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WE GUARD

Web-based Education | Guidelines Updates, Advances & Researches in Dyslipidemia

Module 1 Part 1:

Guidelines-Based Dyslipidemia Management

SA-6751 Expiration Date: 16/08/2025

AGENDA

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- Pathophysiology
- Clinical presentation

02 **Triglycerides (TG)**

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- Hypertriglyceridemia

03 **Lipoproteins types and role**

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- Lipoprotein interpretation

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- Pathophysiology

05 **Atherosclerosis**

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- Pathophysiology
- Risk factors and their modification

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- Lipid abnormalities with diabetes
- Pathophysiology

07 **Local epidemiological data**

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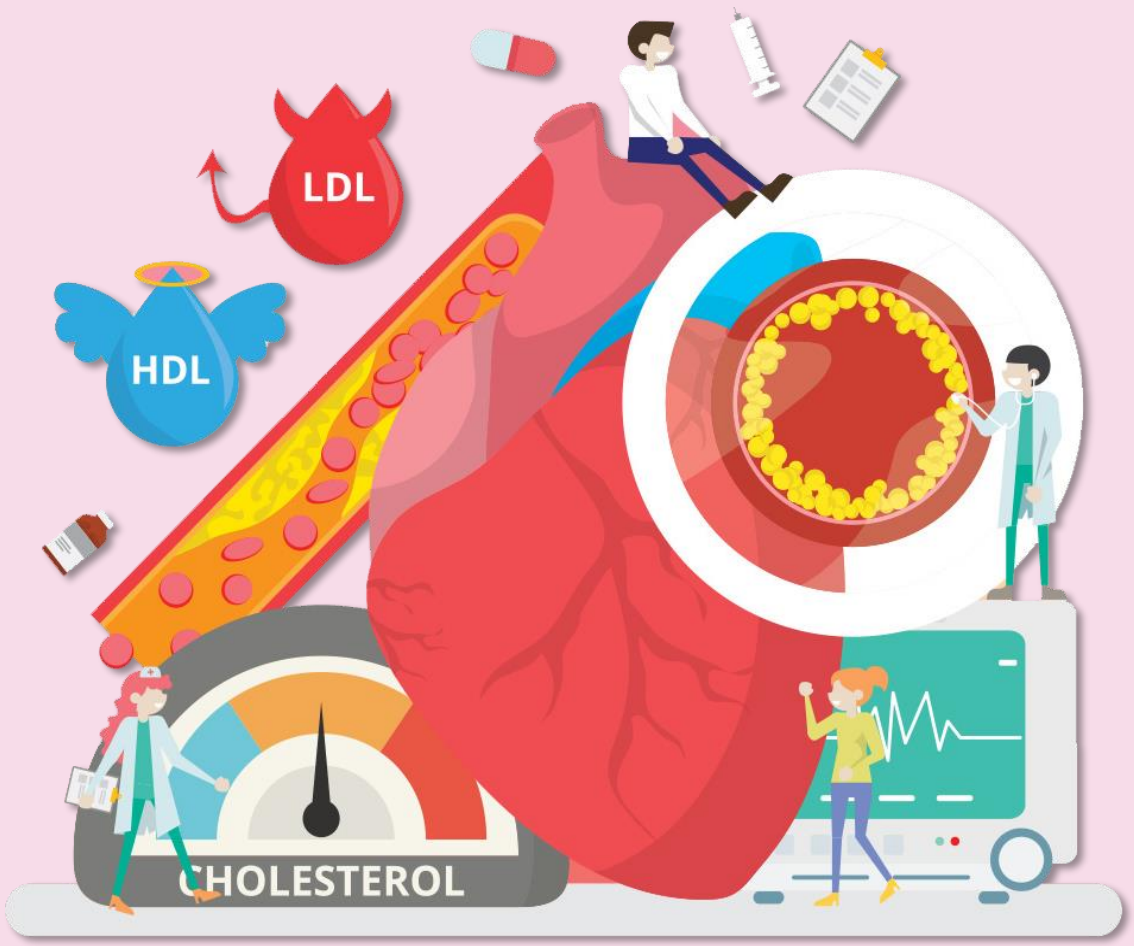

1. Introduction to Dyslipidemia

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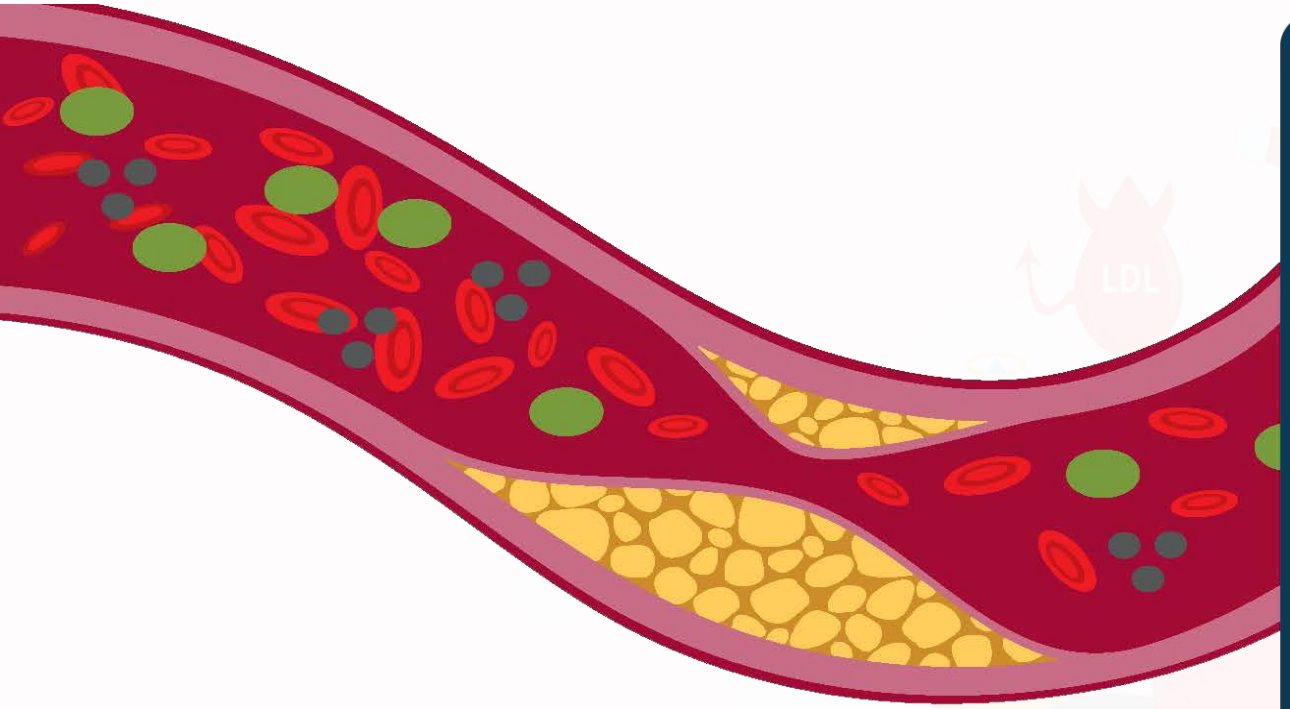
Dyslipidemia Definition[1]



↑Elevated ↑

- Total Cholesterol
- **L**ow-**D**ensity **L**ipoprotein (**LDL**)
- Triglycerides

↓Reduced ↓

- **H**igh-**D**ensity **L**ipoprotein (**HDL**)

Or a combination of these abnormalities.

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1. Di Ciaula A, Garruti G, Lunardi Baccetto R, Molina-Molina E, Bonfrate L, Wang DQ, Portincasa P. Bile Acid Physiology. Ann Hepatol. 2017 Nov;16(Suppl. 1: s3-105.):s4-s14.

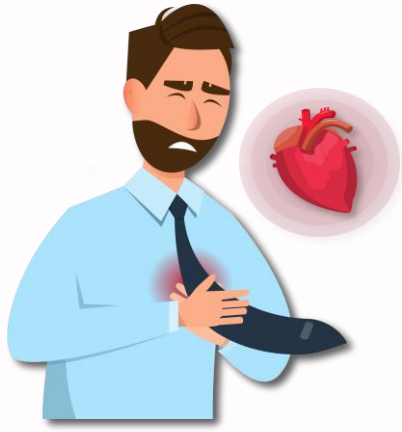
Pathophysiology(1)

Triglycerides

Cholesterol

Phospholipids

Are transported in blood as complexes of lipids and proteins (lipoproteins).



↑ Total & LDL cholesterol

↓ HDL cholesterol

Development of Coronary Heart Disease (CHD).

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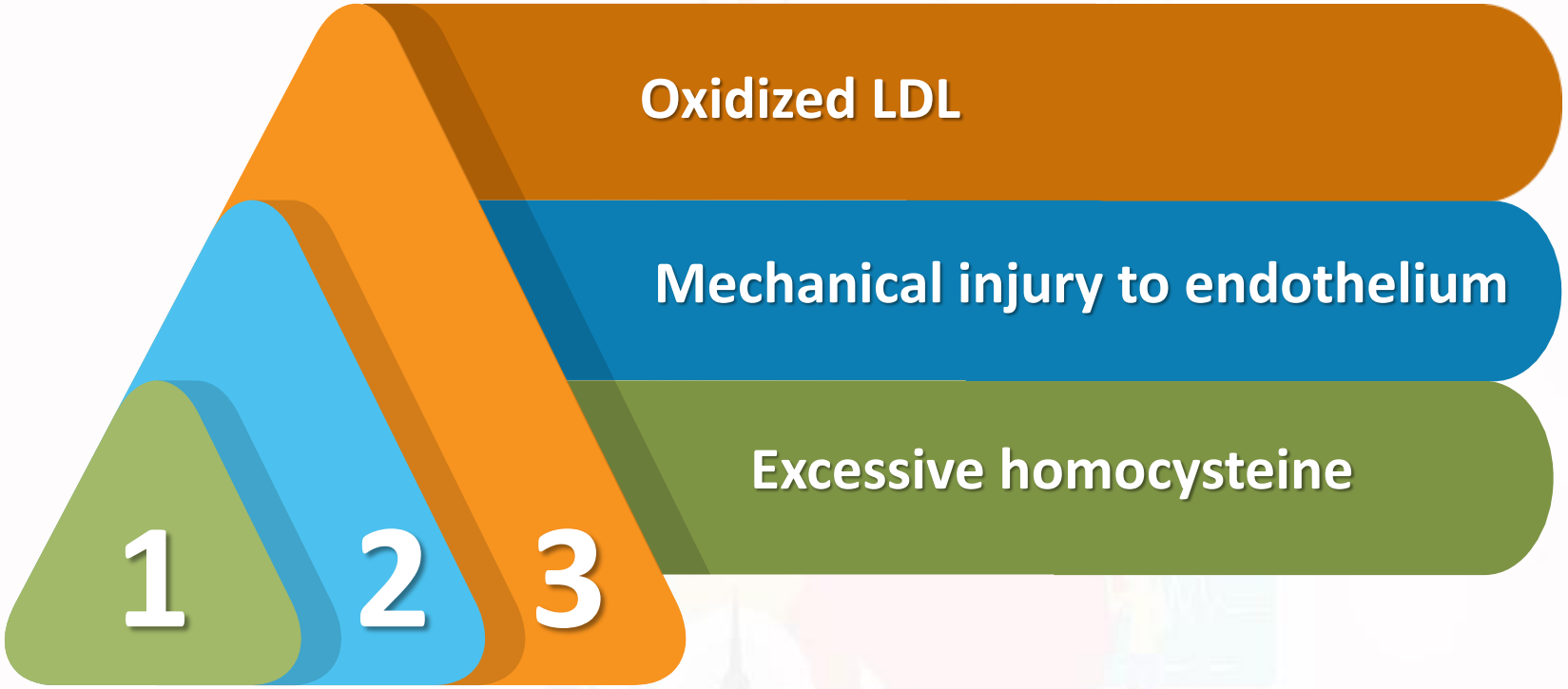
1. Di Ciaula A, Garruti G, Lunardi Baccetto R, Molina-Molina E, Bonfrate L, Wang DQ, Portincasa P. Bile Acid Physiology. Ann Hepatol. 2017 Nov;16(Suppl. 1: s3-105.):s4-s14.

Pathophysiology[1]

☠ Risk factors such as :



Can lead to endothelial dysfunction and cellular interactions culminating in atherosclerosis.

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1. Di Ciaula A, Garruti G, Lunardi Baccetto R, Molina-Molina E, Bonfrate L, Wang DQ, Portincasa P. Bile Acid Physiology. Ann Hepatol. 2017 Nov;16(Suppl. 1: s3-105.):s4-s14.

Pathophysiology[1]

A. Atherosclerotic lesions arise from transport and retention of plasma LDL through the endothelial cell layer into the extracellular matrix of the subendothelial space.

B. Once in the artery wall, LDL is chemically modified through oxidation and nonenzymatic glycation.

C. Mildly oxidized LDL recruits monocytes into the artery wall, which transform into macrophages that accelerate LDL oxidation.

D. Oxidized LDL provokes an inflammatory response mediated by chemoattractants and cytokines.

1. Di Ciaula A, Garruti G, Lunardi Baccetto R, Molina-Molina E, Bonfrate L, Wang DQ, Portincasa P. Bile Acid Physiology. Ann Hepatol. 2017 Nov;16(Suppl. 1: s3-105.):s4-s14.

Pathophysiology(1)

✓ **Repeated injury and repair within an atherosclerotic plaque eventually lead to a fibrous cap protecting the underlying core of :**

Maintenance of the fibrous plaque is critical to prevent plaque rupture and coronary thrombosis.

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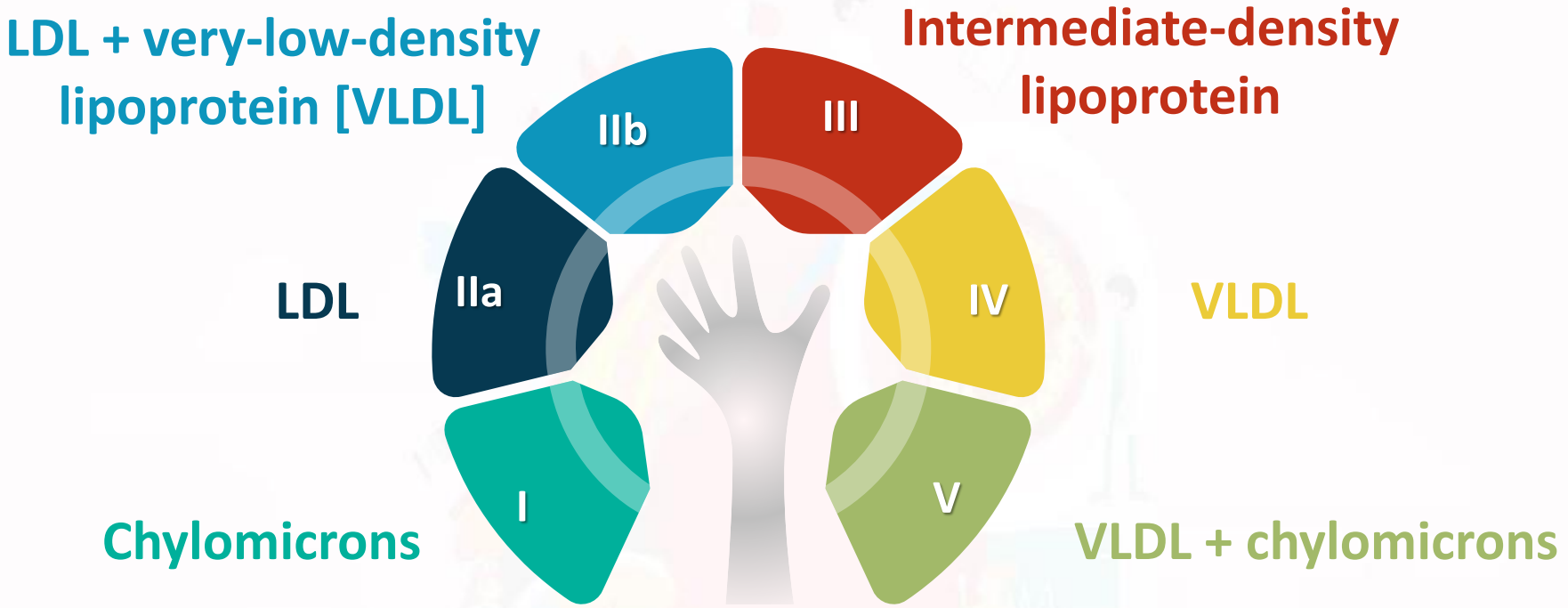
1. Di Ciaula A, Garruti G, Lunardi Baccetto R, Molina-Molina E, Bonfrate L, Wang DQ, Portincasa P. Bile Acid Physiology. Ann Hepatol. 2017 Nov;16(Suppl. 1: s3-105.):s4-s14.

Pathophysiology(1)

✓ **Primary or genetic lipoprotein disorders are classified into six categories:**



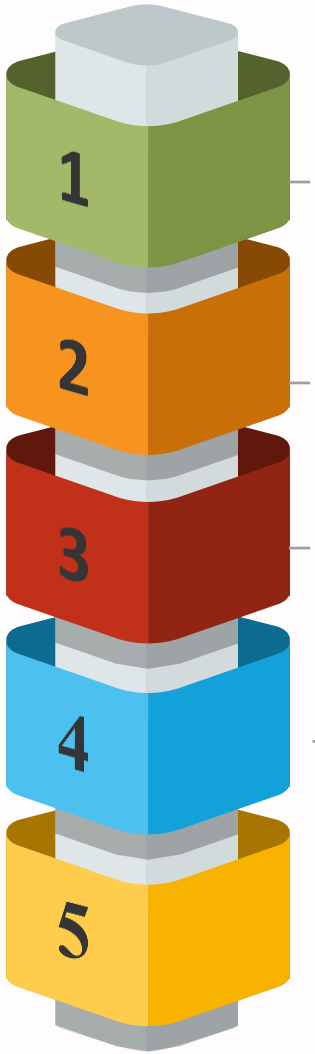
✓**Secondary forms of dyslipidemia also exist.**

✓ The primary defect in familial hypercholesterolemia is inability to bind LDL to the LDL receptor ➔ lack of LDL degradation by cells and unregulated biosynthesis of cholesterol.

1. Di Ciaula A, Garruti G, Lunardi Baccetto R, Molina-Molina E, Bonfrate L, Wang DQ, Portincasa P. Bile Acid Physiology. Ann Hepatol. 2017 Nov;16(Suppl. 1: s3-105.):s4-s14.

Pathophysiology(1)

✓Several drug classes may elevate cholesterol levels:



Progestins, Thiazide Diuretics

Glucocorticoids, B-blockers

Isotretinoin, Protease Inhibitors

Cyclosporine, Mirtazapine

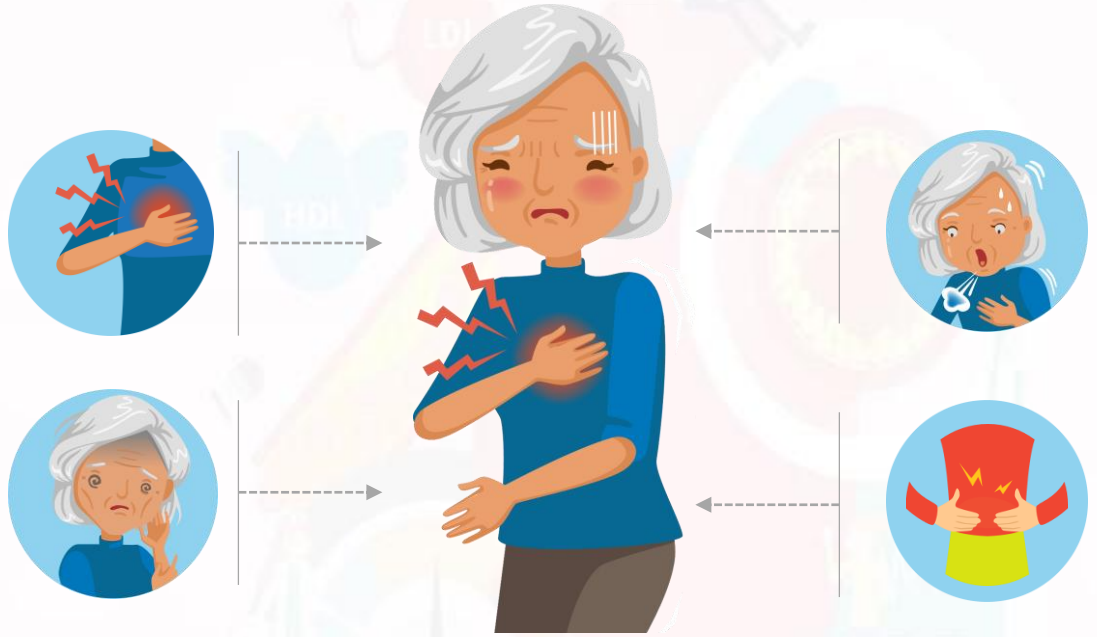
Sirolimus

Clinical presentation[2,3]

- **Most patients are asymptomatic for many years.**
- **Symptomatic patients may complain of :**

Palpitations, Chest pain

Sweating, Anxiety



Shortness of breath

Abdominal pain

Depending on the lipoprotein abnormality, signs on physical examination may include cutaneous xanthomas, peripheral polyneuropathy, ↑ BB , and ↑ BMI or waist size.

