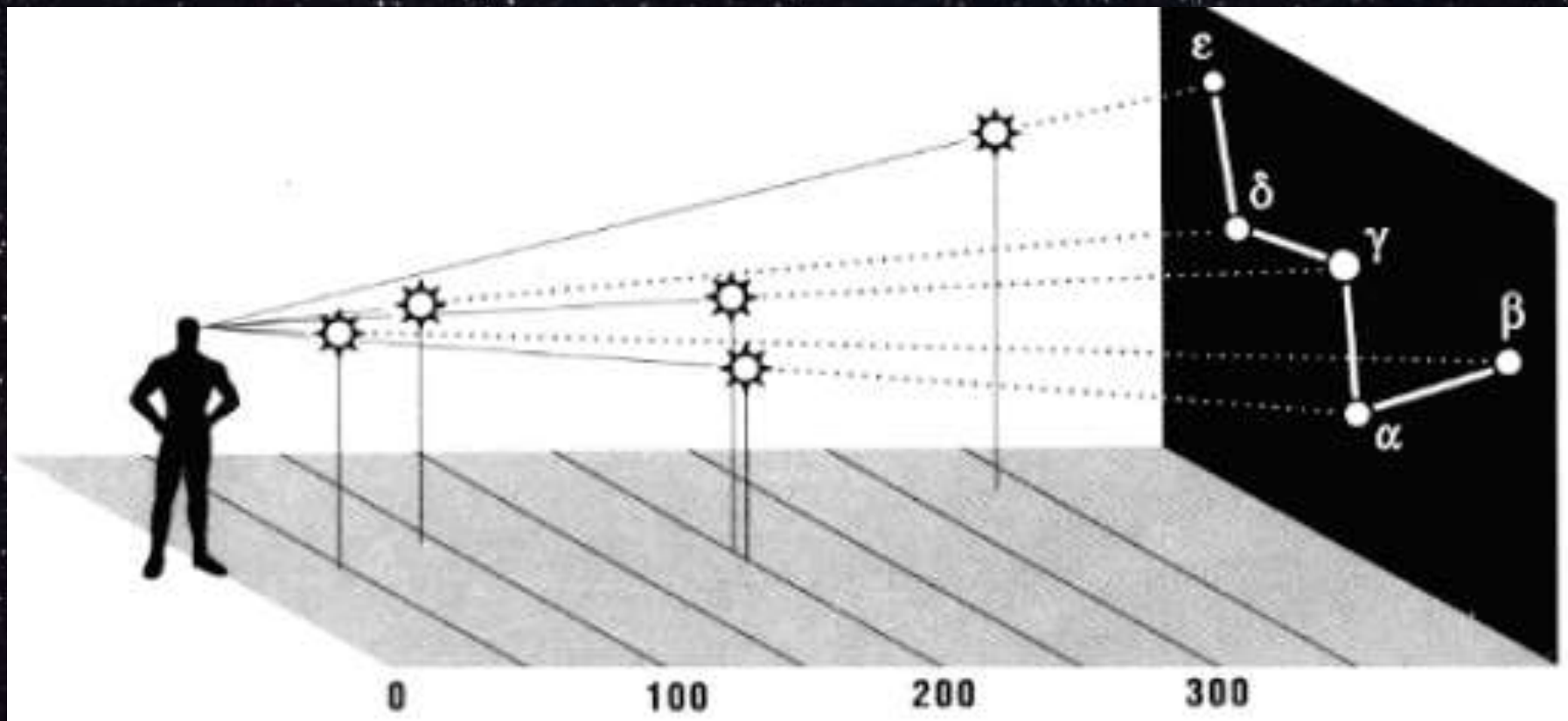


Sindrome metabolica nella malattia psoriasica

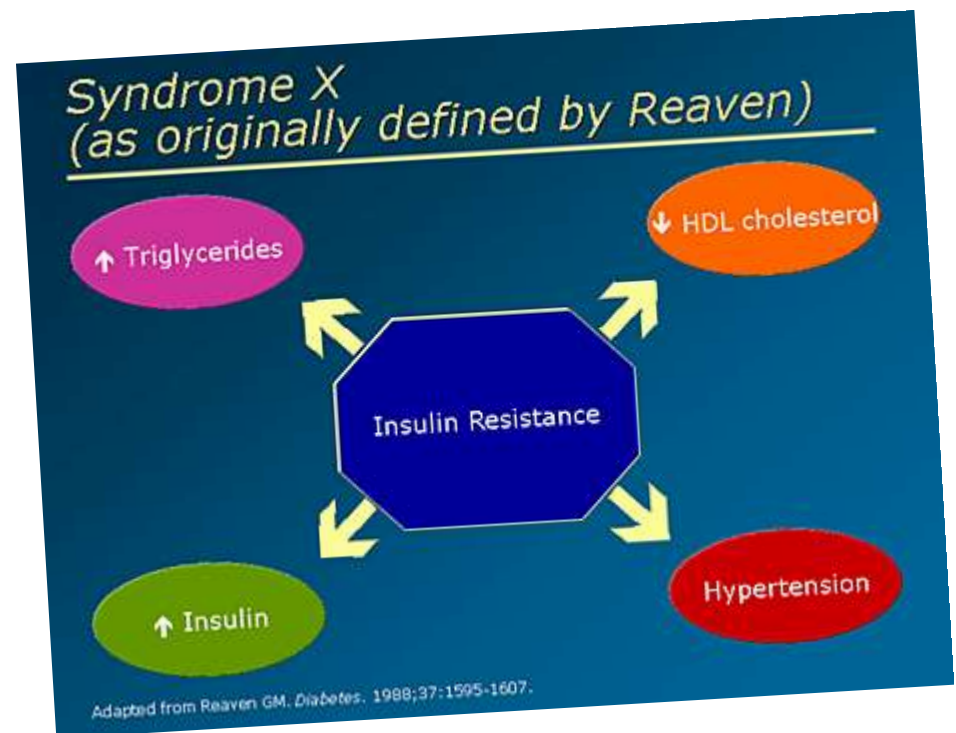
Fabio Broglio

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Università degli Studi di Torino



Dalla «Sindrome X»....

- insulin resistance
- hyperinsulinaemia
- glucose intolerance
- ↑ VLDL triglyceride
- ↓ HDL cholesterol
- Hypertension



...alla «Sindrome Metabolica»....

	WHO (1999)	NCEP-ATP III (2001)	NCEP-R (2004)	IDF (2005)	AACE
Obesity	WHR >0.90(male) >0.85(female) or BMI>30 kg/m ²	WC ≥ 102 cm (male) ≥ 88 cm (female)	WC ≥ 102 cm (male) ≥ 88 cm (female)	[REQUIREMENT] WC ≥ 94 cm (male) ≥ 80 cm (female)	Overweight/ Obesity BMI ≥ 25 kg/m ²
Serum triglycerides	≥ 150mg/dl	≥ 150 mg/ dl	≥ 150 mg/ dl or medication	≥ 150 mg/ dl or medication	≥ 150 mg/ dl
Serum HDL	< 35 mg/ dl (male)	< 40 mg/ dl (male)	< 40 mg/ dl (male)	<40 mg/ dl (male)	<40 mg/ dl (male)
Cholesterol	< 39 mg/ dl (female)	< 50 mg/ dl (female)	< 50 mg/ dl (female) or medication	<50 mg/ dl (female) or medication	<50 mg/ dl (female)
Blood pressure	≥ 140/ 90 mmHg	≥ 130/85 mmHg or medication	≥ 130/85 mmHg or medication	≥ 130/85 mmHg or medication	≥130/ 85 mmHg or medication
Fasting plasma glucose	[REQUIREMENT] FPG≥110 mg/ dl	≥ 100mg/ dl	≥ 100mg/ dl	≥ 100mg/ dl or previously diagnosed T2DM	110-126 mg/ dl
Other risk factors	Urinary albumin excretion rate ≥ 20µg/ min or albumin / creatinine ratio ≥ 30 mg/g				Family history of T2DM, HTN, or CVD. Polycystic ovary syndrome, sedentary life stly, Advancing age and ethnic groups having high risk for DM or CVD Physician's judgement
Diagnosis	Impaired FPG+any 2 criteria	Any 3 criteria	Any 3 criteria	WC+any 2 criteria	

T2DM: Type 2 diabetes mellitus, HTN: Hypertension, CVD: Cerebrovascular accident, DM: Diabete mellitus, WC: Waist circumference. NCEP ATP III : National cholesterol education program adult tretment panel III, NCEP-R: NCEP-R: revised NCEP, IDF: International diabetes federation, ACE: American association of clinical endocrinologists, WHO: World Health Organization, WHR: Waist-to-hip ratio, BMI: Body mass index, HDL: high density lipoprotein

The Metabolic Syndrome: Time for a Critical Appraisal

Joint statement from the American Diabetes Association and the European Association for the Study of Diabetes

RICHARD KAHN, MD¹
JOHN BOYK, MD, PhD²

LEE FERRIGNANI, MD³
MICHAEL STERN, MD⁴

Table 3—Summary of concerns regarding the metabolic syndrome

- 1) Criteria are ambiguous or incomplete.
Rationale for thresholds are ill defined.
- 2) Value of including diabetes in the definition is questionable.
- 3) Insulin resistance as the unifying etiology is uncertain.
- 4) No clear basis for including/excluding other CVD risk factors.
- 5) CVD risk value is variable and dependent on the specific risk factors present.
- 6) The CVD risk associated with the “syndrome” appears to be no greater than the sum of its parts.
- 7) Treatment of the syndrome is no different than the treatment for each of its components.
- 8) The medical value of diagnosing the syndrome is unclear.

The Metabolic Syndrome: Time for a Critical Appraisal

Joint statement from the American Diabetes Association and the European Association for the Study of Diabetes

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Table 8. Clinical Identification of the Metabolic Syndrome

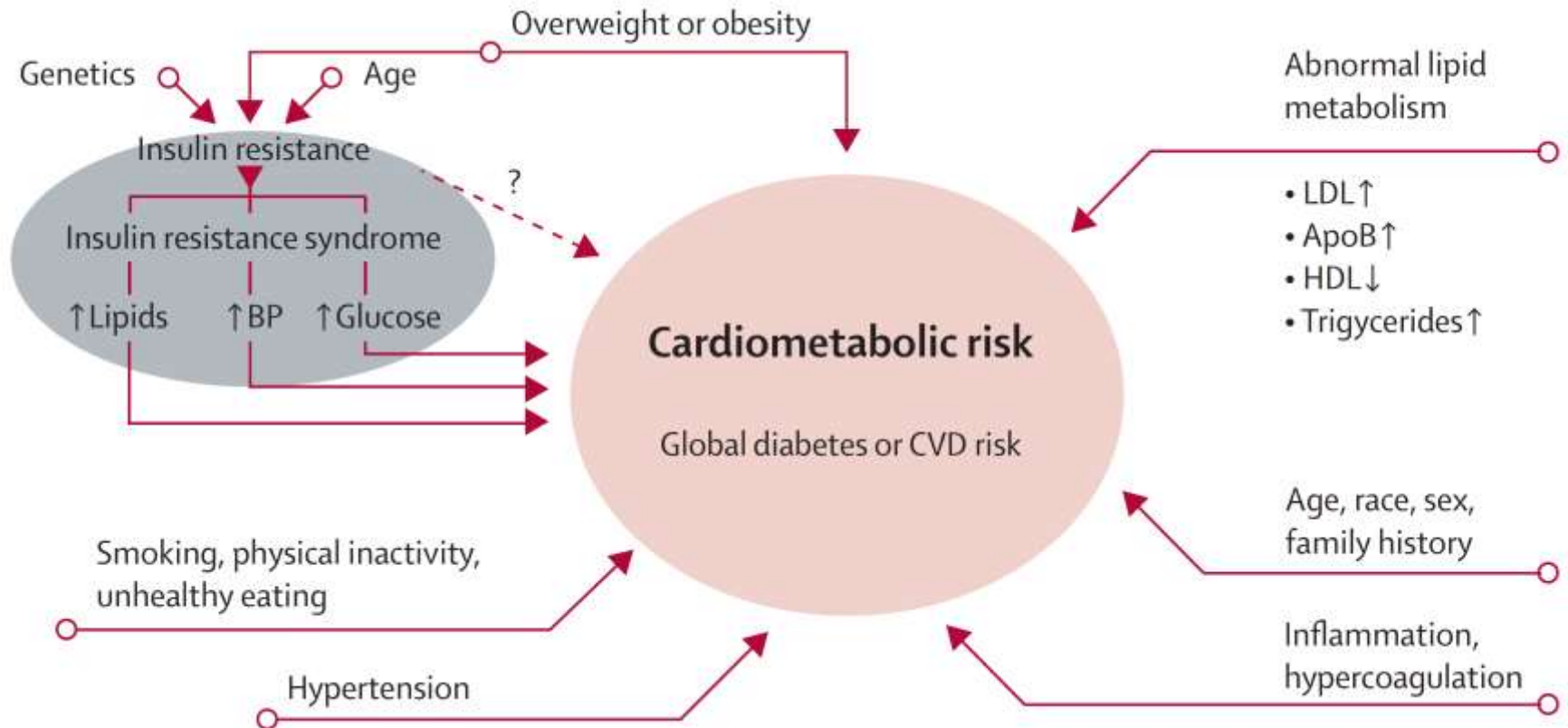
Risk Factor	Defining Level
Abdominal Obesity*	Waist Circumference ¹
Men	>102 cm (>40 in)
Women	>88 cm (>35 in)
Triglycerides	≥150 mg/dL
HDL cholesterol	
Men	<40 mg/dL
Women	<50 mg/dL
Blood pressure	≥130/≥85 mmHg
Fasting glucose	≥110 mg/dL

