

Do We Have the COURAGE to Do the Right Things in Our Aggressive PCI Approach to Coronary Disease: New Perspectives on the ISCHEMIA Trial

UNIT OBJECTIVES

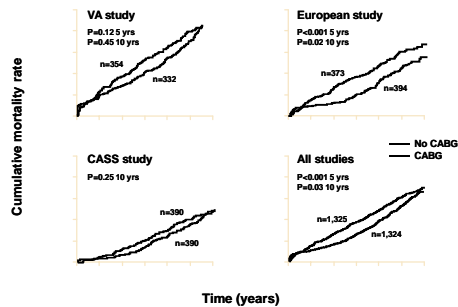
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Faculty Disclosures

- Nothing to Disclose

CABG vs no CABG

CABG Surgery Trialists Collaboration; 10-year outcome



Relevance today is unclear. There was minimal or no use of effective medical therapy (ASA, statins, beta-blockers, ACE inhibitors).

Yusuf et al. Lancet 1994;344:563-570.

Risk Factor Goals In COURAGE

Variable	Goal	
Smoking	Cessation	
Total Dietary Fat / Saturated Fat	<30% calories / <7% calories	
Dietary Cholesterol	<200 mg/day	
LDL cholesterol (primary goal)	60-85 mg/dL	
HDL cholesterol (secondary goal)	>40 mg/dL	
Triglyceride (secondary goal)	<150 mg/dL	
Physical Activity	30-45 min. moderate intensity 5X/week	
Body Weight by Body Mass index	Initial BMI 25-27.5	Weight Loss Goal BMI <25
	>27.5	10% relative weight loss
Blood Pressure	<130/85 mmHg	
Diabetes	HbA1c <7.0%	

Optimal Medical Therapy

Pharmacologic

- Anti-platelet: aspirin; clopidogrel in accordance with established practice standards
- Statin: simvastatin ± ezetimibe or ER niacin
- ACE Inhibitor or ARB: lisinopril or losartan
- Beta-blocker: long-acting metoprolol
- Calcium channel blocker: amlodipine
- Nitrate: isosorbide 5-mononitrate

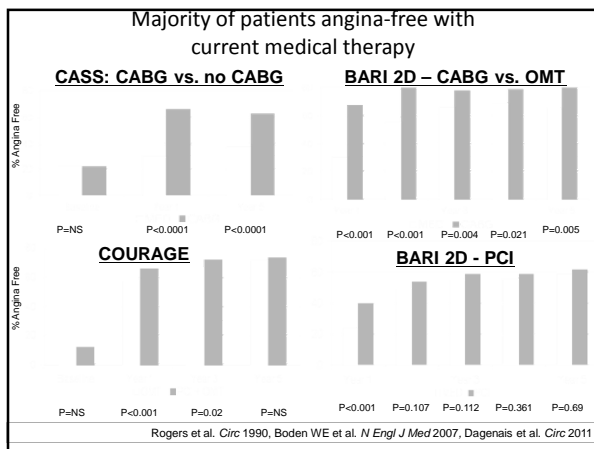
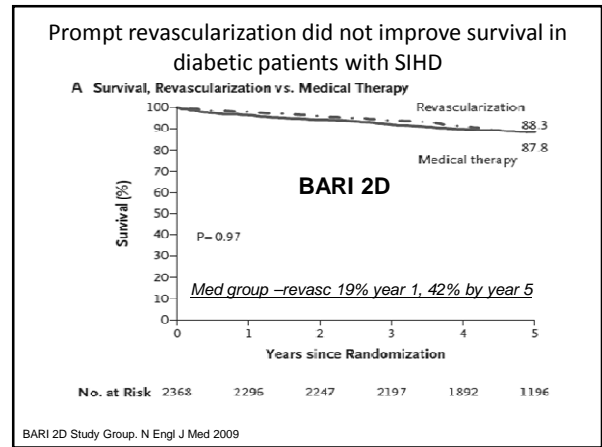
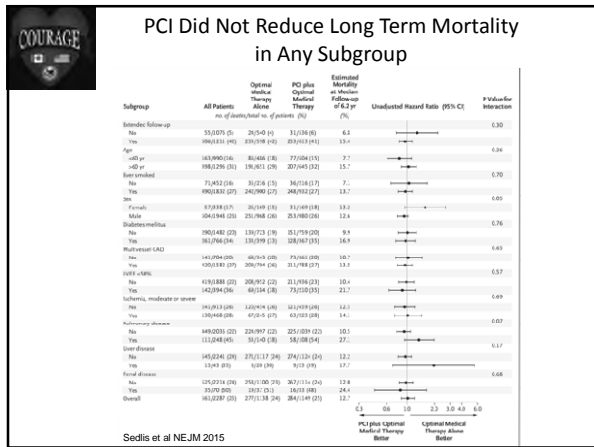
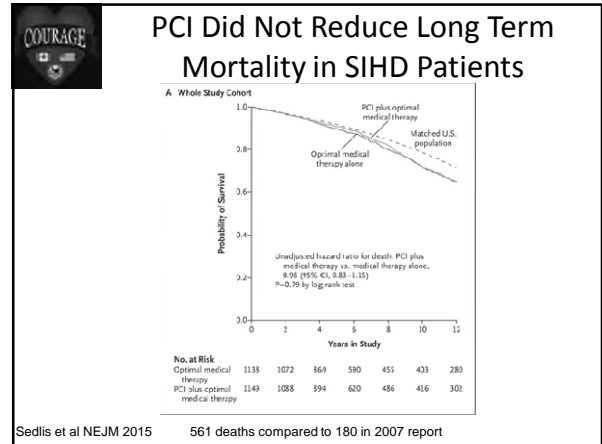
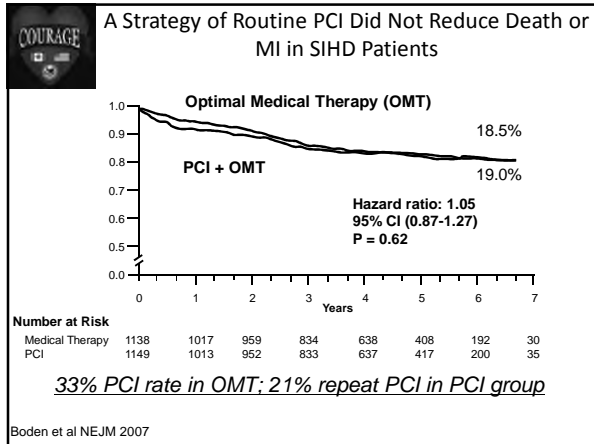
Lifestyle

