Los primeros 1000 días de vida: claves para la prevención de la obesidad

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CIBERESP-Instituto Carlos III, Madrid

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XI CONVENCIÓN

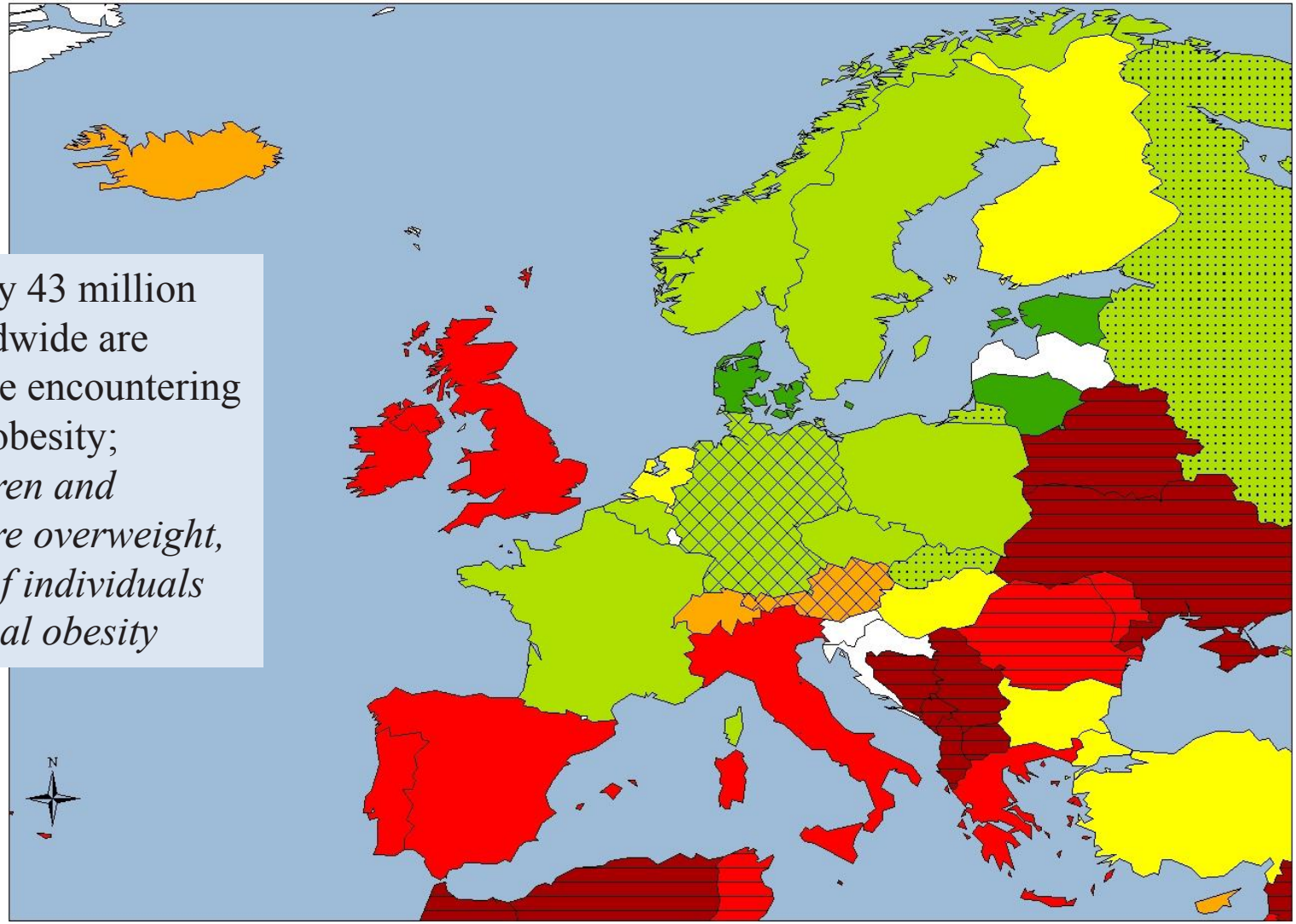
X PREMIOS ESTRATEGIA

22 de NOVIEMBRE de 2017

NAOS

Prevalence of overweight and obesity in European children and adolescents

Approximately 43 million children worldwide are estimated to be encountering a problem of obesity; *21-24% children and adolescents are overweight, and 16-18% of individuals have abdominal obesity*

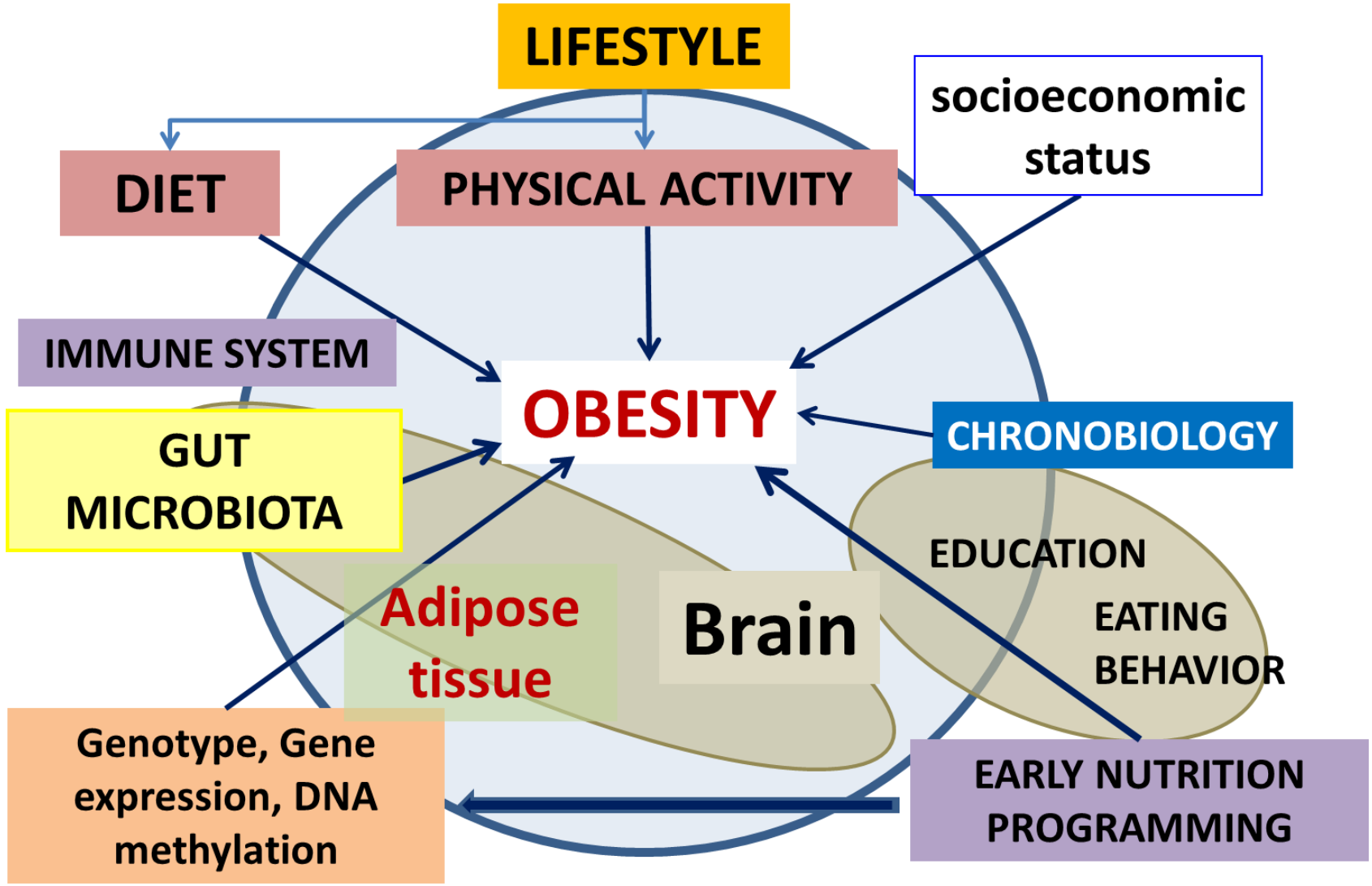


no data | < 10% | 10% - 15% | 15% - 20% | 20% - 25% | 25% - 30% | > 30%

IOTF | CDC | K-H | Other | WHO

Moreno, Pigeot, Ahrens (eds.): Epidemiology of overweight and obesity in children and adolescents. Springer, New York 2011

CAUSES OF CHILDHOOD OBESITY



Symonds ME, Mendez MA, Meltzer HM et al. Early life nutritional programming of obesity: Mother-Child Cohort Studies. Ann Nutr Metab 2013; 62: 137-145.

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Prof. Cristina Campoy. University of Granada. E-mail: ccampoy@ugr.es

Tabaquismo materno durante el embarazo ⇒ Obesidad infantil

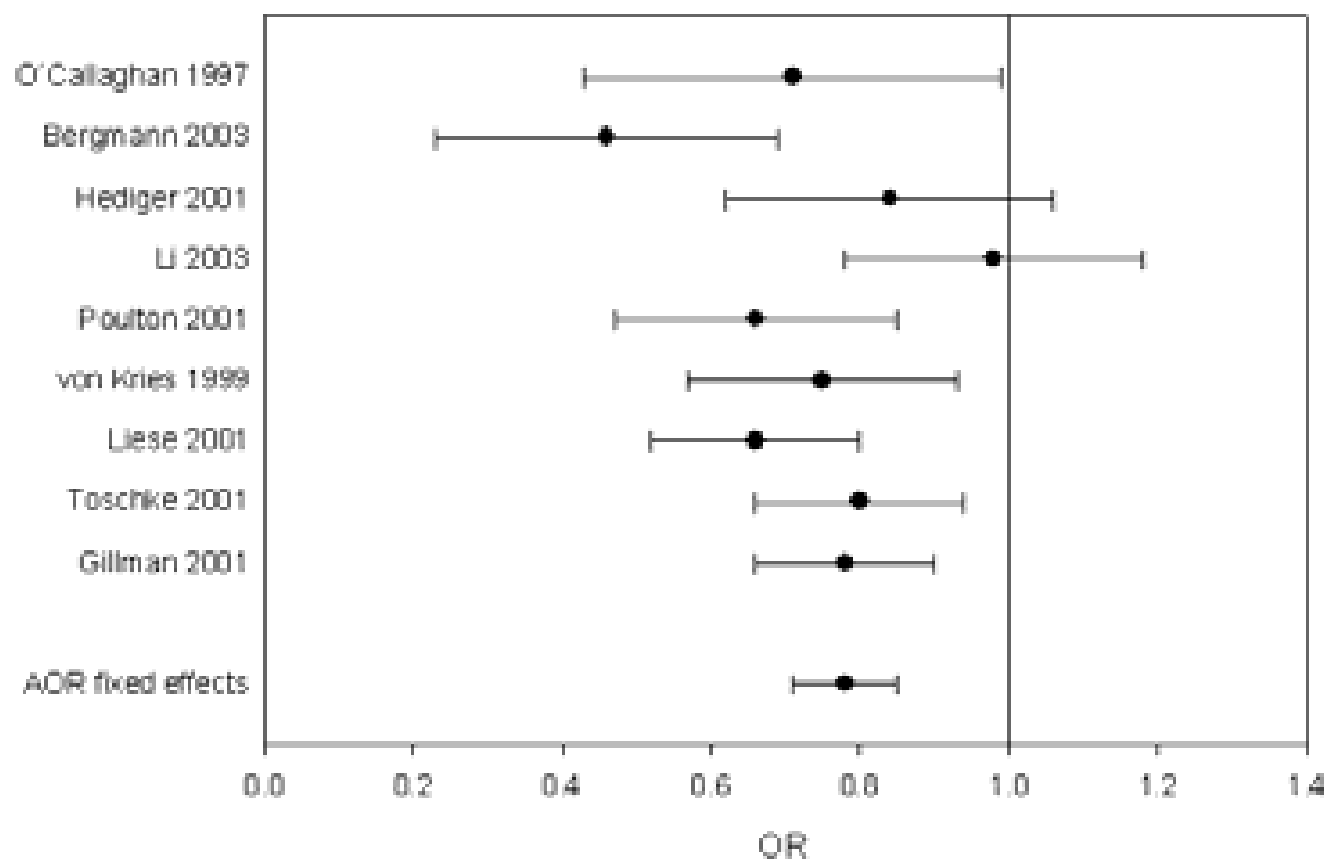
von Kries R, Toschke AM, Koletzko B, Slikker W. Am J Epidemiol 2002;156

Adj. OR sobrepeso 1.43 (1.07; 1.90) Adj. OR obesidad 2.06 (1.31; 3.23)

Lactancia materna y obesidad: Meta-análisis

Covariate adjusted odds ratios, pooled odds ratio

Arenz, Rückerl, Koletzko, von Kries. Int J Obesity 2004



Efecto dosis-respuesta de la duración de la lactancia materna en 4/9 estudios

EARLY NUTRITION

FOLIC ACID

LC-PUFAs

PROTEINS

VITAMINS

MICRONUTRIENTS

GUT-MICROBIOME

EARLY PROGRAMMING

BRAIN DEVELOPMENT, MENTAL PERFORMANCE & BEHAVIOR

DIET DURING INFANCY AND CHILDHOOD

Mother's IQ

LIFESTYLE, PHYSICAL ACTIVITY

ENVIRONMENTAL POLLUTANTS / TOXICS

GENETIC factors

Circadian system

Metabolic illnesses

SOCIOECONOMIC STATUS

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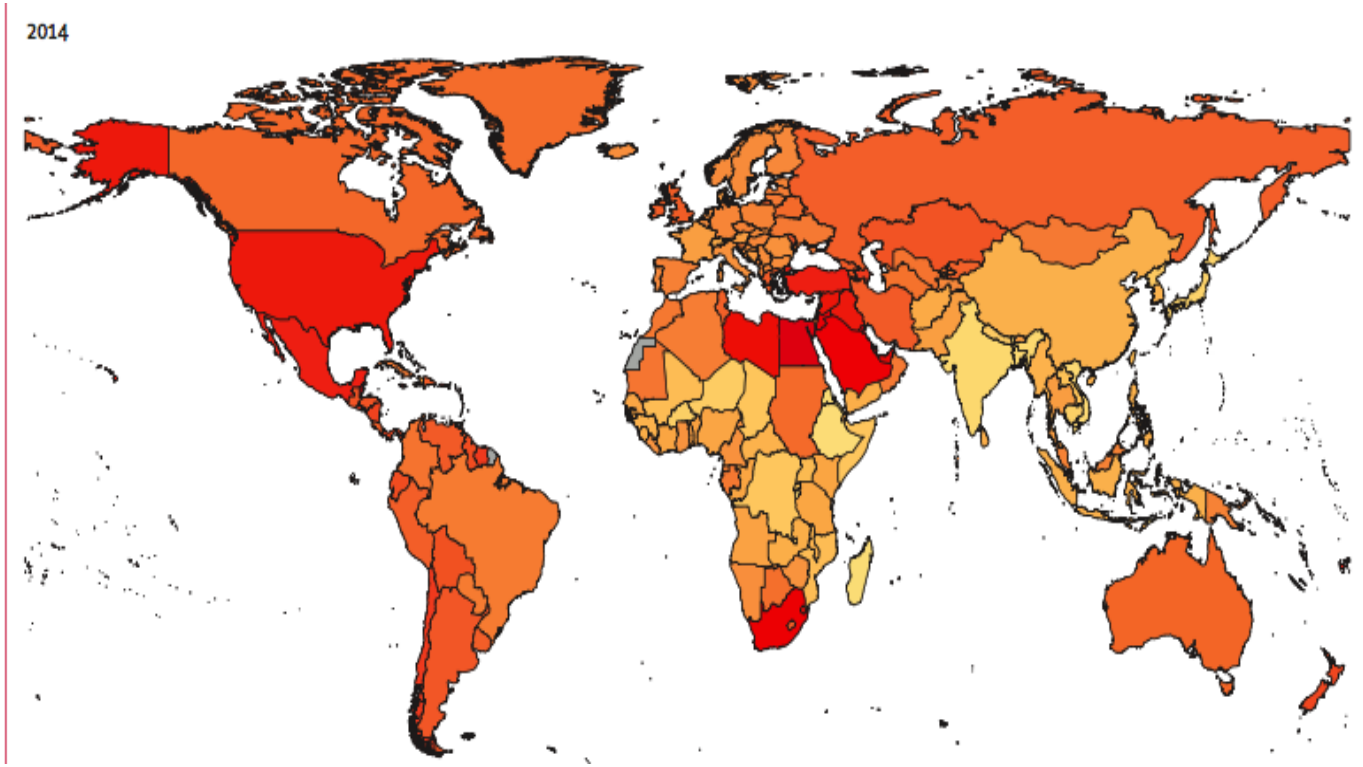
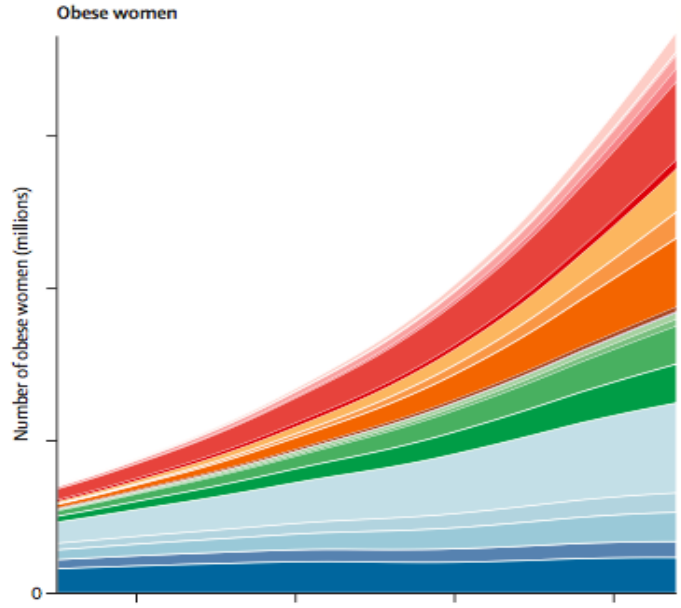
Obesity amongst women 2014

‘By 2025, global obesity prevalence will reach 18% in men and surpass 21% in women’



