DIABETE MELLITO

Tipo 1 :

carenza assoluta di insulina

- esordio in genere in età giovane
- peso in genere normale

Tipo 2 :

carenza relativa + inefficacia dell'insulina (insulinoresistenza)

- esordio in genere in età adulta/senile
- spesso associato a obesità

Effetti di una singola seduta di esercizio sulla omeostasi glucidica

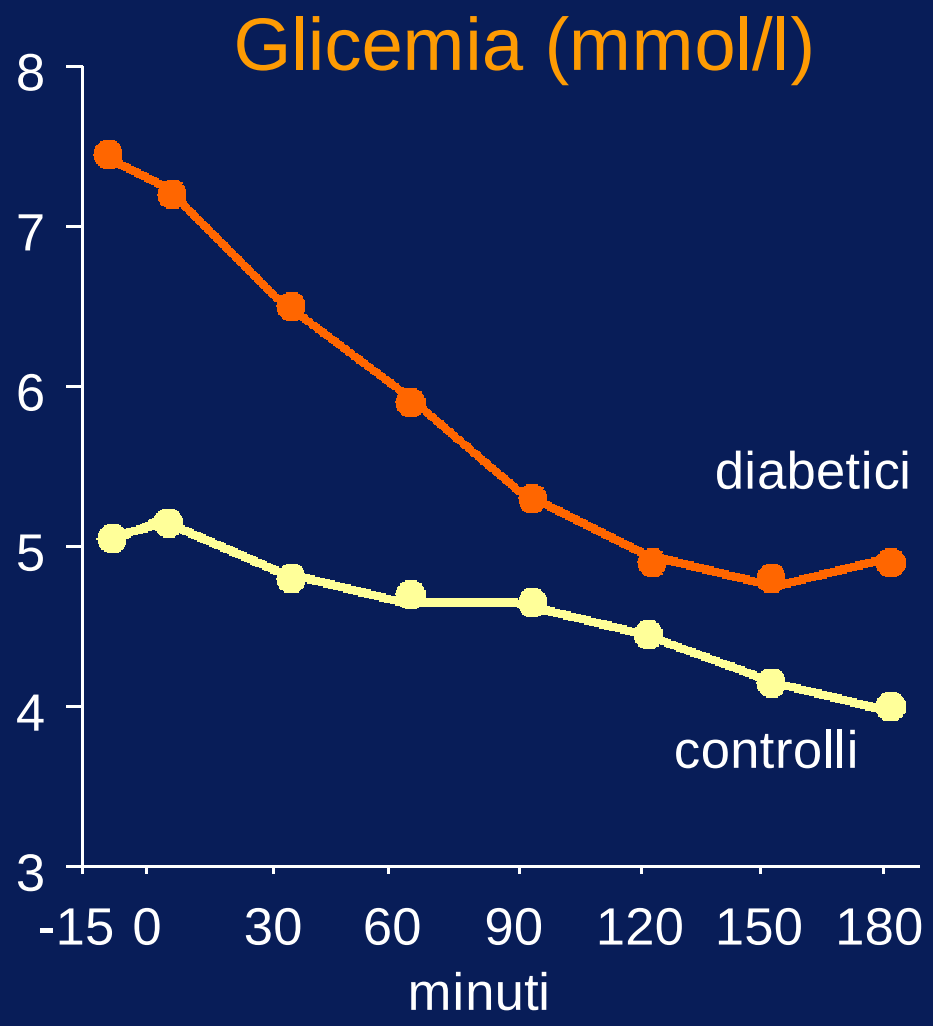
- Aumento dell’utilizzazione del glucosio
- Aumentata sensibilità all’insulina per la captazione del glucosio

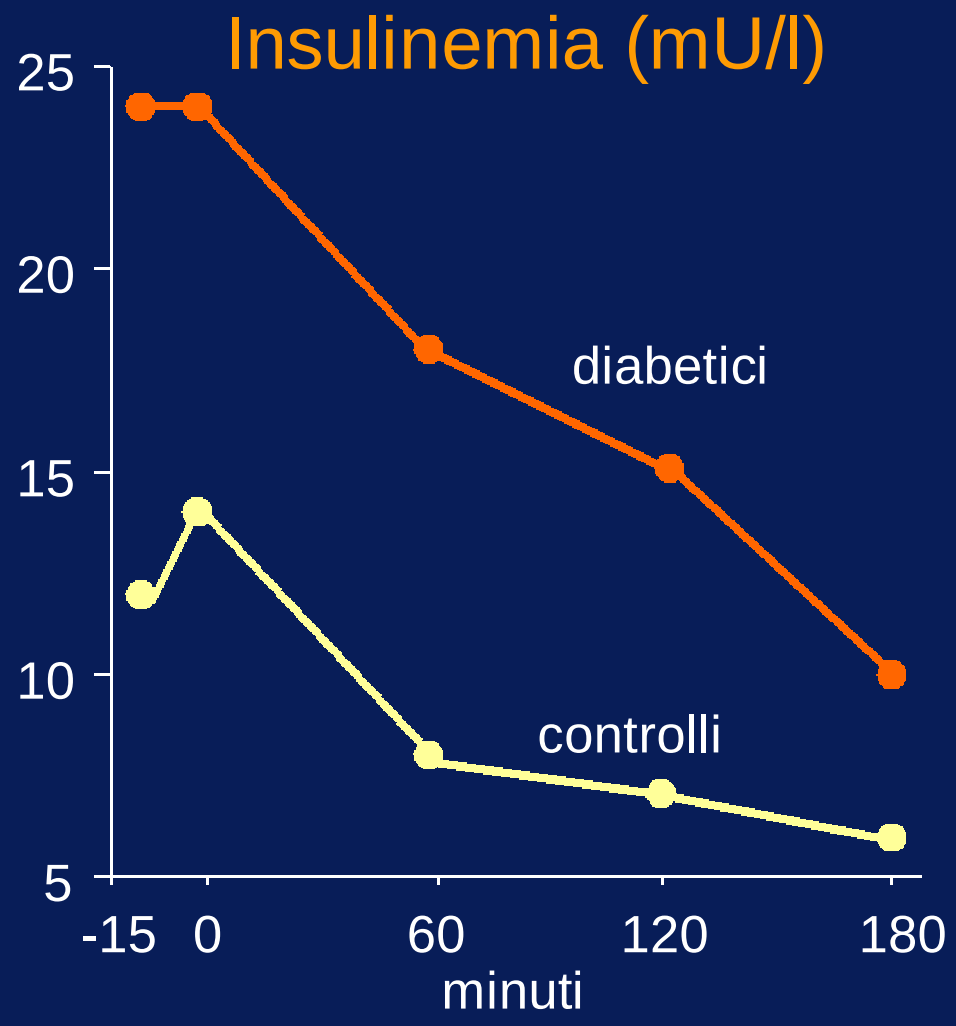
Gli effetti possono persistere per diverse ore dopo la cessazione dell’esercizio

Peculiarità del diabete tipo 2 in relazione all'esercizio fisico

- L'esercizio ha effetti benefici sui meccanismi patogenetici della malattia e sui fattori di rischio cardiovascolare associati al diabete: è uno strumento di cura.
- Nel diabete tipo 2 non vi è ipoinsulinemia assoluta: difficilmente l'esercizio può precipitare uno scompenso metabolico.
- L'eventuale iperinsulinemia è in genere conseguenza dell'insulinoresistenza e si riduce con il miglioramento della sensibilità insulinica (non è così se farmaco-indotta)

Modificazioni di glicemia e insulinemia durante esercizio aerobico moderato protratto in pazienti con diabete tipo 2





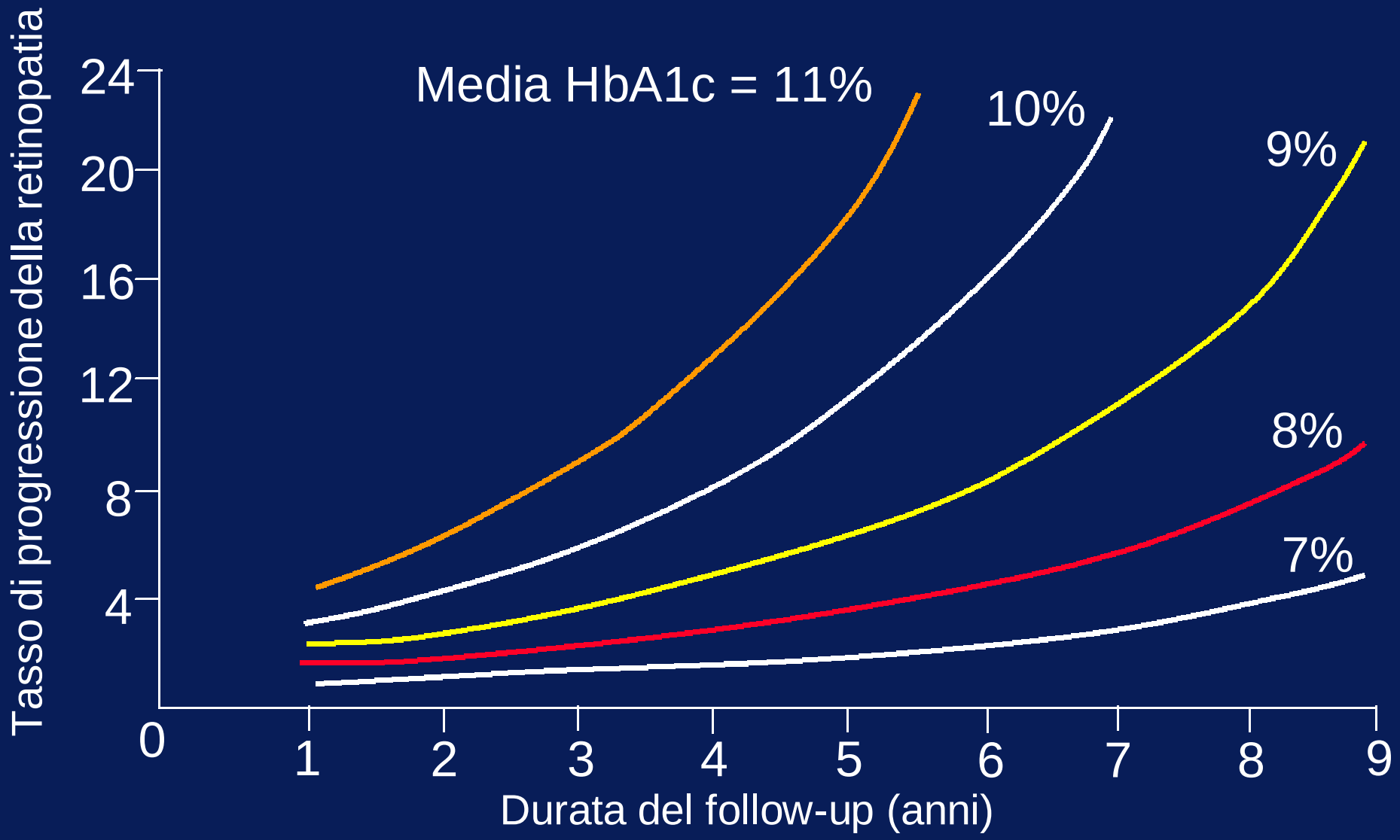
(Devlin et al, 1987)

Effetti favorevoli dell'esercizio fisico sui fattori di rischio cardiovascolare nel diabete tipo 2

- Riduzione glicemia
- Aumento sensibilità insulinica
- Riduzione colesterolo LDL e trigliceridi
- Aumento colesterolo HDL
- Riduzione tessuto adiposo, specie viscerale
- Riduzione fattori pro-coagulanti
- Controllo dell'ipertensione (lieve)

Riduzione mortalità cardiovascolare (?)

Correlazione tra controllo glicemico, durata del diabete e retinopatia diabetica
(Adattata da : The Diabetes Control and Complications Trial Research Group - DCCT 1995)



OBIETTIVI TERAPEUTICI

per la riduzione del rischio cardiovascolare nel diabete mellito di tipo 2

- Riduzione di peso corporeo e obesità viscerale
- HbA1c < 7.0 %
- Colesterolemia LDL < 100 mg/dl
- Colesterolemia HDL > 40 mg/dl
- Trigliceridemia < 150 mg/dl
- Pressione arteriosa < 135/85 mmHg
- Sospensione del fumo
- Attività fisica (≥ 10 MET)

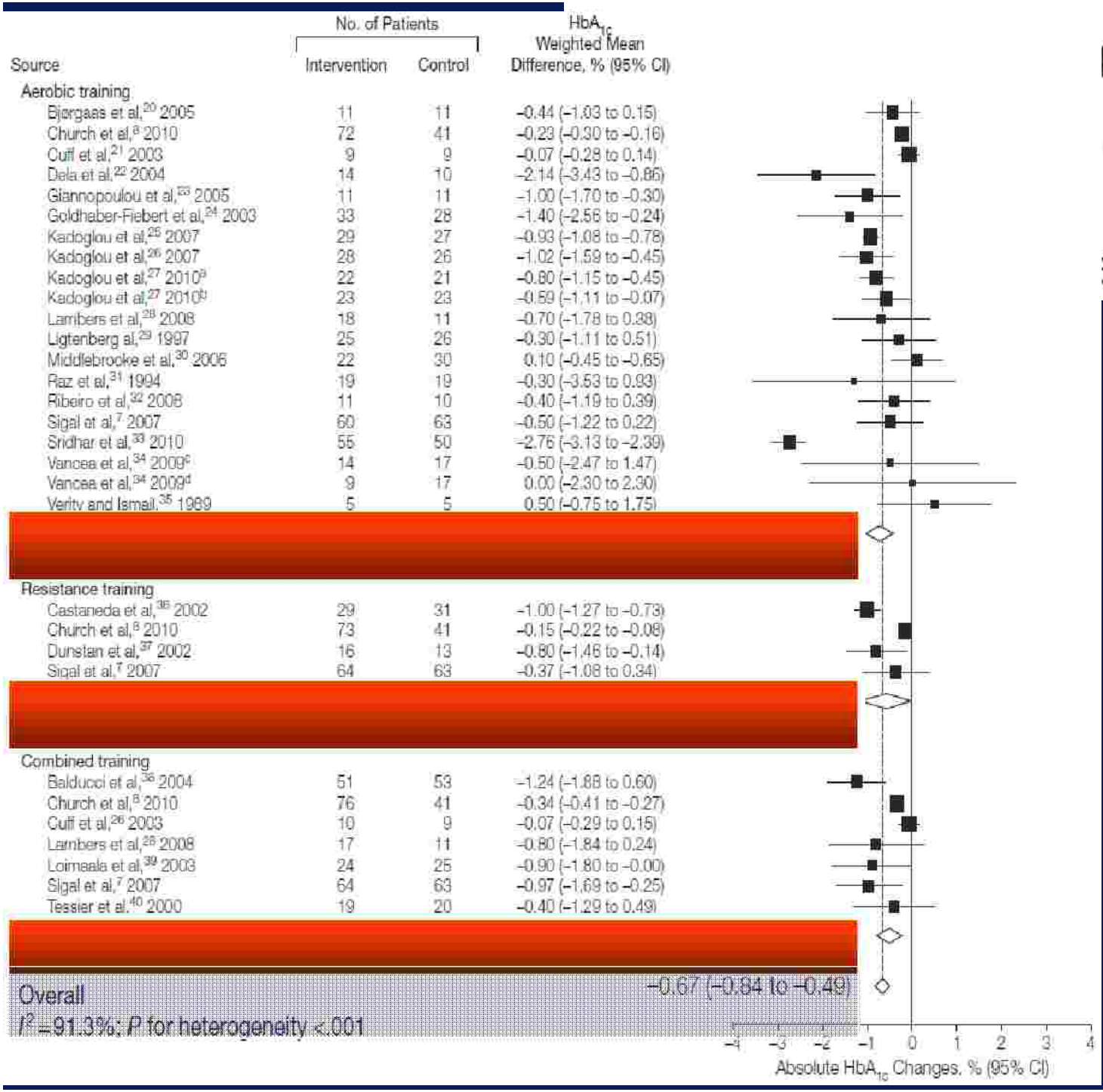
Approccio iniziale raccomandato nell'algoritmo della terapia del diabete tipo 2

Consensus statement ADA/EASD 2012

1. Interventi su stile di vita, considerando l'opportunità di associare dall'inizio farmaci (in genere metformina)

Standard italiani per la cura del diabete AMD/SID 2009-10

1. Interventi su stile di vita
2. Se non sufficiente associare metformina



ce Only or Structured Association Type 2 Diabetes

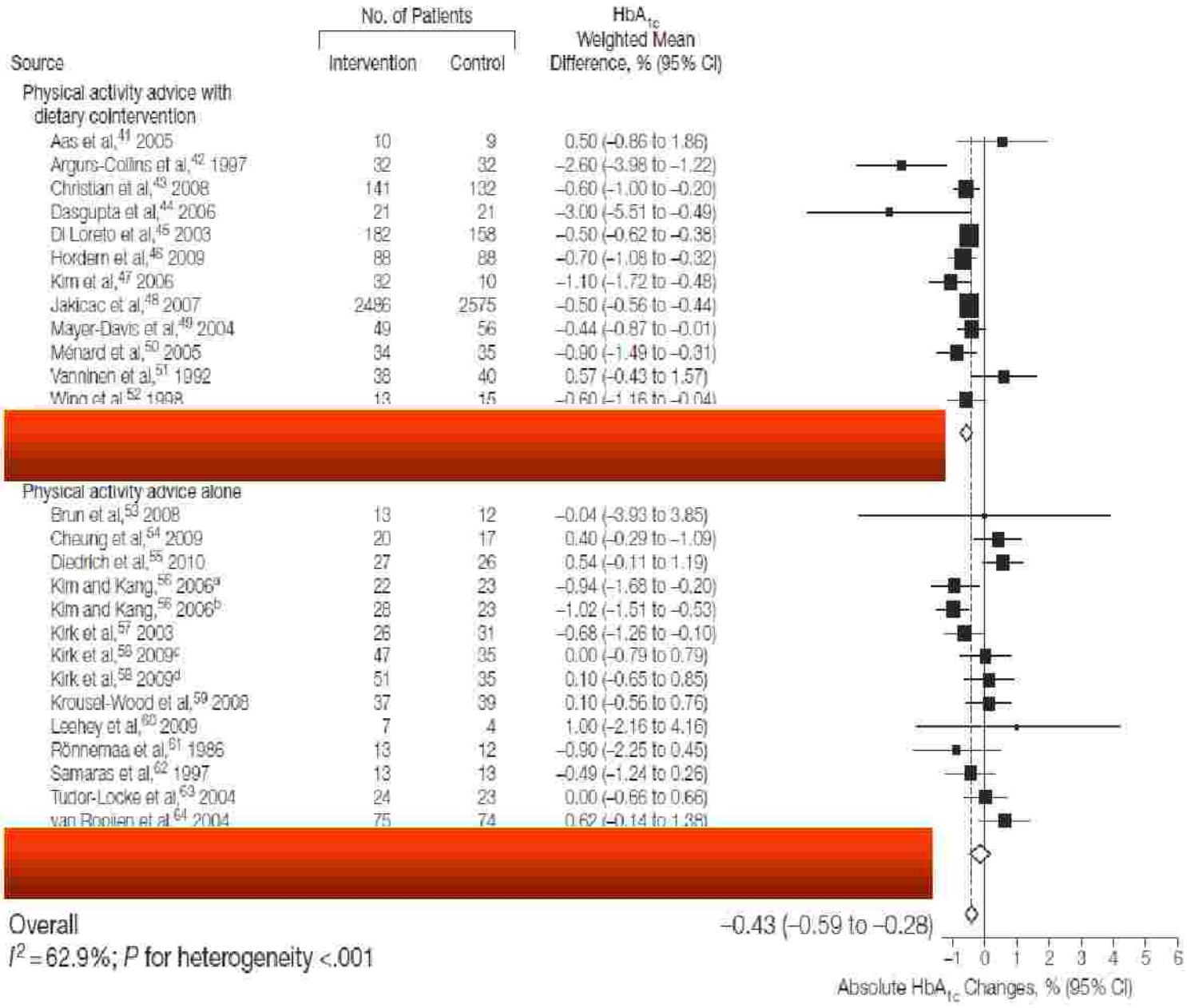
eta-analysis

Effects of aerobic, resistance or combined training on HbA1c

Umpierre et al, JAMA 2011

Physical Activity Advice Only or Structured Exercise Training and Association ype 2 Diabetes

a-analysis

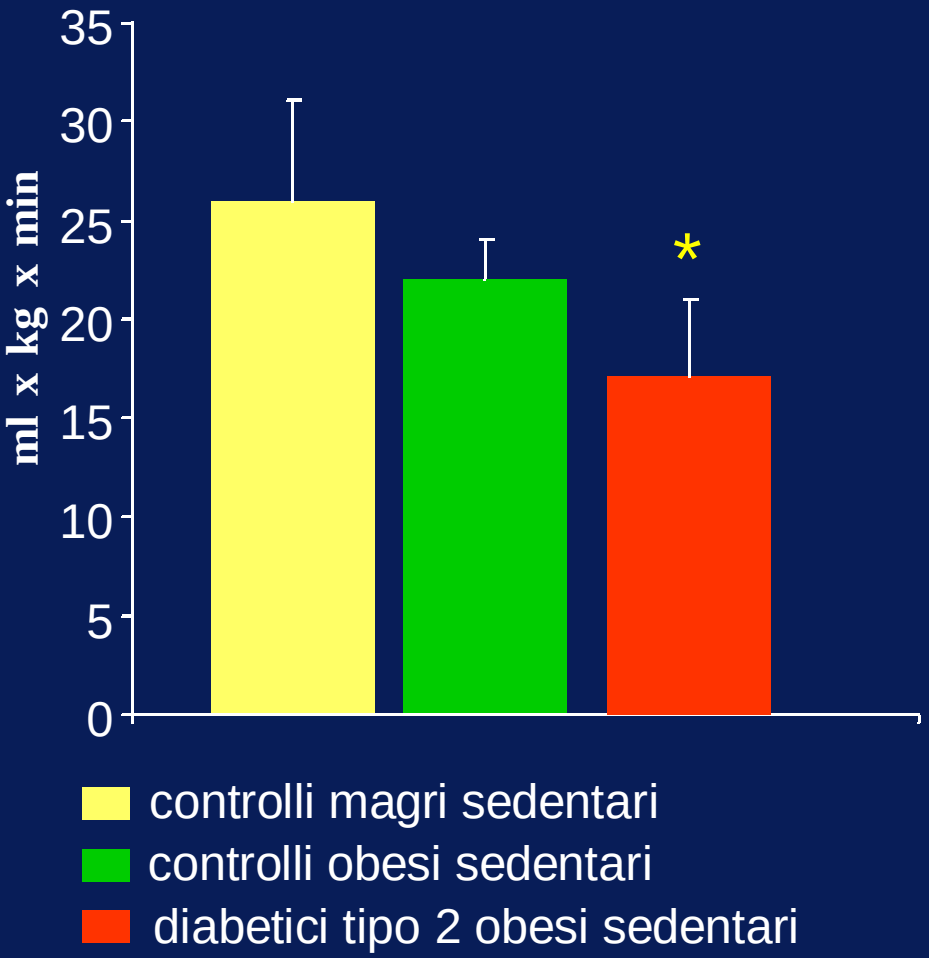


Effects of physical activity advice on HbA1c

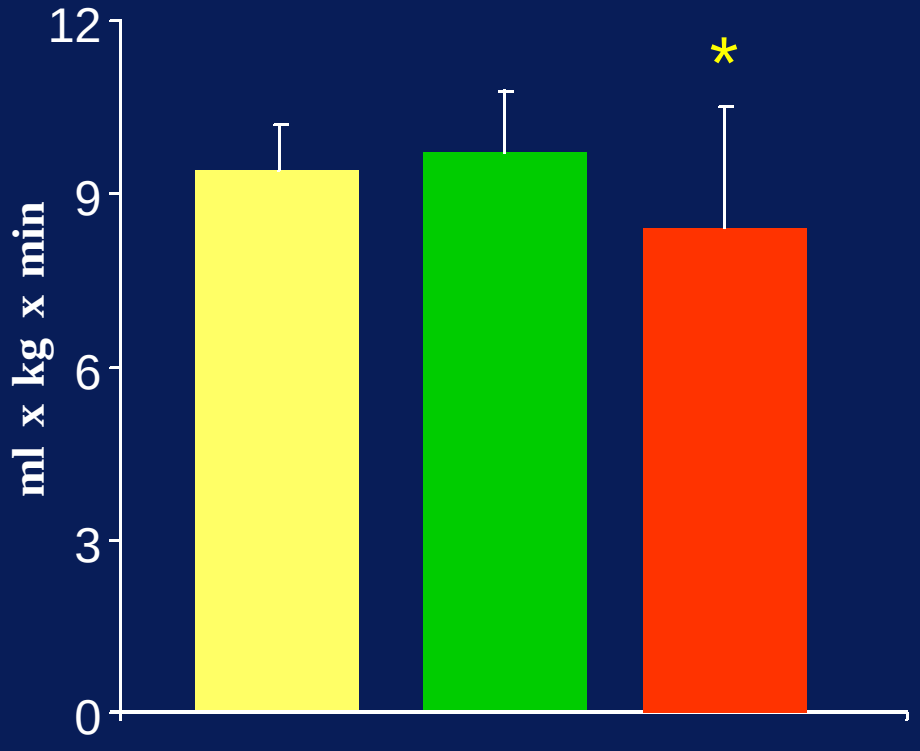
Umpierre et al, JAMA 2011

Captazione di ossigeno durante esercizio al cicloergometro nel diabete tipo 2 non complicato

VO_2 max



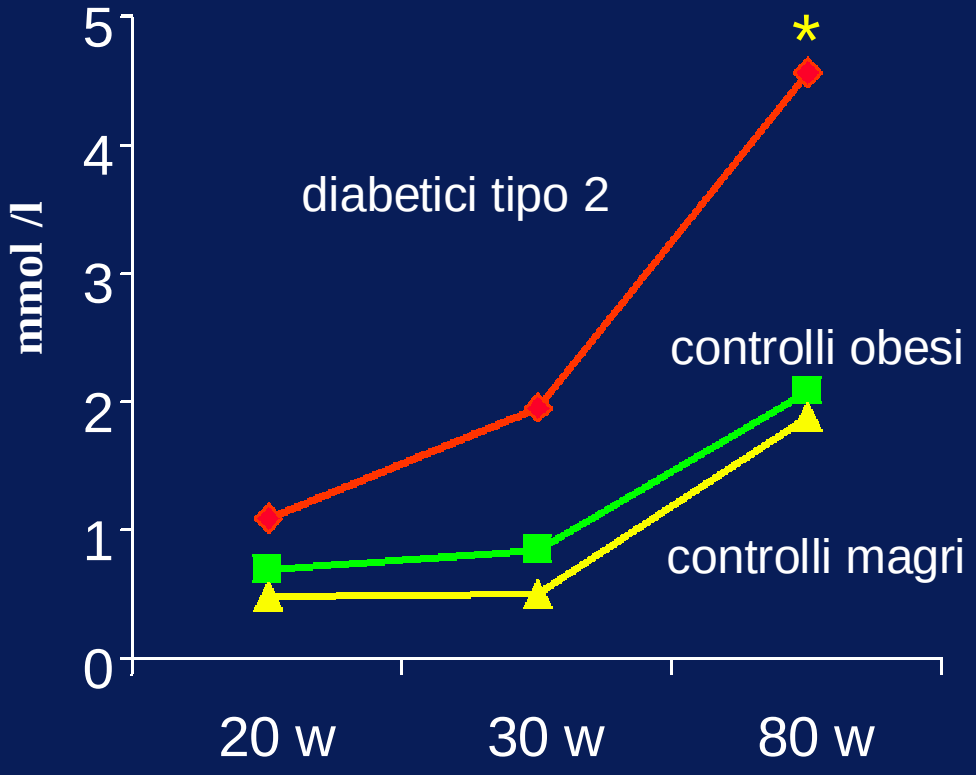
$\Delta VO_2 / \Delta$ lavoro



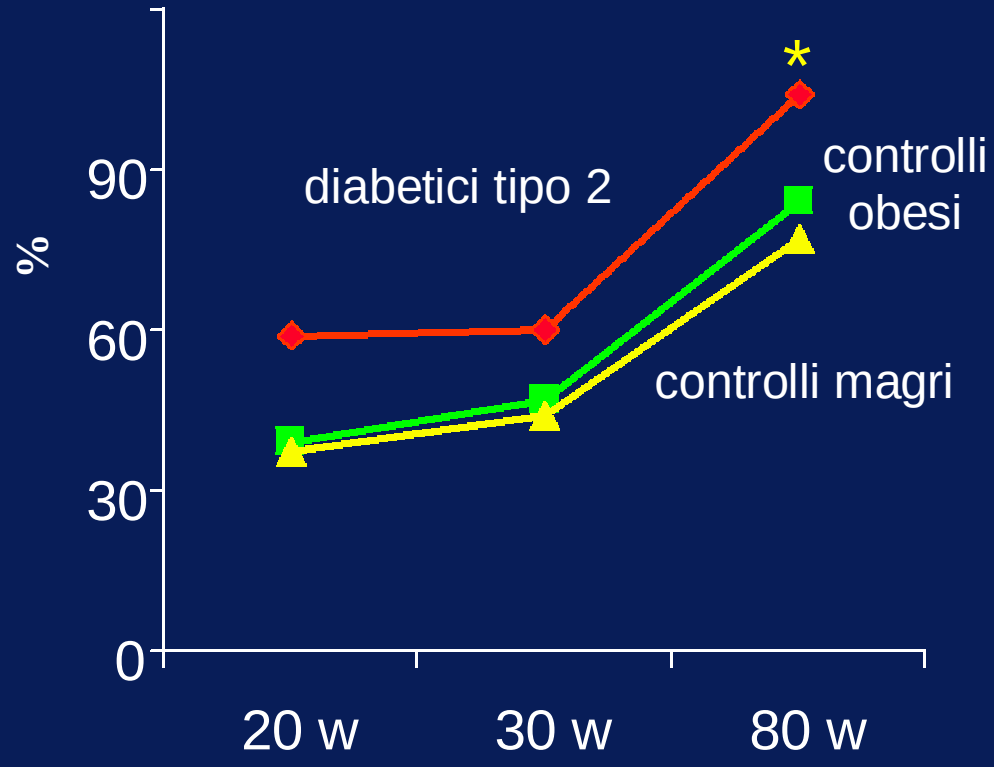
Regensteiner et al, 1998

Risposte all'esercizio submassimale nel diabete tipo 2 non complicato

Lattacidemia

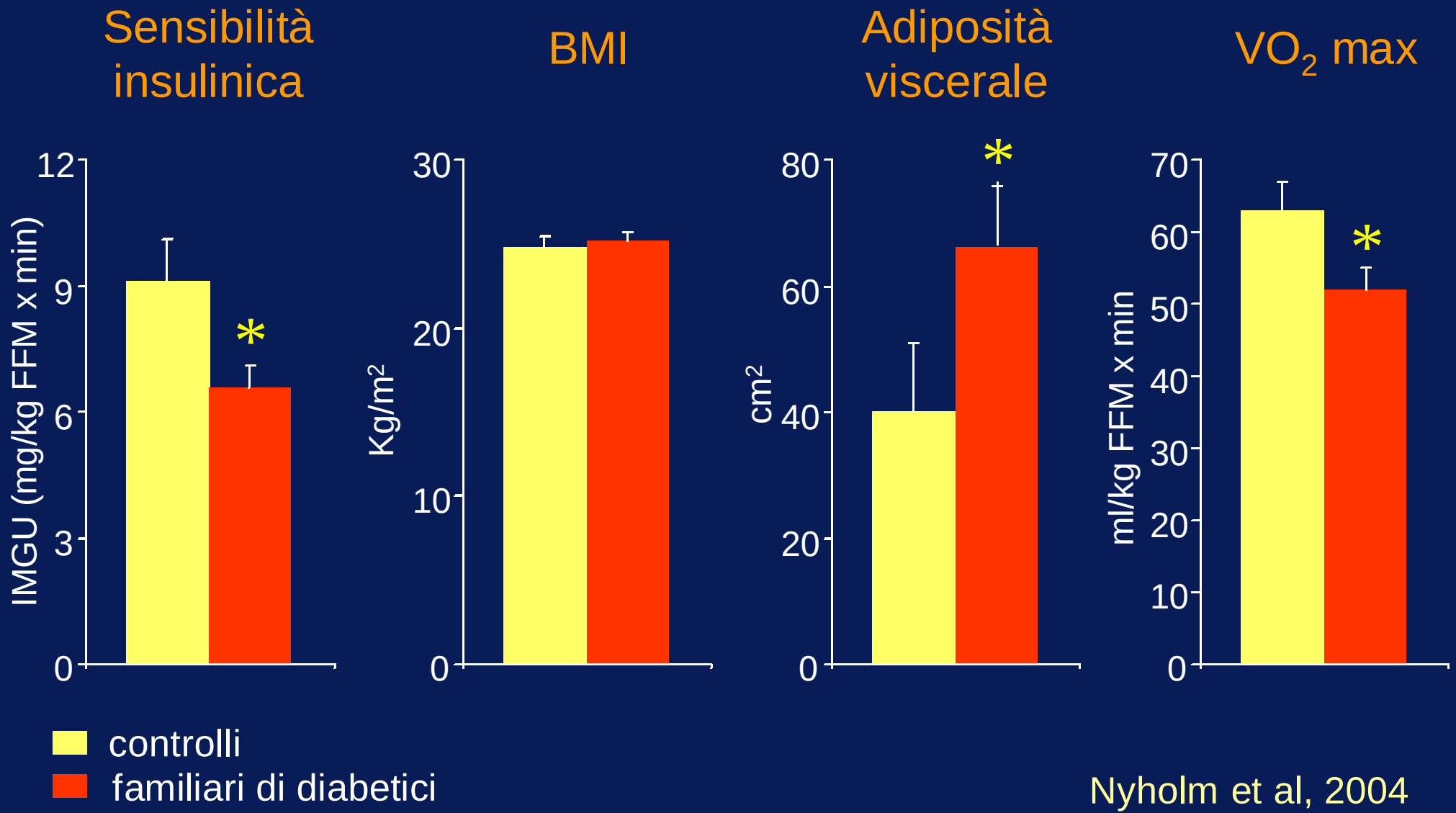


VO_2/ VO_2 max



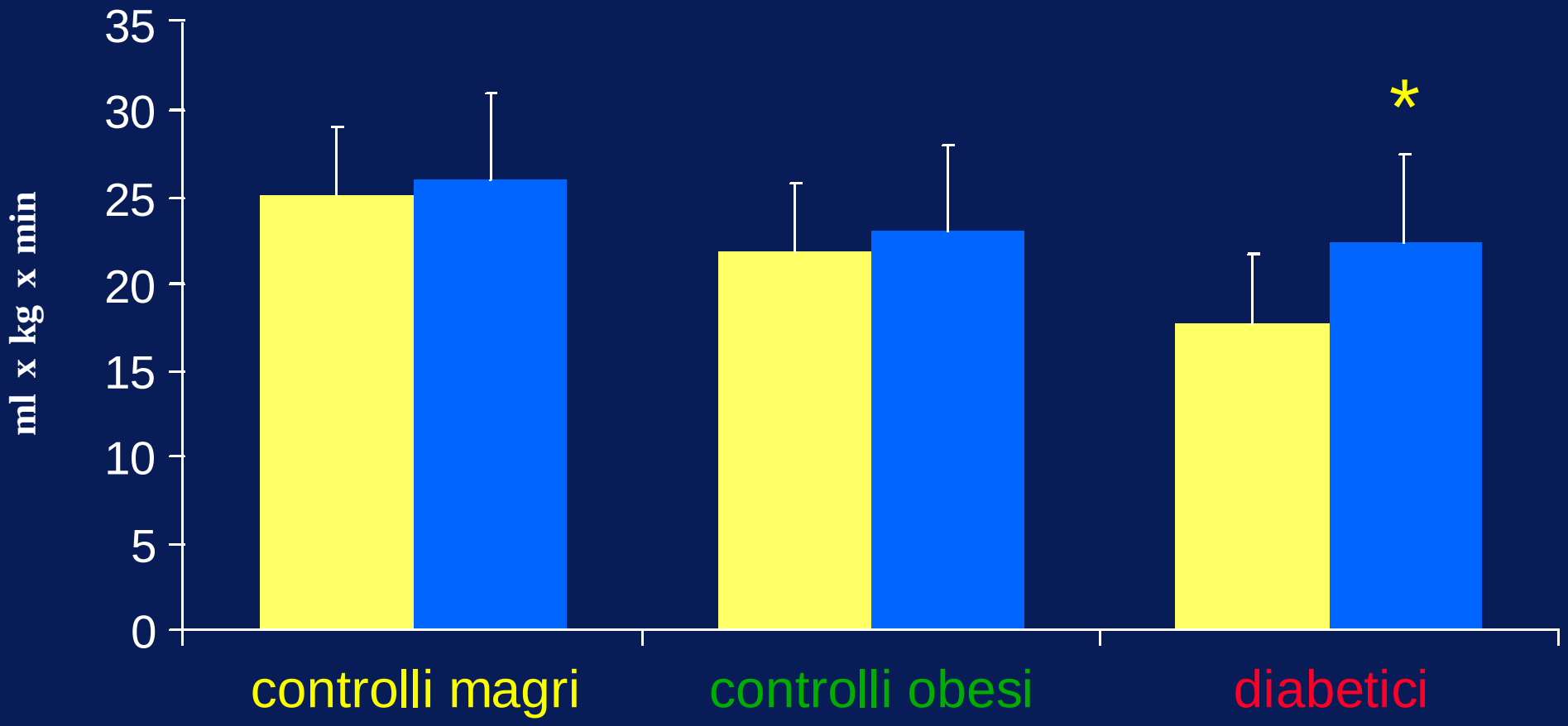
Regensteiner et al, 1998

Adiposità, insulinoresistenza e VO_2 max in soggetti magri normoglicemici con familiarità di 1° grado per diabete tipo 2