- Smoking cessation
- Exercise program
- Nutrition counseling
- Weight control

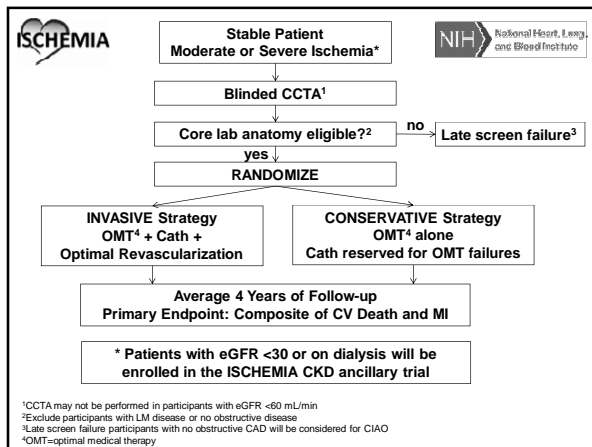
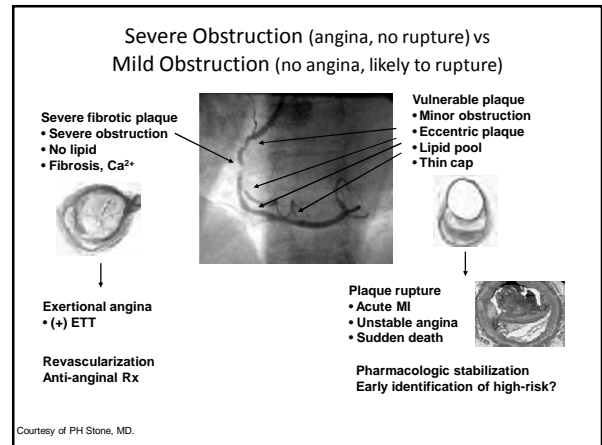
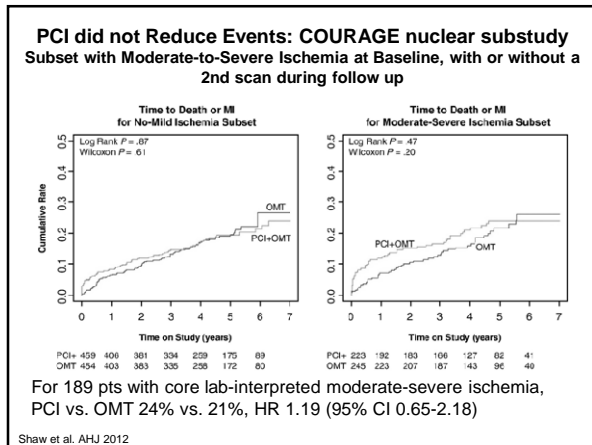
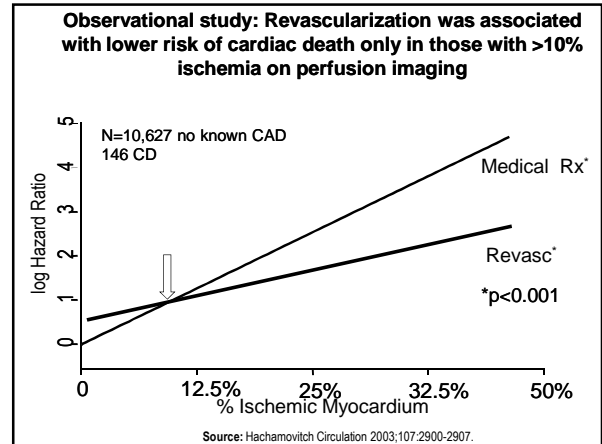
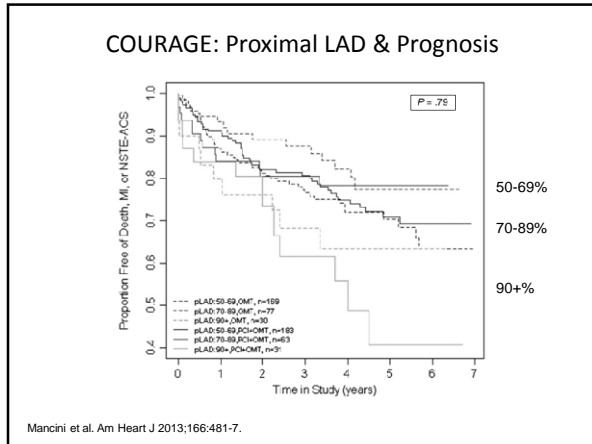
Applied to Both Arms by Protocol and Case-Managed

