Università degli Studi di Messina

Peculiarità del rischio cardiovascolare nella donna diabetica

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XIX CONGRESSO NAZIONALE AMD
Roma 1 Giugno 2013

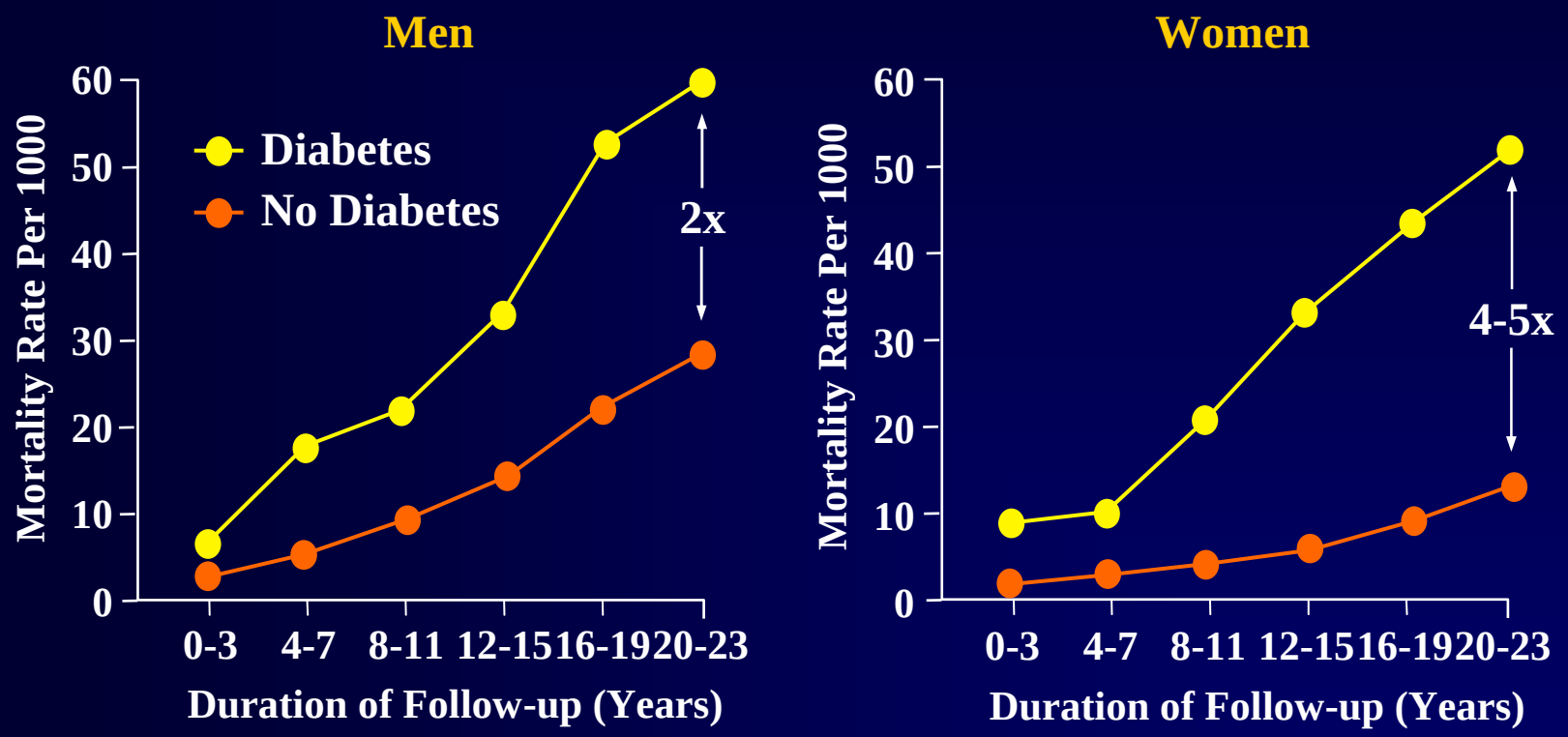
Conflitto di interesse

Bristoll-Mayer-Squibb Astra Zeneca

Boeringer-Ingelheim

✓ **Nei paesi industrializzati le malattie cardiovascolari rappresentano la principale causa di morte nelle donne.**

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

Huxley R et al., BMJ 2006

Stima del rischio relativo di CHD fatale nelle donne e negli uomini con diabete: meta-analisi di 37 studi prospettici

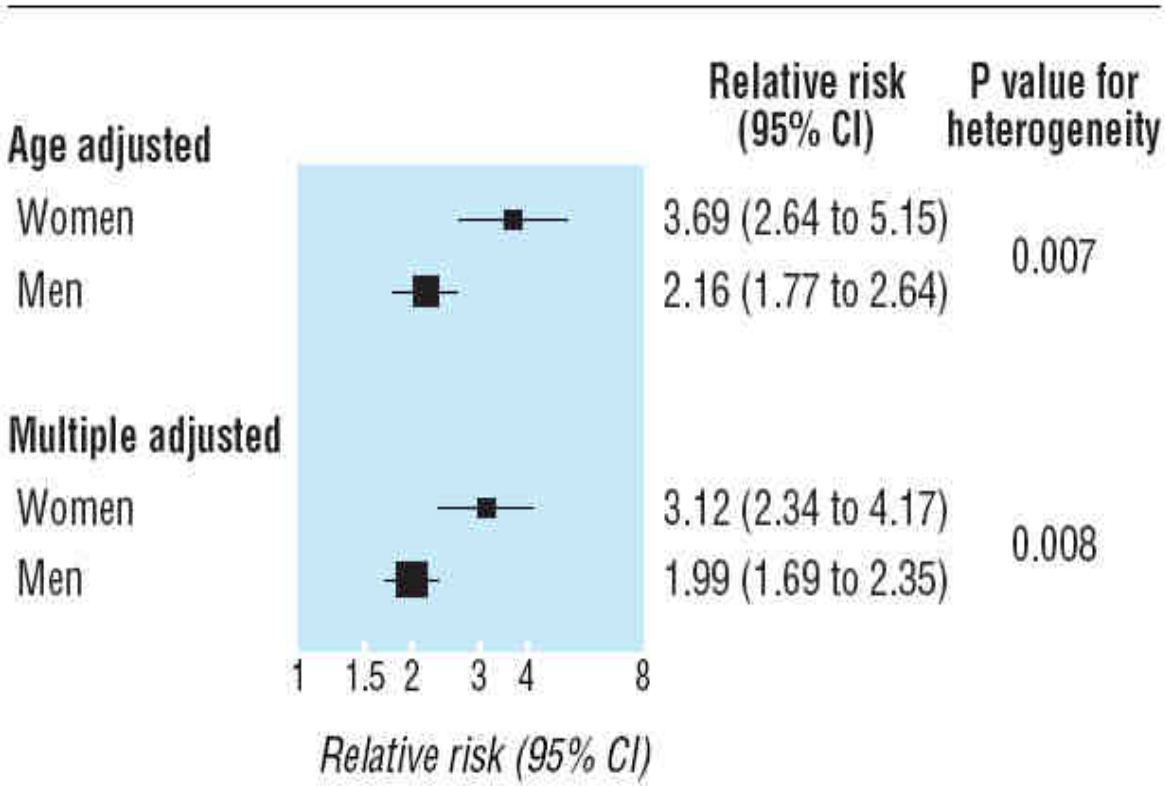


Fig 2 Overall summary estimates of relative risks and 95% confidence intervals for fatal coronary heart disease in men and women with and without diabetes in 22 studies that reported both age and multiple adjusted coefficients

Huxley R et al., BMJ 2006

What is already known on this topic

People with type 2 diabetes are at a much greater risk of fatal coronary heart disease than those without diabetes

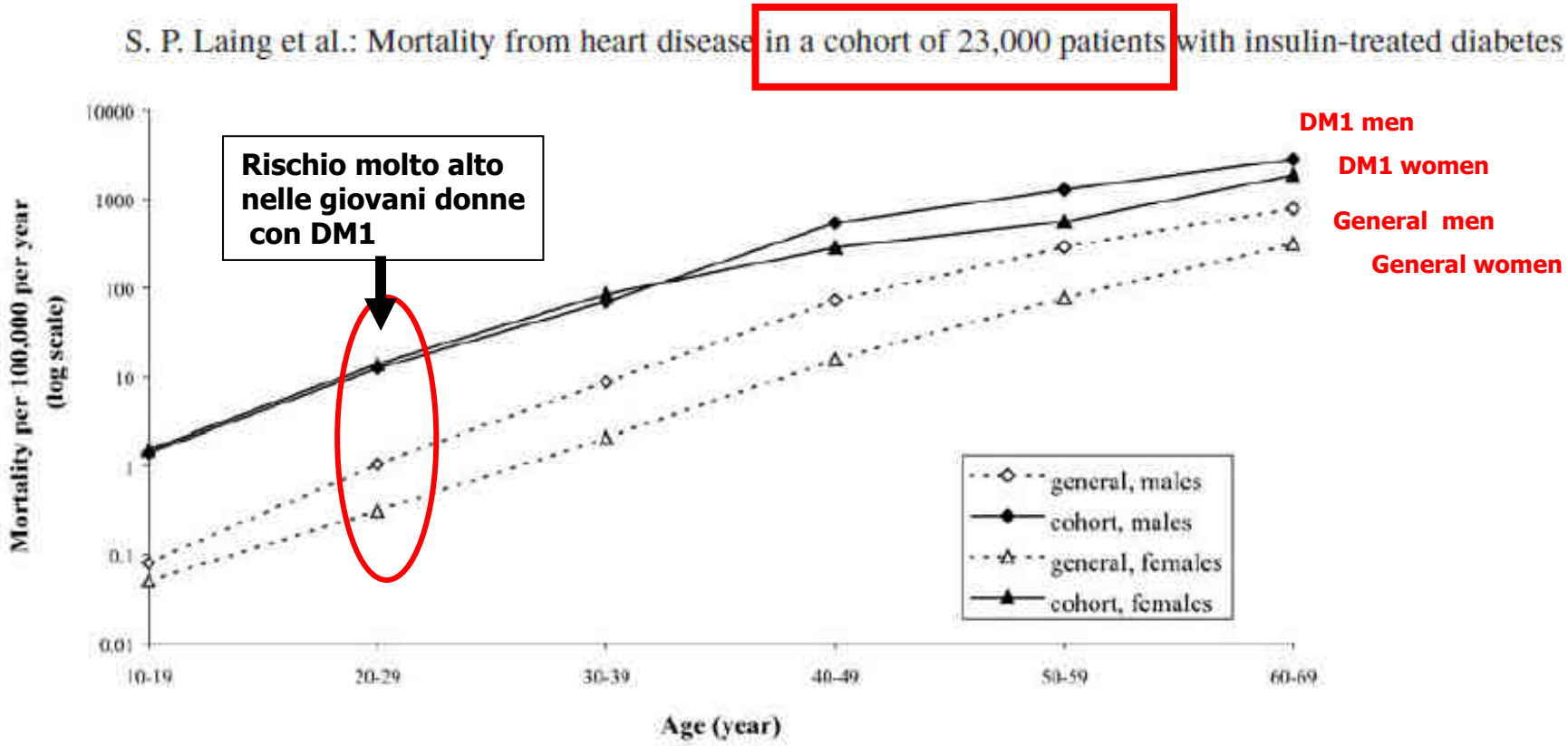
It is unclear whether the adverse effects of diabetes are greater for women than they are for men

What this study adds

The risk of death from coronary heart disease associated with type 2 diabetes is about 50% greater in women than it is in men

Huxley R et al., BMJ 2006

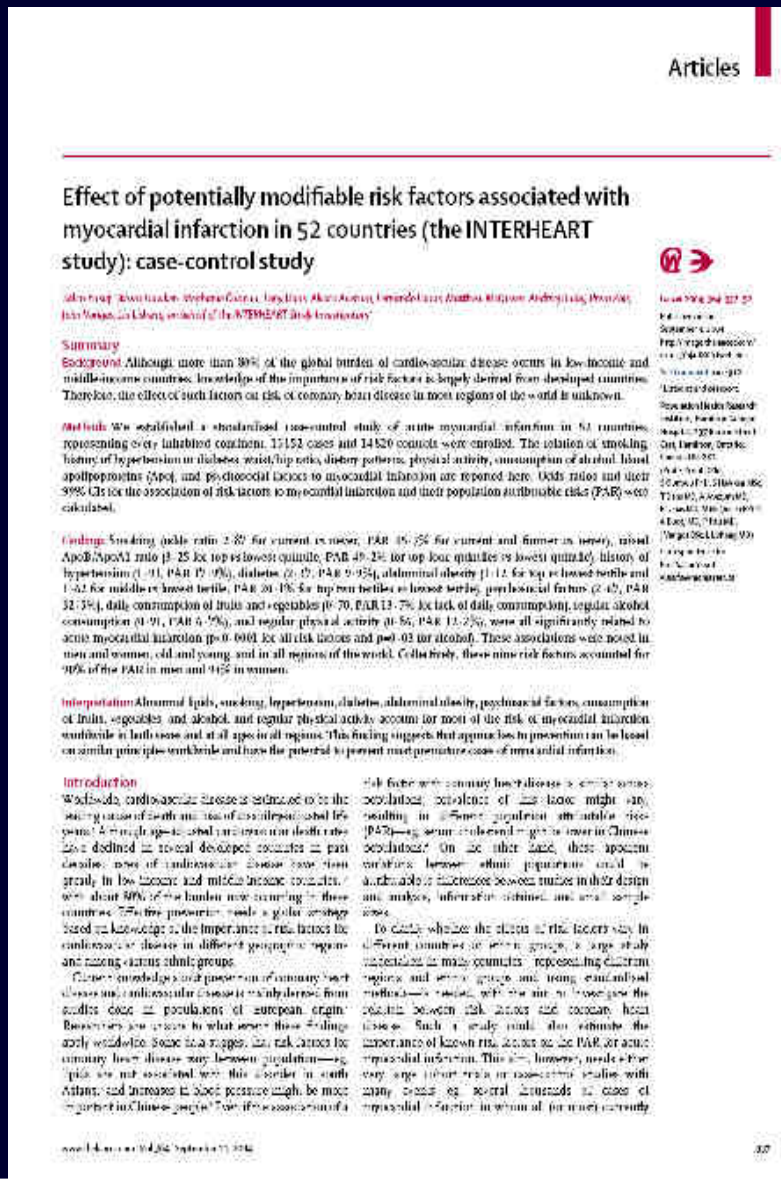
Mortalità per cardiopatia ischemica nel diabete di tipo 1 e nella popolazione generale



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

Laing SP; Diabetologia 2003

Il diabete è un fattore di rischio più importante nelle donne



Articles

Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study

Summary

Background Although more than 80% of the global burden of cardiovascular disease occurs in low-income and middle-income countries, knowledge of the importance of risk factors is largely derived from developed countries. Therefore, the effects of such factors on risk of coronary heart disease in most regions of the world is unknown.

Methods We established a standardised case-control study of acute myocardial infarction in 52 countries, representing every inhabited continent. 15152 cases and 14820 controls were enrolled. The relation of smoking, history of hypertension or diabetes, waist/hip ratio, dietary patterns, physical activity, consumption of alcohol, blood apolipoproteins (Apo), and psychosocial factors to myocardial infarction are reported here. Odds ratios and their 99% CIs for the association of risk factors to myocardial infarction and their population attributable risks (PAR) were calculated.

Findings Smoking (odds ratio 2·87 for current vs never, PAR 35·7% for current and former vs never), raised ApoB/ApoA1 ratio (3·25 for top vs lowest quintile, PAR 49·2% for top four quintiles vs lowest quintile), history of hypertension (1·91, PAR 17·9%), diabetes (2·67, PAR 9·9%), abdominal obesity (1·12 for top vs lowest tertile and 1·62 for middle vs lowest tertile, PAR 20·1% for top two tertiles vs lowest tertile), psychosocial factors (2·67, PAR 32·5%), daily consumption of fruits and vegetables (0·70, PAR 13·7% for lack of daily consumption), regular alcohol consumption (0·91, PAR 6·5%), and regular physical activity (0·86, PAR 12·2%), were all significantly related to acute myocardial infarction (p<0·0001 for all risk factors and p=0·03 for alcohol). These associations were noted in men and women, old and young, and in all regions of the world. Collectively, these nine risk factors accounted for 90% of the PAR in men and 94% in women.

Interpretation Abnormal lipids, smoking, hypertension, diabetes, abdominal obesity, psychosocial factors, consumption of fruits, vegetables and alcohol, and regular physical activity account for most of the risk of myocardial infarction worldwide in both sexes and at all ages in all regions. This finding suggests that approaches to prevention can be based on similar principles worldwide and have the potential to prevent most premature cases of myocardial infarction.

Introduction

Worldwide, cardiovascular disease is estimated to be the leading cause of death and loss of disability-adjusted life years.[1] Although age-specific cardiovascular disease death rates have declined in several developed countries in past decades, rates of cardiovascular disease have risen greatly in low income and middle income countries.[2] ... about 80% of the burden now occurring in these countries. Effective prevention needs a global strategy based on knowledge of the importance of risk factors for cardiovascular disease in different geographic regions and among various ethnic groups.

Current knowledge about prevention of coronary heart disease and cardiovascular disease is largely derived from studies done in populations of european origin. Researchers are unsure to what extent these findings apply worldwide. Some of the risk factors for coronary heart disease may be different between populations—eg, lipids are not associated with this disorder in south Asians, and increases in blood pressure might be more important in Chinese people.[3] Few if any associations of a risk factor with coronary heart disease ... [illegible] ... populations, prevalence of the factor might vary, resulting in different population attributable risks (PARs)—eg, serum cholesterol might be lower in Chinese populations.[4] On the other hand, these apparent variations between ethnic populations could be attributable to differences between studies in their design and analyses, information obtained, and study samples.

