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You are what you eat, are you? How to interpret the evidence from nutrition epidemiology studies – PART 1
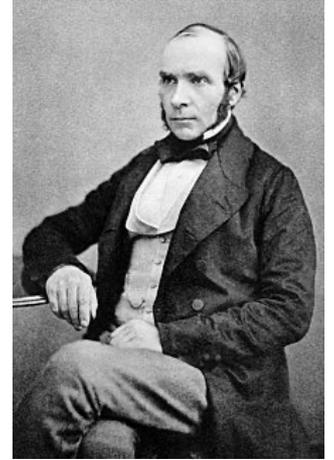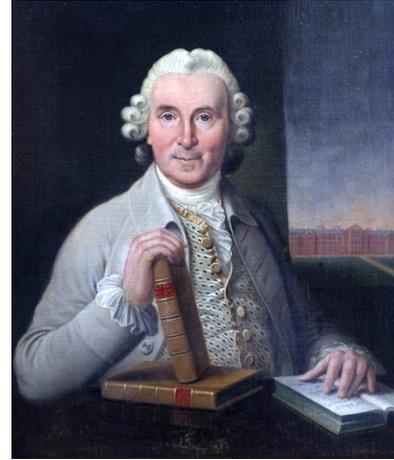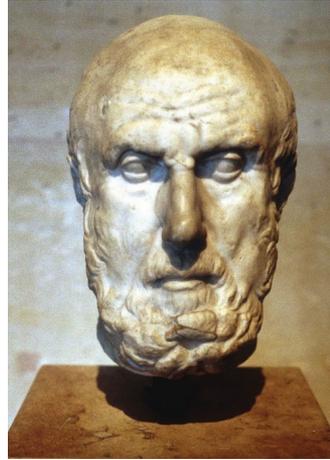
Layout

A bit of history

Determinants of dietary intake

Diet and NCDs: the different study types

- Ecological / geographical

- Cross-sectional

- Prospective

- Interventions

How food fed epidemiological methods

A BIT OF HISTORY

Huang Di (2600 BC)

Huang Di asked, "I've heard that in the days of old everyone lived one hundred years without showing the usual signs of aging. In our time, however, people age prematurely, living only fifty years. Is this due to a change in the environment, or is it because people have lost the correct way of life?"

Qi Bo replied, "In the past, people practiced the Tao, the Way of Life. They … **ate a balanced diet at regular times**, arose and retired at regular hours, avoided overstressing their bodies and minds, … thus, it is not surprising that they lived over one hundred years."
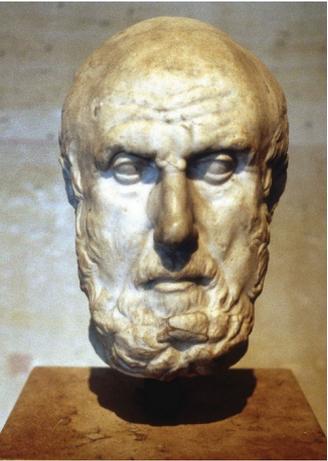
"These days, people have changed their way of life. They drink wine as it were water,... They **fail to regulate their lifestyle and diet**, and sleep improperly. So it is not surprising that they look old at fifty and die soon after."

Hippocrates of Cos (400 BC)

Let food be thy medicine: wrongly attributed to him.

On Regimen in Acute Diseases

One must determine by such marks as these, when sweet, strong, and dark wine, hydromel, water and oxymel, should be given in acute diseases. Wherefore the sweet affects the head less than the strong, attacks the brain less, evacuates the bowels more than the other, but induces swelling of the spleen and liver; it does not agree with bilious persons, for it causes them to thirst; it creates flatulence in the upper part of the intestinal canal, but does not disagree with the lower part, as far as regards flatulence; and yet flatulence engendered by sweet wine is not of a transient nature, but rests for a long time in the hypochondria.

James Lind - The first clinical trial (1747)

192 *Of the prevention of the scurvy.* Part II.

have them. They all in general had putrid gums, the spots and lassitude, with weakness of their knees. They lay together in one place, being a proper apartment for the sick in the fore-hold; and had one diet common to all, *viz.* water-gruel sweetened with sugar in the morning; fresh mutton-broth often times for dinner; at other times puddings, boiled biscuit with sugar, &c.; and for supper, barley and raisins, rice and currants, sago and wine, or the like. Two of these were ordered each a quart of cyder a-day. Two others took twenty-five gutts of *elixir vitriol* three times a-day, upon an empty stomach; using a gargle strongly acidulated with it for their mouths. Two others took two spoonfuls of vinegar three times a-day, upon an empty stomach; having their gruels and their other food well acidulated with it, as also the gargle for their mouth. Two of the worst patients, with the tendons in the ham rigid, (a symptom none of the rest had), were put under a course of sea-water. Of this they drank half a pint every day, and sometimes more or less as it operated, by way of gentle physic. Two others had each two oranges and one lemon given them every day. These they eat with greediness,

Chap. IV. *Of the prevention of the scurvy.* 193

diness, at different times, upon an empty stomach. They continued but six days under this course, having consumed the quantity that could be spared. The two remaining patients, took the bigness of a nutmeg three times a-day, of an electuary recommended by an hospital-surgeon, made of garlic, mustard-seed, *rad. raphan.* balsam of *Peru*, and gum myrrh; using for common drink, barley-water well acidulated with tamarinds; by a decoction of which, with the addition of *cremor tartar*, they were gently purged three or four times during the course.

The consequence was, that the most sudden and visible good effects were perceived from the use of the oranges and lemons; one of those who had taken them, being at the end of six days fit for duty. The spots were not indeed at that time quite off his body, nor his gums sound; but without any other medicine, than a gargarism of *elixir vitriol*, he became quite healthy before we came into *Plymouth*, which was on the 16th of *June*. The other was the best recovered of any in his condition; and being now deemed pretty well, was appointed nurse to the rest of the sick.

B b

John Snow – geographical epidemiology (1854)

"I found that nearly all the deaths had taken place within a short distance of the pump ... With regard to the deaths ... there were sixty-one instances in which I was informed that the deceased persons used to drink the water from Broad Street, either constantly or occasionally..."

"The result of the inquiry then was that there has been no particular outbreak or increase of cholera, in this part of London, except among the persons who were in the habit of drinking water of the above-mentioned pump-well. I had an interview with the Board of Guardians of St. James parish, ... the handle of the pump was removed the following day."
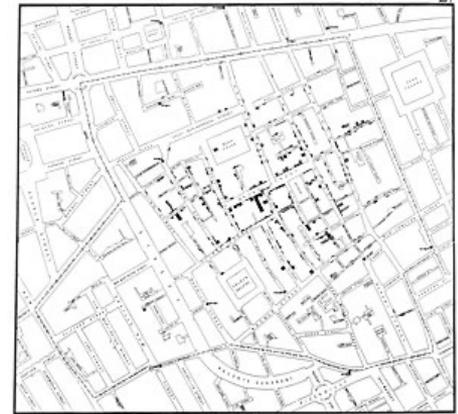
Determinants of dietary intake
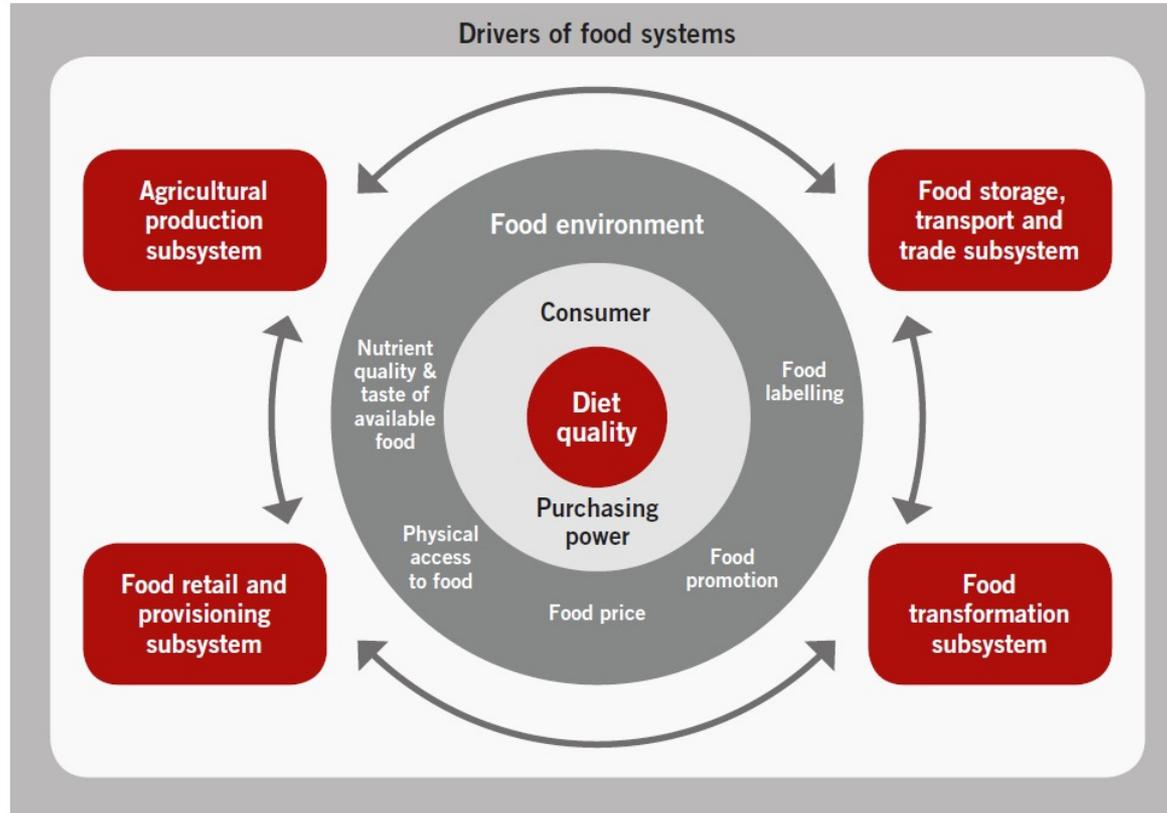
Food expenditures, 2012, % of budget

