The Impact of Processed Food on Cardiovascular Health

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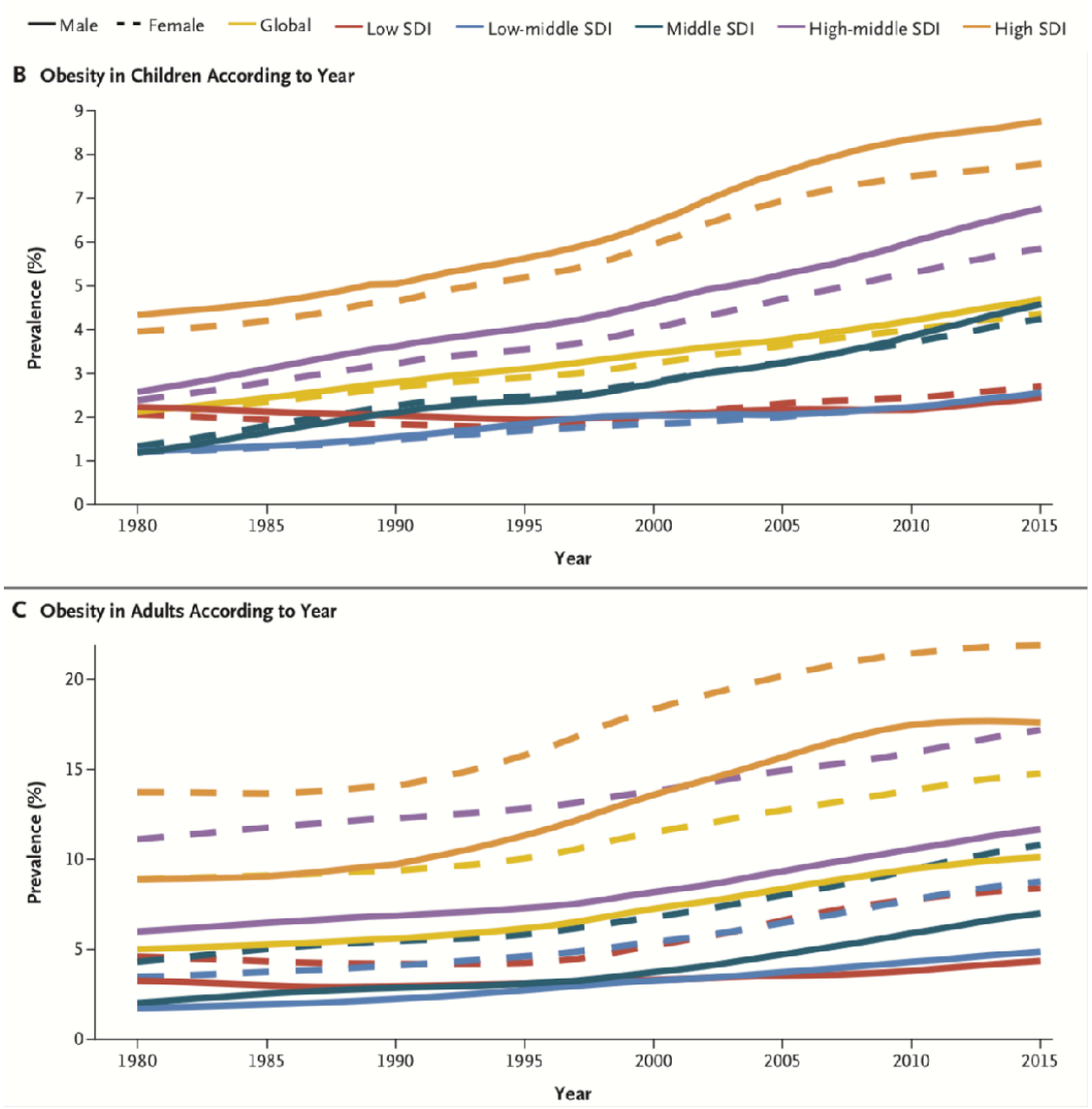
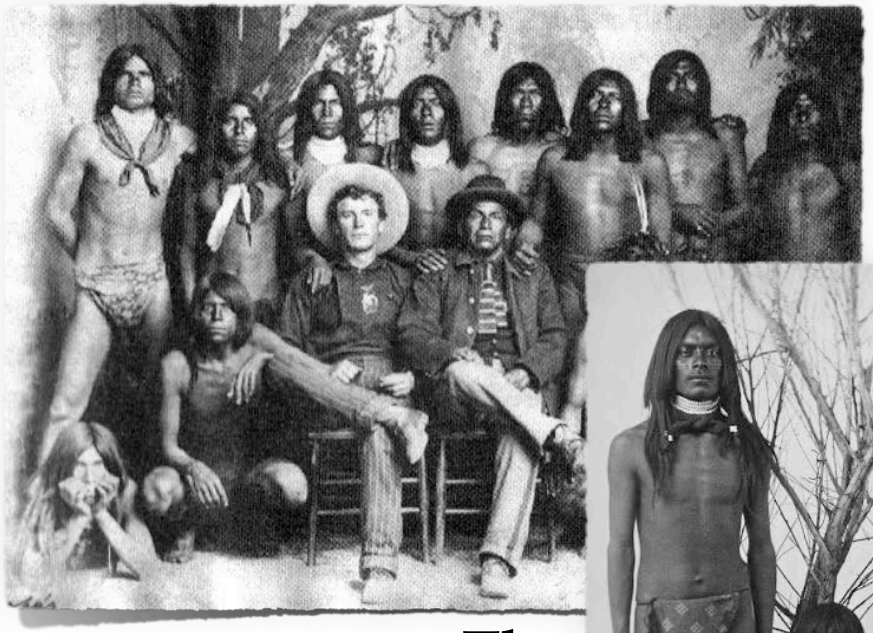
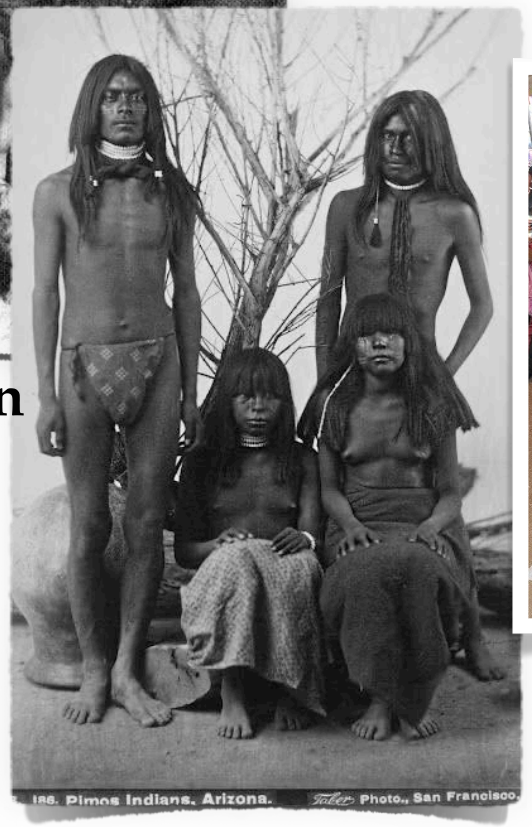
The Obesity Problem



The GBD 2015 Obesity Collaborators. New Engl J Med 2017

The Pima Indians (Arizona)





Then

Now

Diabetes in Pima Indians (Arizona)

son-years. The age- and sex-specific inci-

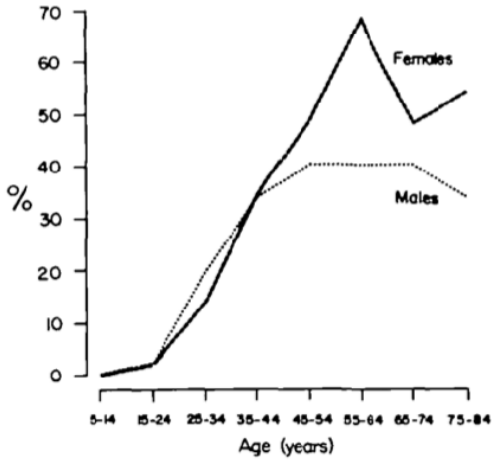


FIGURE 1. Prevalence of diabetes in the Pima Indians, ages 5–84.

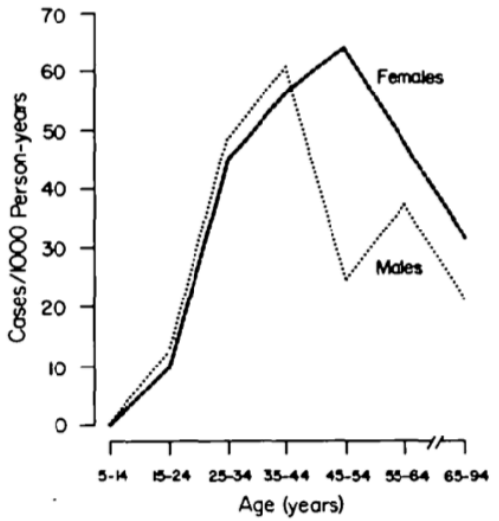


FIGURE 2. Incidence of diabetes in the Pima Indians, ages 5–94.

TABLE 2

Age-sex standardized prevalence and incidence (± 1 standard error) of diabetes and summary ratios (Pima/Rochester) with 95% confidence intervals. Standardized to the US white population, 1970 Census.

	Pima	Rochester*	Summary ratios (95% confidence interval)
Prevalence (%)			
Males	18.9 ± 1.0	1.84 ± 0.10	
Females	22.9 ± 1.0	1.43 ± 0.07	
Both	21.1 ± 0.7	1.62 ± 0.06	12.7 (11.5, 14.0)
Incidence (cases/1000 person-years)			
Males	23.6 ± 2.6	1.58 ± 0.07	
Females	29.0 ± 2.7	1.13 ± 0.05	
Both	26.5 ± 1.9	1.34 ± 0.04	18.7 (16.0, 21.8)

* Calculated from data provided by Dr. P. J. Palumbo of the Mayo Clinic, Rochester, MN.

Knowler et al. Am J Epidemiol 1978


Healthy Eating
Be mindful
EAT
... (only) when you're hungry.
... real food (no added sugar!).
... more slowly and enjoy.
DON'T
... snack.
... think too much about food.
Weight Loss (is hard...)
Cut added sugars cold turkey
Exercise for 5 hours per week
Portion control
(Intermittent) fasting

It's not exercise and diets typically don't work

The number to treat for classic diets to prevent diabetes is 25.

Haw et al. JAMA Intern Med 2017

"This study did not support that physical inactivity as reported in the freely living adult population in the long term is associated with the development of obesity, but the study indicates that obesity may lead to physical inactivity."

Petersen et al. Int J Obesity 2005

"[The studies] are uncertain in their conclusions about whether increasing activity will be effective in preventing obesity."

Wareham et al. Proc Nutr Soc 2005

Obesity and metabolic syndrome

- 80% of obese people have metabolic syndrome, but 20% don't.
- 40% of normal weight people have metabolic syndrome.
- Insulin resistance predicts diabetes and is a cause of obesity.
- Ectopic fat, a consequence of insulin resistance, triggers further metabolic abnormalities, including insulin resistance.
- The main problem is not the weight, but associated metabolic disease.

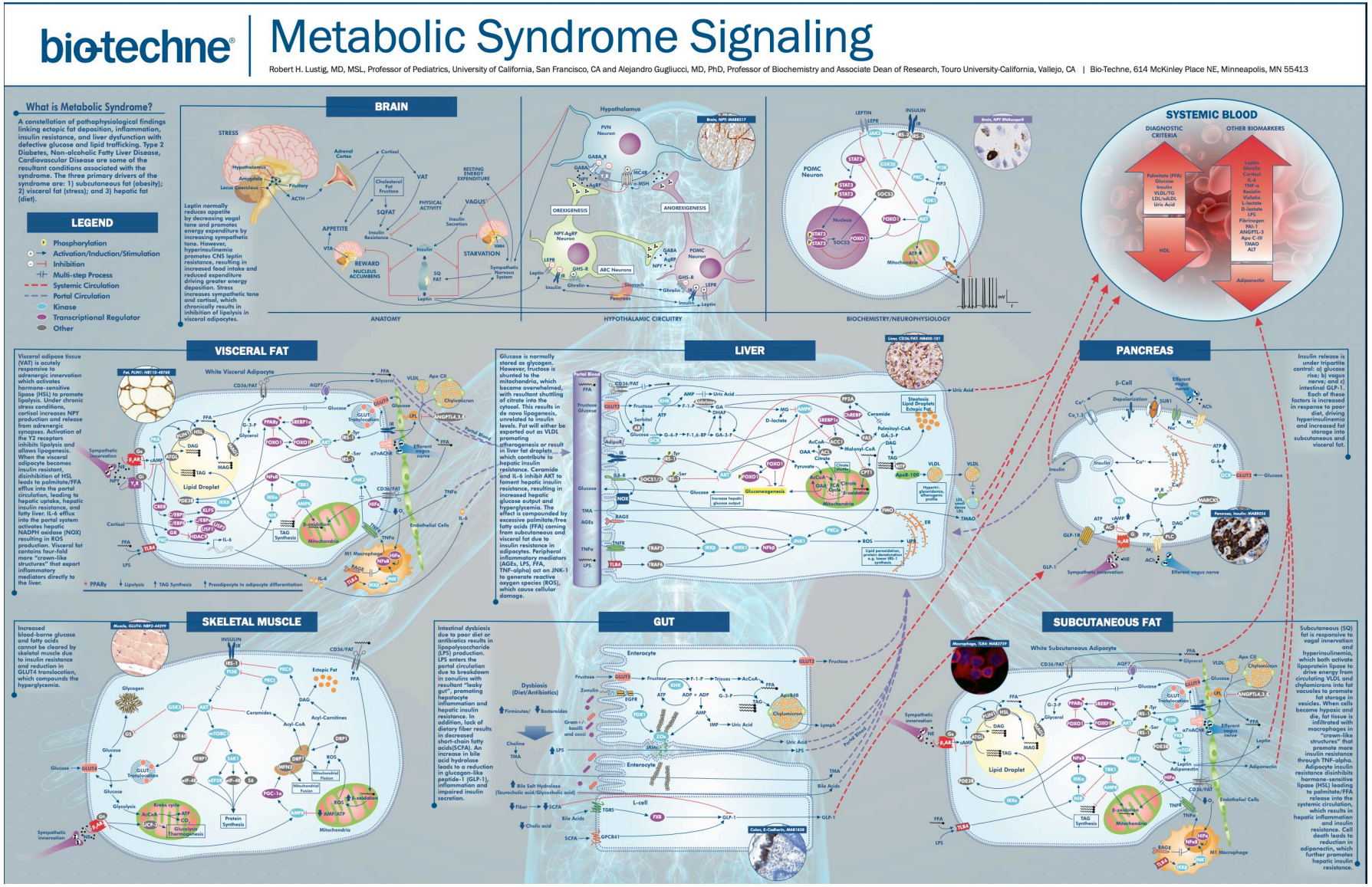
Metabolic Syndrome

At least 3 of the following criteria:

