



XIX
CONGRESSO
NAZIONALE AMD
Roma, 29 maggio - 1 giugno 2013
Rome Marriott Park Hotel

Ictus e diabete

Giuseppe Seghieri, Pistoia

Venerdì 31 maggio 2013
Congresso Nazionale AMD

Il dr Giuseppe Seghieri dichiara di
non avere alcun conflitto di
interesse riguardo al contenuto
della presente comunicazione

Agenda

- **Epidemiologia dell'ictus**
- Ruolo del diabete
- Terapia

Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data



Alan D Lopez, Colin D Mathers, Majid Ezzati, Dean T Jamison, Christopher J L Murray

Ten leading causes of death by income group, 2001

Low-and-middle-income countries				High-income countries		
	Cause	Deaths (millions)	% of total deaths	Cause	Deaths (millions)	% of total deaths
1	Ischaemic heart disease	5.70	11.8%	Ischaemic heart disease	1.36	17.3%
2	Cerebrovascular disease	4.61	9.5%	Cerebrovascular disease	0.78	9.9%
3	Lower respiratory infections	3.41	7.0%	Trachea, bronchus, lung cancers	0.46	5.8%
4	HIV/AIDS	2.55	5.3%	Lower respiratory infections	0.34	4.4%
5	Perinatal conditions	2.49	5.1%	Chronic obstructive pulmonary disease	0.30	3.8%
6	Chronic obstructive pulmonary disease	2.38	4.9%	Colon and rectum cancers	0.26	3.3%
7	Diarrhoeal diseases	1.78	3.7%	Alzheimer's disease and other dementias	0.21	2.6%
8	Tuberculosis	1.59	3.3%	Diabetes mellitus	0.20	2.6%
9	Malaria	1.21	2.5%	Breast cancer	0.16	2.0%
10	Road traffic accidents	1.07	2.2%	Stomach cancer	0.15	1.9%

Table 1: Ten leading causes of death by income group, 2001

Lancet 2006; 367: 1747-57

Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data



Alan D Lopez, Colin D Mathers, Majid Ezzati, Dean T Jamison, Christopher J L Murray

Ten leading causes of burden of disease (DALYs)* by income group, 2001

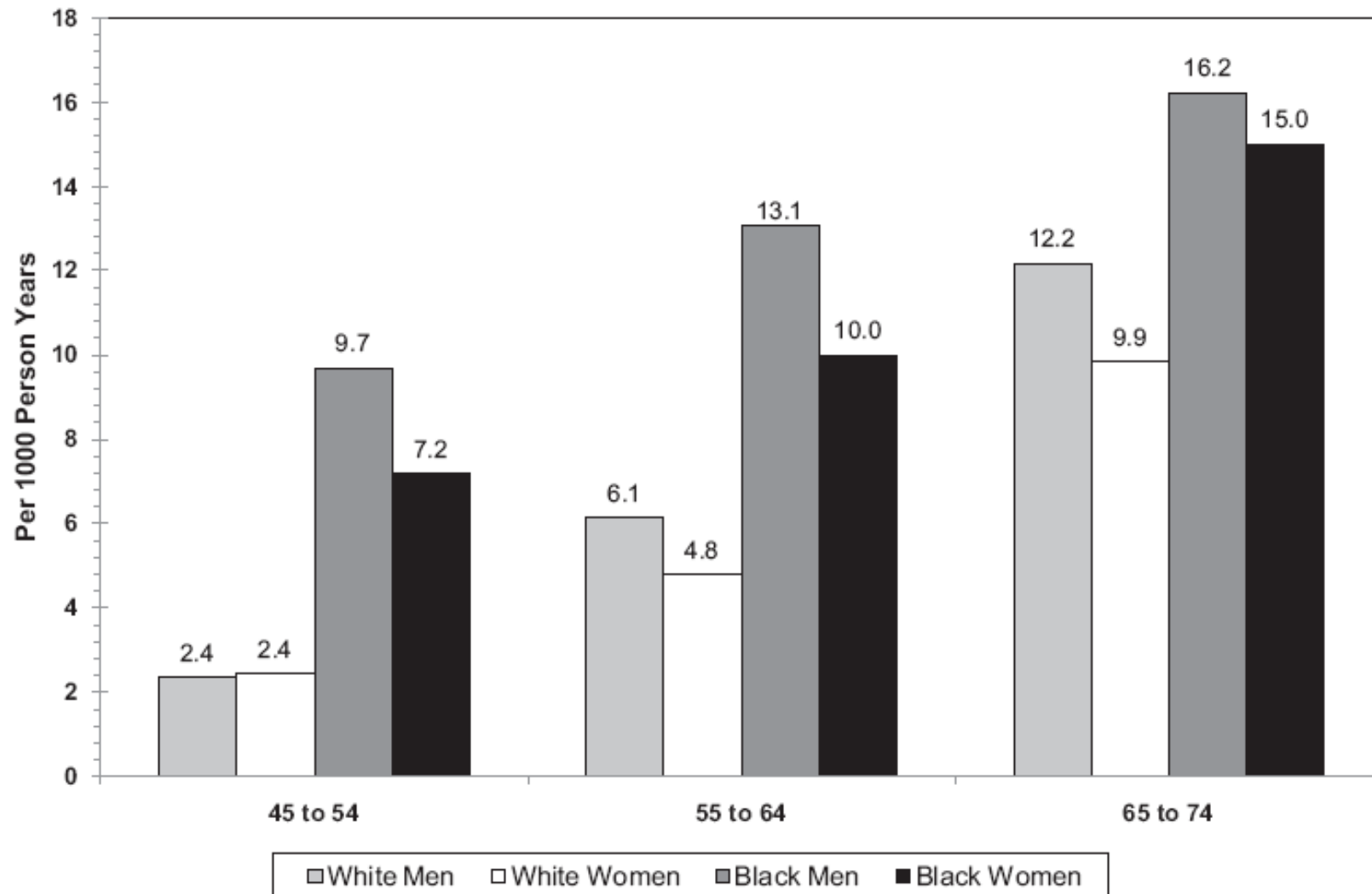
Low-and-middle-income countries			High-income countries			
Cause	DALYs (millions of years)*	% of total DALYs	Cause	DALYs (millions of years)*	% of total DALYs	
1	Perinatal conditions	89.07	6.4%	Ischaemic heart disease	12.39	8.3%
2	Lower respiratory infections	83.61	6.0%	Cerebrovascular disease	9.35	6.3%
3	Ischaemic heart disease	71.88	5.2%	Unipolar depressive disorders	8.41	5.6%
4	HIV/AIDS	70.80	5.1%	Alzheimer's disease and other dementias	7.47	5.0%
5	Cerebrovascular disease	62.67	4.5%	Trachea, bronchus, lung cancers	5.40	3.6%
6	Diarrhoeal diseases	58.70	4.2%	Hearing loss, adult onset	5.39	3.6%
7	Unipolar depressive disorders	43.43	3.1%	Chronic obstructive pulmonary disease	5.28	3.5%
8	Malaria	39.96	2.9%	Diabetes mellitus	4.19	2.8%
9	Tuberculosis	35.87	2.6%	Alcohol use disorders	4.17	2.8%
10	Chronic obstructive pulmonary disease	33.45	2.4%	Osteoarthritis	3.79	2.5%

*Constructed with 3% yearly discount rate and uniform age weights.

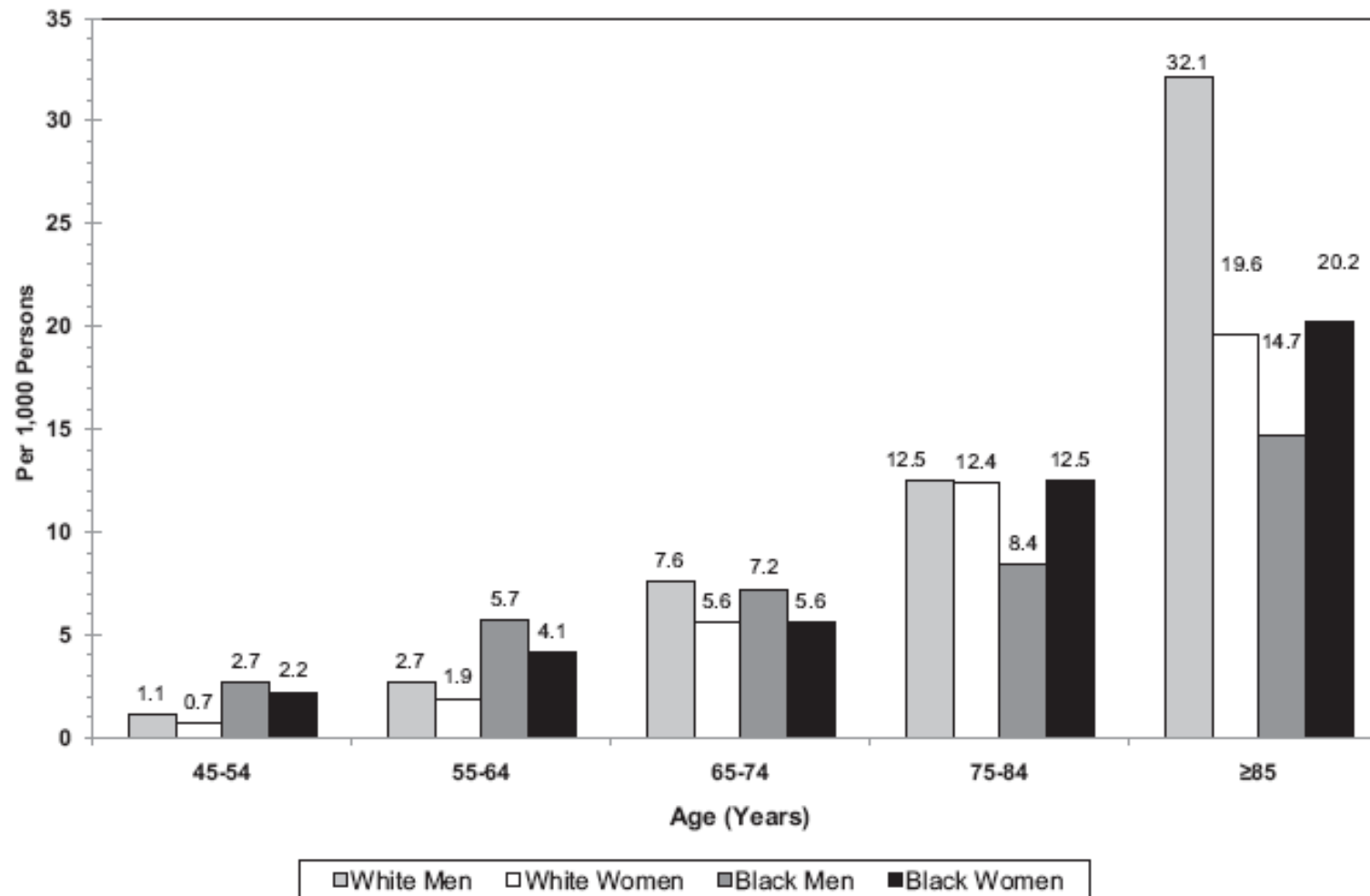
* disability-adjusted life years

Lancet 2006; 367: 1747-57

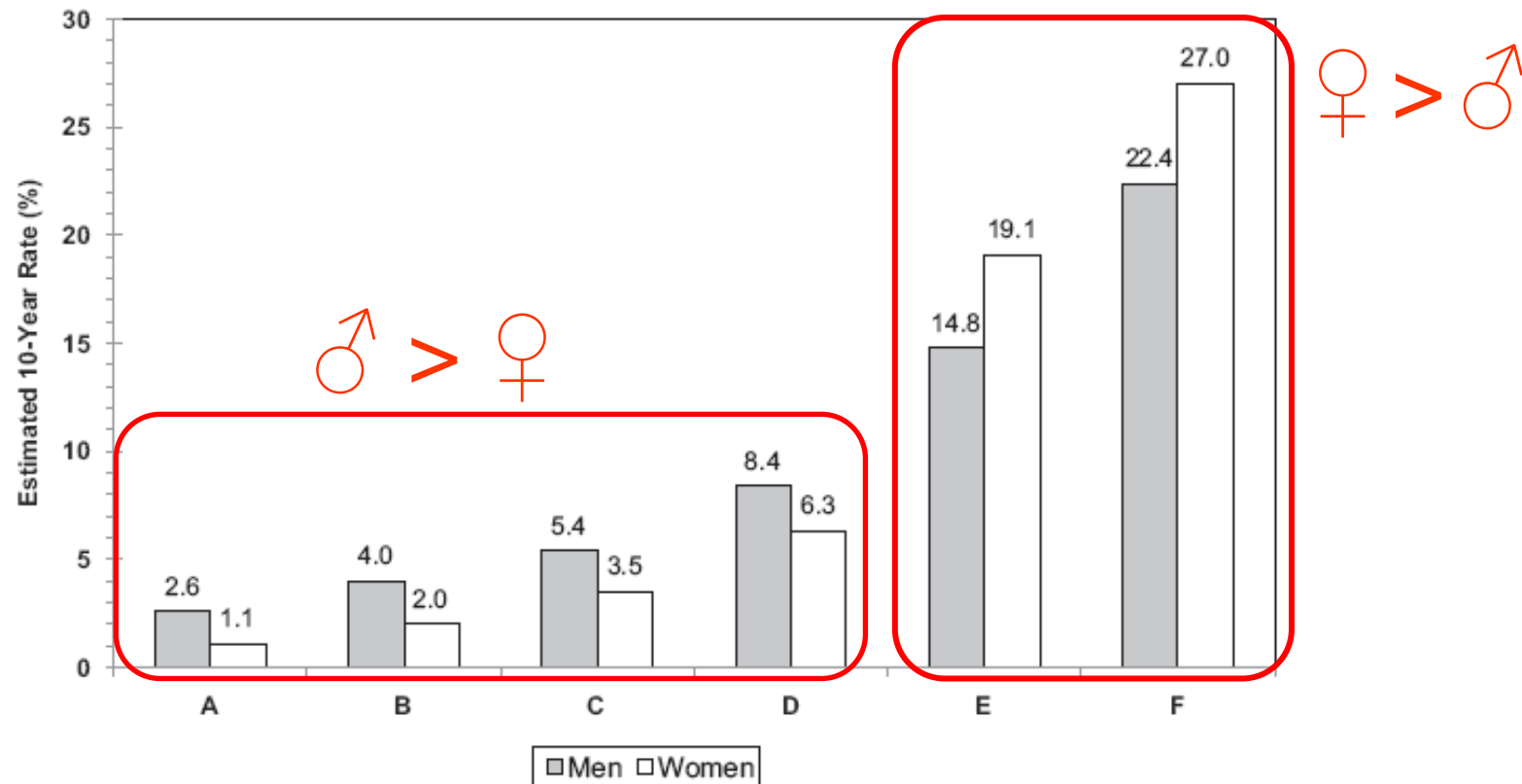
Age-adjusted incidence of stroke/transient ischemic attack by race and sex, ages 45–74 Atherosclerosis Risk in Communities study cohort, 1987–2001. Data derived from National Heart, Lung, and Blood Institute, Incidence and Prevalence Chart Book, 2006.



Annual rate of first cerebral infarction by age, sex, and race (Greater Cincinnati/Northern Kentucky Stroke Study: 1999). Rates for black men and women 45 to 54 years of age and for black men 75 years of age are considered unreliable. Source: Unpublished data from the Greater Cincinnati/Northern Kentucky Stroke Study.



