SID
Società Italiana di Diabetologia
fondata dal 1964

Diagnosi precoce e trattamento efficace della patologia cardionefrometabolica: dalla teoria alla pratica

Milano, 4/5 luglio 2025

SESSIONE 4
PREVENZIONE E TERAPIA CARDIONEFROMETABOLICA

Lifestyle: quanto è importante nel trattamento moderno del diabete tipo 2?

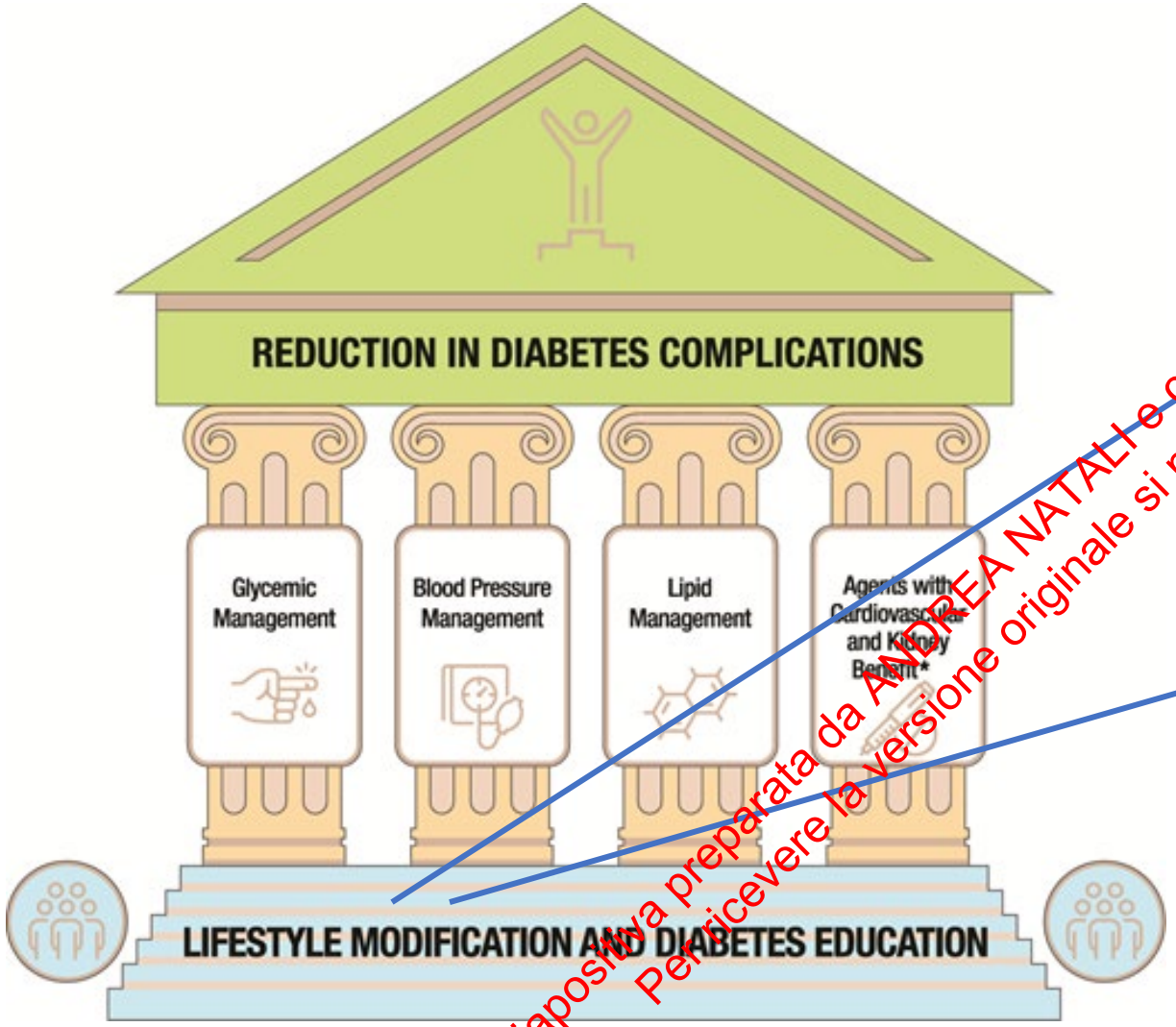
Andrea Natali, UNIPI

IN SUPREMÆ DIGNITATIS
1343

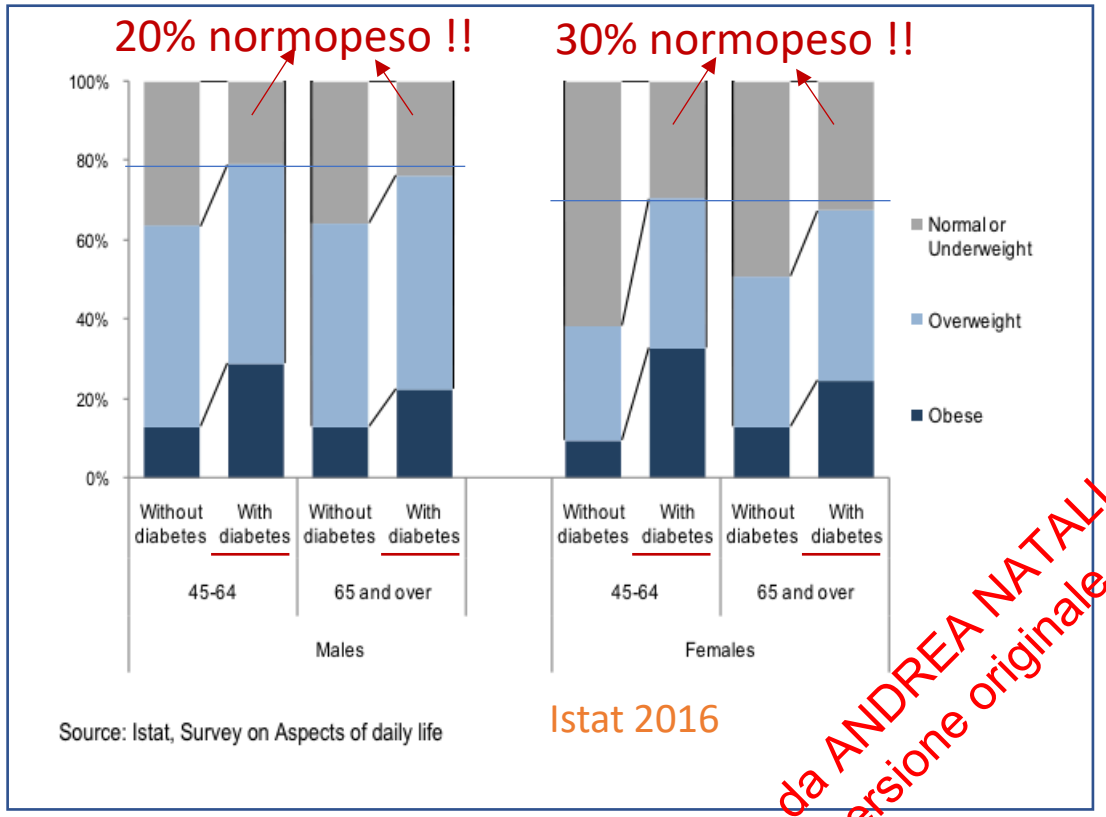
Disclosure

- Finanziamenti alla ricerca: Boehringer Ingelheim, Nestlè
- Inviti a congressi: Eli Lilly, Servier, Amgen
- Consulting board: Eli Lilly

The four (five) pillars approach



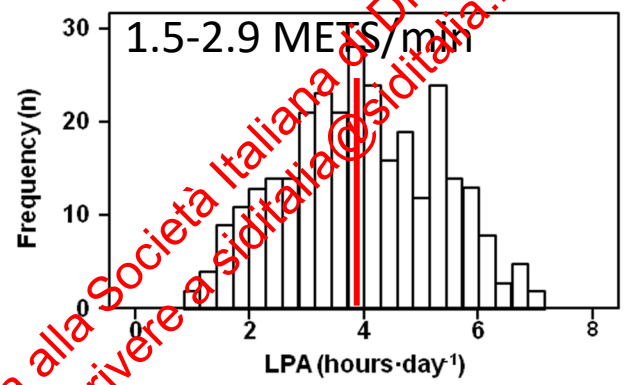
Lifestyle and T2D: La situazione in italia



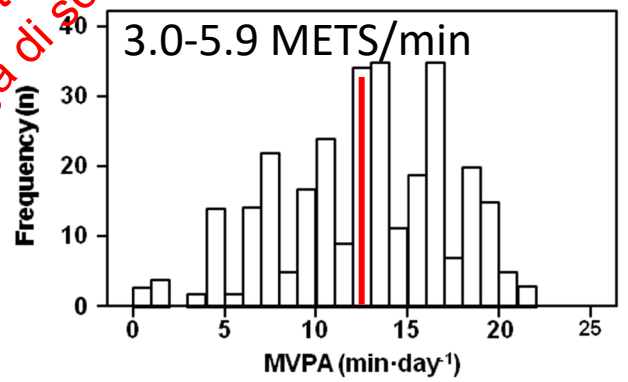
Istat 2016

FUMATORI 26.3% !!!

Annali AMD 2023



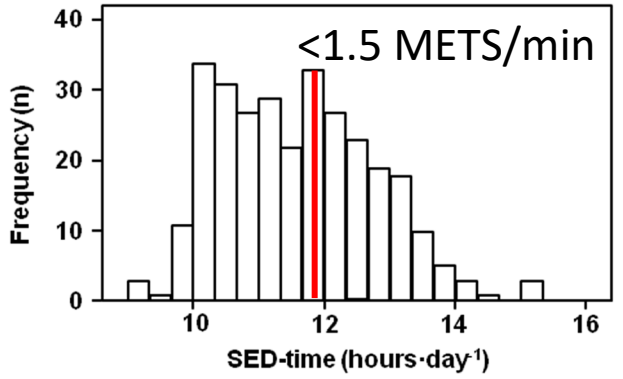
3.89 hours·day-1
(2.96-4.93)



12.9 min·day-1
(9.0-16.0)

364 METs-min/week

91 min/week !!



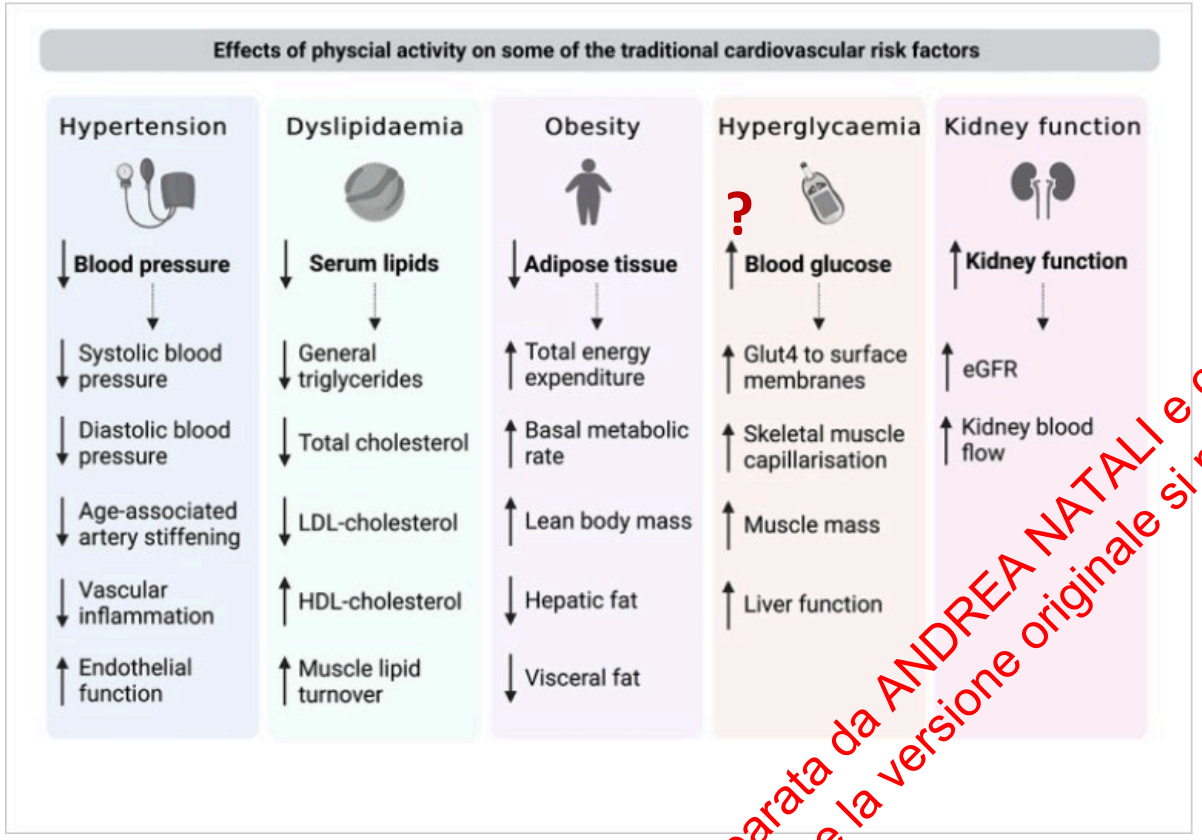
11.6 hours·day-1
(10.6-12.4)

