Hyperlipidemia and Dyslipidemia

Risk & Controversies

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Significance of the Clinical Problem

- Given the well-established strong link between

  lipids and cardiovascular disease

  it is essential that clinicians develop a strategy to decide **who they will treat and which drugs they will use**.

CTTC Meta-analysis: 21 statin trials n=140,000 Major Vascular Events per mmoL(39 mg/dl) LDL-C reduction

	No. of events(%pa)	No. of events(%pa)	Relative risk(CI) per mmol/L LDL-C reduction
	Statin	Control	
Any major vascular event	7136(2.8%)	8934(3.6%)	0.79(0.77-0.81)

Cholesterol Treatment Trialists (CTT) Collaboration **2010** Lancet

Case 1

- A 50-year-old male in good health seeks your advice on reducing risk for CVD. The patient exercises and eats a healthy diet.
- He does not smoke and has no family history of heart disease.
- He is on no medications.
- Height is 178 cm; weight 91 kg; BMI 28.7; WC 91.4 cm; and BP , 130/80 mm Hg.

Case 1:continued

- Total cholesterol is 220 mg/dl
- LDL. 132 mg/dl
- HDL, 40 mg/dl
- Non-HDL cholesterol, 189 mg/dl
- Triglyceride (TG) , 140 mg/dl
- Calculate his 10-year ACC/AHA Risk Score and lifetime risk and decide for his treatment.

Case 1:continued

- His 10-year ACC/AHA Risk Score is 5.1%
- Lifetime risk is 46%.
- Using the QRISK calculator, his 10-year- risk is 5.4% and lifetime risk is 41%.

What would you do next for case 1?

- A. Observe with repeat testing
- B. Start statin therapy
- C. Obtain additional tests: hs-CRP, carotid ultrasound, computed tomography to measure coronary calcium score

What is the "normal" range of serum lipids?

- There is no true "normal" range for serum lipids.
- In Western populations, cholesterol values are about 20% higher than in Asian populations and exceed 300 mg/dL in nearly 5% of adults.
- About 10% of adults have LDL cholesterol levels above 200 mg/dL
- Total and LDL cholesterol levels tend to rise with age even in persons who are otherwise in good health

Prevalence of Hypercholesterolemia, High LDL, and Low HDL in Iran: A Systematic Review and Meta-Analysis

Table 4: The pooled estimate of the prevalence of lipid components according to ATPIII cut-off, based on gender using random effect meta-analysis of data extracted from population-based studies in Iran (2005-2015)

Variable	Cut-off point (mg/dl)	Number of studies	Prevalence (%)	95% CI	I2 (%)
High cholesterol	≥200	T: 16 M: 9 F: 9	T: 39 M: 31 F: 38	T: 35-44 M: 15-46 F: 33-43	T: 99.3 M: 99.9 F: 98.8
	≥240	T: 6 M: 4 F: 6	T: 15 M: 13 F: 14	T: 7-22 M: 5-21 F: 7-22	T: 99.6 M: 99.4 F: 99.2
High LDL-C	≥130	T: 10 M: 4 F: 5	T: 38 M: 34 F: 37	T: 24-52 M: 13-56 F: 14-60	T: 99.9 M: 98.4 F: 99.4
	≥160	T: 5 M: 4 F: 5	T: 18 M: 18 F: 15	T: 12-24 M: 13-24 F: 5-26	T: 95.1 M: 94.5 F: 99.2
Low HDL-C	M: ≤ 40 F: ≤50	T: 9 M: 8 F: 6	T: 45 M: 41 F: 42	T: 34-55 M: 25-57 F: 29-55	T: 99.8 M: 99.8 F: 99.7

T: Total; M: Male; F: Female

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Table 5: The overall prevalence of lipid components according to ATPIII cut-off among sex by random effect meta-analysis of data extracted from population-based studies in Iran

Variable	Cut-off point (mg/dl)	Extracted articles (*n*)	Sample size (*n*)	Prevalence (%)	CI 95%
T-C	>200	M=9	M=48,567	M: 38.9	M: 31.3-46.5
		F=9	F=54,019	F: 41.8	F: 31.5-52.0
		T=14	T=113,874	T: 41.6	T: 36.1-47.0
Heterogeneity T-C	I2square	M: 99.9%	*P*<0.001		
		F: 100.0%	*P*<0.001		
		T: 99.9%	*P*<0.001		
TG	>150	M=9	M=21,013	M: 47.0	M: 44.3-49.7
		F=10	F=20,401	F: 42.5	F: 39.4-45.7
		T=11	T=44,958	T: 46.0	T: 43.3-48.7
Heterogeneity TG	I2square	M: 98.3%	*P*<0.001		
		F: 98.8%	*P*<0.001		
		T: 99.3%	*P*<0.001		
LDL-C	>130	M=6	M=6,798	M: 34.7	M: 16.8-52.6
		F=6	F=10,828	F: 40.2	F: 19.8-60.5
		T=11	T=26,454	T: 35.5	T: 24.0-47.1
Heterogeneity LDL-C	I2square	M: 99.9%	*P*<0.001		
		F: 100.0%	*P*<0.001		
		T: 100.0%	*P*<0.001		
HDL-C	M: <40	M=11	M=33,701	M: 40.6	M: 23.6-57.6
	F: <50	F=11	F=34,574	F: 47.6	F: 30.9-64.2
		T=14	T=74,216	T: 43.9	T: 33.4-54.4
Heterogeneity HDL-C	I2square	M: 100.0%	*P*<0.001		
		F: 100.0%	*P*<0.001		
		T: 100.0%	*P*<0.001		

Prevalence of abnormal lipid profiles in adults, United States.

DATA SOURCE	POPULATION	ABNORMAL LIPID PROFILE	PREVALENCE (%)
NHANES 2003-2006	US, adults, age ≥20 years	Elevated LDL-C (risk-stratum specific)	27
		Depressed HDL-C (males, <40 mg/dL; females <50 mg/dL)	23
		Elevated TGs (≥200 mg/dL)	30
		Elevated non-HDL-C (≥130 mg/dL) and elevated TG (≥200 mg/dL)	13
		Mixed dyslipidemia (elevated LDL-C and depressed HDL-C and/or elevated TGs)	21
		Elevated LDL-C and depressed HDL-C and elevated TG	6

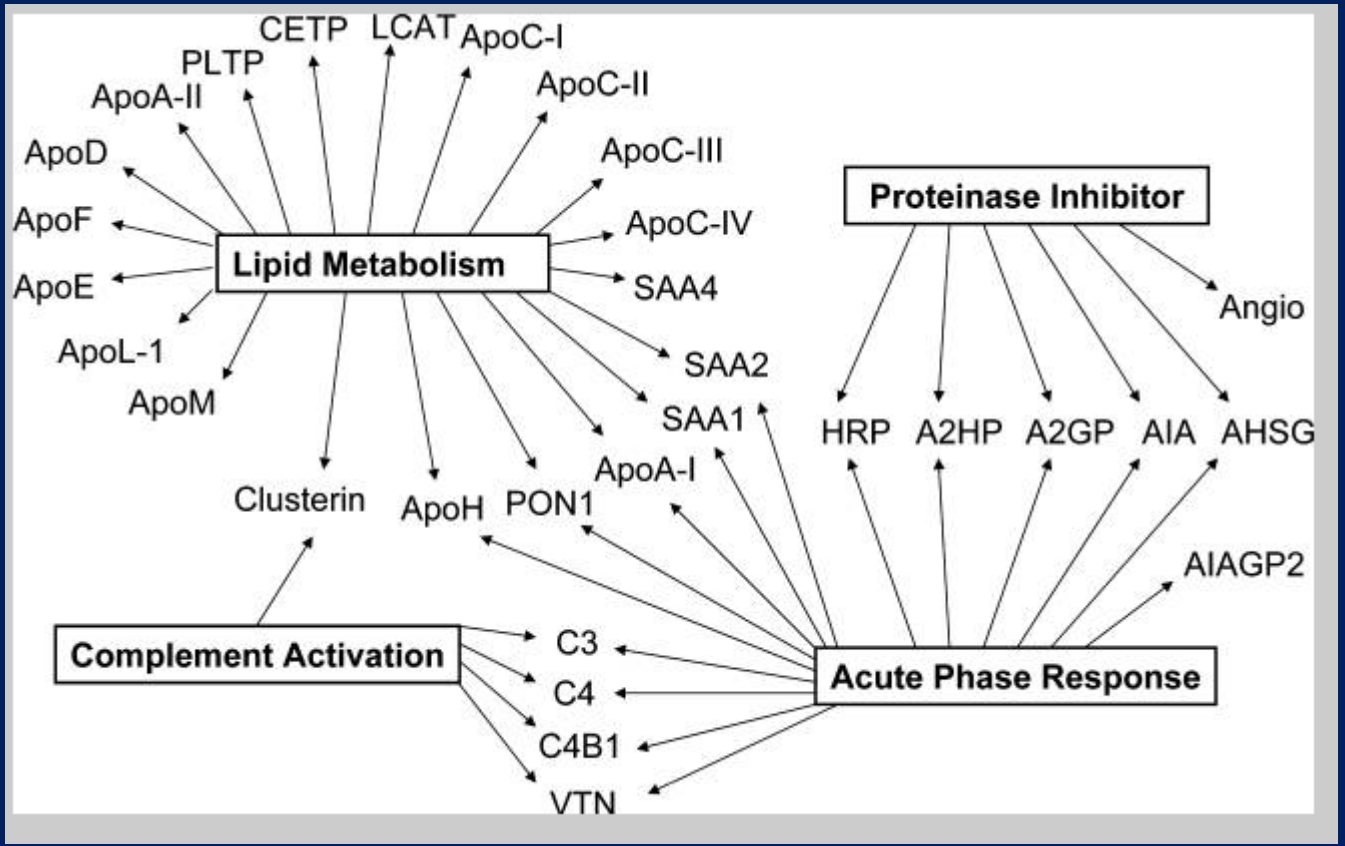
Source: Tóth et al. 2012[4]

Abbreviations: LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides. Fasting blood serum levels are shown.