www.ers.usda.gov/data-products/food-expenditures.aspx
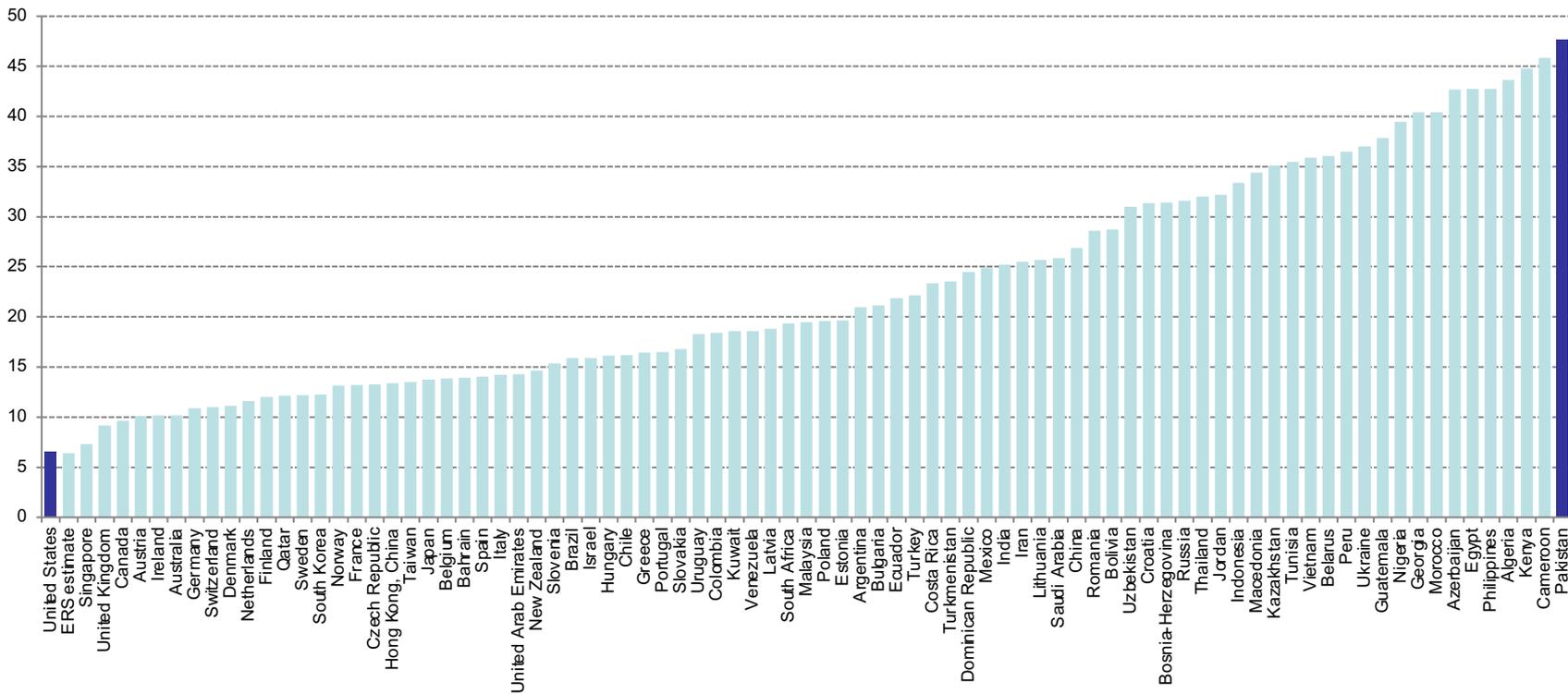
The War in Ukraine Is Creating the Greatest Global Food Crisis Since WWII, the U.N. Says

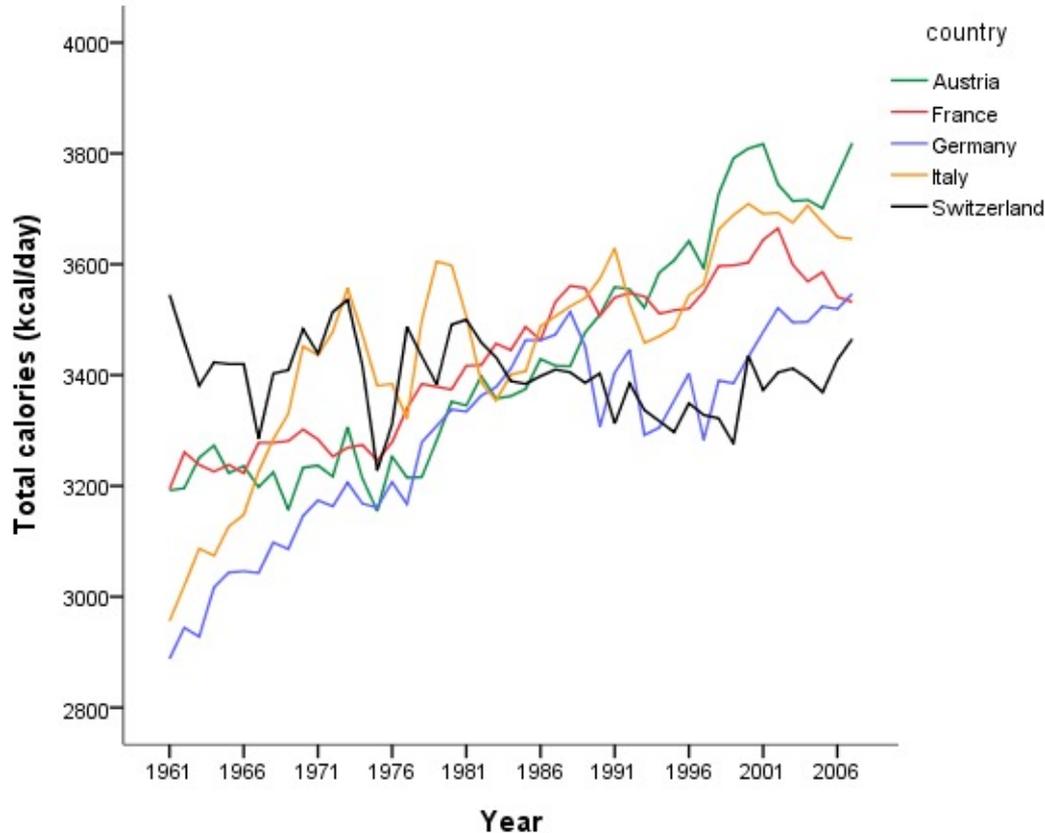BY **EDITH M. LEDERER / AP**   MARCH 30, 2022 12:20 AM EDT

The war in Ukraine is turning "the breadbasket of the world to breadlines" for millions of its people, while devastating countries like Egypt that normally gets 85% of its grain from Ukraine and Lebanon that got 81% in 2020, Beasley said.

Ukraine and Russia produce 30% of the world's wheat supply, 20% of its corn and 75%-80% of the sunflower seed oil. The World Food Program buys 50% of its grain from Ukraine, he said.

As Russia "chokes off Ukrainian exports," food prices are skyrocketing, with wheat prices rising between 20% and 50% so far this year, she said.

"We are particularly concerned about countries like Lebanon, Pakistan, Libya, Tunisia, Yemen and Morocco which rely heavily on Ukrainian imports to feed their population," Sherman said.

