

Clinical Epidemiology

Chapter 2 Measurement of disease

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Here, it is necessary to count.

*---P.C.A. Louis
1787-1872*

(A 19th Century physician and proponent of the “numerical method” (relying on counts, not impressions) to understand the natural history of disease such as typhoid fever.)



Example

A 72-year-old man presents with slowly progressive urinary frequency, hesitancy, and dribbling. A digital rectal examination reveals a symmetrically enlarged prostate gland and no nodules. Urinary flow measurements show a reduction in flow rate, and his serum prostate-specific antigen (PSA) is not elevated. The clinician diagnoses benign prostatic hyperplasia (BPH). In deciding on treatment, the clinician and patient must weigh the benefits and hazards of various therapeutic options. To simplify, let us say the options are medical therapy with drugs or surgery. The patient might choose medical treatment but runs the risk of worsening symptoms or obstructive renal disease because the treatment is less immediately effective than surgery. Or he might choose surgery, gaining immediate relief of symptoms but at the risk of operative mortality and long-term urinary incontinence and impotence.



- **In modern times, clinical research has become sufficiently strong and extensive that it is possible to ground clinical judgment in research-based probabilities---frequencies.**
- **Probabilities of disease, improvement, deterioration, cure, side effects, and death are the basis for answering most clinical question.**
- **For this patient, sound clinical decision making requires accurate estimates of how his symptoms and complications of treatment will change over time according to which treatment is chosen.**



Stages of disease in an individual and in a population



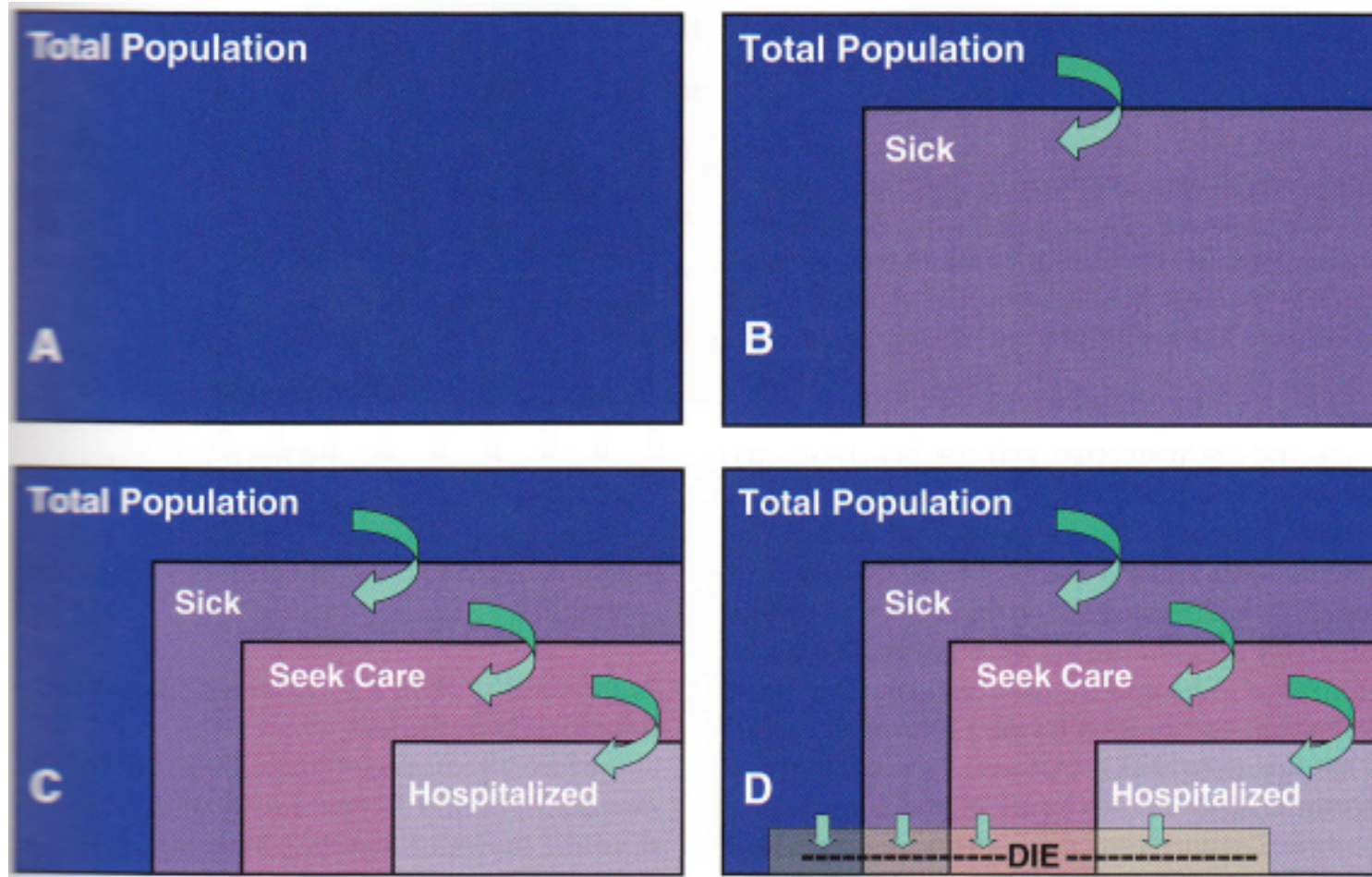
Fig2-1A: The natural history of disease.



B

Fig2-1B: The natural history of disease and some sources of data relating to each interval.

The progression of disease in a population



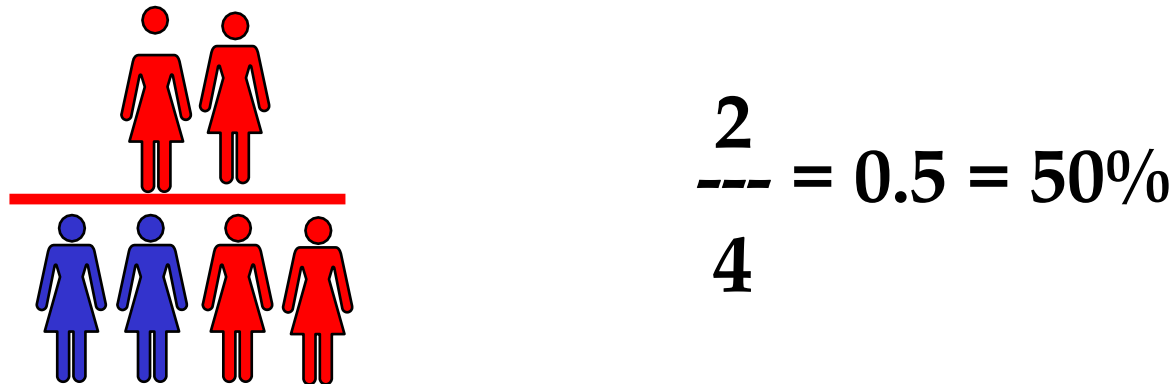
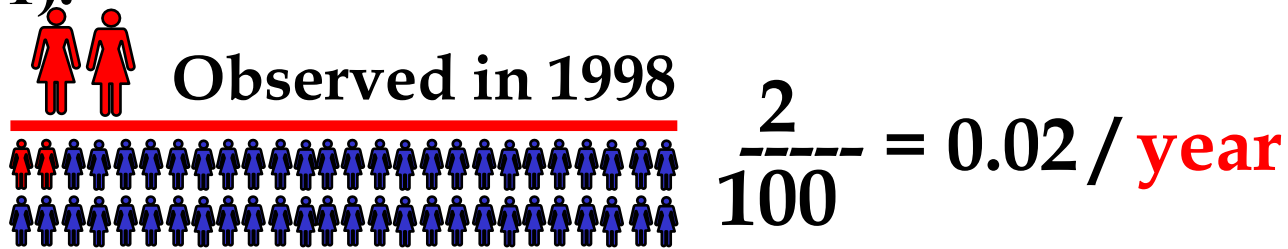


□ What source of data can be used to obtain information about the person's illness?

- **Medical and hospital records (fig2-1B: illness period)**
- **Physicians' records (seek care to outcome)**
- **Questionnaire or an interview (symptoms to outcome)**

□ Occurrence of disease can be measured using rates or proportions

- **Rates:** how fast the disease is occurring in a population.
- **Proportions:** what fraction of the population is affected (0~1).





Measures of Morbidity

□ Incidence rate

is defined as the number of new cases of a disease that occur during a specified period of time in a population at risk of developing the disease.