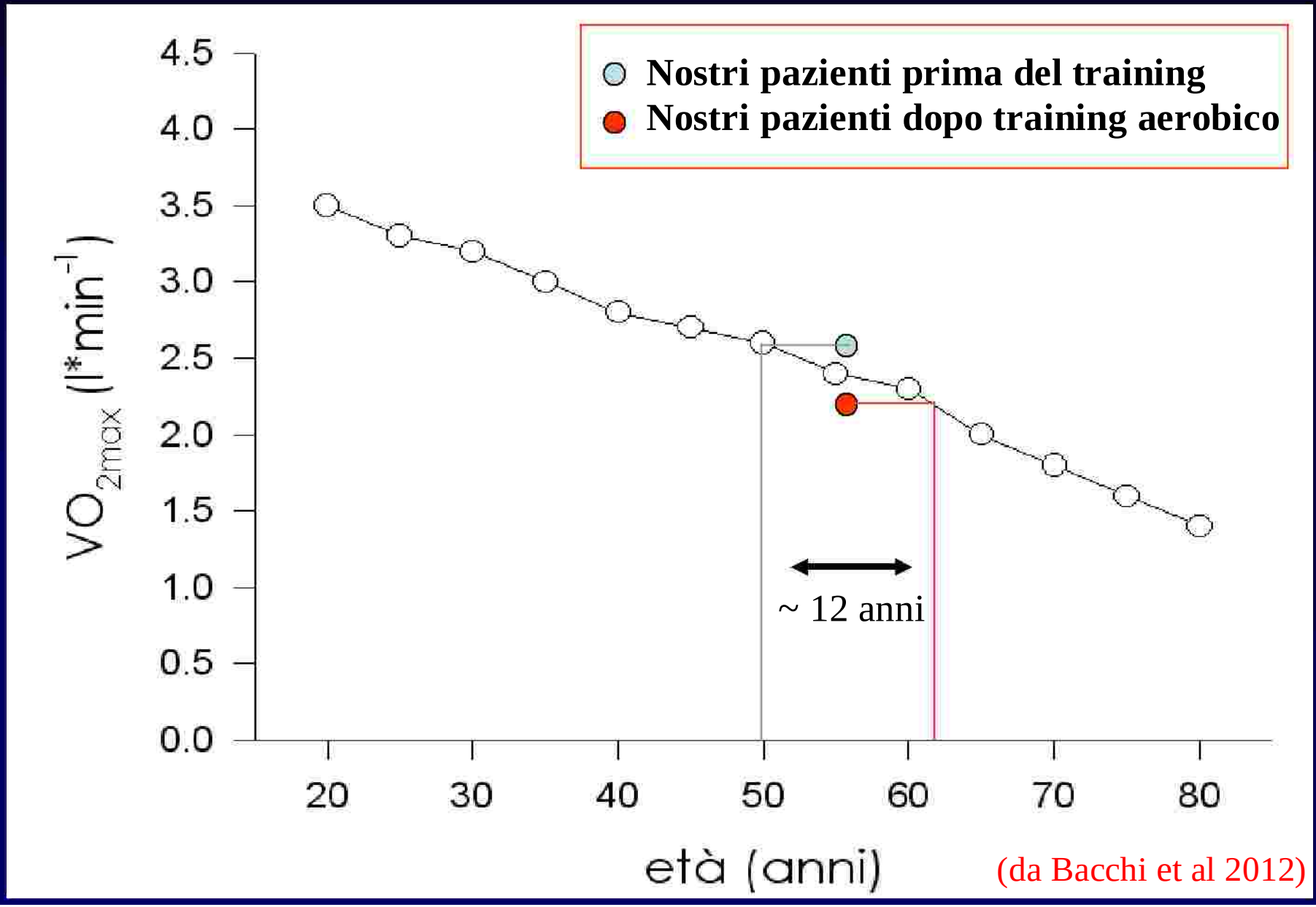
Nyholm et al, 2004

Modificazioni della VO_2 max dopo 3 mesi di training nel diabete tipo 2 (3 h/w 70-85% max)



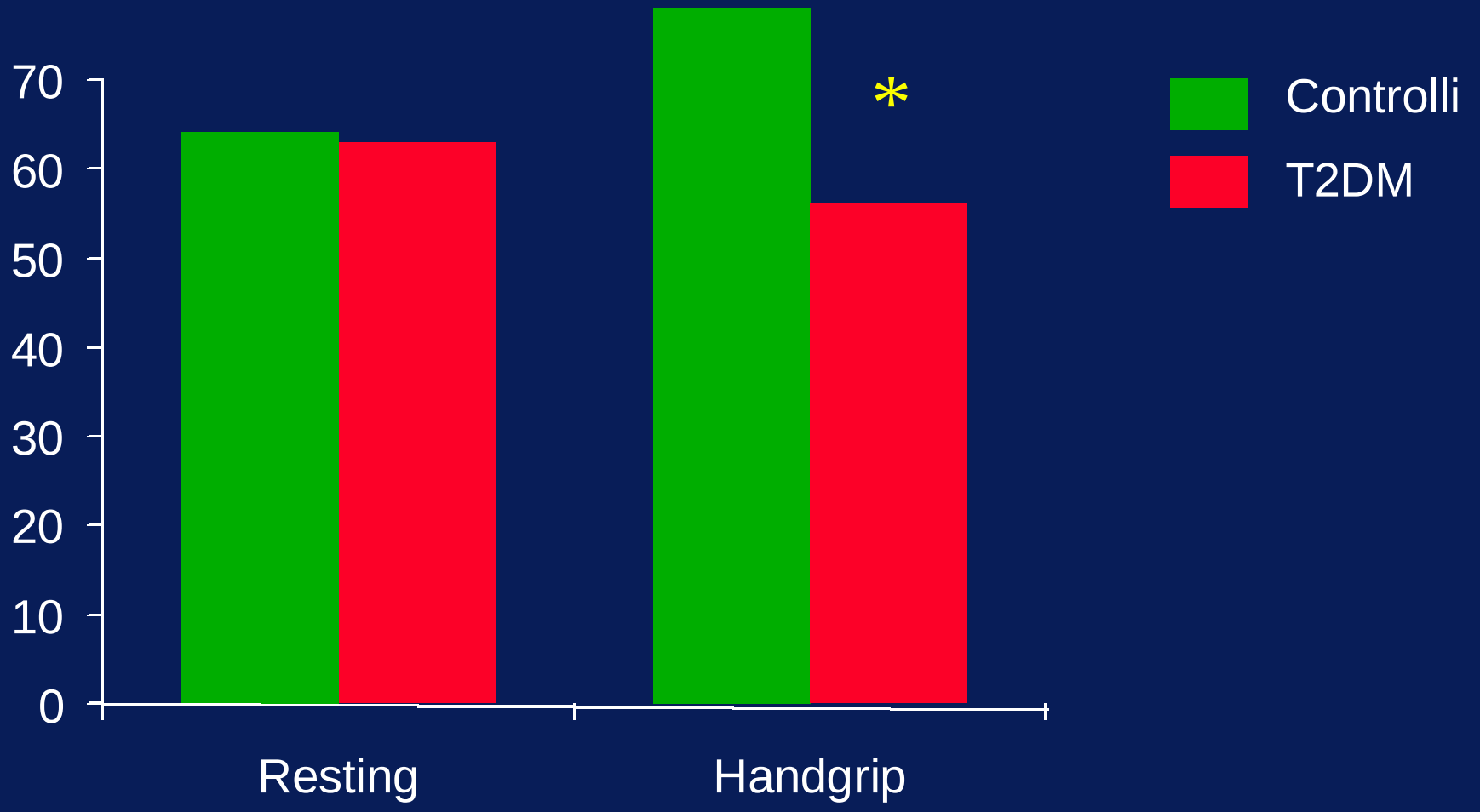
Brandemburg et al, 1999

Modificazioni della capacità aerobica dopo 4 mesi di training rapportate ai valori medi per l'età



(da Bacchi et al 2012)

Frazione di eiezione del ventricolo sinistro in diabetici tipo 2 a riposo e durante handgrip

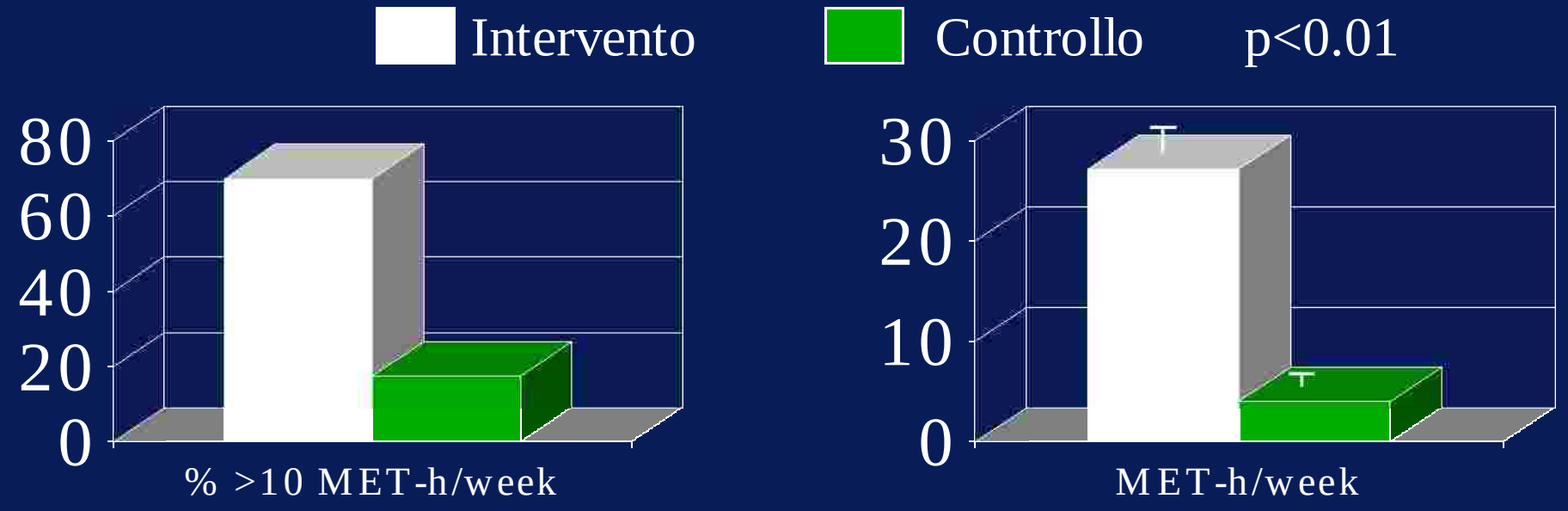


* p<0.01 vs controlli

Scognamiglio et al, 2004


insulinoresistenza
riduzione attività fisica
diabete tipo 2

PERCENTUALE DI SOGGETTI DIABETICI CHE HANNO RAGGIUNTO IL LIVELLO RACCOMANDATO DI ATTIVITA' FISICA E STIME DI ATTIVITA' MEDIA DOPO 2 ANNI DI ATTIVITA' EDUCATIVA INTENSIVA



Di Loreto et al, 2003

Modificazioni osservate in base al livello di attività fisica raggiunto (MET)

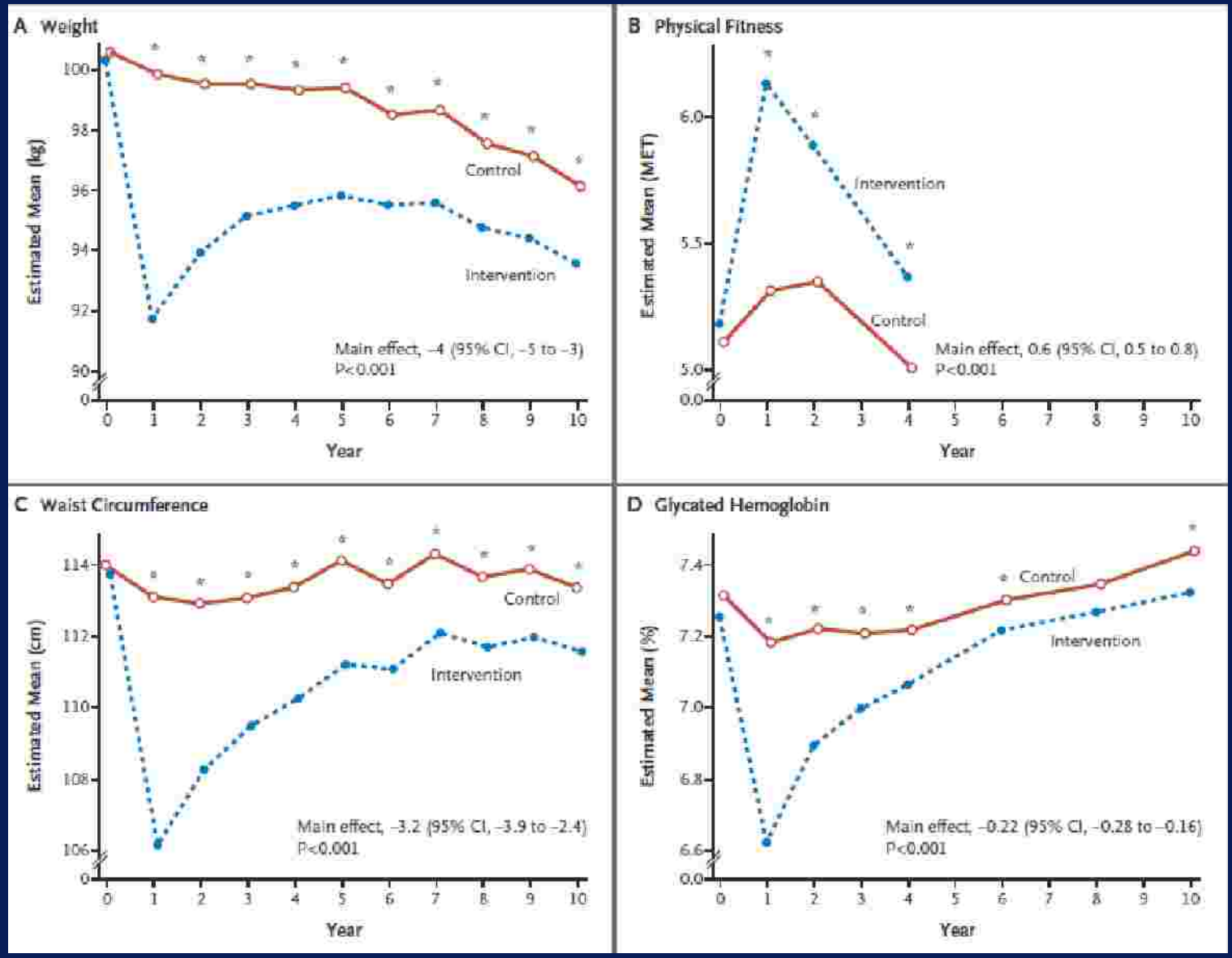
	0	1-10	11-20	21-30	31-40	> 40
Peso Kg	+ 0.8	+ 0.6	+ 0.1	- 2.2	- 3.0	- 3.2
Circonf. vita cm	+ 1.0	+ 1.0	- 0.9	- 3.8	- 5.5	- 7.1
HbA1c %	+ 0.03	- 0.06	- 0.44	- 0.88	- 1.11	- 1.19
PA max mmHg	- 1.8	- 1.5	- 6.4	- 5.5	- 6.6	- 9.2
PA min mmHg	- 4.6	- 2.4	- 2.9	- 4.8	- 5.3	- 7.1
Col. tot mg/dl	- 3.8	- 5.6	- 10.2	- 10.7	- 7.4	- 10.9
Col. LDL mg/dl	- 4.5	- 7.1	- 3.4	- 5.3	- 6.3	- 7.7
Col. HDL mg/dl	+ 0.1	+ 1.1	+ 2.9	+ 5.6	+ 10.4	+ 6.3
TG mg/dl	+ 3.4	+ 2.1	- 48.2	- 55.2	- 57.4	- 68.4
CHD %	+ 0.1	- 0.3	- 2.6	- 3.7	- 4.8	- 4.3

p<0.05

Di Loreto et al, Diabetes Care 2005

Look AHEAD Trial

Changes in weigth, fitness waist and HbA1c after intensive or standard lifestyle intervention

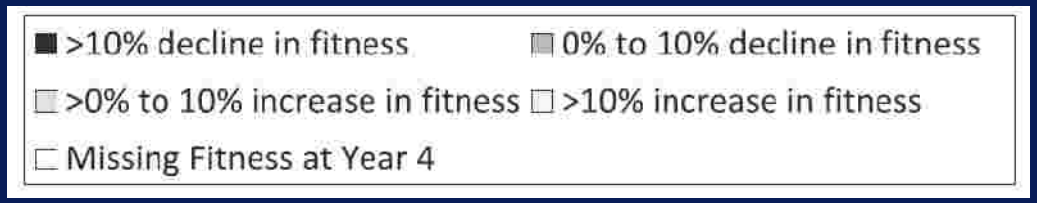


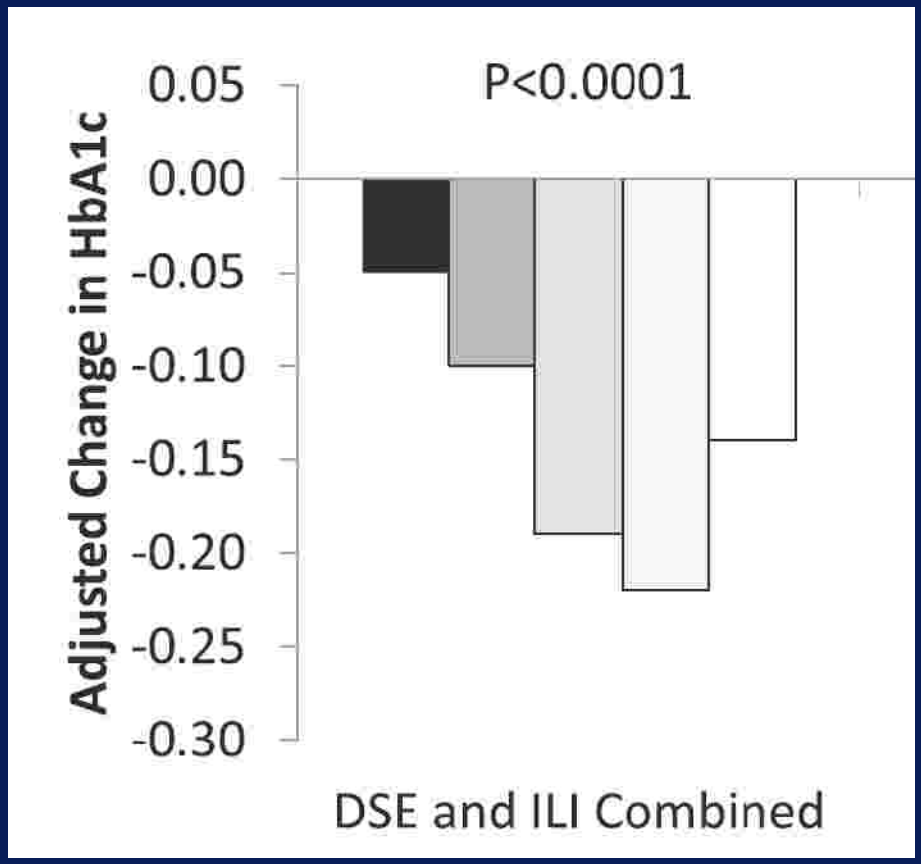
Wing et al, New Engl J Med 2013

Four-Year Change in Cardiorespiratory Fitness and Influence on Glycemic Control in Adults With Type 2 Diabetes in a Randomized Trial

The Look AHEAD Trial

N=3942, mean age 58 yr





(Jakicic et al, Diabetes Care 2013)

Look AHEAD Trial

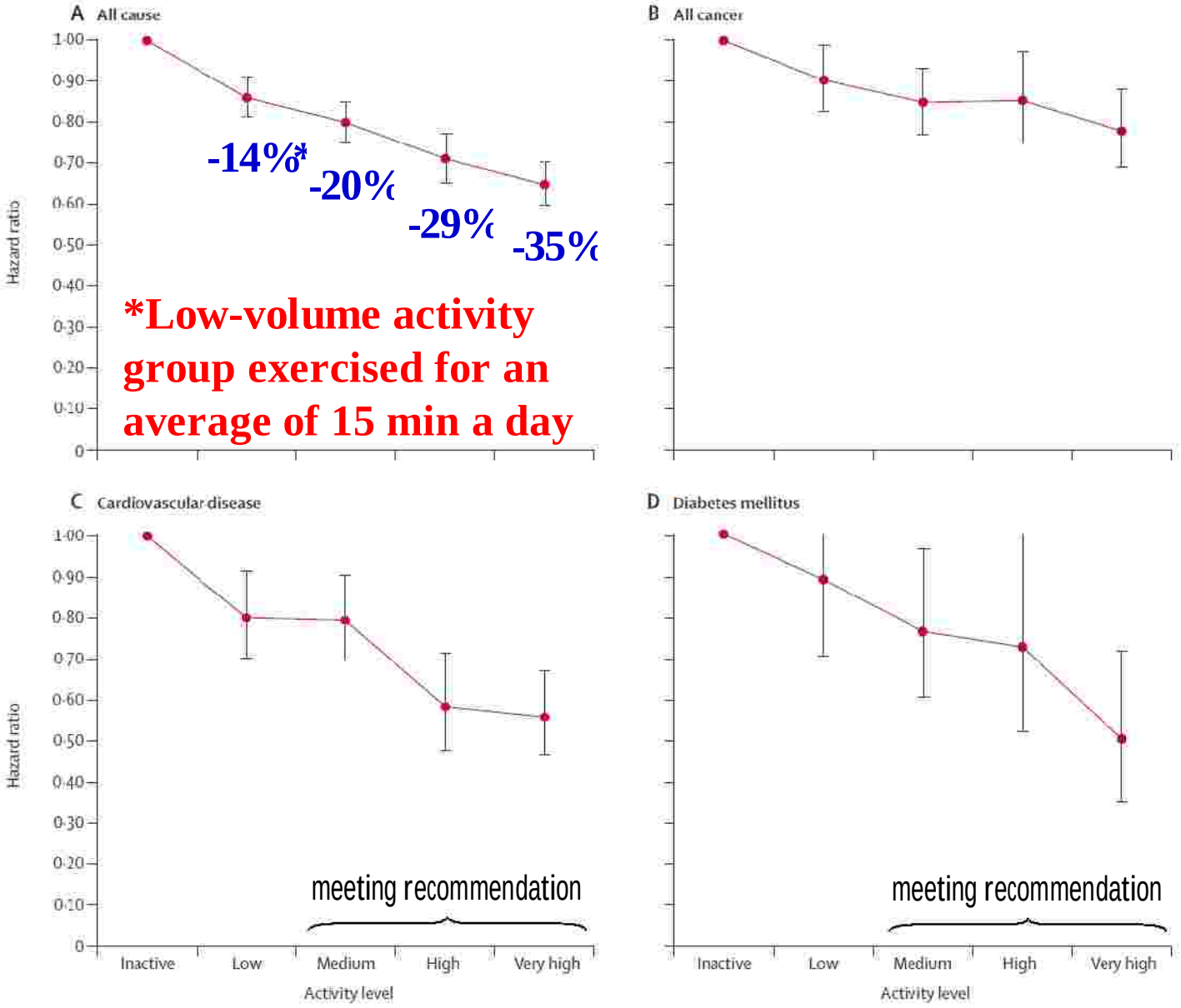
Death and other cardiovascular outcomes after intensive or standard lifestyle intervention

Wing et al, New Engl J Med 2013

Table 2. Primary and Secondary Outcomes and Other Cardiovascular Outcomes.*

Outcome	Patients with Event	Control Group	Intervention Group	Hazard Ratio (95% CI)	P Value
	no.	*no. of events (rate/100 person-yr)*			
Primary outcome					
Death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for angina	821	418 (1.92)	403 (1.83)	0.95 (0.83–1.09)	0.51
Secondary outcomes					
Death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke	550	283 (1.25)	267 (1.17)	0.93 (0.79–1.10)	0.42
Death from any cause, nonfatal myocardial infarction, or nonfatal stroke	1025	529 (2.43)	496 (2.25)	0.93 (0.82–1.05)	0.23
Death from any cause, nonfatal myocardial infarction, nonfatal stroke, hospitalization for angina, CABG, PCI, hospitalization for heart failure, carotid endarterectomy, or peripheral vascular disease	1177	600 (2.81)	577 (2.67)	0.94 (0.84–1.05)	0.29
Other cardiovascular outcomes					
Death					
Any cause	376	202 (0.86)	174 (0.73)	0.85 (0.69–1.04)	0.11
Cardiovascular cause	109	57 (0.24)	52 (0.22)	0.88 (0.61–1.29)	0.52
Myocardial infarction					
Fatal or nonfatal†	354	191 (0.84)	163 (0.71)	0.84 (0.68–1.04)	0.11
Fatal	16	11 (0.05)	5 (<0.02)	0.44 (0.15–1.26)	0.13
Nonfatal	342	183 (0.80)	159 (0.69)	0.86 (0.69–1.06)	0.16
Hospitalization for angina	390	196 (0.87)	194 (0.85)	0.97 (0.80–1.19)	0.79
Stroke	165	80 (0.34)	85 (0.36)	1.05 (0.77–1.42)	0.78
Heart failure	218	119 (0.51)	99 (0.42)	0.80 (0.61–1.04)	0.10
CABG	525	269 (1.21)	256 (1.14)	0.93 (0.78–1.10)	0.41
Carotid endarterectomy	54	25 (0.11)	29 (0.12)	1.10 (0.64–1.87)	0.74

Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study



Relation between level of physical activity and mortality; reference was inactive people (n=416 175 from Taiwan, average follow up 8 yr).

Wen et al, Lancet 2011

Combined effect of diabetes and physical inactivity on CVD death risk - The HUNT 2 cohort study

(n=53587 subjects from Norway, median follow-up 12 yr)

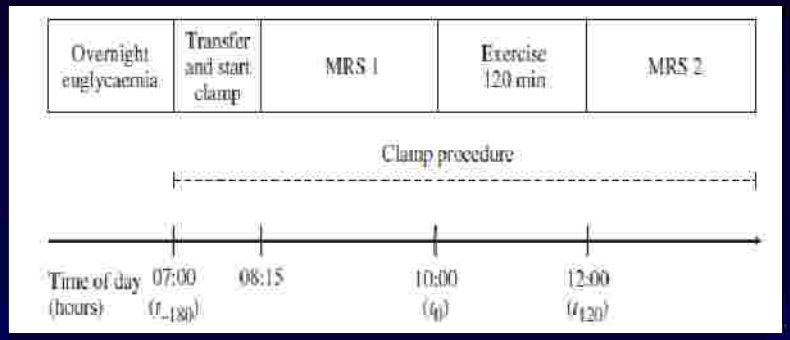
	No diabetes				Diabetes			
Physical activity	Person-years	Deaths N	HR (95% CI)[a]	P_{trend}[b]	Person-years	Deaths N	HR (95% CI)[a]	P_{trend}[b]
Inactive	35,056	215	1.00 (Reference)	—	1,102	33	2.81 (1.93–4.07)	—
Light activity								
<1 h	48,182	153	1.04 (0.84–1.28)	—	997	19	2.81 (1.75–4.51)	—
1–2 h	62,459	192	0.86 (0.71–1.05)	—	1,438	15	1.07 (0.63–1.81)	—
≥3 h	36,220	172	0.78 (0.63–0.96)	0.007	1,055	11	0.89 (0.48–1.63)	<0.001
Total activity[c]								
Low	200,260	648	0.92 (0.78–1.07)	—	2,212	78	1.77 (1.36–2.30)	—
Medium	213,450	507	0.74 (0.63–0.87)	—	4,796	38	1.04 (0.73–1.47)	—
High	181,546	184	0.66 (0.53–0.81)	<0.001	2,387	13	0.91 (0.51–1.60)	<0.001

[a]Adjusted for age (as the time scale), sex (man, woman), smoking status (never, former, current, unknown), alcohol consumption (0, 1, 2–3, ≥4 times last month, total abstainer, unknown), education (<10, 10–12, >13 years, unknown), BMI (kg/m^2), systolic blood pressure (mmHg), and total serum cholesterol (mmol/L). [b]Test for linear trend across categories of physical activity. [c]Total activity level defined as inactive (no light or hard activity, 2), low (<3 h light and/or <1 h hard activity), medium (≥3 h light and/or <1 h hard activity), and high (any light and >1 h hard activity).

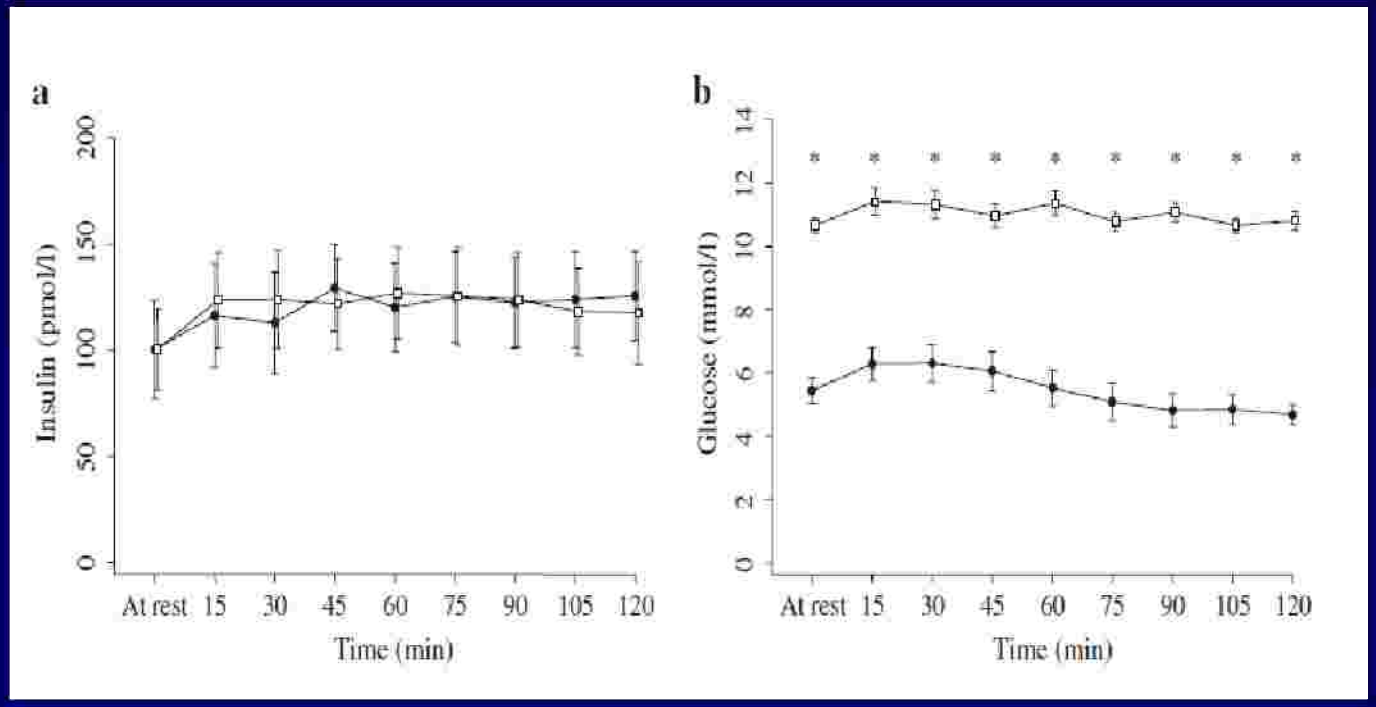
Moe et al, Diab Care 2012

La glicemia di un diabetico condiziona,
a parità di livelli di insulina,
l’utilizzo dei substrati durante esercizio?

