14° CONGRESSO NAZIONALE SINut

SINut Società Italiana di Nutraceutica

12-14 settembre 2024

Bologna

Disglicemia: fattore di rischio cardiometabolico emergente

Gianluca Sanna

Il sottoscritto Gianluca Sanna
ai sensi dell'art. 3.3 sul Conflitto di Interessi, pag. 17 del Reg. Applicativo dell'Accordo Stato-Regione del 5 novembre 2009,

dichiara

che negli ultimi due anni NON ha avuto rapporti diretti di finanziamento con soggetti portatori di interessi commerciali in campo sanitario

che negli ultimi due anni ha avuto rapporti diretti di finanziamento con i seguenti soggetti portatori di interessi commerciali in campo sanitario:

- *S.p.A.*
- *……*
- *……..*

Diabetes is a cardiovascular disease

Heart disease leading cause of death in 67% of adults with diabetes ≥ 65 years

Mortality risk and CV disease is increased with diabetes

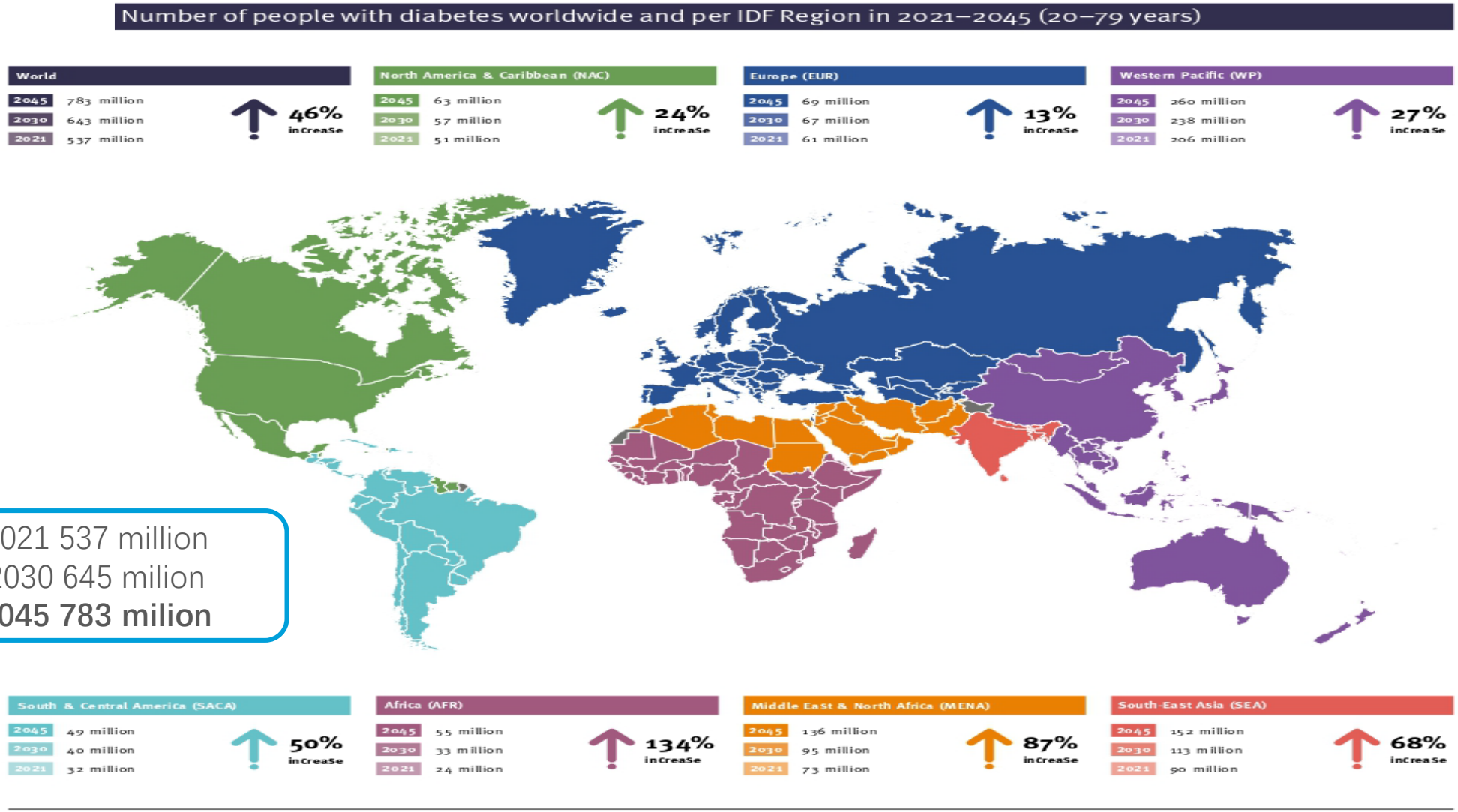
Hazard ratio for **all-cause mortality: 1.80**

Hazard ratio for **CV death: 2.32**

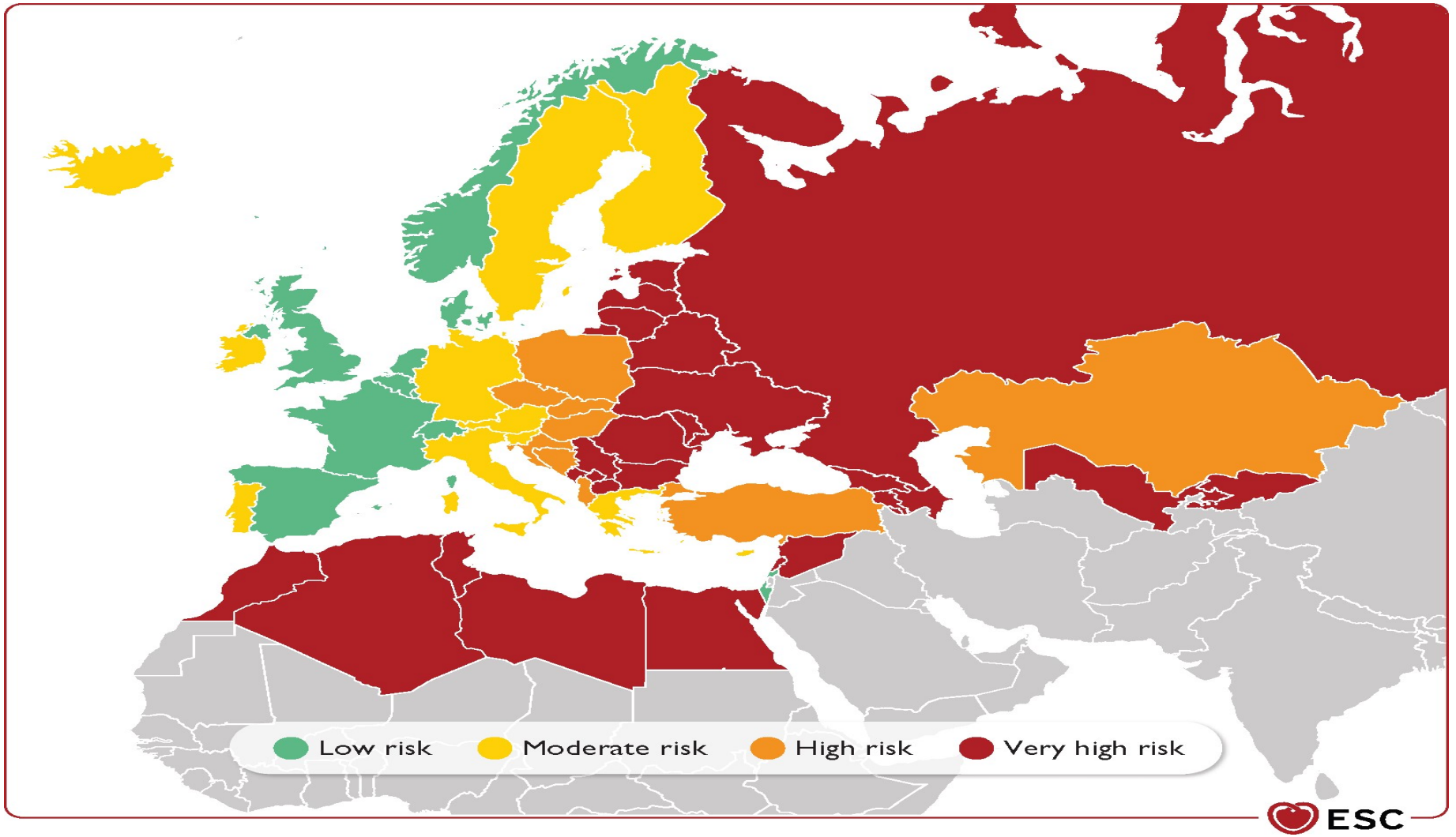
*Mortality risk associated with diabetes vs no diabetes (n=820,900) CV, cardiovascular.

IDF 2019; Rao Kondapally Seshasai S et al. *N Engl J Med* 2011;364:829–41.

Diabetes is a cardiovascular disease



2021 537 million
2030 645 milion
2045 783 milion



2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

Diabetes is a cardiovascular disease

Disglicemia
Disfunzione delle betacellule
Insulino-resistenza

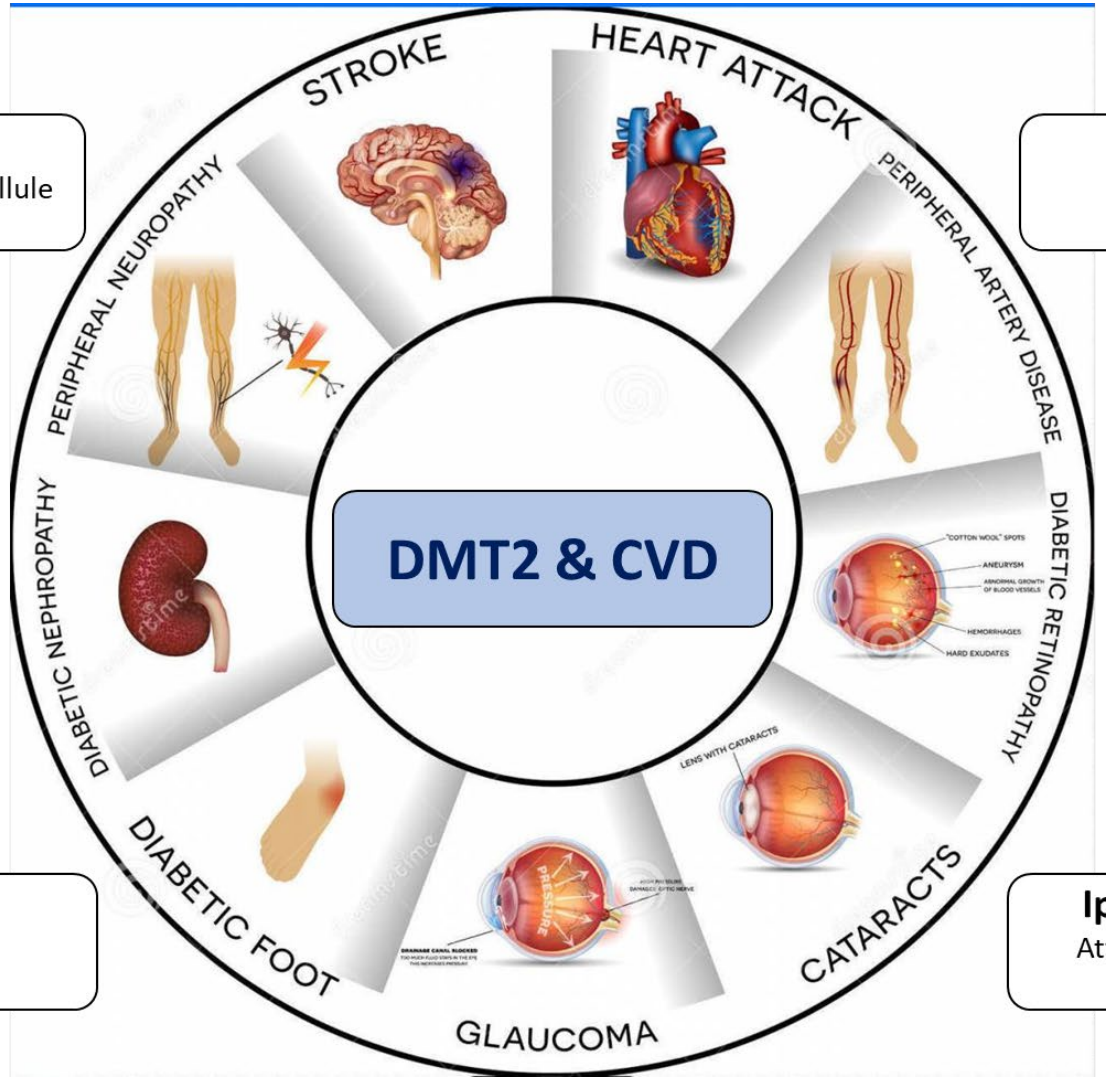
Stress ossidativo
oxLDL

Disfunzione endoteliale

Infiammazione
hsPCR
IL-1, IL-6, TNF-α

Dislipidemia
LDL, FFAs, ApoB, ApoA-1

Ipercoagulabilità
Attività antitrombinica, fibrinogeno



Prediabetes or Dysglycemia?

Esiste uno stato intermedio tra i valori normali alti di glicemia e diabete (100-125 mg%), che siamo abituati a chiamare prediabete/iperglicemia non diabetica, che sicuramente non è benigno: infatti è associato ad un aumento degli eventi micro e macrovascolari.

Il termine che negli ultimi anni viene utilizzato per descriverlo è disglicemia.