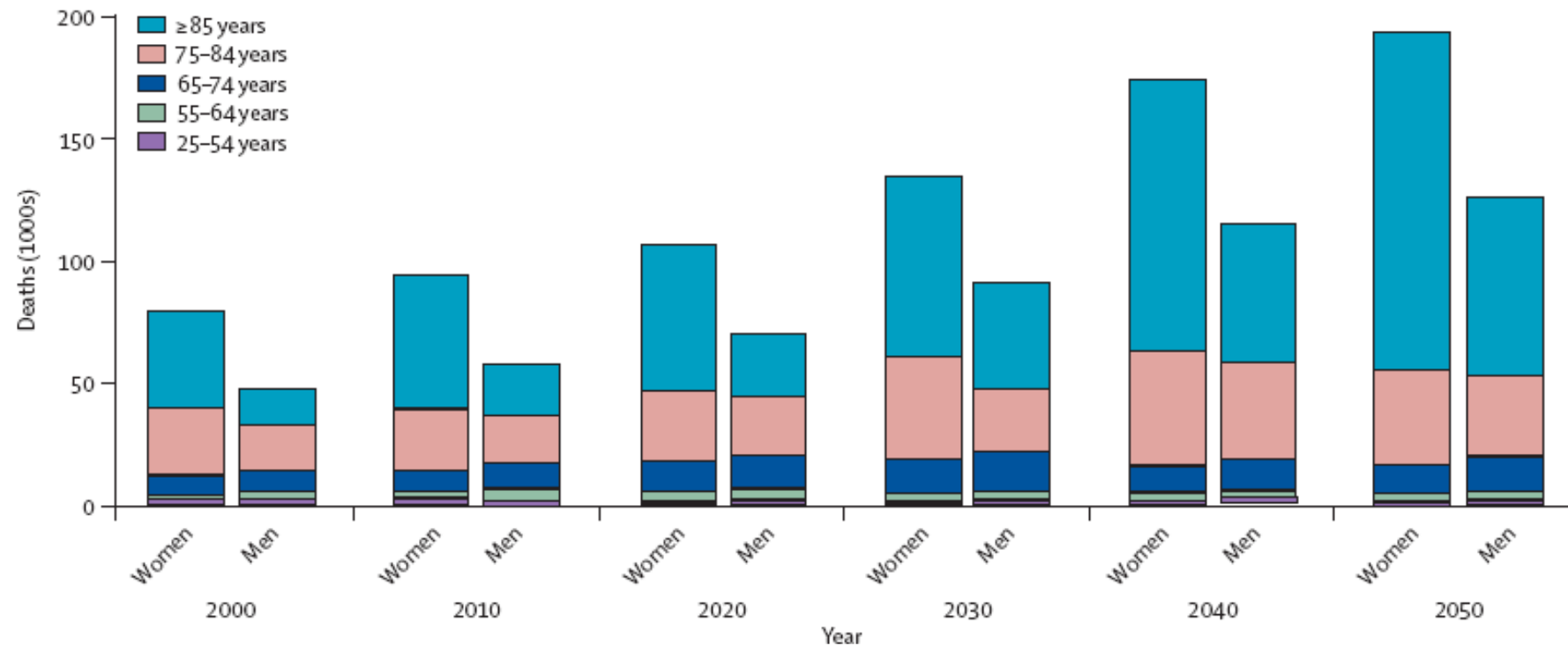
Estimated 10-year stroke risk in adults 55 years of age according to levels of various risk factors (Framingham Heart Study). AF indicates atrial fibrillation; CVD, cardiovascular disease. Data derived from Wolf et al



	A	B	C	D	E	F
Blood Pressure*	95-105	138-148	138-148	138-148	138-148	138-148
Diabetes	No	No	Yes	Yes	Yes	Yes
Cigarette Smoking	No	No	No	Yes	Yes	Yes
Prior AF	No	No	No	No	Yes	Yes
Prior CVD	No	No	No	No	No	Yes

* - Closest ranges for women are : 95-104 and 115-124.

Projected number of deaths from stroke among whites (USA, 2000–2050)

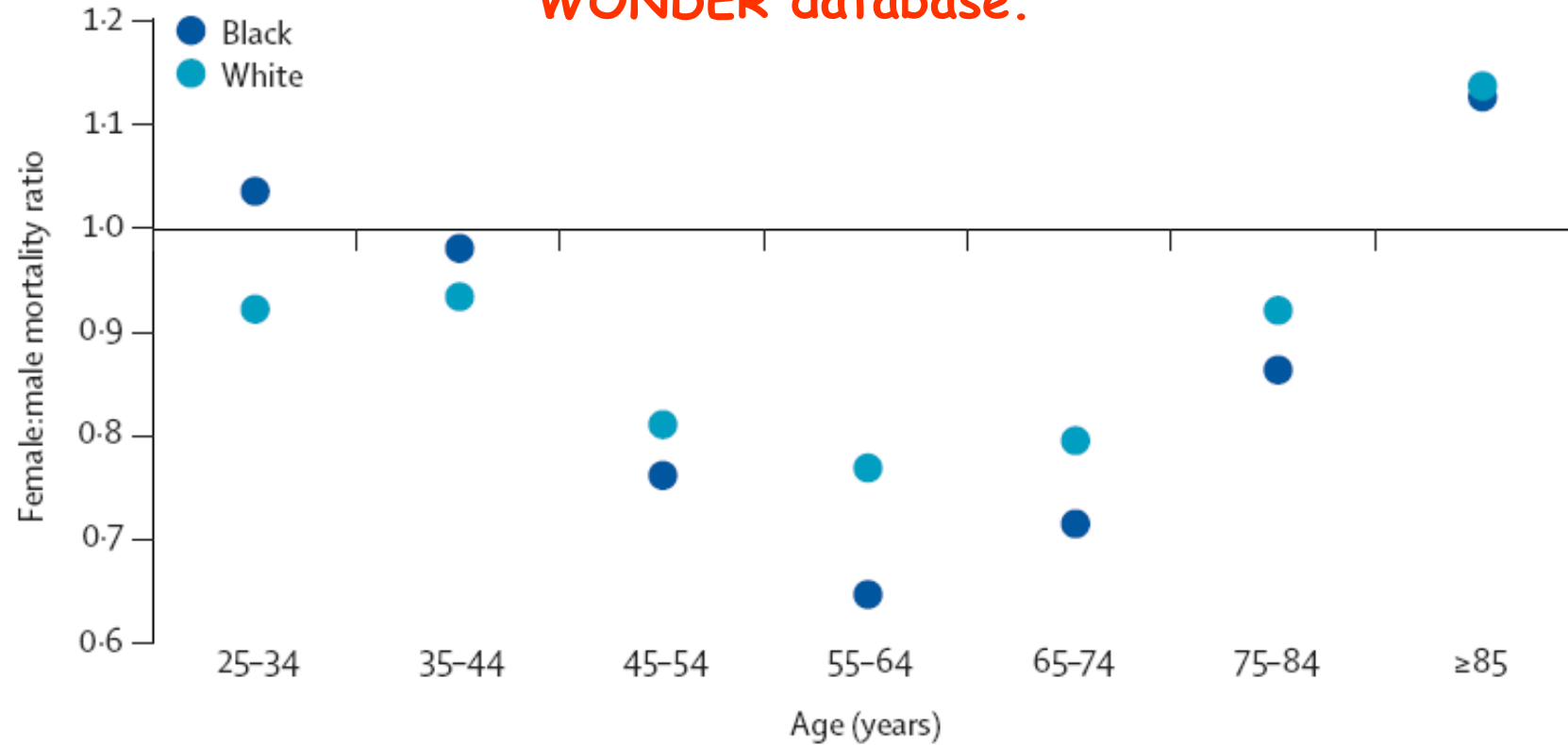


Age-specific and sex-specific mortality estimates were obtained from the US Centers for Disease Control and Prevention WONDER database, and age-specific and sex-specific population projections from the US Census Bureau middle series.² Projected deaths were calculated by applying age-specific and sex-specific mortality data to the population projections.

Reeves MJ et al. Lancet Neurol 2008; 7: 915–26

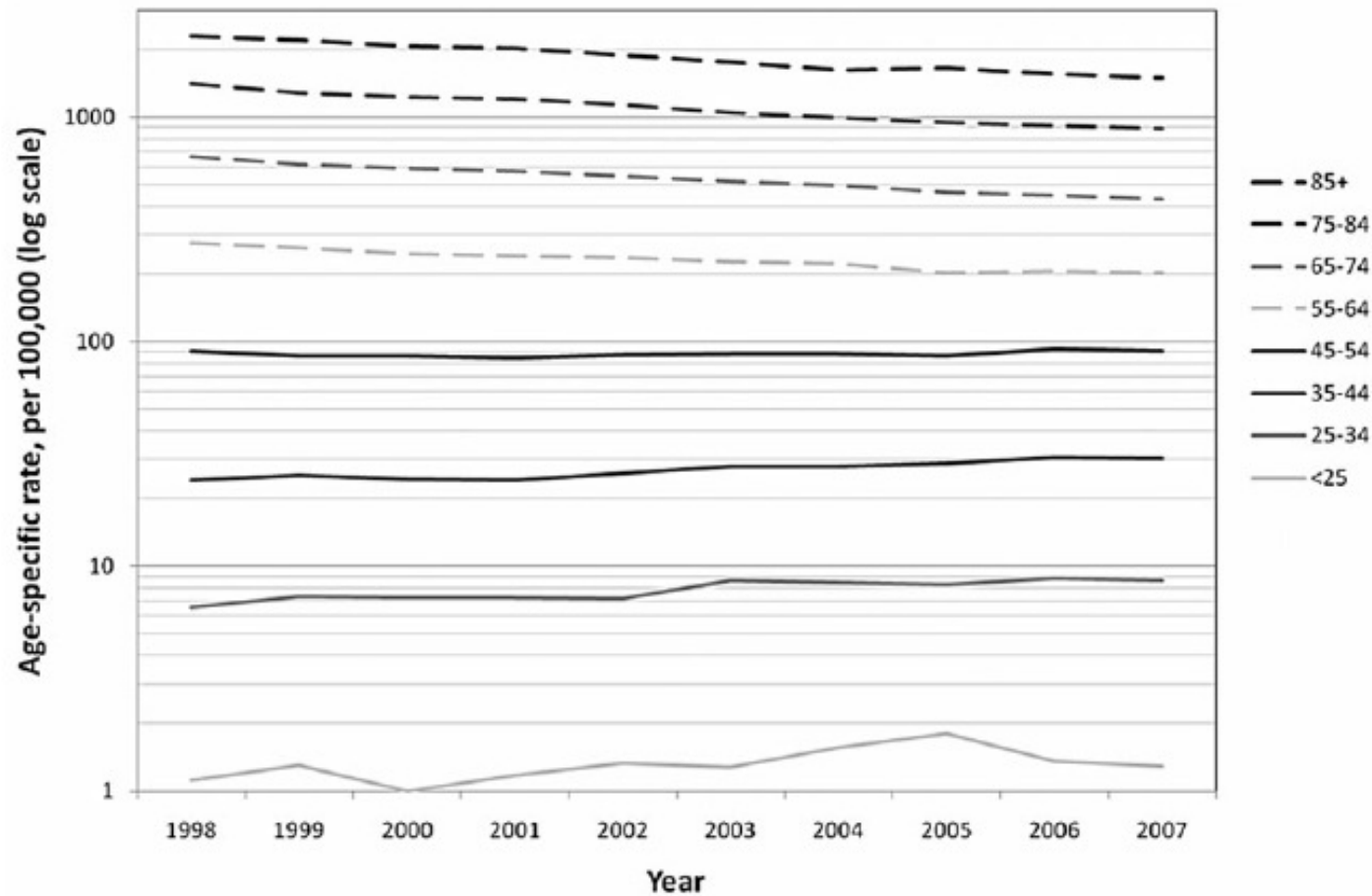
Female:male mortality ratios for stroke by age (USA, 1999–2003)

Data from the US Centers for Disease Control and Prevention WONDER database.



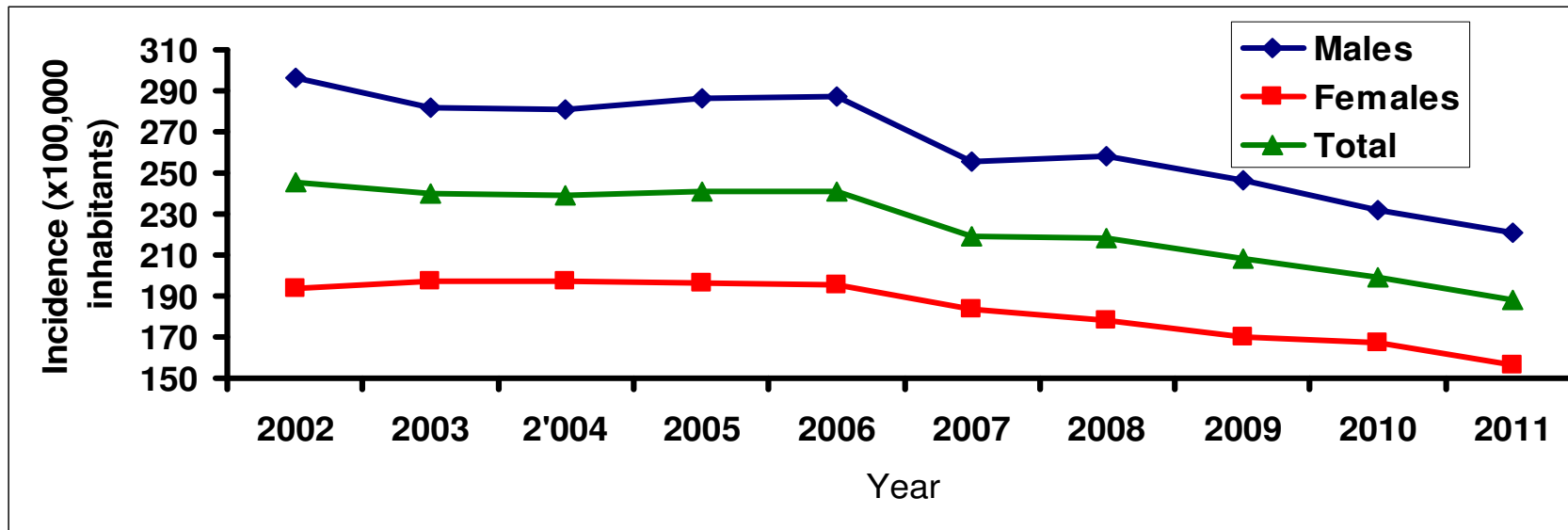
Reeves MJ et al. Lancet Neurol 2008; 7: 915–26

Annual age-specific rates of ischemic stroke hospitalization in the United States. Rates for those age 55–65, 65–75, 75–85, and 85 decreased significantly ($P < 0.0001$ each). Rates for those 25–35 and 35–45 increased significantly ($P < 0.001$ and $P < 0.0001$, respectively). Rates for those <25 and 45–55 were unchanged.

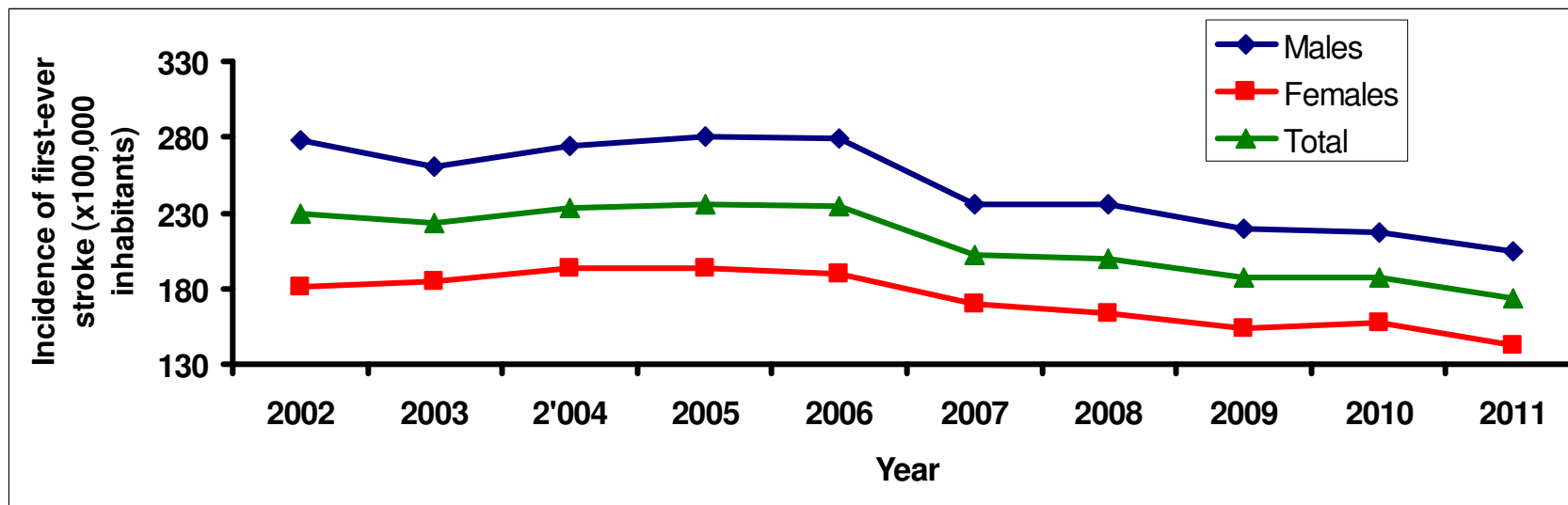


Incidenza di stroke ischemico (totale e first- ever)in Toscana (2002-2011)

Stroke totali



First-ever stroke



Take home messages

- Lo stroke è importante causa di mortalità e di disabilità nella nostra popolazione,
- L'incidenza è maggiore nell'uomo in tutte le classi di età, con l'eccezione per la donna con polimorbosità che ha incidenza più elevata nella classe di età più avanzata,
- In questi ultimi anni vi è una tendenza alla riduzione di incidenza dei nuovi casi sia totali che first-ever nella nostra popolazione
- La mortalità è maggiore nel sesso maschile, con l'eccezione della fascia di età più avanzata, dove prevalgono le donne

