

# Kaiser Permanente's Aspirin, Lisinopril, Lovastatin (ALL) Program: From Consensus to Outcomes

R. James Dudl, MD



*care management* | institute

# Agenda

- What is PHASE/ALL? How did it develop?
- Is it More effective to treat pts with hi LDL/BP or Hi CVD risk?
- Is a “bundle” of meds with ACEI’s more effective than just titrating a statin?
- Treating for primary prevention: “How Low can you go” in treating risk before statins do more harm than good?

Slide 2

# What is ALL/PHASE?



Slide 3

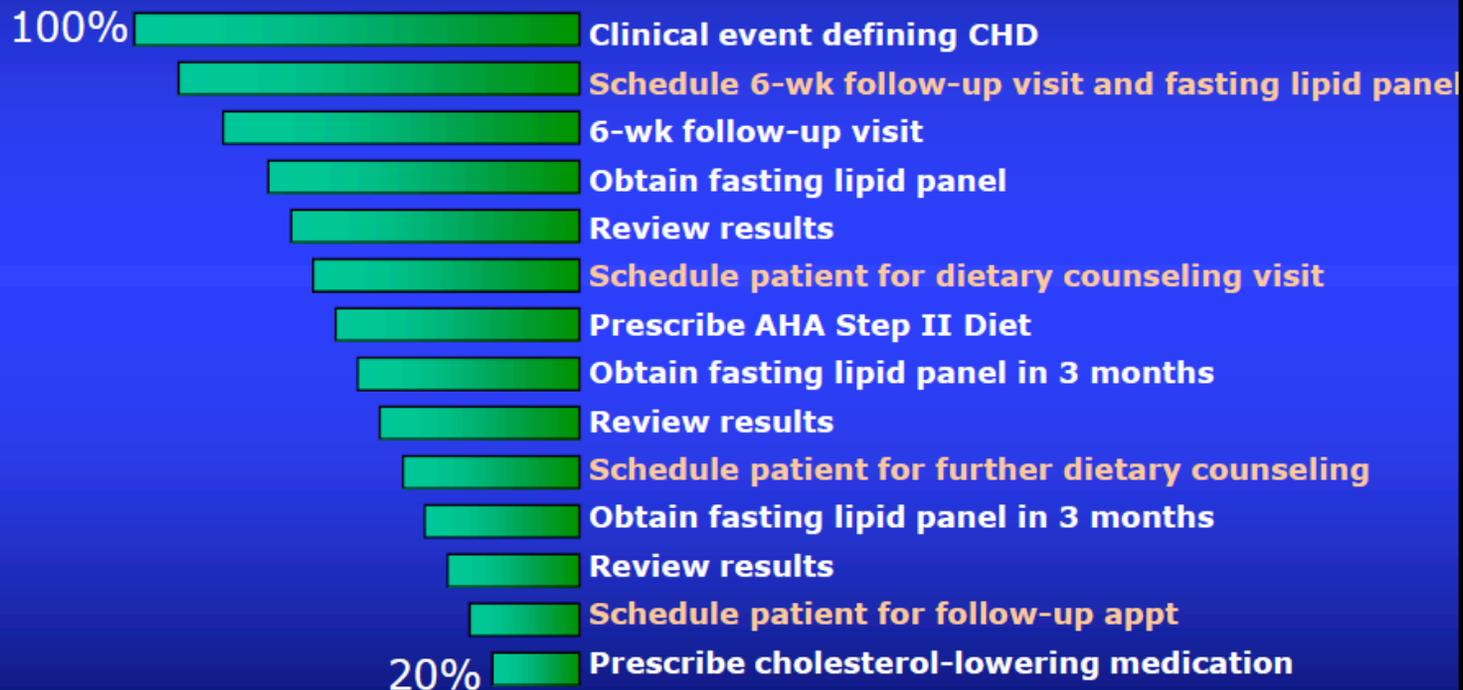
# How Did It Develop: The Consensus Phase

- By 1990's Evidence emerged that lowering cholesterol decreased heart attacks & strokes
- The 1995 program: Treat all eligible patients who came to clinic with niacin
  - Nurse Practitioners to make calls to do 6 titrations
- Tested cholesterol every 3 months to address adherence

Slide 4

# Why Not Just Keep Titrating up Statin Dose? ?

## NCEP ATP I and II Guidelines for the Detection and Treatment of Hypercholesterolemia: Secondary Prevention Treatment Algorithm



Slide 5

# Consensus Phase Results

Evaluated by Archimedes medical-economic model

## ➤ NO effect on Heart Attacks

- Treating low risk patients (“worried well”), Avg 7% five yr CVD risk
- Titrations didn’t work
  - 1 per patient accomplished when 6 were needed

## ➤ Benefit/Savings

- No benefit therefore no savings
- Cost of tests exceeded savings

## ➤ Lessons:

- Treating low risk patients is not effective
- Titrating is very difficult in our system
- Testing is expensive and didn’t lower heart attacks & strokes

Slide 6

# Next step: Risk Stratification Phase

- To find high-risk patients
  - Initiated population-based cholesterol screening
    - Rapidly increased to ~80% tested in 2 years
- To increase efficacy:
  - Added Lovastatin treatment (not yet generic)

Slide 7

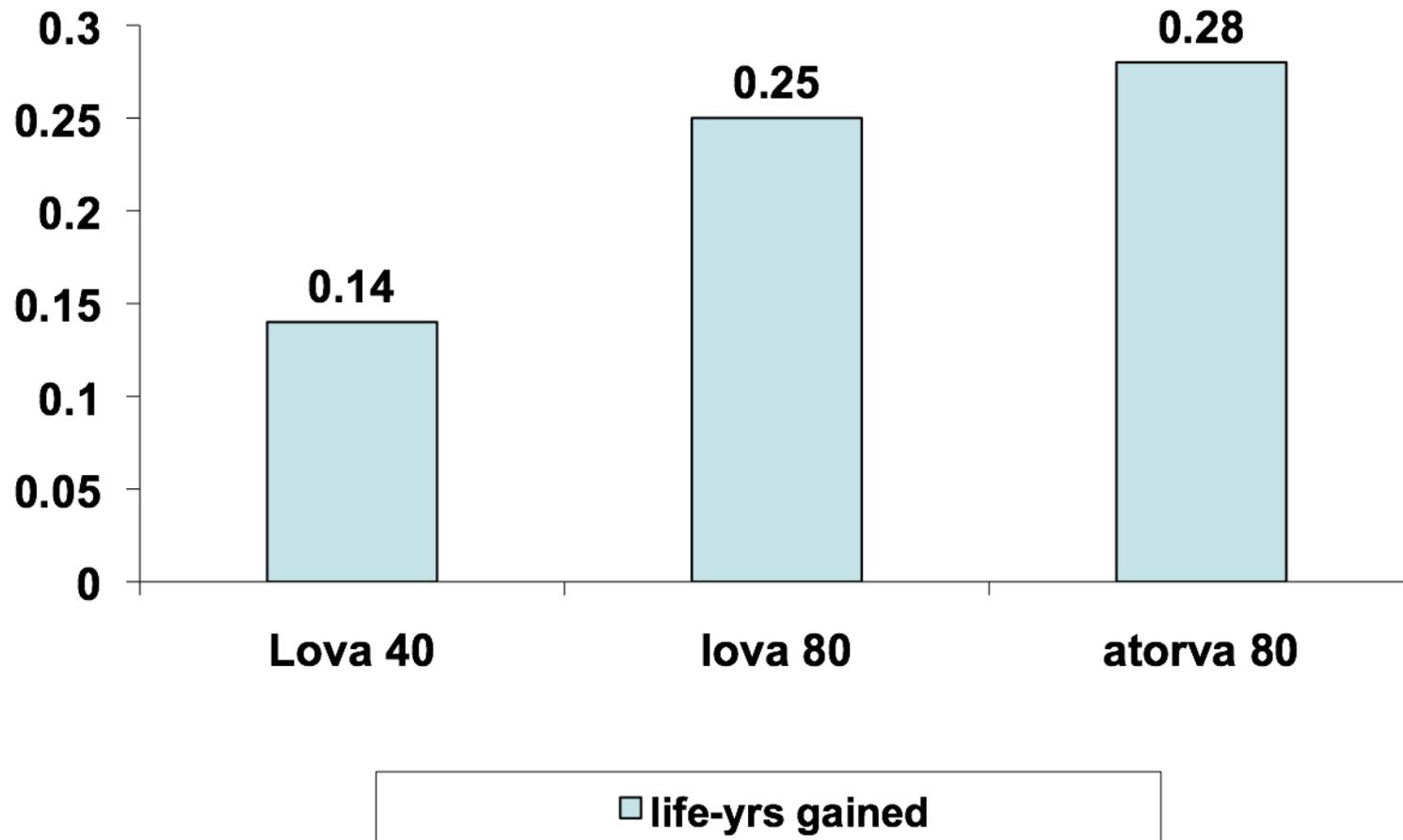
# Risk Stratification Phase

## Archimedes Results

- Still no drop in heart attacks and strokes
  - MI's 1998 15/1000 DM members
  - MI's 2001 16/1000 DM members, Why?
    - Many with high cholesterol tests & hi risk were not treated!
- Lessons:
  - Testing still did not decrease events
    - To start meds, the program needs to focus on starting meds
  - Treating cholesterol alone won't decrease heart attacks and strokes in low to medium CVD risk pts
- Program modeled: Statins were high cost and lower LDL but little drop in heart attacks and strokes