IR per 1,000=

$$\frac{\text{No. of *new cases* of a disease during a specified period of time}}{\text{No. of persons who are *at risk of developing* the disease during that period of time}} \times 1,000$$



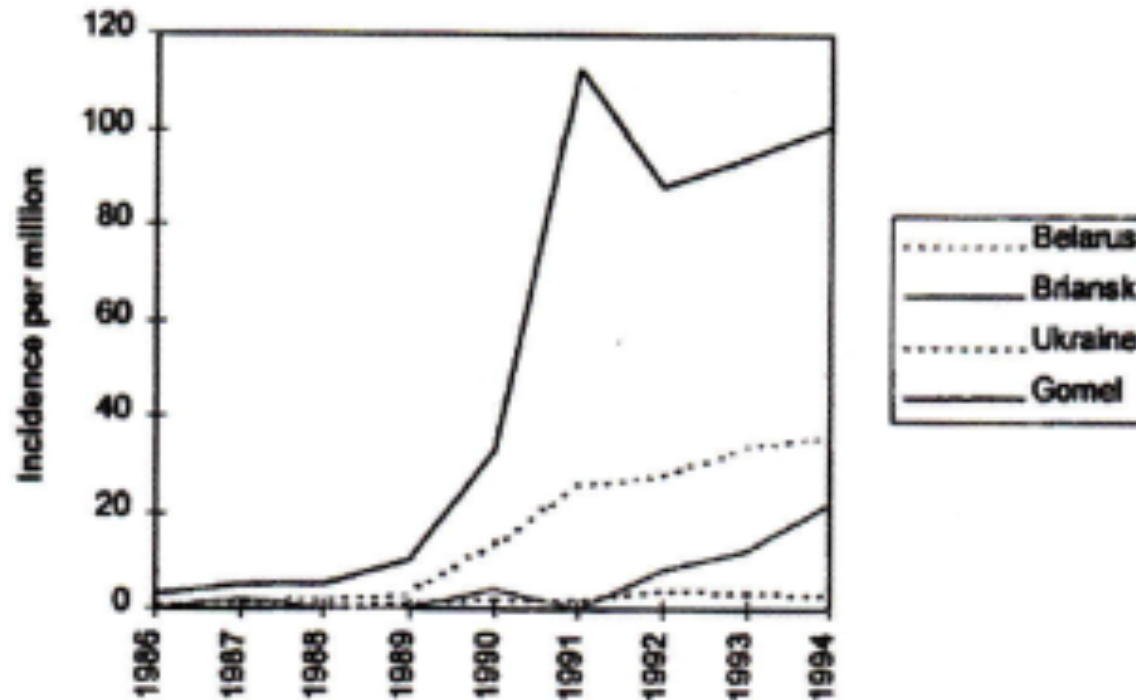
□ Incidence rate

- Numerator: **new** cases of disease.

*The incidence rate is **a measure of events**-----the disease is identified in a person who develops the disease and did not have the disease previously (a measure of risk).*

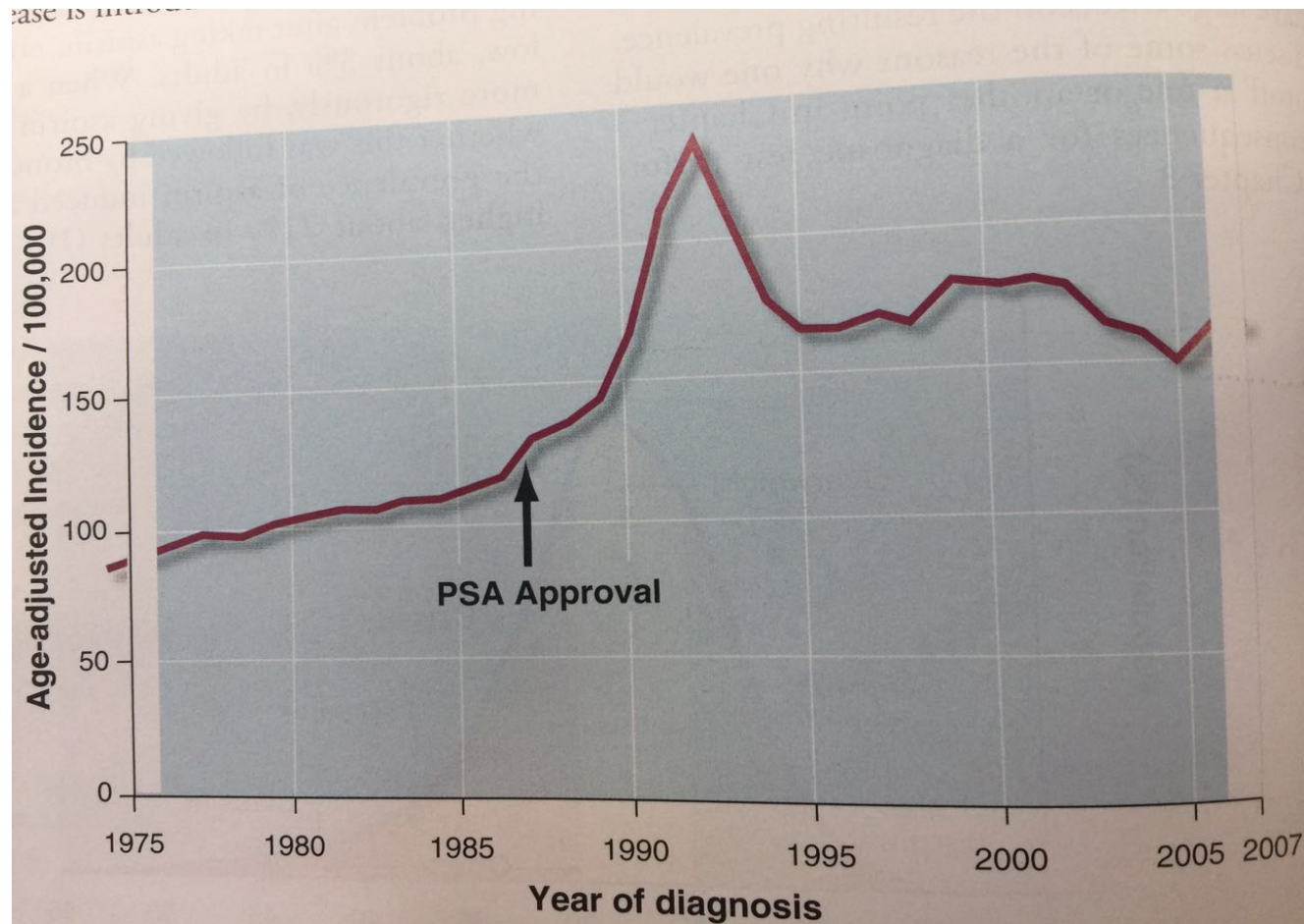
***Intensive screening** could have identified diseases that might otherwise not have been detected.*

Trends of incidence of childhood thyroid cancer in Belarus, Ukraine and Russia, 1986-1994



- *Such screening in Belarus could have identified thyroid tumors that might otherwise not have been detected.*

Incidence depends on the intensity of efforts to find cases





□ Incidence rate

- **Denominator:** The number of people who are **at risk** for developing the disease.

Any individual who is included in the denominator must have the potential to become part of the group. (a high risk).

*e.g. Incidence rate of **Uterine cancer**, the denominator must include only women, because men would not have the potential to become part of the group.*



□ Incidence rate

- Denominator: **the issue of time**

- 1) people at risk who are observed **throughout** a defined time period.
- 2) When all people **are not observed for the full time** period, person-time (or units of time when each person is observed).



□ Incidence rate

- People at risk who are observed **throughout** a defined time period.
 - 1) the denominator have been followed up for that entire period. (1 week, 1 month, 1 year, 5 years, and so on.)
 - 2) All individuals included in the calculation must have been observed (at risk) for the entire period. (**Cumulative incidence**)



□ Incidence rate

- When all people are not observed for the full time period, **person-time** (or units of time when each person is observed).
 - 1) Loss to follow-up or death from a cause.
 - 2) Different individuals are observed for different lengths of time.
 - 3) **Incidence density: the denominator consists of the sum of the units of time that each individual was at risk and was observed.(person-time, person-years, person-months)**

When all the people in the population being studied are observed for the entire period: person-years of observation

