

Adopting New Guidelines into Practice : Implications for Korea

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LDL Cholesterol Goals and Cutpoints (2004)

Risk Category	LDL Goal (mg/dL)	LDL (mg/dL) - Therapeutic Lifestyle Changes (TLC)	LDL (mg/dL) - Drug Therapy
<ul style="list-style-type: none"> ■ CHD or CHD Risk Equivalents (10-year risk > 20 %) 	<p><100</p> <p>Optional < 70*</p>	<p>≥100</p>	<p>≥100</p> <p>(<100 : drug optional)</p>
<ul style="list-style-type: none"> ■ 2+ Risk Factors (10-year risk 10–20 %) 	<p><130</p> <p>Optional <100*</p>	<p>≥130</p>	<p>≥130</p> <p>(100–129 : drug optional)</p>
<ul style="list-style-type: none"> ■ 2+ Risk Factors (10-year risk <10 %) 	<p><130</p>	<p>≥130</p>	<p>≥160</p>
<ul style="list-style-type: none"> ■ 0–1 Risk Factor 	<p><160</p>	<p>≥160</p>	<p>≥190</p> <p>(160–189 : drug optional)</p>

European guideline

- Estimate absolute CHD risk using coronary risk chart
 - Initial total cholesterol

Absolute CHD risk < 20%

TC \geq 190 mg/dL

Life style advice with the goal

TC < 190 mg/dL (5.0 mmol/l)

LDL < 115 mg/dL (3.0 mmol/l)

F/U at 5 years interval

Absolute CHD risk \geq 20%

Measure fasting TC, TG, HDL
and calculate LDL

Life style advice for **3 months**

Increased CHD risk

HDL < 40 mg/dL

TG > 180 mg/dL

TC < 190 mg/dL

LDL < 115 mg/dL

: Continue life style
advice with **annual F/U**

TC \geq 190 mg/dL

LDL \geq 115 mg/dL

Maintain life style advice
with **drug therapy**

Japanese guideline

(mg/dL)

Risk group	CHD	risk factors	1997 goal		2001 goal		ATPIII LDL
			TC	LDL	TC	LDL	
A	-	0	<220	<140	<240	<160	<160
B1	-	1	<200	<120	<220	<140	
B2	-	2					<130
B3	-	3			<200	<120	
B4	-	> 4					
C	+		<180	<100	<180	<100	<100

Risk factors : age (M \geq 45, F \geq 55), smoking, hypertension, diabetes (DM B2)

Goal : HDL \geq 40 mg/dL, TG < 150 mg/dL

International Lipid Guidelines

- Guidelines developed for the prevention of CHD
- Based on major clinical trial evidence
- Help assess and assist in the management of patients at risk of CHD

Risk Category	NCEP LDL-C goal	European LDL-C goal
CHD or CHD risk equivalents (10-year risk >20%)	≤100mg/dl (≤2.6mmol/l)	≤115mg/dl (≤3.0mmol/l)
2+ risk factors (10-year risk ≤20%)	<130mg/dl (≤3.4mmol/l)	≤115mg/dl (≤3.0mmol/l)

(1998-2000)

20

7,962

	Mean	SD	Percentile					
			5th	25th	50th	75th	90th	95th
TC	188.3	37.5	134	162	185	210	237	255
LDL	113.6	33.8	64	90	111	133	157	173
TG	123.3	61.8	48	77	110	158	203	228
HDL	50.1	12.6	32	41	48	57	67	73

(2002)

(mg/dL)

≥ 240

≥ 200

LDL-

≥ 160

≥ 130

HDL-

< 40

HDL-

≥ 60

≥ 200

≥ 150

LDL-

Risk Category

LDL Goal (mg/dL)

CHD and
CHD risk equivalents

<100

Multiple (2+) risk factors

<130

0 - 1 risk factor

<160

Western studies to assess the rate of target goal achievement

American College of Cardiology Evaluation of
Preventive Therapeutics project (ACCEPT)

Am J Cardiol 1997;80(8B):45H-52H.

Lipid Treatment Assessment Project (L-TAP)

Arch Intern Med 2000;160:459-467.

European Action on Secondary Prevention through
Intervention to Reduce Events (EUROASPIRE II)

EUROASPIRE II Euro Heart Survey Programme

Euro Heart J 2001;22:554-772.

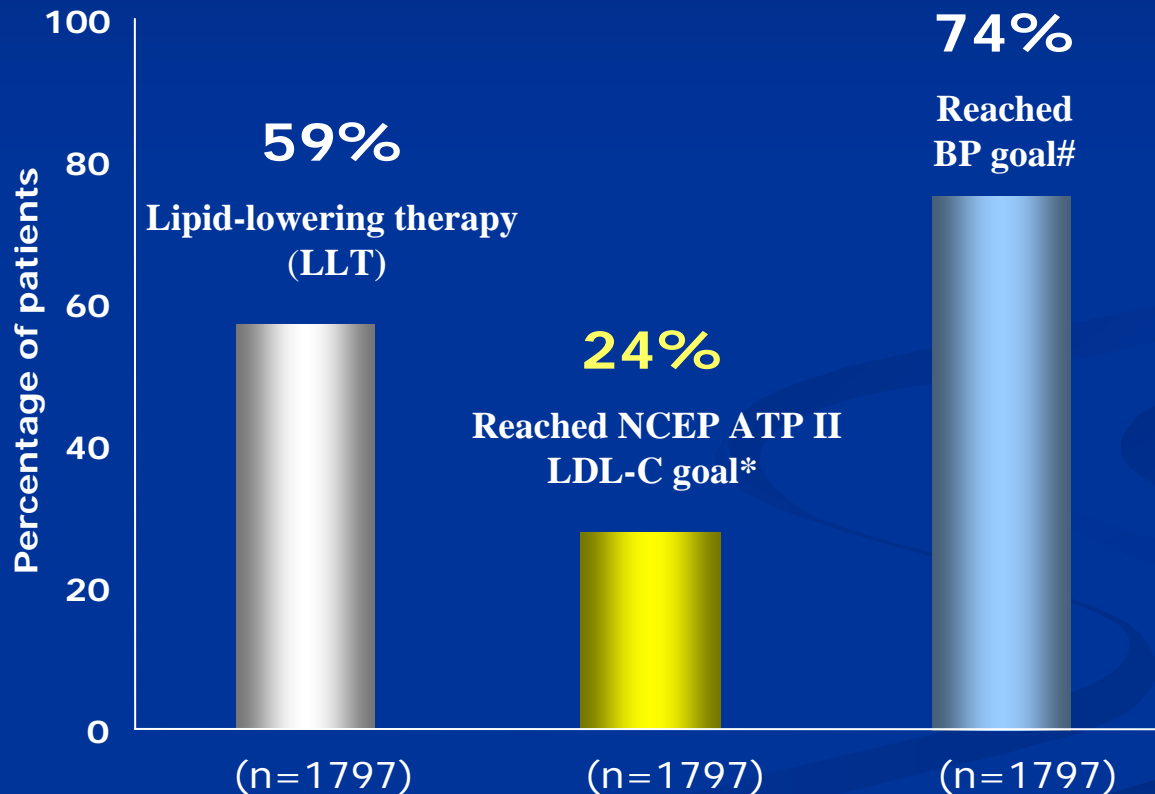
American College of Cardiology Evaluation of Preventive Therapeutics project (ACCEPT)

- 1797 CHD patients in 1996
 - : first CABG, first PTCA, AMI, myocardial ischemia
 - : medical record and interview
 - : 6 months after discharge
- 25 % smoker
- 87 % with Aspirin, 63 % with beta-blocker
- 74% reached BP goal (SBP < 140 mmHg)
- 59% received lipid-modifying therapy

Am J Cardiol 1997;80(8B):45H-52H.