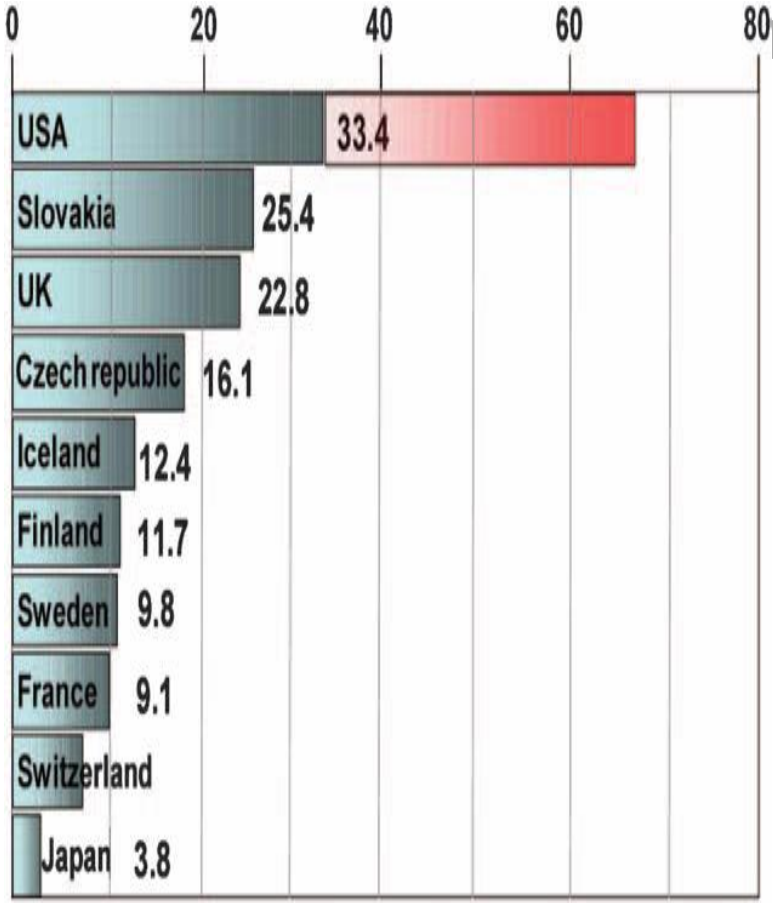
Change 1975- 2014



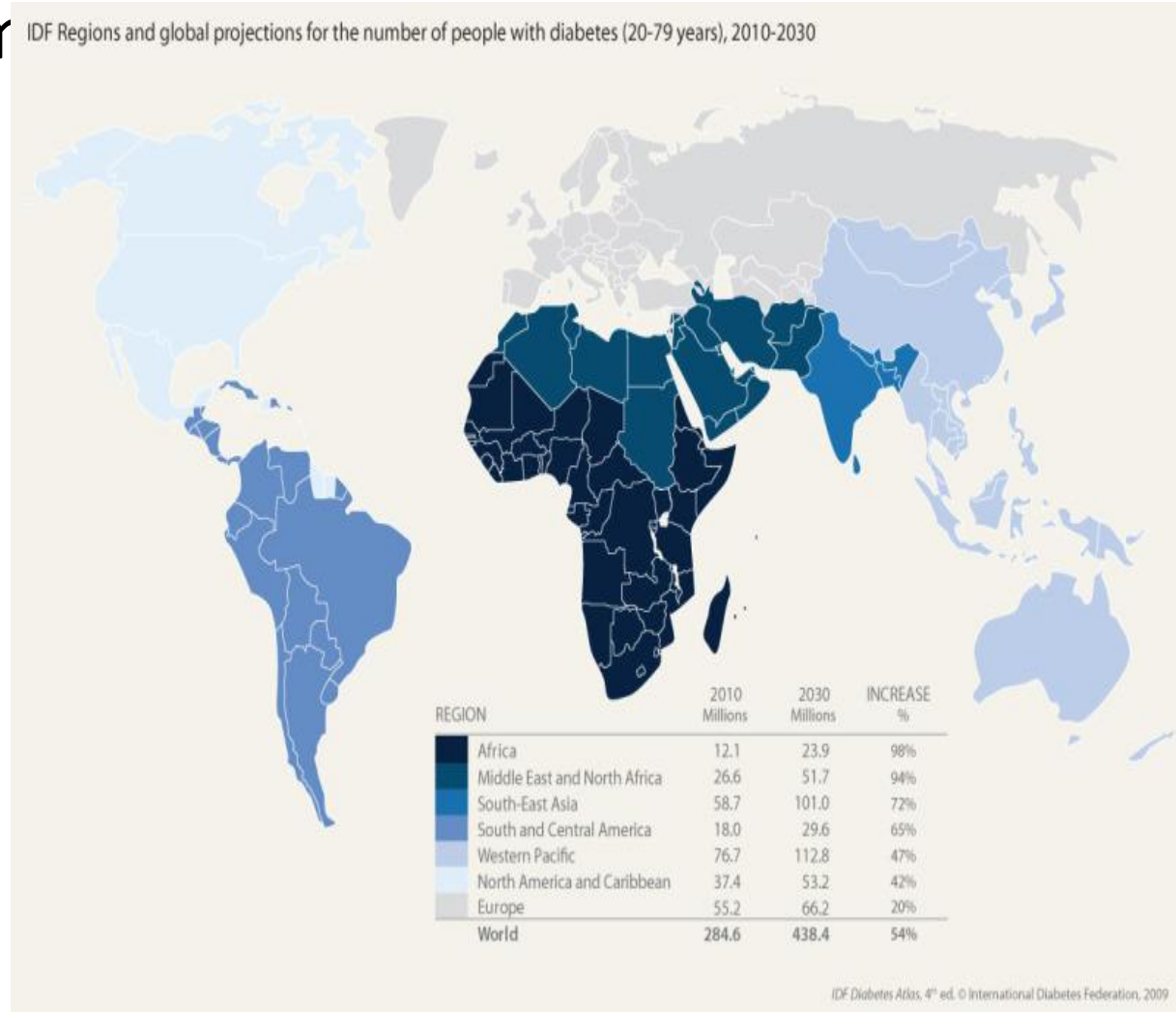
NCD Risk factor Collaboration, Lancet 2016

Metabolic diseases during Pregnancy

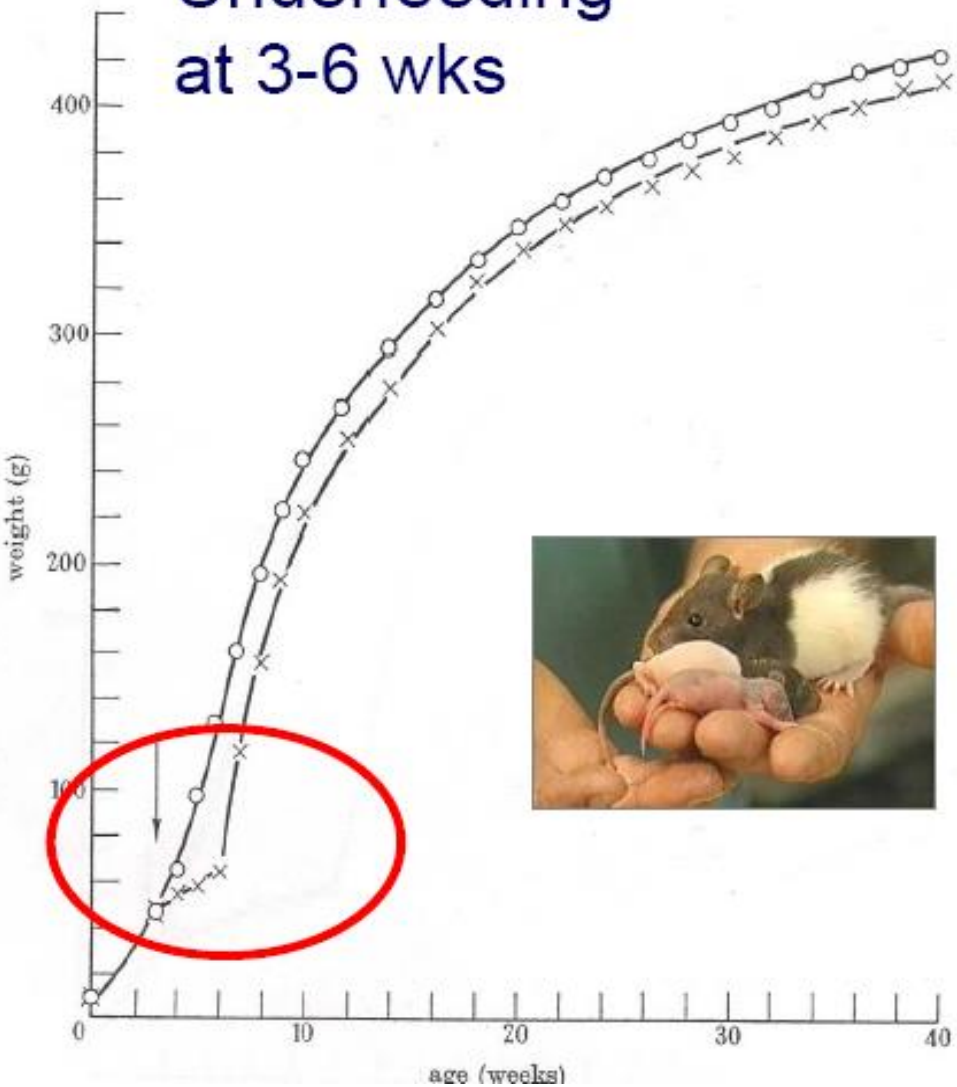
Metabolic diseases (*obesity, type 2 diabetes, hypertension*) have increased in the modern m



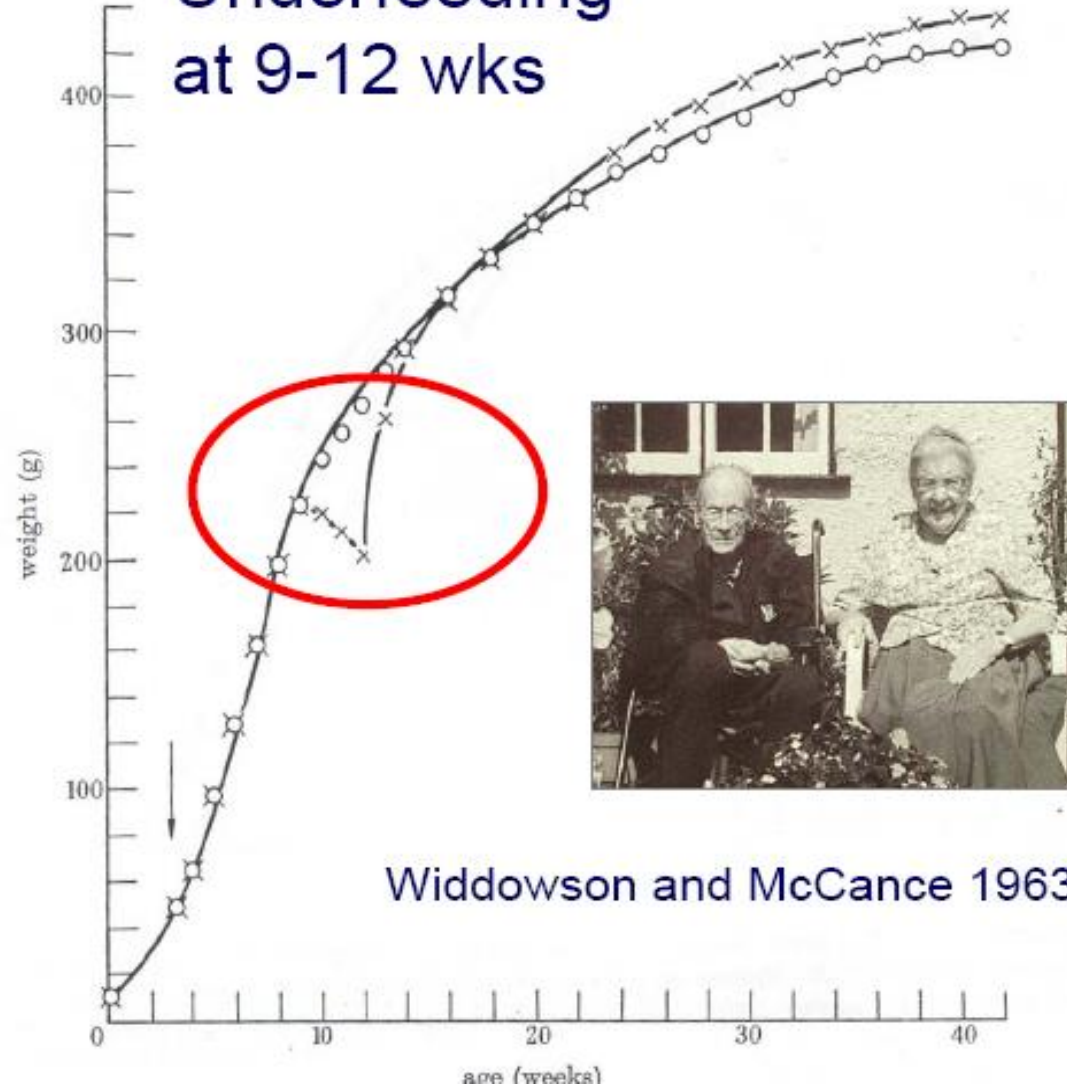
The percentage of women with a BMI>30 in several countries. USA data also includes BMI>25 (*Catalano, 2006*)



Underfeeding at 3-6 wks



Underfeeding at 9-12 wks

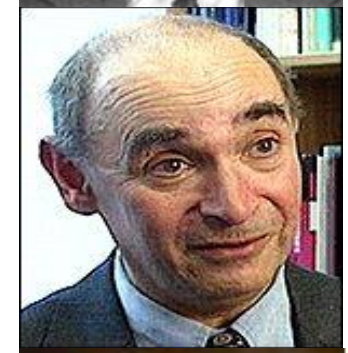


Widdowson and McCance 1963

❖**La malnutrición en animales durante la vida precoz, y no durante la adultez, determina el tamaño corporal**
Elsie Widdowson & MacCance, Cambridge 1970

❖**Programación (Programming) de las funciones del adulto y de las enfermedades, mediante hormonas, metabolitos y neurotransmisores durante periodos críticos del desarrollo.** ***Günter Dörner, Berlin, Germany 1974***

❖**Programación mediante la nutrición precoz en el humano**
Alan Lucas, Cambridge, UK 1991



❖**Orígenes del desarrollo de las enfermedades del adulto por malnutrición fetal y bajo peso al nacimiento**
David Barker, Nick Hales, Oxford, Southamptom, UK 1992

TIPO A

RETRASO de CRECIMIENTO POSTNATAL

CIR SIMÉTRICO

NO SE OBSERVA FENÓMENO DE RECUPERACIÓN

MAL PRONÓSTICO A LARGO PLAZO

↓Peso al nacimiento ⇒ ↑ índice de mortalidad a los 20-74 años en 10,141 hombres nacidos en Hertfordshire 1911-1930

Barker, 1994

Recién nacidos con bajo peso al nacimiento → riesgo a largo plazo de enfermedad coronaria

TIPO B

¿Efectos de la malnutrición prenatal?

- **Pobre crecimiento fetal**
  - ✓Hipótesis del origen fetal de las enfermedades del adulto

¿Efectos de la nutrición postnatal?

- **Efecto compensador con un crecimiento postnatal excesivo**
  - ✓ Hipótesis de una aceleración del crecimiento postnatal

CIR ASIMÉTRICO

BAJO PESO PARA LA EDAD DE GESTACIÓN

MALNUTRICIÓN FETAL

SECUELAS a LARGO PLAZO

RETRASO POSTNATAL de CRECIMIENTO

OBESIDAD y CO-MORBILIDADES

HIPERTENSION ARTERIAL DIABETES TIPO II, ALTERACIONES SISTEMA INMUNE

NEUROLÓGICAS

Parálisis cerebral infantil

Epilepsia

Disfunción cerebral mínima

PSÍQUICAS

Déficit mental

ANOMALIAS ASOCIADAS A LA CAUSA

Promoting growth – risks and benefits Preterm Infants

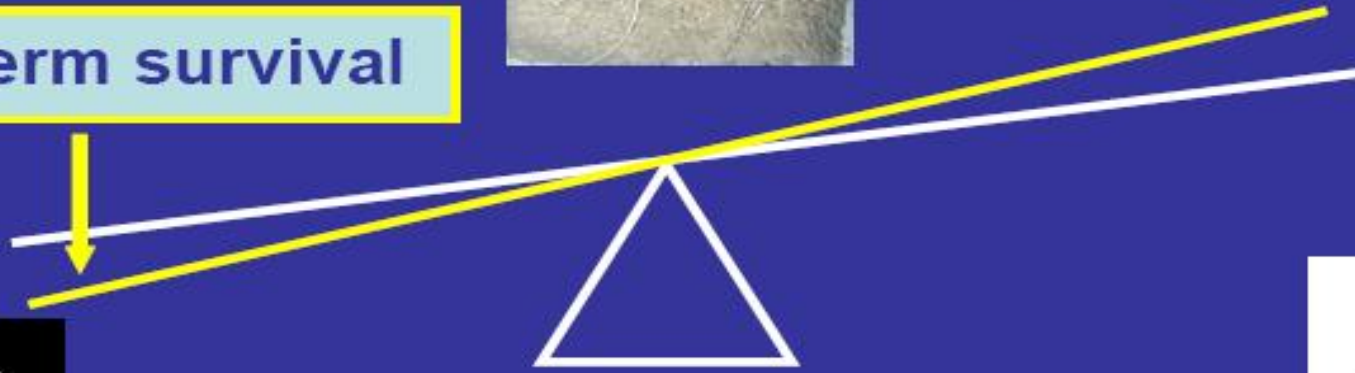
BENEFIT

Bone health
Cognitive function

RISK

Cardiovascular disease

Short-term survival



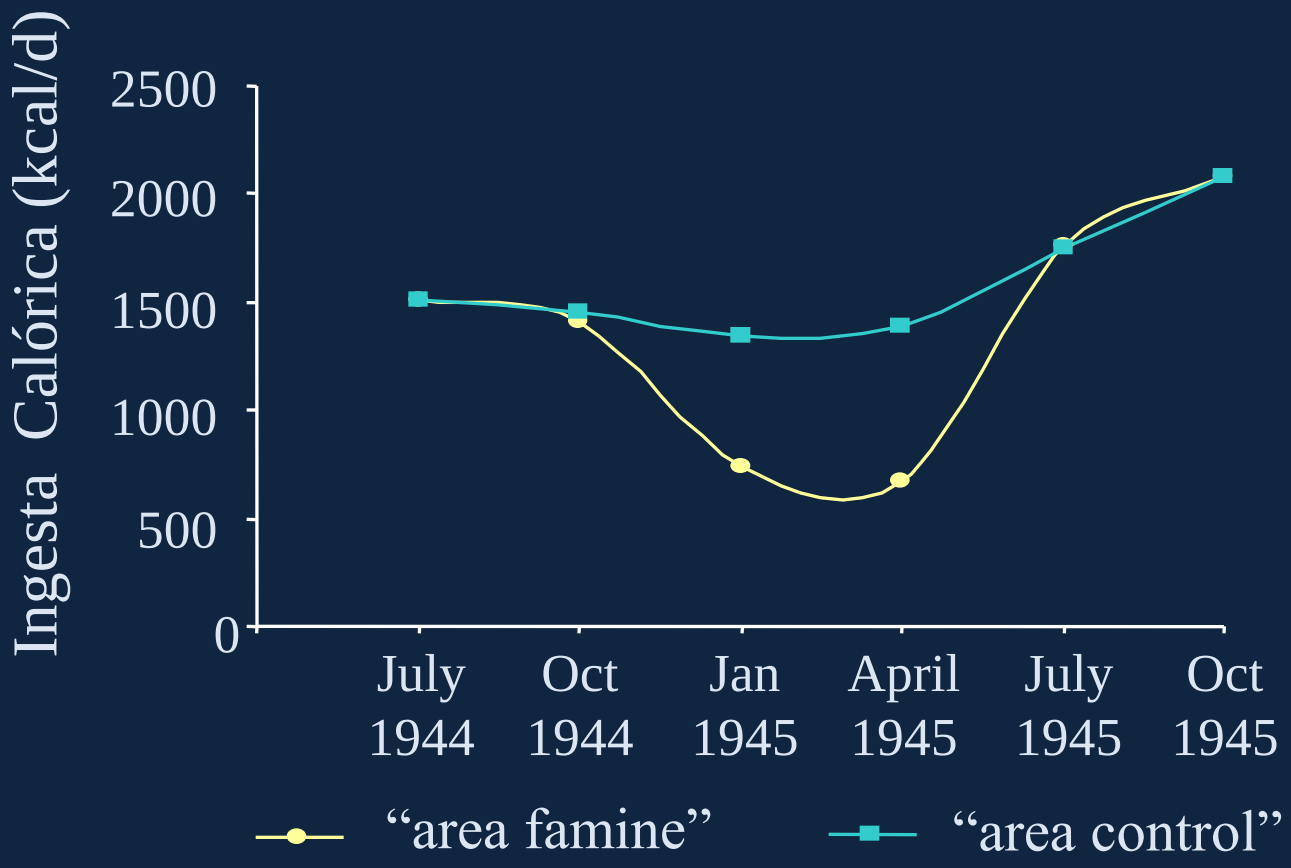
‘Grow now – pay later’