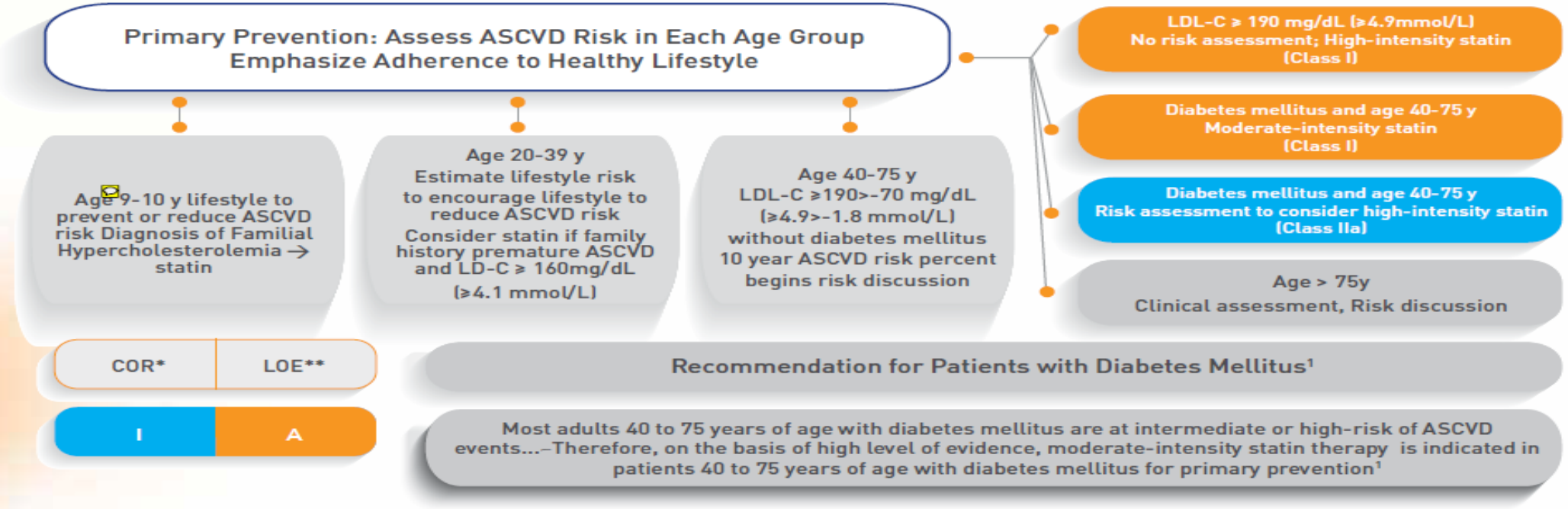
2. Ibrahim MA, Jialal I. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Jan 7, 2020. Hypercholesterolemia.
3. Wang HH, Garruti G, Liu M, Portincasa P, Wang DQ. Cholesterol and Lipoprotein Metabolism and Atherosclerosis: Recent Advances In reverse Cholesterol Transport. Ann

2018 Guideline on the management of blood cholesterol

2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APHA/ASPC/NLA/PCNA GUIDELINE ON THE MANAGEMENT OF BLOOD CHOLESTEROL[1]

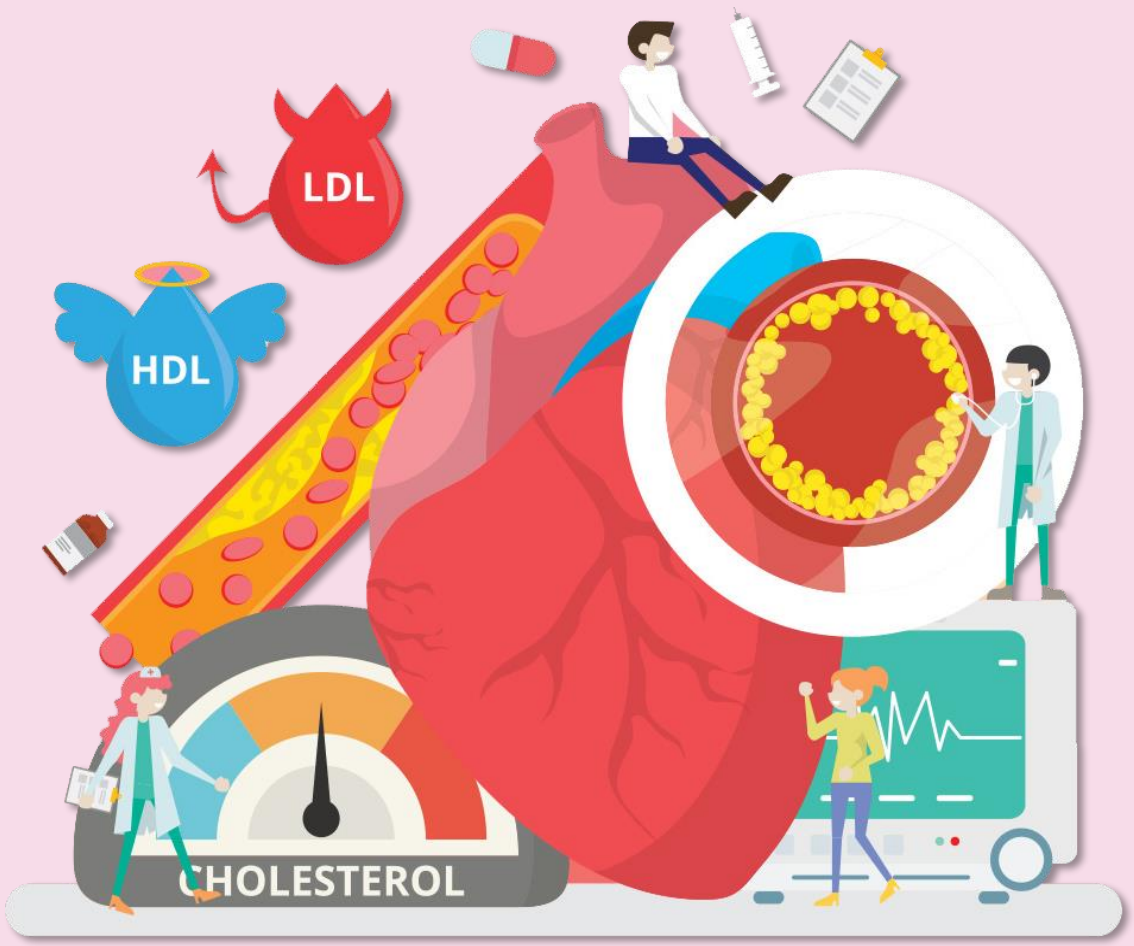
In primary prevention, statins are recommended for patients with severe hypercholesterolemia and in Adults 40 to 75 years of age either with diabetes mellitus or at higher ASCVD risk.[1]

Primary Prevention[1]



*COR: Class (STRENGTH) Of Recommendation/Class I: Highest (Strongest recommendation)
**LOE: Level (Quality) Of Evidence/ Level A: Highest Quality of evidence

Adapted from Grundy SM, et al. 2018



2. Triglycerides (TG)

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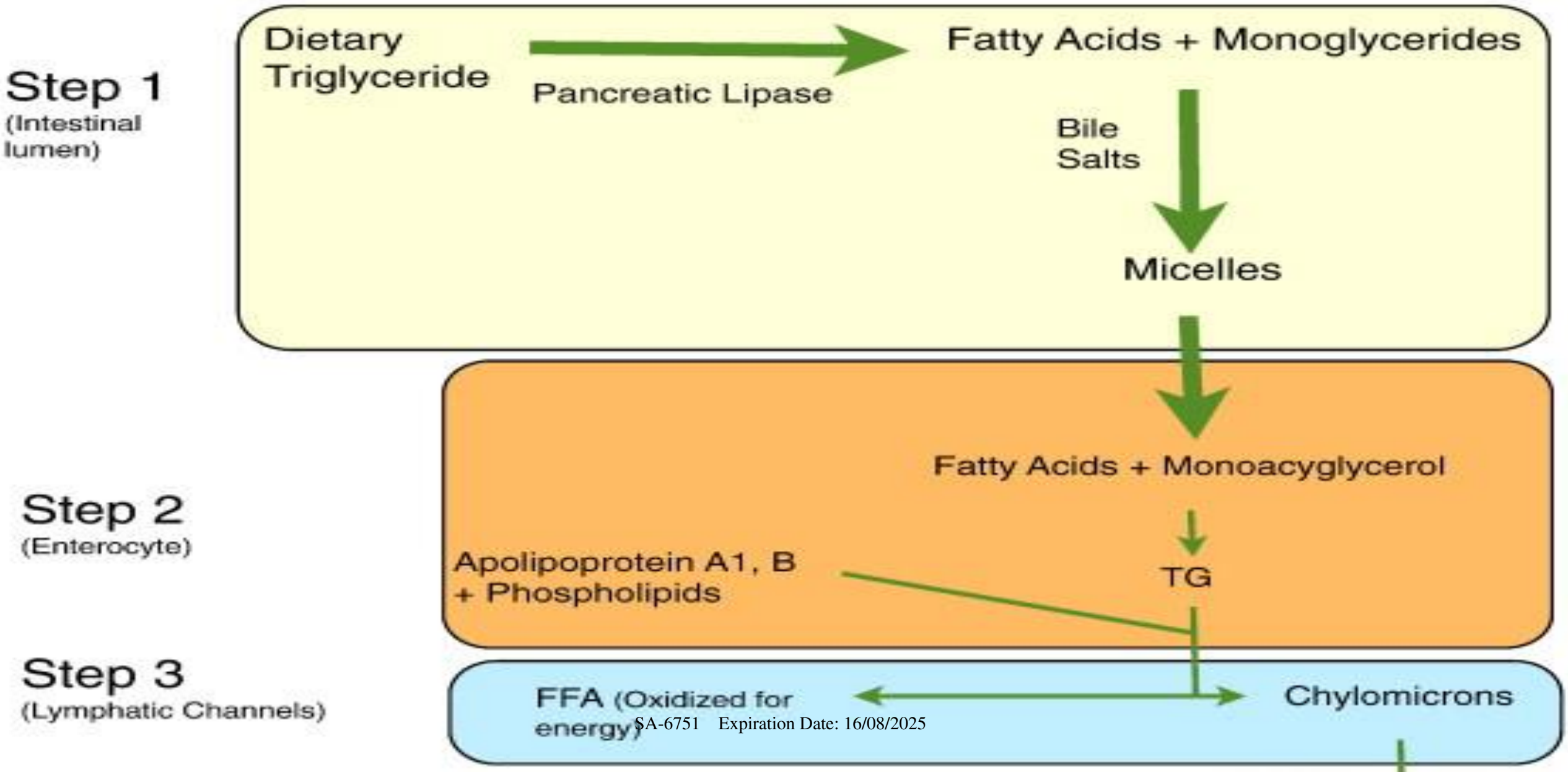
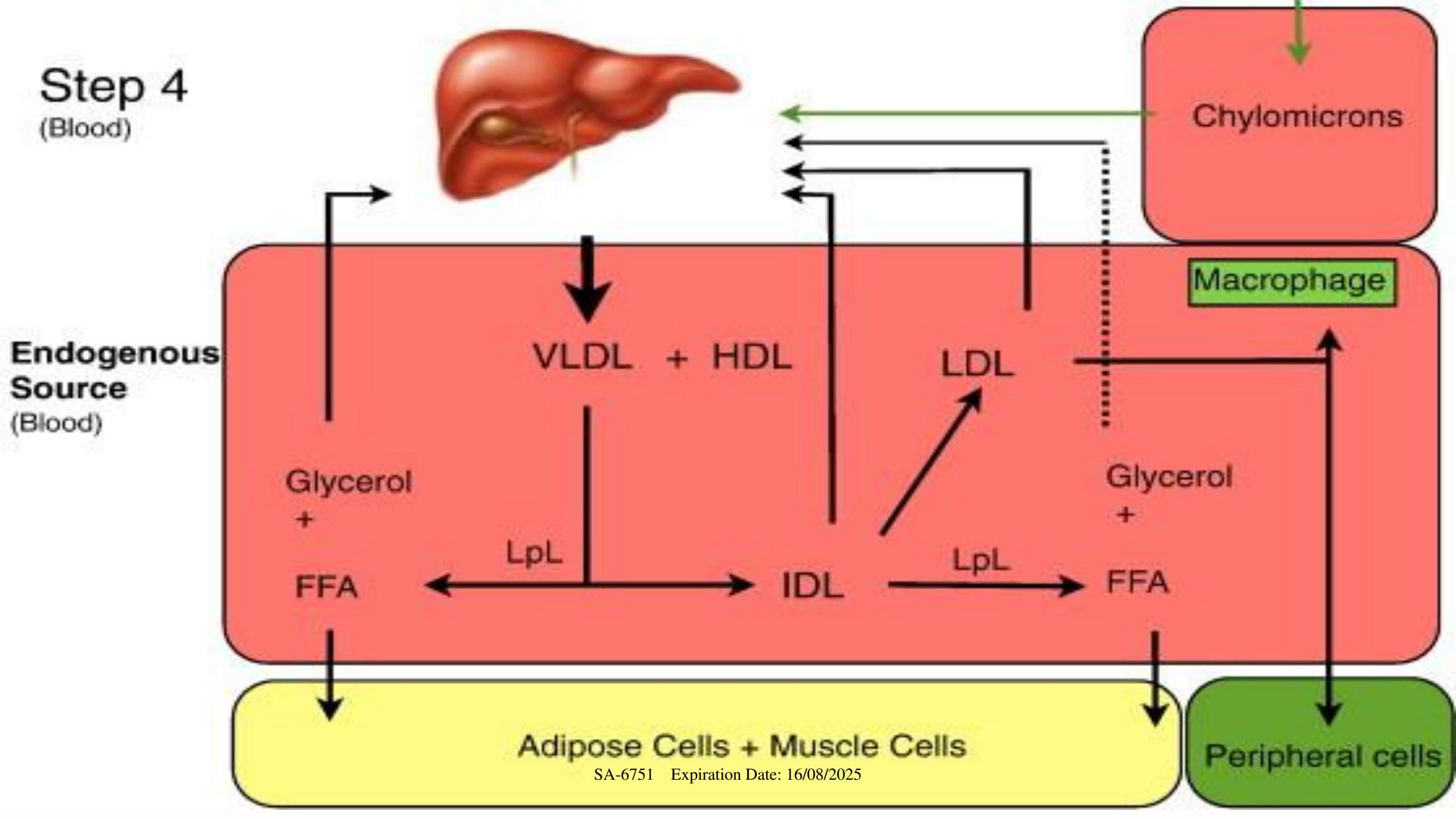
Triglyceride metabolism



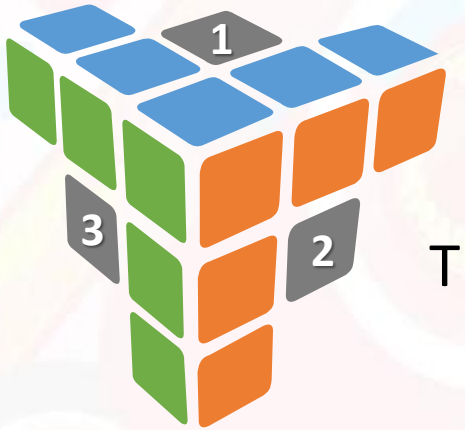

Step 4
(Blood)
Chylomicrons
Macrophage
Endogenous Source
(Blood)
VLDL + HDL
LDL
Glycerol
+
FFA
LpL
IDL
LpL
Glycerol
+
FFA
Adipose Cells + Muscle Cells
Peripheral cells

Hypertriglyceridemia[3,4]

Hypertriglyceridemia is often observed in patients with:

Type 2 **D**iabetes **M**ellitus (**DM**)

Familial **C**ombined **H**yperlipidemia (**FCHL**).



The **Met**abolic **S**yndrome (**MetS**),

The hallmark of these clinical phenotypes is the presence of:

Insulin Resistance.

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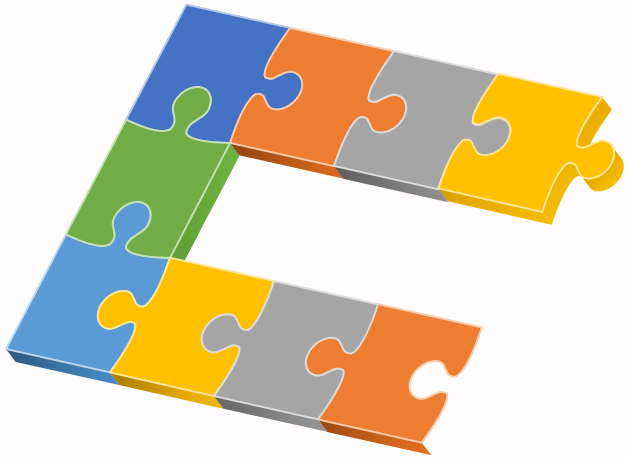
3. Wiesner P, Watson KE. Triglycerides: A reappraisal. Trends Cardiovasc Med. 2017;27(6):428–432. doi:10.1016/j.tcm.2017.03.004.
4. Harchaoui, K. E., Visser, M. E., Kastelein, J. J., Stroes, E. S., & Dallinga-Thie, G. M. (2009). Triglycerides and cardiovascular risk. Current cardiology reviews, 5(3), 216–222. https://doi.org/10.2174/157340309788970315

Hypertriglyceridemia[3,4]



In the insulin resistant state, the normal response to insulin is attenuated.

This will eventually lead to abnormalities in lipid handling in those organs that are particularly sensitive to insulin regulation such as adipose tissue, liver and skeletal muscle.

In the fed state, insulin activates LPL in adipose tissue and thereby set the switch to uptake of **F**ree **F**atty **A**cids (**FFA**) into the adipocytes which will then be stored in lipid droplets.

