XXII CONGRESSO NAZIONALE SOCIETÀ ITALIANA DI TABACCOLOGIA

Fumo di Tabacco e Sindrome Metabolica



Lecce, 15 ottobre 2026

Antonio Sacchetta

Conegliano

2026 AHA/ACC/ADA/ASN: Cardiovascular-Kidney-Metabolic (CKM) Syndrome

2025 ERS: Systemic Metabolic disorders

2005 IDF: Sindrome Metabolica

2003 AACE: Sindrome dell'insulino-resistenza

2001 NCEP-ATP III: Sindrome Metabolica

1998 WHO: Sindrome metabolica

1991 De Fronzo: Sindrome dell'insulino-resistenza

1988 Reaven: Sindrome X

1966 Avogaro, Crepaldi: Sindrome plurimetabolica

1956 J.Vague: Sindrome dell'obesità androide

70 anni di storia per la sindrome metabolica…..

Criterio	AHA (2023) 3 criteri
Obesità	circonferenza vita: uomini ≥ 102 cm donne ≥ 88 cm
Dislipidemia	Triglic.: ≥ 150 mg/dl. e/o Terapia oppure HDL- Col: uomini <40 mg/dl; donne <50 mg/dl e/o Terapia
Ipertensione	≥ 130/85 mmHg. e/o Terapia
Glicemia	≥ 100 mg/dl. e/o Terapia
Insulino - Resistenza	*Nessun marker*

Circulation. 2023 Nov 14. 148 (20):1636-1664

Cardiovascular-Kidney-Metabolic (CKM) Syndrome

"CKM syndrome is a systemic disorder characterized by pathophysiological interactions among metabolic risk factors, CKD, and the cardiovascular system, leading to multiorgan dysfunction and a high rate of adverse cardiovascular outcomes.
CKM syndrome includes both individuals at risk for CVD due to the presence of metabolic risk factors, CKD, or both, and individuals with existing CKD or CVD that is potentially related to or complicates metabolic risk factors.
The increased likelihood of CKM syndrome and its adverse outcomes is further influenced by ***unfavorable conditions for lifestyle and self-care*** resulting from policies, economics, and the environment"

Circulation Volume 154, Issue 4, 28 July 2026; Pages e50-e158

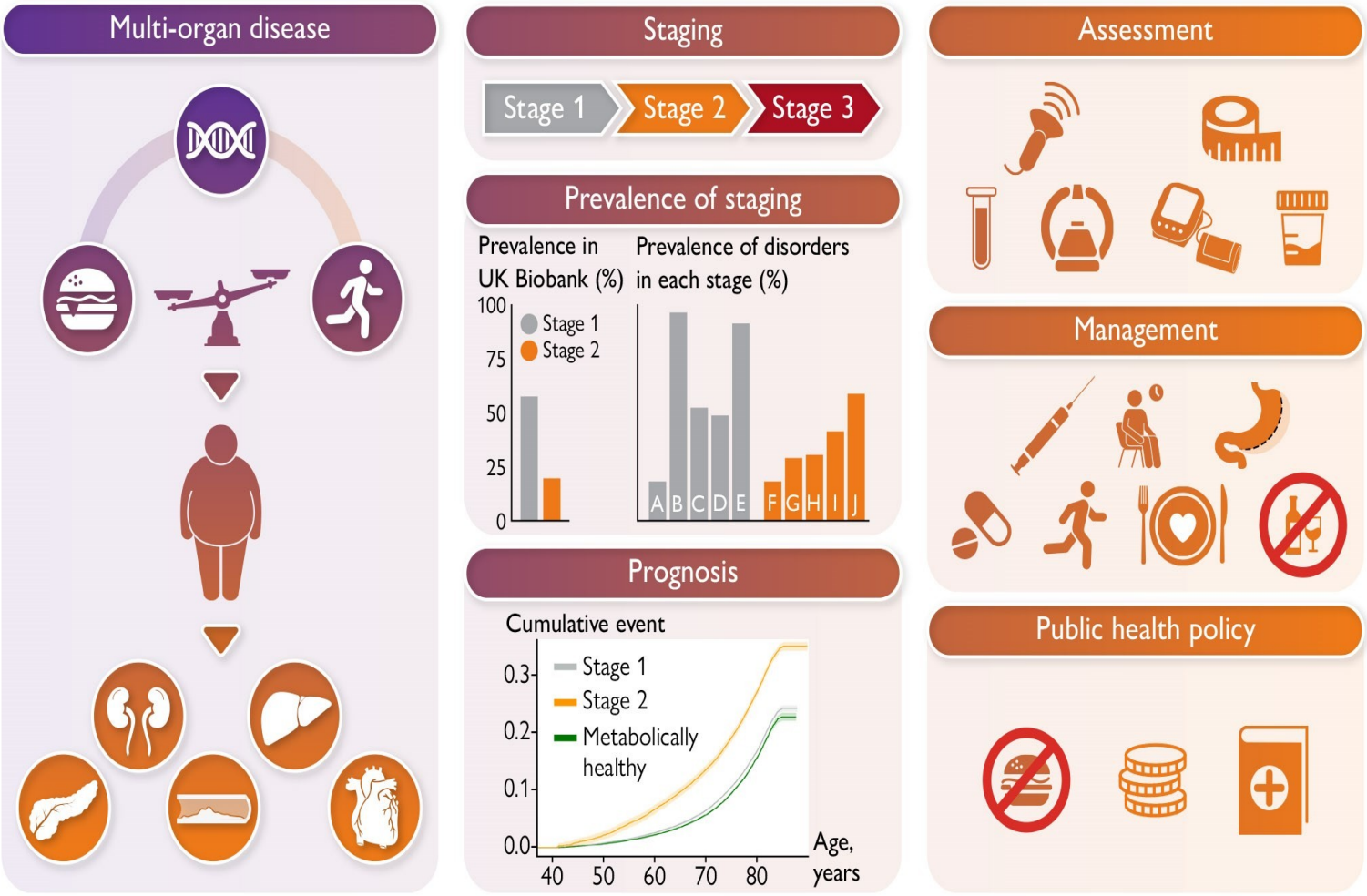
Systematic Metabolic Disorder (SMD)

"a cluster of metabolic abnormalities affecting multiple organs, leading to increased morbidity and mortality from both cardiovascular and non-cardiovascular causes"

SMD's definition is broader than CKM syndrome and includes liver diseases affected by metabolic risk factors.

Eur Heart J.2025 Oct 7. 46 (38):3685-3713.

EAS consensus statement on systemic metabolic disorders



A: prediabetes; B: overweight; C: liver steatosis; D: hypertension; E: dyslipidaemia; F: type 2 diabetes; G: asymptomatic diastolic dysfunction; H: metabolic-associated steatohepatitis; I: chronic kidney disease; J: subclinical atherosclerosis

Eur Heart J, Volume 46, Issue 38, 7 October 2025, Pages 3685–3713, https://doi.org/10.1093/eurheartj/ehaf314

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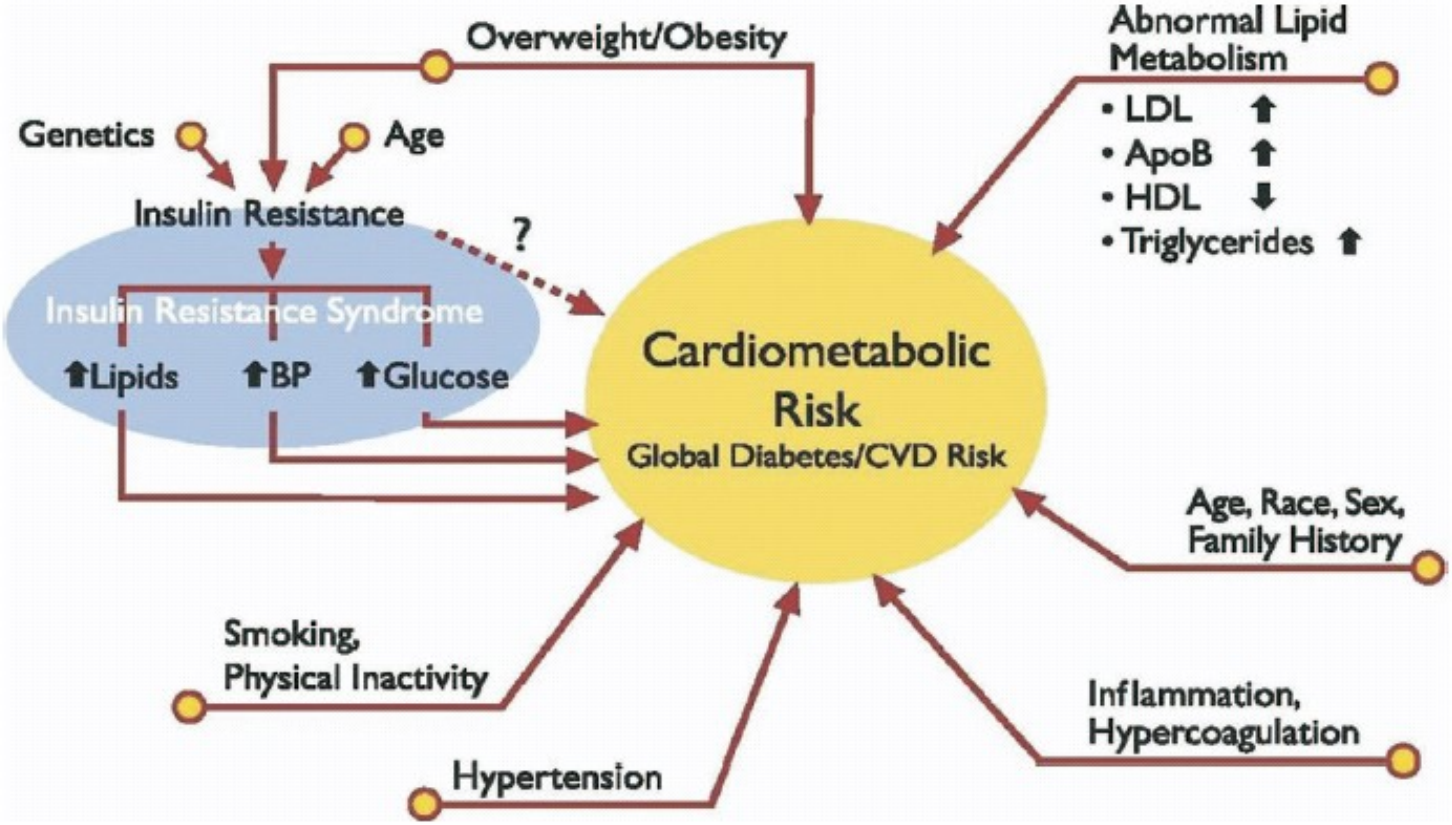