To clarify whether the effects of risk factors vary in different countries or ethnic groups, a large study was undertaken in many countries representing different regions and ethnic groups and using standardised methods—the aim was to investigate the relation between risk factors and coronary heart disease. Such a study could also estimate the importance of known risk factors as the PAR for acute myocardial infarction. This aim, however, needs a fairly very large cohort study or case-control studies with many cases (eg, several thousands of cases of myocardial infarction in whom all (or most) currently

INTERHEART Study:

- Più di 15000 casi di infarto miocardico
- Più di 14800 controlli
- 52 Paesi nel mondo

Ysuf et al, the Lancet 2004

Il diabete è un fattore di rischio più importante nelle donne

Risk factor	Sex	Control (%)	Case (%)	Odds ratio (99% CI)	PAR (99% CI)
Current smoking	F	9·3	20·1	2·86 (2·36–3·48)	15·8% (12·9–19·3)
	M	33·0	53·1	3·05 (2·78–3·33)	44·0% (40·9–47·2)
Diabetes	F	7·9	25·5	4·26 (3·51–5·18)	19·1% (16·8–21·7)
	M	7·4	16·2	2·67 (2·36–3·02)	10·1% (8·9–11·4)
Hypertension	F	28·3	53·0	2·95 (2·57–3·39)	35·8% (32·1–39·6)
	M	19·7	34·6	2·32 (2·12–2·53)	19·5% (17·7–21·5)
Abdominal obesity	F	33·3	45·6	2·26 (1·99–2·68)	35·9% (28·9–43·6)
	M	33·3	46·5	2·24 (2·03–2·47)	32·1% (28·0–36·5)
Psychosocial index	F	–	–	3·09 (2·41–5·04)	40·0% (28·6–52·6)
	M	–	–	2·58 (2·11–3·14)	25·3% (18·2–34·0)
Fruits/veg	F	50·3	39·4	0·58 (0·48–0·71)	17·8% (12·9–24·1)
	M	39·6	34·7	0·74 (0·66–0·83)	10·3% (6·9–15·2)
Exercise	F	16·5	9·3	0·48 (0·39–0·59)	37·3% (26·1–50·0)
	M	20·3	15·8	0·77 (0·68–0·85)	22·9% (16·9–30·2)
Alcohol	F	11·2	6·3	0·41 (0·32–0·53)	46·9% (34·3–60·0)
	M	29·1	29·6	0·88 (0·81–0·96)	10·5% (6·1–17·5)
ApoB/ApoA1 ratio	F	14·1	27·0	4·42 (3·43–5·70)	52·1% (44·0–60·2)
	M	21·9	35·5	3·76 (3·23–4·38)	53·8% (48·3–59·2)

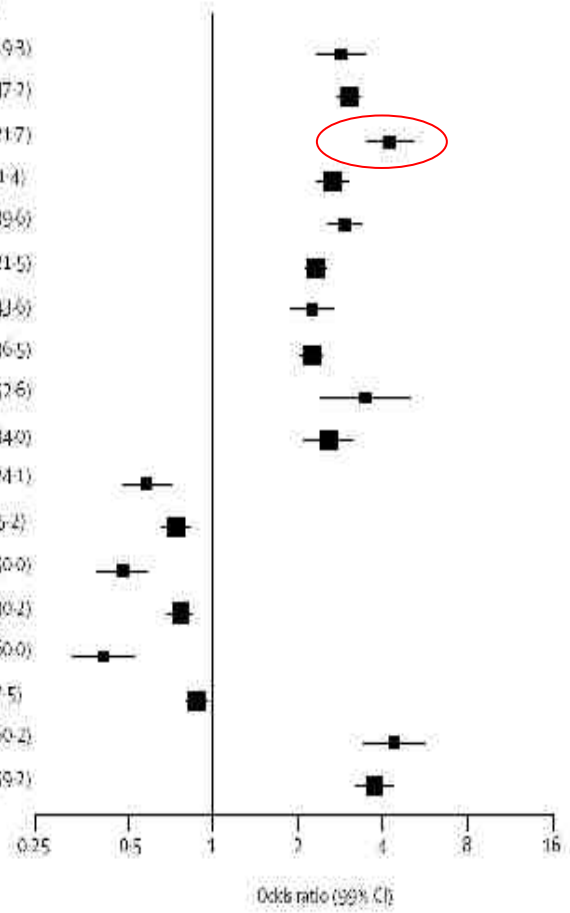
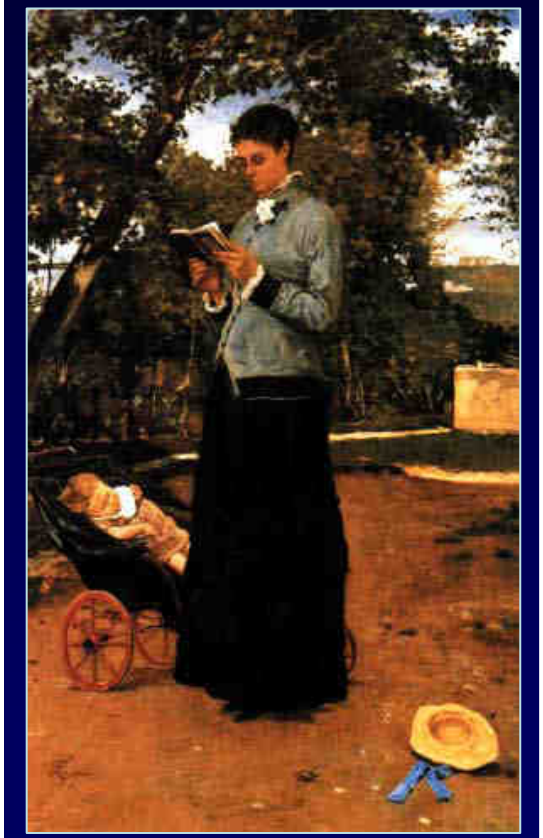
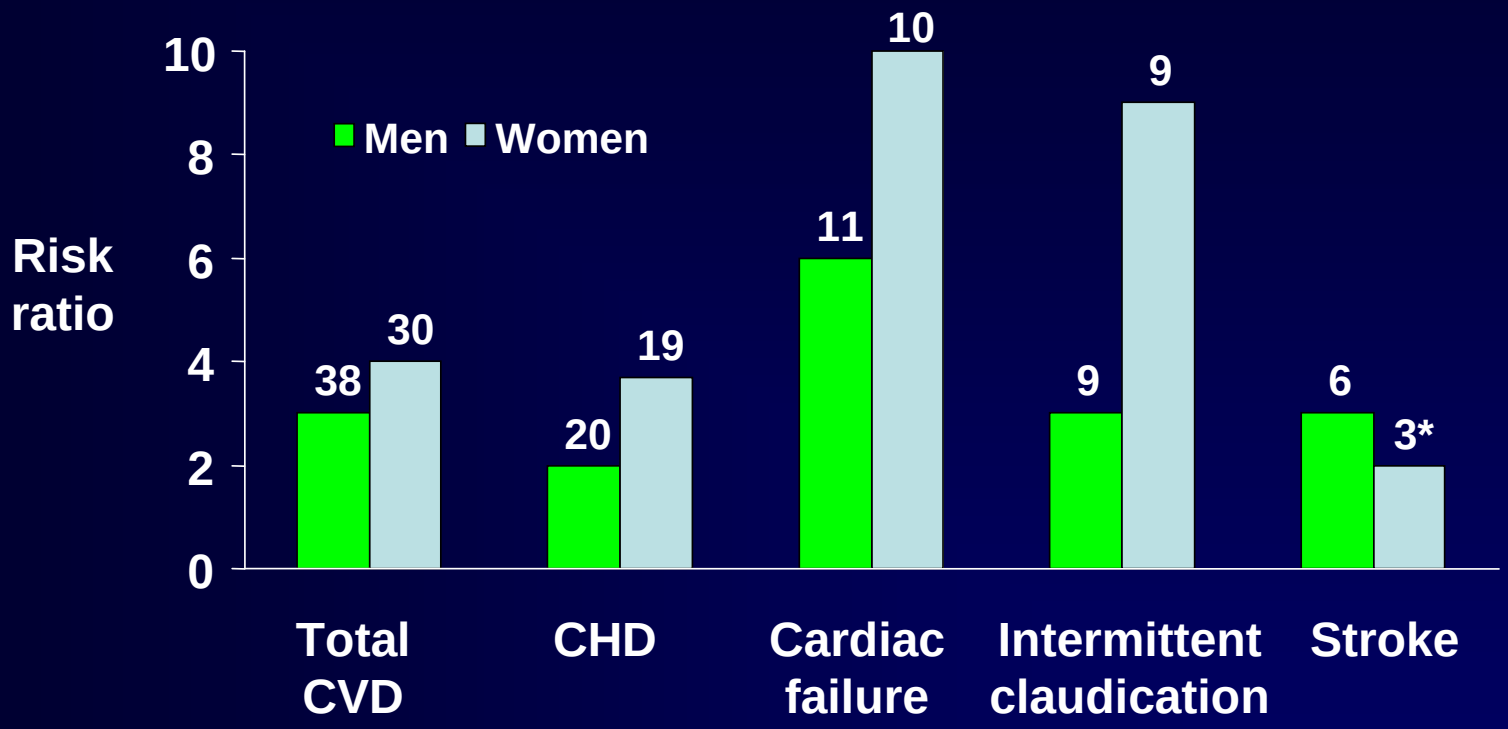


Figure 4: Association of risk factors with acute myocardial infarction in men and women after adjustment for age, sex, and geographic region
For this and subsequent figures, the odds ratios are plotted on a doubling scale. Prevalence cannot be calculated for psychosocial factors because it is derived from a model.



Ysuf et al, the Lancet 2004

Framingham Heart Study 30-Year Follow-Up: CVD Events in Patients With Diabetes



P<0.001 for all values except **P*<0.05.

Wilson PWF, Kannel WB. In: *Hyperglycemia, Diabetes and Vascular Disease.* Ruderman N et al, eds. Oxford; 1992.

Le donne con diabete hanno anche un aumentato rischio di stroke .....

Diabetologia (2006) 49:2859–2865
DOI 10.1007/s00125-006-0493-z

ARTICLE

Risk of stroke in people with type 2 diabetes in the UK: a study using the General Practice Research Database

H. E. Mulnier · H. E. Seaman · V. S. Raleigh · S. S. Soedamah-Muthu · H. M. Colhoun · R. A. Lawrenson · C. S. De Vries

Age-adjusted HR for stroke in DM2 subjects vs non diabetic subjects was:
- 2.08 (95%CI:1.94-2.24) in men
- 2.32 (95%CI: 2.16-2.49) in women.

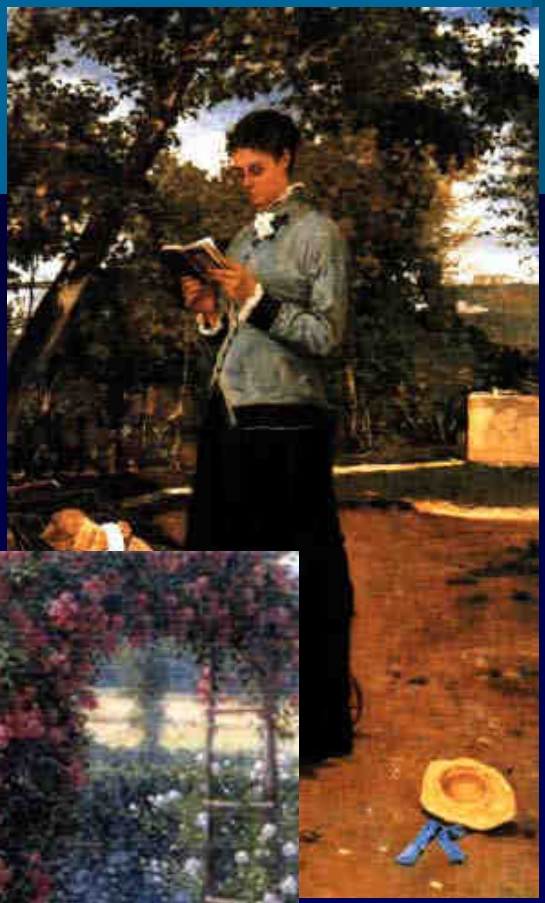
The increase in risk attributable to diabetes was highest
- in young women (HR 8.18; 95%CI 4.31-15.51) and decreased with age.

Table 4 Hazard ratios (95% CI) for stroke in diabetes compared with no diabetes stratified by sex and attained age-group

	All	Men	Women
Diabetes/no diabetes (*n*)	41,799/ 202,733	22,178/ 107,285	19,621/ 95,448
Age (years)			
35–54	5.64 (3.91–8.13)	4.66 (2.96–7.33)	8.18 (4.31–15.51)
55–64	3.81 (3.23–4.49)	3.31 (2.69–4.07)	4.89 (3.71–6.45)
65–74	2.54 (2.31–2.79)	2.35 (2.07–2.65)	2.83 (2.45–3.28)
75–84	1.90 (1.75–2.06)	1.69 (1.49–1.90)	2.10 (1.89–2.34)
≥85	1.69 (1.49–1.92)	1.60 (1.28–1.99)	1.74 (1.49–2.03)
All ages	2.19 (2.09–2.32)	2.08 (1.94–2.24)	2.32 (2.16–2.49)

Mulnier HE, Diabetologia 2006

Le donne diabetiche hanno "poorer outcomes".....

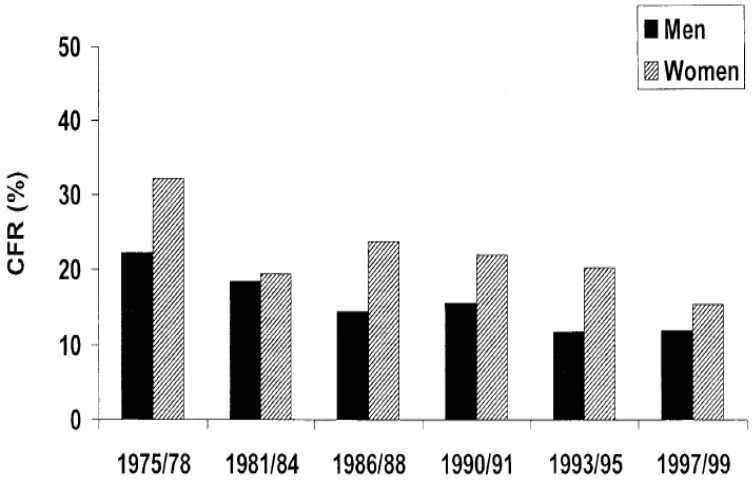


Sex differences in survival after acute myocardial infarction in patients with diabetes mellitus (Worcester Heart Attack Study)

Amber Crowley, MD,[a] Vandana Menon, MD, MPH,[b] Darleen Lessard, MS,[c] Jorge Yarzebski, MD, MPH,[c] Elizabeth Jackson, MD, MPH,[c] Joel M. Gore, MD,[c] and Robert J. Goldberg, PhD[c] *New Haven, Conn, and Boston and Worcester, Mass*

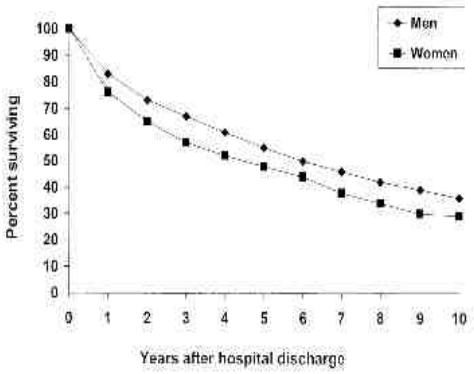
Le morti *intraospedaliere* dopo IMA sono ridotte sia negli uomini che nelle donne con diabete; tuttavia le donne hanno ancora un rischio maggiore di morte intraospedaliera ed 1 anno dopo IMA

Figure 1



Trends in hospital CFRs for men and women with diabetes mellitus and AMI.

Figure 2

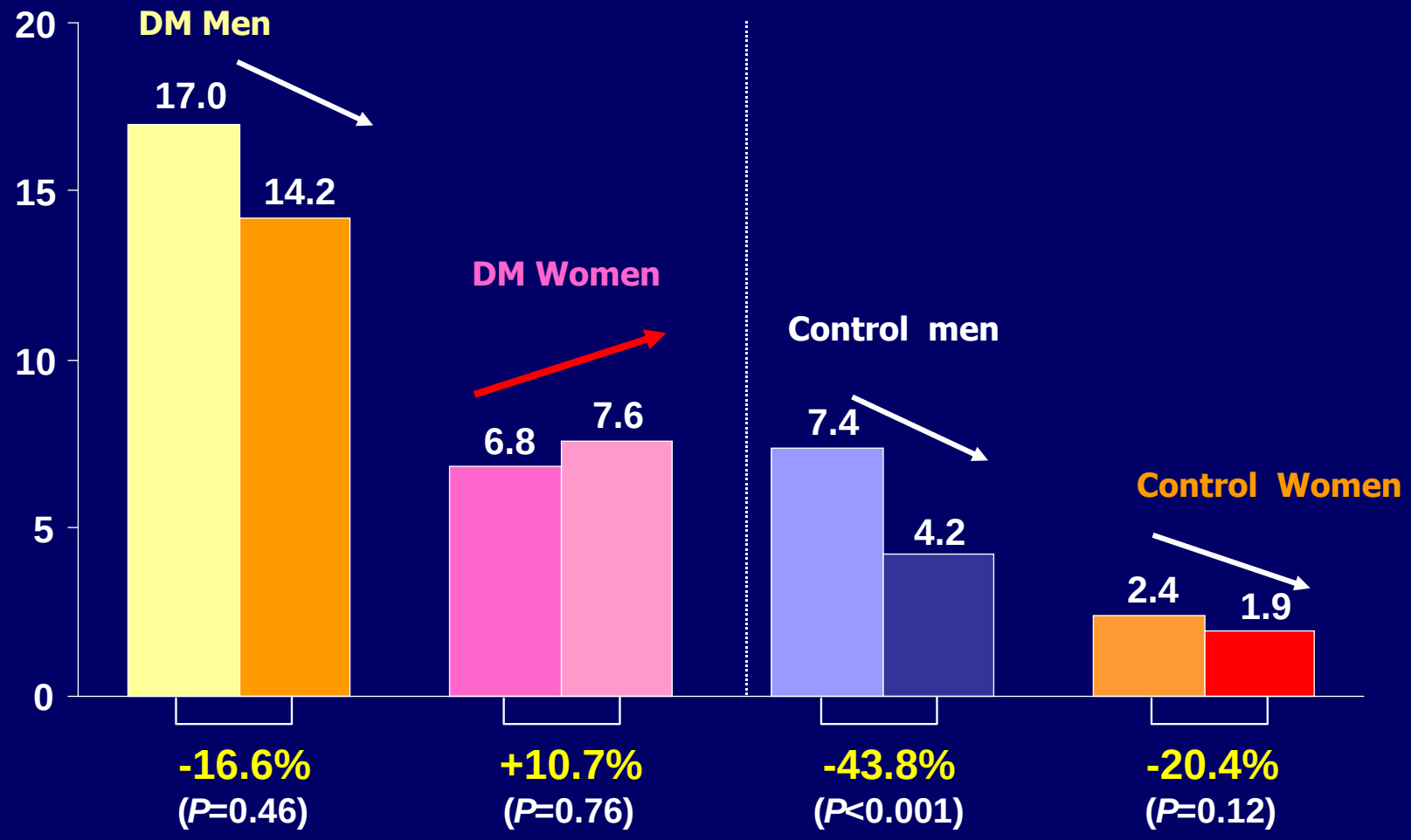


Long-term survival after acute myocardial infarction in men and women with diabetes mellitus.

