Nutrition and Cardiovascular Disease

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Magnitude of the Problem

- Cardiovascular disease (CVD) is the leading cause of death in Western countries, representing almost 30% of all deaths worldwide.

- It is estimated that over 80% of deaths from CVD take place in low-income and middle-income countries. Therefore, it is imperative to develop effective and affordable strategies for the prevention and treatment of CVD.

- Incidence of CVD over the last 25 years has become a public health priority, especially the prevention of CVD (or cardiovascular events) through lifestyle interventions.

- On the one hand, a large body of scientific evidence has reported that nutrition might be the most preventive factor of CVD death and could even reverse heart disease. On the other hand, diet seems to play an important role in the management of other risk factors, such as excess weight, hypertension, diabetes, or dyslipidemia

CVD and Diet

- CVD describes a range of disorders that affect the heart and blood vessels, such as hypertension, stroke, atherosclerosis, peripheral artery disease, and vein diseases.

- The probability of developing CVD is associated with unhealthy dietary patterns (i.e., excessive intake of sodium and processed foods; added sugars; unhealthy fats; low intake of fruit and vegetables, whole grains, fiber, legumes, fish, and nuts), together with a lack of exercise, overweight and obesity, stress, alcohol consumption, or a smoking habit.

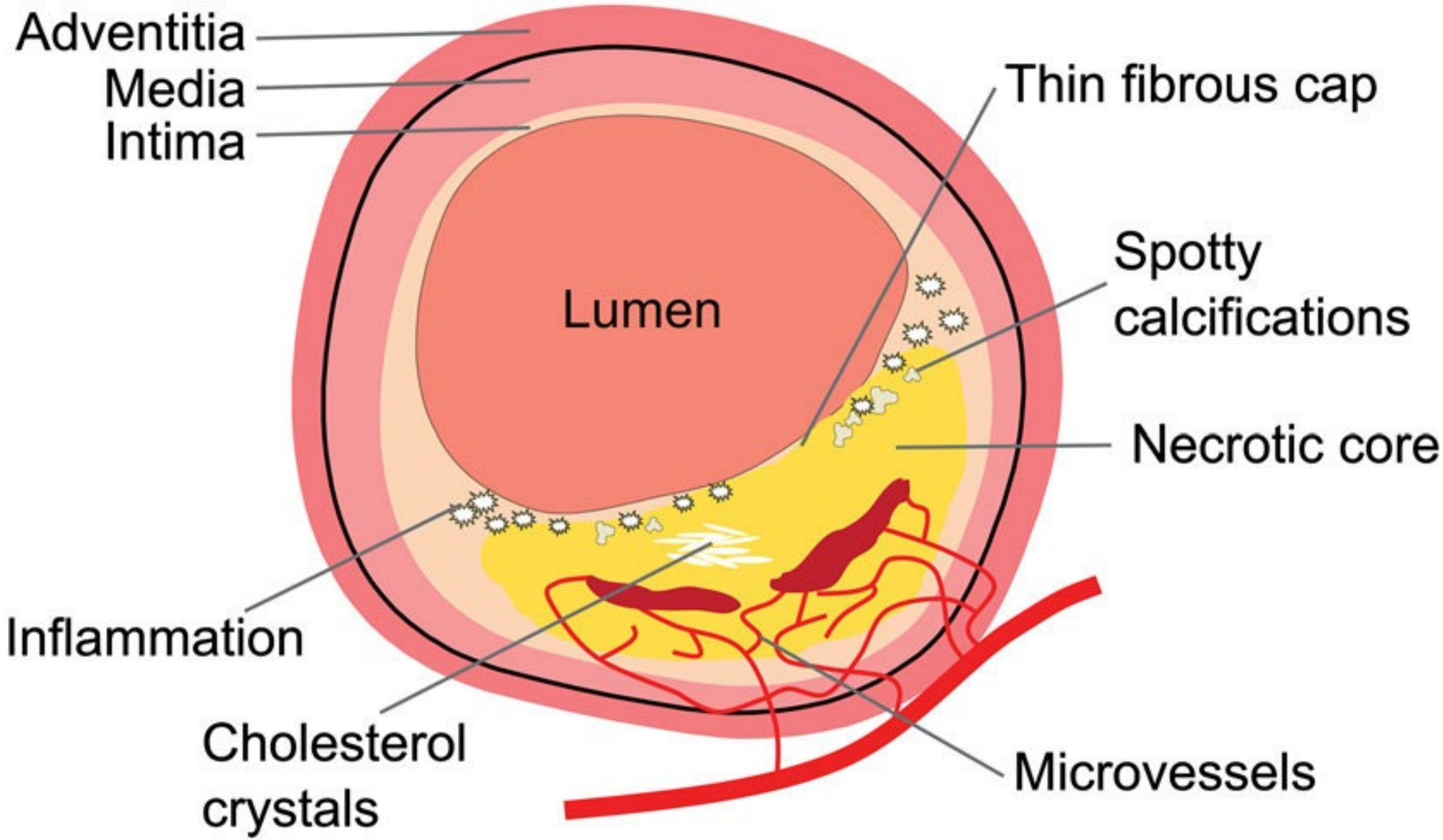
- Additionally, CVD often coincides with multiple co-morbidities, such as obesity, diabetes, hypertension, or dyslipidemia, which represent four of the 10 greatest risk factors for all-cause mortality worldwide

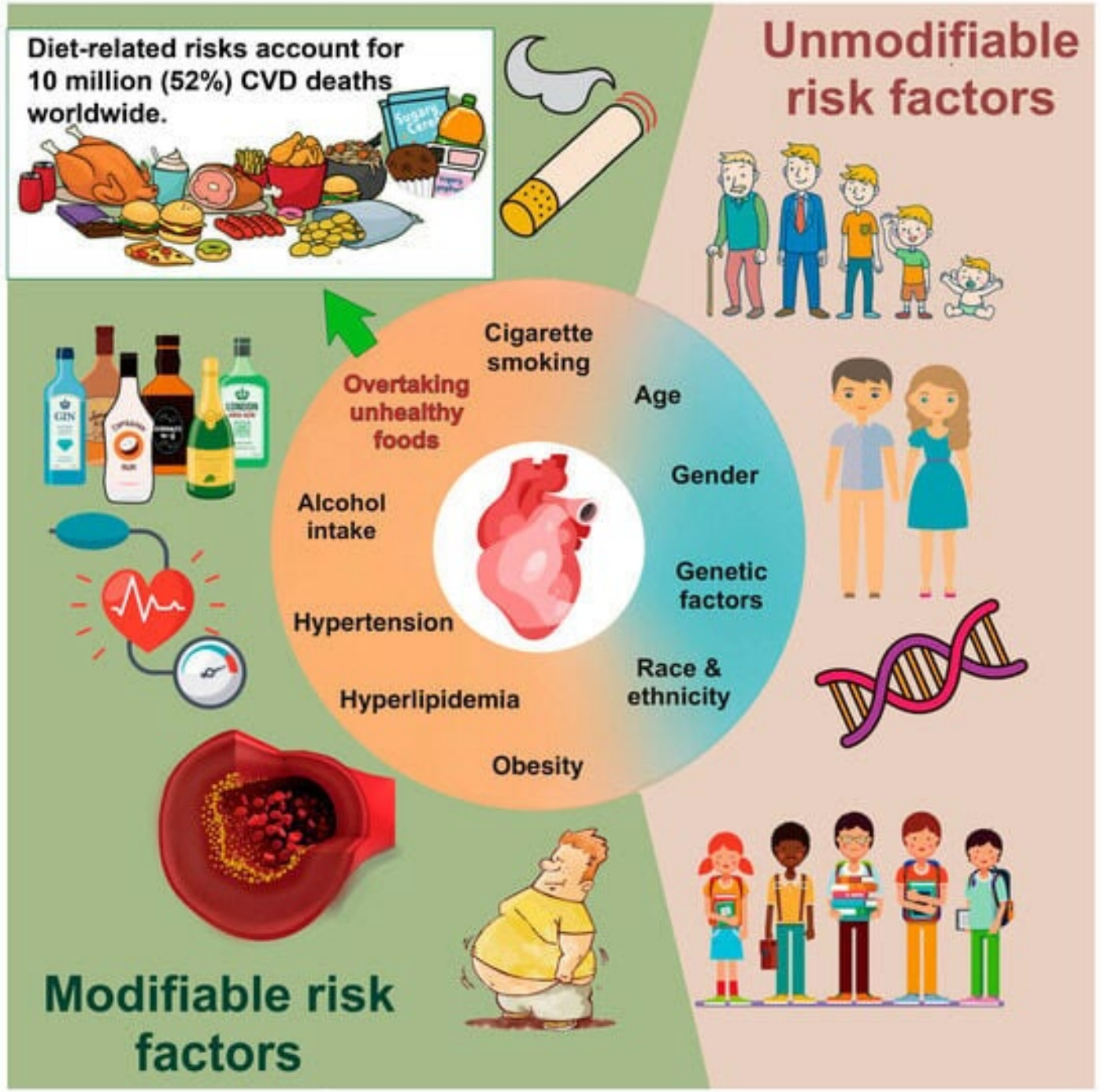
Atherosclerosis

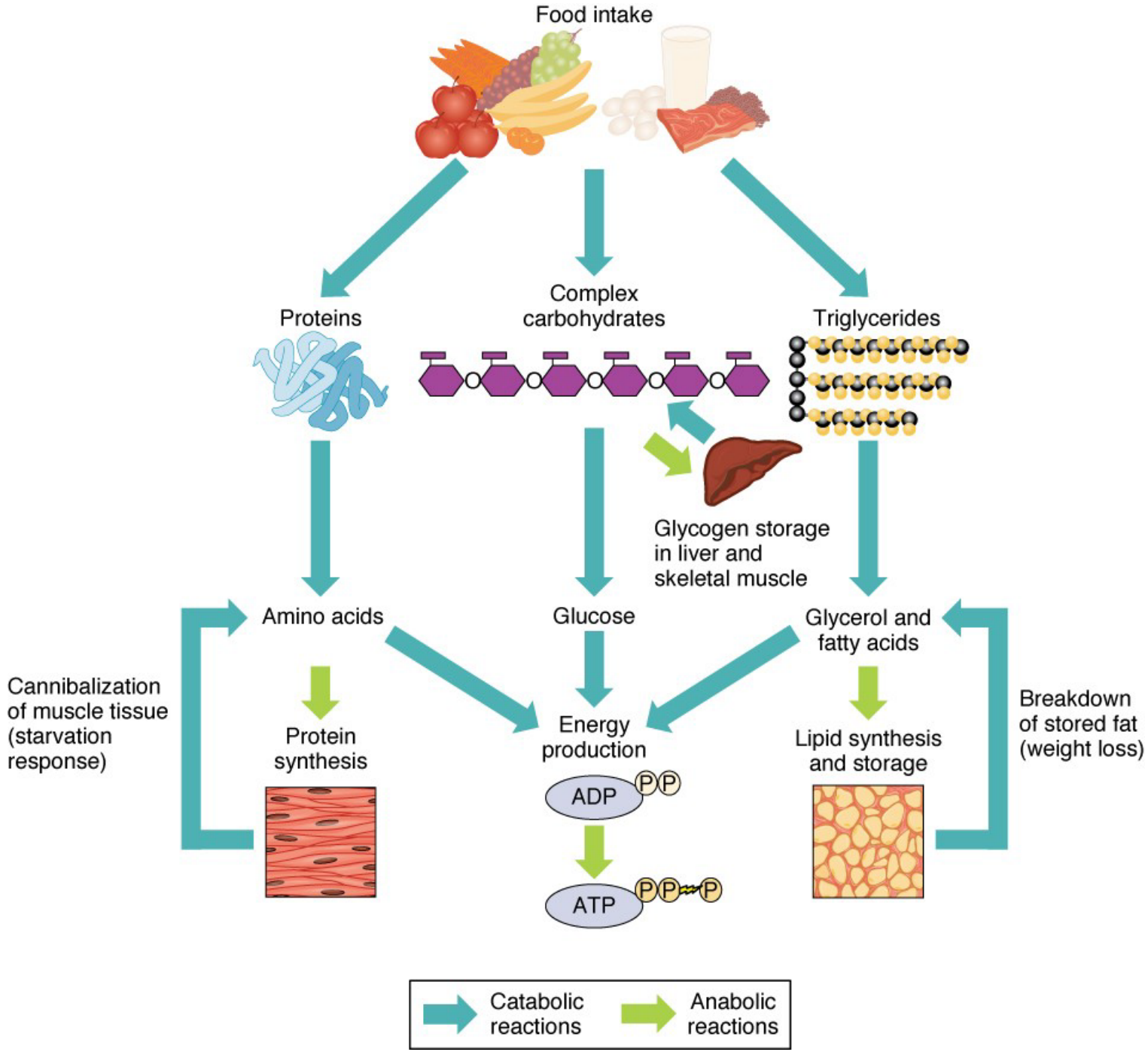
- Atherosclerosis is an inflammatory disease that contributes to major incidence and mortality of CVD.

- Oxidative stress and systemic inflammation are modifiable by nutrition with an excess energy intake and physical inactivity as contributors of pro-inflammatory cytokines' secretion.

