NCEP ATP III Guideline

- Update and their application to the real world

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Talking about…

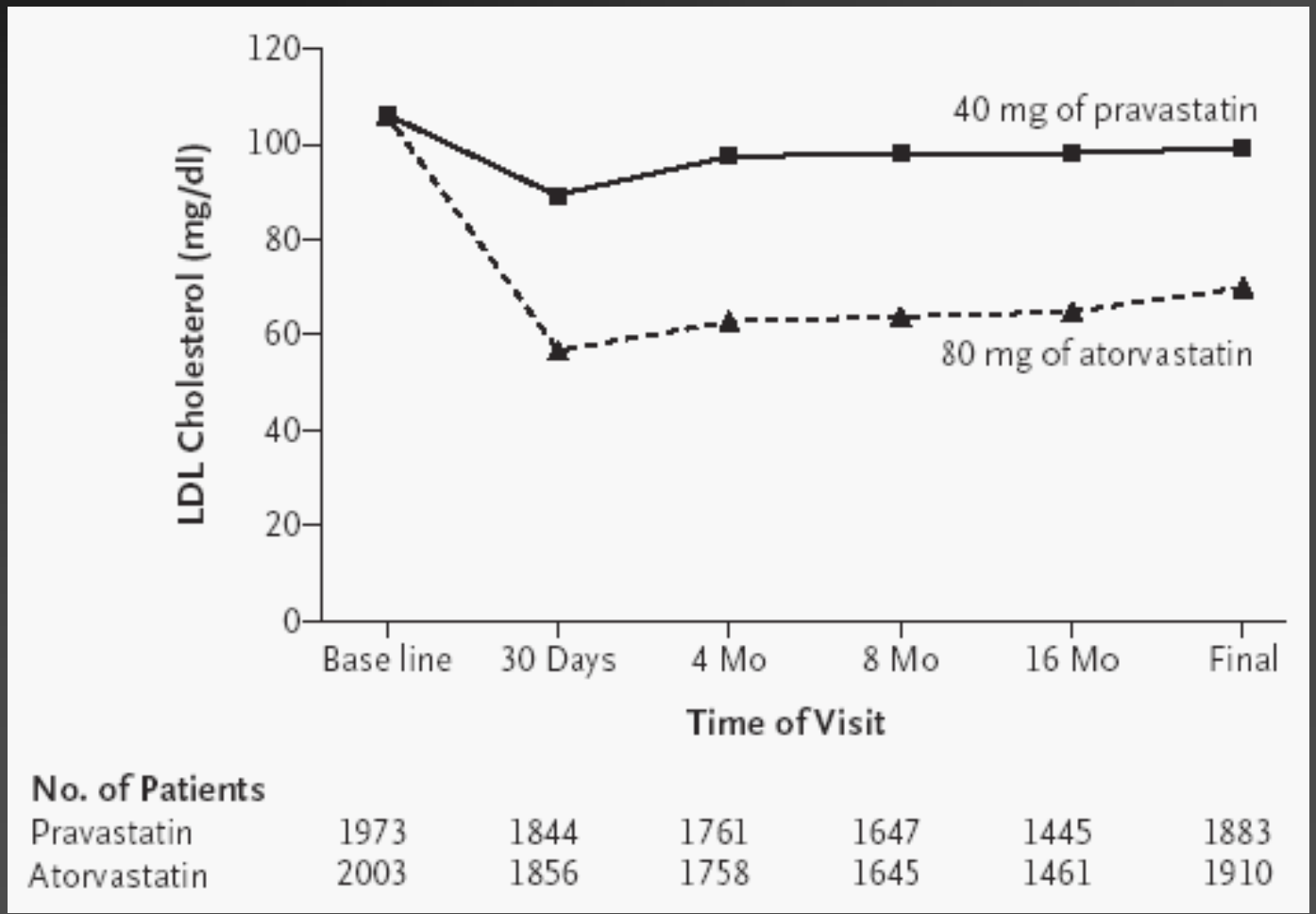
- ‘Ideal?’ world
  - 2004 Update in NCEP ATP III
- ‘Real’ world
  - Treatment gap
  - What about low-risk?

Very high-risk

- Who?
  - Known coronary artery disease, stroke, peripheral artery disease

    plus
  - ACS
  - Metabolic syndrome
  - Multiple major risk factors, esp DM and smoking, severe or poorly controlled
- LDL goal < 70 mg/dL
  - (July 12, 2004 in Circulation)

PROVE-IT



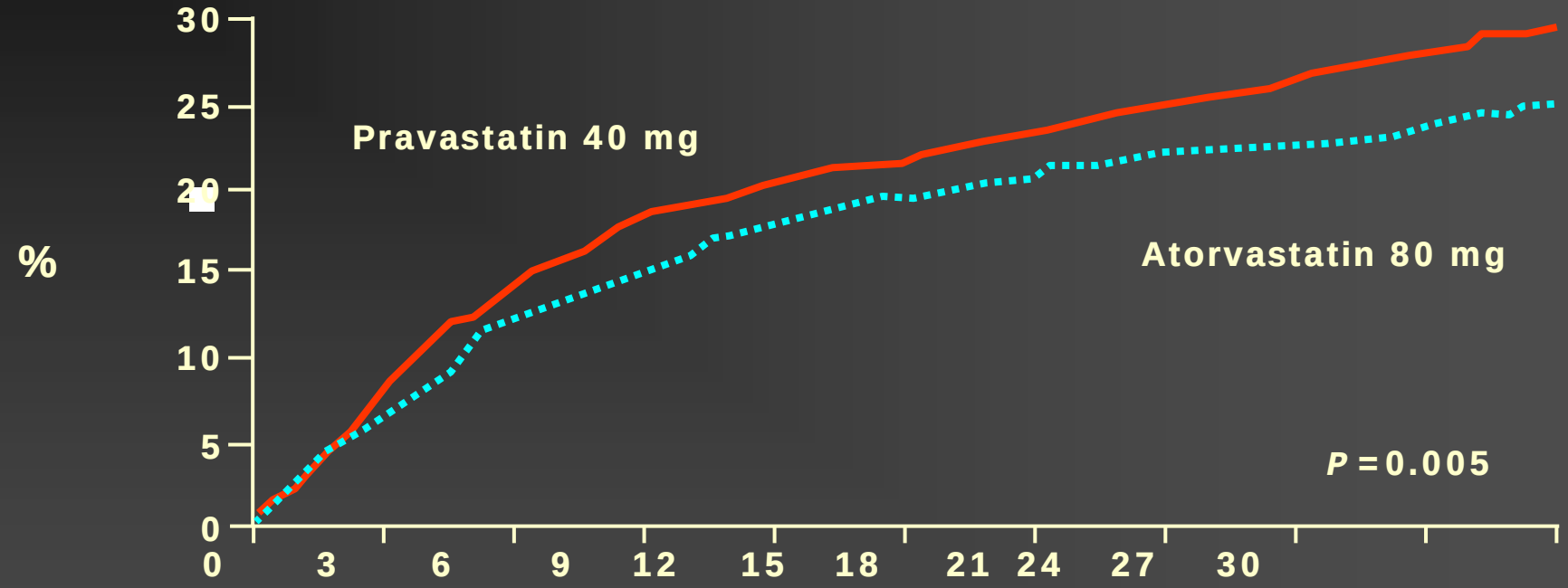
No. of Patients						
Pravastatin	1973	1844	1761	1647	1445	1883
Atorvastatin	2003	1856	1758	1645	1461	1910

