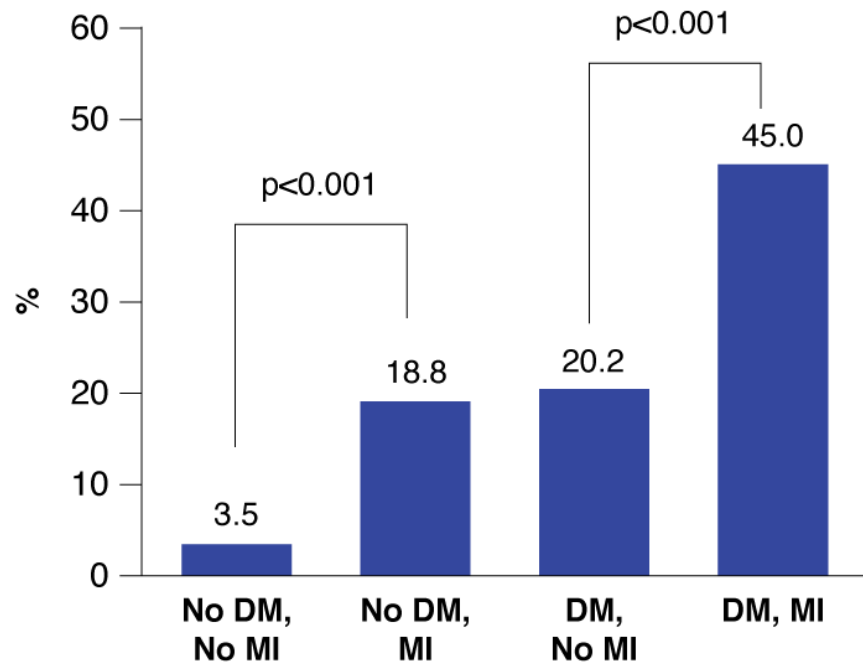


# Diabetes and Cardiovascular Disease

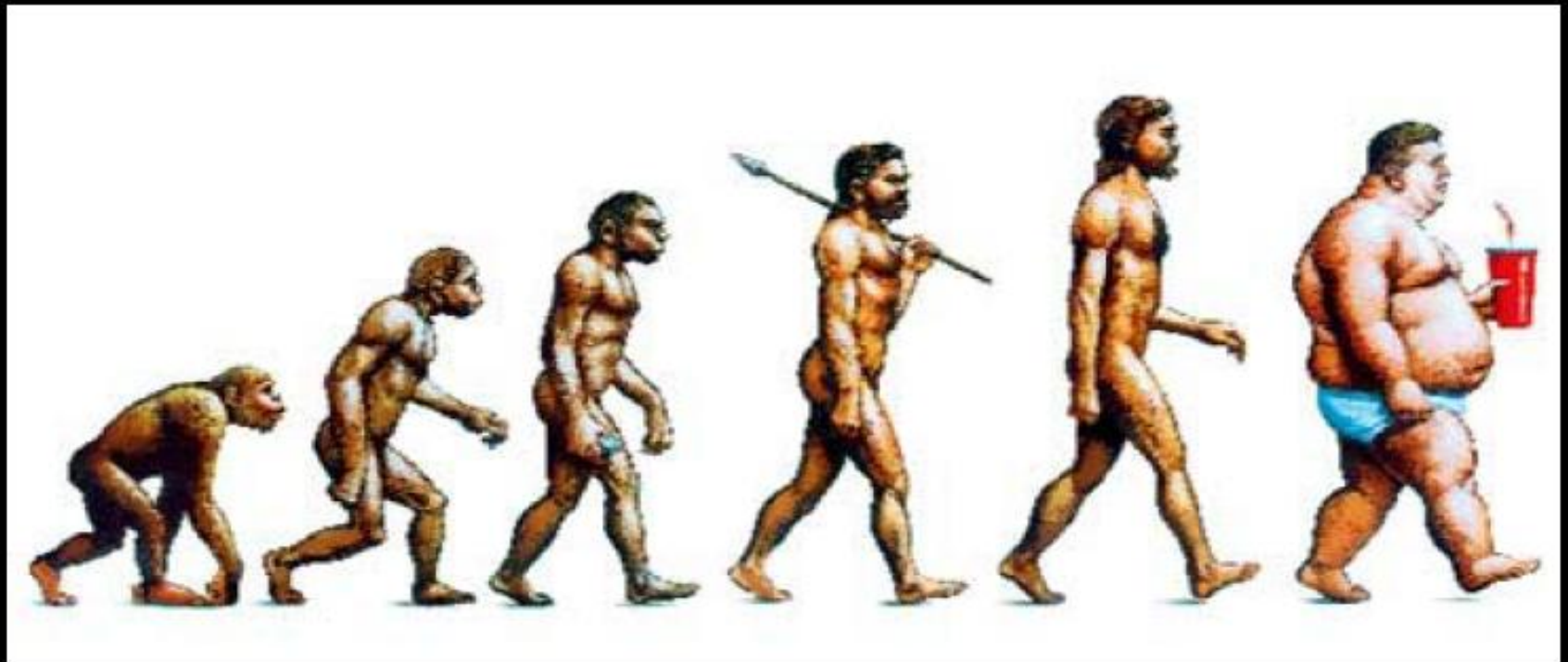
Michael J. Gault, MD, FACC  
Medical Director, Cardiac Services  
Saddleback Memorial Hospital