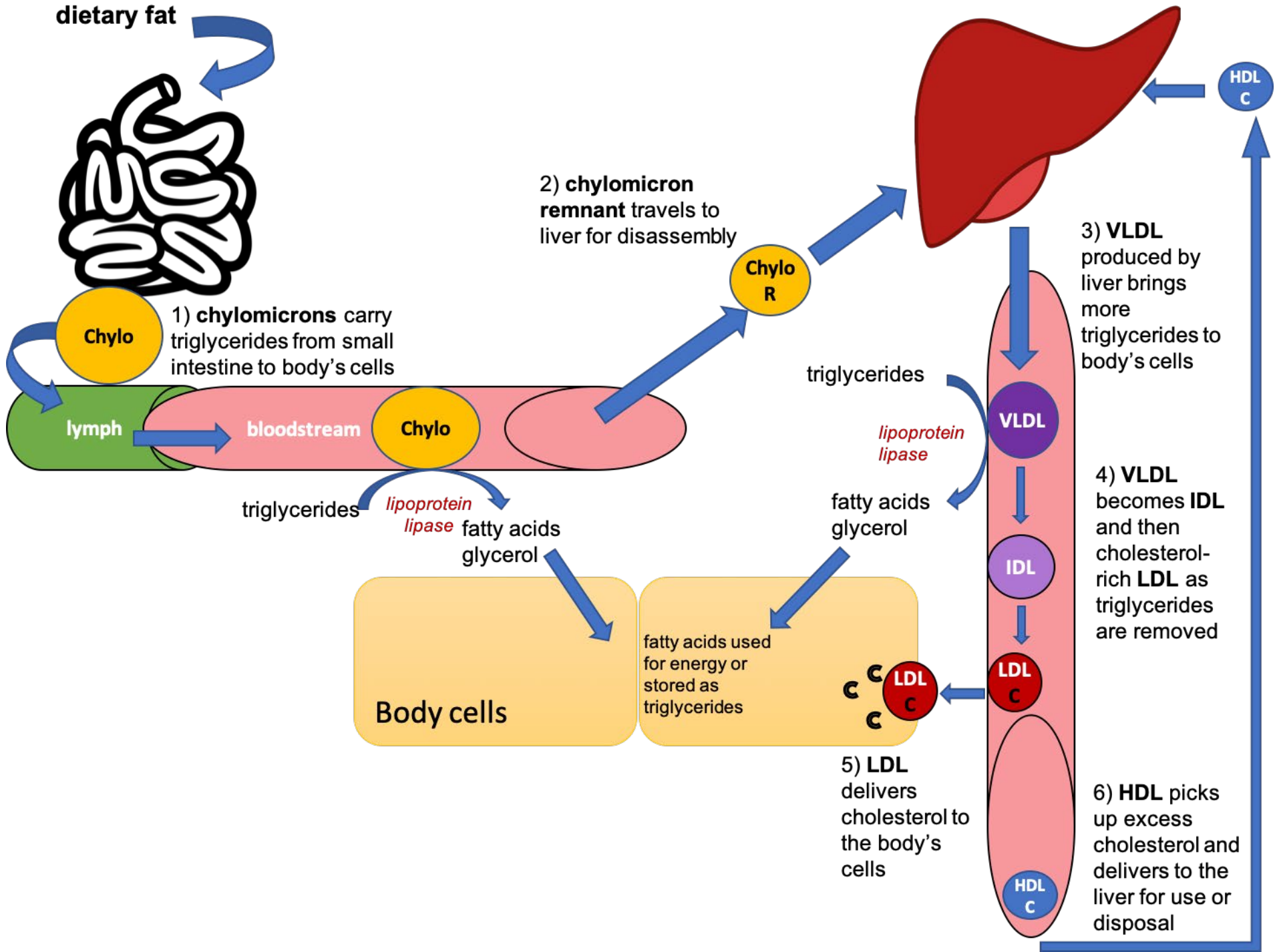
- The causes and risk factor of atherosclerosis and oxidative stress are not well defined. However, certain health conditions and habits may contribute to atherosclerosis development, such as high total cholesterol and low-high-density lipoprotein cholesterol (HDL-c) levels, hypertension, type 2 diabetes mellitus (T2DM), obesity, and physical inactivity. Additionally, healthy dietary patterns and lifestyle modifications are potential strategies for atherosclerosis and oxidative stress prevention.


Adventitia
Media
Intima
Lumen
Thin fibrous cap
Spotty calcifications
Necrotic core
Inflammation
Cholesterol crystals
Microvessels


Diet-related risks account for 10 million (52%) CVD deaths worldwide.
Unmodifiable risk factors
Cigarette smoking
Overtaking unhealthy foods
Age
Gender
Alcohol intake
Genetic factors
Hypertension
Race & ethnicity
Hyperlipidemia
Obesity
Modifiable risk factors


Food intake
Proteins
Complex carbohydrates
Triglycerides
Glycogen storage in liver and skeletal muscle
Amino acids
Glucose
Glycerol and fatty acids
Cannibalization of muscle tissue (starvation response)
Protein synthesis
Energy production
Lipid synthesis and storage
Breakdown of stored fat (weight loss)
ADP
P P
ATP
P P P
Catabolic reactions
Anabolic reactions

Fats


dietary fat
Chylo
1) **chylomicrons** carry triglycerides from small intestine to body's cells
lymph
bloodstream
Chylo
2) **chylomicron remnant** travels to liver for disassembly
Chylo R
triglycerides
lipoprotein lipase
fatty acids
glycerol
Body cells
fatty acids used for energy or stored as triglycerides
HDL C
3) **VLDL** produced by liver brings more triglycerides to body's cells
triglycerides
lipoprotein lipase
fatty acids
glycerol
VLDL
IDL
LDL C
4) **VLDL** becomes **IDL** and then cholesterol-rich **LDL** as triglycerides are removed
LDL C
5) **LDL** delivers cholesterol to the body's cells
HDL C
6) **HDL** picks up excess cholesterol and delivers to the liver for use or disposal

FATS

✗ Trans Fats

- Hydrogenated vegetable oils
- Fast foods
- Cakes/pastries
- Chocolate
- Deep Fried Food

✗ Saturated Fats

Vegetable Fats

- Coconut
- Palm oil
- 3-in-1 & 2-in-1 beverages, creamer, condensed milk

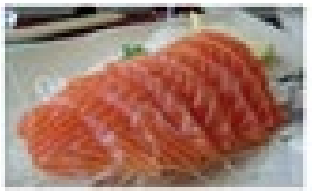
Animal Fats

- Poultry skin
- Fatty meat
- Butter
- Ghee
- Tallow / lard
- Full cream dairy products

✓ Unsaturated Fats

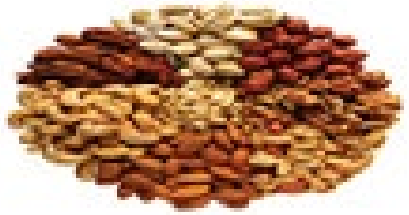
Polyunsaturated

- Corn oil
- Soybean oil
- Sunflower oil
- Seeds
- Cold-water fish



Monounsaturated

- Olive oil
- Canola oil
- Peanut oil
- Sesame oil
- Avocado
- Most nuts



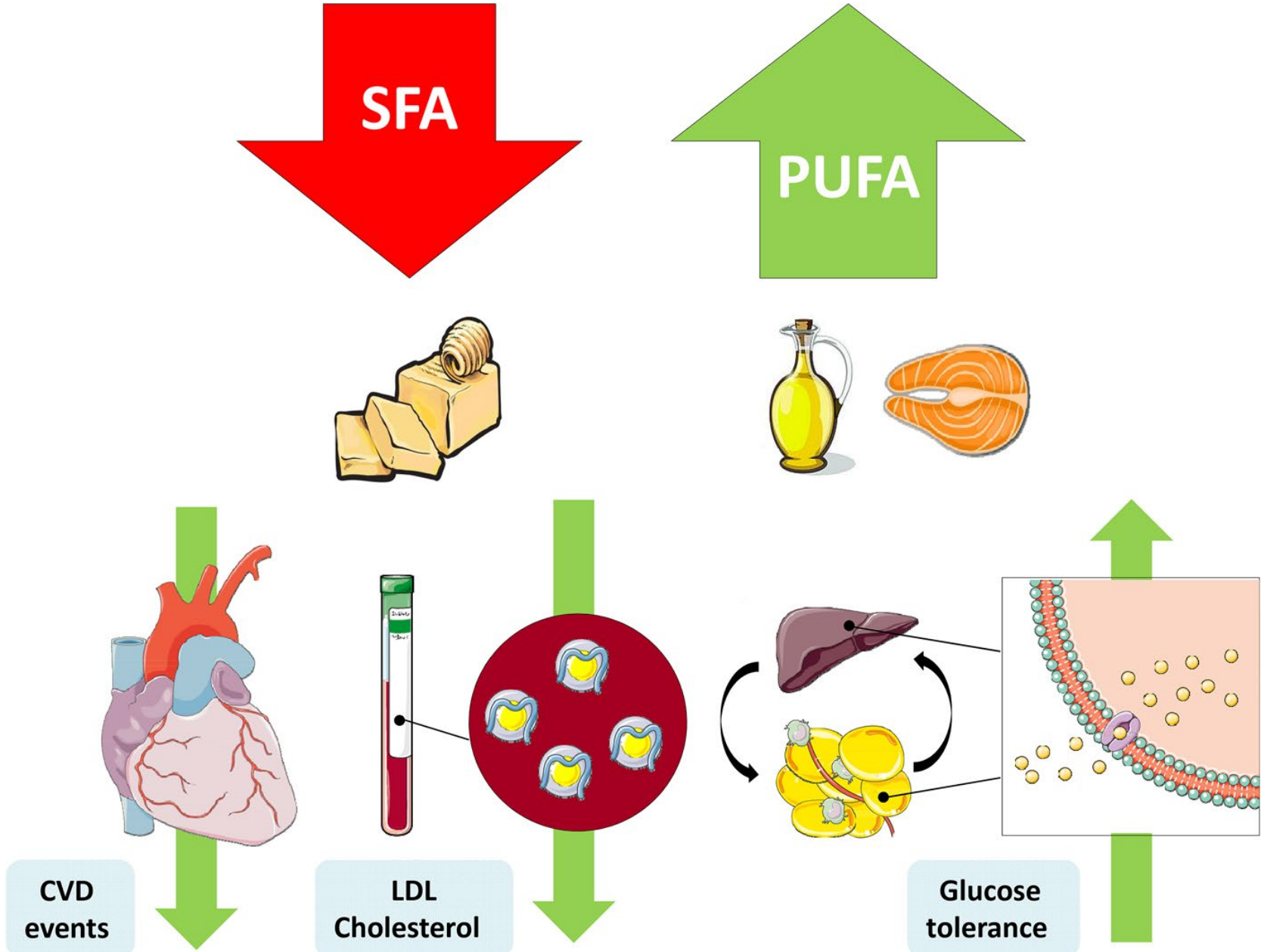
Fats

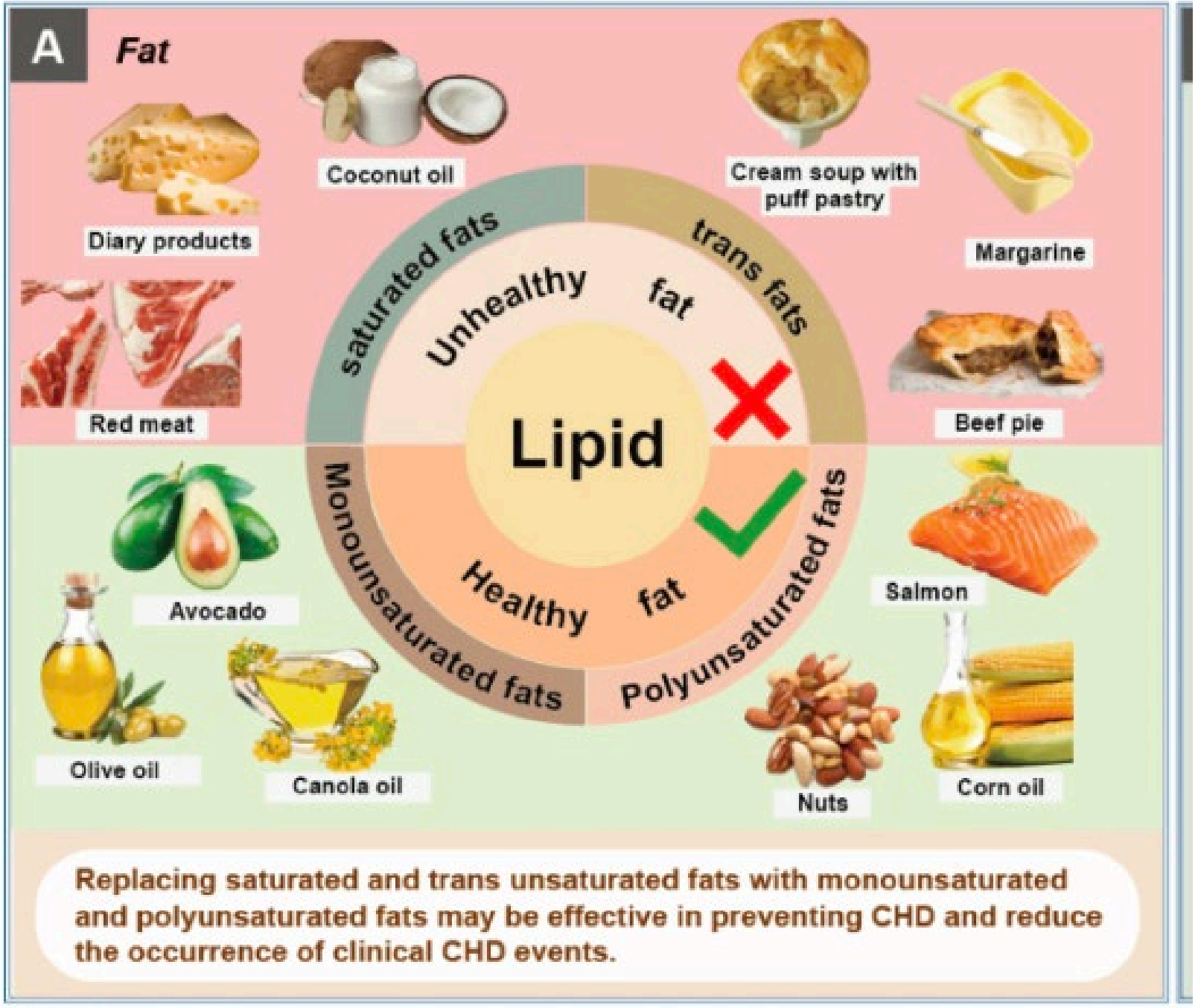
- The dietary fats in foods can be classified into four major types: saturated fats, trans fats, monounsaturated fats, and polyunsaturated fats.

