# Methods in Epidemiology & Nutrition

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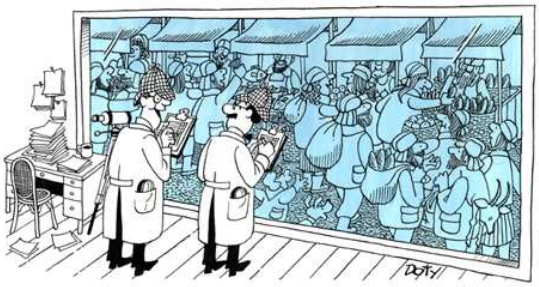
## Observation vs. Experimentation

- *Observations de populations ou d'individus*
  - *ne donne pas de preuve directe*
- *Expérimenter au labo ou "sur le terrain"*
  - *preuve directe que l'action a un effet*



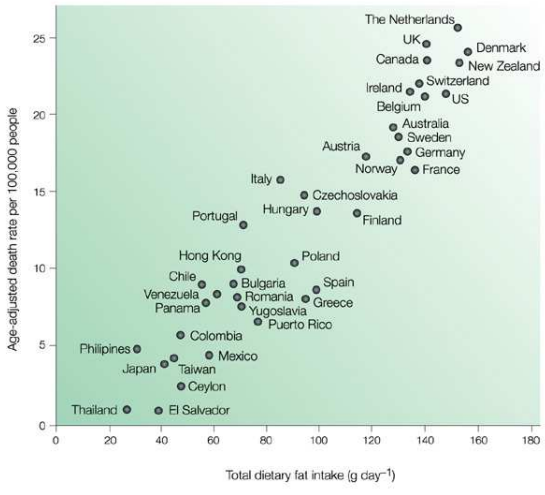
"These studies always remind me of an ant colony I had as a kid!"

# Observation vs. Experimentation

- To observe populations or individuals
  - Correlation studies (international)
  - Retrospective case-control studies
  - Prospective cohort studies
  -
- To do Experimental studies (lab or field)
  - In vitro, cell culture or bacteria
  - In vivo, animal studies (pre-clinical studies)
  - In volunteers: intervention trial

# Observation at Population Level
## **international correlation** studies

*E.g.:*
International correlation between **Fat Intake** & **Breast cancer** mortality
***(correlation is NOT a proof)***

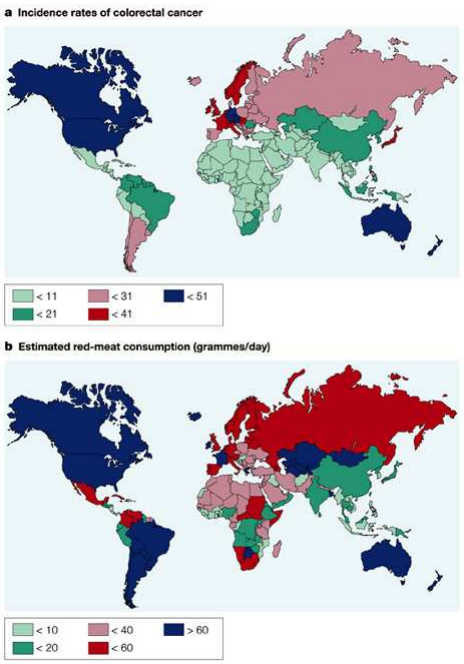



Bingham & Riboli, 2004, Nature Reviews Cancer

***International Correlation shown on a map***

**Red meat**
eating countries
Are also
**Colorectal cancer**
high risk countries

***(correlation is NOT a proof)***

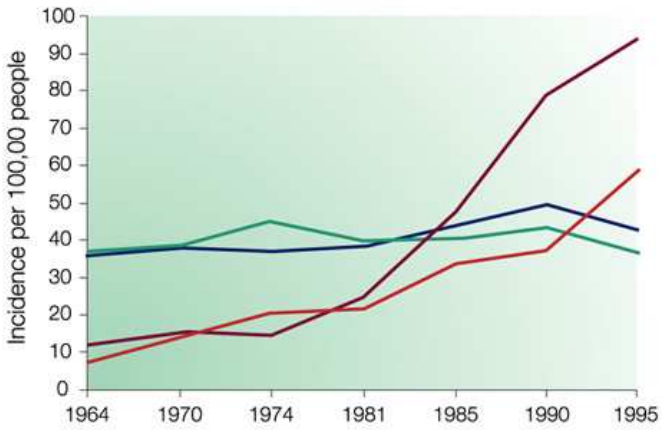



Bingham & Riboli, 2004, Nature Reviews Cancer

# Observation : Population Level Time Trends Studies

- Generates hypotheses on causes of disease : is there a change in the lifestyle that can explain the change in disease rate ?
- Also migrant studies : Observe changes in disease rate when a population migrates from a low-risk country to a high-risk country