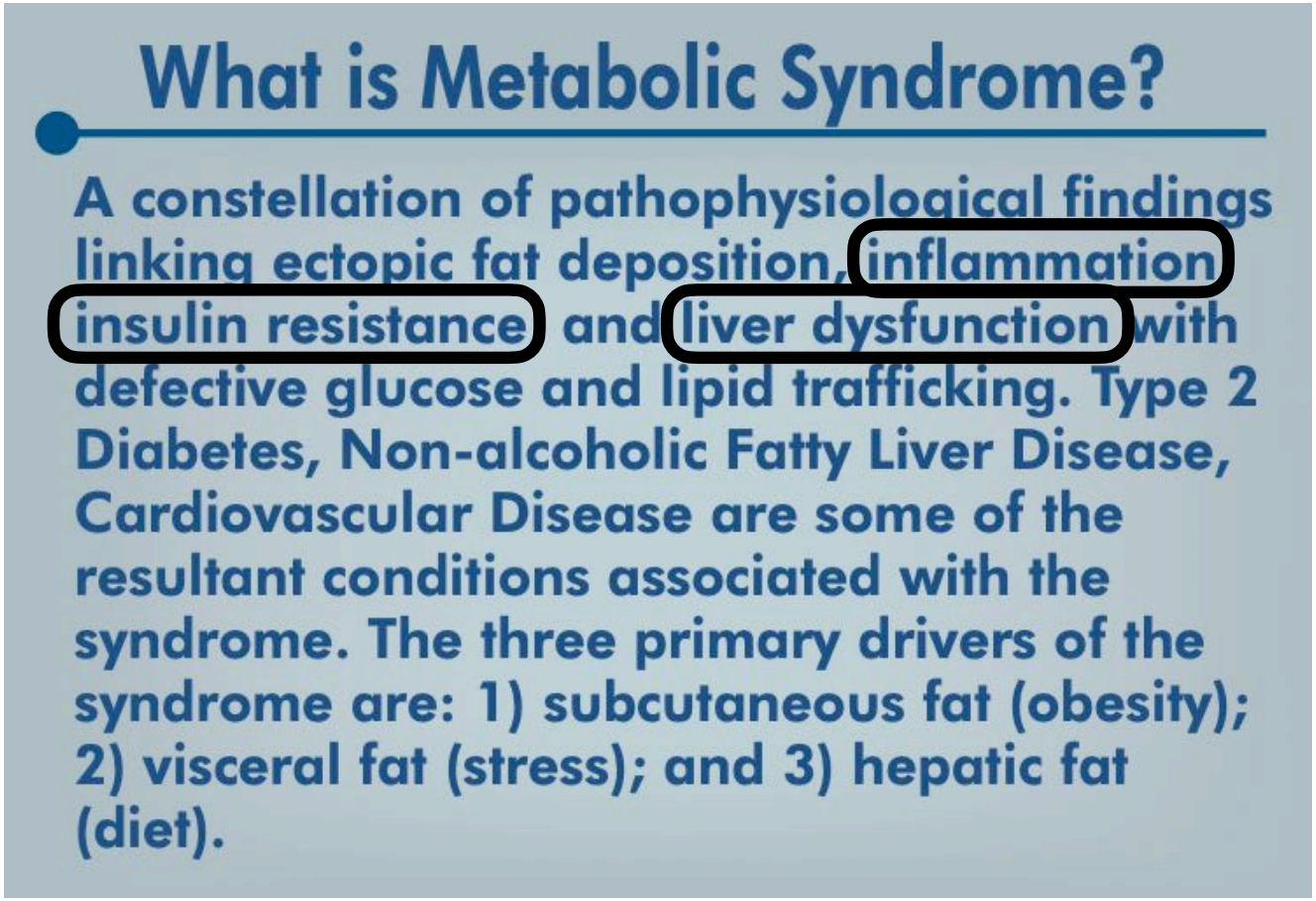
- A **waistline** of 40 inches or more for men and 35 inches or more for women (measured across the belly)
- A **blood pressure** of 130/85 mm Hg or higher or are taking **blood pressure medications**
- A **triglyceride** level above 150 mg/dl
- A fasting **blood glucose** level greater than 100 mg/dl or are taking glucose-lowering medications
- A **high density lipoprotein level** (HDL) less than 40 mg/dl (men) or under 50 mg/dl (women)

https://my.clevelandclinic.org/health/diseases/10783-metabolic-syndrome

The Metabolic Side of Metabolic Syndrome



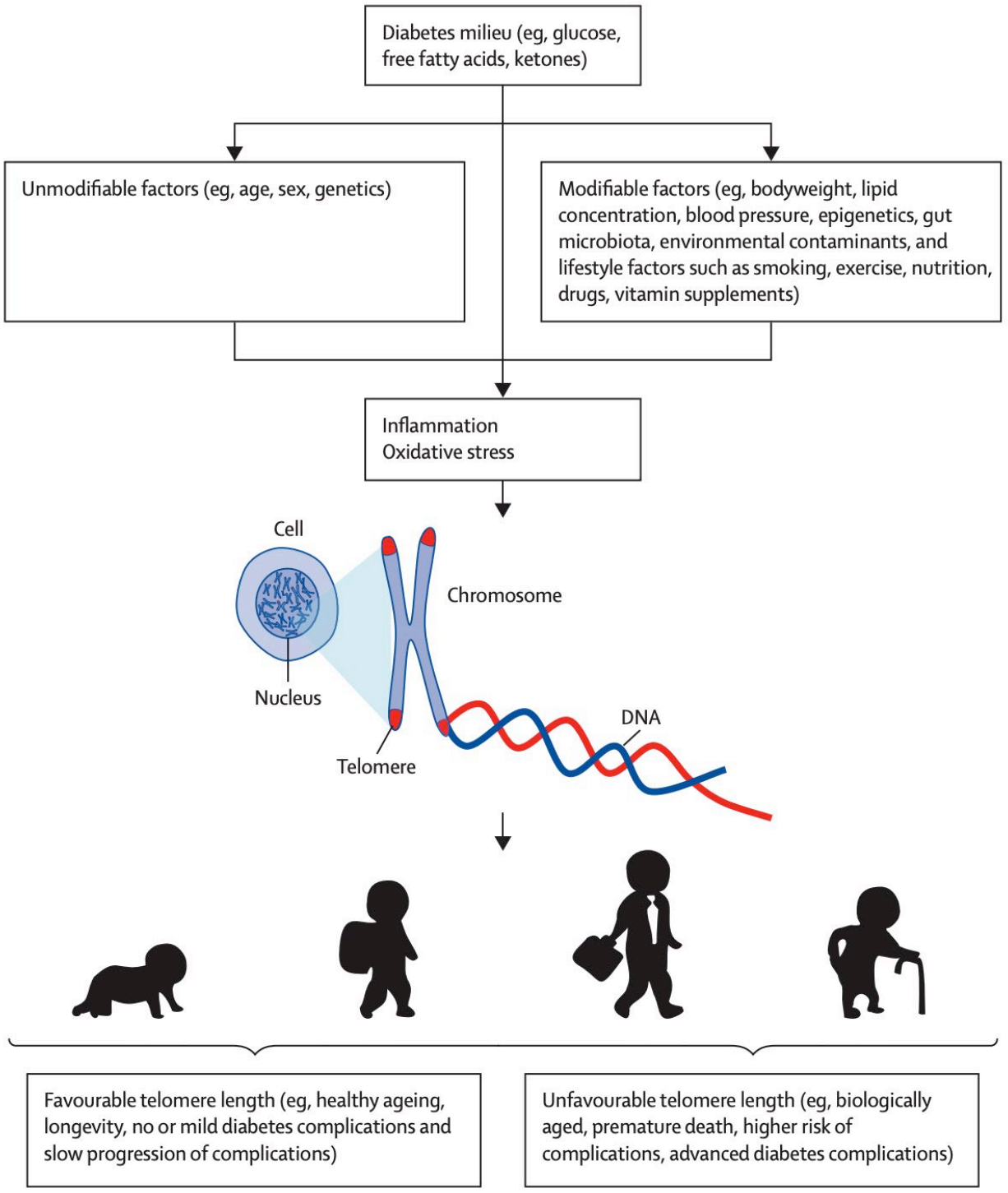
Metabolic Syndrome



Lustig R and Gugliucci A, 2021

Metabolic syndrome and ageing:

Metabolic disease shortens telomeres, and thereby lifespan



Cheng et al.
Lancet Diab Endocrinol 2021

What is processed food?

United States Department of Agriculture (USDA):

"Any raw agricultural commodity that has been subject to washing, cleaning, milling, cutting, chopping, heating, pasteurizing, blanching, cooking, canning, freezing, drying, dehydrating, mixing, packaging or other procedures that alter the food from its natural state.

This may include the addition of other ingredients to the food, such as preservatives, flavors, nutrients, and other food additives or substances approved for use in food products, such as salt, sugars, and fats."

Why do we have processed food?

Food processing for better taste or increasing shelf life

- Fermenting (likely ok)
- Freezing (mostly ok)
- Drying (vitamins and other nutrients may be lost)
- Removing perishable components (e.g. bran and with it important fibres)
- Blending (non-soluble fibres lose their macromolecular structure)
- Heating (extra virgin olive oil turns into transfers at 160°C; BBQ -> carcinogenic molecules)
- Adding salt/sugar (not healthy in added amounts)
- Adding emulsifiers, colorants, preservatives or alike (mostly not ok)

What is ultra-processed food?

NOVA Classification

Group 1: Unprocessed, or minimally processed, foods

Defined as: “edible parts of plants (seeds, fruits, leaves, stems, roots) or of animals (muscle, offal, eggs, milk), and also fungi, algae, and water, after separation from nature.”

Group 2: Processed culinary ingredients

Defined as: “oils, butter, sugar, and salt, are substances derived from Group 1 foods or from nature by processes that include pressing, refining, grinding, milling, and drying.”

Group 3: Processed foods

Defined as: “Processed foods, such as bottled vegetables, canned fish, fruits in syrup, cheeses, and freshly made breads, are made essentially by adding salt, oil, sugar, or other substances from Group 2 to Group 1 foods.”

Group 4: Ultra-processed foods

Defined as: “Ultra-processed foods, such as soft drinks, sweet or savory packaged snacks, reconstituted meat products, and pre-prepared frozen dishes, are not modified foods but formulations made mostly or entirely from substances derived from foods and additives, with little if any intact Group 1 food.”

Monteiro et al.
World Nutr 2016

What is ultra-processed food?

Food or food-like products altered by:

- Pesticides for maximizing harvest yield
- Industrial meat production (corn-fed cattle)
- Additives for reducing production cost
- Alterations/preservatives for long shelf life
- Added salt, sugar, sweeteners, emulsifiers, etc for palatability and texture
- (Environmental toxins such as heavy metals or pesticides)

Foods that have been processed to such a degree that there is a significant nutrient loss and/or a significant addition of unhealthy ingredients (mainly in the form of added sugars, oils, or salt).

What is ultra-processed food?

