

Introduction

Edwin L. Hemwall, PhD

Vice President

Worldwide Regulatory & Scientific Affairs

Johnson & Johnson – Merck Consumer Pharmaceuticals

Johnson & Johnson • **MERCK**

NDA: 21-213

- Nonprescription lovastatin 20 mg
- MEVACOR™ DAILY
- Indication: To help lower LDL “bad” cholesterol, which may prevent a first heart attack

Background

- July 2000: Joint Advisory Committee Review
 - Benefit of 10 mg dose not established
 - Statin OTC safety generally accepted
 - Consumer behavior needs further investigation
- August 2000: FDA withdraws official guidance that discouraged development of OTC cholesterol-lowering drugs

Background

- 2000 to Present: New OTC paradigm established and tested with input from FDA and academic experts
 - OTC dose increased to 20 mg per day; treatment to LDL-C goal
 - Primary prevention target population consistent with NCEP Guidelines (ATP III, May 2001)
 - CUSTOM Actual Use Study
 - 3000+ consumers evaluated OTC option
 - 1000+ used for up to 6 months
 - Comprehensive consumer support program

Key Topics for Discussion Today

- Can an OTC option enable consumers to have a greater role in the prevention of cardiovascular disease?
 - OTC target population and label eligibility criteria
 - Consumer behavior with regard to label benefit and safety directions
 - Role of MEVACOR™ Self-Management System and healthcare professional
 - Overall benefit / risk for lovastatin 20 mg OTC

Agenda

Introduction

Edwin L. Hemwall, PhD

Rationale for MEVACOR™ OTC

Richard Pasternak, MD

OTC Label and Self-Management System

Jerry Hansen, R.Ph.

Consumer Behavior

Robert Tipping, MS

Potential of MEVACOR™ OTC

Jerome Cohen, MD

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Rationale for MEVACOR™ OTC

Richard Pasternak, MD
Vice President

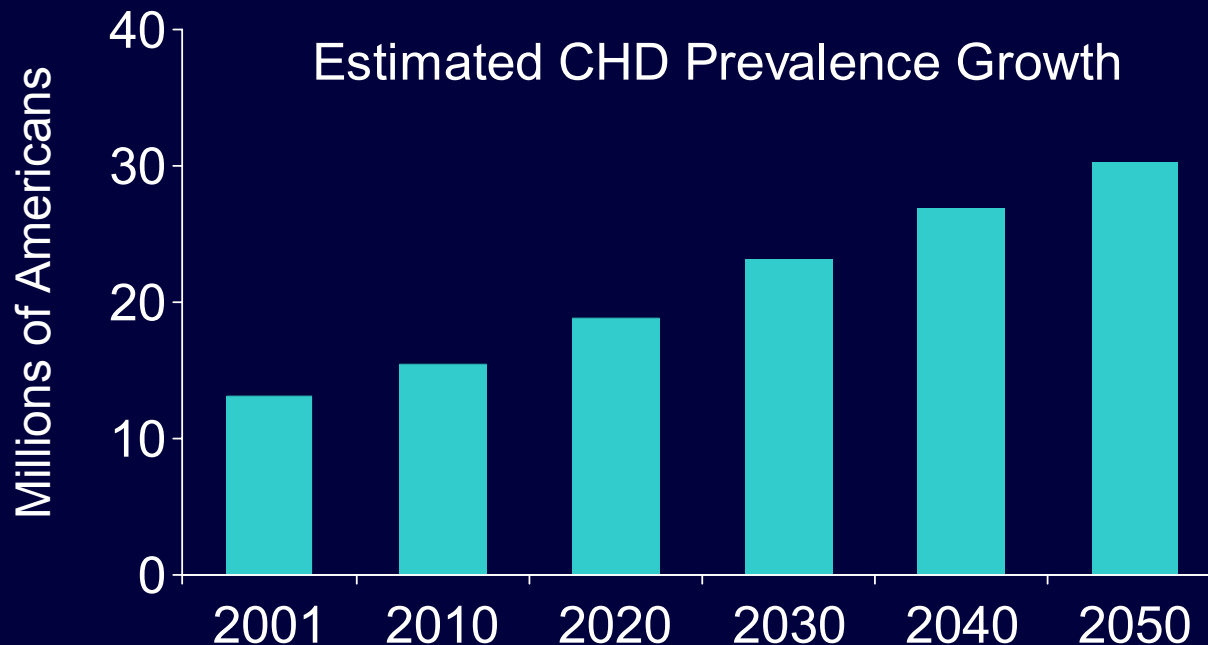
*Clinical Research Cardiovascular & Atherosclerosis
Merck Research Laboratories*

Rationale for MEVACOR™ OTC

- Growing cardiovascular public health problem
- Appropriate OTC target and product profile
- Opportunity to improve public health

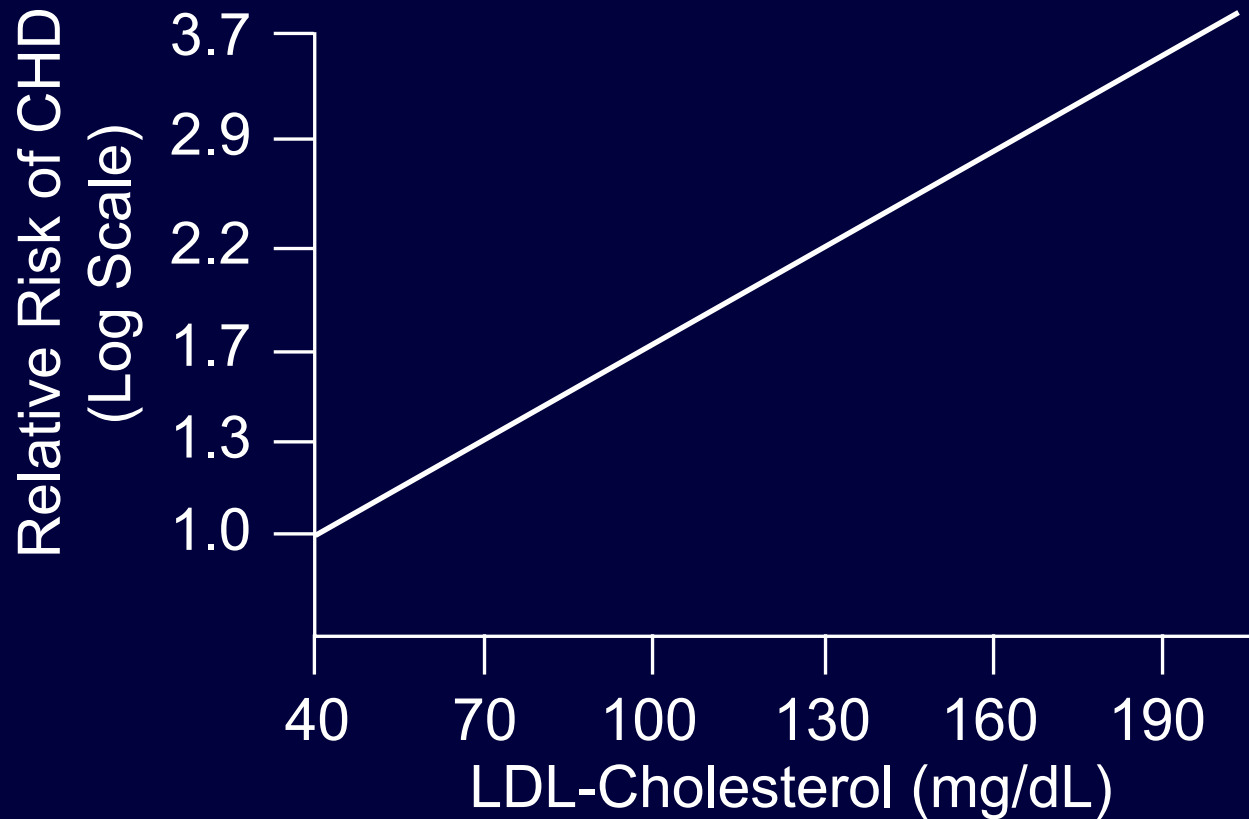
Growing Cardiovascular Public Health Problem

- CVD: The #1 cause of death in the United States*
 - Annual events
 - 1.2 million CHD events
 - Economic burden: \$133 billion for CHD alone



*AHA Heart Disease and Stroke Update 2004; Foot et al. *JACC* 2000; 35:5: 66B-80B.

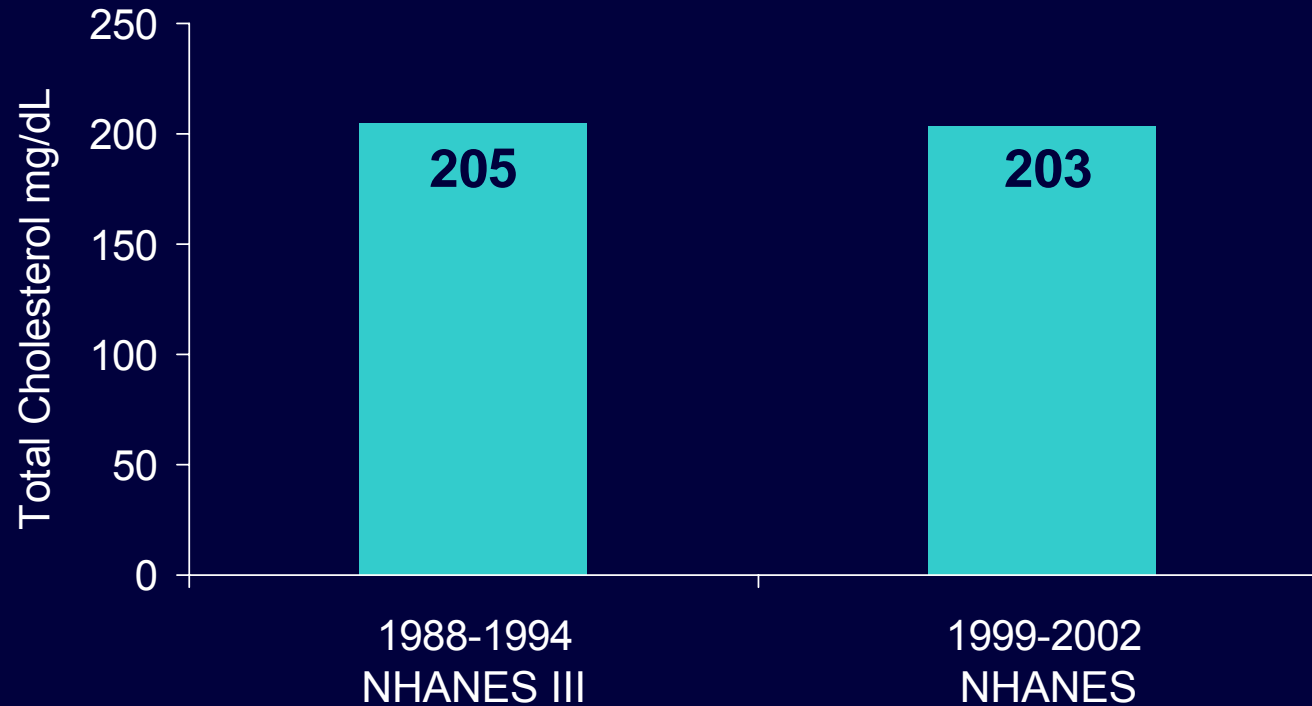
Importance of Cholesterol in Heart Disease Prevention



ATP III Update Grundy et al. *Circulation*: 2004.

Trends in Cholesterol Management

Mean Total Cholesterol Among US Adults*



Healthy People 2000 Goal: <200
Healthy People 2010 Goal: <197

*CDC/NCHS, *Health*, 2004, Table 68, pgs 239-240.

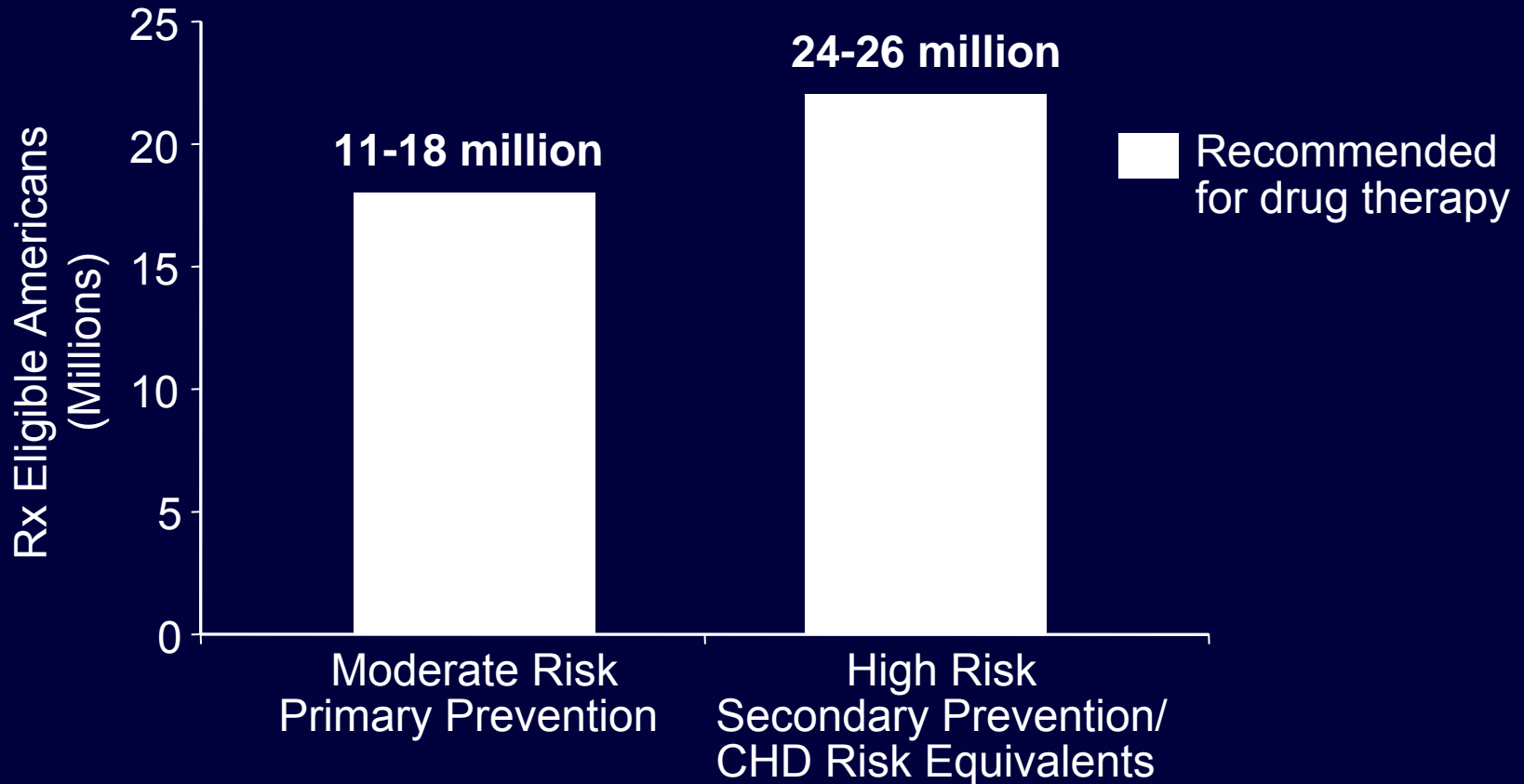
Current Status of Cholesterol Management

NHANES 1999-2000 (N = 4880)

	<u>Tested</u>	<u>Treated</u>
TC > 200 mg/dL or receiving Rx	70%	12%
TC > 240 mg/dL	72%	24%

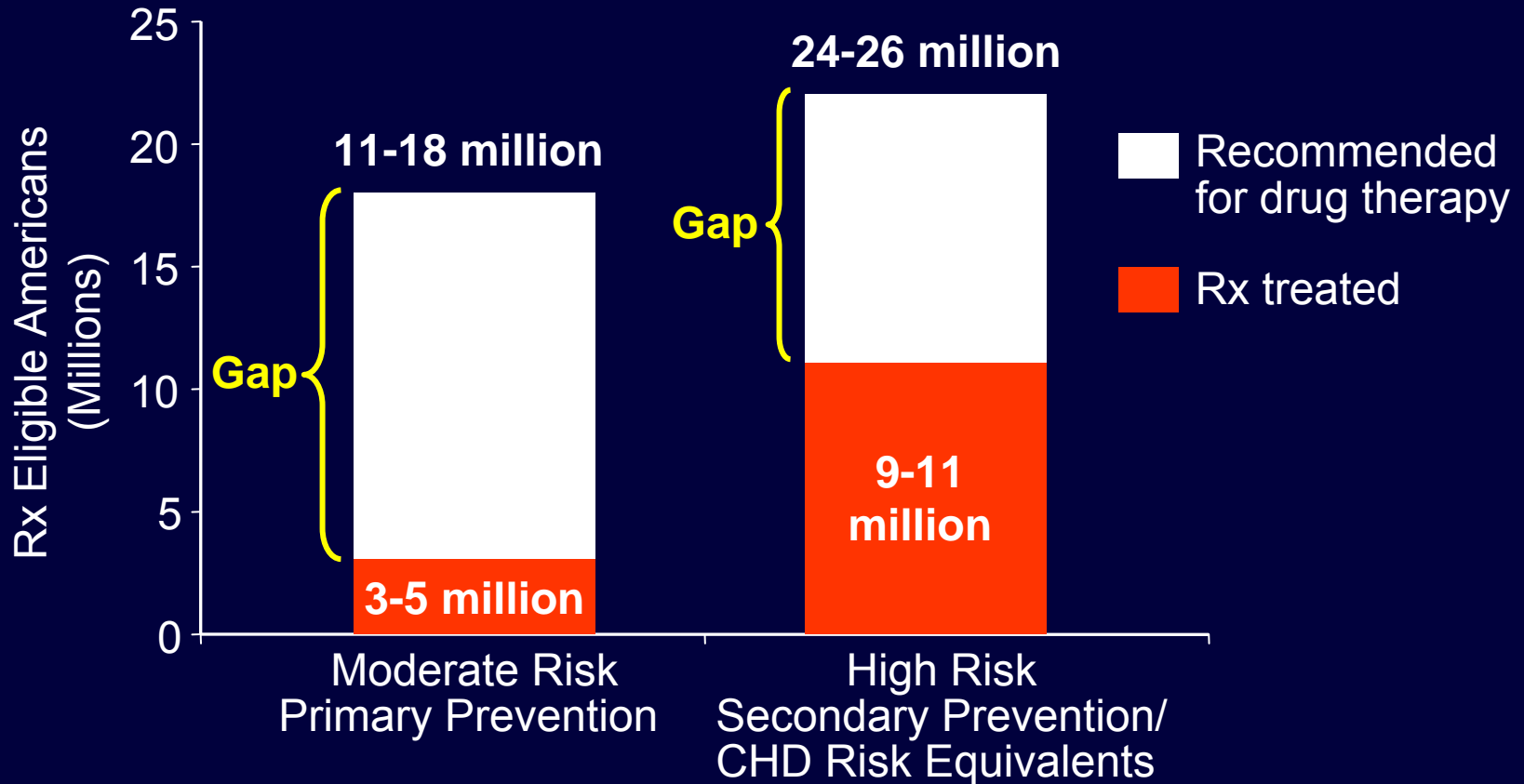
Ford et al. *Circulation* 2003; 107: 2185-89.

Need for Improved Treatment



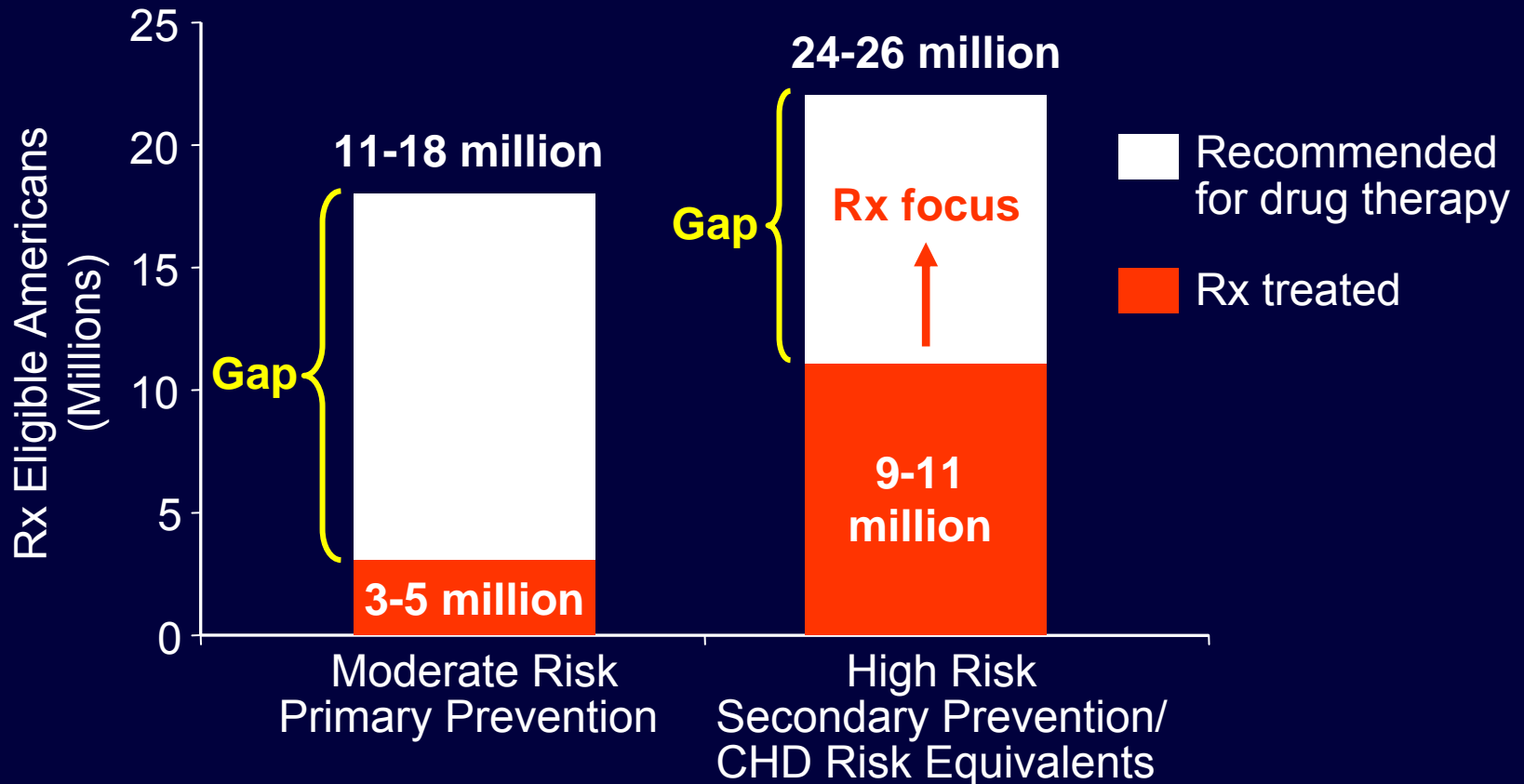
NHANES 1994, IMS 2003, Ingenix Treatment Gap Data 2003.

Need for Improved Treatment



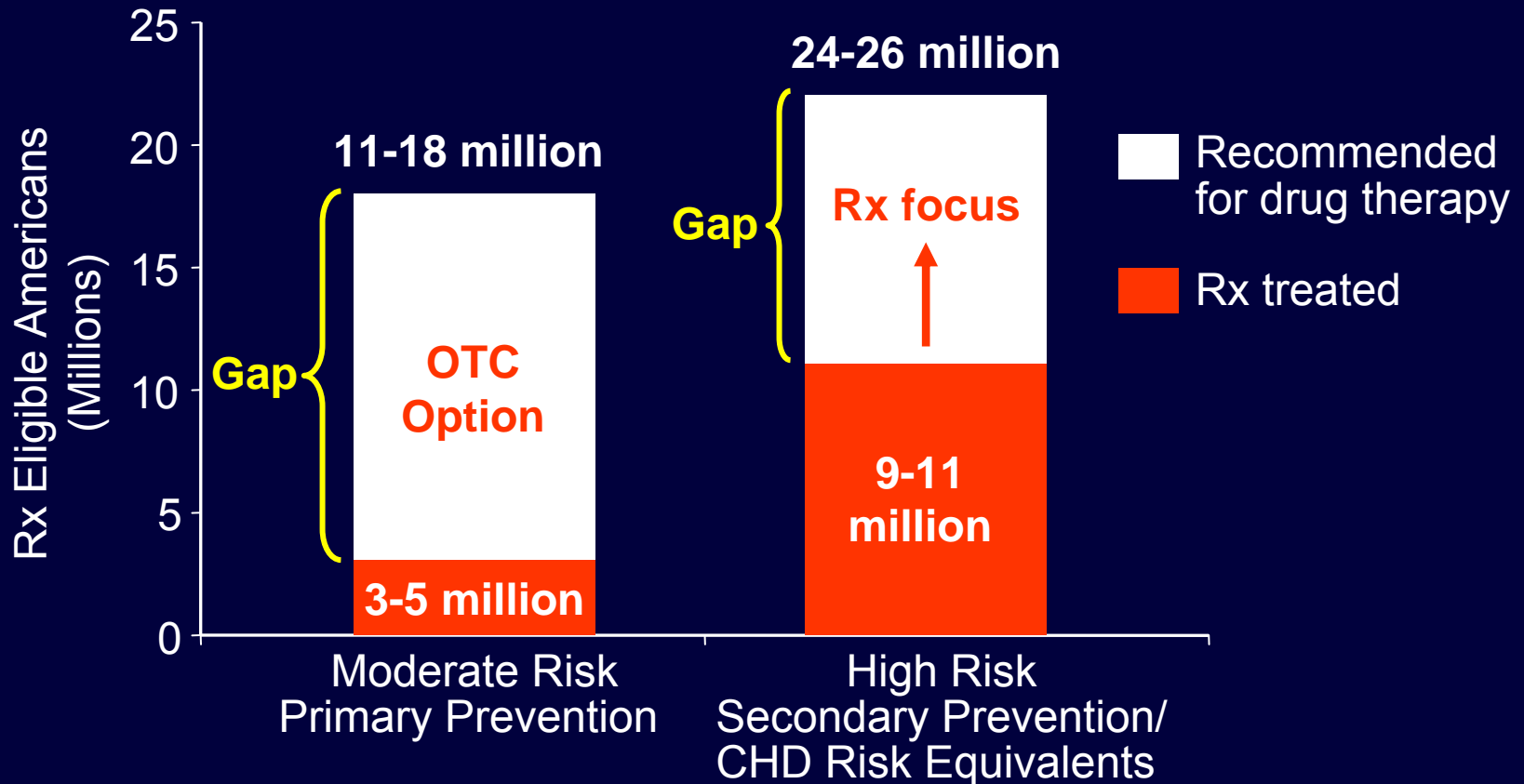
NHANES 1994, IMS 2003, Ingenix Treatment Gap Data 2003.

Need for Improved Treatment



NHANES 1994, IMS 2003, Ingenix Treatment Gap Data 2003.

Need for Improved Treatment



NHANES 1994, IMS 2003, Ingenix Treatment Gap Data 2003.

Rationale for MEVACOR™ OTC

- Growing cardiovascular public health problem
- Appropriate OTC target and product profile
 - Target population consistent with NCEP Guidelines

NCEP-ATP III Treatment Guidelines & 2004 Update Report

Risk Category	LDL-C Goal (mg/dL)	Initiate TLC (mg/dL)	Consider Drug Therapy
High CHD, CHD risk equivalent (10-y risk >20%)	<100 (<70 Optional)	≥100	≥100 (<100 Optional)
Moderately high ≥2 Risk factors (10-y risk 10%-20%)	<130 (<100 Optional)	≥130	≥130 (100-129 Optional)
Moderate ≥2 Risk factors (10-y risk <10%)	<130	≥130	≥160
Low 0-1 Risk factors	<160	≥160	≥190 (160-189 Optional)

Grundy et al. *Circulation*. 2004;110:227.

Proposed OTC Target Population

- “Moderate risk” per NCEP Guidelines
- Label approach
 - LDL 130-170 mg/dL
 - Plus 2 risk factors
 - Treatment to goal: LDL<130 mg/dL
- Comprehensive cholesterol management approach
 - Lifestyle changes - diet and exercise
 - Self-management system reinforces label
 - Collaboration with healthcare professional

Rationale for MEVACOR™ OTC

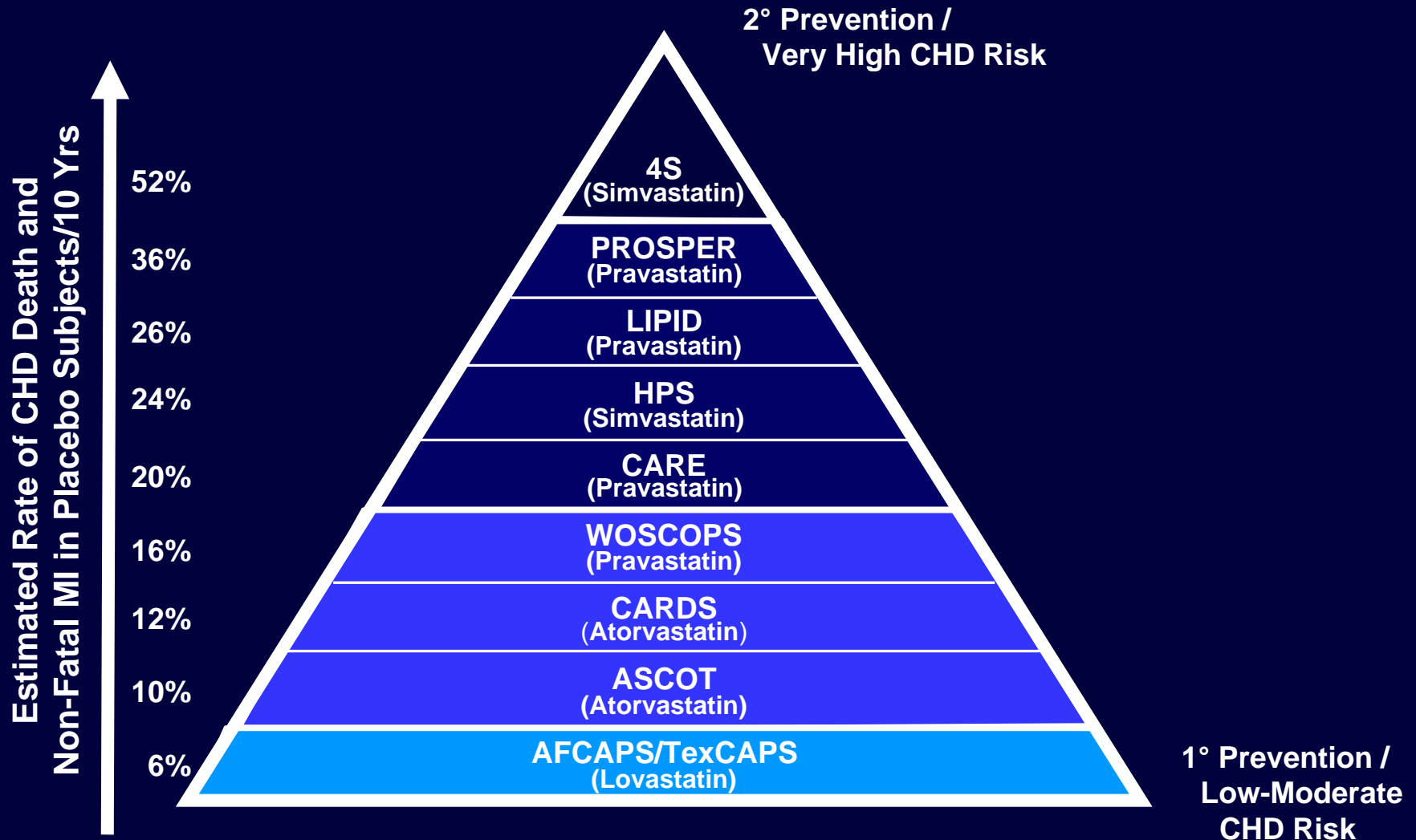
- Growing cardiovascular public health problem
- Appropriate OTC target and product profile
 - Target population consistent with NCEP Guidelines
 - Proven efficacy and safety of lovastatin 20 mg

Statins

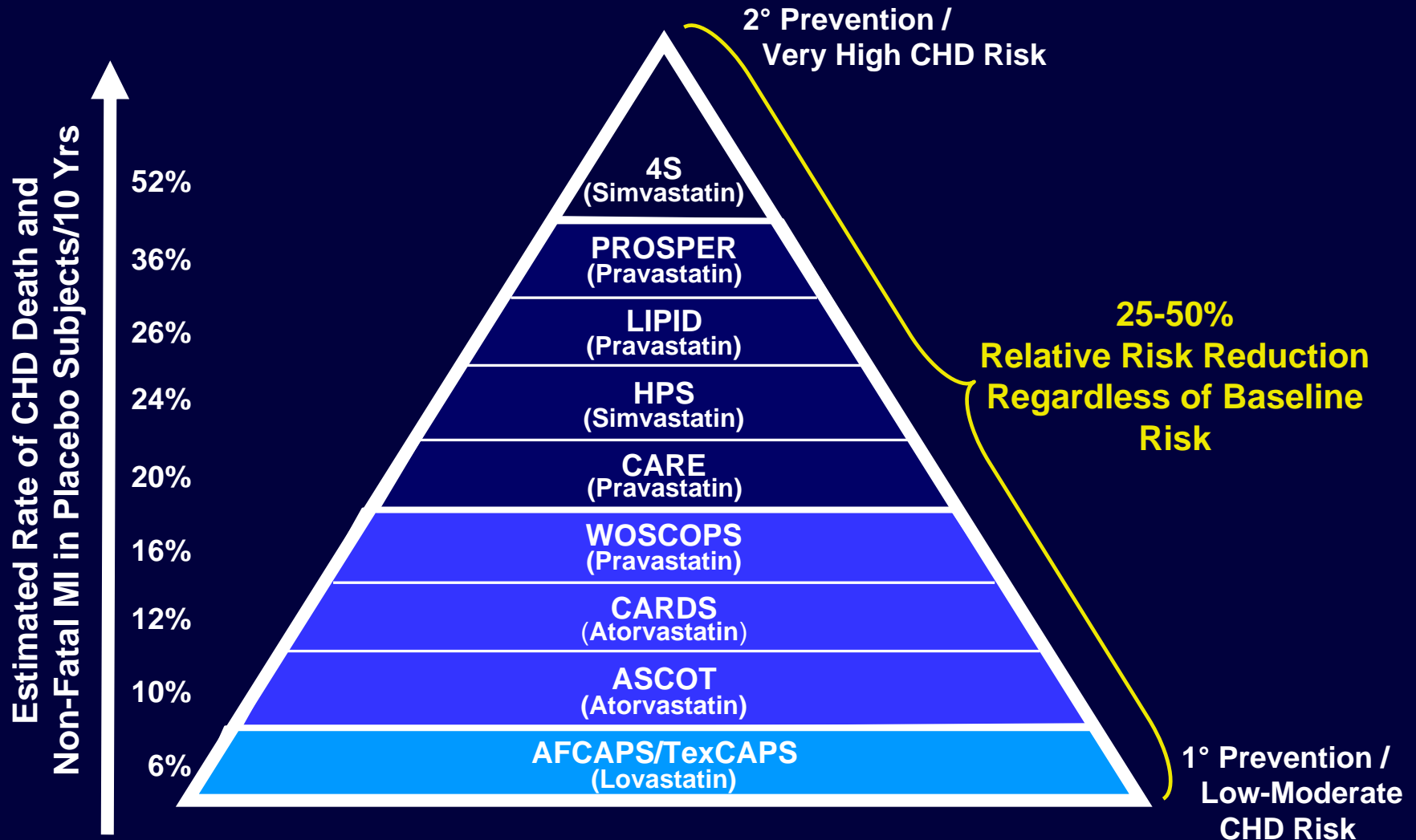
Proven Efficacy, Proven Safety

- 2002 ACC/AHA/NHLBI Clinical Advisory
 - *“Statins have demonstrated a decrease in CHD and total mortality, reductions in myocardial infarctions, revascularization procedures, stroke, and peripheral vascular disease...”*
 - *“Statins have been proved to be extremely safe in the vast majority of patients receiving them...post-marketing reports of adverse events have been very limited when considered in comparison to the very large number of persons safely receiving these drugs.”*

