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Disclosure

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History of Evidence Based
Coronary Revascularization –
Can we identify our mistakes and
not repeat them?

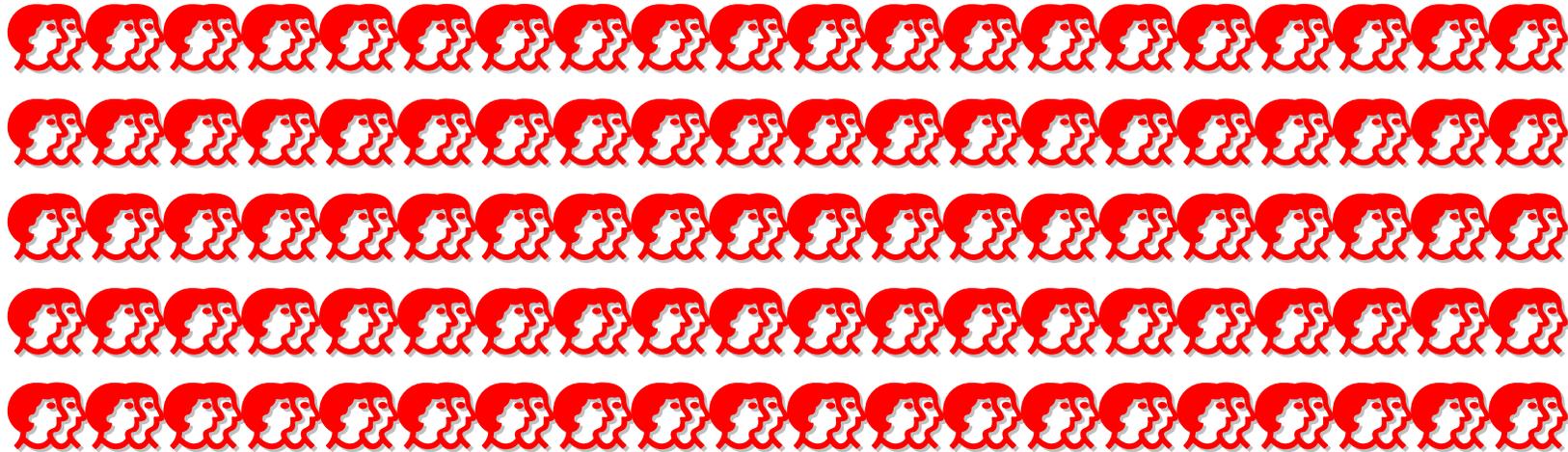
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There Are Problems with RCT's of PCI

- Underpowered.
- Low risk patients .
- Carefully selected.
- Surrogate and “Composite” endpoints.
- Misinterpretation of trial results.

BARI - SELECTIVE ENROLLMENT

PCI Exclusion



BARI was really a study of the ~25% of MVD patients most suitable for PCI, and even then less than half of these were enrolled.

Eligible, not enrolled 



Enrolled 

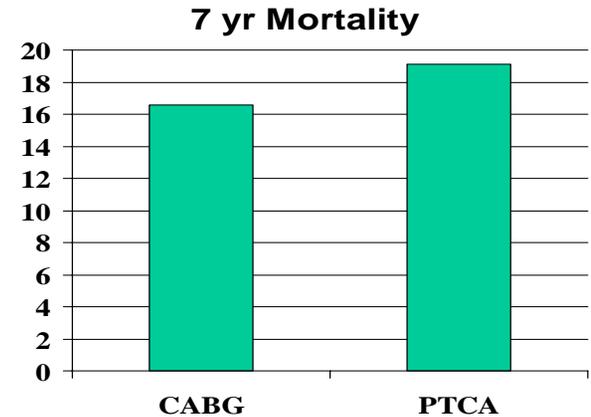
BARI – Problems with Power

- BARI powered to detect a 2.5% mortality difference with 2400 MVD pts intended for enrollment. BUT only 1829 actually enrolled.
- Overall, 5 year mortality difference was 2.9% favoring CABG (*higher than the targeted difference!*), but this was not statistically significant because enrollment was lower than originally intended.
- Erroneous conclusion of clinicians and media–
“No mortality difference between PCI and CABG in MVD”.

STATISTICAL FELONY!!!

