My New Gut:

Insulin Resistance - Linking Modulation of the Gut Microbiome to Dietary Recommendations and Health Claims

to tackle obesity

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MyNewGut

- EU FP7 program project
- Microbiome Influence on Energy balance and Brain Development-Function Put into Action to Tackle Diet-related Diseases and Behavior
- Collaborative Project (large-scale integrating project – 30 partners – 5 non-EU)

MyNewGut - Objectives

- What is the role of the microbiome in the absorption and metabolism of specific macronutrients and energy expenditure?
- What is the role of the dynamic interplay between the gut microbiome and the composite lifestyle and host factors leading to obesity and metabolic disorders during critical stages of life?
- How is it possible to modulate the influence of the gut microbiome in early stages of development to prevent brain-related and metabolic disorders in later stages of life?

MyNewGut - Objectives

- Is it possible to reduce the risk and consequences of metabolic and brain-related disorders via dietary intervention targeting the gut microbiome?

- **MyNewGut** aims to provide proof-of-concept of the possibility of reducing the risk and consequences of metabolic and brain-related disorders via intervention in the gut ecosystem with specific diets and innovative food ingredients and prototypes.

Objectives

- Hypothesis:

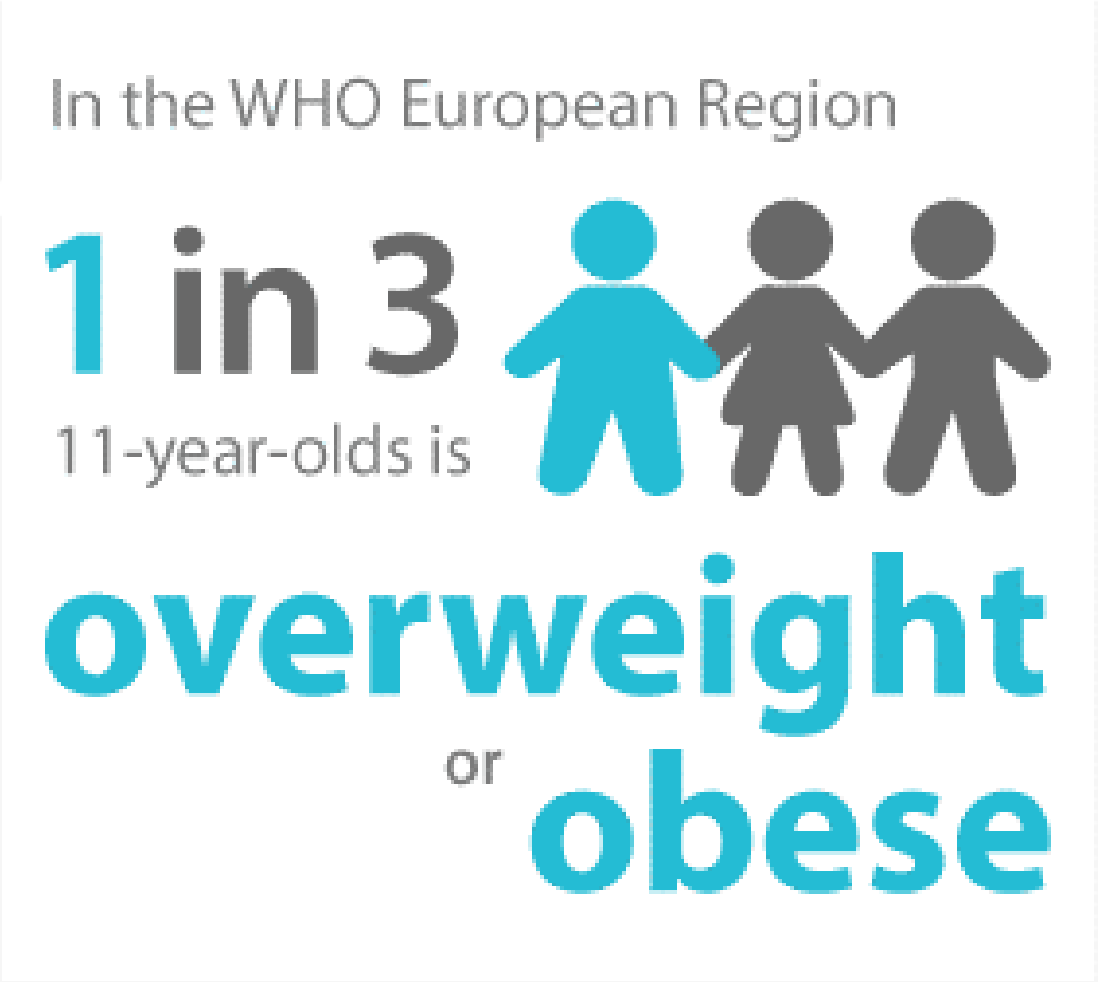
Developing microbiome-based dietary recommendations and interventions targeting the gut ecosystem can provide cost-effective measures to reduce the socioeconomic burden of diet-related diseases and, in particular, obesity and chronic-metabolic and behavioral disorders.

