Équipe de Recherche en Épidémiologie Nutritionnelle

ÉTUDE NUTRINET SANTÉ

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Ultra-processed/Ultra-formulated foods and health: epidemiological evidence

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(ULTRA)PROCESSING / (ULTRA)FORMULATION: SOME RISKS ?

- Food processing: huge progress accross the last century, several advantages (foods that are practical, quick and easy to prepare, low microbiological risk, improved bioavailability and digestibility of some compounds…BUT have we gone too far ?
- In average: more salt, sugar, saturated fats, higher GI, less vitamin, mineral and fibers
- Food additives, recent in vivo / in vitro results of concern for some of them
- Other ingredients / compounds (e.g. Industrial trans fat)
- Contaminant migration following prolonged contact with packaging?
- Neoformed compounds? (some specific to industrial processing)
- Modification of the food matrix (effects on satiety, bioavailability, and transit speed? Favour overconsumption ?)

THE NOVA CLASSIFICATION

NOVA groups	Examples
1) Unprocessed or minimally processed foods Edible parts of plants and animals after separation from nature or modified/preserved by minimal processes (no substances added)	
2) Processed culinary ingredients Substances extracted from foods or nature and used to prepare, cook and season Group 1 foods such as salt, sugar, oils or fats	
3) Processed foods Group 1 foods modified with the addition of salt, sugar, oils or fats to preserve and enhance their sensory qualities	
4) Ultra-processed foods Formulations of substances derived from foods plus cosmetic additives, with little if any intact food, designed to be durable, omnipresent, hyper-palatable, and highly profitable	

Source: Monteiro et al *Public Health Nutrition* 2017

Fruit
(Real food)

≠

"Fruit"
(The imitation)

Ingredientes: Açúcar, maltodextrina, polpa de laranja desidratada, ferro, vitamina C, vitamina A, acidulante ácido cítrico, antiumectante fosfato tricálcico, regulador de acidez citrato de potássio, espessantes: gomas guar e xantana, aromatizante aroma sintético idêntico ao natural, edulcorantes: aspartame, ciclamato de sódio, acesulfame de potássio e sacarina sódica, corante inorgânico dióxido de titânio, espumante extrato de quilária e corantes artificiais: tartrazina e amarelo crepúsculo.
CONTÉM 1% DE POLPA DESIDRATADA

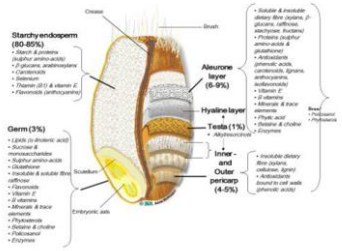
Fruit
(Real food)

≠

"Fruit"
(The imitation)

WATER
SUGAR
MODIFIED MILK INGREDIENTS
GLUCOSE
MILK INGREDIENT
COCONUT OIL
CITRIC ACID
CARRAGEENAN†
CAROB BEAN GUM†
MONO- AND DIGLYCERIDES
MONOSODIUM PHOSPHATE
PROPYLENE GLYCOL
CELLULOSE GUM
COLOUR
FLAVOUR

Cereal
(Real food)



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"Cereal"
(The imitation)

Ingredients: Sugar, corn flour, wheat flour, oat flour, oat fiber, corn fiber, partially hydrogenated vegetable oil, salt, red 40, natural flavor, blue 2, turmeric color, yellow 6, annato color, blue 1, BHT for freshness, vitamin C, niacinamide, reduced iron, zinc oxide, vitamin B6, vitamin B2, vitamin B1, vitamin A, folic acid, viitamin D, vitamin B12

The real meal

Recipe: pasta, chicken, olives, tomato, onions, garlic, salt.

≠

The imitation

Ingredients:

Noodle Cake: Wheat Flour, Palm Oil, Salt, Anti-Caking Agents, Thickener, Humectant.

Flavour Sachet: Salt, Flavour Enhancers (Monosodium Glutamate, Disodium Guanylate, Disodium Inosinate), Sugar, Maize Starch, Flavourings (with Milk and Soya), **Chicken Meat (3%)**, Soya Sauce, Palm Oil, **Chicken Fat (2%)**, Leek, Onion, Garlic, Celery Seed Powder, Acid Turmeric

Source : Pr Carlos Augusto Monteiro, Paris, 2018

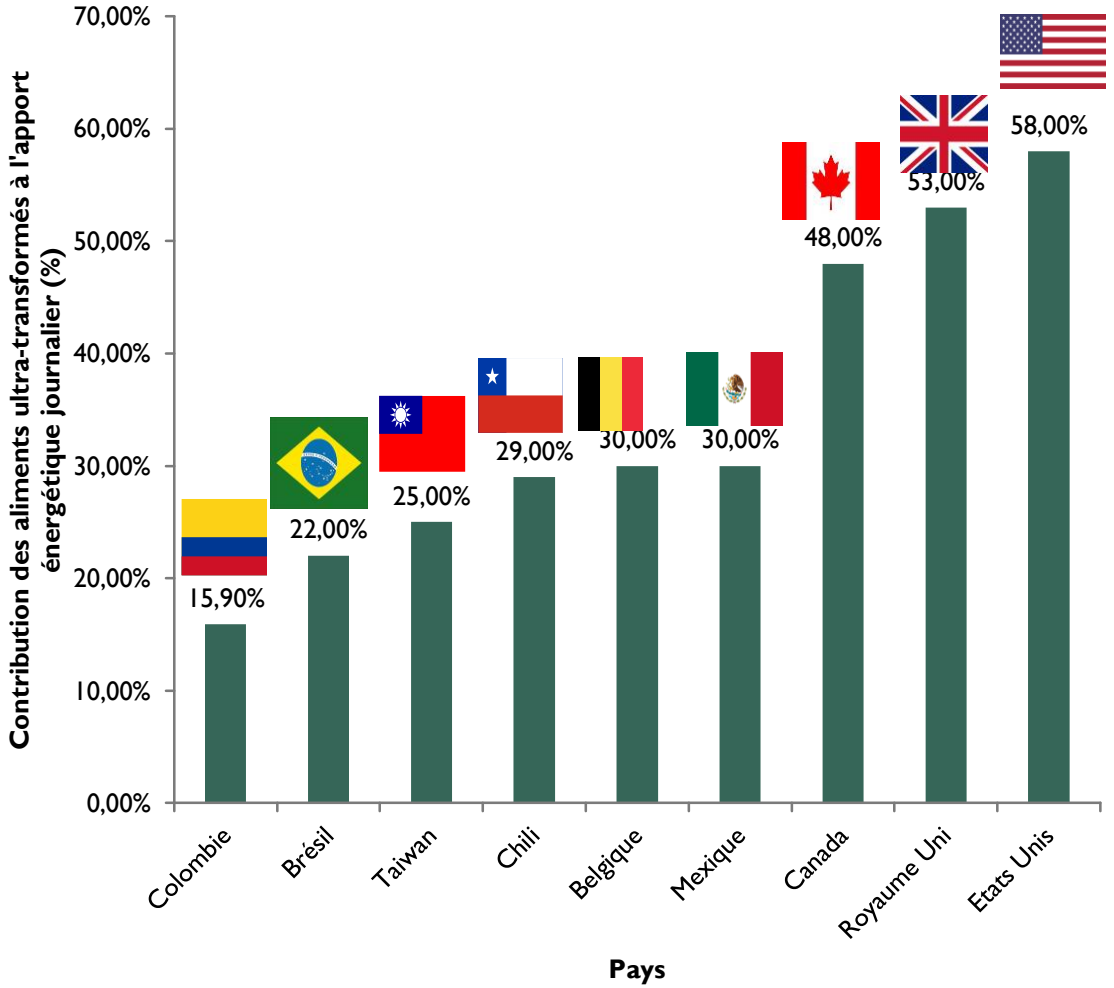
« INDUSTRIAL FOOD » ≠ « UPF » !