Hyperlipidemia and Dyslipidema

- **Low levels of HDL-C** vs. **disturbed functionally of HDL-C**
- The presence of **small, dense LDL particles**
- The presence of **oxidized LDL particles**
- The presence of **atherogenic triglyceride-rich lipoprotein remnants**
- **Insulin resistance** and increased TG (non-HDL-C is the preferred risk indicator and second treatment target)

The HDL proteome: a marker and perhaps mediator of coronary artery disease



Various Forms of Hyperlipidemia

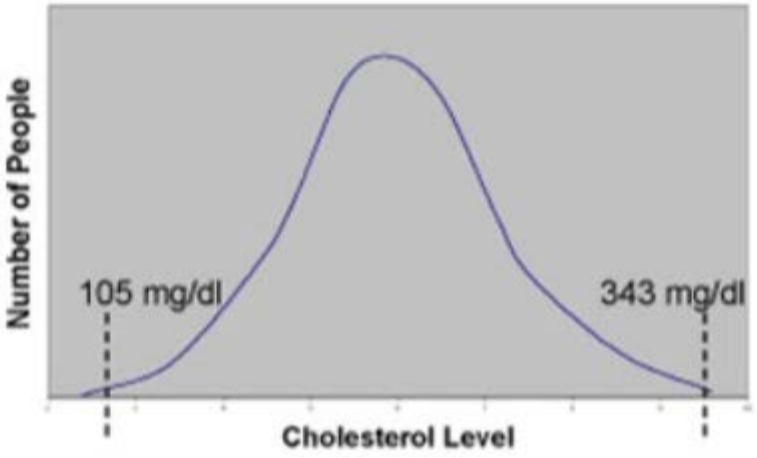
	Incidence	Cholesterol Level
Familial homozygous Hypercholesterolemia	One in one million	>600 mg/dl
Heterozygous FH	One in 300-500 persons	200-300 mg/dl
Polygenic Hypercholesterolemia	Common	
Familial Combined Hyperlipidemia	One in 250 persons	200-400 mg/dl
Familial Dysbeta-lipoproteinemia	~ One in 10,000	300-400 mg/dl
Metabolic Dyslipidemia	Most common cause of mixed hyperlipidemia	Modest elevation of cholesterol

"Pure" Hypercholesterolemia Other causes

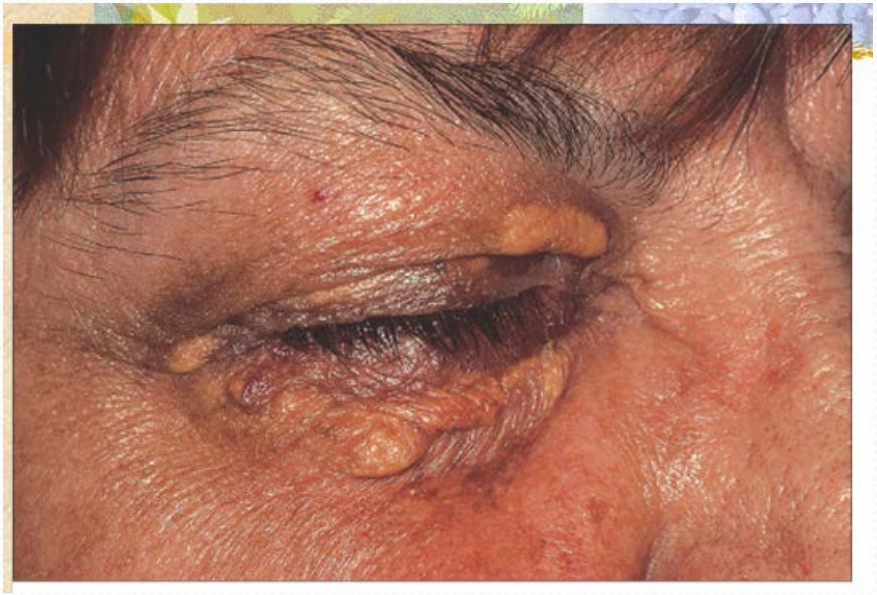
- **Polygenic hypercholesterolemia**
  - Very *Common*
  - Genetics poorly defined
  - Mechanisms poorly defined (likely includes hyperabsorbers)
  - Generally *milder* than FH
- **Diet-induced**
  - Very *common*
  - Generally *much milder* than FH
- "Secondary" causes
  - Hypothyroidism—rel. *common in elderly* but ↑LDL *mild*
  - Other (*rare* hepatic and renal abn., etc.)

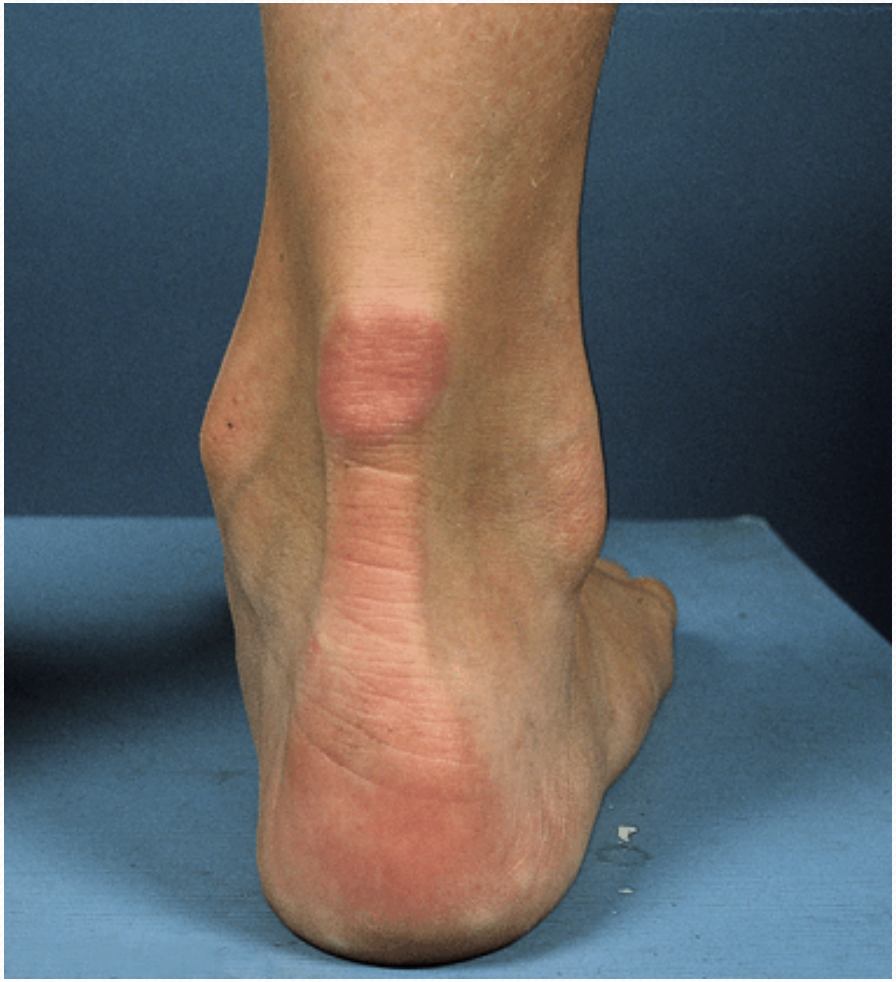
Polygenic Hpercholesterolemia

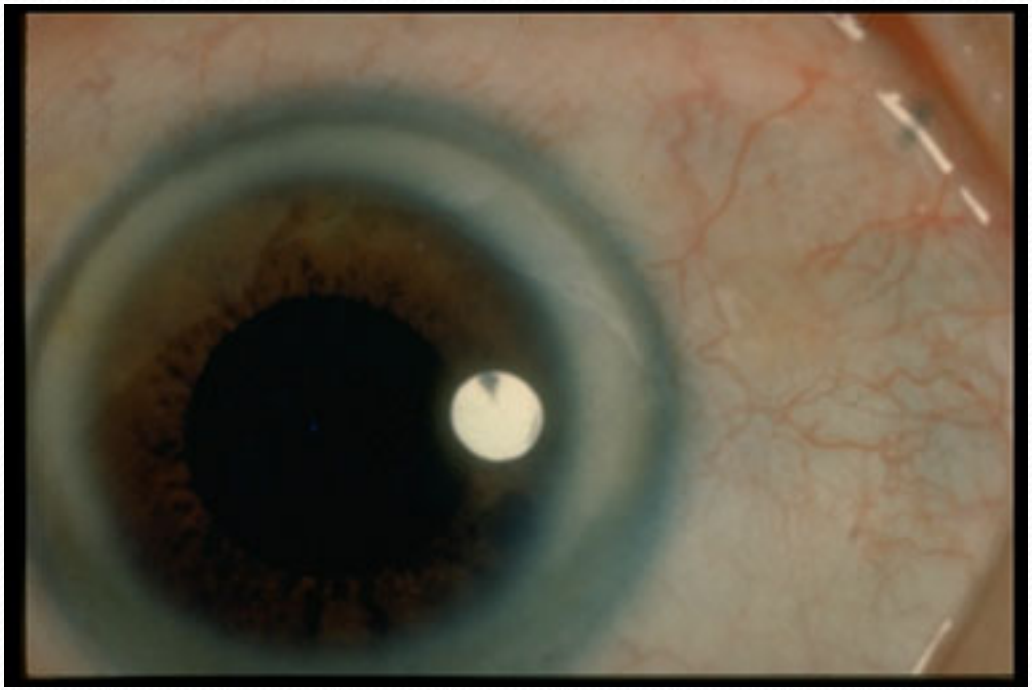
- Hypercholesterolemia is defined as a cholesterol value that exceeds the 95th percentile for the population