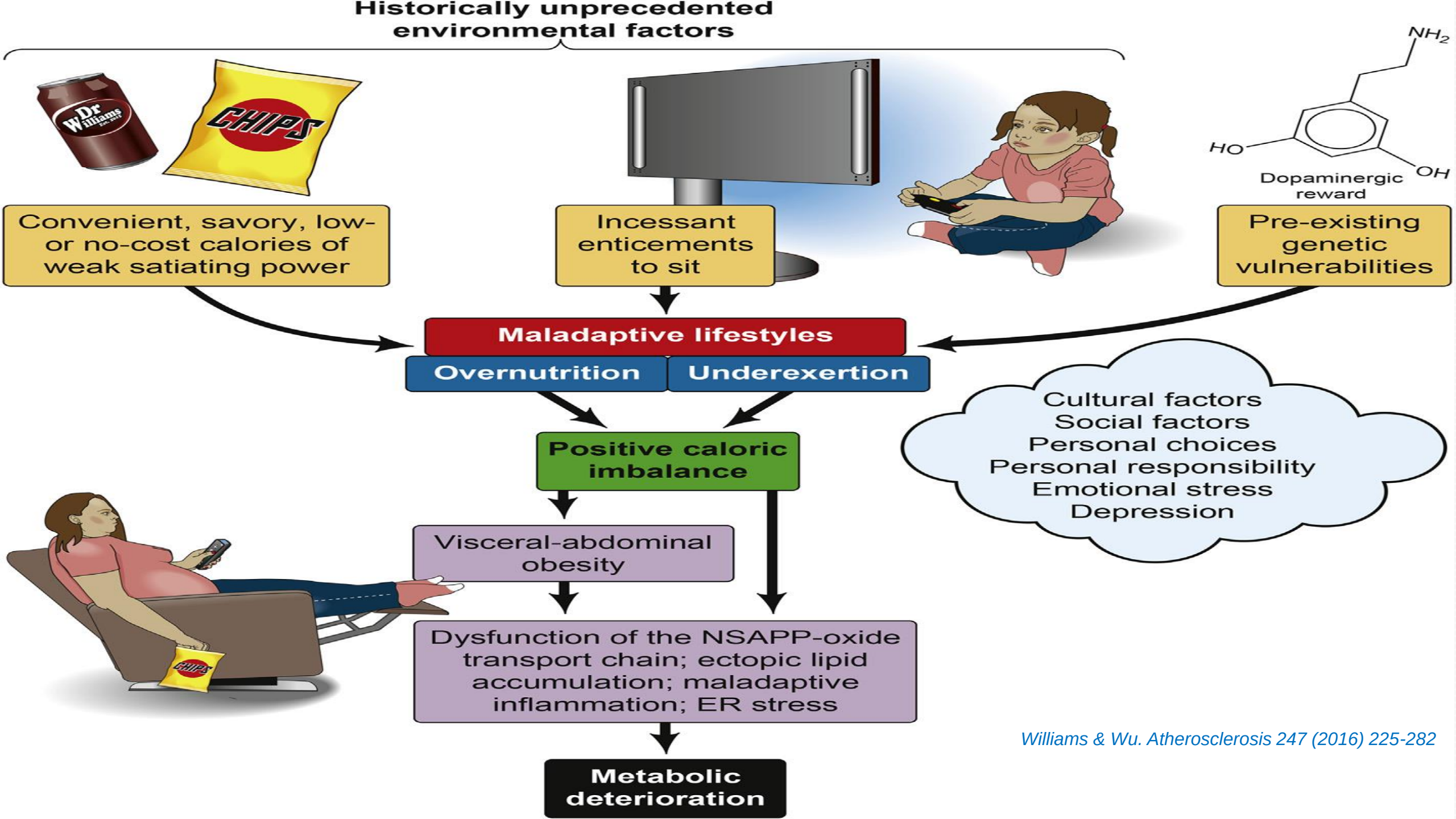
Human studies will be the focus of the project

