Dr Risch

Il vostro laboratorio – oggi e domani

RISCH.CH

Sindrome Metabolica

Labmed Ticino

28.03.2023

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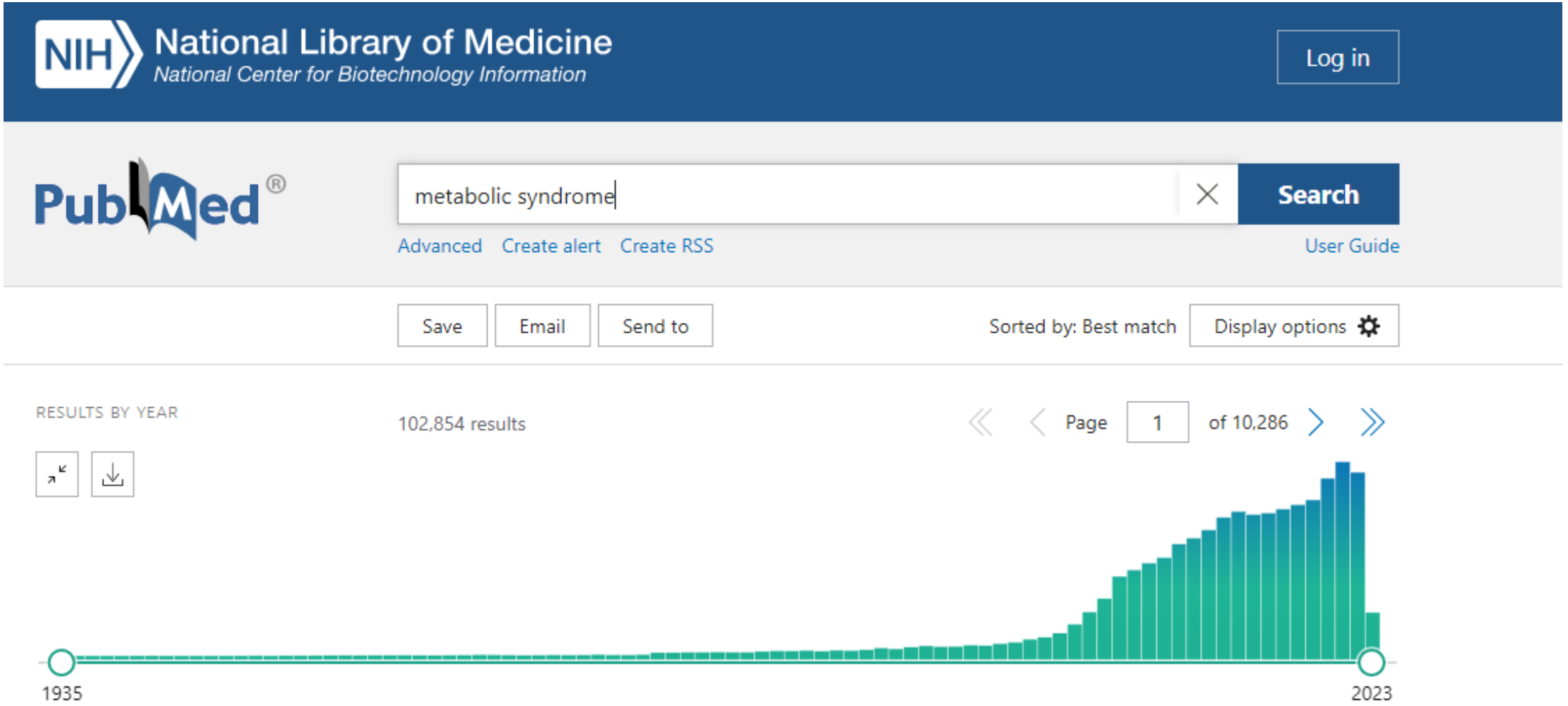
Cosa andremo a vedere: *non é una lezione di biochimica*☺

- Sindrome metabolica
- Adiposità
- Insulino-resistenza
- Lipidi nella pratica di laboratorio
- PCOS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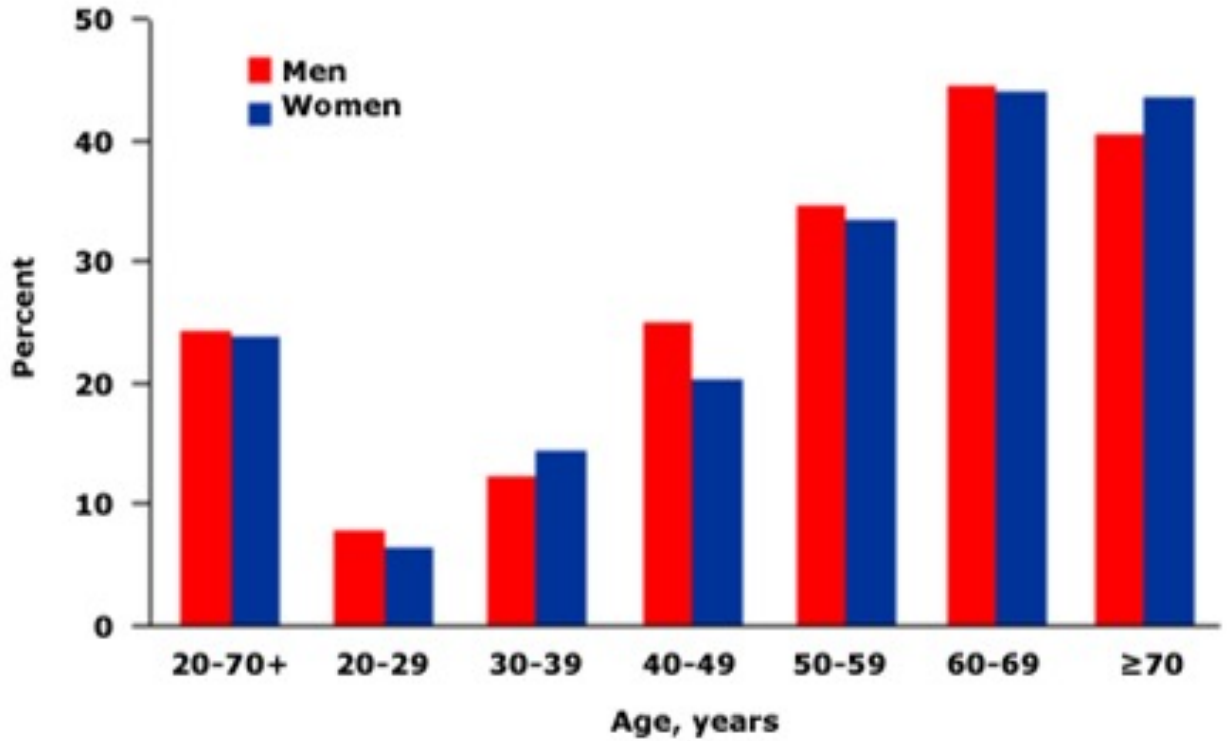
Sindrome metabolica: definizione-1

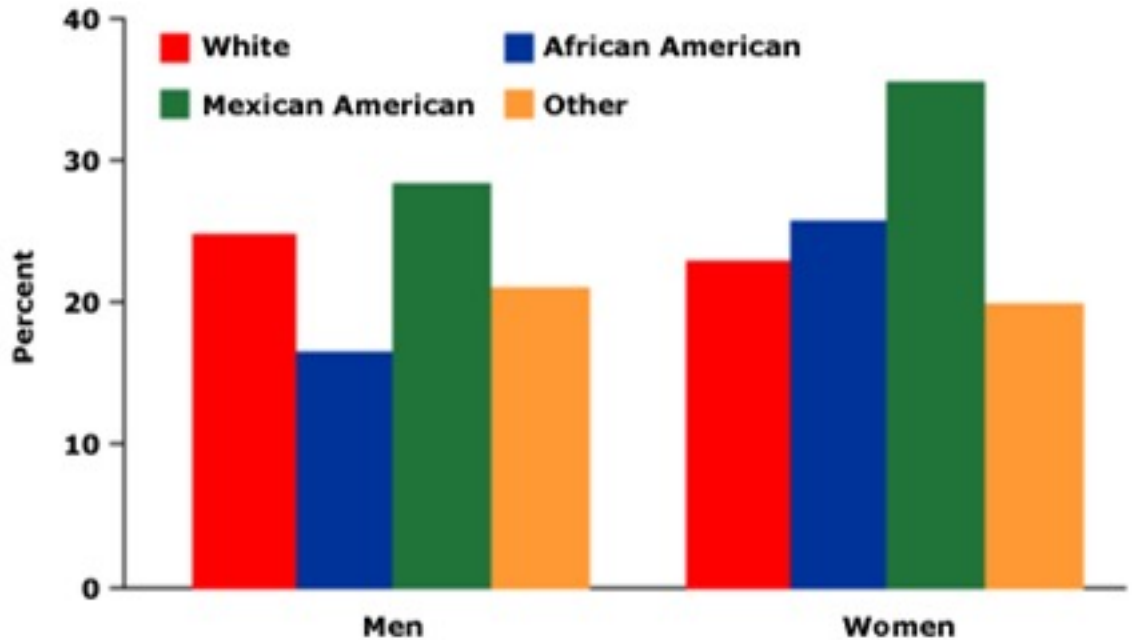
- La sindrome metabolica viene chiamata anche sindrome X
- Who definisce la sindrome metabolica come una condizione patologica caratterizzata da **obesità addominale, insulino-resistenza, ipertensione e iperlipidemia**
- I triggers maggiori per la sindrome metabolica sono cibi ricchi di calorie e poche fibre e la diminuzione di attività fisica
- La sindrome metabolica rappresenta una delle non-communicable disease (NCD)con la maggior causa di mortalità e morbidità

Prevalence of NCEP ATP III metabolic syndrome among subjects in the NHANES III survey, by age



Adapted from: Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA 2002; 287:356.

Prevalence of NCEP ATP III metabolic syndrome among subjects in the NHANES III survey by race/ethnicity and sex



Adapted from: Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA 2002; 287:356.

Noncommunicable diseases

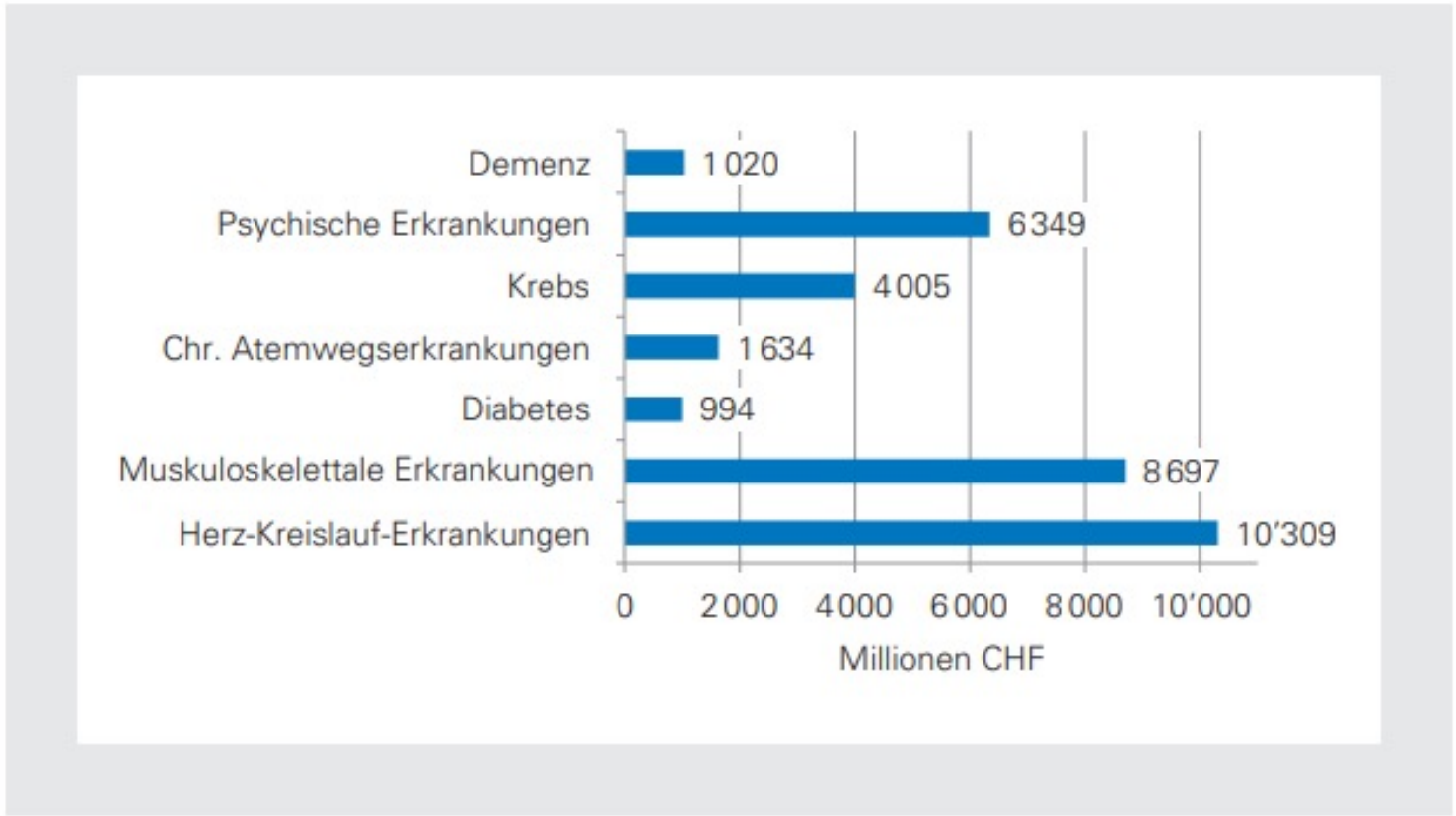
16 September 2022

Key facts

- Noncommunicable diseases (NCDs) kill 41 million people each year, equivalent to 74% of all deaths globally.
- Each year, 17 million people die from a NCD before age 70; 86% of these premature deaths occur in low- and middle-income countries.
- Of all NCD deaths, 77% are in low- and middle-income countries.
- Cardiovascular diseases account for most NCD deaths, or 17.9 million people annually, followed by cancers (9.3 million), chronic respiratory diseases (4.1 million), and diabetes (2.0 million including kidney disease deaths caused by diabetes).
- These four groups of diseases account for over 80% of all premature NCD deaths.
- Tobacco use, physical inactivity, the harmful use of alcohol and unhealthy diets all increase the risk of dying from an NCD.
- Detection, screening and treatment of NCDs, as well as palliative care, are key components of the response to NCDs.

