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AIGEF
Associazione Italiana Ginecologia Estetica e Funzionale
LA GINECOLOGIA E L'OSTETRICIA
AL DI FUORI DELL'OSPEDALE
Fare, non fare, demandare
Milano 22-23 GIUGNO 2018

Gestione della Diabesity: Territorio – Ospedale

Gabriele Rossi

Clinica Luigi Mangiagalli, Milano

Sistema Socio Sanitario
Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico
Regione Lombardia

Diabesity

L’obesità è solo un preambolo per il diabete?

Original Article

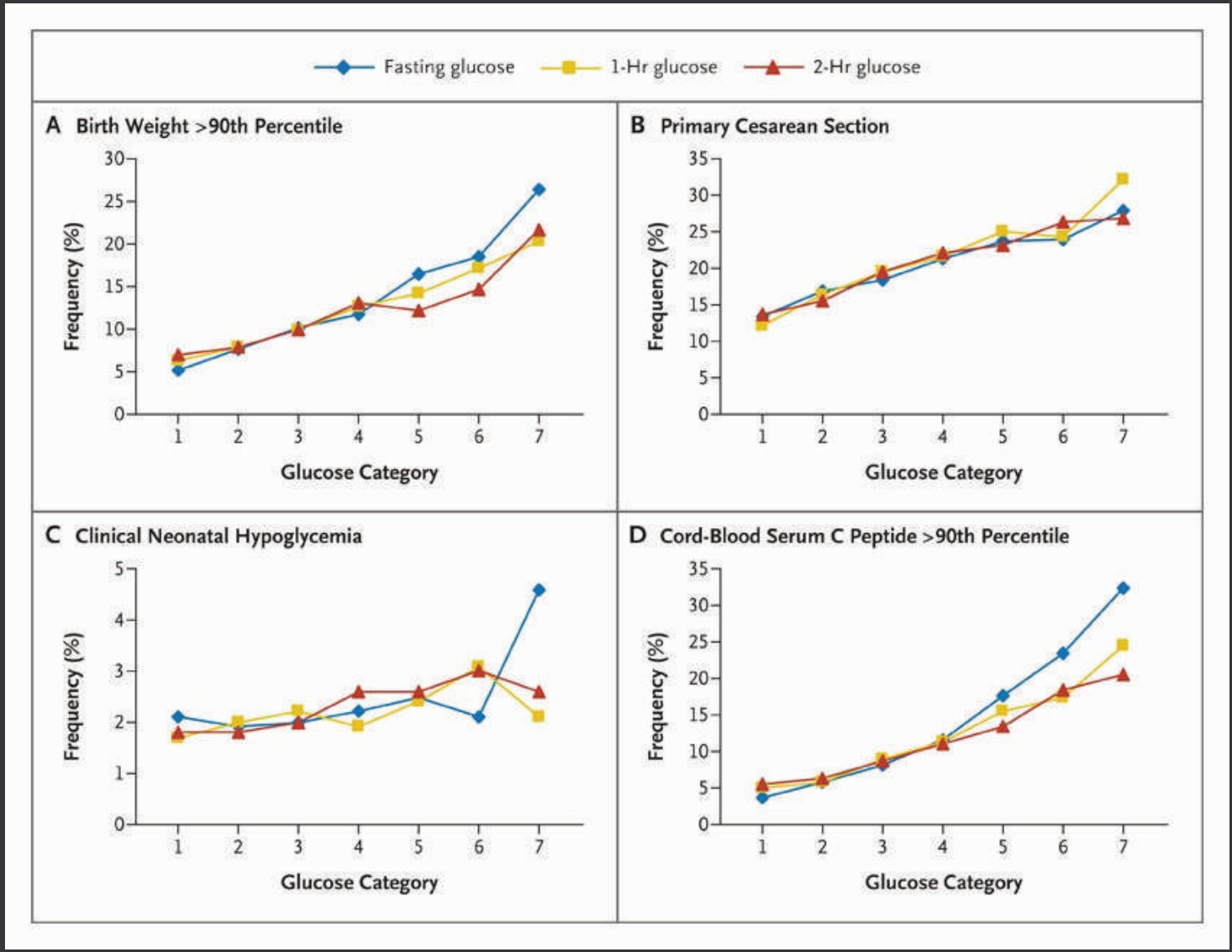
Hyperglycemia and Adverse Pregnancy Outcomes

The HAPO Study Cooperative Research Group

N Engl J Med
Volume 358(19):1991-2002
May 8, 2008

The NEW ENGLAND JOURNAL of MEDICINE

Frequency of Primary Outcomes across the Glucose Categories



The HAPO Study Cooperative Research Group. N Engl J Med 2008;358:1991-2002

The NEW ENGLAND JOURNAL of MEDICINE

DOI: 10.1111/j.1471-0528.2009.02486.x
www.bjog.org

Epidemiology

Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) Study: associations with maternal body mass index

HAPO Study Cooperative Research Group*

Correspondence: Dr BE Metzger, Northwestern University Feinberg School of Medicine, Endocrinology, 645 North Michigan Avenue, Suite 530-22, Chicago, IL 60611, USA. Email: bem@northwestern.edu

Accepted 6 December 2009. Published Online 20 January 2010.

BJOG An International Journal of Obstetrics and Gynaecology

Rischio di LGA

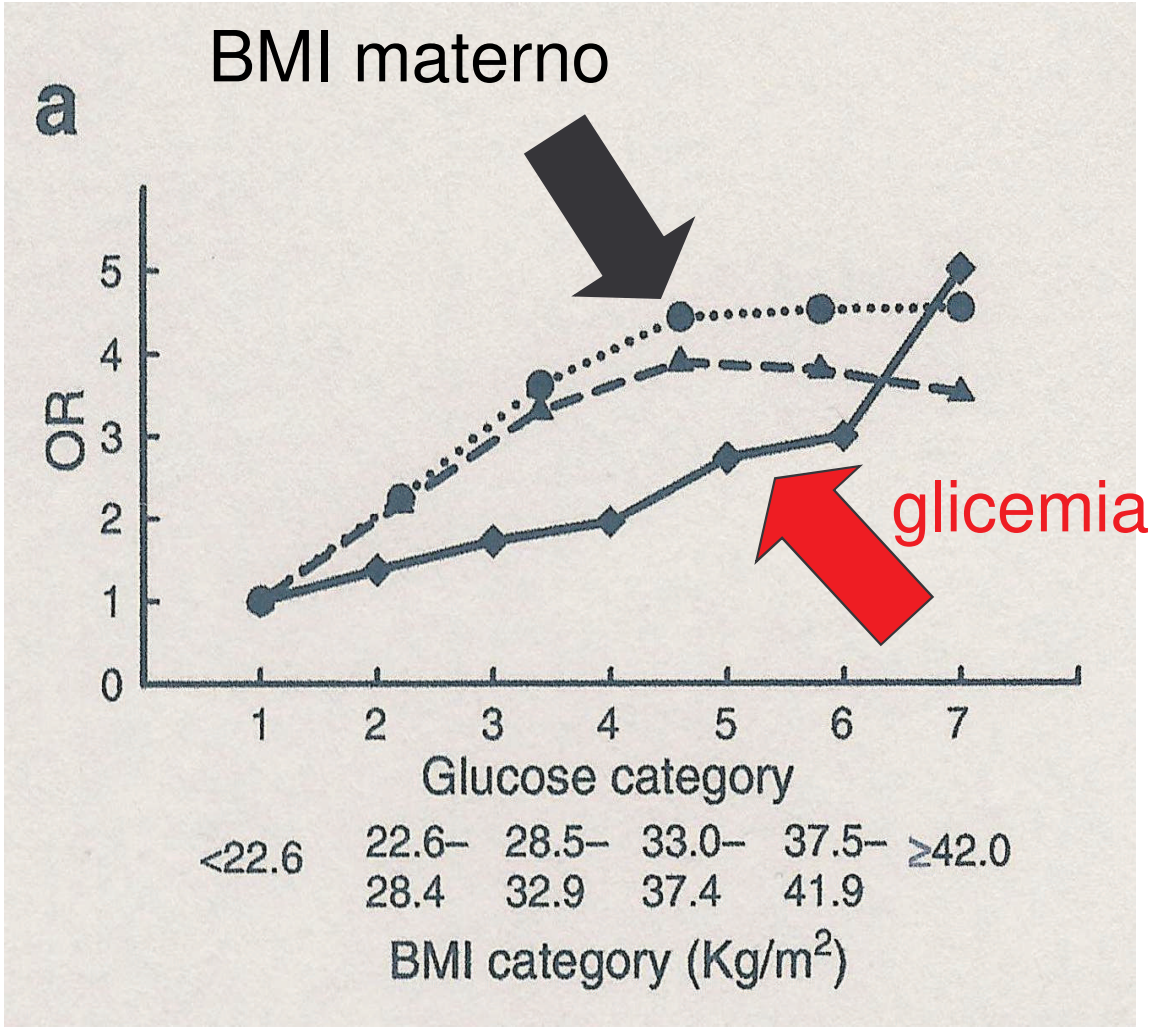
Diabetologia (2011) 54:480–486
DOI 10.1007/s00125-010-2005-4

FOR DEBATE

Diagnosing gestational diabetes

E. A. Ryan

Springer
DIABETOLOGIA
springer.com



Epidemiology/Health Services Research
ORIGINAL ARTICLE

DIABETES CARE, VOLUME 35, APRIL 2012

The Hyperglycemia and Adverse Pregnancy Outcome Study

Associations of GDM and obesity with pregnancy outcomes

American Diabetes Association. Diabetes Care

Table 2—*Relationship between maternal GDM, obesity, and outcomes*

Outcome	N	No.	%	Model I OR	95% CI	Model II OR	95% CI
Newborn percent body fat >90th percentile[5]							
No GDM, no obesity	14,367	1,143	8.0	1.00		1.00	
GDM, no obesity	2,338	331	14.2	1.91	(1.67–2.18)	1.98	(1.73–2.27)
No GDM, obesity	1,854	233	12.6	1.66	(1.43–1.93)	1.65	(1.41–1.93)
GDM, obesity	768	185	24.1	3.67	(3.08–4.38)	3.69	(3.06–4.44)
Cord C-peptide >90th percentile[2]							
No GDM, no obesity	14,886	916	6.2	1.00		1.00	
GDM, no obesity	2,419	386	16.0	2.90	(2.54–3.30)	2.49	(2.17–2.85)
No GDM, obesity	1,829	201	11.0	1.80	(1.52–2.12)	1.77	(1.49–2.11)
GDM, obesity	751	168	22.4	4.14	(3.43–5.00)	3.61	(2.94–4.42)

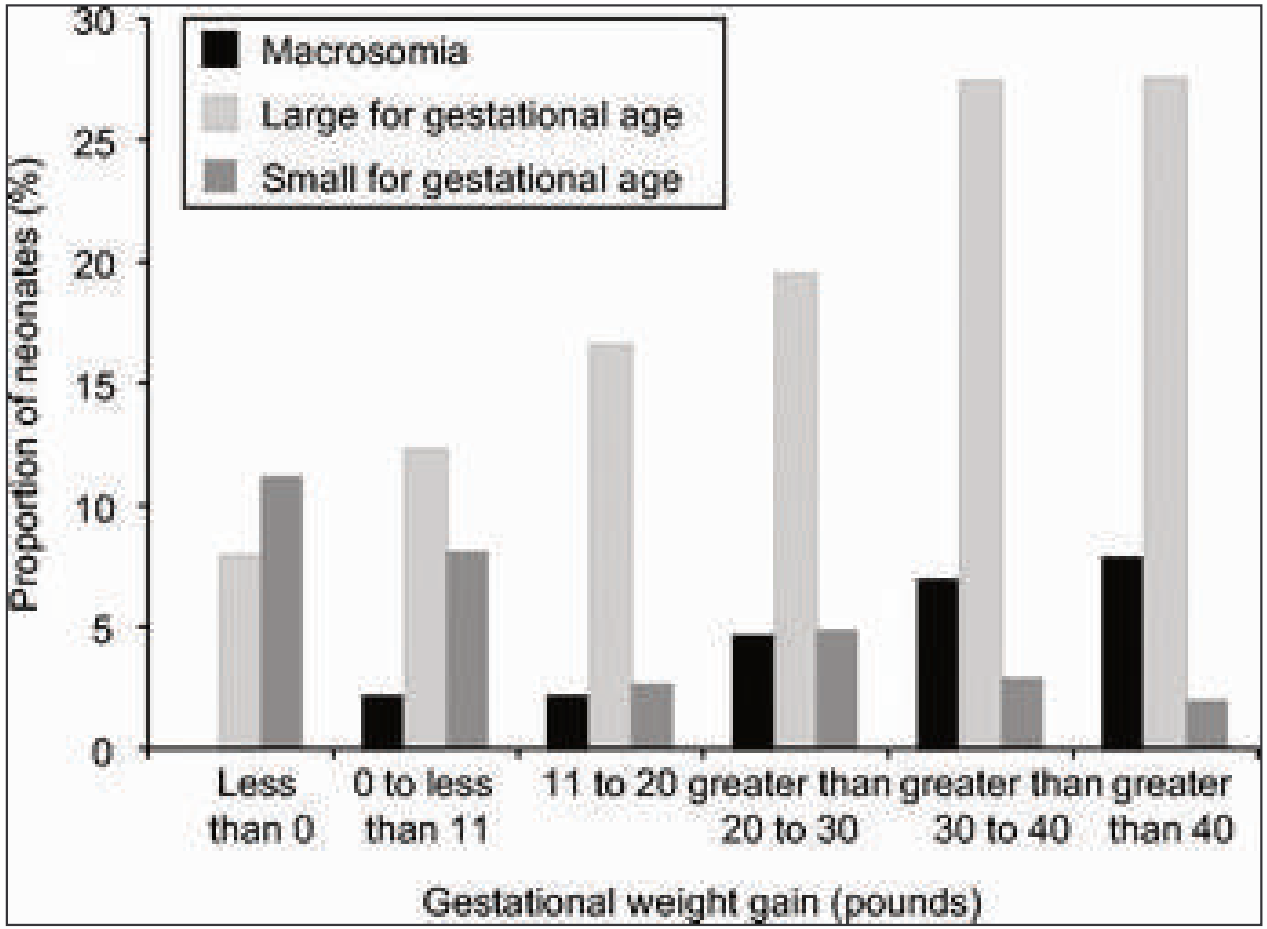
L'obesità indipendentemente dal diabete è un fattore di rischio per l'esito neonatale

Newborn Size Among Obese Women With Weight Gain Outside the 2009 Institute of Medicine Recommendation

Kimberly K. Vesco, MD, MPH, Andrea J. Sharma, PhD, MPH, Patricia M. Dietz, DrPH, MPH, Joanne H. Rizzo, MPA, William M. Callaghan, MD, MPH, Lucinda England, MD, MSPH, F. Carol Bruce, BSN, MPH, Donald J. Bachman, MS, Victor J. Stevens, PhD, and Mark C. Hornbrook, PhD