Slide 8

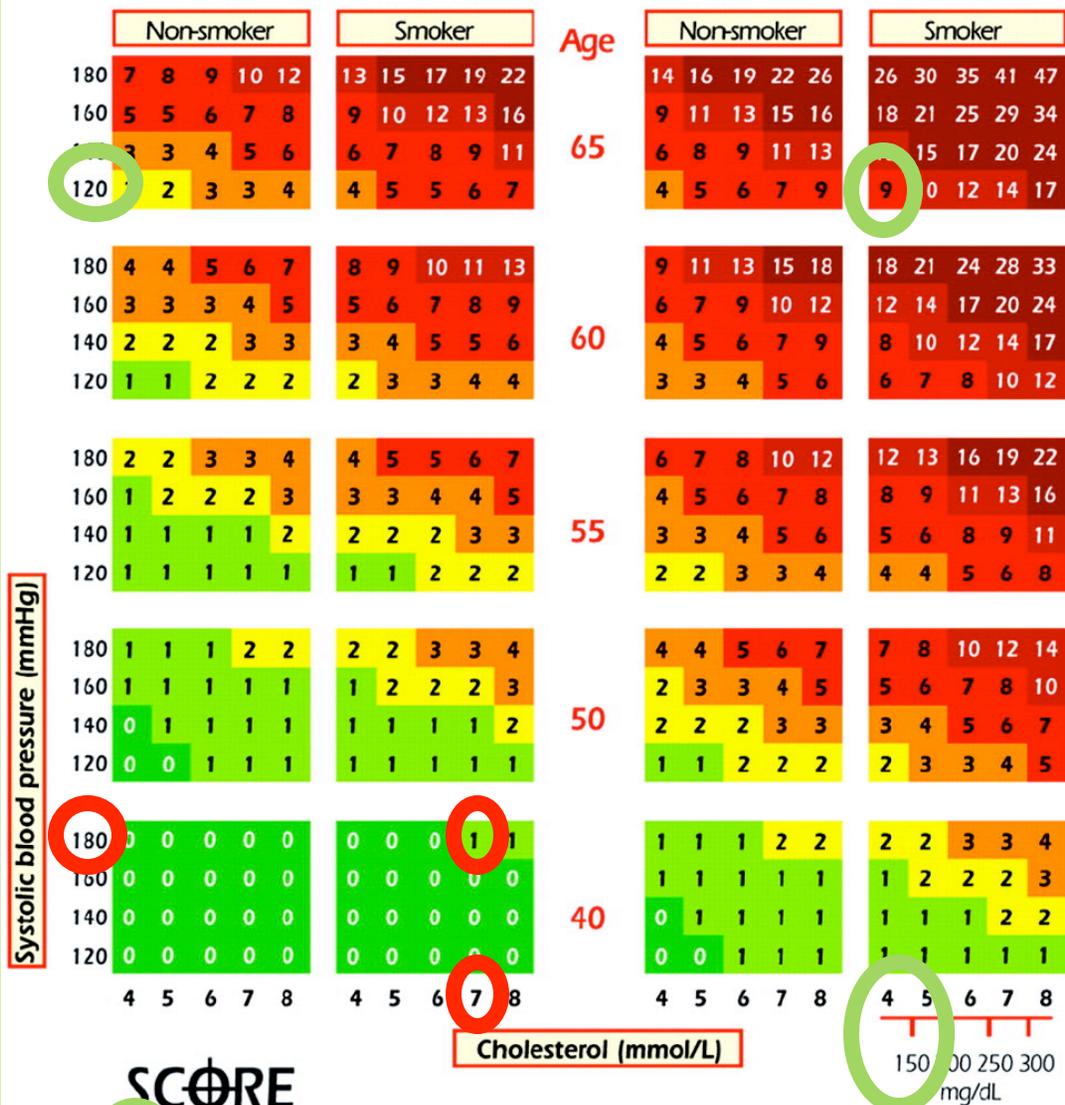
# Does Increasing dose/ strength more matter?



Slide 9

## Women

## Men



Systolic blood pressure (mmHg)

### SCORE



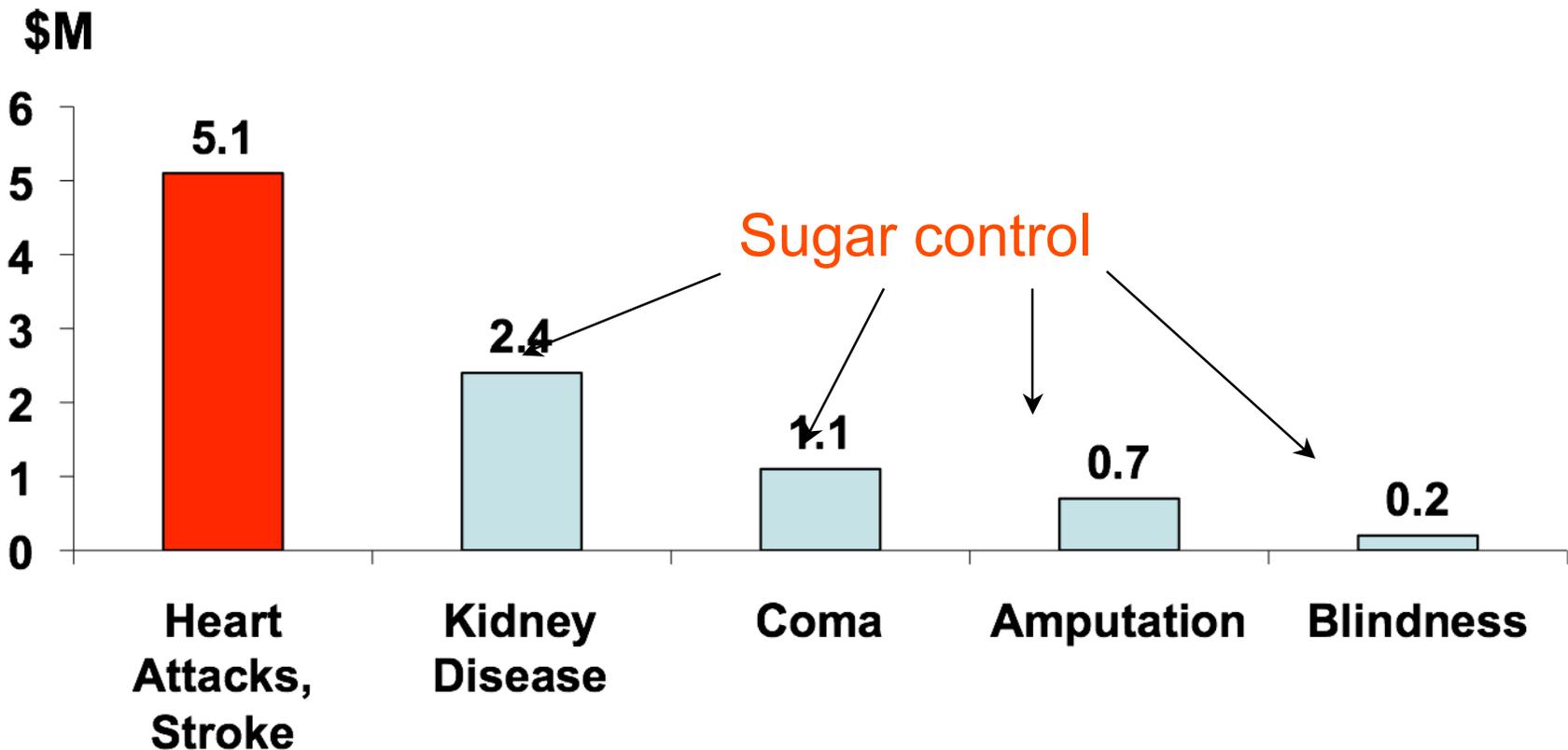
10-year risk of fatal CVD in populations at high CVD risk

Conroy M T et al. Circulation 2010;122:300-310

© 2007 ESC

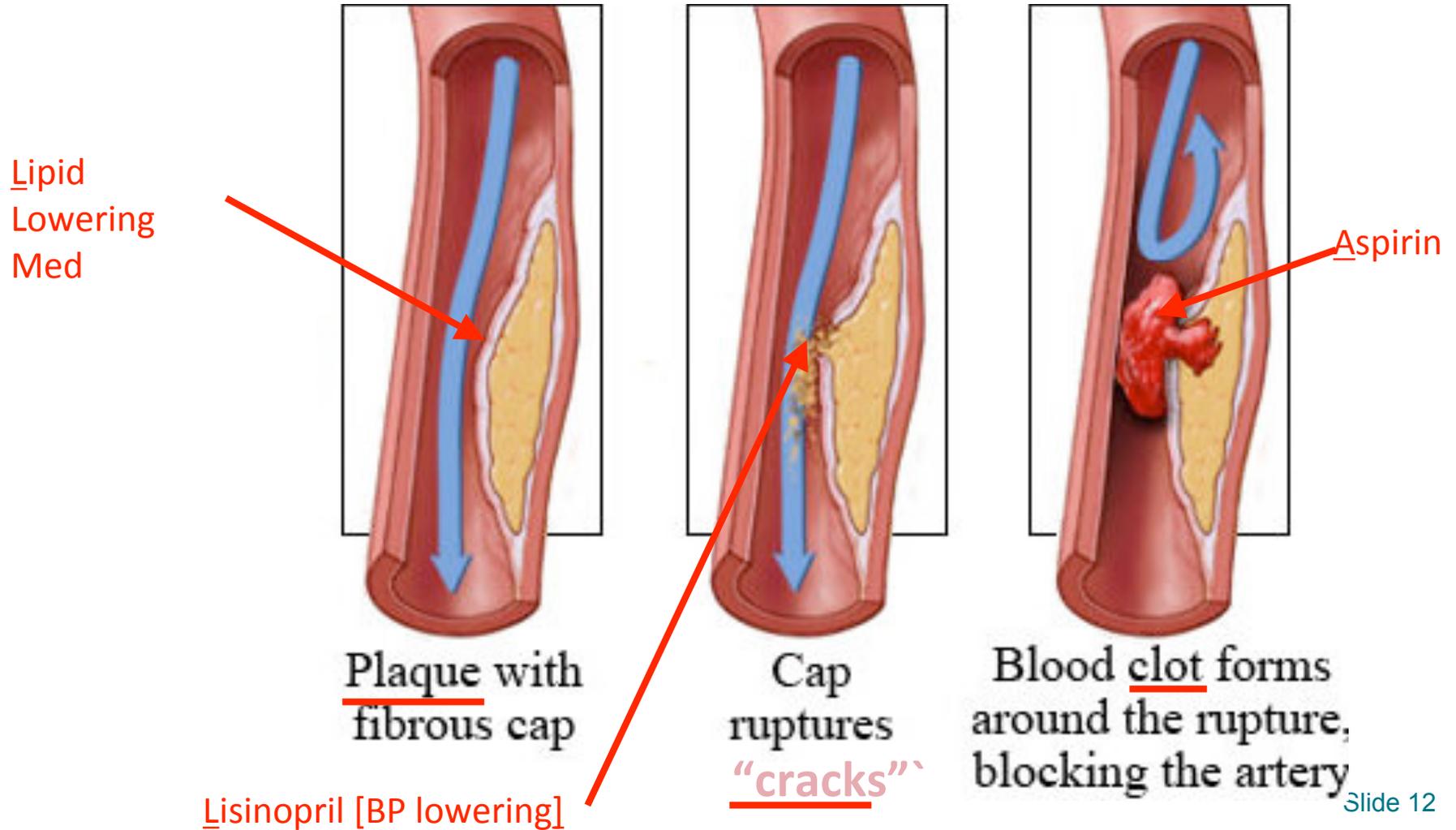
# Why Focus On Heart Attacks & Strokes in DM? It's a CVD Risk Equivalent and...