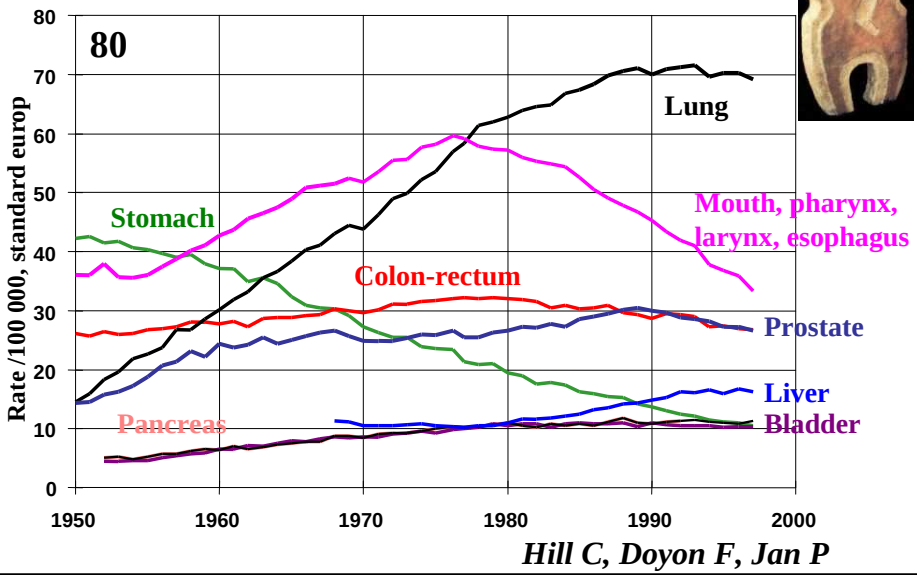
**(still not a proof !)**




Bingham & Riboli, 2004, Nature Reviews Cancer

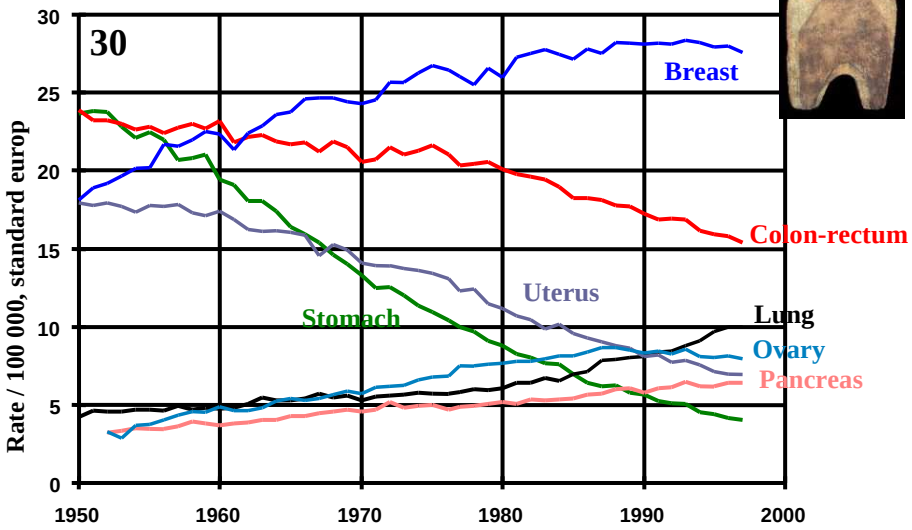
**Change with Time**
ex.: Colon cancer
in the UK (stability)
& in Japan (incrase!)

