CONVEGNO

PREVENZIONE E RIABILITAZIONE PER LA SALUTE CARDIOVASCOLARE

Quattro strategie fondamentali per ridurre il rischio a livello individuale e migliorare l'assistenza alla popolazione

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ITalian Alliance for CArdiovascular REhabilitation and Prevention

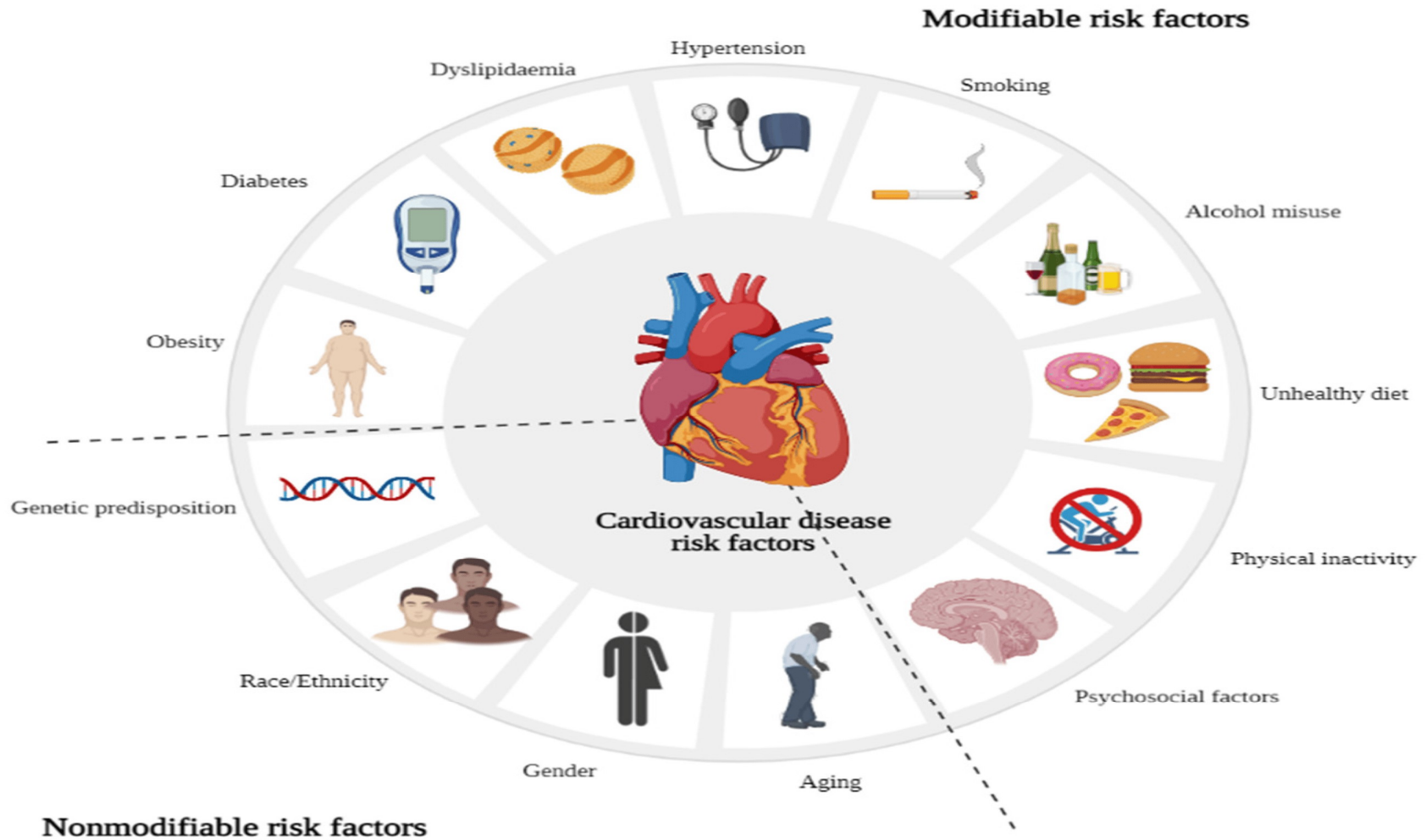# Le relazioni biologiche tra fattori di rischio, aterosclerosi ed eventi cardiovascolari

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Università della Campania «Luigi Vanvitelli»

AORN Sant'Anna e San Sebastiano, Caserta

AORN CASERTA

Università degli Studi della Campania Luigi Vanvitelli

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Cardiovascular Risk Factors

Modifiable risk factors

- Hypertension
- Dyslipidaemia
- Smoking
- Alcohol misuse
- Unhealthy diet
- Physical inactivity
- Psychosocial factors