Circulation 1997;96(8S):733-I

ACCEPT : Achieving NCEP ATP II Goal on Lipid-modifying Therapy



* LDL-C \leq 100 mg/dL

SBP < 140 mmHg

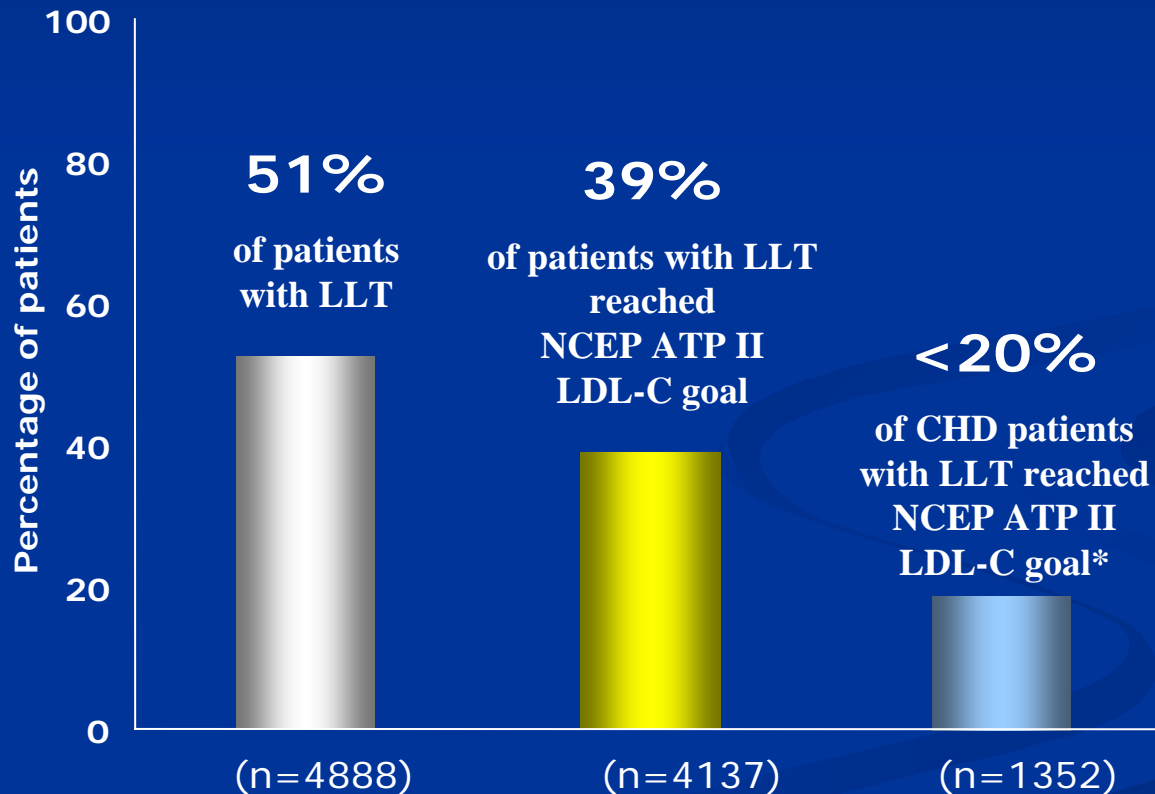
Am J Cardiol 1997;80(8B):45H-52H.

Circulation 1997;96(8S):733-I

Lipid Treatment Assessment Project (L-TAP)

- 4888 primary care patients
from 5 regions of the US were studied.
- Of the total number of patients,
51% received lipid-modifying therapy
and the remainder received non-drug therapy.
- Of those treated with lipid-modifying therapy,
only 39% reached NCEP ATP II LDL-C goal.
- Of those patients with CHD and treated with drug,
less than 20% reached goal.

L-TAP: Achieving NCEP ATP II Goal on Lipid-modifying Therapy



* LDL-C \leq 100 mg/dL

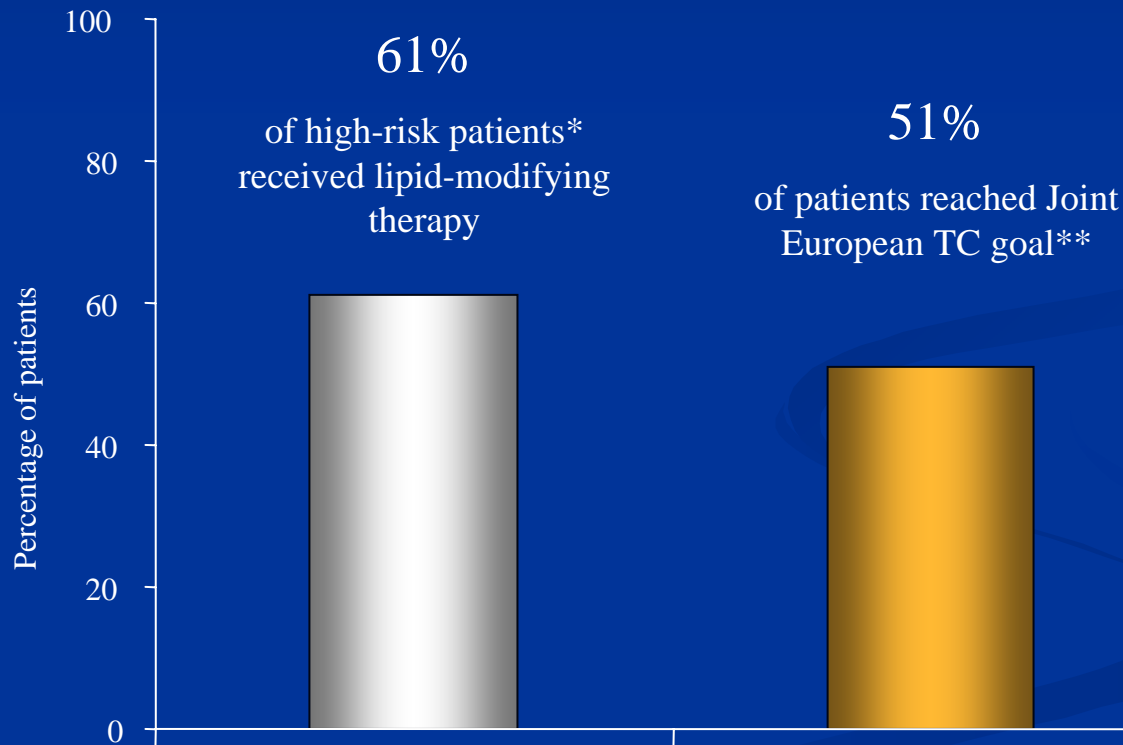
Pearson TA et al. Arch Intern Med 2000;160:459-467.

EUROASPIRE II

- a survey of the medical records of over 5000 patients from 15 European countries
- who had had either
coronary artery bypass grafts
percutaneous transluminal coronary angioplasty
acute myocardial infarction
or myocardial ischaemia 6 months previously.
- **Only 61%** of these high-risk patients actually received lipid-modifying therapy
- **only a half of** these patients reached Joint European Guideline total cholesterol treatment goal

EUROASPIRE II: Achieving Joint European TC Goal

*CABG, PTCA, MI or ischaemia, ** TC <5 mmol/L



*EUROASPIRE II Euro Heart Survey Programme.
Euro Heart J 2001;22:554-772.*

**Current Status of Management for
Dyslipidemia
of CAD patients
In 10 university hospitals in Korea**

Hyo-Soo Kim

On behalf of

National Lipid Advisory Board Members

Inclusion Criteria

- Patients with CAD confirmed by
 - CAG ; stenosis more than 50% or
 - Stress test ; positive or
 - Medical record ; s/p PTCA(PCI), s/p CABG
- OPD F/U within recent 6 months

Investigator

Center	Investigator	Total n (%)
		93 (8.87)
		150 (14.31)
		100 (9.54)
		100 (9.54)
		100 (9.54)
		106 (10.11)
		100 (9.54)
		101 (9.64)
		98 (9.35)
		100 (9.54)
Total		1,048 (100.00)

Current status of management of hyperlipidemia for CAD patients under OPD F/U in 2003 in Korea

- Rate of target goal achievement [LDL-C < 100mg/dl]
 - at presentation ; 20% of pts
 - at F/U after management ; 50% of pts
- Medication rate of lipid lowering drug
 - 58% of CHD patients received
- LDL-C reduction rate
 - in pts with medication [$140 \pm 36 \rightarrow 100 \pm 28$ mg/dl] ; 30%
 - in pts without medication [$112 \pm 44 \rightarrow 100 \pm 28$ mg/dl] ; 10%

Current status of management of hyperlipidemia for CAD patients under OPD F/U in 2003 in Korea

- Among treated CHD patients, only 55% reached goal.
 - SVS user 65%
 - AVS user 50%
 - PVS user 28%

Current status of management of hyperlipidemia for CAD patients under OPD F/U in 2003 in Korea

“10-60% Rule”

- 10% : LDL-C reduction rate in pts without medication
- 20% : rate of TGA at initial time point in CAD pts
- 30% : LDL-C reduction rate in pts with medication
- 40% : rate of pts without lipid drugs
- 50% : rate of TGA at F/U time point in CAD pts
- 60% : rate of pts with lipid drugs

REALITY :

Return on Expenditure Achieved for Lipid Therapy

■ Objectives

- To evaluate treatment gap of lipid management of patients at various risk levels of CHD in clinical practice in Korea
: From 100 doctors from clinics to university hospitals
- To assess treatment pattern among patients on lipid lowering therapy (LLT) associated with goal achievement