Abbildung 1

Direkte Kosten der 7 NCD-Gruppen im Jahr 2011 (daten-gestützte Berechnung)



GzD_BU36_Kostenstudie NCD_D.pdf (med.lab)

Sindrome metabolica: definizione-2

- Ci sono diverse definizione di sindrome metabolica
- Questo rende più complicato la comparazione dei dati a livello di ricerca
- Le definizioni più usate sono quelle
  - The National Cholesterol Education Program (NCEP)
  - Adult Treatment Panel III (ATP III)

Definitions of the metabolic syndrome

Parameters	NCEP ATP3 2005*	IDF 2009	EGIR 1999	WHO 1999	AACE 2003
Required			Insulin resistance or fasting hyperinsulinemia (ie, in top 25% of the laboratory-specific reference range)	Insulin resistance in top 25%Δ; fasting glucose ≥6.1 mmol/L (110 mg/dL); 2-hour glucose ≥7.8 mmol/L (140 mg/dL)	High risk of insulin resistance◇ or BMI ≥25 kg/m^2 or waist ≥102 cm (men) or ≥88 cm (women)
Number of abnormalities	**≥3 of:**	**≥3 of:**	**And ≥2 of:**	**And ≥2 of:**	**And ≥2 of:**
Glucose	Fasting glucose ≥5.6 mmol/L (100 mg/dL) or drug treatment for elevated blood glucose	Fasting glucose ≥5.6 mmol/L (100 mg/dL) or diagnosed diabetes	Fasting glucose 6.1 to 6.9 mmol/L (110 to 125 mg/dL)		Fasting glucose ≥6.1 mmol/L (110 mg/dL); ≥2-hour glucose 7.8 mmol/L (140 mg/dL)
HDL cholesterol	<1.0 mmol/L (40 mg/dL) (men); <1.3 mmol/L (50 mg/dL) (women) or drug treatment for low HDL cholesterol§	<1.0 mmol/L (40 mg/dL) (men); <1.3 mmol/L (50 mg/dL) (women) or drug treatment for low HDL cholesterol	<1.0 mmol/L (40 mg/dL)	<0.9 mmol/L (35 mg/dL) (men); <1.0 mmol/L (40 mg/dL) (women)	<1.0 mmol/L (40 mg/dL) (men); <1.3 mmol/L (50 mg/dL) (women)
Triglycerides	≥1.7 mmol/L (150 mg/dL) or drug treatment for elevated triglycerides§	≥1.7 mmol/L (150 mg/dL) or drug treatment for high triglycerides	or ≥2.0 mmol/L (180 mg/dL) or drug treatment for dyslipidemia	or ≥1.7 mmol/L (150 mg/dL)	≥1.7 mmol/L (150 mg/dL)
Obesity	Waist ≥102 cm (men) or ≥88 cm (women)¥	Waist ≥94 cm (men) or ≥80 cm (women)	Waist ≥94 cm (men) or ≥80 cm (women)	Waist/hip ratio >0.9 (men) or >0.85 (women) or BMI ≥30 kg/m^2	
Hypertension	≥130/85 mmHg or drug treatment for hypertension	≥130/85 mmHg or drug treatment for hypertension	≥140/90 mmHg or drug treatment for hypertension	≥140/90 mmHg	≥130/85 mmHg

NCEP: National Cholesterol Education Program; IDF: International Diabetes Federation; EGIR: Group for the Study of Insulin Resistance; WHO: World Health Organization; AACE: American Association of Clinical Endocrinologists; HDL: high-density lipoprotein; CVD: cardiovascular disease; BMI: body mass index.

* Most commonly agreed upon criteria for metabolic syndrome. Note that abdominal obesity is **not** a prerequisite for diagnosis; the presence of any 3 of the 5 risk criteria constitutes a diagnosis of metabolic syndrome.

¶ For South Asian and Chinese patients, waist ≥90 cm (men) or ≥80 cm (women); for Japanese patients, waist ≥90 cm (men) or ≥80 cm (women).

Δ Insulin resistance measured using insulin clamp.

◇ High risk of being insulin resistant is indicated by the presence of at least 1 of the following: diagnosis of CVD, hypertension, polycystic ovary syndrome, non-alcoholic fatty liver disease or acanthosis nigricans; family history of type 2 diabetes, hypertension or CVD; history of gestational diabetes or glucose intolerance; non-White race; sedentary lifestyle; BMI 25 kg/m^2 or waist circumference 94 cm (men) or 80 cm (women); and age 40 years.

§ Treatment with 1 or more of fibrates or niacin.

¥ In Asian patients, waist ≥90 cm (men) or ≥80 cm (women).

References:

1. *Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009; 120:1640.*
2. *Meigs J. Metabolic syndrome and risk for type 2 diabetes. Expert Rev Endocrin Metab 2006; 1:57. Table 1. Updated data from the International Diabetes Federation, 2006.*
3. *Bloomgarden ZT. American Association of Clinical Endocrinologists (AACE) consensus conference on the insulin resistance syndrome: 25-26 August 2002, Washington, DC. Diabetes Care 2003; 26:933.*

Ethnic specific values for waist circumference

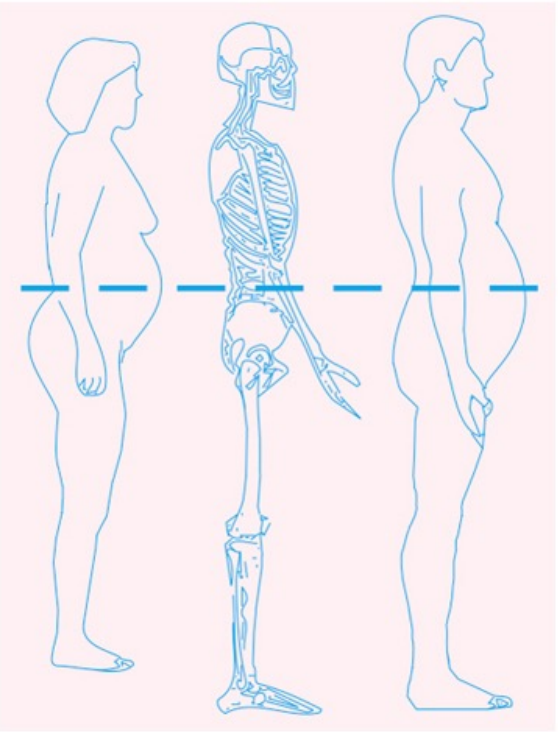
Ethnic group	Waist circumference (as measure of central obesity)
Europid populations*	
Males	≥94 cm
Females	≥80 cm
South Asian populations	
Males	≥90 cm
Females	≥80 cm
Chinese populations	
Males	≥90 cm
Females	≥80 cm
Japanese populations	
Males	≥90 cm
Females	≥80 cm
South and Central American populations	Use South Asian recommendations until more specific data are available
Sub-Saharan African populations	Use European data until more specific data are available
Eastern Mediterranean and Middle Eastern populations	Use European data until more specific data are available

Data are pragmatic cutoffs, and better data are required to link them to risk. Ethnicity should be basis for classification, not country of residence.

* In USA, Adult Treatment Panel III values (102 cm male, 88 cm female) are likely to continue to be used for clinical purposes. In future epidemiological studies of populations of Europid origin (White people of European origin, regardless of where they live in the world), prevalence should be given, with both European and North American cutoffs to allow better comparisons.

Come misurare la circonferenza addominale

Waist circumference measurement



Measuring-tape position for waist (abdominal) circumference in adults. To measure waist circumference, locate the upper hip bone and the top of the right iliac crest. Place a measuring tape in a horizontal plane around the abdomen at the level of the iliac crest. Before reading the tape measure, ensure that the tape is snug, but does not compress the skin, and is parallel to the floor. The measurement is made at the end of a normal expiration.

Reproduced from: National Heart, Lung, and Blood Institute. The Practical Guide: Identification, Evaluation, and Treatment of Overweight and Obesity in Adults. US Department of Health and Human Services, Public Health Service, National Institutes of Health, National Heart Lung and Blood Institute, Bethesda, MD, October 2000.

Adiposità negli adulti

- Grasso sottocutaneo ➔ Stoccaggio Energetico

- Grasso viscerale➔ da vedersi più come un organo endocrino attivo piuttosto che come il posto di stoccaggio energetico
  - Densità cellulare Alta
  - Molto ben irrorato
  - Presenza elevata di recettori di glucocorticoidi (ormoni steroidei prodotti dal surrene)
    - Viene stimolato dagli ormoni
    - Può cambiare il metabolismo lipidico
  - Sintesi di citochine proinfiammatorie

- Concentrazione glucosio a digiuno
- Trigliceridi
- Colesterolo totale

} Hanno una correlazione positiva con il grasso viscerale

Fujioka et al. (1987)

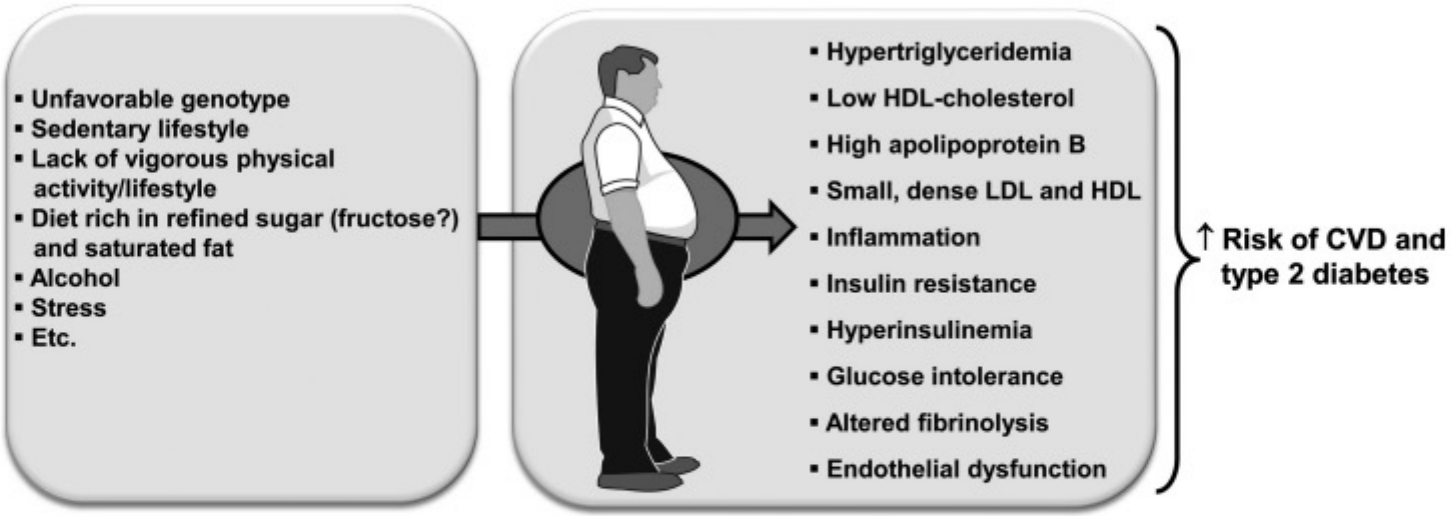
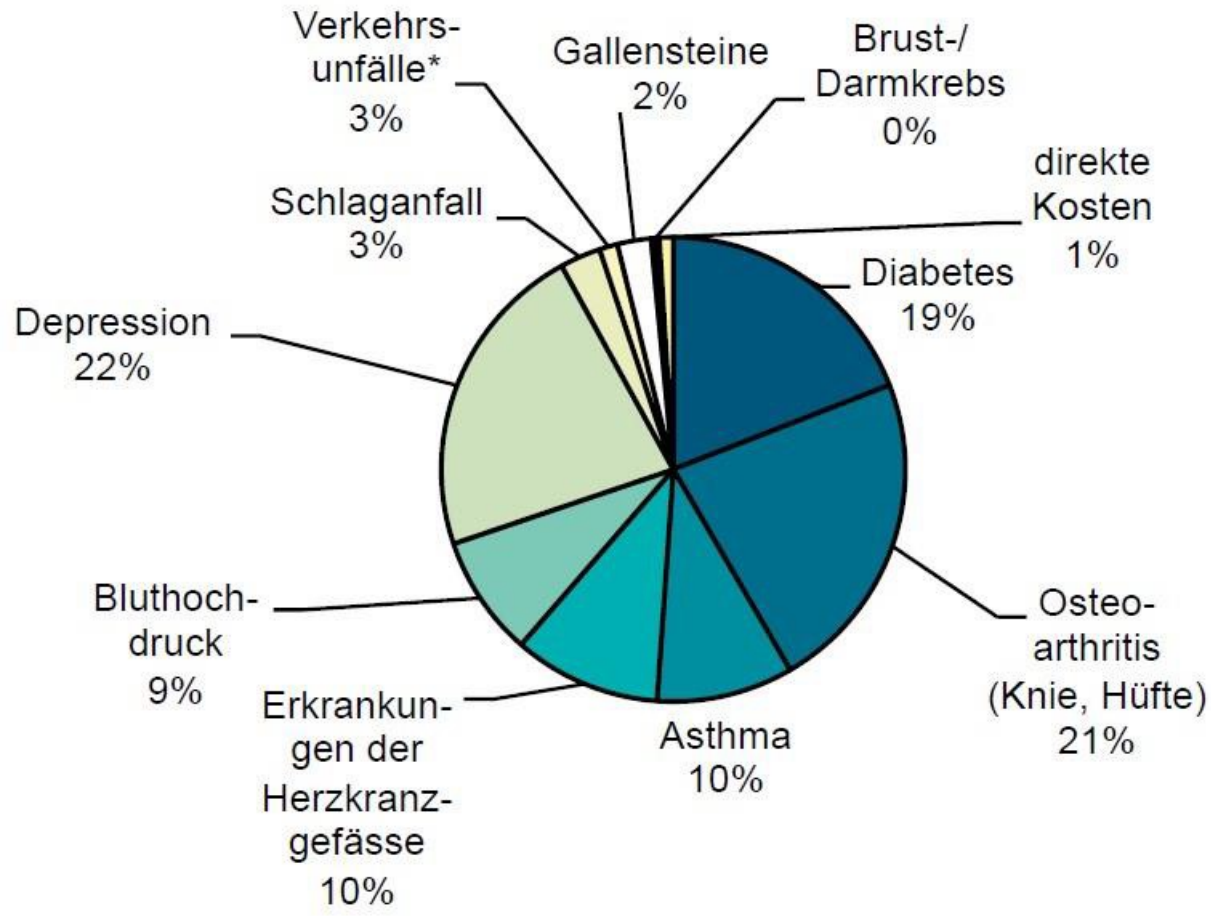


Figure 1. Some of the alterations in the metabolic risk profile that have been found to be related to abdominal obesity assessed by anthropometry and later to excess visceral adiposity/ectopic fat assessed by imaging techniques. This constellation of metabolic abnormalities increases the risk of type 2 diabetes mellitus and of various cardiovascular outcomes. CVD indicates cardiovascular disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Profili di rischio relazionati all'obesità addominali ➔ relazionati ad adiposità viscerale ectopica come dimostrato Da imaging

Conseguenze dell’adiposità



BAG Adipositas Kosten ind-5-2

Adiposità-Eziologia in Europa (WHO) Bilancio energetico positivo

- Aumento di cibi poco sani, ricchi di energia e a basso costo
- Diminuzione della consapevolezza di uno stile di vita sano
- Aumento di quartieri poco privilegiati con diminuzione di
- attività fisica e accesso a cibi poco sani
- Con l'aumento della tecnologia si assiste a una diminuzione dell'attività fisica…. Meno tempo libero…

Cluster sociale

Adipositià in	– Aumenta il rischio di adipositià per se stesso:
Amici	– 57%
Fratelli	– 40%
Compagni	– 37%