Fuel metabolism during exercise in euglycaemia and hyperglycaemia in patients with type 1 diabetes



7 Physically active men with type 1 diabetes
Byke, 55-60% VO2max



Lattacidemia (mmol/L)

basale		**picco**
0.6	→	**1.3**
0.7	→	**1.4**

(Jenni et al, Diabetologia 2008)

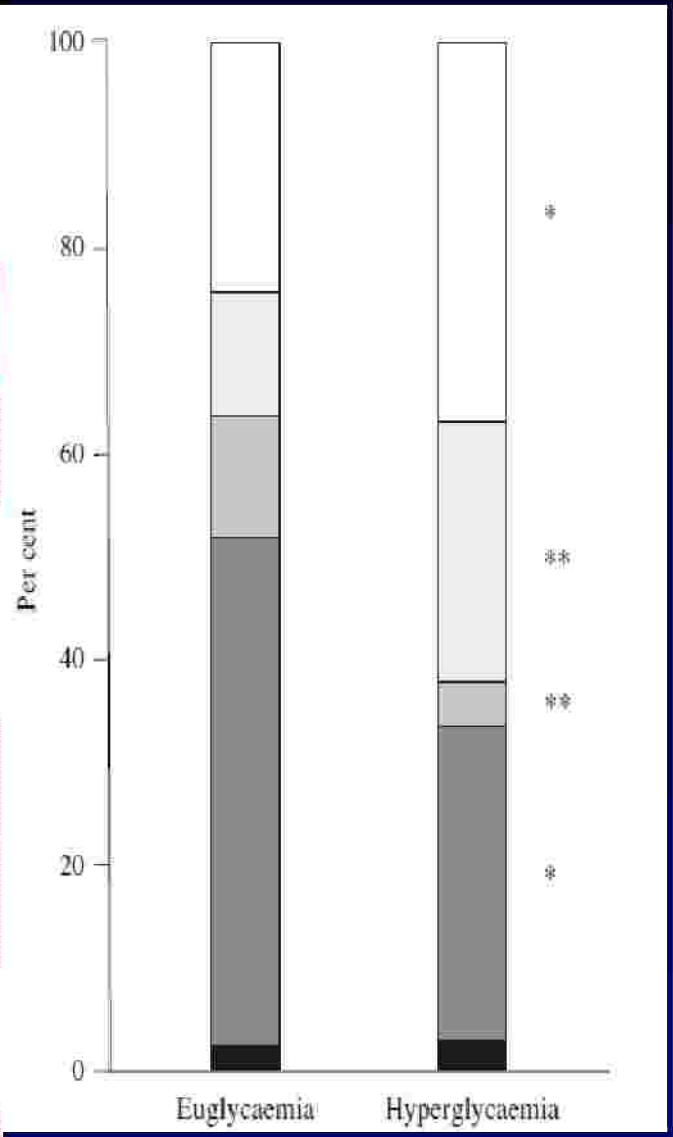
Fuel metabolism during exercise in euglycaemia and hyperglycaemia in patients with type 1 diabetes

Table 1 Respiratory gas exchange and net substrate oxidation rates

Parameter	Rest	Exercise	
		60 min	120 min
$\dot{V}O_2$ (ml min^{-1} kg^{-1})			
Euglycaemia	4.4±0.8	28.6±2.4[c]	29.7±2.1[c,d]
Hyperglycaemia	5.0±0.2	28.2±2.0[c]	28.4±2.0[a,c]
$\dot{V}CO_2$ (ml min^{-1} kg^{-1})			
Euglycaemia	3.4±0.6	24.5±2.0[c]	24.9±1.9[c]
Hyperglycaemia	3.9±0.2	25.0±1.7[c]	25.4±1.8[c]
Lipid oxidation (mg min^{-1} kg^{-1})			
Euglycaemia	1.6±0.4	6.6±0.8[c]	7.7±0.8[c,d]
Hyperglycaemia	1.7±0.2	5.1±0.9[b]	4.8±0.8[a,b]

Table 2 Glucose turnover

Parameter	Rest	Exercise
Endogenous glucose production (mg min^{-1} kg^{-1})		
Euglycaemia	2.4±0.2	4.0±0.6[c]
Hyperglycaemia	1.9±0.6	1.9±0.8[b]
Glucose disposal (mg min^{-1} kg^{-1})		
Euglycaemia	2.6±0.1	8.4±0.8[c]
Hyperglycaemia	2.9±0.3	11.3±1.6[d]
Oxidation rate of systemic glucose (mg min^{-1} kg^{-1})		
Euglycaemia	1.9±0.3	8.4±1.1
Hyperglycaemia	1.6±0.1	10.3±1.3[c]
Glycogen breakdown rate (mg min^{-1} kg^{-1})		
Euglycaemia	−0.8±0.6	9.3±2.4[d]
Hyperglycaemia	−0.6±0.4	13.2±1.8[a,c]



Contributo relativo dei diversi substrati

Glycogen

Glucose infused

Endogenous glucose

Lipids

Proteins

(Jenni et al, Diabetologia 2008)

Caratteristiche peculiari dei pazienti con diabete tipo 2

- Spesso anziani
- Spesso in sovrappeso/obesi
- Spesso in terapie poli-farmacologiche
- Rischio di ipoglicemia farmaco-indotta
- Complicanze croniche frequenti, anche al momento della diagnosi di diabete
- Alterata efficienza metabolica

Implicazioni energetiche delle alterazioni metaboliche del diabete tipo 2

- Iperglicemia = difficoltà ad utilizzare il glucosio, stato di carenza energetica cellulare
- Insulinoresistenza = ridotta e alterata risposta all'insulina, presenza di multipli fattori di rsichio cardiovascolare
- Ridotta flessibilità metabolica = ridotta capacità di adattare l'ossidazione dei substrati alle variazioni omeostatiche

La capacità aerobica massima dei diabetici tipo 2 è in media di ~22 ml/kg min, cioè 6.4 MET *

Questo implica che nel diabetico “medio” si possono prescrivere esercizi aerobici di intensità fino a 4.8 MET (75% del massimo).

* *Boulè et al, Diabetologia 2003*

Measuring Habitual Walking Speed of People With Type 2 Diabetes

Are they meeting recommendations?

Table 1—*Median, 25th, and 75th percentiles of 3-day averaged ambulatory characteristics obtained from an AMP**

Ambulation characteristic	Median	25th percentile	75th percentile
Total daily steps	9,150	5,394	11,469
Locomotion steps	5,331	2,444	7,015
Locomotion walking speed (km/h)	3.3	2.9	3.7
Locomotion cadence (steps/min)	106	102	111
Time spent in locomotion (min)	49.4	26.1	58.5
Distance in locomotion (km)	2.7	1.2	4.2
Time spent at or above 4.0 km/h (min:sec)	06:13	02:06	27:25

***Activity Monitoring Pod 331**

Johnson et al, Diabetes Care 2005

Supervised Walking Groups to Increase Physical Activity in Type 2 Diabetic Patients

Diabetes Care 33:1–2, 2010

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Table 1—*Comparison of changes observed in subjects who attended at least 50% of supervised walking sessions and in control subjects*

	Intervention group		Control group		
	Baseline	4 months	Baseline	4 months	*P*
n	21	21	20	20	
Age (years)	65.7 ± 4.9		65.7 ± 5.2		
Duration of diabetes (years)	10.7 ± 7.4		11.9 ± 8.4		
Body weight (kg)	75.4 ± 11.5	74.5 ± 11.3	77.7 ± 12.7	77.4 ± 12.8	0.49
BMI (kg/m^2)	29.2 ± 4.2	28.9 ± 4.2	29.5 ± 4.9	29.3 ± 4.7	0.63
Total cholesterol (mg/dl)	179 ± 32	175 ± 28	177 ± 34	178 ± 36	0.32
HDL cholesterol (mg/dl)	51.4 ± 10.9	52.0 ± 12.4	54.7 ± 11.4	52.7 ± 11.1	0.29
LDL cholesterol (mg/dl)	104.2 ± 29.8	100.9 ± 25.1	98.9 ± 28.4	101.6 ± 29.5	0.24
Triglyceride (mg/dl)	119 ± 51.1	109 ± 49.4	116 ± 43.0	118 ± 48.4	0.21
Systolic blood pressure (mmHg)	133 ± 14.5	134 ± 13.9	133 ± 16.0	134 ± 16.1	0.96
Diastolic blood pressure (mmHg)	80 ± 6.2	78 ± 7.1	75 ± 6.5	77 ± 8.0	0.15
6-mWT (m)	521 ± 37.2	612 ± 78.8*	554 ± 49.2	574 ± 60.8†	0.001
Energy expenditure through voluntary physical activity (MET h × week)	10.0 ± 11.2	18.6 ± 10.1*	11.9 ± 11.9	14.9 ± 10.3	0.008
Changes to antidiabetic medication regimen					
Dose increased	—	5	—	5	
Dose decreased or therapy discontinued	—	33	—	5	0.05
No change to regimen	—	62	—	90	

-33 %

-5 %

Data are means ± SD or percent, unless otherwise indicated. *P* values refer to comparison between intervention and control groups by ANOVA for repeated measures or, for comparison in changes to antidiabetic regimen, by Fisher exact test. In this analysis, subjects were grouped according to whether or not they had a reduction in antidiabetic medications. *<0.001 intragroup comparison; †<0.05 intragroup comparison.

Exercise and Type 2 Diabetes
ACSM & ADA Joint Position Statement 2010

- Attività aerobica: almeno 3 ma meglio 5 giorni/settimana
- Per almeno 150 min/settimana se moderata (40-60% VO2 max) o 60-75 min se vigorosa (61-75% VO2max)
- Se moderata, valutare la possibilità di una intensificazione

Colberg et al, Diabetes Care

Exercise and Type 2 Diabetes
ACSM & ADA Joint Position Statement 2010

- Attività di forza: da associare all'attività aerobica, almeno 2 ma meglio 3 giorni/settimana, per migliorare forza e azione insulinica
- Moderata (~50% 1-RM) o meglio vigorosa (75-80% 1-RM)
- Lenta progressione fino a 1-4 serie di 8-10 ripetizioni di 5-10 esercizi, con uso di macchine di resistenza e pesi liberi, a carico dei principali muscoli di arti superiori, arti inferiori e tronco
- Se autogestita può essere meno efficace per il control o metabolico, adeguata per massa muscolare e forza

Colberg et al, Diabetes Care

Exercise and Type 2 Diabetes
ACSM & ADA Joint Position Statement 2010

- Initial instruction and periodic supervision by a qualified exercise trainer is recommended for most persons with type 2 diabetes, particularly if they undertake resistance exercise training.
- Use of objective measures such as step counters may enhance reaching daily goals.

Colberg et al, Diabetes Care

Strength Training Increases Insulin-Mediated Glucose Uptake, GLUT4 Content, and Insulin Signaling in Skeletal Muscle in Patients With Type 2 Diabetes

Mads K. Holten,[1,2] Morten Zacho,[2] Michael Gaster,[3] Carsten Juel,[2,4] Jørgen F.P. Wojtaszewski,[2,5] and Flemming Dela[1,2]

DIABETES, VOL. 53, FEBRUARY 2004

- disegno sperimentale -

10 diabetici tipo 2
7 controlli

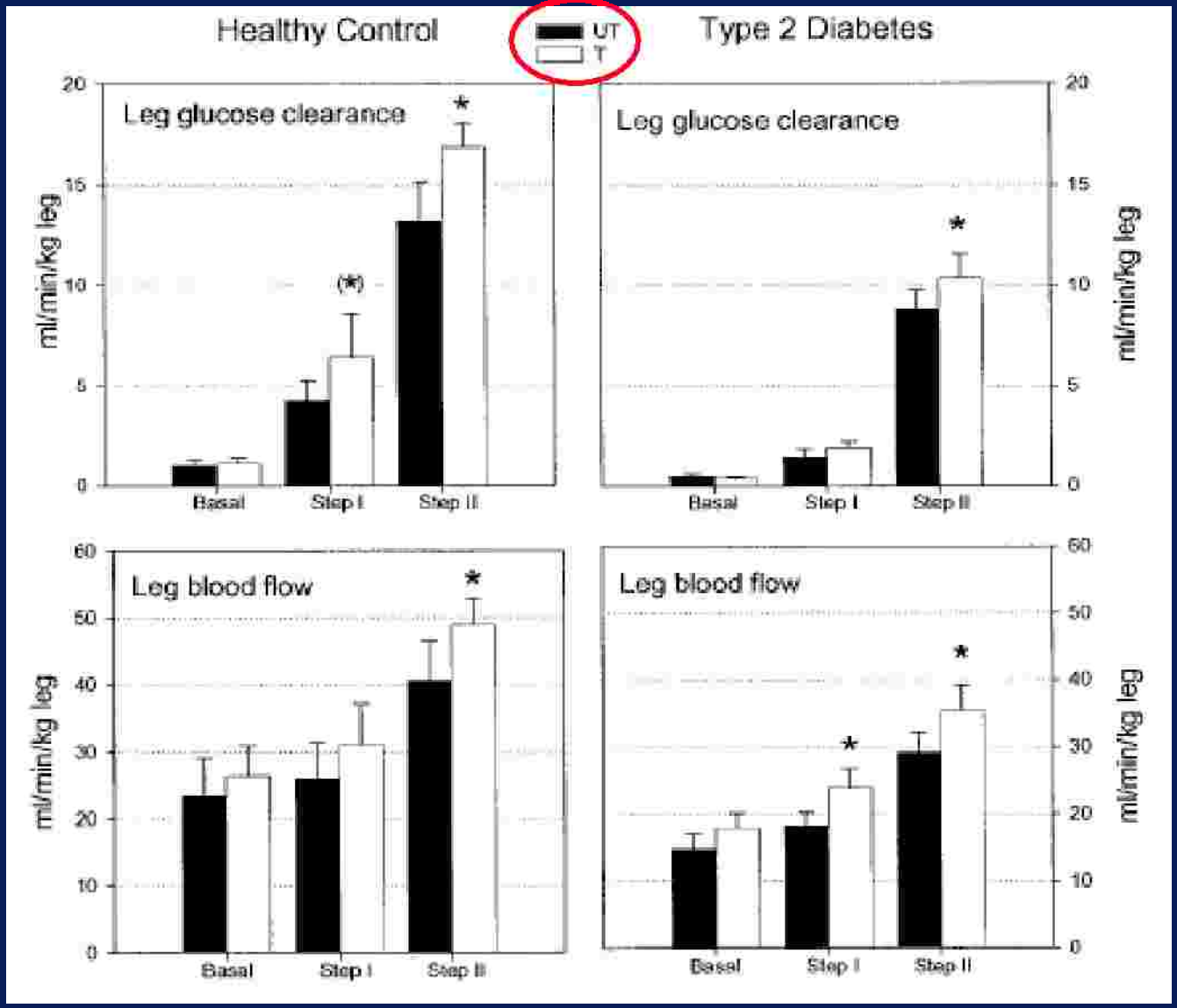
Un arto sottoposto ad allenamento di forza

Un arto non sottoposto ad allenamento

Dopo 6 settimane di allenamento moderato supervisionato (30’ x 3/settimana):

- clamp euglicemico con cateterismo artero-venoso femorale bilaterale
- biopsia muscolare su entrambi gli arti

Clearance del glucosio e flusso sanguigno alla gamba, basali e durante clamp, nell'arto sottoposto ad allenamento di forza e in quello non allenato in controlli e diabetici tipo 2



Allenamento supervisionato:
30'x3/settimana x 6 settimane

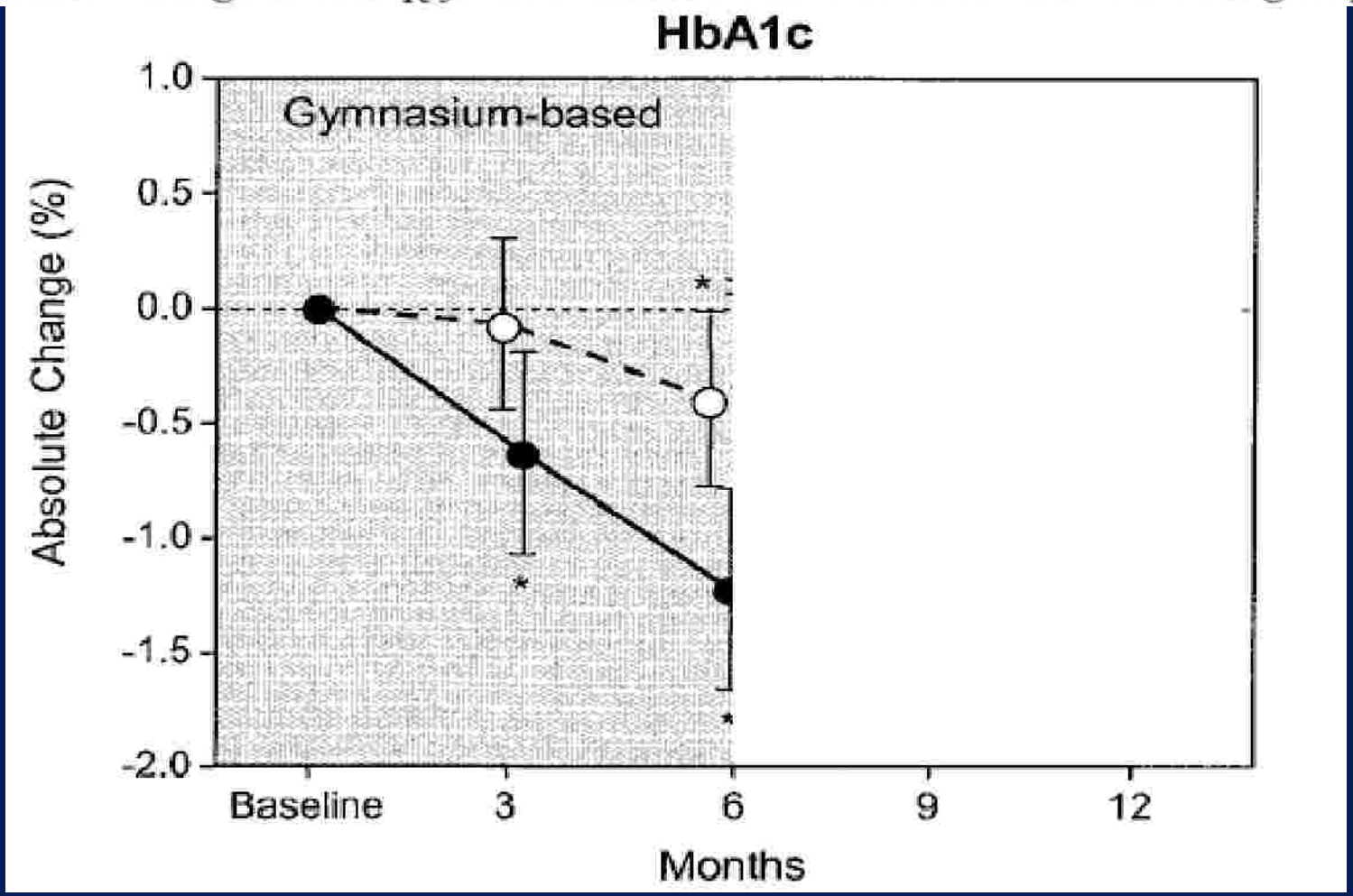
Infusione insulinica nel clamp:
28 and 480 mU/m2 min

Holten et al, Diabetes 2004

Home-Based Resistance Training Is Not Sufficient to Maintain Improved Glycemic Control Following Supervised Training in Older Individuals With Type 2 Diabetes

Dunstan et al,
Diabetes Care 2005

Absolute change in HbA_{1c} from baseline in RT&WL (●) and WL (○) groups



- High intensity resistance training + weight loss vs weight loss alone
- 6 months of supervised training + 6 months of home-based training

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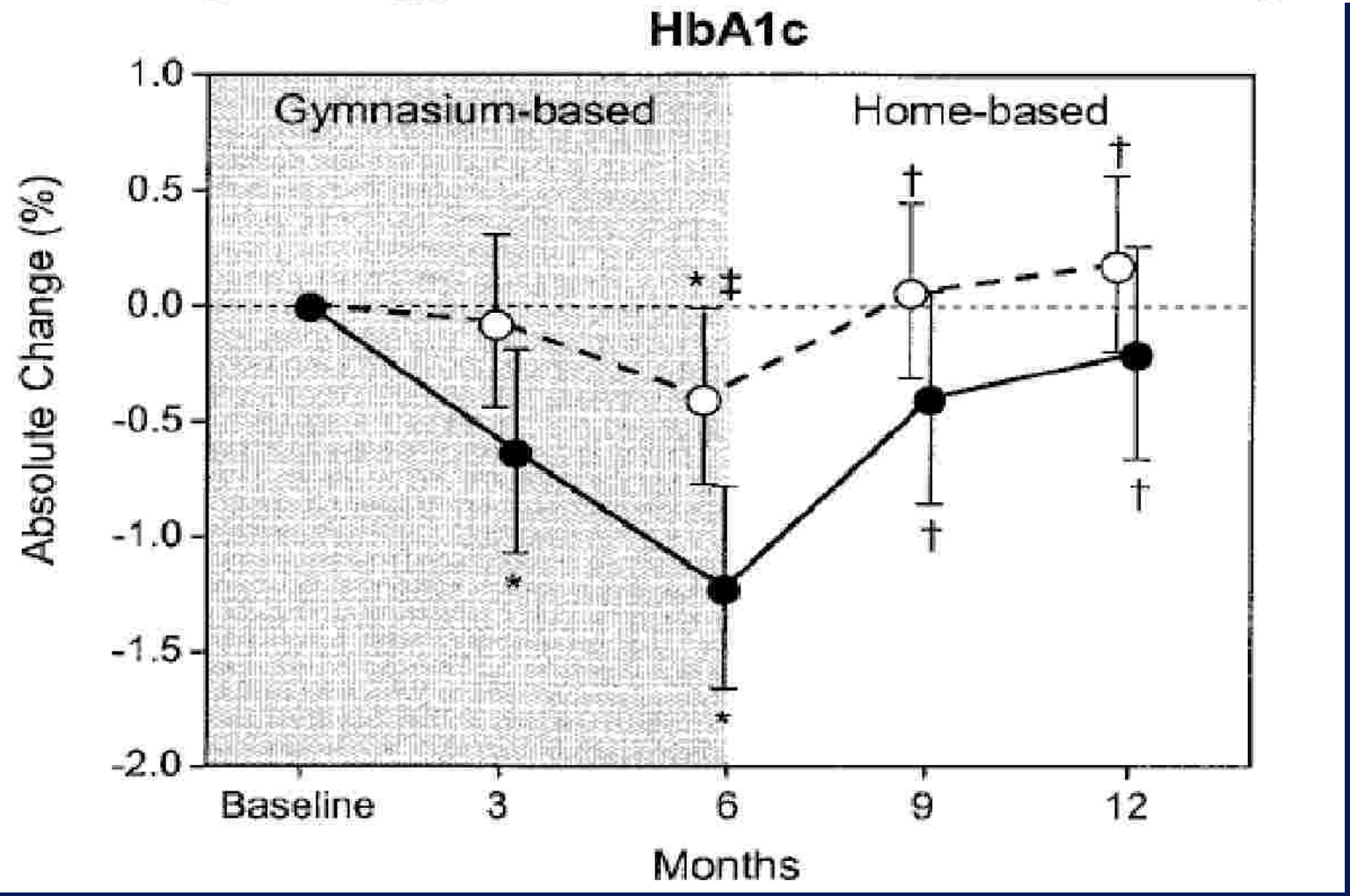

- High intensity resistance training + weight loss vs weight loss alone
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Annals of Internal Medicine 2007;147:357 | ARTICLE

Effects of Aerobic Training, Resistance Training, or Both on Glycemic Control in Type 2 Diabetes

A Randomized Trial

Ronald J. Sigal, MD, MPH; Glen P. Kenny, PhD; Normand G. Boulé, PhD; George A. Wells, PhD; Denis Prud'homme, MD, MSc; Michelle Fortier, PhD; Robert D. Reid, PhD, MBA; Heather Tulloch, MSc; Douglas Coyle, PhD; Penny Phillips, MA; Alison Jennings, MA; and James Jaffey, MSc

N=251 T2DM (multicentrico)

Durata intervento: 22 settimane (3 sedute/settimana)

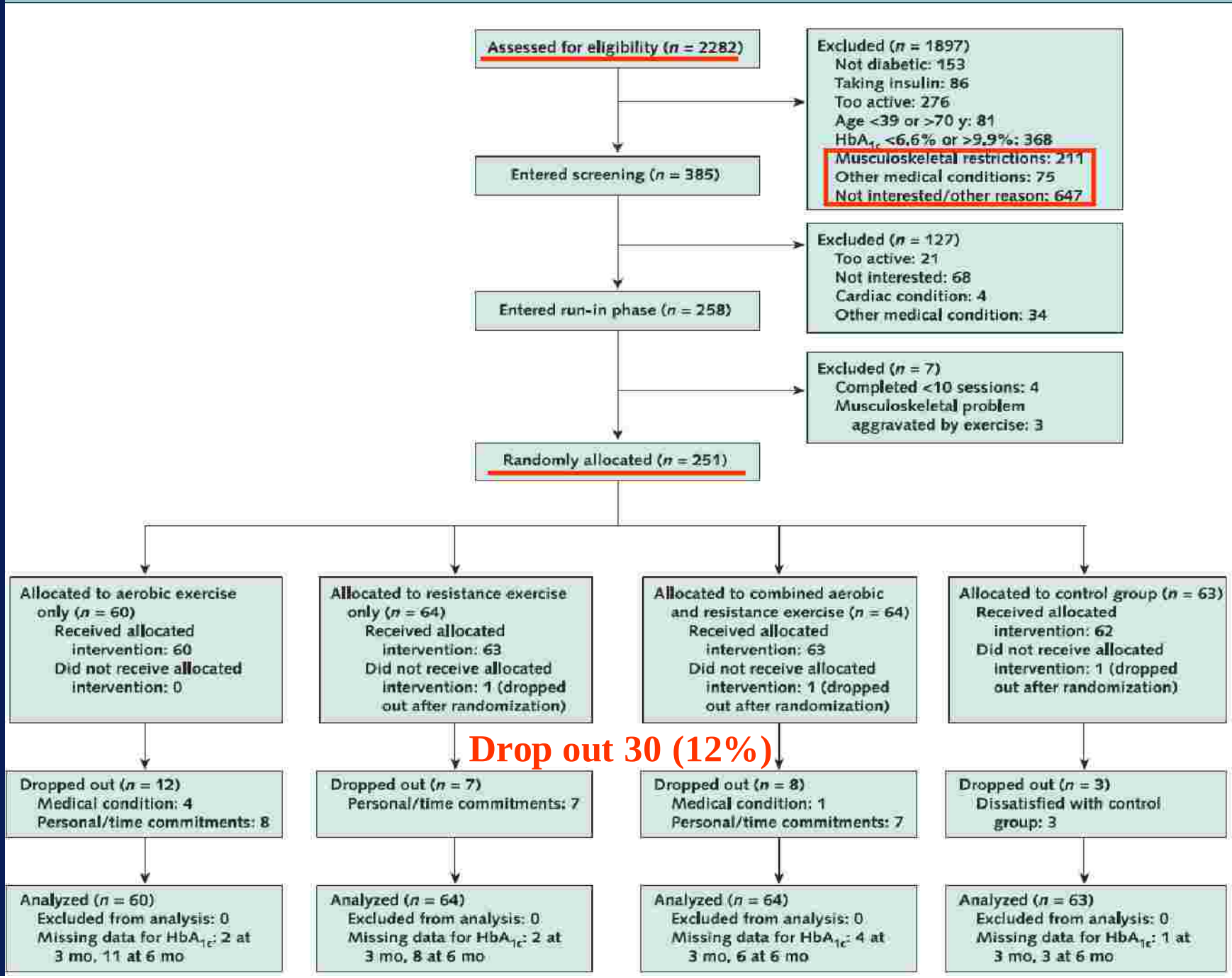
Dieta stabile

Randomizzazione a 4 gruppi:

- a) a. aerobica (treadmill, cicloergometro): 45' al 75% HRmax
- b) a. di resistenza (macchine): 3 serie di 7 esercizi a 7-9 RM
- c) a. combinata: a+b
- d) gruppo di controllo

Figure. Study flow diagram.

Sigal et al, Ann Intern Med 2007



Annals of Internal Medicine 2007;147:357 | ARTICLE

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Variable	Mean Value (SD)			Difference in Change from Baseline to 6 Months (95% CI)	*P* Value
	Baseline	3 mo	6 mo		
Body weight, *kg*					
Combined exercise group	101.9 (30.4)	100.2 (30.4)	99.3 (30.4)	–	–
Aerobic training group	103.5 (31.0)	101.8 (30.2)	100.9 (30.2)	–	–
Resistance training group	99.1 (30.4)	98.1 (30.4)	98.0 (30.4)	–	–
Control group	101.3 (28.6)	100.5 (27.8)	101.0 (27.8)	–	–
Intergroup comparisons					
Aerobic training vs. control	–	–	–	−2.2 (−3.9 to −0.6)	0.008
Resistance training vs. control	–	–	–	−0.7 (−2.4 to 0.9)	0.36
Combined exercise vs. aerobic training	–	–	–	0.0 (−1.6 to 1.7)	0.98
Combined exercise vs. resistance training	–	–	–	−1.5 (−3.1 to 0.1)	0.075

Annals of Internal Medicine 2007;147:357 | ARTICLE

Effects of Aerobic Training, Resistance Training, or Both on Glycemic Control in Type 2 Diabetes

A Randomized Trial

Ronald J. Sigal, MD, MPH; Glen P. Kenny, PhD; Normand G. Boulé, PhD; George A. Wells, PhD; Denis Prud'homme, MD, MSc; Michelle Fortier, PhD; Robert D. Reid, PhD, MBA; Heather Tulloch, MSc; Douglas Coyle, PhD; Penny Phillips, MA; Alison Jennings, MA; and James Jaffey, MSc

Variable	Mean (SD) Value			Difference in Change from Baseline to 6 Months (95% CI)	*P* Value
	Baseline	3 mo	6 mo		
Hemoglobin A_{1c} [patients], % *[n]*†					
Combined exercise group	7.46 (1.48) [64]	6.99 (1.56) [60]	6.56 (1.55) [58]	–	–
Aerobic training group	7.41 (1.50) [60]	7.00 (1.59) [58]	6.98 (1.50) [49]	–	–
Resistance training group	7.48 (1.47) [64]	7.35 (1.57) [62]	7.18 (1.52) [56]	–	–
Control group	7.44 (1.38) [63]	7.33 (1.49) [62]	7.51 (1.47) [59]	–	–
Intergroup comparisons					
Aerobic training vs. control	–	–	–	−0.51 (−0.87 to −0.14)	0.007
Resistance training vs. control	–	–	–	−0.38 (−0.72 to −0.22)	0.038
Combined exercise vs. aerobic training	–	–	–	−0.46 (−0.83 to −0.09)	0.014
Combined exercise vs. resistance training	–	–	–	−0.59 (−0.95 to −0.23)	0.001

Effects of Aerobic and Resistance Training on Hemoglobin A_{1c} Levels in Patients With Type 2 Diabetes

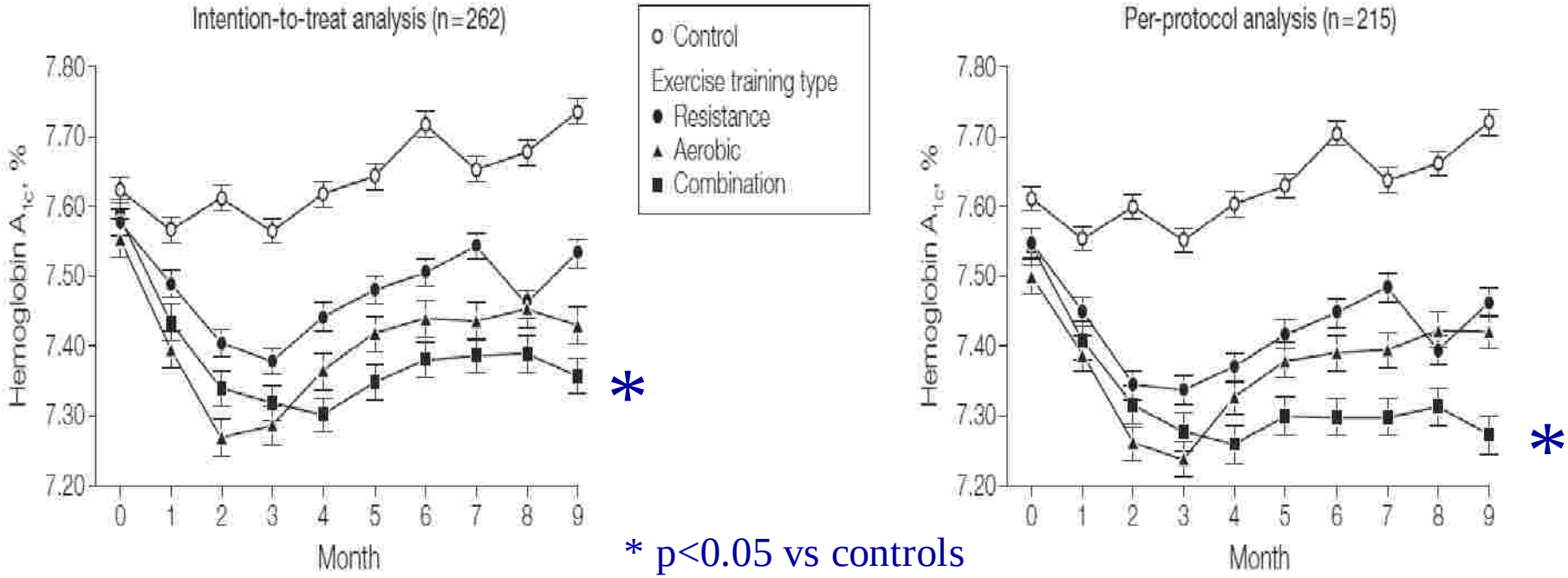
Church et al, JAMA 2010

- 262 diabetici tipo 2 sedentari
- RCT
- 9 mesi di intervento (impegno di tempo sovrapponibile)
  - Aerobico (n=72): 12 kcal/kg per settimana, 50-80% VO2max
  - Resistenza muscolare (n=73), 1-12 ripetizioni di 2-3 set di 9 esercizi, 3 volte/w
  - Combinato (n=76), 10 kcal /kg per settimana attività aerobica + 1 set di 9 esercizi, 2 volte/w
  - Non-esercizio (n=41)

Effects of Aerobic and Resistance Training on Hemoglobin A_{1c} Levels in Patients With Type 2 Diabetes

Church et al, JAMA 2010

Figure 2. Monthly Hemoglobin A_{1c} Levels



* $p<0.05$ vs controls

No. of patients										
Exercise training type										
Control	41	37	34	35	33	33	31	35	33	35
Resistance	73	73	72	71	66	64	64	62	60	55
Aerobic	72	65	62	60	56	57	55	54	51	53
Combination	76	73	73	69	69	68	69	65	57	57

No. of patients										
Exercise training type										
Control	41	37	34	35	33	33	31	35	33	35
Resistance	60	60	60	60	59	58	59	60	58	52
Aerobic	52	51	52	52	48	51	50	51	46	49
Combination	62	62	62	59	60	60	61	60	54	54

Training aerobico vs di resistenza muscolare nel diabete tipo 2 - Protocolli

Tipo Training	Durata	Frequenza	Tempo sessione	Intensità di training	Strumenti	Dieta
AEROBICO 	4 mesi	3 volte settimana	60 minuti	Incremento progressivo fino al 60-65% Frequenza Cardiaca di Riserva	Macchine allenamento cardiovascolare	regime alimentare stabile, nel rispetto linee guida ADA. Incontro Dietista
FORZA 	4 mesi	3 volte settimana	60 minuti 3 serie di 8-12 ripetizioni intervallate da 1 minuto di recupero	Incremento progressivo del carico fino a 70÷80% 1RM	8-10 esercizi dei maggiori gruppi muscolari, utilizzando macchine isotoniche e pesi liberi	regime alimentare stabile, nel rispetto linee guida ADA. Incontro Dietista

Metabolic Effects of Aerobic Training and Resistance Training in Type 2 Diabetic Subjects

A randomized controlled trial (the RAED2 study)