## No Cal 1996 costs of DM Complications



Slide 11

# Back to Basics: What Causes a Heart Attack?



# Cumulative Impact of Simple Cardiovascular Protective Medications

	Relative-risk	5yr CV event rate
None	--	20%
Aspirin	↓ 25%	15%
Beta blocker	↓ 25%	11.3%
ACE inhibitor	↓ 25%	8.4%
Lipid lowering Rx	↓ 30%	5.9%
LDL 100 → 70 mg/dl	↓ 22%	4.6%

Cumulative risk reduction if all four therapies are used: 77%

Absolute risk reduction: 15.4% NNT = 6

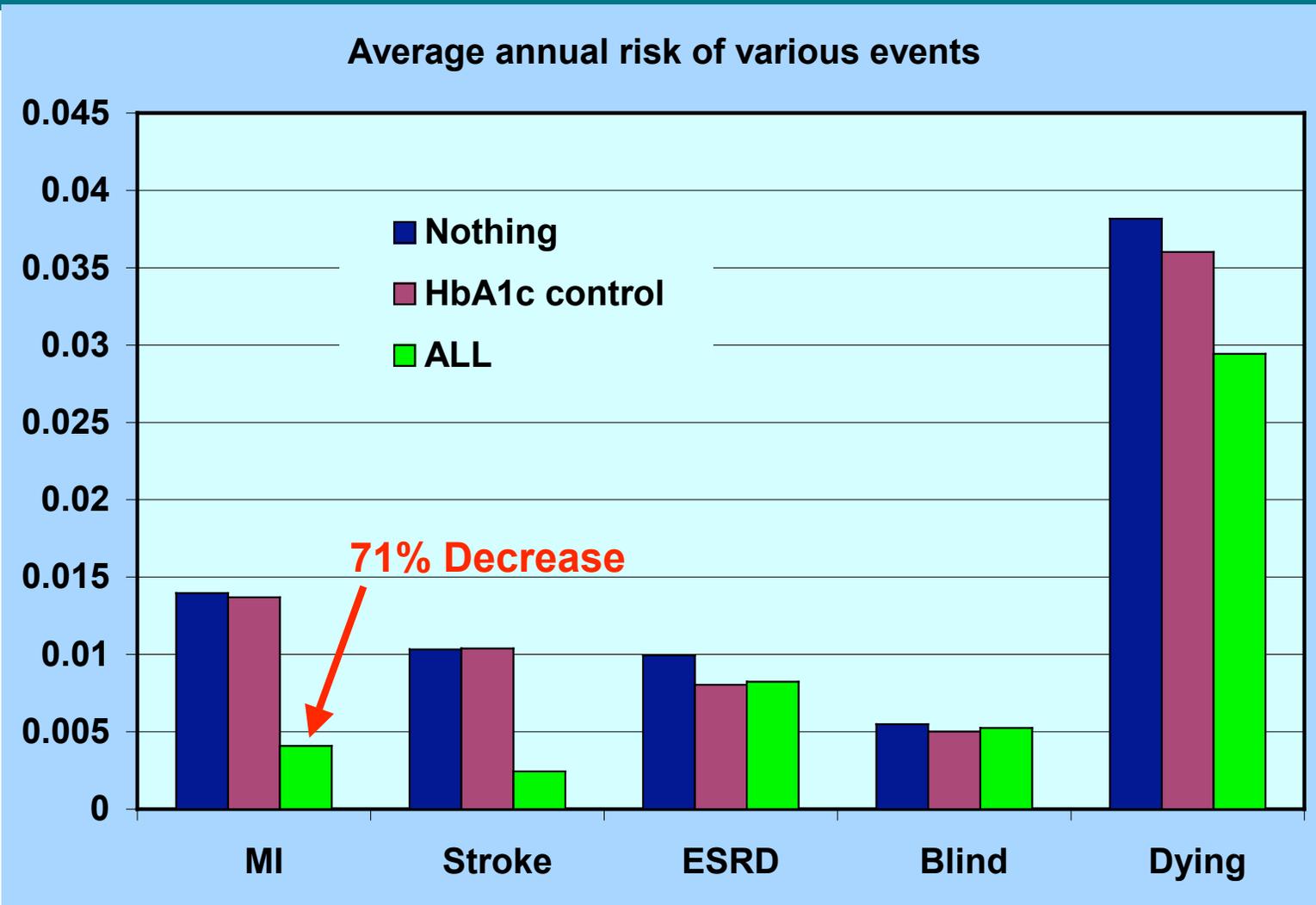
CV event = CV death, MI, or stroke

# Model of the Outcomes Phase: A.L.L.

- Systematic implementation in all pts with:
  - Diabetes (age  $\geq 55$ yo) or
  - Cardiovascular disease (prior heart attack or stroke)
- To insure they are offered daily dose of:
  - Aspirin 75-235 mg
  - Lovastatin 40mg
  - Lisinopril 20 mg

Slide 14

# Archimedes Modeling of A.L.L. & A1C in Diabetes : Effect on Morbidity & Mortality



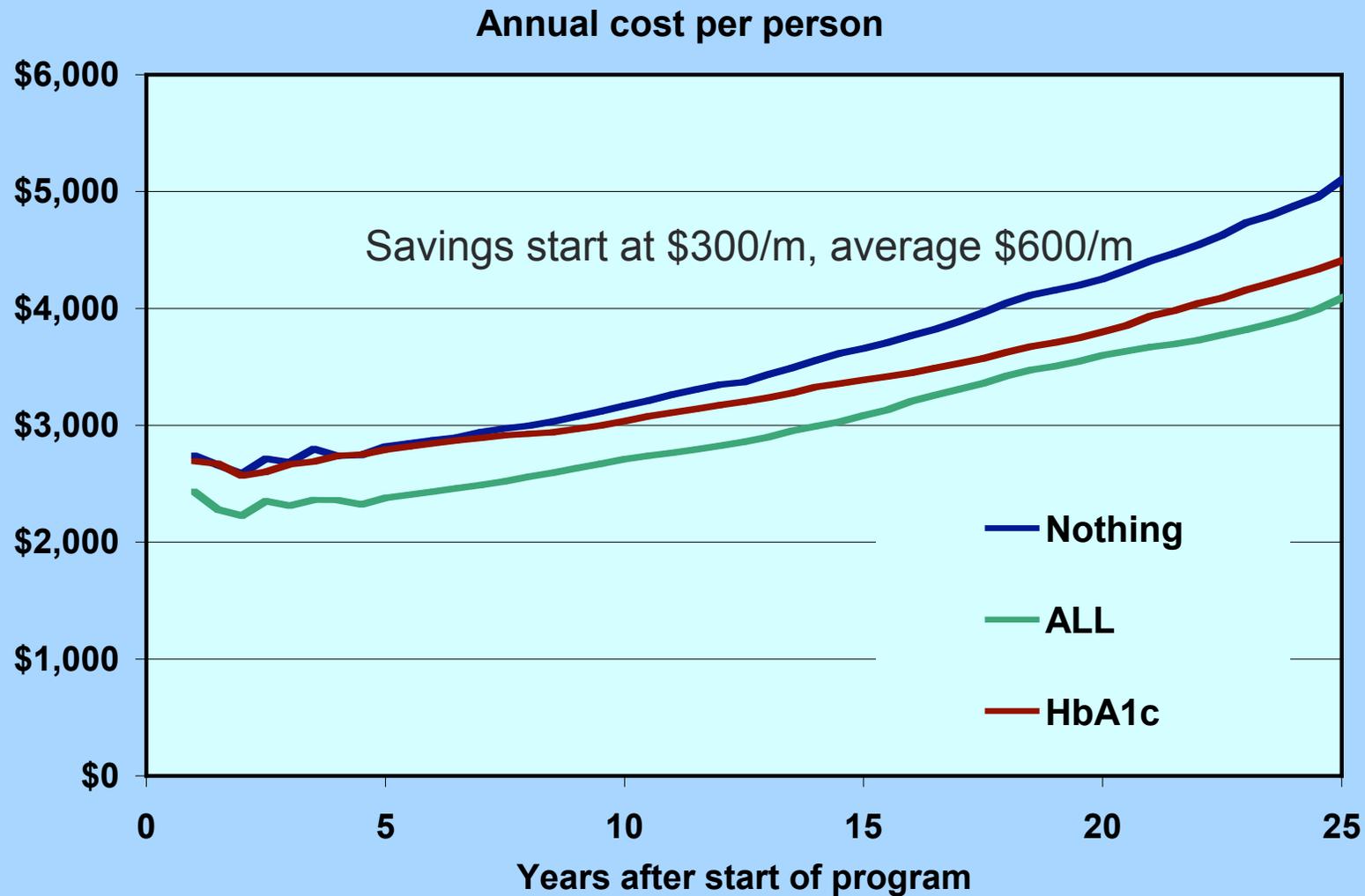
Slide 15

# How We Increased Efficacy and Efficiency

- Identify high-risk with minimal testing:
  - Diabetes (age  $\geq 55$ yo) or history of heart attack or stroke
  
- Simplify implementation and cut costs:
  - Eliminate titrations
    - No change on effect of medications
    - Less visits and testing