WHO European Regional Obesity Repost 2022.pdf

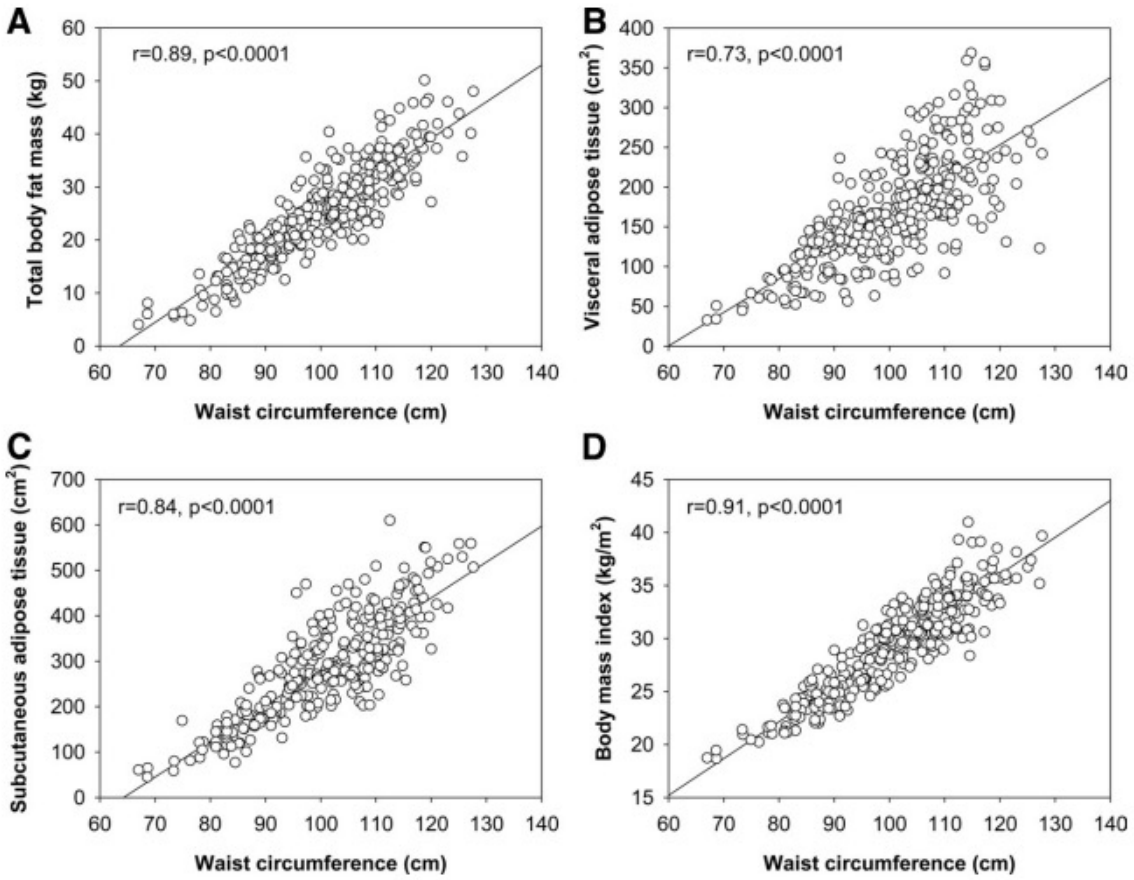


Figure 2. Relationship between waist circumference and total body fat content (in kilograms) assessed by underwater weighing (**A**), visceral adiposity (cross-sectional area in centimeters squared) assessed by computed tomography (**B**), subcutaneous abdominal adiposity (cross-sectional area in centimeters squared) assessed by computed tomography (**C**), and body mass index (in kilograms per meter squared) (**D**) in a convenience sample of 313 men used in various studies of the author. These results show that. when used in isolation, waist circumference is an index of total adiposity that cannot distinguish visceral from subcutaneous abdominal adiposity.

L'uso della sola circonferenza della vita, **non permette di distinguere tra grasso sottocutaneo e grasso Viscerale**. La circonferenza della vita, rappresenta il **grasso totale**

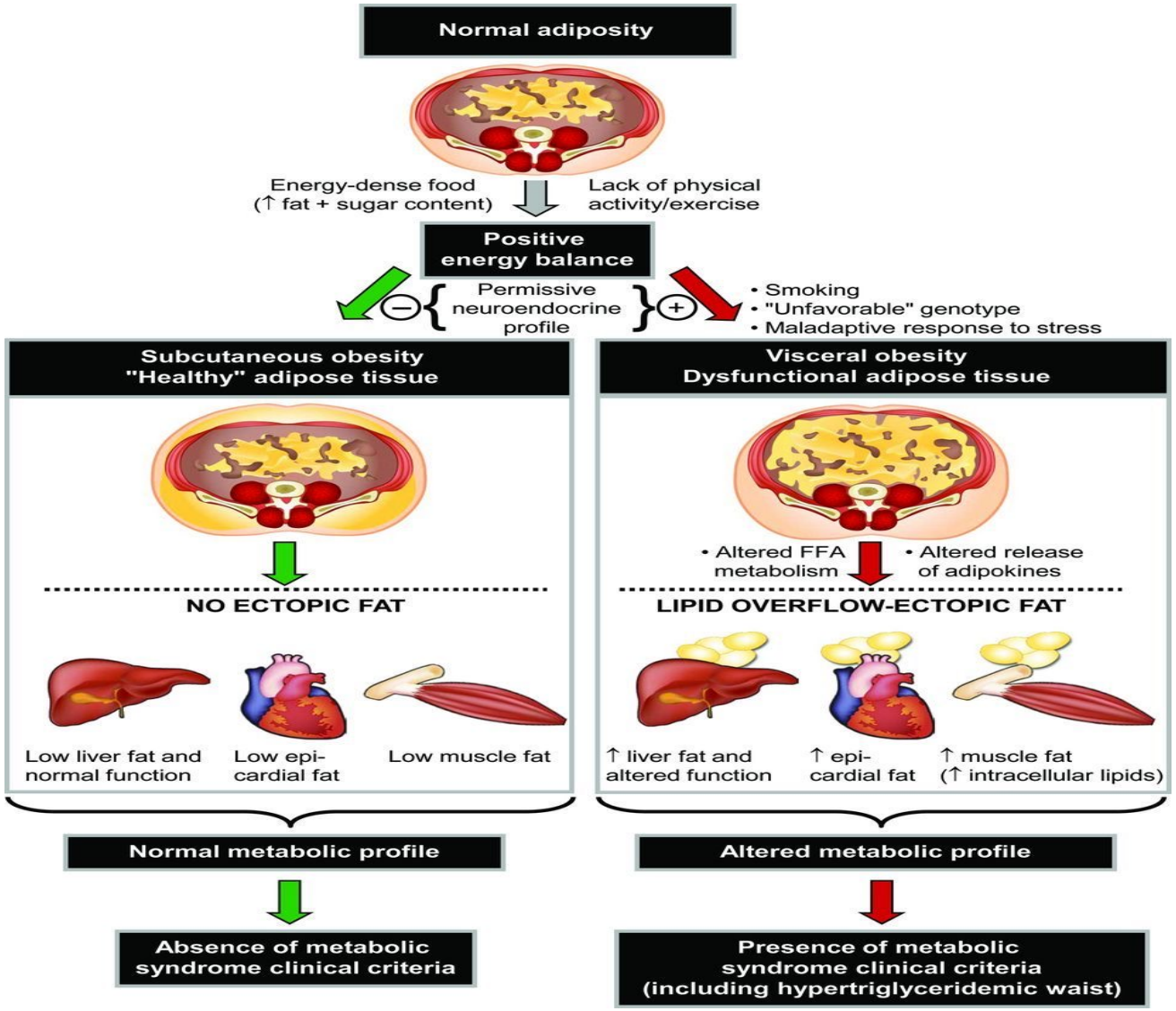
Adiposità viscerale eccessiva, quo vadis?

- Un deposito di grasso viscerale espanso (metabolicamente attivo con lipolisi abbondante➔ espone il fegato a concentrazioni maggiori di acidi grassi e contribuisce allo sviluppo dello stato iperinsulemico, iperglicemico e ipertriglicemico che caratterizza la sindrome metabolica

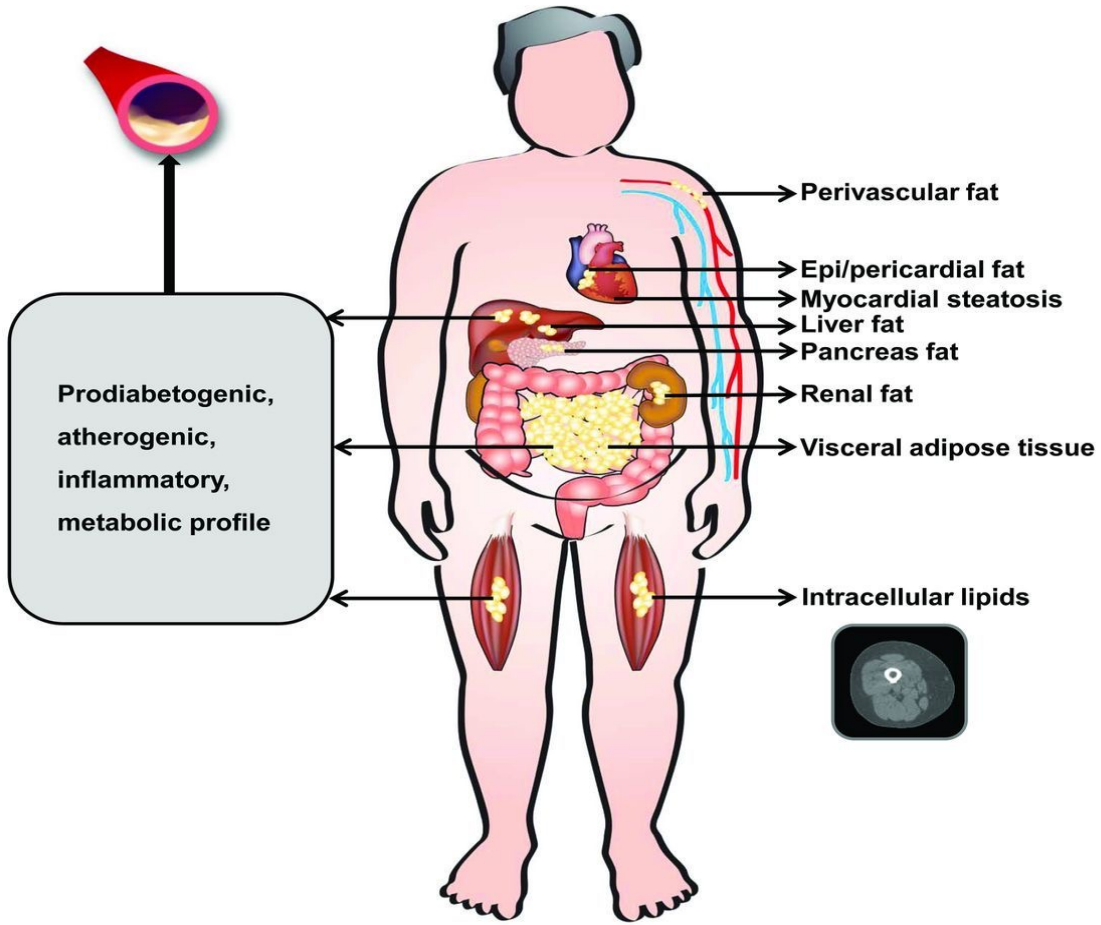
Cibi elaborati come fonte di dipendenza

- Cibo come dipendenza
- 14% degli adulti/12 % die bambini sono colpiti
  - Perdita di controllo sull'assunzione di cibo
  - Desiderio intenso
  - Difficoltà a smettere
  - Comportamento protratto nonostantante la consapevolezza delle conseguenze negative

Gearhardt(2022) Highly processed foods can be considered addictive substances based on established scientific criteria -Addiction



Jean-Pierre Després. Circulation. Body Fat Distribution and Risk of Cardiovascular Disease, Volume: 126, Issue: 10, Pages: 1301-1313, DOI: (10.1161/CIRCULATIONAHA.111.067264)

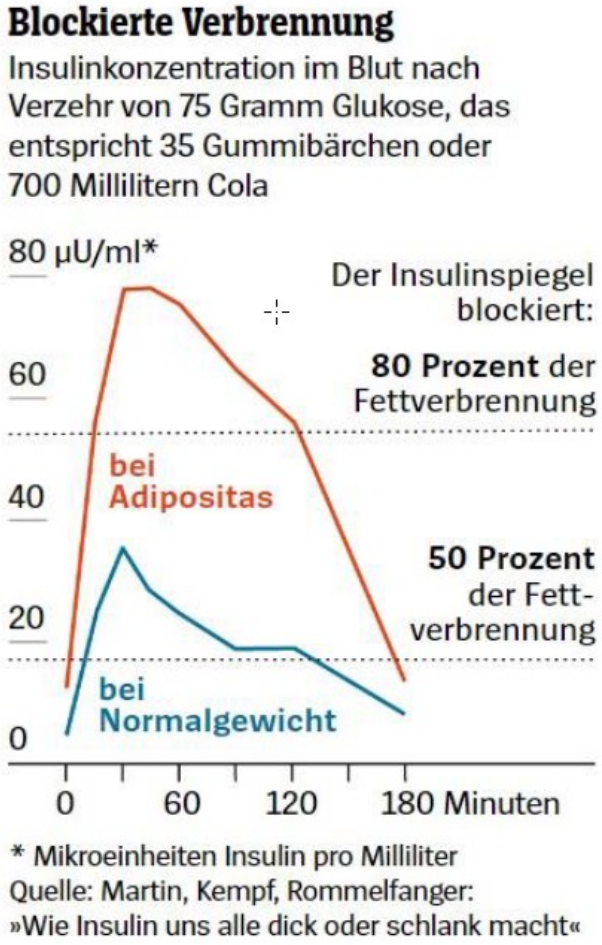


Ectopic fat depots with systemic effects:
- Liver fat
- Visceral adipose tissue
- Intracellular lipids
- Pancreas fat

Ectopic fat depots with local effects:
- Perivascular fat
- Epi/pericardial fat
- Renal fat
- Etc.

Zucchero come potenziale di dipendenza, non tanto i grassi

Adiposità-eziologia: il modello zucchero-insulina



»Es kommt nicht so sehr auf die Kalorienzahl an, sondern auf die Zusammensetzung der Nahrung. Je weniger Kohlenhydrate, desto besser fürs Abnehmen«

«Patient:innen sollen Industriezucker ebenso weglassen wie Honig, Brötchen, Brot, Kuchen, Kartoffeln, Reis, Nudeln, Bier (auch Obst meiden, da viel Fruchtzucker) »

«Stattdessen … Möhren, Blumenkohl … Salat … Gemüse mit Olivenöl … Fisch … Fleisch, Eier, Milch-produkte und Käse essen, so viel man will»

Therapeutic goals for management of metabolic syndrome

	Goals
Lifestyle risk factors	
Abdominal obesity	Year 1: Reduce body weight 7 to 10 percent
	Continue weight loss thereafter with ultimate goal BMI <25 kg/m^2
Physical inactivity	At least 30 min (and preferably ≥60 min) continuous or intermittent moderate intensity exercise 5 times per week, but preferably daily
Atherogenic diet	Reduced intake saturate fat, trans fat, cholesterol
Metabolic risk factors	
Dyslipidemia	
Primary target elevated LDL cholesterol	High risk*: <100 mg/dL (2.6 mmol/>L); optional <70 mg/dL
	Moderate risk: <130 mg/dL (3.4 mmol/L)
	Lower risk: <160 mg/dL (4.9 mmol/L)
Secondary target elevated non-HDL cholesterol	High risk*: <130 mg/dL (3.4 mmol/L); optional <100 mg/dL (2.6 mmol/L) very high risk
	Moderate risk: <160 mg/dL (4.1 mmol/L)
	Lower risk: <190 mg/dL (4.9 mmol/L)
Tertiary target reduced HDL cholesterol	Raise to extent possible with weight reduction and exercise
Elevated blood pressure	Reduce to at least <140/90 (<130/80 if diabetic)
Elevated glucose	For IFG, encourage weight reduction and exercise
	For type 2 DM, target A1C <7 percent
Prothrombotic state	Low-dose aspirin for high-risk patients
Proinflammatory state	Lifestyle therapies; no specific interventions

LDL: low-density lipoprotein; HDL: high-density lipoprotein; DM: diabetes mellitus; IFG: impaired fasting glucose.

* High-risk: diabetes, known coronary artery disease.

Data from: Grundy S, Cleeman J, Daniels S, 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.