The evolving continuum of dysglycaemia: Non-diabetic hyperglycaemia in older adults. *Diabetic Medicine. 2023;40:e15177.*

Linee Guida ADA

La diagnosi di prediabete/disglicemia viene stabilita sulla base di una delle seguenti condizioni:

- una glicemia a digiuno alterata tra **100 e 125** mg/dl (IFG: impaired fasting glucose);

- dopo una curva da carico orale (75 g di glucosio [OGTT] con determinazione della **glicemia** al tempo 0 e a 120 minuti), con valori compresi tra **140 e 199** mg/dl (IGT:impaired glucose tolerance);

- un livello di **emoglobina glicata** (HbA1c) di **5,7-6,4**%.

Le raccomandazioni dell'ADA sottolineano l'importanza di uno screening per il prediabete e il diabete di tipo 2.

American Diabetes Association Professional Practice Committee. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes – 2022. Diabetes Care 2022;45(Suppl. 1):S17–S38.

Prediabetes or Dysglycemia?

	HbA1c (mmol/mol)	IFG (mmol/L)	IGT (mmol/L)
American Diabetes Association (ADA)[4]	39–47	5.5–7.0	7.8–11.0
National Institute of Clinical Excellence (NICE)[5]	42–47	6.1–7.0	7.8–11.0
World Health Organisation (WHO)[6]	N/A	6.1–7.0	7.8–11.0
International Expert Committee (IEC)[7]	42–47	N/A	N/A

Abbreviations: IFG, impaired fasting glucose; IGT, impaired glucose tolerance.

The evolving continuum of dysglycaemia: Non-diabetic hyperglycaemia in older adults. *Diabetic Medicine. 2023;40:e15177.*

Prediabetes or Dysglycemia?

La prevalenza della disglicemia continua ad aumentare a livello globale.
Le stime indicano che probabilmente saranno interessati il 10-33% della popolazione adulta

Per la riduzione del rischio cardiovascolare e l'eventuale progressione verso il diabete di tipo II è diventato essenziale identificare i pazienti con iperglicemia non diabetica.

ITALIA

- La prevalenza di IGT è pari all'8,4%, con numeri superiori nelle donne (1.549.000) rispetto agli uomini (1.105.00).
- La prevalenza di IFG è pari al 2,8%.
- Il tasso di conversione a diabete in 10 anni è del 7,6%,
- Soggetti con IFG presentano un rischio > 11 volte di sviluppare diabete di tipo 2,
- Soggetti con IGT presentano un rischio > 4 volte di sviluppare diabete di tipo 2,
- Soggetti con la combinazione IFG/IGT presentano un rischio >20,5 di sviluppare diabete di tipo 2.

The evolving continuum of dysglycaemia: Non-diabetic hyperglycaemia in older adults. *Diabetic Medicine. 2023;40:e15177.*

International Diabetes Federation. IDF Diabetes Atlas. 10th Edition, 2021. *Italy – Diabetes report 2000-2045.*

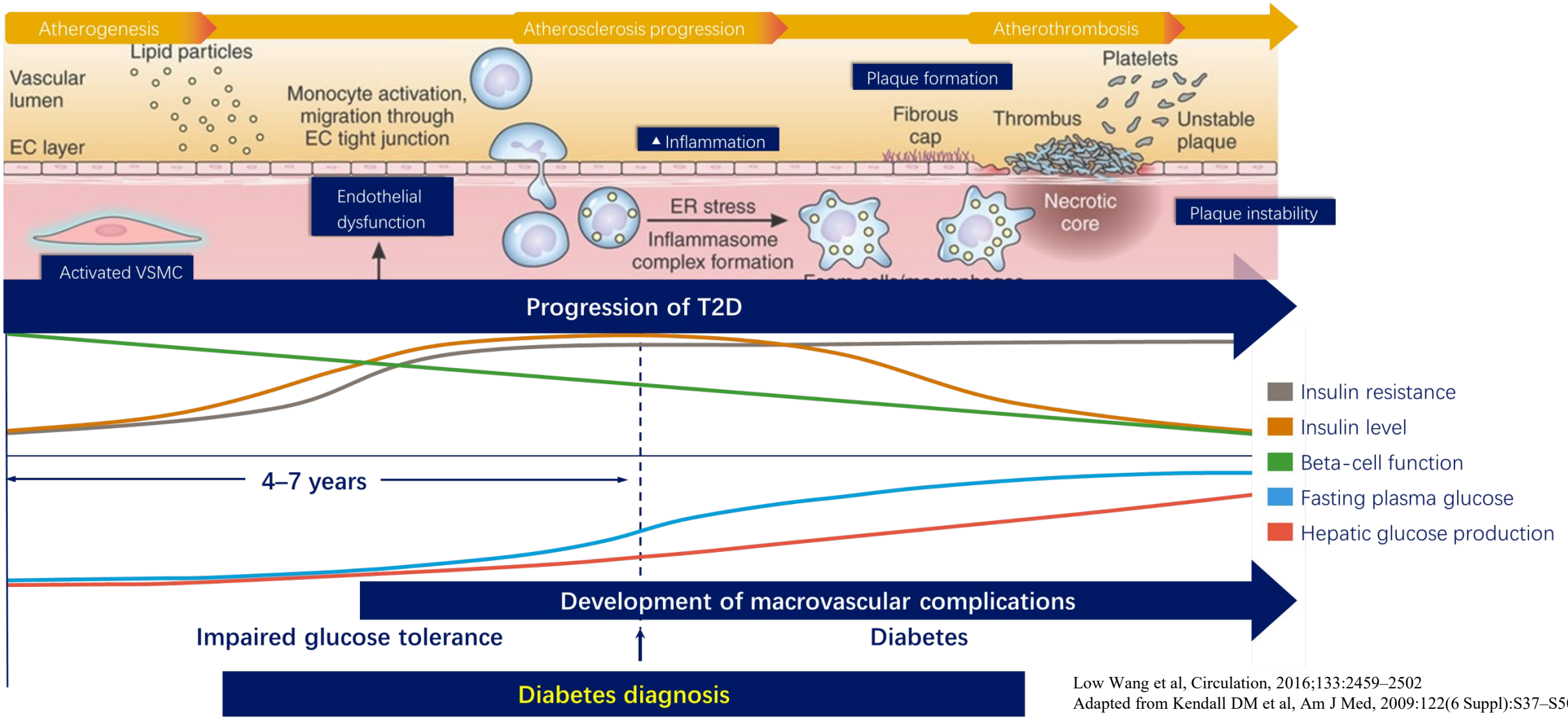
Approach to Screening, Diagnosis, and Management of dysglycemia

Adulti in sovrappeso o obesi con ≥1 fattori di rischio:

- Familiarità di primo grado per il diabete
- Malattia cardiovascolare pregressa o in corso
- Ipertensione
- Ipercolesterolemia e/o ipertrigliceridemia
- Sindrome dell'ovaio policistico
- Altre condizioni cliniche

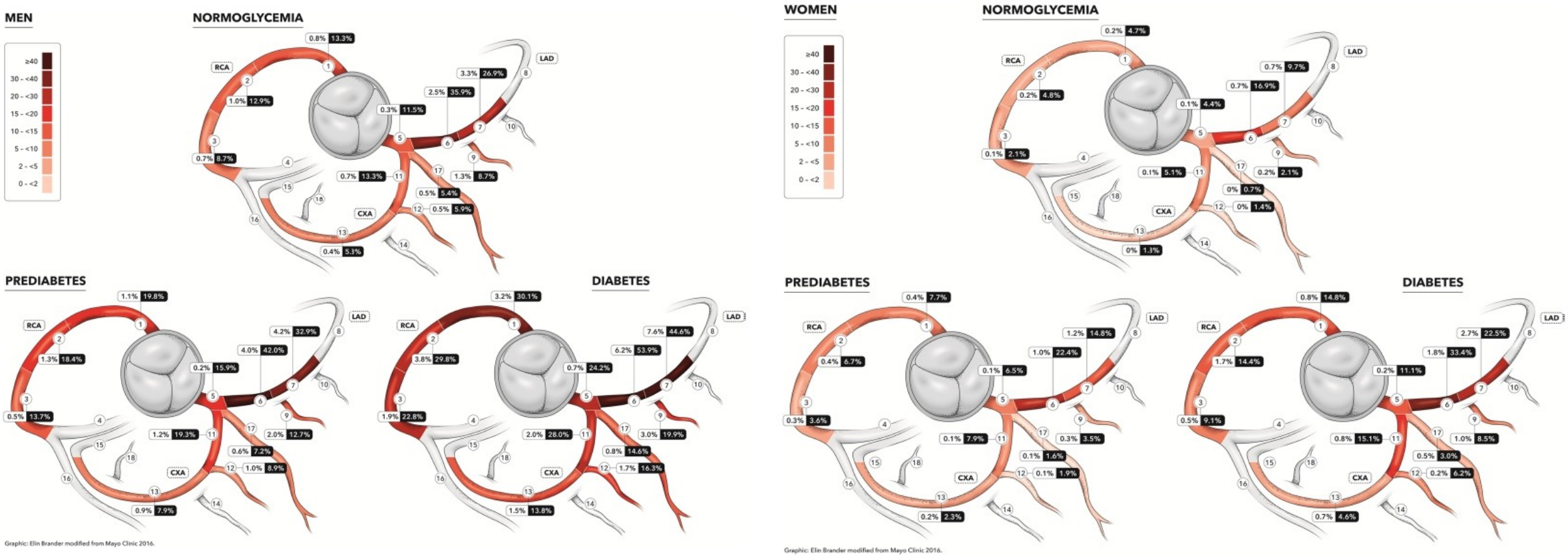
American Diabetes Association Professional Practice Committee. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes – 2022. Diabetes Care 2022;45(Suppl. 1):S17–S38.

ASCVD prima della diagnosi di diabete di tipo II



Low Wang et al, Circulation, 2016;133:2459–2502
Adapted from Kendall DM et al, Am J Med, 2009:122(6 Suppl):S37–S50

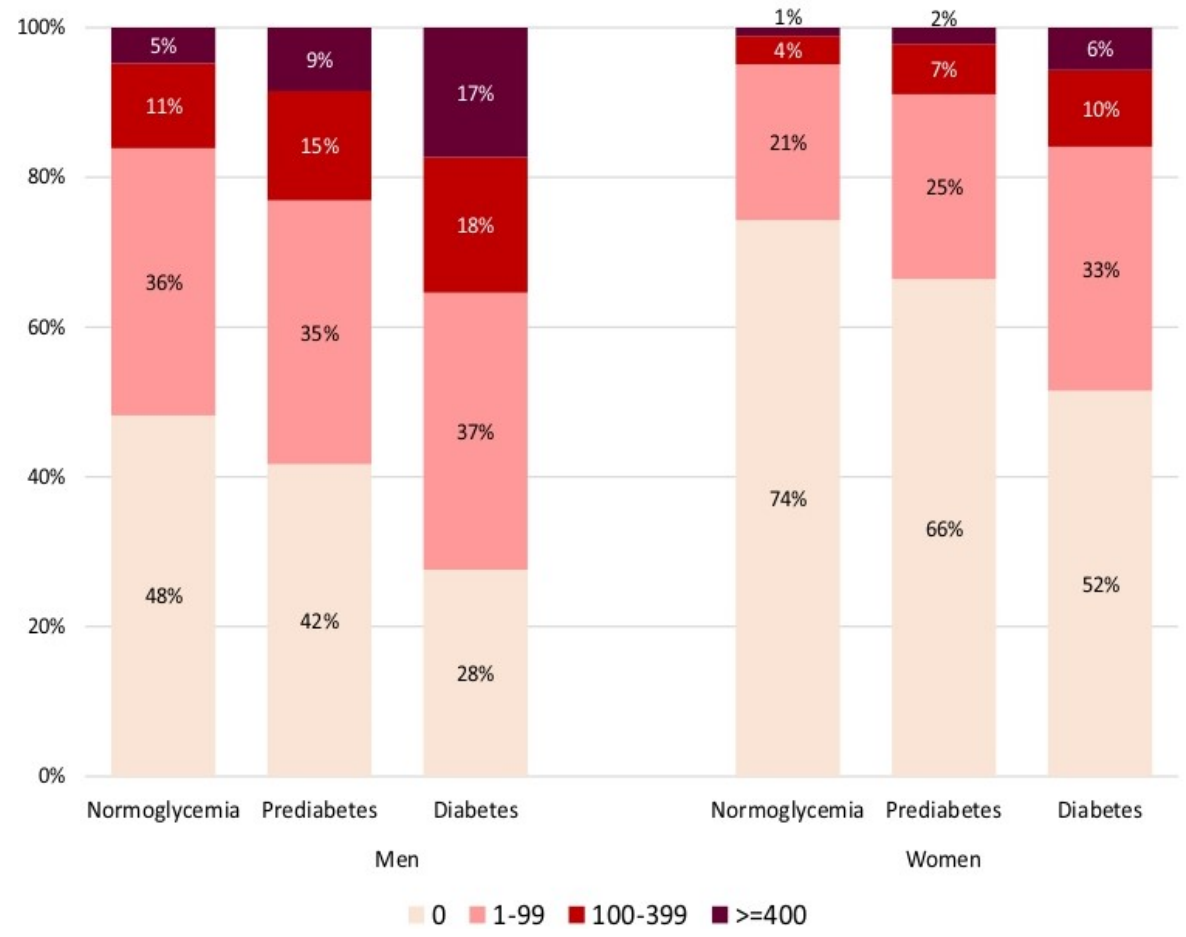
ASCVD prima della diagnosi di diabete di tipo II