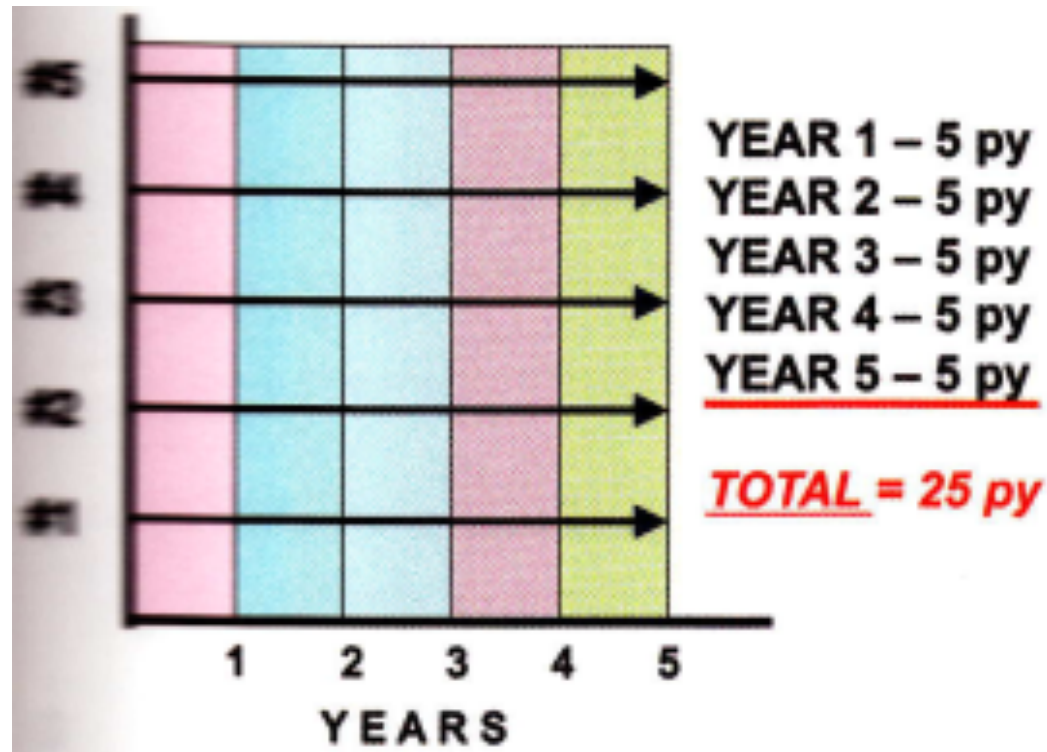


Fig 2-5 (A-I)
Calculation of
person times as
person-years (py)
observed

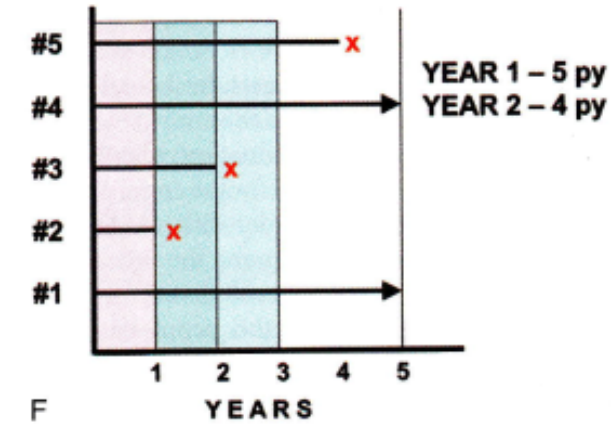
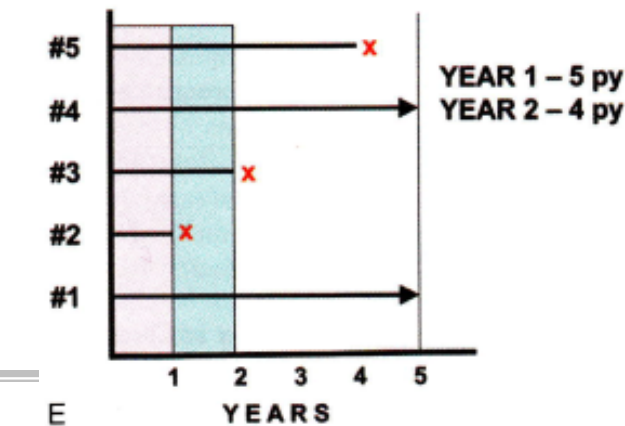
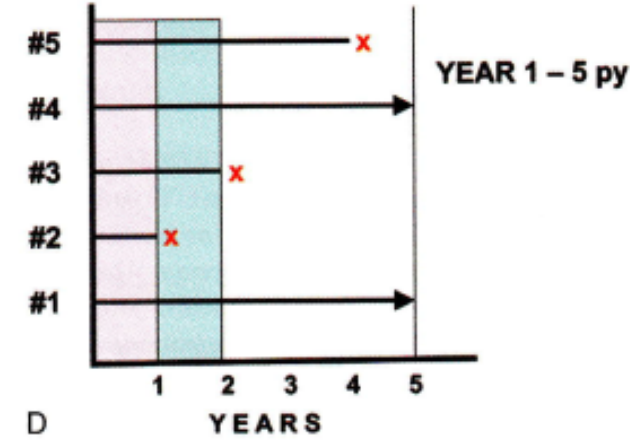
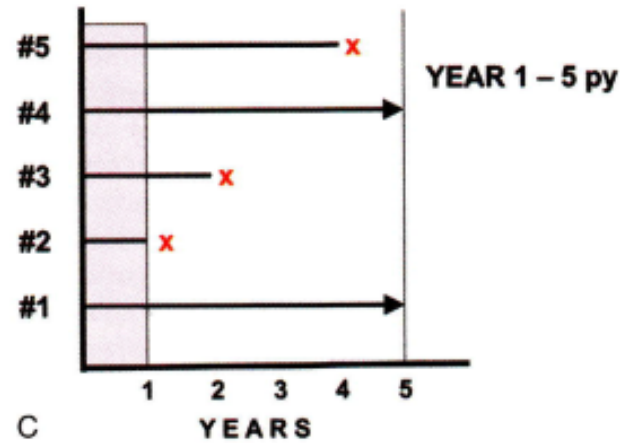
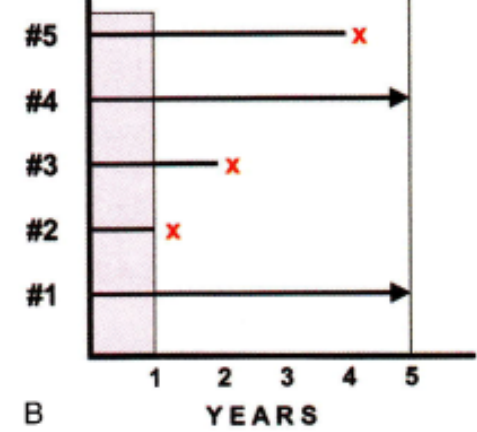
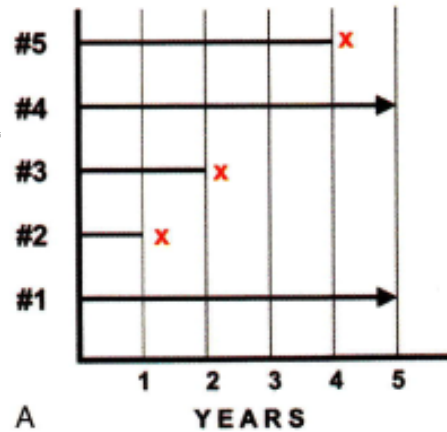


Fig 2-5 (G-H)
Calculation of
person times as
person-years (py)
observed

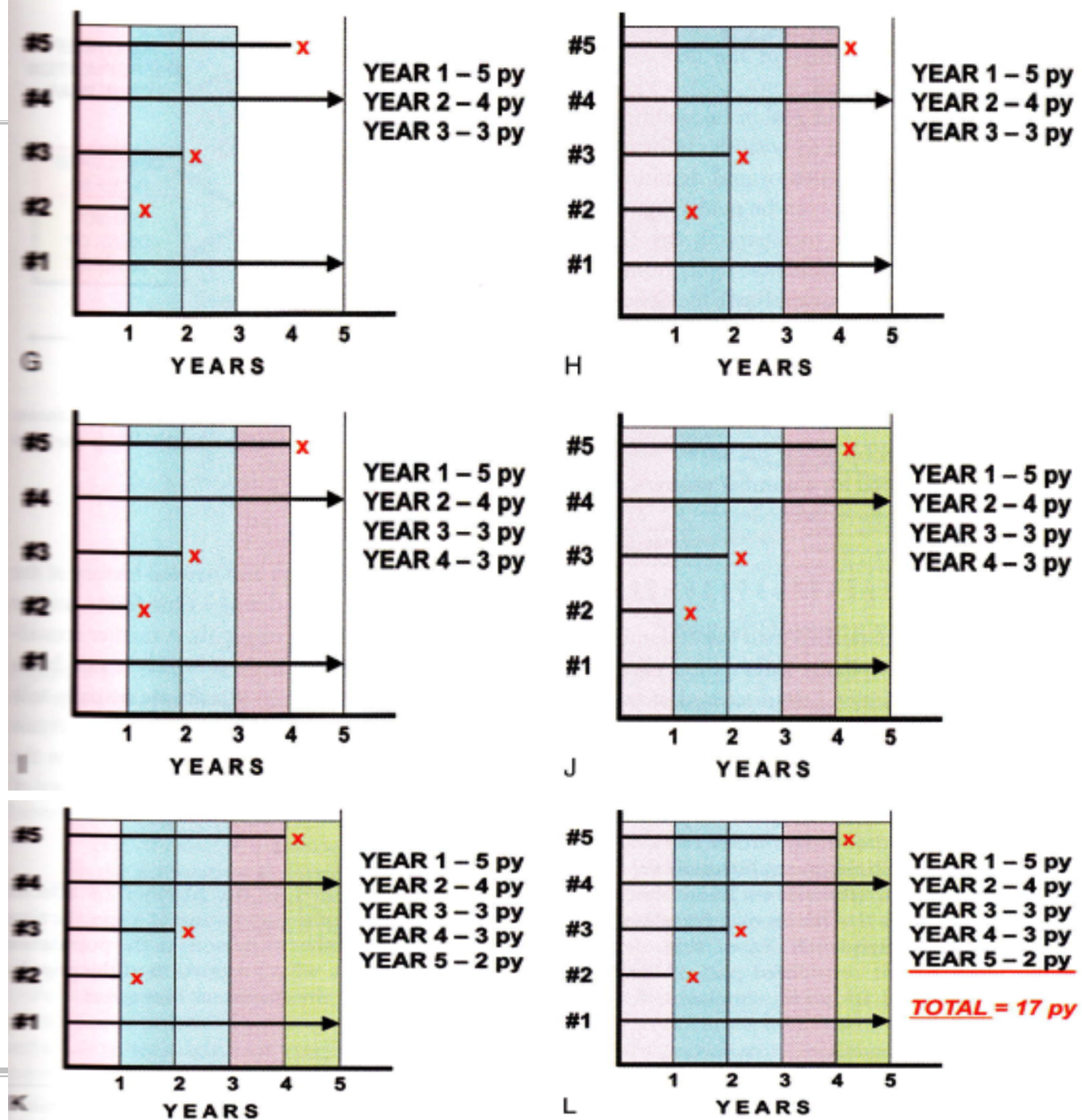
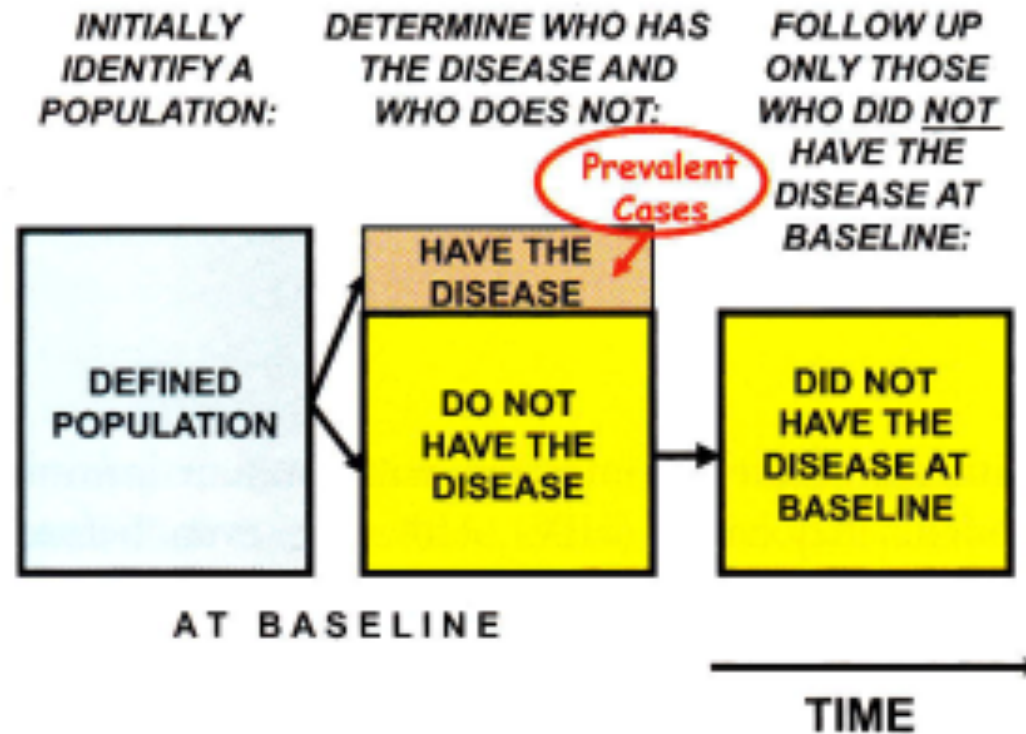