Normal Distribution of Healthy Cholesterol Levels



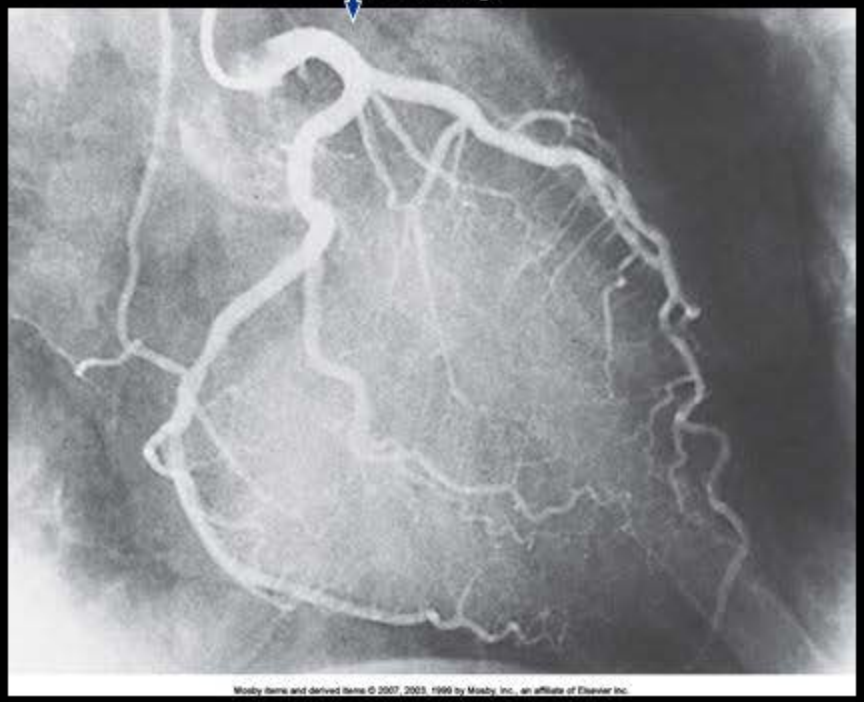




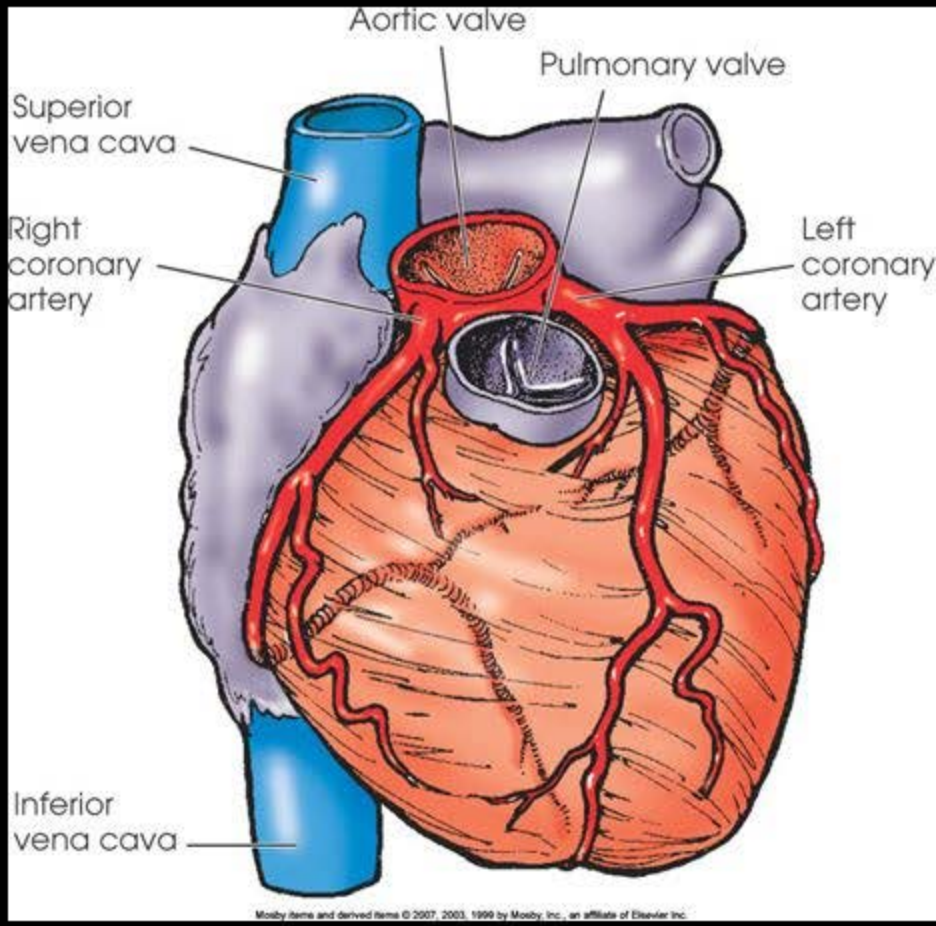
Common Secondary Causes of Dyslipidemia

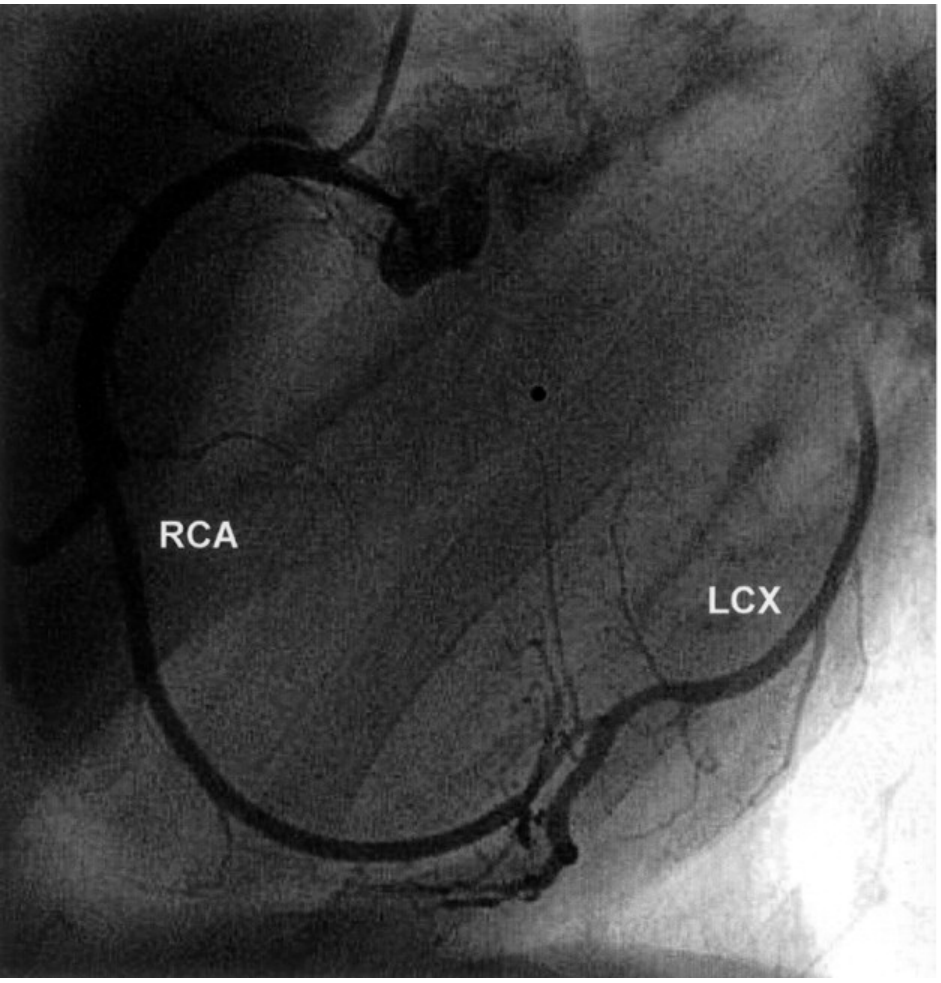
Affected lipids	Conditions
↑ Total cholesterol and LDL-C	• 1- Hypothyroidism
	• 2- Nephrosis
	• 3- Dysgammaglobulinemia (systemic lupus erythematosus, multiple myeloma)
	• 4- Progestin or anabolic steroid treatment
	• 5- Cholostatic diseases of the liver
	• 6-Protease inhibitors for treatment of HIV infection
↑ Triglycerides and VLDL-C	• 7-Chronic renal failure
	• 8-T2DM
	• 9-Obesity
	• Excessive alcohol intake
	• Hypothyroidism
	• Antihypertensive medications (thiazide diuretics and b-adrenergic blocking agents)
	• Corticosteroid therapy
	• Orally administered estrogens, oral contraceptives, pregnancy
	• Protease inhibitors for treatment of HIV infection