- Excess intake of dietary saturated fat may lead to increased levels of low-density lipoprotein cholesterol, which is a crucial risk factor for CVD progression

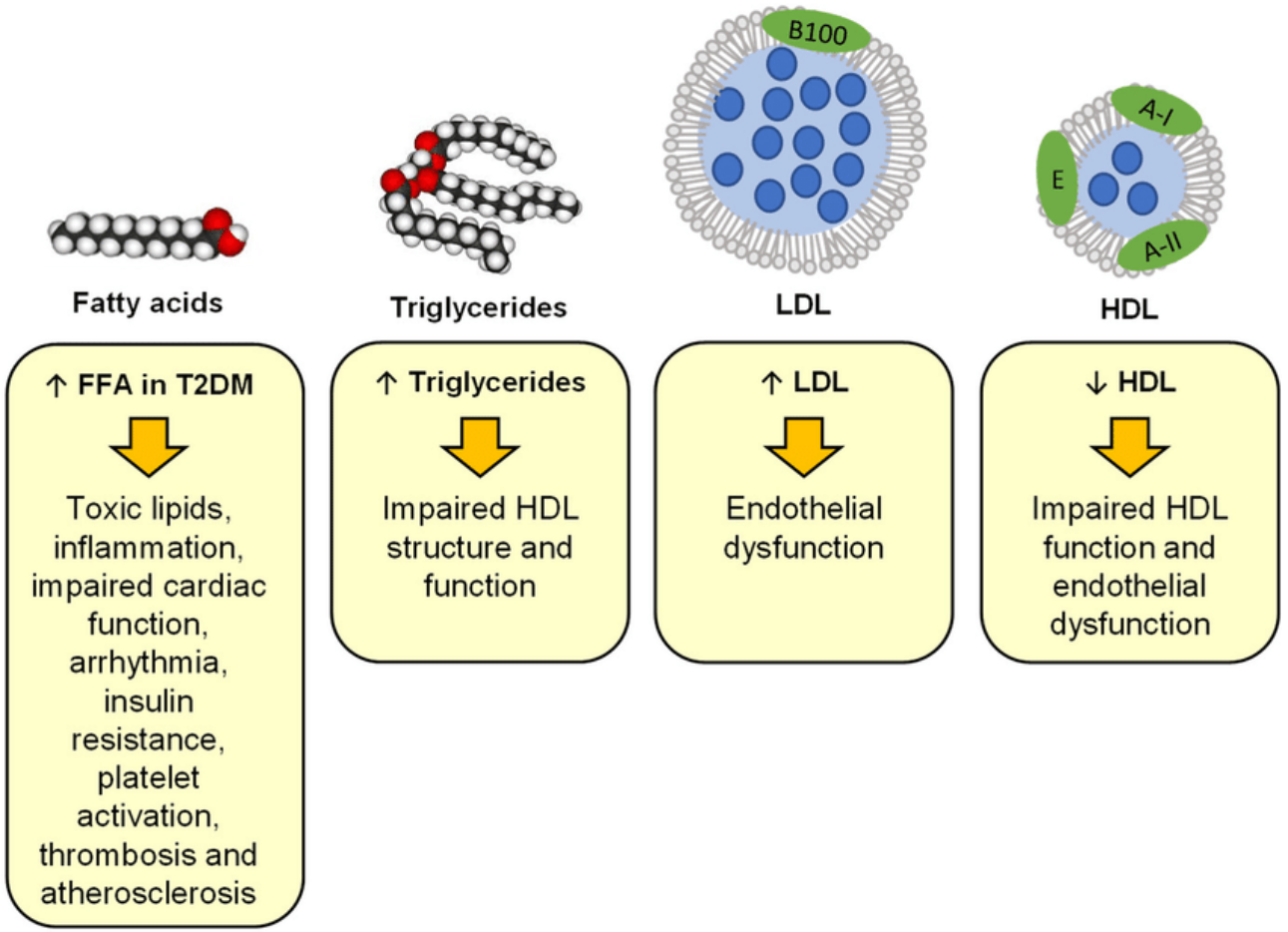
- A prospective analysis of the PREvención con DIeta MEDiterránea (PREDIMED) study with 7038 participants at high CVD risk reports that saturated fatty acid and trans fat intake are associated with a high risk of CVD, whereas intake of monounsaturated fatty acids and polyunsaturated fatty acids are inversely associated with CVD death
- The Mediterranean diet, which is high in monounsaturated fatty acids and polyunsaturated fatty acids, and low in saturated fatty acids and trans fatty acids, is observed to effectively prevent the risk of major cardiovascular events

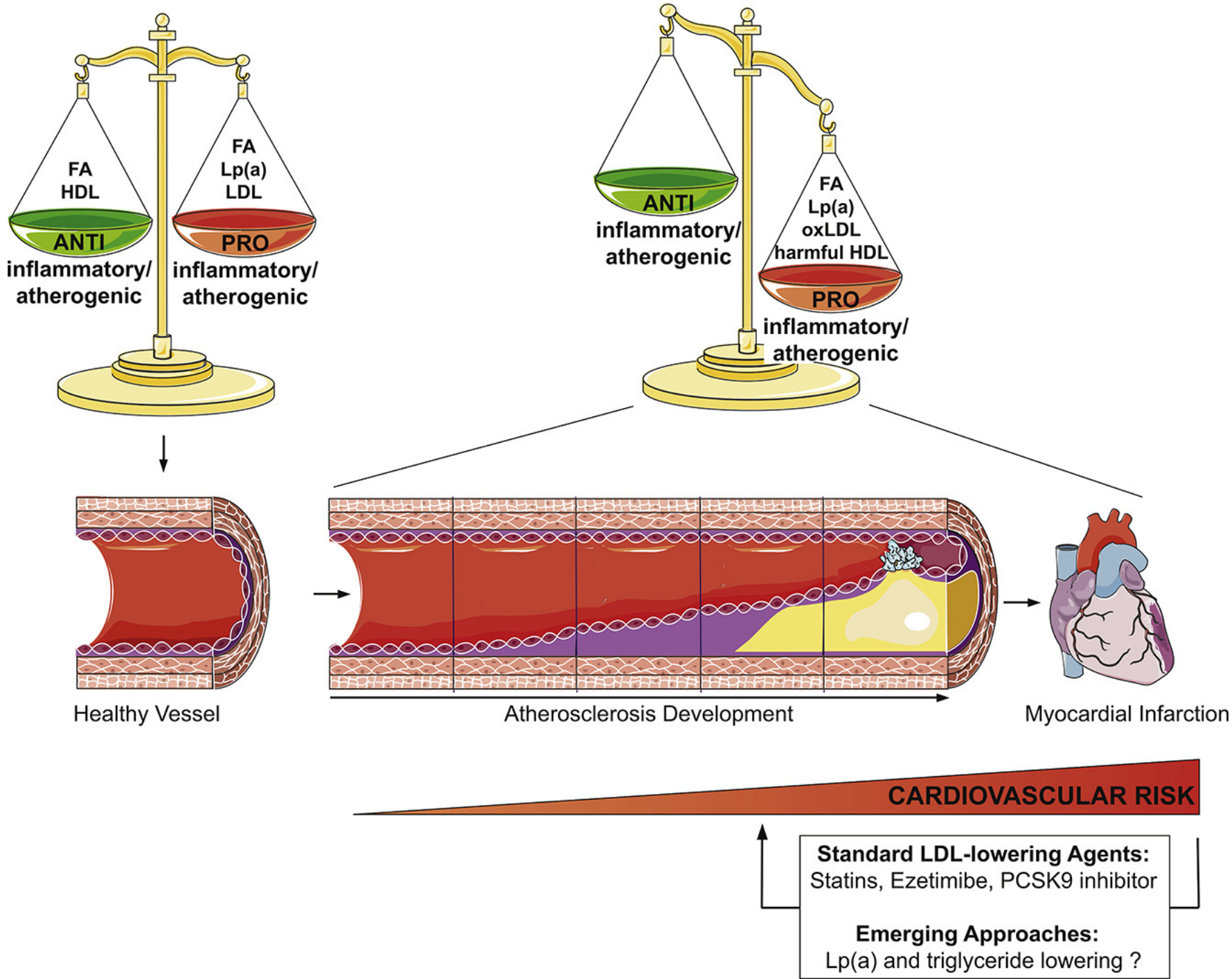
- Specifically, increased intake of linoleic acid, the n-6 polyunsaturated fat primarily from vegetable oils and nuts, is associated with a low risk of both total CHD events and deaths


SFA
PUFA
CVD events
LDL Cholesterol
Glucose tolerance


A
Fat
Coconut oil
Cream soup with puff pastry
Diary products
Margarine
saturated fats
trans fats
Unhealthy fat
Red meat
Beef pie
Lipid
Monounsaturated fats
Polyunsaturated fats
Healthy fat
Avocado
Salmon
Olive oil
Canola oil
Nuts
Corn oil
Replacing saturated and trans unsaturated fats with monounsaturated and polyunsaturated fats may be effective in preventing CHD and reduce the occurrence of clinical CHD events.

Lipid Factions and Effects on CVD




FA
HDL
ANTI
inflammatory/
atherogenic
FA
Lp(a)
LDL
PRO
inflammatory/
atherogenic
ANTI
inflammatory/
atherogenic
FA
Lp(a)
oxLDL
harmful HDL
PRO
inflammatory/
atherogenic
Healthy Vessel
Atherosclerosis Development
Myocardial Infarction
CARDIOVASCULAR RISK
Standard LDL-lowering Agents:
Statins, Ezetimibe, PCSK9 inhibitor
Emerging Approaches:
Lp(a) and triglyceride lowering ?

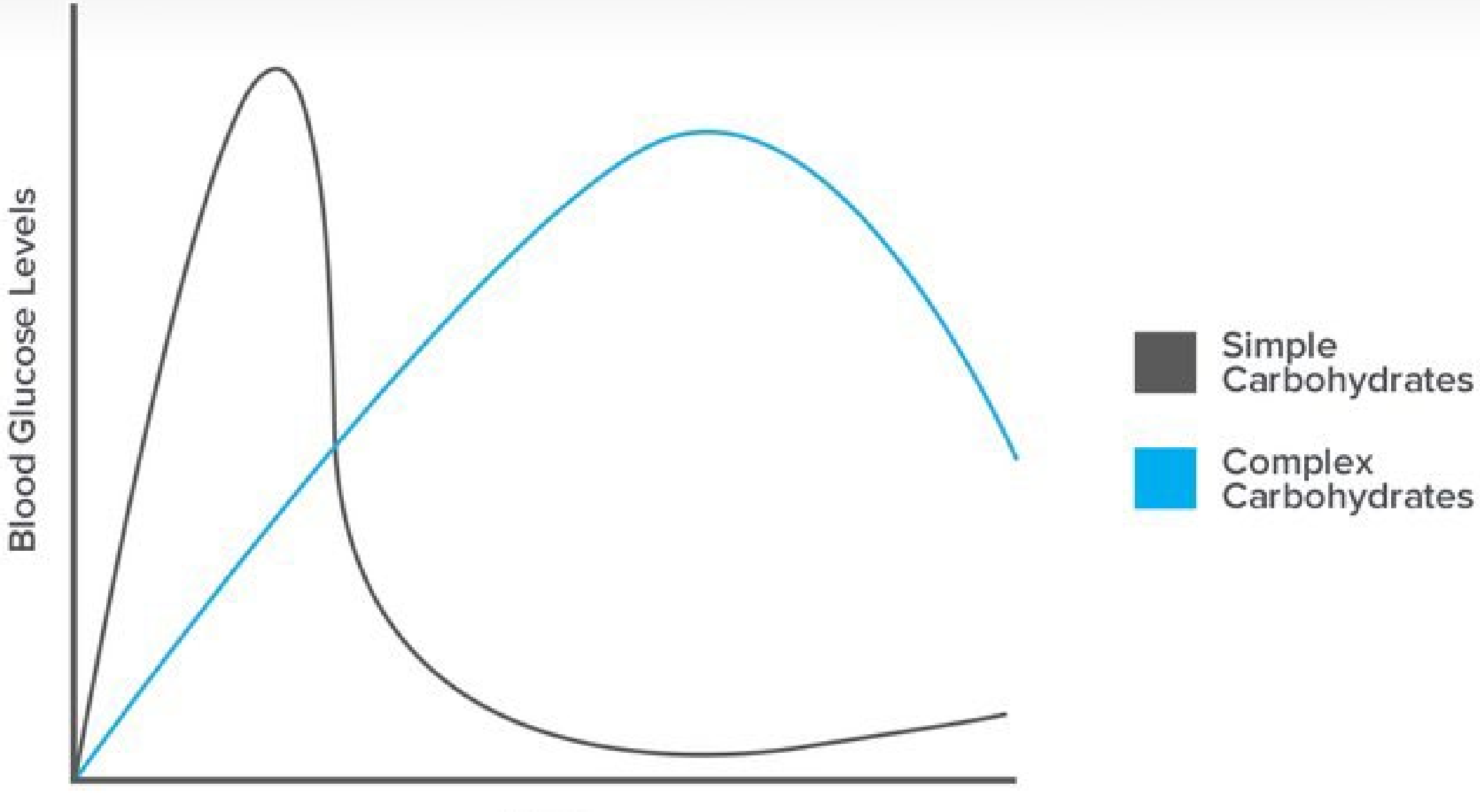
Carbohydrates

SIMPLE CARBS VS. COMPLEX CARBS

Simple Carb vs. Complex Carb Structures:

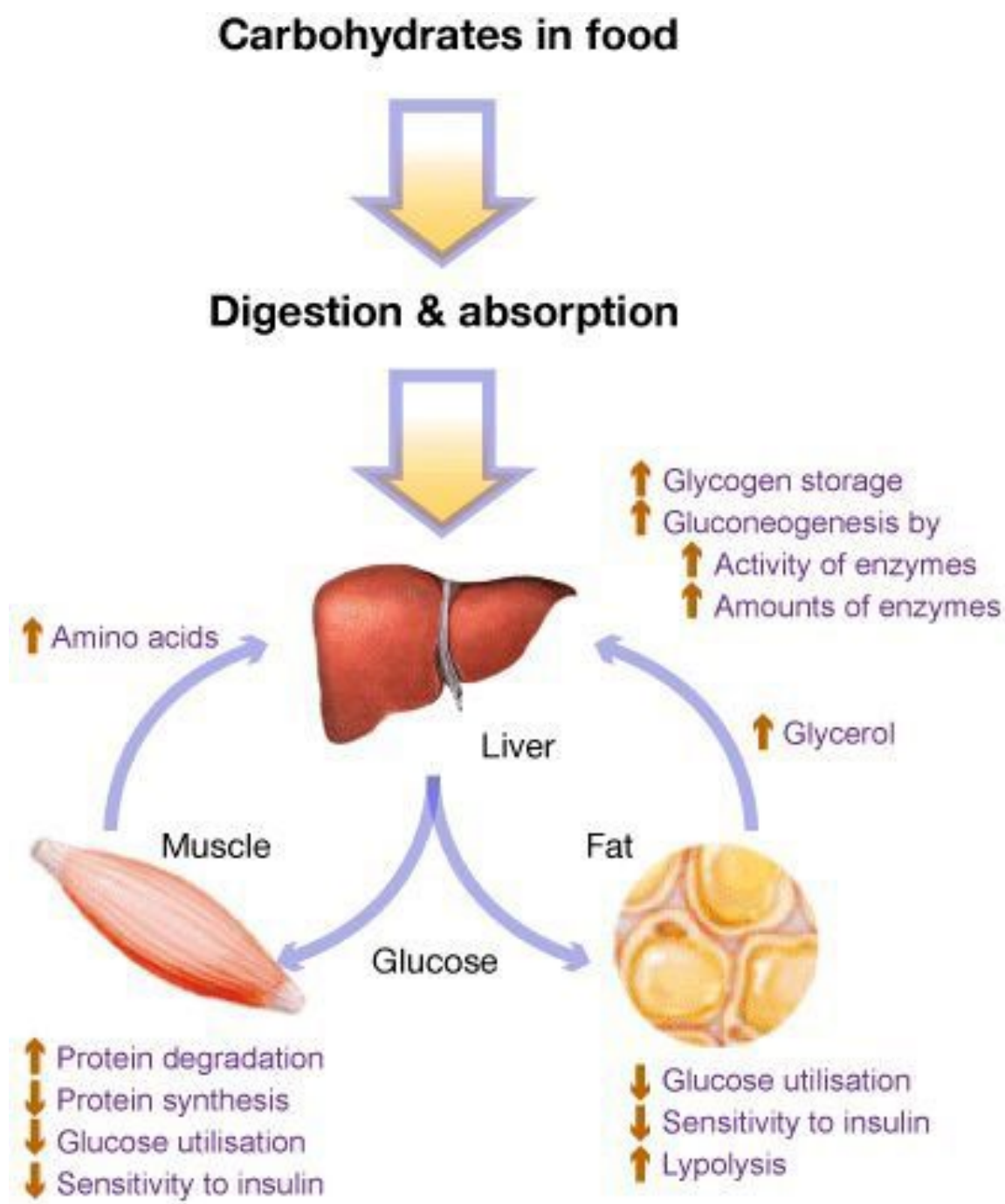
mono-, di- and oliogosaccharides as well as polysaccharides