## 7-year Incidence of Fatal and Nonfatal Myocardial Infarction in Diabetics vs. Non-Diabetics

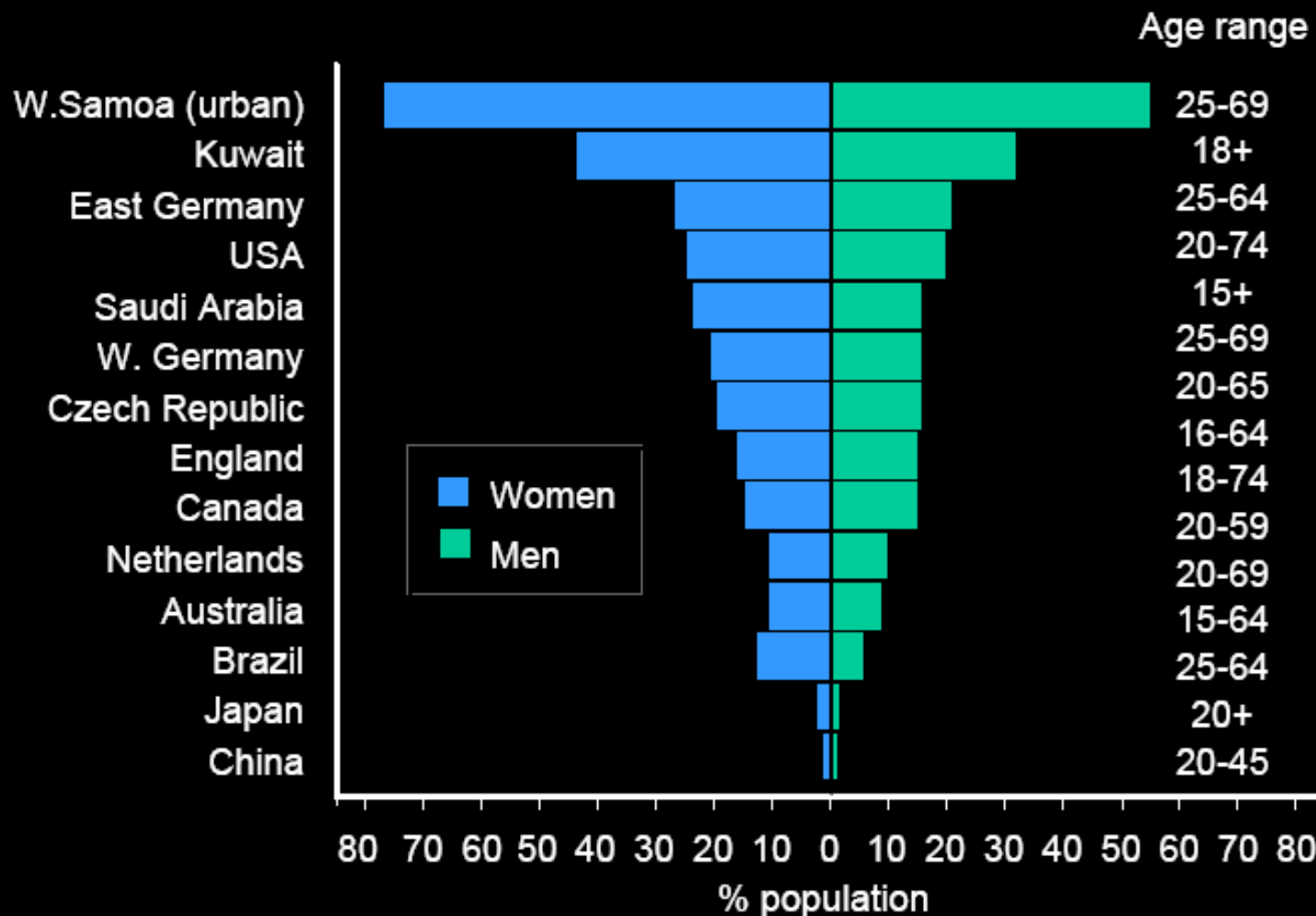


# A Further View of Evolution...

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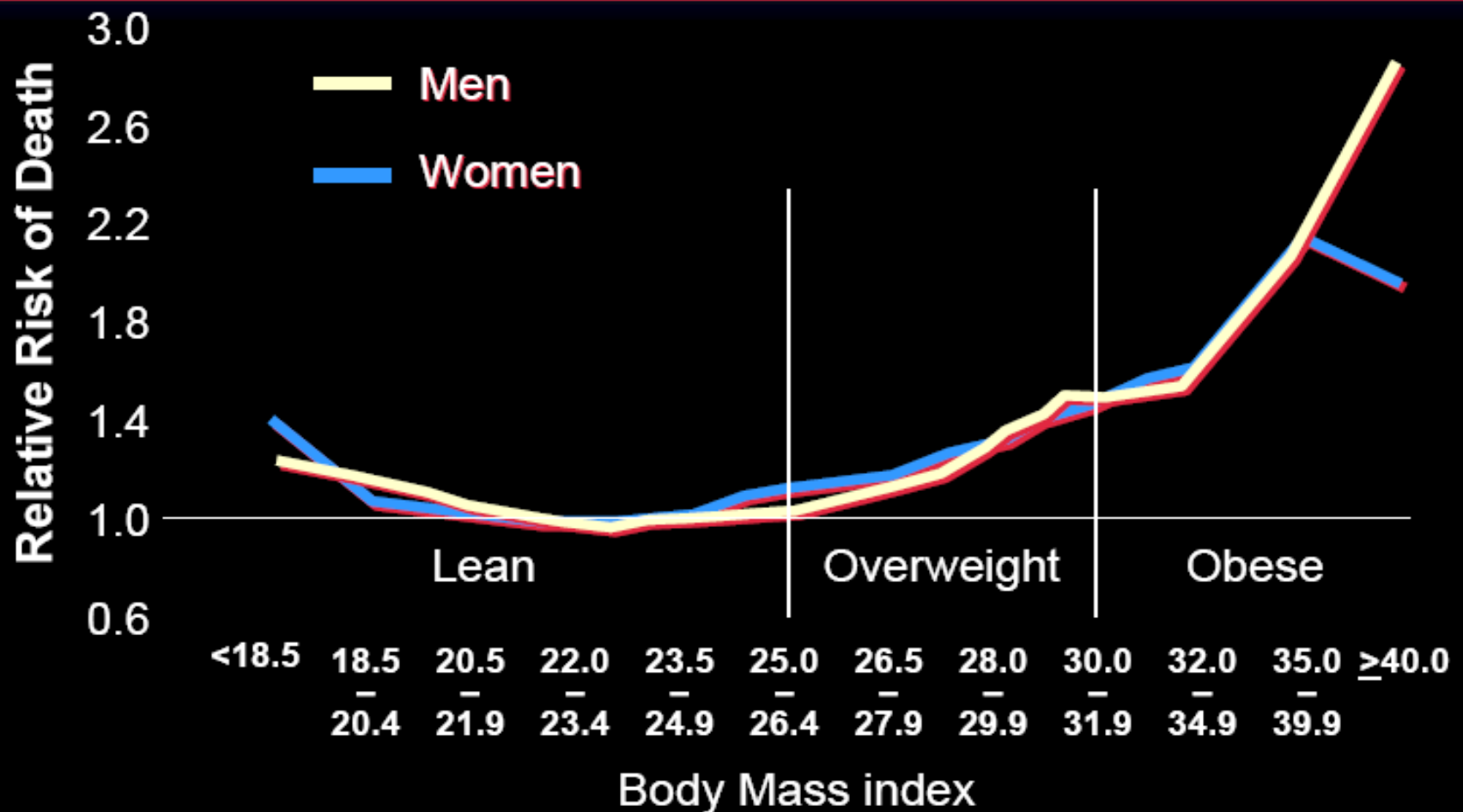


# Global Prevalence of Obesity (BMI $\geq 30$ )



\* Most recent available data. Surveys conducted between 1988 and 1994.

# Relationship Between BMI and Cardiovascular Disease Mortality



## The ABC's of Diabetes and CVD

- A A1C test, aspirin
- B Blood pressure
- C Cholesterol management
- D Diabetes and pre-diabetes management
- E Exercise
- F Food

# Convergence of CVD & T2DM: ABCs for Providers: A

## Aspirin

- Patients with
  - T2DM > 40 years of age, or
  - Prevalent CVD
- 81 mg
- Soluble aspirin

# The ABC's of Diabetes and CVD

## Tests For the Diagnosis of Diabetes

- A1C (hemoglobin A1C) test
- Fasting plasma glucose (FPG)
- Oral glucose tolerance test (OGTT)

## The ABC's of Diabetes and CVD

### A1C: (hemoglobin A1C) Test

- Goal: <7% (normal: 4 - 5.9%)
- Prevents microvascular disease (i.e., retinal, kidney, and nerve damage)

## The ABC's of Diabetes and CVD

### Oral Glucose Tolerance Test (OGTT)

- Impaired glucose tolerance: 2-h plasma glucose  $\geq 140$  mg/dl
- Diabetes: 2-h plasma glucose  $\geq 200$  mg/dl