https://time.com/6162598/ukraine-war-food-shortage/

Trends in caloric availability

Guerra et al. *Eur J Clin Nutr*. 2012;66:273-5

Trends in vegetable oil availability

Guerra et al. *Eur J Clin Nutr*. 2012;66:273-5
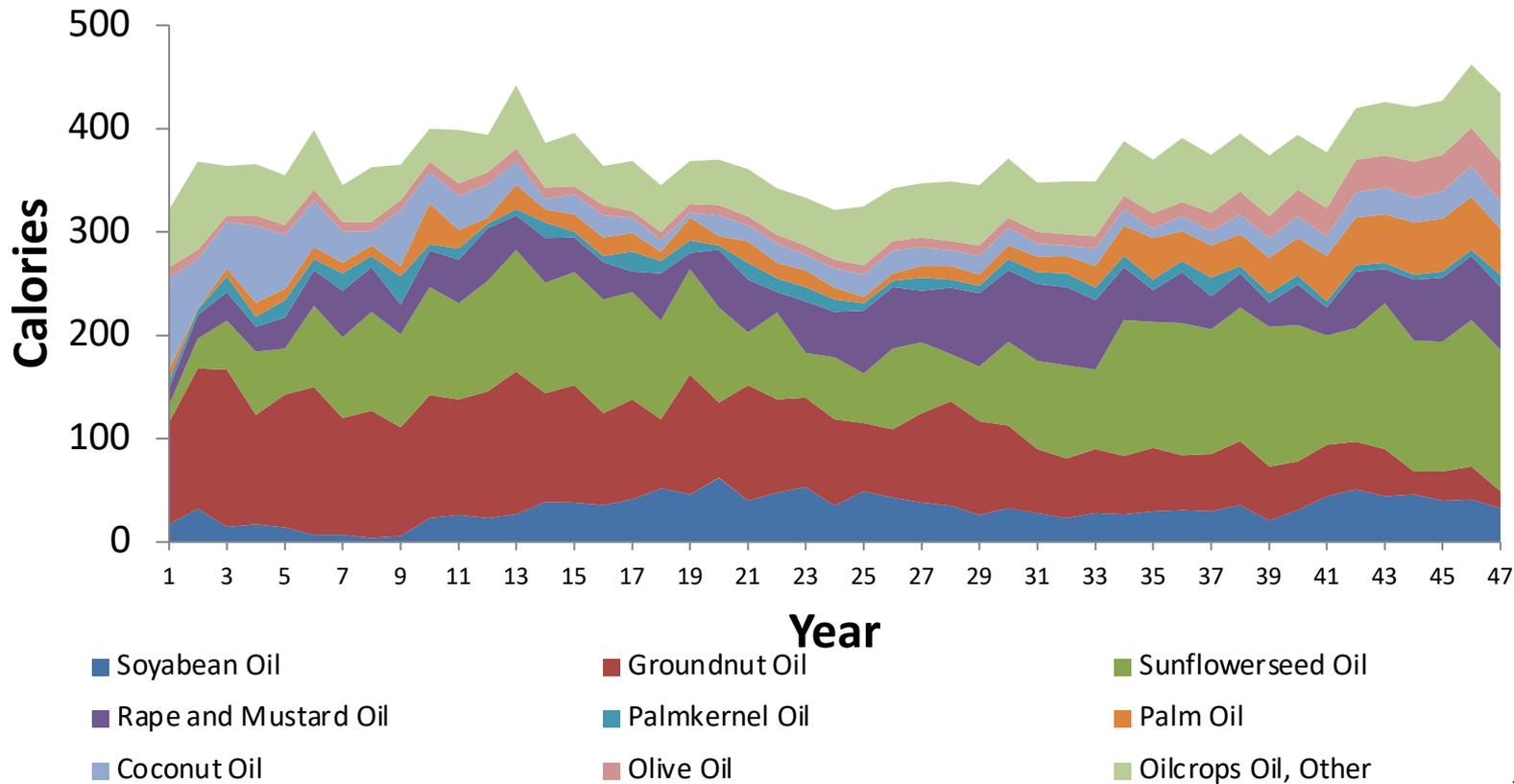
Different types of studies

DIET AND NCDs

A major burden
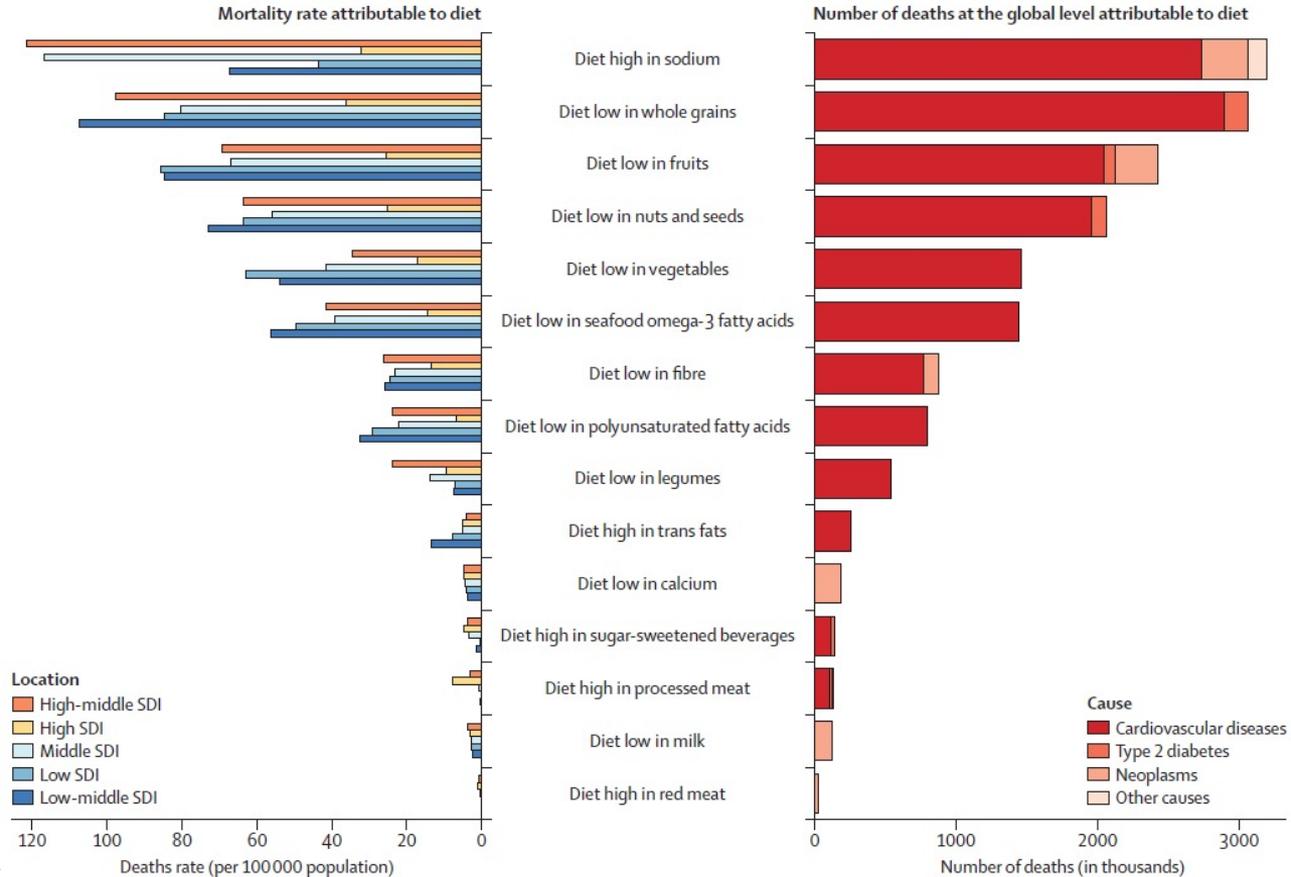
GBD 2017 Diet collaborators, *Lancet* 2019;393:1958–72

And many possible markers

Individual foods: beef, fish, bananas, bread, water…

Food categories: meat, dairy, fruit, vegetables…

Nutrients: protein, lipids, vitamins, minerals

Other: AA, flavonoids, phytosterols, polyphenols…

**Non-food**: additives, pollutants, microplastics, toxins…

Dietary patterns: *a priori* or *a posteriori*…

Compliance to dietary guidelines: yes/no, score…

Behaviours: number and timing of meals, fasting, diets…

Ecological correlations

Food balance sheets
production
+ imports
- exports
- waste
- animal consumption
= food availability

Hoerr et al. *J Epidemiol Glob Health* 2017;7:81-89.
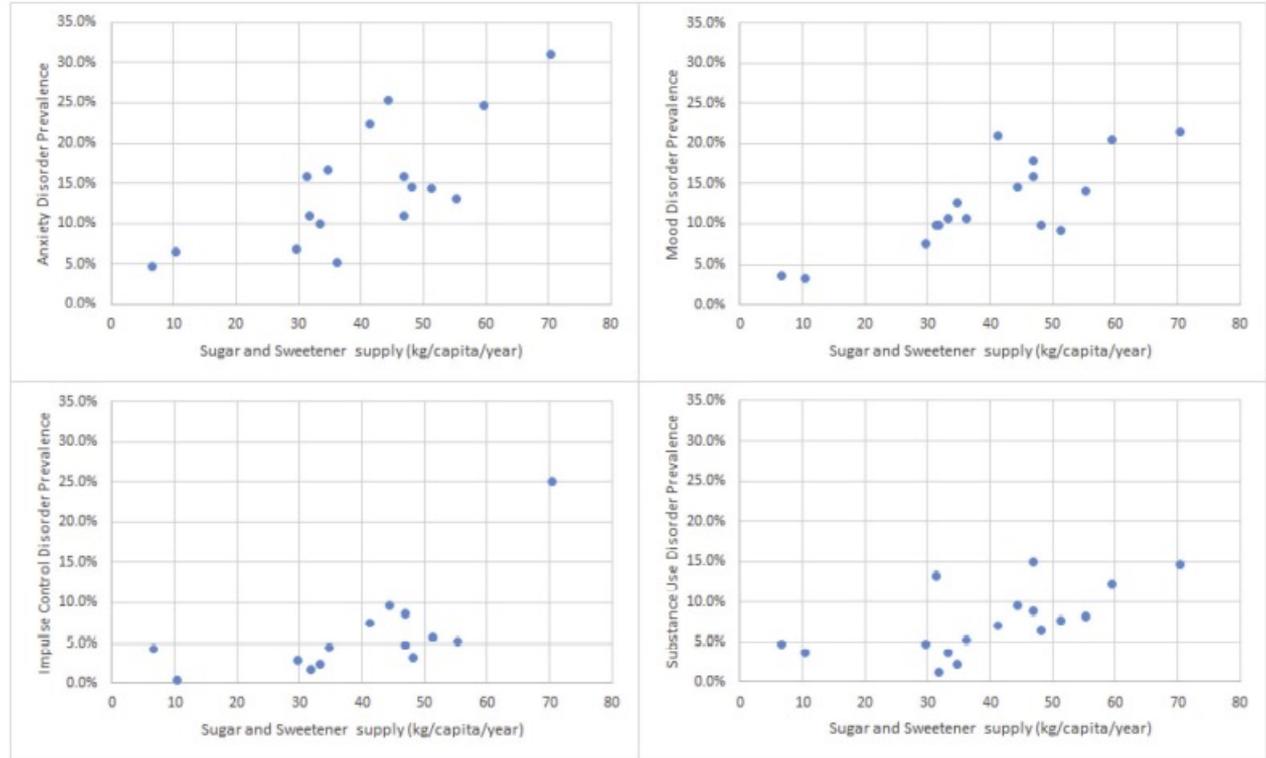
Ecological temporal correlations

