You are what you eat, are you? How to interpret the evidence from nutritional epidemiology studies – PART 2

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SSPH+/ETHZ Lecture Series "This Is Public Health" . May 2022

Overview

- What is nutritional epidemiology?

- Criticism to nutritional epidemiology

- Can we reliably measure dietary intakes in individuals and populations?

- Translating science into policy: Food Pyramids

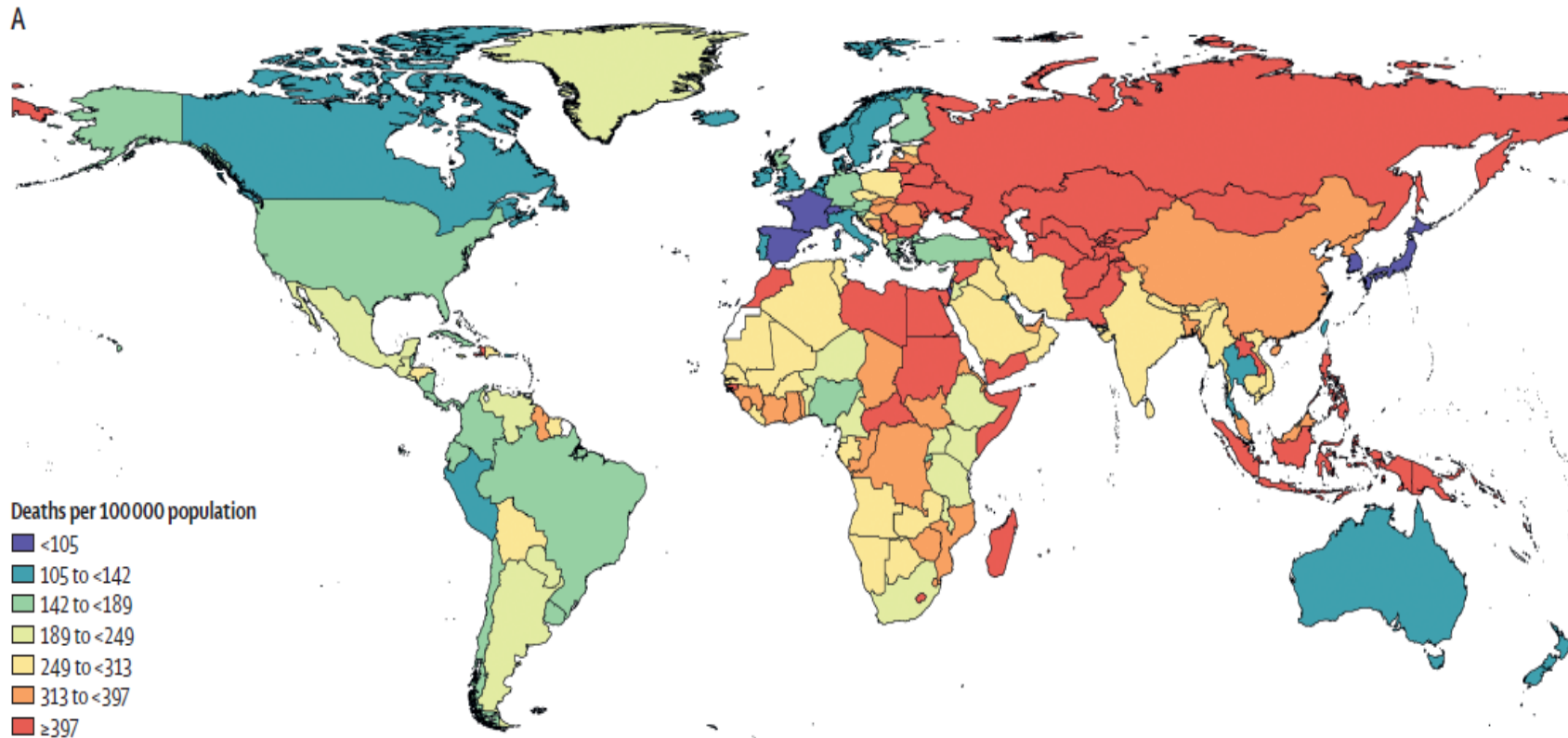# What is "nutritional epidemiology"?

Definition

- Nutritional epidemiology examines dietary or nutritional factors in relation to disease occurrence in populations. (M. Mccullough and E. Giovannucci, Nutritional Oncology, 2006)

- Nutritional epidemiology is the application of epidemiological methods to the study of how diet is related to health and disease in humans at the population level. (K. Thornton and E. Villamor, Encyclopedia of Food and Health, 2016)

It's directly relevant to human health.