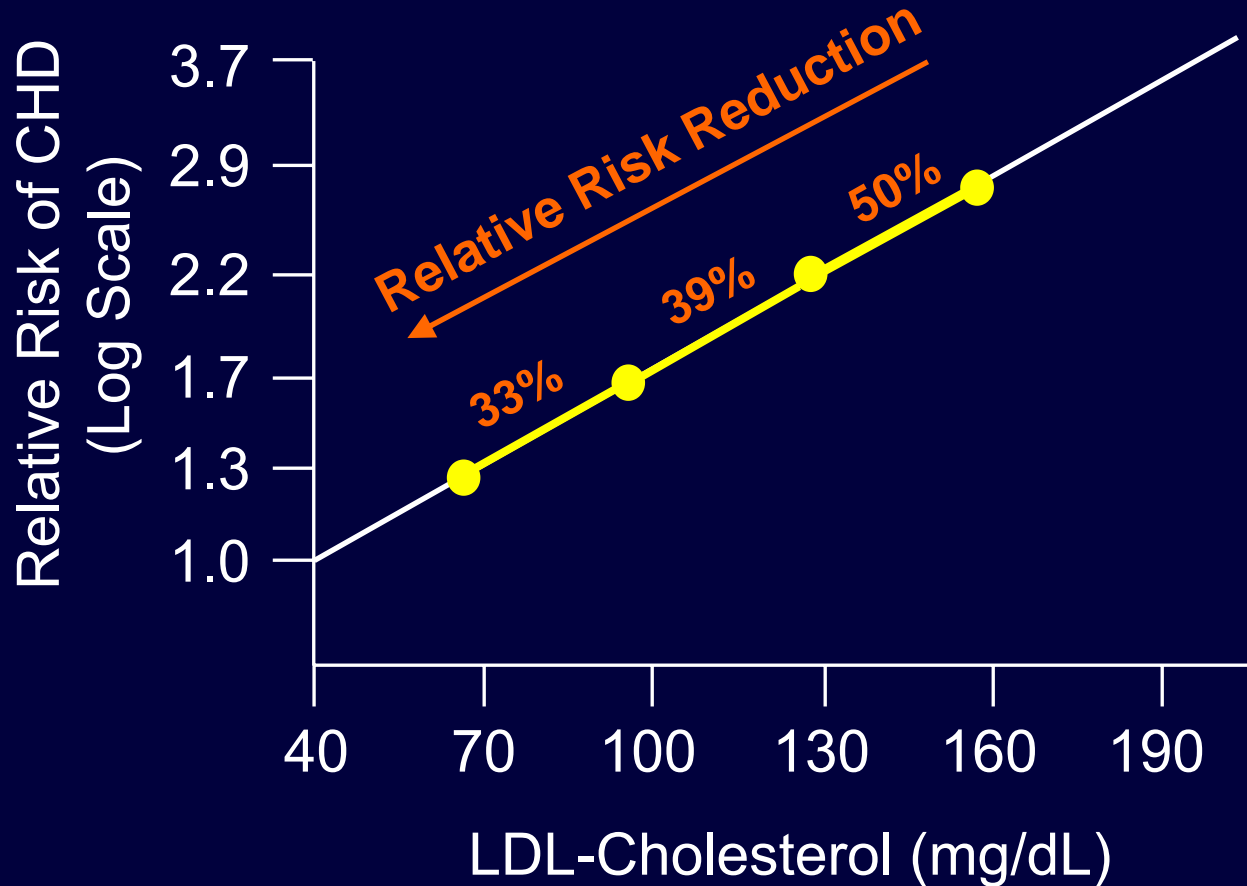
Proven Benefit Across Risk Groups



Proven Benefit Across Risk Groups



Significant Risk Reduction Across LDL Levels



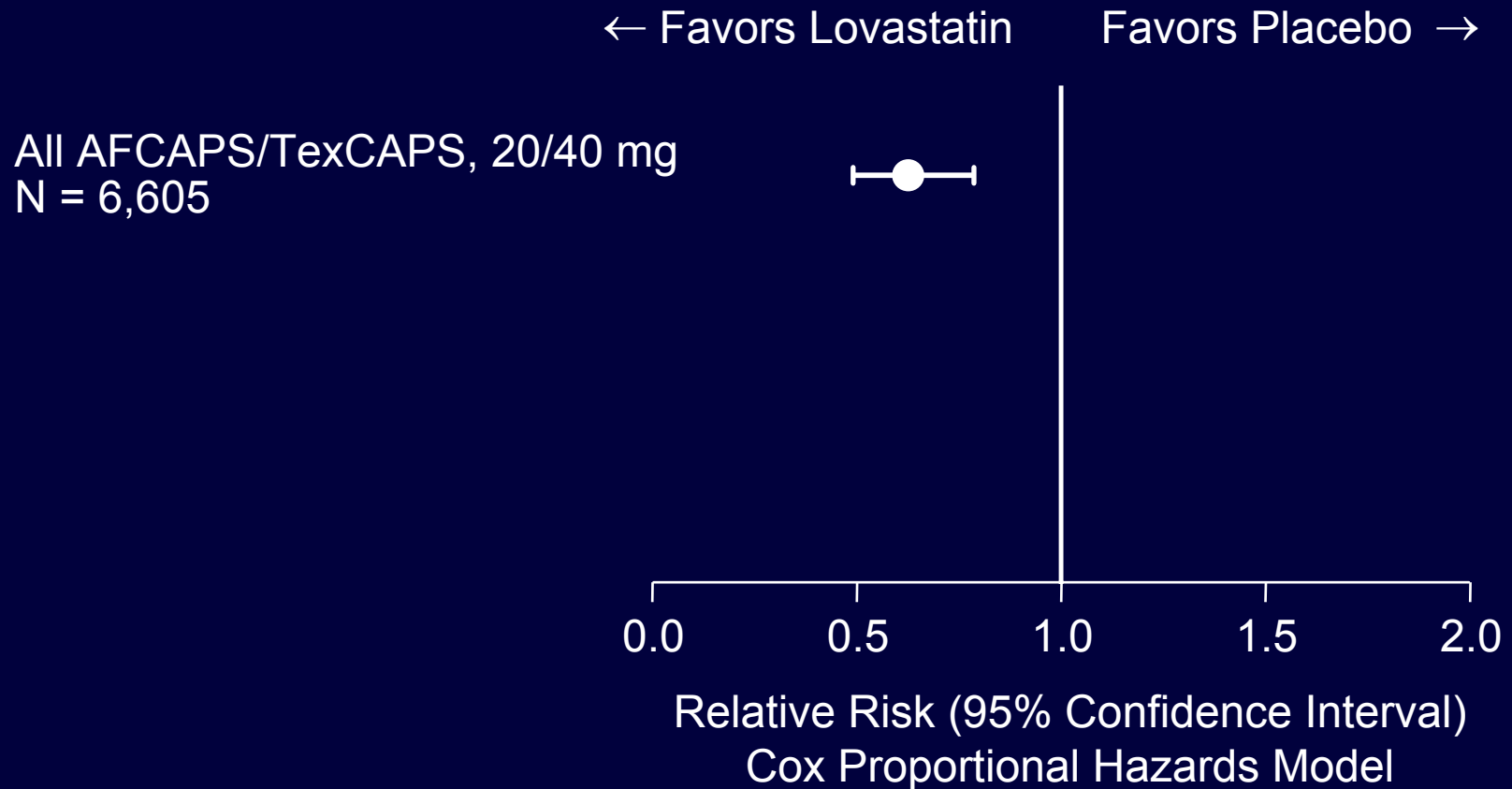
Grundy et al. *Circulation*: 2004.

Efficacy of Lovastatin

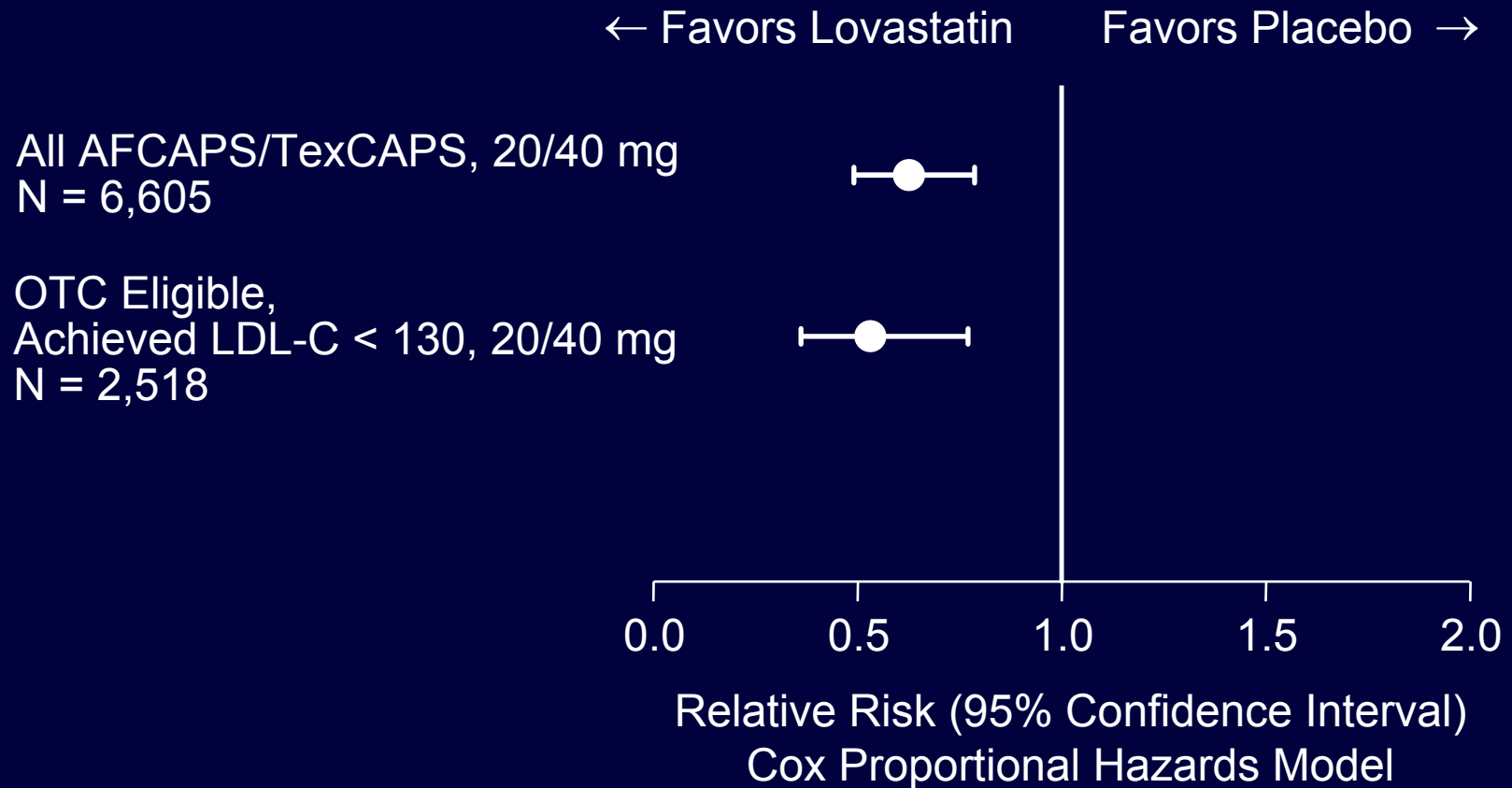
Proven Benefit

- Megatrials in ~15,000 patients
 - EXCEL: 20-80 mg/day, 48 weeks
 - AFCAPS/TexCAPS: 20-40 mg/day, 5 yrs
- Lovastatin 20 mg:
 - Improves Lipid Profile:
 - LDL-C -24%, HDL-C +6%, Total-C -17%
- Reduces the risk of a first coronary event by 37% in moderate risk individuals (AFCAPS/TexCAPS)

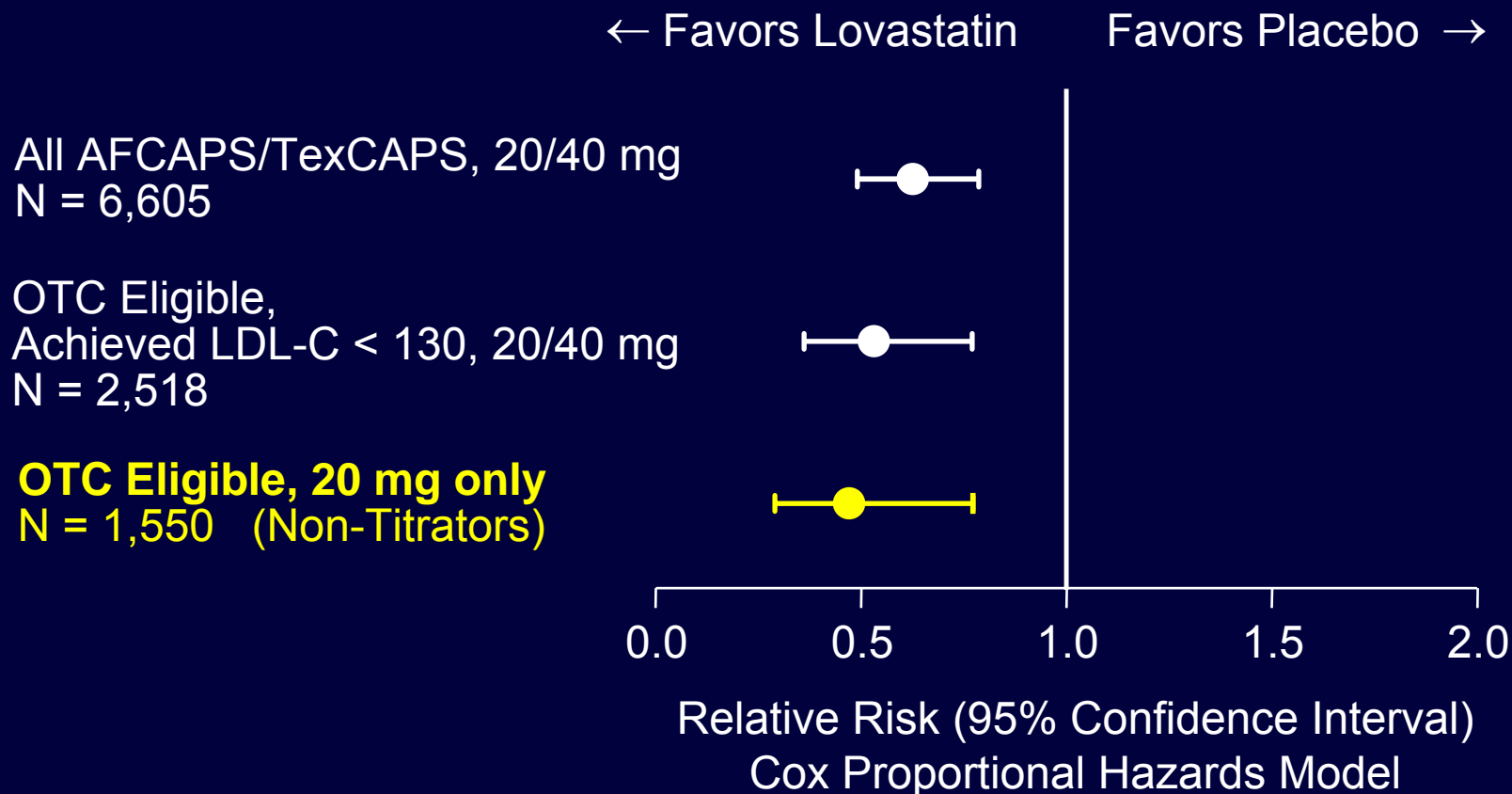
Potential Benefit in OTC Eligible Population



Potential Benefit in OTC Eligible Population



Potential Benefit in OTC Eligible Population



Safety of Lovastatin

Proven Safety

- Extensive experience
 - 17+ years in market
 - 27+ million patient-treatment years
- Strong clinical data
 - AFCAPS/TexCAPS & EXCEL
 - ~15,000 patients
 - Doses from 20-80mg
 - 20-40mg comparable to placebo for potential safety concerns
 - Liver, muscle, drug interactions

Lovastatin Safety: Liver

- Asymptomatic minor elevations of LFTs are:
 - Seen with all statins, fibrates, niacin
 - Dose and potency dependent
 - Often transient and resolving on therapy
 - Not associated with clinical liver disease
- Liver function testing not proposed for OTC dose

Lovastatin Safety: Liver

Clinical Data

	Liver Enzymes ALT Consecutive Elevations 3X Upper Limit of Normal		
	Placebo N (%)	20 mg N (%)	40 mg N (%)
EXCEL (1 year)	2/1639 (0.1%)	2/1625 (0.1%)	12/1629 (0.9%)
AFCAPS/TexCAPS (5+ years)	11/3248 (0.3%)	20/40 mg 18/3243 (0.6%)	
		20 mg 11/1586 (0.7%)	40 mg 7/1657 (0.4%)

Worldwide Adverse Experience System (WAES)

- Spontaneous reports of adverse events in postmarketing experience
- Voluntary reporting system
- Includes all reports independent of perceived causality
- Does not provide incidence rate

Lovastatin Safety: Liver

Worldwide Adverse Experience System (WAES)

- Acute liver failure
 - Background rate
 - 1-10 cases/million annually
 - Reports with lovastatin
 - 25 cases
 - ~1 report/million patient-treatment-years

WAES reports from health care professionals up to 01-Nov-2003.

Lovastatin Safety: Muscle

- Muscle toxicity is rare for low-dose statins:
 - Occurs with all statins and fibrates
 - Dose related
 - Self-recognizable muscle symptoms
 - Prompt recovery on discontinuation
 - Rarely severe (rhabdomyolysis)

Thompson et al. *JAMA*. 2003;289:1681-90.; Gotto. *Arch Intern Med* 2003;163:657-9;
Bradford et al. *Arch Int Med*. 1991;151:43-9; Downs et al. *Am J Cardiol*. 2001;87:1074-79.

Lovastatin Safety: Muscle

Clinical Data

	Muscle Enzymes CPK>10X Upper Limit of Normal		
	Placebo N (%)	20 mg N (%)	40 mg N (%)
EXCEL (1 year)	7 (0.4%)	3 (0.2%)	3 (0.2%)
AFCAPS/TexCAPS (5+ years)	21 (0.6%)	20/40 mg: 21 (0.6%)	
		20 mg: 11 (0.7%)	40 mg: 10 (0.6%)

No significant difference between lovastatin 20-40 mg and placebo

Lovastatin Safety: Muscle

Myopathy: Myalgia with CPK > 10x ULN

Rhabdomyolysis: Myopathy with end-organ damage

	AFCAPS/TexCAPS		EXCEL	
	Lovastatin 20-40 mg (N=3304)	Placebo (N=3301)	Lovastatin 20 mg (N=1642)	Placebo (N=1663)
Myopathy	0	0	0	0
Rhabdomyolysis	1	2	0	0

Lovastatin Safety: Muscle

Worldwide Adverse Experience System (WAES)

- Rhabdomyolysis rare
 - 336 spontaneous reports
 - 1.2 / 100,000 patient-treatment-years
 - 158 without potentially interacting drugs[†]
 - 41 reports with lovastatin 20 mg

[†] Fibrates, niacin, cyclosporine, and/or strong CYP3A4 inhibitors.
WAES reports from Health Care Professionals up to 01-Nov-2003.

Lovastatin Safety: Drug Interactions

- Strong CYP3A4 inhibitors
 - May increase risk of myopathy with concomitant administration
- OTC label instructs: Ask doctor or pharmacist if taking any prescription medicine
 - Package insert and education materials list potentially interacting drugs

Lovastatin Safety: Drug Interactions

Clinical Experience with Strong CYP3A4 Inhibitors‡
AFCAPS/TexCAPS (N=6605)

<u>Adverse Experience†</u>	<u>Lovastatin 20 to 40 mg (N=535) n (%)</u>	<u>Placebo (N=512) n (%)</u>
Musculoskeletal adverse experience	42 (8.0)	39 (8.0)
Myalgia	3 (1.0)	4 (1.0)
Muscle weakness	1 (0.2)	2 (0.4)
Myopathy/rhabdomyolysis	0 (0.0)	0 (0.0)

† Serious, drug-related, or caused discontinuation.

‡ Erythromycin, clarithromycin, ketoconazole, itraconazole, nefazodone.

Lovastatin Safety: Drug Interactions

Worldwide Adverse Experience System (WAES)

- Rhabdomyolysis with Interacting Drugs
 - 178 of 336 reports include potentially interacting drugs
 - Fibrates (97)
 - Cyclosporine (34)
 - Niacin (34)
 - Strong CYP3A4 Inhibitors (41)
 - With strong CYP3A4 inhibitor only (28/41)
 - Erythromycin/clarithromycin (16)
 - Itraconazole/ketoconazole (5)
 - Nefazodone (3)
 - Mibefradil (3)
 - Protease inhibitor (1)

Lovastatin Safety: Pregnancy

- Prescription label: pregnancy Category X
 - Non-specific animal findings at 10-80 times maximum human dose (80 mg) based on plasma AUC values
 - No benefit of short-term treatment during pregnancy
- Proposed OTC label
 - “Do NOT use if you are pregnant or breast-feeding”

Strong Product Profile for OTC Use

- Data demonstrates
 - Significant benefit of 20 mg in OTC target population
 - Cholesterol lowering efficacy
 - Reduction in cardiovascular outcomes
 - Safety profile comparable to placebo up to 40 mg
 - No apparent risk of liver adverse events
 - Low risk of muscle adverse events
 - Labeling will further minimize risks

Rationale for MEVACOR™ OTC

- Growing cardiovascular public health problem
- Appropriate OTC target and product profile
- Opportunity to improve public health
 - Consumer interest in an OTC option

Consumer Interest in OTC Options

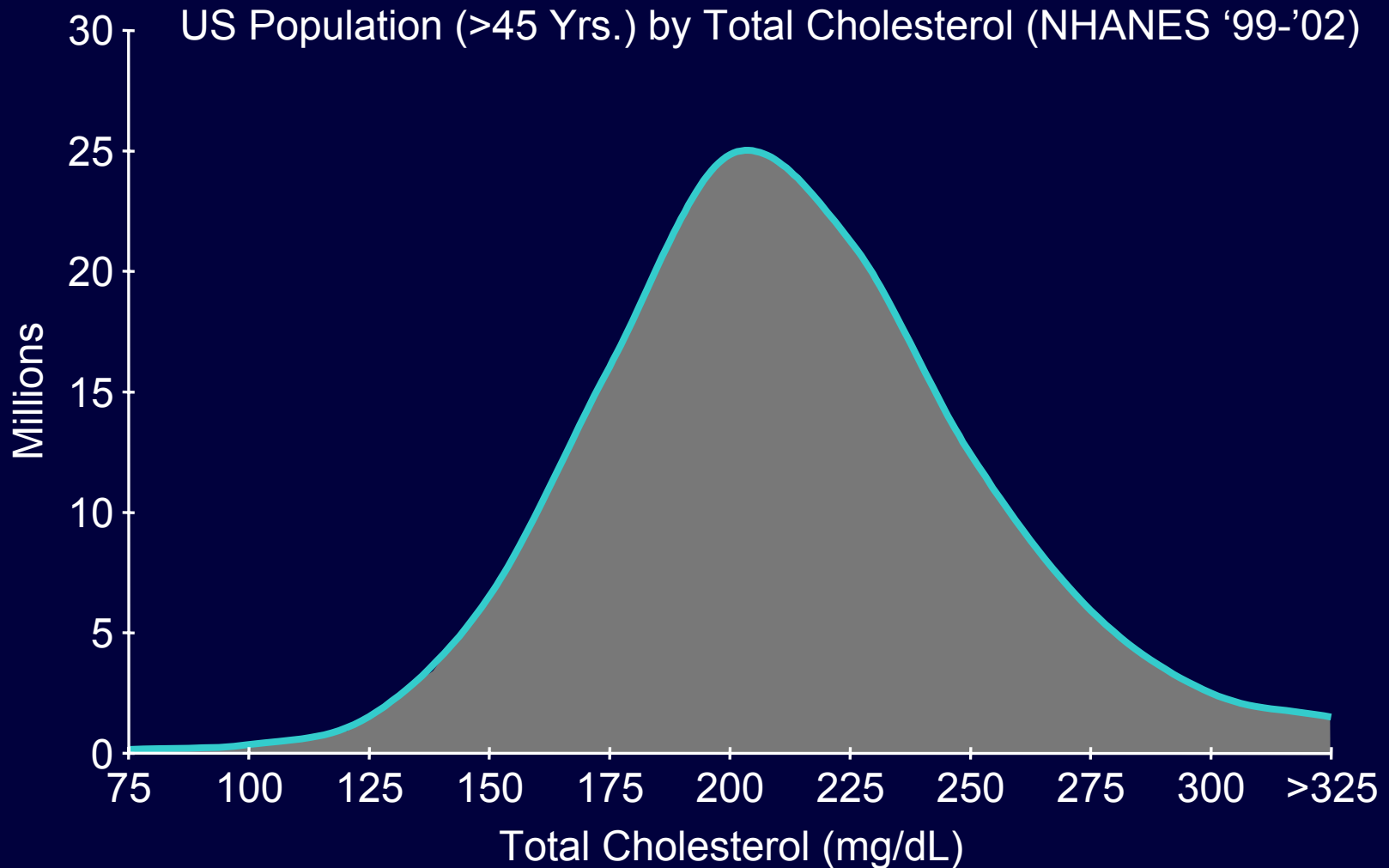
- National Lipid Association 2004 survey*
 - Majority of consumers are making more health decisions on their own
 - 72% of cholesterol concerned consumers are interested in learning more about an OTC statin option
- National Consumer's League 2004 survey**
 - 3 of 4 consumers at moderate risk and not taking prescription therapy say they prefer OTC for heart health prevention
- Consumers spend more than \$1 billion per year on heart health OTC and food products***
- UK approved non-prescription ZOCOR

*Pearson et al. AJC. 2004;94:16F-21F; **National Consumer League/Harris Interactive 2004 Survey Q#611; ***Information Resources Inc.

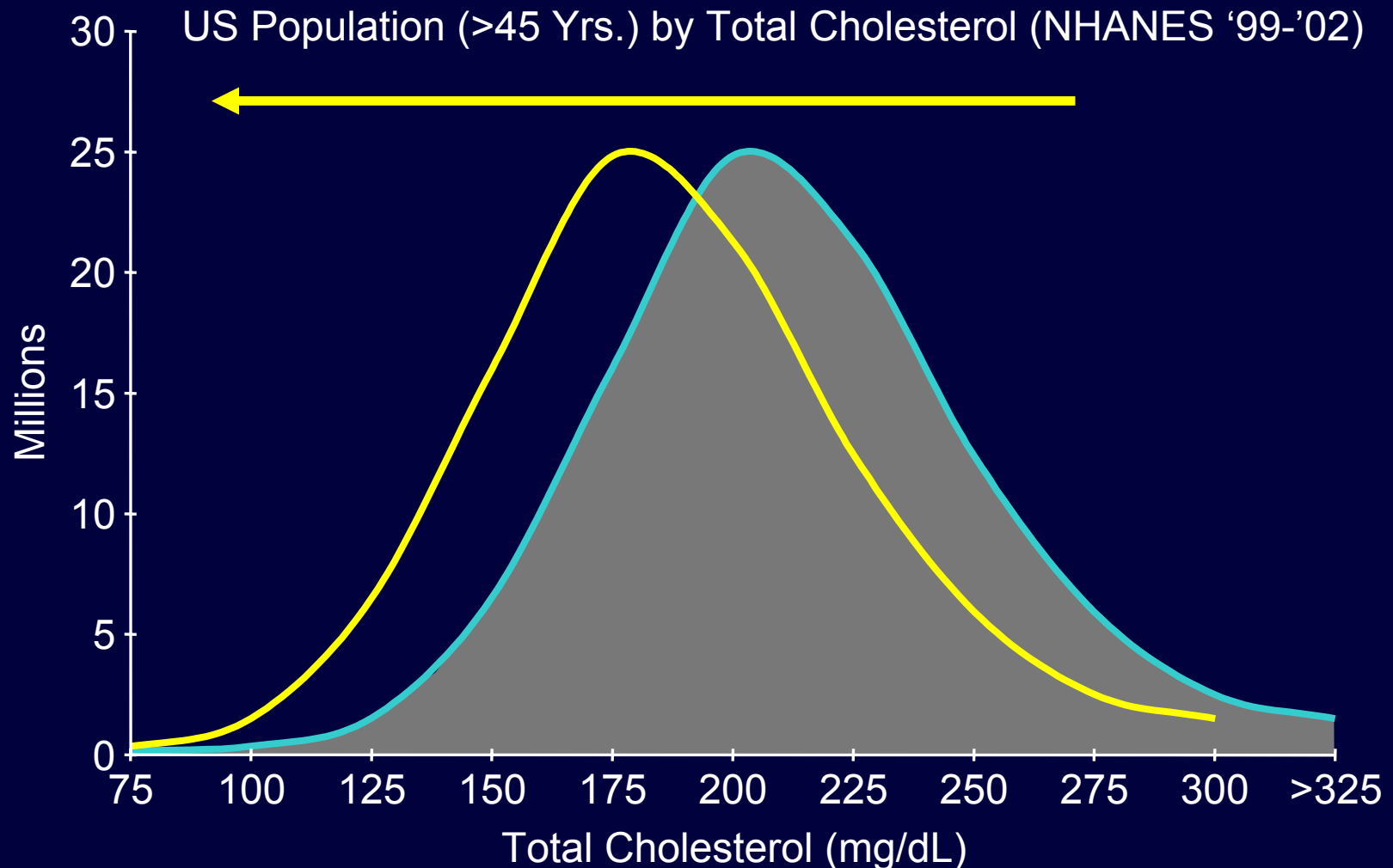
Rationale for MEVACOR™ OTC

- Growing cardiovascular public health problem
- Appropriate OTC target and product profile
- Opportunity to improve public health
 - Consumer interest in OTC option
 - Public health prevention approach

Need for Comprehensive Approach to Cholesterol Management



Need for Comprehensive Approach to Cholesterol Management



Summary

Rationale for MEVACOR™ OTC

- Growing cardiovascular public health problem
- Appropriate OTC target and product profile
- Opportunity to improve public health

Rationale for MEVACOR™ OTC

- Growing cardiovascular public health problem
- Appropriate OTC target and product profile
- Opportunity to improve public health
- Demonstrated appropriate consumer behavior

MEVACOR™ OTC Label & Self-Management System

Jerry Hansen, RPh
Vice President

*New Product Development and Consumer Research
Johnson & Johnson – Merck Consumer Pharmaceuticals*

Extensive Consumer Research

<u>Research</u>	<u>Approximate Number of Participants</u>
Consumer understanding (attitude & behavior)	10,600
Label development & comprehension	8,900
Self-Management System development	2,700
Actual use studies (lovastatin 10 & 20 mg)	<u>12,400</u>
Total	34,600

People Likely to Take Action with OTC Option

- Demographics representative of US population
 - Older (45+)
 - Other factors similar to US averages
 - Gender
 - Income
 - Race
 - Education

People Likely to Take Action with OTC Option

- Attitudes and behaviors not representative
 - Very active in own healthcare - more likely to:
 - Knowledgeable about health issues
 - Diet & exercise
 - Take aspirin for heart health
 - Take vitamins & supplements

People Likely to Take Action with OTC Option

- Attitudes and behaviors not representative
 - Very active in own healthcare
 - Strong relationship with physician
 - 80%+ see doctor at least once a year
 - 70%+ had a cholesterol test in past year
 - 80% have discussed cholesterol with doctor
 - “Motivated health-conscious”

Higher Interest in OTC vs. Rx

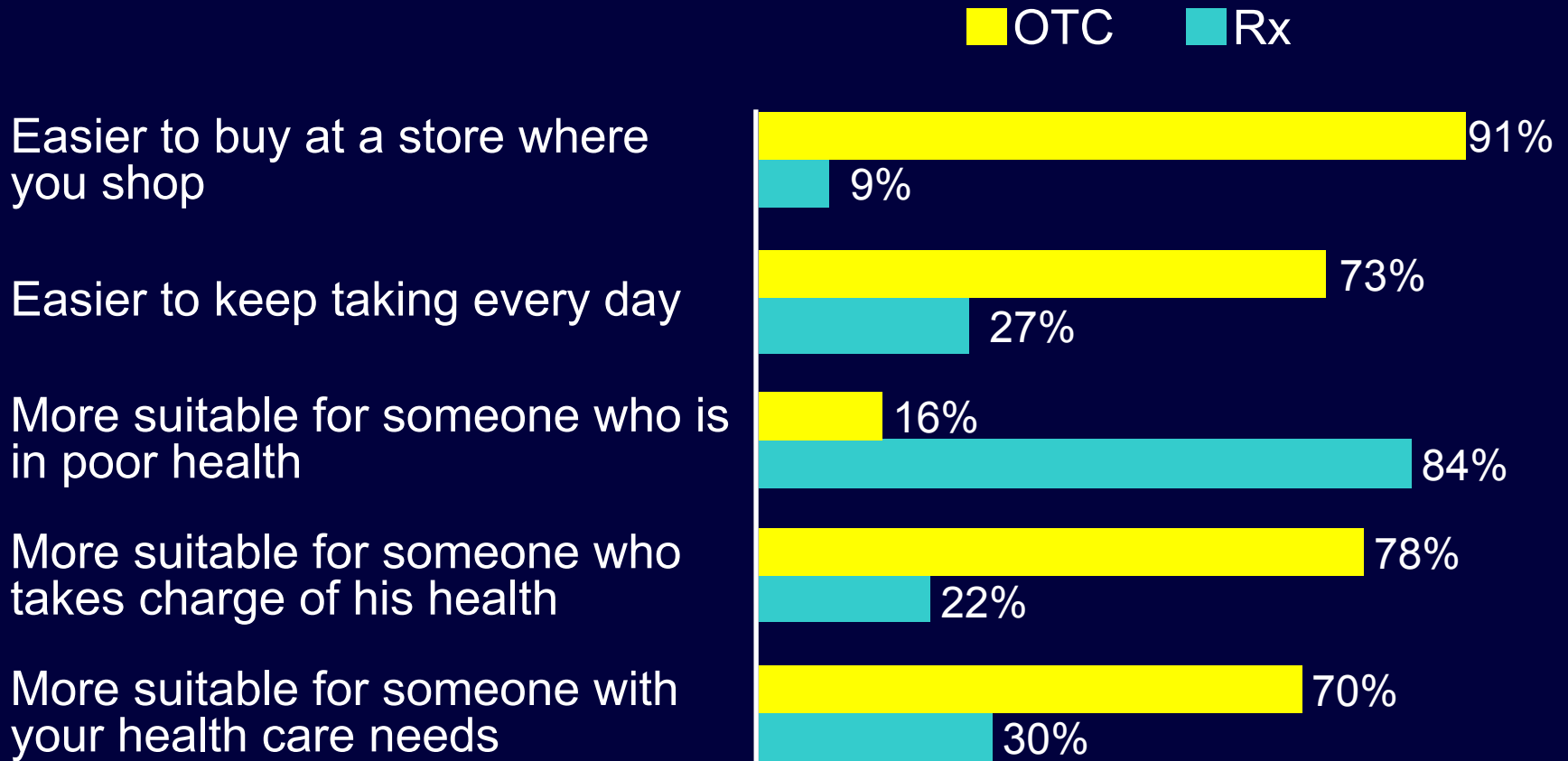
Untreated Potential or Known Moderate Risk

N=730

<u>Please tell us which product you would be more likely to...</u>	<u>OTC %</u>	<u>Rx %</u>
Consider taking	76	24
Recommend to family member or friend	76	24
Seek more information about	75	25

Why Moderate Risk Untreated Prefer OTC to Rx

N=730



Q#606: Please tell us which product you believe would be....
Untreated Potential or Known Moderate Risk.
National Consumer League/Harris Interactive 2004 Survey.

