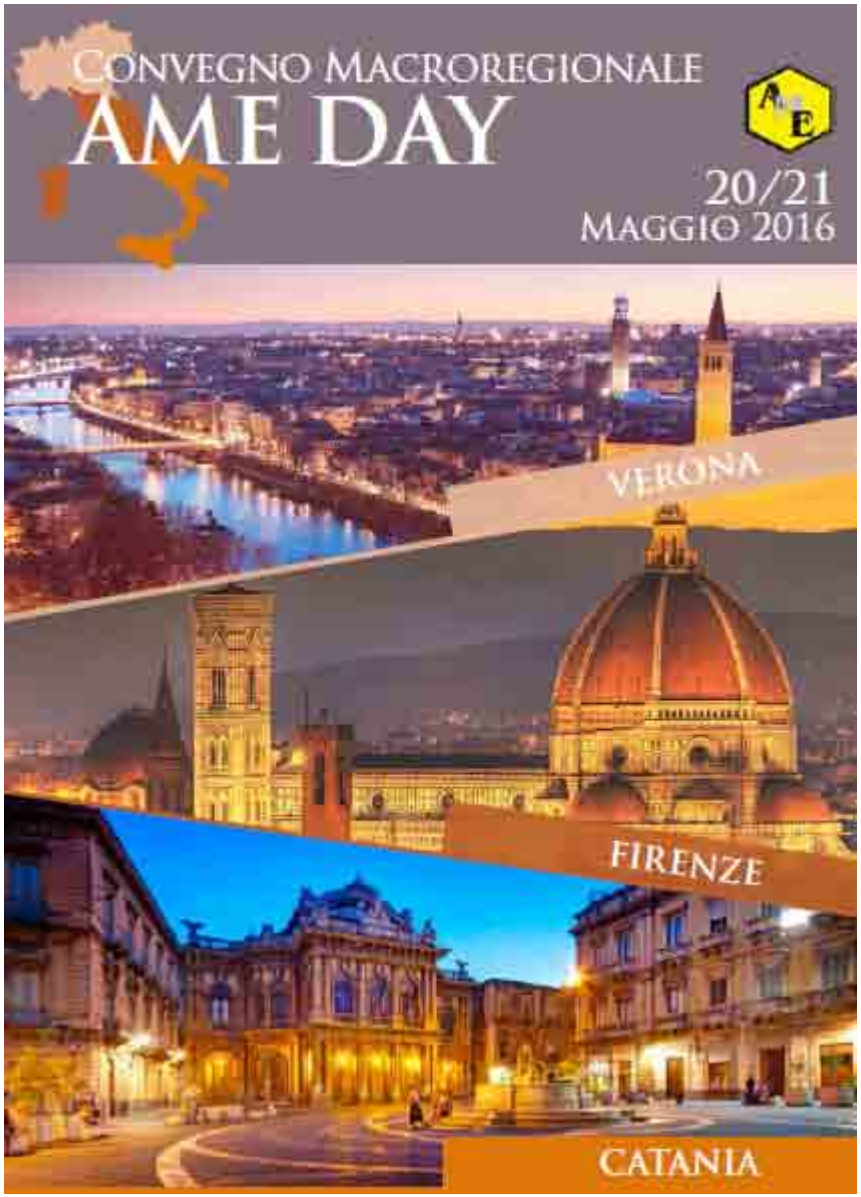


# LE DISLIPIDEMIE
## Classificazione e quadri clinici

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**Genova**


depositi di grasso

| | |
|---|---|
| **I** | **Chilomicronemia; ipertrigliceridemia marcata** |
| **IIa** | **Aumento delle LDL; ipercolesterolemia** |
| **IIb** | **Incremento di LDL e VLDL; dislipidemia mista** |
| **III** | **Elevati livelli di IDL; dislipidemia mista severa** |
| **IV** | **Incremento VLDL; ipertrigliceridemia** |
| **V** | **Iperchilomicronemia ed incremento delle VLDL; ipertrigliceridemia marcata** |

http://www.endowiki.it

da Cecil Medicine, 24° Ed

LIPOPROTEIN CHARACTERISTICS

| LIPOPROTEIN | APOLIPOPROTEIN CONTENT | MAJOR LIPIDS | SIZE (NM DIAMETER) | DENSITY (G/ML) |
|---|---|---|---|---|
| Chylomicrons, chylomicron remnants | Apo B48, apo E, apo AI, apo AII, apo AIV, apo CII, apo CIII | Triglycerides from diet | 80-500 | <<1.006 |
| VLDL | Apo B100, apo E, apo CII, apo CIII | Triglycerides from liver | 30-80 | <1.006 |
| IDL | Apo B100, apo E | Cholesteryl esters, triglycerides | 25-35 | 1.006-1.019 |
| LDL | Apo B100 | Cholesteryl esters | 18-25 | 1.019-1.063 |
| HDL | Apo AI, apo AII, apo AV | Cholesteryl esters, phospholipids | 5-12 | 1.063-1.210 |
| Lp(a) | Apo B100, apo(a) | Cholesteryl esters | ~30 | 1.055-1.085 |

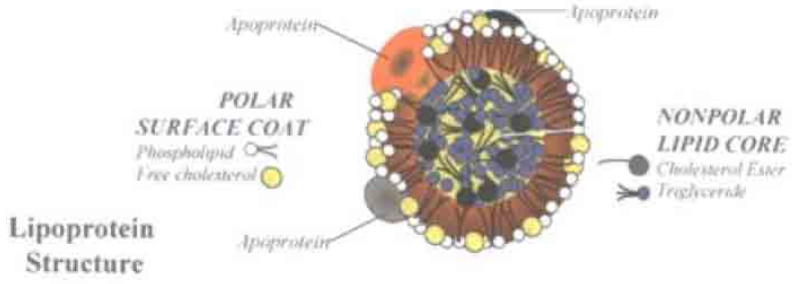
Apo = apolipoprotein; HDL = high-density lipoprotein; IDL = intermediate-density lipoprotein; LDL = low-density lipoprotein; Lp(a) = lipoprotein (a); VLDL = very low density lipoprotein.

Le **apolipoproteine** sono le proteine costituenti le lipoproteine, attivano gli enzimi chiave del metabolismo lipidico ed interagiscono con i recettori cellulari:

- Apo A-I, sintetizzata nel fegato e nell'intestino, è presente in tutte le HDL;
- Apo A-II è contenuta in circa i due terzi delle HDL;
- Apo B-48, sintetizzata nell'intestino, è l'apoproteina presente nei chilomicroni;
- Apo B-100, sintetizzata dal fegato, è presente nelle LDL, IDL e VLDL;
- Apo C sono coinvolte nel metabolismo delle lipoproteine ricche in trigliceridi;
- Apo E sono presenti nei chilomicroni, nelle VLDL e nelle IDL.

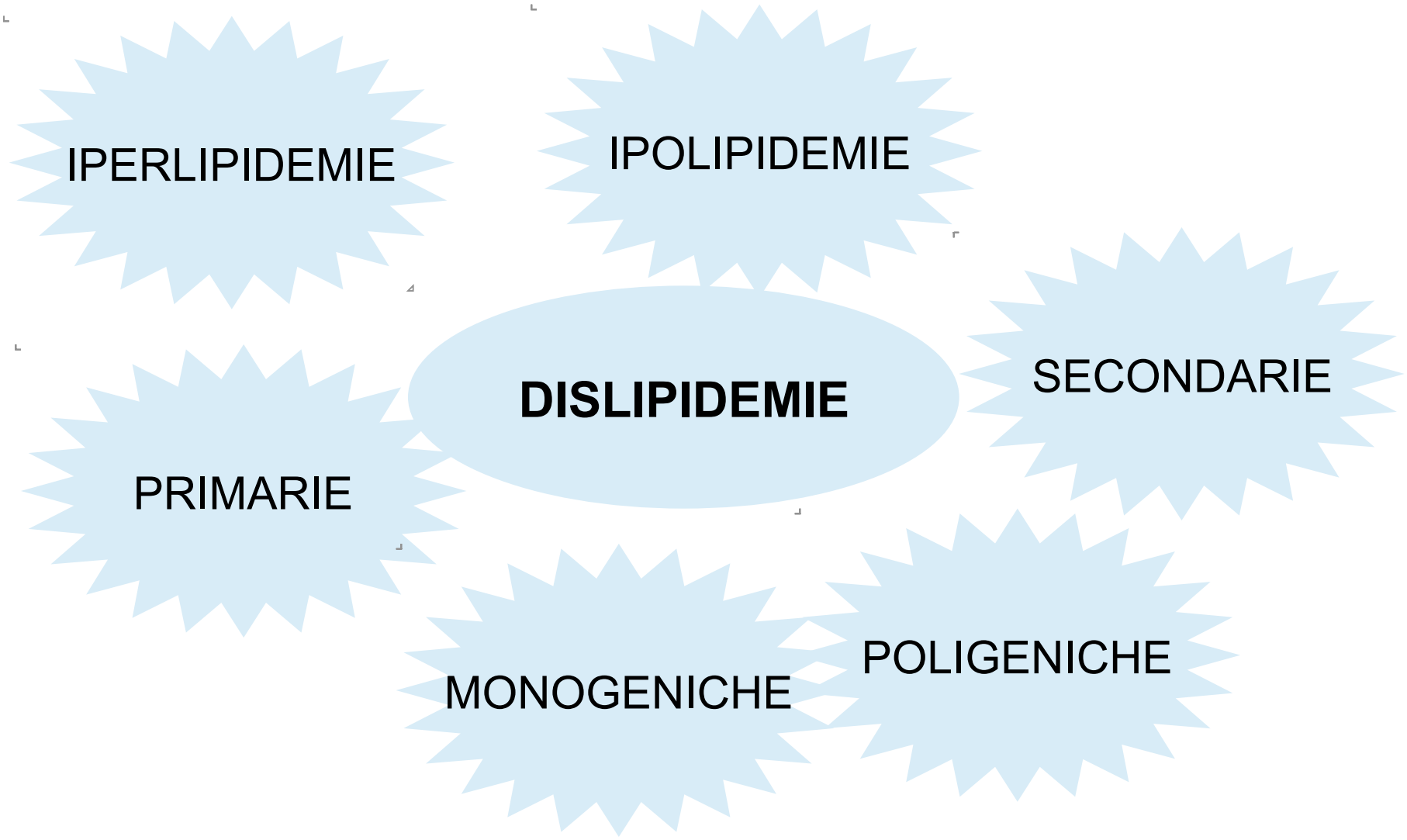
Le lipoproteine circolanti trasportano i lipidi assorbiti dall'intestino (via esogena), quelli sintetizzati dal fegato (via endogena) e il colesterolo rilasciato dai tessuti periferici (trasporto inverso).