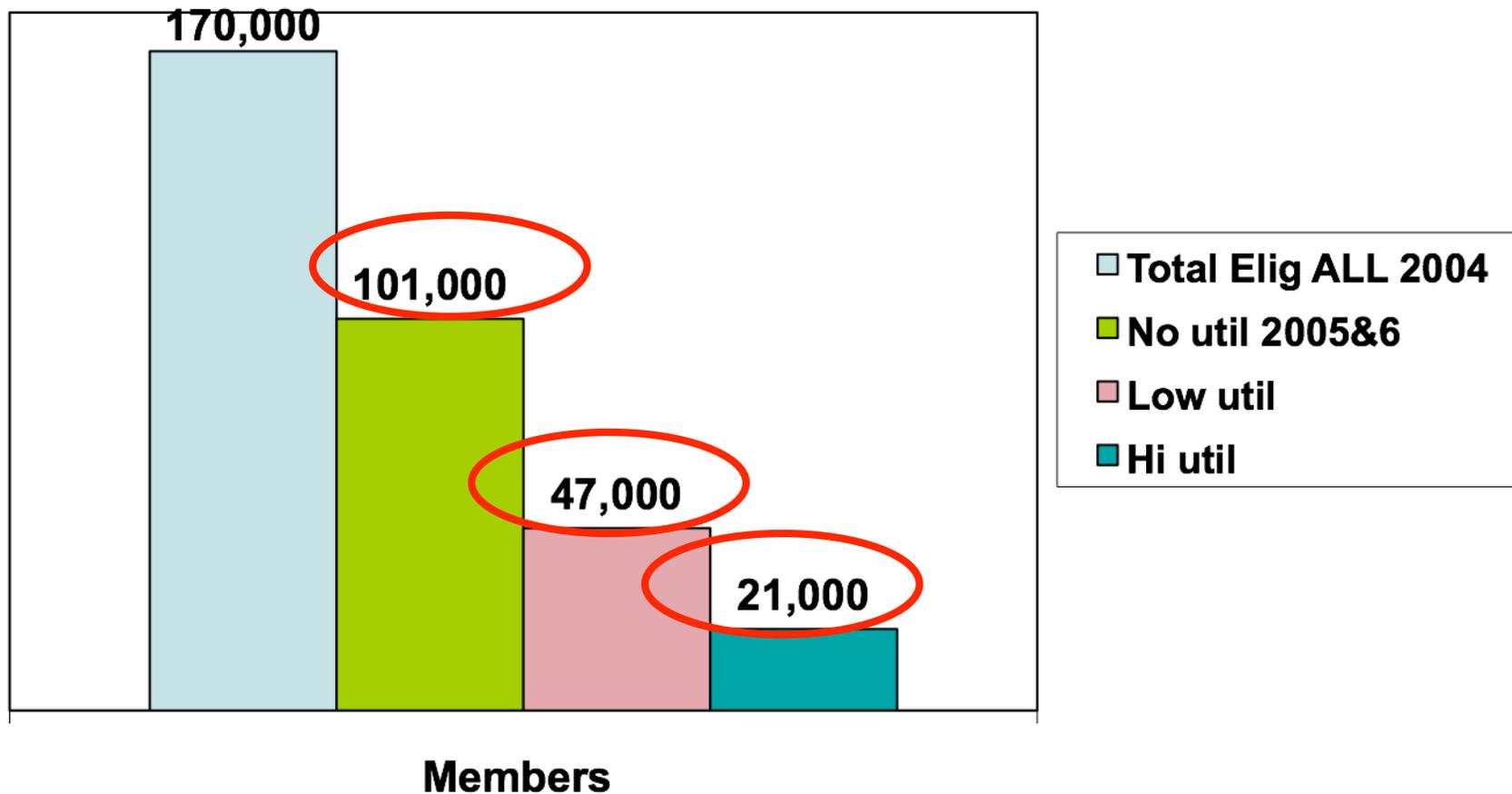
Slide 16

# A.L.L. reduces cost in patients with diabetes



Slide 17

# Did we do it and did it work?

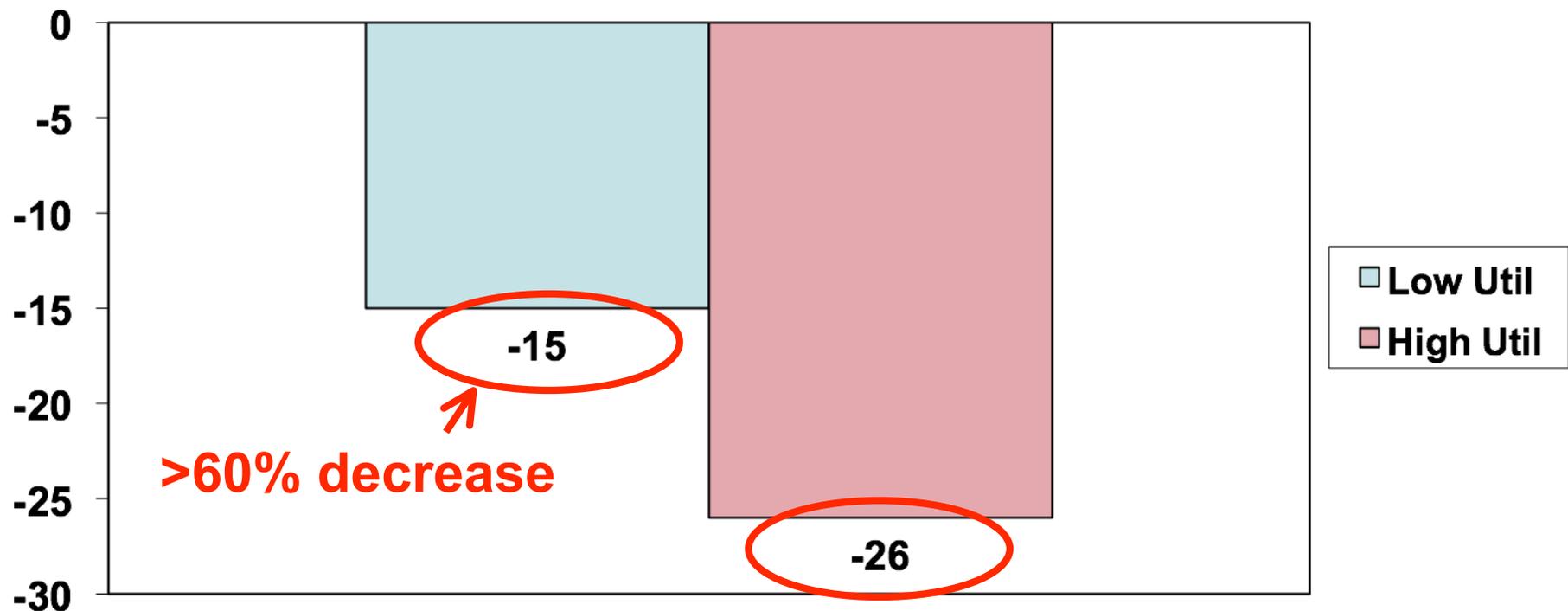


\*90,000 patients from No Cal ("PHASE" program), remainder of patients from So Cal. MPR=Mean Possession Ratio

Slide 18

# The effect per group was significant

## Reduction in Heart Attacks & Strokes/1000 pers/yr



- Even 1 day of 5 utilization was significant
- But taking it 2/3 of the time was much more beneficial

Slide 19

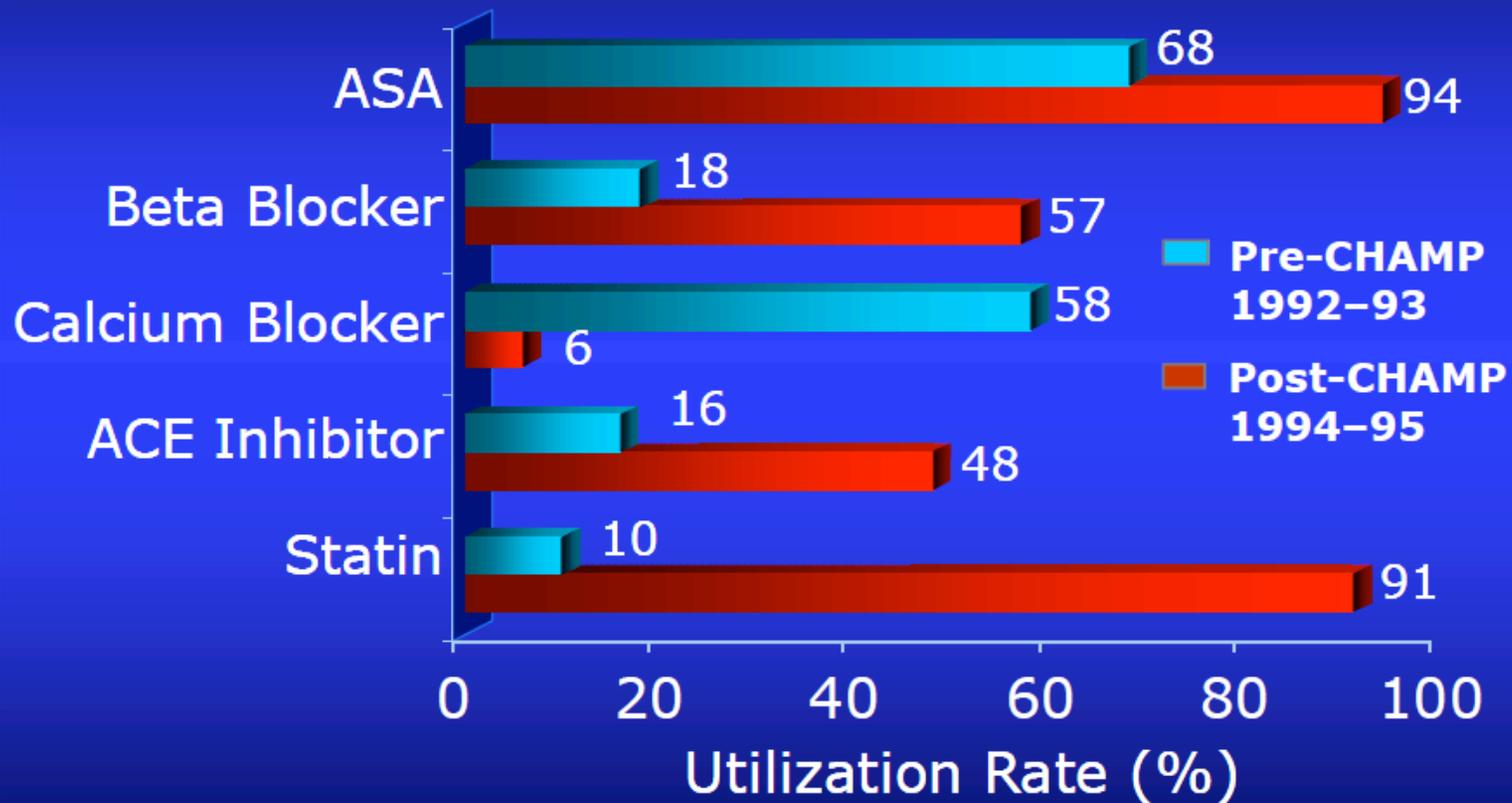
## Archimedes Planned Outcomes Phase :

- A.L.L. medications prescribed to a large number of patients
- Heart attacks and strokes significantly decreased
- Costs of meds were contained using A.L.L.

