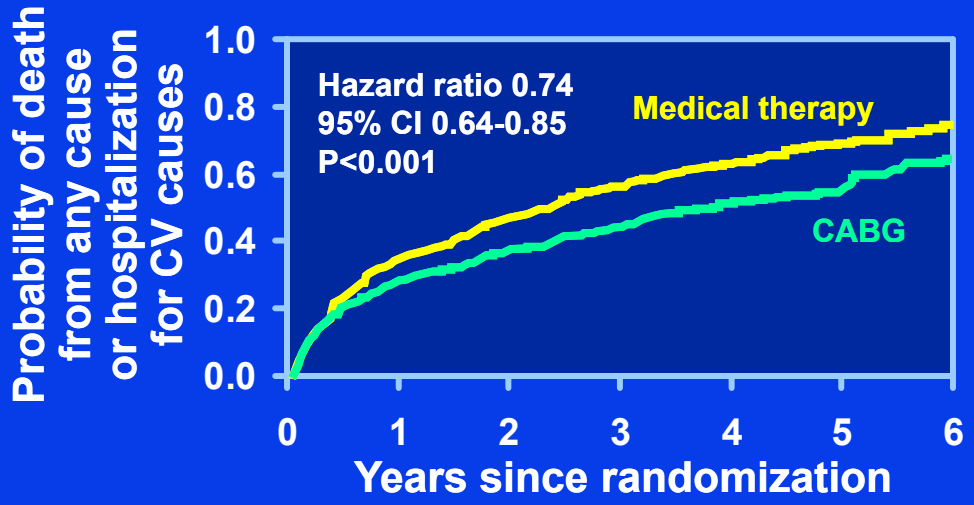
- 1,212 pt
- 2002-2007
- EF <0.35
- CCS angina ≤2 (95%)
- NYHA ≤3 (97%)

All Cause Mortality



CV Mortality and CHF Hospitalization





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Velasquez: NEJM, 2011

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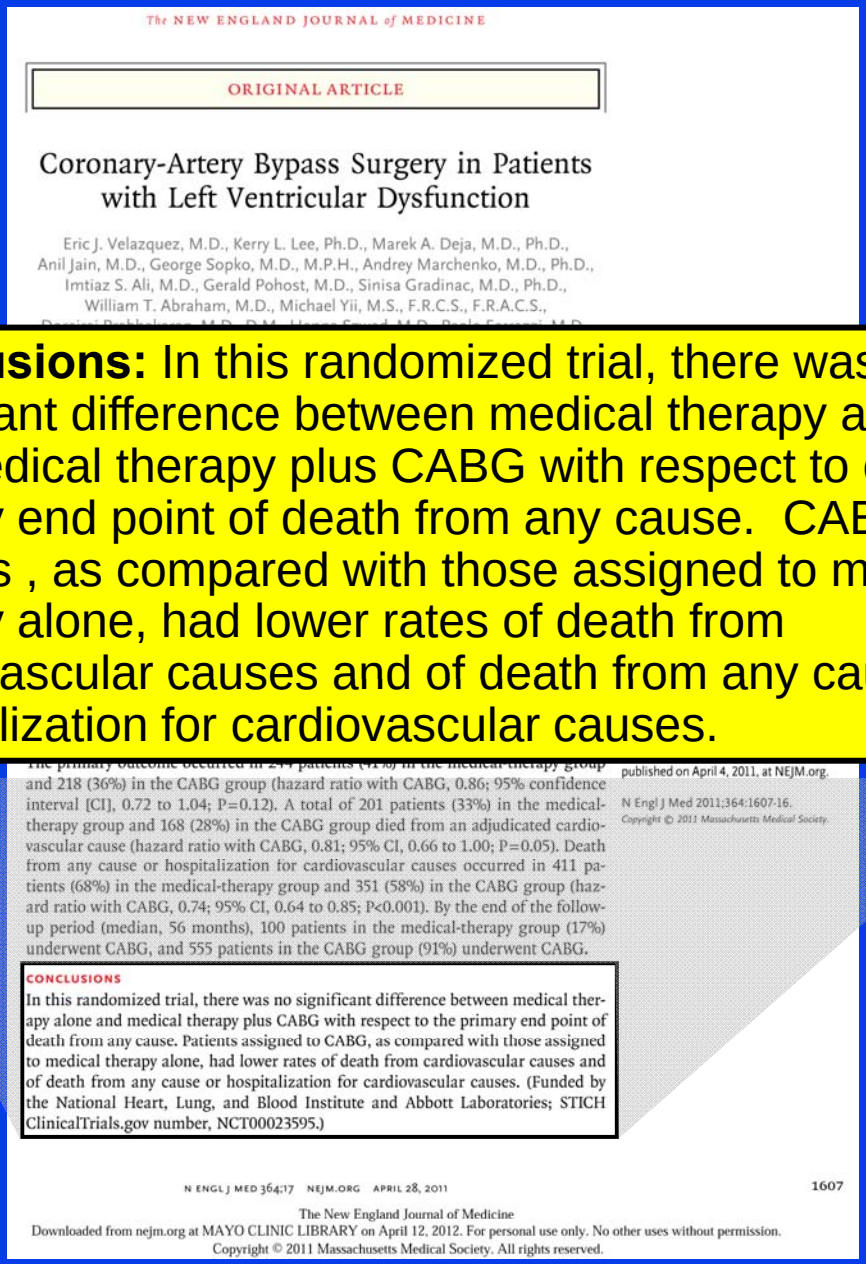