http://www.endowiki.it




Lipoprotein Structure

da J.L. Jameson, L.J. De Groot, 7th Ed


IPERLIPIDEMIE
IPOLIPIDEMIE
DISLIPIDEMIE
SECONDARIE
PRIMARIE
MONOGENICHE
POLIGENICHE

Journal of Clinical Lipidology (2016) 10, S1-S43

**Table 2: Genetic causes of hypolipidemias.**

| Genetic Abnormality | Mechanism | Clinical Manifestations |
|---|---|---|
| | | |
| **LOW HDL-C GENETIC ABNORMALITIES** | | |
| | | |
| ApoA-1 Milano | Increased HDL particle turnover | Decreased risk of ASCVD |
| ApoA1 deficiency (Familial hypoalphalipoproteinemia | Underproduction of HDL-C | Increased risk for ASCVD<br>Flat planar xanthoma |
| ABCA1 deficiency (Tangier's disease) | Defective ABCA1 transporter protein<br>Autosomal recessive | Possible premature ASCVD, especially if combined with other ASCVD risk factors<br>Orange tonsils<br>Splenomegaly<br>Hepatomegaly<br>Neuropathy |
| Complete LCAT deficiency | Absense of LCAT | Corneal opacification, anemia, proteinuria, renal failure |
| Partial PCAT deficiency (Fish eye disease) | Partial absence of LCAT | Corneal opacities |
| | | |
| **LOW APOB CONTAINING LIPOPROTEIN GENETIC ABNORMALITIES** | | |
| | | |
| Hypobetalipoproteinemia (HBL) | Apo B mutation; autosomal dominant | Heterozygous HBL = Total cholesterol < 100 mg/dL; LDL-C levels < 60 mg/dL, with a possible decrease risk of ASCVD<br>Homozygous HBL = total cholesterol and LDL-C are very low (lower than heterozygous), and may present with fat malabsorption, progressive neurologic degenerative disease, retinitis pigmentosa, and acanthocytosis, similar to patients with abetalipoproteinemia |
| Abetalipoproteinemia | Absent microsomal triglyceride transfer protein; autosomal recessive | Very low levels of total cholesterol, and absent VLDL, LDL, and apoB<br>Spinocerebellar and retinal degeneration (diability and blindness)<br>Severe vitamin E deficiency, along with variable deficiencies of other fat soluble vitamins (e.g. A, D, K) |

Ipertrigliceridemia

Iperlipidemia combinata

Ipercolesterolemia

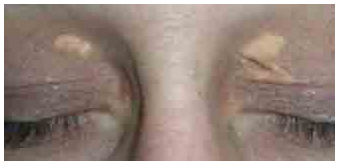
**Tabella 2**
**Iperlipoproteinemie primitive causate da mutazioni di un singolo gene noto**

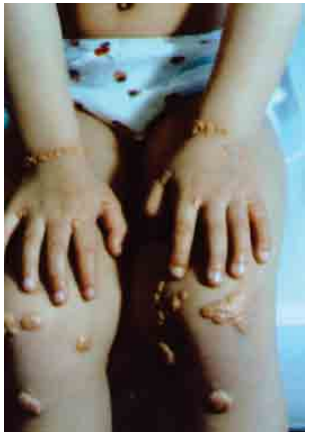
| Alterazione Genetica | Difetto genico | Lipoproteine elevate | Segni clinici | Trasmissione | Incidenza stimata |
|---|---|---|---|---|---|
| Deficit di lipasi lipoproteica | LPL (*LPL*) | Chilomicroni | Xantomi eruttivi, epato-splenomegalia, pancreatiti | AR | 1/1.000.000 |
| Deficit familiare di apolipoproteina C-II | ApoC-II (*APOC2*) | Chilomicroni | Xantomi eruttivi, epato-splenomegalia, pancreatiti | AR | <1/1.000.000 |
| Deficit di ApoA-V | ApoA-V (*APOA5*) | Chilomicroni, VLDL | Xantomi eruttivi, epato-splenomegalia, pancreatiti | AD | <1/1.000.000 |
| Deficit di GPIHBP1 | GDIHBP1 | Chilomicroni | Xantomi eruttivi, pancreatiti | AD | <1/1.000.000 |
| Deficit familiare di lipasi epatica | Lipasi epatica (*LIPC*) | Residui VLDL | Aterosclerosi precoce, pancreatiti | AR | <1/1.000.000 |
| Dis-beta-lipoproteinemia familiare | ApoE (*APOE*) | Chilomicroni e residui VLDL | Xantomi palmari e tuberoeruttivi, CHD, PVD | AR/AD | 1/10.000 |
| Ipercolesterolemia familiare | Recettore per le LDL (*LDL-R*) | LDL | Xantomi tendinei, CHD | AD | 1/500 |
| ApoB-100 difettiva familiare | apoB-100 (*APOB*) | LDL | Xantomi tendinei, CHD | AD | <1/1000 |
| Ipercolesterolemia autosomica dominante | PCSK9 (*PCSK9*) | LDL | Xantomi tendinei, CHD | AD | <1/1.000.000 |
| Ipercolesterolemia autosomica recessiva | LDLRAP | LDL | Xantomi tendinei, CHD | AR | <1/1.000.000 |
| Sitosterolemia | *ABCG5* o *ABCG8* | LDL | Xantomi tendinei, CHD | AR | <1/1.000.000 |

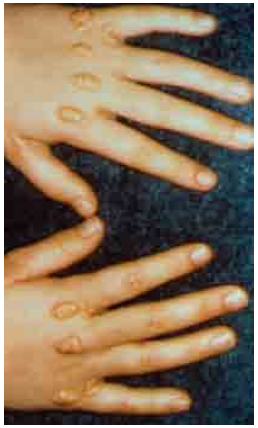
ABCG: ATP-binding cassette G; AD: autosomica dominante; AR: autosomica recessiva; ARH: Ipercolesterolemia autosomica recessiva; CHD: malattia coronarica; GDIHBP1: glycosylphosphatidylinositol-anchored high density lipoprotein binding protein1; LDL: low-density lipoprotein; LDLRAP: LDL receptor associated protein; LIPC: lipasi epatica; LPL: lipoprotein-lipasi; PCSK9: proprotein convertase subtilisin/kexin type 9; PVD: vasculopatia periferica; VLDL: very low density lipoprotein

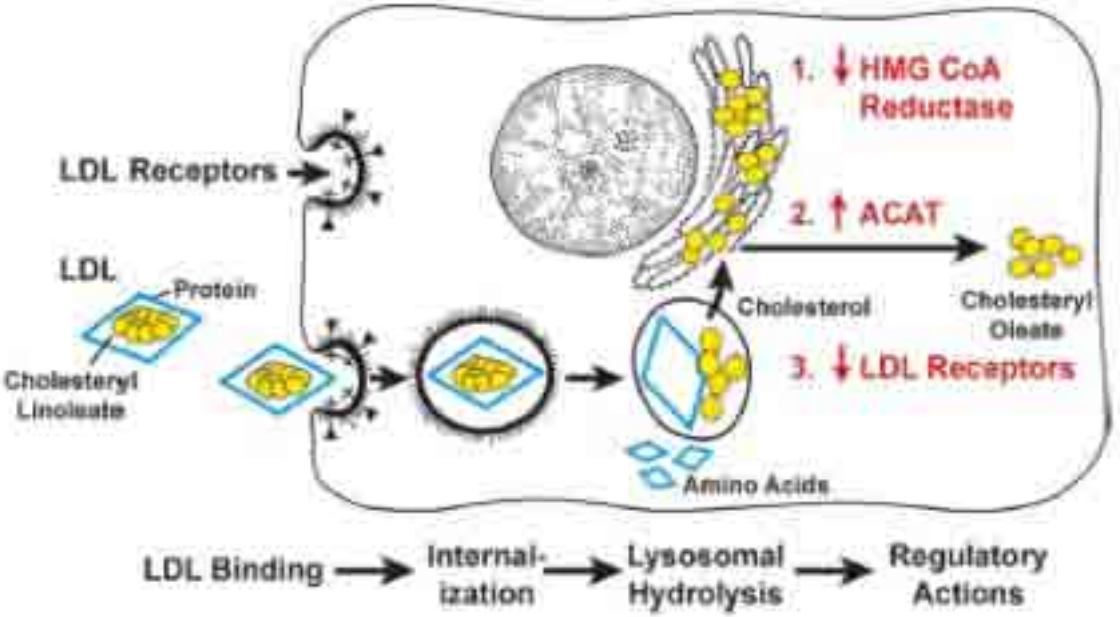
Per quanto riguarda le ipolipoproteinemie, sono state identificate condizioni caratterizzate da bassi livelli delle lipoproteine LDL (ipobetaliproteinemia familiare, abetalipoproteinemia) o da bassi livelli delle lipoproteine HDL (ipoalfalipoproteinemia).

