AEX: CAMPANHA COR(AÇÃO)

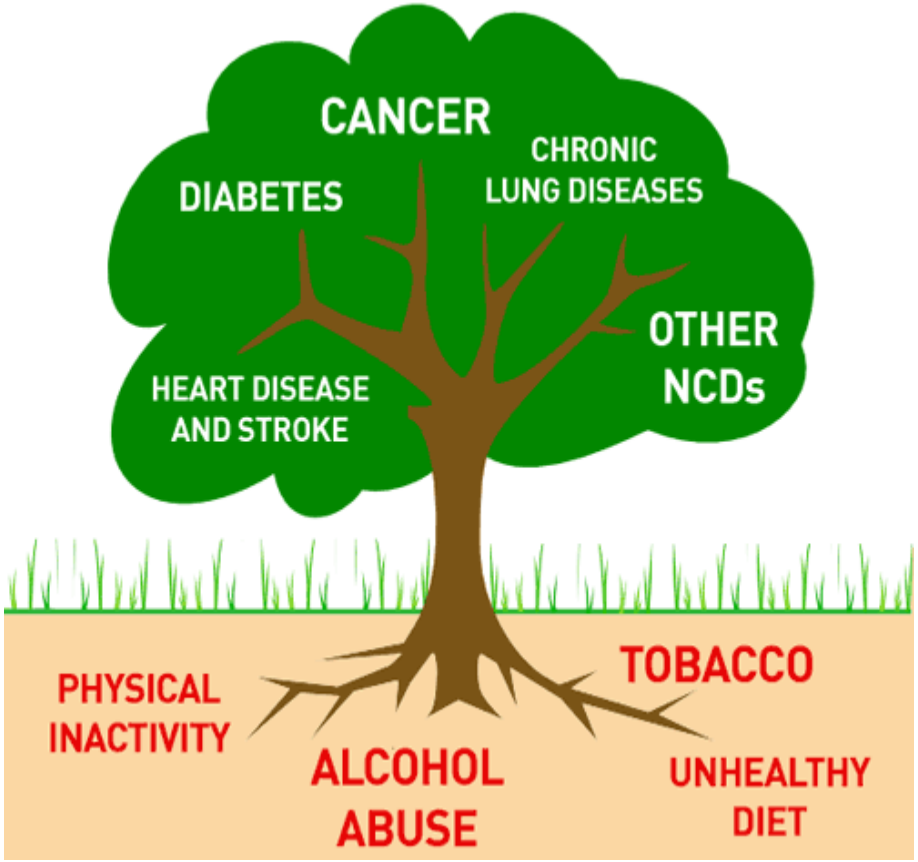
Aterosclerose e Doenças Cardiovasculares

Profa. Inar Castro

2024

Tópicos

1. Doenças Cardiovasculares
2. Fisiopatologia da Aterosclerose
3. Diretrizes
4. Dieta & Aterosclerose

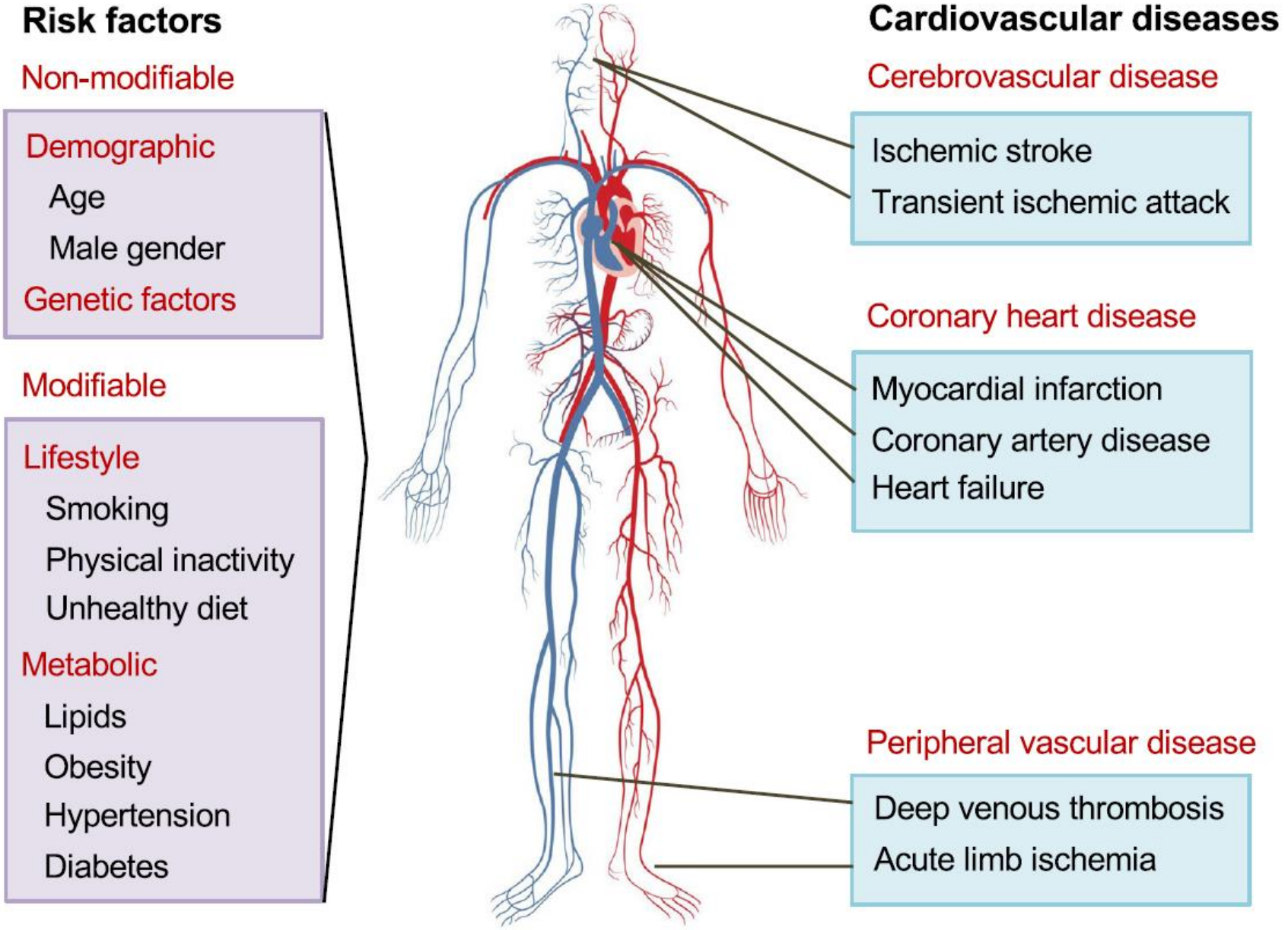


1. Doenças Cardiovasculares

Cardiovascular diseases (CVDs) are a group of disorders of the heart and blood vessels. They include:

- **coronary heart disease** – a disease of the blood vessels supplying the heart muscle;
- **cerebrovascular disease** – a disease of the blood vessels supplying the brain;
- **peripheral arterial disease** – a disease of blood vessels supplying the arms and legs;
- **rheumatic heart disease** – damage to the heart muscle and heart valves from rheumatic fever, caused by streptococcal bacteria;
- **congenital heart disease** – birth defects that affect the normal development and functioning of the heart caused by malformations of the heart structure from birth; and
- **deep vein thrombosis and pulmonary embolism** – blood clots in the leg veins, which can dislodge and move to the heart and lungs.

https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)



Cellular and Molecular Life Sciences (2021) 78:2565–2584

Heart attack and stroke

Often, there are no symptoms of the underlying disease of the blood vessels. A heart attack or stroke may be the first sign of underlying disease. Symptoms of a heart attack include:

- **pain or discomfort in the centre of the chest; and/or**
- **pain or discomfort in the arms, the left shoulder, elbows, jaw, or back.**

In addition the person may experience difficulty in breathing or shortness of breath; nausea or vomiting; light-headedness or faintness; a cold sweat; and turning pale. Women are more likely than men to have shortness of breath, nausea, vomiting, and back or jaw pain.

The most common symptom of a stroke is sudden weakness of the face, arm, or leg, most often on one side of the body.

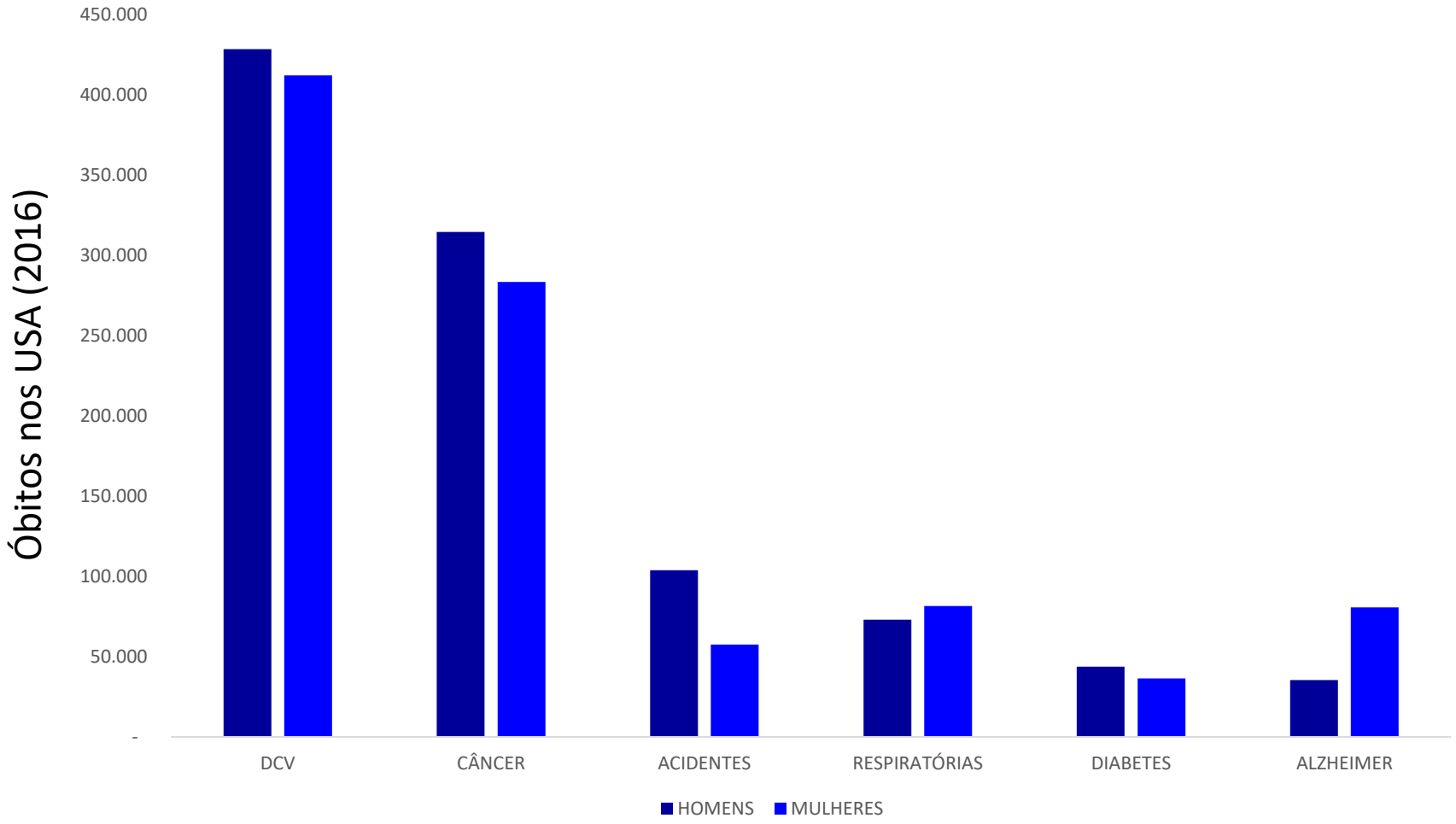
Other symptoms include sudden onset of:

- numbness of the face, arm, or leg, especially on one side of the body;
- confusion, difficulty speaking or understanding speech;
- difficulty seeing with one or both eyes;
- difficulty walking, dizziness and/or loss of balance or coordination;
- severe headache with no known cause; and/or
- fainting or unconsciousness.

People experiencing these symptoms should seek medical care immediately.

https://www.who.int/health-topics/cardiovascular-diseases#tab=tab_2

Doenças cardiovasculares e outras causas de mortalidade



National Heart, Lung and Blood Institute

2030 → 23 milhões óbitos

Benjamin et al. ***Circulation***, 2019.