Are there any other studies that show >60% benefit of bundled therapy?

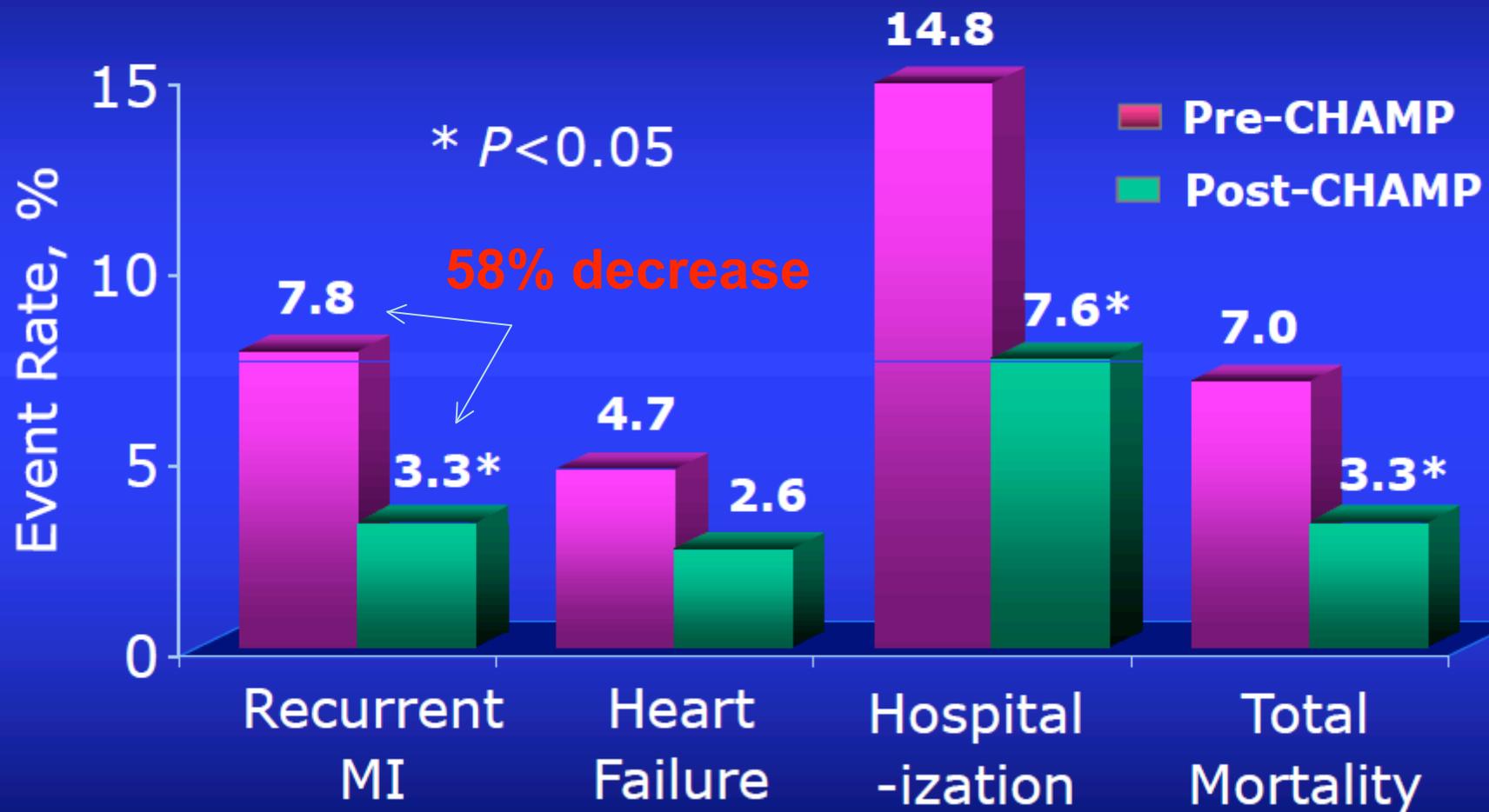
# CHAMP: Start BALL in Hosp New MI

## CHAMP: Impact on Long-Term Treatment Utilization

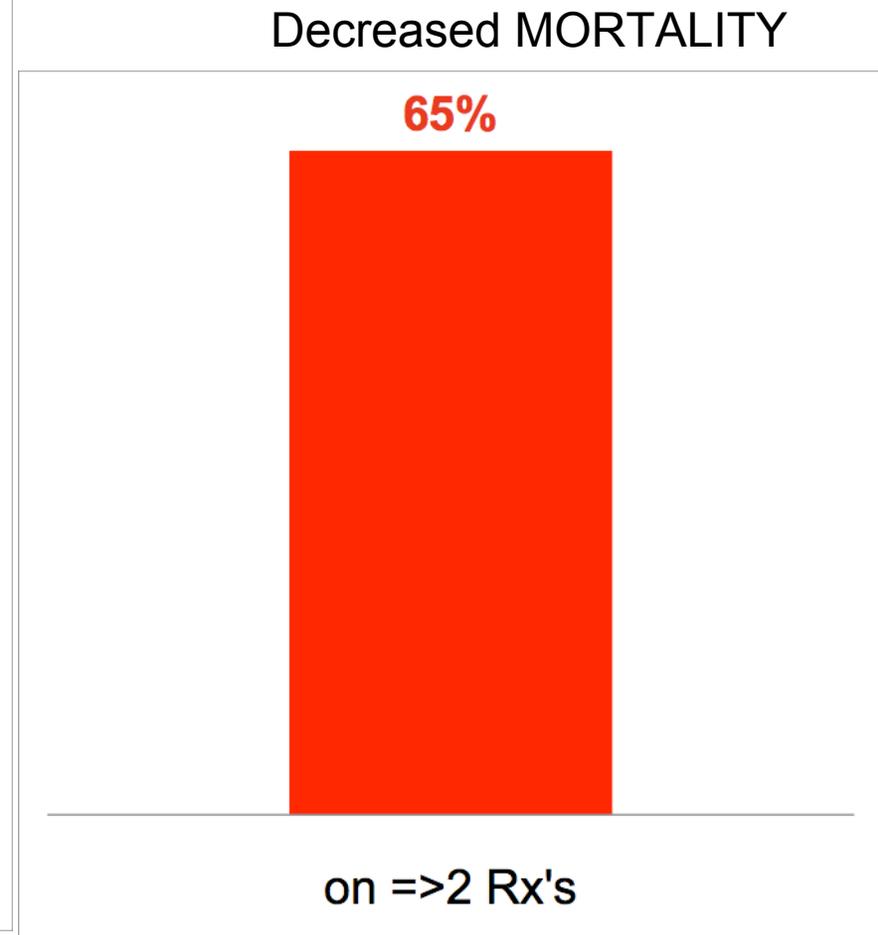
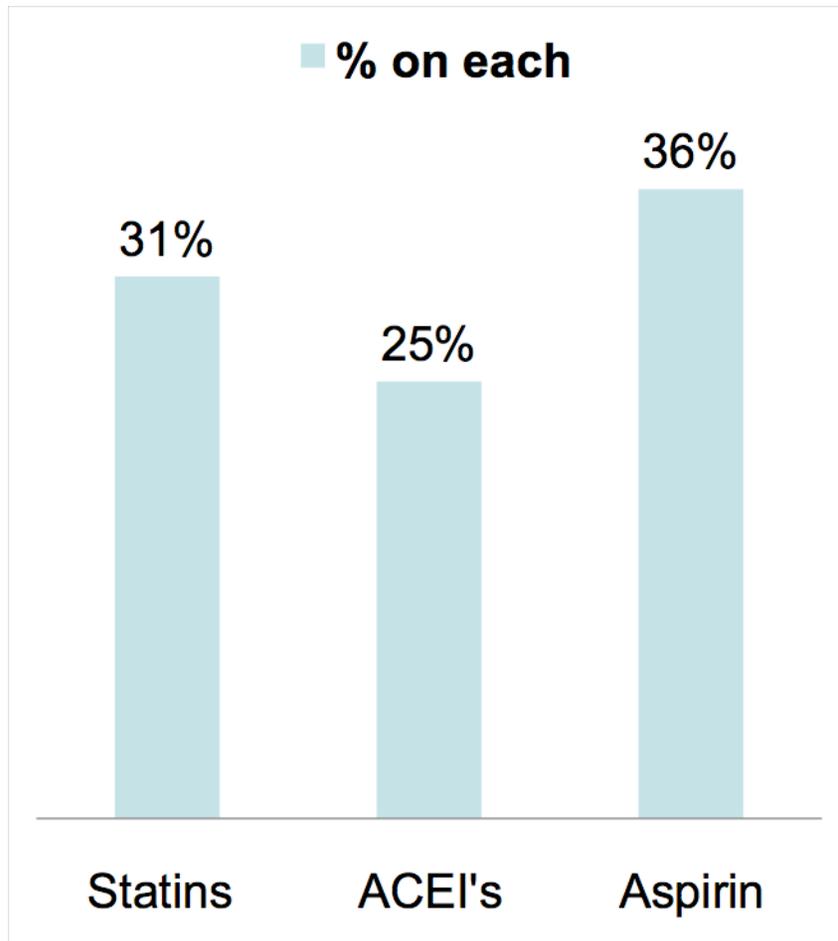