Joseph L. Goldstein (left) and Michael S. Brown on the day of announcement of their Nobel Prize in Physiology or Medicine on October 15, 1985.










## History of Discovery: The LDL Receptor

**Joseph L. Goldstein** and **Michael S. Brown**
Department of Molecular Genetics, University of Texas Southwestern Medical Center, Dallas, TX

*Arterioscler Thromb Vasc Biol*. 2009 April ; 29(4): 431–438. doi:10.1161/ATVBAHA.108.179564.

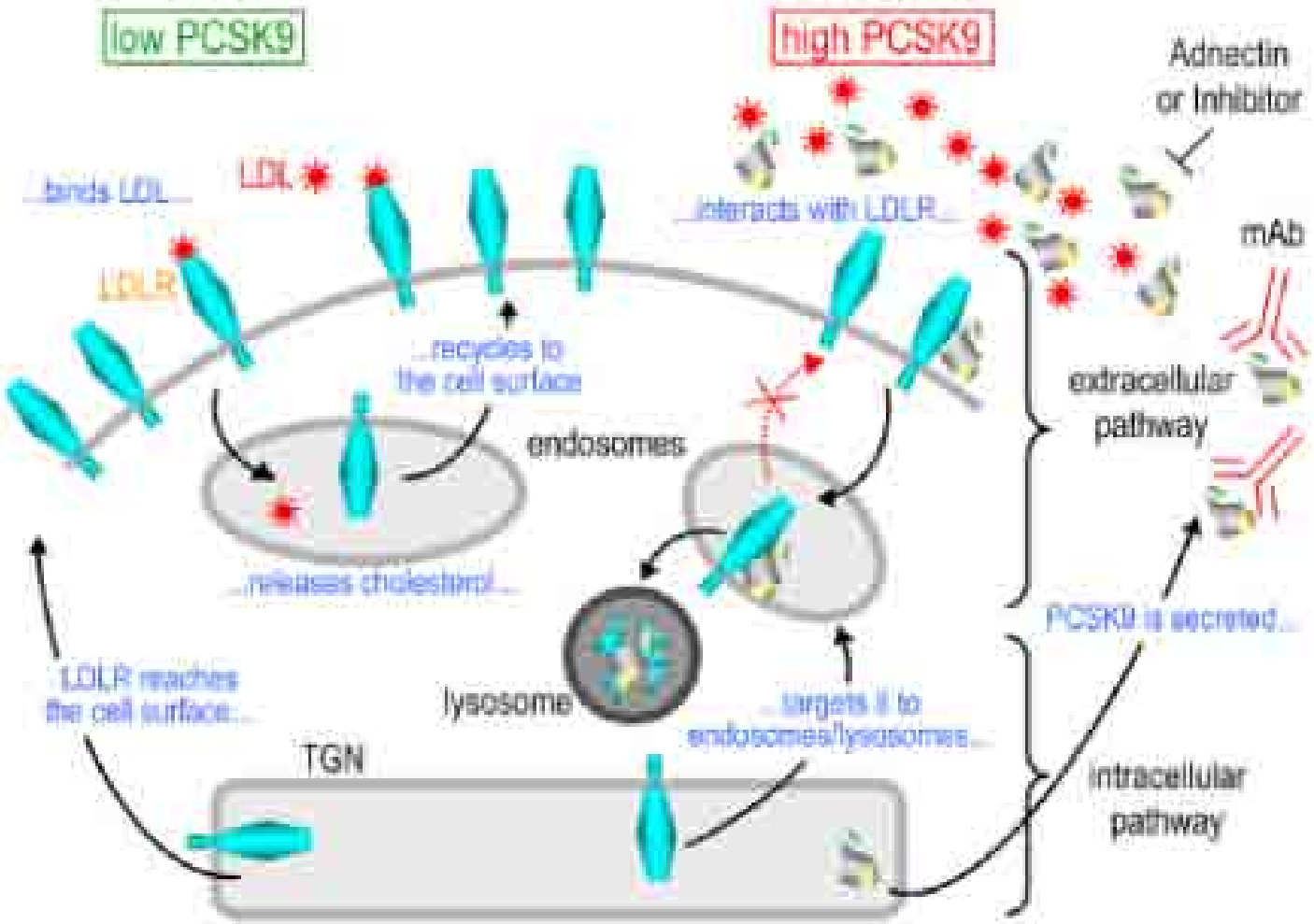
# PCSK9

## A Key Modulator of Cardiovascular Health

Nabil G. Seidah, Zuhier Awan, Michel Chrétien, Majambu Mbikay

*Circulation Research* March 14, 2014

DOI: 10.1161/CIRCRESAHA.114.301621



# Screening for familial hypercholesterolemia: Recommendations from the National Lipid Association

| |
|---|
| Universal screening for elevated serum cholesterol is recommended. Suspect FH in untreated patients with the following fasting cholesterol levels:<br>• Patients age ≥20: LDL ≥190 mg/dL or non-HDL ≥220 mg/dL<br>• Patients age <20: LDL ≥160 mg/dL or non-HDL ≥190 mg/dL |
| For all patients with these cholesterol levels, assess for a family history of high cholesterol and heart disease in first-degree relatives |
| Consider cholesterol screening beginning at age 2 for children with a family history of premature cardiovascular disease or elevated cholesterol. All patients should be screened by age 20 |
| Strongly suspect FH (and obtain lipid measurements) in patients with:<br>• Tendon xanthomas at any age (most common in Achilles tendon and finger extensor tendons, but also can occur in patellar and triceps tendons)<br>• Tuberous xanthomas or xanthelasma in patients younger than age 20 to 25<br>• Arcus corneae in patients younger than age 45 |
| Strongly consider a diagnosis of FH and obtain further family information in patients with the following LDL levels:<br>• ≥250 mg/dL in those age ≥30<br>• ≥220 mg/dL in those age 20 to 29<br>• ≥190 mg/dL in those age <20 |

FH, familial hypercholesterolemia; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Adapted with permission from: Hopkins PN, et al. *J Clin Lipidol.* 2011;5:S9-17.[19]

**Table 4. Dutch Lipid Clinic Network diagnostic criteria for Familial Hypercholesterolemia[1-3]**

| | Points |
|---|---|
| Criteria<br>**Family history** | |
| First-degree relative with known premature* coronary and vascular disease, OR<br>First-degree relative with known LDL-C level above the 95th percentile | 1 |
| First-degree relative with tendinous xanthomata and/or arcus cornealis, OR<br>Children aged less than 18 years with LDL-C level above the 95th percentile | 2 |
| **Clinical history** | |
| Patient with premature* coronary artery disease | 2 |
| Patient with premature* cerebral or peripheral vascular disease | 1 |
| **Physical examination** | |
| Tendinous xanthomata | 6 |
| Arcus cornealis prior to age 45 years | 4 |
| **Cholesterol levels mg/dl (mmol/liter)** | |
| LDL-C >= 330 mg/dL ( ≥8.5) | 8 |
| LDL-C 250 – 329 mg/dL (6.5–8.4) | 5 |
| LDL-C 190 – 249 mg/dL (5.0–6.4) | 3 |
| LDL-C 155 – 189 mg/dL (4.0–4.9) | 1 |
| **DNA analysis** | |
| Functional mutation in the *LDLR, apo B or PCSK9* gene | 8 |
| **Diagnosis (diagnosis is based on the total number of points obtained)** | |
| Definite Familial Hypercholesterolemia | >8 |
| Probable Familial Hypercholesterolemia | 6 – 8 |
| Possible Familial Hypercholesterolemia | 3 – 5 |
| Unlikely Familial Hypercholesterolemia | <3 |

* Premature = < 55 years in men; < 60 years in women
LDL-C = low density lipoprotein cholesterol; FH, familial hypercholesterolemia.
LDLR = low density lipoprotein receptor
Apo B = apolipoprotein B
PCSK9 = Proprotein convertase subtilisin/kexin type 9

[1]Austin MA, Hutter CM, Zimmern RL, Humphries SE. Genetic causes of monogenic heterozygous familial hypercholesterolemia: a HuGE prevalence review. *American journal of epidemiology.* 2004;160:407-420.

[2]Haase A, Goldberg AC. Identification of people with heterozygous familial hypercholesterolemia. *Current opinion in lipidology.* 2012;23:282-289.

[3]Nordestgaard BG, Chapman MJ, Humphries SE, et al. Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease: consensus statement of the European Atherosclerosis Society. *European heart journal.* 2013;34:3478-3490a.