Table 2—Treating the metabolic syndrome

Characteristic	Patient A	Patient B	Patient C
Waist circumference (cm)	110	103	114
Triglycerides (mmol/l) (x 89= 1 mg/dl)	1.62 (144)	0.34 (30)	1.34 (119)
Systolic/diastolic blood pressure (mmHg)	170/95	135/90	125/80
HDL (mmol/l) (x 39= 1 mg/dl)	1.06 (41)	1.68 (65)	1.29 (50)
Fasting plasma glucose (mmol/l) (x 18= 1 mg/dl)	5.28 (95)	6.1 (110)	7.22 (130)
LDL (mmol/l) (x 39= 1 mg/dl)	4.65 (181)	1.81 (70)	1.94 (75)
Other	Patient smokes; taking no drugs	None; taking no drugs	Patient had previous MI 4 years ago; taking a β blocker and aspirin

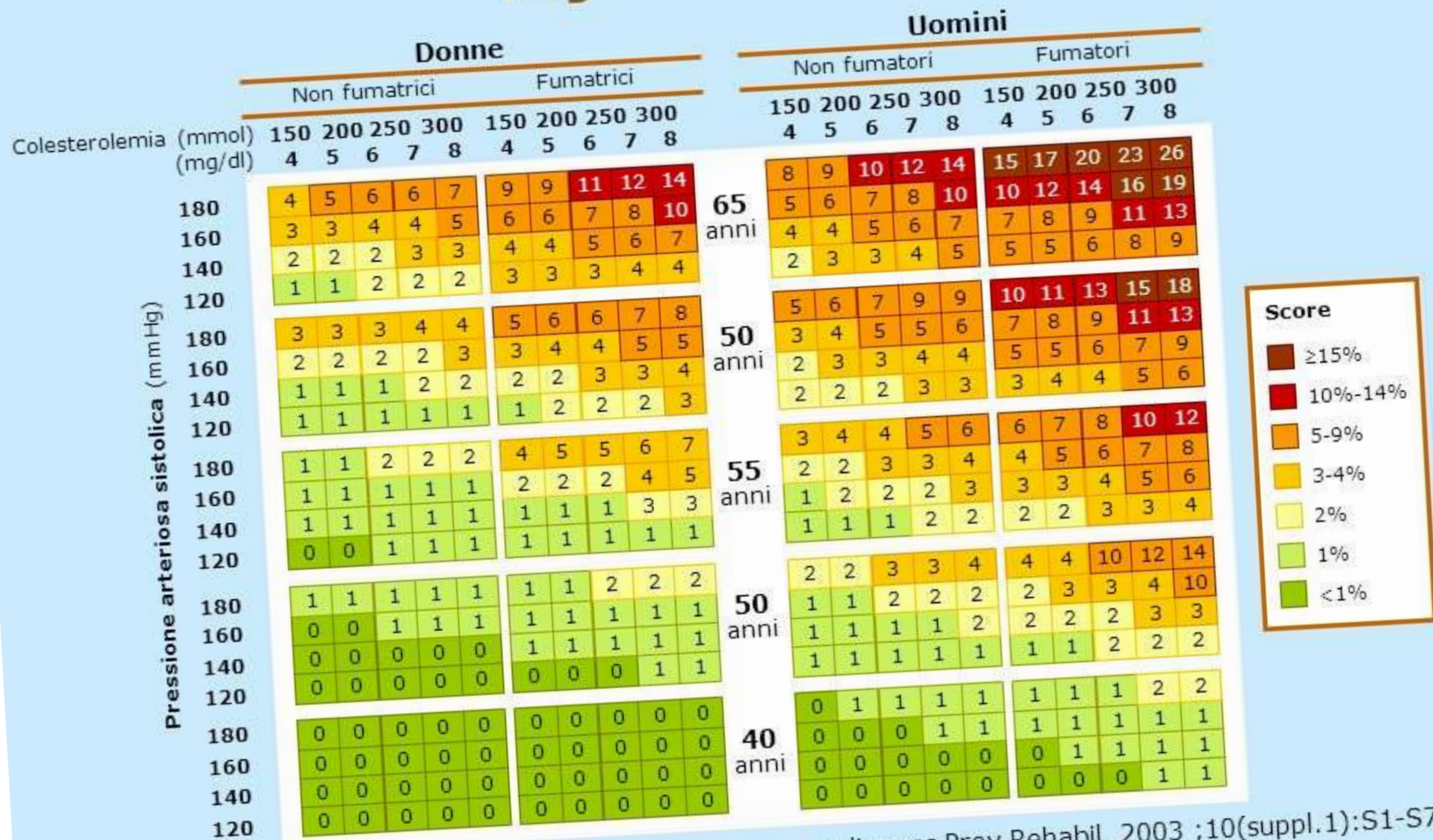
All three patients are 50 years old, white males, with no symptoms of CVD and no family history of diabetes, CHD, or stroke. They present for a routine physical examination. Based on the findings above, what factor(s) should be treated and what is the goal of therapy?

... al «Rischio Cardiometabolico»



La carta europea (Heart Score)

Regioni a basso rischio



De Backer G. et al. Eur J Cardiovasc Prev Rehabil. 2003 ;10(suppl.1):S1-S78

An update on metabolic syndrome: Metabolic risk markers and adipokines in the development of metabolic syndrome

Reena Kumari ^a, Sandeep Kumar ^{b,*}, Ravi Kant ^b

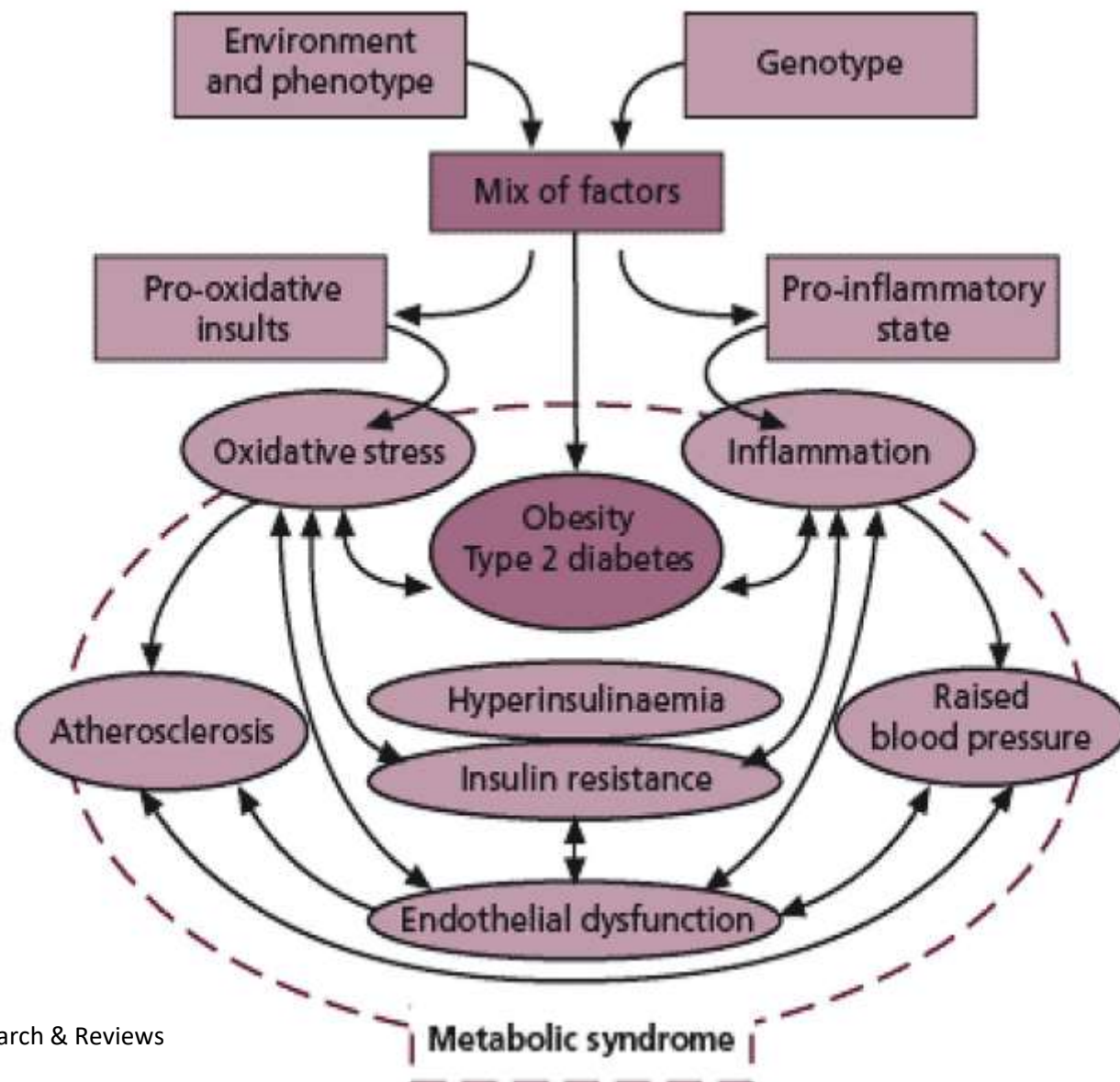


Fig. 2. Pathophysiology of metabolic syndrome.

An update on psoriasis and metabolic syndrome: A meta-analysis of observational studies

Sanminder Singh¹, Paulina Young², April W. Armstrong^{2*}

Fig 2. Prevalence of metabolic syndrome in psoriasis patients. This is a forest plot examining observational studies. The diamond represents the exact estimate from the study. The width of the line extending from each diamond represents the 95% confidence interval (CI). OR, odds ratio; MetSyn, Metabolic syndrome.

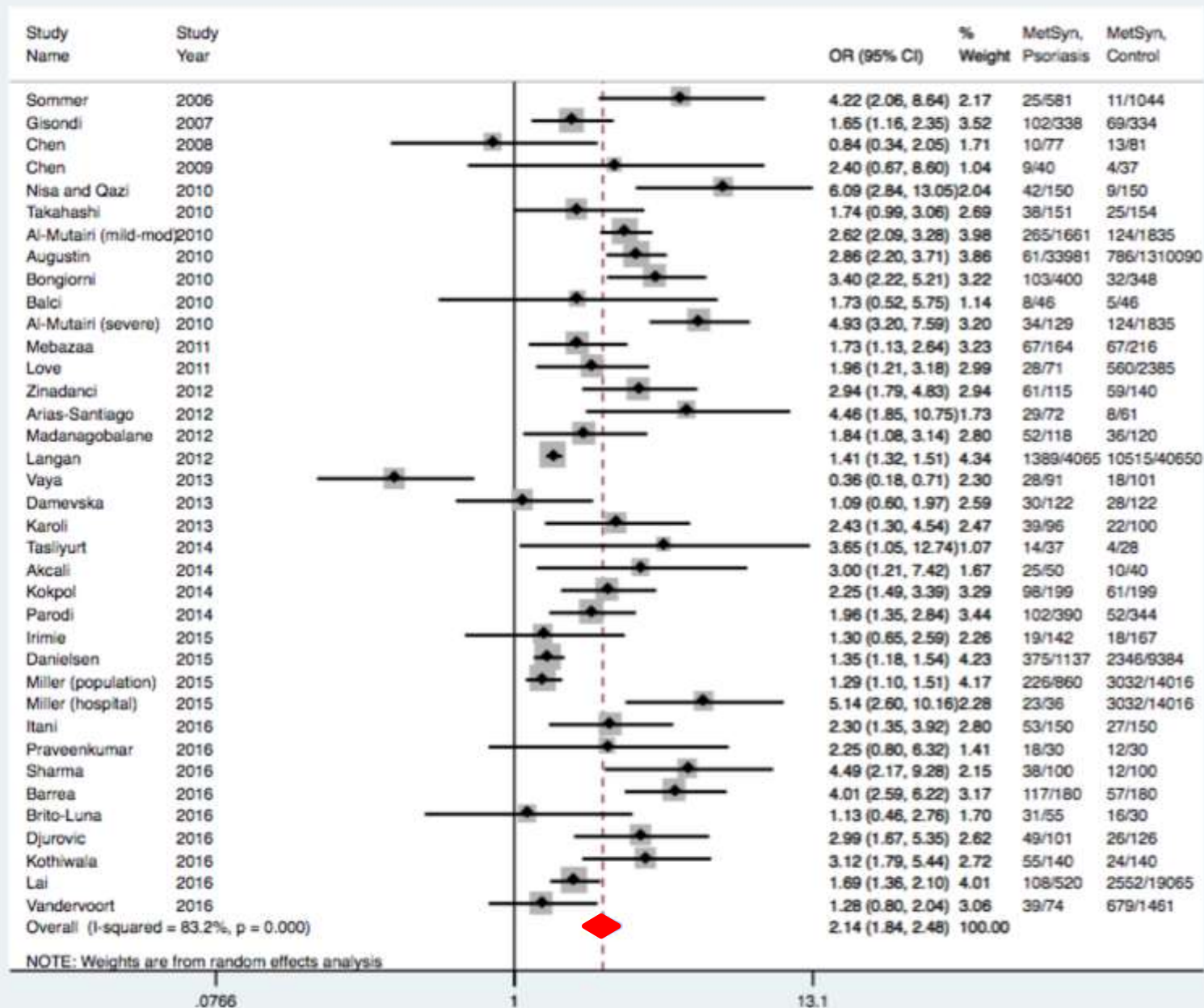
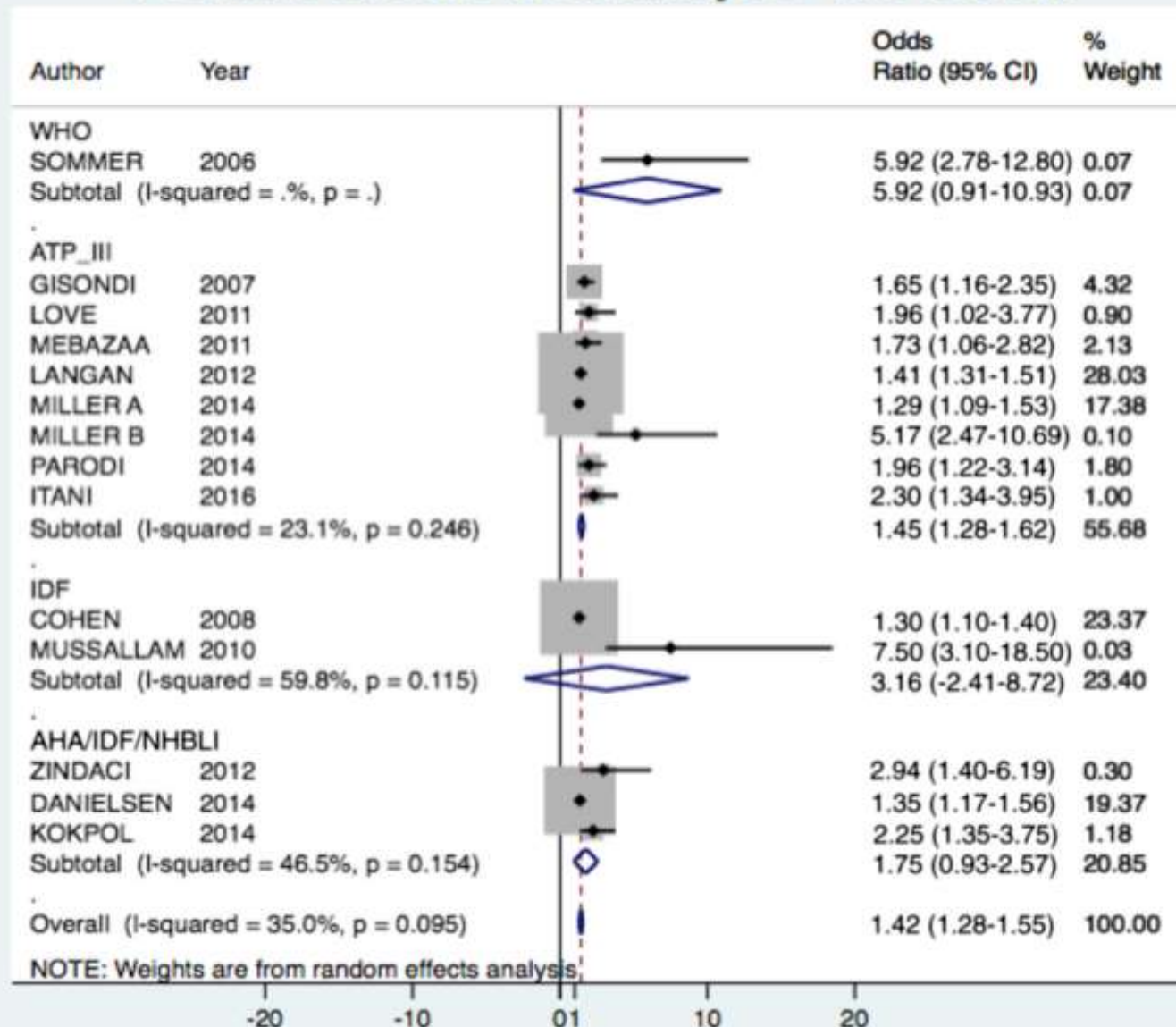


