Clinical Epidemiology

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Clinical Epidemiology

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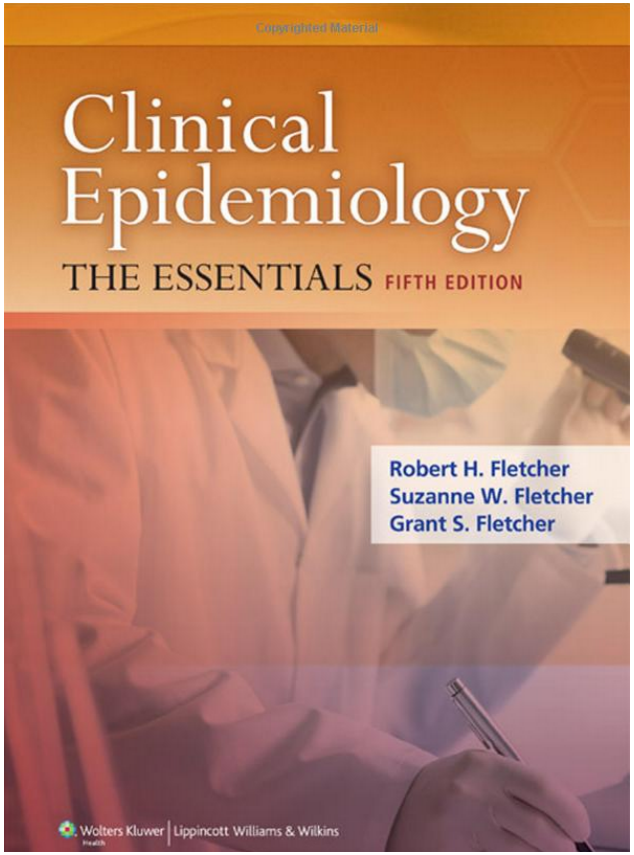


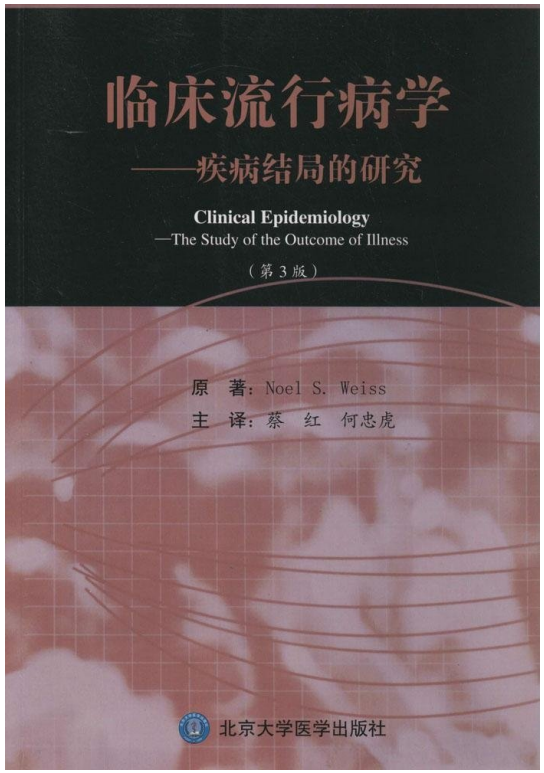
Why use this book as the text book?

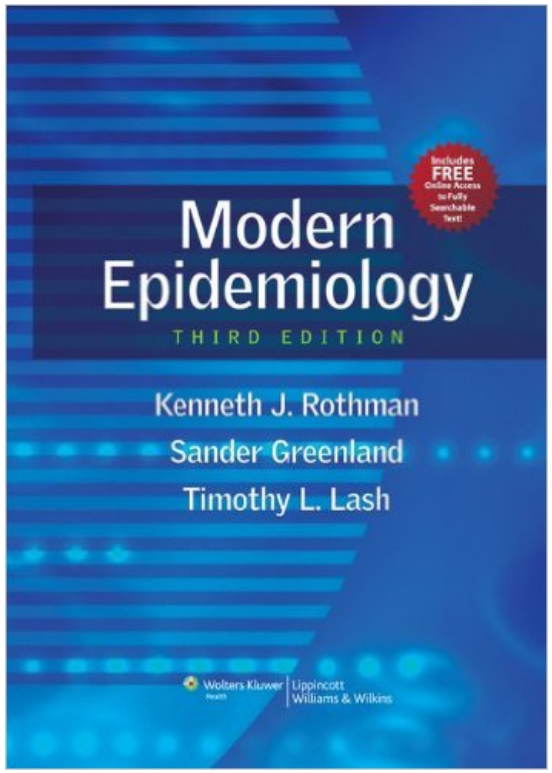
- It is written concisely.
- Understandable
- Interesting topic
- Clinical Epidemiological practices

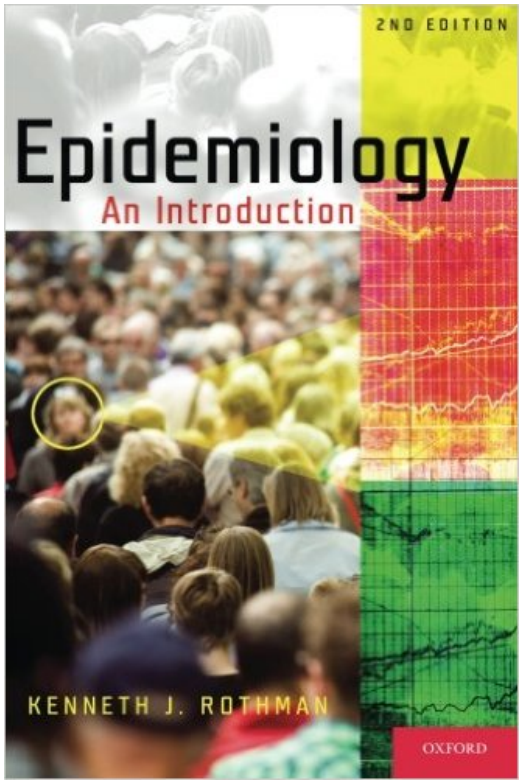
- We should study “the benefits of medical interventions in relation to their hazards and costs”.

---Kerr L.White,1992

Reference Books







Chapter 1 Introduction

- **Clinical questions and clinical epidemiology**
- **Health outcomes**
- **Scientific basis for clinical medicine**
- **Basic principles**
  - Variables
  - Numbers and probability
  - Populations and samples
  - Bias (systematic error)
  - Chance
  - The effects of bias and chance are cumulative
  - Internal and external validity
- **Information and decisions**

Patient profile

- A 51-year-old man asks to see you because of chest pain that he thinks is "indigestion". He was well until 2 weeks ago, when he noticed tightness in the center of his chest after a large meal and while walking uphill. The tightness stopped after 2 to 3 minutes of rest. A similar discomfort has occurred several times since then, sometimes during exercise and sometimes at rest. He gave up smoking one pack of cigarettes per day 3 years ago and has been told that his blood pressure is "a little high". He is otherwise well and takes no medications, But he is worried about his health, particularly about heart disease. He lost his job 6 months ago and has no health insurance. A complete physical examination and resting electrocardiogram are normal except for a blood pressure of 150/96mmHg.

This patient has many questions as following:

- **Am I sick?**
- **How sure are you?**
- **If I am sick, what is causing my illness?**
- **How will it affect me?**
- **What can be done about it?**
- **How much will it cost?**
- **……**

As a clinician, you may have the same kinds of questions:

- Is the probability of serious, treatable disease high enough to proceed immediately beyond simple explanation and reassurance to diagnostic tests?
- How well do various tests distinguish among the possible causes of chest pain: angina pectoris, esophageal spasm, muscle strain, anxiety, and the like.
- How accurately will an exercise stress test be in either confirming or ruling out coronary artery disease?
- If coronary artery disease is found, how long can the patient expect to have the pain?
- How likely is it that other complications---congestive heart failure, myocardial infarction, or atherosclerotic disease of other organs---will occur?

As a clinician, you may have the same kinds of questions:

- Will the condition shorten his life?
- Will reduction of his risk factors for coronary artery disease reduce his risk?
- Should other possible risk factors be sought?
- If medications control the pain, would a coronary revascularization procedure add benefit --- by preventing a future heart attack of cardiovascular death?
- Since the patient is unemployed and without health insurance, can less expensive diagnostic workups and treatments achieve the same result as more expensive ones?

Clinical questions and clinical epidemiology

- **The questions confronting the patient and doctor in the example are the types of clinical questions at issue in most doctor-patient encounters:**

  - **What is "abnormal"?**
  - **How accurate are the diagnostic tests we used?**
  - **How often does the condition occur?**
  - **What are the risks for a given disease, and how do we determine the risks?**
  - **Does the medical condition usually get worse, stay the same, or resolve (prognosis)?**
  - **Does treatment really improve the patients or just the test results?**
  - **Is there a way to prevent the disease?**
  - **What is the underlying cause of the disease or condition? And how can we give good medical care most efficiently?**

Clinical Issues and Questions

Issues	Questions
Frequency	How often does a disease occur?
Abnormality	Is the patient sick or well?
Risk	What factors are associated with an increased risk of disease?
Prognosis	What are the consequences of having a disease?
Diagnosis	How accurate are tests used to diagnose disease?
Treatment	How does treatment change the course of disease?
Prevention	Does an intervention on well people keep disease from arising? Does early detection and treatment improve the course of disease?
Cause	What conditions lead to disease? What are the origins of the disease?

Clinicians use various sources of information to answer the question:

- **Their own experiences**
- **The advice of their colleagues**
- **The reasoning from their knowledge of the biology of disease.**
- **……**

In many situations

- The most credible source is clinical research, which involves the use of past observations on other similar patients to predict what will happen to the patient at hand.
- The manner in which such observations are made and interpreted determines whether the conclusions reached are valid, and thus how helpful the conclusions will be to patients.

Health outcomes

Outcomes of Disease (the 5 Ds)	
Death	**A bad outcome if untimely**
Disease	**A set of symptoms, physical signs, and laboratory abnormalities**
Discomfort	**Symptoms such as pain, nausea, dyspnea, itching, and tinnitus**
Disability	**Impaired ability to go about usual activities at home, work, or recreation**
Dissatisfaction	**Emotional reaction to disease and its care, such as sadness or anger**

Example

- The incidence of type 2 diabetes mellitus is increasing dramatically in the United States. Diabetics' risk of dying from heart disease is two to four times greater than that among people without diabetes, and cardiovascular disease accounts for approximately 70% of all deaths in diabetic patients. New pharmacologic efforts to control diabetes have produced a class of drugs, thiazolidinediones, that increase insulin sensitivity in muscle, fat and the liver. Several studies showed that these drugs lower hemoglobin A_1C levels in diabetic patients.
- One such drug, rosiglitazone, was approved for use in 1999. However, over the ensuing years, several follow-up studies demonstrated a surprising result: patients on the drug were likely to experience more, not less, heart trouble, with different studies showing increases in heart attacks, heart failure, stroke, and cardiovascular or all-cause mortality. Because many of the drug on glucose and hemoglobin A1C levels were not originally designed to examine longer-term cardiovascular results, most follow-up studies were not rigorous trials.
- Nevertheless, enough concern was raised that, in 2010, the U.S. Food and Drug Administration restricted use of rosiglitazone; in Europe, sales of the drug were suspended.

Example

- What kind of conclusions can you draw from this example?
- The clinical trial on a new drug should not only include the efficient of the drug but also the adverse drug reaction.
- All the research of the new drugs should test on the patients but not only on the animals.

The Scientific Basis for Clinical Medicine

- **Clinical Epidemiology is one of the basic sciences that clinicians rely on in the care of patients.**
- **Other health sciences are also integral to patient care. Many of the sciences overlap with each other.**

The health sciences and their complementary relationships

Research Field	Primary Focus
Biologic sciences	Animal models Cells and transmitters Molecules Genes Drug development
Clinical sciences	Individual patients
Clinical epidemiology	Individual patient questions Population methods
Epidemiology	Populations
Health services	Health care systems

Clinical epidemiology

- **Is a science of making predictions about individual patients by counting clinical events (the 5 Ds) in groups of similar patients and using strong scientific methods to ensure that the predictions are accurate.**

- **The purpose of clinical epidemiology is to develop and apply methods of clinical observation that will lead to valid conclusions by avoiding being misled by systematic error and the play of chance.**

- **It is an important approach to obtaining the kind of information clinicians need to make good decisions in the care of patients.**

Clinical epidemiology

- **Two disciplines: clinical medicine and epidemiology.**
- **"Clinical": because it seeks to answer clinical questions and to guide clinical decision making with the best available evidence.**
- **"Epidemiology": because many of the methods used to answer questions about how to best care for patients have been developed by epidemiologists and because the care of individual patients is seen in the context of the larger population of which the patient is a member.**

Clinical epidemiology

- **Clinical science: provide the questions and approach that can be used to care for individual patients. E.g., knowing the anatomy of the body helps determine possibilities for diagnosis and treatment of many symptoms.**

- **Population sciences: the study large groups of people.**

- **Epidemiology: is the study of disease occurrence in human population by counting health-related events in people in relation to the naturally members.**

. Clinical Epidemiology

- For example: epidemiology studies are used as the basis for advice about avoiding behaviors such as smoking and inactivity that place patients at increased risk.

- Other epidemiologic studies, such as those showing harmful effects of passive smoking and other environmental and occupational hazards, are the basis for public health recommendations.

- Clinical epidemiology is a subset of the population sciences useful in the care of patients.

Evidence-based medicine

- **Is a modern term for the application of clinical epidemiology to the care of patients.**

- **It includes formulating specific "answerable" clinical questions, finding the best available research evidence bearing on those question, judging the evidence for its validity, and integrating the critical appraisal with the clinician's expertise and the patient's situation and values.**

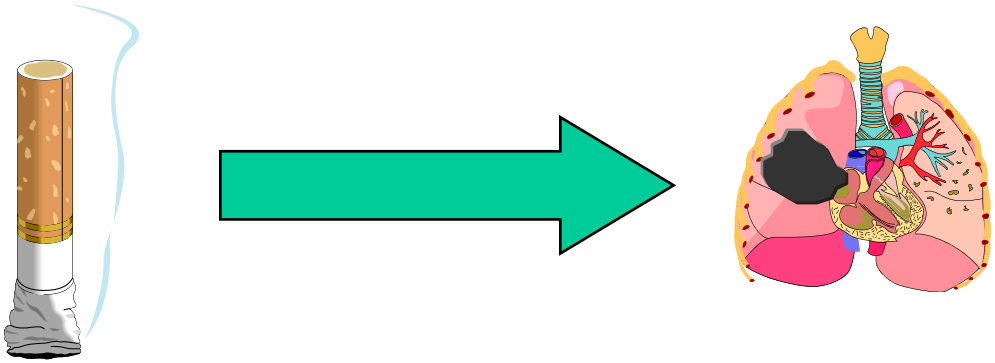
Factors other than evidence-based medicine that may influence clinical decisions

Evidence-based medicine	Senior colleagues who believe experience trumps evidence
Vehemence-based medicine	Substitution of volume and stridency for evidence
Eloquence (or elegance)- based medicine	Sartorial elegance and verbal eloquence
Providence-based medicine	The decision is best left in the hands of the Almighty
Diffidence-based medicine	Too timid to make any medical decision
Nervousness-based medicine	Fear of litigation is a powerful stimulus to overinvestigation and overtreatment
Confidence-based medicine	Bravado

What is Epidemiology?