	Total mortality	Diseases of the circulatory system	Ischemic heart disease	Cerebrovascular diseases
Total energy	0.265	0.254	0.193	0.266
Animal products				
All	0.388	0.468	0.730	0.373
Meat	0.357	0.431	0.707	0.335
Fish	−0.905	−0.908	−0.681	−0.932
Milk	0.302	0.397	0.534	0.329
Animal fats	0.567	0.606	0.754	0.543
Vegetal products				
All	−0.479	−0.578	−0.902	−0.460
Cereals	0.074	−0.001	−0.127	0.041
Sugar/sweeteners	−0.762	−0.812	−0.952	−0.737
Vegetable oils	−0.429	−0.479	−0.781	−0.374
Fruits	0.855	0.874	0.889	0.834
Vegetables	−0.519	−0.470	−0.125	−0.521
Alcoholic beverages	0.815	0.838	0.789	0.801

Geographic associations

SSBs

Obesity

Overlap

Joost et al. *Nutr Diabetes* 2019;9(1):35
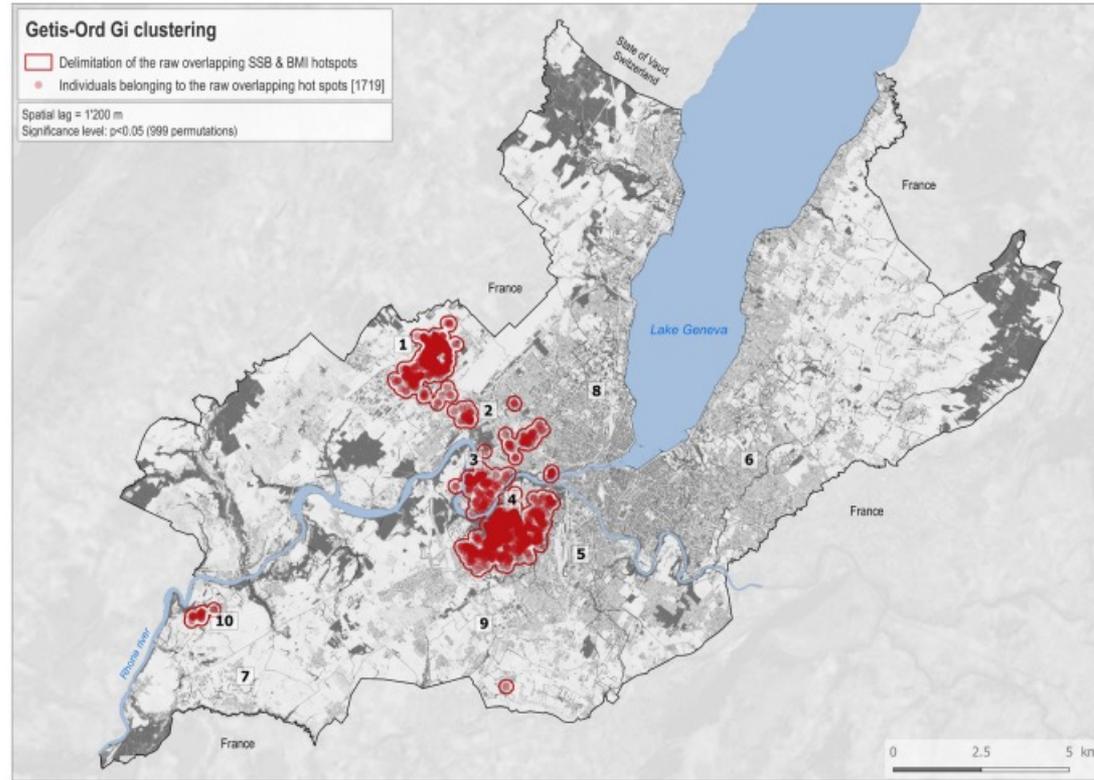
Ecological correlations

Easy to perform

Aggregated data available

Hypotheses-making

Wide range in consumption or disease rates needed

Correlation is not causation

Prone to confounding

Cross-sectional studies

Dietary patterns

- Hypothesis-oriented or *a priori*: selected beneficial foods
- Naïve or *a posteriori*: determined by dimension reduction methods (PCA, RRR, cluster analysis)

	Western	Mediterranean	Sweet-Dairy
Fries	0.559	−0.065	−0.070
Sausage	0.458	−0.012	0.092
Dried sausage, salami	0.453	−0.083	0.142
Burger	0.421	0.079	0.004
Pizza	0.405	0.052	0.060
White bread	0.402	−0.156	0.062
Beer	0.381	−0.113	−0.096
Steaks	0.368	0.110	−0.066
Pâté, terrine	0.367	−0.017	0.097
Croissant, pastry	0.366	−0.064	0.077
Ham, stew	0.365	0.076	0.076
Roast chicken	0.361	0.033	−0.038
Fried fish	0.356	0.076	−0.019
Sweetened beverages	0.339	−0.093	0.079
Ravioli	0.331	0.101	0.120
Mayonnaise (as condiment)	0.325	−0.063	0.197
Cervelas (sausage)	0.324	−0.081	−0.025
Pasta	0.316	0.117	0.122
Carrots	−0.014	0.485	0.059
Green beans, spinach	0.128	0.468	−0.145
Lean fish	−0.039	0.457	−0.032
Cauliflower, broccoli	0.023	0.448	−0.009
Tomatoes	0.151	0.433	−0.216
Green salad	0.043	0.404	−0.017
Salmon (smoked or fresh)	0.020	0.392	−0.003
Kiwi	−0.177	0.389	0.058
Berries	0.078	0.363	−0.083
Olive oil	−0.013	0.347	0.046
Shrimps, sea food	0.187	0.346	−0.153
Peach, nectarine, apricot, melon	0.113	0.345	−0.175
Chicken breast	0.011	0.344	−0.061
Banana, apple, pear, plum, grapes	−0.168	0.338	0.196
Wheat semolina, couscous	0.023	0.331	0.113
Peas, corn	0.282	0.324	−0.050
Avocado	0.030	0.322	0.052
Dressing (as condiment)	0.037	0.314	0.044

Cross-sectional studies

	Major Depressive Disorder Subtypes						
	Current Atypical OR (95CI)	Current Melancholic OR (95CI)	Current Unspecified OR (95CI)	Remitted Atypical OR (95CI)	Remitted Melancholic OR (95CI)	Remitted Unspecified OR (95CI)	Never Depressed
Model 2							
Western	1.44 * (1.05, 1.96)	0.64 ** (0.45, 0.90)	1.07 (0.86, 1.34)	1.05 (0.87, 1.26)	0.87 * (0.76, 1.00)	0.98 (0.88, 1.09)	1 (ref.)
Mediterranean	1.09 (0.82, 1.45)	0.83 (0.62, 1.10)	0.93 (0.76, 1.13)	1.00 (0.85, 1.18)	1.01 (0.89, 1.13)	1.00 (0.91, 1.10)	1 (ref.)
Sweet-Dairy	0.97 (0.72, 1.32)	1.39 * (1.03, 1.88)	0.97 (0.79, 1.19)	0.94 (0.80, 1.11)	1.03 (0.91, 1.17)	0.99 (0.90, 1.09)	1 (ref.)