- Epidemiologists study real life.
- They do not need to extrapolate from animal models or in vitro systems.
- The results of their work can be translated into specific recommendations for changes in nutrient intakes or food consumption patterns.

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According to the 2019 Global Burden of Disease study of 195 countries, dietary factors are the single leading cause of death (greater health burden than smoking)

A

Deaths per 100000 population

- <105
- 105 to <142
- 142 to <189
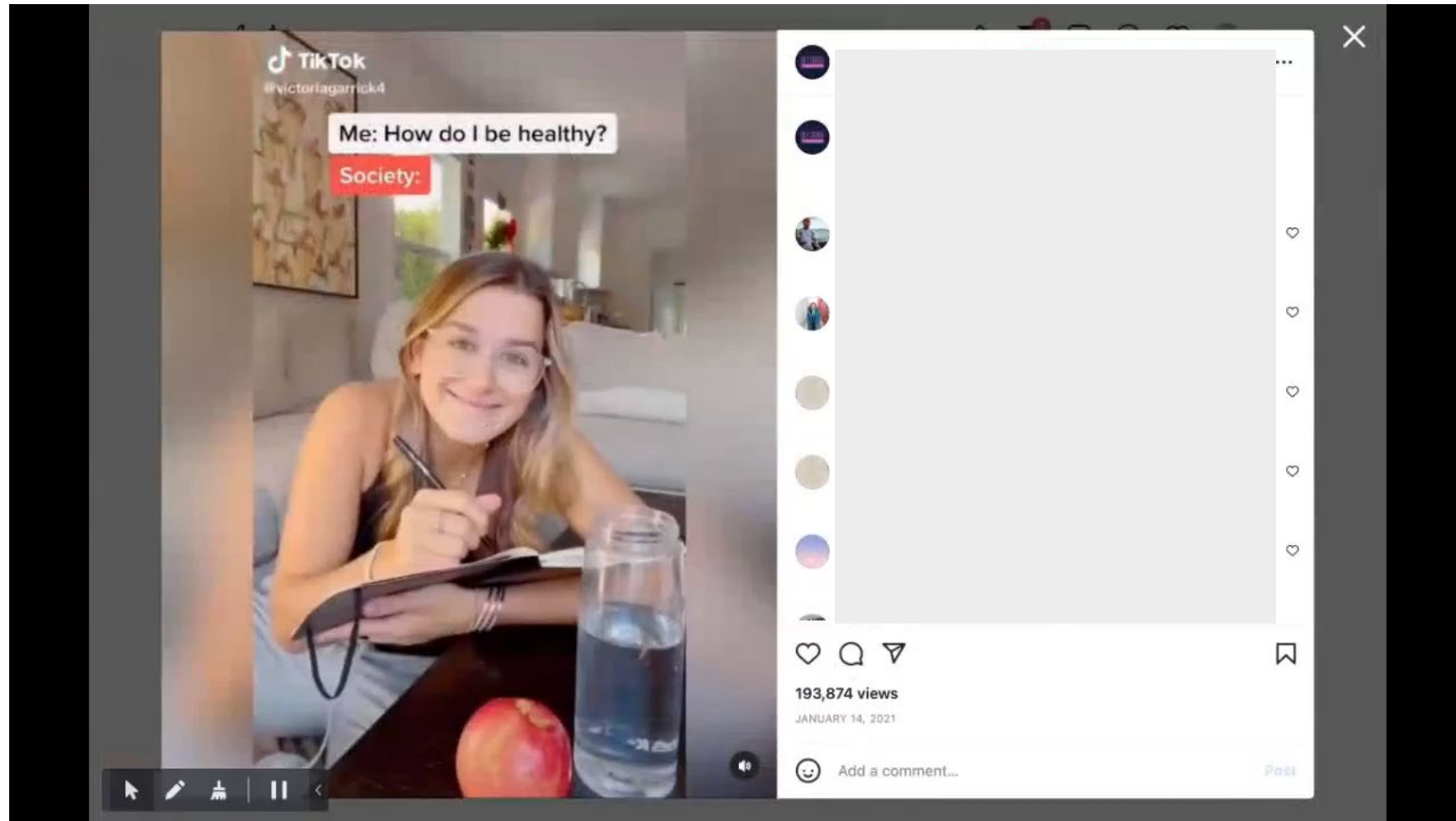- 189 to <249
- 249 to <313
- 313 to <397
- ≥397

GBD 2017 Diet Collaborators. Health effects of dietary risks in 195 countries, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2019;393(10184):1958-1972