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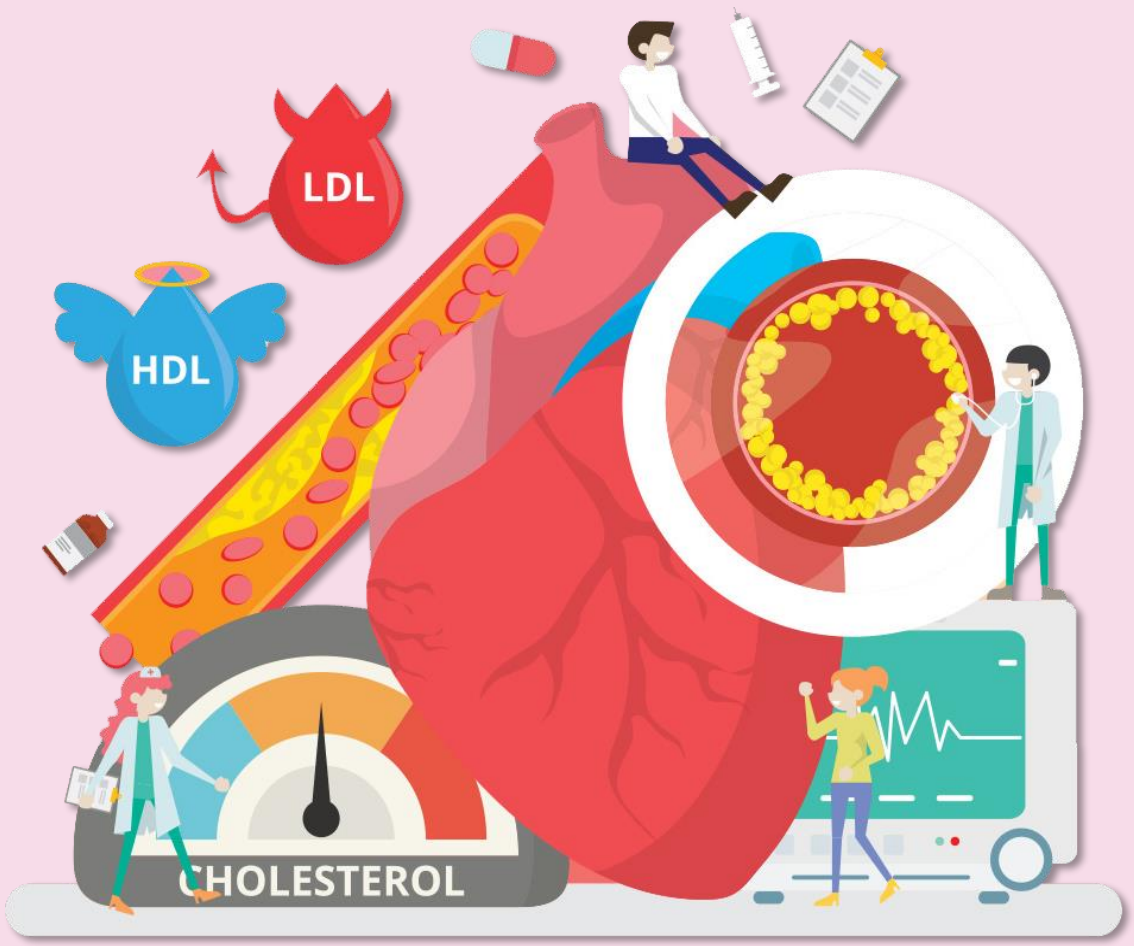
3. Wiesner P, Watson KE. Triglycerides: A reappraisal. Trends Cardiovasc Med. 2017;27(6):428–432. doi:10.1016/j.tcm.2017.03.004.
4. Harchaoui, K. E., Visser, M. E., Kastelein, J. J., Stroes, E. S., & Dallinga-Thie, G. M. (2009). Triglycerides and cardiovascular risk. Current cardiology reviews, 5(3), 216–222. https://doi.org/10.2174/157340309788970315

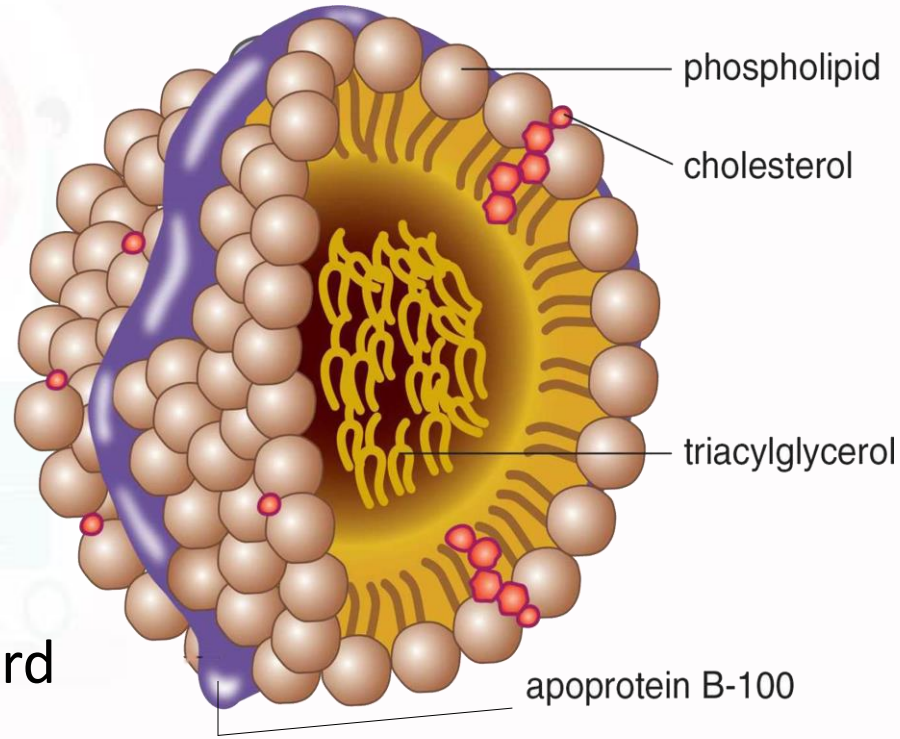


3. Lipoproteins types and their role

Introduction[5]

A lipoprotein is a biochemical assembly whose purpose is to transport hydrophobic lipid (a.k.a. fat) molecules in water, as in blood or extracellular fluid.

1. They have a single-layer phospholipid and cholesterol outer shell
2. Hydrophilic portions oriented outward toward the surrounding water
3. Lipophilic portions oriented inwards toward the lipids molecules within the particles.



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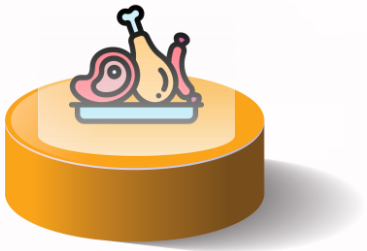
5. Wang HH, Garruti G, Liu M, Portincasa P, Wang DQ. Cholesterol and Lipoprotein Metabolism and Atherosclerosis: Recent Advances In reverse Cholesterol Transport. Ann Hepatol. 2017 Nov;16(Suppl. 1: s3-105.):s27-s42.

Function[5]

The handling of lipoprotein particles in the body is referred to as **lipoprotein particle metabolism.**

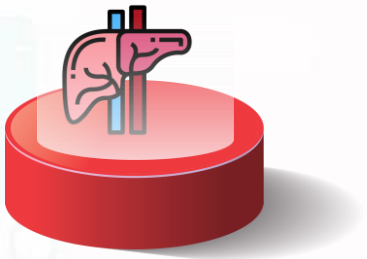
- It is divided into two pathways:

Exogenous



The lipoprotein particles in question are composed chiefly of **dietary lipids**

Endogenous



The lipoprotein originated in the **liver** through de novo synthesis of triacylglycerols.

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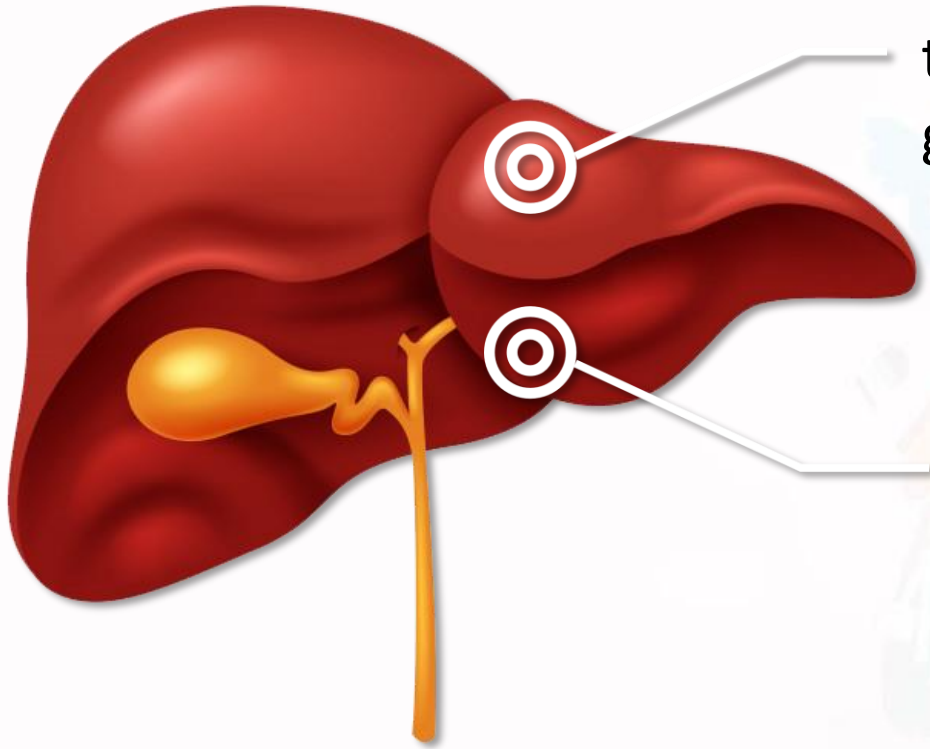
5. Wang HH, Garruti G, Liu M, Portincasa P, Wang DQ. Cholesterol and Lipoprotein Metabolism and Atherosclerosis: Recent Advances In reverse Cholesterol Transport. Ann Hepatol. 2017 Nov;16(Suppl. 1: s3-105.):s27-s42.

Function[5]



The **hepatocytes** are the main platform for the handling of triacylglycerols and cholesterol and store certain amounts of glycogen and triacylglycerols.

While **adipocytes** are the main storage cells for TG, they do not produce any lipoproteins.

5. Wang HH, Garruti G, Liu M, Portincasa P, Wang DQ. Cholesterol and Lipoprotein Metabolism and Atherosclerosis: Recent Advances In reverse Cholesterol Transport. Ann Hepatol. 2017 Nov;16(Suppl. 1: s3-105.):s27-s42.

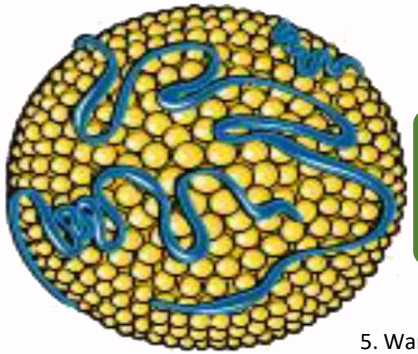
Types of lipoprotein(5)

High density lipoprotein (HDL) 1 — Highest in density due to high protein/protein ratio.

Low density lipoprotein (LDL) 2 — Highest in cholesterol esters as % of weight.

IDL 3 — Intermediate density lipoprotein.

Very low density lipoprotein (VLDL) 4 — 2nd highest in triacylglycerols as % of weight .



CHYLOMICRON 5 — Largest ,lowest in density due to high lipid/protein ratio: highest in triacylglycerols as % of weight.

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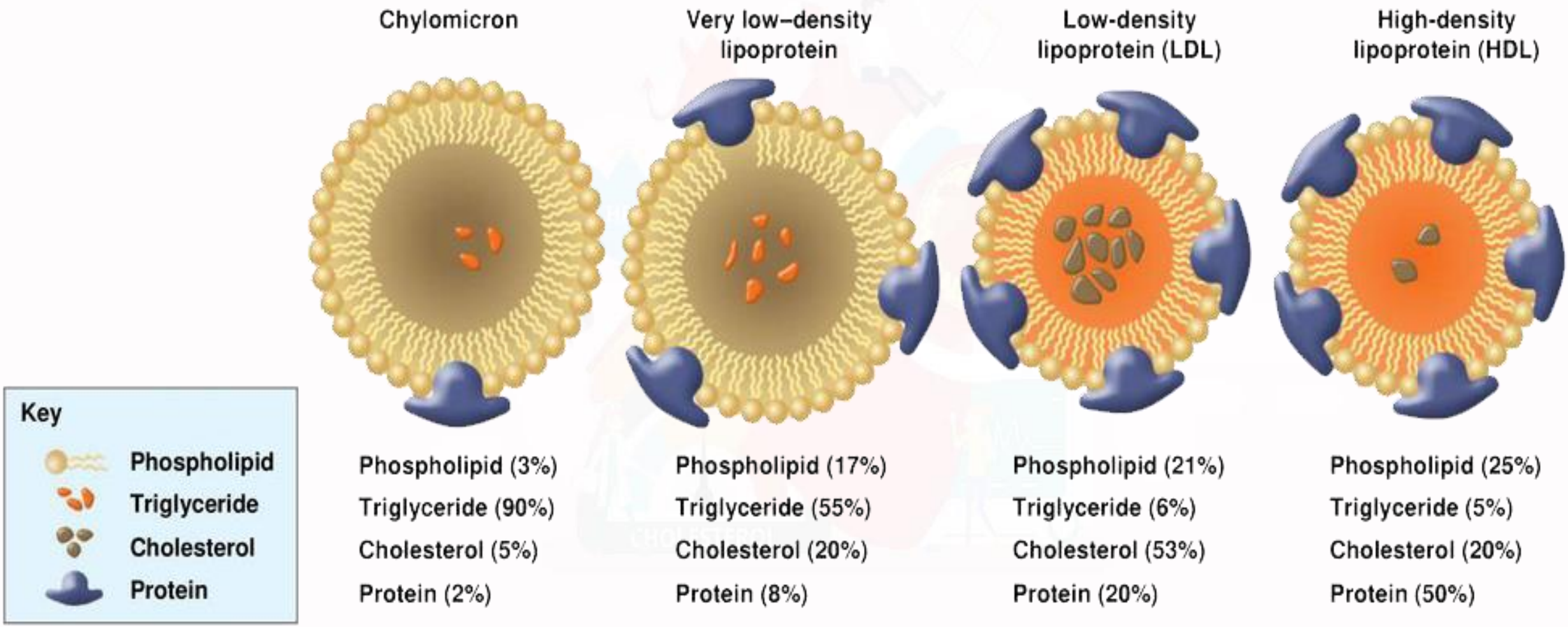
5. Wang HH, Garruti G, Liu M, Portincasa P, Wang DQ. Cholesterol and Lipoprotein Metabolism and Atherosclerosis: Recent Advances In reverse Cholesterol Transport. Ann Hepatol. 2017 Nov;16(Suppl. 1: s3-105.):s27-s42.

Types of lipoprotein(5)



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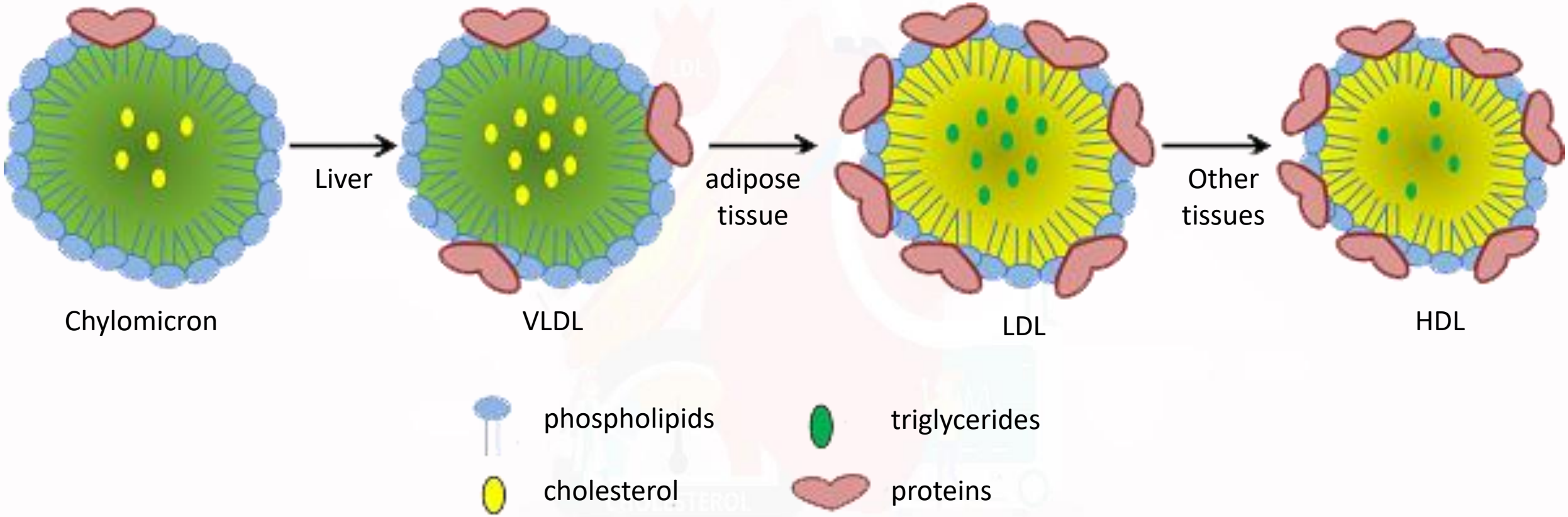
Types of lipoprotein(5)



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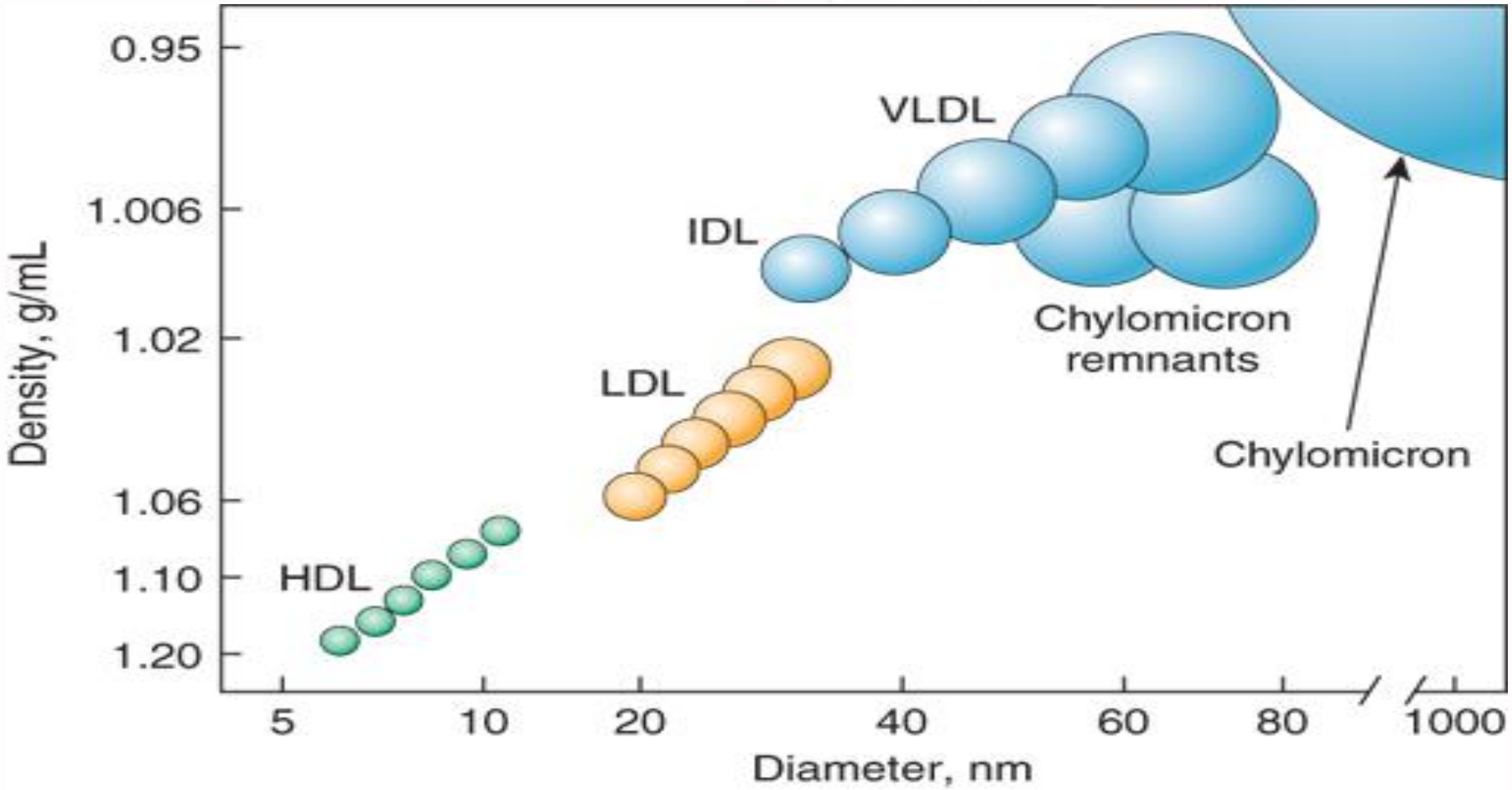
5. Wang HH, Garruti G, Liu M, Portincasa P, Wang DQ. Cholesterol and Lipoprotein Metabolism and Atherosclerosis: Recent Advances In reverse Cholesterol Transport. Ann Hepatol. 2017 Nov;16(Suppl. 1: s3-105.):s27-s42.

