

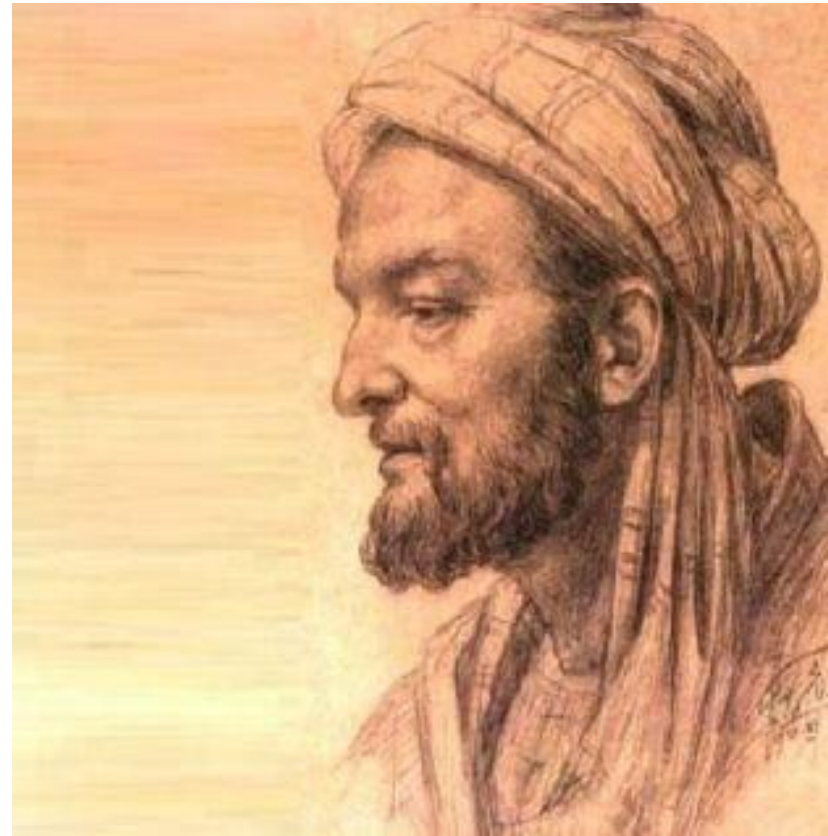
# The State of Nutritional Epidemiology

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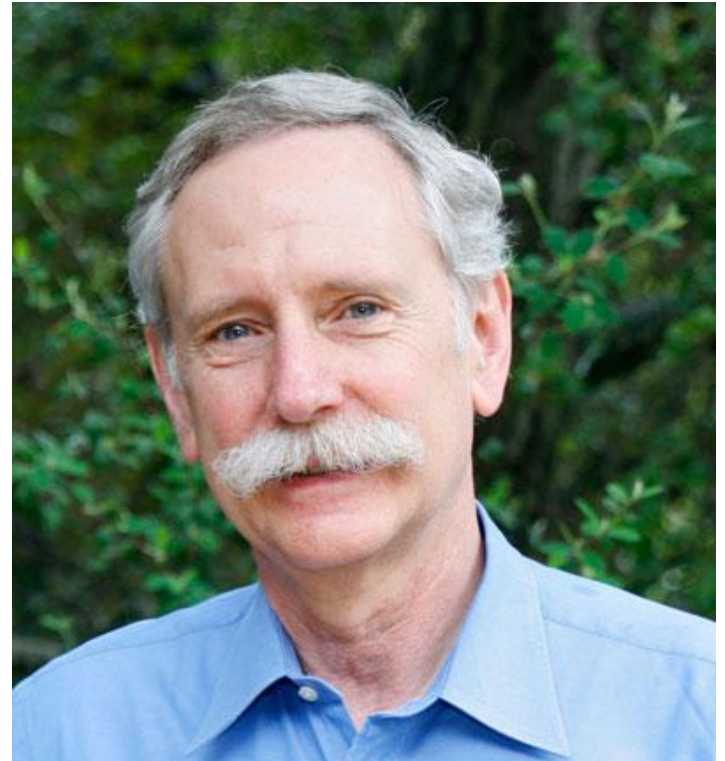
# Avicenna, 1000 years ago

- Most illnesses arise solely from long-continued errors of diet and regimen.
- The meal should include:
  - (1) flesh, especially that of baby kids of goats, veal, and year-old lamb;
  - (2) wheat, which is cleaned of extraneous matter and gathered during a healthy harvest without ever having been exposed to injurious influences . . . .”