JORNAL DA USP – QUARTA DIA 07/08/24

Lei Maria da Penha: 18 anos ser | Doenças cardiovasculares são a

jornal.usp.br/radio-usp/doencas-cardiovasculares-sao-a-principal-causa-de-mortes-no-brasil-segundo-o-ministerio-da-saude/

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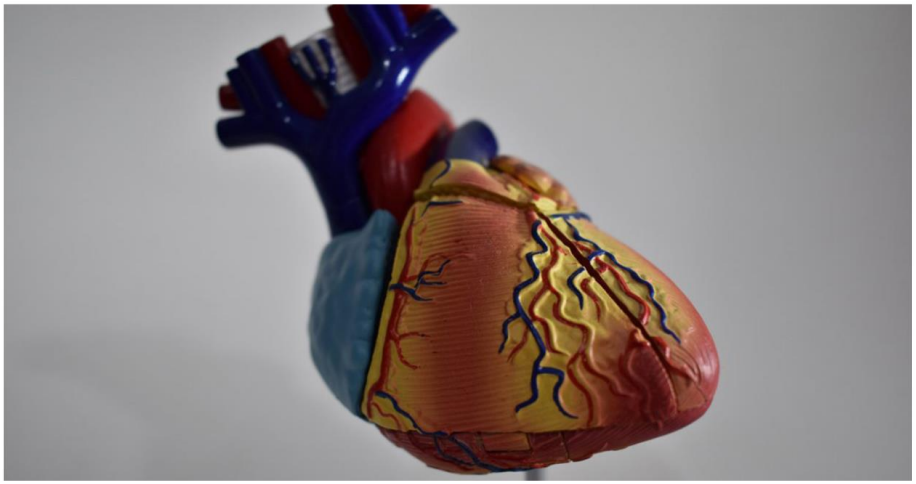
Doenças cardiovasculares são a principal causa de mortes no Brasil, segundo o Ministério da Saúde

Sérgio Timerman explica como identificar a angina, dor no peito relacionada ao infarto, e afirma que nesses casos é necessário agir rapidamente

Atualidades / Jornal da USP no Ar 1ª edição / Rádio USP - https://jornal.usp.br/?p=789024

Publicado: 06/08/2024



A realização de exames preventivos é uma boa dica no combate às doenças cardiovasculares – Foto: Jorge Romero por Pixabay

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06/08/2024
Por Horrara Moreira, pesquisadora da Cátedra Oscar Sala do Instituto de Estudos Avançados (IEA) da USP

É possível termos transparência de algoritmos para sistemas de

Key facts

- **Cardiovascular diseases (CVDs) are the leading cause of death globally.**

- **An estimated 17.9 million people died from CVDs in 2019, representing 32% of all global deaths. Of these deaths, 85% were due to heart attack and stroke.**

- **Over three quarters of CVD deaths take place in low- and middle-income countries.**

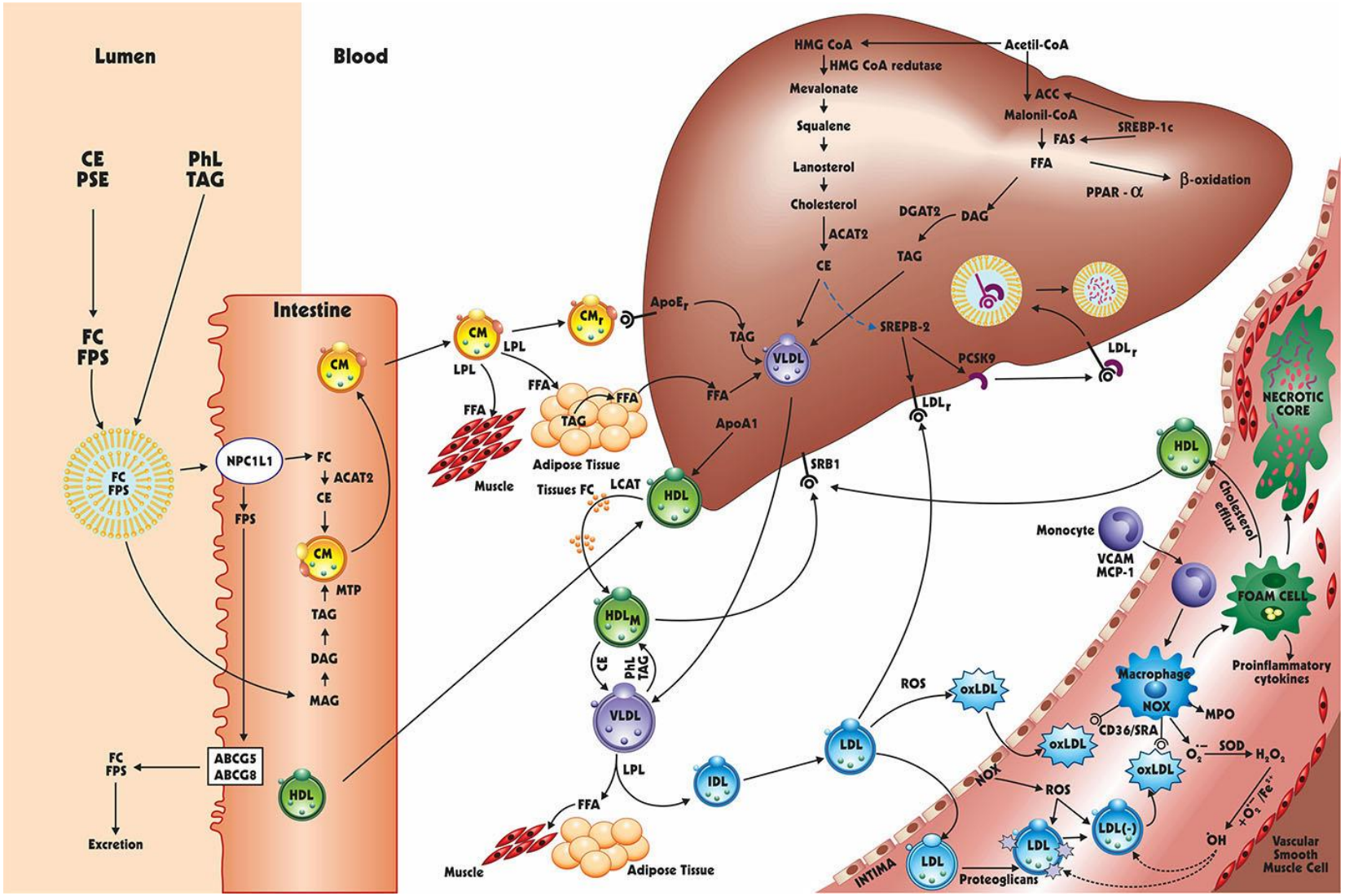
- **Out of the 17 million premature deaths (under the age of 70) due to noncommunicable diseases (não transmissíveis) in 2019, 38% were caused by CVDs.**

- **Most cardiovascular diseases can be prevented by addressing behavioural risk factors such as tobacco use, unhealthy diet and obesity, physical inactivity and harmful use of alcohol.**

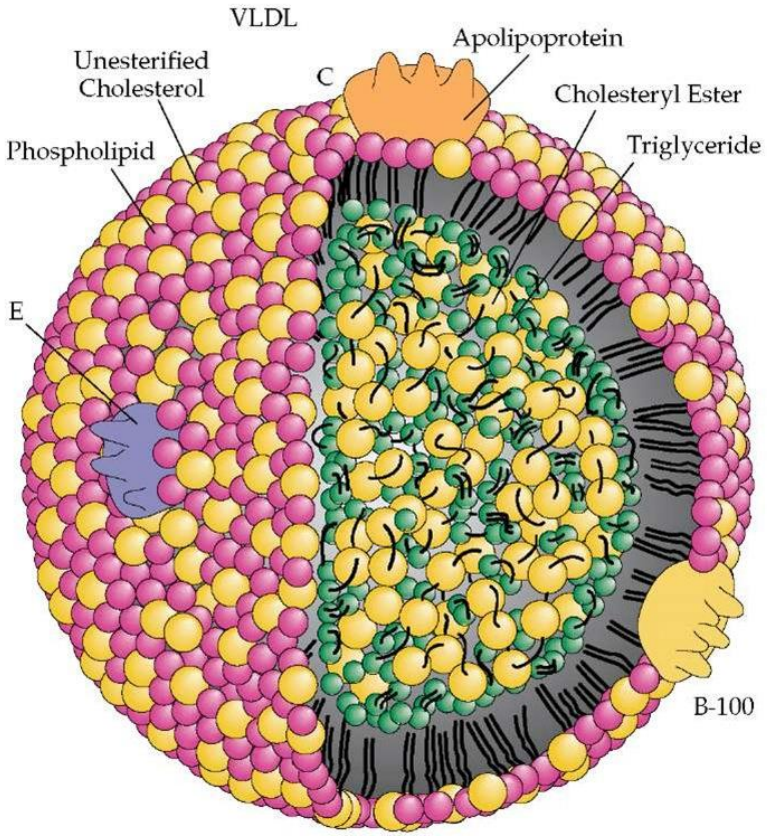
- **It is important to detect cardiovascular disease as early as possible so that management with counselling and medicines can begin.**