Metcalfe

TEE 2001;16:254

Typical diet during the Dutch famine

Estudios en humanos- Estudio Famine 1944-45



Adultos:

Tiempo de la restricción nutricional

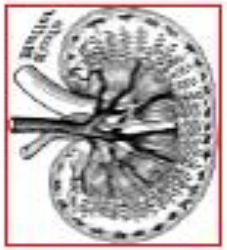
Precoz Mitad Tardía

CVD

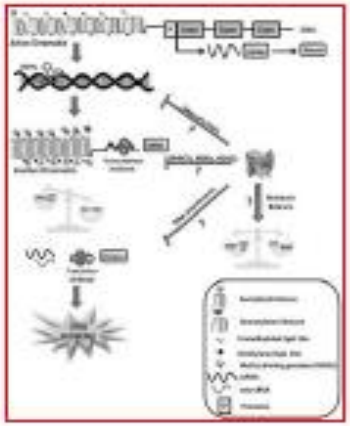
Riñón

Metabolismo

Structural changes

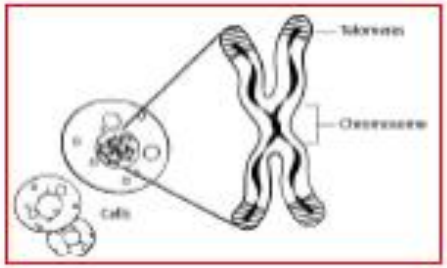


Epigenetics

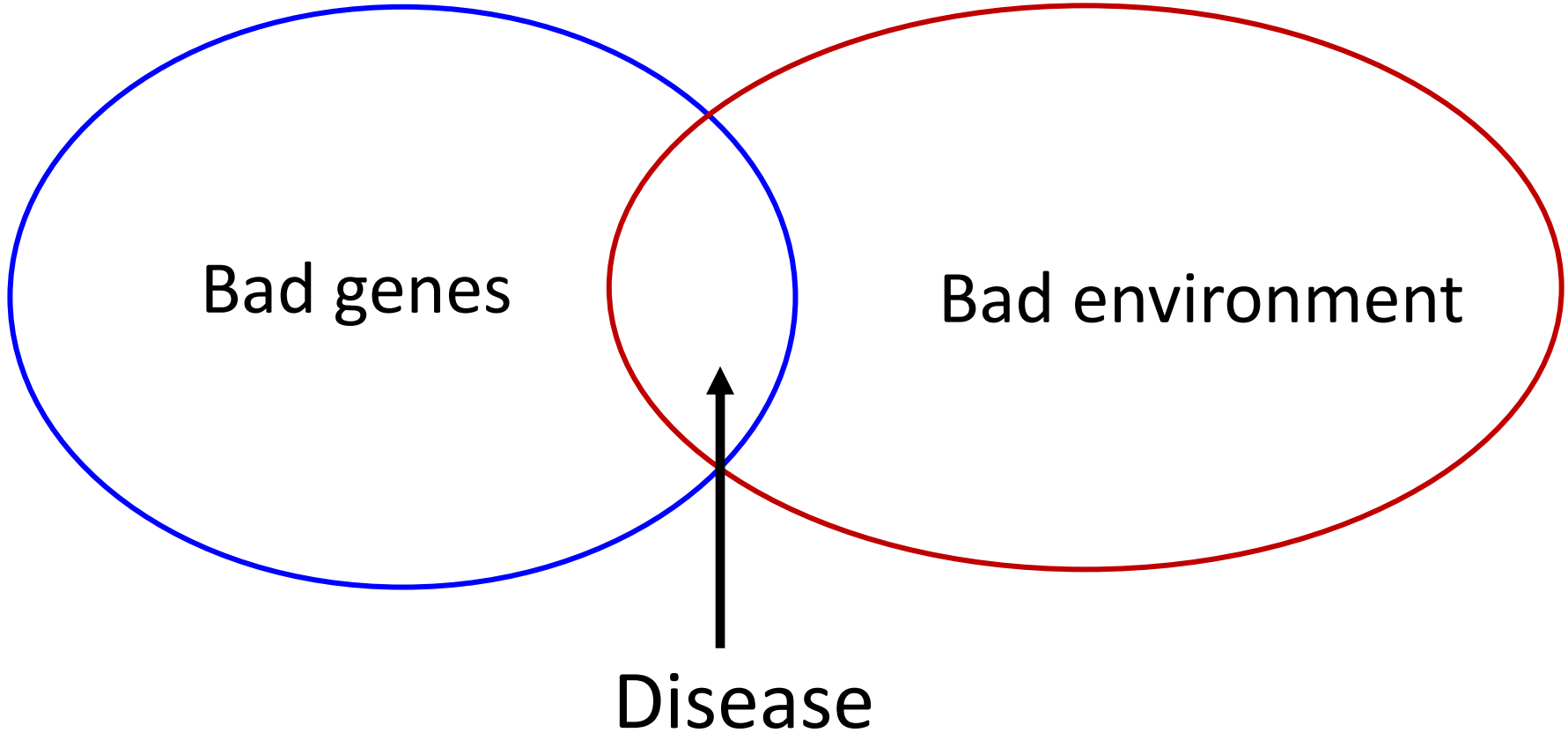


Microbiome

Cellular ageing



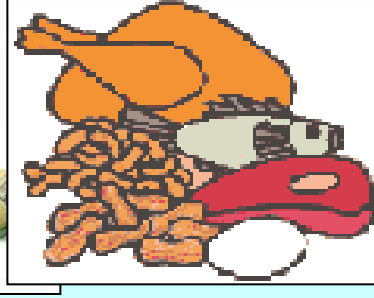
Gene: Environment interaction



Potential environmental epigenetic regulators

- animal models

- Maternal care & stress
- Endocrine disruptors
- Folate and micronutrients
- Multiple dietary compounds
- Assisted reproduction
  - superovulation and/or embryo culturing
- Alcohol exposure
- Smoking
- Pollution/heavy metals/particulates
- Many others emerging