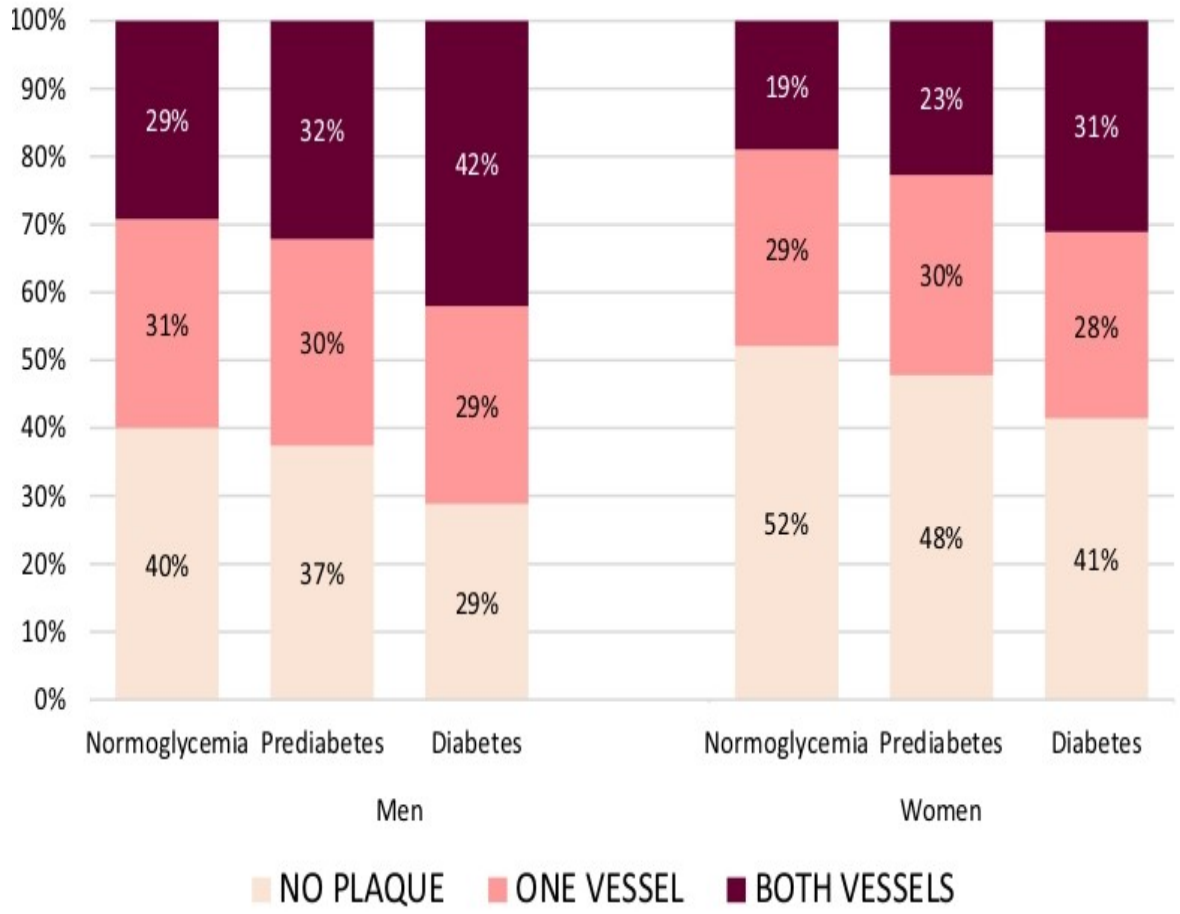
Östgren *et al. Cardiovascular Diabetology (2023) 22:261*

ASCVD prima della diagnosi di diabete di tipo II

Frequency of CACS categories, by glycaemic status



Frequency of plaque in carotid arteries, by glycaemic status



Östgren *et al. Cardiovascular Diabetology (2023) 22:261*

Theraphy of Dysglycemia

The results of the present study show that asymptomatic atherosclerotic burden increases with increasing dysglycaemia in major vascular beds, as the coronary arteries, in a large population-based cohort. The data may have future implications for screening strategies and tailored preventive interventions for people with dysglycaemia.

Östgren *et al. Cardiovascular Diabetology (2023) 22:261*

Approach to Screening, Diagnosis, and Management of Prediabetes

La disglicemia è associata ad un incremento del rischio di sviluppare diabete, eventi cardiovascolari e mortalità.

La first-line therapy consiste nel cambiamento dello stile di vita, soprattutto esercizio fisico e perdita di peso.

La modifica dello stile di vita è associato a benefici superiori rispetto alla terapia con metformina.

Diagnosis and Management of Prediabetes
JAMA. 2023;329(14):1206-1216.

Randomized Clinical Trials of Medications for Prevention of Type 2

Source	Country/year of publication	Prediabetes phenotype	BMI at entry, mean (SD)	Study groups	Study size, No.	Mean follow-up, y	Relative risk reduction for intervention vs placebo (95% CI), %	Absolute risk reduction related to intervention
TRIPOD[78]	US/2002	IGT (women with a history of gestational diabetes)	30 (5.7)	Troglitazone vs placebo	266	2.5	55 (17 to 75)	Annual diabetes incidence rate: 12.1% in placebo group vs 5.4% in troglitazone group
STOP-NIDDM[79]	International/ 2002	IGT and IFG	31 (4.2)	Acarbose vs placebo	1429	3.3	25 (10 to 37)	Cumulative incidence: 42% in the placebo group vs 32% in the acarbose group
DPP[34]	US/2002	IGT and IFG	34 (6.7)	Metformin vs placebo	3234	2.8	31 (17 to 43)	Incidence rate per 100 person-years: 11.0 in the placebo group vs 7.8 in the metformin group
DPP[80]	US/2005	IGT	NR	Troglitazone vs placebo	585	0.9	75 (NR)	Incidence rate per 100 person-years: 3.0 in the troglitazone group vs 12.0 in the placebo group
XENDOS[81]	International/ 2006	Normal glucose regulation and IGT	37 (4.4)	Orlistat vs placebo	3305	4	37 (14 to 54)	Cumulative incidence: 9% in the placebo group vs 6.2% in the orlistat group
Indian DPP-1[35]	India/2006	IGT	25.8 (3.5)	Metformin vs placebo	531	2.5	26.4 (19.1 to 35.1)	Cumulative incidence: 55.0% in the placebo group vs 40.5% in the metformin group
Indian DPP-2[97]	India/2006	IGT	25.9 (3.3)	Pioglitazone vs placebo	407	3	2 (−44 to 33)	Cumulative incidence: 31.6% in the placebo group vs 29.8% in the pioglitazone group
DREAM[82]	International/ 2006	IGT and IFG	30.9 (5.6)	Rosiglitazone vs placebo	5269	3	62 (56 to 67)	Cumulative incidence: 25.0% in the placebo group vs 10.6% in the rosiglitazone group
DREAM[83]	International/ 2006	IGT and IFG	30.9 (5.6)	Ramipril vs placebo	5269	3	9 (−3 to 20)	Cumulative incidence: 19.5% in the placebo group vs 18.1% in the ramipril group
Voglibose trial[84]	Japan/2006	IGT	25.8 (3.8)	Voglibose vs placebo	1780	0.9	40 (18 to 57)	Cumulative incidence: 17% in the placebo group vs 8% in the voglibose group
NAVIGATOR[85]	International/ 2010	IGT and IFG	30.5 (5.4)	Nateglinide vs placebo	9306	5	−7 (−15 to 0)[a] (Favors placebo)	Cumulative incidence: 34% in the placebo group vs 34% in the nateglinide group
NAVIGATOR[86]	International/ 2010	IGT and IFG	30.5 (5.4)	Valsartan vs placebo	9306	5	14 (8 to 20)	Cumulative incidence: 36.8% in the placebo group vs 33.1% in the valsartan group
ACT NOW[87]	US/2010	IGT	33.7 (SE, 0.4)	Pioglitazone vs placebo	602	2.4	72 (51 to 84)	Incidence rate per 100 person-years: 7.6 in the placebo group vs 2.1 in the pioglitazone group
CANOE[88]	Canada/2010	IGT	31.7 (27.1-36.8)	Metformin and rosiglitazone vs placebo	207	3.9	66 (41 to 80)	Cumulative incidence: 39% in the placebo group vs 14% in the treatment group
SCALE[89,90]	International/ 2010	IGT and IFG	38.9 (6.4)	Liraglutide vs placebo	2254	3	79 (66 to 87)	Cumulative incidence: 6% in the placebo group vs 2% in the liraglutide group
ACE[91]	China and Hong Kong/ 2010	IGT	24.5 (3.1)	Acarbose vs placebo	6522	5	18 (6 to 29)	Incidence rate per 100 person-years: 3.8 in the placebo group vs 3.2 in the acarbose group

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); DPP, Diabetes Prevention Program; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; NR, not reported.

[a] Denotes a lack of risk reduction.

Diagnosis and Management of Prediabetes *JAMA*. 2023;329(14):1206-1216.

Efficacy of Lifestyle Intervention From Randomized Trials to Prevent Type 2 Diabetes

Source	Country	Study duration	Prediabetes definition	Age, y/BMI, mean (SD)	Study groups (No.)	Weight target	Mean follow-up, y	Intervention vs control		Reversal of prediabetes, %	Years of follow-up after active intervention
								Relative risk reduction for diabetes, %	Absolute risk reduction for diabetes		
Da Qing[32]	China	1986-1992	IGT	45 (9)/25.8 (3.8)	Diet (130) Exercise (141) Diet and exercise (126) Control (133)	No specific target	6	Diet, 31.5 Exercise, 46 Diet and exercise, 42	Cumulative incidence: 65.9% in control vs 47.1% in diet, 44.2% in exercise, and 44.6% in diet and exercise groups	NR	30
Finnish DPS[33]	Finland	1993-2001	IGT	55 (7)/31 (4.5)	Diet and exercise (265) Control (257)	>5% Weight loss	4	Diet and exercise, 58	Incidence rate per 1000 person-years: 32 cases in diet and exercise group vs 78 in control group	NR	13
DPP[34]	US	1996-2001	IGT (+ IFG in some)	51 (10.7)/34 (6.7)	Diet and exercise (1079) Metformin (1073) Control (1082)	7% Weight loss	2.8	Diet and exercise, 58 Metformin, 31	Incidence rate per 100 person-years: 10.8 in placebo vs 7.8 in metformin groups and 4.8 in lifestyle (diet and exercise) intervention groups	Lifestyle, 40 Metformin, 20	15
Japanese trial[59]	Japan	1984-2003	IGT (men only)	NR/24 (2.2)	Diet and exercise (102) Control (356)	No specific target	4	Diet and exercise, 67.4	Cumulative incidence: 9.3% in control group vs 3.0% in intervention group (diet and exercise)	Lifestyle, 53.8	NR
Indian DPP-1[35]	India	2003-2005	IGT	46 (5.7)/25.8 (3.5)	Diet and exercise (133) Metformin (133) Diet, exercise, and metformin (136) Control (136)	No specific target	3	Diet and exercise, 28.5 Metformin, 26.4 Diet, exercise, and metformin, 28.2	Cumulative incidence: 55.0% in control group vs 39.3% in diet and exercise, 40.5% in metformin, 39.5% in diet, exercise, and metformin groups	NR	NR
Indian DPP-2[60]	India	2003-2005	IGT	45 (6.2)/26 (3.3)	Diet and exercise (203) Diet, exercise, and pioglitazone (204)	No specific target	3	Diet, exercise, and pioglitazone (vs diet and exercise), 1.8	Cumulative incidence: 31.6% in diet and exercise group vs 29.8% in pioglitazone group	Lifestyle, 32.3 Pioglitazone, 40.9	NR

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); DPP, Diabetes Prevention Program; DPS, Finnish Diabetes Prevention Study; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; NR, not reported.

Diagnosis and Management of Prediabetes *JAMA*. 2023;329(14):1206-1216.

Opzioni terapeutiche

Affrontare i fattori di rischio cardiovascolari in fase precoce ha un ruolo fondamentale nella pianificazione degli interventi terapeutici.

Agire in maniera efficace su una popolazione di pazienti moderatamente ipercolesterolemici, ipertesi, iperglicemici, in sovrappeso a rischio intermedio o in fasce di età nelle quali la somministrazione di farmaci specifici non ha rapporto rischio/beneficio determinato con precisione.

Il primo intervento da proporre al paziente è adeguarsi ad un corretto stile di vita.

Theraphy of Dysglycemia

"Know your numbers" suggested plain-language communication points to patients.

Parameter	What it tells us	What's normal	What's risky	The direction we want it to go[a]
General health (all patients)				
BMI	Whether your weight puts you at risk for other diseases. BMI is your weight (in kilograms) divided by your height (in meters)	18 to 25	30 or more	Lower
Waist circumference	A way of measuring how much fat you have around your stomach area; too much puts you at risk for other diseases	Women ≤88 cm (35 in); men ≤102 cm (40 in)	More than these	Lower
BP	The amount of pressure your blood puts against the walls of your blood vessels (like the water in a hose)	Less than 120 over 80	More than 140 over 90	Lower
HDL-C	How much "good" cholesterol you have, which helps keep the blood flowing in your body	More than 50	Less than 40	Higher
Triglycerides	How much fat is in your blood	Less than 100	More than 135	Lower
LDL-C	How much "bad" cholesterol you have; too much can clog up your blood vessels	Less than 100	More than 55, 70, or 100[b]	Lower
Non-HDL-C	Total cholesterol minus HDL-C ("good" cholesterol)	Less than 130	More than 85, 100, or 130[b]	Lower
Diabetes				
A1C	How well your diabetes is controlled overall	Less than 5.7	More than 6.5 or 7 or 7.5[c]	Lower
FPG	How much sugar is in your blood when you haven't eaten for 8 h, such as in the morning before breakfast	More than 70 and less than 100	Less than 70 and more than 140	Stay between 70 and 140
TIR	The percentage of time each day your blood sugar is well controlled	100 %	Less than 70 %	Longer (more time)
Diabetes and CKD				
eGFR	How well your kidneys are working	More than 90	Less than 60	Higher (or at least stay the same)
UACR	How much protein is in your urine, which tells us if your kidneys are damaged	Less than 30	More than 300	Lower (or at least stay the same)

Abbreviations: A1C, hemoglobin A1C; BMI, body mass index; BP, blood pressure; eGFR, estimated glomerular filtration rate; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; TIR, time in range; UACR, urine albumin-creatinine ratio.