BARI Continued Problems

- Despite highly selected patients, at seven years, PCI mortality was 15% relatively higher than CABG. (p=.043) *JACC April 2000*

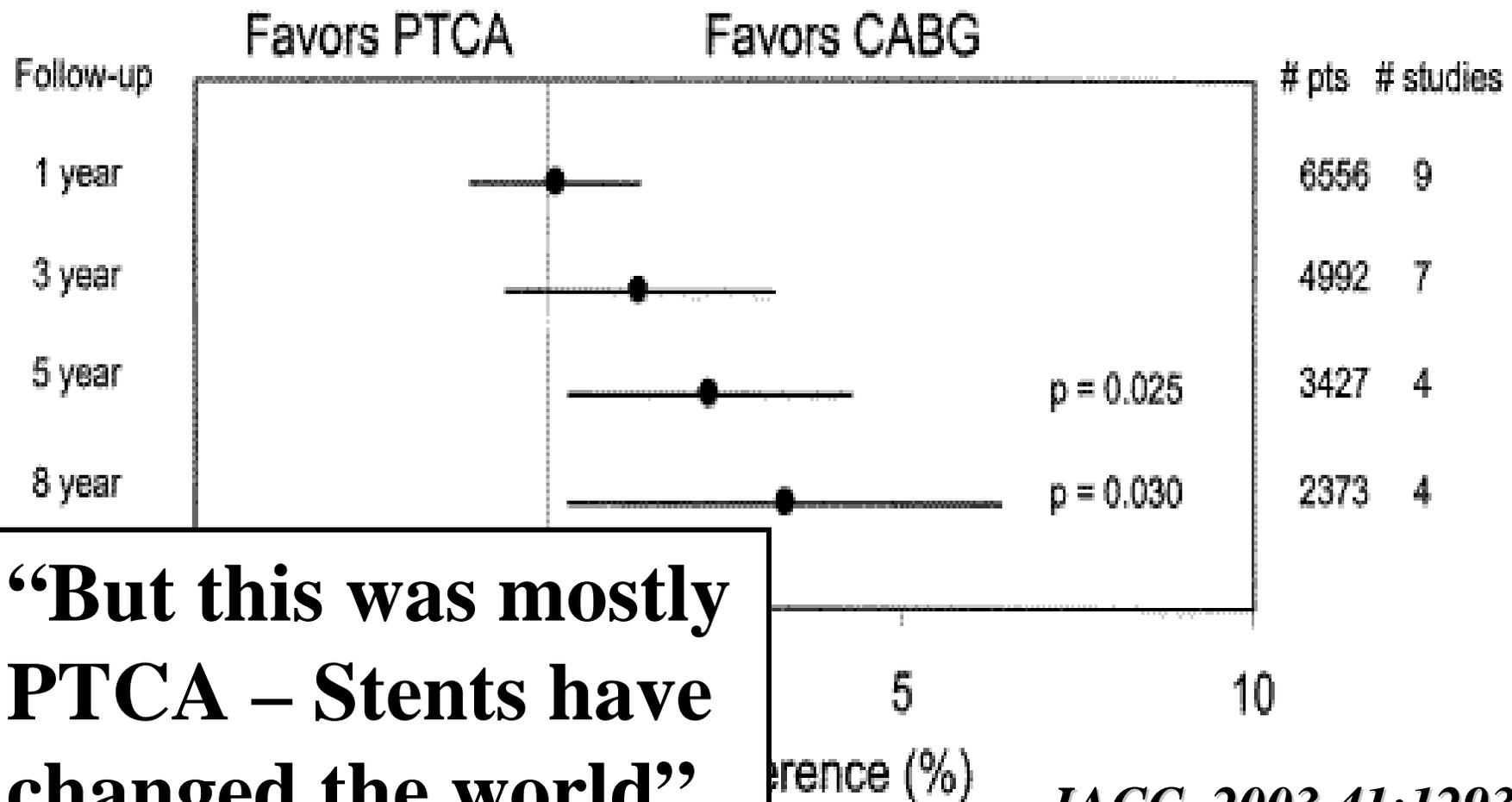


- Response of PCI advocates –

“Let’s take out the diabetic patients. Once we take out the diabetic patients, BARI shows that PCI survival is equal to CABG survival in MVD.”

COMPOUND FELONY!