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Coronary-Artery Bypass Surgery in Patients with Left Ventricular Dysfunction

Eric J. Velazquez, M.D., Kerry L. Lee, Ph.D., Marek A. Deja, M.D., Ph.D., Anil Jain, M.D., George Sopko, M.D., M.P.H., Andrey Marchenko, M.D., Ph.D., Imtiaz S. Ali, M.D., Gerald Pohost, M.D., Sinisa Gradinac, M.D., Ph.D., William T. Abraham, M.D., Michael Yii, M.S., F.R.C.S., F.R.A.C.S.,

Conclusions: In this randomized trial, there was no significant difference between medical therapy alone and medical therapy plus CABG with respect to eh primary end point of death from any cause. CABG patients , as compared with those assigned to medical therapy alone, had lower rates of death from cardiovascular causes and of death from any cause or hospitalization for cardiovascular causes.

and 218 (36%) in the CABG group (hazard ratio with CABG, 0.86; 95% confidence interval [CI], 0.72 to 1.04; P=0.12). A total of 201 patients (33%) in the medical-therapy group and 168 (28%) in the CABG group died from an adjudicated cardiovascular cause (hazard ratio with CABG, 0.81; 95% CI, 0.66 to 1.00; P=0.05). Death from any cause or hospitalization for cardiovascular causes occurred in 411 patients (68%) in the medical-therapy group and 351 (58%) in the CABG group (hazard ratio with CABG, 0.74; 95% CI, 0.64 to 0.85; P<0.001). By the end of the follow-up period (median, 56 months), 100 patients in the medical-therapy group (17%) underwent CABG, and 555 patients in the CABG group (91%) underwent CABG.

CONCLUSIONS

In this randomized trial, there was no significant difference between medical therapy alone and medical therapy plus CABG with respect to the primary end point of death from any cause. Patients assigned to CABG, as compared with those assigned to medical therapy alone, had lower rates of death from cardiovascular causes and of death from any cause or hospitalization for cardiovascular causes. (Funded by the National Heart, Lung, and Blood Institute and Abbott Laboratories; STICH ClinicalTrials.gov number, NCT00023595.)

published on April 4, 2011, at NEJM.org.

N Engl J Med 2011;364:1607-16.