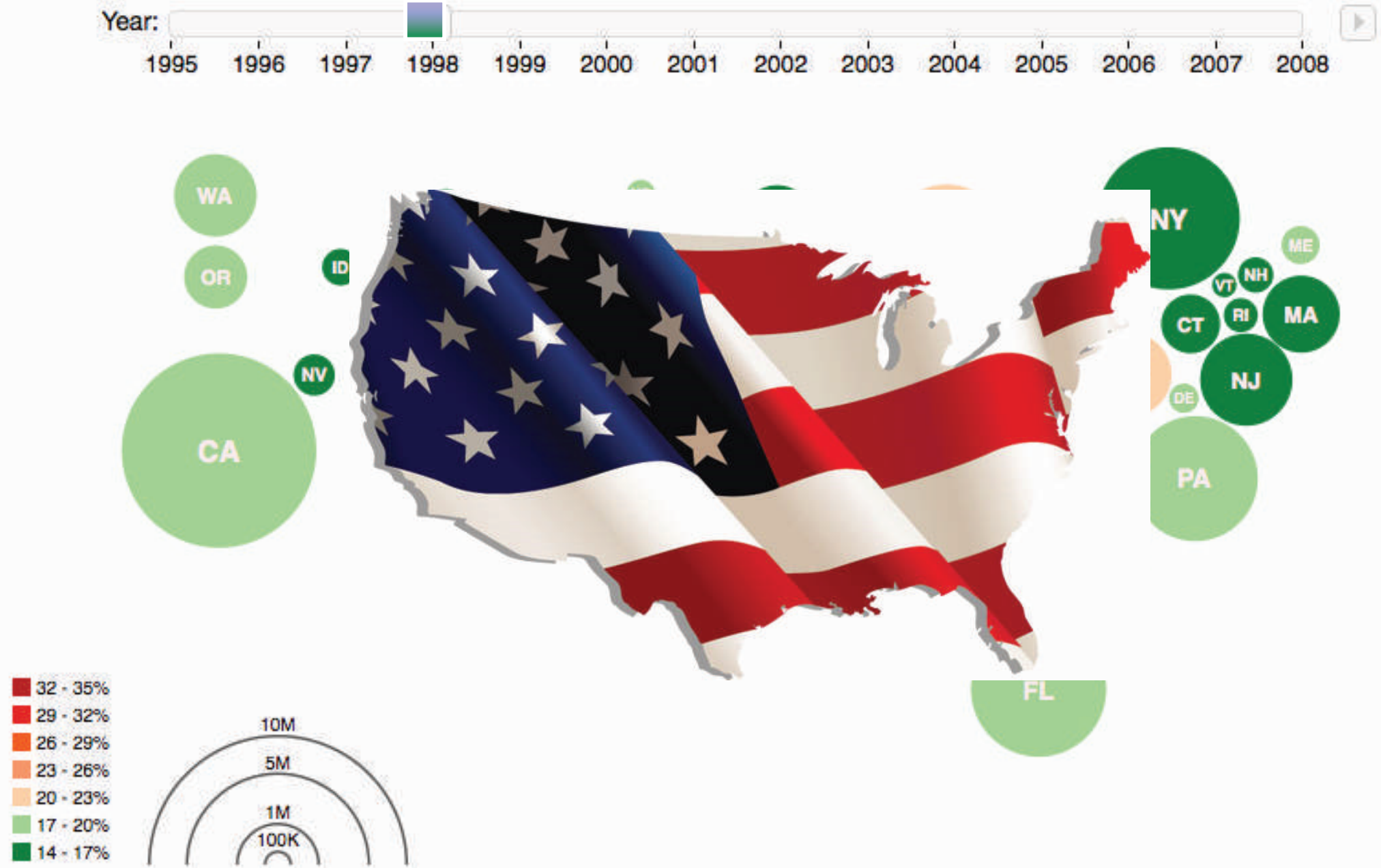
OBSTETRICS & GYNECOLOGY

L'eccessivo incremento ponderale nelle gravide obese è un ulteriore fattore di rischio per la crescita fetale eccessiva

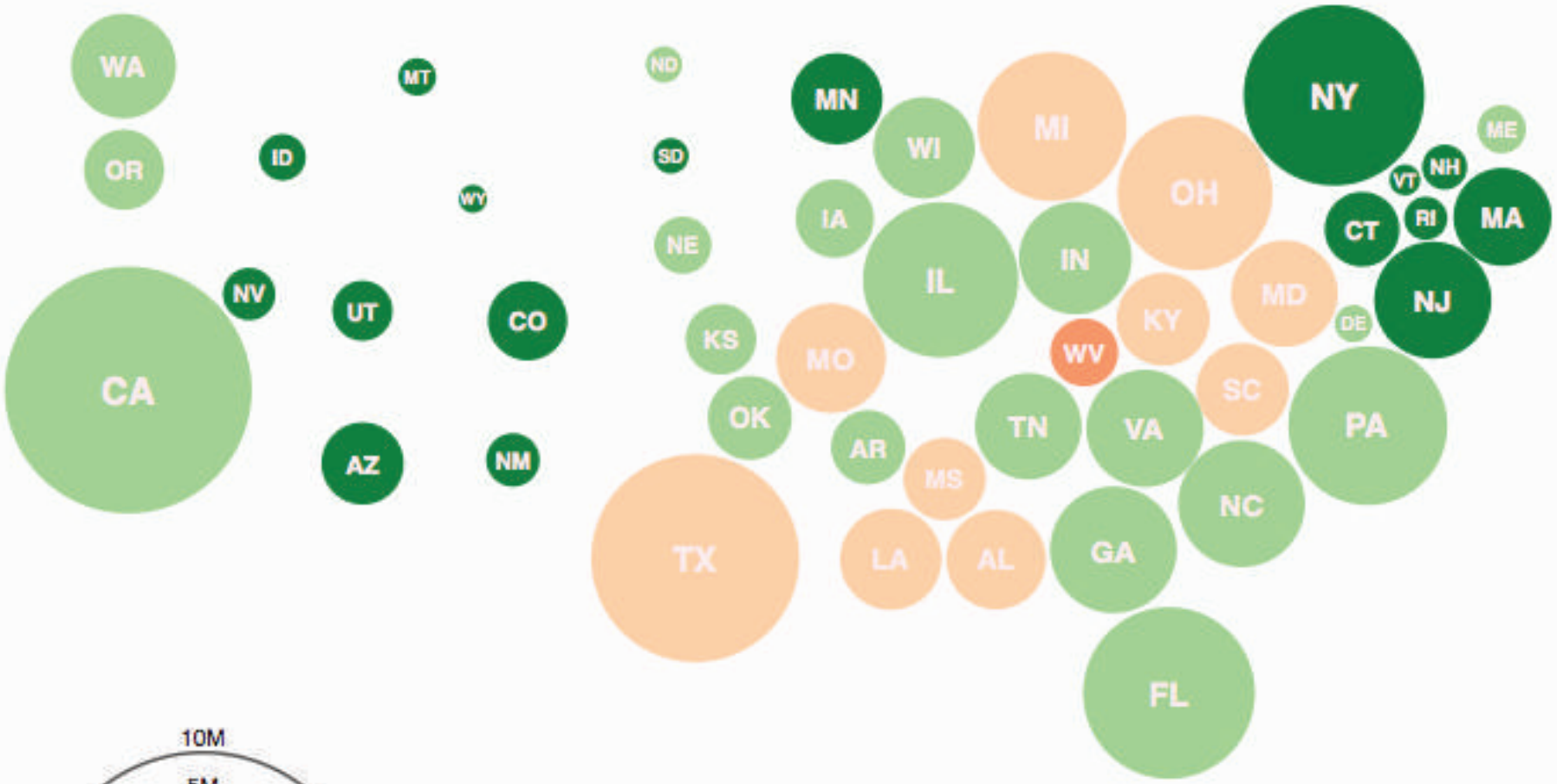


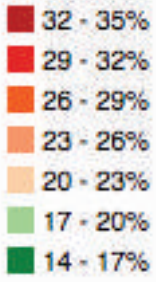
L’incremento dell’obesità è epidemico

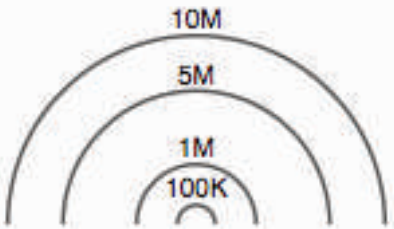
Dorling Cartogram of Obesity in the United States (1995 to 2008)



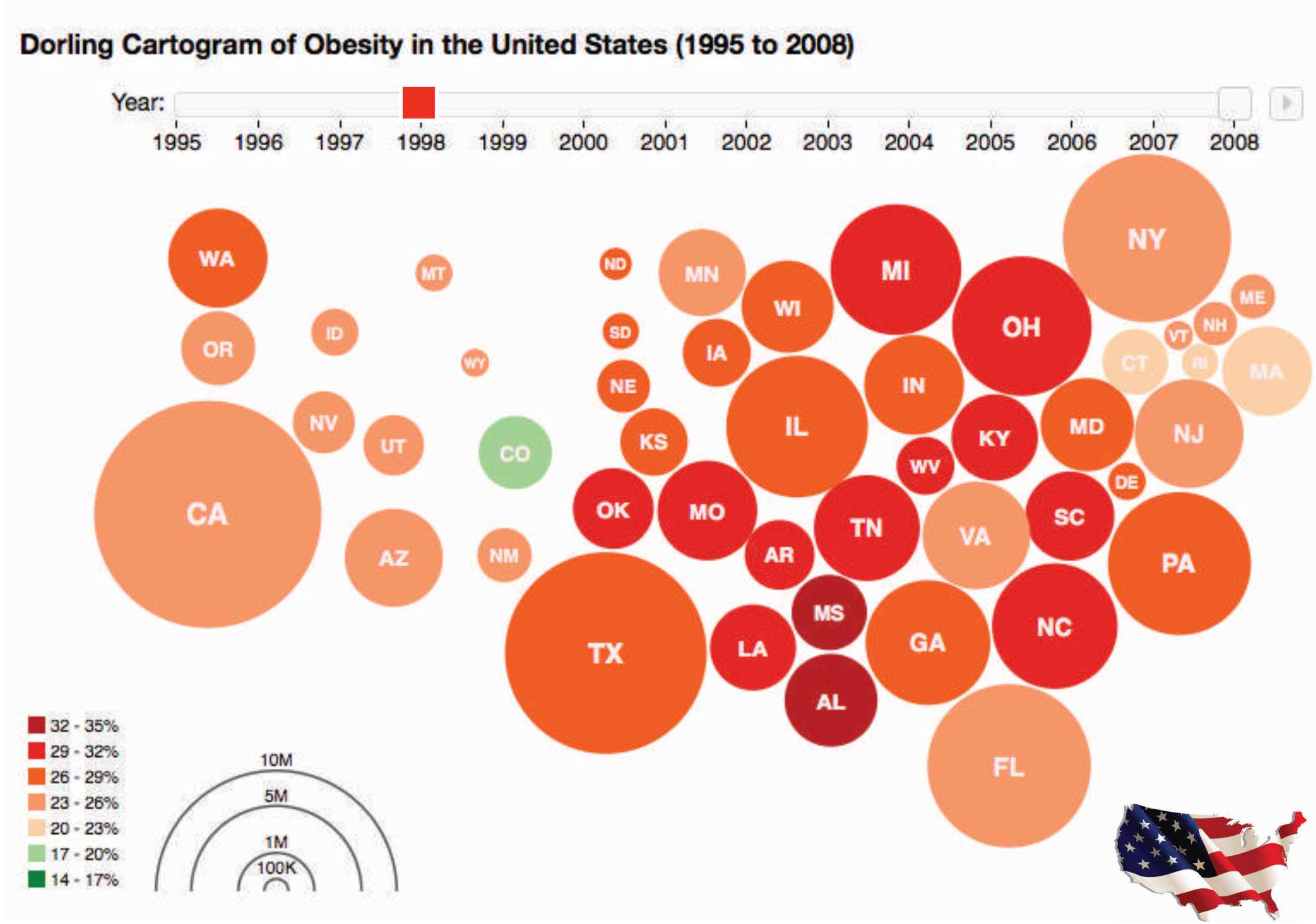
Dorling Cartogram of Obesity in the United States (1995 to 2008)





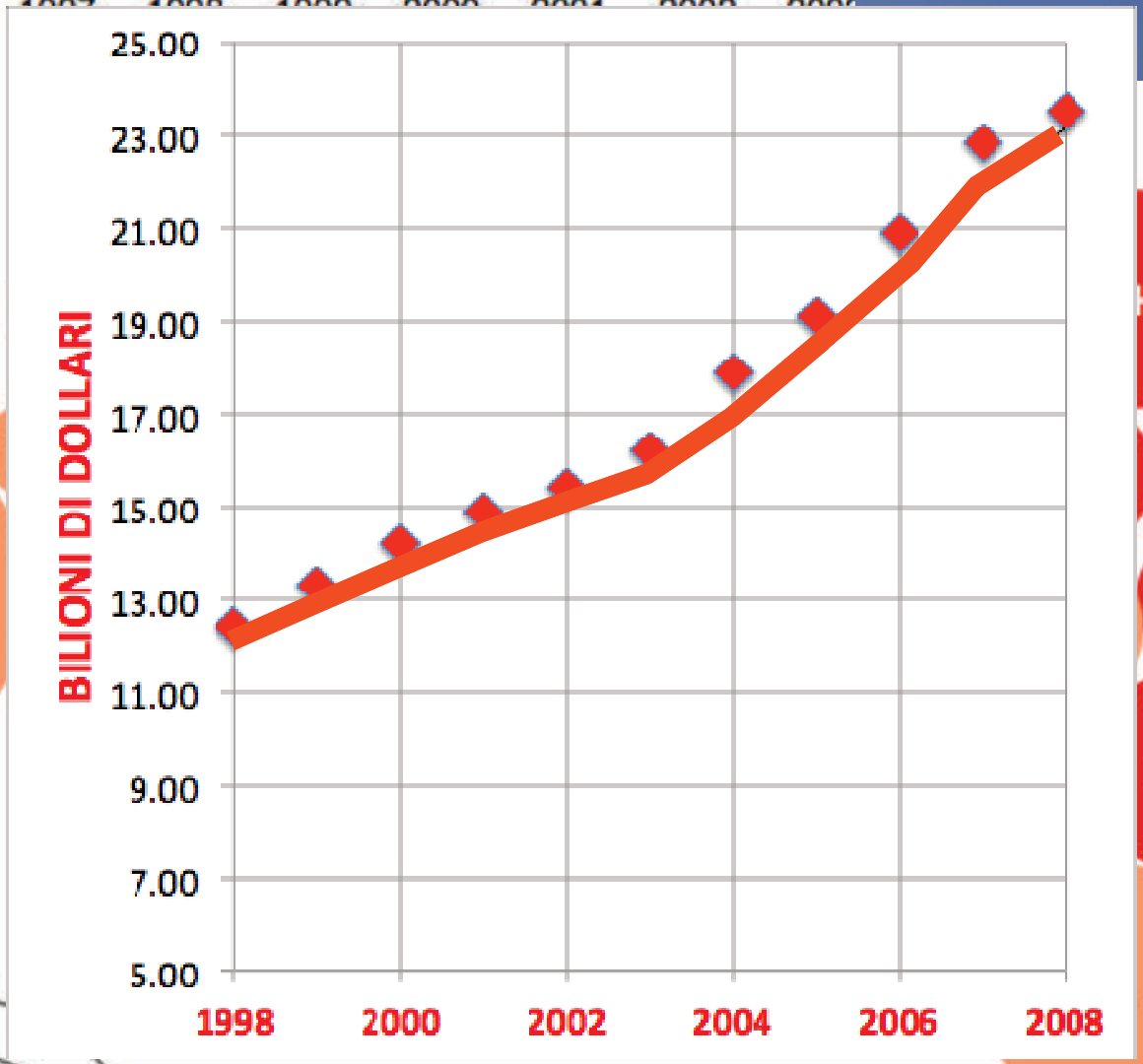


Dorling Cartogram of Obesity in the United States (1995 to 2008)



Dorling Cartogram of Obesity in the United States (1995 to 2008

Year: 1995 1996 ... 2008



WA OR CA NY ME VT NH CT RI MA MD NJ DE SC PA NC

32 - 35%
29 - 32%
26 - 29%
23 - 26%
20 - 23%
17 - 20%
14 - 17%

10M
5M
1M
100K

Zimmet *Clinical Diabetes and Endocrinology* (2017) 3:1
DOI 10.1186/s40842-016-0039-3

Clinical Diabetes and Endocrinology

COMMENTARY **Open Access**

Diabetes and its drivers: the largest epidemic in human history?

Paul Z. Zimmet

Coca

COLONIZATION

L’epidemia colpisce tutto il mondo

grandi civiltà
e
culture isolate

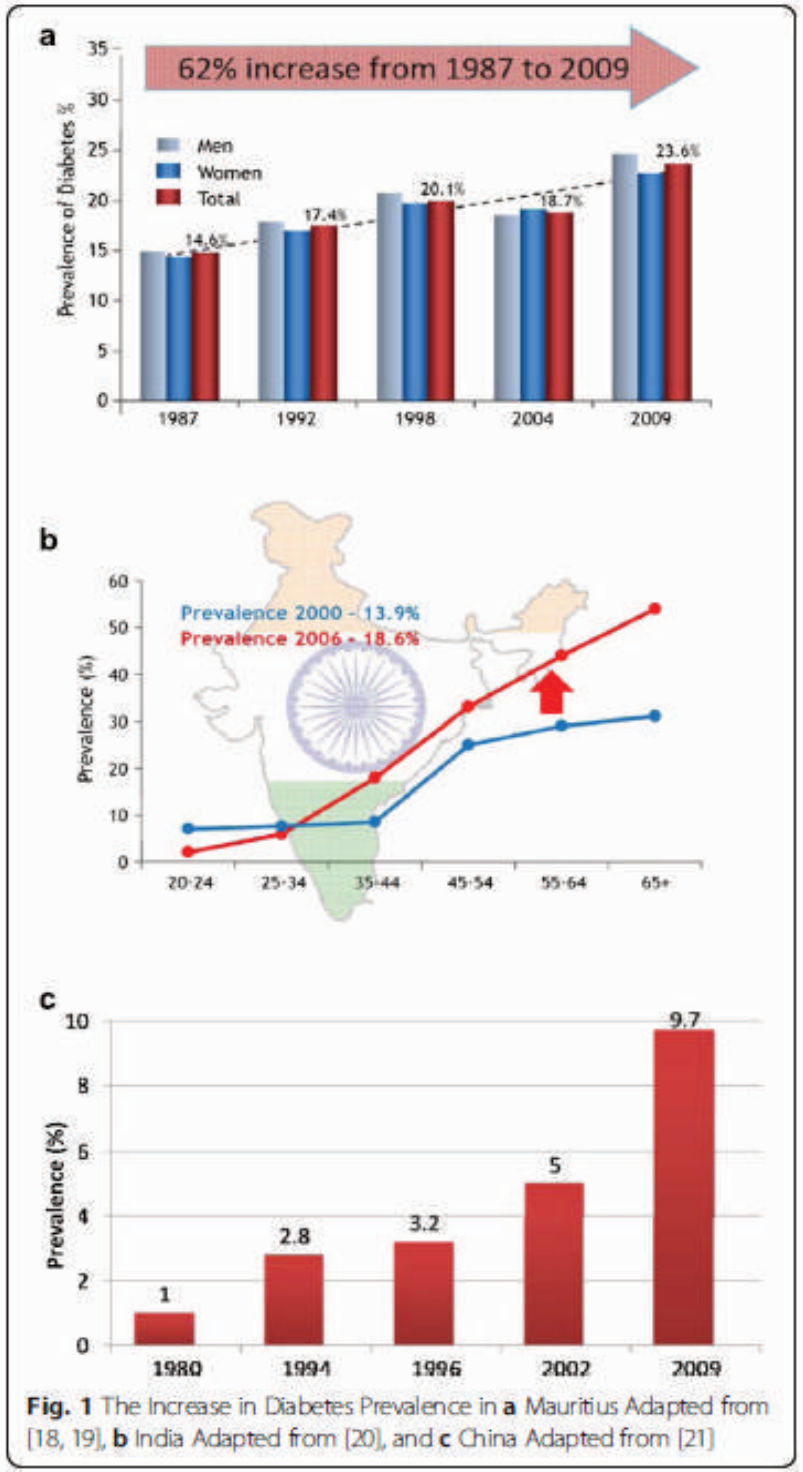


Fig. 1 The Increase in Diabetes Prevalence in **a** Mauritius Adapted from [18, 19], **b** India Adapted from [20], and **c** China Adapted from [21]

Mauritius

India

Cina

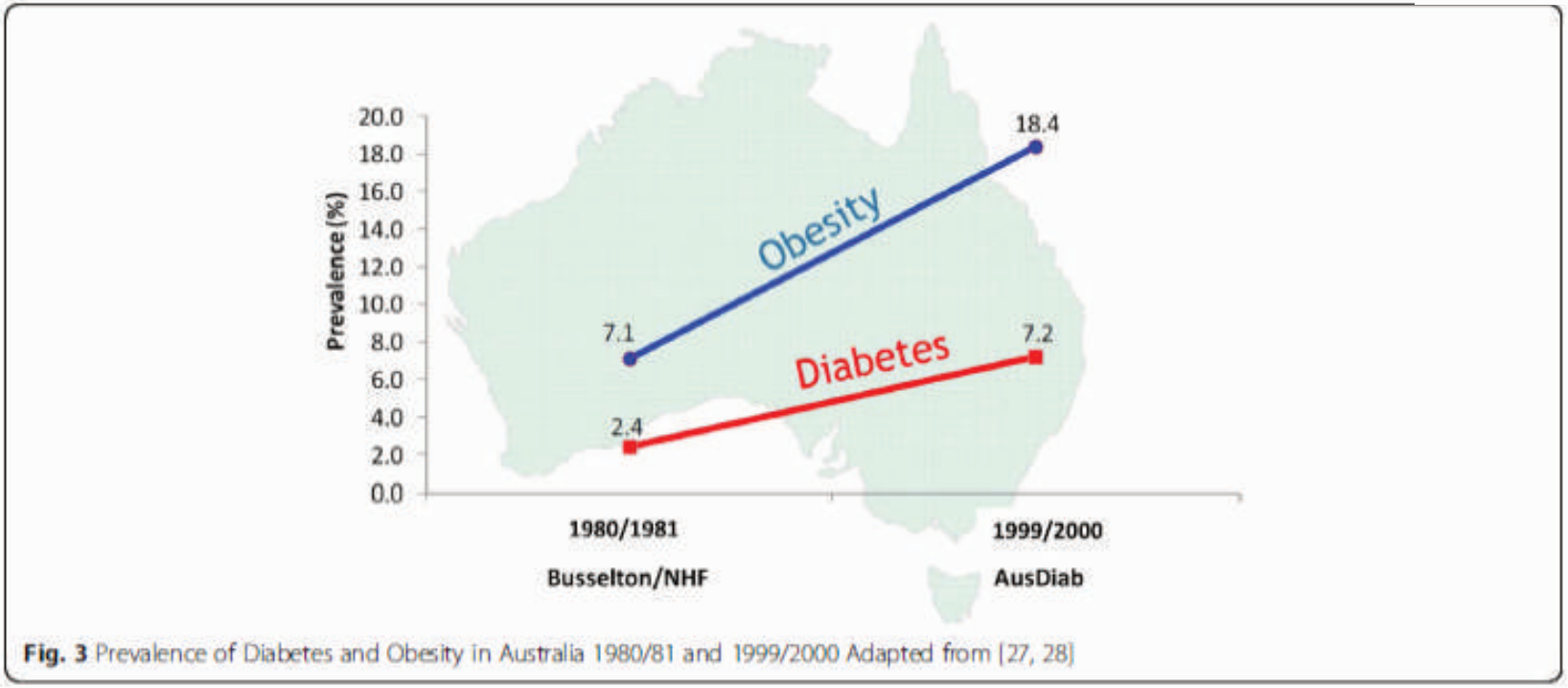


Fig. 3 Prevalence of Diabetes and Obesity in Australia 1980/81 and 1999/2000 Adapted from [27, 28]

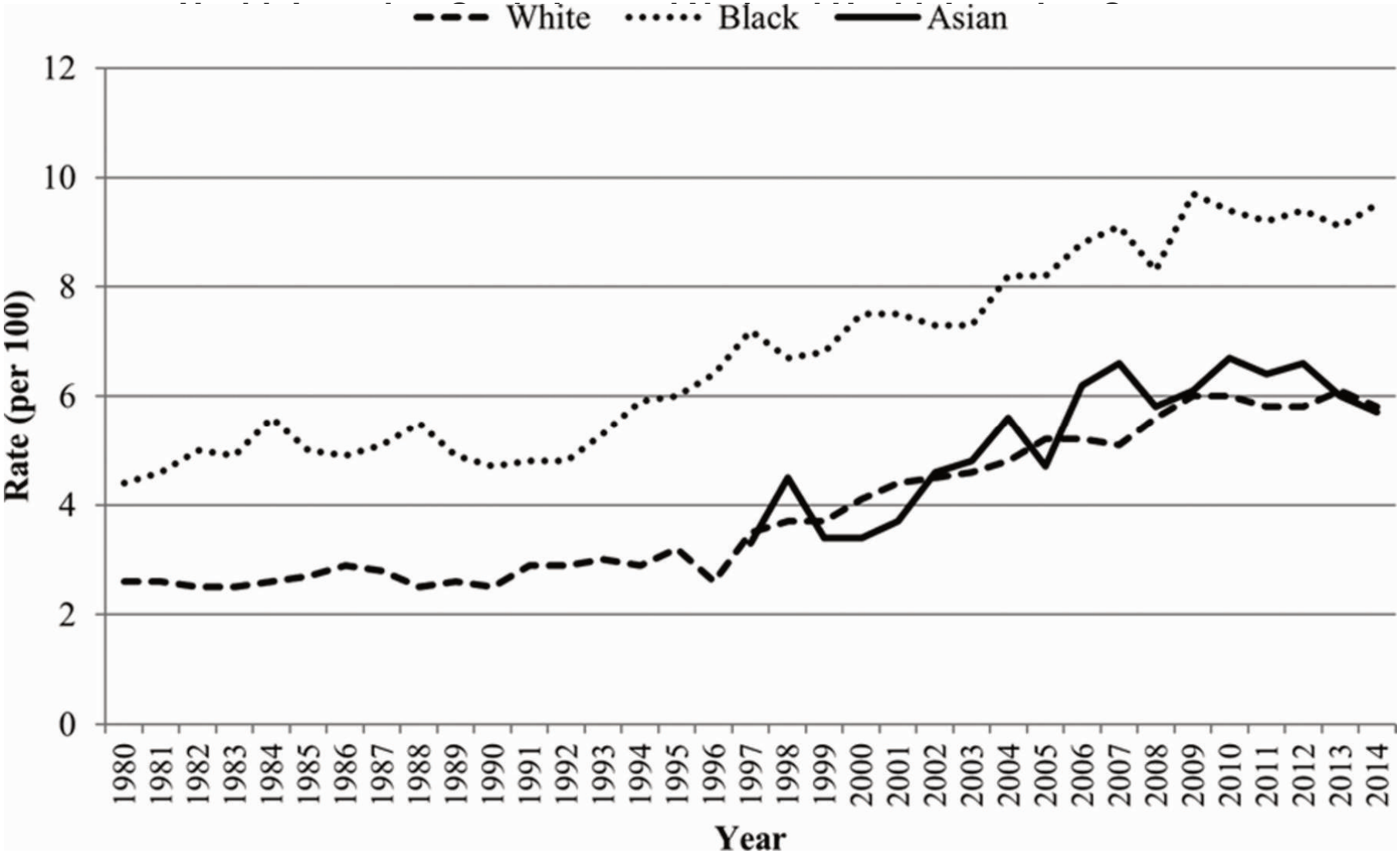
Australia: modello continentale di una colonizzazione alimentare globale

a

b

L’obesità è indipendente dalla razza

Trends in age-adjusted rates of diagnosed diabetes mellitus per 100 civilian, noninstitutionalized population in the United States, by race, 1980–2014.31 Data source: Centers for Disease Control and Prevention, National Center for Health Statistics, Division of



American Heart Association.

Shilpa N. Bhupathiraju, and Frank B. Hu Circ Res. 2016;118:1723-1735

Mol Biol Rep (2015) 42:799–818
DOI 10.1007/s11033-014-3751-z

Obesity and diabetes: from genetics to epigenetics

Ernesto Burgio · Angela Lopomo · Lucia Migliore

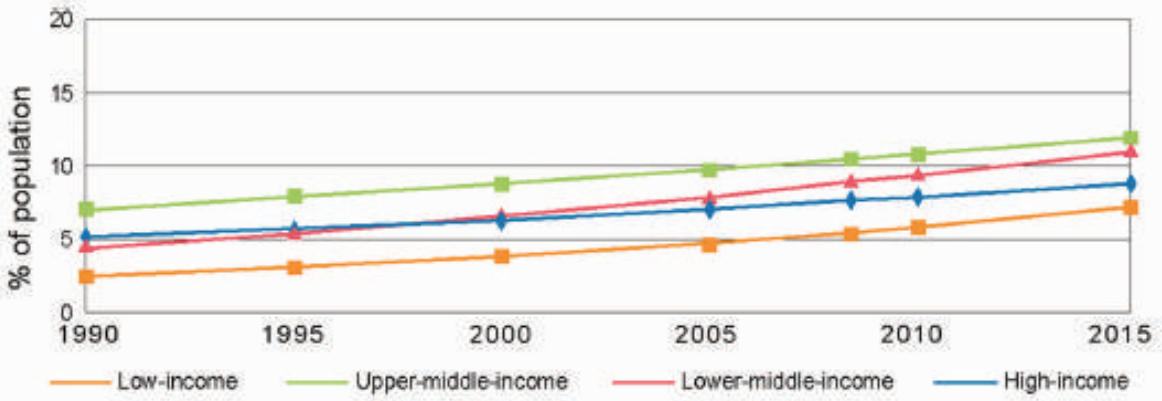


Fig. 1 Infant and young child overweight trends from 1990 to 2015, by World Bank income group (Adapted from WHO, 2010)

L'obesità sta aumentando nell'infanzia
indipendentemente dalle condizioni economiche e sociali

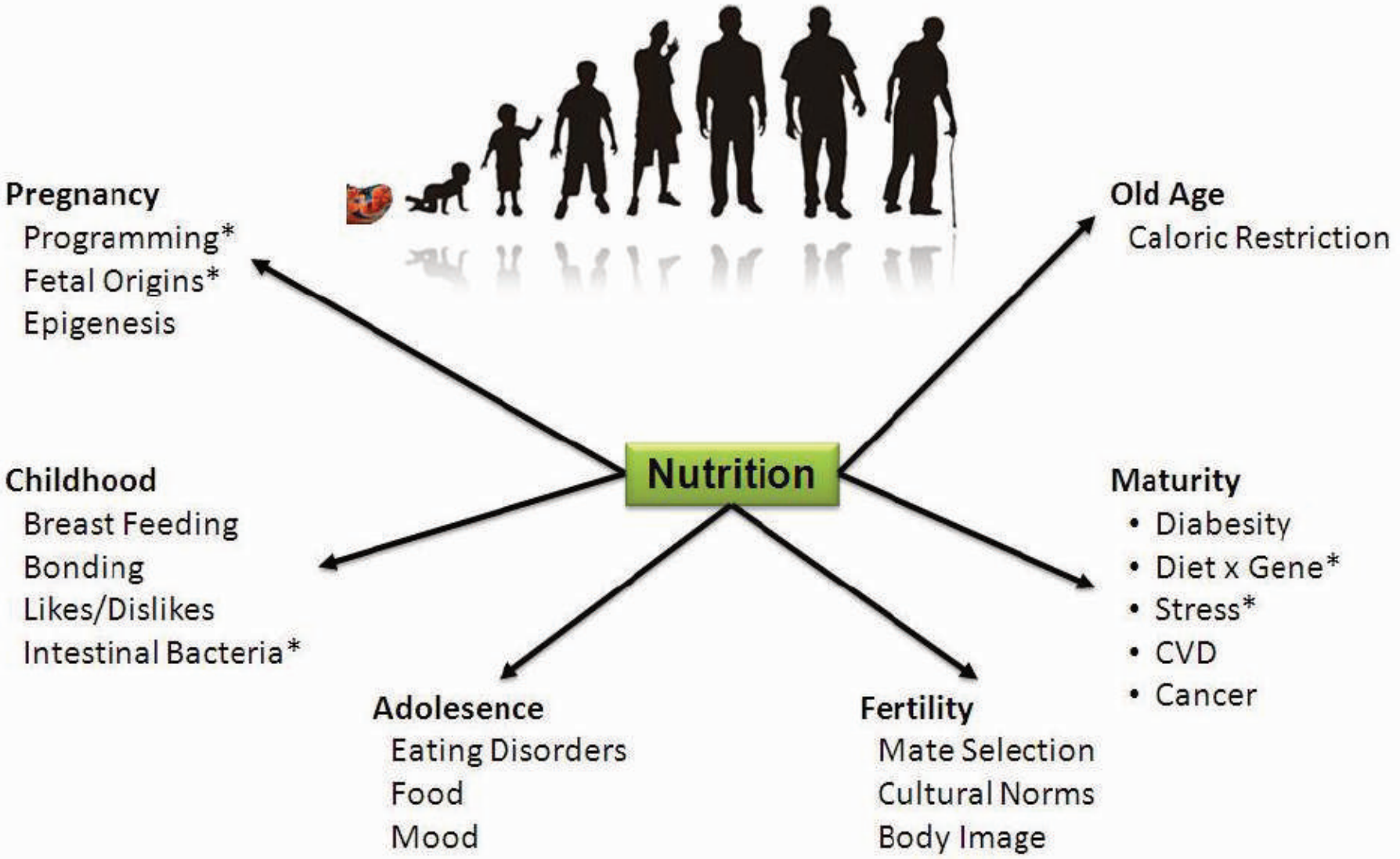


Figure 2. The effects of nutrition on the sociotype during the life cycle.

*Factors involved in the pathogenesis of diabesity as discussed in the text.

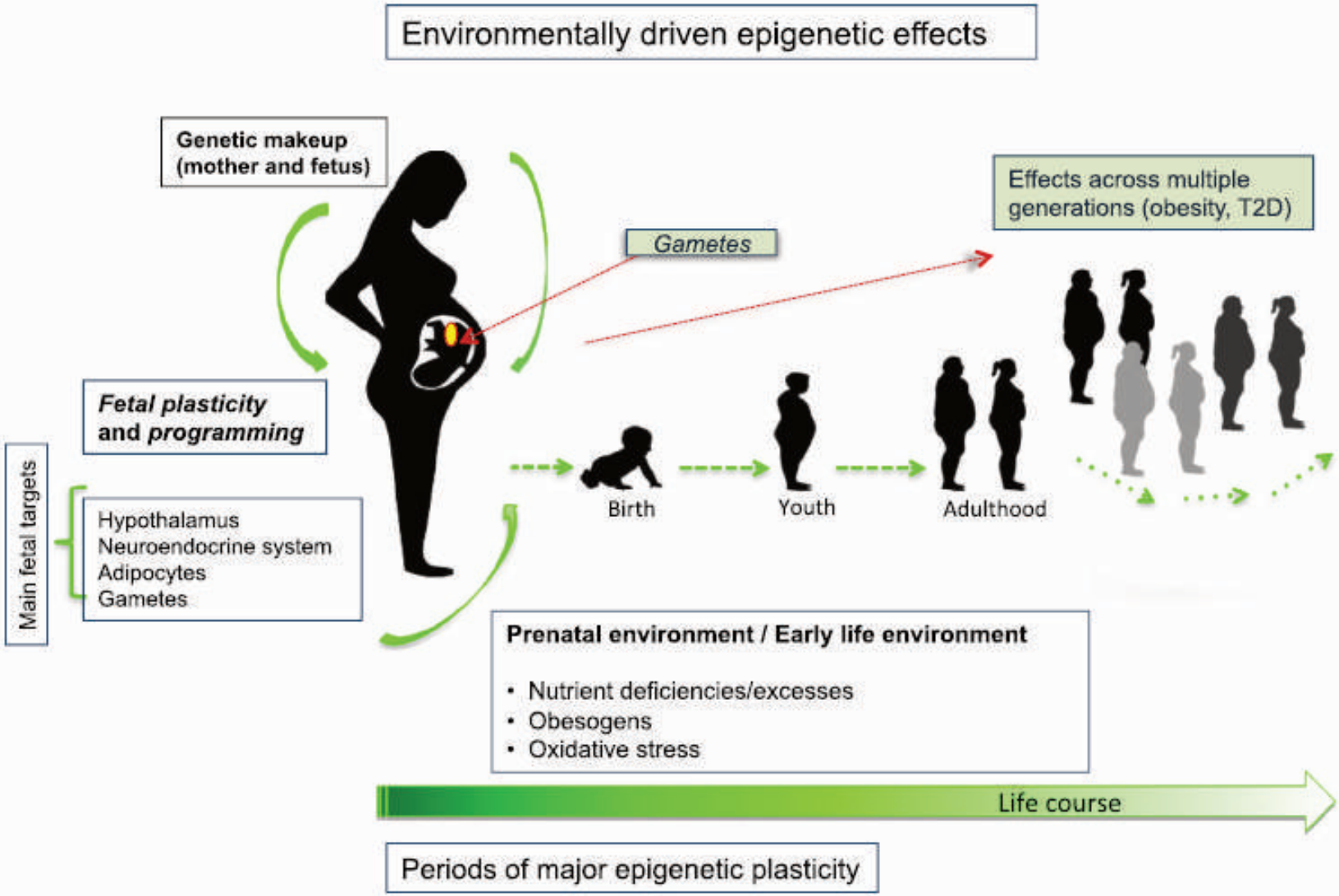


Fig. 3 Importance of environmentally driven epigenetic effects during life course and consequences across generations

Siamo quello che siamo?...

… o siamo quello che subiamo?

Il ruolo dell'alimentazione nell'induzione dell'obesità inizia con la vita intrauterina

Zimmet *Clinical Diabetes and Endocrinology* (2017) 3:1
DOI 10.1186/s40842-016-0039-3

Clinical Diabetes and Endocrinology

COMMENTARY Open Access

Diabetes and its drivers: the largest epidemic in human history?

Paul Z. Zimmet

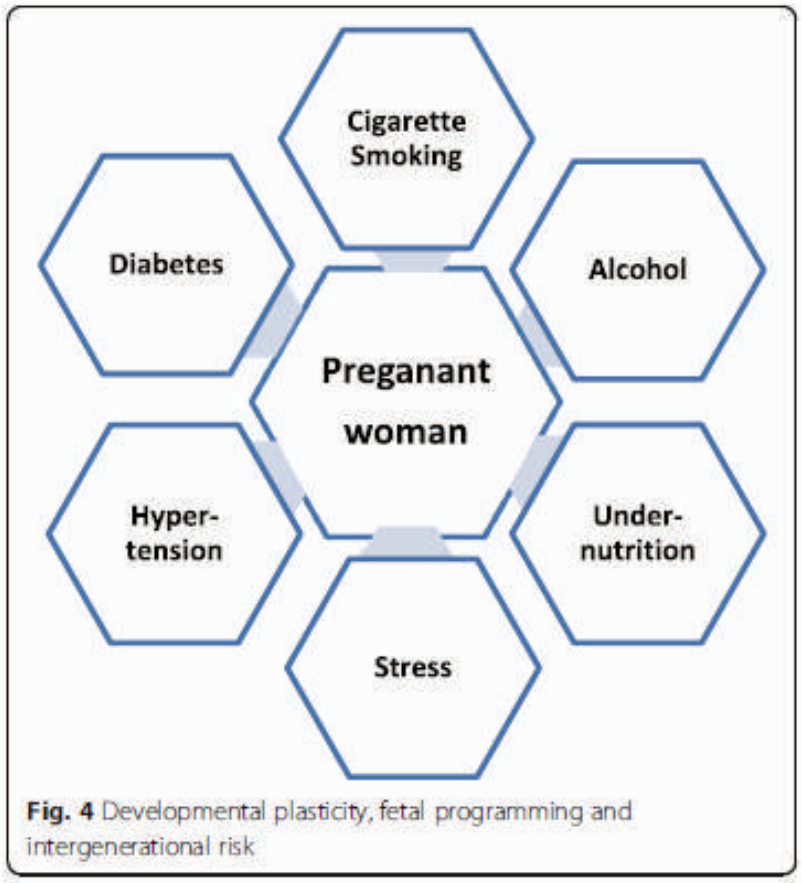


Fig. 4 Developmental plasticity, fetal programming and intergenerational risk

Restrizione alimentare

- Occupazione nazista dell'Olanda
- Grande fame cinese
- Biafra

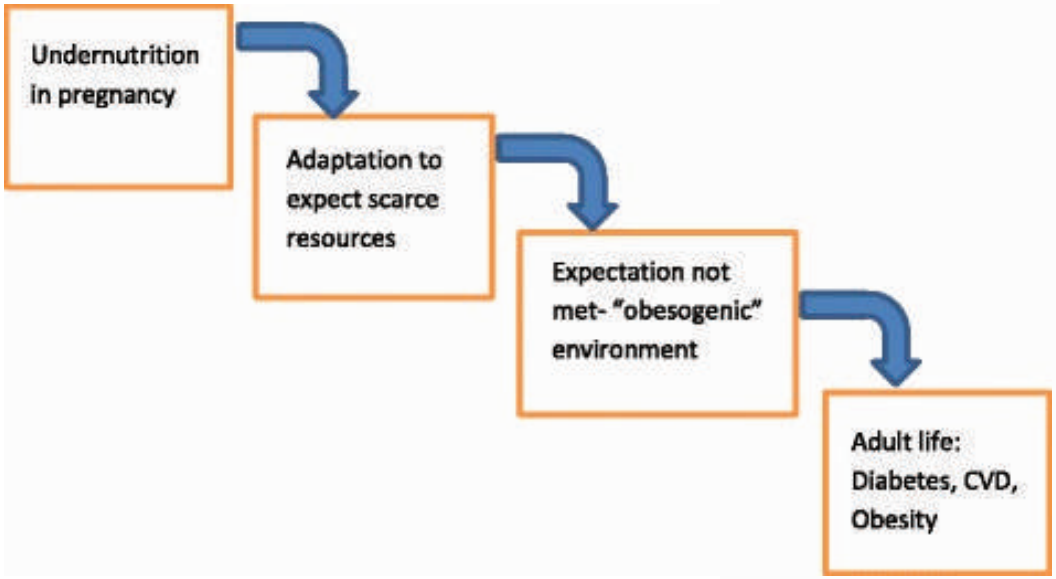
REVIEW ARTICLE

Nutrition Vol. 13, No. 9, 1997

Maternal Nutrition, Fetal Nutrition, and Disease in Later Life

DAVID J. P. BARKER, MD, PHD, FRCP

From the MRC Environmental Epidemiology Unit, University of Southampton, Southampton General Hospital, Southampton, UK



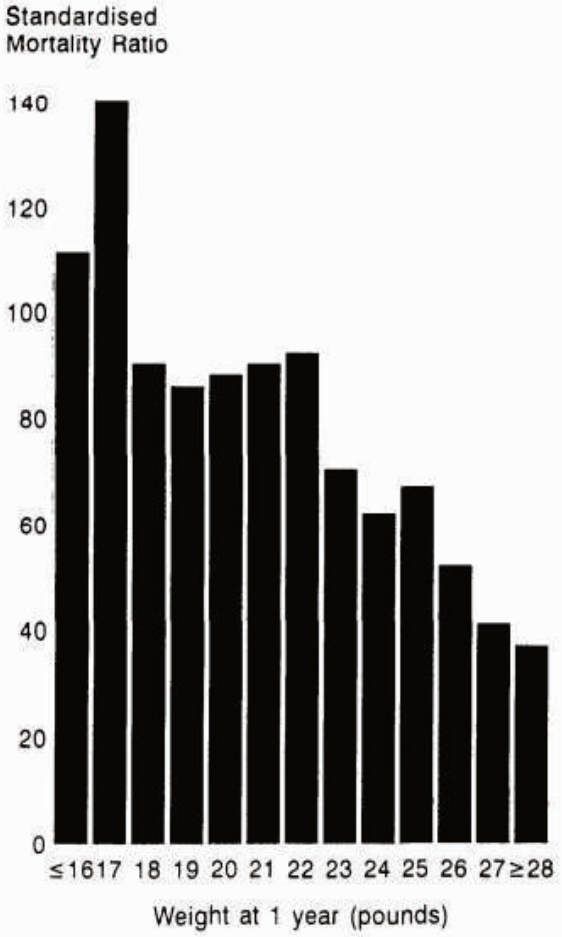


FIG. 1. Mortality from coronary heart disease in 8175 men born during 1911–1930 according to weight at 1 y of age.

diseases

MDPI

Review

Milk's Role as an Epigenetic Regulator in Health and Disease

Bodo C. Melnik [1,*] and Gerd Schmitz [2]

1 Department of Dermatology, Environmental Medicine and Health Theory, Faculty of Human Sciences, University of Osnabrück, Am Finkenhügel 7a, D-49076 Osnabrück, Germany

2 Institute for Clinical Chemistry and Laboratory Medicine, University Hospital Regensburg, University of Regensburg, Franz-Josef-Strauß-Allee 11, D-93053 Regensburg, Germany; gerd.schmitz@ukr.de

* Correspondence: melnik@t-online.de; Tel.: +49-5241-988-060; Fax: +49-5241-25801

Academic Editor: Takeo Kubota

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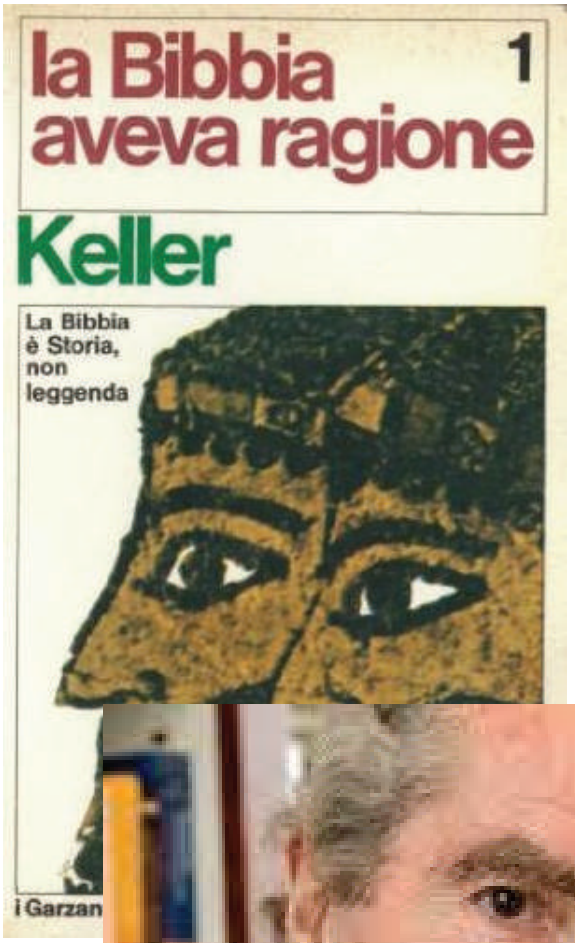
la Bibbia aveva ragione
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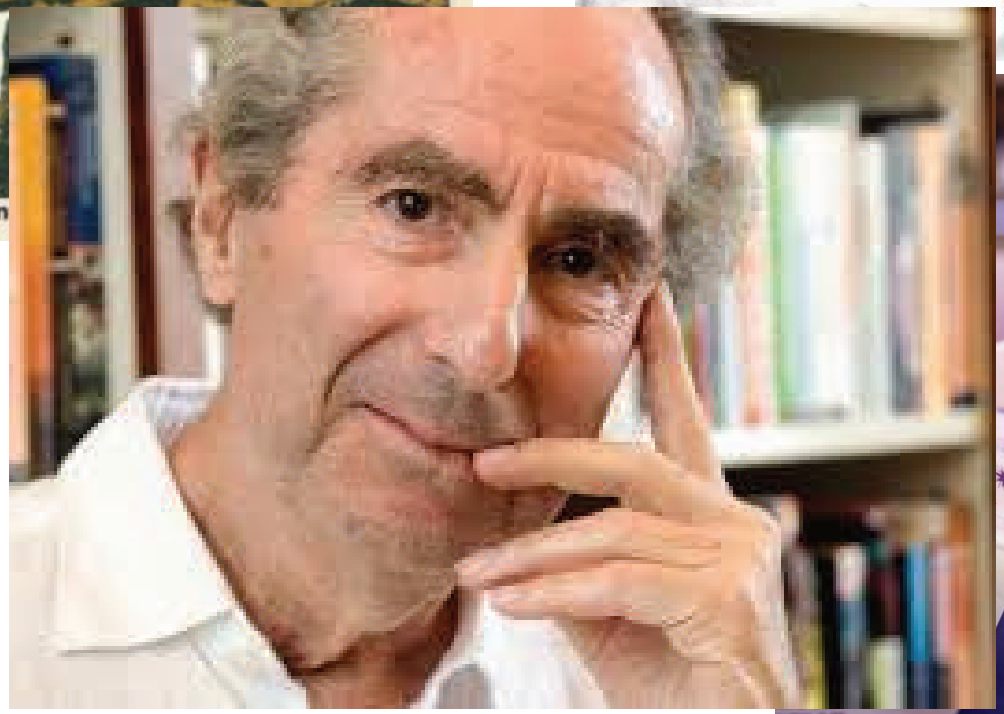
Keller
La Bibbia è Storia, non leggenda
i Garzan




Cheesemas

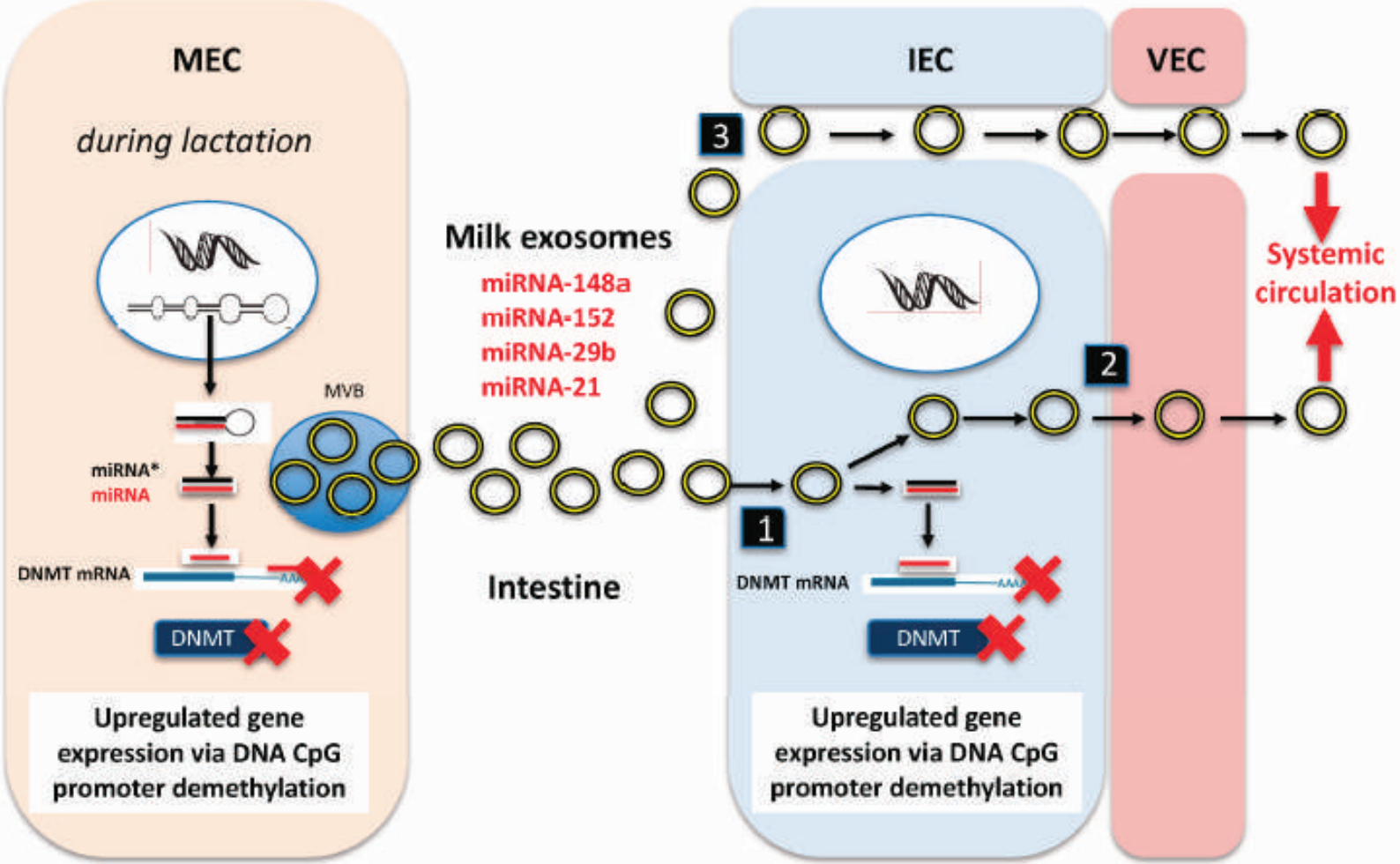


Figure 1. Working model of exosomal transfer of lactation-specific miRNAs that target DNA methyltransferases (DNMT) of the milk recipient. Mammary gland epithelial cells (MEC) secrete DNMT-targeting miRNAs via exosomes, which are taken up by (1) intestinal epithelial cells (IEC) and (2) vascular endothelial cells (VEC) via endocytosis; (3) Especially during the postnatal period, which is associated with high interstinal permeability, milk exosomes may travel along IEC intercellular spaces. After entry into the systemic circulation, milk exosomes may reduce DNA methylation of peripheral target cells.

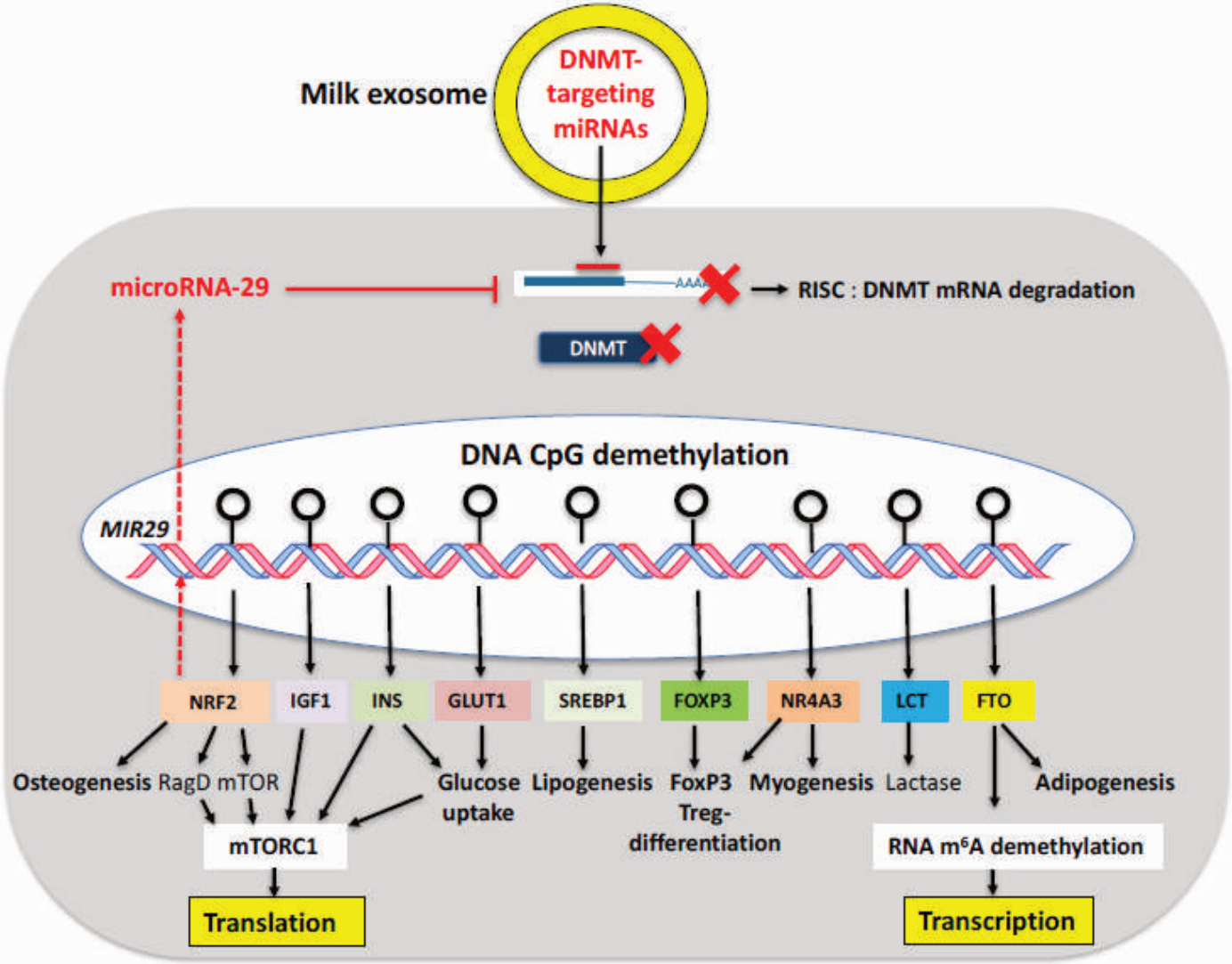


Figure 2. Working model of milk-mediated epigenetic regulation. Milk exosome-derived DNMT-targeting miRNAs enhance DNA promoter demethylation of critical CpG islets involved in the upregulation of gene expression of pivotal transcription factors (NRF2, SREBP1, FOXP3, NR4A3) and key metabolic regulators (INS, IGF1, CAV1, GLUT1, LCT) and the RNA m^6A demethylase FTO. Milk-derived DNMT-targeting miRNAs may thus play a fundamental role in epigenetic enhancement of transcription and translation (see list of abbreviations).

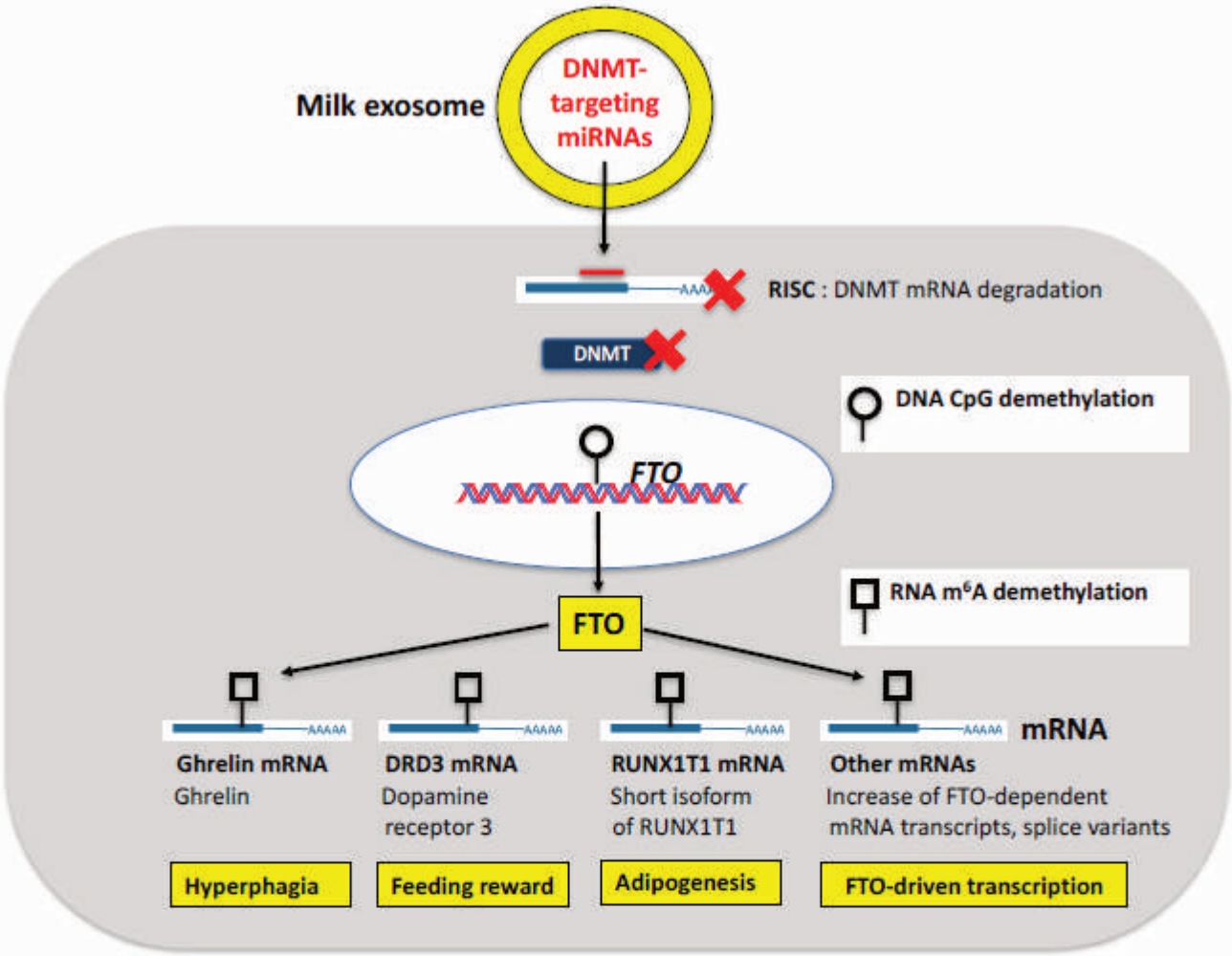
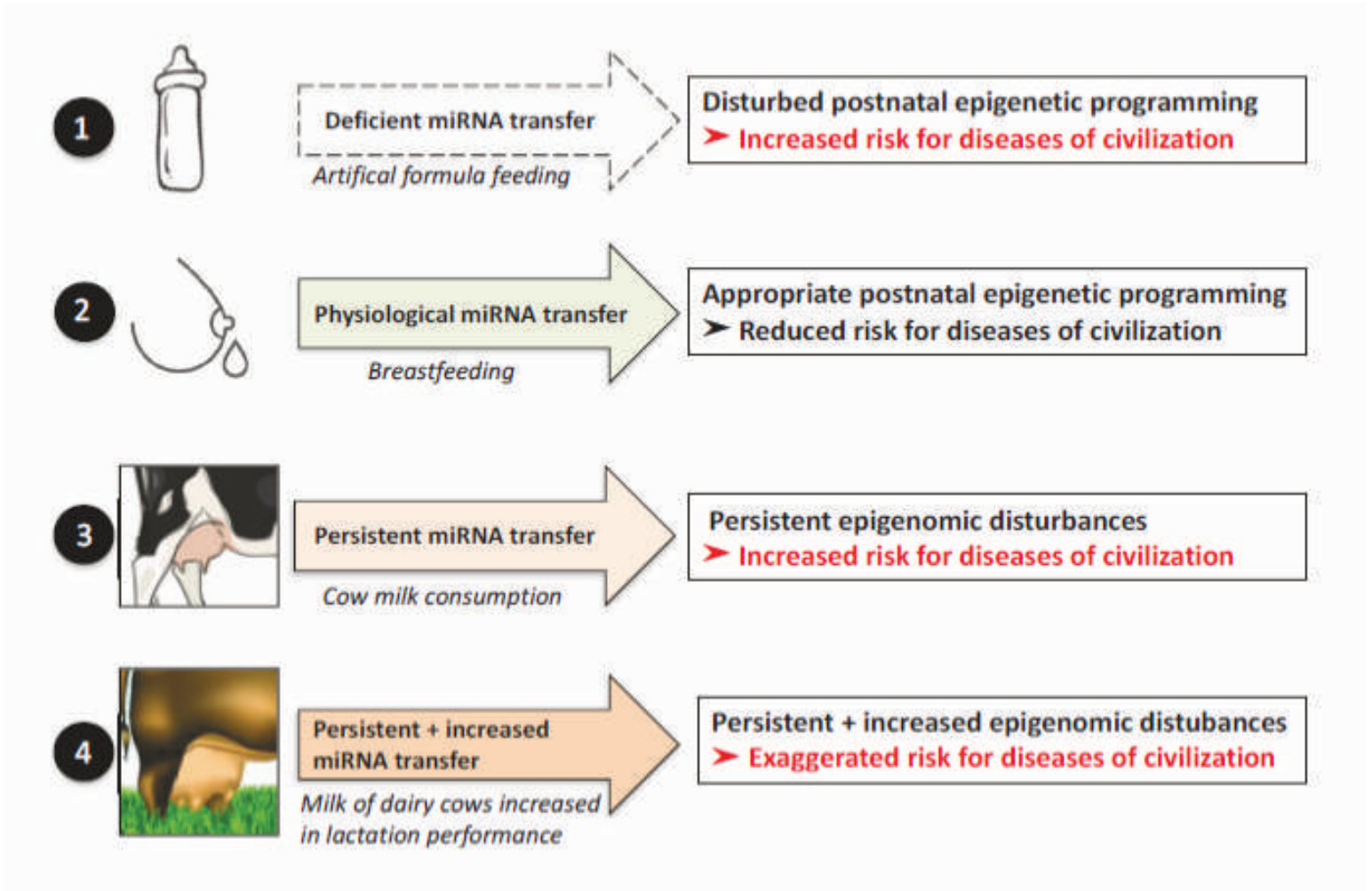
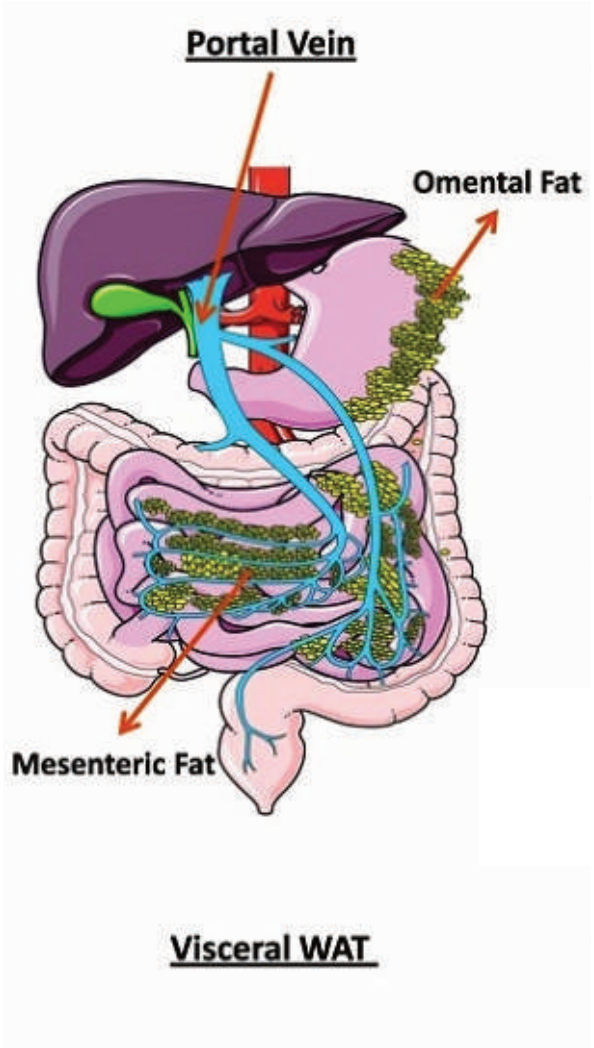


Figure 3. Working model of milk-mediated epigenetic actication of fat mass- and obesity-associated protein (FTO) expression modifying the epitranscriptome. Milk-derived DNMT-targeting miRNAs reduce methylation critical DNA CpG islets thereby increasing FTO gene expression. The RNA m^6A demethylase FTO erases m^6A marks on mRNAs, thereby enhancing FTO-dependent mRNA transcription and mRNA splice variant production such as adipogenic short form of RNX1T1. The mRNAs of ghrelin and dopamine receptor 3 (DRD3) are targets of FTO-mediated upregulation. Resulting hyperphagia and feeding rewards support milk intake for infant growth requirements. Via epigenetic upregulation of FTO expression milk regulates the m^6A-controlled epitranscriptome.


1
Deficient miRNA transfer
Artifical formula feeding
Disturbed postnatal epigenetic programming
➤ Increased risk for diseases of civilization
2
Physiological miRNA transfer
Breastfeeding
Appropriate postnatal epigenetic programming
➤ Reduced risk for diseases of civilization
3
Persistent miRNA transfer
Cow milk consumption
Persistent epigenomic disturbances
➤ Increased risk for diseases of civilization
4
Persistent + increased miRNA transfer
Milk of dairy cows increased in lactation performance
Persistent + increased epigenomic distubances
➤ Exaggerated risk for diseases of civilization

Influenza del tessuto adiposo viscerale sul metabolismo



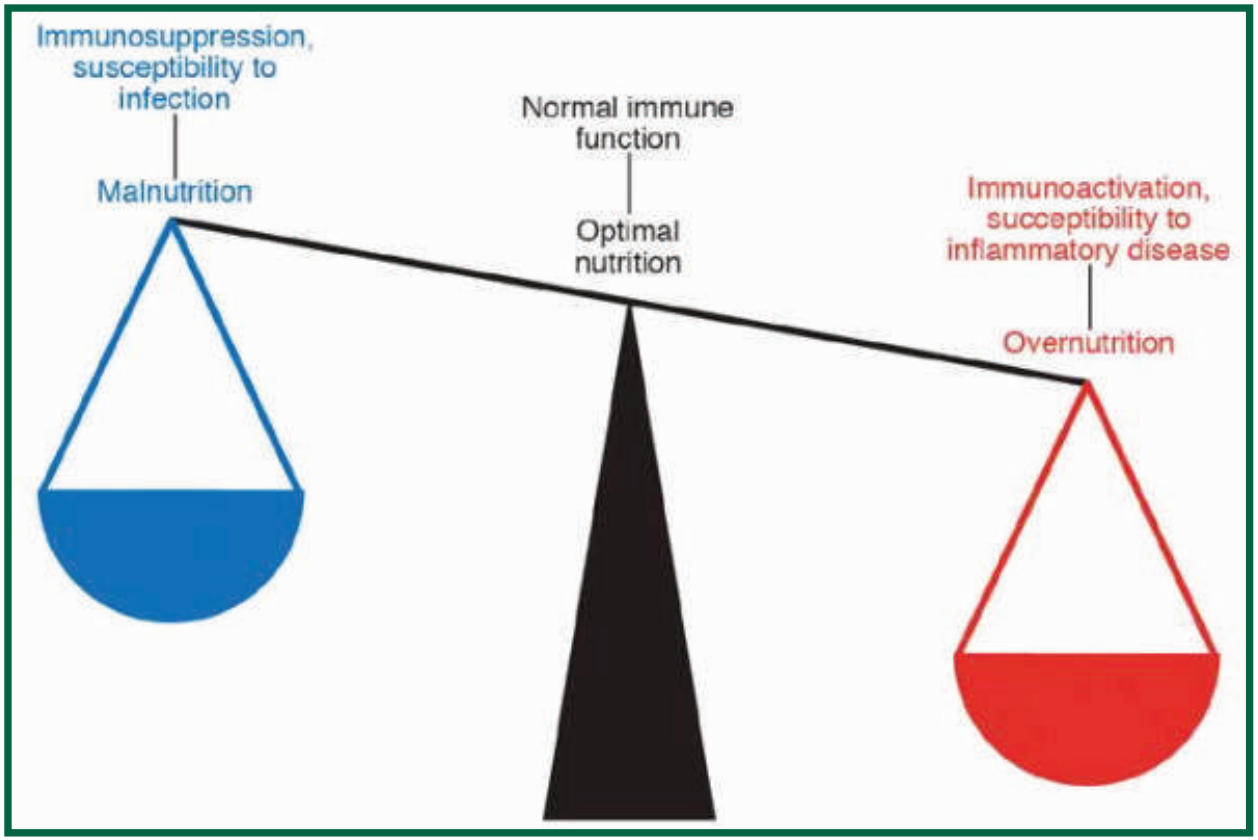
TESSUTO ADIPOSO VISCERALE

- ↑Acidi Grassi liberi
- ↑Citochine pro-infiammatorie
- ↑Recettori β adrenergici
- ↑Insulino resistenza

Tessuto adiposo e infiammazione

Un accumulo eccessivo di tessuto adiposo viscerale favorisce una condizione cronica di infiammazione del tessuto stesso con conseguente sviluppo di insulinoresistenza

Infiammazione, Stress e Diabete



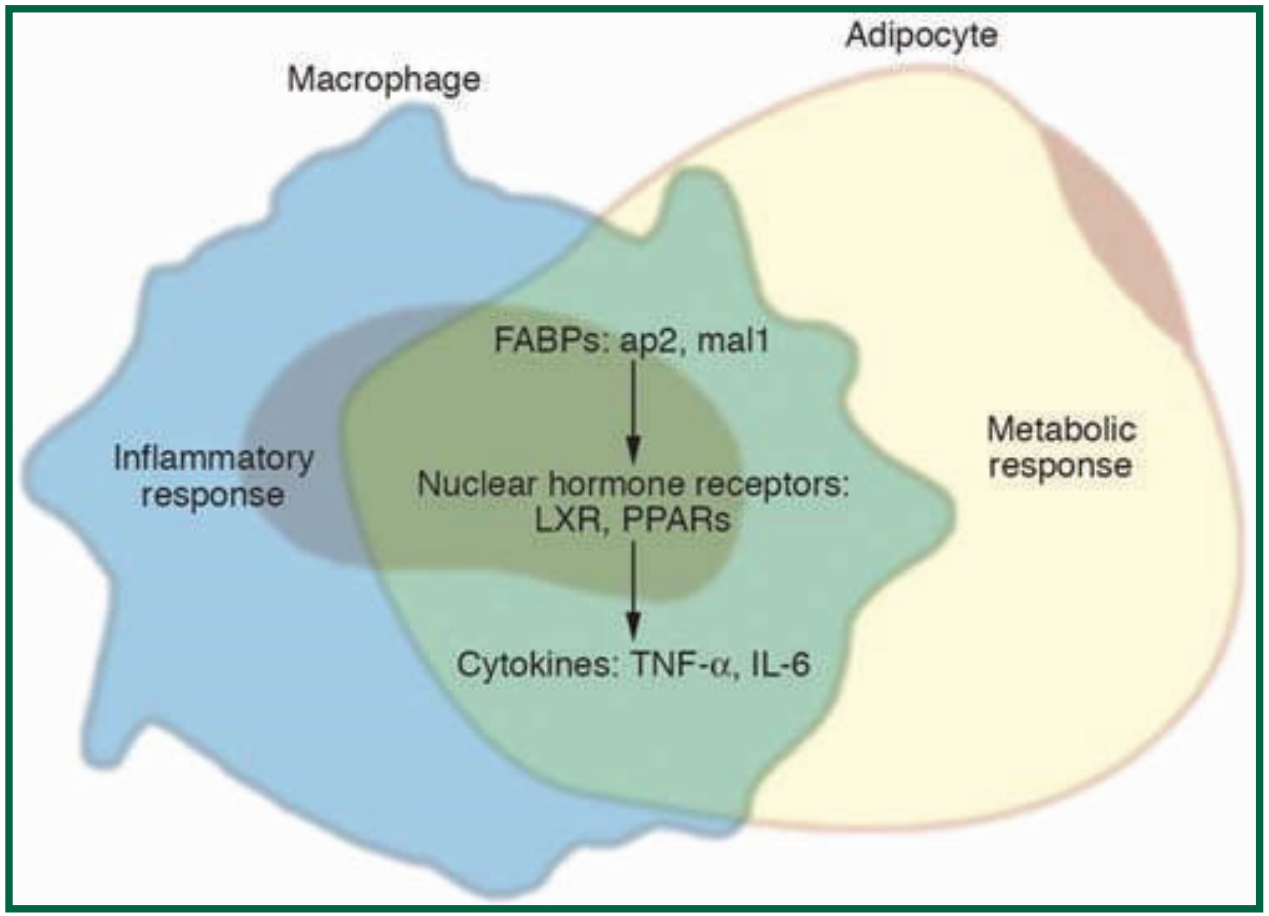
Il tessuto adiposo è un organo complesso suscettibile ad alterazioni metaboliche ed immunologiche

Inflammation, stress, and diabetes.
Wellen, Kathryn; Hotamisligil, Gokhan

Journal of Clinical Investigation. 115(5):1111-1119, May 2005.

JCI The Journal of Clinical Investigation

Infiammazione, Stress e Diabete



Inflammation, stress, and diabetes.
Wellen, Kathryn; Hotamisligil, Gokhan

Journal of Clinical Investigation. 115(5):1111-1119, May 2005.

JCI The Journal of Clinical Investigation

Fetal Diagnosis and Therapy

Fetal Diagn Ther 2018;43:143–147
DOI: 10.1159/000475988

Received: September 5, 2016
Accepted after revision: April 21, 2017
Published online: June 17, 2017

Maternal Subcutaneous and Visceral Adipose Ultrasound Thickness in Women with Gestational Diabetes Mellitus at 24–28 Weeks' Gestation

Francesco D'Ambrosi[a] Francesca Crovetto[a] Enrico Colosi[b] Isabella Fabietti[a]
Floriana Carbone[a] Beatrice Tassis[a] Silvia Motta[a] Alessandro Bulfoni[c]
Luigi Fedele[a] Gabriele Rossi[a] Nicola Persico[a]

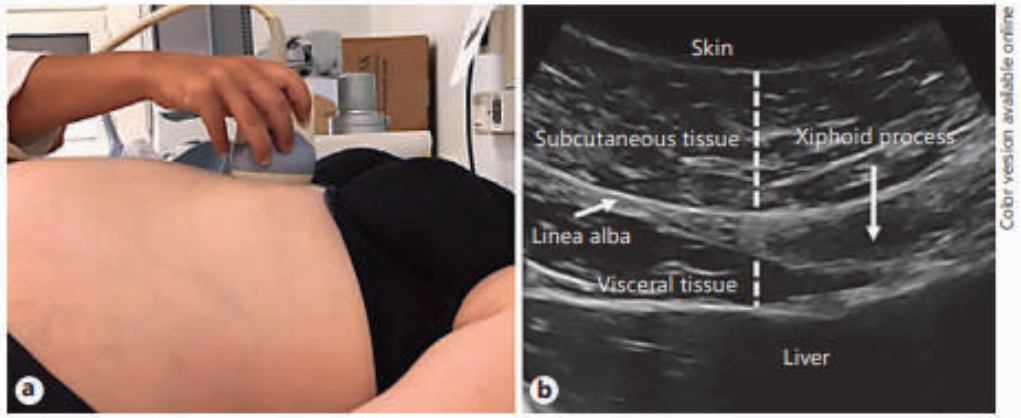
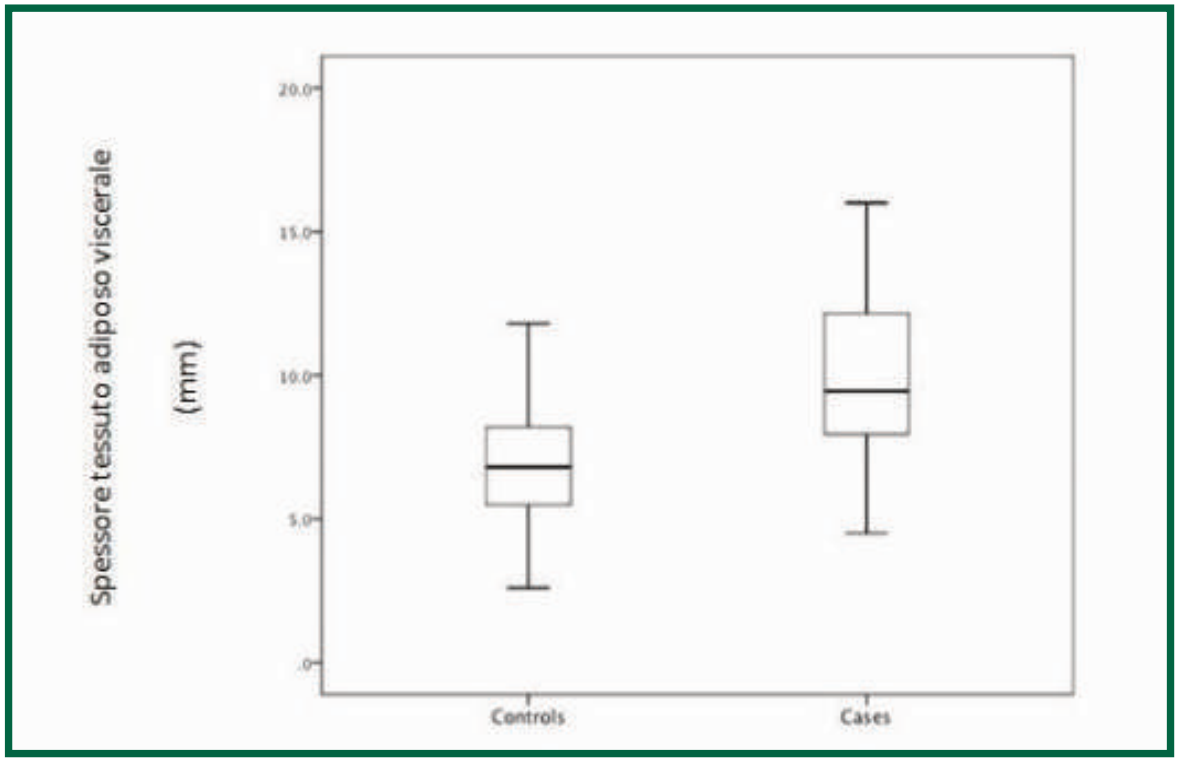


Fig. 1. Images showing the correct placement of the ultrasound transducer on the maternal abdomen (**a**) and the measurement of subcutaneous and visceral adipose thickness (**b**).

Fig. 1. Images showing the correct placement of the ultrasound transducer on the maternal abdomen (**a**) and the measurement of subcutaneous and visceral adipose thickness (**b**).

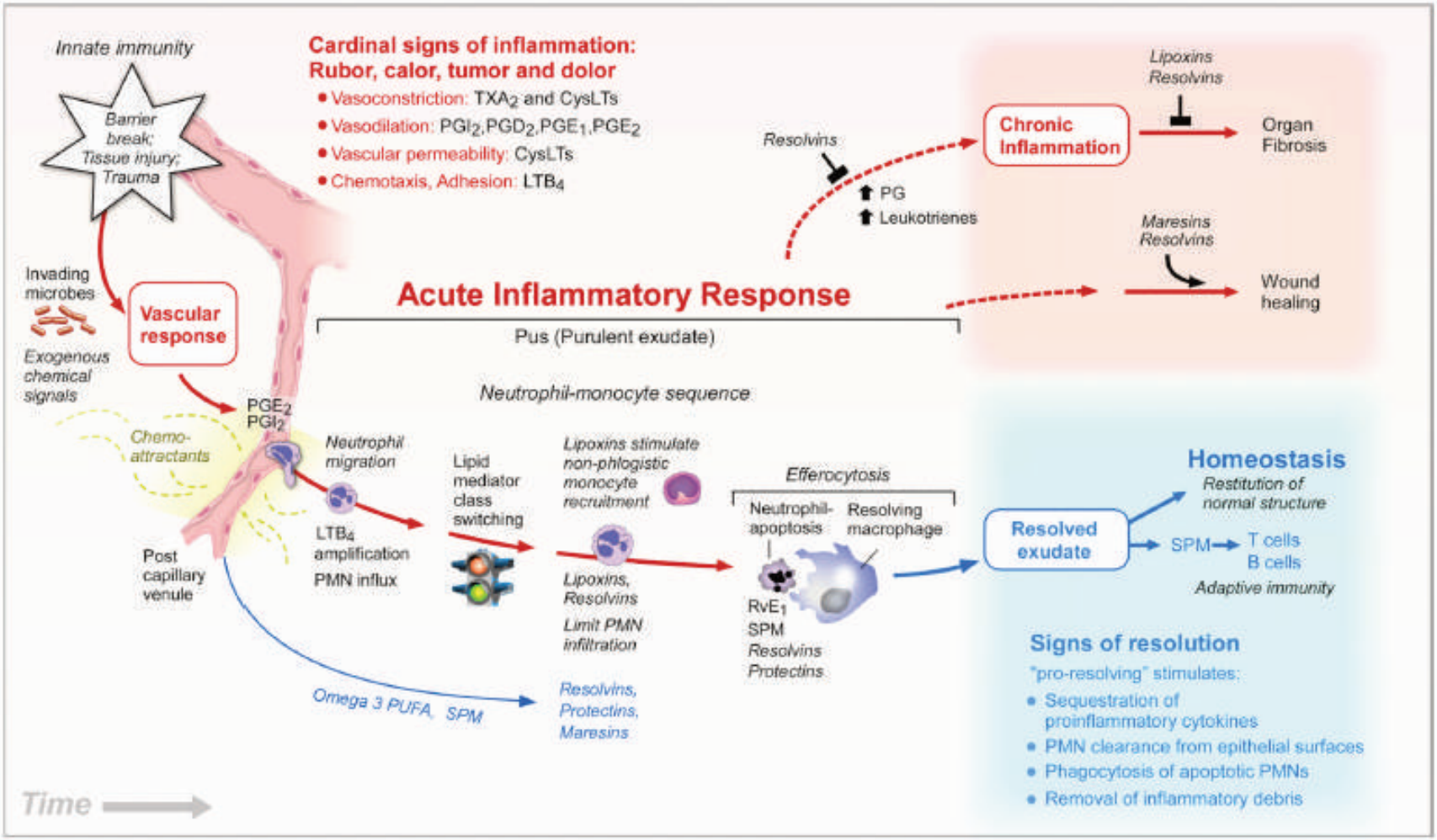


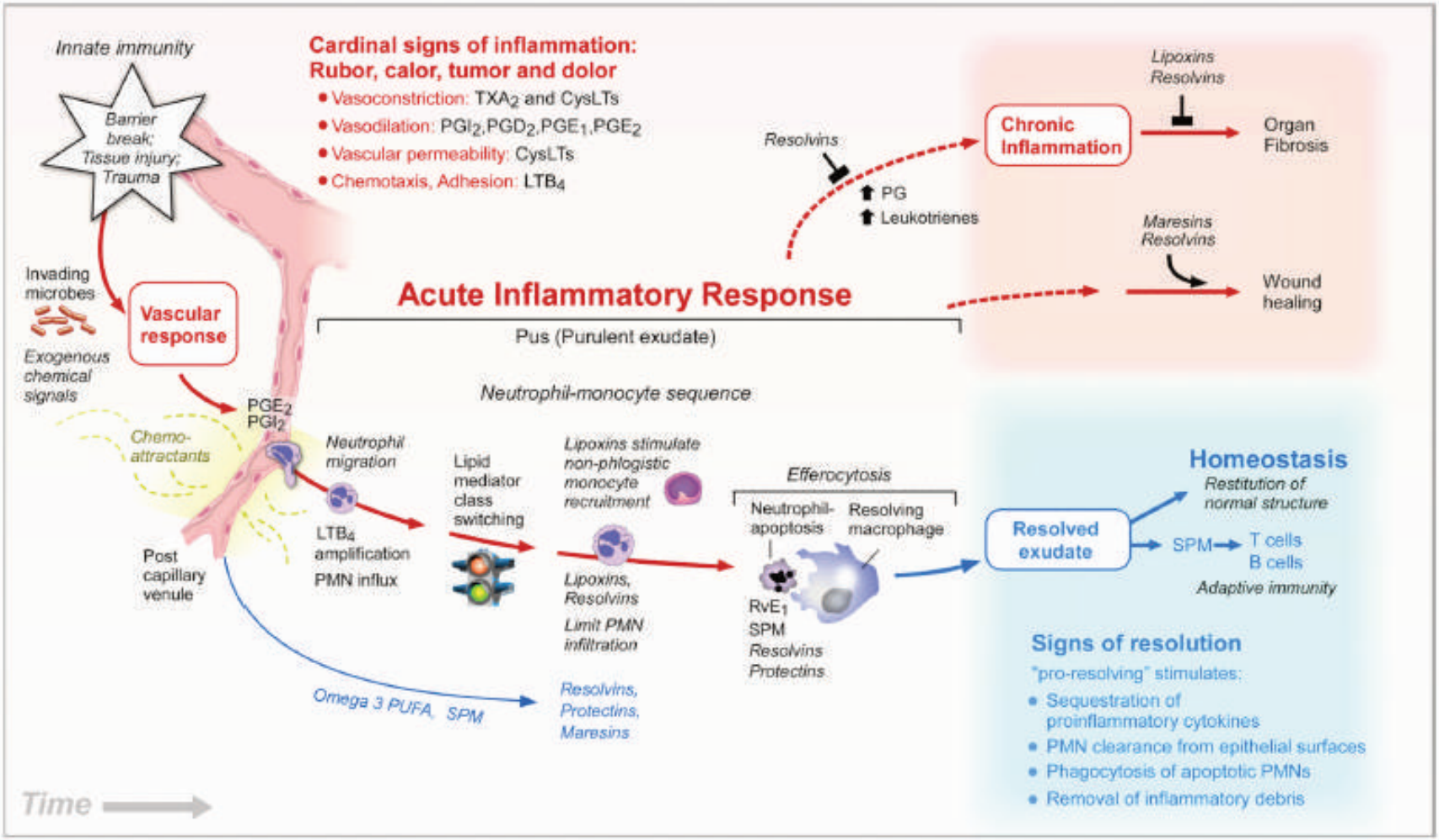
Il tessuto adiposo viscerale è significativamente aumentato nelle pazienti che sviluppano diabete gestazionale

Nature. 2014 June 5; 510(7503): 92–101. doi:10.1038/nature13479.

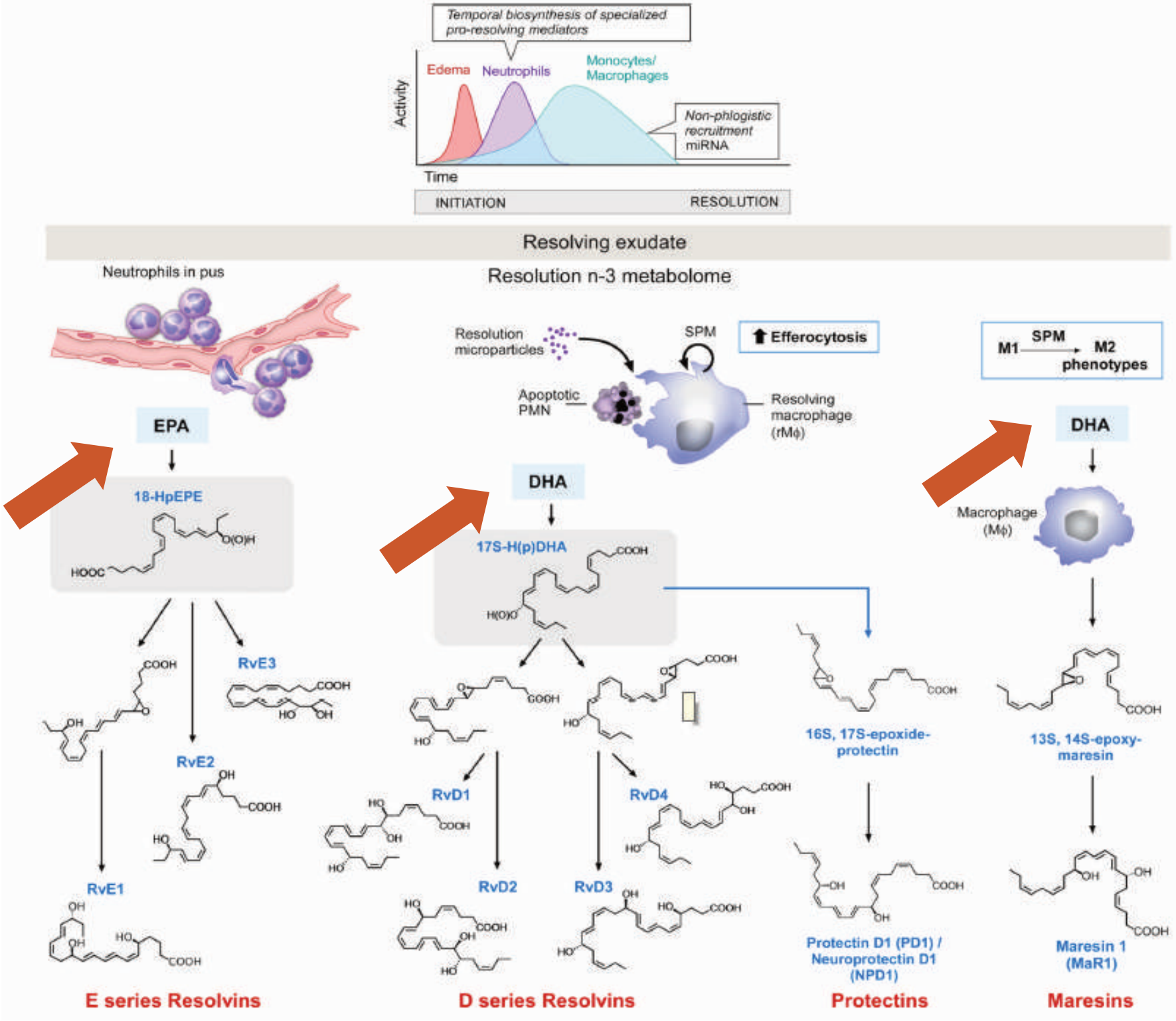
Novel Pro-Resolving Lipid Mediators in Inflammation Are Leads for Resolution Physiology

Charles N. Serhan
Center for Experimental Therapeutics and Reperfusion Injury, Department of Anesthesiology, Perioperative and Pain Medicine, Harvard Institutes of, Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, 02115





Il corpo necessita di un bilanciamento nella dieta di fattori proinfiammatori e antinfiammatori per mantenere un equilibrio nelle fasi di inizio e risoluzione del processo infiammatorio


Temporal biosynthesis of specialized pro-resolving mediators
Edema
Neutrophils
Monocytes/ Macrophages
Activity
Non-phlogistic recruitment miRNA
Time
INITIATION
RESOLUTION
Resolving exudate
Neutrophils in pus
Resolution n-3 metabolome
Resolution microparticles
SPM
Efferocytosis
Apoptotic PMN
Resolving macrophage (rMϕ)
M1 SPM M2 phenotypes
EPA
DHA
DHA
Macrophage (Mϕ)
18-HpEPE
17S-H(p)DHA
RvE3
RvE2
RvE1
RvD1
RvD2
RvD3
RvD4
16S, 17S-epoxide-protectin
13S, 14S-epoxy-maresin
Protectin D1 (PD1) / Neuroprotectin D1 (NPD1)
Maresin 1 (MaR1)
E series Resolvins
D series Resolvins
Protectins
Maresins

Potenziale infiammatorio dei nutrienti

Proinfiammatori	Antinfiammatori
Acidi grassi Omega-6	Acidi grassi Omega-3
Acidi grassi saturi	Polifenoli
Eccesso di carboidrati	

Tessuto adiposo e infiammazione

infiammazione cellulare

↓

resistenza all'azione dell'insulina

↓

elevate quantità di FFA in circolo

↓

FFA si accumulano nel fegato e nel muscolo scheletrico

↓

amplificazione del fenomeno infiammatorio

Condizioni croniche che possono essere curate con una dieta antinfiammatoria

- Obesità
- Sindrome metabolica
- Diabete
- Ipertensione
- Malattia cardiovascolare

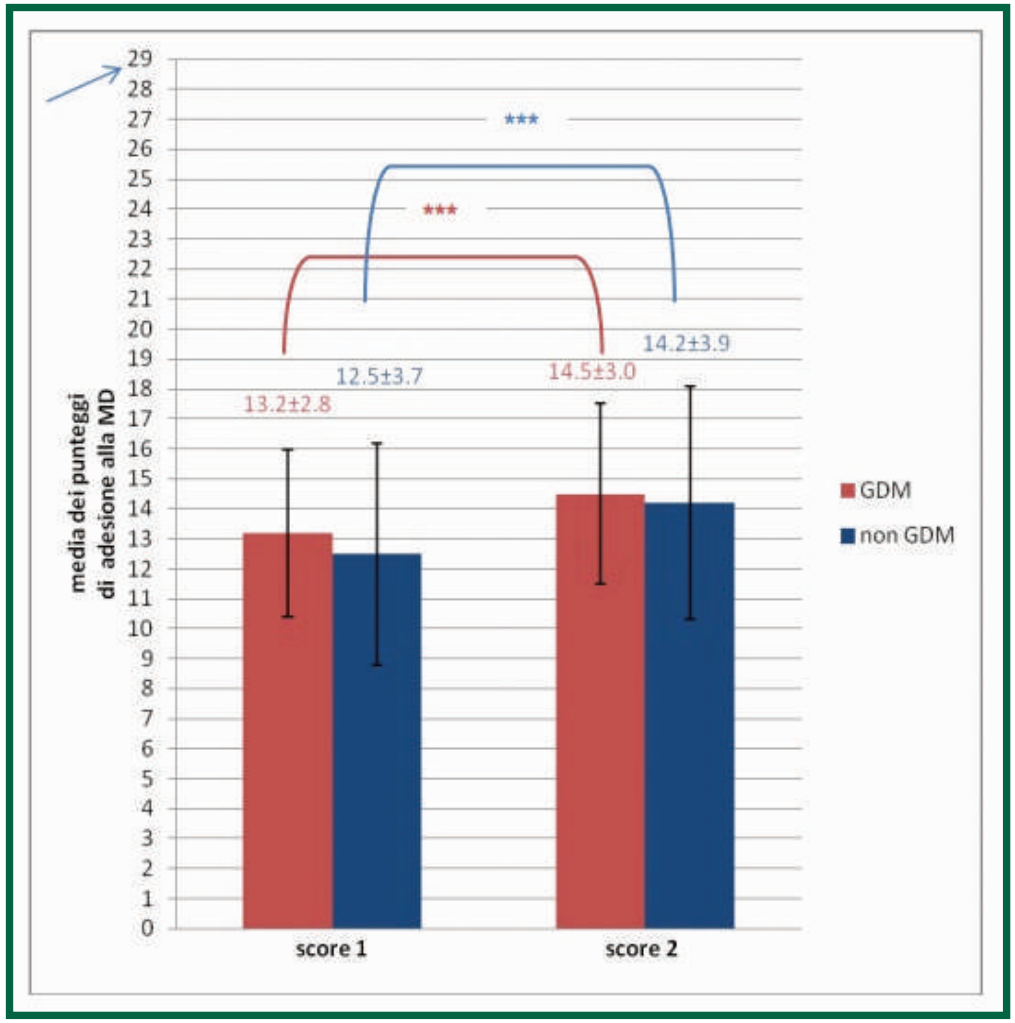
Marker clinici del rischio infiammatorio

- AA/EPA Ratio 1.5-3.0
- TG/HDL Ratio <1 (mg/dl) o <0.4(mmoles/ml)
- HbA1c 5%

Costruire una dieta antinfiammatoria

Questionario alimentare nel II Trimestre

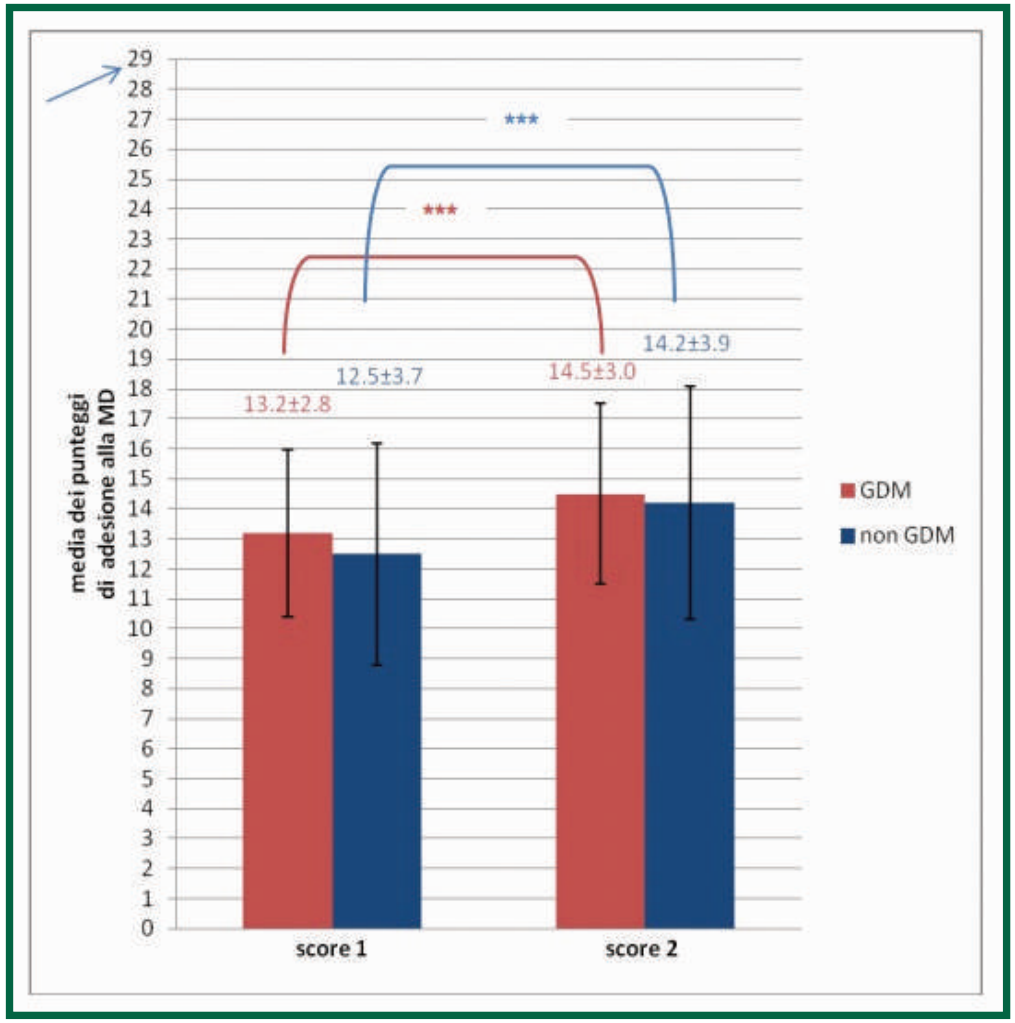
aderenza alla dieta mediterranea



Non esiste differenza nelle modalità di assunzione di cibo prima e durante la gravidanza nei controlli e nelle pazienti con GDM…

Questionario alimentare nel II Trimestre

aderenza alla dieta mediterranea



… e l'aderenza alla dieta mediterranea è bassa in entrambi i gruppi

HARVARD T.H. CHAN
SCHOOL OF PUBLIC HEALTH

The Nutrition Source

Il Piatto del Mangiar Sano (Italian)

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Il Piatto del Mangiar Sano (Italian)

Move your ass and pick up your food!

Uso potenziale di supplementi antinfiammatori

Uso potenziale di supplementi antinfiammatori

Acidi grassi Omega-3

- Utilizzare prodotti altamente raffinati con contenuti irrilevanti di PCB (PolyChlorinated Biphenyls)

- 2.5 gr al giorno di EPA e DHA

Uso potenziale di supplementi antinfiammatori

Polifenoli

- A concentrazioni adeguate i Polifenoli possono attivare AMP-chinasi, che svolge un ruolo centrale nel controllo molecolare del metabolismo

- 500-1000 mg dose suggerita giornaliera

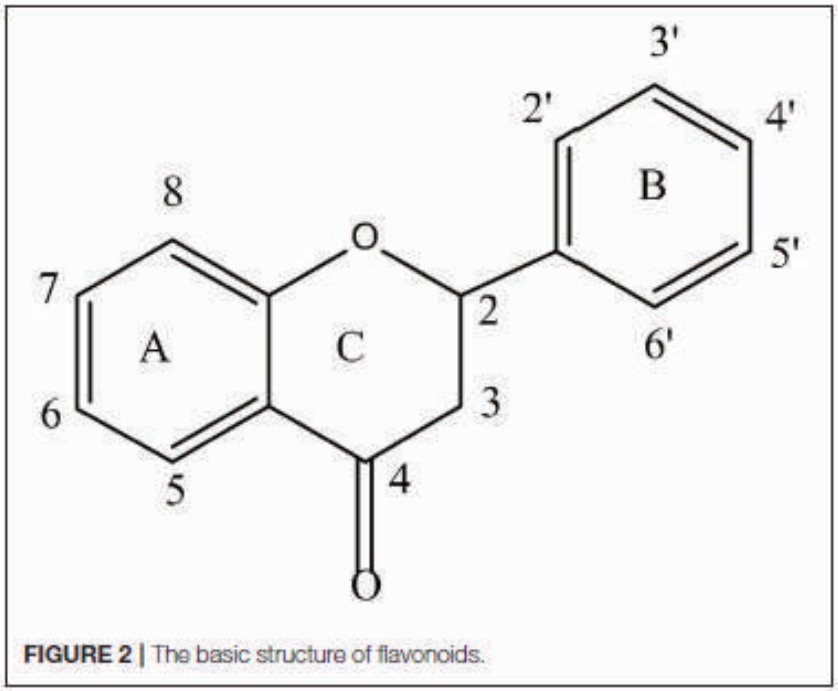

FIGURE 2 | The basic structure of flavonoids.

I polifenoli che sono difficilmente assorbibili a livello intestinale potrebbero svolgere la loro azione interagendo con il microbiota intestinale

frontiers in Pharmacology

REVIEW
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Significance of Microbiota in Obesity and Metabolic Diseases and the Modulatory Potential by Medicinal Plant and Food Ingredients

Hoda M. Eid[1,2,3], Michelle L. Wright[4], N. V. Anil Kumar[5], Abdel Qawasmeh[6], Sherif T. S. Hassan[7], Andrei Mocan[8,9], Seyed M. Nabavi[10], Luca Rastrelli[11], Atanas G. Atanasov[12,13,14] and Pierre S. Haddad[1,2]**

I polifenoli ed i polisaccaridi (destrine, mannani) potrebbero modificare l'assorbimento dei substrati metabolici interagendo con il microbiota

Amelioration of diabesity-induced colorectal ontogenesis by omega-3 fatty acids in mice

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Anche gli Omega-3 possono migliorare il metabolismo agendo a livello intestinale