La prevenzione del sovrappeso e dell'obesità come strumento per la prevenzione del diabete e delle malattie croniche

Genova, 28 novembre 2011

Eccesso ponderale e malattia diabetica

Alberto De Micheli
Agenzia **R**egionale **S**anitaria Liguria
Genova

Dichiaro sotto la mia responsabilità che negli ultimi due anni ho avuto i seguenti rapporti diretti di finanziamento con soggetti portatori di interessi commerciali in campo sanitario:

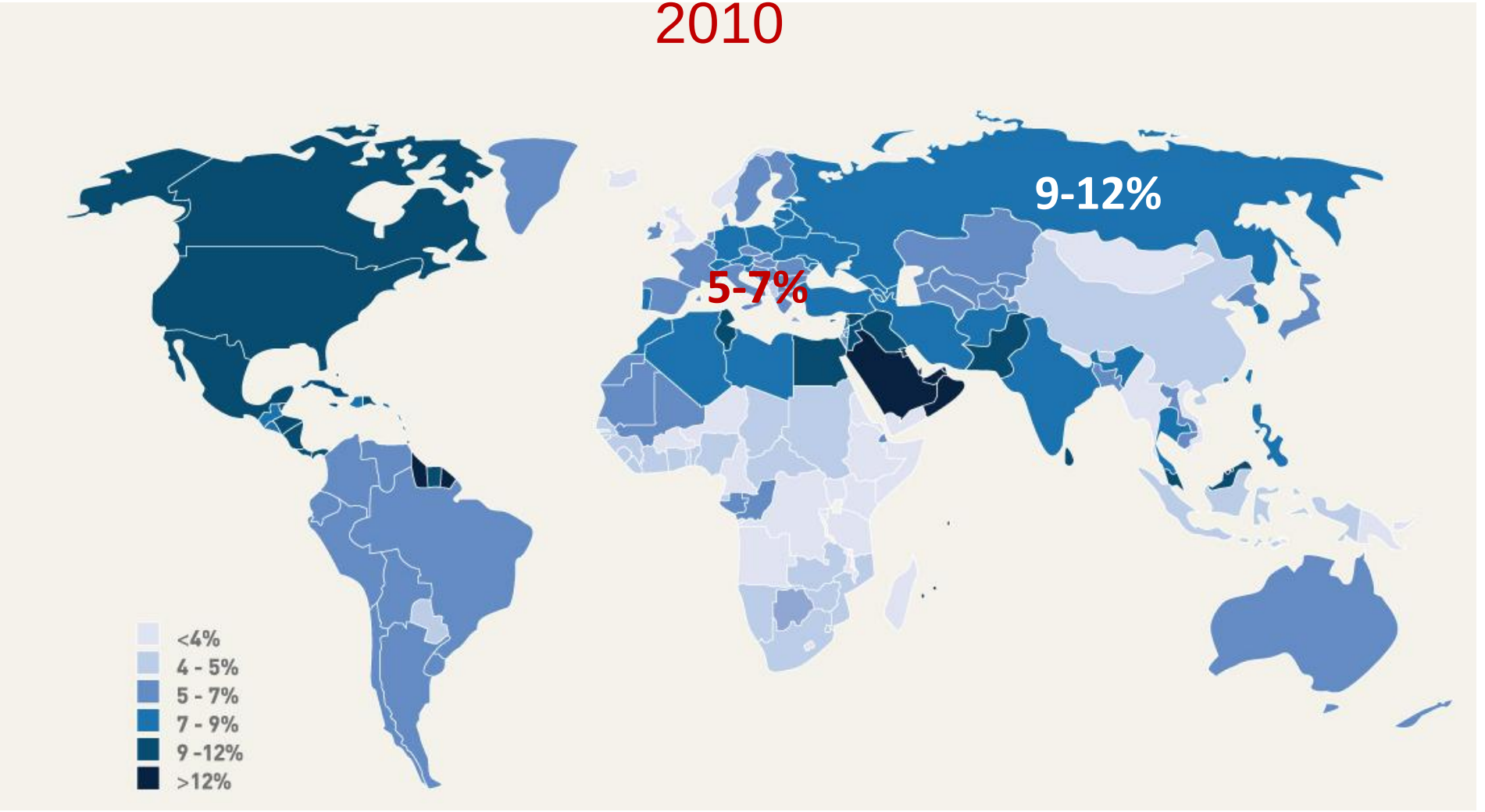
- Bayer
- GSK
- Roche
- Stroder

Il contesto:
L'epidemia diabete

Prevalenza ed incidenza del diabete tipo 2

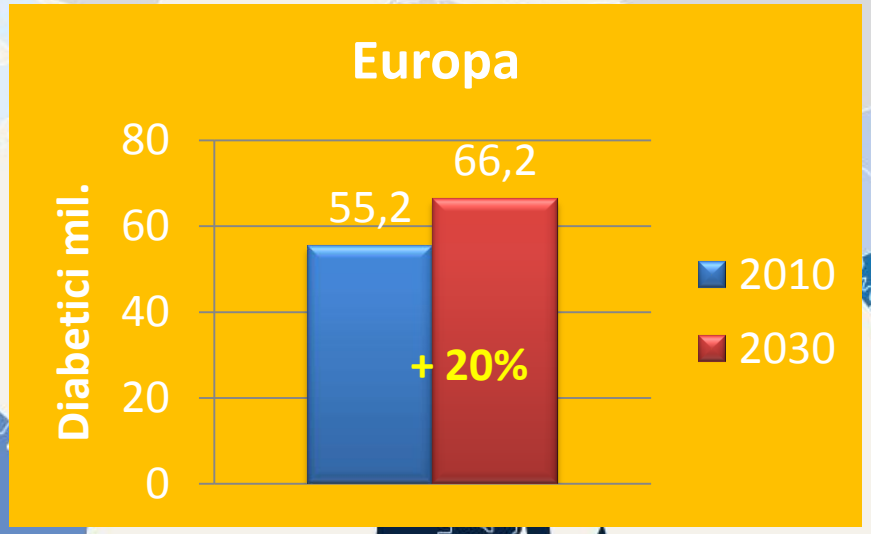
Prevalence (%) estimates of diabetes (20-79 years)

2010



IDF Diabetes Atlas 4th edition© 2009 International Diabetes Federation

IDF Regions and global projections for the number of people with diabetes (20-79 years) 2010-2030

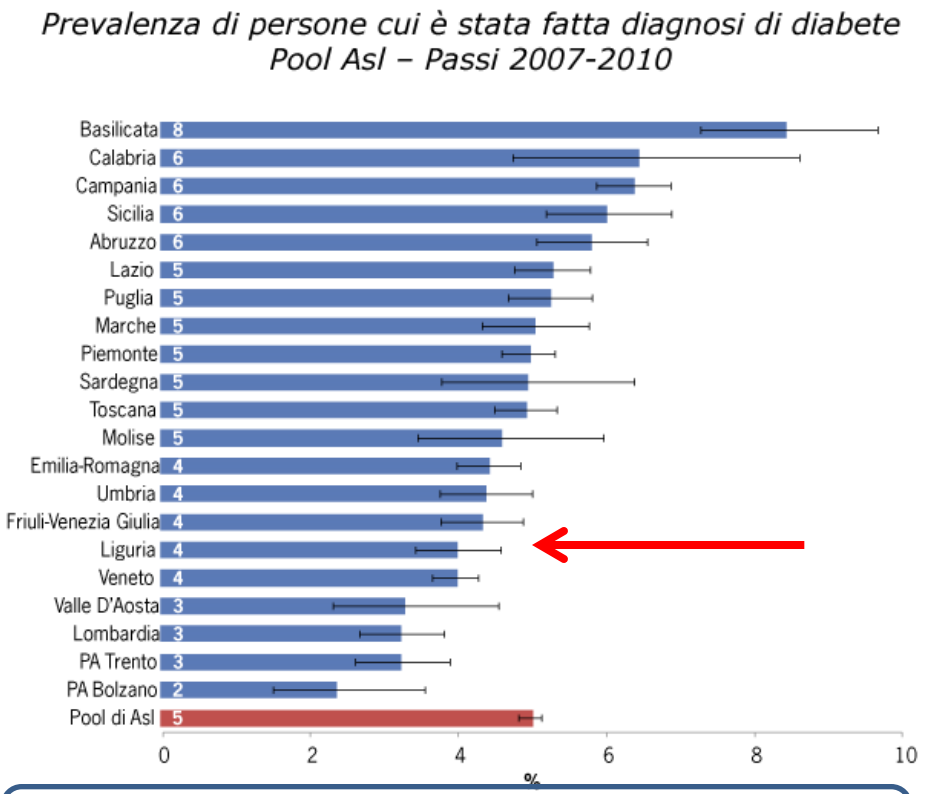


REGION	2010 Millions	2030 Millions	INCREASE %
Africa	12.1	23.9	98%
Middle East and North Africa	26.6	51.7	94%
South-East Asia	58.7	101.0	72%
South and Central America	18.0	29.6	65%
Western Pacific	76.7	112.8	47%
North America and Caribbean	37.4	53.2	42%
Europe	55.2	66.2	20%
World	**284.6**	**438.4**	**54%**

World		
2010 millions	2030 millions	% increase
284.6	438.4	54%

IDF Diabetes Atlas 4th edition© 2009 International Diabetes Federation

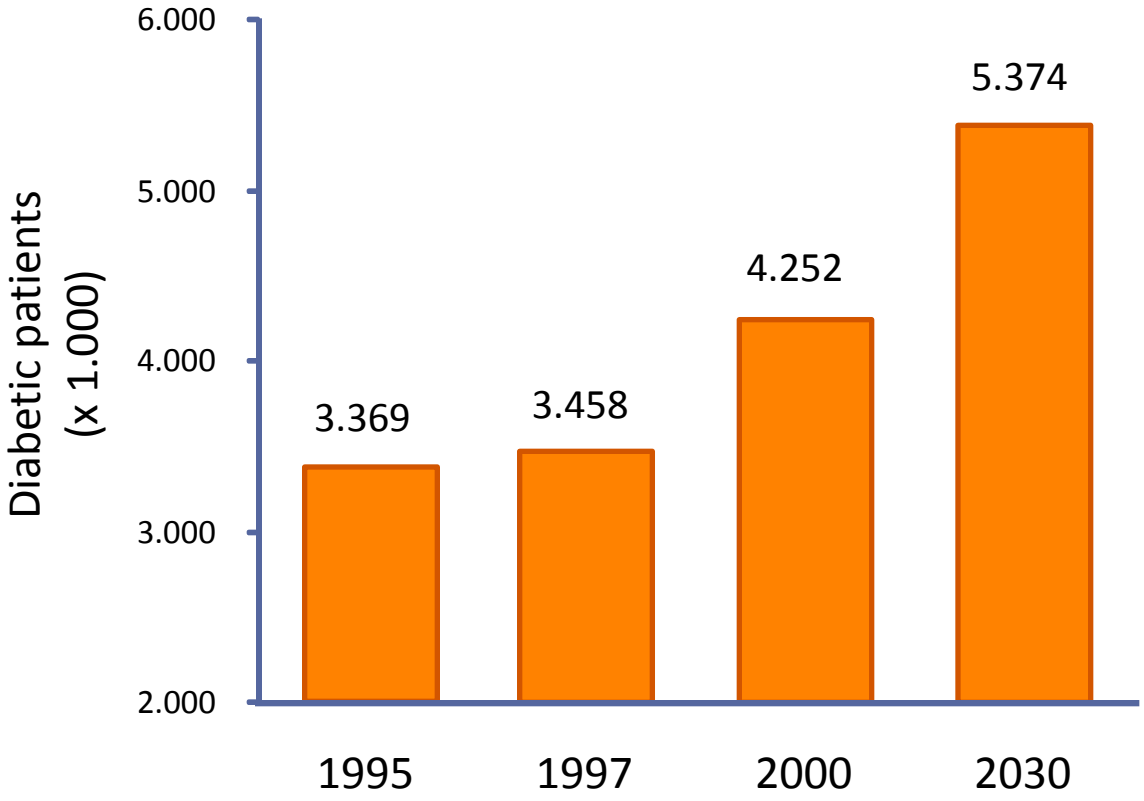
Prevalenza del diabete in Italia: sistema di sorveglianza PASSI



Liguria 89823/ 1616788 = 5.5%

http://www.epicentro.iss.it/passi/R2010Diabete.asp

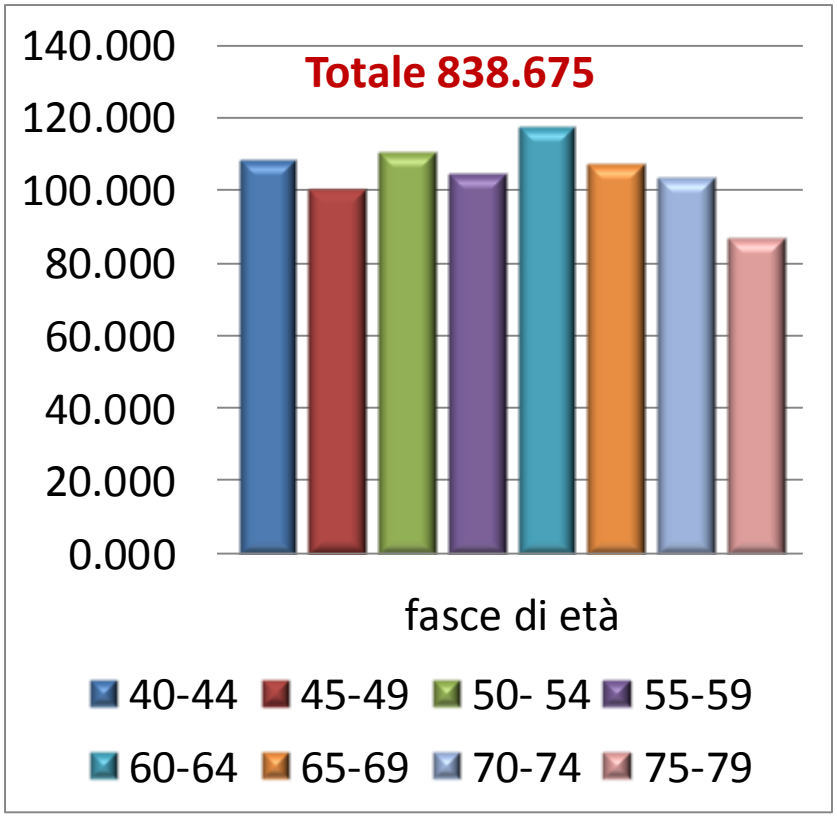
Diabetes epidemic in Italy



OMS (www.who.int/diabetes/facts/world_figures/en/index4.html)

Stima dei nuovi casi di diabete tipo 2 per anno nella regione Liguria

Popolazione della Liguria Età 40- 79 anni



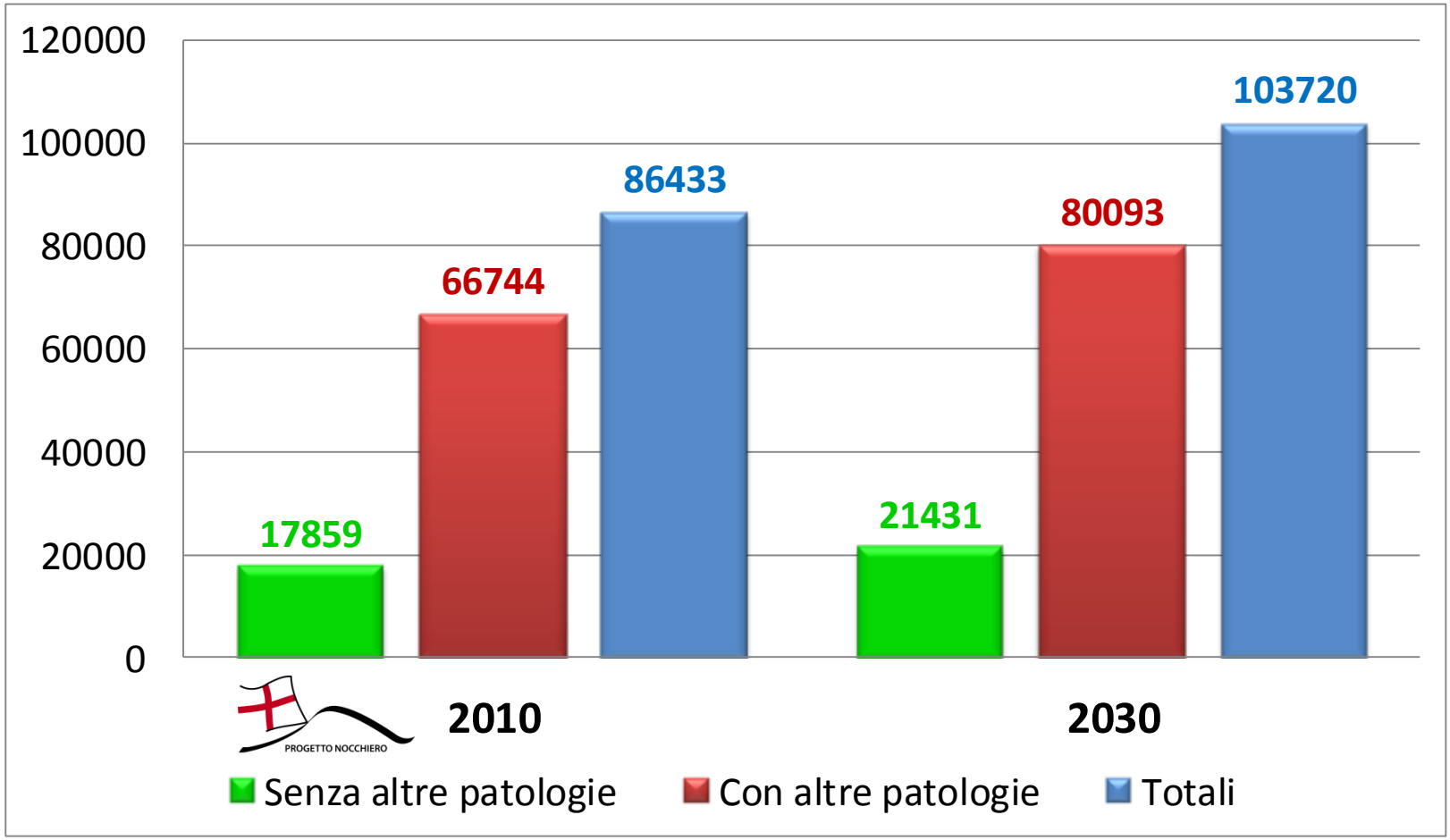
http://www.istat.it/dati/catalogo/20071112_01/

Stima dei nuovi casi di diabete 2 per anno

- Lo studio di Brunico, ha mostrato un'incidenza del diabete tipo 2 in soggetti di 40-79 anni pari a 7,6 casi per 1000 persone-anno
- Si stimano in Liguria 6374 nuovi casi per anno

Bonora E Diabetes 2004;53:1782-1789.

