# Incidenza delle complicanze cardiovascolari – lo studio DAI

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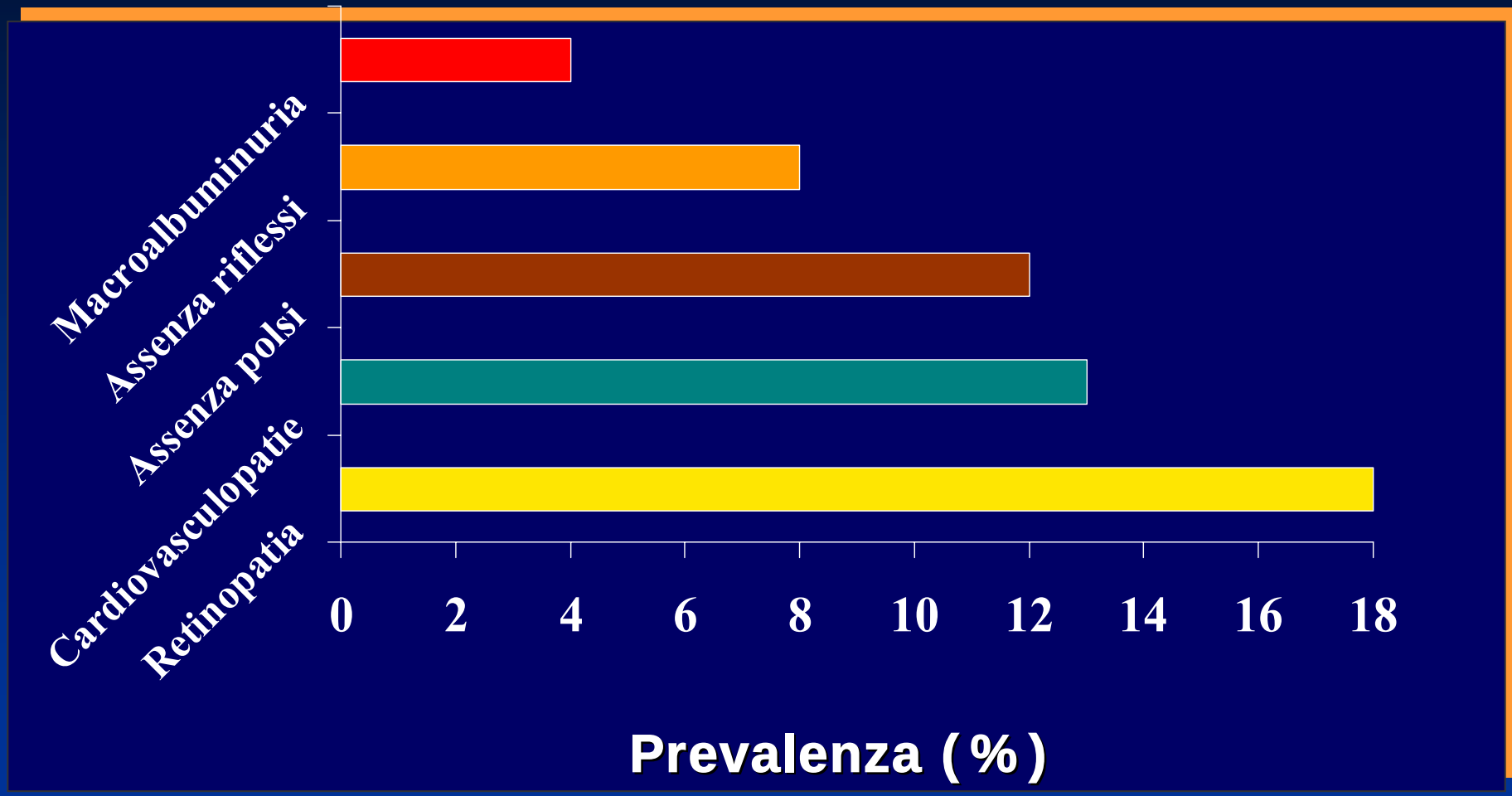
# Diabete Tipo 2
## Complicanze Tardive

- **Le complicanze tardive sono una causa importante di incremento di morbilità e mortalità**
- **Il 25% ha già complicanze in atto al momento della diagnosi[1]**
- **L'incidenza di Cardiopatia Ischemica è da 2 a 4 volte superiore a quella dei non diabetici[2]**
- **La malattia cardiovascolare è la causa maggiore di morbilità e mortalità**