# Walter Willett, 1998

- Nutritional epidemiology has contributed importantly to understanding the etiology of many diseases.
- Suboptimal intake of fruit and vegetables has been related to increased risk of many cancers.
- Substantial epidemiologic evidence has accumulated, indicating that dietary antioxidants are likely to play an important role in preventing coronary heart disease.



# Three Case Studies

- Vegetables and cancer
- Antioxidants and cancer
- Coffee and cancer





## 2013: Pooled cohort analyses for vegetables, comparing Q5 to Q1

- Lung cancer: 0.88 (0.78-1.00), P(trend)= 0.12
- Colon cancer: 0.94 (0.86 to 1.02), P(trend)= 0.17
- Breast cancer: 0.96 (0.89-1.04), P(trend) = 0.54
- Ovarian cancer: 0.90 (0.78-1.04), P(trend) = 0.06
- Prostate cancer: 1.02 (0.99, 1.06)



# Tim Key, 2011

- The possibility that fruit and vegetables may help to reduce the risk of cancer has been studied for over 30 years, but no protective effects have been firmly established.
- The available data suggest that general increases in fruit and vegetable intake would not have much effect on cancer rates.







# Observational studies in the 1970s and 1980s

- Alpha-tocopherol, a form of vitamin E, may reduce the risk of lung cancer.
- Beta-carotene, a precursor of vitamin A, may reduce the risk of lung cancer.

# Observational studies of vitamin A and lung cancer

- Five-year follow-up results for 8,278 men who in mail surveys showed an index for vitamin A intake to be negatively associated with lung cancer incidence at all levels of cigarette smoking. (Bjelke, 1975)
- A previously reported negative association between a high index of dietary vitamin A and lung cancer incidence was confirmed in an extended follow-up, covering 11 1/2 years, of 13,785 men and 2,928 women (Kvale, 1983)

# Observational studies of vitamin A and lung cancer

- A strong inverse association between serum beta-carotene and the risk of squamous-cell carcinoma of the lung was observed, with a relative odds = 4.3. (Menkes, 1986)
- Serum levels of vitamin E in the lowest quintile had a 2.5 times higher risk of lung cancer than persons with levels in the highest quintile. (Menkes, 1986)



**Table 1:** Randomized, double-blind, placebo-controlled, primary prevention trials designed to reduce risk of major chronic diseases

| <b>Study</b>  | <b>Population</b>  | <b>N</b> | <b>Agents, dose, and mean duration</b>  | <b>Main outcomes</b>                          | <b>Results</b>  |
|---|--|----------|---|---|---|
| Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study <sup>[4]</sup> | Male Smokers aged 50 – 69 years (Finland)  | 29,133   | $\alpha$ -tocopherol (50 mg daily) and / or $\beta$ -carotene (20 mg daily) for six years | Lung cancer incidence                         | $\alpha$ -tocopherol did not affect the risk of lung cancer or total mortality, but it increased the risk of hemorrhagic stroke by 50%. $\beta$ -carotene increased the incidence of lung cancer by 18% and total mortality by 8% (mainly due to lung cancer and ischemic heart disease). |
| Beta-Carotene and Retinol Efficacy Trial (CARET) <sup>[7]</sup>               | Smokers, former smokers, and workers exposed to asbestos > 45 years of age (United States) | 18,314   | $\beta$ -carotene (30 mg) plus retinol (25,000 IU) daily for 4 years                      | Lung cancer incidence                         | Supplements increased the incidence of lung cancer by 28% and total mortality by 17%.   |
| Physicians' Health Study (PHS) <sup>[8]</sup>                                 | Male physicians 40 – 84 years old (United States)  | 22,071   | $\beta$ -carotene (50 mg on alternate days) and / or aspirin for 12 years                 | Overall, cardiovascular, and cancer mortality | There was virtually no difference in any of the main outcomes when comparing those who received and did not receive $\beta$ -carotene.  |



# Initial studies of coffee and pancreatic cancer

- After adjustment for cigarette smoking, the relative risk associated with drinking up to two cups of coffee per day was 1.8 (95% confidence limits, 1.0 to 3.0), and that with three or more cups per day was 2.7 (1.6 to 4.7). (MacMahon, 1981)

# Coffee and pancreatic cancer, 2013

- HR = 1.10, 95% CI: 0.81-1.48 (Genkinger 2012)
- HR = 0.82, 95% CI: 0.38-1.76 (Bidel, 2013)
- HR = 1.03; 95% CI: 0.83-1.27 (Bhoo-Pathy, 2013)



# Coffee and all-cause mortality

- Freedman and colleagues (2012) found that, after adjustment for smoking and several other factors, coffee intake was associated with 10% to 15% reduced all-cause mortality.
- Multiple other studies have found beneficial effects for coffee intake.