[a] Assumes patient's levels are abnormal.

[b] Depends on the patient's individual comorbidities; see Section 2.2.3. Lipid disorders.

[c] Depends on patient's individual characteristics; see Section 2.2.6. Antihyperglycemic therapy in type 2 diabetes.

DCRM 2.0: Multispecialty practice recommendations for the management of diabetes, cardiorenal, and metabolic diseases Metabolism. 2024 Jun 4:155931

Theraphy of Dysglycemia

Patient Education

Increase Patient Knowledge and Promote Understanding

- Recognize obesity, diabetes, cardiovascular, kidney, and other cardiorenal and metabolic diseases as chronic conditions
  - Types of diabetes, lipid disorders, etc
  - Vascular complications
  - Risk factor monitoring: BP, glucose, lipids,
  - eGFR + UACR
- Exams and tests to expect for eyes, kidney, heart, liver, feet, hearing
- "Know and understand your numbers": BMI, A1C, TIR, FPG, BP, LDL-C, ApoB, TG, HDL-C, non-HDL-C, FIB-4, eGFR, UACR
- Treatment options: lifestyle, pharmacologic, surgical/invasive interventions
- Health-related technology (apps, wearables, etc)
- Healthcare systems and reimbursement

A1C = hemoglobin A1C (HbA1c); ApoB = apolipoprotein B; BMI = body mass index; BP = blood pressure; eGFR = estimated glomerular filtration rate; FIB-4, fibrosis 4 calculation; FPG = fasting plasma glucose; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; TG = triglycerides; TIR = time in range; UACR = urine albumin-creatinine ratio.

Shared Decision Making

- Elicit patient's priorities
- Emphasize early and aggressive treatment
- Ask open-ended questions
- Affirm personal challenges and goals
- Encourage belief patient can control health outcomes

Dos and Don'ts

- Do provide education every clinic visit
- Don't try to cover all topics at once
- Do repeat and reinforce
- Don't be judgmental

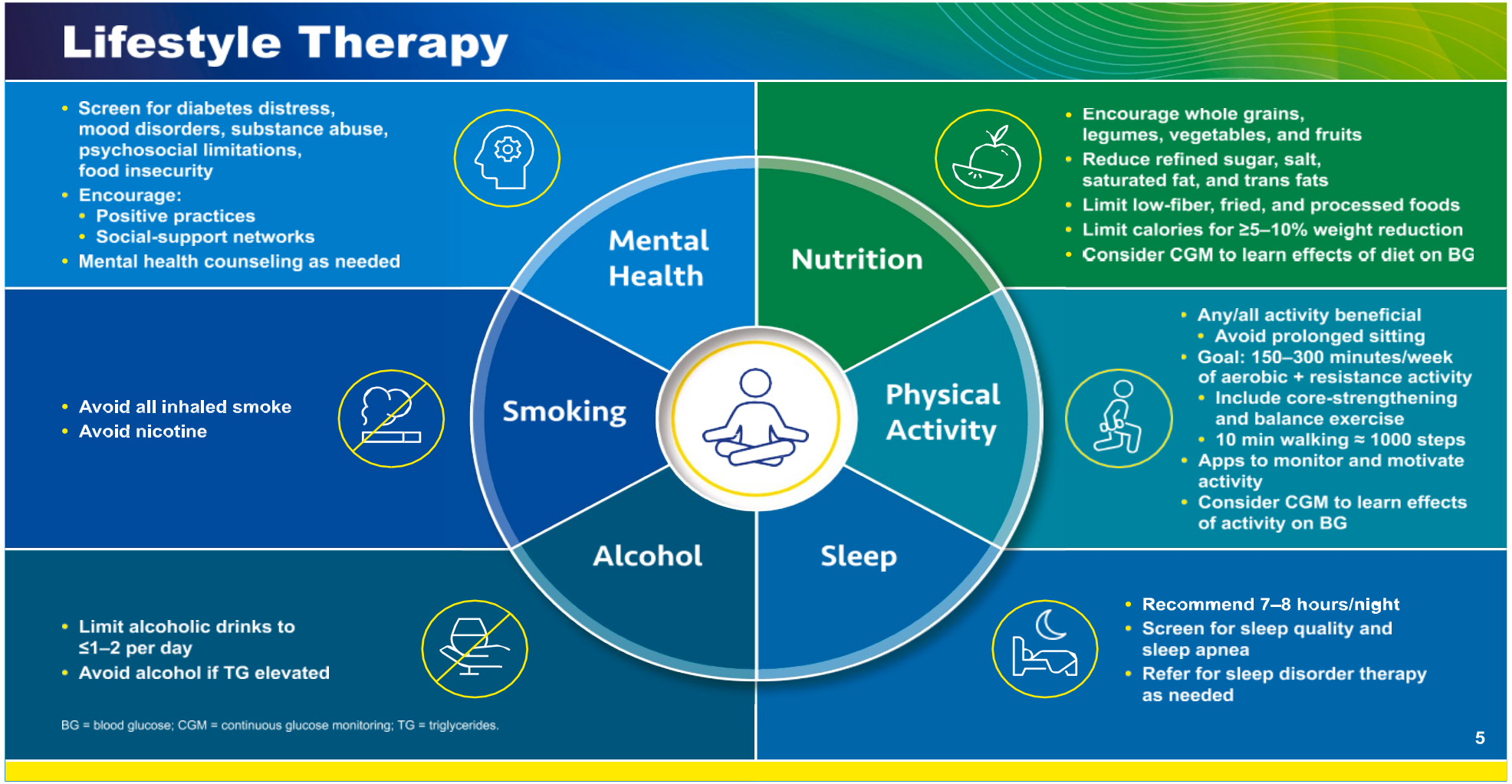
Tailor to Individual Patient

- Evaluate and consider health literacy
- Account for socioeconomic factors and other social determinants of health

Improve Adherence

DCRM 2.0: Multispecialty practice recommendations for the management of diabetes, cardiorenal, and metabolic diseases Metabolism. 2024 Jun 4:155931

Theraphy of Dysglycemia



DCRM 2.0: Multispecialty practice recommendations for the management of diabetes, cardiorenal, and metabolic diseases Metabolism. 2024 Jun 4:155931

Theraphy of Dysglycemia

Virani SS et al. Circulation. 2023

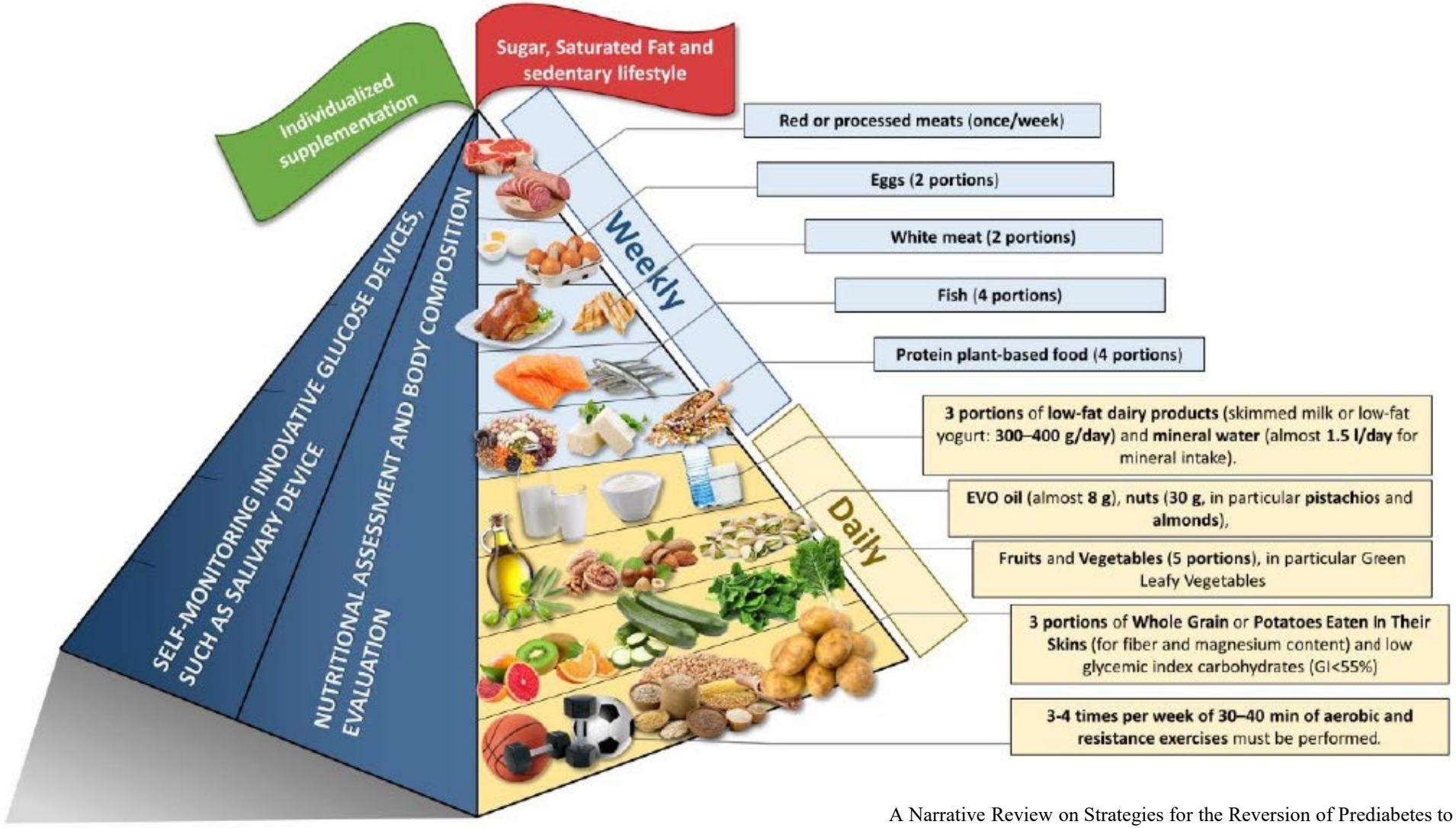
Modificare lo stile di vita

Il primo intervento è la modifica dello stile di vita: una dieta sana per ridurre il sovrappeso o l'obesità, ottenere un adeguato controllo glicemico e prevenire le complicanze.
L'alimentazione dovrebbe essere basata sulla dieta mediterranea e consistere in <30% di grassi, <10% di grassi saturi, >15 g di fibra insolubile e solubile per 1.000 kcal, 45-60% di carboidrati e 15-20% di proteine. Pazienti dovrebbero limitare l'assunzione di grassi saturi al <7% del fabbisogno calorico giornaliero; acidi grassi monoinsaturi, come l'olio d'oliva e altri oli, sono raccomandati (ADA, 2021).

Il secondo intervento è aumentare la proprio attività fisica e impegnarsi in un minimo di 30-40 minuti di attività aerobica almeno tre o quattro volte alla settimana.
Il paziente dovrebbe anche essere consigliato di smettere di fumare e consumare alcolici.

The role of selected nutraceuticals in managment of prediabetes and diabetes An update review of the literature Derosa G, D'Angelo A, Maffioli P.Phytother Res. 2022 Oct;36(10):3709-3765.

Ideal food pyramid for prediabetes



A Narrative Review on Strategies for the Reversion of Prediabetes to Normoglycemia: Food Pyramid, Physical Activity, and Self-Monitoring Innovative Glucose Devices Nutrients 2023, 15, 4943

I limiti

Tuttavia sappiamo che non sempre i pazienti riescono a modificare i propri stili di vita e mantenere uno stile di vita sano in particolare per inerzia, situazioni lavorative (sedentarie), socio-economiche, etc.

L'utilizzo di nutraceutici può essere considerato un valido aiuto.

I risultati di studi osservazionali suggeriscono un ruolo per alcuni nutraceutici in particolare Berberina, Banaba, Curcumina e Gomma Guar, Morus alba, Ilex paraguariensis, Omega-3 nella gestione del prediabete e del diabete.

The role of selected nutraceuticals in managment of prediabetes and diabetes An update review of the literature Phytother Res. 2022 Oct;36(10):3709-3765.

Nutraceutical products and guidelines for type 2 diabetes mellitus.

Nutraceutical Products Mentioned: **Berberine, Morus Alba Extract, other Herbal Extracts, Omega-3 Polyunsaturated Fatty Acids, Viscous Fibre, Plant Stanols/Sterols**		
Year	**Guideline (S) Name**	**Ref.**
2021–2022	American Diabetes Association "Standards of Medical Care in Diabetes"	
	Pharmacologic Approaches to Glycemic Treatment	[33,38]
	Cardiovascular Disease and Risk Management	[39,40]
2019	ESC Guidelines on diabetes, pre-diabetes and cardiovascular diseases developed in collaboration with the EASD	[34]
2018	Management of hyperglycaemia in type 2 diabetes	[41]
	A consensus report by ADA and EASD	
2017	IDF Recommendations for Managing Type 2 Diabetes in Primary Care	[42]
2016	EASL–EASD–EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease	[43]

In conclusion, guidelines for T2DM do not mention any specific nutraceutical approach to this disease, nor to milder forms such as insulin resistance and pre-diabetes, which may be observed in the early phases before proper T2DM development. In any case, if the validation of such products is considered important, robust clinical research will, thus, need to be implemented in this specific area

Nutraceuticals for Dyslipidaemia and Glucometabolic Diseases: What the Guidelines Tell Us (and Do Not Tell, Yet) Nutrients 2022, 14, 606

Pharmacological and non-pharmacological strategies for prediabetes..