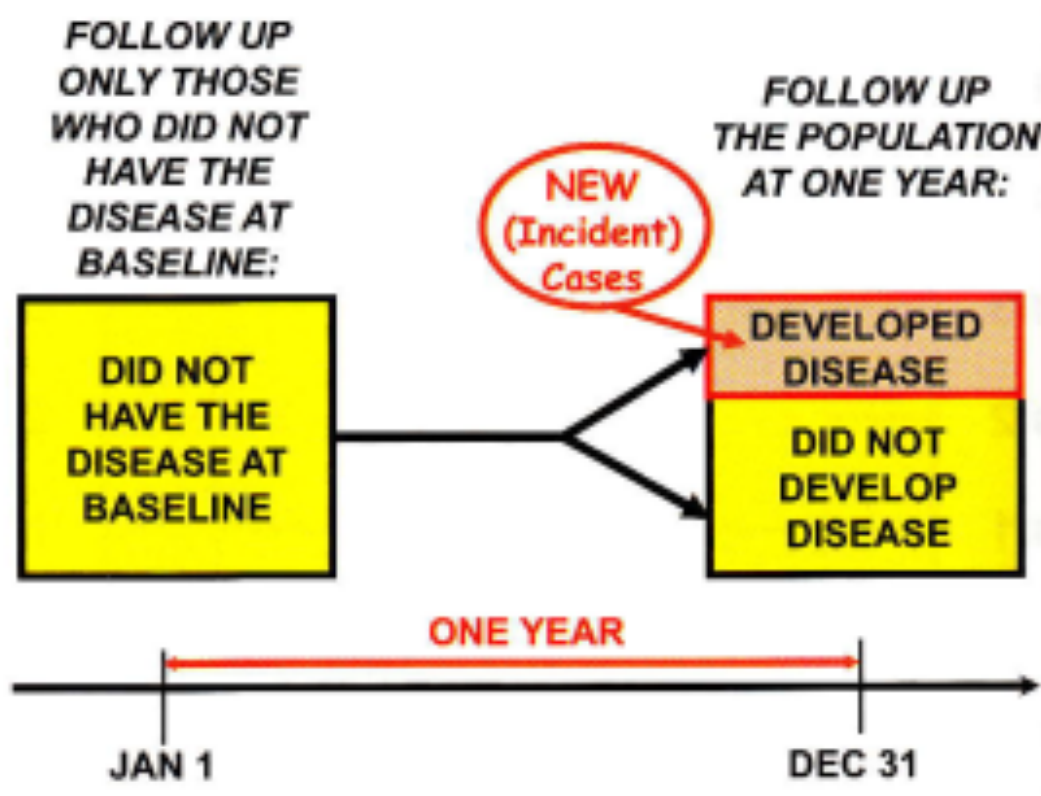
Figure 3-5, cont'd

- Identifying new cases in order to calculate incidence



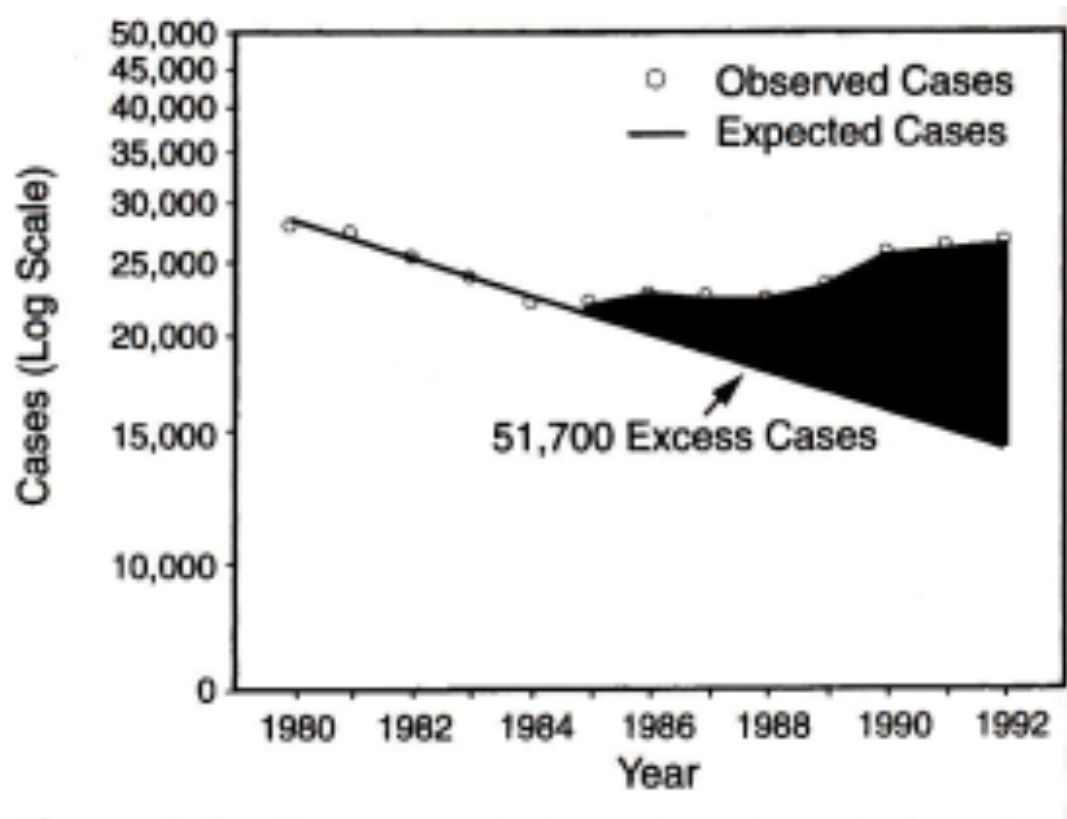
Step 1: Screening for prevalent cases at baseline

- Identifying new cases in order to calculate incidence



Step 2: Follow-up and rescreening at 1 year to identify cases that developed during the year.

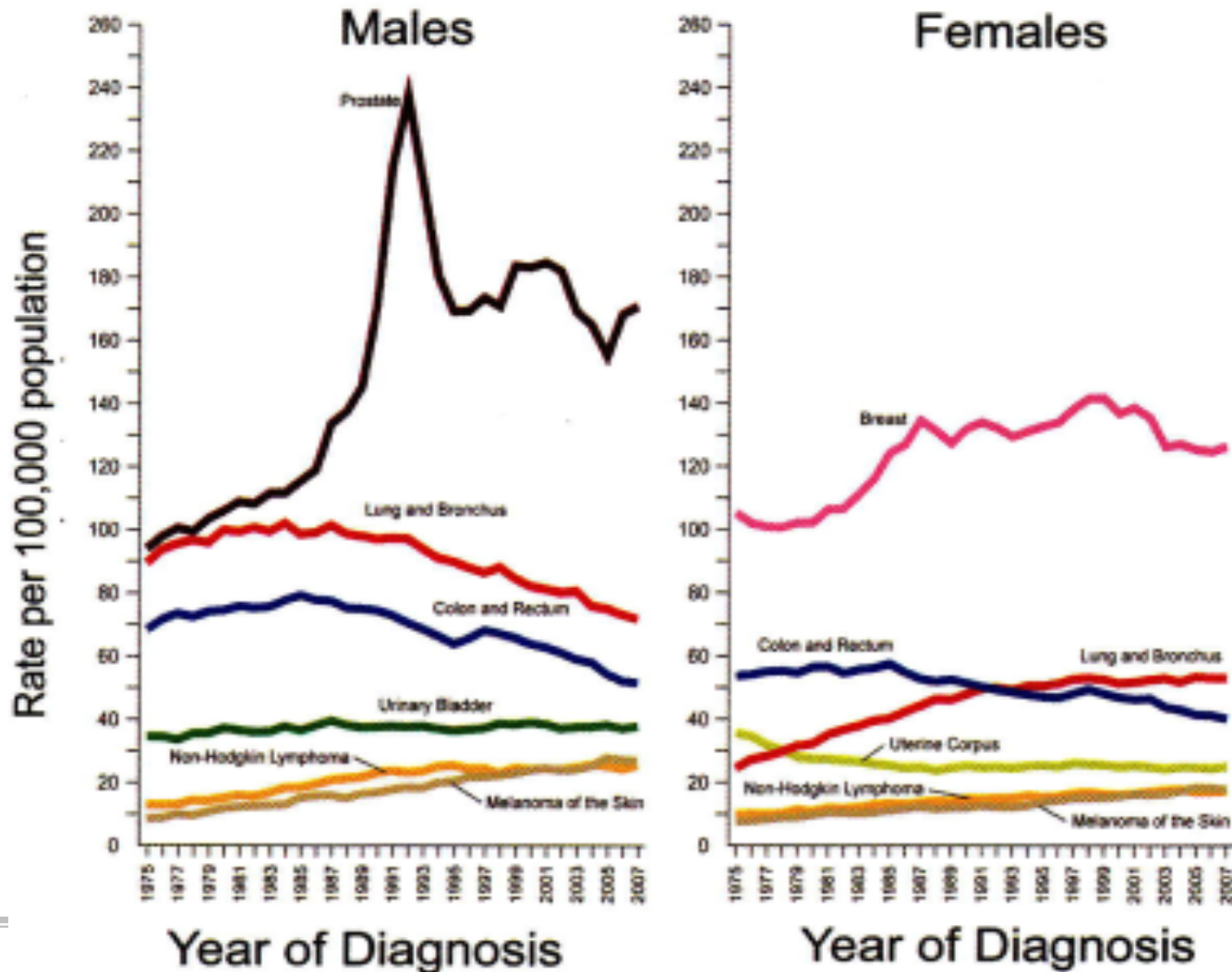
The number of expected and observed cases of tuberculosis reported in the US, 1980-1992



