FETAL PROGRAMMING

NUMBERS = IMPACT

Maternal overweight and obesity during pregnancy are highly prevalent (~30-50%)

NEW RISK FACTORS = NEW POSSIBILITIES TO PREVENT

- Obesity & type 2 diabetes
- Heart failure & cardiovascular disease
- Cognitive decline & dementia

"a stimulus in utero establishes a permanent response in the fetus that impacts functions later in life"

**no early risk-screening policy
no primary prevention solution
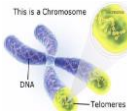no effective therapy**

SPECIFIC TARGETS

Early feeding
Obesity / Diabetes

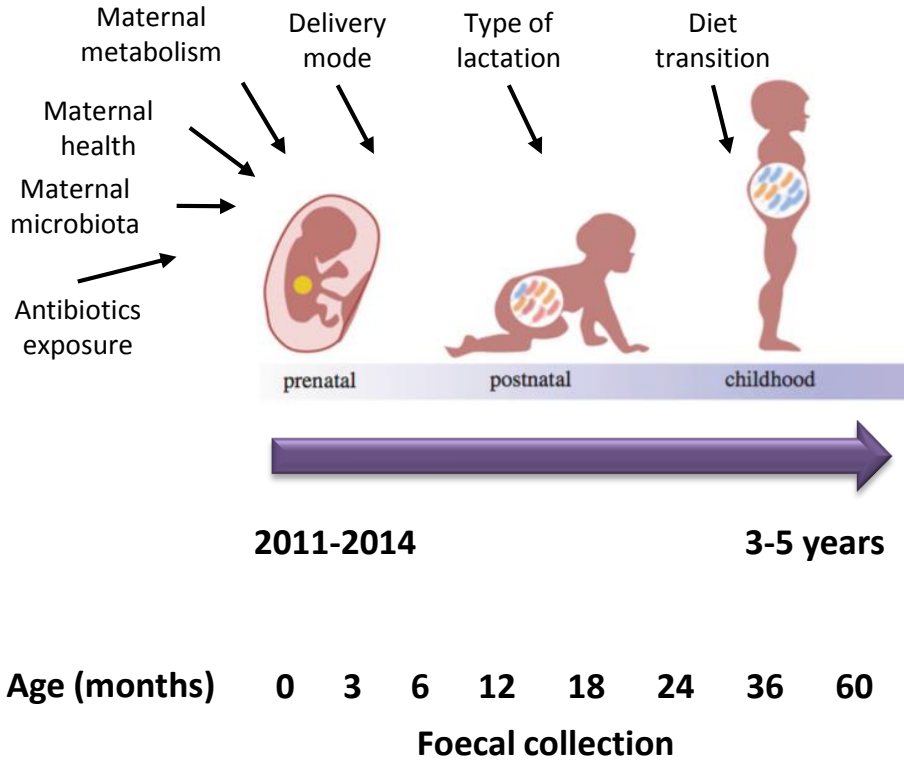**Brain development**
Cognitive dysfunction

Lifecourse & mechanisms

Cell senescence
Telomere length

Cardiac development
Cardiac disease

Maternal metabolism — Delivery mode — Type of lactation — Diet transition

Maternal health

Maternal microbiota

Antibiotics exposure

prenatal — postnatal — childhood

2011-2014 — **3-5 years**

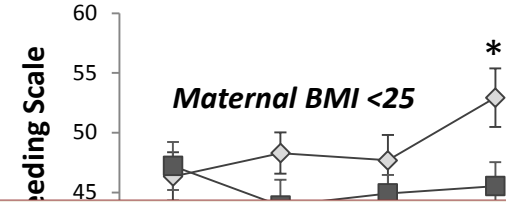**Age (months)** 0 3 6 12 18 24 36 60
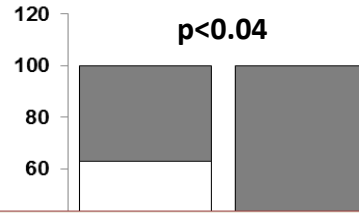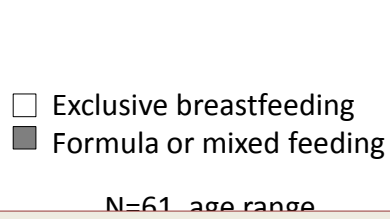
Foecal collection