Figure 1. Factors Contributing to Cardiometabolic Risk

La denominazione

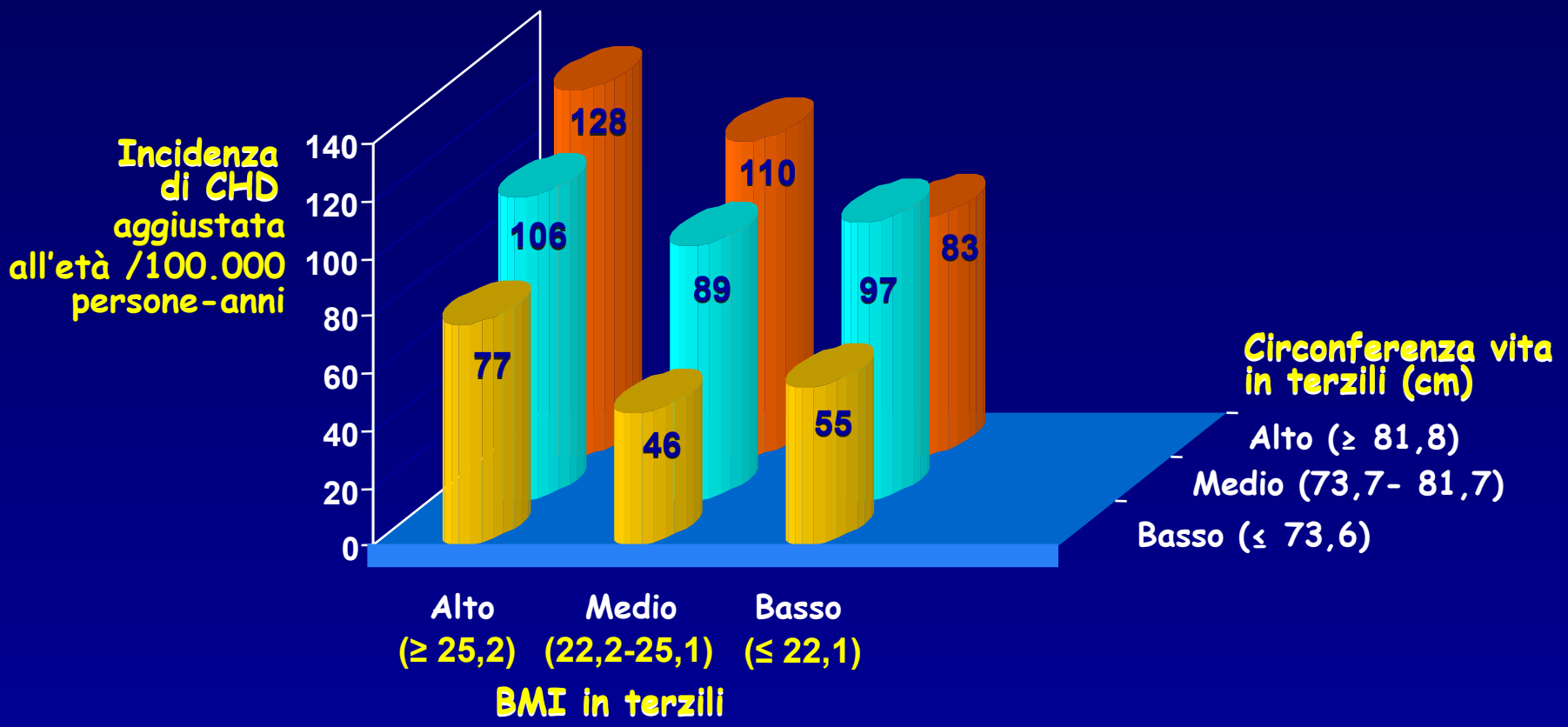
Sindrome da Insulino Resistenza (IRS)

Mette a fuoco il ruolo centrale dell'Insulino Resistenza con iperinsulinemia compensatoria nella patogenesi dell'associato insieme ("cluster") di alterazioni.

E' più utilizzata la denominazione

Sindrome Metabolica

L'obesità addominale aumenta il rischio di CHD indipendentemente dal BMI



Rexrode KM et al. JAMA 1998; 280: 1843-1848

Relationship between smoking and metabolic syndrome

- Composite "healthy lifestyle" scores (typically including nonsmoking, physical activity, and diet) are associated with a 43% lower risk of metabolic syndrome comparing the healthiest vs least-healthy groups, underscoring smoking's role as part of an adverse lifestyle cluster that promotes MetS.
- Smoking is a major modifiable risk factor for hypertension, dyslipidemia, and diabetes, all of which are core MetS components and key drivers of coronary risk.
- Cigarette smoking and Nicotine Addiction amplify the development, expression, and adverse outcomes of metabolic syndrome through shared inflammatory and cardiometabolic pathways

Public Health Pract (Oxf). 2025 Jan 18;9:100585.
International journal of obesity (2005). Meta-Analysis, Systematic Review.

Tobacco drives systemic inflammation, immune dysfunction, oxidative injury

- Tobacco smoke causes immune and inflammatory activation with increased proinflammatory cytokines (IL-1β, IL-6, TNF-α receptor) and impaired NK cytotoxic activity, reflecting heightened inflammation but reduced host defense.
- Smoking also promotes oxidative DNA damage and endothelial dysfunction across vascular beds, processes that dovetail with MetS-related microvascular and atherogenic changes.
- Collectively, these patterns support smoking as an upstream amplifier of the adipose-dysfunction / insulin-resistance axis that underpins metabolic syndrome and CKM syndrome.

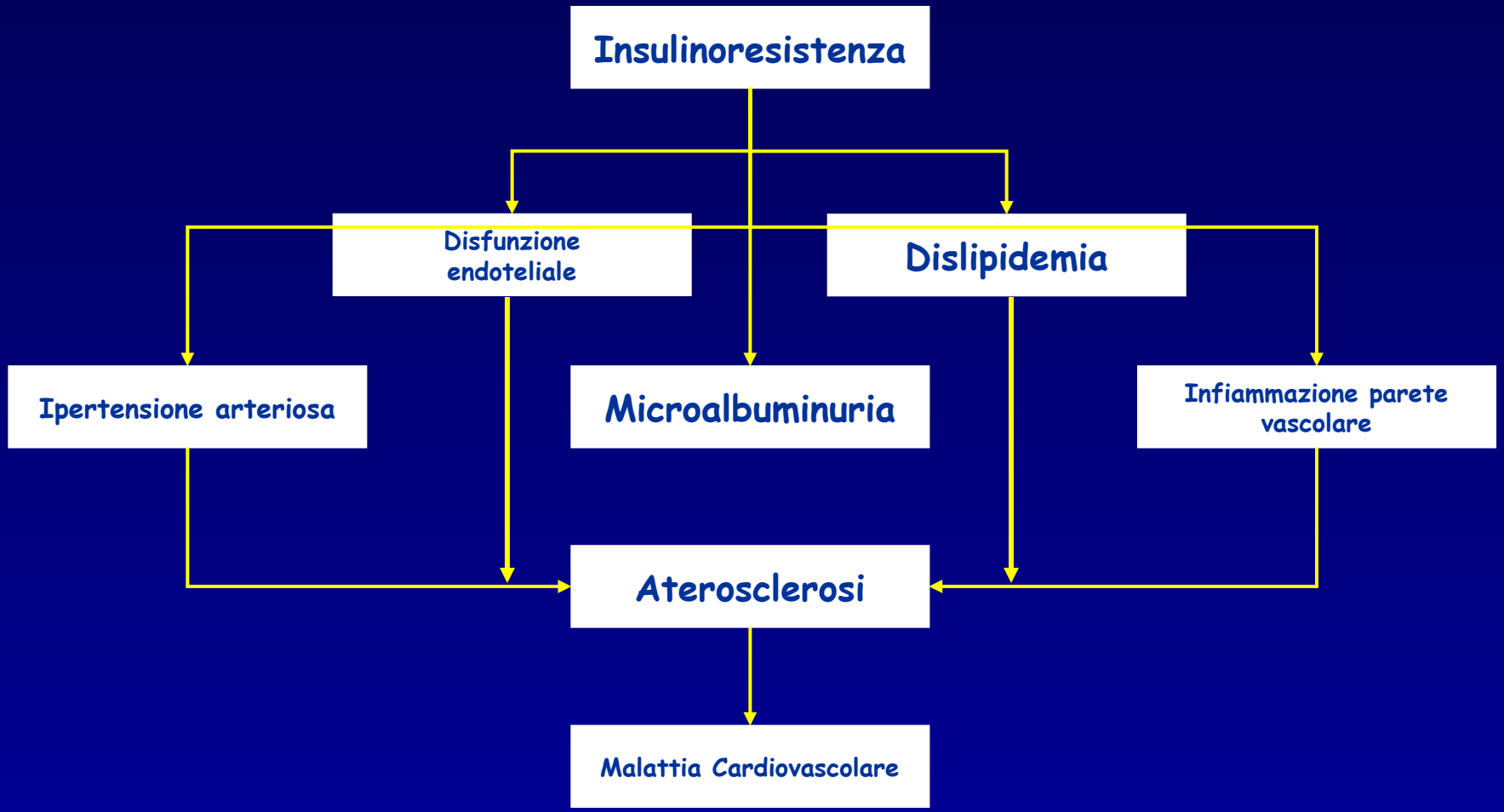
Yu L *et al. Molecular Biomedicine (2026) 7:12*

Active Smoking and Risk of Metabolic Syndrome: A Meta-Analysis of Prospective Studies

Findings of the present meta-analysis show a clear link between smoking and risk of metabolic syndrome. Based on data from 13 prospective cohort studies (56,691 participants; 8,688 incident cases of metabolic syndrome), *active smokers have a 26% increased risk of metabolic syndrome* compared with nonsmoking individuals. The combined estimate of our primary analysis was strong across multiple sensitivity analyses and without significant publication bias.

