

## ***Revascularization for Patients with HFrEF: Lessons Learned from STICH Trial***

The Egyptian Society of Cardiology  
44<sup>th</sup> Annual Congress “CardioEgypt 2017”  
Monday, February 20<sup>th</sup> 2016

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## **Disclosures**

- **Research Grants**
  - *NHLBI*
  - *Amgen*
  - *Novartis*
  - *Pfizer*
  - *Alnylam*
- **Consultant**
  - *Novartis*
  - *Amgen*
  - *Merck*



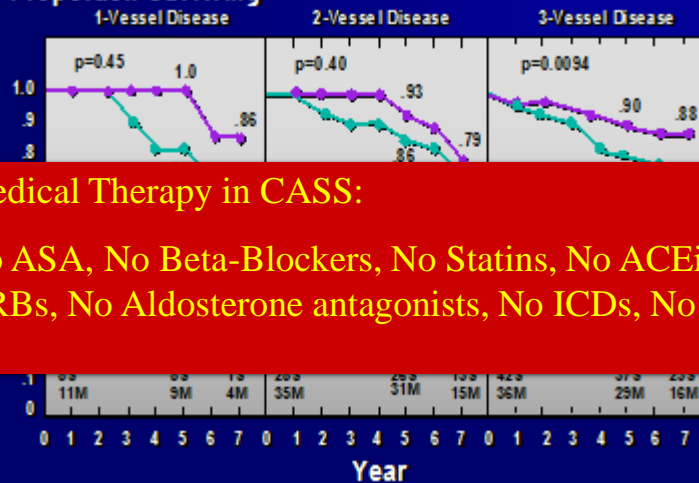


## Outline: Revascularization in HFrEF

- What we knew then
- What we know now
  - *STICH Revascularization Hypotheses*
  - *Patient Selection*
- Personal reflections

## CASS Randomized: Reduced LVEF (EF 35-50%)

### Proportion Surviving



### Medical Therapy in CASS:

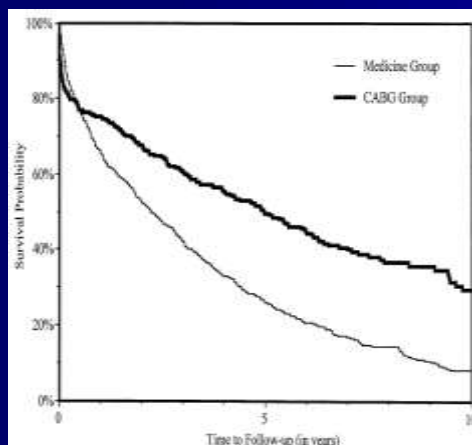
No ASA, No Beta-Blockers, No Statins, No ACEi, No ARBs, No Aldosterone antagonists, No ICDs, No CRTs

## CASS Registry: LVEF $\leq$ 35%

631 patients excluded from CASS RCT

	Medical	Surgical
After 3 years, limiting symptom was		
Angina	26%	0%
Dyspnea	36%	30%
Fatigue	18%	40%*
After 3 years, survival was . . .		
In those presenting with angina	68%	84%*
In those presenting with CHF	55%	55%

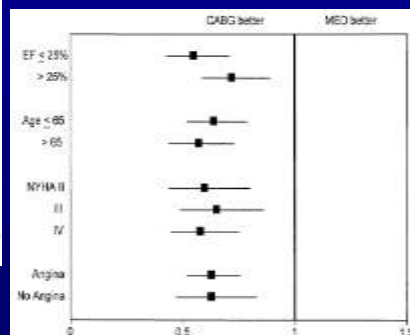
## Duke CV Database



**TABLE 3** Adjusted Cox Proportional-Hazards Survival Estimates\*

	Medical Therapy	CABG
1-yr survival	74%	83%
5-yr survival	37%	61%
10-yr survival	13%	42%

\*p < 0.0001, for all comparisons. Weighted average of 1-, 2-, and 3-yr survival data used to calculate the 1-, 5-, and 10-year survival estimates.