[1]UKPDS: Diabetologia 34, 877, 1991; [2]Haffner et al.: Am J Med 103, 152, 1997

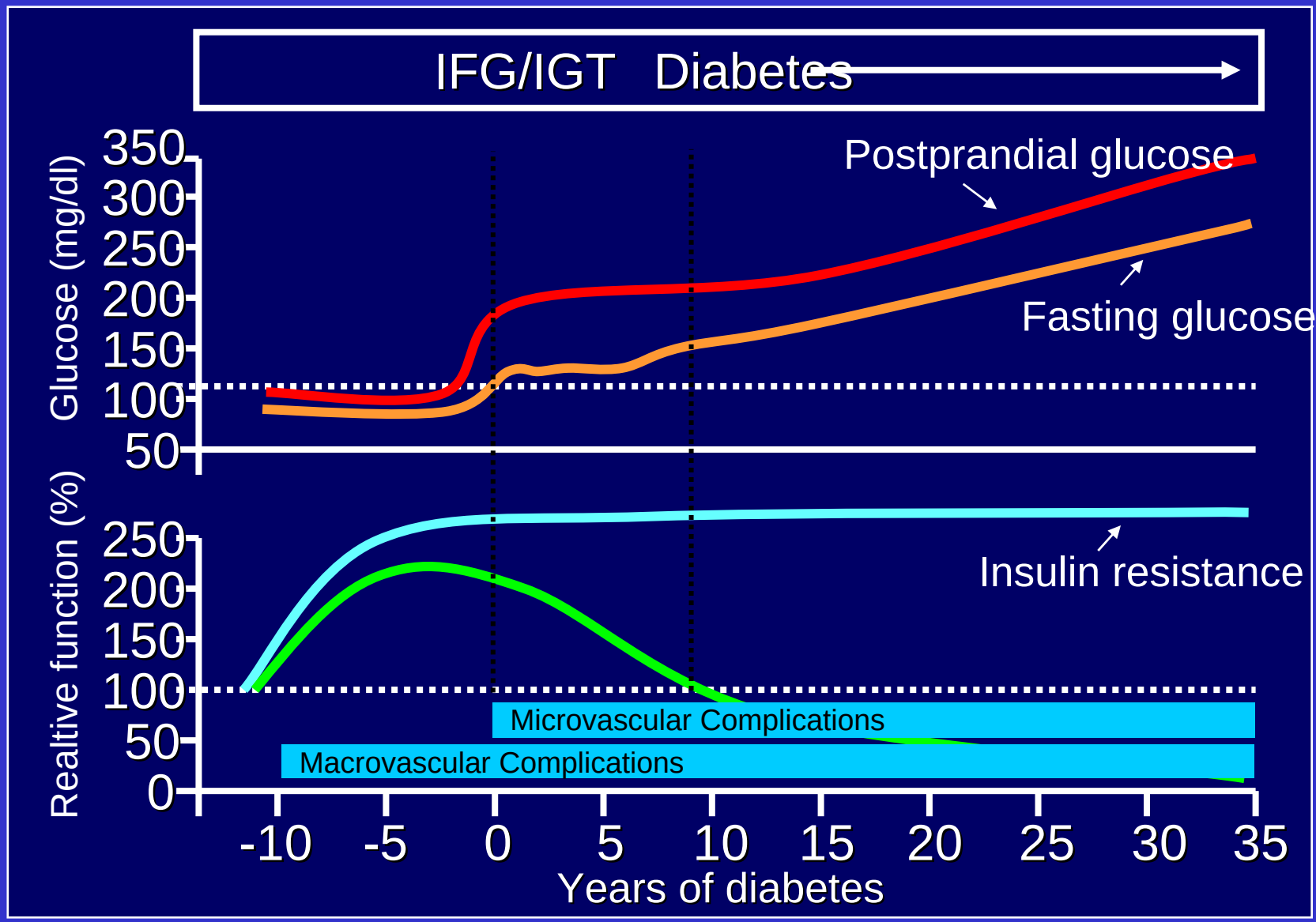
# Diabete tipo 2

## Prevalenza delle complicanze alla diagnosi

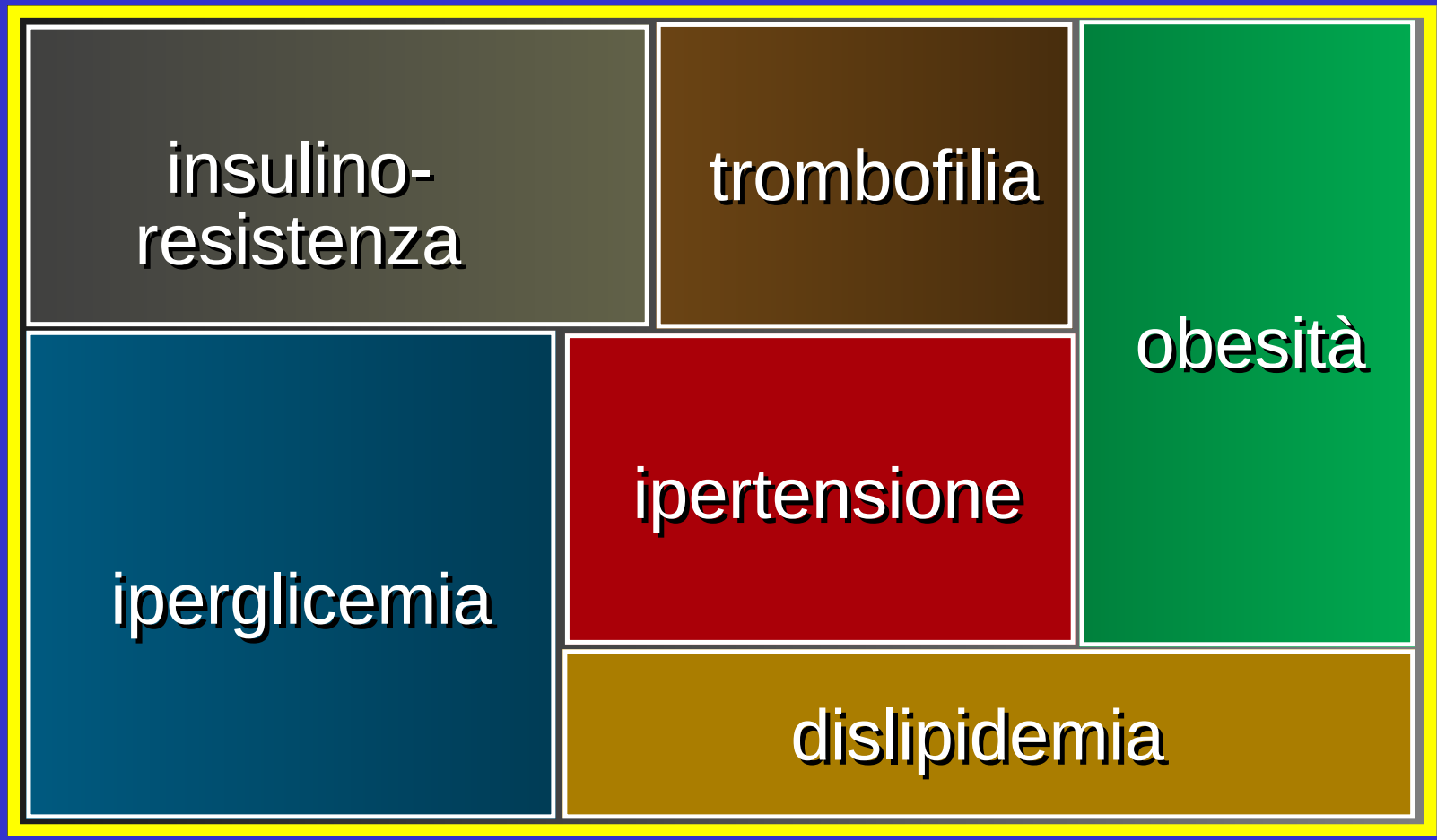



Dagogo-Jack et al.: Arch. Int. Med. 157, 1802, 1997

# Natural history of type 2 diabetes



# IL CONTENITORE DIABETE TIPO 2



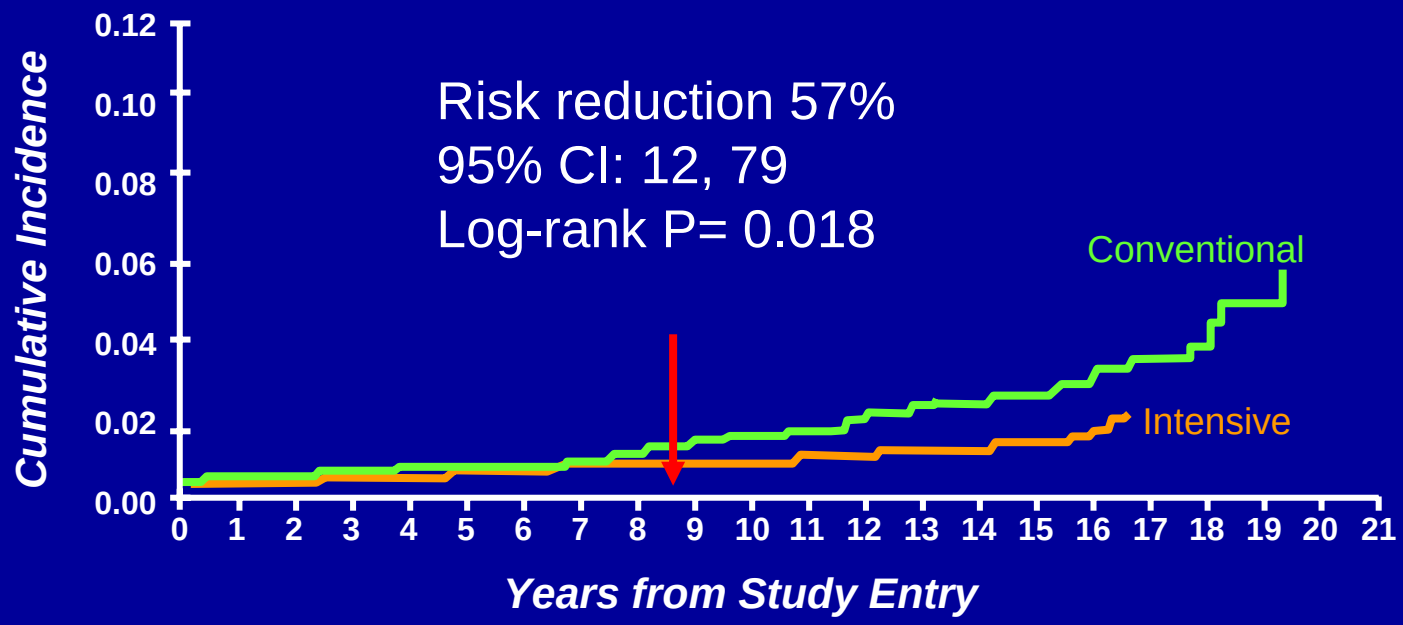
# Intensive Diabetes Treatment and Cardiovascular Disease in Patients with Type 1 Diabetes

DCC/EDIC Research Group

*N Engl J Med, 2005*

# Cardiovascular Events

*Non-Fatal MI, Stroke or CVD Death*




| *Number at Risk* | | | | |
|---|---|---|---|---|
| Intensive | 705 | 686 | 640 | 118 |
| Conventional | 721 | 694 | 637 | 96 |

# Intensive Therapy and Cardiovascular Disease

- The 57% reduction in non-fatal myocardial infarctions and strokes and cardiovascular death in Type 1 diabetes exceeds risk reduction with aggressive management of hypertension and hypercholesterolemia in other populations

# RR e cause di mortalità nel T2DM negli studi Whitehall, Paris Prospective, Helsinki Policemen

| Cause | Whitehall | Paris Prosp | Helsinki Pol |
|---|---|---|---|
| Tutte | 2,48 | 2,16 | 2,06 |
| Malattie CV | 2,56 | 2,17 | 2,75 |
| CHD | 3,19 | 2,12 | 3,52 |
| CerebroVascol | - | 2,39 | 1,54 |
| Neoplasie | 1,47 | 1,76 | 0,53 |
| Altre cause | 4,27 | 2,81 | 2,18 |

**Follow-up 20 anni**

**Balkau B et al: Lancet 350, 1680, 1997**

# RR di mortalità nei diabetici in rapporto ai paesi di origine

| Paese | Studio | Mortalità (RR) | |
|---|---|---|---|
| | | Da ogni causa | Coronarica |
| USA | PHS* | 2,3 | 3,3 |
| Finlandia | Helsinki | 2,06 | 3,52 |
| UK | Whitehall | 2,48 | 3,19 |
| Francia | Paris | 2,16 | 2,12 |
| Europa | DECODE | 1,81 | 1,94 |
| Italia | Verona | 1,42 | 1,41 |

# Variazioni nella mortalità tra il 1971-75* e il 1982-84^ nei due sessi in diabetici e non

| Cause | Diabetici | | Nondiabetici | |
|---|---|---|---|---|
| | Maschi | Femmine | Maschi | Femmine |
| Tutte | - 1,1 | + 10,7 | - 19,7 | - 12,9 |
| Cardiopatie | - 10,0 | + 22,9 | - 32,0 | - 27,1 |
| Card. Ischemica | - 16,6 | + 10,0 | - 43,8 | - 20,4 |

*NHANES I; ^NHANES I epidemiologic follow-up survey

Gu K ET al: JAMA 281, 1291, 1999

# Il diabete come fattore di prognosi negativa

Hazard Ratio* di mortalità per CHD in rapporto alla presenza di cardiopatia e/o diabete*

| Patologia | Uomini | Donne |
|---|---|---|
| Nessuna | 1,0 | 1,0 |
| Solo CHD° | 4,2 | 1,9 |
| Solo Diabete | 2,1 | 3,8 |
| Diabete+CHD° | 6,1 | 5,4 |

*Framingham Study; follow-up 20 a.
°Coronary Heart Disease

Natarajan S et al: Arch Intern Med 163, 1735, 2003

# Prevalenza della malattia CV nei pazienti con diabete di tipo 2 in Italia

- Studio DAI: 19.5%
- Studio SFIDA: 20.1%
- Studio MetaScreen: 16.1%

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- Prevalenza in Francia: 23.5% (C. Delcourt et al, 1998)
- Prevalenza in Germania: 26.7% (Studio CODE-2, 1999)

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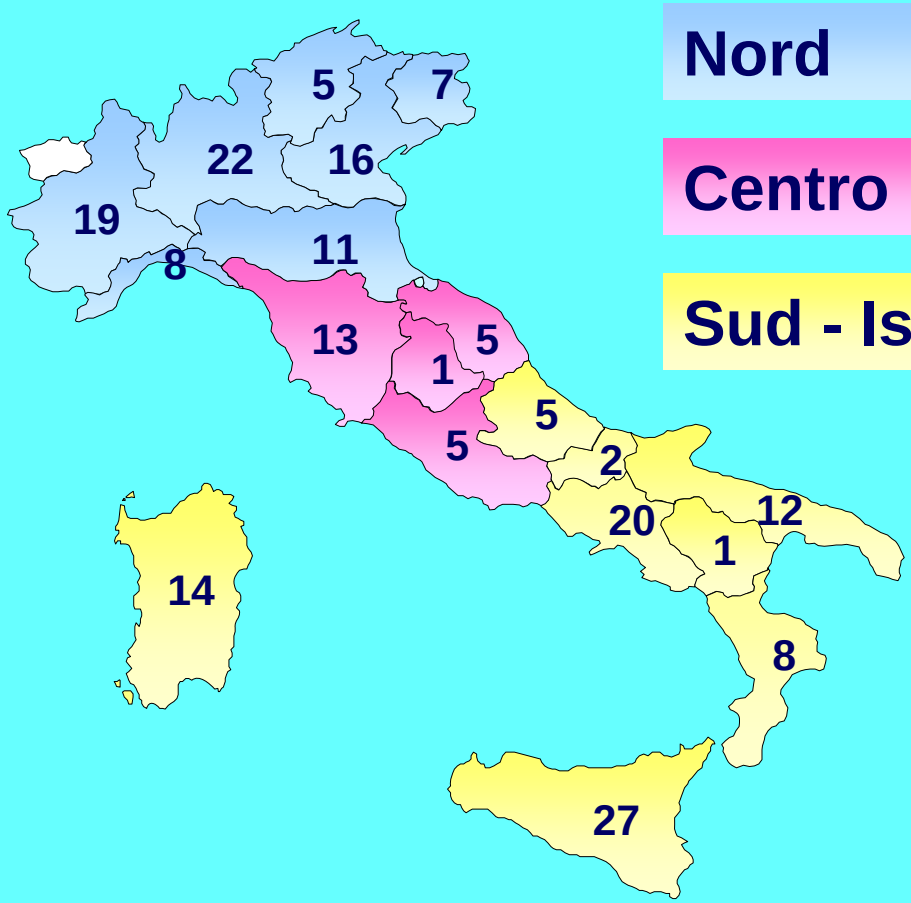
- Prevalenza nella popolazione italiana >45 anni: 3.7% (Dati ISTAT, 1998)