Processed

Ultra-processed

Image sources : Open Food Facts https://uk.openfoodfacts.org/

UPF CONTRIBUTION TO DAILY ENERGY INTAKE (CROSS-SECTIONAL REPRESENTATIVE SURVEYS)



French Data
30-35%
(preliminary results in ESTEBAN study)

SROUR B. et al.

UPF AND CHRONIC DISEASE RISK – EPIDEMIOLOGICAL STUDIES

- In cross sectional studies, several associations were observed between UPF intake and various chronic conditions, e.g.: overweight, obesity, Metabolic syndrome, dyslipidaemia

  (Juul 2015, PAHO 2015, Juul 2018, Louzada 2015, Canella 2014, Tavares 2012)

- Until 2018: few prospective studies

1st Author	Year	Country	Effective	Cohort	Outcome	Journal
Rauber	2015	Brésil	345	Sao Leopoldo (enfants)	Bilan lipidique	Nutr Metab Cardiovasc
Mendonça	2016	Espagne	8451	SUN	Surpoids/obésité	Am J Clin Nutr
Mendonça	2017	Espagne	14790	SUN	Hypertension	Am J Hypertens

NutriNet-Santé cohort

Launched in **2009** in France, 1st **web-cohort** of this size worldwide

>171,000 adult participants (recruitment still ongoing)

- **Very detailed assessment of dietary exposures and emerging nutritional behaviours**
  - ✓ 3 validated repeated 24h dietary records every 6 months, incl. >3500 food items + commercial brands
  - ✓ Huge amount of complementary online questionnaires
    food packaging, cooking practices, mode of production, physical activity, tobacco, drugs, environmental, domestic and professional exposures…

- **Biobank:** n=20,000 (fasting serum, plasma, buffy-coat, urine) / stool collection ongoing for a subsample

- **Health events:** validation by medical committee + linked to National health insurance databases (SNIIRAM) and mortality registry (CépiDC)

2009 — Ongoing, **already >10-year follow-up** and >4000 incident cancers, 2700 CVD, 1300 deaths — 2020…

- **International Expansion** (launched: Belgium, current drivers: Switzerland, Canada, Mexico, Brazil)

→ **Unique platform for multidisciplinary research**

www.etude-nutrinet-sante.fr / https://info.etude-nutrinet-sante.fr/

ÉTUDE NUTRINET SANTÉ

Accueil | L'étude NutriNet-Santé | Actualités | Publications | FAQ

Connexion

Participer à NutriNet-Santé c'est être acteur de la recherche pour améliorer la santé de tous !

Je m'inscris | Je me connecte | Obtenir un nouveau mot de pass

Pour accéder à votre espace personnel et remplir vos questionnaires, cliquez sur « Je me connecte ».

Questionnaire alimentaire

Retour à la liste — Si vous êtes déconnecté ou si vous fermez le questionnaire, vos réponses seront systématiquement sauvegardées

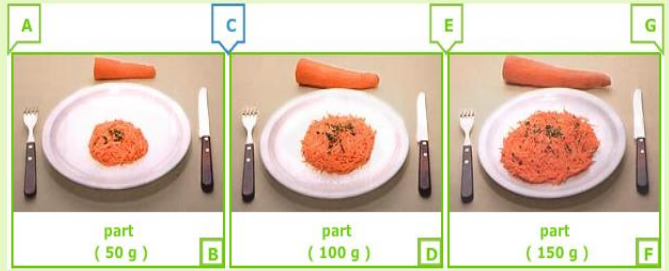
Journée de SAMEDI (17/01/2009) — Aide

petit déjeuner

carottes rapées assaisonnées

déjeuner (4 aliments)

Choisissez la quantité pour "carottes rapées assaisonnées"



Sélectionnez la portion : ○ A ○ B ◉ C ○ D ○ E ○ F ○ G

Sélectionnez le nombre de portions: 1

Si les portions proposées ne conviennent pas à votre consommation, vous pouvez préciser la quantité exacte : g

Annuler — Précédent — Terminer

METHODS & STATISTICAL ANALYSES

UPF: NOVA classification *(Monteiro PHN 2017, World Nutrition 2016, Moubarac 2014)* applied to NutriNet-Santé's food composition database (>3300 generic items) + calculation of the proportion of UPF in the diet (in quantity, g/d)

Exclusion : prevalent cases, participants having <2 R24, energy under-reporters

Cox Proportional Hazard Models to assess the associations between the proportion of ultra-processed foods in the diet (for an increase of 10 points in the percentage, or by quartiles/tertiles) and the risk of chronic diseases

Mixed models for weight change

Adjustments: age and sex, anthorpometric, lifestyle, sociodemographic factors, physical activity and smoking, alcohol intake, nutritional factors (food groups and global scores or patterns), family history of disease, metabolic comorbidities (disease and treatment), and reproductive life for breast cancer analyses

Secondary analyses: associations between unprocessed/minimmally processed foods and health outcomes

Sensitivity analyses (further adjustments, account for reverse causality, stratification by sex, age, BMI, smoking status…)