Fig 3. Meta-analysis of the association between psoriasis and metabolic syndrome (MS) according to the 3 sets of MS diagnostic criteria used in studies. AHA/IDF/NHBLI, American Heart Association/International Diabetes Federation/National Heart, Lung, and Blood Institute Joint Scientific Statement; ATP III, National Cholesterol Education Program Adult Treatment Panel III; CI, confidence interval; IDF, International Diabetes Federation; MS, metabolic syndrome; WHO, World Health Organization.

Psoriasis and MS Meta analysis - MS Criteria



Psoriasis, metabolic syndrome and cardiovascular risk factors. A population-based study

J.M. Fernández-Armenteros,^{1,2,*} X. Gómez-Arbonés,^{1,3} M. Buti-Soler,^{4,5} A. Betriu-Bars,^{1,6} V. Sanmartín-Novell,² M. Ortega-Bravo,⁷ M. Martínez-Alonso,¹ E. Garí,¹ M. Portero-Otín,¹ L. Santamaría-Babi,⁸ J.M. Casanova-Seuma^{1,2,3}

Table 5 Prevalence of cardiovascular risk factors and major cardiovascular events in psoriasis and general population

Risk factor/cardiovascular event	Prevalence in psoriasis	Prevalence in non-psoriasis group	OR (IC 95%)	Author
Ischaemic cardiomyopathy	229 (3.3%)	7116 (1.8%)	1.87 (1.63–2.13, $P < 0.001$)	Our results (2018)
			1.5 (1.2–1.9)	Miller <i>et al.</i> (2013) ²²
Cerebrovascular accident	122 (1.8%)	4520 (1.2%)	1.55 (1.29–1.86, $P < 0.001$)	Our results (2018)
			1.1 (0.9–1.3)	Miller <i>et al.</i> (2013) ²²
Diabetes mellitus	952 (13.9%)	29 171 (7.4%)	2.01 (1.87–2.15, $P < 0.001$)	Our results (2018)
	15 (11.3%)			Jacobi <i>et al.</i> (2013) ²⁶
			1.59 (1.38–1.83)	Armstrong <i>et al.</i> (2013) ⁶
			1.9 (1.5–2.5)	Miller <i>et al.</i> (2013) ²²
			1.76 (1.59–1.96)	Coto-Segura <i>et al.</i> (2013) ²⁷
Dyslipidaemia	1979 (28.8%)	68 201 (17.4%)	1.92 (1.82–2.03, $P < 0.001$)	Our results (2018)
			1.04–5.55	Ma <i>et al.</i> (2013) ⁴
			1.5 (1.4–1.7)	Miller <i>et al.</i> (2013) ²²
Decreased HDL	2067 (38.1%)	71 574 (32.3%)	1.29 (1.22–1.36, $P < 0.001$)	Our results (2018)
	29.8%			Belinchón <i>et al.</i> (2015) ²⁵
	26 (27.37%)	4 (4.21%)	8.57 ($P < 0.001$)	Salunke <i>et al.</i> (2017) ²⁸
Hypertriglyceridaemia	2754 (45.7%)	92 140 (35.2%)	1.55 (1.47–1.63, $P < 0.001$)	Our results (2018)
	34.7%			Belinchón <i>et al.</i> (2015) ²⁵
	43 (45.26%)	11 (11.58%)	6.31 (<0.001)	Salunke <i>et al.</i> (2017) ²⁸
Arterial hypertension	2140 (31.2%)	74 489 (19.0%)	1.93 (1.83–2.03, $P < 0.001$)	Our results (2018)
	52 (39.1%)			Jacobi <i>et al.</i> (2013) ²⁶
			1.8 (1.6–2.0)	Miller <i>et al.</i> (2013) ²²
Obesity	1497 (33.7%)	47 184 (28.1%)	1.58 (1.42–1.76)	Armstrong <i>et al.</i> (2013) ⁶
			1.30 (1.22–1.39, $P < 0.001$)	Our results (2018)
High waist circumference	1787 (75.7%)	58 311 (72.3%)	1.8 (1.4–2.2)	Miller <i>et al.</i> (2013) ²²
	58.8%			Our results (2018)
			1.19 (1.08–1.31, $P < 0.001$)	Belinchón <i>et al.</i> (2015) ²⁵
	31 (32.63%)	15 (15.79%)	2.58 ($P = 0.007$)	Salunke <i>et al.</i> (2017) ²⁸
			1.6 (1.2–2.3)	Miller <i>et al.</i> (2013) ²²

Psoriasis Severity—A Risk Factor of Insulin Resistance Independent of Metabolic Syndrome

Melita Vuksic Polic ^{1,2}, Maja Miskulin ², Martina Smolic ^{2,3}, Kristina Kralik ²,
Ivan Miskulin ², Maja Cigrovski Berkovic ⁴ and Ines Bilic Curcic ^{1,2,*}

Table 3. HOMA-IR and HOMA- β according to disease severity.

Variable	Median (Interquartile Range)			<i>p</i> *
	Mild Form	Moderate to Severe Form	Severe Form	
All Subjects				
HOMA-IR	1.8 (1.2–3.1)	3.6 (2.1–5.3)	3.5 (2.2–5.1)	<0.001
HOMA-β	65.7 (39.3–108.2)	110.4 (52.2–251.7)	120 (67.9–215.4)	0.008
No Metabolic Syndrome				
HOMA-IR	1.9 (1.1–3.1)	3.1 (1.2–4.6)	4.1 (3–5.5)	0.004
HOMA-β	70.9 (39.9–110.2)	113.8 (58.8–230.6)	155.9 (103.3–417.8)	0.007
With Metabolic Syndrome				
HOMA-IR	1.8 (1.3–4.4)	4 (2.2–5.9)	2.8 (2–5)	NS
HOMA-β	51.5 (30–80)	107.1 (47.2–255.8)	90.4 (67.3–204.9)	NS

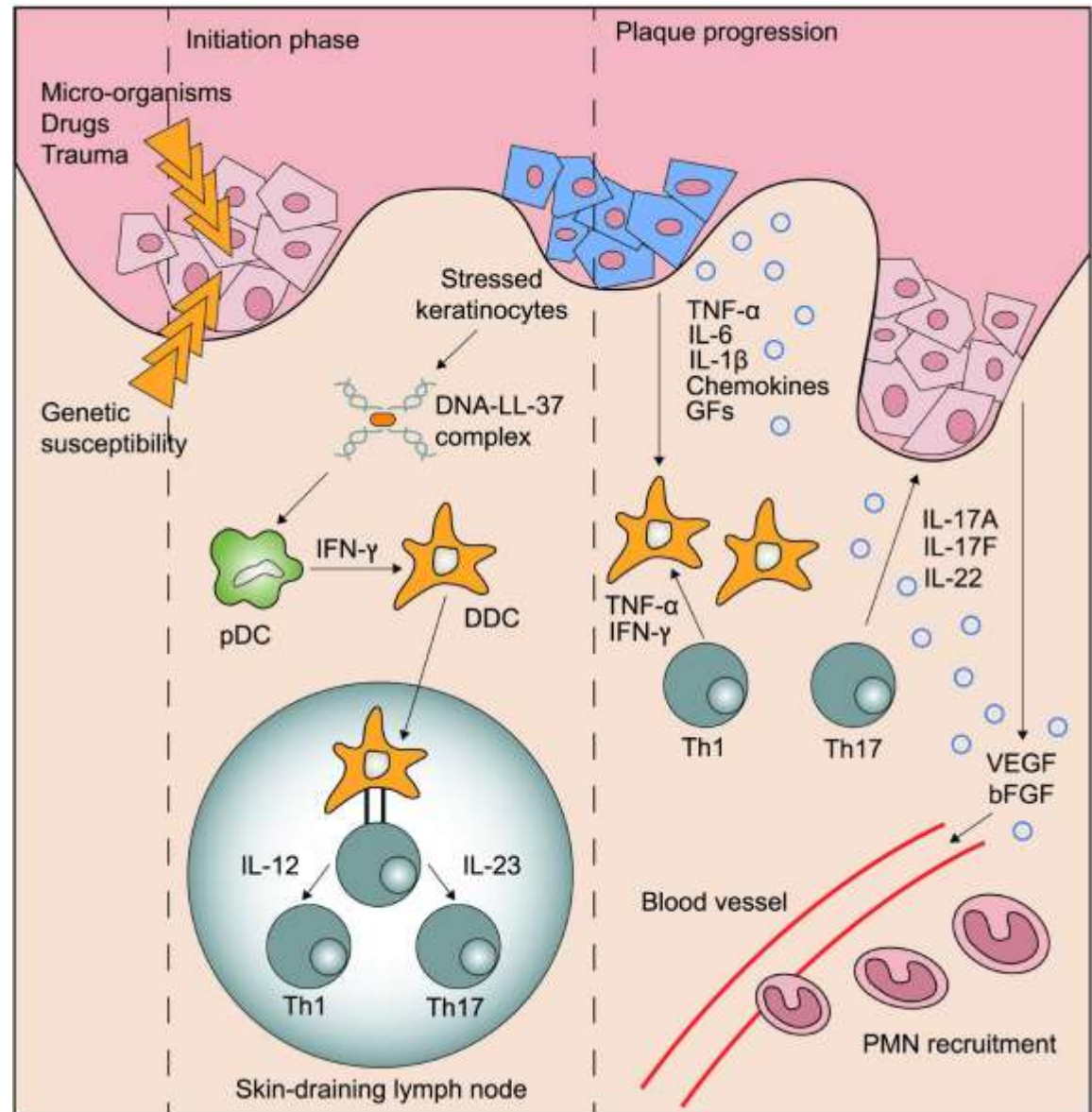
* Kruskal-Wallis test; NS, not significant.