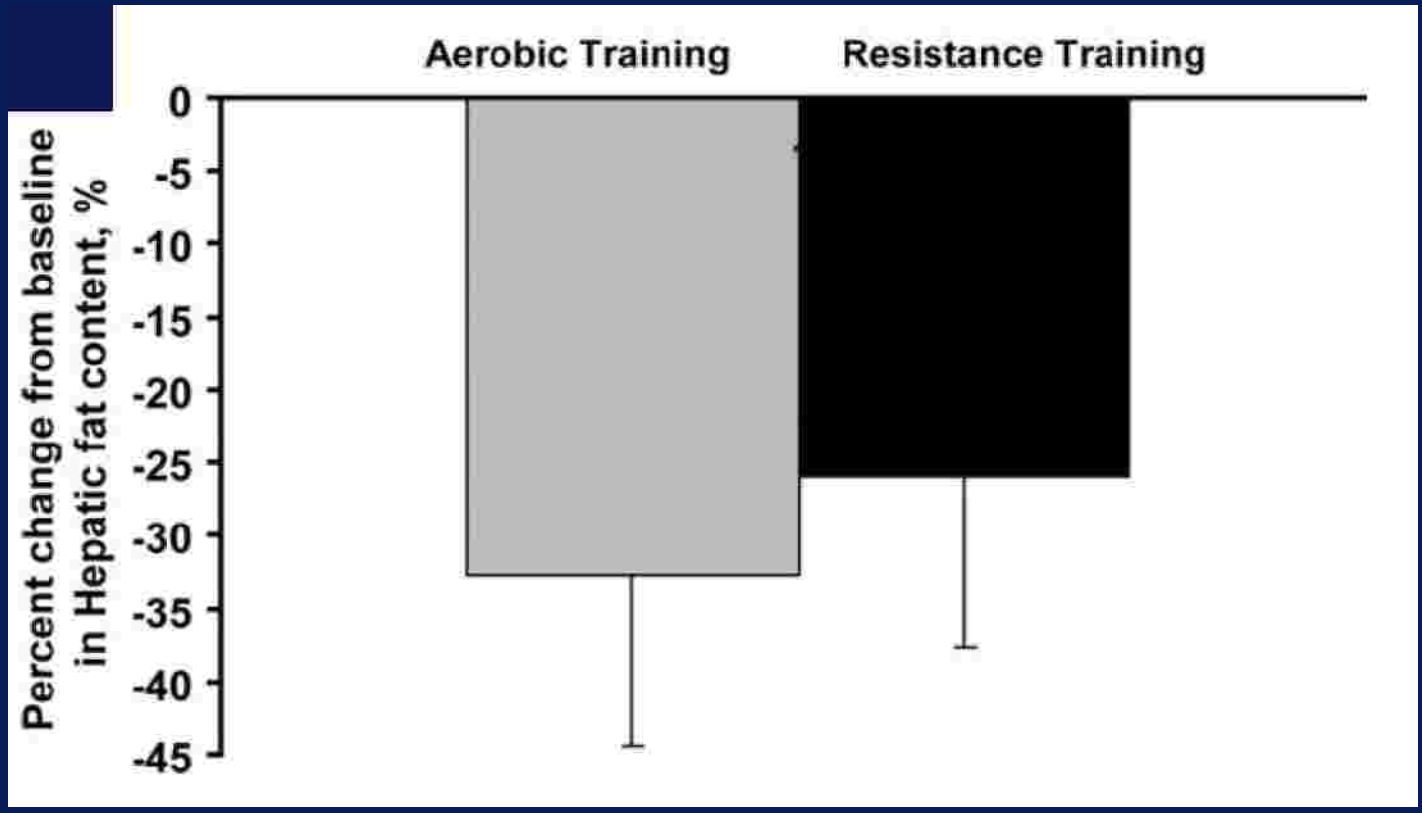
Diabetes Care, 2012

ELISABETTA BACCHI, PHD[1]
CARLO NEGRI, MD[2]
MARIA ELISABETTA ZANOLIN, MSC[3]
CHIARA MILANESE, MSC[4]
NICCOLO FACCIOLI, MD[5]
MADDALENA TROMBETTA, MD, PHD[1,2]
GIACOMO ZOPPINI, MD[1,2]
ANTONIO CEVESE, MD[4]
RICCARDO C. BONADONNA, MD[1,2]
FEDERICO SCHENA, MD, PHD[4]
ENZO BONORA, MD, PHD[1,2]
MASSIMO LANZA, MSC[4]
PAOLO MOGHETTI, MD, PHD[1,2]

	Aerobic group (n = 19)	Resistance group (n = 19)	P value, time	P value, time-by-group interaction
HbA_{1c}, %	−0.40 (−0.61 to −0.18)	−0.35 (−0.59 to −0.10)	<0.0001	0.759
Fasting glycemia, mg/dL	−15.2 (−29.8 to −0.57)	−12.0 (−23.4 to −0.5)	0.004	0.718
Total cholesterol, mg/dL	−0.8 (−15.8 to 14.1)	−0.7 (−8.5 to 7.1)	0.845	0.989
LDL cholesterol, mg/dL	1.8 (−9.9 to 13.5)	2.3 (−4.5 to 9.2)	0.537	0.933
HDL cholesterol, mg/dL	2.9 (−0.28 to 6.1)	1.3 (−1.1 to 3.8)	0.034	0.413
Triglycerides, mg/dL	−27.8 (−57.5 to 1.7)	−23.9 (−49.5 to 1.6)	0.001	0.926
Glucose disposal rate, mg · kg FFM $^{-1}$ · min $^{-1}$	1.15 (0.22–2.07)	0.52 (0.01–1.05)	0.006	0.271
Systolic, mmHg	−6.8 (−15.5 to 1.8)	−5.1 (−12.4 to 2.3)	0.034	0.750
Diastolic, mmHg	−4.6 (−9.3 to 0.06)	−2.0 (−6.6 to 2.6)	0.041	0.407
Vo_{2peak}, mL · kg $^{-1}$ · min $^{-1}$	4.0 (2.7–5.3)†	2.1 (0.6–3.5)†	—	0.045
Watt	20 (10.1–29.9)†	9 (3.2–14.6)†	—	0.044
HR_{peak}, bpm	−0.91 (−6.0 to 4.1)	0.8‡ (−2.7 to 4.4)	0.979	0.546
Chest press, kg	1.3 (−1.1 to 3.7)	10.3 (7.2–13.2)†	—	<0.0001
Leg extension, kg	3.0 (−0.3 to 6.3)	12.3 (9.0–15.5)†	—	<0.0001
Overall physical activity, MET min per week	710 (575–843)	808 (675–941)	<0.0001	0.278
Caloric intake, kcal per day	−96 (−240 to 48)	−76 (−177 to 23)	0.040	0.814
BMI, kg/m^2	−0.76 (−1.1 to −0.4)	−0.54 (−0.85 to −0.22)	<0.0001	0.330
Waist circumference, cm	−3.2 (−4.5 to −1.9)	−2.4 (−3.8 to −0.9)	<0.0001	0.373
Lean total, kg	−0.12 (−0.60 to 0.34)	0.32 (−0.27 to 0.91)	0.592	0.225
Lean mass of limbs, kg	0.43 (0.11–0.76)	0.72 (0.34–1.1)	<0.0001	0.239
Fat total, kg	−1.96 (−2.7 to −1.2)	−1.71 (−2.4 to −1.0)	<0.0001	0.605
Fat trunk, kg	−1.66 (−2.2 to −1.1)	−1.41 (−1.9 to −0.89)	<0.0001	0.506
VAT, cm^2	−61.4 (−98.4 to −24.4)	−33.5 (−52.9 to −14.0)	<0.0001	0.360
SAT, cm^2	−13.8 (−23.9 to −3.7)	−19.5 (−35.4 to −3.6)	0.001	0.627

Both Resistance Training and Aerobic Training Reduce Hepatic Fat Content in Type 2 Diabetic Subjects With Nonalcoholic Fatty Liver Disease (the RAED2 Randomized Trial)

Elisabetta Bacchi,[1] Carlo Negri,[1] Giovanni Targher,[1] Niccolò Faccioli,[2] Massimo Lanza,[3] Giacomo Zoppini,[1] Elisabetta Zanolin,[4] Federico Schena,[3] Enzo Bonora,[1] and Paolo Moghetti[1]



Hepatology, 2013

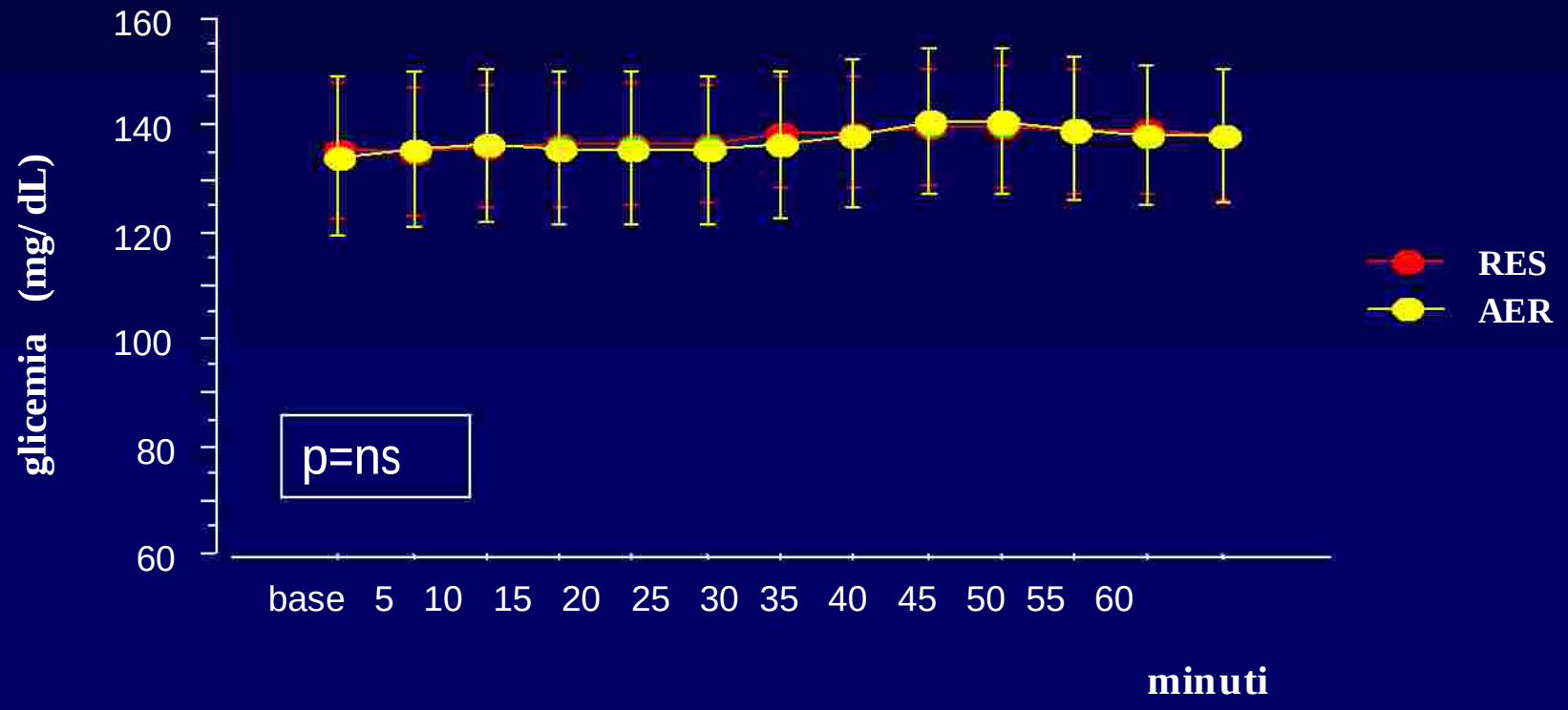
Predictors of HbA1c changes after exercise training by multiple regression analysis

(R^2= 0.55)

	Coefficient	Std. Coeff	p value
Intercept	-1.392	-1.392	**0.008**
HbA1c at baseline (%)	0.175	0.337	**0.017**
Change in VO2 peak (ml/kg min)	-0.049	-0.422	**0.002**
Change in Truncal Fat (kg)	0.110	0.372	**0.006**
Change in Leg extension (kg)	-0.006	-0.152	**0.250**

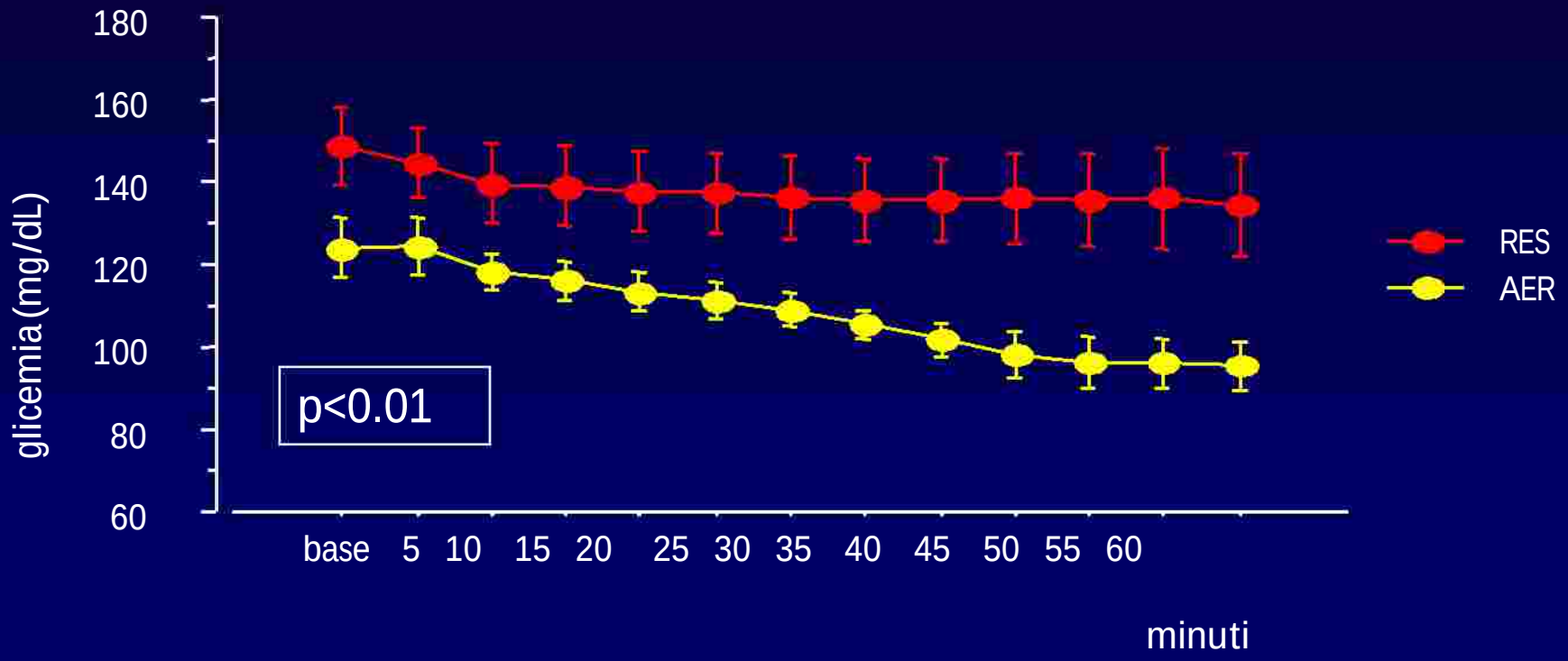
Bacchi et al, Diabetes Care 2012

Andamento della glicemia nel gruppo aerobico e nel gruppo di resistenza muscolare nell' orario del giorno di riposo corrispondente alla sessione di esercizio



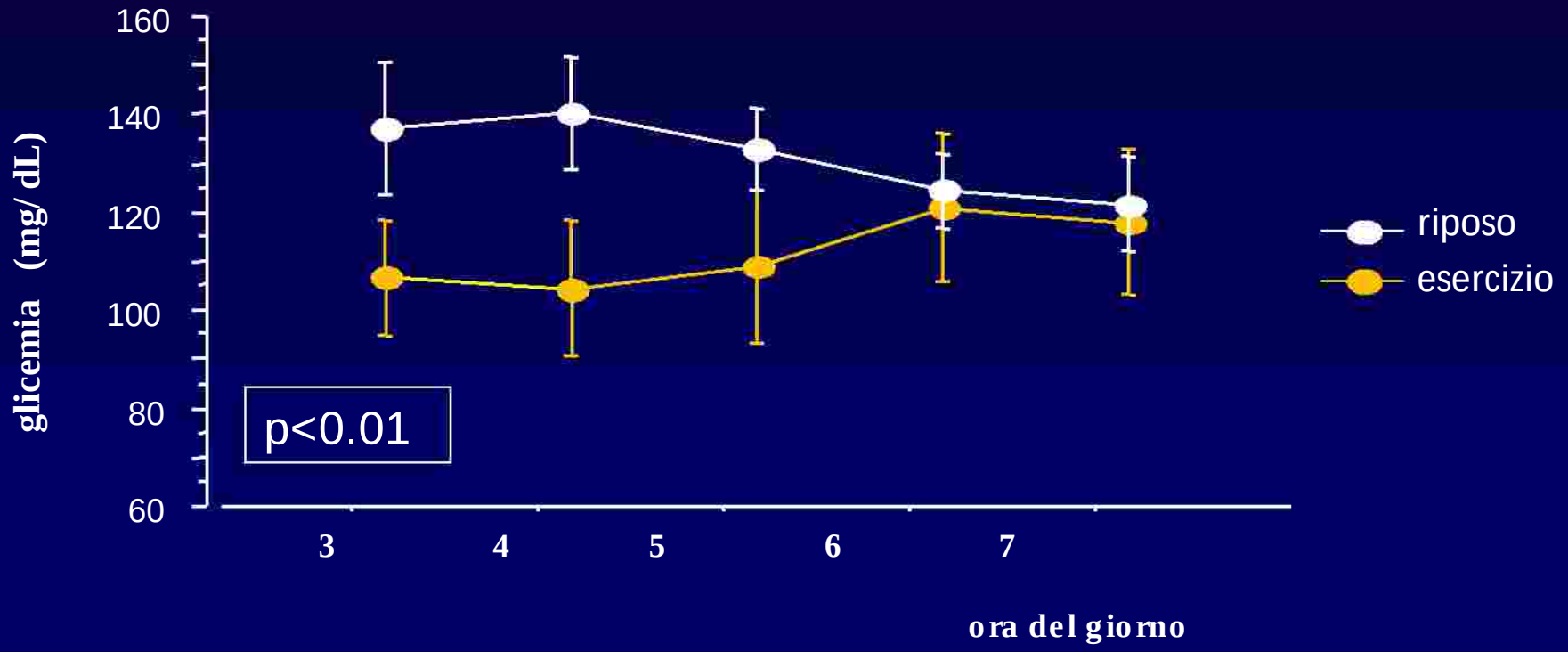
Da Bacchi et al, PLoS One 2012

Andamento della glicemia nel gruppo aerobico e nel gruppo di resistenza muscolare nel corso della seduta di esercizio fisico



Da Bacchi et al, PLoS One 2012

Andamento della glicemia nelle ore notturne dopo una seduta di training Aerobico e nell'orario corrispondente del giorno di riposo



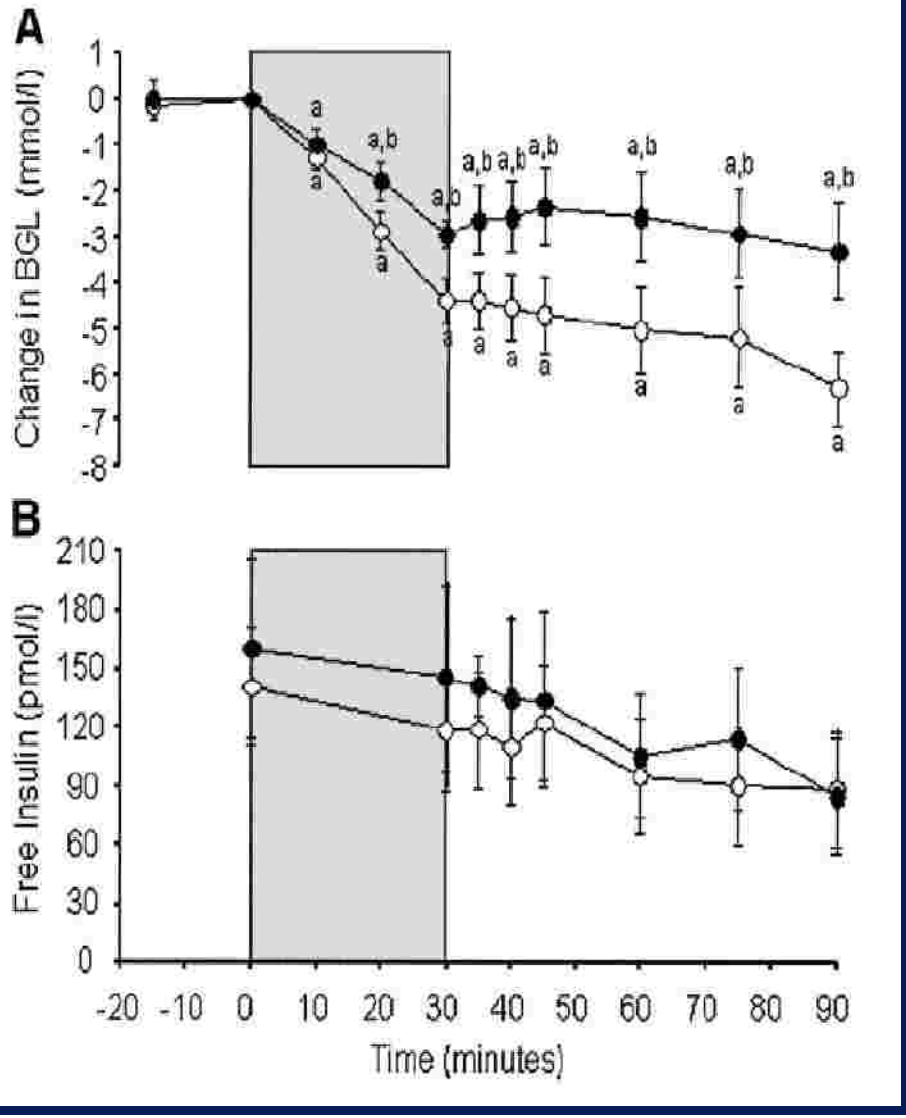
Da Bacchi et al, PLoS One 2012

The Decline in Blood Glucose Levels Is Less With Intermittent High-Intensity Compared With Moderate Exercise in Individuals With Type 1 Diabetes

KYM J. GUELFI, BSC(HONS)[1]
TIMOTHY W. JONES, MD[2,3]
PAUL A. FOURNIER, PHD[1]

Diabetes Care 28:1289–1294, 2005

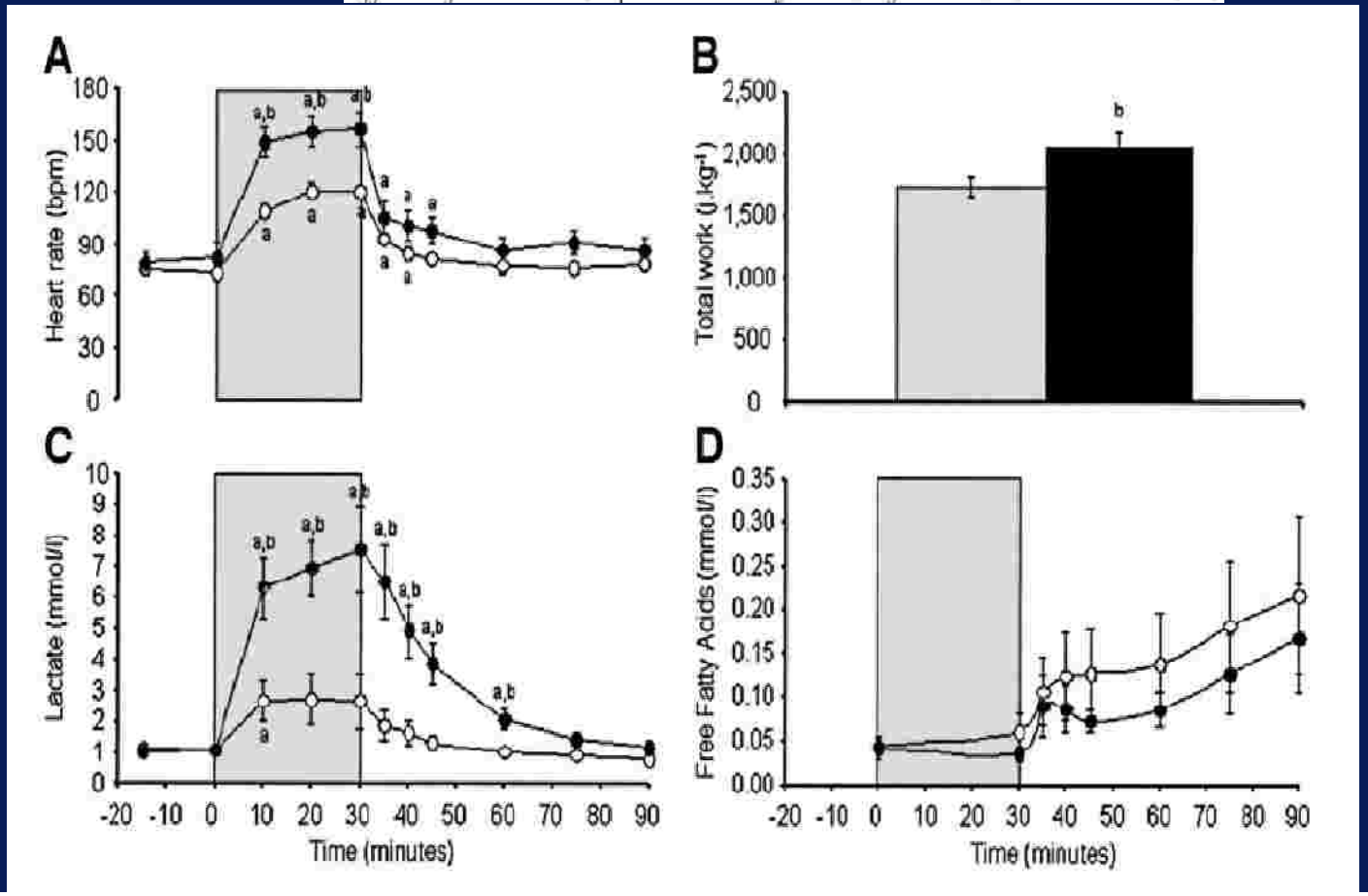
Effect of 30 min (represented by box) of IHE (■) or MOD (□)



Frequenza cardiaca, lavoro totale, livelli di lattato e di FFA durante e dopo esercizio intermittente ad elevata intensità o esercizio di moderata intensità in diabetici tipo 1

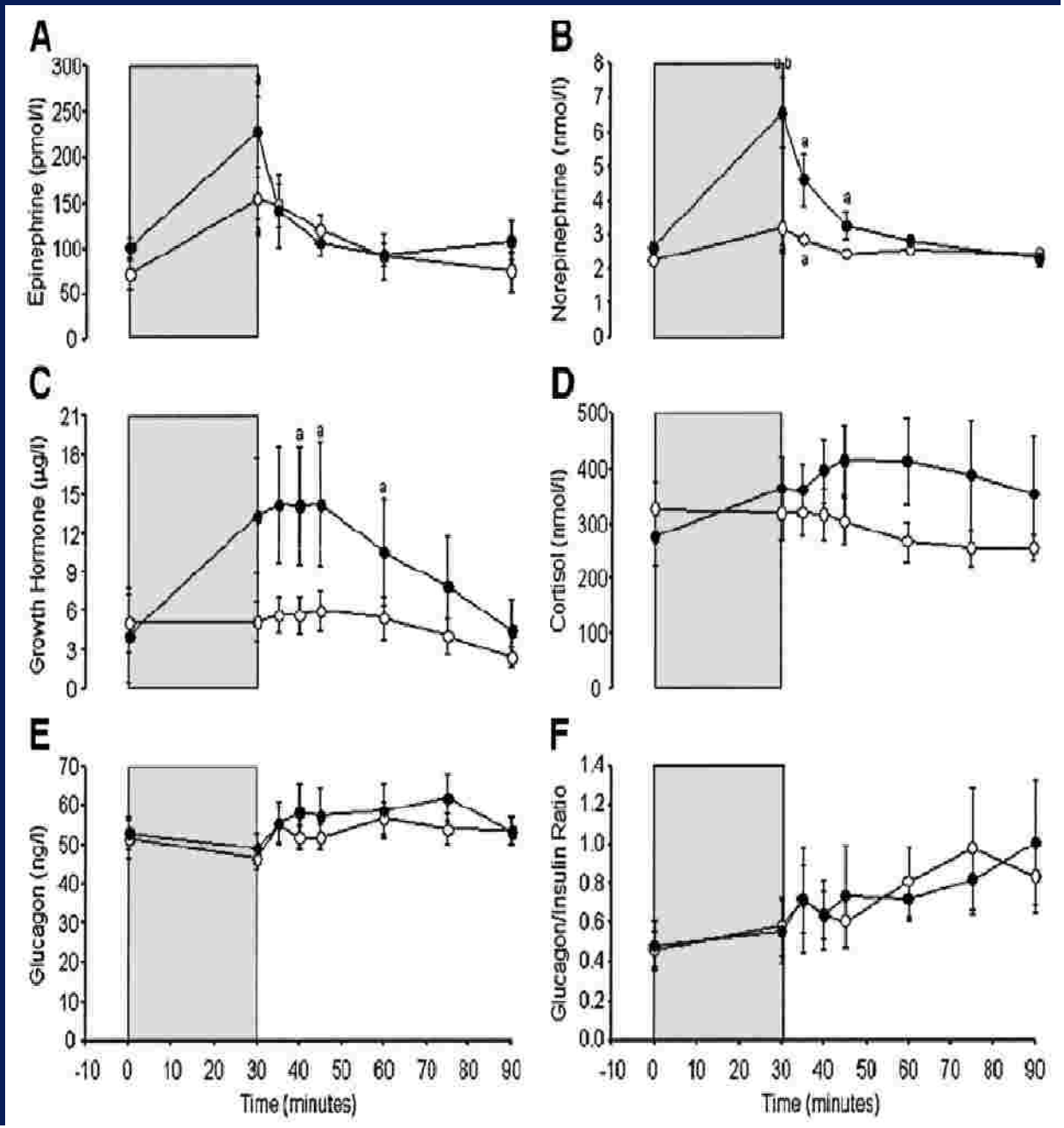
Diabetes Care 28:1289–1294, 2005

Effect of 30 min (represented by box) of IHE (■) or MOD (□)



Diabetes Care 28:1289–1294, 2005

Variazioni dei livelli degli ormoni controinsulari durante e dopo esercizio intermittente ad elevata intensità o esercizio di moderata intensità in diabetici tipo 1



Effect of 30 min (represented by box) of IHE (■) or MOD (□)

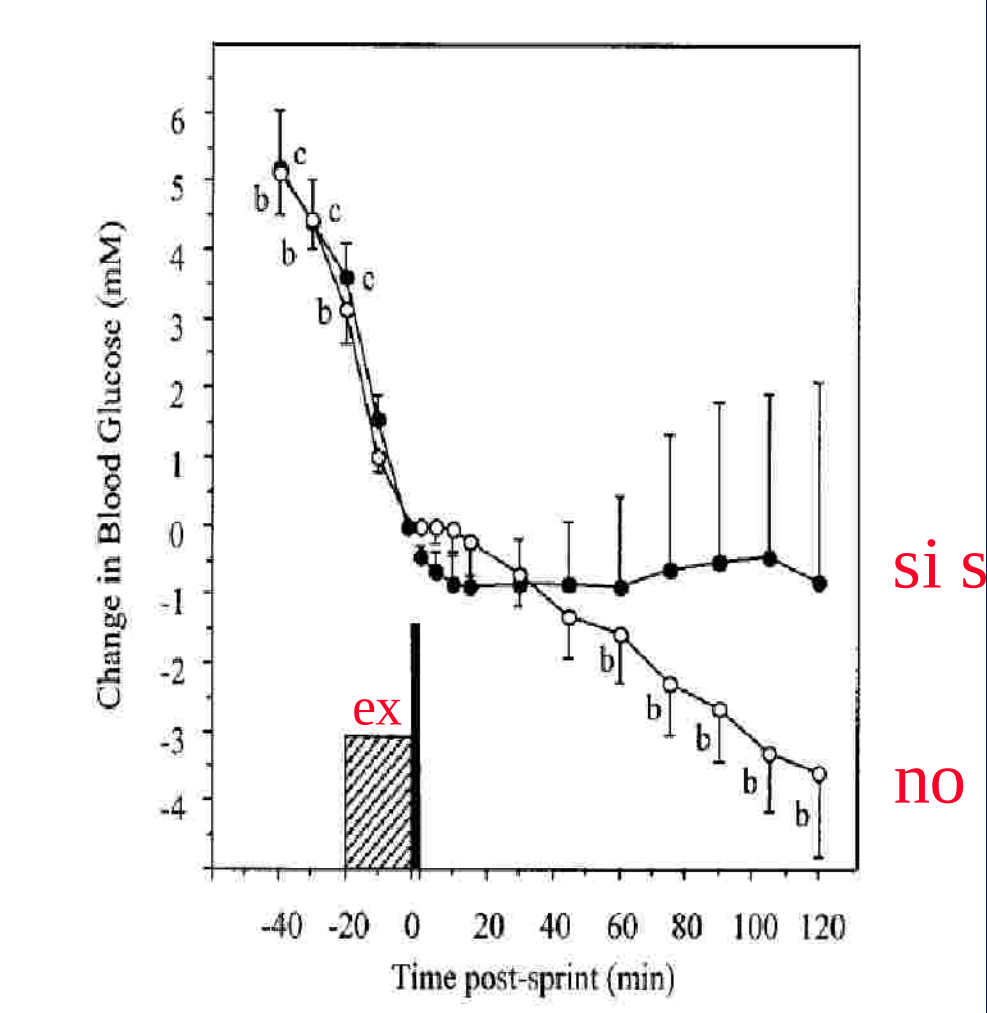
EFFETTI DI UNO SPRINT MASSIMALE SULLA CADUTA GLICEMICA POST-ESERCIZIO NEL DIABETE TIPO 1

Disegno sperimentale

- 7 giovani diabetici tipo 1 sottoposti in due occasioni a 20’ di attività fisica moderata al cicloergometro (40% VO2max), dopo l’iniezione della dose abituale di insulina e la colazione, una volta raggiunta una glicemia di 11 mmol/l (198 mg/ l)
- Successivamente, nelle due occasioni:
  - riposo per 120 minuti
  - sprint massimale per 10’’, poi riposo per 120 minuti
- Registrazione dell’andamento della glicemia e misurazione dei livelli di catecolamine, GH e cortisolo nel corso dello studio

(Bussau et al, Diabetes Care 2006)