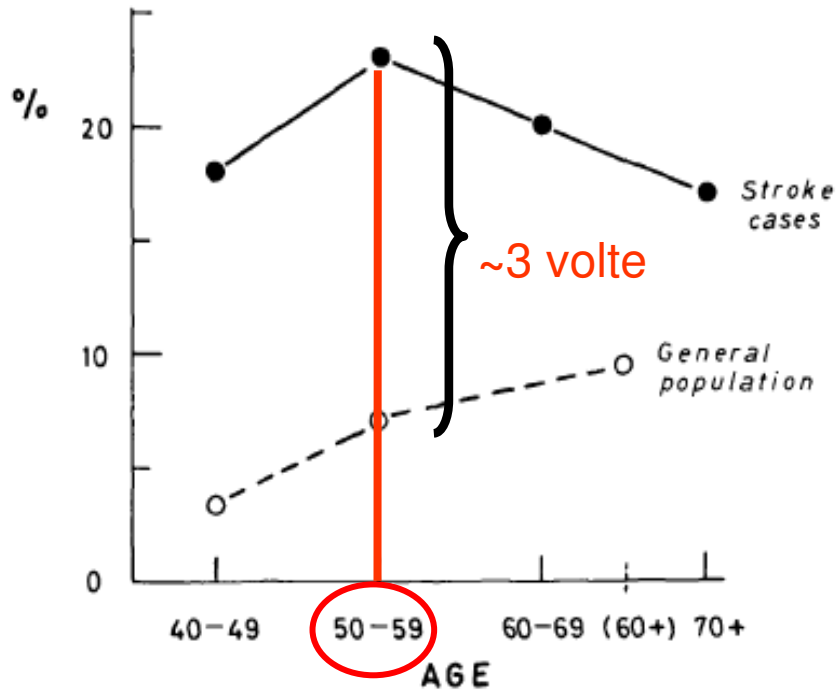
Agenda

- Epidemiologia dell'ictus
- **Ruolo del diabete**
- Terapia

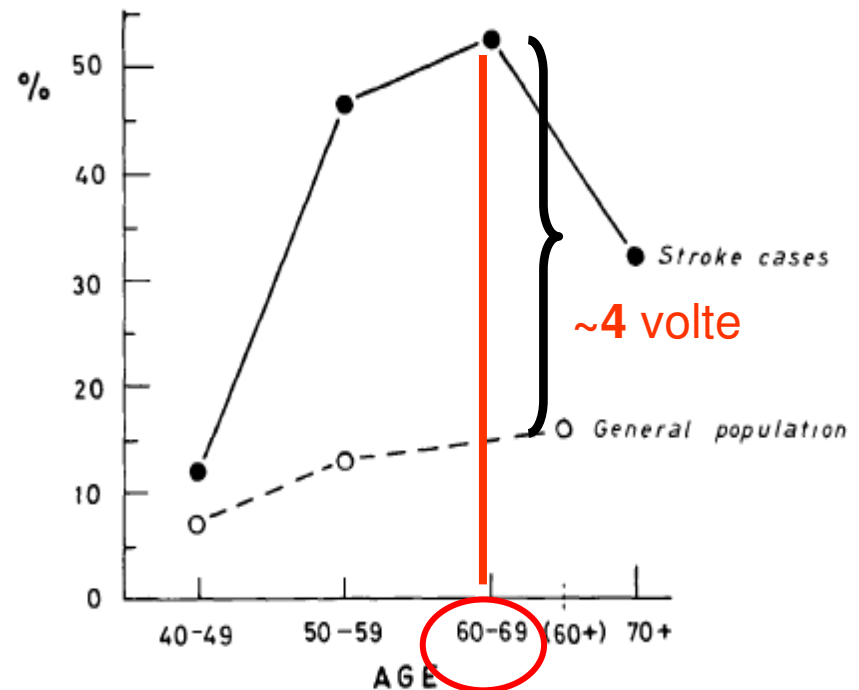
Hypertension and Diabetes as Risk Factors in Stroke Patients

BY SYLVAN LAVY, M.D., ELDAD MELAMED, M.D.,
ESTHER CAHANE, M.D., AND AMIRAM CARMON, M.D.

THE PREVALENCE OF MALE DIABETICS IN STROKE CASES AND IN GENERAL POPULATION

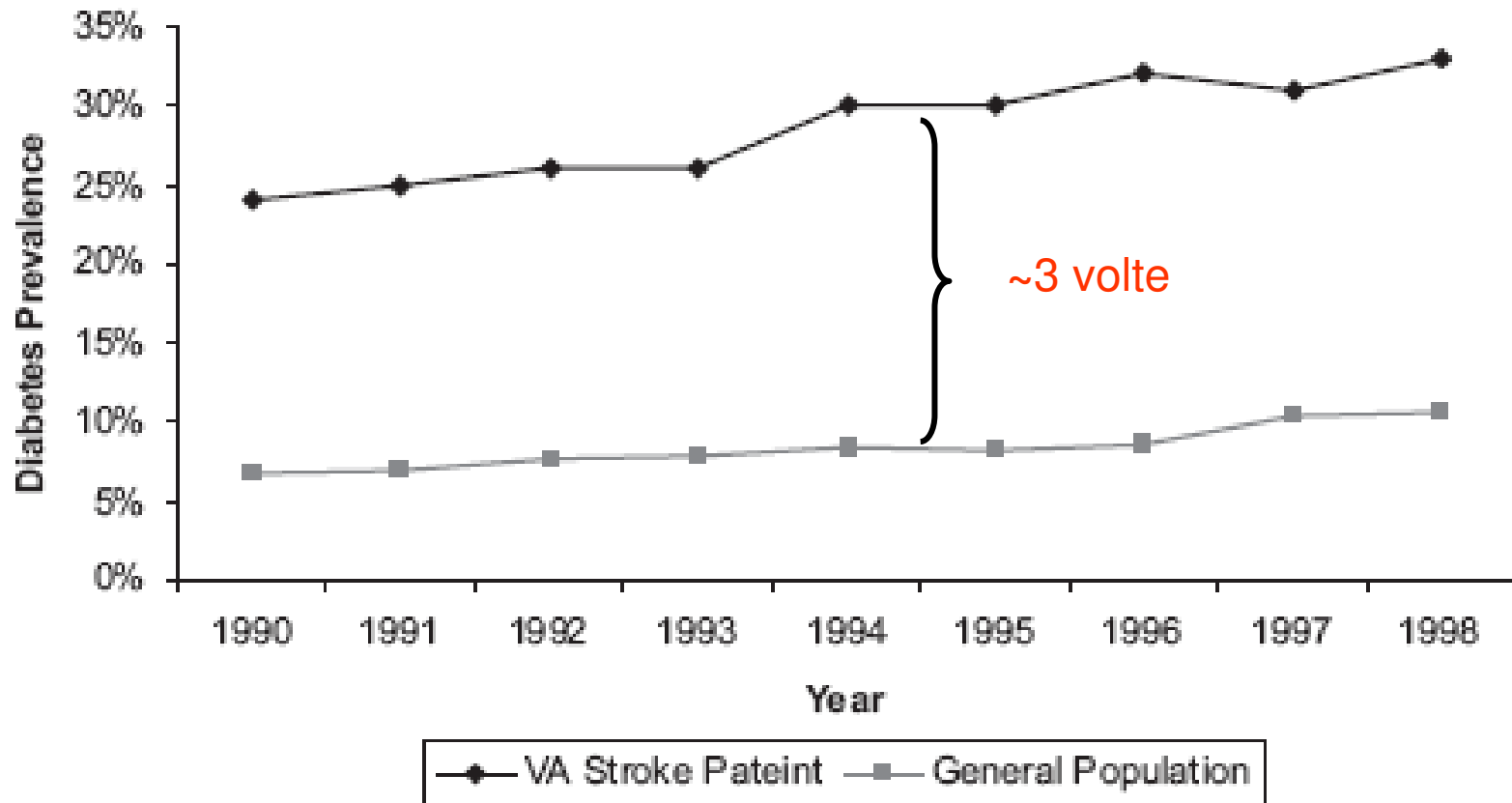


THE PREVALENCE OF MALE HYPERTENSIVES IN STROKE CASES AND IN GENERAL POPULATION



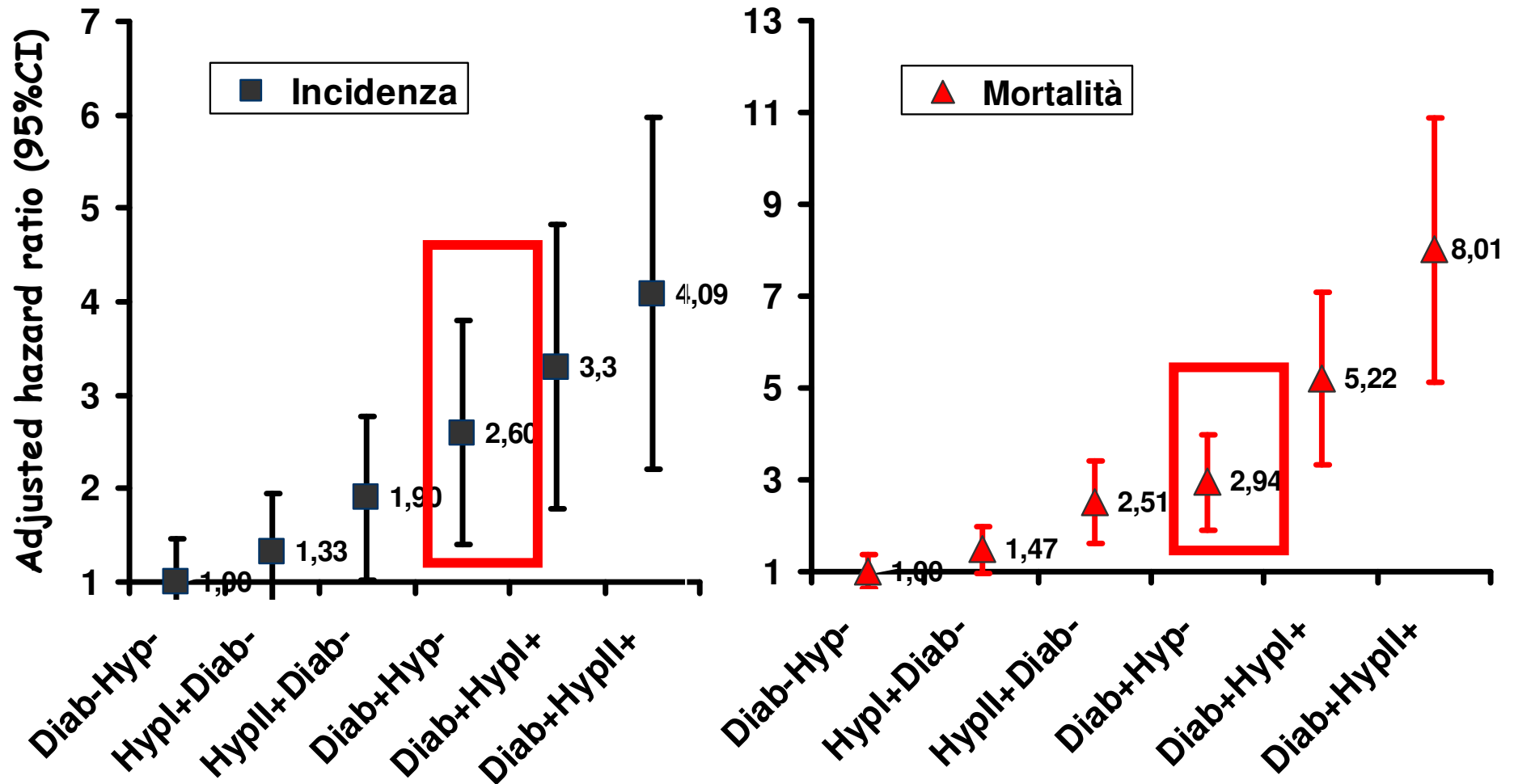
Stroke. 1973;4:751-59

Diabetes prevalence among stroke patients and general population (*Veterans hospital between October 1990 and September 1997 n=48,733 ischemic stroke patients*)



Kamalesh M et al. Stroke. 2008;39:2727-2731

HRs for Stroke Incidence and Stroke Mortality According to the History of Hypertension and Diabetes at Baseline (Finnish subjects aged 25 to 74 years; follow-up of 19.1 yrs)



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 (<i>n</i>)	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 et al Diabetologia (2006) 49:2859–2865

Rischio di stroke ischemico o di FEIS espresso come OR nel diabetico vs. il non diabetico dopo aggiustamento per età in pazienti stratificati per sesso dimessi dagli ospedali toscani (anni 2001-2011)

	Ischemic stroke		First-ever stroke	
	OR	95% CI	OR	95% CI
Males	1.31	(1.28-1.34)	1.29	(1.26-1.32)
Females	1.24	(1.21-1.27)	1.22	(1.19-1.25)

Dati ARS, Toscana

Clinical patterns of stroke in patients with and without diabetes

Clinical	Diabetes	No diabetes
Ischaemic : haemorrhagic	Approx. 10:1	Approx. 5:1
Stroke risk < 55 years	Higher	Lower
RR for male /female	Female > male	Female < male
Infratentorial infarcts	More common	Less common
Lacunar infarction	More common	Less common
Infarction volume	No difference	

Multivariate model of risk factors for stroke case fatality from UKPDS

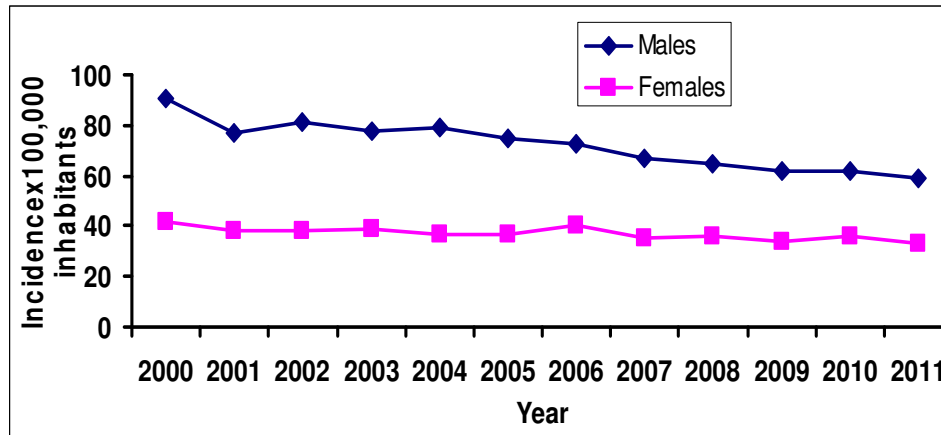
Risk factor	Odds ratio	95% CI	p value*
Sex (female vs. male)	2.33	1.11–4.91	0.025
HbA _{1c} (per 1%)	1.37	1.09–1.72	0.007
Systolic blood pressure (per 10 mmHg)	1.29	1.04–1.54	0.004
Subsequent stroke vs. first stroke	12.6	4.34–36.7	<0.0001
White cell count (per 10 ⁹ /L)	0.82	0.67–0.97	0.0218

Key: CI = confidence incidence

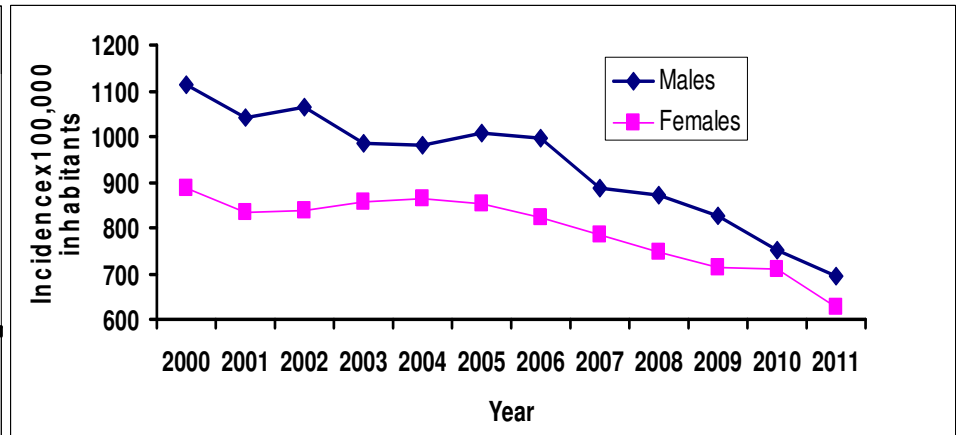
*Values are significant p < 0.05

Incidenza di stroke ischemico in Toscana in non diabetici ed in diabetici (2000-2011)