Cross-sectional studies

Mostly case-control or association

NO causality

Considerable risk of bias

- Information/recall
- Social desirability
- Sampling

Hypothesis-developping

Should not be disregarded

Prospective studies

Glycemic index (GI)
- Capacity to increase glucose levels after consumption
- High GI: white bread, sugary beverages, potatoes
- Low GI: pulses, pasta

Cancer	N cases	Carbo-hydrate	1 HR	2 HR	95% CI	3 HR	95% CI	4 HR	95% CI	5 HR	95% CI	P trend$
Tongue	76	High GI	1	0.75	(0.37–1.53)	0.81	(0.40–1.64)	0.66	(0.31–1.40)	0.59	(0.25–1.36)	0.218
		Low GI	1	1.59	(0.77–3.28)	1.26	(0.58–2.75)	0.99	(0.43–2.30)	1.60	(0.74–3.46)	0.585
Stomach	146	High GI	1	0.63	(0.38–1.05)	0.68	(0.41–1.14)	0.61	(0.36–1.05)	0.51	(0.27–0.94)	0.045
		Low GI	1	1.18	(0.69–2.03)	1.21	(0.70–2.11)	1.10	(0.62–1.94)	1.36	(0.78–2.37)	0.395
Colon	441	High GI	1	1.02	(0.74–1.41)	1.29	(0.94–1.77)	1.18	(0.85–1.66)	1.71	(1.19–2.44)	0.004
		Low GI	1	0.94	(0.71–1.25)	0.86	(0.64–1.16)	0.77	(0.56–1.05)	0.75	(0.54–1.03)	0.032

Prospective studies
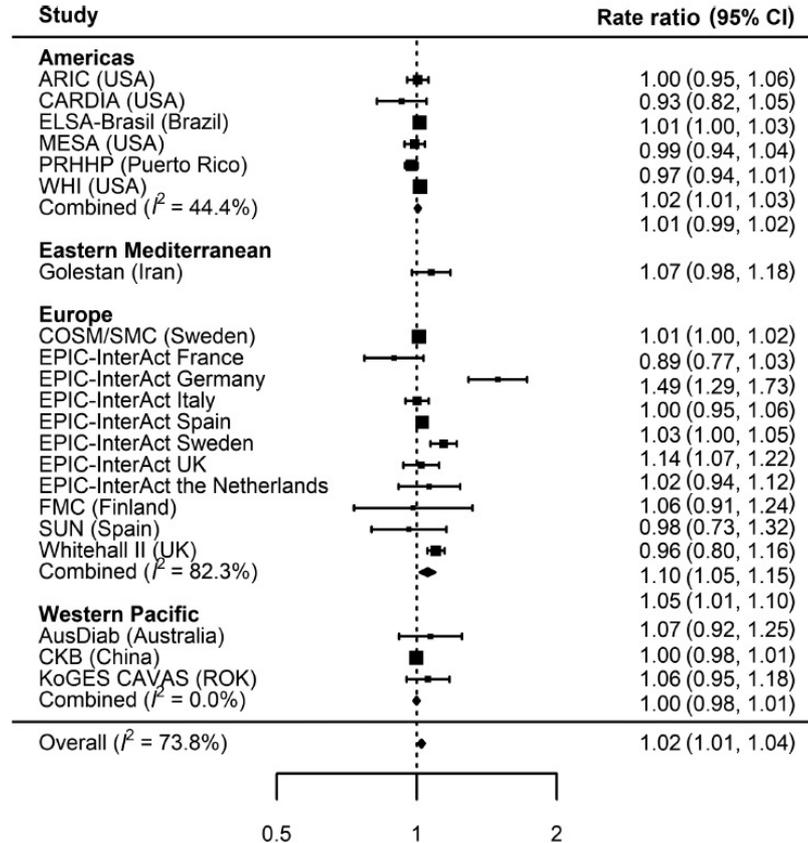
Meta-analysis

- Grouping the information from several prospective studies
- Increased overall sample size, combined effect, heterogeneity, publication bias...

Study	Rate ratio (95% CI)
Americas	
ARIC (USA)	1.00 (0.95, 1.06)
CARDIA (USA)	0.93 (0.82, 1.05)
ELSA-Brasil (Brazil)	1.01 (1.00, 1.03)
MESA (USA)	0.99 (0.94, 1.04)
PRHHP (Puerto Rico)	0.97 (0.94, 1.01)
WHI (USA)	1.02 (1.01, 1.03)
Combined ($I^2 = 44.4\%$)	1.01 (0.99, 1.02)
Eastern Mediterranean	
Golestan (Iran)	1.07 (0.98, 1.18)
Europe	
COSM/SMC (Sweden)	1.01 (1.00, 1.02)
EPIC-InterAct France	0.89 (0.77, 1.03)
EPIC-InterAct Germany	1.49 (1.29, 1.73)
EPIC-InterAct Italy	1.00 (0.95, 1.06)
EPIC-InterAct Spain	1.03 (1.00, 1.05)
EPIC-InterAct Sweden	1.14 (1.07, 1.22)
EPIC-InterAct UK	1.02 (0.94, 1.12)
EPIC-InterAct the Netherlands	1.06 (0.91, 1.24)
FMC (Finland)	0.98 (0.73, 1.32)
SUN (Spain)	0.96 (0.80, 1.16)
Whitehall II (UK)	1.10 (1.05, 1.15)
Combined ($I^2 = 82.3\%$)	1.05 (1.01, 1.10)
Western Pacific	
AusDiab (Australia)	1.07 (0.92, 1.25)
CKB (China)	1.00 (0.98, 1.01)
KoGES CAVAS (ROK)	1.06 (0.95, 1.18)
Combined ($I^2 = 0.0\%$)	1.00 (0.98, 1.01)
Overall ($I^2 = 73.8\%$)	1.02 (1.01, 1.04)

0.5   1   2

Prospective studies

Establish causality

Multiple hypotheses can be tested

Hard to conduct (sample size, follow-up)

Need replication

- Dietary behaviours

- Dietary change

Main source of evidence to establish dietary guidelines

Intervention studies

7447 people randomized into:

- Mediterranean diet + nuts
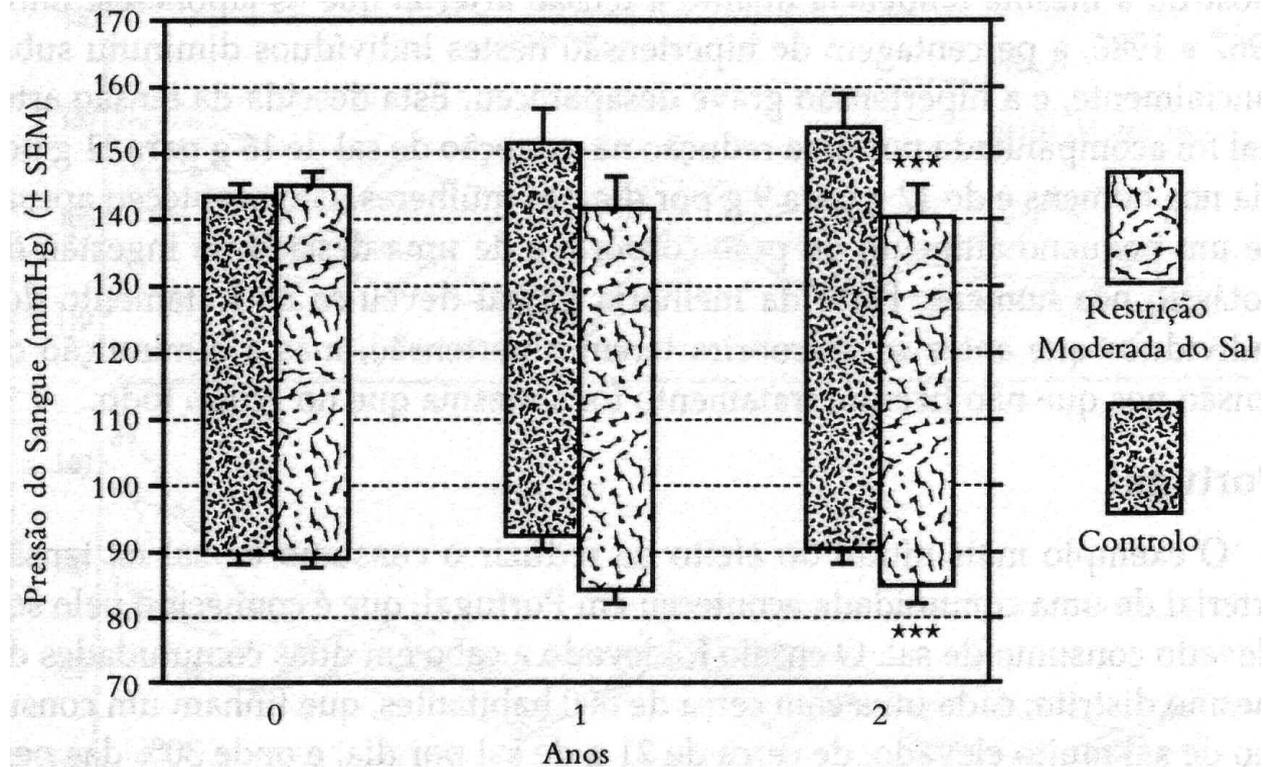- Mediterranean diet + extra-virgin olive oil (EVOO)
- Low fat diet

Primary End Point (acute myocardial infarction, stroke, or death from cardiovascular causes)

Med diet, EVOO: hazard ratio, 0.69 (95% CI, 0.53–0.91)
Med diet, nuts: hazard ratio, 0.72 (95% CI, 0.54–0.95)
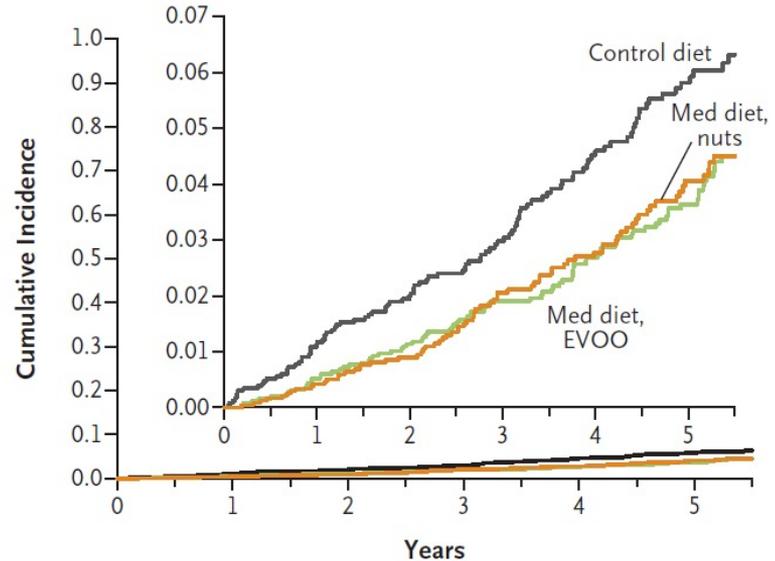
No. at Risk						
Control diet	2450	2268	2020	1583	1268	946
Med diet, EVOO	2543	2486	2320	1987	1687	1310
Med diet, nuts	2454	2343	2093	1657	1389	1031

Estruch et al. *N Engl J Med*. 2018;378:e34.