Crowley, Am Heart J 2003

Mortality trends in diabetic women

Mortality Rates for Ischemic Heart Disease in Patients With and Without Diabetes



*In national sample of adults in NHANES I (1971-75).

Gu K et al. *JAMA* 1999;281:1291-1297.

Trends in mortality are *unfavourable* in diabetic women

Annals of Internal Medicine | ARTICLE

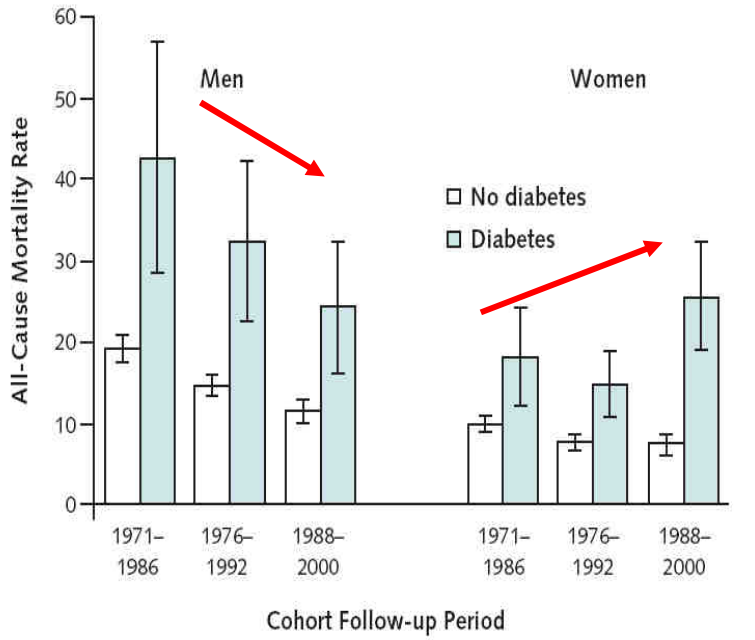
Mortality Trends in Men and Women with Diabetes, 1971 to 2000

Edward W. Gregg, PhD; Qiuping Gu, MD, PhD; Yiling J. Cheng, MD, PhD; K.M. Venkat Narayan, MD, MSc, MBA; and Catherine C. Cowie, PhD

Gregg E et al., Ann Int Med 2007

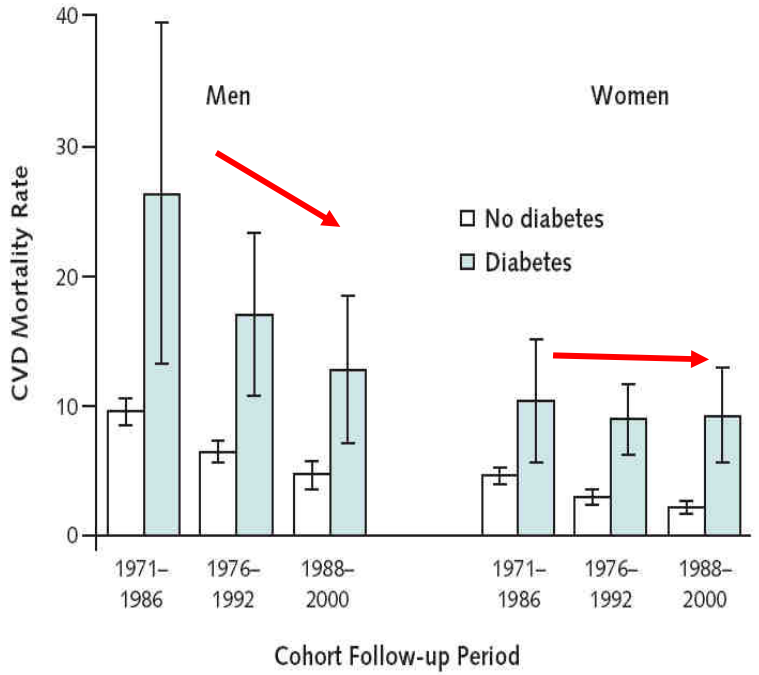
Mortality trends among U.S. Persons with Diabetes: NHANES Surveys I, II, III

Figure 1. Age-adjusted all-cause mortality rates among the U.S. population age 35 to 74 years with and without diabetes, by cohort and sex.



Mortality rates are calculated as annual deaths per 1000 persons. Error bars represent 95% CIs.

Figure 2. Age-adjusted cardiovascular disease mortality rates among the U.S. population age 35 to 74 years with and without diabetes, by cohort and sex.



Mortality rates are calculated as annual deaths per 1000 persons. Error bars represent 95% CIs.

Gregg E et al., Ann Int Med 2007

European Heart Journal (2008) **29**, 1889–1895
doi:10.1093/eurheartj/ehn250

CLINICAL RESEARCH
Prevention and epidemiology

The diabetes-cardiovascular risk paradox: results from a Finnish population-based prospective study

Noël C. Barengo[1*†], Shuichi Katoh[1,2,3,4†], Vladislav Moltchanov[2], Naoko Tajima[3], and Jaakko Tuomilehto[1,5]

[1]Department of Public Health, University of Helsinki, PL 41, PO Box 41 (Mannerheimintie 172), 00014 Helsinki, Finland; [2]Diabetes and Genetic Epidemiology Unit, Department of Epidemiology and Health Promotion, National Public Health Institute, Helsinki, Finland; [3]Division of Diabetes and Endocrinology, Department of Internal Medicine, Jikei University School of Medicine, Tokyo, Japan; [4]Fuji City General Hospital, Fuji, Japan; and [5]South Ostrobothnia Central Hospital, Seinäjoki, Finland

Received 16 November 2007; revised 30 March 2008; accepted 23 May 2008; online publish-ahead-of-print 16 June 2008

Barengo et al., Eur Heart J 2008

Published in final edited form as:
Circulation. 2009 April 7; 119(13): 1728–1735. doi:10.1161/CIRCULATIONAHA.108.829176.

Trends in All-Cause and Cardiovascular Disease Mortality among Women and Men with and without Diabetes in the Framingham Heart Study, 1950-2005

Sarah Rosner Preis, ScD MPH[1,2], **Shih-Jen Hwang, PhD**[1,2], **Sean Coady, MA**[2], **Michael J. Pencina, PhD**[3], **Ralph B. D'Agostino Sr, PhD**[3], **Peter J. Savage, MD**[2], **Daniel Levy, MD**[1,2], and **Caroline S. Fox, MD MPH**[1,2,4]

[1] National Heart, Lung, and Blood Institute's Framingham Heart Study, Framingham, MA

[2] National Heart, Lung, and Blood Institute, National Institutes of Health

[3] Department of Mathematics, Boston University, Boston, MA

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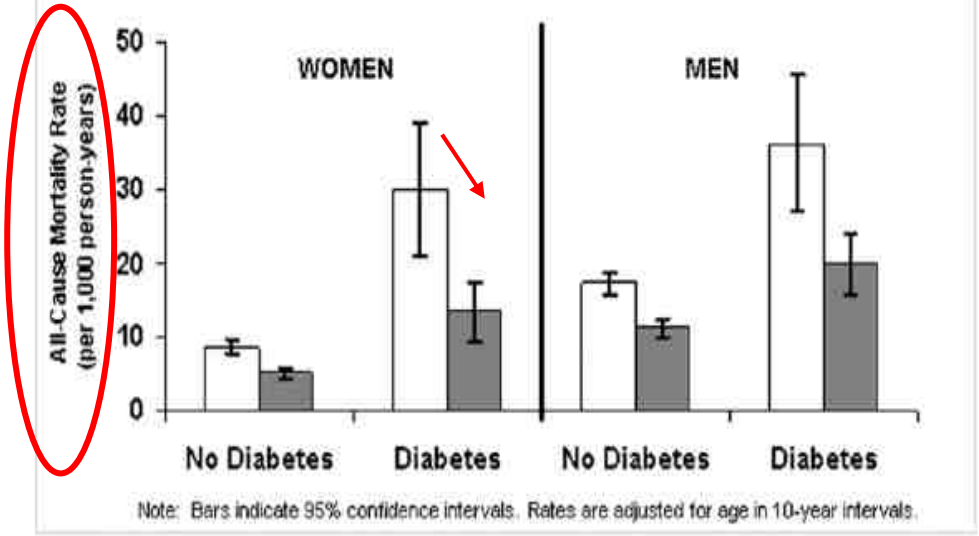
Preis et al., Circulation 2009



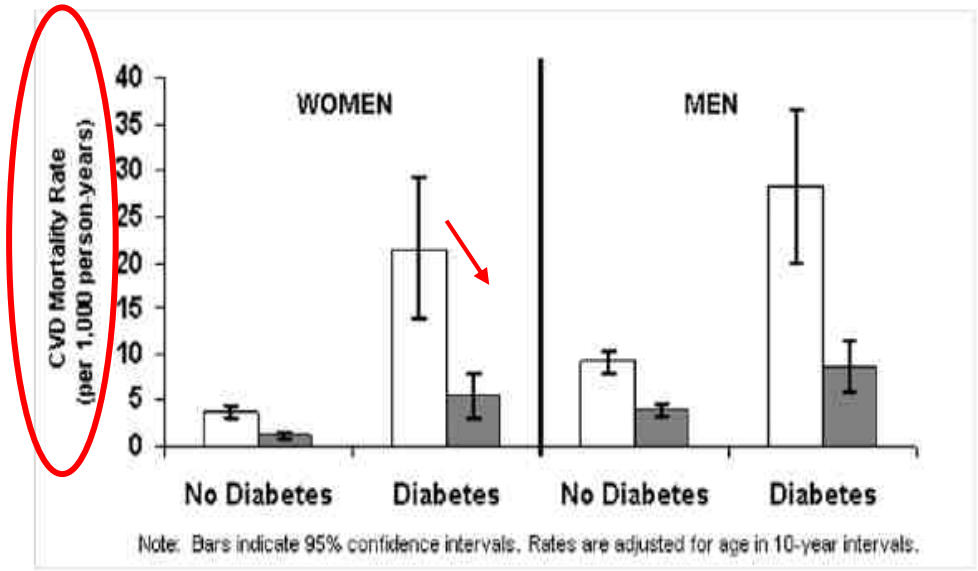


Figure 1.
Figure 1a. Age-adjusted all-cause mortality rates among participants with and without diabetes, by sex and time period.
Figure 1b. Age-adjusted cardiovascular disease (CVD) mortality rates among participants with and without diabetes, by sex and time period.

Mortality rates associates with diabetes in the Framingham Heart Study

Preis et al., Circulation 2009

G Model
JJCC-650; No. of Pages 6
ARTICLE IN PRESS

Journal of Cardiology xxx (2013) xxx–xxx

Contents lists available at SciVerse ScienceDirect

Journal of Cardiology

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

Original article

Gender differences in the impact of diabetes on mortality in patients with established coronary artery disease: A report from the Eastern Taiwan integrated health care delivery system of Coronary Heart Disease (ET-CHD) registry, 1997–2006

Yi-Hwei Li (PhD)[a,**], Gen-Min Lin (MD, MPH)[a,b,*], Chin-Lon Lin (MD)[c], Ji-Hung Wang (MD)[c], Chih-Lu Han (MD, PhD)[d]

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[b] Department of Medicine, Hualien Armed Forces General Hospital, Hualien, Taiwan
[c] Division of Cardiology, Buddhist Tzu-Chi General Hospital, Hualien, Taiwan
[d] Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan

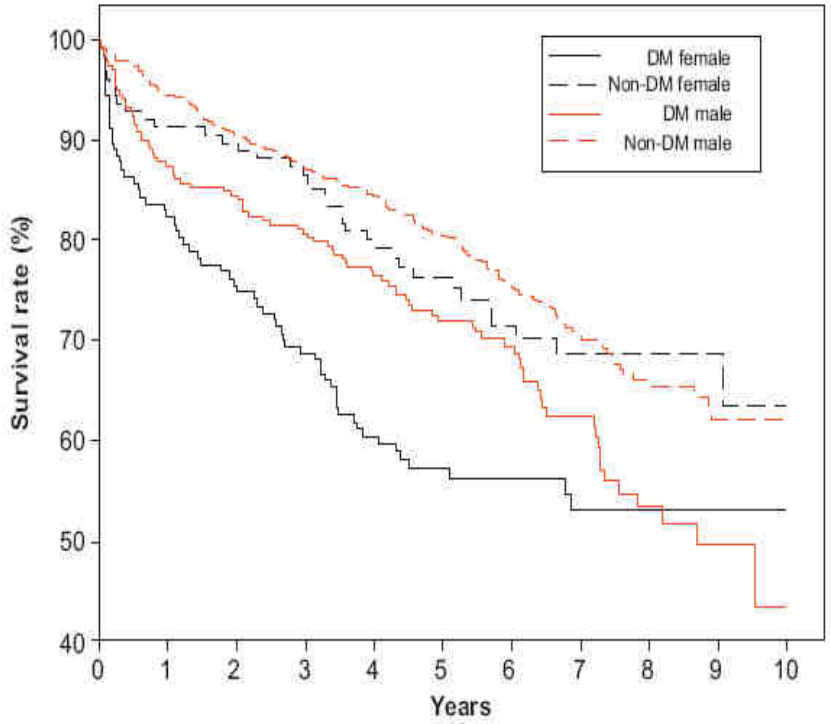

Fig. 1. Kaplan–Meier survival curves for overall mortality by gender and diabetes mellitus (DM) status in coronary artery disease patients.

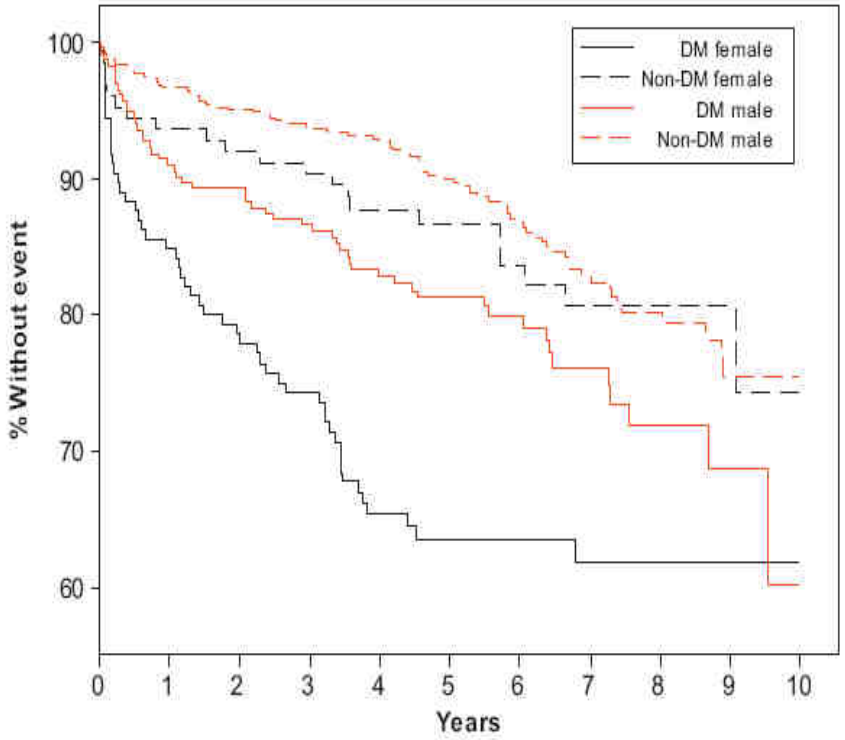

Fig. 2. Kaplan–Meier survival probabilities without cardiac death by gender and diabetes mellitus (DM) status in coronary artery disease patients.

Li et al., J Cardiol 2013

Perché le donne diabetiche hanno questo eccesso di rischio cardiovascolare?

