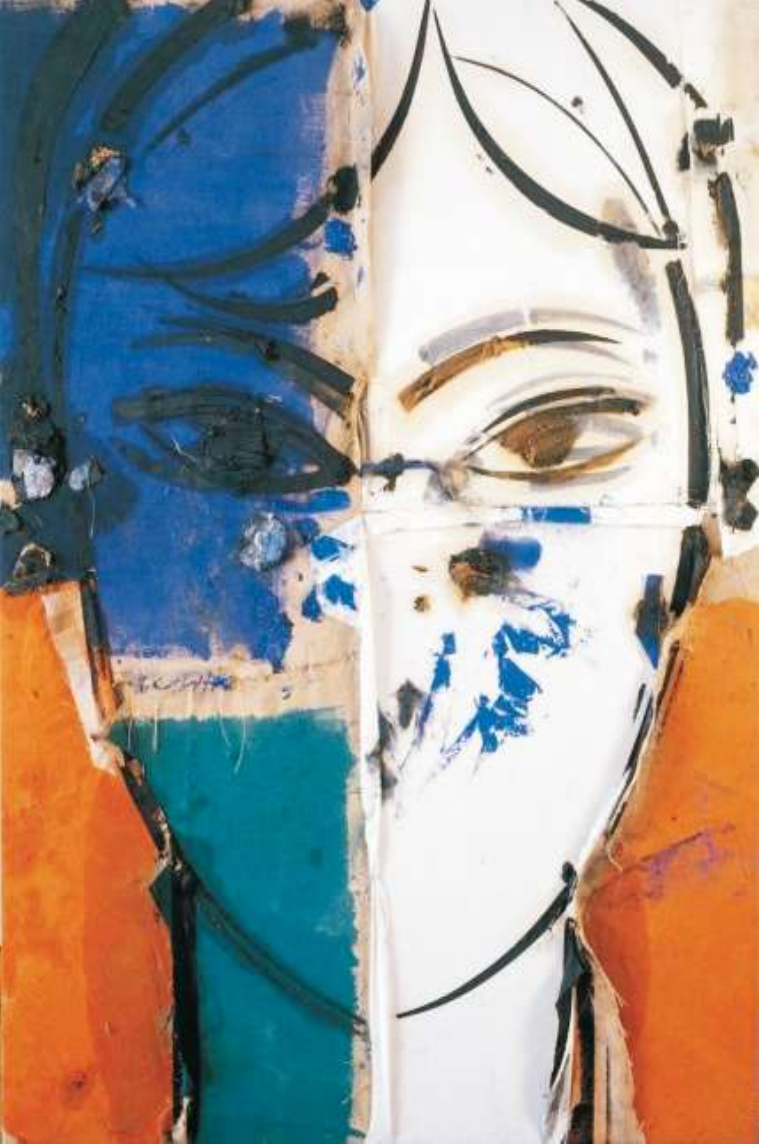


Profilo Lipidico: *differenze di genere e differenze di rischio CV nel DT1 e DT2*

Giuseppina Russo

Dipartimento di Medicina Clinica e Sperimentale
Università di Messina

con il patrocinio di

Reggio Emilia
10 e 11 aprile 2015
Centro Internazionale Loris Malaguzzi

DICHIARAZIONE CONFLITTO D'INTERESSE DOCENTI

In ottemperanza alla normativa ECM ed al principio trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario, il ***docente deve "rilasciare al provider o all'organizzatore la dichiarazione di conflitto d'interessi (ultimi 2 anni rapporti diretti con aziende)***

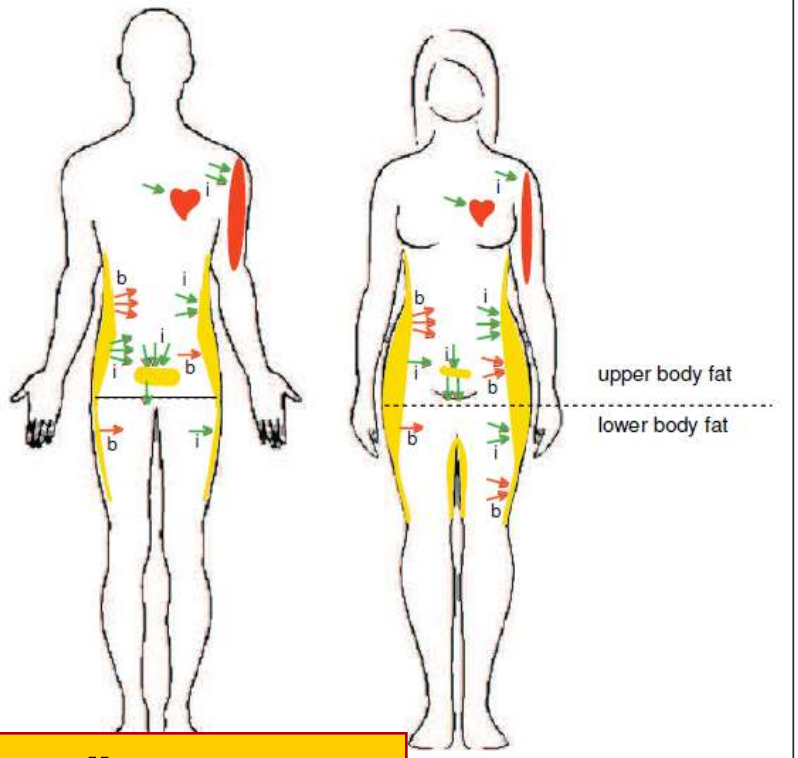
- ✓ **Boehringer-Ingelheim**

Gruppo Donna

Uomini e donne non sono uguali nemmeno sotto il profilo lipidico…..

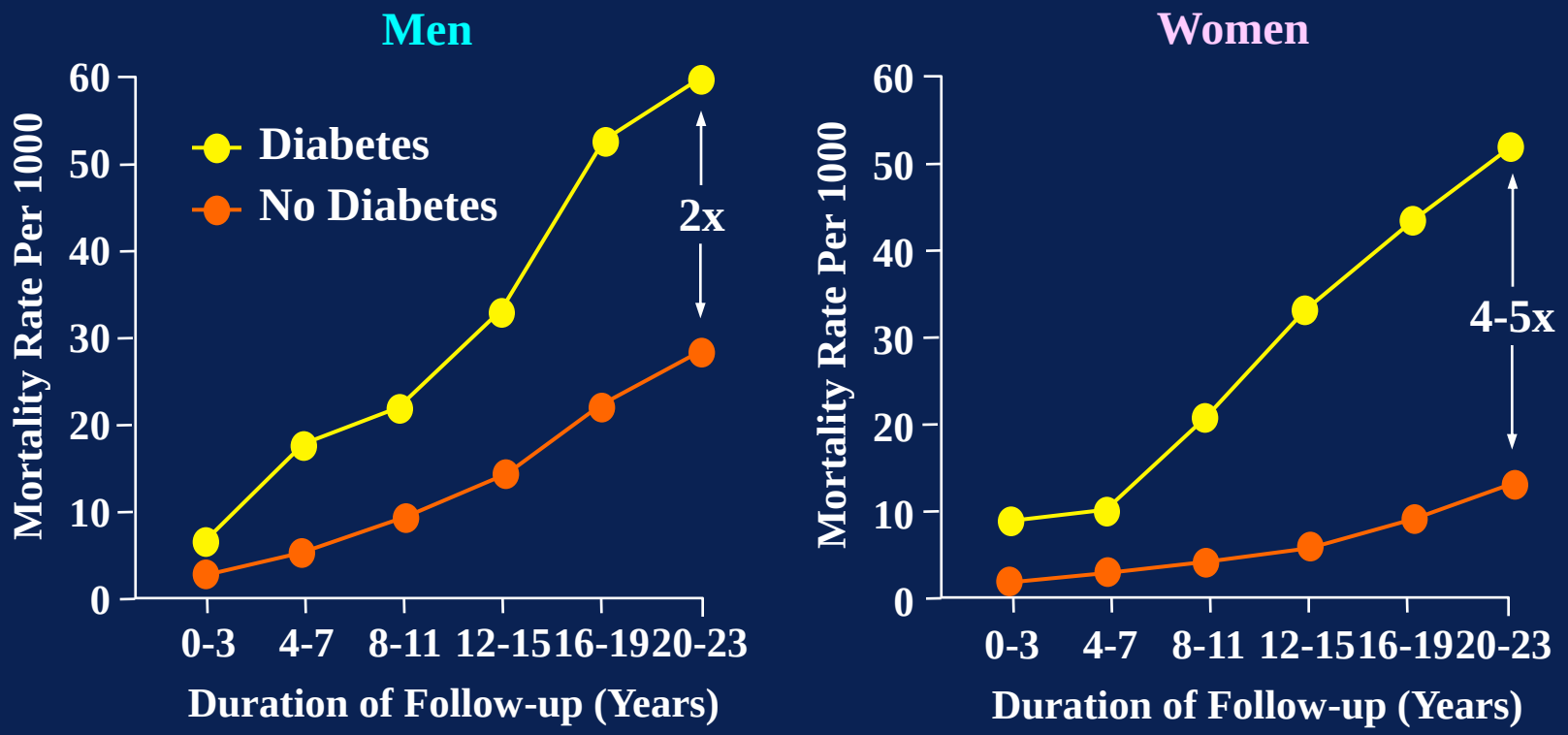
Queste differenze di "genere" emergono anche nei pazienti con diabete?

Il genere ha un impatto diverso sul profilo lipidico nel DT1 e DT2?



ifferences in lipid metabolism in body-fat and lower muscle mass and Vomen also have less V WAT and more SC WAT, both in the abdominal and gluteofemoral regions, than men. Outward arrows indicate basal (b) and insulin-inhibited (i) lipolysis. Inward arrows indicate basal (b) and insulin-stimulated (i) FFA uptake. Under basal post-absorptive conditions, upper-body SC WAT is more lipolytically active both men and women (red outward arrows). FFAs from upper-body SC WAT is less en and FFA release from V WAT is less en outward arrows). A greater percentage of up by upper-body SC WAT in women than in men. Women display higher direct FFA uptake in leg SC WAT than men. Direct FFA uptake is higher in upper SC WAT than in lower SC WAT in men, but not in women. These sex differences in the topography of lipid metabolism may explain higher SC WAT, especially low-body SC WAT, in women compared to men. Higher muscle mass in males is beneficial for more efficient oxidation of FFAs.

Diabetes is a potent CVD Risk Factor in men and women



Krolewski AS, et al. Evolving natural history of coronary disease in diabetes mellitus. *Am J Med* 1991;90(Supp 2A):56S-61S.

Cite this article as: BMJ, doi:10.1136/bmj.38678.389583.7C (published 21 December 2006)

Research

Excess risk of fatal coronary heart disease associated with diabetes in men and women: meta-analysis of 37 prospective cohort studies

Rachel Huxley, Federica Barzi, Mark Woodward

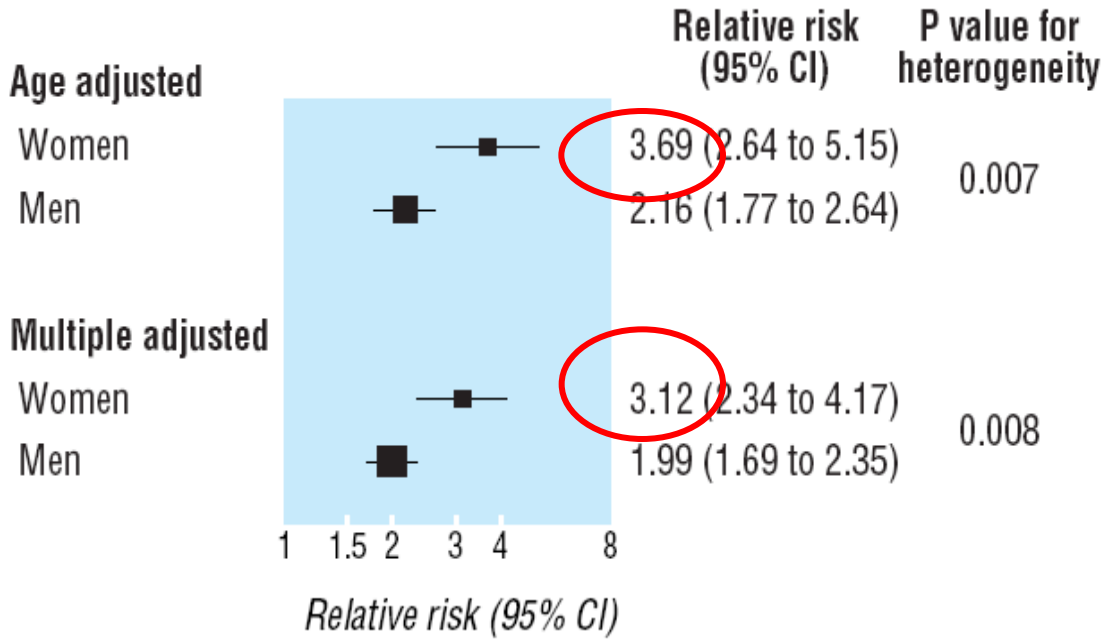


Fig 2 Overall summary estimates of relative risks and 95% confidence intervals for fatal coronary heart disease in men and women with and without diabetes in 22 studies that reported both age and multiple adjusted coefficients

Huxley R et al., BMJ 2006

Fattori di rischio cardiometabolico:

TRADIZIONALI

- Diabete
- Dislipidemie
- Ipertensione
- Obesità
- Inattività fisica
- Fumo
- Familiarità
- Menopausa precoce

NUOVI

- Sindrome metabolica
- Markers infiammatori
- Calcificazione coronarica
- Iperomocisteinemia
- Disfunzione endoteliale
- Fattori psicosociali
- Inquinamento
- altri

Differenze di genere nella dislipidemia nel diabete di tipo 2

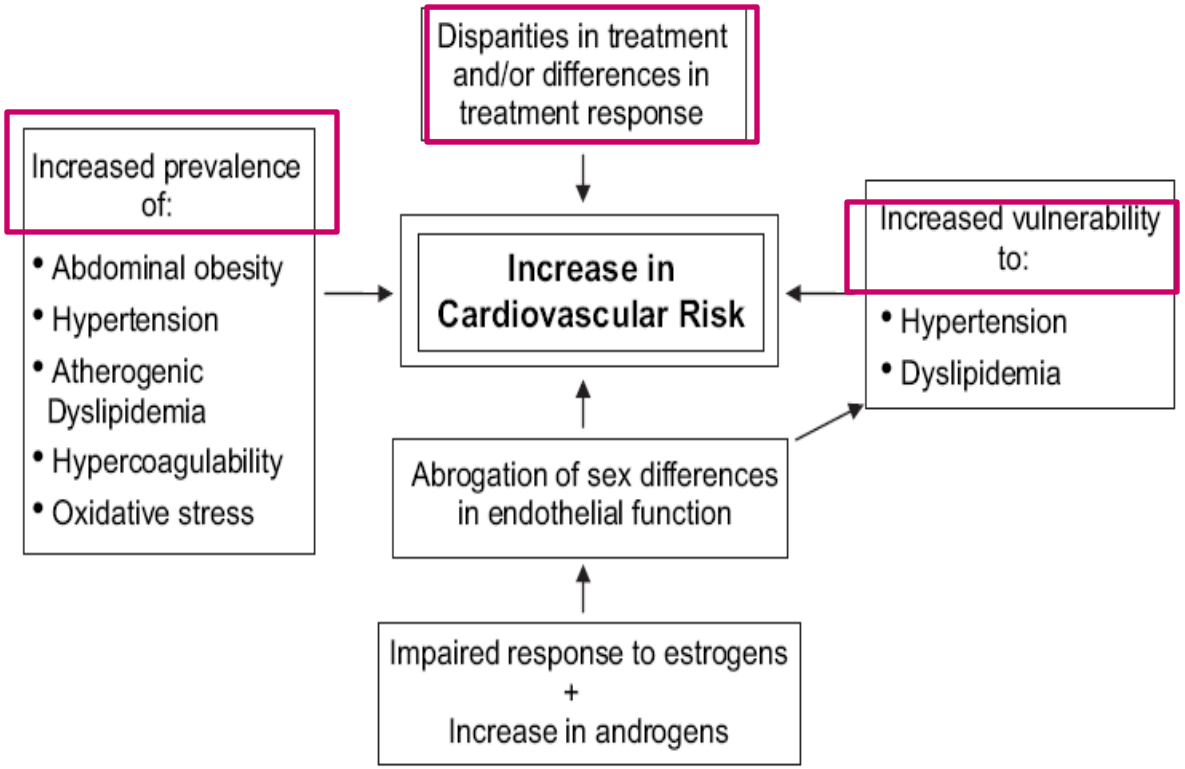


Figure 2 Possible causes of the high cardiovascular risk in women with diabetes.

Modificata da Rivellese et al., NMCD 2010

Maggiore prevalenza dei fattori di rischio cardiovascolare nelle donne diabetiche

Table 3 Mean baseline risk factor levels and differences among men and women with and without diabetes

Risk factor	Difference (diabetes–no diabetes) (95% CI)	
	Men*	Women*
Systolic blood pressure (mm Hg)	7.8 (7.5 to 8.1)	12.5 (12.0 to 13.0)
Total cholesterol (mmol/l)	0.24 (0.22 to 0.26)	0.46 (0.43 to 0.49)
Triglycerides† (mmol/l)	1.53 (1.41 to 1.66)	2.01 (1.88 to 2.14)
High density lipoprotein cholesterol (mmol/l)	–0.076 (–0.1 to –0.05)	–0.13 (–0.16 to –0.1)
Body mass index (kg/m^2)	0.69 (0.65 to 0.74)	1.98 (1.87 to 2.09)

*Data from Asia Pacific Cohort Studies Collaboration.[8]
†Log transformed before analysis and subsequently transformed back.