Types of lipoprotein

Classification according to size



Source: J.L. Jameson, A.S. Fauci, D.L. Kasper, S.L. Hauser, D.L. Longo, J. Loscalzo: Harrison's Principles of Internal Medicine, 20th Edition

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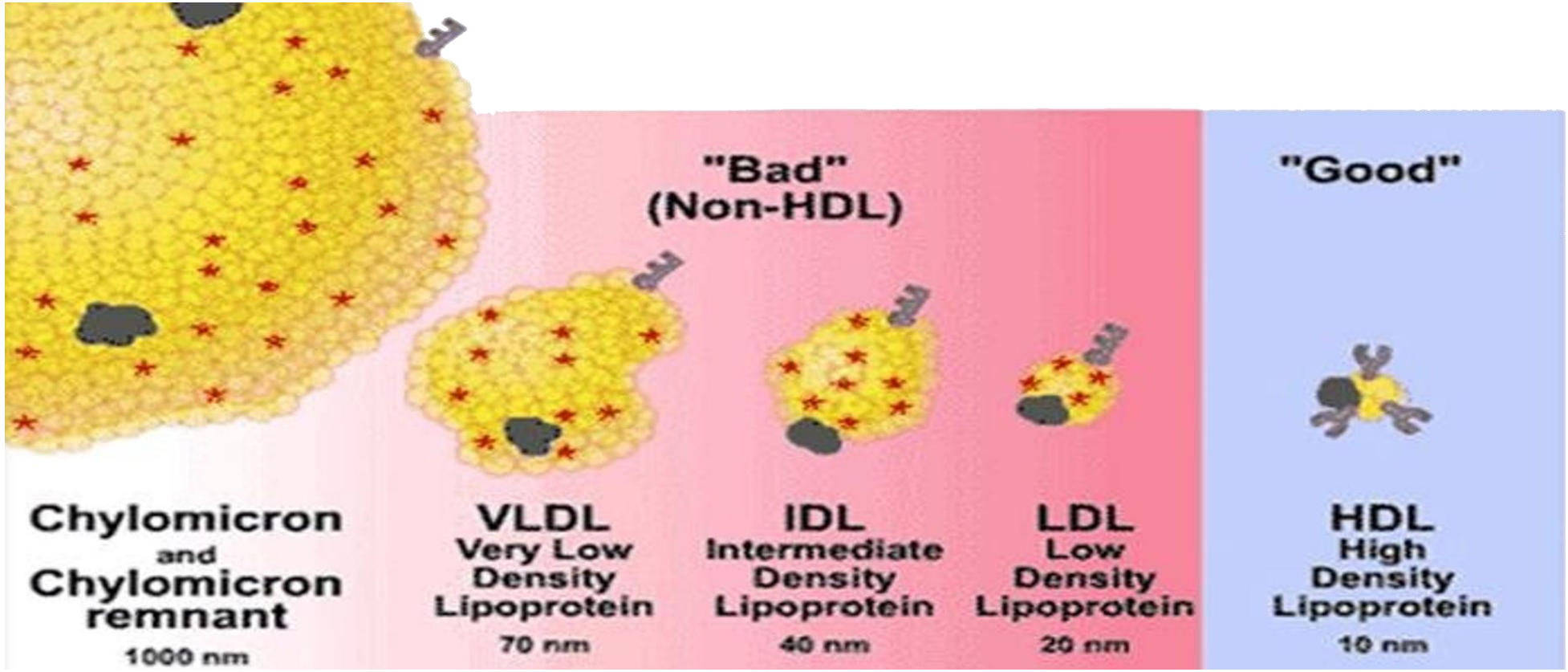
Types of lipoprotein(5)

Classification according to bad and good lipoprotein



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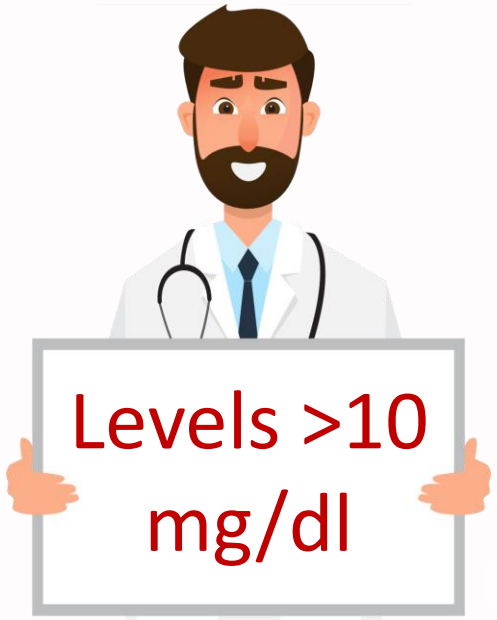
Lipoprotein interpretation(6)



↑↑ Cardiovascular risk.

✓The apolipoproteins have a 1ry responsibility for the transports of lipids and cholesterol.

✓ Apolipoprotein B is a nonexchangeable lipoprotein that exists in two forms in humans:

1 apoB-100

2 apo-48

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6. Karney A, Brągoszewska H, Soluch L, Ołtarzewski M. [Risk factors for atherosclerosis in obese children aged 6-12 years]. Dev Period Med. 2017;21(3):259-265.

Role of lipids and lipoproteins in the pathophysiology of atherosclerosis(7)

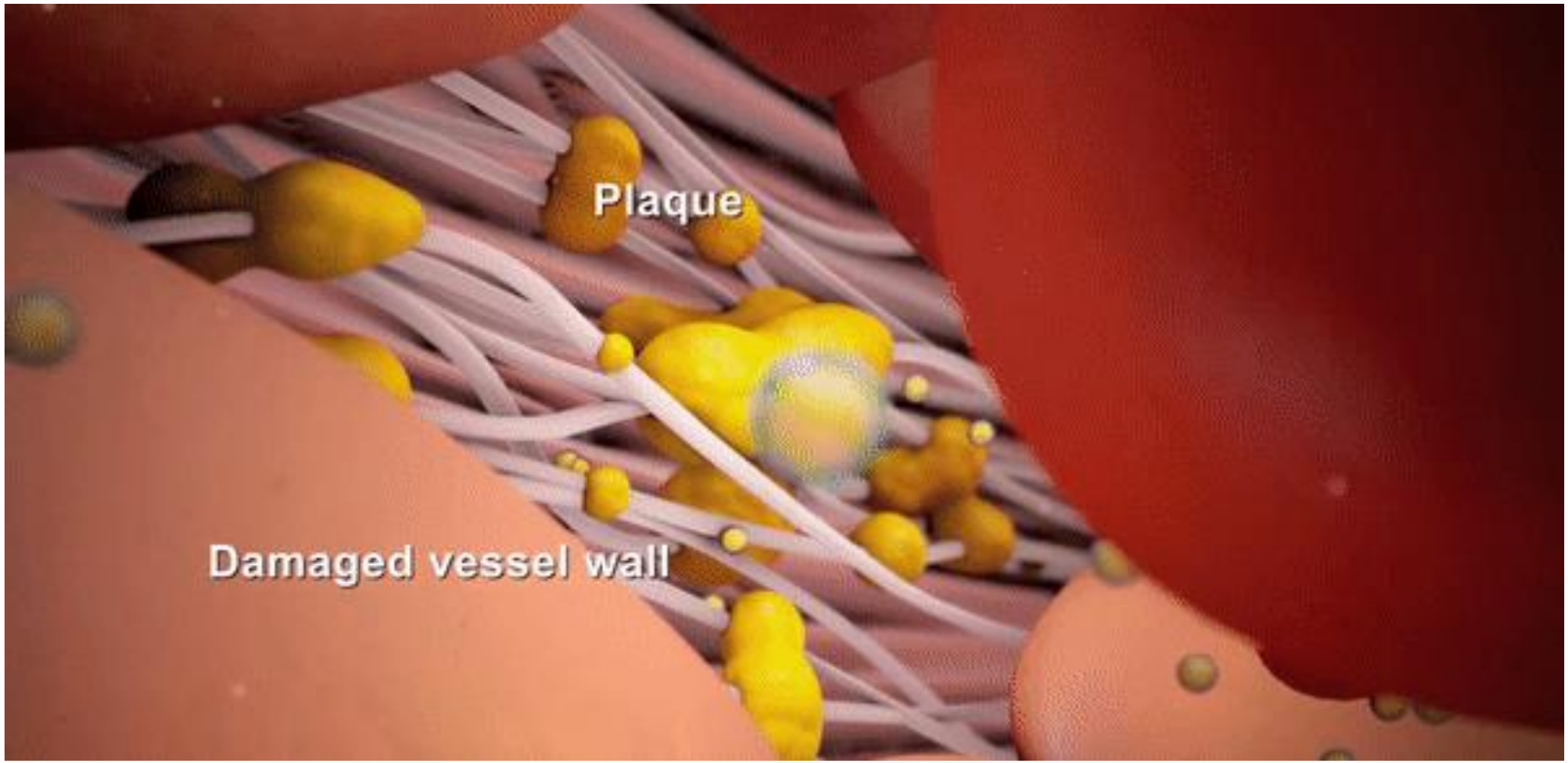
01 All ApoB-containing lipoproteins <70 nm in diameter, including smaller TG-rich lipoproteins can cross the endothelial barrier, especially in the presence of **endothelial dysfunction**, where they can become trapped after interaction with extracellular structures such as **proteoglycans**.

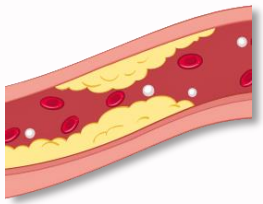
02 ApoBg retained in the arterial wall provoke a complex process that leads to lipid deposition and the initiation of an **atheroma**.

03 Continued exposure to ApoB leads to additional particles being retained over time in the artery wall, and to the growth and progression of ☠**atherosclerotic plaques**☠.

7. Kobiyama, K., & Ley, K. (2018). Atherosclerosis. Circulation research, 123(10), 1118–1120. https://doi.org/10.1161/CIRCRESAHA.118.313816.

Role of lipids and lipoproteins in the pathophysiology of atherosclerosis(7)





People with ↑ conc. of ApoB proteins will retain more particles and accumulate lipids faster → more rapid growth and the progression of atherosclerotic plaques.

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7. Kobiyama, K., & Ley, K. (2018). Atherosclerosis. Circulation research, 123(10), 1118–1120. https://doi.org/10.1161/CIRCRESAHA.118.313816.

Role of lipids and lipoproteins in the pathophysiology of atherosclerosis[7]

☠ The size of the total atherosclerotic plaque burden is determined by both:

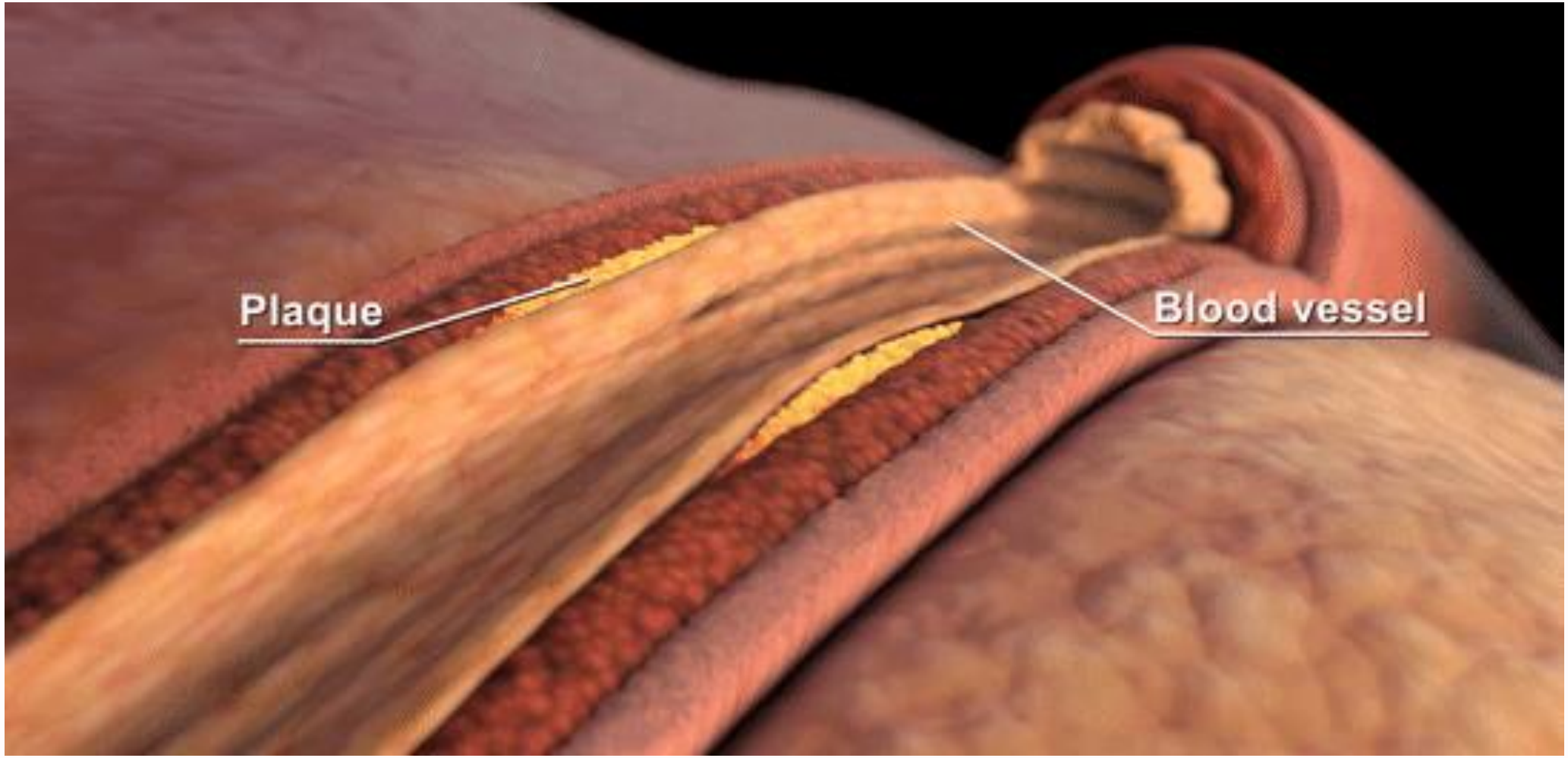
01 The concentration of circulating LDL-C and other ApoB-containing lipoproteins,

02 The total duration of exposure to these lipoproteins.

Therefore, a person's total atherosclerotic plaque burden is likely to be proportional to the cumulative exposure to these lipoproteins.

7. Kobiyama, K., & Ley, K. (2018). Atherosclerosis. Circulation research, 123(10), 1118–1120. https://doi.org/10.1161/CIRCRESAHA.118.313816.

Role of lipids and lipoproteins in the pathophysiology of atherosclerosis[7]



7. Kobiyama, K., & Ley, K. (2018). Atherosclerosis. Circulation research, 123(10), 1118–1120. https://doi.org/10.1161/CIRCRESAHA.118.313816.

Role of lipids and lipoproteins in the pathophysiology of atherosclerosis[7]

☠ Disruption of a plaque with the formation of an overlying thrombus that acutely obstructs blood flow resulting in:

Unstable angina

Myocardial Infarction (MI)

Death

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7. Kobiyama, K., & Ley, K. (2018). Atherosclerosis. Circulation research, 123(10), 1118–1120. https://doi.org/10.1161/CIRCRESAHA.118.313816.

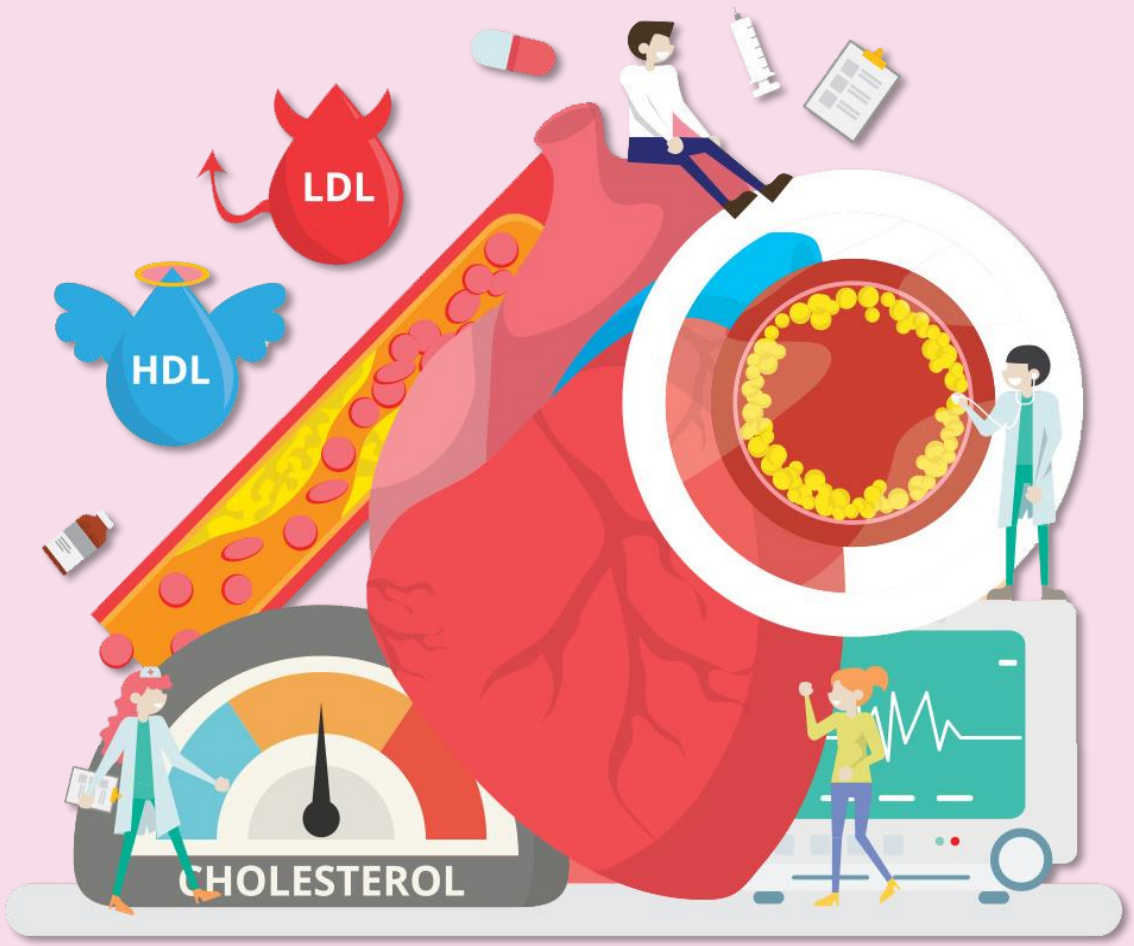
Role of lipids and lipoproteins in the pathophysiology of atherosclerosis[7]

✓ **To slow the progression of atherosclerosis:**

Encouraging a healthy lifestyle to maintain low levels of ApoB-containing lipoproteins throughout life

Recommend treatment to lower LDL-C and other ApoB-containing lipoproteins

7. Kobiyama, K., & Ley, K. (2018). Atherosclerosis. Circulation research, 123(10), 1118–1120. https://doi.org/10.1161/CIRCRESAHA.118.313816.