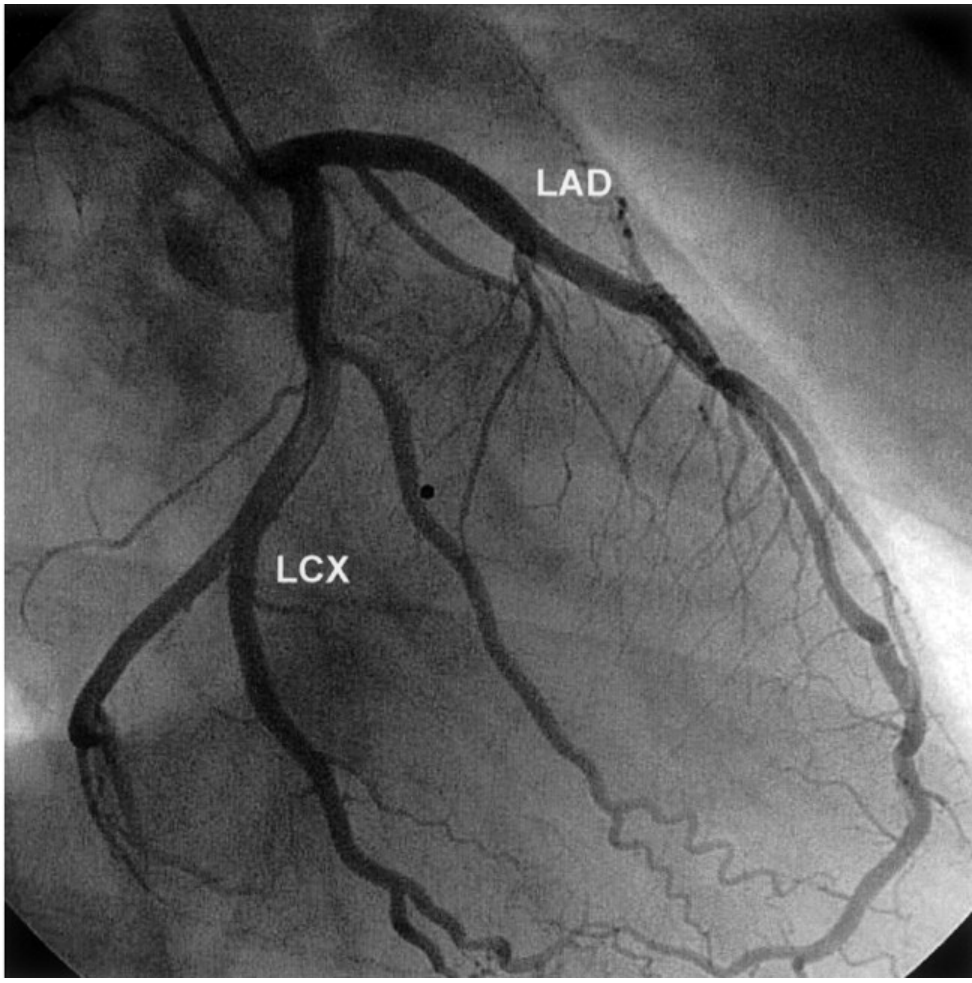
Coronary Angiography

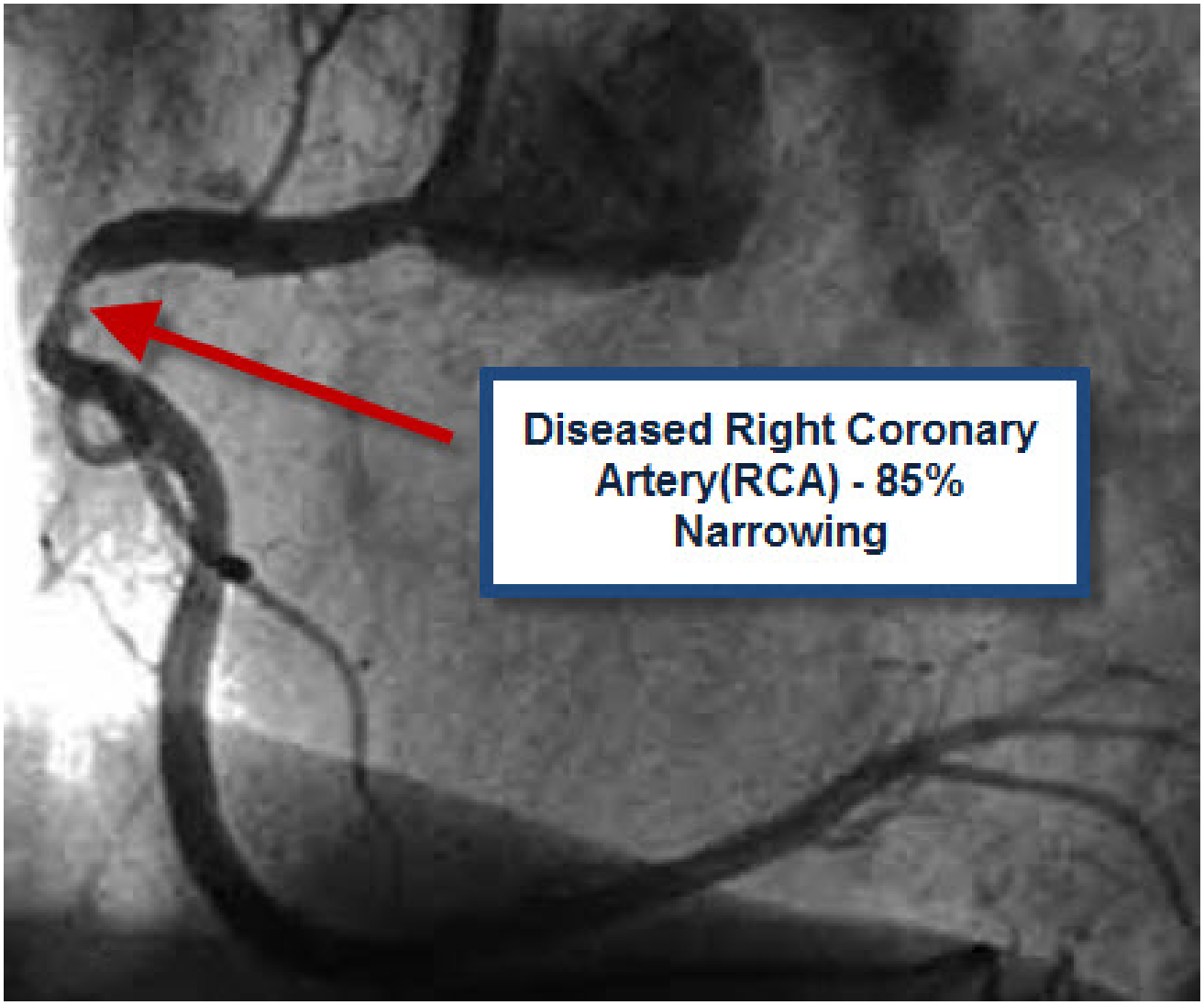


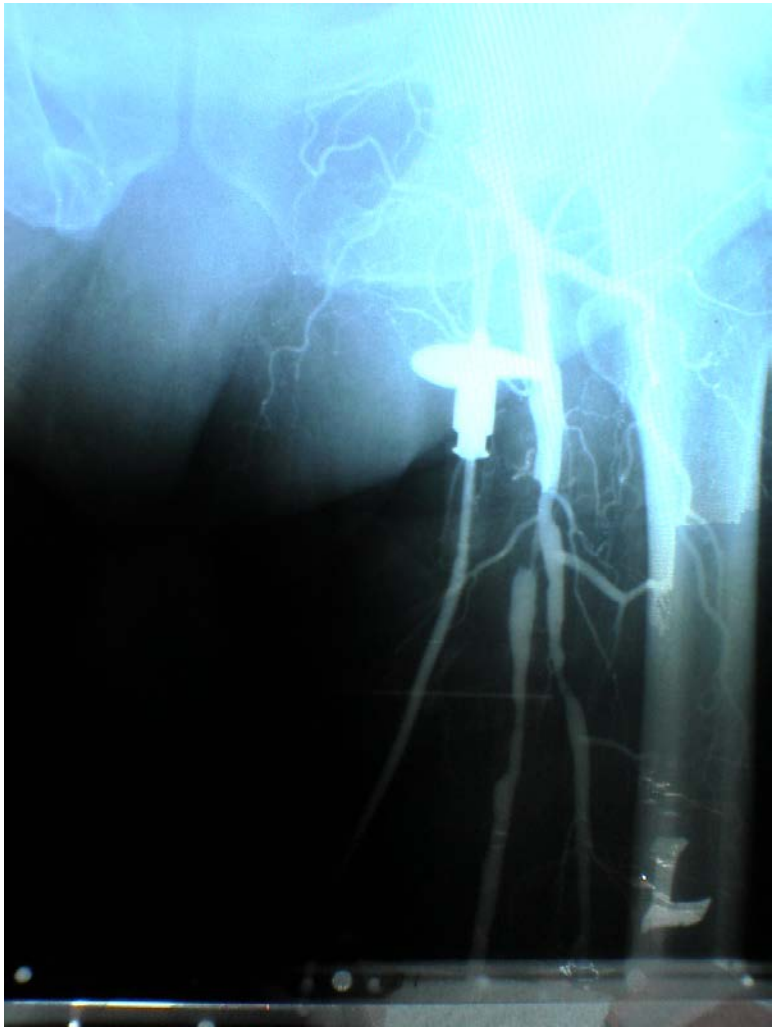
Normal LT coronary Artery

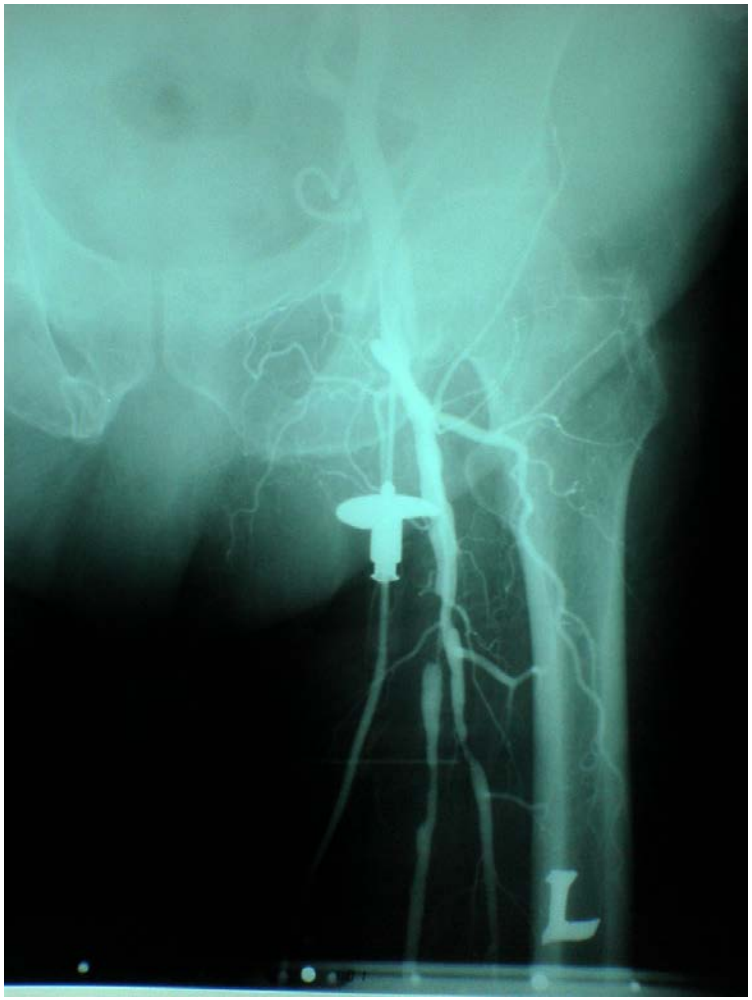


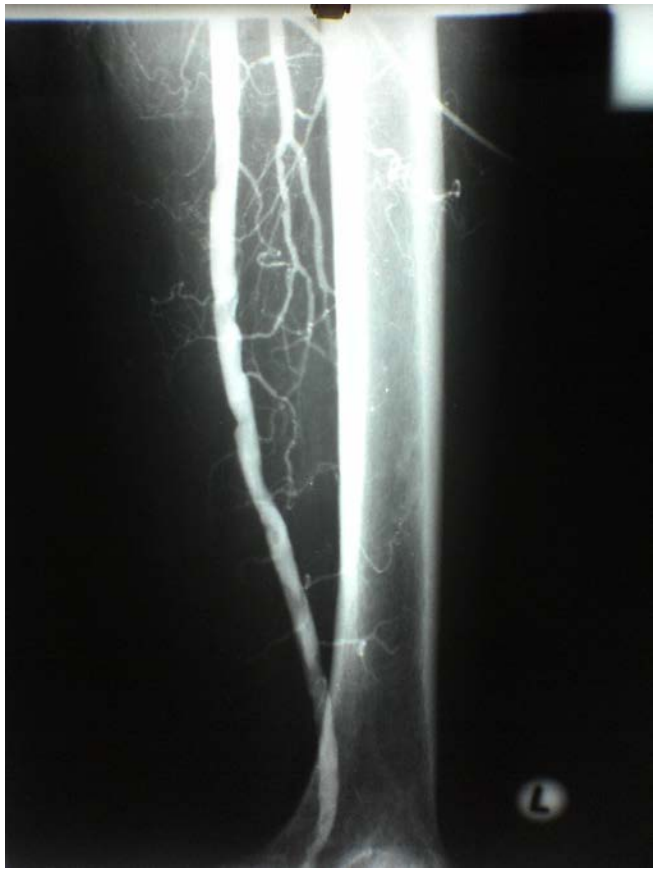

RCA
LCX


LAD
LCX


Diseased Right Coronary Artery(RCA) - 85% Narrowing



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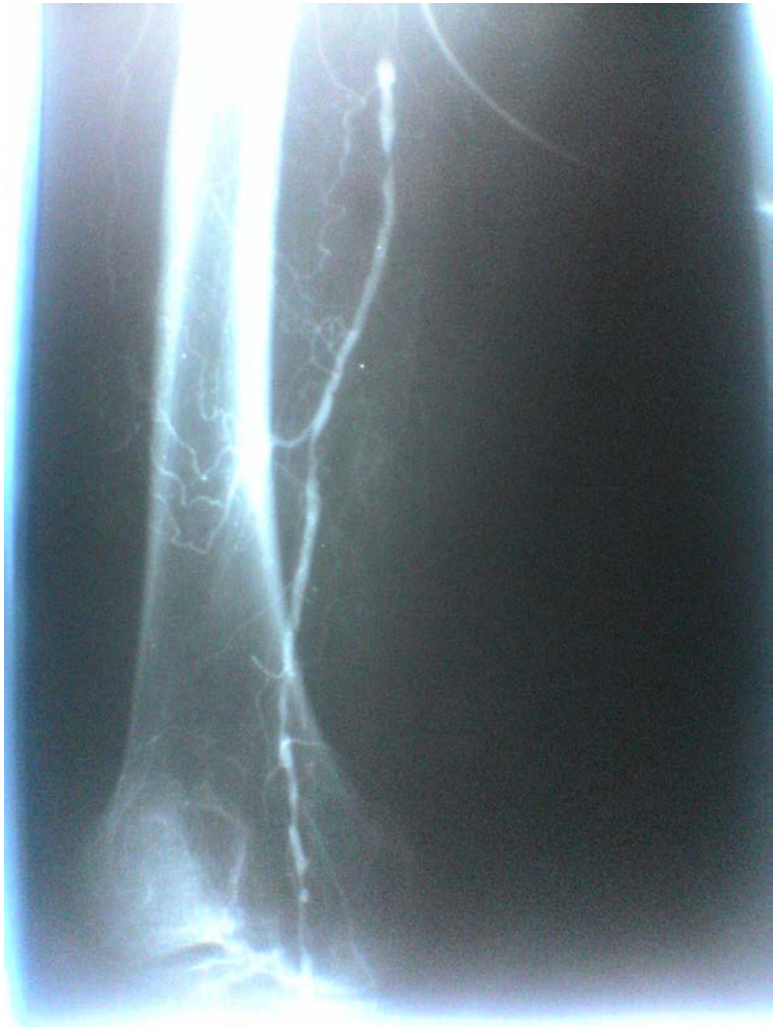


IRAN : CORONARY HEART DISEASE

Deaths	%	Rate	World Rank
89,116	27.47	170.87	35

According to the latest WHO data published in 2017 Coronary Heart Disease Deaths in Iran reached 89,116 or 27.47% of total deaths. The age adjusted Death Rate is 170.87 per 100,000 of population ranks Iran #35 in the world. Review other causes of death by clicking the links below or choose the full health profile.

IRAN : STROKE

Deaths	%	Rate	World Rank
42,356	13.06	83.32	91

According to the latest WHO data published in 2017 Stroke Deaths in Iran reached 42,356 or 13.06% of total deaths. The age adjusted Death Rate is 83.32 per 100,000 of population ranks Iran #91 in the world.