- Translation of the accumulated knowledge into: guidance for microbiome related health claims
- recommendations and policies to improve the EU position in prevention of diet and brain-related disorders.

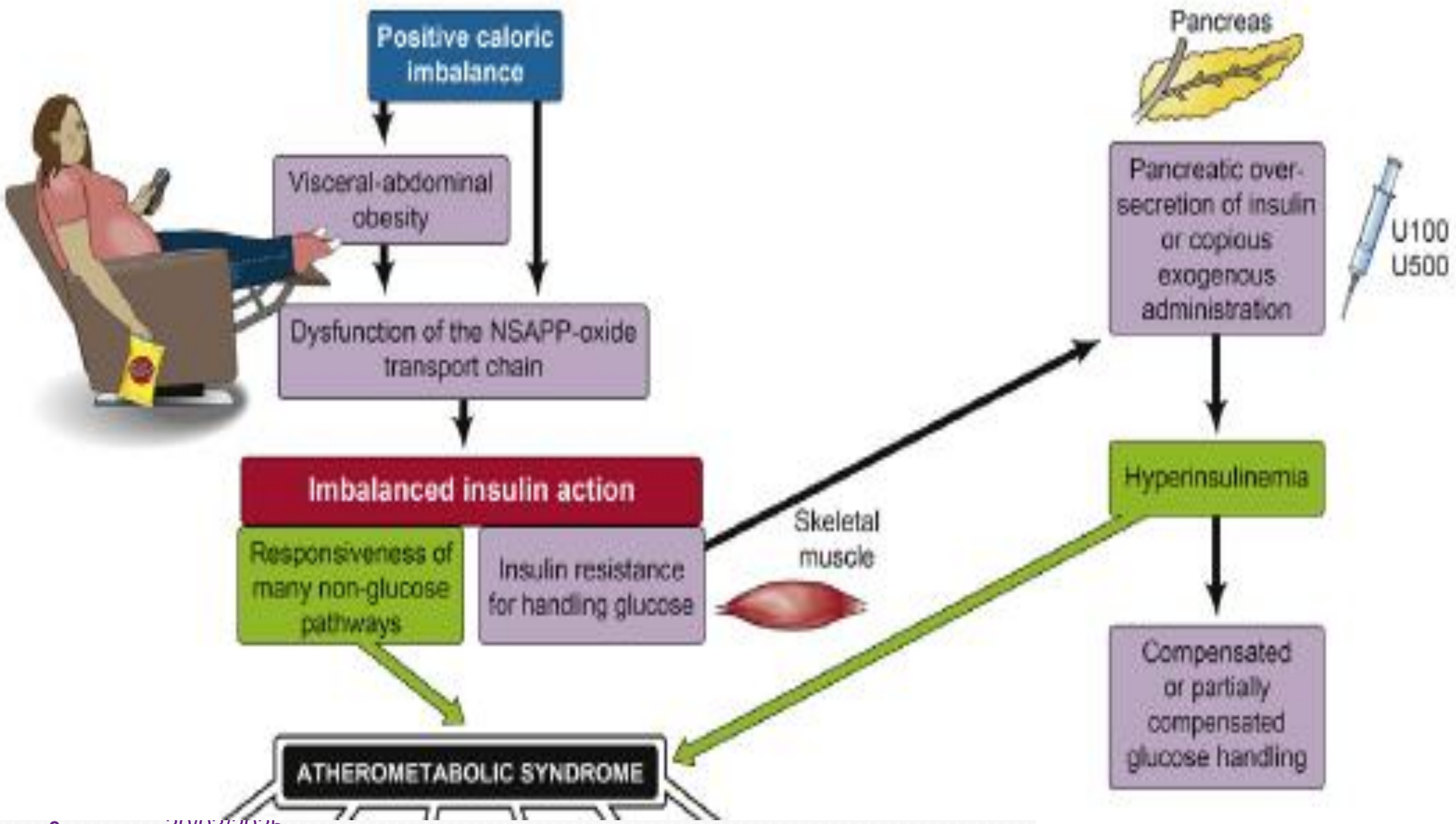