# Studio DAI: 201 centri partecipanti




| | |
|---|---|
| Nord | 43.8% |
| Centro | 11.9% |
| Sud - Isole | 44.3% |

# Uno studio di incidenza (coorte)

Pazienti privi dell'evento

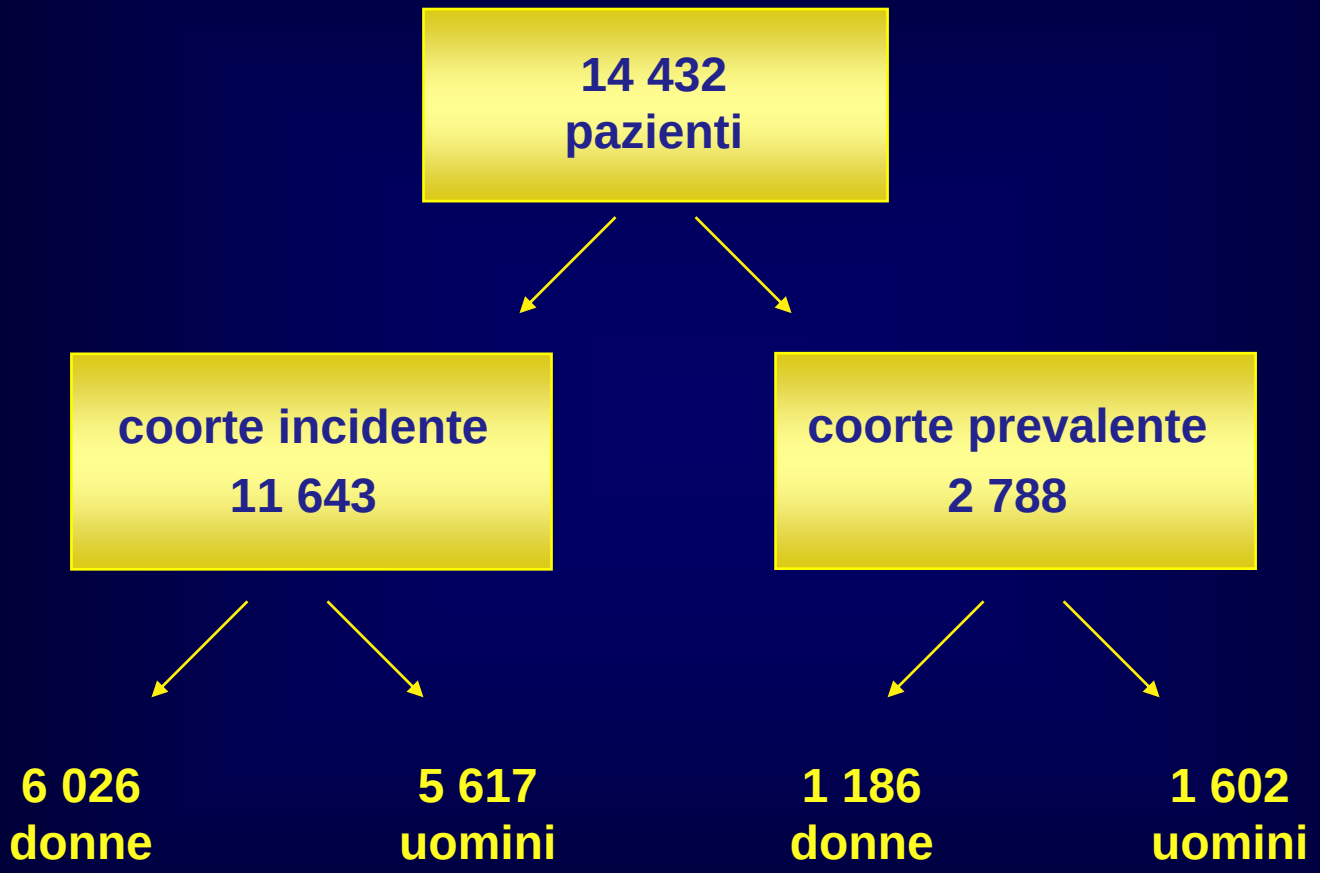
Pazienti con evento

t

Visita di follow-up

Persi

# Lo studio d'incidenza

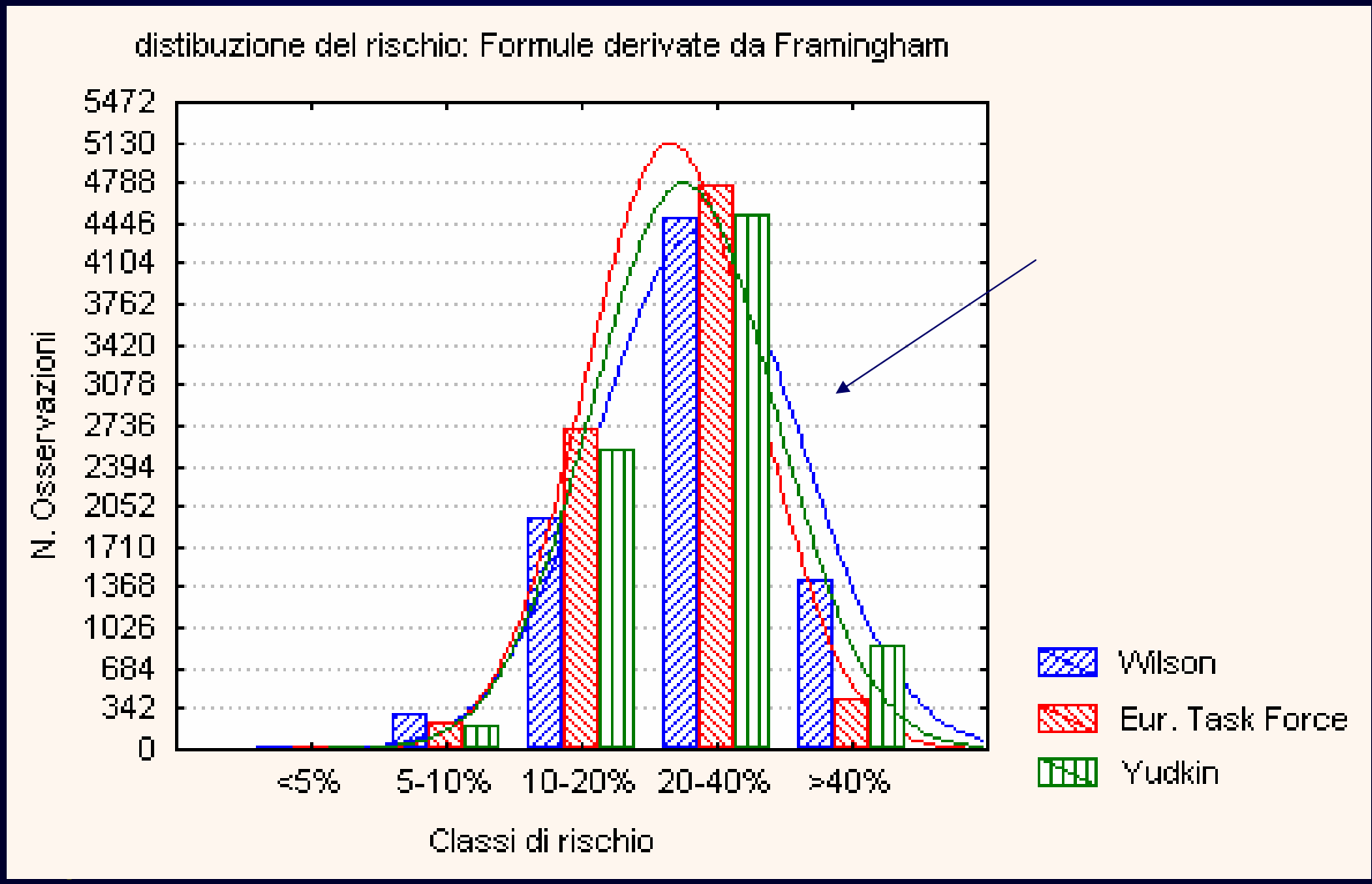


# Studio DAI: una fotografia dei pazienti seguiti dai servizi italiani

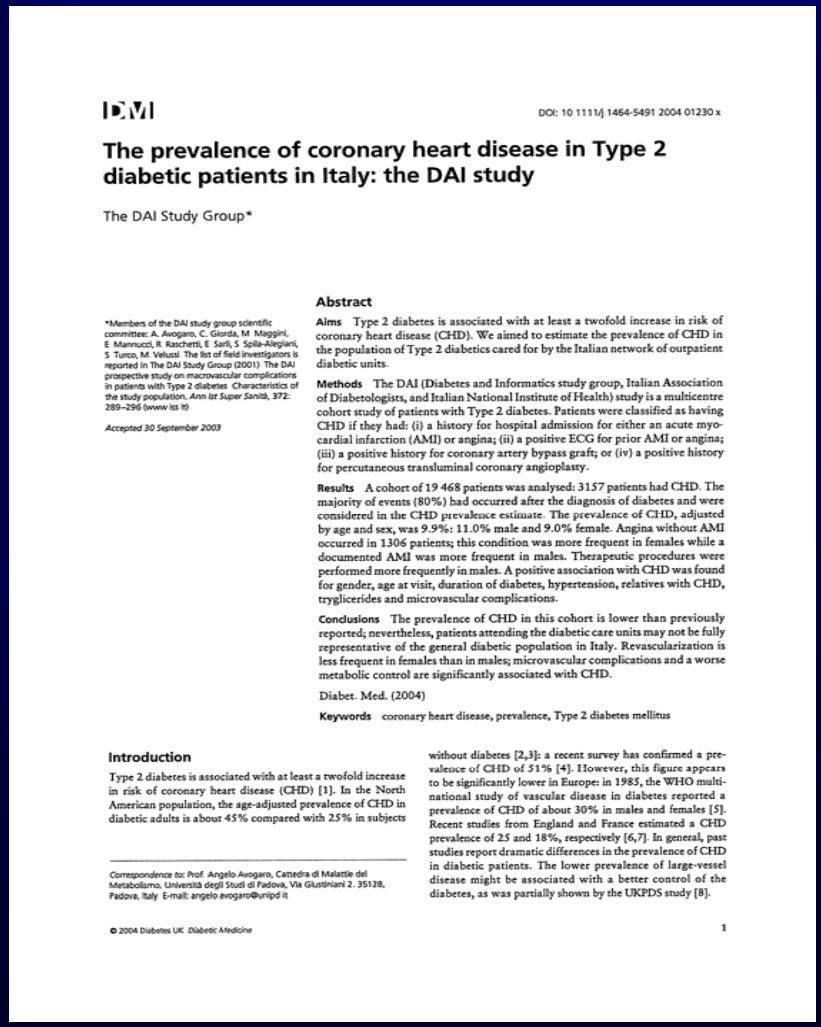
## Fattori di rischio

- Età (mediana) M 65 F67
- Durata (mediana) 8
- Obesi (BMI >30): 38%
- Ipertesi : 82%
- LDL (mediana) 136
- Fumatori: 24,6%
- Microalbuminuria 22%