Life is  
SHORT,  
Enjoy ur  
coffee

# So what is good to eat?

The International Food Information Council's 2012 Food & Health Survey that reported

**More than half of Americans, including 55% of men, think it is easier to do their own taxes than to know how to eat healthy.**

# Reasons for disagreement

- Self-interest of food producers and sellers of diets
  - Meat industry
  - Atkins diet
- Methodological problems

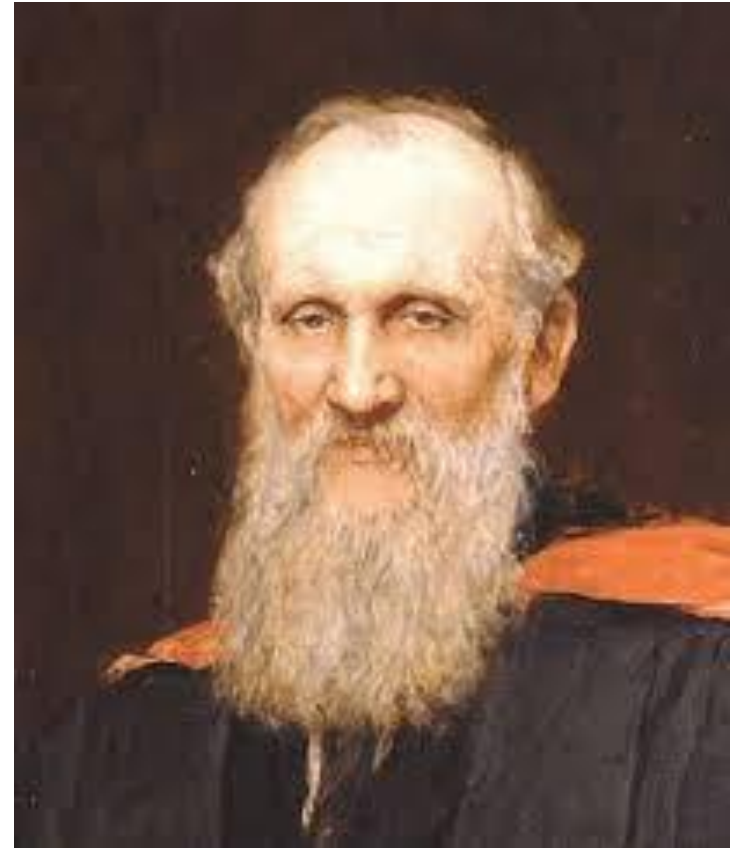


# Methodological problems

- Measurement error
- Confounding
- Variable effects of food items
- Variable reference groups
- Interaction
- Multiple testing

# Measurement error

- “. . . when you can measure what you are speaking about and express it in numbers, you know something about it; but when you cannot measure it, when you cannot express it in numbers, your knowledge is of a meager and unsatisfactory kind”.



# Tools with substantial measurement error

- Food frequency questionnaires
- 24-hour recalls
- Food records

# Confounding

- Many foods are consumed together.
- The intake of many nutrients are correlated.
- Eating patterns are associated with other health-related behaviors.

# Variable effects of food items

- Where and when they have been grown.
  - e.g., selenium content
- Pesticides
- Contaminants

# Variable reference group

- What is that food being compared too?
- For example, what is the effect of eating rice?  
Can be compared to eating
  - Eating white bread
  - Eating wheat bread
  - Eating black beans



# Interactions

- What is the effect of a nutrient in the presence or lack thereof of other nutrients?
- What is the effect of a food item in the presence or lack thereof of others?
- Example: milk and yoghurt

# Multiple testing

- Exposures
  - Many items in food frequency questionnaires
  - Many nutrients
  - Food patterns
- Outcomes
  - Many cancers
  - Cardiovascular diseases
  - Other outcomes