Vitamin B2

Vitamin B6

Vitamin B12

Choline

Folate

one carbon donors

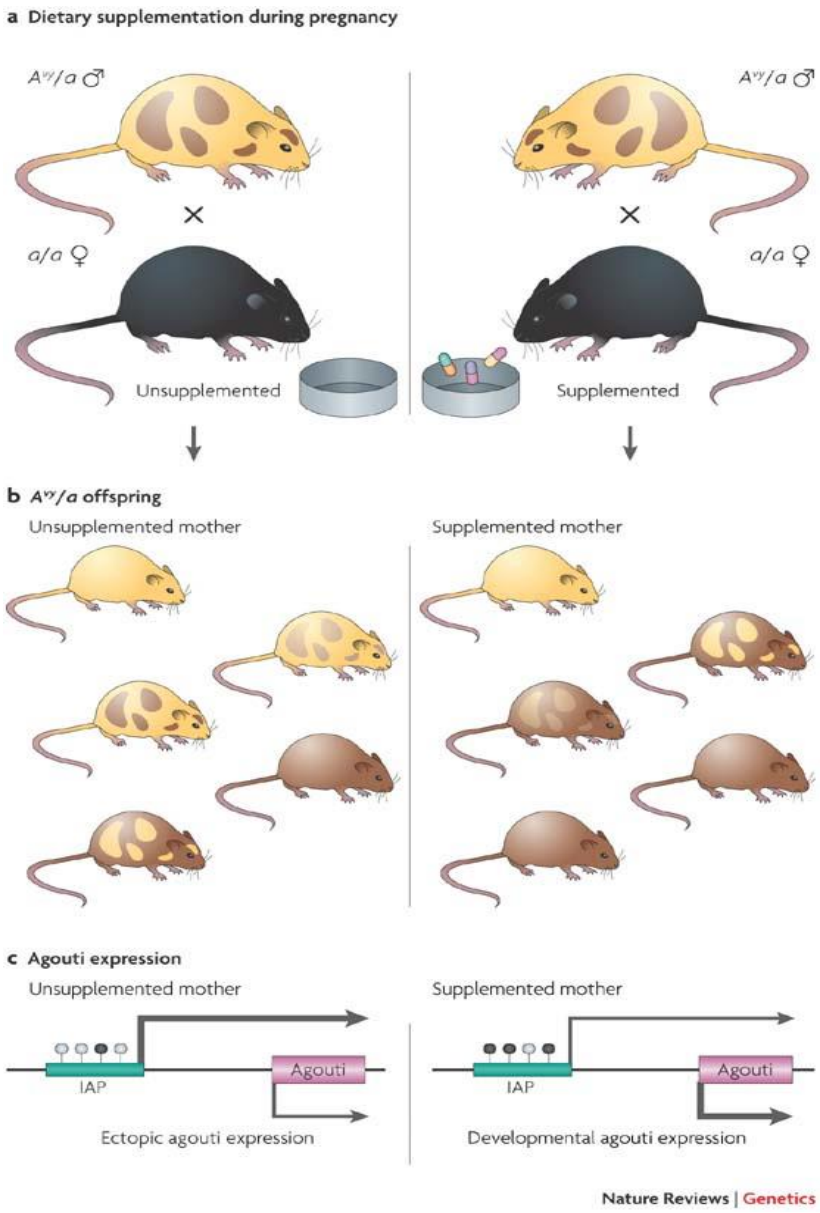
Diet

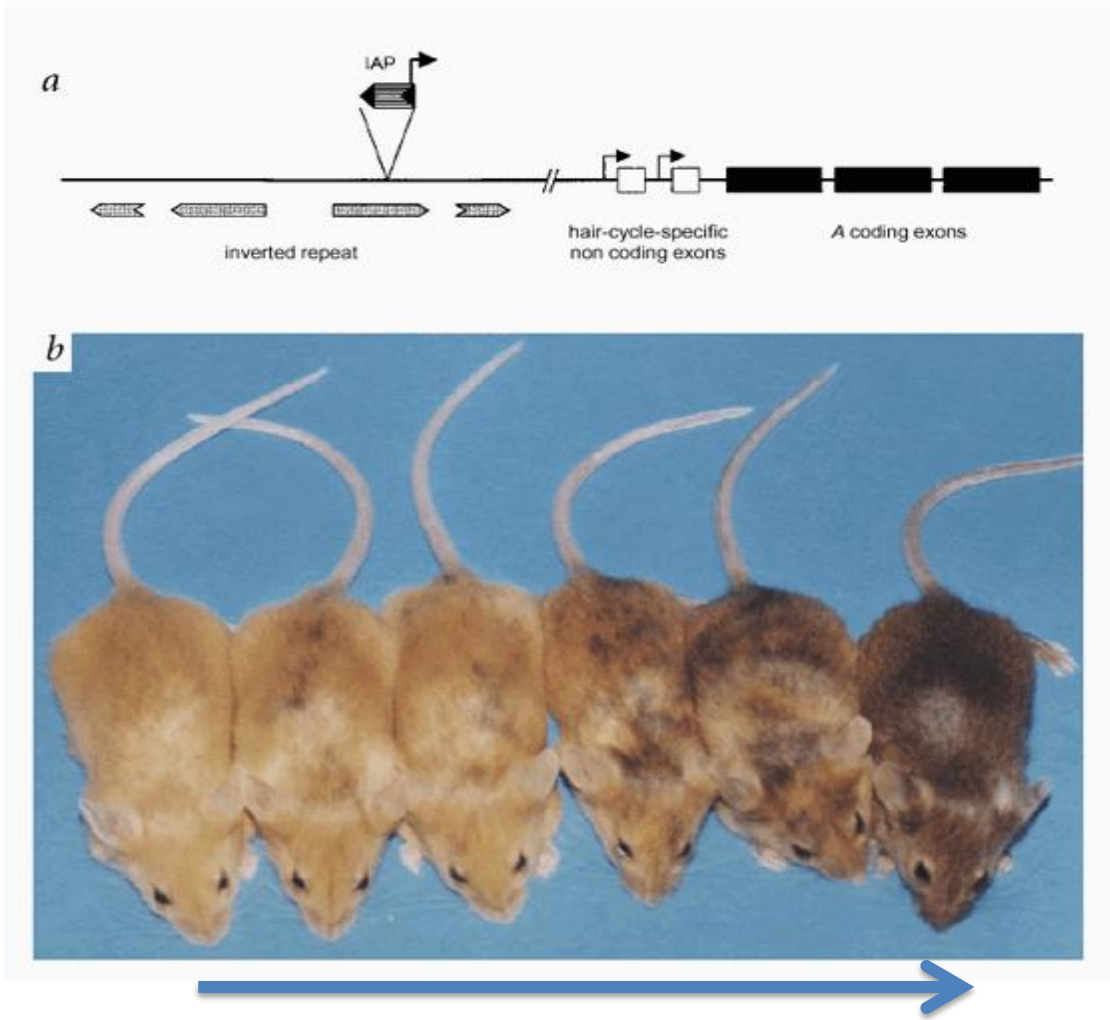
SAM-e

primary methyl donor in all eukaryotes

Addition of methyl group to DNA

Maternal diet and the neonatal epigenome – a focus on folate

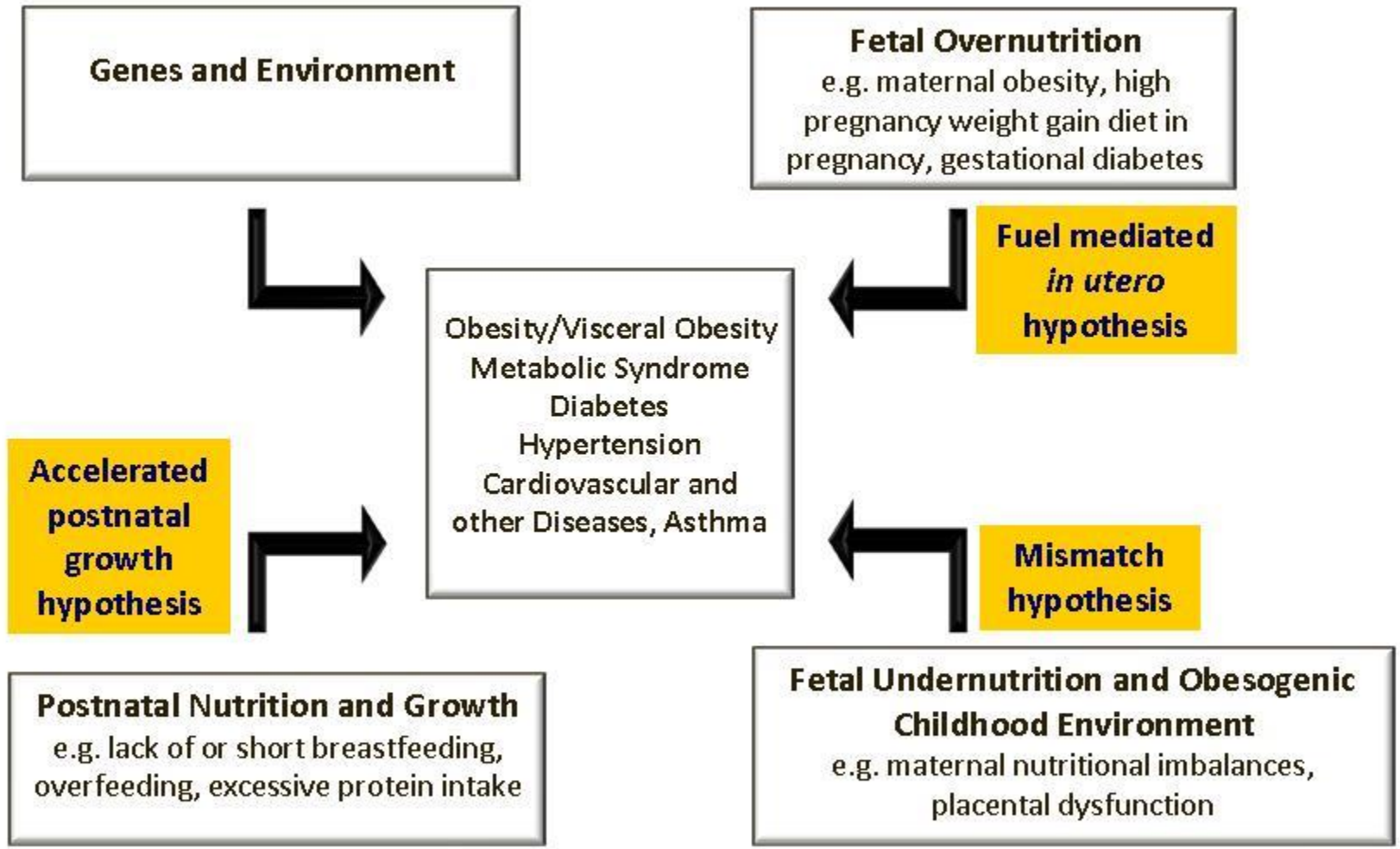




Wolff GL, et al. FASEB J. 1998; 12: 950

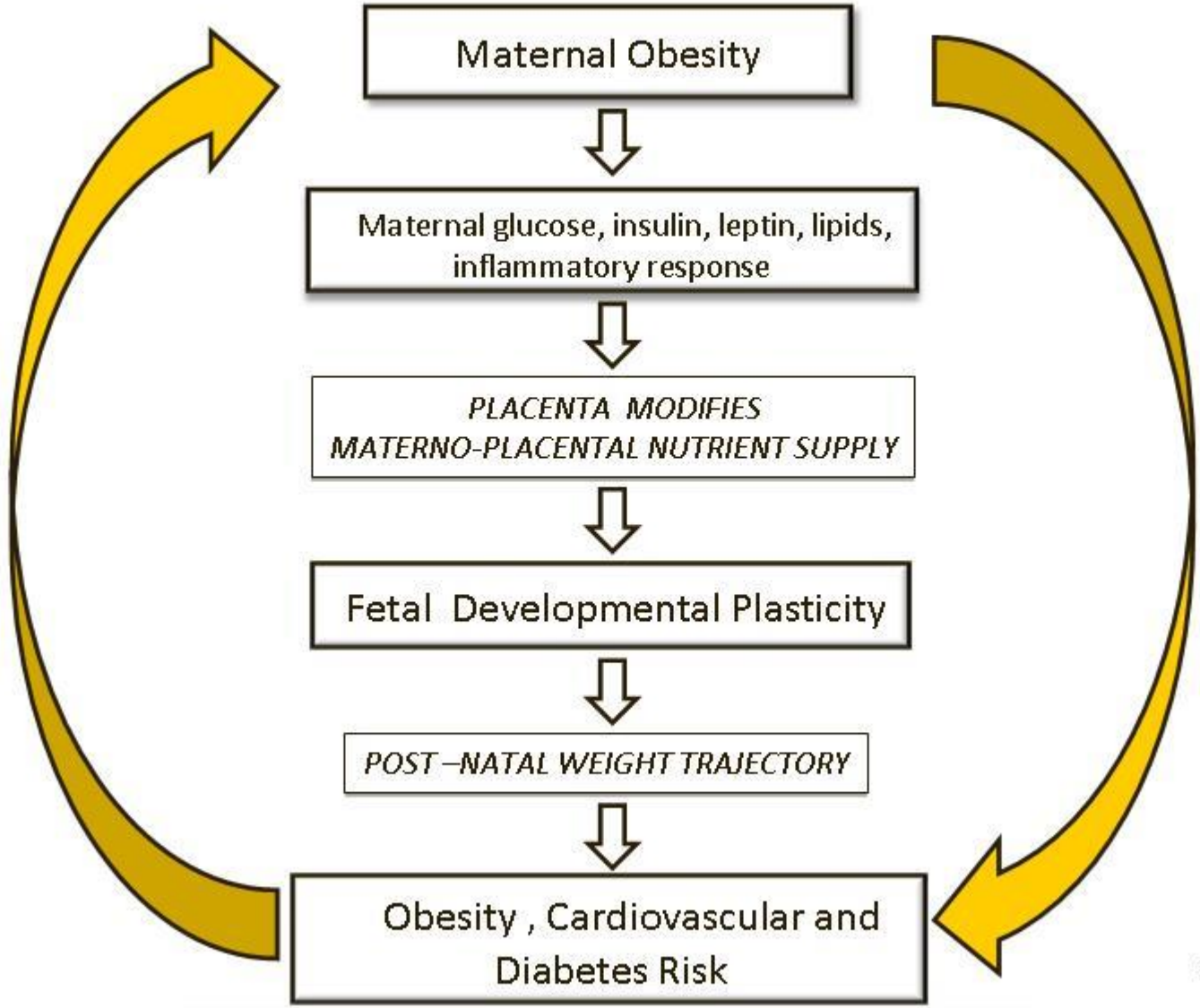
Programación Metabólica Precoz

Key Hypotheses



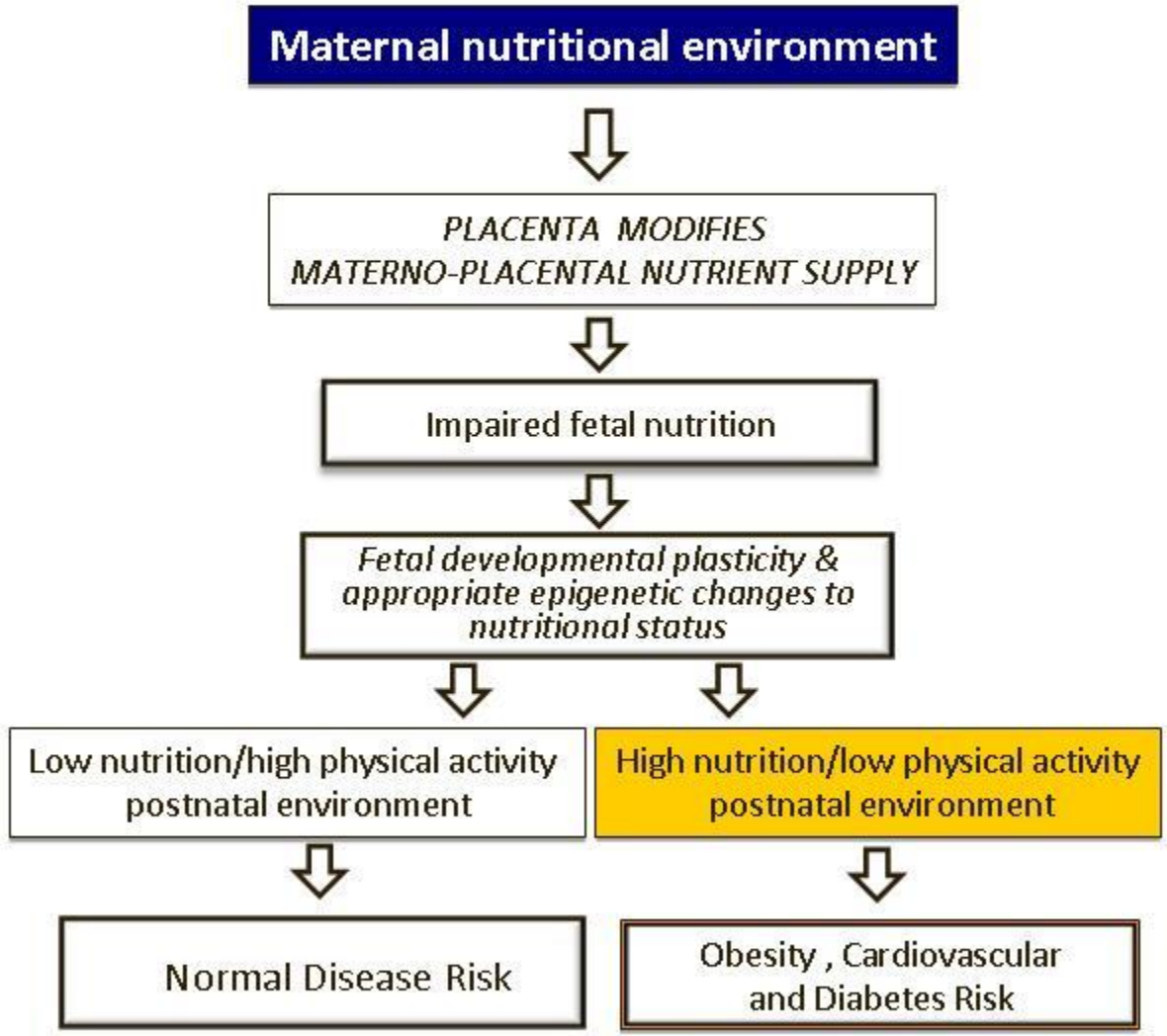
modified from Koletzko et al, Am J Clin Nutr, 2011 Dec;94(6):2036S-2043S.

Transgenerational Circle of Obesity

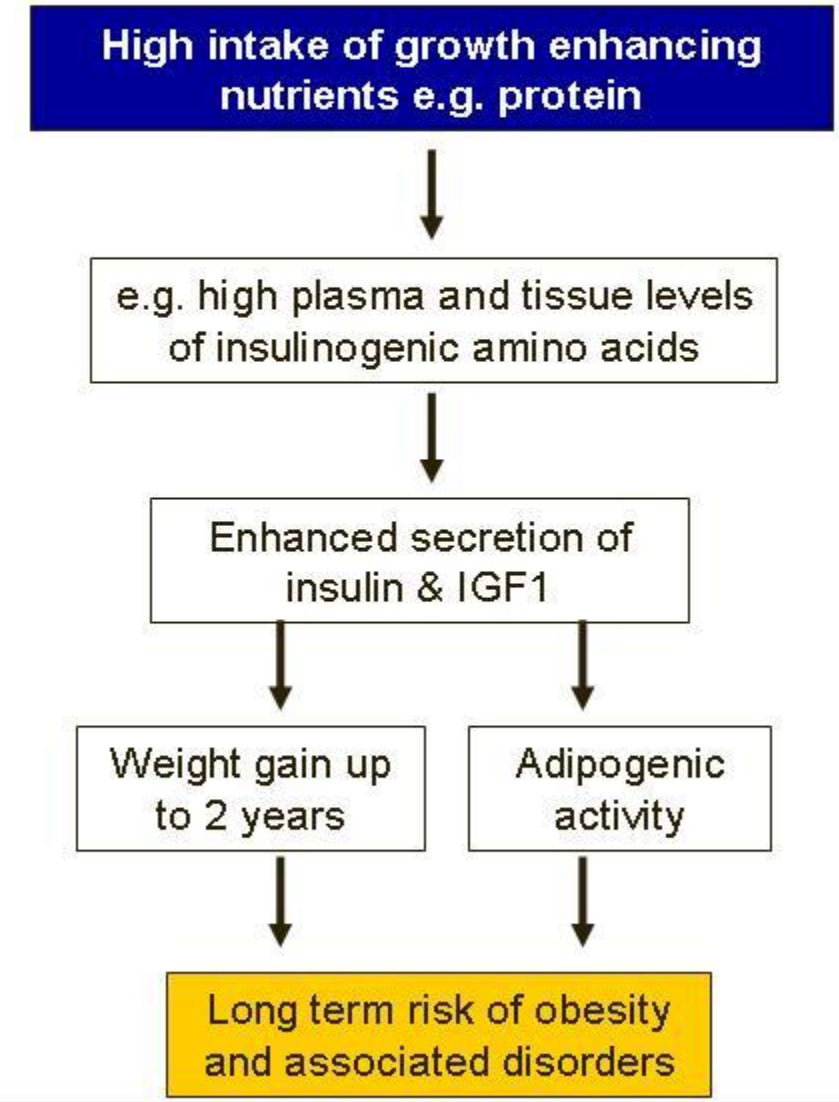


modified from Koletzko et al, Am J Clin Nutr, 2011 Dec;94(6):2036S-2043S.

Mismatch between pre- and postnatal Environment



Postnatal accelerated Weight Gain



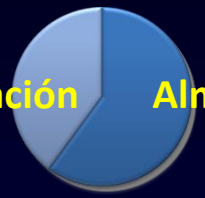
modified from Koletzko et al, 2009

Consecuencias a largo plazo de un ambiente nutricional "materno-fetal-postnatal" subóptimo (Nature Reviews Endocrinology; Symonds et al 2009)

Malnutrición Materna, Diabetes Gestational, Obesidad Materna

Síndrome Metabólico

Alteración homeostasis glucosa, metabolismo lipídico, biogénesis mitocondrial



ER stress
Hipertrofia

Infiltración Lipídica

Resistencia a la Leptina

Alteraciones homeostasis glucosa

Infiltración Lipídica

Resistencia Insulina
Obesidad

Enf. Cardiovasculares
Esteatosis

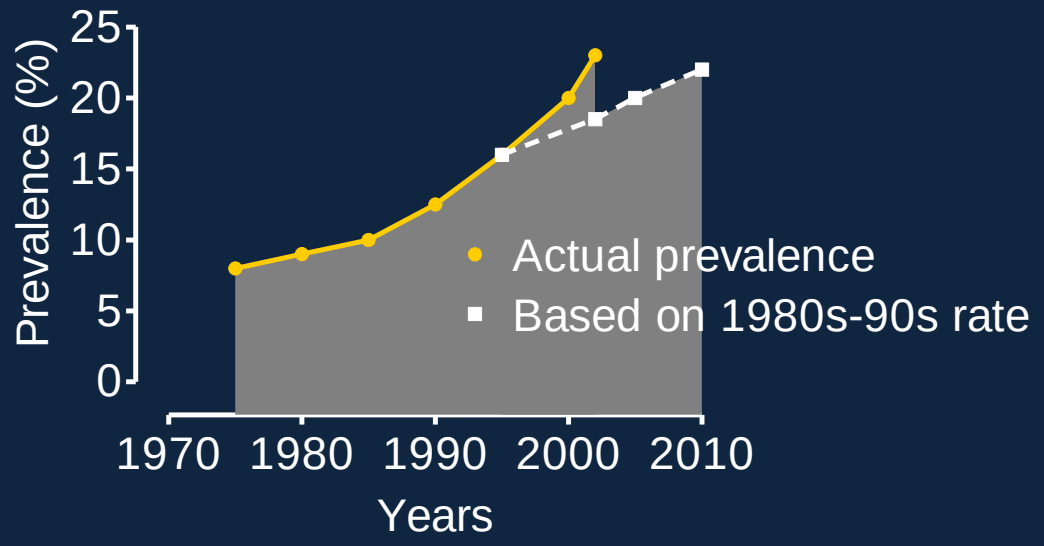
Desórdenes ingesta
Obesidad

Resistencia Insulina
Diabetes Tipo II

“La oportunidad de optimizar la nutrición en la vida precoz”

Acelerada sin control
EU: 14 M sobrepeso, 3 M obesos

Epidemia mundial:
145 M sobrepeso, 30-45 M obesos



La diabetes tipo II se está produciendo en niños y adolescentes

Hace unos años era una ¡patología propia de individuos por encima de los 50 años!

Causas de la obesidad

- Las “2 más importantes” – exceso de ingesta energética/ reducción del gasto energético

- Las “otras 10” – incluyendo: aumento de la edad materna, aumento de la temperatura ambiental, reducción de los fumadores, aumento del uso de antidepresivos, etc.

Keith *et al* (2006) Int J Obesity **30**, 1585-1594

Mother obesity/diabetes determines pathologic phenomena in the mothers and their offspring

MOTHERS

Mortality *(Venous thrombo-embolism,..)*

Morbility *(Gestational diabetes, pre-eclampsia,…)*

Anesthesic complications

Perinatal complications *(Caesaream section, Haemorrhage,..)*

FETUS & NEONATE

Congenital Defects

Perinatal Death

Placental dysfunction

Still birth

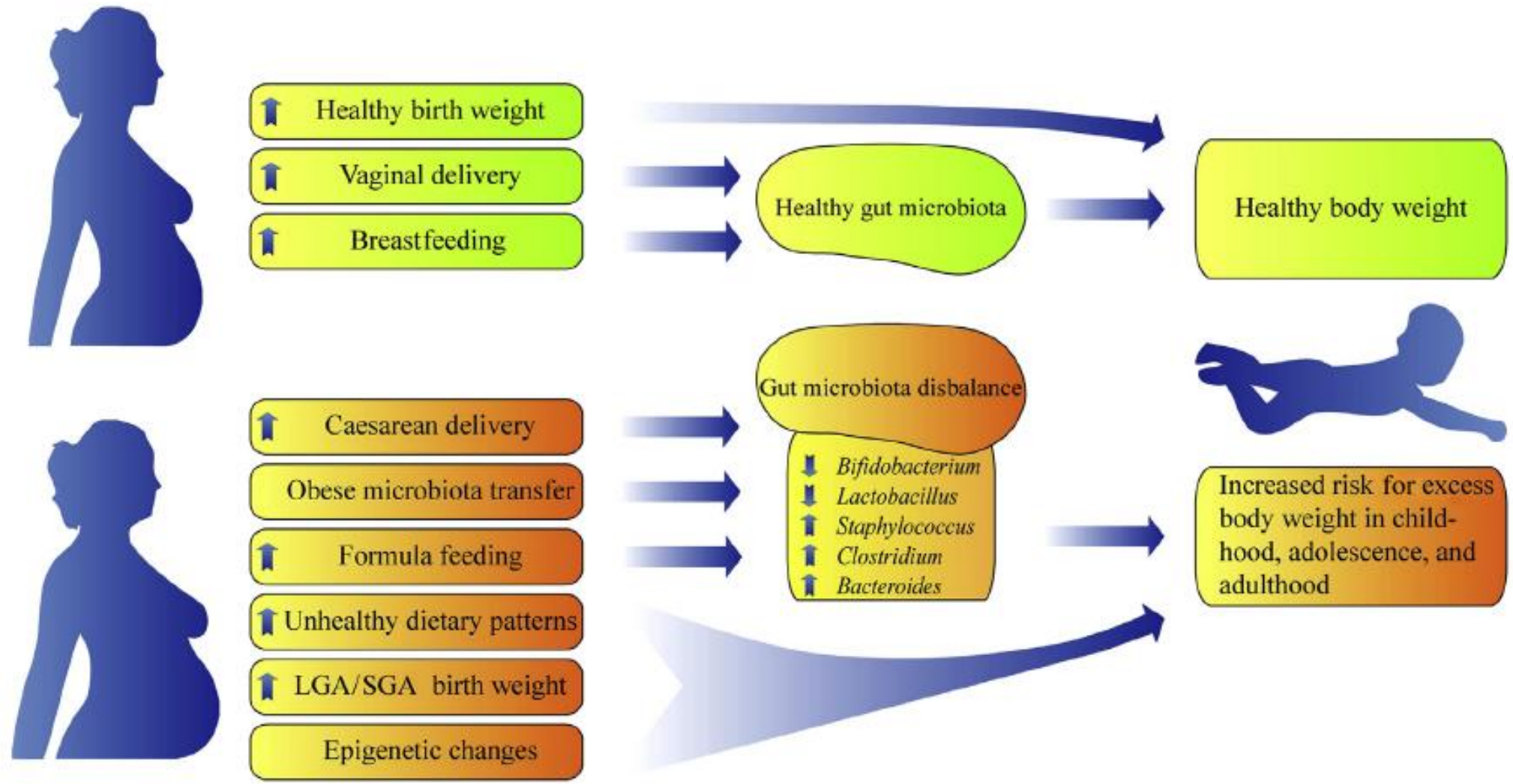
IUGR

Macrosomia

Shoulder distocy

Prof. Cristina Campoy. University of Granada. E-mail: ccampoy@ugr.es

Potential links between mother excess body weight (EBW) during and after pregnancy and elevated risk of EBW in her offspring.