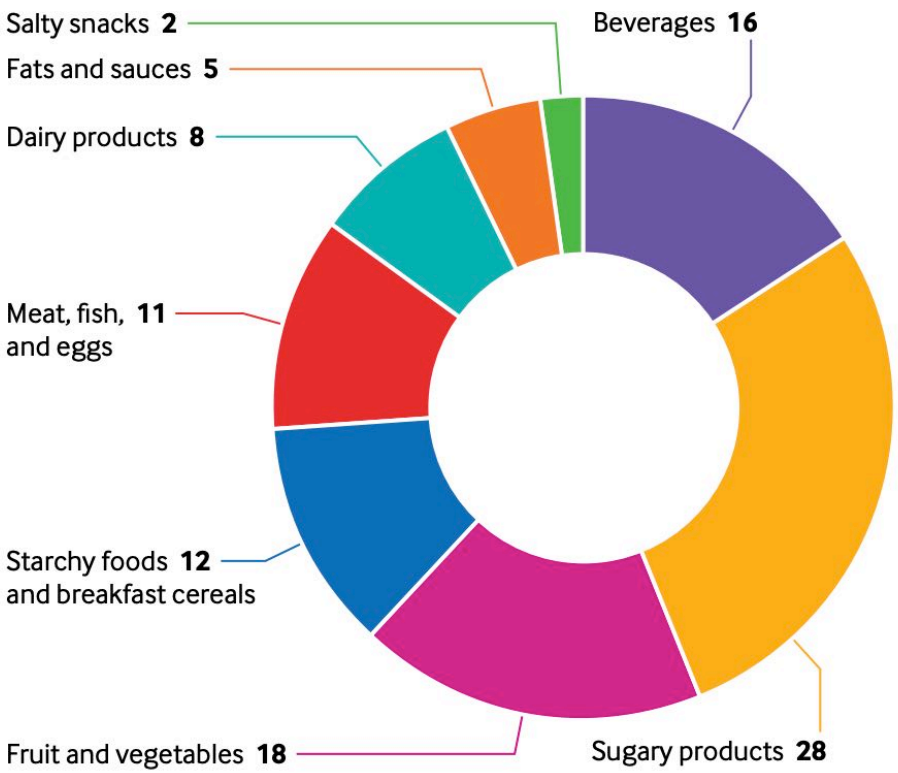
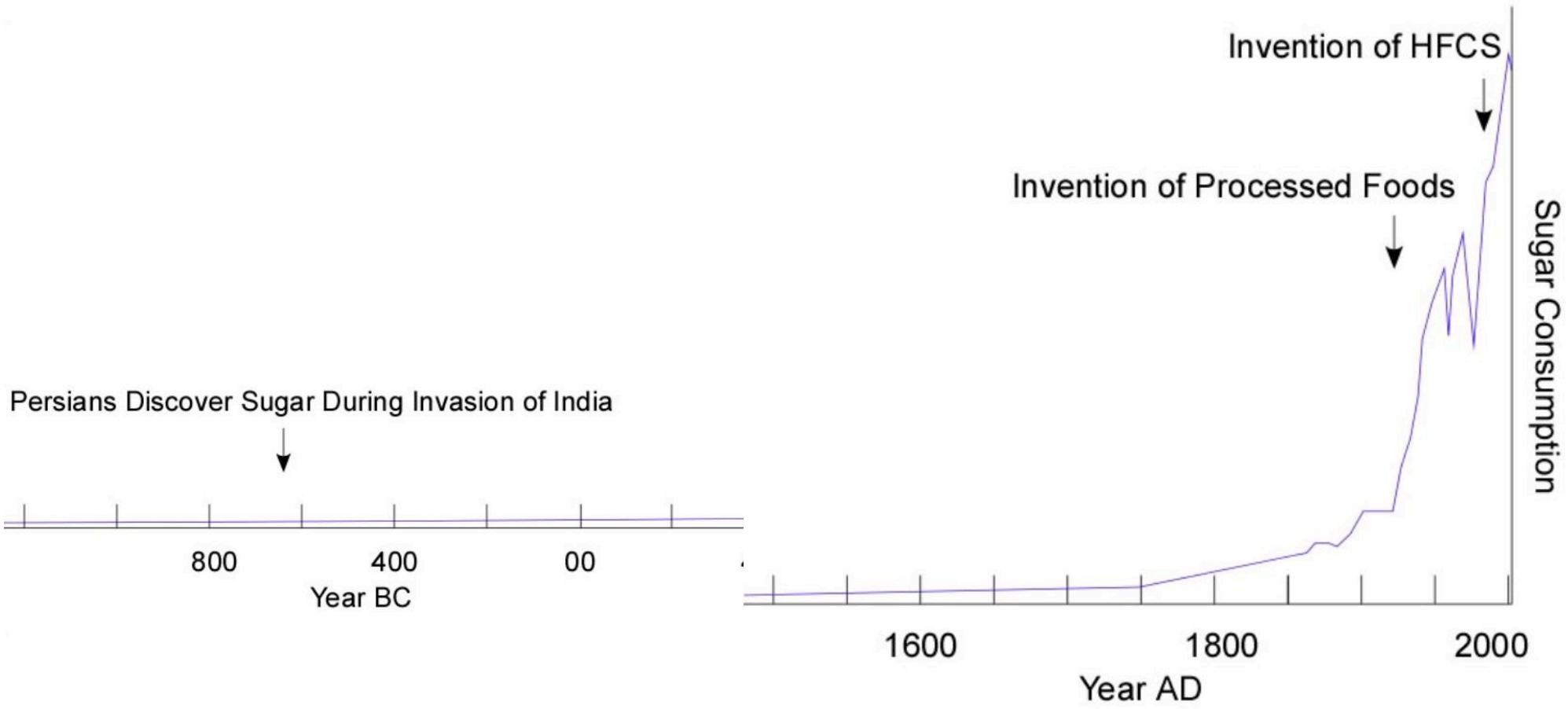


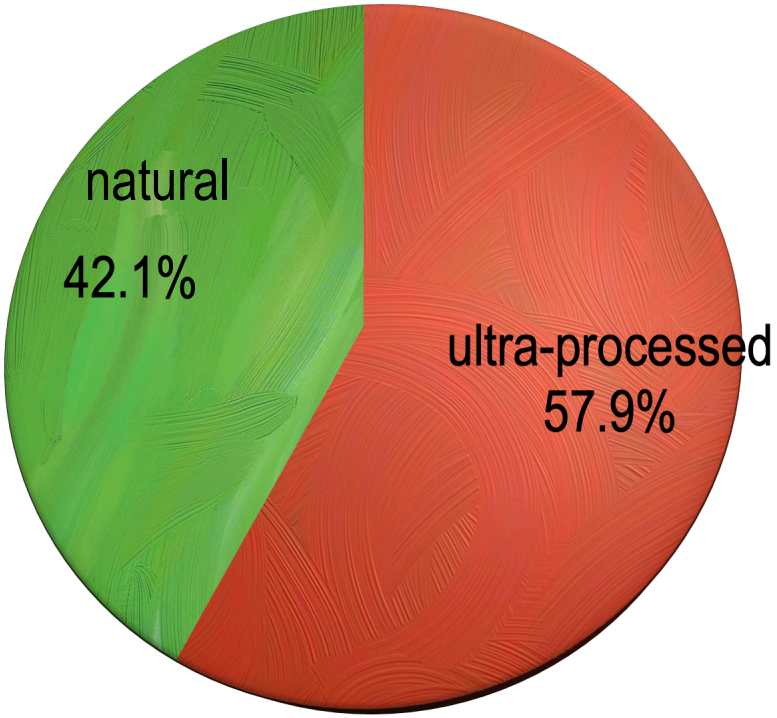
Fig 2 | Relative contribution (%) of each food group to consumption of ultra-processed food in diet

Srour et al. Brit Med J 2019

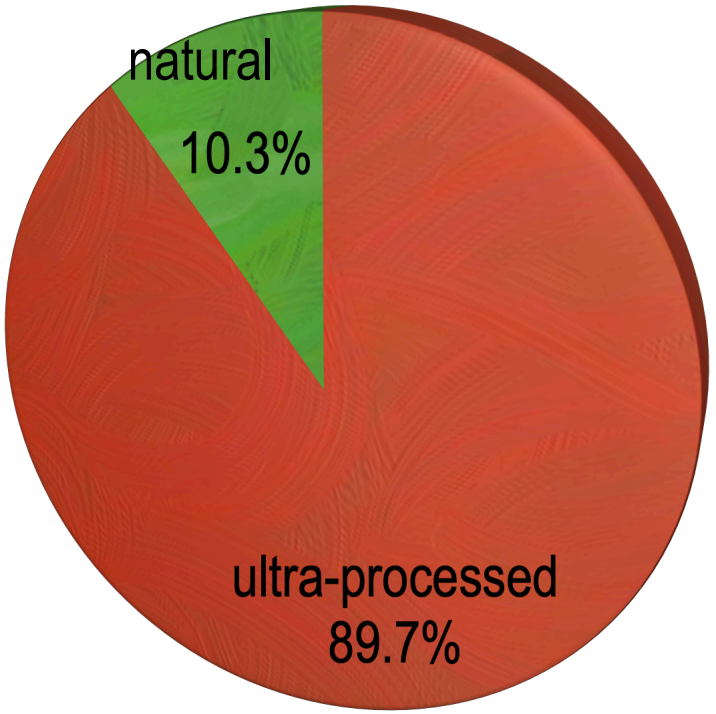
The History of Processed Food Intake



Ultra-processed food in the US diet



Proportion



Calories

Martinez-Steele et al. BMJ Open 2016

Why do we eat ultra-processed food?

On which drug are **you**??

Benefit

Mindfulness

Partner, friends, family

Exercise

Coffee

Alcohol

Nicotine

Marihuana etc.

Cocaine, speed etc.

Damage

Heroine etc.

Ultra-processed food

Food industry interests

Food that is:

- Cheap to produce
- Non-perishable
- Highly palatable
- Attractive

Public opinion:

- Promoting frequent meals
- Leaving it to people with obesity/metabolic syndrome ("lack of discipline")

Withdrawal from processed food is not easy

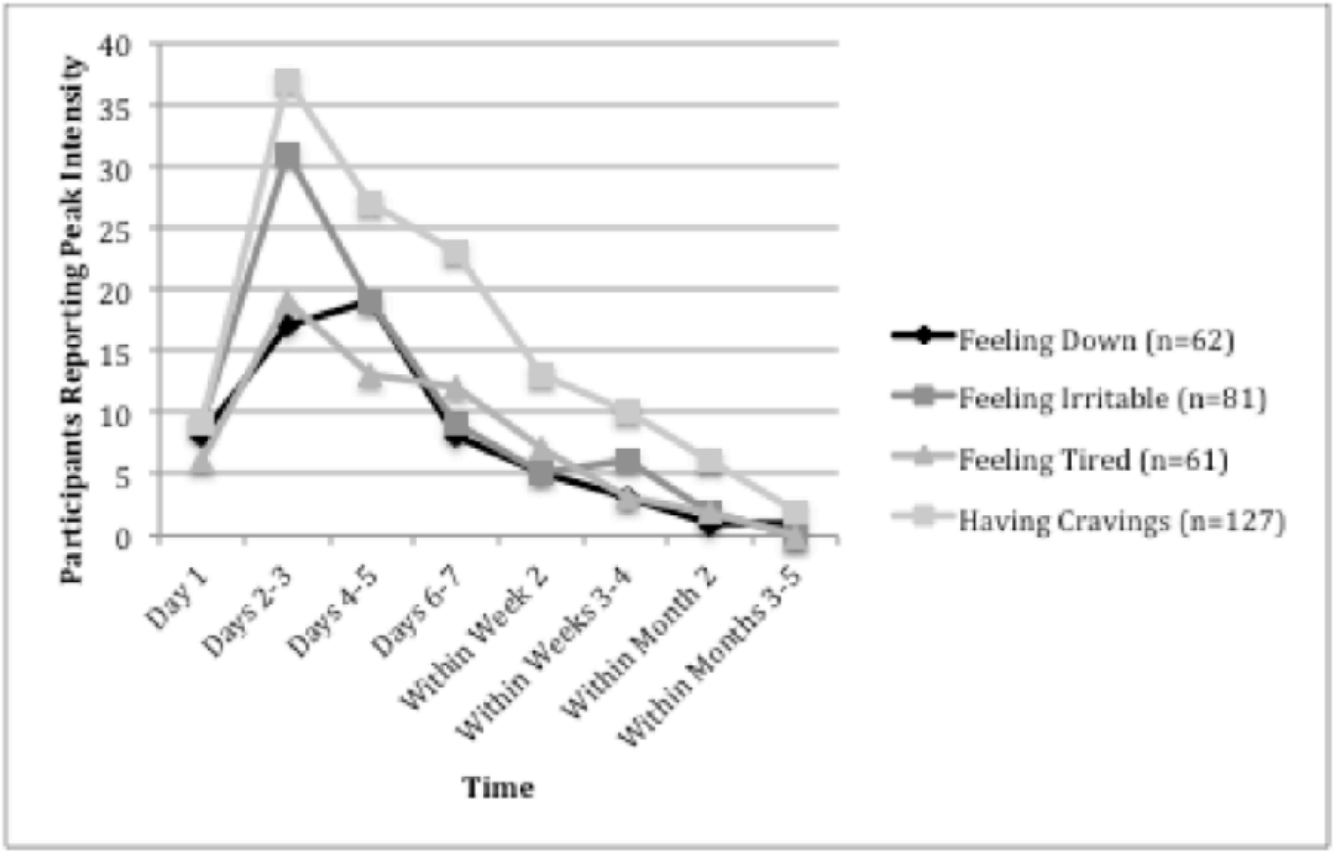
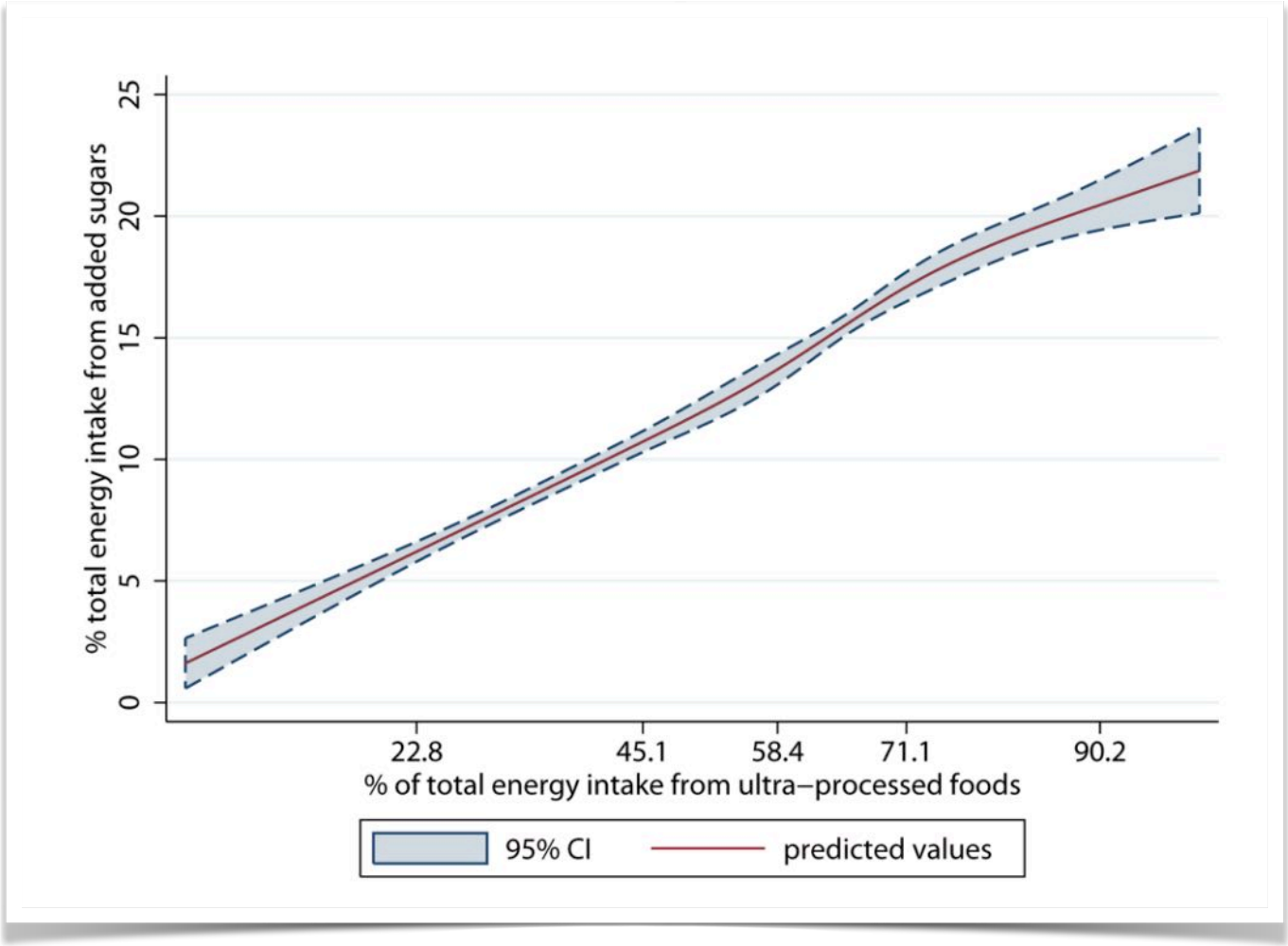