Huxley R et al., BMJ 2006

Epidemiology/Health Services Research
ORIGINAL ARTICLE

Sex Disparities in the Quality of Diabetes Care: Biological and Cultural Factors May Play a Different Role for Different Outcomes

A cross-sectional observational study from the AMD Annals initiative

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SANDRO GENTILE, MD[3]
GIUSEPPE LUCISANO, MSCSTAT[1]
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MARIA FRANCA MULAS, MD[5]
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CARLO GIORDA, MD[8]
ON BEHALF OF THE AMD ANNALS STUDY GROUP*

Gender medicine integrates aspects of biology, sociology, ethnicity, and culture responsible for different responses to care in women and men (1). Gender medicine applied to the field of diabetes care is particularly relevant because women with diabetes, regardless

Table 1—*Patient characteristics according to sex*

Patient characteristics	Mean (SD) or %					
	Overall		Age <75 years		Age ≥75 years	
	M	F	M	F	M	F
n	227,169	188,125	179,807	130,518	47,210	57,230
%	54.7	45.3	57.9	42.1	45.2	54.8
Age (years)	65.7 ± 11.1	68.4 ± 11.4	61.9 ± 9.2	63.1 ± 9.2	79.8 ± 3.7	80.6 ± 4.1
Oral agents	65.4	66.4	65.6	65.6	57.4	54.6
Oral agents + insulin	13.3	16.7	13.5	17.0	12.6	16.1
Insulin	15.5	16.4	13.6	13.1	22.8	23.8
Lipid-lowering agents (%)	41.2	41.2	42.2	43.0	37.3	37.5
Antihypertensive treatment (%)	56.6	61.0	54.6	58.3	64.3	67.3
≥2 antihypertensive agents (%)	33.0	36.1	36.4	41.1	46.7	53.1
Aspirin (%)	29.2	26.0	28.1	23.8	33.4	31.2

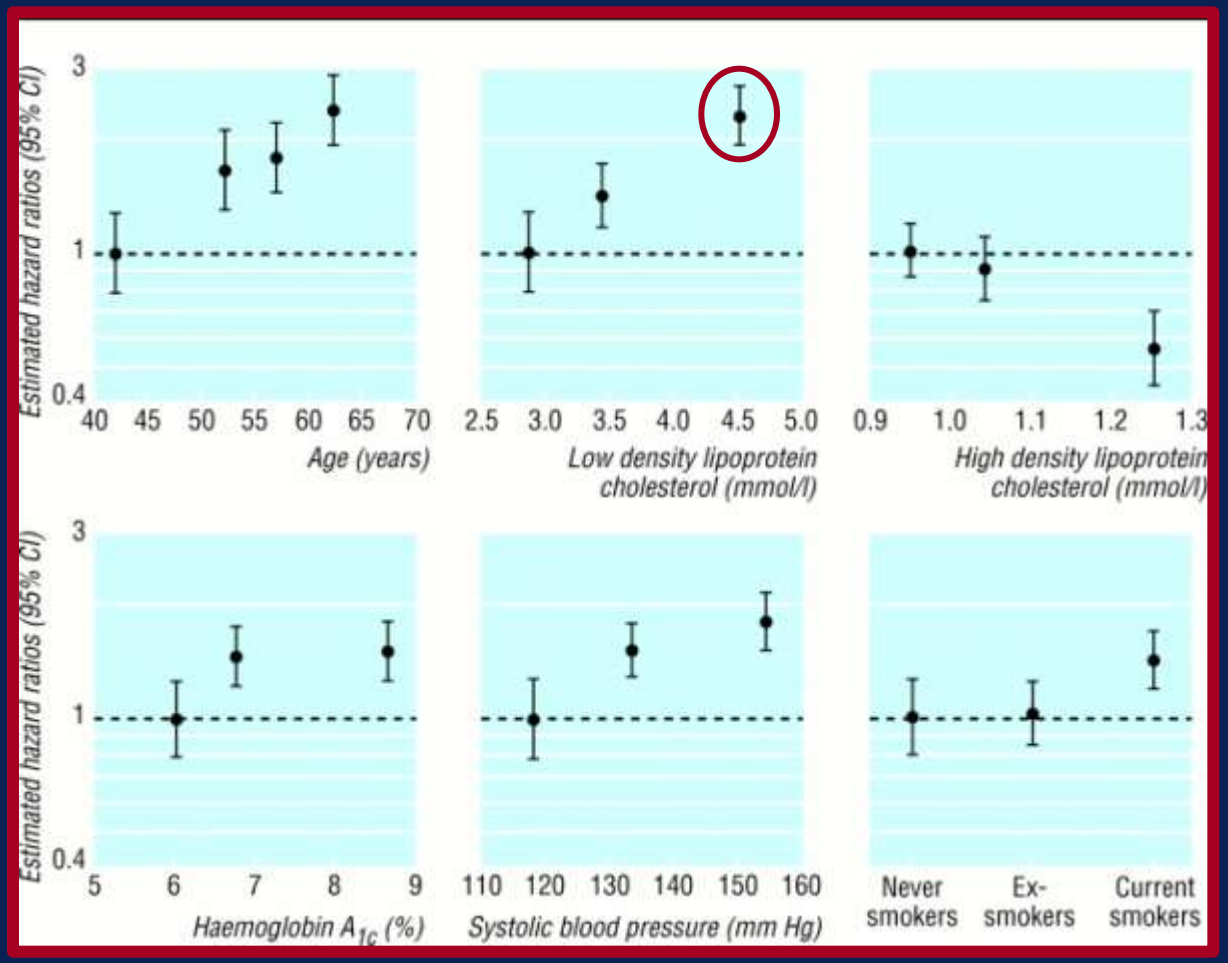
	F	M
Colesterolo totale (mg/dl)	194.4 (40.9)	182.3 (40.8)
Colesterolo HDL (mg/dl)	53.3 (14.0)	46.3 (12.6)
Colesterolo LDL (mg/dl)	112.5 (34.8)	106.6 (34.0)
Trigliceridi (mg/dl)	143.4 (88.3)	151.7 (121.6)

UKPDS Study

Estimated hazard ratios for significant risk factors for coronary artery disease occurring in 335 out of 3055 diabetic patients (expressed as floating absolute risks).

The estimated hazard ratios for the upper third relative to the lower third were:

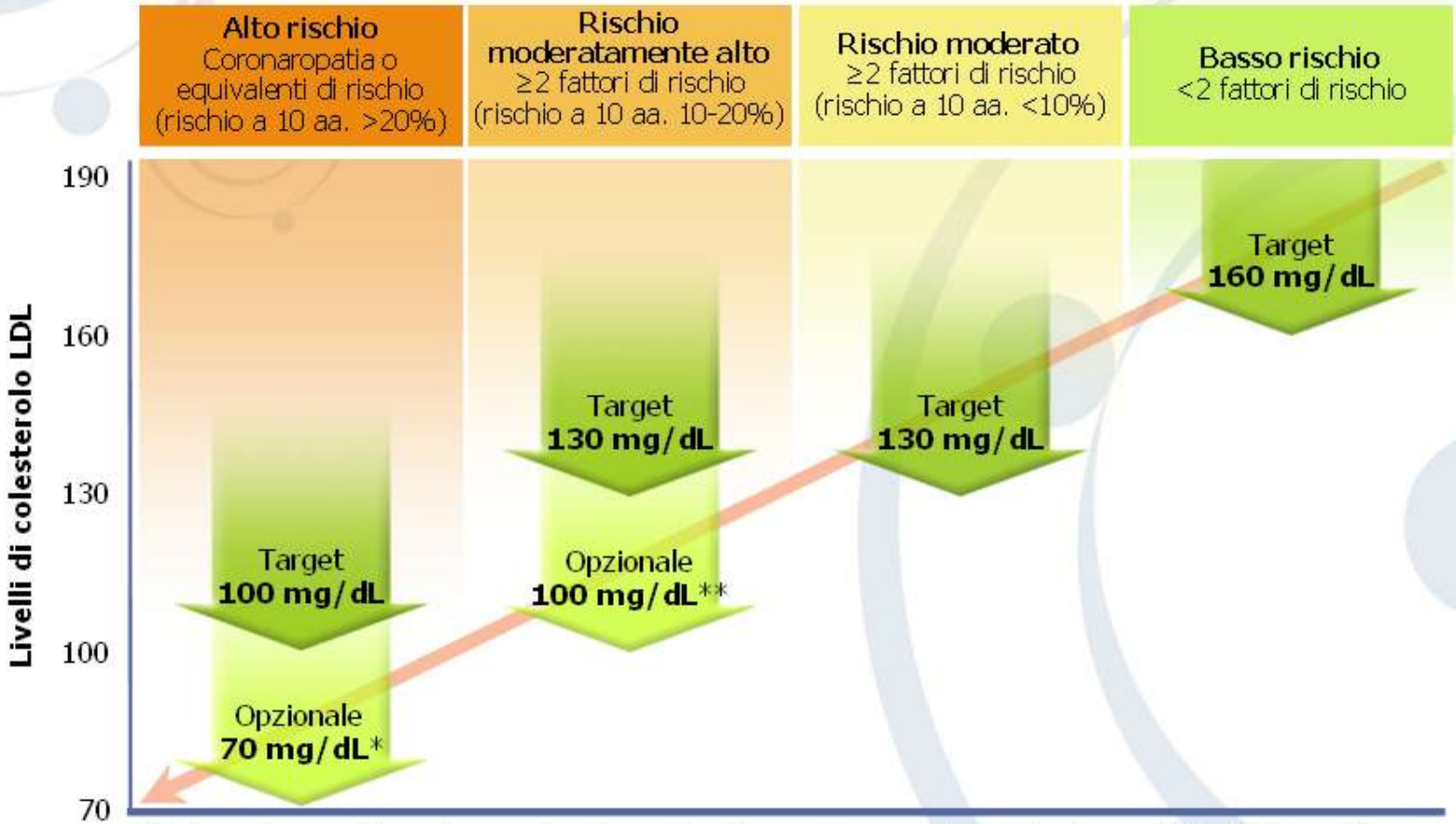
LDL-C: 2.26 (95%CI: 1.70- 3.00)
HDL-C: 0.55 (95% CI: 0.41 - 0.73)
HbA1c:1.52(95% CI: 1.15 - 2.01)
SBP: 1.82 (95% CI:1.34- 2.47)
Smokers:1.41(95% CI: 1.06-1.88)



R C Turner et al. BMJ 1998;316:823-828

ACC/AHA e NCEP ATP III

Target di C-LDL



*Opzione terapeutica nei pz. a rischio molto alto e nei pz. con TG alti e C-non-HDL<100 mg/dL
**Opzione terapeutica

Grundy SM et al. Circulation 2005; 112:2735-2752
Smith CS et al. Circulation 2006: 113:2363-2372

Differenze legate al genere nel profilo Lipidico nel DM2

	Indicatore	M	F	M vs. F (differenza)
PROCESSO	HbA1c	92.6	92.2	+0.4
	Pressione arteriosa	79.1	78.4	+0.7
	Profilo lipidico	74.1	72.4	+1.7
OUTCOME FAVOREVOLI	HbA1c ≤7%	45.5	41.6	+3.9
	PA <130/80 mmHg	15.4	14.9	+0.5
	LDL-C <100 mg/dl	44.6	38.4	+6.2
OUTCOME SFAVOREVOLI	HbA1c >8%	26.9	29.1	-2.2
	PA ≥ 140/90 mmHg	56.1	58.1	-2
	LDL-C ≥130 mg/dl	23.6	28.9	-5.3
FARMACI	Insulina±OHA	29.3	33.8	-4.5
	≥2 antiipertensivi	36.1	33.0	+3.1
	Ipolipemizzanti	41.2	41.3	-0.1
CURA COMPLESSIVA	SCORE Q <15	7.2	8.5	-1.3
	Q SCORE >25	38.0	34.2	3.8

AMD, Annali di Genere DM2

Nutrition, Metabolism & Cardiovascular Diseases (2013) 23, 235–241

Available online at www.sciencedirect.com

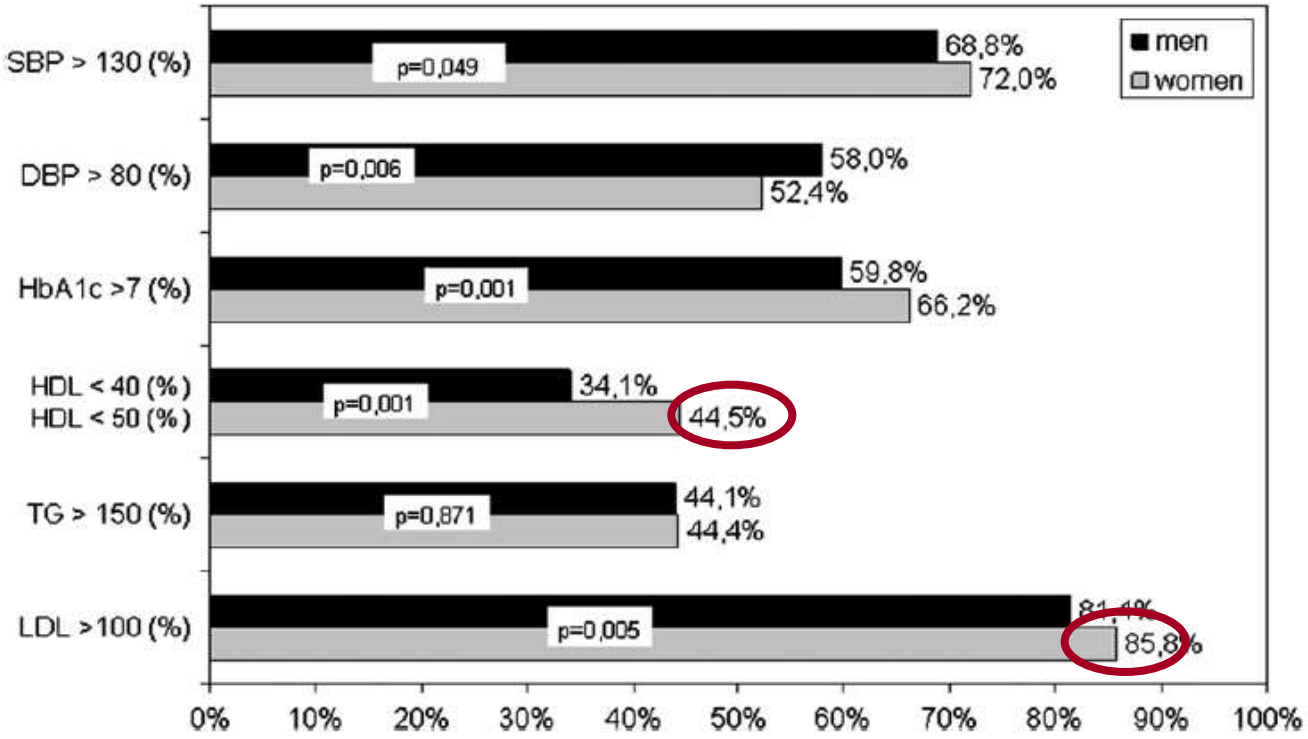
SciVerse ScienceDirect

journal homepage: www.elsevier.com/locate/nmcd

Nutrition, Metabolism & Cardiovascular Diseases

Women show worse control of type 2 diabetes and cardiovascular disease risk factors than men: Results from the MIND.IT Study Group of the Italian Society of Diabetology

L. Franzini [a,*,1], D. Ardigò [a,1], F. Cavalot [b,1], R. Miccoli [c,1], A.A. Rivellese [d,1], M. Trovati [b,1], I. Zavaroni [a,1], O. Vaccaro [d,1]



Il mancato raggiungimento dei target di LDL-C dipende da fattori personali come età e sesso?

Hindawi Publishing Corporation
International Journal of Endocrinology
Volume 2015, Article ID 957105, 8 pages
http://dx.doi.org/10.1155/2015/957105

Hindawi

Research Article

Age- and Gender-Related Differences in LDL-Cholesterol Management in Outpatients with Type 2 Diabetes Mellitus

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Academic Editor: Alexandra Kautzky-Willer

Background. Dyslipidemia contribute to the excess of coronary heart disease (CHD) risk observed in women with type 2 diabetes (T2DM). Low density lipoprotein-cholesterol (LDL-C) is the major target for CHD prevention, and T2DM women seem to reach LDL-C targets less frequently than men. *Aim.* To explore age- and gender-related differences in LDL-C management in a large sample of outpatients with T2DM. *Results.* Overall, 415.294 patients (45.3% women) from 236 diabetes centers in Italy were included. Women were older and more obese, with longer diabetes duration, higher total-cholesterol, LDL-C, and HDL-C serum levels compared to men ($P < 0.0001$). Lipid profile was monitored in ~75% of subjects, women being monitored less frequently than men, irrespective of age. More women did not reach the LDL-C target as compared to men, particularly in the subgroup treated with lipid-lowering medications. The between-genders gap in reaching LDL-C targets increased with age and diabetes duration, favouring men in all groups. *Conclusions.* LDL-C management is worst in women with T2DM, who are monitored and reach targets less frequently than T2DM men. Similarly to men, they do not receive medications despite high LDL-C. These gender discrepancies increase with age and diabetes duration, exposing older women to higher CHD risk.

1. Introduction

Type 2 diabetes (T2DM) is a powerful cardiovascular disease (CVD) risk factor in both men and women. Although the overall CVD risk is higher in T2DM men, the relative risk of coronary heart disease (CHD) is higher in T2DM women when compared to nondiabetic ones, with the loss of the typical oestrogen protection in the premenopausal state [1–3].

Although the mechanism underlying this excessive CHD risk in women with type 2 diabetes (T2DM) has not been fully elucidated yet, several hypotheses suggest that diabetes *per se* may be a stronger CHD risk factor in the female gender, determining a more unfavourable CHD risk profile [4, 5]. This could lead to more complex risk factors and/or disease management in women with T2DM as compared to men.

Chronic hyperglycemia may certainly play a role, but it is not the only responsible for the high CHD burden in subjects with T2DM. Thus, cardiovascular disease (CVD) is a multifactorial condition and major risk factors (i.e., obesity, hypertension, and dyslipidemia) have been all demonstrated to contribute to its occurrence [6].