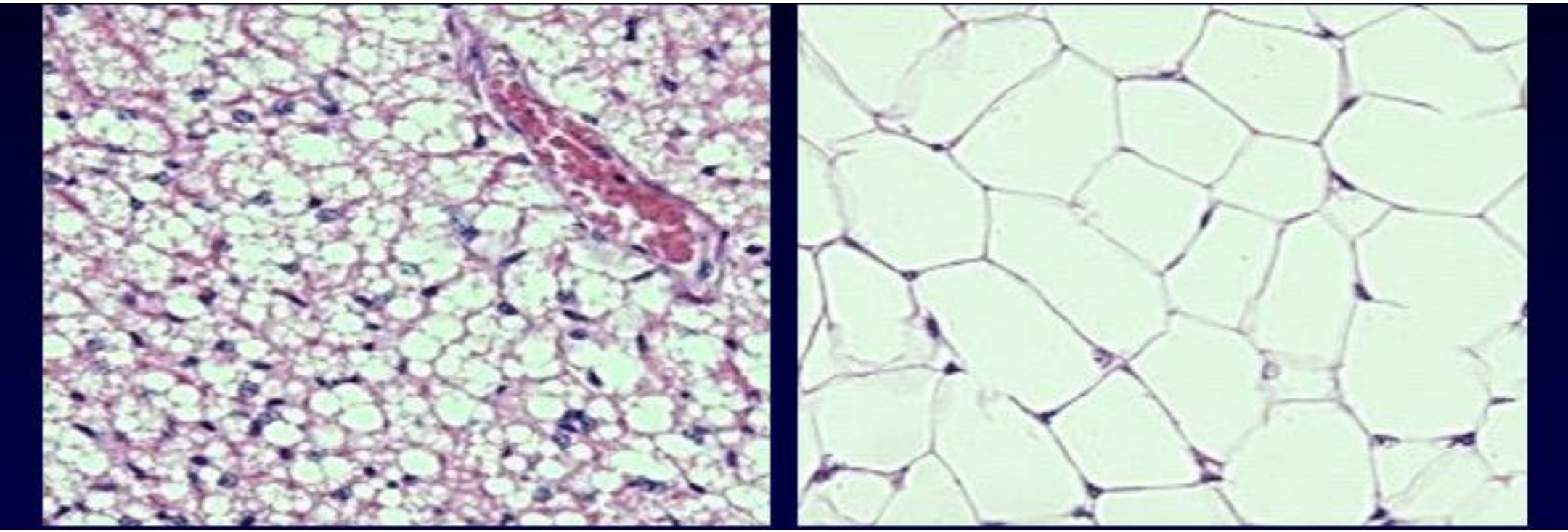


Paliy, et al. Nutrition 2013

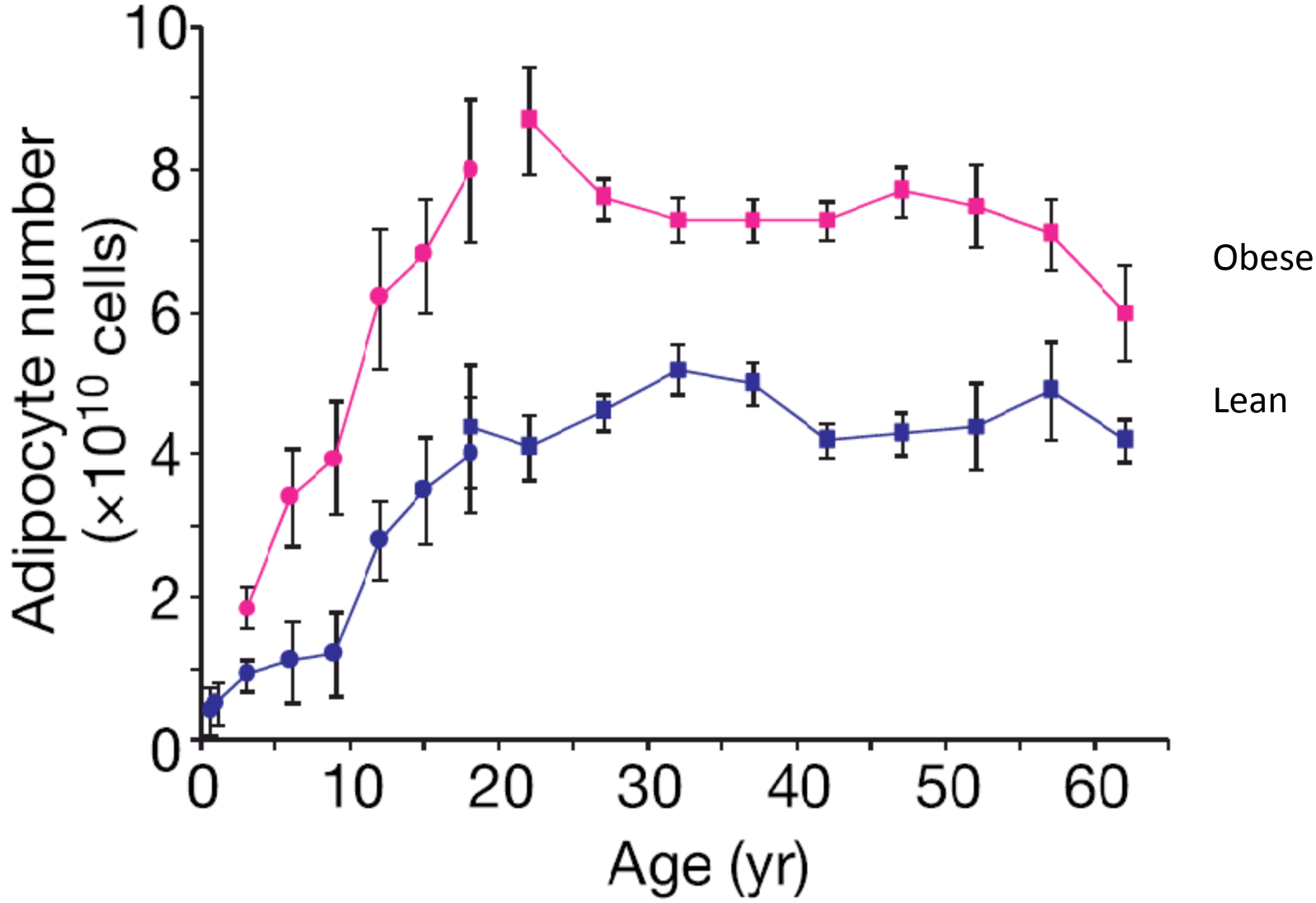
Adipose tissue composition

Brown adipose tissue

White adipose tissue



Fat cell number through the life cycle



Spalding KL *et al* (2008) Nature **453**: 783-787

↑ Birthweight →↑ adult BMI in Danish conscripts aged 18-26 years

Adjusted for gestational age, birth length, maternal factors
Sorensen et al., BMJ 1997.

PERIODOS CRITICOS DE RIESGO DE OBESIDAD

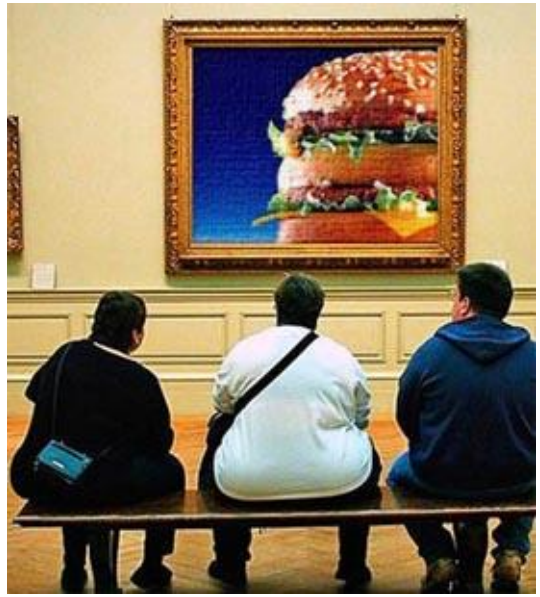
ETAPA FETAL DE DESARROLLO DEL TEJIDO ADIPOSO

14% DE LOS LACTANTES CON SOBREPESO SERÁN ADULTOS OBESOS

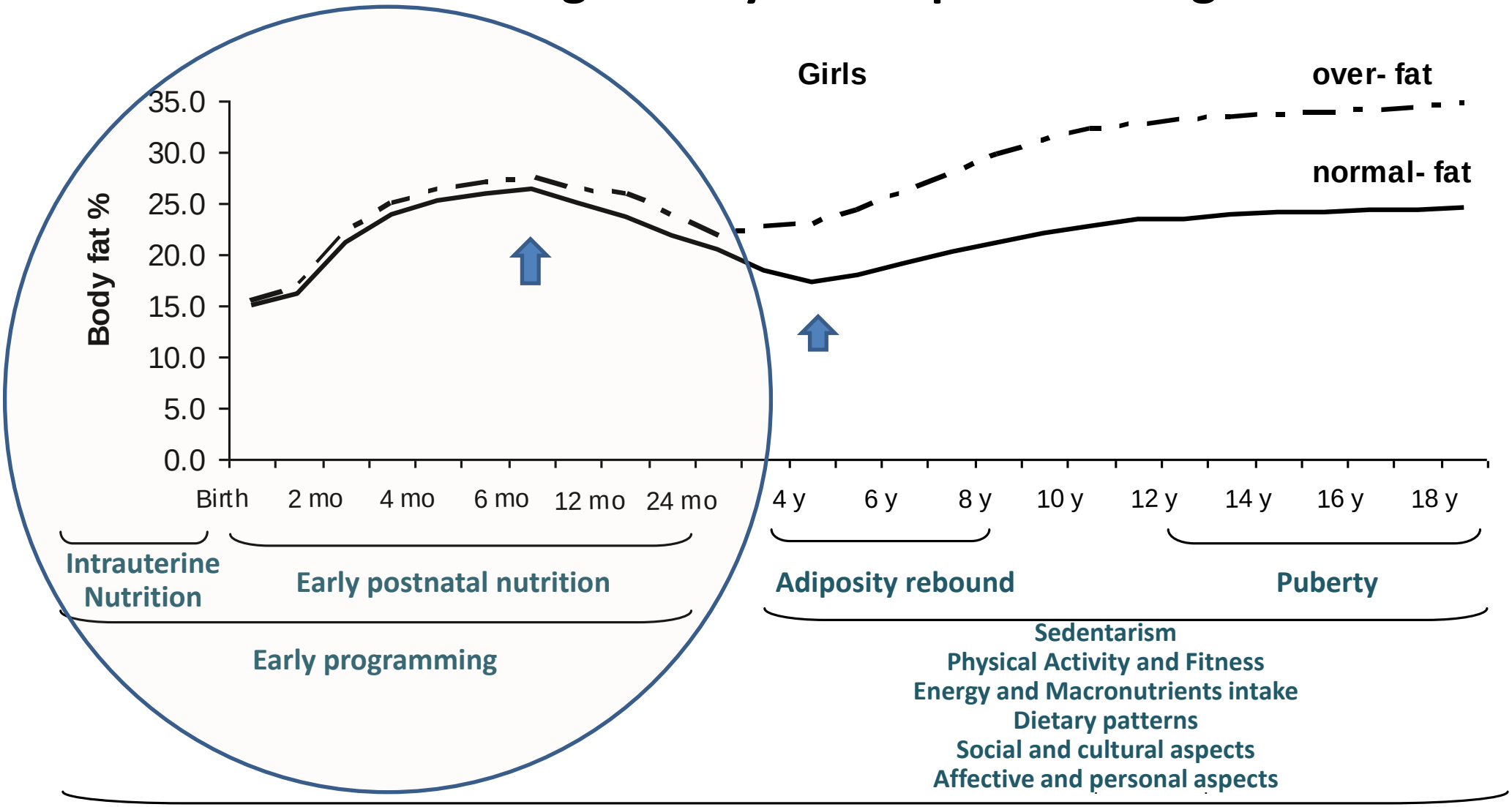
40% DE LOS NIÑOS OBESOS A LOS 6-7 AÑOS SERÁN ADULTOS OBESOS

60% DE LOS ESCOLARES PREPUBERES OBESOS SERÁN ADULTOS OBESOS

80% DE LOS ADOLESCENTES OBESOS SERÁN ADULTOS OBESOS



Factors influencing obesity development along childhood



(Moreno LA et al. World Rev Nutr Diet 2013;106:119-26)

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nuheal
- Nutraceuticals for a healthier life -
EARNEST
Nutri MENTHE
EARLY NUTRITION ACADEMY
European Commission
SEVENTH FRAMEWORK PROGRAMME
My New GUT
THE FRAMEWORK PROGRAMME FOR RESEARCH AND INNOVATION
HORIZON 2020
DynaHEALTH
UNIVERSIDAD DE GRANADA
EURISTIKOS
CENTRO DE EXCELENCIA DE INVESTIGACIÓN PEDIÁTRICA
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Cohort studies analyzing epigenetic influences and the persistence of such signatures

GUSTO study (Asia)

Danish Cohort

Early Nutrition Project (Europe)

Nutritional intervention studies in obese pregnant women

Limit Trial (Australia)

Upbeat Study (UK)

Nigo-Health (Spain)

Rolo Study (Ireland)

>470.000 pregnant women and their offspring

SCIENTIFIC EVIDENCES

EARLYNUTRITION

- Evidence that **diet and lifestyle modifications during pregnancy** can reduce the increased risk of obesity in offspring of obese pregnant women helping to break an intergenerational cycle of obesity and related disorders.
- Evidence that **excessive weight gain in pregnancy and/or rapid early infant weight gain** leads to later obesity will help to formulate policies to reverse the increasing rates of childhood obesity and co-morbidities.
- Evidence that **dietary modifications in infancy**, in particular relating to breastfeeding and complementary feeding practices, as well as novel compositional approaches to infant formula, can reduce the risk of obesity and related disorders in offspring.

This project receives funding from the European Union Seventh Framework Programme (FP7/2007-2013) under grant agreement n° 289346

Nutrición Precoz: 10 recomendaciones para la planificación familiar

EarlyNutrition Priority Recommendations

Preconcepción, Embarazo, Lactancia al pecho & Lactante

European Commission

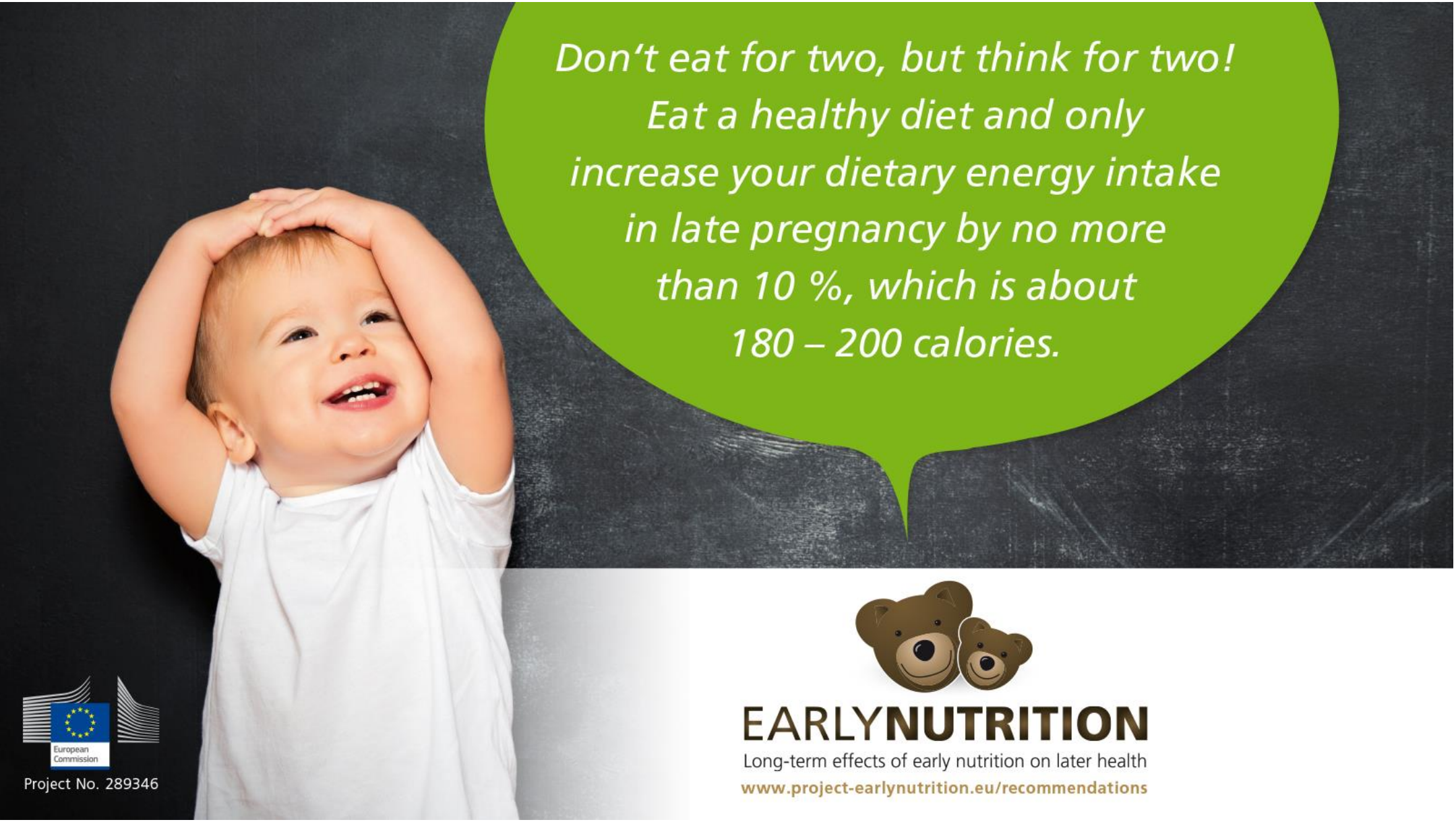
Project No. 289346

EARLYNUTRITION

Long-term effects of early nutrition on later health

www.project-earlynutrition.eu/recommendations


A healthy weight before conception gives your baby the best possible chance of lifelong health!
European Commission
Project No. 289346
EARLYNUTRITION
Long-term effects of early nutrition on later health
www.project-earlynutrition.eu/recommendations



European Commission

Project No. 289346

EARLYNUTRITION

Long-term effects of early nutrition on later health

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European Commission

Project No. 289346

Breastfeeding women should eat a balanced diet!

EARLYNUTRITION

Long-term effects of early nutrition on later health

www.project-earlynutrition.eu/recommendations

EARLYNUTRITION

Long-term effects of early nutrition on later health

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European Commission

Project No. 289346

SEVENTH FRAMEWORK PROGRAMME

EARLYNUTRITION
Long-term effects of early nutrition on later health

LMU LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN

- 5000 students all over the world
- In English, and translated into Chinese and Arabian, and comming in Spanish!