## 2000 – time to revisit revascularization

- HF is increasingly prevalent; CAD is the most common associated etiology
- Substantial improvements in HFrEF medical therapy
- Risks and benefits of cardiac surgery among patients with HFrEF and CAD was not well studied
- Stabilizing or reversing ventricular remodeling is a successful medical target in HFrEF; unclear if a surgical approach provides additional benefit?
- The role of myocardial imaging and other diagnostic strategies in treatment selection for revascularization unclear in the contemporary era

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## STICH Inclusion Criteria

- LVEF  $\leq 0.35$  within 3 months of trial entry
- CAD suitable for CABG
- MED eligible
  - Absence of left main CAD as defined by an intraluminal stenosis of  $\geq 50\%$
  - Absence of CCS III angina or greater (angina markedly limiting ordinary activity)
- SVR eligible
  - Dominant LV anterior akinesia/dyskinesia
  - Experienced surgeon

Velazquez EJ et al. JTCVS 2007



## Major Exclusion Criteria



- Recent acute MI (within 30 days) judged to be an important cause of LVD
- Cardiogenic shock (within 72 hours of randomization)
- Plan for percutaneous intervention of CAD
- Aortic valve disease clearly indicating the need for aortic valve repair or replacement

## Revascularization Hypothesis Conduct



- Age (median) 60 years; 12% women
- Prior MI 77%; Diabetes 39%
- Baseline NYHA II-IV 89%
- LVEF 28% and ESVI 78 ml/m<sup>2</sup> (median)
- Multi-vessel disease 74%; Proximal LAD 68%

*Velazquez EJ et al. New Engl J Med 2016*



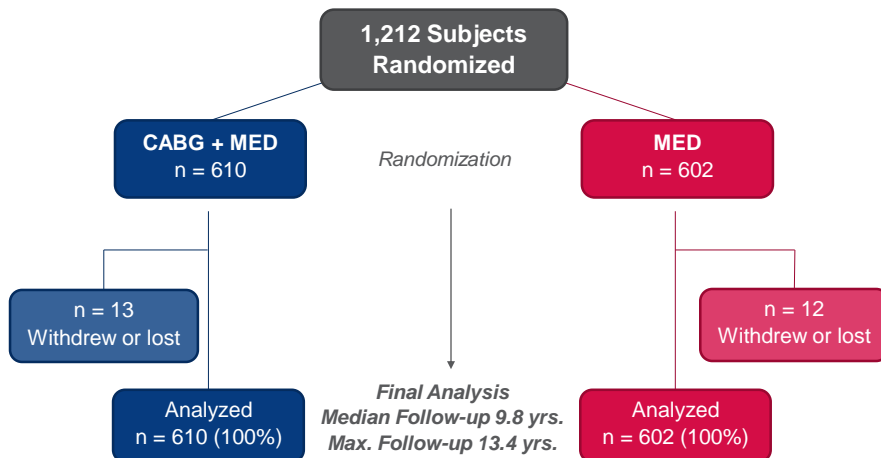
## CABG Conduct



Variable	Randomized to CABG (N=610)
CABG received — no (%)	555 (91)
Time to CABG, days — Median (IQR)	10 (5, 16)
Performed electively — %	95
Arterial conduits $\geq$ 1, %	91
Total conduits $\geq$ 3, %	56