Le cause sono ancora non del tutto note

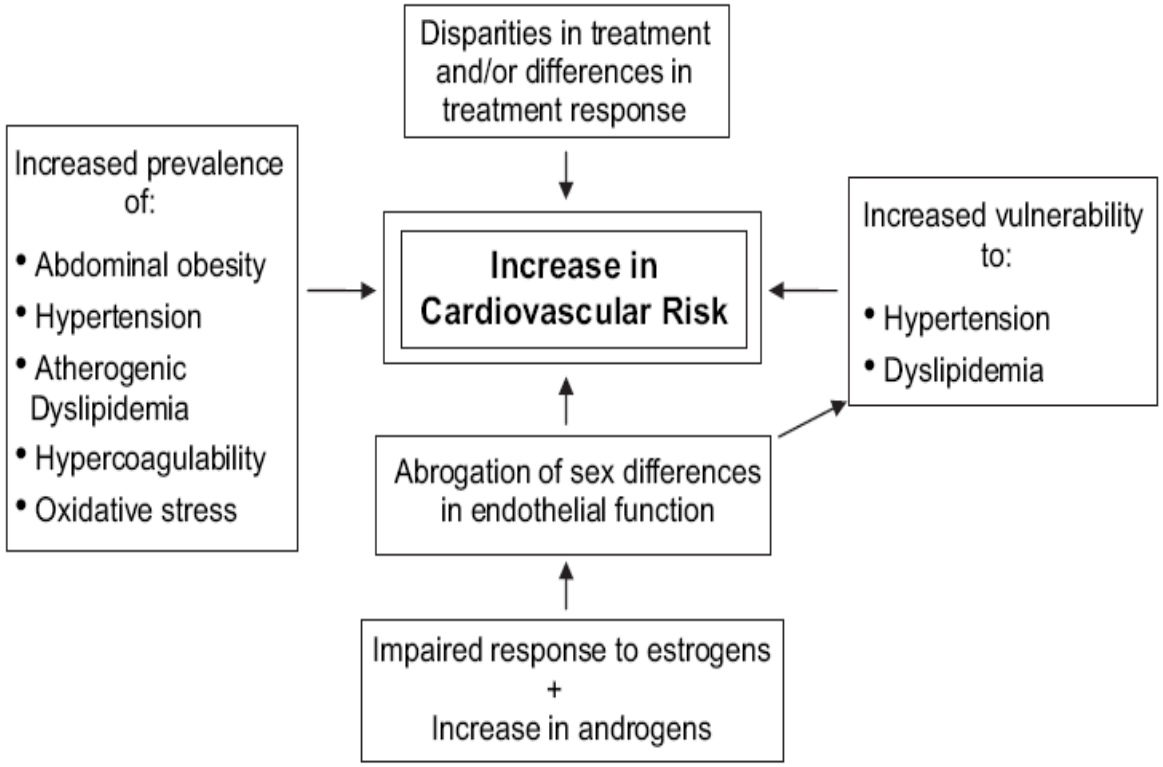

Figure 2 Possible causes of the high cardiovascular risk in women with diabetes.

Rivellese et al., NMCD 2010

Diverse ipotesi per spiegare l'eccesso di rischio nelle donne diabetiche

1. Maggior numero di fattori di rischio
2. Maggiore impatto dei fattori di rischio
3. Differenze "strutturali" e/o "funzionali"dell'albero cardiovascolare
4. Differente presentazione clinica
5. Disparità nel trattamento o nella risposta al trattamento

Diverse ipotesi per spiegare l'eccesso di rischio nelle donne diabetiche

1. **Maggior numero di fattori di rischio**
2. **Maggiore impatto dei fattori di rischio**
3. **Differenze "strutturali" e/o "funzionali" dell'albero cardiovascolare**
4. **Differente presentazione clinica**
5. **Disparità nel trattamento o nella risposta al trattamento**

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

Incidence of Coronary Heart Disease in Type 2 Diabetic Men and Women

Impact of microvascular complications, treatment, and geographic location

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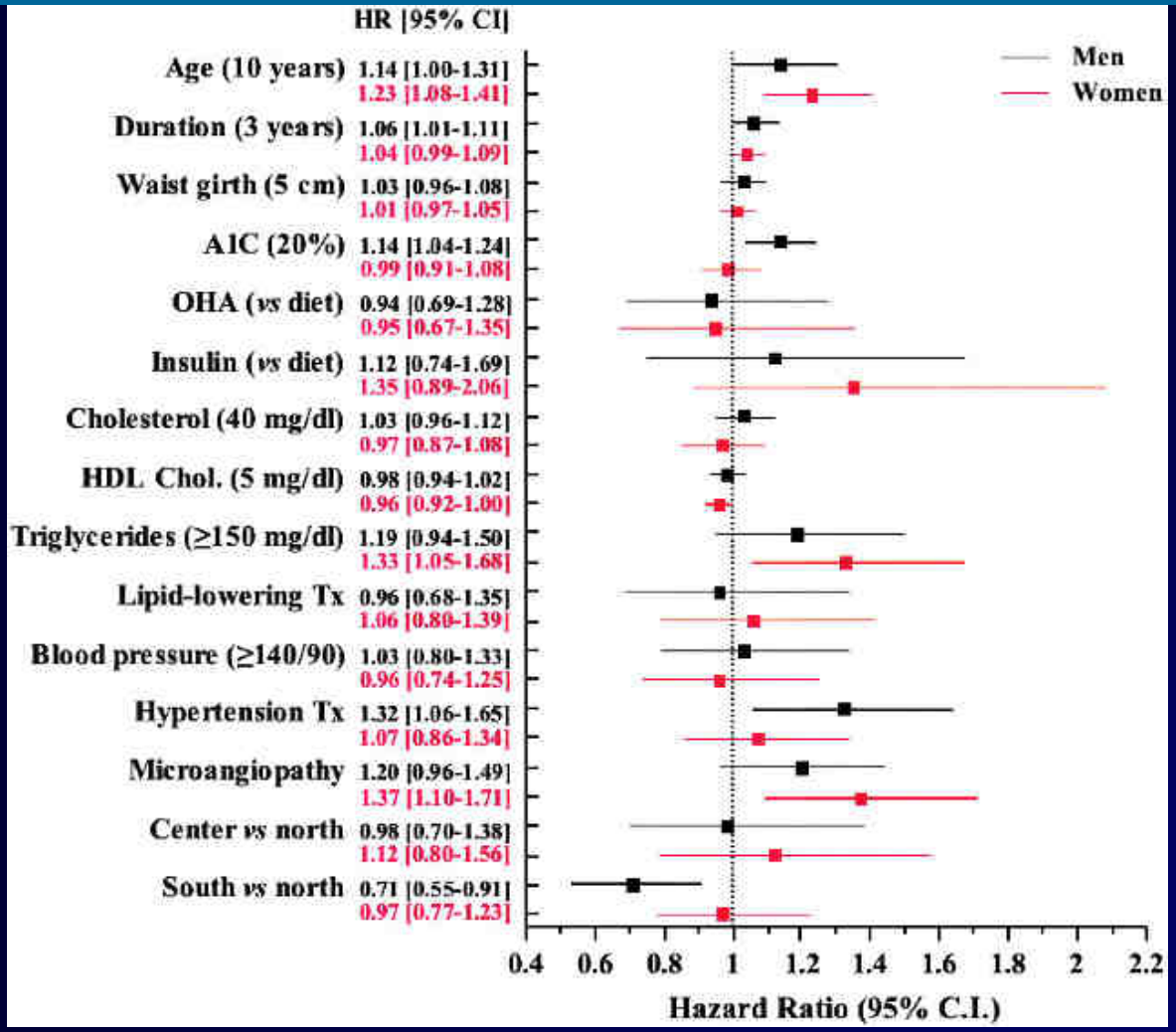
CARLO GIORDA, MD[2]
MARINA MAGGINI, PHD[3]
EDOARDO MANNUCCI, MD[4]
ROBERTO RASCHETTI, PHD[3]
FLAVIA LOMBARDO, PHD[3]
STEFANIA SPILA-ALEGIANI, PHD[3]
SALVATORE TURCO, MD[5]
MARIO VELUSSI, MD[6]
ELE FERRANNINI, MD[7]
FOR THE DIABETES AND INFORMATICS STUDY GROUP, ASSOCIATION OF CLINICAL DIABETOLOGISTS, ISTITUTO SUPERIORE DI SANITÀ

Diabetes is estimated to be responsible for 5.2% of all deaths (1). Since the Framingham Study (2), epidemiology has consistently shown that diabetes confers an increased risk for coronary heart disease (CHD) and cardiac mortality (3–6). Salient features of this association are the following: *1*) relative

CONCLUSIONS — In CVD-free patients with type 2 diabetes, risk of first CHD event depends on sex, geographic location, and presence of microvascular disease. Hyperglycemia and hypertension, particularly in men, and diabetic dyslipidemia, especially in women, are risk factors amenable to more aggressive treatment.

Diabetes Care 30:1241–1247, 2007

Independent predictors of incident CHD in diabetic men (black) and women (red).



Avogaro A et al. Dia Care 2007;30:1241-1247

American Diabetes Association.

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

Obesity and the risk of MI in 27000 participants from 52 countries: a case-control study

INTERHEART study

AMI

BMI quintiles

Waist-to-hip quintiles

Yusuf S et al, Lancet, 366:1640-1649, 2005

Fattori di rischio cardiometabolico:

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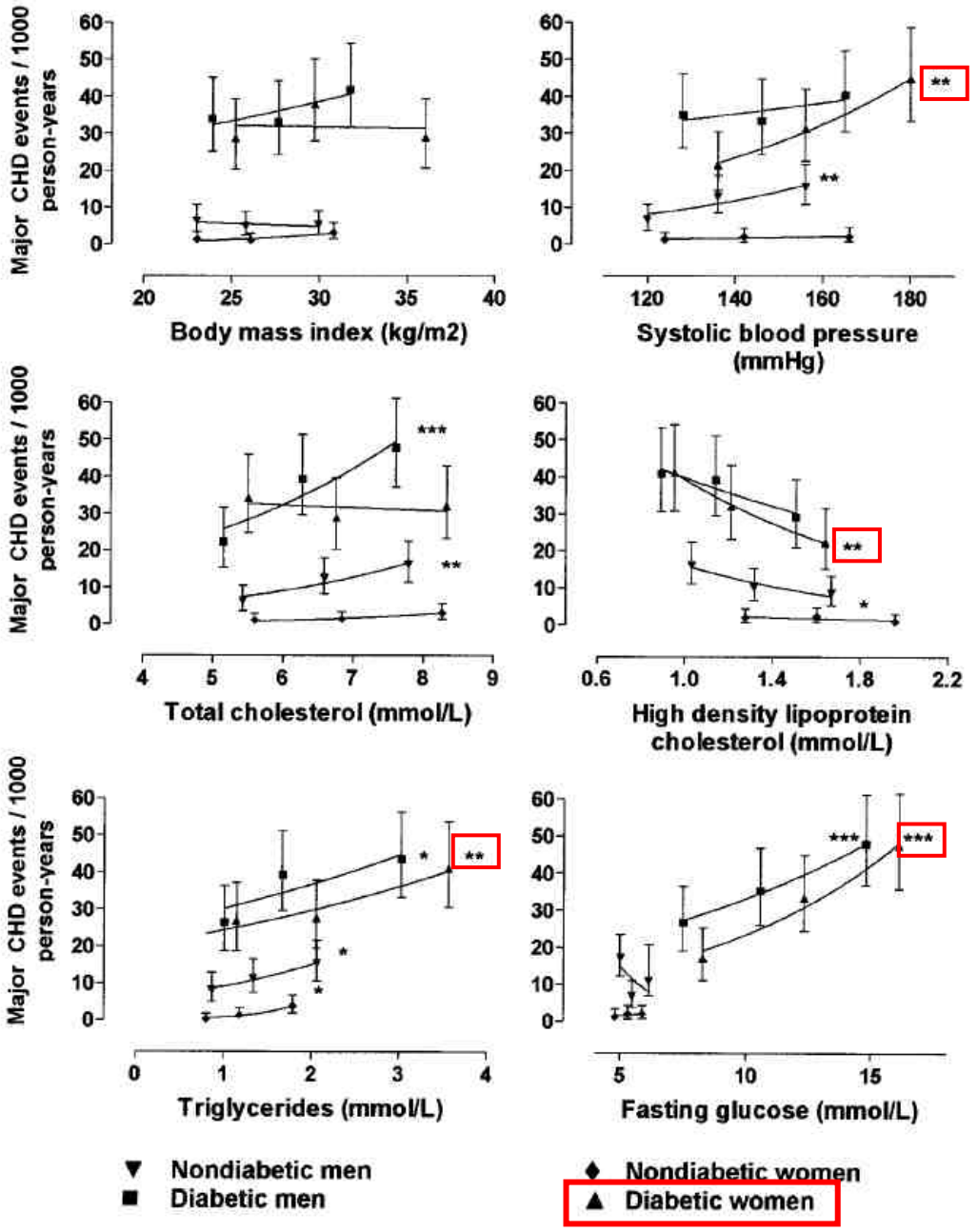

Figure 2—*Event rates for major CHD per 1,000 person-years according to tertiles of risk factors in nondiabetic and diabetic men and women. Event rates and their 95% CIs are plotted by median values of the diabetes status- and gender-specific tertiles of risk factors in nondiabetic men, nondiabetic women, diabetic men, and diabetic women. χ^2 test for trend: *P < 0.05; **P < 0.01; ***P < 0.001.*

Juutilainen A., Diabetes Care 2004

Rischio cardiovascolare nelle donne- Le nostre ricerche

Fattori di rischio cardiometabolico:

TRADIZIONALI

- Diabete
- Dislipidemie
- Ipertensione
- Obesità
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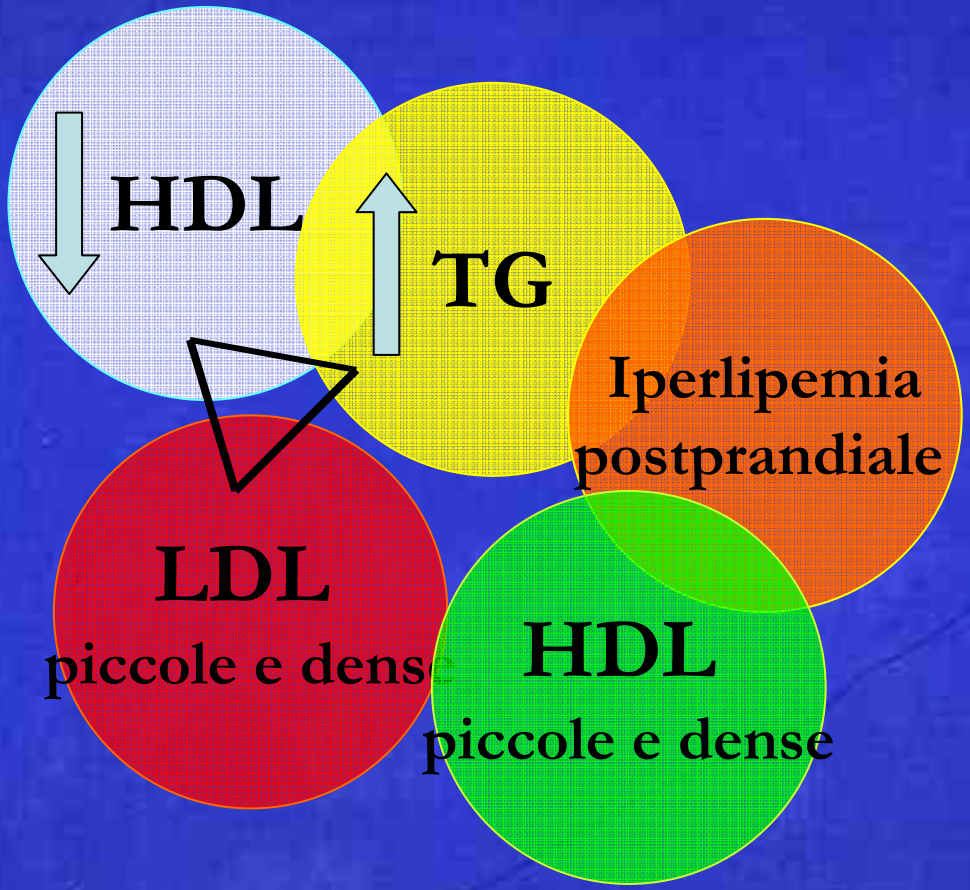
- altri

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.