Meta-analysis of 9 RCT's of PTCA vs. CABG
PCI Significantly INFERIOR at 5 yrs and 8 yrs



**“But this was mostly
PTCA – Stents have
changed the world”**

JACC 2003 41:1293

ARTS Trial

- Mostly European, Funded by Industry
- Very PCI -friendly trial – enrollment only if equivalent revascularization could be achieved with either method - only ~ 5 % of screened patients enrolled.
- Problem with timeliness of Rx:
- Rx with stents 11 days after randomization
- Rx with CABG 27 days after randomization – 3 deaths, 4 MI's, 1 stroke in this interval →
- 0.5% mortality and >1% MACCE before CABG performed, but not in stent group.

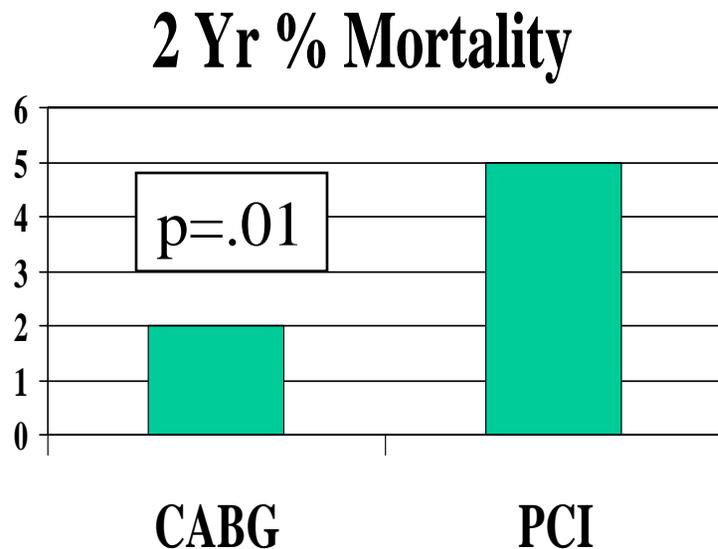
ARTS Trial – 5 year follow-up

- Mortality after Rx was 7.1% at 5 years with CABG, 8% with Stenting, Relative Risk favoring CABG was 1.13.
- 5 year Death, MI, or Stroke - Relative Risk favoring CABG was 1.33.
- Conclusion of paper in abstract – “At five years there was no difference in mortality between stenting and surgery for multivessel disease. Furthermore the incidence of stroke or myocardial infarction was not significantly different between the groups.”

Conclusion NOT justified. It is worse than wrong. It is powerfully misleading.

Stent or Surgery Trial

- 988 patients from 53 centers in Europe and Canada, also funded by industry.
- Revascularization indicated and “appropriate by either strategy” – broader selection of MVD patients than the “equivalent revascularization” of ARTS.



5 yr follow-up WCC 2006:
3% difference at 2 yr
increased to 4.3%
difference at 5 yr. (p=.016)

Lancet 2002;360:965

RESPONSE to early Stent or Surgery results:

“But those were Bare Metal Stents, Drug Eluting Stents Have Changed the World”

Not SO →

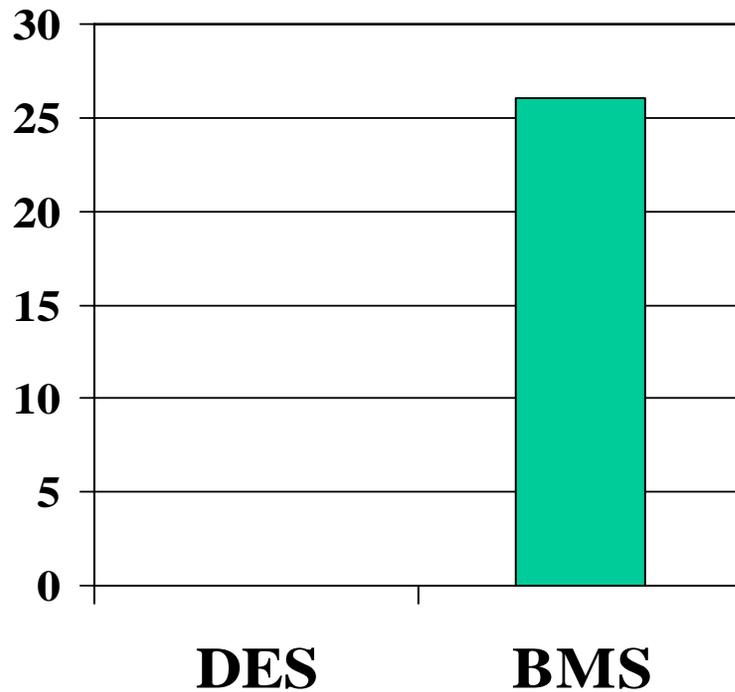
NO mortality benefit of Drug Eluting Stents compared to Bare Metal Stents.