Kan Sun et al: PLOS ONE 1 October 2012 | Volume 7 | Issue 10 | e47791,

L' insulinoresistenza è legata a una serie di fattori di rischio cardiovascolare



Misura dell'insulinoresistenza

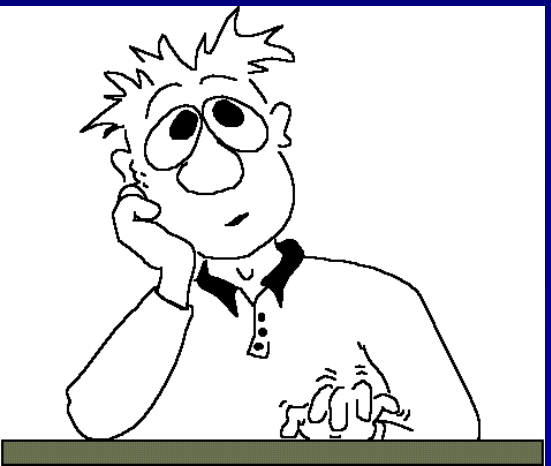
- La tecnica del clamp iperinsulinemico euglicemico, considerato il *'gold standard'*, misura l'insulino-resistenza in condizioni di 'iperinsulinemia'[1]
- L'HOMA stima l'insulinoresistenza nella condizione a digiuno da un singolo campione e correla con altri tests di insulinoresistenza compreso il clamp[2,3]

[1]DeFronzo RA, *et al. Am J Physiol* 1979; 237:E214–E223.
[2]Matthews DR, *et al. Diabetologia* 1985; 28:412–419.
[3]Bonora E, *et al. Diabetes Care* 2000; 23:57–63.

Homeostasis Model Assessment

- A digiuno:

$$\frac{\text{Insulinemia mU/ml} \times \text{Glicemia mmol/L}}{22.5}$$



Triglyceride-Glucose Index As A Biomarker Of Insulin Resistance, Diabetes Mellitus, Metabolic Syndrome, And Cardiovascular Disease: A Review

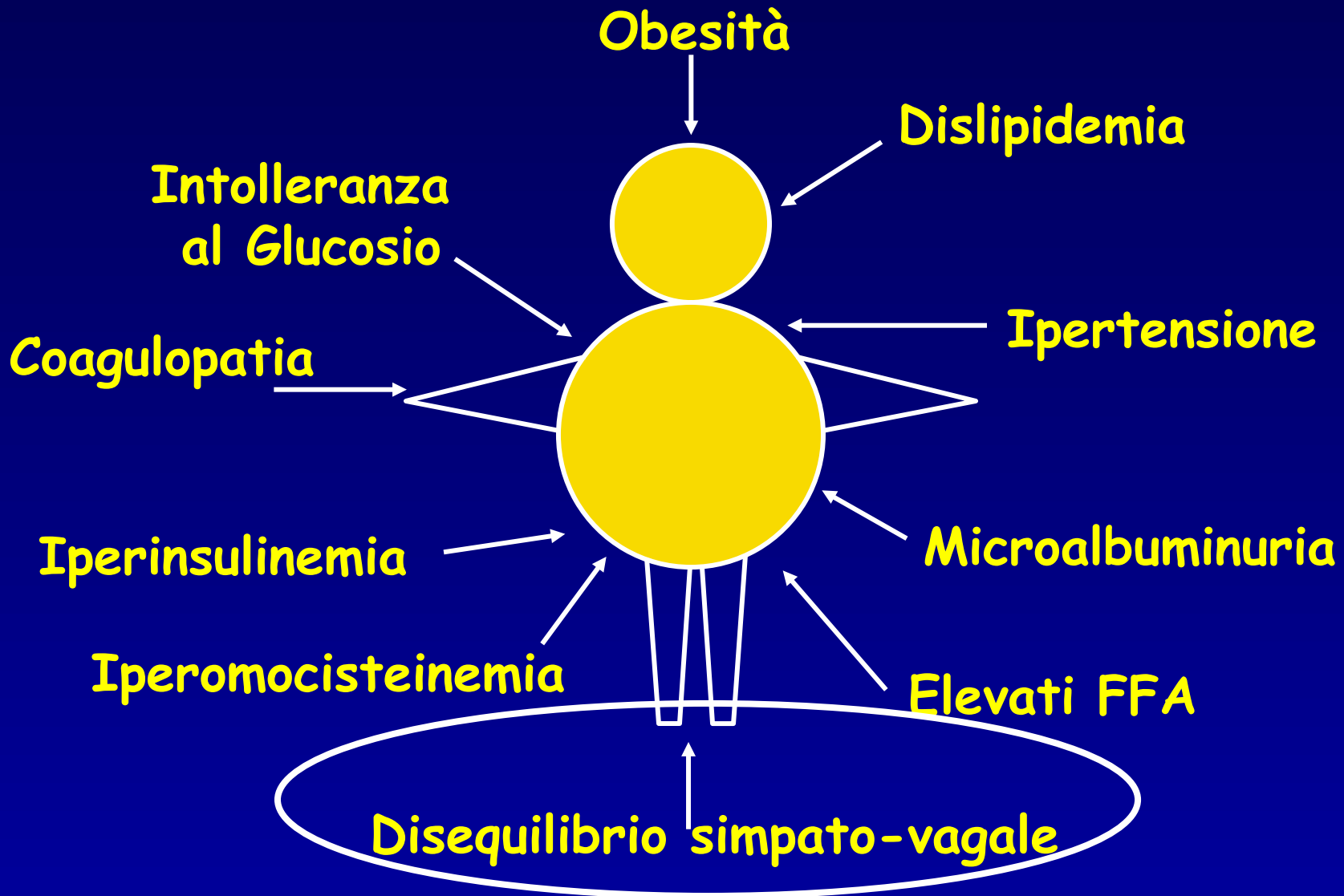
TyG index =
Ln (fasting triglycerides [mg/dL] x fasting glucose [mg/dL])/2
or
TyG index =
Ln (fasting triglycerides [mmol/L] x 88.57 x f. glucose [mmol/L] x 18)/2)

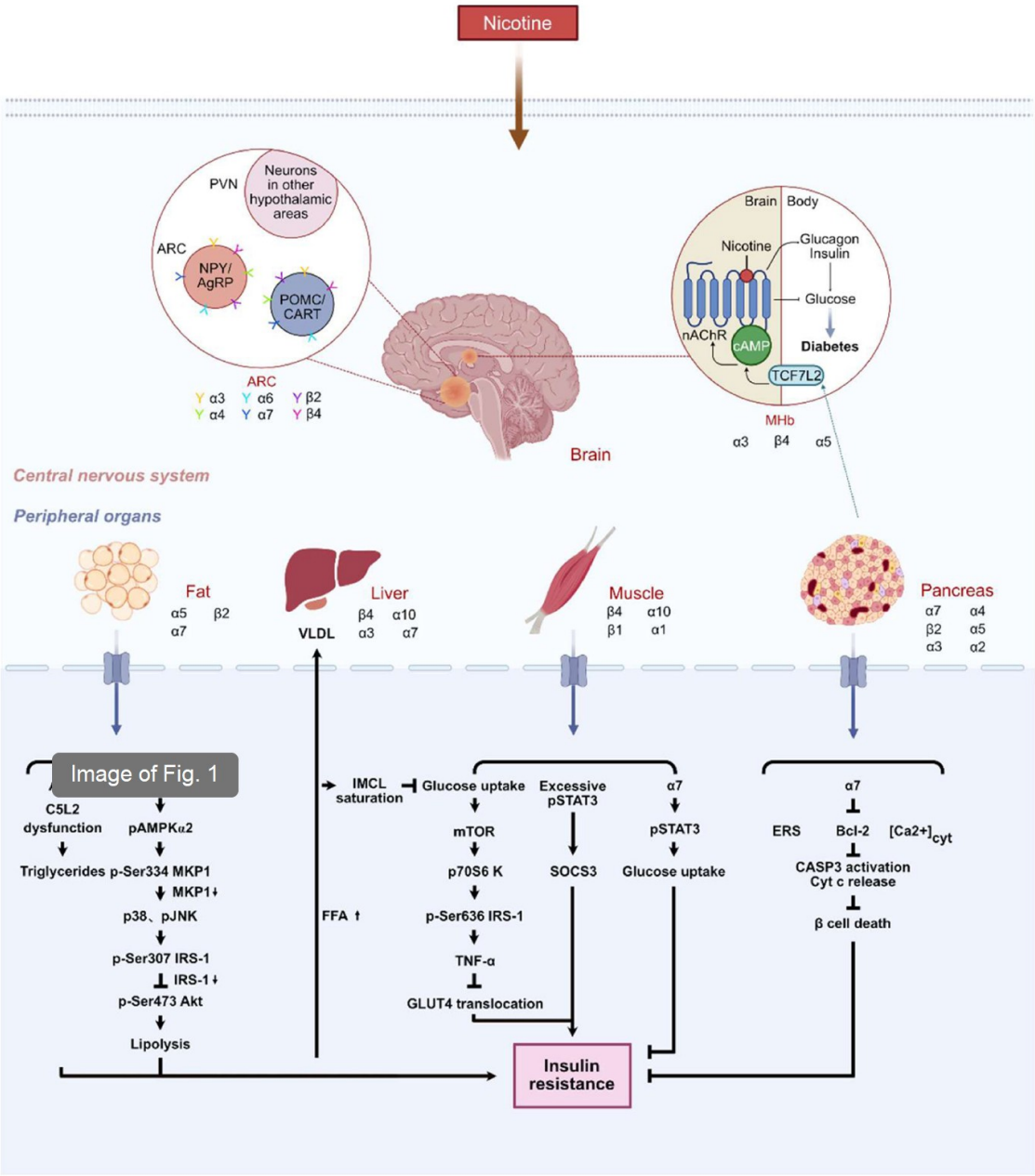
	Cutoff point	Positive likelihood ratio	Negative likelihood ratio	Sensitivity, %	Specificity, %
HOMA-IR	3.23	1.83	0.58	78	70.1
TyG	4.72	2.24	0.44	87	88.2

HOMA-IR, homeostasis model assessment; TyG, triglyceride-glucose index. Statistical differences between groups ($p < 0.05$).

Kurniawan LB eJIFCC 2024 Vol35No1pp44-51
Primo D et al. Ann Nutr Metab 2023;79(2):238-245.