# THM forme genetiche

LDL- C molto alto

Storia familiare di LDL-C alto

Familiarità per precoce insorgenza di ASCVD

Storia personale di precoce insorgenza di ASCVD

Esame clinico (xantomi, xantelasmi, arco corneale …)

Essenziale controllare i familiari

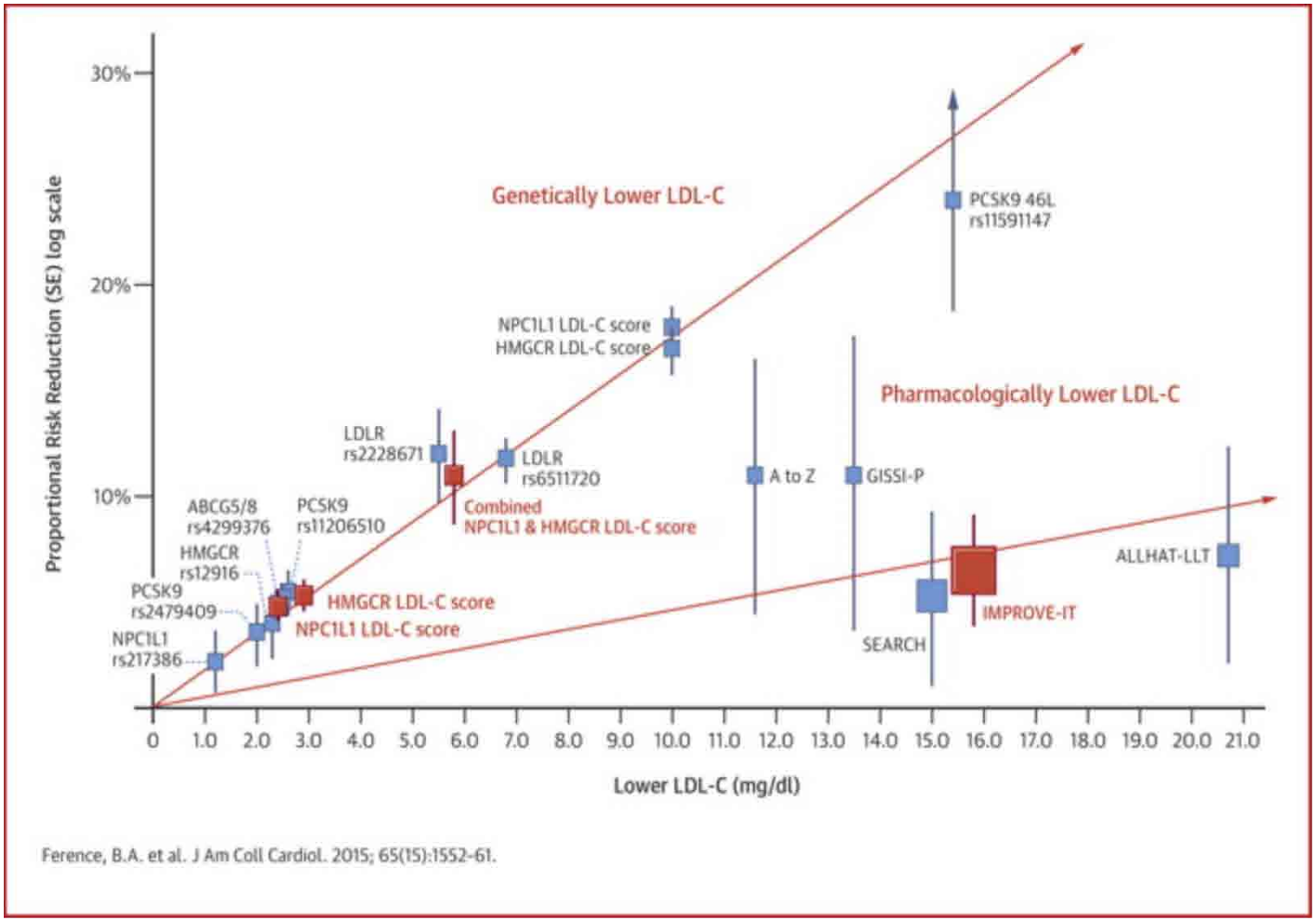
I test genetici non sono essenziali (30% non definibile)

Precocità di diagnosi

Precocità di trattamento

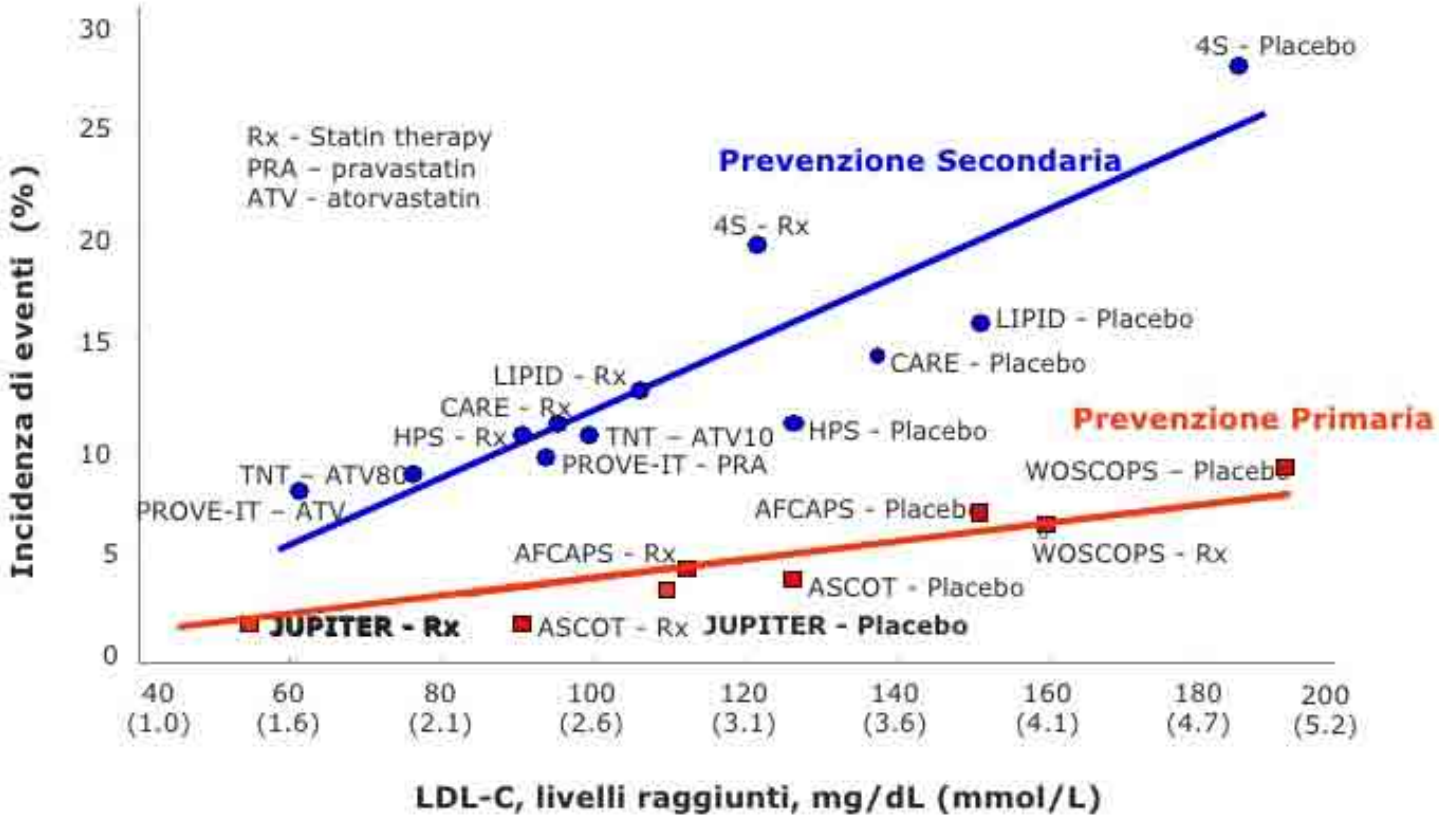

Framingham,MA
Stati Uniti
Ottawa
Montreal
Toronto
Chicago
New York
San Francisco
Los Angeles
San Diego
Dallas
Las Vegas
MONTANA
OREGON
IDAHO
NEVADA
UTAH
NEBRASKA
KANSAS
OHIO
INDIANA
ILLINOIS
KENTUCKY
TENNESSEE
ARIZONA

Effect of naturally random allocation to lower low-density lipoprotein cholesterol on the risk of coronary heart disease mediated by polymorphisms in NPC1L1, HMGCR, or both.
A 2 × 2 factorial Mendelian Randomization Study