Label & Self-Management System

- Development process
 - Consistent with NCEP Guidelines but understandable by consumers
 - Incorporated iterative consumer feedback
 - Developed language & tools to ensure effective communication
 - Comprehensive approach to cholesterol management
 - Diet, exercise

Label & Self-Management System

- Healthcare professional collaboration
 - Before using any OTC for the first time, healthcare professionals are frequently consulted*
 - Doctor (79%)
 - Pharmacist (64%)
 - Data is consistent for those likely to use MEVACOR™ OTC**
 - 80% claim they will talk to a doctor prior to, or shortly after beginning use

**Prevention Magazine National Survey. **BASES, NLA , NCL.*

Key Label Messages

- OTC target consistent with NCEP Guidelines
 - LDL (130-170 mg/dL)
 - Male \geq 45; female \geq 55
 - Plus one additional risk factor
 - Family history
 - Smoking
 - Low HDL
 - High blood pressure

Key Label Messages (Cont'd)

- Do not use if:
 - Liver disease
 - Pregnant or breast-feeding
 - Allergy to lovastatin
- Do not use – see doctor about Rx therapy:
 - CHD
 - Diabetes
 - Taking cholesterol medicine
 - Triglycerides \geq 200 mg/dL
- Clear Safety Warnings
 - Drug interactions
 - Muscle pain

Key Label Messages (Cont'd)

- **Encourage lifestyle changes & testing**
 - Before using you must have:
 - Tried diet & exercise to reduce cholesterol
 - Had a fasting cholesterol test within the past year
 - Test at 6 weeks to see if you got to goal
 - If yes, keep taking daily and test yearly
 - Continue diet & exercise while taking MEVACOR™ OTC

Key Label Messages (Cont'd)

- **Drives ongoing healthcare professional interaction**
 - Consult doctor or pharmacist if questions
 - If do not reach LDL goal, talk to doctor: “OTC may not be enough for you”
 - Talk to doctor if there is a change in your health
 - Talk to your doctor or pharmacist if you are taking a new prescription

Package Label Comprehension Study

- Methodology

- Representative sample tested

- Projectable representative sample: n=696
- Low literacy subgroup: n=203 (REALM)
- Ethnic subgroup: n=207

- Respondents reviewed label & answered questions

- Identical label used in CUSTOM

- “Correct” and “correct/acceptable” scoring

- “Acceptable” often referred to checking with doctor

Package Label Comprehension Study

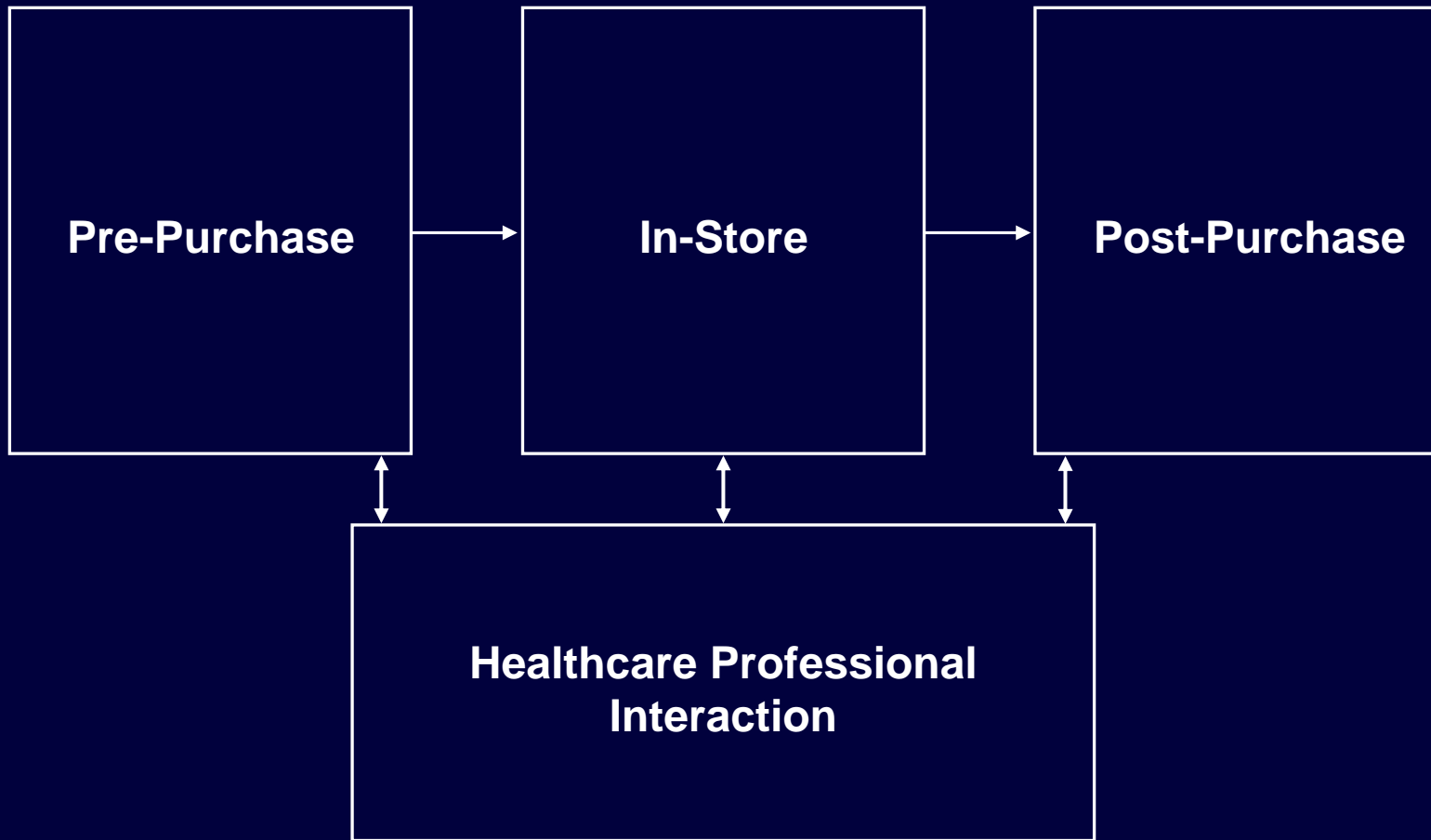
- Results
 - $\geq 80\%$ correct/acceptable for most measures
 - $\geq 90\%$ correct/acceptable for key safety messages
- Conclusions
 - Very effective at communicating key messages in all groups (low literacy/ethnic)
 - Consumers understood to ask healthcare professionals if questions

Self-Management System

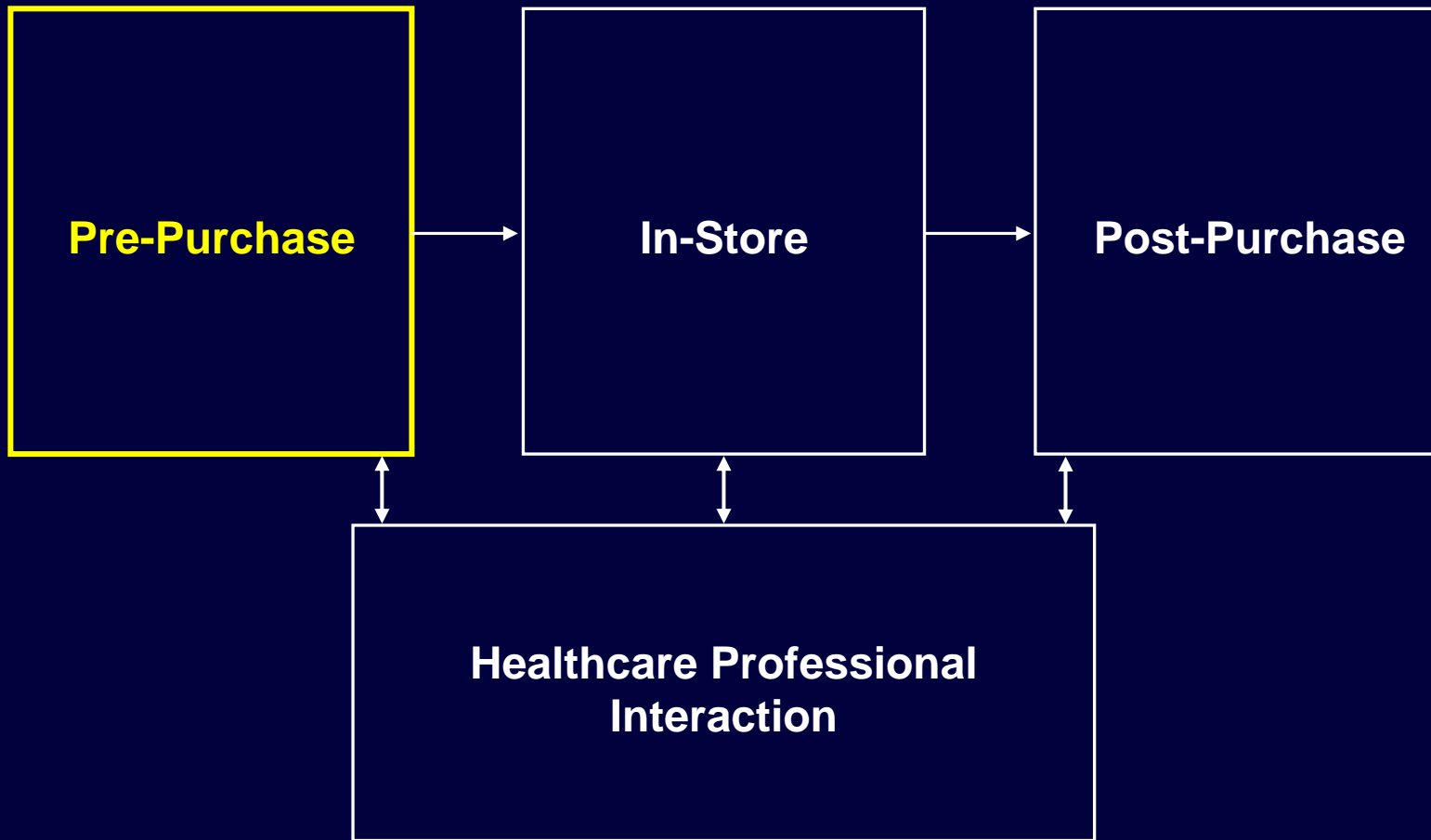
Overview

- Goal: To provide additional information & tools to reinforce key label messages
 - Incorporated input from external experts
 - Multiple methods of delivering information to appeal to different learning styles
 - All elements part of proposed NDA labeling
 - Required in-market
 - Self-Management System tested in CUSTOM

MEVACOR™ OTC Self-Management System



MEVACOR™ OTC Self-Management System



Pre-Purchase Assistance

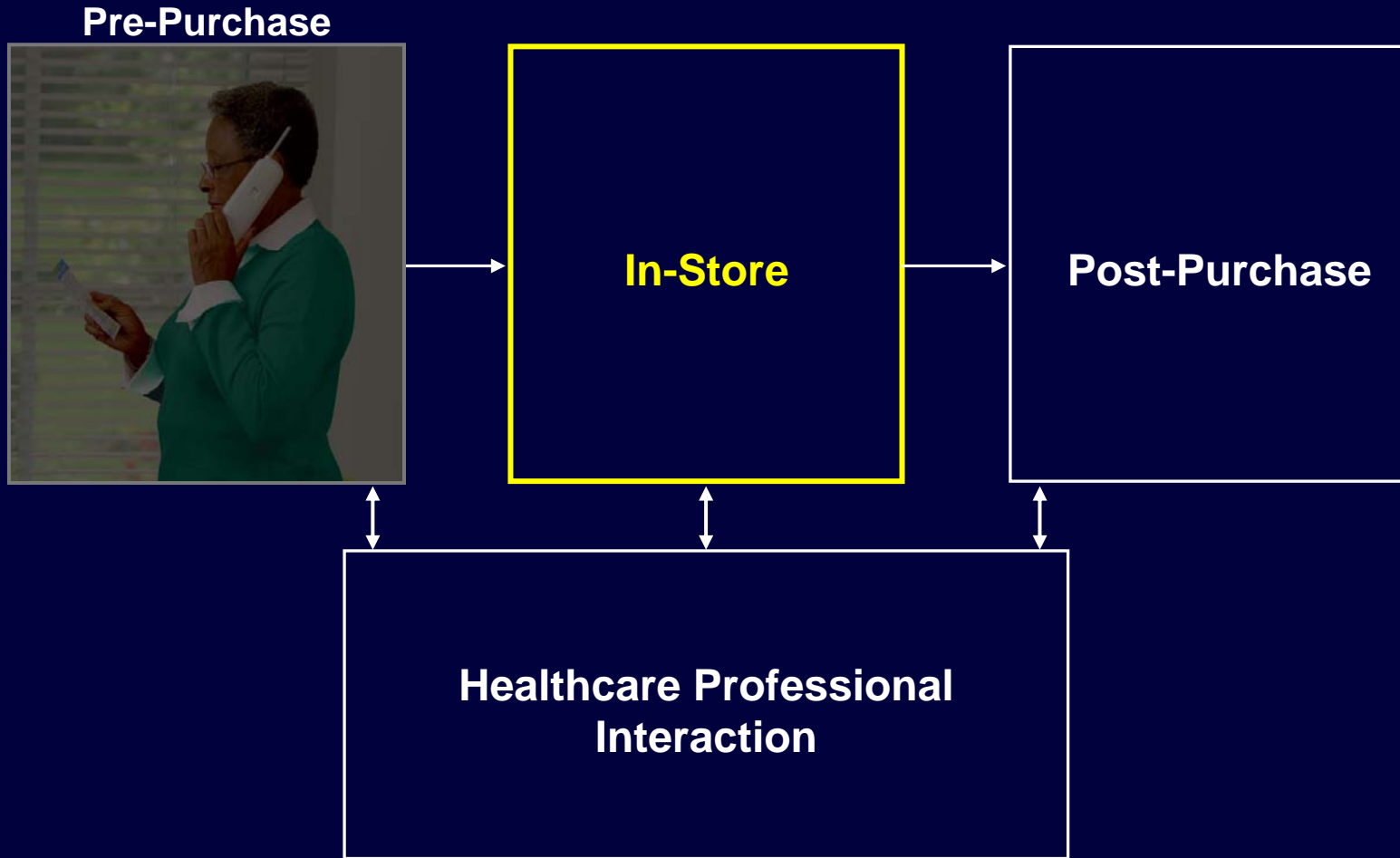


- Communication & Education
 - Know your numbers
 - OTC is not right for everyone, ask if you're not sure



- Eligibility Assistance
 - Physician & pharmacist
 - Trained product specialist
 - Toll-free & on-line
 - Questions and related services

MEVACOR™ OTC Self-Management System



In-Store Assistance



- Pharmacy Support
 - “Pharmacy Care OTC”
 - Pharmacist & staff training



- Enhanced Retail Communication
 - Interactive tools to support label

“Pharmacy Care OTC”

- New approach developed by American Pharmacists Association (APhA) and other leading pharmacy groups
- Features
 - Distributed voluntarily only in stores with a pharmacy
 - On open shelf with current OTC products
 - Does not require pharmacist intervention but strongly supports it
 - Expands supportive services
 - Cholesterol testing, counseling

Store Shelf Communication

First-Time Buyers

Should you take it?

Repeat Buyers

Did you make it?

Important
TAKE ONE

First-Time Buyers

Should you take it?

Use this guide to find out.

1. Any questions, ask the study pharmacist or pharmacist's assistant.
2. Find out your goal numbers. Write your doctor's instructions on the back of this card. Bring your doctor's instructions and this card to the pharmacist.

NOTE: Don't confuse TOTAL with LDL "bad" cholesterol.

1. Total cholesterol	1-129 mg/dL	130-159 mg/dL	160-199 mg/dL
2. LDL "bad" cholesterol	1-129 mg/dL	130-159 mg/dL	160-199 mg/dL
3. HDL "good" cholesterol	1-49 mg/dL	50-59 mg/dL	60-69 mg/dL
4. Triglycerides	1-100 mg/dL	101-150 mg/dL	151-200 mg/dL

See your numbers right for MEVACOR[®] OTC

ALL BLUE NUMBERS: See reverse side. ANY YELLOW NUMBERS: Must not use. Talk to your doctor or pharmacist.

Once-a-day
MEVACOR[™]
OTC

Lovastatin 20 mg
CHOLESTEROL REDUCER

- For people with elevated LDL "bad" cholesterol between 130-170 mg/dL.
- To reduce LDL cholesterol to 129 or below and keep it down

Read back for more information

Once-a-day
MEVACOR[™]
OTC

Lovastatin 20 mg
CHOLESTEROL REDUCER

- For people with elevated LDL "bad" cholesterol between 130-170 mg/dL.
- To reduce LDL cholesterol to 129 or below and keep it down

Read back for more information

Important
TAKE ONE

Repeat Buyers

Did you make it?

Use this guide to find out.

1. Did you get a fasting cholesterol test at 6 weeks? If not, ask the study pharmacist for test information.
2. Did you get to the required 6 week goal: LDL 1-129? If not, ask the study pharmacist before you buy. At 6 weeks, you need to get a fasting cholesterol test to see if you should continue taking MEVACOR[®] OTC. If you have not had your 6 week test, see below. If you know your results, see reverse side.

Schedule your cholesterol test now.

1. Ask the study pharmacist for information on cholesterol testing.
2. Use your \$5 savings. Call 1-800-MEVACOR (633-3226) for details.

Your LDL 6 week test result must be 1-129 for you to continue taking MEVACOR[®] OTC. LDL test result is the number you need - see step 3 on back.

Download: Call 1-800-MEVACOR or visit www.mevacor.com

See if it's right for you. Turn all 5 wheels!

1
4 choices

Gender & Age?

2
4 choices

LDL "bad" Cholesterol?

3
5 choices

Any conditions that increase heart risk?

4
5 choices

Any warnings apply to you?

Should you take it?

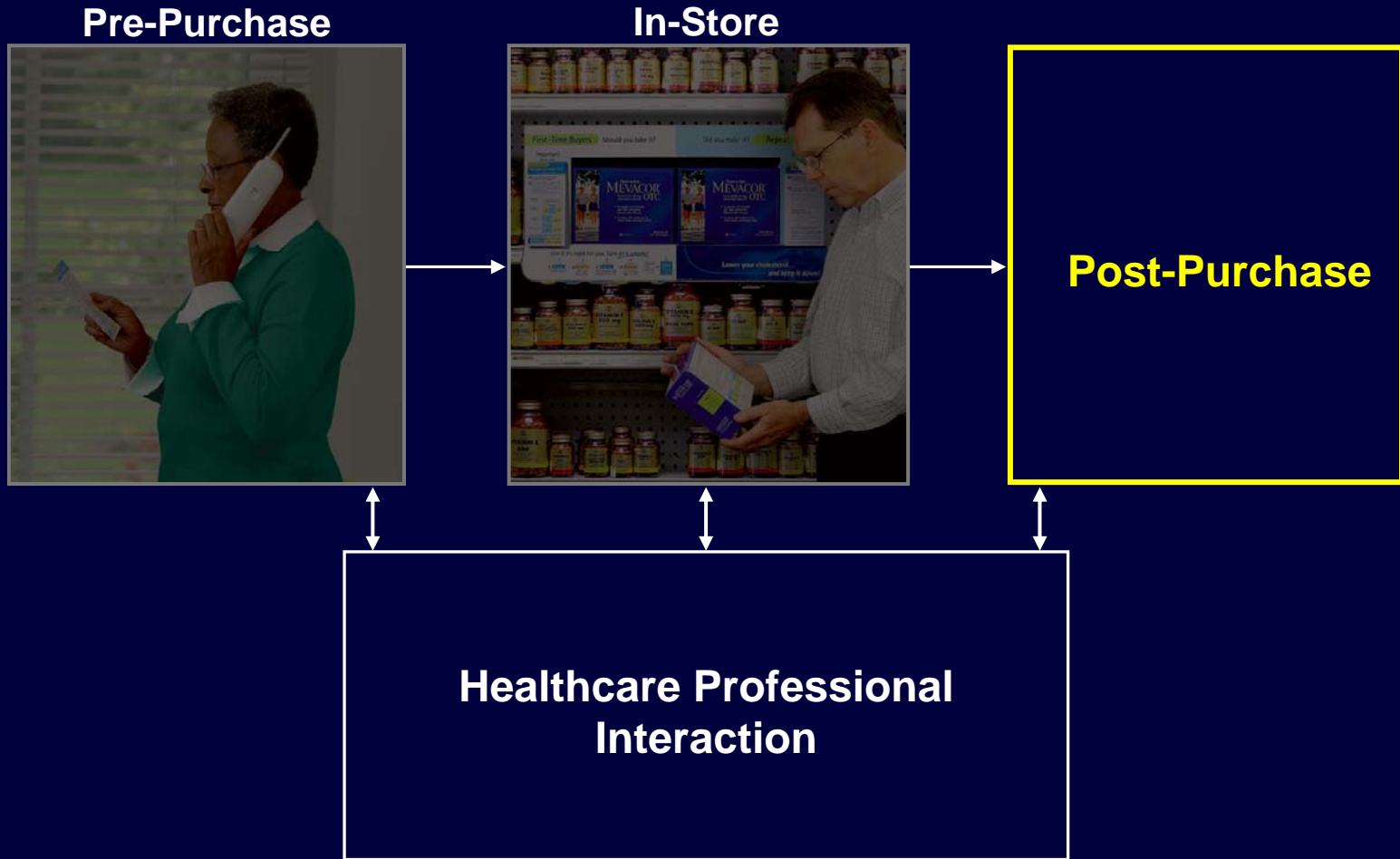
5
ALL BLUE ANSWERS

MEVACOR[®] OTC may be right for you. Talk to your doctor or pharmacist.

Lower your cholesterol...
and keep it down!

- Highlights two decision processes
- Interactive tools
- Encourages dialogue with pharmacist

MEVACOR™ OTC Self-Management System



Post-Purchase Assistance



- In-package materials
 - Educational brochure
 - Package insert & Q&A
 - “Quick Start Guide”
 - Cholesterol testing

Cholesterol Testing

- Cholesterol testing referral system
- Coupon for six-week cholesterol test
- Options
 - Doctor's office/laboratory/hospital
 - Retail setting
 - Walk-in clinics
 - At-home kit

Post-Purchase Assistance



- Adherence Program
 - Toll-free hotline & website
 - Video & AHA cookbook
 - Newsletters, postcards, e-mail reminders

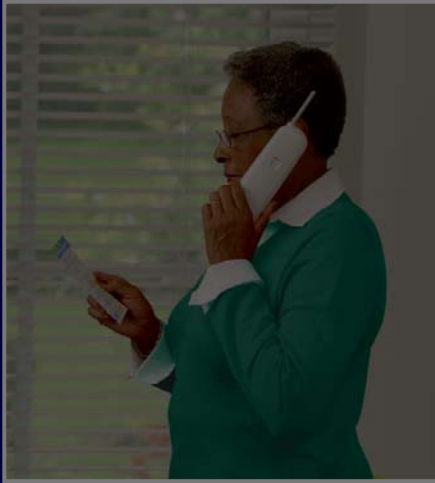
Adherence Program

- Customized to start date
- First three months focus on
 - Eligibility
 - Treatment to goal
- Subsequent focus
 - Diet & exercise
 - Adherence
 - Healthcare professional interaction



MEVACOR™ OTC Self-Management System

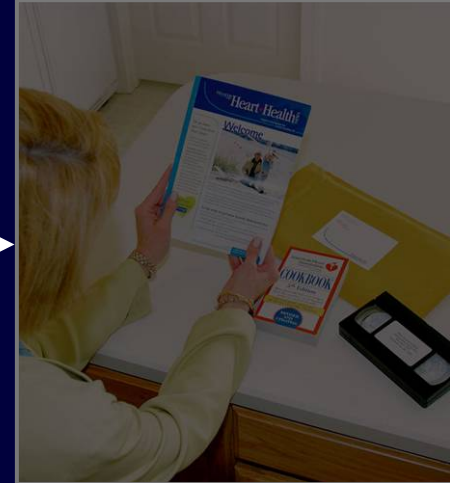
Pre-Purchase



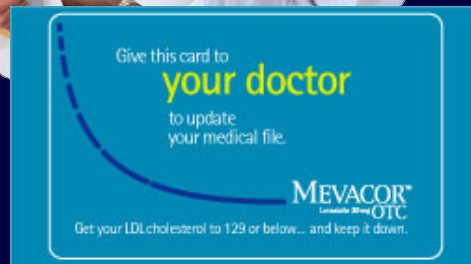
In-Store



Post-Purchase



Healthcare Professionals



- Encourages ongoing dialogue concerning
 - OTC questions
 - Testing & monitoring
 - Higher CHD risk referral

MEVACOR™ OTC Self-Management System

Pre-Purchase



In-Store



Post-Purchase



Healthcare Professional Interaction

Conclusions

- Those likely to take action: “Motivated Health Conscious”

Conclusions

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- Self-Management System offers multi-faceted support to reinforce key label messages
 - Included as part of proposed NDA labeling and required in-market
 - Demonstrated feasibility with key partners
 - Retail, pharmacy, testing companies

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 - Demonstrated feasibility with key partners
 - Retail, pharmacy, testing companies
- Committed to extensive post-marketing surveillance
- Self-Management System fully evaluated in CUSTOM

CONSUMER BEHAVIOR

Robert W. Tipping, MS
Director, Clinical Biostatistics
Merck Research Laboratories

Key Questions

- Will the MEVACOR™ OTC Self-Management System allow consumers to:
 1. Make appropriate initial use decisions?
 2. Self-manage the potential safety risks over time?
 3. Self-manage their cholesterol over time and obtain benefit?

The CUSTOM Study

Consumer Use Study of OTC MEVACOR™

Demonstrating Consumer Behavior in an OTC Setting

CUSTOM Study Design

OTC-like Recruitment

- TV
- Print
- Radio

- No specific label eligibility criteria
- 14 sites in 7 geographic areas
- Minority ads

CUSTOM Study Design

Naturalistic Observation

OTC-like Recruitment

- TV
- Print
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- Minority ads

Site Visit Initial Use Decision



- Naturalistic retail setting
- In-store components of System
- All comers accepted

Self Assessment

- Review of label
- Option to leave to obtain information
- Purchase cholesterol test (optional)
- Pharmacist available to answer questions if asked
- Purchase of drug required

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On-going Use

Visits not scheduled

← 6 months →

Self-guided Behavior & Product Use

- Follow-up test
- Treatment to goal
- New conditions

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End Of Study Questions

CUSTOM Study Design

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Pre & post lipid values obtained

End Of Study Questions

Post CUSTOM Survey

MEVACOR™ OTC Self-Management System

Pre-Purchase



In-Store



Post-Purchase



Healthcare Professional Interaction

CUSTOM Study Design

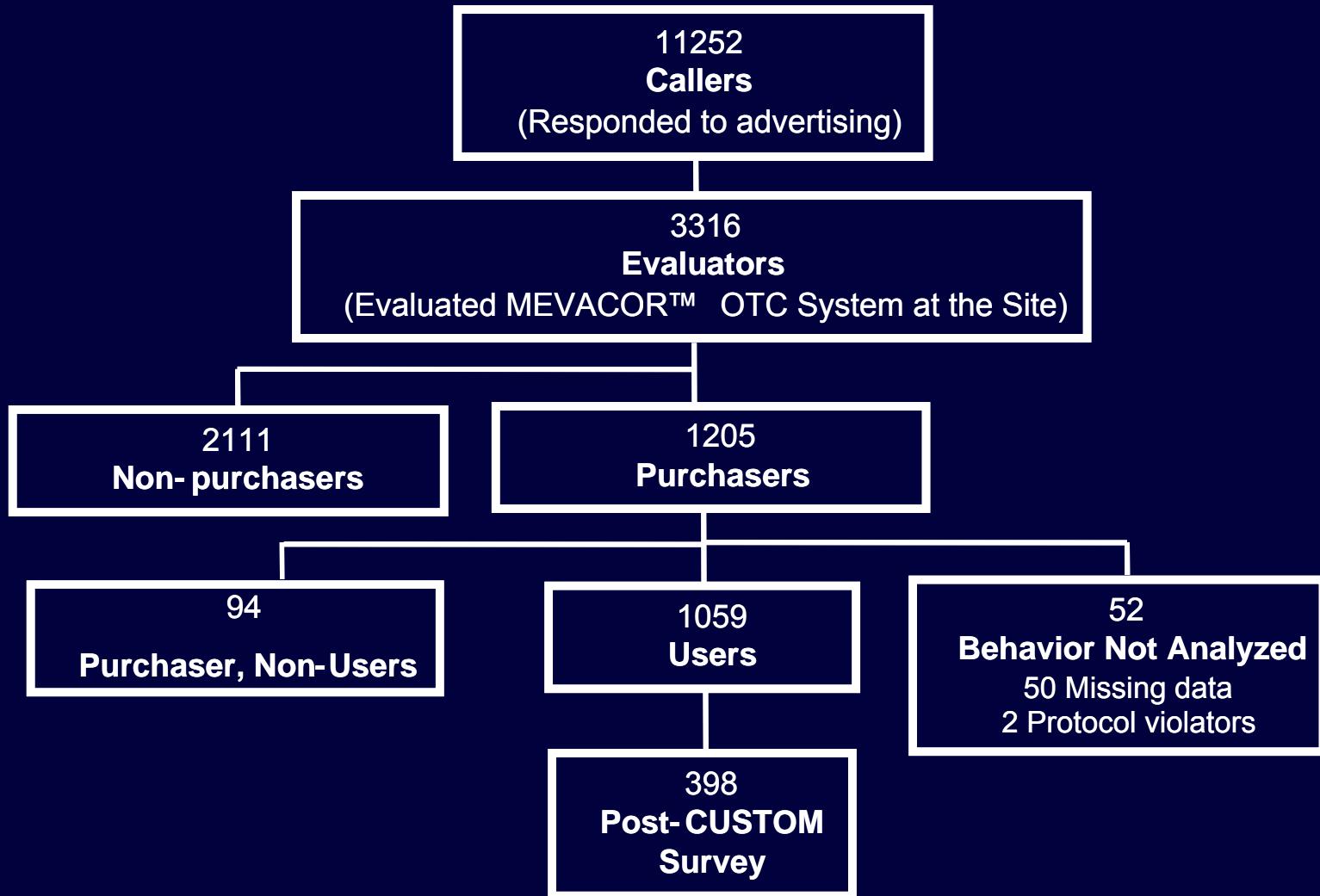
Analysis of Behavior

- Decisions about product purchase and use
 - Initial decision to use
 - Ongoing decisions regarding continued use
- Interactions with healthcare professionals
 - Important factor in determining appropriateness of product use
 - Creating and maintaining partnerships
- Diet and exercise

CUSTOM Actual Use Results

CUSTOM Results

Participant Flow Through Study



CUSTOM Results

Population Profile
Evaluators
(n=3316)

- 59% men
- Median age – 53 yrs
- 28% Non-Caucasian
- 12% Low-literacy

CUSTOM Results

Safety Summary

Users

(n=1061)

- 1 serious, drug-related AE
 - 63 year-old female with acute allergic reaction
- 1 death, probably not related to drug
 - 50 year-old male with CVA
- No serious, drug-related muscle or liver AEs
- No new safety issues identified
- MEVACOR™ was generally safe and well tolerated in this OTC population

CUSTOM Label

Safety Warnings

Initial Use

Benefit Criteria

Initial Use

Safety Warnings

Ongoing Use

Benefit Criteria

Ongoing Use

CUSTOM Label

Safety Warnings – Initial Use

- Pregnant/breast feeding
- Liver disease
- Previous muscle pain
- Interacting meds
- Rx Lipid-lowering therapy

Benefit Criteria

Initial Use

Safety Warnings - Ongoing Use

- New Rx
- New medical condition
- Unexplained muscle pain

Benefit Criteria

Ongoing Use

CUSTOM Label

Safety Warnings

Initial Use

Benefit Criteria – Initial Use

- Age
- Lipids
- Risk Factors

Safety Warnings

Ongoing Use

Benefit Criteria – Ongoing Use

- Follow up Lipid Test
- LDL-C Goal

CUSTOM Label

Safety Warnings – Initial Use

- Pregnant/breast feeding
- Liver disease
- Previous muscle pain
- Interacting meds
- Rx Lipid-lowering therapy

Benefit Criteria – Initial Use

- Age
- Lipids
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- New Rx
- New medical condition
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Benefit Criteria – Ongoing Use

- Follow up Lipid Test
- LDL-C Goal

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Key Questions

- Will the MEVACOR™ OTC Self-Management System allow consumers to:
 1. Make appropriate initial use decisions?
 - 3316 Evaluators
 - 2111 Chose not to purchase
 - 64 Purchased but chose not to use
 - 659 Chose to use appropriately (safety and benefit criteria)

Key Questions

- Will the MEVACOR™ OTC Self-Management System allow consumers to:

1. Make appropriate initial use decisions?

➤ 3316 Evaluators

– 2111
– 64
– 659 } = 2834 (86%)