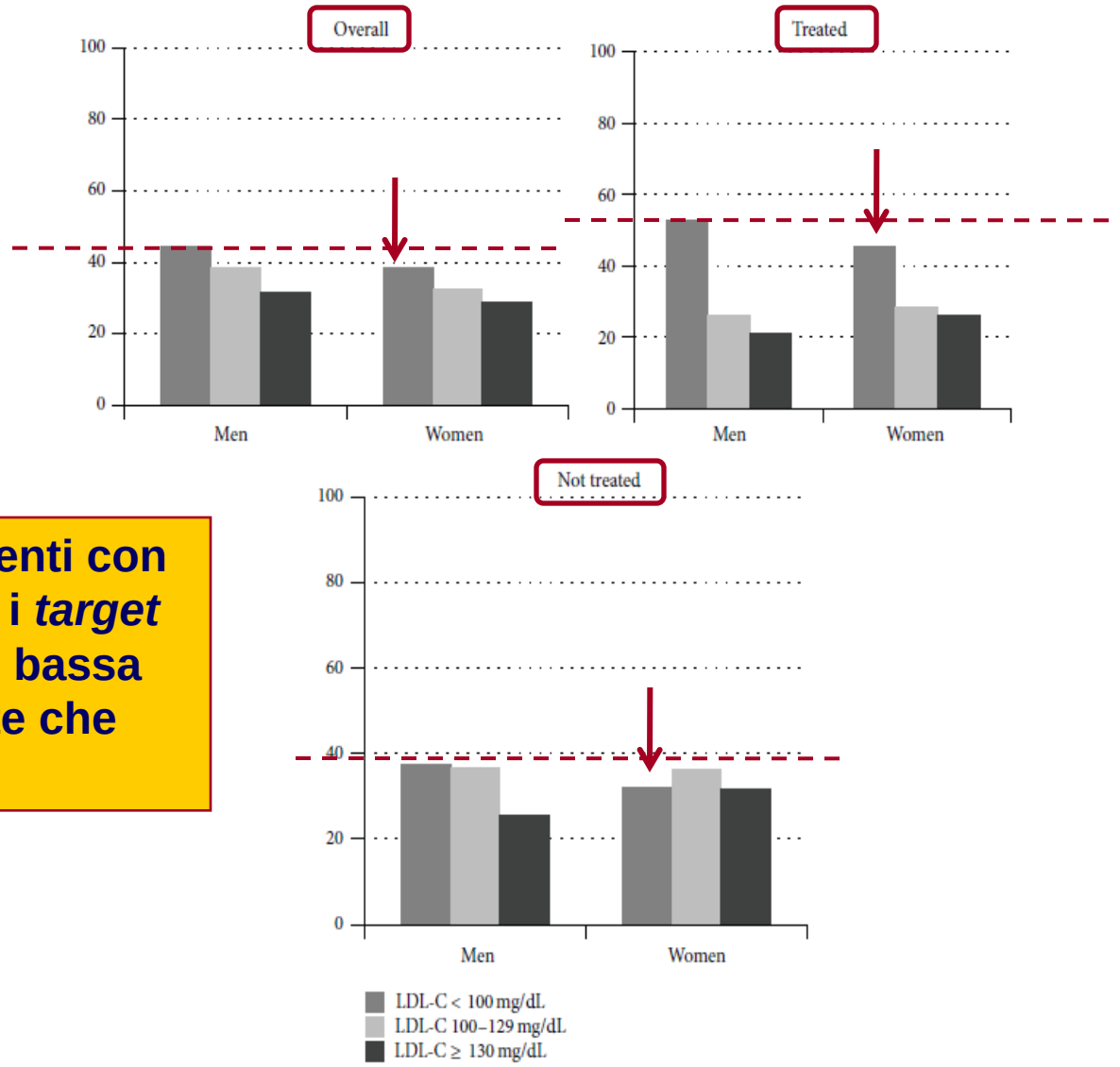


FIGURE 1: LDL-C classes according to gender and lipid-lowering treatment.

La percentuale di pazienti con DM2 che raggiungono i *target* di LDL-C è sempre più bassa nelle donne, sia trattate che non trattate

La discrepanza nella gestione dei livelli di LDL-C a svantaggio delle donne con DM2 peggiora con l'età e la durata del diabete

Table 2: Management of LDL-C values in T2DM outpatients according to gender and age.

	<55 years			55–65 years			65–75 years			>75 years		
	F	M	P	F	M	P	F	M	P	F	M	P
n	22069	37422		42914	62970		65535	79415		57230	47210	
Age (yrs)	47.1 ± 7.3	47.7 ± 6.4	<0.0001	60.6 ± 2.7	60.4 ± 2.8	<0.0001	70.1 ± 2.8	69.9 ± 2.8	<0.0001	80.6 ± 4.1	79.8 ± 3.7	<0.0001
Diabetes duration (yrs)	6.6 ± 7.2	5.7 ± 6.2	<0.0001	8.6 ± 8.0	8.3 ± 7.5	0.0007	11.4 ± 9.4	11.1 ± 9.2	<0.0001	14.3 ± 11.0	13.9 ± 10.9	<0.0001
Patients monitored for lipid profile (%)	72.2	74.3	<0.0001	75.5	76.4	0.0002	74.9	75.4	0.07	67.3	69.0	<0.0001
Patients with LDL-C <100 mg/dL (%)	32.3	35.4	<0.0001	35.8	43.3	<0.0001	40.6	47.6	<0.0001	40.1	48.4	<0.0001
Patients with LDL-C ≥130 mg/dL (%)	34.9	31.7	<0.0001	31.6	25.4	<0.0001	27.0	20.7	<0.0001	26.8	19.6	<0.0001

Data are *n*, %, and means ± standard deviation.

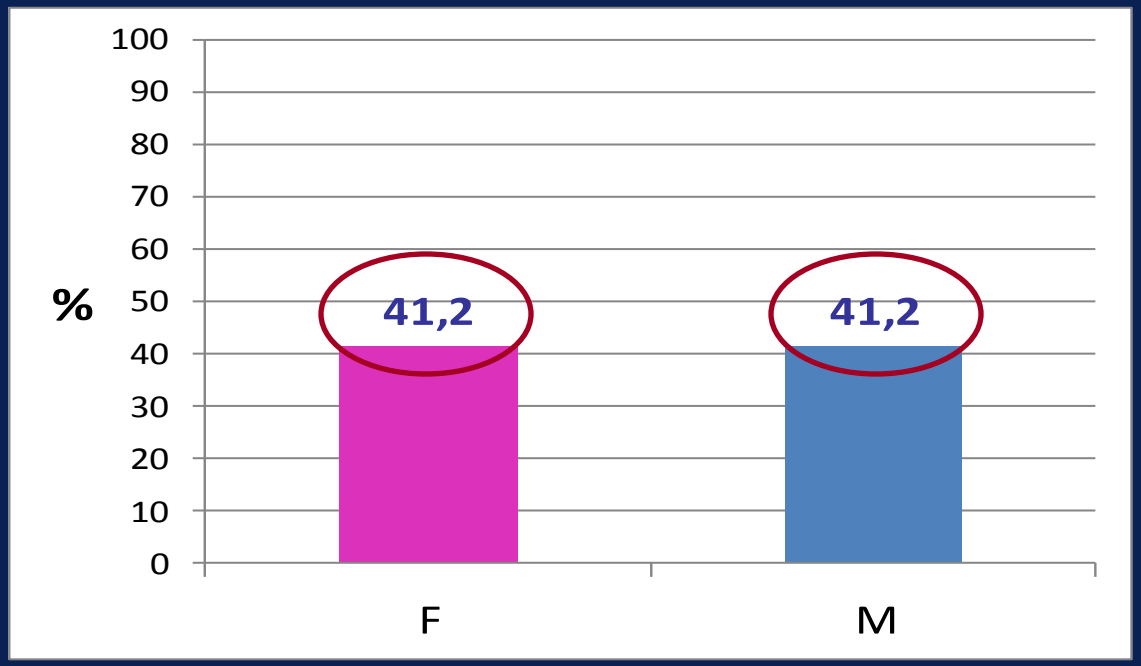
Table 3: Management of LDL-C values in T2DM outpatients according to gender and diabetes duration.

	<2 years			2–5 years			6–10 years			>10 years		
	F	M	P	F	M	P	F	M	P	F	M	P
n	26736	36068		28475	37097		40272	52163		81651	89045	
Age (years)	64.4 ± 12.7	61.4 ± 12.1	<0.0001	65.5 ± 11.7	62.7 ± 11.4	<0.0001	67.2 ± 11.0	64.8 ± 10.5	<0.0001	71.3 ± 10.2	69.1 ± 9.8	<0.0001
Patients monitored for lipid profile (%)	69.8	71.4	<0.0001	74.7	76.4	<0.0001	74.4	75.9	<0.0001	72.4	74.3	<0.0001
Patients with LDL-C <100 mg/dL (%)	28.4	33.9	<0.0001	36.3	41.8	<0.0001	39.2	45.8	<0.0001	42.0	49.3	<0.0001
Patients with LDL-C ≥130 mg/dL (%)	41.6	34.9	<0.0001	30.9	25.6	<0.0001	27.6	22.1	<0.0001	24.9	19.2	<0.0001

Data are *n*, %, and means ± standard deviation.

Terapia : Farmaci Ipolipemizzanti

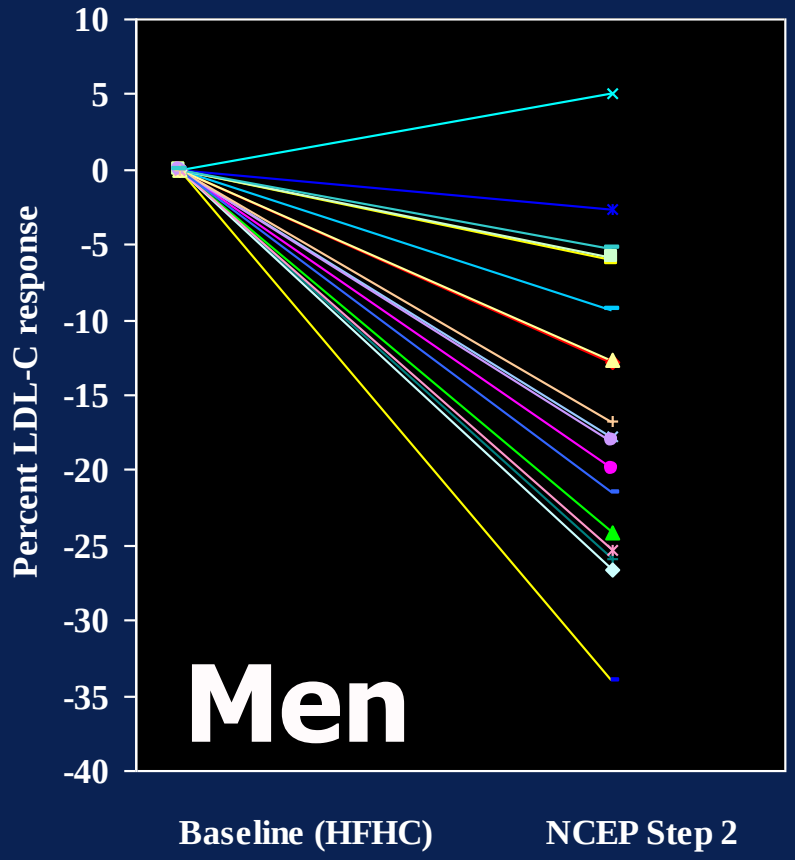
Percentuale di pazienti trattati con ipolipemizzanti per genere

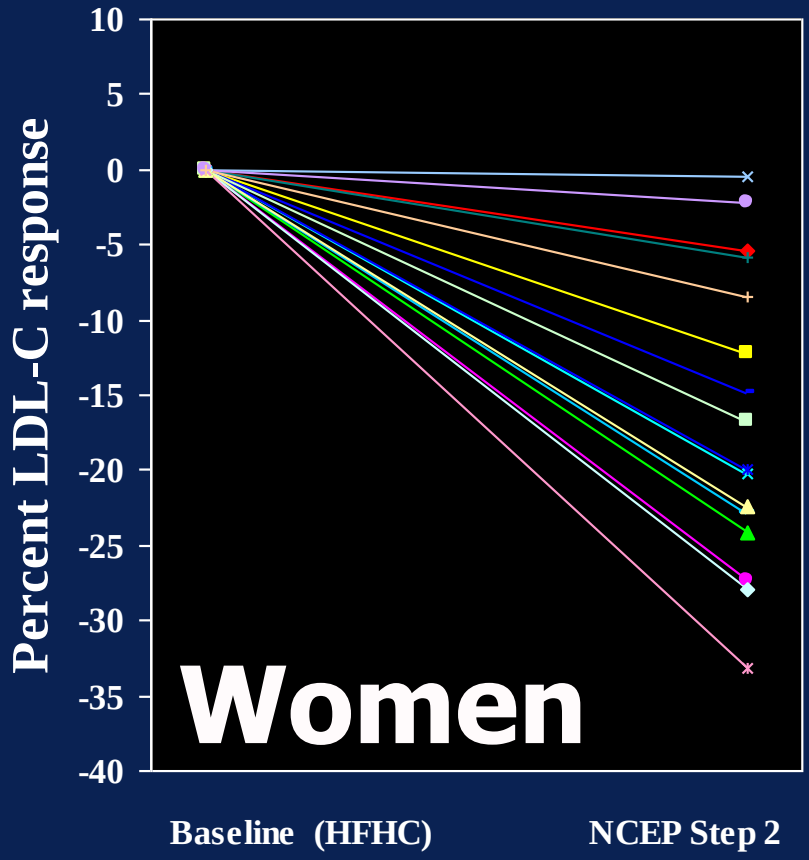


La percentuale di pazienti in trattamento ipolipemizzante risulta del tutto sovrapponibile nei due sessi.

AMD, Annali di Genere DM2

Variability in LDL-C response following Diet Therapy



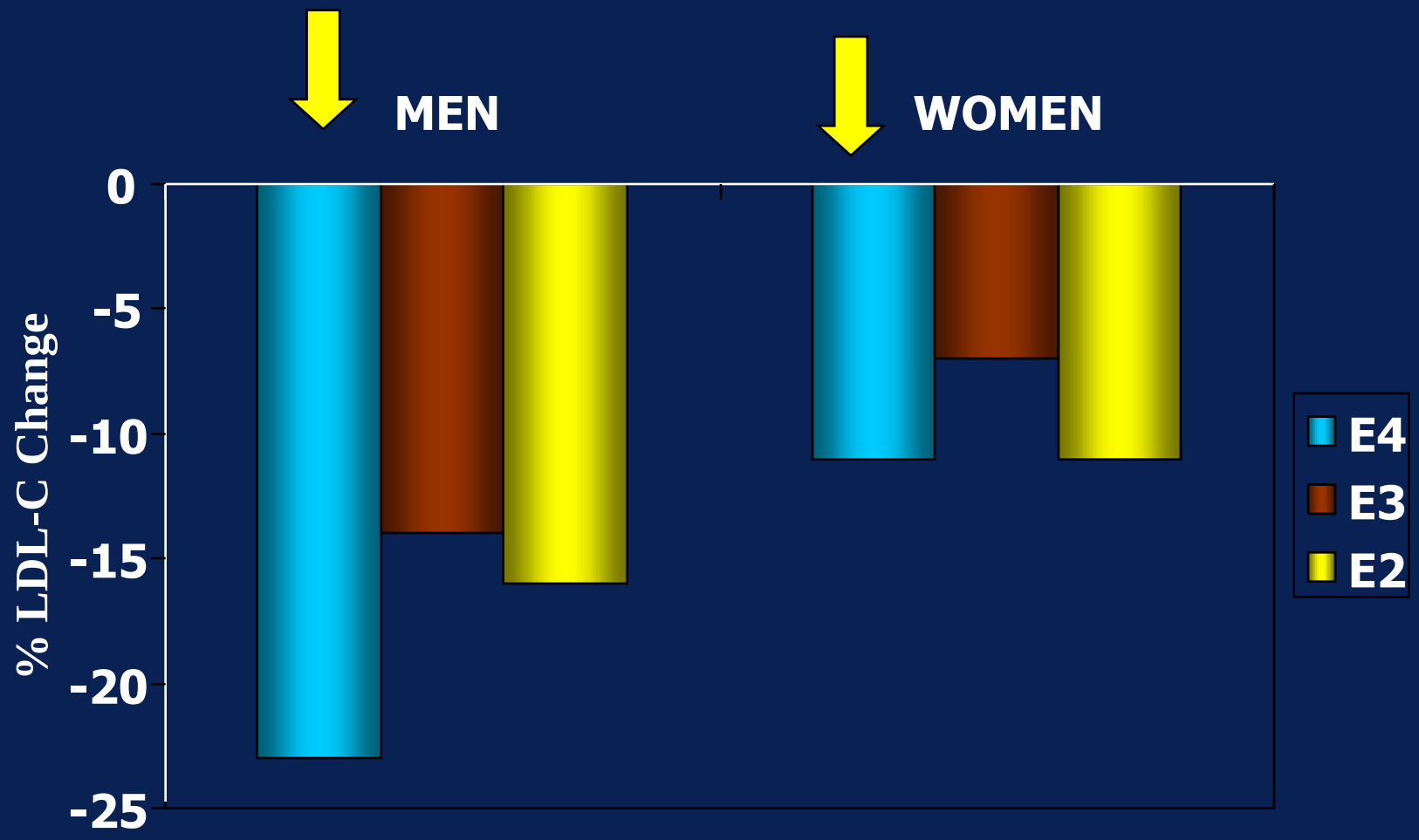


Fattori personali : Età, sesso, etnia

Lipidi = ∫esposizione all'ambiente x *genetica*

Quantità e qualità *dieta*
attività fisica

LDL-C Response to a Therapeutic Diet by *APOE* allele



Lopez-Miranda et al. J Lipid Res. 1994;35:1965-75.