Cardiovascular disease risk factors

Nonmodifiable risk factors

- Diabetes
- Obesity
- Genetic predisposition
- Race/Ethnicity
- Gender
- Aging

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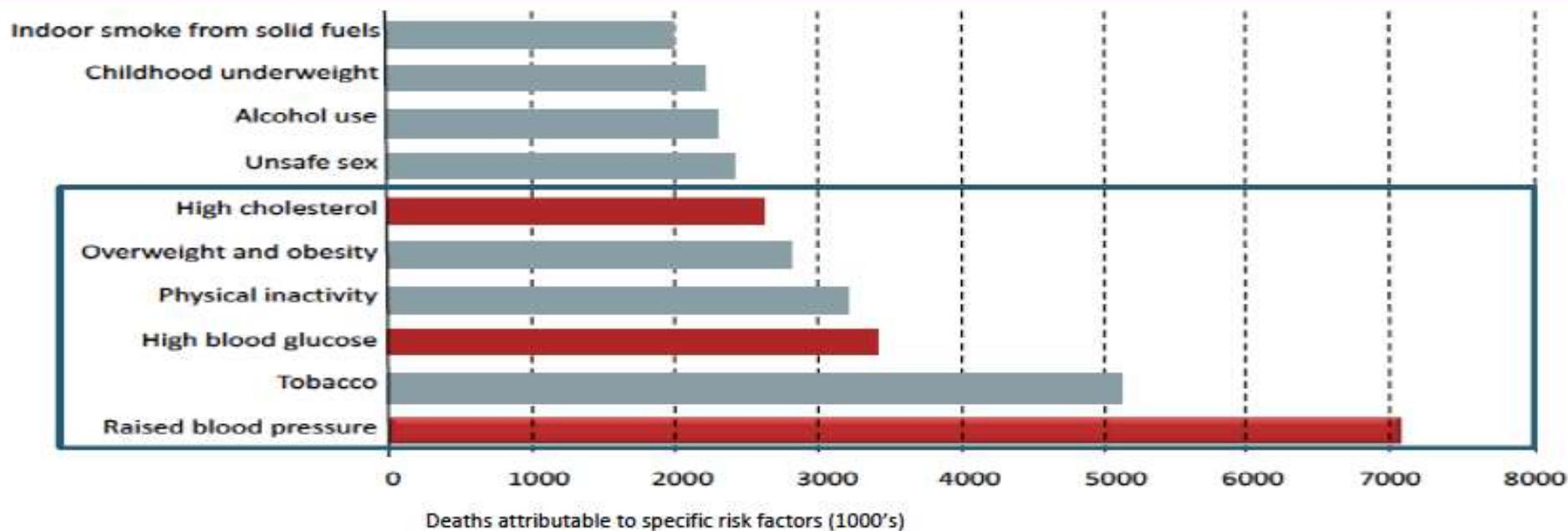REhabilitation and Prevention
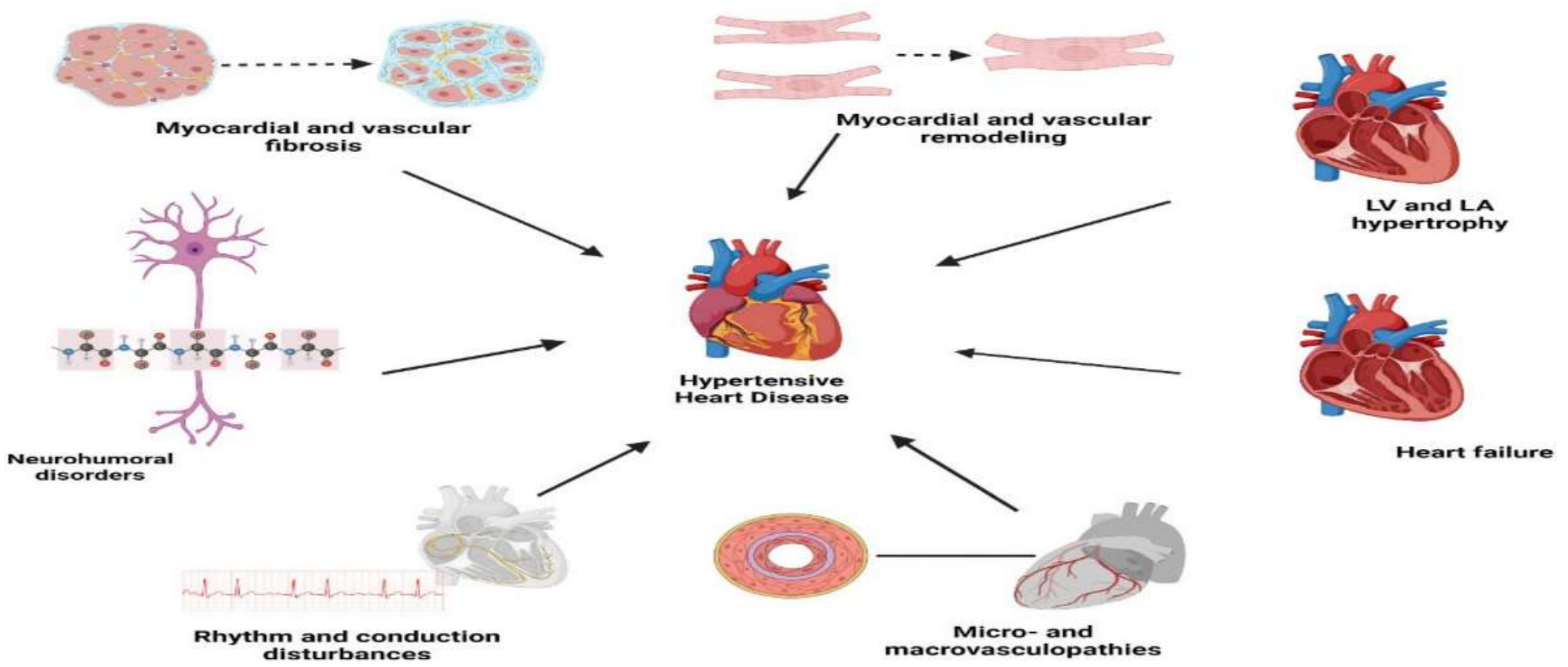
Main Preventable Causes of Death Globally