Insulinoresistenza: unico paradigma per il paziente a rischio di DM tipo 2





Central and peripheral actions of nicotine that influence blood glucose homeostasis and the development of diabetes: Pharmacological Research 194 (2023) 1068601043-6618

Le Influenze adrenergiche riducono la sensibilità insulinica

- Vasocostrizione arteriolare
- Lipolisi aumentata (aumento FFA)
- Spillover di adrenalina aumentato dall'Insulina
- Drive del simpatico aumentato nell'obesità viscerale
- Gli obesi hanno un RAAS attivato

J Hypertension, 25: 909-920, 2007

Adiposità Normale

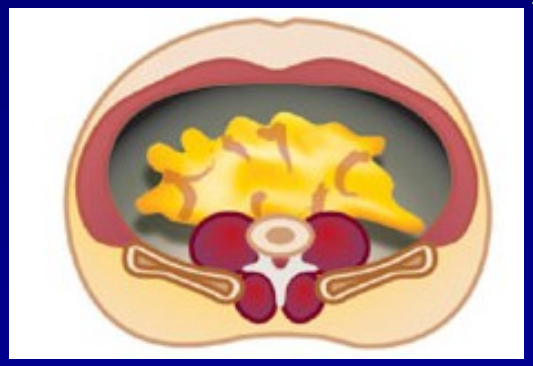


Cibo ad alta Energia
(el. Contenuto di grassi e zucchero)

Mancanza di attività fisica/Esercizio

Bilancio Energetico Positivo

- Fumo
- Genotipo "Sfavorevole"
- Milieu Endocrino
- Anomala Risposta allo stress



Obesità Sottocutanea
Tessuto Adiposo "Sano"



Obesità Viscerale
Tessuto Adiposo "Disfunzionale"

Després a. Lemieux, Nature 2006; 444:881-887

Obesità Viscerale = Tessuto Adiposo Disfunzionale



⇧ Rilascio di citochine

⇧ IL-6
⇧ TNF-α
⇧ AT-II

⇩ Adiponectina
⇧ PAI-1

Profilo Metabolico Alterato

- Milieu Insulinoresistente
- Stato Pro-infiammatorio
- Disfunzione Endoteliale
- Stato Pro-trombotico
- Stato Pro-ipertensivo

Després et al. Arterioscl Thromb Vasc Biol 2008 (pubblicato online il 20 Marzo)

Obesità Viscerale = Tessuto Adiposo Disfunzionale

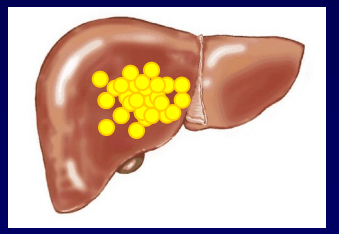


Mancanza o disfunzione del Grasso sottocutaneo

Alterata clearance e

Deposito dei TG nel TA sottocutaneo

Deposizione Ectopica del grasso





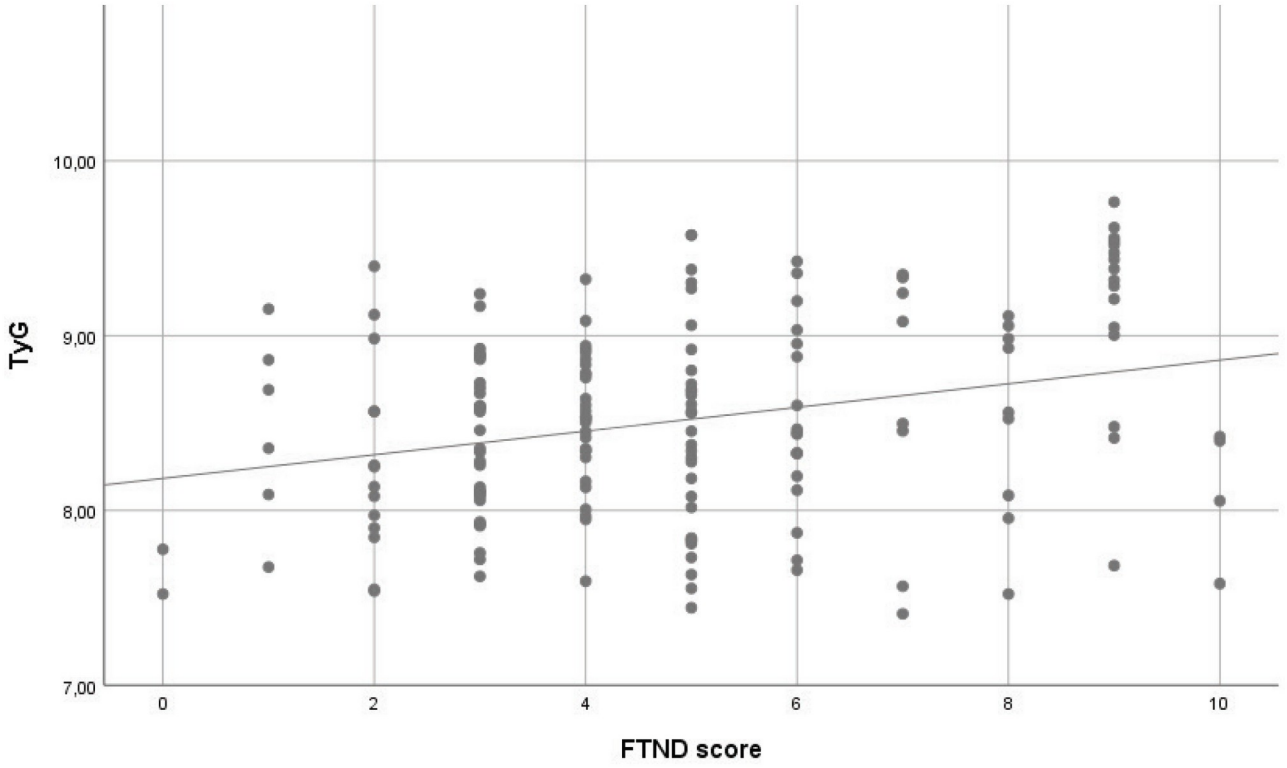




Després et al. Arterioscl Thromb Vasc Biol 2008 (pubblicato online il 20 Marzo)

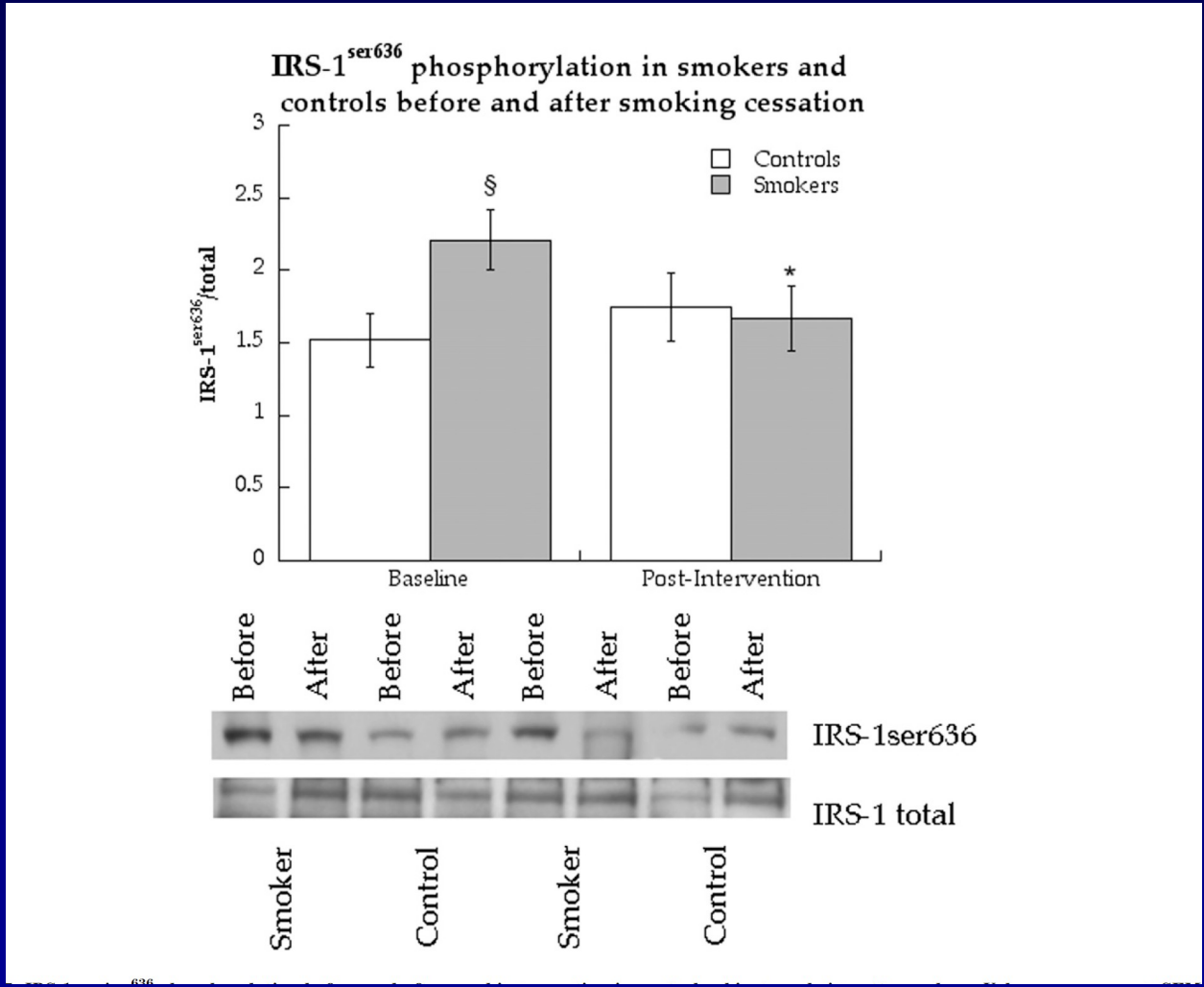
Evaluation of the relationship between insulin resistance and nicotine dependence: A cross-sectional study

Figure 3. Scatter plot illustrating the association between FTND score and TyG index among adult exclusive combustible cigarette smokers in a cross-sectional study conducted at Trabzon Kanuni Training and Research Hospital, Türkiye, 2025 (N=169)



Saruhan S. et al. Tob. Induc. Dis. 2026;24(February):28

Novel and Reversible Mechanisms of Smoking-Induced Insulin Resistance in Humans



Bergman B.C. ed al. DIABETES, vol. 61, December 2012

Obesità ed Infiammazione: TNFa

- Iperespresso nell'obesità
- Riduce l'espressione di PPAR-g^ e di SREBPt
- Fosforilazione in tirosina di IRS-1*, e quindi del recettore dell'Insulina
- Mediatore di insulino-resistenza nella maggior parte dei modelli animali

➢ ***L'Obesità è uno stato infiammatorio!***

^Peroxisome Proliferator Activated Receptor; tSterol Regulatory Element Binding Protein; *Insulin Receptor Substrate 1