Velazquez EJ et al. *New Engl J Med* 2016

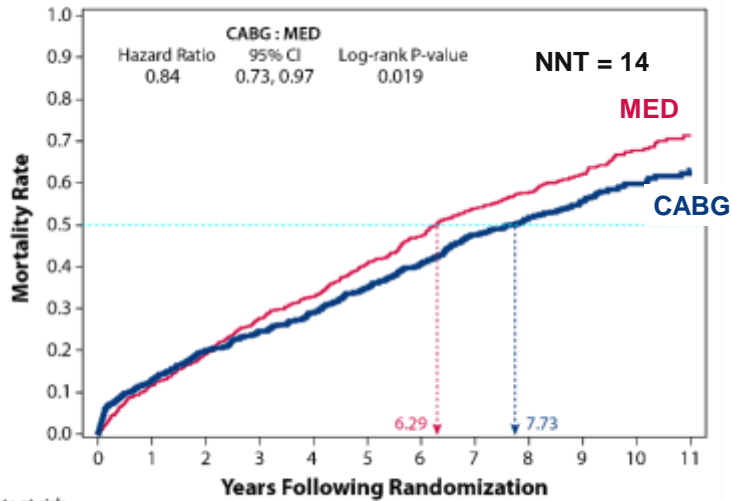
## Study Conduct



Velazquez EJ et al. *New Engl J Med* 2016



## All-cause Mortality

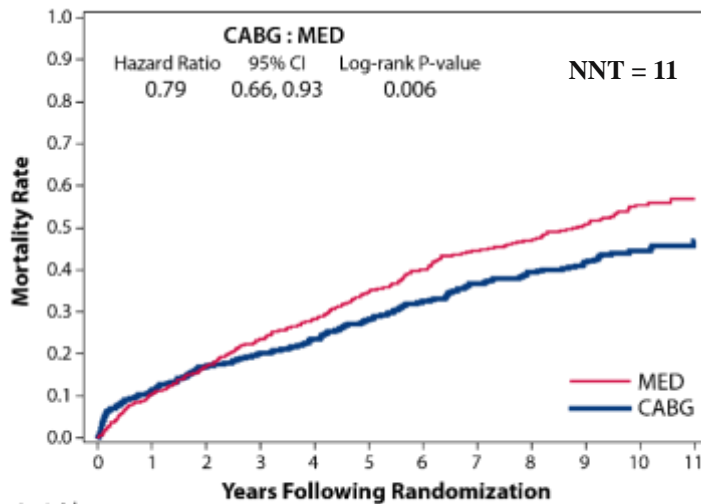


Patients at risk:

MED	602	532	487	435	404	357	315	274	248	164	82	37
CABG	610	532	487	460	432	392	356	312	286	205	103	42

Velazquez EJ et al. N Engl J Med 2016

## Cardiovascular Mortality



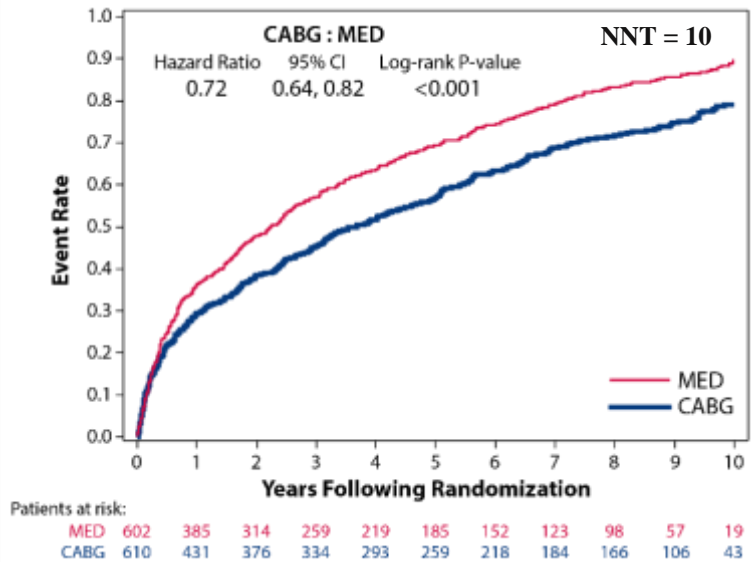
Patients at risk:

MED	602	532	487	435	404	357	315	274	248	164	82	37
CABG	610	532	487	460	432	392	356	312	286	205	103	42

Velazquez EJ et al. N Engl J Med 2016



# All-cause Mortality or Cardiovascular Hospitalization



Velazquez EJ et al. N Engl J Med 2016

# Other Outcomes



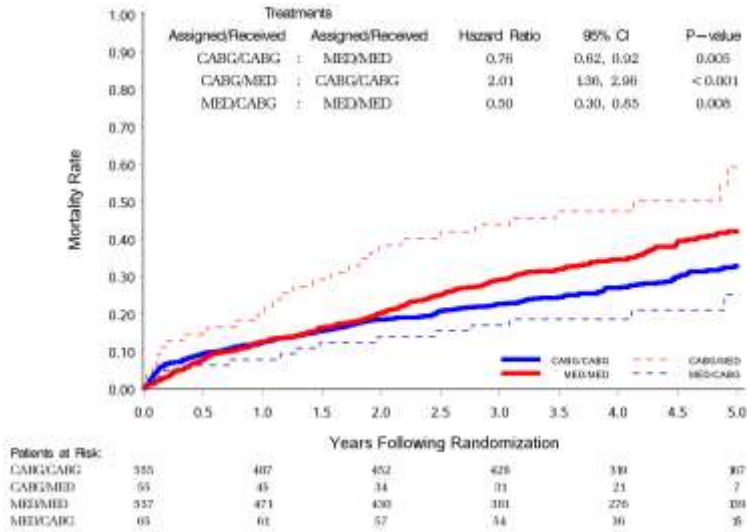
Outcomes	CABG (N=610)	MED (N=602)	Hazard Ratio (95% CI) (CABG vs. MED)	P-value
Death or heart failure hospitalization	404 (66.2%)	450 (74.8%)	0.81 (0.71, 0.93)	0.002
Death or all-cause hospitalization	506 (83.0%)	538 (89.4%)	0.81 (0.71, 0.91)	0.001
Death or revascularization (PCI or CABG)	388 (63.6%)	478 (79.4%)	0.63 (0.55, 0.73)	<0.001
Death or non-fatal myocardial infarction	376 (61.6%)	409 (67.9%)	0.86(0.74, 0.98)	0.032
Death or non-fatal stroke	367 (60.2%)	406 (67.4%)	0.85 (0.74, 0.98)	0.032