Non diabetici

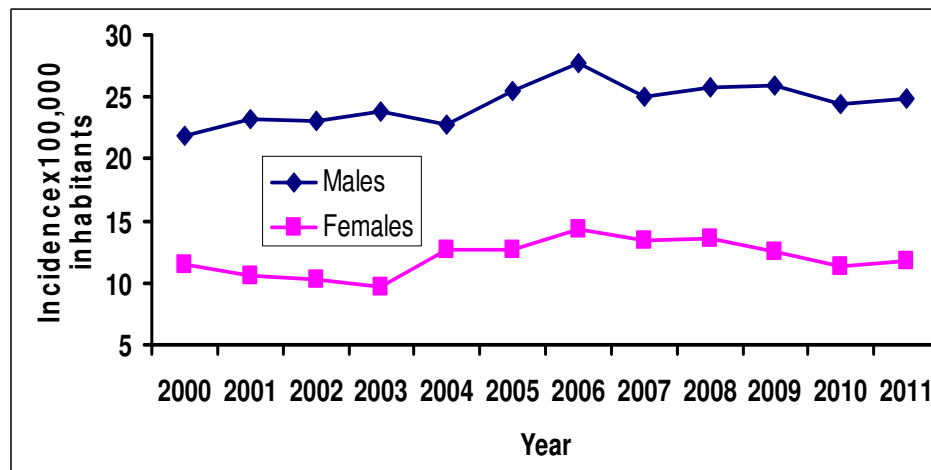


< 70 years

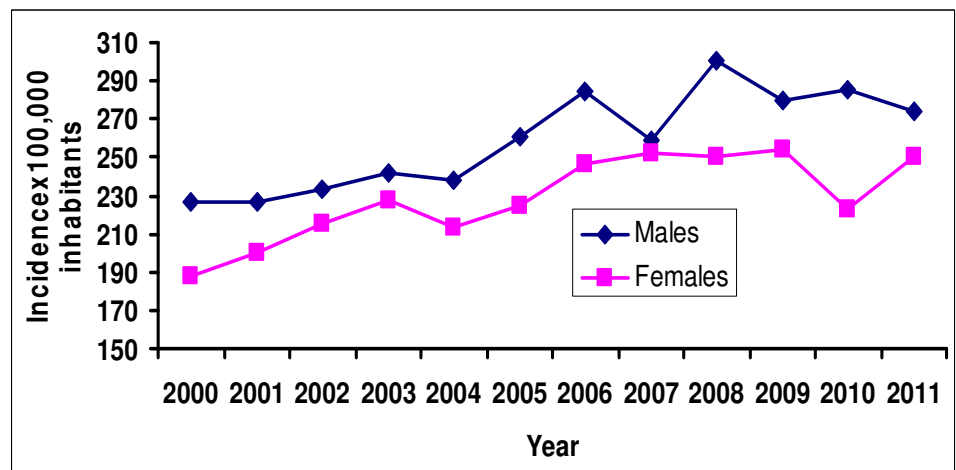


≥ 70 years

Diabetici



< 70 years



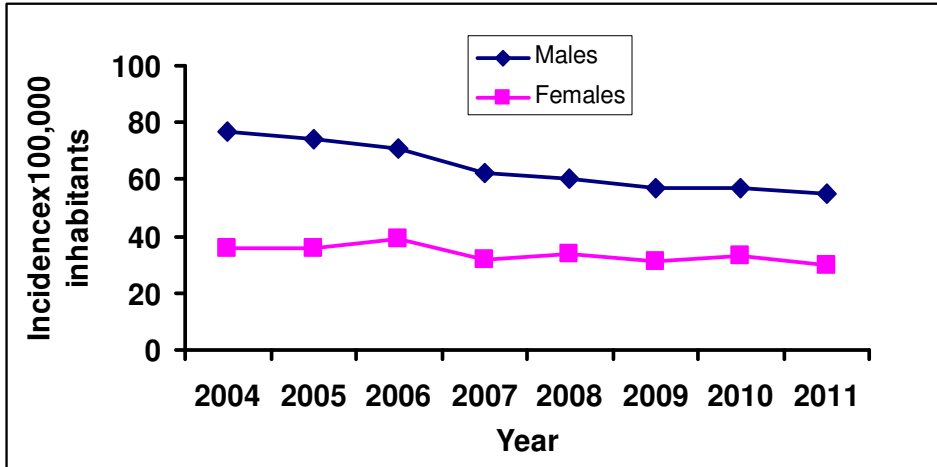
≥ 70 years

Incidenza di stroke ischemico in Toscana nel periodo 2000-2011, suddivisa per fascia di età e per sesso e per presenza di diabete

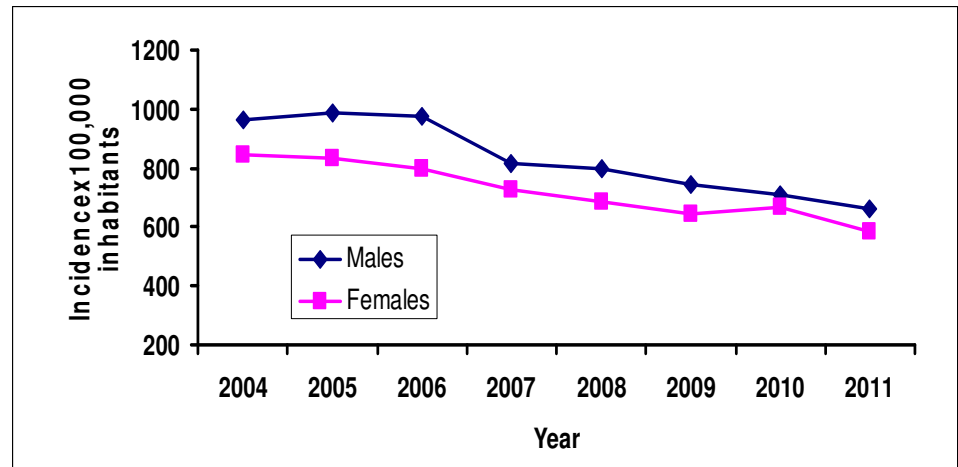
	No. of cases (2000/2011)	Rate x 100,000 (2000/2011)	Yearly change (% ± SE)	95% CI	p
<i>Non Diabetic patients</i>					
<i>Age <70 yr</i>					
Men	1229/807	91/59	-3.2±0.3	-3.8 to -2.7	<0.0001
Women	579/466	42/33	-1.3±0.4	-1.9 to -0.5	0.0007
<i>Age > 70 yr</i>					
Men	2238/1732	1112.71/694.17	-1.8±0.2	-2.2 to -1.5	<0.0001
Women	2834/2320	886.85/627.20	-1.3±0.2	-1.6 to -0.9	<0.0001
<i>Diabetic patients</i>					
<i>Age <70 yr</i>					
Men	296/342	21.93/24.92	1.5±0.4	0.6 to 2.3	0.0014
Women	157/166	11.48/11.84	1.8±0.6	0.5 to 3.1	0.0057
<i>Age > 70 yr</i>					
Men	456/683	226.72/273.74	4.2±0.3	3.5 to 4.9	<0.0001
Women	602/924	188.38/249.80	3.4±0.3	2.8 to 3.9	<0.0001

Incidenza di primo stroke in Toscana in non diabetici ed in diabetici dimessi dai reparti ospedalieri (2004-2011)

Non diabetici

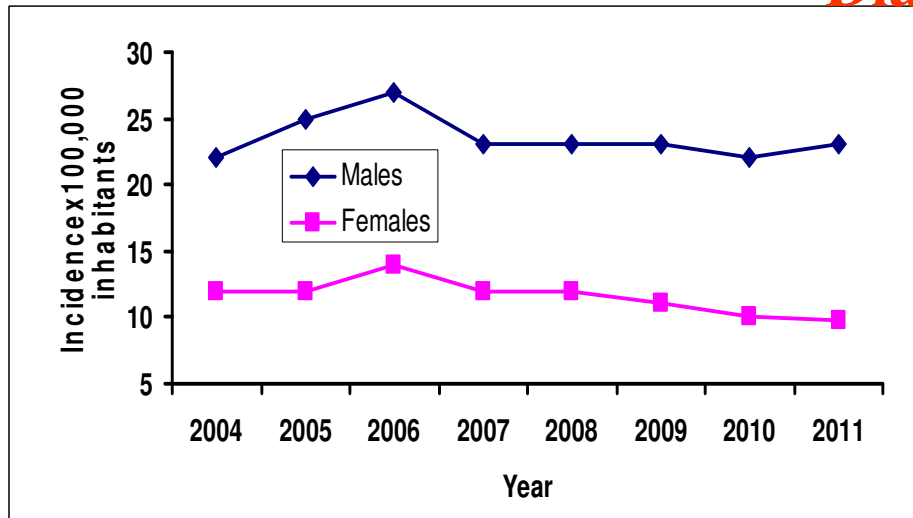


< 70 years

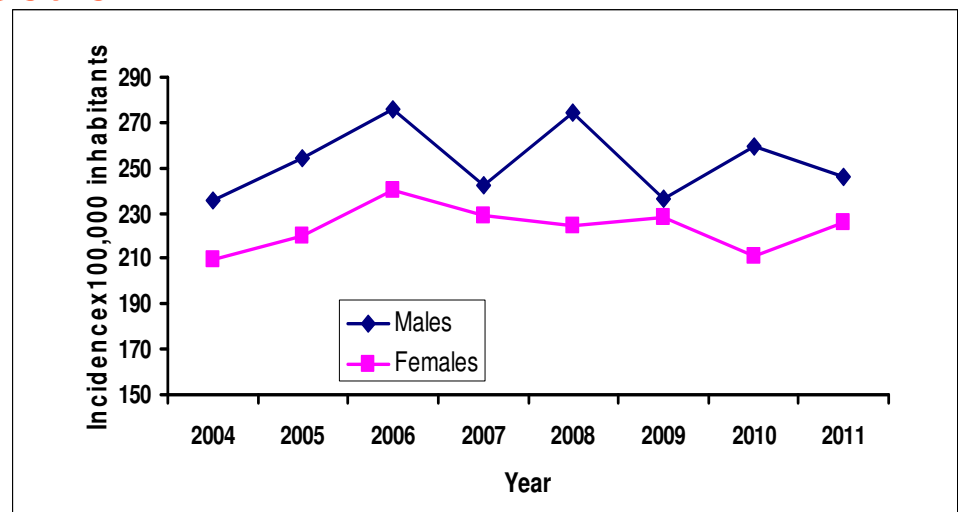


≥ 70 years

Diabetici



< 70 years



≥ 70 years

Incidenza di FEIS in Toscana nel periodo 2004-2011, suddivisa per fascia di età e per sesso e per presenza di diabete

	No. of cases (2004/2011)	Rate x 100,000 (2004/2011)	Yearly change (% ± SE)	95% CI	p
<i>Non Diabetic patients</i>					
<i>Age <70 yr</i>					
Men	1033/750	77.07/54.66	-4.8±0.5	-5.9 to -3.8	<0.0001
Women	494/428	36.38/30.53	-2.2±0.7	-3.6 to -0.8	0.0016
<i>Age > 70 yr</i>					
Men	2108/1626	964.25/651.69	-4.3±0.3	-5 to -3.6	<0.0001
Women	2881/2154	839/582.32	-4.1±0.3	-4.7 to -3.5	<0.0001
<i>Diabetic patients</i>					
<i>Age <70 yr</i>					
Men	296/319	22.08/23.25	-0.71±0.8	-2.4 to 0.9	NS
Women	167/137	12.30/9.77	-3.2±1.2	-5.6 to -0.8	0.0078
<i>Age > 70 yr</i>					
Men	515/614	235.57/246.08	1.9±0.6	0.7 to 3.2	0.0024
Women	715/836	209.81/226	1.3±0.5	0.2 to 2.4	0.0170

Dati ARS

Global and regional mortality from ischaemic heart disease and stroke attributable to higher-than-optimum blood glucose concentration: comparative risk assessment

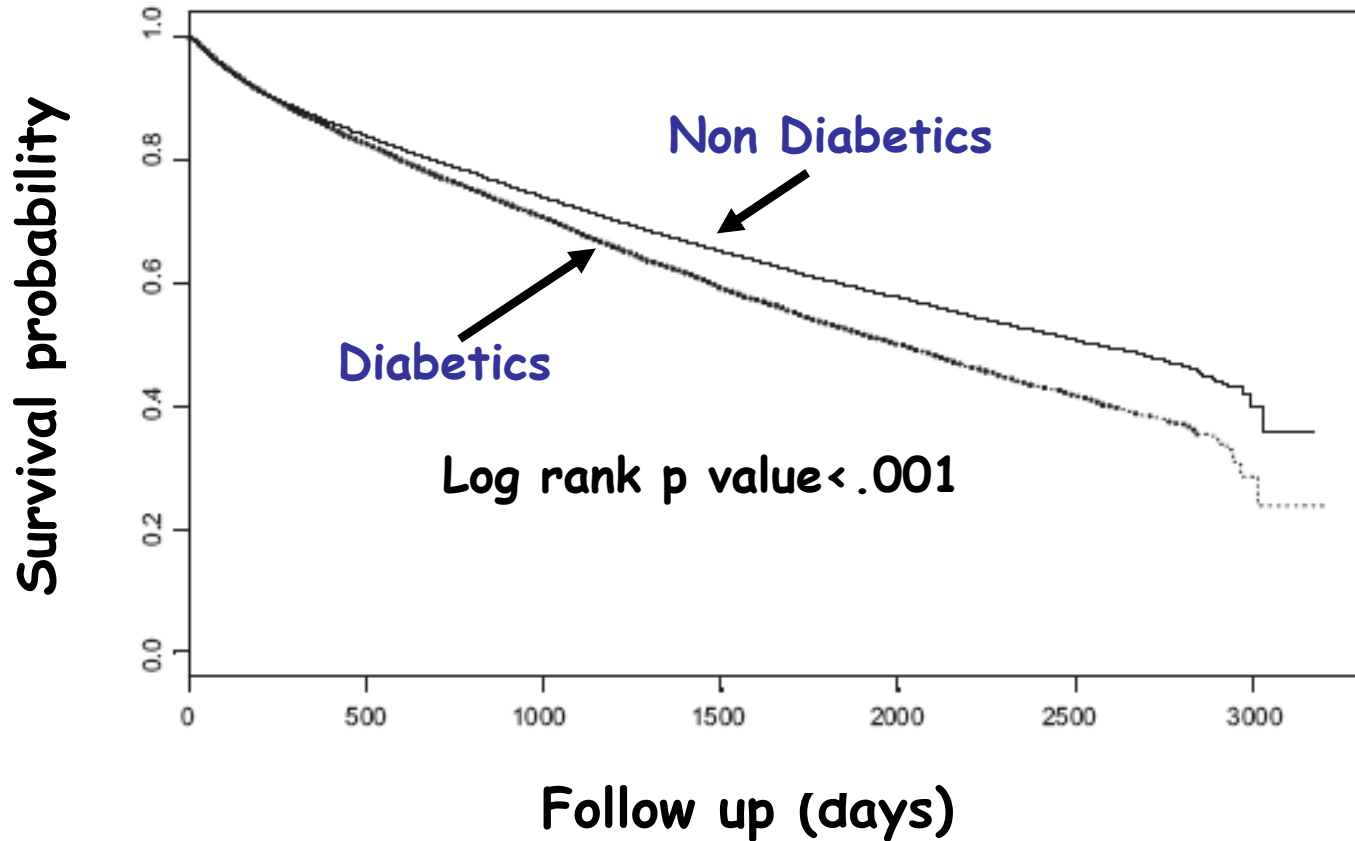
Goodarz Danaei, Carlene M M Lawes, Stephen Vander Hoon, Christopher J L Murray, Majid Ezzati

Relative risk for 1 mmol/L (18mg/dl) increase in FPG, by age group (after adjustment for confounding and regression dilution bias)

	<60 years	60–69 years	≥70 years
Ischaemic heart disease	1.424	1.196	1.196
Stroke	1.360	1.284	1.081