- WHO: A glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water

- Kids good for your health? Parents have lower blood pressure

---USA Today

# Convergence of CVD & T2DM: ABCs for Providers: C

## Cholesterol Management

- *First target LDL-C:* Statins to achieve LDL-C <100 mg/dL (optional <70 mg/dL)

## Cigarette Smoking

- The 5As of smoking cessation:
  1. Ask
  2. Advise
  3. Assess
  4. Assist
  5. Arrange

## The ABC's of Diabetes and CVD

### Diabetes and Pre-Diabetes Management:

- High Risk of Type 2 Diabetes
  - Obesity (especially at the waist)
  - Hypertension
  - High or borderline high triglycerides ( $\geq 150$  mg/dl)
  - Low HDL ( $< 35$  mg/dl)

## The ABC's of Diabetes and CVD

### Exercise:

- Daily moderate exercise (e.g., brisk walking, 30 minutes 5 times/week)
- Increase in daily activities (e.g., walking breaks at work, gardening , housework)
- Encourage resistance training (e.g., weight machines, free weights) 2 days per week
- Move more, eat less

## The ABC's of Diabetes and CVD

### Food:

- Low glycemic load diet
- Limited intake of saturated and trans fats and cholesterol
- Less processed food, more portion control
- Weight loss (weigh daily)
- Protein 3x/day
- Greater awareness of food intake, food choices

# Tape Worms-Not Advised!

**EAT! EAT! EAT!**  
& ALWAYS STAY THIN!

NO DIET - NO BATHS -  
NO EXERCISE!