## Evolution of cancer mortality in France 1950-2000 MEN




*Hill C, Doyon F, Jan P*

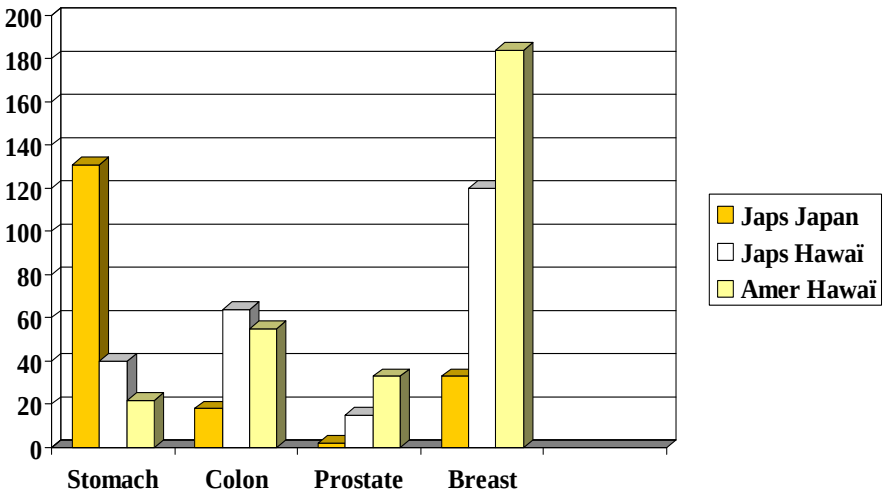
## Evolution of cancer mortality in France 1950-2000 WOMEN




*Hill C, Doyon F, Jan P*

## Migrants Japan=>Hawaï

Cancer Incidence /100 000 (Haenszel JNCI 1968)

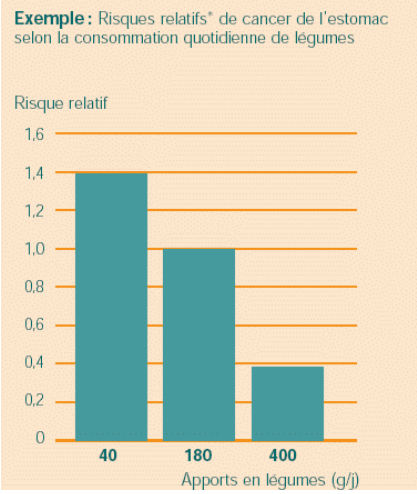


## Analytical Observation of **Individuals :** **case-control** studies (retrospectives)

- Go to the hospital, at the patient's bed (case)
- Ask many questions on past life
- Make a similar survey for similar controls
- Compare cases answers to controls answers, many questions, many people
- Ex: Stomach cancer and fruits & veg. intake

## Analytical Observation of **Individuals :** **Case-Control** studies (retrospectives)

- Population cut in 3 to 5 groups (tertiles, quartiles, quintiles)
- Relative Risk to get the condition (e.g., cancer) in the "big eater" group compared to the "small eater" group



## Analytical Observation of **Individuals :** **Case-Control** studies (retrospectives)

- Relative Risk (precisely, Odd Ratio)
- And 95% Confidence Interval

  RR=2,1 (95% C.I.= 1,2 – 4,3)
- If **ONE** is not included in the 95%CI, the risk is significant
- Other example (protection):

  RR=0.38 (IC95= 0.15-0.89)

## Analytical Observation of **Individuals :** **Case-Control** studies (retrospectives)

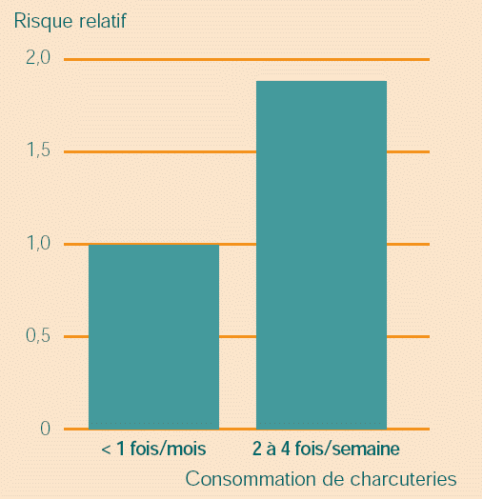
- Advantage: fast & cheap (all cases & controls are "already" there : you only need to ask them questions)
- Drawbacks: Hard to remember past diet (**recall bias**): elapsed time, and illness yield false answers
- No ideal control (Hospital? Home? Street?)
- And multiple **confusion factors**