- Epidemiology is the study of how disease is distributed in populations and the factors that influence or determine this distribution.

- Why does a disease develop in some people and not in others?



- Disease, illness and ill health are not randomly distributed in human populations.

A generalized view of epidemiology:

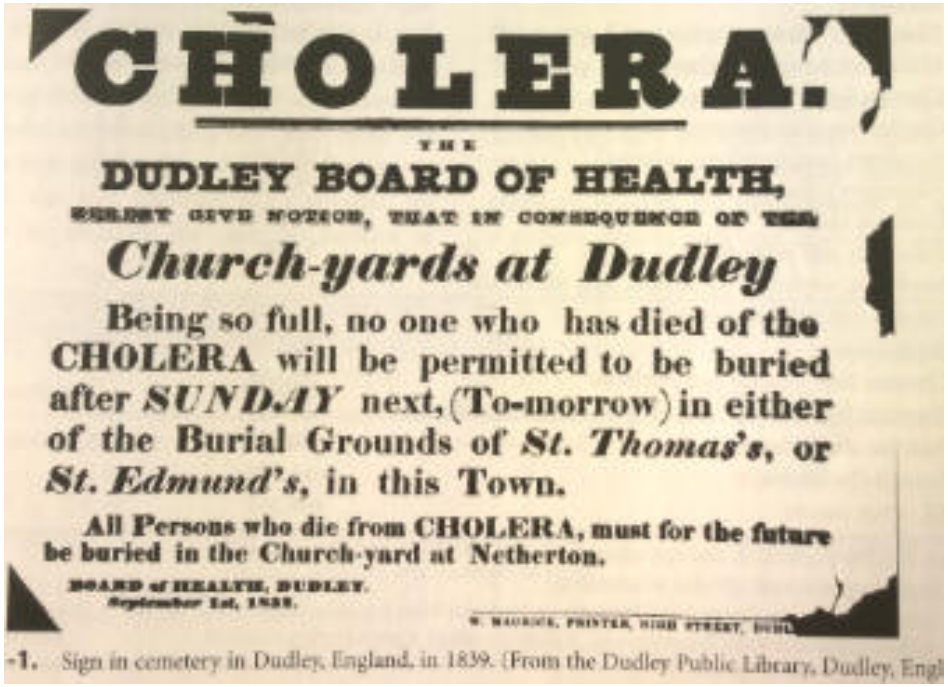
In a **human** population:

Exposures ? Disease

Epidemiology seeks to measure (quantify) these relationships

Changing Patterns of Health Problems

- Providing a clue to changes that take place over time in the health problems presenting in the community.


CHOLERA.

THE

DUDLEY BOARD OF HEALTH,

HEREBY GIVE NOTICE, THAT IN CONSEQUENCE OF THE

Church-yards at Dudley

Being so full, no one who has died of the CHOLERA will be permitted to be buried after *SUNDAY* next, (To-morrow) in either of the Burial Grounds of *St. Thomas's*, or *St. Edmund's*, in this Town.

All Persons who die from CHOLERA, must for the future be buried in the Church-yard at Netherton.

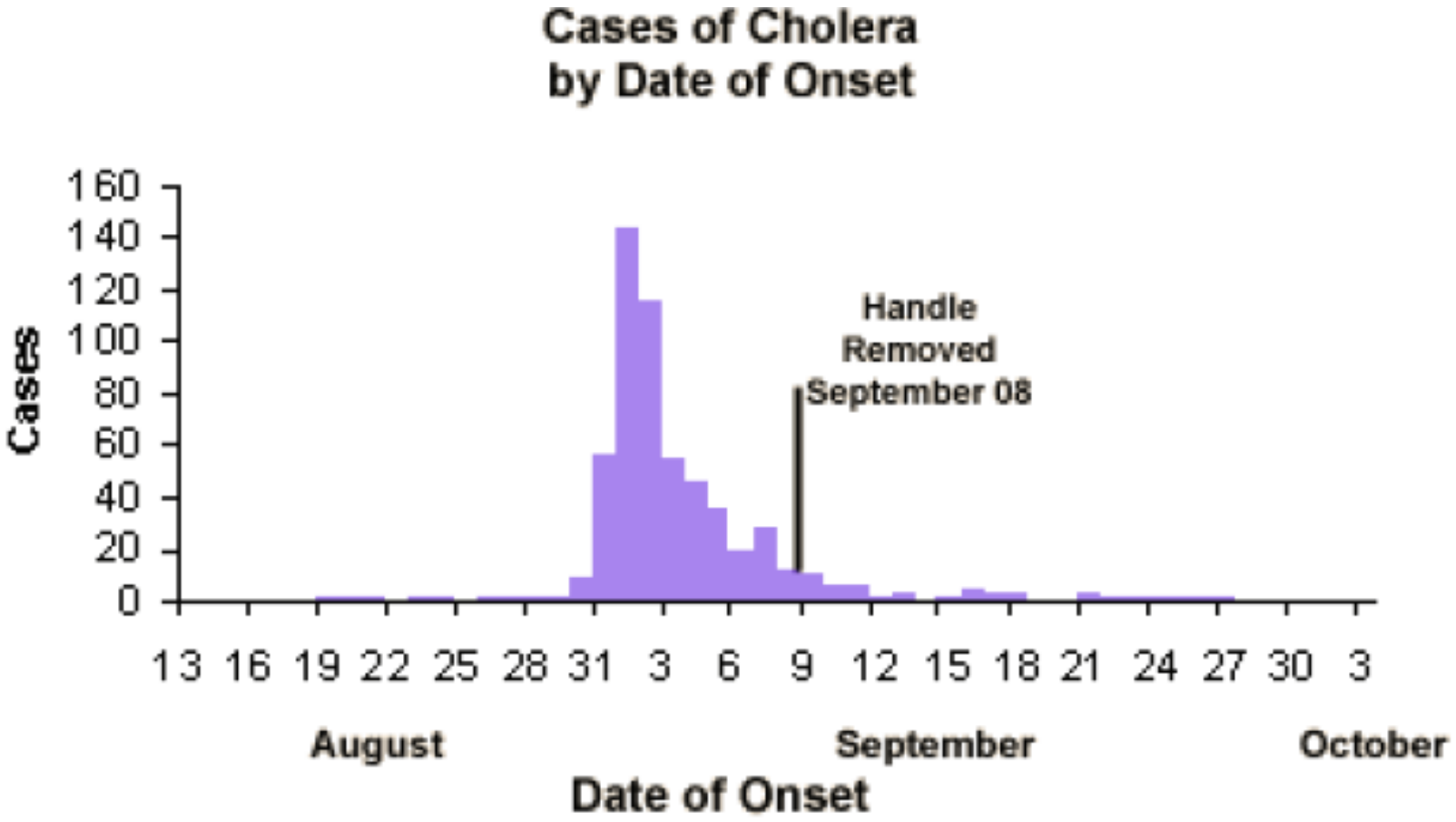
BOARD of HEALTH, DUDLEY.
September 1st, 1831.

W. MACKIE, PRINTER, HIGH STREET, DUDLEY.

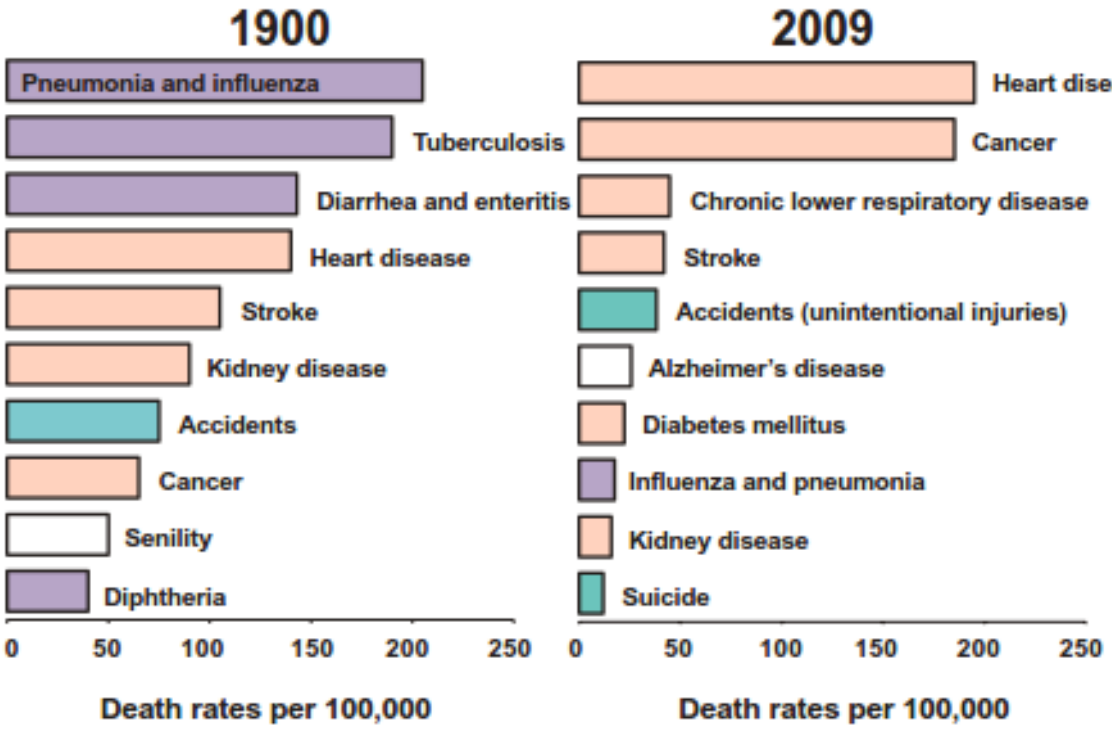
-1. Sign in cemetery in Dudley, England, in 1839. (From the Dudley Public Library, Dudley, Engl

- "No burials of persons who died of cholera would henceforth be permitted."
- The sign conveys an idea of the importance of cholera in the public's consciousness in the early 19th century.

John Snow and Cholera in London



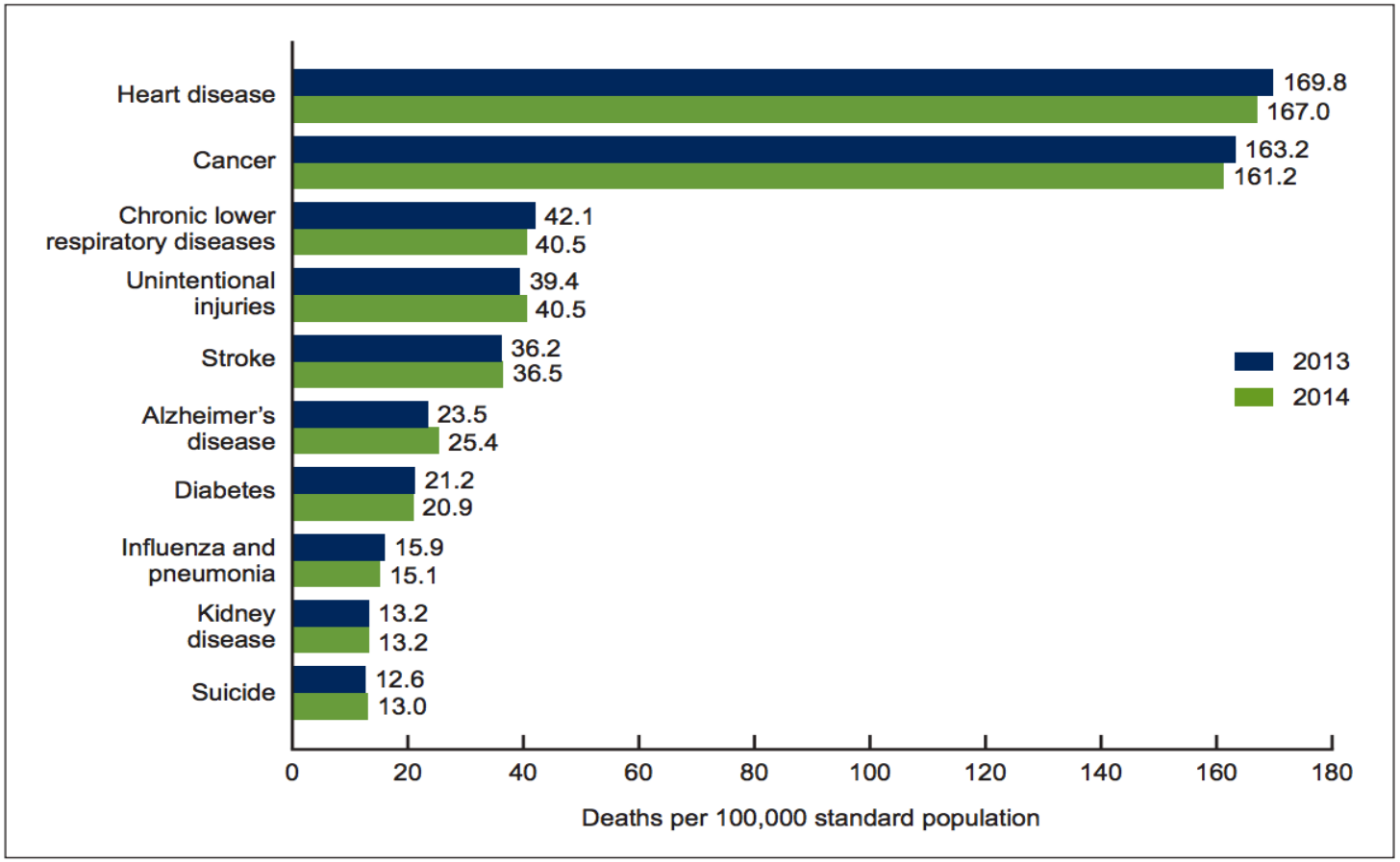
Changing Patterns of Health Problems



- The leading causes of death in the USA, 1900 and 2009. ***What change has occurred?***
- A ***dramatic shift*** in the causes of death in USA.
- **The *pattern of disease occurrence*** is different between developed countries and developing countries.