**FAT**  
the ENEMY that is shortening Your Life  
**BANISHED!**

HOW?  
with  
SANITIZED  
**TAPE WORMS**  
Jar Packed

FRIENDS FOR A  
FAIR FORM!

Easy To  
Swallow!

No Ill  
Effects!

W. T. BRIDGE, Chicago  
SEND NO  
MONEY  
PARTICULARS  
WRITE  
FREE.

www.StrangePersons.com

The advertisement features a central illustration of a woman in a long, flowing dress and a large, ornate hat, standing amidst a large pile of various food products. The products include cans of 'CASWELL'S NATIONAL CHEESE', 'PRIMES', and 'ROYAL MILK', as well as boxes of 'BREAD' and 'COFFEE'. The woman is holding a small jar, presumably the 'Tape Worms' product. The background is a light, textured color, and the overall style is characteristic of early 20th-century commercial art.

## The ABC's of Diabetes and CVD

### Metformin:

- Prevents diabetes in high-risk patients (e.g., A1c >6%, low HDL, elevated triglycerides, BMI  $\geq 35$  kg/m<sup>2</sup>, and age <60 years)
- Promotes weight loss
- Does not induce hypoglycemia
- Renal insufficiency is contraindication

## Summary

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- In patients with type 2 diabetes and a previous MI:
  - Pioglitazone significantly reduced the risk of recurrent fatal/non-fatal MI by 28%
  - Pioglitazone significantly reduced the risk of ACS by 37%
- Pioglitazone significantly improved glycaemic control, HDL cholesterol and triglycerides
- There were fewer patients with serious adverse events in the pioglitazone group (47%) vs placebo group (51%)
- Reports of serious heart failure were increased in the pioglitazone group vs placebo; however, there was no difference in the absolute number of deaths in these patients

## Conclusions

- Pioglitazone, on a background of optimal medical therapy, prevented progression of coronary atherosclerosis,  $P = 0.002$  compared with glimepiride.
- Compared with glimepiride, pioglitazone produced similar, although more durable, glucose-lowering.
- Pioglitazone favorably affected BP, raised HDL-C (16.0% vs. 4.1%), lowered triglycerides (-15.3% vs. +0.6%) and reduced hsCRP (-44.9% vs. -18.0%).
- Hypoglycemia and angina were more common with glimepiride treatment; edema, fractures and weight gain more frequent with pioglitazone treatment.

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# Combination Therapy with TZDs:*Complementary Effects*

- **Dyslipidemia**

- TZDs:

- Lower CRP and inflammation
    - Preserve Beta Cell Function
    - Increase LDL particle density
    - Increase HDL and selectively increase HDL<sub>2</sub>

- Statins:

- Decrease total LDL particle numbers
    - Decrease triglycerides
    - Don't raise HDL significantly
    - Lower CRP

# The Diabetic Dyslipidemic Profile

## Increased Atherogenic Risk

- ↓ HDL/HDL2 cholesterol
- ↑ Small, dense LDL with normal to slightly elevated LDL
- ↑ Triglyceride levels

# Smoking Cessation!!!

*According to repeated nationwide surveys,*

## More Doctors Smoke **CAMELS** than any other cigarette!

Doctors in every branch of medicine were asked, "What cigarette do you smoke?" The brand named most was Camel!

You'll enjoy Camels for the same reason so many doctors enjoy them. Camels have cool, mild nicotine, pack after pack, and a flavor unmatched by any other cigarette. Make this smokable test. Smoke only Camels for 30 days and see how well Camels please your taste. How well they suit your throat as you steadily smoke. You'll see how enjoyable a cigarette can be!

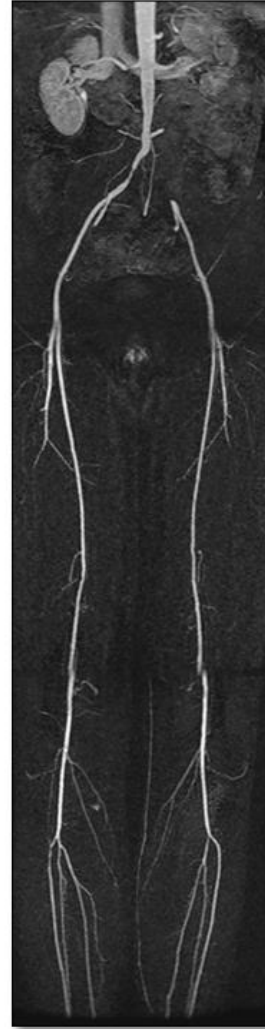
**THE DOCTORS' CHOICE IS AMERICA'S CHOICE!**



*For 30 days, test Camels in your "T-Zone" (T for Throat, T for Taste).*

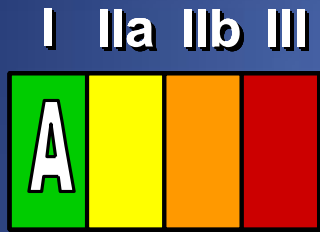
[www.StrangeCosmos.com](http://www.StrangeCosmos.com)

# PAD-Iliac Artery Occlusion

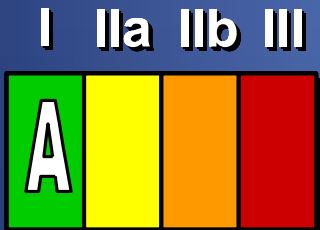


# Supervised Exercise Rehabilitation

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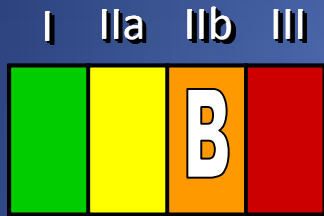
A program of supervised exercise training is recommended as an initial treatment modality for patients with intermittent claudication.