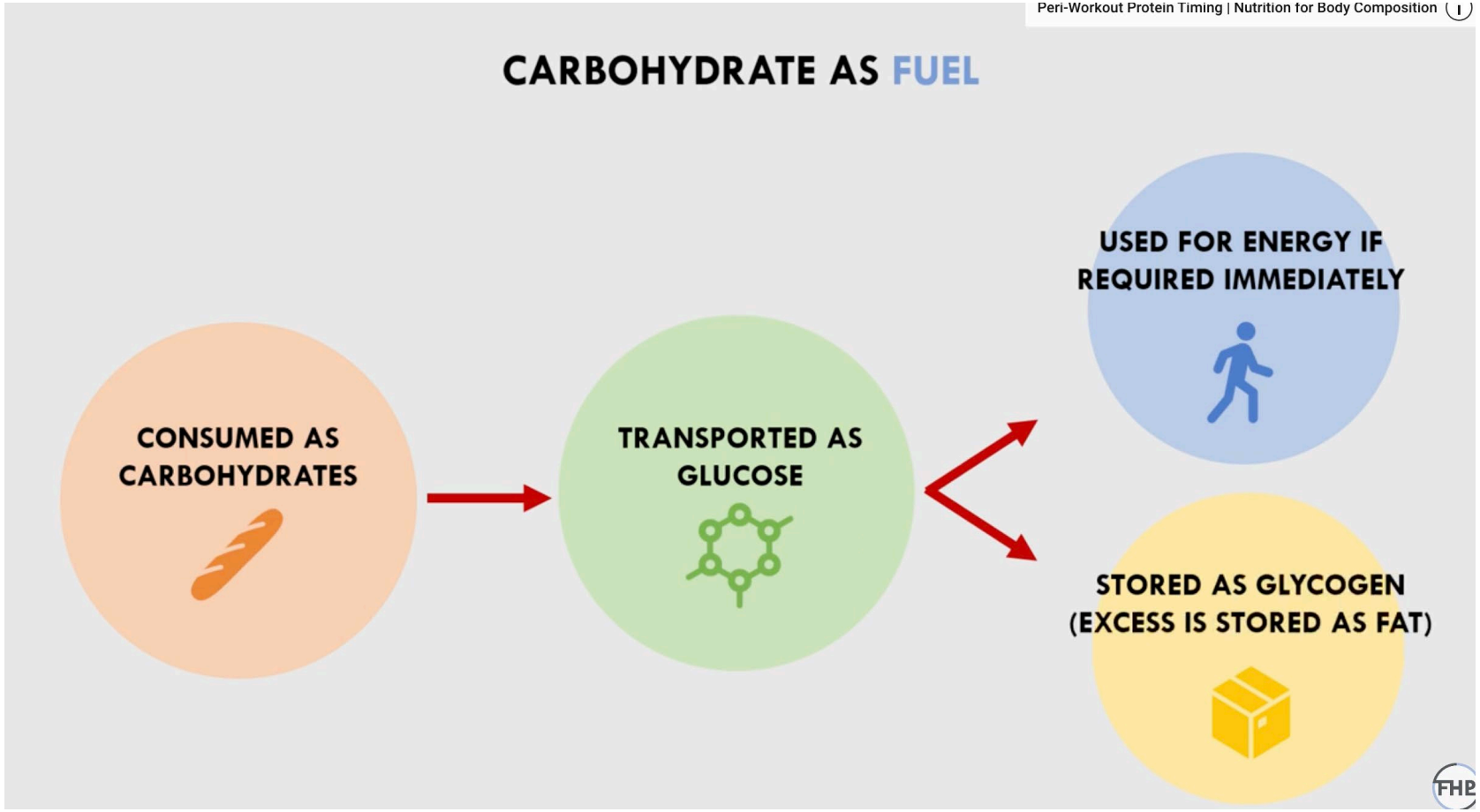
Simple vs. Complex CHO Energy

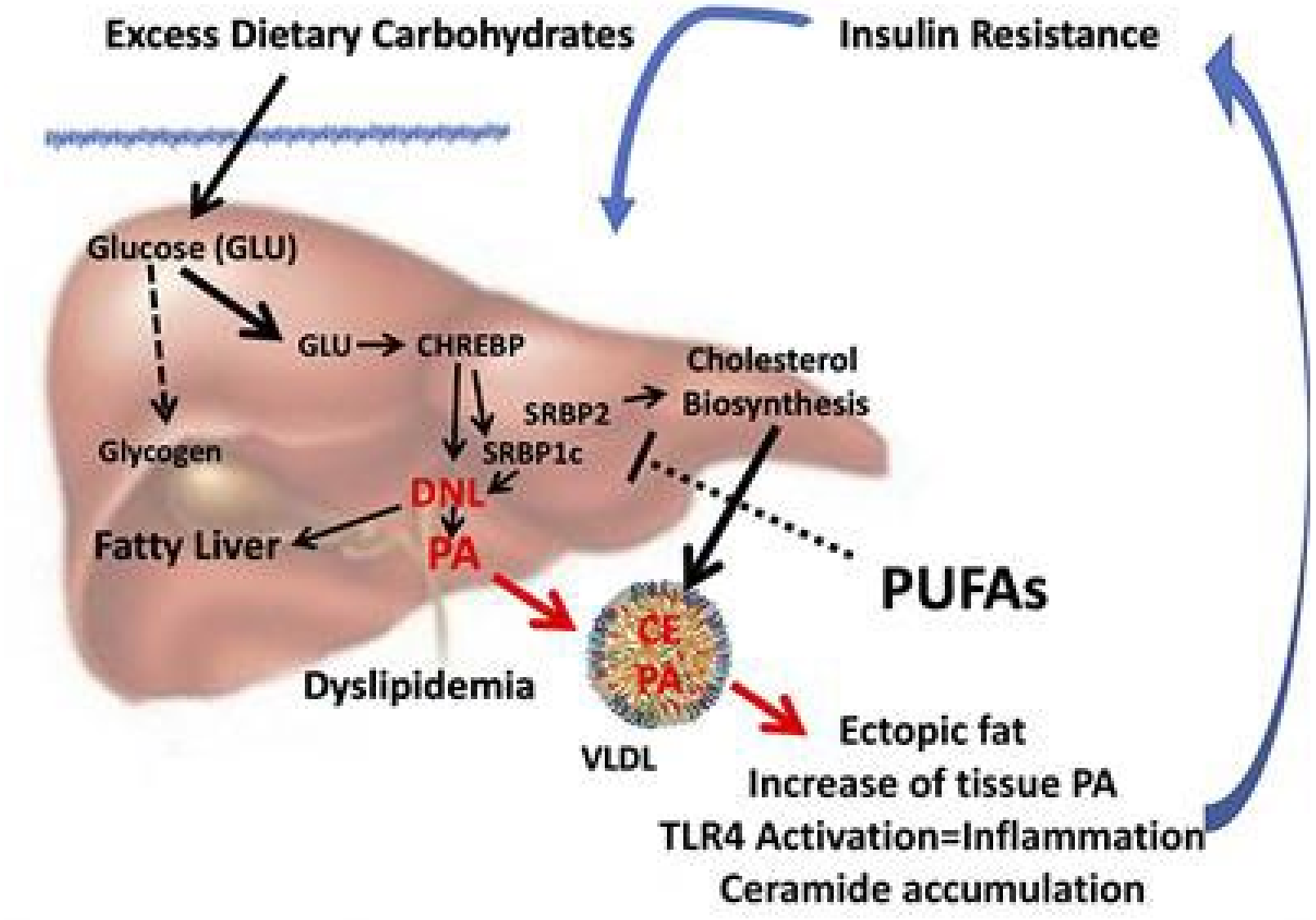


B Carbohydrate

The sources and types of carbohydrates, such as sugar, starch, and fibre, but not the total carbohydrate, should be taken into account by the dietary guidelines. Glycemic index may be used as an indicator of carbohydrate quality related to CVD.


Carbohydrates in food
Digestion & absorption
Glycogen storage
Gluconeogenesis by
Activity of enzymes
Amounts of enzymes
Amino acids
Liver
Glycerol
Muscle
Fat
Glucose
Protein degradation
Protein synthesis
Glucose utilisation
Sensitivity to insulin
Glucose utilisation
Sensitivity to insulin
Lypolysis


CARBOHYDRATE AS FUEL
CONSUMED AS CARBOHYDRATES
TRANSPORTED AS GLUCOSE
USED FOR ENERGY IF REQUIRED IMMEDIATELY
STORED AS GLYCOGEN (EXCESS IS STORED AS FAT)
FHP


Excess Dietary Carbohydrates
Insulin Resistance
Glucose (GLU)
GLU → CHREBP
Glycogen
SRBP2
Cholesterol Biosynthesis
SRBP1c
DNL
Fatty Liver
PA
PUFAs
CE
PA
Dyslipidemia
VLDL
Ectopic fat
Increase of tissue PA
TLR4 Activation=Inflammation
Ceramide accumulation

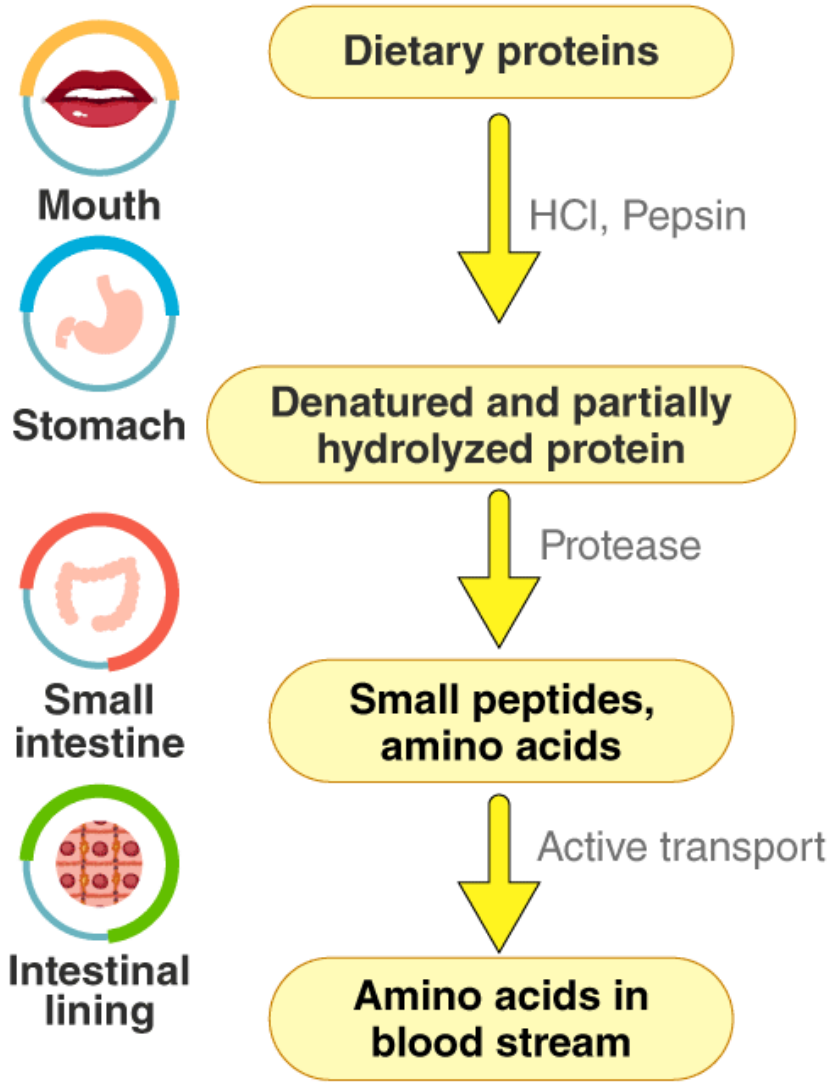
Carbohydrates

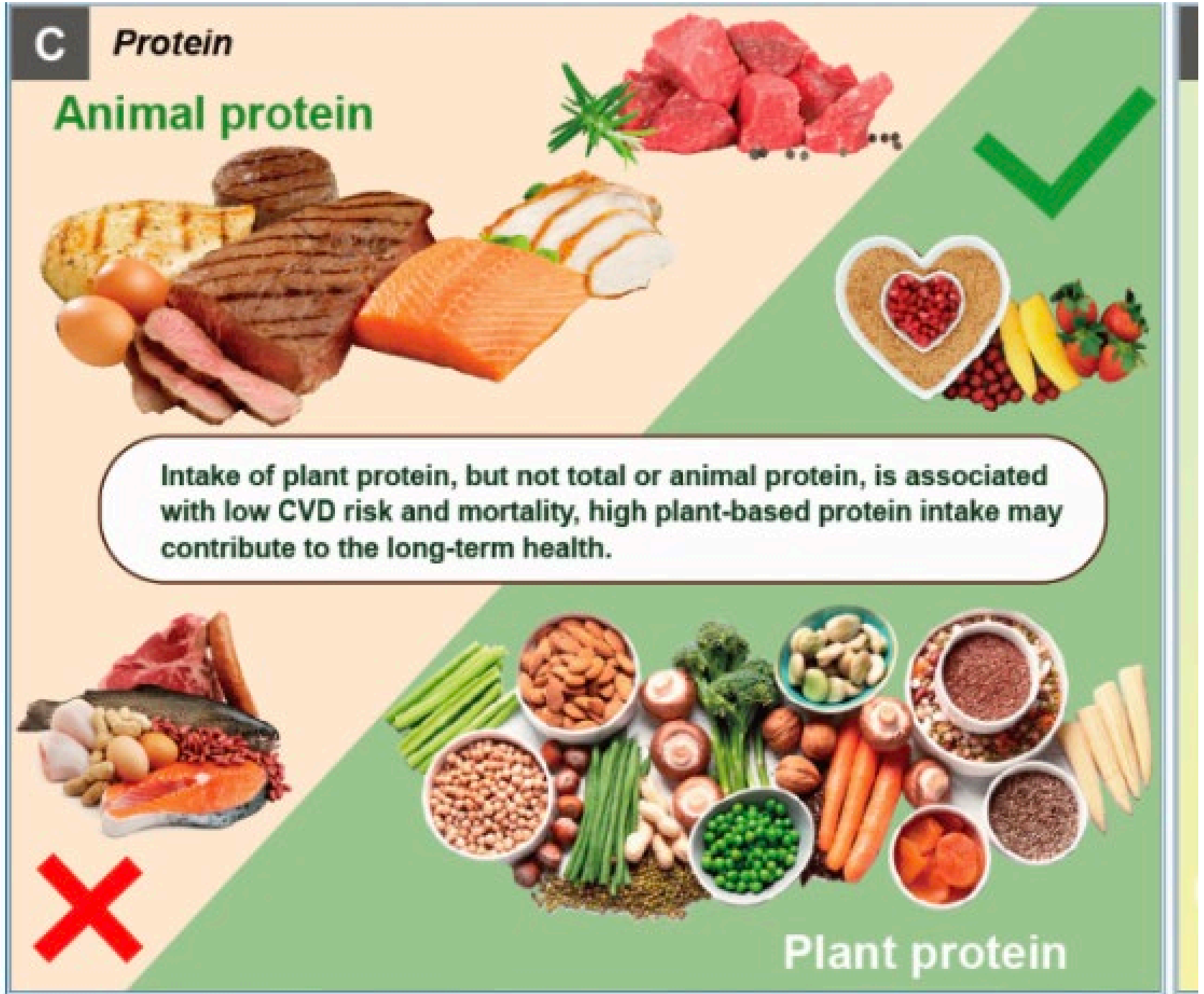
- Low-carbohydrate, high-protein, high-fat diet is found to be beneficial in reducing body weight and improving risk factors for CHD in obese persons