UPF – CANCER RISK

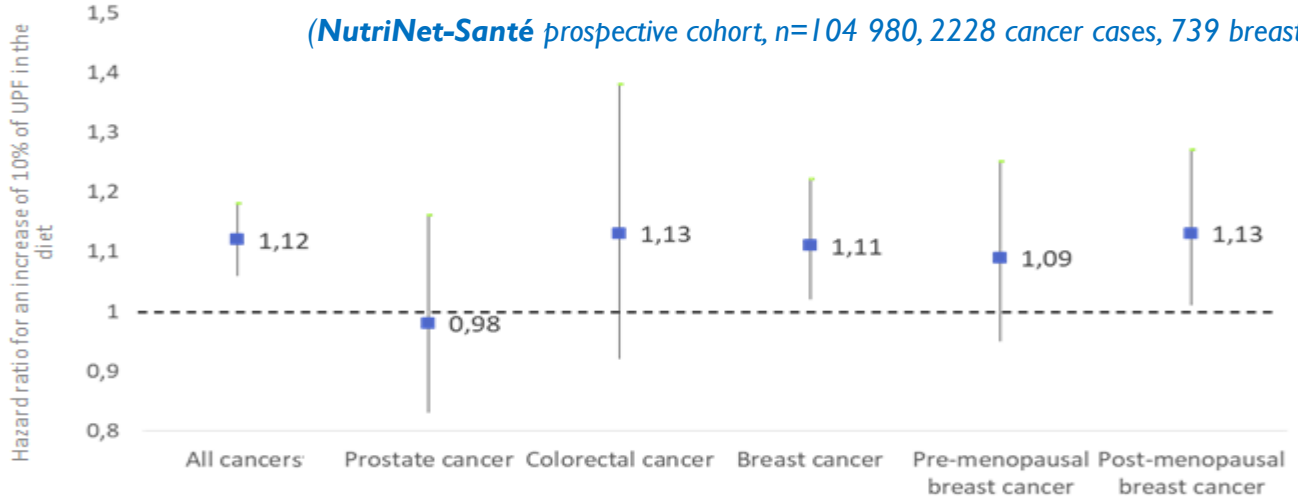
thebmj

Consumption of ultra-processed foods and cancer risk: results from NutriNet-Santé prospective cohort

Thibault Fiolet,[1] Bernard Srour,[1] Laury Sellem,[1] Emmanuelle Kesse-Guyot,[1] Benjamin Allès,[1] Caroline Méjean,[2] Mélanie Deschasaux,[1] Philippine Fassier,[1] Paule Latino-Martel,[1] Marie Beslay,[1] Serge Hercberg,[1,4] Céline Lavalette,[1] Carlos A Monteiro,[3] Chantal Julia,[1,4] Mathilde Touvier[1]

"A 10% increase in proportion of ultra-processed foods in the diet associated with a 12% significant increase in overall cancer risk and 11% for breast cancer risk"

*(**NutriNet-Santé** prospective cohort, n=104 980, 2228 cancer cases, 739 breast cancer cases)*



Fiolet & Srour et al, BMJ, 2018

UPF – CVD RISK

thebmj

Ultra-processed food intake and risk of cardiovascular disease: prospective cohort study (NutriNet-Santé)

Bernard Srour,[1] Léopold K Fezeu,[1] Emmanuelle Kesse-Guyot,[1] Benjamin Allès,[1] Caroline Méjean,[2] Roland M Andrianasolo,[1] Eloi Chazelas,[1] Mélanie Deschasaux,[1] Serge Hercberg,[1,3] Pilar Galan,[1] Carlos A Monteiro,[4] Chantal Julia,[1,3] Mathilde Touvier[1]

Models by disease type	Quarters of ultra-processed food consumption†				P trend	Continuous‡	P value
	First (low intake)	Second	Third	Four (high intake)			
All cardiovascular diseases							
No of cases/non-cases	446/25 950	410/26 008	330/25 996	223/25 796		1409/103 750	
Model 0	1	1.06 (0.93 to 1.22)	1.08 (0.93 to 1.24)	1.25 (1.06 to 1.47)	0.01	1.13 (1.06 to 1.21)	<0.001
Model 1	1	1.04 (0.91 to 1.19)	1.07 (0.93 to 1.23)	1.23 (1.04 to 1.45)	0.02	1.12 (1.05 to 1.20)	<0.001
Model 2	1	.05 (0.92 to 1.20)	1.08 (0.93 to 1.25)	1.25 (1.05 to 1.47)	0.02	1.13 (1.05 to 1.20)	<0.001
Model 3	1	1.03 (0.90 to 1.18)	1.05 (0.91 to 1.22)	1.20 (1.01 to 1.42)	0.05	1.11 (1.03 to 1.19)	0.003
Model 4	1	1.03 (0.90 to 1.18)	1.06 (0.90 to 1.23)	1.21 (1.02 to 1.45)	0.05	1.12 (1.04 to 1.20)	0.002
Model 5	1	1.05 (0.92 to 1.20)	1.08 (0.93 to 1.24)	1.26 (1.07 to 1.48)	0.01	1.13 (1.06 to 1.21)	<0.001
Model 6	1	1.04 (0.91 to 1.19)	1.06 (0.92 to 1.23)	1.23 (1.04 to 1.45)	0.03	1.12 (1.05 to 1.20)	0.001
Coronary heart diseases§							
No of cases/non-cases	208/26 188	194/26 224	166/26 160	97/25 922		665/104 494	
Model 0	1	1.08 (0.89 to 1.31)	1.19 (0.97 to 1.46)	1.23 (0.96 to 1.57)	0.04	1.15 (1.04 to 1.26)	0.006
Model 1	1	1.07 (0.87 to 1.30)	1.19 (0.97 to 1.46)	1 20 (0.93 to 1.53)	0.07	1.13 (1.02 to 1.24)	0.02
Model 2	1	1.07 (0.87 to 1.30)	1.20 (0.97 to 1.47)	1.22 (0.95 to 1.56)	0.05	1.14 (1.03 to 1.26)	0.01
Model 3	1	1.05 (0.86 to 1.28)	1.17 (0.95 to 1.44)	1.16 (0.90 to 1.49)	0.1	1.11 (1.00 to 1.23)	0.04
Model 4	1	1.05 (0.86 to 1.28)	1.17 (0.95 to 1.46)	1.18 (0.91 to 1.53)	0.1	1.12 (1.01 to 1.24)	0.03
Model 5	1	1.07 (0.88 to 1.31)	1.20 (0.97 to 1.47)	1.22 (0.96 to 1.57)	0.05	1.14 (1.03 to 1.26)	0.009
Model 6	1	1.06 (0.87 to 1.29)	1.18 (0.96 to 1.45)	1.18 (0.93 to 1.52)	0.08	1.12 (1.02 to 1.24)	0.02
Cerebrovascular diseases¶							
No of cases/non-cases	267/26 129	238/26 180	188/26 138	136/25 883		829/104 330	
Model 0	1	1.03 (0.87 to 1.23)	1.01 (0.84 to 1.22)	1.24 (1.00 to 1.53)	0.1	1.11 (1.02 to 1.21)	0.02
Model 1	1	1.01 (0.85 to 1.21)	0.99 (0.82 to 1.20)	1.24 (1.00 to 1.53)	0.1	1.11 (1.01 to 1.21)	0.02
Model 2	1	1.02 (0.86 to 1.22)	1.01 (0.84 to 1.22)	1.25 (1.01 to 1.55)	0.1	1.12 (1.02 to 1.22)	0.02
Model 3	1	1.00 (0.84 to 1.20)	0.99 (0.81 to 1.19)	1.21 (0.98 to 1.51)	0.2	1.10 (1.00 to 1.20)	0.04
Model 4	1	1.01 (0.84 to 1.21)	1.00 (0.82 to 1.21)	1.23 (0.98 to 1.54)	0.2	1.11 (1.01 to 1.22)	0.03
Model 5	1	1.02 (0.85 to 1.21)	1.00 (0.83 to 1.21)	1.26 (1.01 to 1.55)	0.1	1.11 (1.02 to 1.22)	0.01
Model 6	1	1.01 (0.85 to 1.21)	0.99 (0.82 to 1.20)	1.23 (1.00 to 1.53)	0.1	1.11 (1.01 to 1.21)	0.02