Long-Term Improvement in Treatment Targets (Group Median ± SE Data)

Treatment Targets	Baseline		60 Months	
	PCI +OMT	OMT	PCI +OMT	OMT
SBP	131 ± 0.77	130 ± 0.66	124 ± 0.81	122 ± 0.92
DBP	74 ± 0.33	74 ± 0.33	70 ± 0.81	70 ± 0.65
Total Cholesterol mg/dL	172 ± 1.37	177 ± 1.41	143 ± 1.74	140 ± 1.64
LDL mg/dL	100 ± 1.17	102 ± 1.22	71 ± 1.33	72 ± 1.21
HDL mg/dL	39 ± 0.39	39 ± 0.37	41 ± 0.67	41 ± 0.75
TG mg/dL	143 ± 2.96	149 ± 3.03	123 ± 4.13	131 ± 4.70
BMI Kg/M ²	28.7 ± 0.18	28.9 ± 0.17	29.2 ± 0.34	29.5 ± 0.31
Moderate Activity (5x/week)	25%	25%	42%	36%



- ### Design Limitations of Prior Trials
- Low risk patients included, limited ischemia
 - Revascularization procedures not contemporary in COURAGE and BARI 2D (little DES, no FFR)
 - Referral bias by randomizing after cath
 - Small sample size (FAME 2)



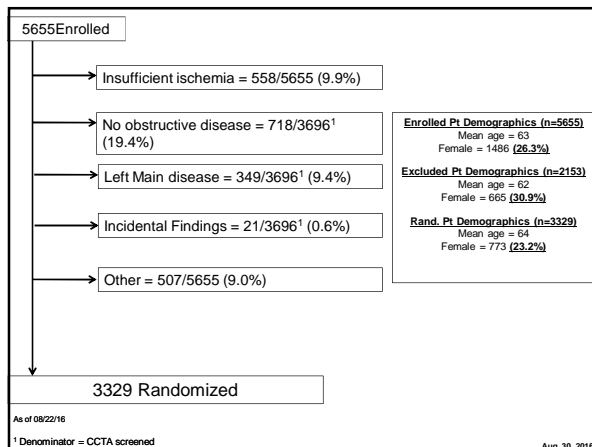
- ### ISCHEMIA Major Exclusion Criteria
- LVEF < 35%
 - Coronary anatomy unsuitable for either PCI or CABG
 - Unacceptable level of angina despite maximal medical therapy or very dissatisfied with medical management of angina
 - Canadian Cardiovascular Society Class III angina of recent onset, OR angina of any class with a rapidly progressive or accelerating pattern
 - Canadian Cardiovascular Society Class IV angina, including unprovoked rest angina
 - Prior CABG, unless cath already done to show anatomy amenable to revascularization
 - ACS within 2 months
 - PCI within 12 months
 - Stroke within 6 months
 - NYHA Class III-IV heart failure at entry or hospitalization for exacerbation of chronic heart failure within the previous 6 months