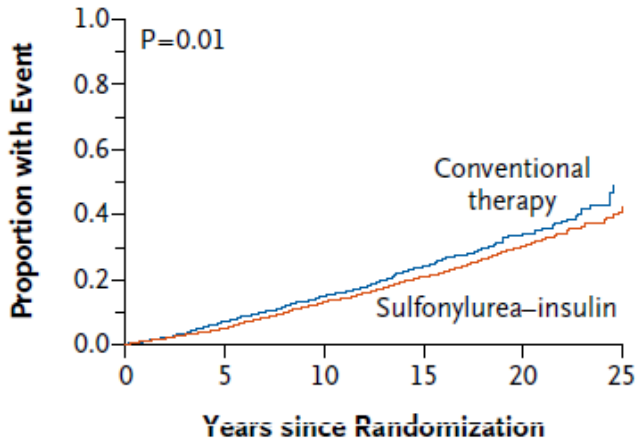
Epidemia del diabete in Liguria: proiezione sul numero dei casi



Epidemiologia delle complicanze del diabete

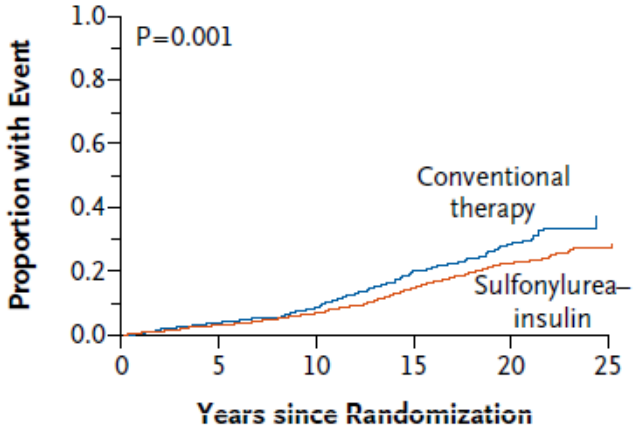
Incidenza cumulativa di complicanze macro e microangiopatiche fino a 25 anni di malattia: il follow up dell'UKPDS

Infarto del miocardio



No. at Risk						
Conventional therapy	1138	1013	857	578	221	20
Sulfonylurea–insulin	2729	2488	2097	1459	577	66

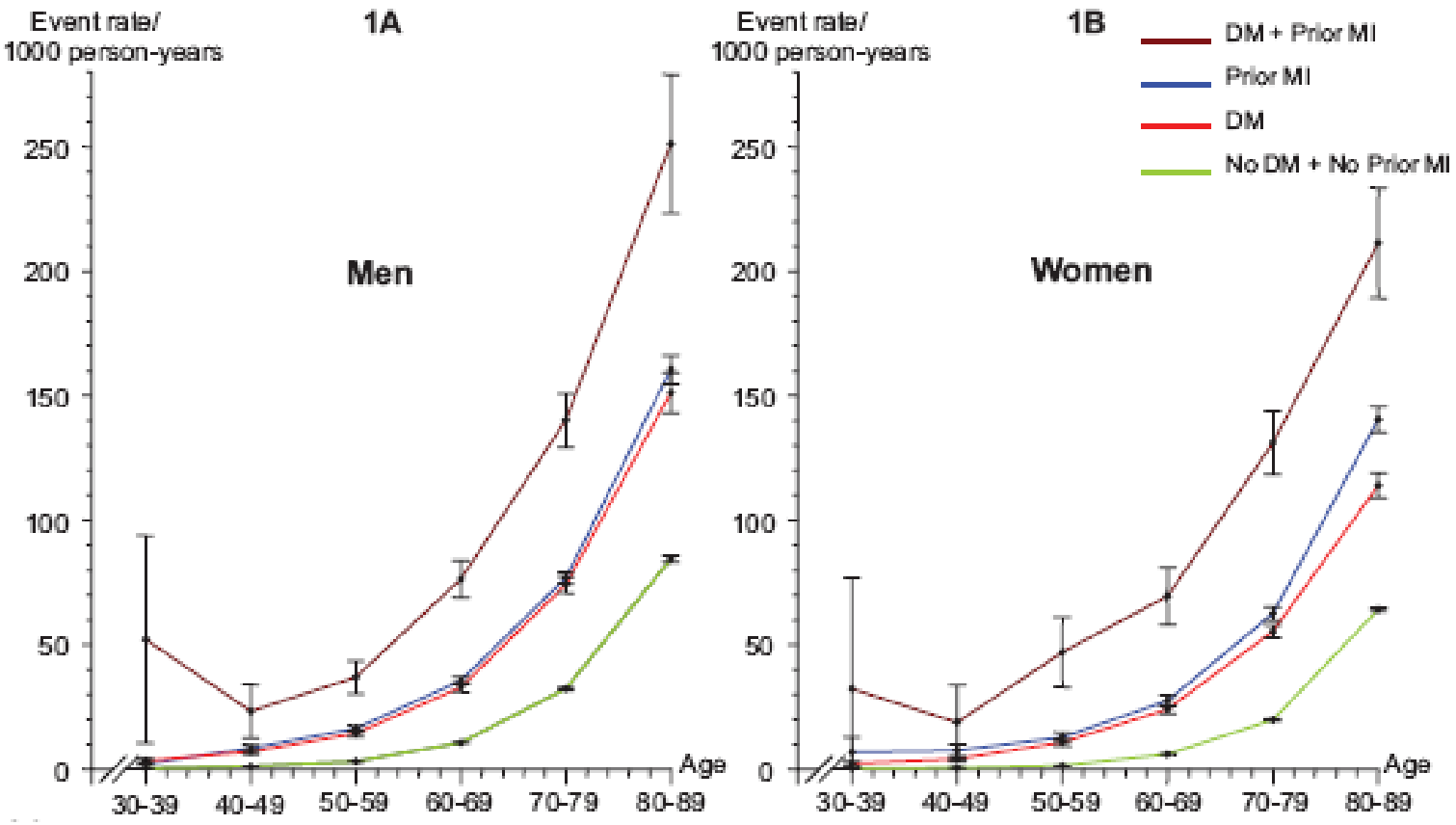
Complicanze microangiopatiche



No. at Risk						
Conventional therapy	1138	1018	844	508	172	13
Sulfonylurea–insulin	2729	2465	2076	1368	488	53

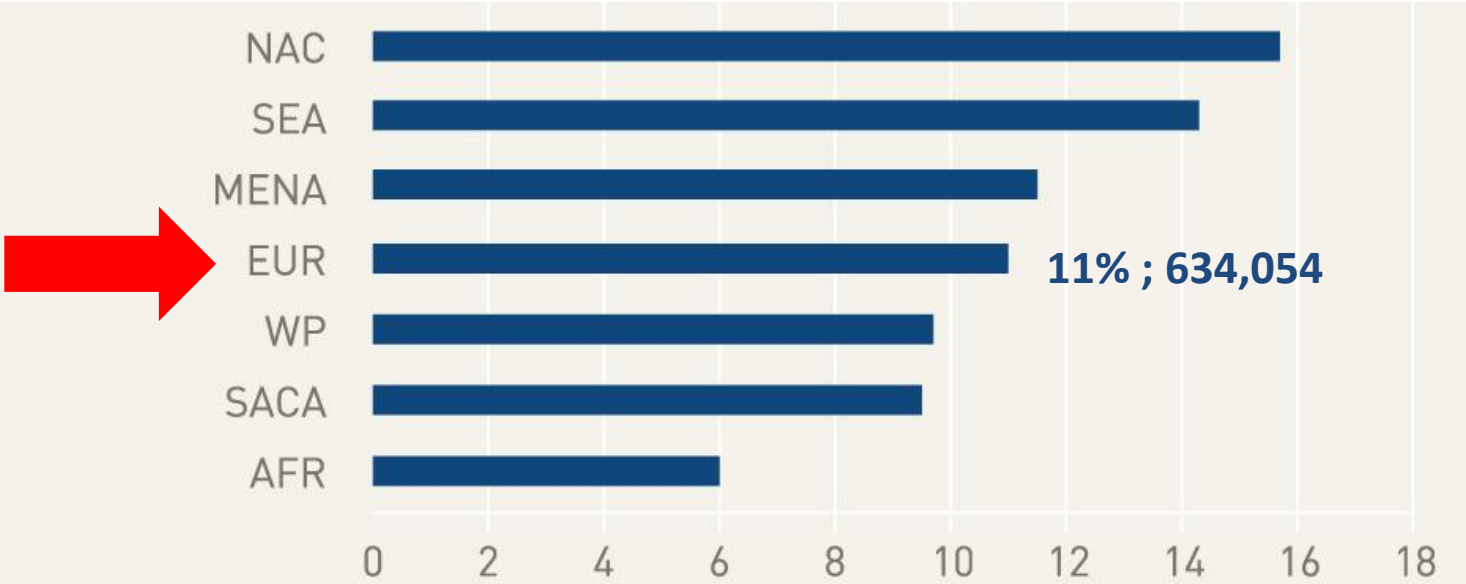
Holman RR N Engl J Med 2008; 359: 1577- 89

Mortalità CV in maschi e femmine stratificati per età in relazione a diabete mellito e pregresso infarto del miocardio



Schramm TK Circulation. 2008; 117: 1945-54

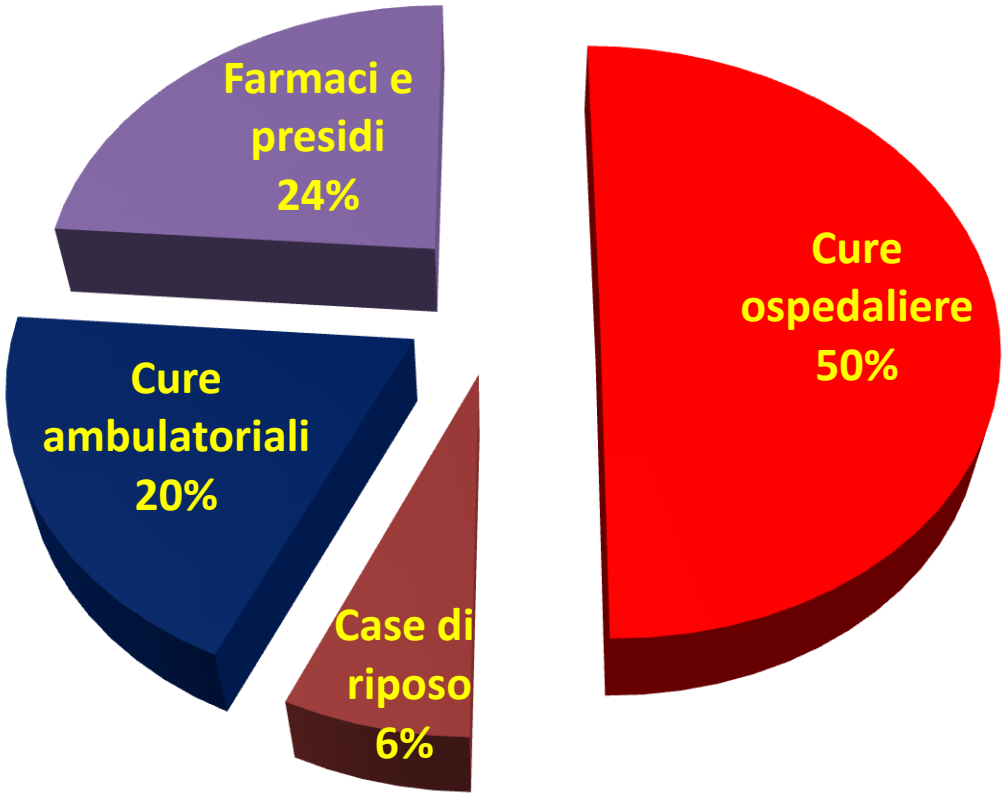
Deaths attributable to diabetes as percentage of all deaths (20-79 years) by region, 2010



AFR: Africa
WP: Western Pacific
SACA: South and Central America
EUR: Europe
SEA: South- East Asia
MENA: Middle East, North Africa
NAC : North America and Caribbean

I costi del diabete

Spesa sanitaria per il diabete

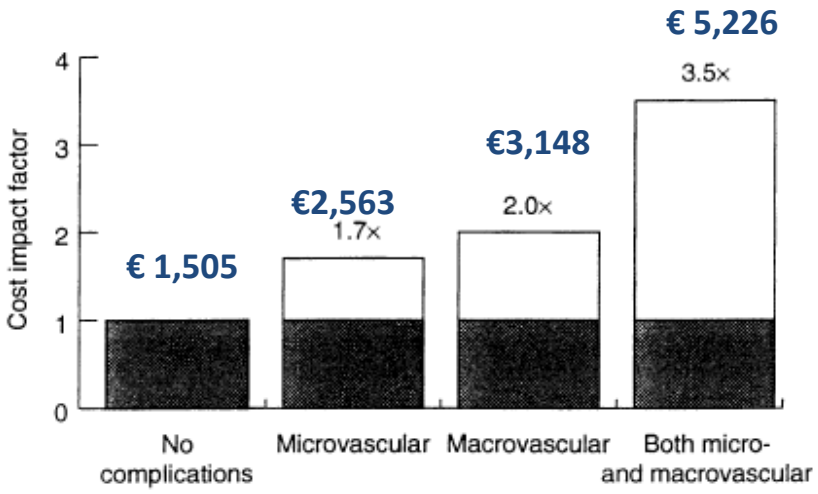


ADA Statement Diabetes Care 31: 596– 615, 2008

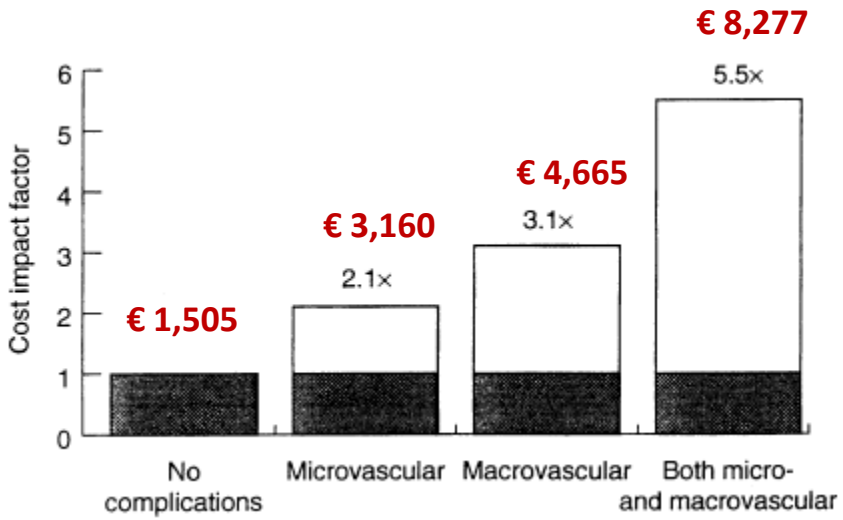
Costs of diabetes-related complications among people with diabetes in Europe

'The Cost of Diabetes in Europe –Type II (CODE-2) study

Effect of complications on the average cost per patient*



Effect of complications on hospitalisation costs*

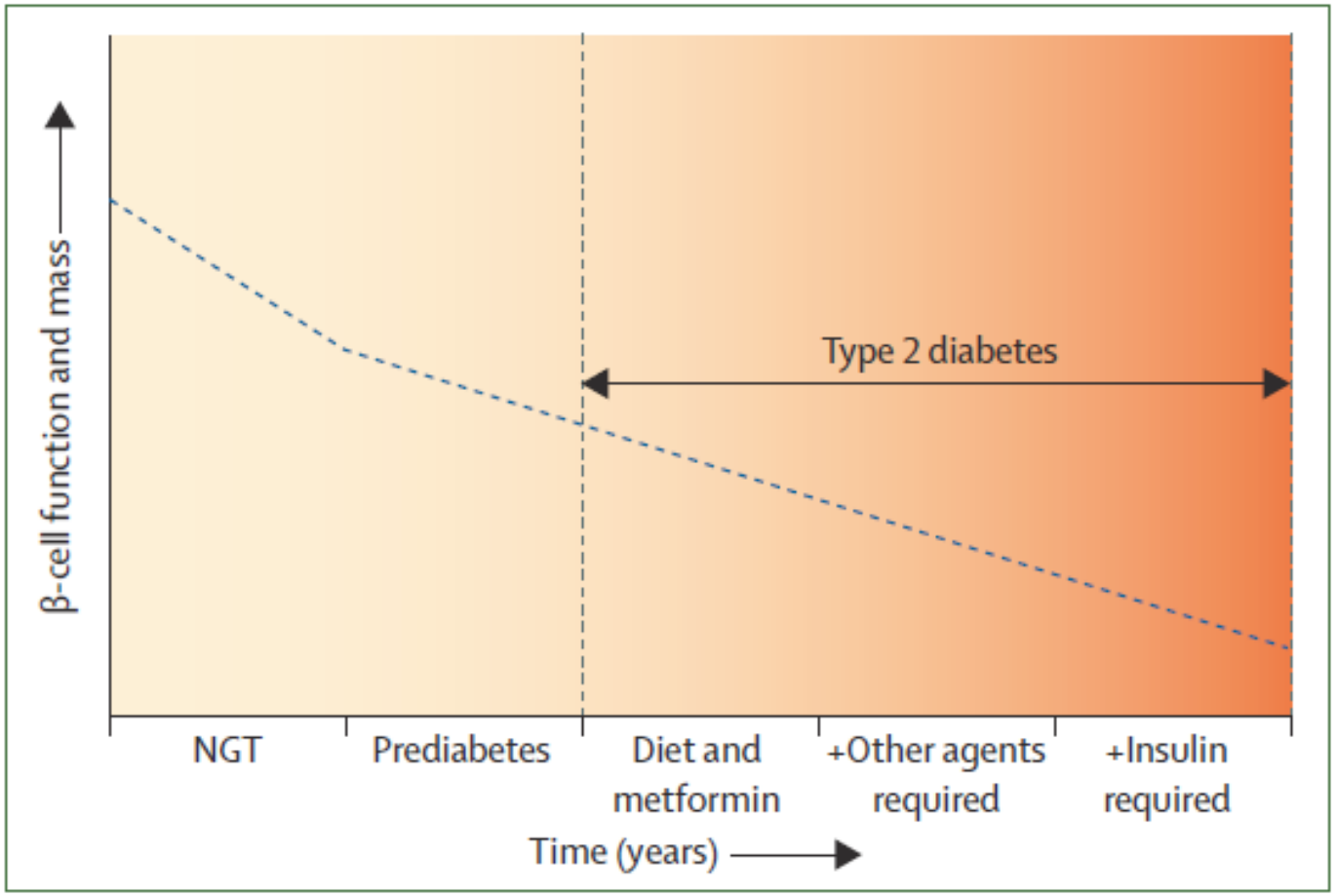


*direct medical costs per year

Williams R Diabetologia 2002; 45: S13– S17

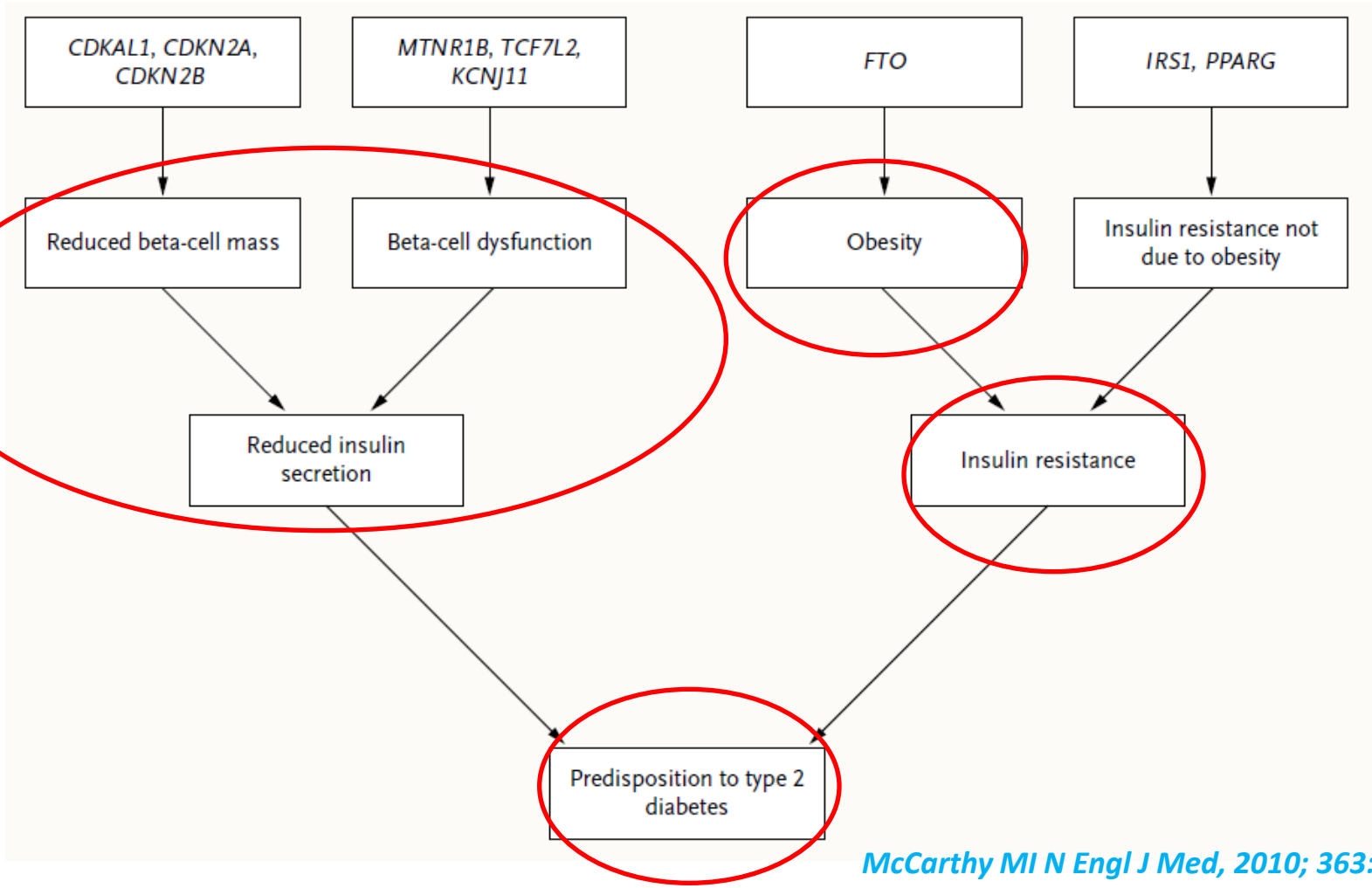
L’obesità come fattore di rischio di diabete