Srour et al, BMJ, 2019

UPF – MORTALITY RISK

JAMA Internal Medicine | Original Investigation

Association Between Ultraprocessed Food Consumption and Risk of Mortality Among Middle-aged Adults in France

Laure Schnabel, MD, MSc; Emmanuelle Kesse-Guyot, PhD; Benjamin Allès, PhD; Mathilde Touvier, PhD; Bernard Srour, PharmD; Serge Hercberg, MD, PhD; Camille Buscail, MD, PhD; Chantal Julia, MD, PhD

Table 3. Association Between the Proportion of Ultraprocessed Food in the Diet and Overall Mortality Risk in Study Participants

	Proportion of Ultraprocessed Food in the Diet (in Weight)		
Imputed Data	No. of Cases/Noncases	HR (95% CI)[d]	Continuous *P* Value[e]
Model 1[a]	602/43 949	1.20 (1.08-1.32)	<.001
Model 2[b]	602/43 949	1.15 (1.04-1.27)	.005
Model 3[c]	602/43 949	1.14 (1.04-1.27)	.008

JAMA Internal Medicine

Schnabel et al, JAMA Int Med, 2019

UPF – DEPRESSIVE SYMPTOMS

Prospective association between ultra-processed food consumption and incident depressive symptoms in the French NutriNet-Santé cohort

BMC Medicine

Moufidath Adjibade[1*], Chantal Julia[1,2], Benjamin Allès[1], Mathilde Touvier[1], Cédric Lemogne[3,4,5], Bernard Srour[1], Serge Hercberg[1,2], Pilar Galan[1], Karen E. Assmann[1] and Emmanuelle Kesse-Guyot[1]

Table 3 Association between ultra-processed food intake and incident depressive symptoms, NutriNet-Santé study

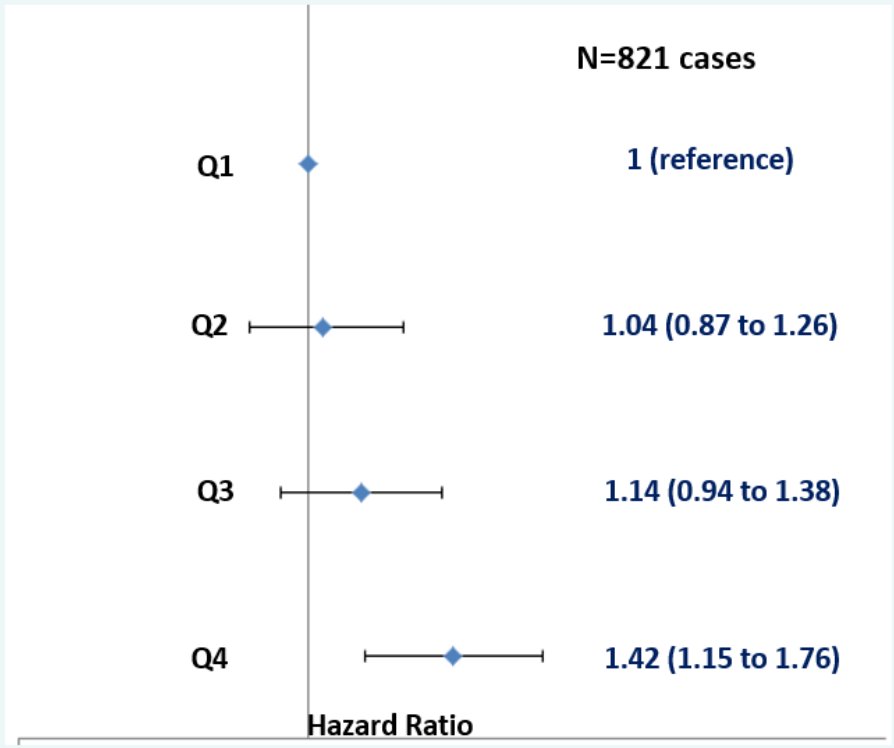
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	*P* trend	Continuous[a]	*P*[b]
UPF, range	0%–10%	10%–14%	14%–19%	19%–76%			
UPF, median (IQR)	7% (3%)	12% (2%)	16% (2%)	23% (8%)			
n	6682	6683	6683	6682		26,730	
Number of cases	491	459	557	714		2221	
Person years	21,597	21,097	20,468	19,918		83,080	
Model 1[c]	1 (ref)	0.90 (0.79; 1.02)	1.07 (0.94; 1.21)	1.31 (1.16; 1.47)	< 0.0001	1.23 (1.17; 1.29)	< 0.0001
Model 2[d]	1 (ref)	0.91 (0.80; 1.04)	1.09 (0.96; 1.23)	1.30 (1.15; 1.47)	< 0.0001	1.21 (1.15; 1.27)	< 0.0001
Model 3[e]	1 (ref)	0.91 (0.80; 1.04)	1.08 (0.95; 1.23)	1.29 (1.13; 1.47)	< 0.0001	1.22 (1.16; 1.29)	< 0.0001
Model 4[f]	1 (ref)	0.92 (0.81; 1.04)	1.09 (0.97; 1.24)	1.31 (1.16; 1.48)	< 0.0001	1.21 (1.15; 1.27)	< 0.0001
Model 5[g]	1 (ref)	0.88 (0.77; 1.00)	1.00 (0.88; 1.13)	1.13 (1.00; 1.28)	0.01	1.14 (1.09; 1.20)	< 0.0001
Model 6[h]	1 (ref)	0.88 (0.78; 1.00)	1.06 (0.94; 1.20)	1.27 (1.13; 1.44)	< 0.0001	1.21 (1.15; 1.27)	< 0.0001
Model 7[i]	1 (ref)	0.86 (0.76; 0.98)	1.00 (0.88; 1.13)	1.13 (1.00; 1.28)	0.01	1.15 (1.09; 1.21)	< 0.0001