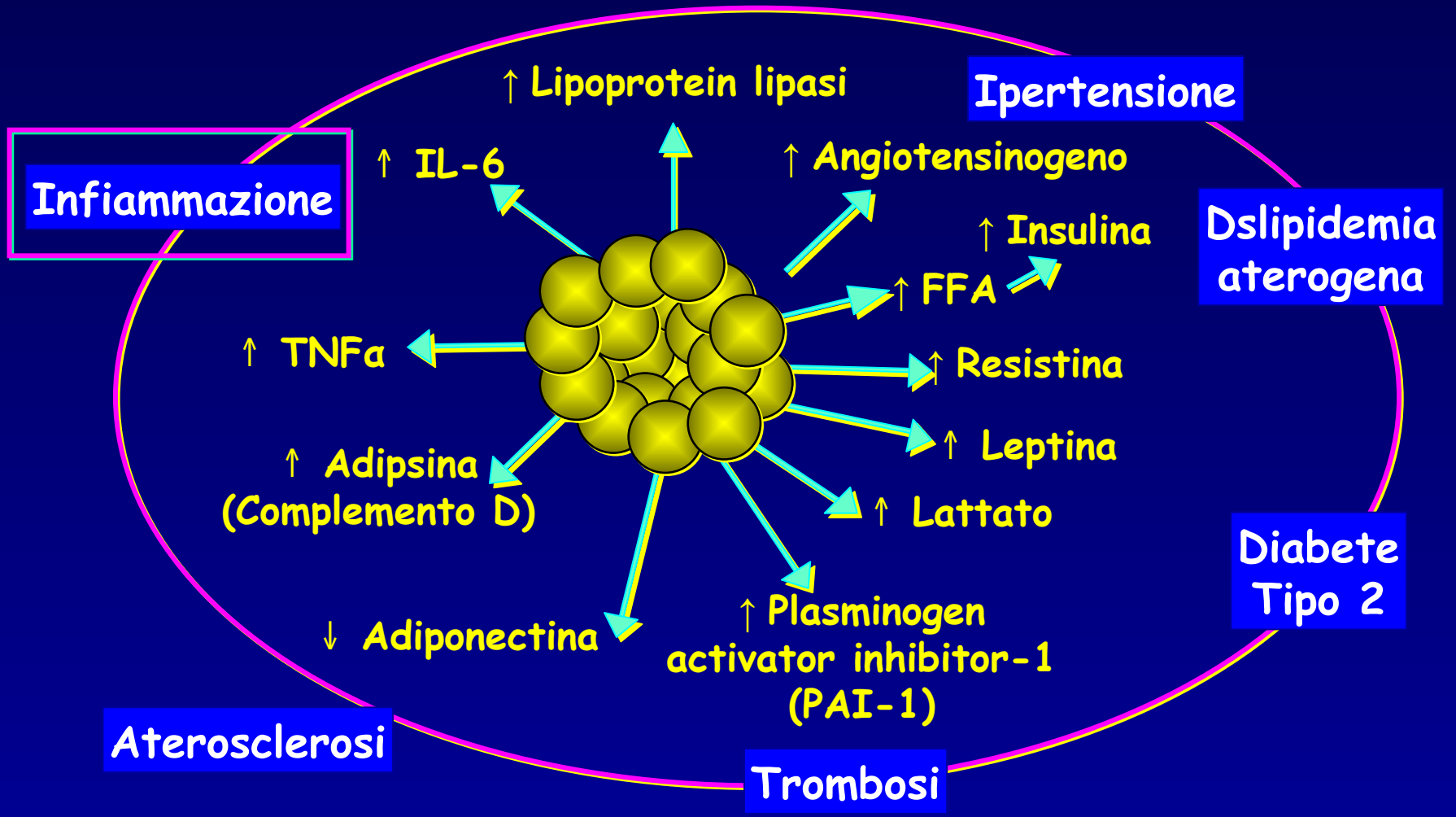
Activation of PPARg Attenuates the Expression of Physical and Affective Nicotine Withdrawal Symptoms through Mechanisms Involving Amygdala and Hippocampus Neurotransmission

- **Smoking cessation leads the occurrence of physical and affective withdrawal symptoms representing a major burden to quit tobacco use.**

- **Activation of PPAR prevents the expression of both somatic and affective signs of nicotine withdrawal.**
- **At molecular levels results PPAR expression increases in GABAergic cells in the hippocampus and in GABA- and glutamate-positive cells in the basolateral amygdala.**
- **Hippocampal microinjections of pioglitazone reduce the insurgence of the physical withdrawal signs, whereas anxiety linked to protracted abstinence is attenuated by pioglitazone injected into the amygdala.**
- **Results in male Wistar rats and in male mice demonstrate the implication of neuronal PPAR in nicotine withdrawal and suggest that PPAR agonism may represent a promising treatment to aid smoking cessations**

Domi E et al: Journal of Neuroscience, December 4, 2019 • 39(49):9864 –9875

Effetti cardiometabolici avversi dei prodotti degli adipociti



Lyon 2003; Trayhurn et al 2004; Eckel et al 2005

Effects of smoking cessation on serum leptin and adiponectin levels

Table 1 Samples' characteristics at baseline and 3 months and 6 months after smoking cessation

Participants' characteristics	Baseline	3 months	6 months
Age (years)[a]	56.1 ± 9.4	–	–
Female sex[a]	16 (45.7)	–	–
BMI (kg/m^2)	27.1 ± 3.7	28.6 ± 3.6*	29.2 ± 3.5*,**
Smoking (pack-years)[a]	54.3 ± 26.7	–	–
Exhaled CO	14.7 ± 9.4	4.3 ± 2.5*	4.0 ± 2.7*
Serum leptin (ng/ml)	6.9 ± 3.1	10.5 ± 6.8*	6.5 ± 5.2**
Serum adiponectin (μg/ml)	9.5 ± 2.8	11.8 ± 5.5*	9.6 ± 5.2
CRP (mg/dl)	0.8 ± 1.1	0.3 ± 0.3*	0.3 ± 0.3*

Data are expressed as number of subjects (%) or mean value ± standard deviation. Differences not marked with one of the above symbols are not significant

*$p < 0.05$ vs. baseline

**$p < 0.05$ vs. 3 months

[a]Assessment applicable only at baseline

Kryfti et al. Tobacco Induced Diseases (2015) 13:30
DOI 10.1186/s12971-015-0054-7

Effects of smoking cessation on serum leptin and adiponectin levels

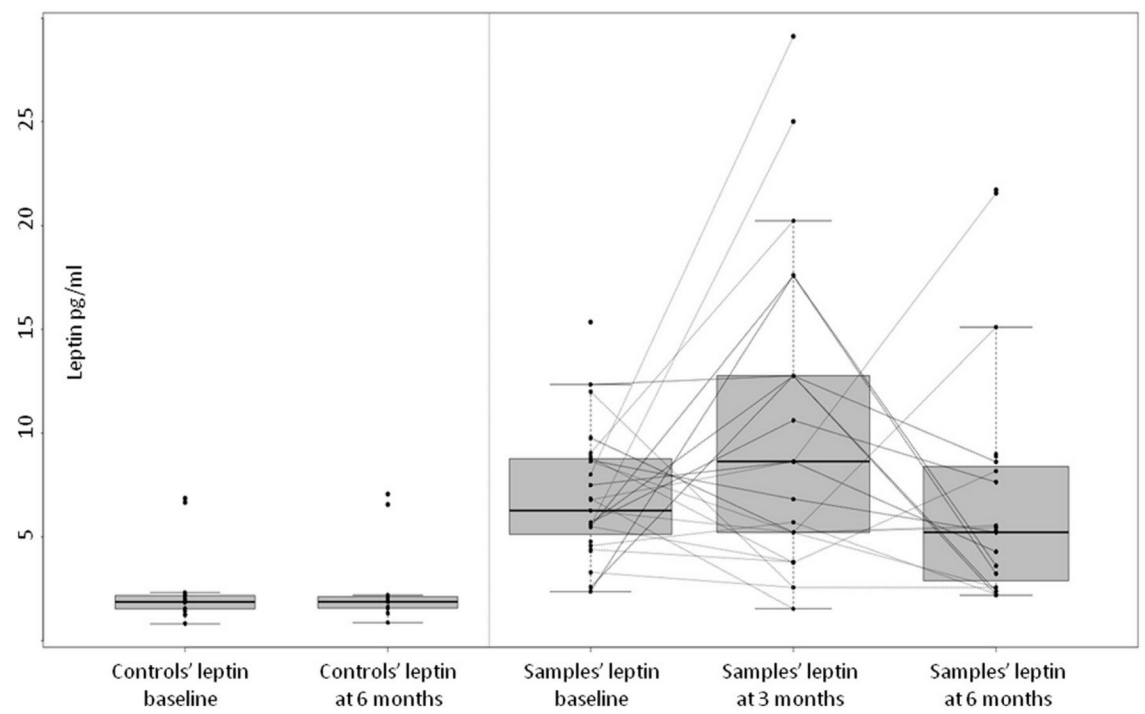
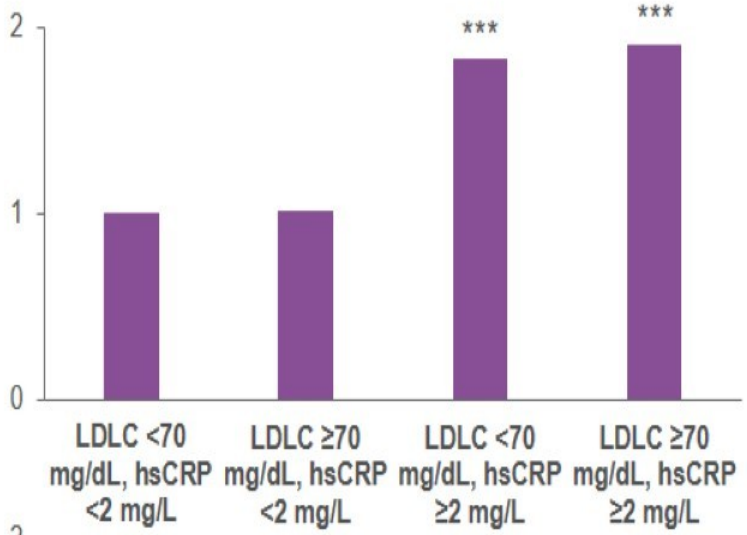


Fig. 1 Scatterplot of samples and controls' leptin at baseline and after smoking cessation