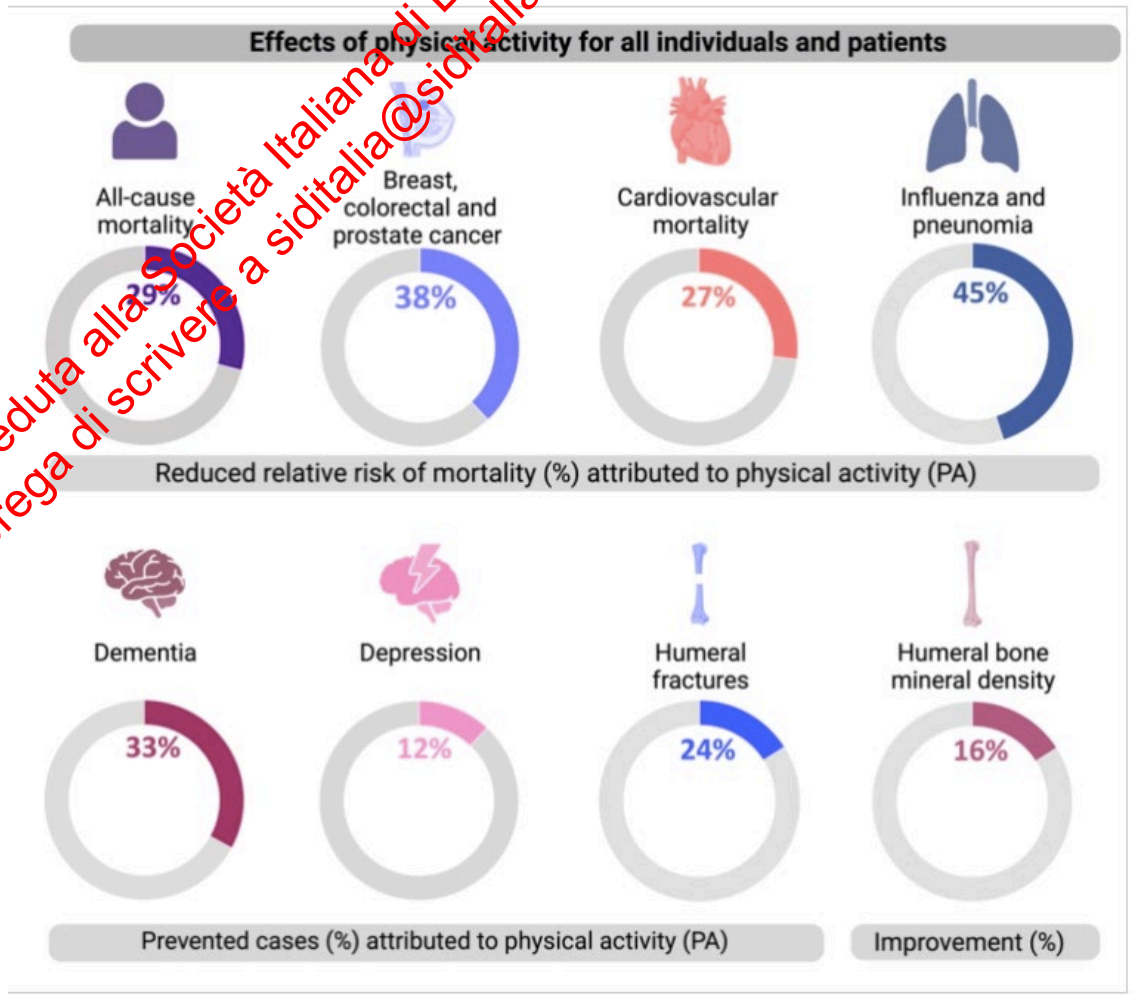
Balducci S. *PlosOne* 2017

Esercizio fisico

1. Cosa dicono le LG
2. Quale tipo di esercizio e come si misura
3. Curva dose-risposta quantità di esercizio *vs* HbA1c
4. Quale tipo di esercizio è più efficace su HbA1c

I benefici dell'attività fisica (ESC 2024)





Physical inactivity was seen to be responsible for the loss of **13.4 million disability-adjusted life years (DALYs) worldwide**, these DALYs were estimated for **coronary heart disease, stroke, type 2 diabetes, breast cancer, and colon cancer** [11].

EASD GUIDELINES

Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

≥150 min/sett moderata intensità

Oppure

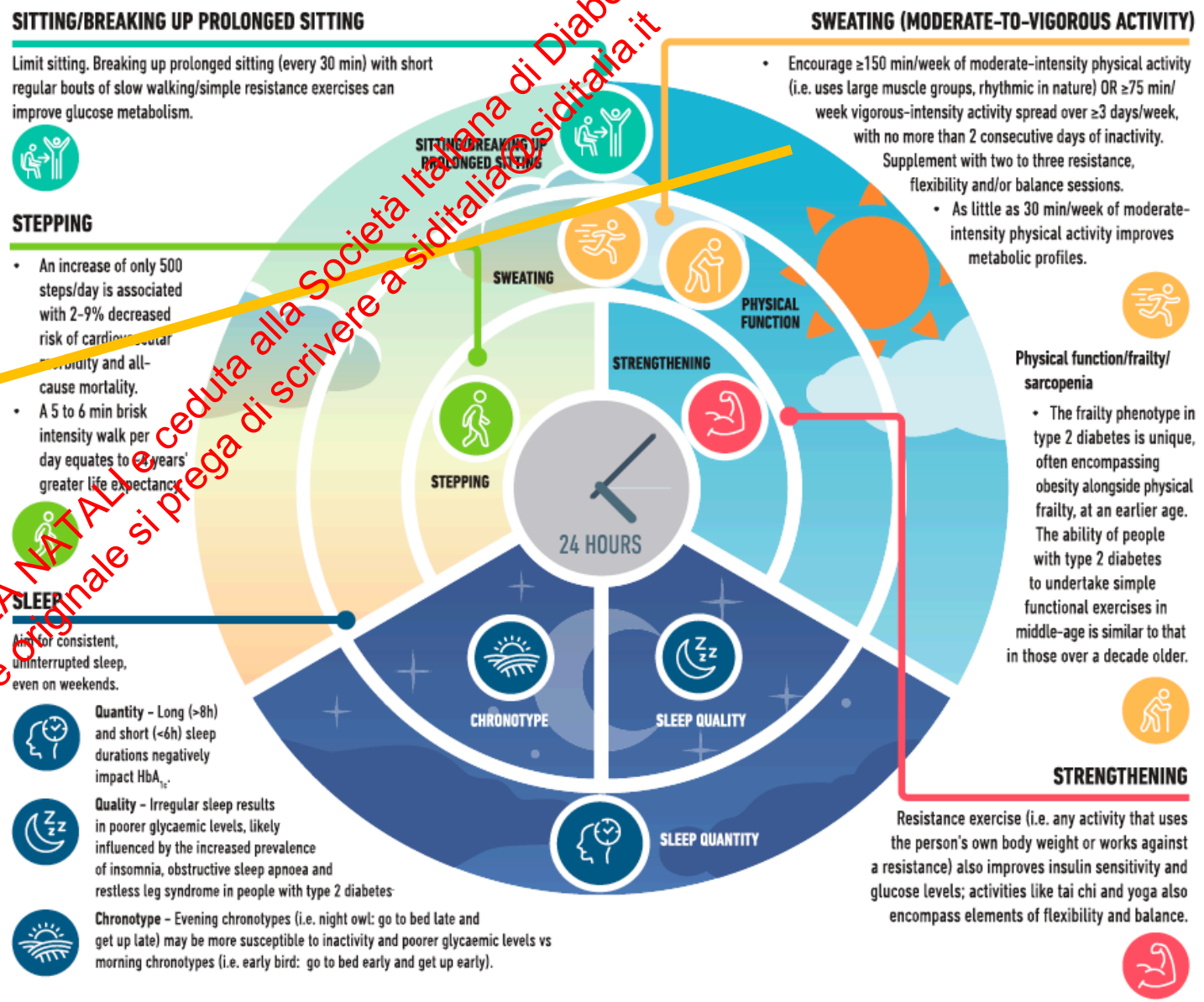
≥75 min/sett alta intensità

Suddivisa in ≥3 giorni senza superare 2 giorni di inattività

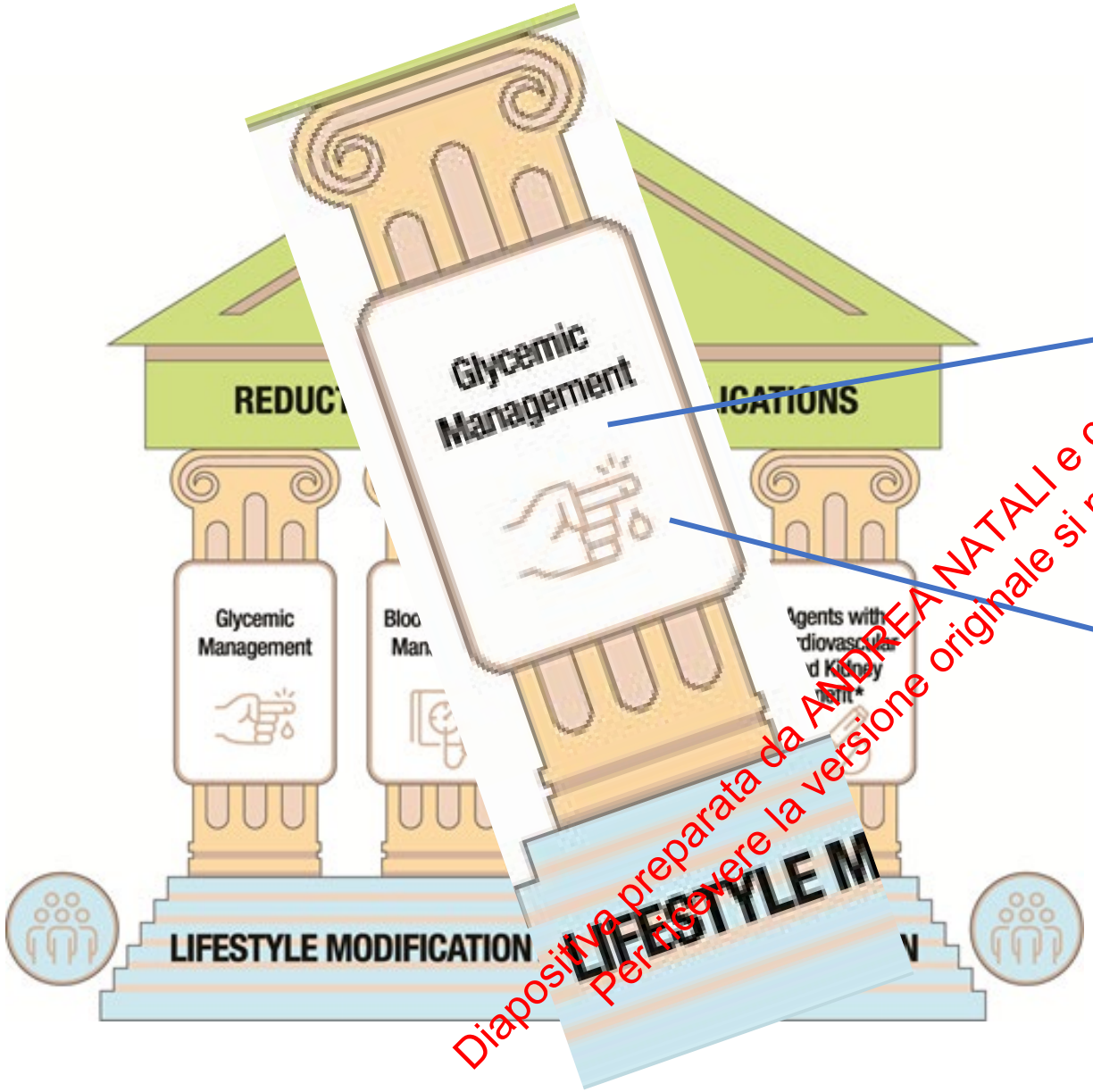
Aggiungere esercizi di equilibrio/flessibilità o contro resistenza.