- The data from the UK Biobank cohort show that distinct carbohydrates display different associations with mortality and CVD risk, indicating that the sources and types of carbohydrates, such as sugar, starch, and fiber, but not the total carbohydrates, should be taken into account

- GI may be used as an indicator of carbohydrate quality related to CVD or other chronic diseases. Improving carbohydrate quality by lowering the GI is important for dietary intervention in preventing the adverse outcomes associated with CVD

Proteins


Dietary proteins
Mouth
HCl, Pepsin
Stomach
Denatured and partially hydrolyzed protein
Protease
Small intestine
Small peptides, amino acids
Active transport
Intestinal lining
Amino acids in blood stream


C
Protein
Animal protein
Intake of plant protein, but not total or animal protein, is associated with low CVD risk and mortality, high plant-based protein intake may contribute to the long-term health.
Plant protein

Protein

- Protein plays a critical role in promoting health. It acts on the metabolic targets involved in satiety, appetite, and energy metabolism. The early studies showed that consumption of high-protein diets may contribute to the prevention of obesity and metabolic syndrome.
- studies have shown that replacing carbohydrates with protein is associated with a low risk of ischemic heart disease (IHD) and an improvement in cardiometabolic risk factors

Vitamins

- In postmenopausal women, intake of vitamin E, but not vitamins A and C, has been reported to be inversely associated with the risk of CHD. The preventive benefits of folic acid and B vitamins in stroke prevention are also reported

CENTRAL ILLUSTRATION: Vitamin D and Calcium Supplements for Cardiovascular Health: Evidence From Observational and Interventional Studies and Clinical Recommendations

	Vitamin D Supplements	Calcium Supplements
Observational Studies	Multiple studies report associations between low blood Vitamin D levels and worse CV health Potential for confounding, reverse causation and other biases	Several studies suggest calcium supplements might increase risk of CVD Potential for confounding, reverse causation and other biases
RCTs	In RCTs, Vitamin D supplements did not prevent CVD 	Some RCTs and trial meta-analyses suggest that calcium supplements increase risk of MI and stroke 
Recommendations	Obtain Vitamin D through adequate diet plus moderate sun exposure   Consider supplementation if Vitamin D inadequacy/insufficiency, although effects for bone health likely modest 	To improve bone health, increase physical activity and intake of calcium from diet  If supplements are considered, incorporate potential risks of CVD into the clinician-patient discussion 

Michos, E.D. et al. J Am Coll Cardiol. 2021;77(4):437–49.

MTHFR

- The *MTHFR* gene provides instructions for making an enzyme called methylenetetrahydrofolate reductase. This enzyme plays a role in processing amino acids, the building blocks of proteins. Methylenetetrahydrofolate reductase is important for a chemical reaction involving the vitamin folate (also called vitamin B9)

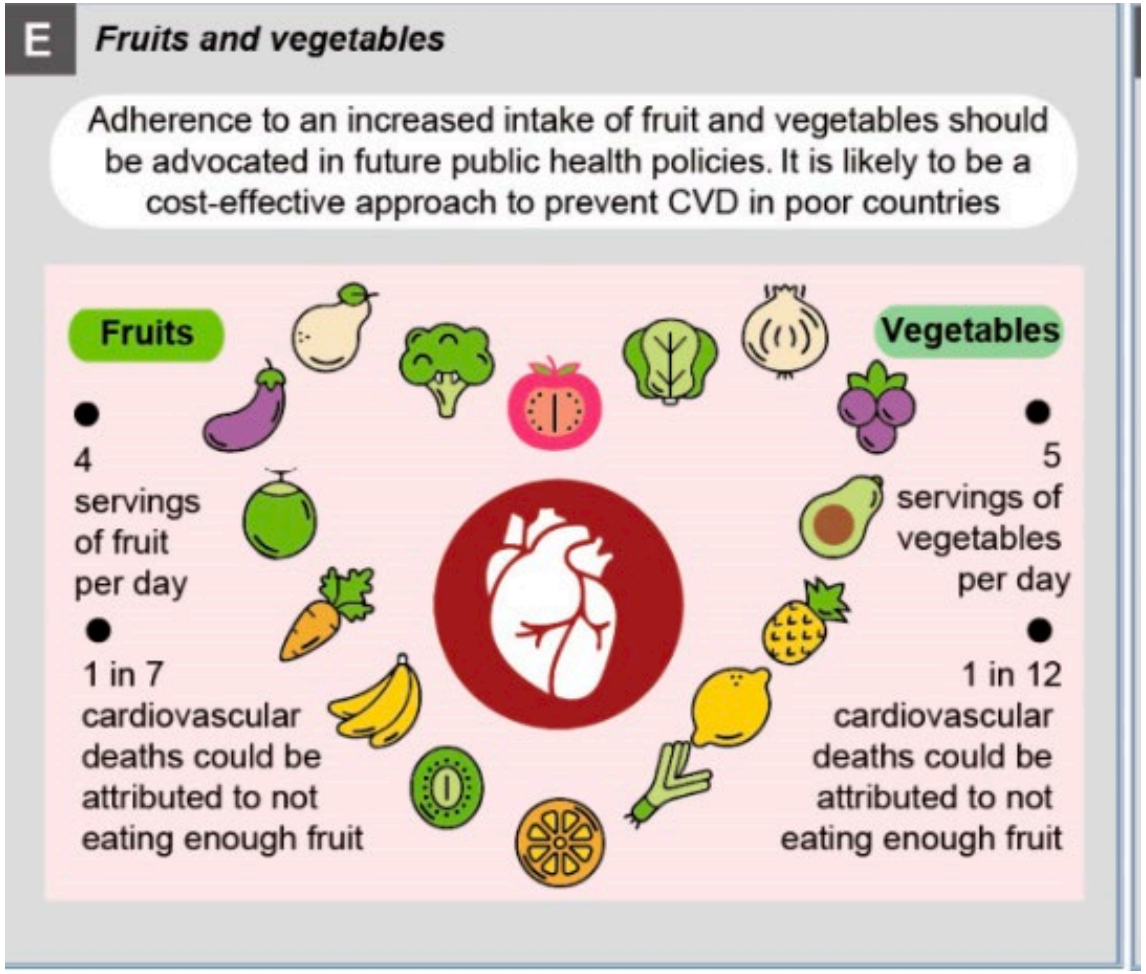
- Its deficiency leads to an increased serum level of homocysteine, which is well-known to be associated with premature coronary artery disease (CAD). Our case demonstrates the association of MTHFR polymorphism with premature CAD and myocardial infarction (MI) despite normal homocysteine levels. Screening for MTHFR polymorphisms in addition to homocysteine levels may be considered for patients presenting with premature CAD and a normal lipid profile.

Fiber

- The regular consumption of fruits, vegetables, and cereals has been encouraged by dietary guidelines as important sources of dietary fiber.
- WHO states that a healthy diet should contain more than 25 g of dietary fiber per day. Intakes in the range of 25–30 g of fiber daily is recommended by most European countries

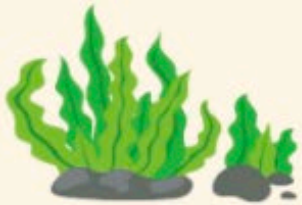
Fiber

- A fruit and vegetable intake over five servings/day has been reported to be associated with lower risk of CHD [125]. An intake of 800 g/day of combined apples/pears, citrus fruits, green leafy vegetables/salads, and cruciferous vegetables is able to reduce the risk of CVD