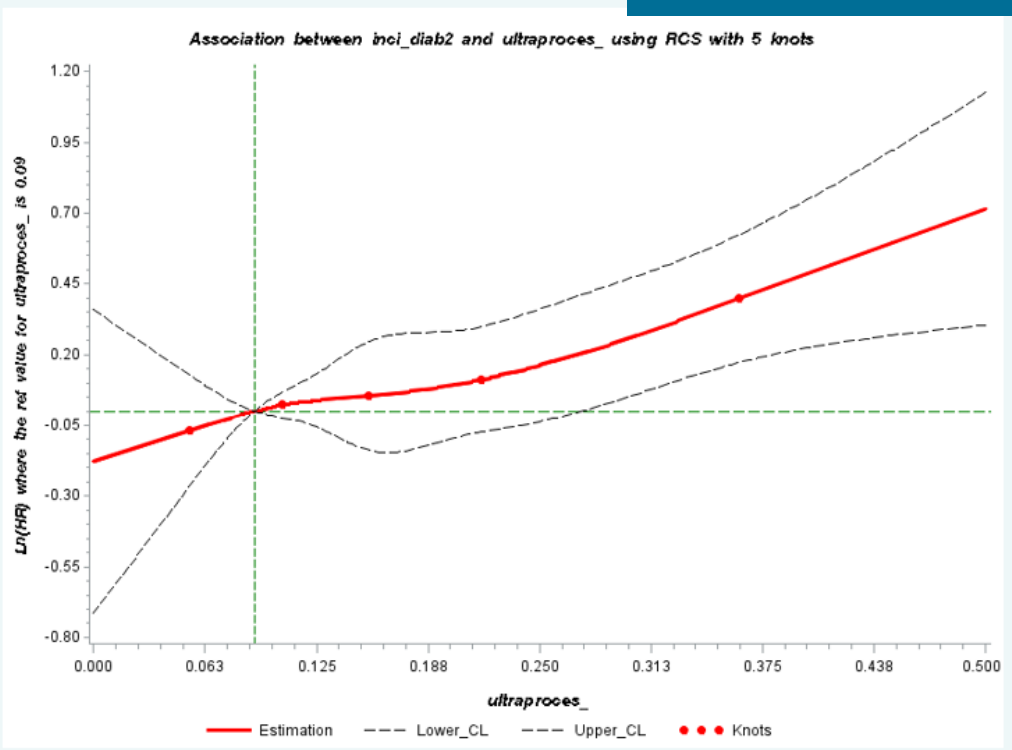
Adjibade et al, BMC Medicine, 2019

UPF – TYPE 2 DIABETES RISK

JAMA Internal Medicine

N=104 707





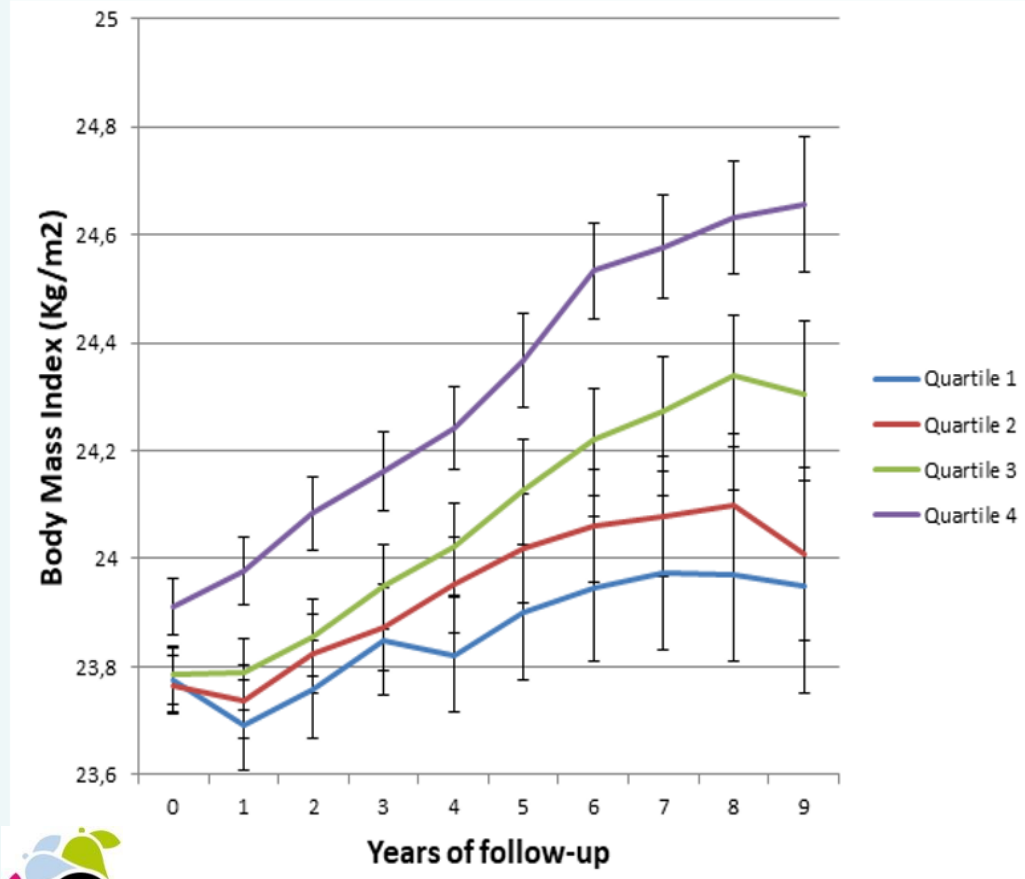
An absolute increment of 10 in the percentage of UPF in the diet was associated with a 20% increase in the risk of T2D (HR=1.20 (1.10 to 1.30), p<0.0001)