LDL 106mg/dL

95 mg/dL

62 mg/dL

PROVE-IT: Primary Composite End Point*



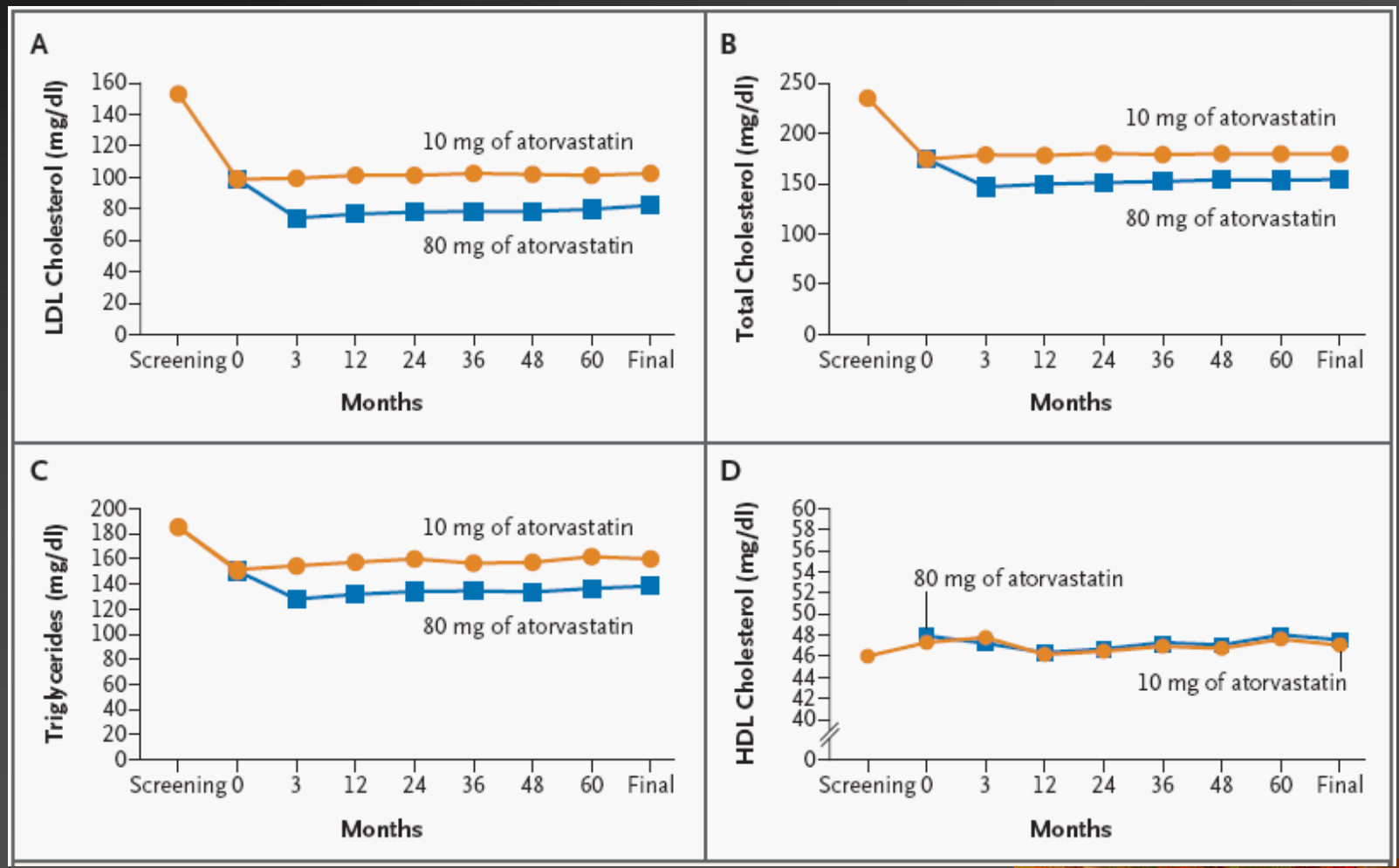
No. at risk						
Pravastatin	2,063	1,688	1,536	1,423	810	138
Atorvastatin	2,099	1,736	1,591	1,485	842	133