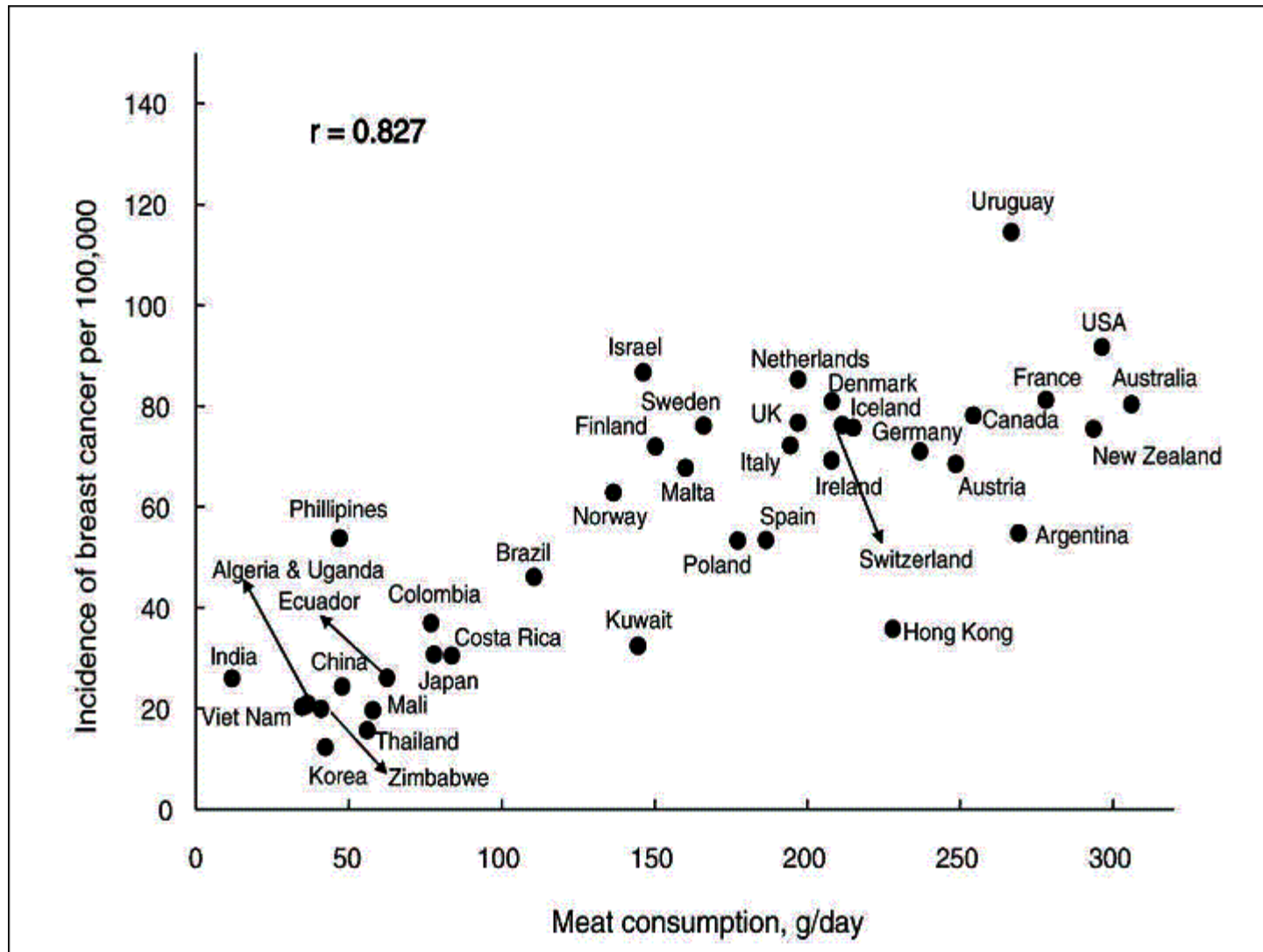
# Other designs

- Much of what was discussed here about measurement error applies to observational studies in individuals
  - Cohort
  - Case-control
  - Cross-sectional
- However, there are other designs too.
  - Ecological studies
  - Randomized trials

# Other designs

- These studies have certain strengths, but have major limitations too.
- For example, trials:
  - are very expensive;
  - may have started too late;
  - may have problems of sample attrition and non-compliance.