Patofisiologia della sindrome metabolica

- Processo complicato e non del dutto chiarito

- Grasso viscerale➔ con funzioni endocrine, ipertensione, displipidemia rappresentano i capisaldi che portano alla sindrome metabolica
- Recentemente a questi vengono aggiunti: stress ossidativo, infiammazione sitemica

- Grasso viscerale rappresenta un noxa per la progressione a sindrome metabolica

Patofisioloia della sindrome metabolica

- Adiposità viscerale rappresenta la fonte primaria di FFA (acidi grassi liberi), prima al fegato poi alla circolazione sistemica
- Adiposità viscerale é fonte di prouduzione di citochine che portano alla sindrome metabolica
- Il tessudo adiposo disfunzionale viscerale porta all'aumento di FFA che portano al deposito di lipidi locali
- Questa esposizione cronica provoca un disfunzionamento cellulare del fegato, pancreas e muscolo scheletrico

Patofisiologia della sindrome metabolica: il fegato

- Il fegato é fondamentale nell'assorbimento die FFA, sintesi e stoccaggio e trasporto dei metaboliti dei lipidi

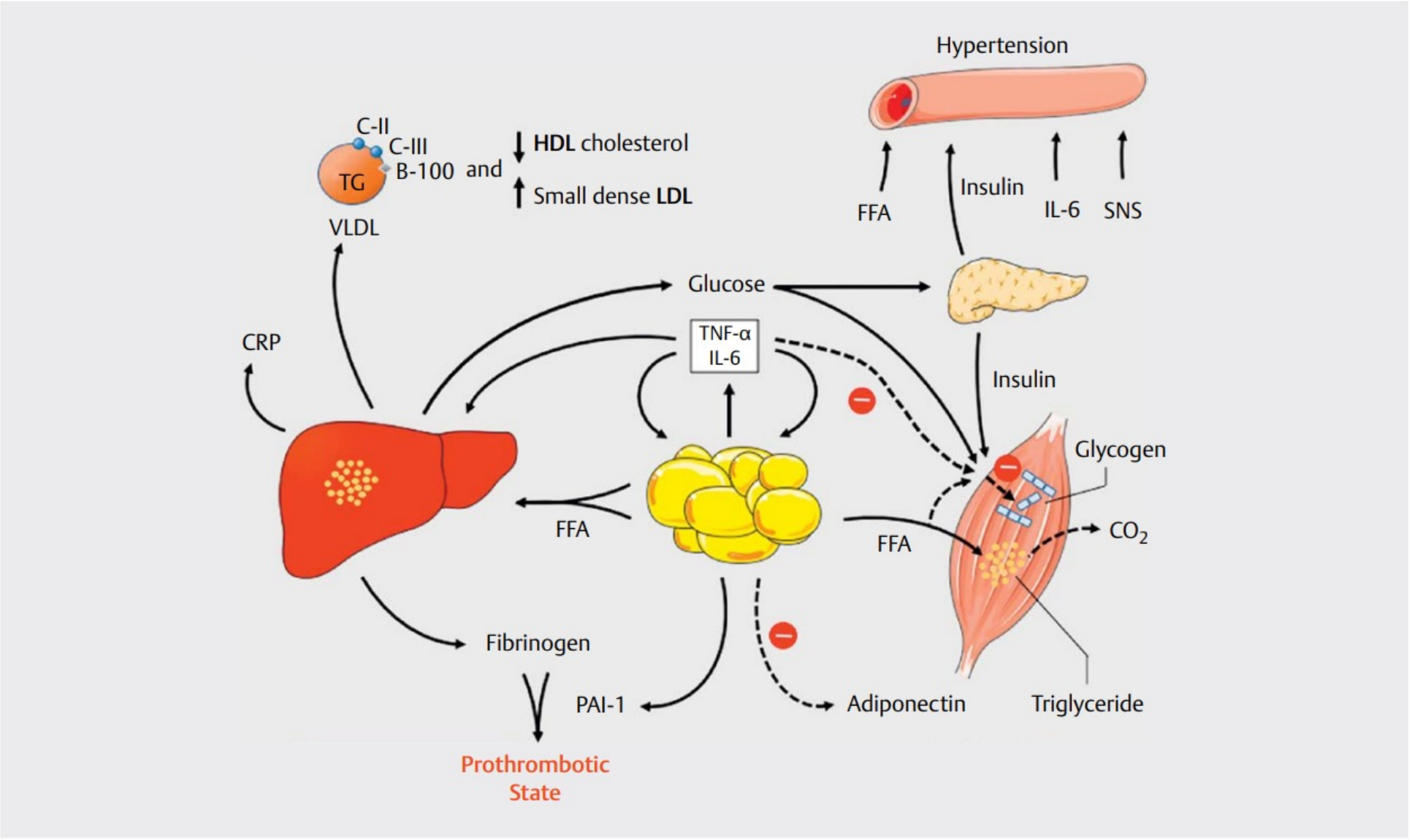
- Il fegato risponde all'alto dosaggio di FFA con la produzione di lipoproteine

Patofisiologia della sindrome metabolica

- Parallelamente alla definizione, non esiste un consenso sulla patofisiologia, quello che é assodato é una forte dipendenza tra fattori genetici e ambientali
- Grasso addominale influisce sull'asse ormonale e immunologico
- L'adiposità viscerale é la principale fonte di FFA che arrivano prima al fegato e poi alla circolazione sistemica.
- L'adiposità viscerale é una fonte cruciale di citochine

La patofisiologia della sindrome metabolica

- Il grasso addominale é la fonte principale di FFA con relativo deposito ectopico
- L'esposizione cronica a livelli elevati di FFA porta a disfunzioni cellulari di fegato, pancreas e muscoli scheletrici con lo sviluppo di insulino-resistenza
- Adipociti hanno una funzione centrale regolando l'appetito e hanno un effetto periferico sulla sensibilità all'insulina
- L'eccesso di FFA provoca un aumento dello stress ossidativo che porta a una disregolazione delle adipocitochine (PAI-1, Il-6)➔ infiammazione cronica
- L'ipertrofia e l'iperplasia degli adipociti porta a un'over-expression della leptina➔ associata con un effetto anti-anoressico➔ insulino-resistenza….



▶ **Fig. 1** Proposed Metabolic Syndrome Pathophysiology. CRP, C-reactive protein; HDL, high density lipoprotein; FFA, free fatty acids; IL-6, interleukin 6; LDL, low-density lipoprotein; PAI-1, plasminogen activator inhibitor 1; SNS, Sympathetic Nervous System; TG, triglyceride; TNF α, tumor necrosis factor α; VLDL, very low density lipoproteins.

Definizione di insulino-resistenza

- Incapacità di una quantità definita di insulina endogena o esogena di aumentare l'uptake cellulare di glucosio➔ rischio aumentato di sindrome metabolica

- Una certa quantità di insulina é legata a una risposta anormale del glucosio

Cause di insulino-resistenza

Major causes of insulin resistance

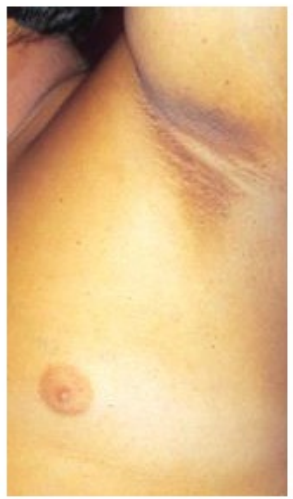
Inherited states of target cell resistance
Leprechaunism (insulin-receptor mutations)
Rabson-Mendenhall syndrome (insulin-receptor mutations)
Type A syndrome of insulin resistance (insulin-receptor mutations in some, unknown signaling defect in most)
Some lipodystrophies
Secondary insulin resistance
Obesity (free fatty acids and adipocytokines may contribute)
Stress, infection due to excess counterregulatory hormones (cortisol, catecholamines, growth hormone, glucagon)
Medications (eg, glucocorticoids, HIV antiretrovirals, oral contraceptives)
Inactivity
Pregnancy (placental lactogen)
Immune mediated (anti-insulin antibodies, anti-insulin receptor antibodies in type B syndrome)
Miscellaneous (starvation, uremia, cirrhosis, ketoacidosis)
Consequences of insulin resistance
Most cases of type 2 diabetes mellitus
Cardiovascular disease, hypertension
Polycystic ovary syndrome
Metabolic syndrome
Obesity-related cancers

HIV: human immunodeficiency virus.

Clinical manifestations of insulin resistance

Glucose homeostasis
Variable, including overt diabetes, impaired glucose tolerance, normal, and hypoglycemia
Cutaneous
Acanthosis nigricans
Skin tags
Alopecia
Reproductive
Amenorrhea
Hirsutism
Virilization
Infertility (in females)
Linear growth
Variable, including normal, impaired, increased
Adipose tissue
Variable, including normal, lipoatrophy, lipohypertrophy, obesity
Musculoskeletal
Variable, including normal, cramps, muscle hypertrophy, pseudoacromegaly
Lipid metabolism
Normal or hypertriglyceridemia
Autoimmunity
Type B syndrome with variety of immune phenotypes

Acanthosis nigricans

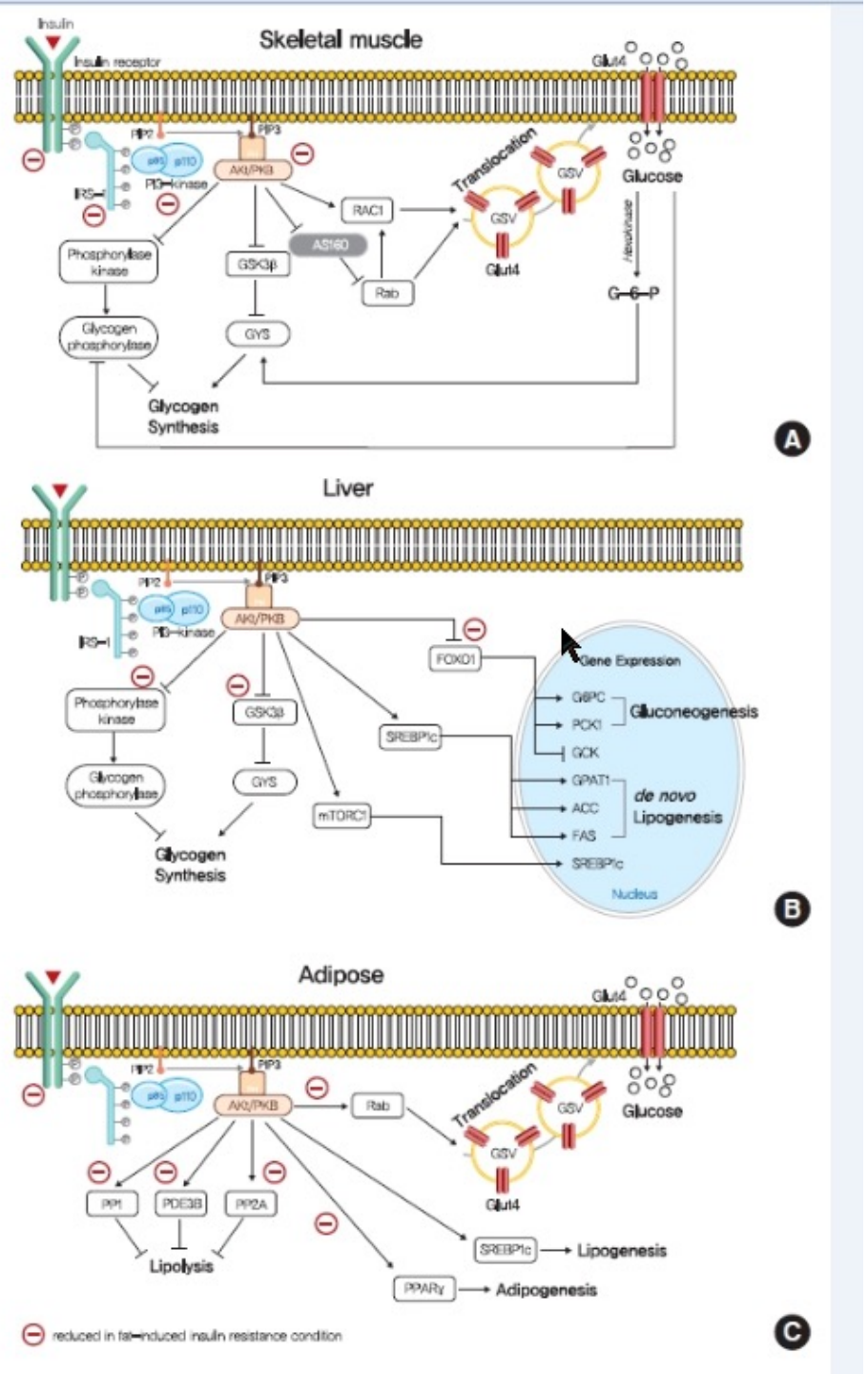


Classic hyperpigmented axillary lesion in acanthosis nigricans.

Courtesy of Jeffrey Flier, MD.

Fattori per lo sviluppo di insulino-resistenza

- Accumulo di lipidi ectopici e dei loro metaboliti
- Sviluppo di Stress a livello di ER
- Sviluppo di risposta sistemica infiammatoria a basso grado


Skeletal muscle
Insulin
Insulin receptor
Glut4
PIP2
PIP3
p85
p110
PI3-kinase
IRS
AKt/PKB
RAC1
Translocation
GSV
Glucose
AS160
Phosphorylase kinase
GSK3β
Rab
Hexokinase
G-6-P
Glycogen phosphorylase
GYS
Glycogen Synthesis
A
Liver
FOXO1
Gene Expression
G6PC
PCK1
Gluconeogenesis
SREBP1c
GCK
GPAT1
ACC
FAS
de novo Lipogenesis
mTORC1
Nucleus
B
Adipose
PPI
PDE3B
PP2A
Lipolysis
PPARγ
Adipogenesis
reduced in fat-induced insulin resistance condition
C

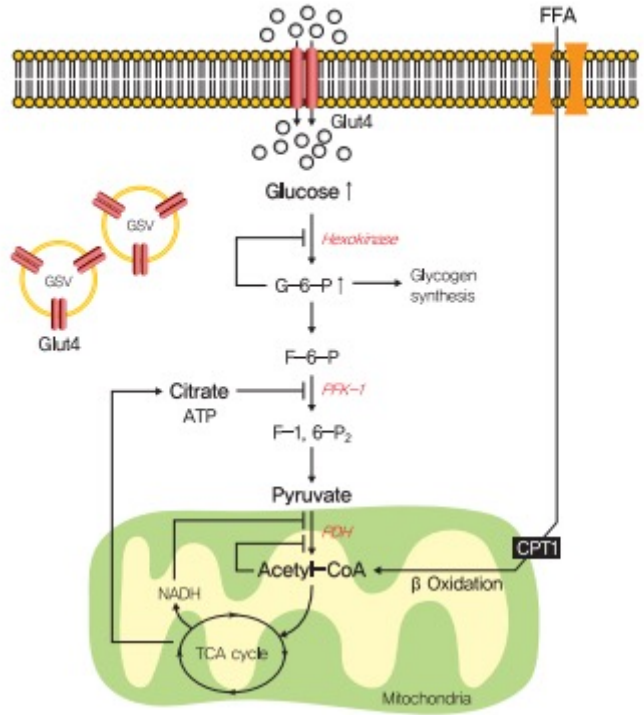


Fig. 2. The glucose-fatty acid cycle hypothesis in insulin resistance. Randle et al. [52] proposed that lipid-induced insulin resistance in skeletal muscle is attributed to limited insulin-stimulated glucose utilization caused by increased fatty acid oxidation. Fatty acid oxidation might increase mitochondrial acetyl-CoA levels and subsequently inactivate pyruvate dehydrogenase (PDH), which in turn, would increase intracellular citrate levels and inhibit phosphofructokinase 1 (PFK-1), and lead to the accumulation of intramyocellular glucose-6-phosphate (G-6-P), which inhibits hexokinase activity and causes the accumulation of intramyocellular glucose and reduced glucose uptake. FFA, free fatty acid; GLUT4, glucose transporter type 4; GSV, GLUT4 storage vesicle; ATP, adenosine triphosphate; CPT1, carnitine palmitoyltransferase 1; NADH, reduced nicotinamide adenine dinucleotide; TCA, trichloroacetic acid.