PROVE-IT=Pravastatin or Atorvastatin Evaluation and Infection Therapy

*Death or major cardiovascular event

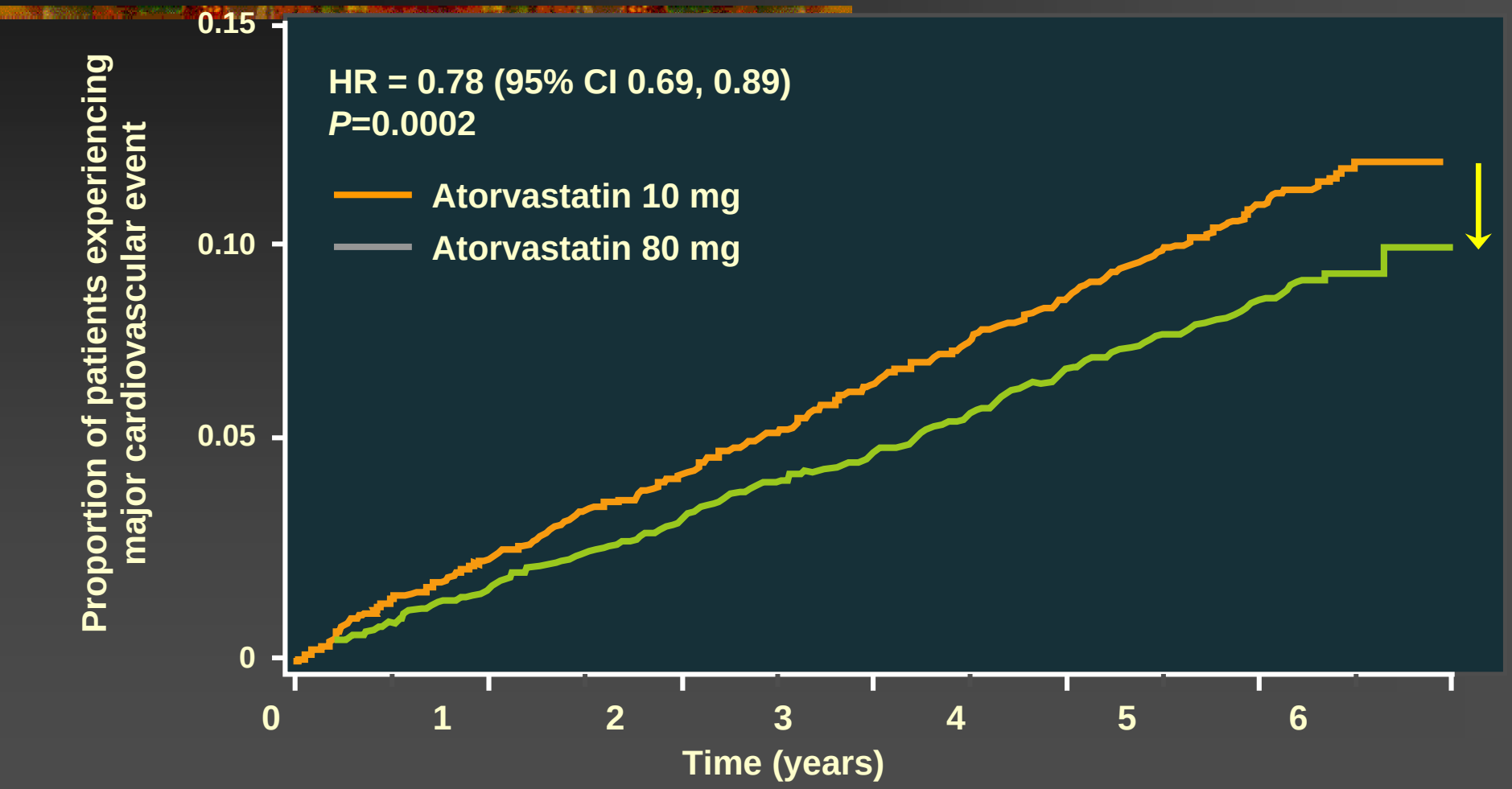
Cannon CP et al. *N Engl J Med*. 2004;350:1495-1504.

Treating to New Targets (TNT) – lipid profile change



N Engl J Med 2005;352.

Primary Efficacy Outcome Measure: Major Cardiovascular Events*



LaRosa JC, *et al.* [illegible] 2[illegible]352

Moderately high-risk

- Who?
  - Without clinical vascular disease
  - With at least 2 major risk factors
  - 10-20% estimated 10-year risk
- LDL goal was < 130 mg/dL but <100 mg/dL is also an option is significant proportion of this group.
- Additional option for drug Tx at 100-129 mg/dL in selected groups

Who has more risk?

- Older subjects
- Severe risk factors
- Metabolic syndrome
- ‘Emerging’ risk factors
  - CRP > 3
  - Coronary calcium > 75 percentile

ATP III: Additional CHD Risk Factors

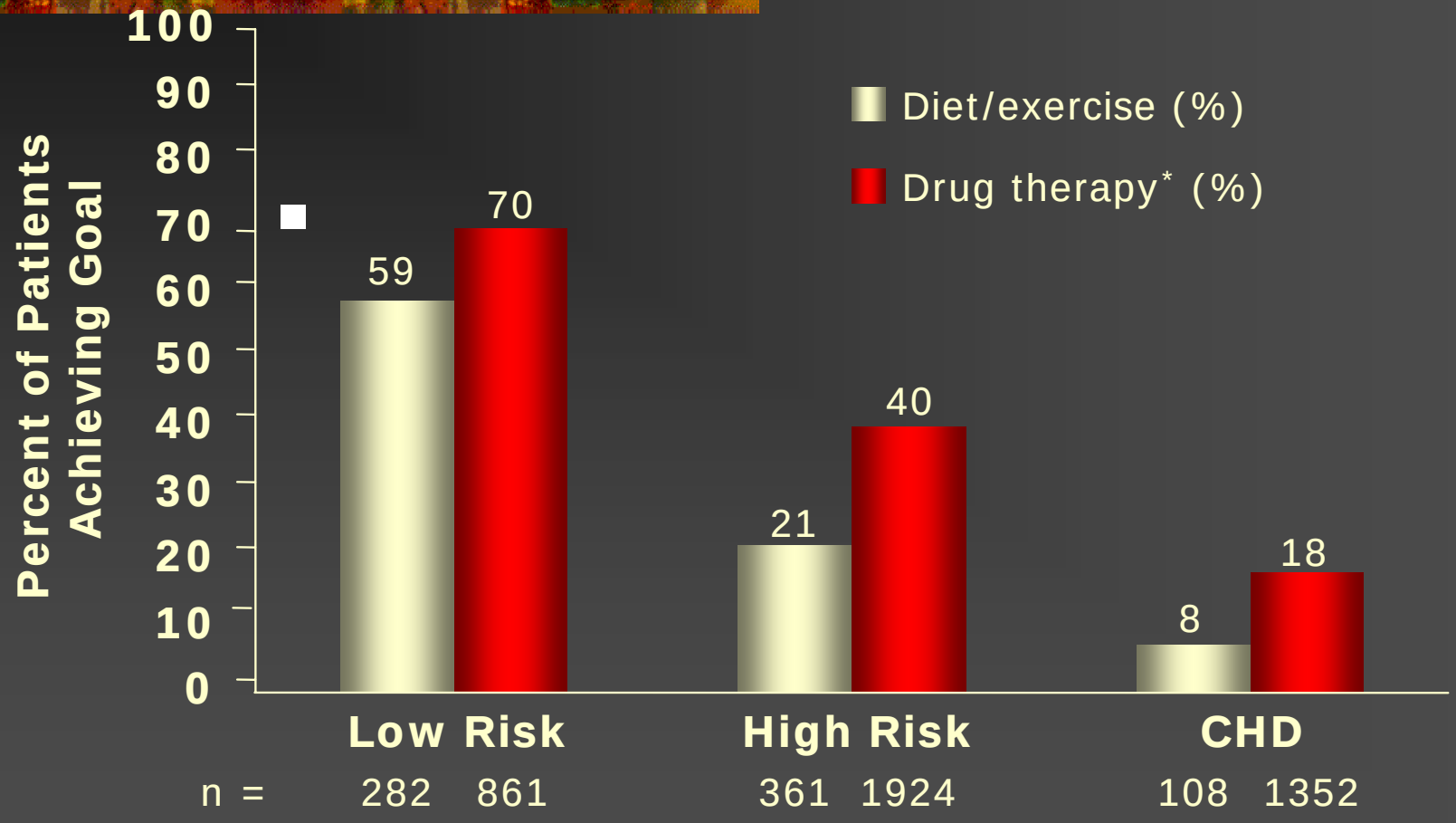
- **Life-habit risk factors: targets for intervention; not used to set lower LDL-C goal**
  - obesity
  - physical inactivity
  - atherogenic diet
- **Emerging risk factors: can help guide intensity of risk-reduction therapy; do not categorically alter LDL-C goals**
  - lipoprotein(a)
  - impaired fasting glucose
  - subclinical atherosclerotic disease
  - homocysteine
  - prothrombotic and proinflammatory factors