The Big 6

Blood Pressure, Smoking, Glucose, Inactivity, Obesity and Cholesterol
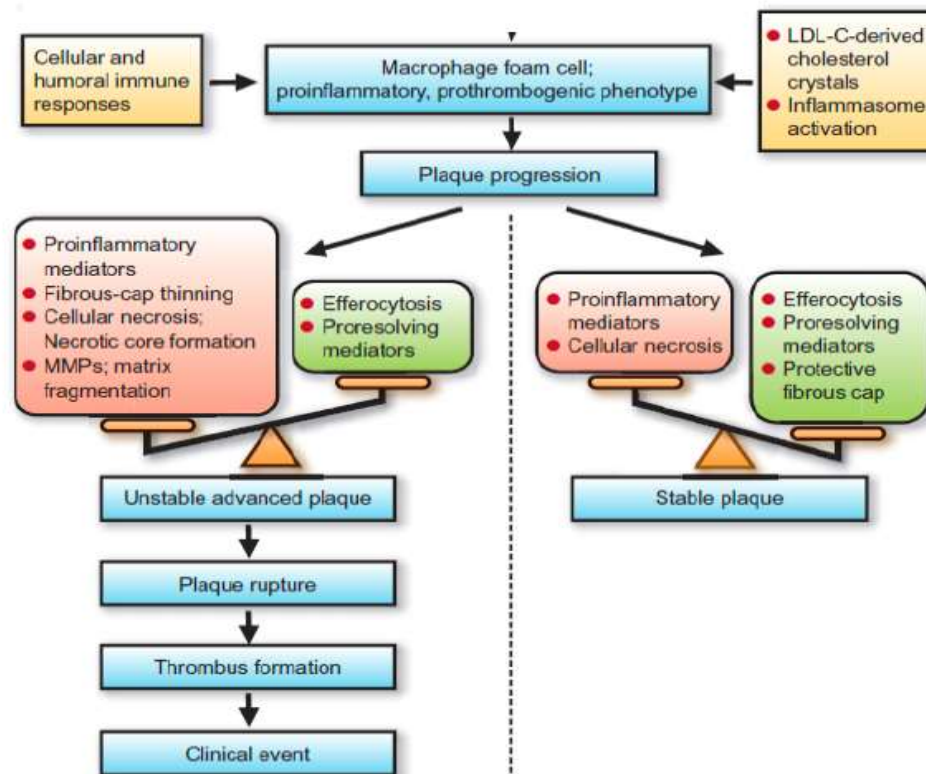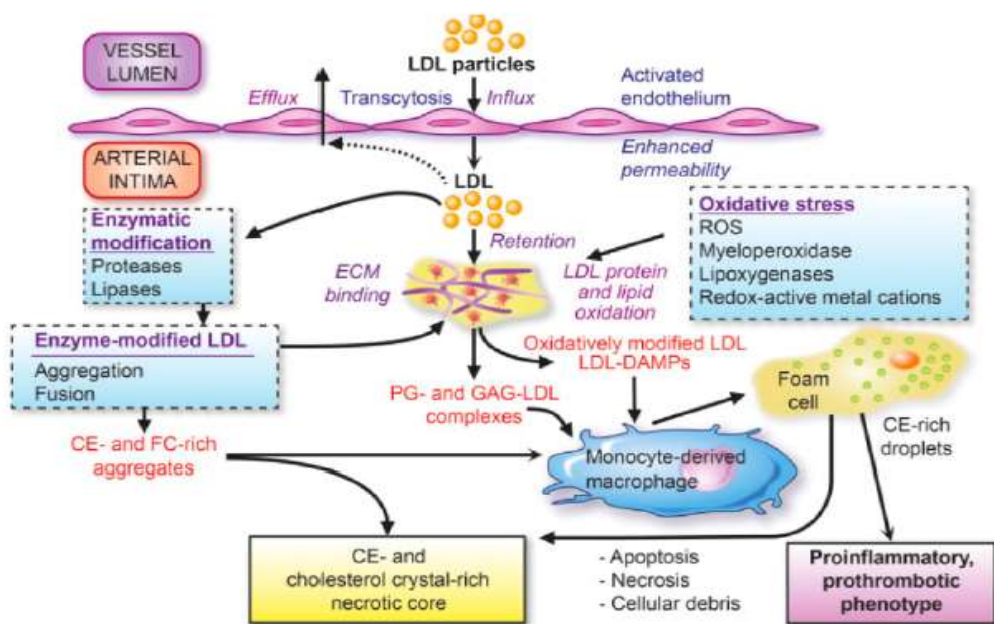are the main global risk factors for mortality
(WHO 2011)

Deaths attributable to specific risk factors (1000's)

World Health Organisation. Global atlas on cardiovascular disease prevention and control. 2011.

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Arterial Hypertension

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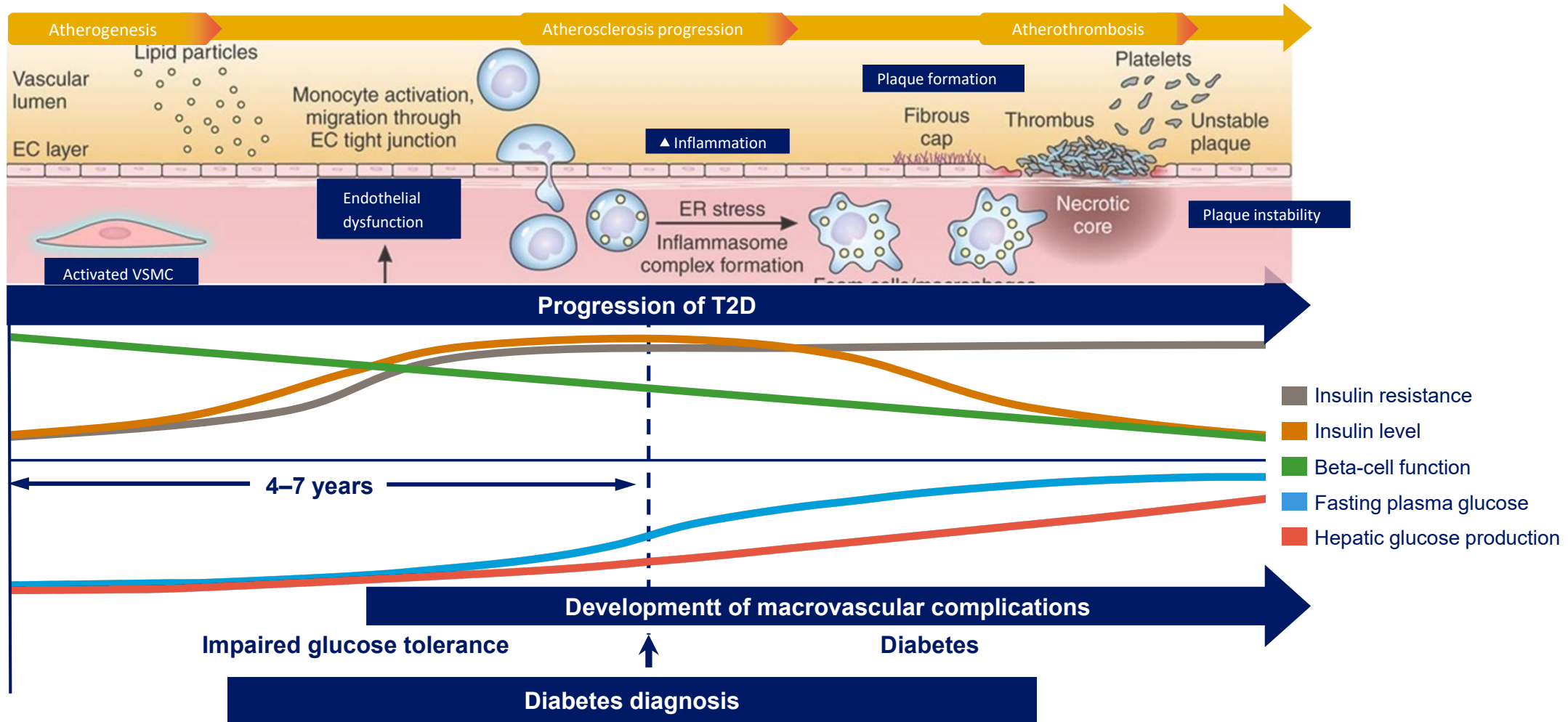REhabilitation and Prevention