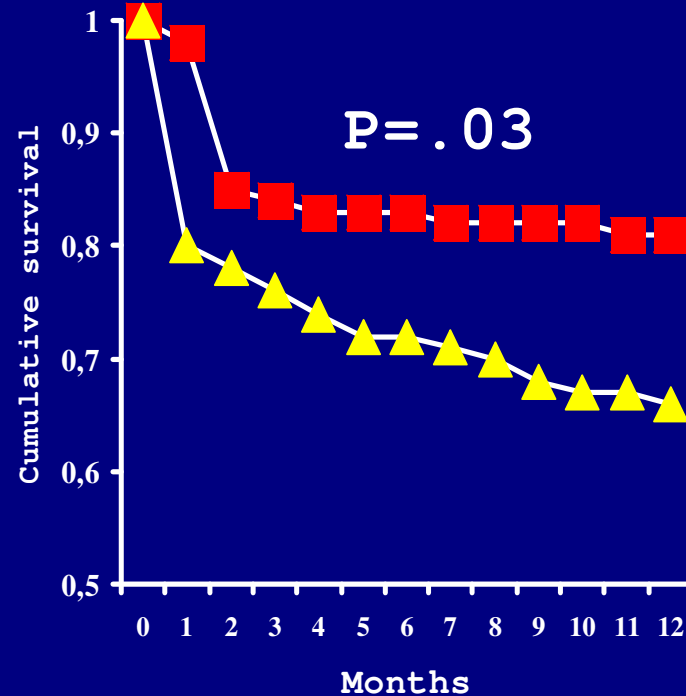
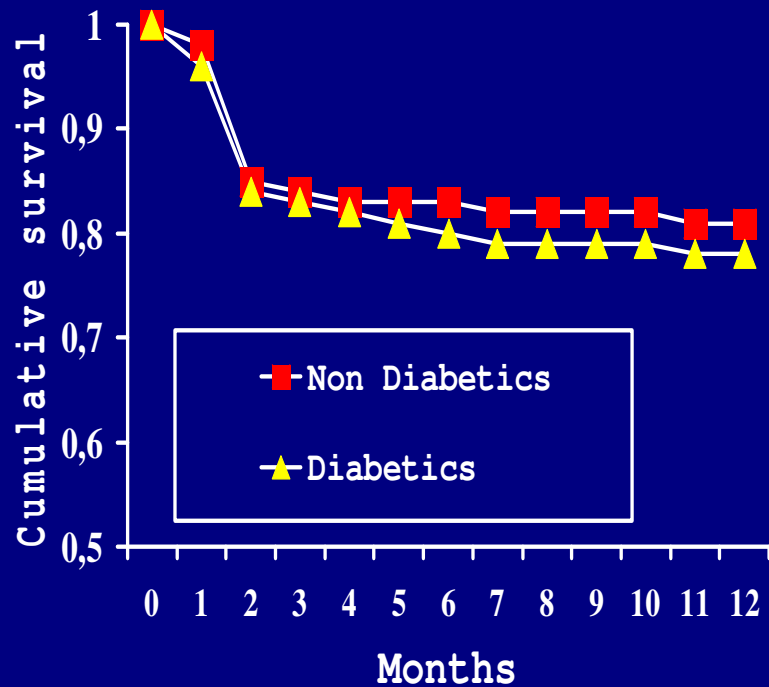
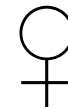
Lancet 2006; 368: 1651–59

Kaplan-meier plot of time to death (in days) for diabetic and nondiabetic groups (*Veterans hospital between October 1990 and September 1997 ; n=48733 ischemic stroke patients*)



Kamalesh M et al. Stroke. 2008;39:2727-2731

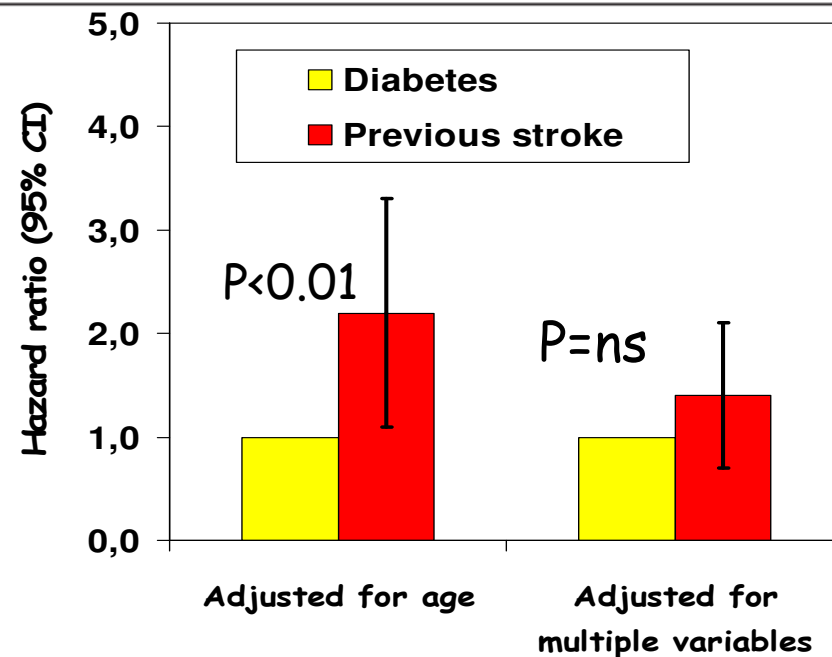
Kaplan-Meier Estimates of Cumulative Survival in the Group of Patients Stratified by Presence of Diabetes



Seghieri G et al, unpublished data

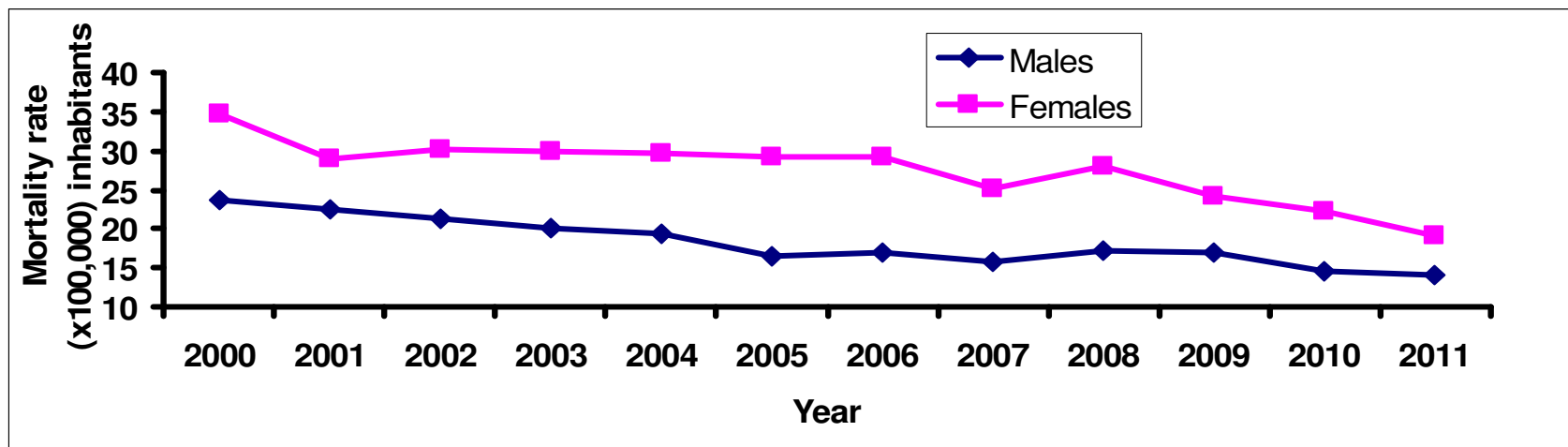
Stroke mortality HRs comparing nondiabetic subjects, those with previous MI or with previous stroke to diabetic subjects without CVD and with previous stroke (Age-adjusted 10-y stroke mortality rate per 1000 person-years).

Subgroup	Fatal Strokes, n	n	Stroke Mortality Rate*	Adjusted for Age		Adjusted for Multiple Variables‡	
				HR‡	95% CI	HR	95% CI
No. CVD, no diabetes	141	23 876	0.75	1.00		1.00	
Previous MI	5	567	0.59	0.66	(0.27–1.61)	0.71	(0.29–1.76)
Diabetes	42	2091	2.53	3.37	(2.38–4.77)	3.07	(2.01–4.68)
Previous stroke	31	432	6.66	6.77	(4.56–10.05)	4.67	(2.91–7.50)
Diabetes, previous stroke	8	95	7.95	7.82	(3.81–16.06)	5.40	(2.11–13.83)

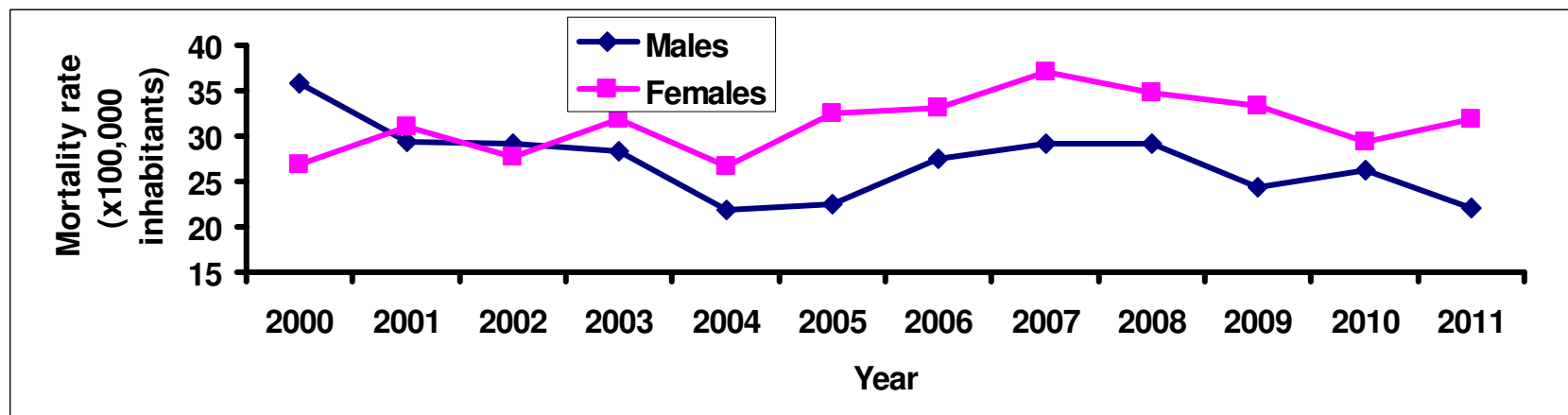


Mortalità per stroke in Toscana in non diabetici ed in diabetici su popolazione > 70 anni (2000-2011)

Non diabetici



Diabetici



Mortalità introspedaliera per stroke ischemico in Toscana nel periodo 2000-2011, in dimessi con eta > 70 anni suddivisa per sesso e per presenza di diabete

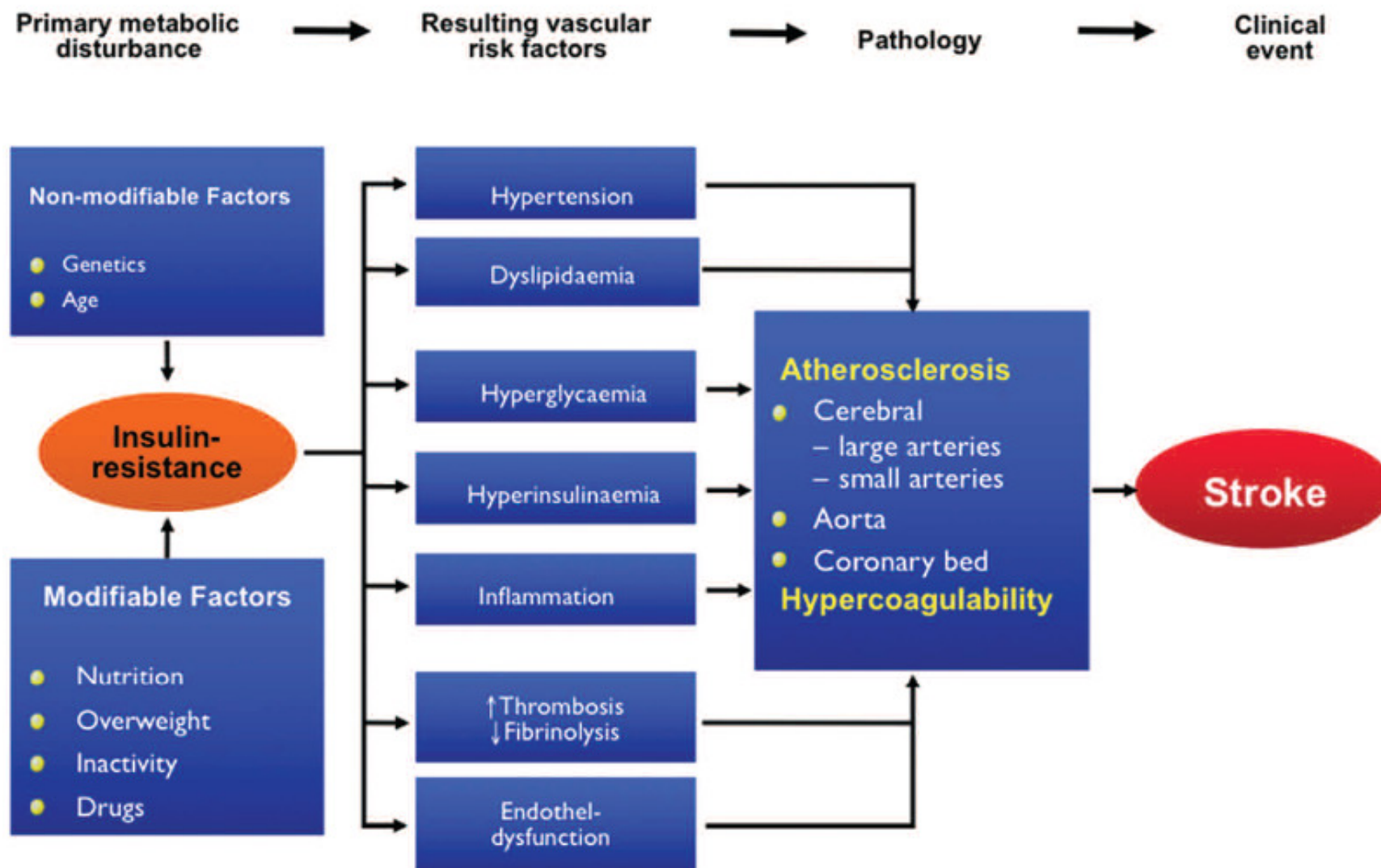
	No. of cases (2000/2011)	Rate x 100,000 (2000/2011)	Yearly change (% ± SE)	95% CI	p
<i>Non diabetic patients</i>					
<i>Age > 70 yr</i>					
Men	320/194	23.2/14.1	-4.2±0.5	-5.3 to -3.2	<0.0001
Women	476/268	34.8/19.1	-3.6±0.4	-4.4 to -2.7	<0.0001
<i>Diabetic patients</i>					
<i>Age > 70 yr</i>					
Men	72/55	35.8/22	-0.4±1.1	-2.5 to 1.7	NS
Women	86/118	26.9/31.9	2.6±0.8	1.0 to 4.2	<0.0012

Rischio di associazione tra diabete e mortalità
intraospedaliera espresso come OR in pazienti con stroke
ischemico o con FEIS stratificati per sesso dimessi dagli
ospedali toscani (anni 2000-2011)

