

The Impact of Different Treatment Strategies on Cardiac Death and MI Rates in Patients with Type 2 Diabetes and Stable Coronary Disease: A Report from BARI 2D

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The BARI 2D Trial is coordinated by the Epidemiology Data Center at the University of Pittsburgh, Graduate School of Public Health

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BARI 2D Trial

Randomized controlled trial that tested 2 treatment strategies in a 2 x 2 factorial design among patients in whom angina symptoms were controlled (82%) or asymptomatic (18%)

Comparison of prompt coronary revascularization and intensive medical therapy, with intensive medical therapy alone with later revascularization only for clinical indications

Choice of the intended PCI or CABG procedure was selected by the treating physicians before randomization

Comparison of an insulin sensitizing strategy to an insulin provision strategy for glycemic management



BARI 2D Inclusion/ Exclusion Criteria

Inclusion Criteria

- Type 2 Diabetes
- CAD suitable for elective REV
- Documented ischemia

Exclusion Criteria

- REV in the prior 12 mo
- LMCD
- Class III or IV HF
- Hepatic dysfunction
- Creatinine > 2 mg/ dL
- HbA1c > 13.0%

REV= coronary revascularization
LMCD= left main coronary disease



BARI 2D Trial: Demographic Characteristics of the 2368 Randomized Patients

•Age	62 yrs	•Hx PVD	24%
•Female	30%	•TIA/CVA	10%
•Duration DM	10 yrs	•Prior MI	32%
•Albuminuria	33%	•Prior REV	26%
•Neuropathy	50%	•MVD	67%
•HbA1c	7.7%	•LVEF <50%	17%

PVD= peripheral vascular disease
TIA/CVA=transient ischemic attack/stroke
MVD= multivessel disease
LVEF= left ventricular ejection fraction



Atherosclerotic Risk Factors

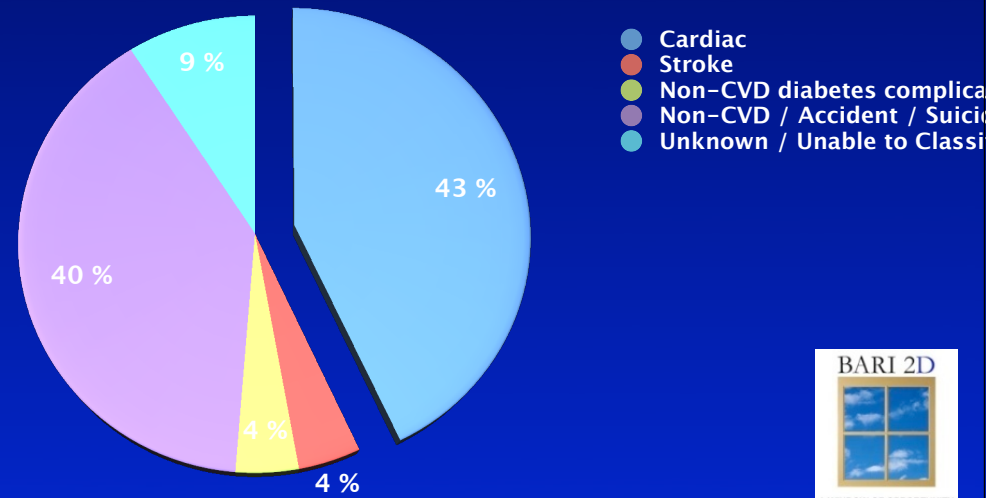
All patients received intensive medical therapy regardless of initial treatment strategy

% Pts Meeting Target Values	Baseline	Three Yrs
Glycated HbA1c <7.0%	40	48
LDL cholesterol <100 mg/dl	60	83
BP \leq 130/80 mm Hg	48	71
% that smoked in prior year	22	11
All 3 at target values	13	28

BARI 2D Trial Group: *NEJM* 2009;360:2503-15



BARI 2D (n=2,368): Causes of Death During 5.3 Year Follow-Up (n=316)