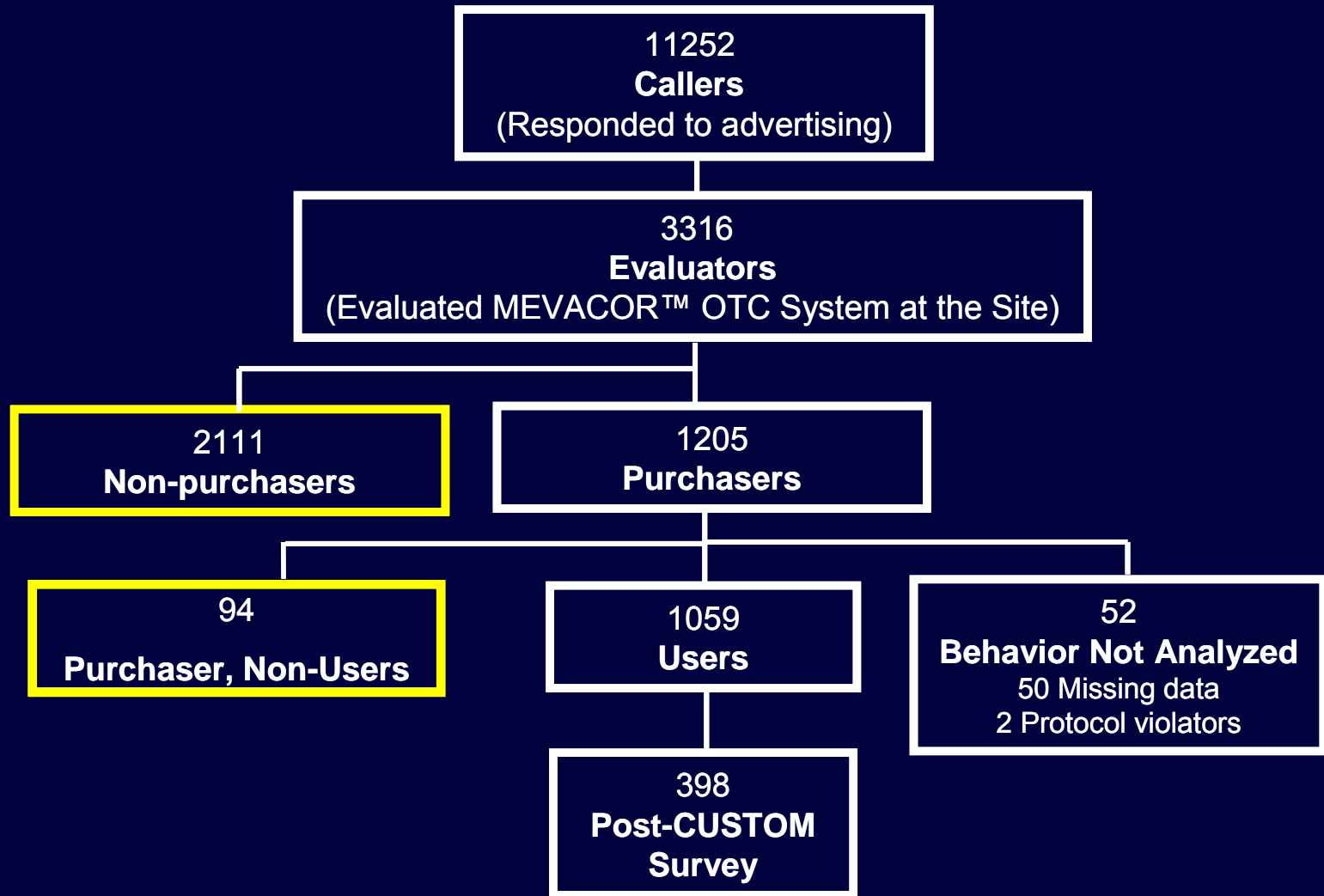
Key Questions

- Will the MEVACOR™ OTC Self-Management System allow consumers to:
 1. Make appropriate initial use decisions?
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 - 2111
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} = 2834 (86%)
 - 109 (3%) use inconsistent with label safety warnings

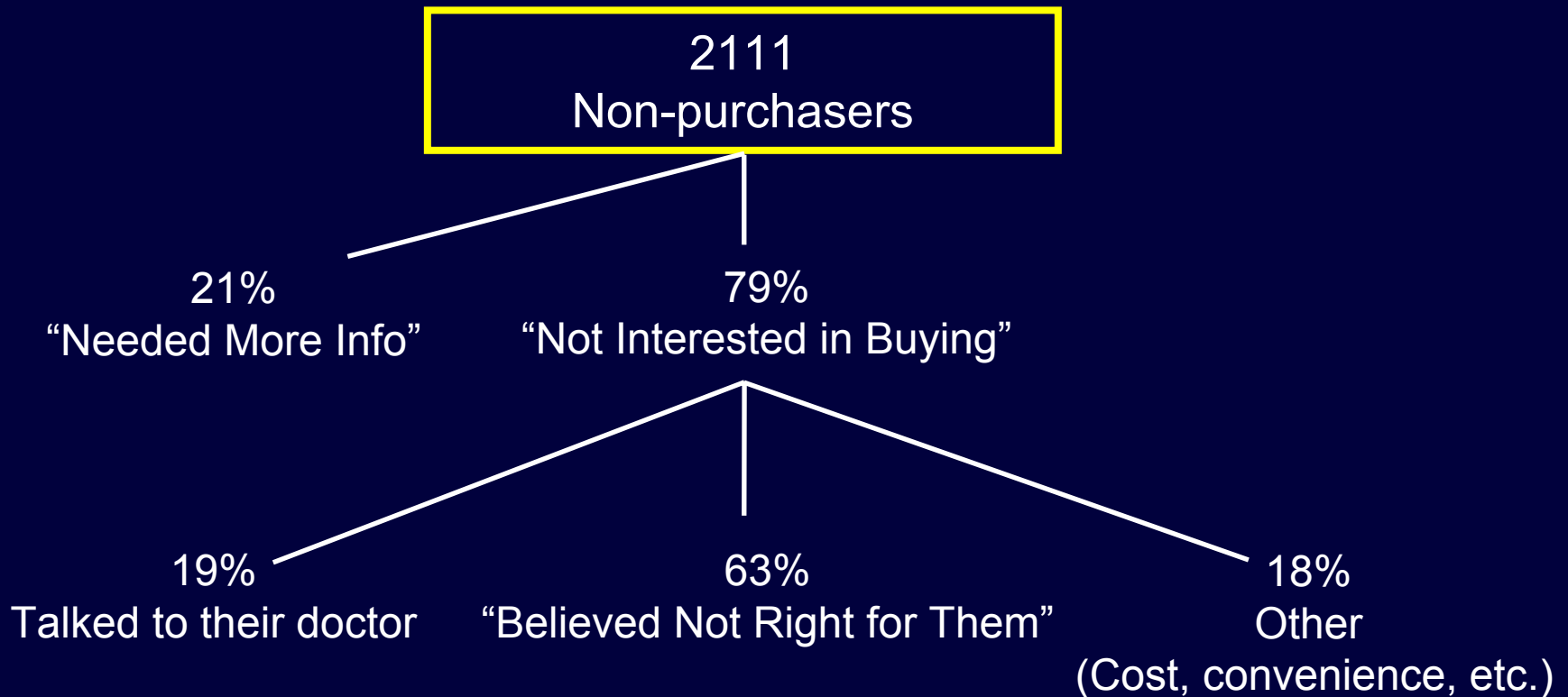
CUSTOM Results

Participant Flow Through Study



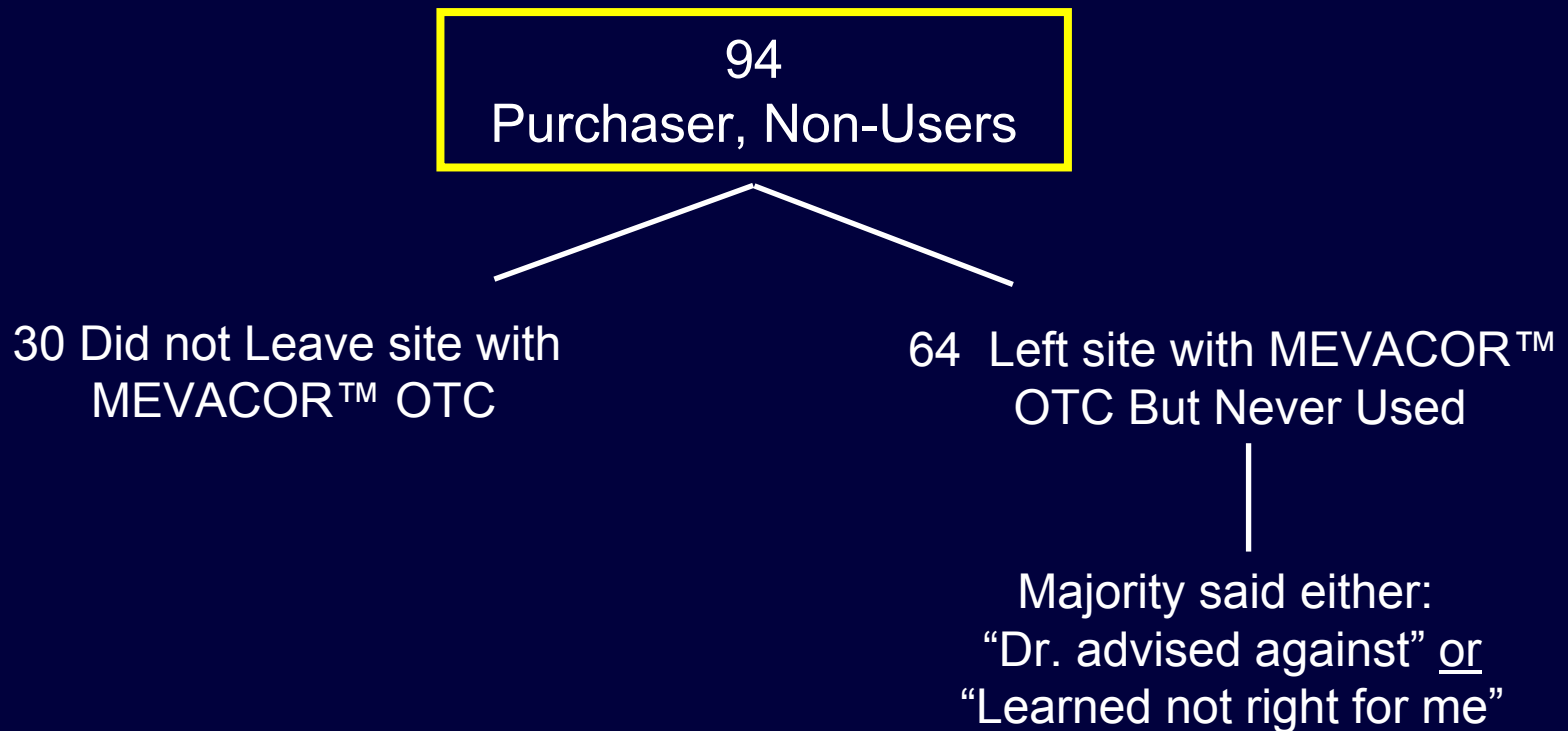
CUSTOM: Non-Purchaser Behavior

In-Store OTC System Discouraged
Inappropriate People from Purchasing



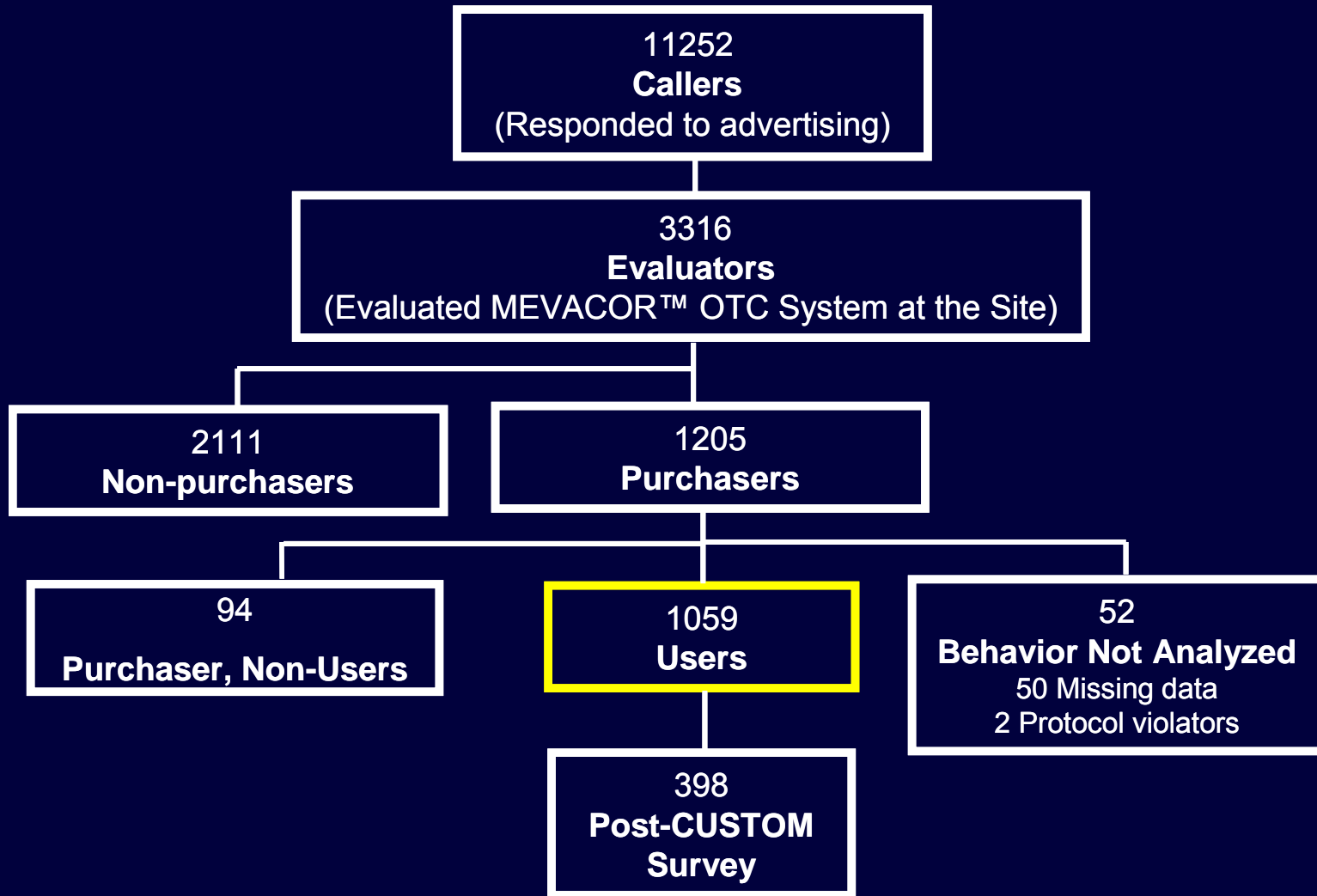
CUSTOM: Purchaser, Non-User Behavior

Post-Purchase OTC System Discouraged Additional Inappropriate People from Using



CUSTOM Results

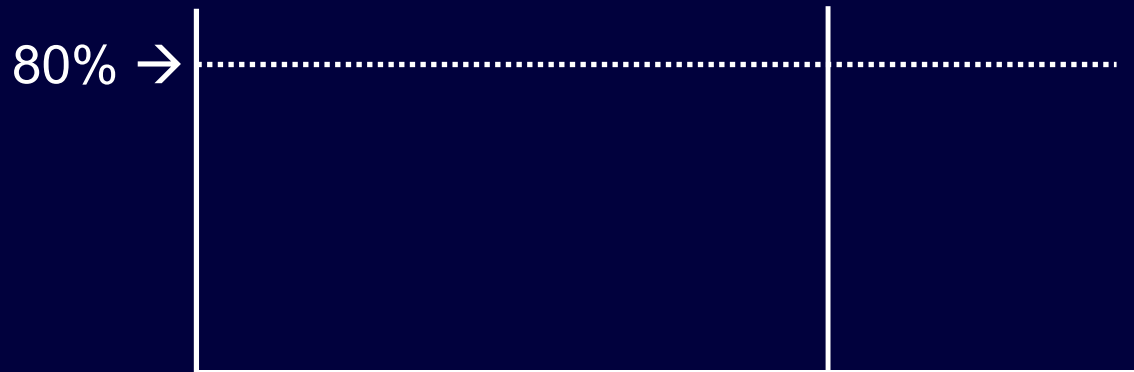
Participant Flow Through Study



CUSTOM Results

Benefit and Safety Behavioral Assessment

Initial Decision to Use
(N=1059)

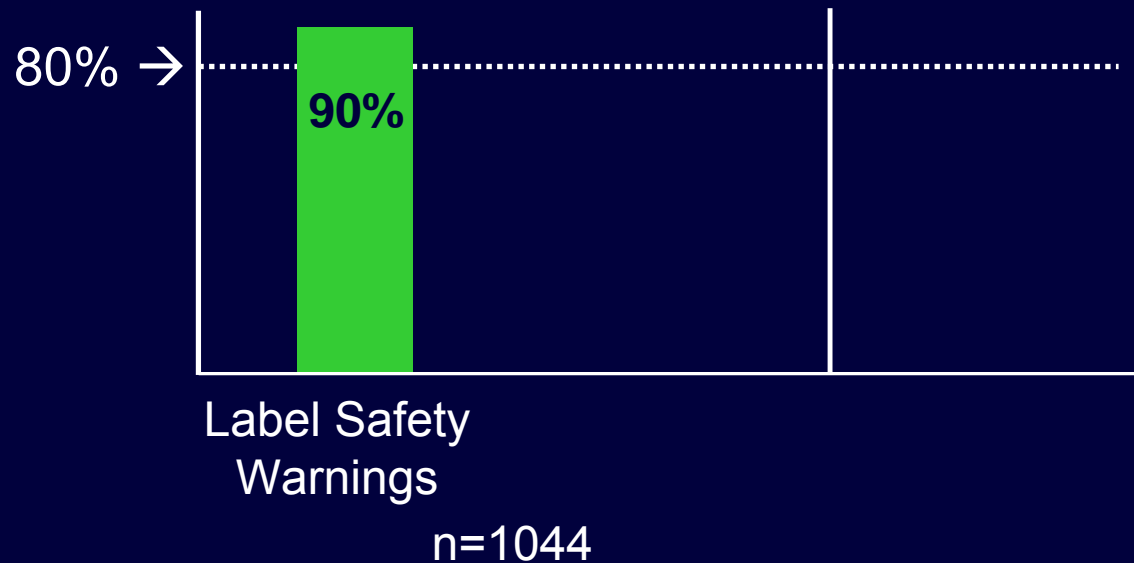


CUSTOM Results

Benefit and Safety Behavioral Assessment

Initial Decision to Use
(N=1059)

Supplemental
Analyses

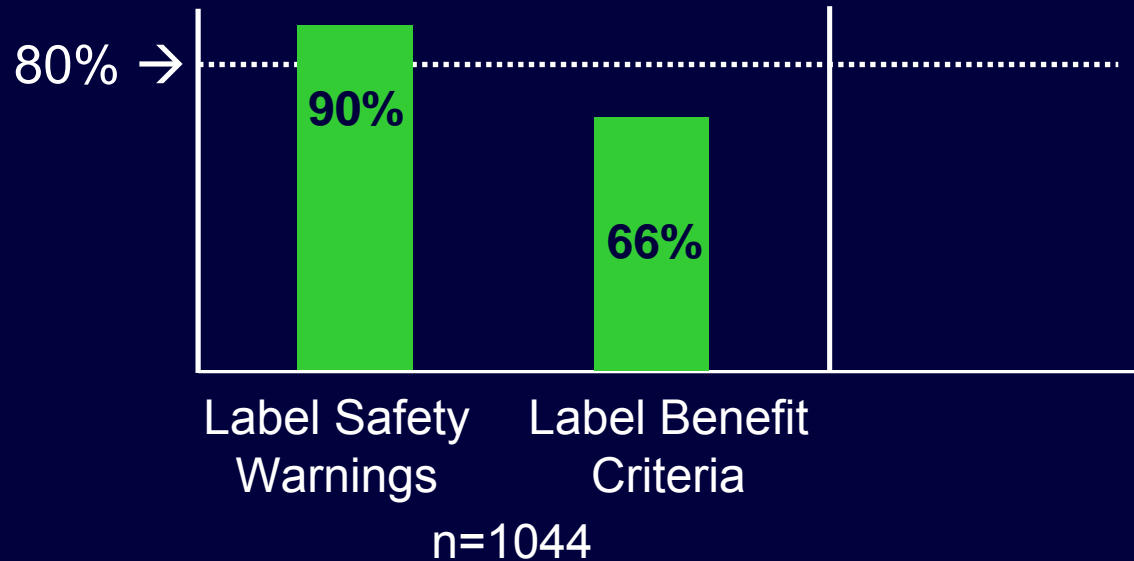


CUSTOM Results

Benefit and Safety Behavioral Assessment

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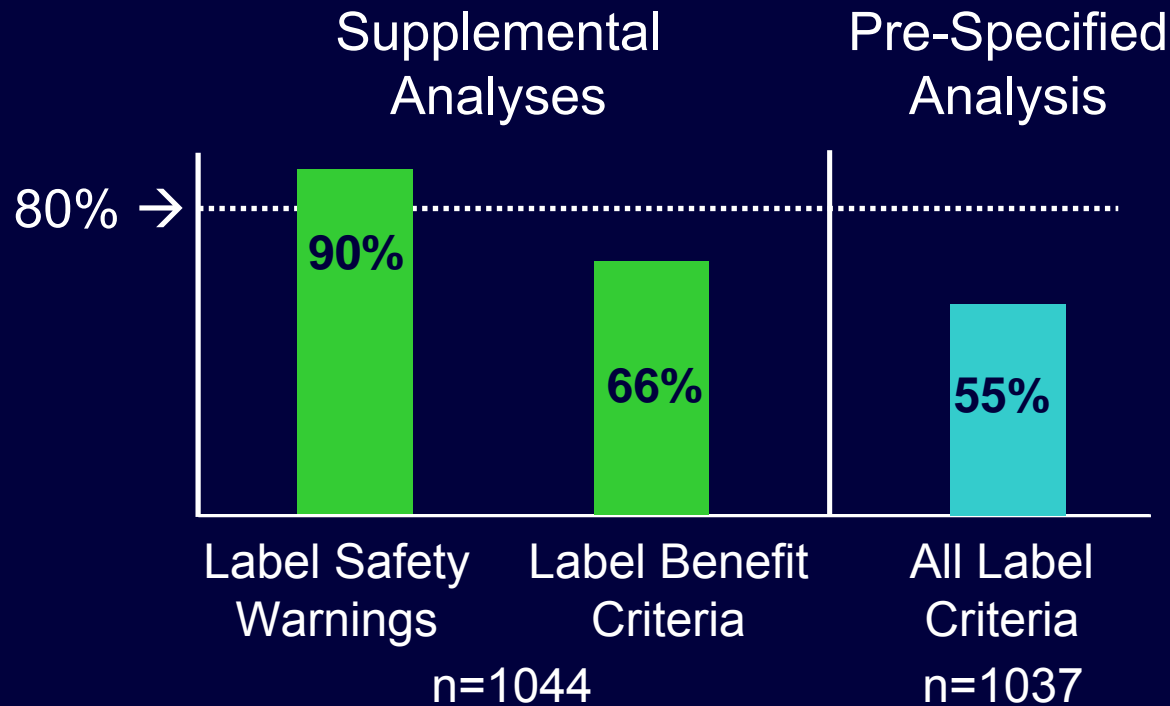
Supplemental
Analyses



CUSTOM Results

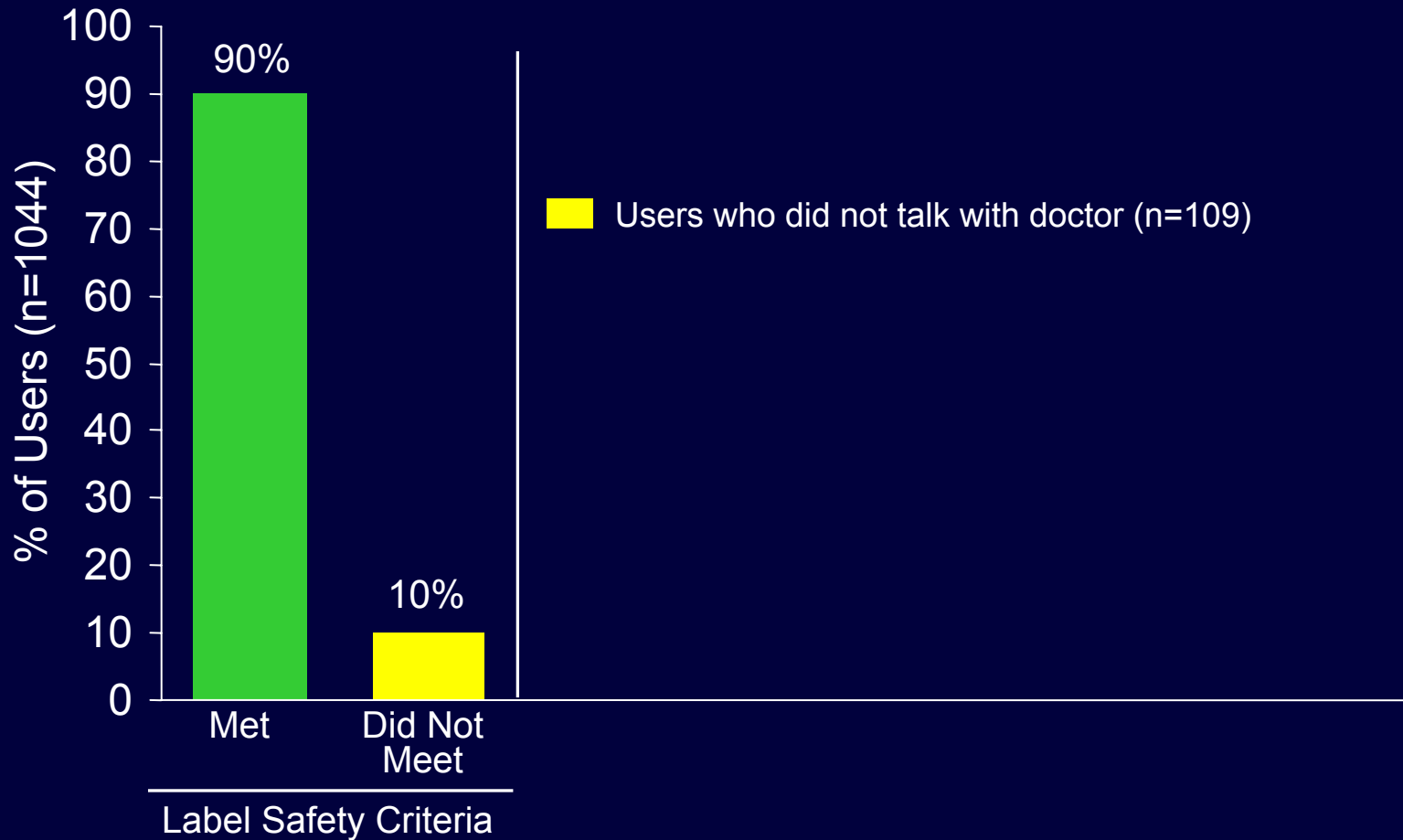
Benefit and Safety Behavioral Assessment

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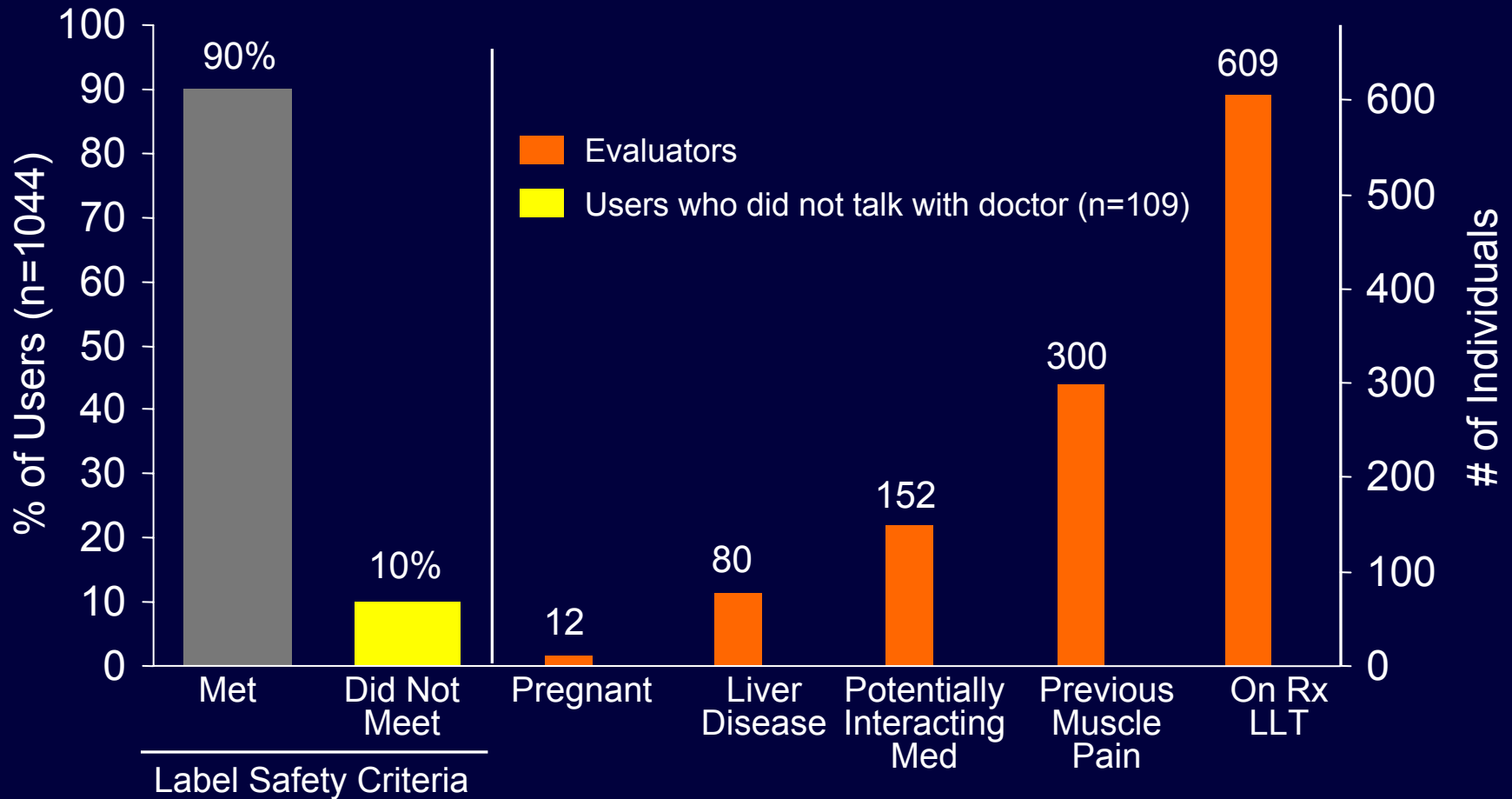
CUSTOM Results