# Lo Studio DAI (20000 pazienti DM2 italiani): Short-term Risk



# Il passato dello Studio DAI
# LE COMPLICANZE CV NEI DIABETICI ITALIANI



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DOI: 10.1111/j.1464-5491.2004.01230.x

## The prevalence of coronary heart disease in Type 2 diabetic patients in Italy: the DAI study

The DAI Study Group*

*Members of the DAI study group scientific committee: A. Avogaro, C. Giorda, M. Maggini, E. Mannucci, R. Raschetti, E. Sarfi, S. Spila-Alegiani, S. Turco, M. Velussi. The list of field investigators is reported in The DAI Study Group (2001) The DAI prospective study on macrovascular complications in patients with Type 2 diabetes: Characteristics of the study population. *Ann Ist Super Sanità*, 37(2): 289–296 (www.iss.it)

*Accepted 30 September 2003*

**Abstract**

**Aims** Type 2 diabetes is associated with at least a twofold increase in risk of coronary heart disease (CHD). We aimed to estimate the prevalence of CHD in the population of Type 2 diabetics cared for by the Italian network of outpatient diabetic units.

**Methods** The DAI (Diabetes and Informatics study group, Italian Association of Diabetologists, and Italian National Institute of Health) study is a multicentre cohort study of patients with Type 2 diabetes. Patients were classified as having CHD if they had: (i) a history for hospital admission for either an acute myocardial infarction (AMI) or angina; (ii) a positive ECG for prior AMI or angina; (iii) a positive history for coronary artery bypass graft; or (iv) a positive history for percutaneous transluminal coronary angioplasty.

**Results** A cohort of 19 468 patients was analysed: 3157 patients had CHD. The majority of events (80%) had occurred after the diagnosis of diabetes and were considered in the CHD prevalence estimate. The prevalence of CHD, adjusted by age and sex, was 9.9%: 11.0% male and 9.0% female. Angina without AMI occurred in 1306 patients; this condition was more frequent in females while a documented AMI was more frequent in males. Therapeutic procedures were performed more frequently in males. A positive association with CHD was found for gender, age at visit, duration of diabetes, hypertension, relatives with CHD, tryglicerides and microvascular complications.

**Conclusions** The prevalence of CHD in this cohort is lower than previously reported; nevertheless, patients attending the diabetic care units may not be fully representative of the general diabetic population in Italy. Revascularization is less frequent in females than in males; microvascular complications and a worse metabolic control are significantly associated with CHD.

Diabet. Med. (2004)

**Keywords** coronary heart disease, prevalence, Type 2 diabetes mellitus

**Introduction**

Type 2 diabetes is associated with at least a twofold increase in risk of coronary heart disease (CHD) [1]. In the North American population, the age-adjusted prevalence of CHD in diabetic adults is about 45% compared with 25% in subjects without diabetes [2,3]: a recent survey has confirmed a prevalence of CHD of 31% [4]. However, this figure appears to be significantly lower in Europe: in 1985, the WHO multinational study of vascular disease in diabetes reported a prevalence of CHD of about 30% in males and females [5]. Recent studies from England and France estimated a CHD prevalence of 25 and 18%, respectively [6,7]. In general, past studies report dramatic differences in the prevalence of CHD in diabetic patients. The lower prevalence of large-vessel disease might be associated with a better control of the diabetes, as was partially shown by the UKPDS study [8].

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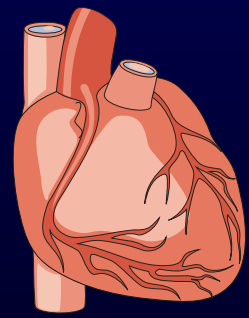
| | Totale |
|---|---|
| Infarto | 6,2 |
| Cardiopatia ischemica | 6,1 |
| Tromboembolia cerebrale | 2,9 |
| Angioplastica coronarica | 0,8 |
| By pass aorto coronarico | 2,0 |
| Amputazioni | 0,7 |

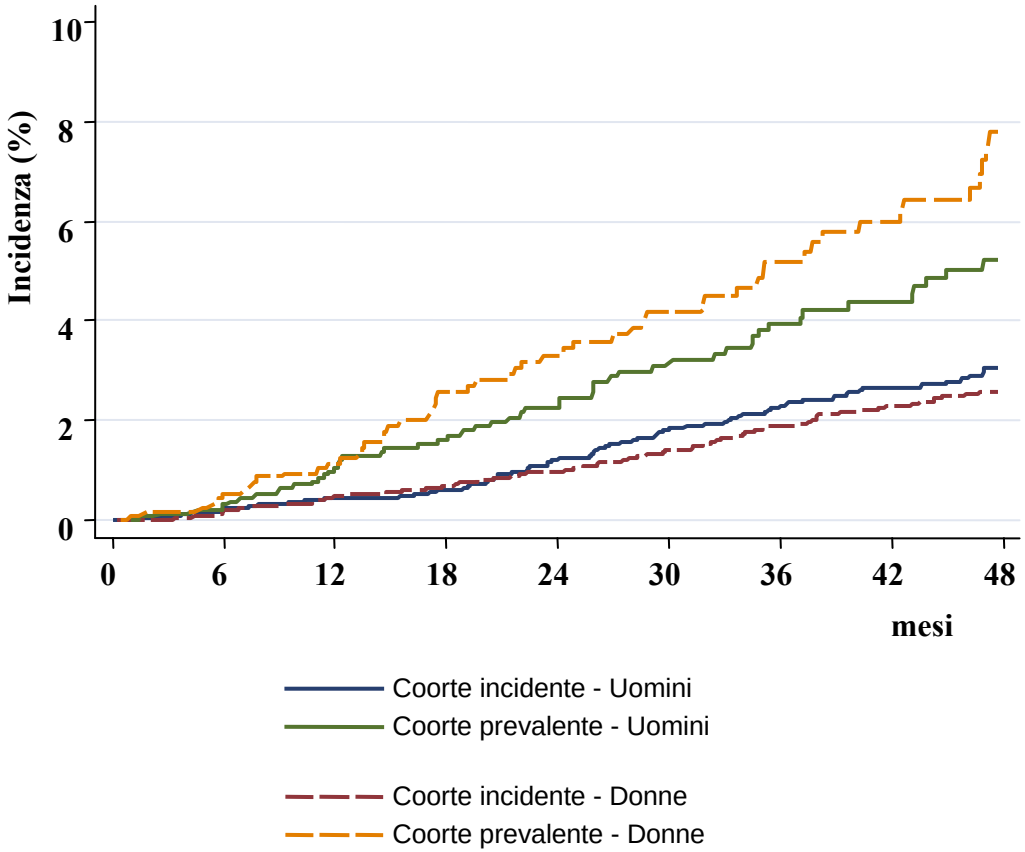
# Eventi coronarici all'arruolamento

| | Totale | | |
|---|---|---|---|
| | Maschi | Femm | Totale |
| Infarto | 9,1 | 3,3 | 6,2 |
| Cardiopatia ischemica | 6,0 | 6,3 | 6,1 |
| Angioplastica coronarica | 1,2 | 0,5 | 0,8 |
| By pass aorto coronarico | 3,0 | 1,0 | 2,0 |