ISCHEMIA Optimal Medical Therapy

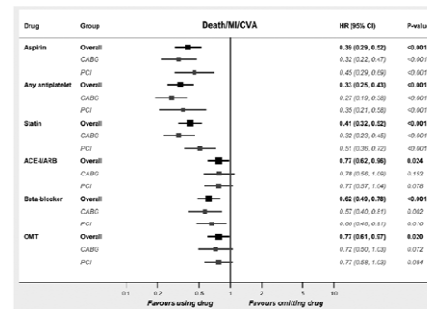
- Applied equally to CON and INV, based on guidelines
- Study team at each site is responsible for implementation of OMT, working with participant's personal MD
- Local circumstances will dictate how study team collaborates with personal physician
- Cath done in conservative strategy for acute ischemic events or refractory symptoms

ISCHEMIA Invasive Strategy

- Cath and revascularize all INV patients
- Revascularization method based on highest likelihood to safely and effectively relieve significant ischemia in viable myocardial territories
- FFR required per algorithm



Optimal Medical Therapy Improves Clinical Outcomes in Patients Undergoing Revascularization With Percutaneous Coronary Intervention or Coronary Artery Bypass Grafting
Insights From the Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery (SYNTAX) Trial at the 5-Year Follow-Up



Iqbal et al. Circulation. 2015;131:1269-

Optimal Medical Therapy Improves Clinical Outcomes in Patients Undergoing Revascularization With Percutaneous Coronary Intervention or Coronary Artery Bypass Grafting

Table 3. Survival Benefit of OMT Versus Non-OMT Across Population Subgroups

Variable	Groups	HR (95% CI)	P Value	P for Interaction
Age	<65 y	0.76 (0.46-1.28)	0.371	0.814
	≥65 y	0.61 (0.44-0.85)	0.003	
Sex	Male	0.67 (0.49-0.92)	0.016	0.555
	Female	0.57 (0.33-1.03)	0.050	
SYNTAX score	0-22	0.68 (0.43-1.09)	0.089	0.425
	23-32	0.76 (0.44-1.31)	0.323	
	>32	0.52 (0.30-0.88)	0.016	
EuroSCORE	0-2	0.77 (0.39-1.53)	0.388	0.506
	3-5	0.68 (0.44-1.05)	0.080	
	≥6	0.58 (0.37-0.93)	0.015	
Revascularization strategy	CABG	0.65 (0.49-0.86)	0.002	0.443
	PCI	0.70 (0.48-1.09)	0.049	
Current smoker	Yes	0.54 (0.30-1.02)	0.059	0.395
	No	0.68 (0.50-0.93)	0.016	
Diabetes mellitus	Yes	0.61 (0.47-0.79)	0.002	0.958
	No	0.62 (0.43-0.90)	0.009	
Dyslipidemia	Yes	0.60 (0.47-0.78)	0.002	0.980
	No	0.68 (0.38-1.16)	0.132	
LVEF	≥50%	0.68 (0.24-2.03)	0.771	0.354
	<50%	0.63 (0.47-0.85)	0.002	
COPD	Yes	0.36 (0.16-0.95)	0.039	0.173
	No	0.71 (0.53-0.95)	0.027	
PVD	Yes	0.78 (0.44-1.39)	0.405	0.452
	No	0.41 (0.14-0.85)	0.003	
Completeness of revascularization	Complete	0.72 (0.50-1.07)	0.110	0.244
	Incomplete	0.64 (0.36-0.92)	0.003	

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Conclusions:

- Adopting a therapeutic lifestyle foundation to preventing events, smoking cessation, exercise, healthy diet
- Pharmacologic primary and secondary prevention will decrease cardiac event rates
- In particular, therapy to lower LDL, anti-platelet therapy, ACE/ARB, beta blockers
- Revascularization is well established in ACS, severe CAD
- Much remains to be learned about individualizing therapy
- The heart team approach and shared decision making is critical