EFFETTI SULLA GLICEMIA DI UNO SPRINT MASSIMALE DOPO ESERCIZIO AEROBICO MODERATO NEL DIABETE TIPO 1

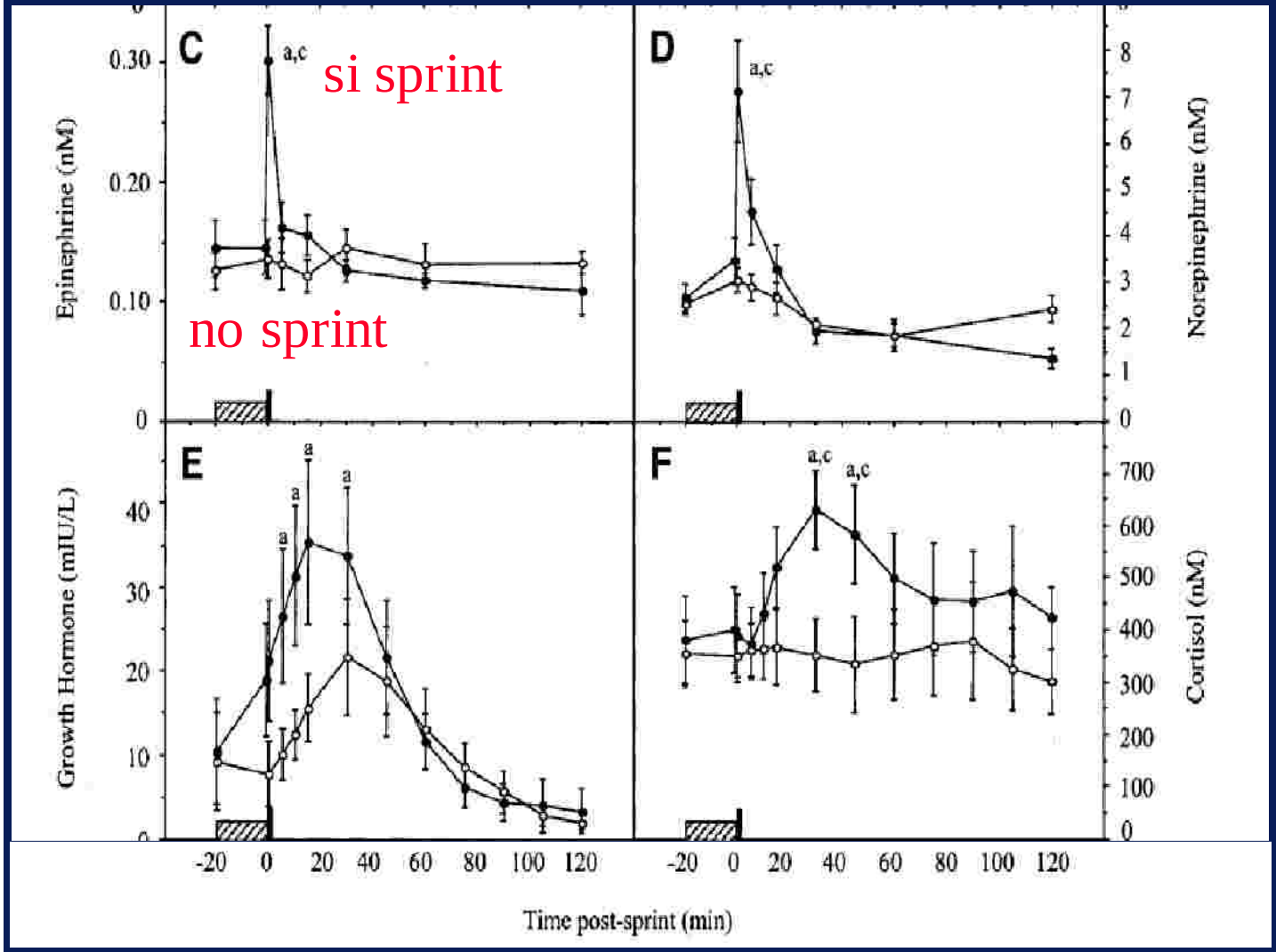


si sprint

no sprint

Bussau et al, Diabetes Care 2006

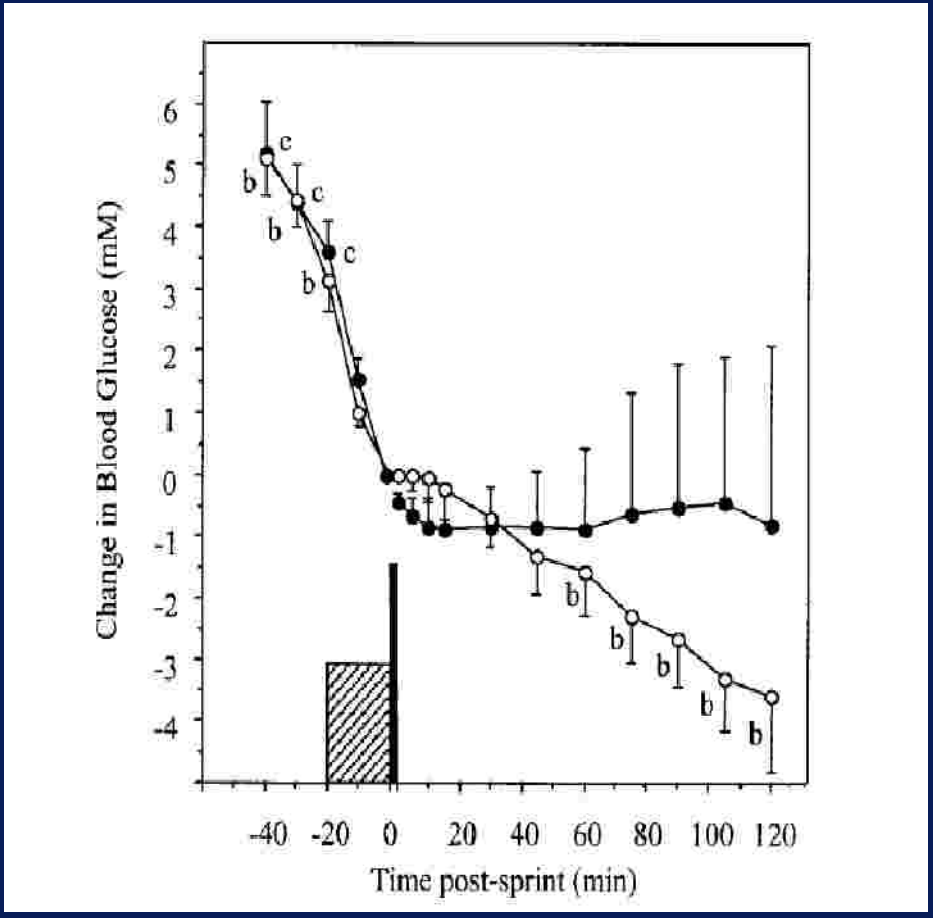
EFFETTI DI UNO SPRINT MASSIMALE DOPO L'ESERCIZIO SUGLI ORMONI CONTROINSULARI NEL DIABETE TIPO 1



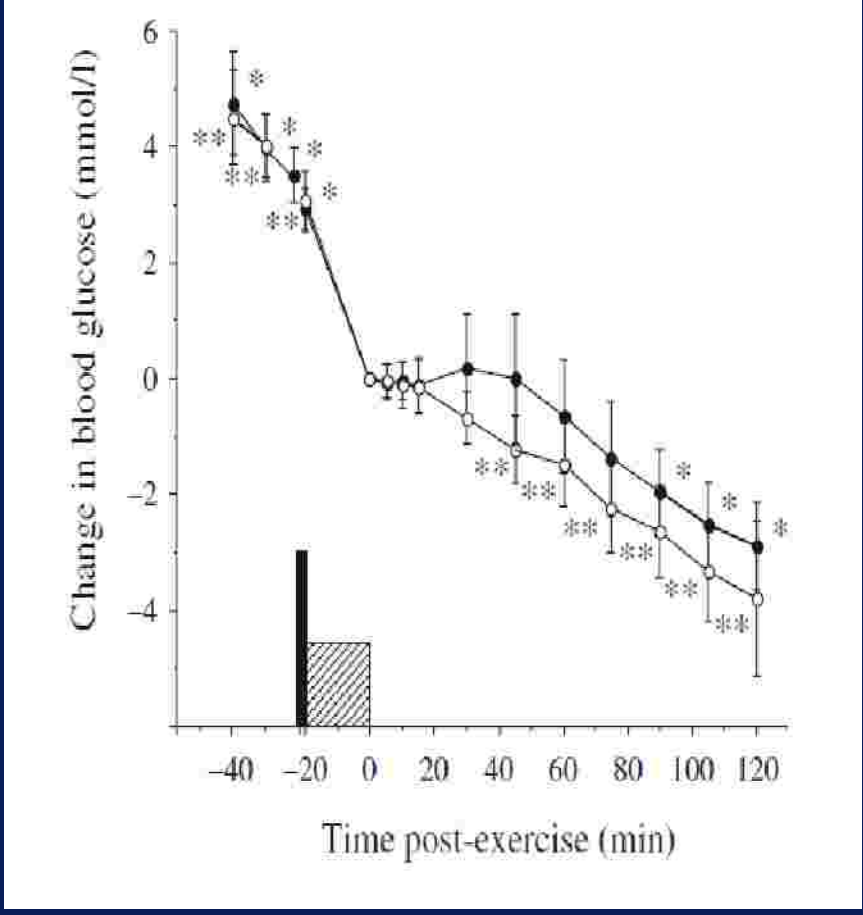
Bussau et al, Diabetes Care 2006

EFFETTI DI UNO SPRINT MASSIMALE PRE O POST-ESERCIZIO SULLA CADUTA GLICEMICA NEL DIABETE TIPO 1

post

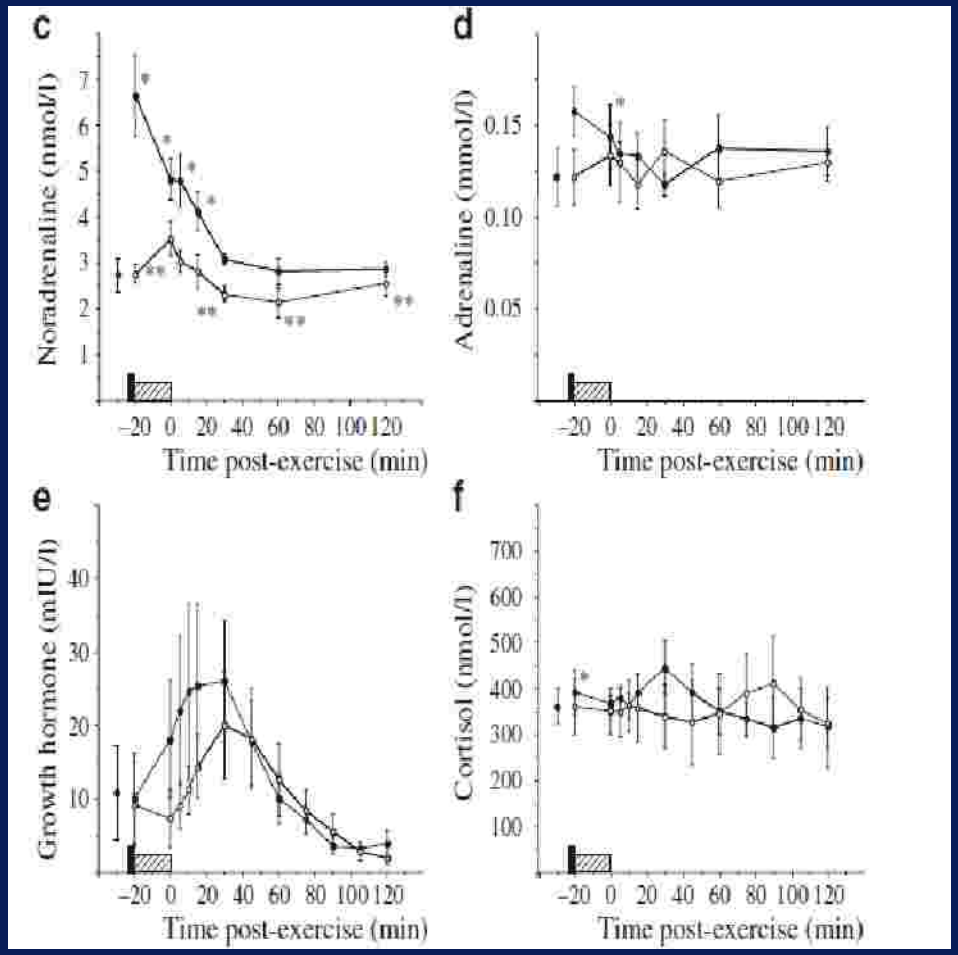


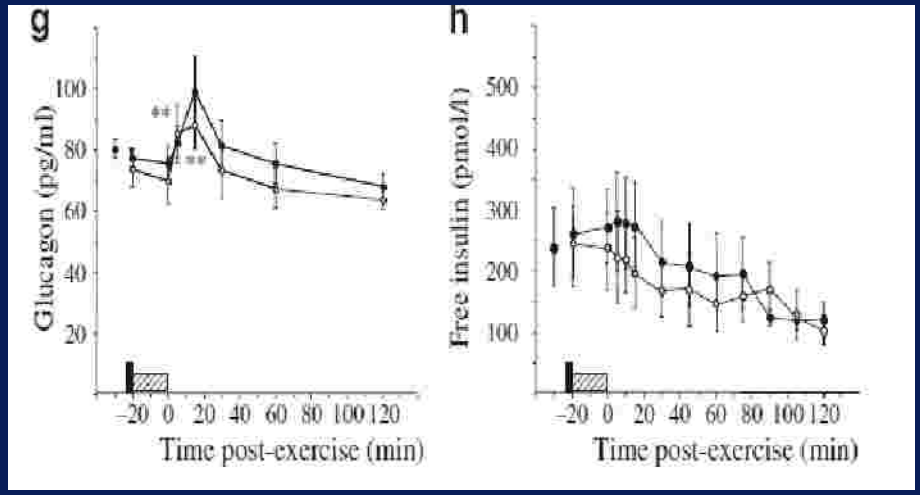
pre



Bussau et al, Diabetologia 2007

EFFETTI DI UNO SPRINT MASSIMALE PRE- ESERCIZIO SUGLI ORMONI CONTROINSULARI NEL DIABETE TIPO 1





Bussau et al, Diabetologia 2007

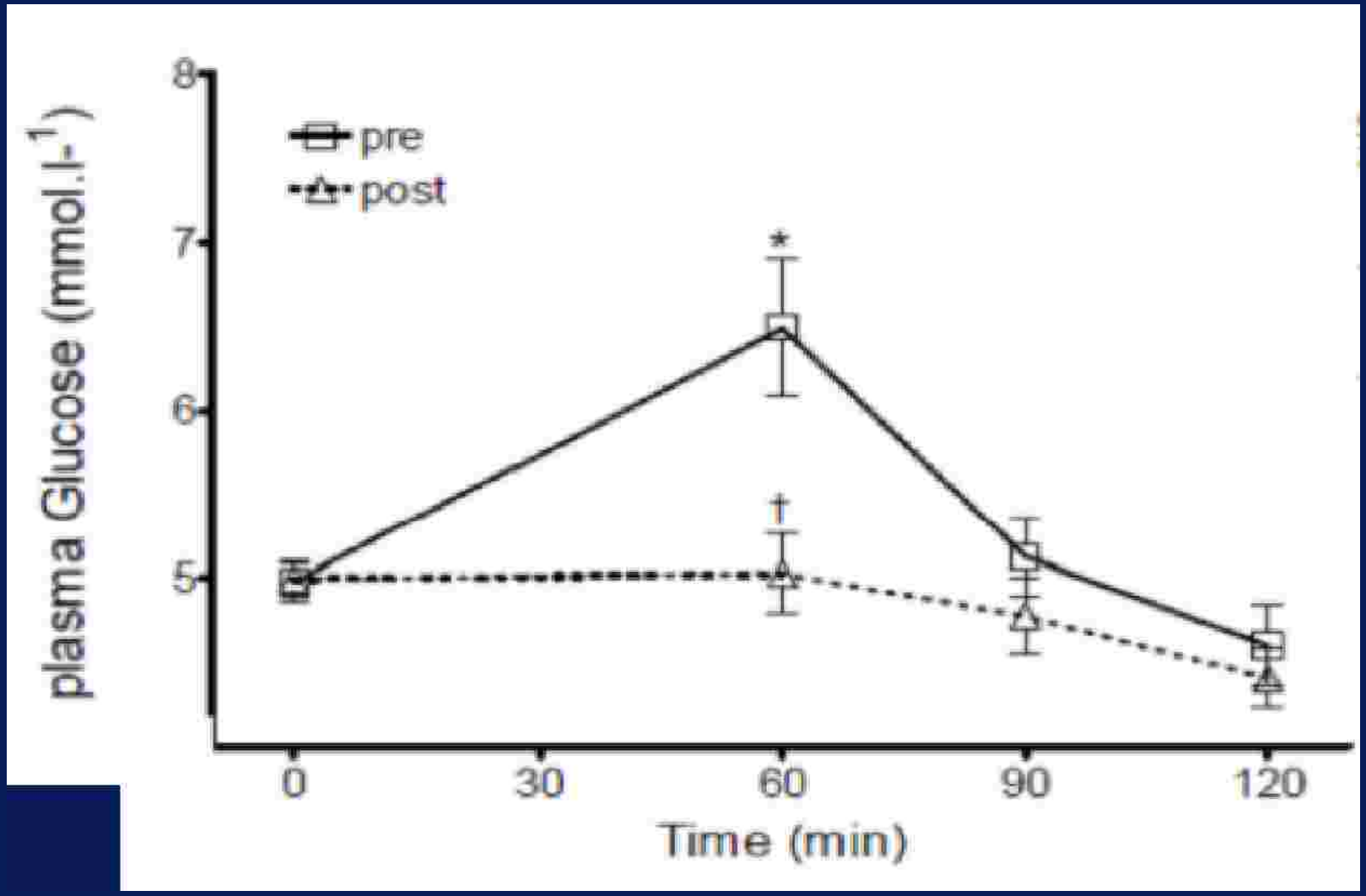
Extremely short duration high intensity training substantially improves insulin action in young sedentary males

Soggetti e protocollo

- 16 giovani soggetti sedentari o moderatamente attivi
  - età 21±2 anni,
  - BMI 23.7±3.1 kg/m^2
  - VO2 picco 48±9 ml/ kg min
- 2 settimane di esercizio supervisionato ad alta intensità (corrispondente a circa 250 kcal /settimana)
  - 6 sessioni di 4-6 sprint di 30” (con recupero di 4’) al cicloergometro al 75% della Wmax (pedalata di 90 rpm)
- Misure prima e dopo le due settimane di allenamento
  - OGTT (con misura di glicemia, insulina, NEFA)
  - Performance (tempo richiesto per un lavoro di 250 kJ)

Babraj et al, BMC Endocrine Disorders 2009

Extremely short duration high intensity training substantially improves insulin action in young sedentary males



Babraj et al, BMC Endocrine Disorders 2009

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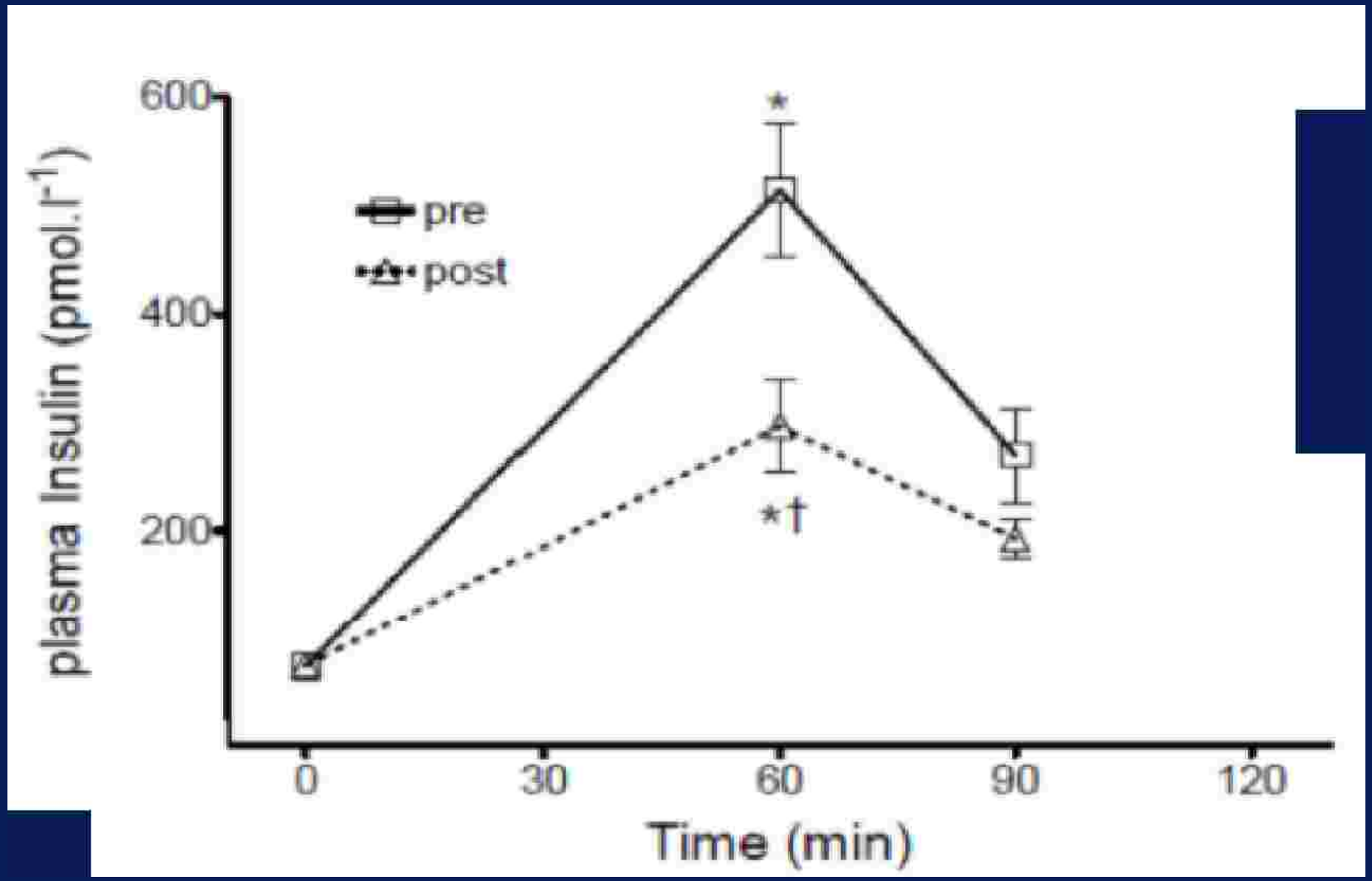
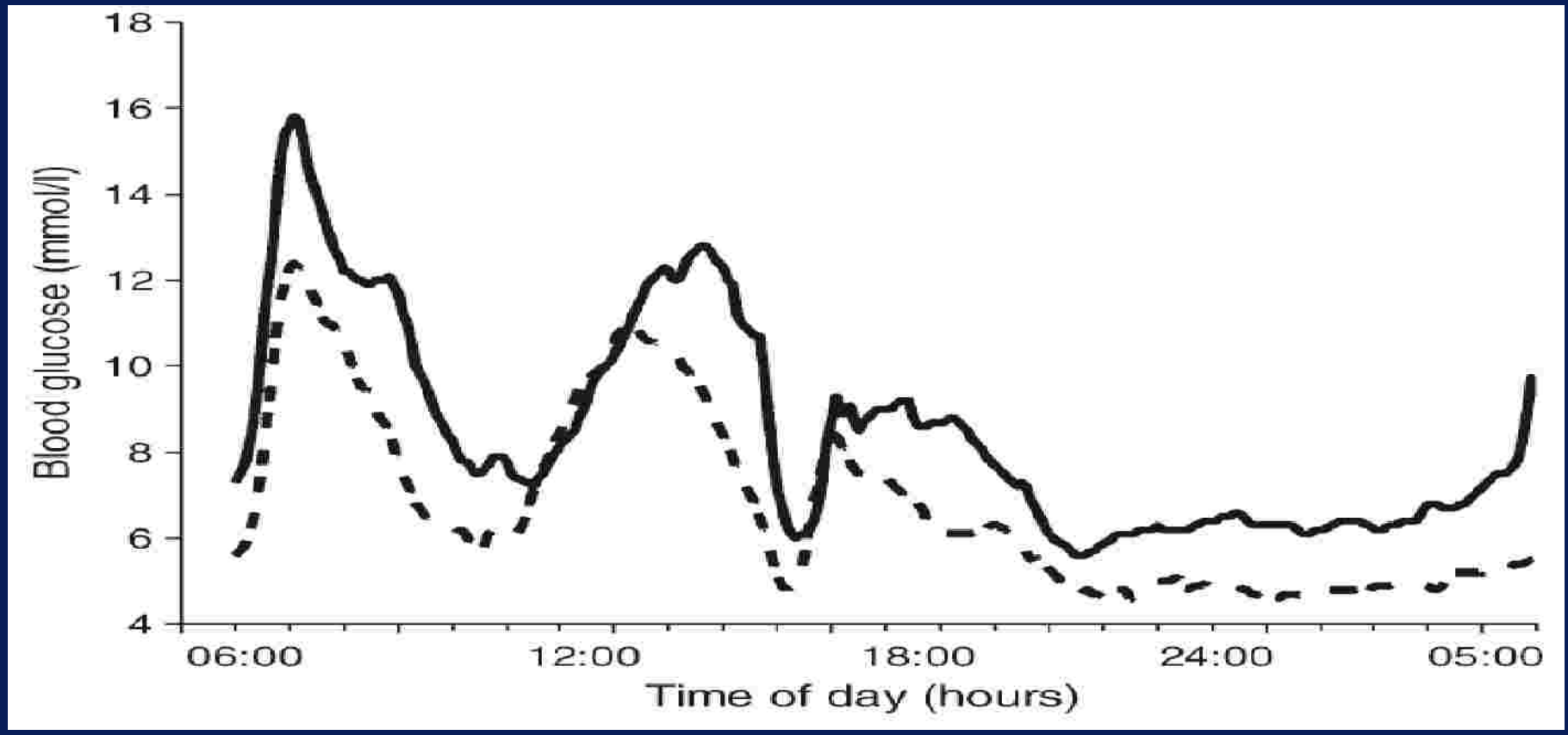


Babraj et al, BMC Endocrine Disorders 2009

High Intensity Interval Training nel diabete tipo 2

(10 x 60 sec + 60 sec recupero, Intensità 90%HRmax)

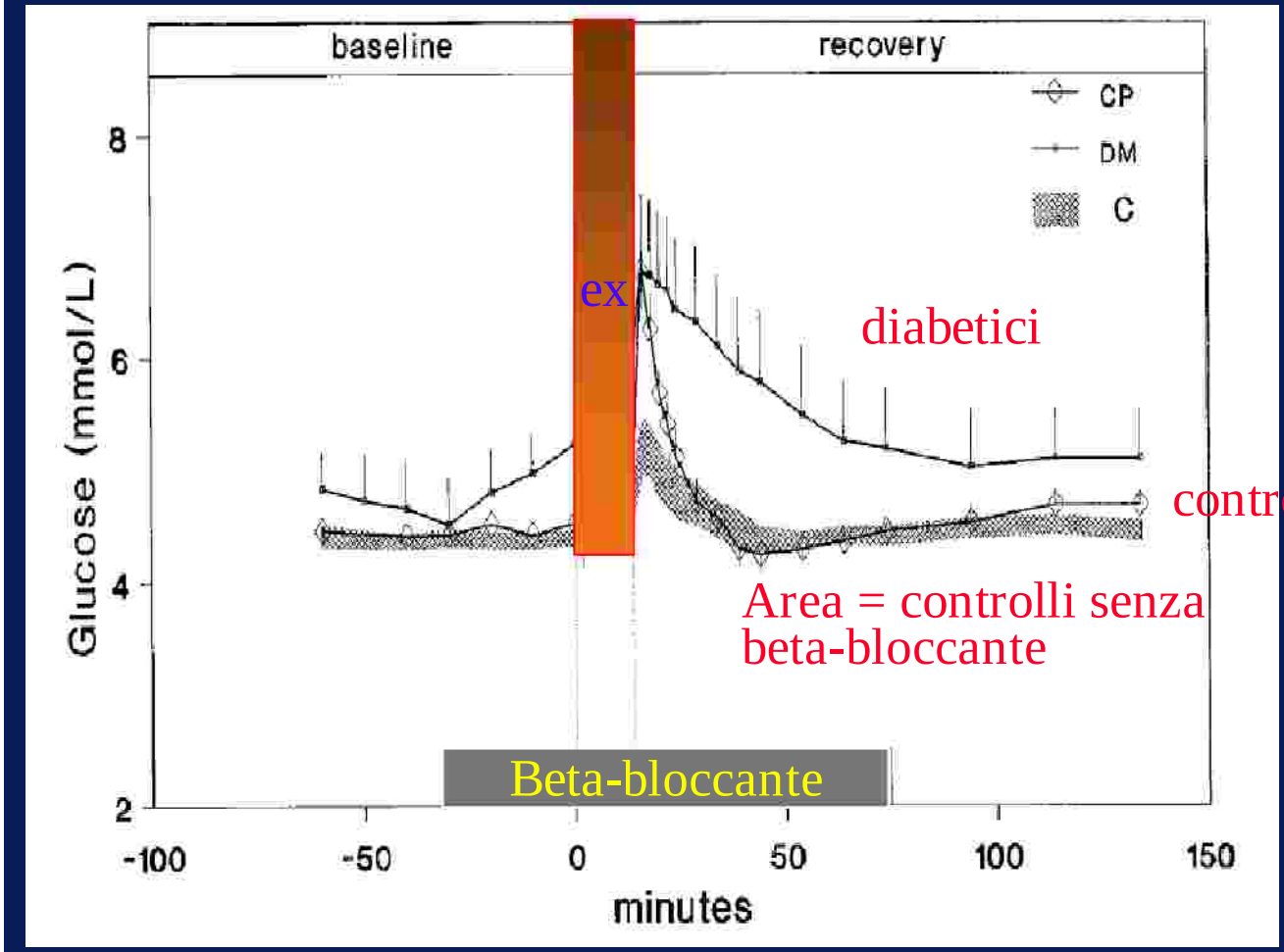
Andamento glicemico nelle 24 ore, prima e dopo due settimane di allenamento



Little et al, 2011

Effetto sulla glicemia dei farmaci beta-bloccanti durante esercizio intenso in soggetti con diabete tipo 1 e controlli

esercizio



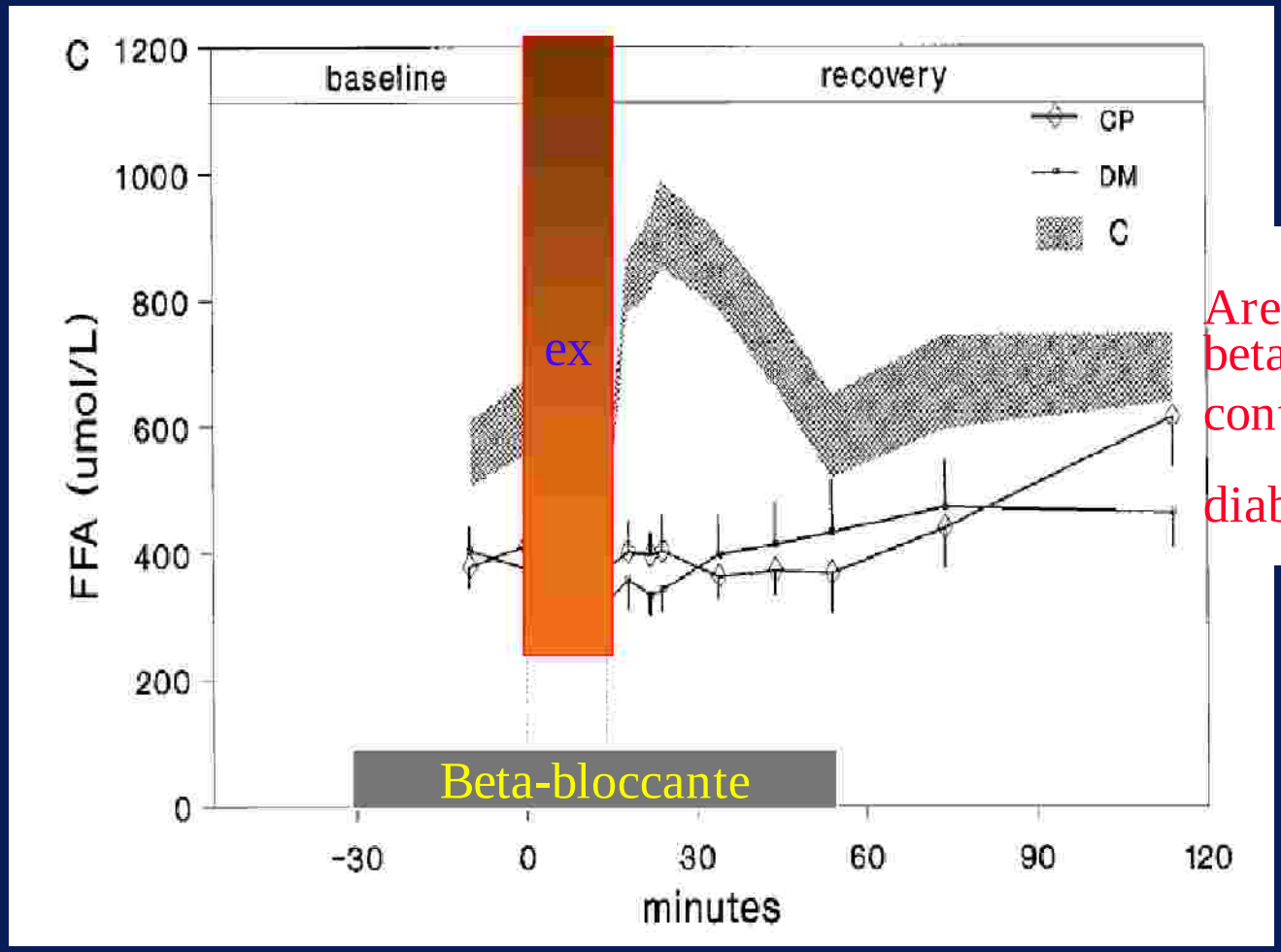
Esercizio all'85-87% della VO2max

Infusione propranololo

(Sigal 1999)

Effetto dei farmaci beta-bloccanti sui livelli di acidi grassi liberi durante esercizio in soggetti con diabete tipo controlli

esercizio



Area = controlli senza beta-bloccante

controlli

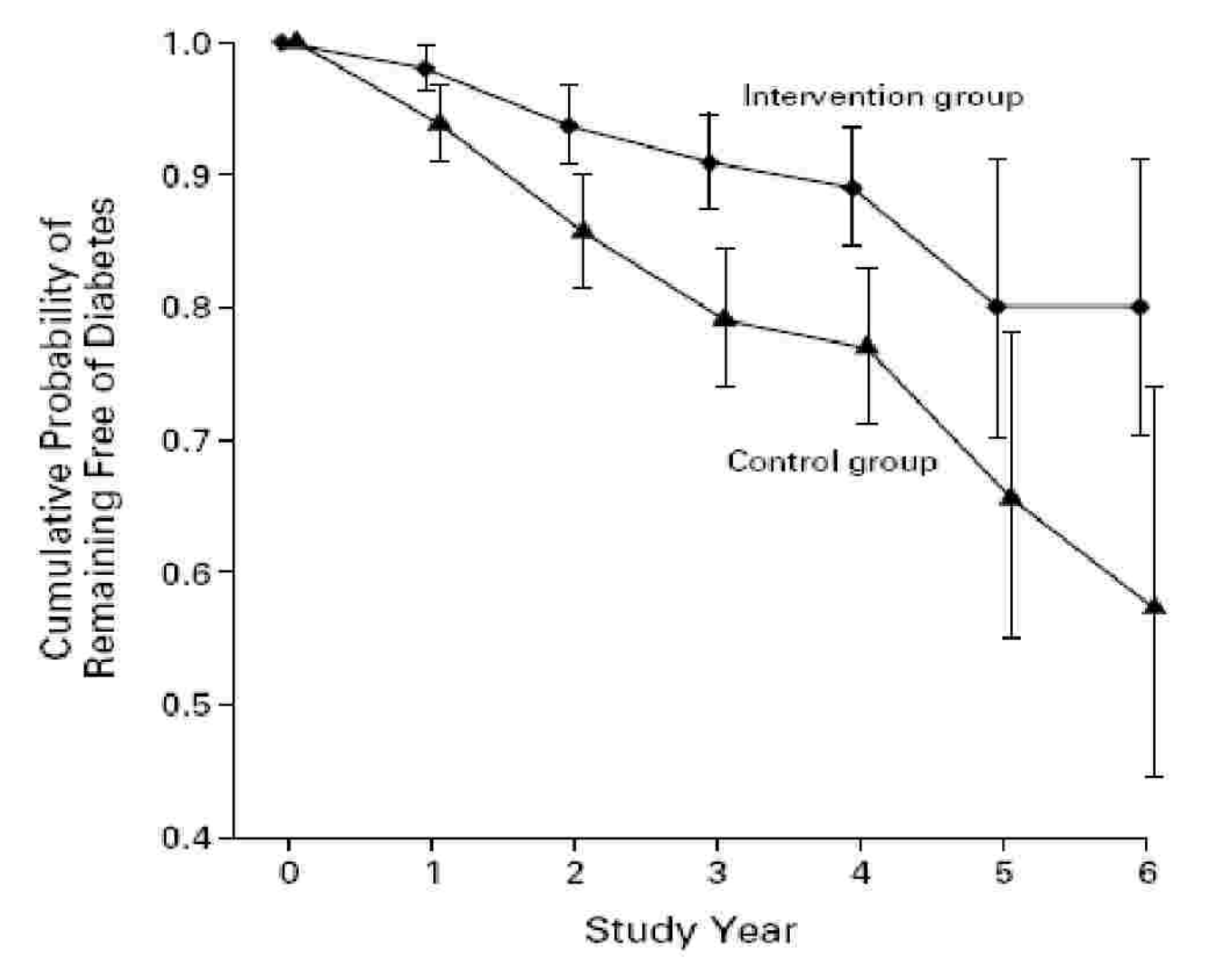
diabetici

(Sigal 1999)