21

# CHAMP Study: Clinical Events for the First Year After Discharge for Acute MI

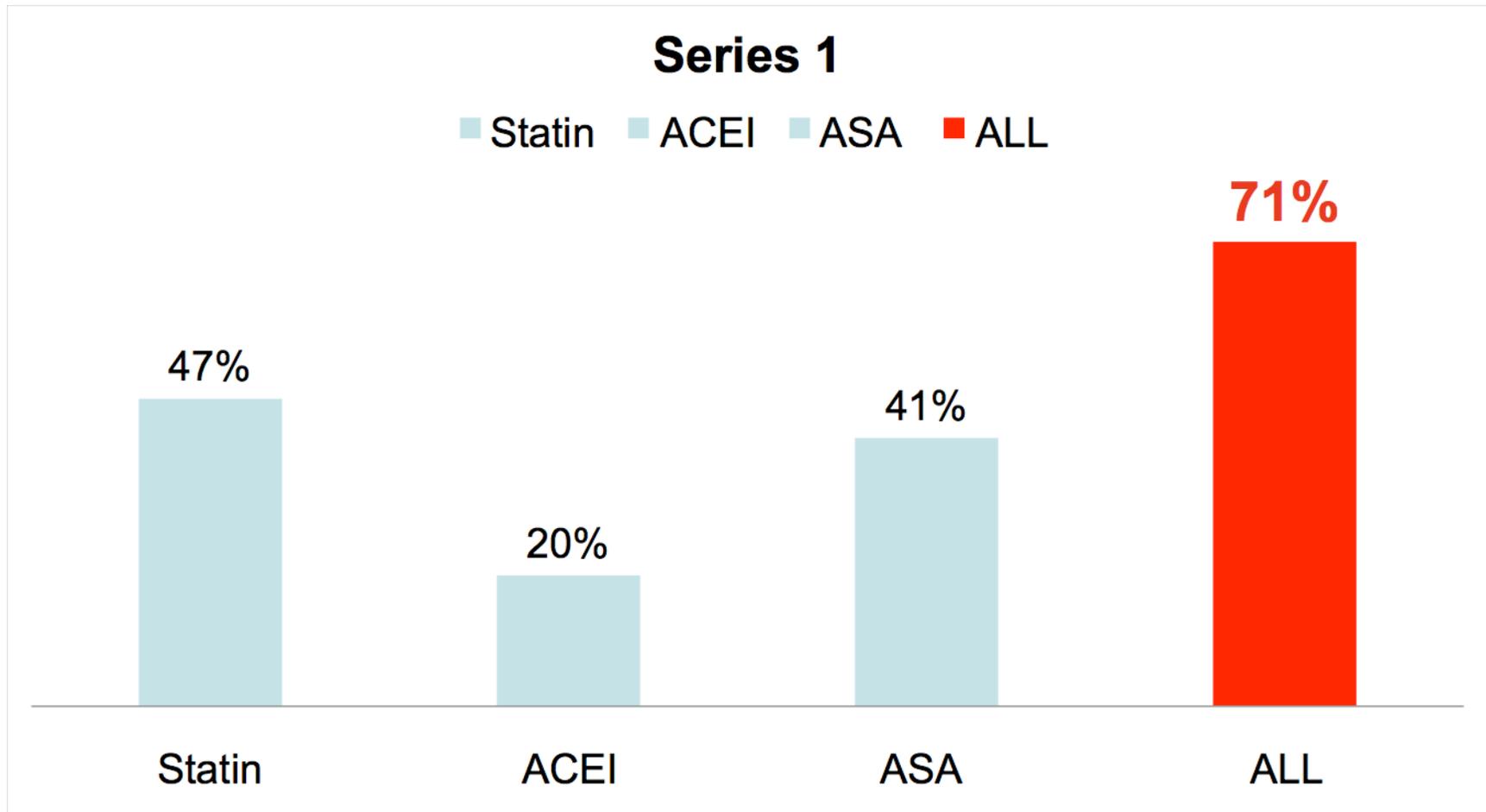


# NHANES : to 2004 7,458 Periph Art Dis pts, ~70% Without CVD



Slide 23

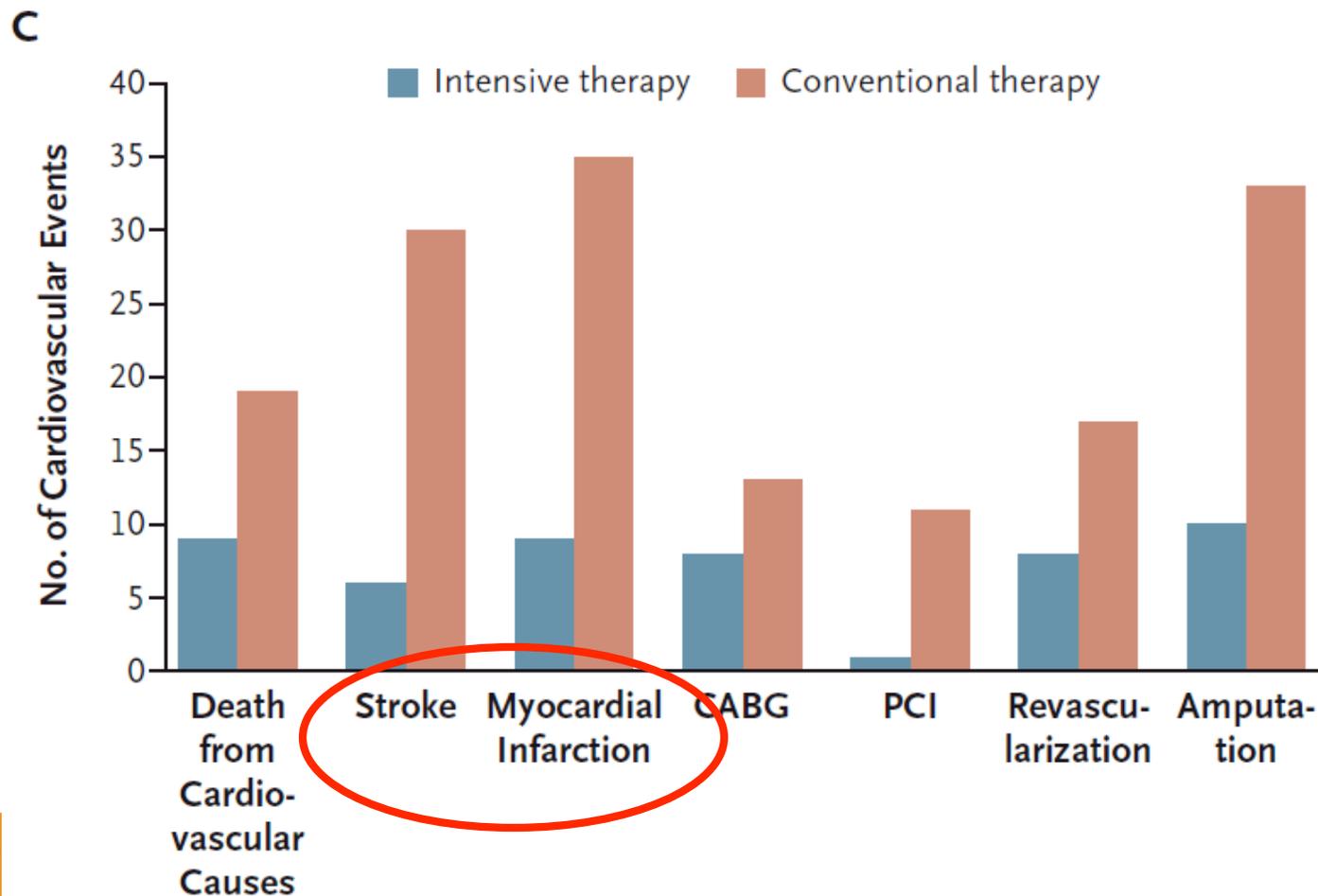
# UK 13,029 Pts with 1<sup>st</sup> MI decr death c/w matched controls not on Meds