- **Much of the increase in TB seen in 1985 was associated with simultaneous infection with HIV.**



Annual age-adjusted cancer incidence rates among males and females for selected cancer, United States, 1975-2007





□ Attack rate

- In a food-borne disease outbreak, **attack rate** is defined as the number of people exposed to a suspect food who became ill, divided by the number of people who were exposed to that food.
- Attack rate does not explicitly specify **the time interval** because for many food-borne outbreaks we know that most cases occur **within a few hours or a few days** after the exposure.
- Actually, attack rate is not truly a rate but a **proportion**.



□ Prevalence

- Prevalence is defined as the number of affected persons present in the population at a specific time divided by the number of persons in the population at that time.
- What **proportion** of the population is affected by the disease at that time?
- *Prevalence per 1,000*

$$\frac{\text{No. of cases of a **disease present** in the population at a specified time}}{\text{No. of persons in the population at that specified time}} \times 1,000$$



- **Point prevalence and period prevalence**
 - ✓ Prevalence can be viewed as a **snapshot** or a **slice** through the population at a point in time at which we determine who has the disease and who does not.
 - ✓ **Point prevalence**: at a certain point in time-----this is the use of the term prevalence that we have just discussed.
 - ✓ **Period prevalence**: how many people have had the disease at any point during a certain time period?



- **Point prevalence and period prevalence**

TABLE 3-1. Examples of Point and Period Prevalence and Cumulative Incidence in Interview Studies of Asthma

Interview Question	Type of Measure
“Do you currently have asthma?”	Point prevalence
“Have you had asthma during the last [<i>n</i>] years?”	Period prevalence
“Have you ever had asthma?”	Cumulative incidence

- What is the difference between incidence and prevalence?

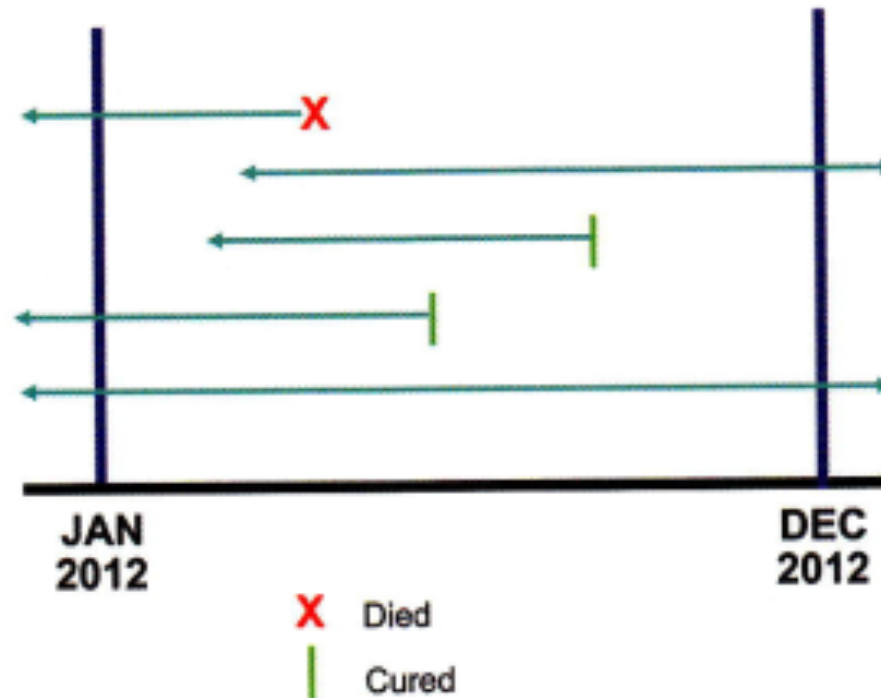
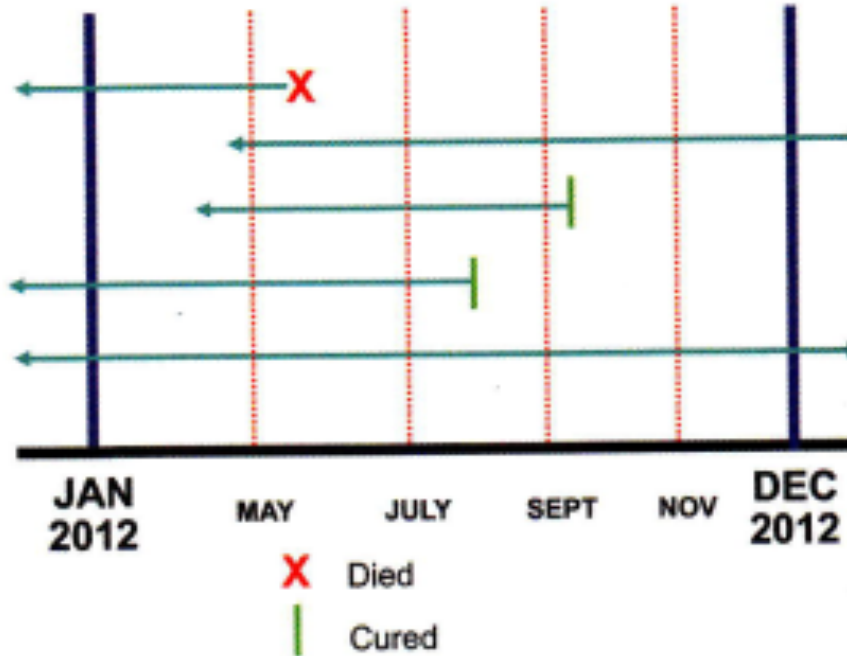


Figure 3-10. Example of incidence and prevalence: I.

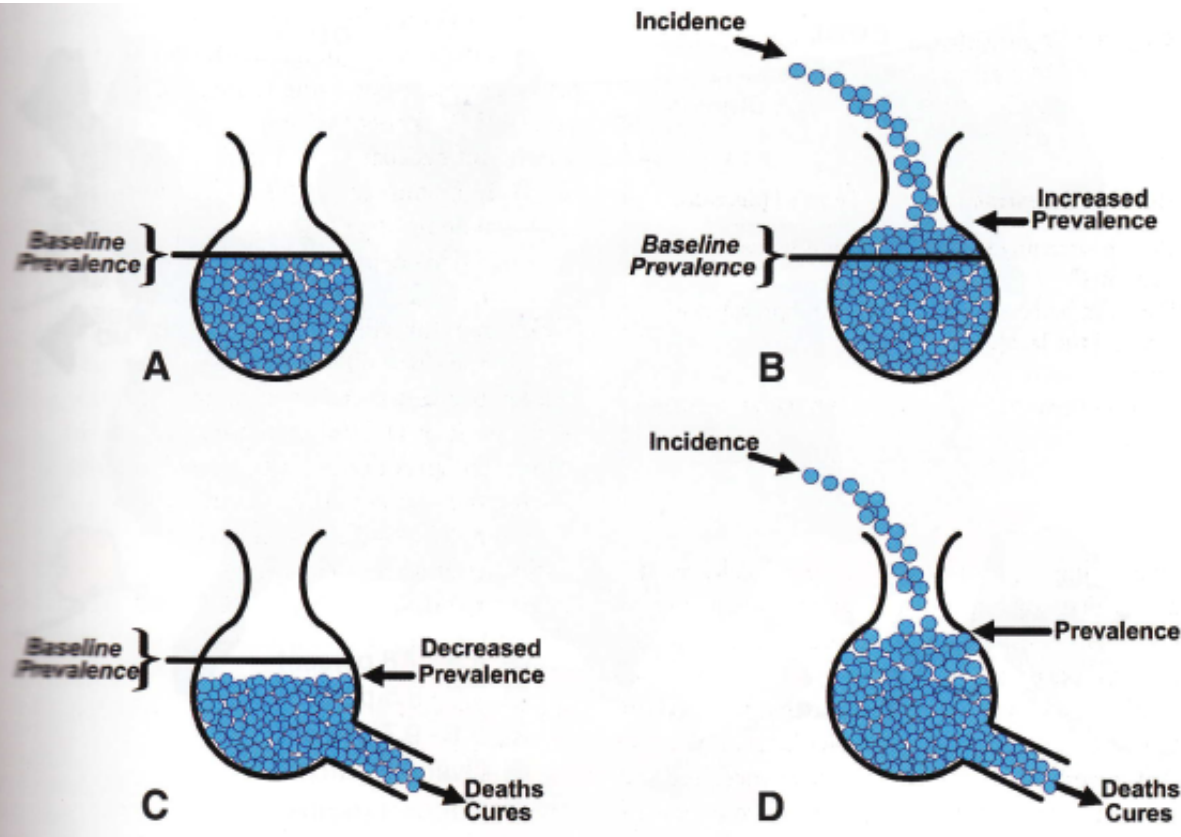


- What is the difference between incidence and prevalence?