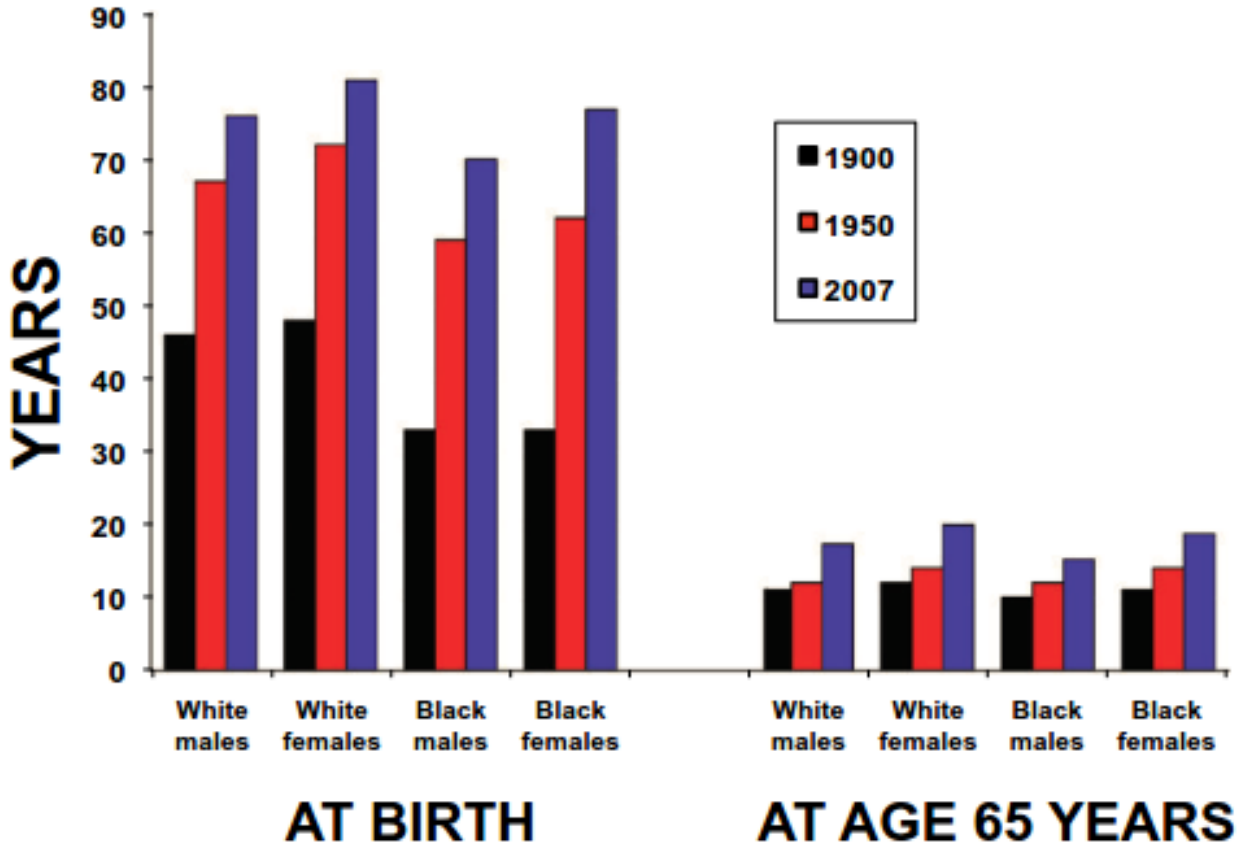
Changing Patterns of Health Problems

Figure 3. Age-adjusted death rates for the 10 leading causes of death: United States, 2013 and 2014



NOTES: A total of 2,626,418 resident deaths were registered in the United States in 2014. The 10 leading causes accounted for 73.8% of all deaths in the United States in 2014. Access data table for Figure 3 at: http://www.cdc.gov/nchs/data/databriefs/db229_table.pdf#1. Causes of death are ranked according to number of deaths.
SOURCE: CDC/NCHS, National Vital Statistics System, Mortality.

Changing Patterns of Health Problems



- What primarily accounts for the increase in remaining years of life at birth are the decreases in infant mortality and in mortality from childhood disease.
- For adults, we have been much less successful in extending the span of life.

- Life expectancy at birth and at 65 years of age, by race and sex, US,1990,1995, 2007.

(NCHS, NVSR,2010)

Epidemiology and Prevention

◆**Why should we identify such high-risk groups?**

- **To direct preventive efforts, such as screening programs for early disease detection.**
- **To identify the specific factors or characteristics that put them at high risk and then try to modify those factors.**

◆Primary, Secondary and Tertiary prevention

TABLE 1-2. Three Types of Prevention

Type of Prevention	Definition
Primary prevention	Preventing the *initial development* of a disease
Secondary prevention	Early detection of *existing disease* to reduce severity and complications
Tertiary prevention	Reducing the *impact of the disease*

To prevent the development of a disease in a person who is well and does not(yet) have the disease.

Identifying people in whom a disease process has already begun but symptoms of the illness.

Denotes preventing complications in those who have already developed signs and symptoms of an illness and have been diagnosed.

◆Two Approaches to Prevention: a Different View

- **A population-based approach**

  e.g. Prudent dietary advice for preventing CAD

  (inexpensive and noninvasive)

- **A high-risk approach**

  e.g. Screening for cholesterol in children might be restricted to children from high-risk families.

  (more expensive and invasive or inconvenient.)

Clinical Practice and Epidemiology

- **The practice of medicine is dependent on the population data.**

  - ✓**Diagnosis**
  - ✓**Prognostication**
  - ✓**Selection of appropriate therapy.**

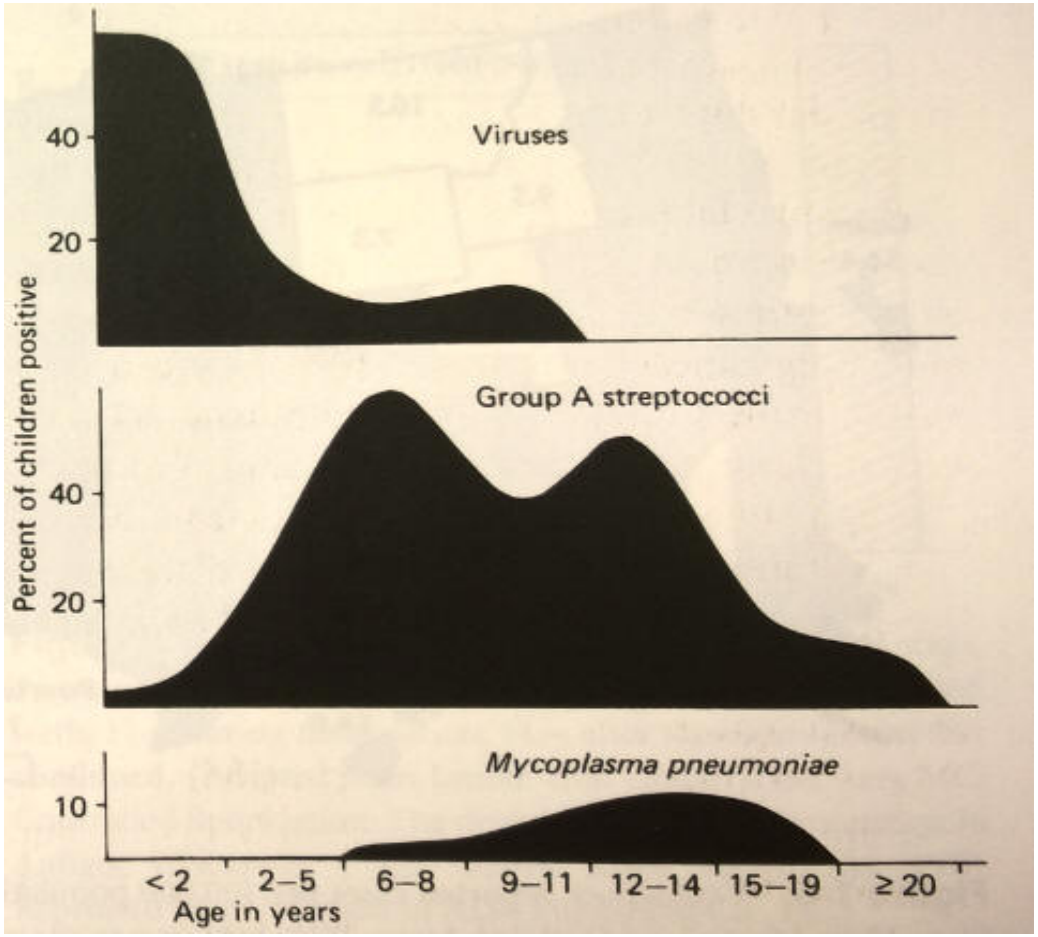
Clinical Practice and Epidemiology

"You've got whatever it is that's going around."

Figure 1-4. "You've got whatever it is that's going around." (© The New Yorker Collection 1975. Al Ross from cartoonbank.com. All rights reserved.)

- e.g. A patient asks his physician, "how long do I have to live, doctor?" and the doctor replies: "Six month to a year."
- On what basis does the physician prognosticate?
- On the basis of experience with large groups of patients who had the same disease, which is based on the population data.

Clinical Practice and Epidemiology



- e.g. If the infection occurs early in life, it is likely to be viral in origin.
- If it occurs at ages 4 to 7 years, it is likely to be streptococcal in origin.
- In an older children Mycoplasma becomes more important.

Frequency of agents by age of children with pharyngitis, 1964-1965.

The Epidemiology Approach

How does the epidemiologist proceed to identify the cause of a disease?

- To determine whether an association exists between exposure to a factor (e.g. an environmental agent) or a characteristic of a person (e.g. an increased serum cholesterol level) and the development of the disease in question.

- To try to derive appropriate inferences about a possible causal relationship from the patterns of the associations that have been found.

Gonorrhea: reported cases per 100,000 population, US and territories, 2010.

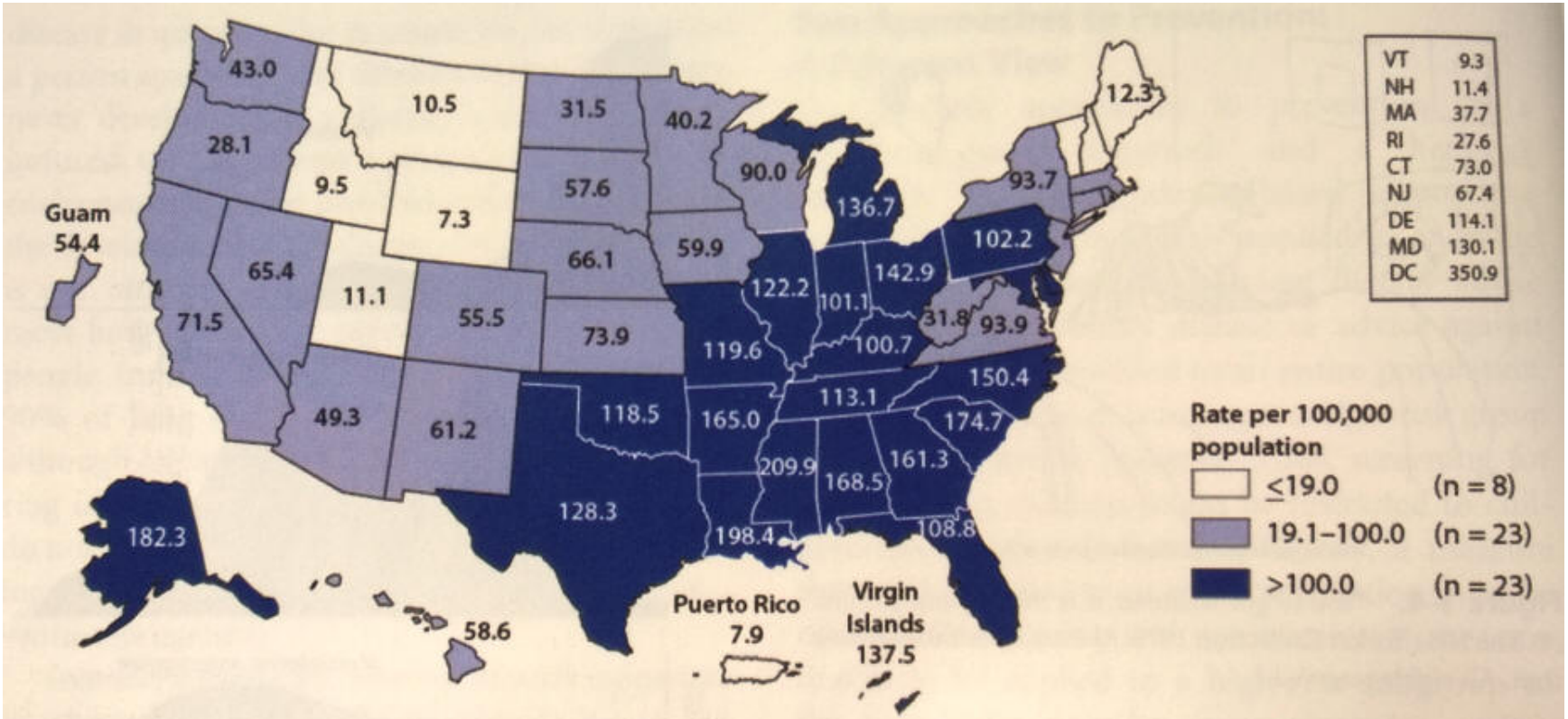


Figure 1-6. Gonorrhea: reported cases per 100,000 population, United States and territories, 2010. (From Gonorrhea—Rates by State, United States and Outlying Areas, 2010. http://www.cdc.gov/std/stats10/figures/17.htm. Accessed January 24, 2013.)

Epidemiology often begins with the descriptive data

- "Are these differences real?"
- "Are the data from each area of comparable quality?
- "Why have these differences occurred?"
- "Are these environmental differences between high-risk and low-risk areas, or are these differences in the people who live in those area?"