IRAN : HYPERTENSION

Deaths	%	Rate	World Rank
16,415	5.06	32.25	17

According to the latest WHO data published in 2017 Hypertension Deaths in Iran reached 16,415 or 5.06% of total deaths. The age adjusted Death Rate is 32.25 per 100,000 of population ranks Iran #17 in the world. Review other causes of death by clicking the links below or choose the full health profile.

TURKEY : CORONARY HEART DISEASE

Deaths	%	Rate	World Rank
81,029	20.34	108.59	105

According to the latest WHO data published in 2017 Coronary Heart Disease Deaths in Turkey reached 81,029 or 20.34% of total deaths. The age adjusted Death Rate is 108.59 per 100,000 of population ranks Turkey #105 in the world. Review other causes of death by clicking the links below or choose the full health profile.

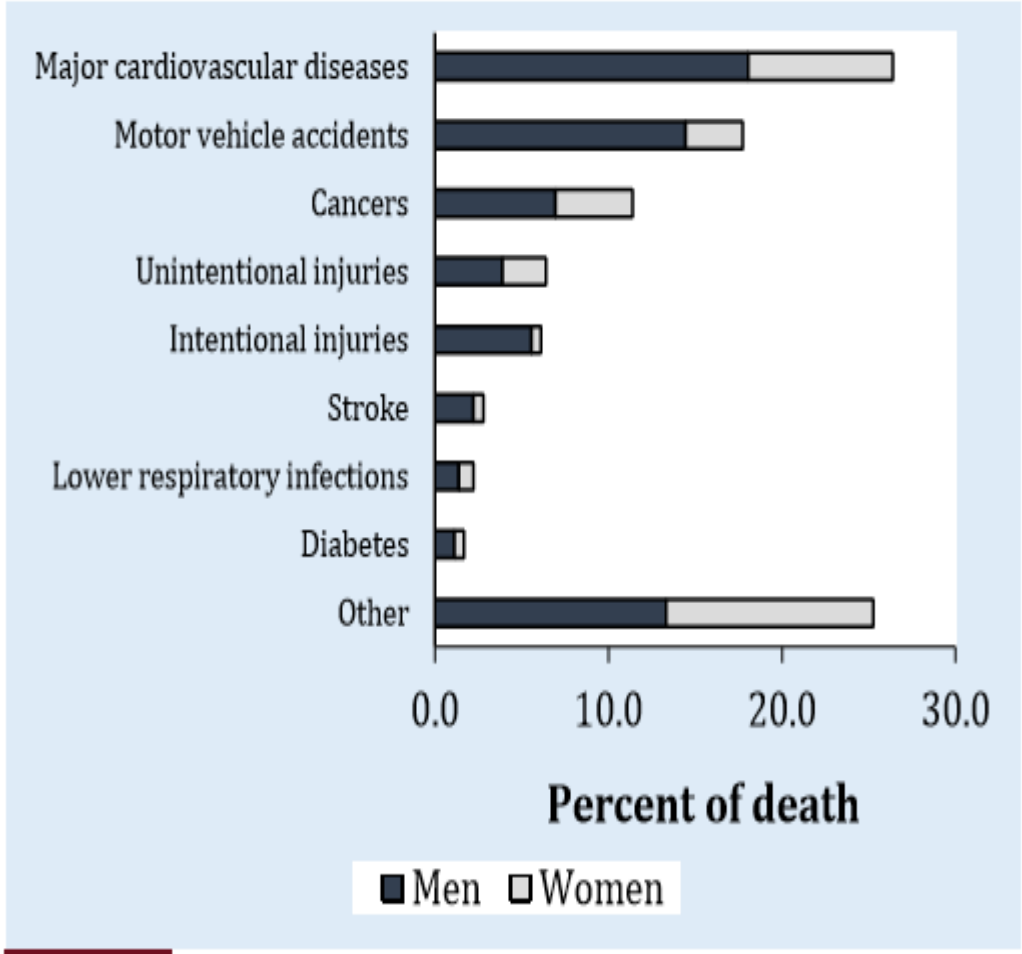


Figure 1: The most common causes of death in the studied population

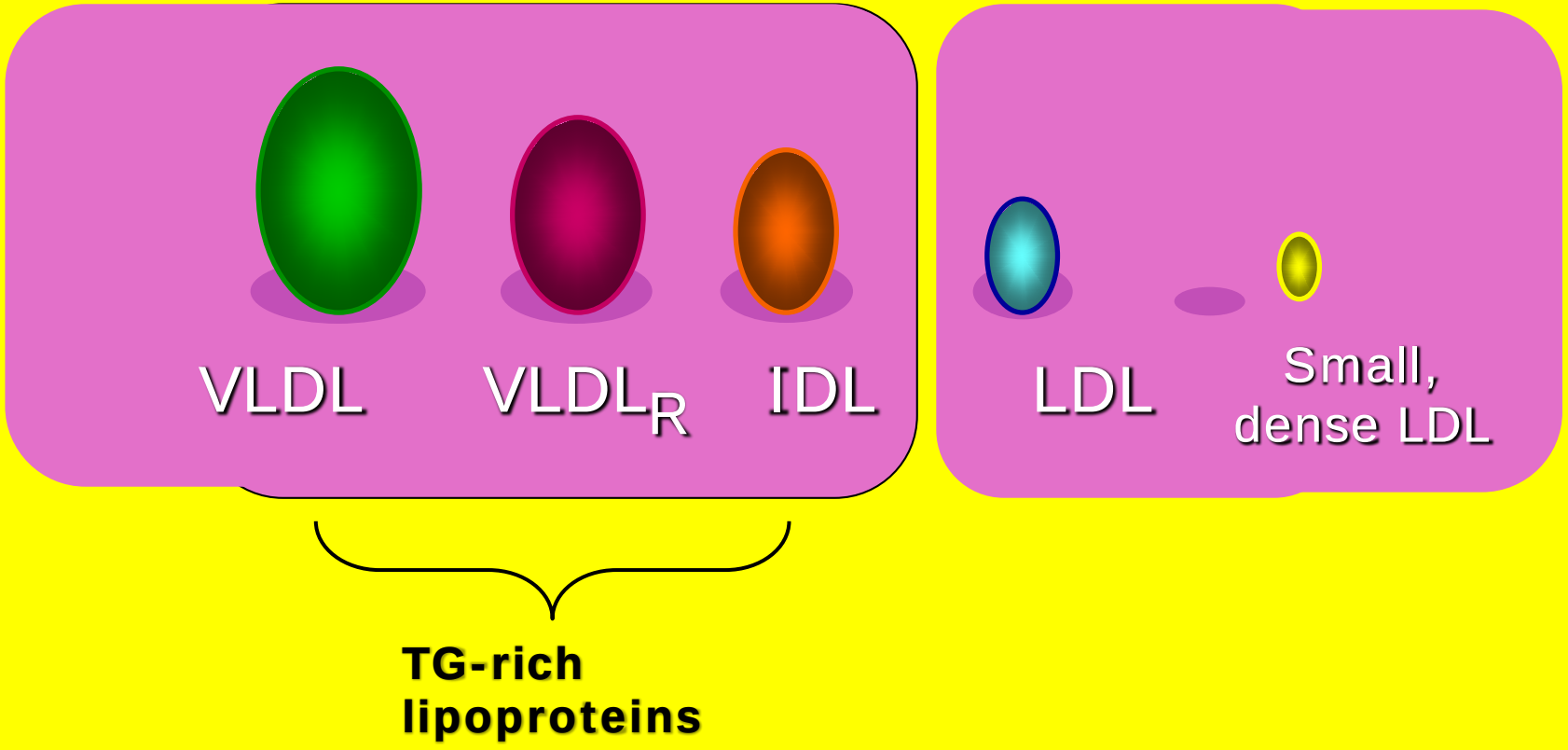
Atherosclerotic cardiovascular disease [ASCVD]