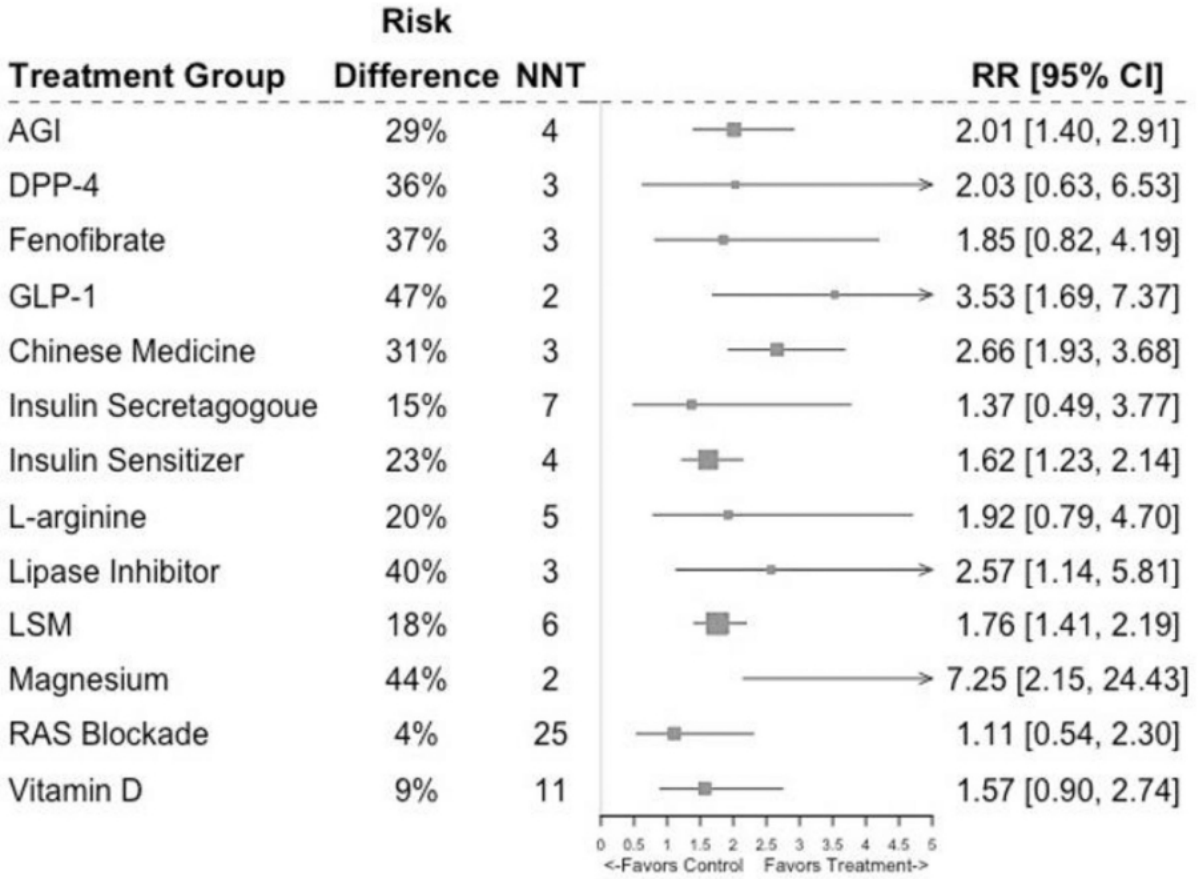


Figure 2.
Forest plot showing pooled effects for each treatment against control/placebo.
AGI, alpha-glucosidase inhibitors; DPP-4, dipeptidyl peptidase 4 inhibitors; GLP-1, glucagon-like peptide 1 receptor agonists; LSM, lifestyle modification; RAS, renin-angiotensin system; NNT, number needed to treat; RD, risk difference; RR, relative risk.

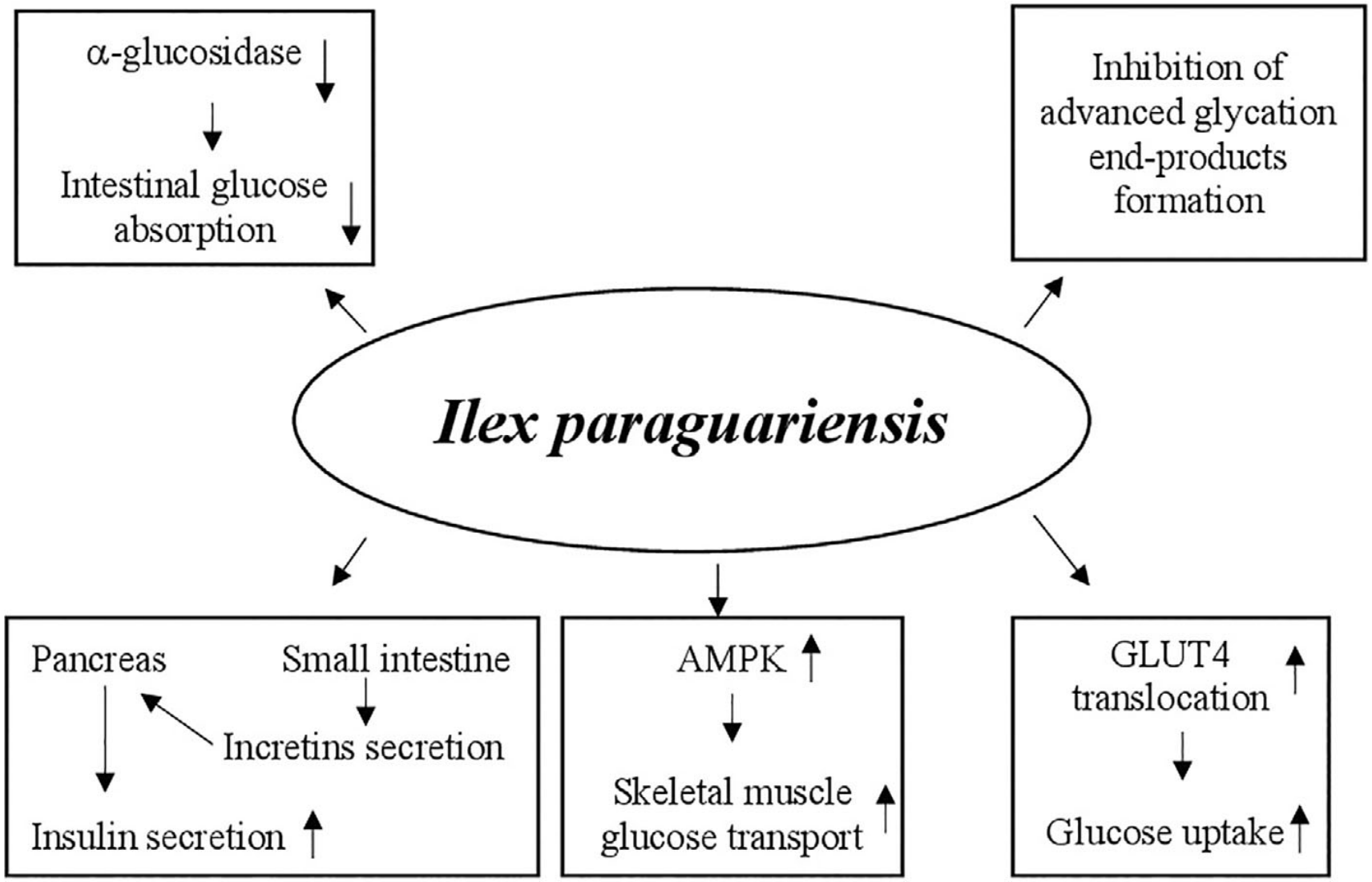
Only lifestyle modification interventions provide strong evidence of effectiveness, which supports current expert statements recommending this as the first-line approach for treating prediabetes. To date, neither medications nor alternative approaches are recommended in expert statements or have been approved by regulatory authorities for treating prediabetes—the present findings support these conclusions.

Interventions for Reversing Prediabetes: A Systematic Review and Meta-Analysis)
Am J Prev Med. 2022 April ; 62(4): 614–625

Ilex paraguariensis

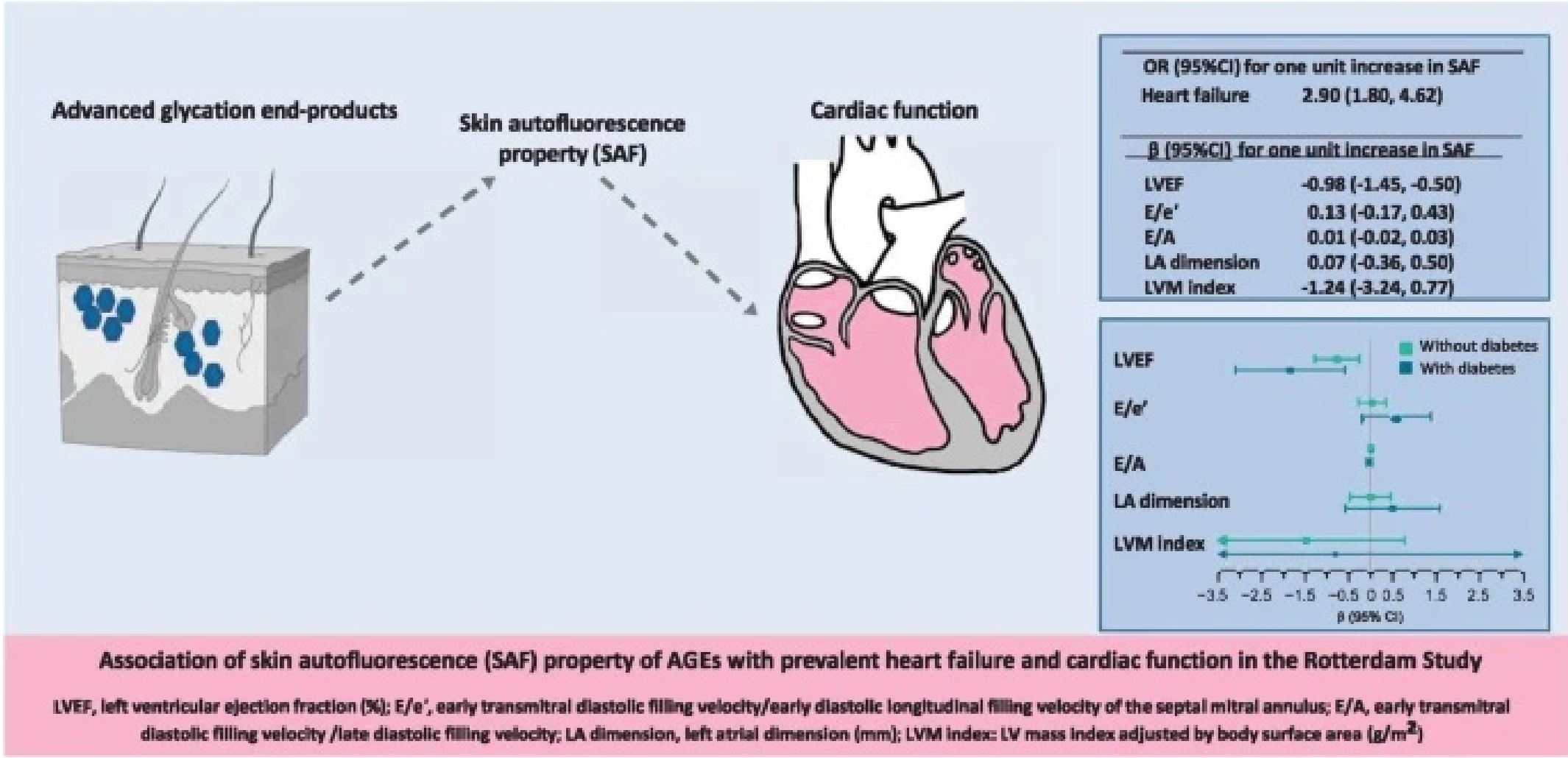
Ilex paraguariensis è una pianta localizzata in Sud America, appartenente alla famiglia delle Aquifoliaceae.
È un albero sempreverde dioico, che può raggiungere un'altezza di 8-15 m. Le foglie verde oliva lunghe 8 cm sono perenni, alterne, coriacee, obovate con margini dentati leggermente crenati e apice ottuso, e hanno una base a forma di cuneo. I piccioli sono lunghi fino a 15 mm.
La fase di fioritura avviene durante la stagione primaverile, producendo piccoli fiori unisessuali con quattro petali bianchi. In alcune specie tropicali o subtropicali, il numero di petali può essere cinque, sei o sette. Questi possono essere raggruppati in gruppi di 1-15 fiori che appaiono nelle ascelle delle foglie.
I frutti sono bacche di colore rosso contenenti da quattro a cinque semi

Bracesco et al., 2011



Hypoglycemic effects of Ilex paraguariensis:
AMPK, adenosine monophosphate-activated protein kinase;
GLUT4, glucose transporter 4