(30 min di att. fis/sett migliora il profilo metabolico)

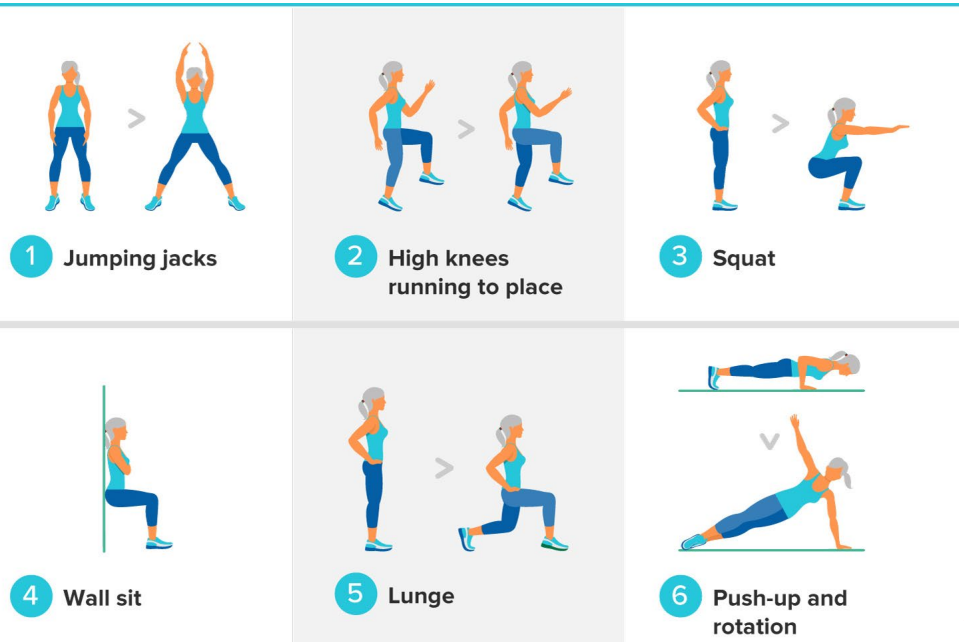
	Glucose/insulin	Blood pressure	HbA_{1c}	Lipids	Physical function	Depression	Quality of life
SITTING/BREAKING UP PROLONGED SITTING	↓	↓	↓	↓	↑	↓	↑
STEPPING	↓	↓	↓	↓	↑	↓	↑
SWEATING (MODERATE-TO-VIGOROUS ACTIVITY)	↓	↓	↓	↓	↑	↓	↑
STRENGTHENING	↓	↓	↓	↓	↑	↓	↑
ADEQUATE SLEEP DURATION	↓	↓	↓	↓	?	↓	↑
GOOD SLEEP QUALITY	↓	↓	↓	↓	?	↓	↑
CHRONOTYPE/CONSISTENT TIMING	↓	?	↓	?	?	↓	?



The four (five) pillars approach



HIIT



30 - 60 sec 8 Mets

1 - 2 min Rest

20 min approx. 70 METS

RESISTANCE TRAINING

3-4 METS

20 min approx. 70 METS

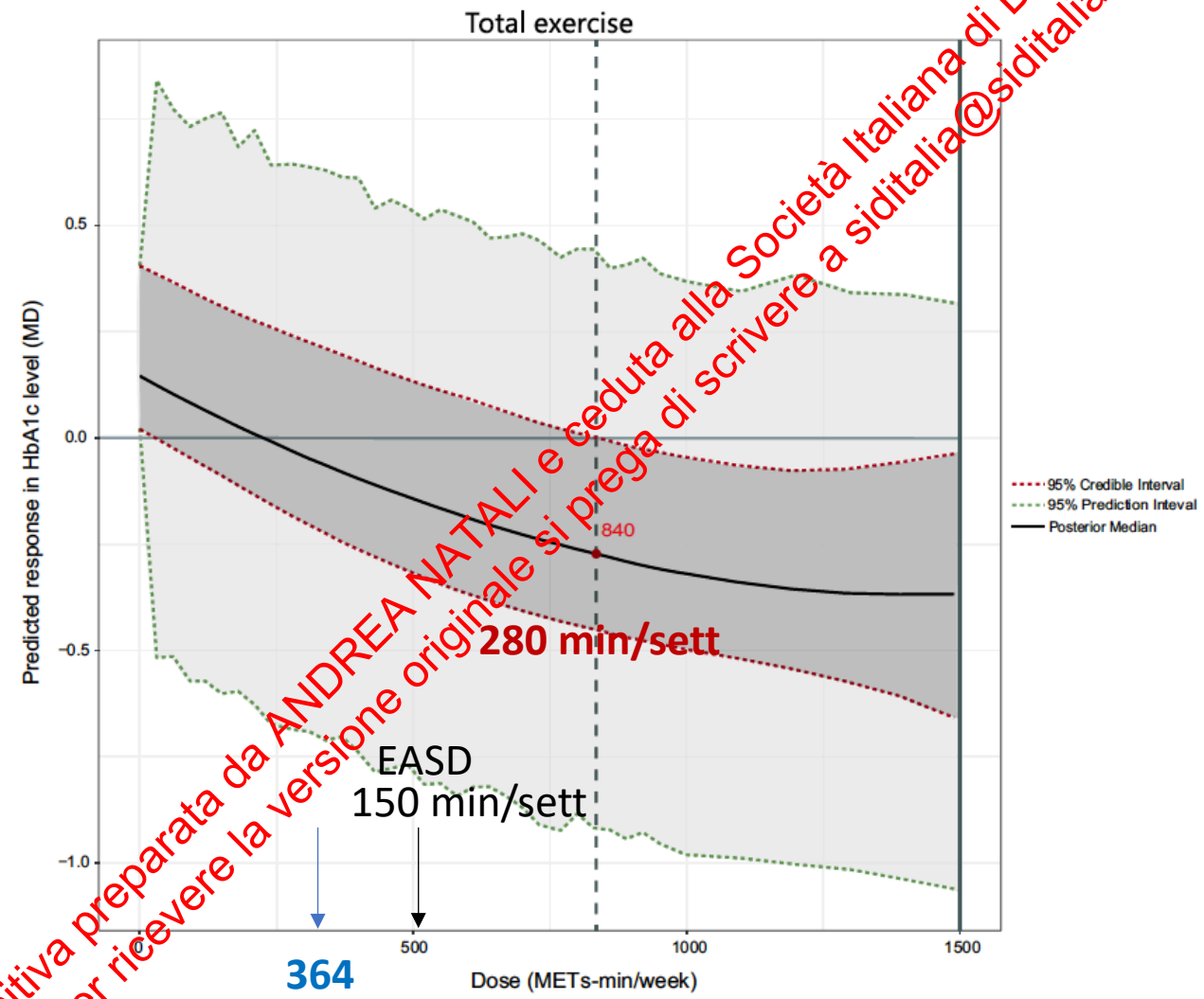
Aerobic exercise

Exercise type
Walking
Houseworks
Yoga
Bicycling <10 km/h

3-4 METS

20 min approx. 70 METS

Esercizio ed HbA1c: quale volume è efficace ?