Safety Warnings - Initial Use



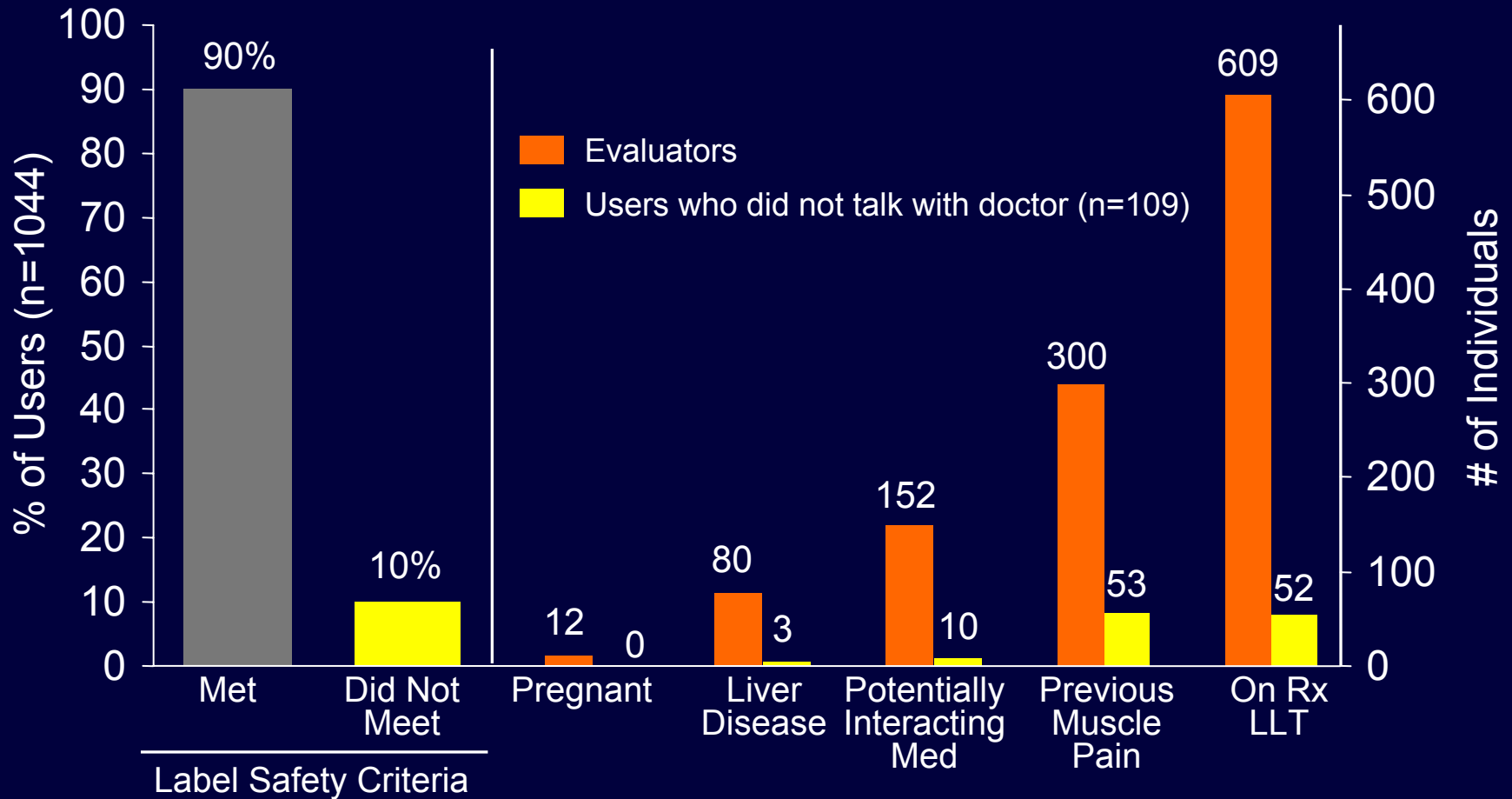
CUSTOM Results

Safety Warnings - Initial Use



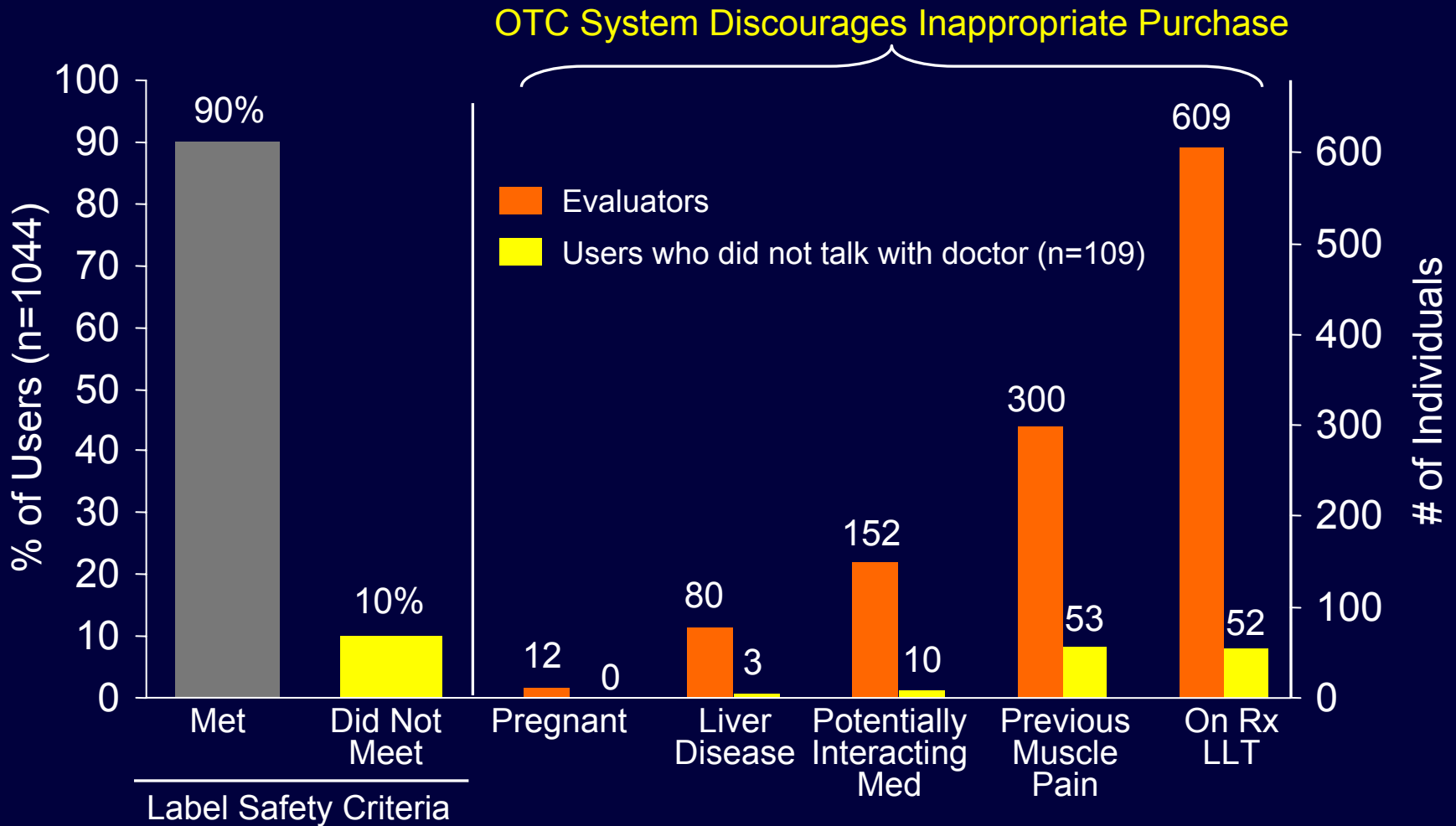
CUSTOM Results

Safety Warnings - Initial Use



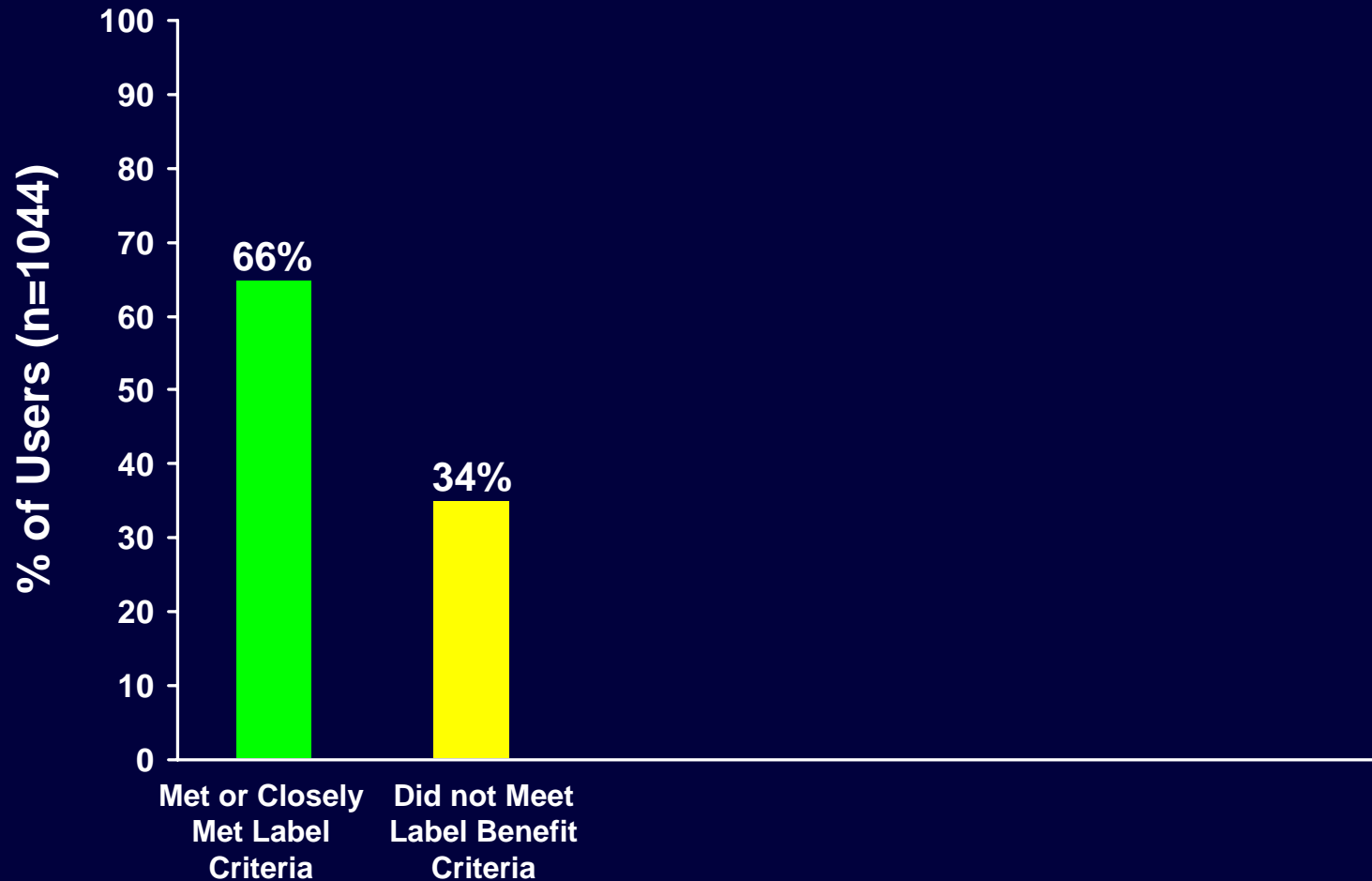
CUSTOM Results

Safety Warnings - Initial Use



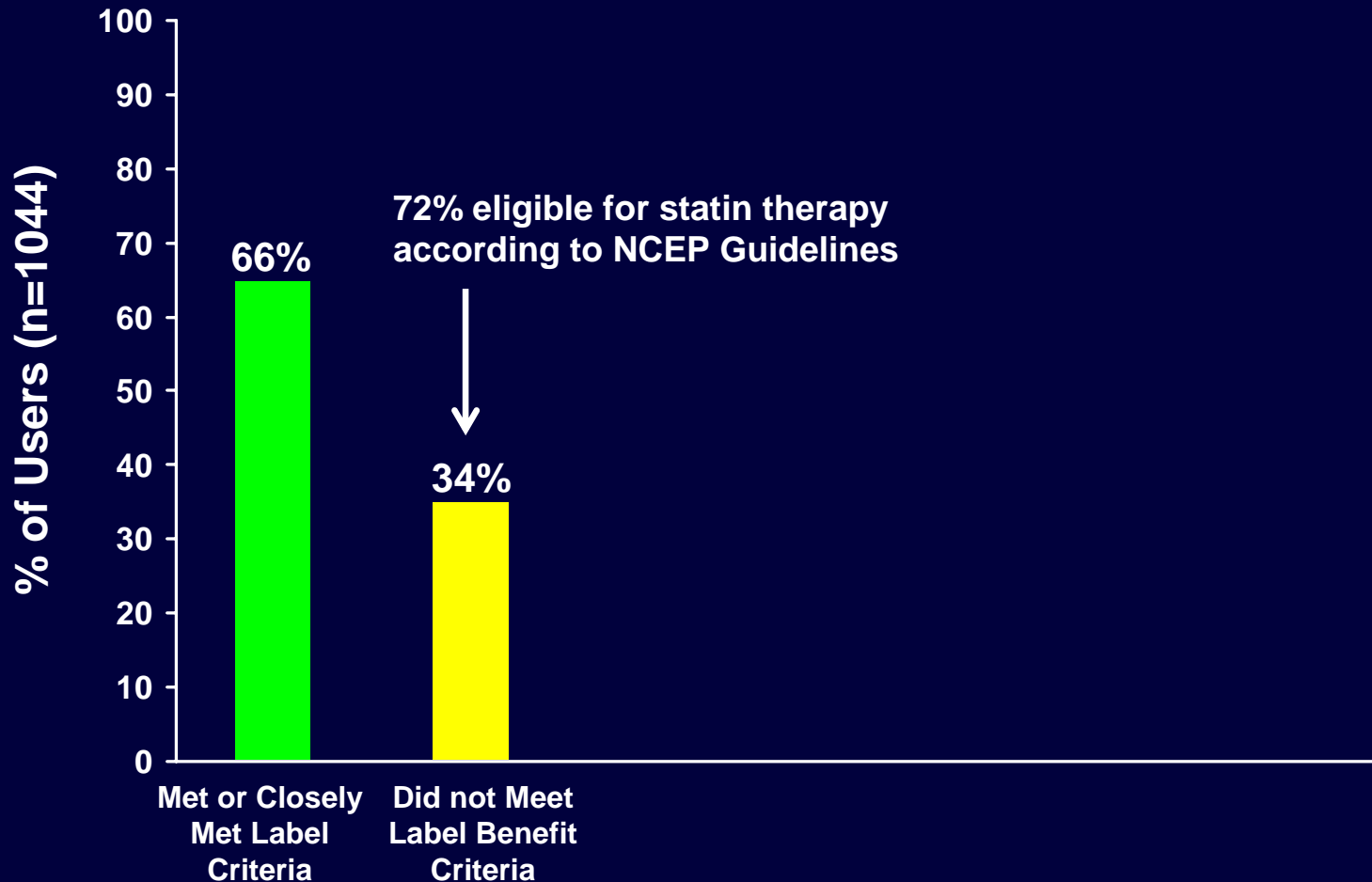
CUSTOM Results

Benefit Criteria - Initial Use



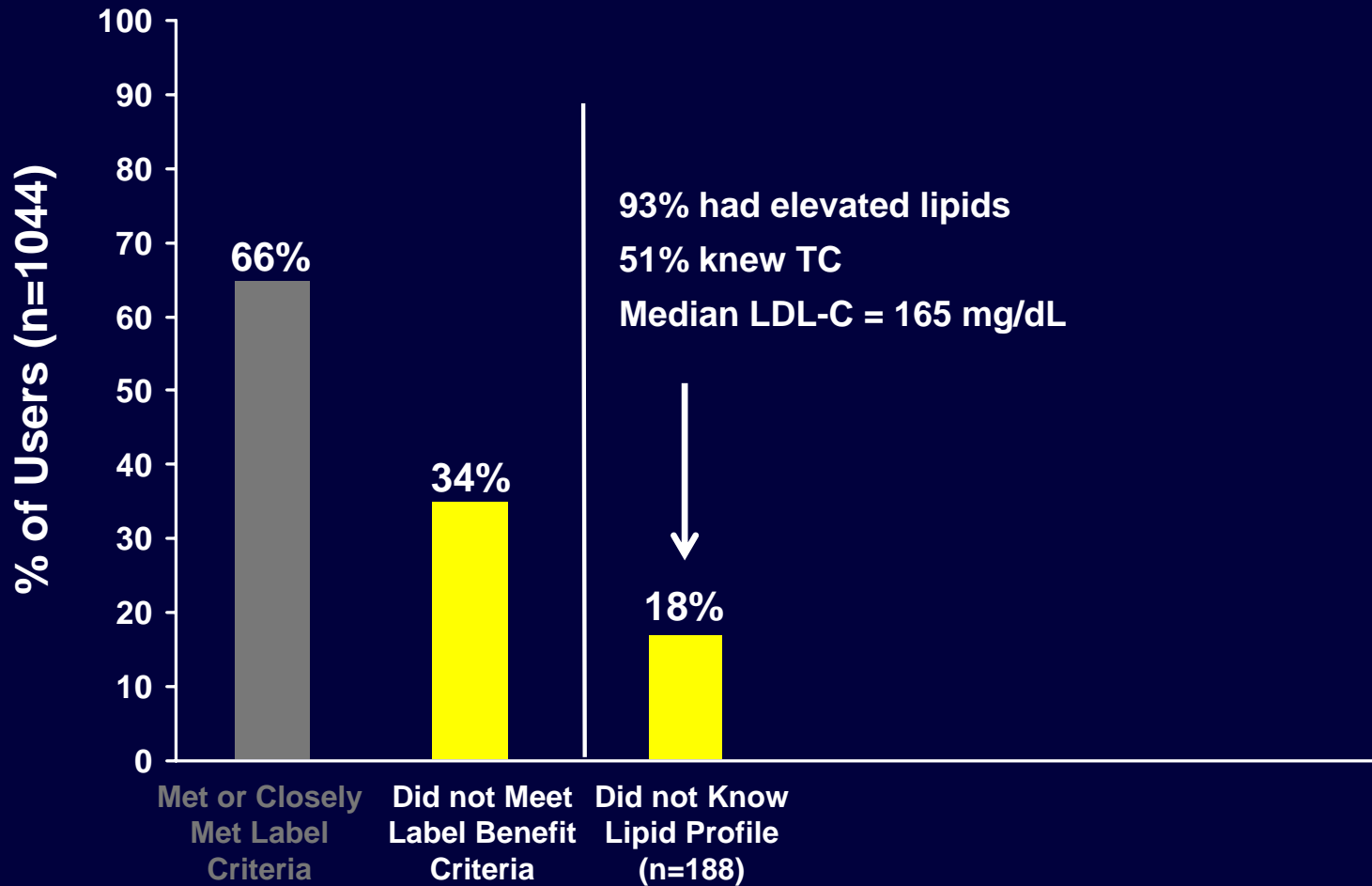
CUSTOM Results

Benefit Criteria - Initial Use



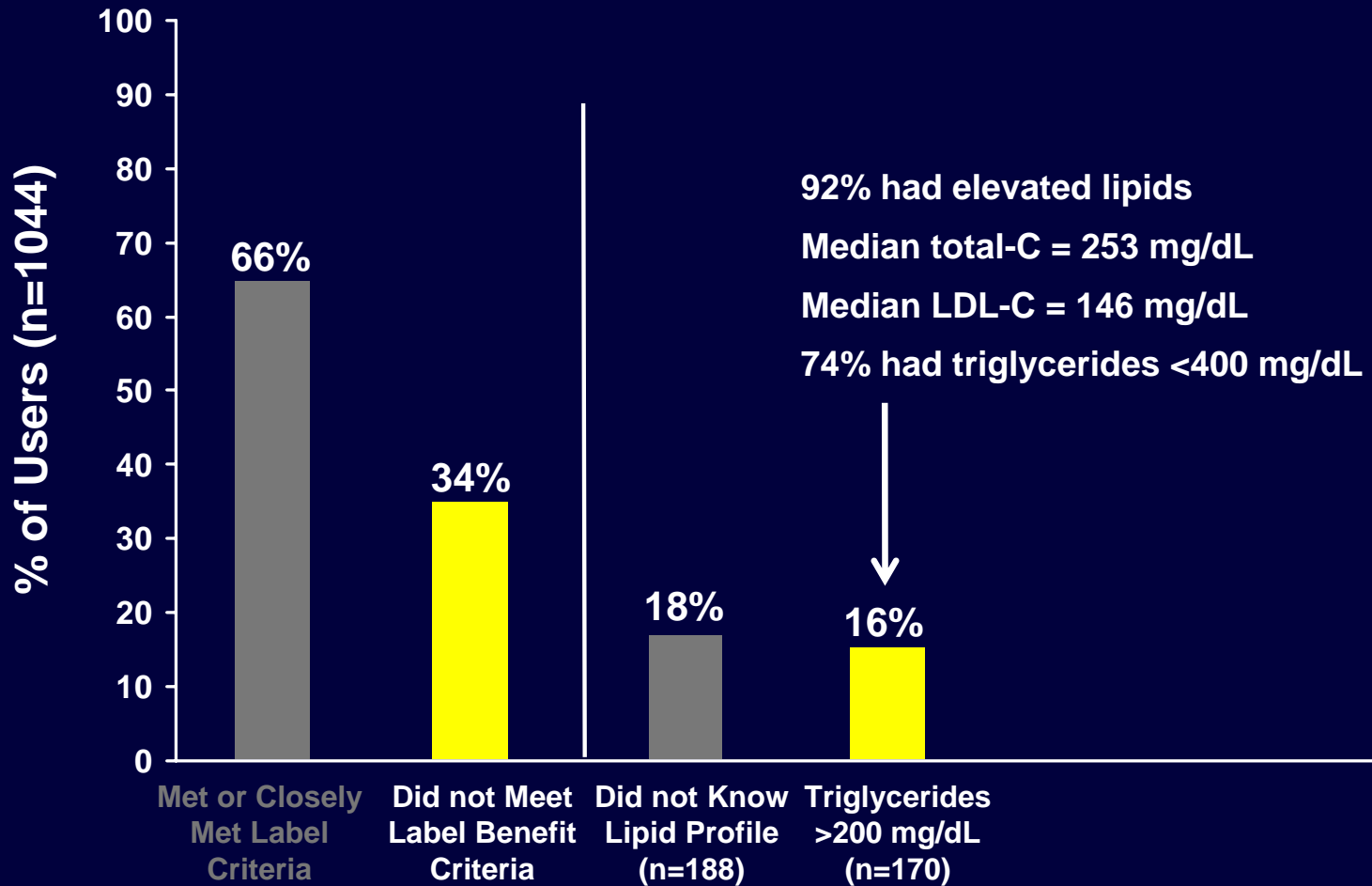
CUSTOM Results

Benefit Criteria - Initial Use



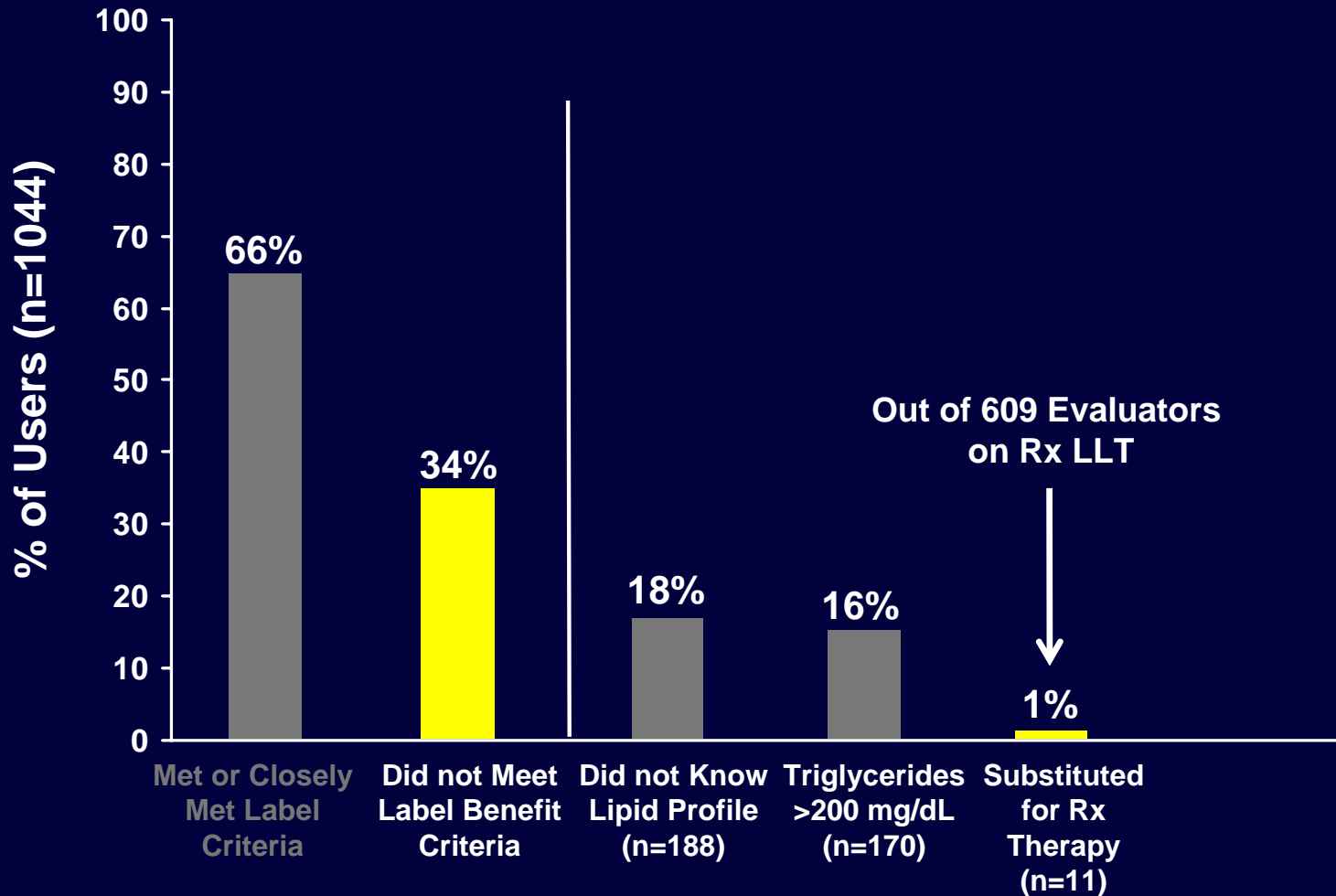
CUSTOM Results

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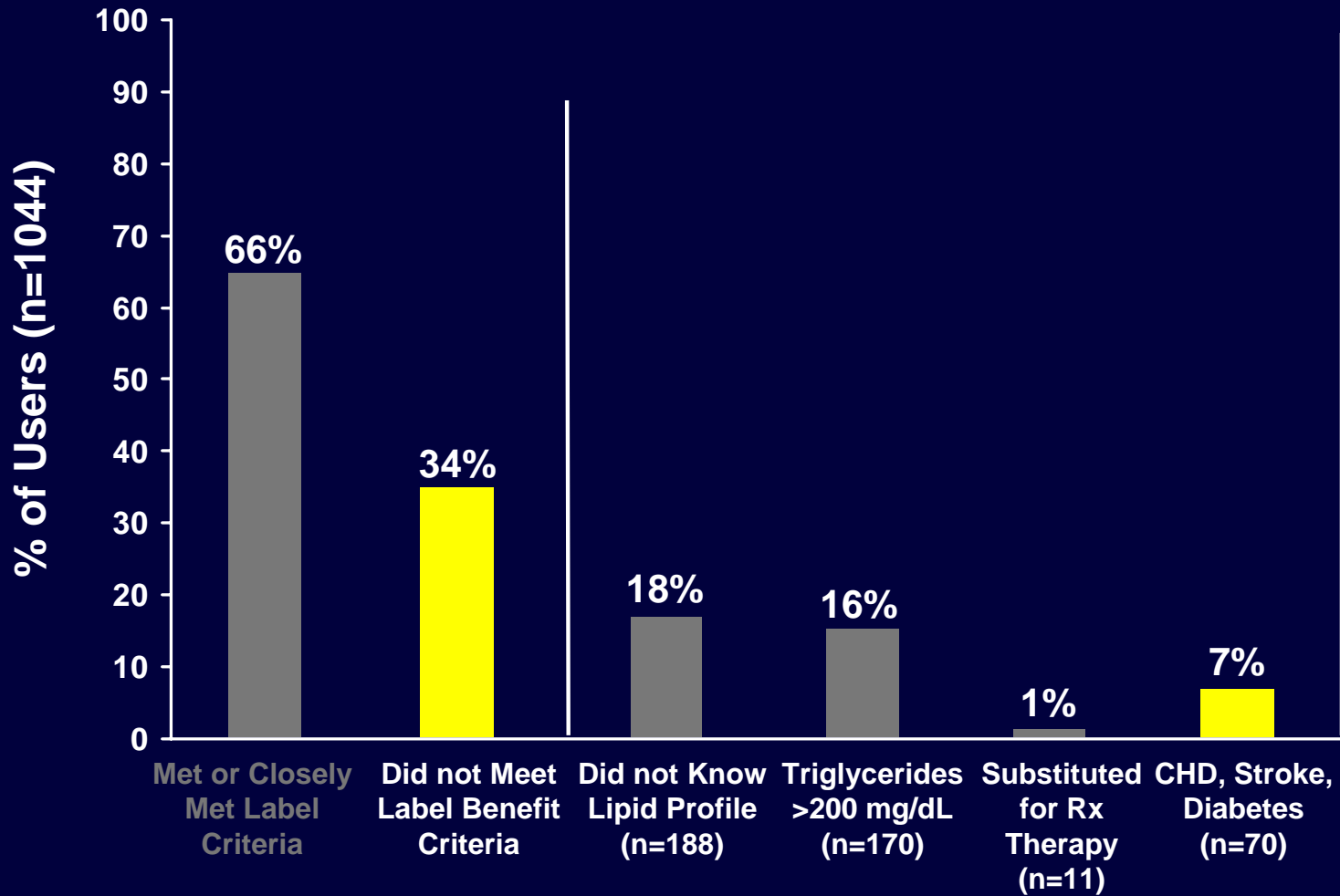
CUSTOM Results

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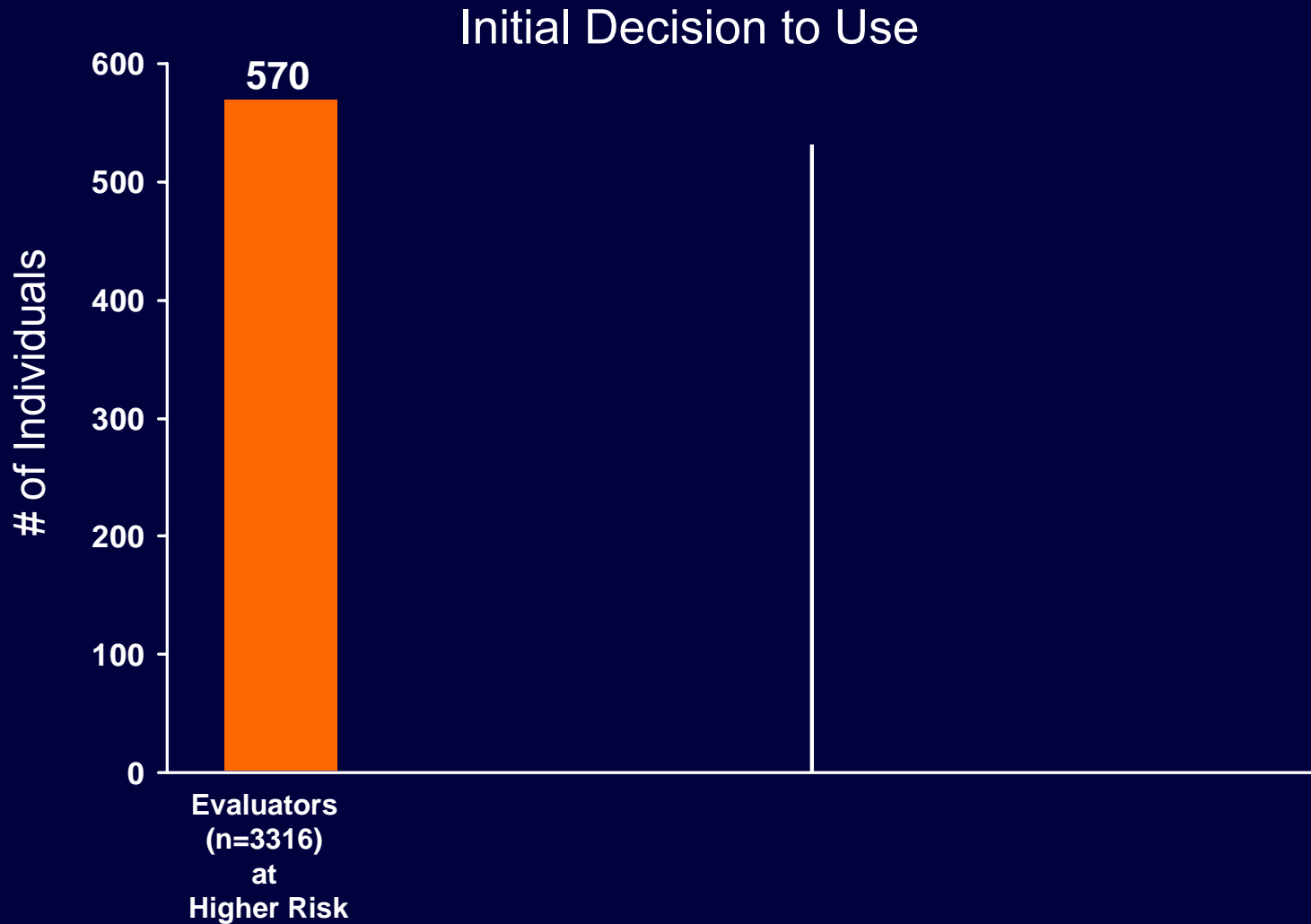
CUSTOM Results

Benefit Criteria - Initial Use



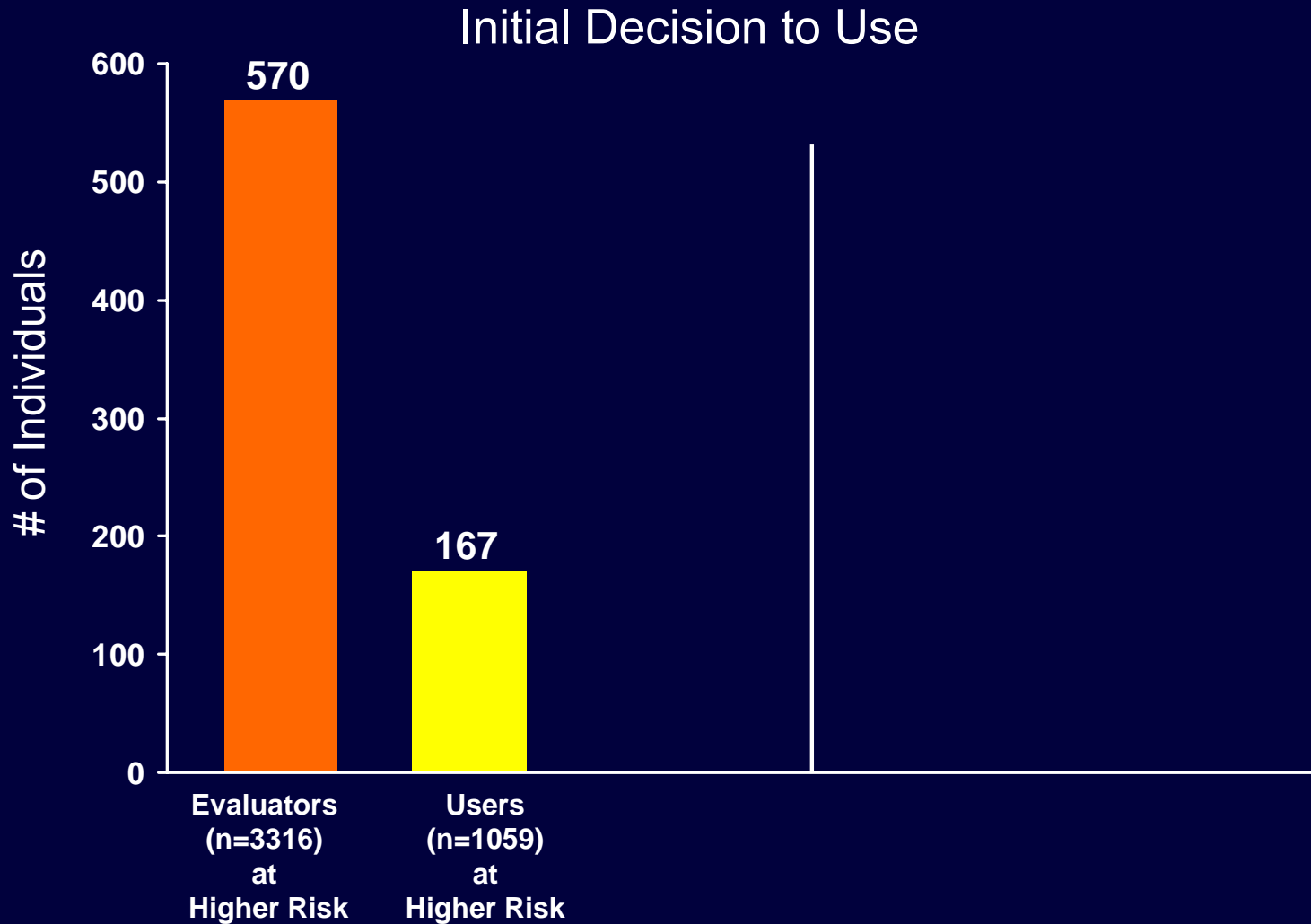
CUSTOM Results

Consumers at Higher Risk (CHD, Stroke, Diabetes)