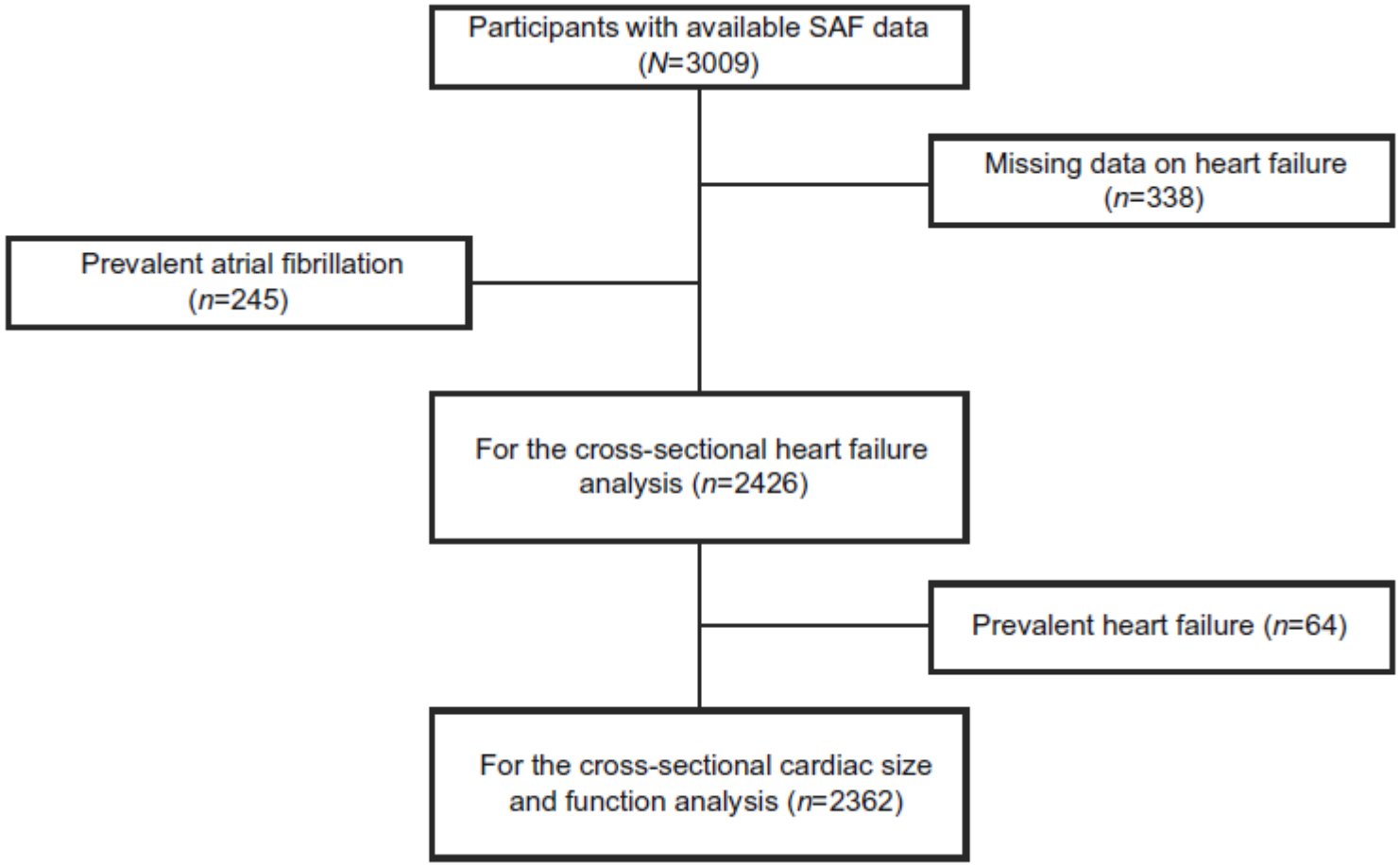
the role of selected nutraceuticals in managment of prediabetes and diabetes An update review of the literature Derosa G, D'Angelo A, Maffioli P.Phytother Res. 2022 Oct;36(10):3709-3765.



Association of skin autofluorescence (SAF) property of AGEs with prevalent heart failure and cardiac function in the Rotterdam Study

LVEF, left ventricular ejection fraction (%); E/e', early transmitral diastolic filling velocity/early diastolic longitudinal filling velocity of the septal mitral annulus; E/A, early transmitral diastolic filling velocity /late diastolic filling velocity; LA dimension, left atrial dimension (mm); LVM index: LV mass index adjusted by body surface area (g/m^2)

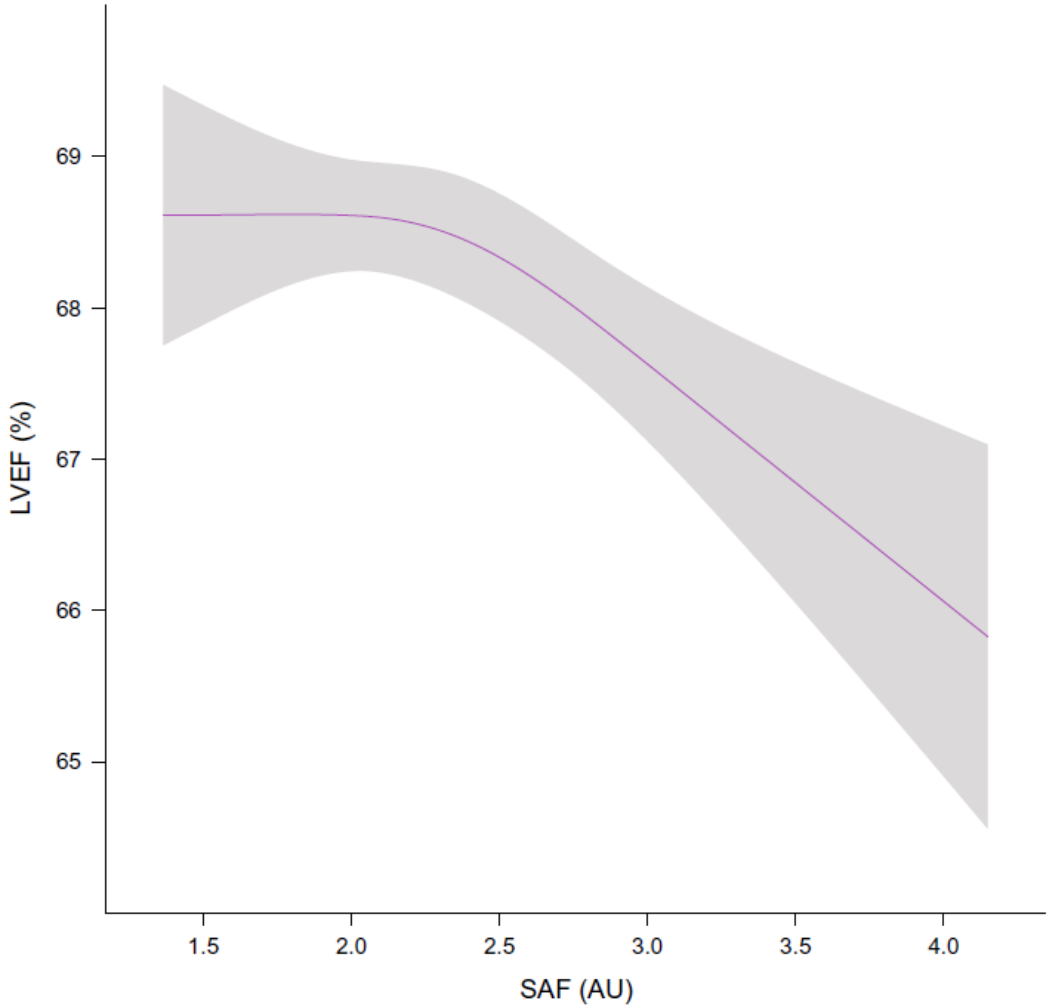
Advanced glycation end-products, cardiac function and heart failure in the general population: The Rotterdam Study Diabetologia (2023) 66:472–481



Advanced glycation end-products, cardiac function and heart failure in the general population: The Rotterdam Study Diabetologia (2023) 66:472–481

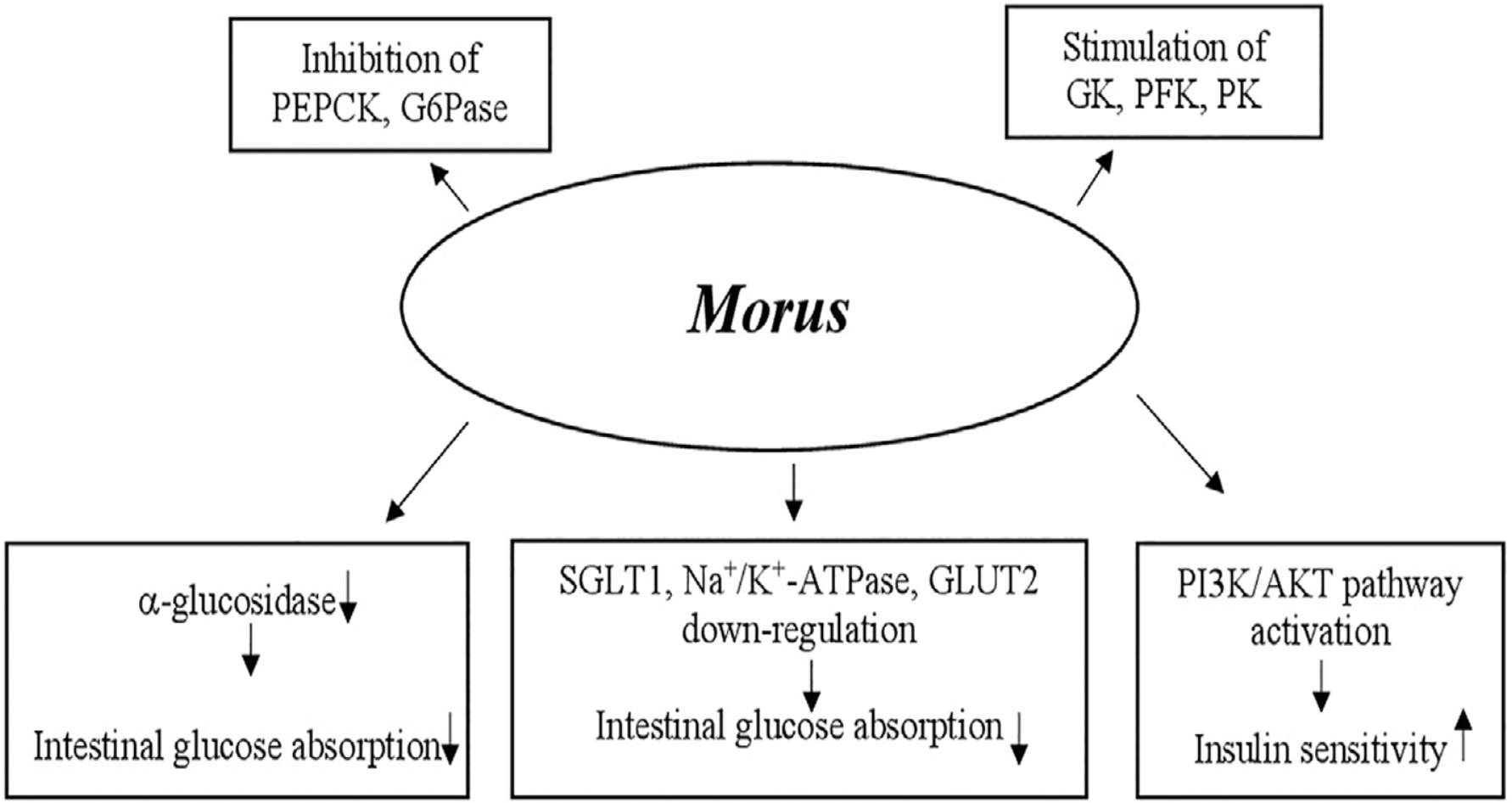
Levels of LVEF in association with SAF levels. The number of individuals with available data on LVEF and SAF was 2328 in the original data

Conclusions Higher levels of SAF were associated with prevalent heart failure irrespective of diabetes status. Among individuals free of heart failure, higher SAF levels were associated with poorer LV systolic and diastolic function, although the associations were more prominent for systolic function. Sex-stratified analyses suggested an inverse association between AGEs and parameters of diastolic function that was more prominent in men with diabetes. Further prospective research on the mechanisms linking AGEs to heart failure is warranted.



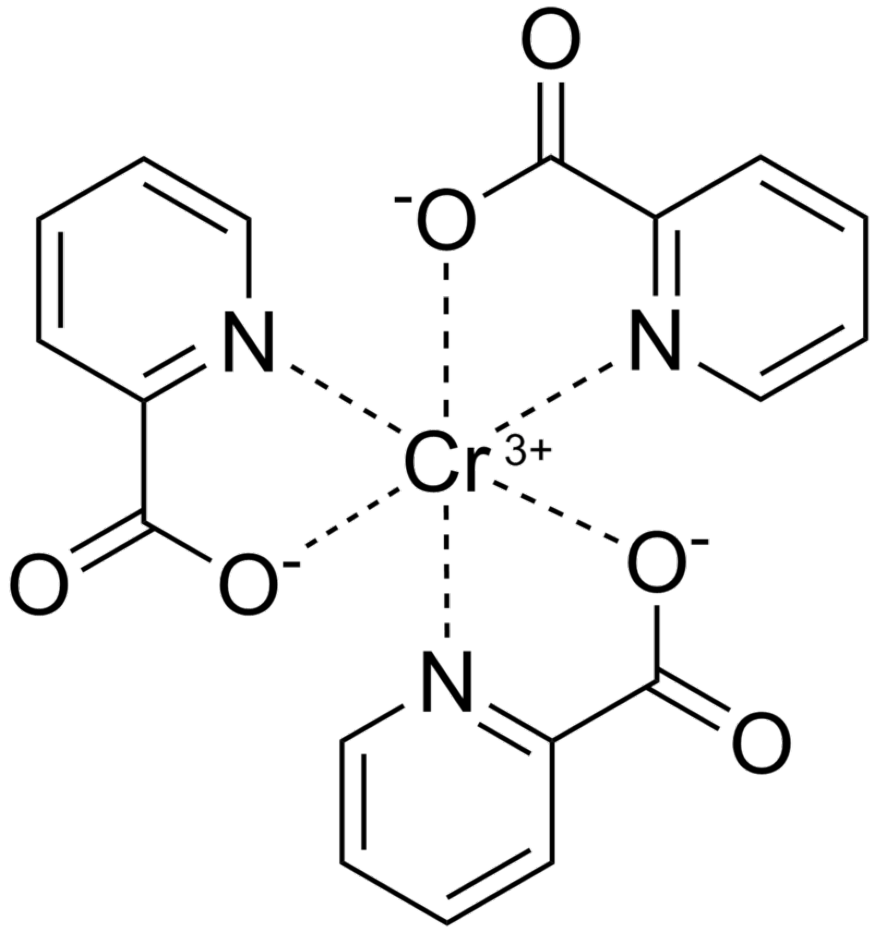
Advanced glycation end-products, cardiac function and heart failure in the general population: The Rotterdam Study Diabetologia (2023) 66:472–481


XLVII
Morus alba, Linn.