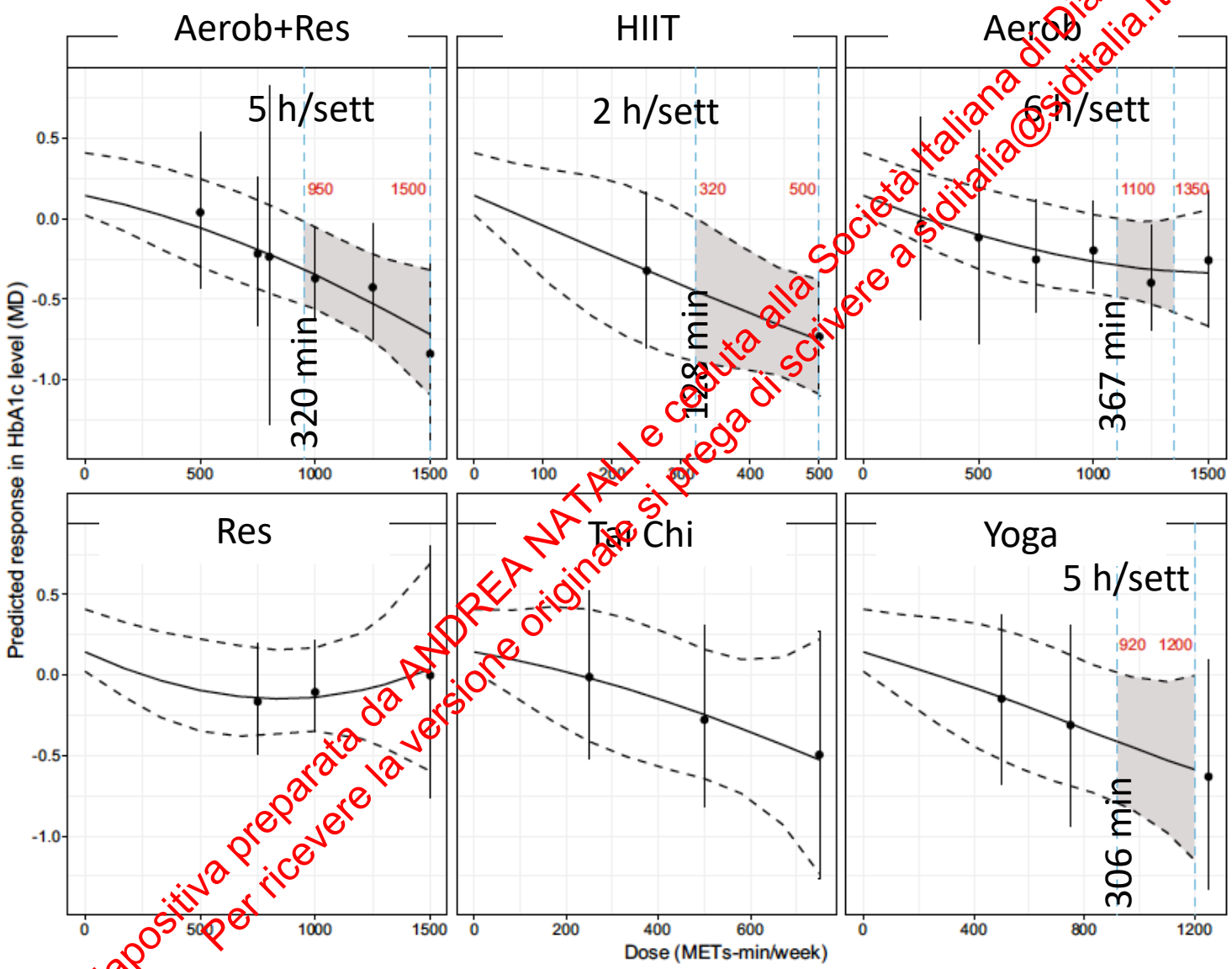
280 min/sett

EASD
150 min/sett

364
Media IDES
104 min/sett

Liang Z et al Sports Medicine (2024) 54:2557–2570

Esercizio ed HbA1c: Quanti minuti e quale tipo di esercizio



Liang Z et al Sports Medicine (2024) 54:2557–2570

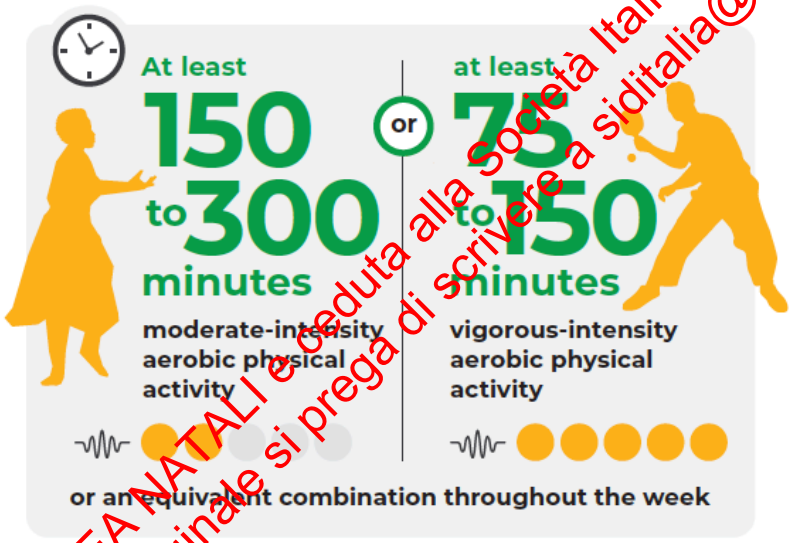
2020

World Health Organization

It is recommended that:

› All adults and older adults with type 2 diabetes should undertake regular physical activity.

Strong recommendation, moderate certainty evidence



› Adults and older adults with type 2 diabetes should do at least 150–300 minutes of moderate-intensity aerobic physical activity; or at least 75–150 minutes of vigorous-intensity aerobic physical activity; or an equivalent combination of moderate- and vigorous-intensity activity throughout the week for substantial health benefits.

Strong recommendation, moderate certainty evidence

› Adults and older adults with type 2 diabetes should also do muscle-strengthening activities at moderate or greater intensity that involve all major muscle groups on 2 or more days a week, as these provide additional benefits.

Strong recommendation, moderate certainty evidence

ISBN 978-92-4-001513-5 ISBN 978-92-4-001512-8
https://iris.who.int/bitstream/handle/10665/336656/9789240015128-eng.pdf?sequence=1

IDES-2 Study

300 sedentary T2D

150 Treatment

PA volume: +198 METS/week

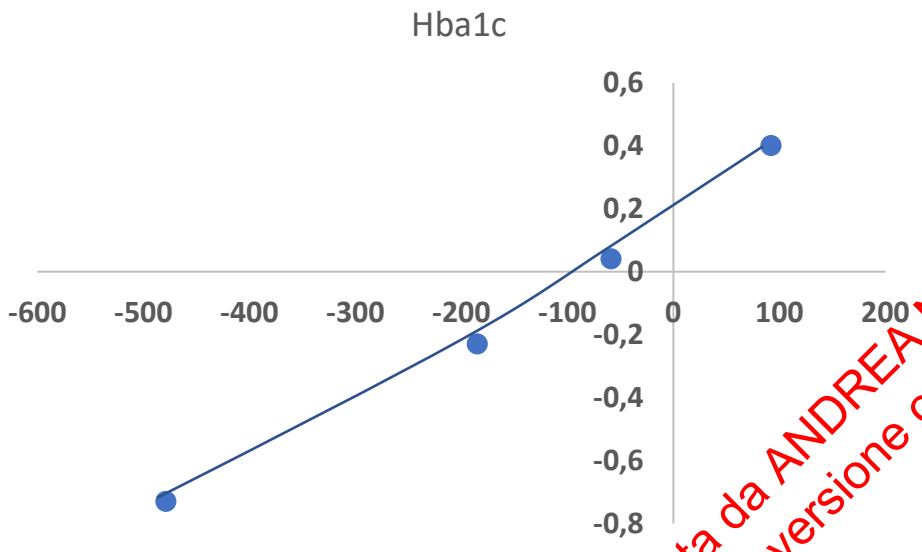
Sedentary time: -336 min/week

MVPA: + 45 min/week

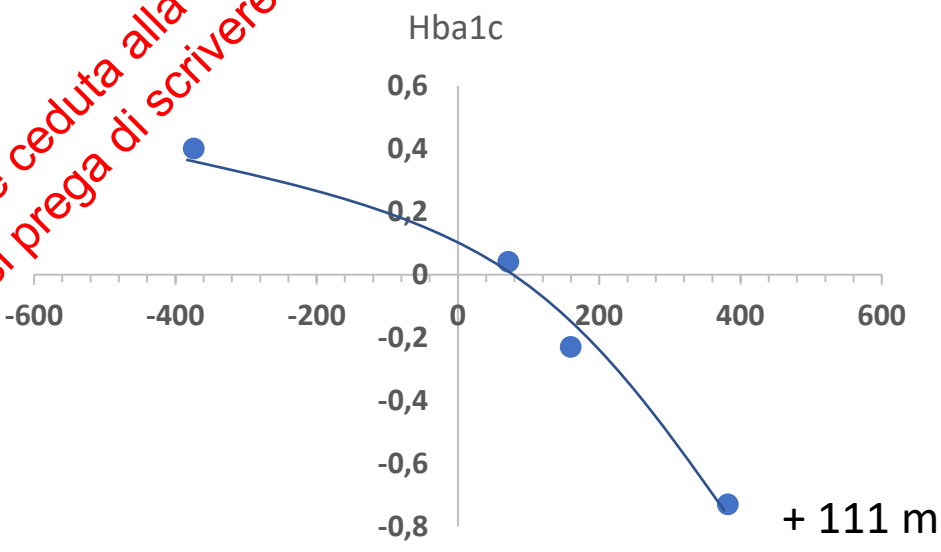
150 Standard Care

Follow-up 3 years

Quartiles of MVPA



Variazione attività sedentaria (min/set)



+ 111 min/week
(+104 = 215)

Variazione attività fisica (METS/set)

Balducci S *et al Diab Care* 2022

Dieta ed HbA1c

1) Linee guida
3) Peso
2) Macronutrienti
3) Colazione

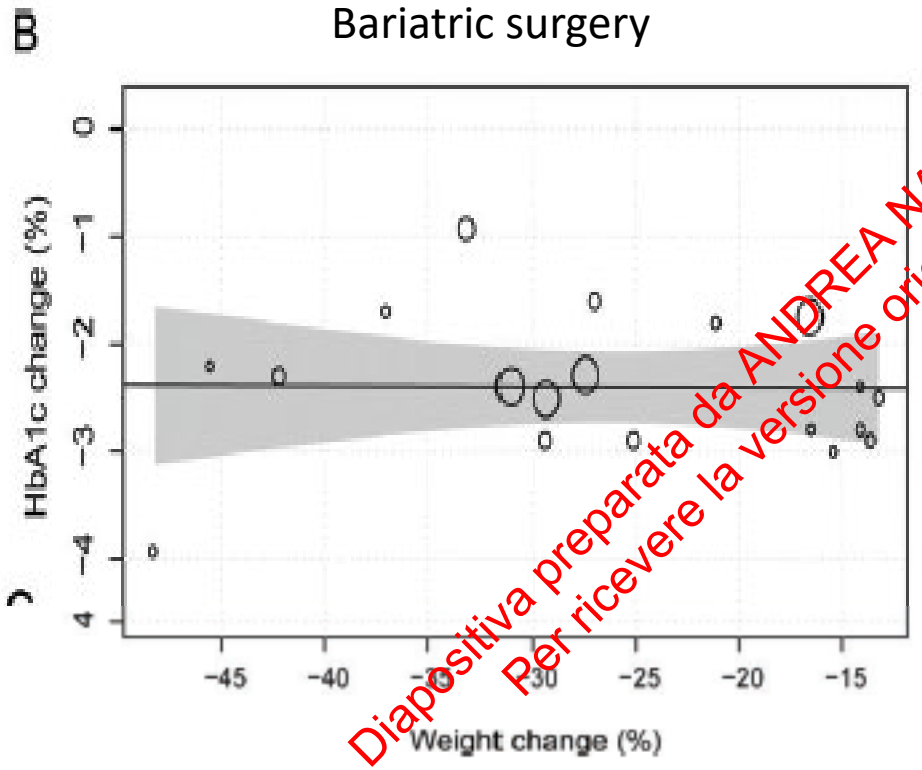
Weight management ADA Standard of Care 2024

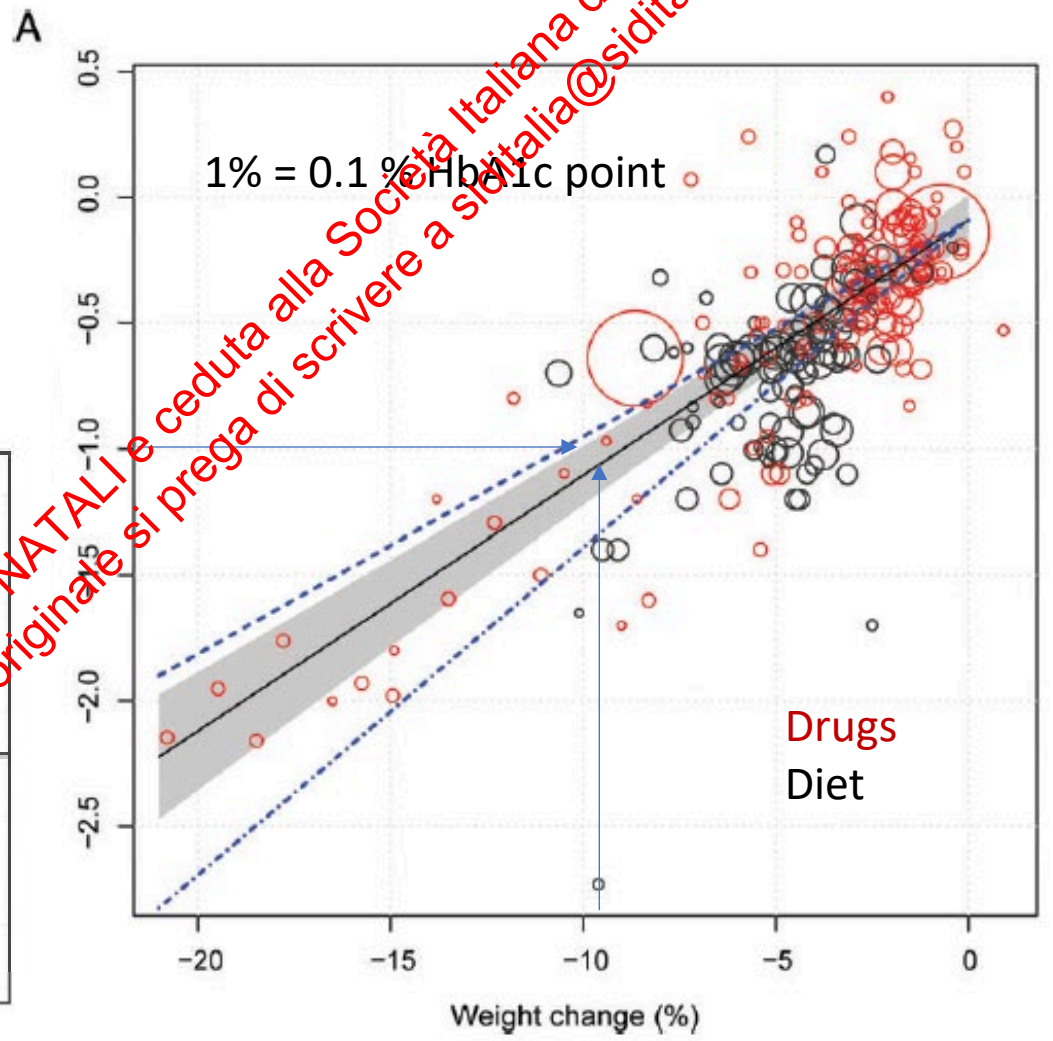
8.4 In people with type 2 diabetes and overweight or obesity, weight management should represent a primary goal of treatment along with glycemic management. A

8.5 People with diabetes and overweight or obesity may benefit from any magnitude of weight loss. Weight loss of 3–7% of baseline weight improves glycemia and other intermediate cardiovascular risk factors. A

8.6 Individualize initial treatment approaches for obesity (i.e., lifestyle and nutritional therapy, pharmacologic agents, or metabolic surgery) A based on the person's medical history, life circumstances, preferences, and motivation. Consider combining treatment approaches if appropriate.