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. *JAMA*. 2001;285:2486-2497.

Summary of NCEP ATP III update

Risk Category	LDL-C Goal	Initiate TLC	Consider Drug Therapy**
High risk: CHD* or CHD risk equivalents† (10-year risk >20%)	<100 mg/dL (optional goal: <70 mg/dL)‖	≥100 mg/dL#	≥100 mg/dL†† (<100 mg/dL: consider drug options)**
Moderately high risk: 2+ risk factors‡ (10-year risk 10% to 20%)§§	<130 mg/dL¶	≥130 mg/dL#	≥130 mg/dL (100–129 mg/dL; consider drug options)‡‡
Moderate risk: 2+ risk factors‡ (10-year risk <10%)§§	<130 mg/dL	≥130 mg/dL	≥160 mg/dL
Lower risk: 0–1 risk factor§	<160 mg/dL	≥160 mg/dL	≥190 mg/dL (160–189 mg/dL: LDL-lowering drug optional)

Many Patients Are Not Reaching Their LDL-C Goal



*Included statins (fluvastatin, lovastatin, pravastatin, simvastatin), gemfibrozil, bile acid sequestrants, niacin, psyllium fiber, or combination drug therapy

Current Status of Treatment for Hyperlipidemia & Gap to Target Goal in Patients with CAD in Korea

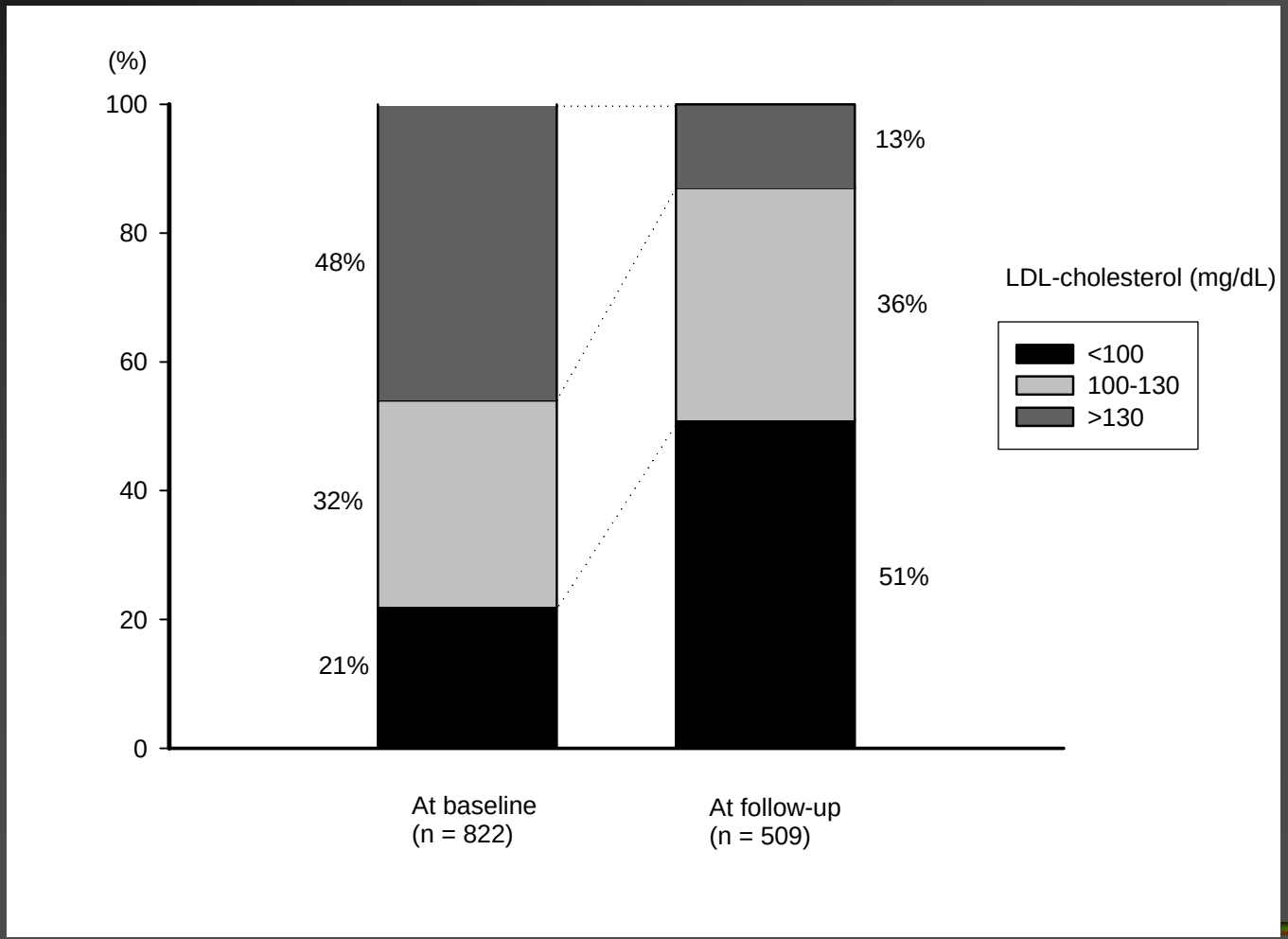
성지동, 김상현, 김영대, 백상홍, 안영근, 임도선,
조홍근, 채성철, 한기훈, 김효수

(In Press)