- 1) What is the numerator for incidence rate in 2012?
- 2) What about the numerator for **point prevalence** in 2012?
(Depends on when do our prevalence survey, May, July or Sept.)

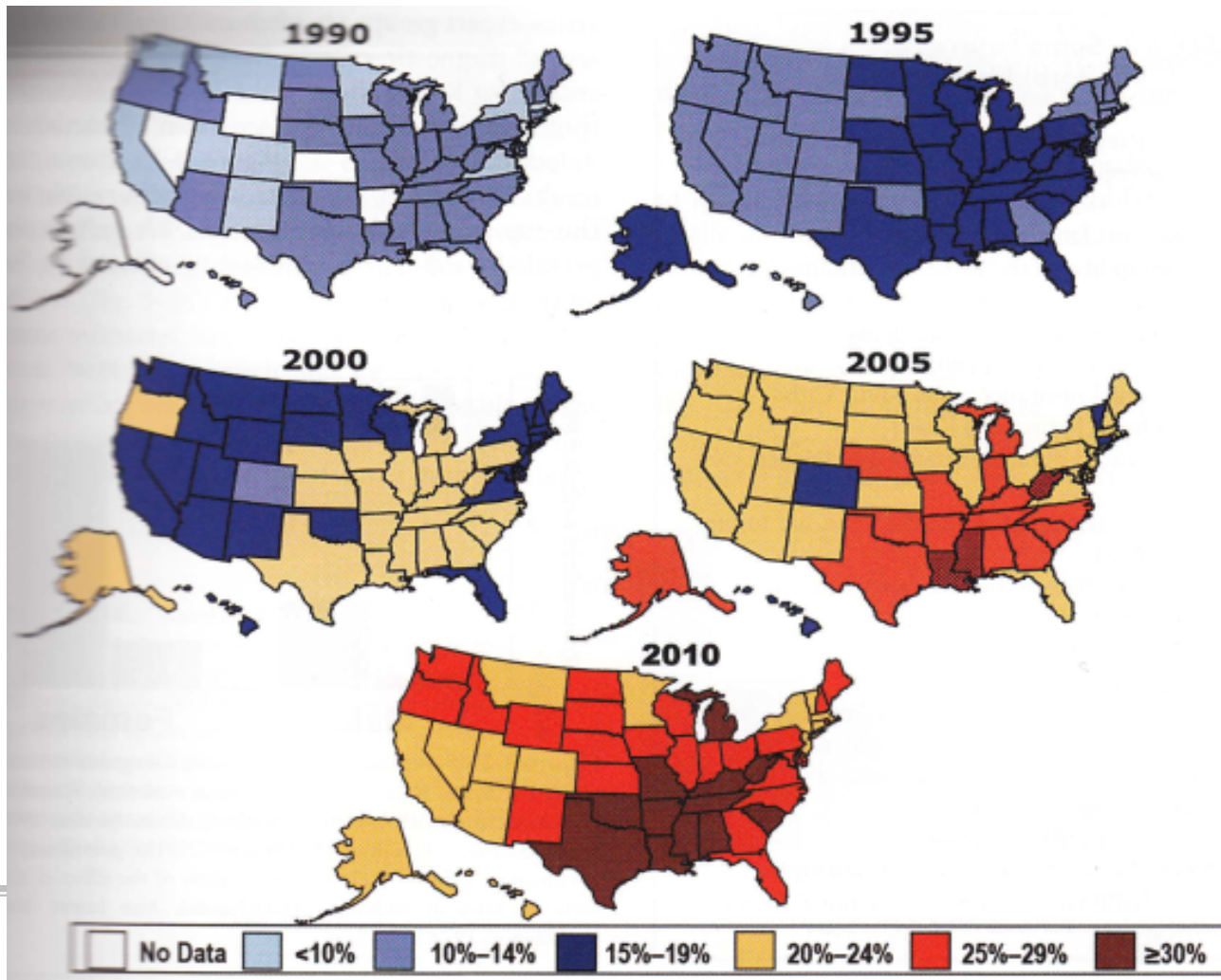
- What is the difference between incidence and prevalence?



- A:** level of prevalence in the population
- B:** Increased prevalence resulting from incidence.
- C:** Decreased prevalence resulting from deaths and /or cures.
- D:** Overall impact on prevalence of incidence.



- Trends in prevalence of obesity, by state, United State, 1990, 1995, 2000,2005, and 2010, based on self-reported height and weight**



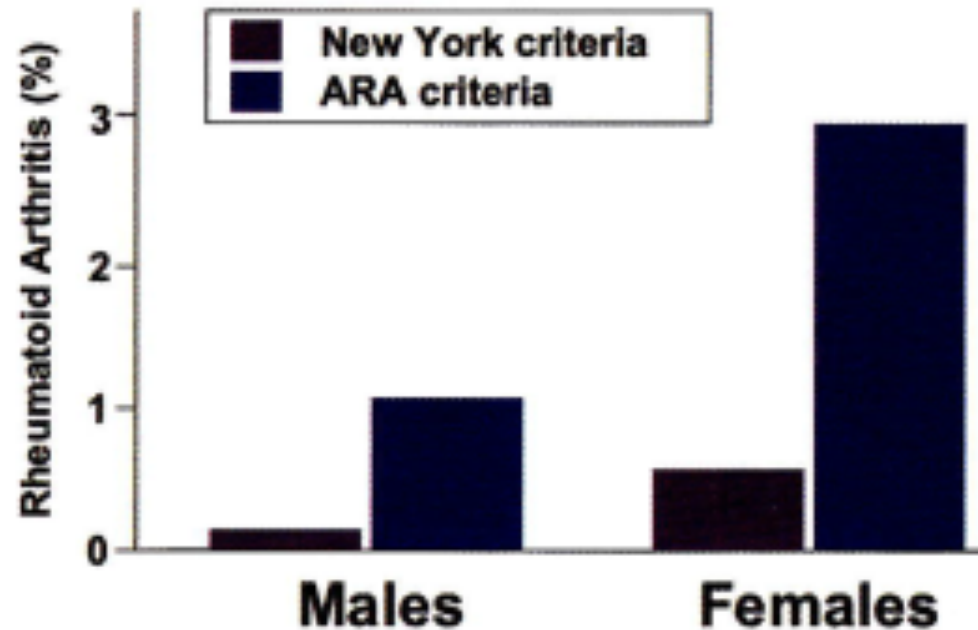


• Some sources of Morbidity statistics

1. Disease reporting—communicable diseases, cancer registries
2. Data accumulated as a by-product of insurance and prepaid medical care plans
 - a. Group health and accident insurance
 - b. Prepaid medical care plans
 - c. State disability insurance plans
 - d. Life insurance companies
 - e. Hospital insurance plans—Blue Cross
 - f. Railroad Retirement Board
3. Tax-financed public assistance and medical care plans
 - a. Public assistance, aid to the blind, aid to the disabled
 - b. State or federal medical care plans
 - c. Armed Forces
 - d. Veterans Administration
4. Hospitals and clinics
5. Absenteeism records—industry and schools
6. Pre-employment and periodic physical examinations in industry and schools
7. Case-finding programs
8. Records of military personnel
9. Morbidity surveys on population samples (e.g., National Health Survey, National Cancer Surveys)