Criticism to nutritional epidemiology studies

Public perception

Conflicting messages from media (and scientists?) regarding nutrition

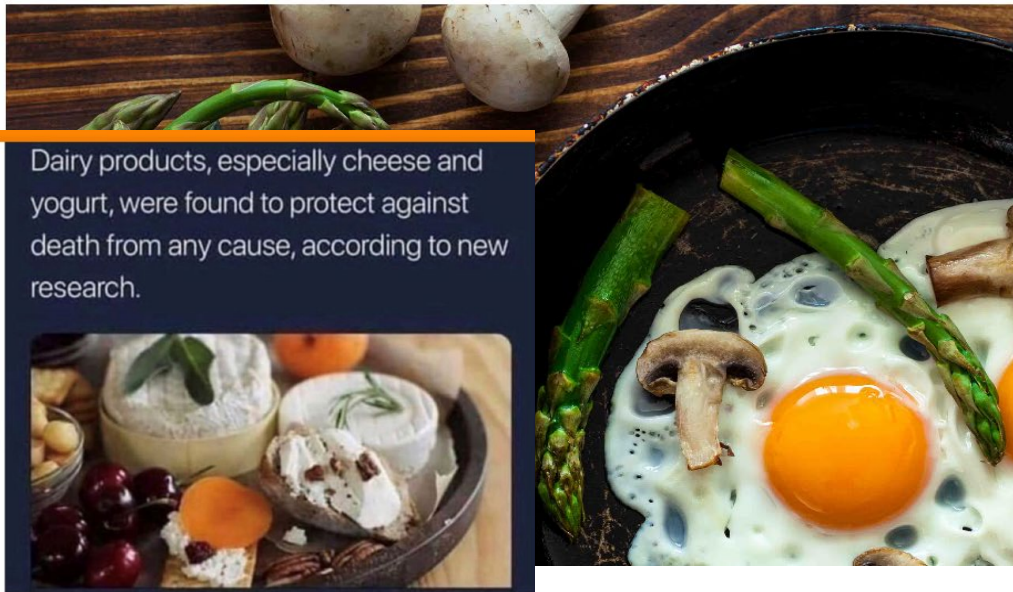CROSS SECTIONS / *Essays & Opinion*

Nutrition Science Is Broken. This New Egg Study Shows Why.

At turns lauded and vilified, the humble egg is an example of everything wrong with nutrition studies.

07.18.2019 / BY Timothy F. Kirn

322 COMMENTS

REPUBLISH

Dairy products, especially cheese and yogurt, were found to protect against death from any cause, according to new research.

Walter Grant Thornburgh
30 August

Assassin: *drops empty gun* why won't you die

Me: *eating my 28th block of cheese* I came prepared

Associations of Dietary Cholesterol or Egg Consumption With Incident Cardiovascular Disease and Mortality

Victor W Zhong [1], Linda Van Horn [1], Marilyn C Cornelis [1], John T Wilkins [1], Hongyan Ning [1], Mercedes R Carnethon [1], Philip Greenland [1], Robert J Mentz [2] [3], Katherine L Tucker [4], Lihui Zhao [1], Arnita F Norwood [5], Donald M Lloyd-Jones [1], Norrina B Allen [1]

Affiliations + expand
PMID: 30874756 PMCID: PMC6439941 DOI: 10.1001/jama.2019.1572
Free PMC article

Abstract

Importance: Cholesterol is a common nutrient in the human diet and eggs are a major source of dietary cholesterol. Whether dietary cholesterol or egg consumption is associated with cardiovascular disease (CVD) and mortality remains controversial.

Objective: To determine the associations of dietary cholesterol or egg consumption with incident CVD and all-cause mortality.

Design, setting, and participants: Individual participant data were pooled from 6 prospective US cohorts using data collected between March 25, 1985, and August 31, 2016. Self-reported diet data were harmonized using a standardized protocol.

Exposures: Dietary cholesterol (mg/day) or egg consumption (number/day).

Main outcomes and measures: Hazard ratio (HR) and absolute risk difference (ARD) over the entire follow-up for incident CVD (composite of fatal and nonfatal coronary heart disease, stroke, heart failure, and other CVD deaths) and all-cause mortality, adjusting for demographic, socioeconomic, and behavioral factors.