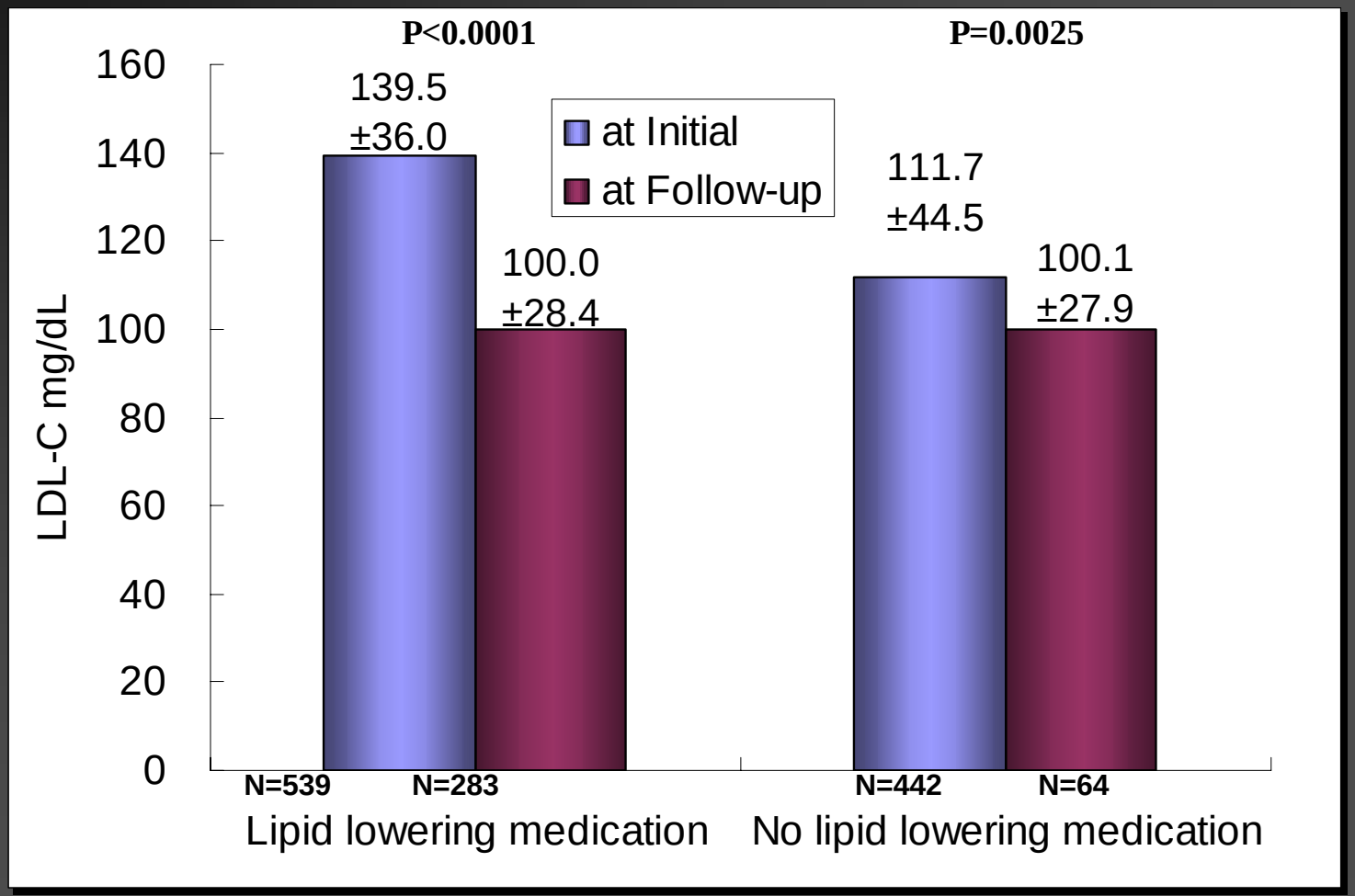
Investigators

Center	Investigator	Total	
		n	(%)
경북대병원	채성철	93	(8.87)
고대안암병원	임도선	150	(14.31)
동아의대	김영대	100	(9.54)
보라매병원	김상현	100	(9.54)
삼성서울병원	성지동	100	(9.54)
서울대병원	김효수	106	(10.11)
성빈센트병원	백상홍	100	(9.54)
아산병원	한기훈	101	(9.64)
연세의료원	조홍근	98	(9.35)
전남대병원	안영근	100	(9.54)
Total		1,048	(100.00)

LDL-C Distribution in Whole Patients at Initial & F/U Point



LDL-C Reduction
with or without Lipid Lowering Medication



Korean standard(?) for cholesterol lowering

- Without cardiovascular diseases: > 250 mg/dL
- With cardiovascular diseases: > 220 mg/dL
- Rationale?
  - Evidence?
  - Cost-effectiveness?

Economical consideration

Study	Persons	Duration	Statin Drug (dose/d)	Baseline LDL-C (mg/dL)	LDL-C Change	Major Coronary Events	Revascu-larization	Coronary Mortality	Total Mortality
WOSCOPS	6595	4.9 yrs	Pravastatin 40 mg	192	-26%*	-31%*	-37%*	-33%*	-22%*
AFCAPS/ TexCAPS	6605	5 yrs	Lovastatin 20/40 mg	150	-25%*	-37%*	-33%*	NS	NS

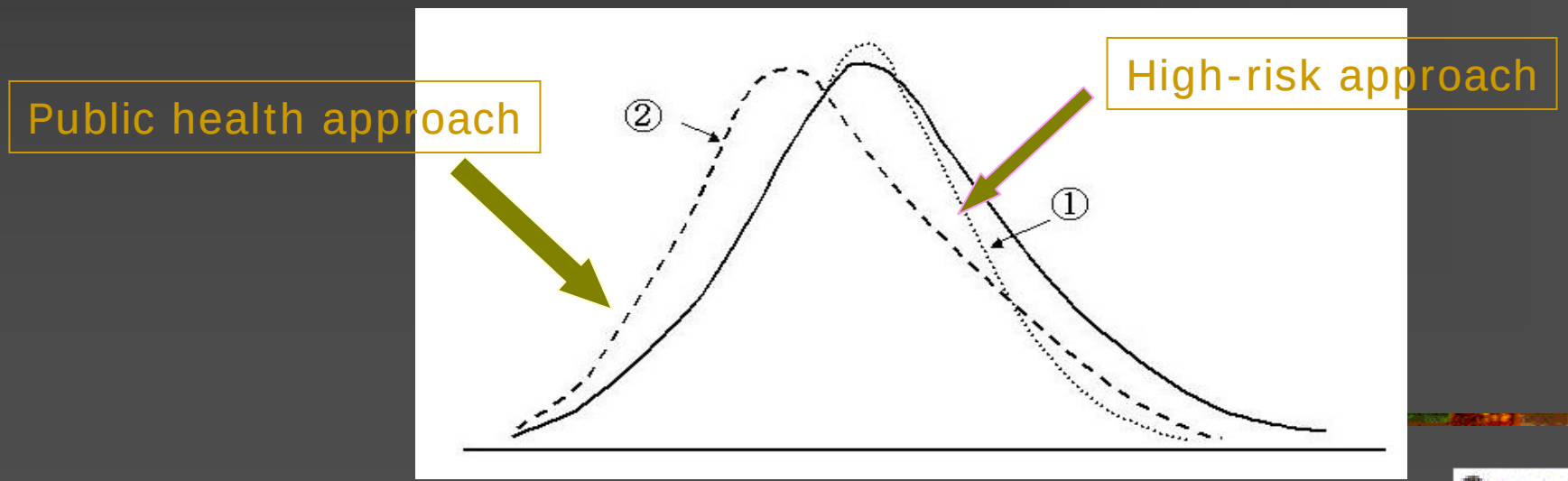
* Changes significant at $p<0.05$ or lower.