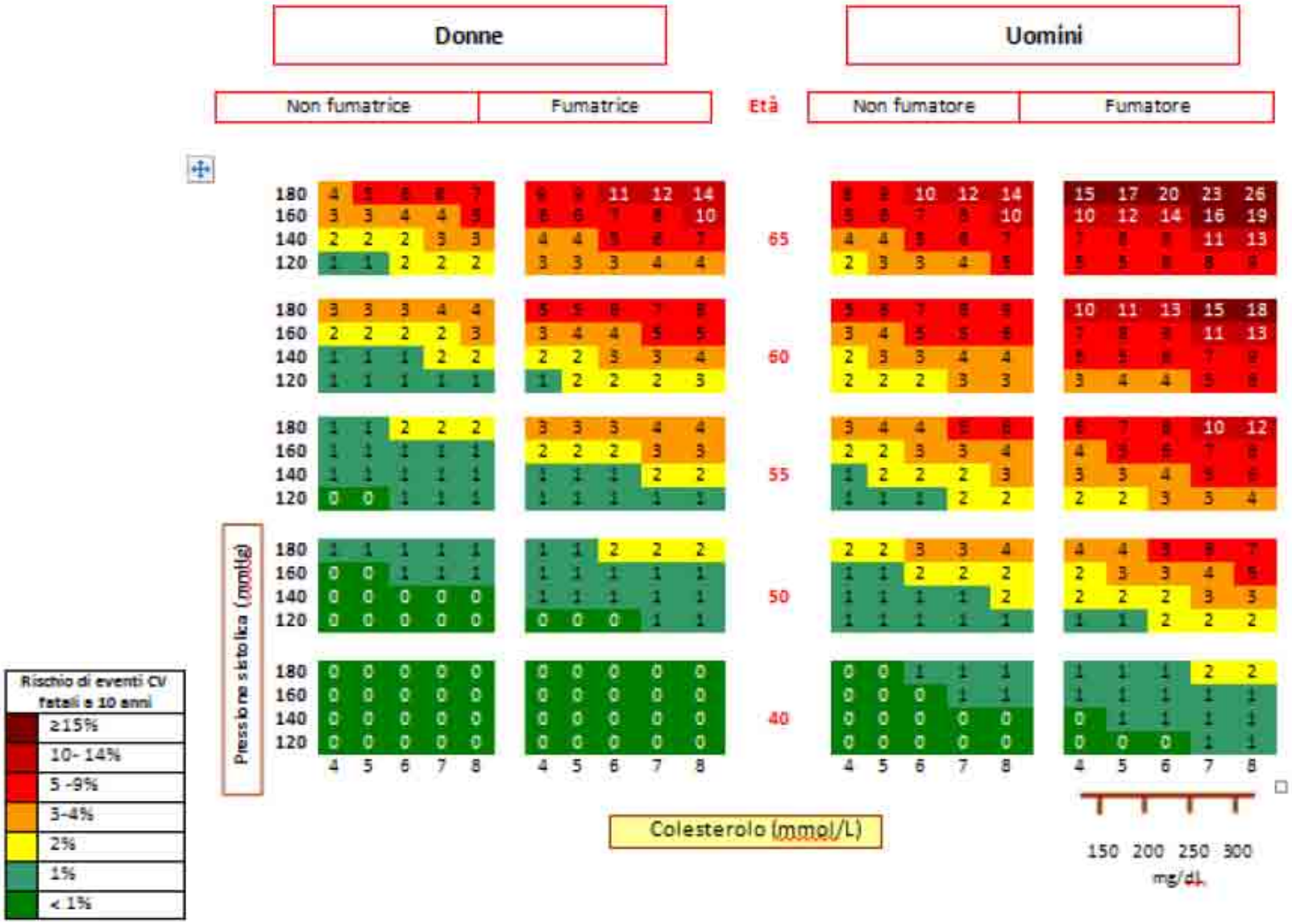



Ference, B.A. et al. J Am Coll Cardiol. 2015; 65(15):1552-61.

# Incidenza di eventi in funzione dei livelli di C-LDL raggiunti nei trial con statine



# Carta del rischio



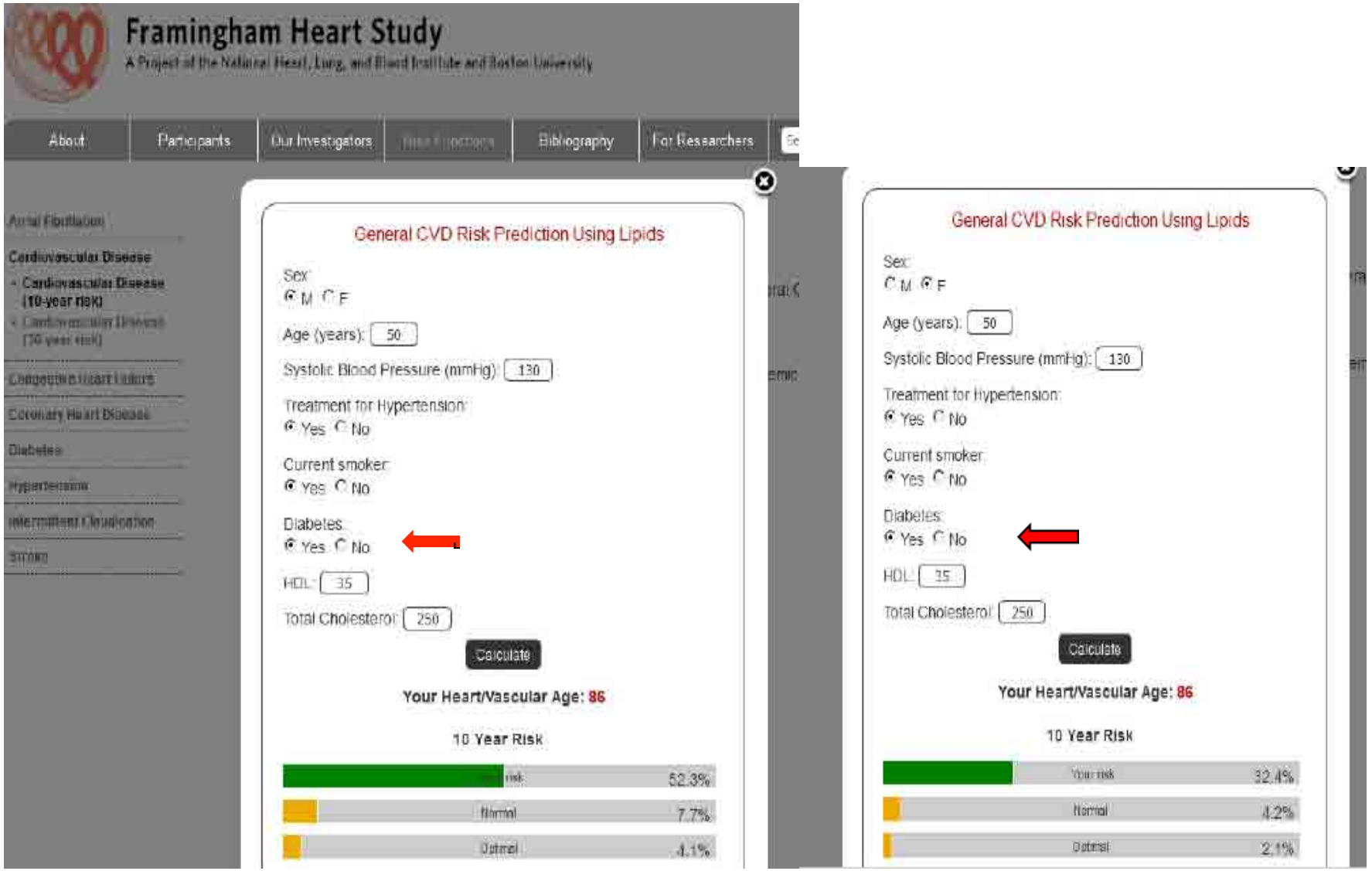

Framingham Heart Study
A Project of the National Heart, Lung, and Blood Institute and Boston University
About
Participants
Our Investigators
Bibliography
For Researchers
Cardiovascular Disease
Cardiovascular Disease (10-year risk)
General CVD Risk Prediction Using Lipids
Sex:
M F
Age (years): 50
Systolic Blood Pressure (mmHg): 130
Treatment for Hypertension:
Yes No
Current smoker:
Yes No
Diabetes:
Yes No
HDL: 35
Total Cholesterol: 250
Calculate
Your Heart/Vascular Age: 86
10 Year Risk
52.3%
Normal
7.7%
Optimal
4.1%
General CVD Risk Prediction Using Lipids
Sex:
M F
Age (years): 50
Systolic Blood Pressure (mmHg): 130
Treatment for Hypertension:
Yes No
Current smoker:
Yes No
Diabetes:
Yes No
HDL: 35
Total Cholesterol: 250
Calculate
Your Heart/Vascular Age: 86
10 Year Risk
32.4%
Normal
4.2%
Optimal
2.1%

**Table 5**
**Major Coronary Artery Disease Risk Factors (10 [EL 4], 11 [EL 4], 12 [EL 4], 13 [EL 4], 14 [EL 2], 15 [EL 4], 16 [EL 2], 17 [EL 4], 18 [EL 2], 19 [EL 2], 20 [EL 4], 21 [EL 3])**

| Major risk factors | Additional risk factors | Nontraditional risk factors |
|---|---|---|
| Advancing age[a,d] | Obesity, abdominal obesity[c,d] | Elevated lipoprotein (a) |
| High total serum cholesterol level[a,b,d] | Family history of hyperlipidemia[d] | Elevated clotting factors |
| High non–HDL-C[d] | Small, dense LDL-C[d] | Inflammation markers (hsCRP; Lp-$PLA_2$) |
| High LDL-C[a,d] | ⇧ Apo B[d] | Hyperhomocysteinemia |
| Low HDL-C[a,d,e] | ⇧ LDL particle number | Apo E4 isoform |
| Diabetes mellitus[a,b,c,d] | Fasting/postprandial hypertriglyceridemia[d] | Elevated uric acid |
| Hypertension[a,b,c,d] | PCOS[d] | |
| Cigarette smoking[a,b,c,d] | Dyslipidemic triad[f] | |
| Family history of CAD[a,d,g] | | |

Abbreviations: apo, apolipoprotein; CAD, coronary artery disease; HDL-C, high-density lipoprotein cholesterol; hsCRP, highly sensitive C-reactive protein; LDL-C, low-density lipoprotein cholesterol; Lp-$PLA_2$, lipoprotein-associated phospholipase $A_2$; PCOS, polycystic ovary syndrome.