4. Metabolic Syndrome

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Definition[8,9]

✓**Met**abolic **S**yndrome (**MetS**) is defined by a constellation of an interconnected :

Physiological

Biochemical

Clinical

Metabolic factors

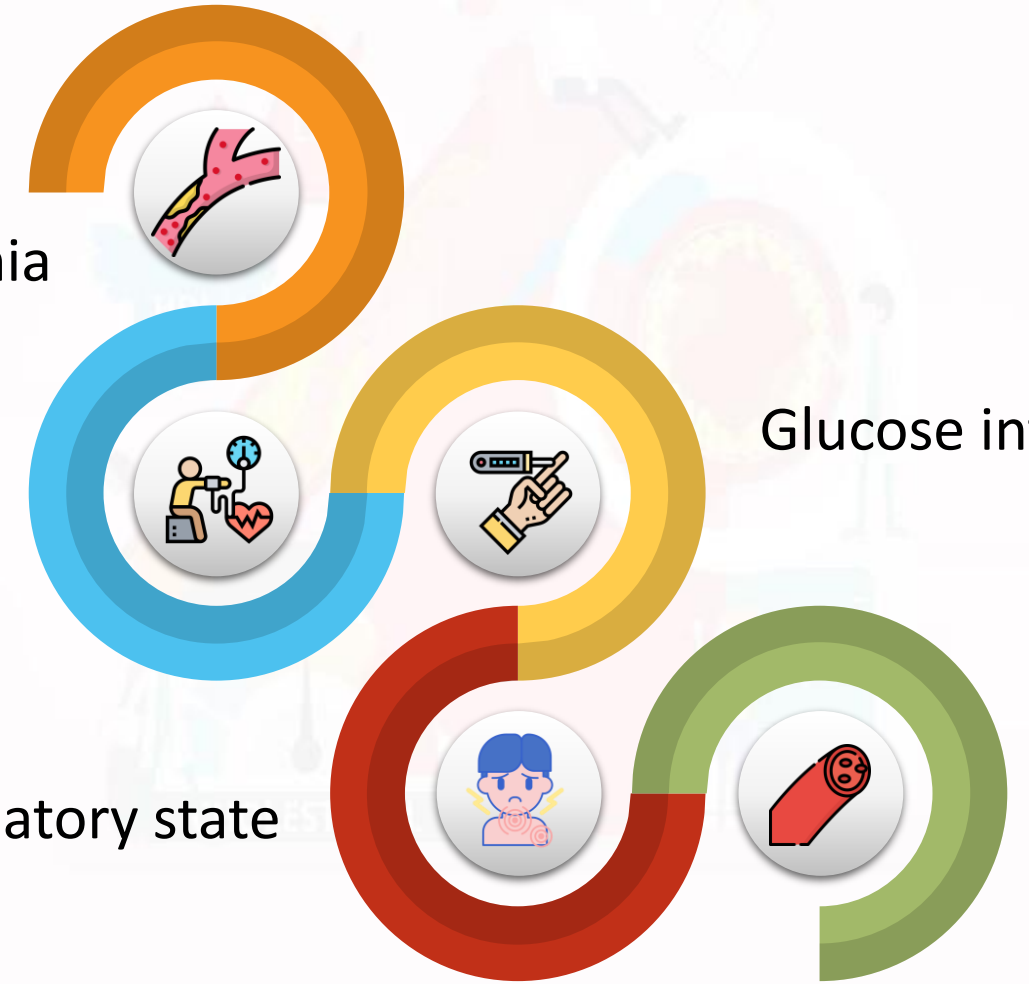
That directly increases the risk of **a**thero**s**clerotic **c**ardiovascular **d**isease (**ASCVD**), **T**ype **2 d**iabetes **m**ellitus (**T2DM**) and all-cause mortality.

SA-6751 Expiration Date: 16/08/2025

8. Kaur J. (2014). A comprehensive review on metabolic syndrome. Cardiology research and practice, 2014, 943162. https://doi.org/10.1155/2014/943162 (Retraction published Cardiol Res Pract. 2019 Jan 31;2019:4301528).
9. Han, Jong-Min; Kim, Hyeong-Geug; Lee, Jin-Seok; Choi, Min-Kyung; Kim, Young-Ae; Son, Chang-Gue (2015): Graphical summary of the metabolic syndrome by a repeated hunger sense.. PLOS ONE. Figure. https://doi.org/10.1371/journal.pone.0098276.g009.

Definition[8,9]

☠ This collection of unhealthy body measurements and abnormal laboratory test results include :



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8. Kaur J. (2014). A comprehensive review on metabolic syndrome. Cardiology research and practice, 2014, 943162. https://doi.org/10.1155/2014/943162 (Retraction published Cardiol Res Pract. 2019 Jan 31;2019:4301528).
9. Han, Jong-Min; Kim, Hyeong-Geug; Lee, Jin-Seok; Choi, Min-Kyung; Kim, Young-Ae; Son, Chang-Gue (2015): Graphical summary of the metabolic syndrome by a repeated hunger sense.. PLOS ONE. Figure. https://doi.org/10.1371/journal.pone.0098276.g009.

Epidemiology (8,9)

Worldwide prevalence of MetS ranges from <10% to 84% depending on :

- The region
- Urban or rural environment
- Composition (sex, age, race, and ethnicity) of the population studied
- The definition of the syndrome used

The IDF estimates that one-quarter of the world's adult population has the MetS.

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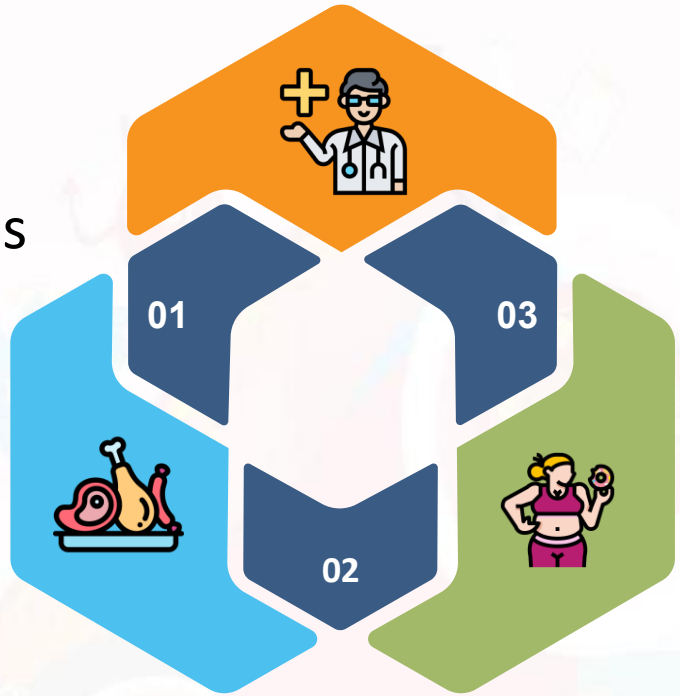
8. Kaur J. (2014). A comprehensive review on metabolic syndrome. Cardiology research and practice, 2014, 943162. https://doi.org/10.1155/2014/943162 (Retraction published Cardiol Res Pract. 2019 Jan 31;2019:4301528).
9. Han, Jong-Min; Kim, Hyeong-Geug; Lee, Jin-Seok; Choi, Min-Kyung; Kim, Young-Ae; Son, Chang-Gue (2015): Graphical summary of the metabolic syndrome by a repeated hunger sense.. PLOS ONE. Figure. https://doi.org/10.1371/journal.pone.0098276.g009.

Epidemiology (8,9)

Higher socioeconomic status



↑ Body mass index (BMI)

Sedentary lifestyle

☠ Were significantly associated with MetS.

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8. Kaur J. (2014). A comprehensive review on metabolic syndrome. Cardiology research and practice, 2014, 943162. https://doi.org/10.1155/2014/943162 (Retraction published Cardiol Res Pract. 2019 Jan 31;2019:4301528).
9. Han, Jong-Min; Kim, Hyeong-Geug; Lee, Jin-Seok; Choi, Min-Kyung; Kim, Young-Ae; Son, Chang-Gue (2015): Graphical summary of the metabolic syndrome by a repeated hunger sense.. PLOS ONE. Figure. https://doi.org/10.1371/journal.pone.0098276.g009.

Epidemiology (8,9)

☠ The prevalence of the MetS in National Health and Nutrition Examination Survey was :

5% Of normal weight

22% Of overweight

60% Of the obese

10% Aged 20–29

20% Aged 40–49

45% Aged 60–69

☠ The prevalence of MetS (based on NCEP-ATP III criteria, 2001) varied from:

8% to 43% In men

7% to 56% In women

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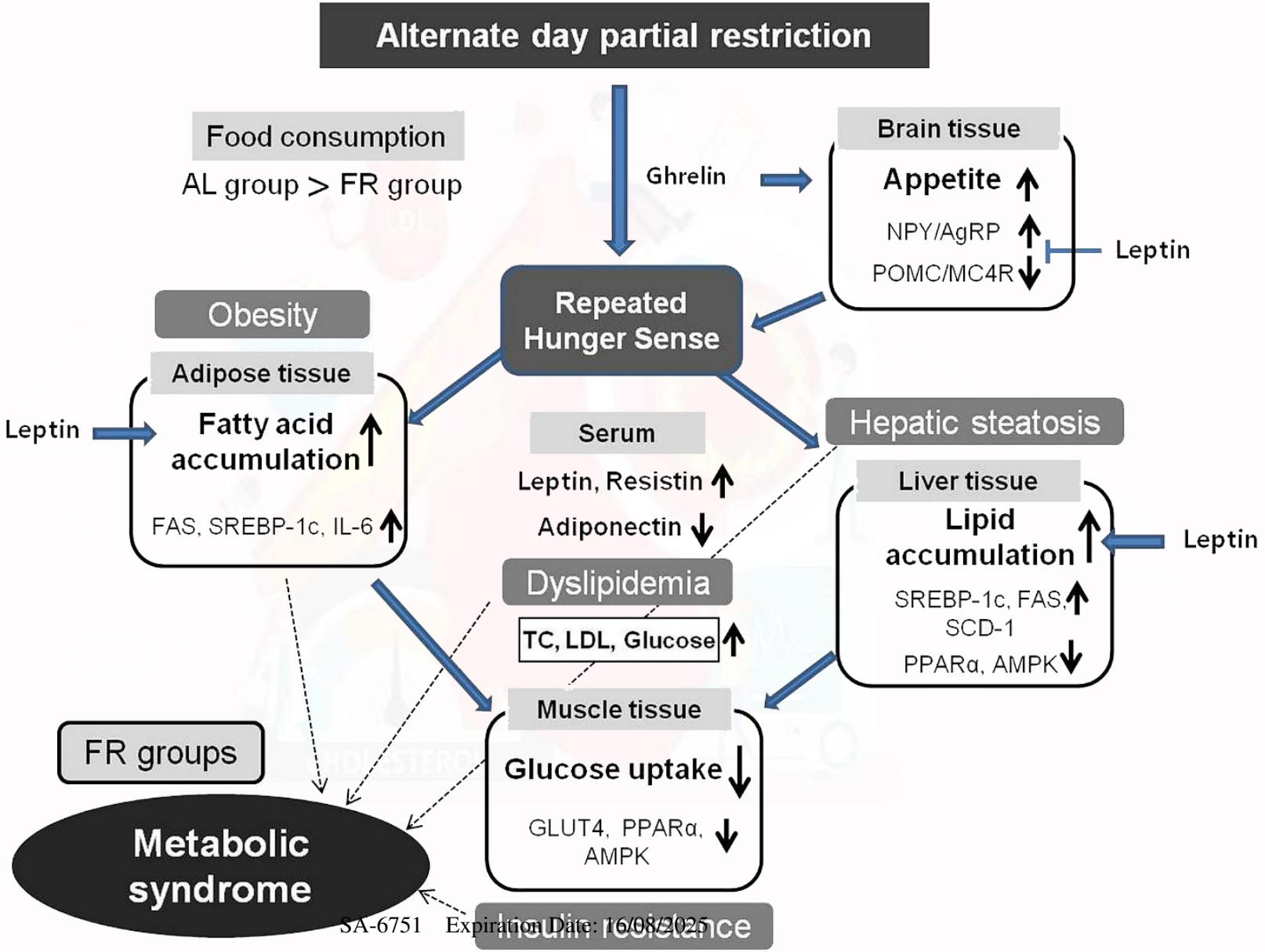
8. Kaur J. (2014). A comprehensive review on metabolic syndrome. Cardiology research and practice, 2014, 943162. https://doi.org/10.1155/2014/943162 (Retraction published Cardiol Res Pract. 2019 Jan 31;2019:4301528).
9. Han, Jong-Min; Kim, Hyeong-Geug; Lee, Jin-Seok; Choi, Min-Kyung; Kim, Young-Ae; Son, Chang-Gue (2015): Graphical summary of the metabolic syndrome by a repeated hunger sense.. PLOS ONE. Figure. https://doi.org/10.1371/journal.pone.0098276.g009.

Pathophysiology

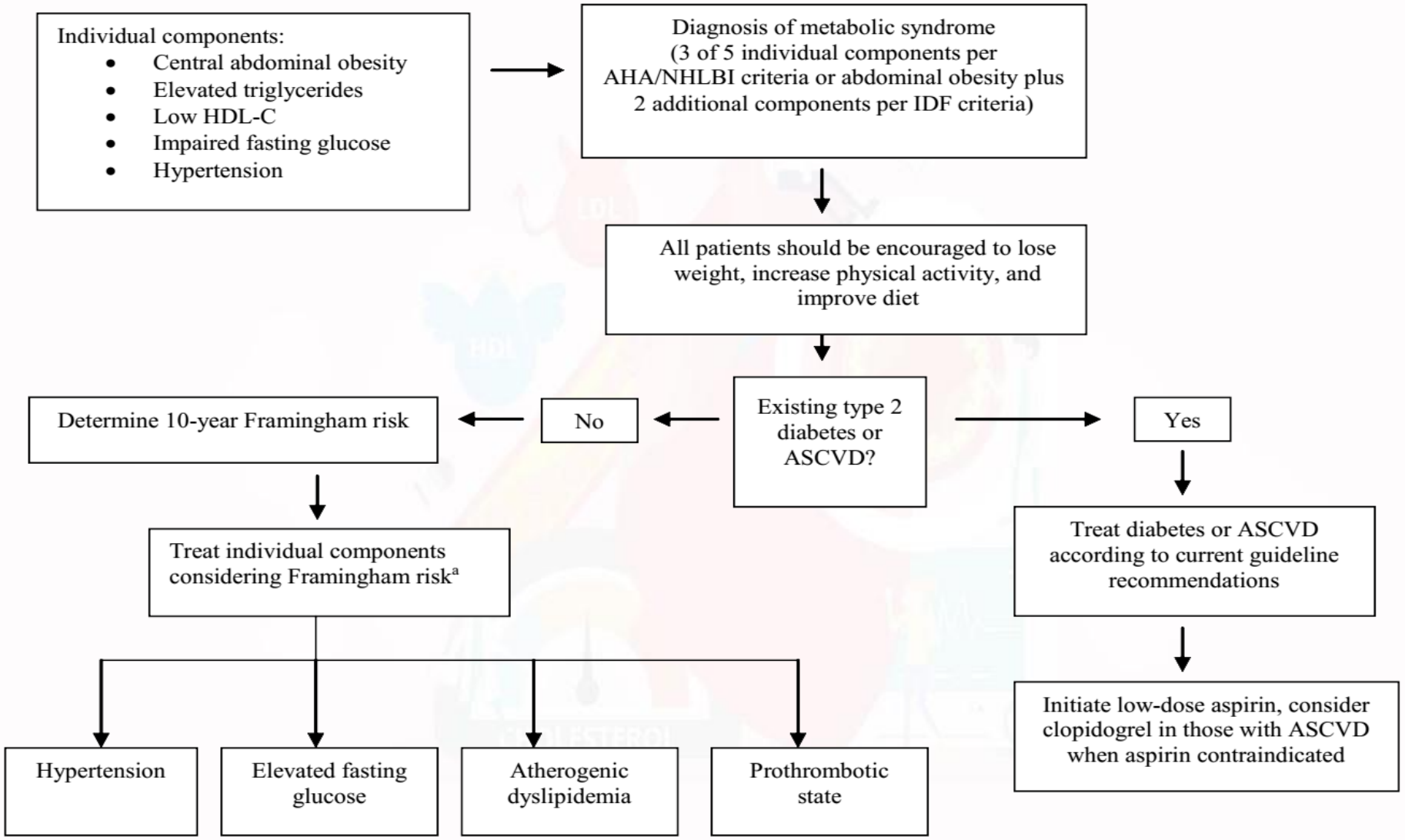


Treatment Goals by Framingham Risk for Patients Without Existing Disease

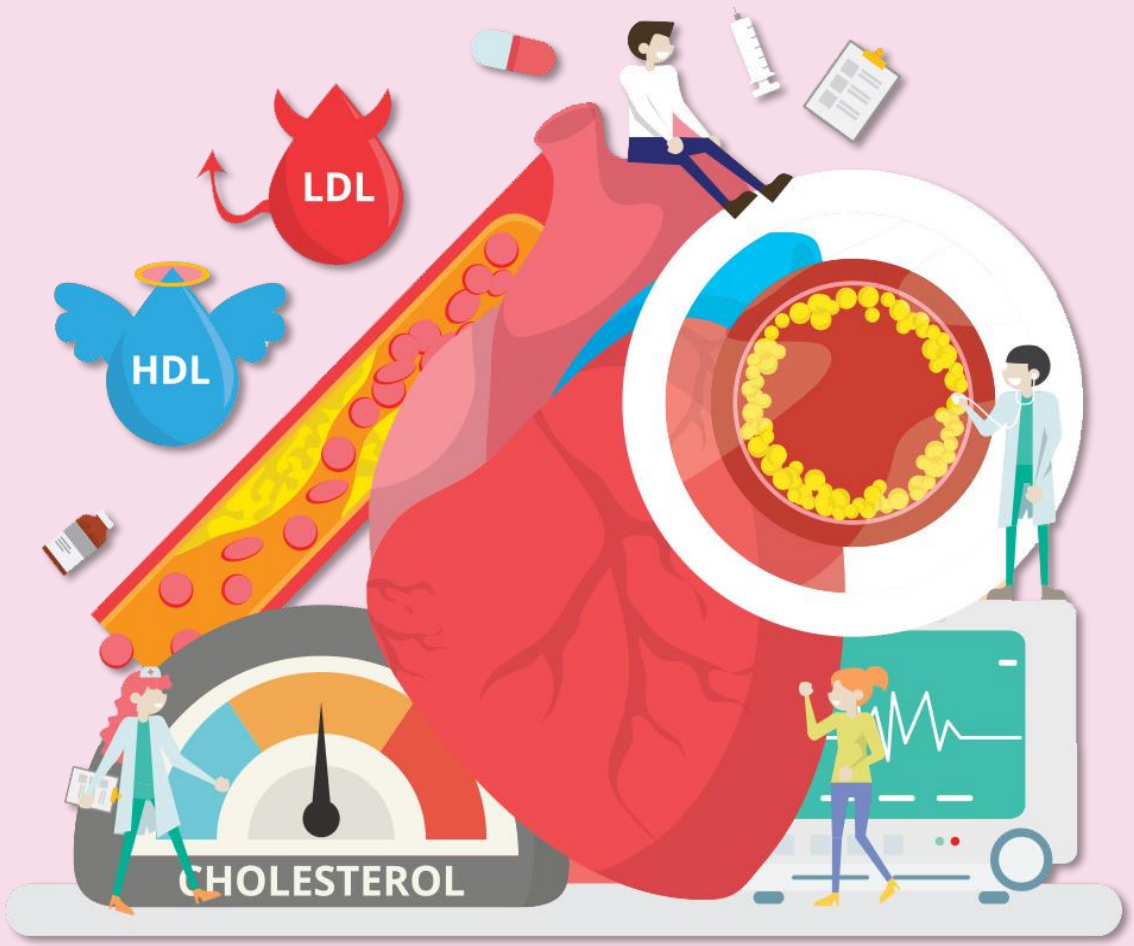
Framingham Risk (%)	Blood Pressure (mm Hg)	LDL-C (mg/dL)	Non–HDL-C (mg/dL)	FPG (mg/dL)	Aspirin
< 10	< 140/90	< 160,[a] < 130[a]	< 190,[b] < 160[b]	< 100	Consider[c]
10–20	< 130/80	< 130, < 100[d]	< 160, < 130[d]	< 100	Yes
> 20	< 130/80	< 100, < 70[e]	< 130, < 100[e]	< 100	Yes

[a]Goal less than 160 mg/dL for patients with 0 or 1 major risk factor (i.e., cigarette smoking, hypertension, low HDL-C, premature coronary heart disease, or age); goal less than 130 mg/dL for patients with two or more major risk factors.
[b]Goal less than 190 mg/dL for patients with 0 or 1 major risk factor; goal less than 160 mg/dL for patients with two or more major risk factors.
[c]Some patients with metabolic syndrome will meet criteria according to the U.S. Preventive Services Task Force statement concerning the use of aspirin for the prevention of cardiovascular disease.
[d]Multiple major risk factors, severe and poorly controlled risk factors (especially continued cigarette smoking), or metabolic syndrome.
[e]Established coronary heart disease plus any of the following: multiple major risk factors (especially diabetes), severe and poorly controlled risk factors (especially continued cigarette smoking), metabolic syndrome, or recent acute coronary syndrome.
FPG = fasting plasma glucose; LDL-C = low-density lipoprotein cholesterol; non–HDL-C = non–high-density lipoprotein cholesterol.
Information from Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation 2005;112:2735–52; Rosendorff C, Black HR, Cannon CP, Gersh BJ, Gore J, Izzo JL Jr, et al. Treatment of hypertension in the prevention and management of ischemic heart disease: a scientific statement from the American Heart Association Council for High Blood Pressure Research and the Councils on Clinical Cardiology and Epidemiology and Prevention. Circulation 2007;115:2761–88; and National Institutes of Health. Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Available at *www.nhlbi.nih.gov/guidelines/cholesterol/index.htm*. Accessed June 5, 2009.