AIM: Death and MI Endpoints

Primary endpoint: All-cause death*

Principal Secondary endpoint: Death/MI/
stroke*

Secondary endpoints

- Cardiac death
- Myocardial infarction
- All-cause death/MI
 - Cardiac death/MI

*BARI 2D Trial Group: *NEJM* 2009; 360:2503-15



Methods

Data were analyzed by intent to treat; Kaplan-Meier analyses were used to estimate 5-yr cumulative event rates for (i) all cause death (ii) cardiac death (iii) MI, and (iv) cardiac death/MI

Kaplan Meier estimates of event rate distributions were compared using the log-rank test

A p-value of 0.05 was used to determine statistical significance. Nominal p-values are presented. Adjustment for multiple testing was performed using Bonferroni correction



BARI 2D: Five Year Kaplan Meier End-Point Estimates

	Rev	IMT	IP	IS
All-Cause Death	11.7	12.2	12.1	11.8
Cardiac Death	5.9	5.7	6.0	5.7
Sudden Cardiac Death	4.0	4.2	4.2	4.0
Myocardial Infarction	11.5	14.3	13.6	12.2
Cardiac Death or Myocardial Infarction	15.9	16.7	17.1	15.6

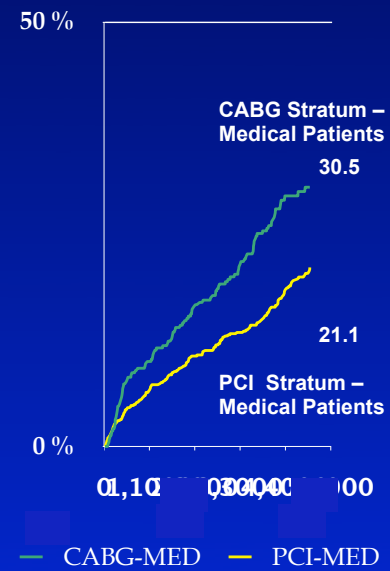
Treatment comparisons (Revascularization (Rev) vs. Intensive Medical Therapy (IMT)) and (Insulin Provision (IP) vs. Insulin Sensitization (IS)) are not statistically significant for any of the end-points listed



**Baseline Characteristics
By Randomization Stratum**

	PCI Intended (n=1605)	CABG Intended (n=763)
Age	62.0	63.2
Male	68%	76%
Proximal LAD	10%	19%
3 Vessel Dx	20.3%	52.4%
Total Occlusions	32%	61%
MJI	37.2	59.7
LVEF < 50	18%	18%
Prior revascularization	29%	13%