Intervention studies

Cluster randomization:
- Low salt
- Control

Forte et al *J Human Hypertens* 1989;3:179-184

Intervention studies

Very few randomized controlled trials

- Dietary changes hard to sustain in the long term

- Need for large sample sizes

- One hypothesis = one RCT

- Replications needed…

Intervention [studies]

Non-randomized interventions due to changes in

- Policy or legislation
- Economics
- Food availability
- Lifestyle

USA: water chlorination

Figure 1-1

Death Rates for Typhoid Fever in the USA

Chlorination begins

Rates per 100,000 Population
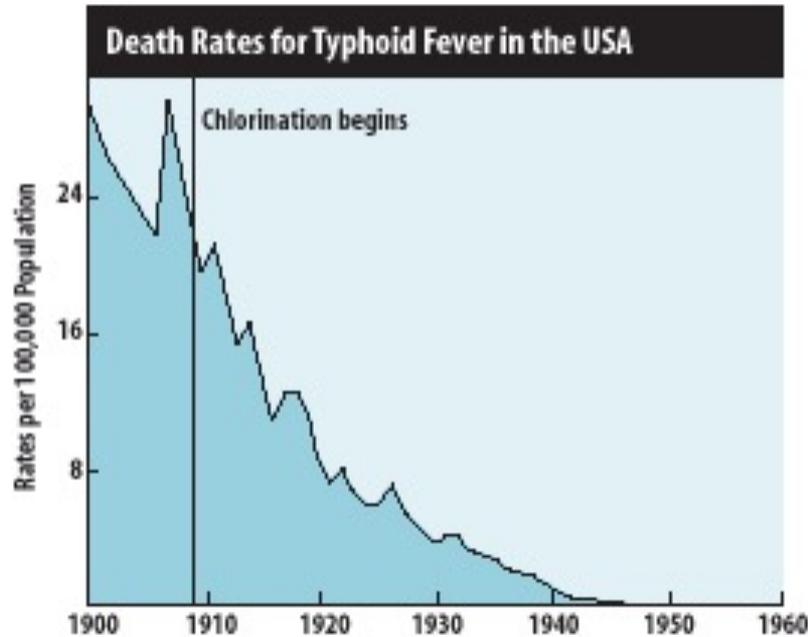
Similar decreases in cholera and hepatitis A cases

Life magazine (1997) declared, "The filtration of drinking water plus the use of chlorine is probably the most significant public health advancement of the millennium."

Switzerland: iodized salt

Conscripts with goiter
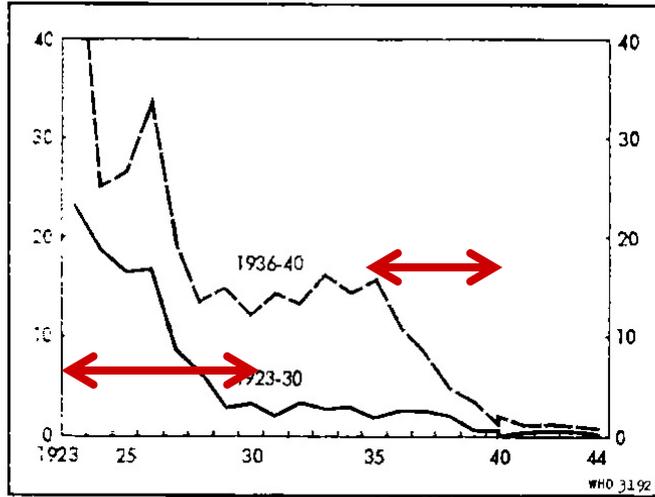
Cantons ayant introduit la prophylaxie par le sel iodé de 1923 à 1930

Cantons ayant introduit la prophylaxie par le sel iodé de 1936 à 1940
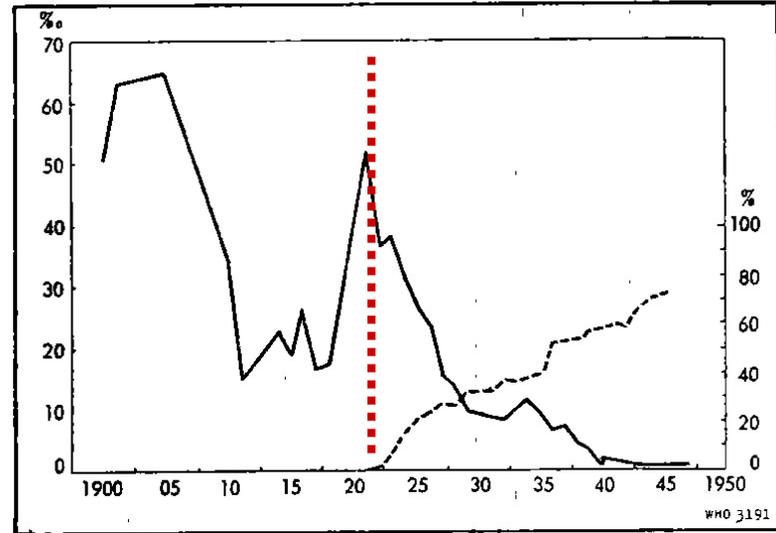
Réformés pour goitre

Consommation de sel iodé
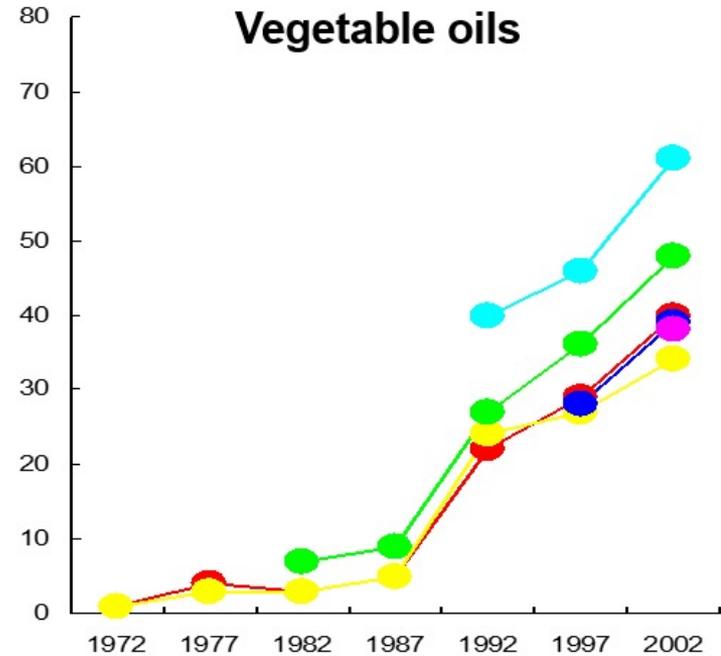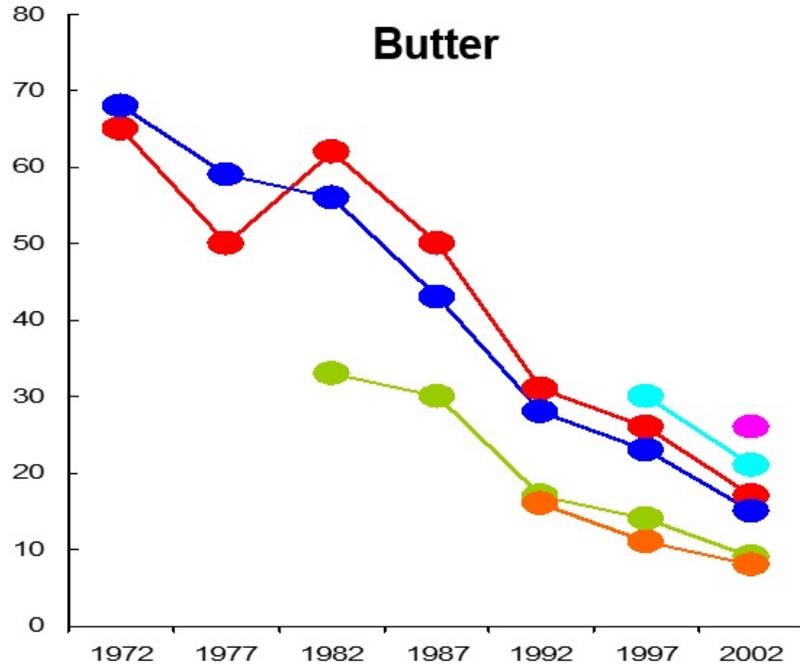
Nicod, *Bull World Hlth Org* 1953;9:259-73