Psoriatic disease and body composition: A systematic review and narrative synthesis

Tim Blake^{1,2*}, Nicola J. Gullick³, Charles E. Hutchinson^{2,3}, Thomas M. Barber^{2,4}

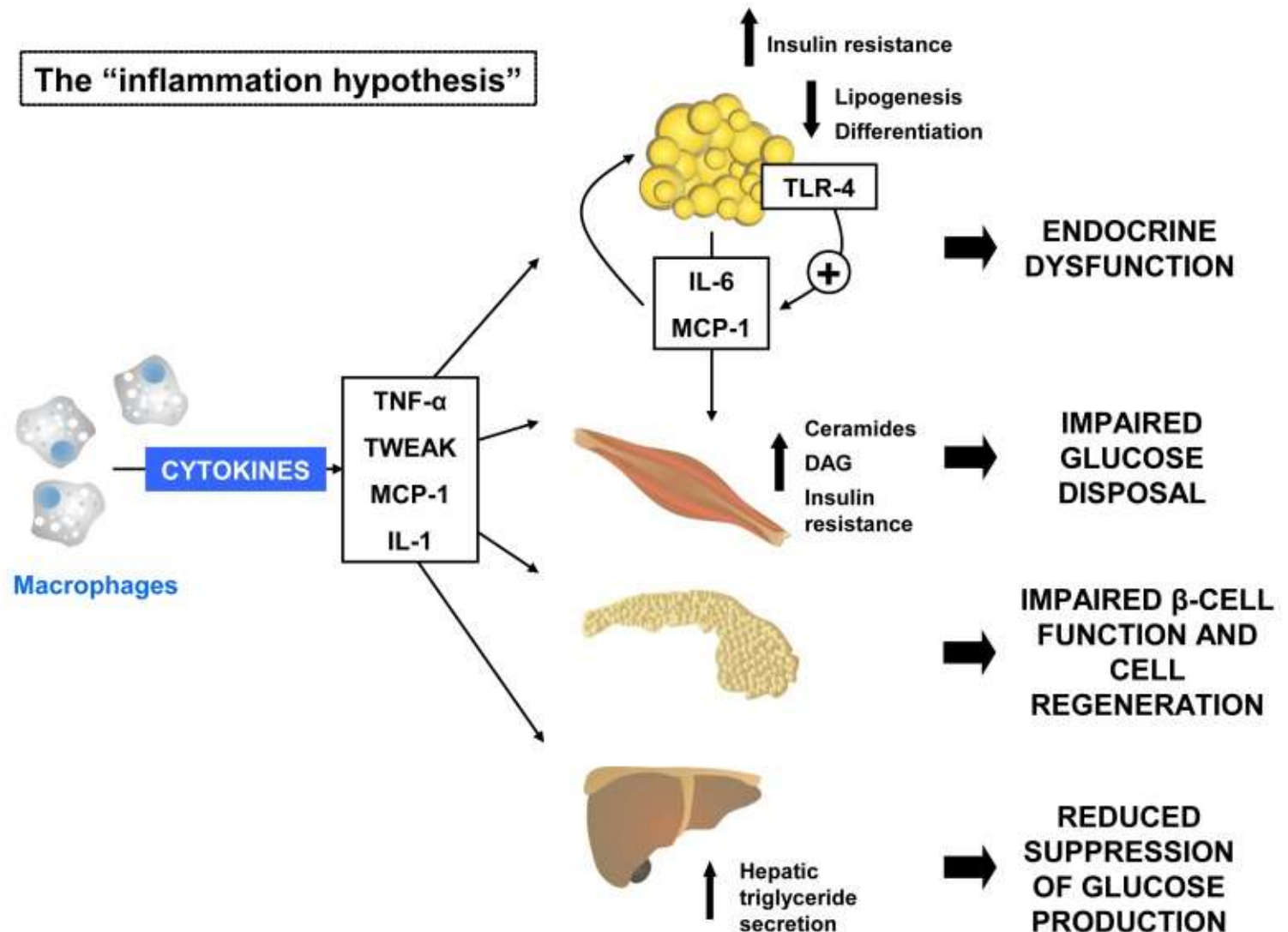
1 Rheumatology Department, University Hospitals Coventry and Warwickshire NHS Trust, Coventry, United Kingdom, **2** Warwick Medical School, University of Warwick, Coventry, United Kingdom, **3** Department of Imaging, University Hospitals Coventry and Warwickshire NHS Trust, Coventry, United Kingdom, **4** Warwickshire Institute for the Study of Diabetes, Endocrinology and Metabolism, University Hospitals Coventry and Warwickshire NHS Trust, Coventry, United Kingdom

Fig 1. Immunopathogenesis of psoriasis. Cell subsets and cytokine signaling pathways implicated in the pathogenesis of psoriasis. Damage to the epidermis triggers release of antimicrobial peptides including LL-37, which complexes with self-DNA released from cellular membrane rupture. DNA-LL-37 complexes are autoantigens of psoriasis, which are taken up by dendritic cells, resulting in IL-12 and IL-23 production. The IL-23/Th17 axis actuates a feedforward loop that favors keratinocyte proliferation, ultimately forming a psoriatic plaque. bFGF: basic fibroblast growth factor; DDC: dermal dendritic cell; GFs: growth factors; pDC: plasmacytoid dendritic cell; VEGF: vascular endothelial growth factor.

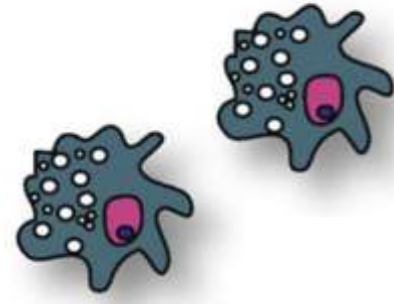


Molecular links between Obesity and Diabetes: “Diabesity”

A. Chadt, S. Scherneck, H.-G. Joost, H. Al-Hasani

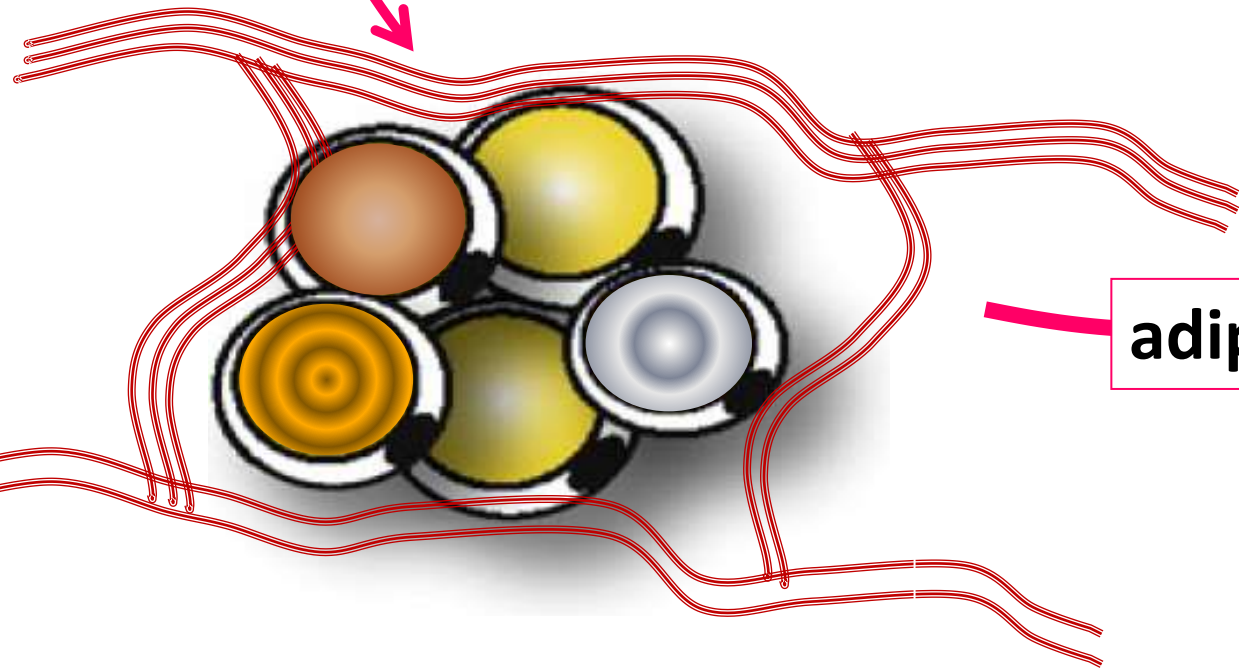


**citochine
(TNF- α , IL-6, ...)**



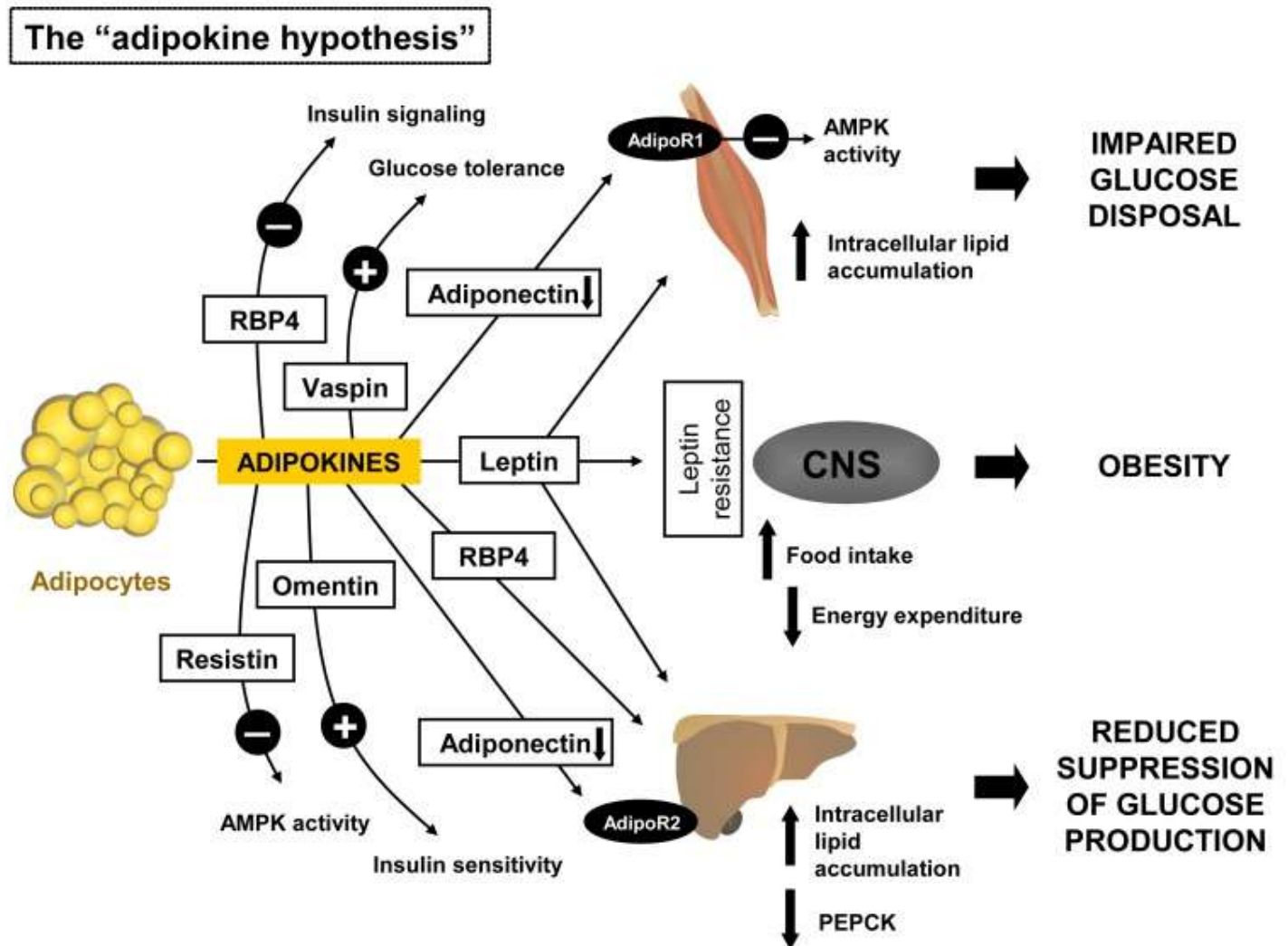
**attivazione e
migrazione macrofagi
(M1 proinfiammatori)**

adipochine

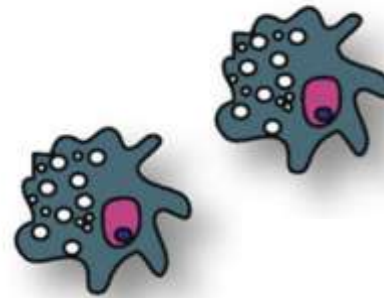


Molecular links between Obesity and Diabetes: “Diabesity”

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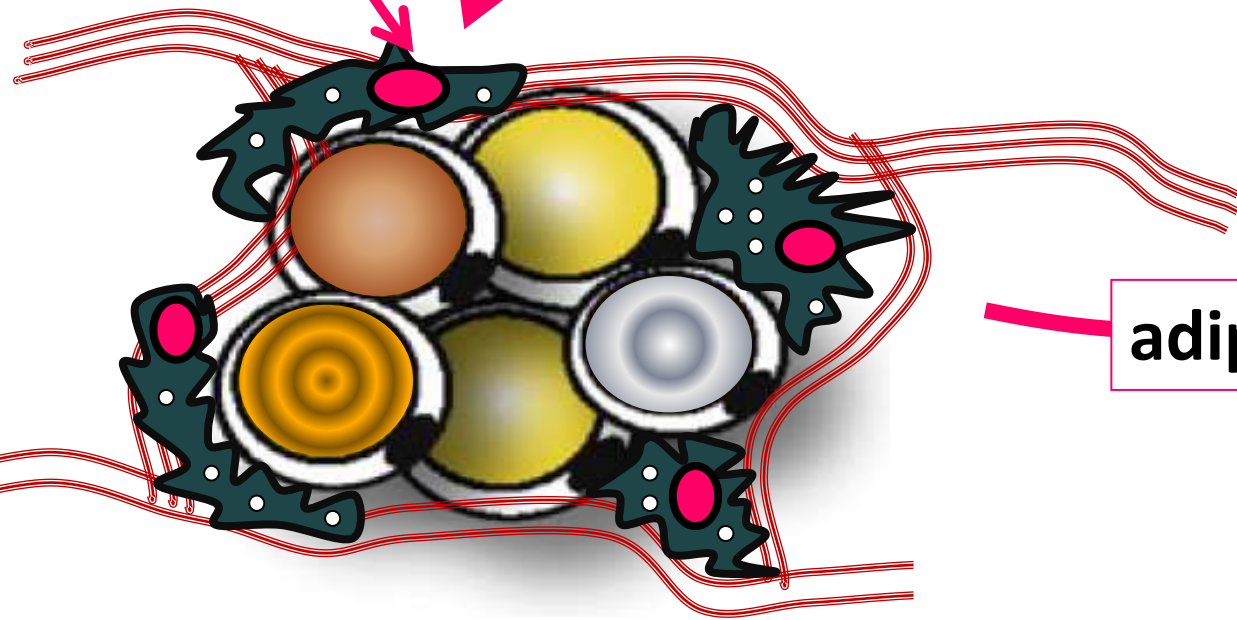