Hypoglycemic effects of Morus:
G6Pase, glucose-6-phosphatase;
GK, glucokinase; GLUT2, glucose transporter 2;
PEPCK, phosphoenolpyruvate carboxykinase;
PFK, phosphofructokinase;
PI3K/AKT, phosphatidylinositol-3-kinase/protein kinase B;
PK, pyruvate kinase; SGLT1, intestinal sodium glucose co-transporter 1

The role of selected nutraceuticals in managment of prediabetes and diabetes An update review of the literature Derosa G, D'Angelo A, Maffioli P.Phytother Res. 2022 Oct;36(10):3709-3765.



Il cromo (Cr) è un integratore comune utilizzato da molti pazienti con DMT2 allo scopo di migliorare regolazione del glucosio.
Un adeguato apporto di Cr per gli uomini e le donne sono 35 e 25 µg / giorno.
Il cloruro di cromo è la varietà trivalente presente in natura di cromo trovato in fonti alimentari comuni come: cereali integrali, broccoli, funghi e fagiolini.
Il Cr picolinato è il fratello sintetico del cloruro di Cr.
Cromo è un micronutriente essenziale legato alla regolazione di molti processi nel corpo umano tra cui l'omeostasi del glucosio attivando i recettori dell'insulina attraverso il oligopeptide cromudulina aumentando così la trasduzione e la sensibilità del segnale insulinico.

Effect of chromium supplementation on glycated hemoglobin and fasting plasma glucose in patients with diabetes mellitus Raynold V Yin, Olivia J Phung Nutr J 2015 Feb 13;14:14.

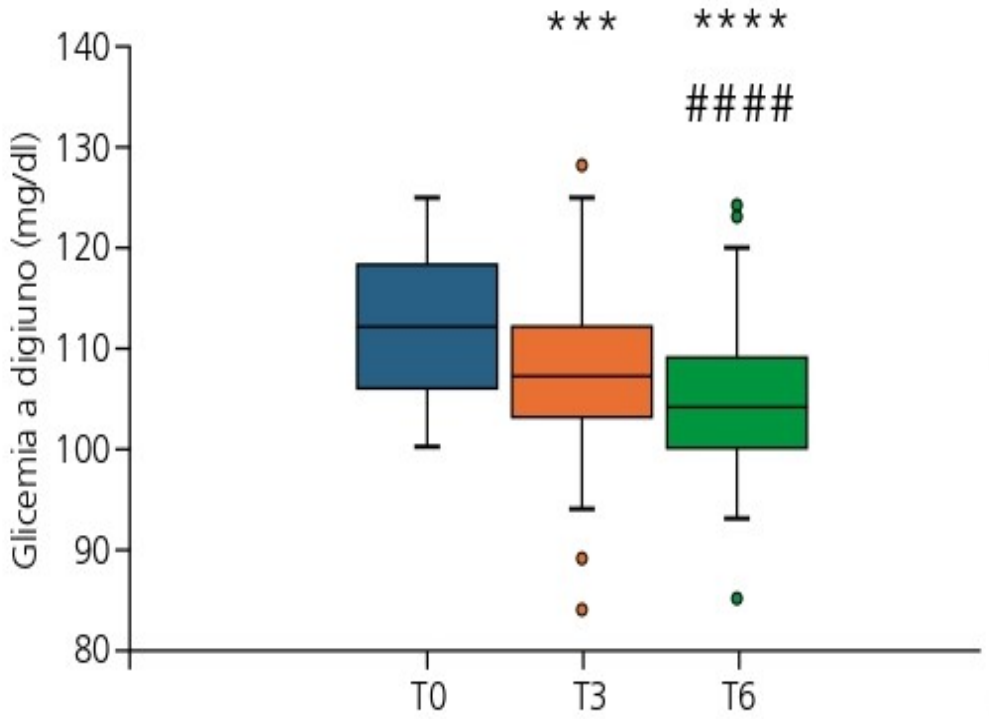
VARIAZIONE DEI PARAMETRI SELEZIONATI NELLO STUDIO AL BASELINE (T0) E DOPO TRE (T3) E SEI (T6) MESI DI TRATTAMENTO

	T0	T3	T6
Peso (Kg)	81,42 ± 18,58	78,90 ± 17,06	79,16 ± 16,80
BMI (Kg/m²)	29,52 ± 7,21	28,63 ± 6,64	28,71 ± 6,57
Circonferenza vita (cm)	101,12 ± 13,50	98,37 ± 12,64	97,54 ± 12,63
Glicemia a digiuno (mg/dL)	111,89 ± 6,79	107,38 ± 7,57***	104,22 ± 6,83****####
HbA1c (mmol/mol)	40,97 ± 3,35	40,40 ± 3,41	40,35 ± 3,91
Insulina (µU/ml)	11,55 ± 7,34	9,35 ± 4,08	9,34 ± 4,04
Colesterolemia totale (mg/dL)	197,94 ± 41,69	183,32 ± 36,78**	185,17 ± 35,78*
HDL-C (mg/dL)	50,01 ± 12,16	50,54 ± 12,70	50,78 ± 11,21
LDL-C (mg/dL)	125,45 ± 36,67	110,65 ± 38,90	112,99 ± 36,34
non HDL-C (mg/dL)	155,22 ± 38,44	136,91 ± 37,33	141,74 ± 30,88
Trigliceridi (mg/dL)	139,48 ± 65,31	119,62 ± 49,76	111,84 ± 41,72
ALT/GPT (U/L)	27,01 ± 18,52	25,99 ± 14,33	25,02 ± 12,02
AST/GOT (U/L)	25,14 ± 16,15	25,39 ± 12,48	24,13 ± 11,46
GGT (U/L)	31,57 ± 24,59	26,59 ± 16,17	25,82 ± 13,95
Piastrine (unità/µl)	258,55 ± 76,79	240,52 ± 78,91	243,65 ± 63,57
Hb (g/dL)	14,01 ± 1,11	14,00 ± 1,05	14,07 ± 1,04
Htc (%)	42,73 ± 4,09	42,34 ± 3,74	43,38 ± 4,29
PAS (mmHg)	129,30 ± 15,23	130,98 ± 13,58	129,41 ± 10,81
PAD (mmHg)	75,99 ± 9,36	76,81 ± 8,55	76,77 ± 7,06
Uricemia (mg/dL)	5,51 ± 1,34	5,65 ± 1,23	5,05 ± 1,16*##
Creatinina (mg/dL)	0,94 ± 0,22	0,92 ± 0,19	0,92 ± 0,17

Tutti i valori riportati in tabella sono espressi in media ± deviazione standard.
*p<0,05; **p<0,01; ***p<0,001; ****p<0,0001 (vs T0); ##p<0,01; ####p<0,0001 (vs T3).
Abbreviazioni: BMI, body mass index; HbA1c, emoglobina glicata A1c; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ALT, alanina aminotransferasi; GPT, glutammico piruvato transaminasi; AST, aspartato aminotransferasi; GOT, glutammico ossalacetico transaminasi; GGT, γ-glutamil transferasi; Hb, emoglobina; Htc, ematocrito; PAS, pressione arteriosa sistolica; PAD, pressione arteriosa diastolica.

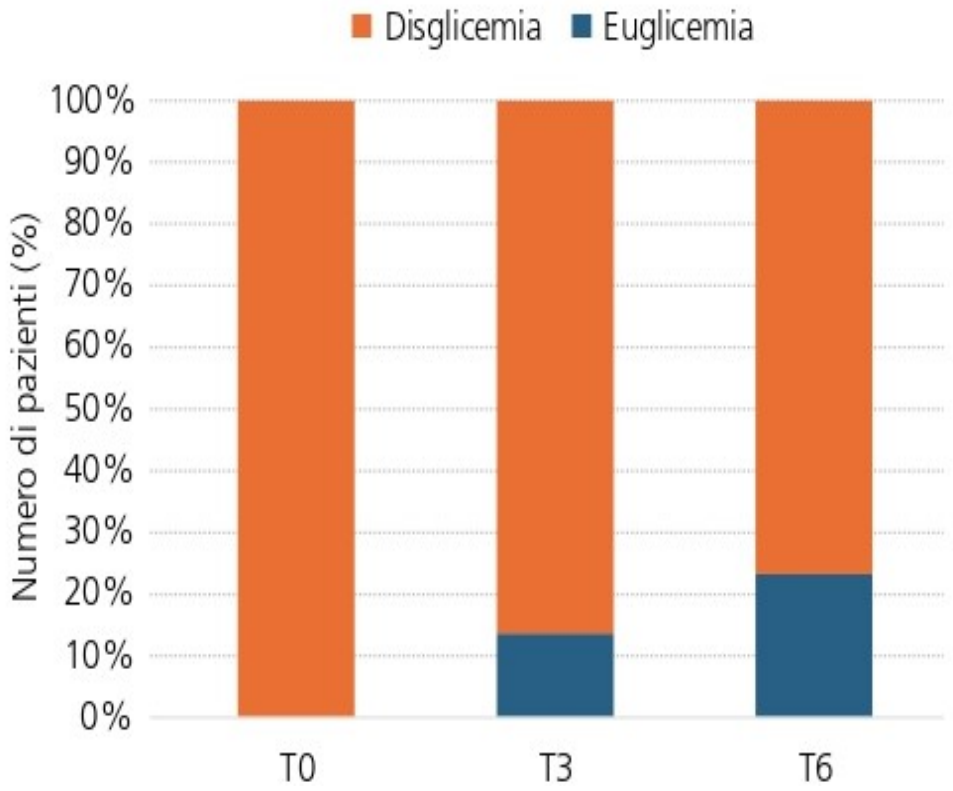
Prediabetes, from epidemiology to treatment:the role of nutraceuticals.
Pharmanutrion Anno IX, N. 2 - Giugno 2024

Concentrazione ematica della glicemia a digiuno (mg/dl) al basale e dopo 3 e 6 mesi di trattamento



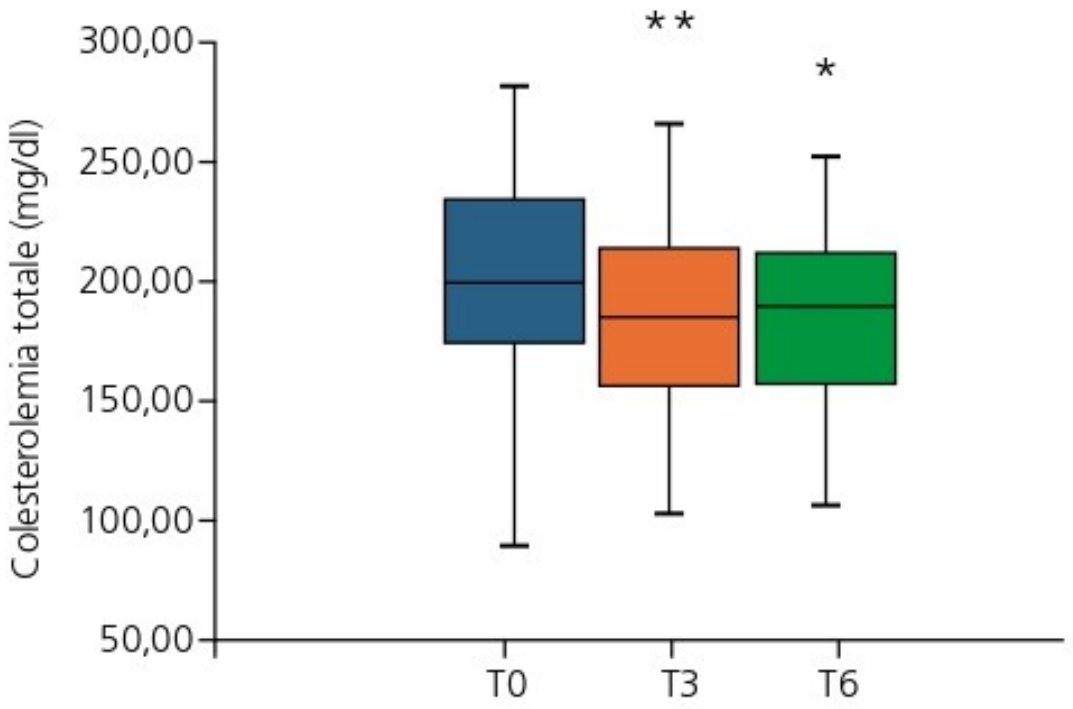
***p= 1,17x10^{-4}; ****p= 5,63x10^{-12} (vs T0); ####p= 1,86x10^{-3} (vs T3).