Algorithm for the management of metabolic syndrome



AHA/NHLBI = American Heart Association/National Heart, Lung and Blood Institute; ASCVD = atherosclerotic cardiovascular disease; HDL-C = high-density lipoprotein cholesterol; IDF = International Diabetes Federation.



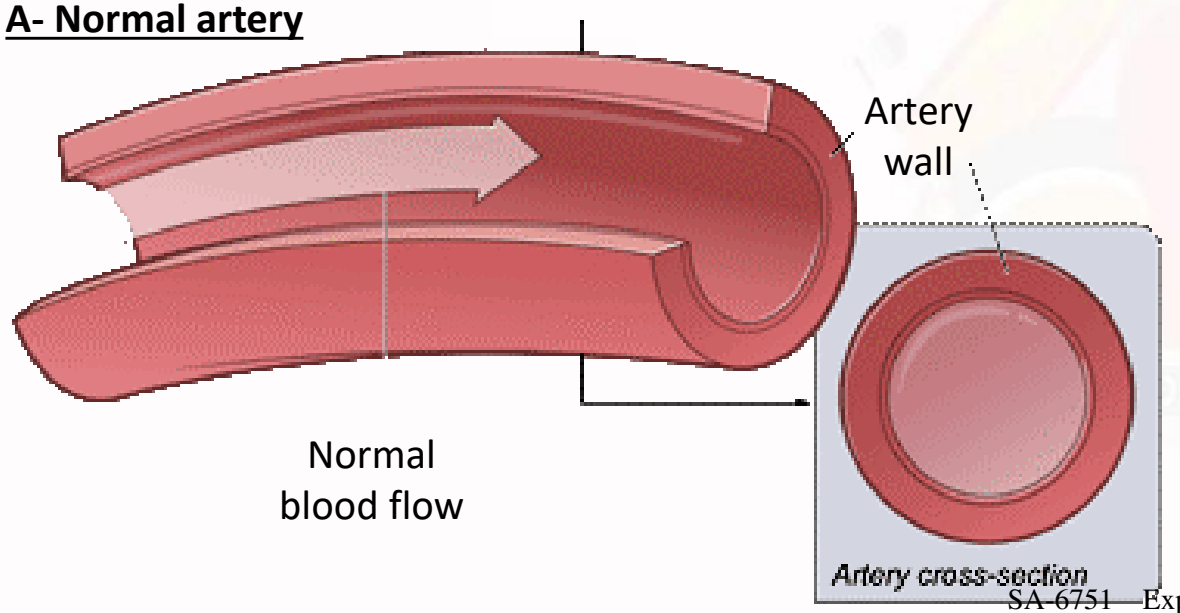
5. Atherosclerosis

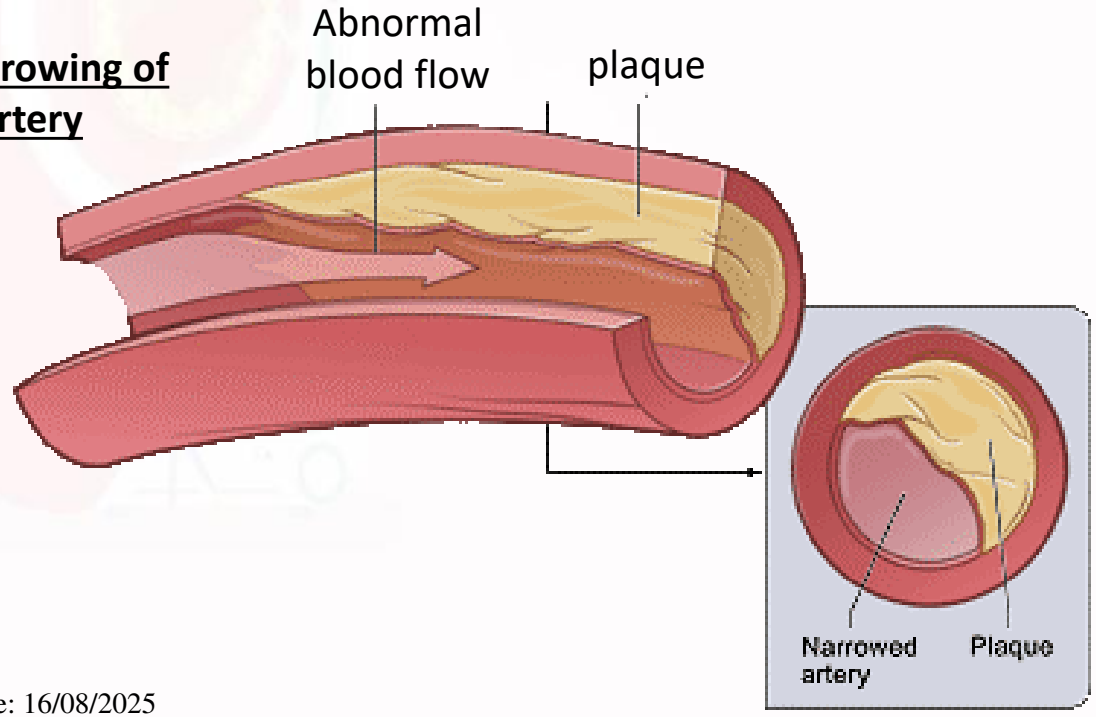
SA-6751 Expiration Date: 16/08/2025

Definition(10)

Atherosclerosis

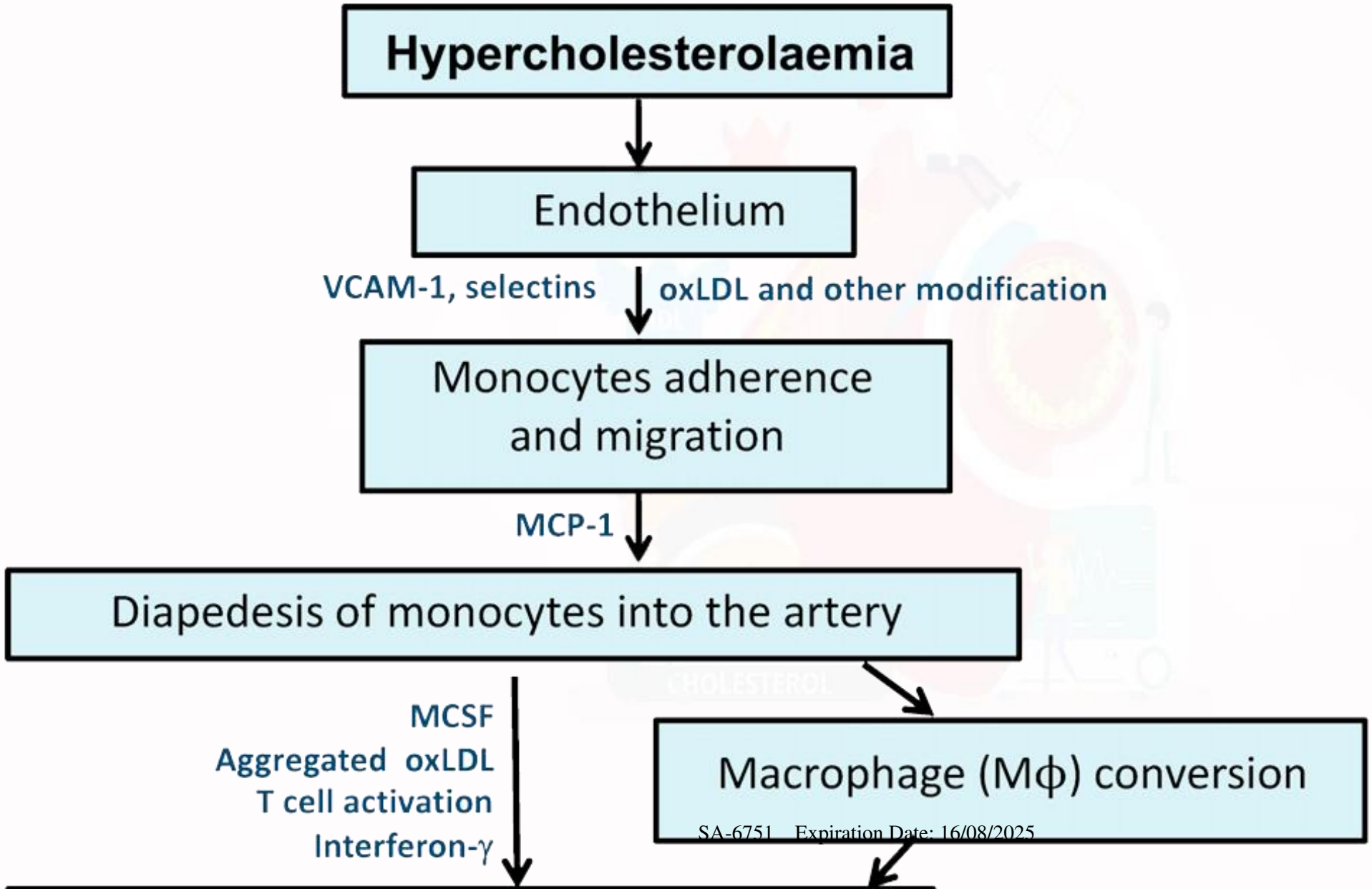
A chronic inflammatory disease of large and medium-sized arteries that causes ischemic heart disease, strokes, and peripheral vascular disease, collectively called cardiovascular disease (CVD).





10. Sacks FM, Lichtenstein AH, Wu JHY, Appel LJ, Creager MA, Kris-Etherton PM, Miller M, Rimm EB, Rudel LL, Robinson JG, Stone NJ, Van Horn LV., American Heart Association. Dietary Fats and Cardiovascular Disease: A Presidential Advisory From the American Heart Association. Circulation. 2017 Jul 18;136(3):e1-e23.

Pathophysiology(11)



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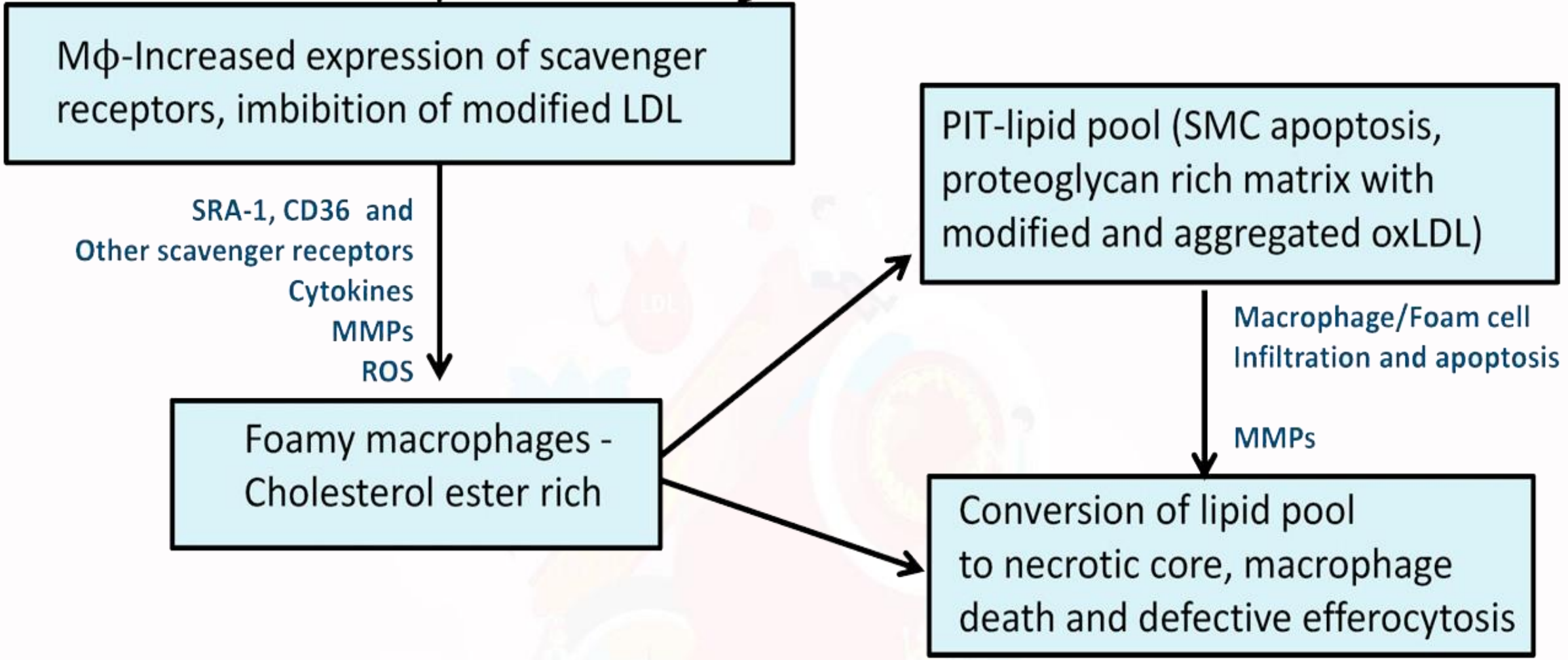
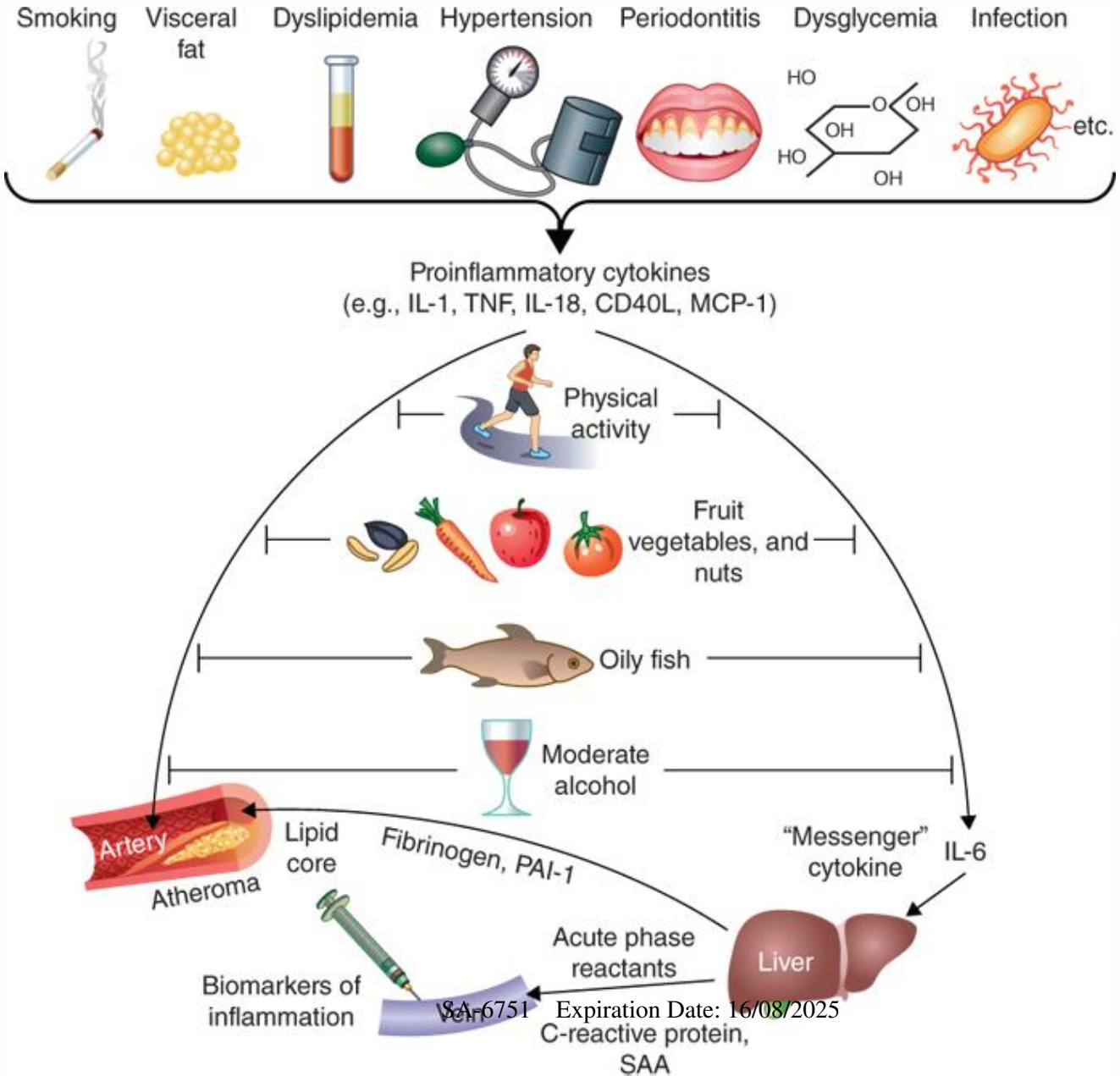


11. Wang HH, Garruti G, Liu M, Portincasa P, Wang DQ. Cholesterol and Lipoprotein Metabolism and Atherosclerosis: Recent Advances In reverse Cholesterol Transport. Ann Hepatol. 2017 Nov;16(Suppl. 1: s3-105.):s27-s42.

Risk factors and their modification



Rheumatologic conditions can ↑ the pathogenesis of atherosclerosis[12]

☠ **Patients with inflammatory rheumatic diseases such as:**

Rheumatoid arthritis

Systemic lupus erythematosis

Vasculitides

Have a higher burden of traditional risk factors for atherosclerosis than well individuals.