https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases

2. Fisiopatologia da aterosclerose



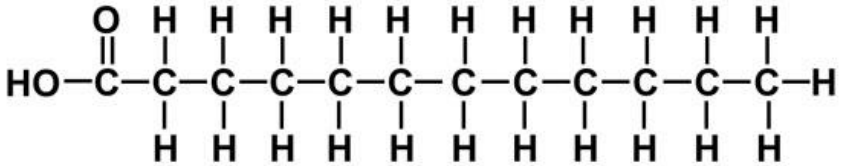
LDL - PARTICLE



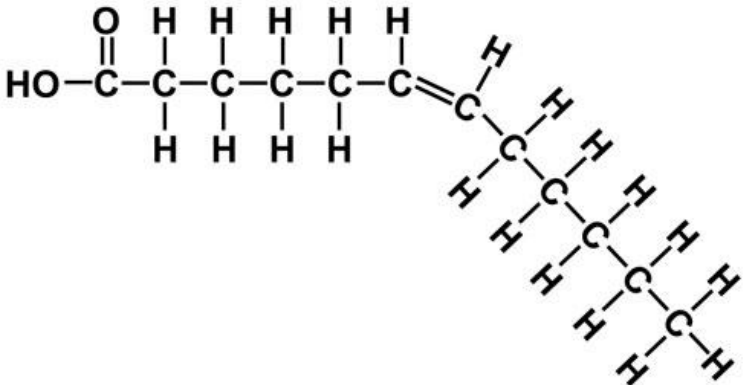
FATTY ACIDS

SATURATED
TRANS
POLYUNSATURATED

Saturated Fatty Acid

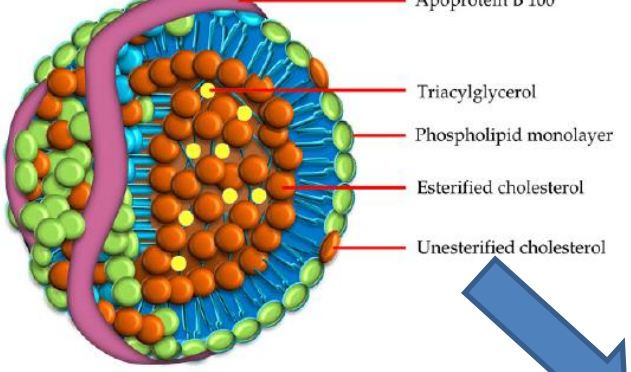


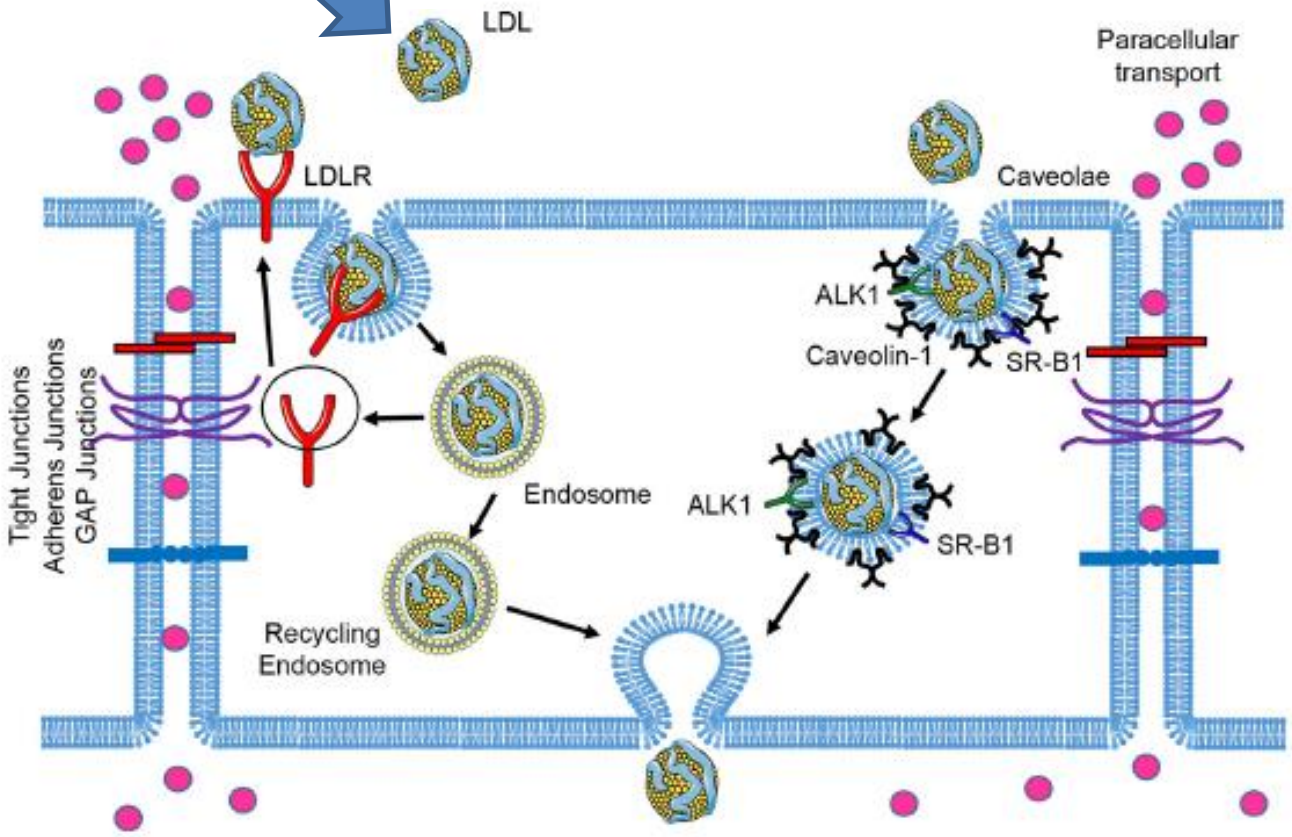
Unsaturated Fatty Acid



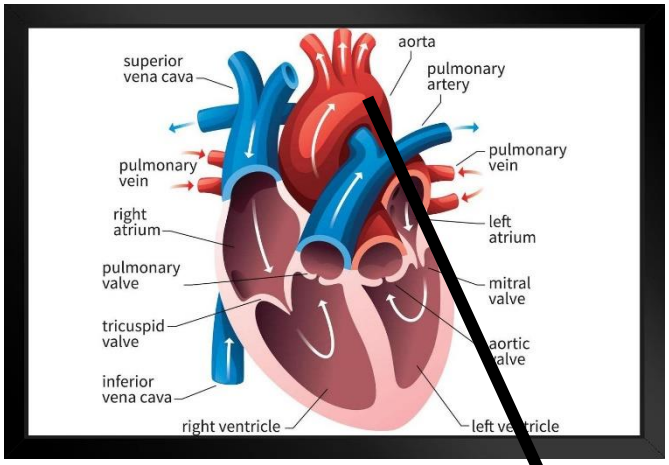
https://www.revolutionhealth.org/ldl-p/

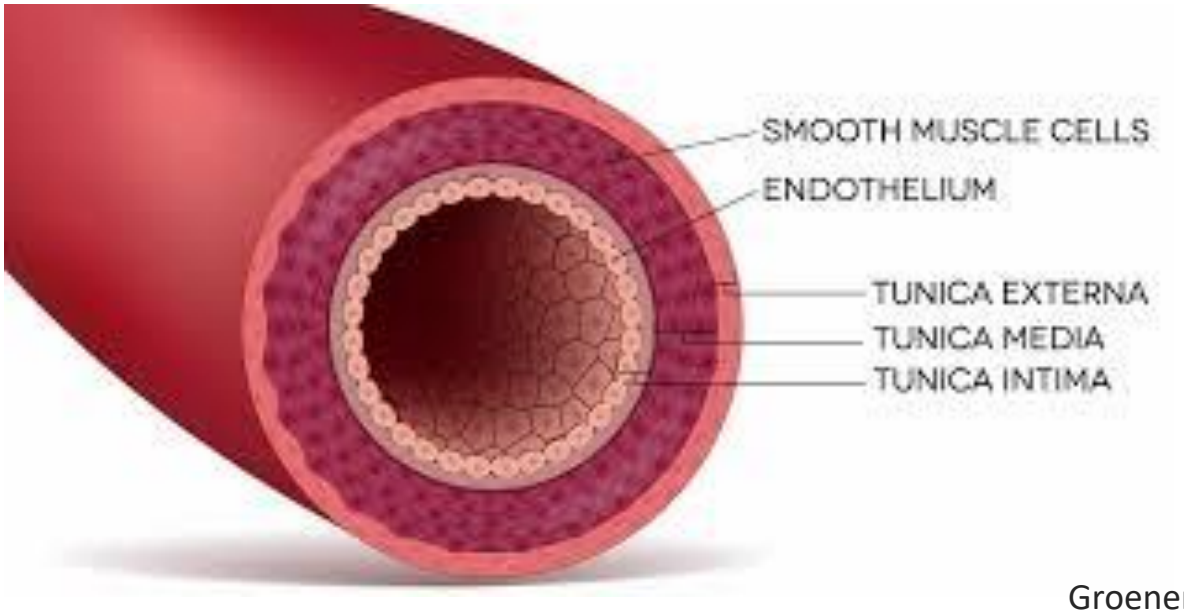
https://dlc.dcccd.edu/biology1-3/lipids





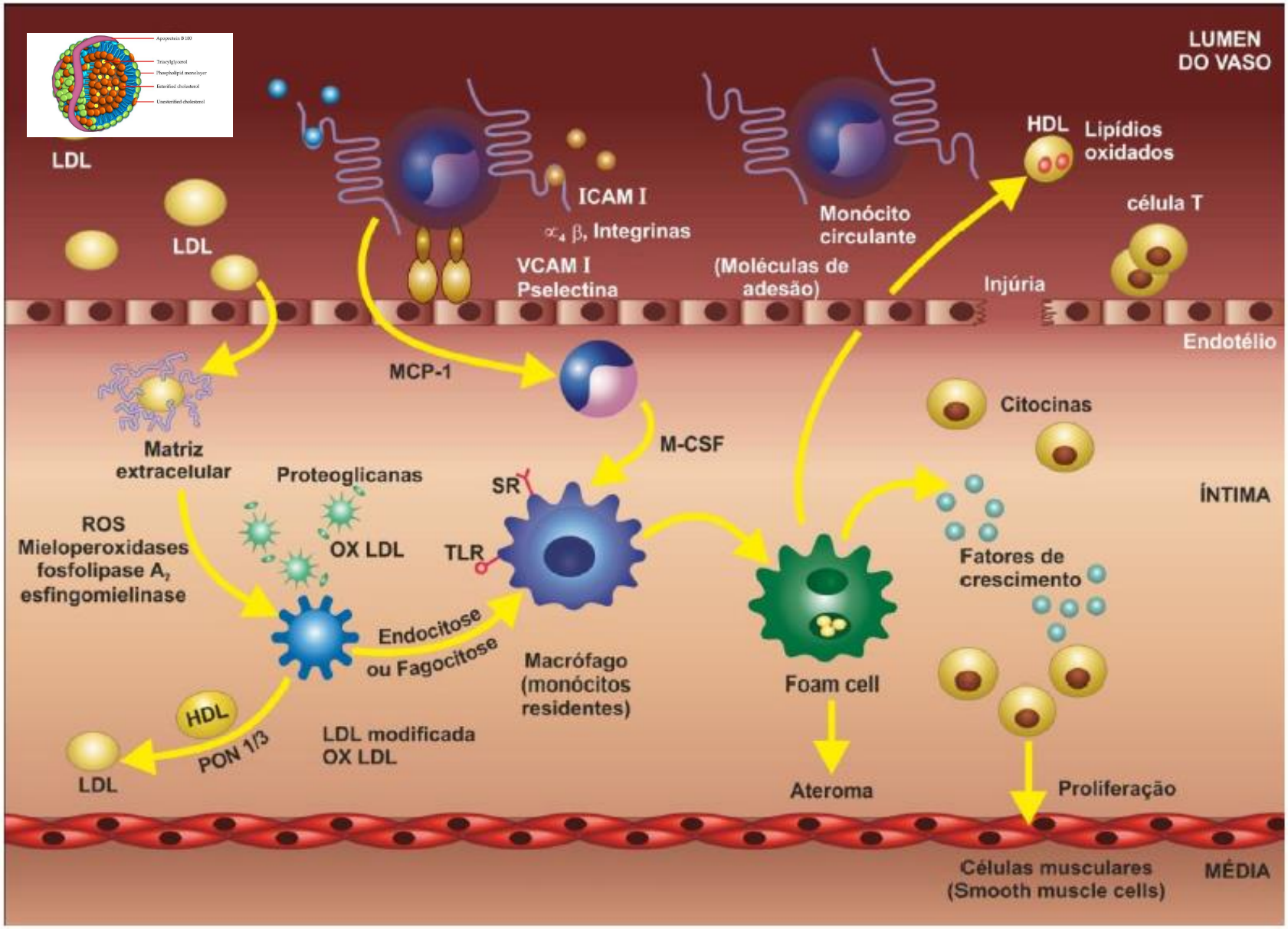
Zhang et al. (2018)





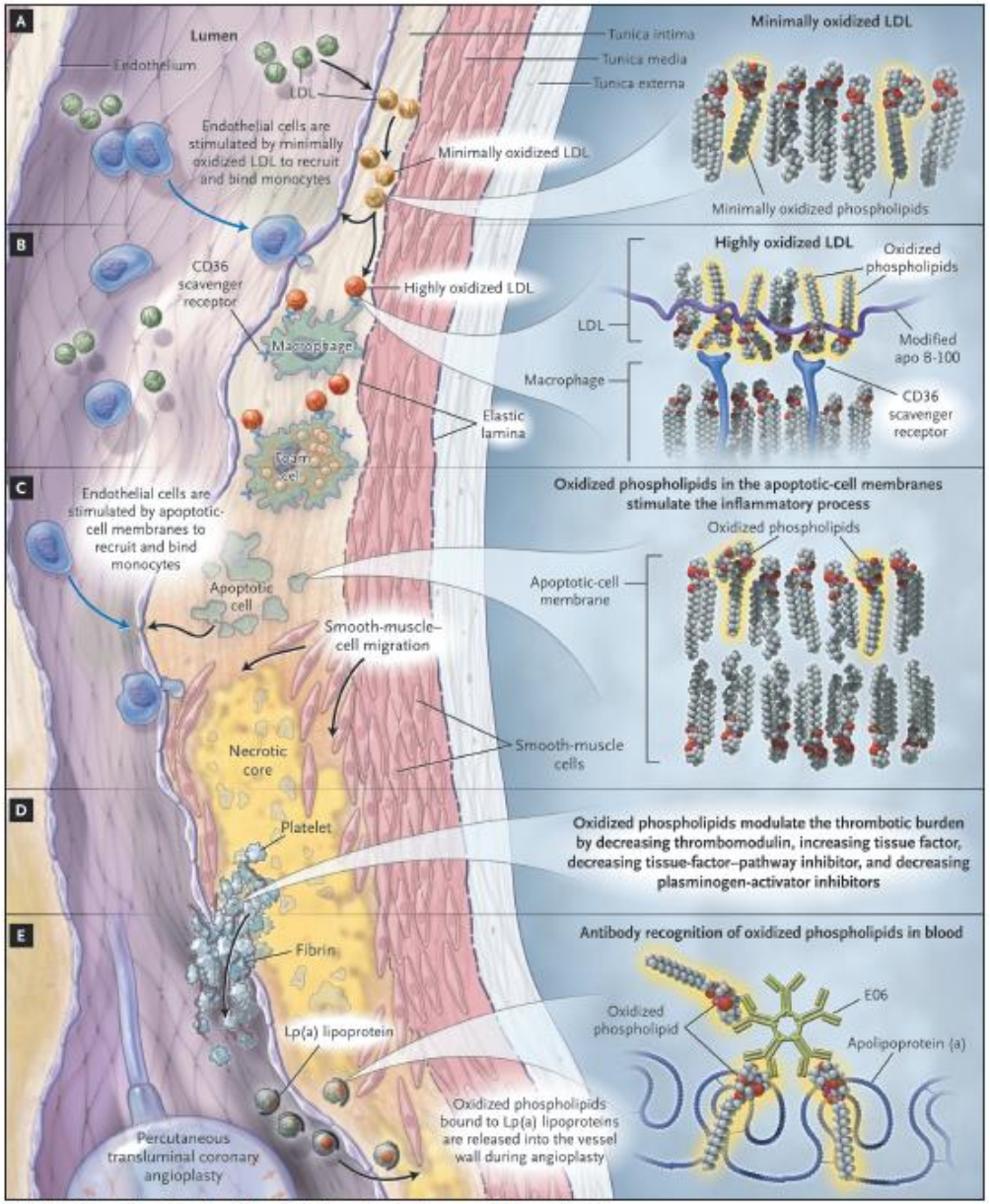
Groenendyk & Metha . ***BJM*** (2018)

Aterosclerose

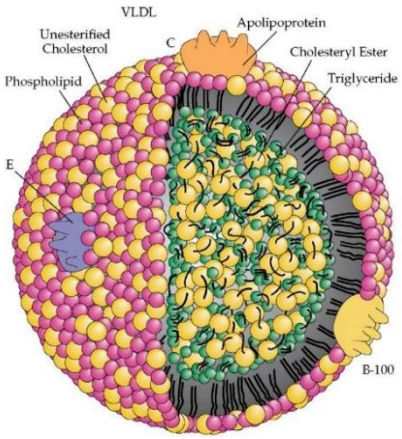


Adaptado de Rader & Daugherty. ***Nature*** (2008)

Pró-aterogenicidade de fosfolipídios oxidados

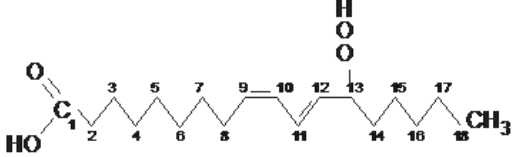


A Model of the Roles of Oxidized Phospholipids in the Development of Atherosclerosis.