Fig. 1. Time course of highly processed food withdrawal symptoms.

Schulte et al. Appetite 2018

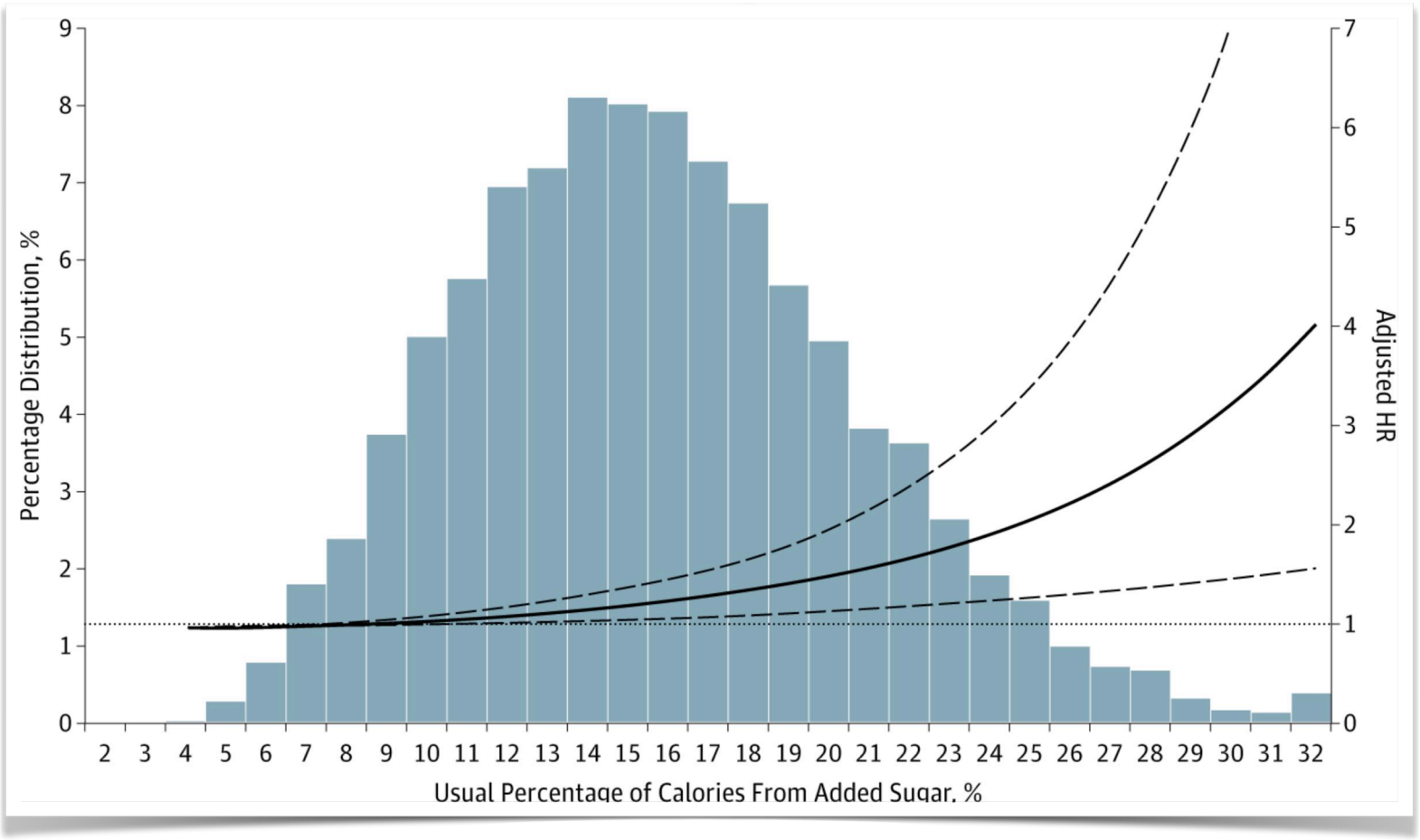
Is ultra-processed food really bad?

Processed Food and Sugar Intake



Steele et al. BMJ Open 2016

Added sugar and mortality



Yang et al. JAMA Int Med 2014

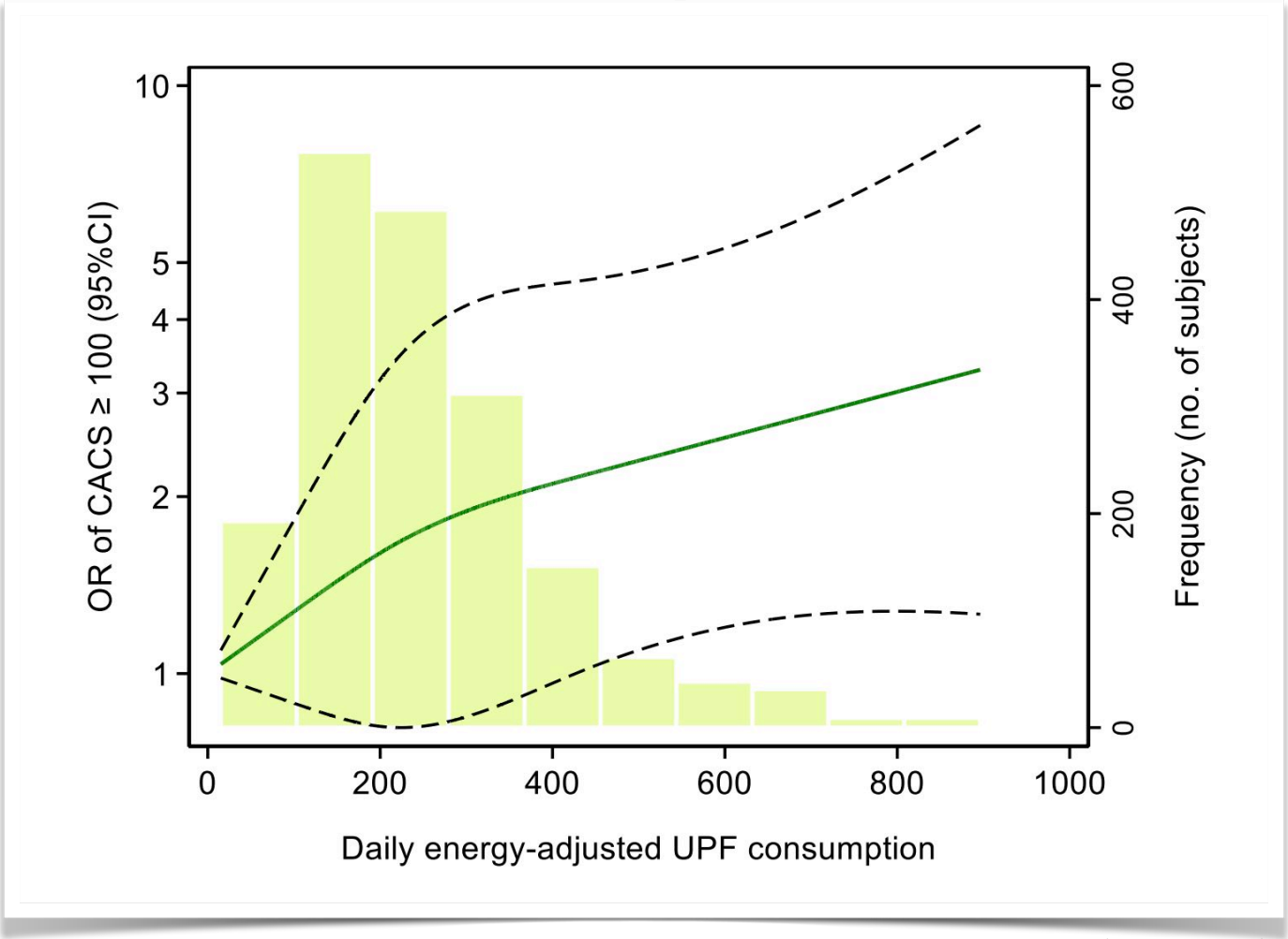
Processed Food and Health Outcomes

Negative impact on outcomes have been shown for

- Metabolic syndrome
- Cardiovascular diseases
- Cerebrovascular diseases
- Respiratory diseases
- Mental health disorders
- Cancer
- All-cause mortality

Chen et al. Nutr J 2020

Ultra-processed food and coronary calcium



Montero-Salazar et al. BMC Med 2020

Ultra-processed food and cancer risk

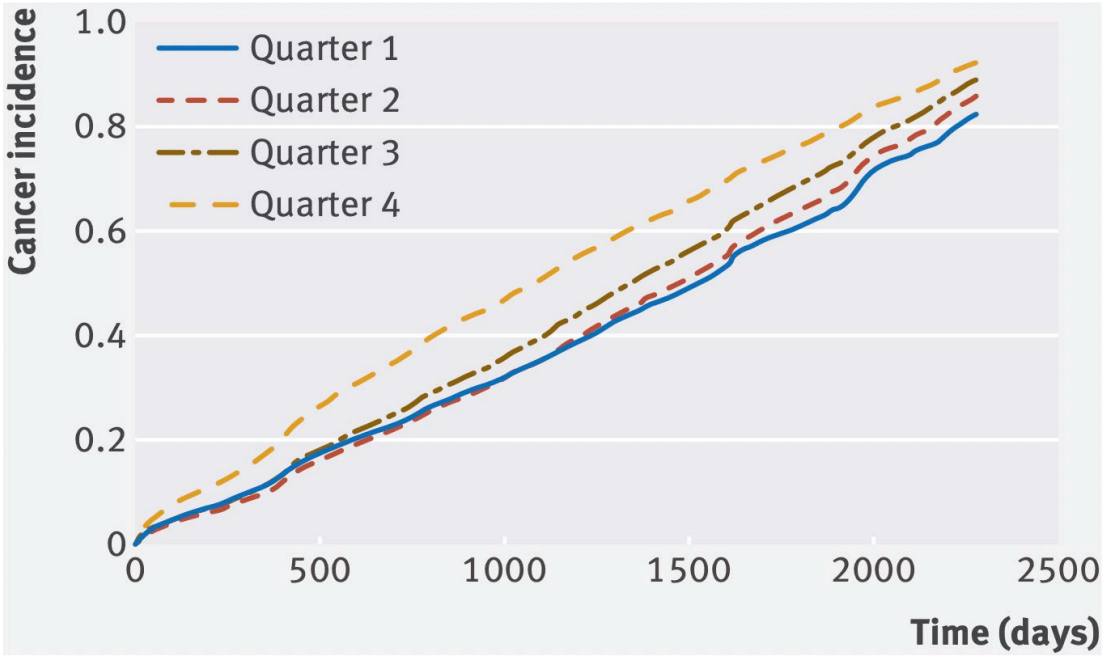
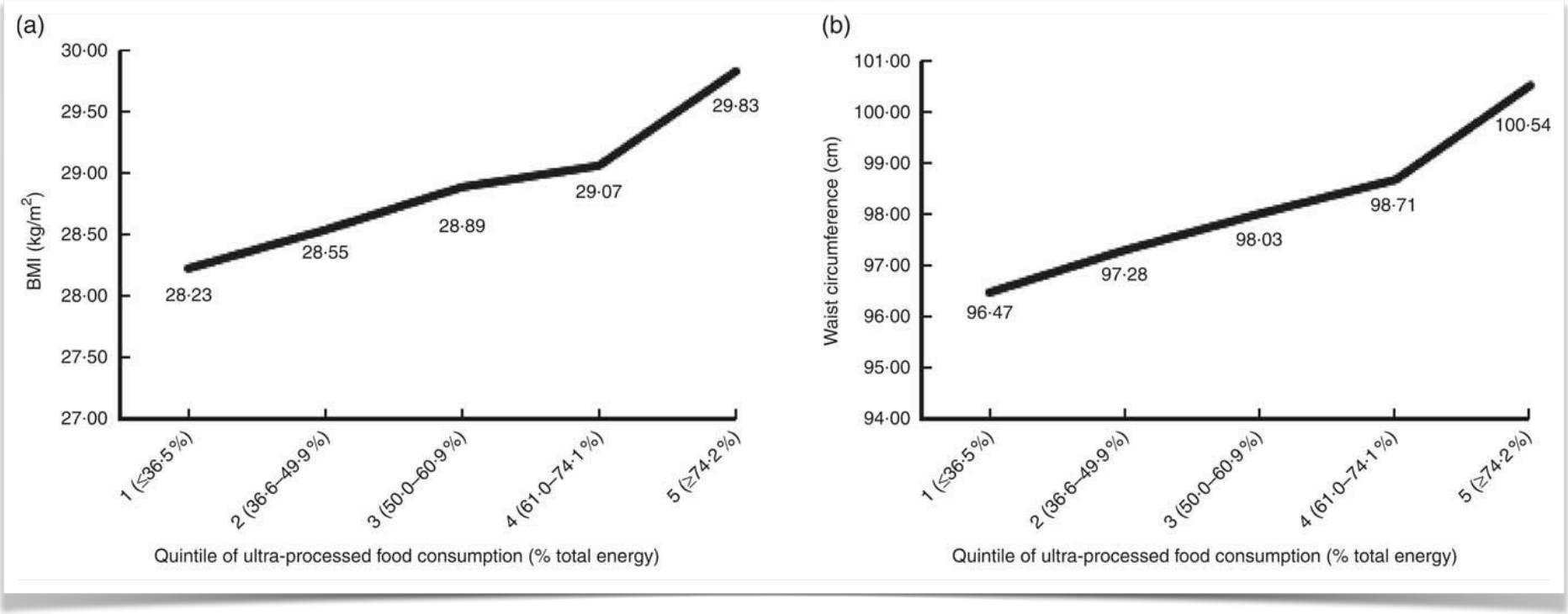