ESPGHAN

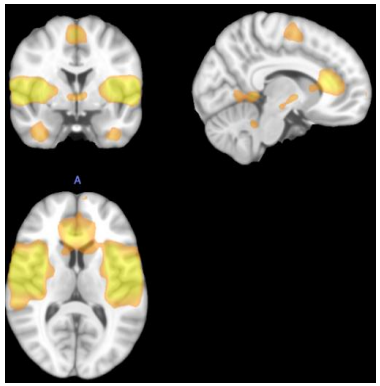
Early programming of gut microbiota-brain axis

Cristina Campoy, Prof. MD.
Department of Paediatrics. School of Medicine
EURISTIKOS Excellence Centre for Paediatric Research
Institute of Neurosciences. Health Sciences Technological Park
University of Granada. Spain

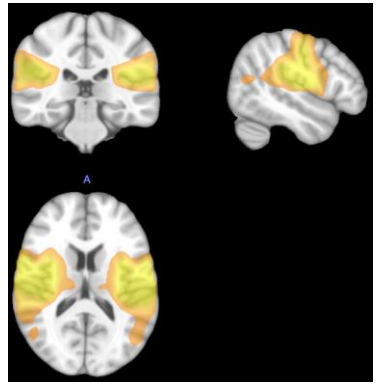
3rd Annual meeting of the MyNewGut project
22-23 August 2017, Cork, Ireland

Grant Agreement no: 613979
www.mynewgut.eu

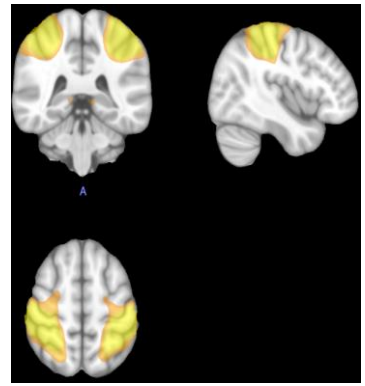
Brain Networks Studied



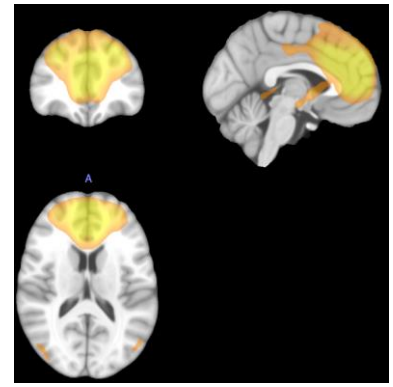
Salience *Network (Attention)*



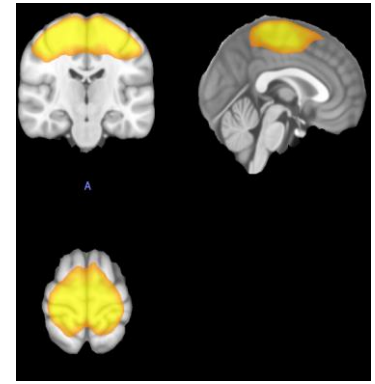
Auditory Network



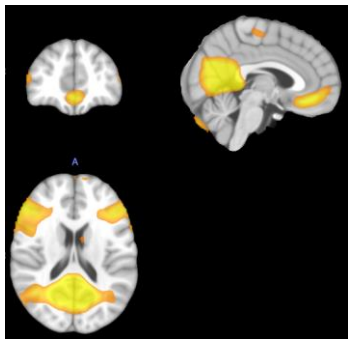
Somatosensorial Network

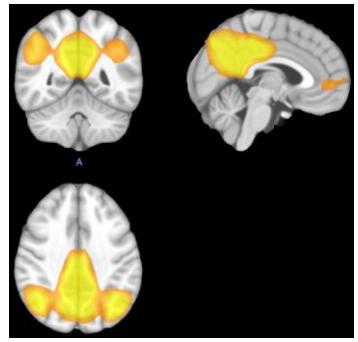


Executive Control Network

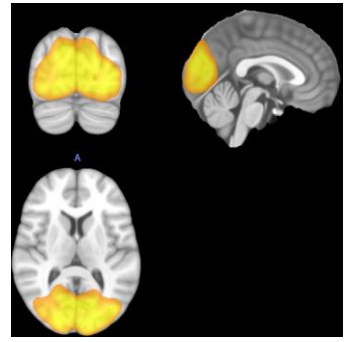


Motor Network: Motor Coordination

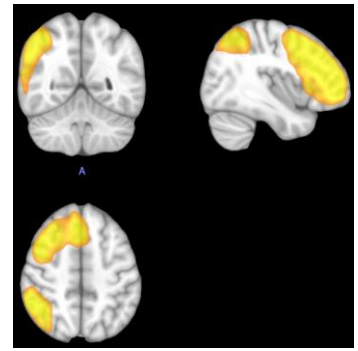


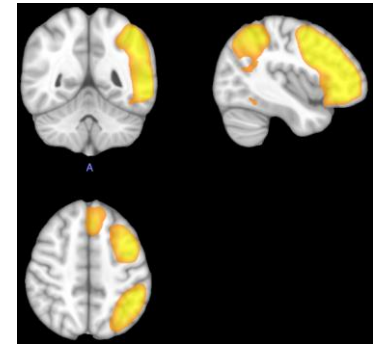


Default Mode Network: **Ventral Area** (left) **Dorsal Area** (right). Responsible of the brain activity when mind is in resting state



Visual Network

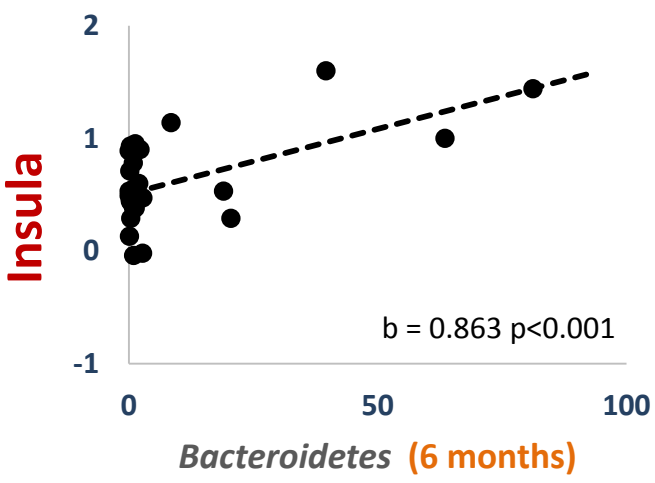


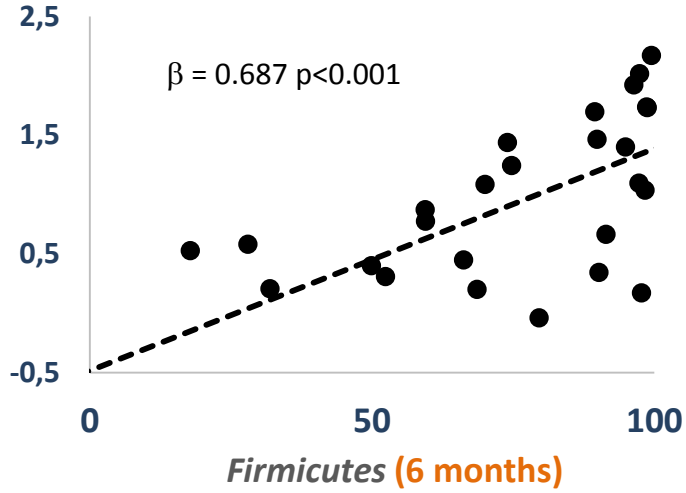


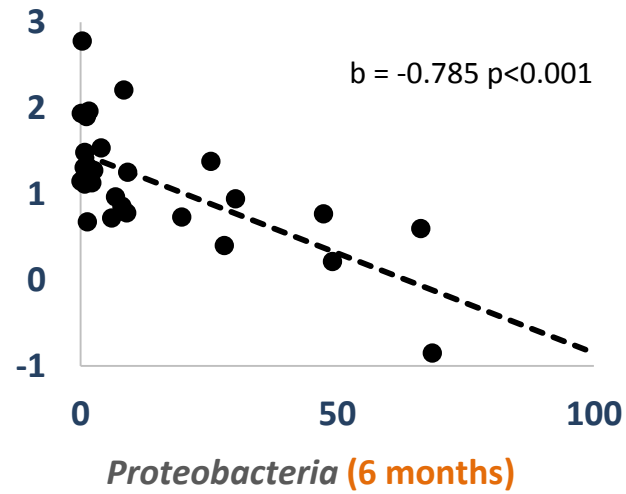
Fronto-Parietal Attention Network (left and right)

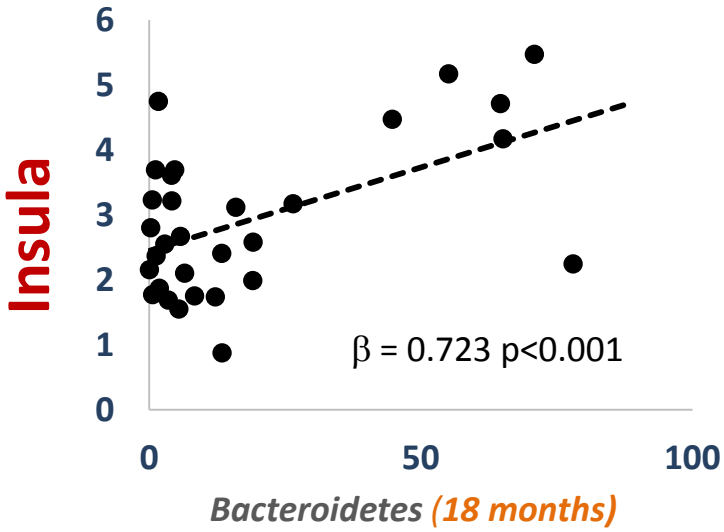
My New GUT

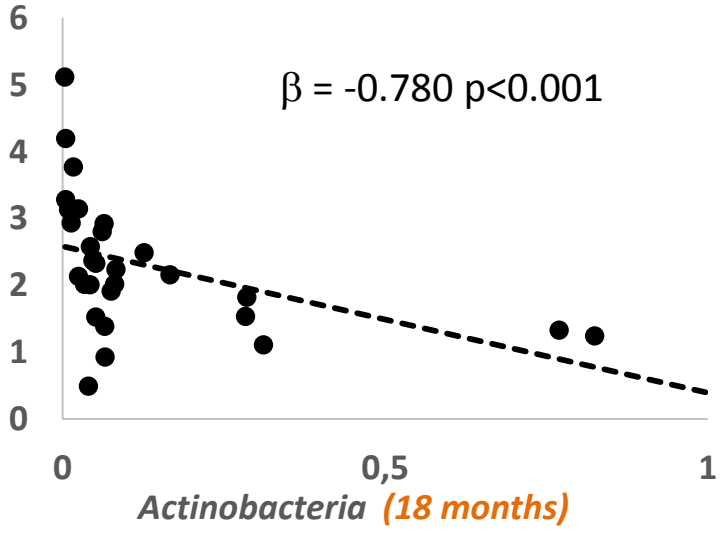
Salience Network (6.5 yrs)

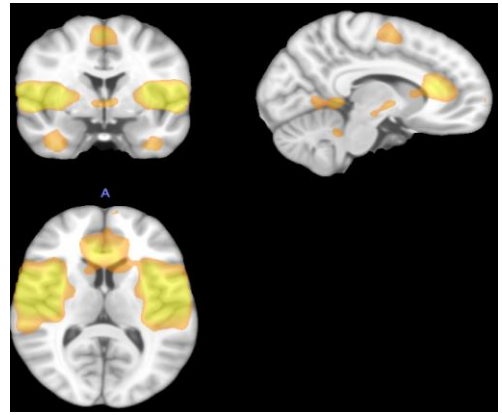








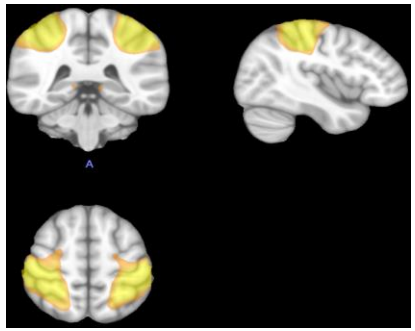




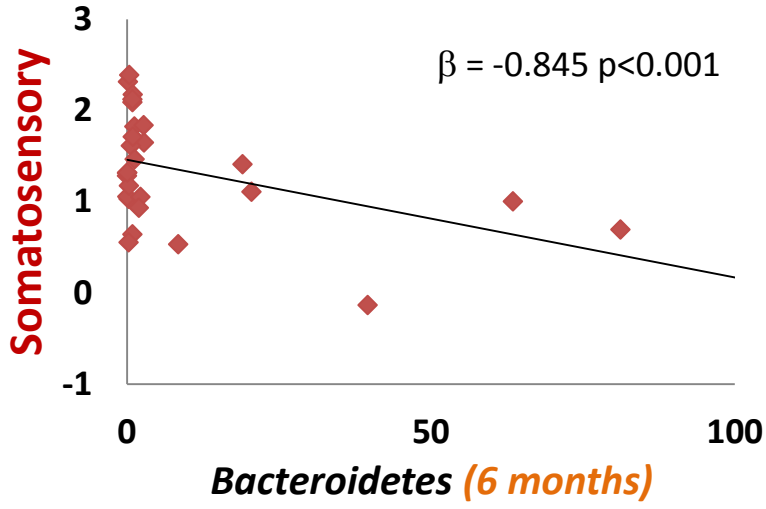
PREOBE Follow up

My New GUT

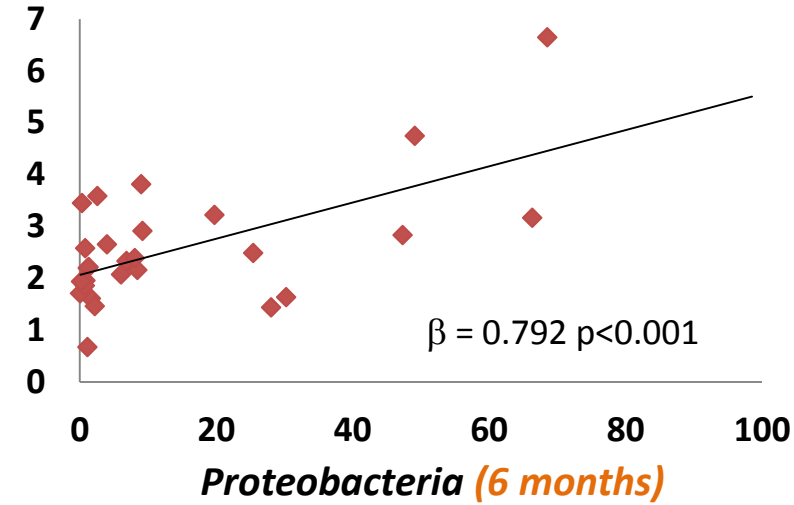
Somatosensorial Network (6.5 yrs)



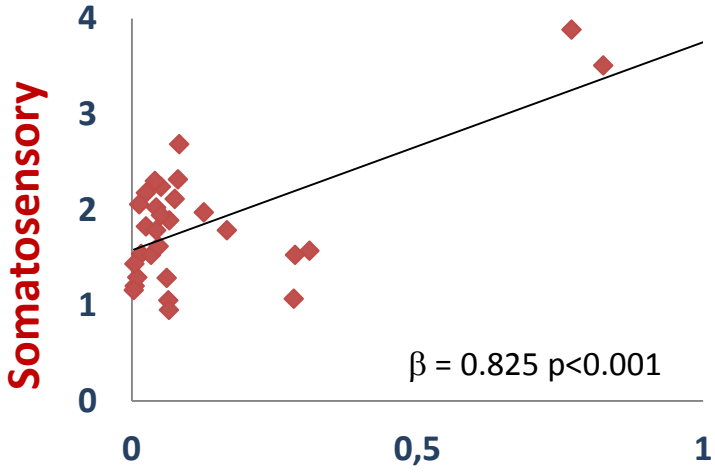
XPREOBE Follow up



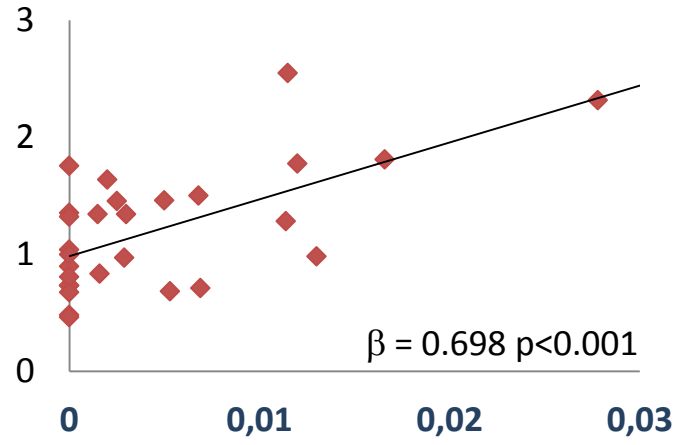
***Bacteroidetes** (6 months)*



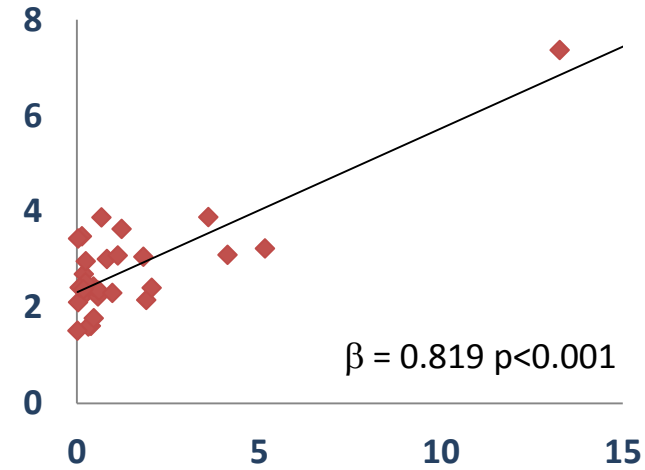
***Proteobacteria** (6 months)*



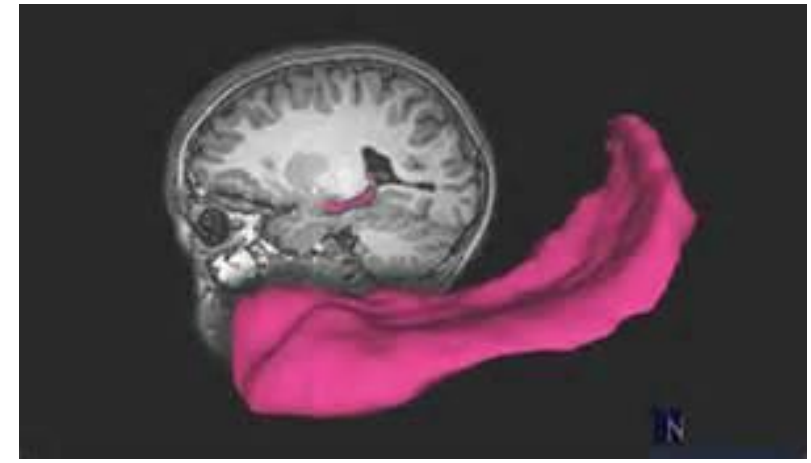
***Actinobacteria** (18 months)*



***Fusobacteria** (18 months)*



***Proteobacteria** (18 months)*



Children brain volumes as a function of Maternal Obesity

My New GUT

European Commission

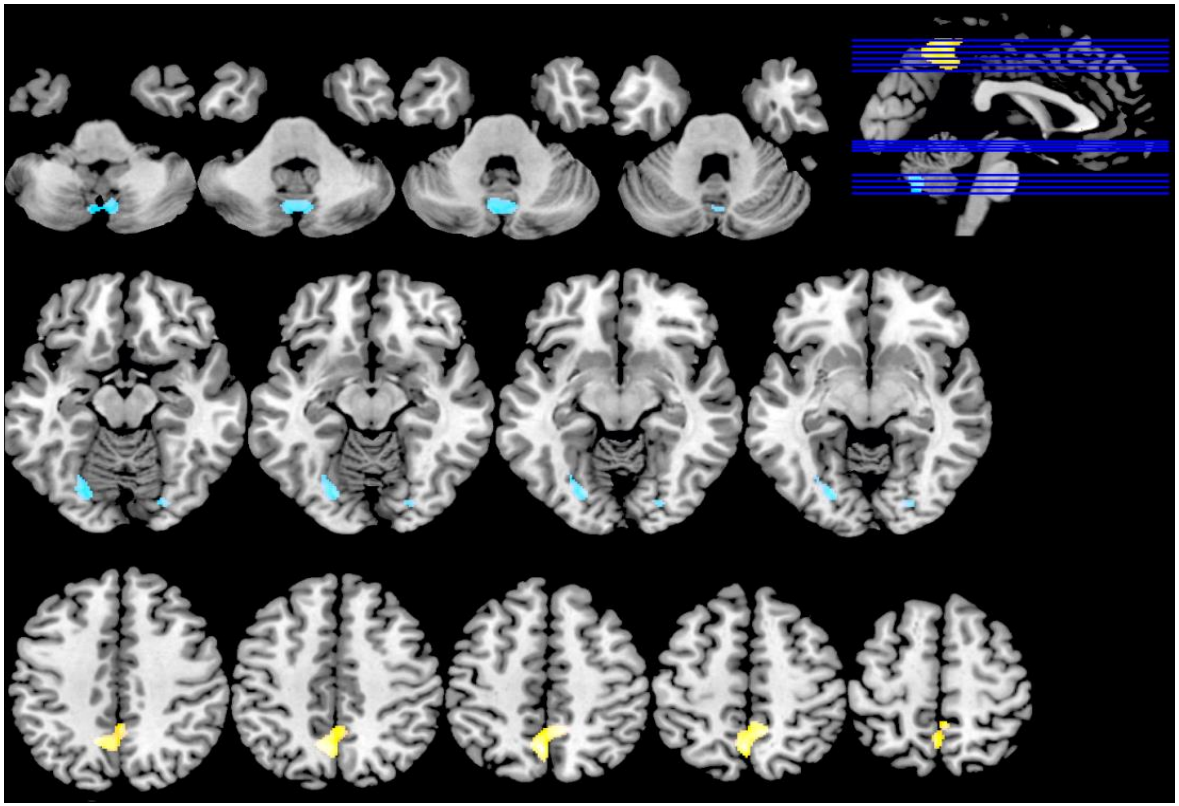
EURISTIKOS
Centro de Excelencia de Investigación Pediátrica

ugr Universidad de Granada

cimcyc

VBM results

- Obesity vs. Normal weight



Children born to Normal Weight Mothers showed **larger volumes** than those born to Obese pregnant mothers in a cluster that peaks at the *left Precuneus*, embracing also part of the *right Precuneus* and a small part of *Left Mid Cingulate*

The Obesity group had **larger volumes** in cluster speaking at the *left Fusiform* and *Lingual Gyrus*, and parts of the *left and right cerebelum*.