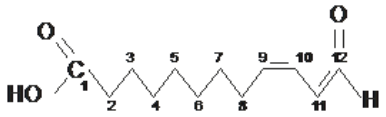
Que et al. **Nature** (2018)

Oxidação LNA



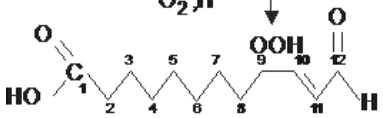
Linoleato 13 - Hidroperóxido

Clivagem



+ Hexanal

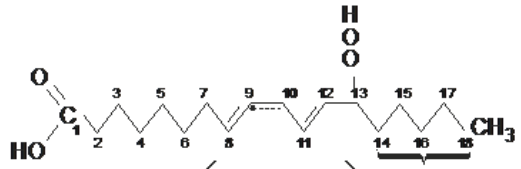
O_2, H^*



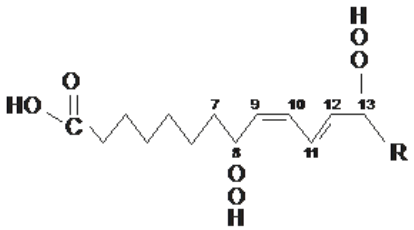
+

9 - Hidróxi - 12 OxO - 10 - Ácido Dodecenóico

11 - OxO - 9 - Ácido Undecenóico



O_2, H^*

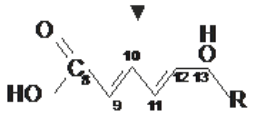


8,13 - dihidroperóxido

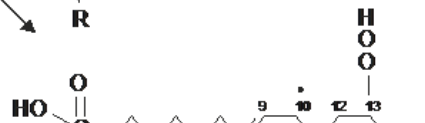
6 - hidroperoxi - 2,4 - Nonadienal

+

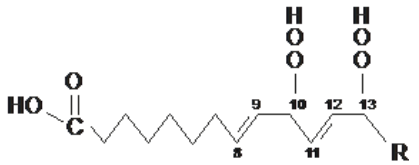
Ácido Heptanóico



6 - Hidroxi - 2,4 - Nonadienal



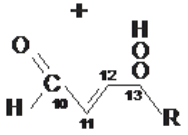
O_2, H^*



10,13 - dihidroperóxido

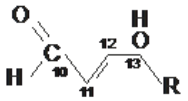
9 - ácido - 9 OxO - nonanóico

+



4 - hidroperoxi - 2 - Nonenal

Redução

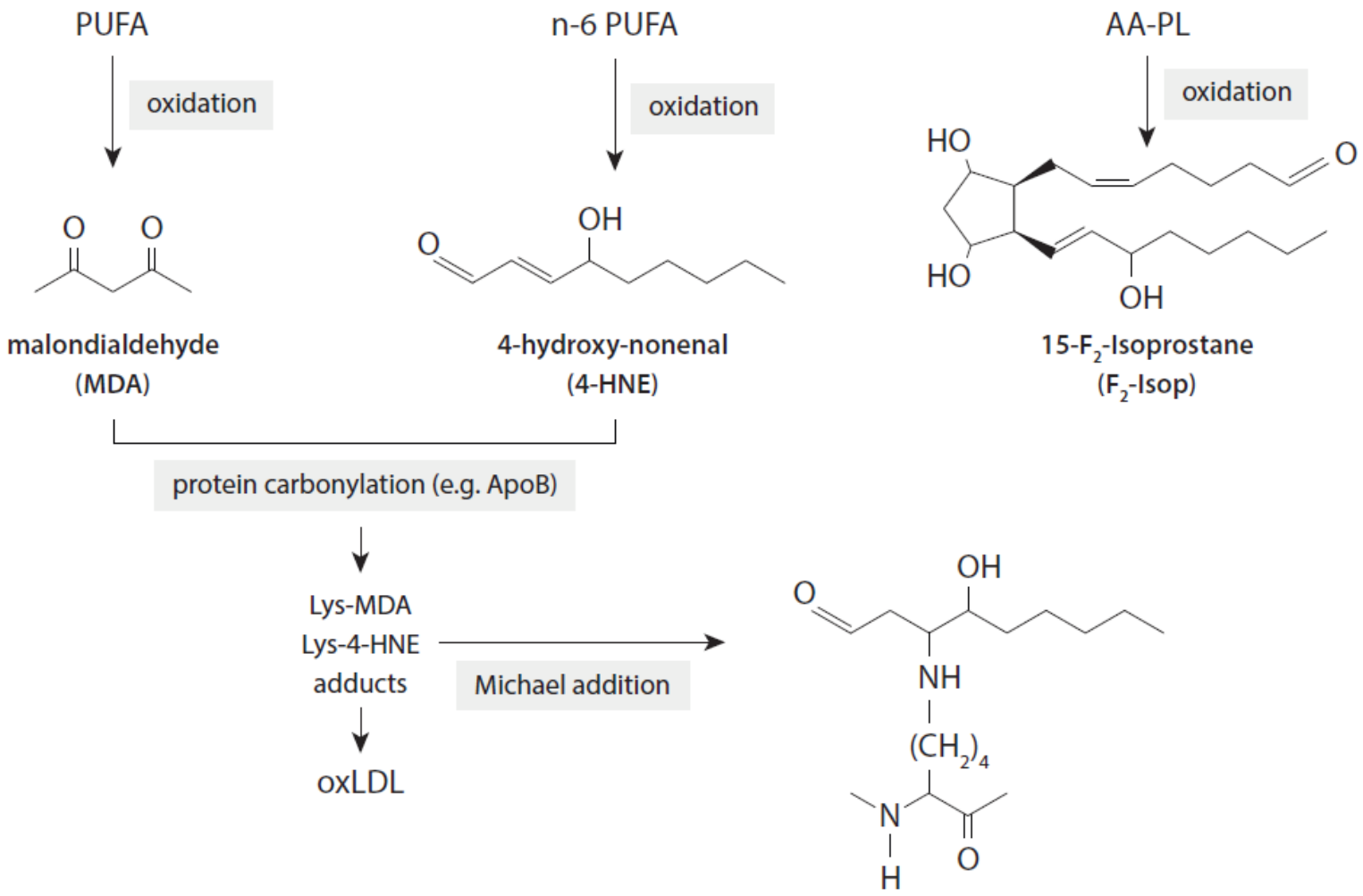


4 - HIDROXI - 2 - NONENAL

4-HNE

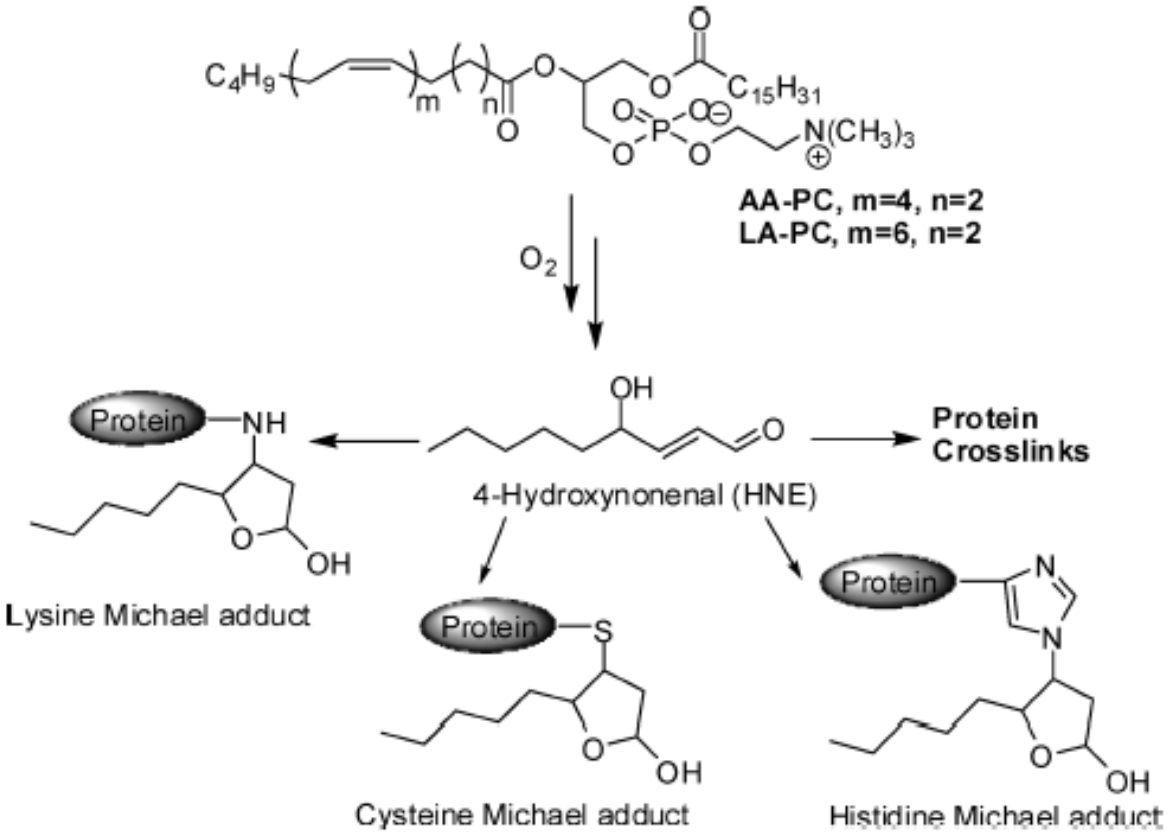
Frankel, 2005;Choe & Min, 2006

Oxidação da LDL



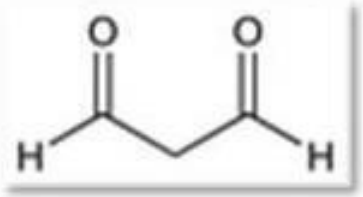
Síntese de 4-HNE e formação de adutos com aminoácidos

Scheme 1. Generation of HNE and Amino Acid Michael Adducts from Polyunsaturated Fatty Acids

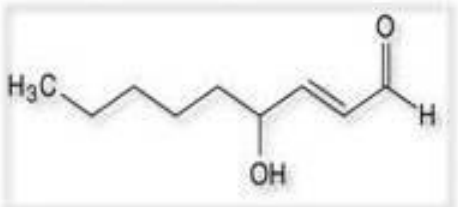


PRODUTOS DA OXIDAÇÃO LIPÍDICA

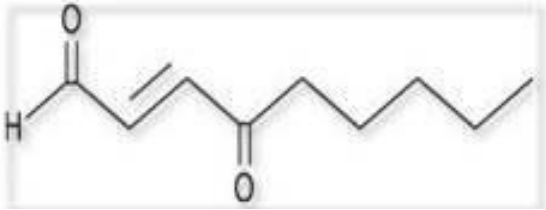
Malondialdehyde



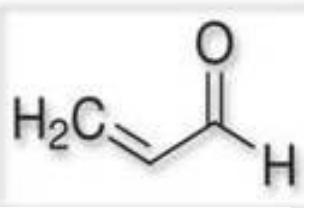
4-Hydroxynonenal

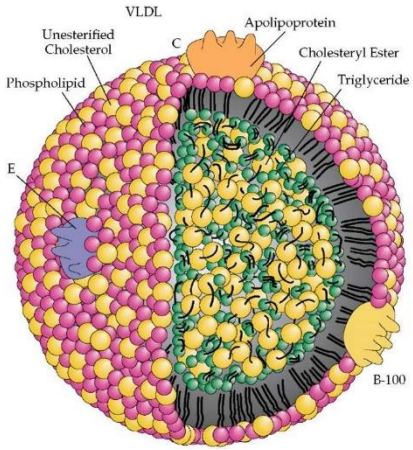


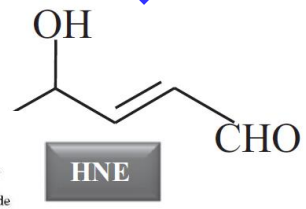
4-oxo-2-nonenal



Acrolein







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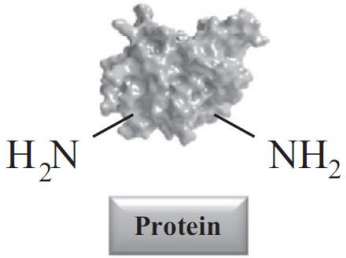
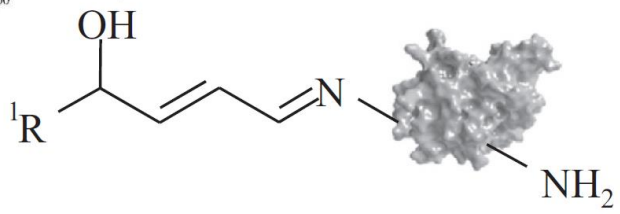
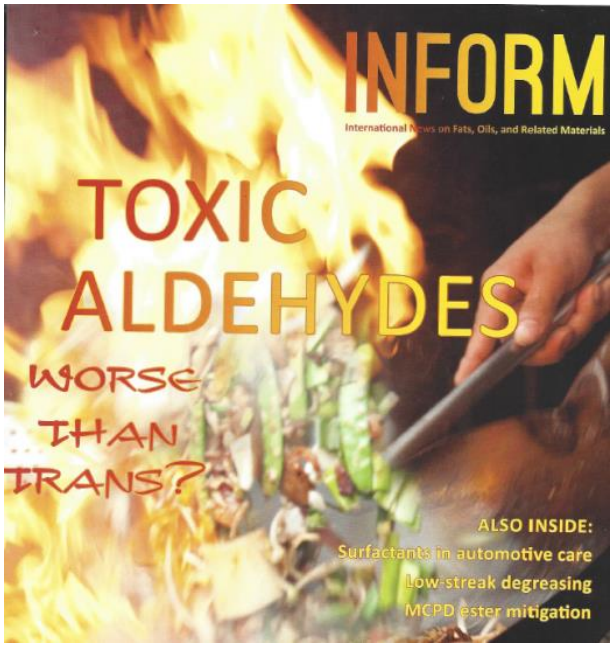