Epidemiology often begins with the descriptive data

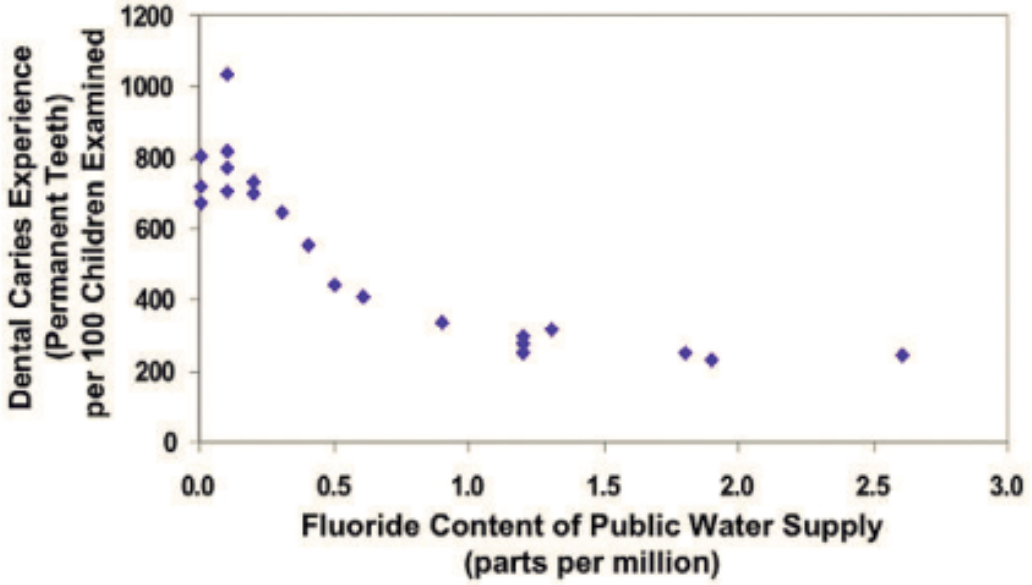
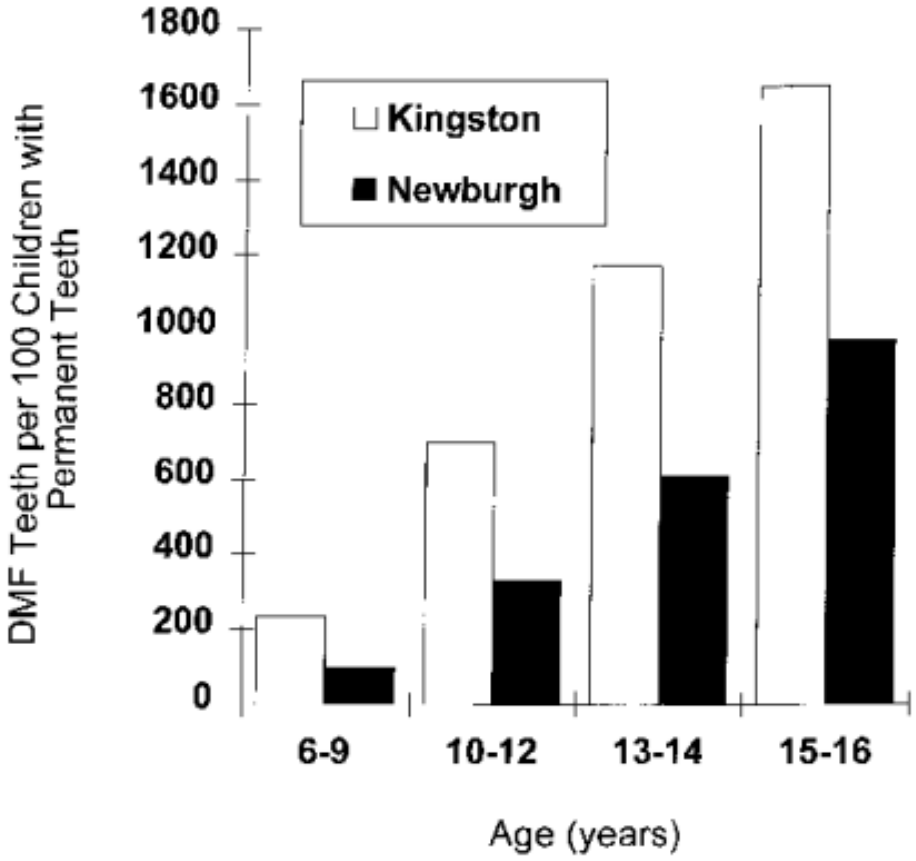


Figure 1-7. Relationship between rate of dental caries in children's permanent teeth and fluoride content of public water supply. (Adapted from Dean HT, Arnold FA Jr, Elvove E: Domestic water and dental caries: V. Additional studies of the relation of fluoride in domestic waters to dental caries experience in 4,425 white children aged 12 to 14 years of 13 cities in 4 states. Public Health Rep 57:1155–1179, 1942.)

- **Hypothesis:**

Fluoride might be an effective prevention of caries if it were artificially added to the drinking water supply.

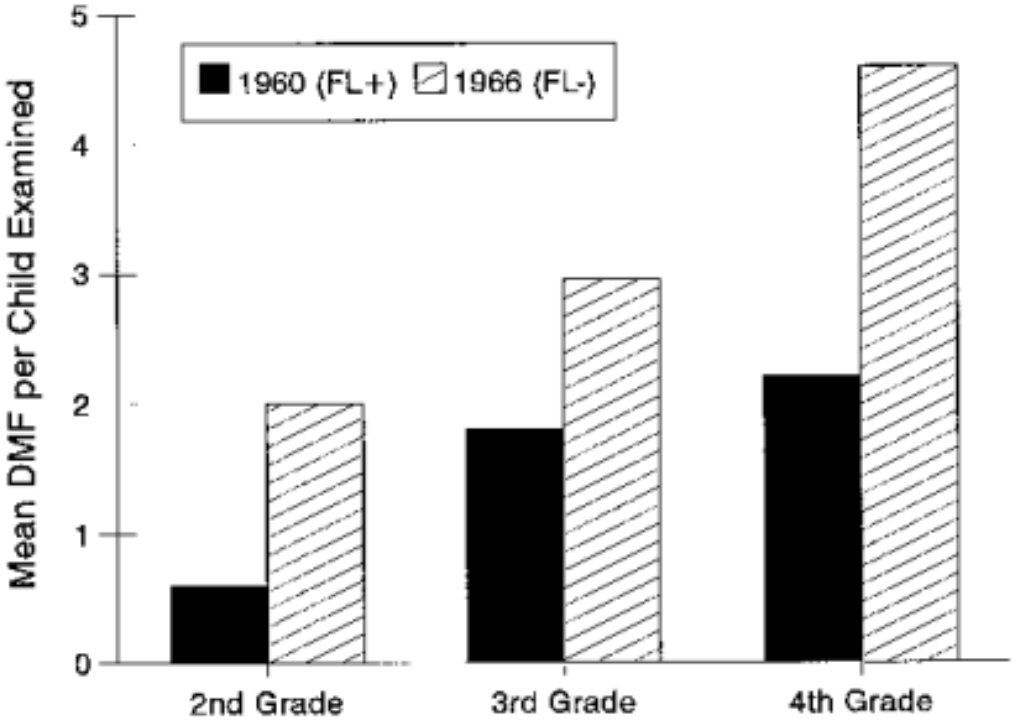
A trial was therefore carried out to test the hypothesis



- The baseline data from the two cities was comparable.
- **Intervention:** The water in Newburgh was fluoridated.
- **Follow-up:** DMF indices after 10 year of fluoridation, 1954-1955. (DMF, a count of decayed, missing and filled teeth.)

A causal relationship between fluoride ingestion and low rates of caries.

Another trial was carried out to test the hypothesis



- Effect of discontinuing fluoridation in Antigo, Wisconsin,1960.

- FL(+): during fluoridation
- FL(-): after fluoridation was discontinued.

This provide a further piece of evidence that fluoride acted to prevent dental caries.

From Observations to Preventive Actions

- Ignaz Semmelweis and Childbed Fever

  - Ignaz Semmelweis was born on July 1, 1818 in Tabán, neighbourhood of Buda, Hungary,
  - Ignaz Semmelweis began studying law at the University of Vienna in the autumn of 1837, but by the following year, he had switched to medicine.

From Observations to Preventive Actions

- Ignaz Semmelweis and Childbed Fever

- The first clinic was staffed by physicians and medical students.
- The second clinic by midwives.
- Physicians and students began their days performing autopsies on women who had died from childbed fever; they then proceeded to provide clinical care for childbirth.
- The midwives staffing the second clinic did not perform autopsies.

Maternal mortality due to childbed fever, first and second clinics, General Hospital, Vienna, Austria,1842.

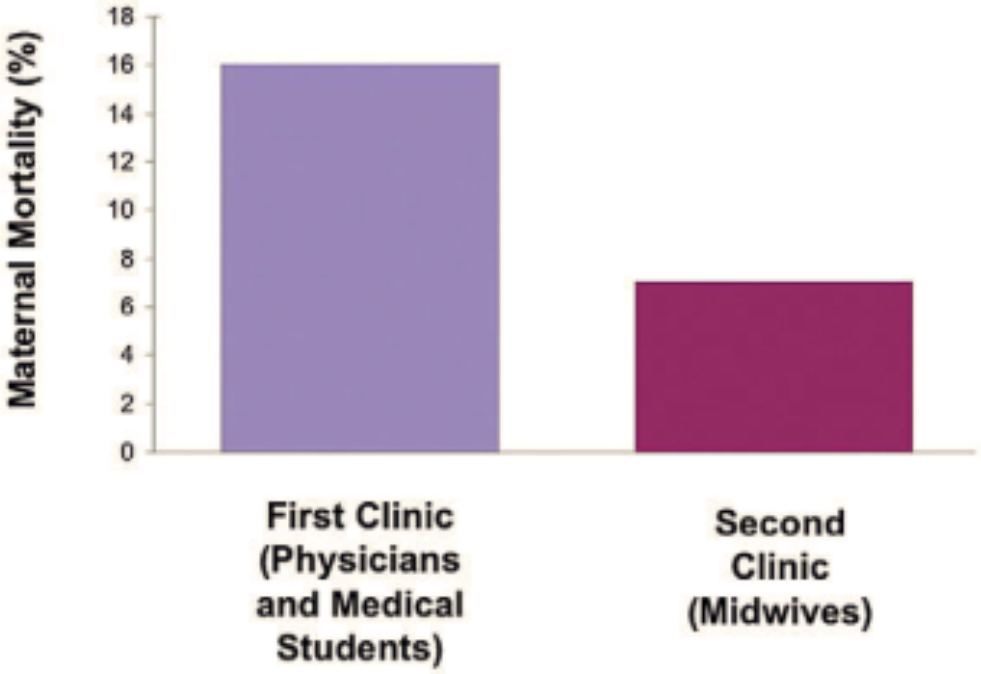
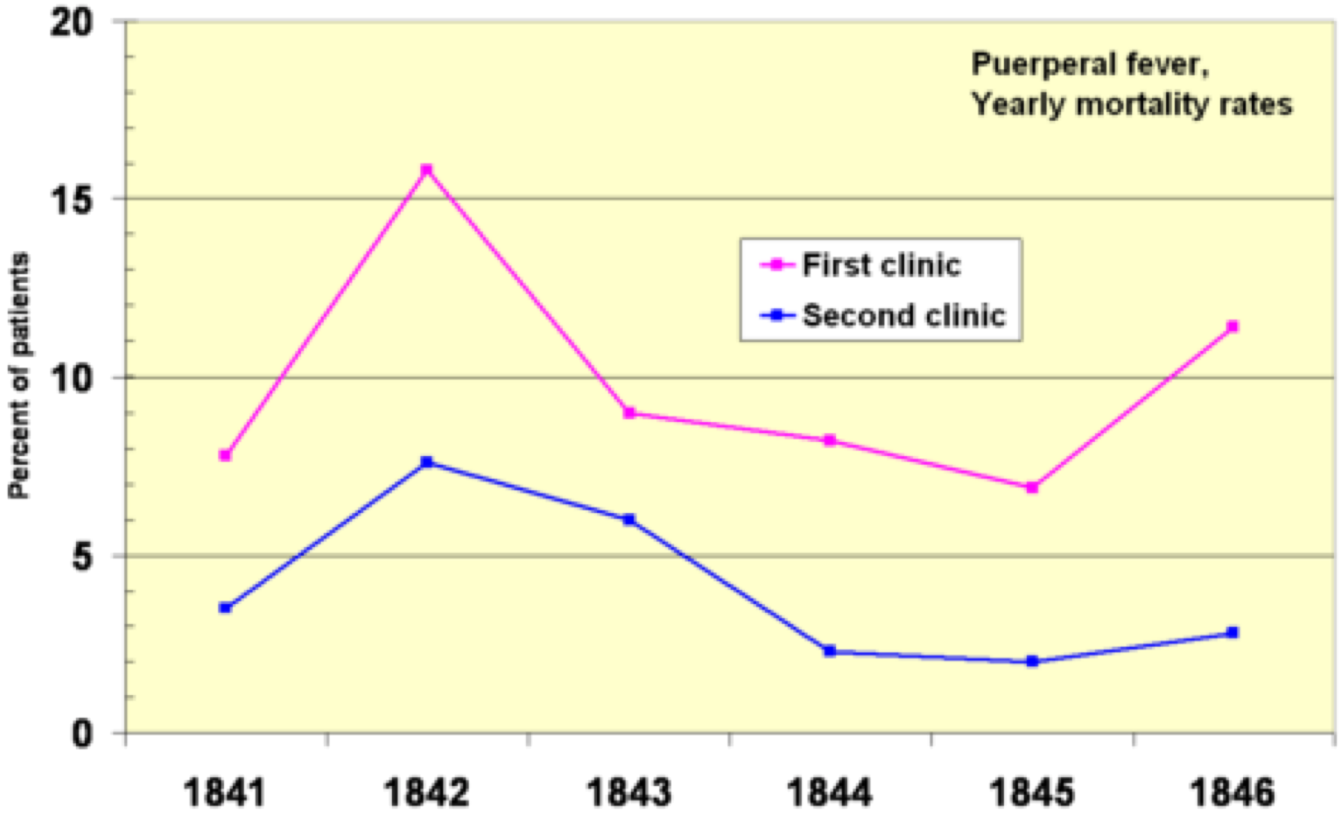


Figure 1-11. Maternal mortality due to childbed fever, First and Second Clinics, General Hospital, Vienna, Austria, 1842. (Adapted from the Centers for Disease Control and Prevention: Hand hygiene in health care settings—Supplemental. www.cdc.gov/handhygiene/download/hand_hygiene_supplement.ppt. Accessed April 11, 2013.)

Puerperal fever mortality rates for the First and Second Clinic at the Vienna General Hospital 1841–1846.