Bassi livelli di colesterolo HDL aumentano il rischio cardiovascolare

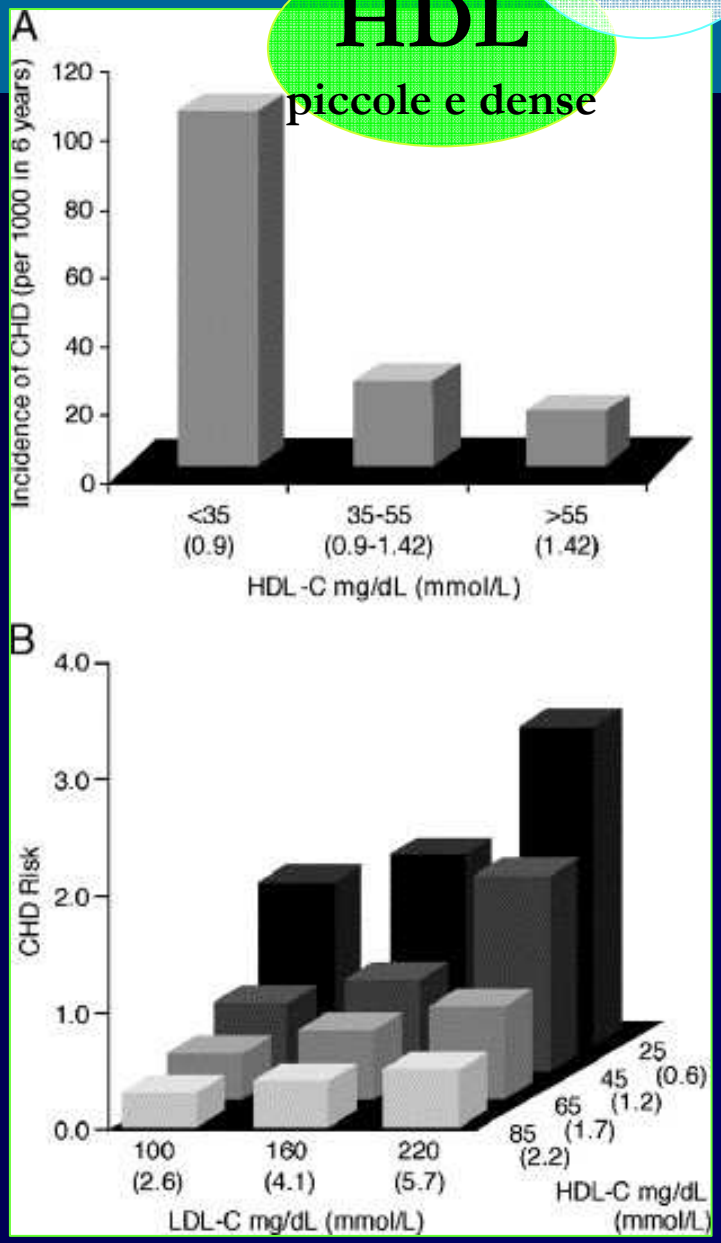
HDL

HDL
piccole e dense

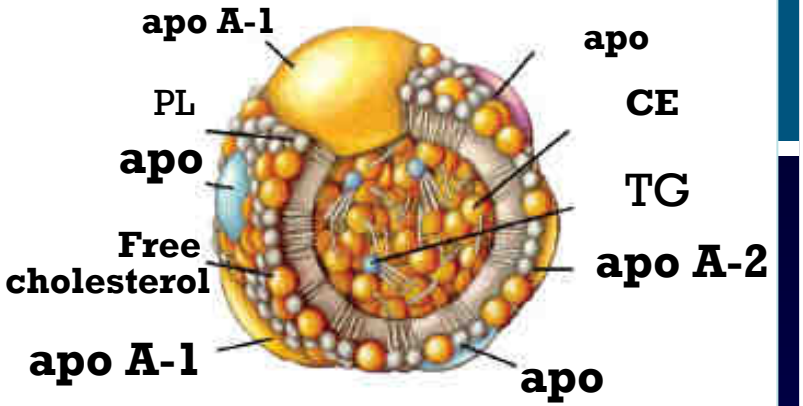
HDL-C as a predictor of CHD risk.
(A) Data from a 6-year follow up of the PROCAM study showing that the incidence of CHD decreases with higher levels of HDL-C (Assmann et al., 1996).

(B) Data from the Framingham study showing that high levels of HDL-C reduce the risk of CHD at all levels of LDL-C (Gordon et al., 1977).

HDL cholesterol ≥60 mg/dL counts as a "negative" risk factor; its presence removes one risk factor from the total count.
(Adult Treatment Panel III- ATP III Guidelines)



Le sottopopolazioni di HDL



✓ L'associazione ateroprotettiva delle HDL non sembra riconducibile solo alle **concentrazioni basali di HDL-C**, ma anche a **modificazioni qualitative delle HDL**.

✓ Le HDL sono una classe **eterogenea** di particelle che differiscono per composizione, dimensioni, carica e densità.

✓ Le HDL possono infatti essere suddivise, utilizzando diverse metodiche, in **SOTTOFRAZIONI**, che potrebbero avere funzioni differenti e, conseguentemente, diversi gradi di associazione con la CHD, nonostante concentrazioni basali simili di HDL-C.

✓ Alcuni autori hanno dimostrato come la presenza di **CHD** sia associata più fortemente alle **dimensioni delle HDL ed alle sottopopolazioni HDL** che ai livelli di HDL-C (*Cheung MC, J Lipid Res 1991; Asztalos, Arterioscler Thromb Vasc Biol 2004*).

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

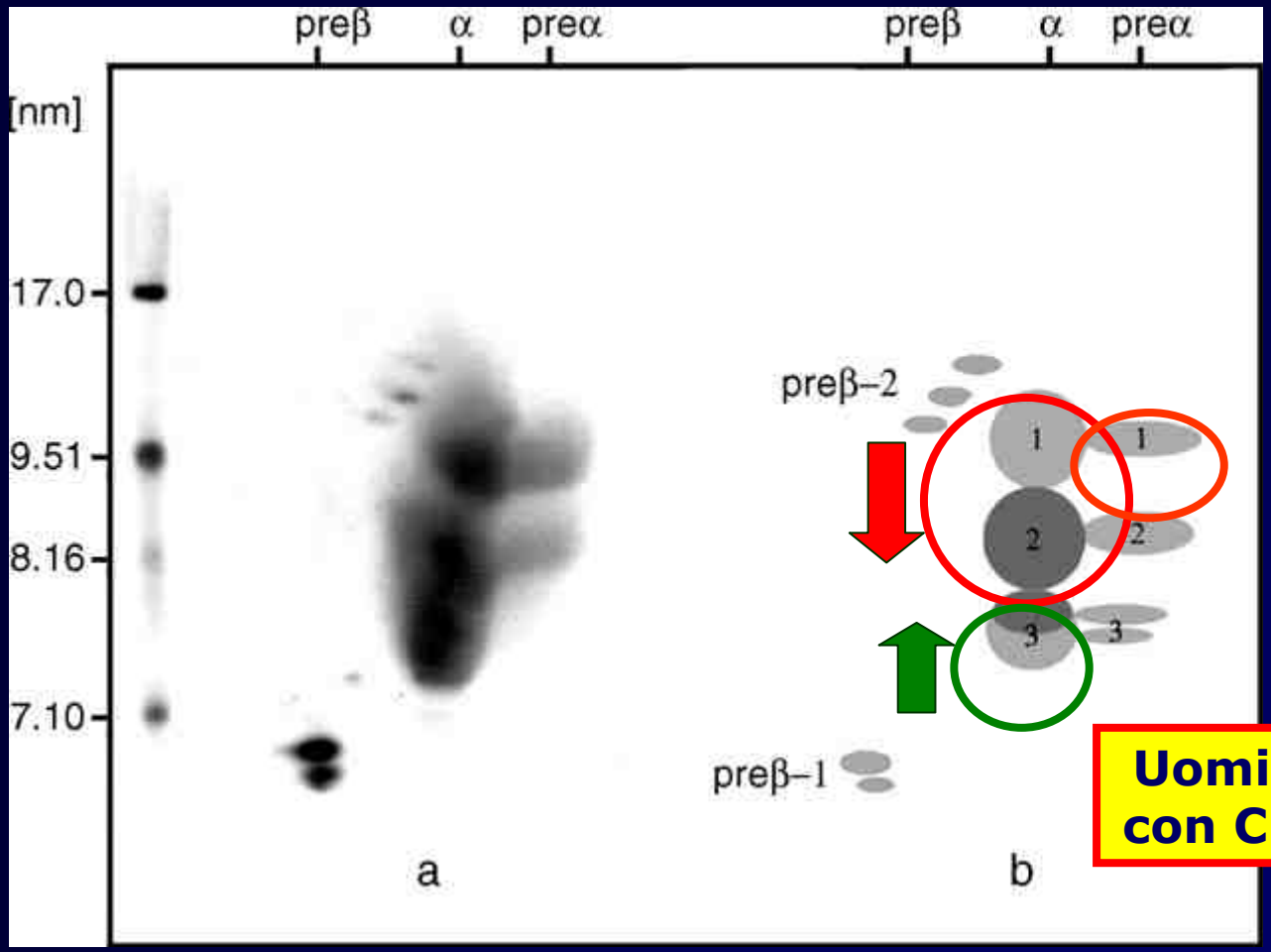
- preβ

- 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
[b] Lipid Metabolism Laboratory, JM-USDA-Human Nutrition Research Center on Aging at Tufts University, Boston, MA, USA

ARTICLE INFO

Article history:

ABSTRACT

The common *Taq*IB variant in the gene coding for cholesteryl ester transfer protein (CETP), a key enzyme

in B2 allele carriers with lower $HOMA_{IR}$, BMI or triglycerides levels.

At multivariate analysis, CETP polymorphism, apoA-I, triglycerides and BMI were independent determinants of HDL-C concentration in diabetic women; apo-A-I, triglycerides, age and creatinine in controls.

Type 2 diabetes is associated with a more atherogenic lipid profile; the CETP *Taq*IB variant may partly prevent these modifications in diabetic women with a milder degree of insulin resistance and its related disorders.

Scopo dello studio:

Valutare gli effetti della menopausa e del diabete sul profilo lipidico e sulle sottopopolazioni HDL in donne con e senza diabete di tipo 2.

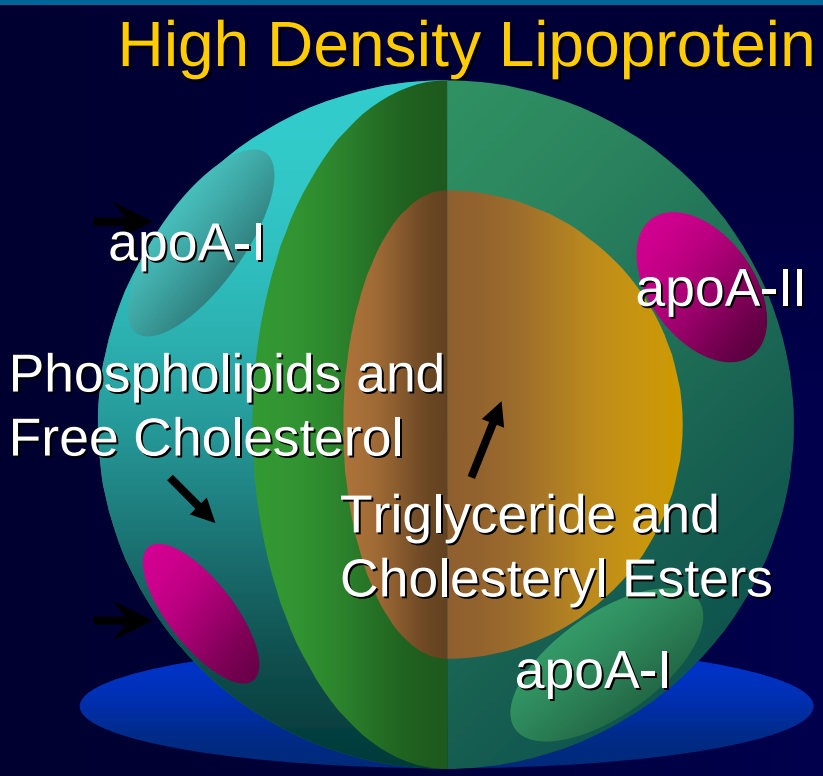
Sottopopolazioni HDL nelle donne con e senza Diabete Mellito di tipo 2

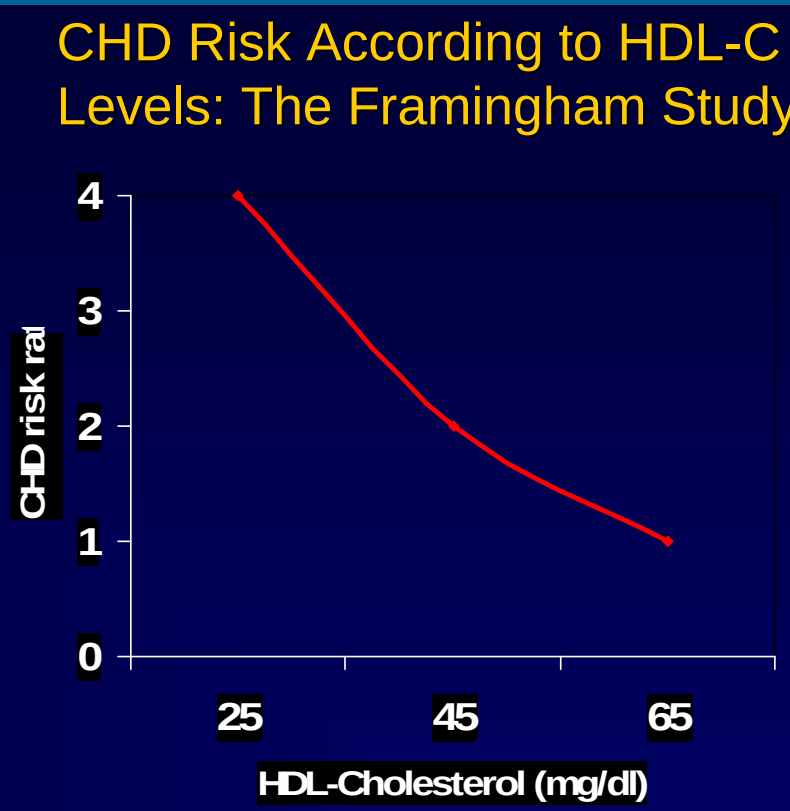
	Donne con DM2	Donne non diabetiche	P
α-1 (mg/dl) ↓	19.32±8.97	23.35±9.58	0.006
α-2 (mg/dl) ↓	41.29±9.62	45.47±8.99	0.005
α-3 (mg/dl) ↑	18.18±5.56	16.36±3.74	0.02
α-4 (mg/dl)	10.90±3.58	9.71±3.07	0.02
Pre-α1 (mg/dl) ↓	5.51±3.39	6.74±3.46	0.02
Pre-α2 (mg/dl)	6.77±2.99	7.10±2.48	-
Pre-α3 (mg/dl)	2.46±0.97	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

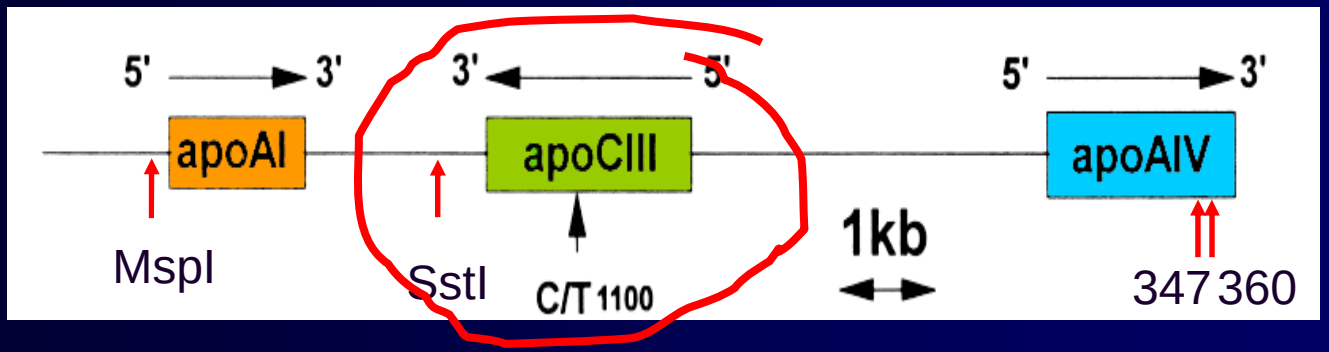
I dati sono n, %, medie ± SD. Sono presentati solo i valori di P significativi

Russo GT et al; Atherosclerosis 2010

I livelli di HDL-C e trigliceridi sono in parte geneticamente determinati: ruolo del APOA1-APOC3-APOA4-APOA5 locus







Impatto polimorfismo CETP taq1B sui livelli di HDL-C nelle donne diabetiche di tipo 2

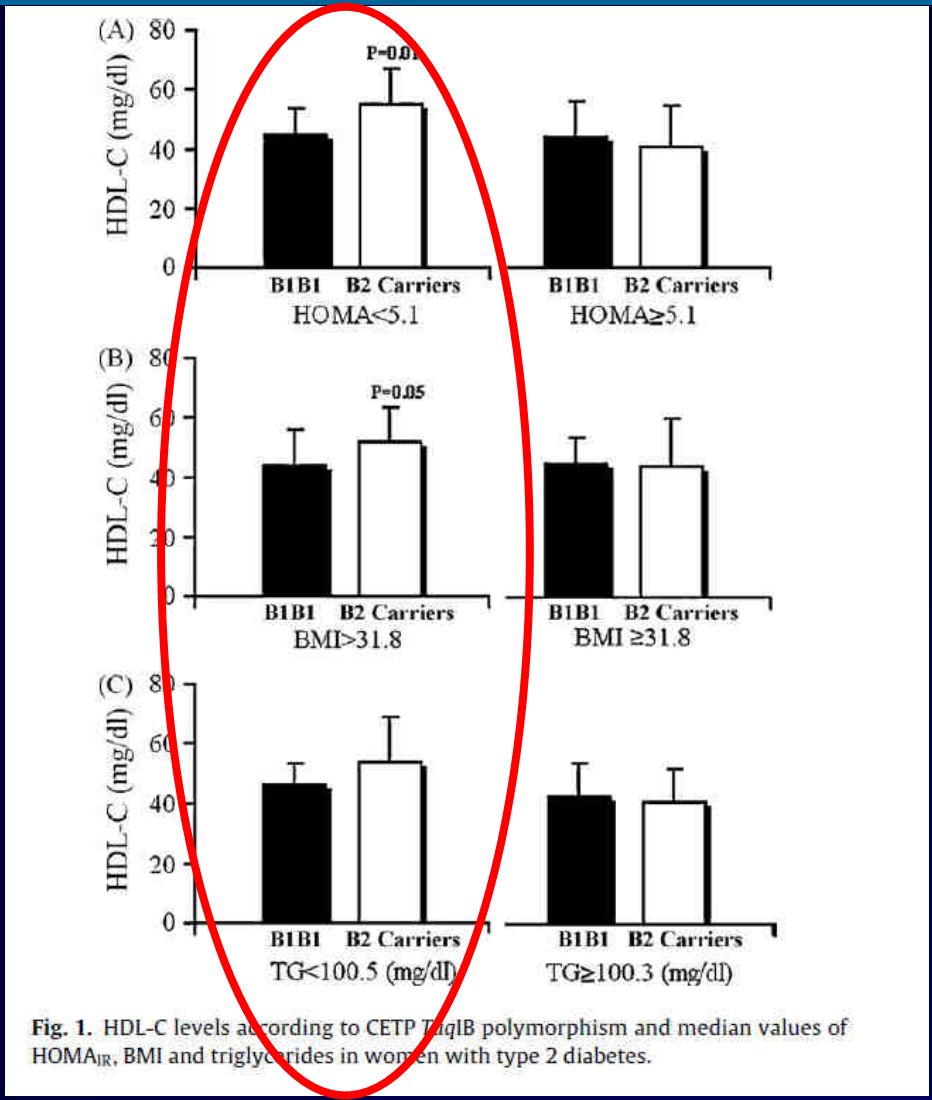


Fig. 1. HDL-C levels according to CETP TaqIB polymorphism and median values of $HOMA_{IR}$, BMI and triglycerides in women with type 2 diabetes.