Kryfti et al. Tobacco Induced Diseases (2015) 13:30
DOI 10.1186/s12971-015-0054-7

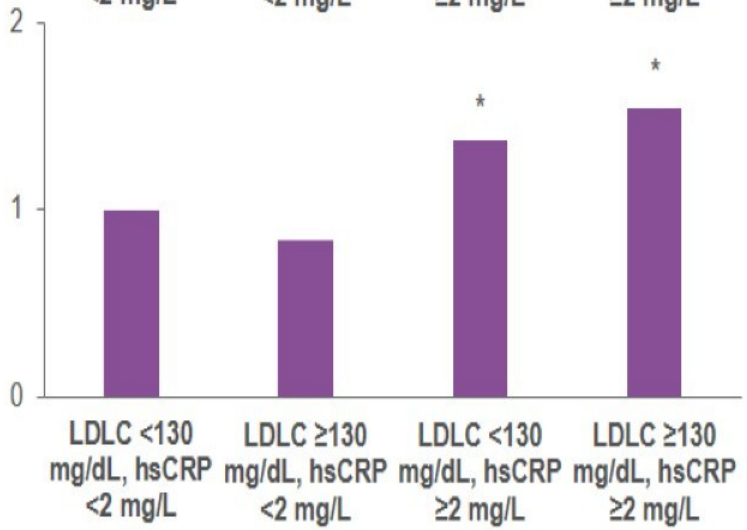
Inflammation Measured by hsCRP Is a Major Risk Factor for CV Death (cont)

Patients treated with statins[1]
N = 31,245



Highest Risk
hsCRP ≥ 2 mg/L with
LDL-C ≥ or < 70 mg/dL

Patients who cannot tolerate statins[2]
N = 13,970



Highest Risk
hsCRP ≥ 2 mg/L with
LDL-C ≥ or < 130 mg/dL

*$P < .05$; ***$P < .0001$.

1. Ridker PM, et al; PROMINENT, REDUCE-IT, and STRENGTH Investigators. Lancet. 2023;401:1293-1301; 2. Ridker PM, et al; CLEAR Outcomes Investigators. Circulation. 2024;149:28-35.

Evaluation of hSCRP and microalbumin levels in smokers

Table 2
Shows the comparison of hsCRP and microalbumin levels in smokers and non-smokers

	Smokers	Non-smokers	P value
hSCRP (mg/L)	2.78	1.01	<0.001
Urine spot microalbumin in mg/dL	31.56	14.98	<0.001

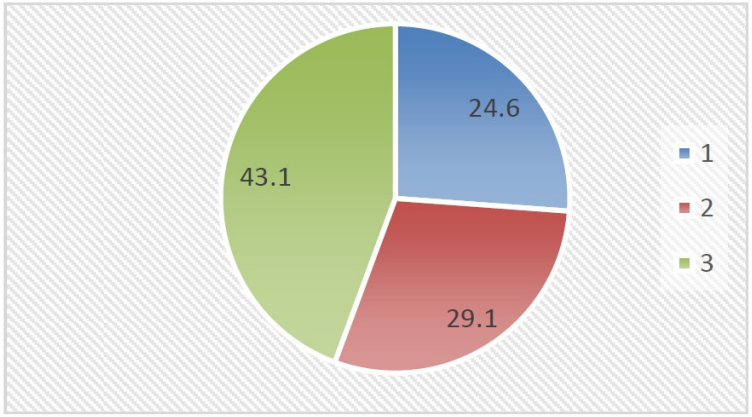
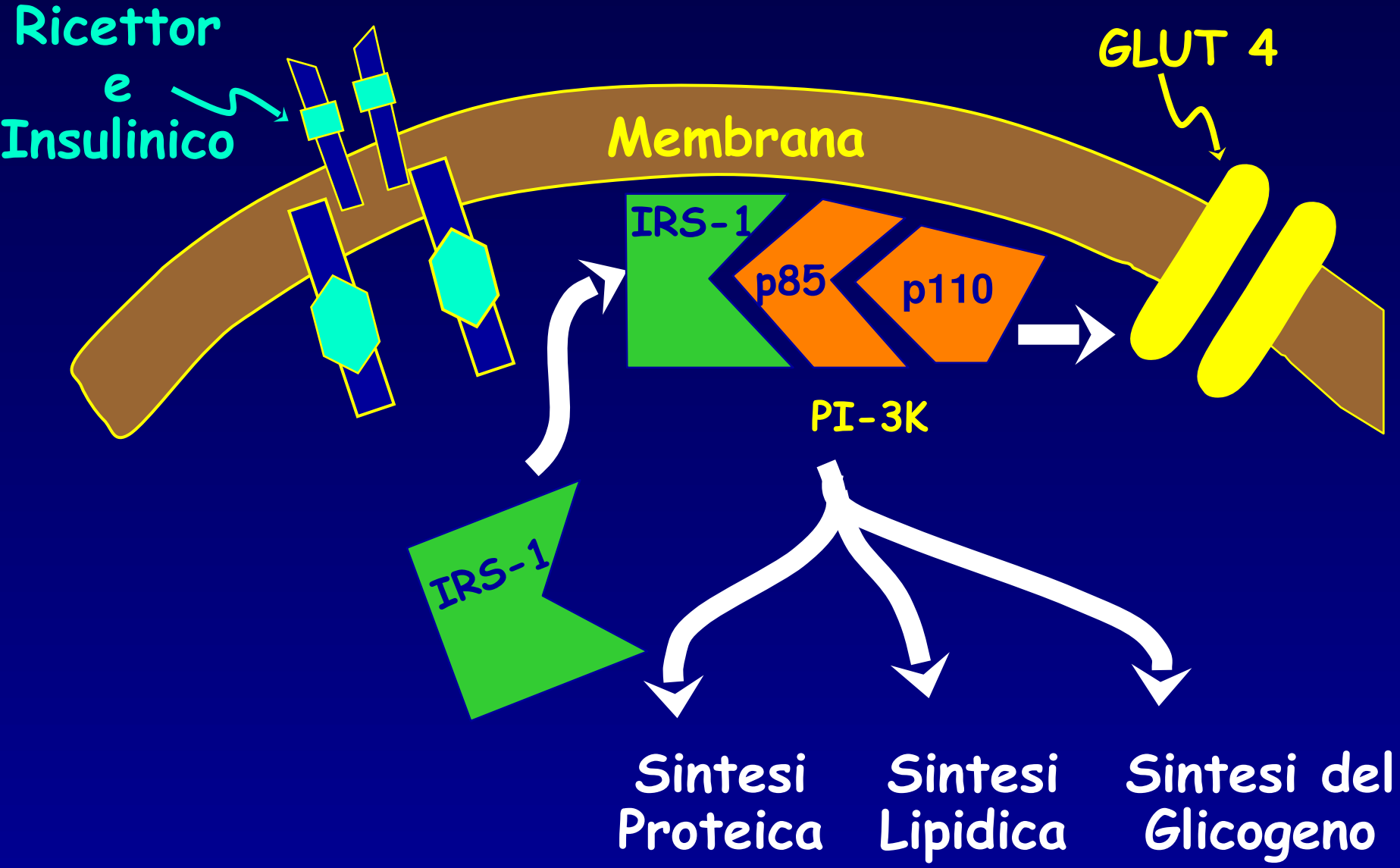


Figure 1. Shows comparison of mean levels urine microalbumin levels (mg/L) among smokers

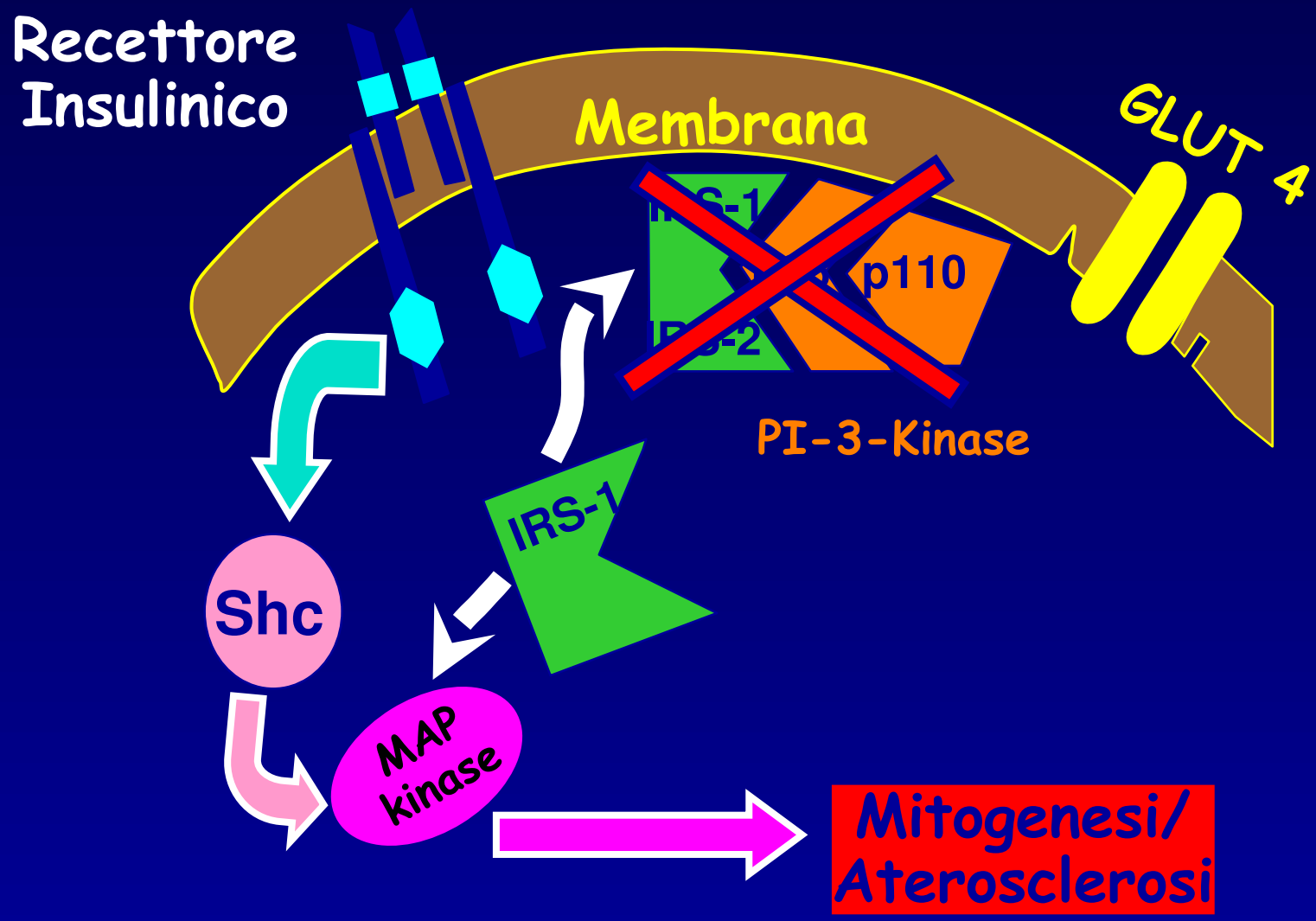
1= light smokers (10-14 pack-years), 2 = moderate smokers (15-19 pack-years) and 3 = heavy smokers (>20 pack-years)

International Journal of Health Sciences, 6(S3), 11578–11584. (2022)

SISTEMA DI TRADUZIONE DEL SEGNALE INSULINICO



SISTEMA DI TRADUZIONE DEL SEGNALE INSULINICO



Molecular Mechanisms: Nicotine

- Increases IRS-1 phosphorylation at serine 636 through an mTOR-dependent mechanism, reducing insulin sensitivity in skeletal muscle.
- In adipose tissues, nicotine activates AMPKa2, leading to increased lipolysis and elevated free fatty acids, which impair insulin sensitivity.
- Recovery: Notably, insulin sensitivity of human smokers can recover within 2–3 weeks of smoking cessation.