LDL-C and Atherogenesis

CE, cholesteryl ester; **DAMPs**, damage-associated molecular patterns; **ECM**, extracellular matrix; **FC**, free cholesterol; **GAG**, glycosaminoglycans; **LDL**, low-density lipoprotein; **LDL-C**, low-density lipoprotein cholesterol; **PG**, proteoglycans; **ROS**, reactive oxygen species

Borén J, et al. Eur Heart J. 2020;41:2313–2330

European Job ID: BIL/23/0459 | Date of preparation: August 2023

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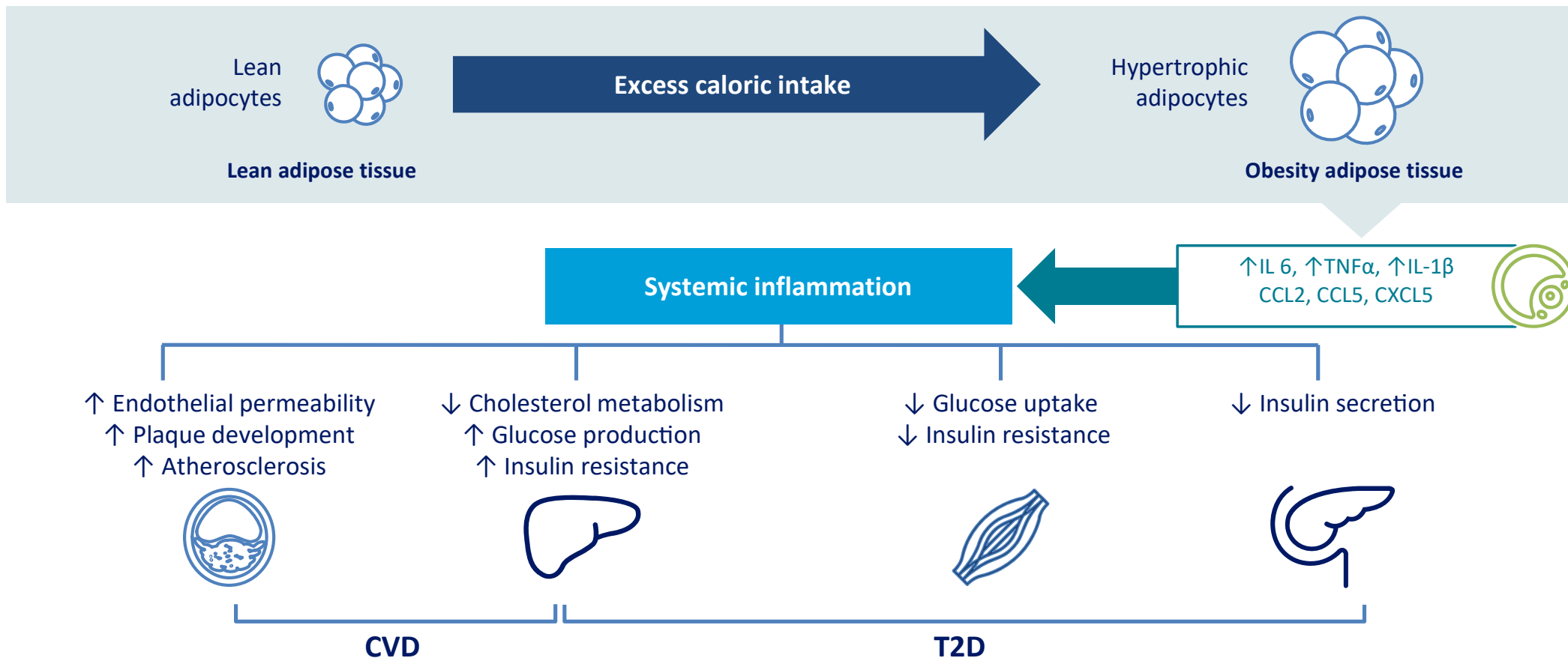# Nel Diabete l'esordio della Malattia CV inizia ancor prima della diagnosi

Low Wang et al, *Circulation*, 2016;133:2459–2502
Adapted from Kendall DM et al, *Am J Med*, 2009:122(6 Suppl):S37–S50

Systemic inflammation increases risk of CVD and T2D

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Lean adipocytes

Excess caloric intake

Hypertrophic adipocytes

Lean adipose tissue

Obesity adipose tissue

↑IL 6, ↑TNFα, ↑IL-1β
CCL2, CCL5, CXCL5

Systemic inflammation

↑ Endothelial permeability
↑ Plaque development
↑ Atherosclerosis

↓ Cholesterol metabolism
↑ Glucose production
↑ Insulin resistance

↓ Glucose uptake
↓ Insulin resistance

↓ Insulin secretion

CVD

T2D

CCL, chemokine (C-C motif) ligand; CVD, cardiovascular disease; CXCL5, chemokine (C-X-C motif) ligand 5; IL, interleukin; T2D, type 2 diabetes; TNFα, tumour necrosis factor alpha.
Yao L et al. J Immunol Res 2014;2014:181450.

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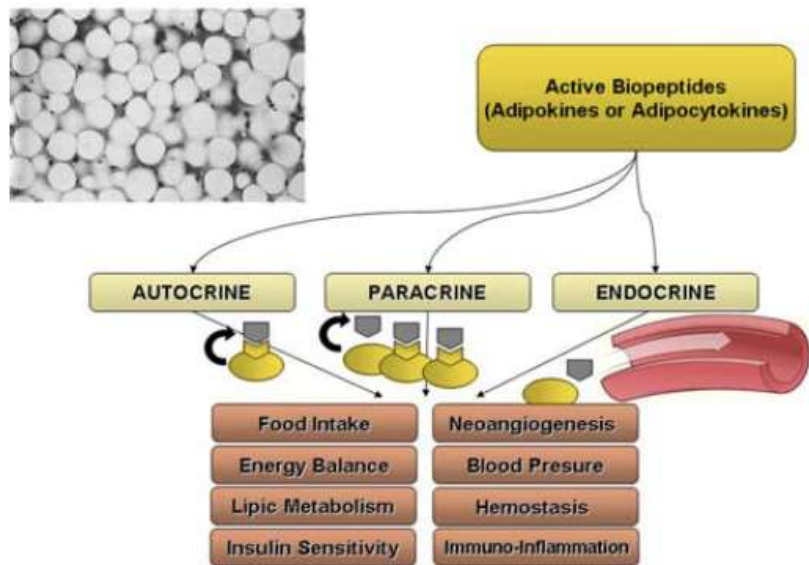
ADIPOSE TISSUE AS AN ENDOCRINE ORGAN