Fig 2 | Cumulative cancer incidence (overall cancer risk) according to quarters of proportion of ultra-processed food in diet

Fiolet et al. Brit Med J 2018

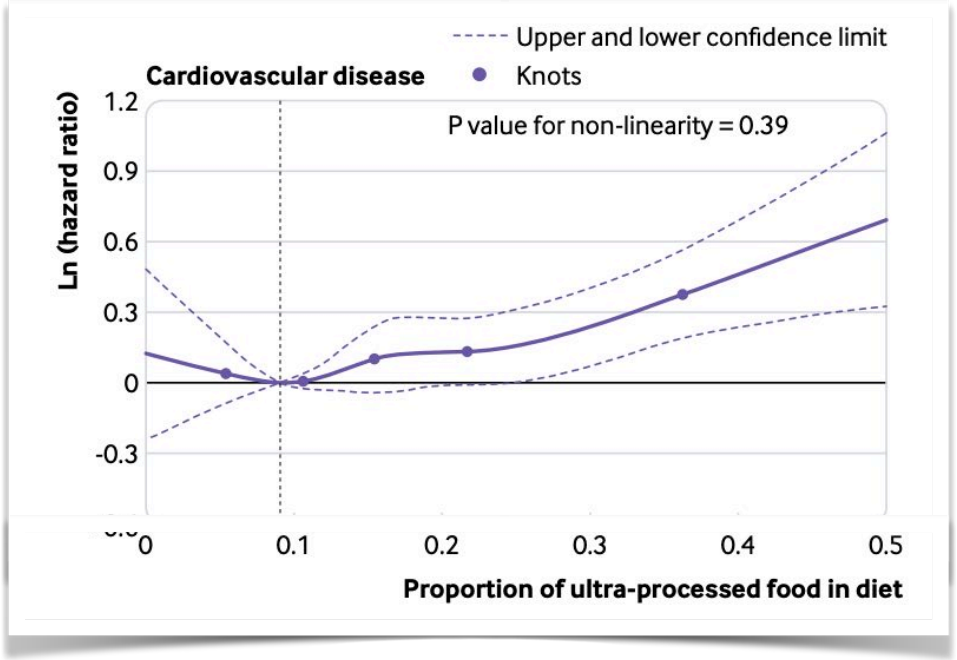
Ultra-processed food and risk for obesity

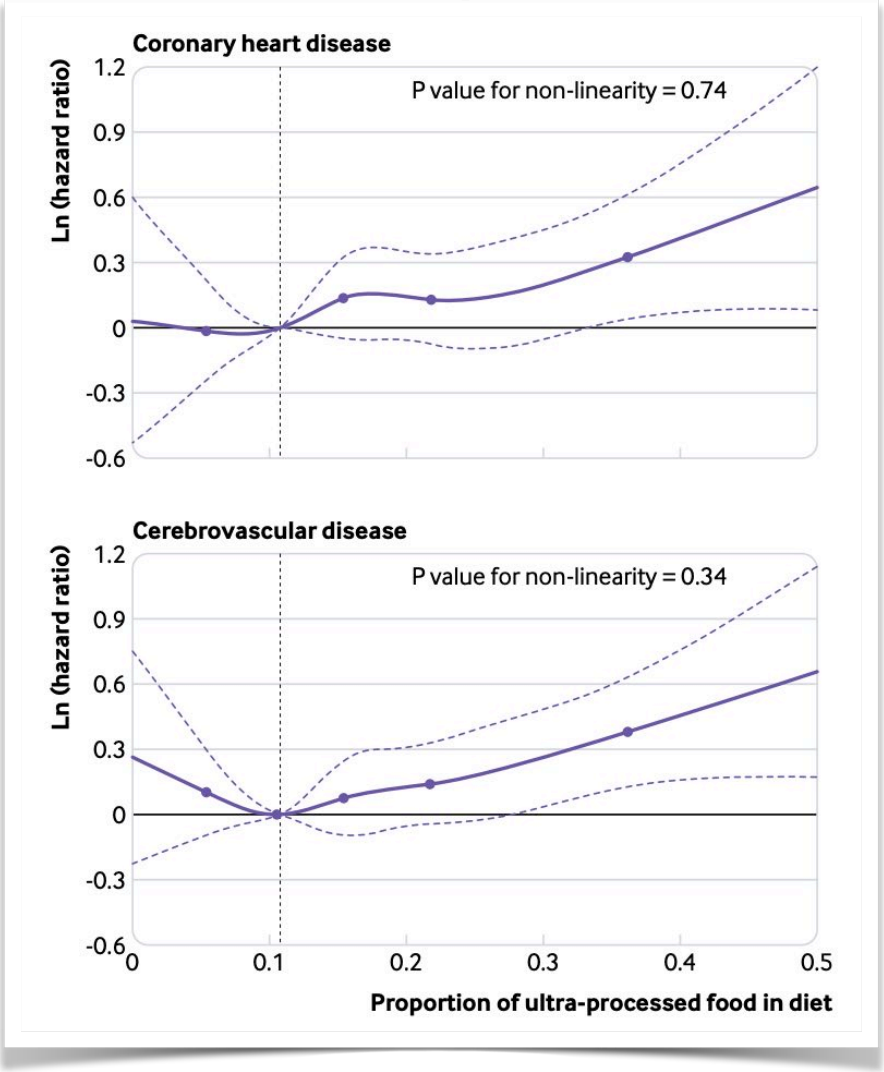


Juul et al. Brit J Nutr 2018

Ultra-processed food and outcomes

Prospective cohort study (NutriNet-Santé)
n = 105,159





Srour et al. Brit Med J 2019

Processed meat and outcomes

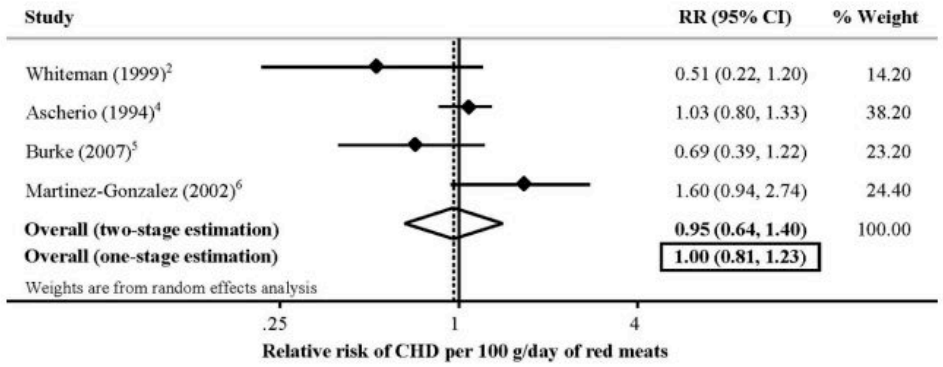
Red and Processe
Coronary Hear
A Sy

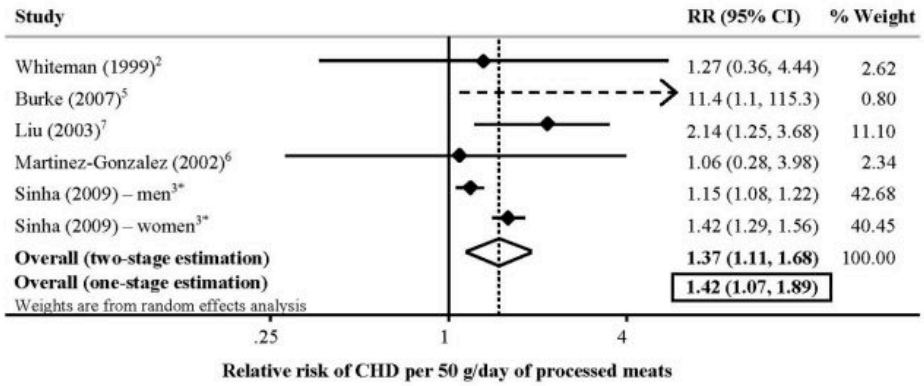
Renata Micha, RD,

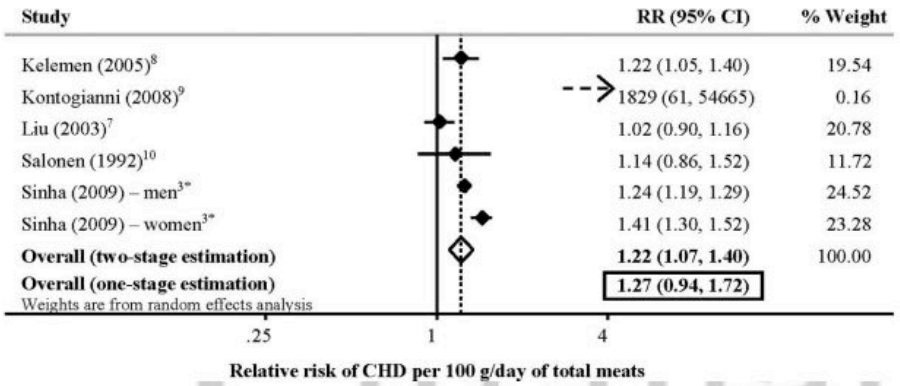
Background—Meat consumption is
and diabetes mellitus, limiting qu
different outcomes, as well as of
Methods and Results—We perfor
(unprocessed), processed, and tot
for any cohort study, case-contro
healthy adults. Of 1598 identifie
case-control studies. All data we
models for trend estimation were
individuals and 23 889 CHD, 228
CHD (n=4 studies; relative risk
heterogeneity=0.36) or diabetes
Conversely, processed meat intak
per day=1.42; 95% confidence in
risk=1.19; 95% confidence inter
Consumption of red and processe
Conclusions—Consumption of proc
diabetes mellitus. These results h
particular focus on processed me

Key Words: cardiov

Conclusions—Consump
diabetes mellitus. Th







42% higher risk

with higher incidence of CHD and
otential mechanisms of effects and for

Micha et al. Circulation 2010

Processed Food and All-Cause Mortality

Table 3 Hazard ratios (HR) and 95 % CI for all-cause mortality, according to quartile of frequency of ultra-processed food intake (times/d), among adults aged ≥20 years (*n* 11 898), Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994)

	Quartile of frequency of ultra-processed food intake								
	Quartile 1 (*n* 2982)		Quartile 2 (*n* 2989)		Quartile 3 (*n* 2985)		Quartile 4 (*n* 2942)		
	HR	95 % CI	HR	95 % CI	HR	95 % CI	HR	95 % CI	*P*-trend
Deaths due to all causes, *n*	625		588		617		621		
Model 1*	1·00	Reference	0·98	0·82, 1·16	1·02	0·83, 1·24	1·29	1·09, 1·53	0·002
Model 2†	1·00	Reference	0·98	0·83, 1·17	1·06	0·85, 1·29	1·31	1·09, 1·58	0·001
Model 3‡	1·00	Reference	0·99	0·83, 1·18	1·06	0·87, 1·30	1·30	1·08, 1·57	0·001

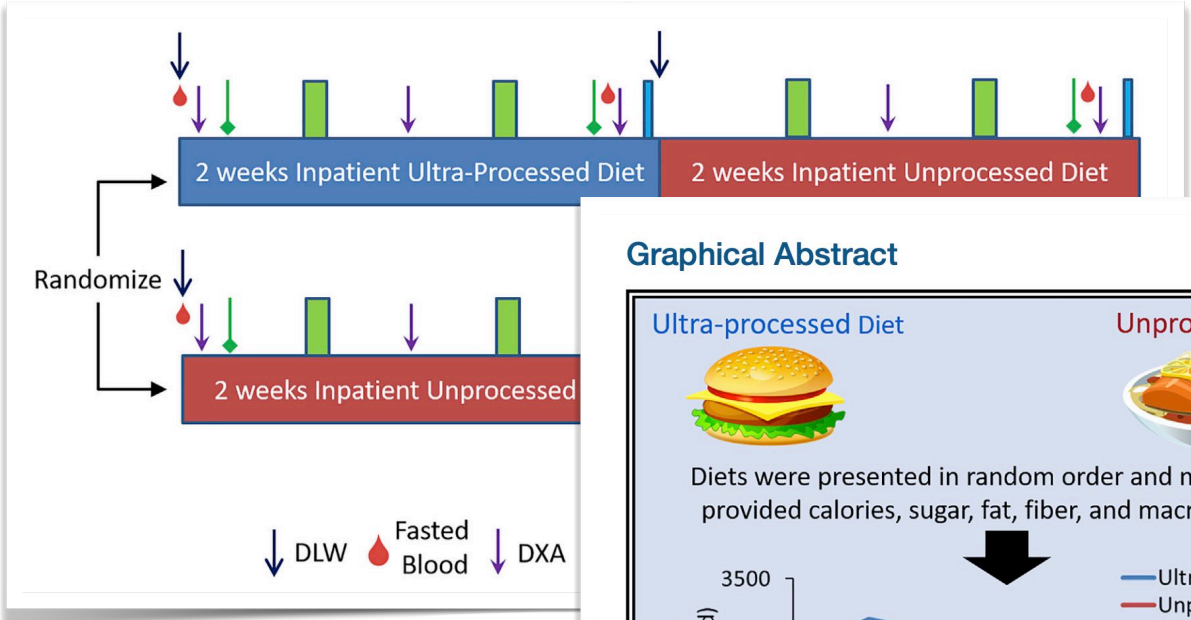
*Model 1 was adjusted for age, sex, race/ethnicity and total energy intake.
†Model 2 was adjusted for the variables in Model 1 plus poverty level, education level, smoking status, physical activity and alcohol intake.
‡Model 3 was adjusted for the variables in Model 2 plus BMI, hypertension status, total cholesterol and estimated glomerular filtration rate.