Finland: North Karelia Project

Vartiainen et al, *BMJ* 1995;311:589

Finland: North Karelia Project

Vartiainen et al, *BMJ* 1995;311:589
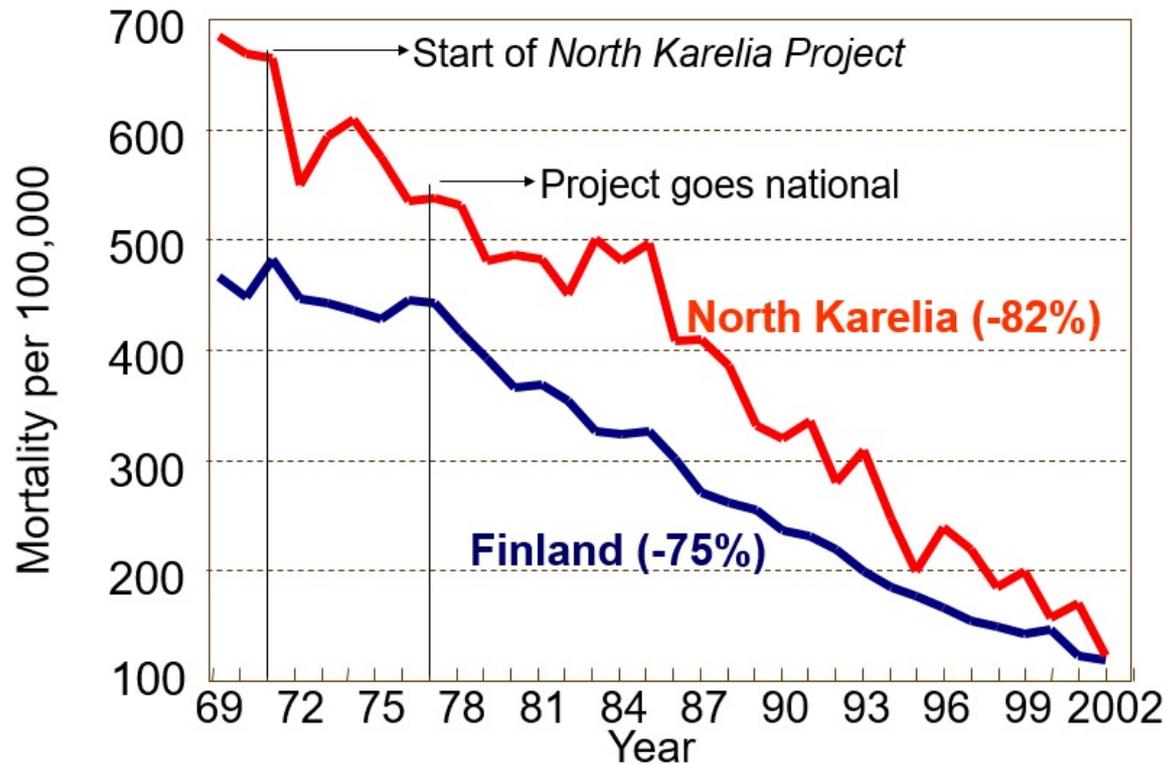
Cuba

Economic crisis after the fall of Soviet Union

Cuba

Obesity cut by **half**!

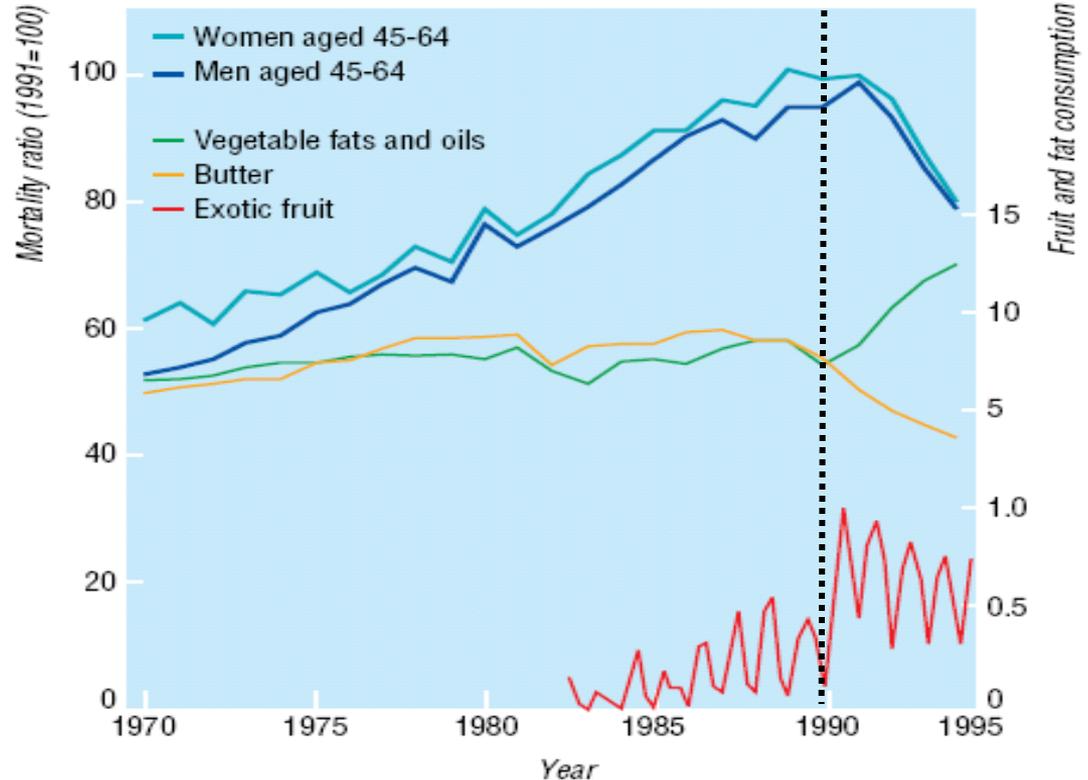1991 (mean BMI = 24.83)
1995 (mean BMI = 23.34)

Franco et al, *Am J Epidemiol*;2007;166:1374-80
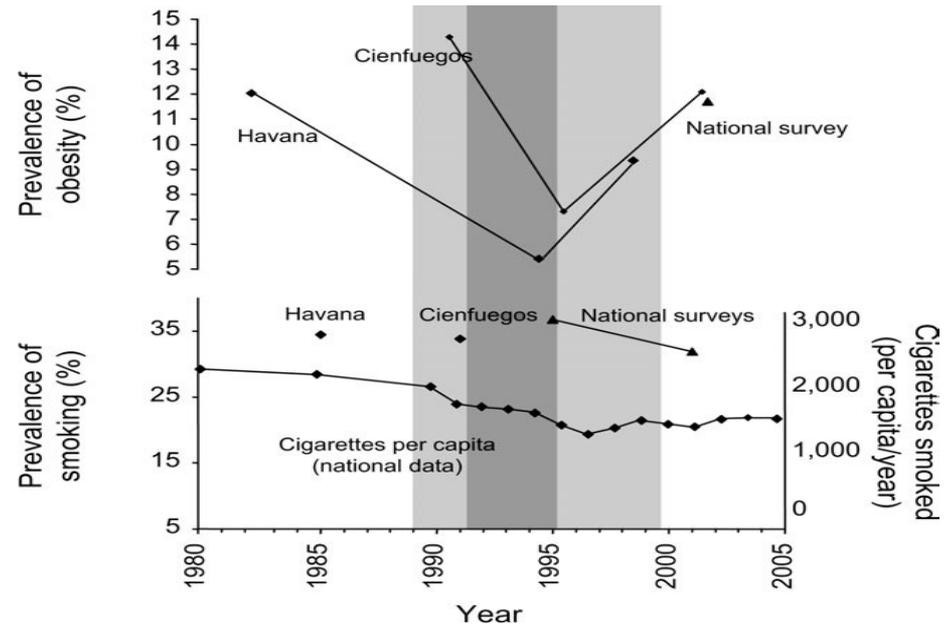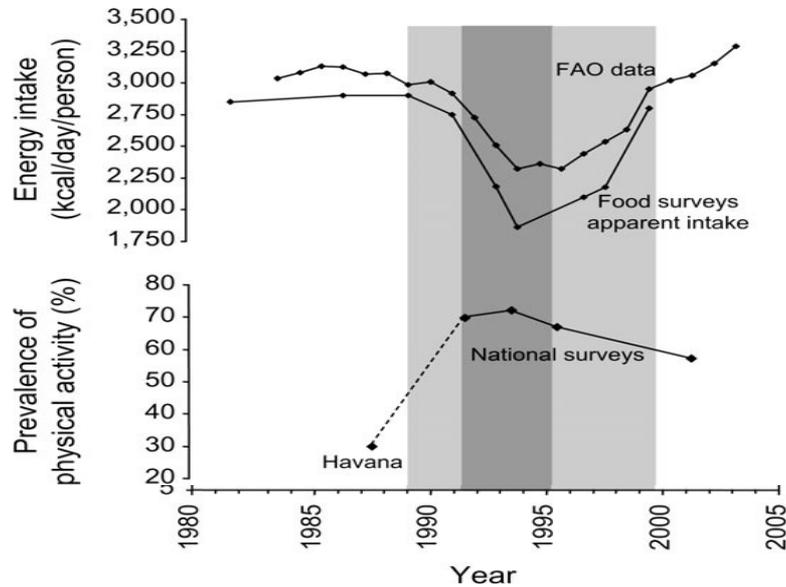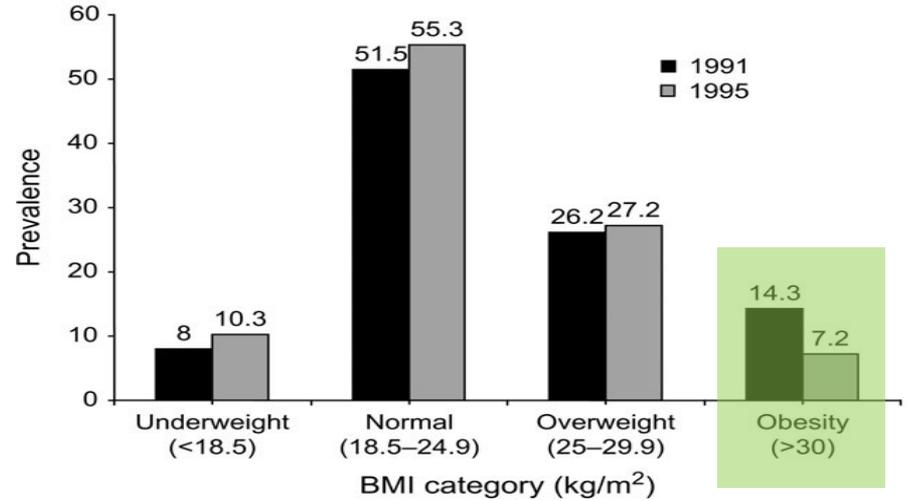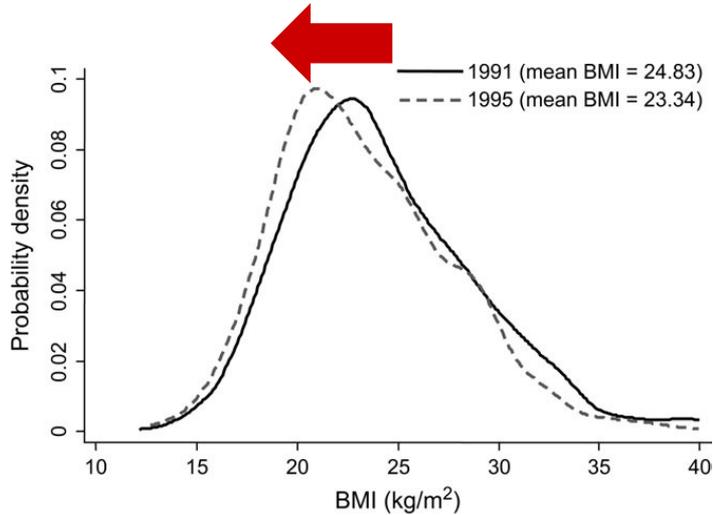
Cuba