Velazquez EJ et al. New Engl J Med 2016



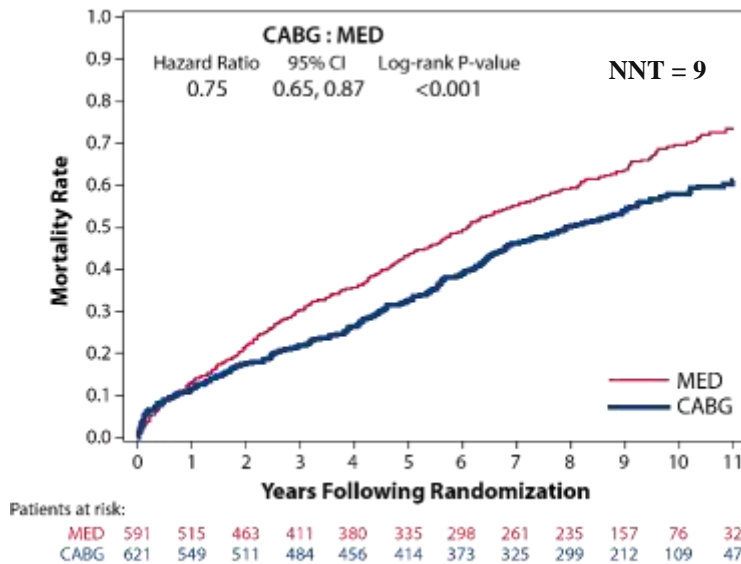


# STICH: Impact of Crossovers



Doenst T et al. Circ Heart Failure 2013

# All-cause Mortality as Treated



Velazquez EJ et al. N Engl J Med 2016

## 2000- Patient Selection for CABG in HFrEF

### No Controversy

- Left main disease
- Severe angina
  - +/- HF symptoms
  - +/- ischemia
  - +/- viability
  - +/- remodeling

### Controversy

- No Left main disease
- No to minimal angina
  - +/- HF symptoms
  - +/- ischemia
  - +/- viability
  - +/- remodeling

Depends on who and when you ask

Could imaging for ischemia or viability help?



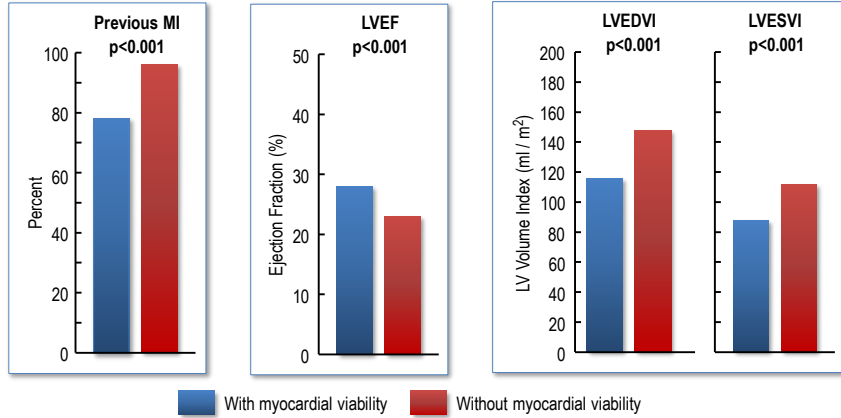
### Hypothesis of viability testing:

In patients with CAD and LV dysfunction, assessment of myocardial viability will identify those patients who will have the greatest survival benefit from adding CABG to aggressive medical therapy