Modalità di intervento sullo stile di vita adottate nel Finnish Diabetes Prevention Study

- Obiettivi:
  - riduzione peso ≥5%
  - introito lipidi <30% delle calorie totali (saturi <10%)
  - fibre >15 g/1000 Cal
  - attività fisica moderata ≥ 30 min/die
- Strumenti utilizzati:
  - counseling intensivo individuale
    - 7 incontri con dietista 1° anno; ogni 3 mesi in seguito (media 20)
  - incentivazione attività fisica
  - disponibilità gratuita supervisione per training di resistenza muscolare

Effetto della modifica dello stile di vita sulla comparsa di diabete tipo 2 nei soggetti con IGT del Finnish Diabetes Prevention Study



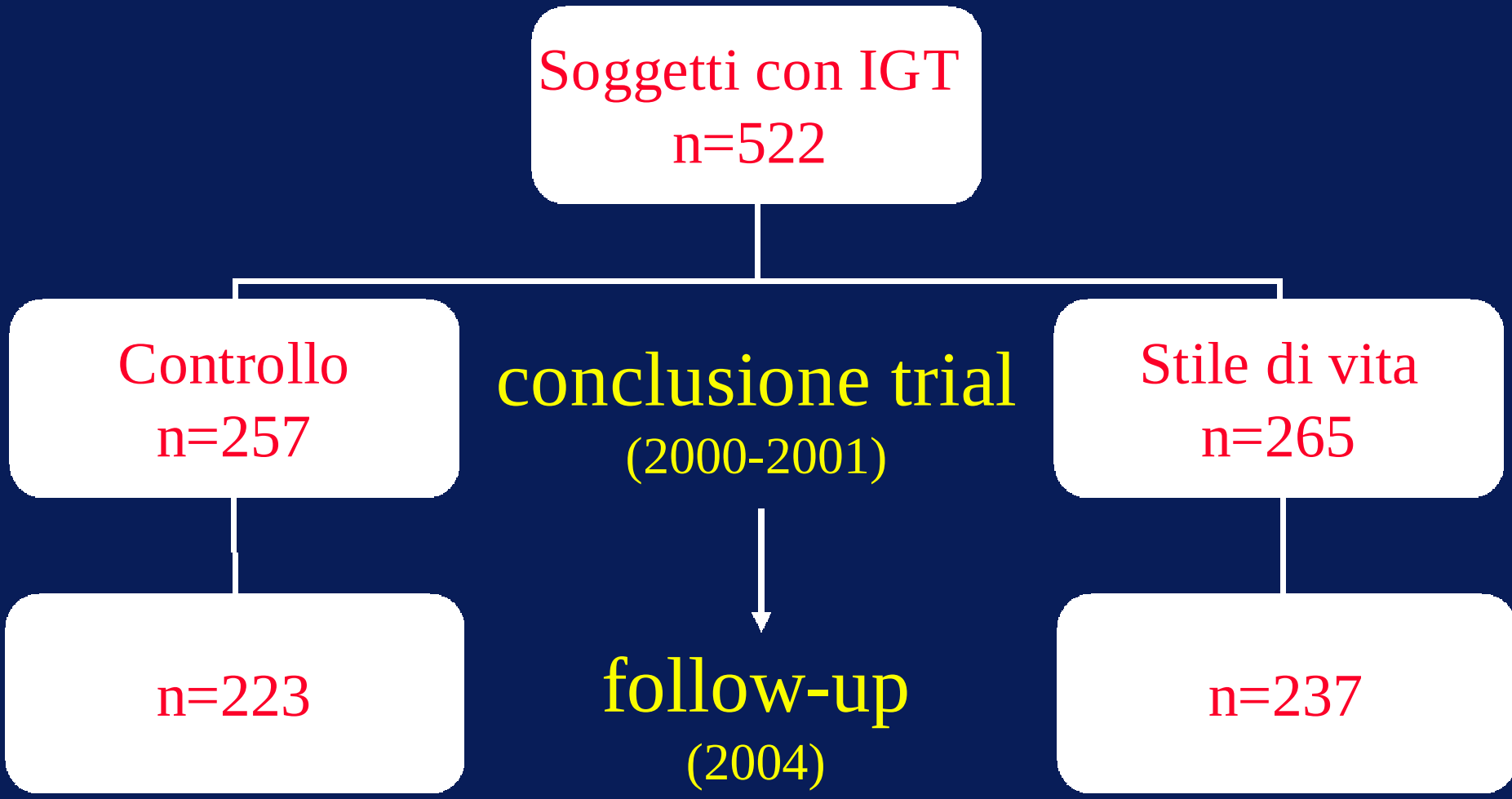
-58%

-p<0.001

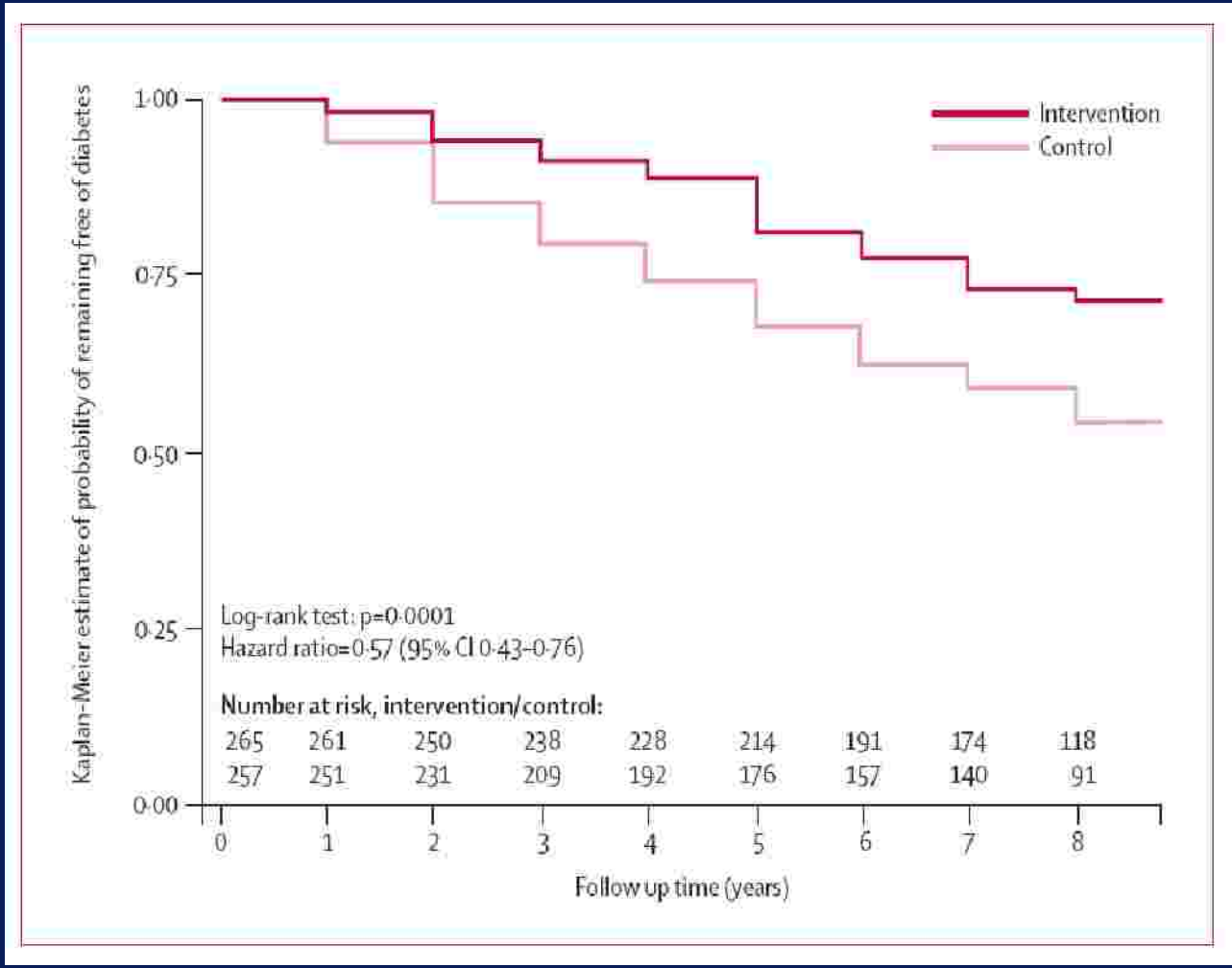
Tuomilehto et al, NEJM 2001

Finnish Diabetes Prevention Study

- schema di randomizzazione (1993-1998) -

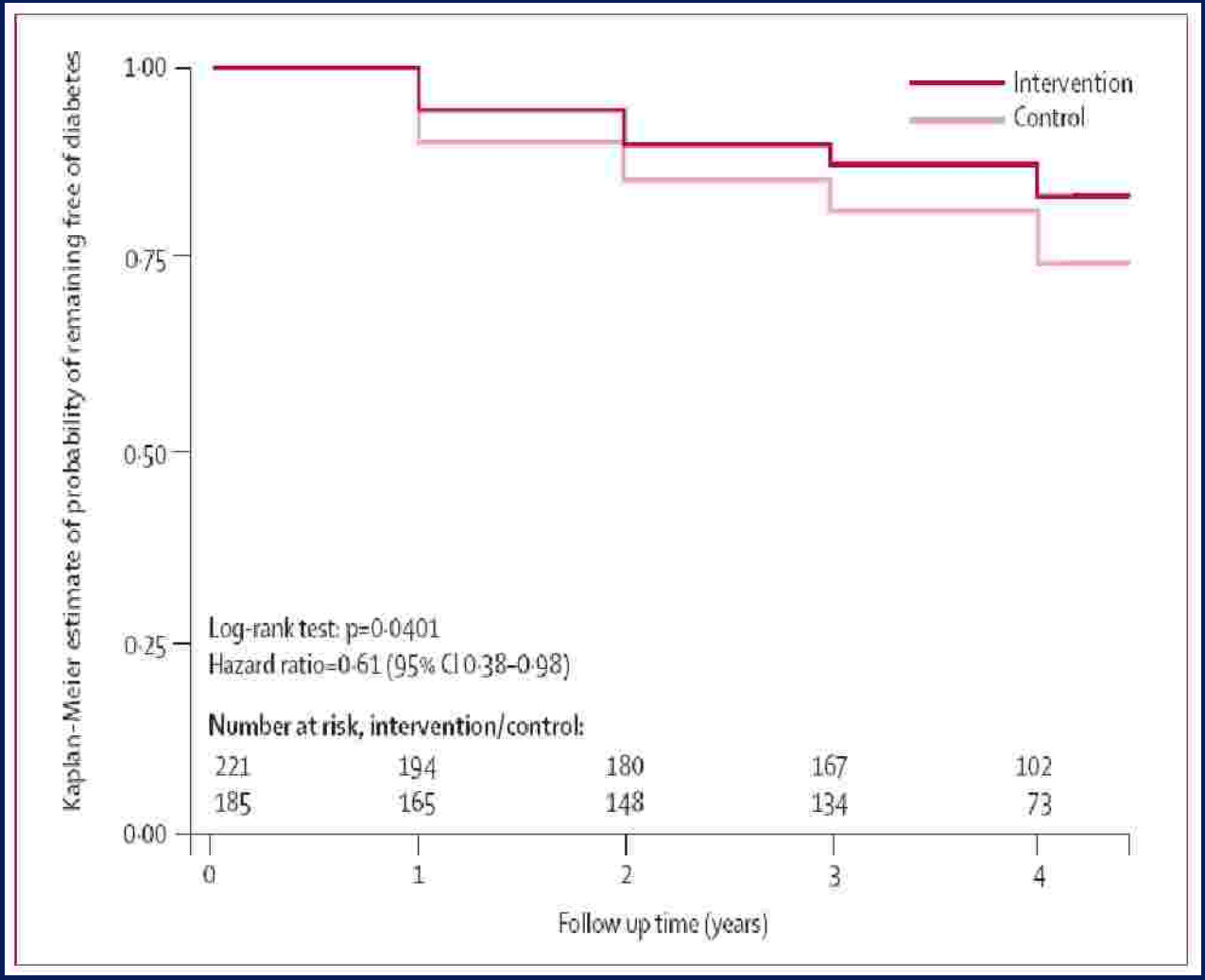


Effetto a lungo termine della modifica dello stile di vita sulla comparsa di diabete tipo 2 nei soggetti con IGT del Finnish Diabetes Prevention Study



Peltonen et al, Lancet 2006

Rischio di diabete nei soggetti con IGT del Finnish Diabetes Prevention Study riesaminati nel follow-up a lungo termine dopo la conclusione del trial



Peltonen et al, Lancet 2006

Caratteristiche dei soggetti del Finnish Diabetes Prevention Study nel corso del trial

	Intervention		Control		p*
	n	Mean	n	Mean	
Bodyweight (kg)					
Baseline	265	86·7	257	85·5	0·3267
Year 1	256	82·2	250	84·8	<0·0001
Year 3†	256	83·4	251	85·2	<0·0001
Last intervention period visit†	257	84·3	251	85·6	<0·0001
Proportion of physically active (%)‡					
Baseline	261	64	257	67	0·5192
Year 1	252	86	245	69	<0·0001
Year 3†	256	82	251	71	0·0003
Last intervention period visit†	256	81	251	71	0·0013
Energy proportion of fat (%)					
Baseline	264	36	255	37	0·0670
Year 1	254	33	245	35	0·0001
Year 3†	254	32	246	34	<0·0001

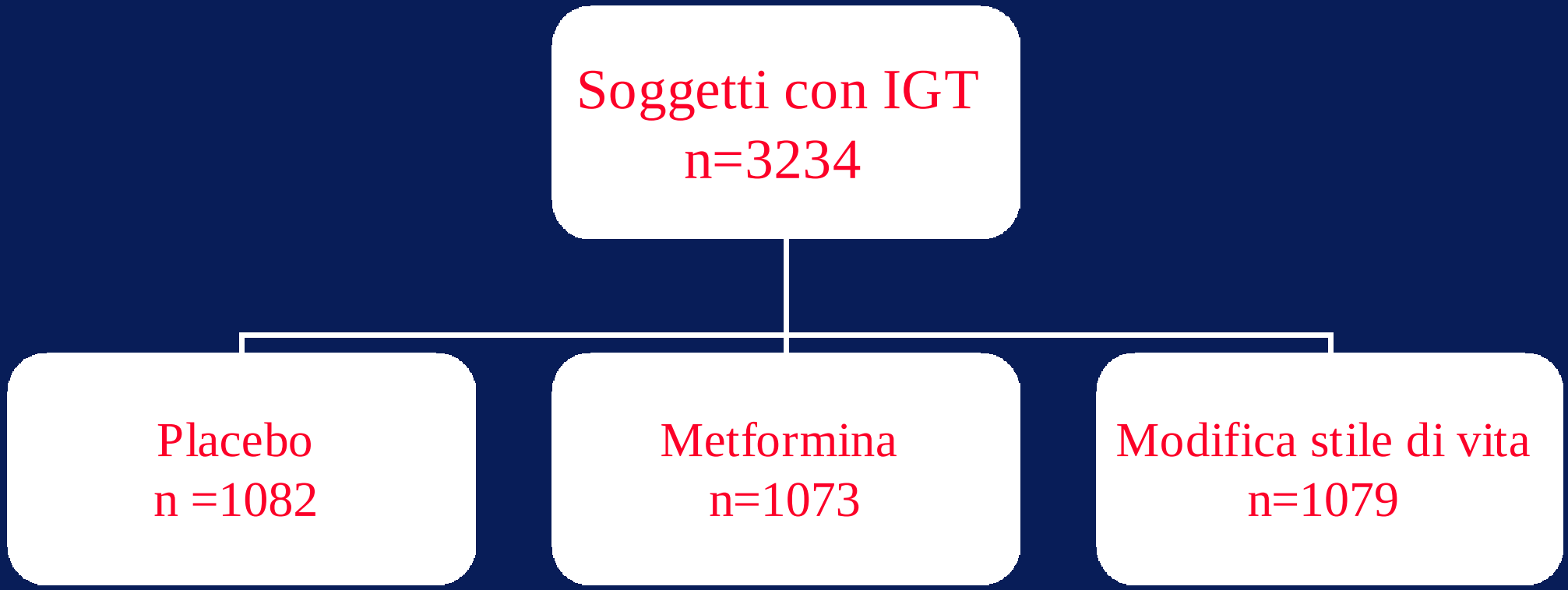
*p for test of equality between groups, adjusting for baseline level. †Last observation brought forward for individuals who dropped out or became diabetic during the study. ‡Individuals who reported walking, cycling, or other moderate intensity activity for at least 4 h per week categorised as physically active.

Table 1: Bodyweight, physical activity, and dietary intake during the intervention period of the study

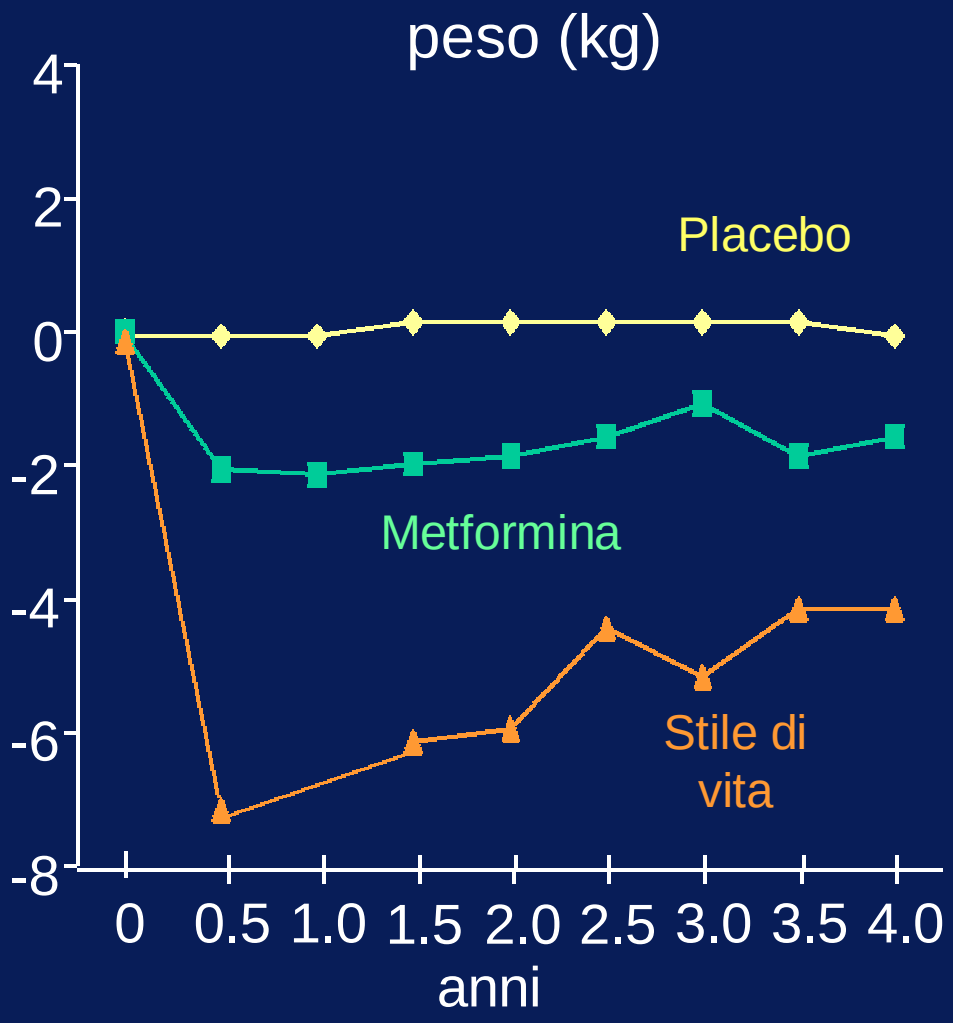
Peltonen et al, Lancet 2006

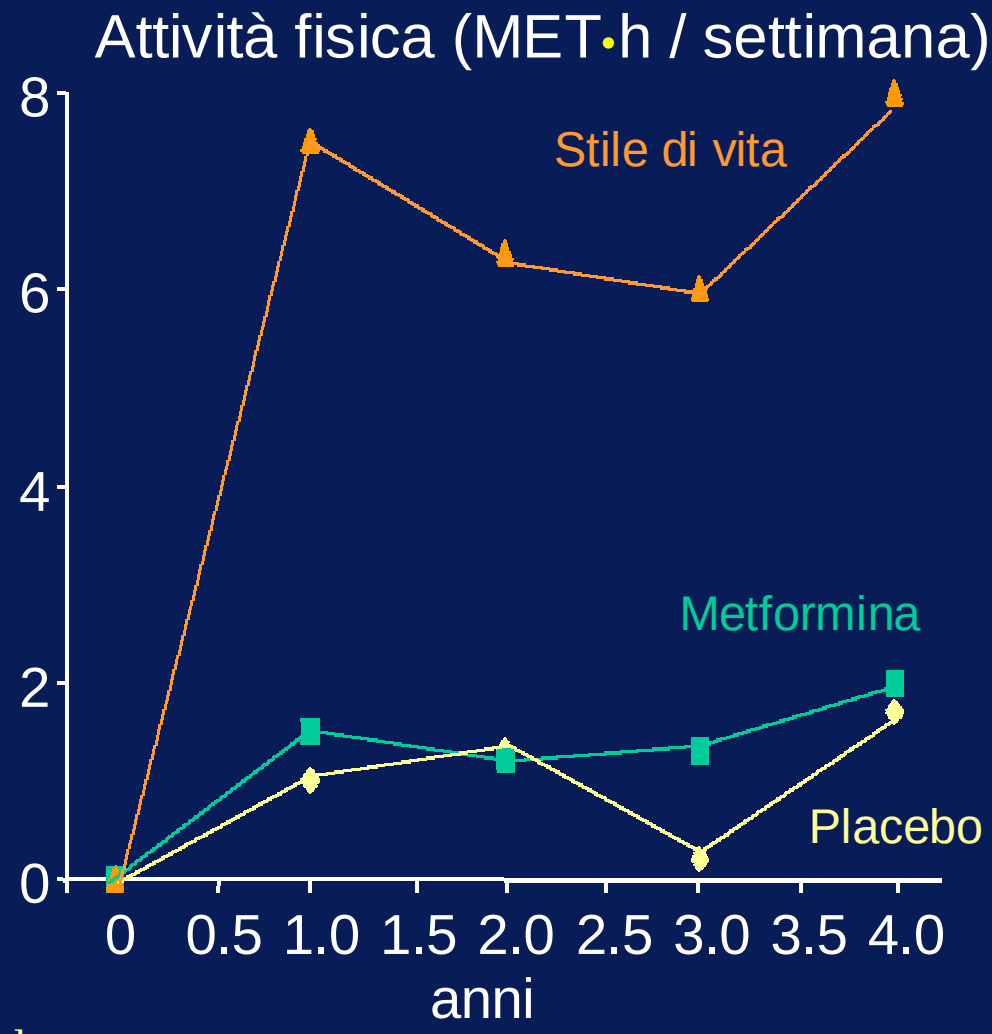
Diabetes Prevention Program

- schema di randomizzazione -



Cambiamenti nel peso e nell'attività fisica in 3234 soggetti con IGT assegnati a un programma intensivo di modifica dello stile di vita*, metformina o placebo

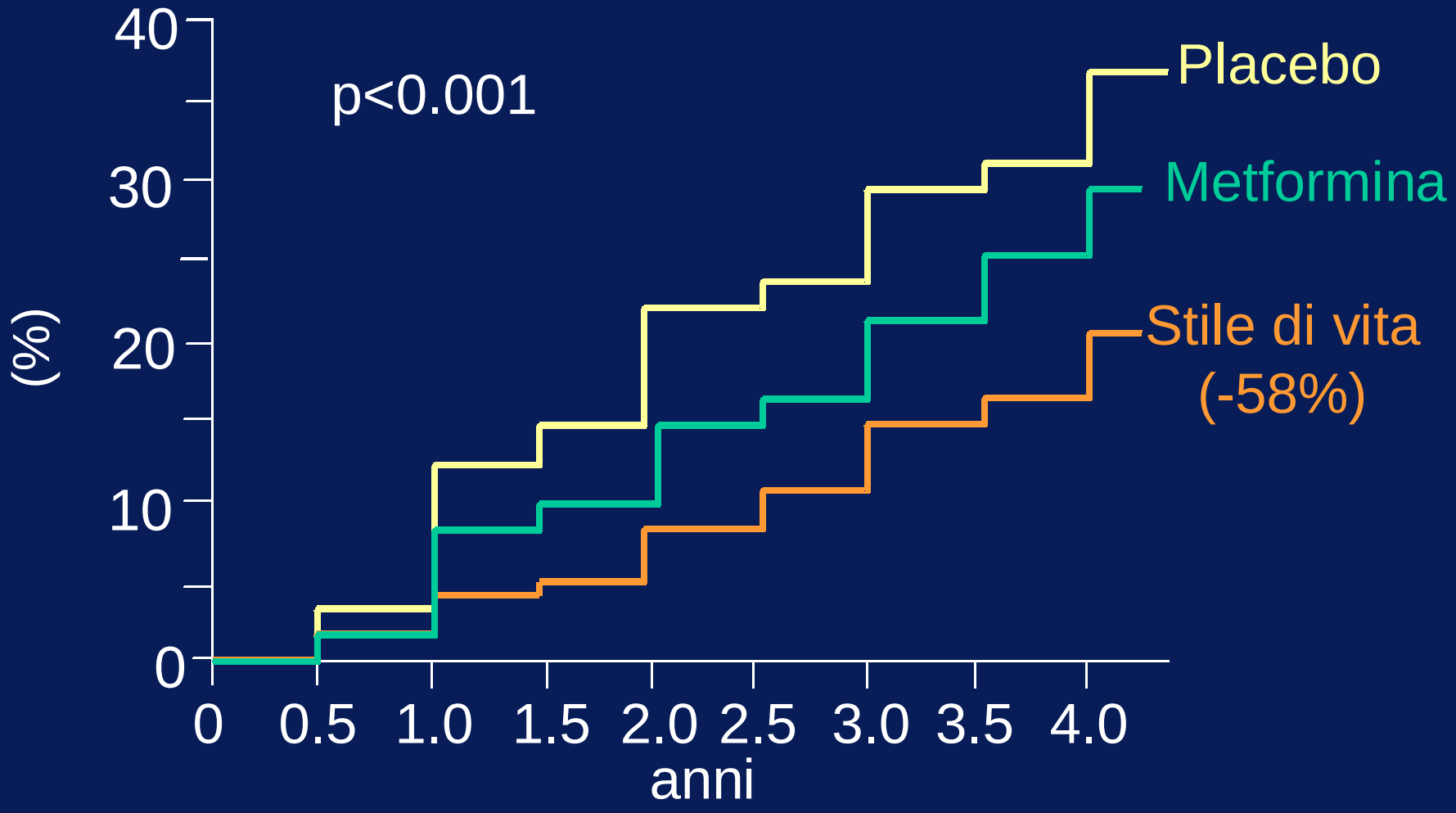




* dieta ipocalorica ipolipidica (obiettivo: calo ponderale =7%) + attività fisica moderata =150 min/settimana

Diabetes Prevention Program, NEJM 2002

Effetto della modifica dello stile di vita o della terapia con metformina sulla comparsa di diabete tipo 2 in 3234 soggetti con IGT



Diabetes Prevention Program, NEJM 2002

DPP Outcomes Study

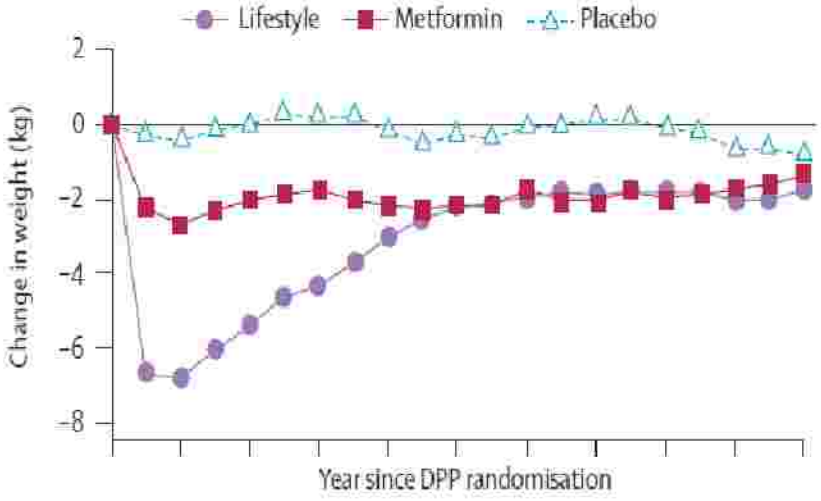
- 2766 of 3150 eligible subjects (88%) enrolled after completion of the randomised trial (mean duration 2.8 yr)
- Mean additional follow-up 5.7 yr
- All 3 groups offered lifestyle intevention. Lifestyle group offered additional counseling sessions for weight loss.
- Attendance at lifestyle session was 18% in the original lifestyle, 15% in the metformin and 14% in the placebo groups.
- 70% of subjects in the metformin group maintained therapy
- Intention-to-treat analysis

10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study

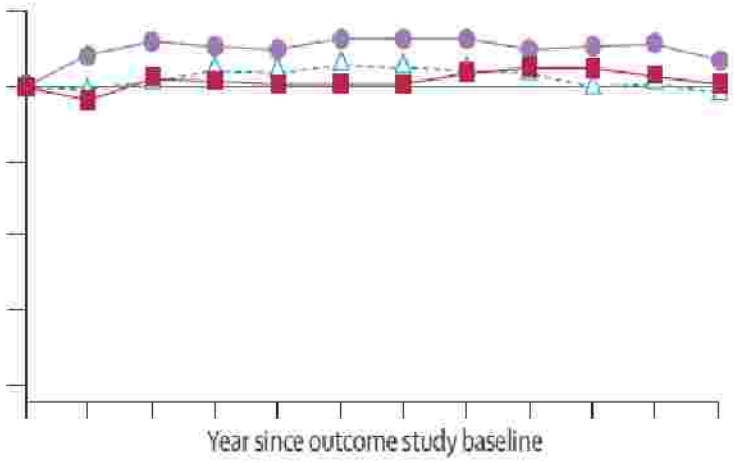
Lancet, November 2009

Mean weight change

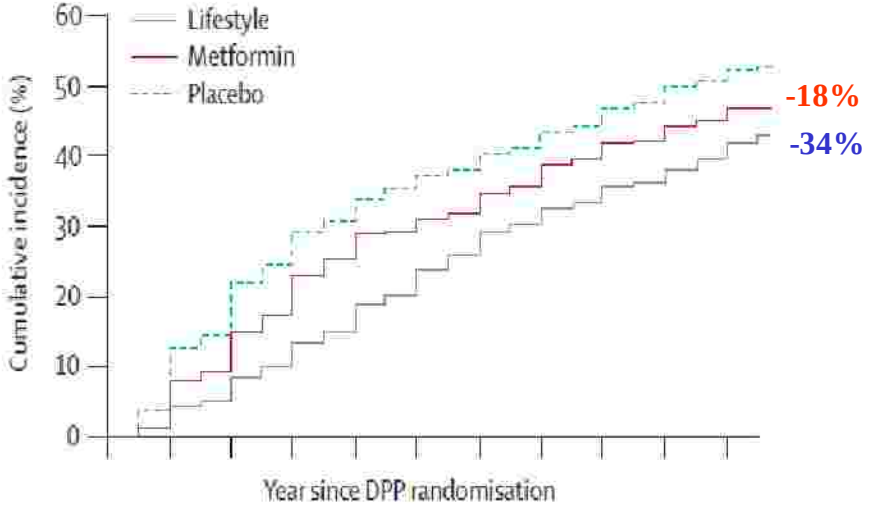
Years since randomization

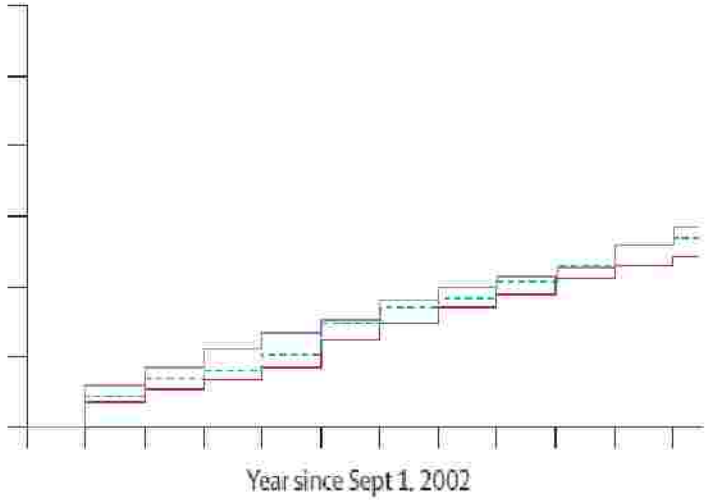


Years since outcome study baseline



Cumulative frequency of diabetes





10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study

Lancet, November 2009

Table 4: [redacted] since randomisation to DPP

	ILS group (n= 910)	Metformin group (n=924)	Placebo group (n= 932)
Antihypertensive drugs	32·9% (32·2–33·6)	37·1% (36·4–37·8)	35·6% (34·9–36·3)
Lipid-lowering drugs	18·4% (17·8–19·0)	22·6% (22·0–23·2)	22·7% (22·1–23·3)
Systolic/diastolic blood pressure (mm Hg)	120·8/74·4 (120·2/74·1–121·3/74·8)	122·4/75·6 (121·9/75·3–122·9/75·9)	122·3/75·6 (121·8/75·3–122·8/75·9)
Serum cholesterol (mmol/L)	4·92 (4·89–4·95)	4·93 (4·90–4·96)	4·97 (4·94–5·00)
Geometric serum triglycerides (mmol/L)	1·37 (1·34–1·39)	1·45 (1·42–1·47)	1·45 (1·43–1·48)

Data are % (95% CI) or mean (95% CI). DPP=Diabetes Prevention Program. ILS=intensive lifestyle intervention.