	First clinic			Second clinic		
Year	Births	Deaths	Rate (%)	Births	Deaths	Rate (%)
1841	3,036	237	7.8	2,442	86	3.5
1842	3,287	518	15.8	2,659	202	7.6
1843	3,060	274	9.0	2,739	164	6.0
1844	3,157	260	8.2	2,956	68	2.3
1845	3,492	241	6.9	3,241	66	2.0
1846	4,010	459	11.4	3,754	105	2.8

Puerperal fever mortality rates for the First and Second Clinics at the Vienna General Hospital 1841–1846

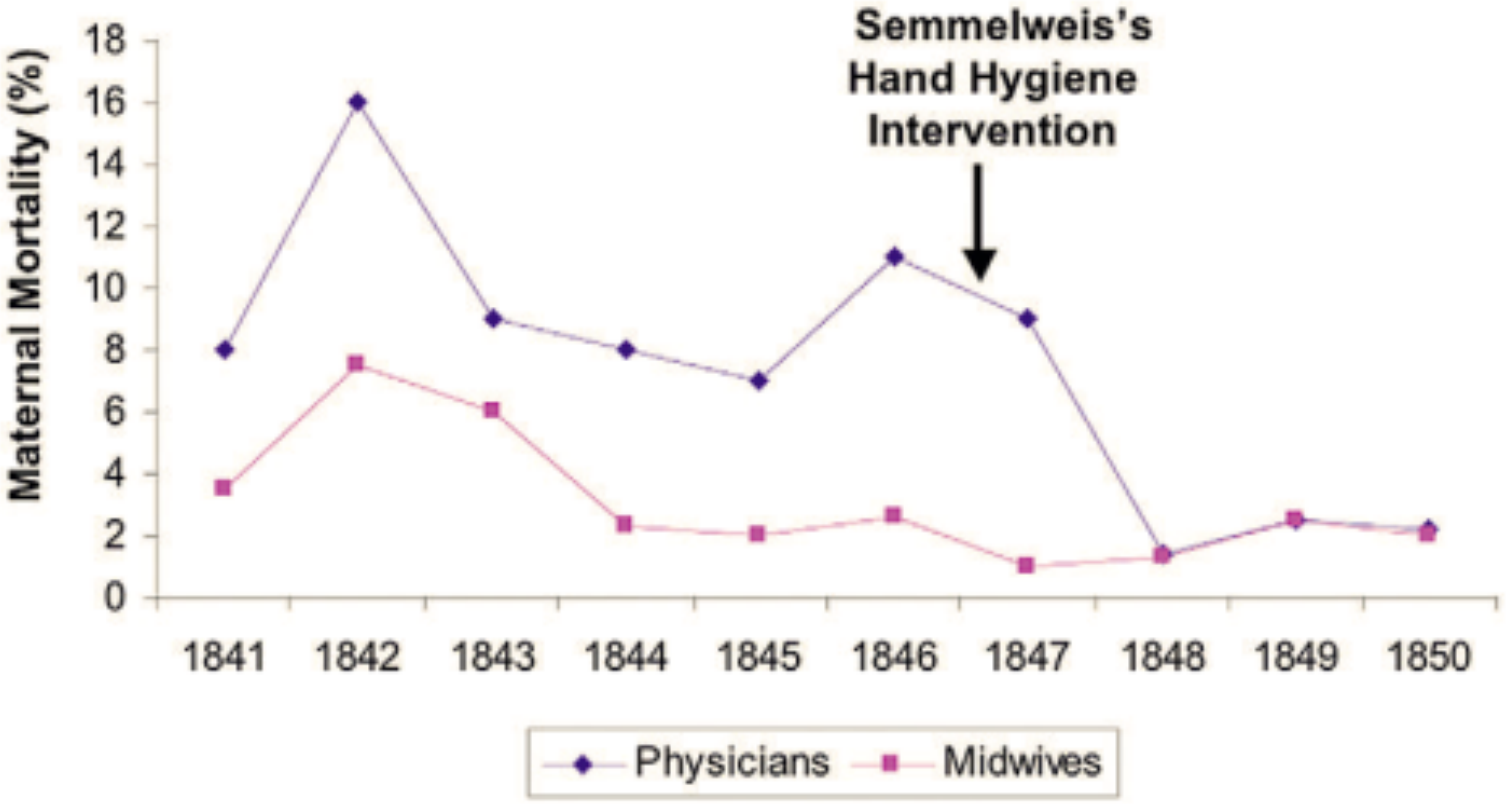


- Semmelweis developed and implemented a policy for the physicians and medical students in the first clinic after they had finished the autopsies and before they came in contact with any of the patients:

  (1)wash their hands

  (2)brush under their fingernails

Mortality in the first clinic dropped from 12.2% to 2.4%, a rate comparable to that seen in the second clinic.



Summary on Ignaz Semmelweis and Childbed Fever

- Many years passed before a policy of hand washing was broadly adopted.
- Years later, the major cause of childbed fever was recognized to be a streptococcal infection.
- However, recent studies have reported that many physicians in hospitals in the US and in other countries still fail to wash their hands as prescribed.

TABLE 1-3. Compliance with Hand Hygiene among Physicians, by Specialty, at University of Geneva Hospitals

Physician Specialty	Number of Physicians	Compliance with Hand Hygiene (% of Observations)
Internal medicine	32	87.3
Surgery	25	36.4
Intensive care unit	22	62.6
Pediatrics	21	82.6
Geriatrics	10	71.2
Anesthesiology	15	23.3
Emergency medicine	16	50.0
Other	22	57.2

Data from Pittet D: Hand hygiene among physicians: Performance, beliefs, and perceptions. Ann Intern Med 141(1):1–8, 2004.

From Observations to Preventive Actions

- Edward Jenner and Smallpox

  - Edward Jenner was born in Berkeley, Gloucestershire on 17 May 1749. At the age of 14, he was apprenticed to a local surgeon and then trained in London.
  - In 1772, he returned to Berkeley and spent most the rest of his career as a doctor in his native town.

From Observations to Preventive Actions

- Edward Jenner and Smallpox
  - In 1796, he carried out his now famous experiment on eight-year-old James Phipps. Jenner inserted pus taken from a cowpox pustule and inserted it into an incision on the boy's arm.
  - He was testing his theory that milkmaids who suffered the mild disease of cowpox never contracted smallpox, one of the greatest killers of the period, particularly among children.
  - Jenner subsequently proved that having been inoculated with cowpox Phipps was immune to smallpox.

From Observations to Preventive Actions

- Edward Jenner and Smallpox

- He submitted a paper to the Royal Society in 1797 describing his experiment, but was told that his ideas were too revolutionary and that he needed more proof.
- Undaunted, Jenner experimented on several other children, including his own 11-month-old son.
- In 1798, the results were finally published and Jenner coined the word vaccine from the Latin 'vacca' for cow.

Summary on Edward Jenner and Smallpox

- In 1967, WHO began international efforts to eradicate smallpox using vaccinations with vaccinia virus(cowpox).
- It has been estimated that, until that time, smallpox afflicted 15 million people annually throughout the world.
- In 1980, the WHO Smallpox Eradication Program certified that smallpox had been eradicated, which is one of the greatest disease prevention achievements in human history.

From Observations to Preventive Actions

- **John Snow and Cholera**
  - John Snow was a famous doctor in London and he attended Queen Victoria as her personal physician. But he became inspired when he thought about helping ordinary people exposed to cholera.
  - This was the deadly disease of its day. Neither its cause nor its cure was understood. So many thousands of terrified people died every time there was an outbreak.
  - John Snow wanted to face the challenge and solve this problem. He knew that cholera would never be controlled until its cause was found.

• John Snow and Cholera

- In 1854, about 600 people living within a few blocks of the broad Street pump in London died of cholera.
- The registrar General was William Farr, who had a disagreement about the cause of cholera with Snow.
- Farr adhered to what was called the miasmatic theory of disease: disease was transmitted by a **miasm** or cloud , that clung low on the surface of the earth.

TABLE 1-4. **Deaths from Cholera in 10,000 Inhabitants by Elevation of Residence above Sea Level, London, 1848–1849**

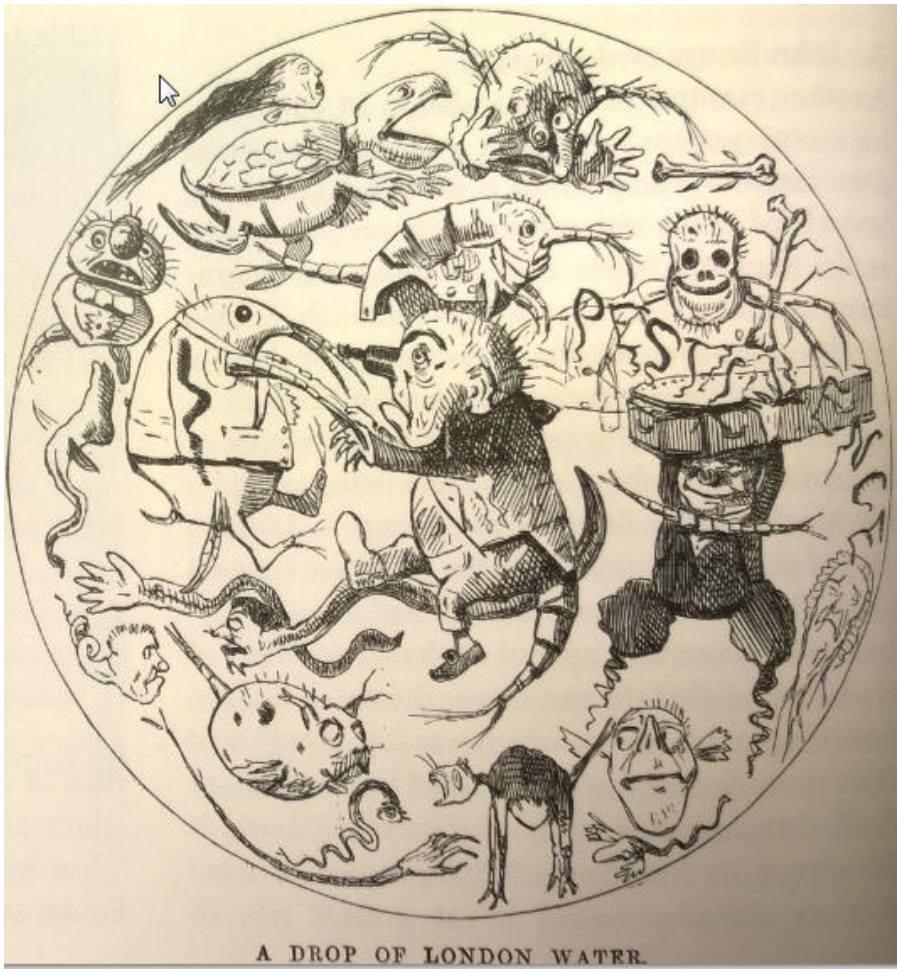
Elevation above Sea Level (ft)	Number of Deaths
<20	120
20–40	65
40–60	34
60–80	27
80–100	22
100–120	17
340–360	8

Data from Farr W: Vital Statistics: A Memorial Volume of Selections from the Reports and Writings of William Farr (edited for the Sanitary Institute of Great Britain by Noel A. Humphreys). London, The Sanitary Institute, 1885.

• John Snow and Cholera

- Snow believed that cholera was transmitted through contaminated water.

- In London at that time, two water supply companies intake the polluted water from Thames river. Lambeth Company shifted its water intake upstream in the Thames to a less polluted part of river, the other company did not move the locations of their water intakes.



- **John Snow and Cholera**

"Shoe-leather epidemiology"---going from house to house, counting all deaths from cholera in each house, and determining which company supplied water to each house.

- **John Snow and Cholera**

TABLE 1-5. Deaths from Cholera per 10,000 Houses, by Source of Water Supply, London, 1854

Water Supply	Number of Houses	Deaths from Cholera	Deaths per 10,000 Houses
Southwark and Vauxhall Co.	40,046	1,263	315
Lambeth Co.	26,107	98	38
Other districts in London	256,423	1,422	56

Data adapted from Snow J: On the mode of communication of cholera. In Snow on Cholera: A Reprint of Two Papers by John Snow, M.D. New York, The Commonwealth Fund, 1936.

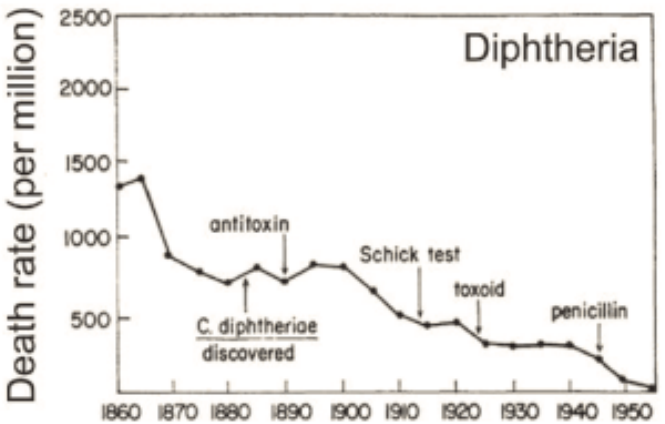
Summary on John Snow and Cholera

- **Remember that, in Snow's day, the enterotoxin *Vibrio cholera* was unknown.**

- **Snow's conclusion that contaminated water was associated with cholera was based entirely on observational data.**

- **When the frequency of a disease declines, who deserved the credit?**

A



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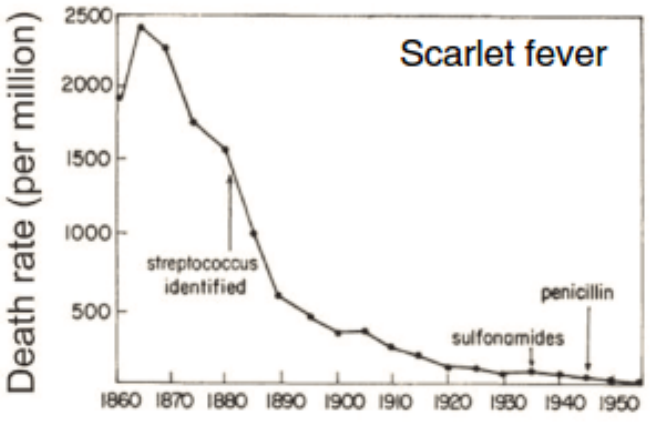

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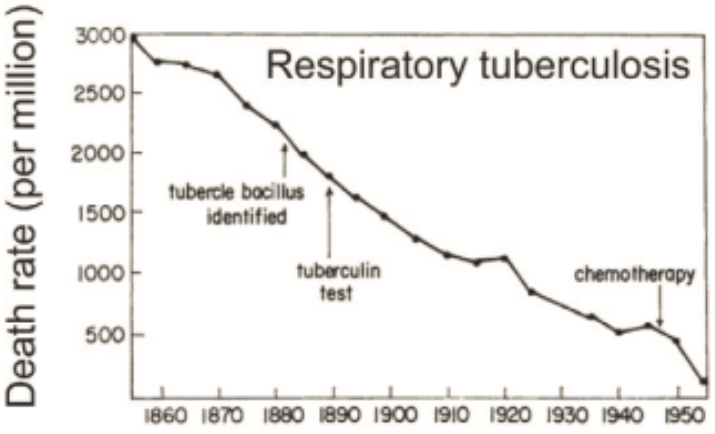