Prevalence Obesity Adults EU

Prevalence Obesity Children EU





Williams & Wu. Atherosclerosis 247 (2016) 225-282



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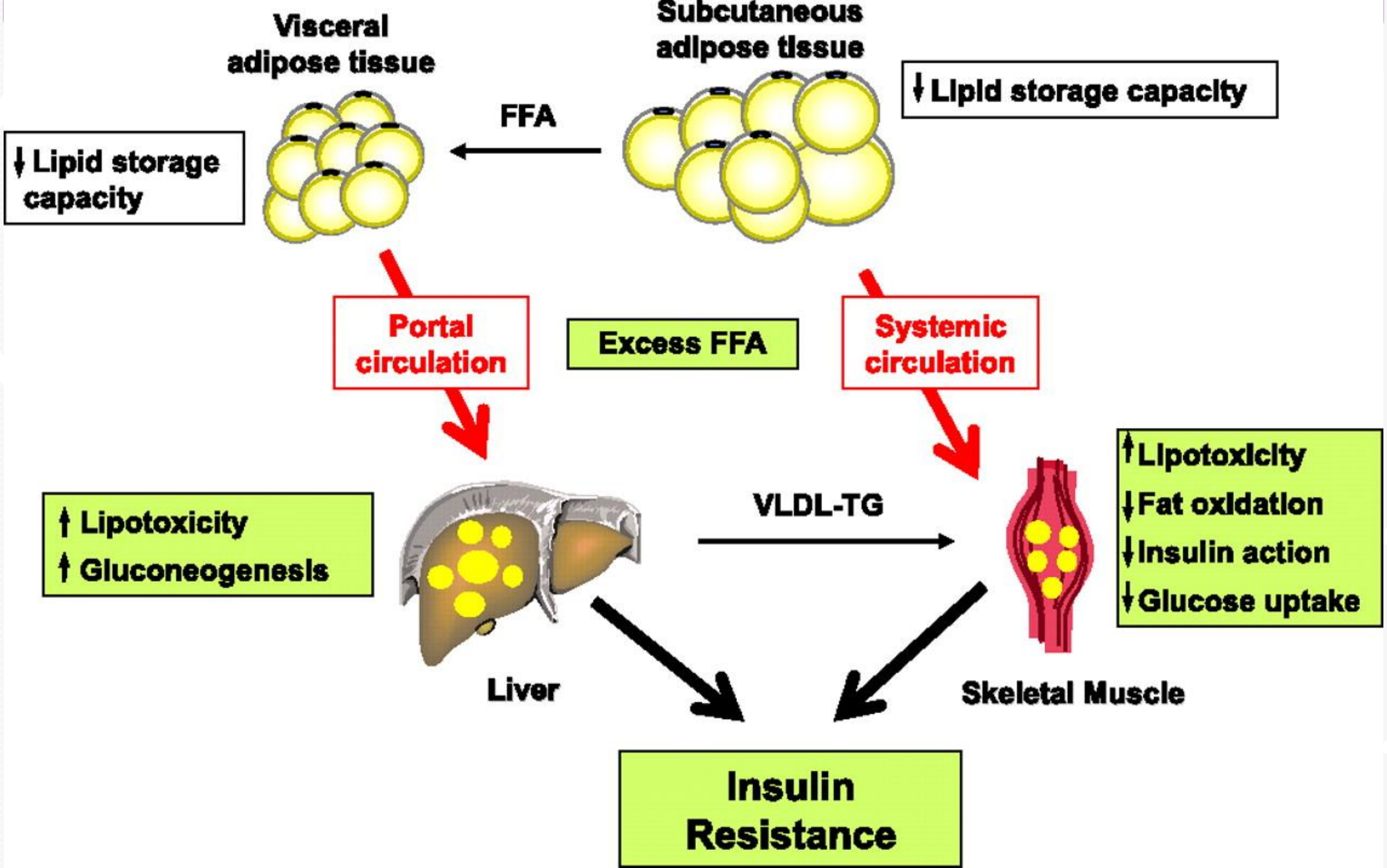