[a] Risk factors identified in the Framingham Heart study.

[b] Risk factors identified in the MRFIT study (Multiple Risk Factor Intervention Trial).

[c] Risk factors identified in the INTERHEART study.

[d] Risk factors identified in guidelines and position statements (National Cholesterol Education Program Adult Treatment Panel III, American Association of Clinical Endocrinologists Polycystic Ovary Syndrome Position Statement, American Association of Clinical Endocrinologists Insulin Resistance Syndrome Position Statement, American Diabetes Association Standards of Care 2009, American Diabetes Association/American College of Cardiology Consensus Statement on Lipoprotein Management in Patients with Cardiometabolic Risk).

[e] Elevated high-density lipoprotein cholesterol is a negative risk factor.

[f] Hypertriglyceridemia; low high-density lipoprotein cholesterol; and small, dense low-density lipoprotein cholesterol.

[g] Definite myocardial infarction or sudden death before age 55 years in father or other male first-degree relative or before age 65 years in mother or other female first-degree relative.

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS' GUIDELINES FOR MANAGEMENT OF DYSLIPIDEMIA AND PREVENTION OF ATHEROSCLEROSIS

**Table 9**
**Optimal/Near-Optimal, Borderline, and High-Risk Serum Lipid Concentrations**
(10 [EL 4])

| Lipid | Optimal/near-optimal serum concentration | Borderline serum concentration | High-risk/very high-risk serum concentration |
|---|---|---|---|
| TC, mg/dL | <200 | 200-239 | ≥240 |
| HDL-C, mg/dL | ≥60 (negative risk factor) | 40-59 (men)<br>50-59 (women) | <40 men<br><50 women[b] |
| LDL-C, mg/dL | <100 optimal<br>(100-129 near-optimal) | 130-159 | 160-189 high<br>≥190 very high |
| TG[a], mg/dL | <150 | 150-199 | 200-499 high<br>≥500 very high |
| Apo B, mg/dL | <90 (patients at risk of CAD, including those with diabetes)<br><80 (patients with established CAD or diabetes plus ≥1 additional risk factor) | | |

Abbreviations: apo, apolipoprotein; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides.

[a] Both borderline and high-risk values may signify familial combined dyslipidemia or dyslipidemia of diabetes; values >1000 indicate high risk for pancreatitis.

[b] Moderate reductions of high-density lipoprotein cholesterol in women may indicate insulin resistance syndrome.

**Table 6**
**Coronary Artery Disease Risk Categories and Low-Density Lipoprotein Treatment Goals**
(20 [EL 4], 22 [EL 4], 23 [EL 4])

| Risk category | Risk factors[a]/10-year risk[b] | LDL-C treatment goal |
|---|---|---|
| Very high risk | Established or recent hospitalization for coronary, carotid, and peripheral vascular disease or diabetes plus 1 or more additional risk factor(s) | <70 mg/dL |
| High risk | ≥2 risk factors and 10-year risk >20% or CHD risk equivalents[c], including diabetes with no other risk factors | <100 mg/dL |
| Moderately high risk | ≥2 risk factors and 10-year risk 10%-20% | <130 mg/dL |
| Moderate risk | ≥2 risk factors and 10-year risk <10% | <130 mg/dL |
| Low risk | ≤1 risk factor | <160 mg/dL |

Abbreviations: CHD, coronary heart disease; LDL-C, low-density lipoprotein cholesterol.

[a] Major independent risk factors are high low-density lipoprotein cholesterol, polycystic ovary syndrome, cigarette smoking, hypertension (blood pressure ≥140/90 mm Hg or on hypertensive medication), low high-density lipoprotein cholesterol (<40 mg/dL), family history of coronary artery disease (in male first-degree relative younger than 55 years; in female first-degree relative younger than 65 years), and age (men ≥45; women ≥55 years). Subtract 1 risk factor if the person has high high-density lipoprotein cholesterol (≥60 mg/dL) (10 [EL 4], 11 [EL 4]).

[b] Framingham risk scoring is applied to determine 10-year risk (10 [EL 4]).

[c] Coronary artery disease risk equivalents include diabetes and clinical manifestations of noncoronary forms of atherosclerotic disease (peripheral arterial disease, abdominal aortic aneurysm, and carotid artery disease).

## Table 12
## Lipid Goals for Patients at Risk for Coronary Artery Disease
(20 [EL 4], 37 [EL 1], 38 [EL 1], 39 [EL 1], 40 [EL1], 41 [EL 4])

| Lipid Parameter | Goal | EL |
|---|---|---|
| TC, mg/dL | <200 | EL 1 |
| LDL-C, mg/dL | <100; <70 (*all* very high risk patients) | EL 1 |
| HDL-C, mg/dL | As high as possible, but at least >40 in both men and in women | EL 1 |
| Non–HDL-C, mg/dL | 30 above LDL-C goal | EL 1 |
| TG, mg/dL | <150 | EL 1 |
| Apo B, mg/dL | <90 (patients at risk of CAD, including those with diabetes)<br><80 (patients with established CAD or diabetes plus ≥1 additional risk factor) | EL 4 |

Abbreviations: apo, apolipoprotein; EL, evidence level; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides.

**Tabella 5**
**Inquadramento clinico-diagnostico delle dislipidemie primarie**

| Tipo di dislipidemia | Assetto lipidico | Clinica |
|---|---|---|
| **Ipercolesterolemia pura** | | |
| Ipercolesterolemia poligenica comune | Colest totale 250-350 mg/dL | Molto comune<br>Asintomatica sino a comparsa di evento CV<br>Xantomi assenti |
| Ipercolesterolemia familiare eterozigote | Colest totale 275-500 mg/dL | Prevalenza 1/500<br>Elevato rischio CV<br>Xantomi nell'adulto |
| Ipercolesterolemia familiare omozigote | Colest totale > 500 mg/dL | Prevalenza 1/1.000.000<br>Malattie vascolari e xantomi nell'infanzia |
| **Ipertrigliceridemia pura** | | |
| Ipertrigliceridemia familiare | Tg 250-750 mg/dL | Prevalenza 1/1000<br>Rischio aumentato di vasculopatie<br>Rischio di pancreatite |
| Deficit familiare di lipoprotein-lipasi o apo C II | Tg > 750 mg/dL (plasma lattescente) | Prevalenza 1-2/1.000.000<br>Possibile associazione con pancreatite ed epato-splenomegalia |
| **Ipercolesterolemia + ipertrigliceridemia** | | |
| Iperlipemia familiare combinata | Tg 250-750 mg/dL<br>Colest totale 250-500 mg/dL | Molto comune (prevalenza 1/100)<br>Rischio elevato di cardiopatia ischemica<br>La forma familiare può manifestarsi anche con aumento isolato di Tg o di colesterolo-LDL |

**DISLIPIDEMIE SECONDARIE** (tab 7)

**Tabella 7**
**Dislipidemie secondarie**

| Fenotipo | Cause |
|---|---|
| Ipercolesterolemia | Epatopatie ostruttive<br>Ipotiroidismo<br>Porfiria acuta intermittente<br>Sindrome nefrosica<br>Farmaci: estroprogestinici, ciclosporina, tiazidi |
| Ipertrigliceridemia | Alcool<br>Gravidanza<br>Diabete mellito<br>Obesità<br>Epatite acuta<br>Gammopatie monoclonali: mieloma, linfomi<br>Insufficienza renale cronica<br>Glicogenosi<br>By-pass ileale<br>Lipodistrofia<br>LES<br>Sepsi<br>Stress<br>Farmaci: estrogeni, isotretinoina, ß-bloccanti, glucocorticoidi, resine chelanti acidi biliari, tiazidi |
| Riduzione HDL | Fumo<br>Malnutrizione<br>Obesità<br>Farmaci: ß-bloccanti, steroidi anabolizzanti |