Relazione tra weight loss e ∂HbA1c





Gummesson A DOM 2017

MACRONUTRIENTI

Evidence-based European recommendations for the dietary management of diabetes

Aprile 2023

The Diabetes and Nutrition Study Group (DNSG) of the European Association for the Study of Diabetes (EASD)

Carboidrati

Preferire i cereali integrali (ricchi in fibre), non importa la quantità ma meglio evitare gli estremi.

- **Preferire cibi con basso indice glicemico.**
- **Evitare zuccheri semplici (<10% Kcal tot)**

Grassi

- **Preferire grassi vegetali (MUFA e PUFA)**
- **Evitare grassi saturi (<10% Kcal tot) e trans (<1% Kcal tot)**

Dolcificanti

Tutti OK, ma non è chiaro se aiutino

Fibre

- **Almeno 35 g/die**
- **Fonti: cereali integrali, verdura, frutta, legumi, semi, frutta a guscio.**
- **Considerare supplementi per raggiungere il target.**

Proteine

-10-20% Kcal tot se < 65 aa

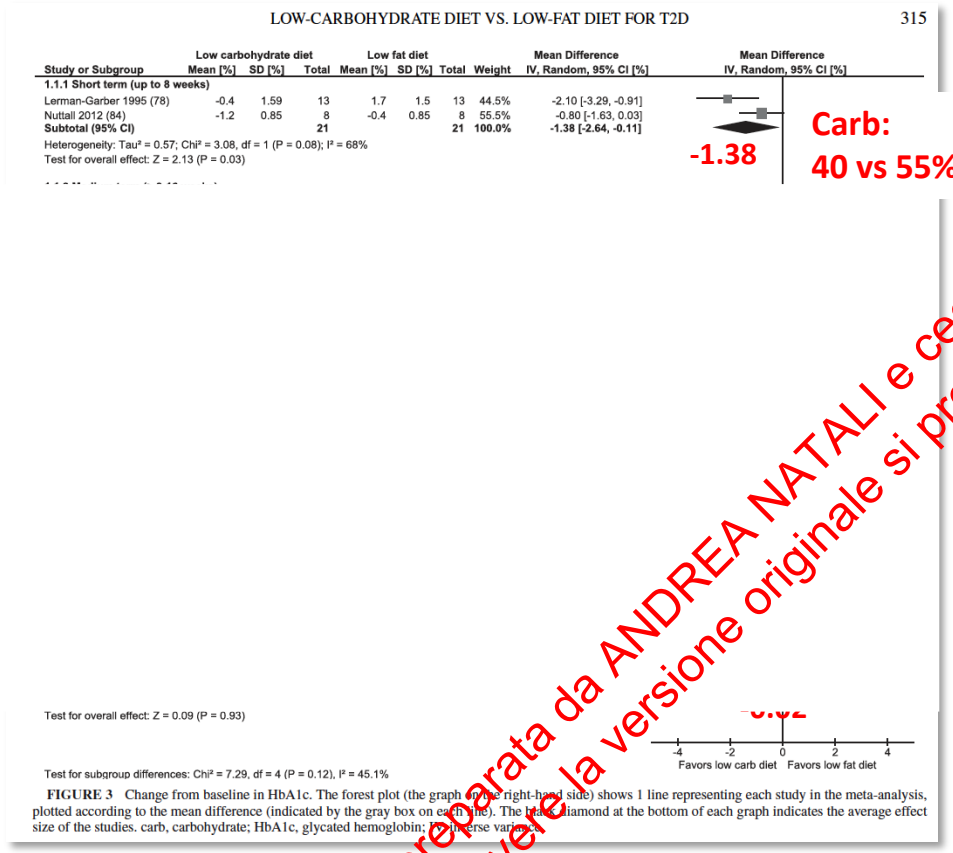
-15-20% Kcal tot se >65 aa

-23-32% Kcal tot durante calo ponderale

-Se eGFR 60-45 ml/min: max 10-15%

Low-carb & HbA1c: time and dose

≤8 weeks



LOW-CARBOHYDRATE DIET VS. LOW-FAT DIET FOR T2D 315

Study or Subgroup	Low carbohydrate diet Mean [%]	SD [%]	Total	Low fat diet Mean [%]	SD [%]	Total	Weight	Mean Difference IV, Random, 95% CI [%]
1.1.1 Short term (up to 8 weeks)								
Lerman-Garber 1995 (78)	-0.4	1.59	13	1.7	1.5	13	44.5%	-2.10 [-3.29, -0.91]
Nuttall 2012 (84)	-1.2	0.85	8	-0.4	0.85	8	55.5%	-0.80 [-1.63, 0.03]
Subtotal (95% CI)			**21**			**21**	**100.0%**	**-1.38 [-2.64, -0.11]**

Heterogeneity: Tau² = 0.57; Chi² = 3.08, df = 1 (P = 0.08); I² = 68%
Test for overall effect: Z = 2.13 (P = 0.03)

Test for overall effect: Z = 0.09 (P = 0.93)

Test for subgroup differences: Chi² = 7.29, df = 4 (P = 0.12), I² = 45.1%

Favors low carb diet Favors low fat diet

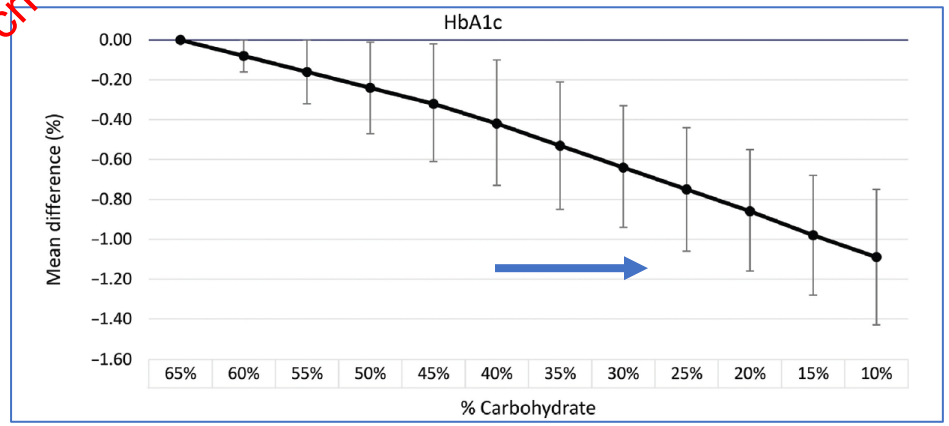
FIGURE 3 Change from baseline in HbA1c. The forest plot (the graph on the right-hand side) shows 1 line representing each study in the meta-analysis, plotted according to the mean difference (indicated by the gray box on each line). The black diamond at the bottom of each graph indicates the average effect size of the studies. carb, carbohydrate; HbA1c, glycated hemoglobin; IV, inverse variance.

-1.38

Carb: 40 vs 55% !!!!!!!!

Van Cauwenberg EJ, *Am J Nutr* 2018

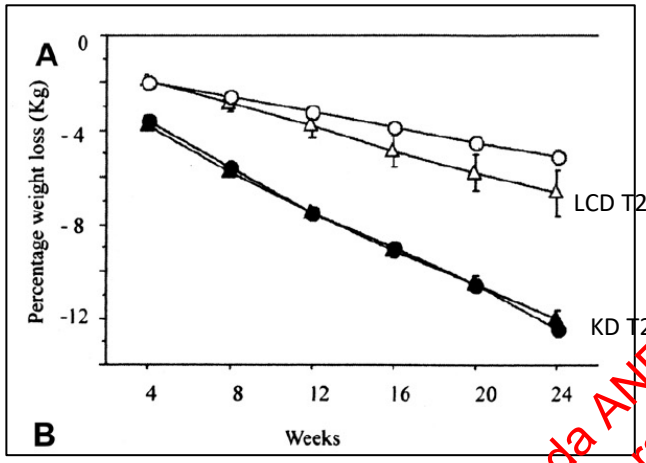
6-month follow-up (*n* = 29 trials)

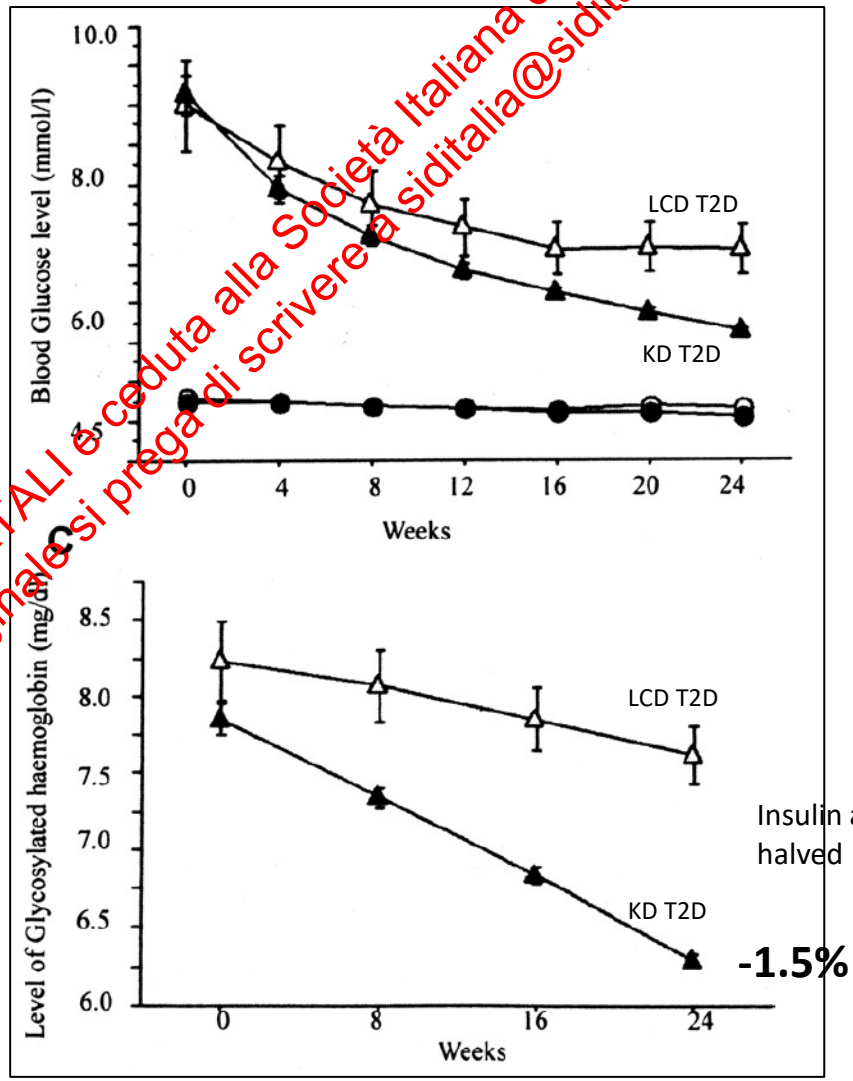


Jayedi A et al *Am J Clin Nutr* 2022

Very Low carb diet

Free choice
363, LCD, cal restriction
220, KD 20 g/die, no cal restriction





Insulin and SU dose halved !!