# L’incidenza di ictus in 4 anni di studio DAI

# Fig1:Incidenza di ictus per incidenti e prevalenti per sesso



# L’incidenza di ictus nei pazienti seguiti dai servizi italiani per 1000 persone/anno

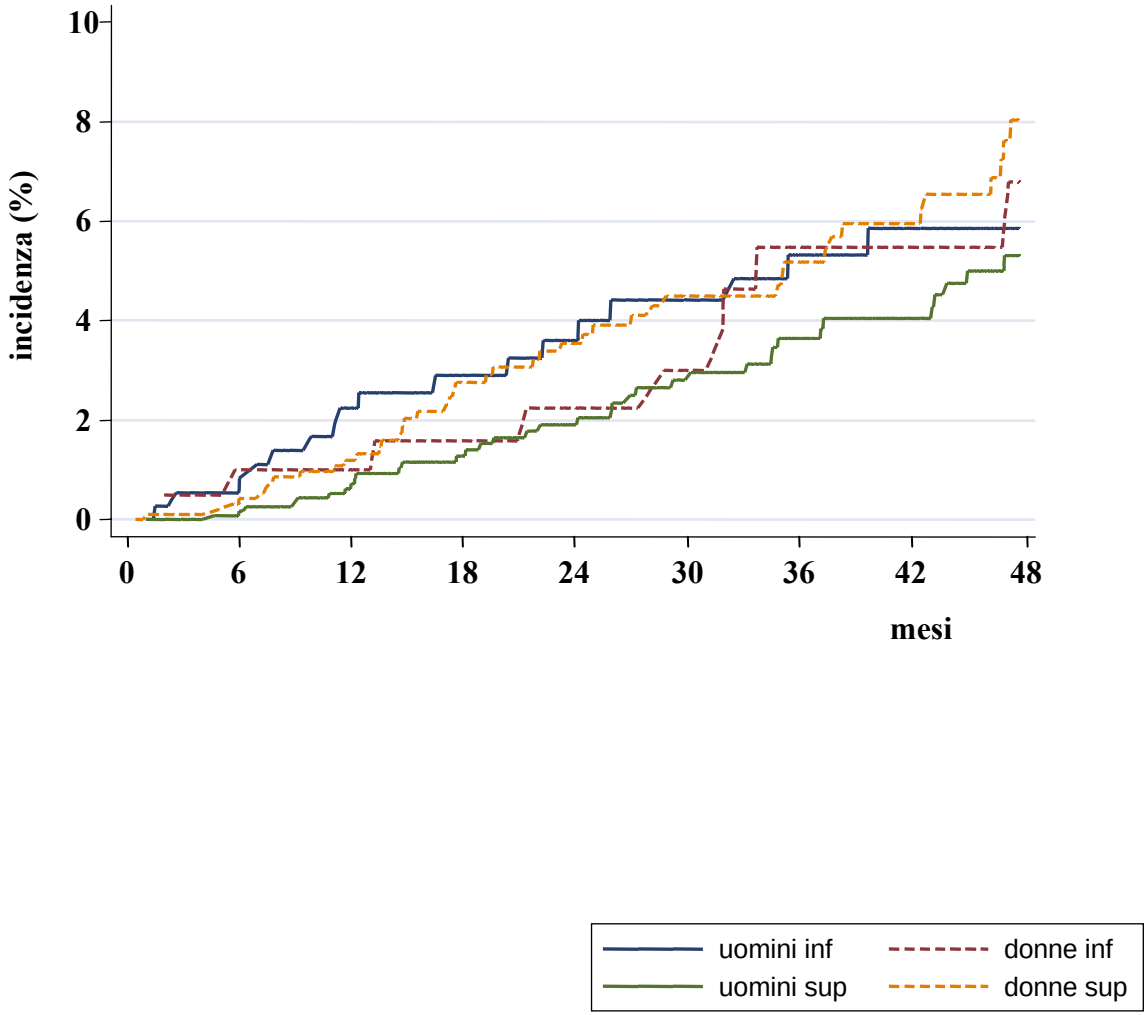
*In prevenzione primaria:*

5.5 (95% C.I. 4.2-6.8) nei maschi e 6.3 (95% C.I. 4.5-8.2) nelle donne

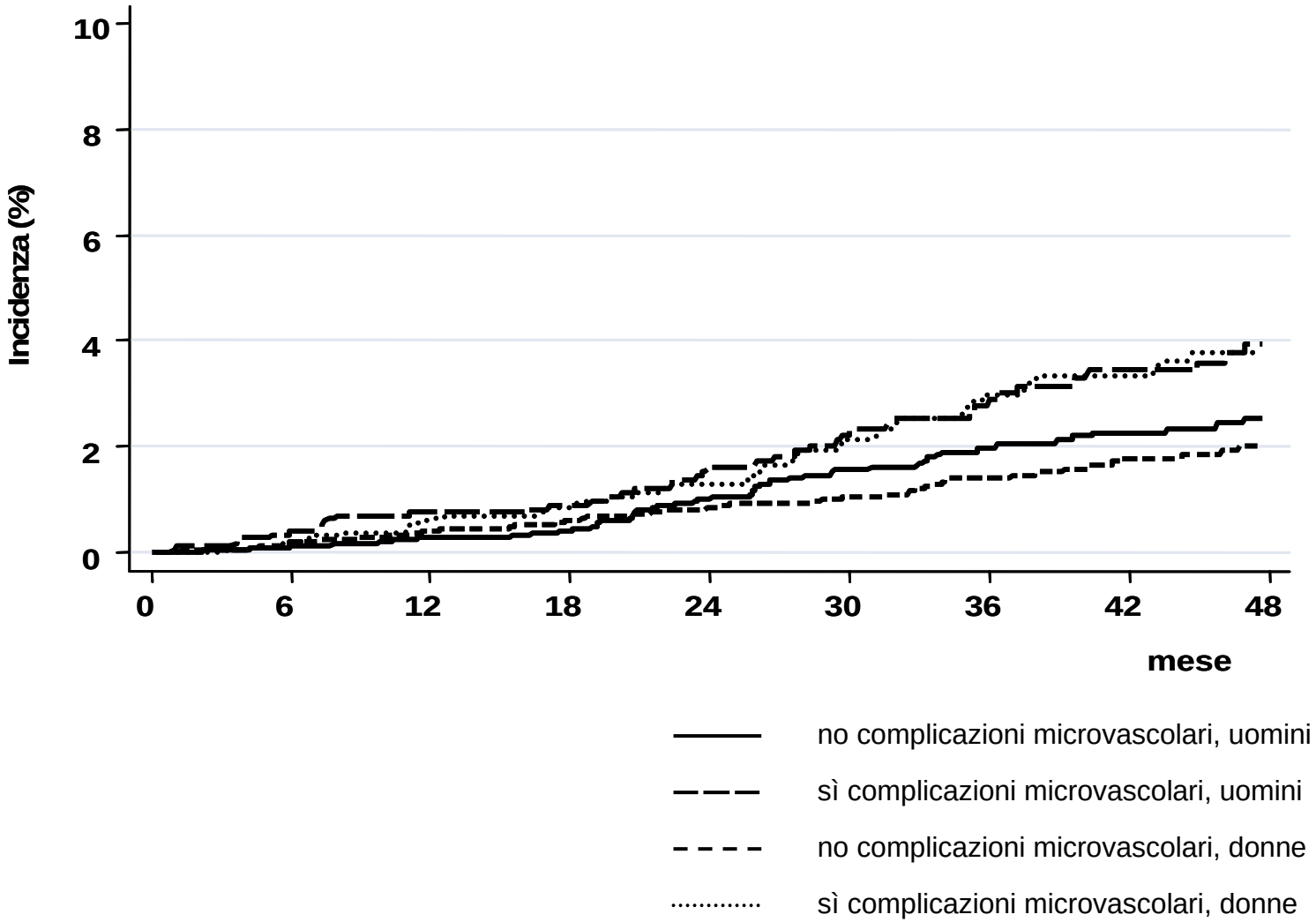
*In prevenzione secondaria (precedenti eventi ats):*

13.7 (95% C.I. 7.5-19.8) nei maschi e 10.8 (95% C.I. 7.3-14.4) nelle donne

# Fig2b:Incidenza di ictus prevalenti per Hba1c



**Incidenza di ictus per presenza/assenza di complicanze microvascolari**



# Predictors of stroke for 11644 patients without previous CVD (Cox proportional hazards analysis).

| Risk factors | Males | P | Females | P |
|---|---|---|---|---|
| **Age at visit (10 years increments)** | 1.94 (1.46-2.57) | 0.00 | 2.15 (1.66-2.78) | 0.00 |
| **Duration (3 years increments)** | 1.03 (0.94-1.12) | 0.54 | | |
| **Waist circumference (5 cm increments)** | 1.09 (0.99-1.19) | 0.09 | | |
| **HbA1c (20% increments)** | 1.22 (1.04-1.43) | 0.01 | | |
| **Smoke** | | | | |
| No | 1 | | | |
| Yes | 2.29 (1.36-3.87) | 0.00 | | |
| Former | 1.17 (0.70-1.96) | 0.55 | | |
| **Microvascular complications** | | | | |
| No | 1 | | 1 | |
| Yes | 1.15 (0.74-1.80) | 0.53 | 1.53 (1.01-2.33) | 0.05 |

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# Predictors of stroke for 11644 patients without previous CVD (Cox proportional hazards analysis).

| | | | | |
|---|---|---|---|---|
| **Antihypertensive therapy** | | | | |
| No | 1 | | | |
| Yes | 1.41 (0.90-2.21) | 0.13 | | |
| **Antihyperglycemic therapy** | | | | |
| Diet | 1 | | 1 | |
| Oral agents (OA) | 1.19 (0.58-2.46) | 0.63 | 2.15 (0.86-5.36) | 0.10 |
| Insulin + OA | 2.10 (0.80-5.51) | 0.13 | 2.63 (0.91-7.56) | 0.07 |
| Insulin | 1.61 (0.61-4.21) | 0.34 | 2.28 (0.78-6.66) | 0.13 |
| **Geographic area** | | | | |
| North | 1 | | | |
| Centre | 0.52 (0.22-1.21) | 0.13 | | |
| South | 0.62 (0.37-1.01) | 0.06 | | |

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# *Predictors of stroke for 2788 patients with previous CVD (Cox proportional hazards analysis).*

| Risk factor | Adjusted for multiple variables | | | | | |
|---|---|---|---|---|---|---|
| | Men | | | Women | | |
| | HR | (95% CI) | p | HR | (95% CI) | p |
| Age at visit (10 years increments) | 1.86 | (1.28-2.70) | 0.00 | 2.54 | (1.67-3.88) | 0.00 |
| HDL (5mg/dl increments) | 099 | (0.89-1.11) | 0.89 | 0.88 | (0.79-0.98) | 0.02 |
| Microvascular complication | | | | | | |
| No | 1 | | | 1 | | |
| Yes | 0.74 | (0.41-1.33) | 0.32 | 1.89 | (1.04-3.43) | 0.04 |

Giorda et al. submitted

# *Predictors of stroke for 2788 patients with previous CVD (Cox proportional hazards analysis).*

| | | | | | | |
|---|---|---|---|---|---|---|
| **Antihyperglycemic therapy** | | | | | | |
| Diet | 1 | | | 1 | | |
| Oral agents | 1.94 | (0.59-6.40) | 0.28 | 3.37 | (0.46-24.82) | 0.23 |
| Insulin + oral agents | 5.01 | (1.35-18.50) | 0.02 | 4.77 | (0.61-37.32) | 0.14 |
| Insulin alone | 1.79 | (0.42-7.71) | 0.43 | 3.95 | (0.50-31.14) | 0.19 |
| **Previous stroke at enrolment** | | | | | | |
| No | 1 | | | 1 | | |
| Yes | 2.83 | (1.58-5.07) | 0.00 | 3.12 | (1.75-5.57) | 0.00 |
| **Total Cholesterol (40mg/dl increments)** | 0.68 | (0.47-0.98) | 0.04 | 1.09 | (0.78-1.53) | 0.60 |
| **Lipid-lowering therapy** | | | | | | |
| No | 1 | | | 1 | | |
| Yes | 1.07 | (0.50-2.29) | 0.87 | 1.80 | (0.90-3.61) | 0.10 |
| **Cholesterol x lipid-lowering therapy** | 1.92 | (1.09-3.39) | 0.02 | 0.75 | (0.44-1.30) | 0.31 |