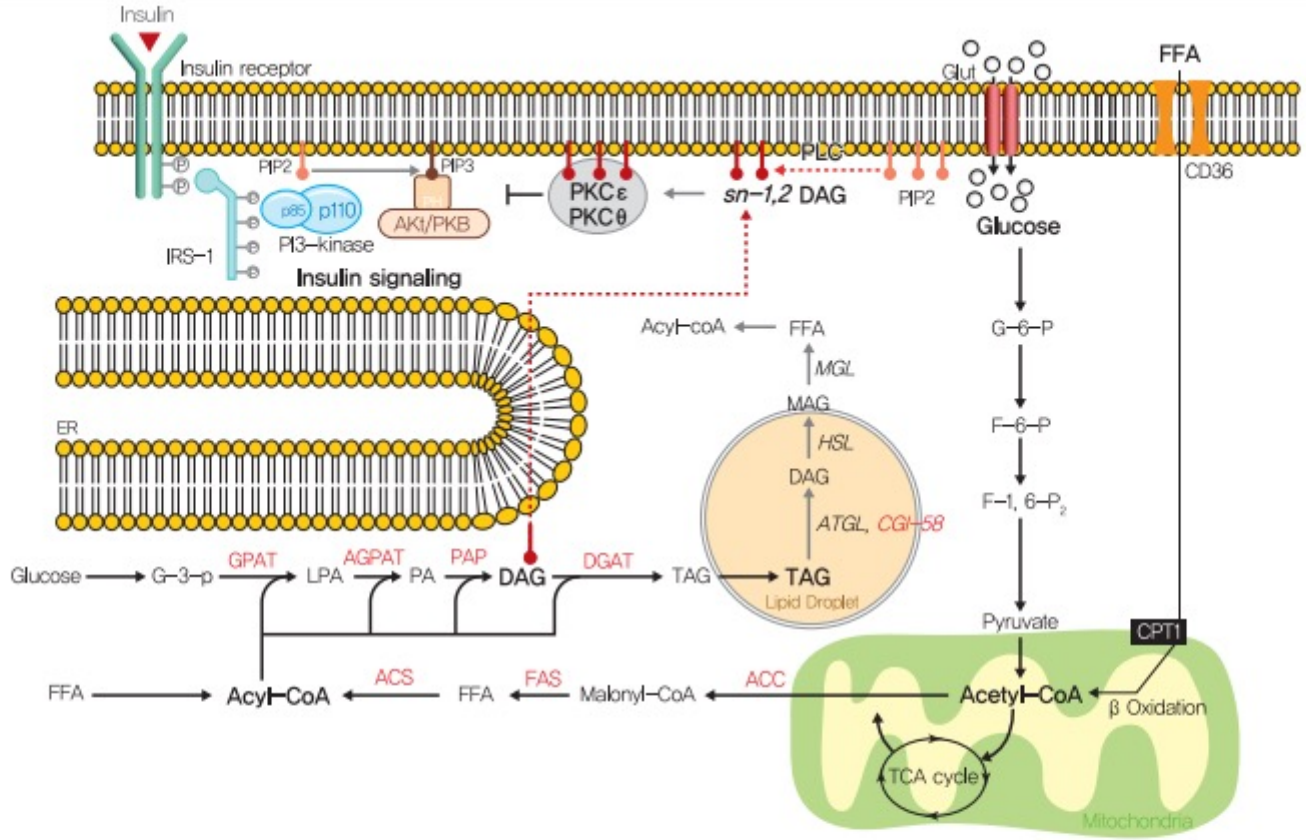


Fig. 4. Diacylglycerol (DAG)-protein kinase C (PKC) hypothesis in insulin resistance. Fatty acids are rapidly esterified in cells to fatty acyl-CoA, which form lysophosphatidic acid (LPA), DAG, and triacylglycerol (TAG) through lipogenesis. Increased hepatic DAG levels induced the translocation of nPKC (PKCε and PKCθ in liver and skeletal muscle, respectively) to the plasma membrane and inhibited insulin receptor tyrosine kinase (IRTK) tyrosine kinase activity by phosphorylating it at Thr1160, which inactivate insulin receptor substrate 2 (IRS-2), phosphatidylinositol-3-OH kinase (PI3K), and Akt2. PIP2, phosphatidylinositol-4,5-bisphosphate; PIP3, phosphatidylinositol-3,4,5-trisphosphate; PKB, protein kinase B; PLC, phospholipase C; FFA, free fatty acid; MGL, monoacylglycerol lipase; MAG, monoacylglycerol; HSL, hormone-sensitive lipase; ATGL, adipose triglyceride lipase; CGI-58, comparative gene identification-58; GPAT, glycerol-3-phosphate acyltransferase; AGPAT, acylglycerolphosphate acyltransferase; PA, phosphatidic acid; PAP, phosphatidic acid phosphatases; DGAT, diacylglycerol acyltransferase; ACS, acyl-CoA synthetases; FAS, fatty acid synthase; ACC, acetyl-CoA carboxylase; CPT1, carnitine palmitoyltransferase 1; TCA, trichloroacetic acid.

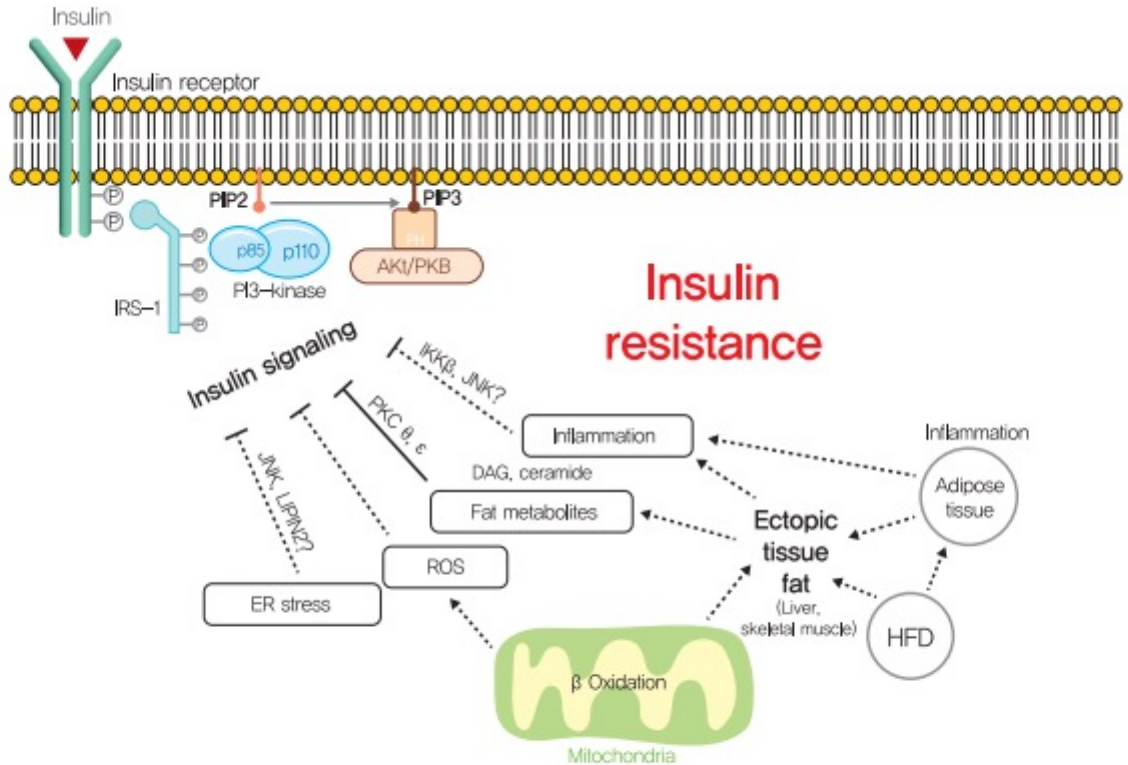


Fig. 5. Other potential mechanisms for insulin resistance. Other hypotheses, such as endoplasmic reticulum (ER) stress, reactive oxygen species (ROS), and inflammation, have been proposed to explain the mechanism responsible for obesity-induced insulin resistance. PIP2, phosphatidylinositol-4,5-bisphosphate; PIP3, phosphatidylinositol-3,4,5-trisphosphate; PKB, protein kinase B; IKK, inhibitor of nuclear factor κ-B kinase; JNK, c-Jun N-terminal kinase; PKC, protein kinase C; LIPIN2, phosphatidic acid phosphatases; DAG, diacylglycerol; HFD, high-fat diet .

Come valutare l’indice HOMA

VERKLEINERN QUIZ STARTEN

HOMA-Index: Nüchternblutzucker (mg/dL) × Insulin nüchtern (mIE/L) / 405

HOMA-Index	Auswertung
<2	Insulinresistenz unwahrscheinlich
2–2,5	Hinweis auf Insulinresistenz
2,6–5	Insulinresistenz wahrscheinlich
>5	Durchschnittswert bei Diabetes mellitus Typ 2

Precauzione nella valutazione dell'indice HOMA

- Homeostasis model Assessment (HOMA): viene calcolato a partire da un prelievo ematico a digiuno misurando il glucosio e l'insulina
- Attenzione alla preanalitica

- Gli assay non sono ancora completamente standardizzati
- Rare mutazioni dell'insulina che mostrano un'attività non normale, ma una normale immunoreattività

I lipidi nel laboratorio

- Chilomicroni derivanti dall'intestino e VLDL derivanti dal fegato, vengono metabolizzati in lipoproteine ricche di trigliceridi (TGRL remnants)

- Secrezione di chilomicroni é regolata dall'alimentazione, VLDL invece dall'insulina

Review

Residual Cardiovascular Risk at Low LDL: Remnants, Lipoprotein(a), and Inflammation

Ron C. Hoogeveen and Christie M. Ballantyne *

Clinical Chemistry 67:1
143–153 (2021)

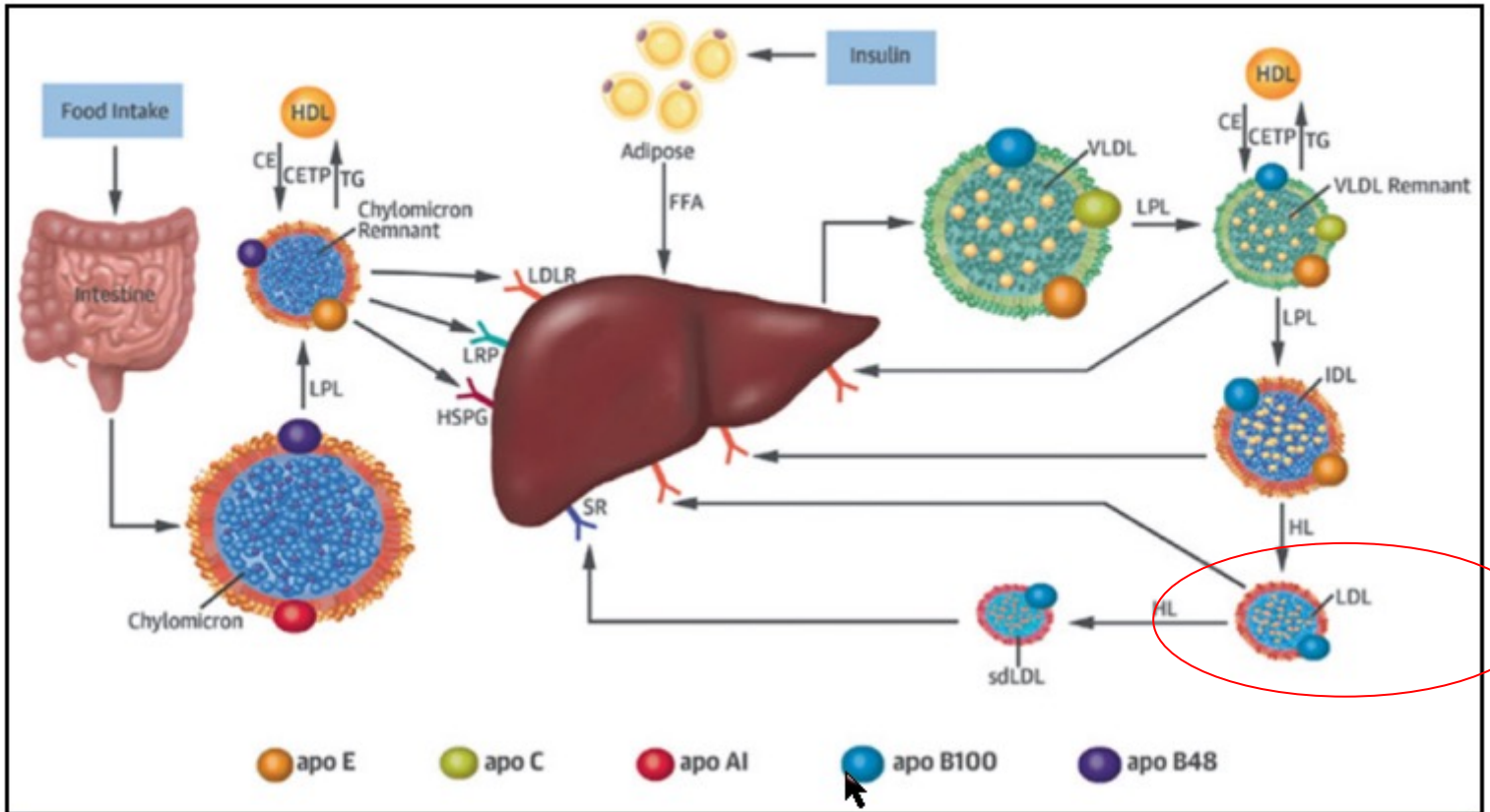
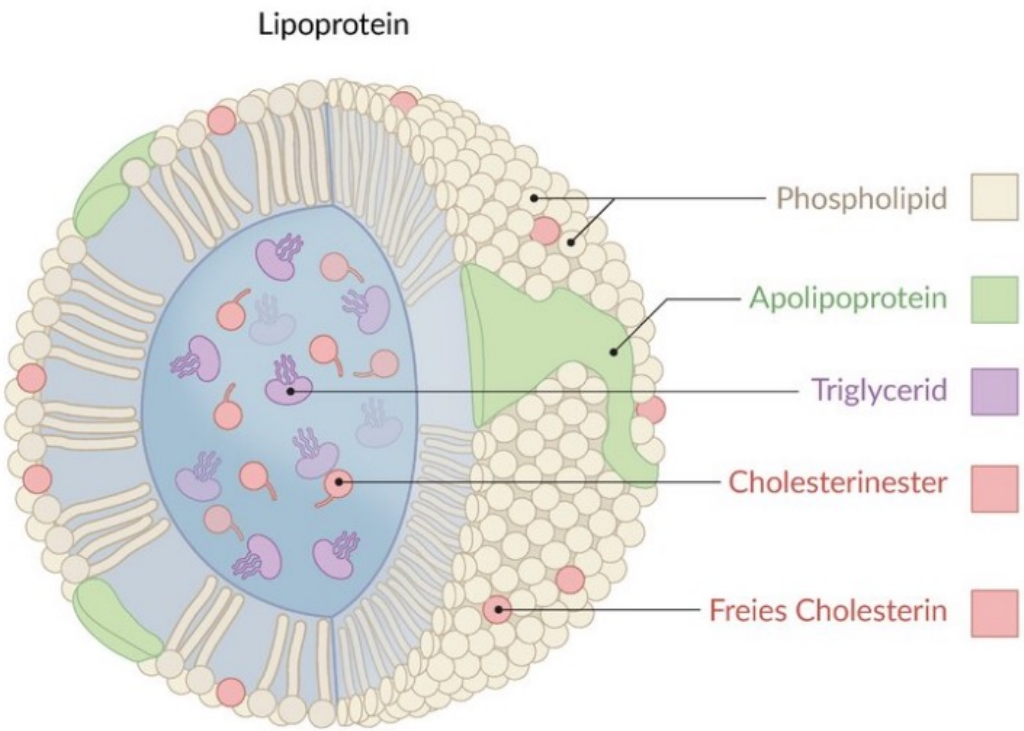
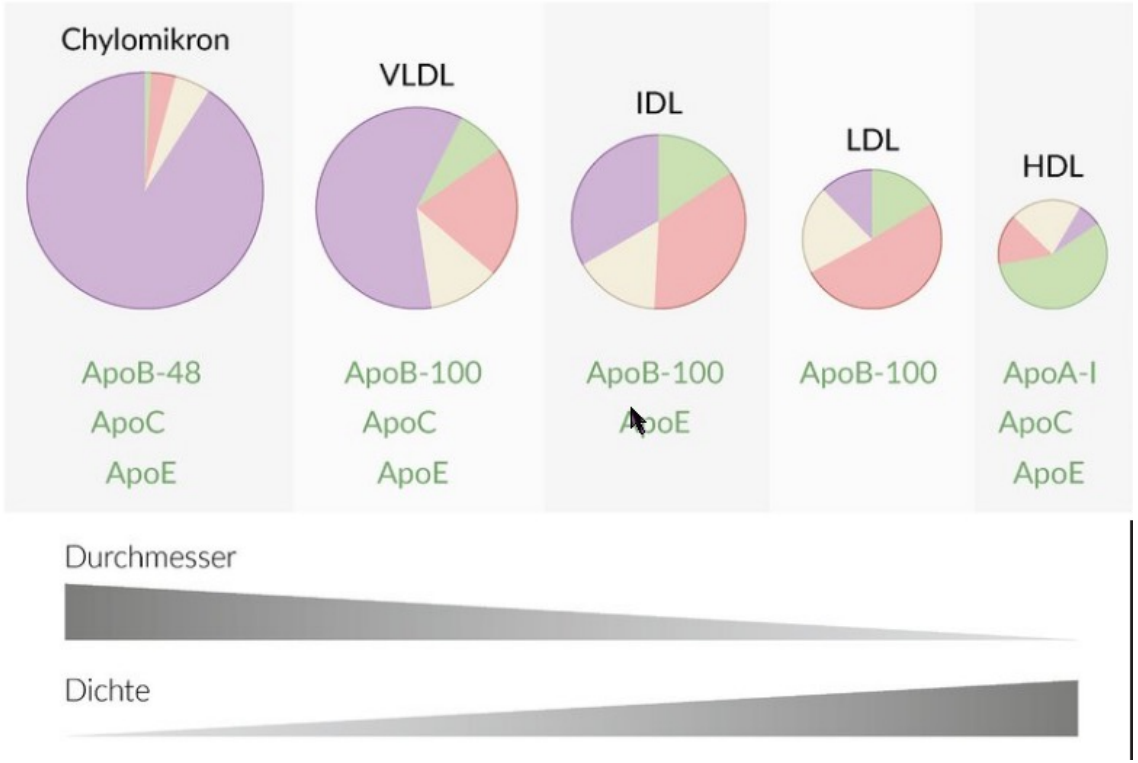