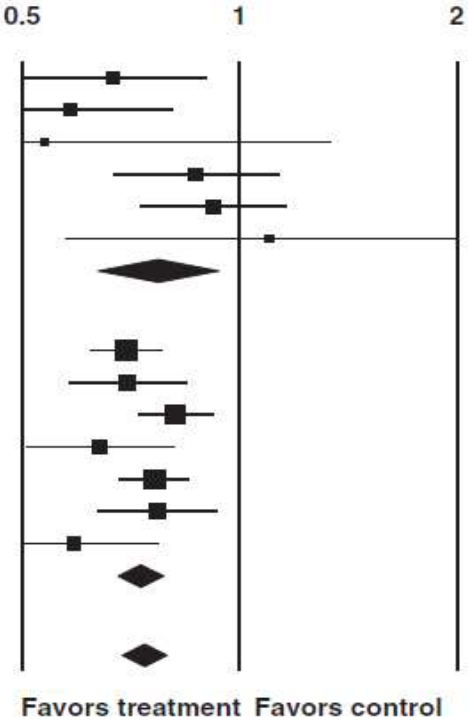
British Journal of Clinical Pharmacology DOI:10.1111/j.1365-2125.2003.02060.x

Meta-analysis of large randomized controlled trials to evaluate the impact of statins on cardiovascular outcomes

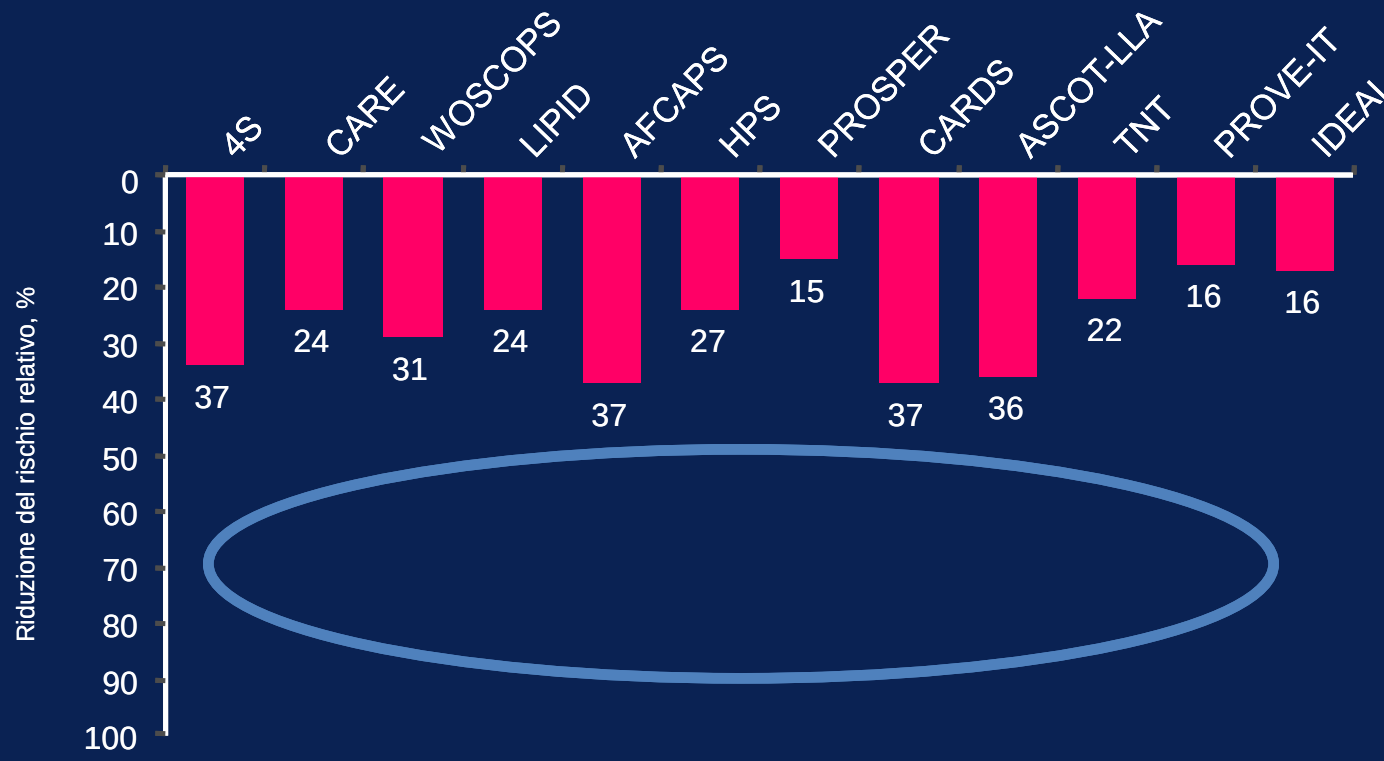
Bernard M. Y. Cheung, Ian J. Lauder,[1] Chu-Pak Lau & Cyrus R. Kumana
Department of Medicine and [1]Statistics and Actuarial Science, University of Hong Kong, Queen Mary Hospital, Hong Kong

Major coronary events

sex	Citation	Treated	Control	Effect	Lower	Upper
F	4S	59 / 407	91 / 420	.67	.50	.90
F	CARE	46 / 286	80 / 290	.58	.42	.81
F	AFCAPS/TexCAPS	7 / 499	13 / 498	.54	.22	1.34
F	LIPID	90 / 756	104 / 760	.87	.67	1.13
F	PROSPER	125 / 1495	137 / 1505	.92	.73	1.16
F	ASCOT-LLA	19 / 979	17 / 963	1.10	.57	2.10
F (6)		**346 / 4422**	**442 / 4436**	**.77**	**.64**	**.94**
M	4S	372 / 1814	531 / 1803	.70	.62	.78
M	WOSCOP	174 / 3302	248 / 3293	.70	.58	.84
M	CARE	384 / 1795	469 / 1788	.82	.72	.92
M	AFCAPS/TexCAPS	109 / 2805	170 / 2803	.64	.51	.81
M	LIPID	467 / 3756	611 / 3742	.76	.68	.85
M	PROSPER	167 / 1396	219 / 1408	.77	.64	.93
M	ASCOT-LLA	81 / 4189	137 / 4174	.59	.45	.77
M (7)		**1754 / 19057**	**2385 / 19011**	**.73**	**.68**	**.78**
Combined (13)		**2100 / 23479**	**2827 / 23447**	**.74**	**.69**	**.79**



Un’esigenza clinica ancora insoddisfatta: un *rischio CV residuo* persiste nonostante il trattamento con una statina



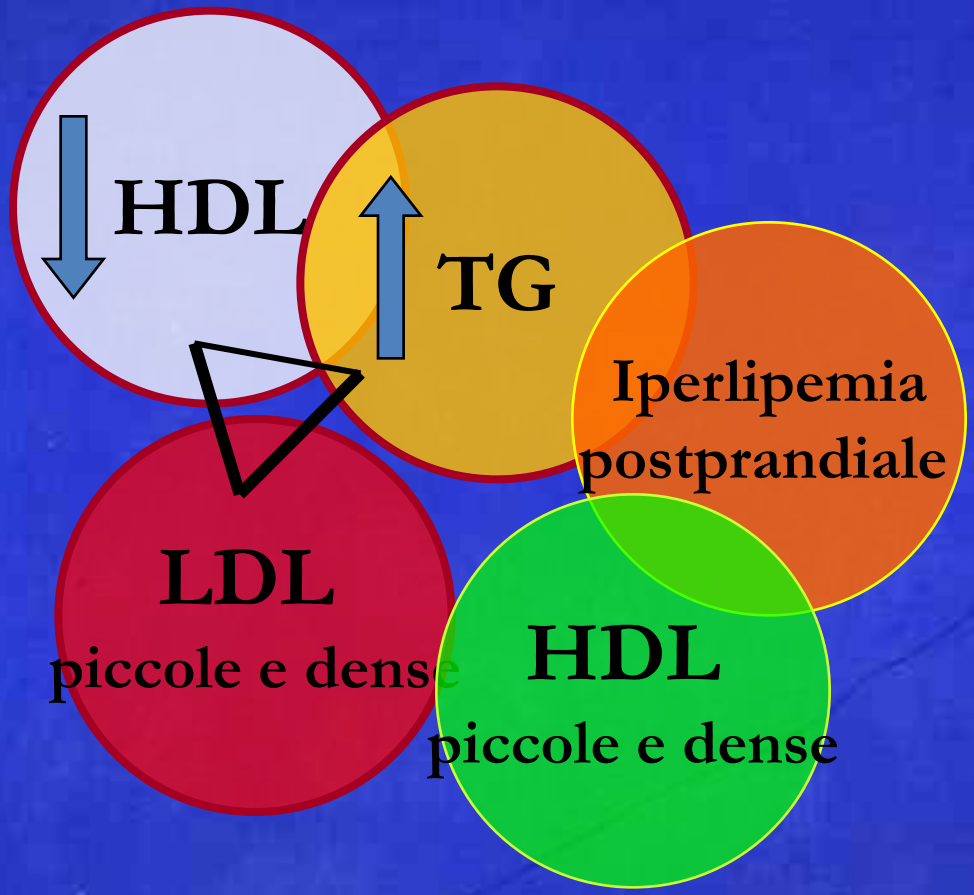
- Le terapie basate sulla riduzione del C-LDL riducono il rischio di malattia coronarica
- Il rischio residuo è determinato sia da fattori di rischio tradizionali che da ulteriori alterazioni del profilo lipidico

4S = Scandinavian Simvastatin Survival Study; CARE = Cholesterol And Recurrent Events; WOSCOPS = West of Scotland Coronary Prevention Study; LIPID= Long-term Intervention with Pravastatin in Ischemic Disease; AFCAPS = Air Force/Texas Coronary Atherosclerosis Prevention Study; HPS = Heart Protection Study; PROSPER = Prospective Study of Pravastatin in Elderly at Risk; CARDS = Collaborative Atorvastatin Diabetes Study; ASCOT-LLA = Anglo-Scandinavian Cardiac Outcomes Trial—Lipid-Lowering Arm; TNT = Treating to New Targets; PROVE-IT = PRavastatin Or atorVastatin Evaluation and Infection Therapy; IDEAL = Incremental Decrease in Endpoints through Aggressive Lipid lowering; CV = cardiovascolare.

Tratto da Chapman J. *Eur Heart J*. 2005;7(suppl F):F56–F62.[Gruppo di studio 4S]. *Lancet.* 1994;344:1383–1389; Sacks FM et al. *N Engl J Med.* 1996;335:1001–1009; Shepherd J et al. *N Engl J Med.* 1995;333:1301–1307; The Long-Term Intervention With Pravastatin in Ischaemic Disease (LIPID) Study Group. *N Engl J Med.* 1998;339:1349–1357; Downs JR et al. *JAMA*. 1998;279:1615–1622; Heart Protection Study Collaborative Group. *Lancet.* 2002;36:7–22; Shepherd J et al. *Lancet.* 2002;360:1623–1630; Colhoun HM et al. *Lancet.* 2004;364:685–696; Sever PS et al. *Lancet.* 2003;361:1149–1158; LaRosa JC et al. *N Engl J Med.* 2005;352:1425–1435; Cannon CP et al. *N Engl J Med.* 2004;350:1495–1505; Pedersen TR et al. *JAMA*. 2005;294:2437–3092..

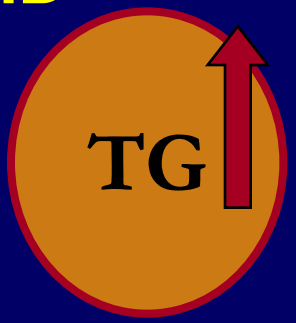
DISLIPIDEMIA

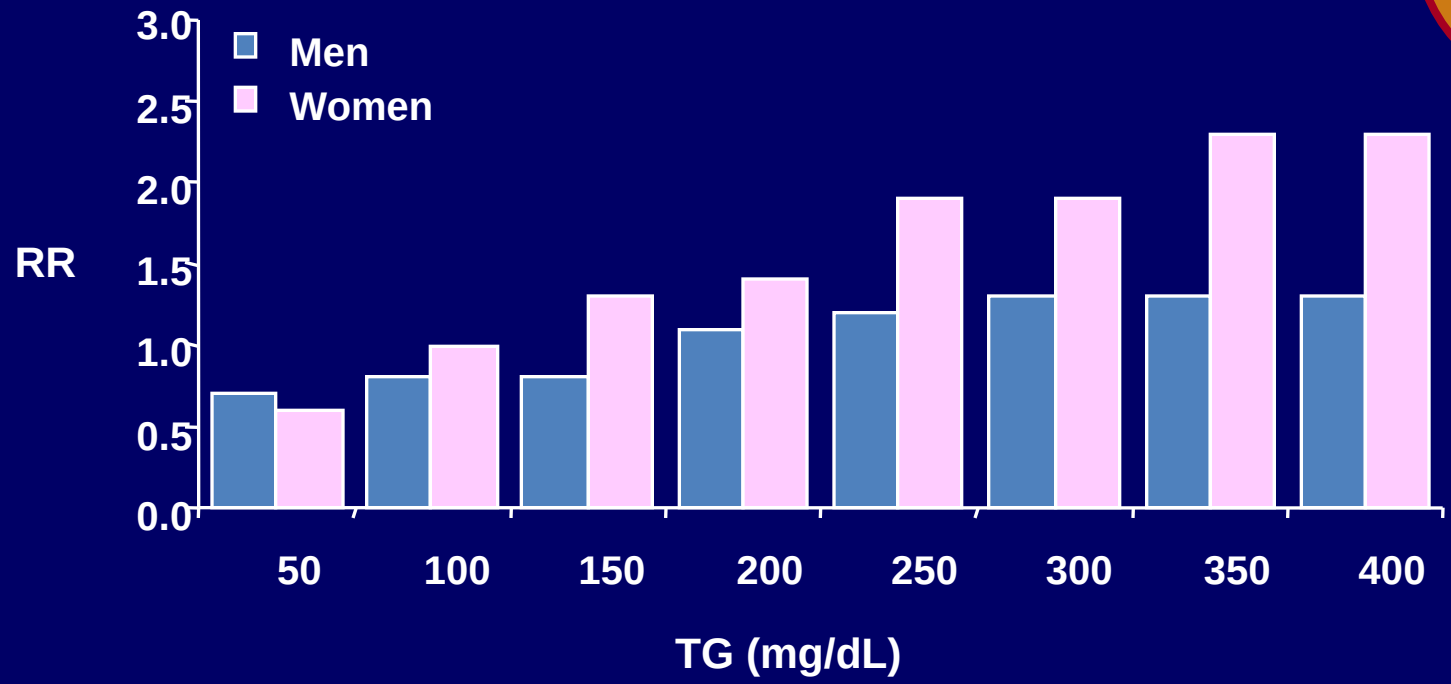
nel diabete di tipo 2 e nell'insulino-resistenza



La fisiopatologia della dislipidemia diabetica si può **ricondurre ad un alterato metabolismo delle TRL**, in larga parte secondario al deficit dell'azione insulinica.

Impact of TG Levels on Relative Risk of CHD in the Framingham Heart Study





Castelli WP. Can J Cardiol 1988;4:5A-10A.

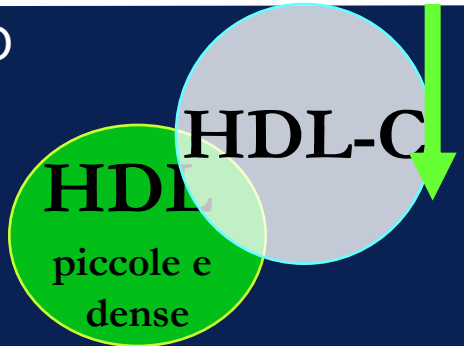
Fattori di rischio CVD maggiori secondo le Linee Guida NECP ATPIII

Fattori di rischio maggiori (escluso LDL-C) che modificano i target di LDL-C

- Fumo di sigaretta
- Ipertensione (PA≥140/90 o terapia)
- Basso HDL-C (<40 mg/dl)*
- Familiarità per CHD prematura (CHD in un parente di primo grado <55 anni se maschio, < 65 anni se femmina)
- Età (uomini ≥ 45 anni; donne ≥ 55 anni)

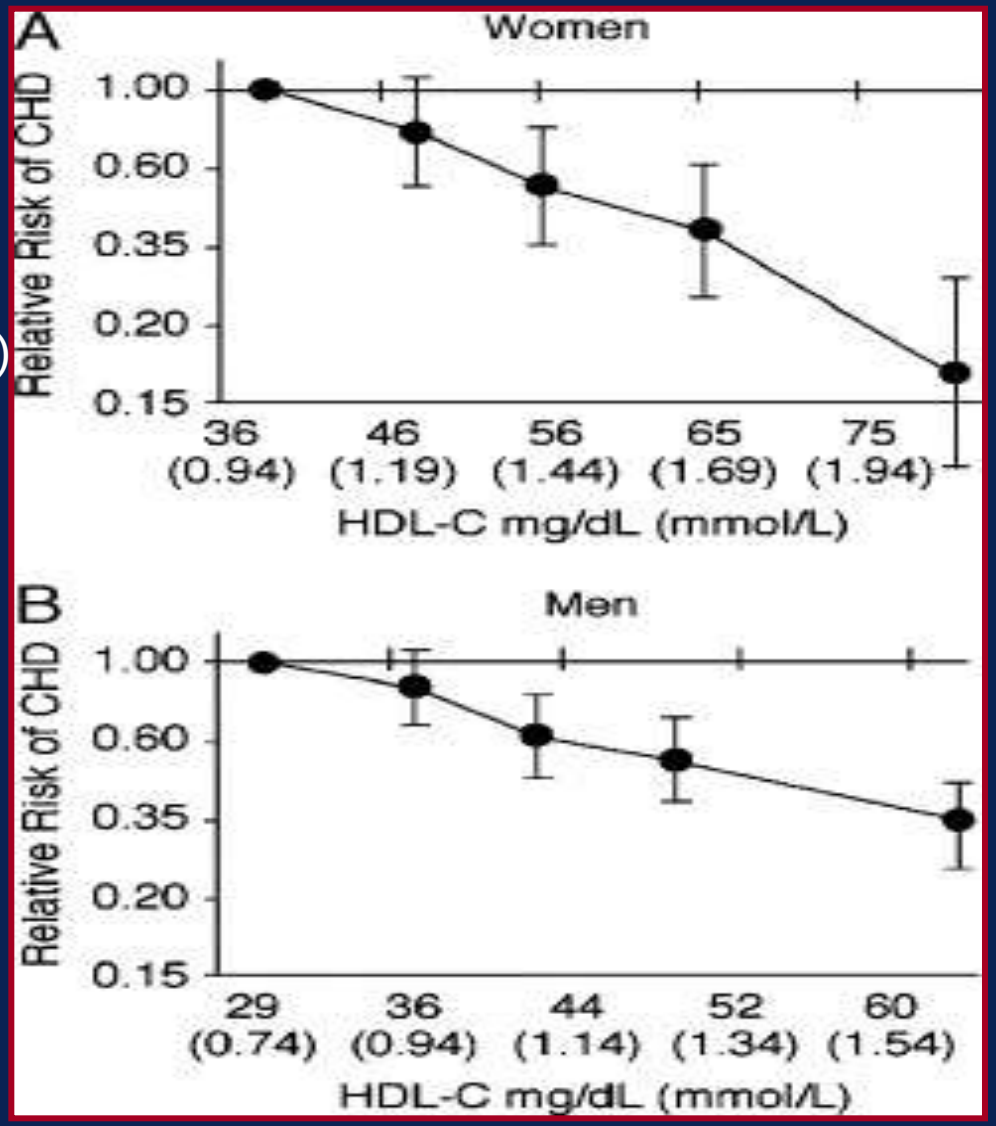
**** Livelli di HDL-C ≥ 60 mg/dl sono un fattore di rischio "negativo", la loro presenza rimuove un fattore di rischio dal conteggio totale.***

Note: nello ATPIII il diabete è considerato un equivalente CHD



HDL-C quintiles and relative risk of CHD in the ARIC study

(adjusted for age and race)