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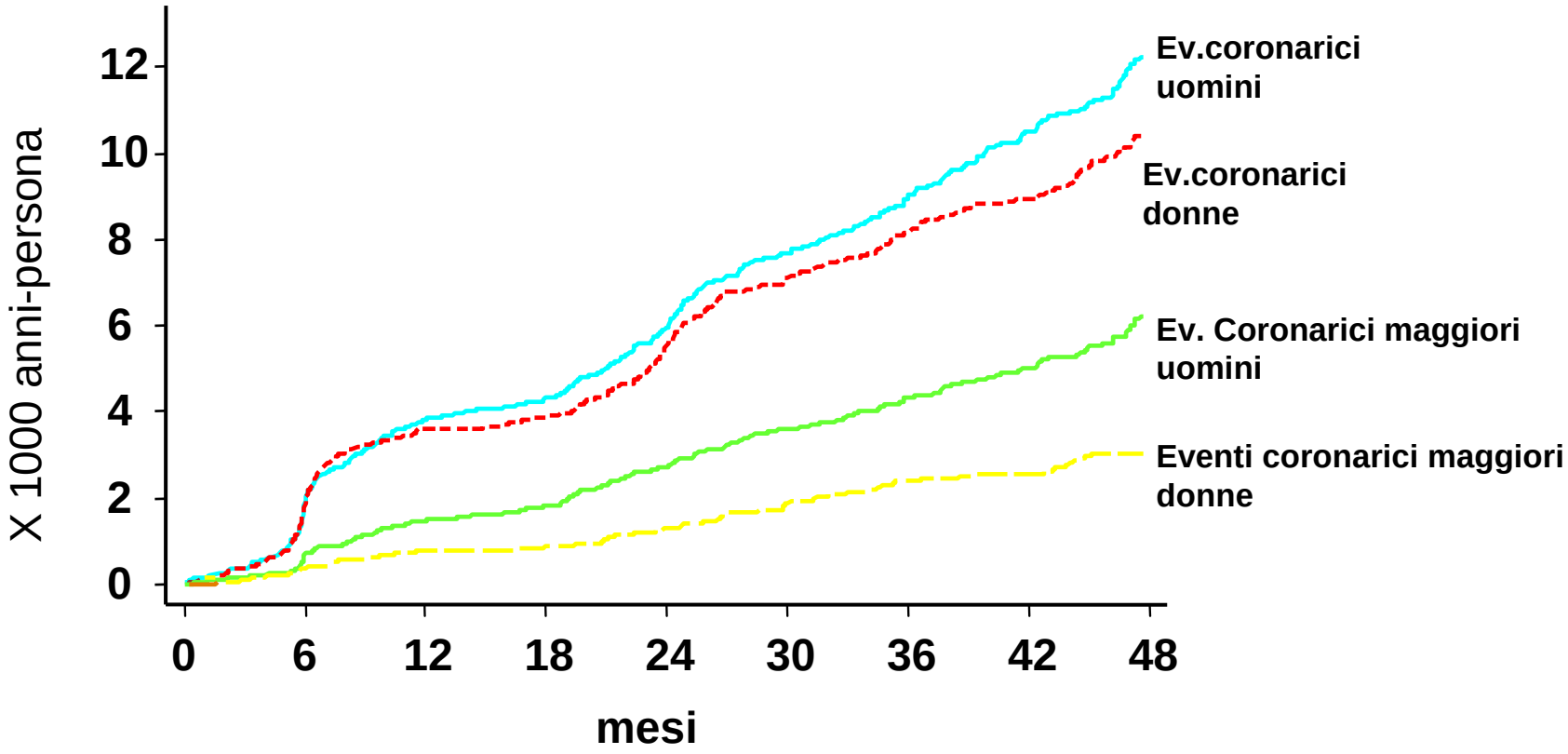
# La cardiopatia ischemica in 4 anni di studio DAI

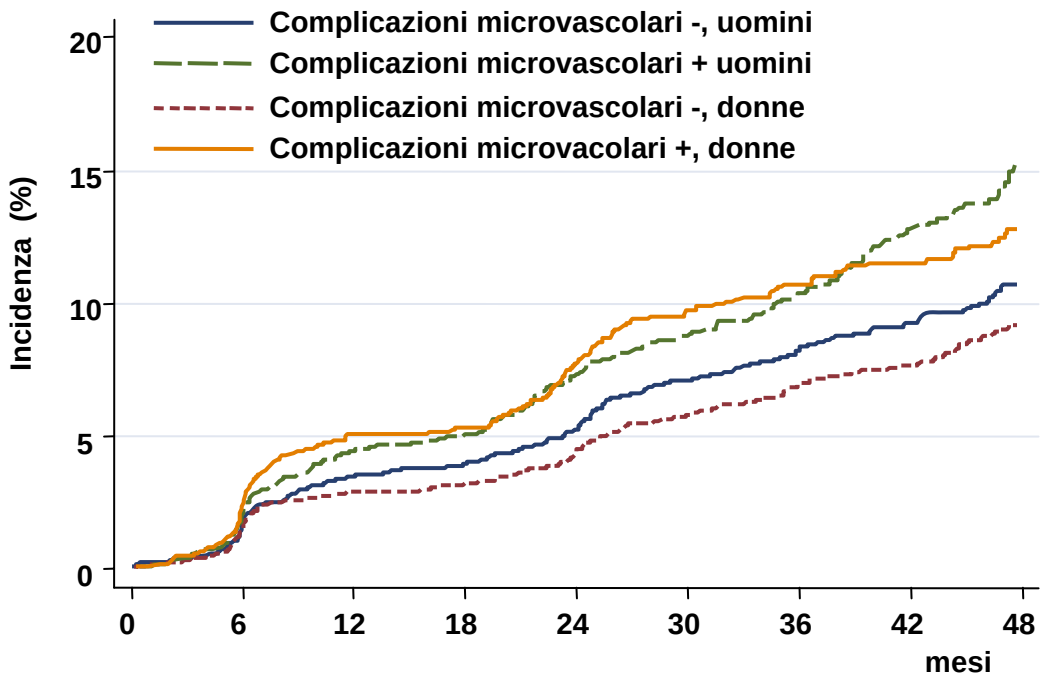

X 1000 anni-persona
12
10
8
6
4
2
0
0
6
12
18
24
30
36
42
48
mesi
Ev.coronarici uomini
Ev.coronarici donne
Ev. Coronarici maggiori uomini
Eventi coronarici maggiori donne

# EVENTI CORONARICI

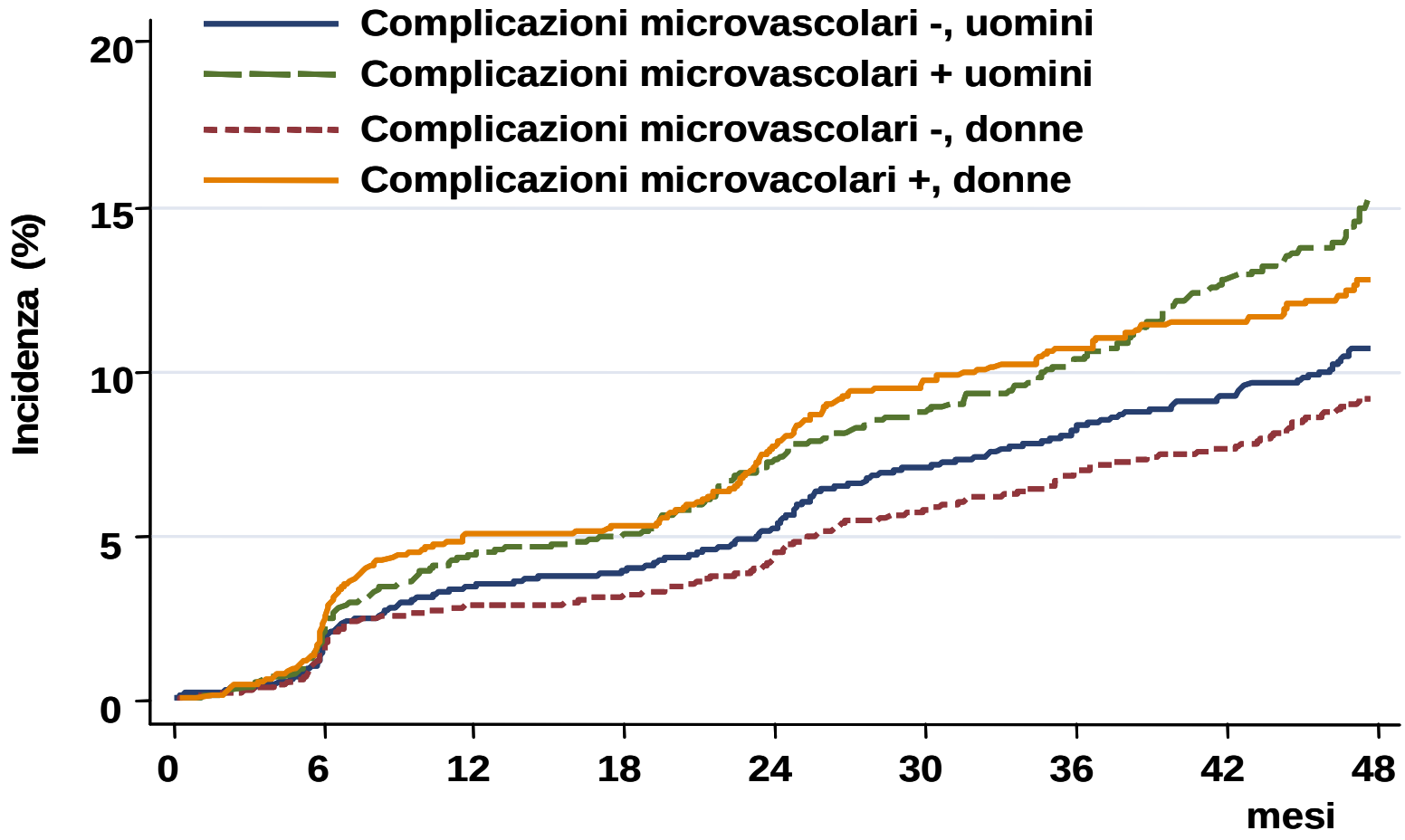
**Tasso di incidenza di primo evento coronario (Inc. per 1000 anni persona) standardizzato per età**