PISA, ITALY

N=91 Families (children born 2011-2014)

CHARACTERIZATION

- Cord blood (inflammatory, metabolic, hormonal)
- Body growth (weight, height)
- Breastfeeding / formula
- Dietary information (complementary)
- Cardiac development (echocardiography)
- Neurodevelopment (Griffith Mental Scale)
- Eating behaviour (Montreal Children Scale)

Gut colonisation

☐ Exclusive breastfeeding
■ Formula or mixed feeding

N=61, age range

p<0.04

Maternal BMI <25

*

N=57, age 20±1 months
mean±sem

**Late pregnancy BMI: stronger predictor than early pregnancy BMI
of an obesogenic nutrition/behavior**

% Energy intake

r=0.28, p=0.04

Body weight

r=0.33, p=0.01

Maternal BMI (kg/m²)

Sanguinetti et al submitted
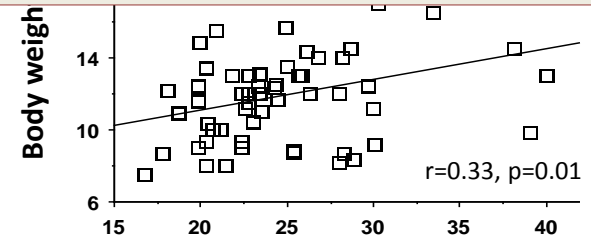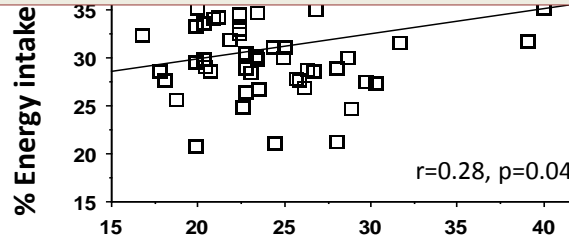
Helsinki Birth Cohort Study (70-80 years)
LED BY JOHAN ERIKSSON (FINLAND)

OBESITY
IN THE OLDER OFFSPRING

An increase in late pregnancy BMI led to

- A proportional increase in BMI and body fat % in the adult offspring
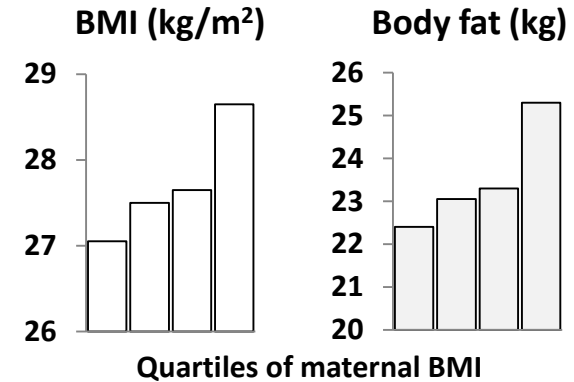
- Increase in diabetes risk, especially in women (10 % for each one BMI unit = 2 kg)

OBESITY & DIABETES

BMI (kg/m²)

29
28
27
26

Body fat (kg)

26
25
24
23
22
21
20

Quartiles of maternal BMI

Eriksson J Ann Med 2014, 2015

Helsinki Birth Cohort Study (70-80 years)
LED BY JOHAN ERIKSSON (FINLAND)

TELOMERES
IN THE OLDER OFFSPRING
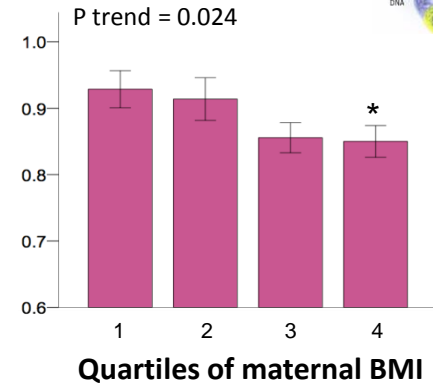
An increase in late pregnancy BMI led to