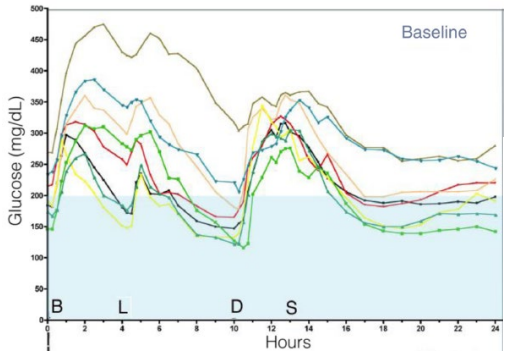
-1.5%

Hussain TA, *Nutrition* 2012

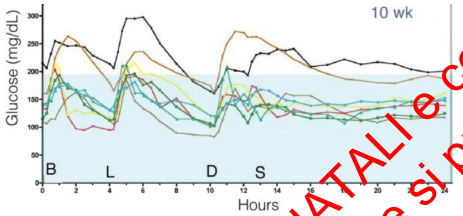
Low carb diet

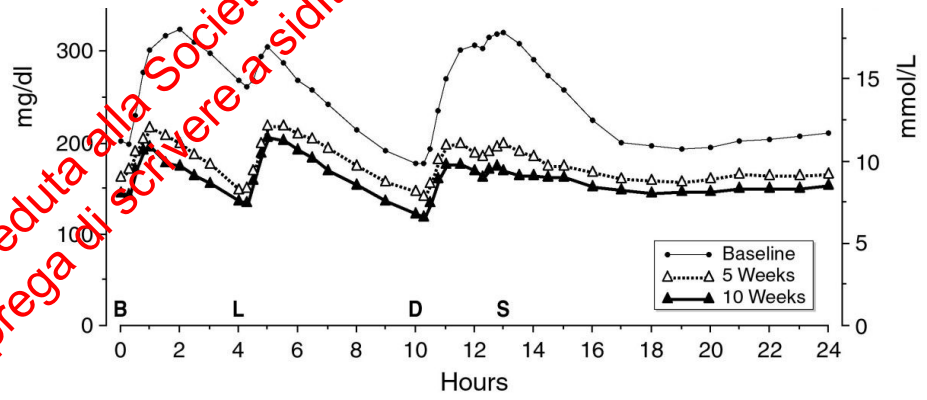
Non-ketogenic diet, no weight loss
30% carbohydrate, 30% protein, 40% fat (30:30:40)

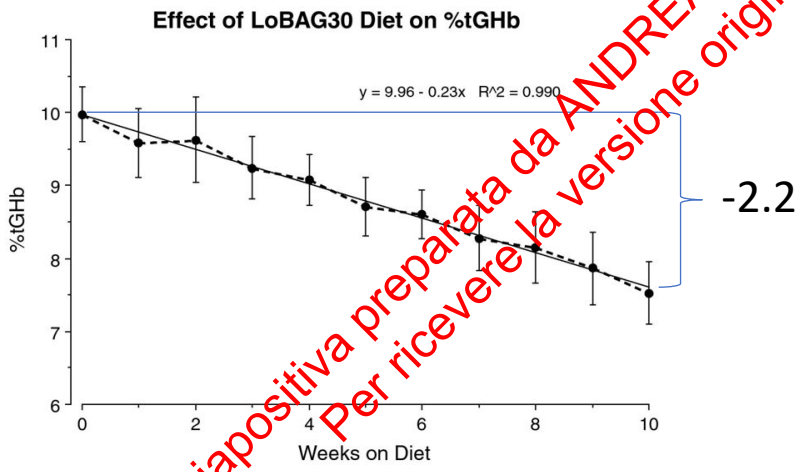
55:15:30



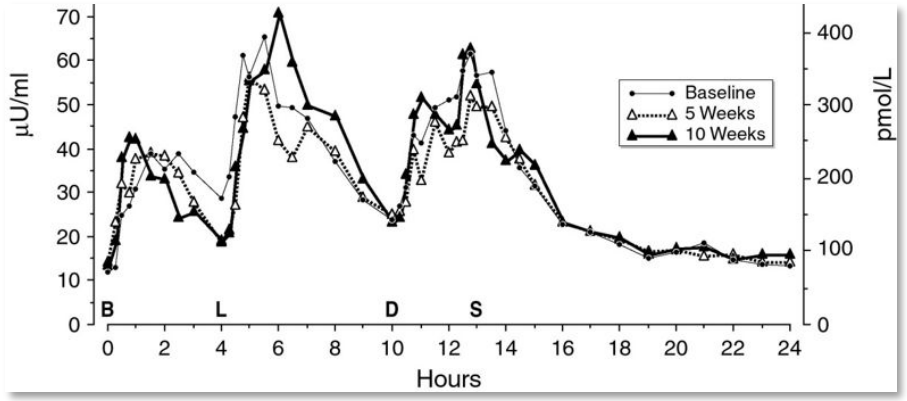
30:30:40







-2.2



Gannon MC, *Nutrition&Metabolism* 2010

Low fat vs Low carb vs Med: Studio DIRECT

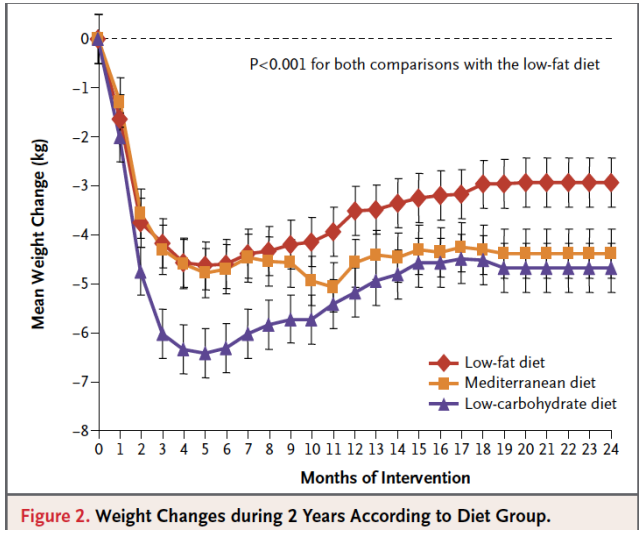
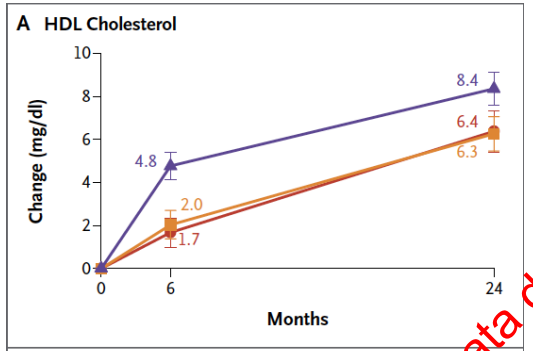
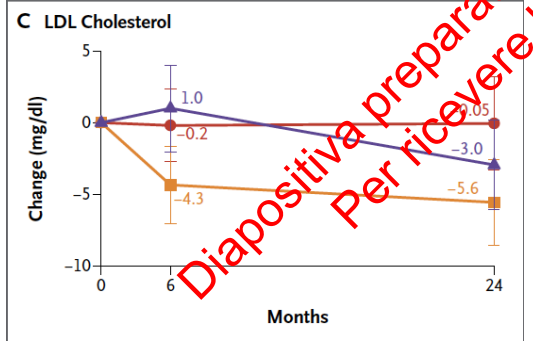


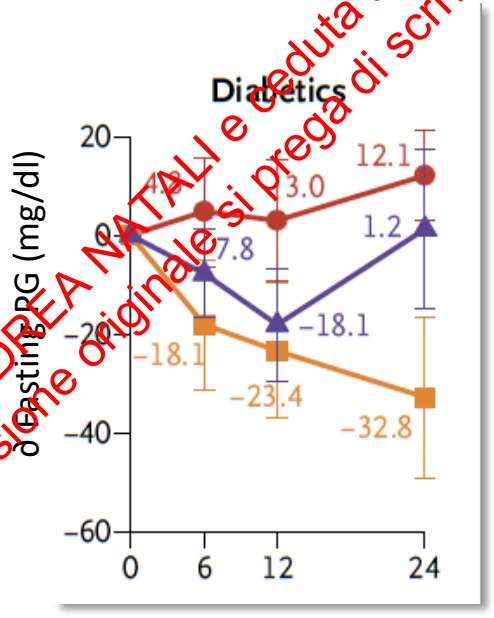
Figure 2. Weight Changes during 2 Years According to Diet Group.

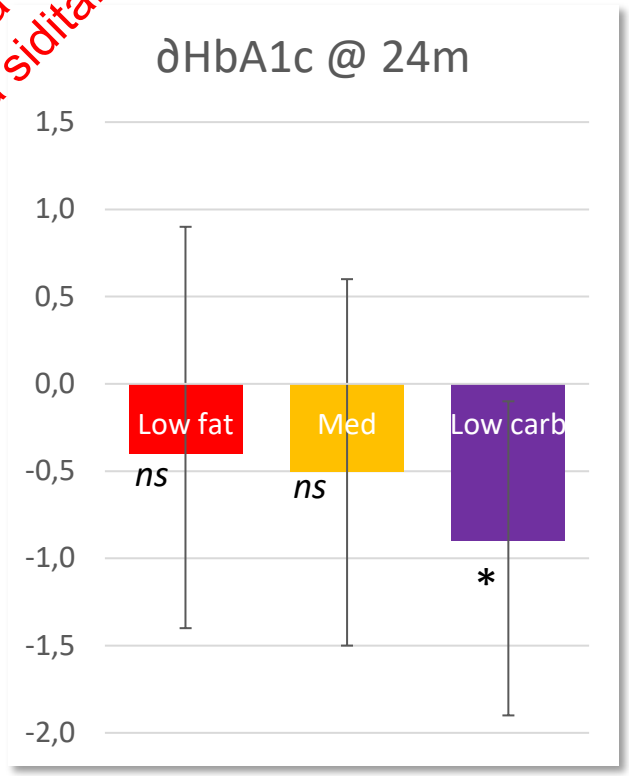
BMI 30, 100 (15 T2D) per group

	C	P	L
Low-fat:	51	19	30 (low cal)
Med	50	18	32 (low cal)
Low-carb:	40	22	38 (free!)









Shai I, *N Eng J Med* 2008

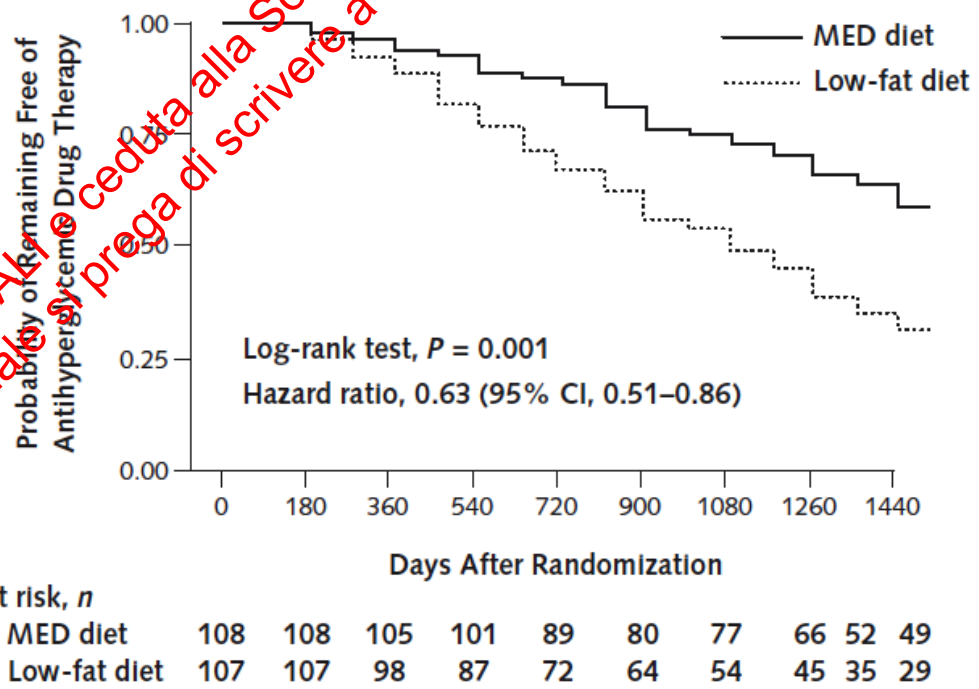
Dieta mediterranea

Overweight newly diagnosed T2D; therapy indicated for follow-up HbA1c >7%

MED diet (hypocaloric)
Rich in vegetables and whole grains and low in red meat, which was replaced with poultry and fish.
<50% carb
20% protein
30-40% lipids (olive oil)

Low fat diet (hypocaloric)
Rich in whole grains and restricted additional fats, sweets, and high-fat snacks
<30% fat
20% protein
50-60% carb

Figure 2. **Probability of remaining free of antihyperglycemic drug therapy.**



MED = low-carbohydrate, Mediterranean-style.