VBM results

- **Precuneus**:
  - **Restraint eaters** have reduced *Precuneus* vol. (Joos et al., 2011, van der Laan et al. 2016).
  - It is linked to **altered functional connectivity in obeses** (Kullman et al., 2012).
  - It has been involved in *episodic memory retrieval*, *self-awareness*, and *visuo-spatial imagery* (Cavanna & Trimble, 2006).

- **Cerebellum**:
  - **Obese people** (Pannacciulli et al., 2006) and **restraint eaters** have *reduced Cerebellar volumes*, that seem to recover after psychological interventions (Eynde, et al. 2012).
  - It has a role in ***feeding and emotion regulation*** (Amianto et al., 2013).

VBM results

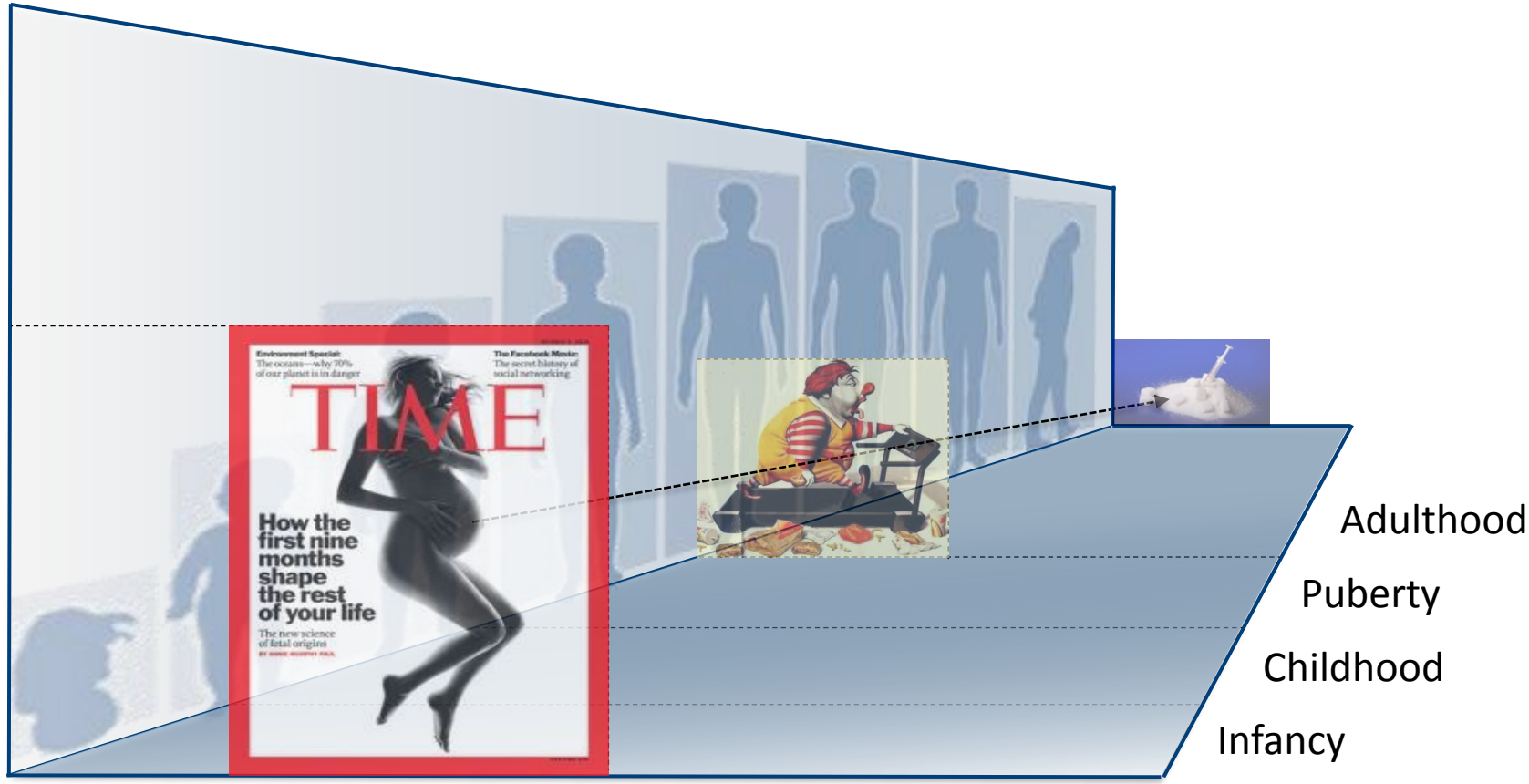
- **Fusiform gyrus**:
  - Has a *negative correlation* with BMI (Taki et al., 2008).
  - It is involved in the *processing of visual information*, and to elicit enhanced responses to high-caloric foods (Killgore et a., 2007, Frank et al., 2010).
  - Its activation after wheight-loss programs predicts *less successful weight maintenance* (Murdaugh et al, 2012).

- **Lingual Gyrus**:
  - *Negatively correlated with waist circunference* (Kurth et al, 2013)
  - *Enhanced response to high-caloric foods* (Murdaugh et al., 2012)

- **Middle Temporal**:
  - *Positive correlation with BMI* (Taki et al, 2008).

FETAL ORIGINS

Genes



Environment

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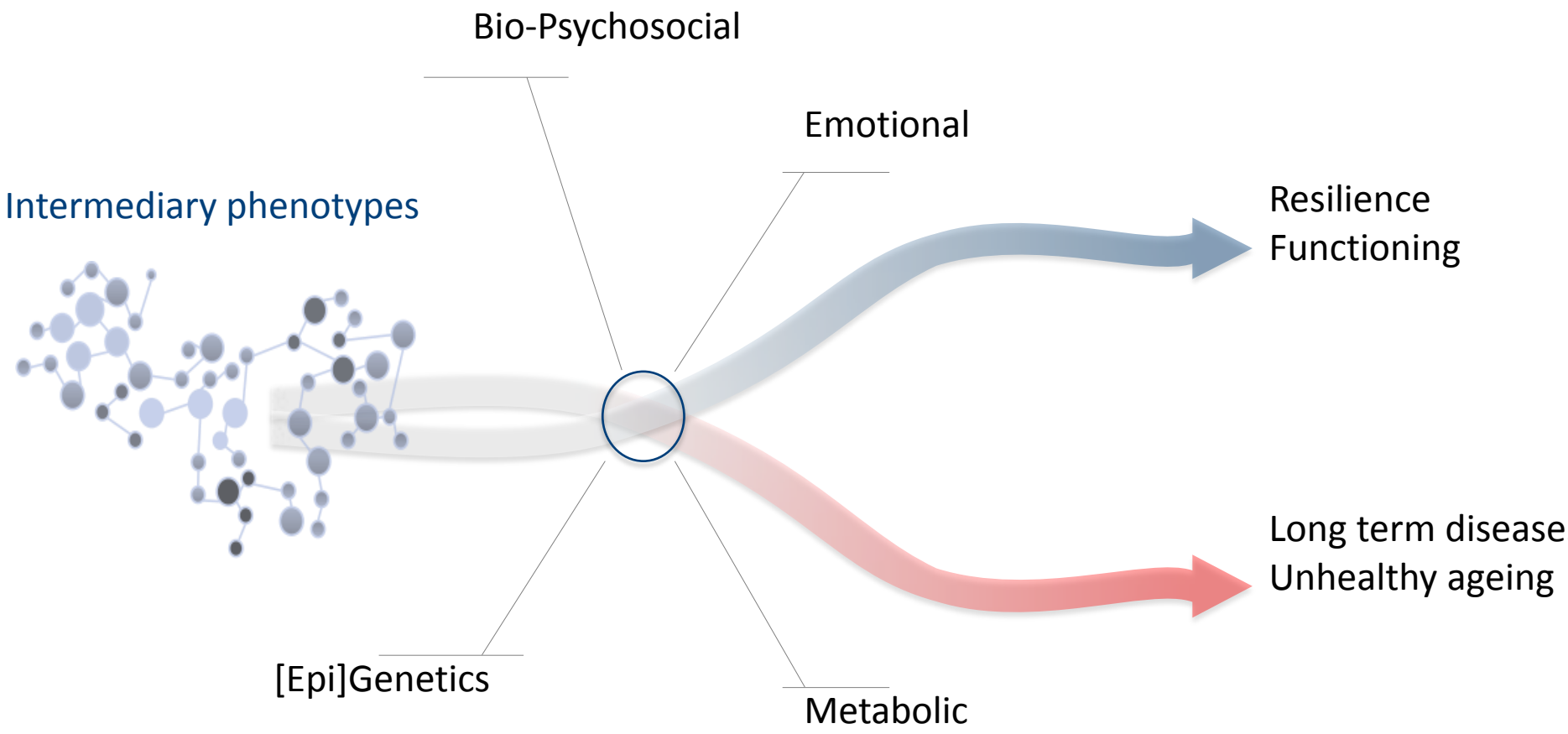
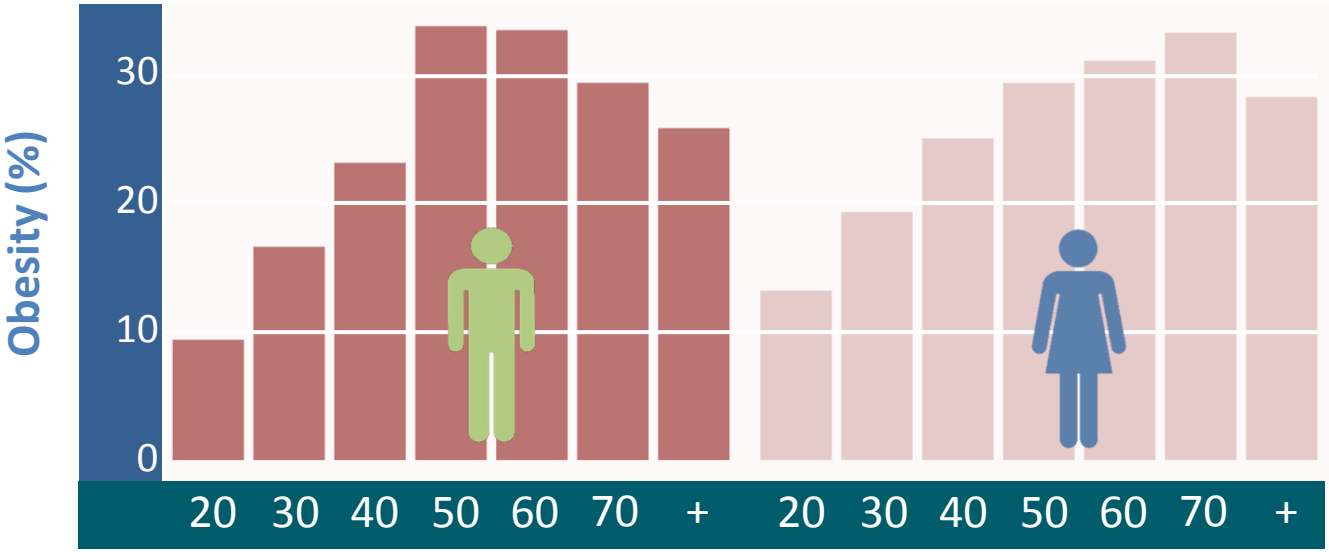
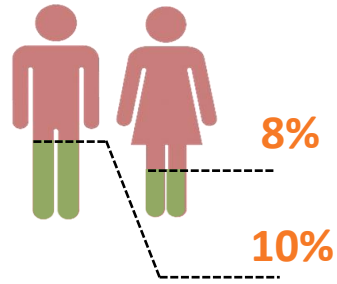
Life-course determinant of Health



Some basic statistics





Adults with
T2 diabetes
Europe

25% of Adults
men living with
Pre-diabetes

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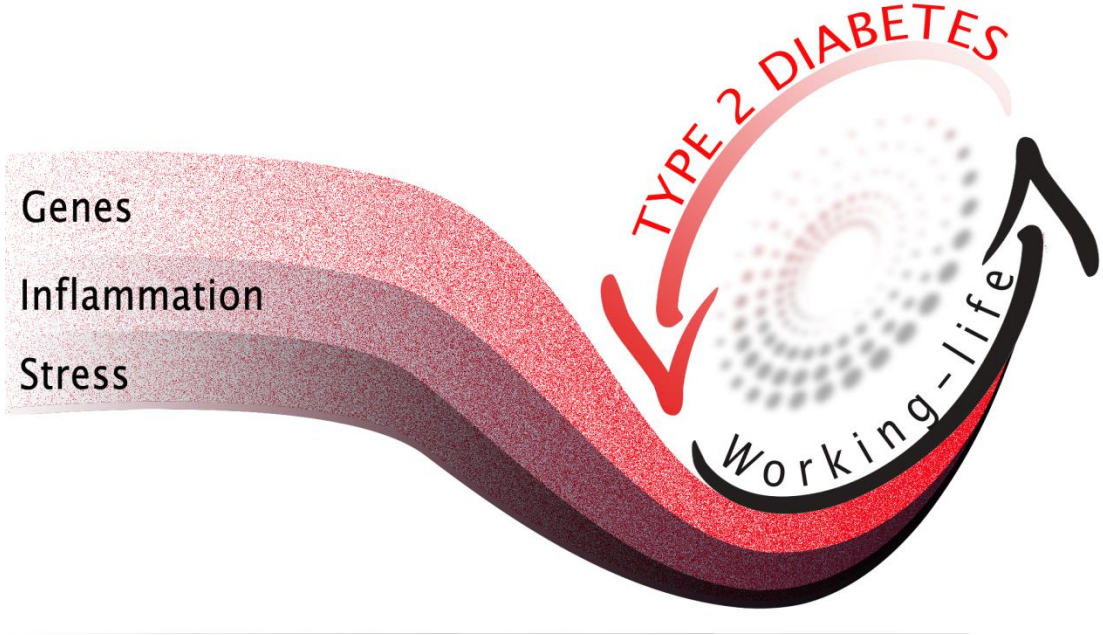
Diabetes and aging

bi-directional relation affecting social factors and economy



Unhealthy & inactive aging

++ Life-long treatment
+ Cognitive decline
+++ Loss of productivity
+ Early retirement
++ Job loss

Total cost (US – 2012)

$176	Healthcare cost
$69	Loss of productivity
$245 billions	

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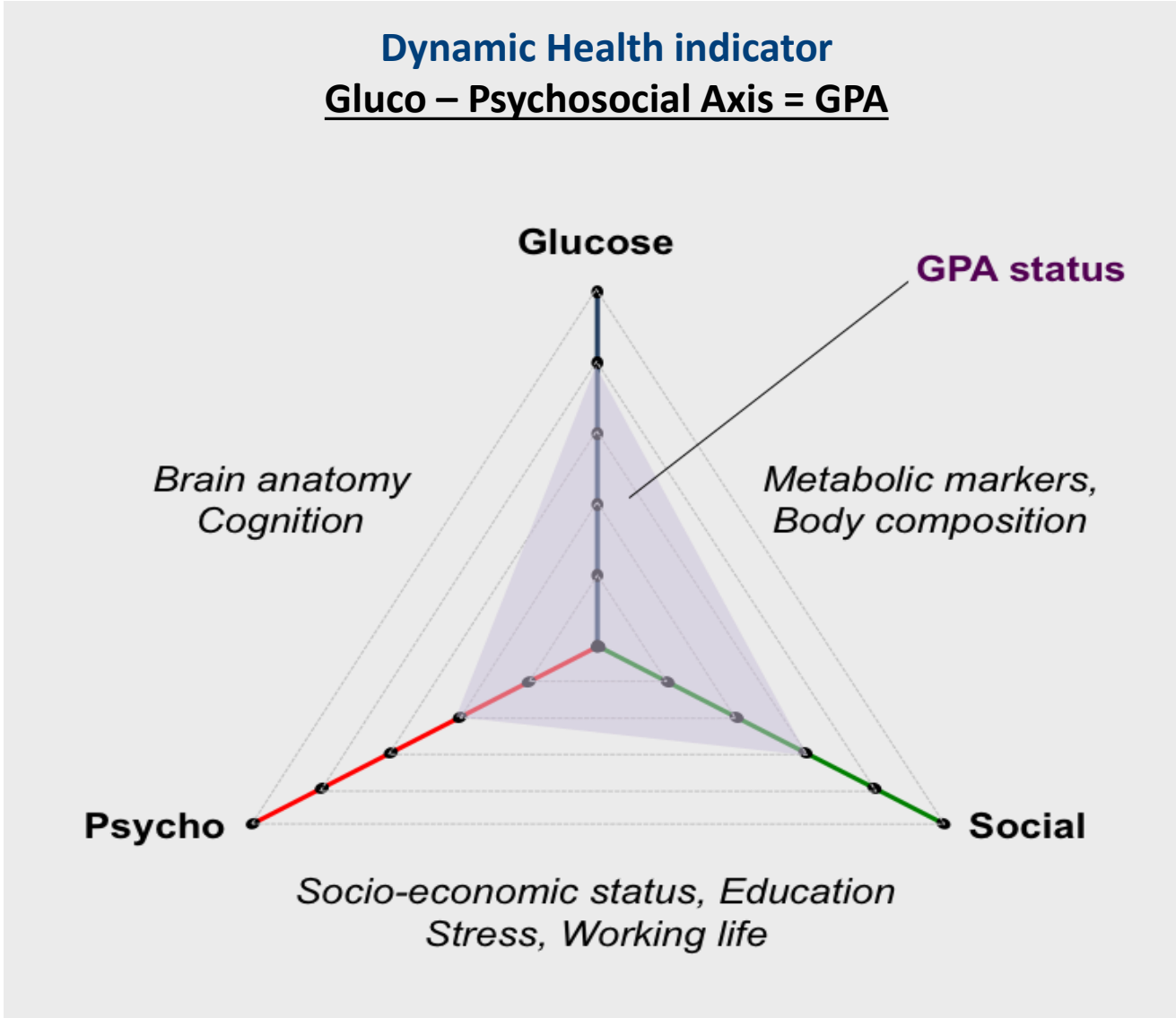
DynaHEALTH project – THE GPA