Storia naturale del diabete tipo 2



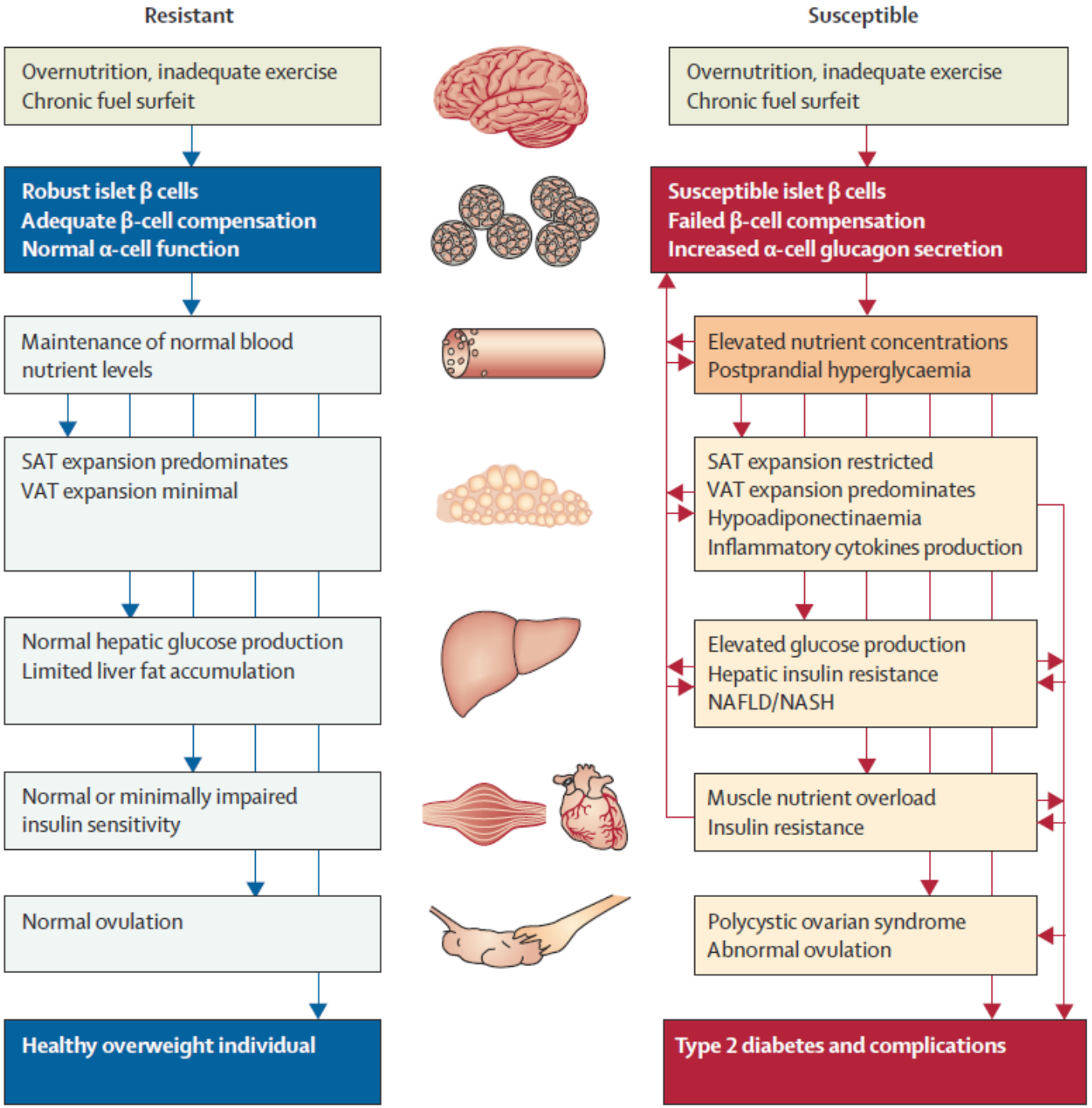
Nolan CJ Lancet. 2011; 378: 169- 81

Aspetti generali della relazione obesità- diabete



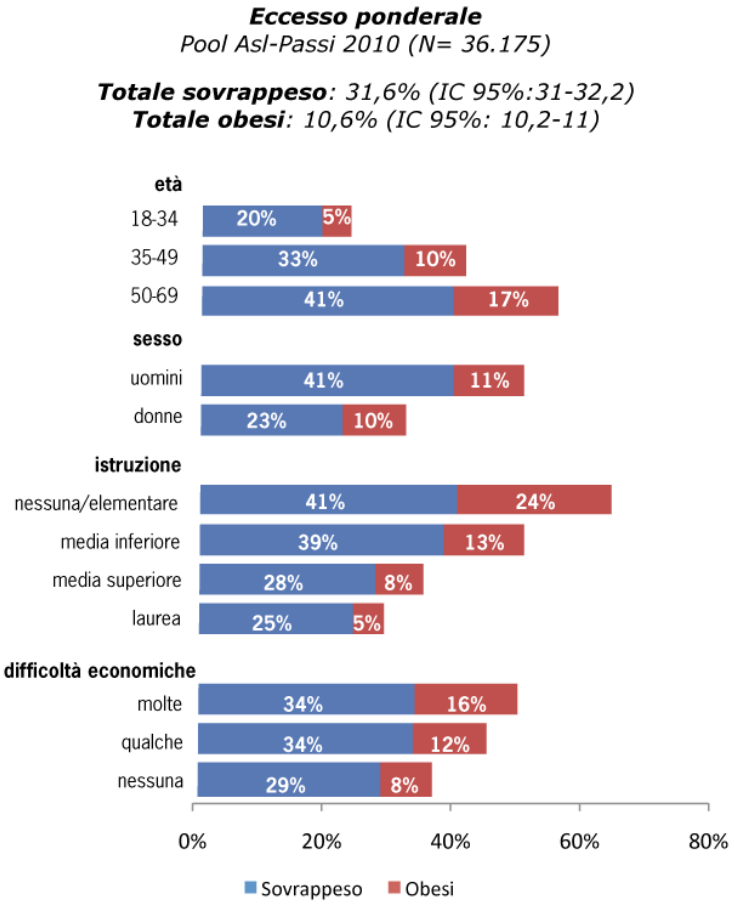
McCarthy MI N Engl J Med, 2010; 363:2339- 50

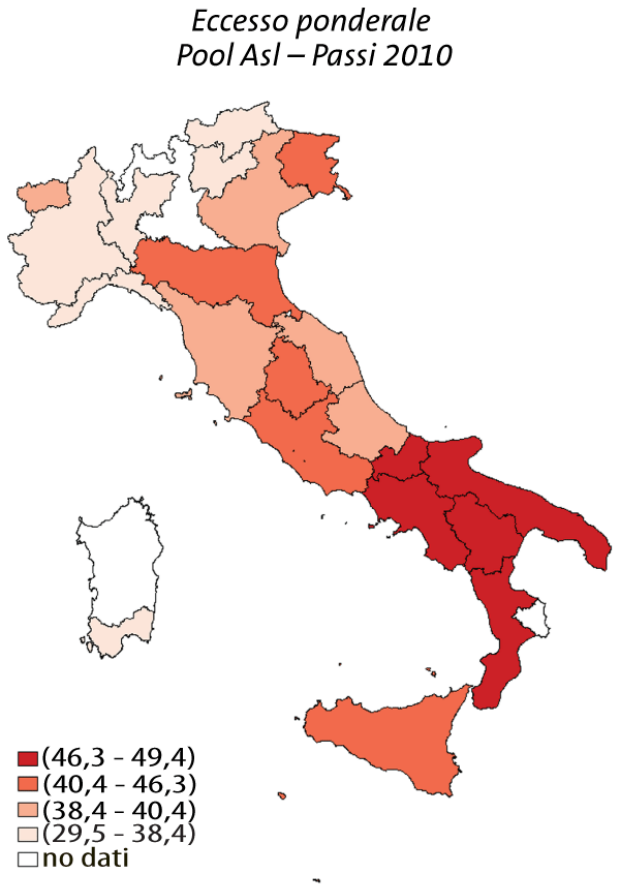
Vie metaboliche verso il diabete e le sue complicanze



Nolan CJ Lancet. 2011; 378: 169- 81

Prevalenza dell'eccesso ponderale in Italia sistema di sorveglianza PASSI





http://www.epicentro.iss.it/passi/R2010SovrappesoObesita.asp

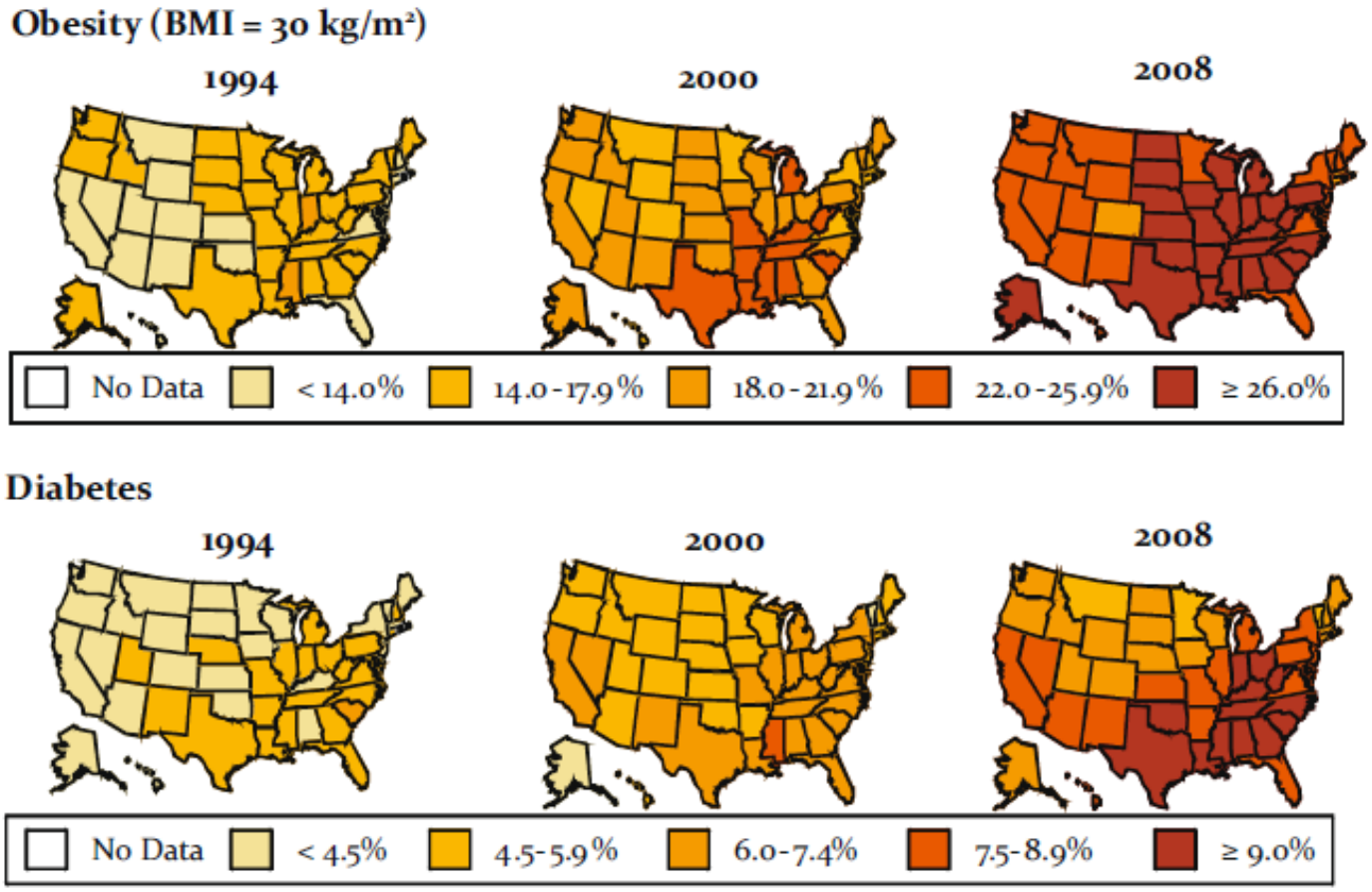
Sovrappeso ed obesità in Italia dal 2001 al 2009

Prospetto 14.1 - Persone di 18 anni e più per indice di massa corporea - Anni 2001-2009 *(per 100 persone di 18 anni e più)*

ANNI	Indice di massa corporea				Totale
	Sottopeso	Normopeso	Sovrappeso	Obesi	
2001	3,3	54,2	33,9	8,5	100,0
2002	3,2	54,7	33,6	8,5	100,0
2003	3,2	53,9	33,8	9,0	100,0
2005	2,8	52,6	34,7	9,9	100,0
2006	2,8	52,0	35,0	10,2	100,0
2007	2,8	51,7	35,6	9,9	100,0
2008	3,0	51,5	35,5	9,9	100,0
2009	2,8	50,9	36,1	10,3	100,0

ISTAT - La vita quotidiana nel 2009 Indagine multiscopo annuale sulle famiglie "Aspetti della vita quotidiana" Anno 2009 http://www3.istat.it/dati/catalogo/20110121_00/

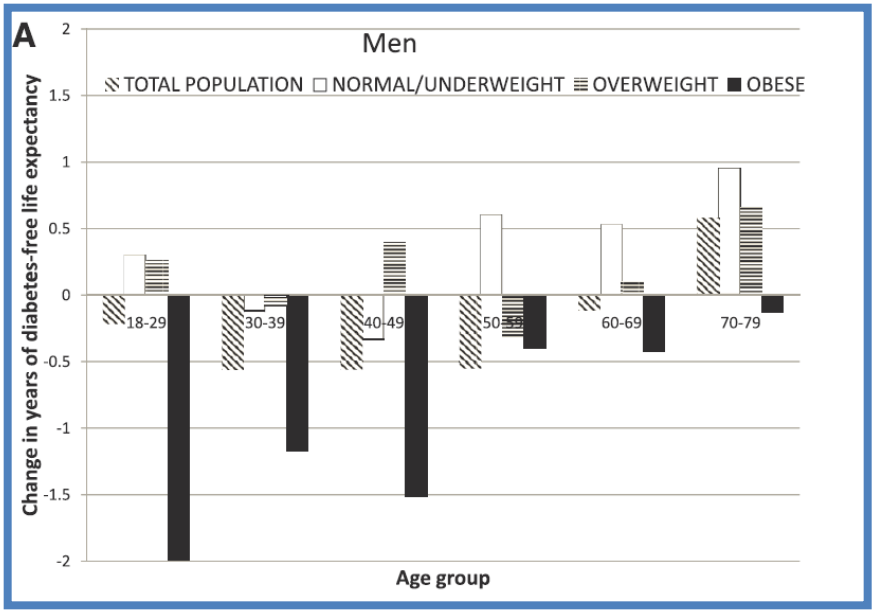
Parallelismo fra incremento dell'obesità ed incremento del diabete



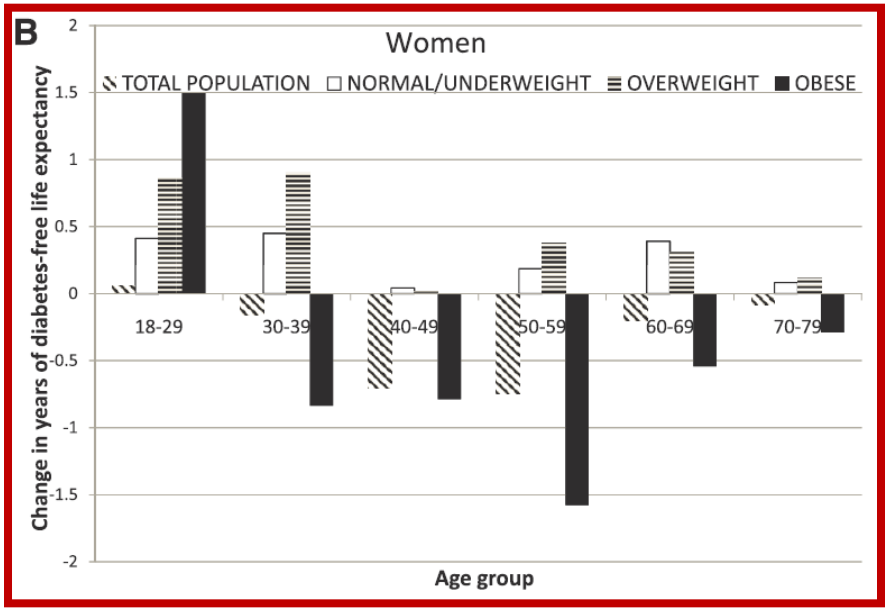
Barnes AS. Tex Heart Inst J. 2011; 38: 142- 4

Riduzione dell'aspettativa di vita priva di diabete: periodo 1980-89 vs. 2000-2004

Maschi

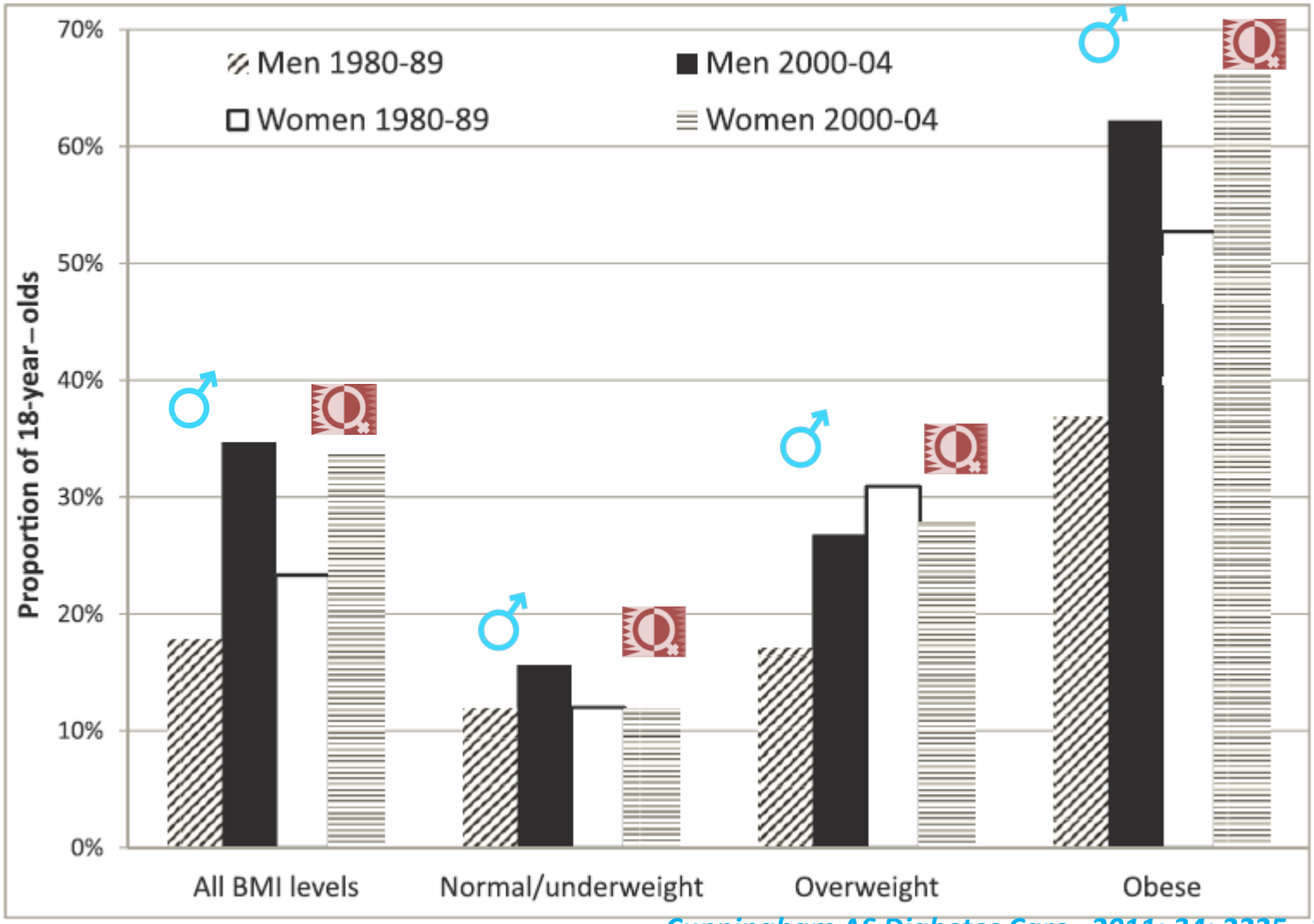


Femmine



Cunningham AS Diabetes Care , 2011; 34: 2225– 2230

Proporzione si soggetti di 18 anni destinati a sviluppare diabete: periodo 1980-89 vs. 2000-2004