- According to ATP-III guideline, majority of people who are eligible to AFCAPS/TexCAPS would not be pharmacologically treated, despite expected risk reduction. Why?

Cost-effectiveness

Public health vs. High-risk approach

- High-risk group has high incidence rate. Intervention in this group is highly cost-effective.
- However, *majority* of cardiovascular disease occurs in less-than-high-risk group because of absolutely larger sized of this population



What about low-risk population?

- Three possible strategies
  - ‘Return to hunter-gatherer’
  - ‘Tap water statin-ization’
  - ‘Pinpoint fortune teller’

‘Return to hunter-gatherer’ strategy

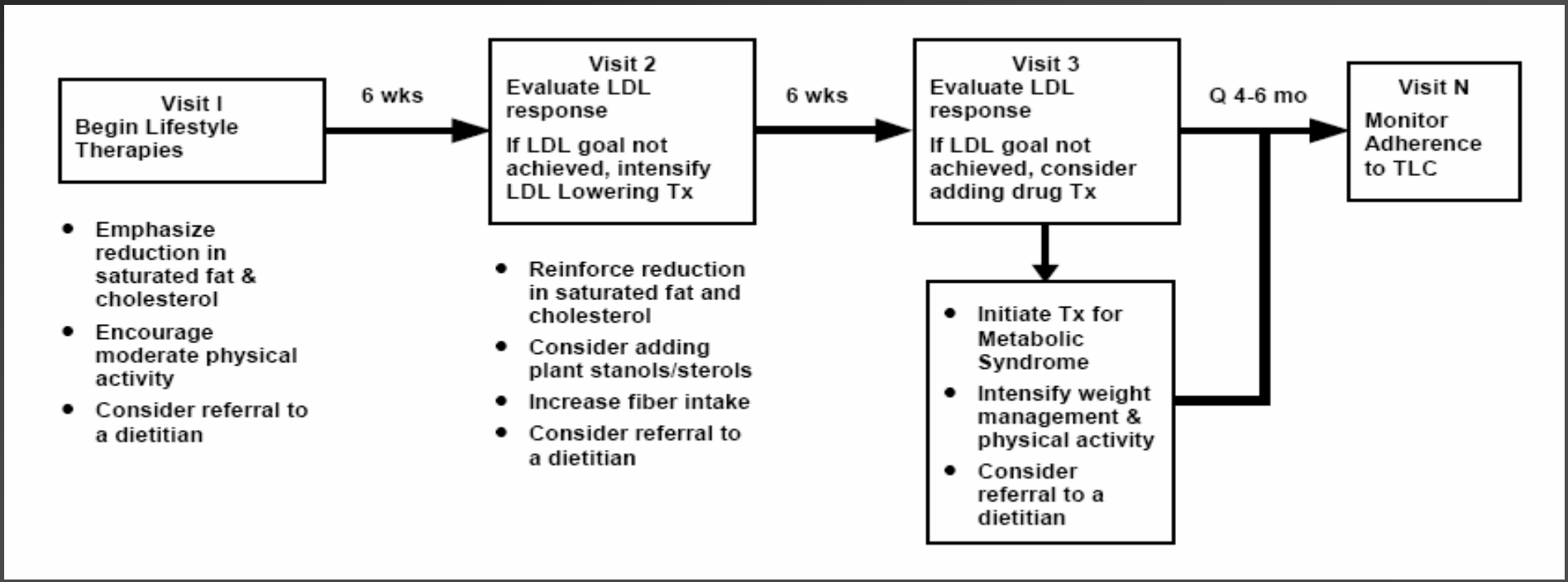
- Hunter-gather’s total cholesterol ≈ 110mg/dL
- No BP elevation
- Almost free of atherosclerosis-related diseases

Essential Components of Therapeutic Lifestyle Changes (TLC)

Component	Recommendation
LDL-raising nutrients	
Saturated fats*	Less than 7% of total calories
Dietary cholesterol	Less than 200 mg/day
Therapeutic options for LDL lowering	
Plant stanols/sterols	2 grams per day
Increased viscous (soluble) fiber	10–25 grams per day
Total calories (energy)	Adjust total caloric intake to maintain desirable body weight/prevent weight gain
Physical activity	Include enough moderate exercise to expend at least 200 Kcal per day

* *Trans* fatty acids are another LDL-raising fat that should be kept at a low intake