Russo GT, Atherosclerosis 2010

ELSEVIER

Atherosclerosis 158 (2001) 173–181

ATHEROSCLEROSIS

www.elsevier.com/locate/atherosclerosis

Association of the Sst-I polymorphism at the *APOC3* gene locus with variations in lipid levels, lipoprotein subclass profiles and coronary heart disease risk: the Framingham offspring study

Giuseppina T. Russo [a], James B. Meigs [b], L. Adrienne Cupples [c], Serkalem Demissie [c], James D. Otvos [d], Peter W.F. Wilson [e], Carlos Lahoz [a], Domenico Cucinotta [f], Patrick Couture [a], Tonya Mallory [g], Ernst J. Schaefer [a], Jose M. Ordovas [a,*]

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associations were observed in women. Despite the described associations with lipid and glucose metabolism related risk factors, we did not find any significant increase in CHD risk associated with the S2 allele in this population.

Nelle donne, S2 allele (mutato) associato con TC, LDL-C e ApoB;

Negli uomini, S2 allele (mutato) associato con sdLDL e insulinemia

Nessuna associazione con CHD in entrambi i sessi.

Russo GT et al, Atherosclerosis 2001

Altri fattori di rischio: quale impatto nella donna diabetica?

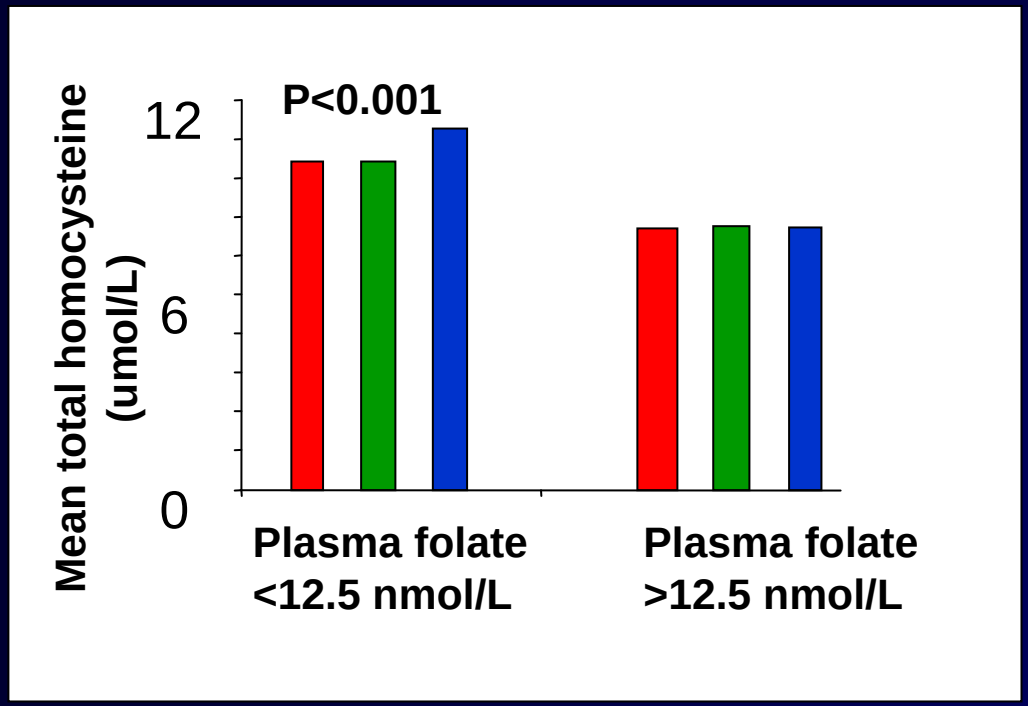
TRADIZIONALI

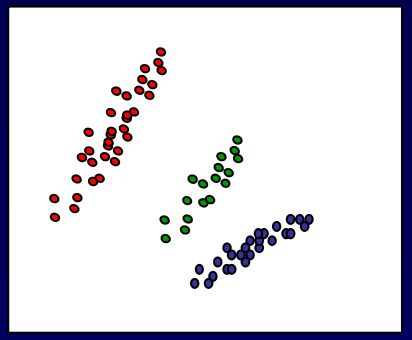
- Diabete
- Lipidi
- Ipertensione
- Obesità
- Inattività fisica
- Fumo
- Familiarità
- Menopausa precoce

NUOVI

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

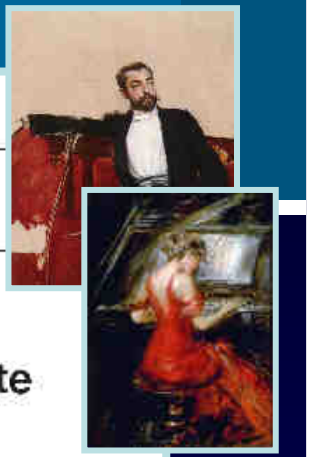
Plasma total Homocysteine (tHcy) concentration of Framingham Offspring Study participants according to MTHFR C677T genotype and plasma folate status





CC
CT
TT

Russo GT et al, J Nutr 2003



Nutrient-Gene Interactions

Age and Gender Affect the Relation between Methylenetetrahydrofolate Reductase C677T Genotype and Fasting Plasma Homocysteine Concentrations in the Framingham Offspring Study Cohort[1,2]

Giuseppina T. Russo,* Simonetta Friso,† Paul F. Jacques,[3] Gail Rogers, Domenico Cucinotta,* Peter W. F. Wilson,** Jose M. Ordovas, Irwin H. Rosenberg and Jacob Selhub

*Jean Mayer-U.S. Department of Agriculture Human Nutrition Research Center on Aging at Tufts University, Boston, MA; *Department of Internal Medicine, University of Messina, Messina, Italy; †Department of Clinical and Experimental Medicine, Policlinico G.B. Rossi, University of Verona, Verona, Italy; **Boston University School of Medicine and The Framingham Heart Study, National Heart, Lung, and Blood Institute, Framingham, MA*

- ✓ Anche "fattori personali" possono influenzare l'effetto del genotipo.
- ✓ L'associazione tra il genotipo MTHFR TT e i livelli di tHcy era modulata dall'età e dal sesso e più evidente in soggetti più giovani di sesso maschile.

Russo GT et al, J Nutr 2003

J. Endocrinol. Invest. 31: 546-551, 2008

Menopause modulates homocysteine levels in diabetic and non-diabetic women

G.T. Russo[1], A. Di Benedetto[1], E. Alessi[1], A. Giandalia[1], A. Gaudio[1], R. Ientile[2], K.V. Horvath[3], B. Asztalos[3], G. Raimondo[1], and D. Cucinotta[1]

[1]Department of Internal Medicine; [2]Department of Biochemical Sciences, University of Messina, Messina, Italy; [3]Lipid Metabolism Laboratory, JM-USDA- Human Nutrition Research Center on Aging at Tufts University, Boston, MA-USA

- ✓ **In healthy women tHcy concentration usually increases after menopause and decreases with HRT.**
- ✓ **To date, data on the role of menopause and other factors modulating tHcy in diabetic women are scarse.**

AIM: to evaluate plasma tHcy concentrations and its major determinants in a group of pre- and postmenopausal women with and without type 2 diabetes

Fasting tHcy plasma levels according to Menopause and MTHFR genotype in type 2 diabetic women

	Geometric mean tHcy (95% CI)µmol/L				
	CC	CT	TT	P^1	P^2
Diabetic women					
Premenopause	6.8* (5.5-8.4)	9.4 (8.3-10.6)	12.7 (10.3-15.8)	0.001	0.09
Postmenopause	10.9 * (9.3-12.8)	11.7 (9.9-13.9)	11.3 (9.3-13.7)	-	-
Non diabetic women					
Premenopause	8.4* (6.5-10.7)	9.5 (7.9-11.5)	14.5 (10.8-19.3)	0.01	-
Postmenopause	10.5* (8.7-12.7)	10.5 (9.2-11.9)	13.5 (10.8-16.8)	-	-

Russo GT , Cucinotta D. et al., J Endocr Invest 2008

Acta Diabetol
DOI 10.1007/s00592-009-0169-5

ORIGINAL ARTICLE

Mild hyperhomocysteinemia, C677T polymorphism on methylenetetrahydrofolate reductase gene and the risk of macroangiopathy in type 2 diabetes: a prospective study

Giuseppina Tiziana Russo · Antonino Di Benedetto · Domenico Magazzù · Annalisa Giandalia · Carlo Bruno Giorda · Riccardo Ientile · Marcello Previti · Enrico Di Cesare · Domenico Cucinotta

Russo GT, Acta Diabetologica 2011

Fattori di rischio: quale impatto nella donna?

TRADIZIONALI

- Diabete
- Lipidi
- Ipertensione
- Obesità
- Inattività fisica
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NUOVI

- Sindrome metabolica
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- Iperomocisteinemia
- Disfunzione endoteliale
- Fattori psicosociali
- Inquinamento
- altri

ORIGINAL INVESTIGATION Open Access

Diabetes abrogates sex differences and aggravates cardiometabolic risk in postmenopausal women

Filipa Mascarenhas-Melo[1], Daniela Marado[2], Filipe Palavra[1,3], José Sereno[1], Álvaro Coelho[2], Rui Pinto[4], Edite Teixeira-Lemos[1,5], Frederico Teixeira[1] and Flávio Reis[1*]

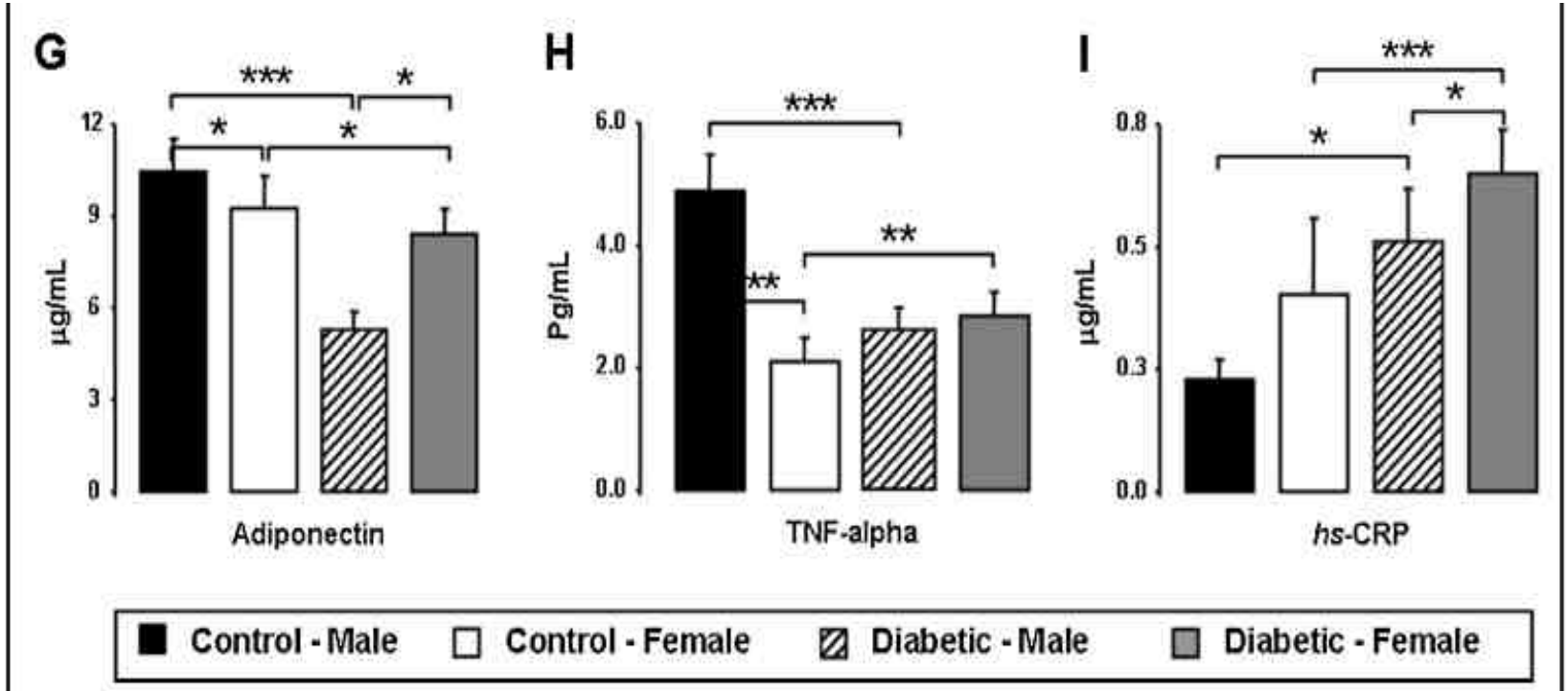


Figure 1 Gender effect on control and diabetic populations. Serum total HDL-c (**A**), large HDL-c (**B**), small HDL-c (**C**), waist circumference (**D**), VEGF (**E**), uric acid (**F**), adiponectin (**G**), TNF-α (**H**) and *hsCRP* (**I**), in male and female diabetic patients and controls. Results are presented as mean ± SEM. *p<0.05, **p<0.01 and ***p<0.001.

Cardiovasc Diabetol 2013

Lipid and non-lipid cardiovascular risk factors in postmenopausal type 2 diabetic women with and without coronary heart disease.

Russo G.T. [a*], Giandalia A. [a], Romeo E.L. [a], Marotta M. [a], Alibrandi A. [c], Horvath K.V. [b], Asztalos B. [b], Cucinotta D. [a]

[a] *Department of Clinical and Experimental Medicine, University of Messina, Italy;*

[b] *Lipid Metabolism Laboratory, JM-USDA- Human Nutrition Research Center on Aging at Tufts University, Boston, MA-USA.*

[a] *Department of Statistic Sciences, University of Messina, Italy;*

Pazienti & Metodi → **95 donne con diabete mellito di tipo 2 post-menopausa (36 CON CHD; 59 SENZA CHD)**

Criteri di esclusione → **Terapia con farmaci estroprogestinici, anti-infiammatori, glitazoni, ipolipemizzanti.**

Russo GT, submitted

Table 2- Lipid and non-lipid risk factors in type 2 diabetic women with and without coronary heart disease.

	Diabetic women without CHD	Diabetic women with CHD	P	P 1
Fasting blood glucose (mg/dl)	160.12 ± 45.65	163.06 ± 54.35	-	-
HOMA-IR	5.77±5.11	7.97±6.52	-	-
HbA1c (%)	7.60 ± 1.49	7.56 ± 1.53	-	-
Creatinine (mg/dl)	0.87 ± 0.13	1.02 ± 0.29	0.003	0.05
Creatinine clearance (ml/min)*	81.21 ± 24.91	63.24 ± 20.00	0.0004	
Total cholesterol (mg/dl)	188.53 ± 29.16	178.51 ± 27.26	-	-
LDL-C (mg/dl)	117.32 ± 26.81	112.81 ± 25.09	-	-
HDL-C (mg/dl)	49.83 ± 13.66	48.29 ± 13.54	-	-
Triglycerides (mg/dl)	102.36 ± 40.80	134.80 ± 57.63	0.003	0.002
RLP-C (mg/dl)	7.22 ± 3.96	9.31 ± 5.93	0.04	0.06
SdLDL (mg/dl)	8.67 ± 7.85	12.41 ± 7.23	0.02	0.01
Apo A I (mg/dl)	123.63 ± 17.84	122.06 ± 19.99	-	-
tHcy (mmol/l)	12.67 ± 5.43	16.33 ± 7.37	0.002	-
Folate (ng/mL)	4.97 ± 2.52	4.92 ± 1.93	-	-
Vitamin B12 (pg/mL)	396.59 ± 181.79	409.48 ± 203.98	-	-
hsCRP (mg/L)	5.02 ± 7.34	4.90 ± 4.55	-	-
IL-6 (pg/ml)	3.04 ± 3.84	3.35 ± 2.03	-	-
sVCAM-1 (ng/ml)	748.18 ± 194.80	940.11 ± 481.97	0.048	-

Russo GT, submitted

Table 3- Factors associated with coronary heart disease (CHD) in type 2 diabetic women.