E *Dietary fiber*

Foods rich in soluble fiber



Kelp

Konjak

Beans

Apple

Foods rich in insoluble fiber

Brown rice

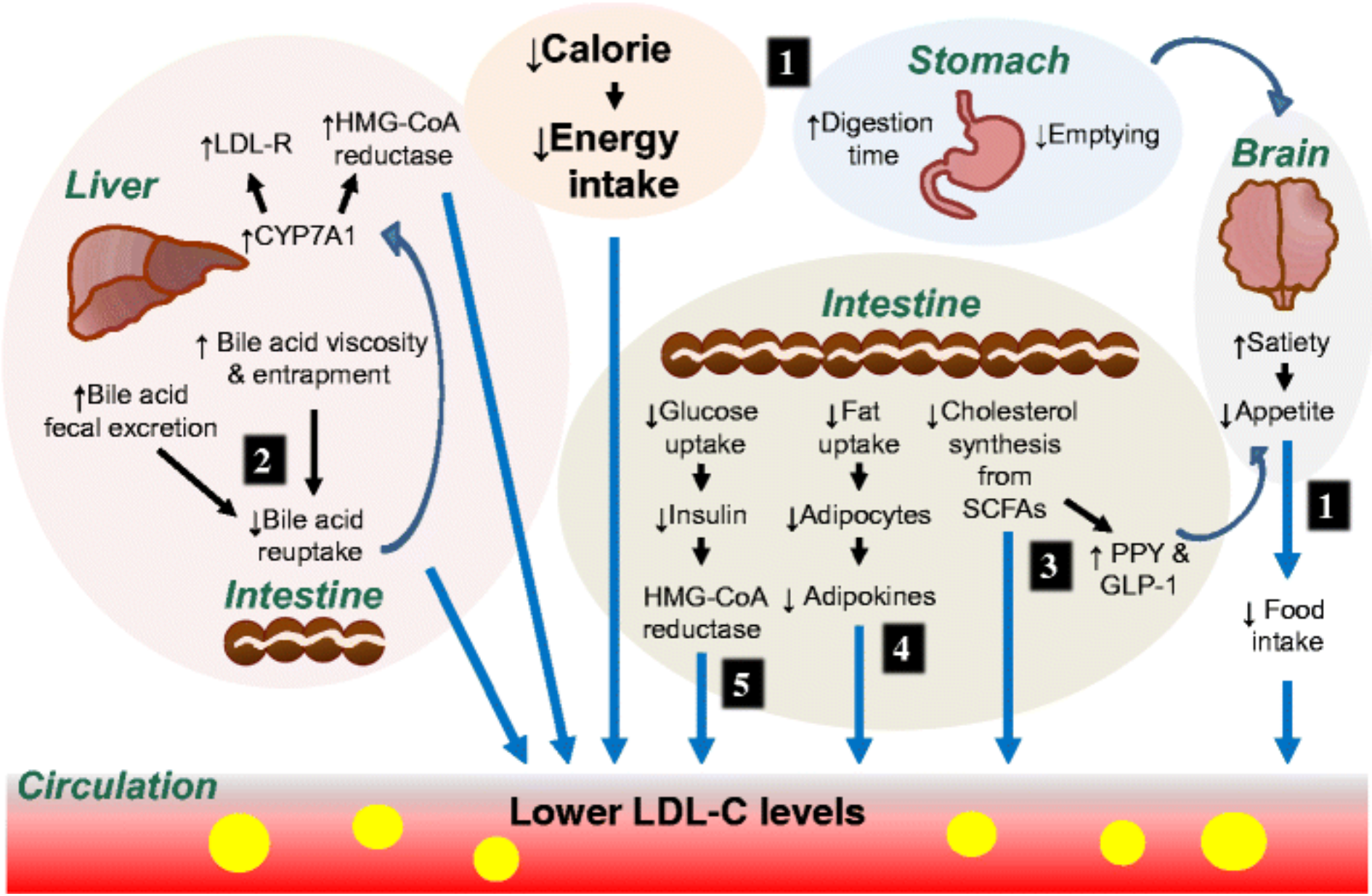
Corn

Broccoli

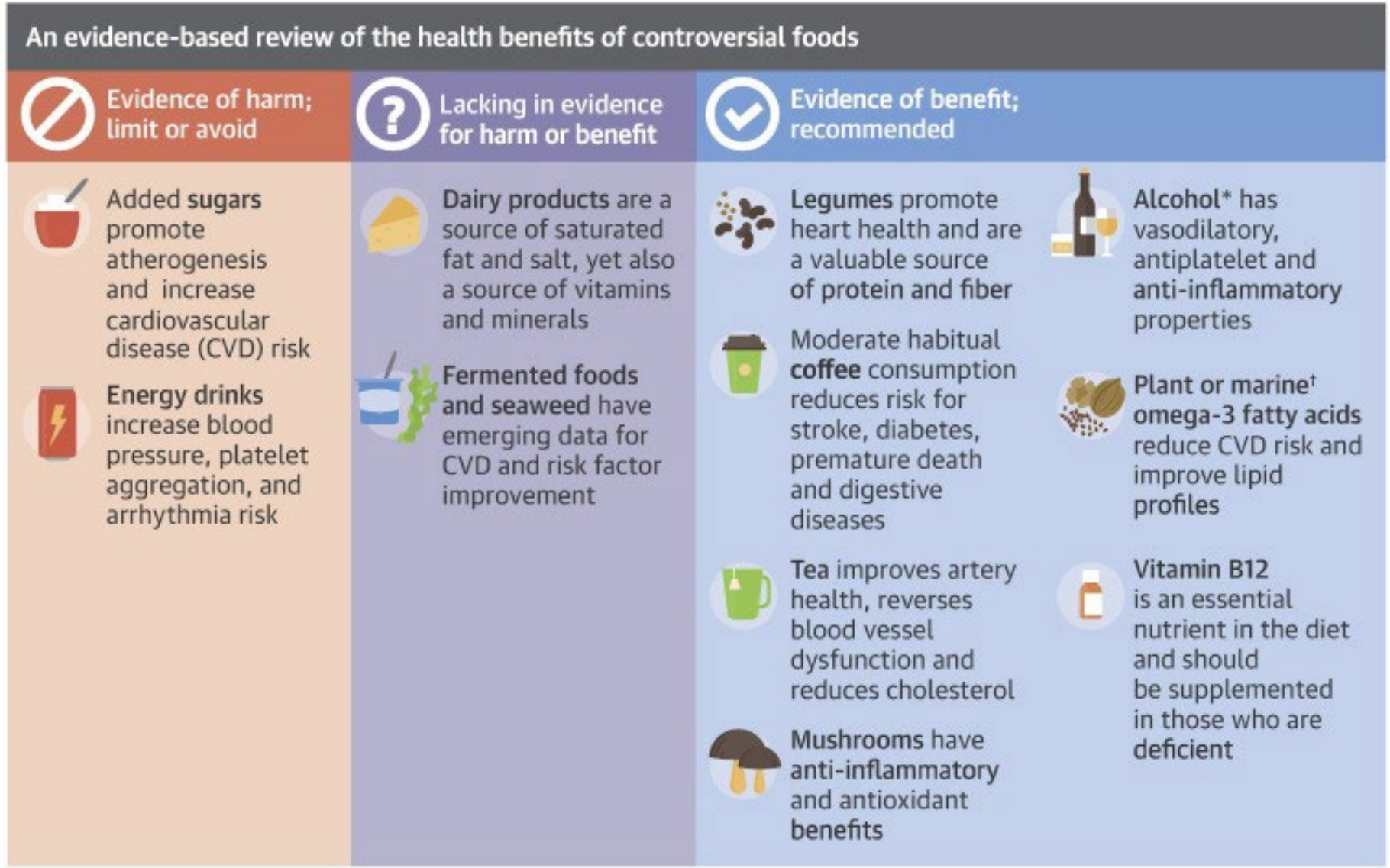
Bamboo shoot

The available evidence strongly support that intake of dietary fiber is associated with improved CVD risk factors.

Dietary Fiber

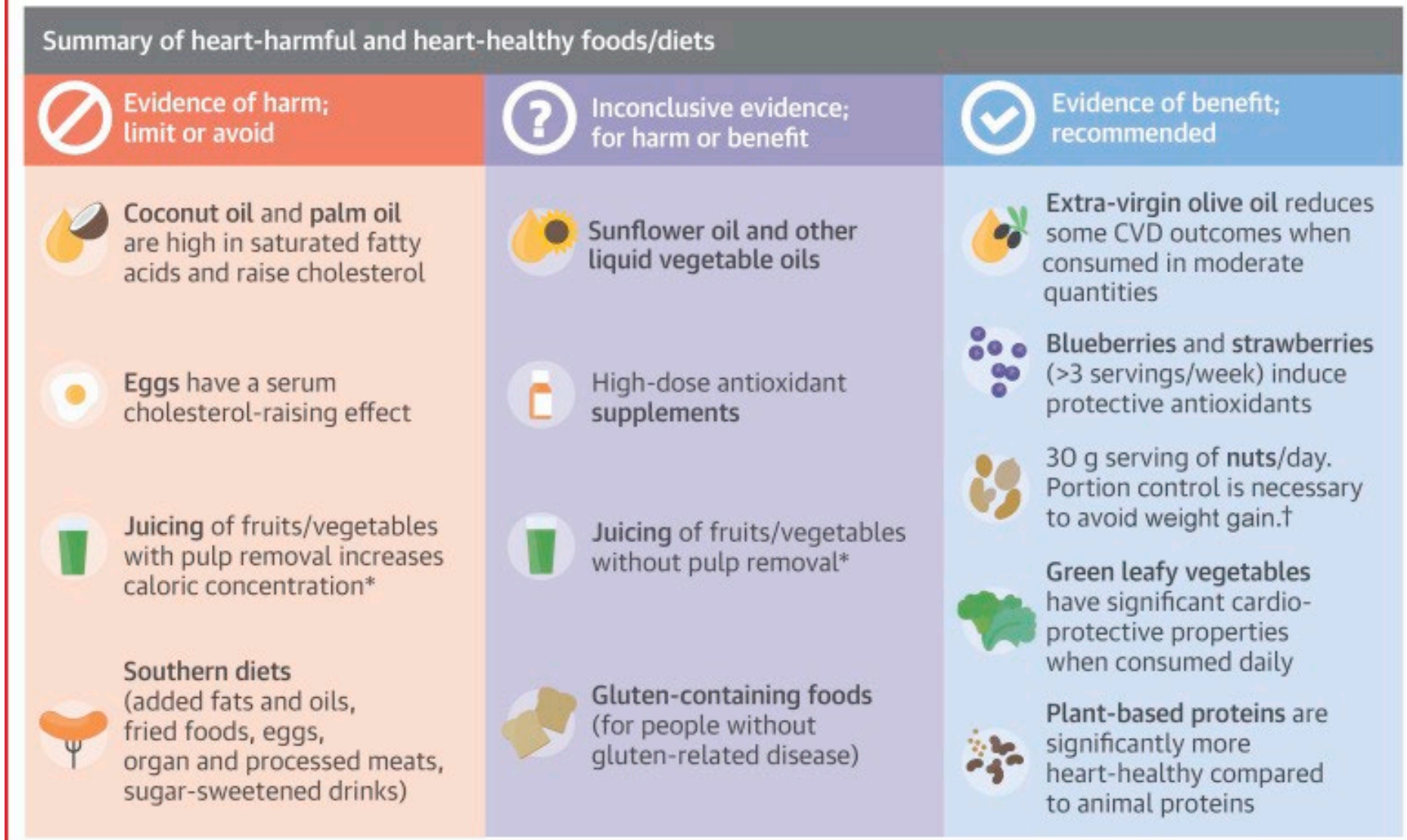


CENTRAL ILLUSTRATION: Cardiovascular Health Benefits Based on Evidence of Controversial Foods



Freeman, A.M. et al. J Am Coll Cardiol. 2018;72(5):553-68.

CENTRAL ILLUSTRATION: Evidence for Cardiovascular Health Impact of Foods Reviewed

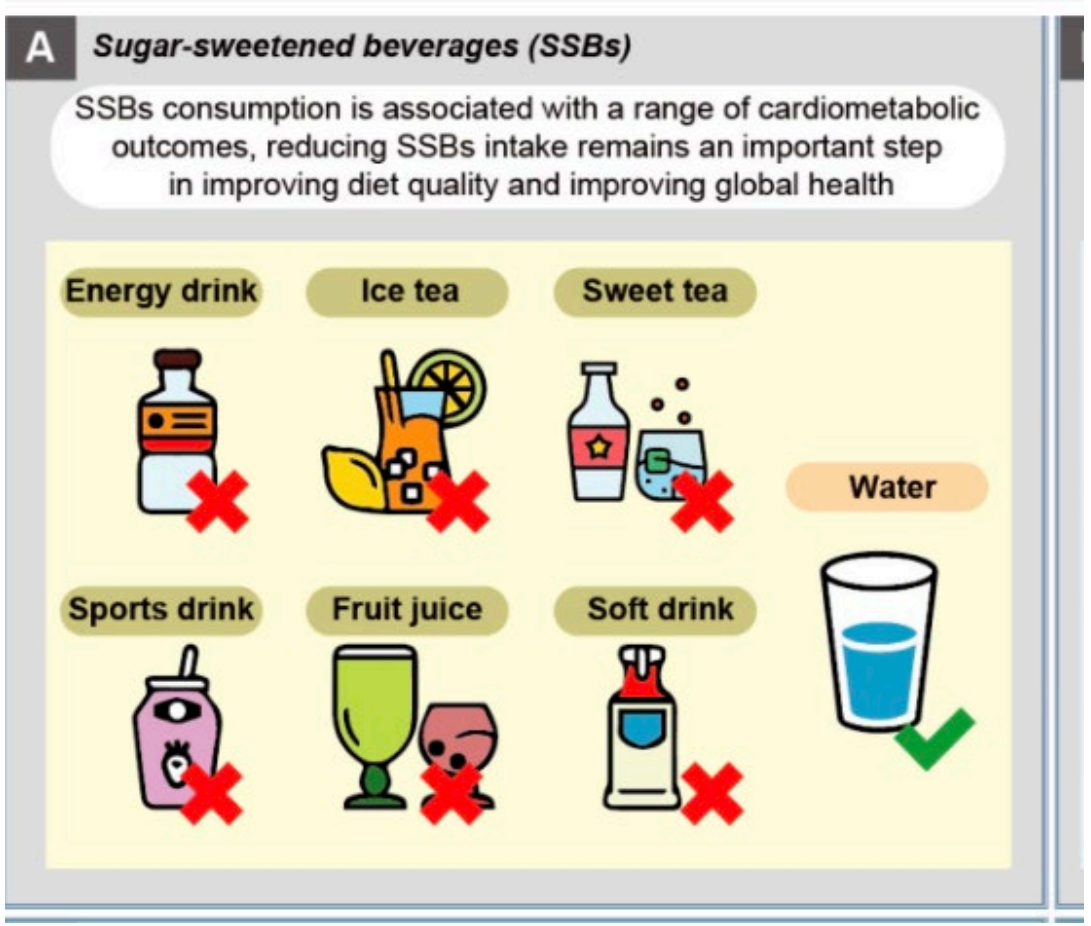


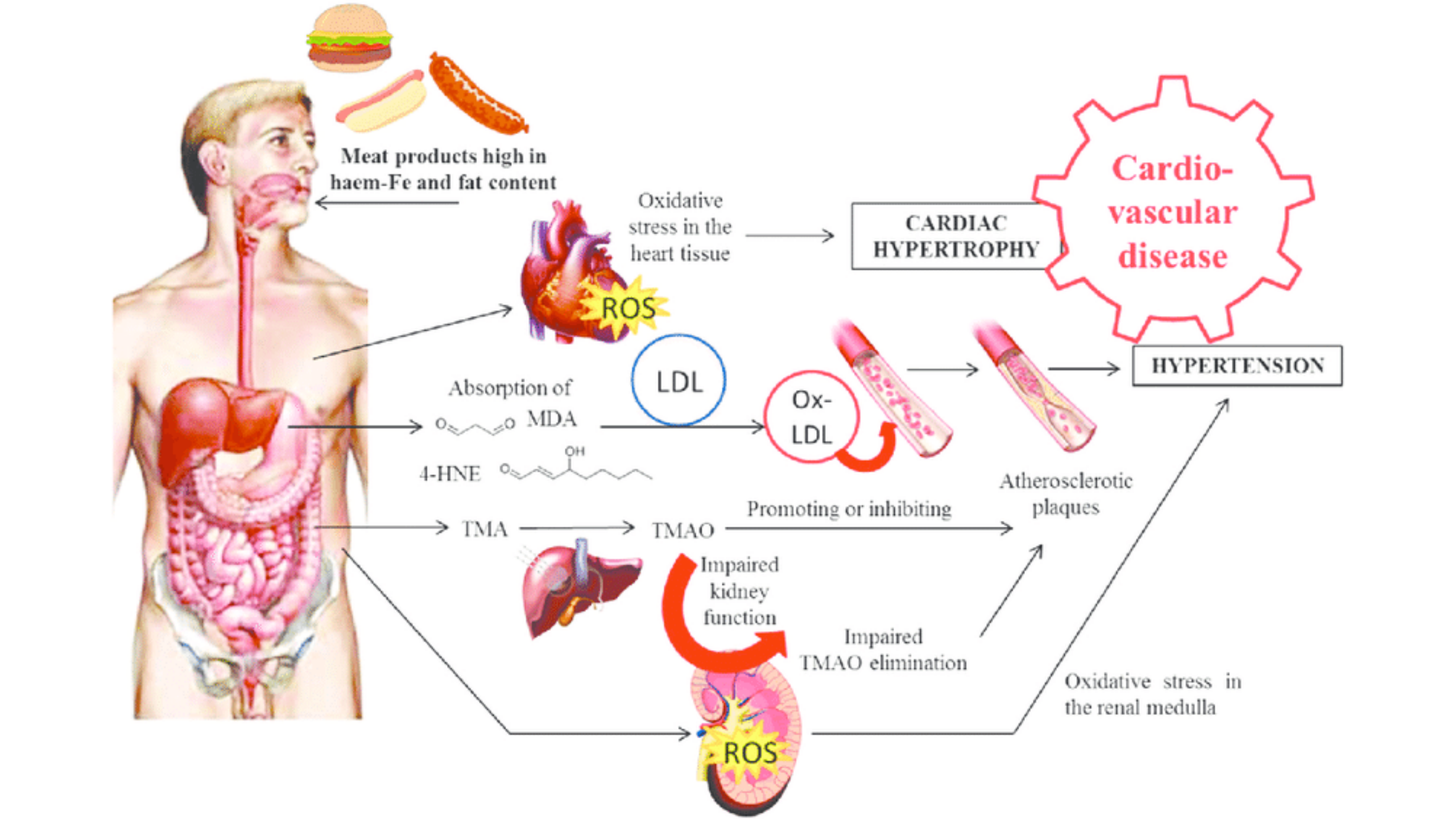
Freeman, A.M. et al. J Am Coll Cardiol. 2017;69(9):1172-87.