Cunningham AS Diabetes Care , 2011; 34: 2225– 2230

L’indice di massa corporea

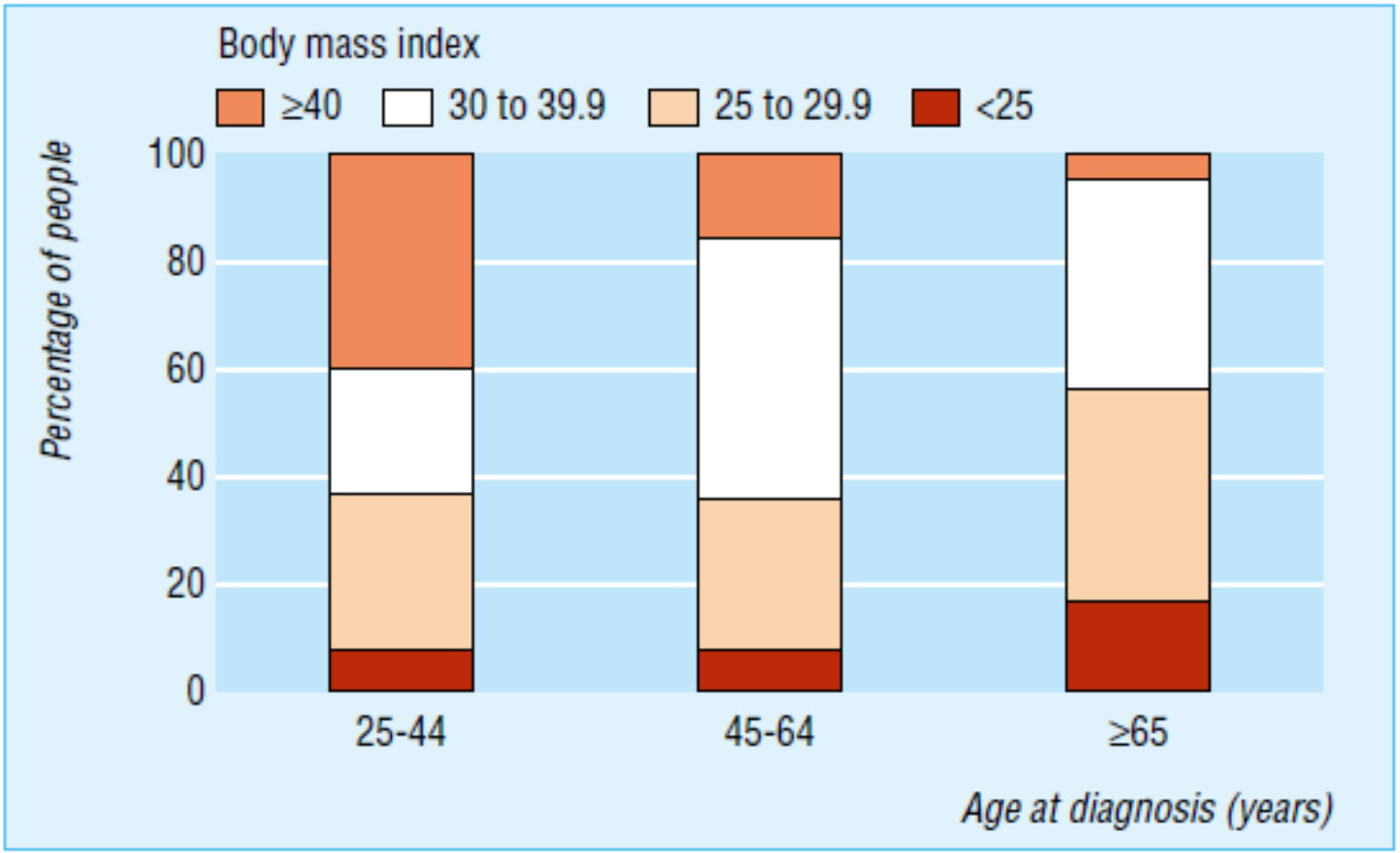
Ruolo prevalente dell'obesità quale fattore di rischio per l'incidenza di diabete tipo 2

Rischio attribuibile nella popolazione per i FR modificabili del diabete tipo 2

Variable[a]	MFH		Health 2000		Pooled		P^b
	PAF	95% CI	PAF	95% CI	PAF	95% CI	
Model 1[c]							
A. Body mass index	0.71	0.55, 0.82*	0.84	0.59, 0.94*	0.75	0.59, 0.85*	0.27
B. Exercise	0.11	−0.03, 0.23	0.10	−0.04, 0.23	0.11	0.01, 0.19*	0.95
C. Alcohol consumption[d]	0.03	−0.02, 0.08	0.10	−0.01, 0.20	0.05	−0.01, 0.11	0.25
D. Smoking[e]	0.05	−0.04, 0.14	0.08	−0.06, 0.20	0.06	−0.02, 0.13	0.73
E. Serum vitamin D	0.21	0.03, 0.35*	0.14	−0.11, 0.34	0.18	0.04, 0.30*	0.64
Model 2[f]							
A. Body mass index	0.71	0.54, 0.81*	0.87	0.59, 0.96*	0.77	0.53, 0.88*	0.20
B. Exercise	0.03	−0.11, 0.16	0.07	−0.09, 0.20	0.05	−0.06, 0.14	0.76
C. Alcohol consumption[d]	0.02	−0.03, 0.07	0.08	−0.05, 0.19	0.03	−0.02, 0.07	0.42
D. Smoking[e]	0.10	0.01, 0.18*	0.10	−0.05, 0.23	0.10	0.02, 0.17*	0.98
E. Serum vitamin D	0.17	−0.02, 0.32	0.01	−0.28, 0.23	0.11	−0.06, 0.25	0.30
B, C, D	0.15	−0.01, 0.28	0.21	0.02, 0.37*	0.17	0.05, 0.28*	0.59
B, C, D, E	0.30	0.03, 0.45*	0.22	−0.06, 0.43	0.27	0.11, 0.40*	0.63
A, B, C, D, E	0.80	0.65, 0.88*	0.90	0.67, 0.97*	0.82	0.70, 0.90*	0.30

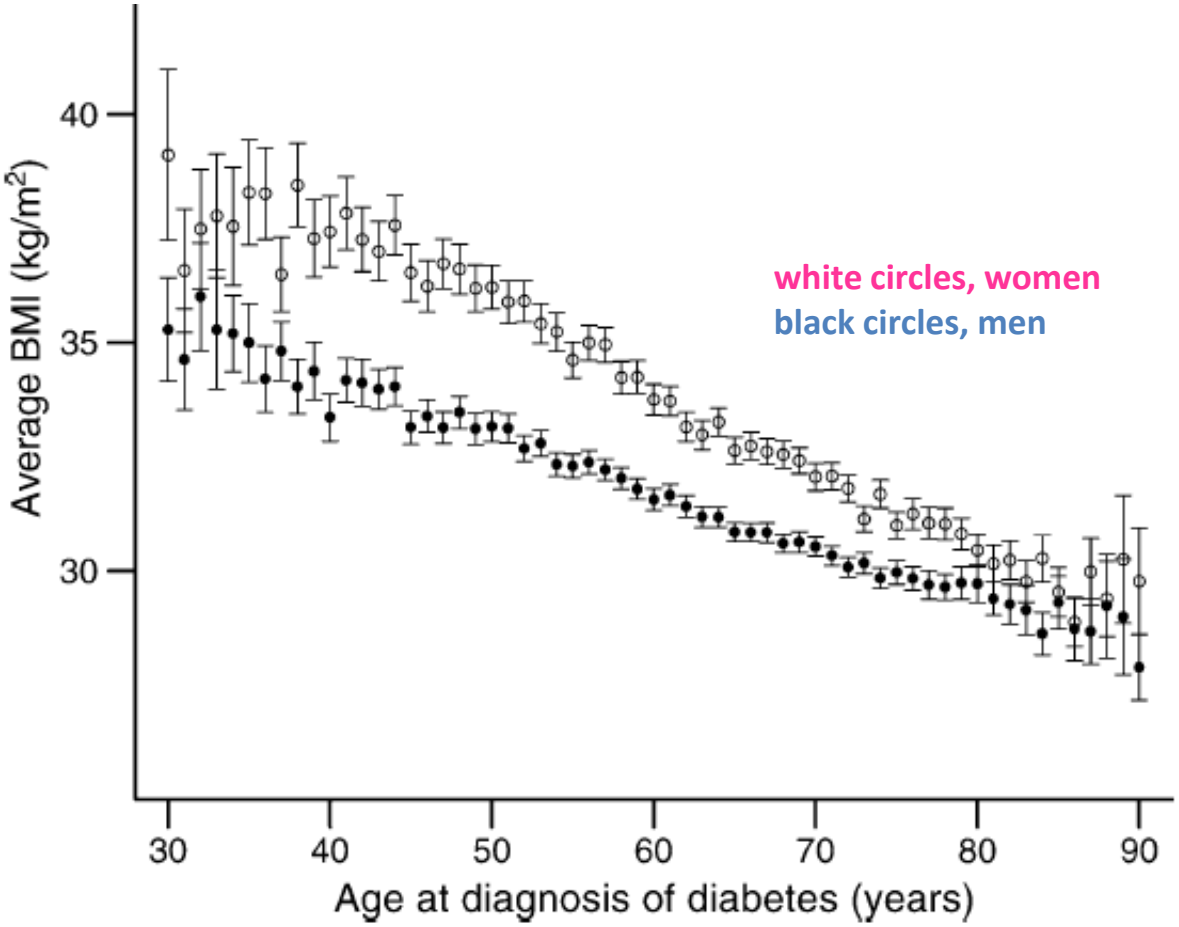
Laaksonen MA Eur J Epidemiol, 2010; 25: 115– 124

Distribuzione del BMI alla diagnosi di diabete per fasce di età



Wild SH, BMJ 2006; 333: 1009- 1011

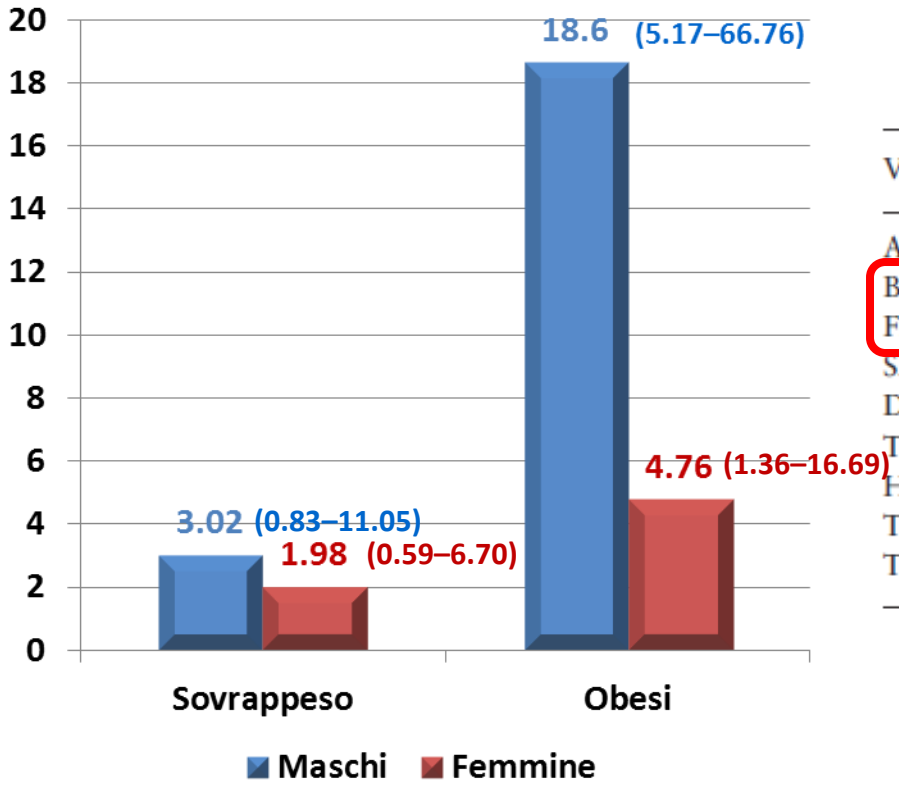
Relazione inversa fra BMI ed età di insorgenza del diabete



Logue J Diabetologia 2011, DOI 10.1007/s00125-011-2313-3, published on line: 30 september 2011

Lo studio di Brisighella: follow up 8 anni

HR per diabete in soggetti obesi ed in sovrappeso vs. normopeso



Ruolo relativo dei diversi fattori di rischio

Variable (1988)	Exp (B) (95% CI)	Significance
Age	1.0090 (0.9612–1.0504)	0.6314
BMI	1.1946 (1.1553–1.4908)	< 0.001
FPG	1.1117 (1.0459–1.1317)	< 0.001
SBP	1.0126 (0.9656–1.0353)	0.2922
DBP	0.9687 (0.9127–1.0235)	0.1691
TG	0.9998 (0.9947–1.0090)	0.9445
HDL-C	0.7159 (1.1553–1.4908)	0.7159
Total physical activity	0.8917 (0.8547–1.0004)	0.0634
Total energy intake	0.9148 (0.8843–1.0037)	0.0759

Cicero AFG Diabet. Med. 2005; 22: 1263–1266

Nurses' Health Study: BMI e incidenza di diabete

Table 1. Attained Body Mass Index and Relative Risk for Non–Insulin-Dependent Diabetes Mellitus in U.S. Women Aged 30 to 55 Years in 1976 and Followed for 14 Years

Body Mass Index	Cases	Person-Years of Follow-up	Age-Standardized Incidence Rate*	Age-Adjusted Relative Risk (95% CI)
kg/m^2	*n*		%	
>22.0	55	466 052	13.0	1.0 (reference)
22.0–22.9	71	194 433	37.4	2.9 (2.0 to 4.1)
23.0–23.9	88	156 770	54.9	4.3 (3.1 to 5.8)
24.0–24.9	94	142 392	62.9	5.0 (3.6 to 6.6)
25.0–26.9	227	198 484	103.5	8.1 (6.2 to 10.5)
27.0–28.9	267	119 662	200.4	15.8 (12.7 to 19.8)
29.0–30.9	329	84 880	354.5	27.6 (22.7 to 33.5)
31.0–32.9	263	47 119	521.2	40.3 (33.7 to 48.3)
33.0–34.9	224	29 885	703.6	54.0 (45.6 to 64.0)
≥35.0	579	46 636	1190.5	93.2 (81.4 to 106.6)

* Rate per 100 000 persons standardized to the age distribution of length of follow-up in the cohort.

Colditz GA Ann Intern Med. 1995; 122: 481- 6

Nurses' Health Study: incremento ponderale fra i 18 anni e l'inizio dello studio e rischio di diabete

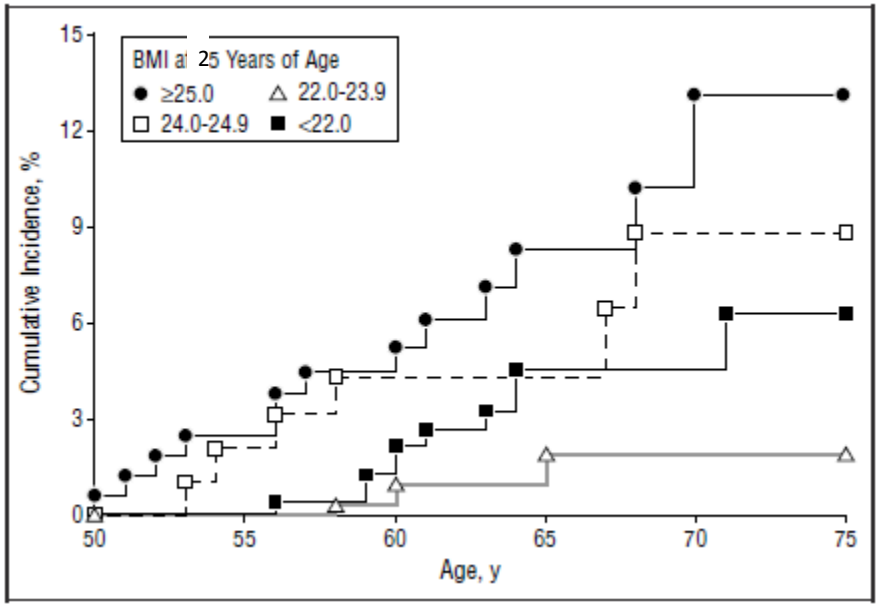
Table 3. Age-Adjusted Relative Risk for Diabetes Mellitus during 14 Years of Follow-up and Weight Change between Age 18 Years and 1976

Weight Change (Amount)	Cases, *n**	Person-Years of Follow-up	Age-Adjusted Relative Risk	Relative Risk Adjusted for Age and Body Mass Index at Age 18 Years (95% CI)
Loss (≥20.0 kg)	5	5921	1.9	0.13 (0.1 to 0.3)
Loss (11.0 to 19.9 kg)	17	22 493	1.8	0.23 (0.1 to 0.4)
Loss (5.0 to 10.9 kg)	43	73 645	1.4	0.54 (0.4 to 0.8)
Loss (4.9 to a gain of 4.9 kg)	197	464 001	1.0	1.0 (reference)
Gain (5.0 to 7.9 kg)	130	192 123	1.5	1.9 (1.5 to 2.3)
Gain (8.0 to 10.9 kg)	143	132 630	2.2	2.7 (2.1 to 3.3)
Gain (11.0 to 19.9 kg)	545	211 126	5.2	5.5 (4.7 to 6.3)
Gain (≥20.0 kg)	724	93 840	15.1	12.3 (10.9 to 13.8)

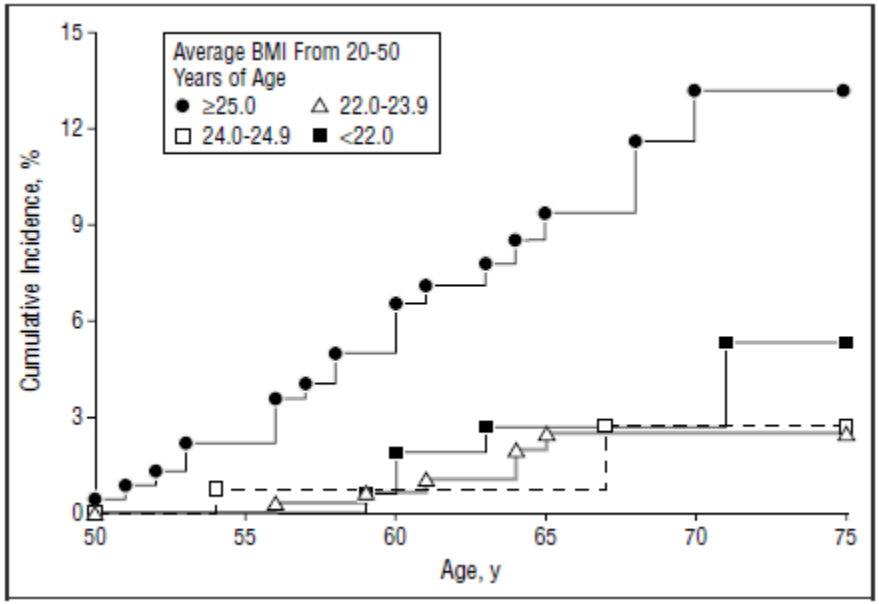
Colditz GA Ann Intern Med. 1995; 122: 481- 6