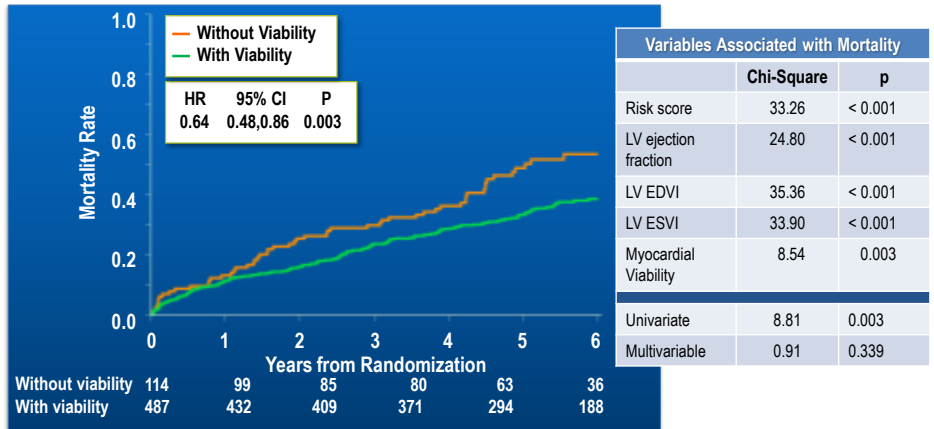




## Baseline Characteristics Patients With and Without Myocardial Viability

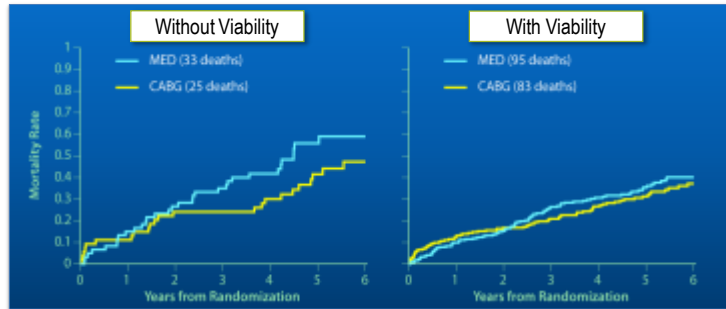


## Myocardial Viability and Mortality

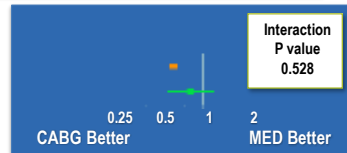




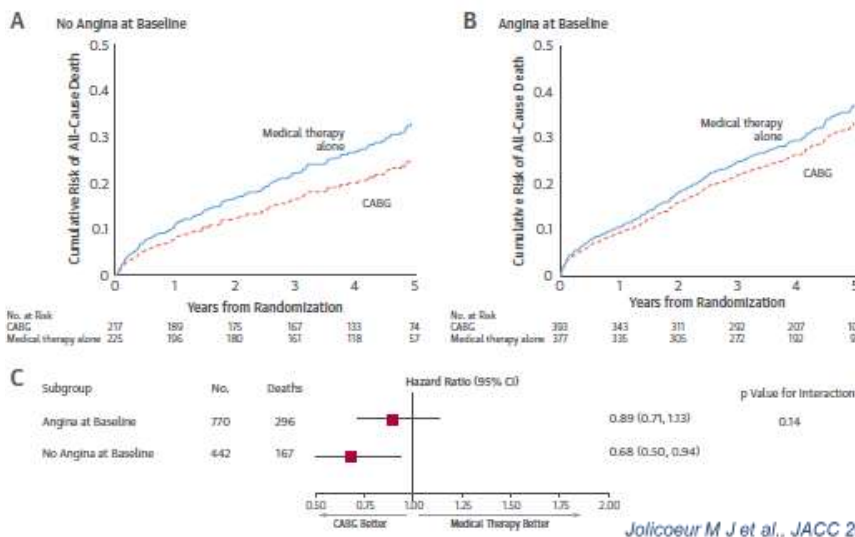
## Treatment, Viability and Mortality



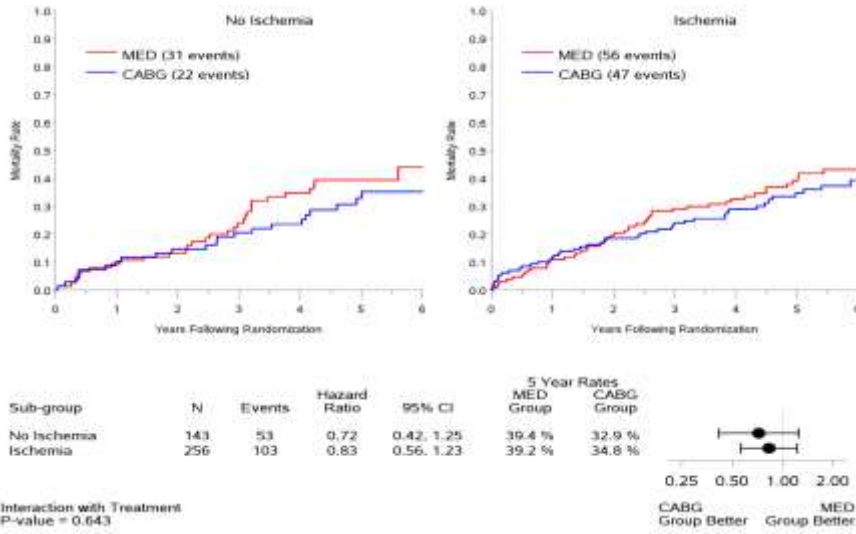
Subgroup	N	Deaths	HR	95% CI
Without Viability	114	58	0.70	0.41, 1.18