In 2016, approximately 660,000 U.S. residents will have a new coronary event

The estimated annual incidence of MI is 550,000 new and 200,000 recurrent attacks

Approximately 305,000 will have a recurrent event

Atherogenic Particles



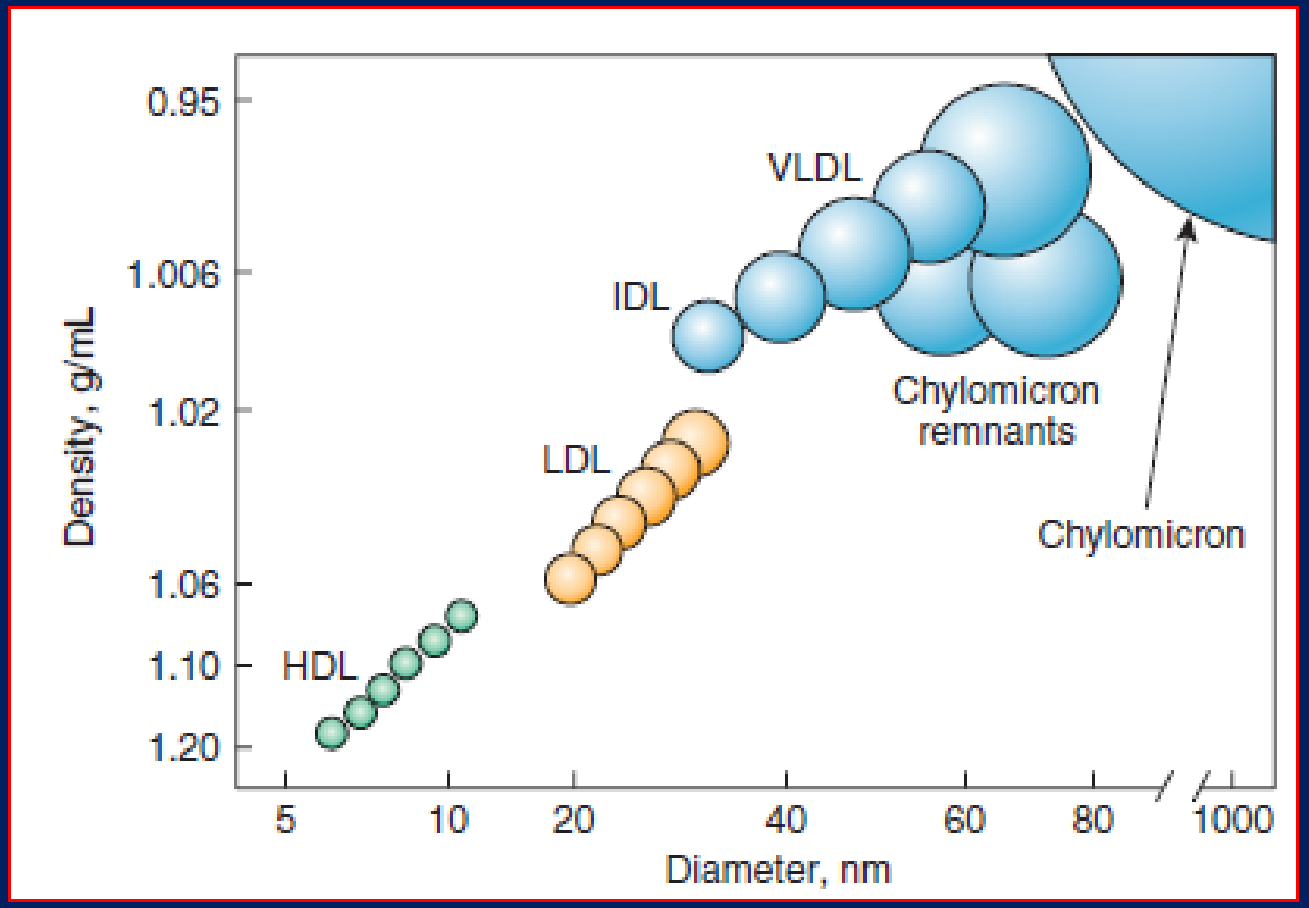

0.95
1.006
1.02
1.06
1.10
1.20
Density, g/mL
VLDL
IDL
LDL
HDL
Chylomicron remnants
Chylomicron
5
10
20
40
60
80
1000
Diameter, nm

TABLE 400-1 Major Lipoprotein Classes

LIPOPROTEIN	DENSITY, g/mL[a]	SIZE, nm[b]	ELECTROPHORETIC MOBILITY[c]	APOLIPOPROTEINS	
				MAJOR	OTHER
Chylomicrons	0.930	75–1200	Origin	ApoB-48	A-I, A-V, C-I, C-II, C-III, E
Chylomicron remnants	0.930–1.006	30–80	Slow pre-β →	ApoB-48	A-I, A-V, C-I, C-II, C-III, E
VLDL	0.930–1.006	30–80	Pre-β →	ApoB-100	A-I, A-II, A-V, C-I, C-II, C-III, E
IDL	1.006–1.019	25–35	Slow pre-β →	ApoB-100	C-I, C-II, C-III, E
LDL	1.019–1.063	18–25	β	ApoB-100	
HDL	1.063–1.210	5–12	α →	ApoA-I	A-II, A-IV, A-V, C-III, E
Lp(a)	1.050–1.120	25	Pre-β	ApoB-100	Apo(a)

NON-HDL-CHOLESTEROL

Non-HDL cholesterol level goal should be 30 mg/dL higher than your LDL **cholesterol** level goal.

For example, if you are aiming for an LDL **cholesterol** of 100 mg/dL, then your goal for **non-HDL** should be 130 mg/dL.

Non-HDL-C =Total cholesterol – HDL-C

LDL-C = Total cholesterol – HDL-C – (TG/5)

Awareness of the potential benefits of non-HDL-C screening

Evidence indicates that compared with LDL-C, non-HDL-C is an equally strong or superior predictor of risk in groups of individuals with :

Diabetes, Insulin Resistance Syndrome

Moderately elevated TG (200 to 500 mg/dL)

Established ASCVD

Awareness of the potential benefits of non-HDL-C screening

- Non-HDL-C is highly correlated but not concordant with total apo B
- Provides a simple way to estimate risk from VLDL-C, LDL-C, intermediate-density lipoprotein cholesterol, and lipoprotein (a)

Screening

The guidelines discuss the use of four tools to assess the 10-year risk of a coronary event:

1-Framingham Risk Assessment Tool

2-Multi-Ethnic Study of Atherosclerosis 10-year Atherosclerotic Cardiovascular Disease (ASCVD) Risk with Coronary Artery Calcification Calculator

3-Reynolds Risk Score,

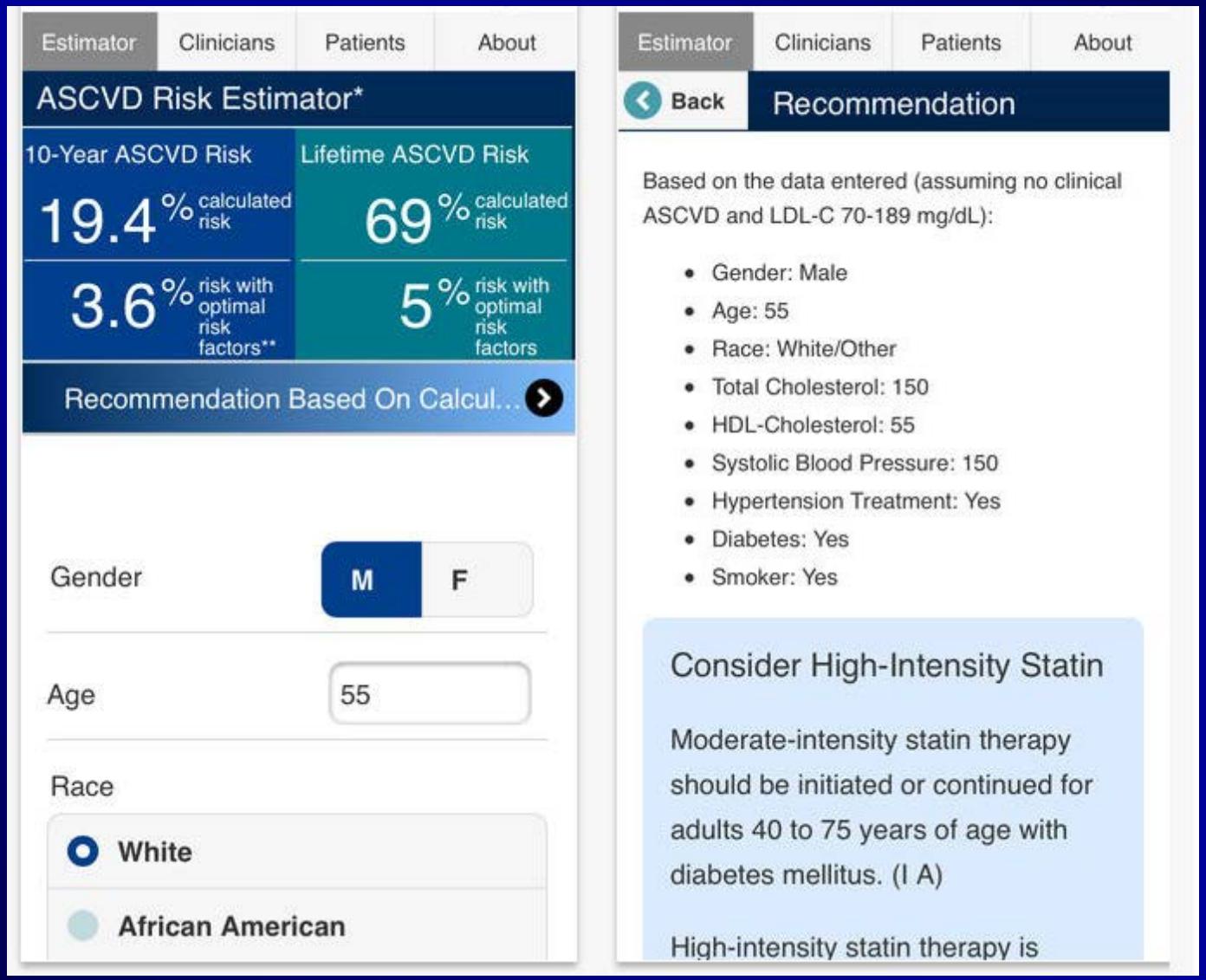
4-United Kingdom Prospective Diabetes Study risk engine to calculate ASCVD risk in those with type 2 diabetes.