NHANES Study

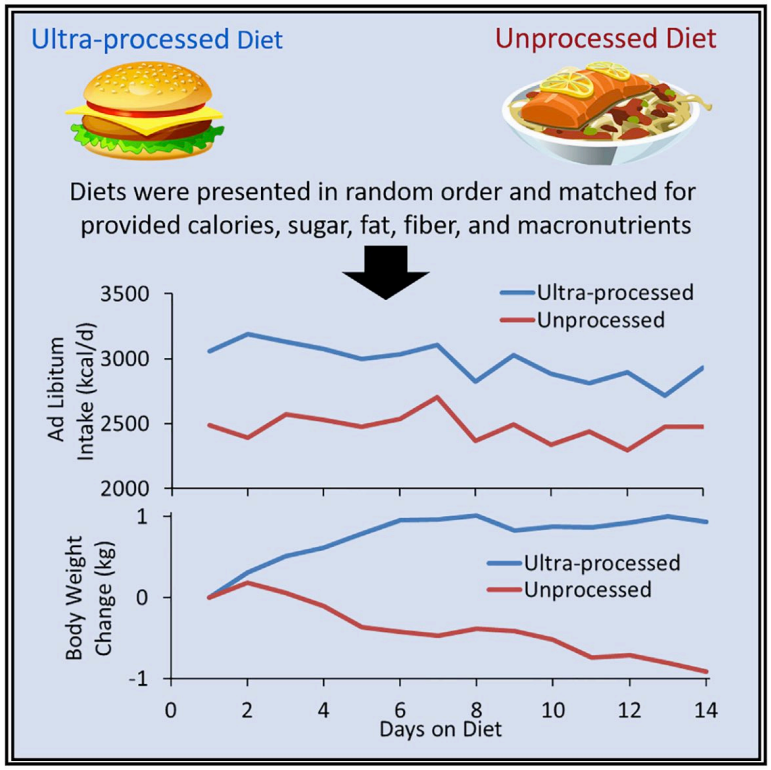
Kim et al. Publ Health Nutr 2019

What
does ultra-processed food do
to our bodies?

Impact of processed food on overall food intake and weight



Graphical Abstract



Authors

Kevin D. Hall, Alexis Ayuketah, Robert Brychta, ..., Peter J. Walter, Shanna Yang, Megan Zhou

Correspondence

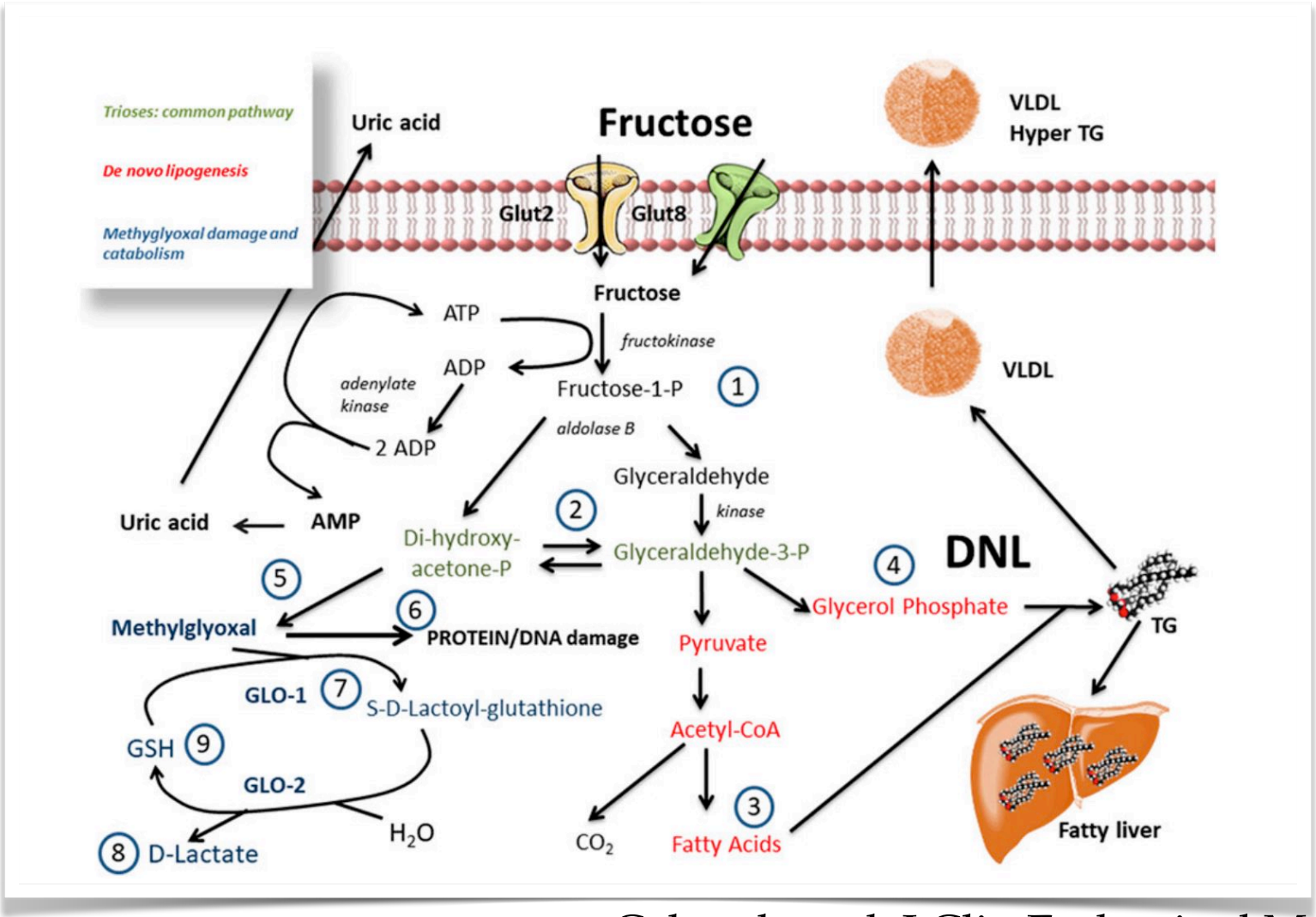
kevinh@nih.gov

In Brief

Hall et al. investigated 20 inpatient adults who were exposed to ultra-processed versus unprocessed diets for 14 days each, in random order. The ultra-processed diet caused increased *ad libitum* energy intake and weight gain despite being matched to the unprocessed diet for presented calories, sugar, fat, sodium, fiber, and macronutrients.