D

- **When the frequency of a disease declines, who deserved the credit?**

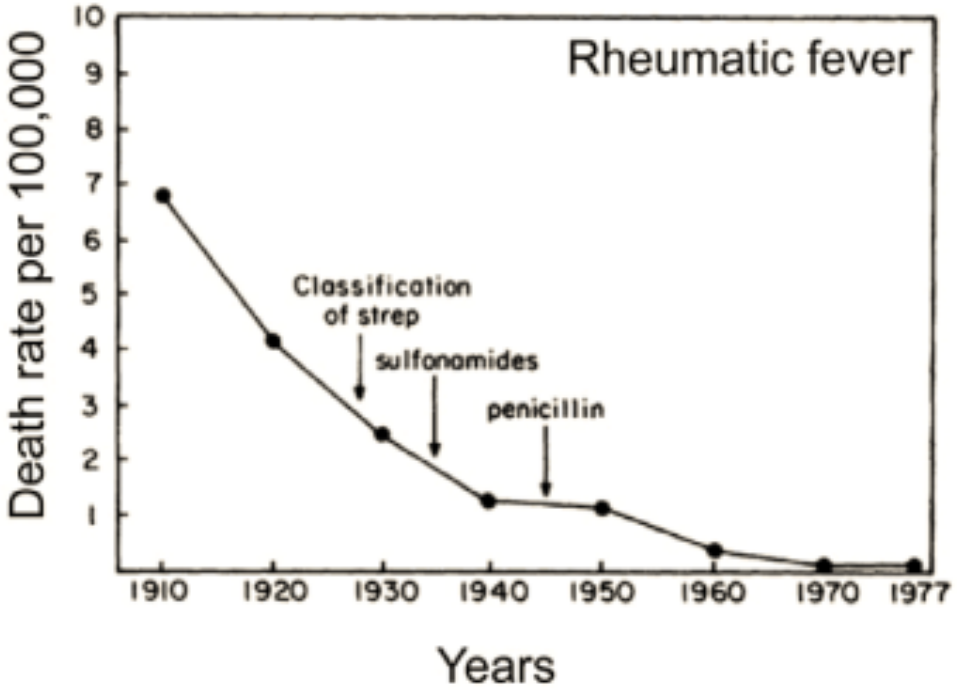
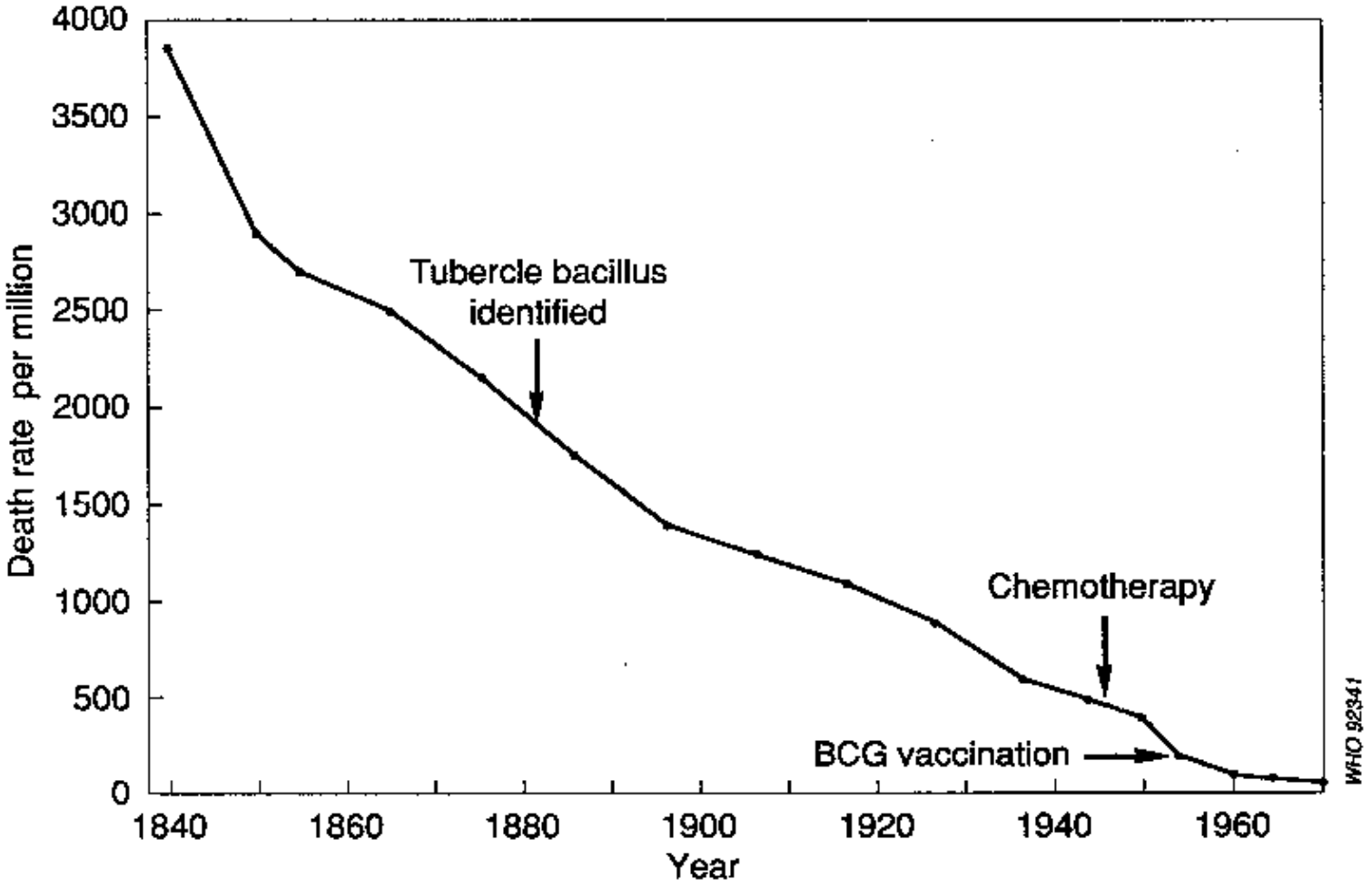


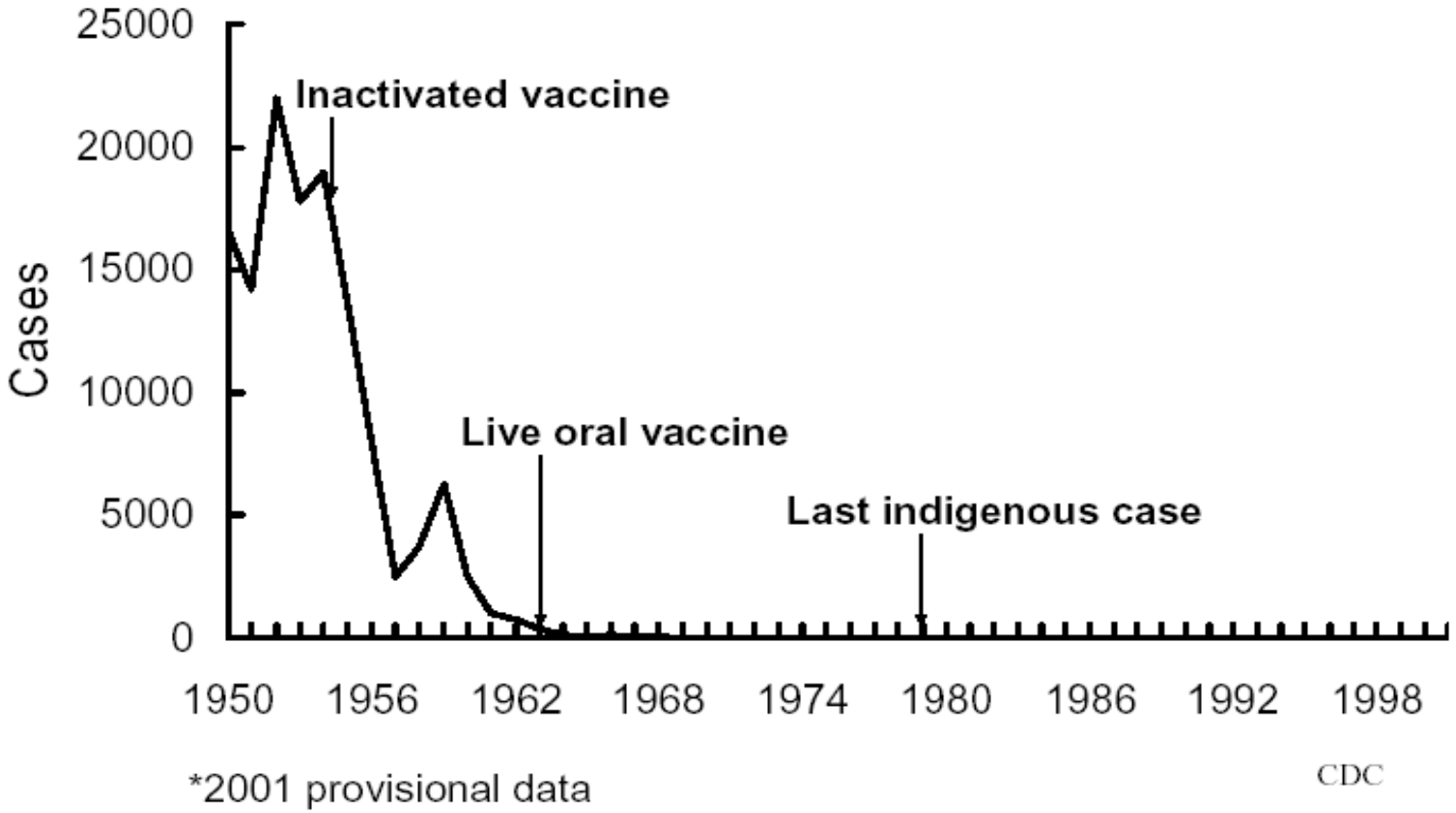
Figure 1-20. Decline in crude death rates from rheumatic fever, United States, 1910–1977. (From Gordis L: The virtual disappearance of rheumatic fever in the United States: lessons in the rise and fall of disease. T. Duckett Jones Memorial Lecture. Circulation 72:1155–1162, 1985.)

Fig. 6.1. Age-standardized death rates from tuberculosis in England and Wales, 1840–1968

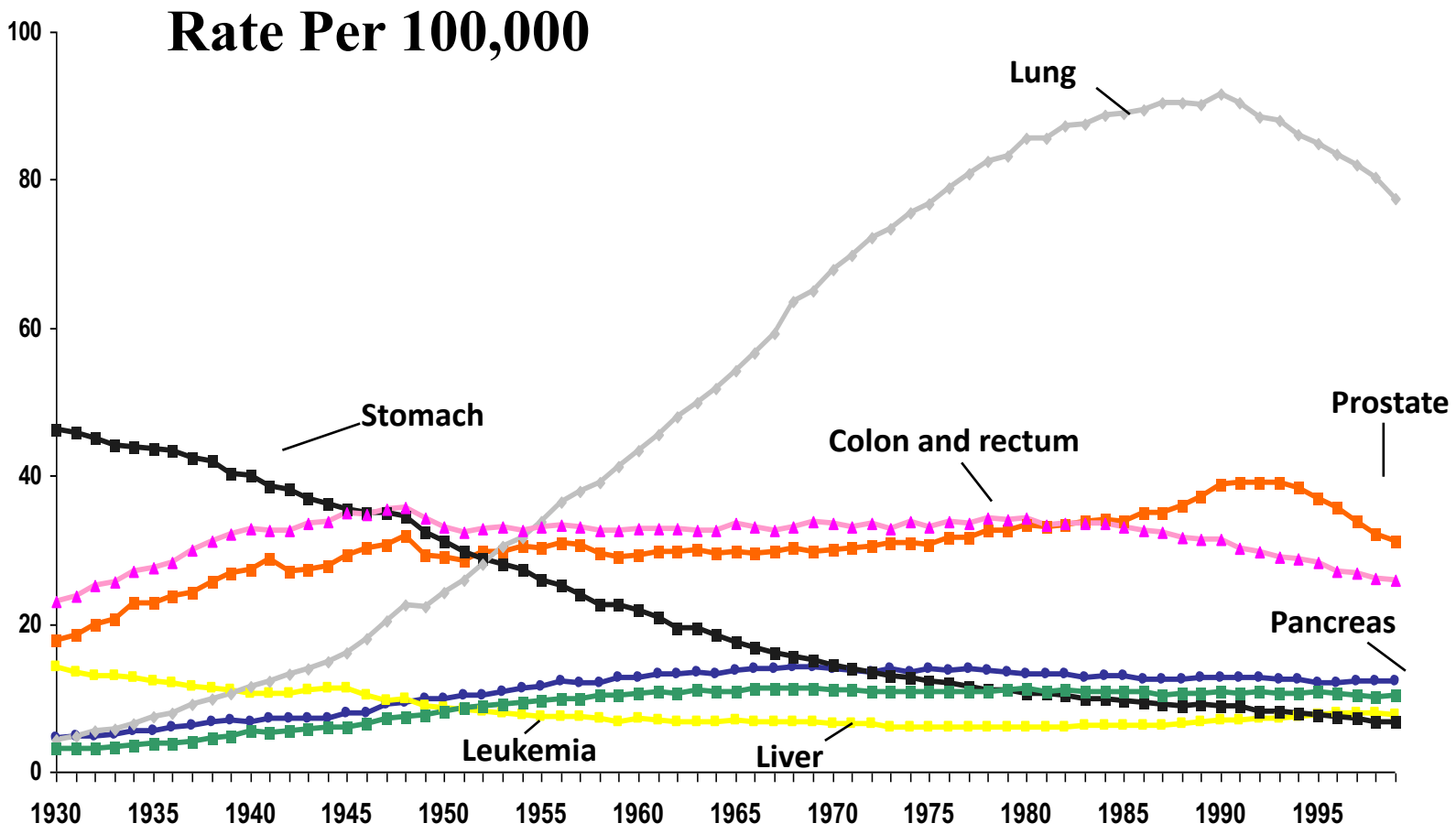


Source: McKeown, 1976. Reproduced by kind permission of the publisher.