# Ecological study of meat and breast cancer



# Ecological study of chocolate consumption and Nobel prize

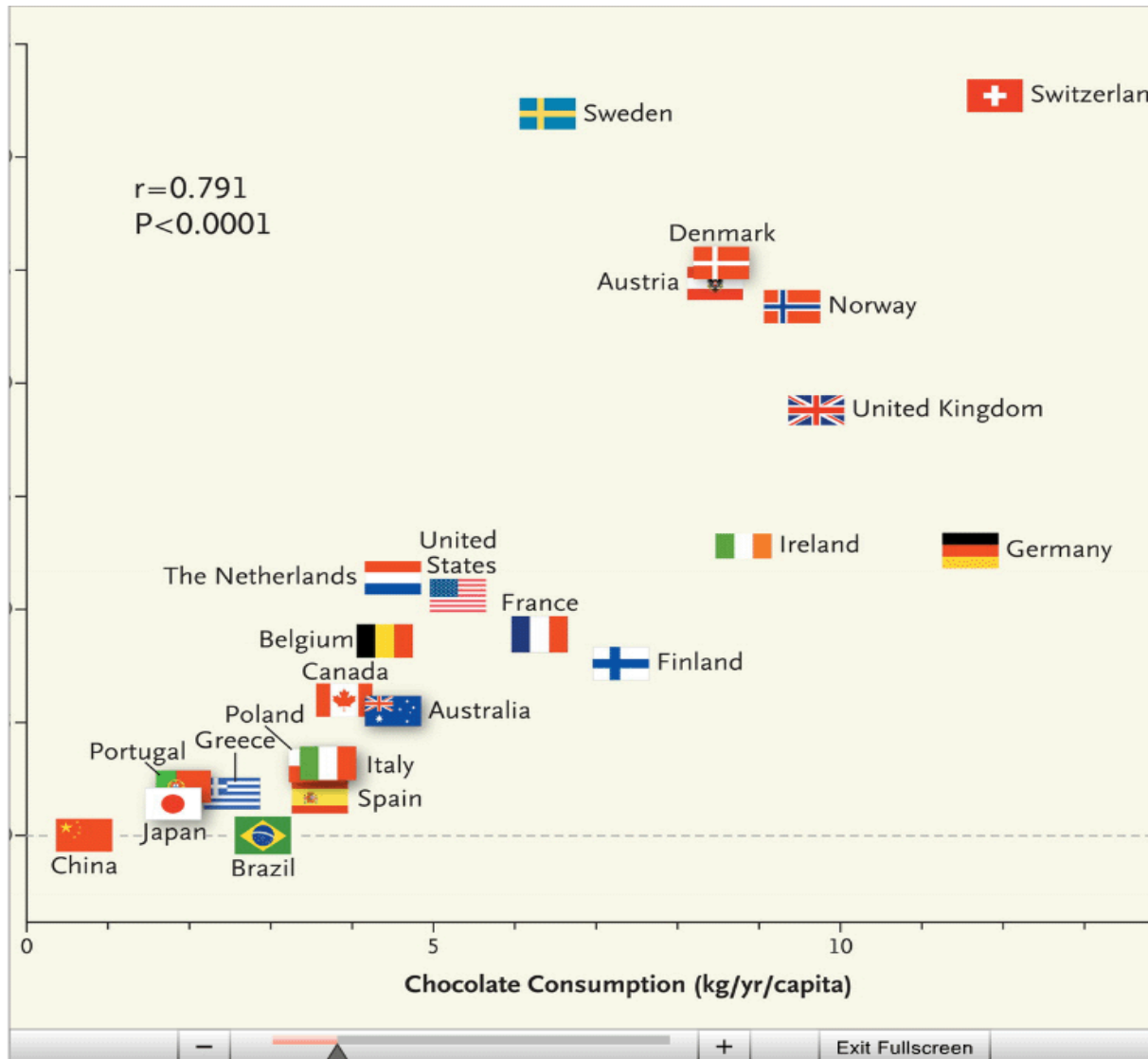


Figure 1. Correlation between Countries' Annual Per Capita Chocolate Consumption and the Number of Nobel Laureates per 10 Million Population.





# Some success, but much to be done

- The collective information gathered so far suggests that the following are good for health:
  - avoiding excessive calories
  - eating white meat rather than red meat (particularly processed red meat)
  - increasing consumption of fruits and vegetables
  - replacing saturated fat with mono- and poly-unsaturated fats
- However, progress in this field has been slowed by the contradictory results that have frequently emerged in the peer-reviewed literature. Questions of what specific food items (e.g., apples or oranges) are healthiest remain almost completely unanswered.

# Basic Dietary Principles

- Eat less
- Move more
- Eat fruits, vegetables and whole grains
- Avoid too much junk food



# Future steps

- First and foremost:
  - Find ways to reduce measurement error
- Conduct various types of studies. If they converge, the results may be believable.