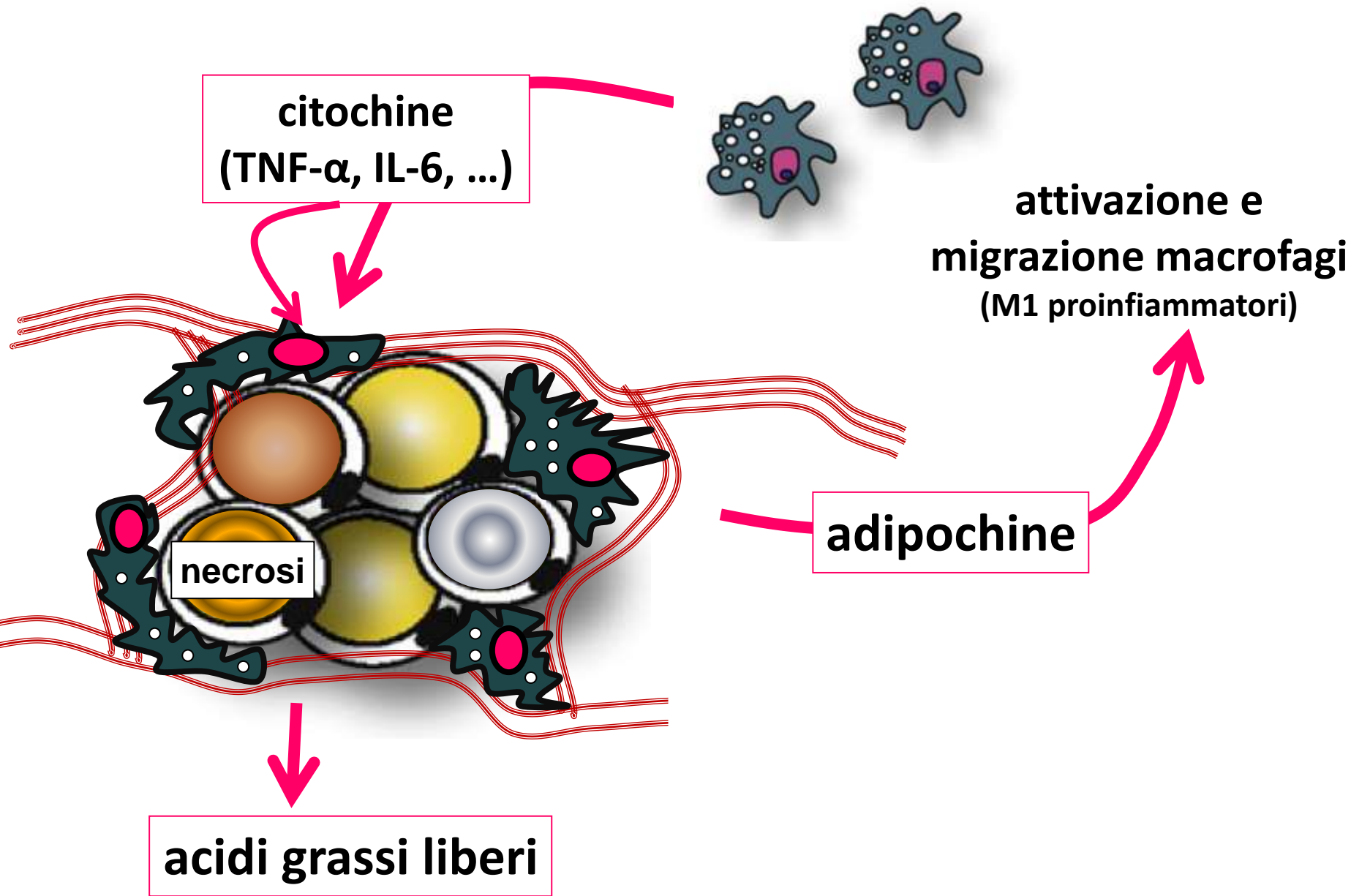
citochine
(TNF- α , IL-6, ...)

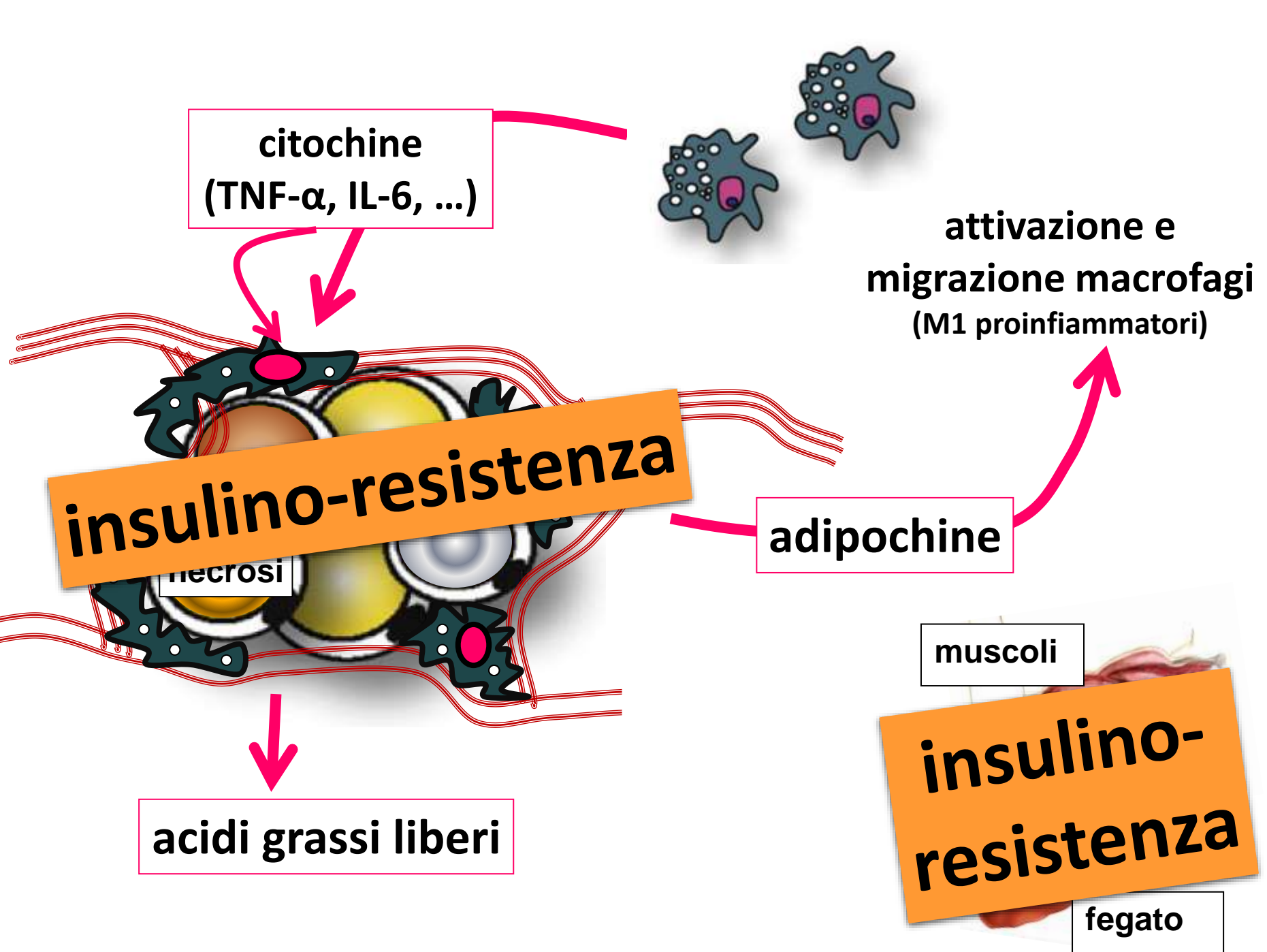


**attivazione e
migrazione macrofagi**
(M1 proinfiammatori)

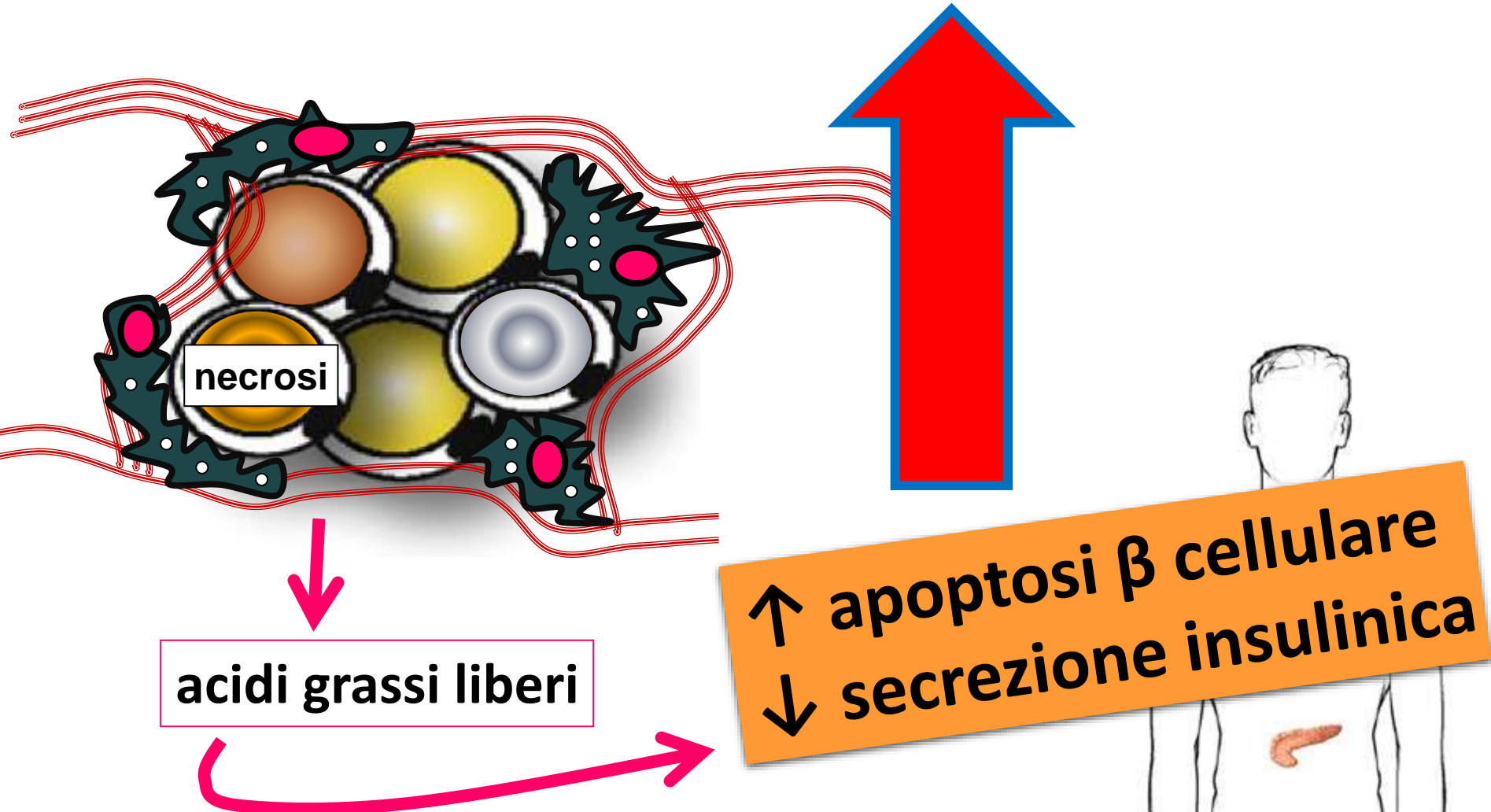
adipochine





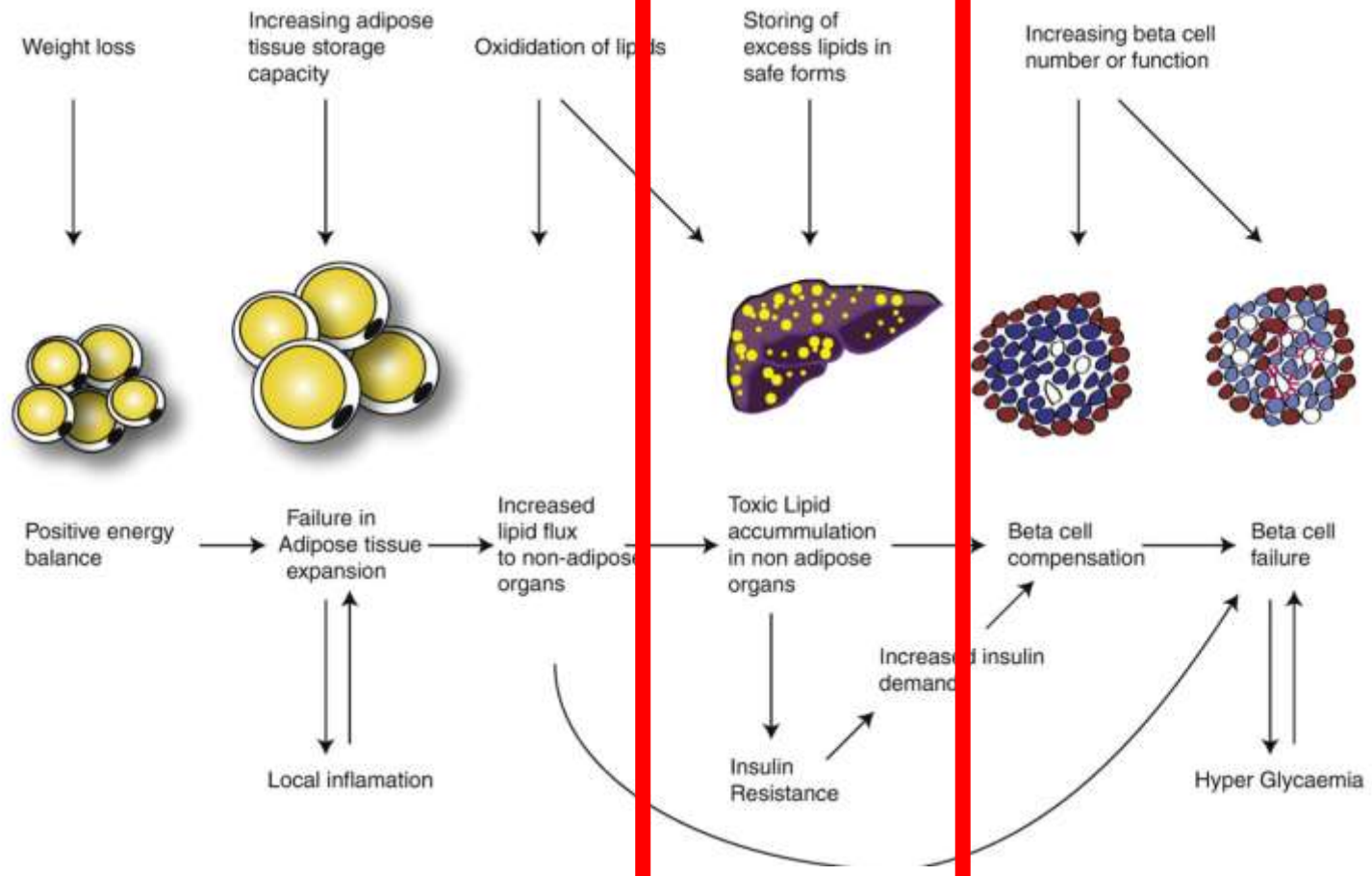


Diabete Mellito



Adipose tissue expandability, lipotoxicity and the Metabolic Syndrome – An allostatic perspective