Method

- **Design**

- : multi-center retrospective review of medical records

- **Study investigators** : 100 investigators across Korea

- 30 Internists working at clinic

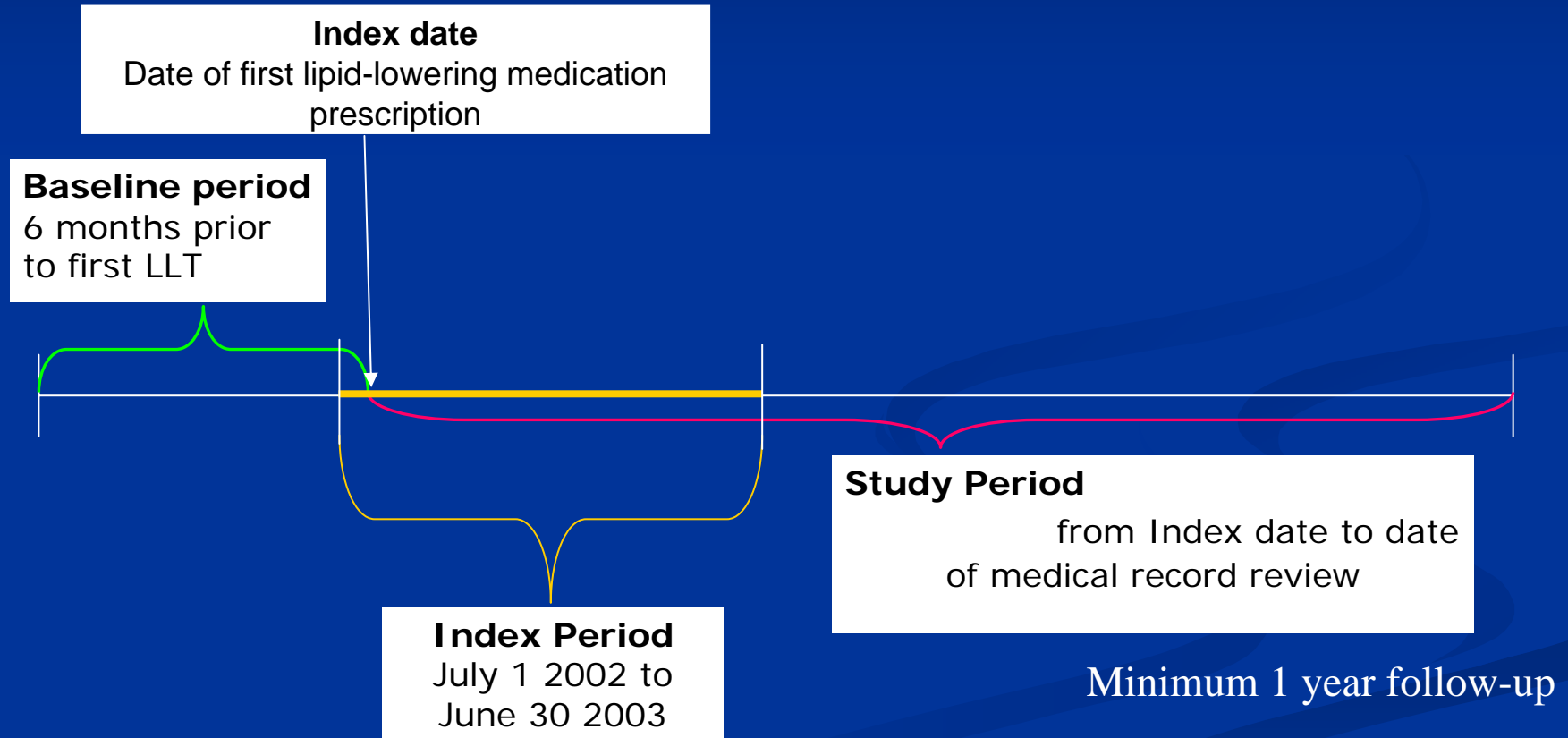
- 30 Endocrinologist working for General Hospitals

- 40 Cardiologist working for General Hospitals

- **Study population**

- : 5 patients/investigator, total 500 patients

Study Flow Chart



Inclusion Criteria

■ During Baseline period

(up to six months prior to first LLT)

- 18 < adults < 75 years
- not receive any lipid lowering medication for previous 6 months
- minimum of one TC and LDL-C measurement
- any one of the following risk factors:
 - Diabetes
 - Hypertension ($\geq 140/90$ mm Hg)
 - history of myocardial infarction (MI)
 - Ischemic heart disease

Analysis

- Monitoring
 - cholesterol measurement
 - lipid-lowering medication
- Treatment goal : KSLA guideline
(referred to NCEP ATP III guidelines)
- Percentage of patients attaining the goal
- Determinants on goal attainment

Baseline characteristics by risk factors

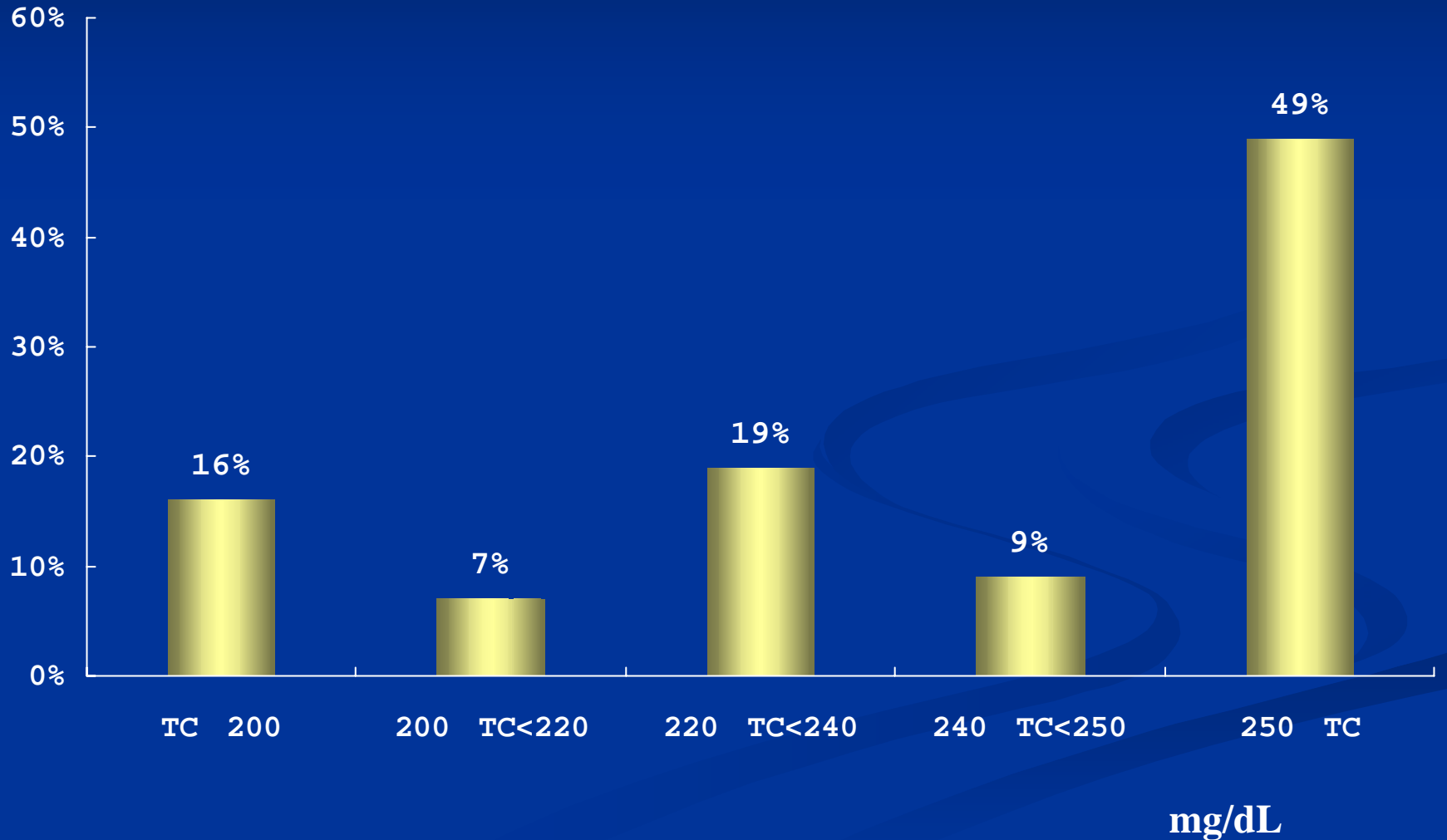
	CHD/CHD equivalent	Non-CHD or Non-DM	≤ 1 Risk	2+ Risk	All
	N = 369	N = 131	N = 45	N = 86	N = 500
%	74%	26%	9%	17%	100%
Gender					
male (%)	198 (54)	56 (43)	12 (27)	44 (51)	254 (51)
female (%)	171 (46)	75 (57)	33 (73)	42 (49)	246 (49)
Age					
18 < age ≤ 39	17 (5)	4 (3)	4 (9)	0	21 (4)
39 < age ≤ 49	60 (16)	28 (21)	21 (47)	7 (8)	88 (18)
49 < age ≤ 59	114 (31)	49 (37)	18 (40)	31 (36)	163 (33)
59 < age ≤ 69	130 (35)	40 (31)	1 (2)	39 (45)	170 (34)
69 < age	48 (13)	10 (8)	1 (2)	9 (10)	58 (12)