Results: This analysis included 29 615 participants (mean [SD] age, 51.6 [13.5] years at baseline) of whom 13 299 (44.9%) were men and 9204 (31.1%) were black. During a median follow-up of 17.5 years (interquartile range, 13.0-21.7; maximum, 31.3), there were 5400 incident CVD events and 6132 all-cause deaths. The associations of dietary cholesterol or egg consumption with incident CVD and all-cause mortality were monotonic (all P values for nonlinear terms, .19-.83). Each additional 300 mg of dietary cholesterol consumed per day was significantly associated with higher risk of incident CVD (adjusted HR, 1.17 [95% CI, 1.09-1.26]; adjusted ARD, 3.24% [95% CI, 1.39%-5.08%]) and all-cause mortality (adjusted HR, 1.18 [95% CI, 1.10-1.26]; adjusted ARD, 4.43% [95% CI, 2.51%-6.36%]). Each additional half an egg consumed per day was significantly associated with higher risk of incident CVD (adjusted HR, 1.06 [95% CI, 1.03-1.10]; adjusted ARD, 1.11% [95% CI, 0.32%-1.89%]) and all-cause mortality (adjusted HR, 1.08 [95% CI, 1.04-1.11]; adjusted ARD, 1.93% [95% CI, 1.10%-2.76%]). The associations between egg consumption and incident CVD (adjusted HR, 0.99 [95% CI, 0.93-1.05]; adjusted ARD, -0.47% [95% CI, -1.83% to 0.88%]) and all-cause mortality (adjusted HR, 1.03 [95% CI, 0.97-1.09]; adjusted ARD, 0.71% [95% CI, -0.85% to 2.28%]) were no longer significant after adjusting for dietary cholesterol consumption.

Conclusions and relevance: Among US adults, higher consumption of dietary cholesterol or eggs was significantly associated with higher risk of incident CVD and all-cause mortality in a dose-response manner. These results should be considered in the development of dietary guidelines and updates.

Journal of the American Heart Association

ORIGINAL RESEARCH

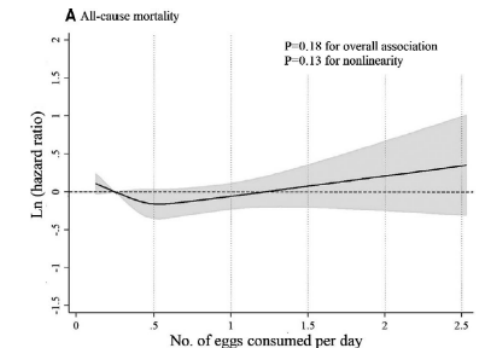## Dietary Intakes of Eggs and Cholesterol in Relation to All-Cause and Heart Disease Mortality: A Prospective Cohort Study

Peng-Fei Xia, MBBS*; Xiong-Fei Pan, PhD*; Chen Chen, MBBS; Yi Wang, MBBS; Yi Ye, MBBS; An Pan, PhD

BACKGROUND: The aim of this study was to identify associations between dietary intakes of eggs and cholesterol and all-cause and heart disease mortality in a US population.

METHODS AND RESULTS: Data from the National Health and Nutrition Examination Survey 1999–2014 were used in this study, which included 37 121 participants ≥20 years of age. Dietary information was assessed via 24-hour dietary recalls at baseline. Mortality status was documented until December 31, 2015. Cox proportional hazards models were used to examine the associations between dietary intakes of eggs and cholesterol and all-cause and heart disease mortality. During a median follow-up of 7.8 years, 4991 deaths were documented, including 870 deaths from heart disease. No significant association was observed between additional daily consumption of half an egg and all-cause mortality (multivariable-adjusted hazard ratio, 1.04; 95% CI, 0.96–1.13), or heart disease mortality (0.96; 0.80–1.14). Each 50-mg/day increase of cholesterol intake was inversely associated with all-cause mortality among participants with daily intake <250 mg (0.87; 0.77–0.98), but positively associated with all-cause mortality among participants with daily intake ≥250 mg (1.07; 1.01–1.12). No significant association was found between dietary cholesterol intake and heart disease mortality.

CONCLUSIONS: No significant association was found between egg consumption and mortality in US adults. The association between dietary cholesterol intake and all-cause mortality depended on the baseline intake levels, with an inverse association in those with lower intake levels (<250 mg/day) but a positive association in those with higher intake levels (≥250 mg/day).

Key Words: cardiovascular disease ■ cohort study ■ dietary cholesterol ■ egg ■ mortality

A All-cause mortality

P=0.18 for overall association
P=0.13 for nonlinearity

Ln (hazard ratio)

No. of eggs consumed per day

Why is nutrition so hard to study?

Written by Tim Newman on February 24, 2020 —
Fact checked by Yella Hewings-Martin, Ph.D.

Is dairy good or bad for health? Is cholesterol evil? Does red meat kill or cure? Is the ketogenic diet a godsend or a health hazard? Can the vegan, vegetarian, pescatarian, or raw food diet extend disease-free life?