Lifestyle intervention for prevention of type 2 diabetes in primary health care: 1 yr follow-up of the Finnish National Diabetes Prevention Program (FIN-D2D)

Saaristo et al, Diabetes Care 2010

- 10,149 subjects at high risk for diabetes (IGT, IFG, CV disease or GDM)
- 1yr follow-up data available in 2,798 subjects
  - Mean age 56 yr
  - BMI 30.9 kg/m2

Lifestyle intervention for prevention of type 2 diabetes in primary health care: 1 yr follow-up of the Finnish National Diabetes Prevention Program (FIN-D2D)

Saaristo et al, Diabetes Care 2010

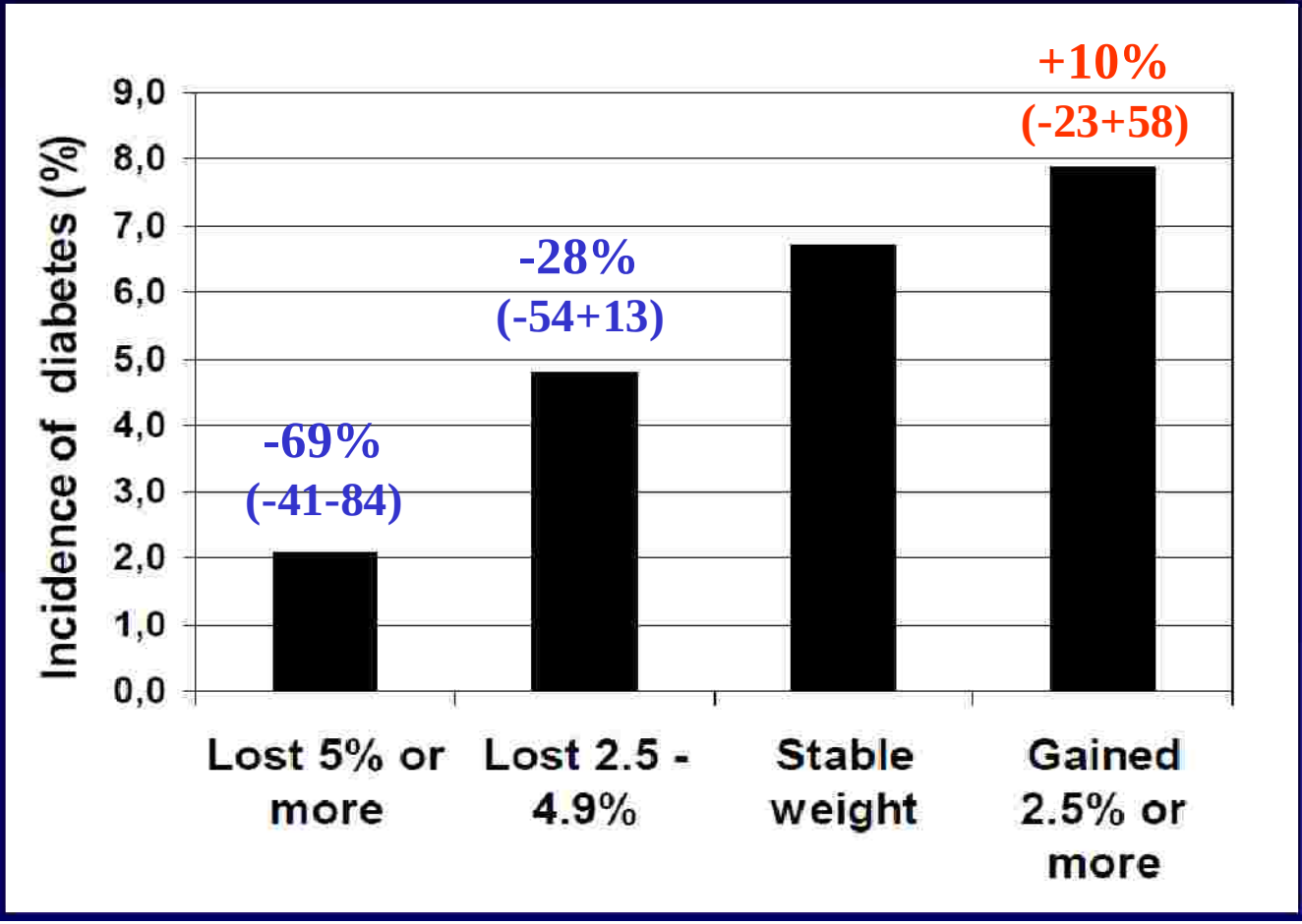
Table 2. Changes in risk factors from baseline to one-year visit according to weight loss

	Weigt loss 5% or more		Weight loss 2.5 – 4.9 %		Stable weight		Gained 2.5% or more		
	N	Mean (SD)[†]	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	ANCOVA p-value[‡, §]
									<0.001
BMI (kg/m^2)[†]	489	-3.0[‖¶] (2.3)	470	-1.1[‖¶] (0.3)	1285	-0.04 (0.46)	541	1.6[‖¶] (1.0)	<0.001
Waist (cm)	477	-6.6[‖¶] (6.1)	449	-2.7[‖¶] (4.2)	1258	-0.4 (4.2)	525	2.6[‖¶] (5.1)	<0.001
SBP (mmHg)[†]	480	-4.4[‖¶] (14.4)	464	-3.1[‖¶] (15.4)	1267	-0.7 (14.5)	536	0.5[‖] (15.1)	<0.001
DBP (mmHg)[†]	480	-3.8[‖¶] (8.4)	464	-2.2 (8.3)	1267	-1.1 (8.4)	536	-0.1 (8.7)	<0.001
Lipids (mmol/l)									
Total cholesterol	438	-0.35[‖¶] (0.78)	411	-0.23 (0.92)	1148	-0.15 (0.78)	482	-0.02[‖¶] (0.81)	<0.001
HDL cholesterol[†]	430	0.10[‖¶] (0.25)	408	0.05 (0.29)	1138	0.02 (0.27)	476	-0.01 (0.31)	<0.001
LDL cholesterol[†]	420	-0.33[‖¶] (0.71)	400	-0.22 (0.89)	1111	-0.17 (0.72)	463	-0.07[‖] (0.74)	<0.001
Triglycerides	430	-0.29[‖¶] (0.66)	406	-0.15[‖¶] (0.95)	1133	-0.01 (0.76)	473	0.12[‖¶] (0.95)	<0.001

Lifestyle intervention for prevention of type 2 diabetes in primary health care: 1 yr follow-up of the Finnish National Diabetes Prevention Program (FIN-D2D)

Saaristo et al, Diabetes Care 2010

Diabetes incidence according to weight loss



Diabete: le complicanze

Prima causa
di cecità

Causa maggiore
di insufficienza
renale & dialisi

Diabete

Prima causa
di amputazione
non traumatica

Concausa
nel 40-50% di
infarti e ictus

Rischi connessi con l'esercizio fisico nel diabete tipo 2

Aggravamento complicanze croniche severe (retinopatia, piede diabetico)

Evento cardiovascolare acuto

- cardiopatia ischemica (silente!)
- neuropatia autonomica

Attività fisica nella cura del diabete tipo 2

Indagini preliminari

Valutare la presenza e la gravità di:

1. Retinopatia
2. Nefropatia
3. Coronaropatia (forme silenti!) e macroangiopatia
4. Neuropatia somatica
5. Neuropatia autonomica

Prima di avviare un paziente diabetico a programmi di esercizio fisico va prescritto un test da sforzo?

- L'utilizzo del test da sforzo in soggetti diabetici asintomatici a basso rischio di coronaropatia, intenzionati a intraprendere un programma di attività fisica (moderata), non è raccomandato (rischio di evento cardiaco a 10 anni < 10%).

- (Livello della prova VI, Forza della raccomandazione D)

ACSM & ADA Joint Position Statement 2010

- Ecg stress test before exercise programs in diabetic patients -

- Before undertaking exercise more intense than brisk walking… ECG exercise stress testing is not recommended for asymptomatic individuals at low risk of CAD
- ECG stress testing may be indicated for individuals matching one or more of the following criteria…

ACSM & ADA Joint Position Statement 2010

- Criteria for a preliminary ecg stress test in diabetic patients -

? Age > 40 years

? Age > 30 years and:

- Diabetes duration > 10 years
- Hypertension, Cigarette smoking, Dyslipidemia
- Proliferative or preproliferative retinopathy, nephropathy (including microalbuminuria)

? Any of the following, regardless of age:

- Known or suspected vascular disease
- Autonomic neuropathy
- Advanced nephropathy with renal failure

Joint Position Statement – ACSM & ADA, 2009

Esercizio fisico e diabete

Raccomandazioni in presenza di microangiopatia

Retinopatia proliferante:

- evitare qualsiasi attività strenua o che comporti una manovra di Valsalva, colpi o scuotimenti bruschi

Nefropatia:

- porre attenzione al controllo pressorio

NEUROPATIA DIABETICA AUTONOMICA
SEGNI E SINTOMI CARDIOVASCOLARI

- Tachicardia fissa
- Ipotensione ortostatica
- Infarto indolore
- Arresto cardiaco

NEUROPATIA DIABETICA AUTONOMICA
TURBE DELLA CONTROREGOLAZIONE

- Ipoglicemie inavvertite

- Ipoglicemie protratte

Joint Position Statement – ACSM & ADA, 2009

Esercizio fisico e diabete

Raccomandazioni in presenza di neuropatia periferica

- I pazienti con neuropatia periferica, senza ulcerazioni in atto, possono effettuare attività fisica moderata con carico sulle estremità.

- Si raccomanda attenta cura dei piedi, con uso di calzature idonee e ispezione quotidiana.

Il problema della neuropatia autonomica

- Altera il compenso emodinamico allo sforzo
- Si associa ad un aumentato rischio cardiovascolare e di lesioni al piede
- Interferisce con la possibilità di usare la frequenza cardiaca come indice di intensità dello sforzo
- Comporta una ridotta capacità di contrastare e percepire l'ipoglicemia
- Può provocare incoordinazione temporale fra effetto dei farmaci ipoglicemizzanti e assorbimento dei nutrienti
- Può comportare difficoltà nel controllo termico

Necessario non far superare livelli di attività fisica percepiti come sforzo moderato

Criteri Diagnostici della Sindrome Metabolica
Revisione IDF 2009 criteri ATP III 2001

Tre o più alterazioni fra le seguenti:

- Glicemia a digiuno ≥ 100 mg/dl
- Trigliceridi ≥ 150 mg/dl
- HDL <40 mg/dl M, <50 mg/dl F
- Ipertensione arteriosa (≥ 130/85 mmHg)
- Obesità addominale (circonf.vita >94 cm M, >80 cm F)

Sindrome metabolica

- Predittore di:
  - Diabete tipo 2
  - Patologia cardiovascolare

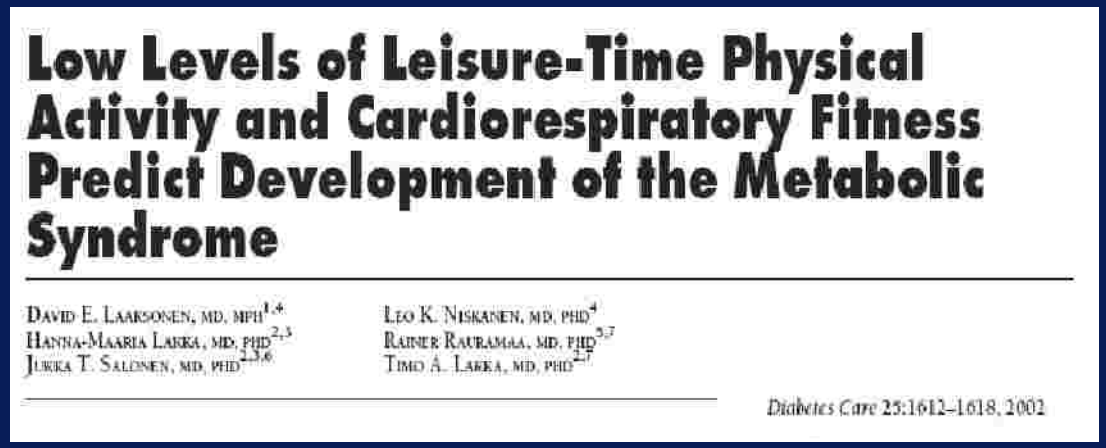
Rischio di comparsa di anomalie metaboliche associato alla ridotta fitness cardiorespiratoria* nel CARDIA Study (n=4487; età 18-30 anni; follow-up 15 anni)

- 3 categorie in base a test massimale al treadmill: 1° vs 2°-3° vs 4°-5° quintile -

Anomalie metaboliche	bassa vs alta (HR e 95% CI)	moderata vs alta (HR e 95% CI)
Ipertensione	2.17 (1.69-2.78)	1.34 (1.07-1.67)
Diabete	1.75 (1.01-3.04)	1.25 (0.75-2.09)
Sindrome metabolica (ATP III)	1.87 (1.42-2.48)	1.64 (1.29-2.09)
Ipercolesterolemia	1.02 (0.76-1.36)	1.01 (0.81-1.27)

• Corretto per età, razza, sesso, scolarità, BMI, circonferenza vita, fumo, storia familiare di IMA precoce.

Carnethon et al, JAMA 2003



Low Levels of Leisure-Time Physical Activity and Cardiorespiratory Fitness Predict Development of the Metabolic Syndrome

David E. Laaksonen, MD, MPH[1,4]
Hanna-Maaria Lakka, MD, PHD[2,3]
Jukka T. Salonen, MD, PHD[2,5,6]
Leo K. Niskanen, MD, PHD[4]
Rainer Rauramaa, MD, PHD[3,7]
Timo A. Lakka, MD, PHD[2,7]

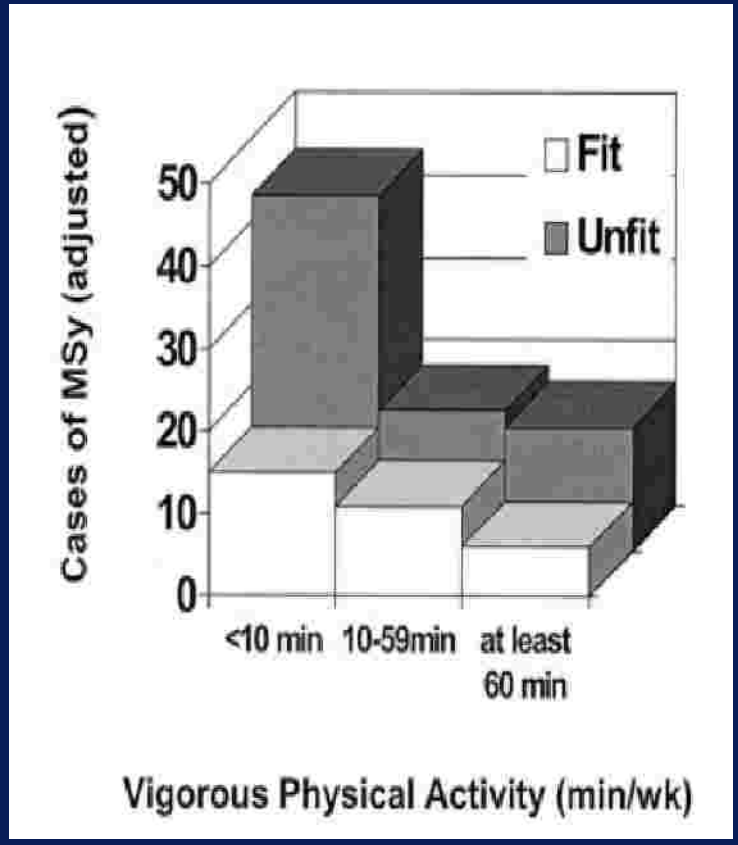
Diabetes Care 25:1612–1618, 2002

612 uomini del KIHD Study senza sindrome metabolica (età media 52 anni, BMI 26 kg/m^2)

- Questionario su attività fisica nell'anno precedente
- Test al cicloergometro

Dopo un follow-up di 4 anni, 107 (17.5%) rientravano nei criteri della diagnosi di sindrome metabolica (WHO)

Comparsa di sindrome metabolica in rapporto alla fitness cardiorespiratoria (50° centile superiore vs inferiore) e alla quantità di attività fisica vigorosa (≥7.5 MET) svolta



Laaksonen et al, KIHD Study, Diabetes Care 2002

Rischio di sviluppo di sindrome metabolica in 3233 uomini suddivisi in quartili di forza muscolare - Aerobics Center Longitudinal Study (1980-2003) -

	Muscular Strength				*P* Value for Trend
	Q1 (Low)	Q2	Q3	Q4 (High)	
Participants (*N*)	808	809	808	808	
Man-years of follow-up	5129	5289	5602	5685	
Cases (*N*)	144	130	120	86	
Age-adjusted rate per 1000 man-years	28.1	24.6	21.3	15.2	<0.0001
HR (95% CI), Model 1*	1.00	0.88 (0.69–1.12)	0.77 (0.60–0.98)	0.54 (0.42–0.71)	<0.0001
HR (95% CI), Model 2†	1.00	0.93 (0.73–1.17)	0.89 (0.70–1.13)	0.66 (0.50–0.86)	0.004
HR (95% CI), Model 3‡	1.00	0.95 (0.75–1.21)	0.93 (0.73–1.18)	0.76 (0.57–0.99)	0.06

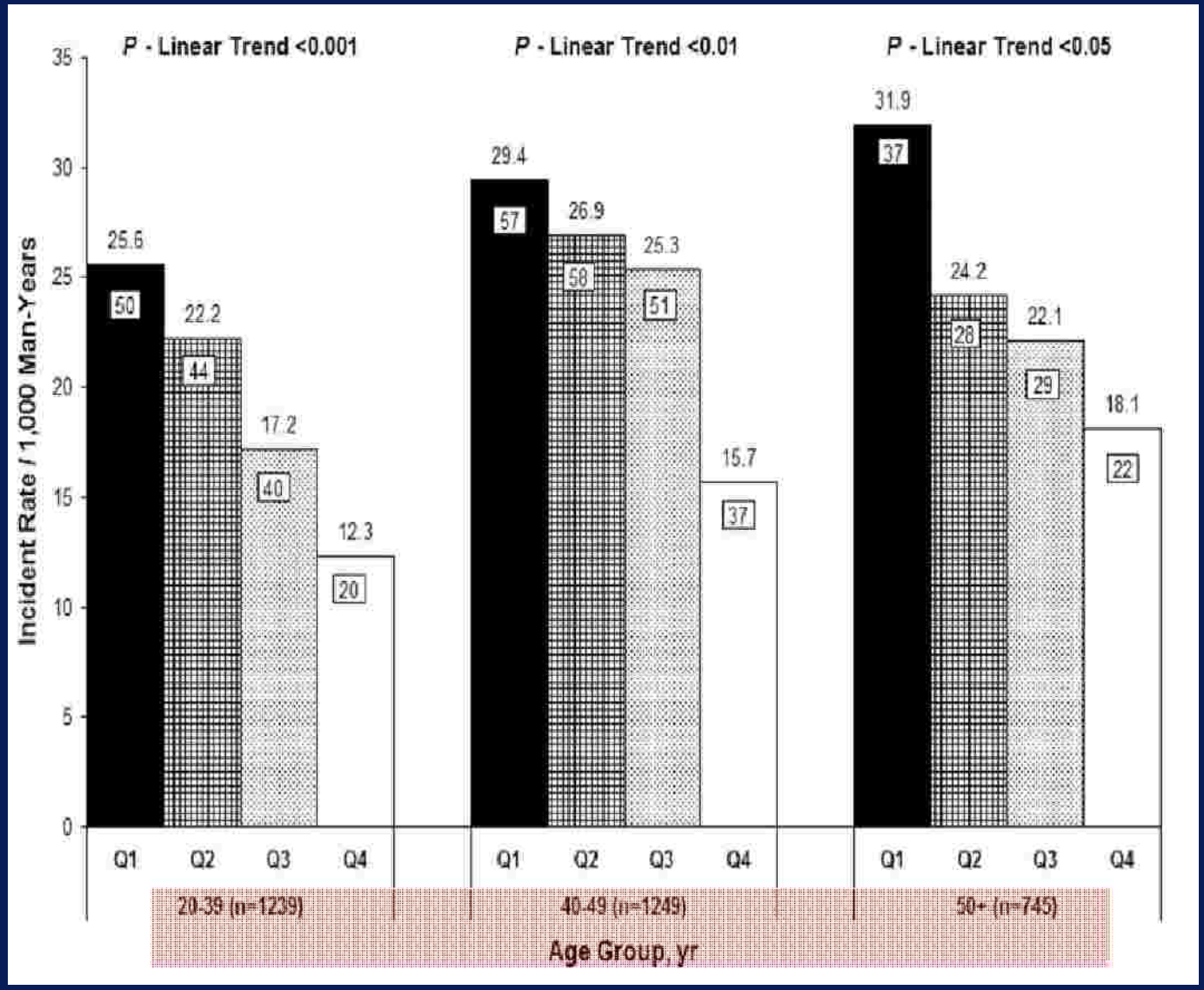
HR, hazard ratio; CI, confidence interval.
* Adjusted for age and examination date.
† Additionally adjusted for smoking, alcohol intake, number of metabolic syndrome risk factors at baseline, and family history of diabetes, hypertension, and premature coronary disease.
‡ Additionally adjusted for maximal treadmill time.

Follow-up medio 7 anni.

Al basale età media 43 anni, BMI medio 25 kg/m^2

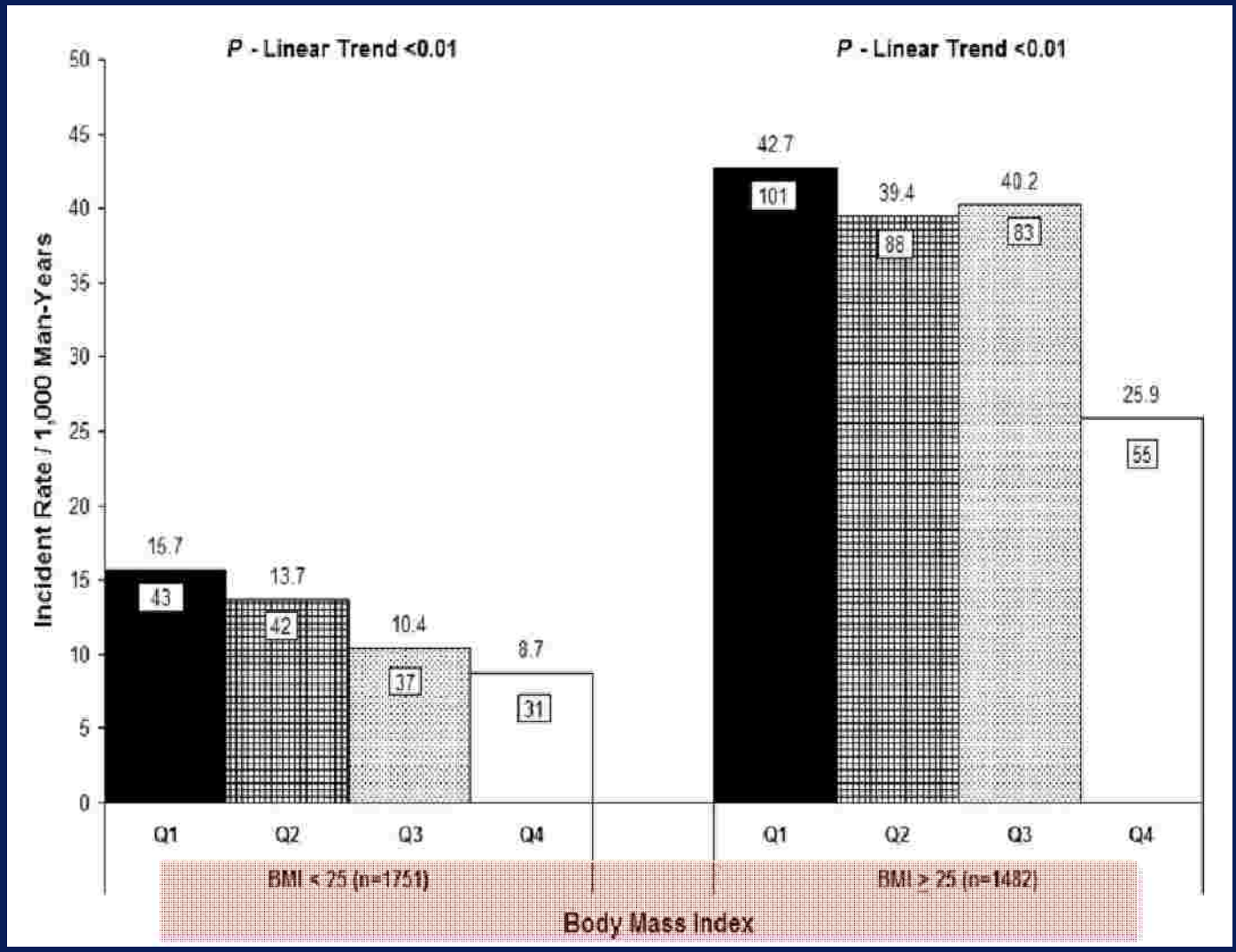
Jurca et al, Med Sci Sports Exerc 2005

Incidenza di sindrome metabolica in uomini suddivisi p età e per quartili di forza muscolare



Jurca et al, Med Sci Sports Exerc 2005

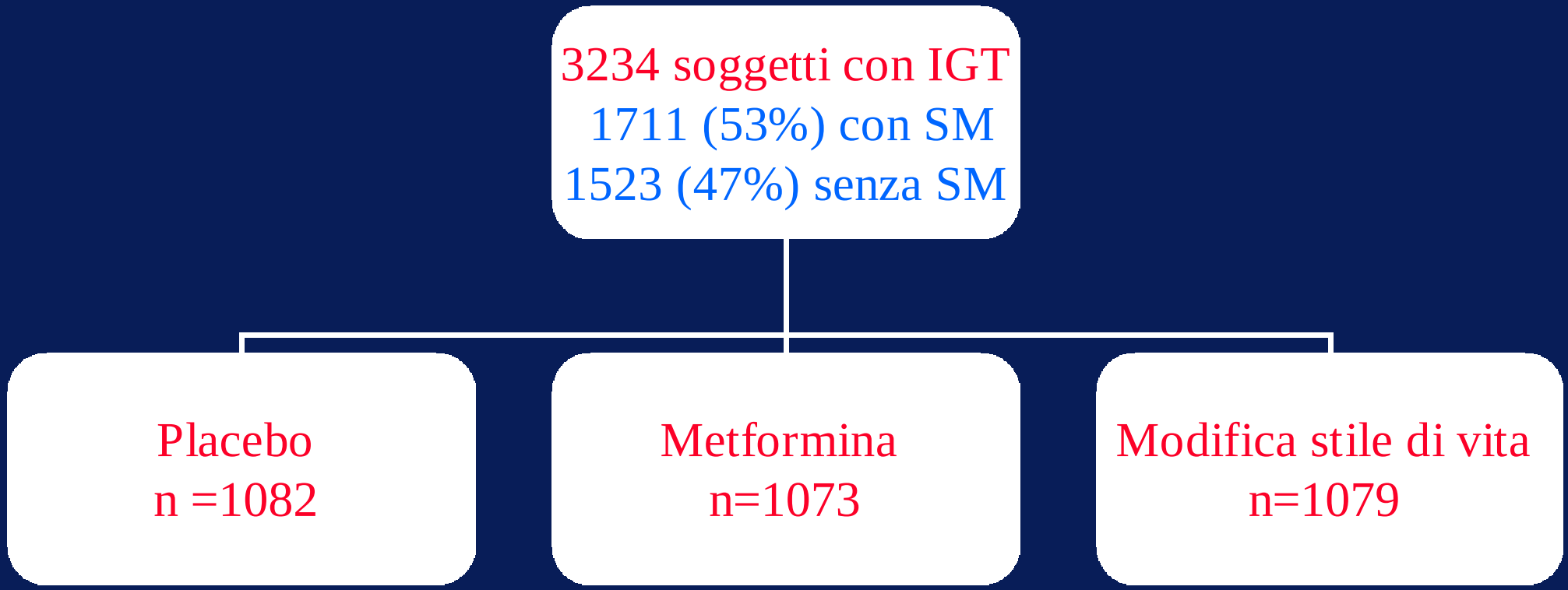
Incidenza di sindrome metabolica in uomini suddivisi p BMI e per quartili di forza muscolare



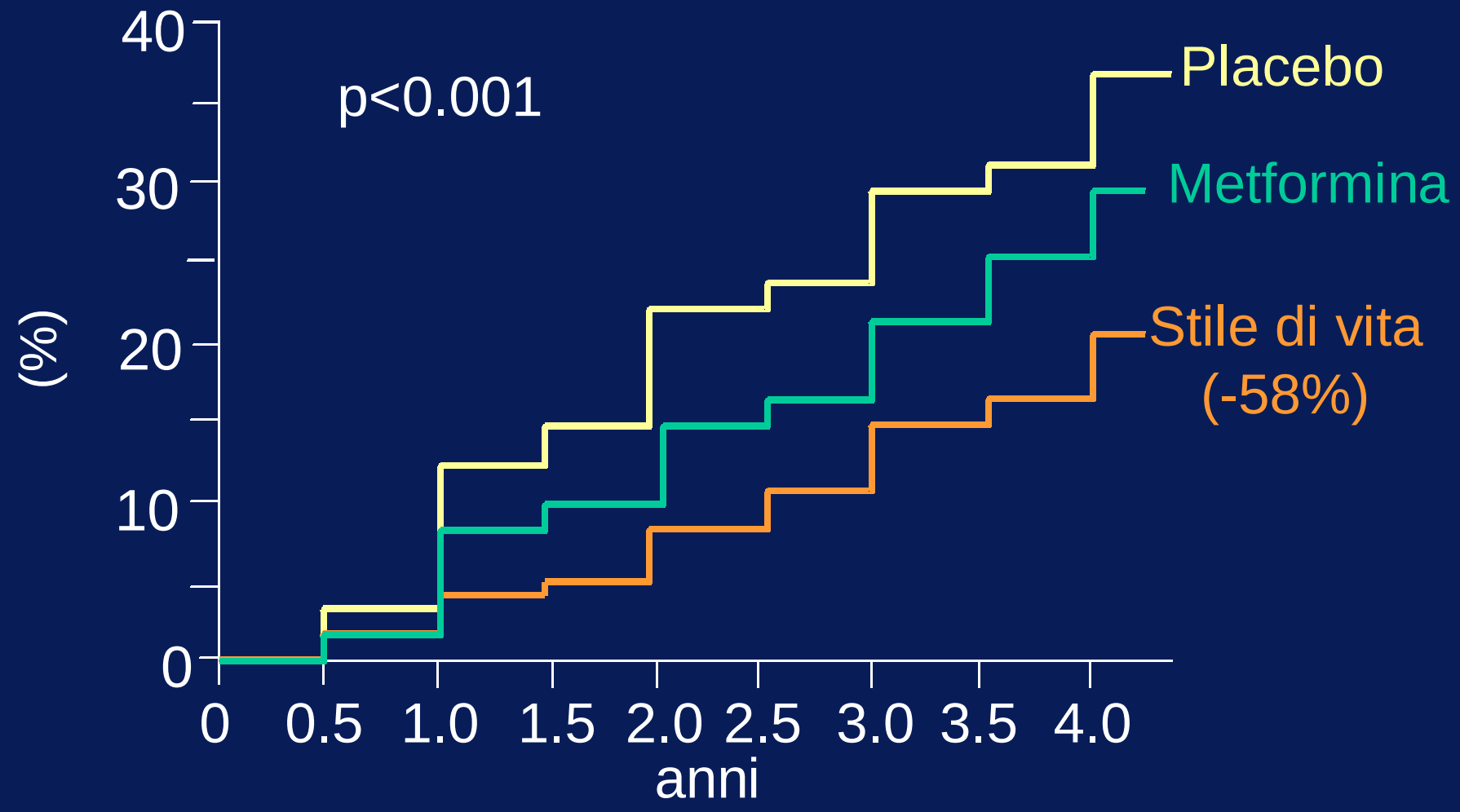
Jurca et al, Med Sci Sports Exerc 2005

Diabetes Prevention Program

- schema di randomizzazione -

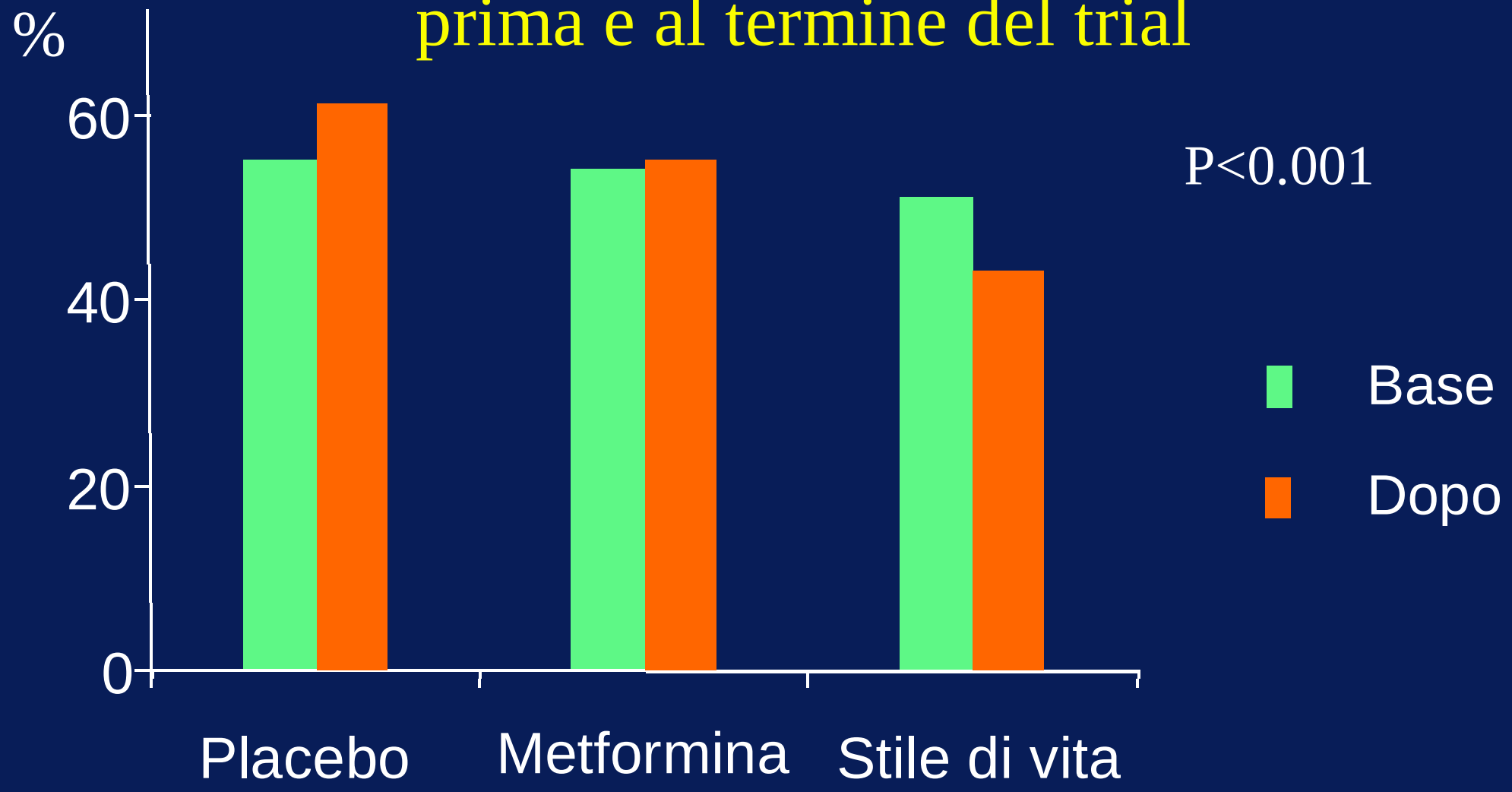


DPP - Effetto della modifica dello stile di vita o della terapia con metformina sulla comparsa di diabete tipo 2 in 3234 soggetti con IGT