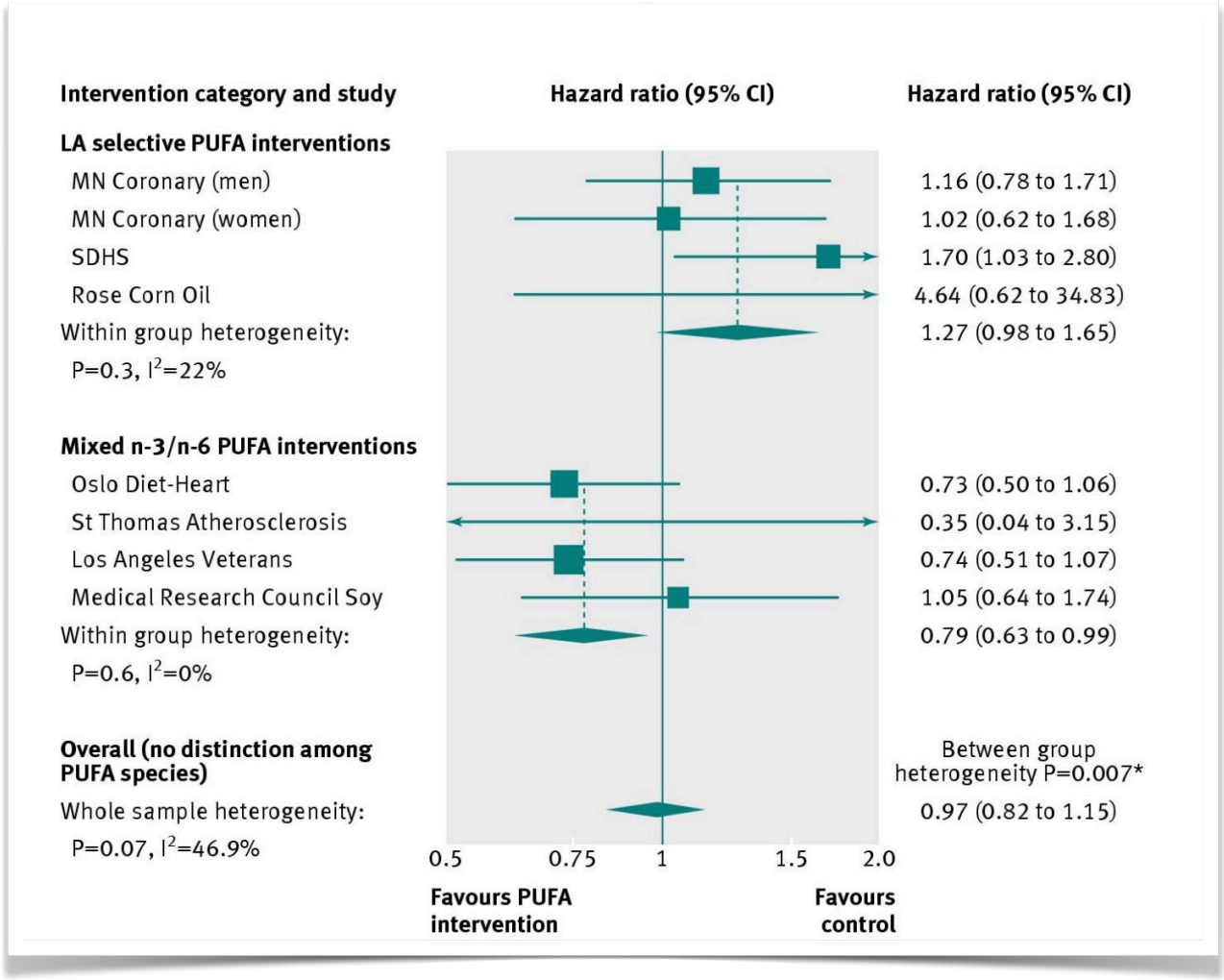
Hall et al. Cell Metab 2019

De-novo lipogenesis from fructose



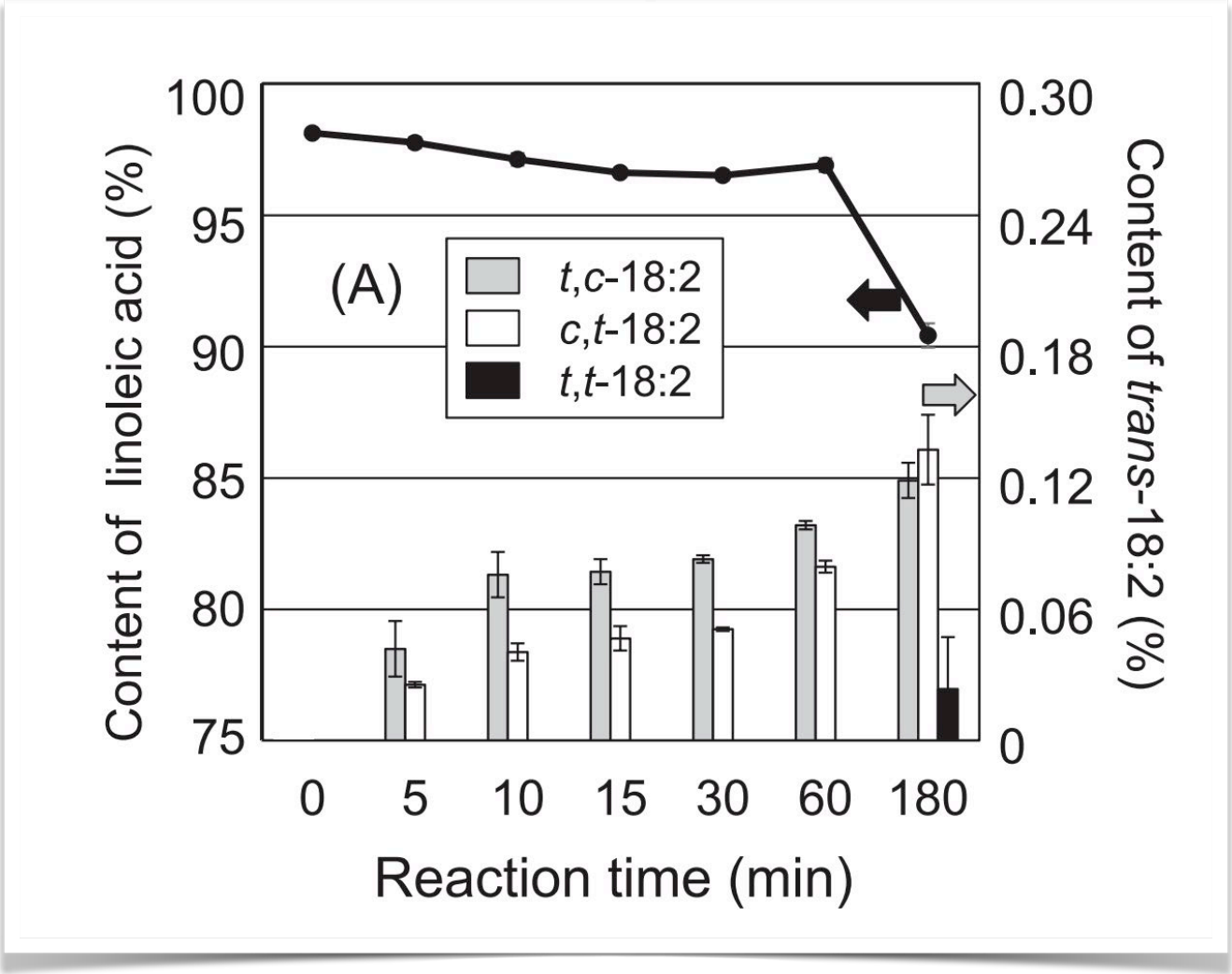
Cakmak et al. J Clin Endocrinol Metab 2019

Omega-6 (linoleum acid) vs mixed (omega-3 and 6) fatty acid supplementation



Ramsden et al. Brit Med J 2013

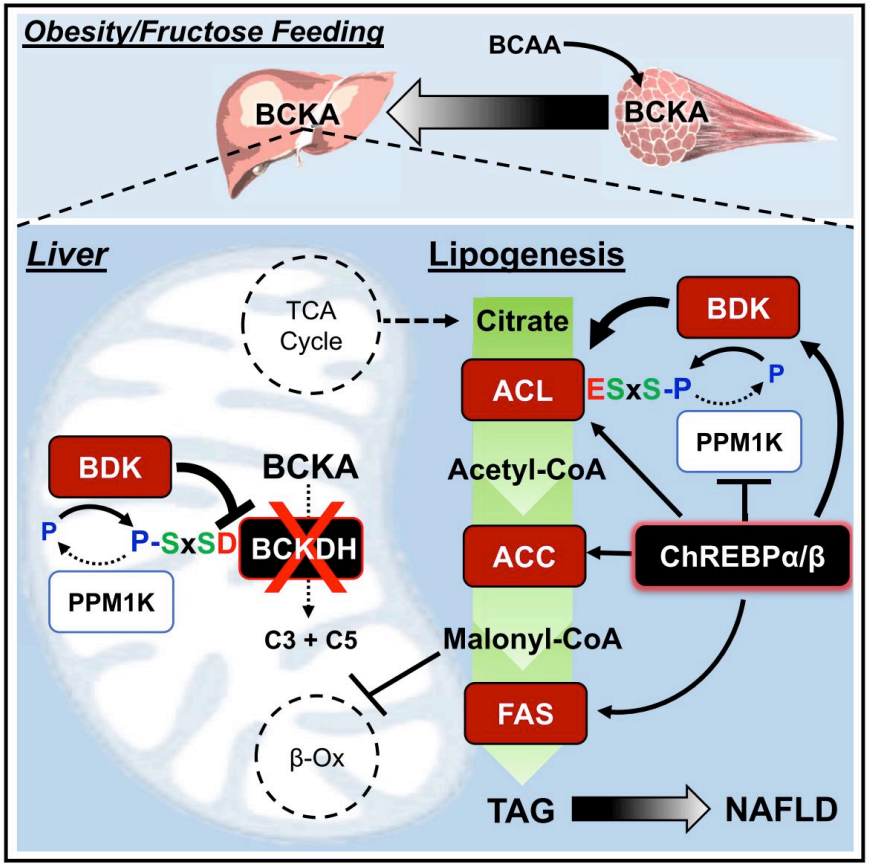
Trans-Fats from Heating



Gotoh, Journal of Oleo Science 2018

Branched-chain amino acids from corn(-fed animals) and metabolic disease

Graphical Abstract



Authors

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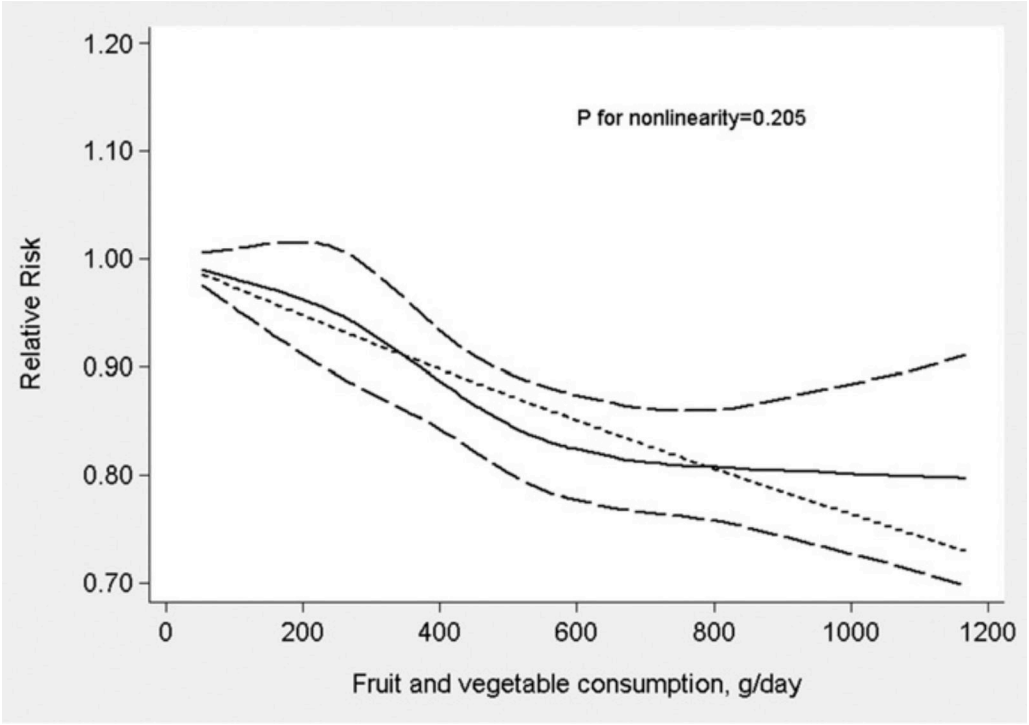
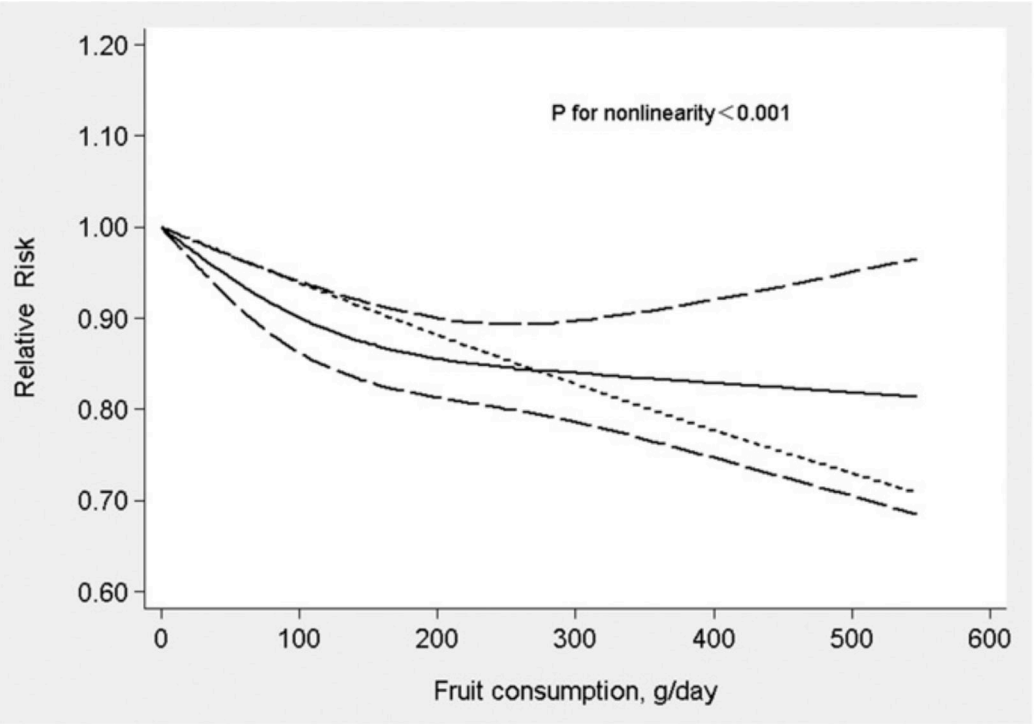
In Brief

Branched-chain amino acids (BCAA) are strongly associated with metabolic diseases. White et al. demonstrate that the kinase (BDK) and phosphatase (PPM1K) that regulate a rate-limiting BCAA metabolic enzyme, BCKDH, also regulate ATP-citrate lyase, a key lipogenic enzyme, thus identifying a new regulatory node that integrates BCAA and lipid metabolism.

White et al. Cell Metabol 2018

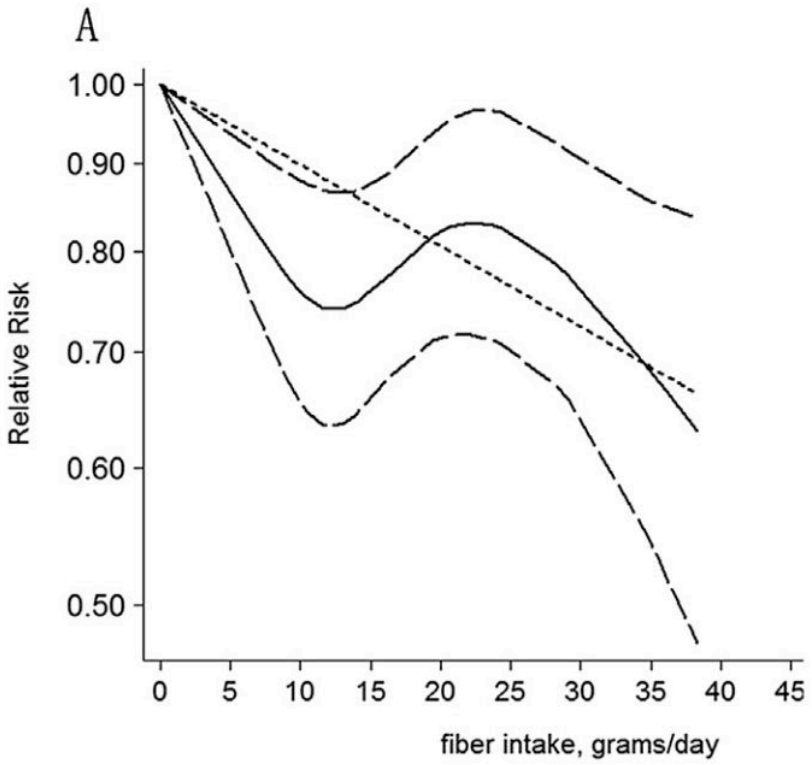
Fruits/vegetables and risk for coronary artery disease