Fig. 1. Remnant lipoprotein metabolism. Chylomicrons secreted from the intestine and very-low-density lipoprotein (VLDL) secreted from the liver are lipolyzed by lipoprotein lipase (LPL), leading to triglyceride-rich lipoprotein (TGRL) remnants. Chylomicron secretion is largely regulated by food intake, whereas VLDL secretion is controlled by insulin. Remnant particles undergo remodeling via the enzymatic action of cholesteryl ester transfer protein (CETP) with high-density lipoprotein (HDL), hepatic lipase (HL), and the exchange of soluble apolipoproteins such as E, C-I, C-II, and C-III. TGRL remnants are cleared from the circulation via receptor-mediated uptake involving the low-density lipoprotein (LDL) receptor (LDLR), LDL receptor–like protein (LRP), and heparan sulfate proteoglycans (HSPG). Chylomicron remnants and VLDL remnants compete for the same lipolytic pathway, a process mediated by apoE. While chylomicron remnant clearance may be mediated by LDLR, LRP, or HSPG, VLDL remnants are believed to be cleared predominantly via LDLR. Individuals with apoE2 isoforms have reduced remnant clearance and are postulated to have compensatory upregulation of cellular LDLR expression that may lead to decreased LDL-TG and LDL-C concentrations. The purported role of HL in the lipolytic conversion of IDL to LDL may at least partly explain why individuals with decreased HL activity due to genetic variation in the *LIPC* gene (e.g., rs 2070895) have high LDL-TG concentrations. Reproduced with permission from Saeed et al. (7).


Lipoprotein
Phospholipid
Apolipoprotein
Triglycerid
Cholesterinester
Freies Cholesterin


Chylomikron
VLDL
IDL
LDL
HDL
ApoB-48
ApoC
ApoE
ApoB-100
ApoC
ApoE
ApoB-100
ApoE
ApoB-100
ApoA-I
ApoC
ApoE
Durchmesser
Dichte

VERKLEINERN QUIZ STARTEN

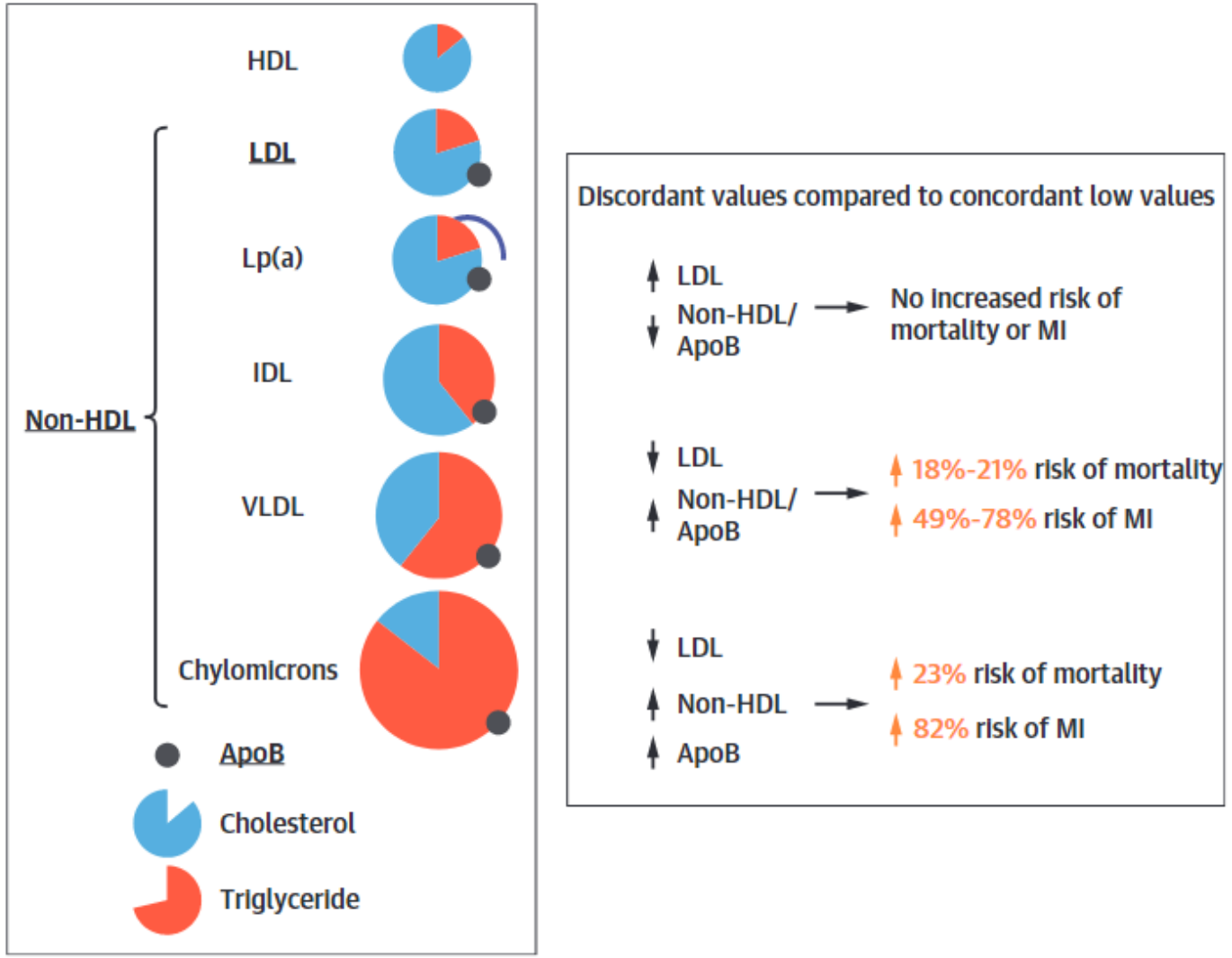
Lipoproteinklasse	Durchmesser (nm)	Wichtige enthaltene Apolipoproteine	Zusammensetzung (in %)				
			TAG	Freies Cholesterin	Cholesterinester	Phospholipid	Apolipoprotein
Chylomikronen	• 75–1200	• B-48, C, E	• 86	• 1	• 4	• 7	• 2
VLDL (Very Low Density Lipoproteins)	• 30–80	• B-100, C, E	• 55	• 5	• 15	• 20	• 5
IDL (Intermediate Density Lipoproteins)	• 15–35	• B-100, E	• 30	• 10	• 30	• 20	• 10
LDL (Low Density Lipoproteins)	• 18–25	• B-100	• 10	• 10	• 40	• 20	• 20
HDL (High Density Lipoproteins)	• 7,5–20	• A-I, C, E	• 5	• 5	• 20	• 30	• 40

	Chilomicroni	VLDL	LDL	HDL
Funzione	Trasporto dei TG	Sintetizzati nel fegato per il trasporto di TG e colesterolo dal fegato ad organi extra-epatici	Trasporto di colesterolo e esteri di colesterolo dal fegato a tessuti extra-epatici	Trasporto di colesterolo e esteri di colesterolo dai tessuti periferici al fegato

Ipercolesterolemia

- Fattore casuale più importante per lo sviluppo di CVD.
- LDL é il target primario utilizzato per il monitoraggio della terapia contro l'ipercolesterolemia
- Tuttavia controllando solamente LDL si tralasciano alltri fattori di rischio con altre lipoproteine aterogeniche
- Conseguentemente apoliproprotein B (apoB) e non-HDL, sono target secondari nel trattamento dell'ipercolesterolemia

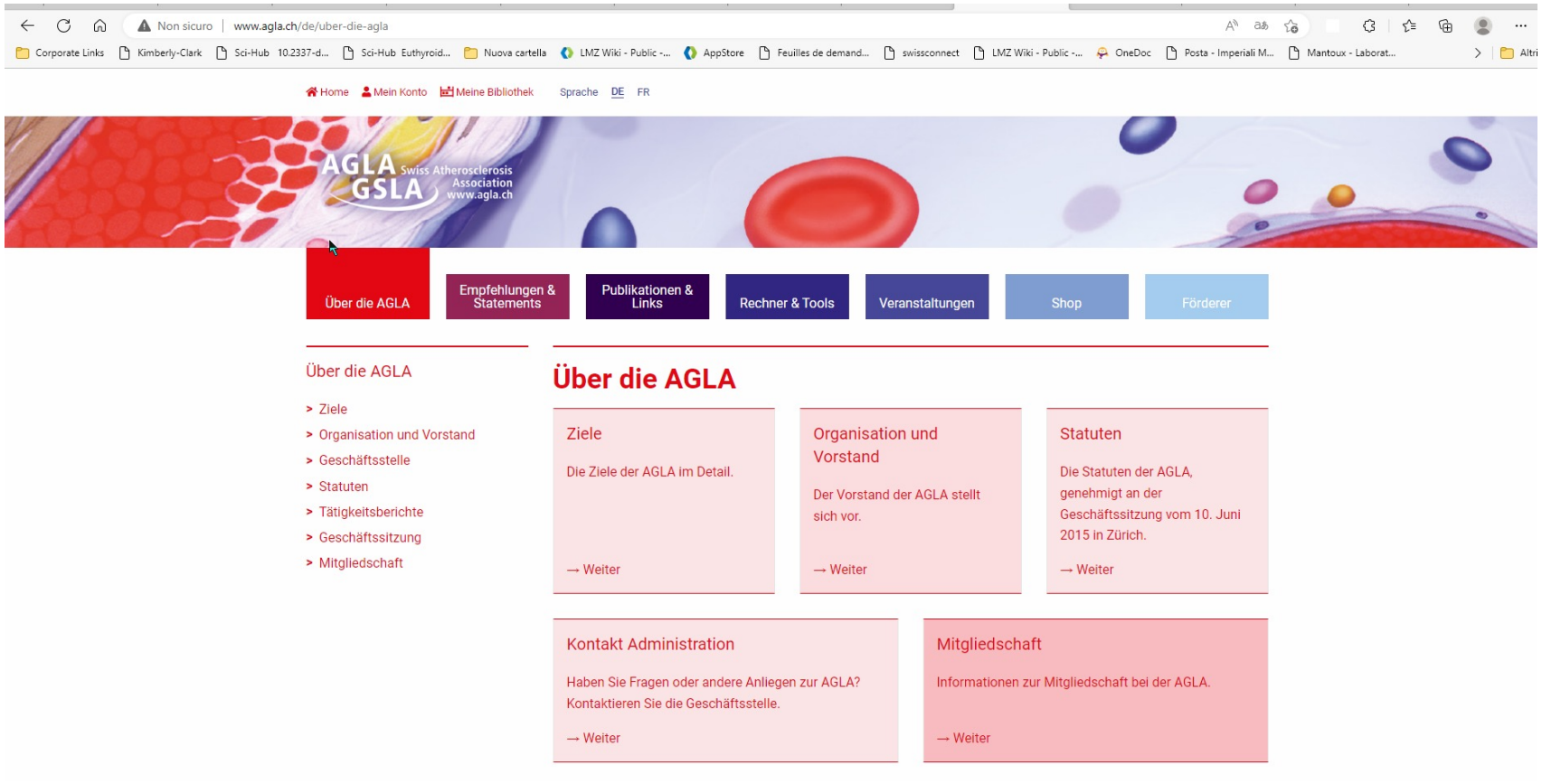
CENTRAL ILLUSTRATION **Multivariable-Adjusted Risk of All-Cause Mortality and Myocardial Infarction in 13,015 Statin-Treated Patients From the Copenhagen General Population Study**



Johannesen, C.D.L. et al. J Am Coll Cardiol. 2021;77(11):1439-50.

Concordance and discordance were defined by median values of each lipid trait. apoB = apolipoprotein B; HDL = high-density lipoprotein; IDL = intermediate-density lipoprotein; LDL = low-density lipoprotein; MI = myocardial infarction; VLDL = very low-density lipoprotein.