With Viability	487	178	0.86	0.64, 1.15



## Mortality According to Angina and Treatment Arm



## Interaction Between Ischemia and Treatment All-Cause Mortality

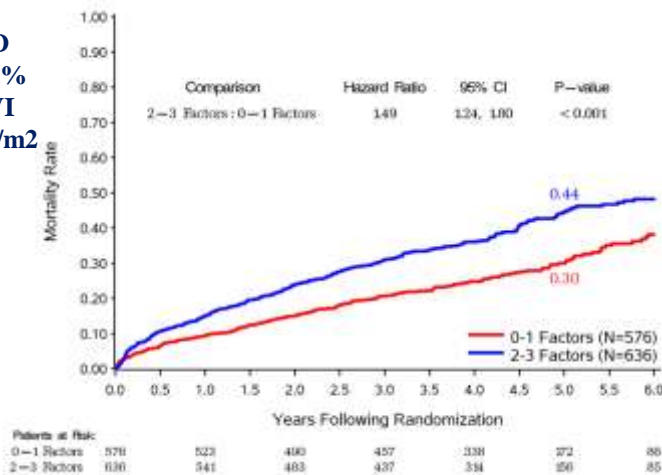


Panza et al. JACC 2013

## Impact of severity of CAD, LVEF and LVESVI regardless of treatment selection



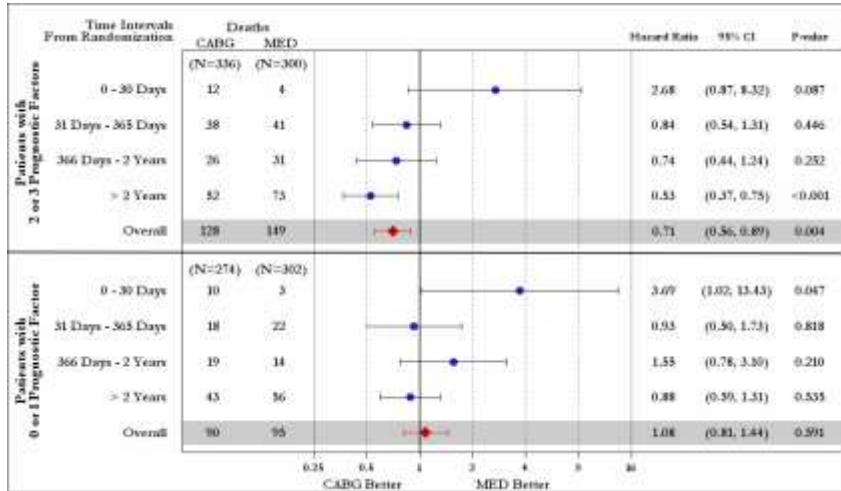
3v CAD  
EF <27%  
LVESVI  
>79 ml/m<sup>2</sup>