- Shorter telomeres (biological aging marker) in the adult offspring, especially in women

- Shorter telomeres were expectedly associated with cardiovascular disease and diabetes

HEART DISEASE & DIABETES

P trend = 0.024

Quartiles of maternal BMI

Guzzardi MA et et al Int J Obesity 2016

Eriksson J Ann Med 2014

Heart in the first year

- Thicker, heavier, more dilated, higher contractility

Heart in adults

- Higher contractility, hyperdynamic function

Preclinical models
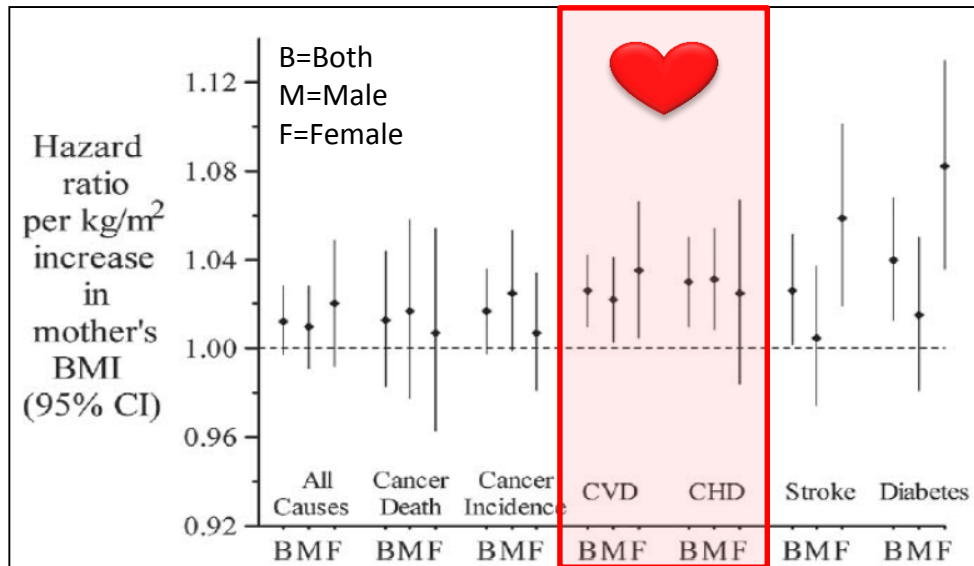
- Congruent data in a longitudinal fashion

- Mechanistic insights on metabolic pathways

(excess glucose exposure, insulin resistance, low glucose oxidation)

Lean mother

Overweight mother
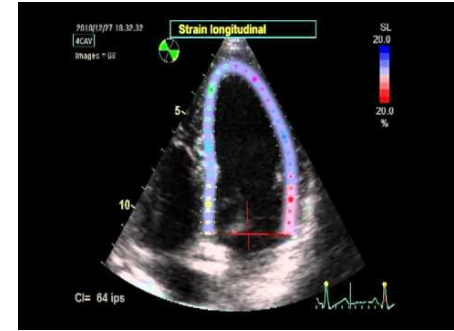
Vulnerability to ischemic damage & heart failure
Late pregnancy BMI: stronger predictor than early pregnancy BMI

Guzzardi et al J Am Coll Cardiol – Cardiovasc Imaging, in press

6 months   **36 months**   **60 months**

Maternal BMI

110

uotient

100

*

110

easoning

100

*

*
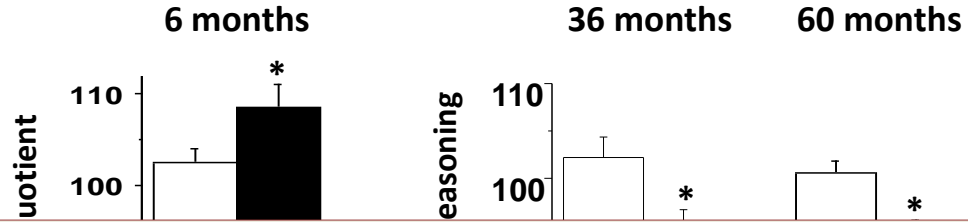
Animal data confirm cognition is high at weaning and low in adults
It goes with brain metabolism and insulin action (high vs low)