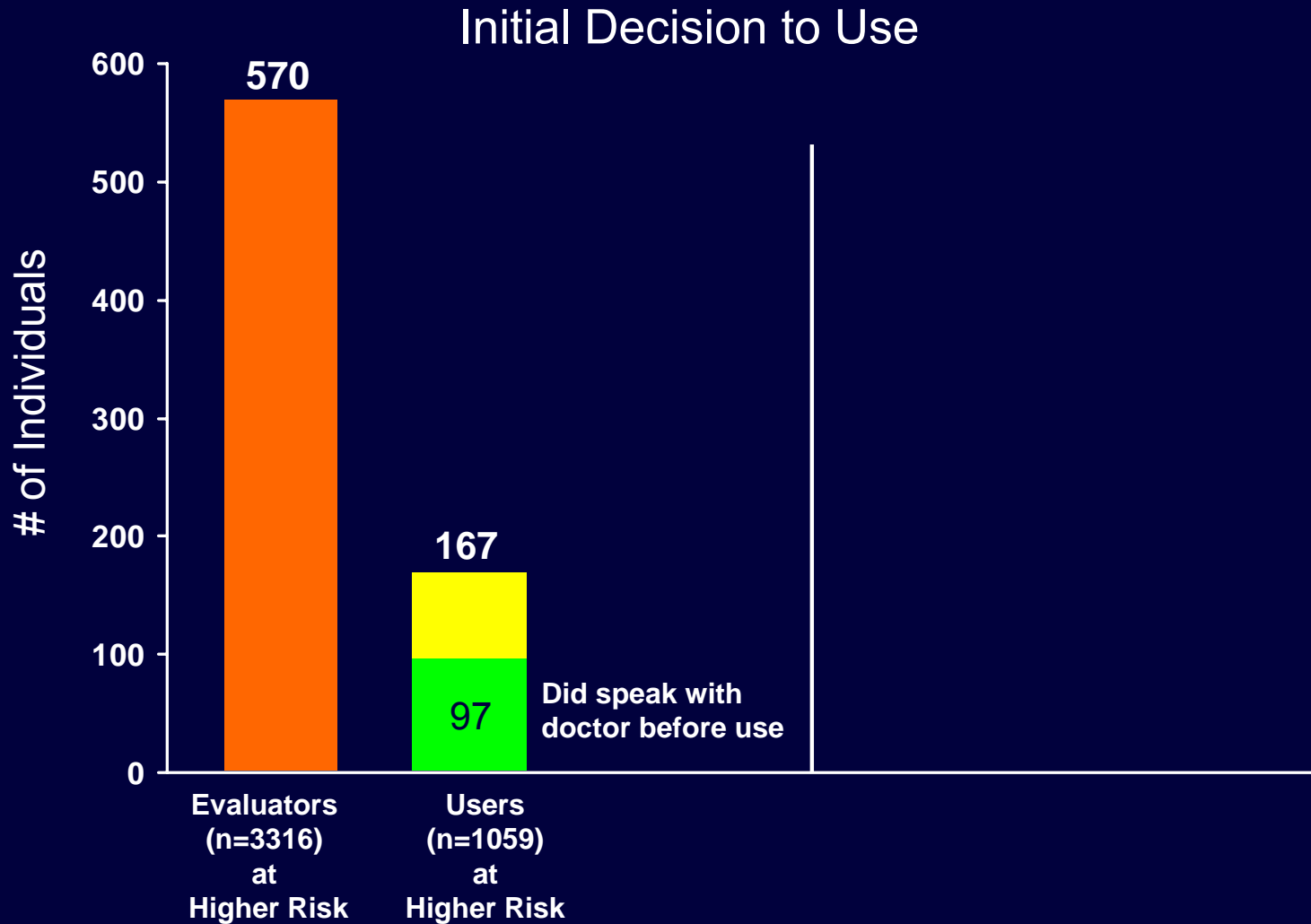
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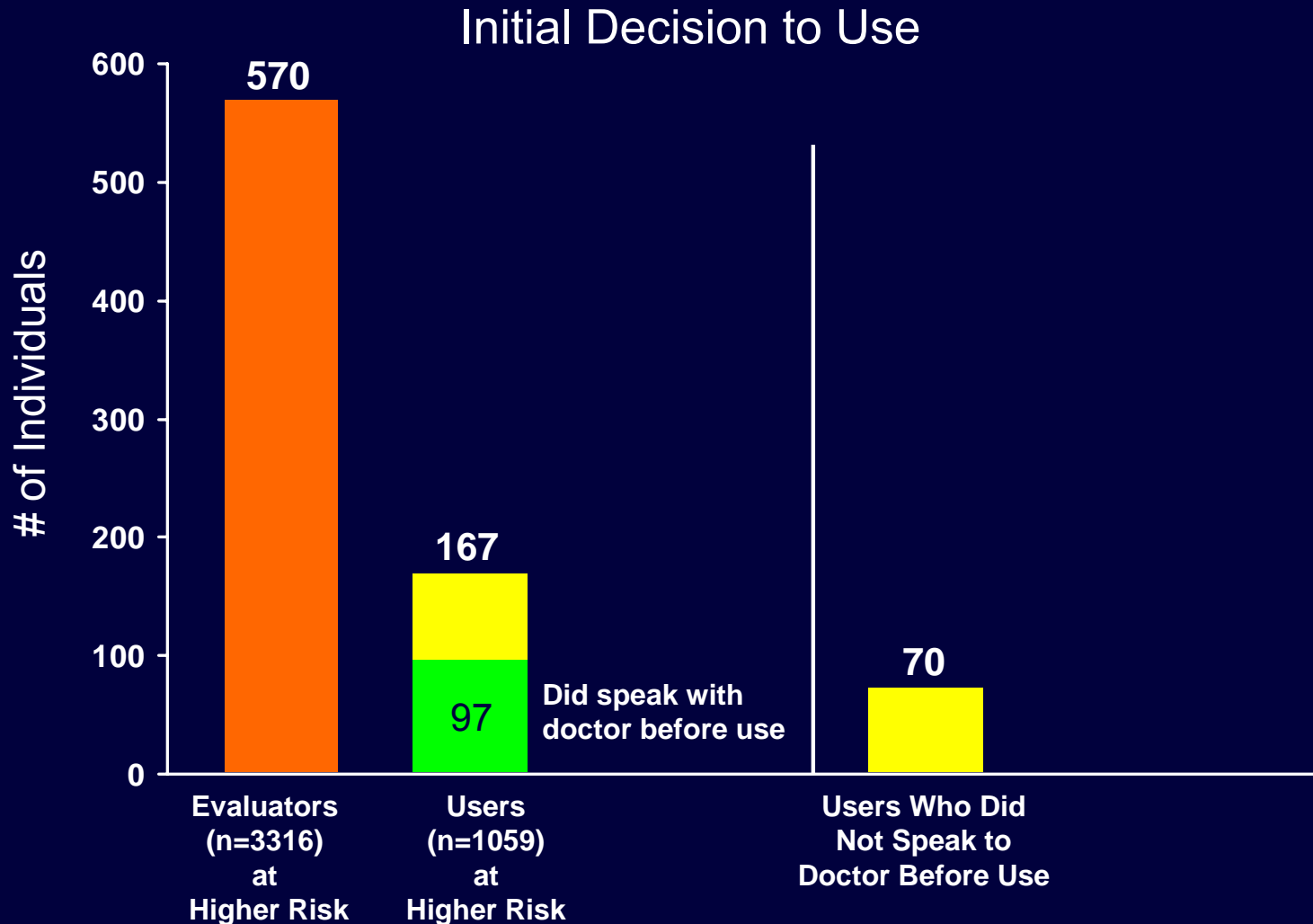
CUSTOM Results

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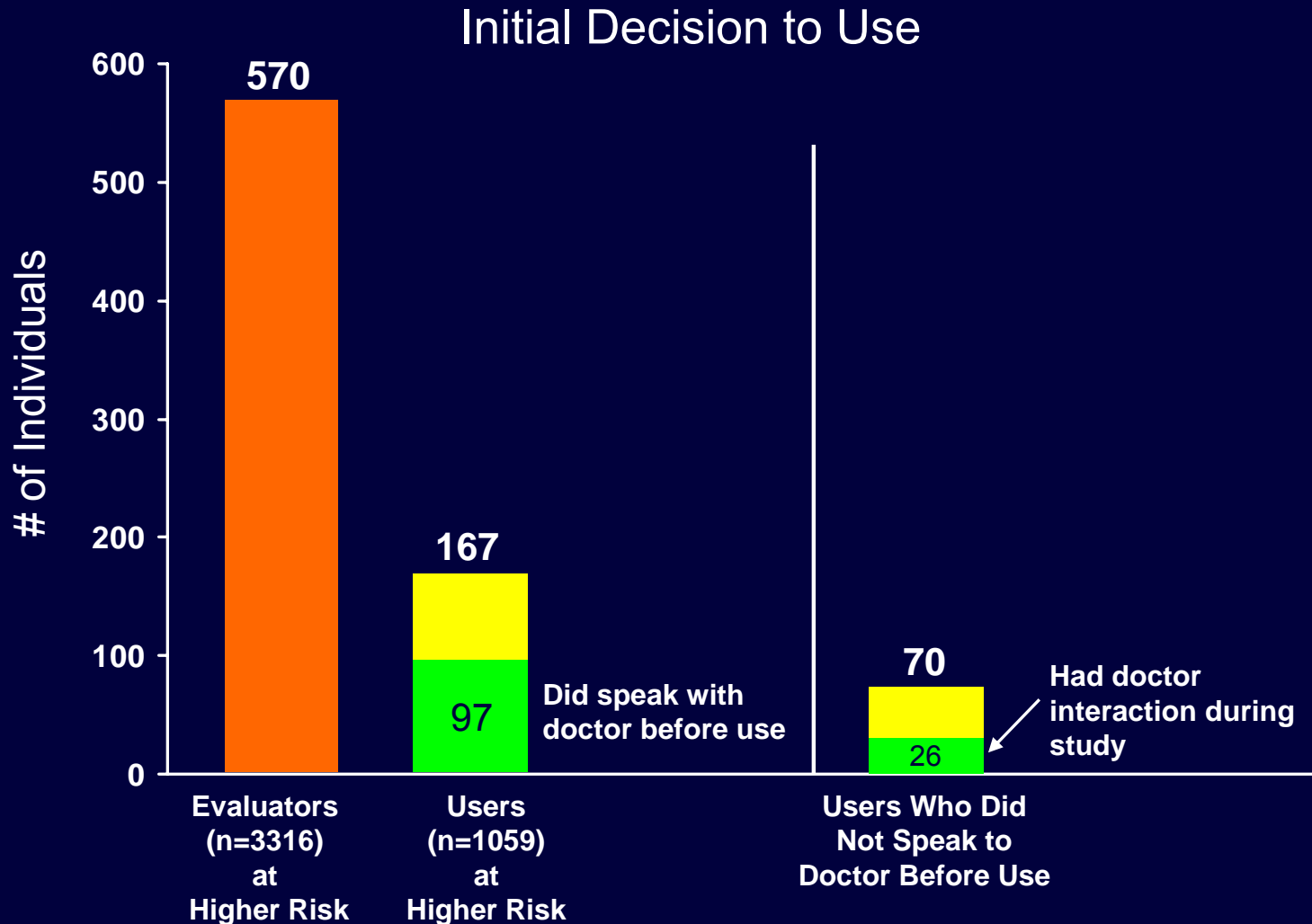
CUSTOM Results

Consumers at Higher Risk (CHD, Stroke, Diabetes)



CUSTOM Results

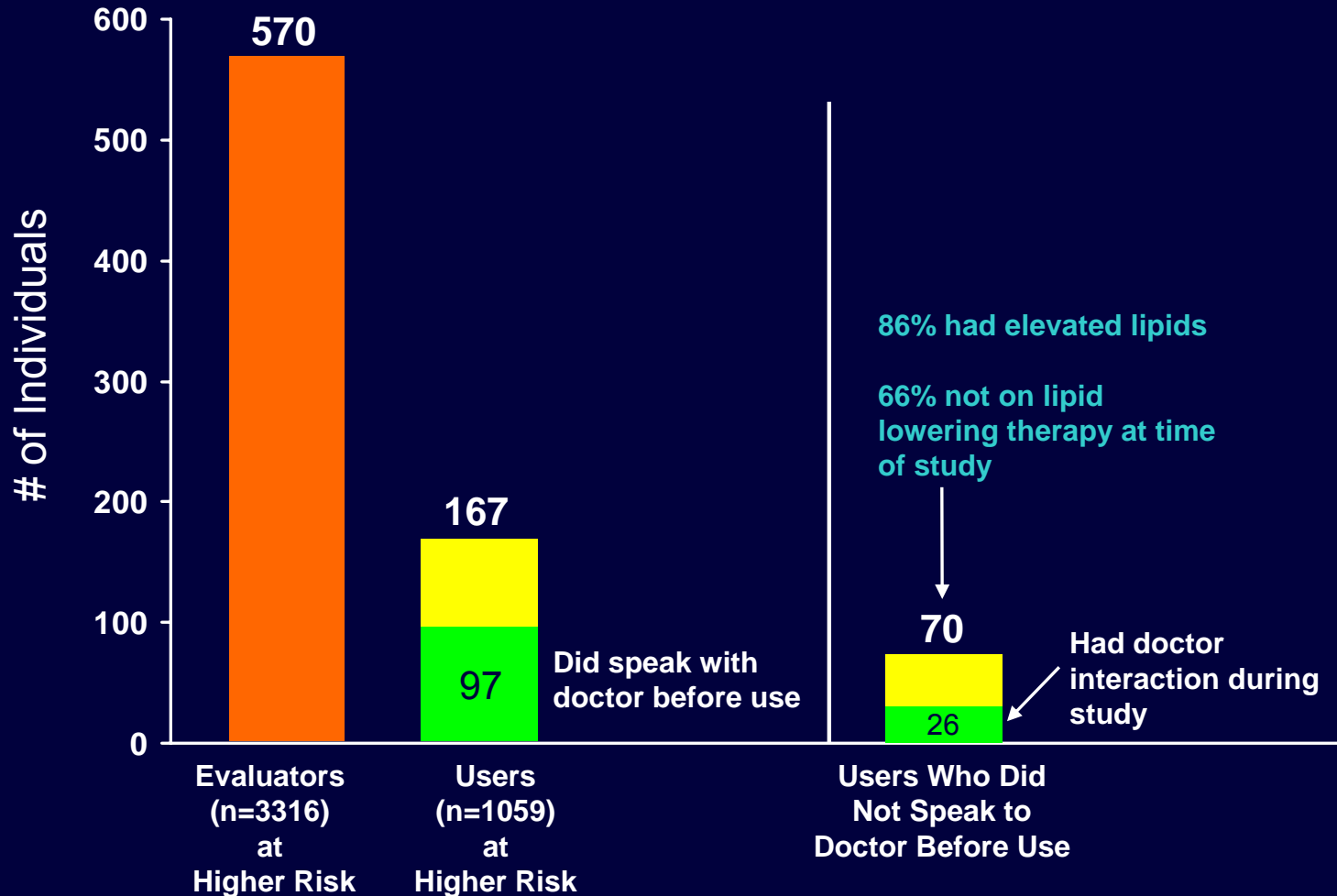
Consumers at Higher Risk (CHD, Stroke, Diabetes)



CUSTOM Results

Consumers at Higher Risk (CHD, Stroke, Diabetes)

Initial Decision to Use

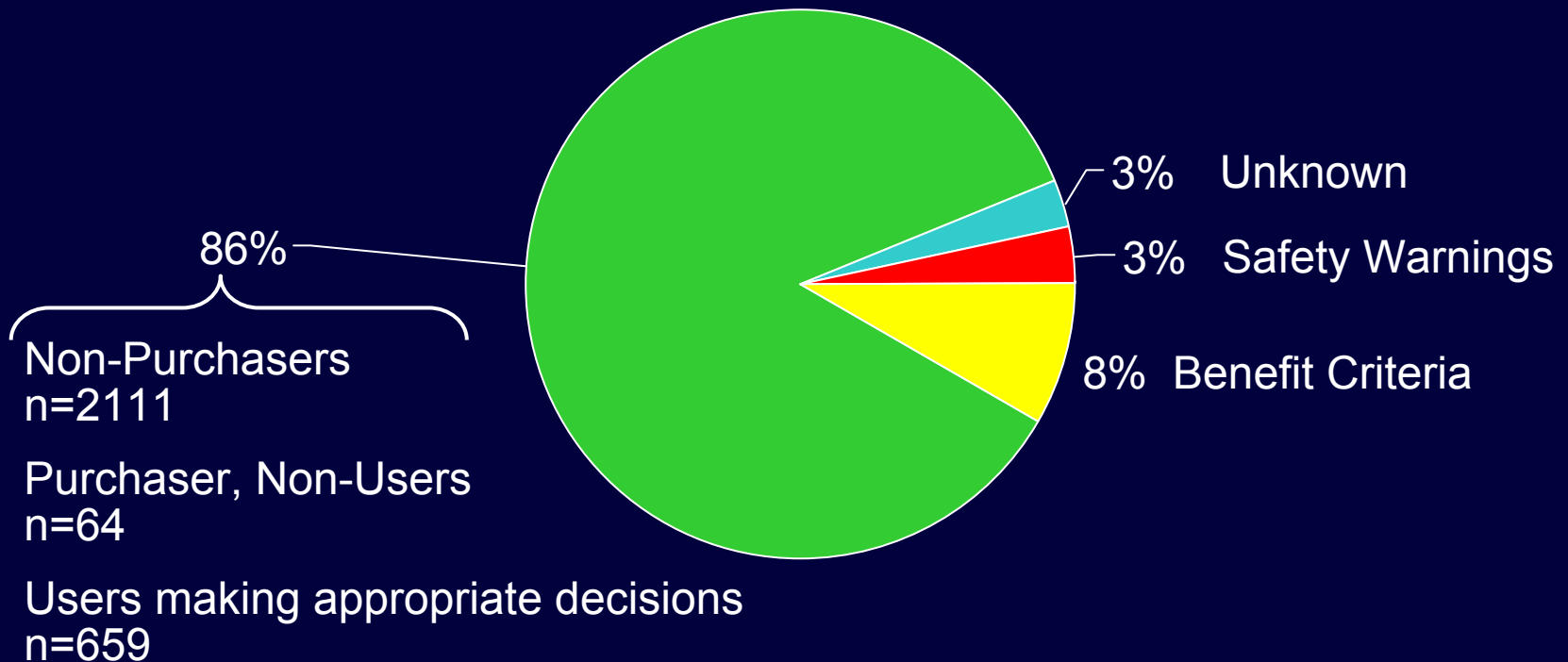


CUSTOM Results

Summary of Initial Use Decisions

N=3316

Consumers Can Select Appropriately



Key Questions

- Will the MEVACOR™ OTC Self-Management System allow consumers to:
 1. Make appropriate initial use decisions?
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 3. Self-manage their cholesterol over time and obtain benefit?

Key Questions

- Will the MEVACOR™ OTC Self-Management System allow consumers to:
 2. Self-manage the potential safety risks over time?
 - 1059 Users
 - 693 No emergent medical condition/situation
 - 366 With emergent medical condition/situation
 - 345 (94%) continued use consistent with label
 - 21 (6%) continued use inconsistent with label

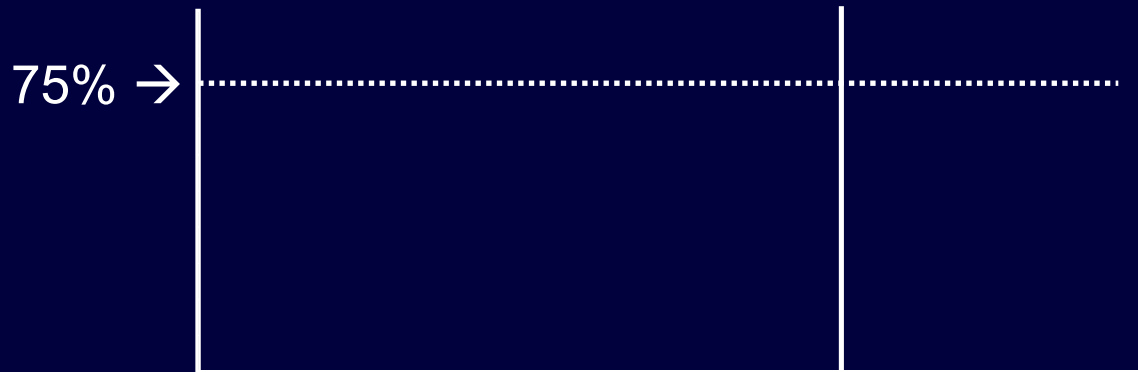
Key Questions

- Will the MEVACOR™ OTC Self-Management System allow consumers to:
 3. Self-manage their cholesterol over time and obtain benefit?
 - 1059 Users
 - 74% of users obtained follow-up test or discontinued before 6 weeks
 - 75% of users with follow-up test followed label directives regarding LDL-C goal
 - 21% reduction in LDL-C

CUSTOM Results

Benefit and Safety Behavioral Assessment

Ongoing Decisions about Use
(N=1059)

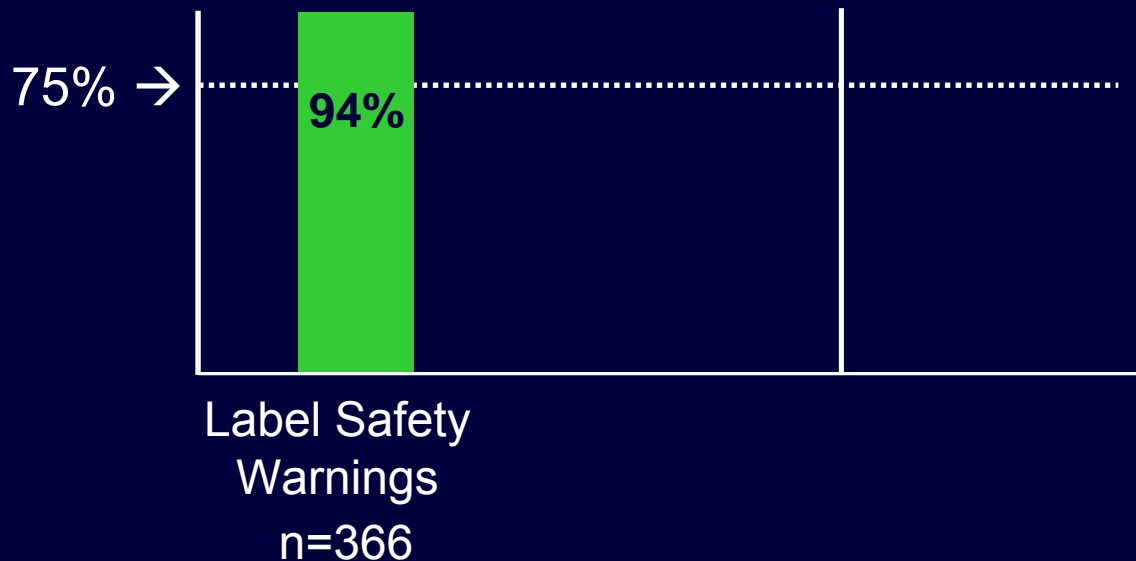


CUSTOM Results

Benefit and Safety Behavioral Assessment

Ongoing Decisions about Use
(N=1059)

Supplemental
Analyses

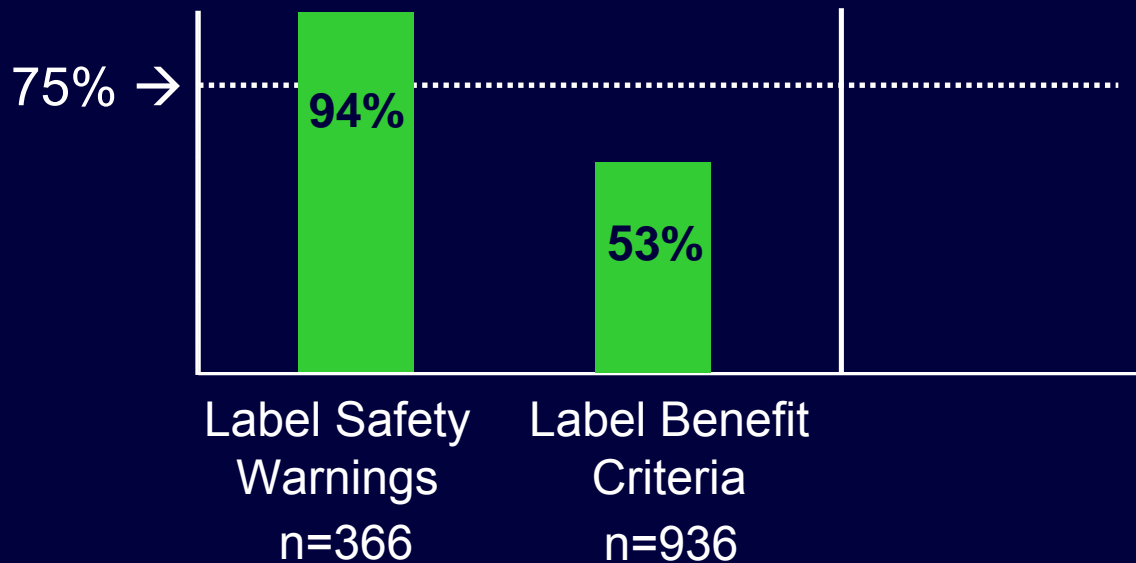


CUSTOM Results

Benefit and Safety Behavioral Assessment

Ongoing Decisions about Use
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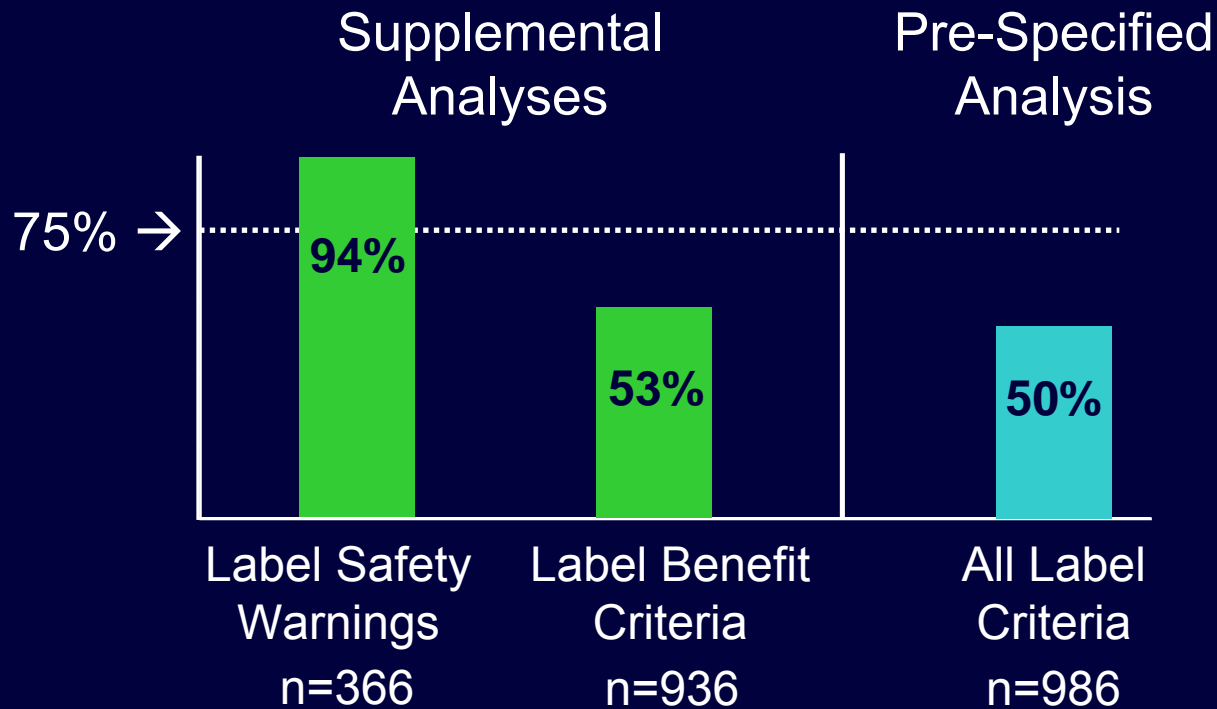
Supplemental
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CUSTOM Results

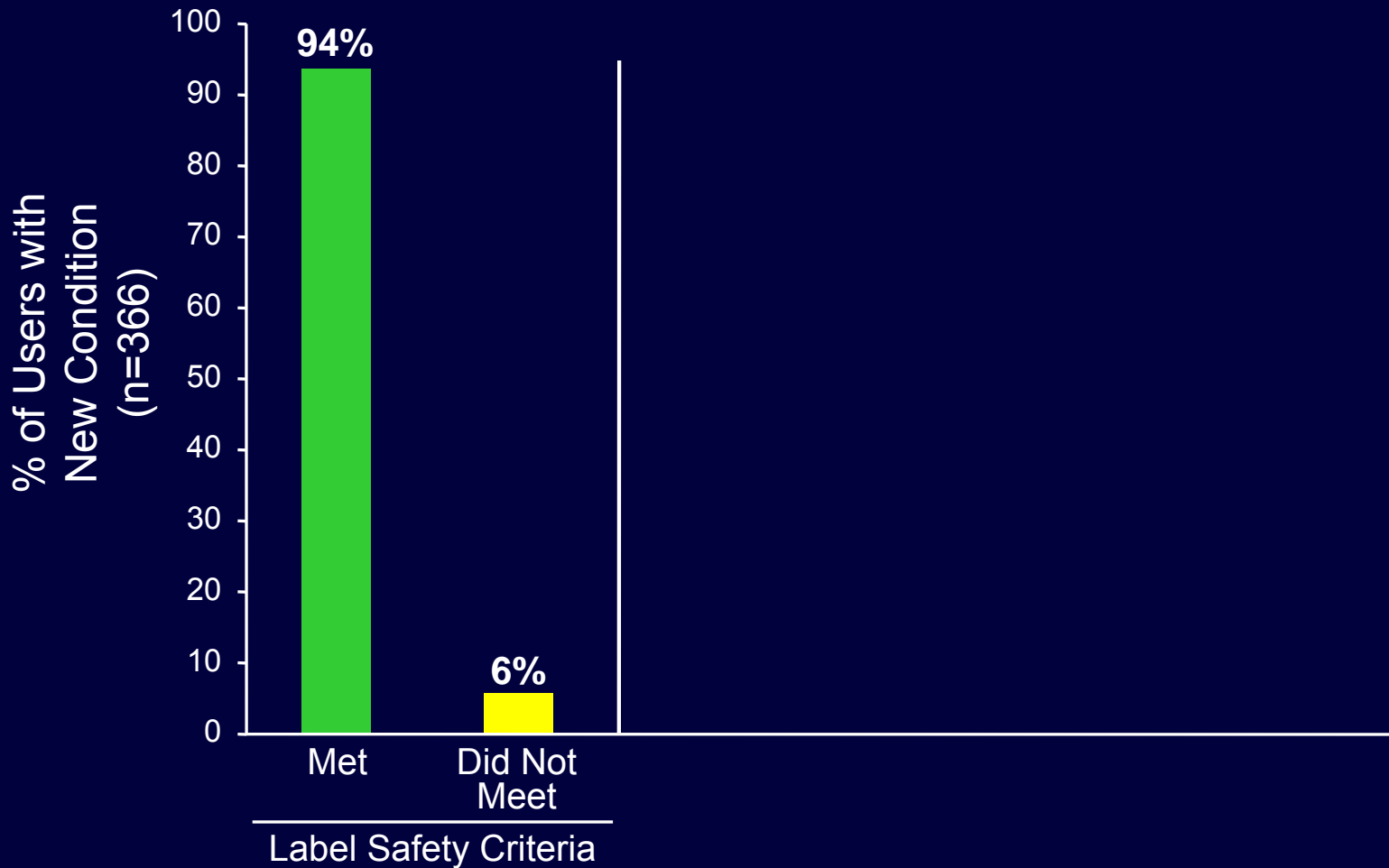
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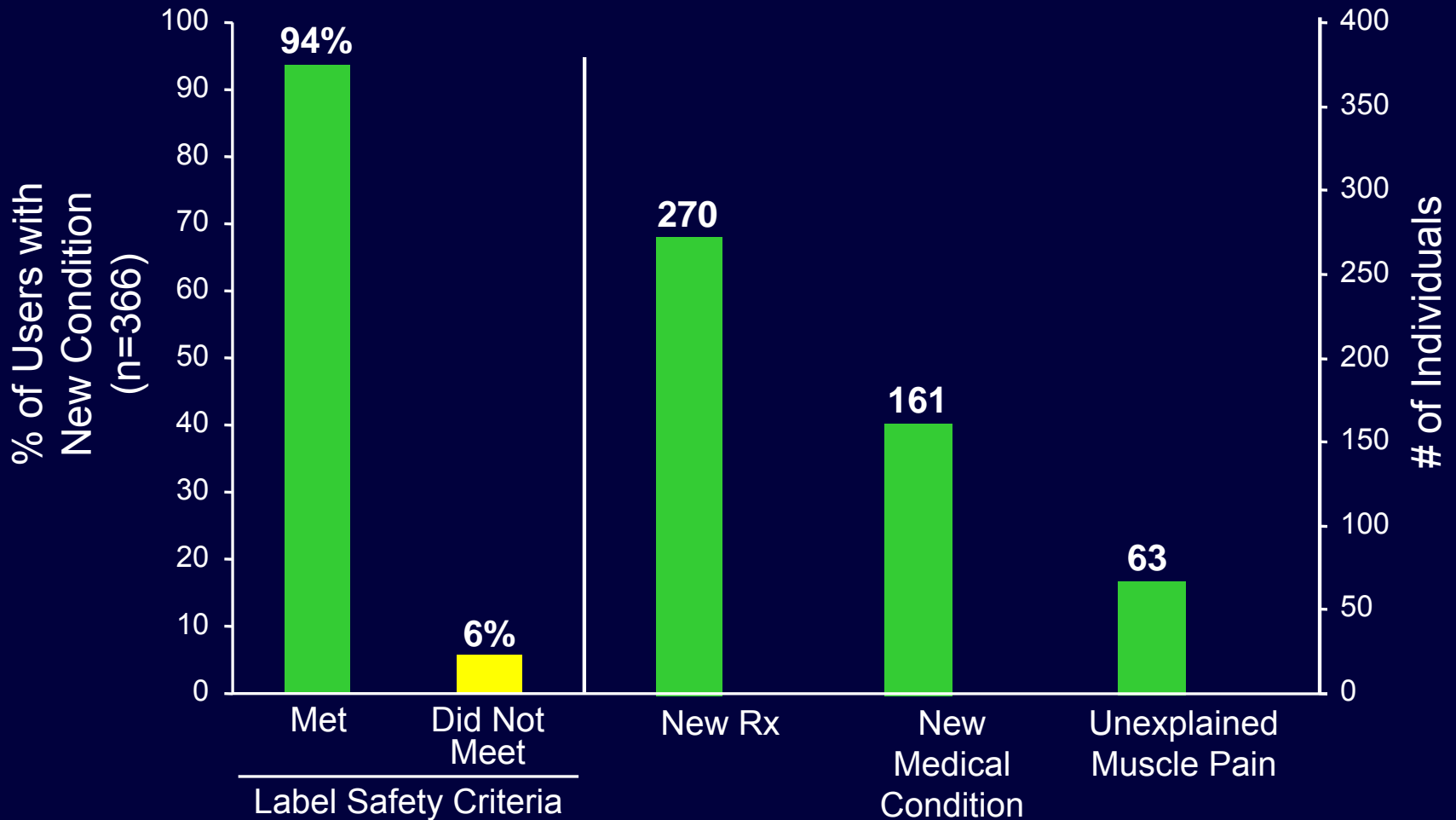
CUSTOM Results