Panza J et al., JACC 2014



## Higher risk leads to earlier and increasing benefit



Panza J et al., JACC 2014

## Cause of death by age

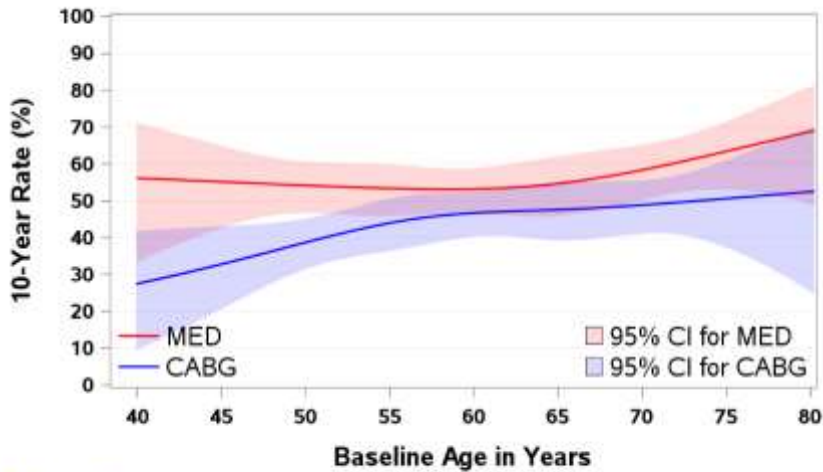


	Age quartiles			
	Q1 (Age ≤ 54 years) (n=330)	Q2 (54 < Age ≤ 60 years) (n=295)	Q3 (60 < Age ≤ 67 years) (n=279)	Q4 (Age > 67 years) (n=308)
<b>All cause, %</b>	53.9	56.3	67.4	73.1
<b>CV, %</b>	42.2	45.1	47.0	45.5
<b>Non-CV, %</b>	5.8	5.8	14.7	21.1
<b>Unknown, %</b>	5.8	5.4	5.7	6.5

Petrie M...Velazquez EJ. Circulation 2016



## Effect of treatment on cardiovascular mortality by age



Interaction  
P-value = 0.3904

*Petrie M ... Velazquez EJ. Circulation 2016*

## Medication Use

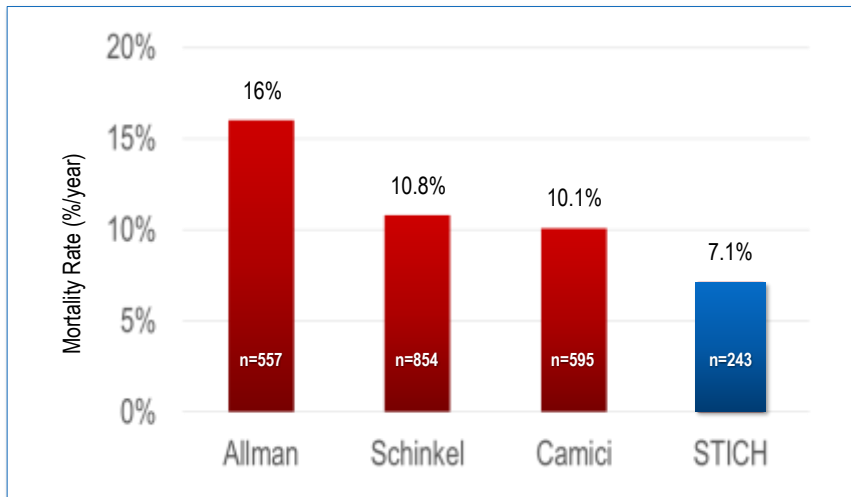


Medication	All Patients Randomized (N=1212)	
	Baseline	Last Follow-Up
Aspirin or clopidogrel, %	86	85
ACE inhibitor or ARB, %	90	84
Beta-blocker, %	85	88
Statin, %	81	85
Loop Diuretics, %	65	72
K+ Sparing Diuretics, %	46	53