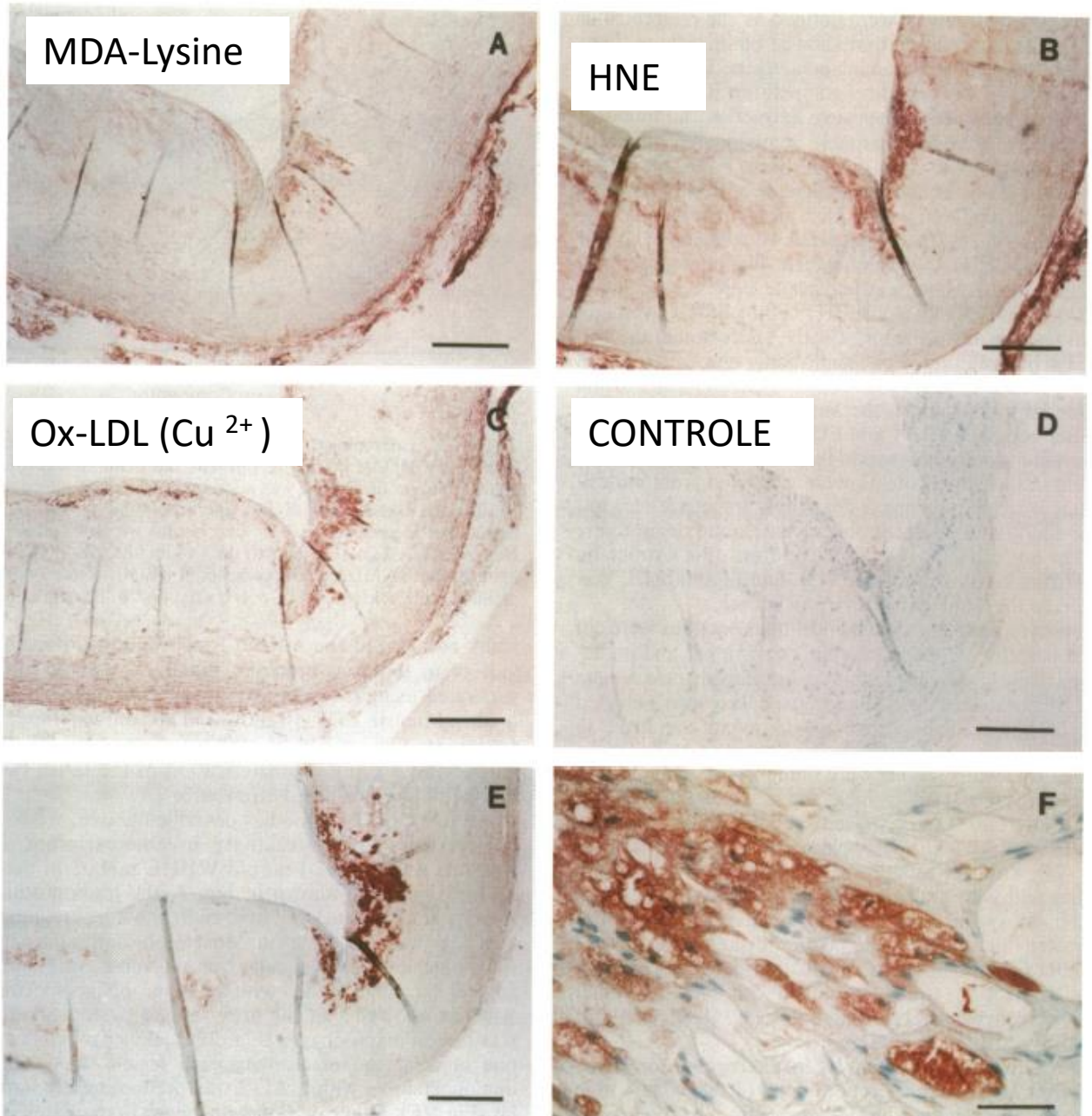




Castro et al. **FRBM(**2017)

Wadhwa et al. **INT J CURR SCI (**2012)

Lesões avançadas em coelhos



Oxidação da LDL e aterosclerose

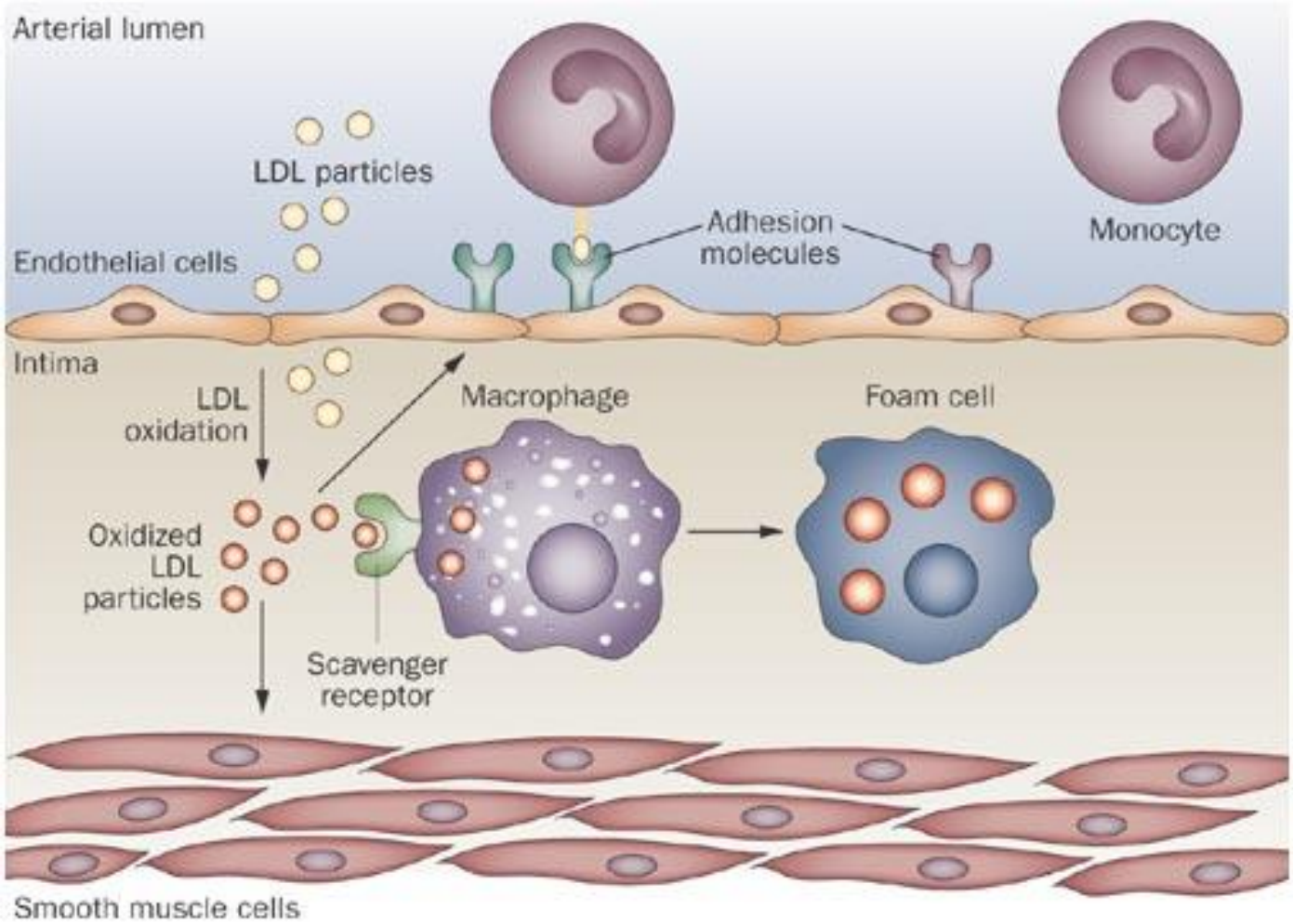
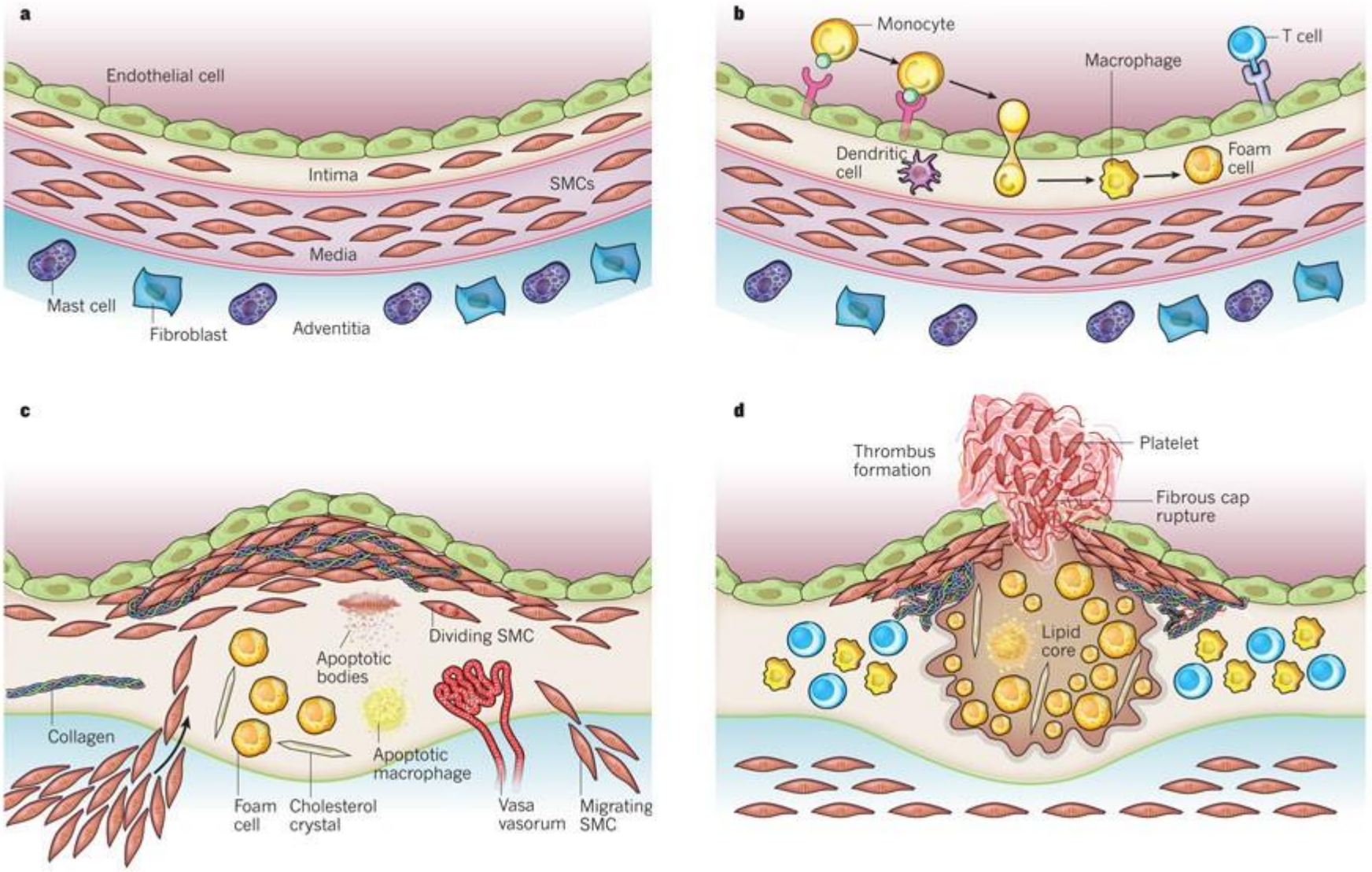
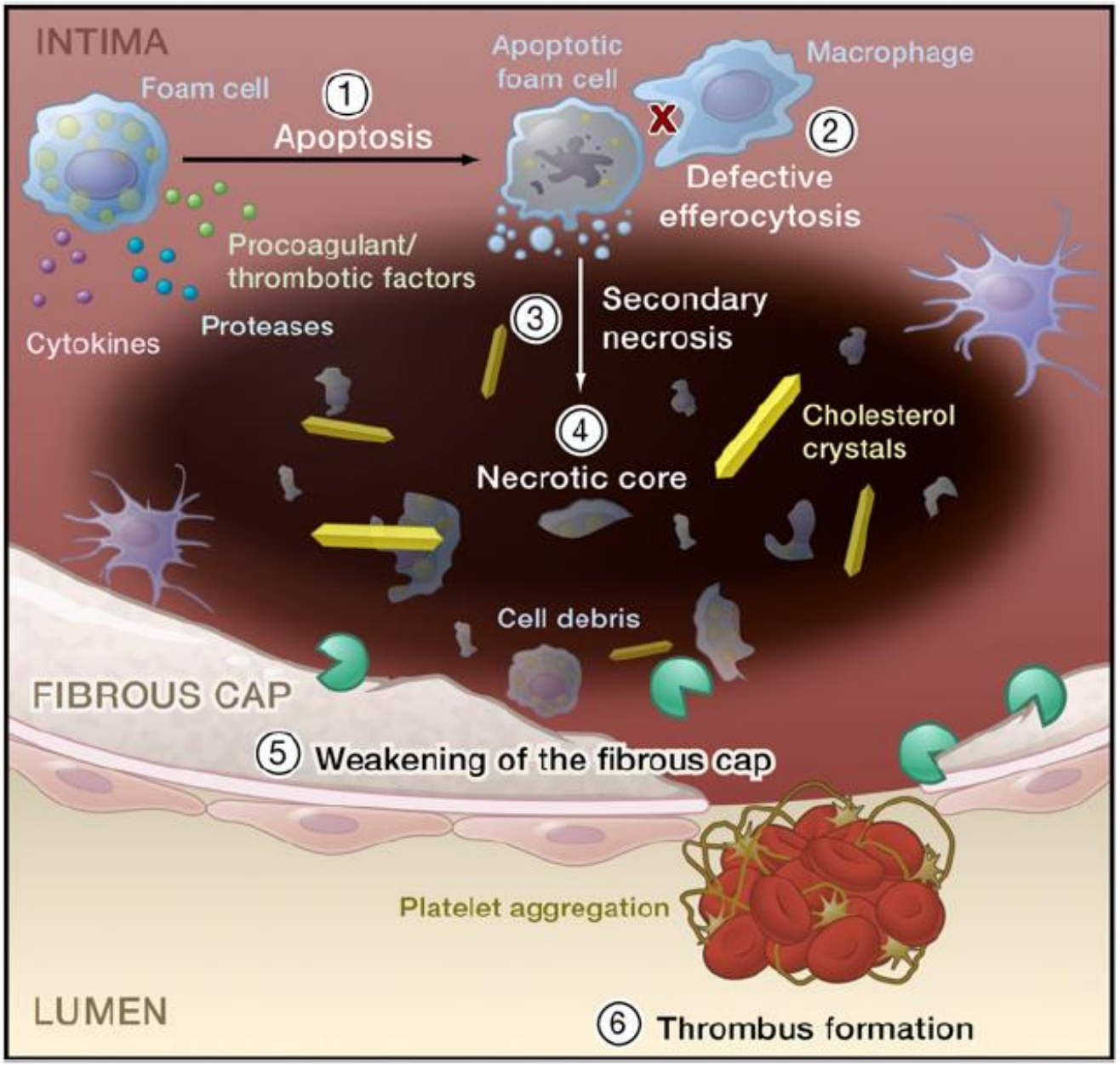