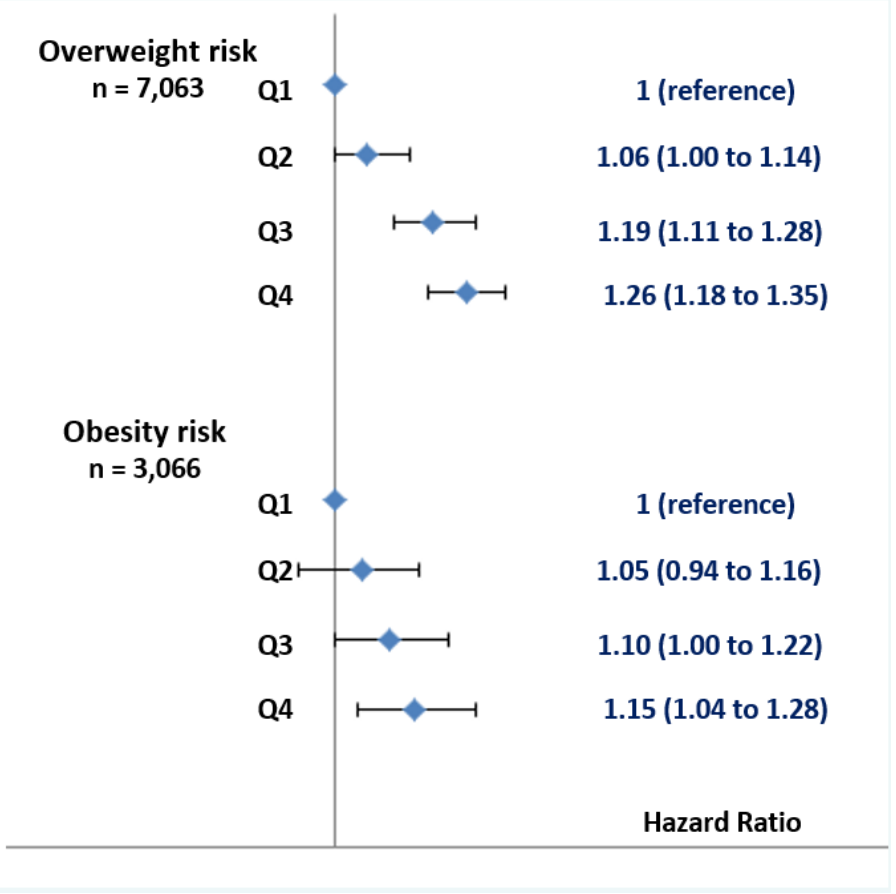
Srour et al, JAMA Int Med 2019

UPF – OVERWEIGHT, OBESITY AND WEIGHT CHANGE

PLOS MEDICINE

N=110,260





Srour&Beslay et al, PLOS Medicine 2020

UPF – GASTROINTESTINAL DISORDERS (CROSS-SECTIONAL)

AJG The American Journal of GASTROENTEROLOGY

Association Between Ultra-Processed Food Consumption and Functional Gastrointestinal Disorders: Results From the French NutriNet-Santé Cohort

Laure Schnabel, MPH[1,2], Camille Buscail, MD[1,2], Jean-Marc Sabate, MD, PhD[3,4], Michel Bouchoucha, MD[3], Emmanuelle Kesse-Guyot, PhD[1], Benjamin Allès, PhD[1], Mathilde Touvier, PhD[1], Carlos A. Monteiro, MD, PhD[5], Serge Hercberg, MD, PhD[1,2], Robert Benamouzig, MD, PhD[3] and Chantal Julia, MD, PhD[1,2]

Table 4 Association between proportion of ultra-processed food in the diet and functional gastrointestinal disorders in adults from the NutriNet-Santé cohort ($n = 33,343$)

Proportion of ultra-processed food in the diet (in weight)											
	Continuous			Quartiles[a]							
				Q1	Q2		Q3		Q4		
	aOR[b]	95% CI	p[c]		aOR	95% CI	aOR	95% CI	aOR	95% CI	p-trend[d]
IBS											
Model 1	1.08	[1.04–1.12]	<0.0001	Ref.	1.07	[0.97–1.19]	1.18	[1.06–1.30]	1.21	[1.09–1.34]	<0.0001
Model 2	1.09	[1.05–1.14]	<0.0001	Ref.	1.07	[0.97–1.19]	1.19	[1.07–1.32]	1.24	[1.12–1.38]	<0.0001
Model 3	1.10	[1.05–1.14]	<0.0001	Ref.	1.07	[0.97–1.19]	1.19	[1.07–1.32]	1.25	[1.12–1.39]	<0.0001
FC											
Model 1	–	–	–	Ref.	0.92	[0.80–1.05]	0.91	[0.79–1.04]	1.02	[0.89–1.16]	0.91
Model 2	–	–	–	Ref.	0.91	[0.80–1.04]	0.90	[0.78–1.03]	1.00	[0.87–1.15]	0.98
Model 3	–	–	–	Ref.	0.90	[0.79–1.03]	0.88	[0.77–1.02]	0.98	[0.85–1.12]	0.66
FDh											
Model 1	–	–	–	Ref.	0.79	[0.59–1.06]	0.89	[0.67–1.19]	1.02	[0.77–1.36]	0.77
Model 2	–	–	–	Ref.	0.77	[0.58–1.04]	0.85	[0.63–1.13]	0.94	[0.71–1.26]	0.82
Model 3	–	–	–	Ref.	0.77	[0.57–1.03]	0.84	[0.62–1.12]	0.92	[0.69–1.24]	0.70
FDy											
Model 1	1.13	[1.06–1.19]	<0.0001	Ref.	1.08	[0.91–1.27]	1.24	[1.06–1.46]	1.32	[1.12–1.55]	0.0002
Model 2	1.10	[1.04–1.17]	0.002	Ref.	1.07	[0.91–1.26]	1.22	[1.03–1.43]	1.26	[1.07–1.48]	0.002
Model 3	1.10	[1.03–1.17]	0.004	Ref.	1.07	[0.90–1.26]	1.21	[1.03–1.43]	1.25	[1.05–1.47]	0.004

aOR adjusted odds ratio, *95% CI* 95% confidence interval, *IBS* irritable bowel syndrome, *CF* functional constipation, *FDh* functional diarrhea, *FDy* functional dyspepsia
[a]Cut-offs for quartiles of UPFp were 9.7, 14.5, and 20.6%
[b]aOR for an increase of 10% of UPFp. Multivariable logistic regression models with continuous variable for UPFp performed only when p-trend < 0.05

Schnabel et al, Am J Gastroenterol 2018

SENSITIVITY ANALYSES

- In secondary analyses: unprocessed/minimally processed food consumption was associated with lower risks of cancer, CVD, mortality, T2D, overweight and obesity
- Robust associations after additional adjustment for various potential confounders, and in different strata of the population and taking into account the risk of reverse causality (exclusion of cases from the first 2-3 years)
- Adjustment for nutritional factors and the nutritional quality of the diet: slight variation but results remain significant → The nutritional quality only partially explained these associations

RECAP UPF-HEALTH STUDIES NUTRINET-SANTÉ

1st Author	Year	Country	Effective	Cohort	Outcome	Journal
Fiolet&Srour	2018	France	104 980	NutriNet-Santé	Cancer	BMJ
Schnabel	2018	France	43 949	NutriNet-Santé	Mortality	JAMA Int Med
Schnabel	2018	France	33 343	NutriNet-Santé	Gastro-intestinal disorders	Am J Gastro
Srour	2019	France	103 750	NutriNet-Santé	Cardiovascular diseases	BMJ
Adjibade	2019	France	26 730	NutriNet-Santé	Depressive symptoms	BMC Med
Srour	2019	France	104 707	NutriNet-Santé	Type 2 Diabetes	JAMA Int Med
Srour&Beslay	2020	France	110 260	NutriNet-Santé	Overweight and obesity	Plos Med

OTHER PROSPECTIVE STUDIES

1st Author	Year	Country	Effective	Cohort	Outcome	Journal
Rauber	2015	Brazil	345	Sao Leopoldo (children)	Lipid profiles	Nutr Metab Cardiovasc
Mendonça	2016	Spain	8451	SUN	Overweight/obesity	Am J Clin Nutr
Mendonça	2017	Spain	14790	SUN	Hypertension	Am J Hypertens
Sandoval-Insausti	2019	Spain	1822	Seniors-Enrica	Frailty	J Gerontol Ser A
Gomez-Donoso	2019	Spain	14907	SUN	Depression	Eur J Nutr
Rico-Compa	2019	Spain	19899	SUN	Mortality	BMJ
Kim	2019	USA	11898	NHANES III	Mortality	Public Health Nutr
Blanco-Rojo	2019	Spain	11898	Enrica	Mortality	Mayo Clin Proc