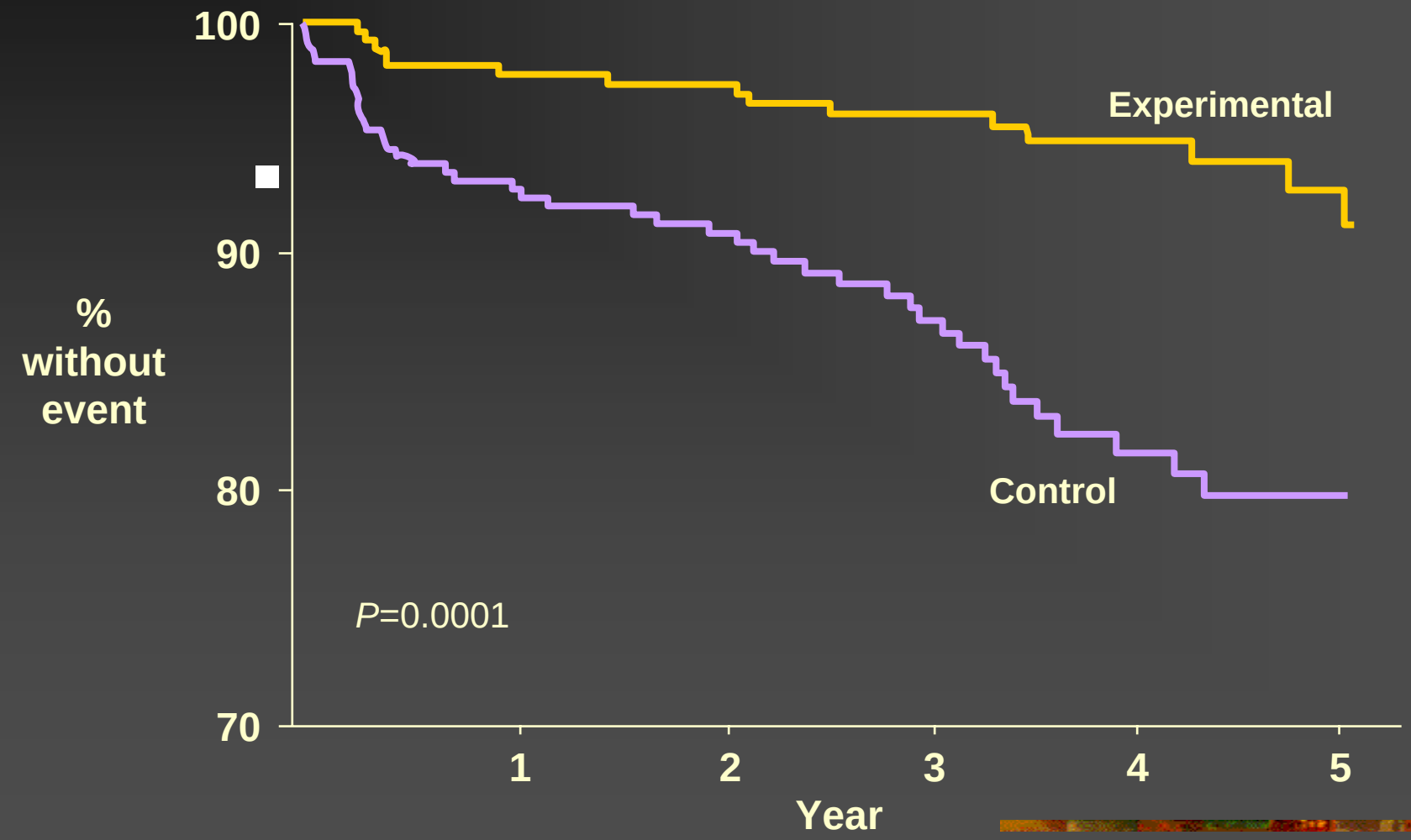
A Model of Steps in Therapeutic Lifestyle Changes (TLC)



Is it effective?

- 1 % reduction in saturated fatty acids intake will reduce serum cholesterol by about 2 %.
- DELTA study: reducing dietary saturated fatty acids from 15 percent of total calories to 6.1 percent of total calories. → 11% LDL lowering
- Meta-analysis of dietary trials (6356 individuals): decreased incidence of CHD by 24%

Lyon Diet Heart Study: Cumulative Survival Without Cardiac Death and Nonfatal MI

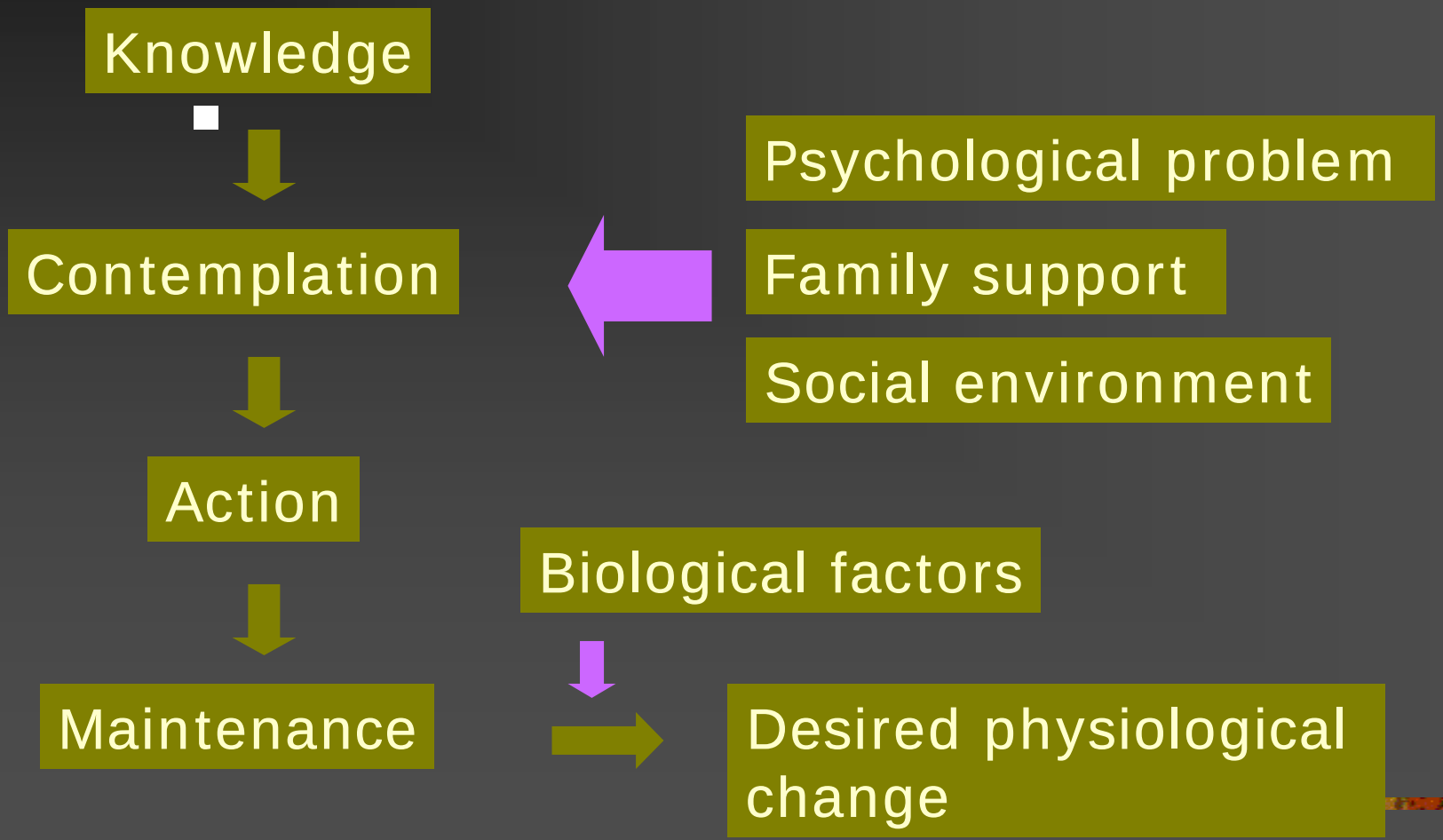


de Lorgeril M et al. *Circulation*. 1999;99:779-785.