Baseline characteristics by risk factors

	CHD/CHD equivalent	Non-CHD or Non-DM	≤ 1 Risk	2+Risk	All
	N = 369	N = 131	N = 45	N = 86	N = 500
%	74%	26%	9%	17%	100%
Hypertension					
Yes	245 (66)	126 (96)	42 (93)	84 (98)	371 (74)
No	123 (33)	5 (4)	3 (7)	2 (2)	128 (26)
Unknown	1	0	0	0	1(<1)
Smoking					
Ever smoking	140 (38)	39 (30)	10 (22)	29 (34)	179 (36)
Never smoking	198 (54)	83 (63)	34 (76)	49 (57)	281 (56)
Unknown	31 (8)	9 (7)	1 (2)	8 (9)	40 (8)

Baseline Total Cholesterol

Patients

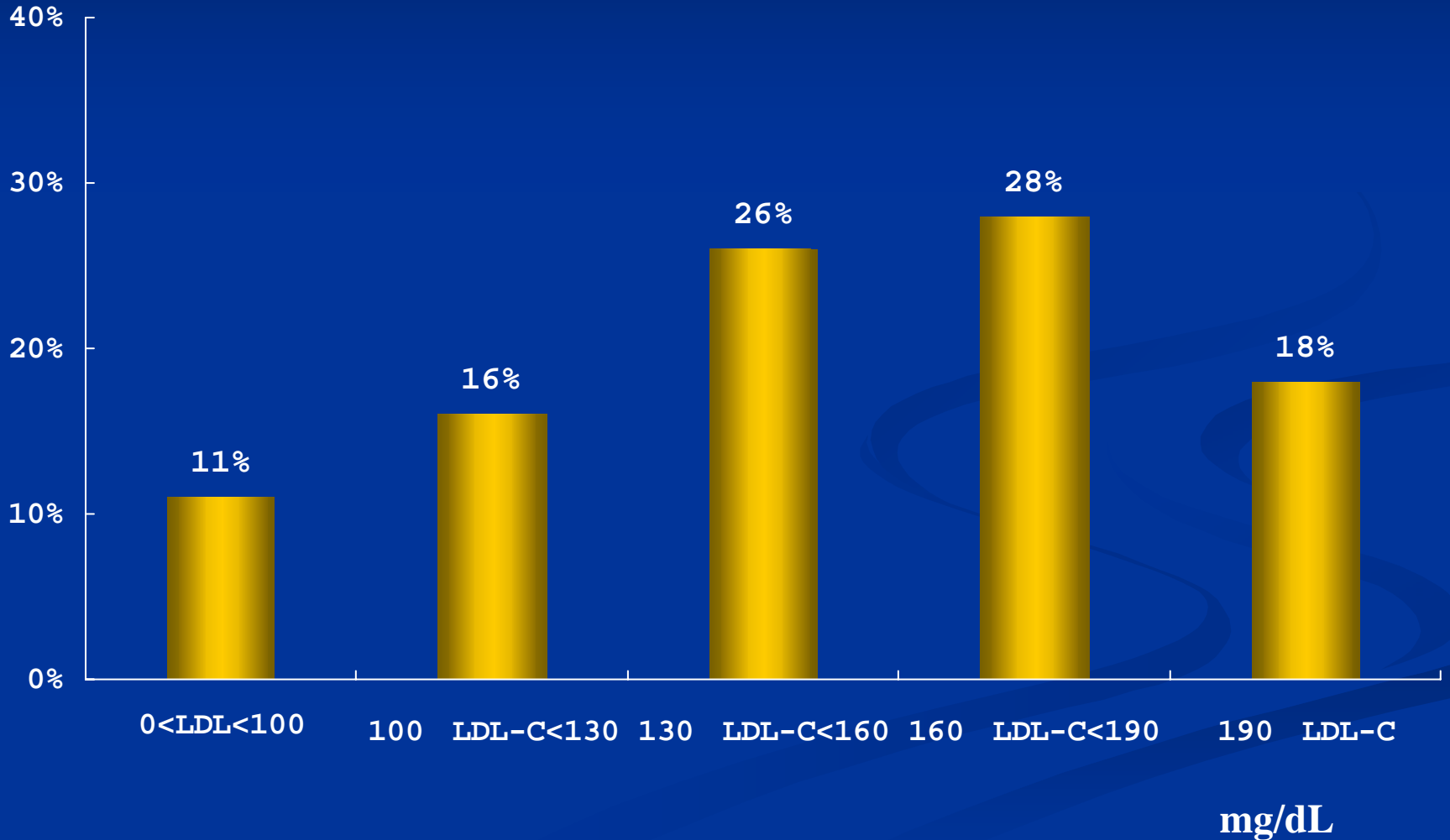


Baseline characteristics by risk factors

		CHD/CHD equivalent	Non-CHD or Non-DM	≤ 1 Risk	2+Risk	All
		N = 369	N = 131	N = 45	N = 86	N = 500
%		74%	26%	9%	17%	100%
Total Cholesterol (mg/dL)						
	TC < 200	71 (19)	11 (8)	6 (13)	5 (6)	82 (16)
200	TC < 220	28 (8)	9 (7)	1 (2)	8 (9)	37 (7)
220	TC < 240	65 (18)	28 (21)	10 (22)	18 (21)	93 (19)
240	TC < 250	32 (9)	12 (9)	4 (9)	8 (9)	44 (9)
250	TC	173 (47)	71 (54)	24 (53)	47 (55)	244 (49)

Baseline LDL Cholesterol

Patients



Baseline characteristics by risk factors

	CHD/CHD equivalent	Non-CHD or Non-DM	≤ 1 Risk	2+Risk	All
	N = 369	N = 131	N = 45	N = 86	N = 500
%	74%	26%	9%	17%	100%
Baseline LDL-C (mg/dL)					
0 < LDL < 100	47 (13)	9 (7)	4 (9)	5 (6)	56 (11)
100 LDL < 130	62 (17)	17 (13)	7 (16)	10 (12)	79 (16)
130 LDL < 160	95 (26)	37 (28)	12 (27)	25 (29)	132 (26)
160 LDL < 190	97 (26)	44 (34)	14 (31)	30 (35)	141 (28)
190 LDL	68 (18)	24 (18)	8 (18)	16 (19)	92 (18)

Baseline characteristics by risk factors

	CHD/CHD equivalent	Non-CHD or Non-DM	≤ 1 Risk	2+Risk	All
	N = 369	N = 131	N = 45	N = 86	N = 500
%	74%	26%	9%	17%	100%
HDL-C					
No data	40 (11)	16 (12)	8 (18)	8 (9)	56 (11)
0 < HDL < 40	122 (33)	30 (23)	9 (20)	21 (24)	152 (30)
40 HDL	207 (56)	85 (65)	28 (62)	57 (66)	292 (58)
CHD					
No-CHD	156 (42)	131 (100)	45 (100)	86 (100)	287 (57)
CHD(AP/MI)	213 (58)	0	0	0	213 (43)
Diabetes					
Yes	220 (60)	0	0	0	220 (44)
no	148 (40)	131 (100)	45 (100)	86 (100)	279 (56)
Unknown	1 (<1)	0	0	0	1 (<1)

Potency :

Individual statins, dosages, stratified by efficacy

<i>Equivalent Potency</i> <u>Statins</u>	<i>1</i> (very low)	<i>2</i> (low)	<i>3</i> (medium)	<i>4</i> (high)	<i>5</i> (very high)
<i>Atorvastatin (mg)</i>	--	5	10	20	40, 80
<i>Simvastatin (mg)</i>	--	10	20	40	80
<i>Pravastatin (mg)</i>	5, 10	20	40	80	--
<i>Fluvastatin (mg)</i>	10, 20	40	80	--	--
<i>Rosuvastatin (mg)</i>	--	--	10	--	--
<i>Lovastatin (mg)</i>	10	20	--	--	--

Potency = 0 in case of gemfibrozil, bezafibrate, fenofibrate, probucol regardless of its strength

Maron DJ et al. Current perspectives on statins. Circulation 2000;101:207-213

REALITY: lipid real world in Korea

- Half (45%) of CHD/CHD equivalent group patients treated with lipid lowering medication in Korea
 - : baseline LDL-C greater than 160 mg/dl
 - requiring LDL-C reduction of 37.5% or greater
 - to attain treatment goal