Insulin regulates cell growth, appetite, glucose metabolism

- word list task
- copying figure task
- delayed memory task

z = 63   z = 51   z = 39

z = 27   z = 15   z = 3

z = -9   z = -21   z = -33

REDUCED WHITE MATTER DENSITY

Bucci et al submitted

Resistance training exercise intervention
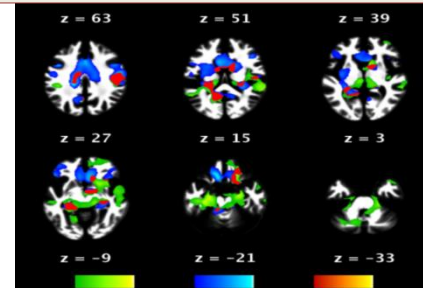
Aging Clin Exp Res (in press). Dynamic changes in p66Shc mRNA expression in peripheral blood mononuclear cells following resistance training intervention in old frail women born to obese mothers: a pilot study

Exercise training effective but should not be discontinued

Reduced white matter density / Cognition pattern

J Appl Physiol 2016. Resistance training enhances insulin suppression of endogenous glucose production in elderly women.

Diabetologia 2016. Resistance training improves skeletal muscle insulin sensitivity in elderly offspring of overweight and obese mothers.

Turku PET Centre
University of Turku, Finland
LED BY PIRJO NUUTILA

Maternal metabolism

Delivery mode

Type of lactation

Diet transition

Maternal
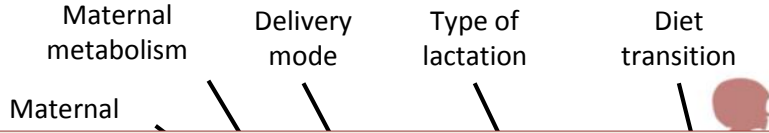
GUT BACTERIA INFLUENCE

- **BEHAVIOUR**

The profile of gut bacteria is different in children with a lean or obese mother & correlates with cardiac size, or with cognition

2011-2014

3-5 years

Age (months)   0   3   6   12   18   24   36   60

Foecal collection

Gut colonisation & development

NOW WE KNOW THAT MATERNAL OVERWEIGHT

ESPECIALLY IN LATE PREGNANCY
- IMPACTS early nutrition, eating behaviour, cardiac development, cognitive development,
- PREDICTS obesity, diabetes, cardiovascular disease, cognitive decline, **death / shorter life**
- MECHANISMS include insulin resistance, oxidative stress, telomere shortening, gut dysbiosis
- EFFECTS are reversible by exercise training in older people

MORE RESEARCH NEEDED IN PRIMARY PREVENTION

Does reversal of maternal obesity reverse consequences?

- Reduce calories? Change composition?
- From before conception? Very difficult
- Mainly in the last trimester? Easier

Is the gut microbiota a promising target for both mother & offspring?

- Existing probiotics do not correct the dysbiosis
- Dysbiosis not the same for e.g. brain and heart
- Personalized microbiota-based prevention

Prove efficacy & effectiveness, time-window need for personalized strategies

Where would you see further needs for policy support? Research is lost in translation, more face-to-face interaction

Developmental ORIgins of healthy and unhealthy AgeiNg
The role of maternal obesity

Members in DORIAN

- Consiglio Nazionale delle Ricerche - Institute of Clinical Physiology *(Italy)*
- Samfundet Folkhälsan i svenska Finland r.f., Helsinki *(Finland)*
- Turun Yliopisto *(Finland)*
- The University of Edinburgh *(United Kingdom)*
- Istituto Superiore di Sanità *(Italy)*
- Max-Planck-Gesellschaft zur Förderung der Wissenschaften e.V. *(Germany)*
- BIOMOL-INFORMATICS SL *(Spain)*
- The European Association for the Study of Obesity *(United Kingdom)*
- Mouvement Mondial des Mères Europe *(Belgium)*
- GABO:milliarium mbH & Co. KG *(Germany)*

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European Foundation for the Study of Diabetes
EFSD
The Research Foundation of the
European Association for the Study of Diabetes