Sam Virtue*, Antonio Vidal-Puig*



Pathways from obesity to hypertension: from the perspective of a vicious triangle

J-P Montani¹*, V Antic¹, Z Yang¹ and Abdul Dulloo¹

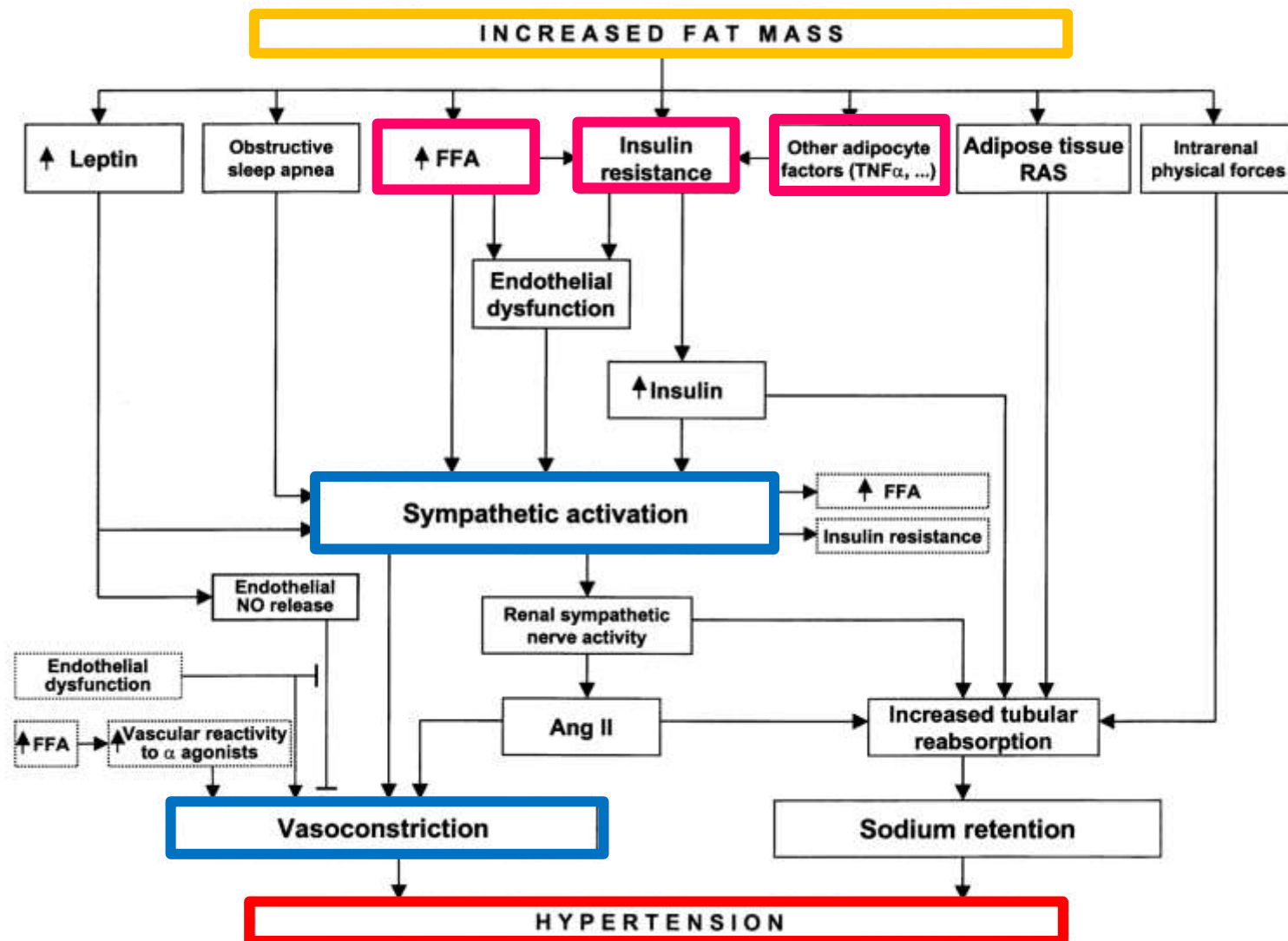


Figure 4 General scheme of mechanisms of obesity-induced hypertension. A number of factors induced or potentiated by obesity lead to sympathetic activation, vasoconstriction and sodium retention, all promoting hypertension. FFA, free fatty acids; TNF- α , tumor necrosis factor; RAS, renin – angiotensin system; NO, nitric oxide; Ang II, angiotensin II.

Metabolic syndrome is associated with an increased risk of psoriasis: A nationwide population-based study

Ha-Na Kim ^a, Kyungdo Han ^b, Yong-Gyu Park ^{b,s,1}, Ji Hyun Lee ^{c,**,1}

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^b Department of Biostatistics, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

^c Department of Dermatology, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

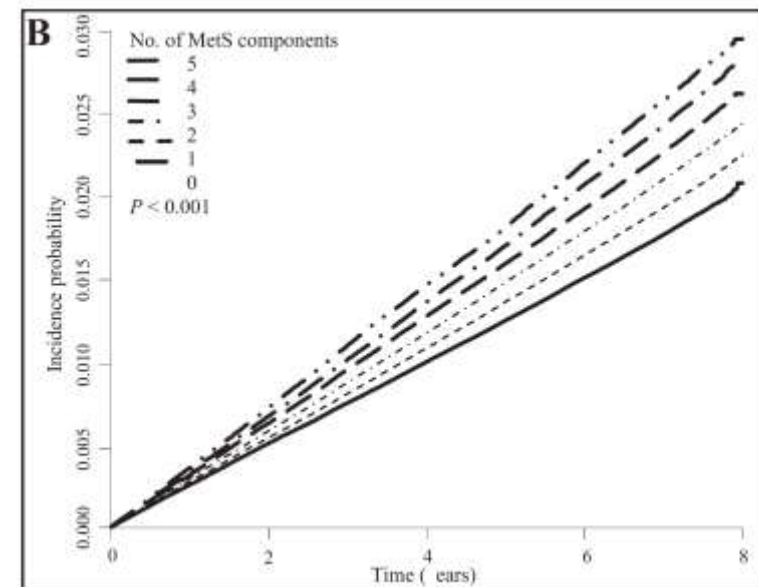
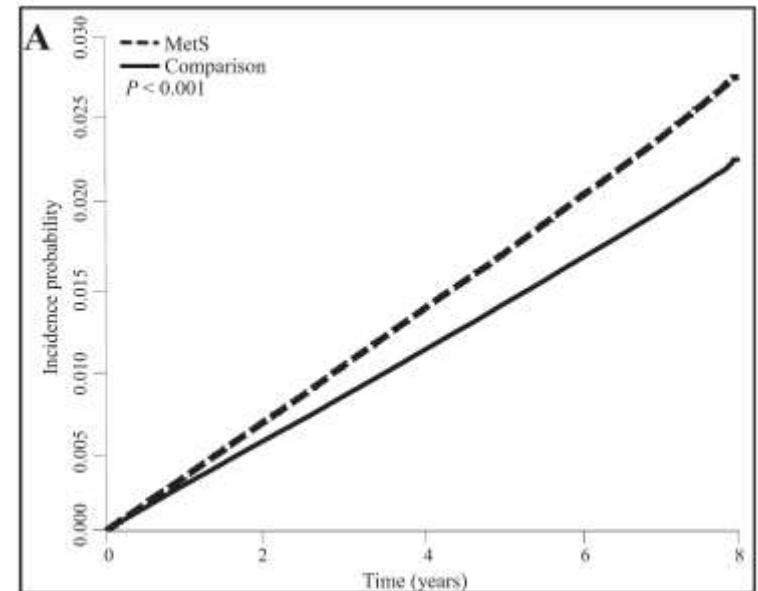





Fig. 2. Cumulative incidence of psoriasis by metabolic syndrome presence/absence (A) and the number of metabolic syndrome components (B) over 8 years of follow-up. P values were determined using the log-rank test. MetS: metabolic syndrome.

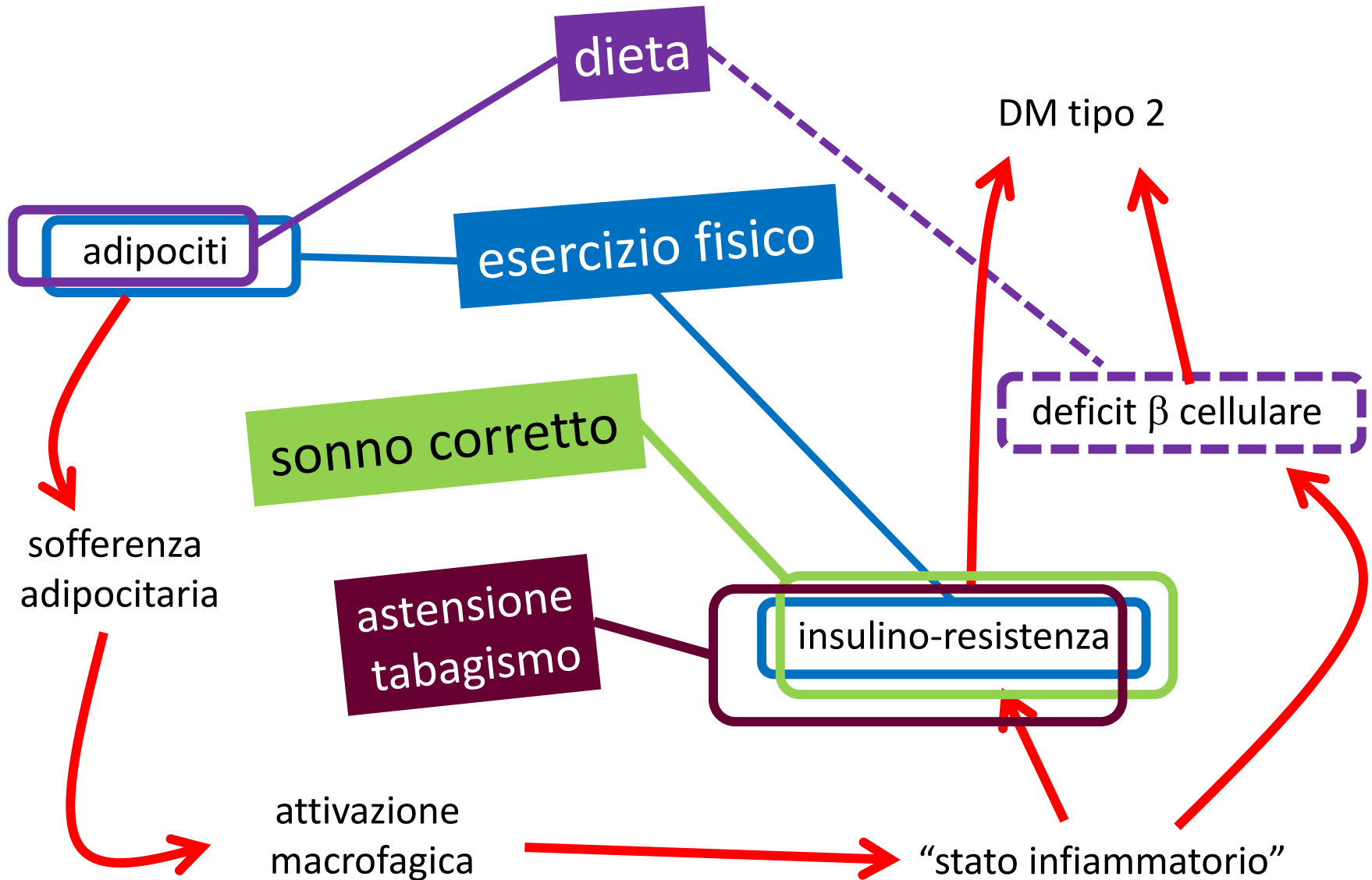
Practical recommendations for systemic treatment in psoriasis according to age, pregnancy, metabolic syndrome, mental health, psoriasis subtype and treatment history (BETA-PSO: Belgian Evidence-based Treatment Advice in Psoriasis; part 1)

J.L.W. Lambert,^{1,*}  S. Segaert,² P.D. Ghislain,³ T. Hillary,⁴  A. Nikkels,⁵ F. Willaert,⁶ J. Lambert,⁷
R. Speeckaert¹ 

Strong recommendation in favour	Weak recommendation in favour	Weak recommendation against: evaluate risk versus benefit case by case	Strong recommendation against	Insufficient evidence to make a recommendation
"Will be efficacious and cause no specific harm in this patient group"	"Will likely be efficacious and likely cause no specific harm in this patient group"	"Might/may be less efficacious or might/may cause harm in this patient group"	"Likely to cause harm in this patient group"	
Psychiatric disorders ACIT, MTX, CYCLO, FUM ADA, CERT, ETA, IFX UST, GUS, RIS, TIL SEC, IXE		APR BROD		
Metabolic syndrome FUM APR ADA, CERT, ETA, IFX UST, GUS, RIS, TIL SEC, IXE, BROD	ACIT, MTX, CYCLO			
Diabetes or insulin resistance ACIT, FUM APR ADA, CERT, ETA, IFX UST, GUS, TIL, RIS SEC, IXE, BROD	MTX, CYCLO			
Obesity FUM APR IFX UST IXE, BROD RIS, GUS	ADA, CERT, ETA SEC TIL	ACIT, MTX, CYCLO		
Cardiovascular risk factors MTX, FUM, APR ADA, CERT, ETA, IFX (case without heart failure) SEC, IXE, BROD UST, GUS, TIL, RIS		ACIT, CYCLO	ADA, CERT, ETA, IFX (case with heart failure)	
Non-alcoholic fatty liver disease CYCLO APR ADA, CERT, ETA, IFX UST, GUS, RIS, TIL SEC, IXE, BROD		ACIT, MTX, FUM		
Nail psoriasis				

ACIT, acitretin; ADA, adalimumab; APR, apremilast; BROD, brodalumab; CERT, certolizumab pegol; CYCLO, cyclosporin; ETA, etanercept; GUS, guselkumab; IFX, infliximab; IXE, ixekizumab; RIS, risankizumab; SEC, secukinumab; TIL, tildrakizumab; UST, ustekinumab. Green: will be efficacious and cause no specific harm in this patient group; Light green: will likely be efficacious and likely cause no specific harm in this patient group; Orange: might/may be less efficacious or might/may cause harm in this patient group; Red: likely to cause harm in this patient group; Grey: insufficient evidence to make a recommendation.