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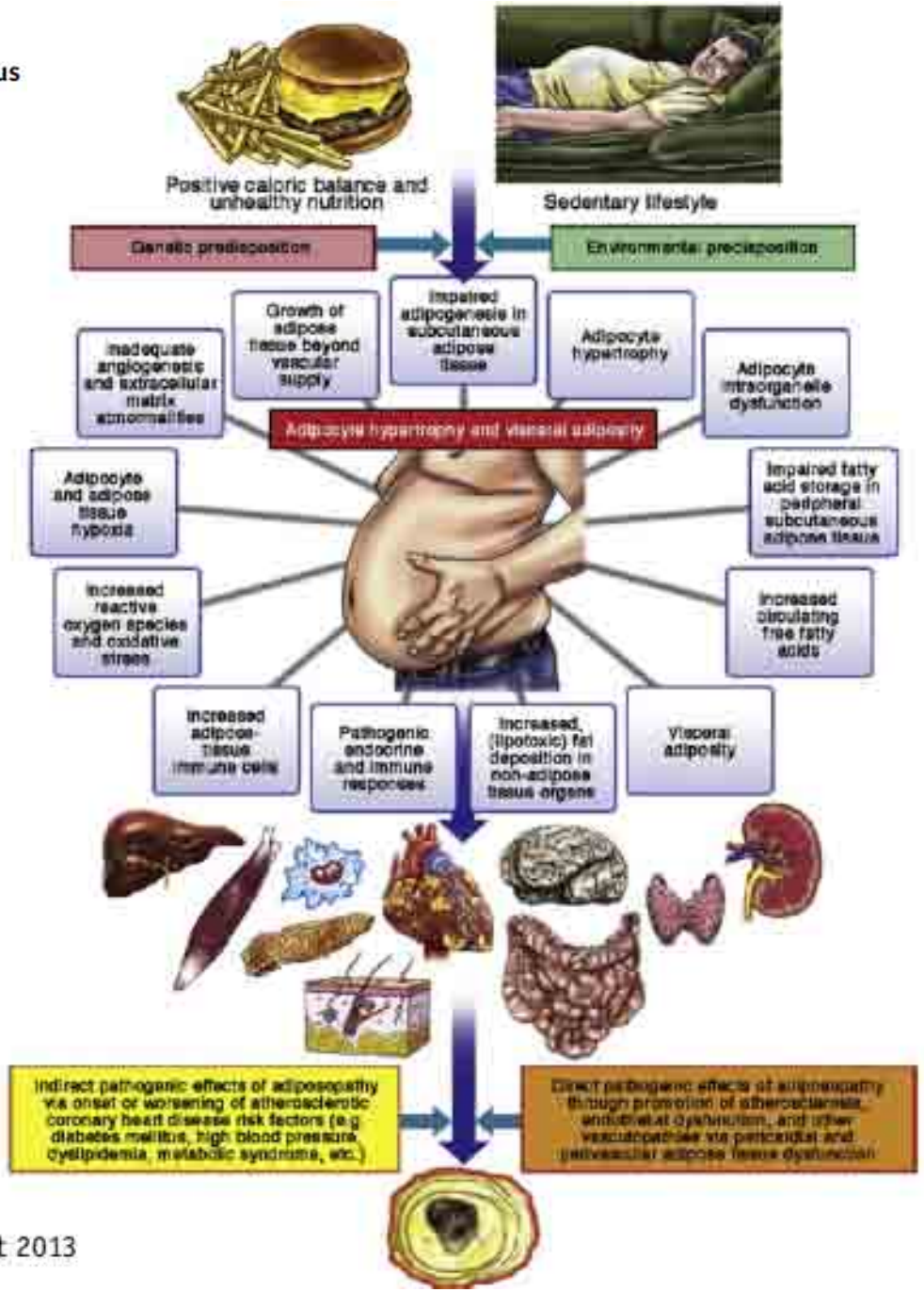
## IV. SECONDARY CAUSES OF DYSLIPIDEMIA[1,24]

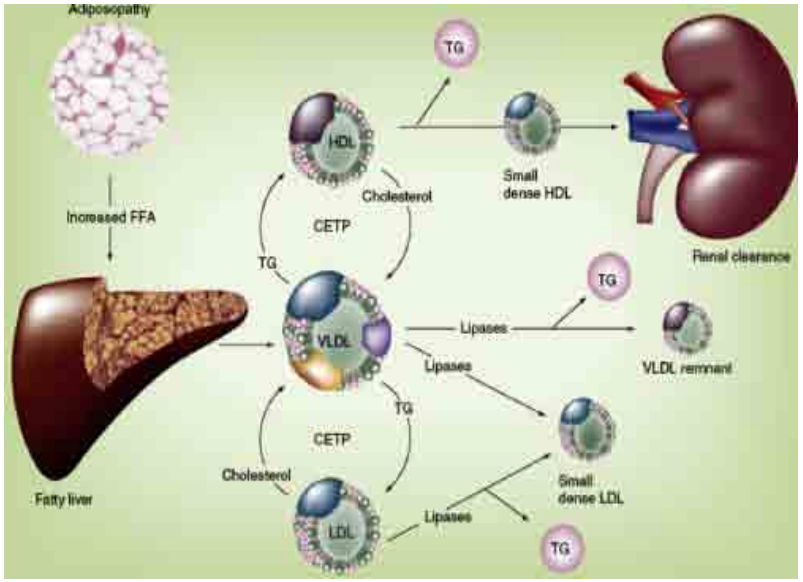
- Beyond genetic considerations, dyslipidemia can also be due to secondary causes.
- A "two hit phenomenon"[24] is commonly encountered in the clinical evaluation and management of patients with primary hyperlipidemia (eg, the relatively common familial combined hyperlipidemia or familial hypertriglyceridemia; the more rare lipoprotein lipase deficiency, apo C-II deficiency, familial dysbetalipoproteinemia).
  - "First hit" = Genetic predisposition.
  - "Second hit" = Exacerbation by secondary factors that worsen lipid levels, often resulting in profound hyperlipidemia.
  - This "second hit" can be of the result of underlying disordered metabolism or disease (e.g., untreated hypothyroidism, inadequately controlled diabetes mellitus) or from drugs that unfavorably alter lipid metabolism.

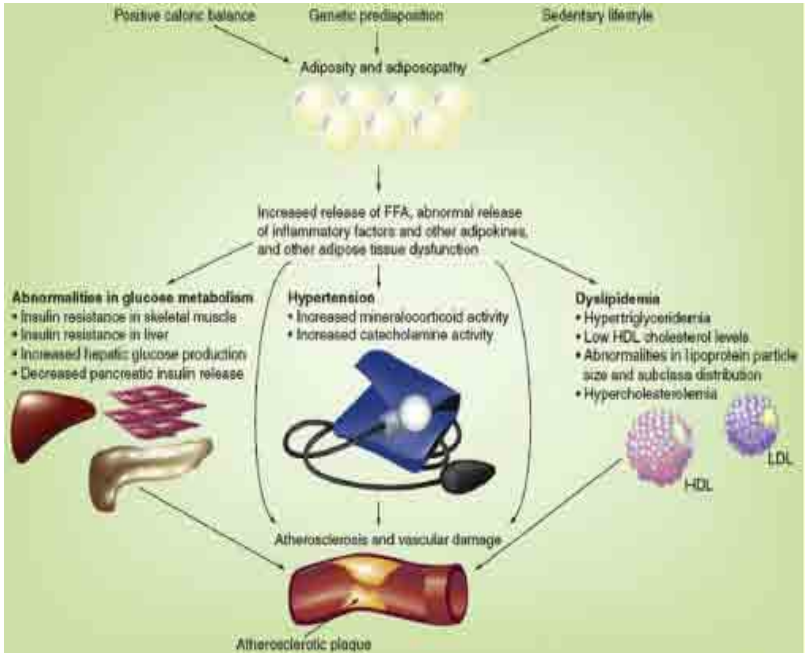
**Obesity, adiposity, and dyslipidemia: A consensus statement from the National Lipid Association**

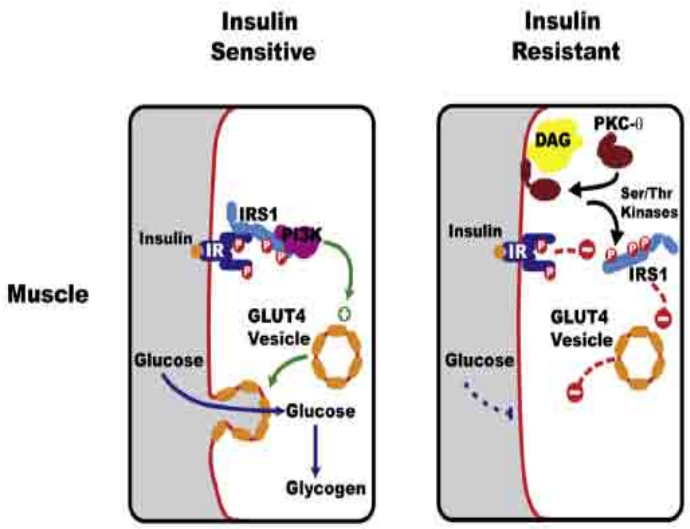


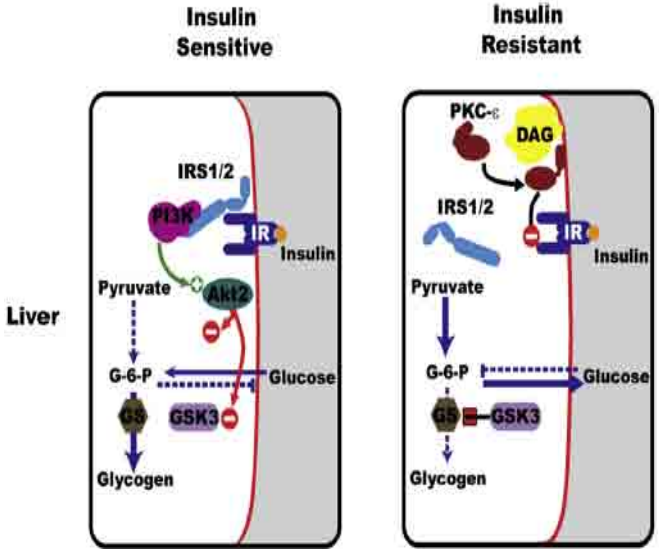
**Obesity, adiposity, and dyslipidemia: A consensus statement from the National Lipid Association**