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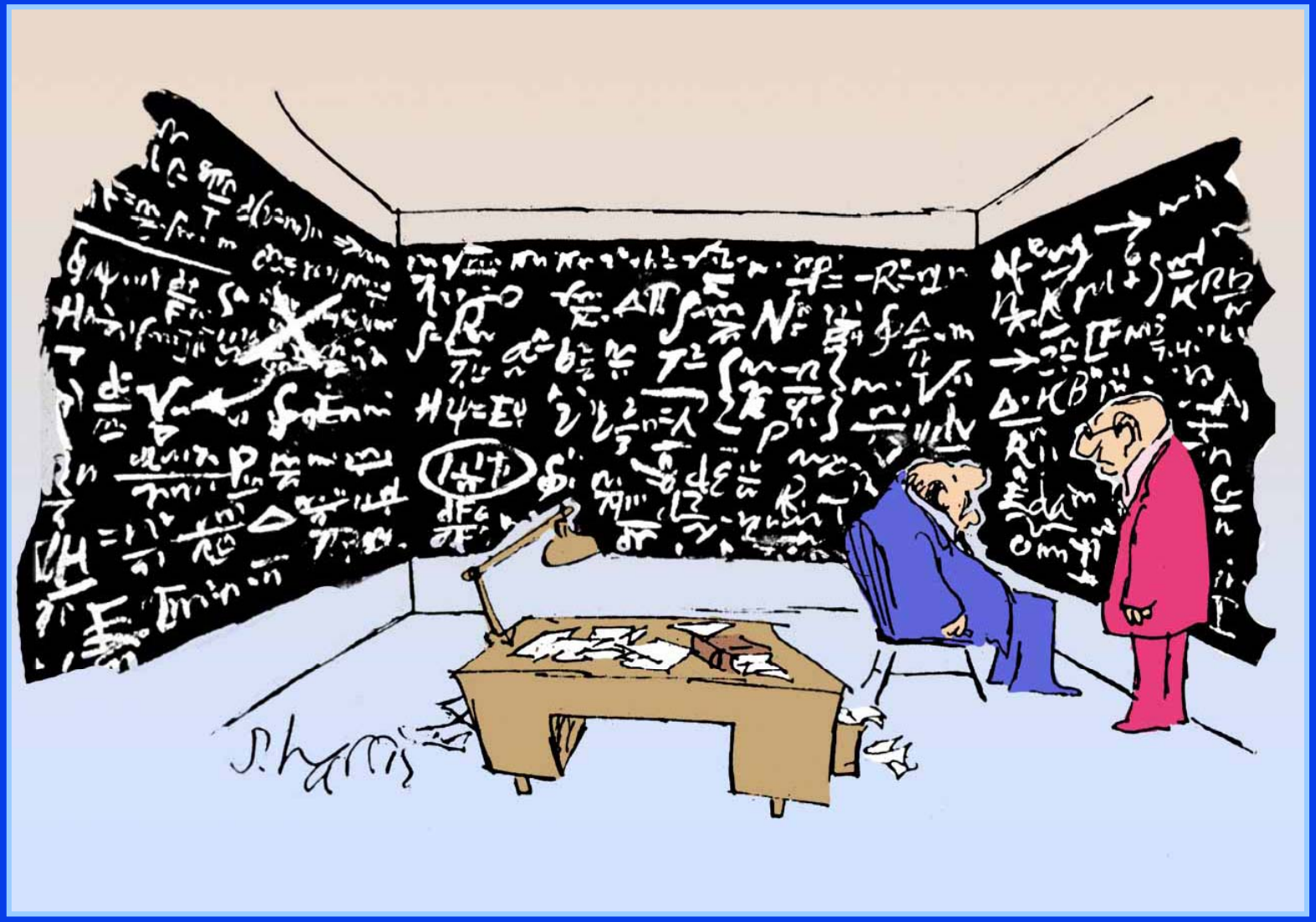
Velazquez et al. N Engl J Med 2011;364;1607-16

Aphorism

All death is sudden – one moment you are alive and the next you are dead



“Whatever happened to *elegant* solutions?”

STICH Trial

- Surgical ventricular reconstruction + CABG is not better than CABG alone
- The presence or absence of myocardial viability does not affect adjusted mortality with either medical therapy or medical therapy + CABG
- In medically treated patients, death from any cause is similar between medically treated patients and those with medical therapy and CABG
- But viability may still be important – perhaps – but not sure

Clinical Scenario

- 70 year-old male with prior MI
  - EF – 32%, anterior severe hypo or akinesis
  - 3 vessel CAD amenable to CABG
  - CHF symptoms – mild to moderate angina
- What to do
  - Work up: ? Assess viability
  - Rx: Optimal medical therapy + ICD
  - CABG + SVR
  - Ischemia guided PCI
  - CABG alone