Quali possibilità di intervento sulle comorbidità metaboliche?



Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis

Clare L Gillies, medical statistician¹, Keith R Abrams, professor of medical statistics¹, Paul C Lambert, senior lecturer in medical statistics¹, Nicola J Cooper, MRC senior training fellow in health services research¹, Alex J Sutton, reader in medical statistics¹, Ron T Hsu, clinical senior teaching fellow in epidemiology and public health¹, Kamlesh Khunti, clinical senior lecturer²

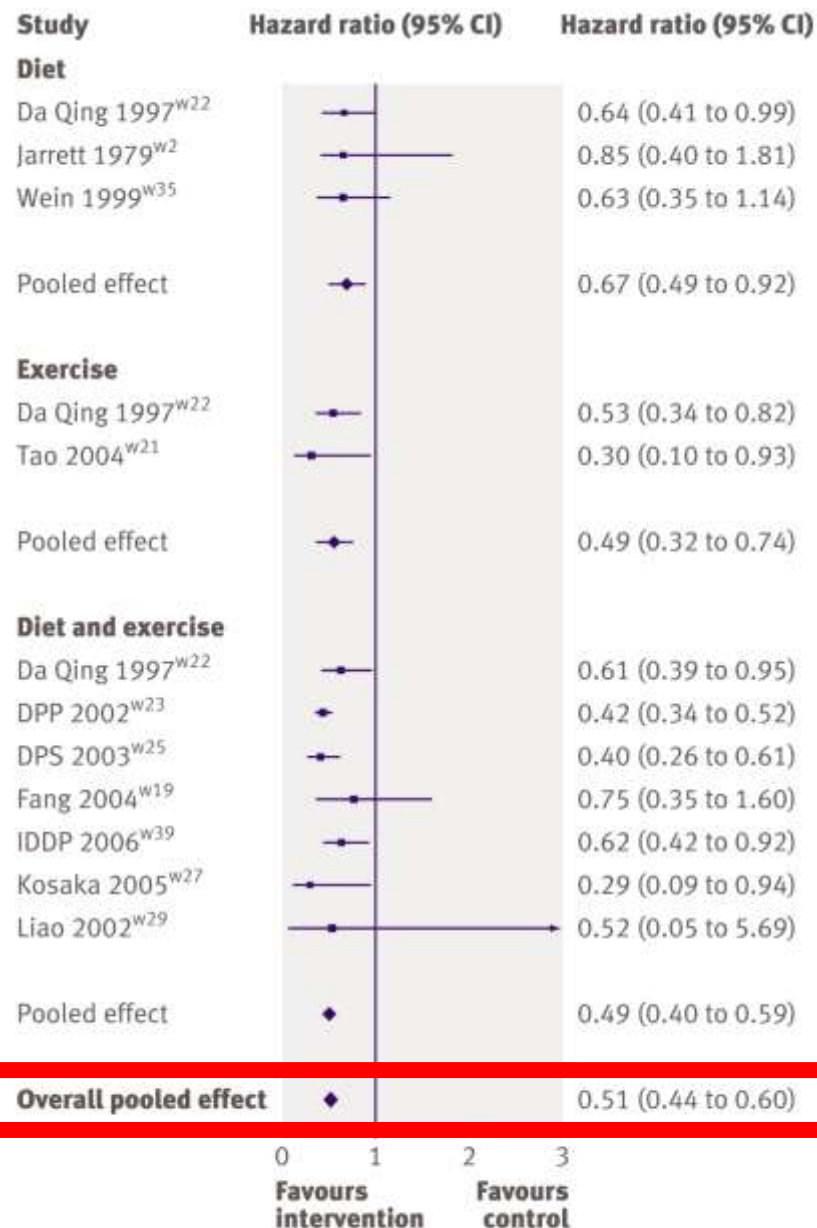
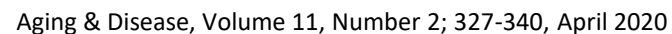


Fig 2 | Meta-analysis of effect of lifestyle interventions on risk of developing type 2 diabetes

Piotr Gronek^{1,4}, Dariusz Wielinski², Piotr Cyganski³, Andrzej Rynkiewicz³, Adam Zając⁴, Adam Maszczyk⁵, Joanna Gronek¹, Robert Podstawski⁶, Wojciech Czarny⁷, Stefan Balko⁸, Cain CT. Clark⁹, Roman Celka¹





Mind&Move Health Specialist

Specialista della Salute Psico-Fisica



**il MASTER universitario
per una rete
"assistenziale" integrata**

obiettivi formativi

formare professionisti che
lavorino **in team**
con una strategia coordinata e
un approccio **interdisciplinare**
per portare i cittadini ad uno
stato di **completo benessere**
fisico, psichico e sociale



VISITA IL NOSTRO
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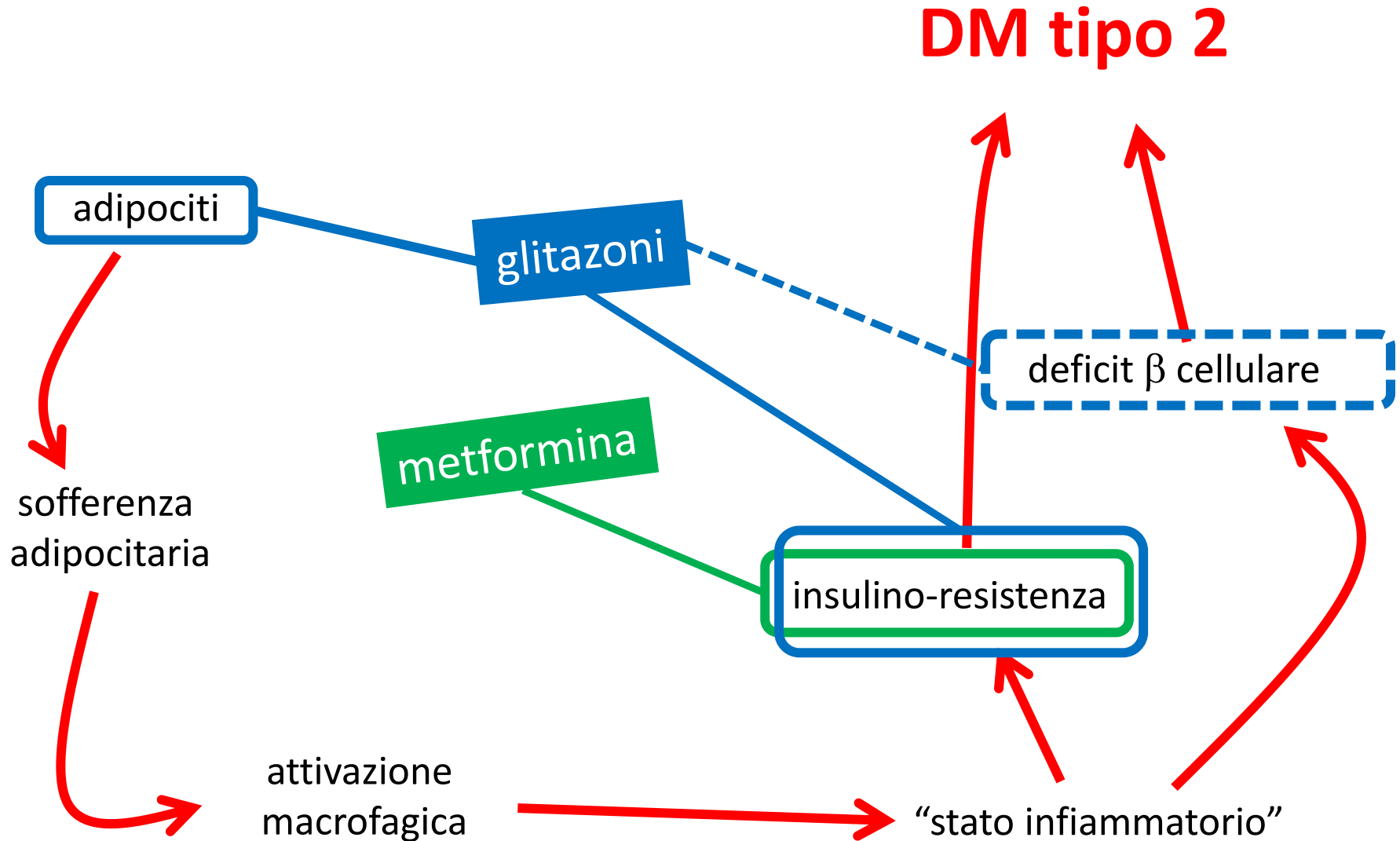
Referenti Amministrative per il Master:
Monica Rege e Ilaria Bisaro, master.medsanluigi@unito.it

MIND & MOVE s.r.l.:
Resp. Segreteria e Amministrazione:
Cristina Fortuna, amministrazione@mindtomove.it

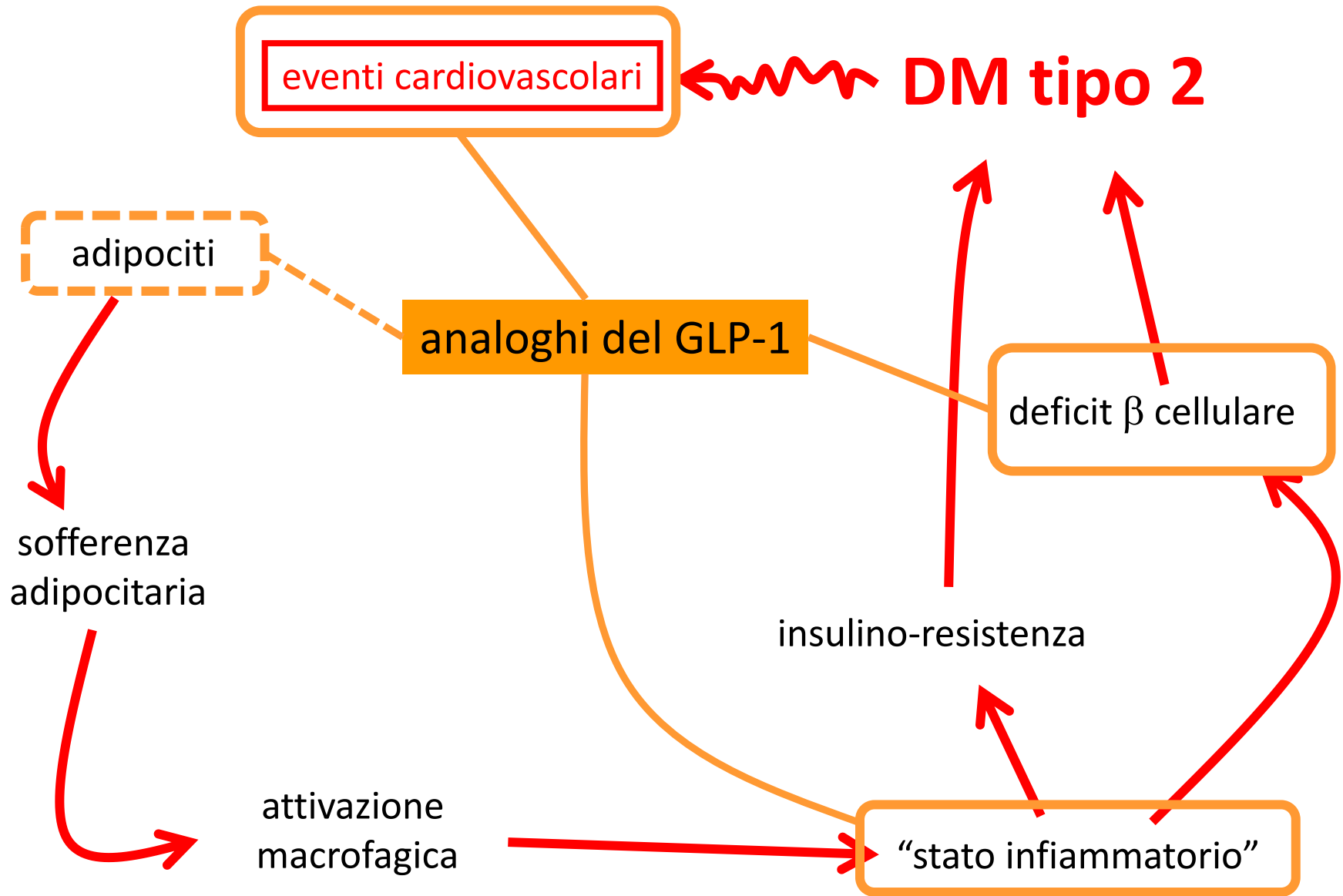


UNIVERSITÀ DEGLI STUDI DI TORINO

Quali possibilità di intervento sulle comorbidità metaboliche?