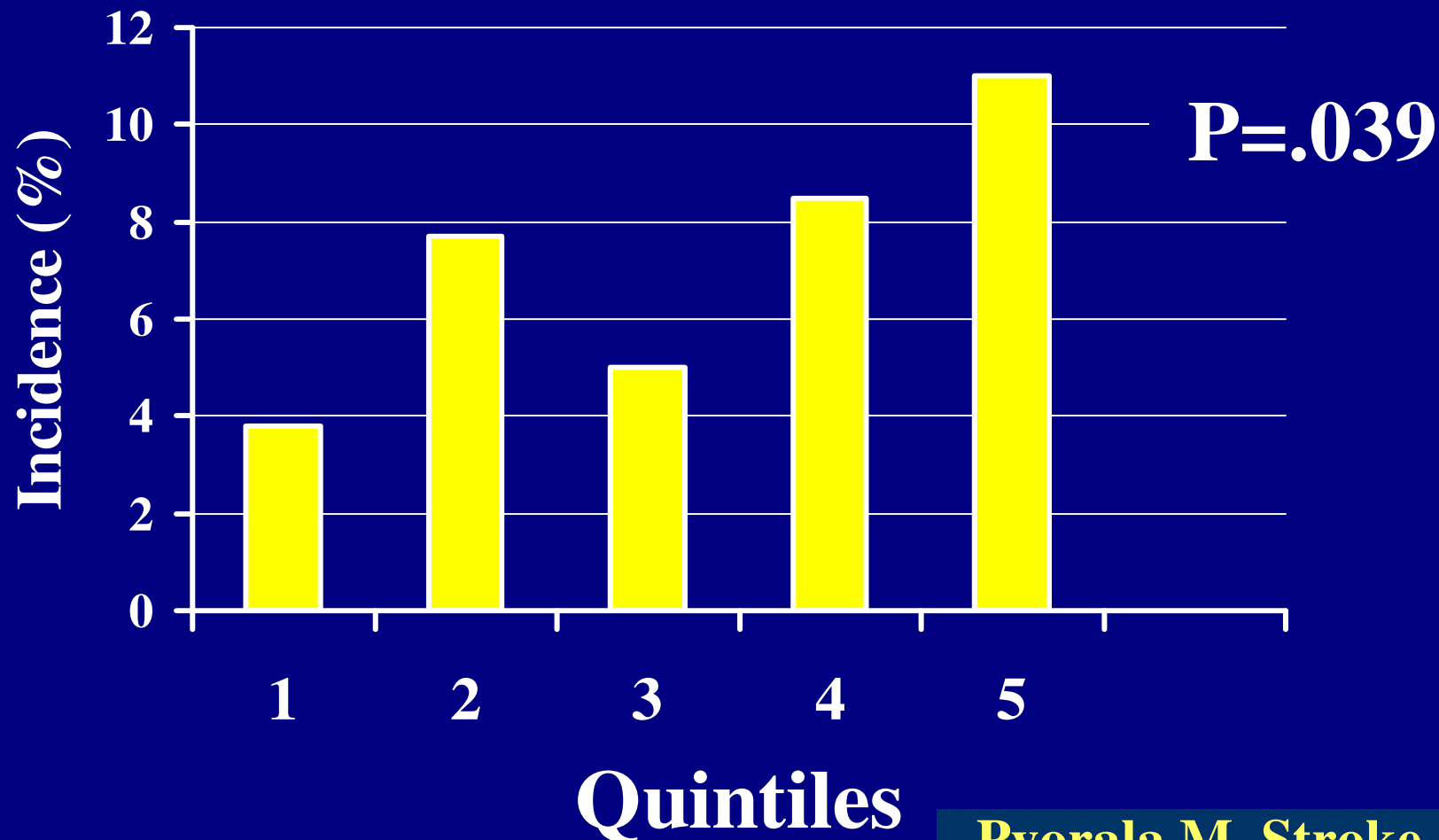
	Ischemic stroke		First-ever stroke	
	OR	95% CI	OR	95% CI
Males	0.93	(0.86-1.01)	0.92	(0.83-1.02)
Females	1.07	(1.002-1.14)	1.10	(1.01-1.19)

Dati ARS, Toscana

Insulin resistance and the development of stroke



Age-adjusted incidence of stroke by quintiles of fasting insulin (22-yr Follow up of the Helsinki Policemen Study)

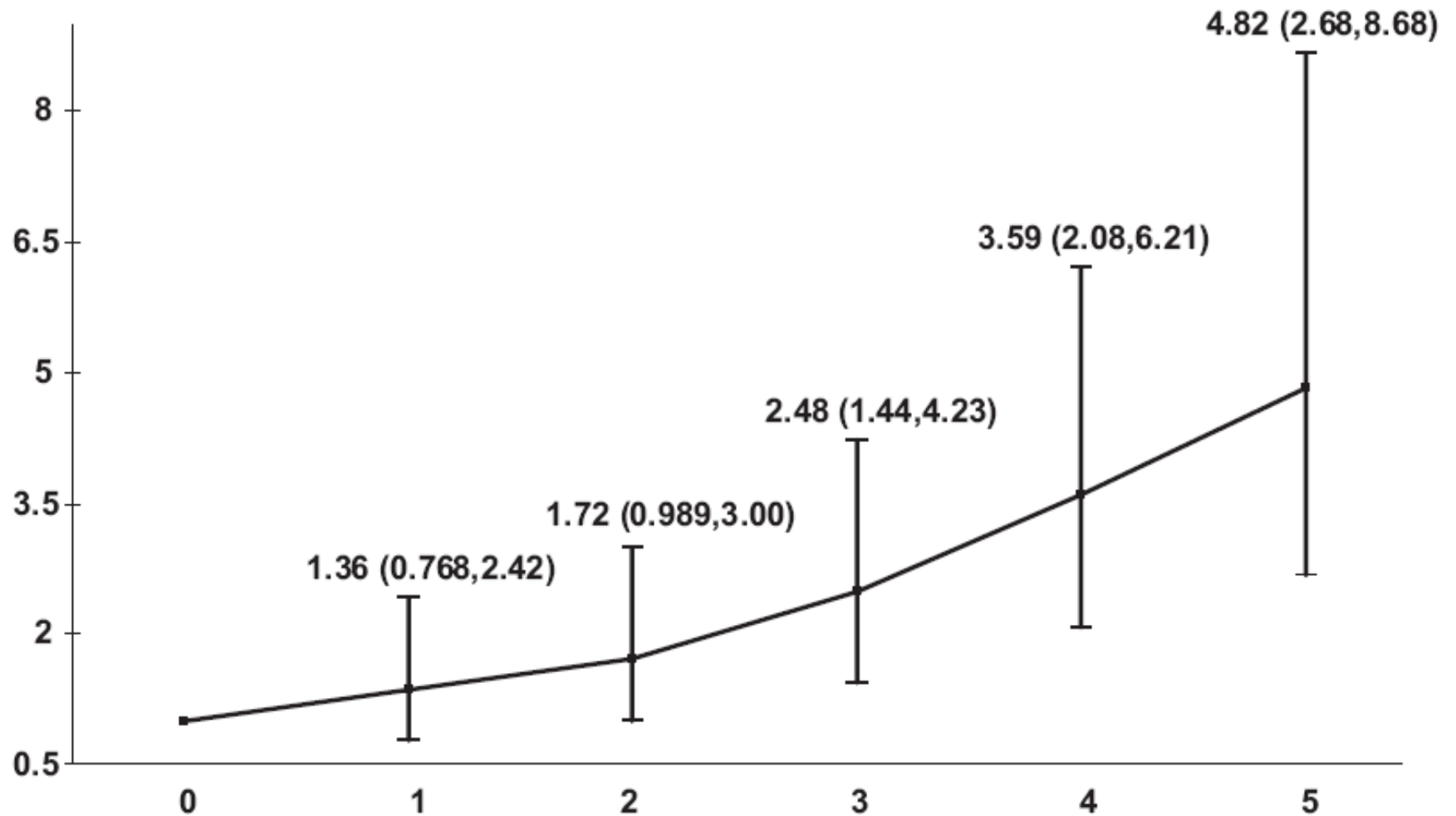


Pyorala M, Stroke, 1998

Dose-response relationship between number of MetS components and the RR of incident (9yr) ischemic stroke.

The Atherosclerosis Risk in Communities (ARIC) Study

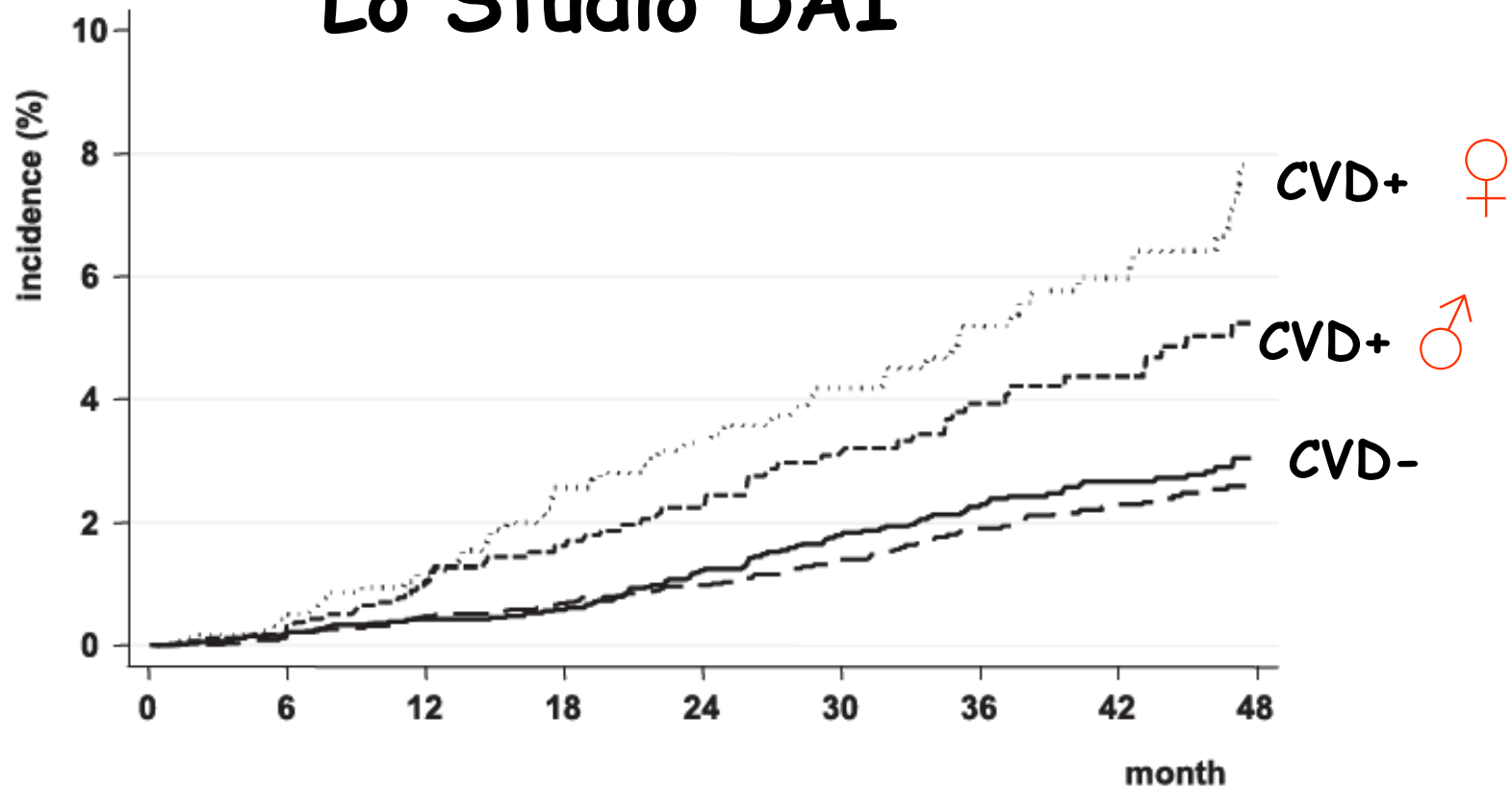
Relative Risk & 95% CI



No. of MetS Components

Rodriguez-Colon SM et al., *Stroke*. 2009;40:200-205

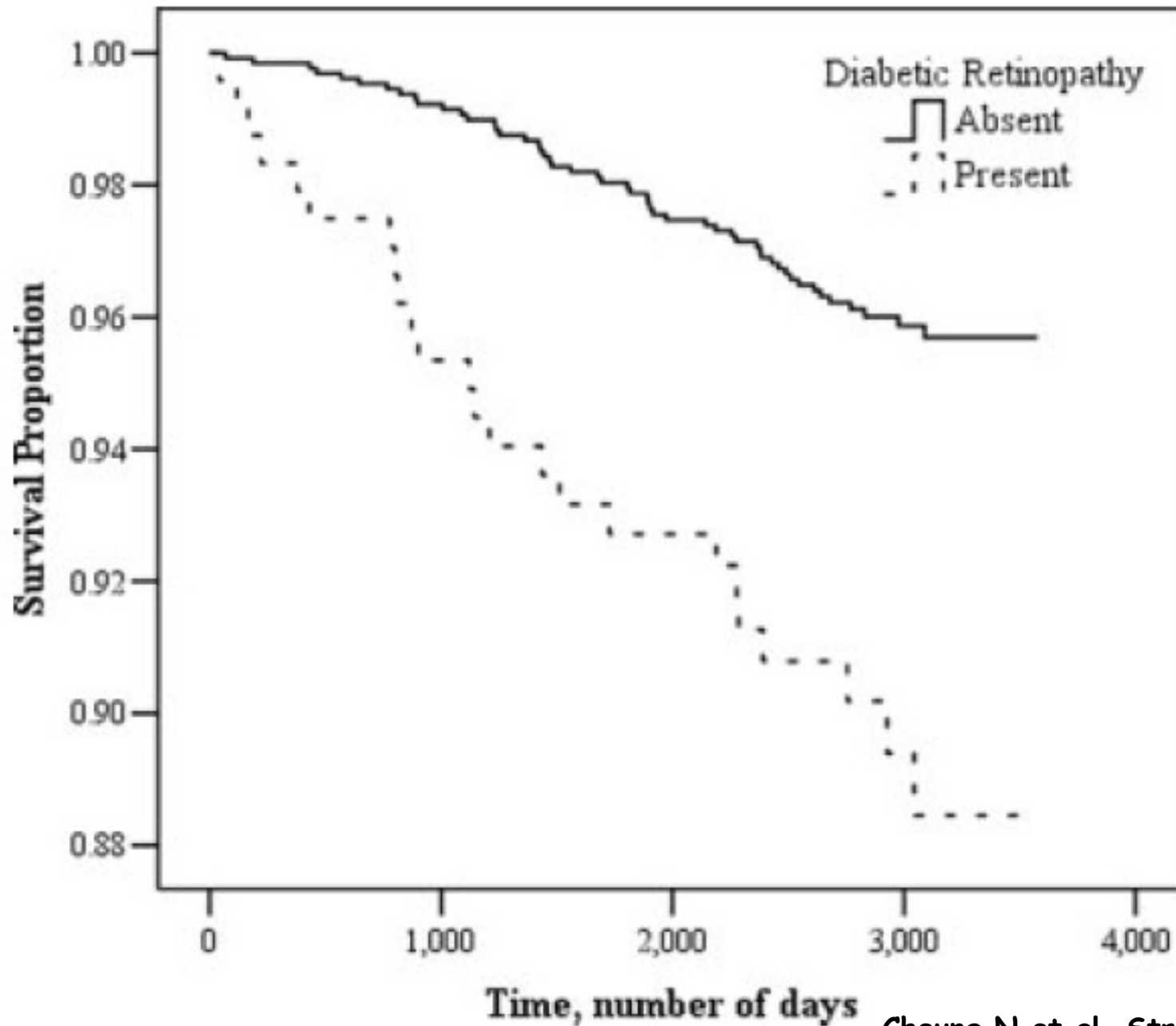
Lo Studio DAI



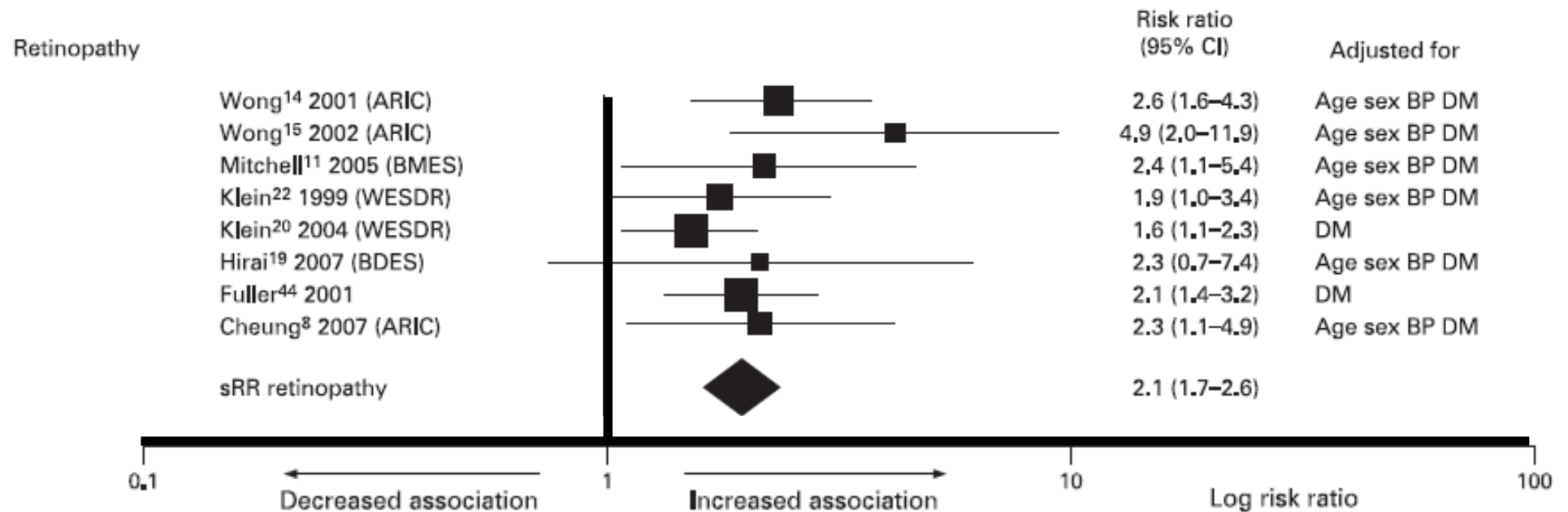
Units:	157	120	97	89
Obs. :	14432	11367	9489	8259