Low HDL-C levels are a stronger CHD RF in women

Sharrett et al, 2001

Negli uomini del Framingham Offspring Study il profilo delle **sottopopolazioni di HDL** è più predittivo dello stesso HDL-C sulla cardiopatia ischemica

Con ELETTROFORESI SU GEL BIDIMENSIONALE

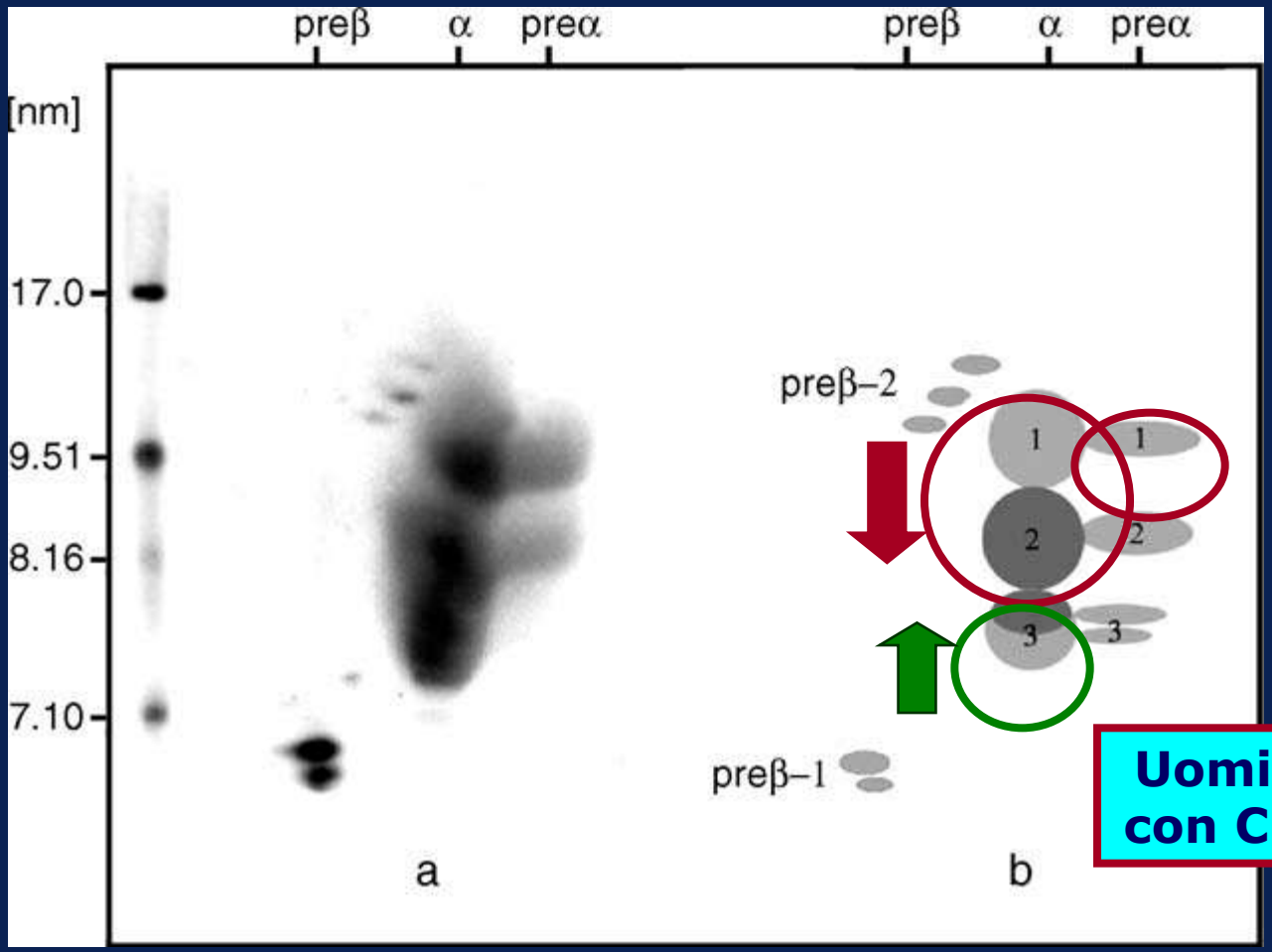
Carica

Motilità

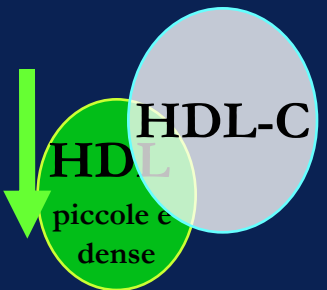
- **preβ**
- **α**
- **preα**

Dimensioni

5.38-13.74 nm



Uomini con CHD



Asztalos BF, Arterioscler Thromb Vasc Biol. 2000

Atherosclerosis 210 (2010) 294–301

Contents lists available at ScienceDirect

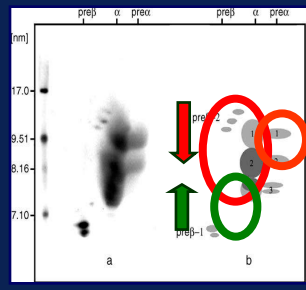
Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

Influence of menopause and cholesteryl ester transfer protein (CETP) *Taq*IB polymorphism on lipid profile and HDL subpopulations distribution in women with and without type 2 diabetes

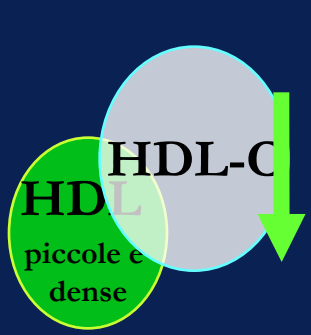
Giuseppina T. Russo[a,*], Kathleen V. Horvath[b], Antonino Di Benedetto[a], Annalisa Giandalia[a], Domenico Cucinotta[a], Bela Asztalos[b]

[a] Department of Internal Medicine, University of Messina, Italy

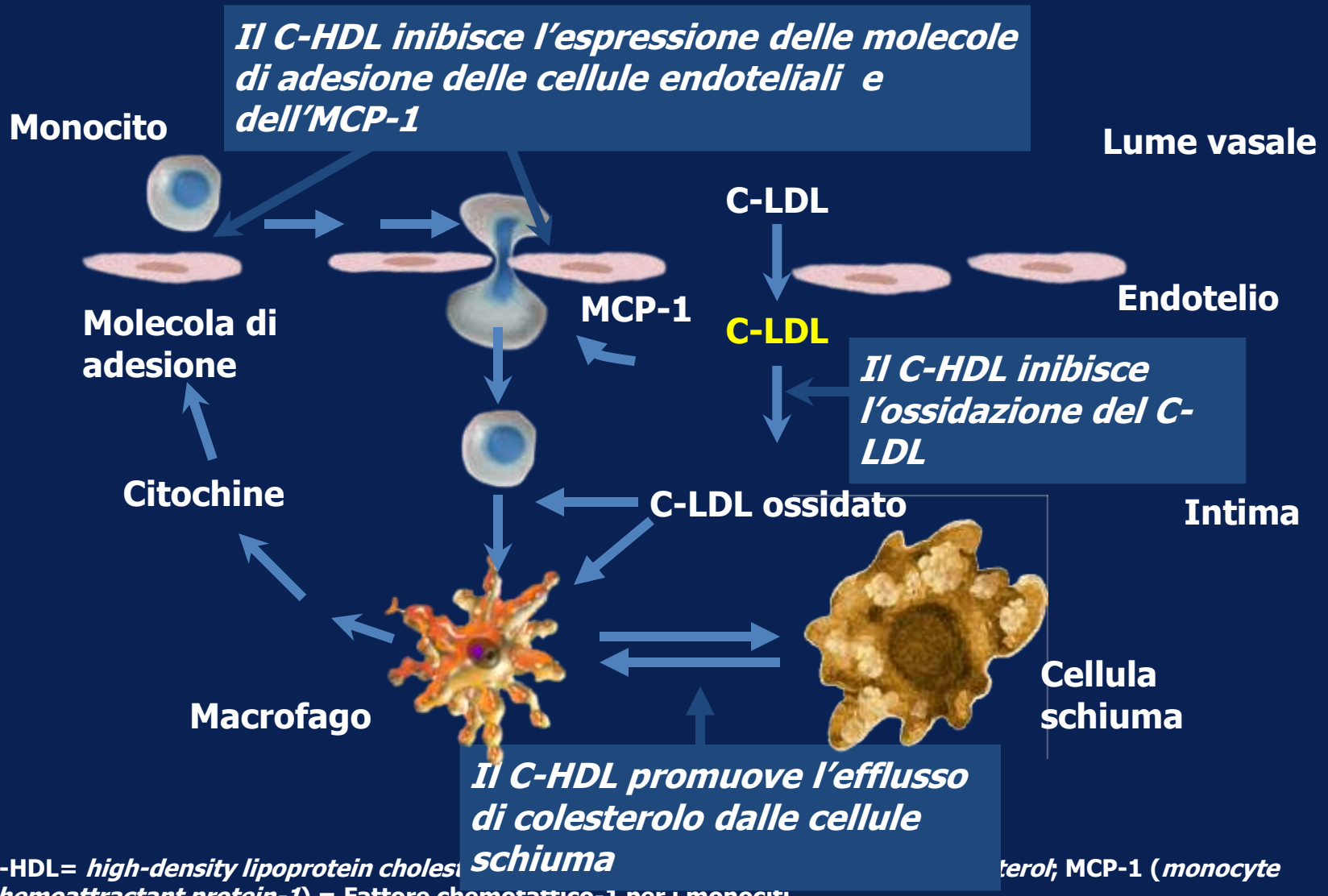


Donne DM2 senza CHD Stesso profilo sottopopolazioni HDL degli uomini con pregresso IMA

	Donne con DM2	Controlli	P
α-1 (mg/dl)	19.32±8.97	23.35±9.58	0.006
α-2 (mg/dl)	41.29±9.62	45.47±8.99	0.005
α-3 (mg/dl)	18.18±5.56	16.36±3.74	0.02
α-4 (mg/dl)	10.90±3.58	9.71±3.07	0.02
Pre-α1 (mg/dl)	5.51±3.39	6.74±3.46	0.02
Pre-α2 (mg/dl)	6.77±2.99	7.10±2.48	-
Pre-α3 (mg/dl)	2.46±0.97	1.95±0.63	0.0001
Pre-α4 (mg/dl)	1.17±0.52	0.92±0.40	0.001
Pre-β1 (mg/dl)	15.30±7.96	15.16±9.81	-
Pre-β2(mg/dl)	1.84±1.02	2.36±1.24	0.004



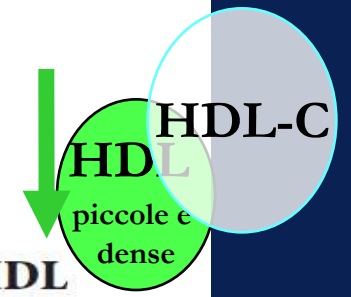
Possibili effetti anti-aterogeni del C-HDL



C-HDL= *high-density lipoprotein choles* *terol*; MCP-1 (*monocyte chemoattractant protein-1*) = Fattore chemotattico-1 per i monociti

Riproduzione autorizzata di Barter PJ et al. *Circ Res*. 2004;95:764–772.

Hindawi Publishing Corporation
International Journal of Endocrinology
Volume 2014, Article ID 607924, 9 pages
http://dx.doi.org/10.1155/2014/607924



Research Article

Markers of Systemic Inflammation and Apo-AI Containing HDL Subpopulations in Women with and without Diabetes

Giuseppina T. Russo,[1] Annalisa Giandalia,[1] Elisabetta L. Romeo,[1] Angela Alibrandi,[2] Katalin V. Horvath,[3] Bela F. Asztalos,[3] and Domenico Cucinotta[1]

[1] *Department of Clinical and Experimental Medicine, University of Messina, Via C. Valeria, 98124 Messina, Italy*

TABLE 3: Univariate and multivariate regression analysis between hsCRP and IL-6 and metabolic, lipid, and Apo-AI containing HDL subpopulations profile in total population.

	hsPCR				IL-6			
	Univariate regression		Multivariate regression		Univariate regression		Multivariate regression	
	B	*P*	*B*	*P*	*B*	*P*	*B*	*P*
Anthropometric and metabolic parameters								
Di								
BM								
W								
Sy								
Fasting BG	0.03	0.005	—	—	0.01	0.009	0.011	0.02
Fasting insulin	0.09	0.004	—	—	0.04	0.009	—	—
Lipid and Apo-AI containing HDL subpopulations profile								
HDL-C	−0.10	0.005			−0.05	0.002	—	
Apo-AI	—	—	—	—	−0.03	0.003	—	—
Apo-AII	−0.21	0.04	—	—	−0.13	0.004	—	—
α-1 HDL	−0.11	0.04	—	—	—	—	—	—
α-2 HDL	—	—	—	—	−0.06	0.009	—	—
α-3 HDL	—	—	—	—	0.11	0.04	—	—
Pre-α-1 HDL	−0.39	0.007	−0.34	0.083	−0.13	0.03	—	—

Only significant *P* are presented. Waist C: waist circumference; BP: blood pressure; BG: blood glucose; Apo: apolipoprotein.

Nelle donne con DM2, le ***sottopopolazioni HDL*** più ***ateroprotettive*** si associano a ridotti livelli di hsPCR e IL-6

Differenze di genere nella dislipidemia nel diabete di tipo 2

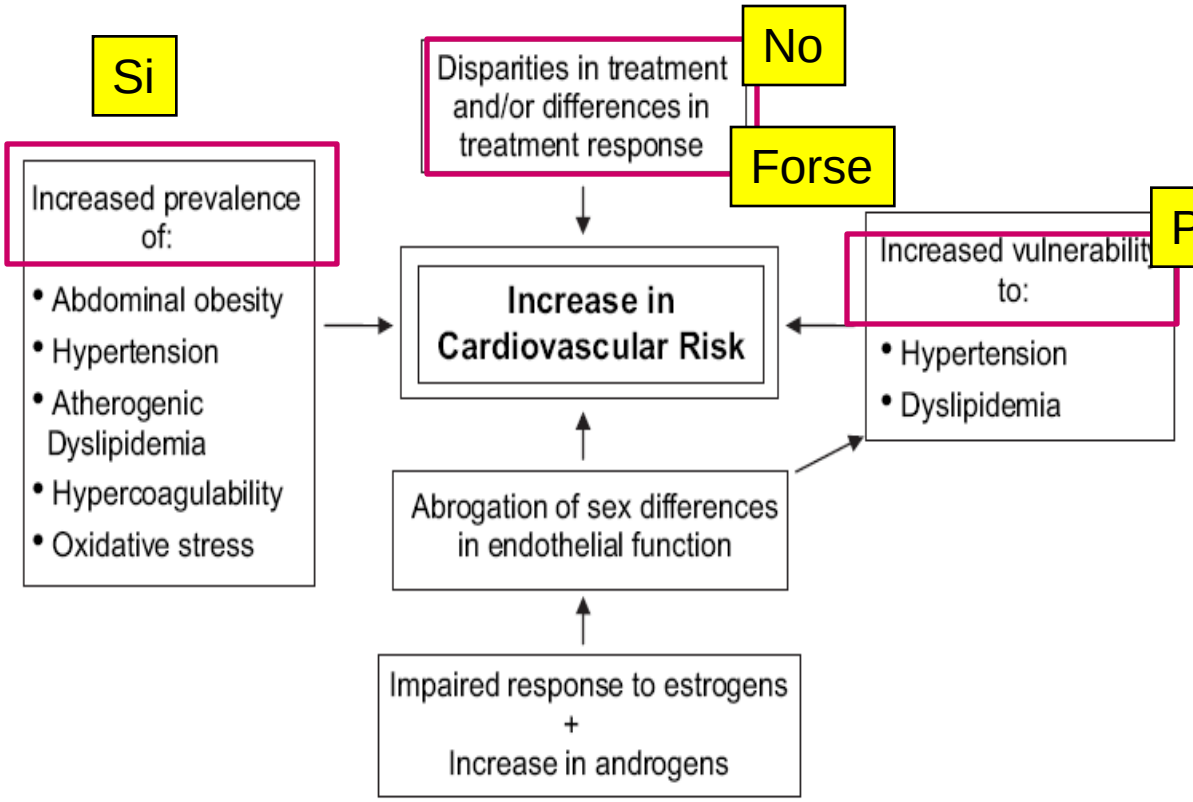


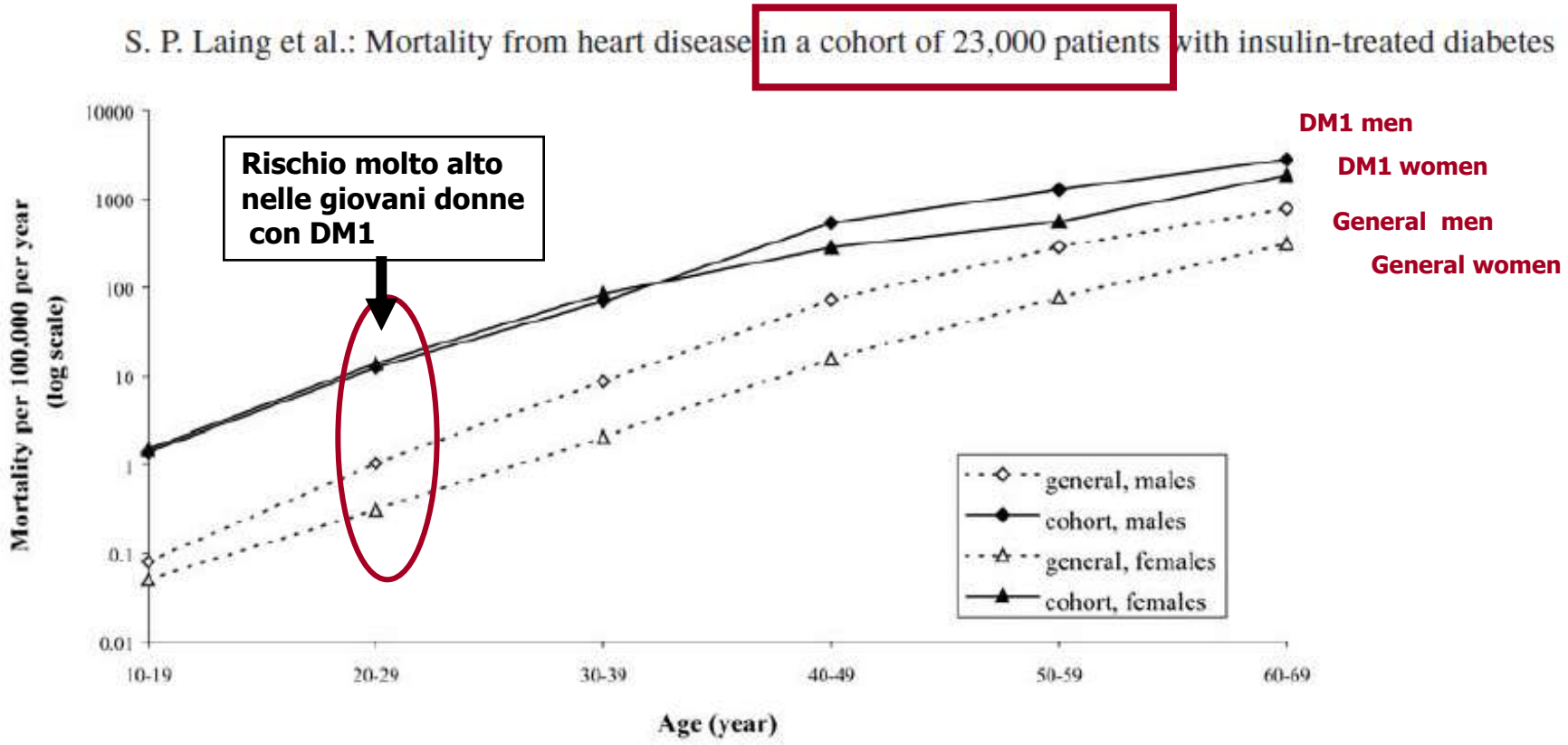
Figure 2 Possible causes of the high cardiovascular risk in women with diabetes.