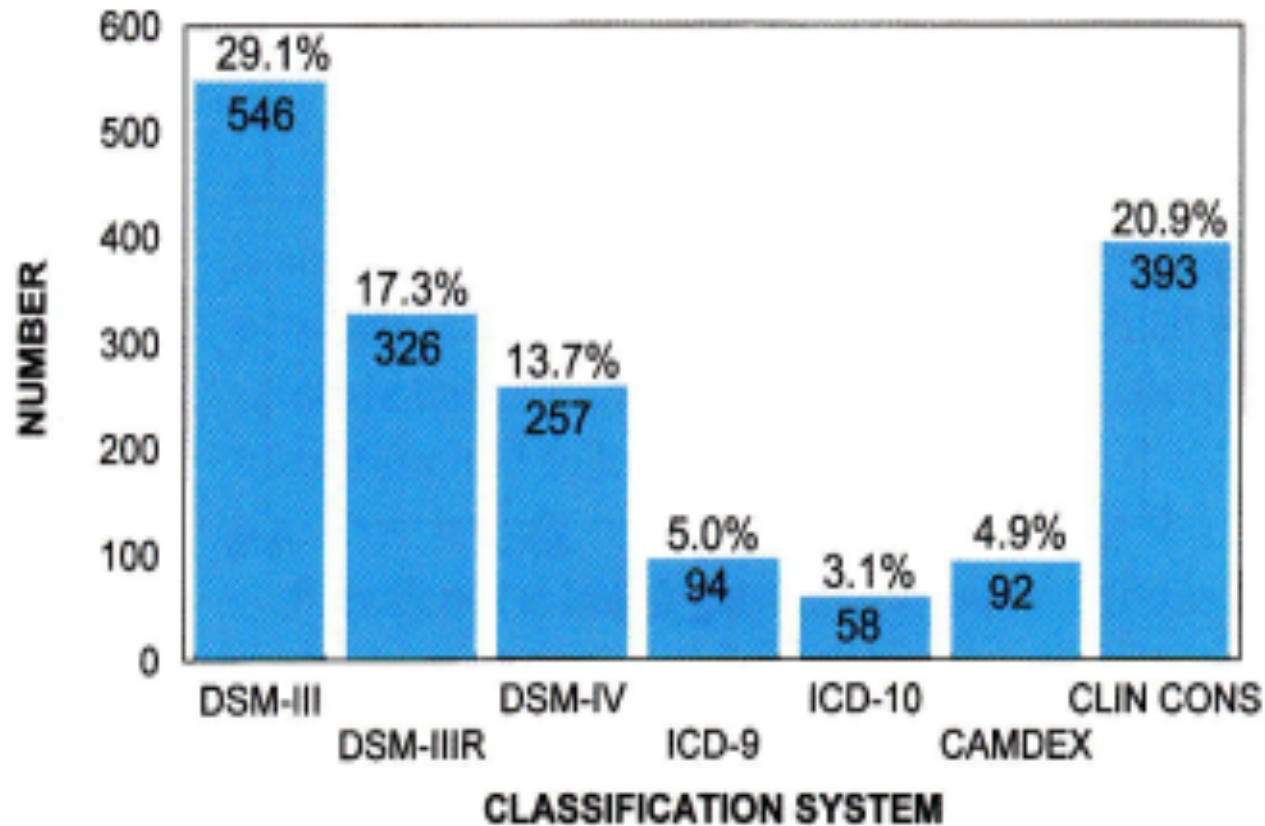


- **Problems with incidence and prevalence measurements**
 - ✓ **Problems with Numerators: define who has the disease**





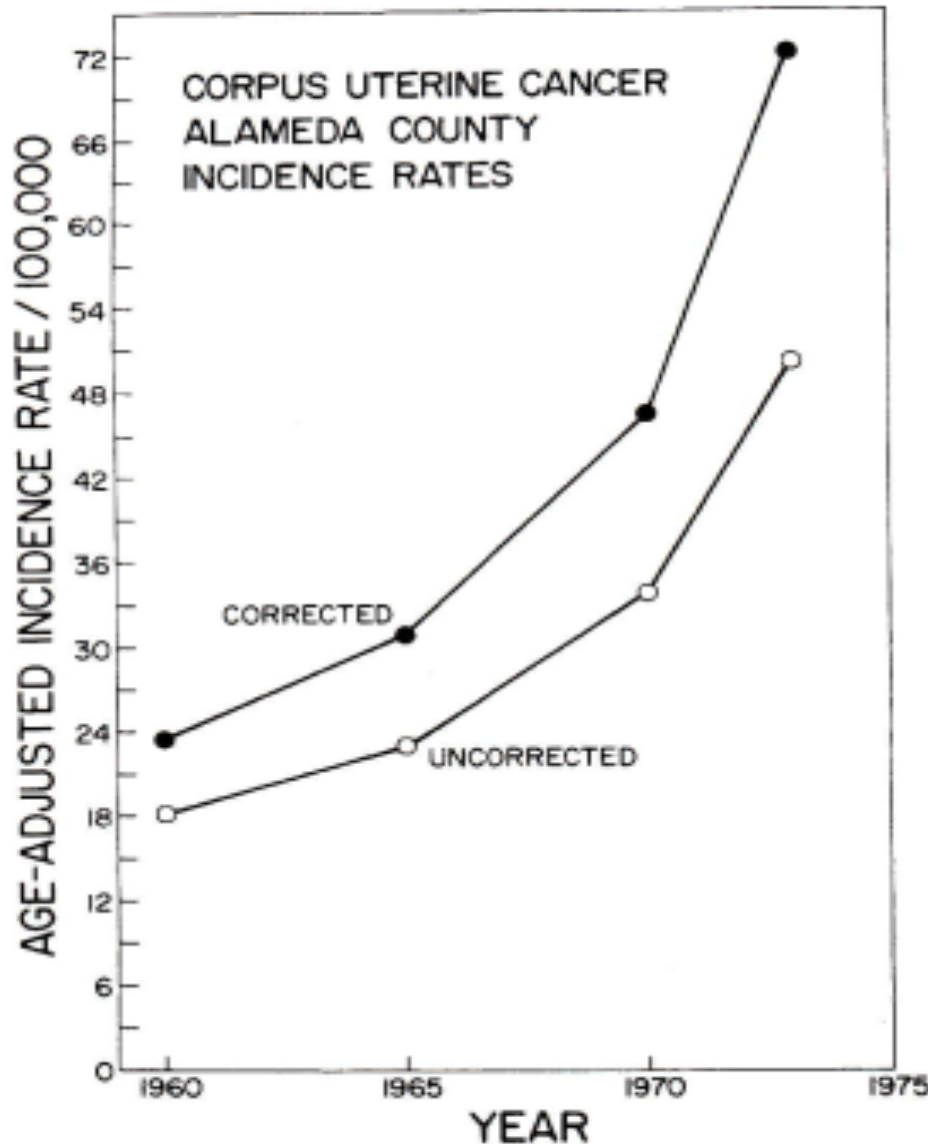
Number of people with and prevalence (%) of dementia in the Canadian Study of health and aging cohort as diagnosed by different classification systems.





- ✓ **Problems with Numerators: ascertaining which persons should be included in the numerator, how do we find the cases?**
 - 1) Use regularly available data
 - 2) Conduct a study specifically designed to gather data

- ✓ **Problems with Denominators: selective undercounting of certain group in the population?**
 - 1) Age-adjusted
 - 2) corrected



Age-adjusted uterine cancer incidence rates, corrected and uncorrected by hysterectomy status, Alameda County, California.