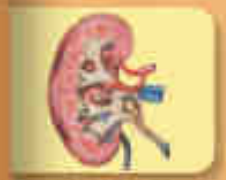
	Univariate associations			Multivariate associations		
	B	**P**	**OR (95% CI)**	**B**	**P**	**OR (95% CI)**
Age	0.126	0.001	1.134 (1.067-1.204)			
Menopause duration	0.131	0.001	1.140 (1.063-1.223)			
Creatinine Clearance	-0.038	0.001	0.963 (0.941-0.985)	-0.70	0.017	0.932 (0.880-0.987)
Hypertension	2.24	0.004	9.395 (2.050-43.058)			
Triglycerides	0.014	0.004	1.014 (1.004-1.023)			
Creatinine	4.19	0.006	65.777 (3.420-1264.983)			
Insulin therapy	2.81	0.01	16.571 (1.975-139.059)			
tHcy	0.09	0.02	1.098 (1.017-1.186)			
sVCAM	0.002	0.02	1.002 (1.000-1.004)			
Diabetes duration	0.055	0.04	1.056 (1.002-1.113)			
CVD Family history	1.306	0.04	3.692 (1.052-12.957)			
SdLDL	0.067	0.04	1.069 (1.003-1.139)	0.206	0.037	1.224 (1.012-1.492)
RLP-C	0.090	0.05	1.094 (0.998-1.199)			

Russo GT, submitted

le Monografie degli Annali AMD 2011

Focus su:

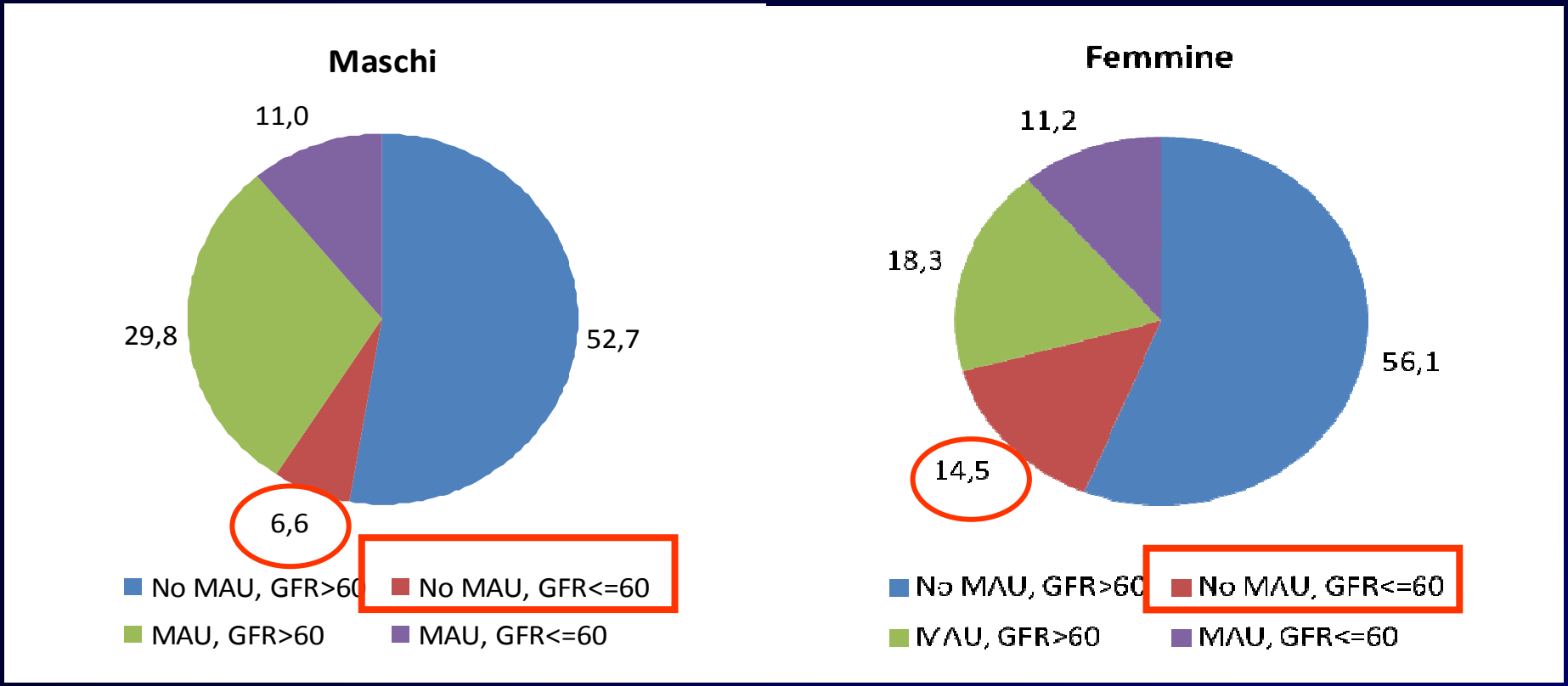
PATTERN ASSISTENZIALI IN BASE AL LIVELLO DI FUNZIONALITÀ RENALE



A. Carrello, S. De Cosmo,
I. Gentile, C.E. Guerra,
A. Nicolucci, R. Pontremoli,
M.C. Rossi, C. Russo

Monografie degli Annali AMD 2011 PATTERN ASSISTENZIALI IN BASE AL LIVELLO DI FUNZIONALITÀ RENALE

Distribuzione della popolazione divisa per SESSO in relazione alla presenza di MAU e di riduzione del GFR (%)



Mentre fra i maschi prevalgono le forme di MAU associate ad un filtrato glomerulare nella norma, fra le donne risultano più comuni le forme isolate di riduzione del GFR. L'associazione delle due alterazioni è invece ugualmente rappresentata nei due sessi.

Logistic regression analysis of coronary, cerebrovascular or peripheral events with CKD phenotypes as covariates

- **Coronary events, *N* = 2,405,**
- **Cerebrovascular, *N* = 1,298,**
- **Peripheral, *N* = 894**

Variable	Coronary events	Cerebrovascular events	Peripheral events
Age (1 year)	1.020 (1.014–1.026)	1.030 (1.022–1.038)	1.013 (1.004–1.021)
Male sex	2.129 (1.906–2.379)	1.16 (1.02–1.33)	1.23 (1.04–1.45)
Smoking status			
Never	1.0	—	1.0
Former	1.508 (1.355–1.678)	—	1.33 (1.13–1.57)
Current	1.065 (0.921–1.233)	—	1.38 (1.12–1.71)
Diabetes duration (1 year)	1.009 (1.004–1.014)	1.024 (1.017–1.030)	1.025 (1.017–1.033)
Glucose-lowering treatment			
Diet	1.0	1.0	1.0
OHA	1.268 (1.075–1.495)	1.20 (0.96–1.51)	1.38 (1.01–1.89)
OHA + insulin	1.743 (1.409–2.155)	0.86 (0.63–1.16)	1.52 (1.05–2.20)
Insulin	2.027 (1.674–2.455)	1.48 (1.15–1.91)	2.12 (1.52–2.86)
Triglycerides (10 mg/dL)	0.992 (0.986–0.998)	—	—
HDL cholesterol (5 mg/dL)	0.934 (0.916–0.954)	0.958 (0.936–0.982)	0.933 (0.905–0.961)
Dyslipidemia	2.730 (2.440–3.055)	1.52 (1.33–1.75)	—
Hypertension	3.050 (2.505–3.715)	1.42 (1.13–1.77)	—
Retinopathy			
Absent	—	1.0	1.0
Nonadvanced	—	1.37 (1.17–1.62)	1.71 (1.41–2.06)
Advanced	—	0.88 (0.72–1.08)	2.52 (2.07–3.07)
CKD phenotype			
No CKD	1.0	1.0	1.0
Stages 1–2 CKD	0.901 (0.794–1.022)	1.41 (1.20–1.65)	1.51 (1.25–1.82)
Nonalbuminuric stage ≥3 CKD	1.514 (1.304–1.757)	1.22 (1.01–1.48)	1.40 (1.11–1.76)
Albuminuric stage ≥3 CKD	1.270 (1.083–1.490)	1.69 (1.40–2.00)	1.88 (1.52–2.34)
Cerebrovascular events	2.472 (2.156–2.834)	2.51 (2.19–2.87)	2.77 (2.37–3.23)
Peripheral events	2.702 (2.306–3.167)	3.75 (3.17–4.44)	3.81 (3.21–4.51)

Results are presented as OR (95% CI). Variables excluded: HbA_{1c}, BMI. OHA, oral hypoglycemic agent.

Solini A. et al, Diabetes Care 2012

Diverse ipotesi per spiegare l'eccesso di rischio nelle donne diabetiche

1. Maggior numero di fattori di rischio
2. Maggiore impatto dei fattori di rischio
3. Differenze "strutturali" e/o "funzionali" dell'albero cardiovascolare
4. **Differente presentazione clinica**
5. Disparità nel trattamento o nella risposta al trattamento

Una differente presentazione clinica può ritardare la diagnosi e modificare la gestione

ARTICLE IN PRESS

Gender Differences in Symptoms During 60-Second Balloon Occlusion of the Coronary Artery

Akira Tamura, MD[a,*], Shigeru Naono, MD[b], Kumie Torigoe, MD[a], Mitsuteru Hino, MD[a], Satoshi Maeda, MD[b], Kazuhiro Shinozaki, MD[b], Hirofumi Zaizen, MD[b], and Junichi Kadota, MD, PhD[a]

Previous investigations have demonstrated the presence of gender differences in the symptoms of angina pectoris and acute coronary syndrome. However, most of these investigations have had certain limitations, including being retrospective, an interview-related bias, a various duration of myocardial ischemia, and a lack of multivariate analysis, all of which would have affected the results. Accordingly, we prospectively examined the presence or absence of chest pain and non−chest pain symptoms during a 60-second balloon inflation in the setting of percutaneous coronary intervention, which provides a unique model of transient myocardial ischemia, in 110 men and 80 women with coronary artery disease. Chest pain and/or non−chest pain symptoms (occipital pain, jaw pain, neck/throat pain, shoulder pain, upper arm pain, back pain, and nausea) were observed during the balloon inflation in 72 men and 52 women. In the 124 patients with any symptoms during the balloon inflation, non−chest pain symptoms were more common in women than in men (31% vs 14%, $p = 0.02$); however, the incidence of chest pain did not differ between the men and women. After adjustment for covariables, including age, body mass index, hypertension, diabetes mellitus, current smoking, previous myocardial infarction, target vessels, β-blocker use, and calcium antagonist use, female gender remained significantly associated with non−chest pain symptoms (odds ratio 3.3, 95% confidence interval 1.2 to 9.9, $p = 0.02$). In conclusion, non−chest pain symptoms during the 60-second balloon occlusion of the coronary artery were more common in women than in men, supporting the presence of the gender difference in myocardial ischemic symptoms. (Am J Cardiol 2013;■:■−■)

Sex Differences in Presentation and Outcome Among Patients With Type 2 Diabetes and Coronary Artery Disease Treated With Contemporary Medical Therapy With or Without Prompt Revascularization

A Report From the BARI 2D Trial (Bypass Angioplasty Revascularization Investigation 2 Diabetes)

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New York, New York; Pittsburgh, Pennsylvania; Washington, DC; Birmingham, Alabama; São Paulo, Brazil; Toronto, Ontario, Canada; and Boston, Massachusetts

Objectives This study evaluated differences in outcome among women and men enrolled in the BARI 2D (Bypass Angioplasty Revascularization Investigation 2 Diabetes) trial.

Background Women and men with coronary artery disease have different clinical presentations and outcomes that might be due to differences in management.

Methods We compared baseline variables, study interventions, and outcomes between women and men enrolled in the BARI 2D trial and randomized to aggressive medical therapy alone or aggressive medical therapy with prompt revascularization.

Results At enrollment, women were more likely than men to have angina (67% vs. 58%, $p < 0.01$) despite less disease on angiography (Myocardial Jeopardy Index 41 ± 24 vs. 46 ± 24, $p < 0.01$; number of significant lesions 2.3 ± 1.7 vs. 2.8 ± 1.8, $p < 0.01$). Over 5 years, no sex differences were observed in BARI 2D study outcomes after adjustment for difference in baseline variables (death/myocardial infarction/cerebrovascular accident: hazard ratio: 1.11, 99% confidence interval [CI]: 0.85 to 1.44). However, women reported more angina than men (adjusted odds ratio: 1.51, 99% CI: 1.21 to 1.89, $p < 0.0001$) and had lower scores for the Duke Activity Status Index (adjusted beta coefficient: −1.58, 99% CI: −2.84 to −0.32, $p < 0.01$).

Conclusions There were no sex differences in death, myocardial infarction, or cerebrovascular accident among patients enrolled in the BARI 2D trial. However, compared with men, women had more symptoms and less anatomic disease at baseline, with persistence of higher angina rates and lower DASI scores after 5 years of medical therapy with or without prompt revascularization. (Bypass Angioplasty Revascularization Investigation in Type 2 Diabetes [BARI 2D]; NCT00006305) (J Am Coll Cardiol 2013;61:1767–76)

JACC 2013

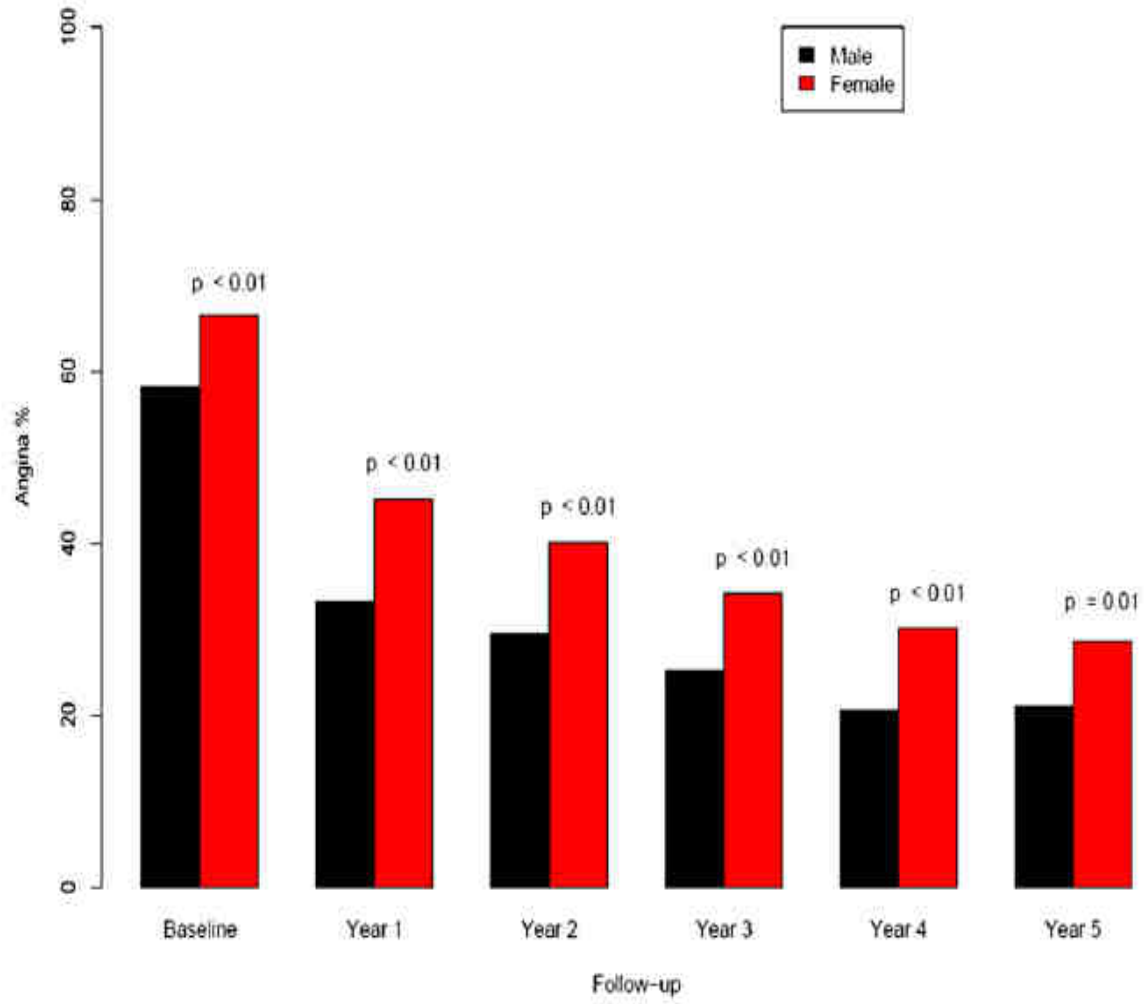

Figure 2 **Angina Prevalence in Women and Men**

Prevalence of angina in women and men at each yearly follow-up visit.

JACC 2013

Diverse ipotesi per spiegare l'eccesso di rischio nelle donne diabetiche

1. Maggior numero di fattori di rischio
2. Maggiore impatto dei fattori di rischio
3. Differenze "strutturali" e/o "funzionali" dell'albero cardiovascolare
4. Differente presentazione clinica
5. **Disparità nel trattamento o nella risposta al trattamento**

Krämer et al. Cardiovascular Diabetology 2012, 11:88
http://www.cardiab.com/content/11/1/88

CARDIO VASCULAR DIABETOLOGY

ORIGINAL INVESTIGATION Open Access

Gender disparities in diabetes and coronary heart disease medication among patients with type 2 diabetes: results from the DIANA study

Heike U Krämer[1†], Elke Raum[1*†], Gernot Rüter[2], Ben Schöttker[1], Dietrich Rothenbacher[3], Thomas Rosemann[4], Joachim Szecsenyi[5] and Hermann Brenner[1]

Kramer HU, cardiovascular Diabetology 2012

Table 3 Coronary heart disease medication by gender and prevalent coronary heart disease

Medication of interest	All				With coronary heart disease			
	Men (n = 624)		Women (n = 522)		Men (n = 147)		Women (n = 67)	
	n	%	n	%	n	%	n	%
Antihypertensive drug	507	81.3	412	78.9	144	98.0	63	94.0
Angiotensin-converting enzyme (ACE) inhibitor	**431**	**69.1**	**316**	**60.5**	**120**	**81.6**	**45**	**67.2**
Diuretic	186	29.9	176	33.7	70	47.9	34	50.7
Beta-blocker	267	42.8	228	43.7	112	76.2	48	71.6
Calcium channel blocker	**168**	**26.9**	**106**	**20.3**	**50**	**34.0**	**10**	**14.9**
Lipid lowering drug	277	44.4	216	41.4	110	74.8	45	67.2
Aspirin	**213**	**34.1**	**133**	**25.5**	102	69.4	45	67.2

Number may not always add up to total because of missing values for some items. Significant results ($p < 0.05$) by X^2 test are printed bold.