The Johns Hopkins Precursors Study: BMI e incidenza di diabete in maschi

BMI a 25 anni e incidenza di diabete

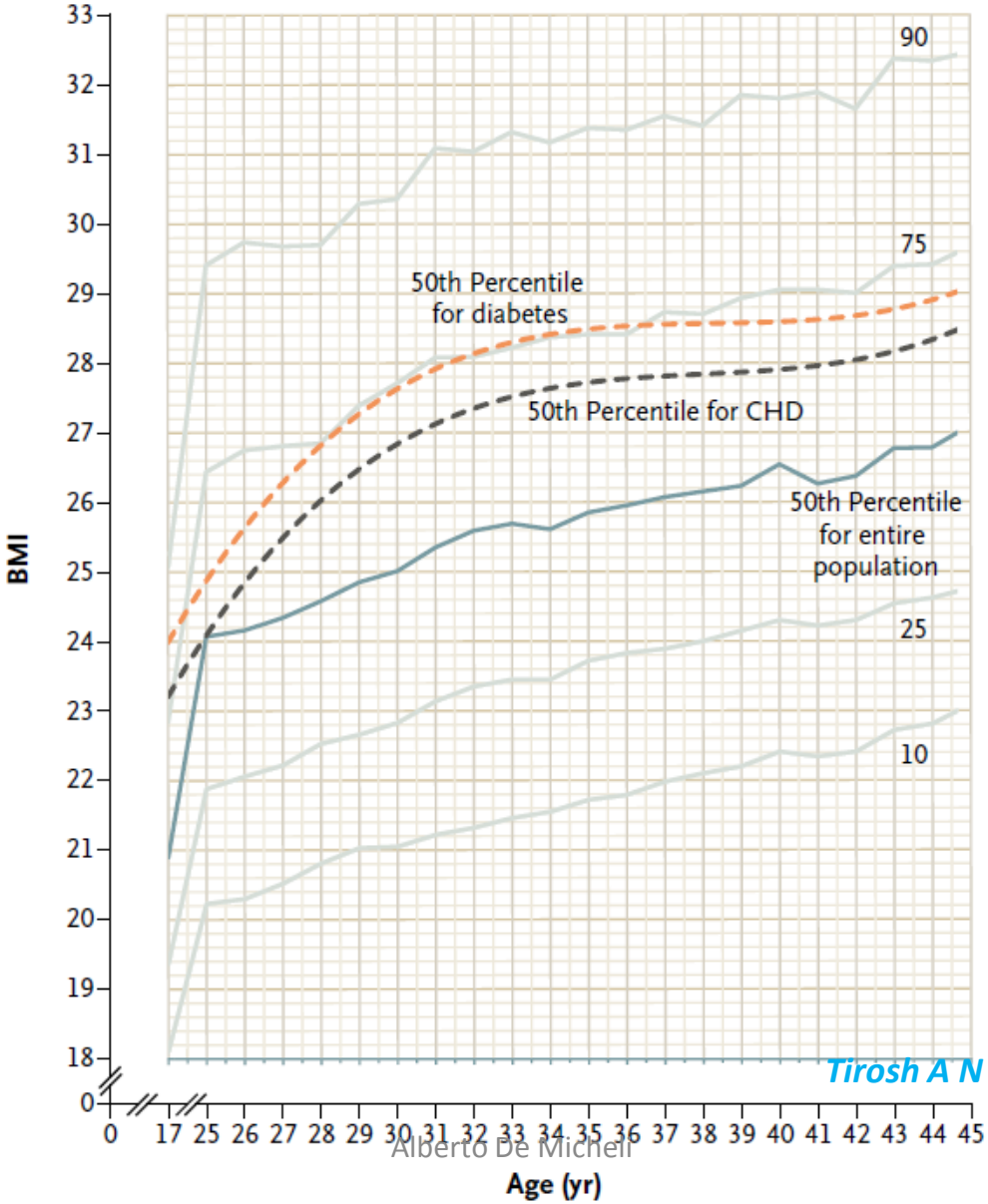


BMI medio da 20 a 50 anni e incidenza di diabete



Brancati FL Arch Intern Med. 1999; 159: 957- 963

Andamento del BMI dall'adolescenza all'età giovane adulta in soggetti con diabete o cardiopatia ischemica



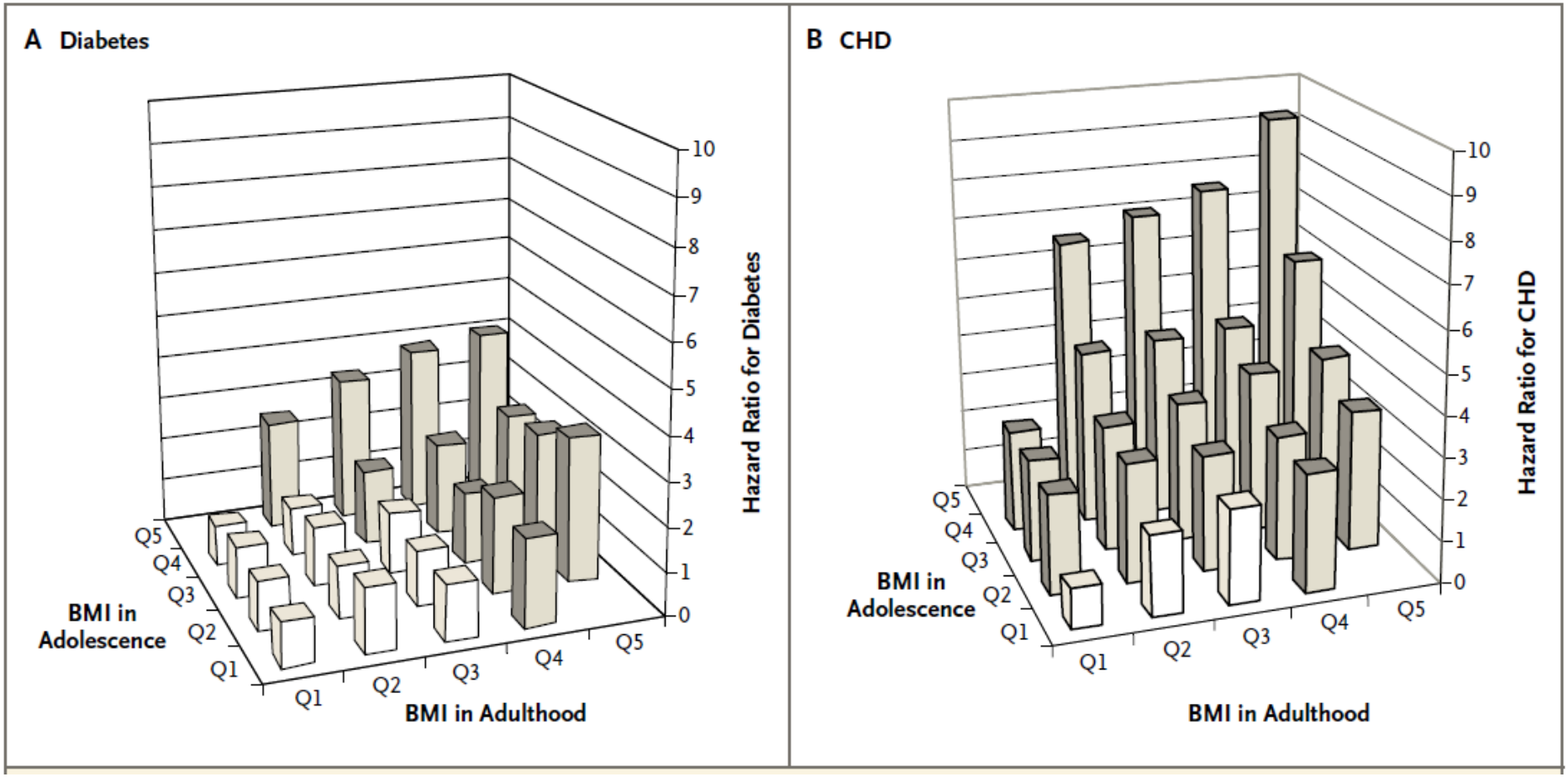
Diabete

CHD

Pop. generale

Tirosh A N Engl J Med 2011;364:1315-25

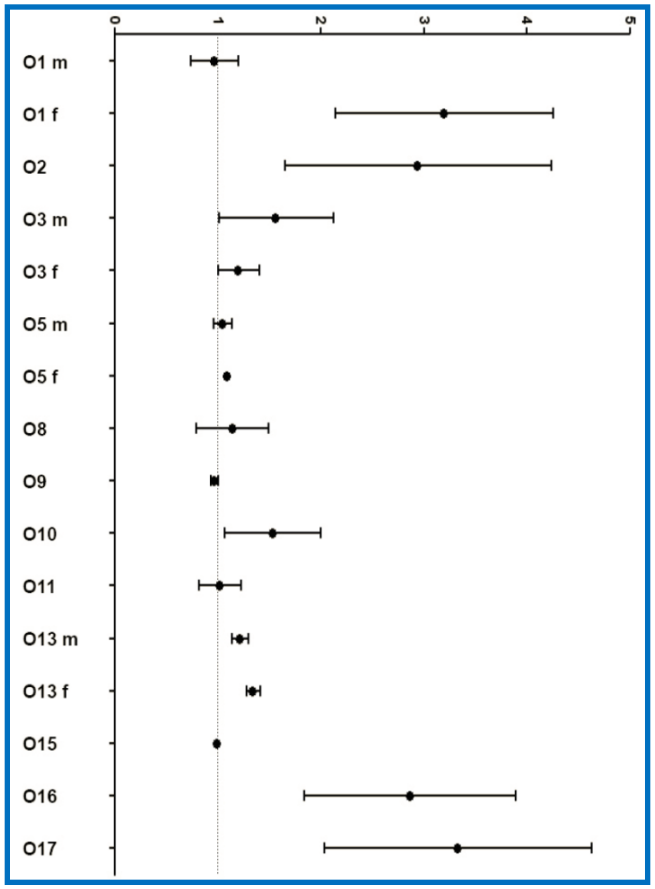
Rischio di diabete e patologia coronarica in relazione al BMI nell'adolescenza e nell'età adulta



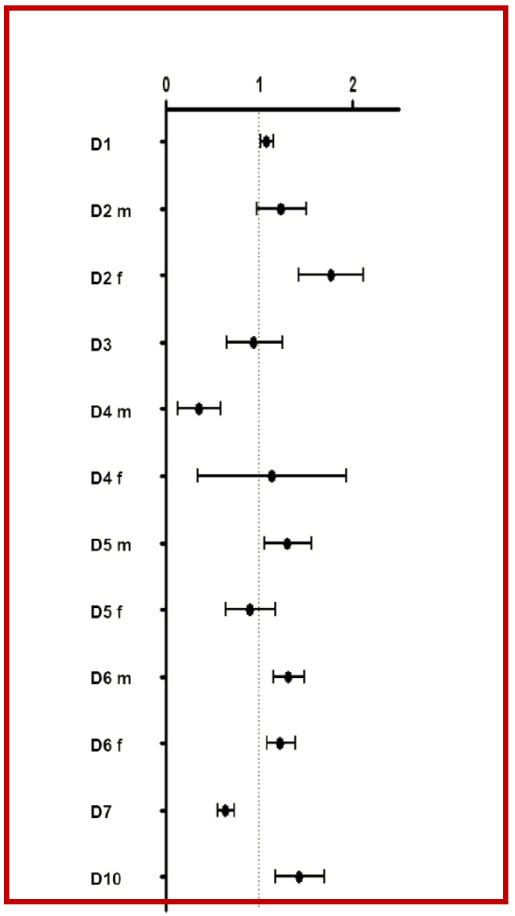
Tirosh A N Engl J Med 2011;364:1315-25

Impatto dello stato socio- economico nell'infanzia sull'incidenza di obesità e diabete: revisione sistematica

Sovrappeso ed obesità



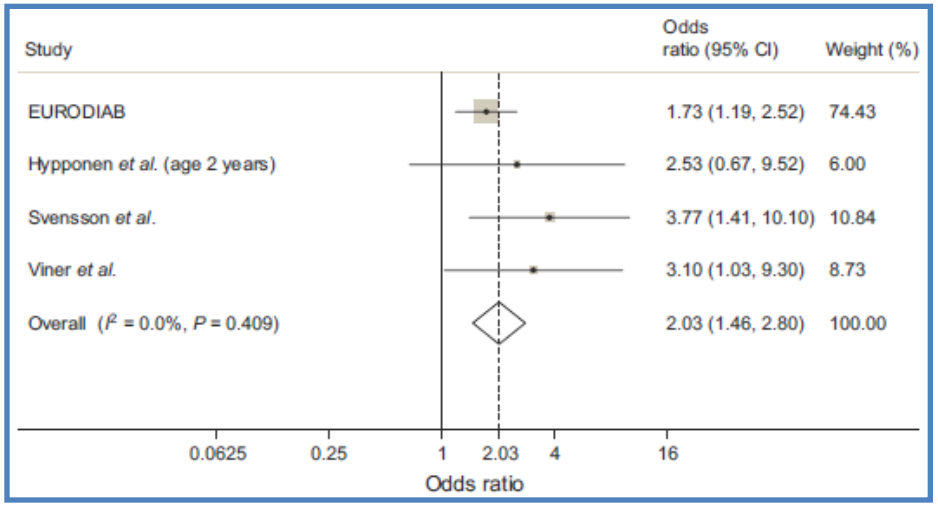
Diabete tipo 2



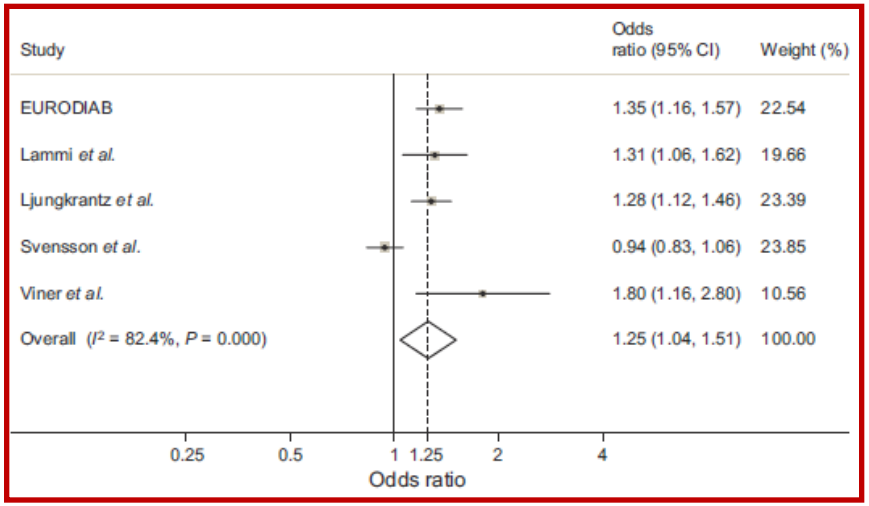
Tamayo T BMC Public Health 2010; 10:525

Associazione fra obesità infantile e rischio di diabete **tipo 1**: revisione sistematica e metanalisi

Obesità



BMI (aumento 1 DS)

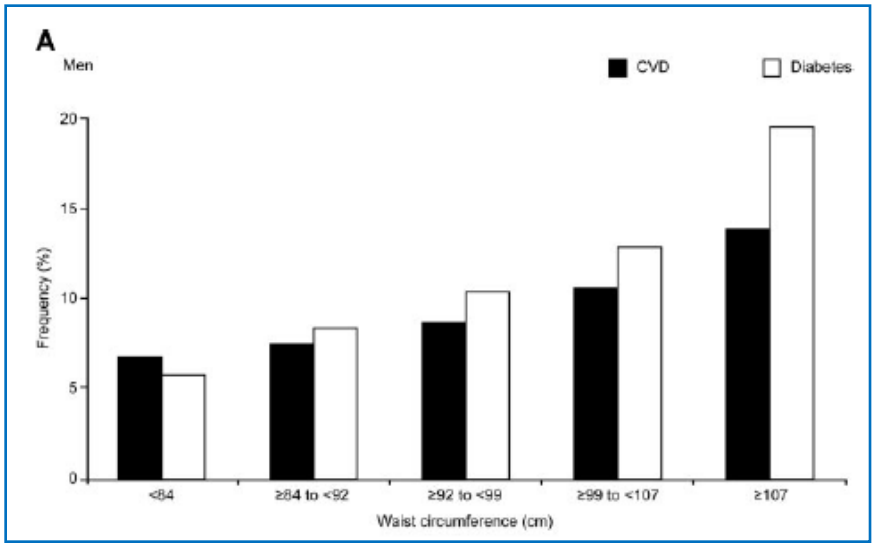


Verbeeten KC Diabet Med 2011; 28: 10–18

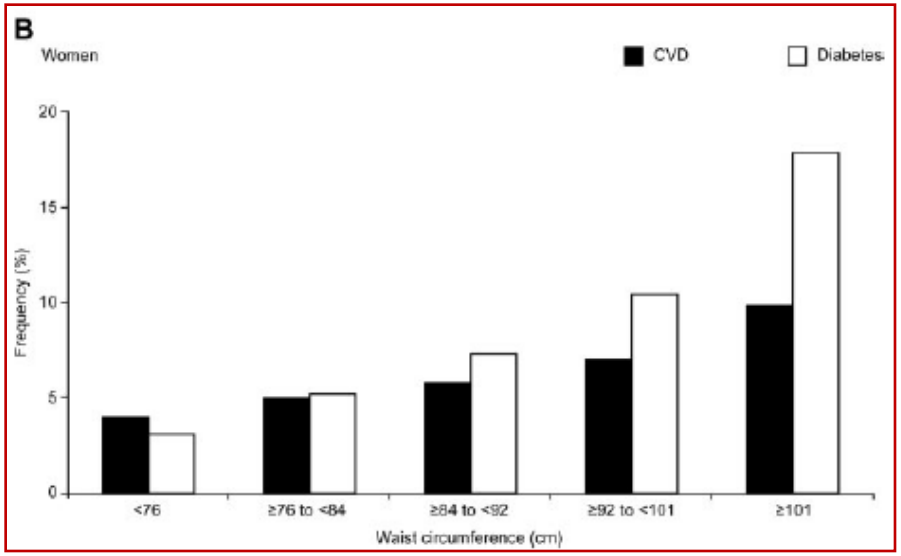
Gli indici di obesità addominale

Frequenza di diabete e malattia cv per quintili di circonferenza vita non aggiustati per BMI (studio trasversale IDEA)

Maschi



Femmine



Balkau M, Circulation. 2007;116:1942-1951

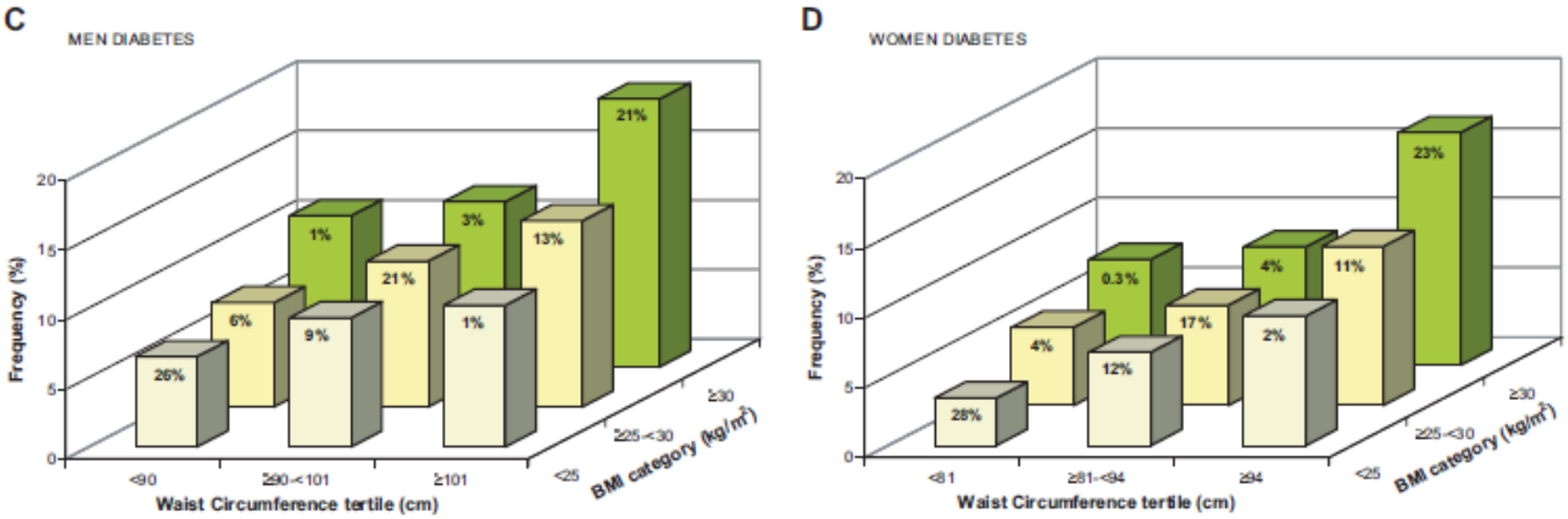
OR per diabete e malattia CV per aumento di 1 DS di circonferenza vita in diverse categorie di BMI

	Men			Women		
BMI Category	1 SD WC (cm)	OR (95% CI) for CVD	OR (95% CI) for Diabetes Mellitus	1 SD WC (cm)	OR (95% CI) for CVD	OR (95% CI) for Diabetes Mellitus
BMI<25 kg/m^2	9.3	1.10 (1.05 to 1.15)*	1.27 (1.21 to 1.33)*	9.3	1.15 (1.11 to 1.19)*	1.43 (1.37 to 1.48)*
BMI 25 to 30 kg/m^2	8.5	1.19 (1.15 to 1.23)*	1.23 (1.18 to 1.27)*	9.2	1.12 (1.08 to 1.16)*	1.32 (1.27 to 1.37)*
BMI≥30 kg/m^2	11.4	1.23 (1.18 to 1.28)*	1.34 (1.29 to 1.39)*	11.9	1.24 (1.20 to 1.29)*	1.43 (1.38 to 1.47)*
Overall	14.0	1.36 (1.33 to 1.39)*	1.59 (1.56 to 1.63)*	14.9	1.40 (1.37 to 1.43)*	1.83 (1.79 to 1.87)*

*P<0.0001.