"Well, if I recall correctly, on April 17 , 1991, at 6:37 p.m. Eastern Time, I ate 6 ounces of grilled salmon steak, farm raised, 2/3 cup of rice, 1/2 cup steamed broccoli, 1 cup of mixed salad greens with 2 tablespoons of French dressing, a 12 ounce glass of unsweetened iced tea and 3 scoops of Tin Roof ice cream for dessert."

## Analytical Observation of **Individuals :** **Cohort** Studies (prospective)

- Choose a large **healthy** cohort
- Ask them how they live **now**
- Wait a long time till some of them get ill (cancer, CVD, diabetes, … any condition you want to study)
- Compare answers from "cases" and "controls" (= the whole cohort, minus the "cases")
- Calculate relative risks (RR) and confidence intervals 95%. If excludes ONE, it's significant

## Analytical Observation of **Individuals :** **Cohort** Studies (prospective)




- Nurses' Health Study = 72000 American nurses (Harvard, USA)
- colorectal cancer & processed meat intake
- (Willet, 1990 : quintiles 1 & 5 are reported here)

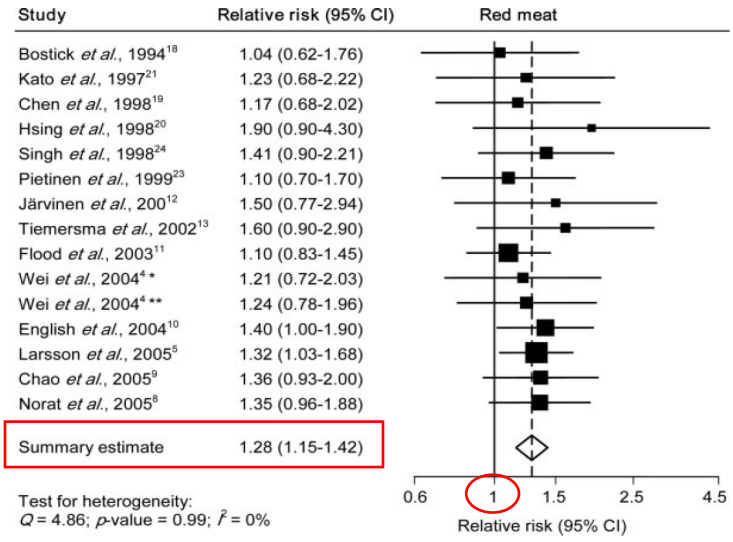
## Analytical Observation of **Individuals :** **Cohort** Studies (prospective)

- Drawback:
  - Very long (*attendre que gens "tombent malades"*)
  - Very expensive (*faut énormément de gens*)
- Advantages:
  - No "recall bias": questions address present time, to healthy people
  - Ideal controls: everybody is similar to start with
- But confusing factors still possible…


# Meta-Analysis
## of Many Cohort Studies

Larsson & Wolk IJC 2006

**Colorectal cancer & Red meat Intake**




# Observation & Expérimentation

- **Observations** *de populations ou d'individus*
  - *Études de corrélation. Evolution dans le temps*
  - *Etudes cas-témoin rétrospectives*
  - *Etudes de cohorte, prospectives*

  **Do not give a direct proof**

- Experimental studies: in the lab or "on the field"

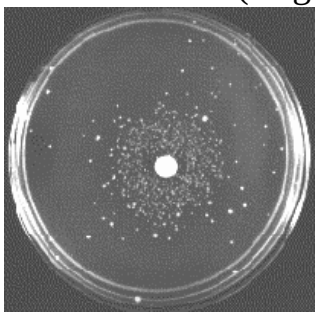
  In vitro, In vivo, in volunteers

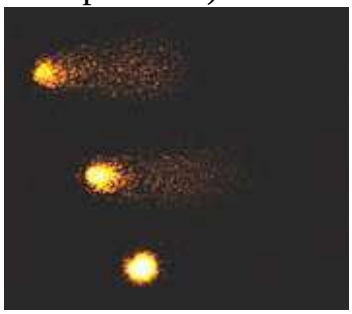
  **Direct solid proof of a cause-effect relationship**