Visceral adipose tissue
Subcutaneous adipose tissue
↓ Lipid storage capacity
FFA
↓ Lipid storage capacity
Portal circulation
Excess FFA
Systemic circulation
↑ Lipotoxicity
↑ Gluconeogenesis
VLDL-TG
↑ Lipotoxicity
↓ Fat oxidation
↓ Insulin action
↓ Glucose uptake
Liver
Skeletal Muscle
Insulin Resistance

The Metabolic Syndrome Associated With Insulin Resistance

Adapted from ADA. *Diabetes Care*. 1998;21:310-314.
Pradhan et al. *JAMA*. 2001;286:327-334.

Microbiota & Obesity

Novel research shows that the gut microbiota is involved in obesity and metabolic disorders

Obese animal and human subjects have alterations in the composition of the gut microbiota compared to their lean counterparts.

Gut microbiota and its influence on obesity

Animal studies:

Perturbations in the composition of gut microbiota associated with genetic or diet-induced obesity seem to be reversible:

- by oral transfer of the gut microbiota from lean or obese mice to a germ-free recipient (Turnbaugh et al. (2008). Cell Host Microbe 17, 213–223; Turnbaugh et al. (2006) Nature 444, 1027–1031). or
- by the administration of prebiotic substrates to animal models at least over short-term periods (Cani et al. (2009) Current Pharmaceutical Design. 15: 1547-1559).

Gut microbiota and its influence on obesity

Human study:

Fecal transfer improves insulin sensitivity in adults with features of metabolic syndrome (Vrieze et al., 2012),

Application as a therapy for other conditions, including obesity, is still experimental.