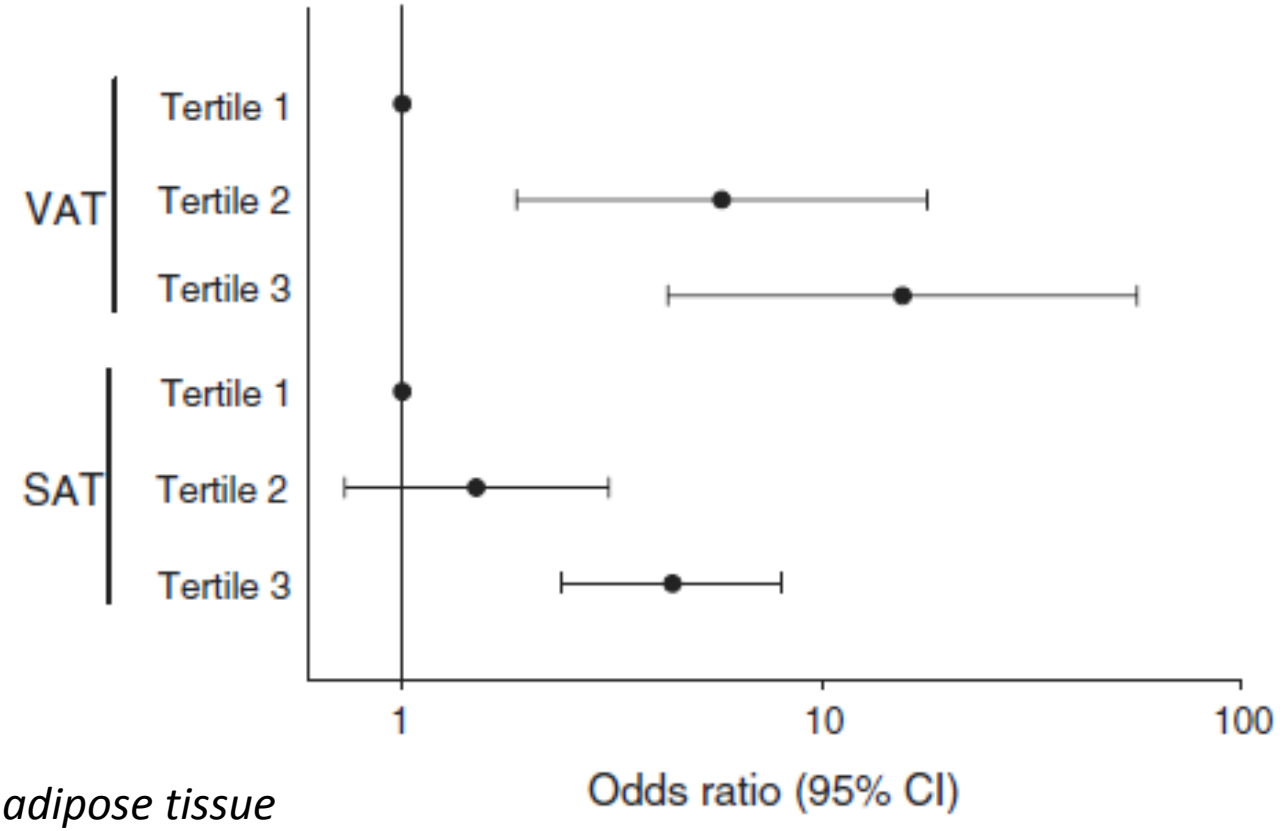
Balkau M, Circulation. 2007;116:1942-1951

Interazione fra BMI e circonferenza vita



Balkau M, Circulation. 2007;116:1942-1951

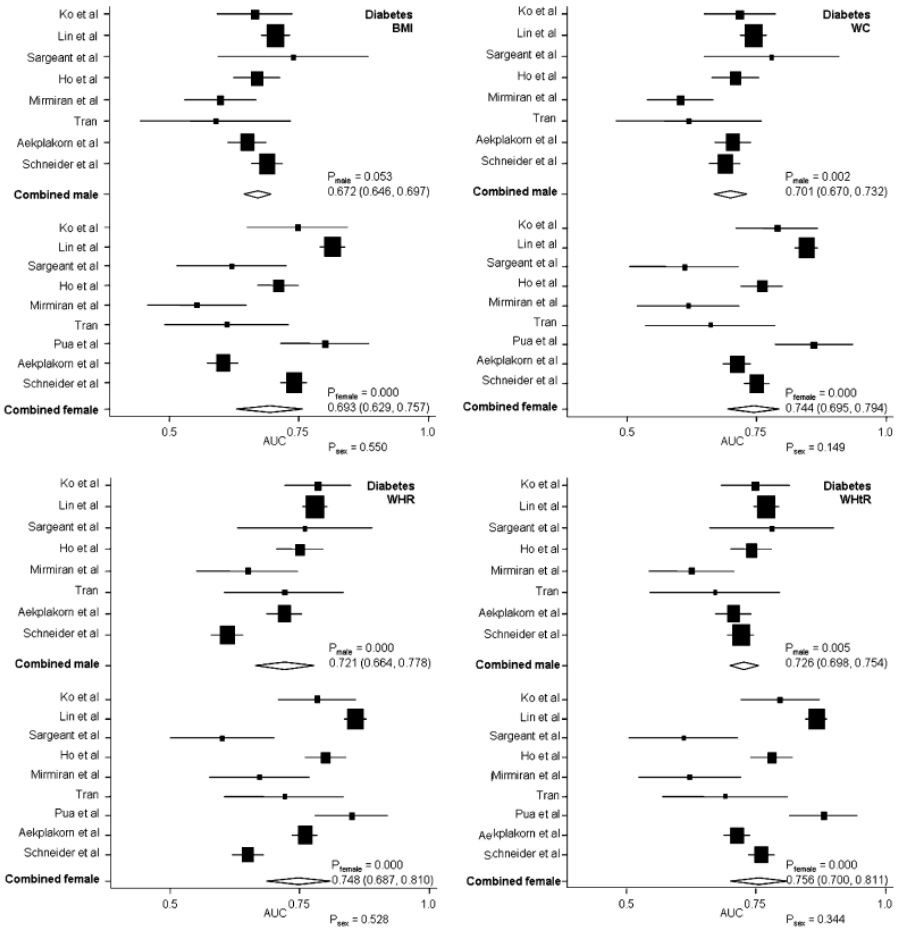
Associazione di terzili di obesità addominale e viscerale con l'incidenza di diabete T2 (IRAS Family Study)



VAT visceral adipose tissue
SAT subcutaneous adipose tissue

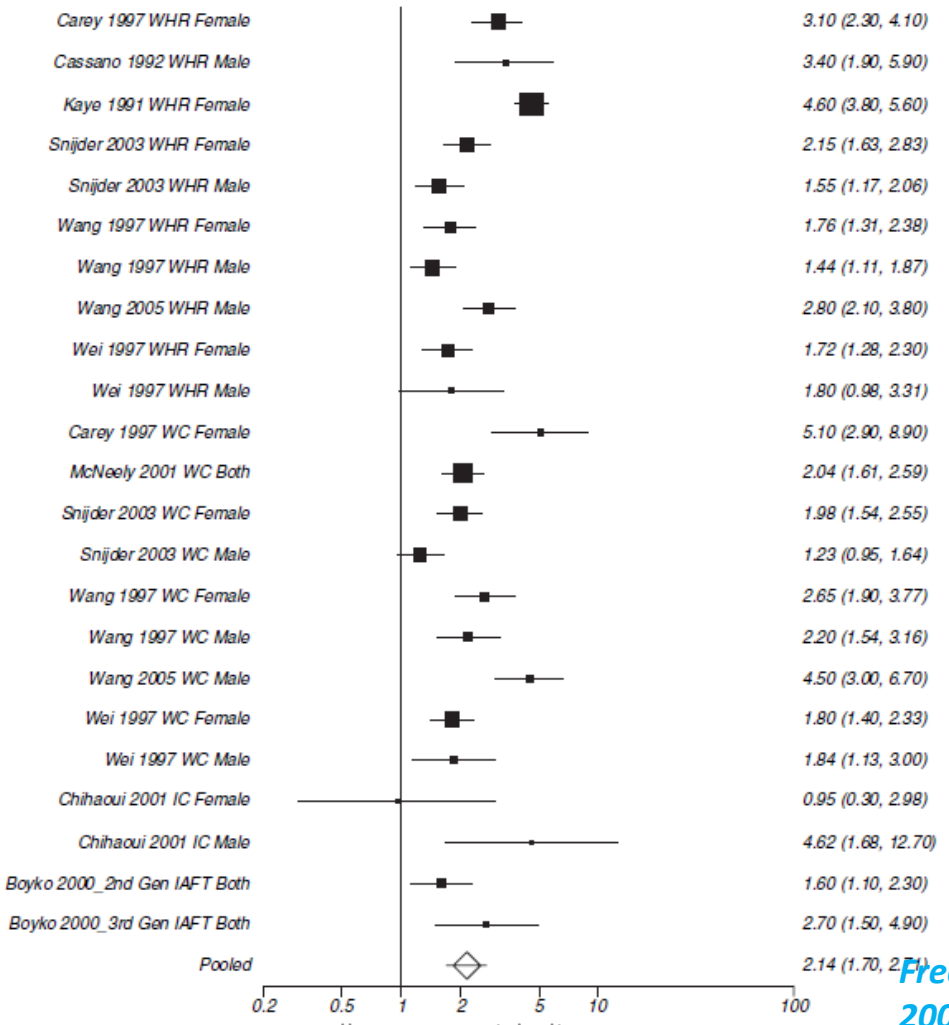
Hanley AJG Diabetologia, 2009; 52: 2079– 2086

Predittività del BMI vs. indici di obesità addominale: metanalisi



Ying Leea CM Journal of Clinical Epidemiology 2008, 61: 646e-653

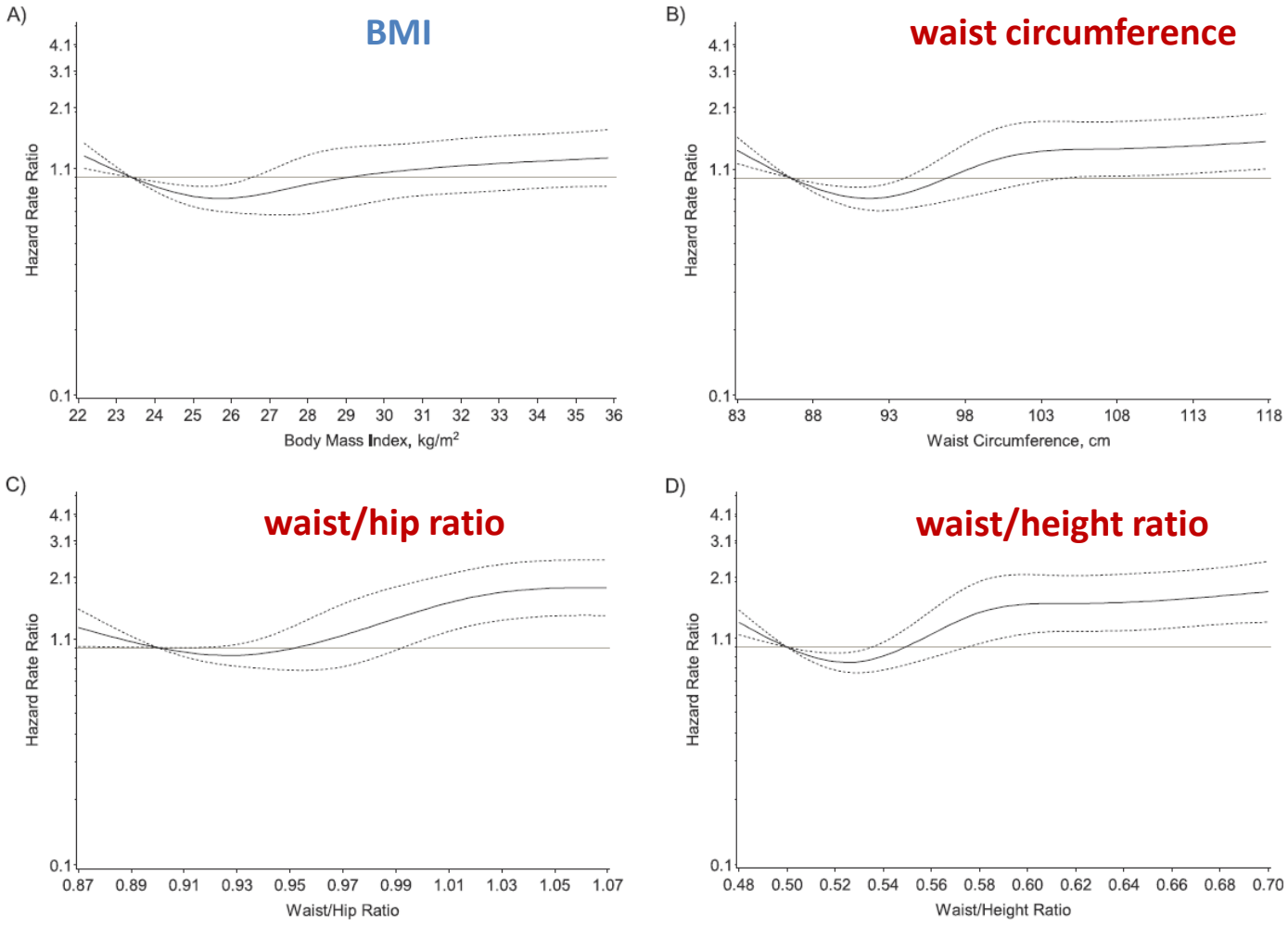
Obesità addominale e incidenza di diabete tipo 2: metanalisi



OR 2.14 (95% CI: 1.70–2.71; p < 0.0001)

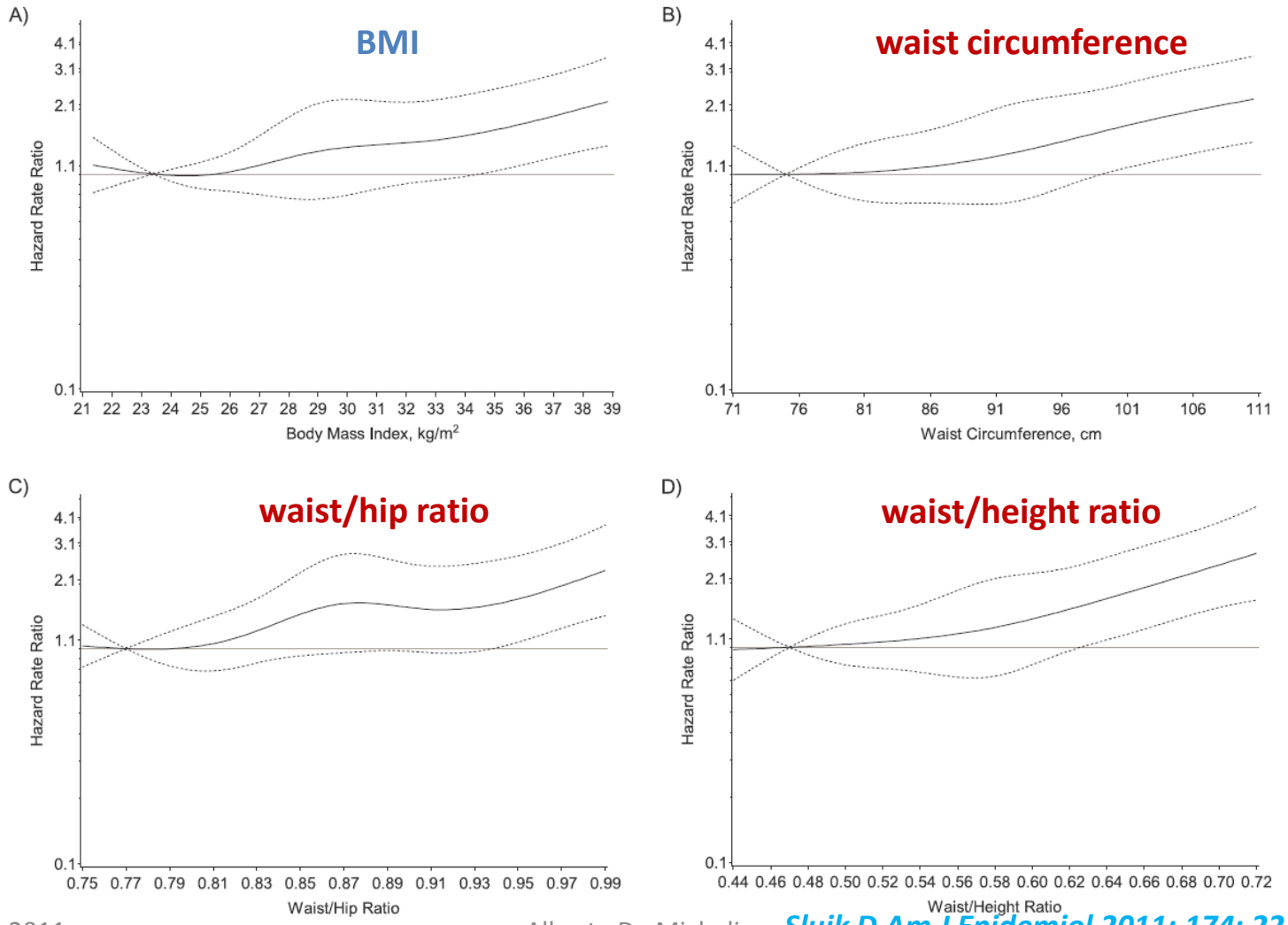
Freemantle N, Int J Clin Pract, 2008,;62: 1391– 1396

Associazione fra obesità generale ed addominale e mortalità nel diabete tipo 2 **(maschi)**