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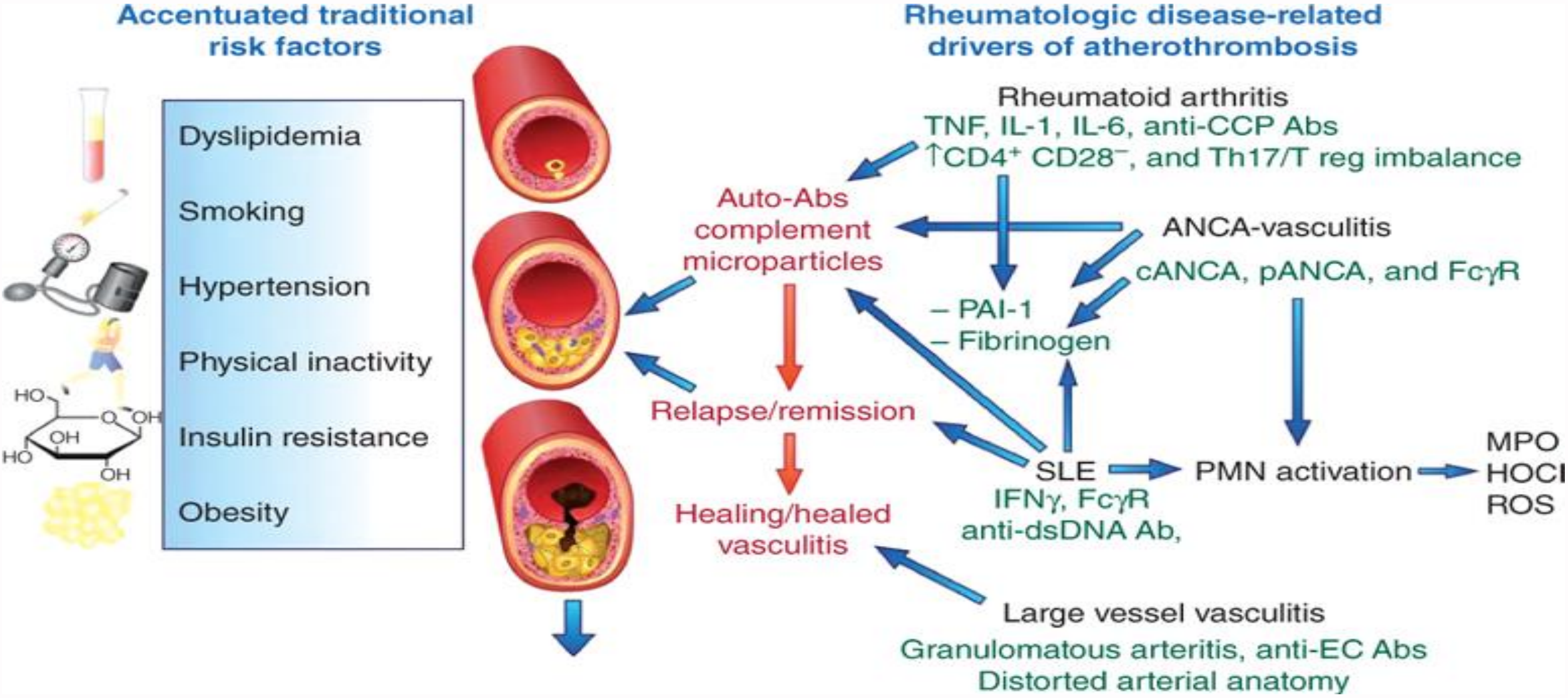
12. Sacks FM, Lichtenstein AH, Wu JHY, Appel LJ, Creager MA, Kris-Etherton PM, Miller M, Rimm EB, Rudel LL, Robinson JG, Stone NJ, Van Horn LV., American Heart Association. Dietary Fats and Cardiovascular Disease: A Presidential Advisory From the American Heart Association. Circulation. 2017 Jul 18;136(3):e1-e23.

Rheumatologic conditions can ↑ the pathogenesis of atherosclerosis



Abbreviations: Ab, antibody; ANCA, antineutrophil cytoplasmic antibody; dsDNA, double-stranded DNA; CCP, cyclic citrullinated peptide; EC, endothelial cells; IFN, interferon; FcγR, Fc gamma receptor; HOCL, hypochloride; MPO, myeloperoxidase; ROS, reactive oxygen species; T reg, regulatory T lymphocytes

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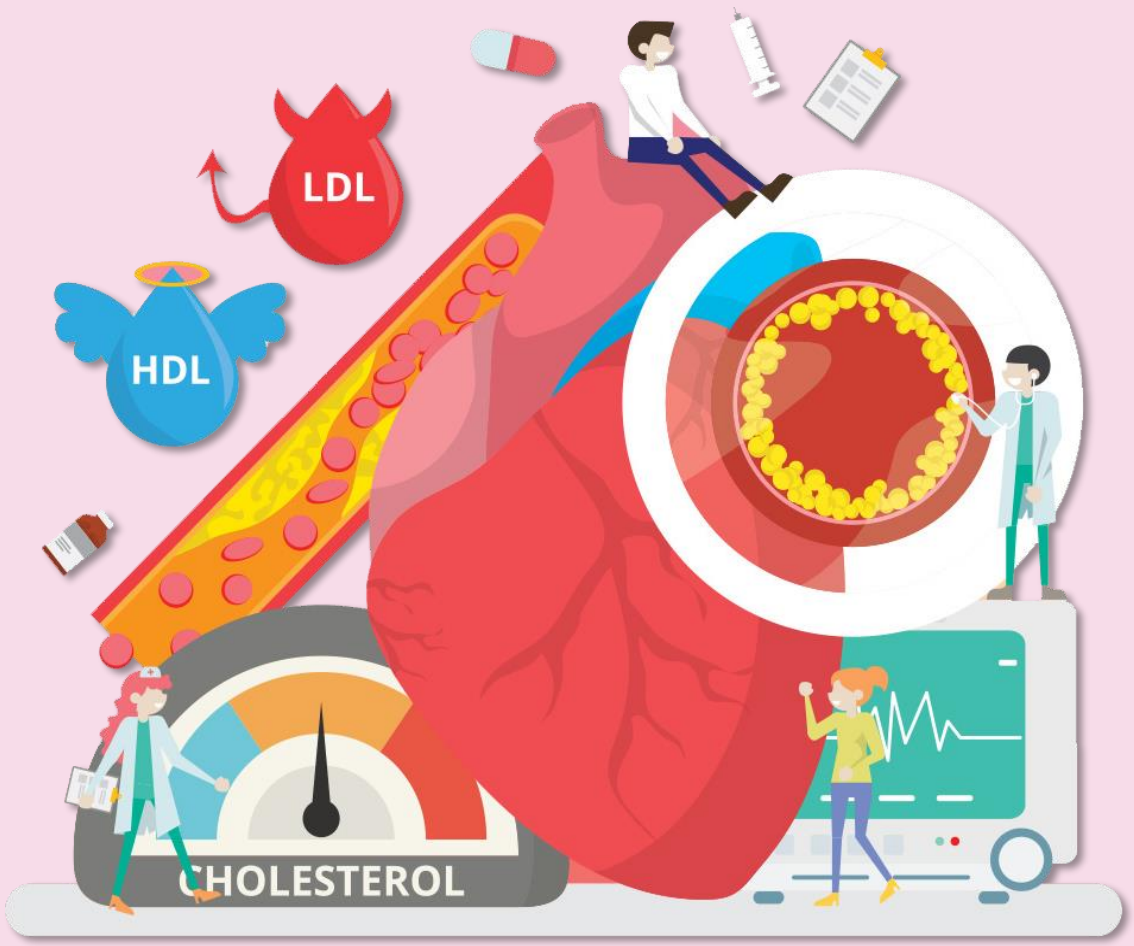

6. Diabetes Dyslipidemia pathophysiolog

SA-6751 Expiration Date: 16/08/2025

Introduction[13,14]

Serum lipid abnormalities (dyslipidemia) are commonly seen in diabetic populations irrespective of insulin deficiency or insulin resistance.

LDL Is the most important risk factor for atherosclerotic cardiovascular disease (CVD) such as coronary artery diseases.

Severe hypercholesterolemia is not frequently observed in diabetic populations, rather hypertriglyceridemia and low HDL are more common.

13. Hirano T. Pathophysiology of Diabetic Dyslipidemia. J Atheroscler Thromb. 2018;25(9):771–782. doi:10.5551/jat.RV17023.
14. Feingold KR, Grunfeld C. Diabetes and Dyslipidemia. [Updated 2019 Jan 3]. In: Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: ncbi.nlm.nih.gov/books/NBK305900/.

Introduction[13,14]

↳A representative cohort study for Japanese populations with type 2 diabetic has revealed that :

The serum TG levels Are a leading predictor of CVD, comparable to LDL-C, which exceeded the predictive power of HbA1c .

Dyslipidemia is more powerful CVD risk than hyperglycemia even in diabetic populations whose blood glucose levels are substantially high.

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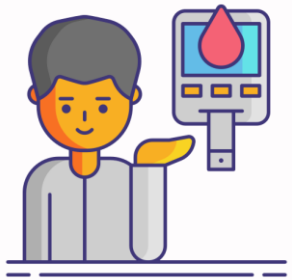
13. Hirano T. Pathophysiology of Diabetic Dyslipidemia. J Atheroscler Thromb. 2018;25(9):771–782. doi:10.5551/jat.RV17023.
14. Feingold KR, Grunfeld C. Diabetes and Dyslipidemia. [Updated 2019 Jan 3]. In: Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: ncbi.nlm.nih.gov/books/NBK305900/.

Lipid abnormalities in patients with diabetes[13,14]

01 In patients with Type 1 diabetes in good glycemic control, the lipid profile is very similar to lipid profiles in the general population.

02 In patients with Type 2 diabetes, even when in good glycemic control, there are abnormalities in lipid levels.



30-60% of patients with Type 2 diabetes have dyslipidemia.

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13. Hirano T. Pathophysiology of Diabetic Dyslipidemia. J Atheroscler Thromb. 2018;25(9):771–782. doi:10.5551/jat.RV17023.
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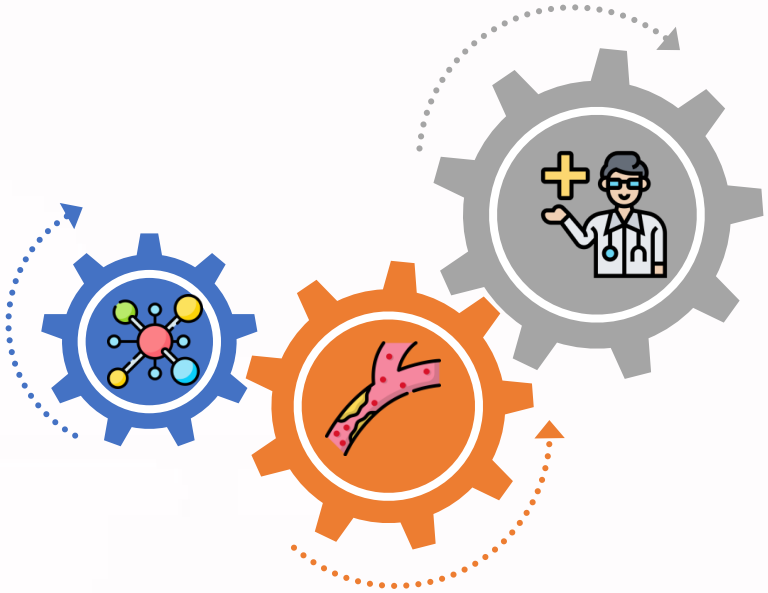
Lipid abnormalities in patients with diabetes[13,14]

01 Non-HDL cholesterol levels are increased due to the increase in VLDL and IDL.

02 LDL cholesterol levels are typically not different than in normal subjects but there is an increase in small dense LDL, a lipoprotein particle that may be particularly pro-atherogenic.



03 As consequences there are more LDL particles, which coupled with the increases in VLDL and IDL, leads to an increase in Apo B.

13. Hirano T. Pathophysiology of Diabetic Dyslipidemia. J Atheroscler Thromb. 2018;25(9):771–782. doi:10.5551/jat.RV17023.
14. Feingold KR, Grunfeld C. Diabetes and Dyslipidemia. [Updated 2019 Jan 3]. In: Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: ncbi.nlm.nih.gov/books/NBK305900/.

Lipid abnormalities in patients with diabetes[13,14]

- ✓ **The ability of HDL to facilitate cholesterol efflux is ↓ in patients with Type 2 diabetes.**
- ✓ **Studies have shown that the HDL isolated from patients with diabetes has :**

1

↓ Anti-oxidant functions

2

↓ Anti-inflammatory functions

Indicating that HDL levels may not fully reflect risk.

The postprandial ↑ in serum TG is accentuated and elevations in postprandial lipids may increase the risk of cardiovascular disease.

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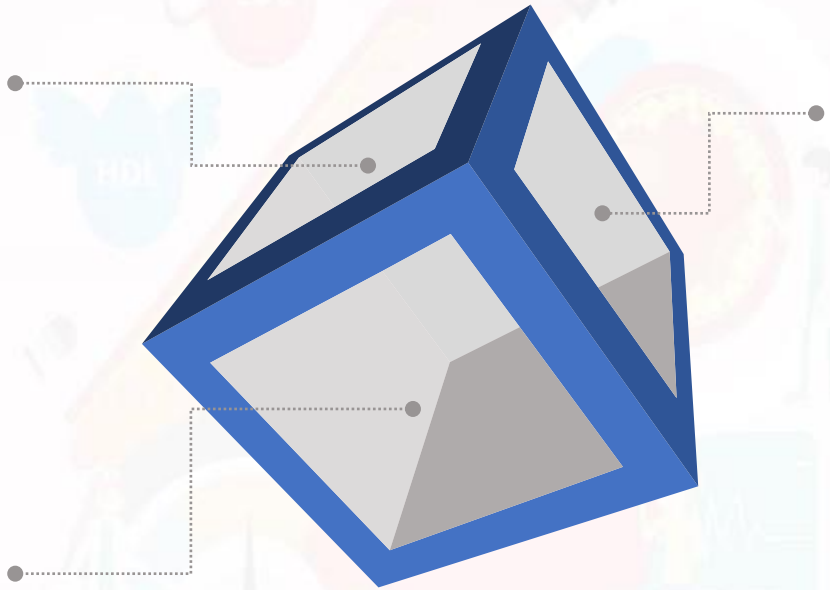
13. Hirano T. Pathophysiology of Diabetic Dyslipidemia. J Atheroscler Thromb. 2018;25(9):771–782. doi:10.5551/jat.RV17023.
14. Feingold KR, Grunfeld C. Diabetes and Dyslipidemia. [Updated 2019 Jan 3]. In: Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: ncbi.nlm.nih.gov/books/NBK305900/.

Lipid abnormalities in patients with diabetes[13,14]

☠ Since a high percentage of patients with Type 2 diabetes are obese, insulin resistant and have the metabolic syndrome, it is not surprising that the prevalence of :

Increased TG

Decreased HDL



Increased LDL

Is common in patients with Type 2 diabetes even when these patients are in good glycemic control.

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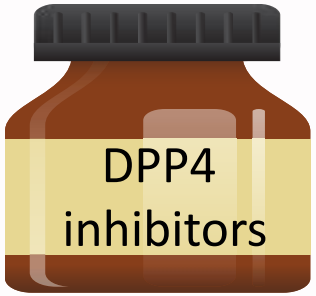
13. Hirano T. Pathophysiology of Diabetic Dyslipidemia. J Atheroscler Thromb. 2018;25(9):771–782. doi:10.5551/jat.RV17023.
14. Feingold KR, Grunfeld C. Diabetes and Dyslipidemia. [Updated 2019 Jan 3]. In: Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: ncbi.nlm.nih.gov/books/NBK305900/.

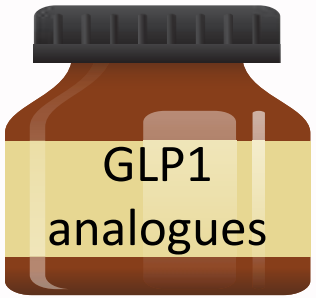
Lipid abnormalities in patients with diabetes[13,14]

↓ TG and modestly ↓ LDLc

No effect

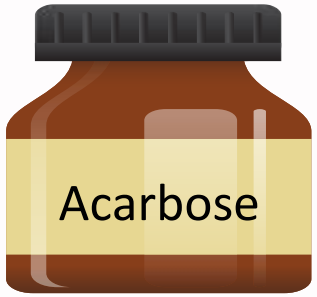


↓ Postprandial TG



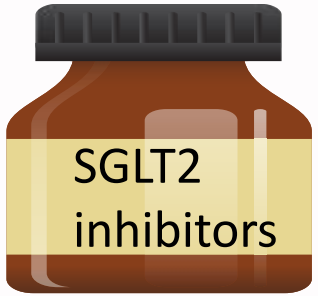
↓ Fasting and postprandial TG and ↑ HDLc

Lipid abnormalities in patients with diabetes[13,14]



↓ Postprandial TG

↓ TG and ↑ HDLc. Small ↑ LDLc but a ↓ in LDL

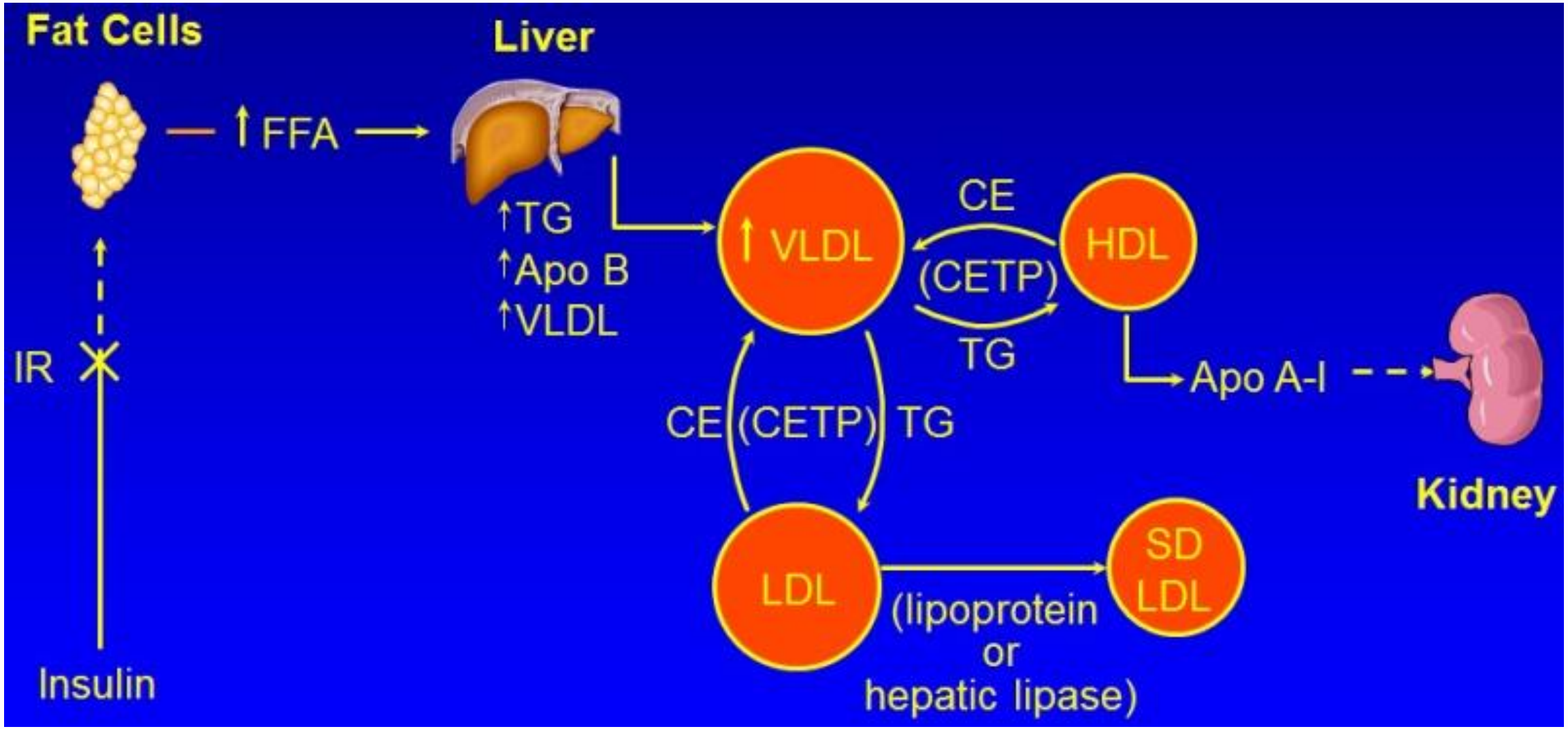


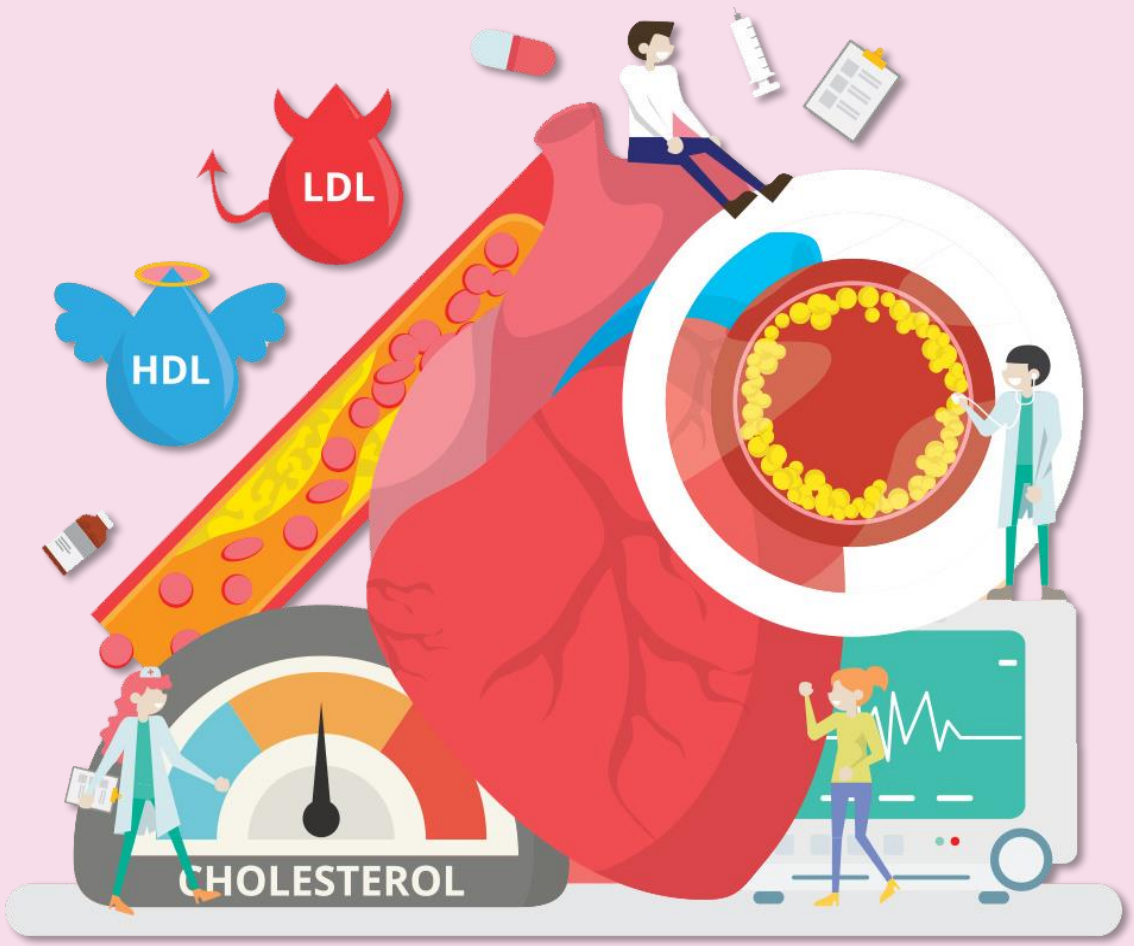
Small ↑ in LDLc and HDLc

Insulin

No effect

Pathophysiology of the dyslipidemia of diabetes





7. Local epidemiological data

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Prevalence of dyslipidemia in the middle east (ME)[15]