Modificata da Rivellese et al., NMCD 2010

Livelli lipidici nel diabete di tipo 1 in base al genere

- ✓ **Il dimorfismo legato al genere nella dislipidemia è presente anche nel *diabete mellito di tipo 1*?**

Mortalità per cardiopatia ischemica nel diabete di tipo 1 e nella popolazione generale



Dati simili ma meno consistenti nelle donne con diabete di tipo 1

Laing SP; Diabetologia 2003

Anche nel DM1 il rischio CVD legato al diabete è maggiore nelle donne

Risk of all-cause mortality and vascular events in women versus men with type 1 diabetes: a systematic review and meta-analysis

Rachel R Huxley, Sanne A E Peters, Gita D Mishra, Mark Woodward

Summary

Background Studies have suggested sex differences in the mortality rate associated with type 1 diabetes. We did a meta-analysis to provide reliable estimates of any sex differences in the effect of type 1 diabetes on risk of all-cause mortality and cause-specific outcomes.

Methods We systematically searched PubMed for studies published between Jan 1, 1966, and Nov 26, 2014. Selected studies reported sex-specific estimates of the standardised mortality ratio (SMR) or hazard ratios associated with type 1 diabetes, either for all-cause mortality or cause-specific outcomes. We used random effects meta-analyses with inverse variance weighting to obtain sex-specific SMRs and their pooled ratio (women to men) for all-cause mortality, for mortality from cardiovascular disease, renal disease, cancer, the combined outcome of accident and suicide, and from incident coronary heart disease and stroke associated with type 1 diabetes.

Findings Data from 26 studies including 214 114 individuals and 15 273 events were included. The pooled women-to-men ratio of the SMR for all-cause mortality was 1·37 (95% CI 1·21–1·56), for incident stroke 1·37 (1·03–1·81), for fatal renal disease 1·44 (1·02–2·05), and for fatal cardiovascular diseases 1·86 (1·62–2·15). For incident coronary heart disease the sex difference was more extreme; the pooled women-to-men ratio of the SMR was 2·54 (95% CI 1·80–3·60). No evidence suggested a sex difference for mortality associated with type 1 diabetes from cancer, or accident and suicide.

Interpretation Women with type 1 diabetes have a roughly 40% greater excess risk of all-cause mortality, and twice the excess risk of fatal and nonfatal vascular events, compared with men with type 1 diabetes.

Funding None.

The Lancet, febbraio 2015

Perché le donne con DM1 hanno questo eccesso di rischio cardiovascolare?

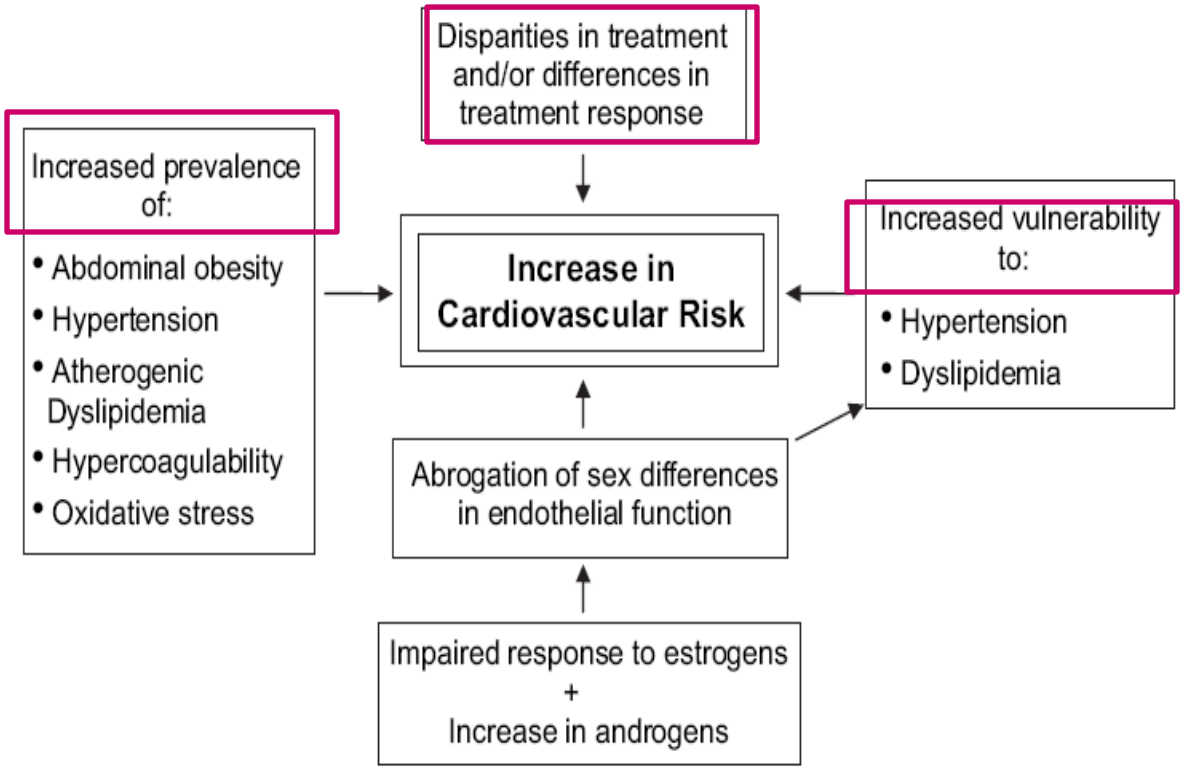


Figure 2 Possible causes of the high cardiovascular risk in women with diabetes.

Modificato da Rivellese et al., NMCD 2010

Risk Factors for Coronary Heart Disease in Type 1 Diabetic Patients in Europe

The EURODIAB Prospective Complications Study

SABITA S. SOEDAMAH-MUTHU, PHD[1]
NISH CHATURVEDI, MD[2]
MONIKA TOELLER, MD[3]
BARRY FERRISS, MD[4]
PAOLO REBOLDI, MD[5]
GEORGES MICHEL, MD[6]
CHRISTOS MANES, MD[7]
JOHN H. FULLER, FRCP[1]
THE EURODIAB PROSPECTIVE COMPLICATIONS STUDY GROUP

type 1 diabetes, and reasons for the greater impact in women are not clear. But there is a lack of large prospective studies in type 1 diabetic patients. Much of the research into CHD risk in diabetes has focused on type 2 diabetes and insulin

Table 3—*Multivariate Cox proportional hazards models for men and women separately in the EURODIAB PCS*

	Standardized hazards ratio (95% CI)*	
	Men	Women
n	1,134 (61 events)	730 (68 events)
Age (years)	1.46 (1.15–1.86)‡	1.51 (1.19–1.92)¶
WHR	1.27 (1.02–1.59)§	
Current smoking	1.54 (0.93–2.55) ($P = 0.10$)	
AER (μg/min)†	1.64 (1.36–1.97)‖	1.33 (1.09–1.63)‡
Systolic BP (mmHg)		1.25 (0.99–1.56) ($P = 0.05$)
FTG (mg/dl)†		1.25 (0.99–1.58) ($P = 0.06$)

*Standardized hazards ratios (Exp[β × SD]); †log transformed; ‡$P \leq 0.01$; §$P < 0.05$; ‖$P \leq 0.0001$; ¶$P \leq 0.001$.

Soedemah-Muthu et al., Diabetes Care 2004

Awareness and Treatment of Dyslipidemia in Young Adults With Type 1 Diabetes

R. Paul Wadwa, MD[1]
Gregory L. Kinney, MPH[2]
David M. Maahs, MD[1]
Janet Snell-Bergeon, MPH[2]
John E. Hokanson, PHD[2]
Satish K. Garg, MD[1]
Robert H. Eckel, MD[3]
Marian Rewers, MD, PHD[1]

ulation and 51% of adults aged 20–59 years with diabetes have hypercholesterolemia (4,5). European data indicate a similar prevalence of 51% of type 1 diabetic adults with dyslipidemia in the

Table 2—*Adjusted mean lipid levels (mg/dl) by sex and diabetes status, adjusted for age and waist-to-hip ratio*

	Men			Women		
	Type 1 diabetic group	Nondiabetic group	*P* value	Type 1 diabetic group	Nondiabetic group	*P* value
n	298	382	—	354	382	—
Total cholesterol	177 (172–181)	196 (192–199)	<0.0001	177 (173–180)	184 (181–187)	<0.01
LDL	105 (102–109)	122 (119–125)	<0.0001	98 (95–101)	106 (103–109)	<0.001
HDL	51 (50–53)	43 (42–44)	<0.0001	61 (59–62)	58 (56–59)	<0.01
Triglycerides*	87 (82–92)	128 (122–134)	<0.0001	81 (77–85)	92 (88–96)	<0.0001

Data are least-squares means adjusted for age and waist-to-hip ratio expressed as mean (95% CI). *Triglycerides analyzed in log scale and reported as geometric mean (95% CI).

DM1 M and W better lipid profile than Controls

Gruppo Donna

Anche nel DM1, la prevalenza di qualsiasi tipo di alterazione lipidica aumenta con l'età.

Epidemiology/Health Services/Psychosocial Research
ORIGINAL ARTICLE

Spectrum and Prevalence of Atherogenic Risk Factors in 27,358 Children, Adolescents, and Young Adults With Type 1 Diabetes

Cross-sectional data from the German diabetes documentation and quality management system (DPV)

K. Otfried Schwab, MD[1]
Jürgen Doerfer, MD[1]
Wolfgang Hecker, MD[2]
Jürgen Grulich-Henn, MD[3]
Peter Beyer, MD[6]
Reinhard W. Holl, MD[7]
on behalf of the DPV Initiative of the German Working Group for

Type 1 diabetes is increasingly recognized as an independent risk factor for premature cardiovascular disease (CVD) and elevated cardiovascular

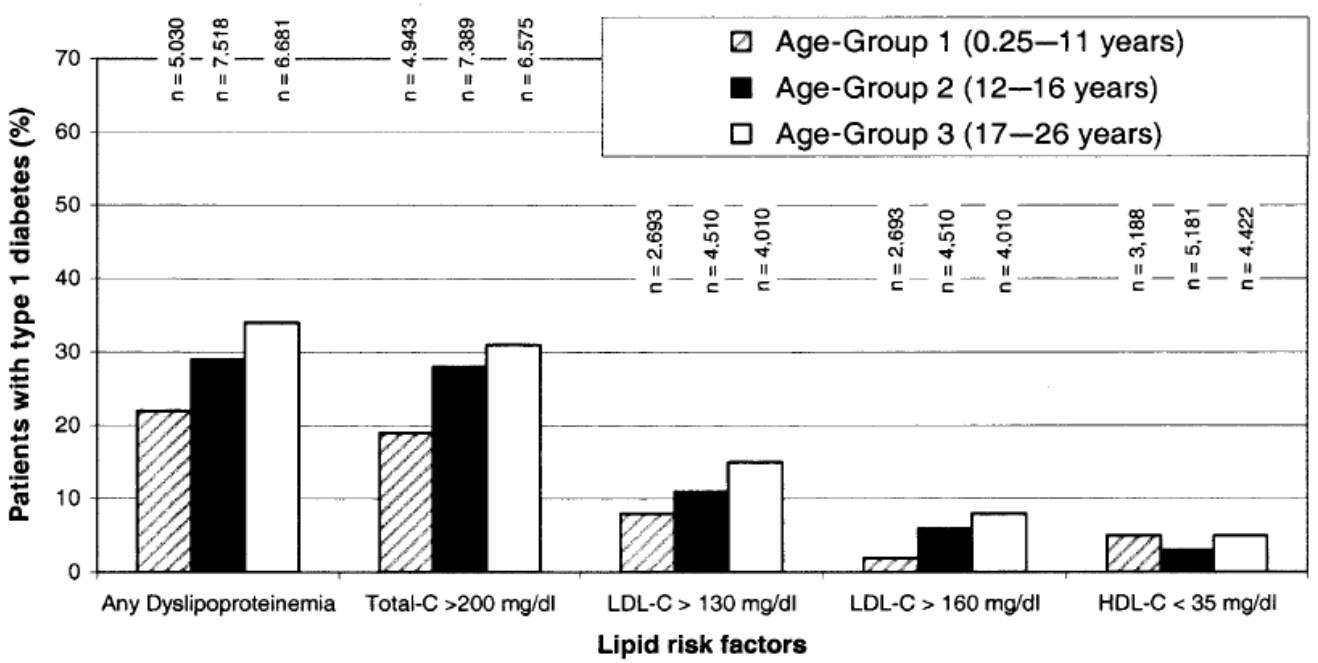


Figure 1—*Age distribution of cardiovascular risk factors, divided into nonlipid and lipid parameters. The total number of patients investigated per age-group is shown above each bar.*

Gruppo Donna

Le donne con DM1 hanno comunque un peggior profilo lipidico rispetto agli uomini con DM1

Epidemiology/Health Services/Psychosocial Research
ORIGINAL ARTICLE

Spectrum and Prevalence of Atherogenic Risk Factors in 27,358 Children, Adolescents, and Young Adults With Type 1 Diabetes

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Olga Kordonouri, MD[5]
Peter Beyer, MD[6]
Reinhard W. Holl, MD[7]
on behalf of the DPV Initiative of the German Working Group for Pediatric Diabetology

Type 1 diabetes is increasingly recognized as an independent risk factor for premature cardiovascular disease (CVD) and elevated cardiovascular death rate in patients aged 20–39 years (1). Postmortem studies in children and youth who had died an unnatural death

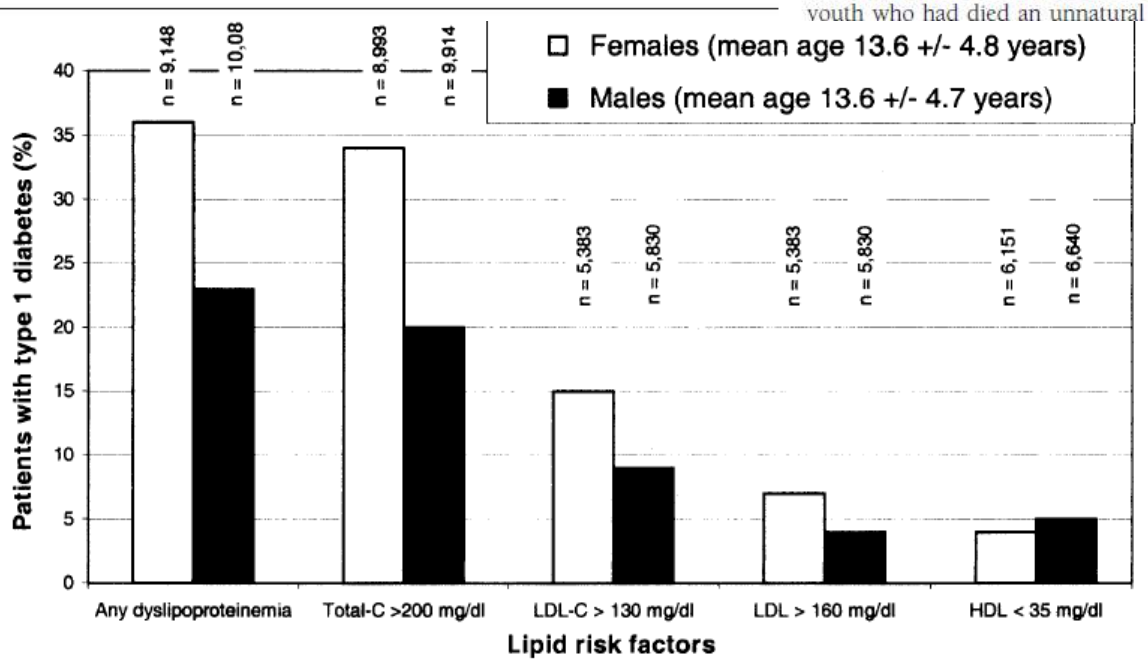

Figure 2—*Sex distribution of cardiovascular risk factors, divided into nonlipid and lipid parameters. The total number of patients investigated is shown above each bar.*

ORIGINAL ARTICLE

Lipoprotein Subfraction Cholesterol Distribution Is Proatherogenic in Women With Type 1 Diabetes and Insulin Resistance

David M. Maahs,[1] John E. Hokanson,[2] Hong Wang,[3] Gregory L. Kinney,[1] Janet K. Snell-Bergeon,[1] Ashley East,[1] Bryan C. Bergman,[3] Irene E. Schauer,[3] Marian Rewers,[1] and Robert H. Eckel[3]

OBJECTIVE—Individuals with type 1 diabetes have a less atherogenic fasting lipid profile than those without diabetes but paradoxically have increased rates of cardiovascular disease (CVD). We investigated differences in lipoprotein subfraction cholesterol distribution and insulin resistance between subjects with and without type 1 diabetes to better understand the etiology of increased CVD risk.