D. Haj Mouhamed, A. Ezzaher, F. Neffati, W. Douki, L. Gaha, M.F. Najjar
Effect of cigarette smoking on insulin resistance risk
Ann. Cardiol. Angeiol., 65 (1) (2016), pp. 21-25

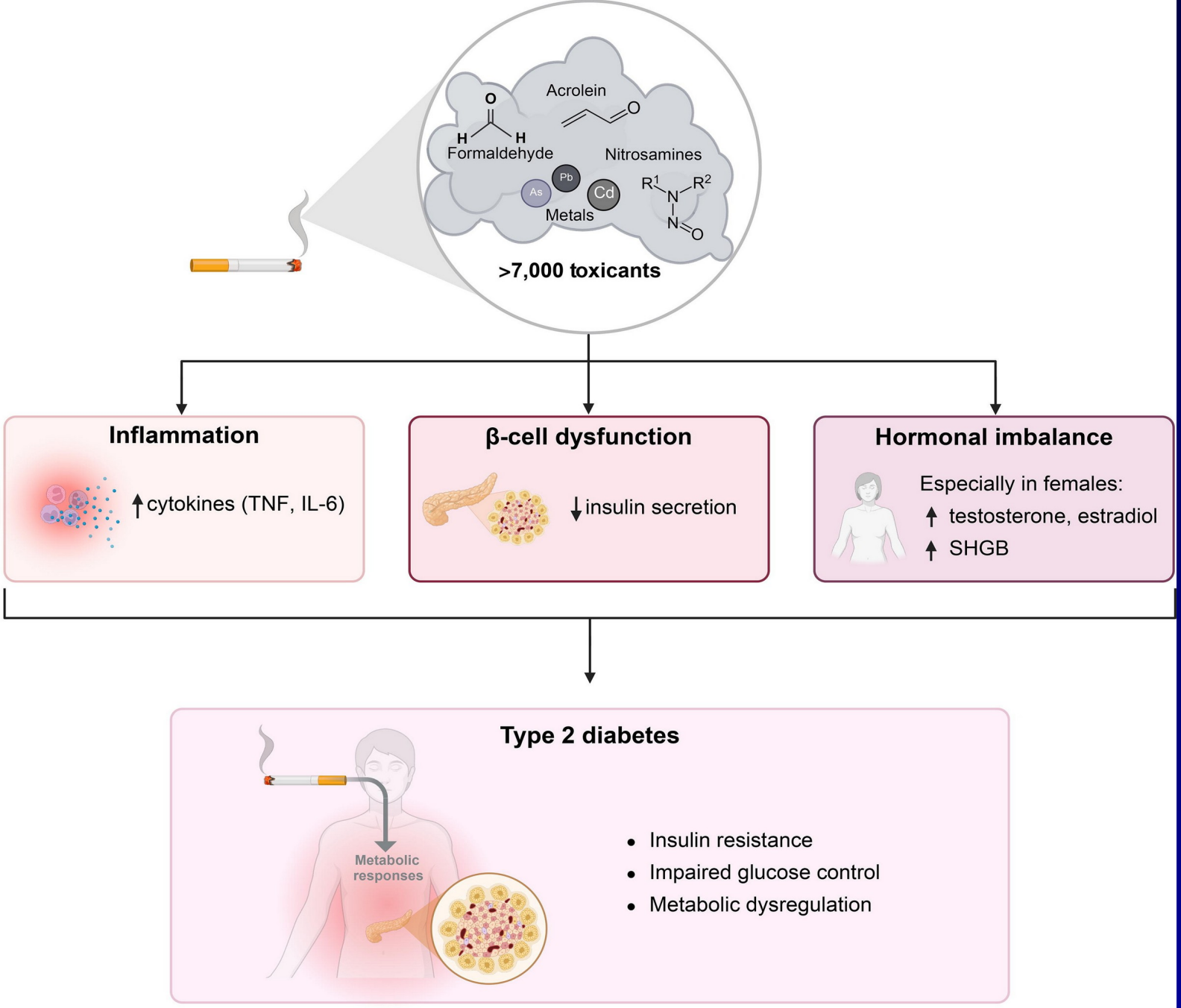
International consensus recommendations for smoking cessation in type 2 diabetes from the DiaSmokeFree Working group

Magdalena Walicka, Cristina Russo, Antonio Ceriello, Jacob George, Davide Campagna, Anoop Misra, Giusy Rita Maria La Rosa, Roberta Sammut, Riccardo Polosa

Diabetes Research and Clinical Practice

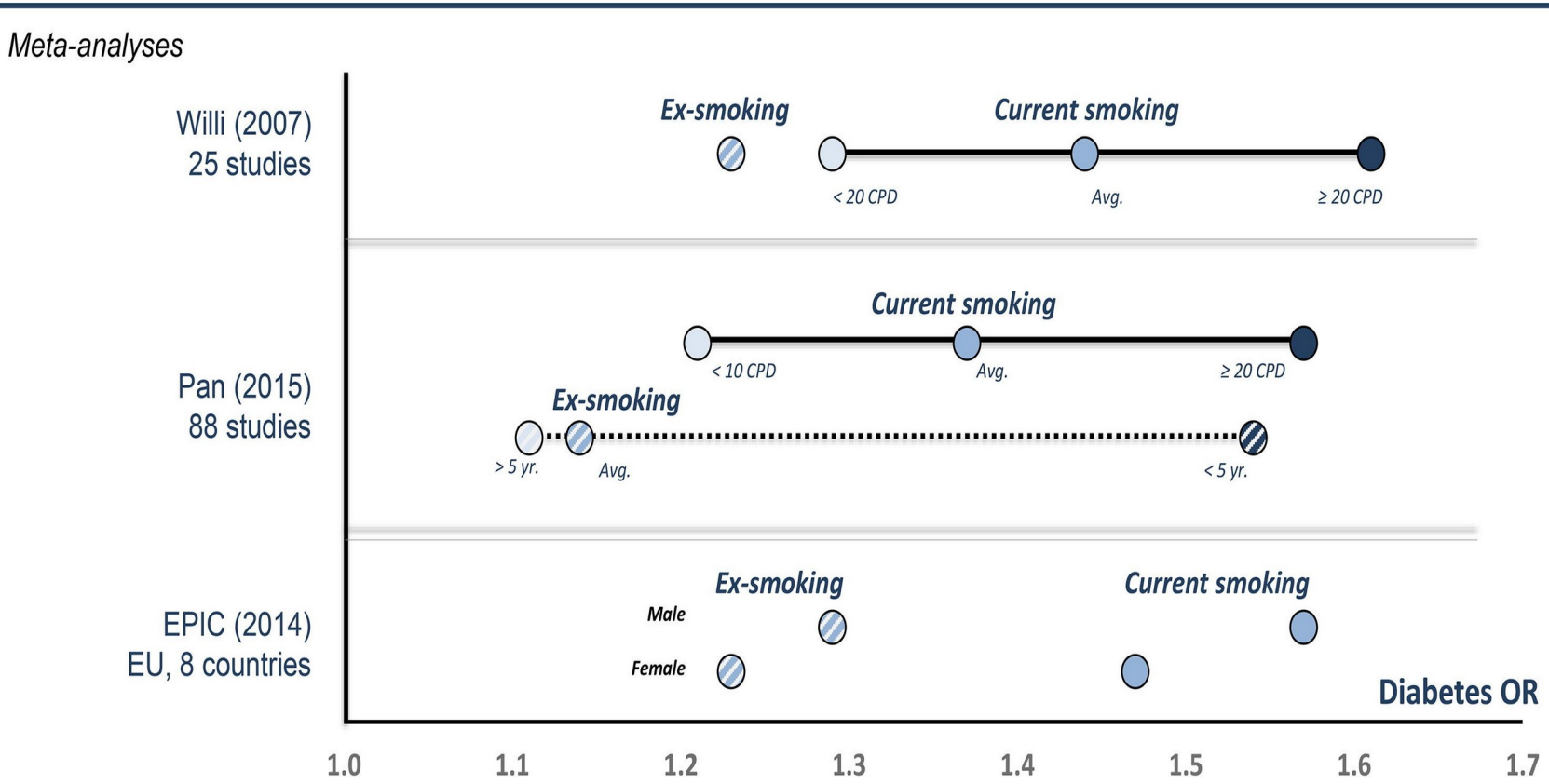
DOI: 10.1016/j.diabres.2026.113528

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Diabetes Research and Clinical Practice DOI: (10.1016/j.diabres.2026.113528)
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Intensity of smoking history impacts diabetes risk