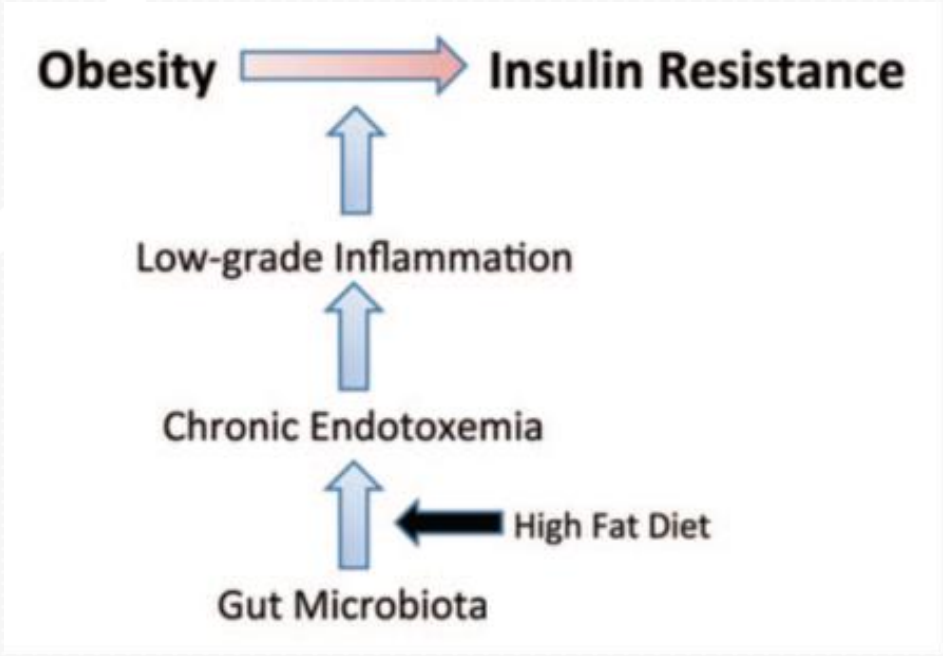
Source: Parekh et al. 2015

Microbiota and health claims
Regulatory issues

EFSA Health claim: primary requirements:

- Claimed effect beneficial to human health (physiologically beneficial effect)?
- Food constituent sufficiently described?
- Cause and effect relationship established?

Obesity & Insulin Resistance



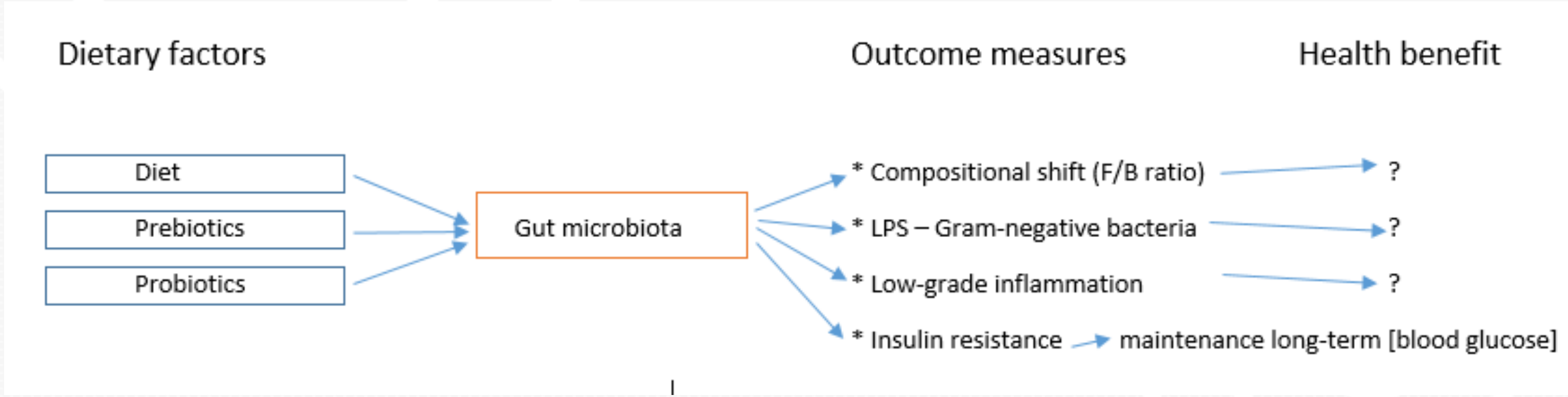
Source: Kemp. Adipocyte 2013, 2:3, 188–190

Nutritional view on Insulin Resistance

Being insensitive to insulin is positively correlated with fat intake, and negatively correlated with dietary fiber intake, and both these factors are also correlated with excess body weight.

Importance of diet !

Claimed effect - Health benefit



Insulin resistance - EFSA-acknowledged health benefit

Claims on (long-term) blood glucose control

Improved blood glucose control is a beneficial physiological effect for subjects with impaired blood glucose tolerance.

HbA1C - EFSA-acknowledged measure of insulin resistance

Claims on (long-term) blood glucose control

Appropriate outcomes for the scientific substantiation of such claims include glycated hemoglobin (HbA1c) measured in intervention studies of appropriate duration (e.g. at least three months).

EFSA-acknowledged supportive measures of insulin resistance

Claims on (long-term) blood glucose control

Measurement of the area under the curve of plasma glucose concentrations after a standard oral glucose tolerance test (OGTT) is considered as supportive.

Take home

Obesity-related, microbiota-targeted research wouldn’t have existed if we, the humans, would have complied to universally agreed dietary recommendations!!


Thank you!
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