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- Research is an ongoing process

- Contradictions are inevitable and part of the scientific process

- Not all studies are created equal

- Newer studies are not necessarily more reliable than older studies

The complex nature of diet

Nutrients can be highly correlated with one another
- Same food sources
- Act synergistically or antagonistically (e.g. compete for intestinal absorption)

Same foods with different preparation methods can have different effects (e.g. coffee)

Eating more of one type of food could be compensated with eating less of another

Foods as part of dietary patterns
→ broader picture of food and nutrient consumption

1. Jacobs et al. Am J Clin Nutr 2003. 2. Hu FB. Curr Opinion Lipid 2002

How to weigh evidence for nutrition studies

- How was diet assessed?

- What type of study?

- How large is the study?

- Animals or humans?

- Real disease endpoints or markers for these diseases?

- Does the given study fit into the entire body of evidence? Weight of the evidence?

Can we reliably measure dietary intakes in individuals and populations?

Everybody eats

- Diet is the main exposure

Also important: relevant period of exposure

- No method is perfect

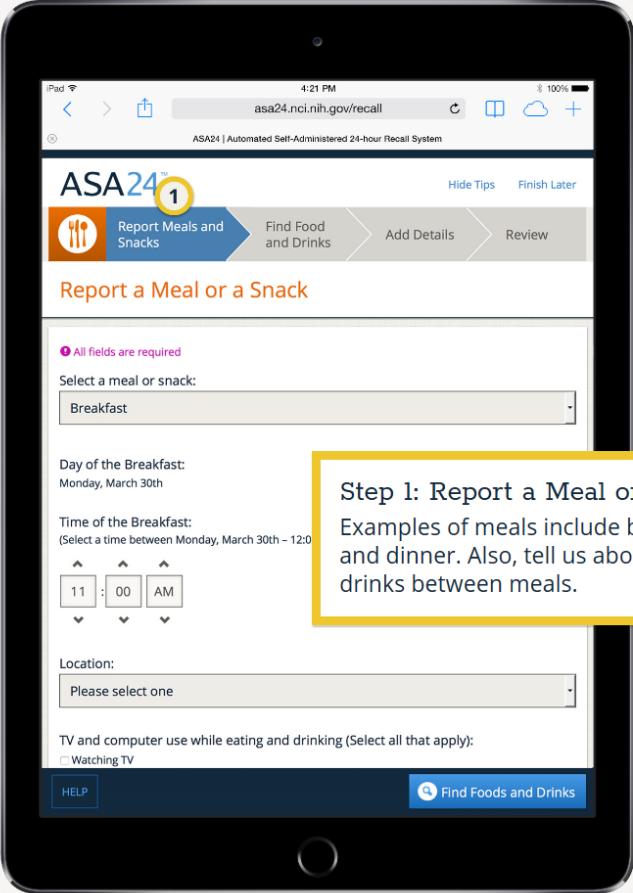- Self-report (subjective methods) and objective methods

Dietary Records

- Participants record everything they eat or drink over several days

- Multiple diet records can be considered as the gold standard of dietary information

✓ Do not rely on memory

✓ Accurately ascertain detailed dietary information

✓ Open ended data

➢ High participant burden (literate, motivated participants)

➢ Resource intensive

➢ Recording can change individual's diet

Repeated 24h diet recalls

Report all foods consumed in the previous 24h to a trained interviewer

✓ Accurate, detailed, open-ended data

✓ Lower participant burden

➤ Relies on memory (short term)

➤ Depends on interviewer's training

Food Frequency Questionnaires

Structured food list and a frequency section – intake of food over a certain period of time in the past (usually 1 year)

✓ Low participant burden/Low cost

✓ Captures long-term dietary intake

✓ Allows repeated assessments over time

➤ Recall error (long term memory)

➤ Fixed food list → omissions

1. Bread and rolls (1 slice or 1 roll or medium serving)		Rarely/ never	1-3 per month	Per week			Per day			
				1	2-4	5-6	1	2-3	4-5	6+
1	Wholemeal or brown bread or Kneipp bread (with or without seeds)	☐	☐	☐	☐	☐	☐	☐	☐	☐
2	White bread (e.g. baguette, rolls, sliced crust(less))	☐	☐	☐	☐	☐	☐	☐	☐	☐
3	Rye bread (any)	☐	☐	☐	☐	☐	☐	☐	☐	☐
4	Naan, Paratha, Chapatti, Pita bread, Piadina	☐	☐	☐	☐	☐	☐	☐	☐	☐
5	Wheat or yeast rusk	☐	☐	☐	☐	☐	☐	☐	☐	☐
6	Thin biscuits (e.g. crackers, knackerbrod, rice-wafer)	☐	☐	☐	☐	☐	☐	☐	☐	☐

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Food Questionnaire Serving Size Pictures