Safety Warnings - Ongoing Use



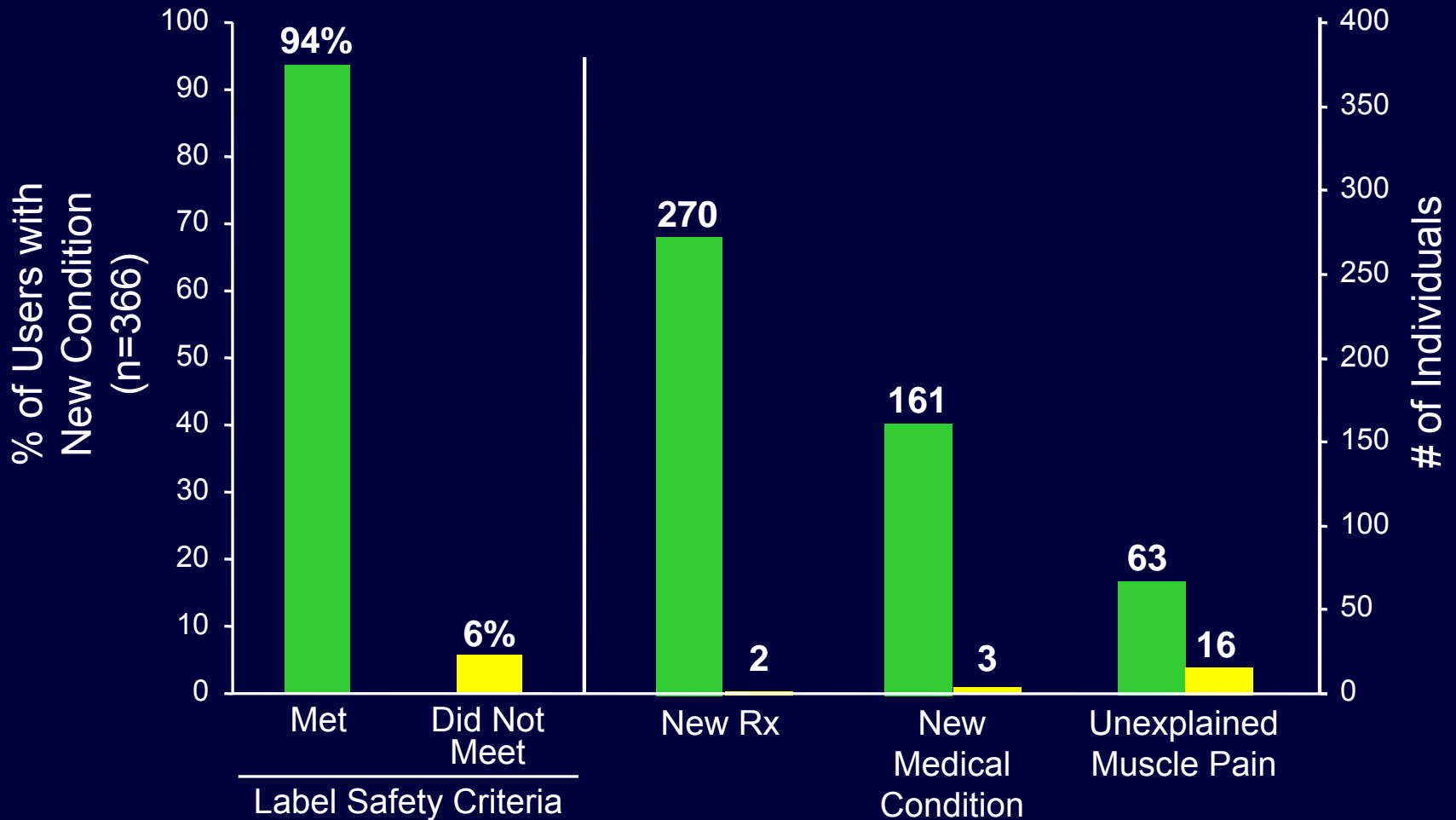
CUSTOM Results

Safety Warnings - Ongoing Use



CUSTOM Results

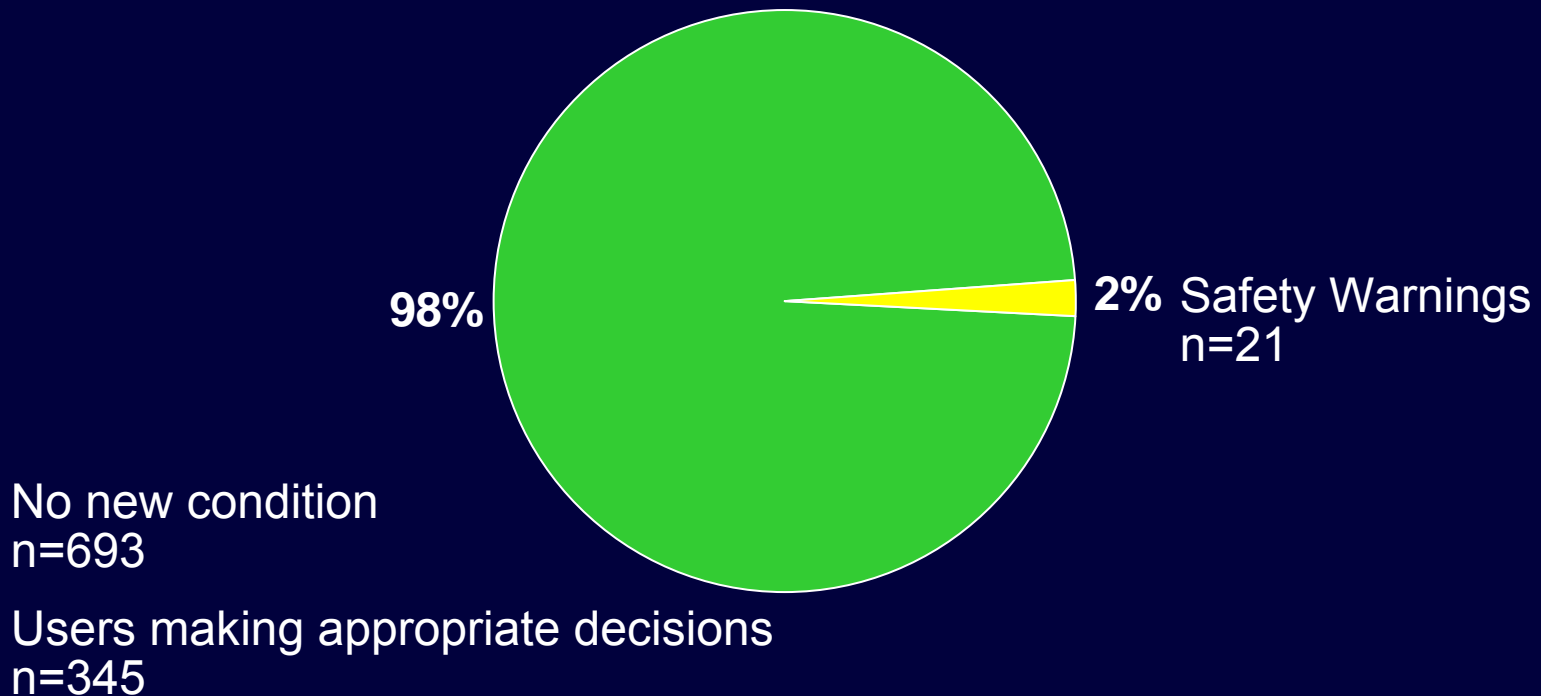
Safety Warnings - Ongoing Use



CUSTOM Results

Summary of Ongoing Use Decisions – Safety Warnings
N=1059

Consumers Can Manage Potential Safety Risks Over Time



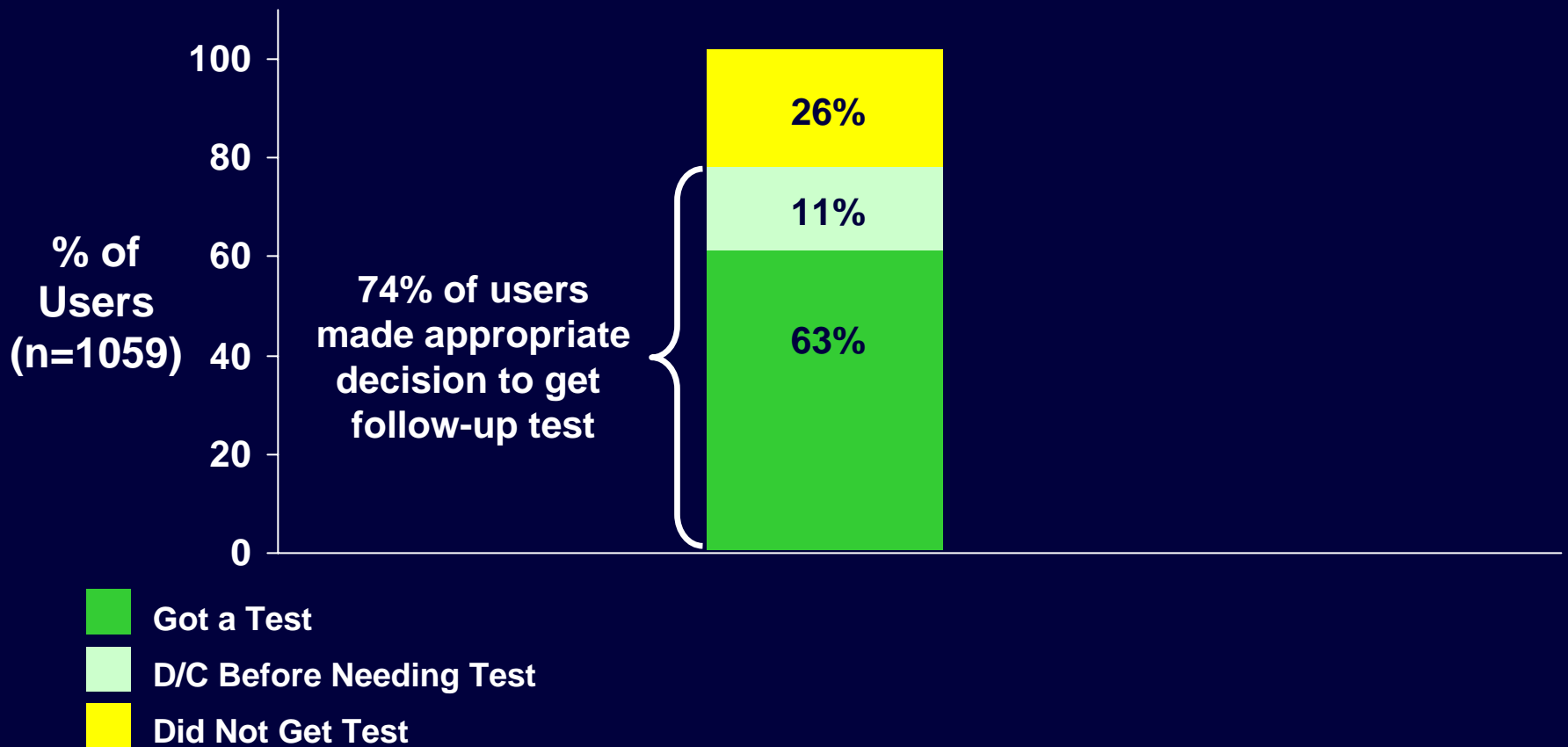
Key Questions

- Will the MEVACOR™ OTC Self-Management System allow consumers to:
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 - Follow-up lipid test

CUSTOM Results

Benefit Criteria - Ongoing Use

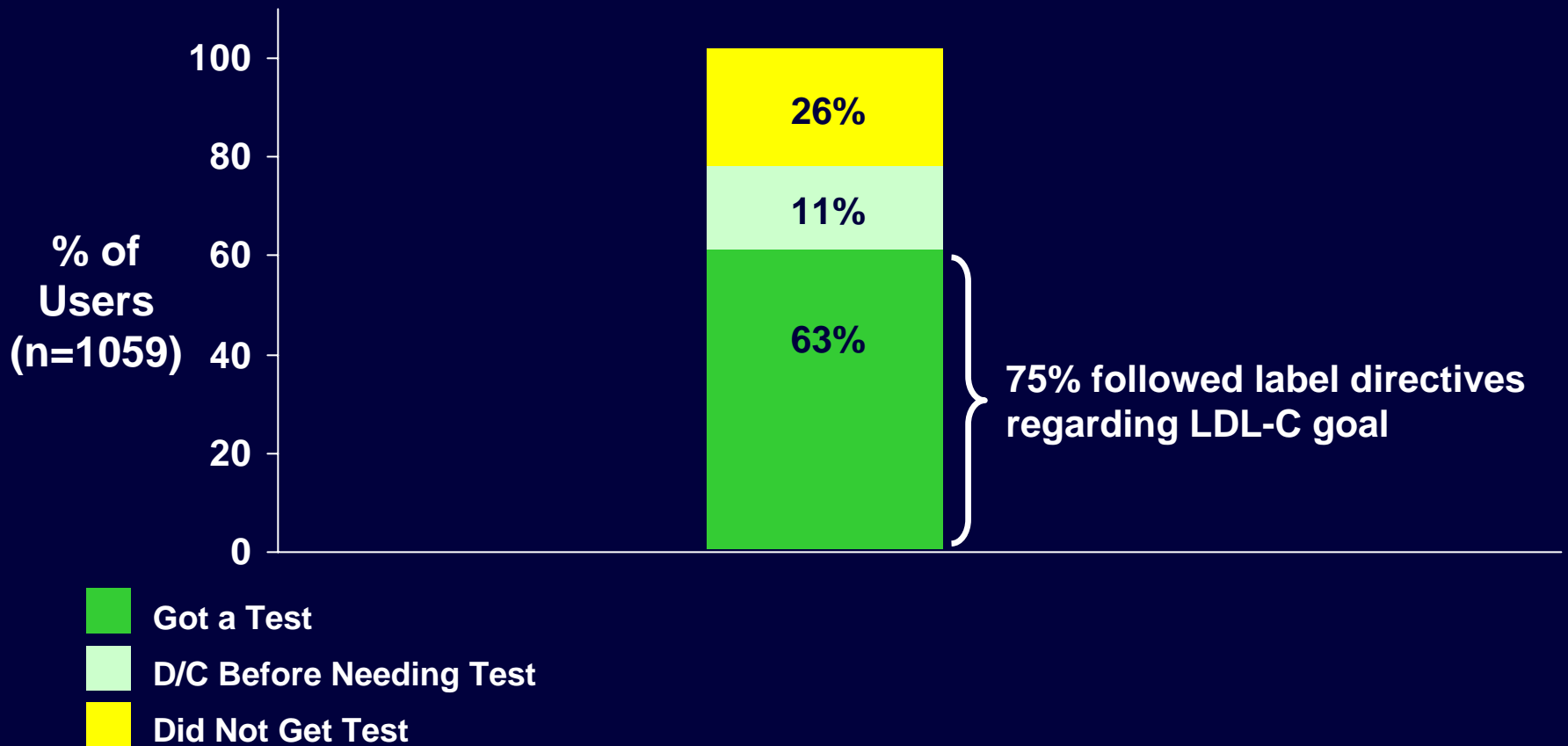
Follow-Up Cholesterol Test



CUSTOM Results

Benefit Criteria - Ongoing Use

Follow-Up Cholesterol Test

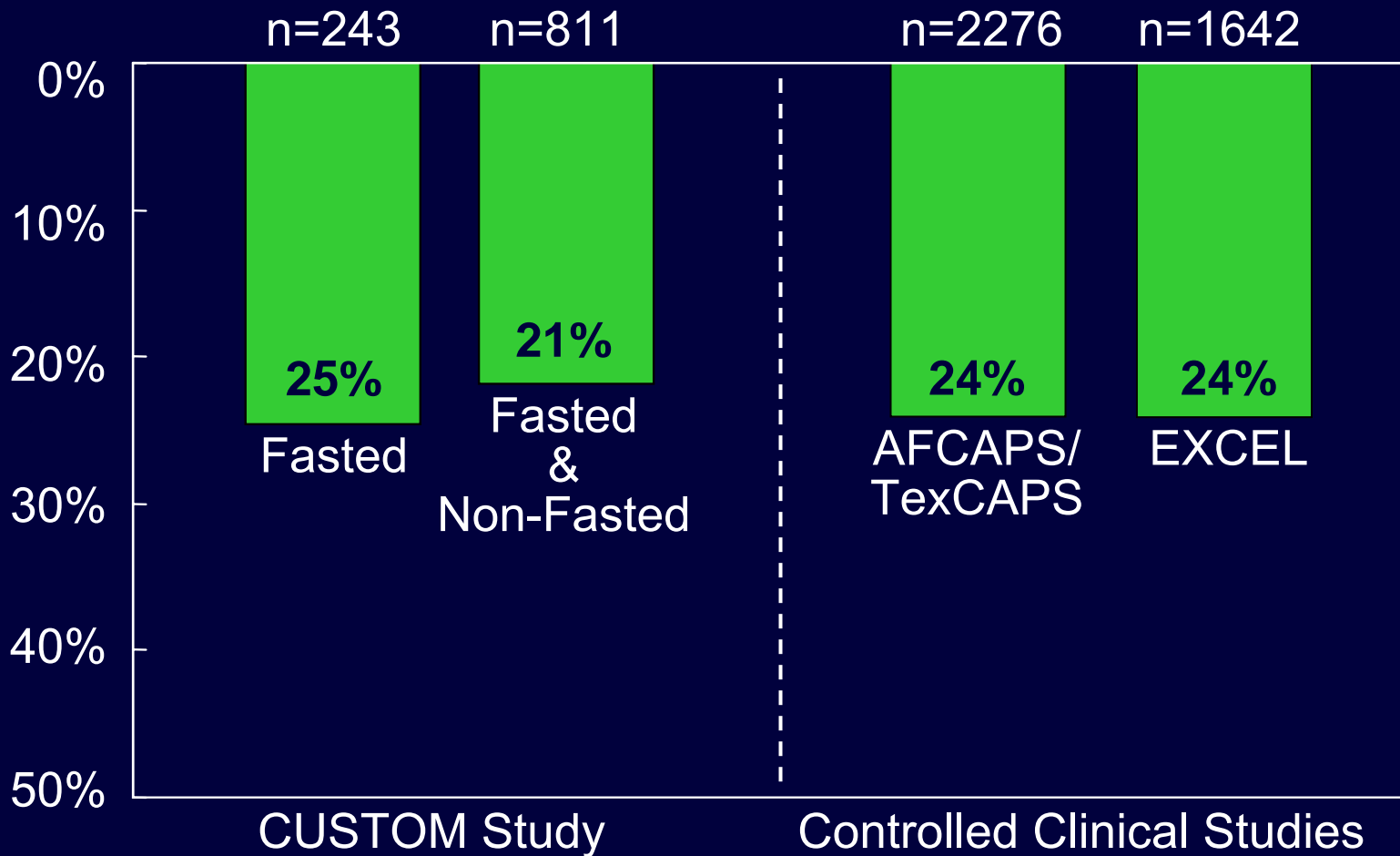


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 - Follow-up lipid test
 - Lipid results

CUSTOM Results

Users Achieved Beneficial Lipid Lowering
with Lovastatin 20 mg/day

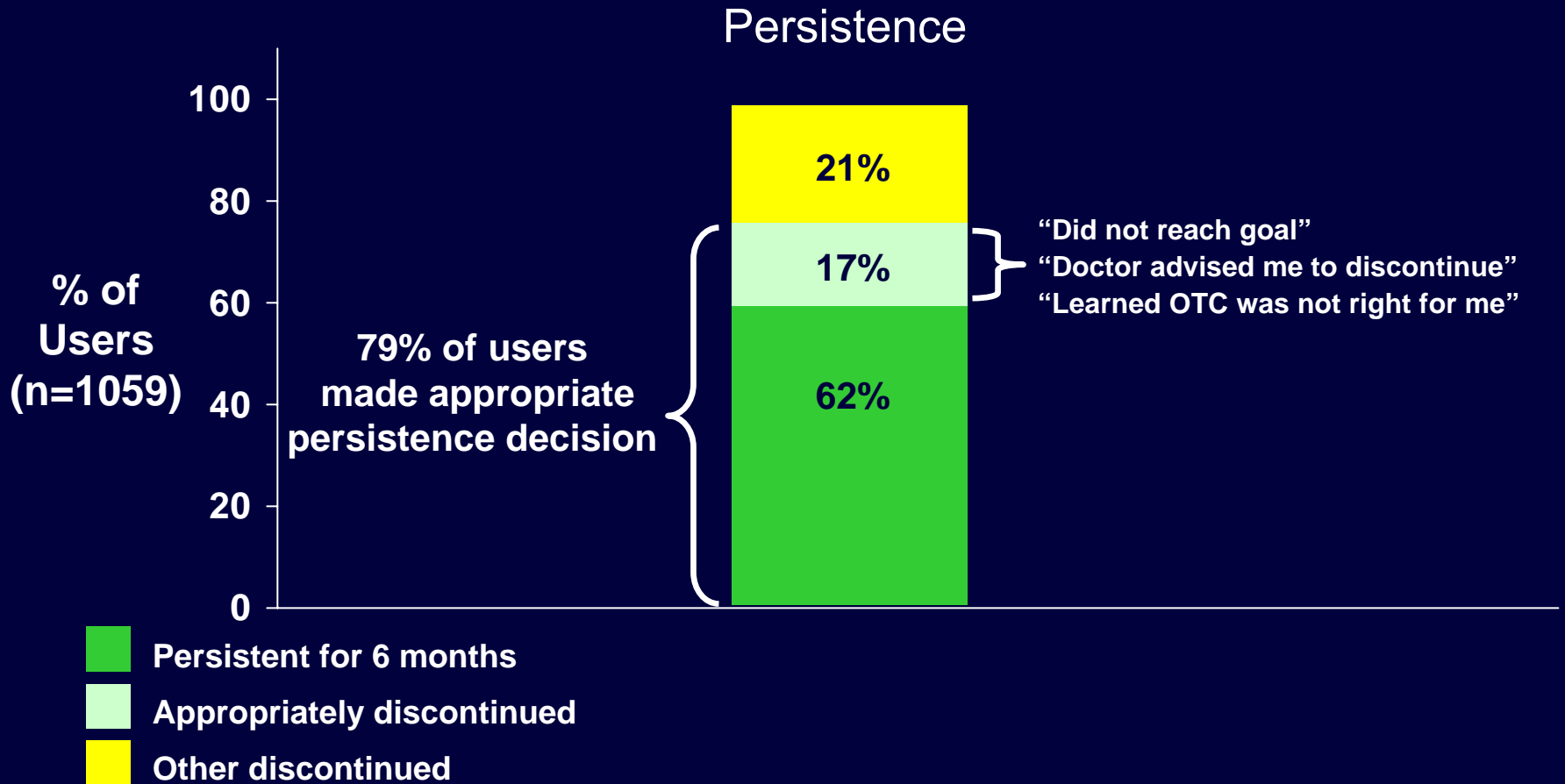


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 - Follow-up lipid test
 - Lipid results
 - Persistence/compliance

CUSTOM Results

Benefit Criteria - Ongoing Use

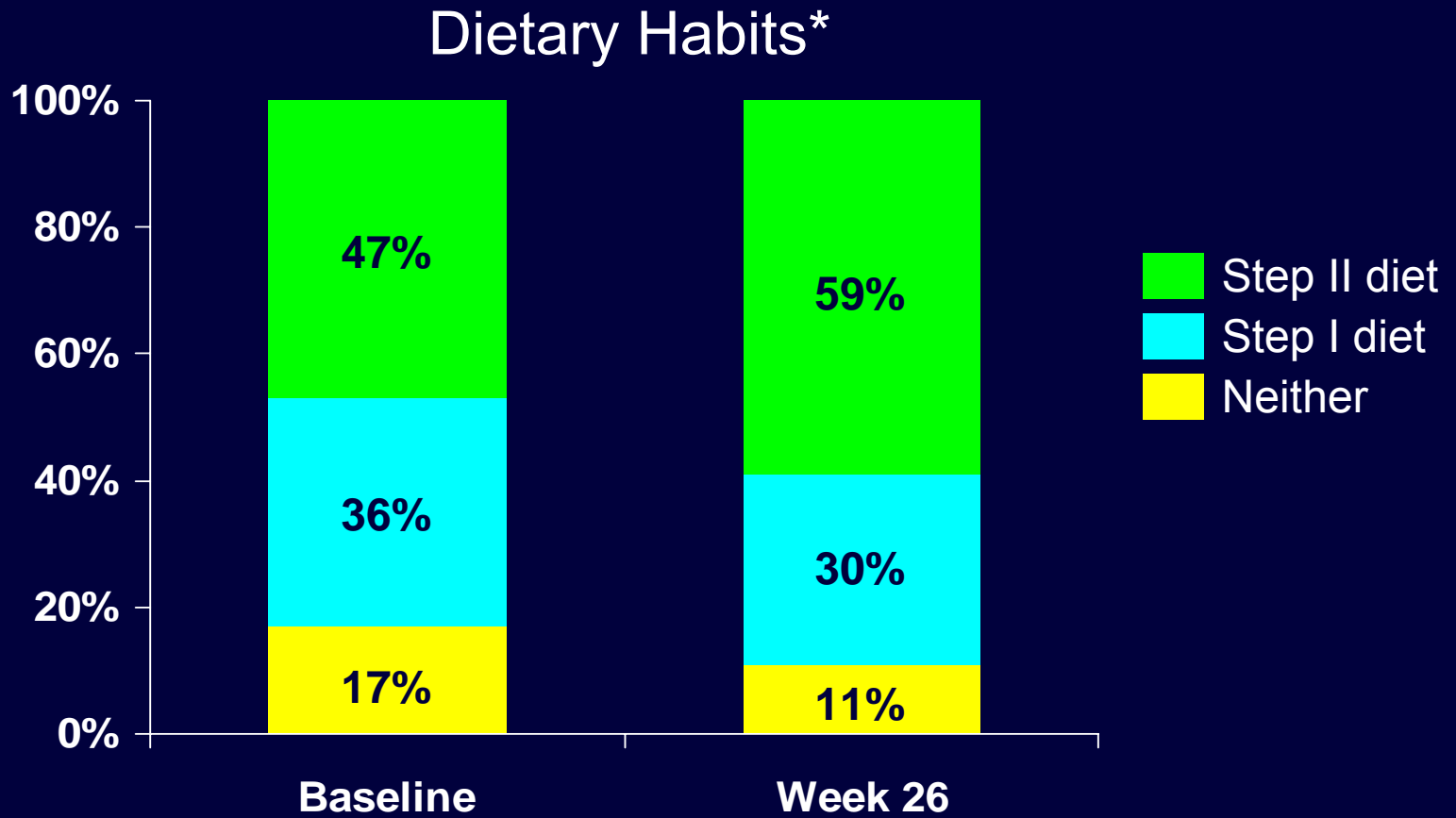


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 2. Self-manage the potential safety risks over time?
 3. Self-manage their cholesterol over time and obtain benefit?
 - Follow-up lipid test
 - Lipid results
 - Persistence/compliance
 - Diet and exercise

CUSTOM Results

Heart-Healthy Lifestyle Behaviors Improve



* Diet assessed with MEDFACTS.

CUSTOM Results

Summary of Ongoing Use Decisions – Benefit Criteria N=1059

- 74% of users obtained follow-up test or discontinued before 6 weeks
- 75% of users with follow-up test followed label directives regarding LDL-C goal
- 21% reduction in LDL-C

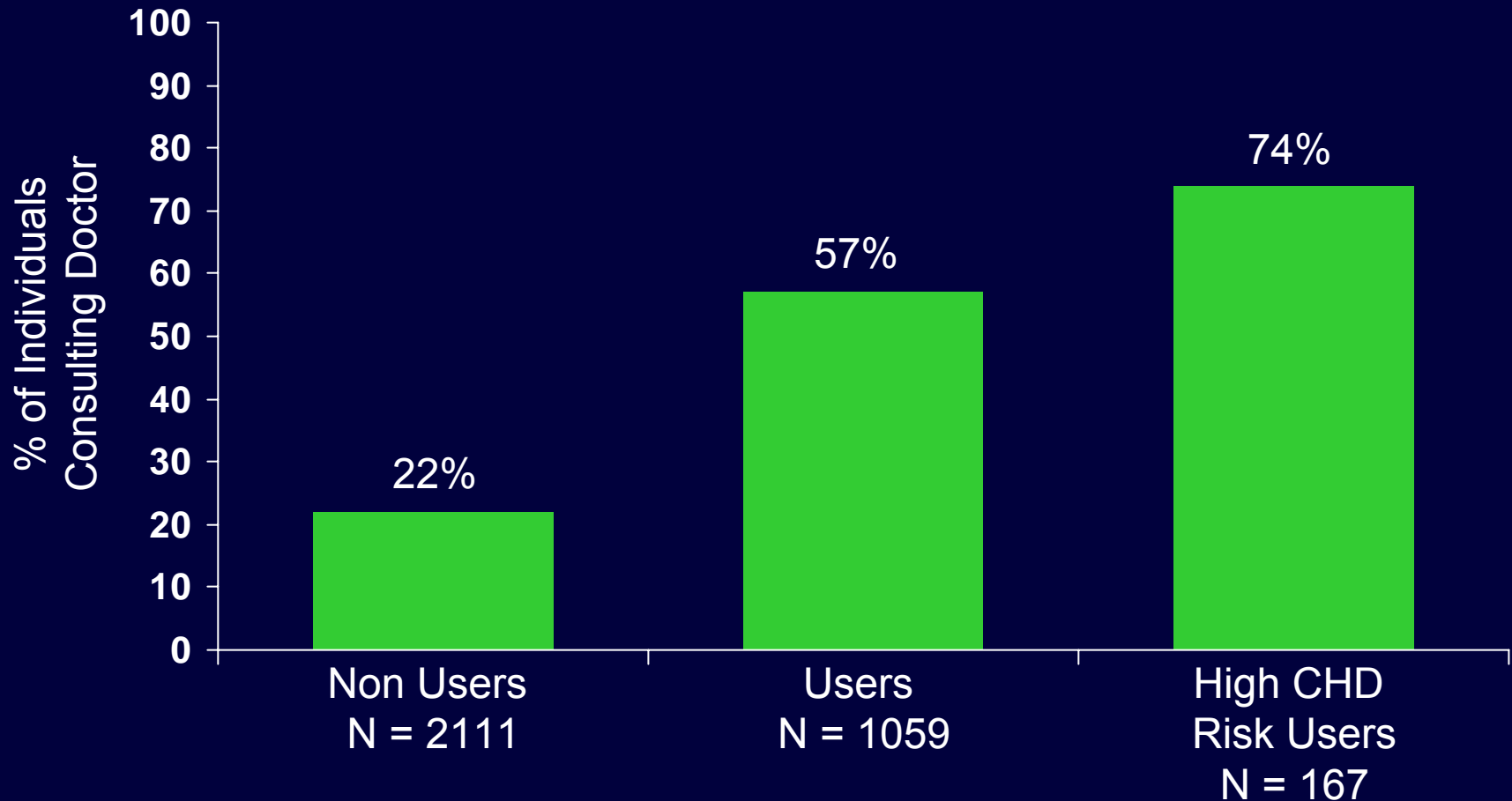
Consumers Can Manage Their Cholesterol Over
Time and Obtain Benefit

CUSTOM Results

Will the MEVACOR™ OTC Self-Management System promote consumer interactions with healthcare professionals?

CUSTOM Results

MEVACOR™ OTC Self-Management System
Encourages Consumer Involvement with HCP



CUSTOM Conclusions

- The Self-Management System discourages inappropriate use

CUSTOM Conclusions

- The Self-Management System discourages inappropriate use
- The majority of consumers who choose to use MEVACOR™ OTC will
 - Be appropriate for self-management
 - Gain clinical benefit
 - Be at minimal safety risk

CUSTOM Conclusions

- The Self-Management System discourages inappropriate use
- The majority of consumers who choose to use MEVACOR™ OTC will
 - Be appropriate for self-management
 - Gain clinical benefit
 - Be at minimal safety risk
- There will be important public health benefits from the Self-Management System including
 - Increased healthcare professional interactions
 - Improved heart health awareness and behavior

The Potential of MEVACOR™ OTC

Jerome D. Cohen, MD, FACC, FACP, FAHA
Professor Internal Medicine
Director of Preventive Cardiology Program
St. Louis University

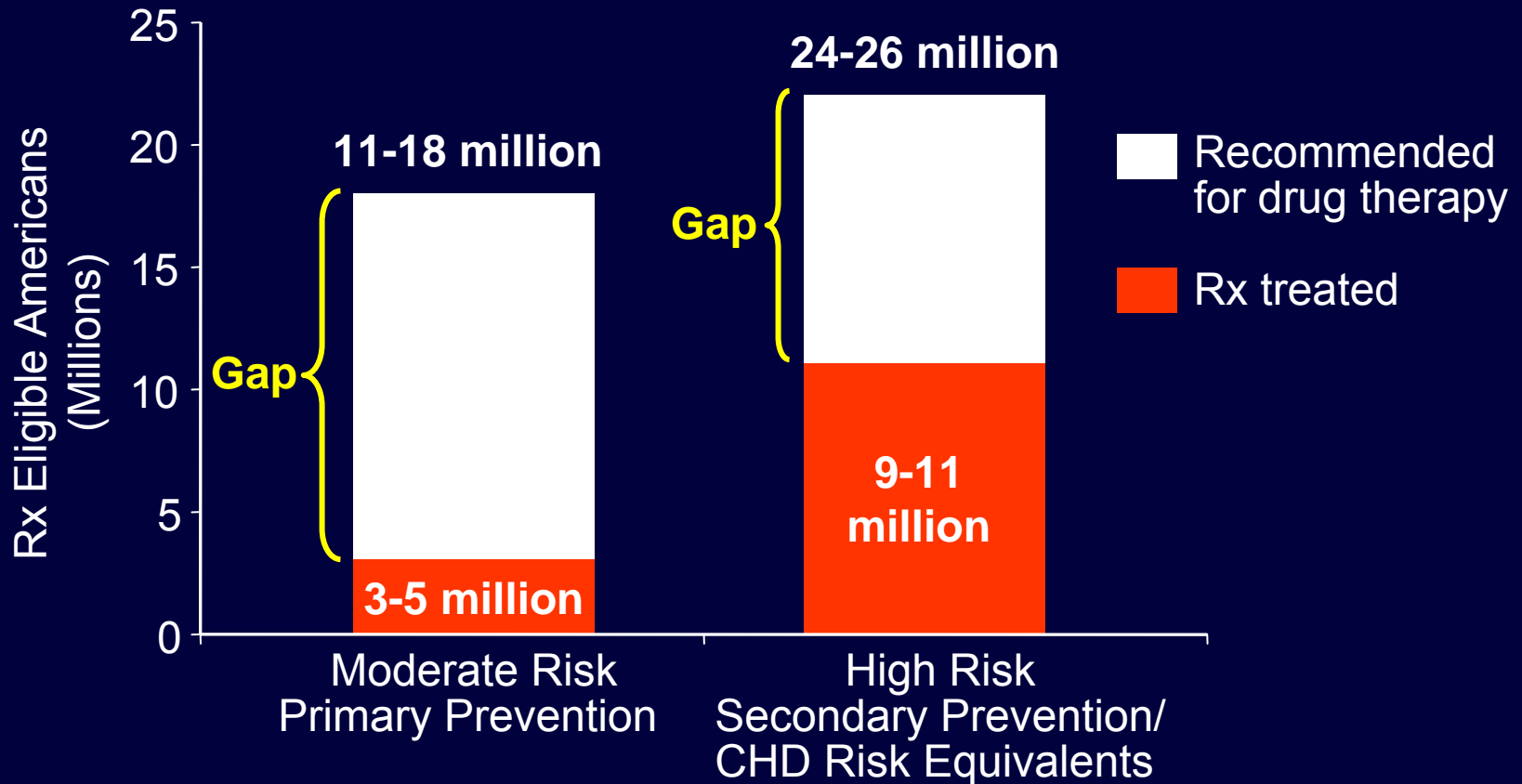
Key Questions

- Is there a need for an OTC option?
- Is MEVACOR™ 20 mg safe for OTC use?
- Can consumers manage cholesterol effectively with OTC?
- Will OTC divert consumers from physician care and from heart-healthy lifestyle practices?
- What's the overall benefit/risk of MEVACOR™ OTC?

Key Questions

- Is there a need for an OTC option?

Large Treatment Gaps Remain



NHANES 1994, IMS 2003, Ingenix Treatment Gap Data 2003.

Key Questions

- Is there a need for an OTC option?
- Is MEVACOR™ 20 mg safe for OTC use?

Proven Safety Profile

- 17+ years in-market experience
- 27+ million patient-years of treatment
- Safety profile comparable to placebo

Key Questions

- Is there a need for an OTC option?
- Is MEVACOR™ 20 mg safe for OTC use?
- Can consumers manage cholesterol effectively with OTC?

Consumers Are Already Using OTC Products for Chronic Asymptomatic Conditions

- ~35 million use calcium*
- ~26 million use aspirin for heart health**
 - 27% self-initiated
- ~14 million use heart health supplements***
 - e.g., Garlic, vitamin E, antioxidants, niacin, red rice yeast

*Osteoporosis Omnibus Study, 2001.

**McNeil Pharmaceutical internal data.

***Cholesterol Omnibus Study, 2004.

Consistent Data Show Consumers Exhibit Appropriate Behavior

	CUSTOM N=1059 %	Lovastatin 10 mg Actual Use Study O76 N=2662* %	Lovastatin 10 mg Actual Use Study 081 N=1229* %
OTC Users:			
Total Cholesterol >200 mg/dL (Pre-treatment)	87	93	n/a
Taking Rx lipid therapy	5	3	5
OTC User Behaviors:			
Appropriately self-select Safety	90	95	97
Benefit	66	66	68

* Made decision to purchase.

Key Results of OTC Therapy Consistent with Prescription Experience

	CUSTOM Results (%)	Current State of Rx Care (Statins) (%)
Obtained goal	62	37 ^a -57 ^b
Appropriate persistence (6 months)	62-79	56 ^c -80 ^d
Average LDL-C reduction	21	24 ^e -25 ^f

^a Pearson et al. *Arch Intern Med* 2000; 160:459-67. ^b Frolkis et al. *Am J Cardiol* 2004; 94:1310-1312.

^c Benner et al. *JAMA* 2002;288:455-461. ^d Grant et al. *Arch Intern Med* 2004; 164:2343-2348.