Prevenzione aterosclerosi



In quali casi proporre lo screening

- Anamnesi famigliare positiva per CVD
- Ipercolesterolemia famigliare
- Fumo
- Ipertensione
- Diabete mellito
- Iperlipidemia
- Adiposità
- Per uomini asintomatici >40 anni o donne asintomatiche >50 anni➔ calcolare il rischo

Ricontrolli previsti

- Rischio basso: ogni 5 anni
- Rischio moderato: 2-5 anni
- Rischio alto/molto elevato: a dipendenza della clinica

Kardiovaskuläres Risiko: Risikokategorie und Risikoschätzung

AGLA Risiko-Score[1,2]

Nur anwendbar bei scheinbar gesunden Personen

1) Punktwerte je Risikofaktor und Ausprägung

LDL-Cholesterin (mmol/l)		HDL-Cholesterin (mmol/l)		Systolischer Blutdruck (mmHg)	
≤2.60	0	≤0.91	11	<110	0
2.61–2.73	1	0.92–0.96	10	110–119	1
2.74–2.86	2	0.97–1.01	9	120–129	2
2.87–2.99	3	1.02–1.06	8	130–139	3
3.00–3.12	4	1.07–1.11	7	140–149	4
3.13–3.25	5	1.12–1.16	6	150–159	5
3.26–3.38	6	1.17–1.21	5	160–169	6
3.39–3.51	7	1.22–1.27	4	170–179	7
3.52–3.64	8	1.28–1.32	3	≥180	8
3.65–3.77	9	1.33–1.37	2	**CV Ereignisse in der Familie***	
3.78–3.90	10	1.38–1.42	1	Nein	0
3.91–4.03	11	≥1.42	0	Ja	5
4.04–4.16	12	**Triglyzeride (mmol/l)**			
4.17–4.29	13	<1.10	0		
4.30–4.42	14	1.10–1.64	2		
4.43–4.55	15	1.65–2.19	3		
4.56–4.68	16	≥2.20	4		
4.69–4.81	17	**Zigarettenraucher zur Zeit**			
4.82–4.94	18	Nein	0		
4.95–5.07	19	Ja	12		
≥5.08	20				

*Myokardinfarkt bei Eltern, Grosseltern oder bei Geschwistern vor dem 55. LJ bei Männern und vor dem 65. LJ bei Frauen

2) Addition der Punktwerte aller Risikofaktoren ergibt die Gesamtrisikopunkte

[1] nach dem PROCAM Weibull-Modell
[2] Bestimmt absolutes Risiko in %, innerhalb von 10 Jahren ein tödliches Koronarereignis oder einen nicht-tödlichen Myokardinfarkt zu erleiden.

3) Altersabhängige Gesamtrisikopunkte für Kategorie «Hohes Risiko» (>20 % in 10 Jahren)

Männer						Frauen			
Alter	Gesamtrisikopunkte					Alter	Gesamtrisikopunkte		
34	70	50	49	66	36	45	70	61	49
35	68	51	48	67	35	46	68	62	47
36	67	52	47	68	34	47	67	63	46
37	65	53	46	69	34	48	65	64	44
38	64	54	45	70	33	49	63	65	43
39	62	55	44	71	32	50	62	66	42
40	61	56	43	72	32	51	61	67	41
41	59	57	42	73	31	52	59	68	40
42	58	58	42	74	30	53	58	69	39
43	57	59	41	75	30	54	56	70	38
44	56	60	40			55	55	71	37
45	54	61	39			56	54	72	36
46	53	62	39			57	52	73	36
47	52	63	38			58	51	74	35
48	51	64	37			59	50	75	34
49	50	65	36			60	49		

4) Ist die errechnete Gesamtpunktzahl grösser oder gleich dem Wert beim entsprechenden Alter, so fällt die Person in die Kategorie «Hohes Risiko» (>20 %)

AGLA Risiko-Algorithmus

Zur direkten Berechnung des kardiovaskulären Gesamtrisikos steht auf **www.agla.ch** ein Algorithmus zur Verfügung. Er ist für Personen bis 75 Jahre anwendbar und erlaubt die Berechnung des absoluten Risikos. Für jede Person soll mindestens eine Berechnung mit dem Algorithmus durchgeführt werden.

2.3 Schätzung des kardiovaskulären Gesamtrisikos mit SCORE2/SCORE2-OP[1]

Nur anwendbar bei scheinbar gesunden Personen

SCORE2 für Personen <70 Jahre

	Frauen								Männer							
	Nichtraucherinnen				Raucherinnen				Nichtraucher				Raucher			
	Non-HDL-Cholesterin[1] (mmol/l)															
Systolischer Blutdruck (mmHg)	3,0–3,9	4,0–4,9	5,0–5,9	6,0–6,9	3,0–3,9	4,0–4,9	5,0–5,9	6,0–6,9	mmol/l	3,0–3,9	4,0–4,9	5,0–5,9	6,0–6,9	3,0–3,9	4,0–4,9	5,0–5,9	6,0–6,9
SCORE2									Alter								
160–179	8	8	8	8	12	12	13	13	65–69	11	12	13	13	15	16	17	19
140–159	7	7	7	7	10	10	11	11		9	10	11	11	13	14	15	16
120–139	6	6	6	6	8	9	9	9		8	8	9	10	11	12	13	13
100–119	5	5	5	5	7	7	7	8		6	7	7	8	9	10	11	11
160–179	6	6	7	7	10	10	11	11	60–64	8	9	10	11	13	14	15	17
140–159	5	5	5	6	8	8	9	9		7	8	7	9	13	14	15	17
120–139	4	4	4	5	6	7	7	8		6	6	7	8	9	14	15	17
100–119	3	3	4	4	5	6	6	6		5	5	6	6	7	8	9	17
160–179	4	5	5	5	8	8	9	10	55–59	7	7	8	9	10	12	13	15
140–159	3	4	4	4	6	7	7	8		5	6	7	8	9	10	11	12
120–139	3	3	3	3	5	6	6	6		4	5	5	6	7	8	9	10
100–119	2	2	3	3	4	4	5	5		4	4	4	5	6	6	7	8
160–179	3	4	4	4	6	7	7	8	50–54	5	6	7	8	9	10	11	13
140–159	3	3	3	3	5	5	6	6		4	5	5	6	7	8	9	10
120–139	2	2	2	3	4	4	5	5		3	4	4	5	6	6	7	8
100–119	2	2	2	2	3	3	4	4		3	3	3	4	4	5	6	7
160–179	2	3	3	3	5	5	6	7	45–49	4	5	6	6	7	8	10	11
140–159	2	2	2	3	4	4	5	5		3	4	4	5	6	7	8	9
120–139	1	2	2	2	3	3	4	4		2	3	3	4	4	5	6	7
100–119	1	1	1	1	2	2	3	3		2	2	3	3	3	4	5	5
160–179	2	2	2	3	4	4	5	6	40–44	3	4	5	5	6	7	8	10
140–159	1	2	2	2	3	3	4	4		2	3	3	4	5	5	6	8
120–139	1	1	1	1	2	3	3	3		2	2	3	3	3	4	5	6
100–119	1	1	1	1	2	2	2	2		1	2	2	2	3	3	4	5

[1] Bestimmt absolutes Risiko, in 10 Jahren ein fatales oder nicht-fatales CV Ereignis (Myokardinfarkt, Schlaganfall) zu erleiden.

Diagnostica e laboratorio delle dislipidemie

4.1 Diagnostik und Zielwerte bei Dyslipidämien

Der Lipidstatus des Nicht-Nüchtern-Plasmas reicht in den meisten Fällen für eine Beurteilung aus. In folgenden Situationen wird eine Nüchtern-Blutentnahme jedoch empfohlen:

- Metabolisches Syndrom
- Nicht-Nüchtern TG >5 mmol/l
- Bekannte Hypertriglyzeridämie
- Nach Hypertriglyzeridämie-induzierter Pankreatitis
- Vor Beginn einer medikamentösen Therapie mit schwerer Hypertriglyzeridämie als möglicher Nebenwirkung
- Wenn zusätzliche Analysen gefordert sind, die nüchtern zu bestimmen sind, z.B. Nüchtern-Glukose, therapeutisches Medikamenten-Monitoring

Screening, Risiko-Stratifizierung und Behandlungsziele bei Dyslipidämie

Lipid-parameter	Screening; Diagnose; Risiko-Stratifizierung	Zielwerte (ZW)
LDL-C	Primär empfohlen. Erforderlich zur Risiko-Schätzung mit AGLA-Risiko-rechner.	■ Patienten <70 Jahre **Sehr hohes Risiko** (vgl. S. 11): LDL-C-Reduktion um ≥50 % und <1.4 mmol/l **Patienten mit ASCVD und erneutem CV Ereignis innerhalb von 2 Jahren trotz maximal tolerierbarer Statin-Dosis:** LDL-C <1.0 mmol/l **Hohes Risiko** (vgl. S. 12): LDL-C-Reduktion um ≥50 % und <1.8 mmol/l **Moderates Risiko** (vgl. S. 12): LDL-C <2.6 mmol/l erwägen **Niedriges Risiko** (vgl. S. 12): LDL-C <2.6 mmol/l kann erwogen werden ■ Patienten ≥70 Jahre: vgl. S. 40
Gesamt-Cholesterin (TC)	Erforderlich zur Berechnung von Non-HDL-C und damit erforderlich zur Risiko-Schätzung mit SCORE2/ SCORE2-OP	■ Kein Behandlungsziel ■ Nur wenn LDL-C oder Non-HDL-C nicht verfügbar

Lipid-parameter	Screening ; Diagnose; Risiko-Stratifizierung	Zielwerte (ZW)
Non-HDL-C (=TC minus HDL-C=Total der athero-genen Lipo-proteine	■ Wird zur Risikoschätzung bei SCORE2/ SCORE2-OP verwendet ■ Empfohlen für Risiko-Assessment, speziell bei folgenden Patienten: • Hohe TG-Werte • DM • Adipositas • Sehr tiefe LDL-C-Werte Kann im Lipidstatus einfach berechnet werden.	**Sehr hohes Risiko:** <2.2 mmol/l **Hohes Risiko:** <2.6 mmol/l **Moderates Risiko:** <3.4 mmol/l
ApoB	Sekundär empfohlen. Kann als Alternative zu LDL-C oder Non-HDL-C verwendet werden. Kann bei folgenden Patienten gegenüber Non-HDL-C bevorzugt werden: • Hohe TG-Werte • Sehr tiefe LDL-C-Werte • DM • Adipositas oder meta-bolisches Syndrom	**Sehr hohes Risiko:** <65 mg/dl **Hohes Risiko:** <80 mg/dl **Moderates Risiko:** <100 mg/dl
Triglyzeride (TG)	Empfohlen als Teil der Routine-Lipid-Analyse. Erforderlich zur Risiko-Schätzung mit AGLA-Risikorechner.	■ Kein Behandlungsziel ■ <1.7 mmol/l bedeutet geringes Risiko, falls höher nach anderen Risikofaktoren suchen ■ Moderate Hypertriglyzeridämie (2–10 mmol/l): vgl. S. 34 ■ Schwere Hypertriglyzeridämie (>10 mmol/l): vgl. S. 34
HDL-C	■ Erforderlich zur Risiko-Schätzung mit AGLA-Risikorechner ■ Erforderlich zur Berechnung von Non-HDL-C	■ Kein Behandlungsziel ■ Tiefes HDL-C geht mit erhöh-tem CV Risiko einher; ■ HDL-C >1.9 mmol/l (Männer) bzw. >2.4 mmol/l (Frauen) ist mit frühzeitigem Tod assoziiert. ■ Bei isoliert niedrigem HDL-C (<1 mmol/l, TG <2.3 mmol/l) Korrektur von Lebensstilfehlern und anderer Risikofaktoren
Lp(a)	Bestimmung sollte bei jeder erwachsenen Person einmal im Leben erfolgen, zur Identifi-kation von Individuen mit hohen Lp(a)-Werten. Besonders stark empfohlen bei: ■ Positiver Familienanamnese bezüglich frühzeitiger CV Erkrankungen ■ Zur Reklassifikation von Patienten, deren Risiko im Bereich moderates und hohes Risiko liegt	■ Kein Behandlungsziel ■ Referenzwerte ASCVD-Risiko: >30 mg/dl (>70 nmol/l): **moderat erhöht** >50 mg/dl (>120 nmol/l): **hoch** >180 mg/dl (>430 nmol/l): **sehr hoch**

Monitoraggio in caso di terapia contro ipercolesterolemia

4.2.4 Labormonitoring bei Cholesterinsenker-Therapie

Kontrollschema			
	Vor Therapie	**Nach Therapiebeginn/ -anpassung**	**Langzeitverlauf**
Lipide	■ Mindestens 2x im Abstand von 1–12 Wochen ■ Ausnahme: Bei ACS oder bei Pat. mit sehr hohem Risiko sofortiger Beginn mit Statin-Therapie	■ 4–12 Wochen nach Beginn mit Lipid-senker ■ 4–12 Wochen nach Therapieanpassung	■ Nach Erreichen der Zielwerte 1x/Jahr, sofern keine Compliance- oder besonderen Gründe vorliegen
Leberenzyme (ALT)	■ Bestimmen	■ 8–12 Wochen nach Therapiebeginn ■ 8–12 Wochen nach Dosisanpassungen ■ Keine Langzeitkontrollen empfohlen, ausser bei Einsatz von Fibraten	
CK	■ Bestimmen ■ Falls CK >4x ULN nicht starten, Test wiederholen	■ Keine Routinekontrollen ■ Tests bei Auftreten von Myalgien ■ Cave: ältere Personen, Begleitmedikamente mit Interaktionsrisiko, Polymedikation, Nierenkrankheiten oder Hypothyreose	

PCSK9-Hemmer: Lipide 4–12 Wochen nach 1. Injektion und 4–12 Wochen nach Therapieanpassung bestimmen.
Langzeitkontrollen gemäss Limitatio S. 46/47.

Management der Statin-Intoleranz vgl. S. 42-45.

Ipercolesterolemia famigliare

- Nel caso di pazienti adulti o in caso di presenza di famigliari di primo grado con:
  - Colesterolo totale >= 8mmol/L
  - Oppure LDL-C>= 5 mmol/L
  - Oppure presenza prematura di aterosclerosi (umoni <55 anni, donne < 60 anni)
  - … (si veda linee guida AGLA)

  - Nel caso di presenza di almeno uno di questi criteri, si consiglia di utilizzare l'algoritmo Duct Lipid clinic Network (DLCN)

Kriterien für die klinische Diagnose der HeFH gemäss Dutch Lipid Clinic Network

Der Algorithmus gilt nur für Erwachsene.

Kategorie	Kriterien*	Score
Familien-anamnese	Verwandter 1. Grades mit vorzeitiger KHK[1] und/oder Verwandter 1. Grades mit LDL-C >95. Perzentile	1
	Verwandter 1. Grades mit Sehnenxanthomen und/oder Arcus lipoides corneae und/oder Kinder <18 J. mit LDL-C >95. Perzentile nach Alter, Geschlecht und Land	2
Persönliche Anamnese	Vorzeitige KHK[1]	2
	Vorzeitige cerebrale/periphere Gefässkrankheit[1]	1
Körperliche Untersuchung	Sehnenxanthome	6
	Arcus lipoides corneae unter 45 J.	4
LDL-C (mmol/l)	≥8.5	8
	6.5–8.4	5
	5.0–6.4	3
	4.0–4.9	1
Genetische Tests	Nachweis kausaler Mutationen in den Genen LDLR, ApoB oder PCSK9	8
TOTAL	**Interpretation der Punktwerte***	**Summe**
Bewertung	■ Definitive HeFH	>8
	■ Wahrscheinliche HeFH	6–8
	■ Mögliche HeFH	3–5
	■ Keine Diagnose	<3

[1] Mann <55 J., Frau <60 J.