- Patients without CVD, males
- - - - Patients with CVD, males
- Patients without CVD, females
- Patients with CVD, females

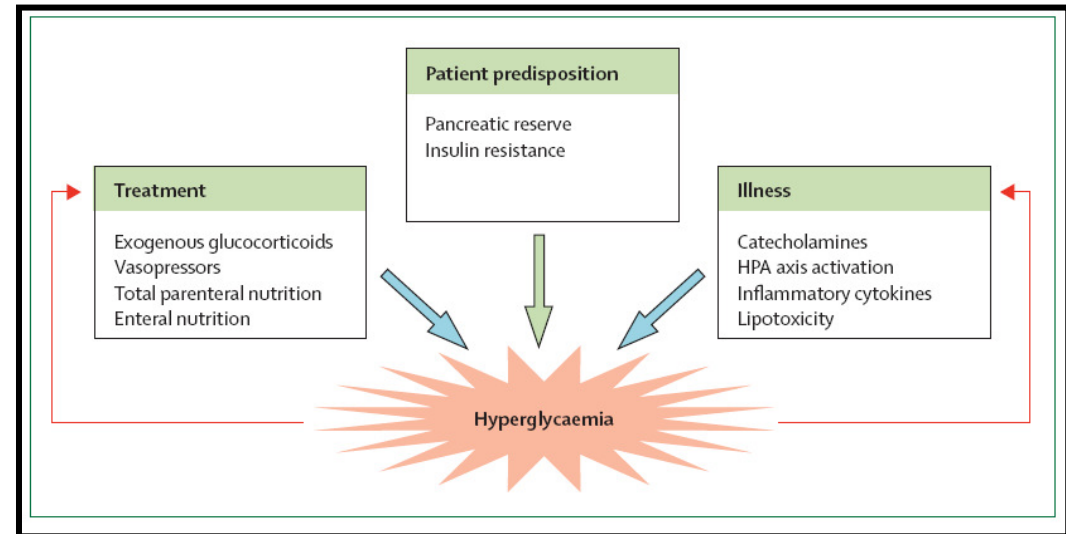
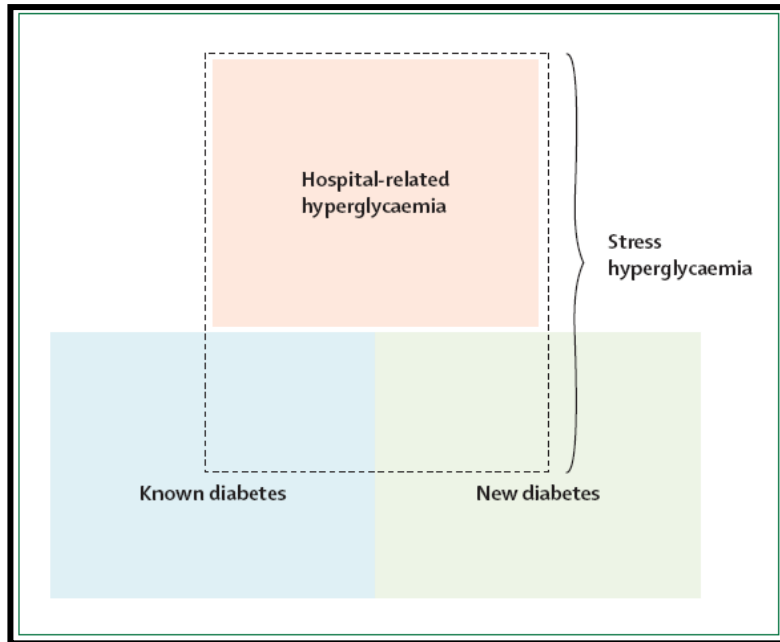
Stroke-free survival in participants with and without diabetic retinopathy



Retinopathy and Stroke: a metanalysis



Expanded view of stress hyperglycaemia



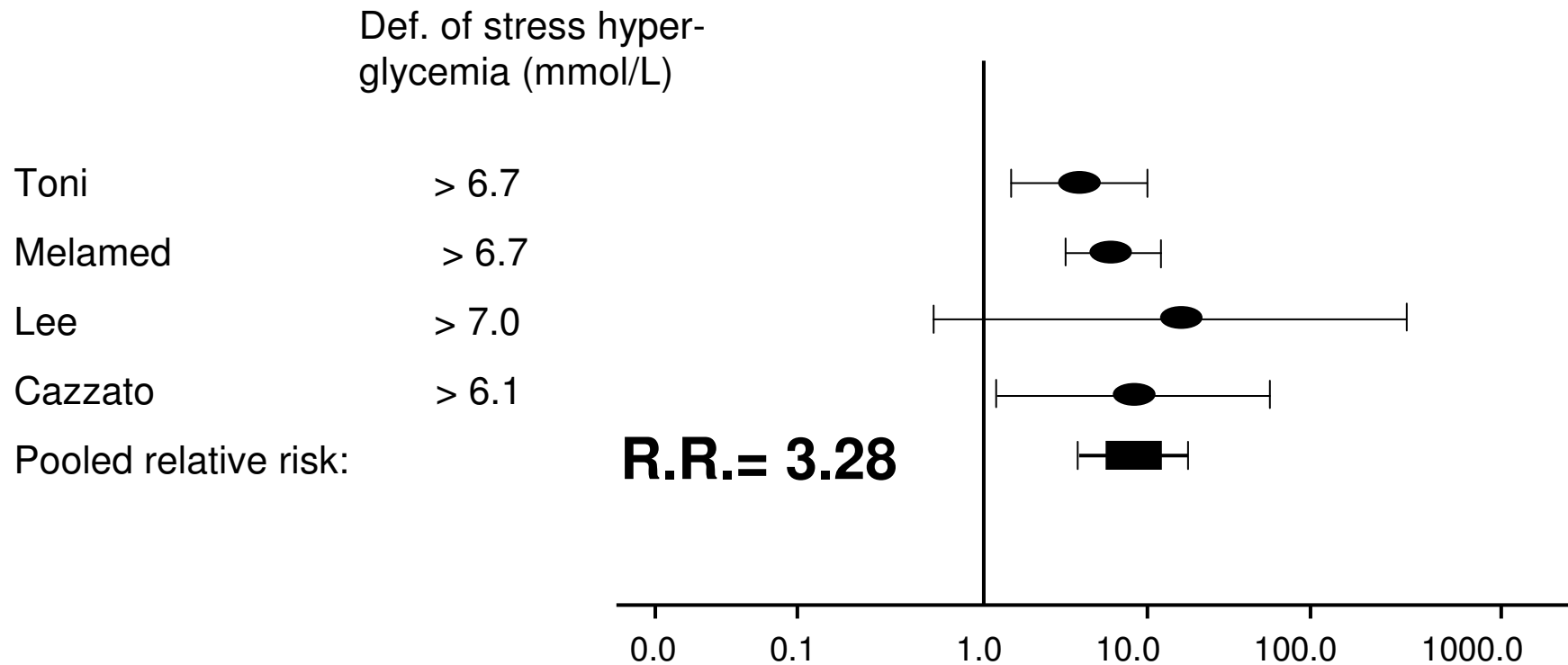
Dungan KM et al Lancet 2009; 373: 1798-807

Stress Hyperglycemia and Prognosis of Stroke in Nondiabetic and Diabetic Patients

A Systematic Overview

Sarah E. Capes, MD; Dereck Hunt, MD, MSc; Klas Malmberg, MD, PhD;
Parbeen Pathak, BSc, MD; Hertzell C. Gerstein, MD, MSc

Relative risk of **in-hospital or 30-day mortality** after **ischemic stroke** in 682 patients with stress hyperglycemia compared with those without stress hypergl.



(Stroke. 2001; 32:2426-2432)

Effects of admission hyperglycemia on mortality and costs in acute ischemic stroke

L.S. Williams, MD; J. Rotich, PhD; R. Qi, MS; N. Fineberg, PhD; A. Espay, MD; A. Bruno, MD;
S.E. Fineberg, MD; and W.R. Tierney, MD

Patients outcome by BG group

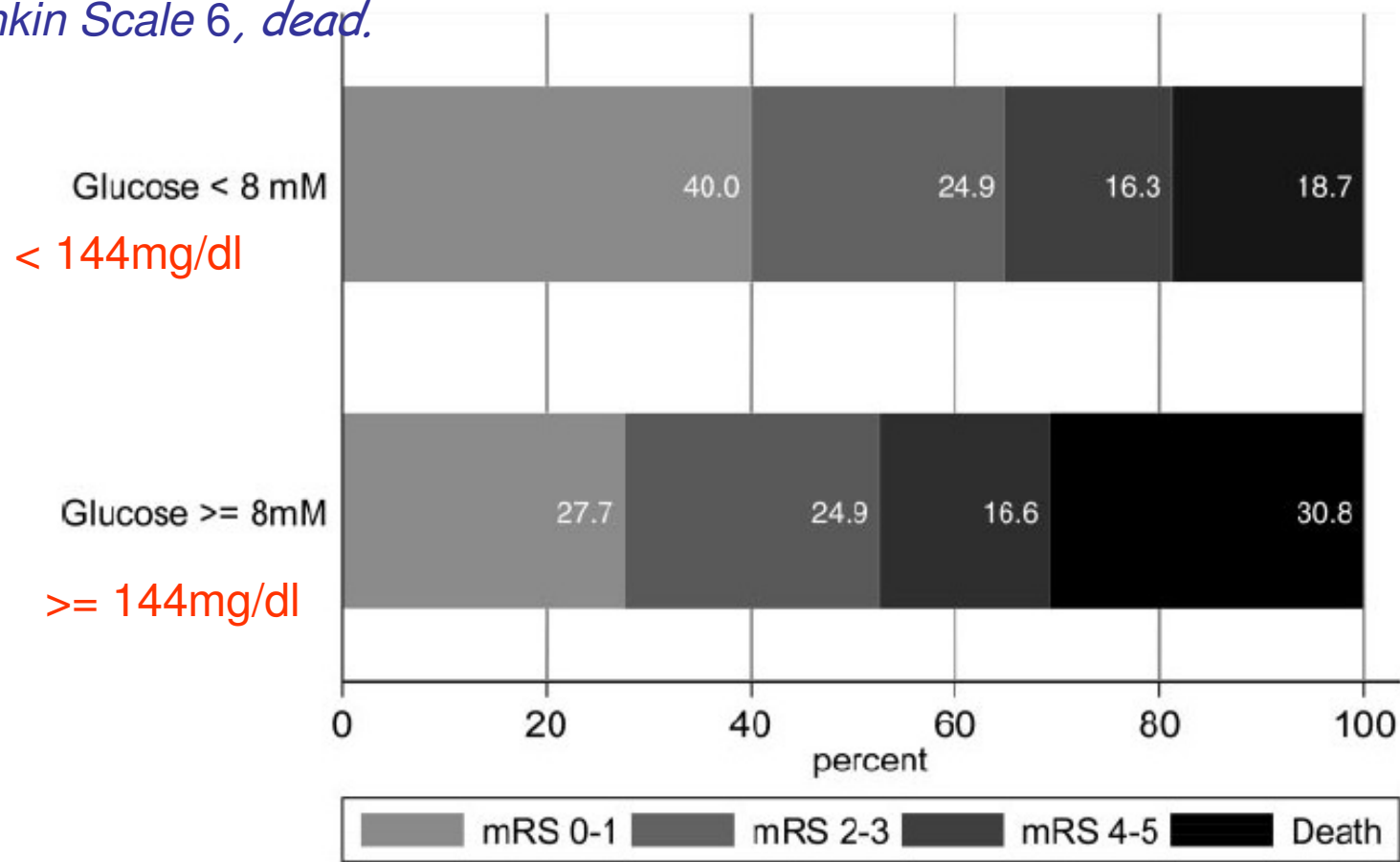
In 656 pazienti ospedalizzati per stroke ischemico acuto

Outcome	Admission BG Groups		p value
	BG < 130 mg/dL n= 385	BG > 130mg/dL n=258	
Mean LOS (days)	6±0.3	7.2±0.4	0.015
In-hospital mortality	18 (5%)	19 (7%)	0.15
30-day mortality	21 (5%)	27 (10%)	0.01
1-year mortality	41 (11%)	46 (18%)	0.009
6-year mortality	82 (22%)	71 (28%)	0.07
Median (range) total charge	\$5,262	\$6,611	<0.001

Neurology 2002; 59:67-71.

Patient outcome at the 90-day follow-up by baseline glucose (unadjusted for other predictors of outcome). [CASES study]

*mRankin Scale 0–1, excellent outcome;
mRankin Scale 2–3, moderate disability;
mRankin Scale 4–5, severe disability;
mRankin Scale 6, dead.*



Poppe AY et al Diabetes Care 32:617–622, 2009

Take home messages

- Il diabete aumenta il rischio di stroke (soprattutto ischemico) di circa 2-3 volte.
- Il cattivo compenso metabolico del diabete espresso da aumento dei valori di FPG e di HbA1c è linearmente correlato con un maggior rischio di stroke,
- Il rischio di stroke è maggiore nella donna soprattutto nelle fasce di età più giovane, anche se i dati non sono concordanti
- La correlazione diabete-stroke sembra essere, almeno in parte, mediata dalla presenza di resistenza insulinica,
- Fattori di rischio importanti nel diabetico sono la presenza di altre complicanze macroangiopatiche o di retinopatia,
- Vi è una tendenza ad incremento della incidenza di stroke ischemico nei diabetici di entrambi i sessi soprattutto nella età più avanzata,
- La mortalità per stroke a breve e lungo termine è aumentata nel diabete, la donna sembra essere a maggior rischio e, contrariamente a quanto avviene nel non diabetico vi è la tendenza in questi ultimi anni ad incremento della mortalità nella ns popolazione,
- L'iperglicemia all'ingresso in ospedale è marcatore di maggior durata di degenza, della mortalità e dei costi della degenza
- Nel diabetico la glicemia all'ingresso è predittore di disabilità futura in pazienti con stroke

Agenda

- Epidemiologia dell'ictus
- Ruolo del diabete
- **Terapia**

LINEE GUIDA SPREAD

- ❑ In pazienti con *ictus acuto* ed *iperglicemia* > 200 mg/dl è **indicata** la correzione con terapia insulinica.

Raccomandazione 11.21 grado D

- ❑ In pazienti con *ictus acuto* ed *ipoglicemia* è **indicata** la pronta correzione tramite infusione di destrosio in bolo ev, associando tiamina 100 mg in caso di malnutrizione o di abuso di alcool.

Raccomandazione 11.22 grado D

LINEE GUIDA EUROPEE

- ❑ E' indicato il controllo della glicemia (Classe IV, GCP).

- ❑ E' indicato il trattamento con insulina dei valori glicemici > 180 mg/dl (10 mmol/l) (Classe IV, GCP).

- ❑ E' indicato trattare l'ipoglicemia grave (< 50 mg/dl [2.8 mmol/l]) con destrosio ev o infusione di glucosio al 10-20% (Classe IV, GCP).

Glucose-potassium-insulin infusions in the management of post-stroke hyperglycaemia: the UK Glucose Insulin in Stroke Trial (GIST-UK)

*Christopher S Gray, Anthony J Hildreth, Peter A Sandercock, Janice E O'Connell, Donna E Johnston, Niall E F Cartlidge, John M Bamford, Oliver F James, K George M M Alberti, for the GIST Trialists Collaboration**

❑ 933 pz con stroke acuto e valori glicemici tra 6.1 e 17 mmol/l (108-306 mg/dl); esclusi pz in tx insulinica prima dell'evento

❑ Tipi di trattamento:

GRUPPO 1 (n=464)

Somministrazione di GKI per 24 h

GRUPPO 2 (n=469)

Infusione di soluzione salina

❑ Obiettivo: mantenere il controllo glicemico tra 4-7 mmol/L (72-126 mg/dl) e valutare la mortalità a 90 giorni.