English GNA FFQ
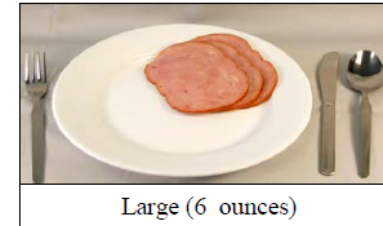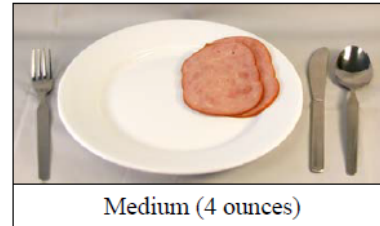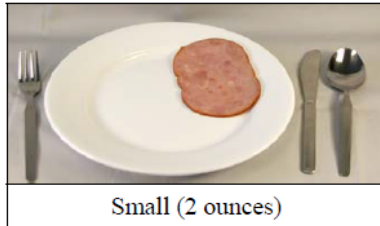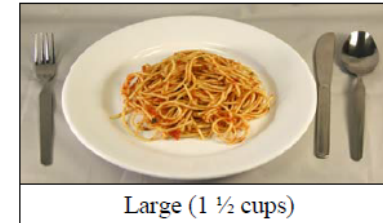
Please note: Use these pictures to help estimate your usual serving sizes.
- Medium serving sizes are given on the Food Questionnaire.
- A small serving is about one-half (1/2) the medium serving size or less.
- A large serving is about one-and-a-half (1 1/2) times the medium serving size or more.
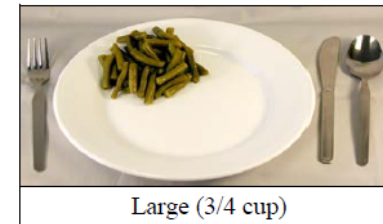
Beef, pork, chicken and fish as a main dish

| Small (2 ounces) | Medium (4 ounces) | Large (6 ounces) |

Spaghetti and casseroles

| Small (1/2 cup) | Medium (1 cup) | Large (1 ½ cups) |

Vegetables such as green beans, corn, and potatoes

| Small (1/4 cup) | Medium (1/2 cup) | Large (3/4 cup) |
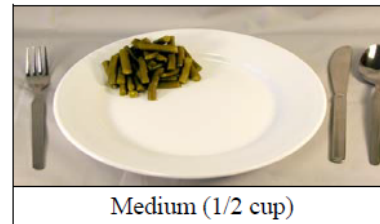
Objective methods for dietary assessment

- Do not rely on written or verbal responses from the individual (or his/her proxy)

- Can be more accurate, less respondent bias (recall error, social desirability)

- Can be costly, intrusive, burdensome for participant and researcher

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Examples of objective methods

❑Direct observation: recording what and how much people are consuming.

❑Duplicate diets: recording or assessing individuals' diets, collecting or preparing as identical meals as possible, and assessing the chemical compositions.

Image-based dietary assessments

When using RFPM, the SmartIntake® app captures images of participants' foods and beverages. A reference card is used for scaling/portion size. A description is included.
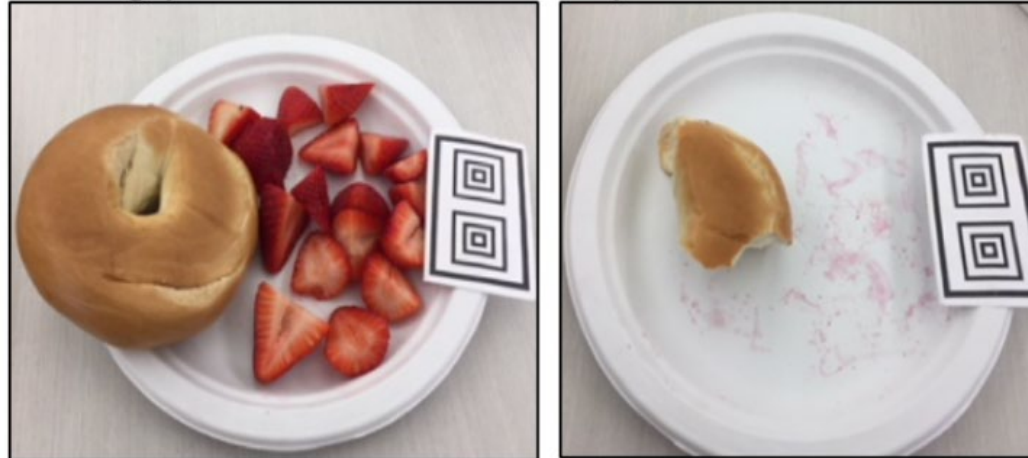
Before image.
Description: "Plain bagel and strawberries"

After image.

Figure 1. The Remote Food Photography Method (RFPM) applied using the SmartIntake app.