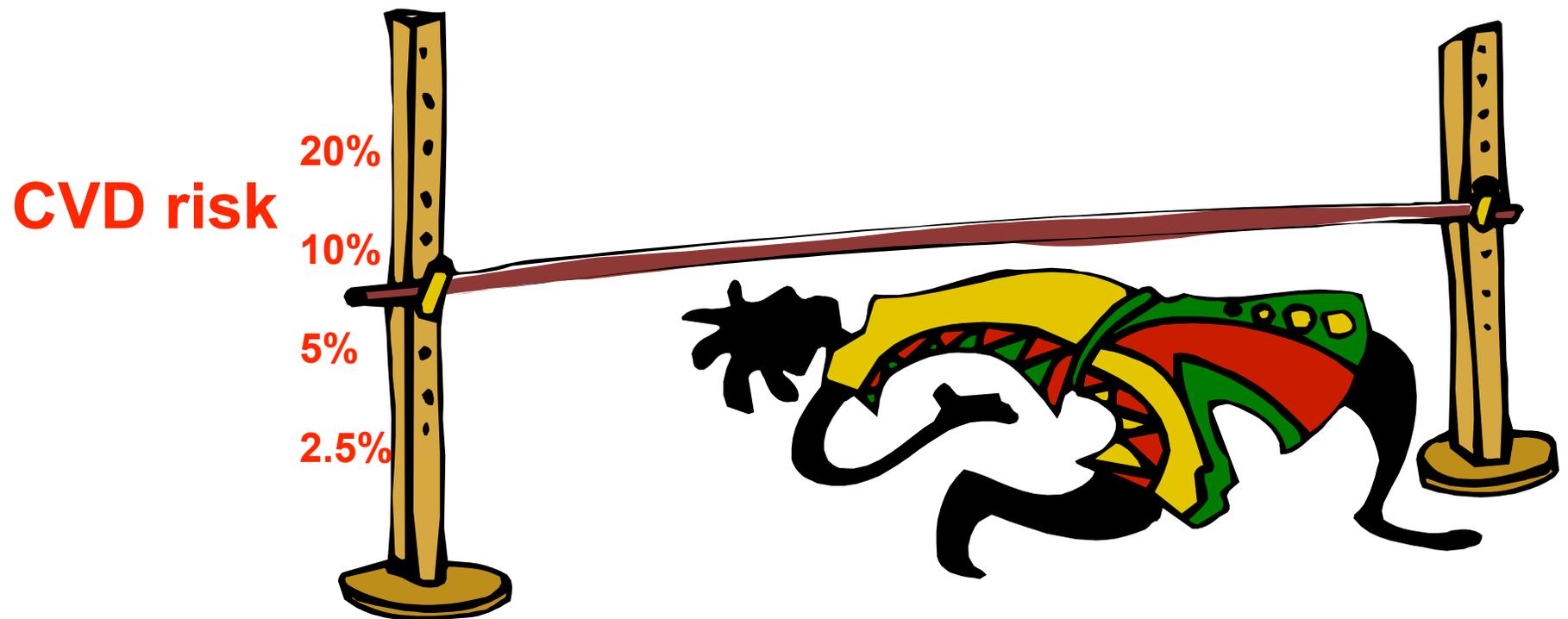
Slide 24

# Steno 2 T2DM w Proteinuria Showed ~60-80% Drop in MI's & Strokes after 13.3 Yrs

ACE/ARB 87% Statins 82% ASA 76% & A1C <8, bb & diuretics if bp high



# But in treating CVD risk “How Low Can You GO!”



Slide 26

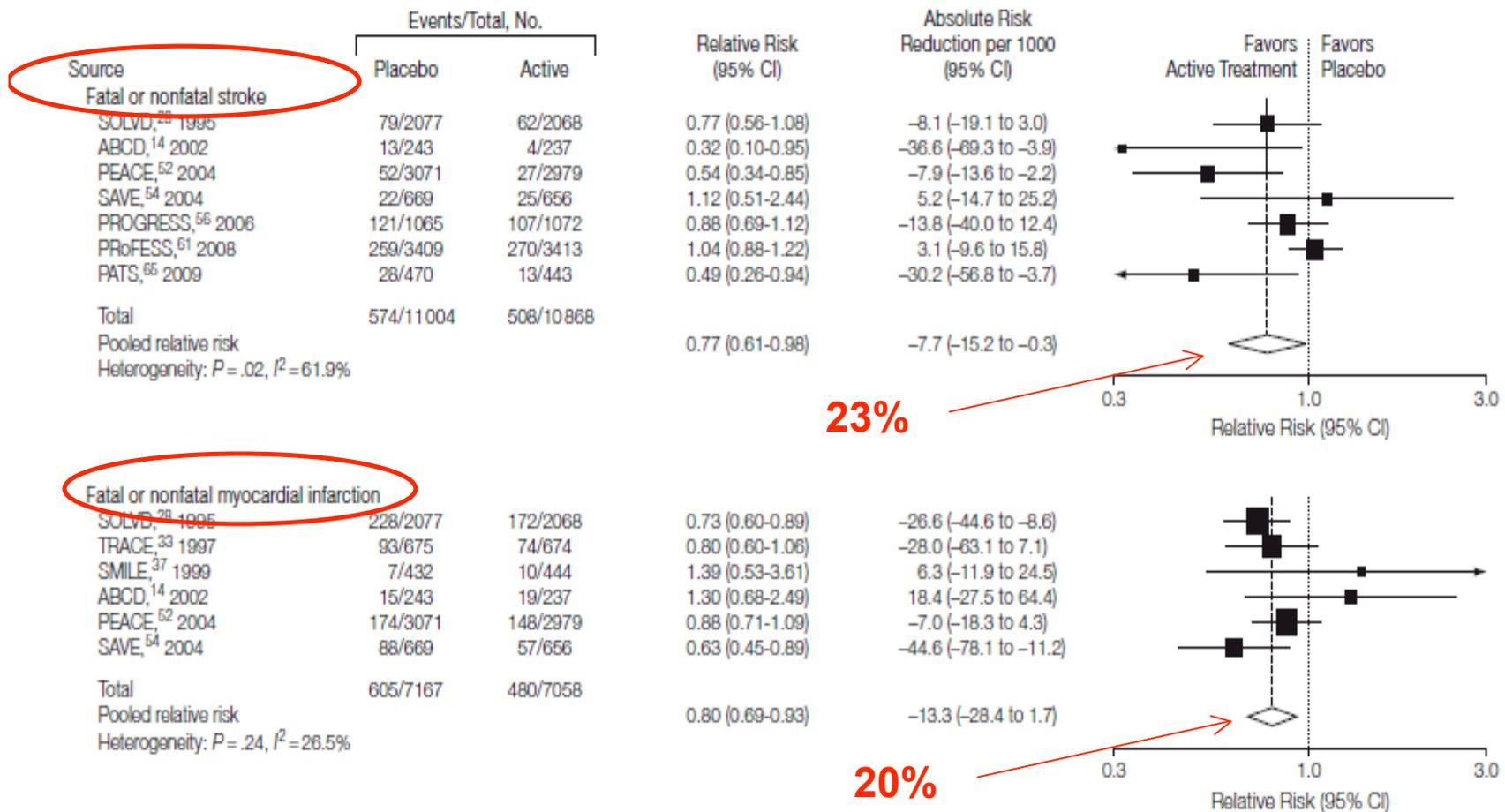
# Why Treat Hi CVD Risk Pts, Not Hi Biomarker LDLc and BP?

- Does therapy decrease with “normal” levels of biomarkers?
  - Are there many people at low levels of that may benefit?
- Are we missing some that have high levels of BP & lipids, but don't come to us?

Slide 27

# Anti HTN drugs Decreased CVD in Normotensive Pts with CVD Event...

**Figure 2.** Pooled Relative Risks and Absolute Risk Reductions for Fatal or Nonfatal Stroke, Myocardial Infarction, and Congestive Heart Failure and Composite Cardiovascular Disease Outcomes