Study name (country) year	N	Age	Guidelines or cut off values	Dyslipidaemia prevalence
NHANESa (USA)	4275	45.4 ± 0.5	Updated NCEP ATP III[b] guideline[g]	0.529
MESAc (USA)	6814	45–84	Updated NCEP ATP IIIb guideline	0.293
Canadian Health Measures Survey (Canada)	1701	20–79	TC/HDL-C ratio ≥ 5; LDL-C ≥ 4.9 mmol/L (190 mg/dL)	0.45
GEMCASd (Germany)	35869	18–99	European guidelinesh	0.76
Brazilian Society of Cardiology (Brazil)	1000	11–16	TC > 4.3 mmol/L (170 mg/dL)	0.61
Gulf RACE-2e (Arabian Gulf Countries)	7930	56 ± 17	Updated NCEP ATP III guideline	0.327
ACEf study (Africa and Middle East)	4378	46 ± 14	Updated NCEP ATP III guideline	0.7

15. Al Rasadi K, Almahmeed W, AlHabib KF, et al. Dyslipidaemia in the Middle East: Current status and a call for action. Atherosclerosis. 2016;252:182–187. doi:10.1016/j.atherosclerosis.2016.07.925.

Dyslipidemia prevalence and groups at increased risk in the ME[16]

	Middle East		
	Egypt	Saudi Arabia	UAE
Overall prevalence in adults	76% overall	High TC, 8.5%; high TG, 8.5%; high LDL-C, 7.4% low HDL-C, 48.7%	44–75% overall
Groups at increased risk	—	Increasing age	Male sex, increasing age

16. Alshamiri M, Ghanaim MMA, Barter P, et al. Expert opinion on the applicability of dyslipidemia guidelines in Asia and the Middle East. Int J Gen Med. 2018;11:313–322. Published 2018 Jul 18. doi:10.2147/IJGM.S160555.

CEPHEUS study[17] (CEntralized Pan-Levant Survey on tHE Undertreatment of hypercholeSterolemia)

Objective

Study evaluated reaching **LDL-C** treatment goals among dyslipidemic individuals using **LLAs** as per international guidelines in the Levant region (Jordan and Lebanon). It also examined the physician- and patient-related factors that influence reaching those goals.

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17. Hammoudeh AJ, Echtay A, Ghanem GY, Haddad J; CEPHEUS-Levant survey investigators. Achieving low-density lipoprotein cholesterol treatment goals among dyslipidemic individuals in the Levant: the CEntralized Pan-Levant survey on tHE Undertreatment of hypercholeSterolemia (CEPHEUS) study. Curr Med Res Opin. 2014;30(10):1957–1965. doi:10.1185/03007995.2014.929095

CEPHEUS study[17] (CEntralized Pan-Levant Survey on tHE Undertreatment of hyperchole Sterolemia)

Methods

It’s a multi-center, cross-sectional survey, enrolled 1002 dyslipidemic patients (August 2010 – January 2011) on LLAs for ≥3 months.

Collection of data and blood samples was done over one visit. Physicians and patients filled out questionnaires pertaining to dyslipidemia diagnosis and treatment.

LDL-C target level were defined according to international guidelines.

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17. Hammoudeh AJ, Echtay A, Ghanem GY, Haddad J; CEPHEUS-Levant survey investigators. Achieving low-density lipoprotein cholesterol treatment goals among dyslipidemic individuals in the Levant: the CEntralized Pan-Levant survey on tHE Undertreatment of hypercholeSterolemia (CEPHEUS) study. Curr Med Res Opin. 2014;30(10):1957–1965. doi:10.1185/03007995.2014.929095

CEPHEUS study[17] (CEntralized Pan-Levant Survey on tHE Undertreatment of hyperchole Sterolemia)

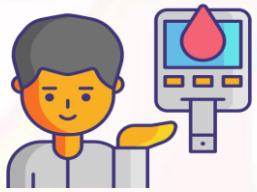
Results

The full analysis set included

992 patients

Mean age was 58.0±11.6 years

41% women



65.7% diabetics

51.5% CHD

LLAs were prescribed for:

1. Primary prevention — **45.8%** of patients
2. Secondary prevention — **52.8%** of patients
3. Familial hypercholesterolemia — **45.8%** of patients

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17. Hammoudeh AJ, Echtay A, Ghanem GY, Haddad J; CEPHEUS-Levant survey investigators. Achieving low-density lipoprotein cholesterol treatment goals among dyslipidemic individuals in the Levant: the CEntralized Pan-Levant survey on tHE Undertreatment of hypercholeSterolemia (CEPHEUS) study. Curr Med Res Opin. 2014;30(10):1957–1965. doi:10.1185/03007995.2014.929095

CEPHEUS study[17] (CEntralized Pan-Levant Survey on tHE Undertreatment of hyperchole Sterolemia)

Results

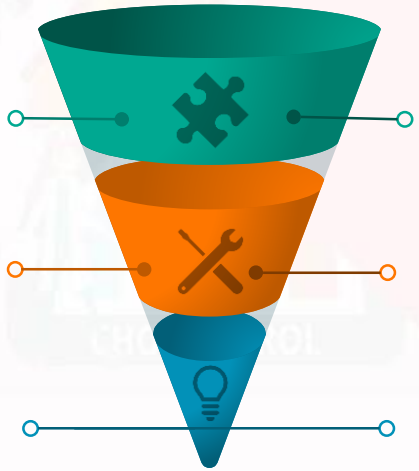
✓ According to the NCEP ATP III guidelines, **64.0%** of patients reached the LDL-C treatment goal.

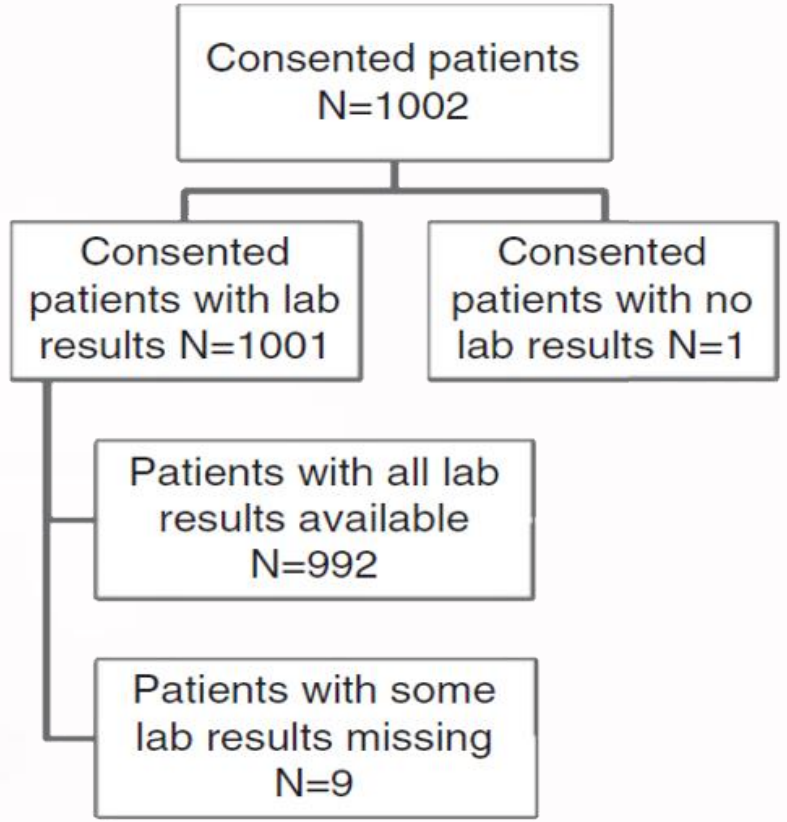
🏳 This goal was reached by:

60.0% of the high-risk patients — n=458

76.1% of the medium risk patients — n=159

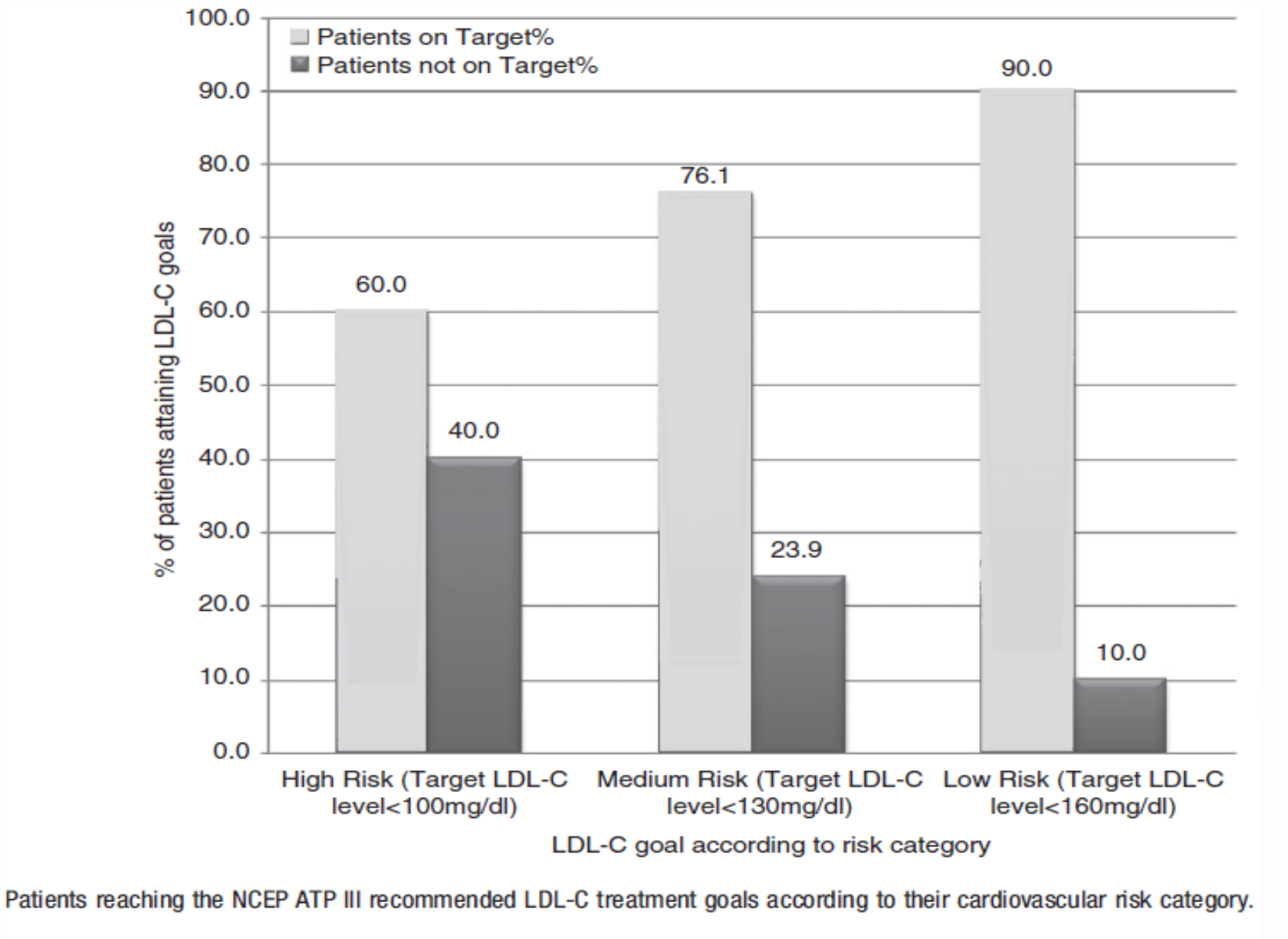
90.0% of the low risk patients — n=18





Patients' disposition.

17. Hammoudeh AJ, Echtay A, Ghanem GY, Haddad J; CEPHEUS-Levant survey investigators. Achieving low-density lipoprotein cholesterol treatment goals among dyslipidemic individuals in the Levant: the CEntralized Pan-Levant survey on tHE Undertreatment of hypercholeSterolemia (CEPHEUS) study. Curr Med Res Opin. 2014;30(10):1957–1965. doi:10.1185/03007995.2014.929095



Patients reaching the NCEP ATP III recommended LDL-C treatment goals according to their cardiovascular risk category.

According to the updated 2004 NCEP ATP III guidelines, **42.3%** of patients reached treatment goals. Moreover, treatment goals were attained by **86.5%** of low risk patients, **77.6%** of low medium risk patients; **52.8%** of the high but not very high risk group and **24.8%** of the very high risk patients.

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CEPHEUS study[17] (CEntralized Pan-Levant Survey on tHE Undertreatment of hyperchole Sterolemia)

Conclusions

A relatively large proportion of hypercholesterolemic patients using LLAs in the Levant area, especially those in the high risk group, **did not attain LDL-C treatment goals**, and thus remain at a substantial risk of developing adverse cardiac events.

✓ Aggressive efforts are urgently needed to :

- Optimize healthcare professionals' implementation of dyslipidemia treatment guidelines
- Enhance patients' awareness of the risk of dyslipidemia
- Enhance the benefits of chronic use of LLAs and the importance of reaching treatment goals.

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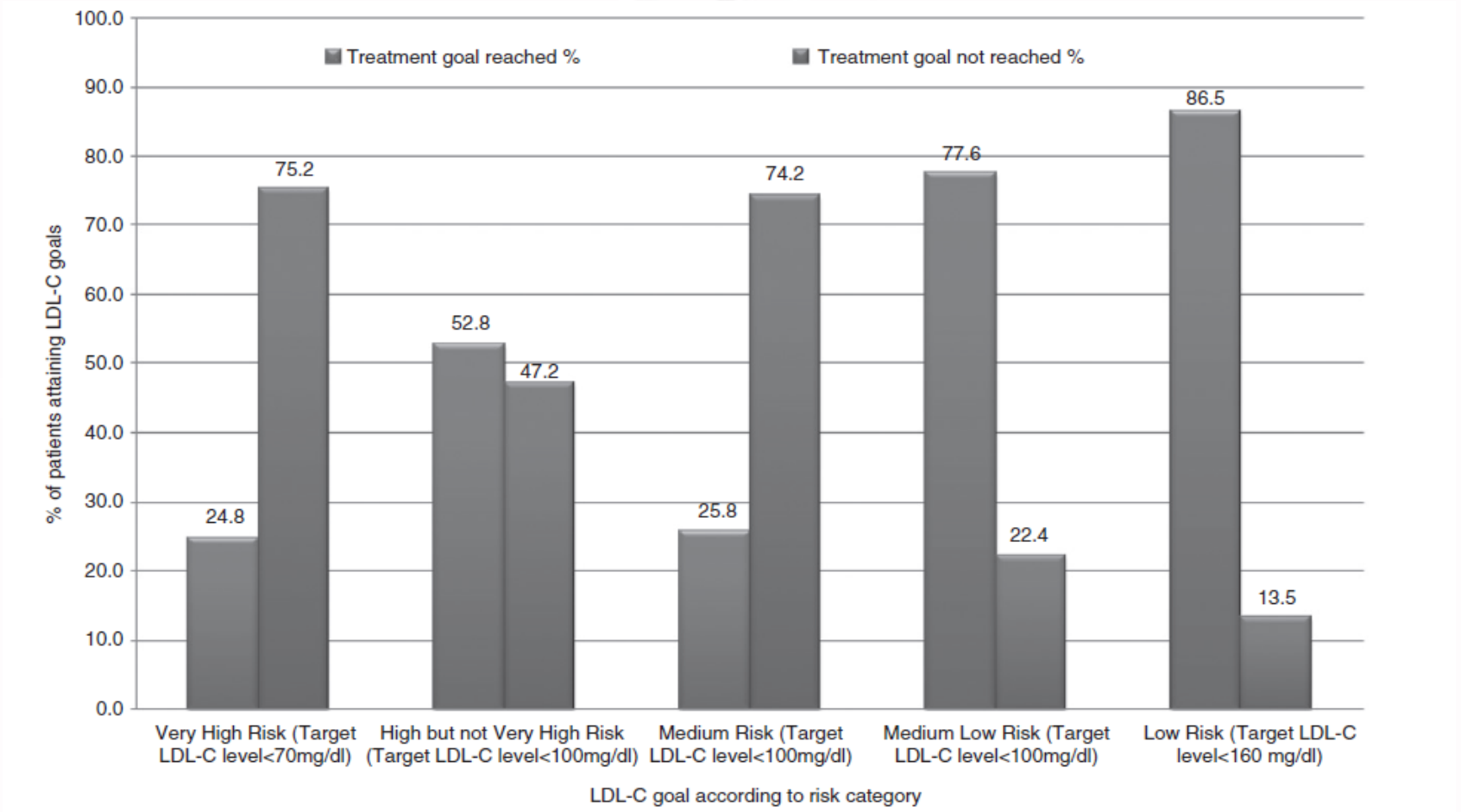
CEPHEUS study[17] (CEntralized Pan-Levant Survey on tHE Undertreatment of hyperchole Sterolemia)

Conclusions



Patients reaching the recommended LDL-C treatment goals according to their cardiovascular risk category as per the 2004 updated NCEP ATP III guidelines.

17. Hammoudeh AJ, Echtay A, Ghanem GY, Haddad J; CEPHEUS-Levant survey investigators. Achieving low-density lipoprotein cholesterol treatment goals among dyslipidemic individuals in the Levant: the CEntralized Pan-Levant survey on tHE Undertreatment of hypercholeSterolemia (CEPHEUS) study. Curr Med Res Opin. 2014;30(10):1957–1965. doi:10.1185/03007995.2014.929095

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Signatory Approval (Certificate)	Noha Mohamed Medical 16-Aug-2023 08:31:06 GMT+0000

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