Biomarkers

Collecting bio-specimens and assaying chemical compositions that reflect dietary exposure, at least partly.

Could be used to calibrate self-reported data in large studies

➤ Sensitivity/Specificity

➤ May not represent long-term intake

➤ Expensive, invasive

➤ Biomarkers not available for many nutrients

'Omics

High-throughput methods for assessing a large number of genomic, epigenomic, transcriptomic, proteomic and metabolomic traits from biological specimens

- Close interplay between food and metabolism

- Can provide additional insights on mechanistic pathways

- Not yet able to accurately distinguish between most specific foods

- Example: Dairy and cognition
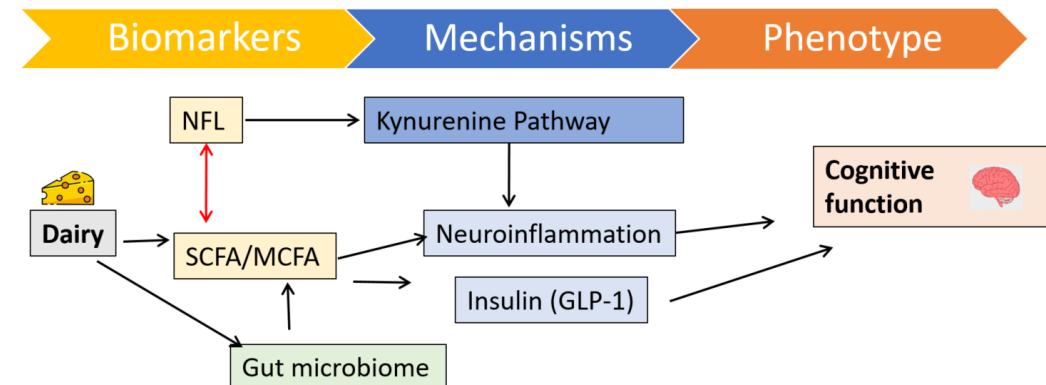
Translating science into policy

Evidence for decision making

- A central goal of nutritional epidemiology and public health research is to improve health and well-being.

- In the absence of large RCTs with hard endpoints, evidence from prospective cohort studies and smaller RCTS with intermediate endpoints is considered.

Satija A, Yu E, Willett WC, Hu FB. Understanding nutritional epidemiology and its role in policy. *Adv Nutr*. 2015;6(1):5-18.

Examples of nutrition policy

- Education and awareness: Dietary guidelines by governments, WHO, organizations such as American Health Association

- Labeling: Nutrition facts on foods/menu

- Economic strategies: taxes/subsidies

- Fortification

- Banning

Recommendations from the Swiss Society for nutrition

- A well-balanced diet is vital in promoting a healthy lifestyle. It influences our mental and physical well-being and helps in prevention of illnesses.

- Switzerland published its first set of dietary guidelines in 1998. The current is the third version and was introduced in 2011.

https://www.sge-ssn.ch

Swiss food pyramid (adults)

Swiss Food Pyramid

Sweets, Salty Snacks & Alcohol
In small quantities.

Oils, Fats & Nuts
Oils and nuts in small quantities daily. Butter/margarine sparingly.

Dairy Products, Meat, Fish, Eggs & Tofu
3 portions of dairy products and 1 portion of meat/fish/eggs/tofu ... per day.

Grains, Potatoes & Pulses
3 portions per day. Grains should preferably be wholegrain.

Vegetables & Fruit
5 portions per day of different colours.

Beverages
1–2 litres of unsweetened beverages per day. Preferably water.

At least 30 minutes of physical activity daily and sufficient relaxation.

© Swiss Society for Nutrition SSN, Federal Food Safety and Veterinary Office FSVO / 2011