OTHER PROSPECTIVE STUDIES

1st Author	Year	Country	Effective	Cohort	Outcome	Journal
Machado Azeredo	2019	Brazil	2190	Pelotas Birth Cohort (children)	Asthma - Null result	Pediatr Allergy Immunol
Canhada	2019	Brazil	11827	ELSA-Brasil cohort	Overweight, obesity	PHN
Costa	2019	Brazil	307	Sao Leopoldo (enfants)	BMI change, anthropometry, metabolism	Nutr Metab Cardiovasc Dis
Zhong	2020	USA	91891	PLCO: Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial	Overall cardiovascular and heart disease mortality	Preprint
Blanco-Rojo	2019	Spain	93599	ENRICA	Mortality	Mayo Clin Proc
Leffa	2020	Brazil	308	Porto-Alegre (children)	Blood lipids	Brit J Nut
Sandoval-Insausti	2020	Spain	652	Seniors-Enrica	Abdominal Obesity	Nutrients

+ many others ongoing worldwide!

RECENT META-ANALYSES ON UPF AND HEALTH

- Pagliai, G., Dinu, M., Madarena, M., Bonaccio, M., Iacoviello, L., & Sofi, F. (2020). Consumption of ultra-processed foods and health status: A systematic review and meta-analysis. British Journal of Nutrition, 1-11. doi:10.1017/S0007114520002688

  *Main findings: "For prospective cohort studies evaluating a total population of 183 491 participants followed for a period ranging from 3·5 to 19 years, highest UPF consumption was found to be associated with increased risk of all-cause **mortality** in five studies (risk ratio (RR) 1·25, 95 % CI 1·14, 1·37; P < 0·00001), increased risk of **CVD** in three studies (RR 1·29, 95 % CI 1·12, 1·48; P = 0·0003), **cerebrovascular disease** in two studies (RR 1·34, 95 % CI 1·07, 1·68; P = 0·01) and **depression** in two studies (RR 1·20, 95 % CI 1·03, 1·40; P = 0·02)."*

- Melissa M. Lane, Jessica A. Davis, Sally Beattie, Clara Gómez-Donoso, Amy Loughman, Adrienne O'Neil, Felice Jacka, Michael Berk, Richard Page, Wolfgang Marx, Tetyana Rocks. Ultraprocessed food and chronic noncommunicable diseases: A systematic review and meta-analysis of 43 observational studies. Obesity Reviews Nov 2020

  Forty-three observational studies were included (N = 891,723): 21 cross-sectional, 19 prospective, two case-control and one conducted both a prospective and cross-sectional analysis. Meta-analysis demonstrated consumption of ultraprocessed food was associated with increased risk of overweight (odds ratio: 1.36; 95% confidence interval [CI], 1.23-1.51; P < 0.001), obesity (odds ratio: 1.51; 95% CI, 1.34-1.70; P < 0.001), abdominal obesity (odds ratio: 1.49; 95% CI, 1.34-1.66; P < 0.0001), all-cause mortality (hazard ratio: 1.28; 95% CI, 1.11-1.48; P = 0.001), metabolic syndrome (odds ratio: 1.81; 95% CI, 1.12-2.93; P = 0.015) and depression in adults (hazard ratio: 1.22; 95% CI, 1.16-1.28, P < 0.001) as well as wheezing (odds ratio: 1.40; 95% CI, 1.27-1.55; P < 0.001) but not asthma in adolescents (odds ratio: 1.20; 95% CI, 0.99-1.46; P = 0.065). In addition, consumption of ultraprocessed food was associated with cardiometabolic diseases, frailty, irritable bowel syndrome, functional dyspepsia and cancer (breast and overall) in adults while also being associated with metabolic syndrome in adolescents and dyslipidaemia in children.

- Askari, M., Heshmati, J., Shahinfar, H. et al. Ultra-processed food and the risk of overweight and obesity: a systematic review and meta-analysis of observational studies. Int J Obes (2020). https://doi.org/10.1038/s41366-020-00650-z

  *Main findings: Fourteen studies (one cohort study and thirteen cross-sectional studies) were included in this review. A significant association was identified between ultra-processed food intake and **obesity** (pooled effect size: 1.26; 95% CI: 1.13, 1.41, p < 0.001).*

RCT

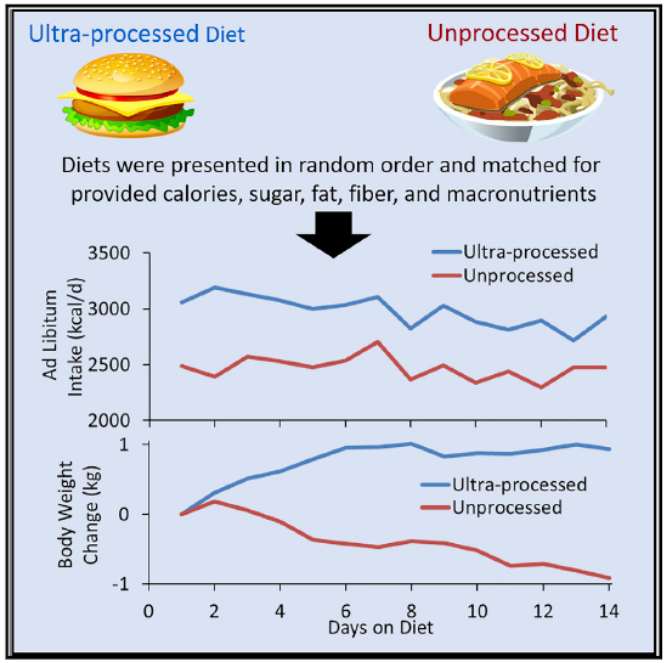
- Long-term RCT not feasible for ethical and practical reasons for lifestyle factors expected to be potentially deleterious
- A short-term RCT (2 * 14 days) showed that an ultra-processed diet increased food intake (ad libitum) and weight (Hall et al., 2019)

Clinical and Translational Report

Cell Metabolism

Ultra-Processed Diets Cause Excess Calorie Intake and Weight Gain: An Inpatient Randomized Controlled Trial of *Ad Libitum* Food Intake