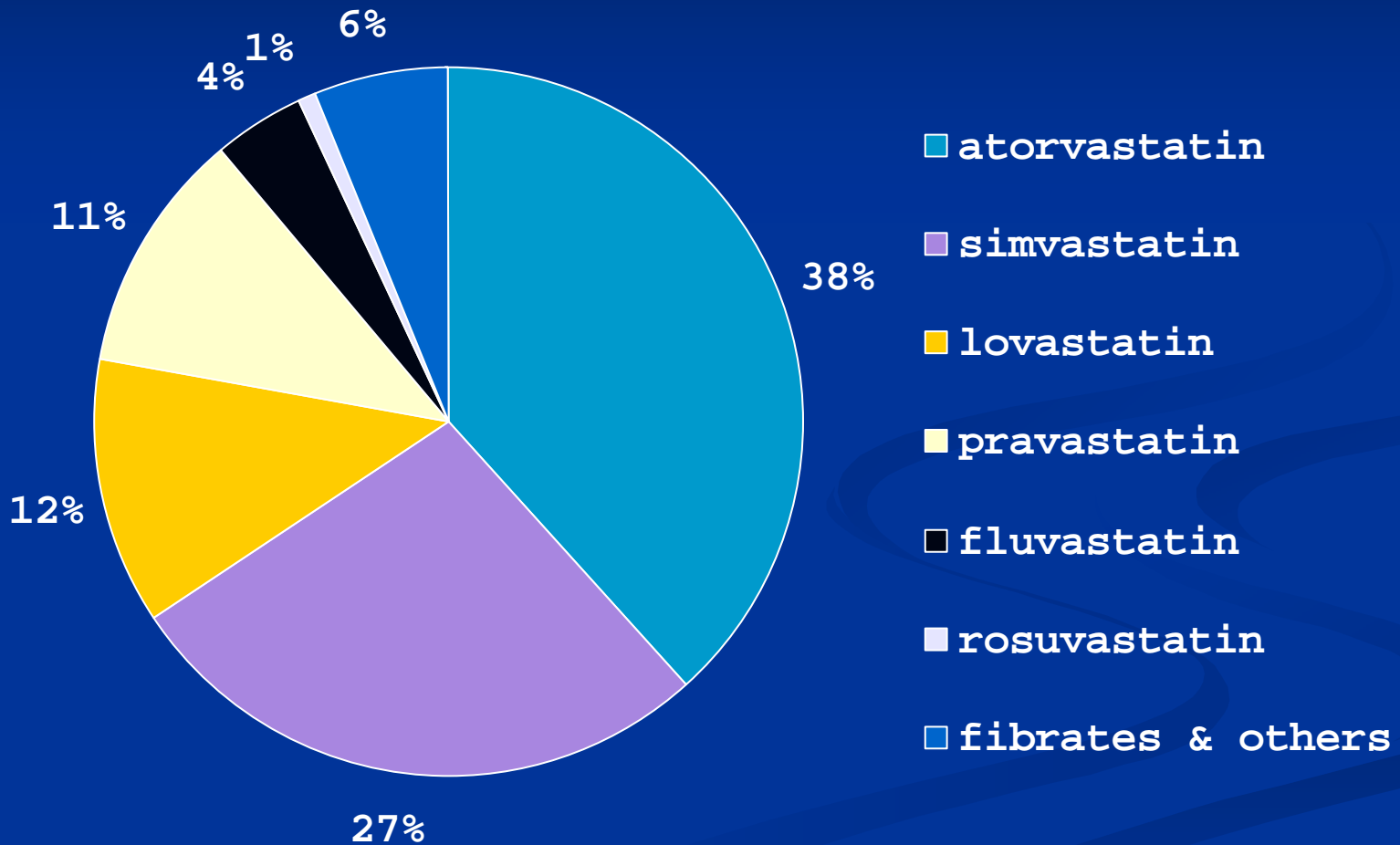
REALITY: lipid real world in Korea

- Most of the patients are either started with
 - medium (66%) potency statin
 - low (28%) potency statin
- Medium potency statins
 - are the most commonly used initial drugs
 - Atorvastatin 10mg: 34.8%
 - Simvastatin 20mg: 24.4%

Initial Lipid Therapy and Baseline LDL-C

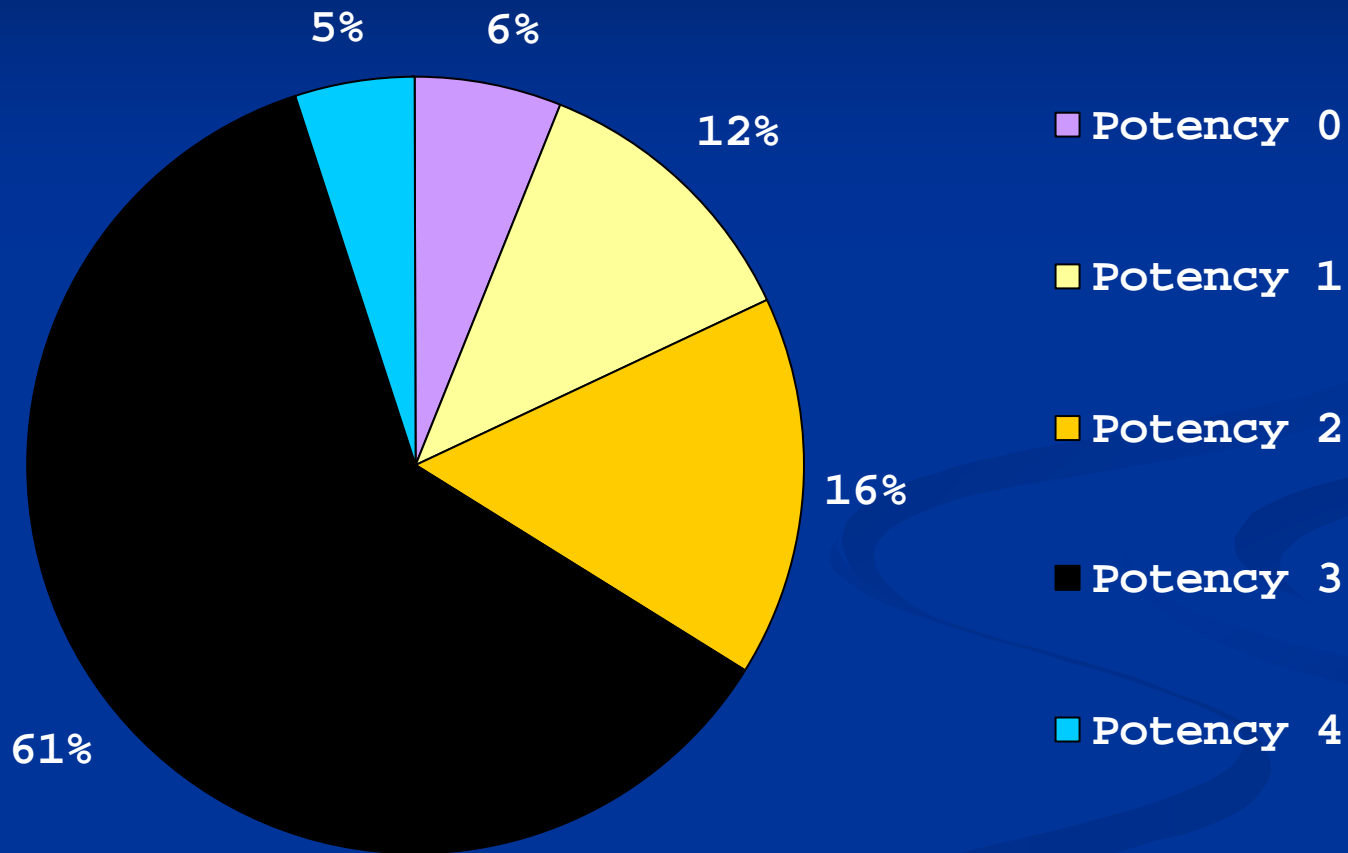
		LDL-C Categories in mg/dl					
	mg	All N=500 (%)	0<LDL-C <100 N=56 (%)	100 LDL-C<130 N=79(%)	130 LDL-C<160 N=132 (%)	160 LDL-C<190 N=141 (%)	190 LDL-C N=92 (%)
atorvastatin	10	174 (35)	15 (27)	25 (32)	55 (42)	51 (36)	28 (30)
	20	18 (4)	2 (4)	2 (3)	2 (2)	8 (6)	4 (4)
simvastatin	10	6 (1)	0	1 (1)	2 (2)	2 (2)	1 (1)
	20	122 (24)	15 (27)	21 (27)	28 (21)	41 (29)	17 (18)
	40	9 (2)	1(2)	0	3 (2)	4 (3)	1 (1)
lovastatin	20	61 (12)	6 (11)	9 (11)	17 (13)	18 (13)	11 (12)
pravastatin	5	19 (4)	1 (2)	2 (3)	4 (3)	3 (2)	9 (10)
	10	33 (7)	5 (9)	8 (10)	11 (8)	3 (2)	6 (7)
	20	1 (<1)	0	0	0	1 (1)	0
	40	1 (<1)	0	0	1 (1)	0	0
fluvastatin	10	1 (<1)	0	0	0	1 (1)	0
	20	3 (1)	0	0	2 (2)	0	1 (1)
	40	11 (2)	1 (2)	1 (1)	3 (2)	3 (2)	3 (3)
	80	7 (1)	0	1 (1)	2 (2)	1 (1)	3 (3)
rosuvastatin	10	3 (1)	0	0	0	1 (1)	2 (2)
bezafibrate	200	7 (1)	1 (2)	0	0	1 (1)	5 (5)
	400	1 (<1)	0	0	0	0	1 (1)
fenofibrate	200	17 (3)	8 (14)	6 (8)	1 (1)	2 (1)	0
	250	2 (<1)	0	0	1 (1)	1 (1)	0
gemfibrozil	300	3 (1)	1 (2)	2 (3)	0	0	0
probucol	250	1 (<1)	0	1 (1)	0	0	0
Total		500 (100)	56 (11)	79 (16)	132 (26)	141 (29)	92 (18)