know more – eat better sge-ssn.ch

Diet in Switzerland

- The swiss food pyramid was followed by <1% of the population.
- 4 in 10 participants met ≥3 criteria.
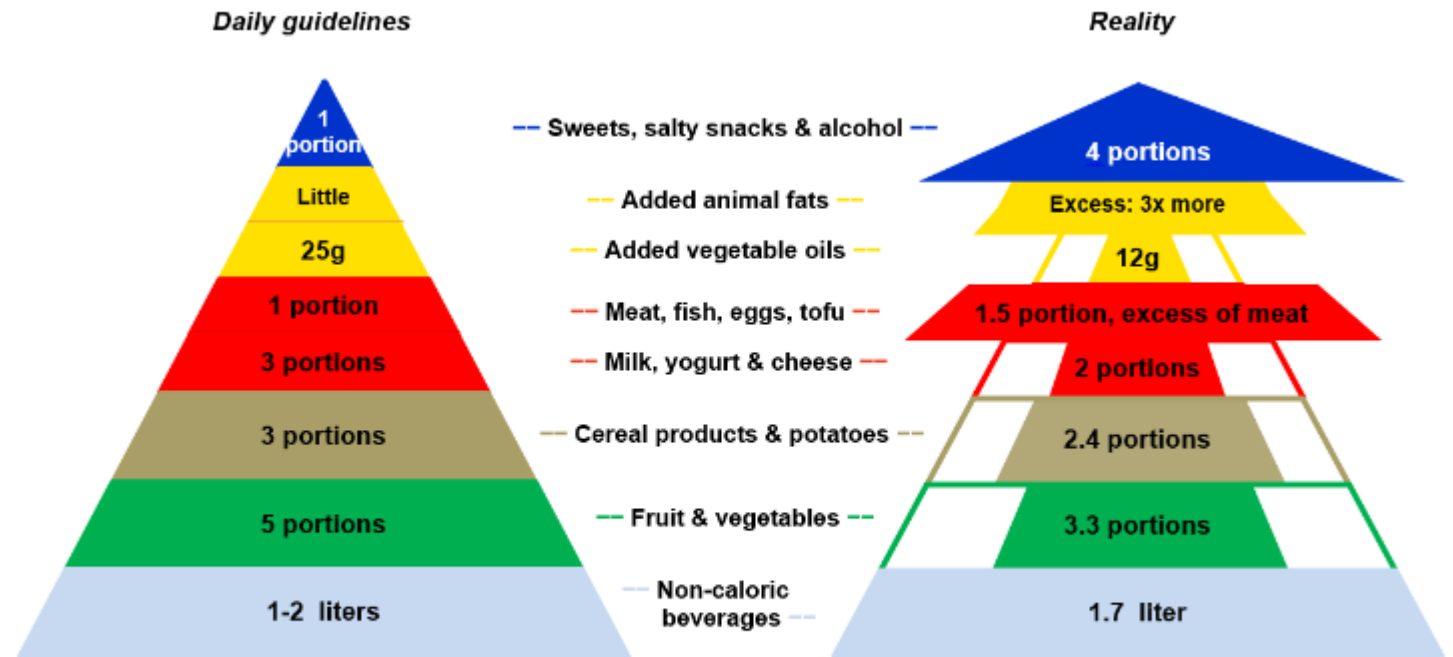- 18% of participants ate ≥5 portions of fruit and vegetables a day, without regional differences.

Daily guidelines

			Reality
1 portion	-- Sweets, salty snacks & alcohol --	4 portions
Little	-- Added animal fats --	Excess: 3x more
25g	-- Added vegetable oils --	12g
1 portion	-- Meat, fish, eggs, tofu --	1.5 portion, excess of meat
3 portions	-- Milk, yogurt & cheese --	2 portions
3 portions	-- Cereal products & potatoes --	2.4 portions
5 portions	-- Fruit & vegetables --	3.3 portions
1-2 liters	Non-caloric beverages	1.7 liter

Figure 2. The daily national food-based dietary guidelines (i.e., Swiss Food Pyramid) **(left)** compared to the actual food consumption for the six stages at a population level **(right)**.

Chatelan A, Beer-Borst S, Randriamiharisoa A, et al. Major Differences in Diet across Three Linguistic Regions of Switzerland: Results from the First National Nutrition Survey menuCH. *Nutrients*. 2017;9(11):1163.

EAT Lancet Commission: Planetary Health Diet

- Guidelines for an optimal diet for human health and environmental sustainability

- It emphasizes a plant-forward diet where whole grains, fruits, vegetables and nuts comprise a greater proportion of foods consumed.

- Meat and dairy significantly smaller proportions

- Discourages overconsumption

Whole grains

Starchy vegetables

Dairy foods

Animal sourced protein

Plant sourced protein

Unsaturated plant oils

Added sugars

https://eatforum.org/eat-lancet-commission/

Precision nutrition

- Dietary guidelines are often based on population average estimates

- Aims to use individualized information (genome, microbiome, metabolome) to receive personalized dietary recommendations for chronic disease prevention and management

- interactions of nutrition with other potentially modifiable exposures such as the microbiome, environment, physical activity...

Brennan L, Hu FB, Sun Q. Metabolomics Meets Nutritional Epidemiology: Harnessing the Potential in Metabolomics Data. Metabolites. 2021 Oct 19;11(10):709

Take home message

- Assessment of diet in free-living individuals is challenging but some methods can classify properly people into different levels of intake

- Evidence on the role of diet on disease is ongoing, with inevitable contradictions as part of the scientific process

- Dietary guidelines are established based on the available evidence

Thank you