Stato glicemico al basale e dopo 3 e 6 mesi di trattamento



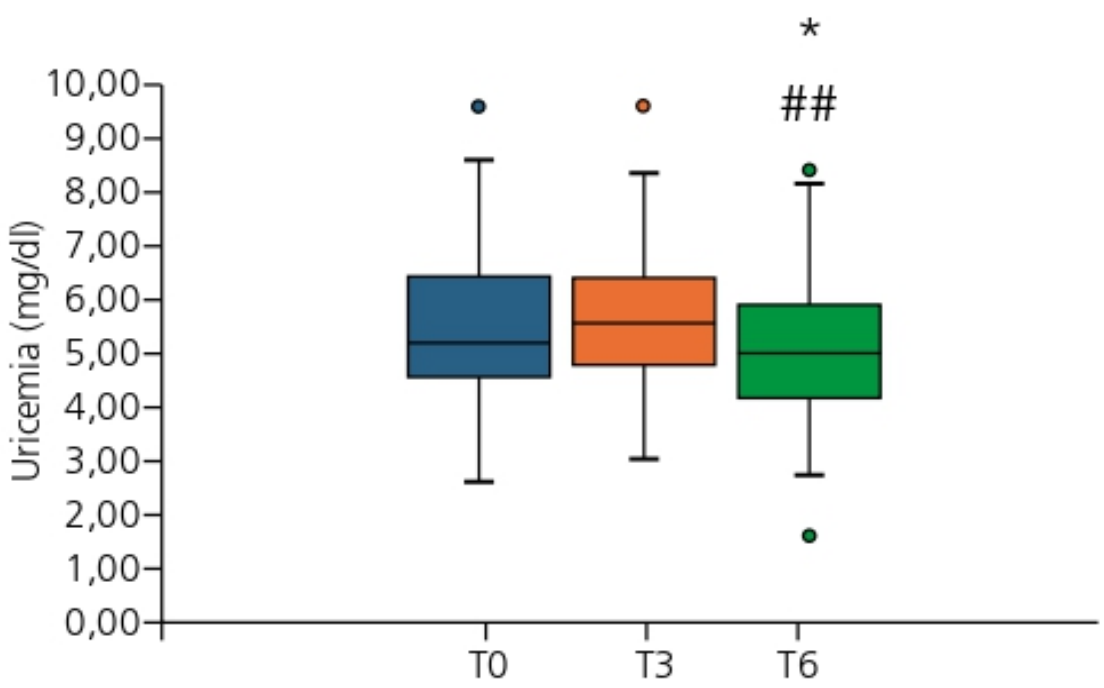
Prediabetes, from epidemiology to treatment:the role of nutraceuticals. Pharmanutrion Anno IX, N. 2 - Giugno 2024

Colesterolemia totale (mg/dl) al basale e dopo 3 e 6 mesi di trattamento



*p= 0,025; **p= 0,0065 (vs T0).

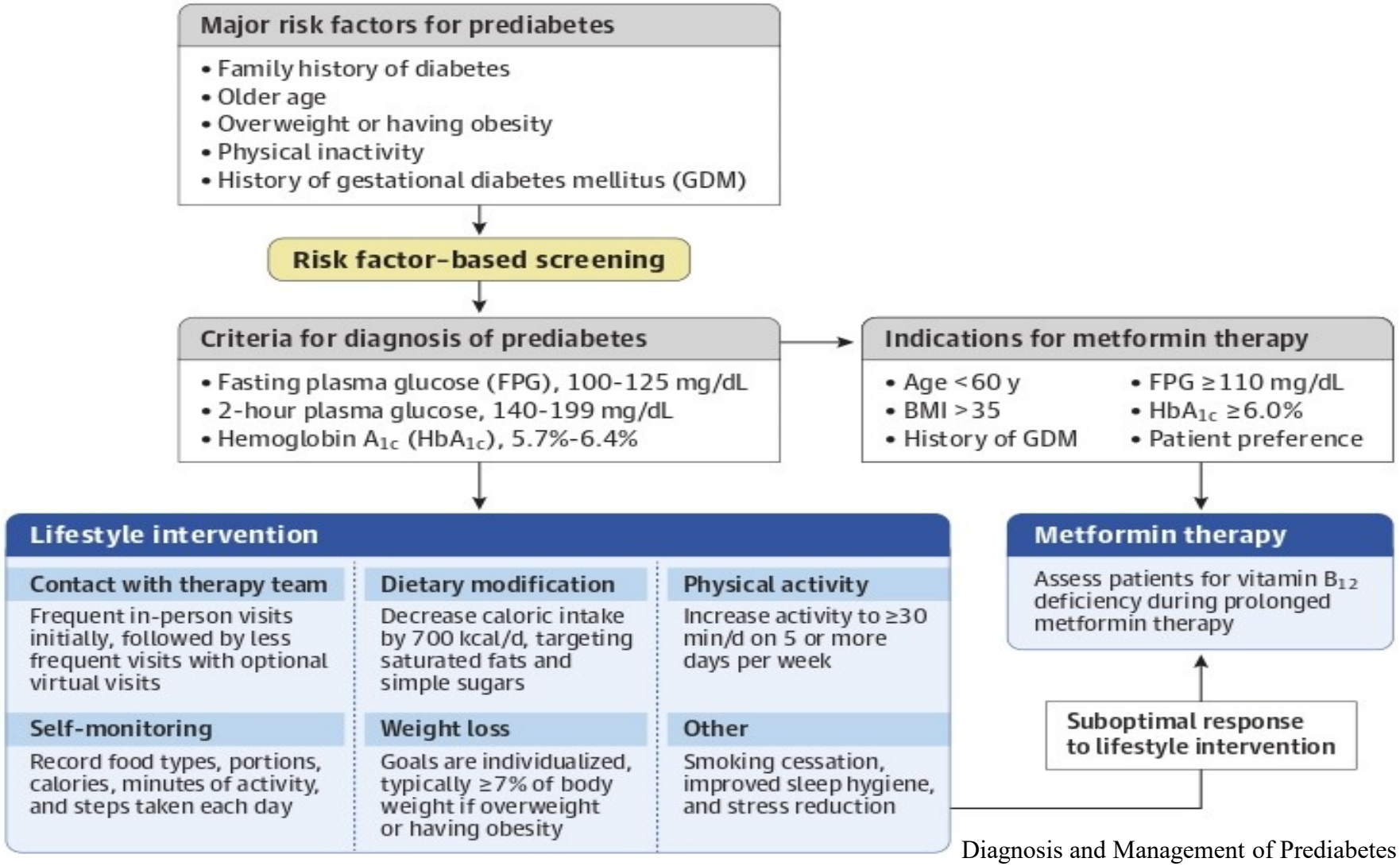
Uricemia (mg/dl) al basale e dopo 3 e 6 mesi di trattamento



*p= 0,040 (vs T0); ##p= 0,002 (vs T3).

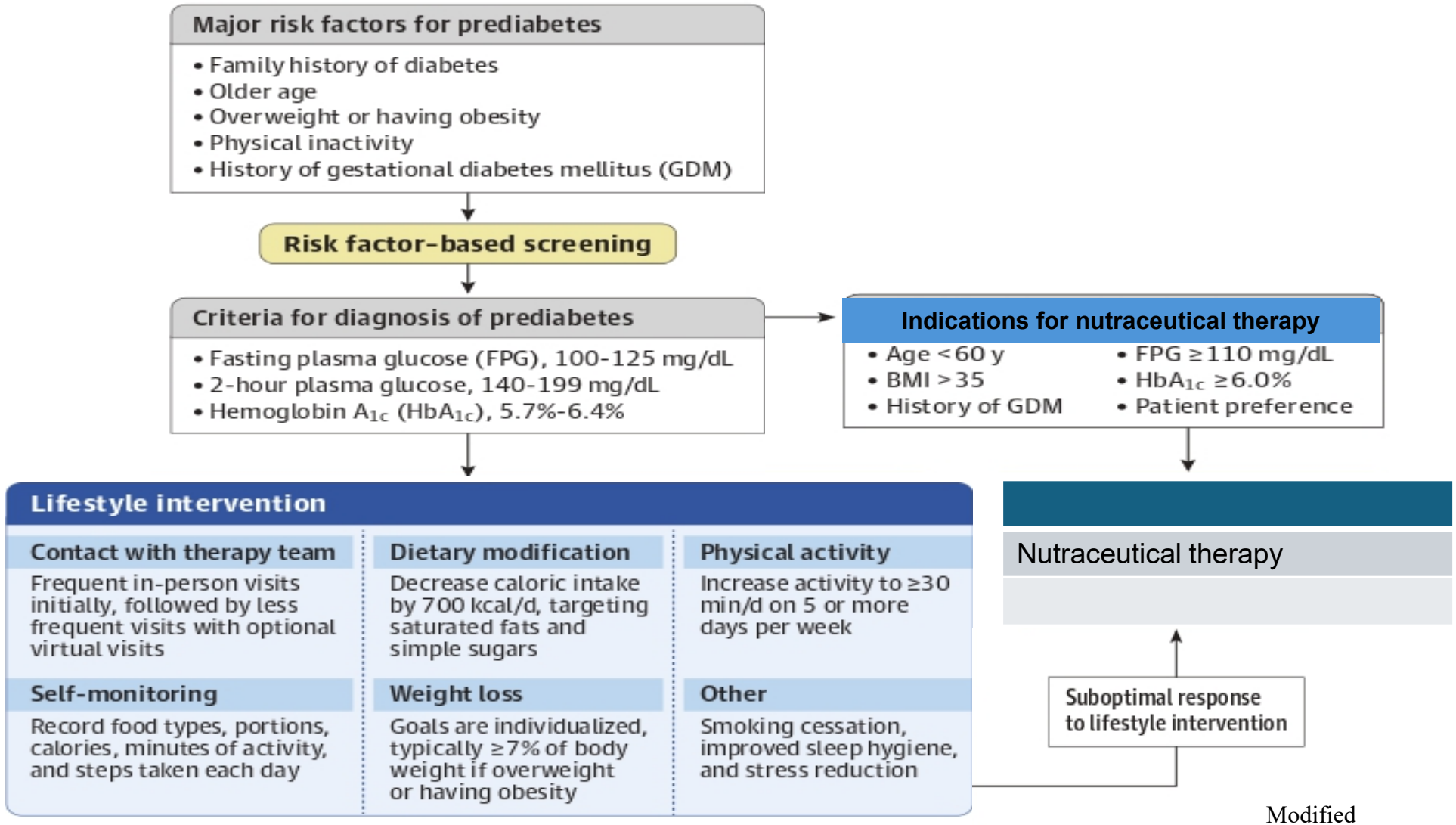
Prediabetes, from epidemiology to treatment:the role of nutraceuticals.
Pharmanutrion Anno IX, N. 2 - Giugno 2024

Approach to Screening, Diagnosis, and Management of Prediabetes



Diagnosis and Management of Prediabetes *JAMA*. 2023;329(14):1206-1216.

Proposal Approach to Screening, Diagnosis, and Management of Prediabetes



Modified

Diagnosis and Management of Prediabetes *JAMA*. 2023;329(14):1206-1216.

Theraphy of Dysglycemia

Prediabetes

Prediabetes Glucose Ranges

<126 / <7.0	<200 / <11.1	<6.5% / <48
IFG[a]	IGT	
FPG, mg/dL / mmol/L	2-h PG, mg/dL / mmol/L	A1C[b], % / mmol/mol
≥100 / ≥5.5	≥140 / ≥7.8	≥5.7% or 6.0% / ≥39 or 42[c]

Risk for CVD and CKD

T2D risk

- All with prediabetes are at risk of CKD, ASCVD, HF
- Risk of progression to T2D increases as prediabetes advances

Lifestyle Intervention for All ≥7% Weight Reduction for Most Persons

CVD Therapies
Start as needed/ indicated:
- Lipid-control agents[d]
- BP-reducing agents
- GLP-1 RA
- SGLT2i
- Pioglitazone[e]
- Other CVD therapies[f]

Weight Reduction Therapies
Start if obesity present and ≥7% weight reduction not achieved with lifestyle alone:
1. GLP-1 RA based[g]
2. Phentermine-topiramate
3. Endoscopic or surgical interventions

Antihyperglycemic Therapies
Start if hyperglycemia progresses:
1. GLP-1 RA based[g]
2. Pioglitazone
3. Metformin
4. SGLT2i
5. Acarbose

Initiate and intensify treatment based on risk of CVD and progression to T2D

Goals

Prevent progression of hyperglycemia and reduce CVD/CKD risk

Achieve normoglycemia with lifestyle and reduce CVD risk factors
- Even short-term regression to normal glucose tolerance with lifestyle may have durable benefits

Initiation of guideline-directed medical therapy for those with CVD, CKD, HF, or progression to T2D

A1C = hemoglobin A1C (HbA1c); ASCVD = atherosclerotic cardiovascular disease; BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; FPG = fasting plasma glucose; GIP = glucose-dependent insulinotropic polypeptide; GLP-1 RA = glucagon-like peptide 1 receptor agonist with proven benefit in indicated population; HF = heart failure; IFG = impaired fasting glucose; IGT = impaired glucose tolerance; MRA = mineralocorticoid receptor agonist; PG = plasma glucose; SGLT2i = sodium glucose cotransporter 2 inhibitor; T2D = type 2 diabetes; WHO = World Health Organization.

[a] WHO definition: 110 to <126 mg/dL / 6.1 to <7.0 mmol/L.
[b] Caution with A1C diagnosis of prediabetes in African American, Latinx, and other ethnic groups.
[c] US, 5.7% / ≥39 mmol/mol; Europe, 6.0% / ≥42 mmol/mol; CV risk elevated at ≥6.0% / ≥42 mmol/mol.
[d] CVD benefit from statins more important than potential A1C increases.
[e] Do not use in HF.
[f] Antiplatelet therapies, MRAs, etc.
[g] GLP-1 RA or GIP/GLP-1 RA.

DCRM 2.0: Multispecialty practice recommendations for the management of diabetes, cardiorenal, and metabolic diseases Metabolism. 2024 Jun 4:155931

Efficacy of Lifestyle Intervention for best horizon

Grazie per l'attenzione