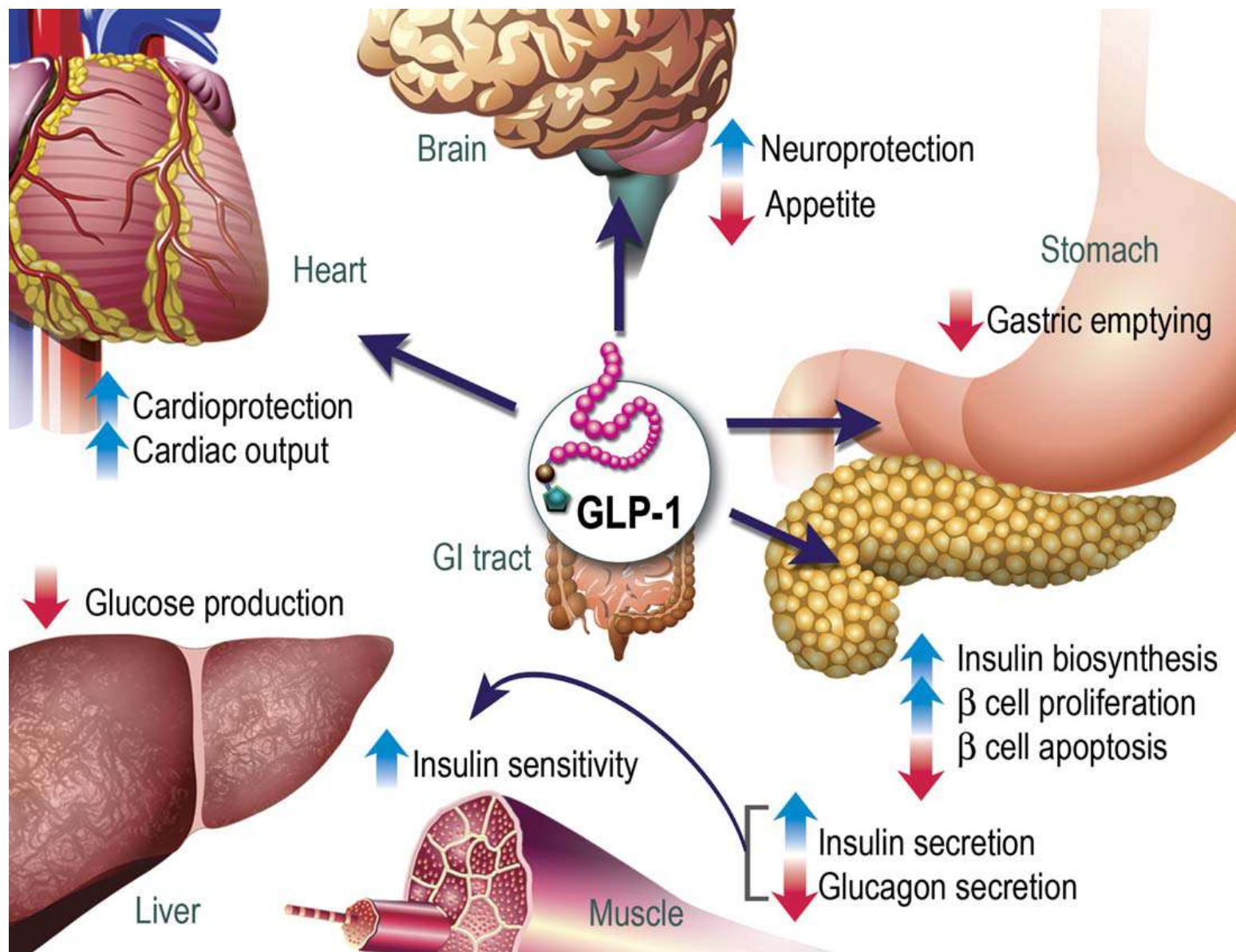
Quali possibilità di intervento sulle comorbidità metaboliche?



Gli analoghi del GLP-1

Drug	Dosing
Exenatide	5-10 mcg SC twice daily prior to meals
Exenatide ER	2 mg SC once weekly without regard to meals
Liraglutide	0.6-1.8 mg SC once daily without regard to meals
Albiglutide	30-50 mg SC once weekly without regard to meals
Dulaglutide	0.75-1.5 mg SC once weekly without regard to meals
Lixisenatide	10 mg SC once daily prior to first meal of the day for 14 days. On day 15, increase dosage to 20 mg SC once daily
Semaglutide	0.25 mg SC once weekly for 1 month, then increase to 0.5 mg weekly for 1 month, then increase to 1.0 mg weekly SC

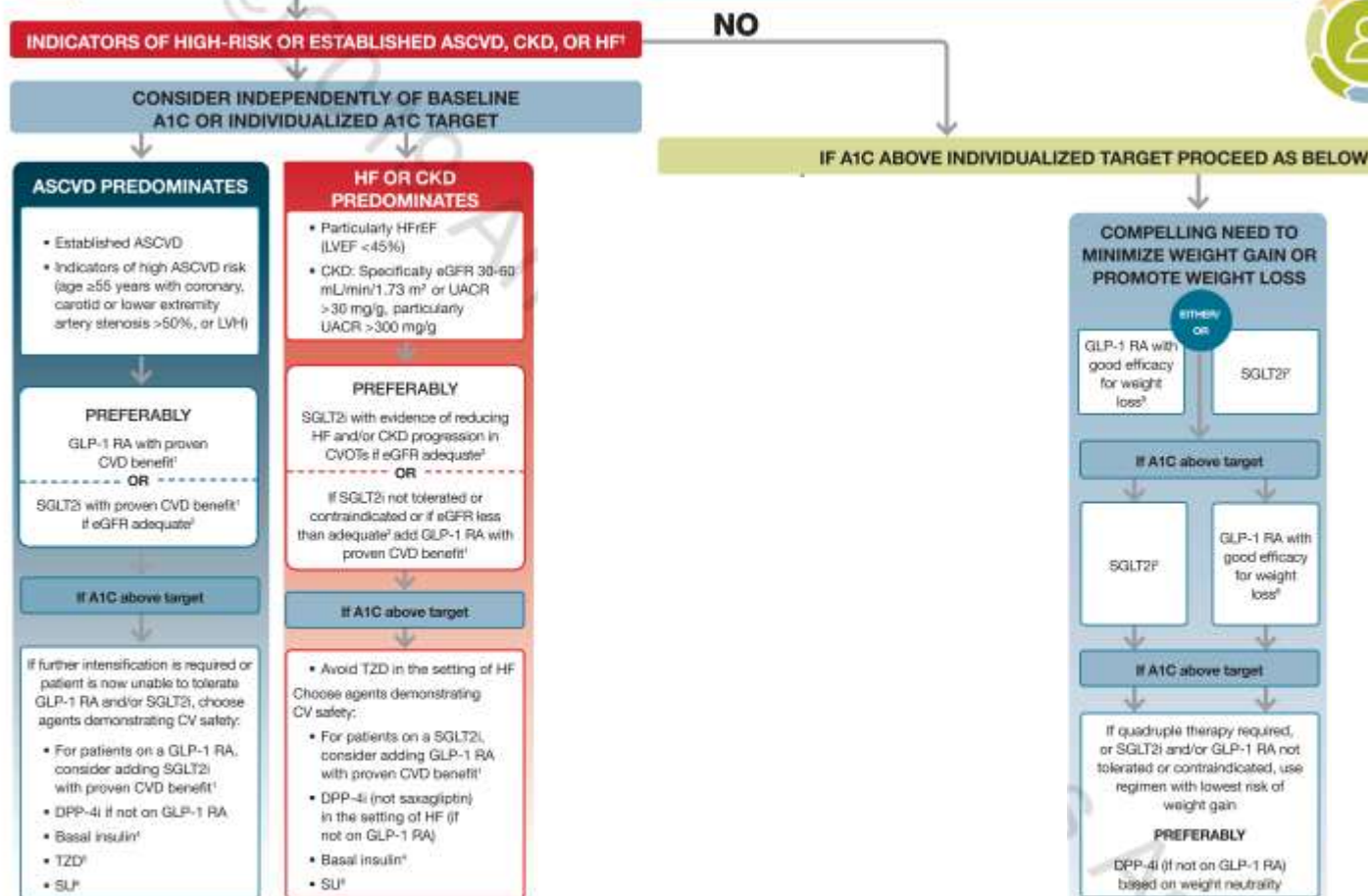
Azioni extra-pancreatiche del GLP-1



STANDARDS OF MEDICAL CARE IN DIABETES—2020



FIRST-LINE Therapy is Metformin and Comprehensive Lifestyle (including weight management and physical activity)



1. Proven CVD benefit means it has label indication of reducing CVD events

2. Be aware that SGLT2i labelling varies by region and individual agent with regard to indicated level of eGFR for initiation and continued use

3. Empagliflozin, canagliflozin and dapagliflozin have shown reduction in HF and to reduce CKD progression in CVDs. Canagliflozin has primary renal outcome data from CREDENCE. Dapagliflozin has primary heart failure outcome data from DAPA-HF

4. Degludec or U100 glargine have demonstrated CVD safety

5. Low dose may be better tolerated though less well studied for CVD effects

† Acted whenever these become new clinical considerations regardless of background glucose-lowering medications.

Effect of glucagon-like peptide-1 receptor agonists in patients with psoriasis

Marwa R. Al-Badri and Sami T. Azar

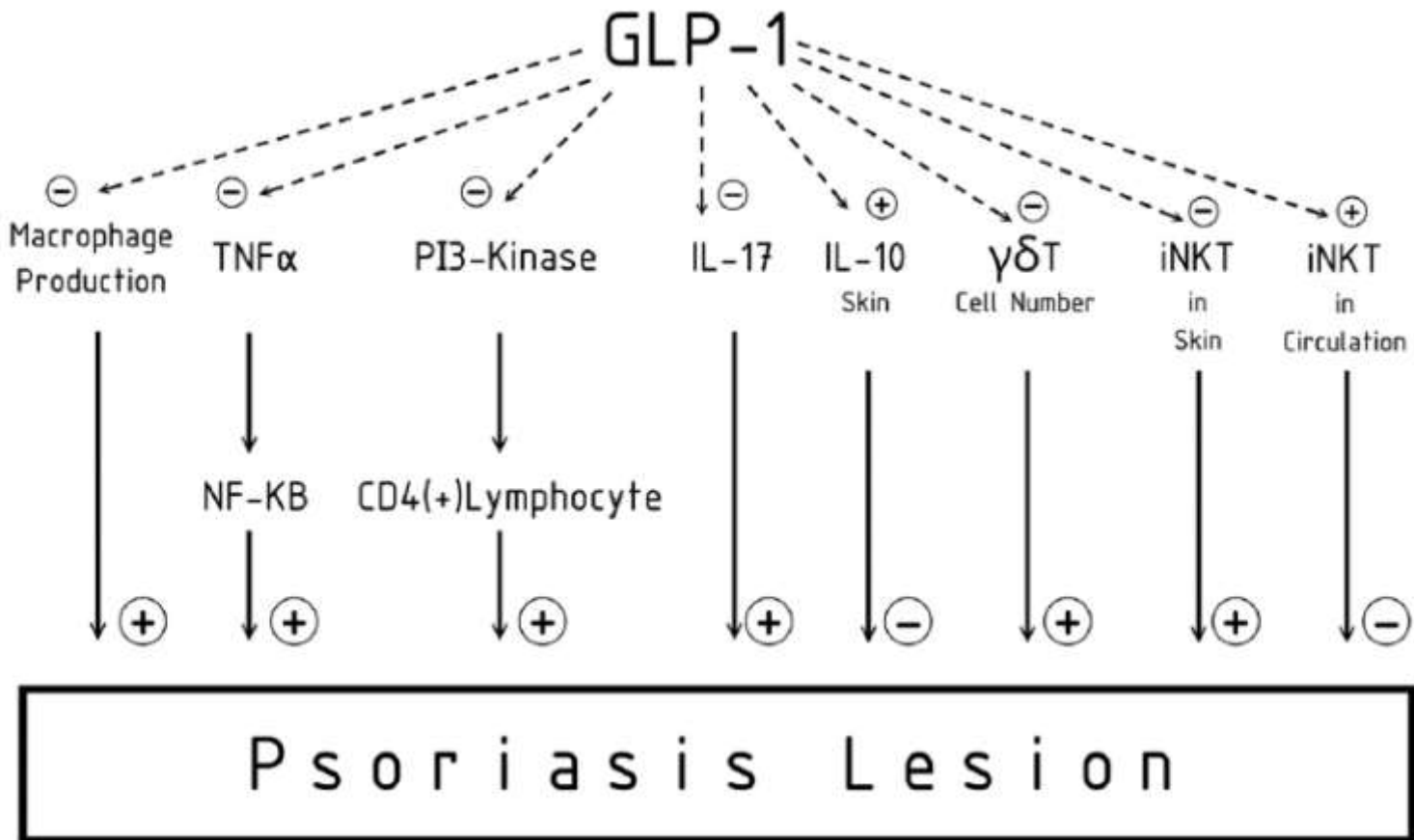


Figure 2. The immunologic role of GLP-1. GLP-1, glucagon-like peptide; IL, interleukin; iNKT, invariant natural killer T cell; NF- κ B, nuclear factor-kappa B; PI3-kinase, phosphatidylinositol-4,5-bisphosphate 3-kinase; TNF- α ; tumor necrosis factor- α .

Conclusioni

Esiste una reciproca relazione in induzione di rischio tra psoriasi e le patologie componenti la sindrome metabolica che esita in un incremento del rischio globale per eventi e mortalità cardiovascolari.

Su tale base, come da indicazione di linee guida è opportuno sottoporre i pazienti affetti da psoriasi ad uno screening periodico delle patologie metaboliche e dei fattori di rischio modificabili ad esse associate tra cui tabagismo, sedentarietà e alterazioni del sonno al fine di permettere una eventuale diagnosi precoce ed un trattamento tempestivo con interventi integrati sullo stile di vita e con terapie farmacologiche mirate.