*Velazquez EJ et al. New Engl J Med 2016*

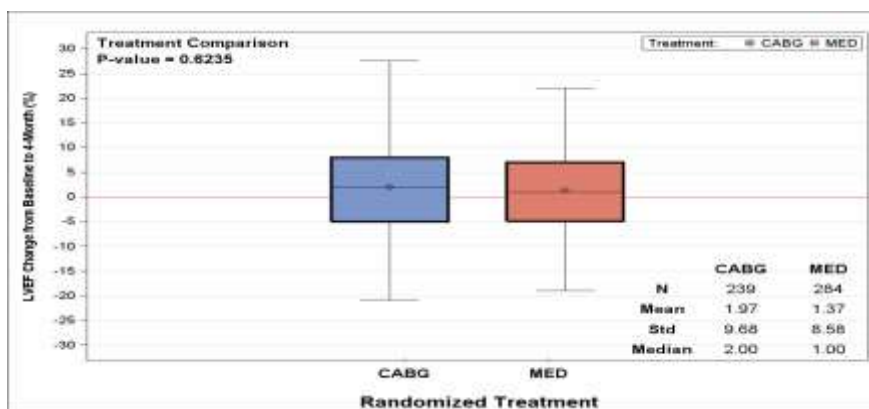


## Evolution of Medical Therapy for HFrEF



Allman et al. JACC 2002; Schinkel et al. Curr Prob Cardiol 2007;  
Camici et al. Circulation 2008; Velazquez EJ NEJM 2011

## Effect of CABG vs MED on LVEF at 4 months



Velazquez EJ et al. AHA Scientific Sessions 2014

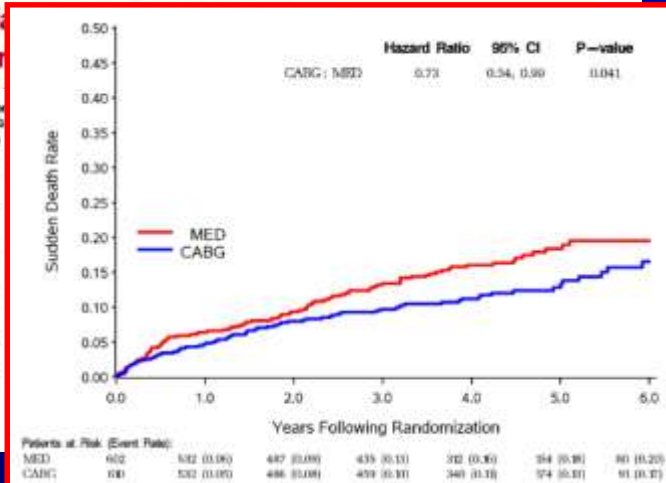




CLINICAL RESEARCH

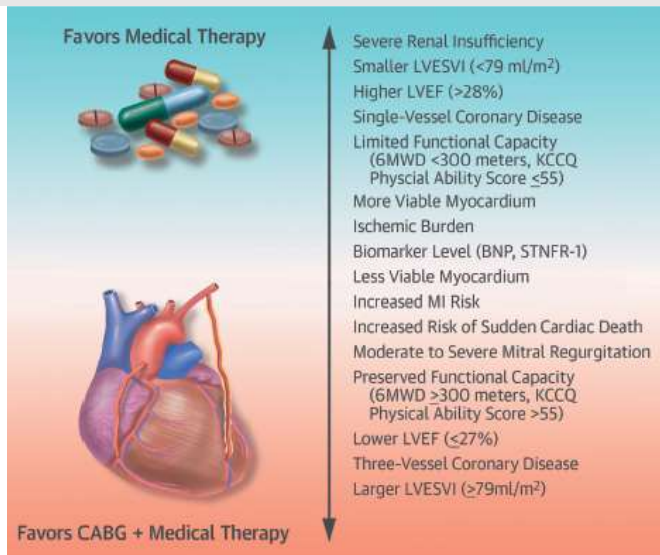
The STICH Trial  
 Ischemic Heart Disease

	Number CABG (n/N)
Sudden Death	74
Pump Failure Death	33
Fatal MI Death	1
Fatal CVA Death	11
CV Procedure Death	28
Other Cardiac Death	14



Patients at Risk (Event Rate)		0.0	1.0	2.0	3.0	4.0	5.0	6.0
MED	602	532 (0.08)	447 (0.08)	435 (0.13)	312 (0.30)	194 (0.38)	80 (0.20)	
CABG	608	532 (0.08)	486 (0.08)	479 (0.11)	340 (0.13)	174 (0.11)	91 (0.11)	

Putting it Together



Velazquez EJ, Bonow RO JACC 2015

## Revascularization in HFrEF: Implications of STICH (so far)

- ▣ Extent of CAD should be assessed and GDMT optimized for all patients presenting with HFrEF
- ▣ CABG improves survival with less morbidity
- ▣ Viability, angina and ischemia status should not define candidacy for CABG in HFrEF
- ▣ Patients at higher risk due to the extent of CAD, LVSD, and remodeling have a greater (earlier) reward with CABG
- ▣ CABG mechanisms of benefit are multifactorial
- ▣ PCI not well studied in HFrEF; available data not favorable