Glucose-potassium-insulin infusions in the management of post-stroke hyperglycaemia: the UK Glucose Insulin in Stroke Trial (GIST-UK)

*Christopher S Gray, Anthony J Hildreth, Peter A Sandercock, Janice E O'Connell, Donna E Johnston, Niall E F Cartlidge, John M Bamford, Oliver F James, K George M M Alberti, for the GIST Trialists Collaboration**

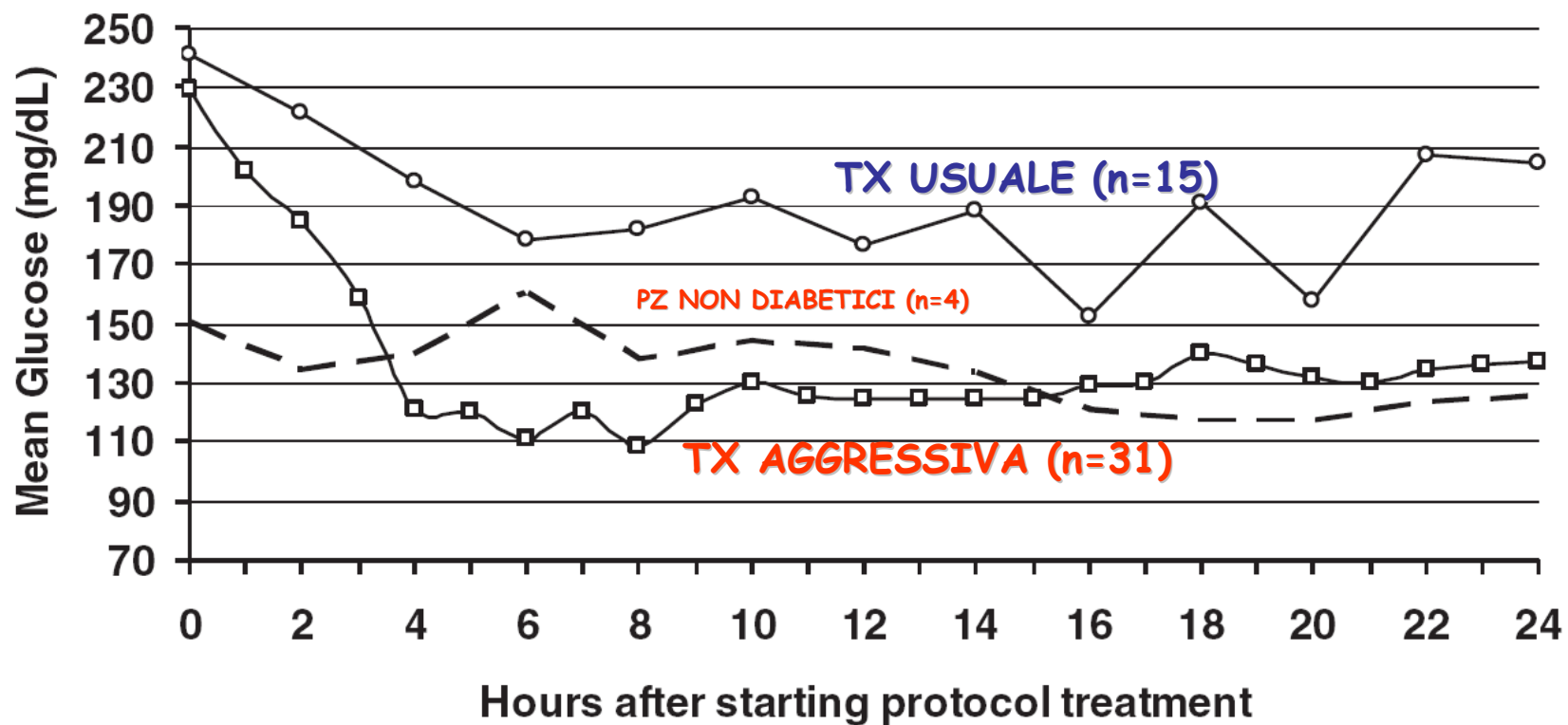
- ❑ Mortalità a 90 gg: 30 % GKI vs 27,3% dei controlli
- ❑ Il delta glicemico con GKI è 0,57 mmol/l (10,26 mg/dl)
- ❑ Analisi posthoc: ↑ della mortalità a 24h nei pz in cui GIK determinava un calo glicemico > 2 mmol/ L (30%) vs calo glicemico < 2 mmol/L (24%).

QUAL È LA FINESTRA TEMPORALE ENTRO CUI PORTARE A TARGET IL CONTROLLO GLICEMICO?

Treatment of Hyperglycemia In Ischemic Stroke (THIS)

A Randomized Pilot Trial

Askiel Bruno, MD; Thomas A. Kent, MD; Bruce M. Coull, MD; Ravi R. Shankar, MD;
Chandan Saha, PhD; Kyra J. Becker, MD; Brett M. Kissela, MD; Linda S. Williams, MD



Il protocollo intensivo è più efficace nel controllo glicemico del pz con ictus ma va verificata la sua efficacia sull'outcome clinico.

Insulin for glycaemic control in acute ischaemic stroke.

With the current evidence, we found that the administration of intravenous insulin with the objective of maintaining serum glucose within a specific range in the first hours of acute ischaemic stroke does not provide benefit in terms of functional outcome, death, or improvement in final neurological deficit and significantly increased the number of hypoglycaemic episodes.

Criteri Inclusione

- Pazienti di ambo i sessi di età compresa fra i 18-80 aa
- Ictus ischemico responsabile di un deficit misurabile di linguaggio, motorio, cognitivo, di sguardo, del visus e/o di neglect. L'ictus ischemico è definito come un evento caratterizzato da un deficit neurologico focale ad esordio improvviso, presumibilmente causato da ischemia cerebrale dopo esclusione CT di una emorragia cerebrale
- Inizio dei sintomi entro 4.5 ore (alla somministrazione di t-PA)
- Sintomi presenti per almeno 30 minuti e non significativamente migliorati prima del trattamento (nota1). I sintomi vanno distinti da quelli di un episodio di ischemia generalizzata (cioè una sincope), di una crisi epilettica o di una crisi di emicrania.
- I pazienti (o un familiare) debbono aver espresso la loro volontà ad essere trattati e aver dato il consenso all'utilizzo dei loro dati e alle procedure di follow-up

Criteri di Esclusione

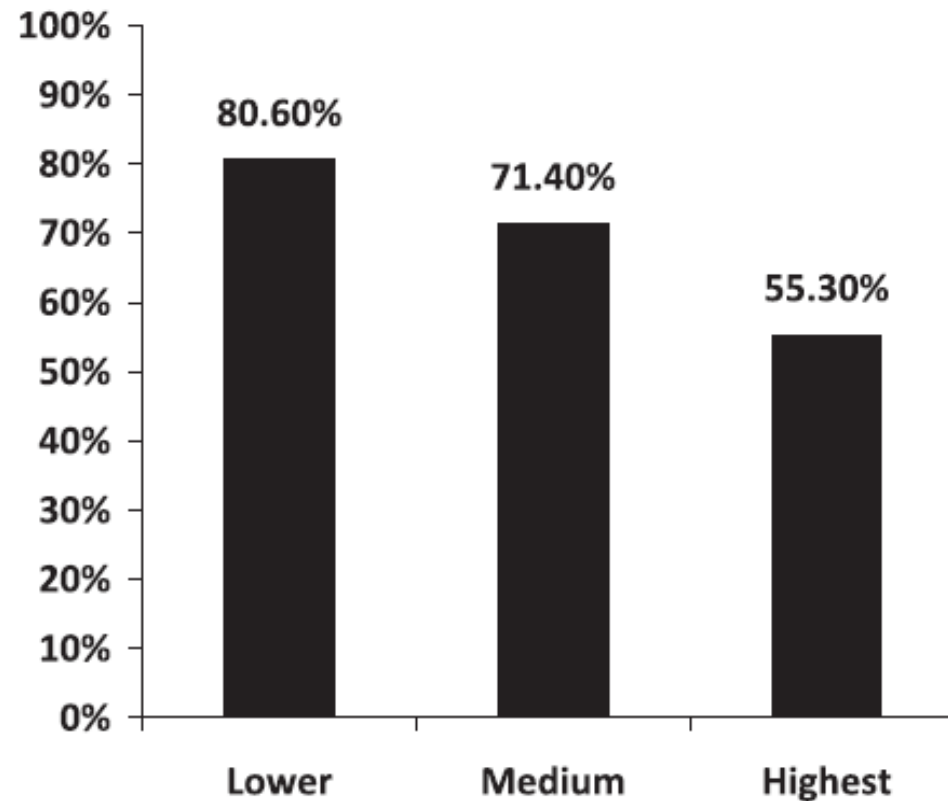
Controindicazioni assolute

- Emorragia intracranica alla TAC cerebrale
- Sospetto clinico di ESA, anche se TAC normale
- Somministrazione di eparina endovena nelle precedenti 48 ore e aPTT eccedente limite normale superiore del laboratorio
- Conta piastrinica < 100.000/mm³
- Diatesi emorragica nota
- Sanguinamento grave in atto o recente
- Storia o sospetto di emorragia intracranica in atto

Controindicazioni relative:

- Ictus grave clinicamente (es. NIHSS >25) e/o sulla base di adeguate tecniche di neuroimmagini
- Insorgenza dell'ictus > 4.5 ore o ora di insorgenza non nota o al risveglio
- Deficit lieve o rapido miglioramento dei sintomi (30 minuti) (NOTA 1)
- Crisi convulsiva all'esordio dell'ictus (VEDI SOTTO)

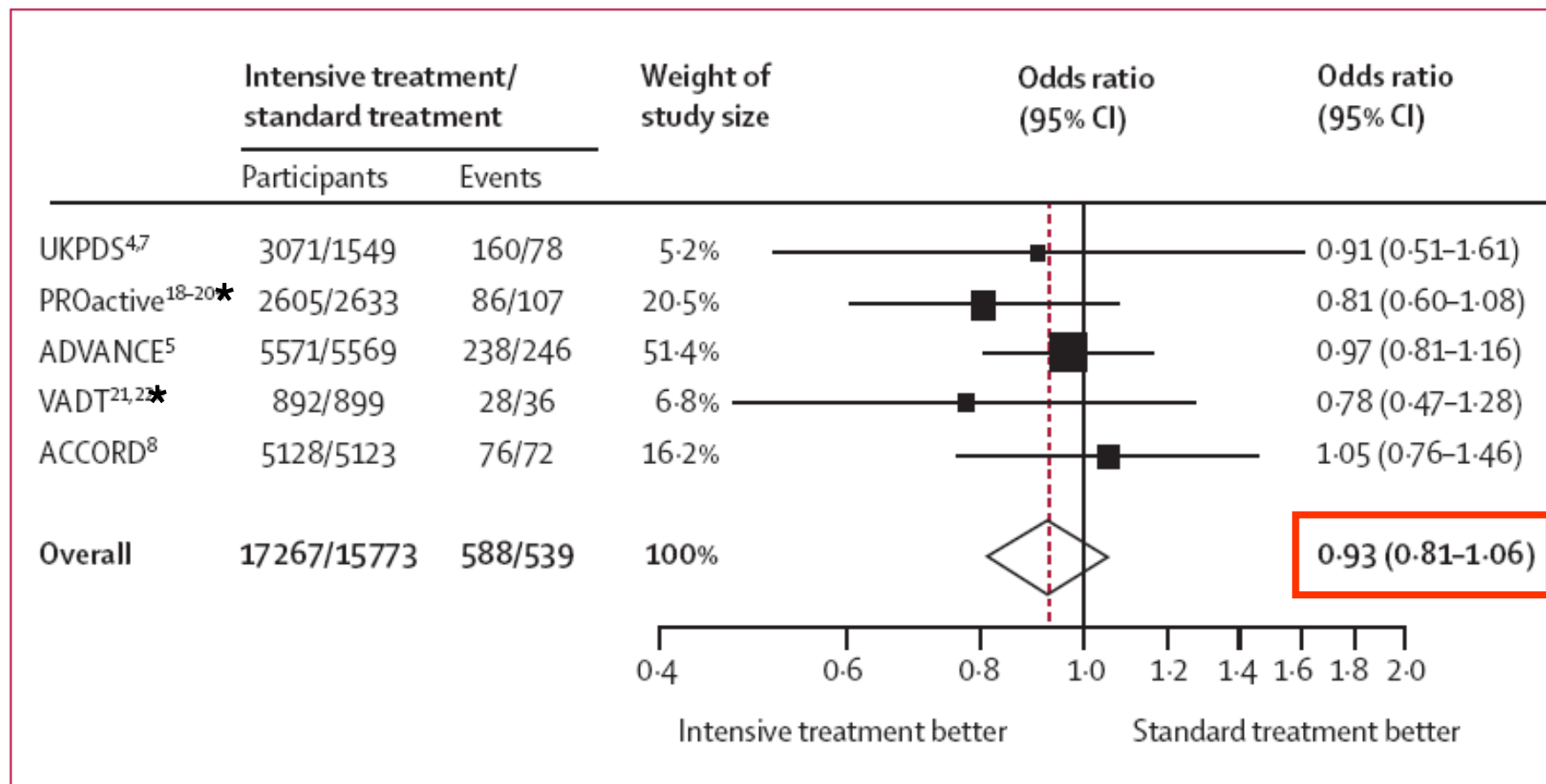
Insulin Resistance Is Associated With a Poor Response to Intravenous Thrombolysis in Acute Ischemic Stroke



Relation between IR and long-term clinical outcome. Bars show the probability of achieving good clinical outcome across HOMA-IR tertiles.

Diabetes Care 34:2413–2417, 2011

Probability of events of stroke with intensive glucose-lowering versus standard treatment



*Included only non-fatal strokes.

Ray KK et al. *Lancet* 2009; 373: 1765-72

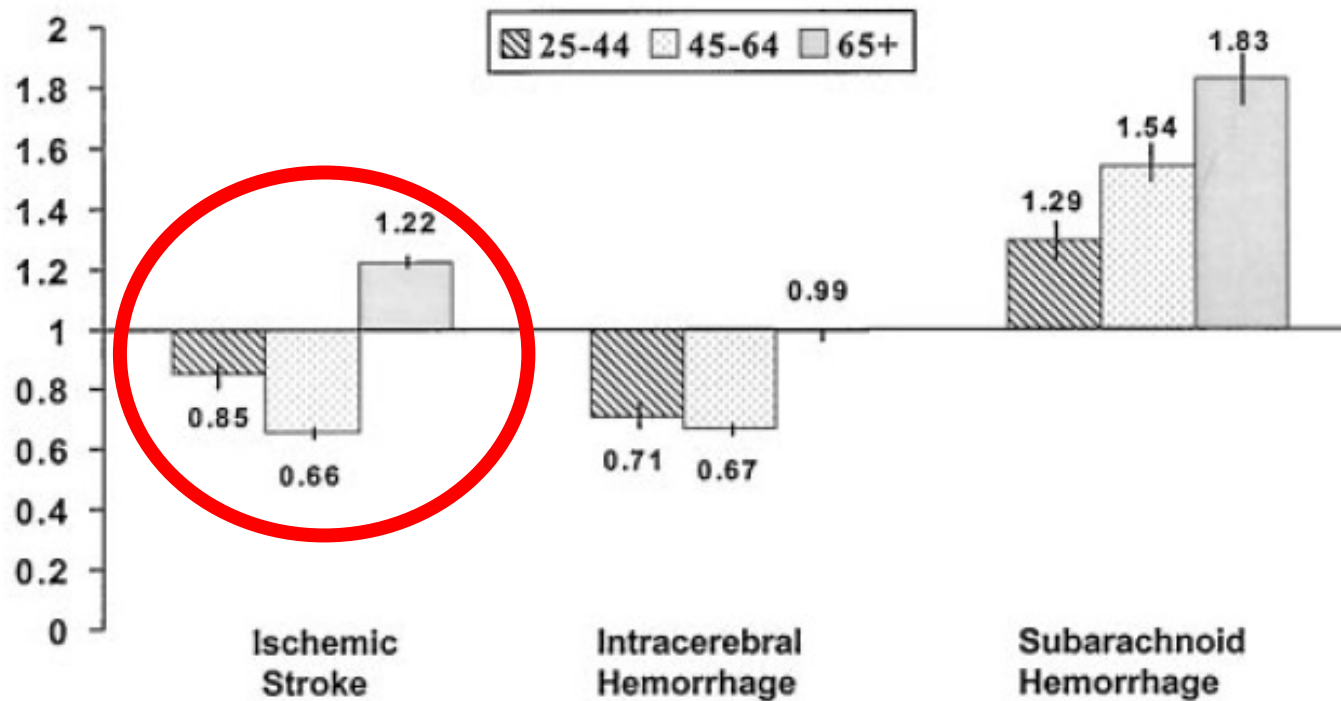
Take home messages

- Anche se vi è consenso sulla necessità di correggere la iperglicemia durante lo stroke non è dimostrato che il raggiungimento di valori glicemici più prossimi al normale mediante infusione ev di insulina siano importanti nella terapia dello stroke e nelle sue conseguenze a distanza, poichè mancano al momento risultati provenienti da CRT,
- Lo stretto controllo metabolico nel diabete tipo 2 non riduce significativamente l'incidenza di stroke ischemico,
- La trombolisi nello stroke ischemico sembra essere meno efficace in particolare nei pazienti diabetici con elevata resistenza insulinica.

Grazie per l'attenzione



Female-to-male mortality rate ratios and 95% CIs for 3 stroke subtypes among adults aged 25 years, by age group (United States, 1995 to 1998). Age groups are as follows: 25 to 44 years, 45 to 64 years, and 65 years.



Ayala C et al, Stroke, 2002