Fig. 1 Mounting evidence supports the idea that adipose tissue is more than a simply storage tissue. It's now clear that it actively releases several mediators, which act in a paracrine way, as well as affecting other tissues in a paracrine or, most notably, an endocrine way. These molecules are involved in the food intake regulation and metabolism, insulin sensitivity and lipid handling; they are involved also in the cardiovascular homeostasis, since they play a role in neoangiogenesis, blood pressure regulation, clot formation, and immuno-inflammatory system. This could represent the pathophysiological basis of the wide spectrum of obesity-related complications
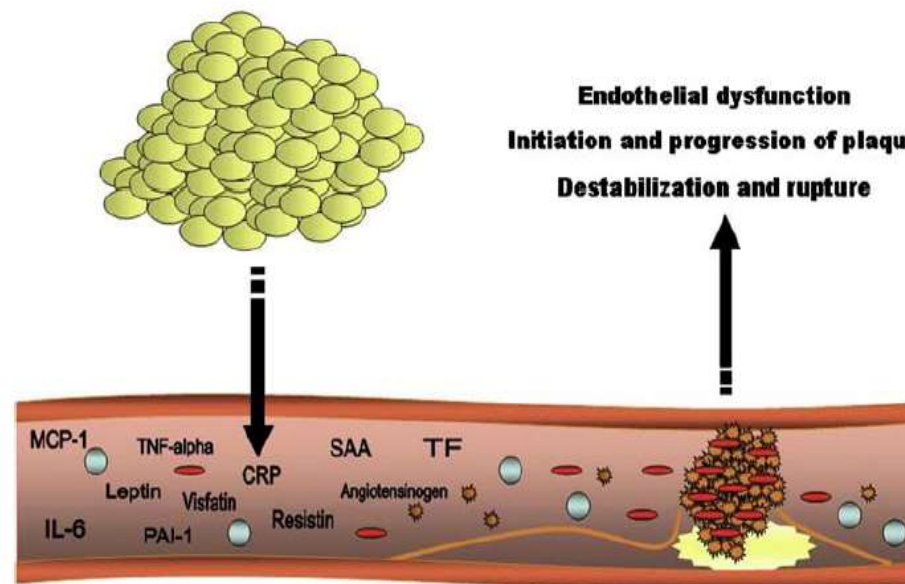

Fig. 2 Adipose tissue releases bioactive peptides known as adipocytokines or adipokines with a number of metabolic and pro-inflammatory functions. These include CRP, SAA, leptin, resistin, angiotensinogen, IL 6, TNF-alpha, and others. Most notably, adipocytes release also protective peptides, such as adiponectin. Growing evidence indicates a key role for the adipokines at the crossroad between obesity and cardiovascular disease, through an early phase of endothelial dysfunction, then the plaque formation, and finally its destabilization. Moreover, a peculiar population of immature adipocytes, known as preadipocytes, is thought to participate to the release of these molecules, acting as macrophage-like cells

Calabrò et al. Adipose tissue-mediated inflammation: the missing link between obesity and cardiovascular disease? - Intern Emerg Med (2009) 4:25–34

Intra-abdominal Adiposity, Inflammation, and Cardiovascular Risk: New Insight into Global Cardiometabolic Risk
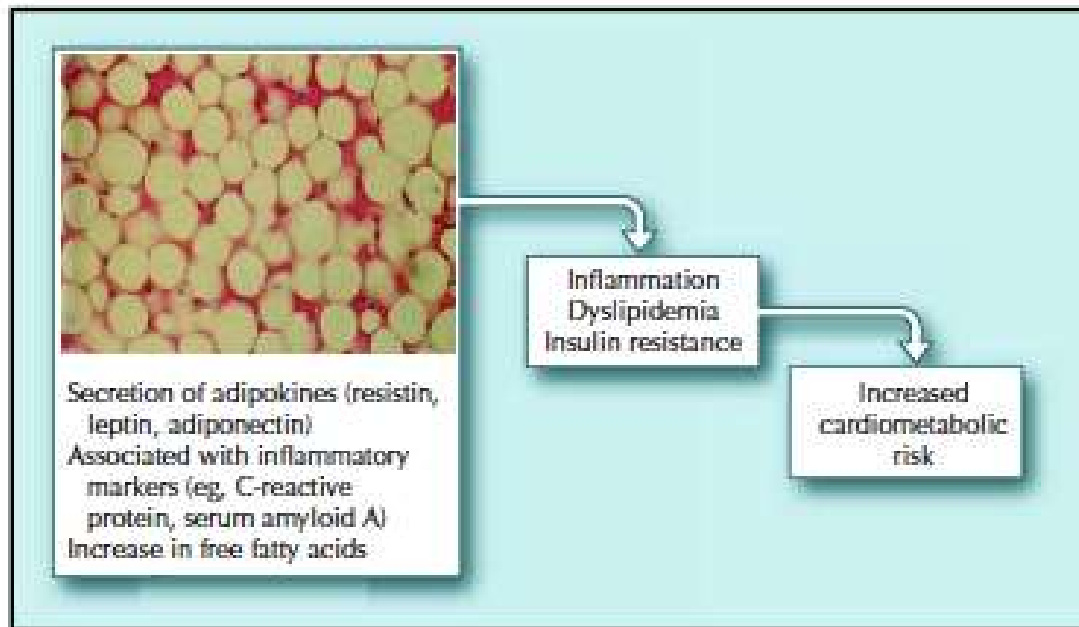
Paolo Calabro, MD, FESC, and Edward T.H. Yeh, MD

Figure 1. Intra-abdominal adiposity as a major contributor to increased cardiometabolic risk.