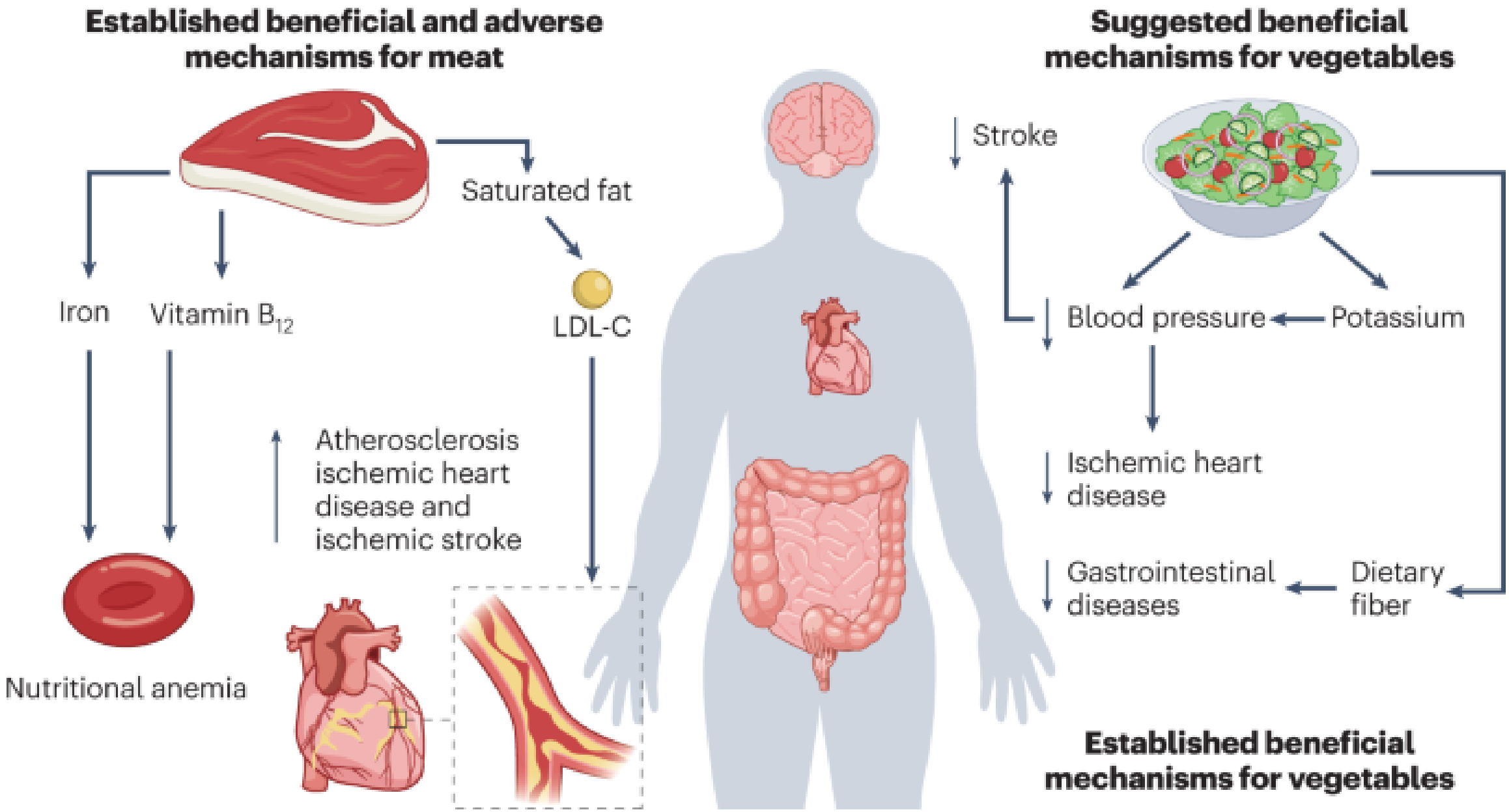
Sugary Drinks

- SSBs, which include carbonated and noncarbonated soft drinks, fruit drinks, and sports drinks that contain added caloric sweeteners, are the largest source of added sugar in the diet in high-income countries. Given the emerging association of added sugars with cardiometabolic risk factors, health authorities including

- For instance, a direct association between high artificial sweetener intake and increased CVD risk has been established, suggesting that ASBs may not be a healthy substitute for SSBs

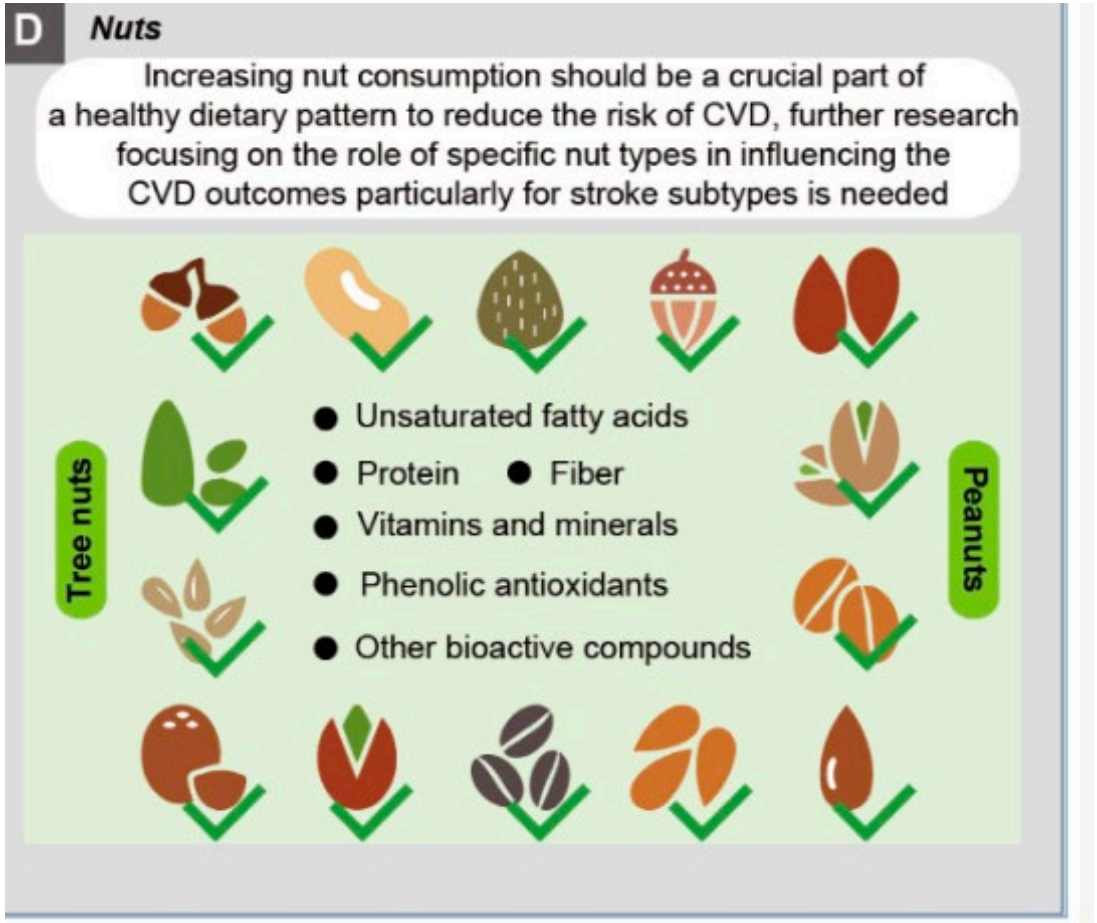



Meat products high in haem-Fe and fat content
Oxidative stress in the heart tissue
CARDIAC HYPERTROPHY
Cardio-vascular disease
ROS
LDL
Absorption of MDA
4-HNE
Ox-LDL
HYPERTENSION
Atherosclerotic plaques
TMA
TMAO
Promoting or inhibiting
Impaired kidney function
Impaired TMAO elimination
Oxidative stress in the renal medulla
ROS


Established beneficial and adverse mechanisms for meat
Saturated fat
Iron
Vitamin B_{12}
LDL-C
Atherosclerosis ischemic heart disease and ischemic stroke
Nutritional anemia
Suggested beneficial mechanisms for vegetables
Stroke
Blood pressure
Potassium
Ischemic heart disease
Gastrointestinal diseases
Dietary fiber
Established beneficial mechanisms for vegetables

Nuts

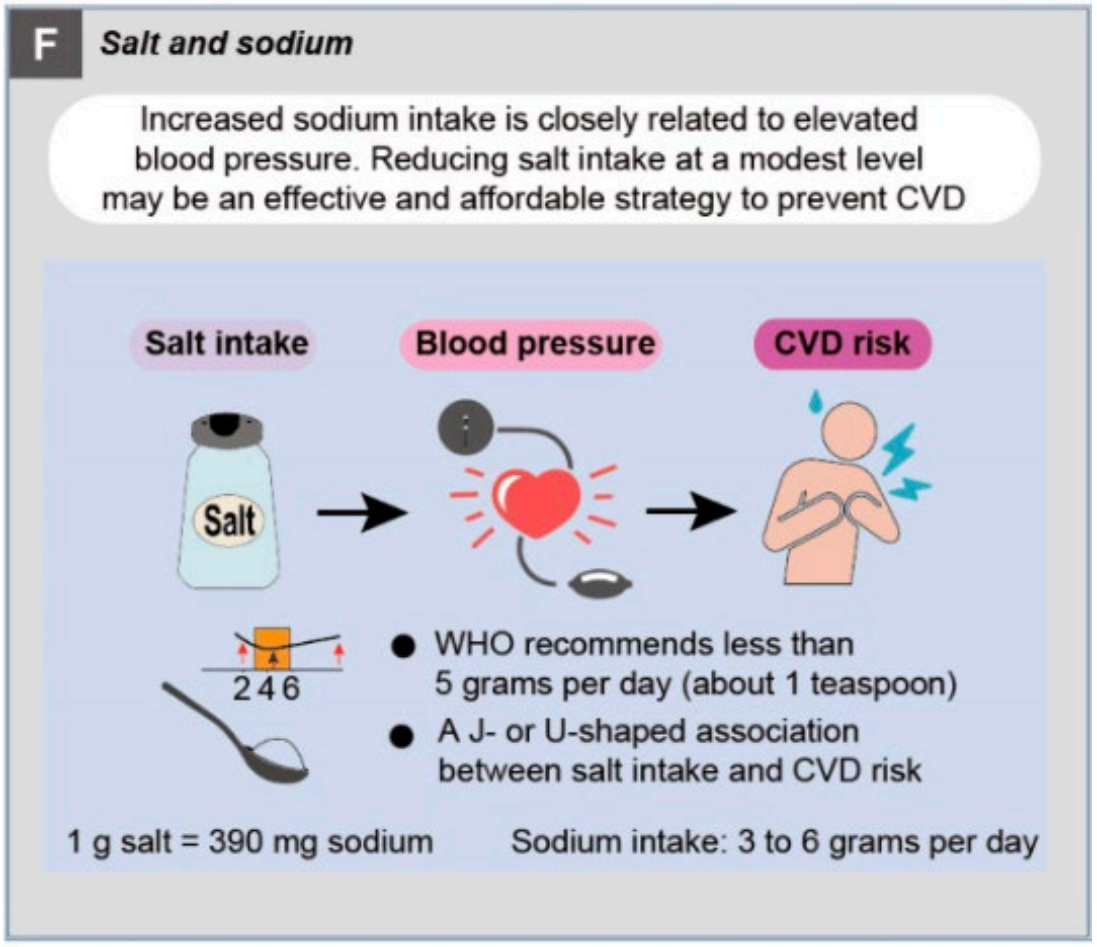
- Studies have shown that a one-serving (28 g) increase in nut intake per day is associated with a 29% and 21% reduction in the relative risk of CHD and CVD, respectively, when compared with not eating nuts



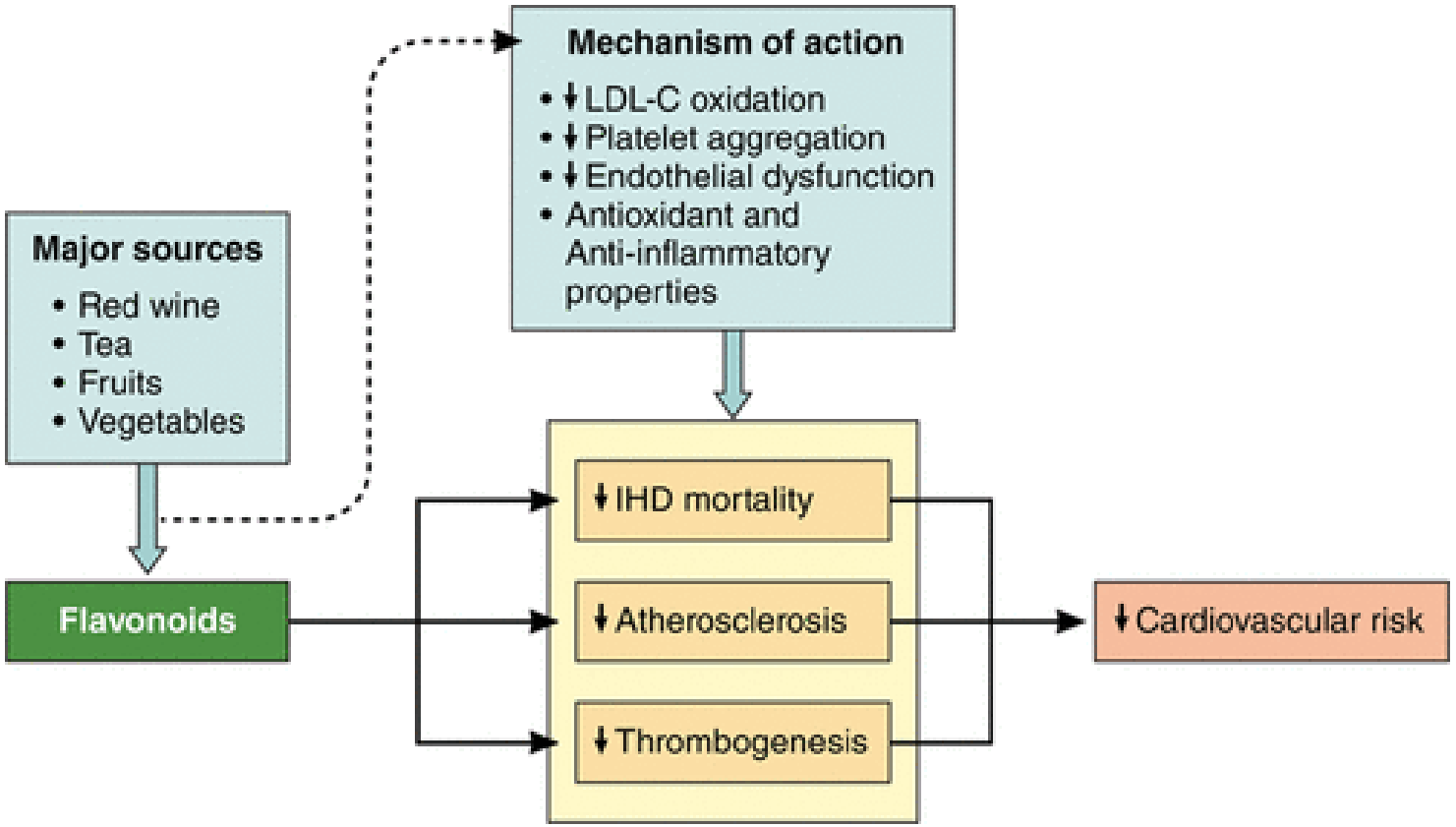
SALT

- Salt is an important nutrient component of a healthy diet, and the human body needs a certain amount of salt to maintain cellular homeostasis