Poliomyelitis–US, 1950-2001*



Cancer Death Rates*, for Men, US, 1930-1999

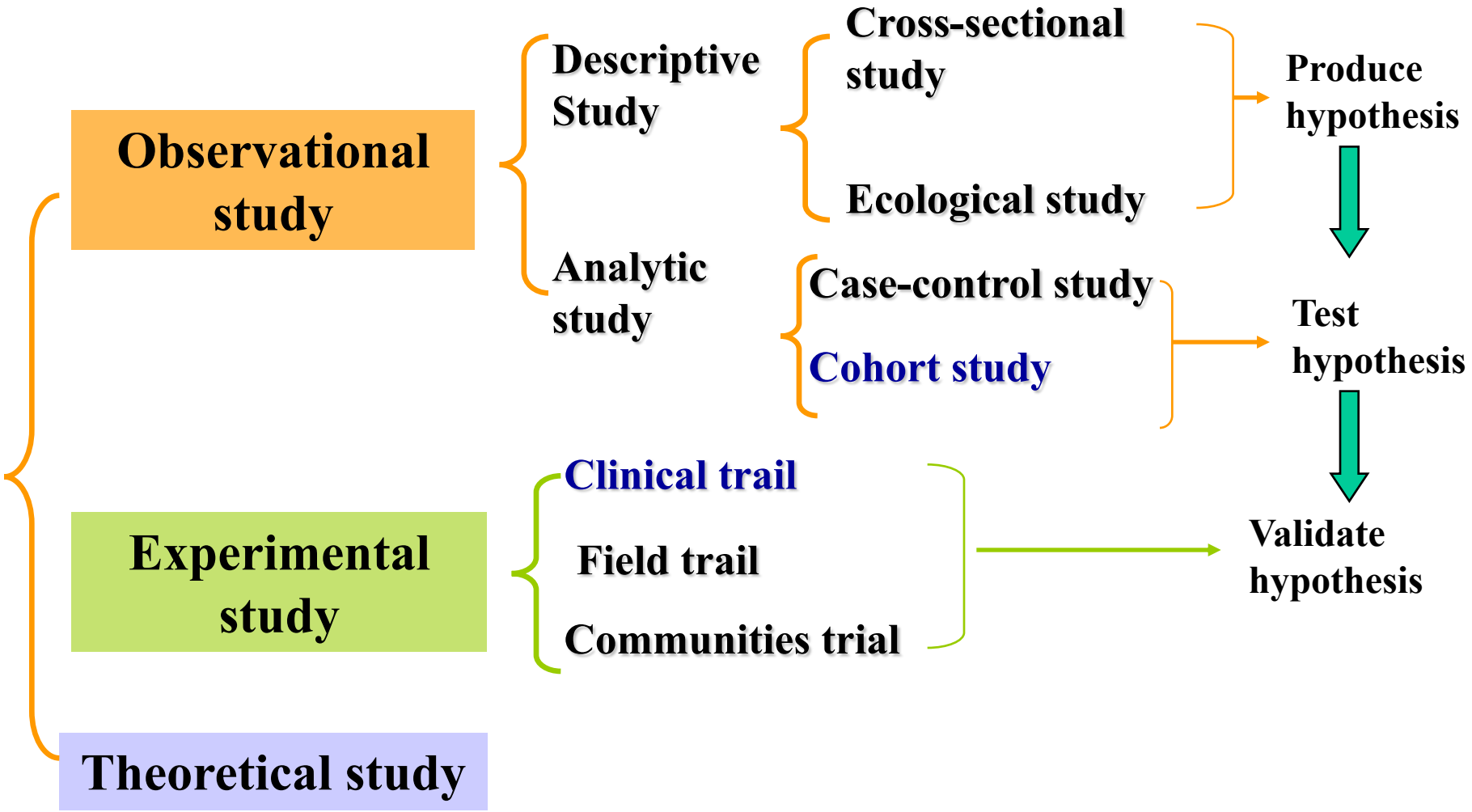


Integrating prevention and treatment

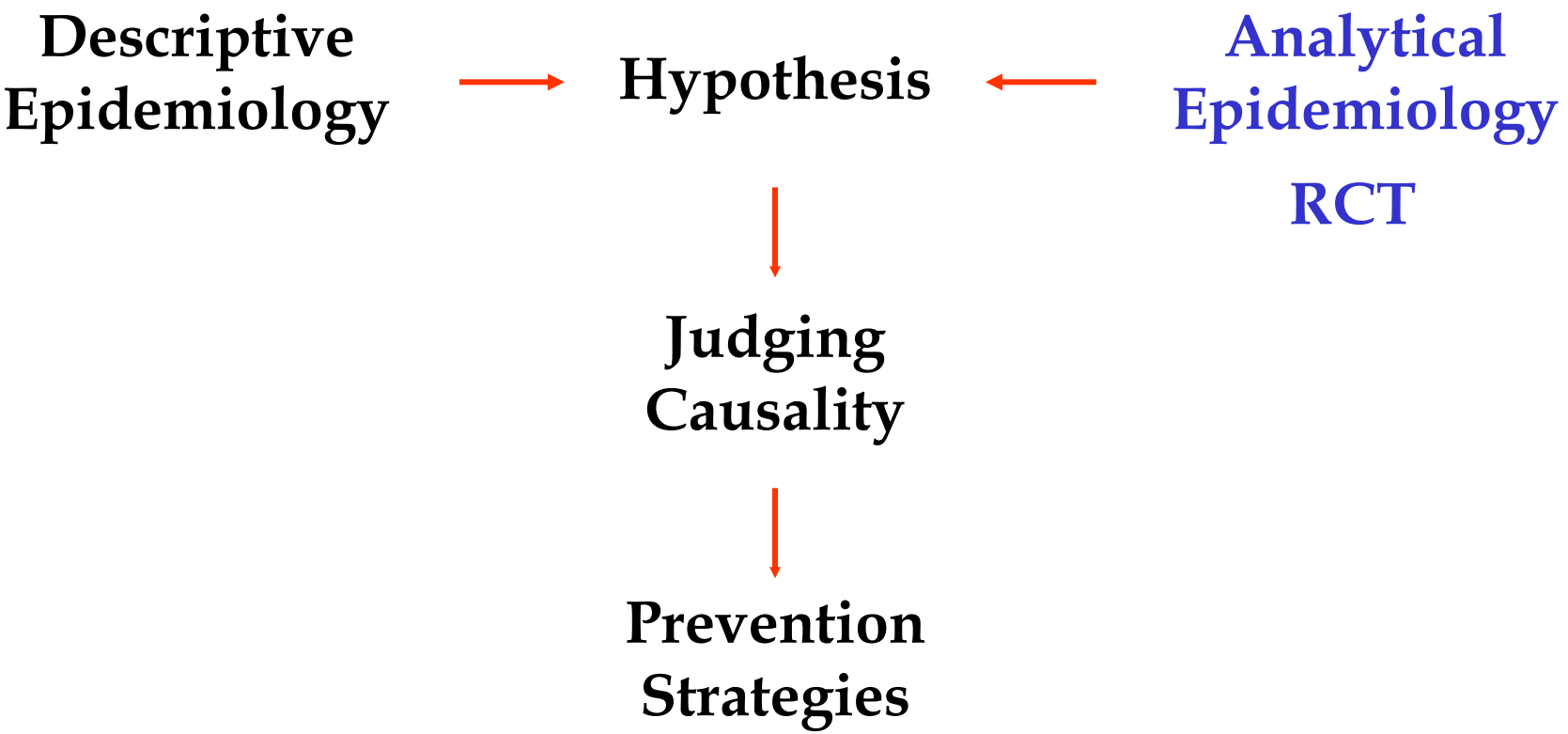
Figure 1-21. Prevention and therapy viewed as mutually exclusive activities. (From Wilson T: Ziggy cartoon. © Universal Press Syndicate, 1986.)

- Therapy involves secondary and tertiary prevention, the latter denoting the prevention of complications such as disability. At times, it also involves primary prevention.
- The entire spectrum of prevention should be viewed as integral to both public health and clinical practice.

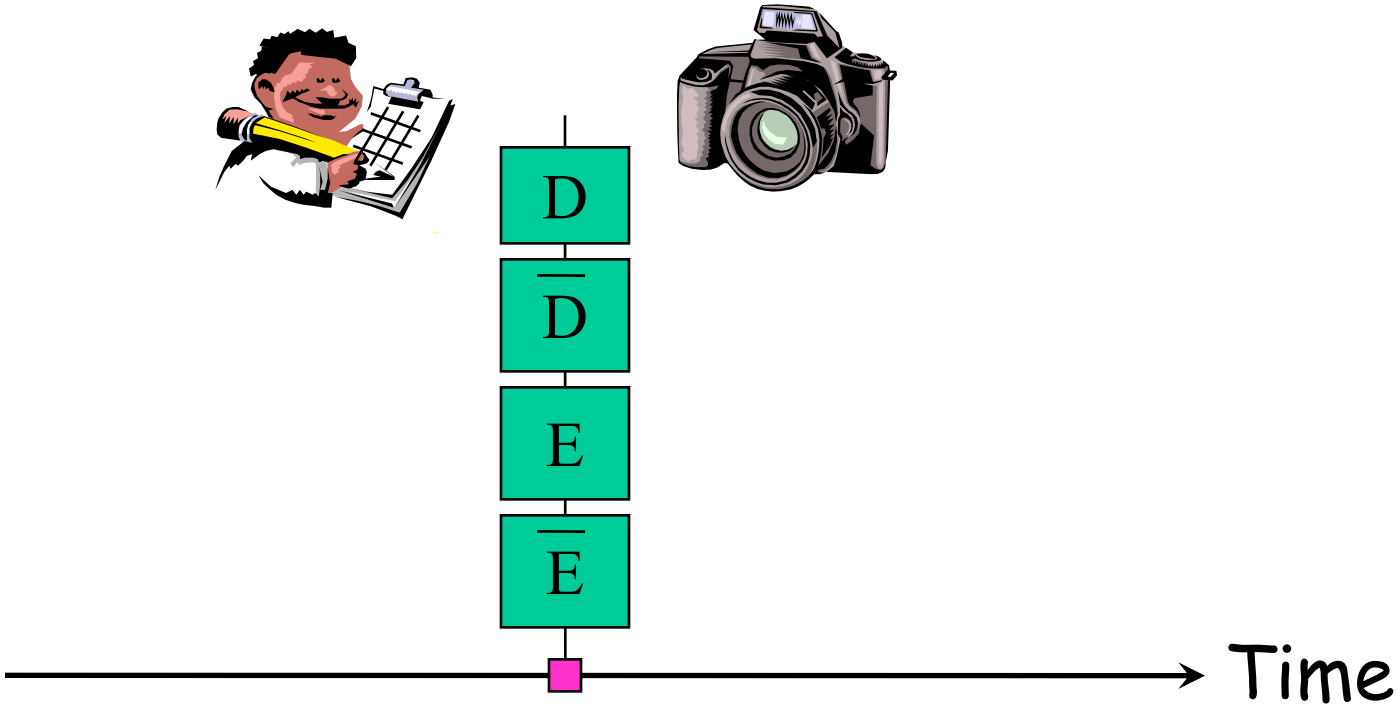
Epidemiology Study Methods



Concept Map


Descriptive Epidemiology
Hypothesis
Analytical Epidemiology
RCT
Judging Causality
Prevention Strategies

cross-sectional study

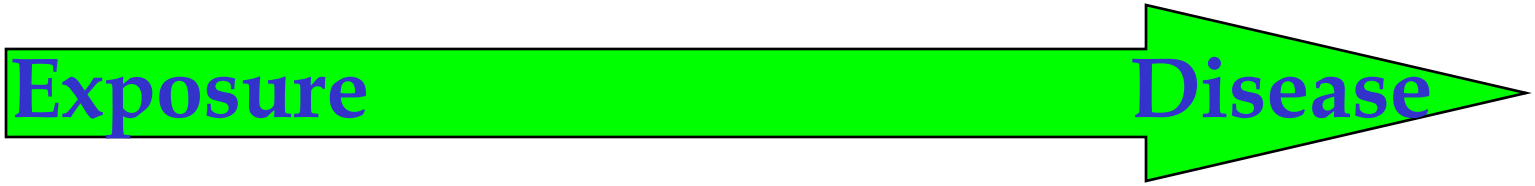


When Where Who

Analytic Epidemiology

The aspect of epidemiology concerned with the search for health-related causes and effects. Uses comparison groups, which provide baseline data, to quantify the association between exposures and outcomes, and test hypotheses about causal relationships.