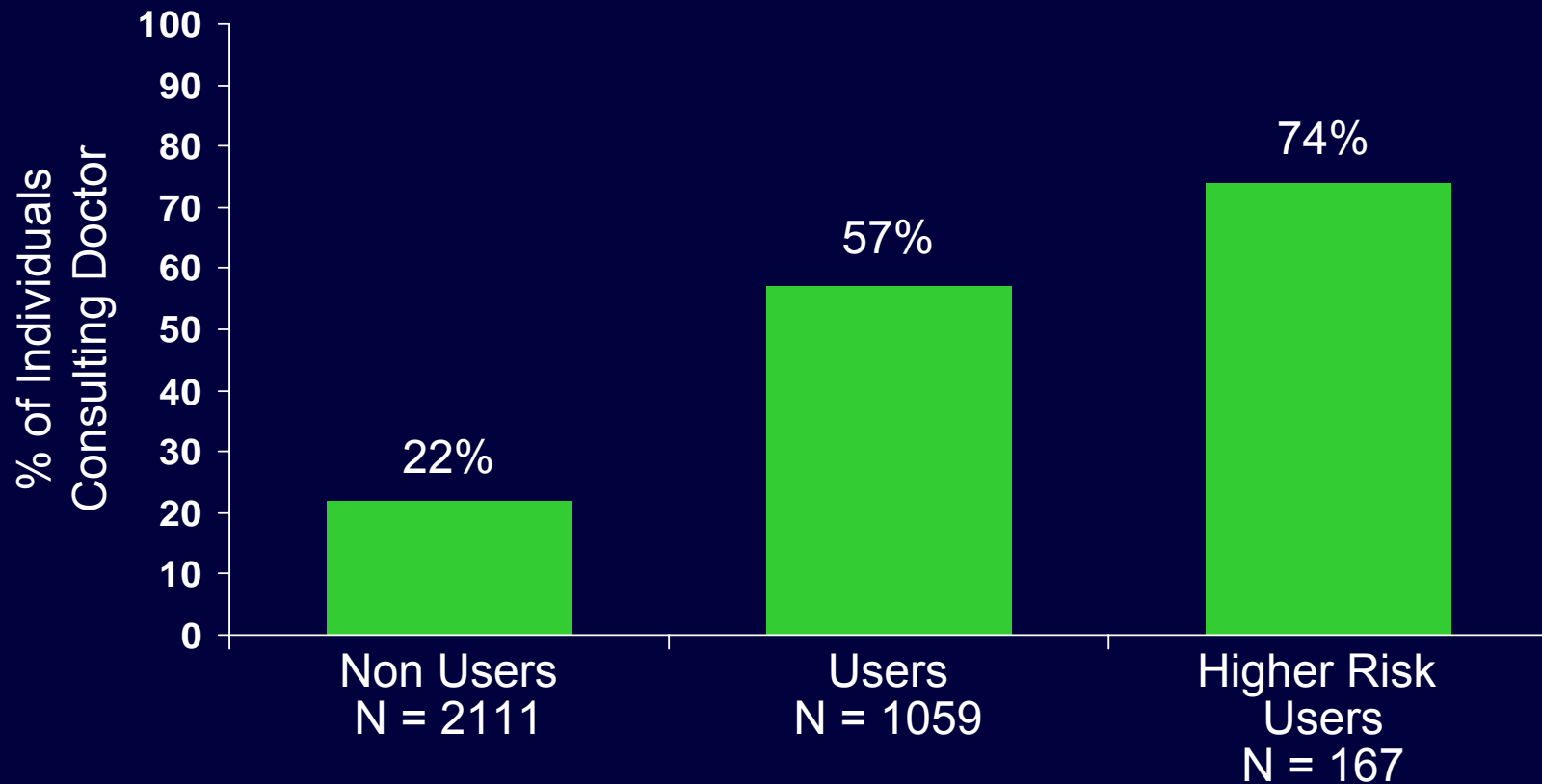
^e AFCAPS data. ^f EXCEL data.

Key Questions

- Is there a need for an OTC option?
- Is MEVACOR™ 20 mg safe for OTC use?
- Can consumers manage cholesterol effectively with OTC?
- Will OTC divert consumers from physician care and from heart-healthy lifestyle practices?

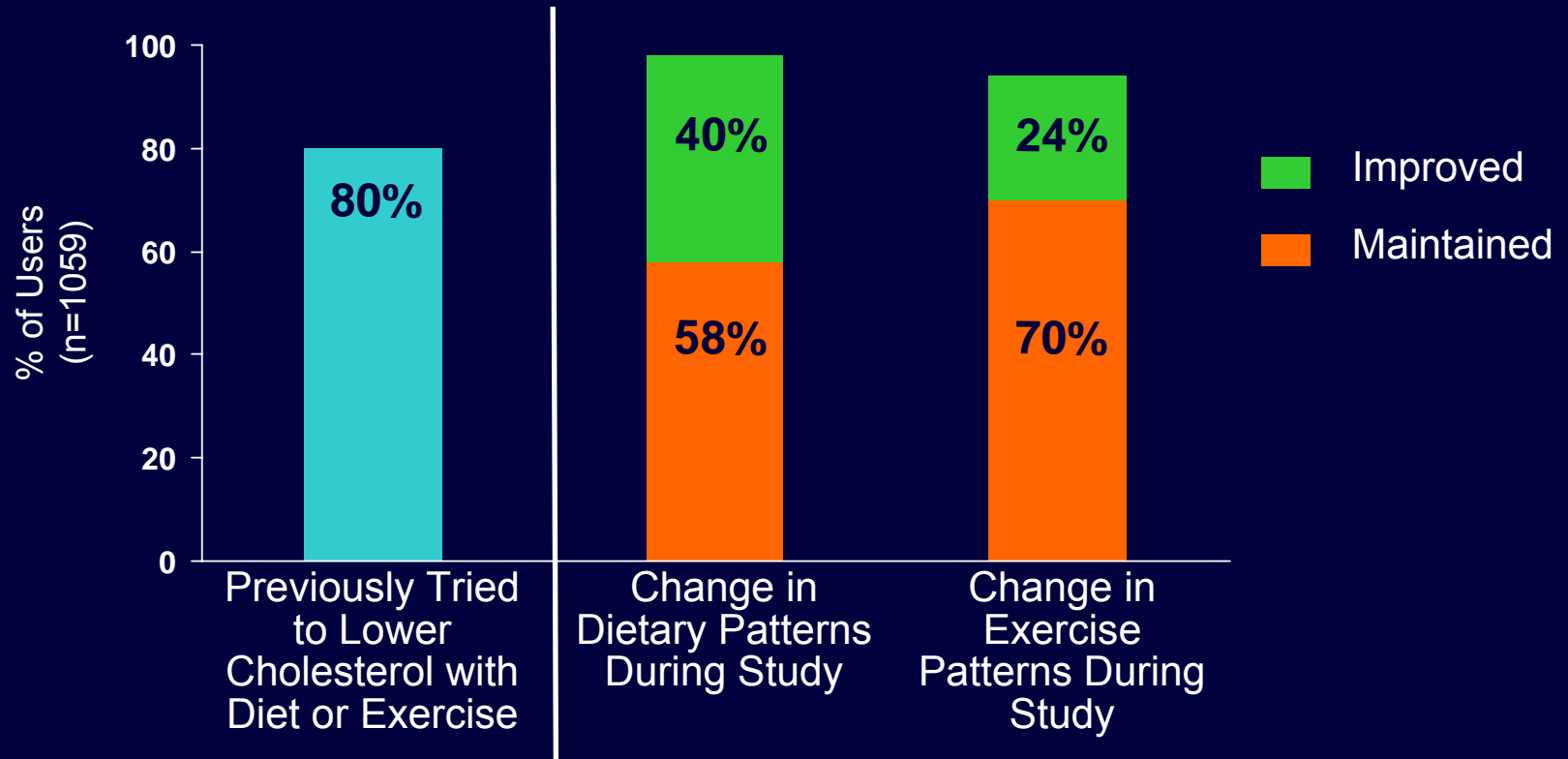
MEVACOR™ OTC System Encourages Interaction with Healthcare Professionals

CUSTOM Results



CUSTOM Results

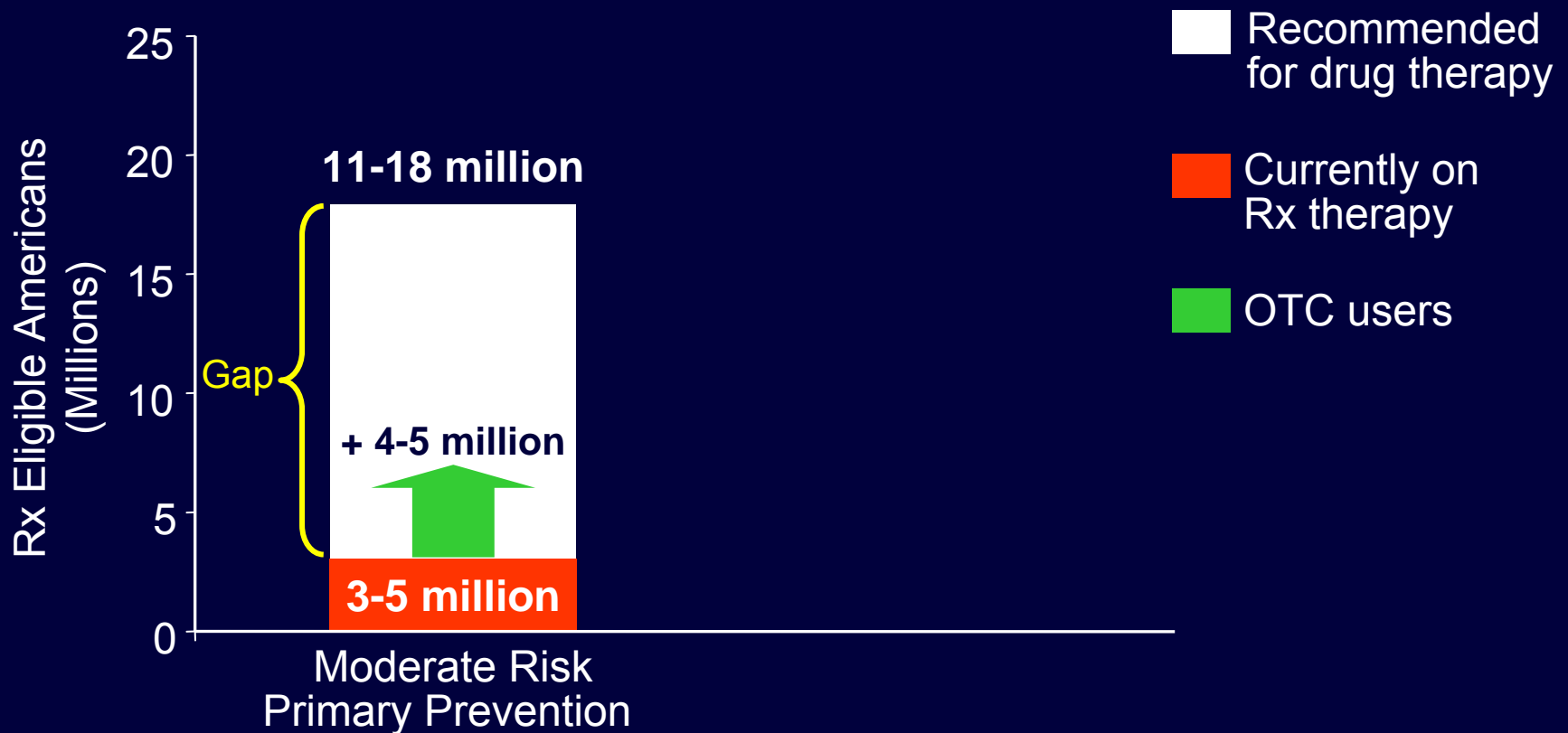
Promotes Lifestyle Changes



Key Questions

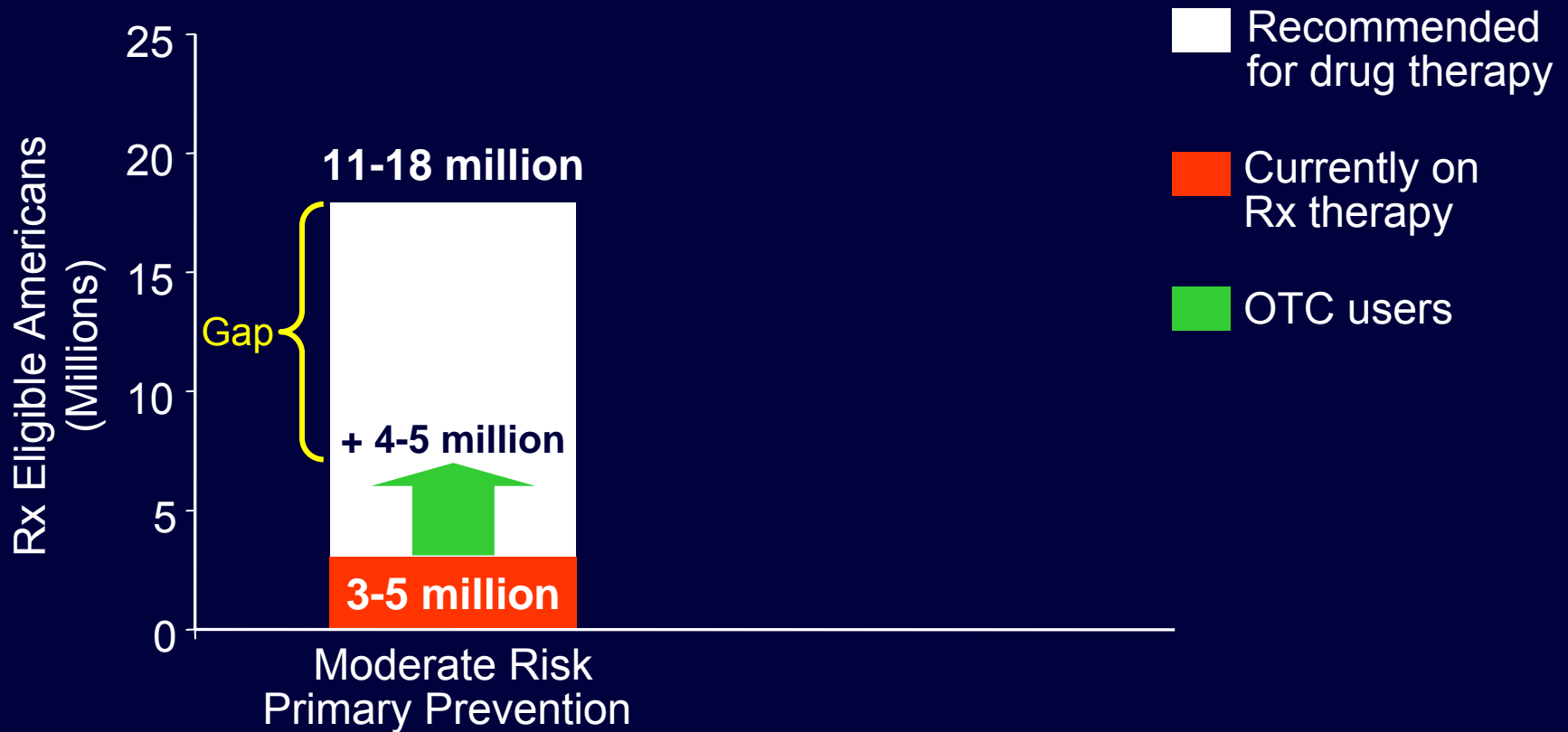
- Is there a need for an OTC option?
- Is MEVACOR™ 20 mg safe for OTC use?
- Can consumers manage cholesterol effectively with OTC?
- Will OTC divert consumers from physician care and from heart-healthy lifestyle practices?
- What's the overall benefit/risk of MEVACOR™ OTC?

OTC Can Narrow Treatment Gap



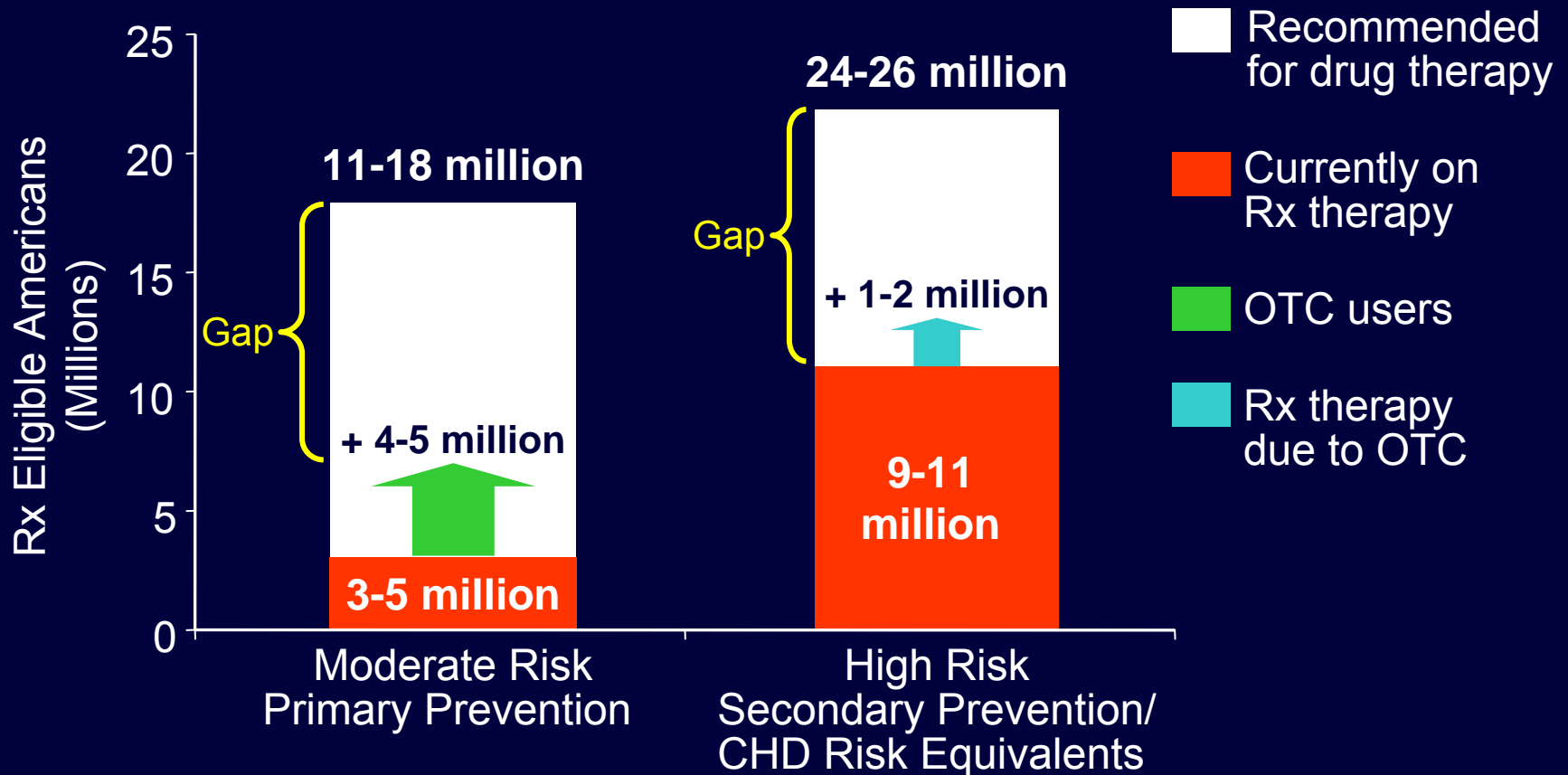
NHANES 1994, IMS 2003, Ingenix Treatment Gap Data 2003. BASES 2002.

OTC Can Narrow Treatment Gap



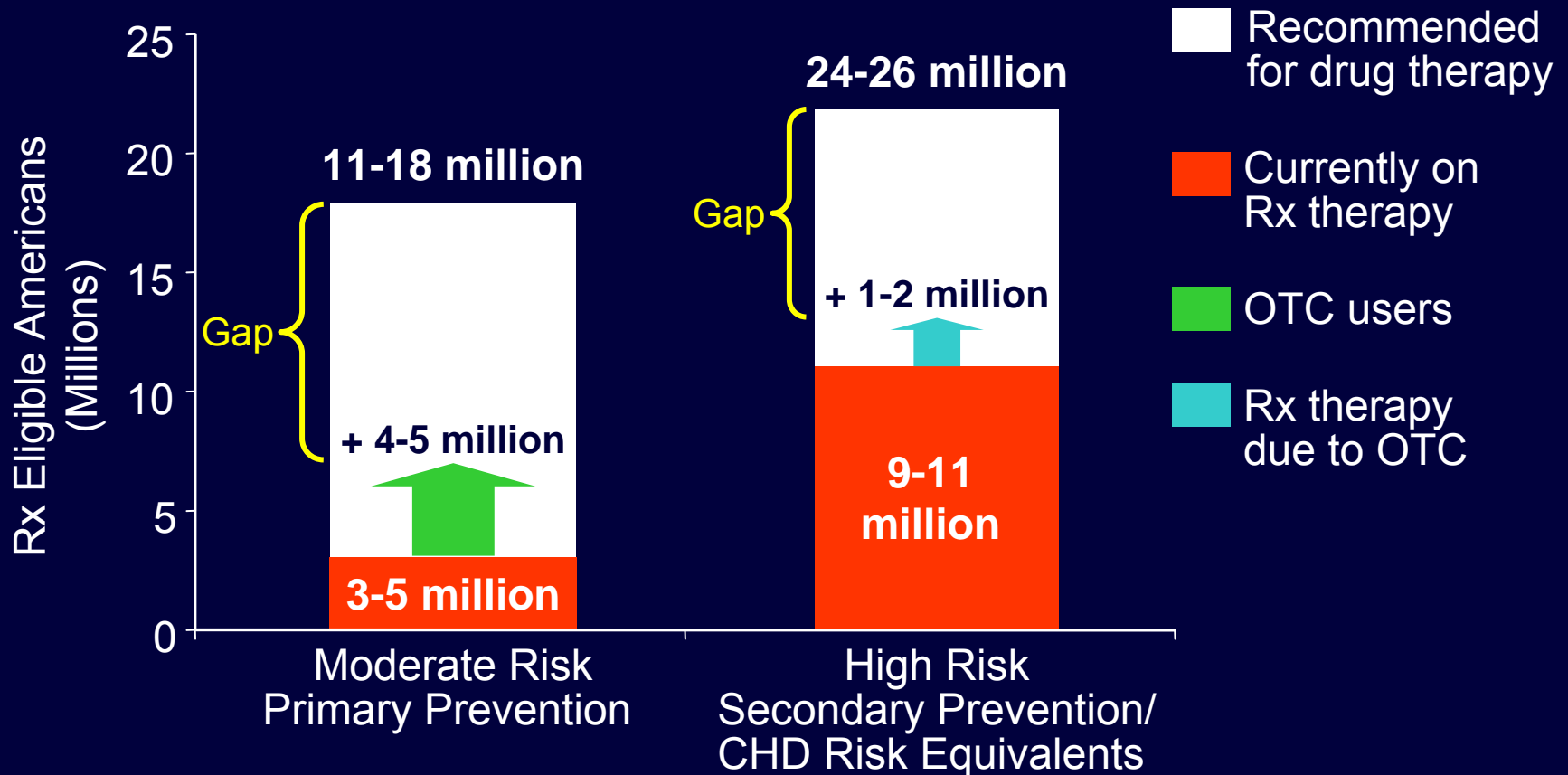
NHANES 1994, IMS 2003, Ingenix Treatment Gap Data 2003. BASES 2002.

OTC Can Narrow Treatment Gap



NHANES 1994, IMS 2003, Ingenix Treatment Gap Data 2003. BASES 2002.

OTC Can Narrow Treatment Gap

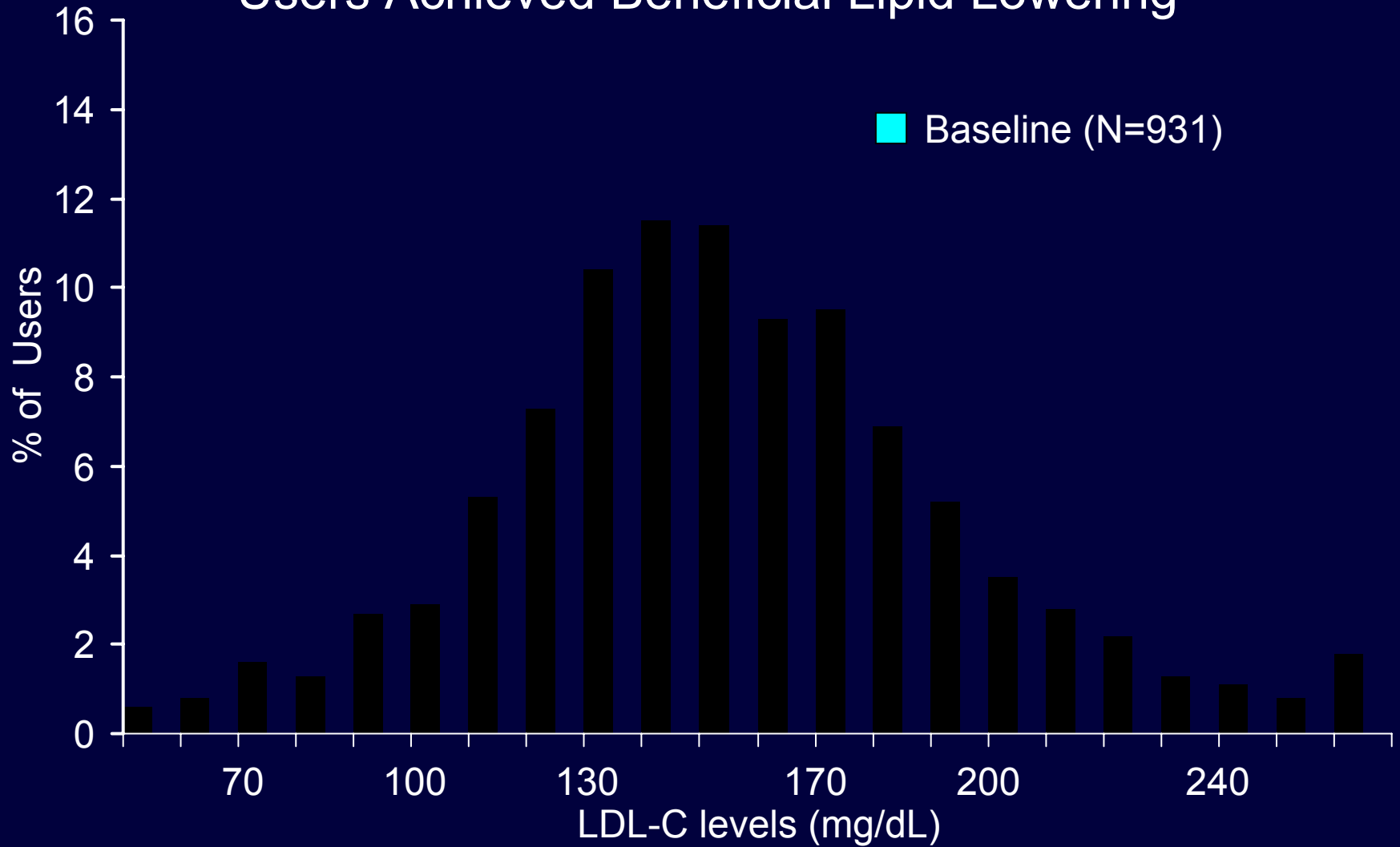


NHANES 1994, IMS 2003, Ingenix Treatment Gap Data 2003. BASES 2002.

OTC Can Help Shift the Curve

CUSTOM Data

Users Achieved Beneficial Lipid Lowering

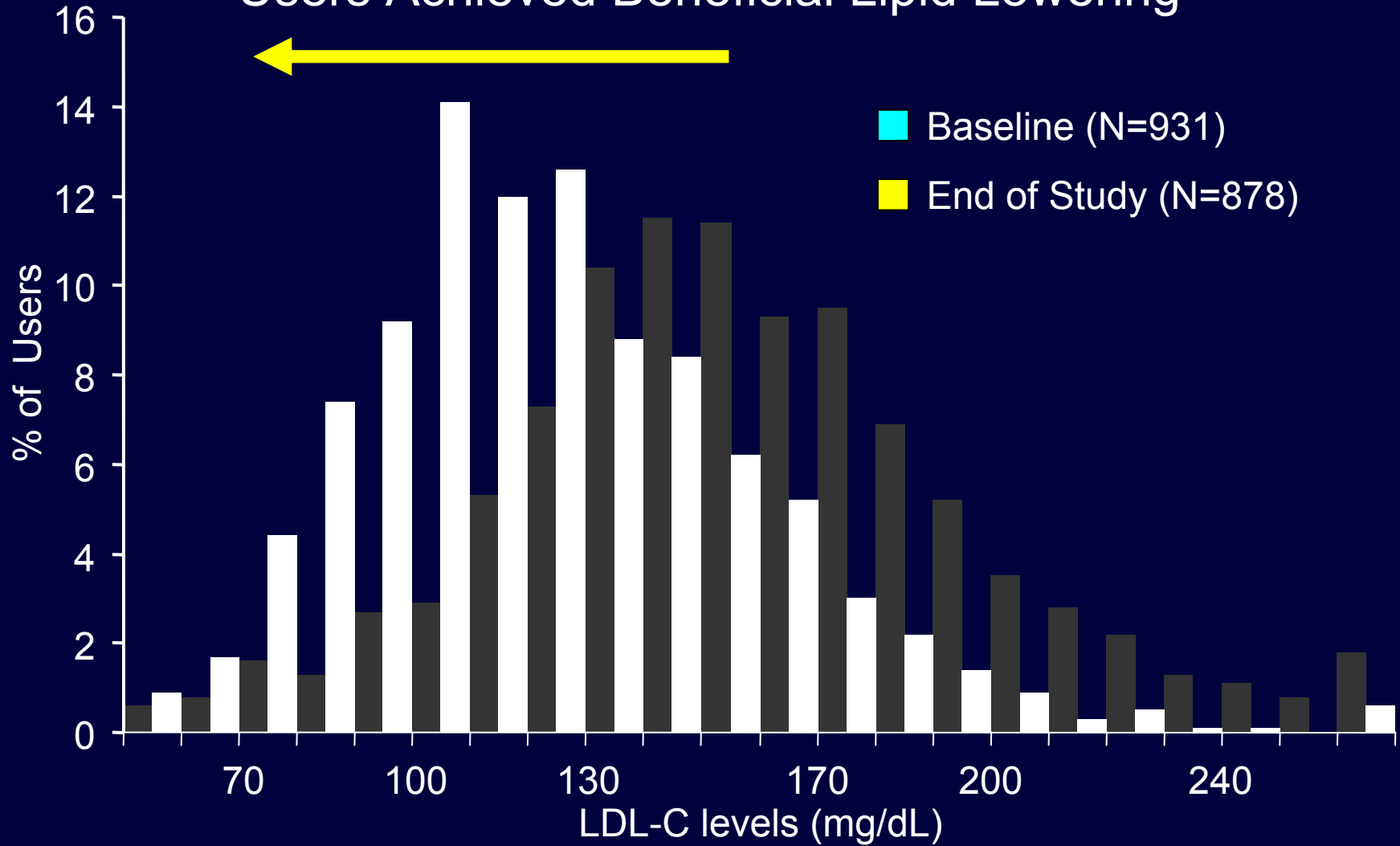


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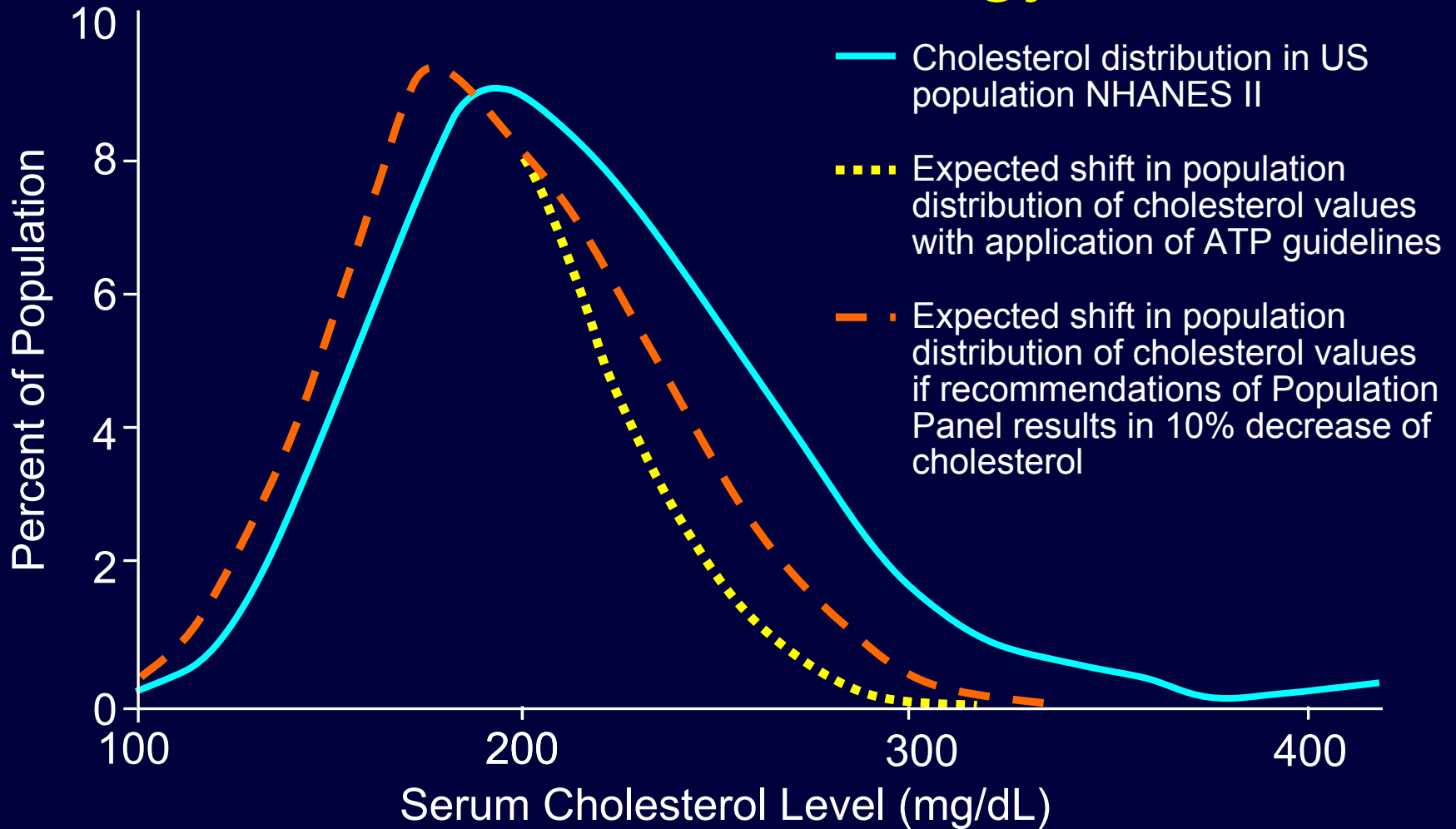
OTC Can Help Shift the Curve

CUSTOM Data

Users Achieved Beneficial Lipid Lowering



The Additive Effect of a Primary Prevention Strategy



Carleton R.A. et al., Circulation 1991, vol 83. 2154-2232.

Overall Benefit of MEVACOR™ OTC

- For example:
 - 1 million OTC users for 10 years
 - Applying CHD risk distribution in CUSTOM population
 - Assumed risk reduction ~25%
 - Benefit
 - 25,000 – 35,000 events prevented