A Final Problem with RCT's

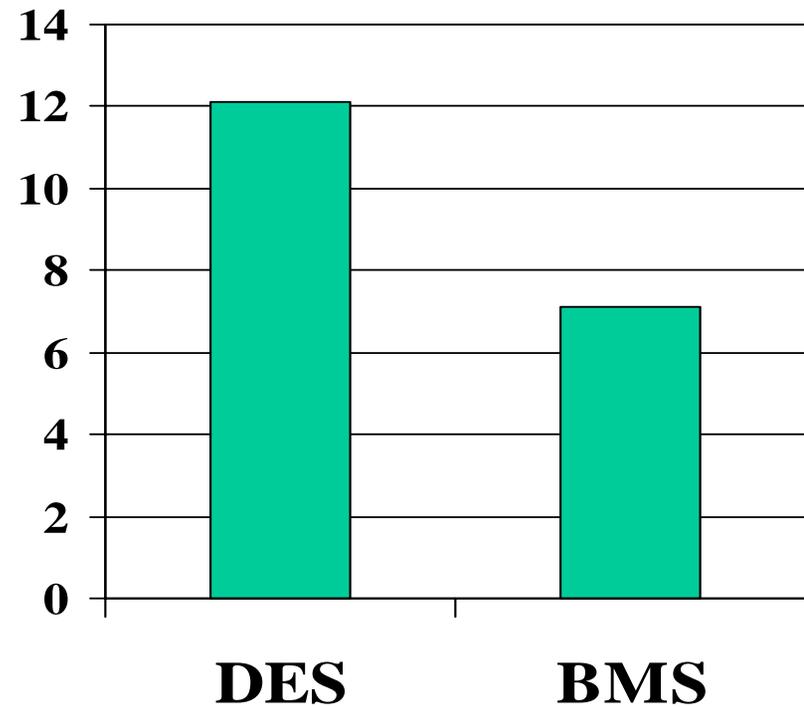
Surrogate Endpoints Can be Hazardous

The RAVEL Trial

% Restenosis – 6mo



% Death – 5 yr

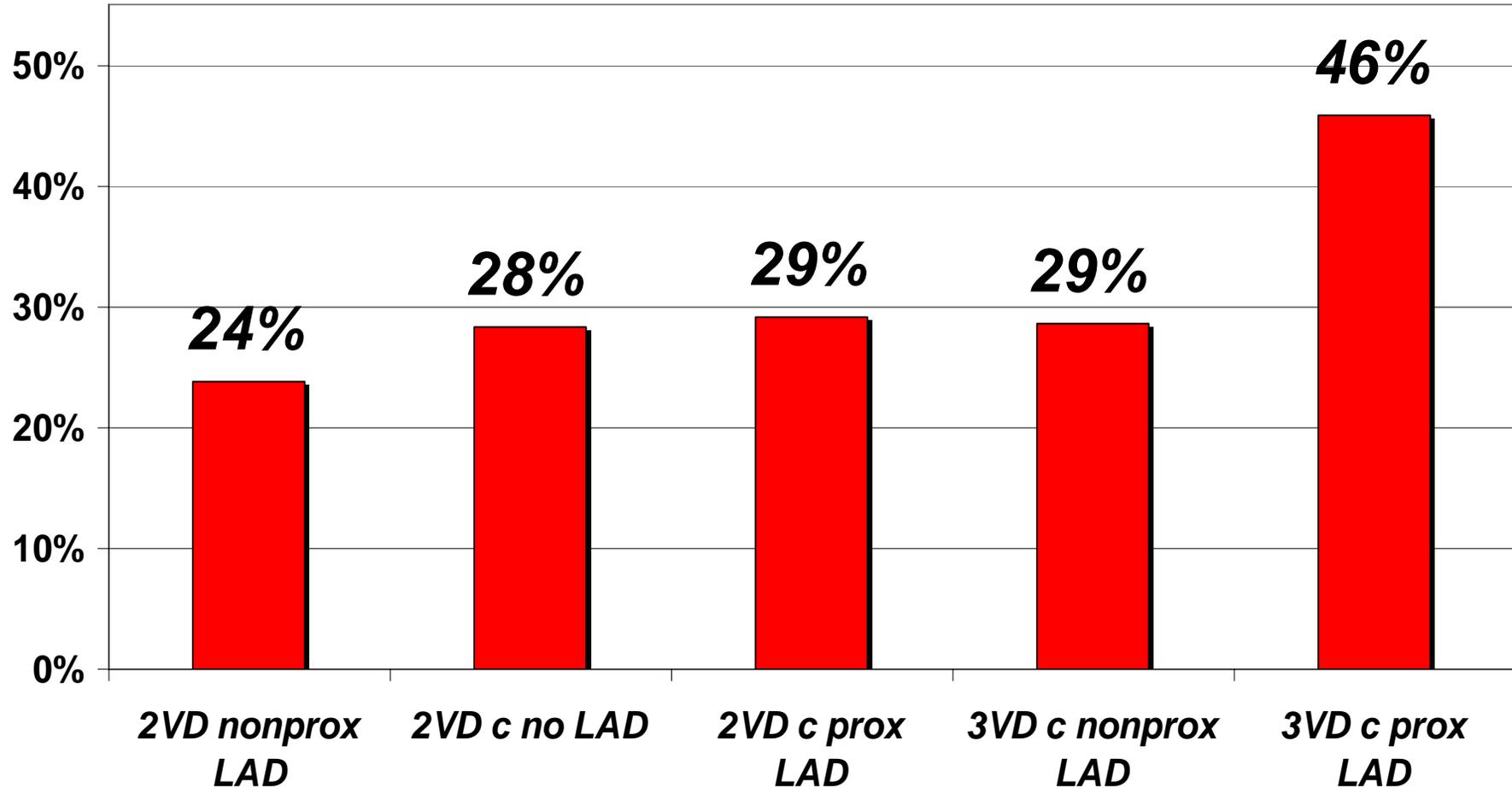


Presented at WCC 2006

Are Stents Excessively Utilized?

- Dramatic increase in Stent use promoted by “solving the restenosis problem”
- We must look to robust comprehensive databases, allowing risk adjusted review of patient subsets.

***Relative Excess Mortality at Three Years with
Initial Stenting vs. Initial CABG***



***NY CABG and Stent Registries
~ 60,000 patients 1997 –2000***

NEJM 2005;352:2174

Mayo Clinic Cardiologists, Gersh and Frye regarding NY State Data:

- “...we are reminded of the limitations of underpowered trials, particularly in lower-risk patients.”
- “...impressive advantage of surgery in the overall cohort and most subgroups.”

Editorial NEJM , May 2005

Where is the Answer – Do we need more RCT's?

- Basic Problem – Clinicians ARE advocates for their patients and they honor their moral obligation to “...do no harm” and to “...not injure one person regardless of the benefits that might come to others.”*
- The patient is enrolled only if the clinician honestly believes the patient will not be harmed by randomization.

*Belmont Report, 1976

Where is the Answer? – continued

- The result is selected enrollment of low risk patients.
- But these selected patients do *not* represent the broader population for whom data is needed.
- There will be limited benefit from more RCT's.