Initial Drug Choice of LLT (All 500 patients)

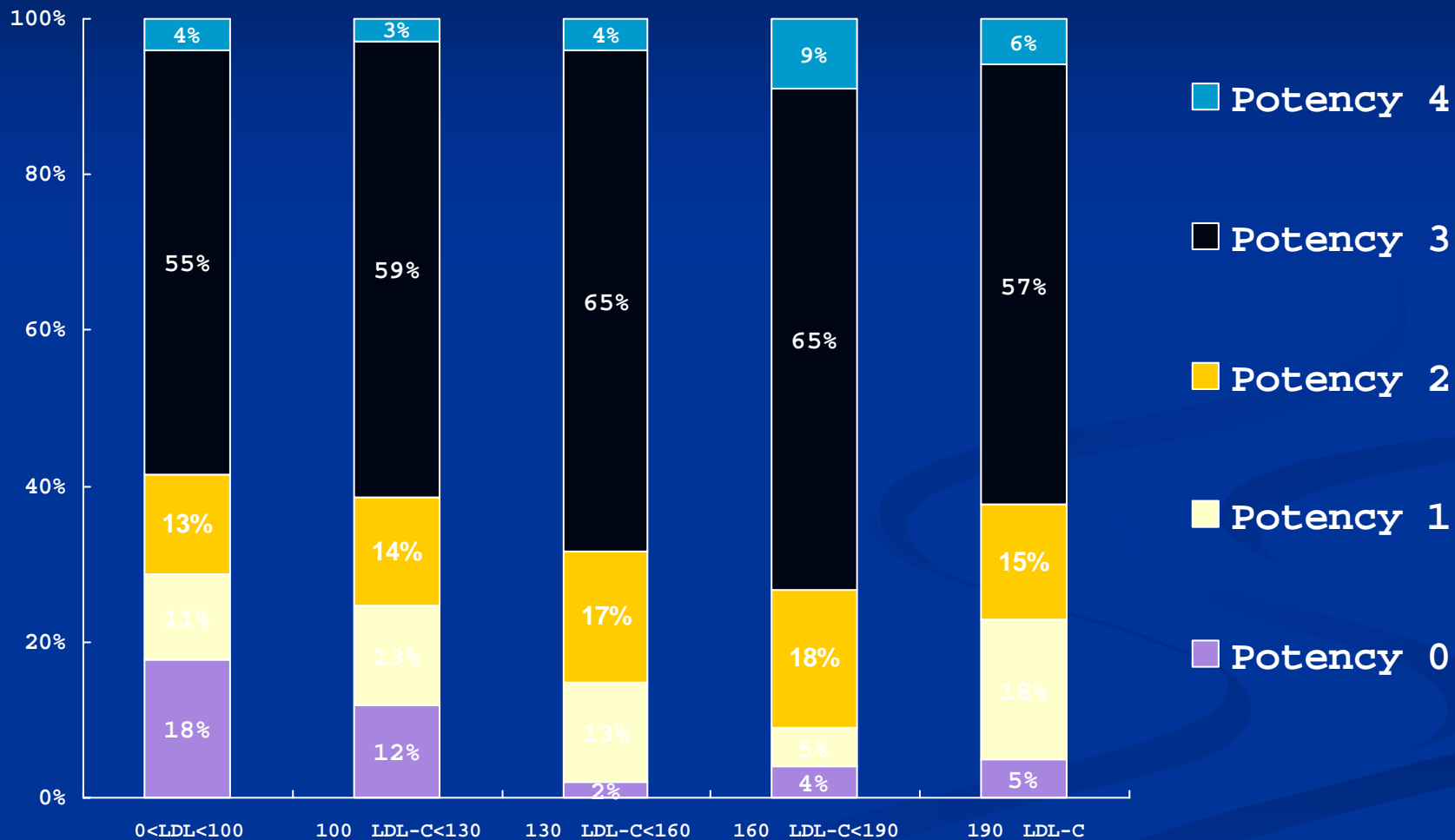


Initial Drug Choice of LLT by Potency

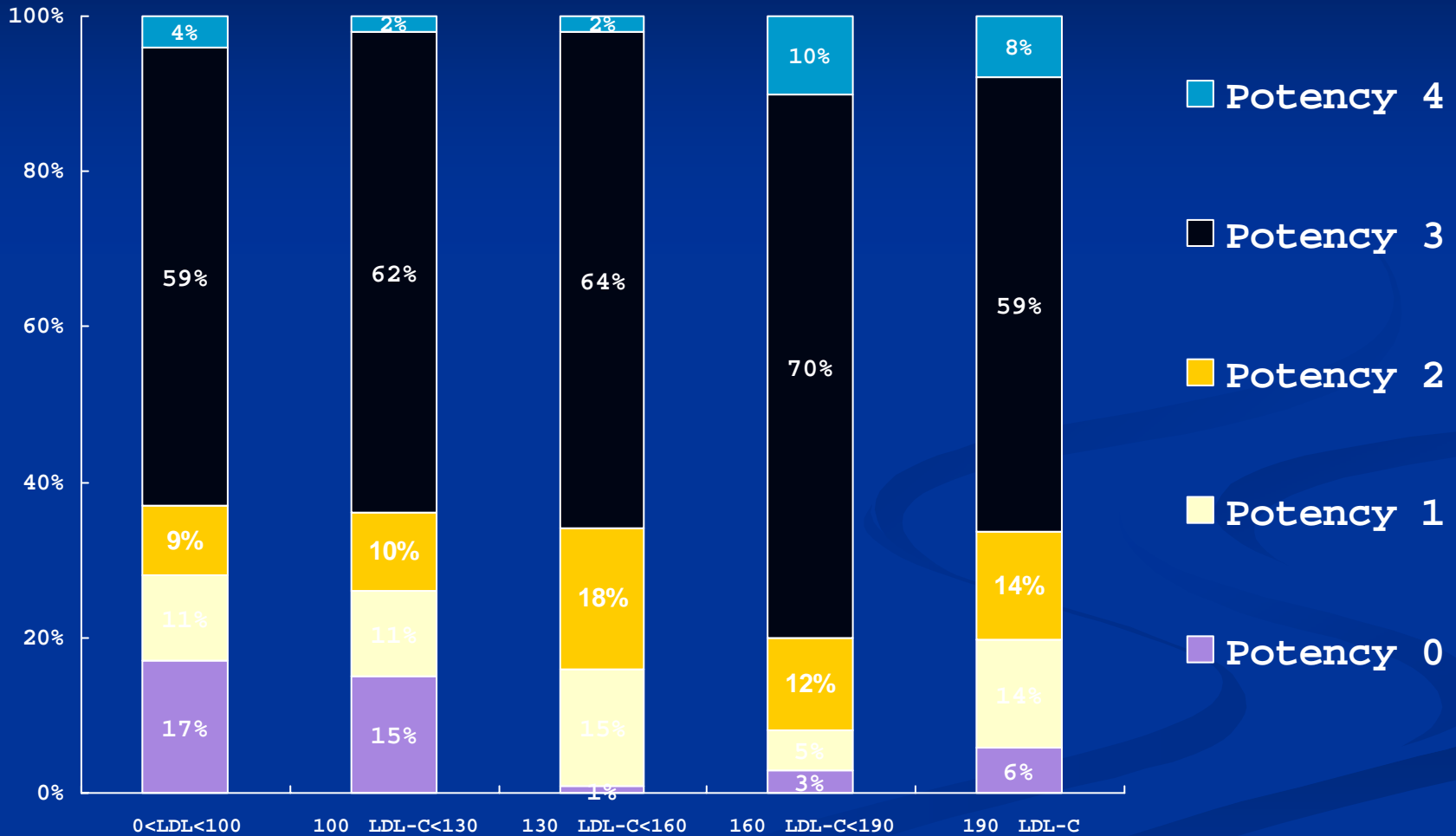
(All 500 patients)



Potency of Initial LLT and baseline LDL-C (All 500 patients)