Figure 1: The excess of LDL particles circulating in the arterial lumen infiltrate the intima monolayer, where they undergo oxidation mediated by ROS. Once oxLDL, there is activation of adhesion molecules, internalization of monocytes that differentiate into macrophages that phagocyte the oxLDL particles forming foam cells, thereby initiating the formation of atherosclerotic plaque. Adapted from Rocha and Libby (2009).



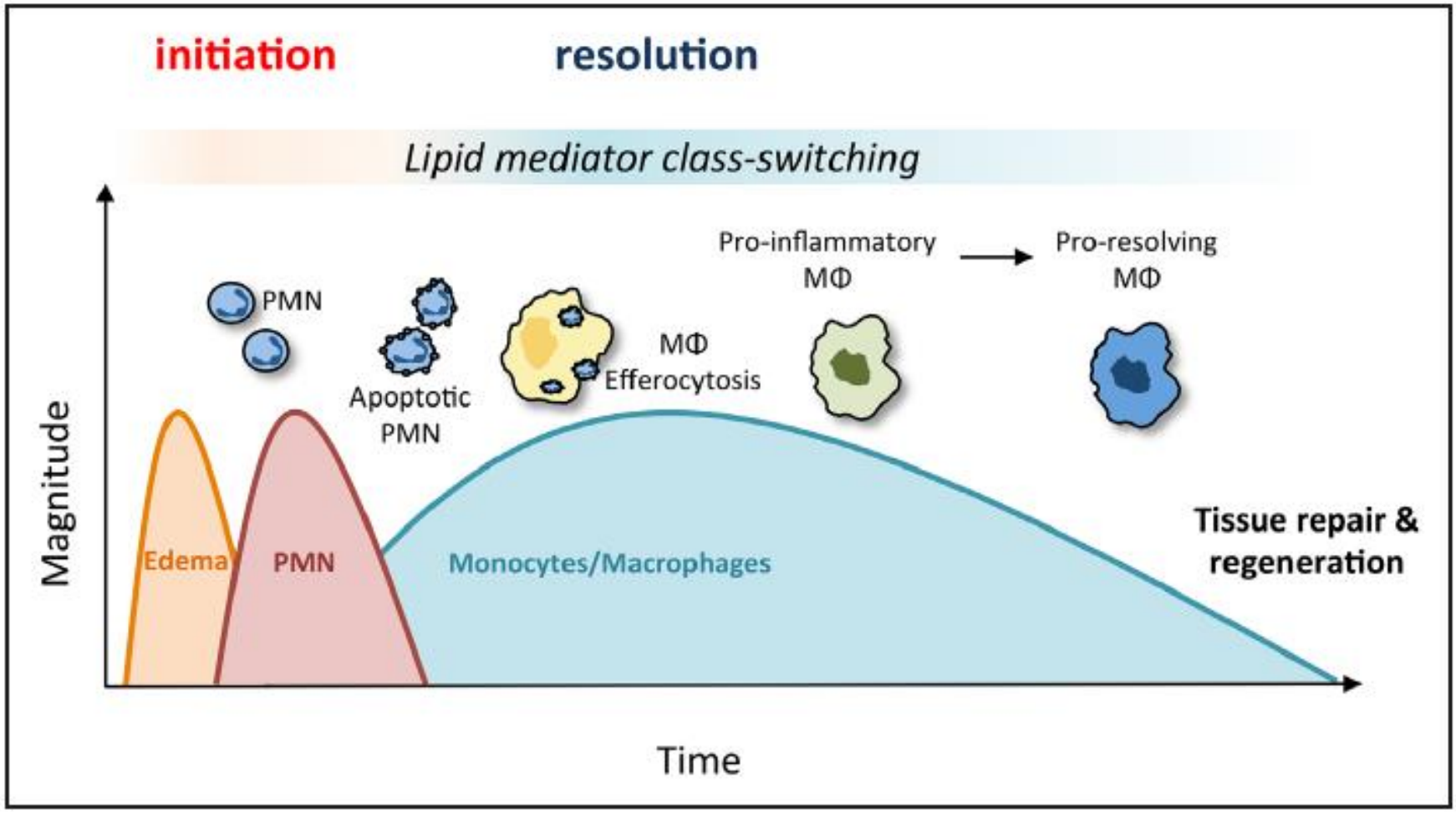
Libby et al (2011)

Características das Lesões Avançadas

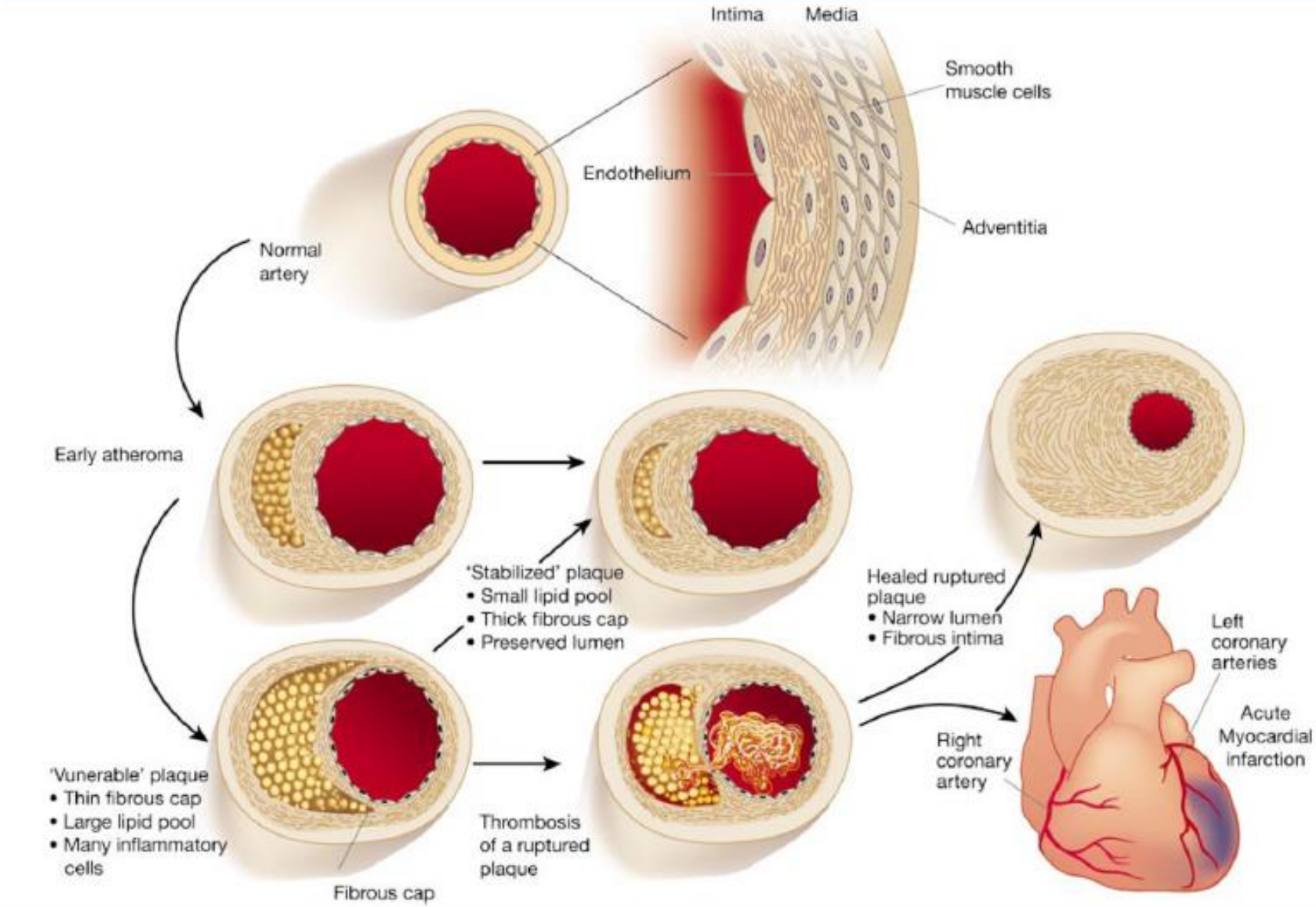


Moore & Tabas. **Cell** (2011).

Sistema Imune



Sansbury and Spite Resolving Cardiovascular Inflammation



Libby et al. 2002

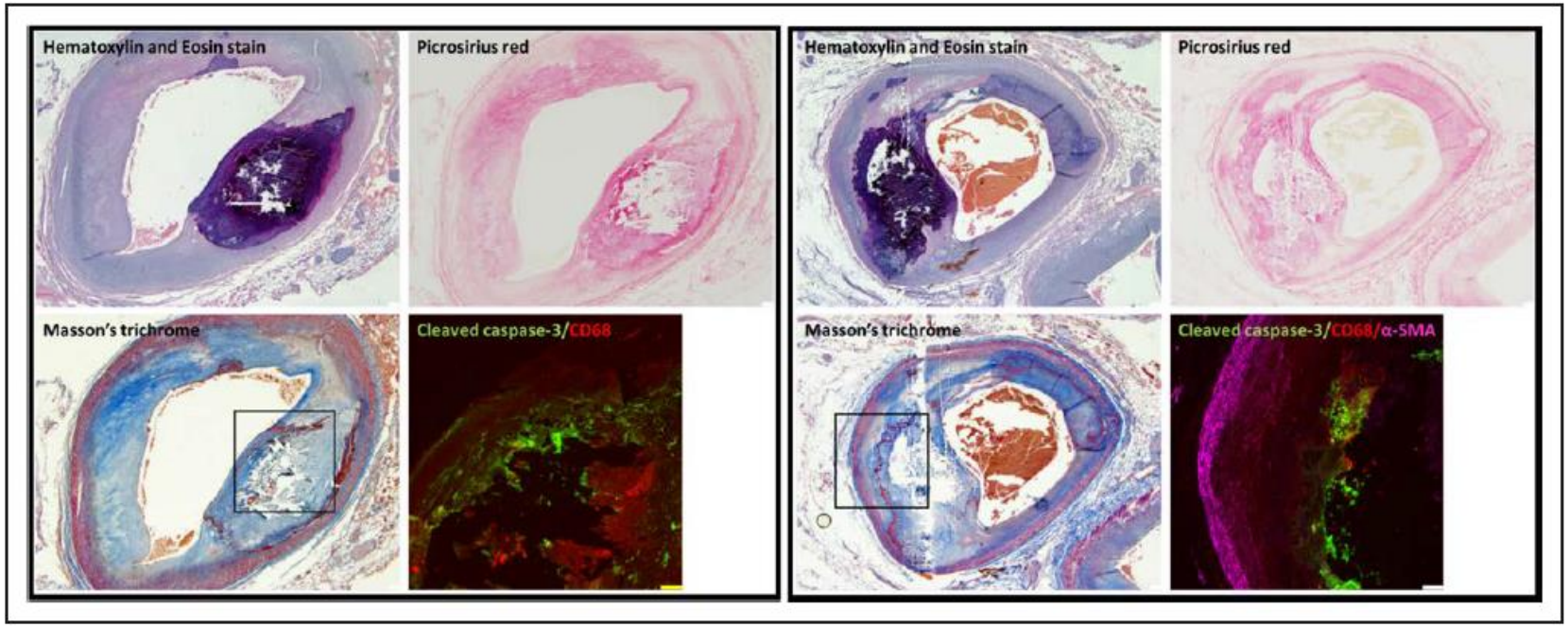
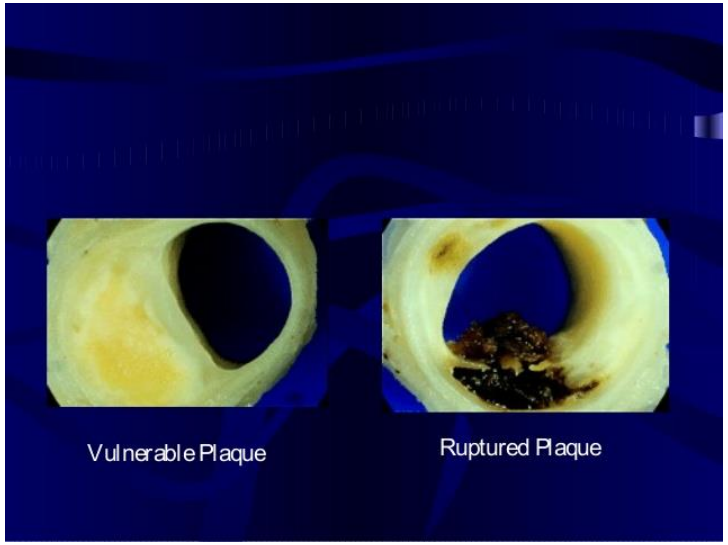


Figure 1. Examples of human atherosclerotic plaques.