Supervised exercise training should be performed for a minimum of 30 to 45 minutes, in sessions performed at least three times per week for a minimum of 12 weeks.

# PAD Guideline-Based Care: Claudication Treatment via Home Exercise

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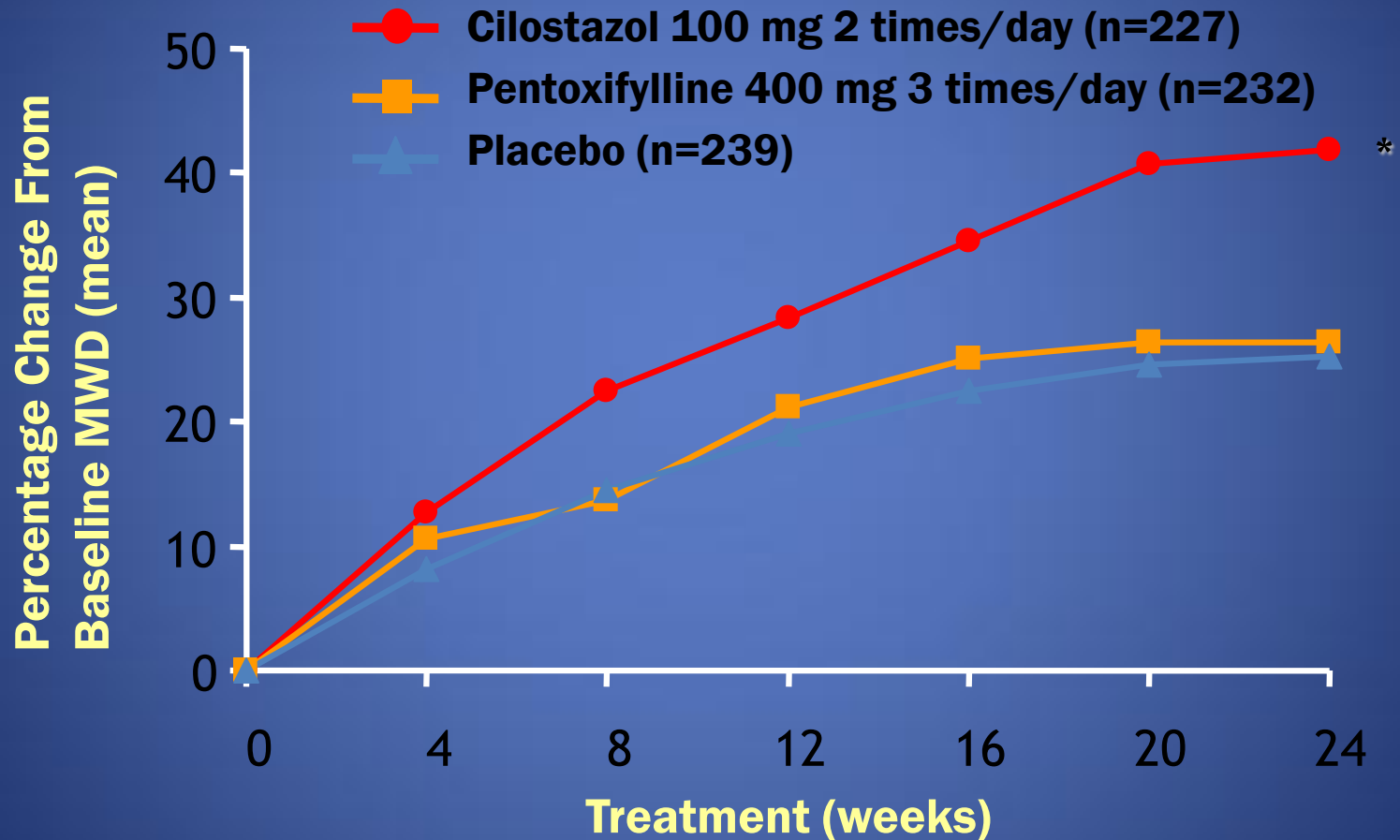
The usefulness of unsupervised exercise programs is not well established as an effective initial treatment modality for patients with intermittent claudication.

The lack of proven efficacy for home-based, unsupervised exercise may be due to:

- A lack of compliance with the minimum “exercise dose”;
- A lack of progression of the workload in the absence of professional supervision;
- A lack of confidence by the patient that it is safe to advance into moderate claudication discomfort severity.

# Cilostazol vs. Pentoxifylline:

## Relative Efficacy to Improve Walking Distance in Claudication



MWD=maximal walking distance.

\*P<0.001 vs pentoxifylline.

Reprinted from Dawson DL, et al. Am J Med. 2000;109:523-530 with permission from Elsevier.