Potency of Initial LLT and baseline LDL-C (CHD/CHD equivalent patients)

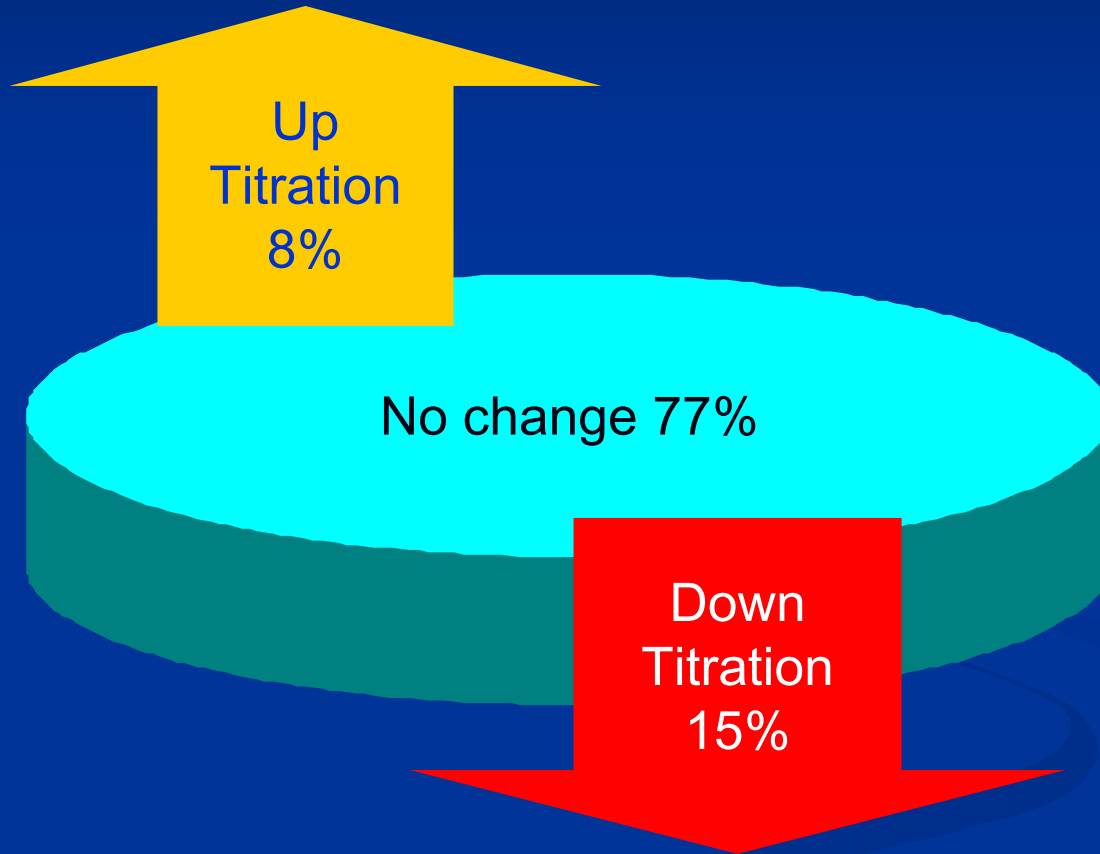


Change of potency to next lipid lowering therapy (All 500 patients) 23 %

Initial Statin Equipotent Dose

		0	1	2	3	4
Next potency	0	22	3	2	15	1
	1	.	32	1	2	.
	2	1	4	39	12	.
	3	6	17	33	268	4
	4	2	.	4	10	22
Total patient that titrated		9(1.8%)	24(4.8%)	40(8%)	39(7.8%)	5(1%)

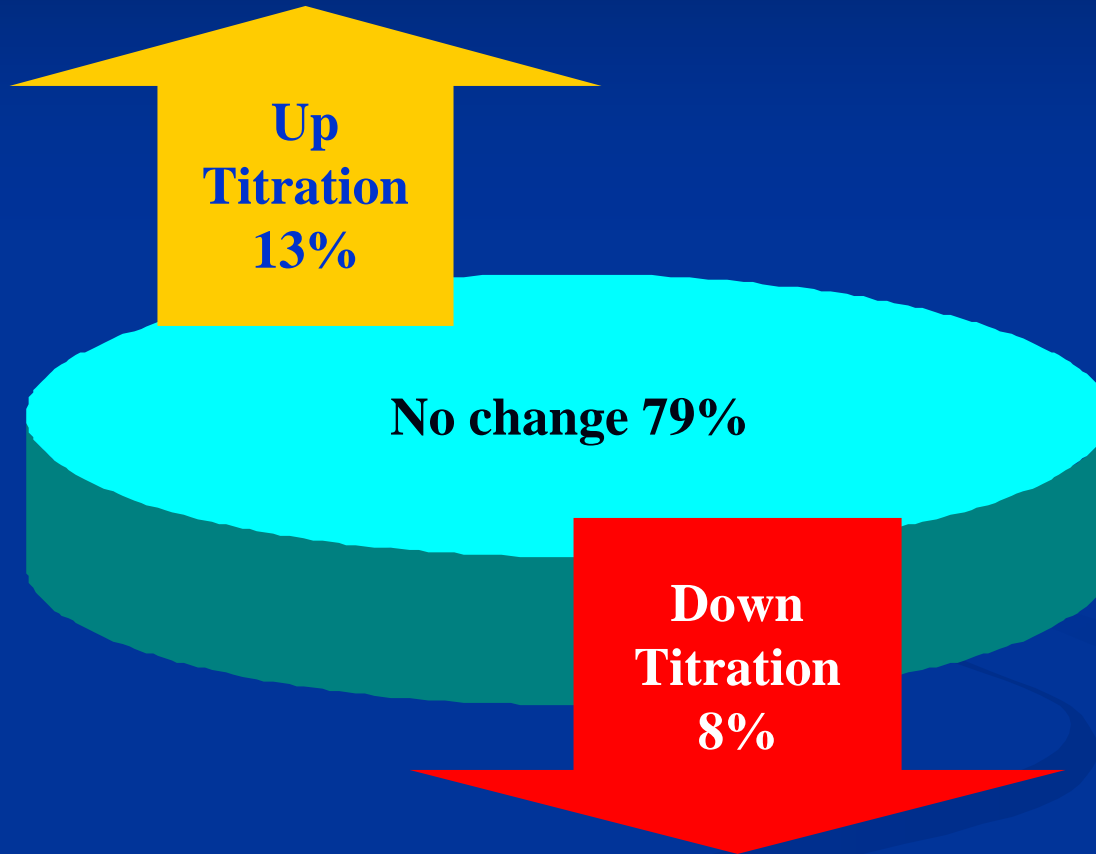
Change of Potency (All 500 patients)



Change of potency to next lipid lowering therapy (CHD/CHD equivalent patients) 21 %

		Initial Statin Equipotent Dose				
		0	1	2	3	4
Next potency	0	19	2	0	10	0
	1	0	24	1	2	0
	2	1	2	27	12	0
	3	4	12	16	203	2
	4	1	0	4	9	18
Total patient that titrated		6(8%)	16(21%)	21(27%)	33(42%)	2(3%)

Change of Potency (CHD/CHD equivalent patients)