Kramer HU, Cardiovascular Diabetology 2012

Original Article

Journal of INTERNAL MEDICINE

doi: 10.1111/joim.12073

Gender differences in cardiovascular disease risk factors, treatments and complications in patients with type 2 diabetes: the RIACE Italian multicentre study

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L. Laviola[10], A. Nicolucci[11] & G. Pugliese[12], for the Renal
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Medicine University of Padua, Padua; [9]Department of Internal Medicine
Endocrinology, Andrology and Metabolic Diseases, Department of Emer
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Molecular Medicine 'La Sapienza' University, Rome Italy*

Results. Although CVD was more prevalent in men, women showed a less favourable CVD risk profile and worse performance in achieving treatment targets for haemoglobin A_{1c}, LDL, HDL and non-HDL cholesterol, systolic blood pressure (BP) and in particular obesity [body mass index (BMI) and waist circumference], but not for triglycerides and diastolic BP. However, women were more frequently receiving pharmacological treatment for hypertension and to a lesser extent hyperglycaemia and dyslipidaemia than men, and female gender remained an independent predictor of unmet therapeutic targets after adjustment for confounders such as treatments, BMI, duration of diabetes and, except for the systolic BP goal, age.

Conclusions. In women with type 2 diabetes from the RIACE cohort, a more adverse CVD risk profile and a higher likelihood of failing treatment targets, compared with men, were not associated with treatment differences. This suggests that factors other than gender disparities in treatment intensity are responsible.

Penno G., Ann Intern Med 2013

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

Available online at www.sciencedirect.com

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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]

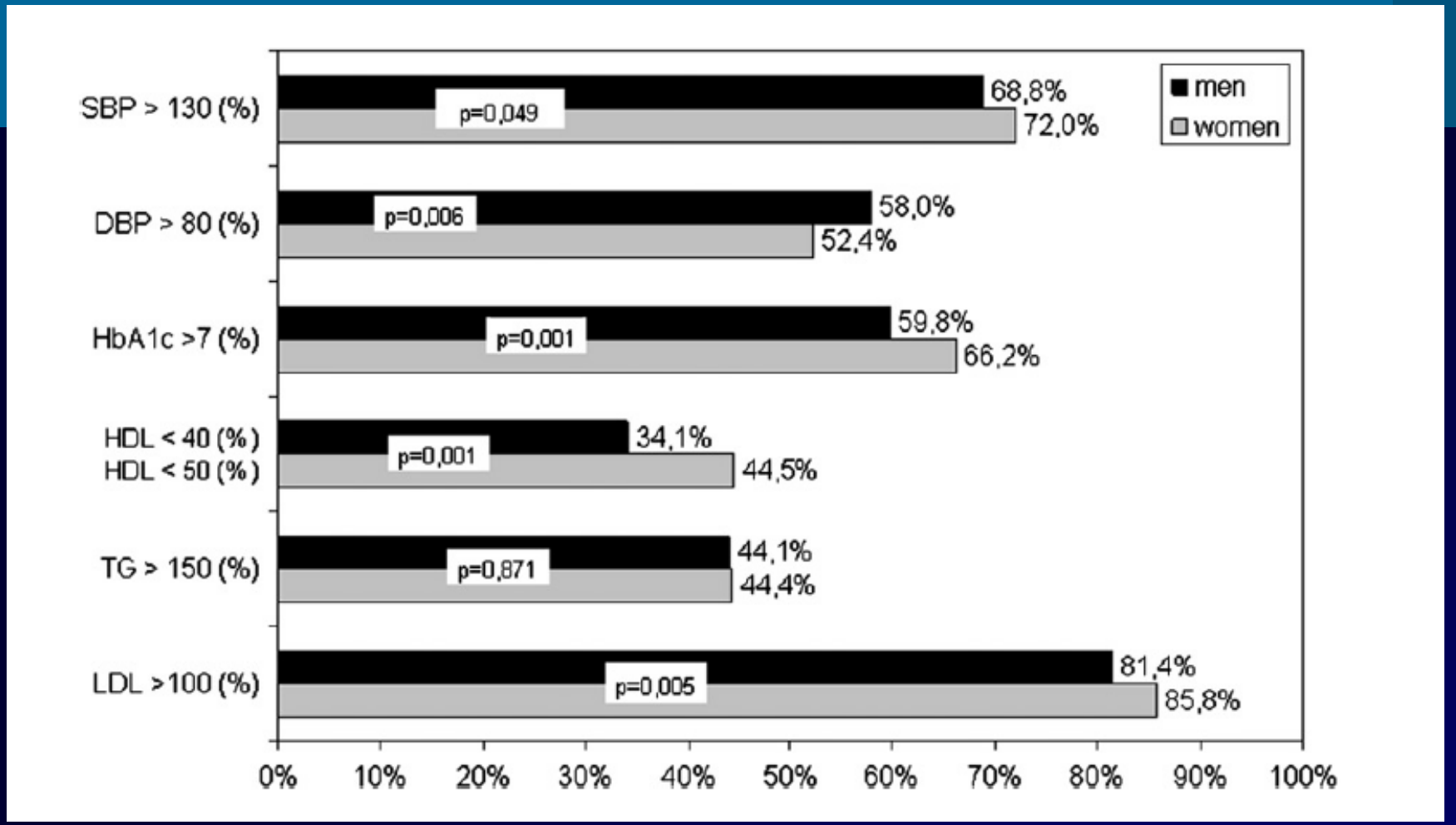

Figure 1 Proportion (%) of men and women out of target for glycated haemoglobin and the cardiovascular risk factors measured in the study. Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA1c, glycated haemoglobin; HDL, HDL cholesterol; TG, triglycerides; LDL, LDL cholesterol.

Franzini L, NMCD 2013

Review

Managing cardiovascular risk factors: Trial evidence in women

J. Hsia*

Hsia J, Nutrition, Metabolism & Cardiovascular Diseases 2010

Riduzione eventi cardiovascolari nelle donne negli studi clinici con statine

Table 2 Cardiovascular event reduction among women in statin trials.

	Number of women	Number of events		RRR (95% CI)
		Placebo	Statin	
Prevalent CHD or equivalent				
4S [10]	827	91	60	34 (9–52)
CARE [11]	576	39	23	43 (4–66)
HPS [12]	5082	396	164	33 (17–43)
LIPID [13]	1516	104	90	11 (–18–33)
PROSPER [14]	3000	194	186	4 (–18–21)
ASCOT [15]	1942	17	19	–10 (–212–43)
No prevalent CHD or equivalent				
West of Scotland [16]	0	NA	NA	NA
AFCAPS/TexCAPS [17]	997	13	7	46 (–31–78)

CHD, coronary heart disease; 4S, Scandinavian Simvastatin Survival Study; CARE, Cholesterol and Recurrent Events; LIPID, Long-term Intervention with Pravastatin in IschemicDisease; HPS, Heart Protection Study; LIPID, Long-Term Intervention with Pravastatin in Ischemic Disease; PROSPER, Prospective Study of Pravastatin in the Elderly at Risk; ASCOT, Anglo-Scandinavian Cardiac Outcomes Trial – Lipid Lowering Arm; AFCAPS/TexCAPS, Air Force/Texas Coronary Artery Prevention Study; RRR, relative risk reduction; NA, not applicable.

Hsia J, Nutrition, Metabolism & Cardiovascular Diseases 2010

Efficacia terapia anti-ipertensiva nelle donne

Table 1 Effectiveness of antihypertensive drug classes vs placebo in men and women.

	BP difference, mm Hg	Major cardiovascular events	
		Risk ratio (95% CI)	*P* value for homogeneity
ACE inhibitor vs placebo			0.80
Women	−4.6/−2.0	0.79 (0.66–0.94)	
Men	−4.4/−2.1	0.81 (0.75–0.88)	
Calcium antagonist vs placebo			0.84
Women	−9.0/−3.5	0.78 (0.59–1.03)	
Men	−7.6/−3.1	0.75 (0.57–0.98)	
Angiotensin receptor blocker vs placebo			0.56
Women	−1.5/−1.0	0.93 (0.81–1.06)	
Men	−1.8/−1.2	0.88 (0.77–1.00)	

ACE, angiotensin-converting enzyme; BP, blood pressure; CI, confidence interval Adapted from Turnbull et al. [5].

Hsia J, Nutrition, Metabolism & Cardiovascular Diseases 2010

Aspirin for primary prevention of cardiovascular events in people with diabetes: meta-analysis of randomised controlled trials

De Bernardis G, Sacco M, Strippoli GFM, Pellegrini F, Graziano G, Tognoni G, Ncolucci A.

Aspirin significantly reduced the risk of myocardial infarction in men (0.57, 0.34 to 0.94) but not in women (1.08, (0.71 to 1.65; P for interaction=0.056).

BMJ 2009

Hindawi Publishing Corporation
Experimental Diabetes Research
Volume 2012, Article ID 570598, 10 pages
doi:10.1155/2012/570598

Review Article

Vascular Disease in Diabetic Women: Why Do They Miss the Female Protection?

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Academic Editor: P. Nilsson

Gender plays a pivotal role in the onset as well as in the progression of the cardiovascular disease with a higher morbidity and mortality being detected in men with respect to women. Type 2 Diabetes Mellitus (T2DM) may reduce gender-related differences in the prevalence of cardiovascular disease by fading the vascular protective effects afforded by estrogen in females. This article will discuss the role of sex and sex hormones on the incidence and mechanisms involved in vascular dysfunction associated to T2DM, which might explain why women with T2DM lack the vascular protection.

IL RUOLO DEGLI ESTROGENI

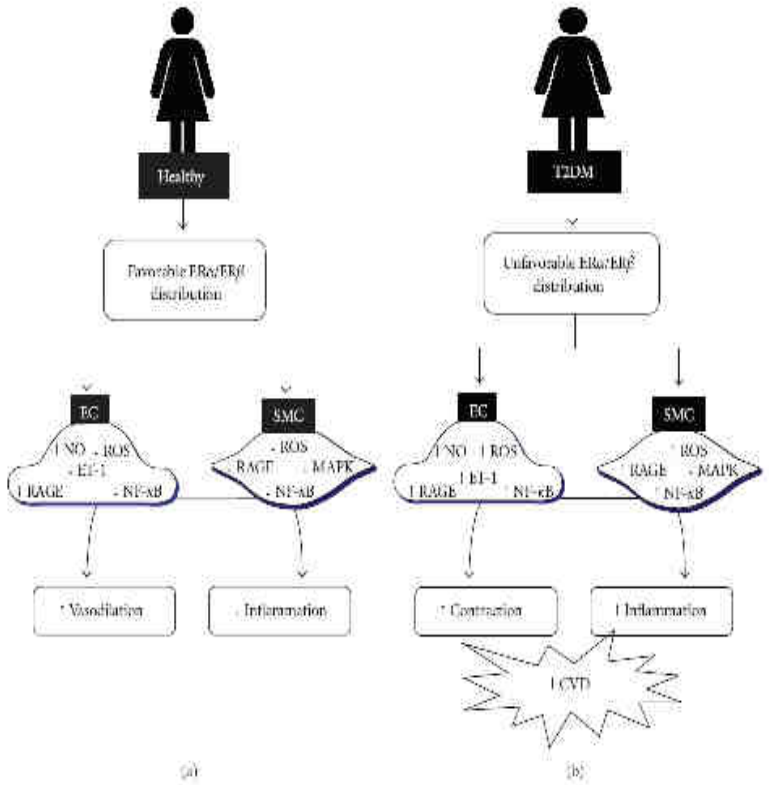


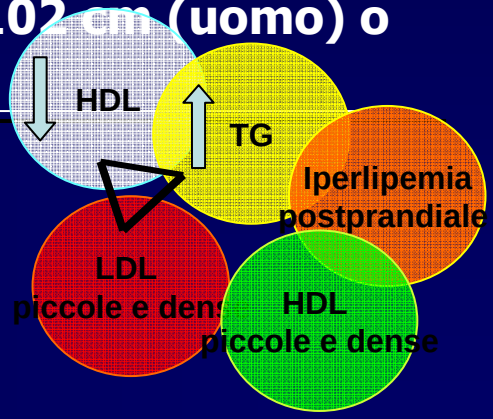
Figure 2: Hypothesis for detrimental estrogen responses in the diabetic vasculature. Type 2 diabetes mellitus (T2DM-) related changes in the vessel wall include decrease of nitric oxide (NO) and concomitant increase of reactive oxygen species (ROS) and endothelin 1 (ET-1) production as well as increased activation of signaling pathways of Nuclear Factor κB (NF-κB), mitogen activated protein kinases (MAPK) and receptors for advanced glycation products (RAGE). In a healthy vasculature (a), with favorable balance of estrogen receptors (ER), estrogen beneficially acts to modulate these factors and to maintain homeostasis. Nevertheless, T2DM adversely modify the balance in expression and/or activity of ERs in a manner that the effects of estrogen are negatively modulated to enhance the existing damage in vascular function (b).

Villela-Dantas 2012

Trattare TUTTI i fattori per ridurre il rischio globale:

Fattori di rischio della cardiopatia coronarica, aterosclerosi inclusa

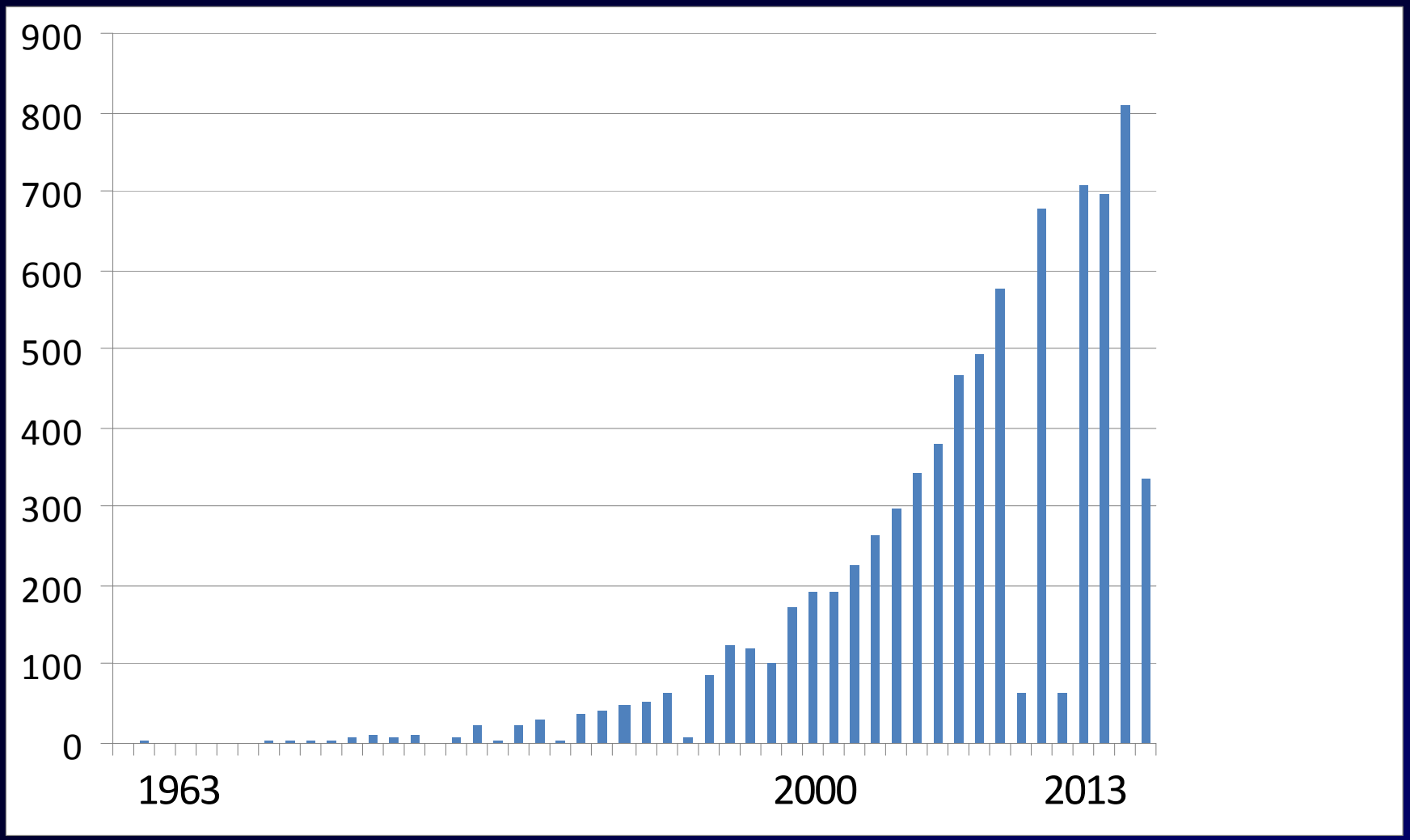
Fattore di rischio	Valori associati alla CHD
Età	>45 anni (uomo) o >55 anni (donna)
Anamnesi familiare	Parente di primo grado con CHD precoce
Tabagismo	Stato di fumatore
Ipertensione	PA >140/90 mmHg o terapia con antipertensivi
C-HDL basso	<40 mg/dl <50 mg/dl nelle donne)
Obesità	BMI >25 kg/m^2 + circ. vita >102 cm (uomo) o >88 cm (donna)



CHD=cardiopatia coronarica; HDL=lipoproteine ad alta densità; PA=pressione arteriosa; BMI=indice di massa corporea

Tratto da Mahley RW, Bersot TP. In: *Goodman & Gilman's The Pharmacological Basis of Therapeutics.* 11° ed. New York: McGraw-Hill Medical Publishing Division, 2006:933–966.

PubMed Results for " cardiovascular –women-diabetes"



GENDER MEDICINE / VOL. 3, NO. 2, 2006

Gender-Specific Care of the Patient with Diabetes: Review and Recommendations

Marianne J. Legato, MD[1]; Andrea Gelzer, MD[2]; Robin Goland, MD[3]; Susana A. Ebner, MD[3]; Sabitha Rajan, MD[4]; Victor Villagra, MD[5]; and Mark Kosowski, MPH; The Writing Group for The Partnership for Gender-Specific Medicine

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CONGRESSO
NAZIONALE
AMD
Rossano Calabro




ndo le donne stanno bene,
to il mondo sta meglio”.

Amartya Sen, premio Nobel per l’economia

Leonardo Da Vinci.
La Dama con l’ermellino.
1485-1490

✓ *Grazie per l’attenzione*