Secretion of adipokines (resistin, leptin, adiponectin)
Associated with inflammatory markers (eg, C-reactive protein, serum amyloid A)
Increase in free fatty acids

Inflammation
Dyslipidemia
Insulin resistance

Increased cardiometabolic risk

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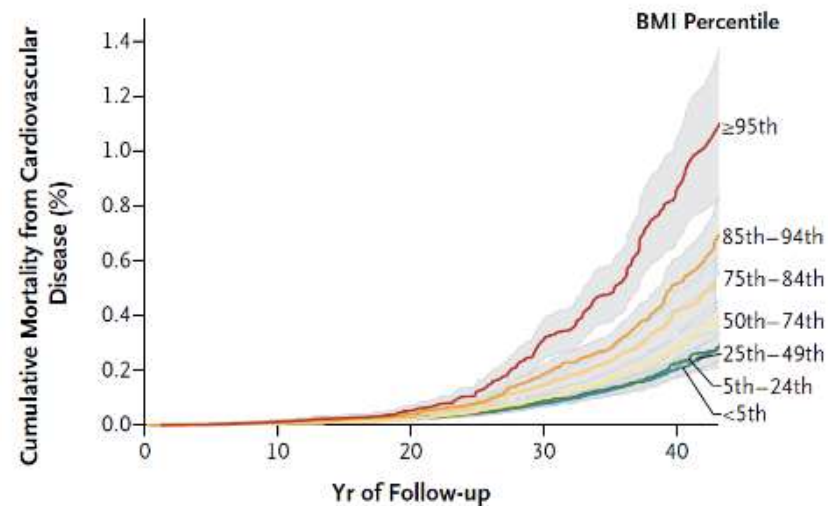REhabilitation and Prevention

The NEW ENGLAND JOURNAL of MEDICINE

Body-Mass Index in 2.3 Million Adolescents and Cardiovascular Death in Adulthood

13 April 2016

➤ **2,3 milioni di adolescenti** nei quali peso e altezza sono stati rilevati nell'arco temporale 1967 - 2010.

➤ È stata valutata l'associazione tra il BMI in tarda adolescenza e la mortalità, in età adulta, improvvisa o per causa cardiovascolare.

➤ Si sono verificati 32.127 decessi, dei quali 2918 per causa cardiovascolare (1497 per malattia coronarica e 528 per infarto) e 893 i decessi improvvisi.

CONCLUSIONI

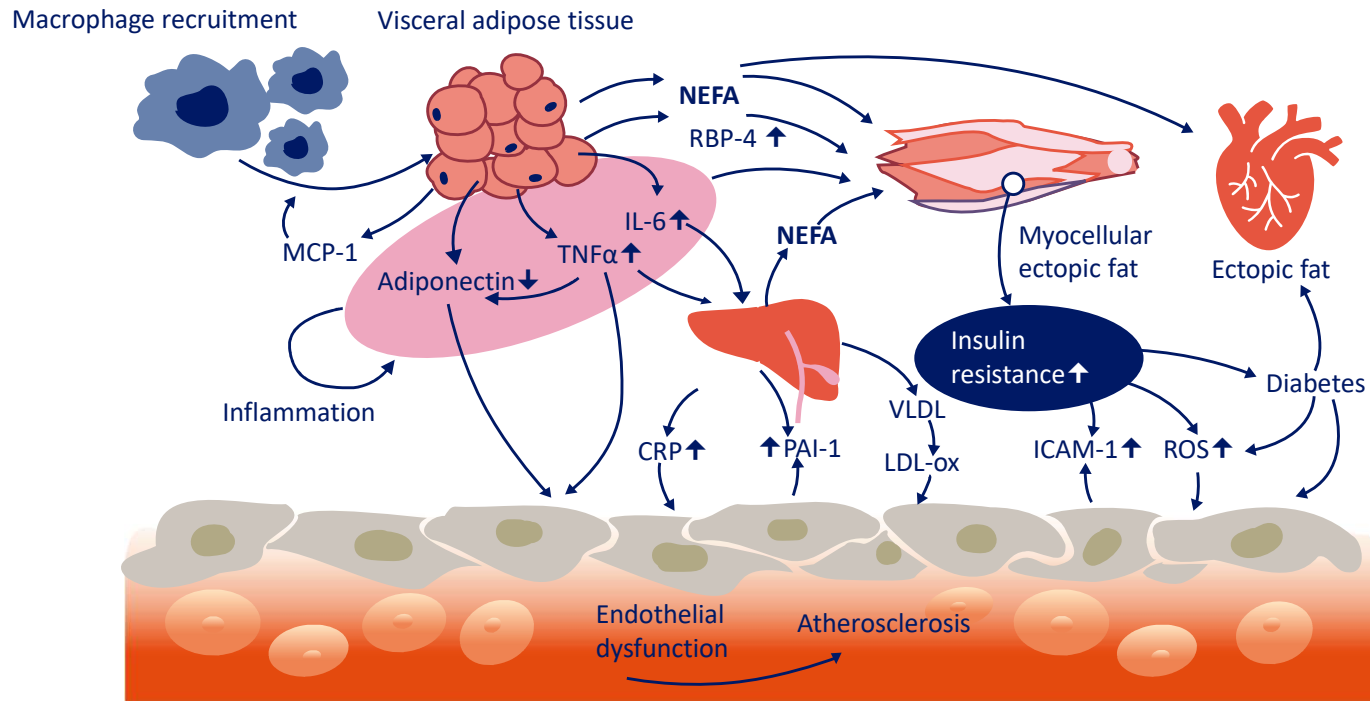➤ L'obesità in fase adolescenziale si associa ad un cospicuo aumento del rischio di morte cardiovascolare in età adulta.

No. at Risk				
Participants at risk	1,712,018	1,042,018	540,636	160,145
Cumulative person-yr	17,201,301	30,718,320	38,472,521	41,926,636
Cumulative cardio-vascular deaths	185	609	1,577	2,676

Figure 2. Body-Mass Index (BMI) during Adolescence and Subsequent Cardiovascular Mortality.

📖 **Body-Mass Index in 2.3 Million Adolescents and Cardiovascular Death in Adulthood** *(Twig G. et al., The New England Journal of Medicine, 2016)*

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The link between obesity, inflammation and CVD