RESULTS: Persistence

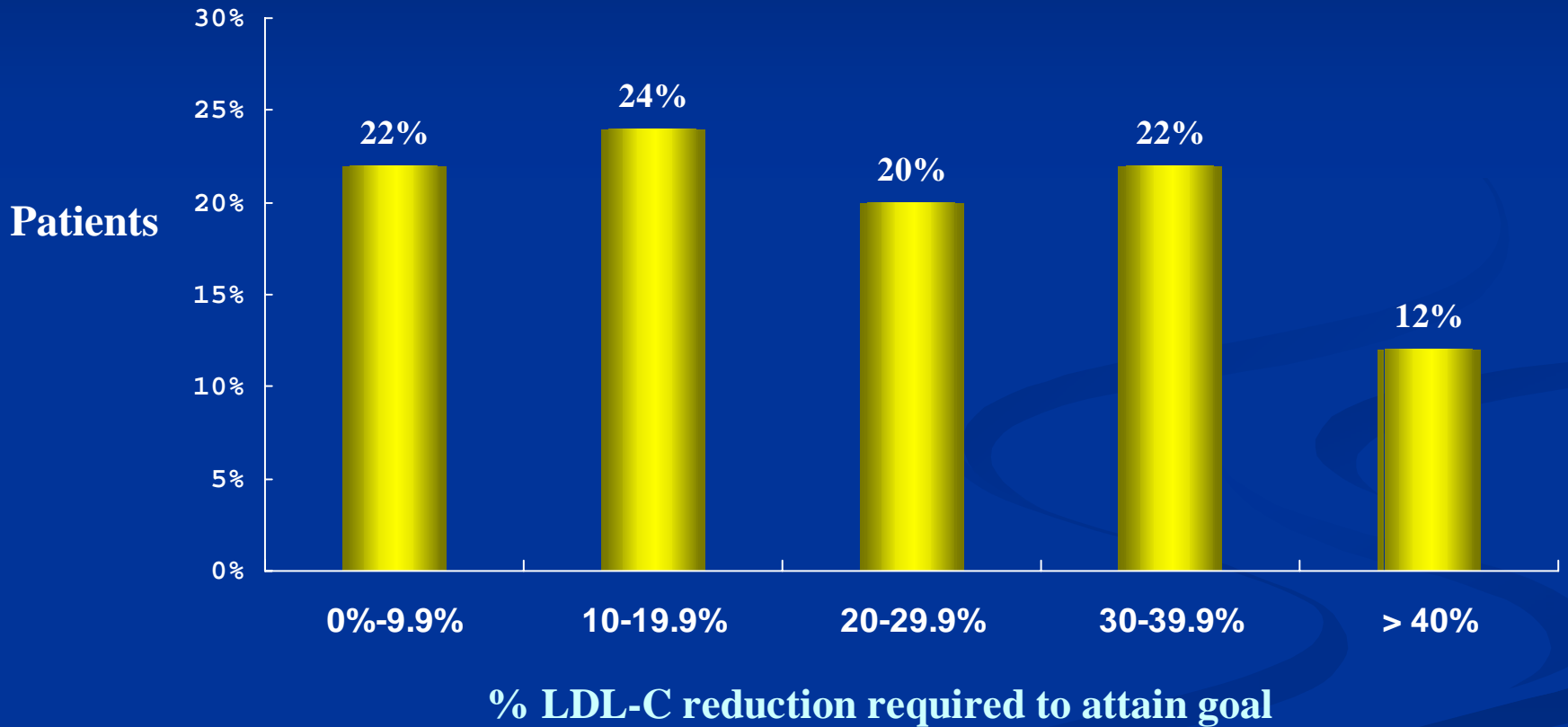
- Persistence with LLT
 - 0.71 during study period (SD 0.35)
 - Treatment duration = last Rx date – first Rx date
 - Total Rx period = Sum of Rx period during study period

$$\text{Persistence} = \frac{\text{Total Rx period}}{\text{Treatment duration}}$$

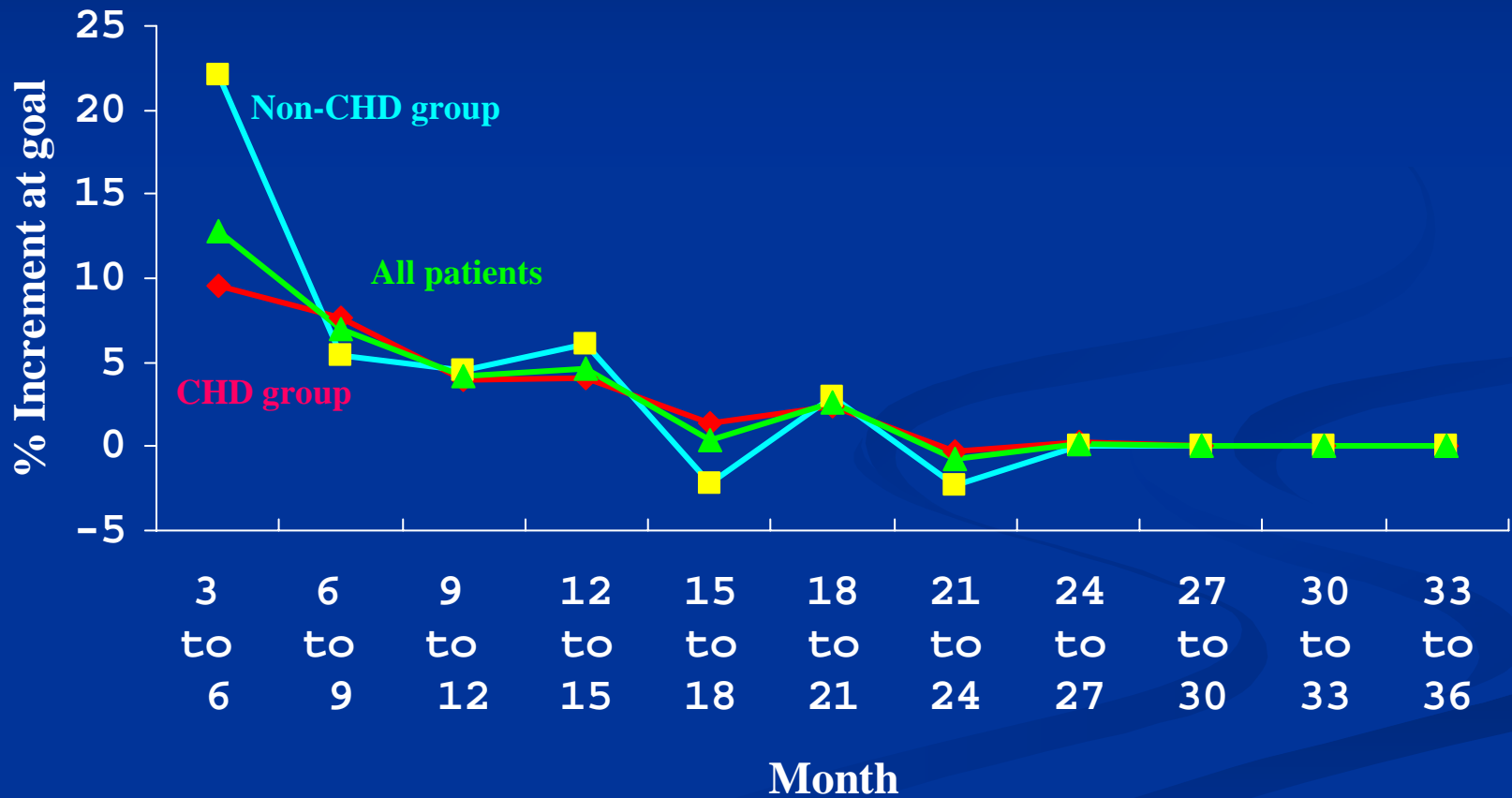
RESULTS: Goal attainment

- LDL-C goal attained during the study period
 - 41% of all patients
 - 37% of CHD/CHD risk equivalent patients
 - 52% of non-CHD patients
- At study end, 34 % of patients who were not at goal
 - : further required LDL-C reductions >30%

LDL-C Reduction Required at Study End for Patients not at Goal



Incremental Goal Attainment Over Time for All, CHD and non-CHD patients



Logistic Regression Model for Goal Attainment

Variables	OR	95% CI
Patient with baseline LDL-C < 130 mg/dL	1.783	1.162-2.735
Patient without a change in potency	0.299	0.139-0.642
Patient with CHD or CHD equivalent	0.445	0.288-0.688
Patient with baseline LDL-C > 190mg/dL	0.283	0.155-0.516

REALITY: summary

- Overall only 41 % patients attained LDL-C goal
 - 37 % CHD/CHD equivalent patients
 - 52 % of non-CHD patients
- Persistence was 71 % during study period
- More effective lipid management therapies are needed to enable patients attain goal

REALITY & Ten Center Study

- Patients with risk factors in general [REALITY STUDY]
 - Overall only **41 %** patients attained **LDL-C goal**
(37 % of CHD patients, 52 % of non-CHD patients)
- CAD patients at OPD of university hospitals [TEN CENTER STUDY]
 - 60 % of patients ; medication for hyperlipidemia
 - 55 % of patients with medication ; achieve target goal
 - **50 %** of whole patients at OPD ; achieve **target goal**
- Insufficient medication rate & dosage of statins
- Future requirements
 - Doctors' awareness of statin therapy for CAD patients
 - Initial adequate dose
 - Super statin or other drugs allowing the use of low dosage with safety
 - Problem of medical insurance

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LDL Cholesterol Goals and Cutpoints (2004)

Risk Category	LDL Goal (mg/dL)	LDL (mg/dL) - Therapeutic Lifestyle Changes (TLC)	LDL (mg/dL) - Drug Therapy
<ul style="list-style-type: none"> ■ CHD or CHD Risk Equivalents (10-year risk > 20 %) 	<p><100</p> <p>Optional < 70*</p>	<p>≥100</p>	<p>≥100</p> <p>(<100 : drug optional)</p>
<ul style="list-style-type: none"> ■ 2+ Risk Factors (10-year risk 10–20 %) 	<p><130</p> <p>Optional <100*</p>	<p>≥130</p>	<p>≥130</p> <p>(100–129 : drug optional)</p>
<ul style="list-style-type: none"> ■ 2+ Risk Factors (10-year risk <10 %) 	<p><130</p>	<p>≥130</p>	<p>≥160</p>
<ul style="list-style-type: none"> ■ 0–1 Risk Factor 	<p><160</p>	<p>≥160</p>	<p>≥190</p> <p>(160–189 : drug optional)</p>