Graphical Abstract



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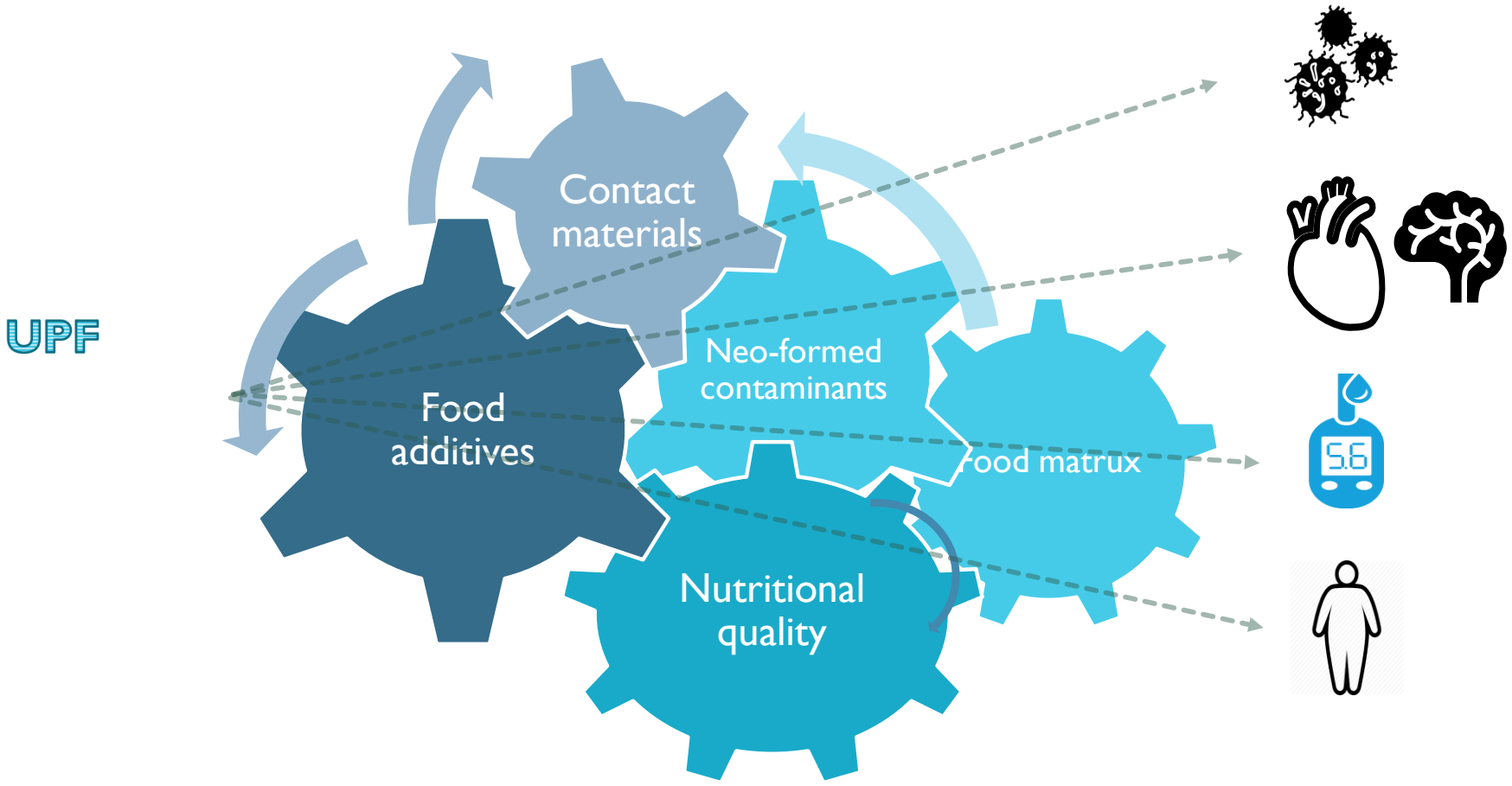
In Brief

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.

MECANISTIC HYPOTHESES



TAKE HOME MESSAGES (1/2):

- Accumulating epidemiological and experimental evidence linking ultra-processing (/ "ultra-formulation") and potential adverse health outcomes (>20 prospective epidemiological studies)

→ Concrete impact on public health policies

- ✓ E.g. :Parliamentary inquiry commission on industrial food in France in 2018-2019
- ✓ Modification of national and international dietary guidelines *(WHO-FAO report 2019, reco France, Brazil…)*

- Research perspectives:
  - To replicate these results in other large-scale cohorts, well designed and taking into account a wide range of confounders + short-term RCT
  - To investigate the biological plausibility of associations through experimental studies and mechanistic epidemiology to understand the mechanisms involved: nutritional aspects, transformation processes, formulation (additives and other substances), contact materials →bring together arguments in favor of causality

Perspectives: research program of EREN on food processing

Équipe de Recherche en Épidémiologie Nutritionnelle

Formulation

- **Additives +++**
  - Chronic disease risk in humans?
  - Potential cocktail effects?
- **Other ingredients**
  - Maltodextrin, inversted sugars, hydrogenated oils, etc.
  - Addes sugars
  - Formulation of meat substitutes

Process

- **Processes**
  - Unitary operations
    →INNOV process Score
  - Modification of food structure/matrix
  - Fermentation
  - Context of transformation (at home vs industrial)
- **Neoformed compounds**
  - Acrylamid, acrolein, furanes, etc.
  - Trans fatty acids
  - AGEs

Contact materials

- **Food packaging**
  - Plastics
  - Cardboard
  - Etc.
- **Culinary practices**
  - Microwave heating of plastic containers, etc.

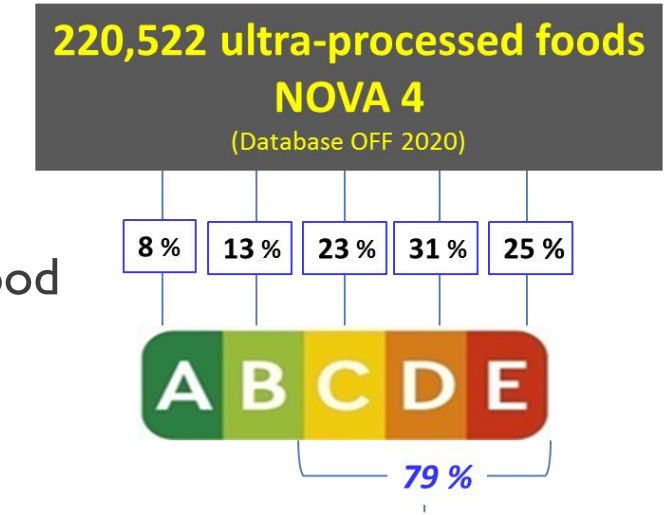
+relative share of these factors and nutritinoal and toxicological quality / organic food and UPF / new WCRF score including UPF / mechanistic understanding of UPF-health / Social sciences / Environnemental impact of UPF and sustainability

TAKE HOME MESSAGES (2/2):

While waiting for additional evidence from ongoing **research** on the impact of food processing on health and underlying mechanisms…

Practical advice for consumers = official public health recommendations in France and several countries:

- 1) Choose foods of better **nutritional quality** (highest level of evidence regarding health impact)→ NutriScore
- 2) Consider two other dimensions (correlated but not colinear) to choose food products:
  - Prefer **minimally processed / unprocessed foods**, limit food additives
  - Prefer **organic products** when possible



Thank you for your attention!

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