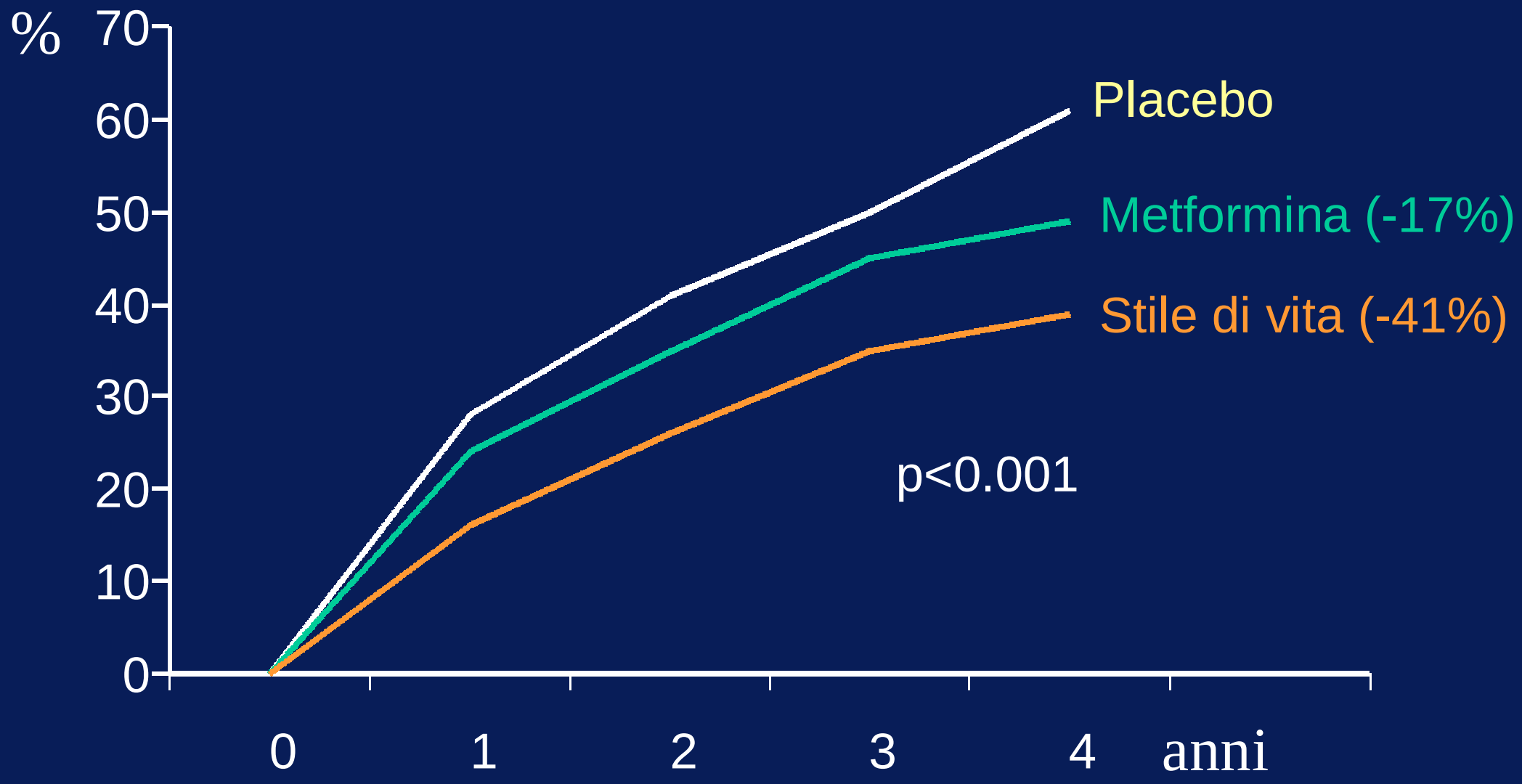
Diabetes Prevention Program, NEJM 2002

Prevalenza della sindrome metabolica nei partecipanti al Diabetes Prevention Program prima e al termine del trial



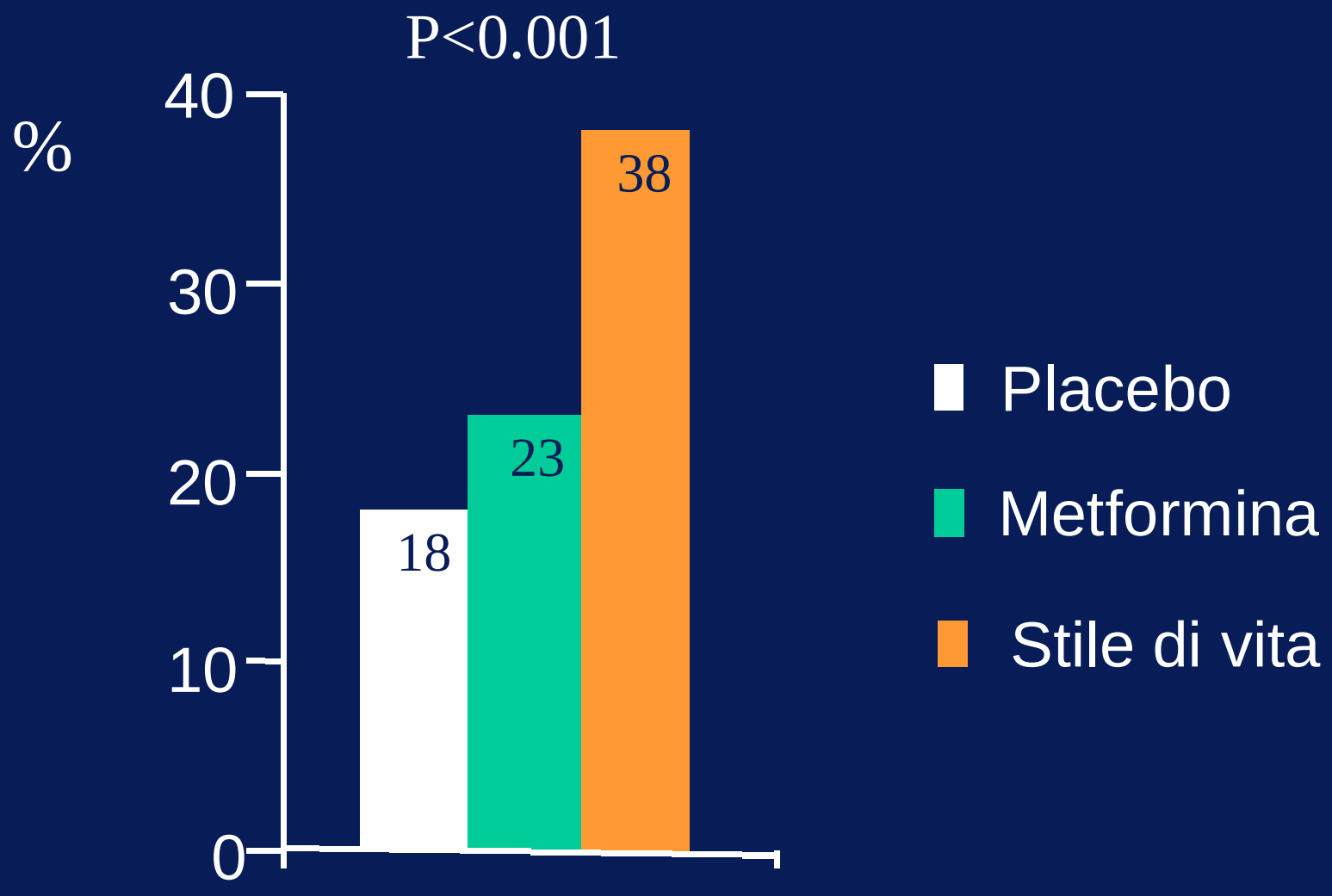
Orchard et al, Ann Intern Med 2005

Incidenza cumulativa di sindrome metabolica nei partecipanti al Diabetes Prevention Program



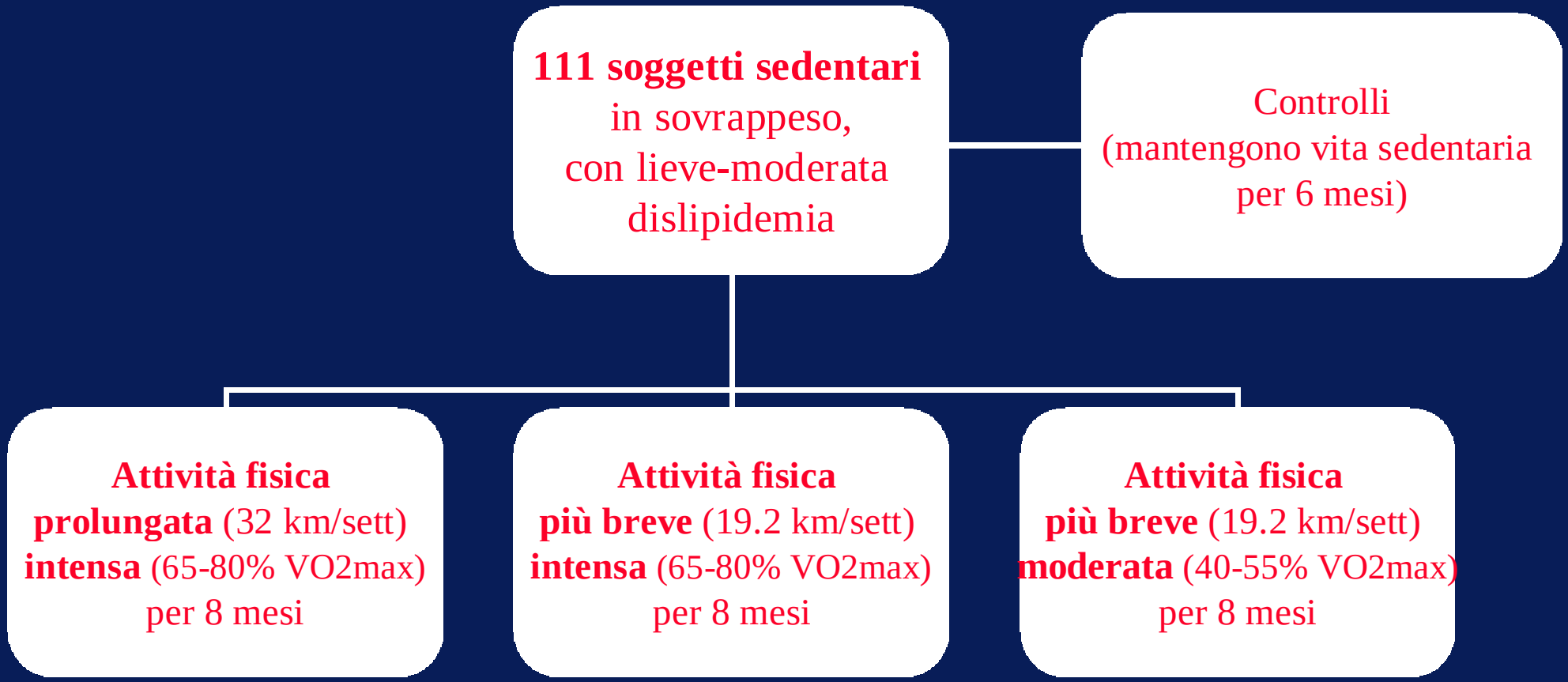
Orchard et al, Ann Intern Med 2005

Frequenza di regressione della sindrome metabolica nei partecipanti al Diabetes Prevention Program



Orchard et al, Ann Intern Med 2005

Attività fisica per ridurre le lipoproteine: quale quantità e quale intensità di esercizio? The STRRIDE Study - disegno sperimentale



Kraus et al, NEJM 2002

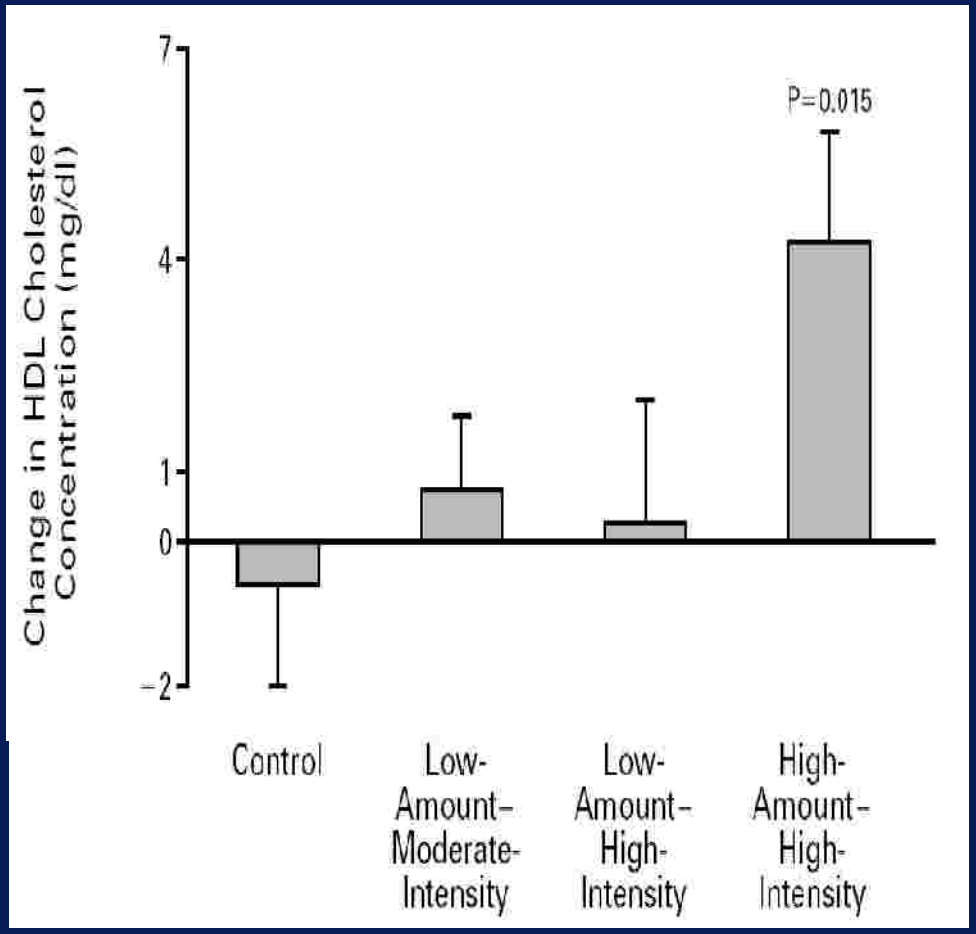
The STRRIDE Study
– aderenza al protocollo e variazioni di peso -

	Control Group (N=26)	Low-Amount–Moderate-Intensity Group (N=19)	Low-Amount–High-Intensity Group (N=17)	High-Amount–High-Intensity Group (N=22)
Prescribed and actual amount and intensity of exercise				
Intensity range — percentage of peak oxygen consumption		40–55	65–80	65–80
Prescribed amount — mi/wk§		12	12	20
Prescribed time — min/wk		191±41	125±26	200±38
Rate of adherence — %		92.1±9.9	91.3±10.6	86.8±8.7
Actual amount — mi/wk¶		11.1	11.0	17.4
Actual time — min/wk‖		176±36	117±26	174±35
Frequency — no. of sessions/wk		3.4±0.6	3.0±0.5	3.8±0.7
Changes from base line				
Body weight — kg	0.95±3.04	−0.55±1.80**	−0.17±1.79	−1.52±2.16††

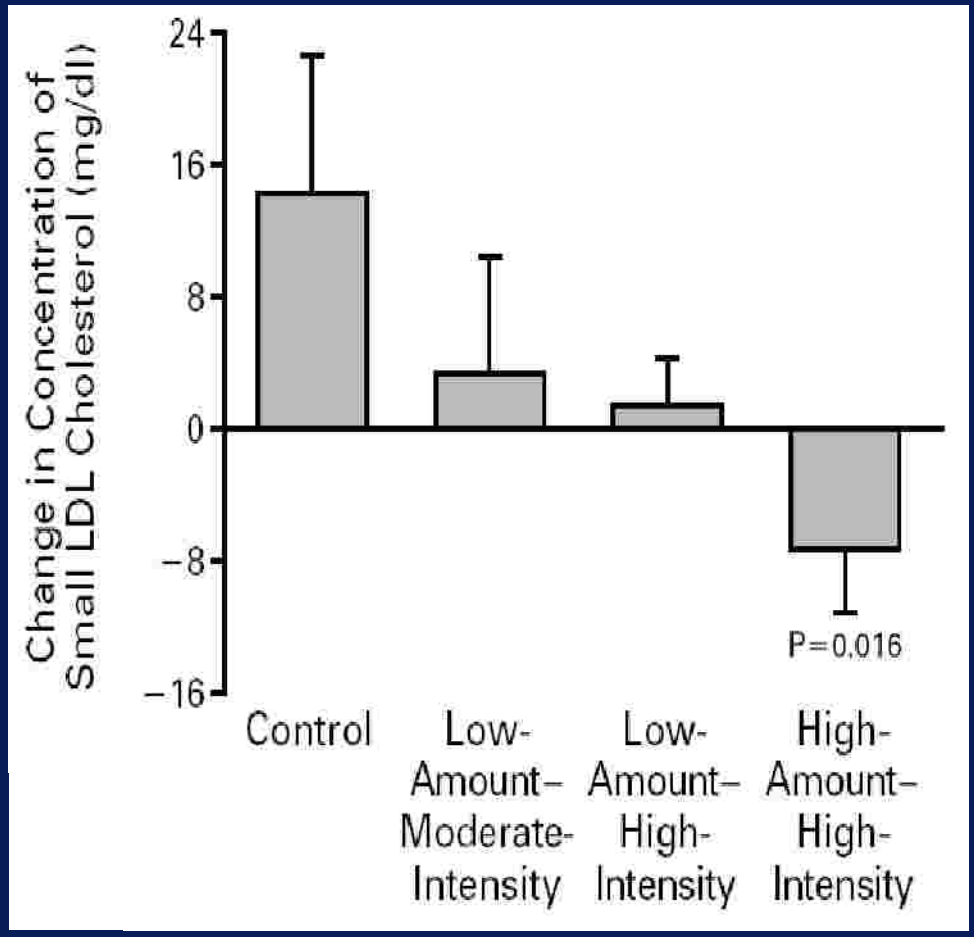
Kraus et al, NEJM 2002

Effetti di varie quantità/intensità di attività fisica su colesterolo HDL e LDL piccole e dense

HDL



LDL piccole e dense



The Strride Study, Kraus et al, NEJM 2002

TABLE 3. EFFECTS OF THE AMOUNT AND INTENSITY OF EXERCISE ON LIPIDS, LIPOPROTEINS, AND LIPOPROTEIN SUBFRACTIONS.*

VARIABLE	EFFECT OF AMOUNT OF EXERCISE	EFFECT OF INTENSITY OF EXERCISE
	rankings	
LDL — Concentration of small LDL particles	High amount, low amount, control	High intensity, moderate intensity, control
LDL — Concentration of LDL particles	High amount, low amount, control	High intensity, moderate intensity, control
LDL — Size of LDL particles	High amount, low amount, control	High intensity, moderate intensity, control
IDL → IDL concentration	High amount, low amount, control	High intensity, moderate intensity, control
HDL — Concentration of large HDL particles	High amount, low amount, control	High intensity, moderate intensity, control
HDL — Size of HDL particles	High amount, low amount, control	High intensity, moderate intensity, control
HDL — HDL cholesterol concentration	High amount, low amount, control	Moderate intensity, high intensity, control
VLDL — Concentration of large VLDL particles	High amount, low amount, control	Moderate intensity, high intensity, control
VLDL — Size of VLDL particles	Low amount, high amount, control	Moderate intensity, high intensity, control
VLDL — Total triglyceride concentration	High amount, low amount, control	Moderate intensity, high intensity, control
VLDL — VLDL triglyceride concentration	High amount, low amount, control	Moderate intensity, high intensity, control

Ordine di efficacia di diverse quantità e intensità dell'attività fisica sulle lipoproteine circolanti

The Strride Study, Kraus et al, NEJM 2002

Diabetologia (2003) 46:1071–1081

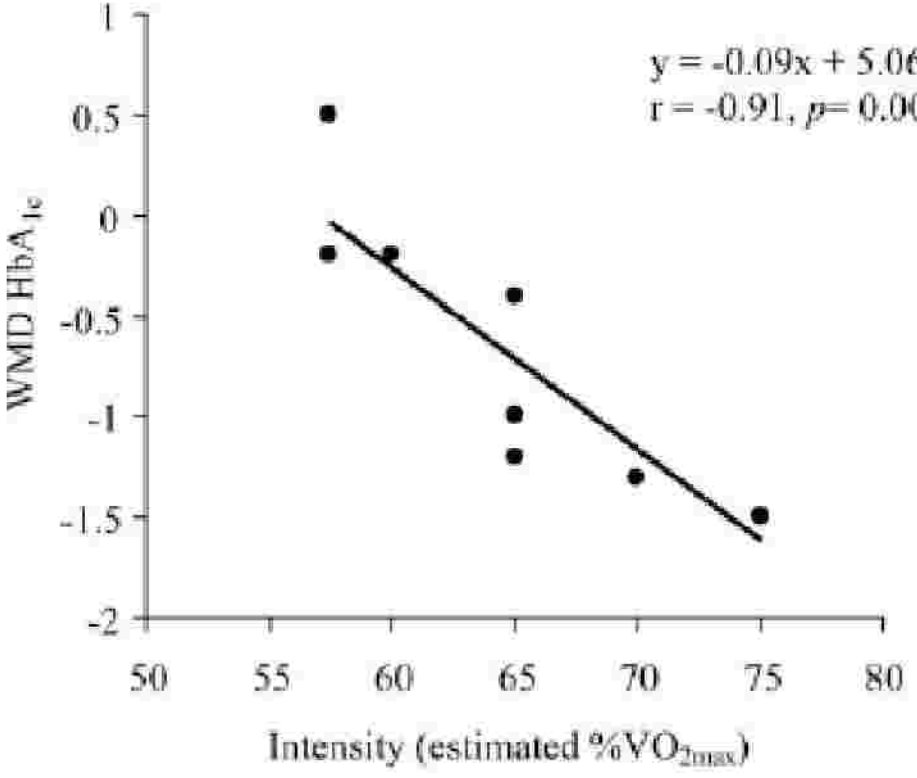
Meta-analysis of the effect of structured exercise training on cardiorespiratory fitness in Type 2 diabetes mellitus

N. G. Boulé[1], G. P. Kenny[1], E. Haddad[2], G. A. Wells[3, 4], R. J. Sigal[1, 3]

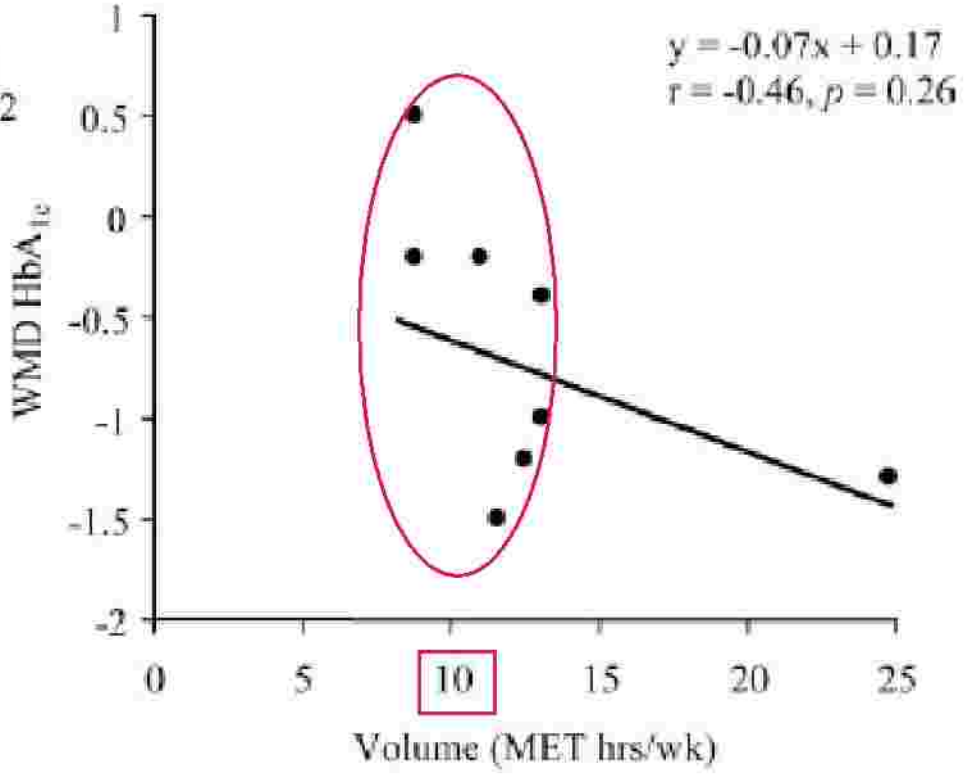
[1] School of Human Kinetics, University of Ottawa, Ottawa, Ontario, Canada
[2] Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada
[3] Department of Medicine, University of Ottawa, Ottawa, Ontario, Canada
[4] Department of Epidemiology and Community Medicine, University of Ottawa, Ottawa, Ontario, Canada

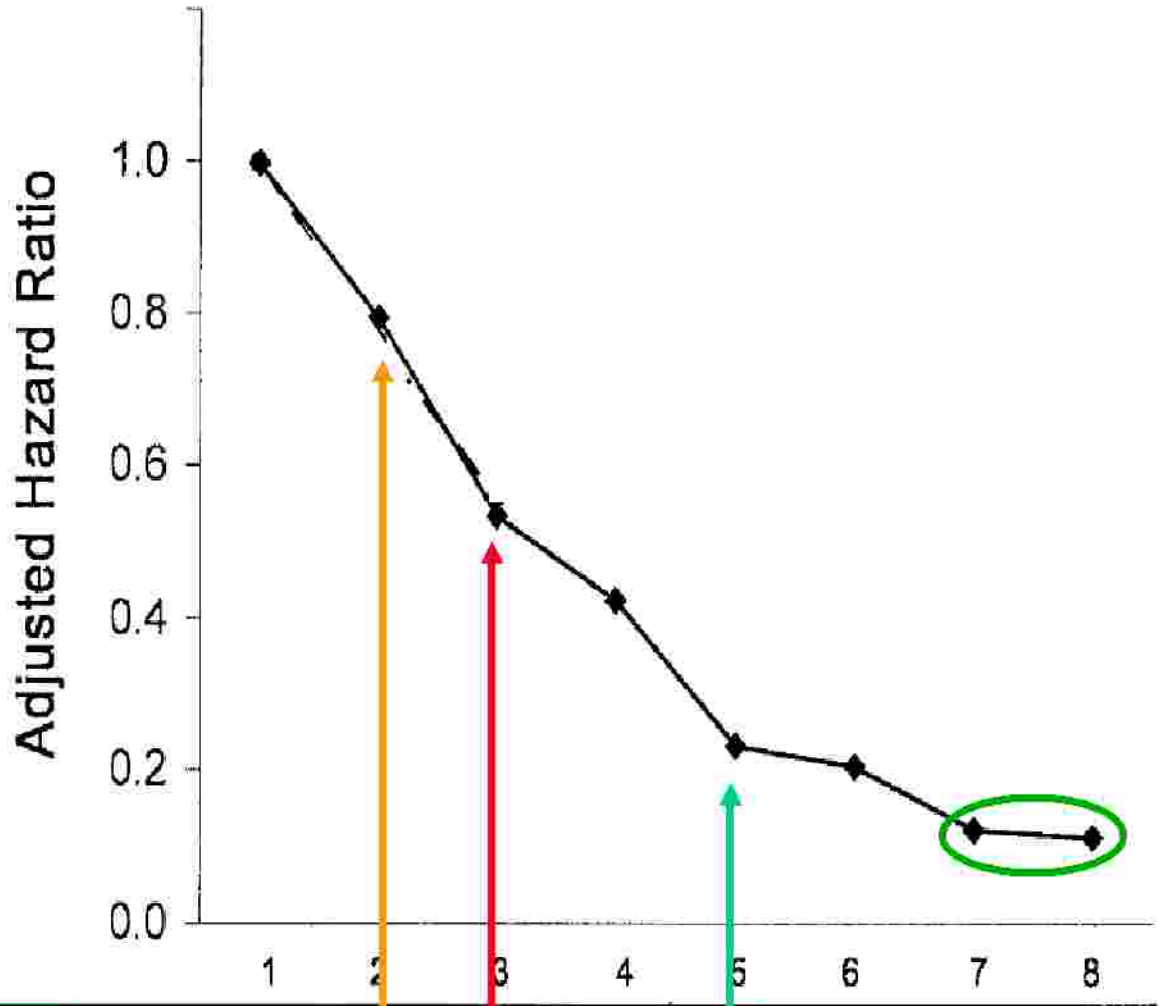
Correlazioni fra caratteristiche del training e riduzione della HbA1c nel gruppo di intervento rispetto al gruppo di controllo non attivo

intensità



quantità





At weight goal	No	No	No	No	Yes	Yes	Yes	Yes
At exercise goal	No	No	Yes	Yes	No	No	Yes	Yes
At fat goal	No	Yes	No	Yes	No	Yes	No	Yes
Mean weight loss (Kg)	-1.5	-2.5	-2.2	-3.5	-11.5	-11.5	-11.8	-13.4
Sample size	134	32	226	103	51	34	208	187

Analisi del contributo relativo di calo ponderale, esercizio e dieta sulla prevenzione di diabete nel braccio con modifica intensiva dello stile di vita del Diabetes Prevention Program

Hamman et al, Diabetes Care 2006

Reduction in Obesity and Related Comorbid Conditions after Diet-Induced Weight Loss or Exercise-Induced Weight Loss in Men

A Randomized, Controlled Trial

Robert Ross, PhD; Damon Dagnone, MSc; Peter J.H. Jones, PhD; Heidi Smith, BSc, RD; Anne Paddags, MSc; Robert Hudson, MD, PhD; and Ian Janssen, MSc

Ann Intern Med. 2000;133:92-103.

- disegno dello studio -

101 maschi obesi
(BMI medio 31 kg/m^2)

Controlli
(non dieta o esercizio)
(con trial concluso n=8)

3 mesi di dieta o esercizio

Dieta ipocalorica
(-700 kcal/die)
(con trial concluso n=11)

Esercizio al treadmill
<70% VO2max
(spesa 700 kcal/die)
(con trial concluso n=16)

Esercizio +
aumento calorie dieta
(con trial concluso n=14)

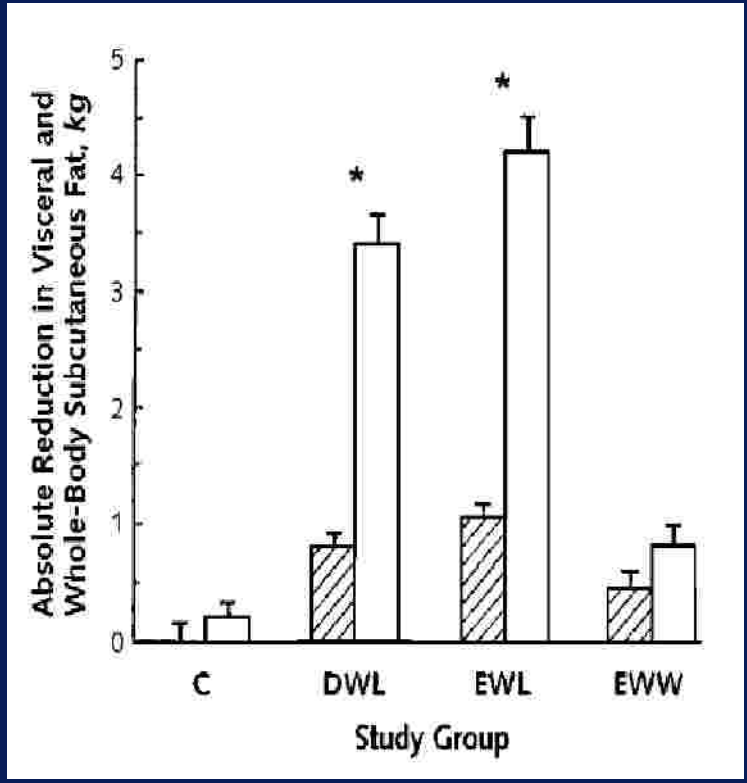
Reduction in Obesity and Related Comorbid Conditions after Diet-Induced Weight Loss or Exercise-Induced Weight Loss in Men

A Randomized, Controlled Trial

Robert Ross, PhD; Damon Dagnone, MSc; Peter J.H. Jones, PhD; Heidi Smith, BSc, RD; Anne Paddags, MSc; Robert Hudson, MD, PhD; and Ian Janssen, MSc

Ann Intern Med. 2000;133:92-103.

Riduzione del grasso viscerale (■) e sottocutaneo (▨) dopo il trial



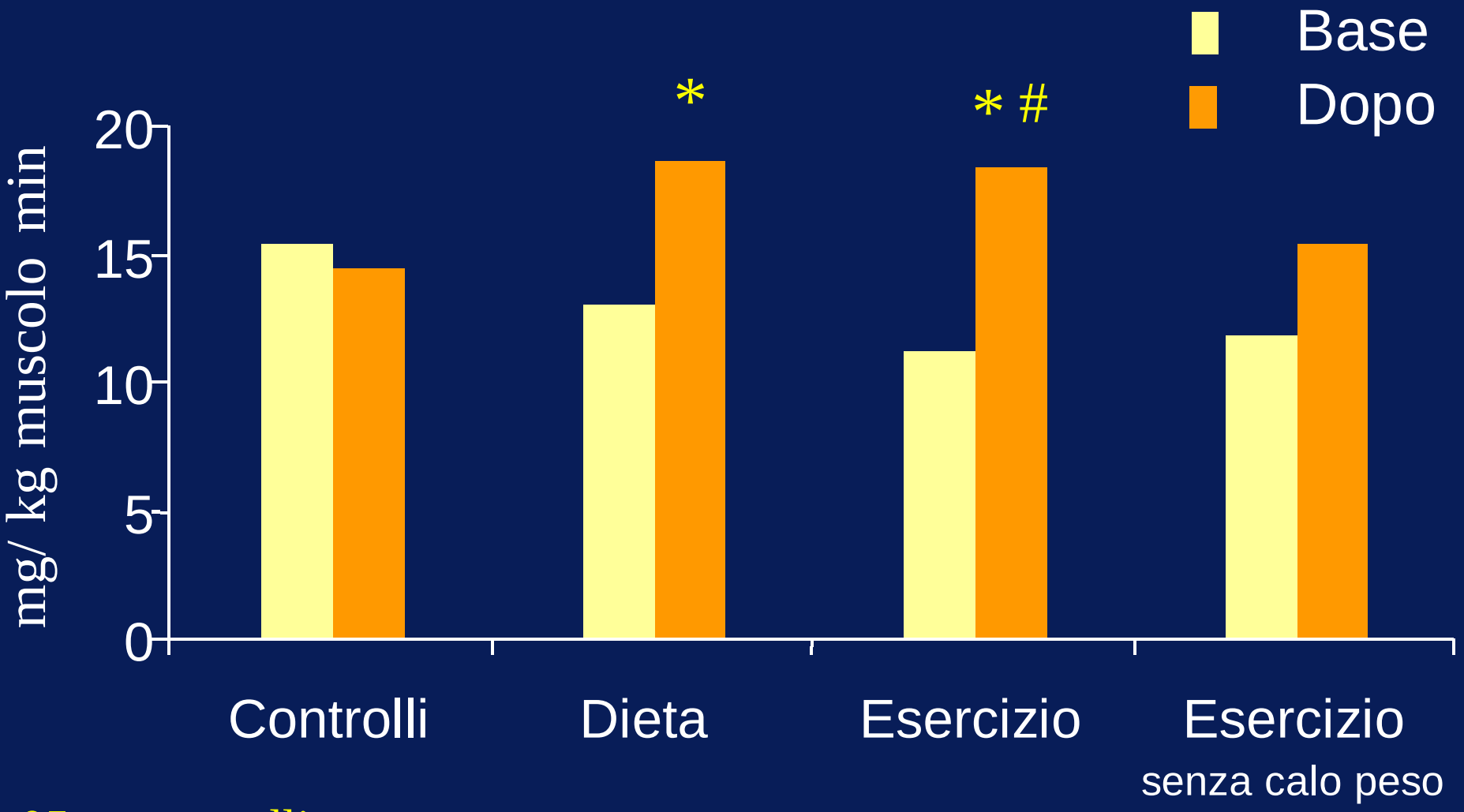
C Controlli

DWL Dieta

EWL Esercizio

EWW Esercizio
senza calo peso

Utilizzazione del glucosio durante clamp prima e dopo dieta o esercizio



* p<0.05 vs controlli

# p<0.05 vs esercizio senza calo peso

Ross et al, Ann Intern Med 2000