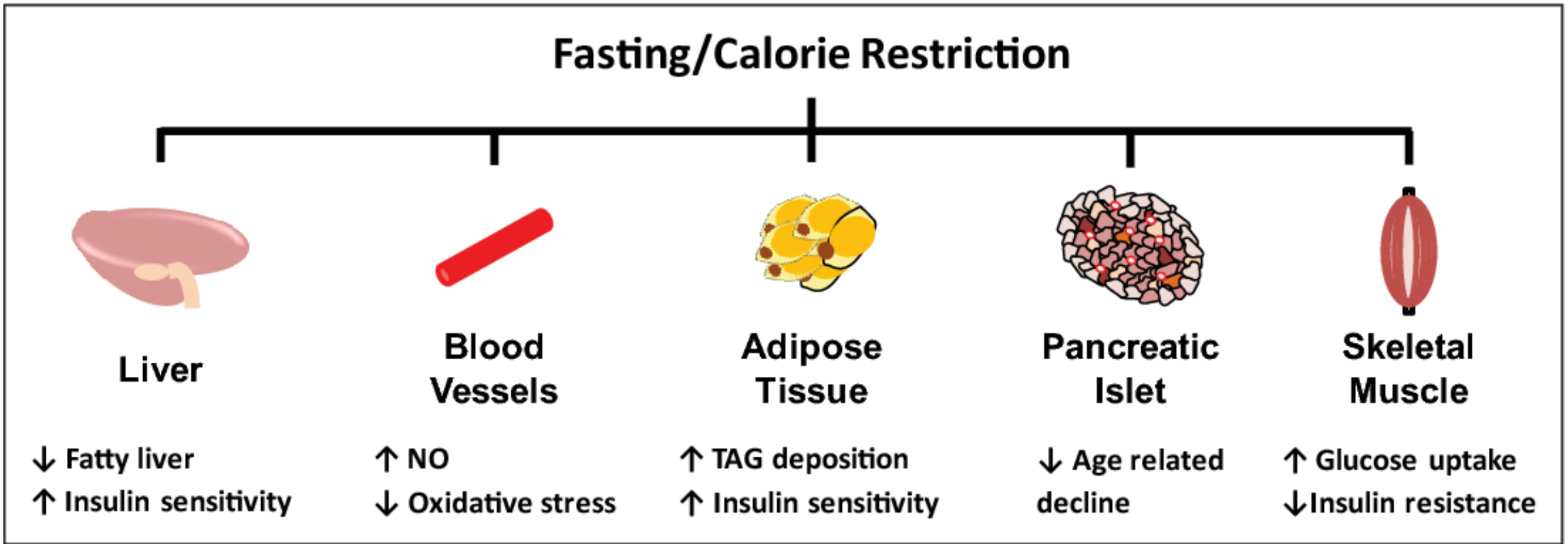
- The role of sodium in cardiovascular health is to maintain intravascular volume. Accumulating evidence has shown that increased sodium intake is closely related to elevated blood pressure, an essential risk factor for CVD.



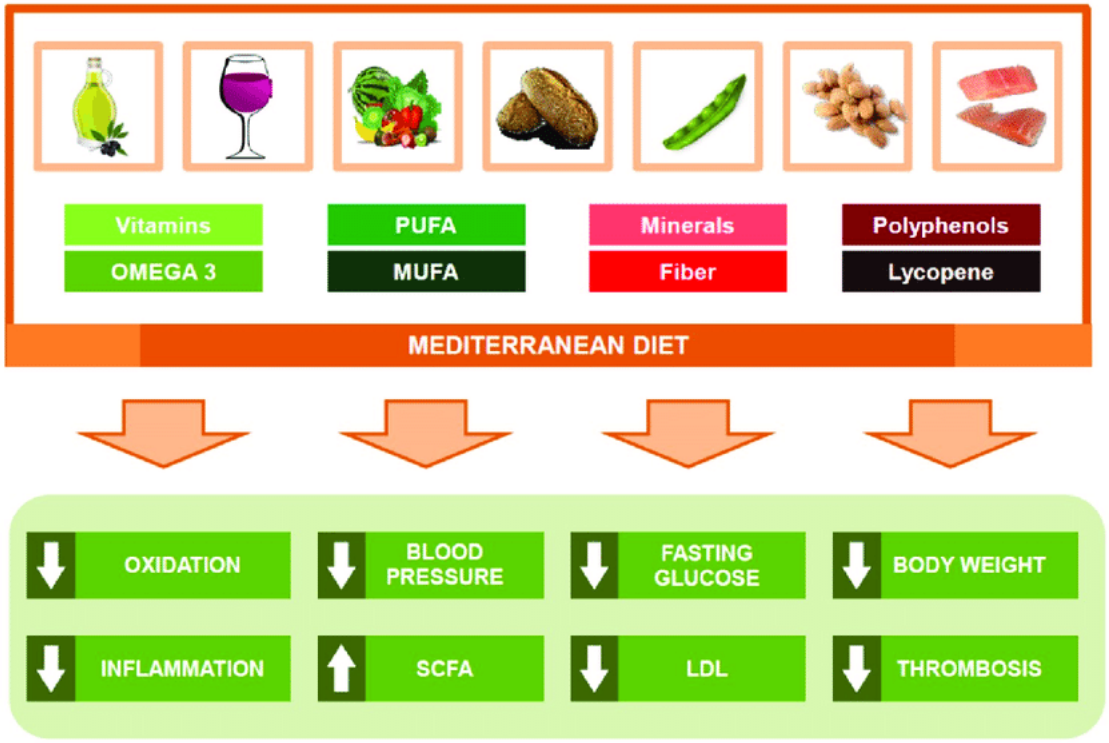
Red Wine

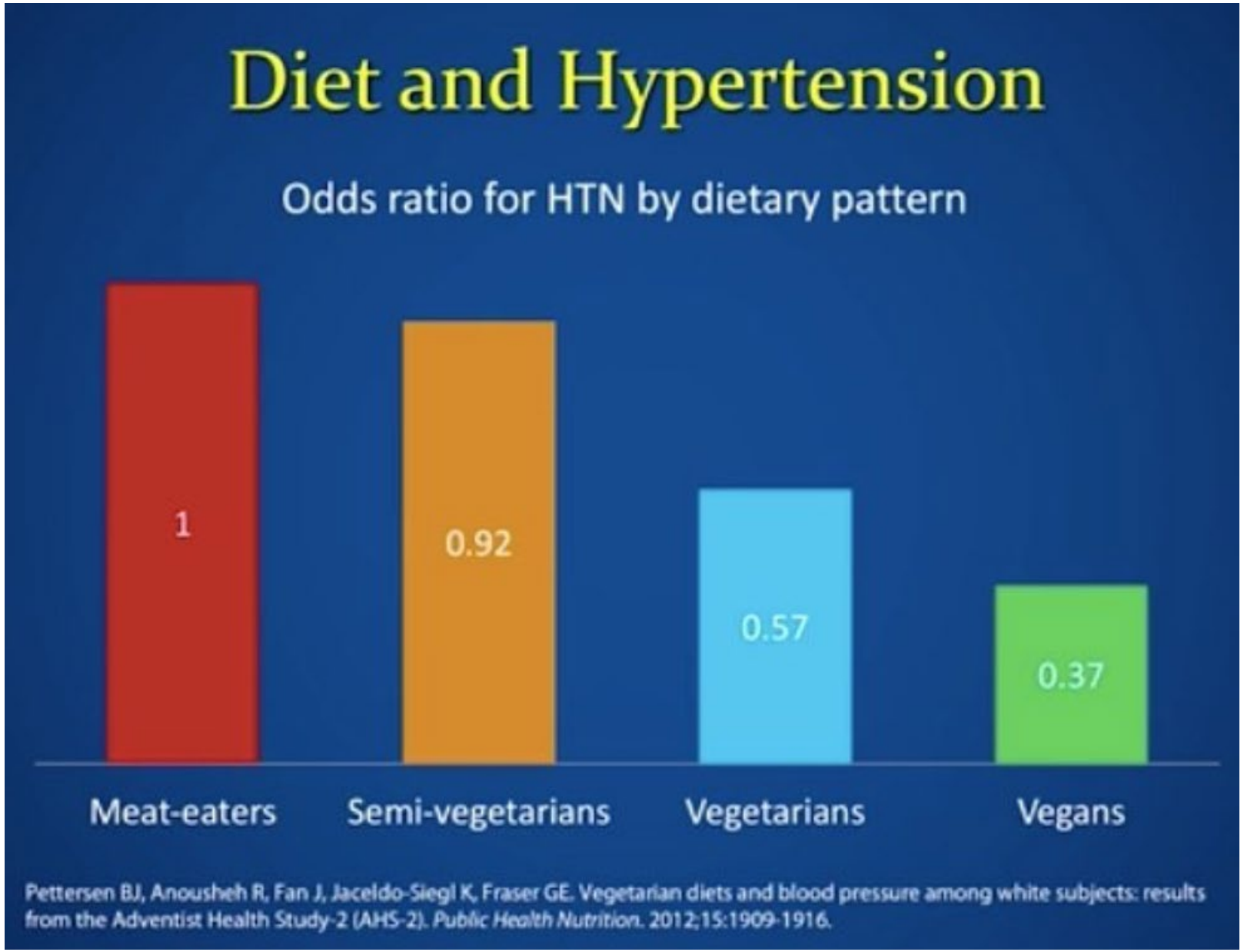

Mechanism of action
• ↓ LDL-C oxidation
• ↓ Platelet aggregation
• ↓ Endothelial dysfunction
• Antioxidant and Anti-inflammatory properties
Major sources
• Red wine
• Tea
• Fruits
• Vegetables
↓ IHD mortality
Flavonoids
↓ Atherosclerosis
↓ Cardiovascular risk
↓ Thrombogenesis

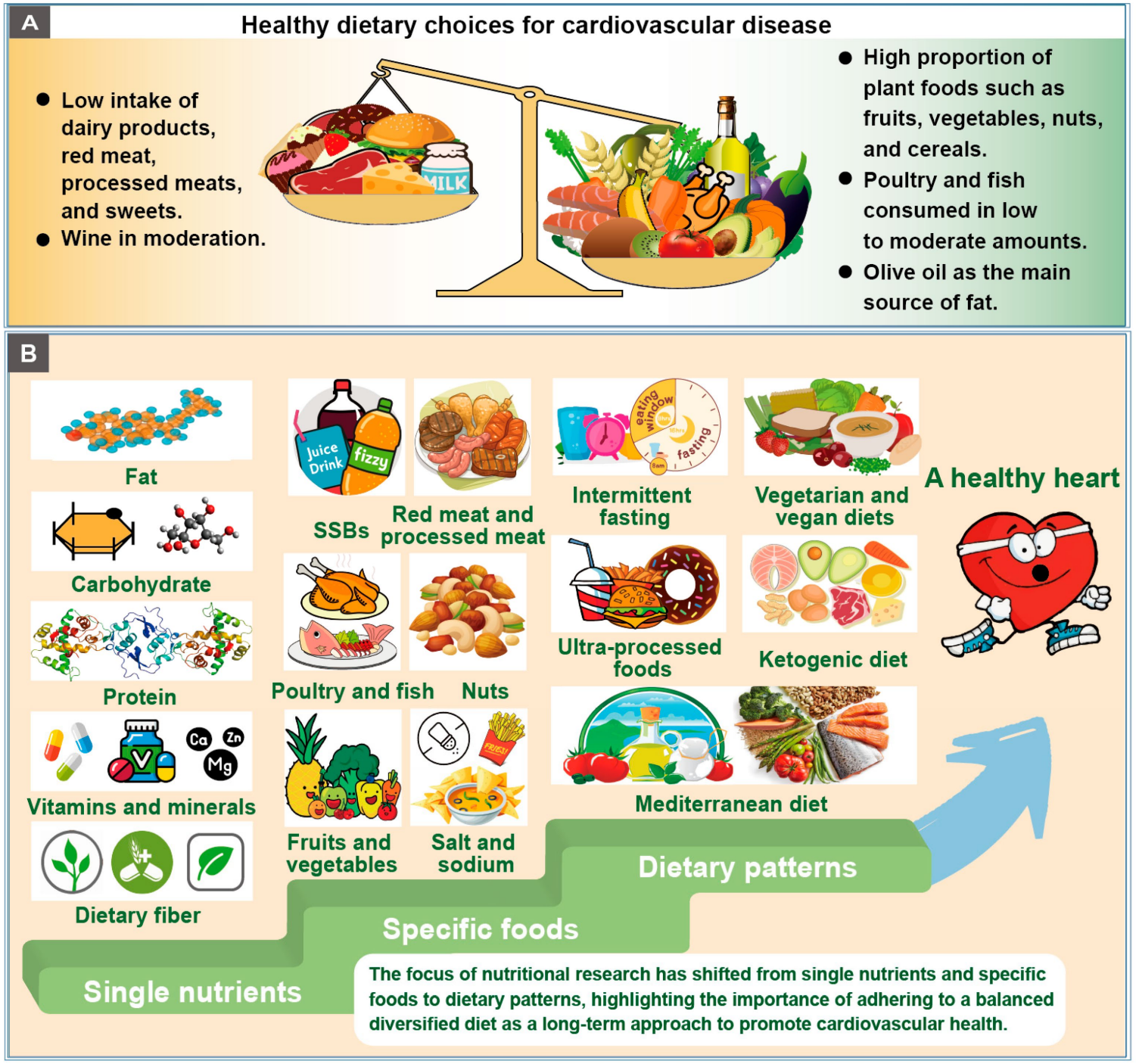
Intermittent Fasting



Mediterranean Diet




Diet and Hypertension
Odds ratio for HTN by dietary pattern
1
0.92
0.57
0.37
Meat-eaters
Semi-vegetarians
Vegetarians
Vegans
Pettersen BJ, Anousheh R, Fan J, Jaceldo-Siegl K, Fraser GE. Vegetarian diets and blood pressure among white subjects: results from the Adventist Health Study-2 (AHS-2). Public Health Nutrition. 2012;15:1909-1916.


A
Healthy dietary choices for cardiovascular disease
Low intake of dairy products, red meat, processed meats, and sweets.
Wine in moderation.
High proportion of plant foods such as fruits, vegetables, nuts, and cereals.
Poultry and fish consumed in low to moderate amounts.
Olive oil as the main source of fat.
B
Fat
Carbohydrate
Protein
Vitamins and minerals
Dietary fiber
SSBs
Red meat and processed meat
Poultry and fish
Nuts
Fruits and vegetables
Salt and sodium
Intermittent fasting
Vegetarian and vegan diets
Ultra-processed foods
Ketogenic diet
Mediterranean diet
A healthy heart
Dietary patterns
Specific foods
Single nutrients
The focus of nutritional research has shifted from single nutrients and specific foods to dietary patterns, highlighting the importance of adhering to a balanced diversified diet as a long-term approach to promote cardiovascular health.

Thank you