We need a robust comprehensive database for treatment of CAD that is sufficiently inclusive that appropriate therapy can be determined in various patient subsets. (*Emphatically NOT just a registry of stent thrombosis – the last thing we need is a registry that focuses on yet another surrogate endpoint*)

Final Point –

The Issue of Informed Consent

- 1981, Andreas Gruntzig: “I can fix your blockage with this little catheter or I can have Dr. Guyton crack your chest.”
- In 1981, there was no counterpoint to Dr. Gruntzig’s statement – there were no data.
- In 2006, PCI Operator, “The Drug Eluting Stents have solved the problem that we used to have with restenosis. Let us fix your blockages with the stents. There is no difference in mortality and we can always

WRONG –

Mortality is NOT the same!

Informed Consent for MVD

- Now all of us would choose Stenting as the first procedure IF mortality were the same, as patients are being led to believe.
- But many patients would rethink their options if they could hear the surgeon say, for 3VD with LAD:
“Coronary Bypass is the procedure that gives you the best chance of being free from angina, and, if you have stenting as your first procedure you have a 46% higher chance of dying in three years compared to Coronary Bypass as your first procedure.”

CONCLUSION

- To guide *future* decisions we need Robust Comprehensive Databases of therapy in MVD patients, not more RCT's of selected low risk patients.
- But Patient Protection and Safety issues need attention *NOW*.
- *DES is inferior to CABG in MVD. Do we not need a DES labeling change to reflect this fact?*
- At the very least, better patient information is of paramount importance!