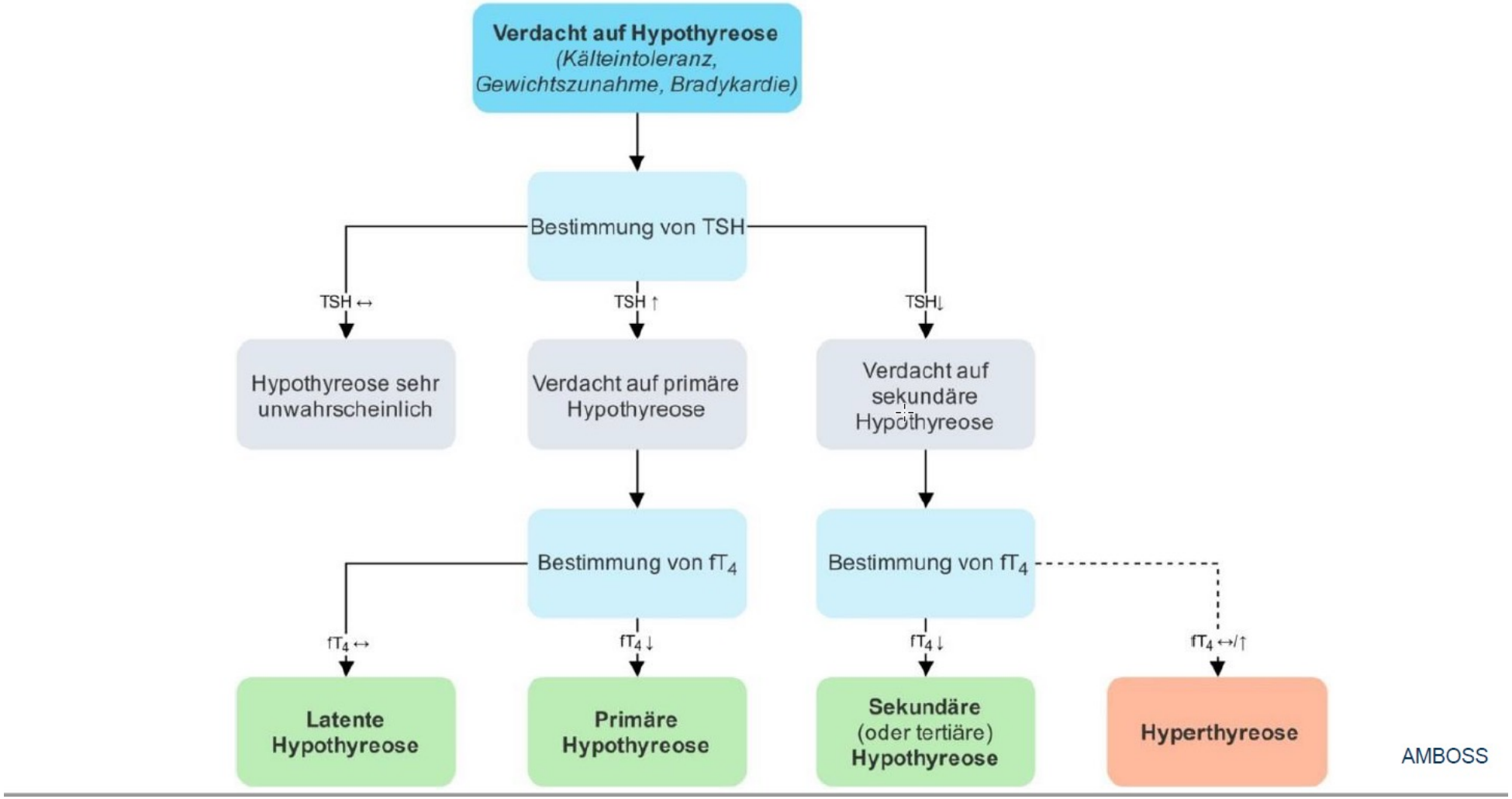
* Benutzung des Algorithmus: pro Kategorie nur den höchsten Score verwenden. Zum Beispiel, wenn KHK und Sehnenxanthome in der Familiengeschichte vorkommen, nur den Score 2 verwenden. Wenn nur Personen mit erhöhtem LDL-Cholesterin und frühzeitiger KHK vorkommen, jedoch niemand mit Xanthomen und keine Kinder mit Hypercholesterinämie, nur den Score 1 verwenden.

Wir empfehlen die Onlineversion des DLCN-Berechnungsalgorithmus auf **www.agla.ch/berechnungshilfen.**
Bitte beachten: Die Kosten der genetischen FH-Analysen werden von den Krankenkassen nicht erstattet.
(Stand Analysenliste des BAG vom August 2022)

Adiposità: cause secondarie

Parametro	Malattia	Feedback	
TSH	Ipoterosi latente	Diminuzione della termogenesi, metabolismo basale diminuito, aumento di peso	0.1-2% (manifesto) 4-10% (latente)
ACTH	Morbo di Cusching	Disturbo nel metabolismo die carboidrati➔ adiposità viscerale	<1%
LH/FSH	PCOS	Si veda di seguito	6-10% delle donne

Ipo/iper tireosi



PCOS: sindrome dell’ovaio policistico

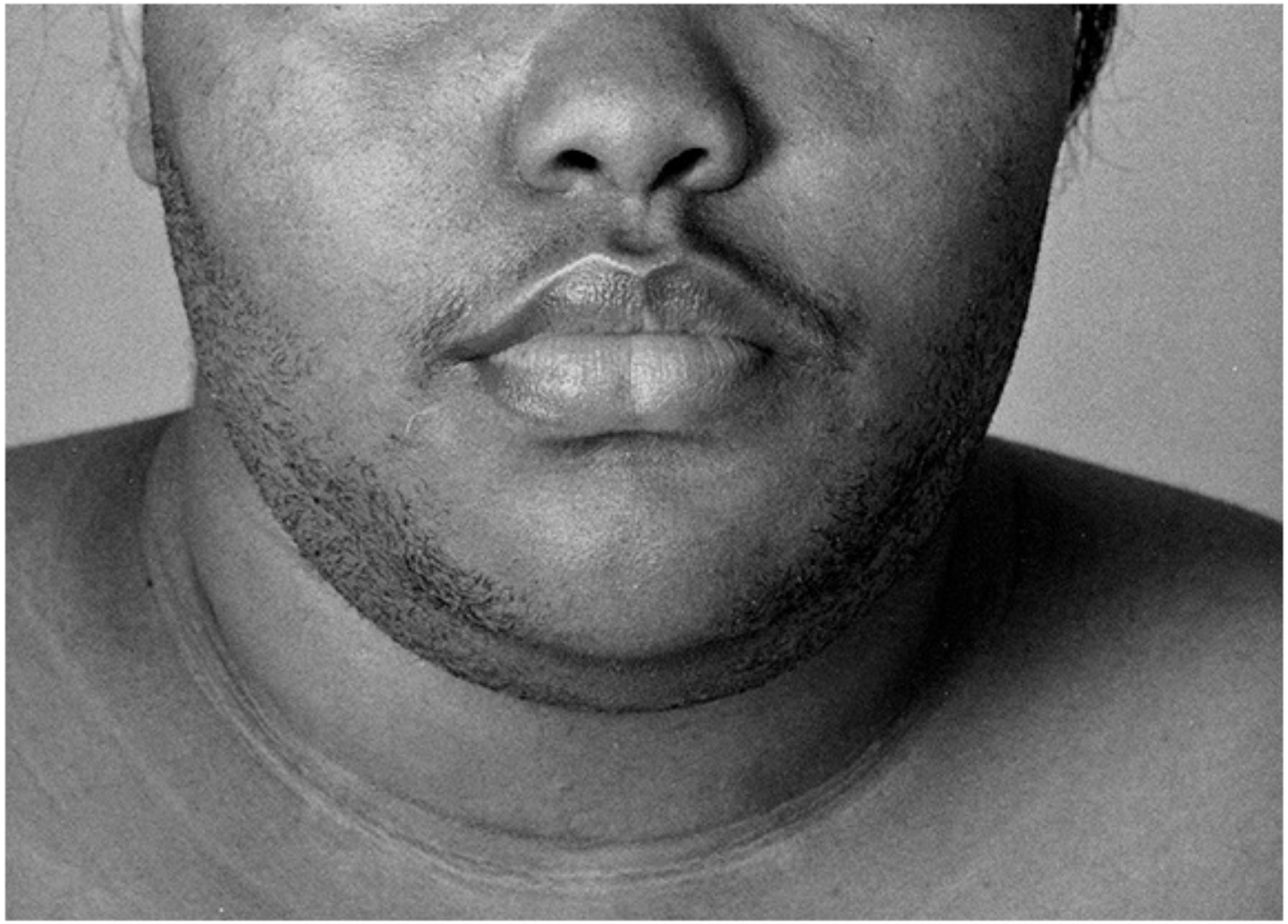
- Causa importante Oligo e/o anovulazione e eccesso di androgeni nelle donne
- Diagnosticata in caso di irsutismo, ciclo irregolare, morfologia da ovaio policistico a US transvaginale
- Se tuttavia i criteri sopra elencati non sono tutti rispettati, i criteri diagnostici diventano piu controversi

Causes of hirsutism in women

Etiology	Clinical features
Common	
PCOS	Peripubertal onset of symptoms, oligomenorrhea, obesity, polycystic ovaries on ultrasound.
Nonclassic 21-hydroxylase deficiency	Similar presentation to PCOS, high serum 17-hydroxyprogesterone concentration, more common in certain ethnic groups.
Uncommon	
Classic 21-hydroxylase deficiency	Diagnosed during infancy, ambiguous genitalia.
Androgen-secreting ovarian tumors (Sertoli-Leydig cell, granulosa-theca cell, hilus cell)	Onset in third decade or later (usually postmenopausal), rapidly progressive hirsutism, virilization.
Androgen-secreting adrenal tumors	Some women with adrenocortical cancer present with just virilization, but a mixed Cushing's and virilization syndrome is more common.
Ovarian hyperthecosis	Onset in third decade or later (usually postmenopausal), rapidly progressive hirsutism, virilization.
Severe insulin-resistance syndromes	Virilization, amenorrhea, infertility, and the ovary shows histologic changes of hyperthecosis.
Cushing's disease	Corticotroph adenoma secreting ACTH results in excess cortisol and adrenal androgens.
Drugs	Use of exogenous androgens (testosterone or DHEA) can cause hirsutism and acne.
Acromegaly	Enlarged jaw (macrognathia) and enlarged, swollen hands and feet, which result in increasing shoe, glove, and ring sizes. Patients with large pituitary tumors may have headaches, visual field defects, and cranial nerve palsies.

PCOS: polycystic ovary syndrome; ACTH: corticotropin; DHEA: dehydroepiandrosterone.

Hirsutism in PCOS



PCOS: polycystic ovary syndrome.

Diagnosi PCOS (Criteri di rotterdam)

- Oligo e/o anovulazione
- Segni clinici e/o biochimici di iperandrogenismo
- Ovaio policistico messo in evidenza da US

PCOS: altri criteri

Proposed diagnostic criteria for polycystic ovary syndrome

NIH consensus criteria 1990[1] (all required)	Rotterdam criteria 2003*[2] (two out of three required)	AES definition 2008[3] (all required)
Menstrual irregularity due to oligo- or anovulation	Oligo- or anovulation	Clinical and/or biochemical signs of hyperandrogenism
Clinical and/or biochemical signs of hyperandrogenism	Clinical and/or biochemical signs of hyperandrogenism	Ovarian dysfunction – oligo/anovulation and/or polycystic ovaries on ultrasound
Exclusion of other disorders: NCCAH, androgen-secreting tumors	Polycystic ovaries (by ultrasound)	Exclusion of other androgen excess or ovulatory disorders

NIH: National Institutes of Health; AES: Androgen Excess Society; NCCAH: nonclassic congenital adrenal hyperplasia; PCOS: polycystic ovary syndrome.

* Rotterdam criteria also require exclusion of other conditions that mimic PCOS. Criteria were developed at a 2003 consensus meeting held in Rotterdam (European Society of Human Reproduction and Embryology [ESHRE]/American Society of Reproductive Medicine [ASRM] consensus workshop group).

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1. *Zawadski JK, Dunaif A. Diagnostic criteria for polycystic ovary syndrome: Towards a rational approach. In: Polycystic Ovary Syndrome (Current Issues in Endocrinology and Metabolism), Dunaif A, Givens JR, Haseltine FP, Merriam GE (Eds), Blackwell Scientific Inc, Boston 1992. p.377.*
2. *Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod 2004; 19:41.*
3. *Azziz R, Carmina E, Dewailly D, et al. The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: The complete task force report. Fertil Steril 2009; 91:456.*

Test Biochimici per PCOS

- Testosterone totale
- SHBG: in genere valori bassi➔ testosterone attivo maggiore➔ fenotipo più severo
- DHEA: si suggerisce di misurare DHEAS in caso di iperandrogenismo severo poichè può essere elevato in carcinoma adrenocorticale
- Androstendione: ruolo non del tutto chiaro, ma può essere elevato
- 17-oh progesterone:
- LH/FSH > 2
- AMH: valori nel range di riferimento superiore o elevati

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Case Report

Metabolic syndrome: A case report

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Abstract

Metabolic syndrome composed of abdominal obesity, atherogenic dyslipidemia, raised blood pressure, insulin resistance and/or glucose intolerance, proinflammatory state and prothrombotic state is a complex multisystem disorder. It is well known that patients with metabolic syndrome have increased cardiovascular risk and risk of developing diabetes type II. But besides these well known risk states, there are other conditions such as polycystic ovary syndrome, fatty liver, cholesterol gallstones, asthma, sleep disturbances and some forms of cancer associated with a metabolic syndrome. In this case report we will present a patient who developed many of these conditions related to the metabolic syndrome and will highlight the novel efforts regarding to the lifestyle changes, primarily weight loss.

More Information

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Case Report

- Uomo 53 anni diagnosticato per sindrome metabolica e nonalcoholic liver disease all'età di 35 anni.
- 120 Kg, 184 cm, Bmi=34.5, circonferenza=113, PA 160/90mmHg

Table 1: Metabolic syndrome with its complications according to organ systems.

System	Comment	Procedure
CNS*	Sleeping disorders, social anxiety	Polysomnography, fundoscopy
CVS*	Hypertension, atherosclerosis	BPM, fundoscopy
GIS*	Nonalcoholic liver disease, polypus in the cecum, chronic gastritis, Barrett's esophagitis	Laboratory findings, liver biopsy, abdominal ultrasound, fibroscan, MSCT of the abdomen, gastroscopy, colonoscopy
Endocrine system	DM* type II, Hashimoto thyroiditis, hyperparathyroidism, hyperaldosteronism	Laboratory findings, parathyroid glands ultrasound, densitometry thyroid ultrasound

*CNS: Central Nervous System; CVS: Cardiovascular System; BPM: Blood Pressure Measurement; GIS: Gastrointestinal System; DM: Diabetes Mellitus

Laboratorio

Laboratory findings

Glucose 7,7 mmol; HbA1c 9%; ALT (Alanine amino-transferase) 134 U/L; AST (Aspartate aminotransferase) 74 U/L; GGT (Gamma-glutamyltransferase) 127 U/L; ALP (Alkaline phosphatase) 101 U/L; PTH (Parathyroid hormone) 13,29 pmol/L; cholesterol 5,1 mmol/L; HDL (High-density lipoprotein) 0,74 mmol/L; LDL (Low-density lipoprotein) 3,581 mmol/L; Vitamin D3 (25-OH) 32 mmol/L; P (Phosporus) 0,82 mmol/L; CRP (C-reaktive protein) 6,8 mg/L; TSH (Thyroid-stimulating hormone) 5,19 mlU/L, fT4 14,8 pmol/LCrC (Creatinine clearance) 151.1 ml/min, Na 139 mmol/, K 3,4 mmol/L, Ca 2,39 mmol/L, proteinuria 0,26 g/24 h, Ca in the urine 17,32 mmol/24 h, P in the urine 54 mmol/24h, aldosterone 622 pmol/L, rennin activity 0,9 mcg/L/h, hepatitis markers negative.

Procedure diagnostiche

- Biopsia epatica: steatoepatite che evolve in cirrosi
- US addominale: nei limiti della norma
- Gastroscopia: esofagite
- Colonscopia: polipus
- Fondo oculare

- ➔ LE evidenze mostrano che la steatoepatite non alcolica é una conseguenza della sindrome metabolica
- ➔ steatoepatite é associata con CVD
- ➔ Insulina-resistenza é associata ad un rischio aumentato di cancro colorettale
- Apnea nottura dovuta all'obesità

Steatoepatite non-alcolica

- «fegato grasso» (5-10% della totalità del fegato)➔ rischi: cirrosi
- Prevalenza: 14.27% in europa
- Laboratorio: ASAT, ALAT, GGT, Ferritina elevati
- Esclusione genesi alcolica: CDT in siero, etilglucuronide urine
- Esclusione forme secondarie: sierologia epatiti B e C

Dr Risch

Il vostro laboratorio – oggi e domani

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