Journal of Clinical Lipidology, Vol 7, No 4, August 2013

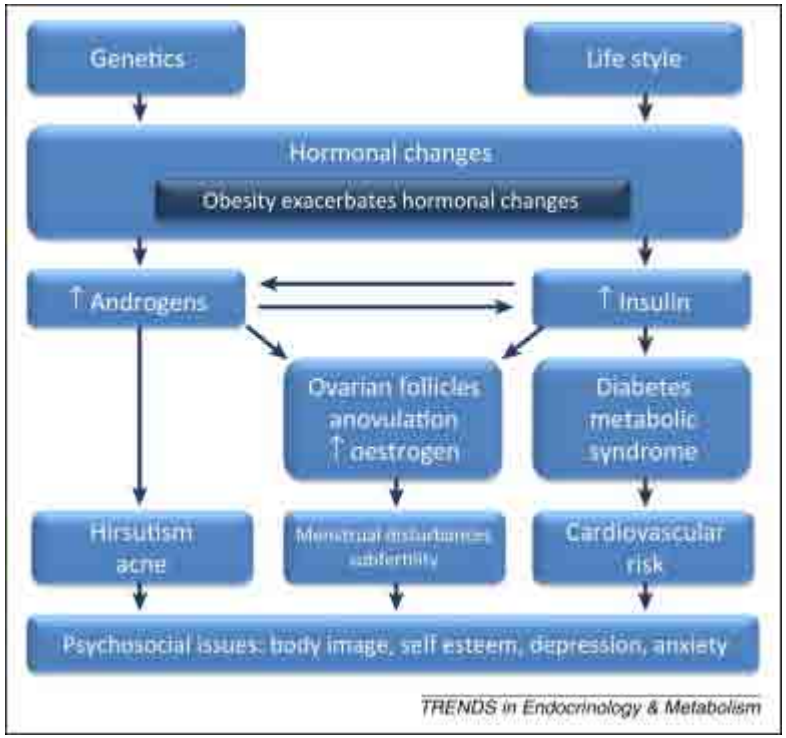


# Metabolic risk in PCOS: phenotype and adiposity impact




Vol 26 March 2015, Pages 136–143

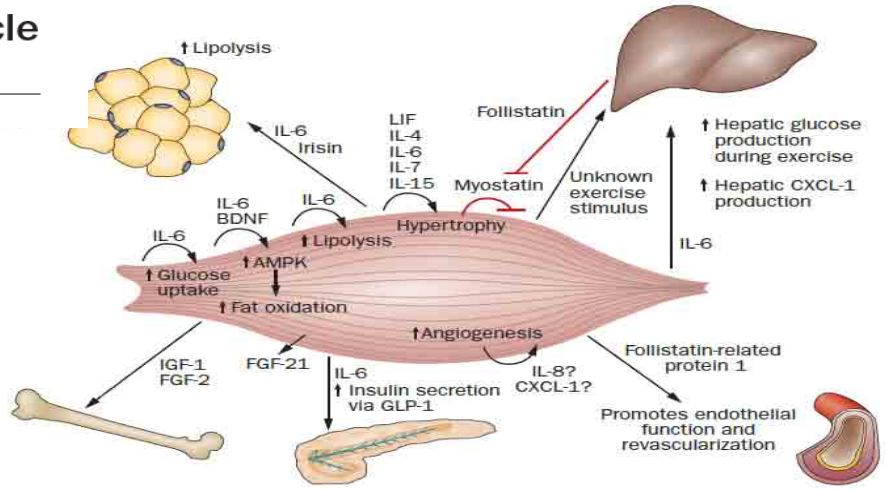
**The polycystic ovary syndrome: a position statement from the European Society of Endocrinology**

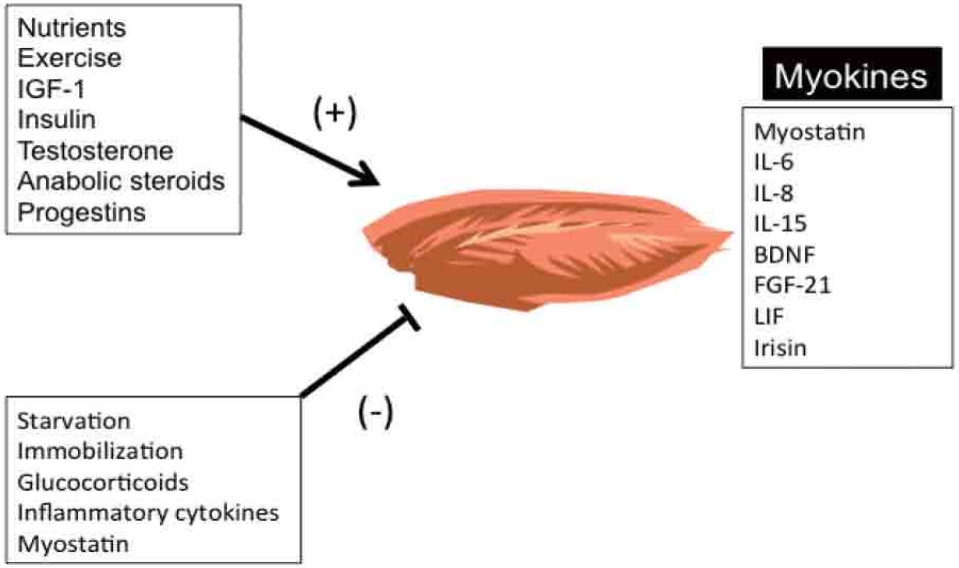
*European Journal of Endocrinology* (2014) **171**, P1–P29

## Muscles, exercise and obesity: skeletal muscle as a secretory organ

*Bente K. Pedersen and Mark A. Febbraio*

Hindawi Publishing Corporation
Mediators of Inflammation
Volume 2013, Article ID 320724, 16 pages
http://dx.doi.org/10.1155/2013/320724




# Connecting Myokines and Metabolism

Rexford S. Ahima[1], Hyeong-Kyu Park[2]

**Review Article**

Endocrinol Metab 2015;30:235-245
http://dx.doi.org/10.3803/EnM.2015.30.3.235
pISSN 2093-596X · eISSN 2093-5978

J Clin Endocrinol Metab 2016, Jan; 101 (1):254-63. doi:10,1210/jc.2015,2724.

**Follicle-Stimulating Hormone Induces Postmenopausal Dyslipidemia Trought Inhibiting Hepatic Cholesterol Metabolism**

- L'aumento del LDL-C che si registra nelle donne in menopausa contribuisce all'aumentato rischio cardiovascolare.
- Sugli epatociti esiste un recettore per l' FSH
- Le donne in post-menopausa che presentavano maggiori livelli di LDL-C avevano maggiori livelli di FSH
- FSH inibisce il recettore delle LDL sugli epatociti in maniera dose e tempo- dipendente (si riduce l'endocitosi del LDL-C e aumentano i livelli circolanti di LDL-C)
- La terapia ormonale sostitutiva riducendo i livelli di FSH > 30% ha prodotto un miglioramento significativo dei livelli lipidici.

# National Lipid Association Annual Summary of Clinical Lipidology 2016

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**Table 7. Secondary causes of dyslipidemia due to drugs[1]**

| Drugs that May Increase LDL-C Levels | Drugs that May Increase Triglyceride Levels |
|---|---|
| **Hormones** | **Hormones or hormone-like agents** |
| • Anabolic steroids (e.g. testosterone) | • Oral estrogens |
| • Glucocorticoids | • Some oral contraceptives |
| • Some progestins | • Glucocorticoids |
| • Danazol | • Tamoxifen |
| **Cardiometabolic pharmacotherapies** | • Raloxifene |
| • Amiodarone | **Cardiometabolic pharmacotherapies** |
| • Thiazide diuretics | • Nonselective beta-blockers |
| • Roziglitazone | • Thiazide diuretics |
| • Fibric acids when administered to patients with severe hypertriglyceridemia | • Bile acid sequestrants |
| • Docosahexaenoic acid when administered to patients with severe hypertriglyceridemia | **Recreational drugs** |
| **Other pharmacotherapies** | • Alcohol |
| • Isotretinoin | • Marijuana |
| • Immunosuppressive drugs (cyclosporine) | **Immuno-active agents** |
| • Sodium glucose co-transporter 2 inhibitors | • Cyclosporin |
| | • Sirolimus |
| | • Interferon |
| | **Anti-neoplastic agents** |
| | • L-asparaginase |
| | • Cyclophosphamide |
| | **Other pharmacotherapies** |
| | • Retinoids |
| | • Protease inhibitors |
| | • Rosiglitazone |
| | **Some neurological & psychiatric drugs (see table 11)** |

Abbreviation: LDL-C = low-density lipoprotein cholesterol

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# THM

Stratificazione del rischio «assoluto» del paziente: valutare non solo i livelli lipidici ma tutti i fattori di rischio, per interventi più mirati e personalizzati

Trattare la patologia di base nelle dislipidemia secondarie

Attenzione alle interferenze farmacologiche

Compliance / Adherence /Persistence