Both abdominal (visceral fat) and insulin resistance may contribute to CVD in obesity
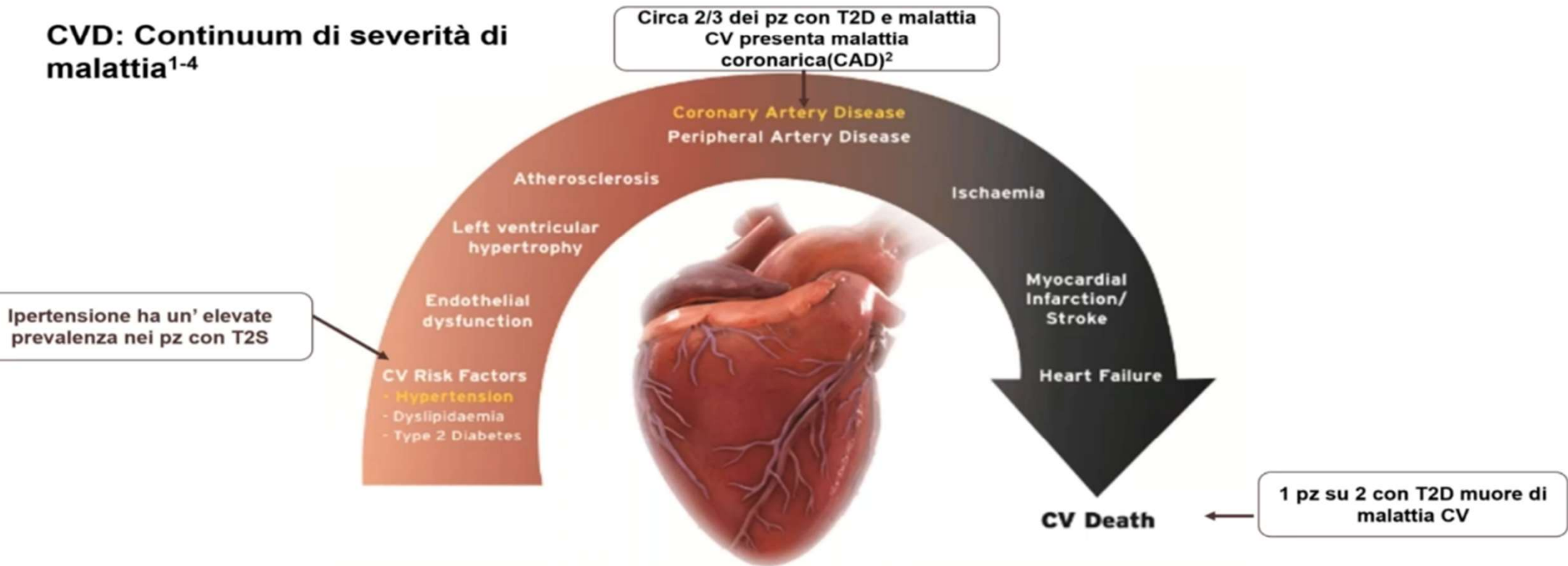

Both abdominal (visceral fat) and insulin resistance may contribute to CVD in obesity

Visceral fat contributes to endothelial dysfunction through activation of inflammatory pathways

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Continuum della malattia cardiovascolare

CVD: Continuum di severità di malattia[1-4]

Circa 2/3 dei pz con T2D e malattia CV presenta malattia coronarica(CAD)[2]

Coronary Artery Disease
Peripheral Artery Disease

Atherosclerosis

Ischaemia

Left ventricular hypertrophy

Endothelial dysfunction

Myocardial Infarction/ Stroke

Ipertensione ha un' elevate prevalenza nei pz con T2S

Heart Failure

CV Risk Factors
- Hypertension
- Dyslipidaemia
- Type 2 Diabetes

CV Death

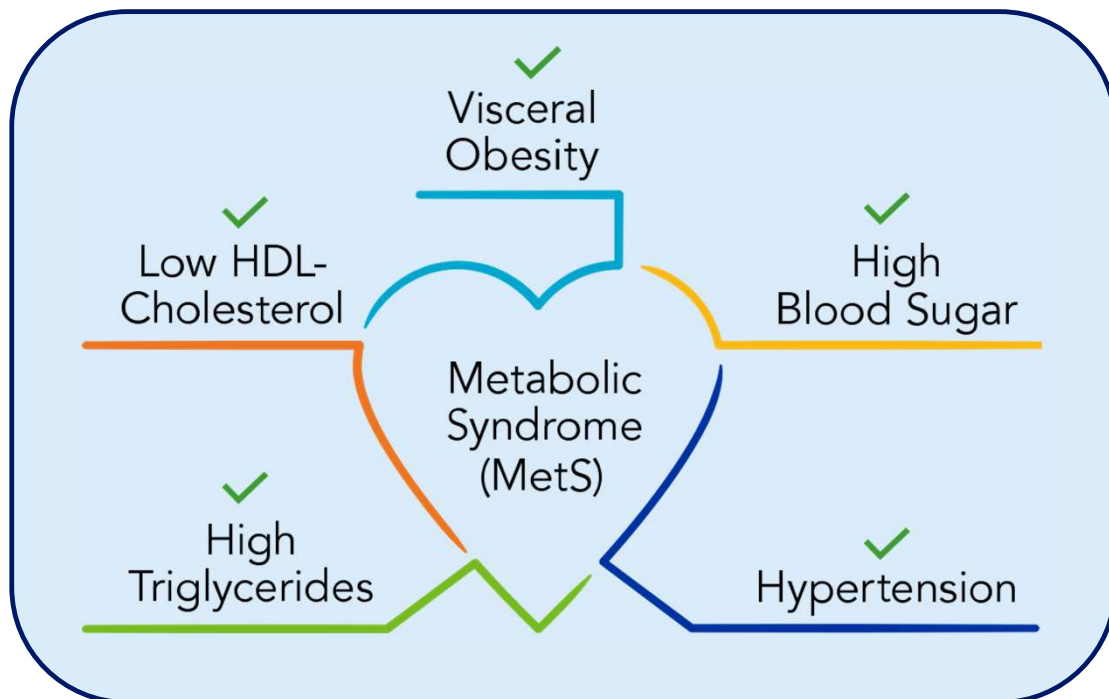1 pz su 2 con T2D muore di malattia CV

References: 1. Dzau VJ, Antman EM, Black HR, et al. The cardiovascular disease continuum validated: clinical evidence of improved patient outcomes: part I: pathophysiology and clinical trial evidence (risk factors through stable coronary artery disease). Circulation. 2006;114(25):2850-2870. 2. Einarson TR, Acs A, Ludwig C, Panton UH. Prevalence of cardiovascular disease in type 2 diabetes: a systematic literature review of scientific evidence from across the world in 2007-2017. Cardiovasc Diabetol. 2018;17(83):1-19. 3. Adelphi. Adelphi Real-World T2D Disease-Specific Programme XIV. Accessed September 20, 2018. 4. Diabetes: Data and Statistics. The challenge of diabetes. World Health Organization European website. http://www.euro.who.int/en/health-topics/noncommunicable-diseases/diabetes/data-and-statistics. Accessed September 20, 2018.