Time



Now E → D

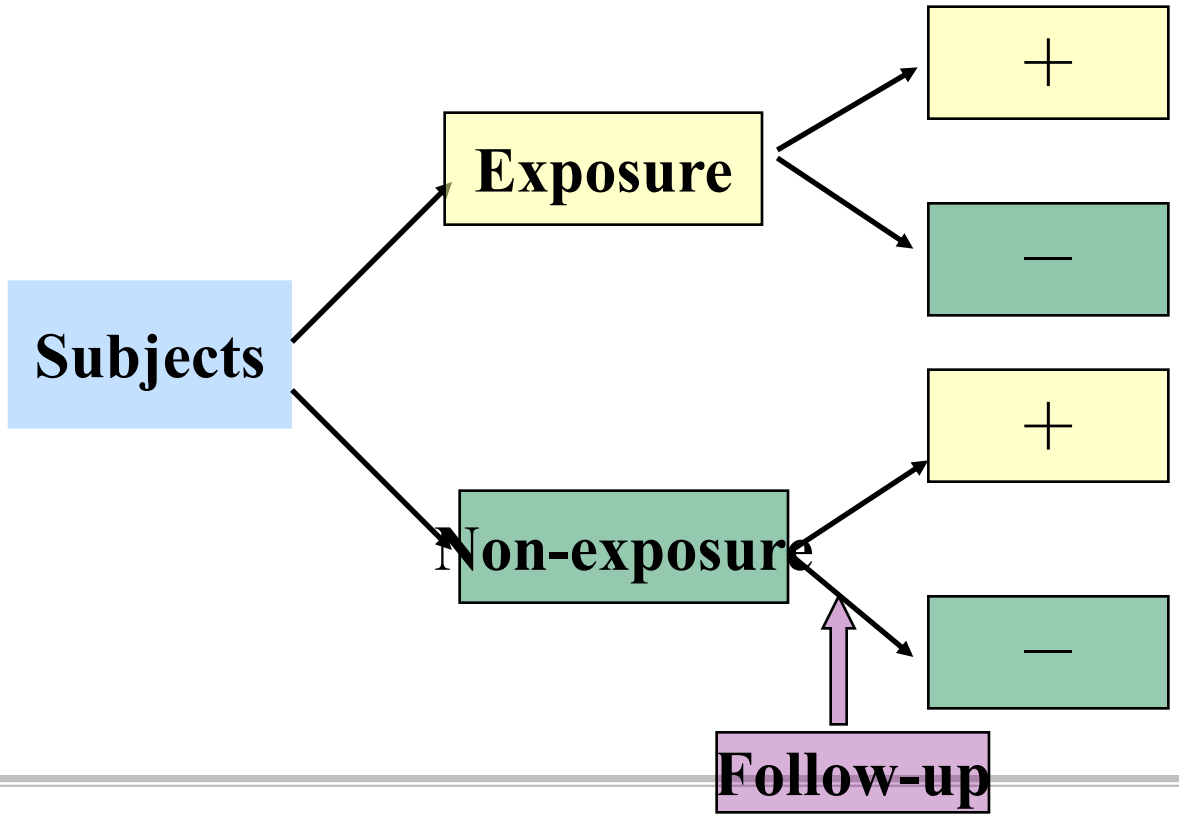
Cohort study

E ⇠ D Now

Case control study

Cohort study

Now Time



a

b

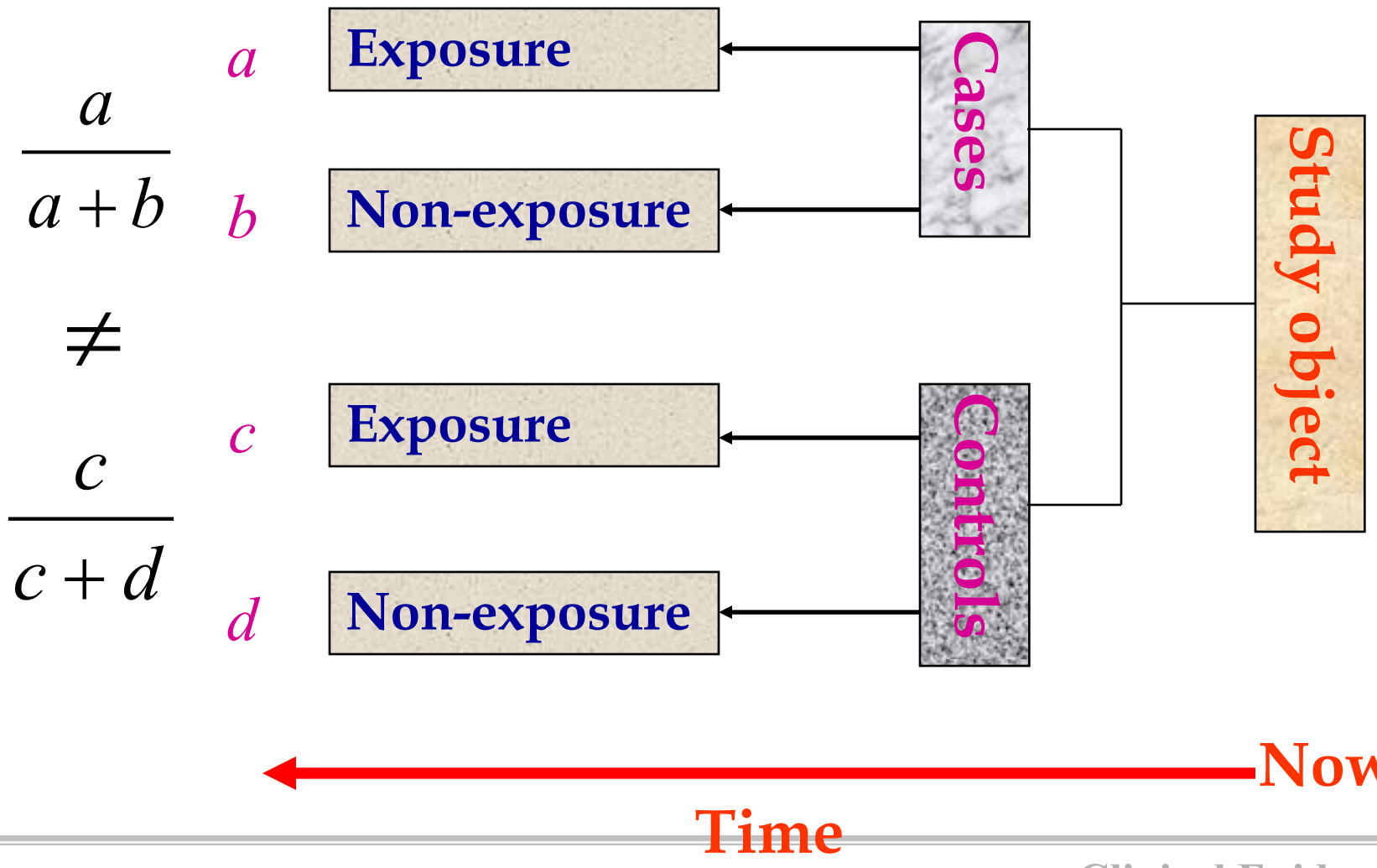
c

d

$$\frac{a}{a+b}$$

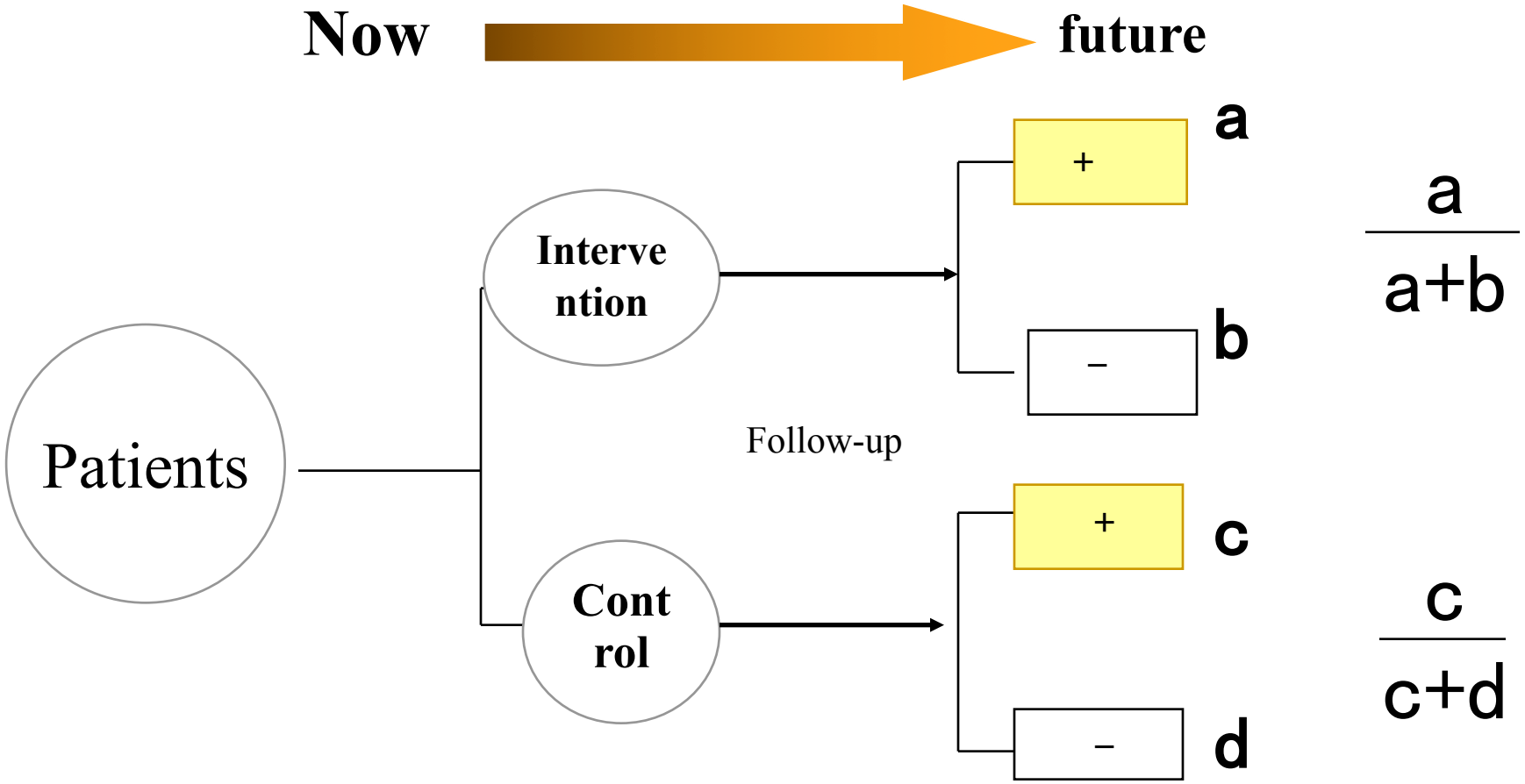
$$\frac{c}{c+d}$$

Case- control study



- **A major limitation of cross-sectional surveys and case-control studies is difficulty in determining if exposure or risk factor preceded the disease or outcome.**

Clinical trial



Basic Principles

- **Variables:** things that vary and can be measured.

✓ **Independent variable** is a purported cause or predictor variable.

✓ **Dependent variable** is the possible effect or outcome variable.

✓ **Extraneous variable (or covariates)** are extraneous to the main question, though perhaps very much a part of the phenomenon under study.

Basic Principles

- **Numbers and probability**

✓ Clinical outcomes, such as occurrence of disease, death, symptoms, or disability, can be counted and expressed as numbers.

✓ An individual will either experience a clinical outcome or will not, and predictions can seldom be so exact. Therefore, a prediction must be expressed as a probability.

✓ A probability for an individual patient is best estimated by referring to past experience with groups of similar patients.

--- for example: the cigarette smoking more than doubles the risk of dying among middle-aged adults, that blood tests for troponins detect about 99% of myocardial infarctions in patients with acute chest pain, and that 2% to 6% of patients undergoing elective surgery for abdominal aortic aneurysm will die within 30 days of the procedure, as opposed to 40% to 80% when emergency repair is necessary.

Basic Principles

- **Population and Samples**

✓ **Population:** are all people in a defined setting (such as Nanjing city), or with certain defined characteristics (such as being age >65 years or having a thyroid nodule).

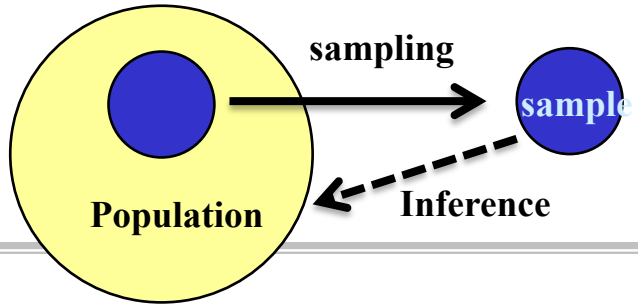
✓ **Clinical populations:** include all patients with a clinical characteristic such as all those with community-acquired pneumonia or aortic stenosis.

✓ One speaks of the general population , a hospitalized population, or a population of patients with a specific disease.

Basic Principles

- **Population and Samples**

  - ✓ **Sample:** clinical research is ordinarily carried out on a sample or subset of people in a defined population
  - ✓ One is interested in the characteristics of the defined population but must, for practical reasons, estimate them by describing the characteristics of people in a sample.
  - ✓ One then makes an inference, a reasoned judgment based on data, that the characteristics of the sample resemble those of the parent population.



Basic Principles

- **Bias (Systematic Error)**

✓ **Bias is "a process at any stage of inference tending to produce results that depart systematically from the true value".**

✓ **It is "an error in the conception and design of a study---or in the collection, analysis, interpretation, publication, or review of data---leading to results or conclusion that are systematically (as opposed to randomly) different from the truth".**

- **Bias (Systematic Error)**

Bias in clinical observation	
Selection bias	Occurs when comparisons are made between groups of patients that differ in determinates of outcome other than the one under study.
Measurement bias	Occurs when the methods of measurement are dissimilar among groups of patients
Confounding	Occurs when two factors are associated (travel together) and the effect of one is confused with or distorted by the effect of the other.

✓ Selection bias

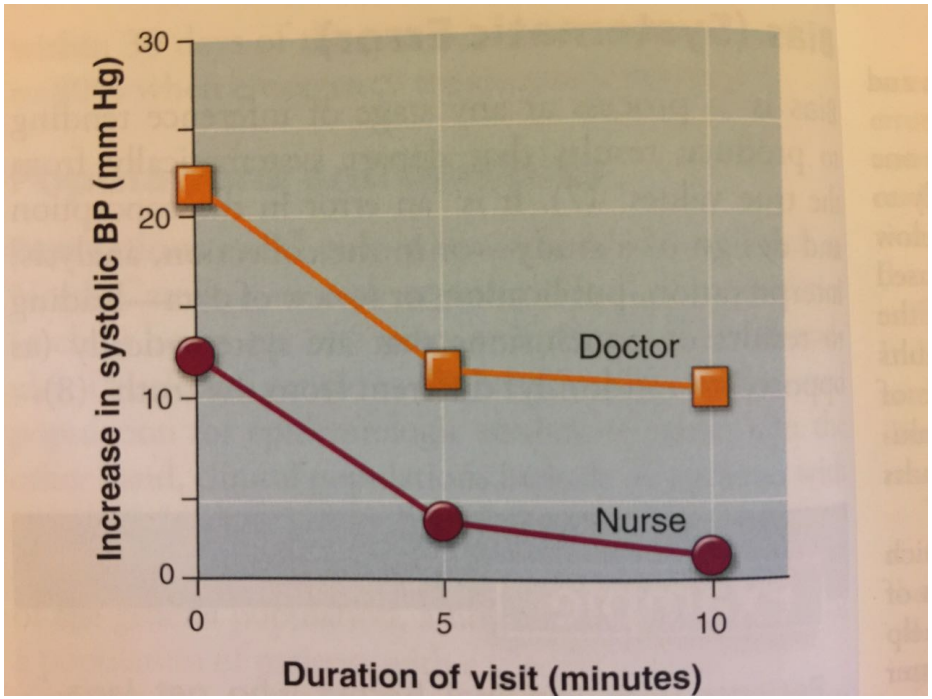
- Occurs when comparisons are made between groups of patients that differ in ways other than the main factors under study, ones that affect the outcome of the study.

- Groups of patients often differ in many ways ---age, sex, severity of disease, the presence of other diseases, the care they receive, and so on.

- If one compares the experience of two groups that differ on a specific characteristic of interest but are dissimilar in these other ways and the differences are themselves related to outcome, the comparison is biased and little can be concluded about the independent effects of the characteristic of interest.

✓ Measurement bias

- **Occurs when the method of measurement leads to systematically incorrect result.**



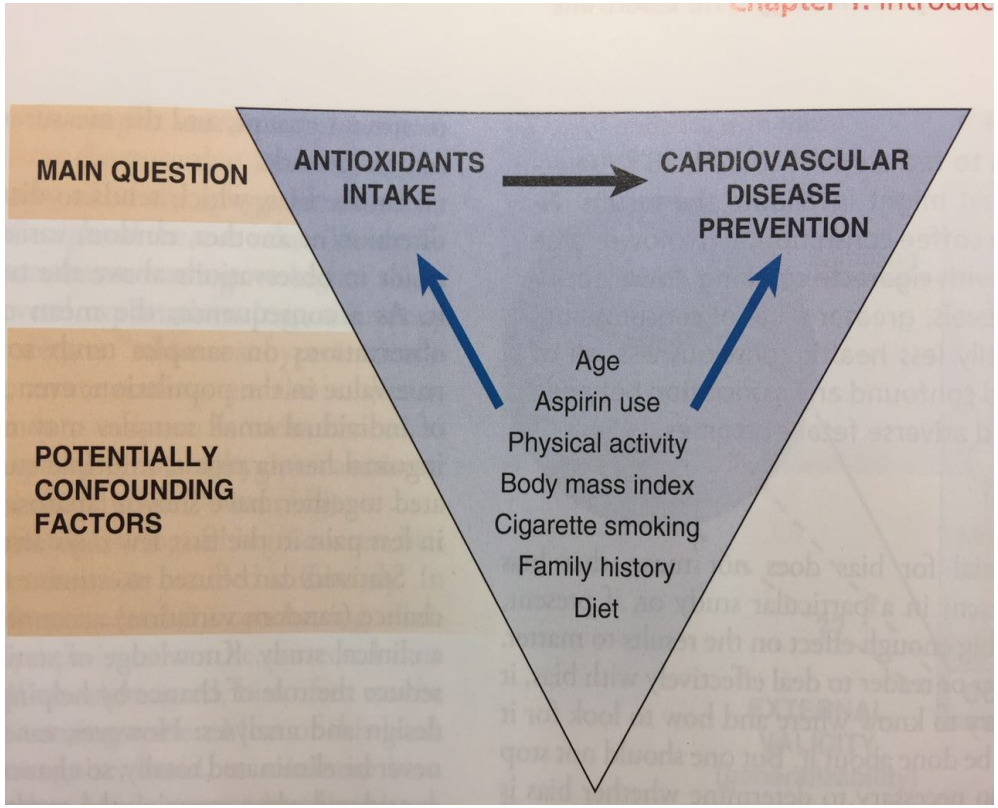
White coat hypertension

✓ confounding bias

- **Confounding can occur when one is trying to find out whether a factor, such as behavior or drug exposure, is a cause of disease in and of itself.**

- **If the factor of interest is associated or "travels together" with another factor, which is itself related to the outcome, the effect of the factor under study can be confused with or distorted by the effect of the other.**

Confounding:



The relationship between antioxidant intake and cardiovascular risk is potentially confounding by patient characteristics and behaviors related to both antioxidant use and development of cardiovascular disease.


Thanks for your attention!