Esposito K, *Ann Int Med* 2008

Perché non fare una low-carb Med ?

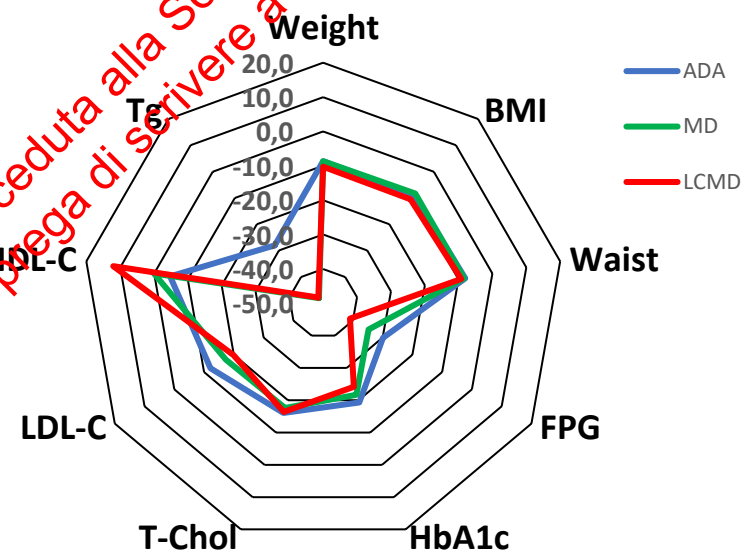
259 overweight diabetic patients (HbA1c=8.3%)

12 month

MD
Carb (50–55%)
low GI
Fat (30%)
Protein (15–20%)

ADA Diet
Carb (50–55%)
Fat (30%)
Protein (15–20%)

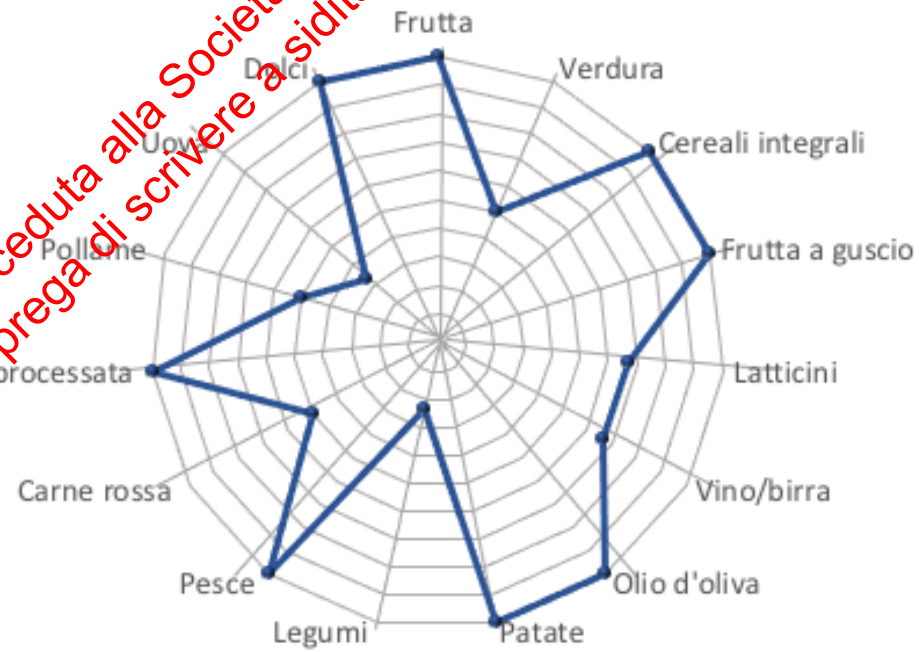
LC-MD
35% Carb
45% Fat (50% MUFA)
20% Prot



Elhaynay A et al DOM 2010

Dieta mediterranea: come si misura ?

		N° porzioni al giorno
5	Frutta	4
6	Verdura	3
7	Cereali integrali	4
8	Frutta a guscio	2
9	Latticini	3
10	Vino/birra	1
11	Olio d'oliva (uso abituale=1)	1
		N° porzioni alla settimana
15	Patate	1
16	Legumi	1
17	Pesce	2
18	Carne rossa	3
19	Carne processata	1
20	Pollame	1
21	Uova	1
22	Dolci	1
24	TOTALE	11.40 / 15
26	ADERENZA	76%

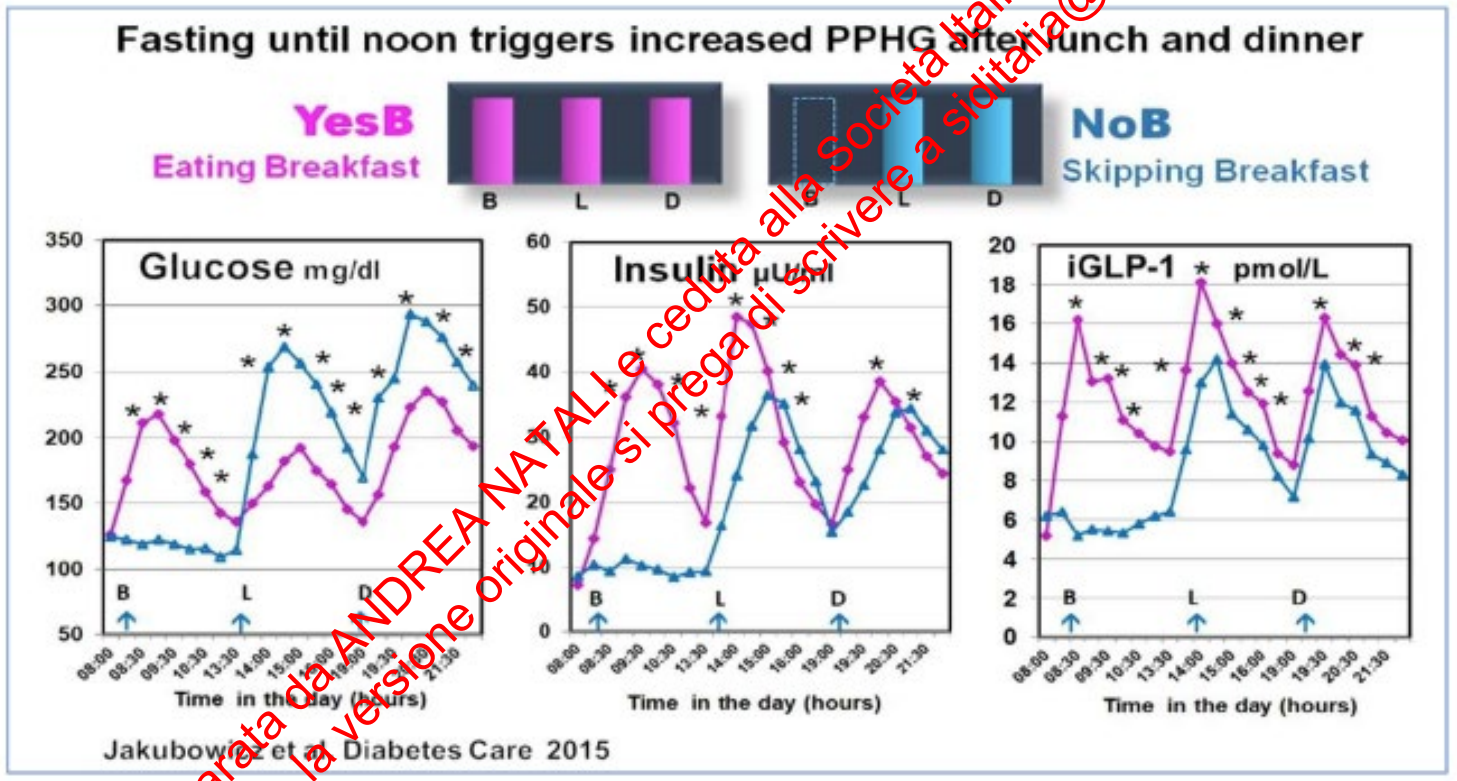


https://www.siditalia.it/clinica/formule-e-calcolatori

SID study group “Dieta e diabete”
Nutrition, Metabolism & Cardiovascular Diseases (2023) 33,724e736

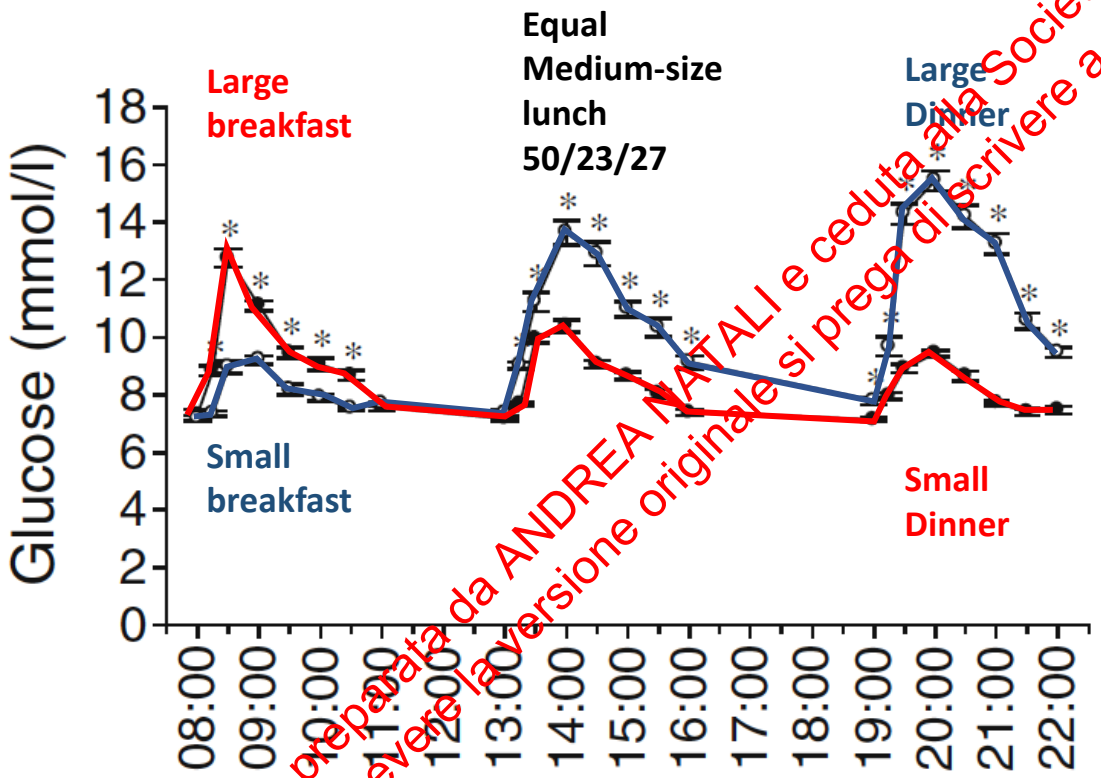
Importanza della colazione

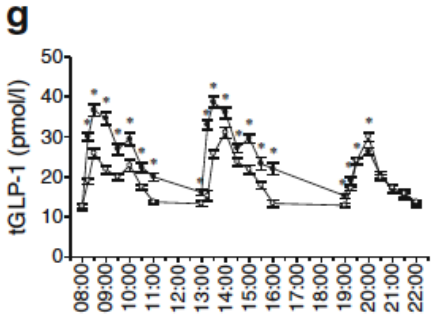
No breakfast !!