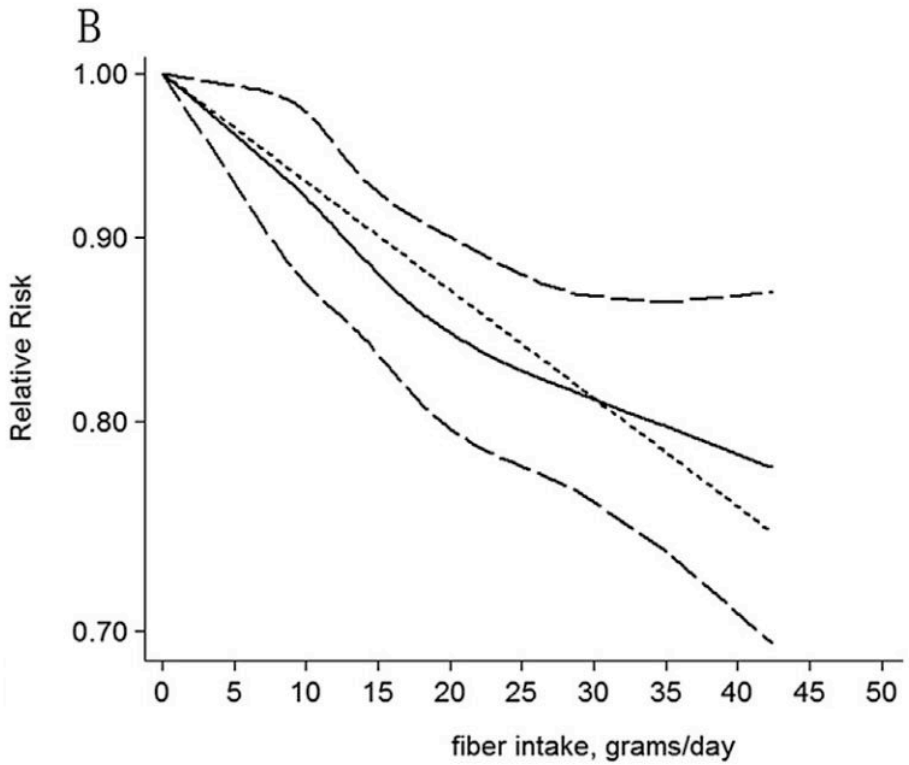




Gan et al. Int J Cardiol 2015

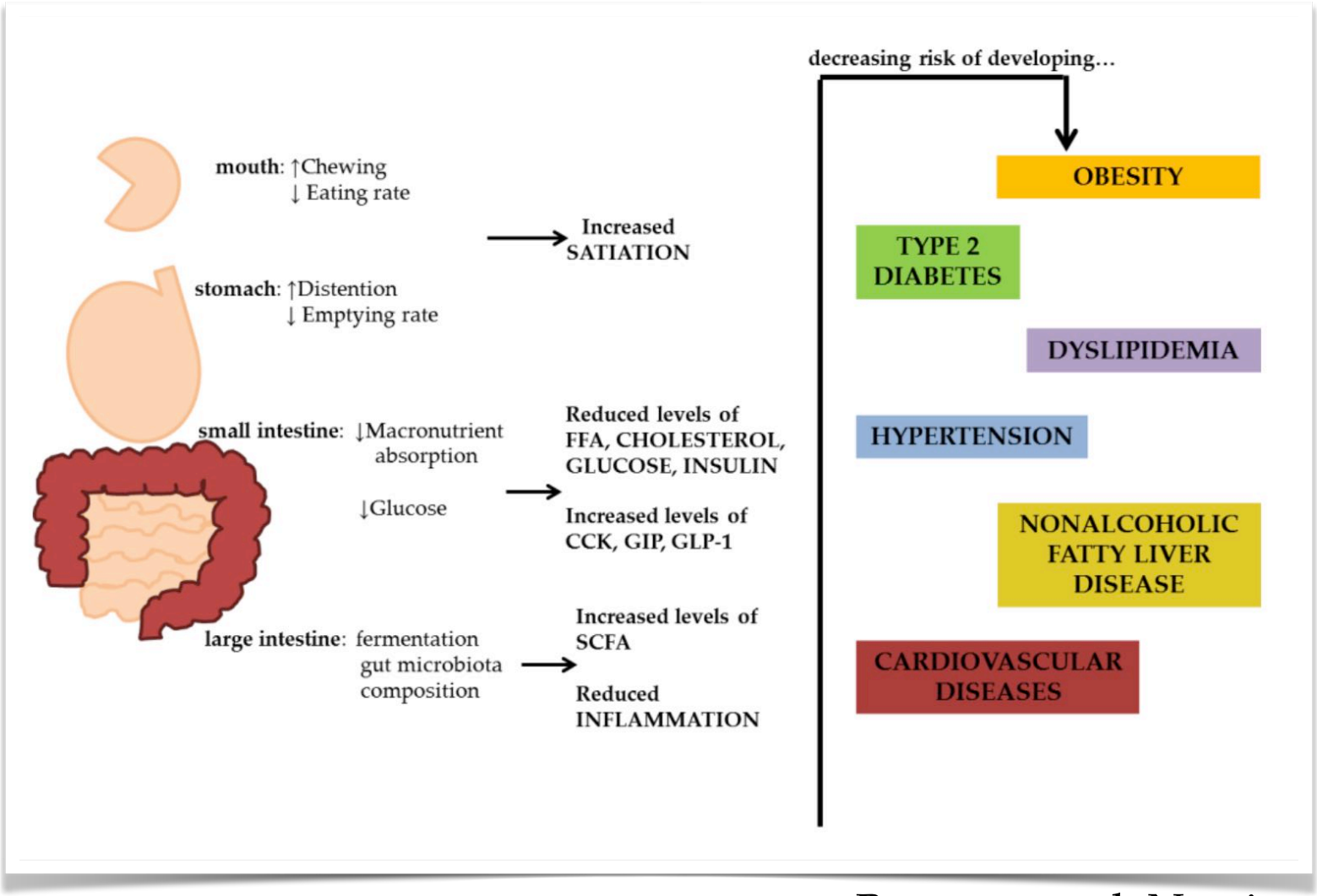
Fibre intake and risk for coronary artery disease





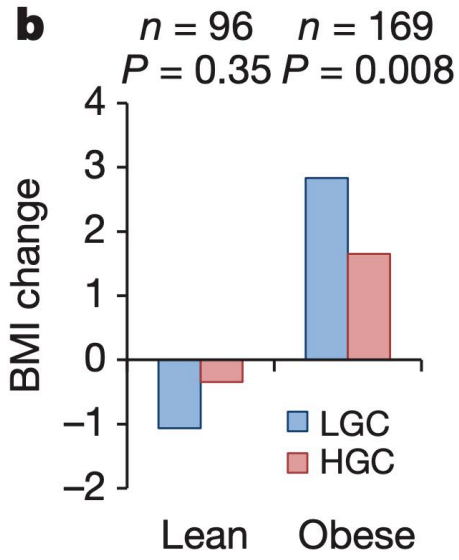
Gu et al. Clin Nutr 2015

Plausible mechanisms for the positive impact of fibres on body weight and CV risk



Bozzetto et al. Nutrients 2018

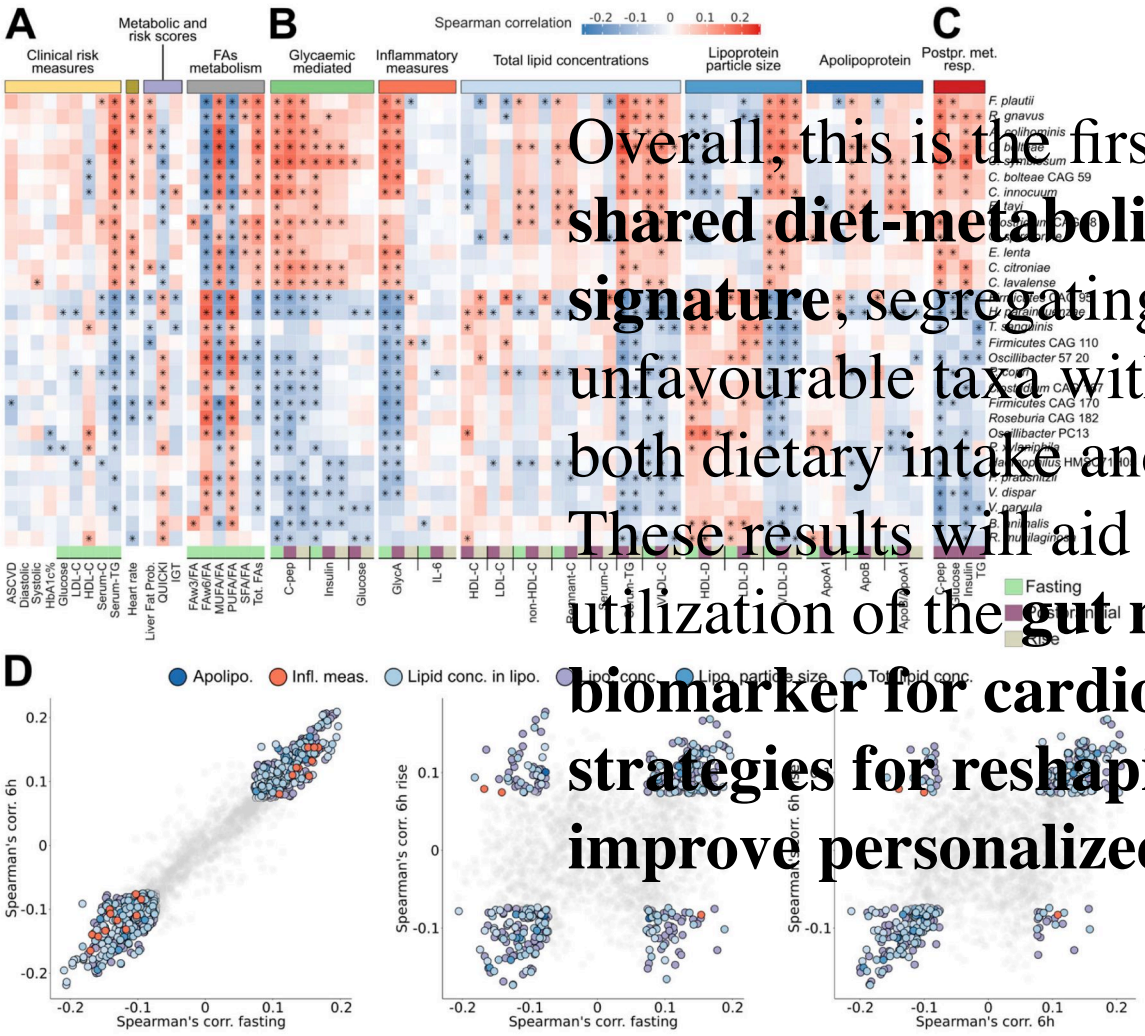
Ultra-processed food and the microbiome



… individuals with a **low bacterial richness** (23% of the population) are characterized by **more marked overall adiposity**, **insulin resistance** and **dyslipidaemia**, and a **more pronounced inflammatory phenotype** when compared with high bacterial richness individuals. The obese individuals among the lower bacterial richness group also gain more weight over time.

Le Chatelier et al. Nature 2013

Ultra-processed food and the microbiome



Overall, this is the first study to identify **a shared diet-metabolic-health microbial signature**, segregating favourable and unfavourable taxa with multiple measures of both dietary intake and cardiometabolic health. These results will aid as a resource both in utilization of the **gut microbiome as a biomarker for cardiometabolic risk and in strategies for reshaping the microbiome to improve personalized dietary health**.

Asnicar et al. Nat Med 2021

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Food Additives	Effect on Microbiota	Effect on Host Physiology	Organism/Treatment	Reference
CMC	Bacterial overgrowth	Intestinal inflammation	Mice ($IL10^{-/-}$). 2% CMC, 3 weeks	[54]
CMC, P-80	Microbiota encroachment, altered species composition, increased pro-inflammatory potential	Colitis, metabolic syndrome	Mice ($IL10^{-/-}$, $TLR5^{-/-}$). 1% CMC/P-80, 12 weeks Mice (WT). 0.1–1% CMC/P-80, 12 weeks	[29]
CMC, P-80	Increased pro-inflammatory potential		Human colon model. 1% CMC/P-80, duration: n/a	[33]
P-80	Microbiota encroachment, altered species composition, increased pro-inflammatory potential	Intestinal inflammation, obesity, liver dysfunction	Mice (WT). 1% P-80 per kg. bw, 4 weeks	[55]
GML	Gut microbiota dysbiosis	Metabolic syndrome, systemic low-grade inflammation	Mice (WT). 150 $mg \cdot kg^{-1}$ GML, 8 weeks	[56]
Titanium dioxide		Decrease in absorptive microvilli, decreased nutrient uptake	Human colon cells. 2.3×10^9 (high), 2.3×10^7 (medium), 2.3×10^5 (low) particles/mL	[63]
Sucralose	Increased expression of bacterial pro-inflammatory mediators	Elevated pro-inflammatory gene expression in the liver	Mice (WT). 0.1 mg/mL sucralose, 6 months	[62]
NAS	Compositional and functional alterations of microbiota associated with obesity	Glucose intolerance	Mice (WT). 0.1 mg/mL^{-1} saccharin, 5 weeks	[28]
Saccharin	Increased pro-inflammatory potential	Liver inflammation	Mice (WT). 0.3 mg/mL saccharin, 6 months	[61]
Aspartame	Compositional alterations of microbiota	Glucose intolerance	Rats (WT). 5–7 mg/kg/d, 10 weeks	[59]
Acesulfame K	Compositional and functional alterations of microbiota associated with obesity	Weight gain (male)	Mice (CD-1). 37.5 mg/kg/d, 4 weeks	[60]
Silver nanoparticles	Gut microbial alterations associated with obesity and inflammatory diseases		Mice (WT). 46, 460 or 4600 ppb Ag NP, 28 days	[64]

Acceptable daily intake (ADI), Polysorbate 80 (P-80), Carboxymethylcellulose (CMC), Non-caloric artificial sweeteners (NAS), Glycerol Monolaureate (GML), Interleukin (IL), Toll like receptor (TLR), Wild type (WT), Not available (n/a), Body weight (bw), Cluster of differentiation 1 (CD1), Part per billion (ppb), Silver (Ag), Nanoparticles (NP).

Zinöcker et al. Nutrients 2018

What ultra-processed food does:

⬆ unnatural contents (sugar/sweeteners, salt, preservatives, emulsifiers, etc.)

⬇ natural contents (non-soluble fibres, omega-3 fatty acids, vitamins, etc.)

↓

⬇ microbiome integrity and diversity,

⬆ inflammation

⬆ ectopic fat

⬆ insulin resistance

↓

Diabetes

Obesity

Non-Alcoholic Fatty Liver Dsease (NAFLD)

Summary

Ultra-processed food has significant implications on eating habits and increases cardiovascular risk, mostly by promoting metabolic disease.

Inflammation and insulin resistance likely promote the development and progression of metabolic disease and subsequent obesity and inactivity.

With a natural diet, it is not necessary to count calories, avoid or focus on certain macronutrients, or curb appetite.

Summary

"Feed the gut
-protect the liver"

Robert Lustig, MD
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