Jarr et al. 2021



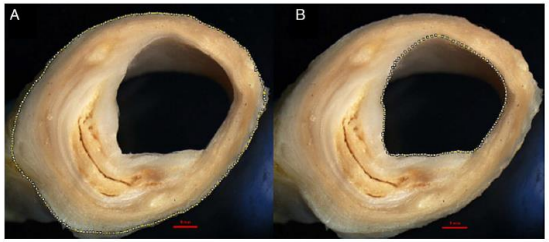
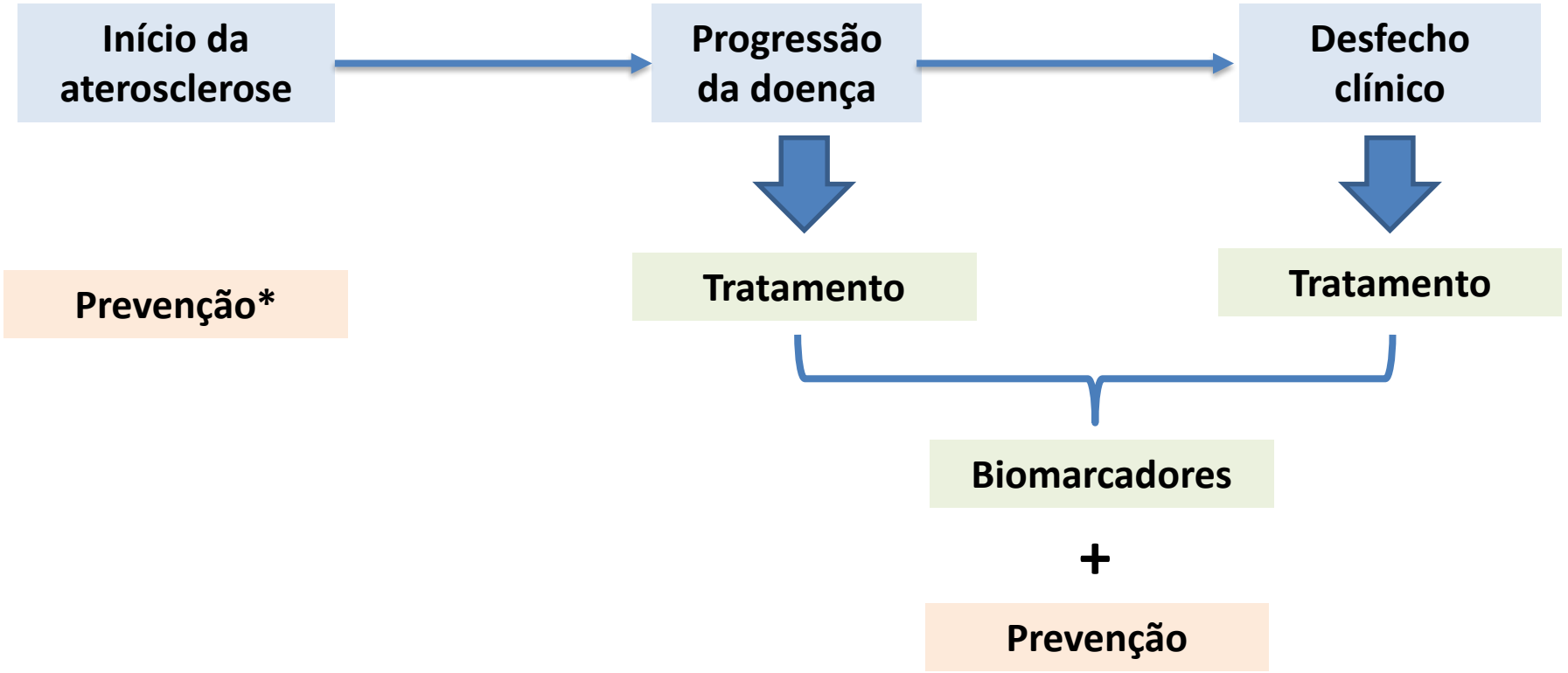


Figure 4 Measures used for the calculation of the carotid artery stenosis index. (A) Area limited by the outer wall of the vessel. (B) Lumen area.

Nishzawa et al. 2016

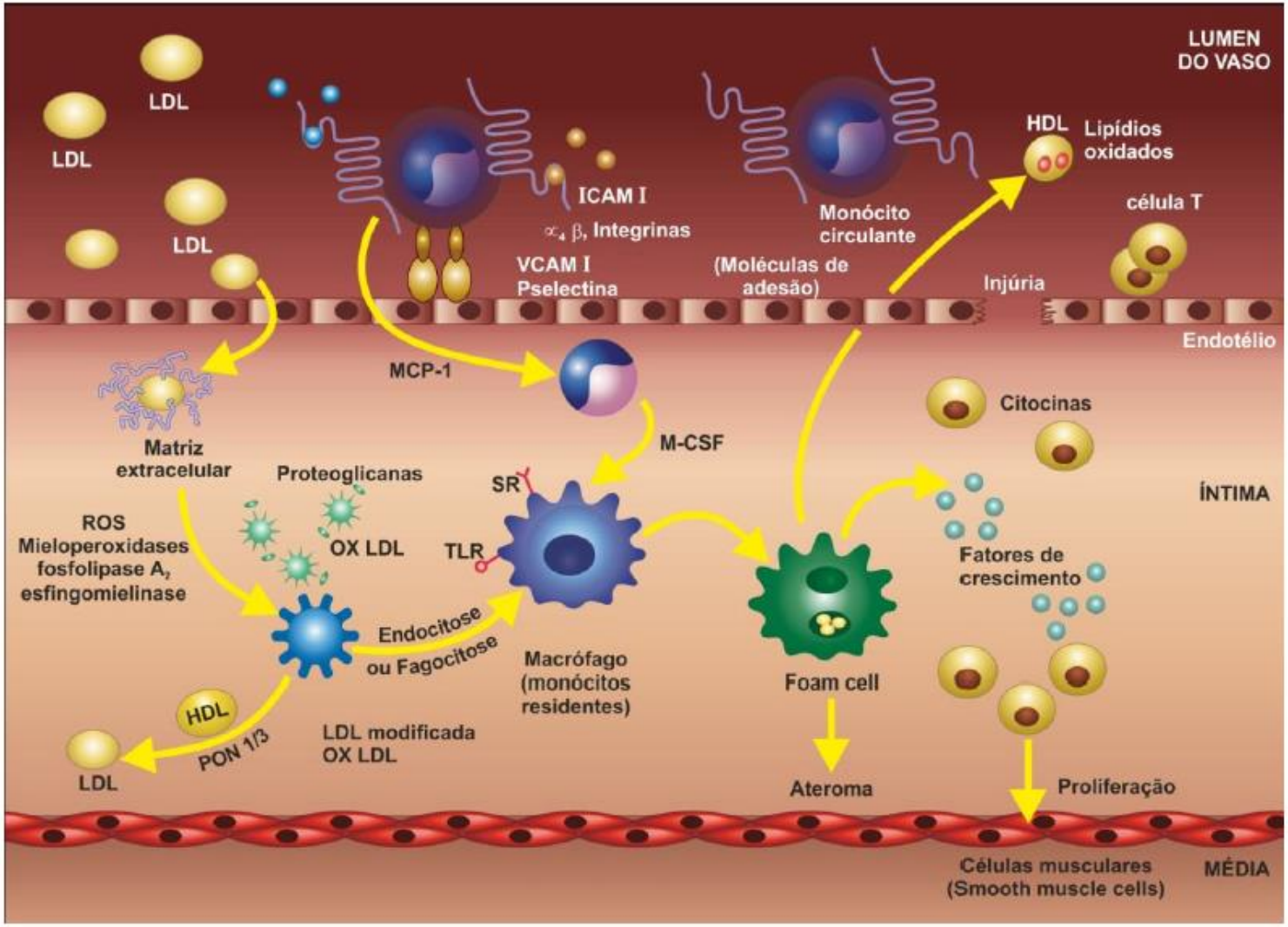
https://www.youtube.com/watch?v=i-KXyVpOobM&t=1s

3. Diretrizes

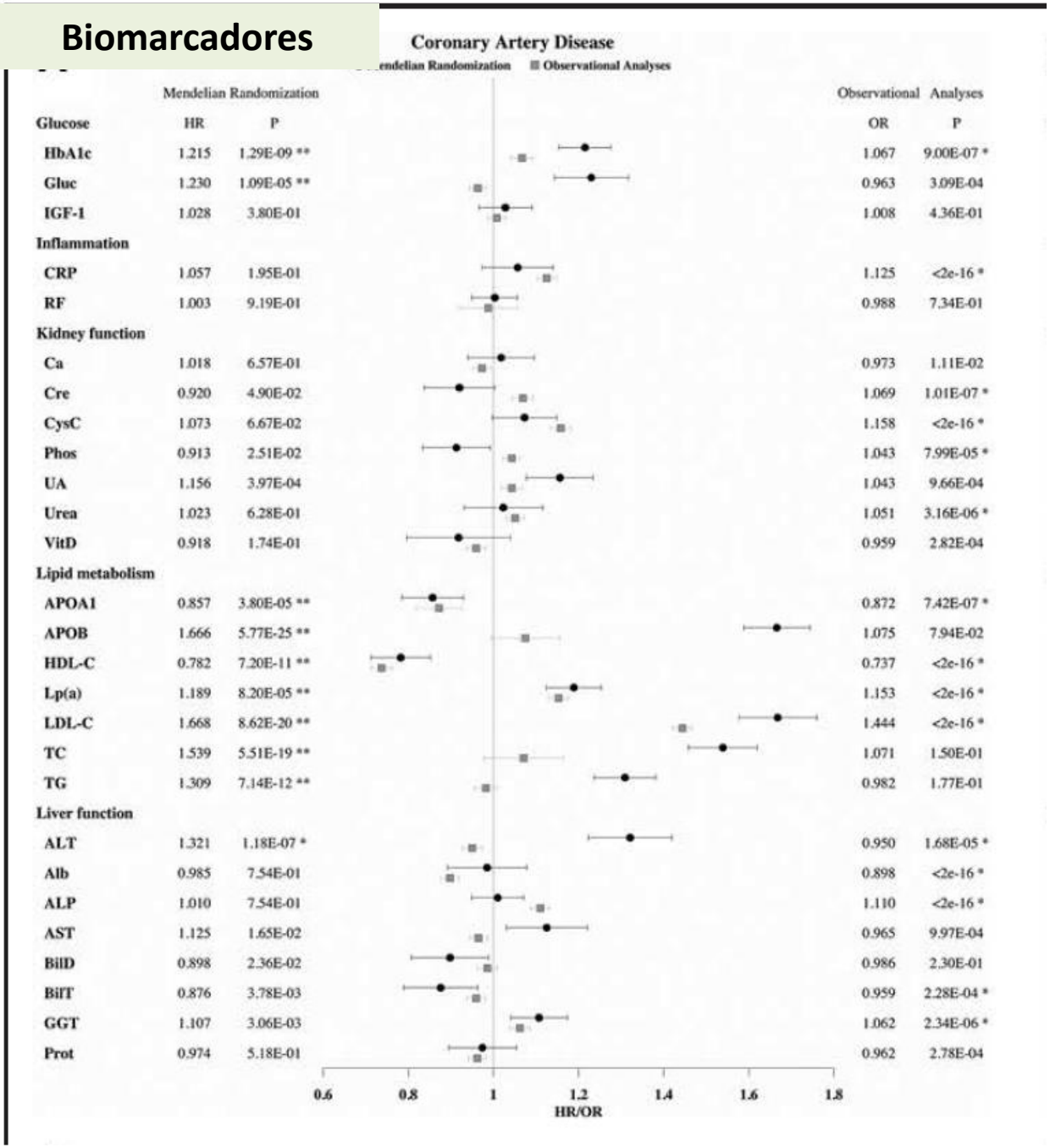


* Casos congênitos

Biomarcadores



Biomarcadores



Zanetti et al.,2020

DIRETRIZES

Tabela 2 – Valores referenciais e de alvo terapêutico* do perfil lipídico (adultos > 20 anos)