Sluik D Am J Epidemiol 2011; 174: 22– 34

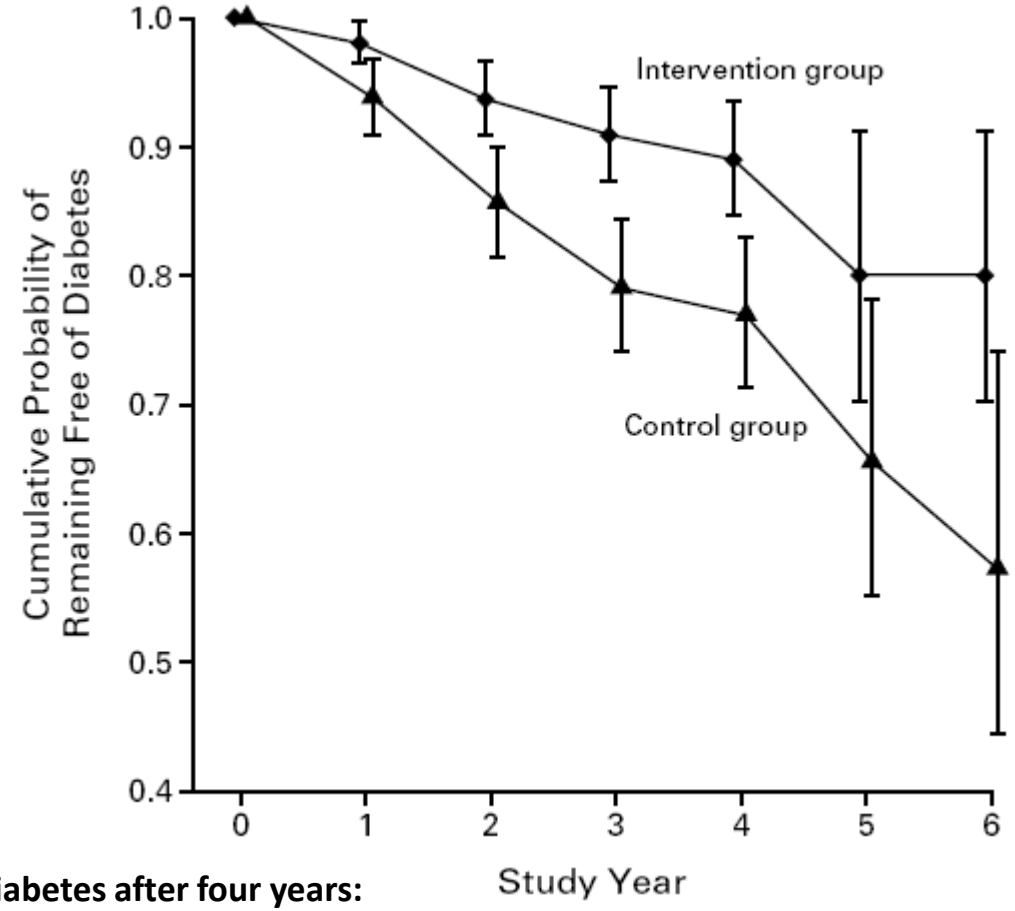
Associazione fra obesità generale ed addominale e mortalità nel diabete tipo 2 **(femmine)**



 Sluik D Am J Epidemiol 2011; 174: 22– 34

Interventi di prevenzione del diabete tipo 2

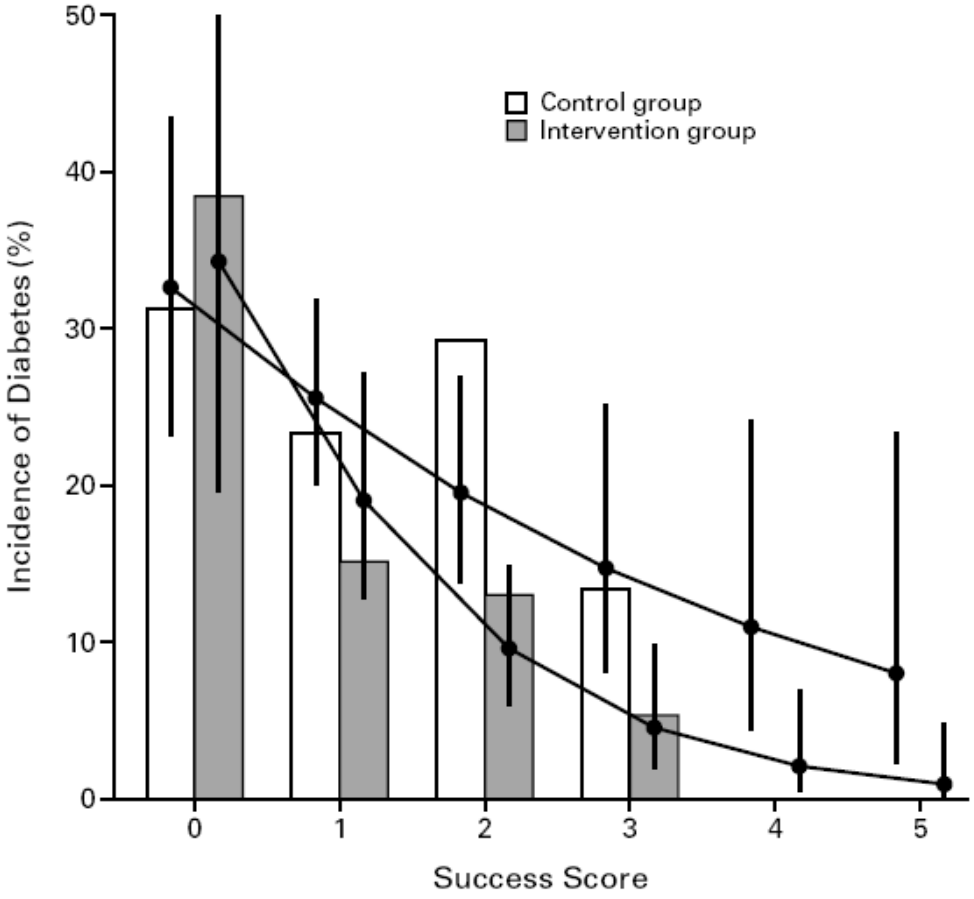
Finnish Study: probabilità di non diventare diabetici



Cumulative incidence of diabetes after four years:
11 percent (95 %CI 6 to 15)in the intervention group
23 percent (95 %CI17 to 29 percent) in the control group

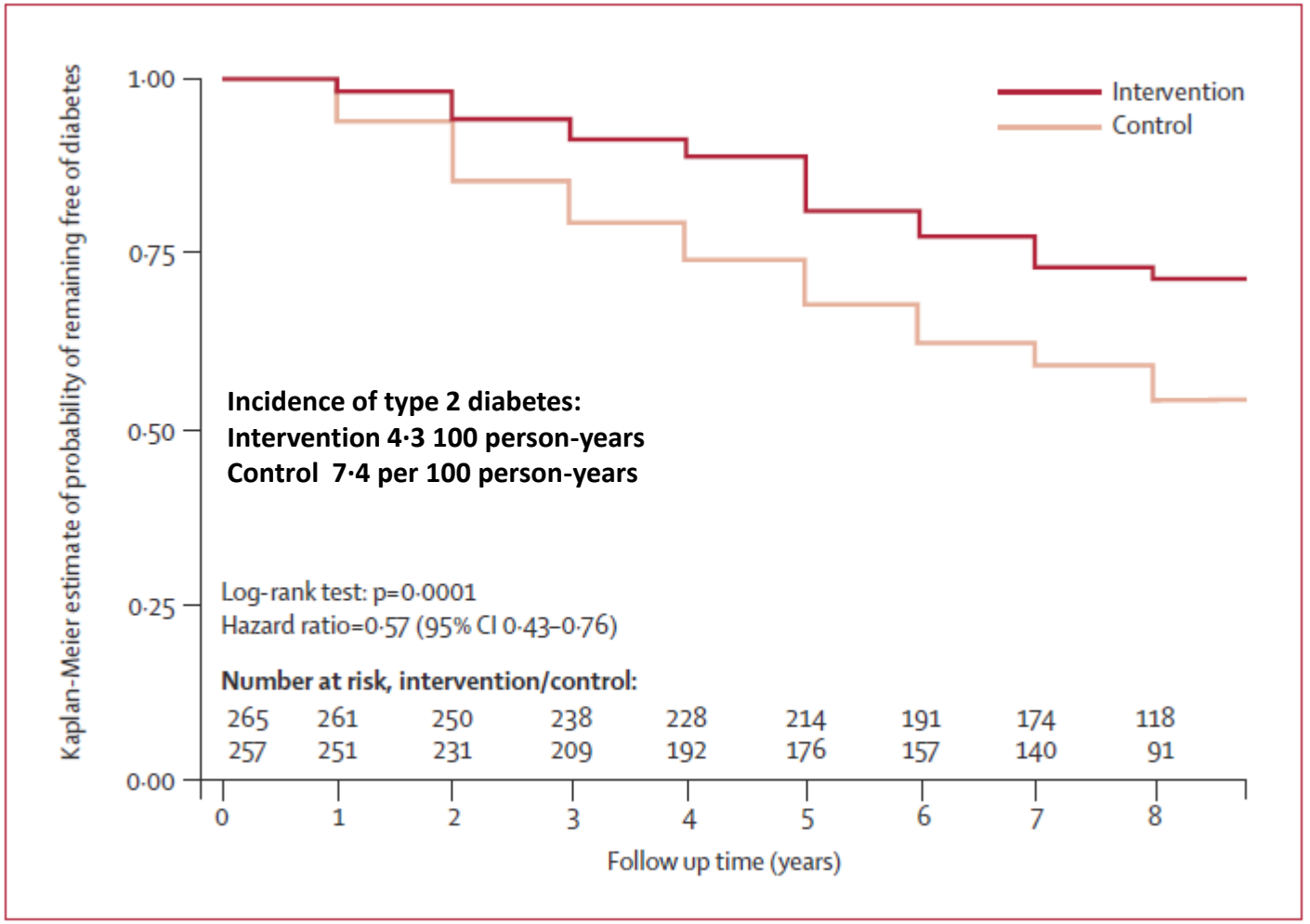
Tuomilehto J, N Engl J Med. 2001 ; 344: 1343- 50

Finnish study: incidenza del diabete in relazione agli obiettivi intermedi raggiunti



Tuomilehto J, N Engl J Med. 2001 ; 344: 1343- 50

Finnish study: probabilità di non diventare diabetici dopo 8 anni



Lindström J Lancet 2006; 368: 1673– 79

Finnish study: effetti indipendenti sulla prevenzione del diabete del raggiungimento di obiettivi diversi

Follow up 8 anni

Variable	Multivariate-adjusted hazard ratios for diabetes (95% CI)
weight reduction	**0·43 (0·30–0·61)**
intake of saturated fat	0·55 (0·26–1·16)
intake of fat	0·80 (0·48–1·34)
physical activity	0·80 (0·57–1·12)
intake of fibre	0·97 (0·63–1·51)

Lindström J Lancet 2006; 368: 1673– 79

Diabetes prevention study: incidenza di diabete

The average follow-up was 2.8 years.
The incidence of diabetes was 11.0, 7.8, and 4.8 cases per 100 person-years in the placebo, metformin, and lifestyle groups, respectively.

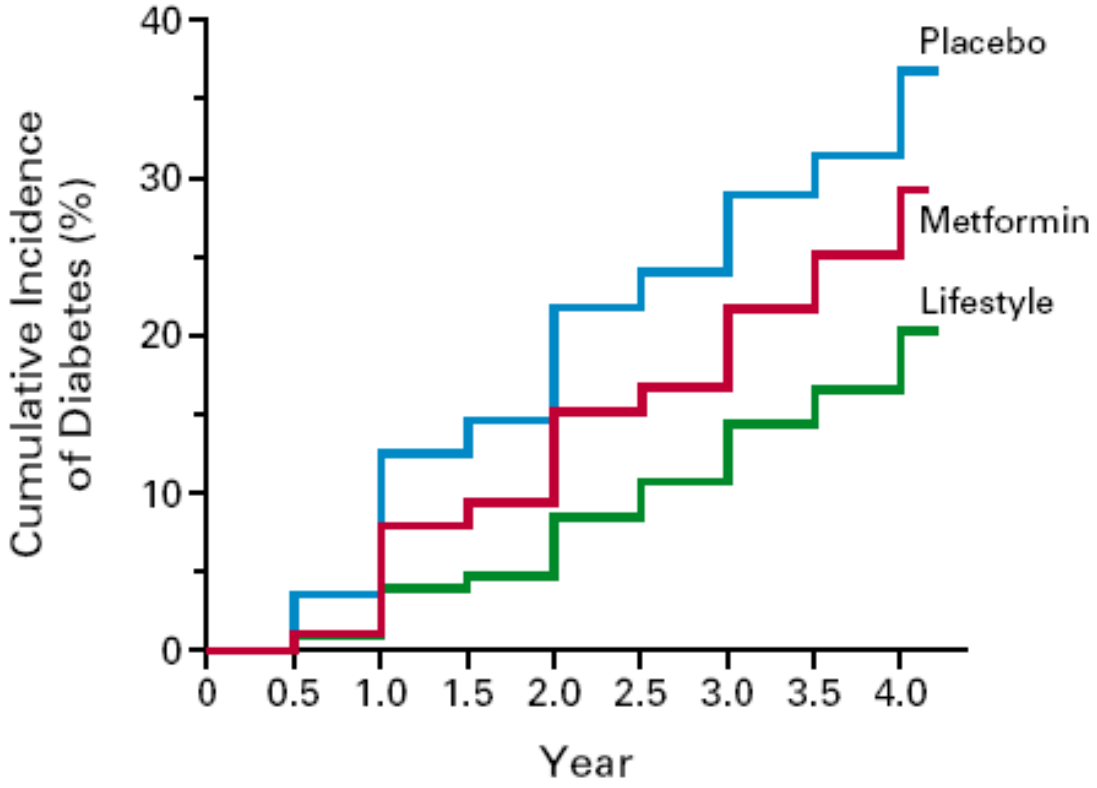


Figure 2. Cumulative Incidence of Diabetes According to Study Group.

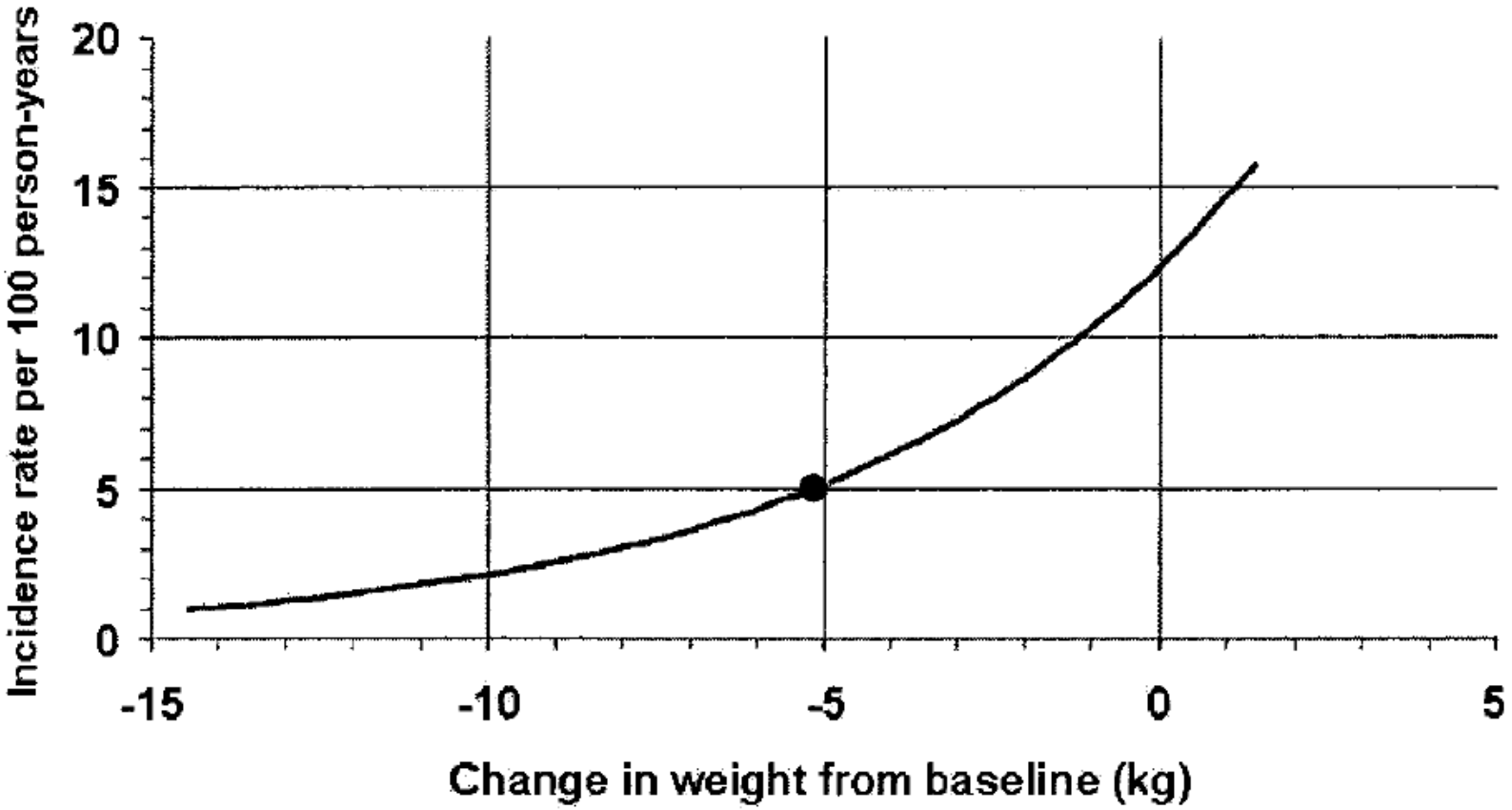
DPP Research Group, N Engl J Med 2002; 346:393- 403

DPP: predittori del ritorno da ipo- a normo- tolleranza glucidica

ILS versus placebo	2.05 (1.66–2.53)	<0.0001
Metformin versus placebo	1.25 (0.99–1.58)	0.0601
Younger age	1.07 (1.02–1.11)	0.0031
Male versus female sex	1.17 (0.98–1.40)	0.0784
Caucasian versus non-Caucasian	1.00 (0.84–1.19)	0.9986
Lower fasting plasma glucose	1.52 (1.36–1.68)	<0.0001
Lower 2-h plasma glucose	1.24 (1.13–1.35)	<0.0001
Greater insulin sensitivity (l/fasting insulin)	1.07 (0.99–1.16)	0.0934
Greater insulin secretion (CIR)	1.09 (1.01–1.17)	0.0353
Higher baseline weight	1.01 (0.92–1.11)	0.8229
Greater weight loss	1.34 (1.21–1.49)	<0.0001

Perreault L Diabetes Care 2009; 32: 1583– 1588

Effetto della perdita di peso sul rischio di diabete

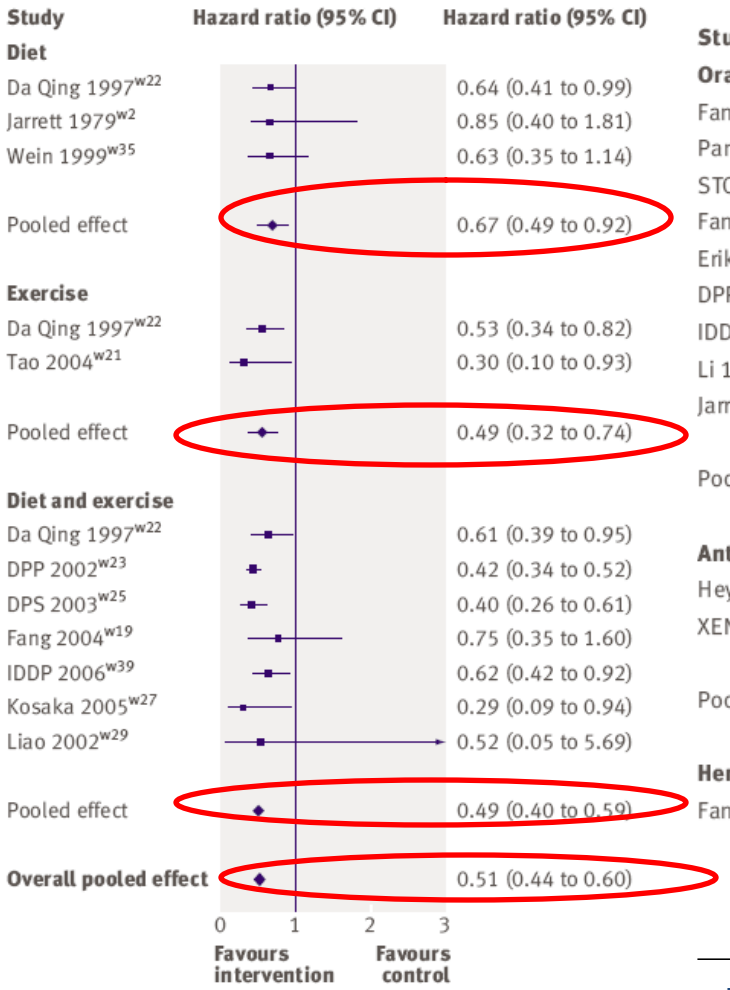


For every kilogram of weight loss, there was a 16% reduction in risk, adjusted for changes in diet and activity