RESEARCH DESIGN AND METHODS—Fast protein liquid chromatography was used to fractionate lipoprotein cholesterol distribution in a substudy of the Coronary Artery Calcification in Type 1 Diabetes (CACTI) study (n = 82, age 46 ± 8 years, 52% female, 49% with type 1 diabetes for 23 ± 8 years). Insulin resistance was assessed by a hyperinsulinemic-euglycemic clamp.

RESULTS—Among men, those with type 1 diabetes had less VLDL and more HDL cholesterol than control subjects ($P < 0.05$), but among women, those with diabetes had a shift in cholesterol to denser LDL, despite more statin use. Among control subjects, men had more cholesterol distributed as VLDL and LDL but less as HDL than women; however, among those with type 1 diabetes, there was no sex difference. Within sex and diabetes strata, a more atherogenic cholesterol distribution by insulin resistance was seen in men with and without diabetes, but only in women with type 1 diabetes.

CONCLUSIONS—The expected sex-based less atherogenic lipoprotein cholesterol distribution was not seen in women with type 1 diabetes. Moreover, insulin resistance was associated with a more atherogenic lipoprotein cholesterol distribution in all men and in women with type 1 diabetes. This lipoprotein cholesterol distribution may contribute to sex-based differences in CVD in type 1 diabetes. *Diabetes* 59:1771–1779, 2010

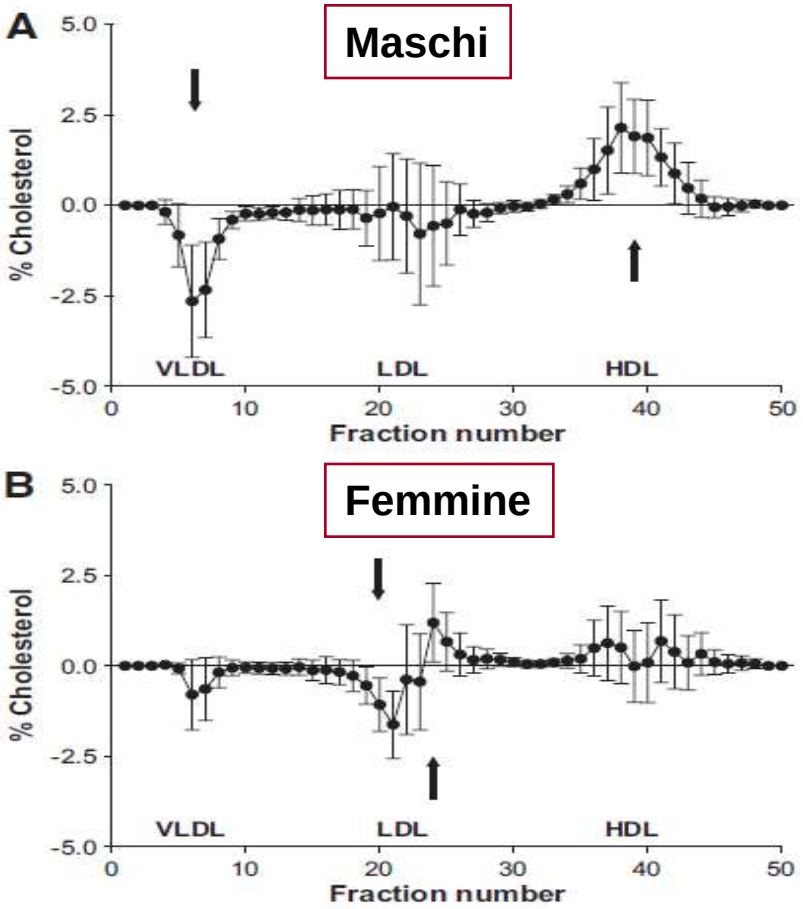

FIG. 4. *A*: Differences in FPLC lipoprotein distribution by type 1 diabetes in male subjects (male type 1 diabetic − male nondiabetic). *B*: Differences in FPLC lipoprotein distribution by type 1 diabetes in female subjects (female type 1 diabetic − female nondiabetic).

Epidemiology/Health Services Research
ORIGINAL ARTICLE

Lipid and Lipoprotein Profiles in Youth With and Without Type 1 Diabetes

The SEARCH for Diabetes in Youth Case-Control Study

Ruolo del compenso glicemico

R. PAUL WADWA, MD[3]
RICHARD F. HAMMAN, MD, DRPH[1]
ELIZABETH J. MAYER-DAVIS, PHD[4]
SANTICA MARCOVINA, PHD[7]
DANA DABELEA, MD, PHD[1]

scribed as comparable to those in nondi-
abetic individuals (5), adults with type 1
diabetes are known to have a higher risk

Lipid and lipoprotein profiles

DM1 better than Controls

DM1 worst than Controls

Table 2—*Lipid levels in nondiabetic control youth and youth with type 1 diabetes with optimal (A1C <7.5%) and suboptimal (A1C ≥7.5%) glycemic control*

Variable	Type 1, A1C <7.5%	*P* value*	Control	*P* value†	Type 1, A1C ≥7.5%
	164		188		348
Cholesterol (mg/dl)	155.6 (151.0–160.3)	0.8	156.2 (152.0–160.5)	<0.0001	169.8 (165.8–174.0)
LDL cholesterol (mg/dl)	91.2 (87.3–95.3)	0.7	91.9 (88.3–95.6)	0.0003	100.1 (96.9–103.5)
Triglyceride (mg/dl)	62.8 (58.5–67.3)	<0.0001	81.2 (75.5–87.4	0.2	76.6 (71.8–81.7)
HDL cholesterol (mg/dl)	50.6 (48.7–52.5)	<0.0001	46.1 (44.4–47.7)	<0.0001	52.3 (50.8–53.8)
Non–HDL cholesterol (mg/dl)	104.5 (100.4–108.8)	0.07	109.4 (105.4–113.5)	0.006	116.5 (112.7–120.4)
Triglyceride-to–HDL cholesterol ratio	1.45 (1.29–1.60)	<0.0001	2.10 (1.89–2.31)	0.9	2.14 (1.73–2.55)
ApoB (mg/dl)	69.1 (65.9–72.5)	<0.0001	54.3 (52.0–56.7)	<0.0001	76.9 (74.1–79.9)
LDL (R_f)	0.283 (0.280–0.286)	0.4	0.282 (0.279–0.285)	<0.001	0.275 (0.272–0.278)

Data are adjusted means (95% CI). *Type 1 diabetes and A1C <7.5 versus control. †Type 1 diabetes and A1C ≥7.5 versus control.

THE JOURNAL OF PEDIATRICS • www.jpeds.com

ORIGINAL ARTICLES

Glucose Control Predicts 2-Year Change in Lipid Profile in Youth with Type 1 Diabetes

David M. Maahs, MD, PhD[1,2,3], Dana Dabelea, MD, PhD[2], Ralph B. D'Agostino, Jr., PhD[4], Jeannette S. Andrews, MS[4], Amy S. Shah, MD[5], Nancy Crimmins, MD[5], Elizabeth J. Mayer-Davis, PhD[6], Santica Marcovina, PhD[7], Giuseppina Imperatore, MD, PhD[8], R. Paul Wadwa, MD[1], Steven R. Daniels, MD, PhD[3], Kristi Reynolds, MPH, PhD[9], Richard F. Hamman, MD, DrPH[2], and Lawrence M. Dolan, MD[5], for the SEARCH for Diabetes in Youth Study*

Se glicata in 2 anni passa da 10% → 8%:

TC: *-11.4 mg/dl*
HDL-C: *+1.3 mg/dl*
LDL-C: *-9.0 mg/dl*
Non HDL-C: -12 mg/dl

Table II. Associations of change in A1c to change in lipids*

Covariates of interest†	β	95% CI Lower	95% CI Upper	P
TC				
Initial A1c, %	−0.084 [−3.234]	−0.170 [−6.559]	0.002 [0.092]	
Time-dependent A1c, %	0.034 [1.307]	−0.033 [−1.286]	0.101 [3.900]	
Initial × TD A1c interaction	0.013 [0.512]	0.005 [0.181]	0.022 [0.843]	.0025
T1D duration, mo	0.002 [0.062]	−0.000 [−0.002]	0.003 [0.126]	.0572
HDL-c				
Initial A1c, %	0.066 [2.569]	0.031 [1.192]	0.102 [3.946]	
Time-dependent A1c, %	0.061 [2.360]	0.033 [1.275]	0.089 [3.444]	
Initial × TD A1c interaction	−0.006 [−0.222]	−0.009 [−0.360]	−0.002 [−0.084]	.0016
T1D duration, mo	0.002 [0.652]	0.001 [0.038]	0.002 [0.093]	<.0001
LDL-c				
Initial A1c, %	−0.034 [−1.326]	−0.104 [−4.022]	0.035 [1.371]	
Time-dependent A1c, %	0.027 [1.041]	−0.027 [−1.032]	0.081 [3.114]	
Initial × TD A1c interaction	0.007 [0.266]	−0.000 [−0.001]	0.014 [0.532]	.0506
T1D duration, mo	−0.002 [−0.067]	−0.003 [−0.116]	−0.001 [−0.019]	.0062
Non–HDL-c				
Initial A1c, %	−0.149 [−5.761]	−0.227 [−8.794]	−0.071 [−2.728]	
Time-dependent A1c, %	−0.025 [−0.974]	−0.086 [−3.336]	0.036 [1.387]	
Initial × TD A1c interaction	0.018 [0.713]	0.011 [0.411]	0.026 [1.015]	<.0001
T1D duration, mo	−0.000 [−0.002]	−0.002 [−0.060]	0.001 [0.056]	.94
TG (log)‡				
Initial A1c, %	−0.121	−0.171	−0.070	
Time-dependent A1c, %	−0.037	−0.078	0.003	
Initial × TD A1c interaction	0.013	0.008	0.018	<.0001
T1D duration, mo	0.004	0.003	0.005	<.0001

*Values given in mmol/L [mg/dL].
†Multivariable model also adjusts for: site, BMI z score, sex, race/ethnicity, age and age², and season of the year.
‡Coefficients are unchanged since log-transformation means that unit conversion is captured in the intercept term.

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Lipoproteins in the DCCT/EDIC cohort: Associations with diabetic nephropathy

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Ruolo del compenso glicemico

Table 1. Clinical characteristics of Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) study subjects at time of sample acquisition

	Women (N = 425)			Men (N = 533)		
	Intensive (N = 222) Mean (SE)	Conventional (N = 203) Mean (SE)	P	Intensive (N = 270) Mean (SE)	Conventional (N = 263) Mean (SE)	P
Age *years*	39.9 (0.5)	38.4 (0.5)	<0.05	39.9 (0.4)	40.2 (0.4)	NS
Duration of type 1 diabetes *years*	17.6 (0.3)	17.8 (0.4)	NS	17.5 (0.3)	16.8 (0.3)	NS
Body mass index *kg/m²*	26.8 (0.3)	25.9 (0.3)	<0.05	27.3 (0.3)	27.0 (0.2)	NS
Waist-to-hip ratio	0.8 (0.0)	0.8 (0.0)	NS	0.9 (0.0)	0.9 (0.0)	NS
Current HbA_{1c} *% hemoglobin*	8.2 (0.1)	8.2 (0.1)	NS	8.1 (0.1)	8.3 (0.1)	<0.05
Mean HbA_{1c} during DCCT *% hemoglobin*	7.3 (0.1)	9.1 (0.1)	<0.0001	7.2 (0.1)	9.0 (0.1)	<0.0001
Systolic blood pressure *mm Hg*	116.9 (1.0)	115.0 (0.9)	NS	121.1 (0.7)	123.6 (0.9)	<0.05
Diastolic blood pressure *mm Hg*	73.3 (0.6)	72.2 (0.6)	NS	76.4 (0.5)	77.3 (0.6)	NS
Total cholesterol *mg/dL*	189.0 (2.2)	187.1 (2.3)	NS	190.0 (2.2)	188.7 (2.2)	NS
HDL (conventional profile; chol.) *mg/dL*	63.0 (1.0)	62.7 (1.0)	NS	51.2 (0.8)	51.7 (0.7)	NS
LDL (conventional profile; chol.) *mg/dL*	110.9 (2.0)	108.8 (2.1)	NS	118.8 (1.9)	118.1 (1.9)	NS
Triglycerides (conventional profile) *mg/dL*	75.7 (2.5)	78.0 (4.0)	NS	98.2 (4.1)	96.2 (4.5)	NS
Log albumin excretion rate *mg/24 hours*	2.3 (0.1)	2.6 (0.1)	0.003	2.5 (0.1)	3.0 (0.1)	<0.001
Albumin excretion rate *mg/24hours*	49.3 (27.7)	74.0 (28.9)	NS	92.2 (43.7)	159.7 (44.3)	NS
Standard creatinine clearance *mL/min*	110.9 (1.6)	110.3 (1.7)	NS	120.6 (1.4)	119.2 (1.6)	NS
ETDRS score	3.2 (0.2)	5.3 (0.3)	<0.0001	3.7 (0.2)	5.7 (0.2)	<0.0001
	% (SE)	% (SE)	P	% (SE)	% (SE)	P
% Body mass index >27.3 in women, >27.8 in men *kg/m²*	39.3 (0.2)	28.2 (0.6)	<0.02	38.5 (0.2)	36.3 (0.5)	NS
% Hypertension[a]	26.1 (0.2)	26.2 (0.6)	NS	42.1 (0.2)	47.3 (0.5)	NS
% Albumin excretion ratio >40 mg/24 hours	6.8 (0.1)	16.8 (0.5)	0.001	11.5 (0.1)	20.5 (0.4)	<0.005
% Current smoker	20.9 (0.2)	17.3 (0.5)	NS	20.3 (0.1)	18.3 (0.4)	NS
% Taking lipid-lowering medications	4.0 (0.1)	3.9 (0.3)	NS	7.3 (0.1)	6.0 (0.2)	NS
% Taking ACE inhibitor	6.7 (0.1)	13.8 (0.5)	<0.02	12.4 (0.1)	17.7 (0.4)	NS

Abbreviations are: ACE, angiotensin-converting enzyme; HDL, high-density lipoprotein; LDL, low-density lipoprotein; HbA_{1c}, hemoglobin A_{1c}.
[a]Hypertension is defined by previously documented or current systolic blood pressure/diastolic blood pressure equal or greater than 140/90 mm Hg

Kautzky-Willer *et al. Cardiovascular Diabetology* 2013, **12**:78
http://www.cardiab.com/content/12/1/78

CARDIO VASCULAR DIABETOLOGY

ORIGINAL INVESTIGATION **Open Access**

Sex-specific-differences in cardiometabolic risk in type 1 diabetes: a cross-sectional study

Alexandra Kautzky-Willer[1*], Kathrin Stich[2], Juliane Hintersteiner[2], Alexander Kautzky[1], Majid Reza Kamyar[2], Johannes Saukel[3], Julienne Johnson[4] and Rosa Lemmens-Gruber[2]

Ci sono solo poche evidenze su differenze di genere nel profilo lipidico in ADULTI con DM1 …..

Table 1 Demographic data and clinical characteristics of T1DM patients

Characteristics	Women (n=102)	Men (n=123)
Age (years)	41.3±13.6	43.1±13.9
Percentage of geriatric patients (>60 years)	8.8	13.8
Age (years) at diagnosis	19.2±10.2	21.4±11.5
Duration (years) of disease	19.3±7.7	17.3±10.4
Smokers (%)	29.1	36.3
Alcohol abstinence (%)	53.5^{555}	20.4
Metabolic syndrome (%)	12.6	14.3
Blood glucose (mg/dl)	122.9±50.4	123.8±56.4
HbA1c (%)	7.6±1.0	7.5±1.1
HbA1c<6.5% (%)	26.5	29.3
Hypertension (%)	44.2	46.7
Systolic blood pressure (mmHg)	135.5±18.9	136.9±17.4
Diastolic blood pressure (mmHg)	82.7±12.3	82.9±8.7
BMI (kg/m^2)	25.5±4.9	26.3±3.4
Overweight (%)	33.3	44.7^{555}
Obese (%)	12.7	13.0
Hyperlipidaemia (%)	46.3	35.2
Total cholesterol (mg/dl)	203.1±38.3	186.7±33.6**
HDL cholesterol (mg/dl)	70.6±19.9	59.1±15.9***
LDL cholesterol (mg/dl)	111.1±32.2	103.4±28.2
Total cholesterol/HDL ratio	3.3±1.6	3.6±1.4
Triglycerides (mg/dl)	106.6±69.1	124.6±71.8

Data are shown as mean±SE.
^{555} $P < 0.001$ by χ^2 test, ** $P < 0.01$ by t test, *** $P < 0.001$ by t test.

Kautzky-Willer et al. Cardiovascular Diabetology 2013, 12:78
http://www.cardiab.com/content/12/1/78

Livelli lipidici nel diabete di tipo 1 in base al genere

Il dimorfismo legato al genere nella dislipidemia è presente anche nel *diabete mellito di tipo 1?*

- **28.802 DT1 *ADULTI* seguiti da 320 servizi di diabetologia in Italia.**
- **M e F sono risultati simili per età** (F: 45±16 a.; M: 45±17a)
- e **durata del Diabete** (F:19±13 a., M:18±13a).

Livelli di *CT* per età, durata diabete e genere nel DM1

Valori medi di colesterolo totale (media e ds) in relazione al genere e alle classi di età e di durata del diabete

	Femmine	Maschi
Popolazione totale	192,6 ± 35,0	184,0 ± 36,0
Classi di età		
≤ 25	183,5 ± 38,0	167,9 ± 34,0
25-45	191,2 ± 35,0	188,4 ± 37,0
45-55	197,4 ± 34,0	189,8 ± 36,0
> 55	194,4 ± 35,0	178,1 ± 35,0
Classi di durata		
≤ 2	188,4 ± 38,0	184,1 ± 41,0
2-5	189,2 ± 34,5	184,3 ± 38,1
5-10	189,8 ± 35,0	183,9 ± 38,0
10-20	193,2 ± 35,0	184,7 ± 35,0
> 20	194,2 ± 35,0	183,4 ± 36,0

Le donne presentano valori di colesterolo totale più elevati di circa 9 mg/dl rispetto agli uomini.

Le differenze più marcate, pari a circa 16 mg/dl, si riscontrano nelle fasce di età più giovane e più avanzata.