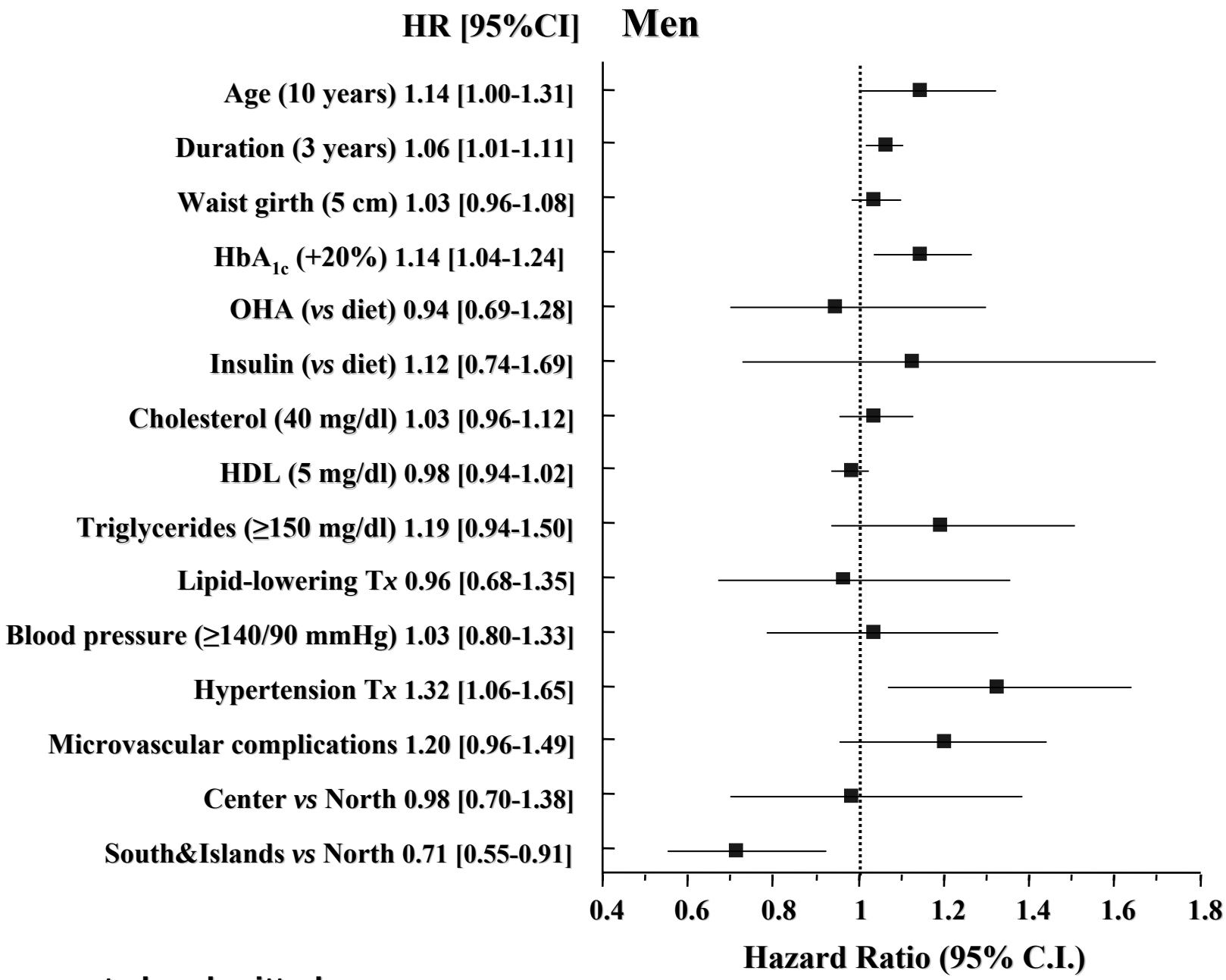
| | Uomini (13.837 anni-persona) | | | Donne (15.232 anni persona) | | |
|---|---|---|---|---|---|---|
| | **n** | **Inc.** | **IC 95%** | **n** | **Inc.** | **IC 95%** |
| **IMA** | 164 | 10,3 | 8,3-12,3 | 88 | 4,7 | 3,3-6,1 |
| **Coronarici no IMA** | 285 | 18,5 | 15,8-21,3 | 344 | 18,6 | 15,9-21,4 |
| **Tutti gli eventi** | **449** | **28,8** | **25,4-32,2** | **432** | **23,3** | **20,2-26,4** |
| **Coronarici maggiori** | 208 | 13,1 | 10,9-15,4 | 114 | 5,8 | 4,3-7,2 |
| **Coronarici letali** | 38 | 2,6 | 1,6-3,5 | 14 | 0,6 | 0,3-0,9 |

Figure 1. Incidence rate of combined (AMI+CHD) events by microvascular complications and sex.



**Incidenze di CHD stimata con Kaplan-Meier per sesso e per complicanze microvascolari negli 11,644 pazienti diabetici di Tipo 2**



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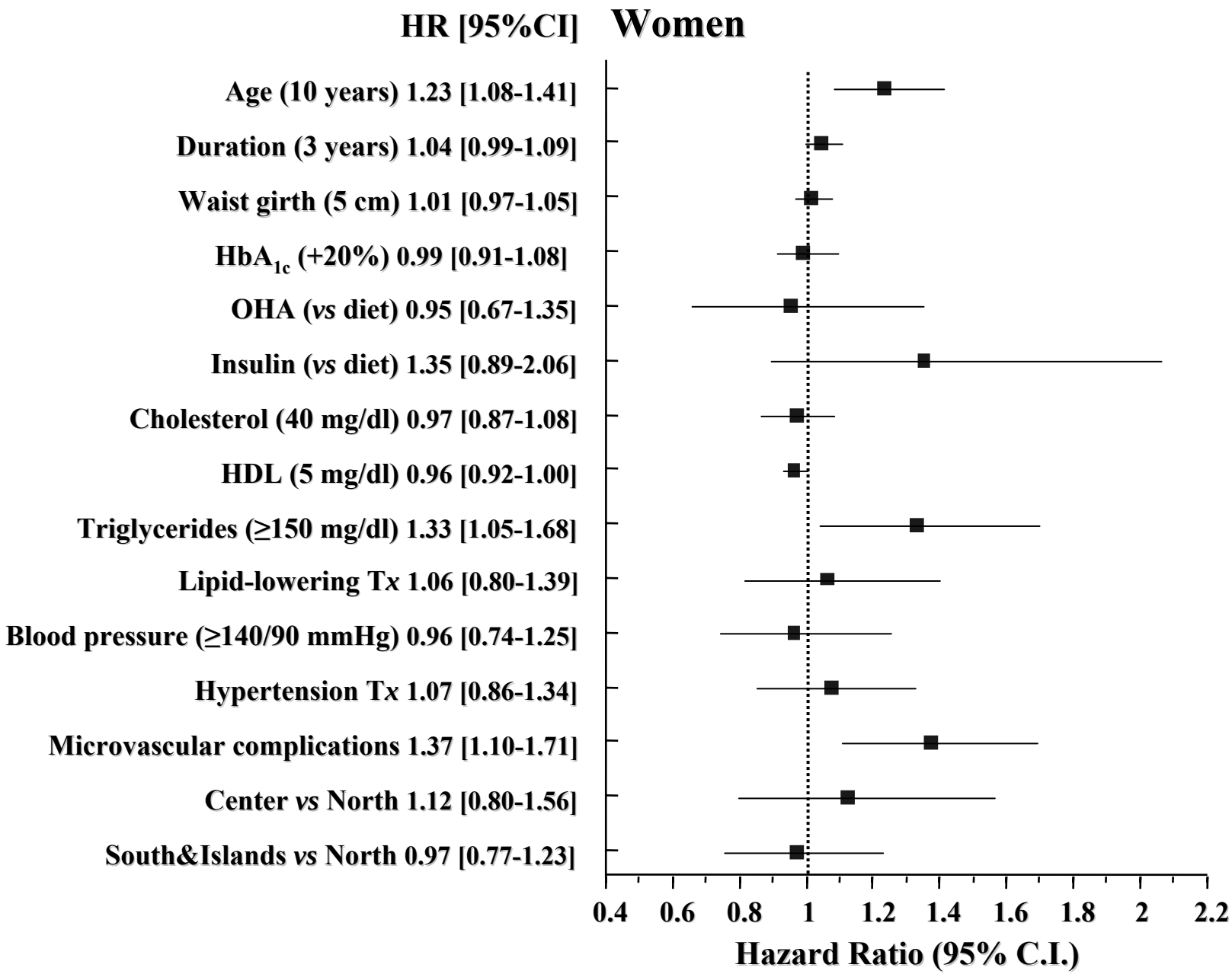
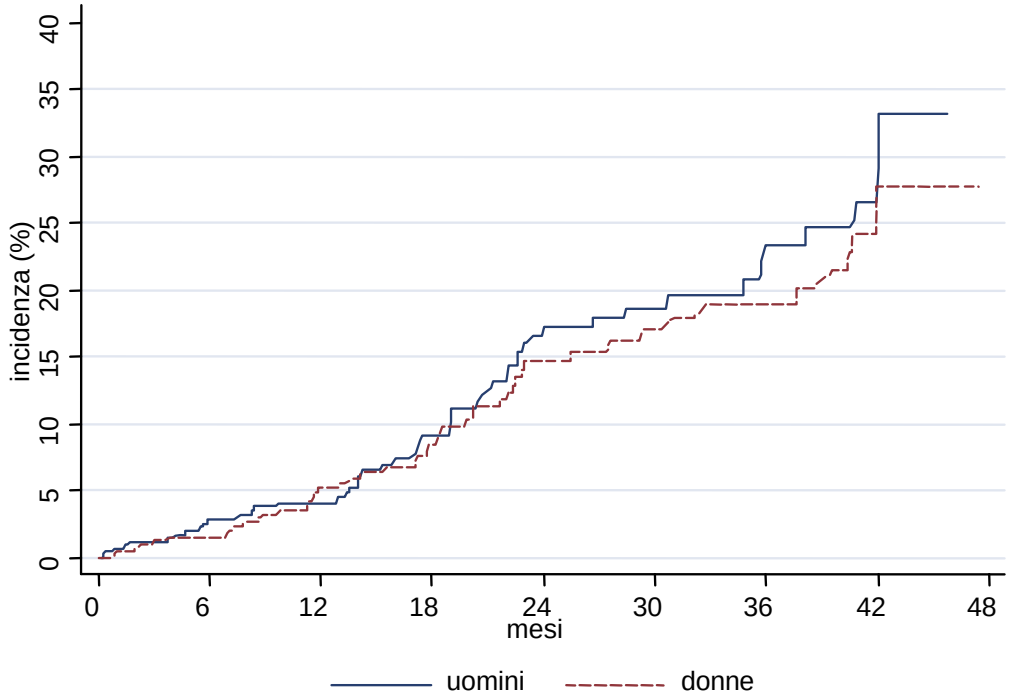