# Contraindications to Cilostazol Use

Cilostazol and several of its metabolites are inhibitors of phosphodiesterase III. Several drugs with this pharmacologic effect have caused decreased survival compared with placebo in patients with Class III-IV CHF. PLETAL<sup>®</sup> is contraindicated in patients with CHF of any severity.

## Provisos:

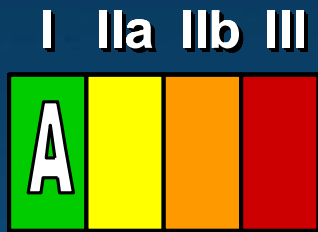
- “CHF of any severity” (systolic dysfunction)
- Any known or suspected hypersensitivity to any of its components

CHF=congestive heart failure.

Pletal<sup>®</sup>(cilostazol) Package Insert. Rockville, Md: Otsuka America Pharmaceutical, Inc; 1999.

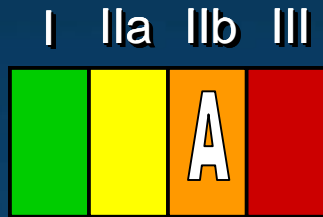
# Pharmacotherapy of Claudication

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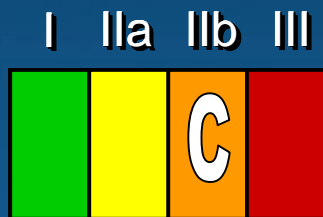


Cilostazol (100 mg orally two times per day) is indicated as an effective therapy to improve symptoms and increase walking distance in patients with lower extremity PAD and intermittent claudication (in the absence of heart failure).

# Pharmacotherapy of Claudication



Pentoxifylline (400 mg 3 times per day) may be considered as second-line alternative therapy to cilostazol to improve walking distance in patients with intermittent claudication.



The clinical effectiveness of pentoxifylline as therapy for claudication is marginal and not well established.

# Diagnostic Testing non invasive

- ECG-Electrocardiogram
- ECHO-Ultrasound, Ejection Fraction  
segmental wall motion.

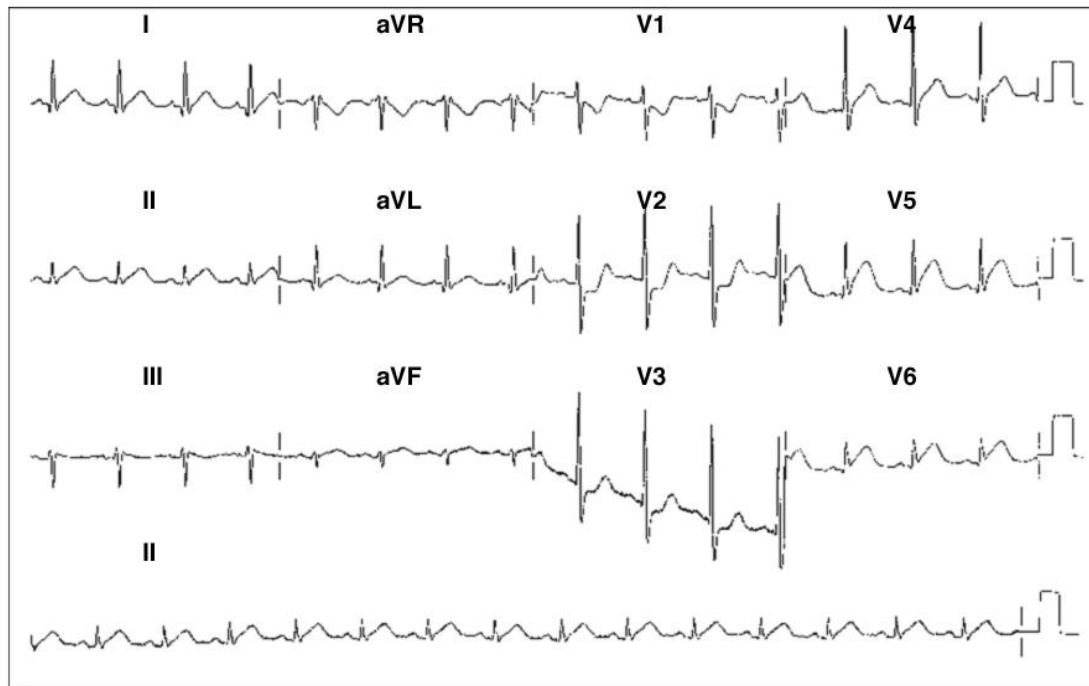
Stress Testing-

Treadmill

Stress Echocardiogram

Nuclear stress test-treadmill vs. adenosine

# Acute MI-Posterior



# Diagnostic Testing non invasive

- ECG-Electrocardiogram
- ECHO-Ultrasound, Ejection Fraction  
segmental wall motion.