# Experimental Studies in Laboratories

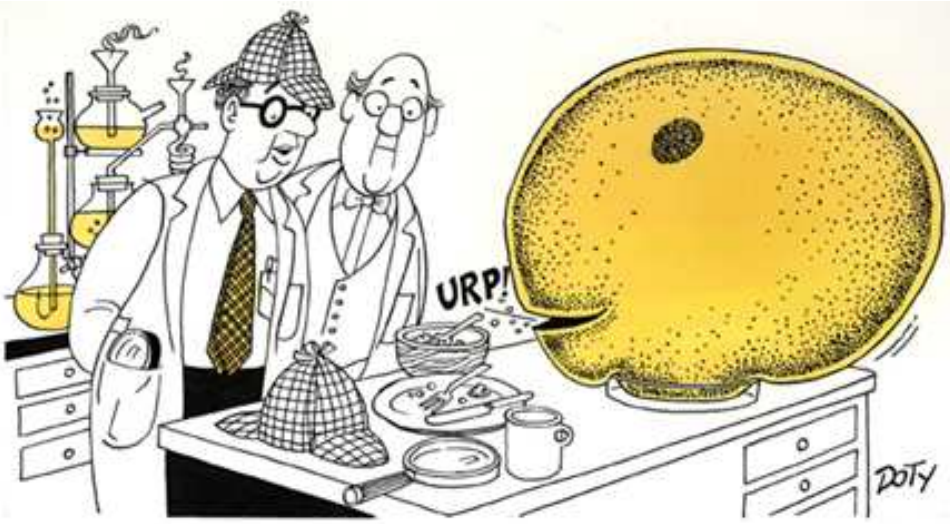
In vitro, cell culture or bacterial

- Mutagens (Ames' test)
- Clastogens (human cells chromosomes)
- Comet Test (single cell gel electrophoresis)





**In vitro**




"Looks like Carstairs finally got a single cell to eat a whole meal. By the way, have you seen Carstairs lately?"

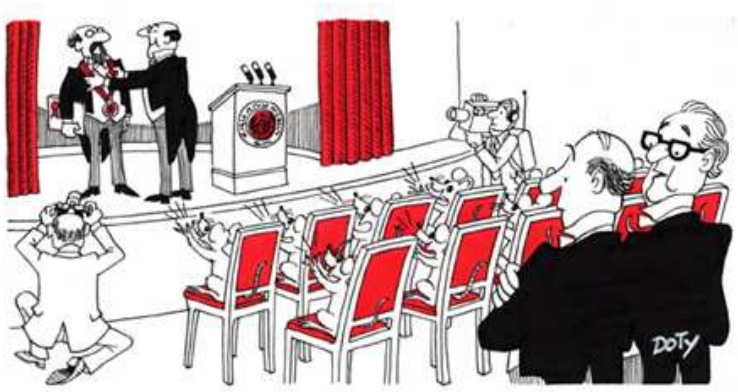
# Experimental Studies in Laboratories

In vitro, cell culture or bacterial

- Mutagens (Ames' test)
- Clastogens (human cells chromosomes)
- Comet Test (single cell gel electrophoresis)

In vivo, animal studies (preclinical)

- Physiological biomarkers
- Carcinogens
- Carcinogenicity studies: protection or promotion




"It's an award for a cancer cure, but it only works on mice."

Human Clinical Trials in Volunteers

## Intervention Studies

- Gold standard: clinical trials for drugs
- **Randomized** trial: treated ones chosen at random
- Treatment compared to a **placebo**
- **Double blinded** study:
  Volunteer AND Investigator
  do not know if placebo or treatment is taken


"Anyone for a game of Blind Man's Bluff after dinner?"

Human Clinical Trials in Volunteers

## Intervention Studies

- Randomized, placebo-controlled, double-blind intervention studies are **the only valid proofs** that a given diet/agent can change a disease risk
  - But testing one agent once costs $10 to 70 millions US dollars, et lasts 3 to 10 ans.
  - This explains why so few agents/diets have already been tested!