**Death / MI/ Stroke
Among Medical Assigned Patients**



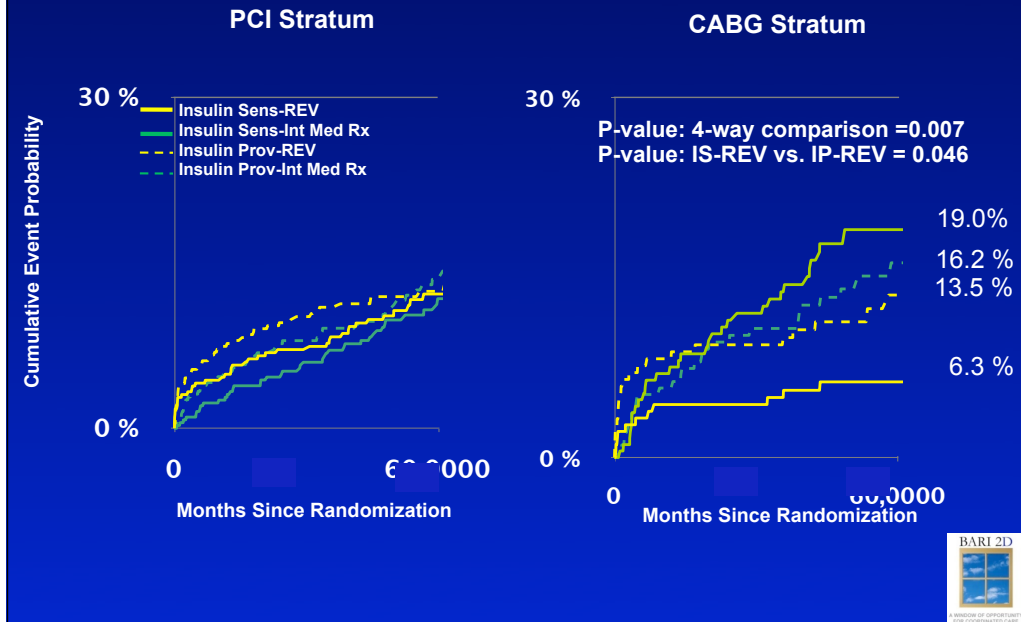
Cardiac Death and First MI rates

	PCI	IMT	P	CABG	IMT	P
Total MI* (n=279)	12.3	12.6	0.42	10.0	17.6	0.003
Non-procedure MI (n=234)	9.4	11.4	0.69	7.6	17.1	<0.001
Cardiac Death (n=136)	5.0	4.2	0.16	8.0	9.0	0.79
Cardiac Death/MI	16.0	14.2	0.05	15.8	21.9	0.03
Cardiac Death/non-procedure MI	13.3	13.2	0.29	13.7	21.4	0.006

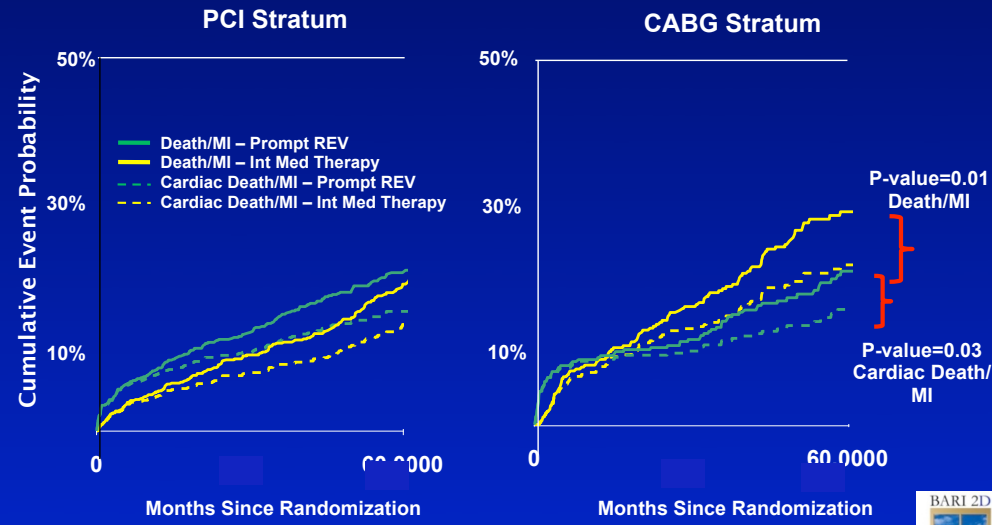
*Of the 279 first MI events, 36 (13%) were fatal;
Myocardial Infarction=MI



Time to First MI by Initial Treatment Strategy



Death/MI and Cardiac Death/MI by Revascularization Strata



Conclusions

- Intensive medical therapy was associated with less cardiovascular mortality/morbidity in patients with T2 diabetes than originally estimated from earlier trials
- The cardiovascular event reduction was observed regardless of type of glycemic strategy used, or whether patients received initial prompt revascularization or intensive medical therapy alone



Conclusions

- In many patients with T2D and stable ischemic CAD, similar to those enrolled in the PCI stratum, an initial strategy of IMT should be considered, and does not require immediate PCI to prevent cardiac death or MI, when angina symptoms are controlled
- In patients with more extensive coronary disease, similar to those enrolled in the CABG stratum, a strategy of prompt CABG, IMT and IS therapy should be considered the preferred strategy to reduce the incidence of spontaneous MI