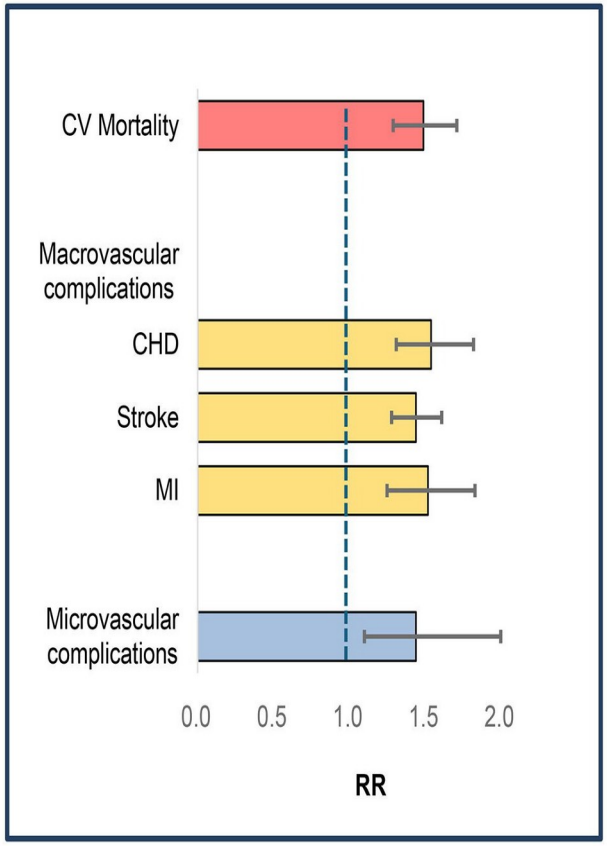




Quitting or reducing smoking can lower diabetes risk, both in males and females
The benefits of quitting increase over time

Diabetes Research and Clinical Practice DOI: (10.1016/j.diabres.2026.113528)
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Relative risk (RR) in type 2 diabetes

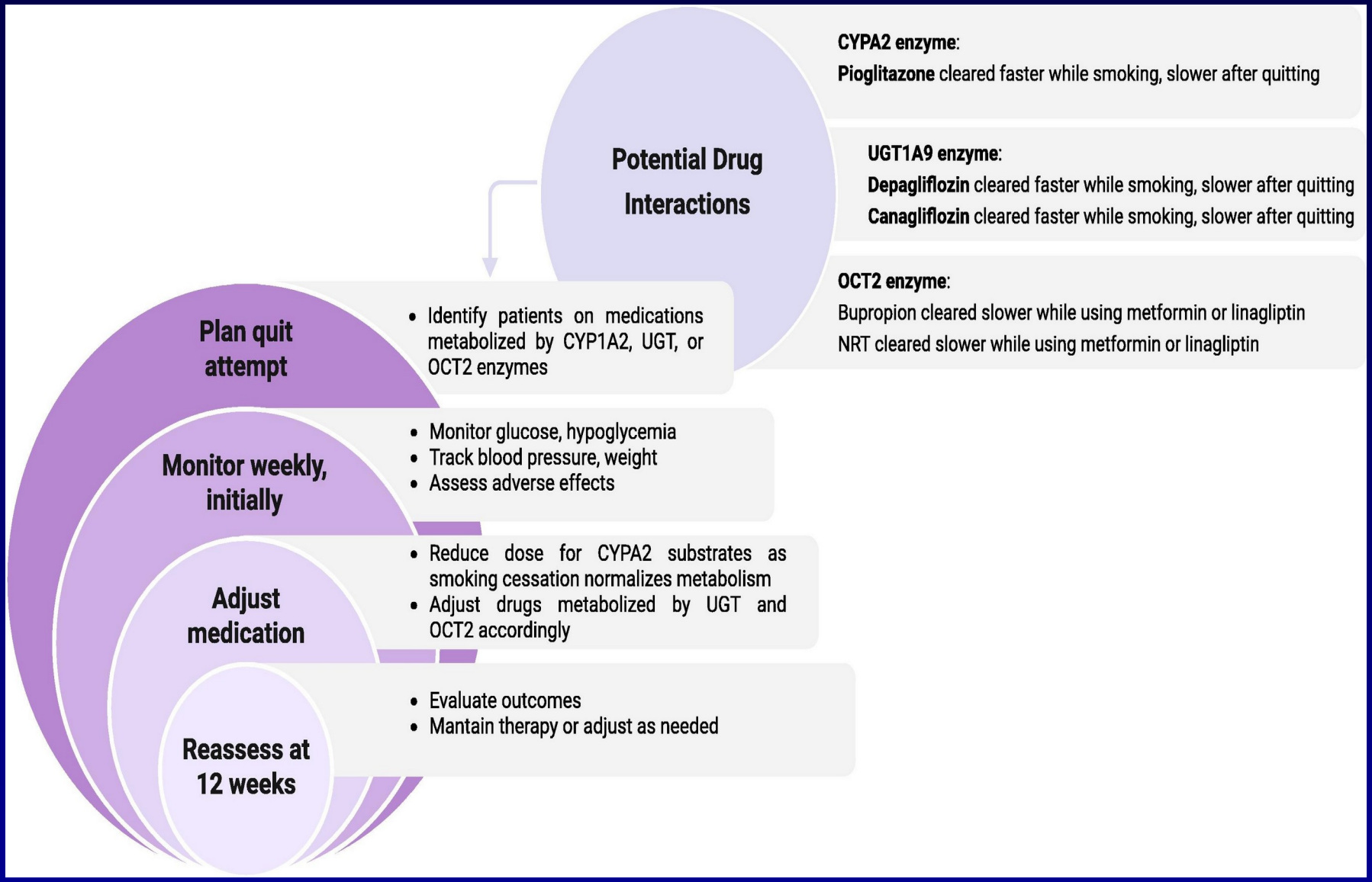


Source: Pan, 2015b

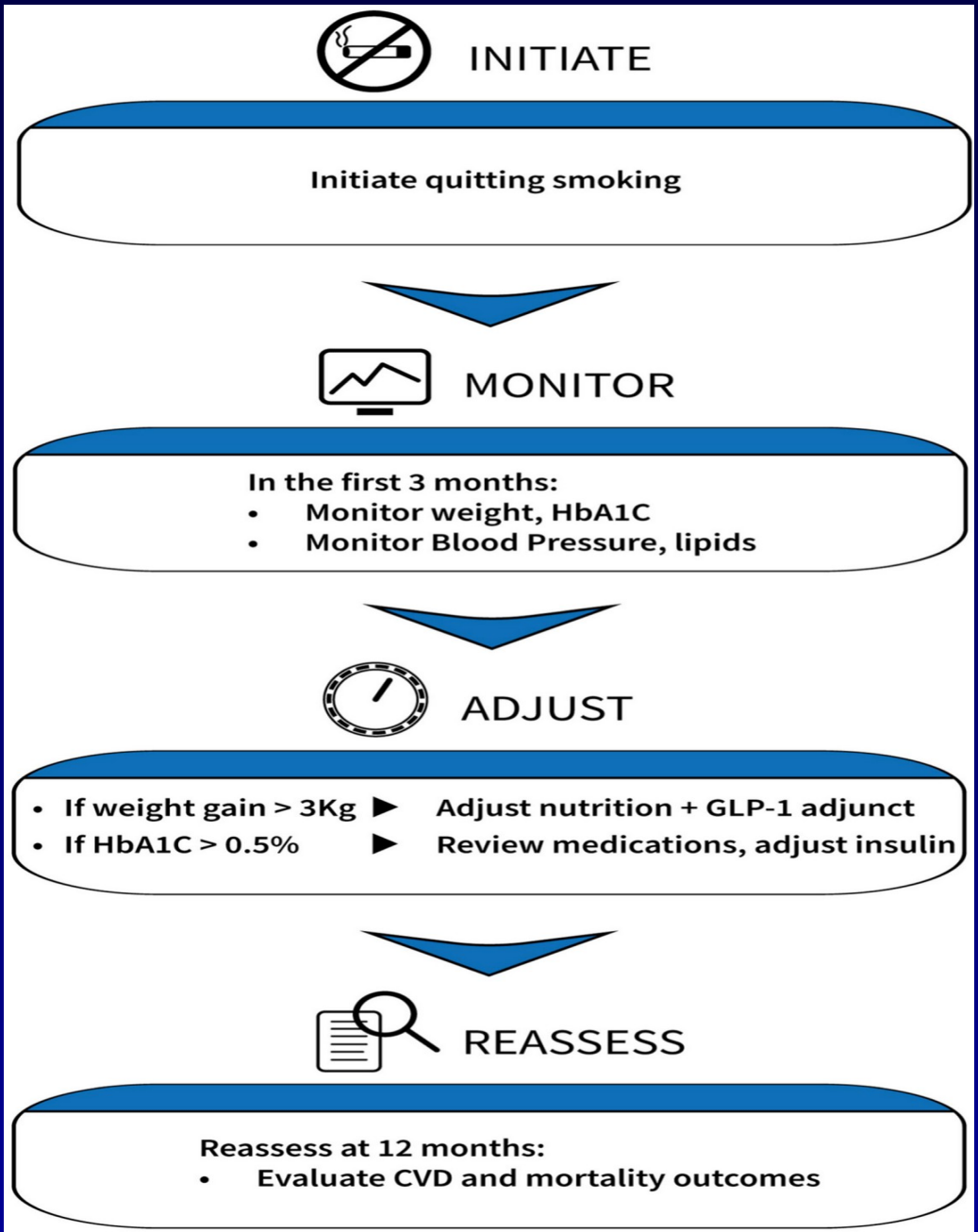
Key insights for healthcare professionals

- Smoking increases mortality by 55% in people with diabetes
- Increased macrovascular risk (CHD, stroke, MI)
- Increased overall microvascular risk (mainly, PAD, and nephropathy)
- Mixed evidence for retinopathy and neuropathy

Diabetes Research and Clinical Practice DOI: (10.1016/j.diabres.2026.113528)
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Diabetes Research and Clinical Practice DOI: (10.1016/j.diabres.2026.113528)
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Diabetes Research and Clinical Practice DOI: (10.1016/j.diabres.2026.113528)
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Is 'Metabolic Syndrome' Obsolete in the GLP-1 Era?

Electronic Cigarette Use and Metabolic Syndrome Development: A Critical Review

-Among 23 studies, 1 was combined in vitro and in vivo study, 6 experimental studies used animal models (Wistar rats, Apoe-/- mice, BALB/cJ mice, C57BL6/J mice), and 16 studies concern the impact of e-cigarettes on their users (mostly adult participants aged 18–96 years).
-Using e-cigarettes did not affect the development of abdominal obesity, insulin resistance, and elevated arterial blood pressure, but could influence the level of glucose and prediabetic state development, and increased risk of obesity and hypertension.
-Increase in the TG level was reported,

Gorna I et al: Toxics 2020, 8, 105; doi:10.3390/toxics8040105

Nicotine and glucose: Key Takeaways

Ma…
Educhiamoli fin da piccoli!