Big breakfast vs big dinner

18 T2D 6 days/cross-over
1,500 Kcal (46/31/23)





Jakubowicz D, *Diabetologia* 2015

Big vs small breakfast

59 T2DM; 1400 Kcal

BB: B= 33% daily cal (rich in fat and protein); L&D 33% calories
SB: B= 12% daily cal (rich in carb); L&D 44% cal

3 months

	BB	SB	
Weight loss (kg)	**-2.4**	**-1.9**	**ns**
HbA1c (%change)	**-4.6**	**-1.5**	**p= 0.047**
Dose reduction (%)	**31**	**0**	**p=0.02**
Dose increase (%)	**3**	**17**	**p=0.002**
Aver. Glucose (mg/dl)	**-13**	**-4**	**p=0.032**
SBP (mmHg)	**-9.6**	**-2.4**	**p=0.04**

Rabinowitz HR, *Ob Biol &Integr Physiol* 2014

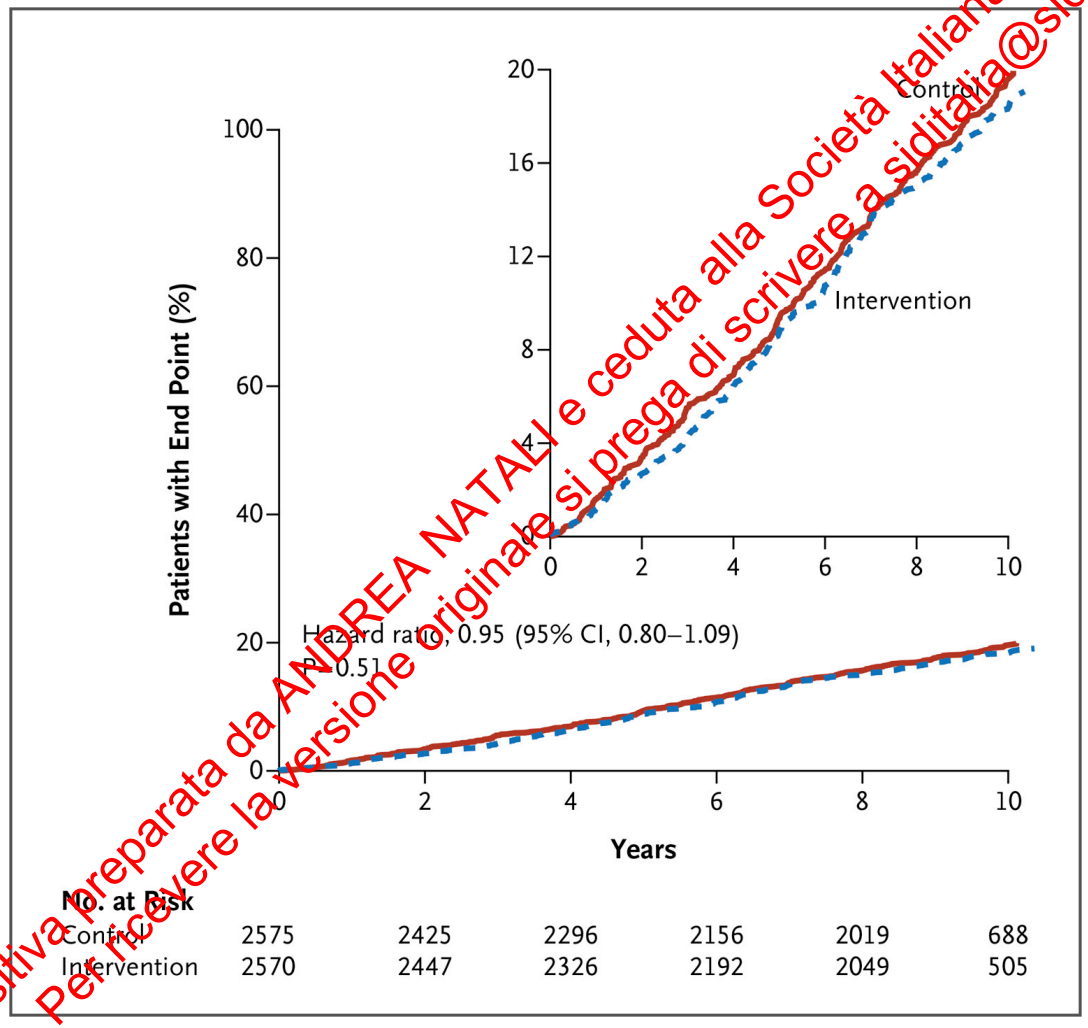
Conclusioni

1) Esiste un margine molto ampio di intervento
2) La dose efficace di attività fisica per migliorare il controllo metabolico è alta (200-300 min di MVPA + 60 min esercizi di resistenza/sett)
3) Perdere peso va sempre bene (5% = 0.5 punti di HbA1c)
4) La dieta migliore: Dieta mediterranea con pochi (40%) di Carb
5) E' meglio rinforzare la colazione e ridurre la cena

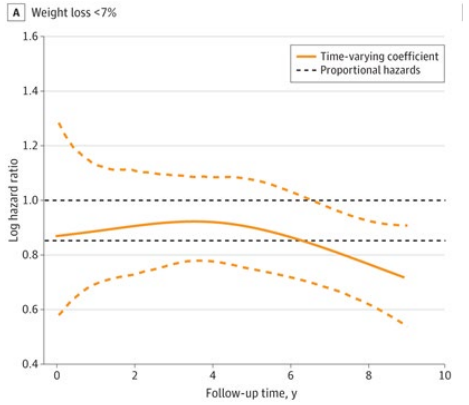
…… e le complicanze cardiovascolari ?

	Glucose/insulin	Blood pressure	HbA_{1c}	Lipids	Physical function	Depression	Quality of life
SITTING/BREAKING UP PROLONGED SITTING	↓	↓	↓	↓	↑	↓	↑
STEPPING	↓	↓	↓	↓	↑	↓	↑
SWEATING (MODERATE-TO-VIGOROUS ACTIVITY)	↓	↓	↓	↓	↑	↓	↑
STRENGTHENING	↓	↓	↓	↓	↑	↓	↑
ADEQUATE SLEEP DURATION	↓	↓	↓	↓	?	↓	↑
GOOD SLEEP QUALITY	↓	↓	↓	↓	?	↓	↑
CHRONOTYPE/CONSISTENT TIMING	↓	?	↓	?	?	↓	?

……. si ma il lookahead è stato deludente



A Post Hoc Analysis of the Look AHEAD Trial



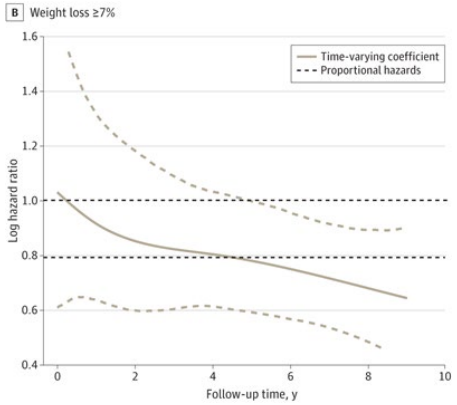


Table 2. Risk of Primary and Secondary Outcomes Stratified by Weight Loss and PA Trajectories

Group	Participants, No. (%)	Model 1, HR (95% CI)[a]	*P* value	Model 2, HR (95% CI)[b]	*P* value	*P* for interaction
Primary outcome: CV death, nonfatal MI or stroke, or hospitalization for angina						
Low PA and no weight loss	105 (15.8)	1 [Reference]	NA	1 [Reference]	NA	.01
Only high PA	39 (16.7)	0.87 (0.59-1.26)	.45	1.04 (0.70-1.53)	.86	
Only weight loss	46 (20.2)	1.29 (0.91-1.83)	.15	1.13 (0.78-1.62)	.52	
High PA and weight loss	8 (7.6)	0.36 (0.17-0.74)	.005	0.39 (0.19-0.81)	.01	
Secondary outcome 1: CV death, nonfatal MI or stroke						
Low PA and no weight loss	68 (10.3)	1 [Reference]	NA	1 [Reference]	NA	.10
Only high PA	22 (9.4)	0.76 (0.47-1.25)	.28	0.96 (0.57-1.59)	.86	
Only weight loss	34 (14.9)	1.46 (0.96-2.21)	.07	1.40 (0.91-2.15)	.13	
High PA and weight loss	6 (5.7)	0.45 (0.19-1.04)	.06	0.57 (0.24-1.36)	.21	
Secondary outcome 2: all-cause death, nonfatal MI or stroke, or hospitalization for angina						
Low PA and no weight loss	121 (18.3)	1 [Reference]	NA	1 [Reference]	NA	.002
Only high PA	43 (18.5)	0.83 (0.59-1.19)	.32	0.98 (0.68-1.42)	.92	
Only weight loss	61 (26.6)	1.48 (1.09-2.02)	.01	1.33 (0.96-1.84)	.08	
High PA and weight loss	9 (8.6)	0.35 (0.18-0.69)	.002	0.38 (0.19-0.75)	.006	
Secondary outcome 3: all-cause death, nonfatal MI or stroke, hospitalization for angina, CABG, PCI, hospitalization for heart failure, carotid endarterectomy, or peripheral vascular disease						
Low PA and no weight loss	154 (23.2)	1 [Reference]	NA	1 [Reference]	NA	.002
Only high PA	52 (22.3)	0.79 (0.57-1.09)	.15	0.88 (0.63-1.22)	.44	
Only weight loss	68 (29.8)	1.27 (0.95-1.70)	.10	1.14 (0.84-1.53)	.40	
High PA and weight loss	10 (9.5)	0.29 (0.15-0.56)	<.001	0.31 (0.16-0.60)	<.001	

Abbreviations: CABG, coronary artery bypass grafting; CV, cardiovascular; MI, myocardial infarction; NA, not applicable; PA, physical activity; PCI, percutaneous coronary intervention.

[a] Model 1 was adjusted for age, race and ethnicity, and sex.

[b] Model 2 was adjusted for age, race and ethnicity, sex, history of cardiovascular disease, fasting plasma glucose level, history of hypertension, insulin use, aspirin use, sedentary time, drinking status, smoking status, triglyceride level, and treatment group.

High PA volume: ≥2000 MET-min/wk

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2) Terapia nutrizionale

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Diabetes Care 1

Nutrition Therapy for Adults With Diabetes or Prediabetes: A Consensus Report

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Alison B. Evert,[1] Michelle Dennison,[2] Christopher D. Gardner,[3] W. Timothy Garvey,[4,5] Ka Hei Karen Lau,[6] Janice MacLeod,[7] Joanna Mitri,[8] Raquel F. Pereira,[9] Kelly Rawlings,[10] Shamera Robinson,[11] Laura Saslow,[12] Sacha Uelmen,[11] Patricia B. Urbanski,[13] and William S. Yancy Jr.[14,15]

(MNT) terapia nutrizionale medica

Perdere peso

1) Effetto proporzionale su HbA1c (>5% - 15%)
2) Non importa il tipo di dieta importa riuscire a convincere il paziente a seguirla

Alcol

1) ≤1 s/die donna, ≤2 uomo
2) Attenzione all'ipoglicemia tardiva

Supplementi

1) Controlla B12 se metformina
2) Cromo, curcuma, cannella, aloe vera, vit D, …. ???

Sodio

≤ 2.3 g/die ?

Proteine

1.0-1.5 g/kg/die (IBW?)

Barriere

Facilitare l'accesso alla MNT

Nutrizione personalizzata (omics)

Qualche osservazione intrigante, ma nessuna solida evidenza