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LA SINDROME METABOLICA

AHA-NHBLI (NCEP-ATP III)

Almeno tre fattori presenti tra quelli elencati:

- **Obesità viscerale**
  - circonferenza vita ≥ 102 cm nell'uomo
  - circonferenza vita ≥ 88 cm nella donna

- **Trigliceridi** ≥ 150 mg/dl o terapie specifiche in atto

- **HDL-Colesterolo**
  - ≤ 40 mg/dl nell'uomo
  - ≤ 50 mg/dl nella donna

- **Pressione arteriosa** ≥ 130/85 mmHg o terapia specifica in atto

- **Glicemia a digiuno** ≥ 100 mg/dl
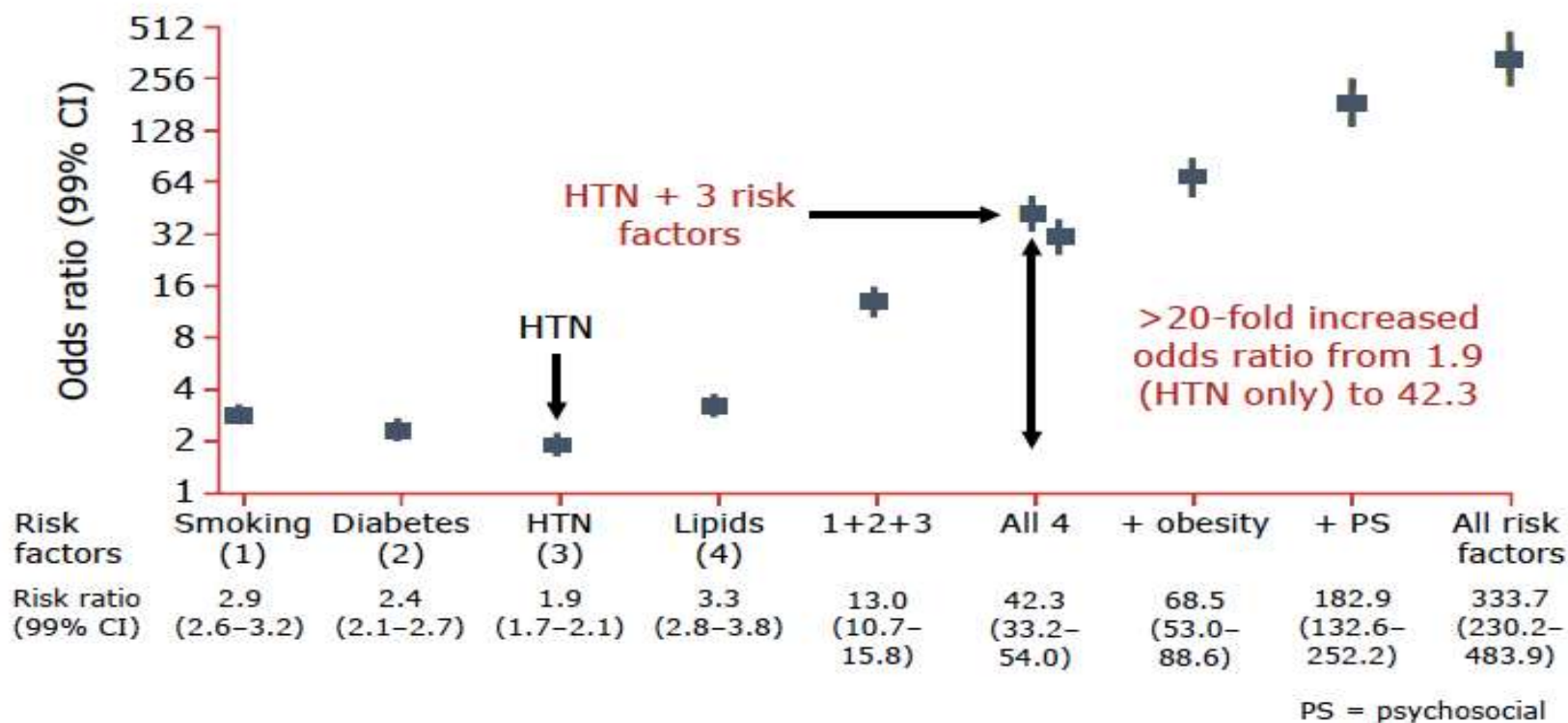
American Heart Association (AHA)
National Heart, Blood and Lung Institute (NHBLI)
National Cholesterol Education Program – Adult Treatment Panel III (NCEP – ATP III)

➢ L'aggregazione di più fattori di **rischio cardiovascolare** nel medesimo soggetto agisce da moltiplicatore del rischio, che sarà tanto più elevato quanti più fattori sono in gioco.

➢ Questa pericolosa associazione di rischio potrebbe essere una delle cause del notevole incremento di patologie coronariche e cerebrali su base aterosclerotica, che rappresentano la prima causa di morte nel mondo.

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Impact of multiple risk factors on total CVD risk: INTERHEART study

Risk factors	Smoking (1)	Diabetes (2)	HTN (3)	Lipids (4)	1+2+3	All 4	+ obesity	+ PS	All risk factors
Risk ratio (99% CI)	2.9 (2.6–3.2)	2.4 (2.1–2.7)	1.9 (1.7–2.1)	3.3 (2.8–3.8)	13.0 (10.7–15.8)	42.3 (33.2–54.0)	68.5 (53.0–88.6)	182.9 (132.6–252.2)	333.7 (230.2–483.9)

PS = psychosocial

Yusuf S, et al. Lancet 2004;364:937–52

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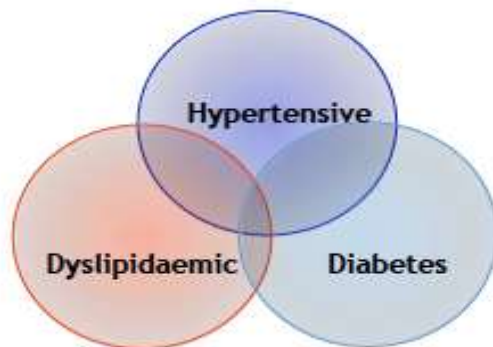REhabilitation and Prevention

Clinical Silos are a barrier to effective CVD Prevention
because most patients have multiple CV risk factors

Multiple comorbidities increase CVD risk by 400-700%

Hypertensive

Dyslipidaemic   Diabetes

Of all people with hypertension:
- 65% have dyslipidaemia
- 16% have type 2 diabetes
- 45% are overweight/obese

Of all people with dyslipidaemia:
- 48% have hypertension
- 14% have type 2 diabetes
- 35% are overweight/obese

Of all people with type 2 diabetes:
- 70% have hypertension
- 60% have dyslipidaemia
- 90% are overweight/obese

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