Livelli di *HDL-C* per età, durata diabete e genere nel DM1

Valori medi di colesterolo HDL (media e ds) in relazione al genere e alle classi di età e di durata del diabete

	Femmine	Maschi
Popolazione totale	67,4 ± 16,4	56,5 ± 15,0
Classi di età		
≤ 25	63,5 ± 15,2	54,3 ± 12,9
25-45	66,7 ± 15,3	55,8 ± 14,4
45-55	68,8 ± 16,5	57,3 ± 15,8
> 55	68,8 ± 17,7	57,8 ± 16,3
Classi di durata		
≤ 2	62,7 ± 16,3	52,2 ± 15,1
2-5	67,2 ± 16,0	56,0 ± 14,7
5-10	67,6 ± 16,7	56,5 ± 14,6
10-20	68,0 ± 16,1	56,2 ± 14,8
> 20	67,9 ± 16,4	57,9 ± 15,4

Maggior parte popolazione a *target* con HDL-C >50 mg/dl nelle F >40 mg/dl negli U

I livelli target di colesterolo HDL sono diversi nei due sessi (sopra i 40 mg/dl per i maschi e sopra i 50 mg/dl per le femmine); la distanza tra valore medio e valore di riferimento è indice di valori di HDL tendenzialmente più favorevoli nelle donne che negli uomini, anche se con leggere differenze tra i sessi.

Livelli di *Trigliceridi* per età, durata diabete e genere nel DM1

Valori medi di trigliceridi (media e ds) in relazione al genere e alle classi di età e di durata del diabete

	Femmine	Maschi
Popolazione totale	82,7 ± 55,6	97,0 ± 89,0
Classi di età		
≤ 25	83,9 ± 78,2	83,4 ± 70,8
25-45	76,8 ± 48,5	97,0 ± 103,0
45-55	80,3 ± 50,9	100,8 ± 77,0
> 55	91,1 ± 55,7	98,8 ± 78,4
Classi di durata		
≤ 2	89,9 ± 79,3	119,6 ± 194,0
2-5	78,7 ± 50,5	97,6 ± 78,5
5-10	81,3 ± 70,1	94,0 ± 86,8
10-20	81,6 ± 54,2	94,0 ± 65,8
> 20	82,4 ± 44,5	93,7 ± 61,1

I livelli di trigliceridi risultano di 15 mg/dl più elevati negli uomini. I valori sono sistematicamente più elevati a partire dai 25 anni di età e in tutte le classi di durata del diabete.

Livelli di *LDL-C* per età, durata diabete e genere nel DM1

Valori medi di colesterolo LDL (media e ds) in relazione al genere e alle classi di età e di durata del diabete

	Femmine	Maschi
Popolazione totale	108,0 ± 29,0	108,2 ± 30,0
Classi di età		
≤25	102,6 ± 29,0	98,2 ± 30,0
25-45	108,5 ± 29,0	113,5 ± 30,0
45-55	111,8 ± 29,0	112,0 ± 31,0
>55	106,7 ± 30,0	100,6 ± 29,0
Classi di durata		
≤2	107,5 ± 30,8	110,2 ± 32,3
2-5	105,4 ± 29,0	108,9 ± 31,0
5-10	105,6 ± 28,0	108,5 ± 31,0
10-20	108,3 ± 29,0	109,6 ± 30,0
>20	109,0 ± 29,0	106,5 ± 30,0

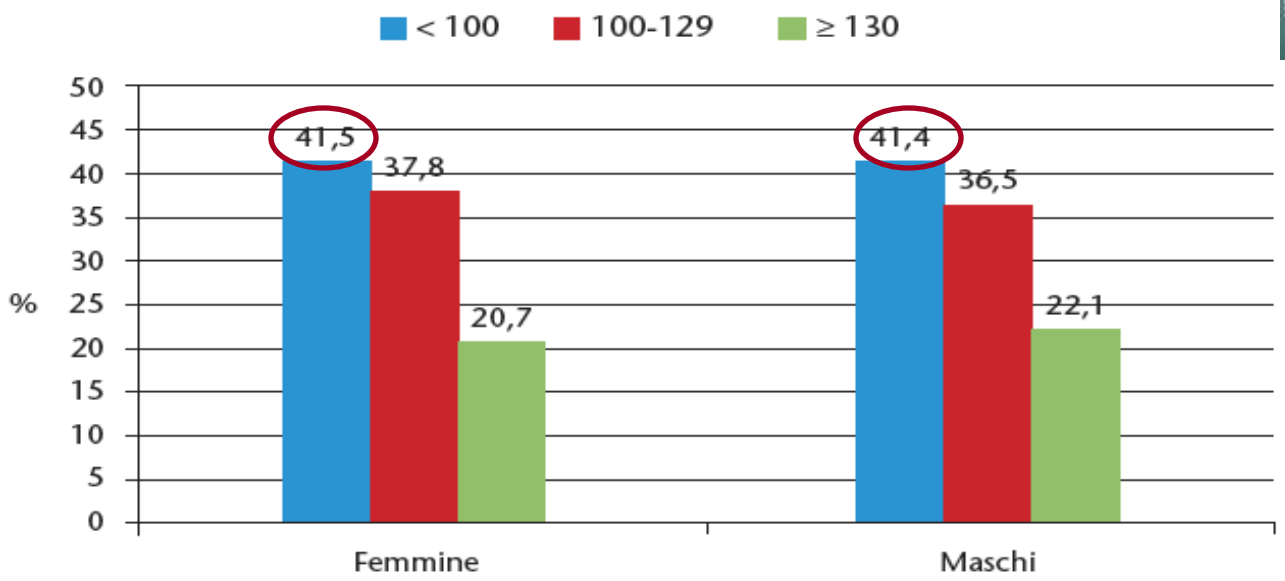
Tra M e F con DM1, differenze minime nei livelli di LDL-C

I valori medi di colesterolo LDL sono del tutto sovrapponibili tra i due sessi. L'esame delle classi di età e di durata mostra che le donne presentano livelli più favorevoli degli uomini per fasce di età intermedie e di durata più basse.

Livelli di *LDL-C* per età, durata diabete e genere nel DM1

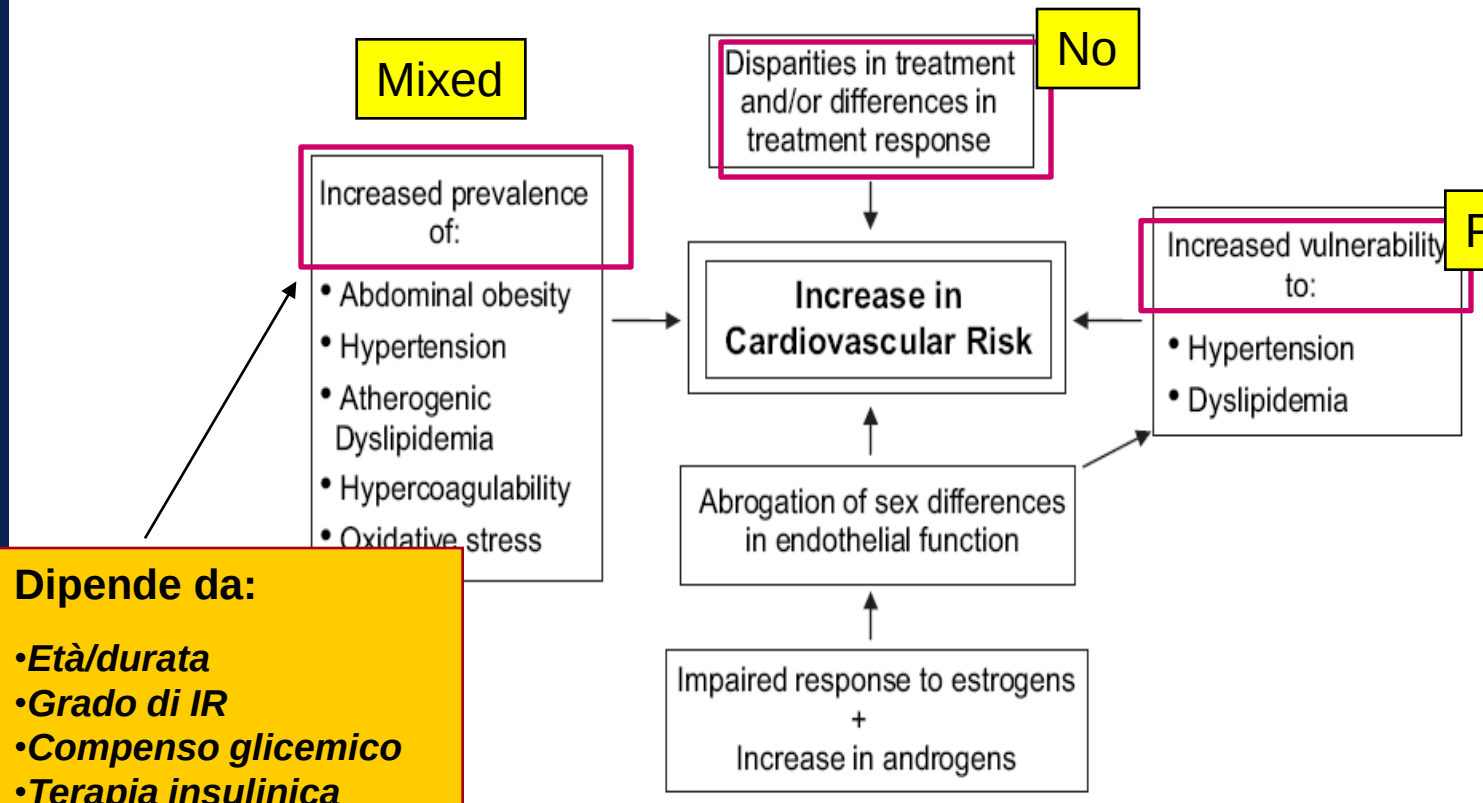
Controllo lipidico

Andamento per classi del colesterolo LDL (mg/dl) (%)



In entrambi i sessi circa il 40% è a target di colesterolo LDL e circa un quinto del campione presenta valori francamente elevati.

Differenze di genere nella dislipidemia nel diabete di tipo 1



Dipende da:

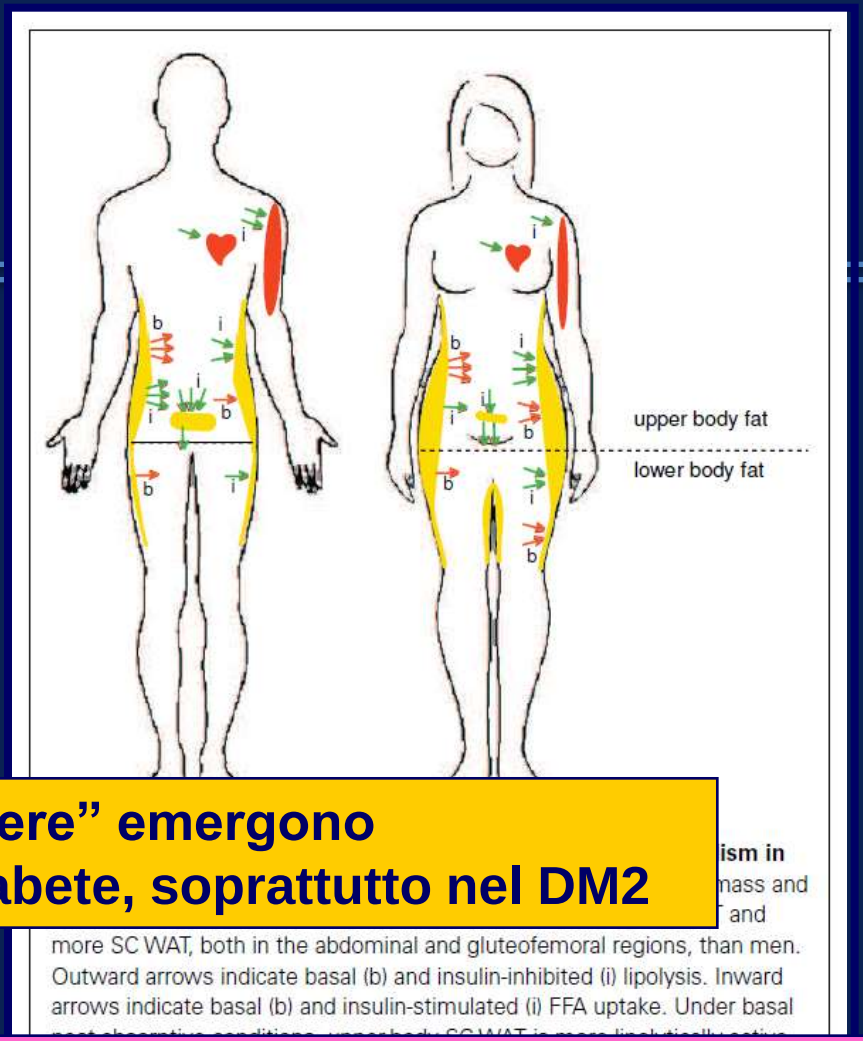
- ***Età/durata***
- ***Grado di IR***
- ***Compenso glicemico***
- ***Terapia insulinica***

Figure 2 Possible causes of the high cardiovascular risk in women with diabetes.

Modificata da Rivellese et al., NMCD 2010

Conclusioni:

Uomini e donne non sono uguali nemmeno sotto il profilo lipidico.



ism in
mass and
and
more SC WAT, both in the abdominal and gluteofemoral regions, than men. Outward arrows indicate basal (b) and insulin-inhibited (i) lipolysis. Inward arrows indicate basal (b) and insulin-stimulated (i) FFA uptake. Under basal

Queste differenze di "genere" emergono anche nei pazienti con diabete, soprattutto nel DM2

Le donne con *DM2* hanno una maggiore prevalenza di dislipidemia e non raggiungono i target desiderati nonostante la terapia, il che potrebbe in parte spiegare il loro elevato rischio cardiovascolare.

Nel *DM1* non ci sono differenze di genere nel raggiungimento dei target lipidici e l'impatto della dislipidemia sul rischio cardiovascolare è ancora controverso.

Gruppo Donna

Grazie per l'attenzione!

G.

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Editorial

Type 2 Diabetes and Cardiovascular Risk in Women

Giuseppina T. Russo,[1] Giovannella Baggio,[2] Maria Chiara Rossi,[3] and Alexandra Kautzky-Willer[4,5]

International Journal Endocrinology 2015

Efficacy of cholesterol-lowering therapy in 18 686 people with diabetes in 14 randomised trials of statins: a meta-analysis

*Cholesterol Treatment Trialists' (CTT) Collaborators**

Summary

Background Although statin therapy reduces the risk of occlusive vascular events in people with diabetes mellitus, there is uncertainty about the effects on particular outcomes and whether such effects depend on the type of diabetes, lipid profile, or other factors. We undertook a prospective meta-analysis to help resolve these uncertainties.

Methods We analysed data from 18 686 individuals with diabetes (1466 with type 1 and 17 220 with type 2) in the context of a further 71 370 without diabetes in 14 randomised trials of statin therapy. Weighted estimates were obtained of effects on clinical outcomes per 1·0 mmol/L reduction in LDL cholesterol.

Findings During a mean follow-up of 4·3 years, there were 3247 major vascular events in people with diabetes. There was a 9% proportional reduction in all-cause mortality per mmol/L reduction in LDL cholesterol in participants with diabetes (rate ratio [RR] 0·91, 99% CI 0·82–1·01; p=0·02), which was similar to the 13% reduction in those without diabetes (0·87, 0·82–0·92; p<0·0001). This finding reflected a significant reduction in vascular mortality (0·87, 0·76–1·00; p=0·008) and no effect on non-vascular mortality (0·97, 0·82–1·16; p=0·7) in participants with diabetes. There was a significant 21% proportional reduction in major vascular events per mmol/L reduction in LDL cholesterol in people with diabetes (0·79, 0·72–0·86; p<0·0001), which was similar to the effect observed in those without diabetes (0·79, 0·76–0·82; p<0·0001). In diabetic participants there were reductions in myocardial infarction or coronary death (0·78, 0·69–0·87; p<0·0001), coronary revascularisation (0·75, 0·64–0·88; p<0·0001), and stroke (0·79, 0·67–0·93; p=0·0002). Among people with diabetes the proportional effects of statin therapy were similar irrespective of whether there was a prior history of vascular disease and irrespective of other baseline characteristics. After 5 years, 42 (95% CI 30–55) fewer people with diabetes had major vascular events per 1000 allocated statin therapy.

Interpretation Statin therapy should be considered for all diabetic individuals who are at sufficiently high risk of vascular events.

Lancet 2008; 371: 117–25

See Comment page 94

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Introduction

At least 170 million people worldwide are estimated to have diabetes mellitus, and this number is predicted to more than double by 2030.[1] The rapid rise in prevalence is mainly attributable to an increased incidence of type 2 diabetes. Since both types of diabetes are associated with a substantially increased risk of atherosclerotic vascular disease,[2–4] identification of treatments for the prevention of major occlusive vascular events is a public-health priority.

Both types of diabetes are associated with dyslipidaemia, but the pattern of abnormality differs between them. In type 2 diabetes, triglyceride concentrations are high but HDL cholesterol concentrations tend to be low, whereas in type 1 diabetes triglyceride concentrations are generally lower than those in type 2 diabetes, and HDL cholesterol levels are average or even high.[5] In both diseases, the concentration of LDL cholesterol in the blood is generally similar to the population average, although this apparently benign pattern can mask an increase in atherogenic small dense LDL particles.[6] Observational studies in different populations have shown that a positive log-linear relation exists between blood LDL cholesterol and the risk of coronary heart disease, with this association continuing well below the range of typical cholesterol levels in developed countries.[4,7,8] For example, in around 360 000 men who were screened for the Multiple Risk Factor Intervention Trial (MRFIT),[4] every 1 mmol/L lower blood total cholesterol was associated with about a 50% lower risk of death from coronary heart disease, irrespective of blood cholesterol at baseline. In the 5000 men who had reported a history of diabetes at the baseline assessment for MRFIT, the relation between blood cholesterol and risk of coronary mortality was of similar magnitude, but the absolute risk of coronary mortality was three to five times higher than it was in those without diabetes.[9]

We have previously reported the results of a collaborative meta-analysis of 14 randomised trials of statin therapy (the Cholesterol Treatment Trialists' [CTT] Collaboration).[10] Our results showed that lowering LDL cholesterol by 1 mmol/L reduces the risk of major vascular events (defined as the composite outcome of myocardial infarction or coronary death, stroke, or coronary revascularisation) by about a fifth in a wide range of high-risk participants, largely irrespective of baseline lipid profile or other presenting characteristics, including diabetes. However, there are still some uncertainties about the effects of statins in people with diabetes. For example, there is little information about