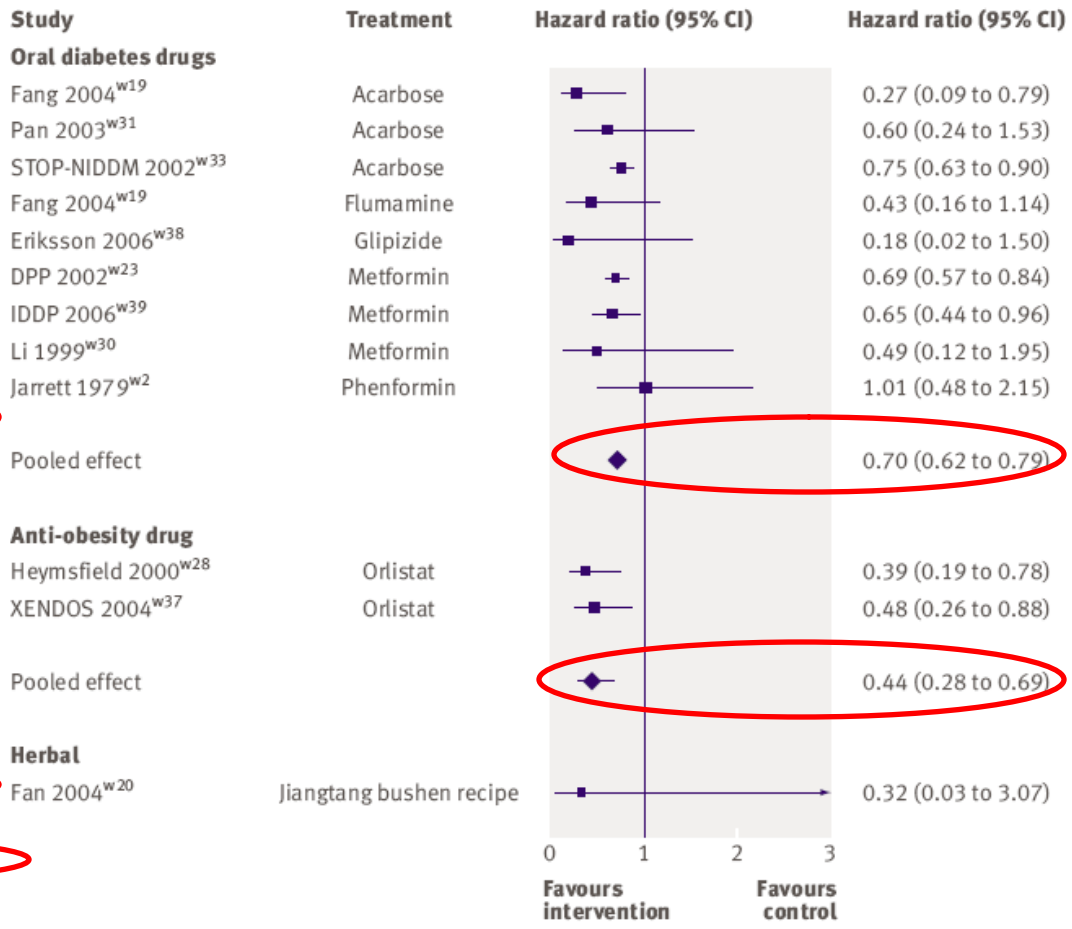
Hamman RF Diabetes Care 29: 2102– 2107, 2006

Metanalisi degli studi di prevenzione del diabete

Stile di vita



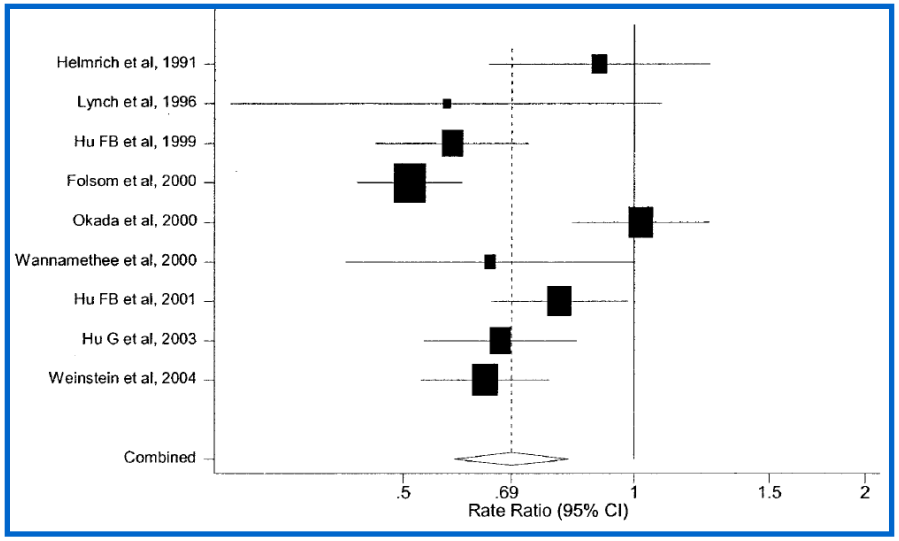
Farmaci



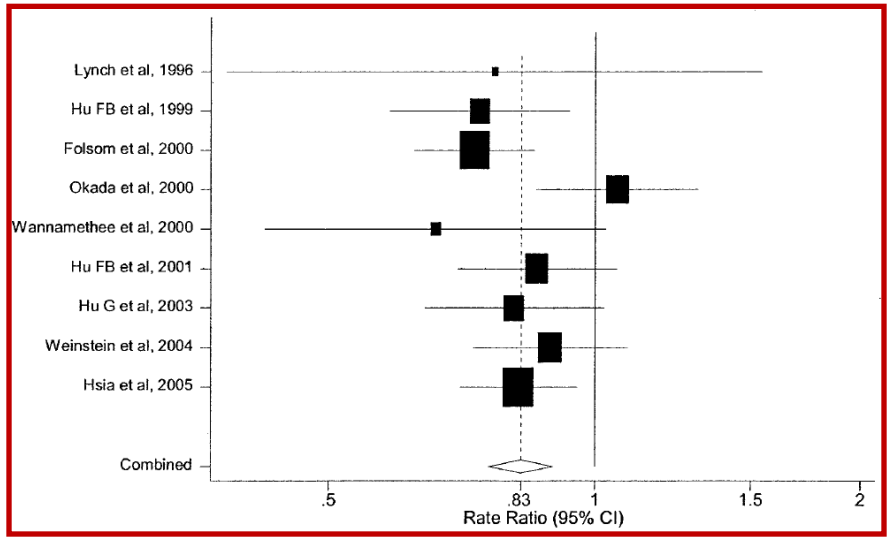
Gillies CL BMJ 2007; 334: 299

Effetto dell'attività fisica di moderata entità sull'incidenza di diabete: revisione sistematica

Senza correzione per BMI



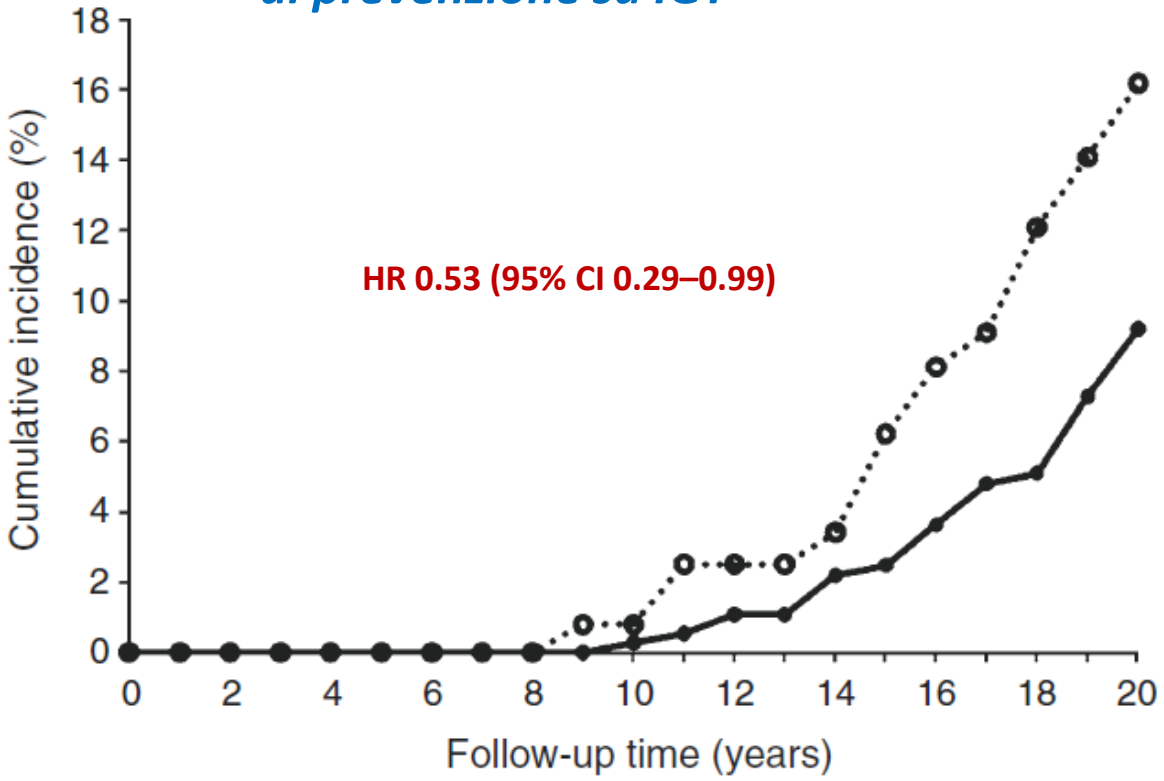
Con correzione per BMI



Jeon CY Diabetes Care 2007; 30: 744– 752

Prevenzione primaria del diabete e delle complicanze:

Incidenza cumulativa di retinopatia severa 20 anni dopo intervento di prevenzione su IGT



Number at risk:

Control	133	132	131	128	128	121	113	107	98	91	82
Intervention	407	407	402	393	387	376	364	355	339	316	290

Gong Q Diabetologia. 2011; 54: 300- 7

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

Neighborhoods, Obesity, and Diabetes — A Randomized Social Experiment

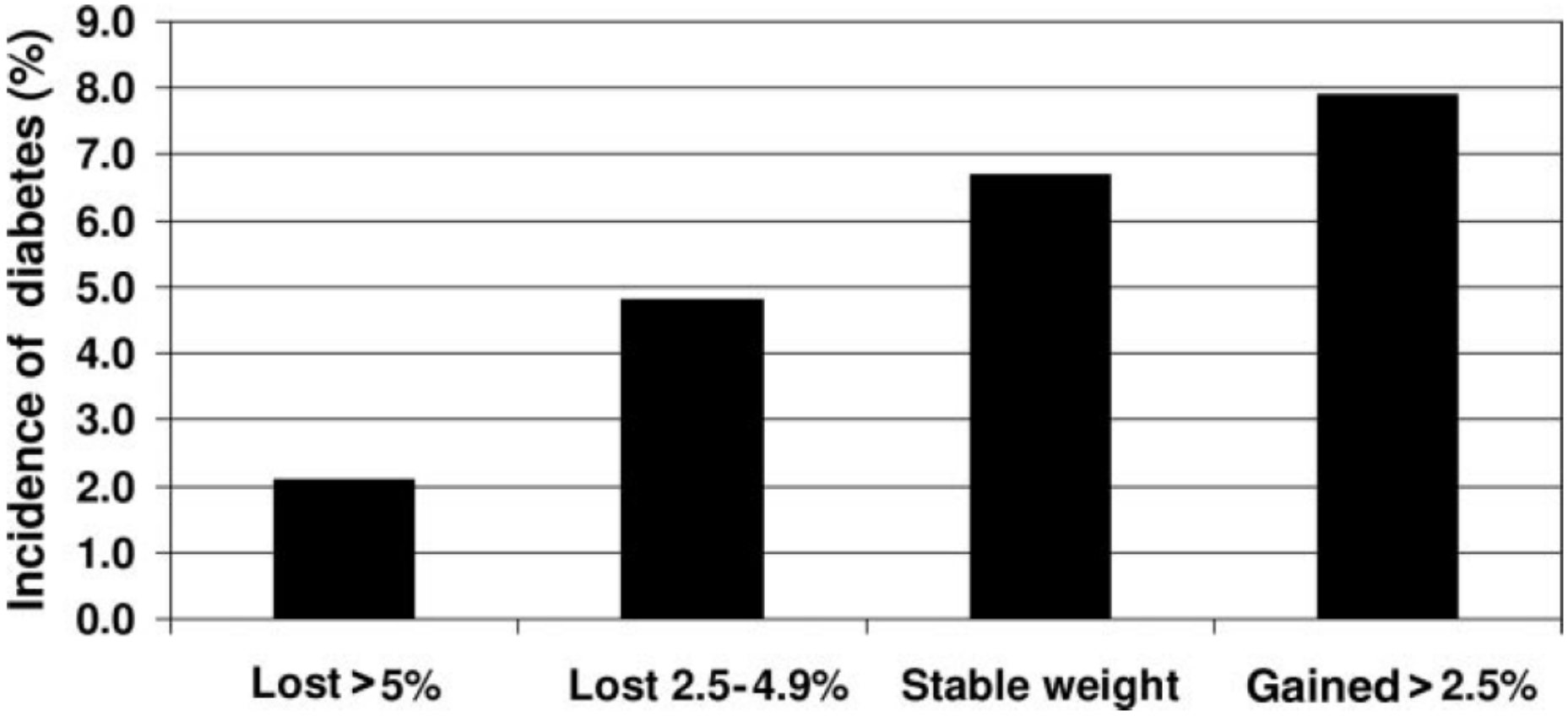
Table 3. Body-Mass Index (BMI) and Glycated Hemoglobin Level at Follow-up, According to Study Group.*

Variable	Control	Low-Poverty Voucher			Traditional Voucher		
	Prevalence (%)	Intention-to-Treat Estimate (95% CI)†	P Value	Prevalence (%)	Intention-to-Treat Estimate (95% CI)†	P Value	Prevalence (%)
BMI‡							
≥30	58.6	−1.19 (−5.41 to 3.02)	0.58	57.5	−0.14 (−6.27 to 5.98)	0.96	58.4
≥35	35.5	−4.61 (−8.54 to −0.69)	0.02	31.1	−5.34 (−11.02 to 0.34)	0.07	30.8
≥40	17.7	−3.38 (−6.39 to −0.36)	0.03	14.4	−3.58 (−7.95 to 0.80)	0.11	15.4
Glycated hemoglobin§							
≥6.5%	20.0	−4.31 (−7.82 to −0.80)	0.02	16.3	−0.08 (−5.18 to 5.02)	0.98	20.6

Ludwig J N Engl J Med 2011; 365: 1509- 19

Finnish National Diabetes Prevention Program (FIN-D2D)
Follow up 1 anno (2798/ 10149 soggetti)

Incidenza di diabete durante il primo anno in relazione alla perdita di peso



Saaristo T, Diabetes Care 2010; 33: 2146– 2151

Considerazioni conclusive

NHS
National Institute for
Health and Clinical Excellence

Preventing type 2 diabetes:
population and community-level interventions in high-risk groups and the general population

2011

NICE Public Health Implementation Tools

NICE public health guidance 35

Background

Key risk factors for type 2 diabetes include:

- Being obese or overweight, a large waist circumference, low physical activity levels

The following people are also particularly at risk:

- Those of South Asian, African-Caribbean, black African and Chinese descent
- Lower socioeconomic groups

Scope

Population and community-level interventions to prevent type 2 diabetes among adults aged 18–74 in high-risk groups and the general population

National recommendations

- Integrating national strategy on non-communicable diseases
- Conveying messages to the whole population
- Promoting a healthy diet
- Promoting physical activity

Local recommendations

- Local joint strategic needs assessments and local strategy
- Interventions for communities at high risk
- Conveying messages to the local population
- Promoting a healthy diet
- Promoting physical activity
- Training

Costs

The following interventions may involve a cost for local organisations, depending on current practice:

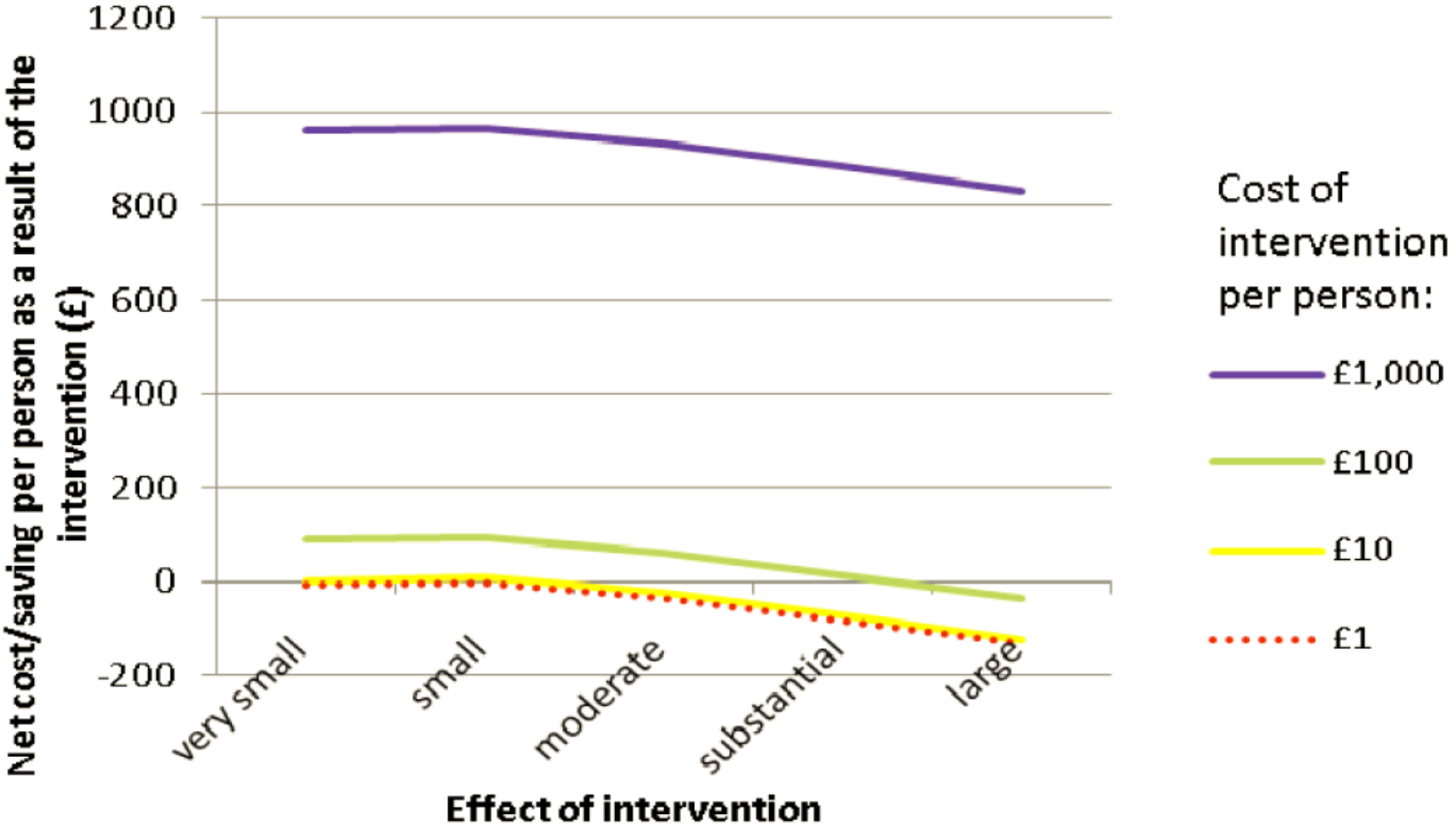
- Weight management programmes
- Nutrition education sessions
- Media campaigns and the associated costs of an increased number of people requiring an intervention as a result of increased awareness

Savings

•Diabetes is estimated to account for at least 5% of UK healthcare expenditure - preventing or delaying the onset of type 2 diabetes and other non-communicable diseases would lead to savings for the NHS and other public service organisations

•The cost of targeting high-risk groups at population level to prevent or delay raised glucose levels is likely to be lower than the cost of one-to-one interventions to stop people with raised glucose levels progressing to type 2 diabetes

Efficacia e costo- efficacia di interventi ad alto e basso costo



NICE public health guidance 35 Preventing type 2 diabetes: population and community interventions
Costing statement: Preventing type 2 diabetes: population and community interventions, May 2011

Grazie per l'attenzione