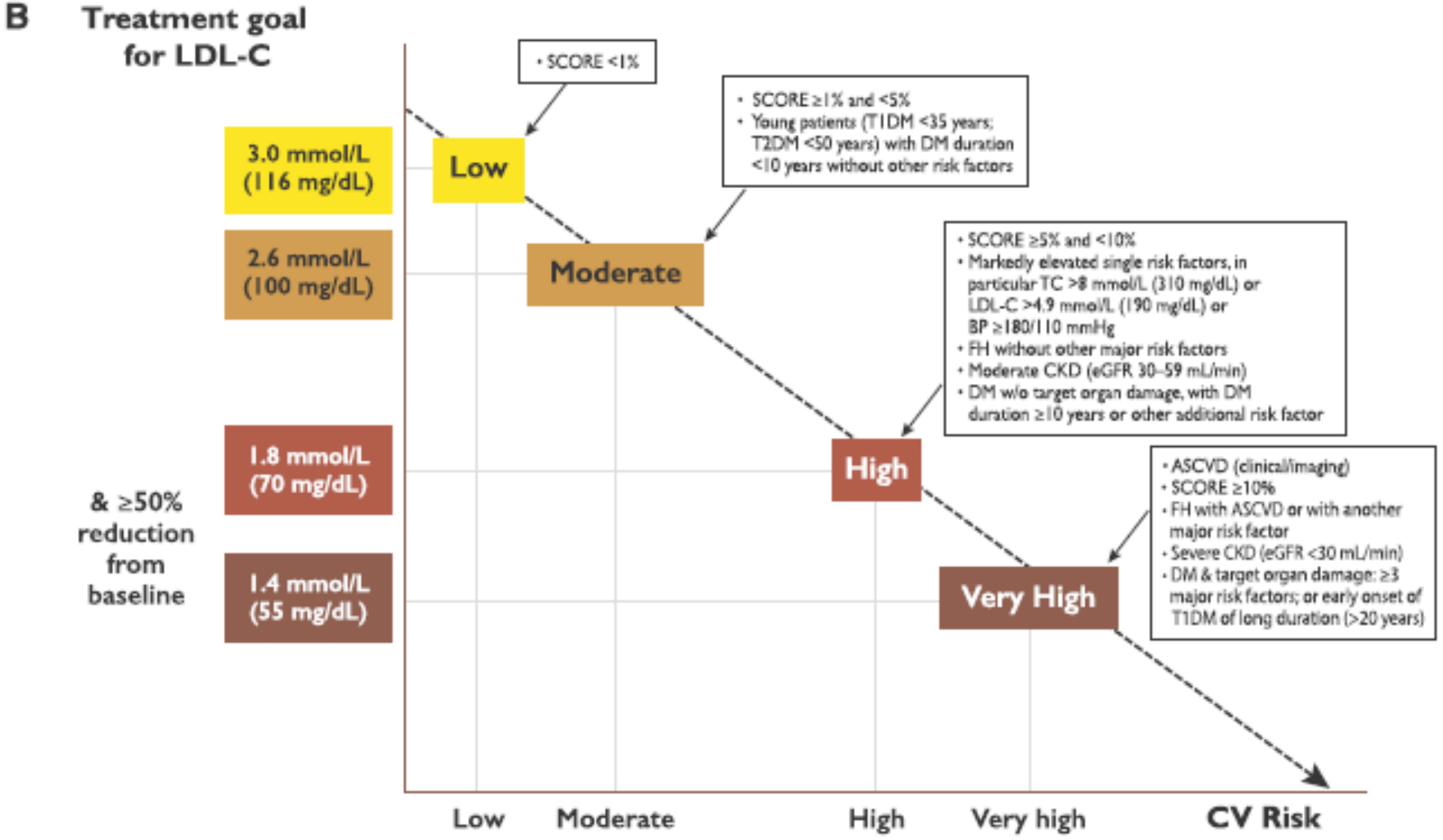
Lípides	Com jejum (mg/dL)	Sem jejum (mg/dL)	Categoria referencial
Colesterol total†	< 190	< 190	Desejável
HDL-c	> 40	> 40	Desejável
Triglicérides	< 150	< 175‡	Desejável
	Categoria de risco		
LDL-c	< 130	< 130	Baixo
	< 100	< 100	Intermediário
	< 70	< 70	Alto
	< 50	< 50	Muito alto
Não HDL-c	< 160	< 160	Baixo
	< 130	< 130	Intermediário
	< 100	< 100	Alto
	< 80	< 80	Muito alto

** Conforme avaliação de risco cardiovascular estimado pelo médico solicitante; † colesterol total > 310 mg/dL há probabilidade de hipercolesterolemia familiar; ‡ Quando os níveis de triglicérides estiverem acima de 440 mg/dL (sem jejum) o médico solicitante faz outra prescrição para a avaliação de triglicérides com jejum de 12 horas e deve ser considerado um novo exame de triglicérides pelo laboratório clínico.*

Quadro 5 – Recomendações para o manejo dos lípides sanguíneos

Recomendação	Grau de Recomendação	Nível de Evidência
Indivíduos de muito alto risco cardiovascular, o LDL-c deve ser reduzido para < 50 mg/dL e o não HDL-c < 80 mg/dL	I	B
Indivíduos de alto risco cardiovascular, o LDL-c deve ser reduzido para < 70 mg/dL e o não HDL-c < 100 mg/dL	I	A
Para indivíduos de alto e muito alto risco cardiovascular, sempre que possível e tolerado, deve-se dar preferência para o uso de estatina de alta intensidade ou ezetimiba associada à estatina (sinvastatina 40 mg ou outra estatina com potência pelo menos equivalente)	I	A
Indivíduos de risco cardiovascular intermediário, o LDL-c deve ser reduzido para < 100 mg/dL e o não HDL-c < 130 mg/dL	I	A
Indivíduos de risco cardiovascular intermediário, sempre que possível e tolerado, deve-se dar preferência para o uso de estatina de intensidade pelo menos moderada	I	A
Indivíduos de baixo risco cardiovascular, a meta de LDL-c deve ser < 130 mg/dL e o não HDL-c < 160 mg/dL	I	A
Não se recomenda tratamento medicamentoso visando à elevação dos níveis de HDL-c	III	A
Indivíduos com níveis de triglicérides > 500 mg/dL devem receber terapia apropriada para redução do risco de pancreatite	I	A
Indivíduos com níveis de triglicérides entre 150 e 499 mg/dL devem receber terapia, com base no risco cardiovascular e nas condições associadas	IIa	B

LDL-c: colesterol da lipoproteína de baixa densidade; HDL-c: colesterol da lipoproteína de alta densidade.


B
Treatment goal for LDL-C
3.0 mmol/L (116 mg/dL)
2.6 mmol/L (100 mg/dL)
1.8 mmol/L (70 mg/dL)
1.4 mmol/L (55 mg/dL)
& ≥50% reduction from baseline
Low
• SCORE <1%
Moderate
• SCORE ≥1% and <5%
• Young patients (T1DM <35 years; T2DM <50 years) with DM duration <10 years without other risk factors
High
• SCORE ≥5% and <10%
• Markedly elevated single risk factors, in particular TC >8 mmol/L (310 mg/dL) or LDL-C >4.9 mmol/L (190 mg/dL) or BP ≥180/110 mmHg
• FH without other major risk factors
• Moderate CKD (eGFR 30–59 mL/min)
• DM w/o target organ damage, with DM duration ≥10 years or other additional risk factor
Very High
• ASCVD (clinical/imaging)
• SCORE ≥10%
• FH with ASCVD or with another major risk factor
• Severe CKD (eGFR <30 mL/min)
• DM & target organ damage: ≥3 major risk factors; or early onset of T1DM of long duration (>20 years)
Low
Moderate
High
Very high
CV Risk

Types of medications and surgical strategies

Basic medicines that should be available include:

•aspirin;
•beta-blockers;
•angiotensin-converting enzyme inhibitors; and
•statins.

An acute event such as a heart attack or stroke should be promptly managed. Sometimes, surgical operations are required to treat CVDs. They include:

•coronary artery bypass;
•balloon angioplasty (where a small balloon-like device is threaded through an artery to open the blockage);
•valve repair and replacement;
•heart transplantation; and
•artificial heart operations.

Tratamento farmacológico

•**ACE inhibitors and beta blockers** help lower blood pressure and lower the heart's workload.
•**Anti-platelet or anti-clotting medicines** may help reduce risk of complications for some people who have atherosclerosis. Aspirin is not recommended for most people.
•**Calcium channel blockers** lower blood pressure by relaxing blood vessels.
•**Medicines to control blood sugar,** such as empagliflozin, canagliflozin, and liraglutide, help lower your risk for complications if you have atherosclerosis and diabetes.
•**Metformin** helps control plaque buildup if you have diabetes.
•**Nitrates,** such as nitroglycerin, dilate your coronary arteries and relieve or prevent chest pain from angina.
•**Ranolazine** treats coronary microvascular disease and the chest pain it may cause.

•Statins treat unhealthy blood cholesterol levels. Your doctor may recommend a statin if you have a higher risk for coronary heart disease or stroke or if you have diabetes and are between ages 40 and 75.

•Other cholesterol-lowering medicines, such as ezetimibe, PCSK9 inhibitor, bempedoic acid, and omega-3 fatty acids, may be used if you are unable to take statins or when statins have not worked to treat unhealthy blood cholesterol and triglyceride levels.

•**Thrombolytic medicines, sometimes called clot busters,** may be used to treat blood clots resulting from atherosclerosis. These medicines can dissolve blood clots that block arteries, causing a stroke, heart attack, mesenteric Ischemia or other problems. Ideally, the medicine should be given as soon as possible.

https://www.nhlbi.nih.gov/health/atherosclerosis/treatment

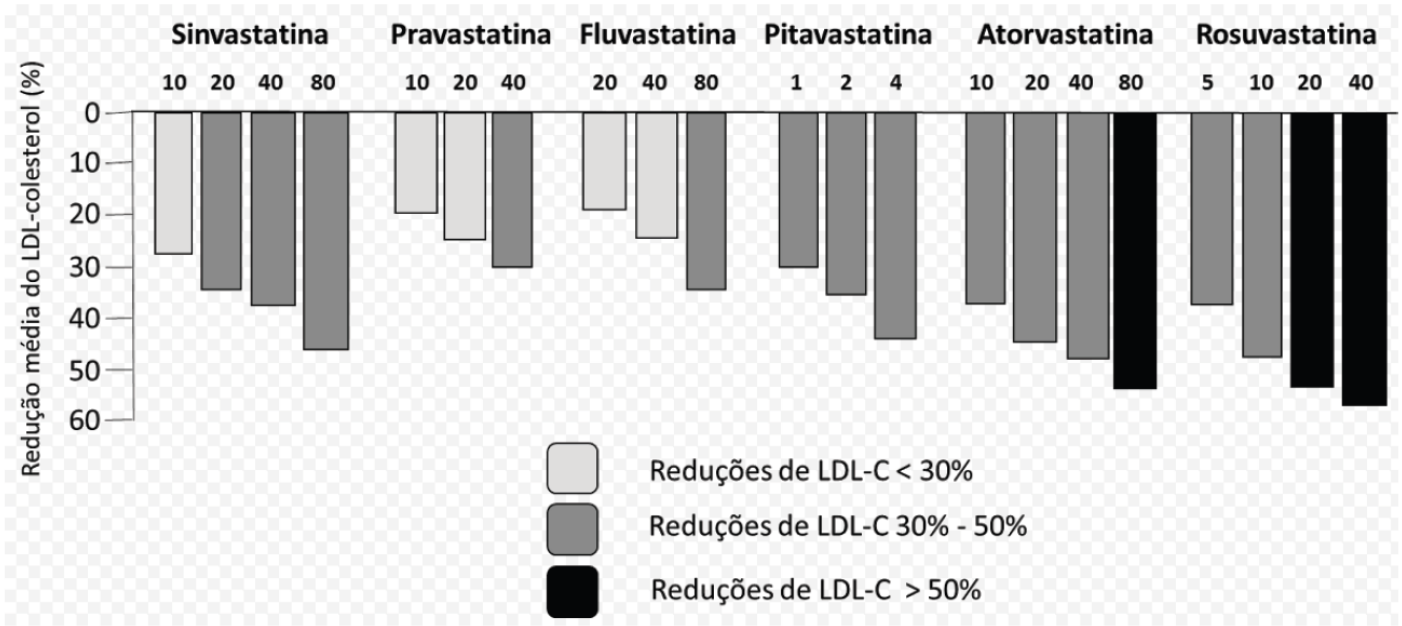


Figura 2 – *Reduções do colesterol da lipoproteína de baixa densidade com as estatinas e as doses disponíveis no mercado nacional.*

TAREFA

V Diretriz Brasileira de Dislipidemias e Prevenção da Aterosclerose", publicada como suplemento número um da edição de setembro de 2013 dos Arquivos Brasileiros de Cardiologia [Arq Bras Cardiol. 2013; 101(4Supl.1): 1-22

Atualização em 2017

Circulation

ACC/AHA CLINICAL PRACTICE GUIDELINE

2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

Circulation
Volume 140, Number 11
https://doi.org/10.1161/CIR.0000000000000678

ESC
European Society of Cardiology

European Heart Journal (2021) **42**, 3227–3337
doi:10.1093/eurheartj/ehab484

ESC GUIDELINES

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

Developed by the Task Force for cardiovascular disease prevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies