



LA GESTIONE DELLA GRAVIDANZA OGGI

Enrico Ferrazzi



Fondazione IRCCS Ca' Granda
Ospedale Maggiore Policlinico



UNIVERSITÀ DEGLI STUDI
DI MILANO

*Direttore -MANGIAGALLI CENTER
IRCCS CA GRANDA POLICLINICO
University of Milan, School of Medicine,*

Gravidanza a basso rischio: counselling e sorveglianza in carico alla Ostetrica Laureata

Gravidanza con rischio intermedi o patologie: specialista ginecologo - MMF

Scenari comuni al bilancio di salute e alla assenza specilistica:
obesità, infiammazione da cibo



**ovvero... gli effetti del “Big Mak”, della “Mutella” e degli antibiotici
sulla riproduzione umana**

**pregnancy and diabetes- foes #1
exploitation of low-income
low-culture people by the agro-
industrial system**

**AMERICAN ASSOCIATION OF ADVERTISING
AGENCIES -1927:**

**final choice of "quantity" over
"quality"**

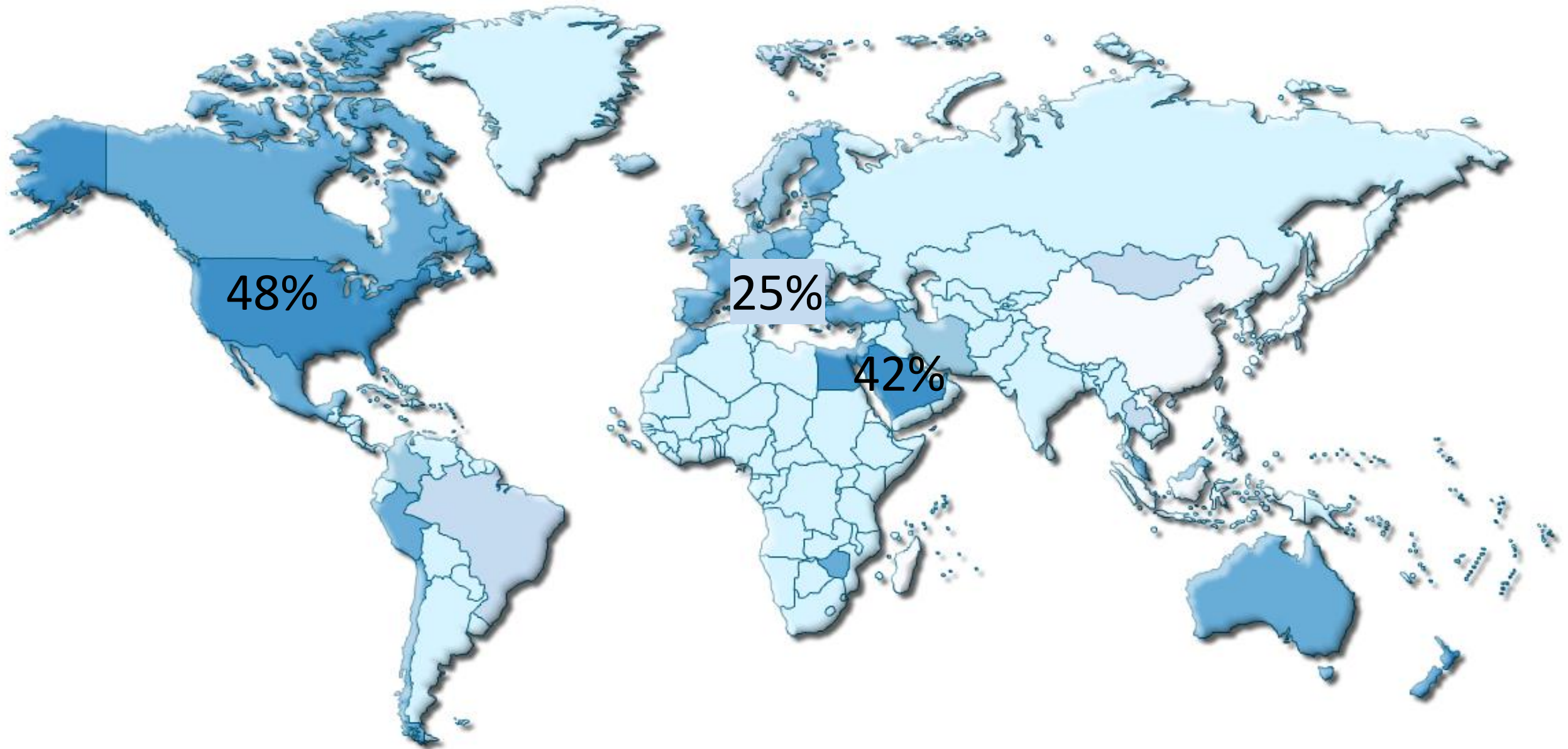
" It is futile to try to appeal to
masses on an intellectual basis

**It might be necessary to fool people
for their own good. Average
intelligence is surprisingly low.**

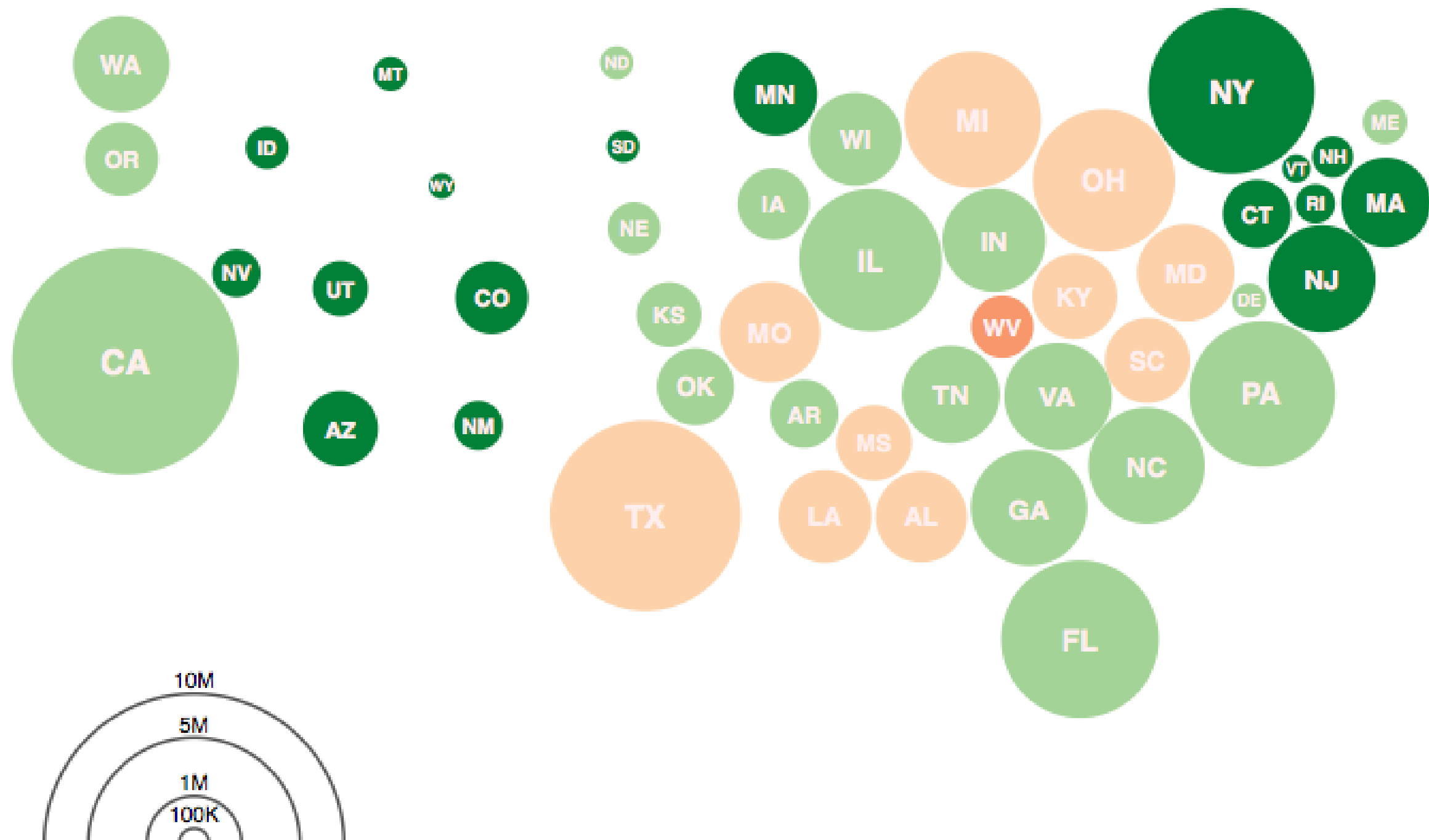
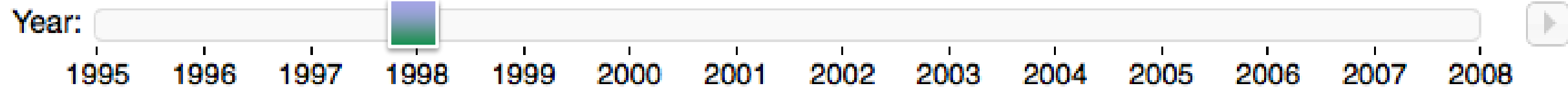
It is so much more effectively guided
by subconscious impulses and
instincts than by reason"

obesità

ADULT FEMALE OBESITY

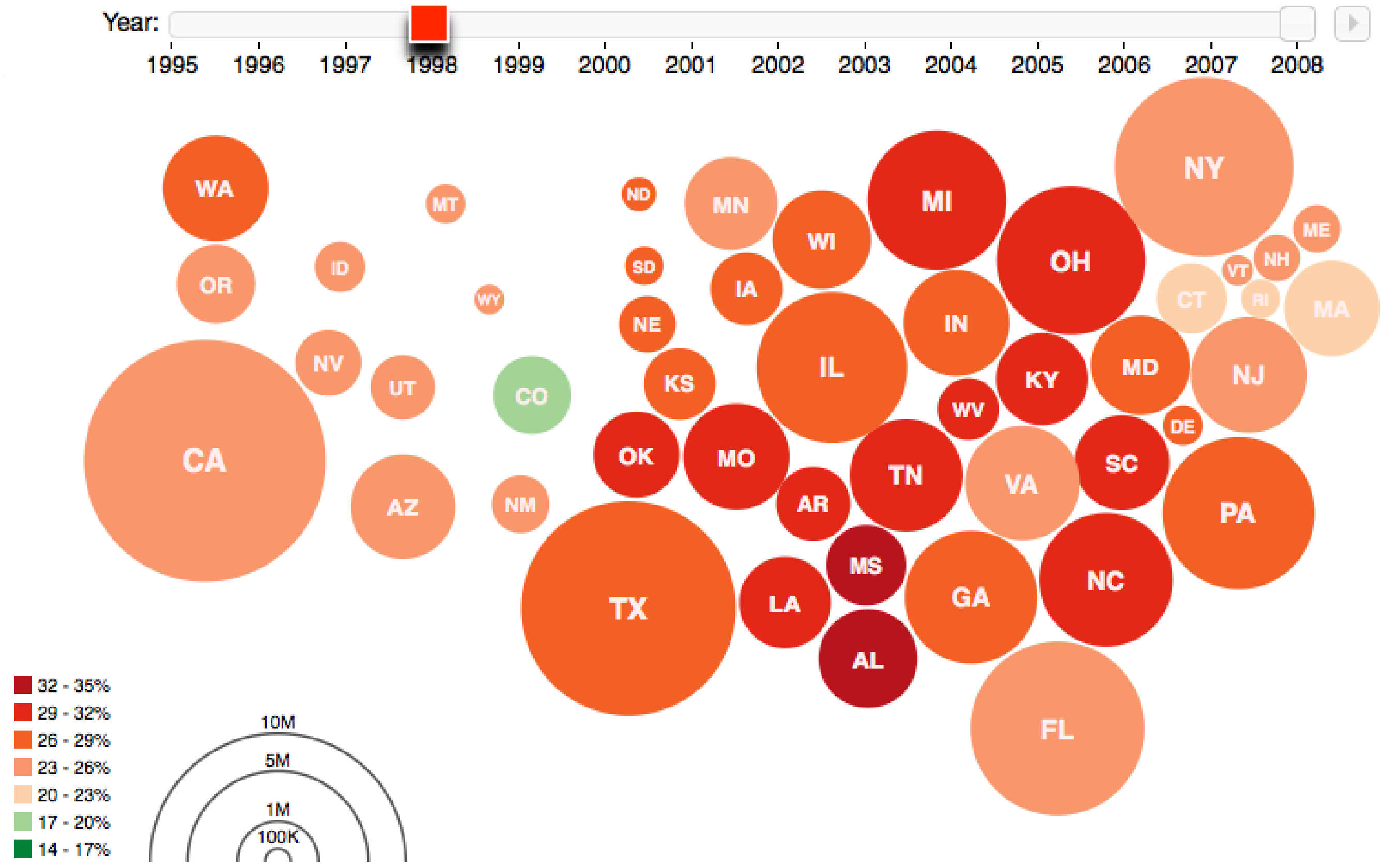


Dorling Cartogram of Obesity in the United States (1995 to 2008)





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 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008

2008 Highlights:

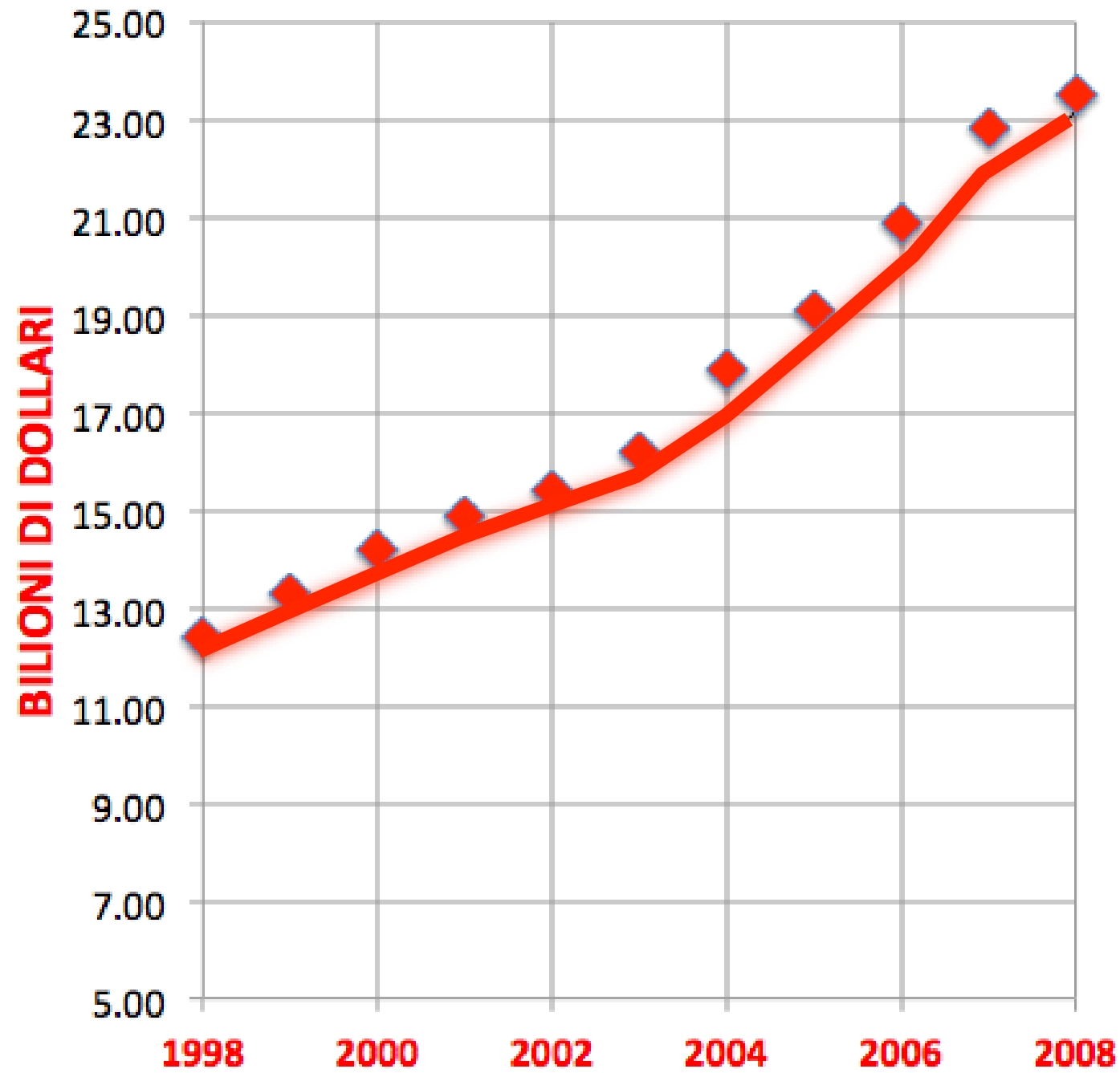
6.9%
Global comparable
sales increase

\$23.5 Billion
Total revenues

\$5.8 Billion
Cash returned
to shareholders via
dividends and share
repurchases



2008



WA

OR

CA

NY

ME

NH

VT

CT

RI

MA

MD

NJ

DE

SC

PA

NC

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

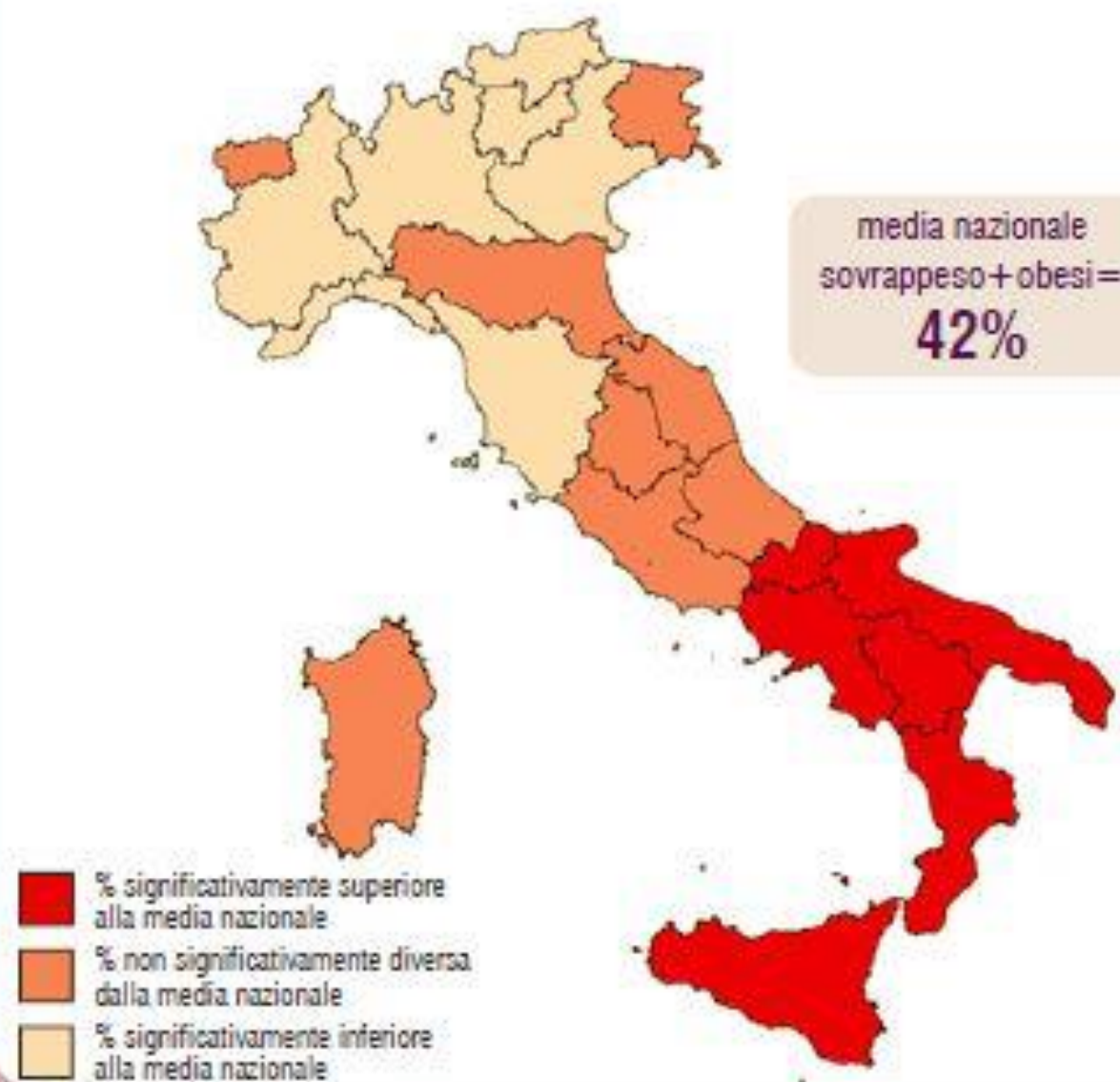
10M

5M

1M

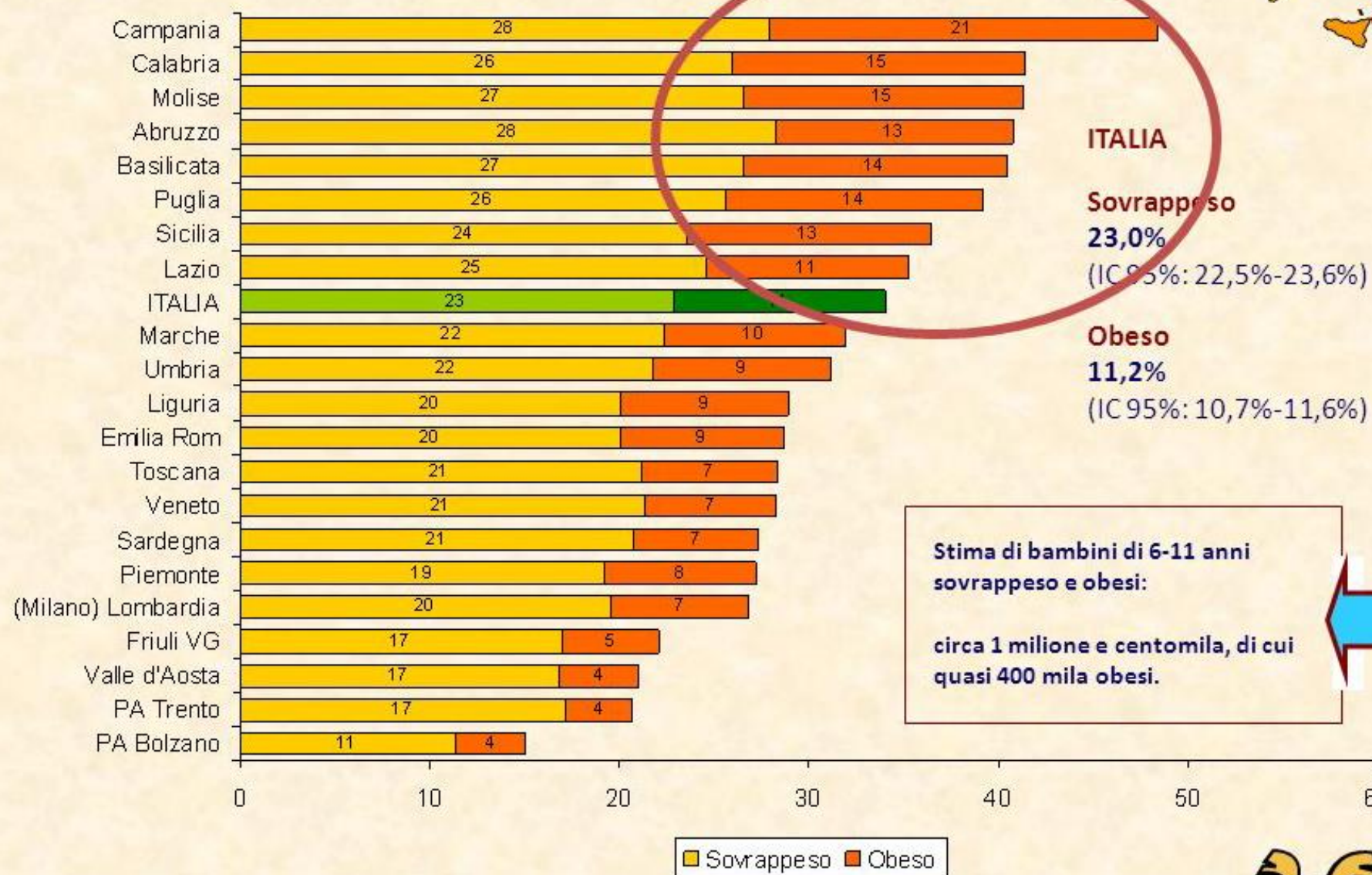
100K

Peso in eccesso nella popolazione delle regioni italiane - PASSI 2009-2012

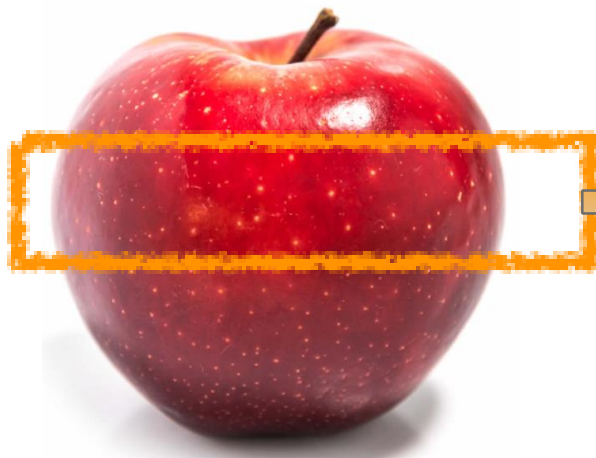




Sovrappeso e obesità per regione, bambini di 8-9 anni della 3^a primaria



infiammazione
da grasso
viscerale



obesità TRUNCALE

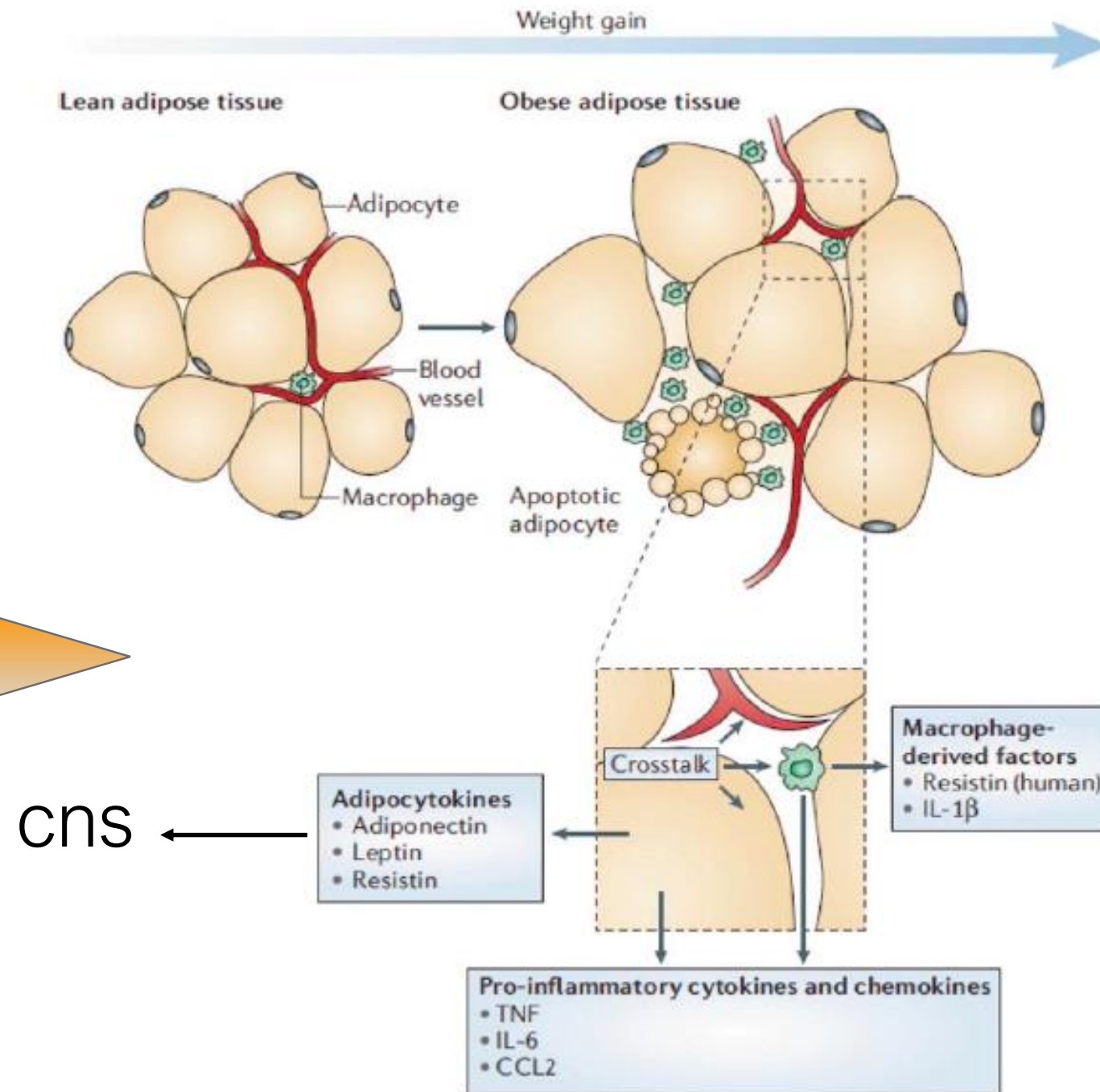
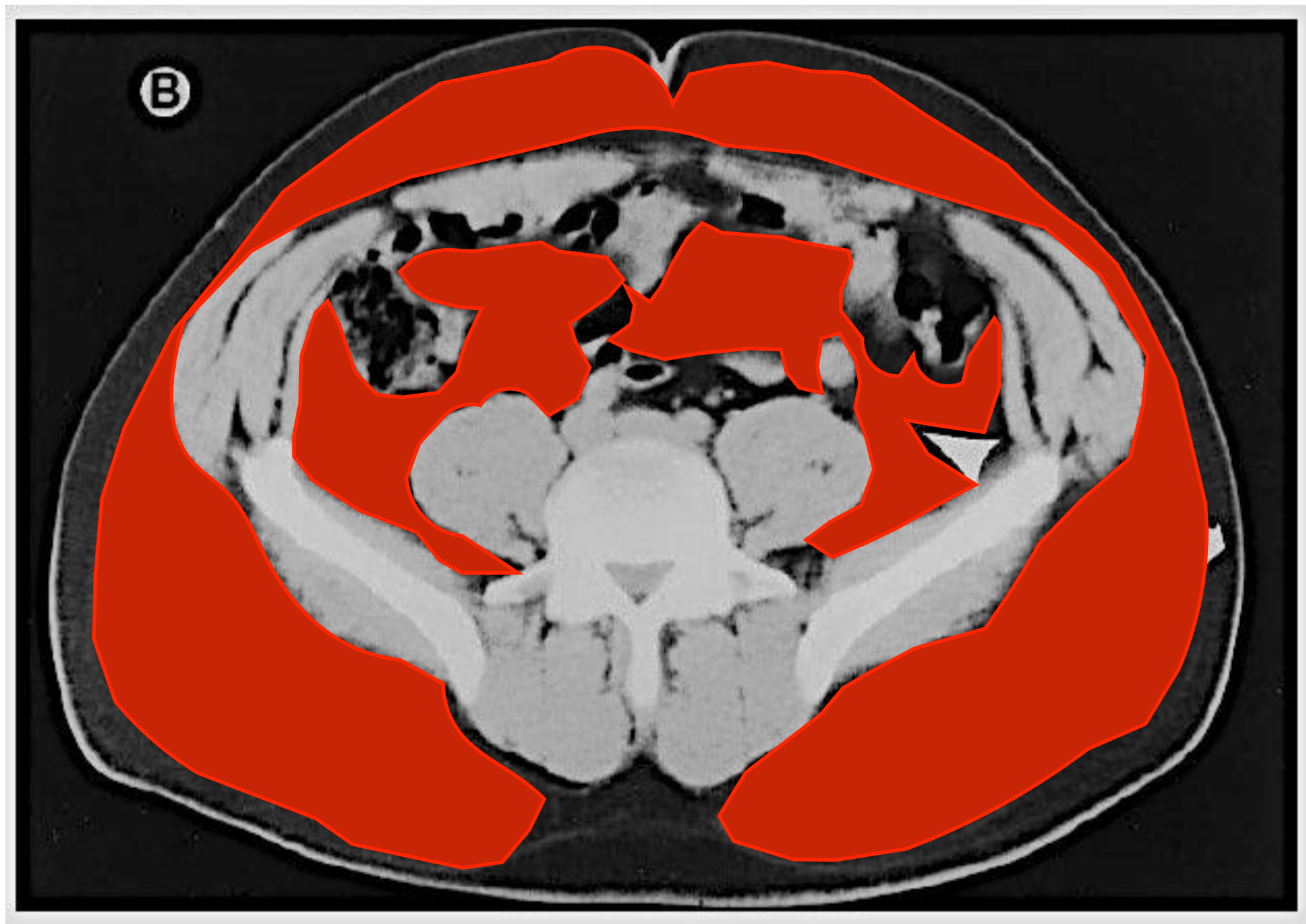


Figure 1 The visceral adipose tissue leads to recruitment of macrophages. These cells, macrophages and adipocytes synthesize a "cytokine-adipocytokines" mix which activates a pro-inflammatory milieu. Tilg H, Moschen AR. Adipocytokines: mediators linking adipose tissue, inflammation and immunity. Nat Rev Immunol 2006; 6(10): 772-83.

Subdivisions of subcutaneous abdominal adipose tissue and insulin resistance

DAVID E. KELLEY, F. LELAND THAETE, FRED TROOST,
TRINA HUWE, AND BRET H. GOODPASTER

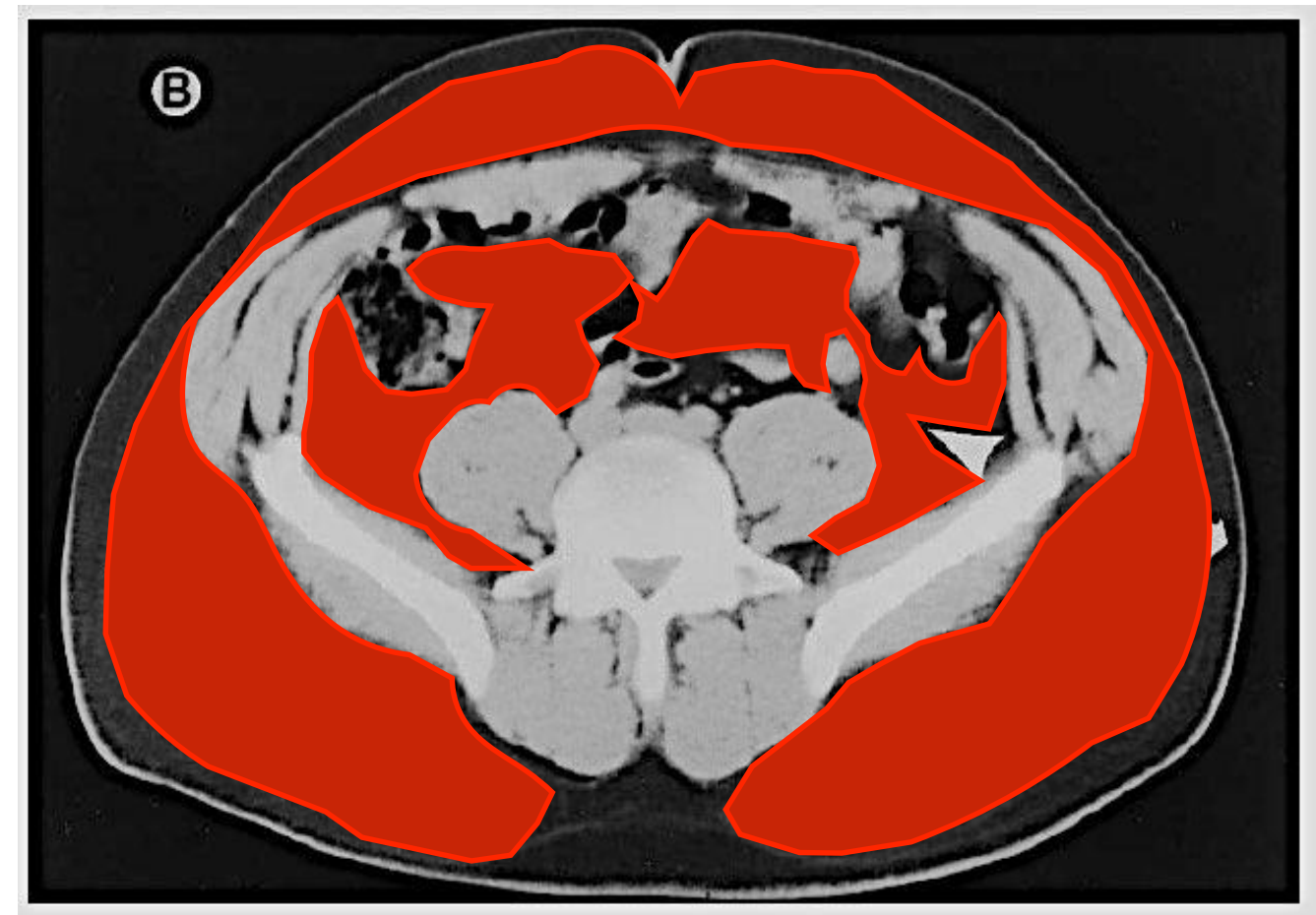
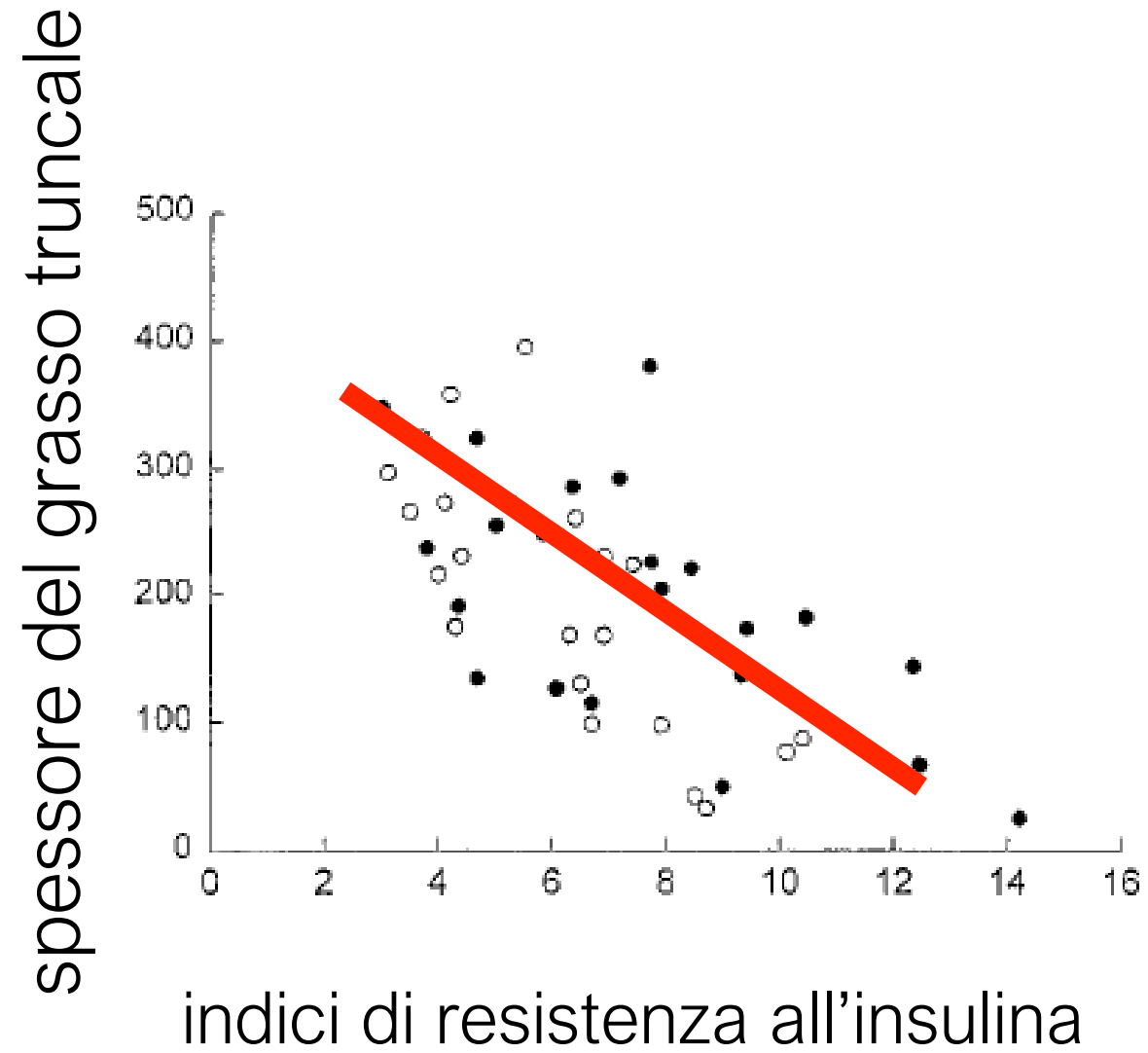
*Division of Endocrinology and Metabolism, Department of Medicine, and Department of Radiology,
University of Pittsburgh, Pittsburgh, Pennsylvania 15261*



Subdivisions of subcutaneous abdominal adipose tissue and insulin resistance

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The combination of obesity and hypertension: a highly unfavorable phenotype requiring attention

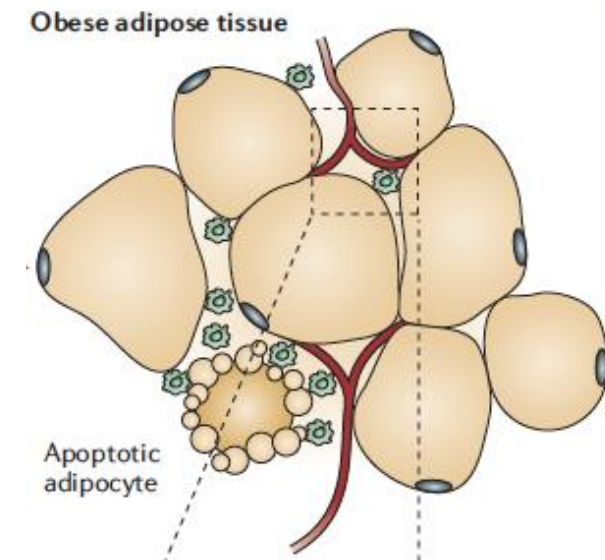
Ross Arena^a, John Daugherty^b, Samantha Bond^b, Carl J. Lavie^c,
Shane Phillips^a, and Audrey Borghi-Silva^d

Pro-inflammatory

- TNF
- IL-6
- CCL2

Adipocytokines

- Adiponectin
- Leptin
- Resistin

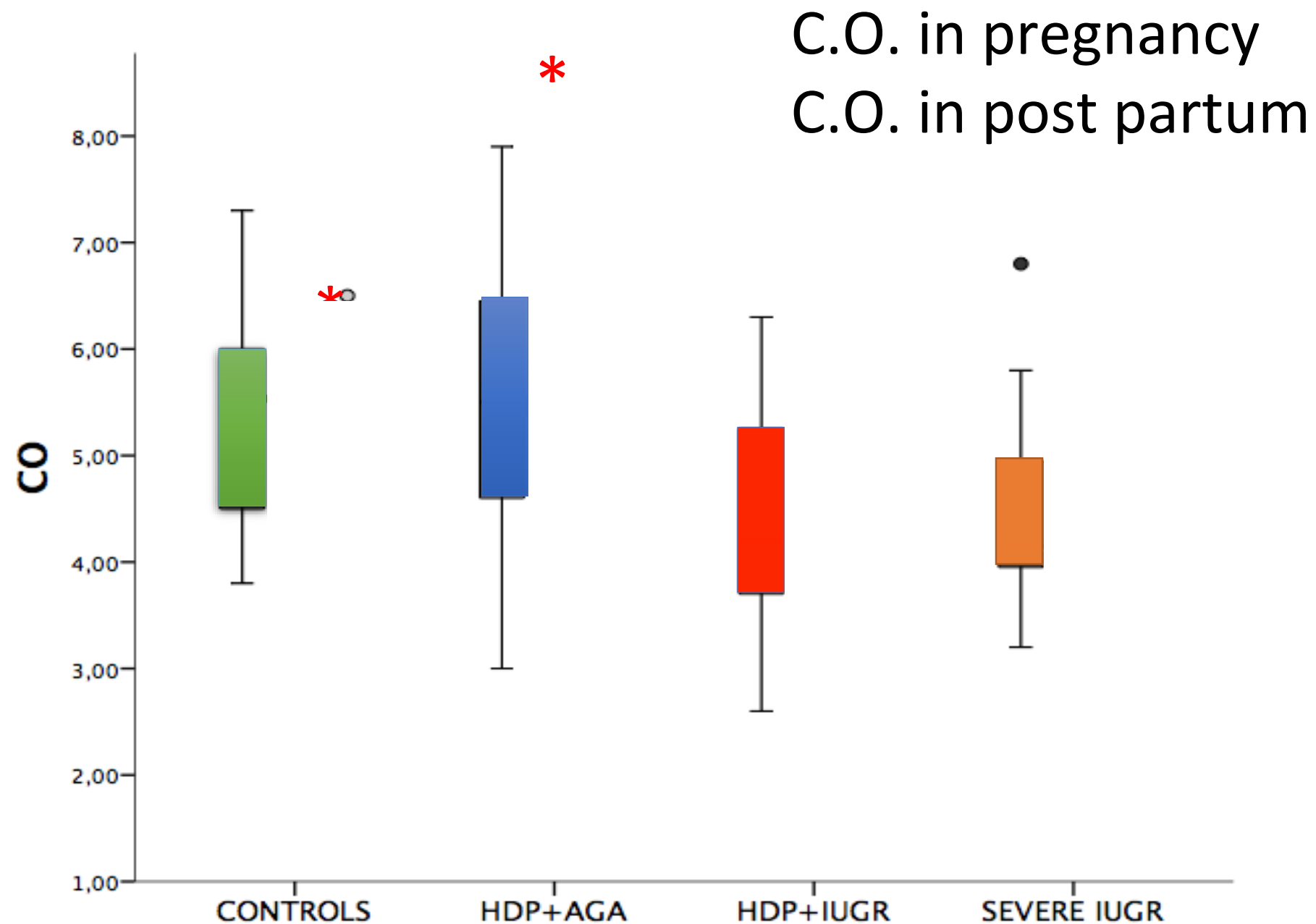


A host of proinflammatory and inflammatory compounds secreted by **adipose tissue**, ... promote **endothelial dysfunction** and thus HTN

Insulin resistance decreases nitric oxide synthesis and ... promotes **vasoconstriction**

obesità =
disordini ipertensivi in gravidanza
diabete gestazionale







Longitudinal assessment of Maternal Hemodynamic in a cohort of HDP



ORIGINAL ARTICLE



The association of first trimester uterine arteries Doppler velocimetry with different clinical phenotypes of hypertensive disorders of pregnancy: a longitudinal study

Tamara Stampalija^a , Lorenzo Monasta^b , Daniela D. Di Martino^c , Mariachiara Quadrifoglio^a,
Leila Lo Bello^a , Giuseppina D'Ottavio^a, Sara Zullino^c, Cristina Mastroianni^c, Daniela Casati^c ,
Valentina Signorelli^c, Eleonora Rosti^c, Vera Cecotti^a, Matteo Ceccarello^a and Enrico Ferrazzi^{d,e} 

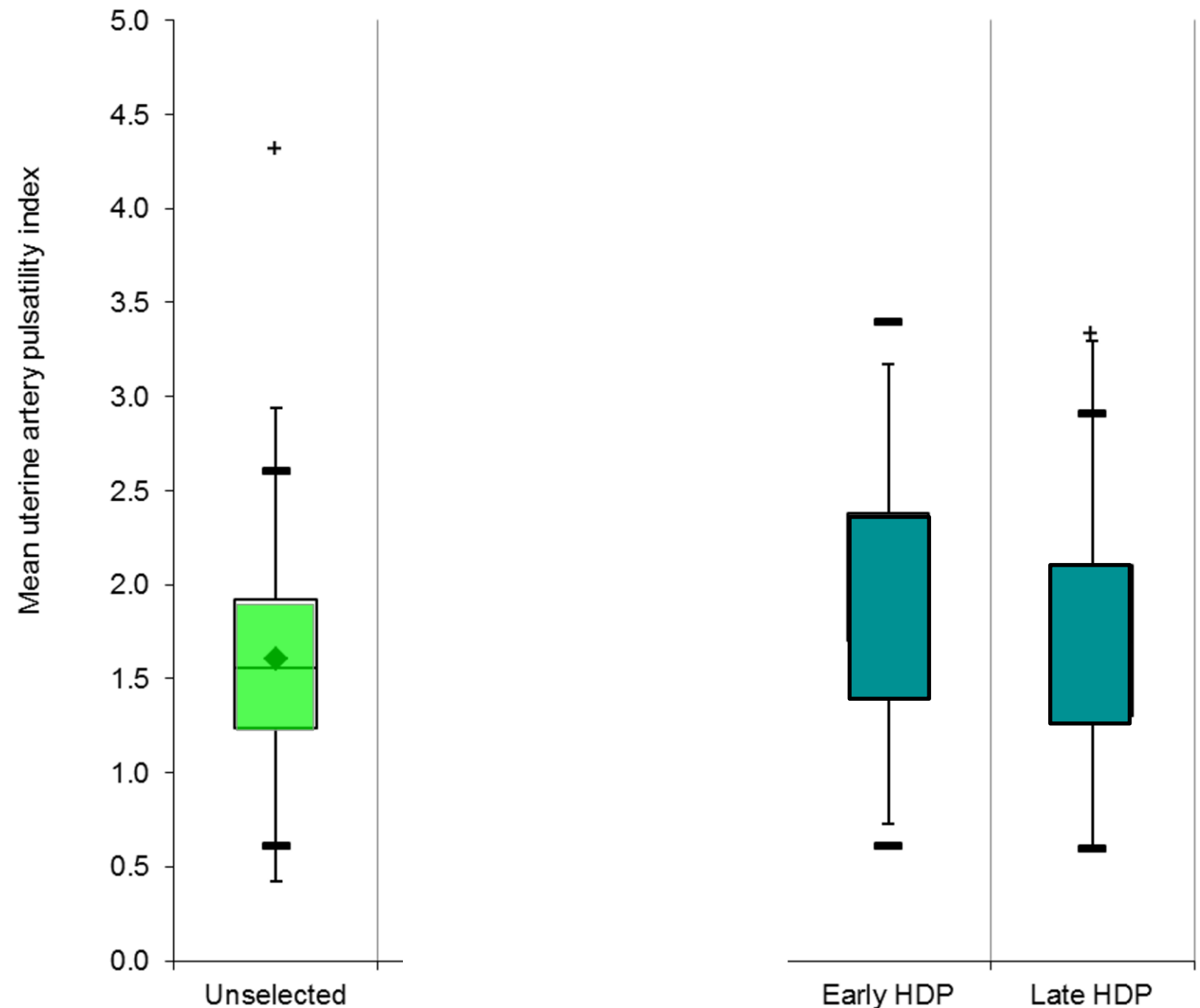
4290 pregnant women

longitudinal follow-up:

Measure of outcome:

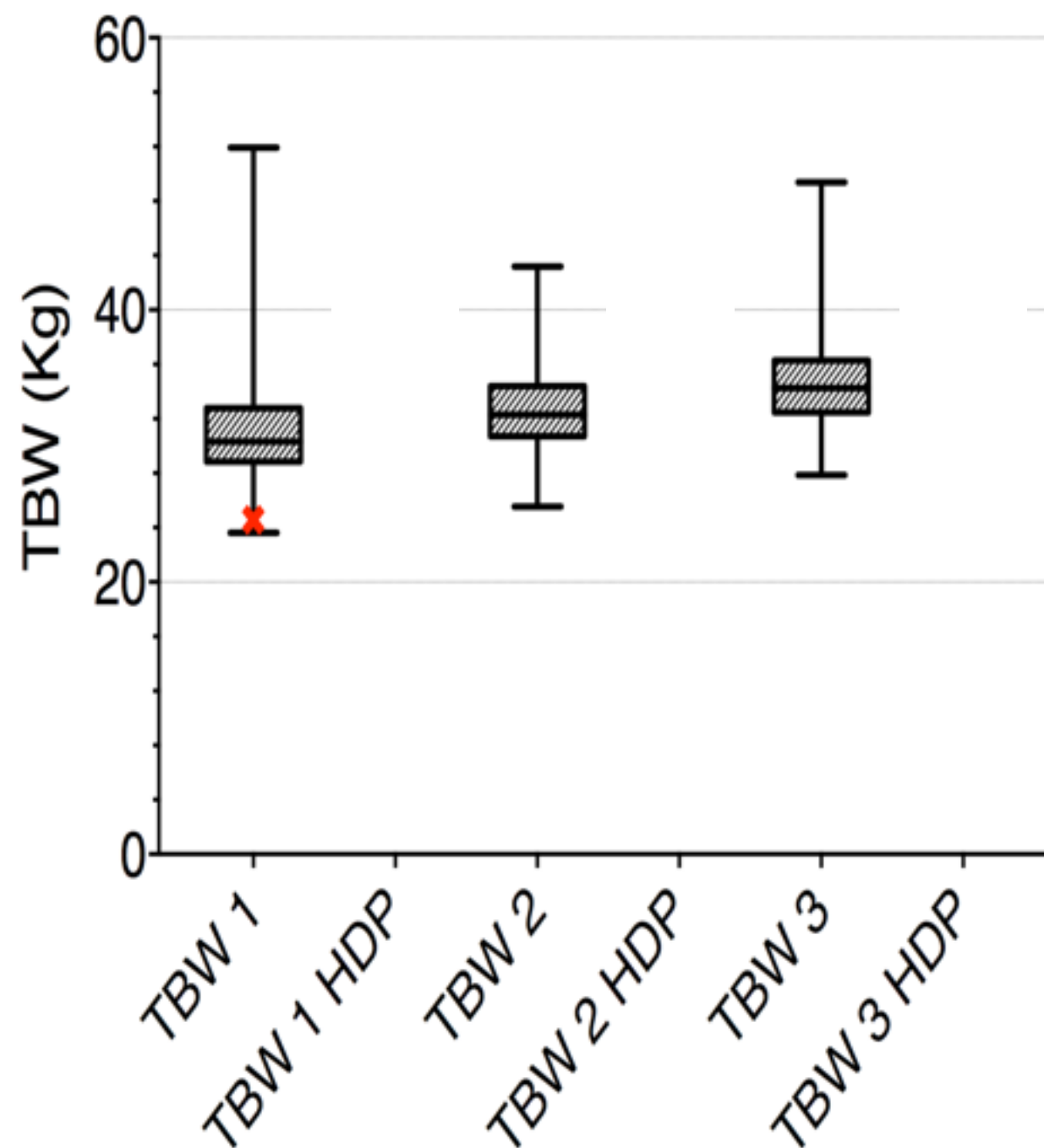
H.D.P.

LONGITUDINAL FETAL



Longitudinal changes and correlations of
bioimpedance and anthropometric measurements
in pregnancy: Simple possible bed-side tools to
assess pregnancy evolution

Gabriele Piuri, Enrico Ferrazzi, Camilla Bulfoni, Luciana Mastricci, Daniela Di
Martino & Attilio Francesco Speciani



**The Hyperglycemia and Adverse Pregnancy Outcome
(HAPO) study: paving the way for new diagnostic
criteria for gestational diabetes mellitus**

Donald R. Coustan, MD; Lynn P. Lowe, PhD; Boyd E. Metzger, MD; Alan R. Dyer, PhD

16% of pregnant population is suffering of a disease called
GDM ?

**Subjects,
cumulative %**

8.3

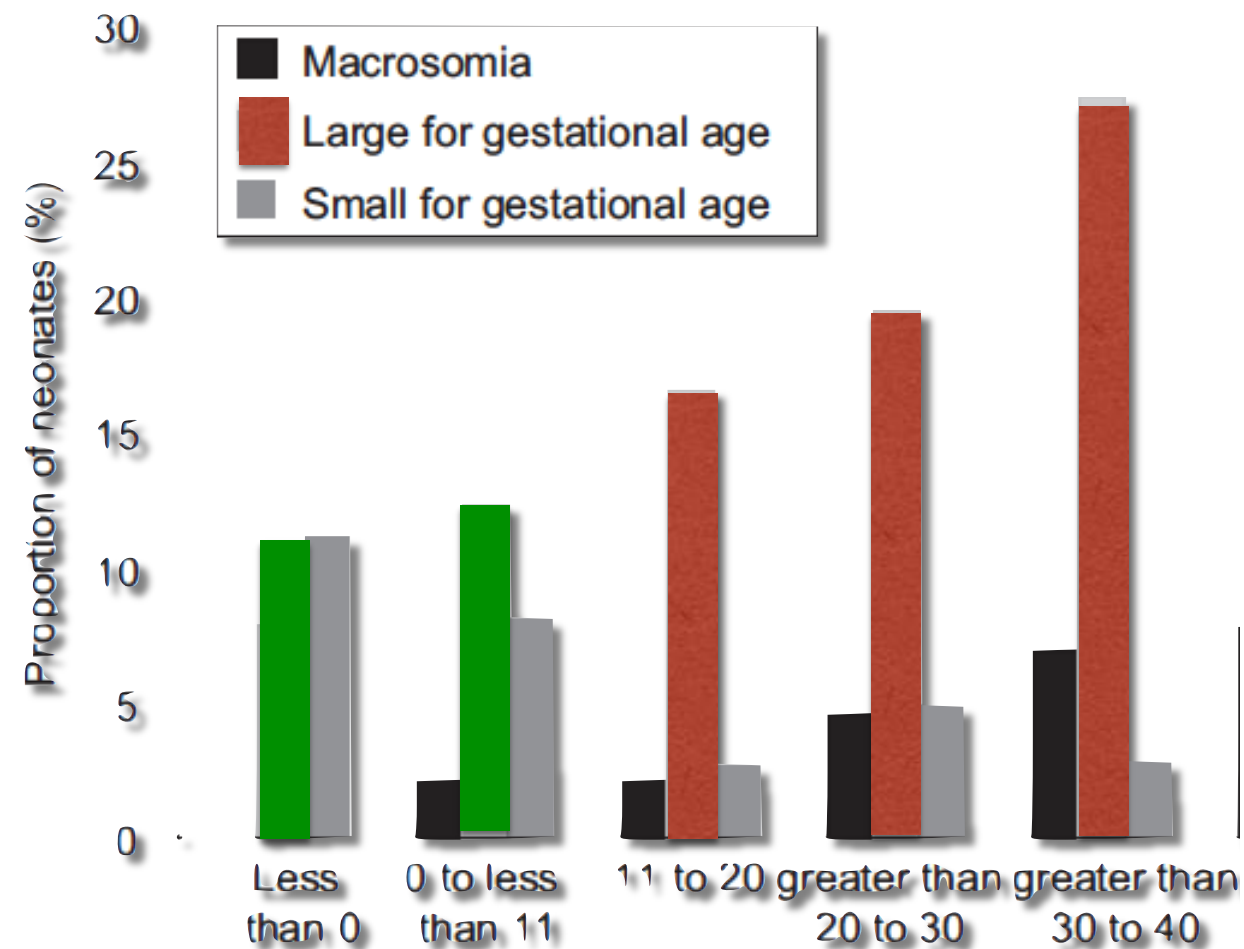
14.0

16.1

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

(Obstet Gynecol 2011;117:812–8)



gestational weight gain

Inflammation da cibo

Fast Food Consumption and Gestational Diabetes Incidence in the SUN Project

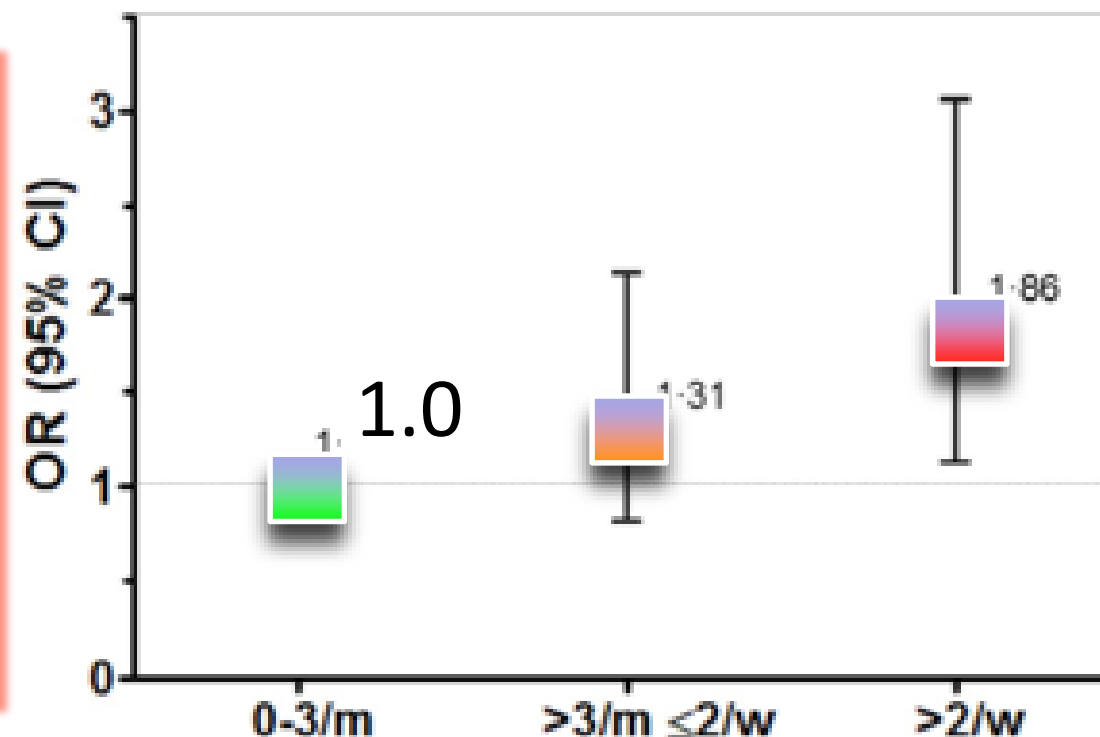
Ligia J. Domínguez^{1*}, Miguel A. Martínez-González², Francisco Javier Basterra-Gortari^{2,3}, Alfredo Gea², Mario Barbagallo¹, Maira Bes-Rastrollo^{2,4}



food
inflammation



- 3038 women
- age 29 years
- BMI = 21
- FamilyHistory of Type 2 diabetes=10%



Odds ratio of GD according to fast food consumption per week

How food can cause inflammation

Saturated fatty acids enhance TLR4 immune pathways in human trophoblasts

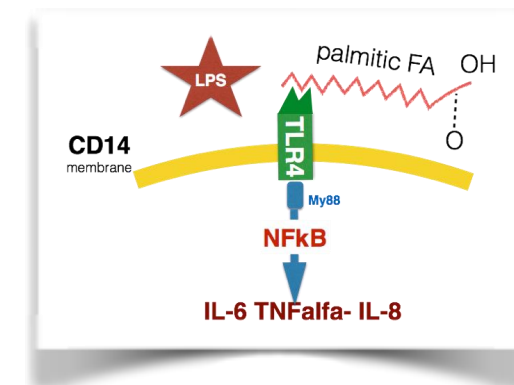
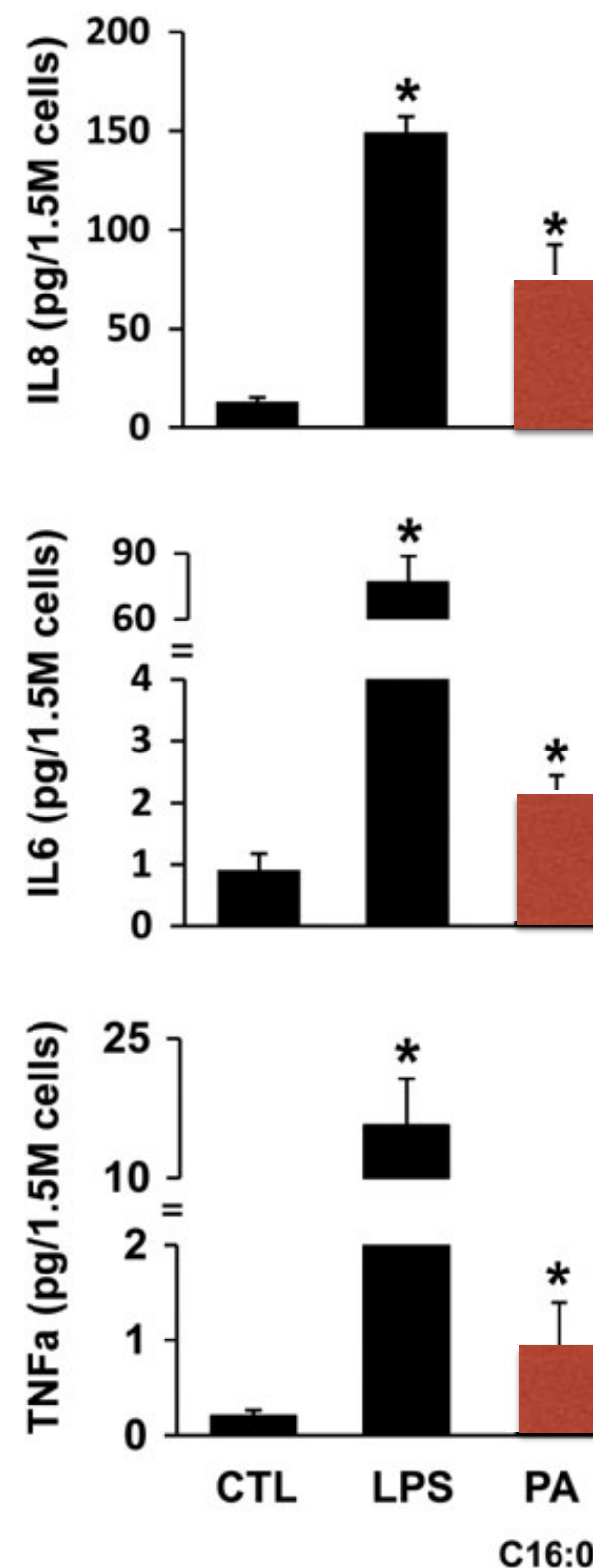
Xiaohua Yang, Maricela Haghiac, Patricia Glazebrook, Judi Minium, Patrick M. Catalano, and Sylvie Hauguel-de Mouzon*

DISCUSSION

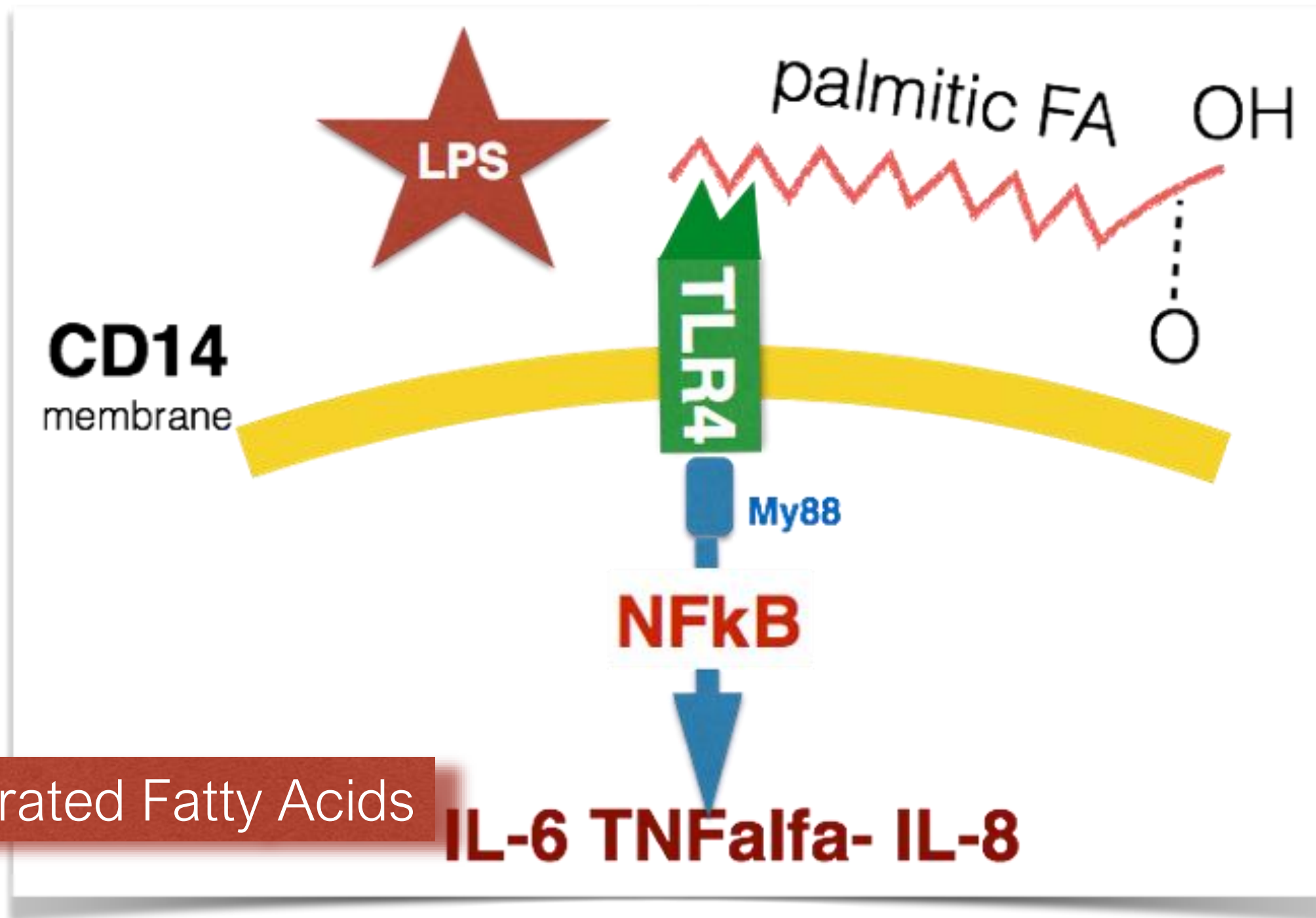
saturated FAs induced an innate immune response in human placental cells.

We demonstrated that in vitro treatment of trophoblast cells with **palmitic acid (PA)** stimulated the **synthesis and release of three major inflammatory cytokines IL-6, IL-8 and TNF- α** , similar to that induced by bacteria **LPS**

Saturated Fatty Acids



Long chain Fatty Acids interact with TLR4 receptors as LPS, and activate intracellular NFkB to produce pro inflammatory cytokines



Hypertension

SCIENTIFIC CONTRIBUTIONS, PART 2

Aging, Acculturation, Salt Intake, and Hypertension in the Kuna of Panama

Norman K. Hollenberg, Gregorio Martinez, Marji McCullough, Terri Meinking, Diane Passan, Mack Preston, Alicia Rivera, David Taplin, Maureen Vicaria-Clement

salt

MIGRATION, ACCULTURATION and BLOOD PRESSURE

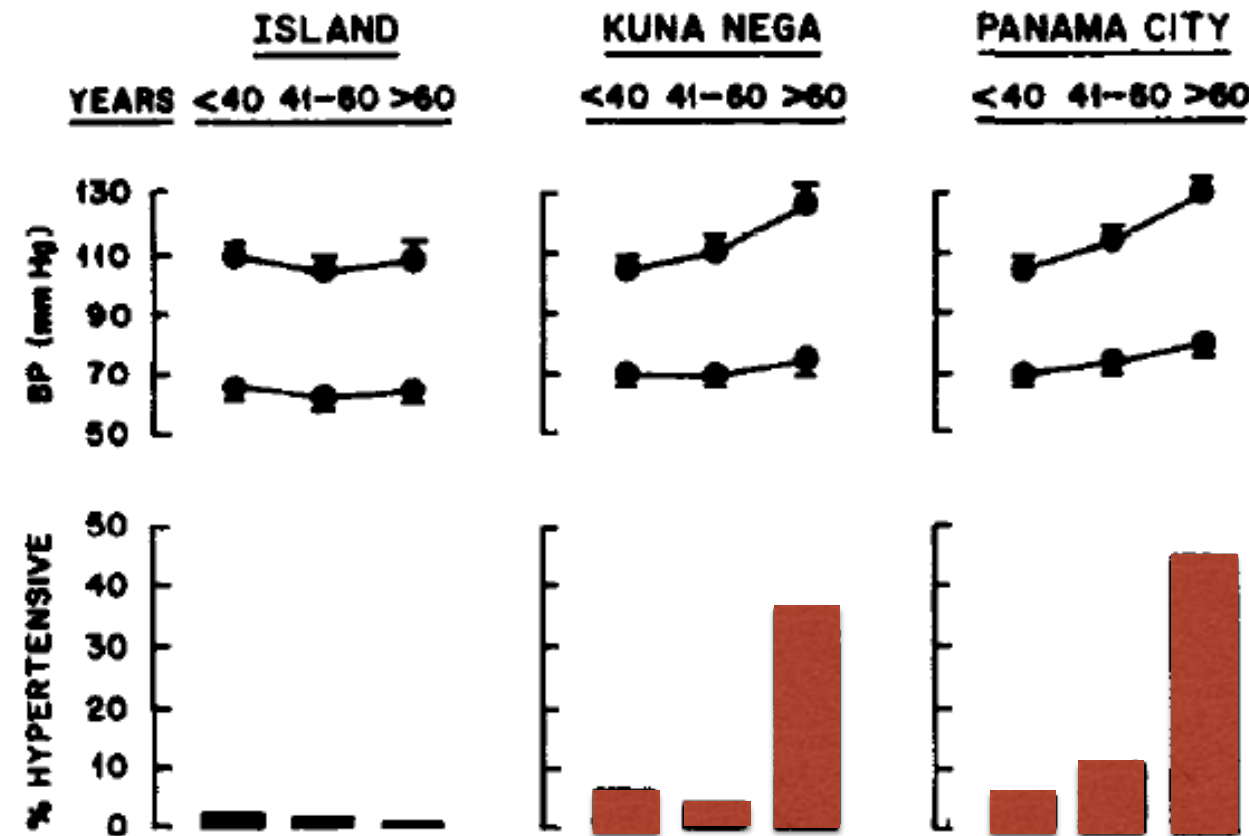
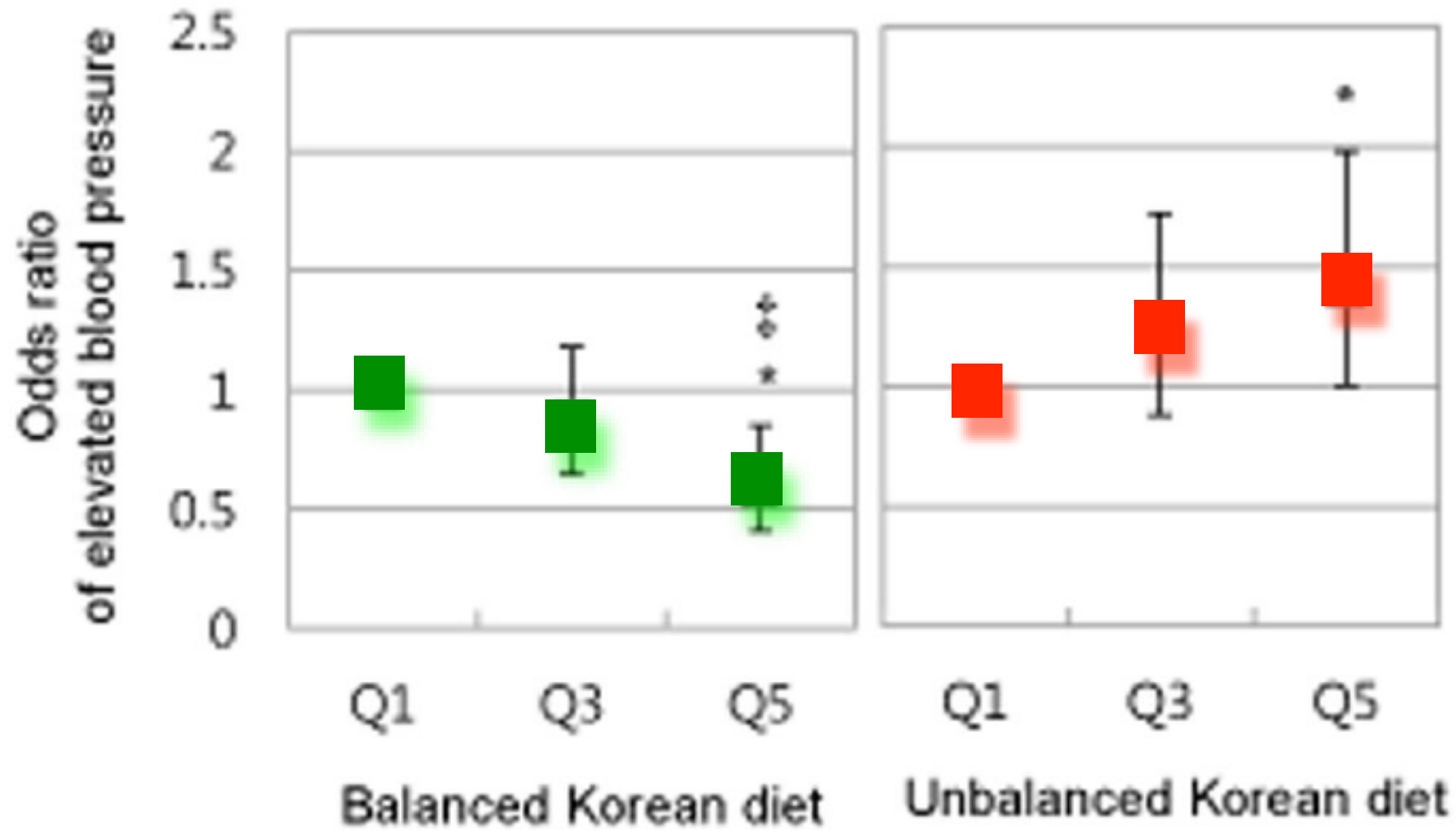


FIG 1 Relation between age, blood pressure (BP), and hypertension prevalence in three Kuna communities. Kuna Nega is a suburban community, which is inhabited only by Kuna Indians and which allows them to maintain some, but not all, of their island lifestyle. Note that both systolic and diastolic blood pressures rise significantly with age in the Kuna residing in Kuna Nega and Panama City, but not on the isolated island ($P < 0.01$). Hypertension is much more prevalent in both communities than in the island dwellers.

Macronutrient Composition and Sodium Intake of Diet Are Associated with Risk of Metabolic Syndrome and Hypertension in Korean Women

Hea Young Oh¹, Mi Kyung Kim^{1*}, Myoungsook Lee², Young Ok Kim³

salt

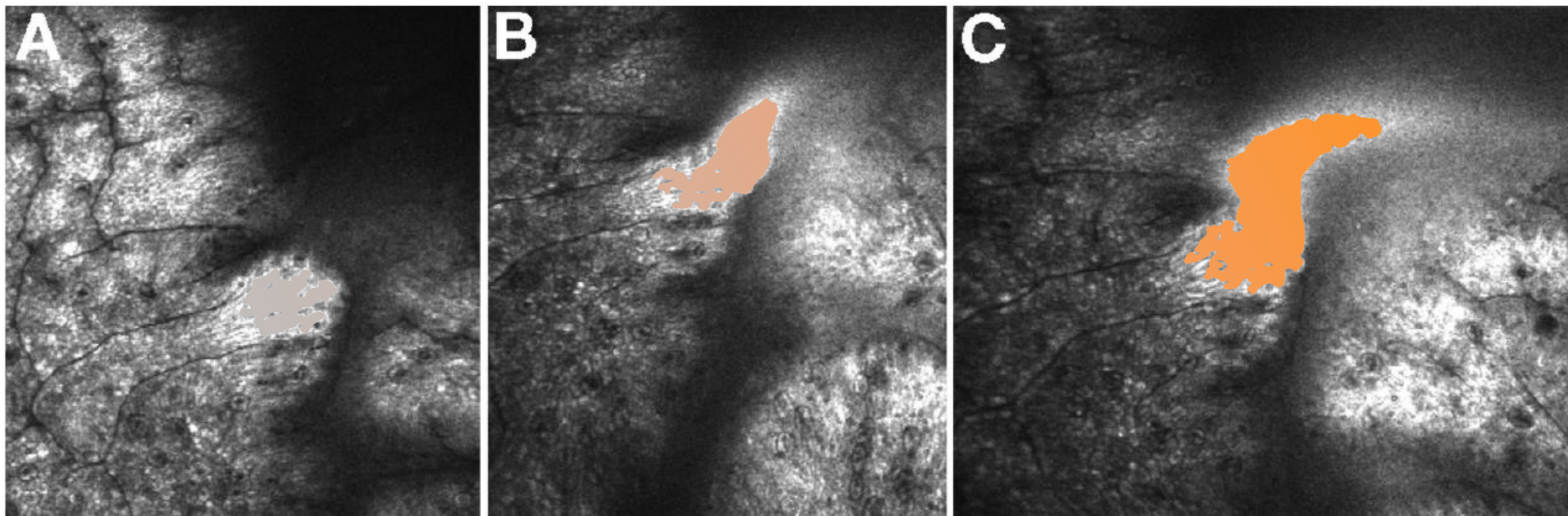


CLINICAL—ALIMENTARY TRACT

Confocal Endomicroscopy Shows Food-Associated Changes in the Intestinal Mucosa of Patients With Irritable Bowel Syndrome



Annette Fritscher-Ravens,¹ Detlef Schuppan,^{2,3,4} Mark Ellrichmann,¹ Stefan Schoch,¹ Christoph Röcken,⁵ Jochen Brasch,⁶ Johannes Bethge,¹ Martina Böttner,⁷ Julius Klose,¹ and Peter J. Milla⁸



Images of a single cell after food challenge shows the onset of mucosal damage. The intact epithelium (A) starts to break its continuity (B), forming a leak with eruption of fluorescein into the gut lumen (C).

excess of similar food
antigens presentation

The European lactase persistence genotype determines the lactase persistence state and correlates with gastrointestinal symptoms in the Hispanic and Amerindian Chilean population: a case–control and population-based study

Eugenia Morales,¹ Lorena Azocar,¹ Ximena Maul,² Claudio Perez,² José Chianale,¹ Juan Francisco Miquel¹

- In a representative sample of the Hispanic Chilean population (Mestizos) and in Amerindians, we observed a high prevalence of the lactose non-persistence genotype (CC) with a clear gradient between ethnic groups (56% and 88%, respectively). Interestingly, the C-13910>T genotype was significantly associated with digestive symptoms and self-reporting intolerance to ingestion of dairy products. This could explain the observed low consumption of dairy products (30 l milk/person/year) in our

lactase non persistence

CONSIDER LACTOSE INTOLERANCE



National
Institute of
Diabetes and
Digestive
and Kidney
Diseases
NATIONAL
INSTITUTES
OF HEALTH

Who is at risk for lactose intolerance?

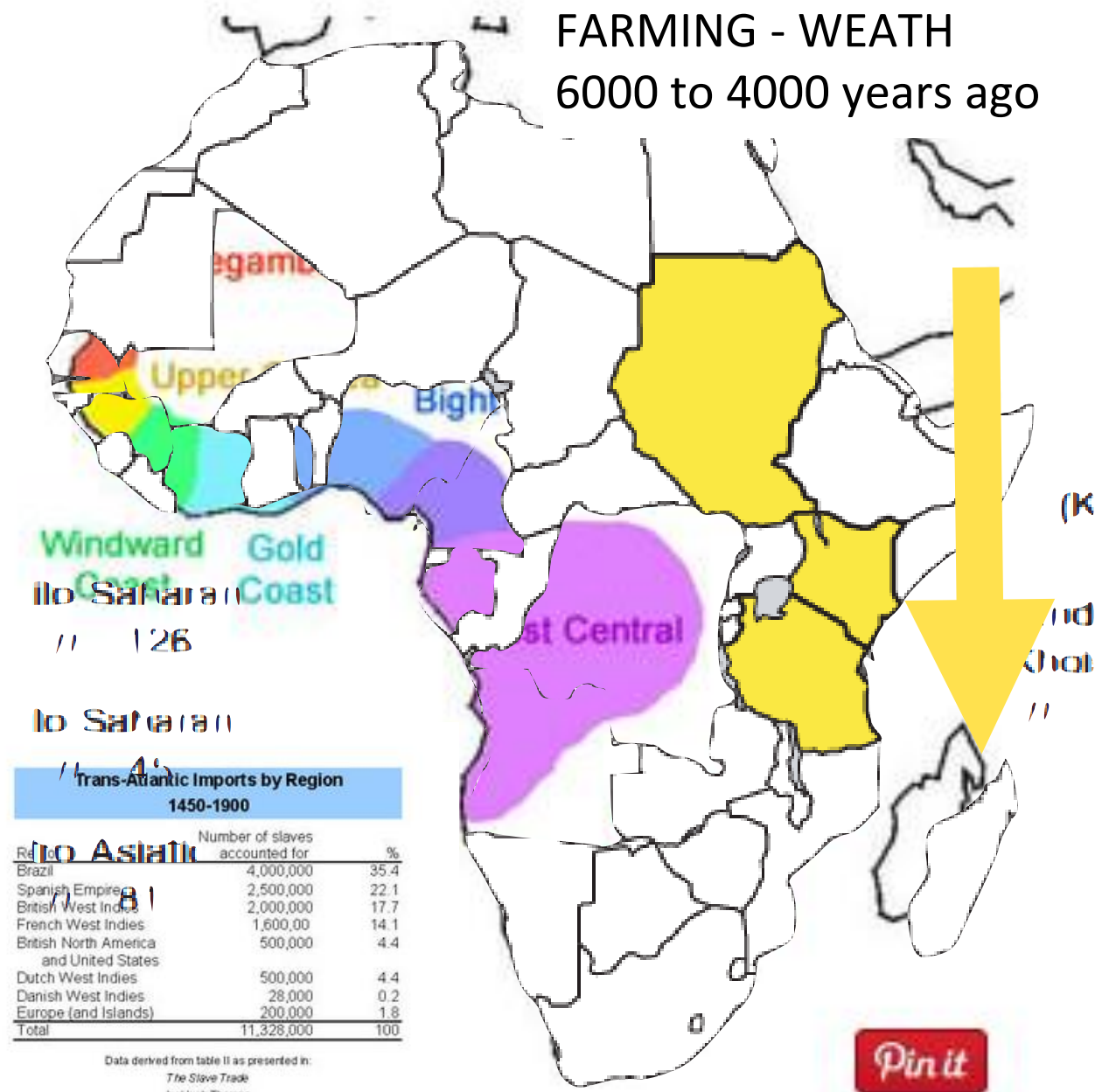
Between 30 and 50 million Americans are lactose intolerant and certain ethnic and racial populations are more affected than others. Up to 80 percent of African Americans, 80 to 100 percent of American Indians, and 90 to 100 percent of Asian Americans are lactose intolerant. The condition is least common among people of northern European descent.

pregnancy - foes #2 inappropriate food for macro ethnicity

CATTLE -COWS AND BUFFALOS

FARMING - WEATH

6000 to 4000 years ago



Pin it

Trans-Atlantic Slave Trade.

Image: © Allstair Boddy-Evans. Used with Permission.

Recent Fast Food Consumption and Bisphenol A and Phthalates Exposures among the U.S. Population in NHANES, 2003–2010

Ami R. Zota, Cassandra A. Phillips, and Susanna D. Mitro

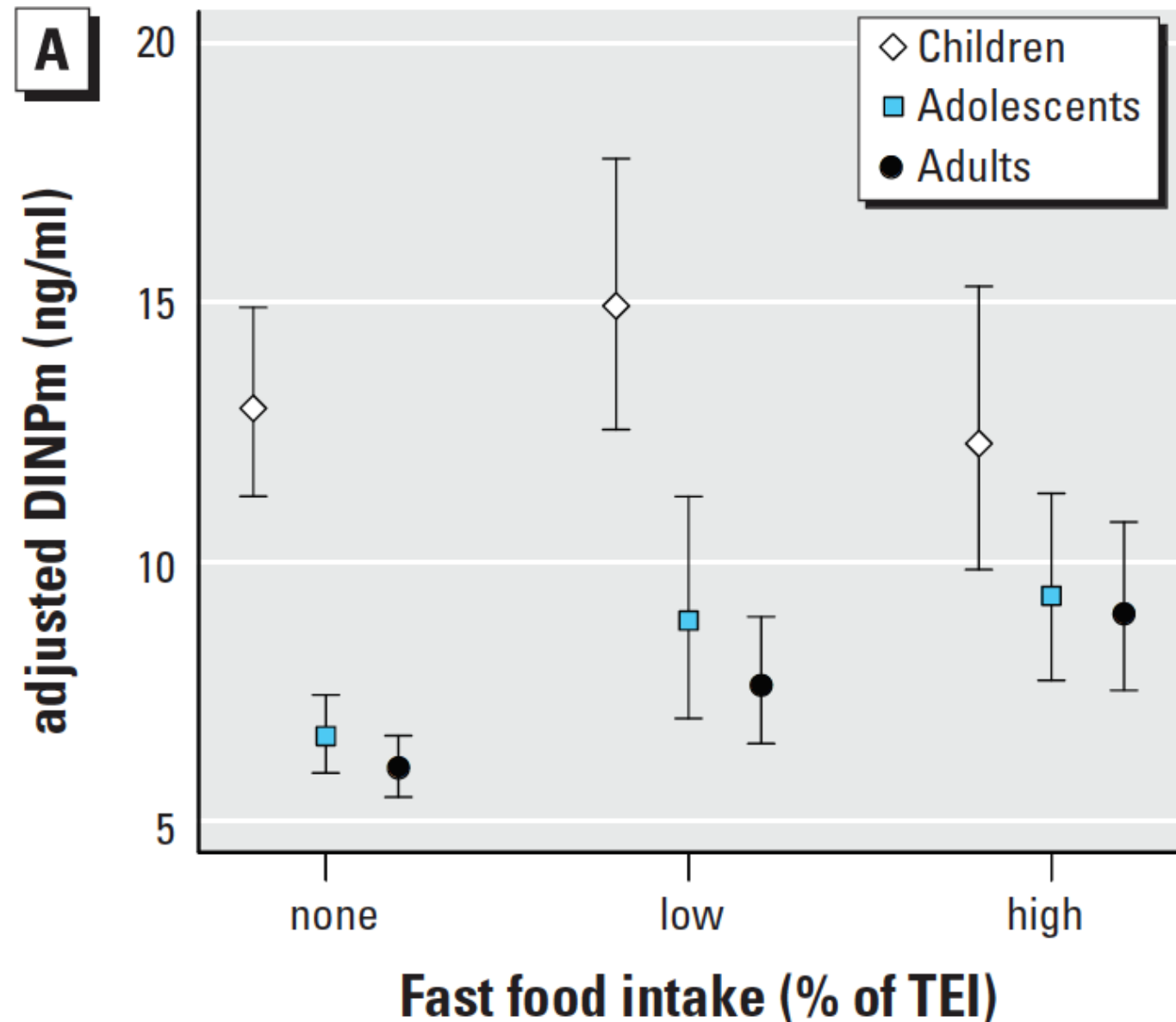
Environmental Health Perspectives • VOLUME 124 | NUMBER 10 | October 2016

Human exposure to DEHP has been associated with a metabolic disease risk factors such as insulin resistance in adolescents and adults

Fast food may be an important source of exposure to phthalates and BPA because it is highly processed, packaged, and handled.

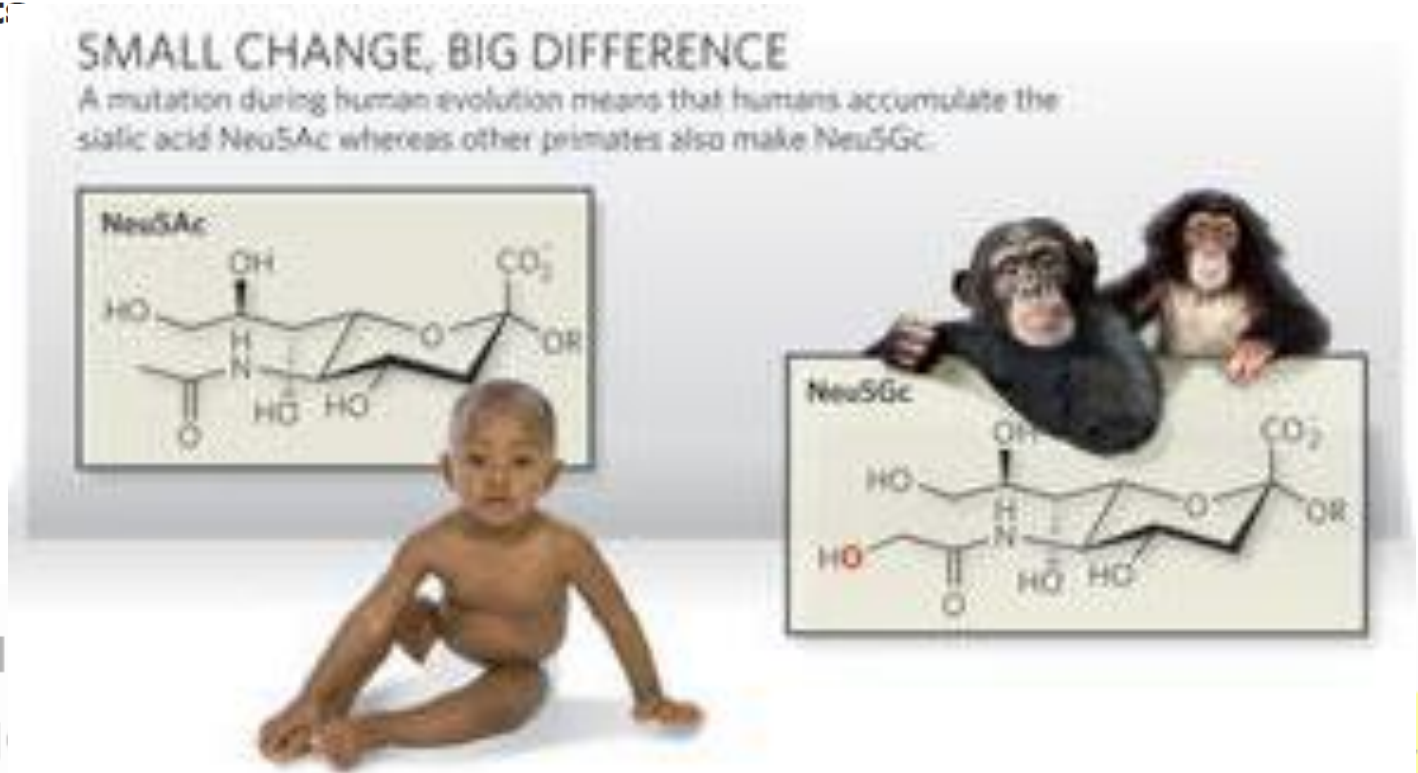
Foods high in fat, such as dairy and meat, may be more contaminated by high-molecular-weight phthalates that are more lipophilic

chemical toxics



Human evolution: Details of being human

A difference in one molecule led physician Ajit Varki to question what sets humans apart from other apes. Bruce Lieberman meets a man who sees a big picture in the finer point.



Varki's recent work has brought back an observation he first observed nearly 25 years ago.

Neu5Gc is found in animal products that contain it, such as meat and milk.

Varki and Gagneux wonder whether — among meat-eaters at least —

Neu5Gc elicits an immune reaction that might contribute to a whole spectrum of human-specific diseases that are associated with chronic

SINGLE GENE MUTATION IN HUMAN SIALIC ACID — such a problem would

not have been such a problem when humans had shorter life spans.



STUDIO GRAAL



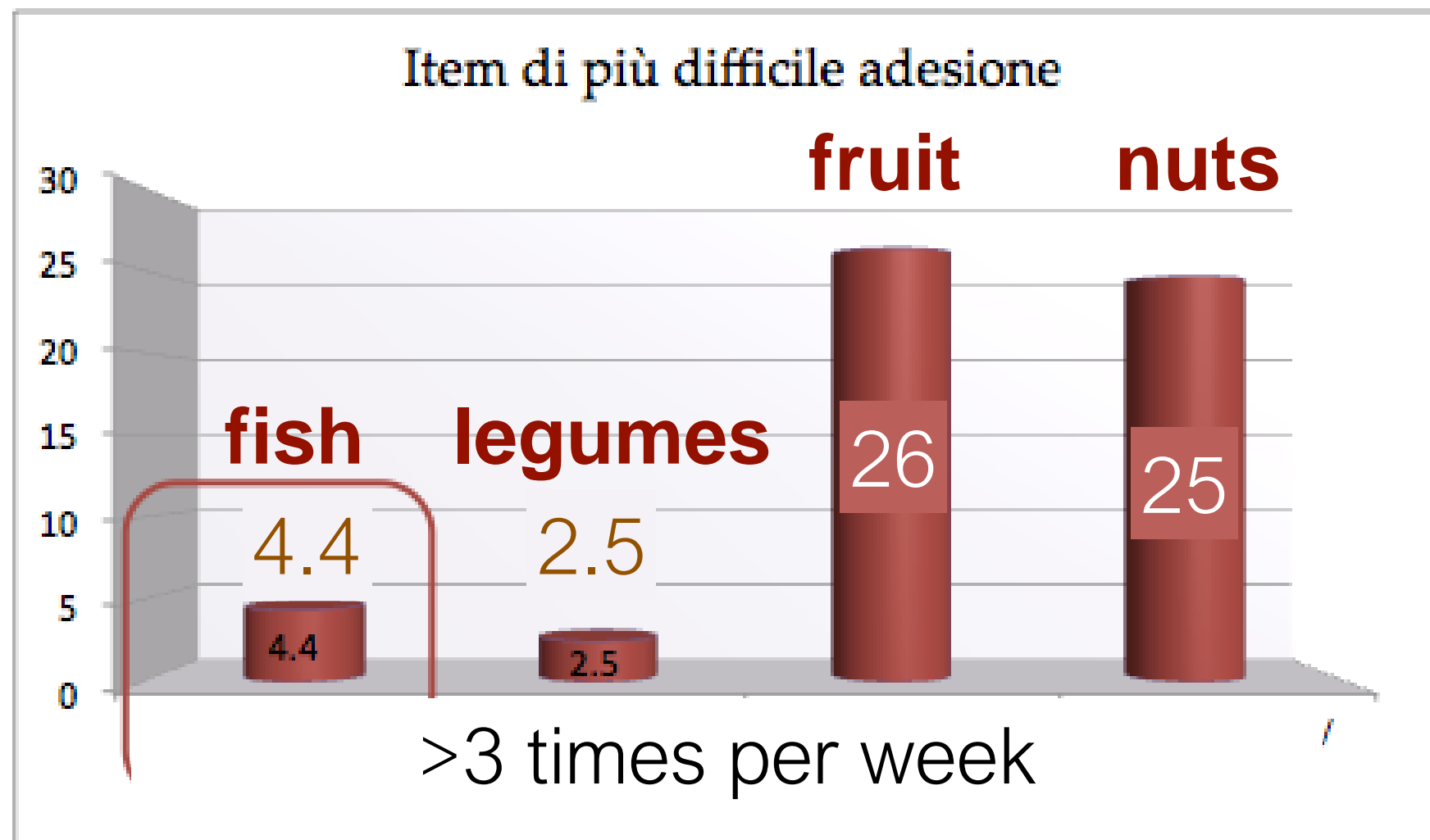
Studio prospettico
20 ÷ 40 anni
Caucasiche
gravidanze singole
gravidanze a basso rischio

Giugno 2012 - Giugno
2014: 120 donne reclutate

120 pregnant women
age 32, BMI 22, nulliparous, 80% graduated,
southern european ancestry



RISULTATI: PROFILO NUTRIZIONALE

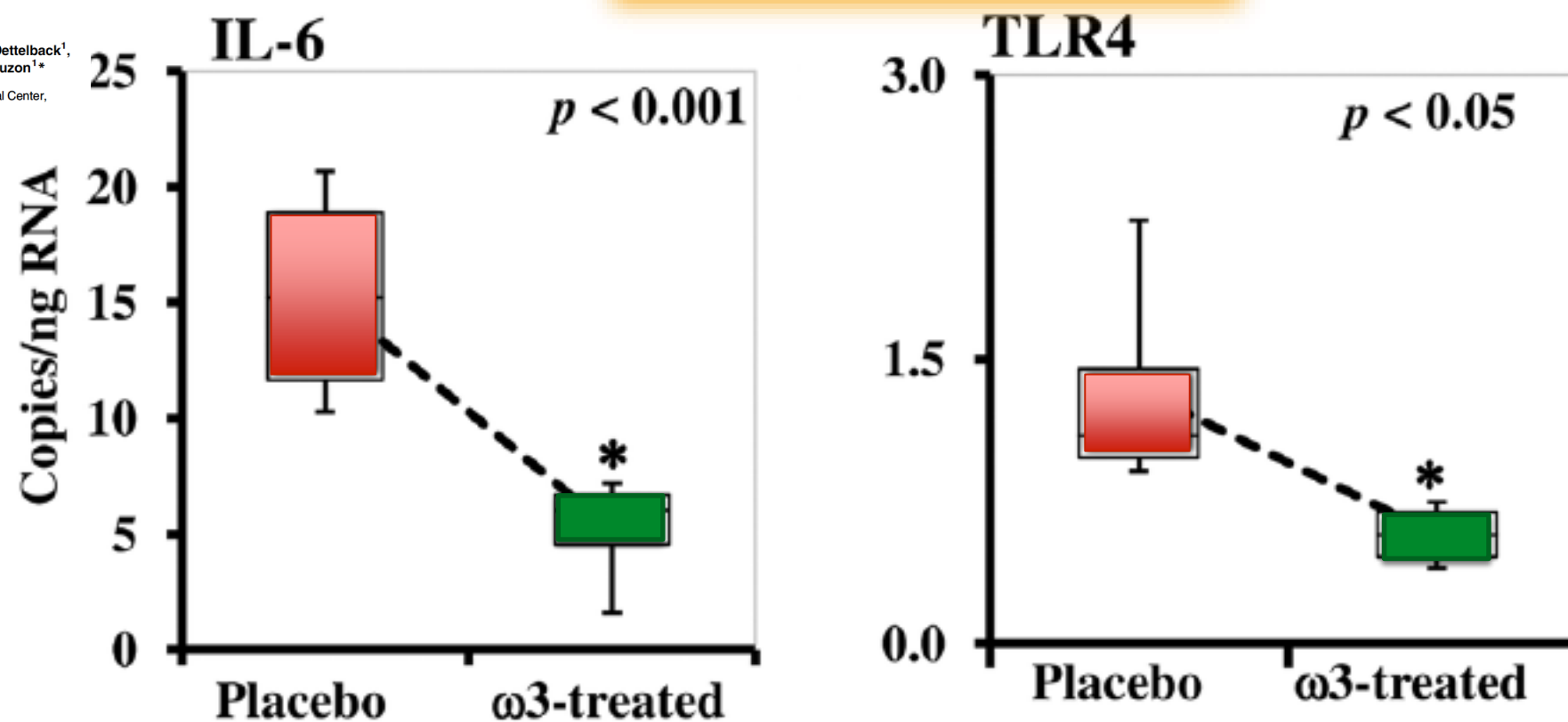


Dietary Omega-3 Fatty Acid Supplementation Reduces Inflammation in Obese Pregnant Women: A Randomized Double-Blind Controlled Clinical Trial

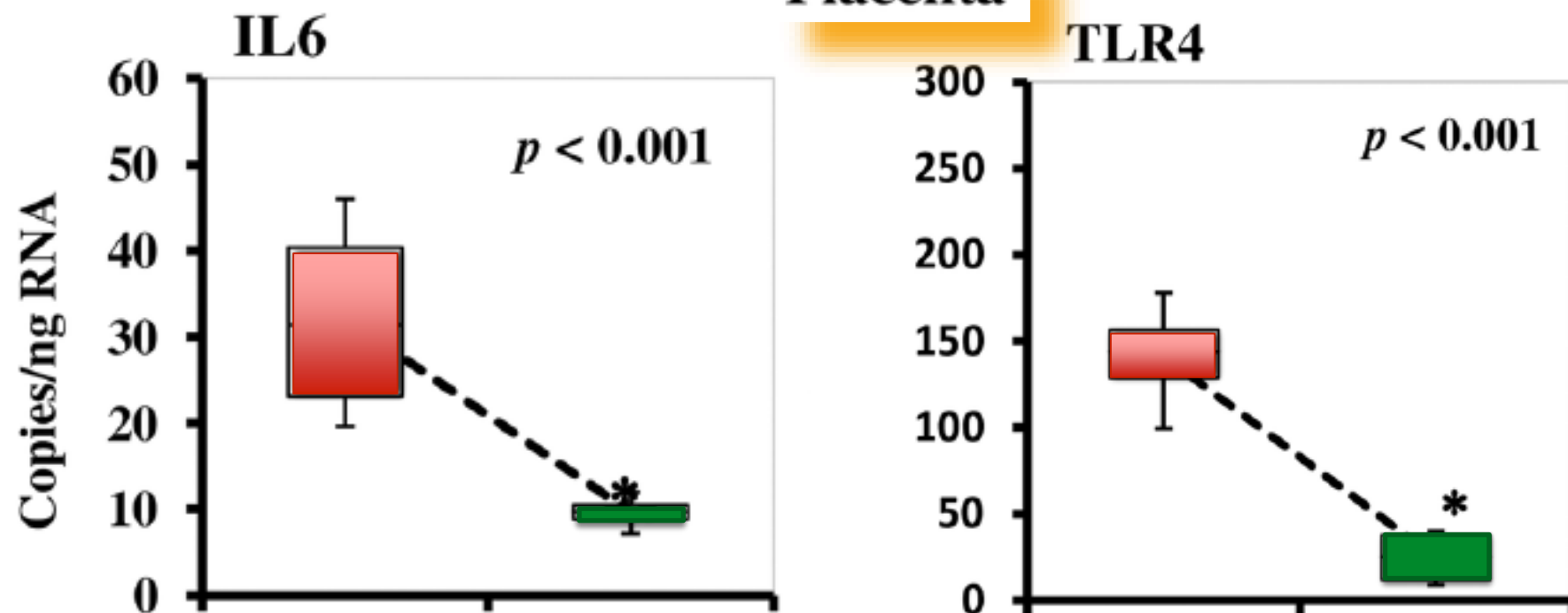
Maricela Haghiac¹, Xiao-hua Yang¹, Lorraine Presley¹, Shoi Smith¹, Shirley Dettelback¹, Judi Minium¹, Martha A. Belury², Patrick M. Catalano¹, Sylvie Hauguel-de Mouzon^{1*}

¹ Department of Reproductive Biology, Center for Reproductive Health, MetroHealth Medical Center,

Maternal adipose tissue



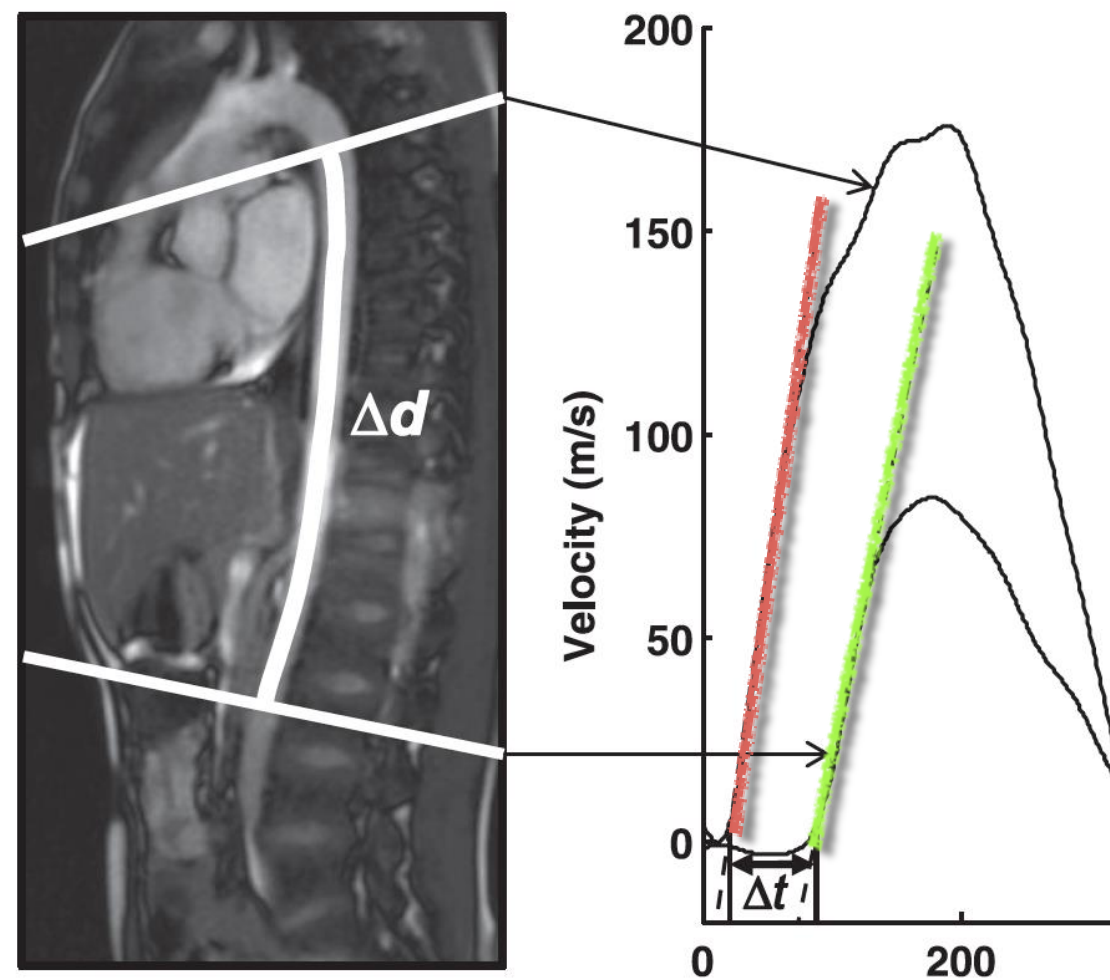
Placenta



**Higher Oily Fish Consumption in Late Pregnancy
Is Associated With Reduced Aortic Stiffness
in the Child at Age 9 Years**
Circ Res. 2015;116:1202-1205.

Jennifer Bryant, Mark Hanson, Charles Peebles, Lucy Davies, Hazel Inskip, Sian Robinson,
Philip C. Calder, Cyrus Cooper, Keith M. Godfrey

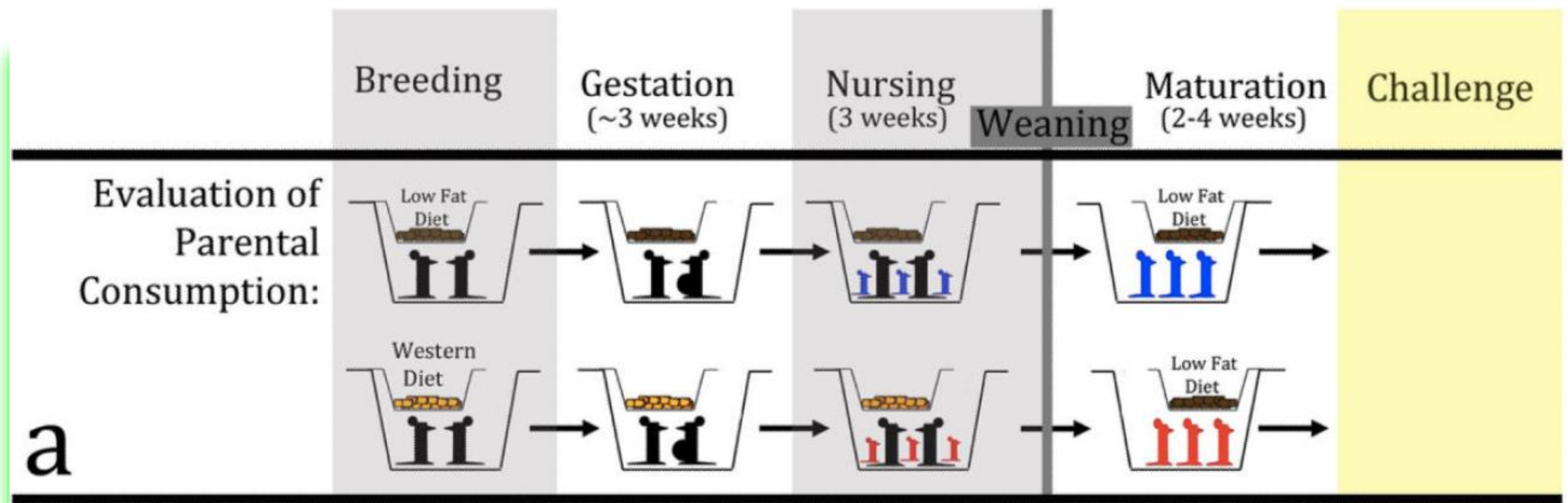
Figure 2. Maternal oily fish intake in late pregnancy vs pulse wave velocity (PWV; means and 95% confidence intervals).



Parental dietary fat intake alters offspring microbiome and immunity¹

Ian A. Myles¹, Natalia M. Fontecilla^{#1}, Brian M. Janelins^{#1}, Paul J. Vithayathil¹, Julia A. Segre², and Sandip K. Datta¹

¹Bacterial Pathogenesis Unit, Laboratory of Clinical Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892

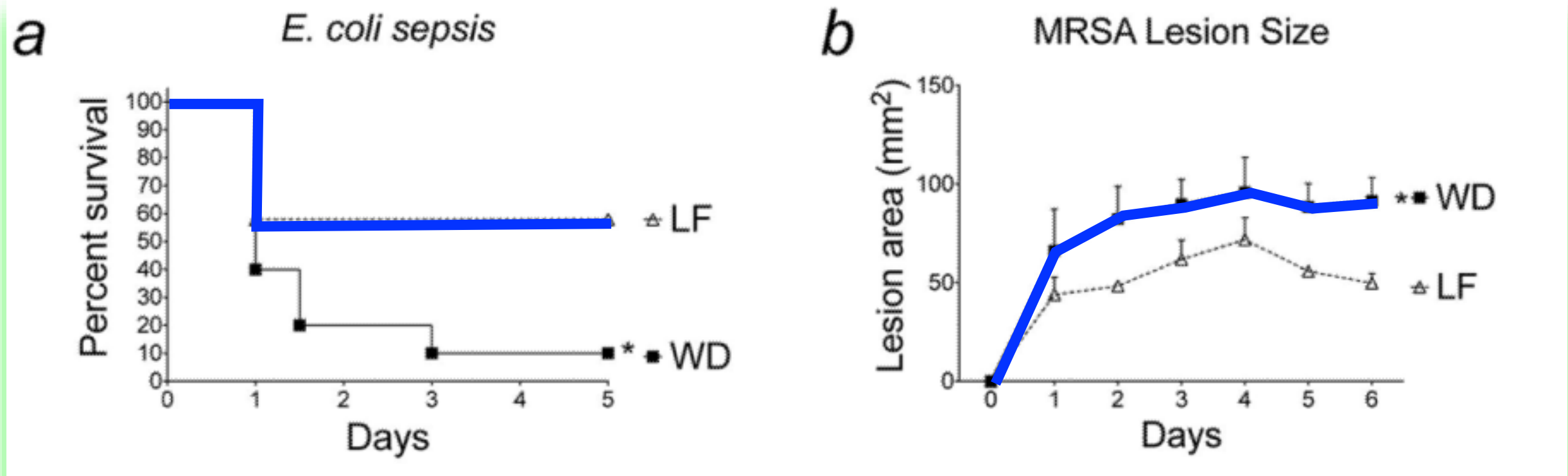


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- a) Survival after infection with *E. coli* S
- b) *Staphylococcus aureus* skin infection

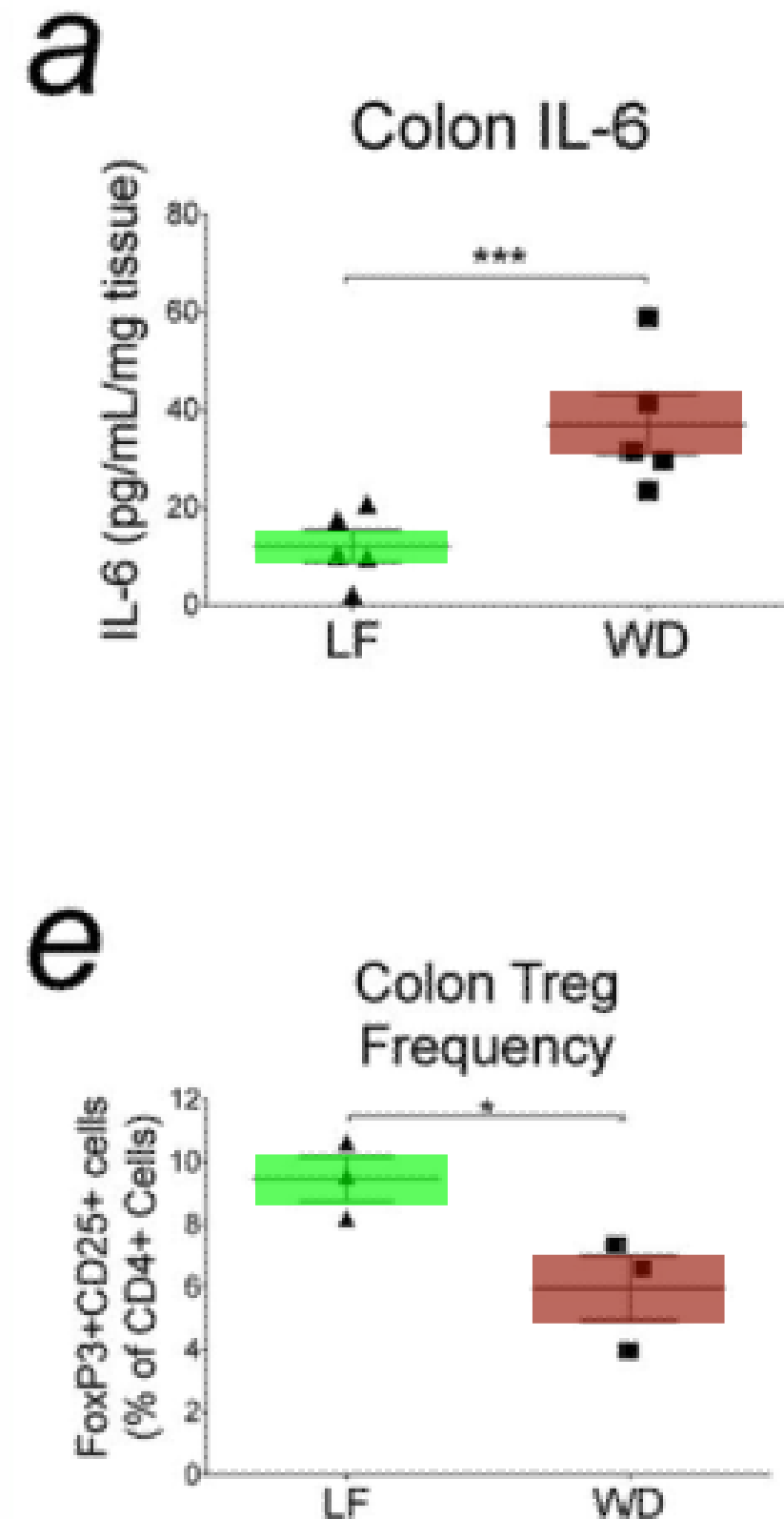


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Cytokine production
and T-reg from female
excised colons
stimulated with LPS for
24-72 hours



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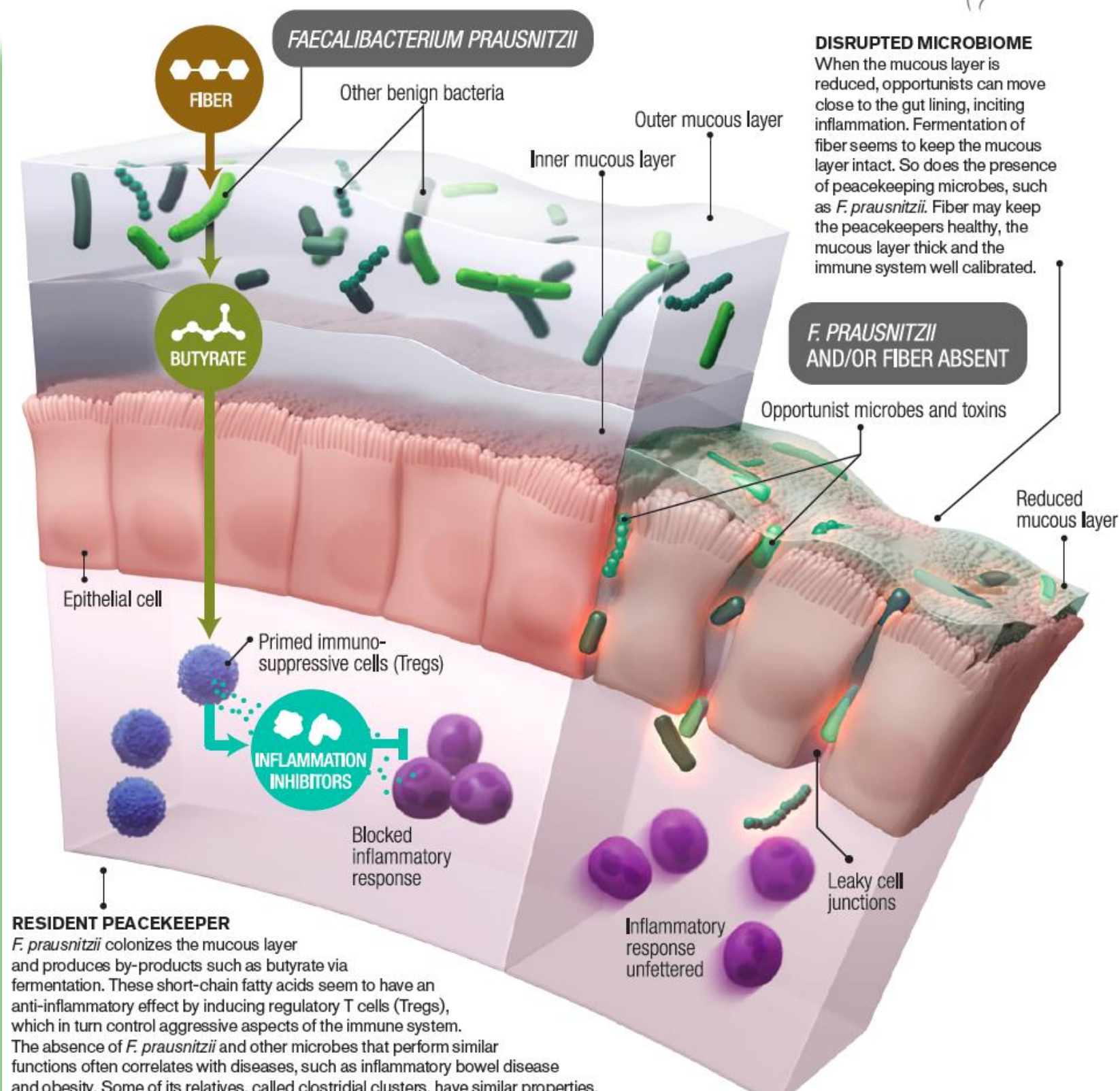
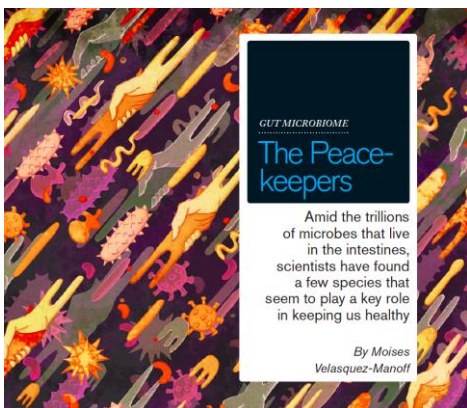
¹Bacterial Pathogenesis Unit, Laboratory of Clinical Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892

Pups from Western diet breeders were not obese or diabetic, - worse outcomes in models of infection, T heightened colonic inflammatory

These deleterious impacts of the Western diet **were associated with alterations of the offspring gut microbiome.**

These results indicate that parental fat consumption can leave a “legacy” impacting offspring immunity and **suggest inheritable microbiota may contribute to the modern patterns of human health and disease.**

fibre, disbiosi, Infiammazione



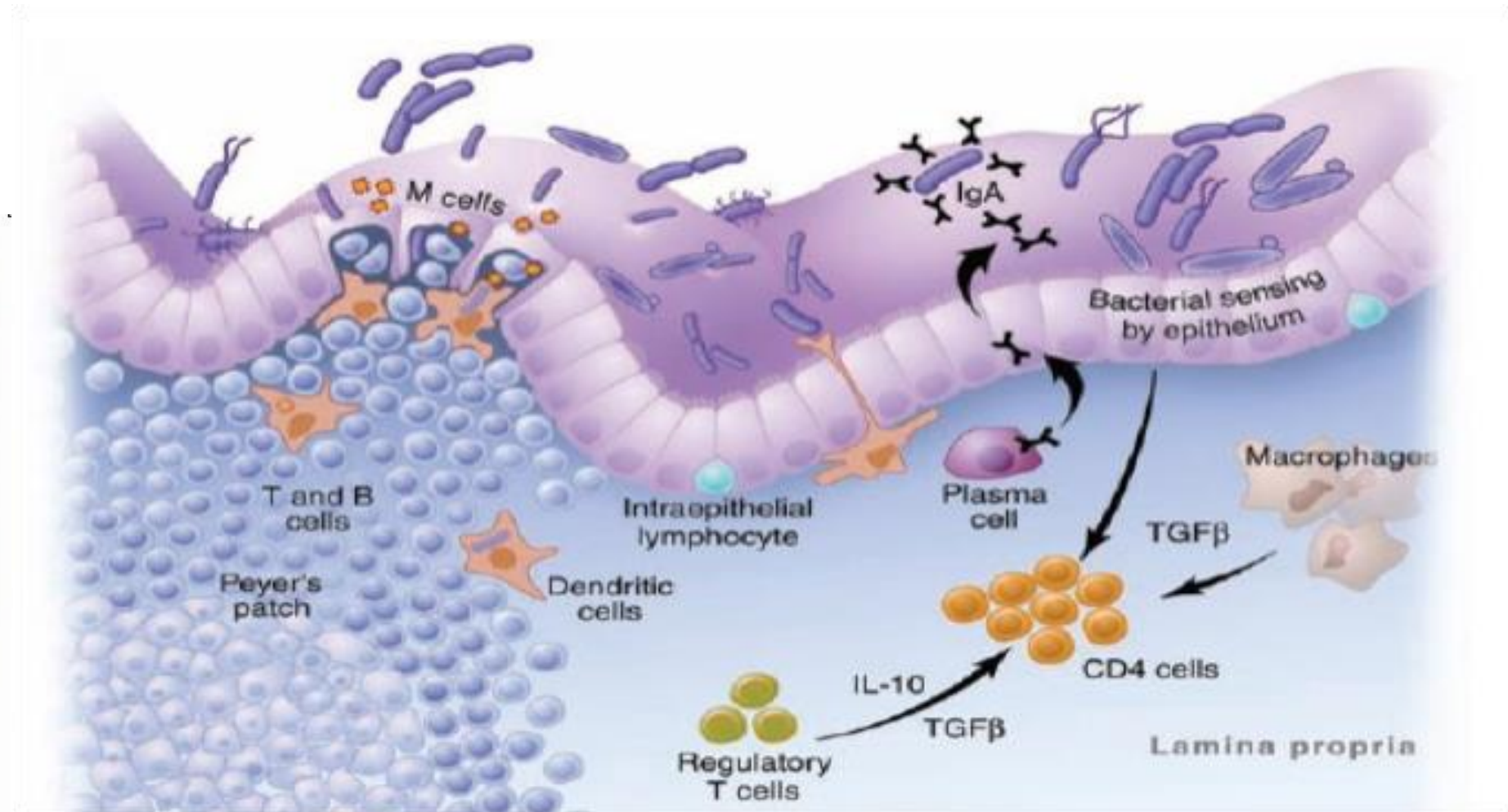
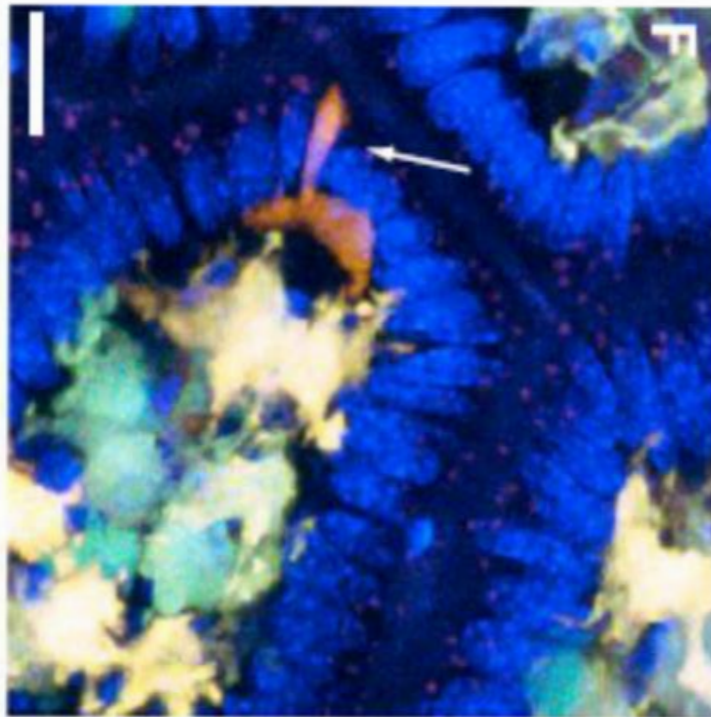
Inflammation da disbiosi

Dendritic cells in intestinal immune regulation

Janine L. Coombes and Fiona Powrie

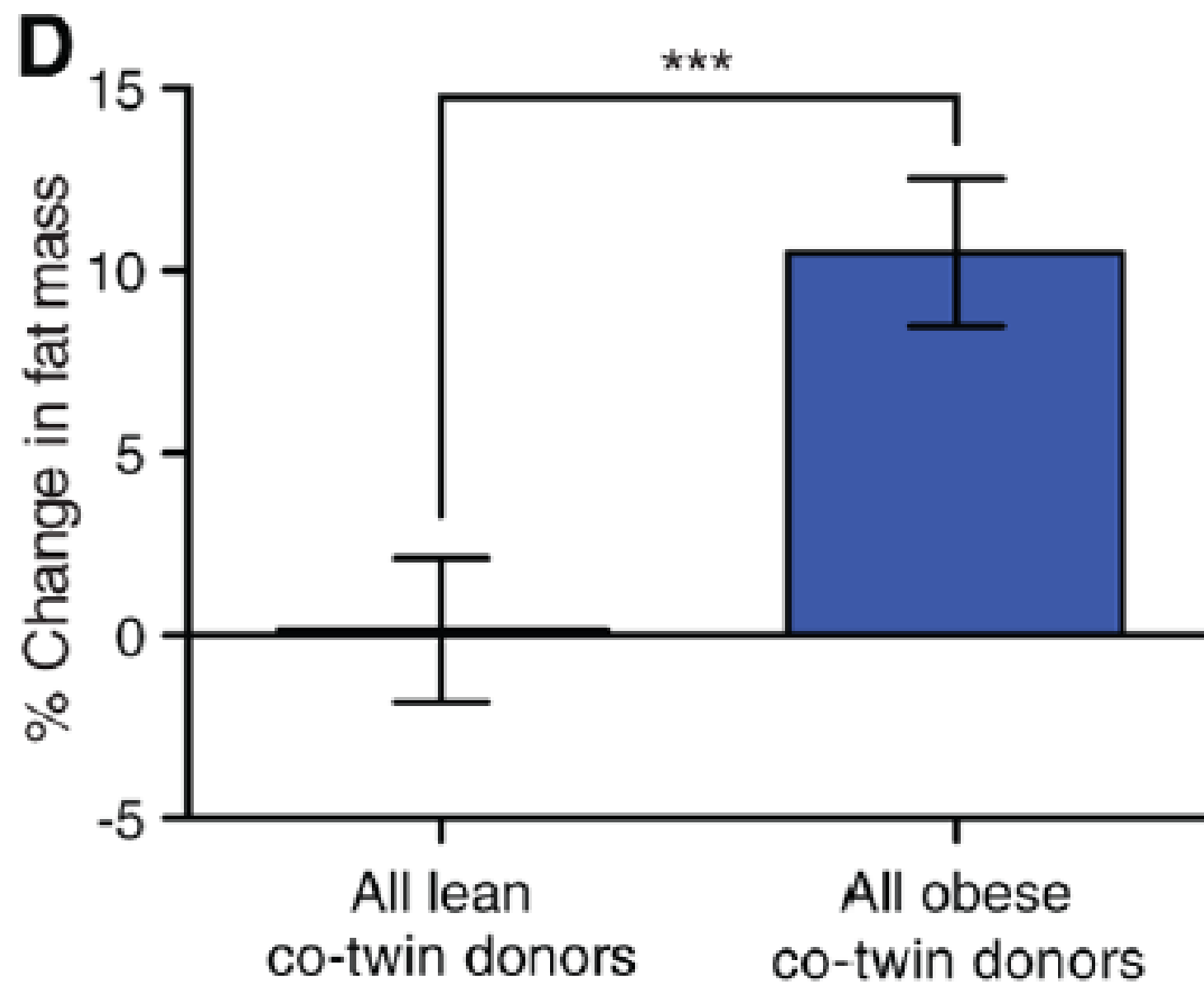
NATURE REVIEWS | IMMUNOLOGY | VOLUME 8 | JUNE 2008 | 435

infiammazione
da disbiosi



Cultured gut microbiota from twins discordant for obesity modulate adiposity and metabolic phenotypes in mice

Vanessa K. Ridaura¹, Jeremiah J. Faith¹, Federico E. Rey¹, Jiye Cheng¹, Alexis E.



Prevenzione possibile

Quantifying the mediating effect of body mass index on the relation between a Mediterranean diet and development of maternal pregnancy complications: the Australian Longitudinal Study on Women's Health^{1,2}

Danielle AJM Schoenaker,^{3} Sabita S Soedamah-Muthu,⁴ and Gita D Mishra³*

Am J Clin Nutr 2016;104:638–45. .

Low adherence to the Mediterranean diet in 3500 pregnant women was associated with:

- **higher risk of GDM (OR: 1.35; 95% CI: 1.02, 1.60)**

- **higher risk of (OR: 1.41; 95% CI: 1.18, 1.56),**

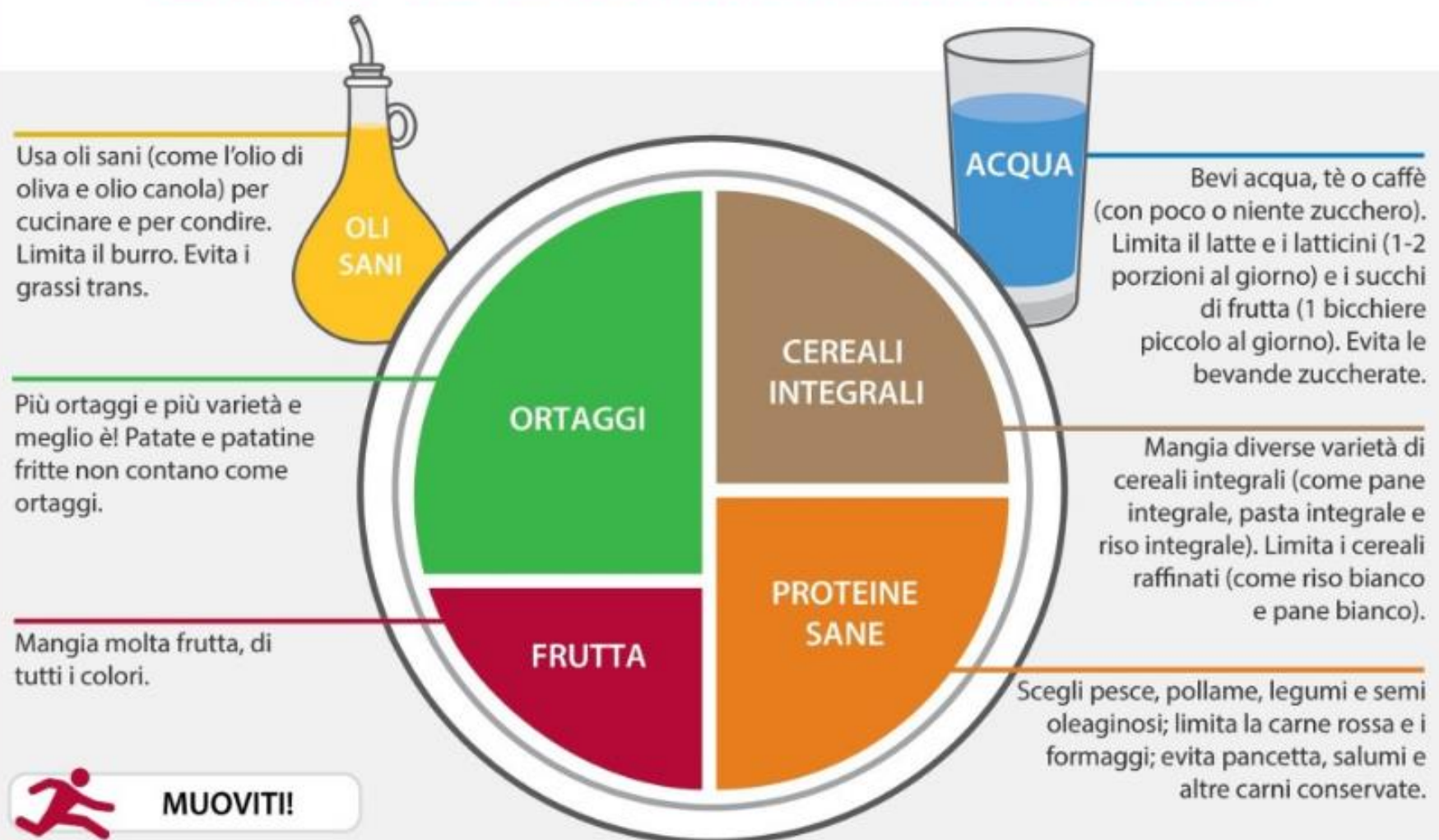
after adjustment for:

education, parity, polycystic ovary syndrome, energy intake, and physical activity.



The Nutrition Source

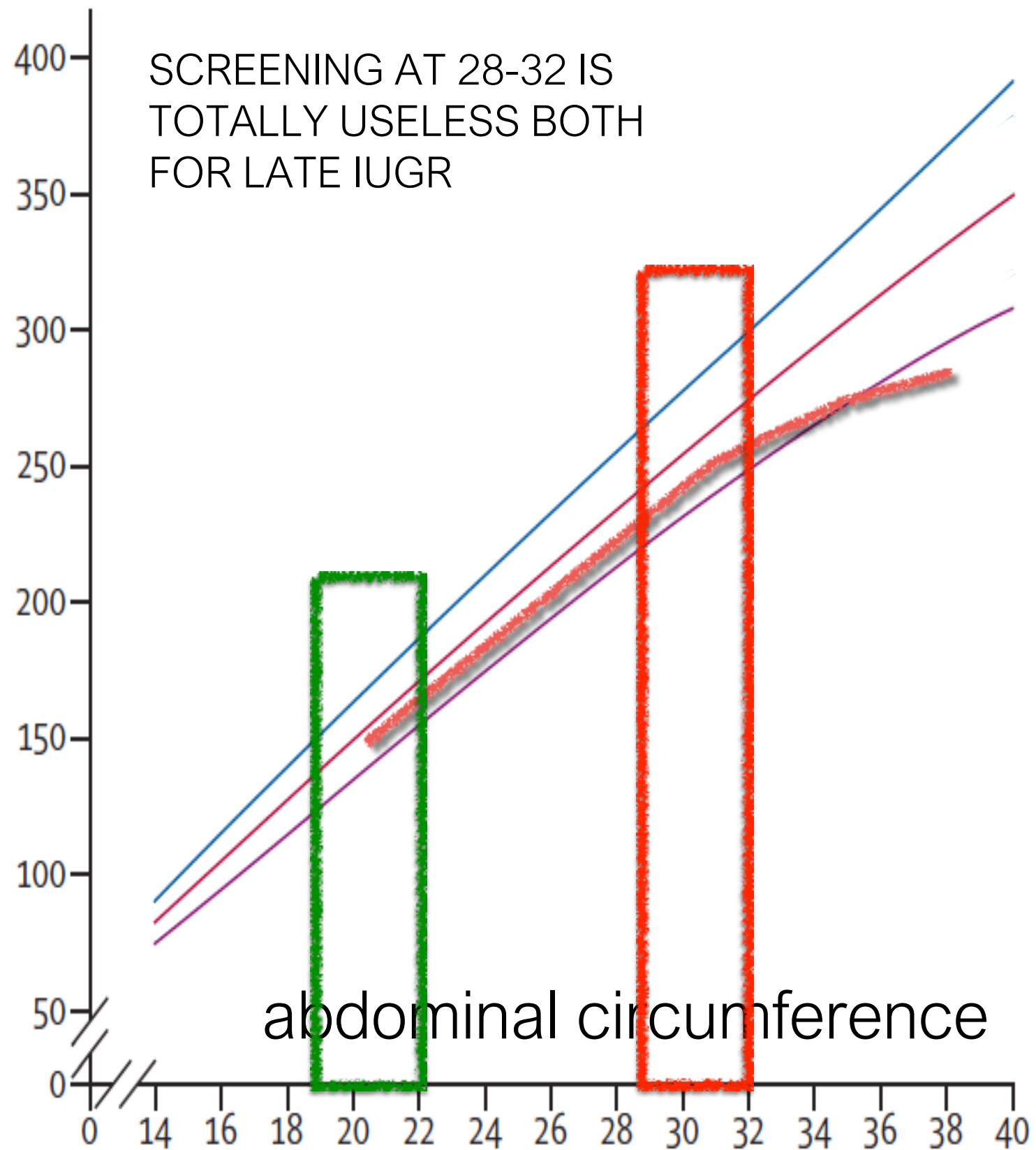
IL PIATTO DEL MANGIAR SANO



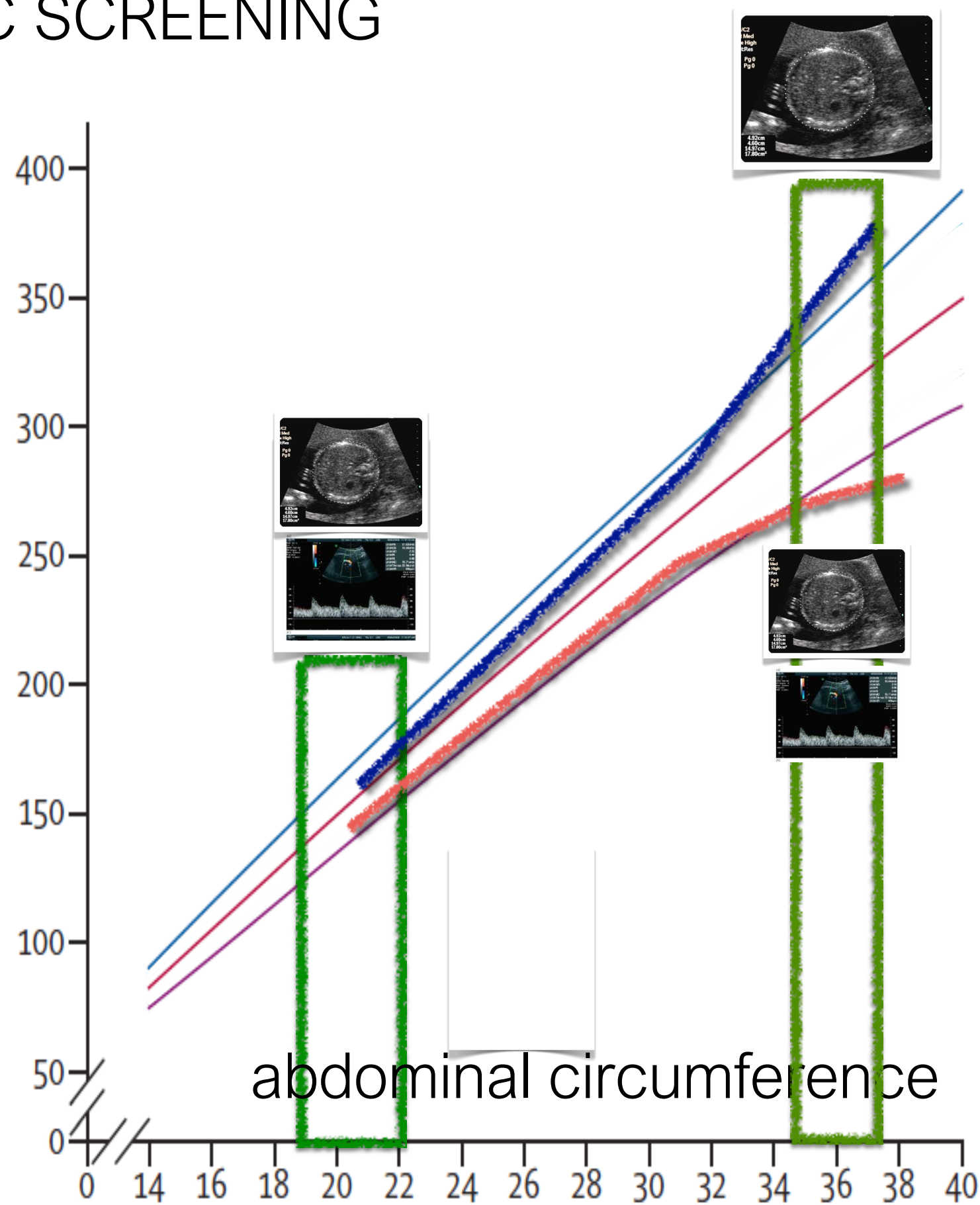
© Harvard University



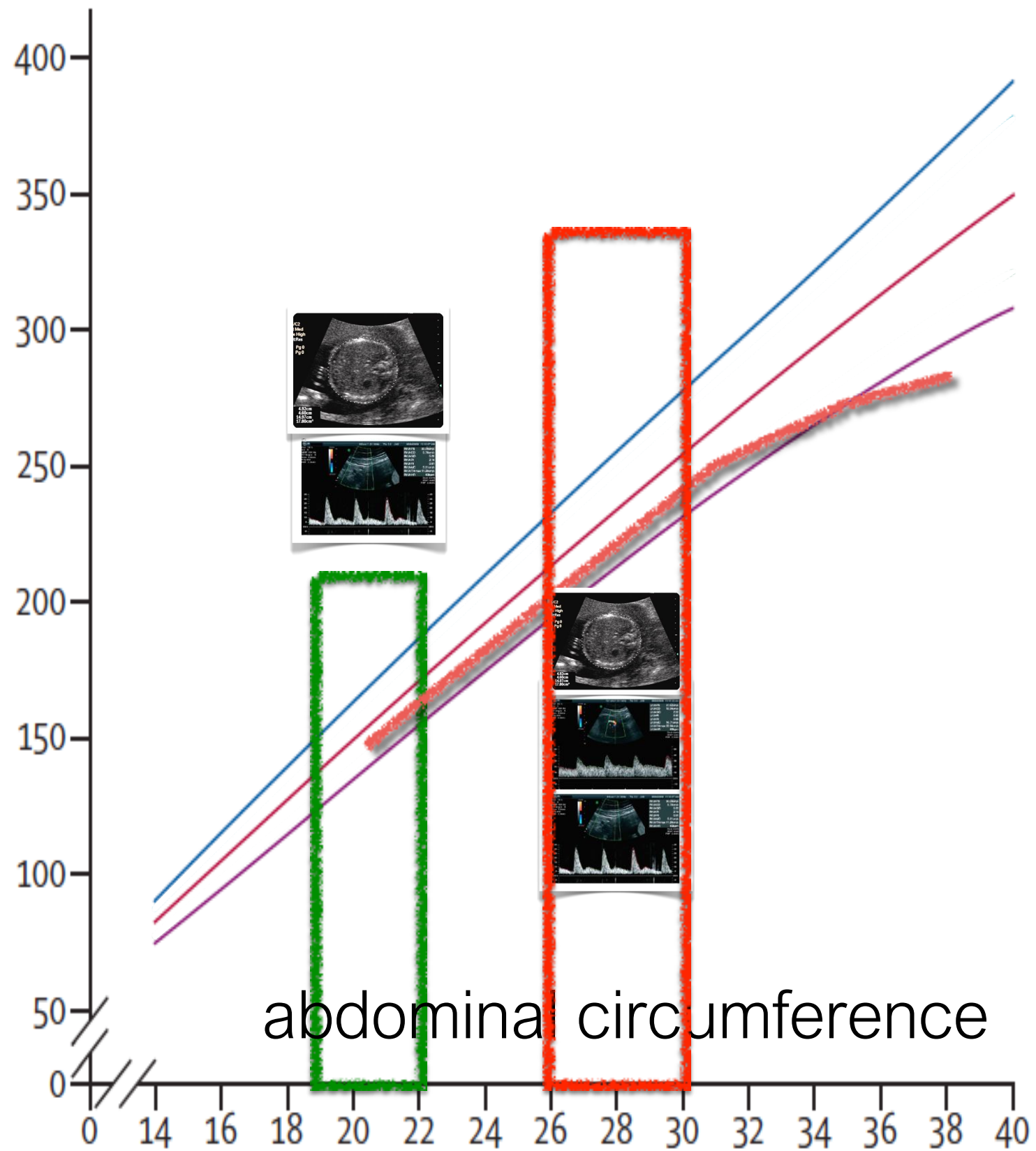
ITALIAN NHS SCREENING



PRAGMATIC SCREENING



PRAGMATIC SCREENING



The Spectrum and Regulatory Landscape of Intestinal Innate Lymphoid Cells Are Shaped by the Microbiome

Gury-BenAri et al., 2016, *Cell* 166, 1231–1246