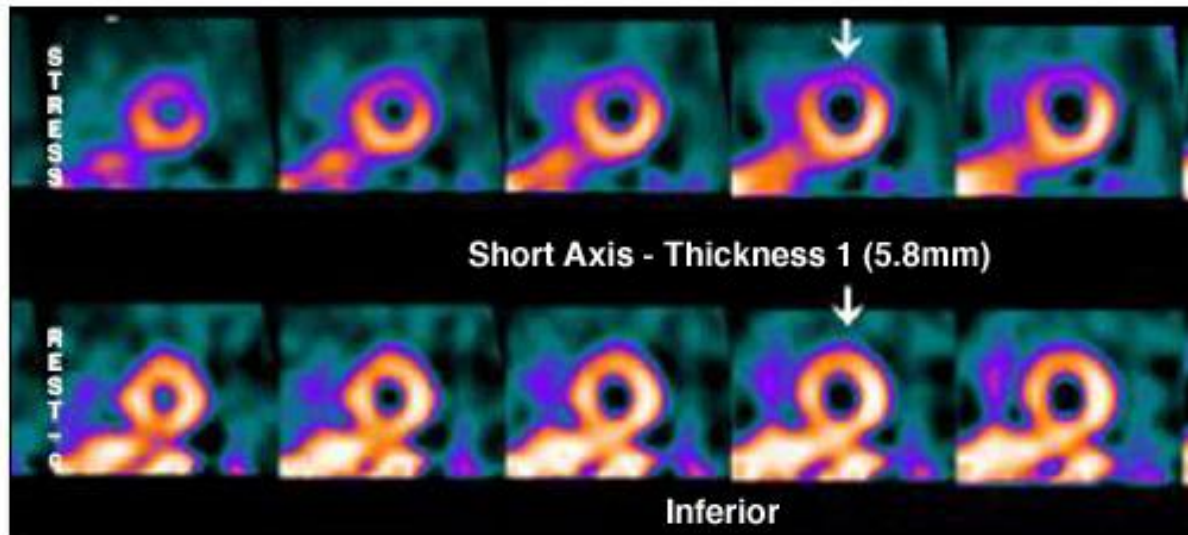
Stress Testing-

Treadmill

Stress Echocardiogram

Nuclear stress test-treadmill vs. adenosine

# Nuclear Stress Testing



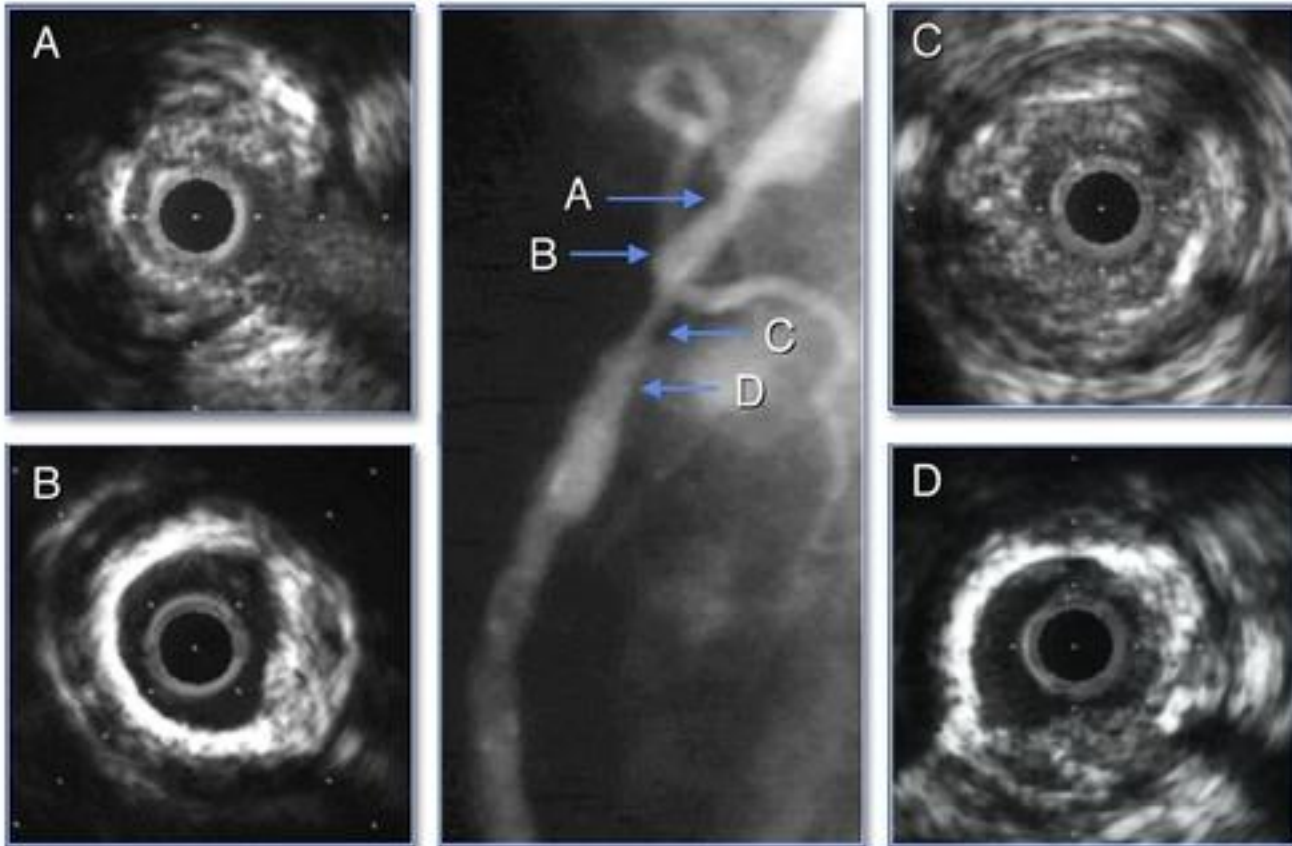
# Diagnostic Testing- non invasive

- EBCT-Cat scan, coronary calcification
- CT Coronary Angiogram
- MRI/A
  
- Peripheral Vascular Disease-
  - Ankle Brachial index
  - Doppler/ultrasound, Carotid US
  - CT Angiography