AMERICAN
COLLEGE of
CARDIOLOGY

2013 Prevention Guidelines Tools

CV RISK CALCULATOR

ASCVD Risk Estimator



Atherosclerotic Cardiovascular Disease Risk Factors

Major risk factors	Additional risk factors	Nontraditional risk factors
Advancing age	Obesity, abdominal obesity	⇧ Lipoprotein (a)
⇧ Total serum cholesterol level	Family history of hyperlipidemia	⇧ Clotting factors
⇧ Non-HDL-C	⇧ Apo B	⇧ Inflammation markers
⇧ LDL-C	Fasting/postprandial	(hsCRP; Lp-PLA_2)
Low HDL-C	hypertriglyceridemia	⇧ Homocysteine levels
Diabetes mellitus	PCOS	⇧ Uric acid
Hypertension	Dyslipidemic triad	
Stage 3 or 4 chronic kidney disease		
Cigarette smoking		
Family history of ASCVD		

Abbreviations: apo, apolipoprotein; ASCVD, atherosclerotic cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; hsCRP, highly sensitive C-reactive protein; LDL-C, low-density lipoprotein cholesterol; Lp-PLA2, lipoprotein-associated phospholipase; PCOS, polycystic ovary syndrome.

Additional Screening Tests

Recommendations associated with this question:

Coronary artery calcification

- **R33.** Coronary artery calcification measurement has been shown to be of high predictive value and is useful in refining risk stratification to determine the need for more aggressive treatment strategies **(Grade B; BEL 2)**.

hsCRP

- **R30.** Use hsCRP to stratify ASCVD risk in individuals with a standard risk assessment that is borderline, or in those with an intermediate or higher risk with an LDL-C concentration less than 130 mg/dL **(Grade B; BEL 2)**.

Lp-PLA_2

- **R31.** Measure lipoprotein-associated phospholipase A_2 (Lp-PLA_2), which in some studies has demonstrated more specificity than hsCRP, when it is necessary to further stratify an individual's ASCVD risk, especially in the presence of hsCRP elevations **(Grade A; BEL 1)**.

Homocysteine

- **R32.** The routine measurement of homocysteine, uric acid, plasminogen activator inhibitor-1, or other inflammatory markers is not recommended because the benefit of doing so is not sufficiently proven **(Grade D)**.

Carotid intima media thickness

- **R34.** Carotid intima media thickness may be considered to refine risk stratification to determine the need for more aggressive ASCVD preventive strategies **(Grade B; BEL 2)**.

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; hsCRP, highly sensitive C-reactive protein; LDL-C, low-density lipoprotein cholesterol.

Jellinger P, Handelsman Y, Rosenblit P, et al. *Endocr Practice*. 2017;23(4):479-497.

Which screening tests should be used

Screening

- The majority of screening guidelines recommend a full fasting lipid profile including
  - total cholesterol,
  - high-density lipoprotein (HDL) cholesterol,
  - triglycerides,
  - although some guidelines allow for a non-fasting lipid panel.

- The age at which to begin screening varies among the guidelines and may differ for men and women.

Measurement of triglyceride levels

- A 2016 consensus statement from the European Atherosclerosis Society (EAS) and the European Federation of Clinical Chemistry and Laboratory Medicine also suggests that ***non-fasting blood*** samples can be routinely used for the assessment of plasma lipid profiles to improve patient compliance with lipid testing.

Random measurement of non-fasting triglyceride levels at 1–6 h after habitual meals compared with fasting triglyceride levels shows maximal mean changes of only −0.2 mmol/l (−8 mg/dl)

NATURE REVIEWS | CARDIOLOGY -2017

High, Moderate, Low Intensity Statin Therapy

High-Intensity	Moderate -Intensity	Low-Intensity
Daily dose lowers LDL-C on average by approximately 50%	Daily dose lowers LDL-C on average by approximately 30 to <50%	Daily dose lowers LDL-C on average by approximately by <30%
Atorvastatin 40-80 mg	Atorvastatin 10-20 mg	Simvastatin 10 mg
Rosuvastatin 20-40 mg	Rosuvastatin 5-10 mg	Lovastatin 20 mg
	Simvastatin 20-40 mg	Fluvastatin 20-40 mg
	Lovastatin 40 mg	Pitavastatin 1mg
	Pitavastatin 2-4 mg	Pravastatin 10-20 mg

ACC/ACC/AHA Statin Benefit Groups

Benefit Group	Management
Clinical atherosclerotic cardiovascular disease (ASCVD)	Age <75 without contraindications: high-intensity statin Age > 75 or with contraindications moderate-intensity statin
LDL-C > 190 mg/dl, age> 21 years	high-intensity statin Consider nonstatin drug if further LDL-C reduction is desirable

ACC/ACC/AHA Statin Benefit Groups

Benefit Group	Management
Primary prevention: diabetes : age 40-75 years, LDL-C 70-189 mg/dl	Moderate-intensity statin If 10-year ASCVD risk is >= 7.5% consider high-intensity statin
Primary prevention: no diabetes : 10-year ASCVD risk is >= 7.5% age 45-75 years, LDL-C 70-189 mg/dl	Moderate to high-intensity statin

New lipid guidelines shift focus back to LDL goals

The AACE/ACE guidelines discuss specific LDL targets.

Of the 87 recommendations included, 45 are Grade A.

New AACE Lipid Guidelines Establish 'Extreme' CVD Risk Category

Targets are very, very useful.

They're strong incentives for both patients and physicians. We have HbA_{1c} goals, we have blood-pressure goals.

Why shouldn't we have LDL goals?

There is strong evidence that the lower, the better

New AACE Lipid Guidelines Establish 'Extreme' CVD Risk Category

In a departure from recommendations by cardiology societies, two endocrine groups have issued new lipid-management guidelines that *bring back LDL-cholesterol "targets"* and are the first ever to *include a new "extreme-risk" category of patient*s, for whom an LDL-cholesterol level of less than 55 mg/dL is now advised

New lipid guidelines shift focus back to LDL goals

Risk categories and treatment goals

Risk category	Risk factors/10-year risk	LDL mg/dL	Non-HDL mg/dL	Apo B mg/dL
Extreme risk	Progressive ASCVD, including unstable angina in patients who already achieved an LDL of <70 mg/dL Established clinical CVD in patients with diabetes, stage 3 or 4 chronic kidney disease, or heterozygous familial hypercholesterolemia History of premature ASCVD (men, <55 y; women, <65 y)	<55	<80	<70
Very high risk	Established or recent hospitalization for an acute coronary syndrome; coronary, carotid, or peripheral vascular disease, 10-year risk >20% Diabetes or stage 3 or 4 chronic kidney disease with one or more risk factor(s) Heterozygous familial hypercholesterolemia	<70	<100	<80
High risk	Two or more risk factors and 10-year risk 10%–20% Diabetes or stage 3 or 4 chronic kidney disease with no other risk factors	<100	<130	<90
Moderate risk	Two or fewer risk factors and 10-year risk <10%	<100	<130	<90
Low risk	No risk factors	<130	<160	Not recommended

Abbreviations used: Apo B, apoprotein B; ASCVD, atherosclerotic cardiovascular disease; CVD, cardiovascular disease.

Case 2

- A 68-year-old female with a history of a MI two years ago is referred for treatment of dyslipidemia.
- The patient eats a healthy diet and follows a daily exercise program.
- She is taking atorvastatin 80 mg daily.

Case 2: Recent lipid panel

- Total cholesterol = 180 mg/dl
- LDL =110 mg/dl;
- HDL= 50 mg/dl
- Non-HDL cholesterol= 130 mg/dl;

And triglyceride (TG) = 100 mg/dl.

New AACE Lipid Guidelines Establish 'Extreme' CVD Risk Category

That evidence, led the AACE and ACE to differ from the controversial American Heart Association /American College of Cardiology guidelines of 2013 that removed LDL targets and instead recommended varying intensities of statin therapy to four groups of primary- and secondary-prevention patients.

New AACE Lipid Guidelines Establish 'Extreme' CVD Risk Category

In contrast, AACE/ACE now recommend LDL goals of

< 55 mg/dL, < 70 mg/dL, < 100 mg/dL, and < 130 mg/dL

for individuals at:

extreme, very high, high/moderate, and low risk

for cardiovascular events, respectively.

2013 ACC/AHA Guidelines

- Emphasis on statins as first-line therapy due to strong body of supporting evidence

- Focus on 'appropriate intensity' statin therapy in 3 groups 'most likely to benefit'

2013 ACC/AHA Guidelines on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults. Stone NJ, et al. Circulation 2013; JACC 2013

2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA

Guideline on the Management of Blood Cholesterol: Executive Summary

AMERICAN COLLEGE of CARDIOLOGY

American Heart Association.

1. In all individuals, emphasize a heart-healthy lifestyle across the life course.

A healthy lifestyle reduces atherosclerotic cardiovascular disease (ASCVD) risk at all ages. In younger individuals, healthy lifestyle can reduce development of risk factors and is the foundation of ASCVD risk reduction.

In young adults 20 to 39 years of age, an assessment of lifetime risk facilitates the clinician–patient risk discussion (see No. 6) and emphasizes intensive lifestyle efforts. In all age groups, lifestyle therapy is the primary intervention for metabolic syndrome.

Top 10 Take Home Messages

2. In patients with clinical ASCVD, reduce low-density lipoprotein cholesterol (LDL-C) with high-intensity statin therapy or maximally tolerated statin therapy.

The more LDL-C is reduced on statin therapy, the greater will be subsequent risk reduction.

Use a maximally tolerated statin to lower LDL-C levels by ≥50%.

3. In very high-risk ASCVD, use a LDL-C threshold of 70 mg/dL (1.8 mmol/L) to consider addition of nonstatins to statin therapy.

- Very high-risk includes a history of multiple major ASCVD events or 1 major ASCVD event and multiple high-risk conditions.
- In very high-risk ASCVD patients, it is reasonable to add ezetimibe to maximally tolerated statin therapy when the LDL-C level remains ≥70 mg/dL (≥1.8 mmol/L).
- In patients at very high risk whose LDL-C level remains ≥70 mg/dL (≥1.8 mmol/L) on maximally tolerated statin and ezetimibe therapy, adding a PCSK9 inhibitor is reasonable,
  although the long-term safety (>3 years) is uncertain and cost-effectiveness is low at mid-2018 list prices.

4. **In patients with severe primary hypercholesterolemia (LDL-C level ≥ 190 mg/dL[≥4.9 mmol/L]) without calculating 10-year ASCVD risk, begin high-intensity statin therapy without calculating 10-year ASCVD risk.**

- If the LDL-C level remains ≥100 mg/dL (≥2.6 mmol/L), adding ezetimibe is reasonable

- If the LDL-C level on statin plus ezetimibe remains ≥100 mg/dL (≥2.6 mmol/L) & the patient has multiple factors that increase subsequent risk of ASCVD events, a PCSK9 inhibitor may be considered,
  although the long-term safety (>3 years) is uncertain and economic value is low at mid-2018 list prices.