Avogaro et al. submitted

# IL FUTURO dello Studio DAI

## Incidenza di recidiva (872 soggetti, 99 eventi)




| Soggetti: | 872 | 536 | 270 | 142 |
|---|---|---|---|---|

# CONCLUSIONI

1. L’incidenza di ictus e di cardiopatia ischemica nella coorte di diabetici DAI è grosso modo 2 volte quella della popolazione italiana

2. I maschi hanno un’ incidenza circa doppia rispetto alle donne

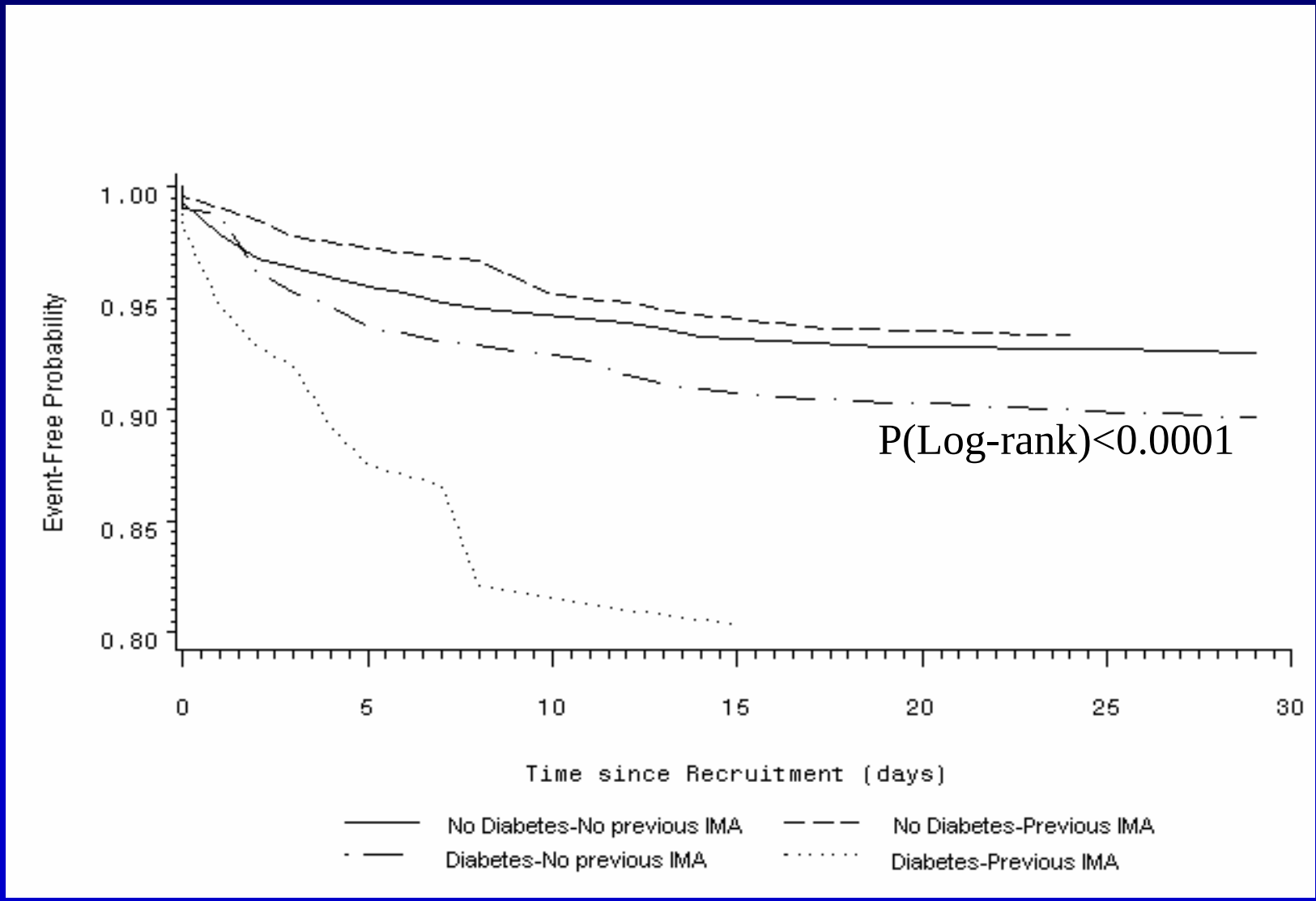
3. Emerge soprattutto nel sesso femminile il ruolo delle complicanze microvascolari (sia nella CHD che nell’ictus)

# CONCLUSIONI 2

1. Nell'ictus età e aver già avuto un precedente evento ats, sono importanti fattori di rischio
2. Nel complesso il ruolo della storia precedente del diabete (*HbA1c,complicanze micro, durata, insulina*) sembra avere un ruolo rilevante nello sviluppo di lesioni vascolari

Grazie per l’attenzione

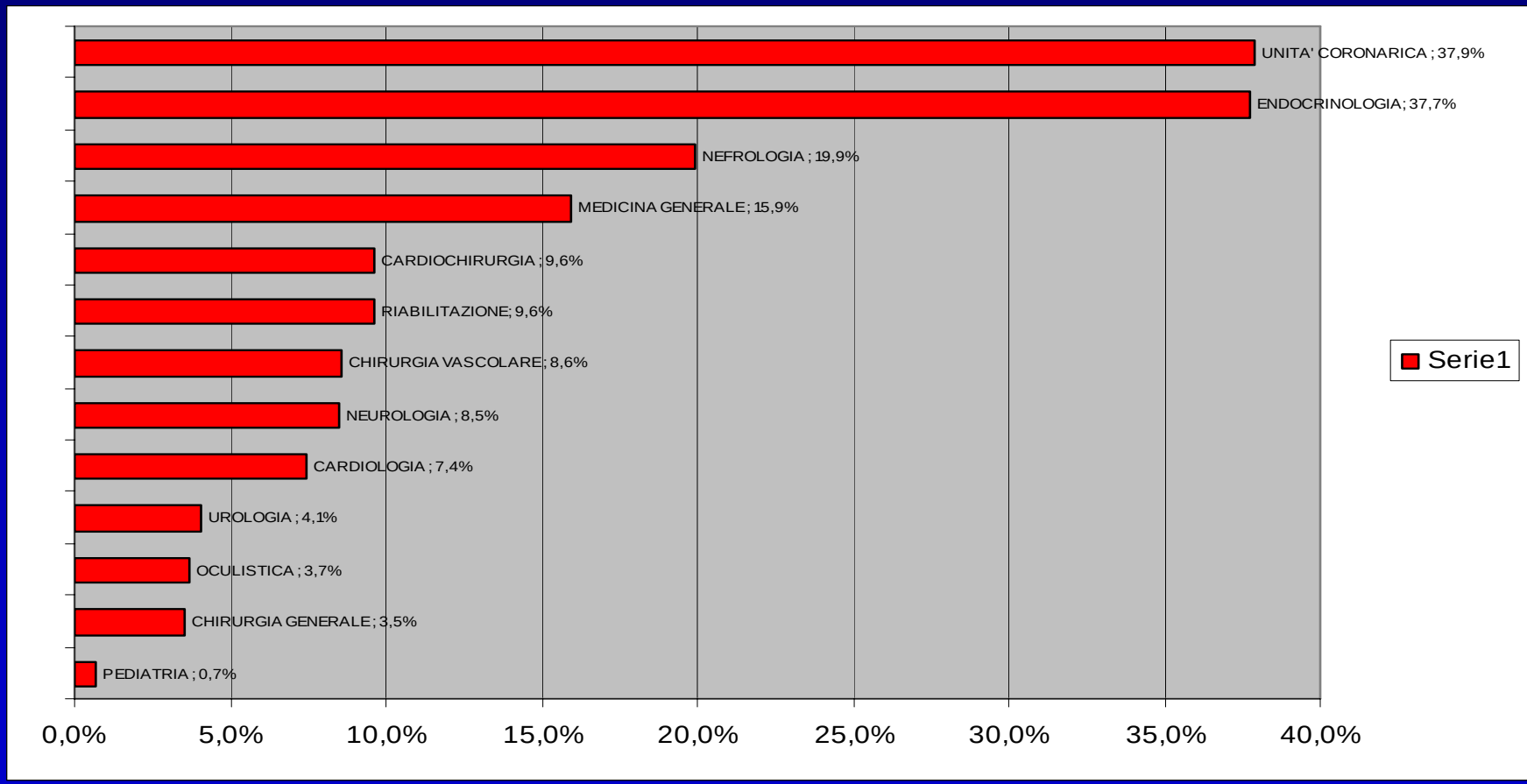
# The BLITZ-1 Registry (ANMCO, UTIC ITALIANE)
# Short – Term Survival after AMI



# Ricoveri ordinari di pazienti diabetici per complicanze Regione Piemonte anno 2001

| RAGGRUPPAMENTO | % | ETA' MEDIANA | RICOVERI urgenti % | DECESSI % |
|---|---|---|---|---|
| Vascolari (escluso cuore e cervello) | 4,6% | 72 | 43,1% | 3,5% |
| Cerebrovascolari | 9,1% | 75 | 72,8% | 11,3% |
| Cardiovascolari | 15,4 % | 70 | 58,4% | 6,8% |
| Scompenso cardiaco | 8,2% | 75 | **75,6%** | 7,1% |
| Neurologici puri | 0,4% | 66 | 17,4% | 0,0% |
| Renali | 2,7% | 70 | 53,5% | 4,1% |
| Oculari | 1,9% | 73 | 16,7% | 0,0% |

# % DI DIABETICI NOTI IN REPARTI DI RICOVERO REGIONE PIEMONTE ANNO 2001



# Effetti della presenza di diabete sulla degenza media ospedaliera per alcune cause di ricovero (Regione Piemonte 2001)