# Diagnostic Testing- Invasive

- Angiogram-heart catheterization
  - Angioplasty/Stenting/CABG
  - Intravascular Ultrasound
  - Radi /flow wire

# Coronary Angio/IVUS



# BARI 2D Trial: Limitations

- Patients who are at high risk for MI and, therefore, stand to benefit the most from revascularization were excluded from the trial.
- The broad applicability of BARI 2D is limited by the fact that the patient population selected represents only a small subset of patients with diabetes and coronary artery disease.

# BARI 2D Trial: Summary

- Neither revascularization nor optimal medical therapy demonstrated a significant reduction in the occurrence of death or major cardiovascular events at 5 years.
- Likewise, there was no demonstrated difference between a strategy of insulin sensitization and insulin provision.
- Further research into defining optimal medical therapy for this group of patients is needed, as evidenced by the fact that 42.1% of patients in the optimal medical therapy alone treatment group eventually required revascularization within 5 years.

# Bari 2D trial summary

- Drug eluting stents have not been shown to favorably impact hard outcomes of death or MI compared to bare-metal stents in either diabetic or non-diabetic patients. Thus, it is unlikely whether the exclusive use of DES in BARI 2D would have resulted in a different outcome.”
- Pre-randomization angiogram is a prerequisite to ensure that patients are eligible for randomization to either an initial strategy of intensive medical therapy or revascularization plus intensive medical therapy. It is, therefore, not a limitation of the trial.
- The mortality rate at 5 years averaged 12% or about 2.4% per year which is consistent with intermediate risk and is somewhat higher than the 1-2% annual mortality rates observed in several recent diabetes trials (ACCORD, VADT, DIAD). It is interesting to note that the mortality in BARI 2D is approximately 50% higher than that observed in the COURAGE trial (8%). Thus, the patients enrolled in BARI 2D do not appear to represent a low-risk population.
- The recommendation for screening for myocardial ischemia in asymptomatic diabetics was not supported in the recently published DIAD trial.
- What BARI 2D tells us is that intensive medical therapy without initial revascularization (especially PCI) can be implemented safely in most diabetic patients with stable CAD without incurring any disadvantage with respect to death or major cardiovascular events.

# SYNTAX

**Trial design:** Patients with severe three-vessel or LM disease were randomized to CABG or DES-PCI with paclitaxel-eluting stents. Clinical outcomes were compared at 12 months.

## Results

- MACCE was significantly lower in CABG arm compared with PCI (12.4% vs. 17.8%,  $p = 0.002$ ), especially for diabetics ( $p = 0.0025$ )
- Significant  $\downarrow$  in the need for repeat revascularization in CABG arm ( $p < 0.001$ )
- Death and MI were similar; CVA  $\uparrow$  with CABG ( $p = 0.003$ )

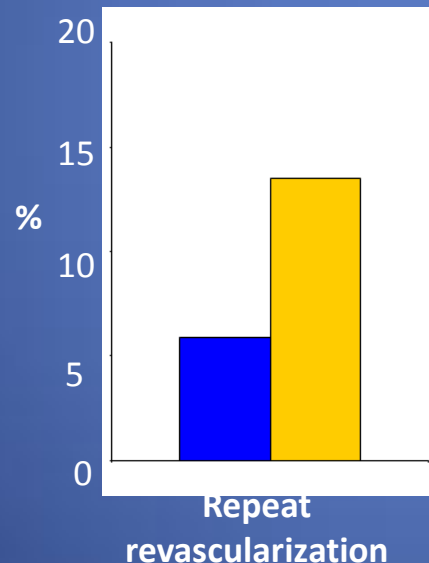
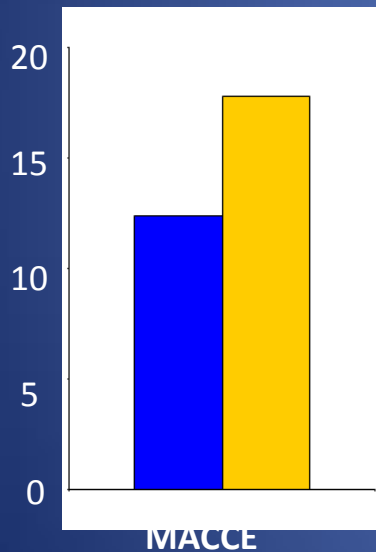
## Conclusions


- CABG was associated with fewer repeat revascularizations compared with DES-PCI in patients with LM or three-vessel disease, but a higher rate of stroke
- No difference in death, MI, or thrombosis
- Diabetics are especially more likely to benefit with CABG compared with DES-PCI


Serruys PW, et al. *N Engl J Med* 2009;360:961-72

( $p = 0.002$ )

$p < 0.001$



 CABG  
(n = 897)

 DES-PCI  
(n = 903)

## 7-year Incidence of Fatal and Nonfatal Myocardial Infarction in Diabetics vs. Non-Diabetics