Decrease in diabetes, cardiovascular disease, but **not** cancer

Franco et al, *Am J Epidemiol*;2007;166:1374-80
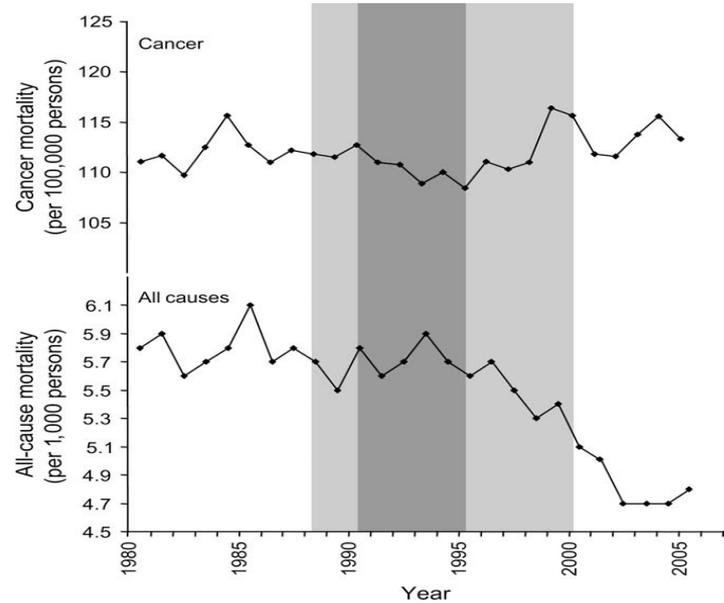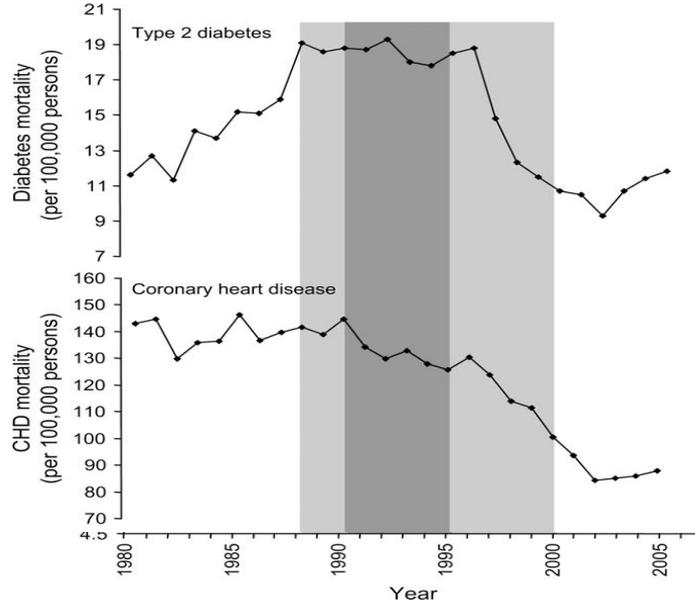
Poland

Very quick effect:
- 20% decrease in 5 years!
- Never achieved by drugs

Zatonski et al, *BMJ* 1998;316:1047

Korea

Negative association with:
- Fruit intake
- Fridge ownership

Park et al. *Cancer Causes Control* 2011;22:1497–502
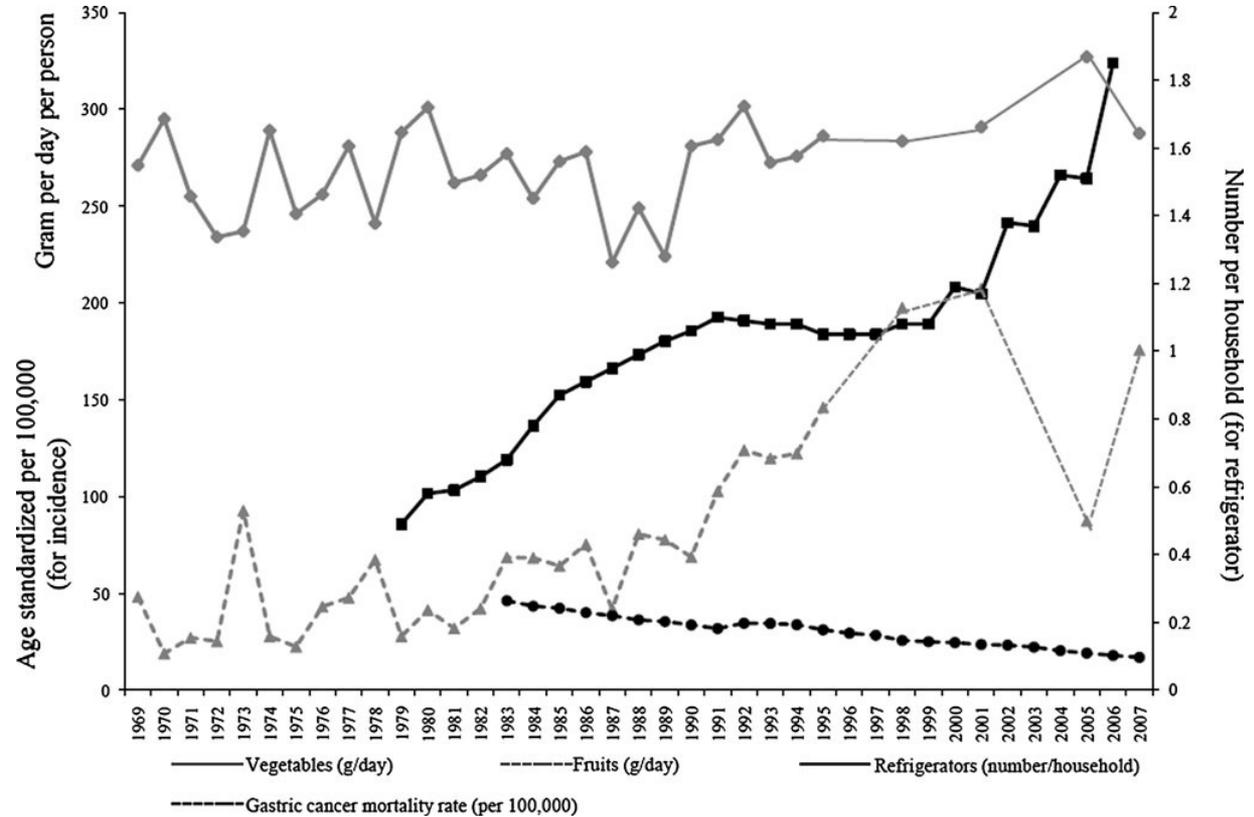
Summary

Dietary intake influenced by multiple factors.

Dietary intake can be assessed via multiple markers.

Diet major determinant of NCDs.

Evidence from prospective studies, few RCTs.