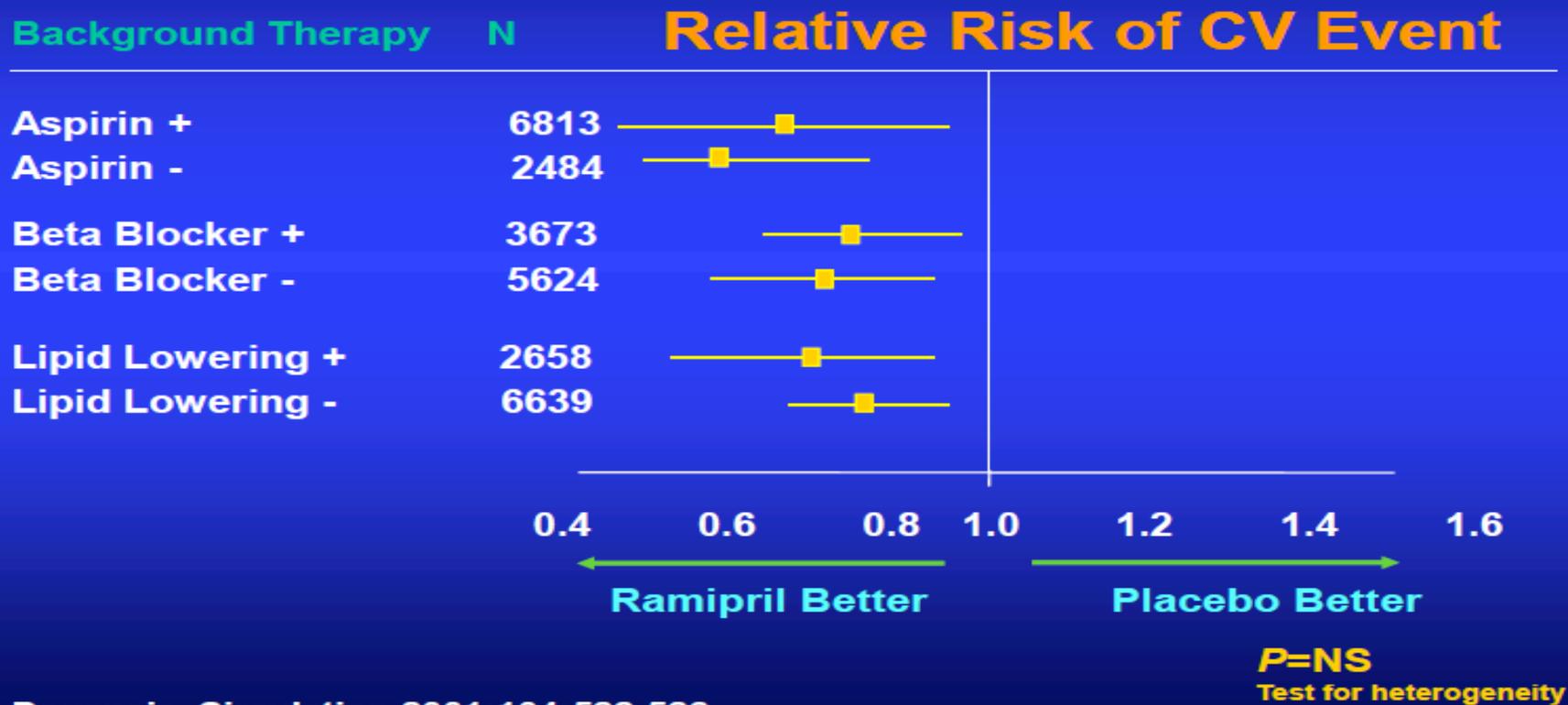


23%

20%

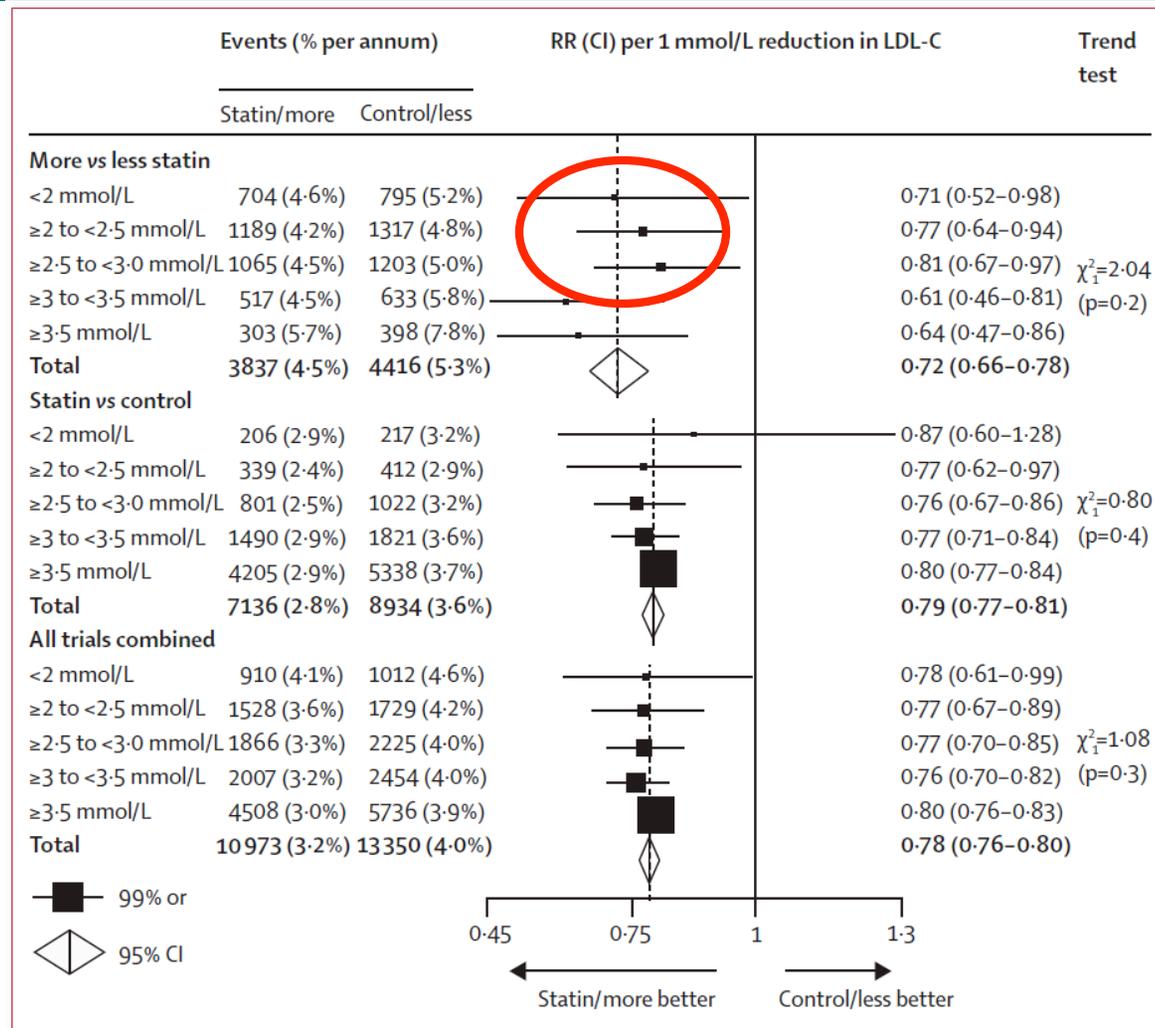
# ACEI's Are Additive in Benefit to ASA & Statins...

**ACEI Therapy is Additive to Other Cardioprotective Therapies in Patients with Atherosclerosis or Diabetes**



Dagenais Circulation 2001;104:522-526.

# Lowering LDL-C reduces CVD events across the range of LDL-C levels



# Statin adverse events

## ➤ Excess risk of myopathy

- 0.5 per 1000 statin-treated persons over 5 years
  - Higher with simvastatin 80 mg (lower doses in Asians)
- 5-year NNH = 2000

## ➤ Excess risk of hemorrhagic stroke/1 mmol/L reduction in LDL-C

- 0.5 per 1000 statin-treated persons over 5 years
  - Might be higher in populations at ↑risk hemorrhagic stroke (eg Asian)
- 5-year NNH = 2000

CTT Collaborators. Lancet 2012; 380: 581-590

# Statin adverse events

## ➤ Excess risk of new diabetes

- 5 per 1000 statin-treated persons over 5 years
  - Meta-analysis of mostly moderate intensity statin therapy
  - 5-year NNH = 200
- 15 per 1000 statin-treated persons over 5 years
  - 54 per 8901 statin-treated persons over 2 years-  
Rosuvastatin 20 mg
  - All cases occurred in those with baseline impaired fasting glucose
  - 5-year NNH = 66

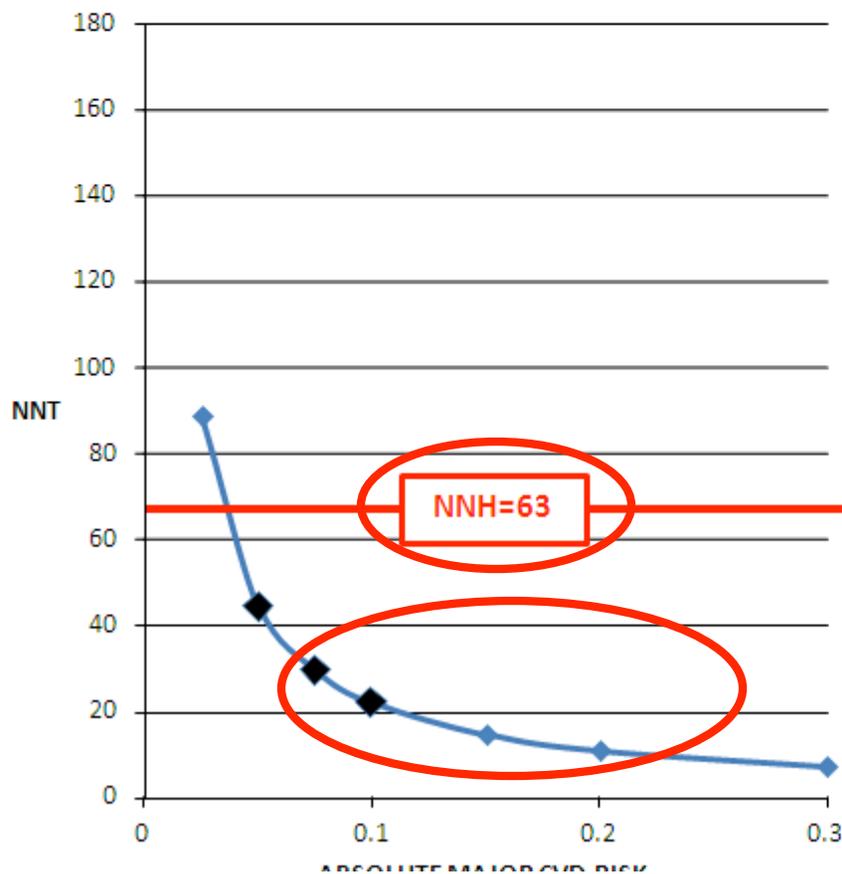
Sattar et al. Lancet 2010; 375: 735-742; Ridker Lancet 2012; 380: 565-571

# Statins for primary prevention 5-10% 5-year major CVD risk

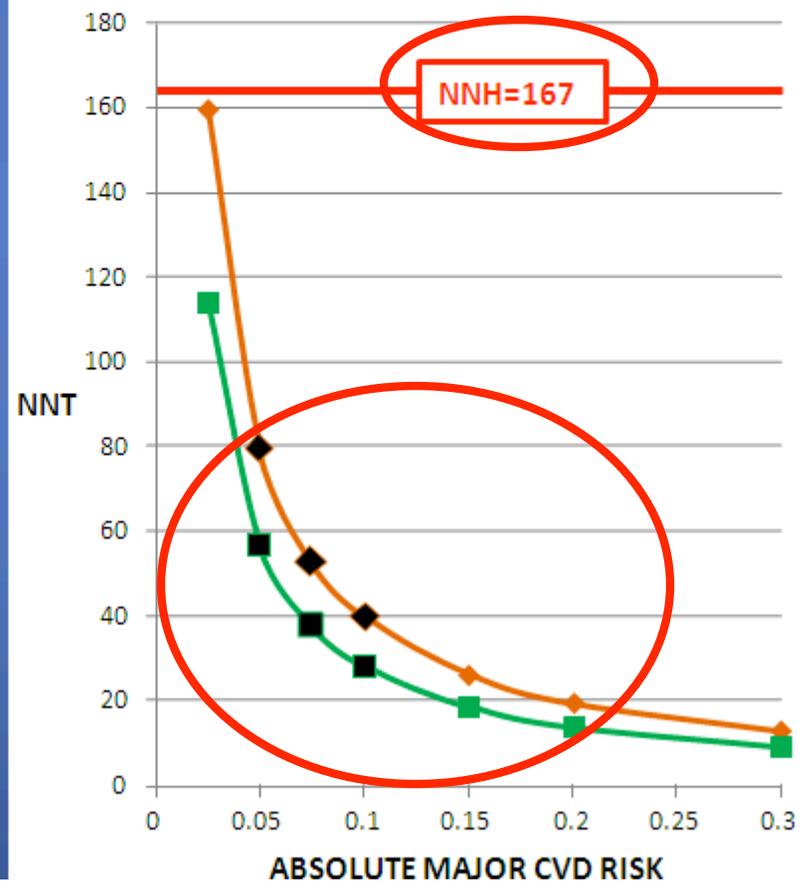
## Major CVD risk reduction benefits >> Adverse effects

Number-needed-to-treat (NNT) to prevent one major CVD event by level of absolute major CVD risk compared to number-needed-to-harm (NNH) over 5 years

### High intensity statin (RRR 45%)



### Low to moderate intensity statin (RRR 25% & 35%)



# In Conclusion

- Treating people with high risk for CVD is more effective than treating high BP or lipids
- Treating with more than statins is more than twice as effective as increasing statin potency or dose
- Combining treating people with over 5% CVD risk with a bundle of ACEI Statin and optionally ASA is so effective it should be implemented now

➤ Questions, Comments or Concerns?

Slide 35

# For More Information:

## Jim Dudl, MD

- National Clinical Lead, ALL Project, Kaiser Permanente Care Management Institute
- [Jim.R.Dudl@kp.org](mailto:Jim.R.Dudl@kp.org)

# I thought Wt Loss & Ex did 75% of benefit, why are we jumping to meds?

- Look Ahead ~5,000 T2DM pts f/u 11 yrs
- “Look AHEAD found that people who are obese and have type 2 diabetes can lose weight and maintain their weight loss with a lifestyle intervention, although it.....
- “did not reduce the number of cardiovascular events”.

NIH News, October 19, 2012 Contact: [Amy Reiter](#)\_301-496-3583

Slide 37