5. **In patients 40 to 75 years of age with diabetes mellitus and LDL-C ≥70 mg/dL (≥1.8 mmol/L), start moderate-intensity statin therapy without calculating 10-year ASCVD risk.**

   In patients with diabetes mellitus at higher risk, especially those with multiple risk factors or those 50 to 75 years of age, it is reasonable to use a high-intensity statin to reduce the LDL-C level by ≥50%.

6. In adults 40 to 75 years of age evaluated for primary ASCVD prevention, have a clinician–patient risk discussion before starting statin therapy.

Risk discussion should include a review of major risk factors (e.g., cigarette smoking, elevated blood pressure, (LDL-C), hemoglobin A1C [if indicated], and calculated 10-year risk of ASCVD);

- the presence of risk-enhancing factors (see No. 8);
- the potential benefits of lifestyle and statin therapies;
- the potential for adverse effects and drug–drug interactions;
- the consideration of costs of statin therapy; and
- the patient preferences & values in shared decision-making.

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American Heart Association.

7. **In adults 40 to 75 years of age without diabetes mellitus and with LDL-C levels ≥70 mg/dL (≥1.8 mmol/L), at a 10-year ASCVD risk of ≥7.5%, start a moderate-intensity statin if a discussion of treatment options favors statin therapy.**

   Risk-enhancing factors favor statin therapy (see No. 8).

   If risk status is uncertain, consider using coronary artery calcium (CAC) to improve specificity (see No. 9). If statins are indicated, reduce LDL-C levels by ≥30%, and if 10-year risk is ≥20%, reduce LDL-C levels by ≥50%.

8. In adults 40 to 75 years of age without diabetes mellitus and 10-year risk of 7.5% to 19.9% (intermediate risk), risk-enhancing factors favor initiation of statin therapy (see No. 7).

Risk-enhancing factors include

- family history of premature ASCVD;
- persistently elevated LDL-C levels ≥160 mg/dL (≥4.1 mmol/L);
- metabolic syndrome;
- chronic kidney disease;

- history of preeclampsia or premature menopause (age <40 yrs)
- chronic inflammatory disorders (e.g., rheumatoid arthritis, psoriasis, or chronic HIV);
- high-risk ethnic groups (e.g., South Asian);
- persistent elevations of triglycerides ≥ 175 mg/dL (≥1.97 mmol/L);

9. In adults 40 to 75 years of age without diabetes mellitus and with LDL-C levels ≥70 mg/dL- 189 mg/dL (≥1.8-4.9 mmol/L), at a 10-year ASCVD risk of ≥7.5% to 19.9%, if a decision about statin therapy is uncertain, consider measuring CAC.

- If CAC is zero, treatment with statin therapy may be withheld or delayed, except in cigarette smokers, those with diabetes mellitus, and those with a strong family history of premature ASCVD.
- A CAC score of 1 to 99 favors statin therapy, especially in those ≥55 years of age.
- For any patient, if the CAC score is ≥100 Agatston units or ≥75th percentile, statin therapy is indicated unless otherwise deferred by the outcome of clinician–patient risk discussion.

10. Assess adherence and percentage response to LDL-C–lowering medications and lifestyle changes with repeat lipid measurement 4 to 12 weeks after statin initiation or dose adjustment, repeated every 3 to 12 months as needed.

- Define responses to lifestyle and statin therapy by percentage reductions in LDL-C levels compared with baseline.
- In ASCVD patients at very high-risk, triggers for adding nonstatin drug therapy are defined by threshold LDL-C levels ≥70 mg/dL (≥1.8 mmol/L) on maximal statin therapy (see No. 3).

Case 2

- A 68-year-old female with a history of a MI two years ago is referred for treatment of dyslipidemia.
- The patient eats a healthy diet and follows a daily exercise program.
- She is taking atorvastatin 80 mg daily.

Case 2: Recent lipid panel

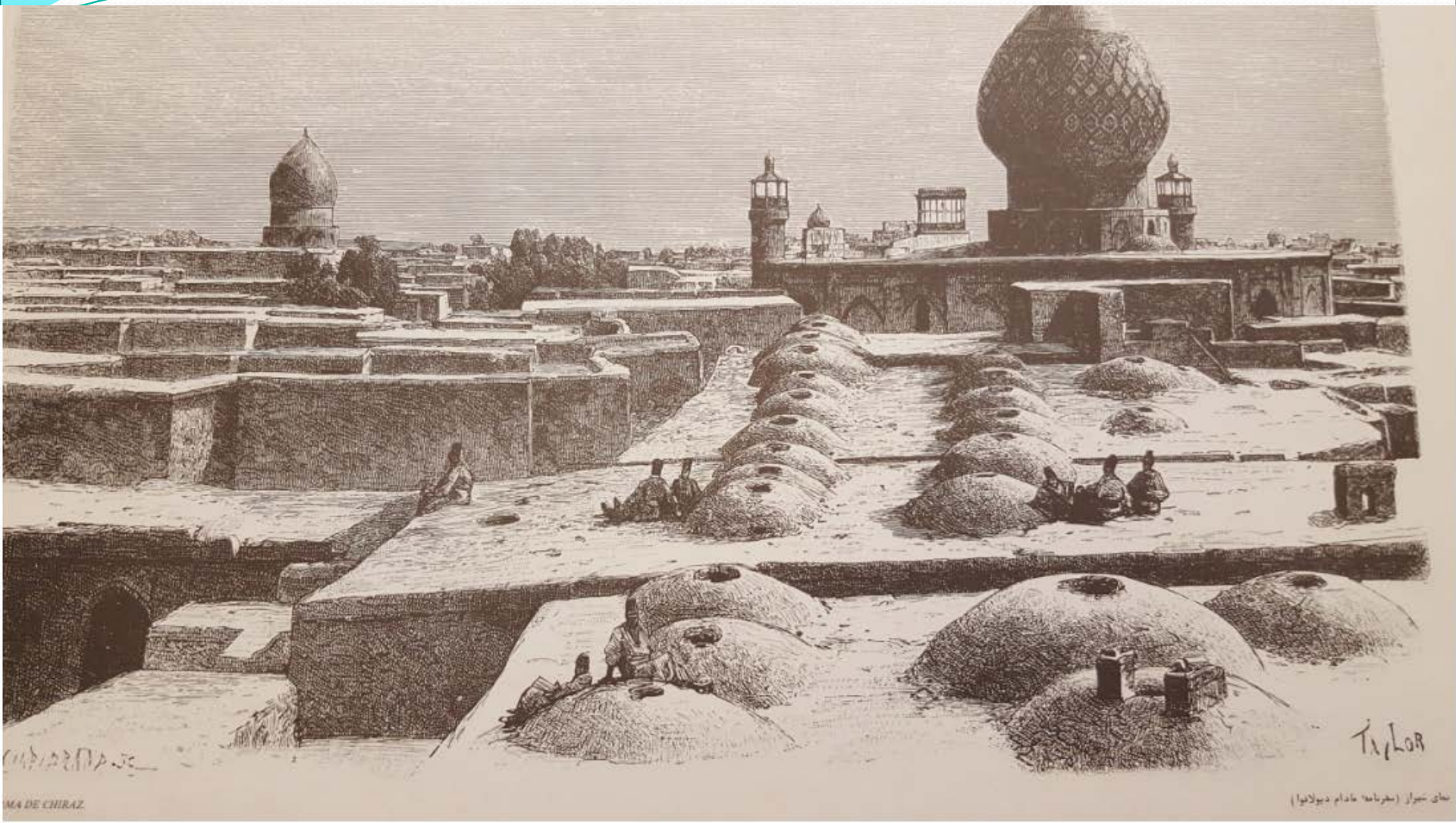
- Total cholesterol = 180 mg/dl
- LDL =110 mg/dl;
- HDL= 50 mg/dl
- Non-HDL cholesterol= 130 mg/dl;

And triglyceride (TG) = 100 mg/dl.

Case 2

What would you do for case 2?

- A. Continue current therapy with no changes
- B. Add fish oil, 1 g three times a day with meals.
- C. Add ezetimibe 10 mg daily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SCREENING

Who should be screened for ASCVD risk and when?

Familial Hypercholesterolemia

- **R9.** Individuals should be screened for FH when there is a family history of:
  - Premature ASCVD (definite MI or sudden death before age 55 years in father or other male first-degree relative or before age 65 years in mother or other female first-degree relative) or
  - Elevated cholesterol levels (total, and/or LDL) consistent with FH **(Grade C;BEL4)**

Adults With Diabetes

- **R10.** Annually screen all adult individuals with T1DM or T2DM for dyslipidemia **(Grade B; BEL 2)**.

Young adults(Men aged 20-45 years ,Women aged 20-55 years)

- **R11.** Evaluate all adults 20 years of age or older for dyslipidemia every 5 years as part of a global risk assessment **(Grade C; BEL 4)**

Young adults(Men aged45-65years,Women aged 55-65 years)

- **R12.** In the absence of ASCVD risk factors, screen middle-aged individuals for dyslipidemia at least once every 1 to 2 years. More frequent lipid testing is recommended when multiple global ASCVD risk factors are present **(Grade A; BEL 1)**

Older Adults (Older Than 65 Years)

- R14. **Annually screen older adults with 0 to 1 ASCVD risk factor for dyslipidemia** (Grade A; BEL 1).
- R15. **Older adults should undergo lipid assessment if they have multiple ASCVD global risk factors (i.e., other than age)** (Grade C; BEL 4)

Screening

Screening in young adults (men 20–45 y; women 20–55 y) should occur every 5 years

Screening in middle-aged adults (men 45–65 y; women 55–65 y) should occur every 1 to 2 years if no CVD risk factors are present.

For patients who are older than 65 years, annual screening is recommended

Children and Adolescents

- R17. **In children at risk for FH (e.g., family history of premature cardiovascular disease or elevated cholesterol), screening should be at 3 years of age, again between ages 9 and 11, and again at age 18** (Grade B; BEL 3)

Children and Adolescents

- R18. **Screen adolescents older than 16 years every 5 years or more frequently if they have ASCVD risk factors, have overweight or obesity, have other elements of insulin resistance syndrome, or have a family history of premature ASCVD** (Grade B; BEL 3)

Screening in Women

- A low HDL cholesterol is a more important risk factor for CHD in women than a high LDL cholesterol.
- Although most experts recommend application of the same primary prevention guidelines for women as for men, clinicians should be aware of the uncertainty in this area.
- Estimating the 10-year cardiovascular risk is particularly important in women
  - a larger percentage of women than men will have estimated 10-year cardiovascular risks below 7.5% per year
  - be advised not to take statins unless their LDL is very high (greater than 190 mg/dL).