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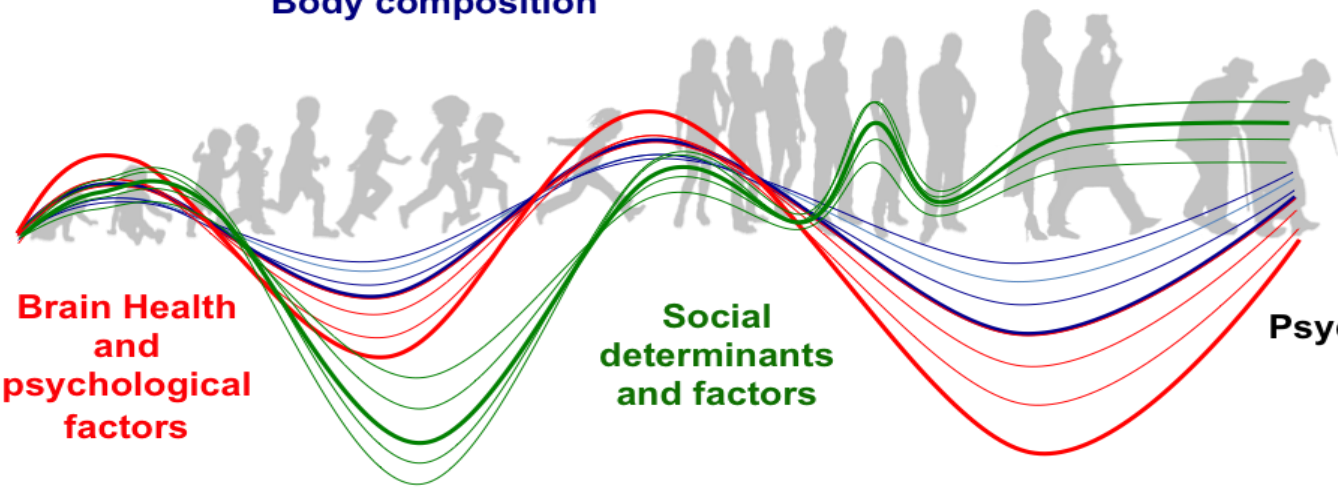
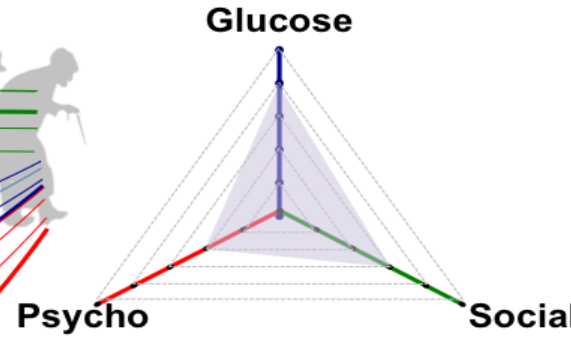
Epigenetic Response

Glycemic Health and Body composition



Brain Health and psychological factors

Social determinants and factors

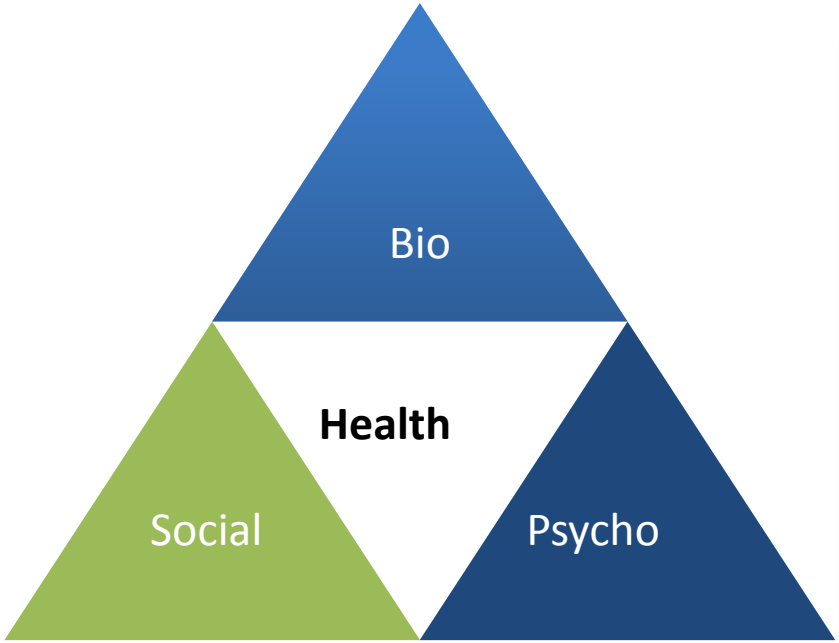


Genetic build-up

Pathways to unhealthy aging

Fetal adversity	Childhood response	Adult health pathways	Unhealthy and inactive aging
Metabolic	Unhealthy early growth	Obesity and Impaired glucose tolerance	Obesity and Type 2 diabetes
Psychological	Impaired cognitive development	High risk behavior	Early dementia and cognitive decline
Social	Low social functioning	Low employability	High social dependency

Rationale



Health[1] and Activity[2] at all age is a composite and/or the results of the **G.P.A. build-up** and of specific investment (or intervention) made to **influence** it.

[1] Accumulation of physical and mental disorders throughout life
[2] Social activity according to age (*e.g.* working, retirement age....)

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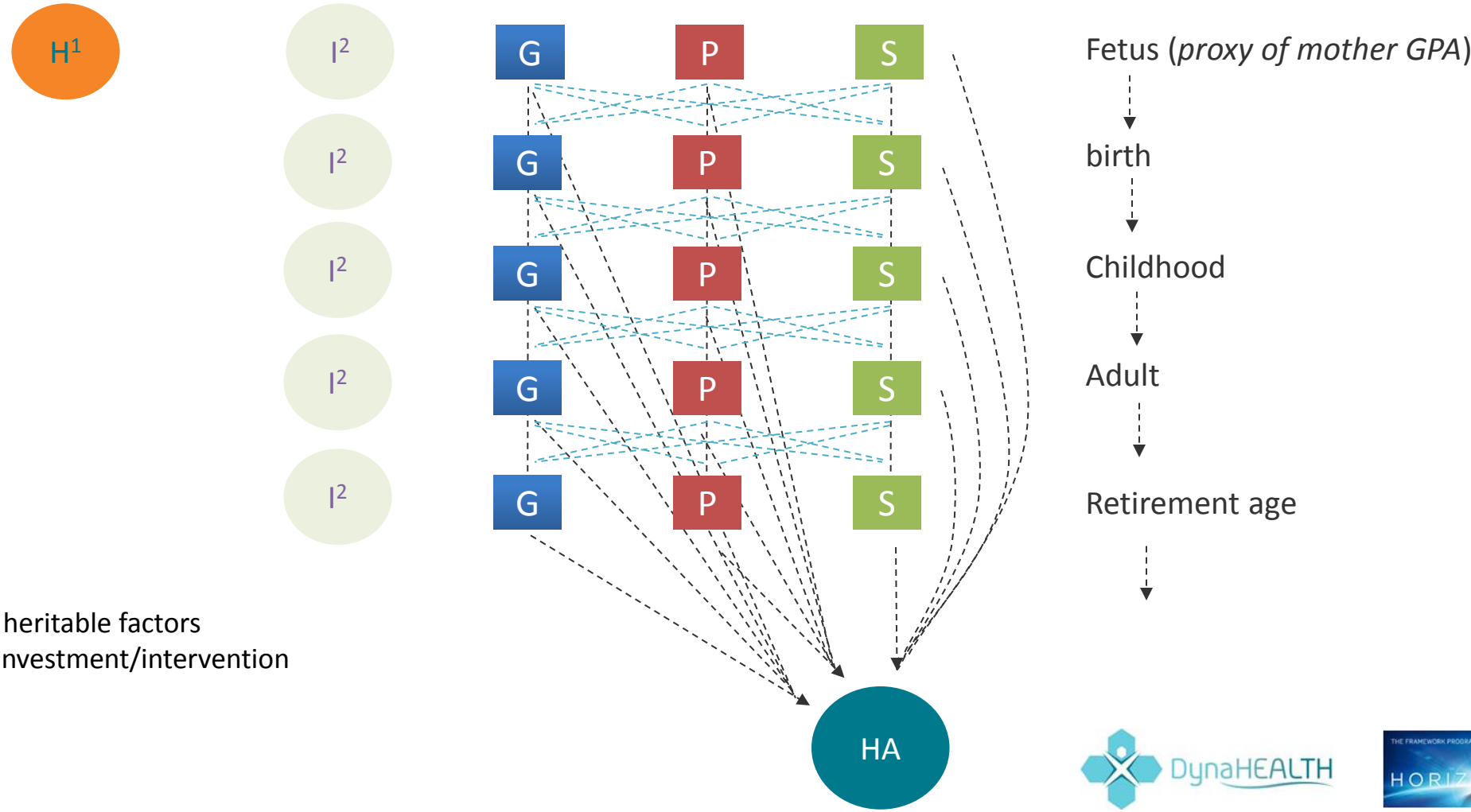
Life-course framework



[1] H= heritable factors
[2] I= Investment/intervention

The model works !

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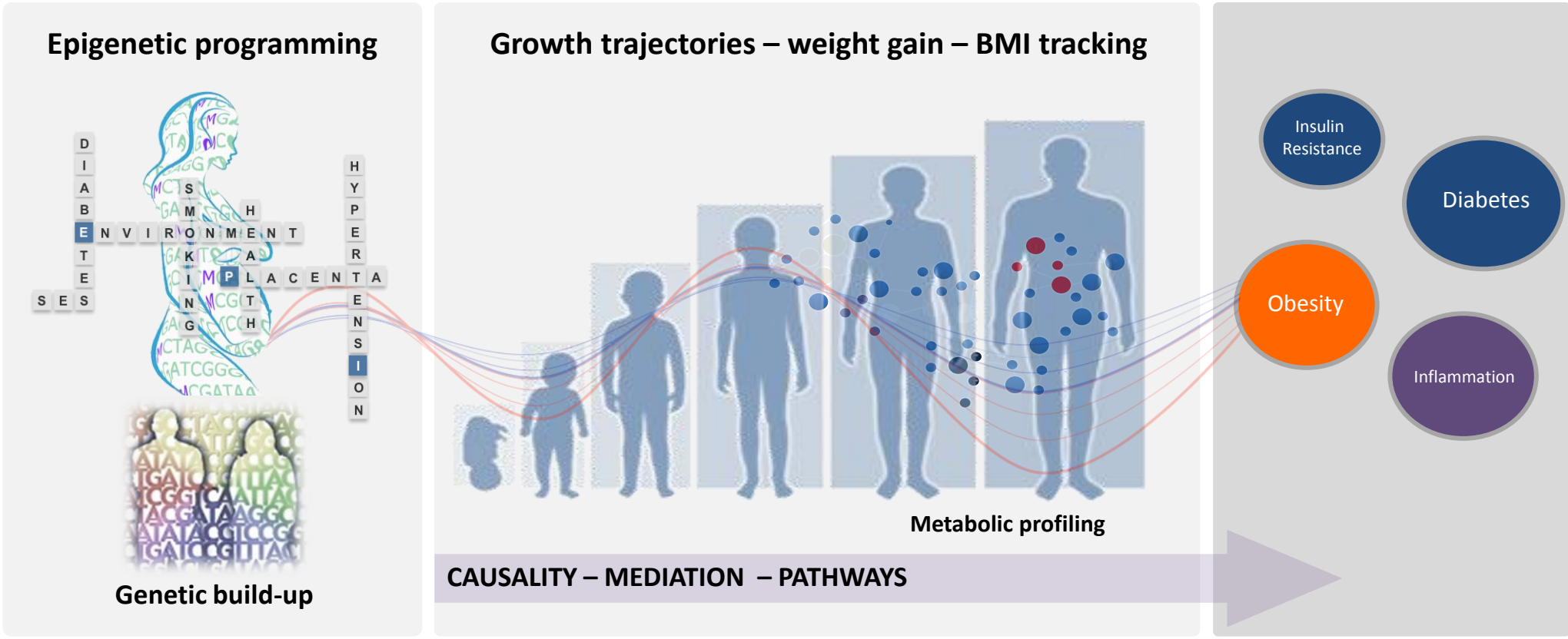
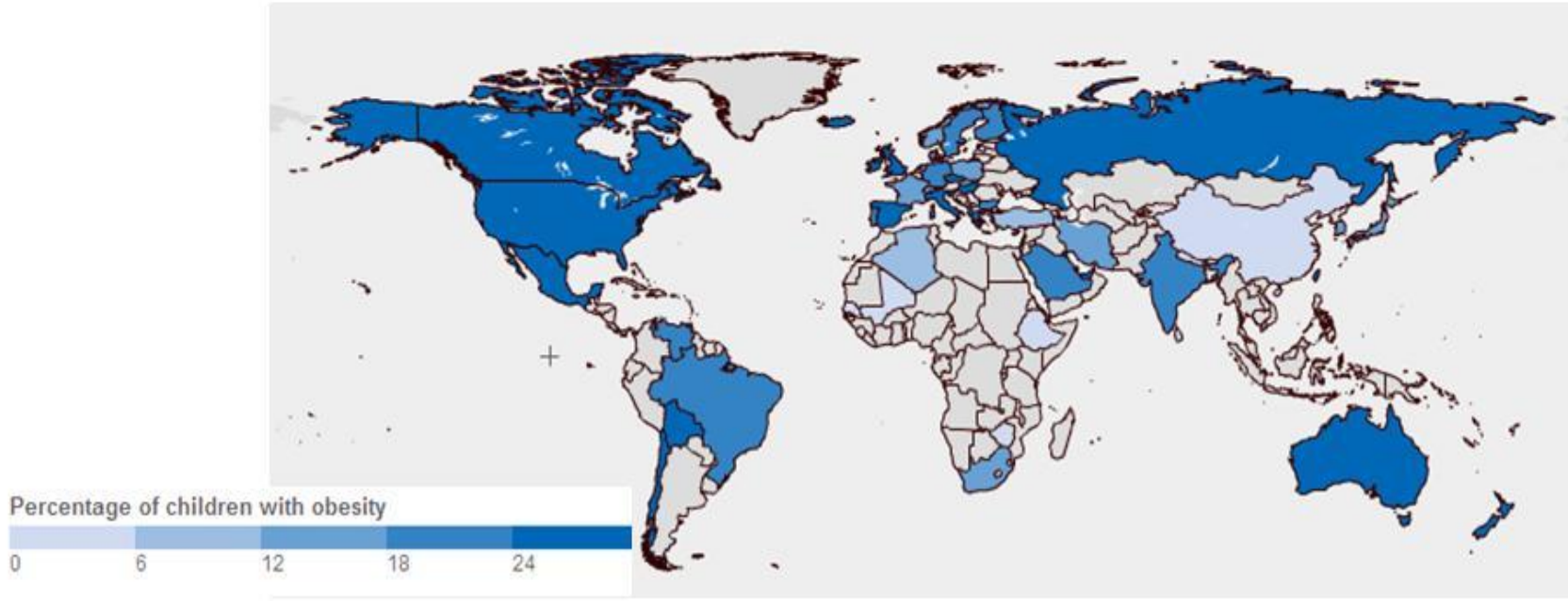
Long path ahead



Why Research on Early Nutrition ⇨ Adiposity?

WHO: overweight & obesity = 5th. leading cause for global deaths

- The growing obesity propels an upsurge of non communicable diseases e.g. diabetes, hypertension and cardiovascular diseases
- Globally, 44% of the diabetes burden, 23% of the ischaemic heart disease burden and between 7% and 41% of certain cancer burdens are attributable to overweight and obesity.



La alimentación precoz programa la salud a largo plazo. Evidencias:

- Riesgo cardiovascular
- Riesgo de alergia e infección
- Enfermedades autoinmunes
  (e.g. diabetes T1, enf. intestinal inflamatoria crónica, enfermedad celíaca,..)
- Función neurológica
- Salud ósea
- Obesidad

Koletzko et al (ed.) Adv Exp Med Biol 2005;569:1-237 & 2009;646:1-196

Interventions to Promote Healthy Eating Habits: Evaluation and Recommendations

I Family is funded by the EC FP7 Project No. 266044 building on

Los primeros 1.000 días

¿Por qué son tan importantes?

Porque en España, ***casi la mitad* de niños y niñas*** *padecen sobrepeso u obesidad*

**4 de cada 10 niños y niñas*

(Según Estudio ALADINO 2015 en niños y niñas de 6 a 9 años)

Por eso, recuerda que en los primeros 1.000 días de tu bebé (embarazo, lactancia y los 2 primeros años):

la alimentación, la actividad física y otros hábitos saludables son claves para el desarrollo neurológico, del sistema inmune y su crecimiento.

270 días

Embarazo

Lleva una alimentación saludable
En el embarazo contribuye al control de tu peso y el de tu bebé.

Come pensando en los 2 ¡pero no comas por 2!

Cuida que la alimentación sea segura durante tu embarazo
Infórmate ¡pincha en la fruta y la ensalada y déjate aconsejar

Realiza una actividad física moderada
Pincha en la zapatilla y mira como se hace:

¡Importante!: no te canses. Debes poder mantener una conversación mientras se realiza la actividad.

Di adiós a los hábitos nocivos

365 días

Primer año de vida

1/6 MESES

6/12 MESES

Lactancia materna exclusiva durante los primeros 6 meses de vida de tu bebé es la mejor prevención. Le aporta las primeras defensas frente a enfermedades infecciosas, reduciendo el riesgo de obesidad y otras enfermedades crónicas en el futuro.

La lactancia materna beneficia a los dos favorece la salud del bebé, creando un vínculo afectivo y disminuyendo el riesgo de diabetes tipo 2, cáncer de ovario y cáncer de mama de la mujer.

Si se utilizan otros alimentos para lactantes y niños de corta edad (siempre por recomendación de los profesionales sanitarios) lee en la etiqueta nutricional el contenido de azúcares, sal y grasas.

El mantenimiento de la lactancia materna es una labor de todos: la familia, los amigos y el entorno laboral.

La Organización Mundial de la Salud (OMS) y otros organismos nacionales e internacionales recomiendan que **los lactantes sean amamantados en exclusiva durante los primeros seis meses y junto con otros alimentos complementarios hasta los dos años de edad o más.**

A partir de los 6 meses de edad, las necesidades nutricionales de un bebé aumentan para facilitar su rápido crecimiento y desarrollo.

Los bebés deben experimentar con una amplia variedad de sabores y alimentos saludables y nutricionalmente adecuados: sigue los consejos de tu pediatra para la introducción de alimentos durante esta etapa.

365 días

Segundo año de vida

Es muy importante que le incorpores a la mesa familiar y al ocio activo.
Porque de forma divertida aprenderá y adquirirá hábitos saludables.
No olvides que lo que aprende hoy le beneficiará mañana y perdurará a lo largo de toda su vida.

En estos 1.000 días, la alimentación de la madre y del bebé (a partir de los 6 meses) **debe ser siempre variada, equilibrada y en cantidades adecuadas:**

Alimentos frescos y de temporada
(frutas, verduras, cereales, legumbres, pescados...)

Alimentos con altos contenidos en sal, azúcares y grasas

¡Consulta el etiquetado nutricional!

Y para la sed: **agua**

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www.earlynutrition.org
www.mynewgut.eu
www.dynahealth.eu

THANK YOU VERY MUCH FOR YOUR ATTENTION!!