Is it effective? - Yes

- Valuable in low-risk, mildly elevated LDL patients.
- Potentiate the effect of pharmacotherapy
- Lower the dose of LDL lowering drugs
- May help to increase adherence to drug treatment

Barriers to adherence



‘Tap water statin-ization’ strategy

- Pharmaceutical company’s dream come true??
- Unacceptibly big cost is the main problem.
- Inexpensive and safe food additives
- Reclassification of statin(s) to over-the-counter drug

OTC statin as a primary prevention strategy

- May 12, 2004, Zocor Heart-Pro (simvastatin 10 mg tab, Johnson & Johnson MSD Consumer Pharmaceuticals) was reclassified as category P (pharmacy only) OTC medicine in the UK.
- Sold to ‘moderate risk’ population
  - First-degree relatives (parent or sibling) with early history of CAD
  - Smoker, either current or in the past 12 mo
  - Overweight (defined as BMI 25) or truncal obesity (defined as waist in men 40 in, in women 35 in)
  - South Asian ethnicity, specifically Indian, Pakistani, Bangladeshi, and Sri Lankan
- Conern for high-risk persons who choose for low-dose self therapy

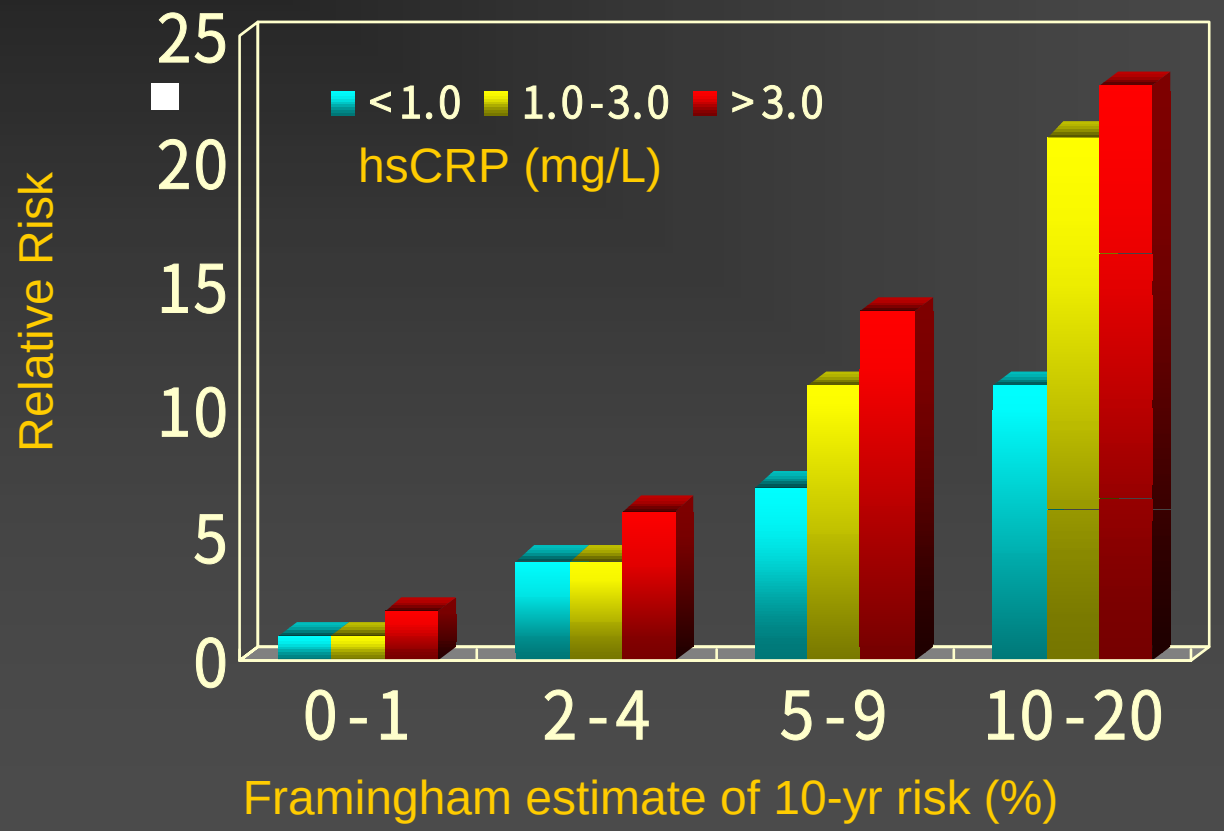
‘Pinpoint fortune teller’ strategy

- Risk assessment by conventional risk factors (Framingham score, etc) is quite useful but has its own limitations
- Is more *individualized* and accurate risk prediction possible?

Emerging risk factors or subclinical disease monitoring

- CRP
- Carotid IMT
- Coronary calcium scoring

CRP



Paul M Ridker et al, circulation 2004

Coronary calcium

- Detected by electron beam CT (EBCT) or multi-detector CT (MDCT)
- Accurate non-invasive estimates of coronary plaque burden
- Predictive of major coronary events
- Quick and convenient (no need for contrast)
- Excellent inter- & intra-individual reproducibility and short learning curve

Coronary calcium scores in various population

	SMC ■		Korean (Yun et al)		Japan (Aizawa et al)		American (wong et al)	
	M	F	M	F	M	F	M	F
<40	1.9	0.5			0.7	0	23.7	1.6
40-50	6.2	0.7	93.9	3.6	7.4	4.9	34.9	7.6
50-60	43.5	35.7	370.0	83.7	25.0	6.0	115.7	36.5
60-70	154.9	28.2	464.9	111.7	147.0	18.6	291.9	69.5
>70	1361.5	210	681.2	549.3	50.6	225.3	928.4	147.3

Conclusion

- Intensive LDL lowering with higher than conventional dose of statin is beneficial and should be considered in the very high-risk group.
  → However, Significant treatment gap exists in ‘real world’ practice, which warrants systematic effort to reduce it.
- Dilemma of cost-effectiveness is a problem in low risk population despite expected benefit of LDL lowering.
  → More refined strategy is needed.