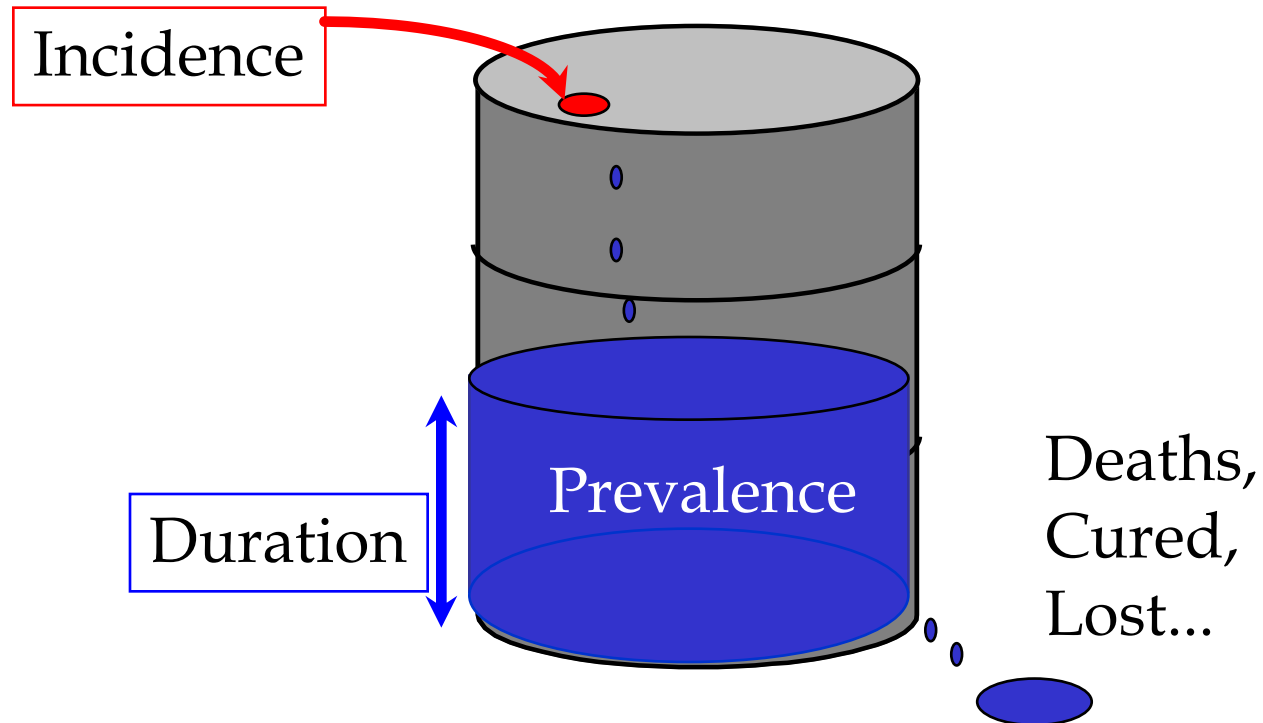


✓ Problems with Hospital Data

TABLE 3-5. **Some Limitations of Hospital Data**

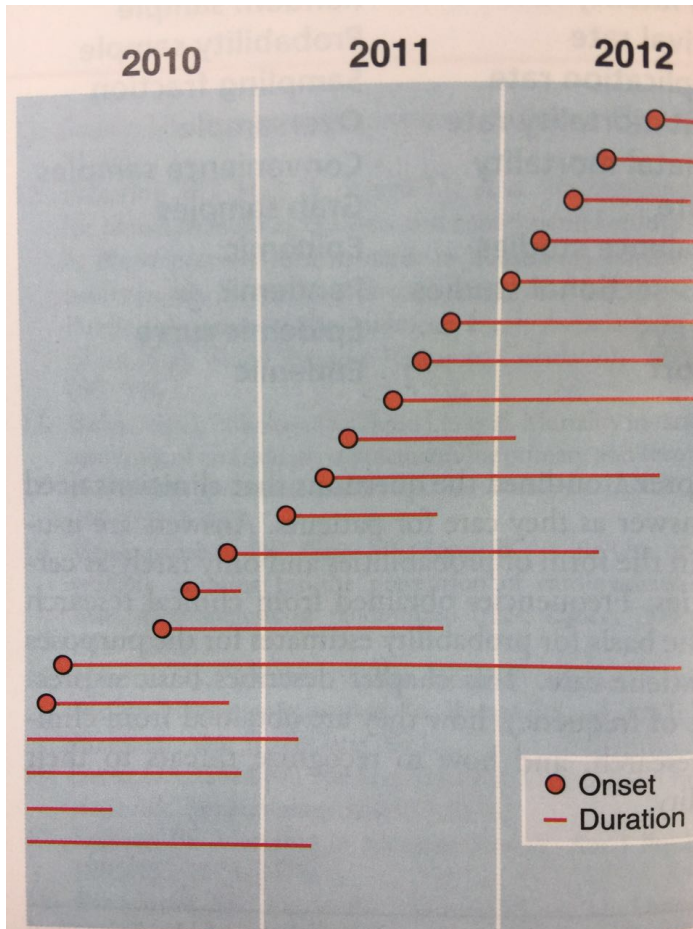
1. Hospital admissions are selective in relation to:
 - a. Personal characteristics
 - b. Severity of disease
 - c. Associated conditions
 - d. Admission policies
2. Hospital records are not designed for research.
They may be:
 - a. Incomplete, illegible, or missing
 - b. Variable in diagnostic quality
3. Population(s) at risk (denominator) is (are) generally not defined

- Relationship between incidence and prevalence



$$\text{Prevalence} = \text{Incidence rate} \times \text{Duration of disease}$$

Occurrence of disease in 10 000 people at risk of lung cancer, 2010 to 2012.



Q1: what was the incidence of lung cancer at the beginning of 2010?

Q2: what was the incidence of lung cancer at the beginning of 2011 and 2012?

Q3: what was the prevalence of lung cancer between 2010 to 2012?

Q4: what were the incidence rate of lung cancer during 2010, 2011 and 2012?



TABLE 3-7. Hypothetical Example of Chest X-Ray Screening: I. Populations Screened and Numbers with Positive X-Rays

Screened Population	Number with Positive X-Ray
1,000 Hitown	100
1,000 Lotown	60

TABLE 3-8. Hypothetical Example of Chest X-Ray Screening: II. Point Prevalence

Screened Population	Number with Positive X-Ray	Point Prevalence per 1,000 Population
1,000 Hitown	100	100
1,000 Lotown	60	60

Can we conclude that the risk of TB is higher in Hitown people than in Lotown people?

TABLE 3-9. Hypothetical Example of Chest X-Ray Screening: III. Prevalence, Incidence, and Duration

Screened Population	Point Prevalence per 1,000	Incidence (Occurrences/yr)	Duration (yrs)
Hitown	100	4	25
Lotown	60	20	3

Prevalence = Incidence × Duration



Percentage of births that were extramarital in New Zealand, 1962-1979

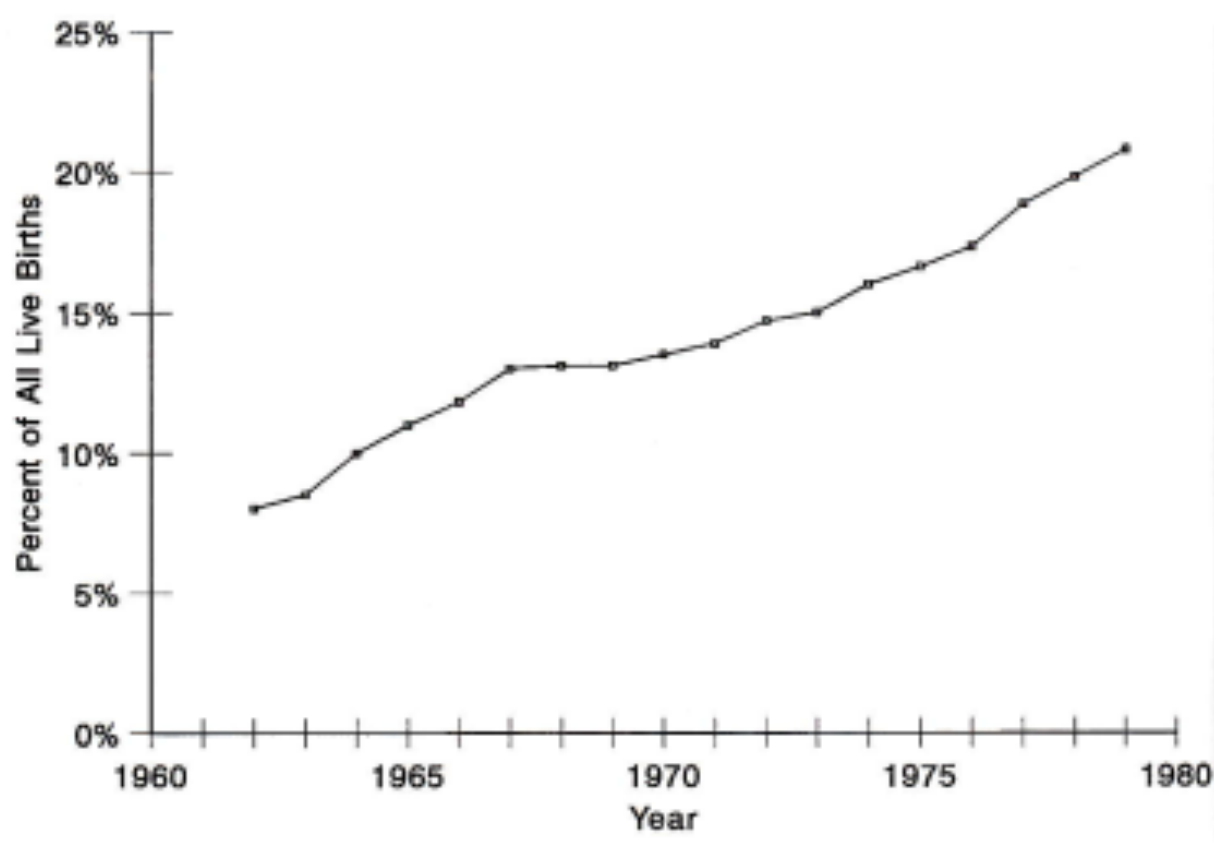
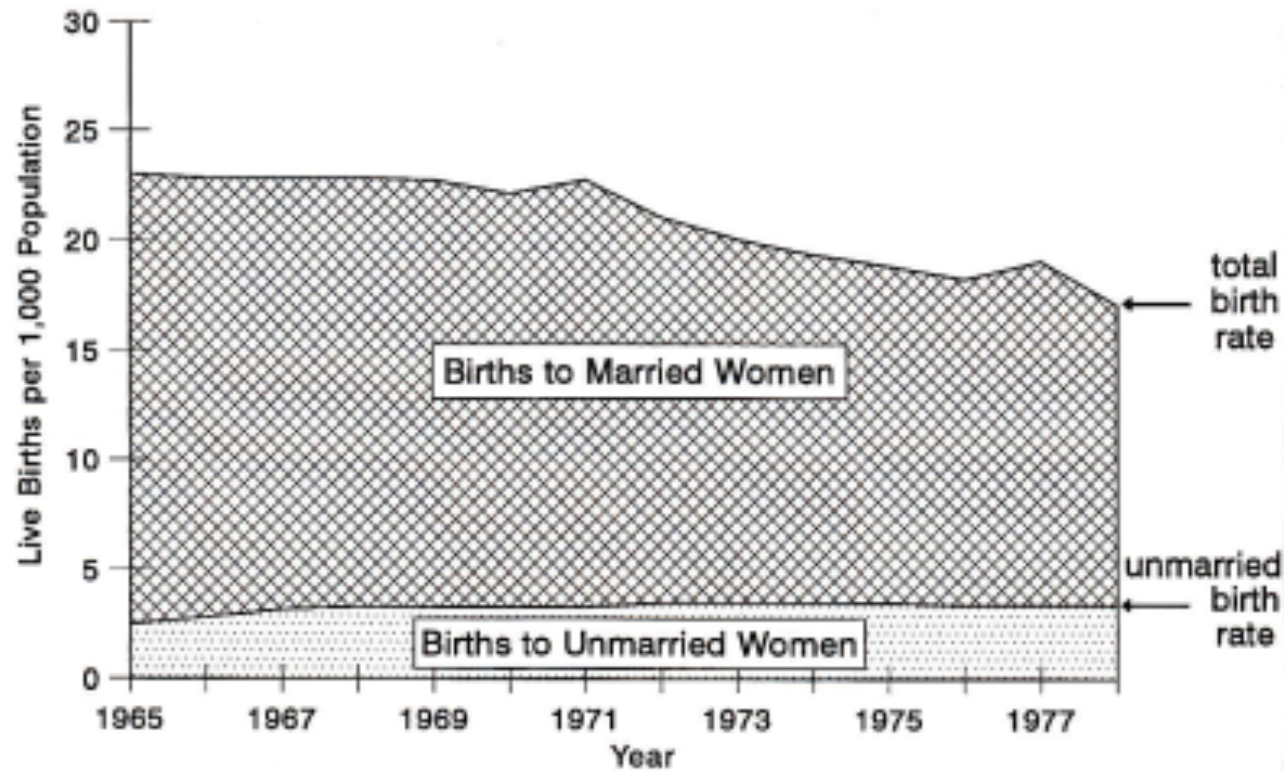
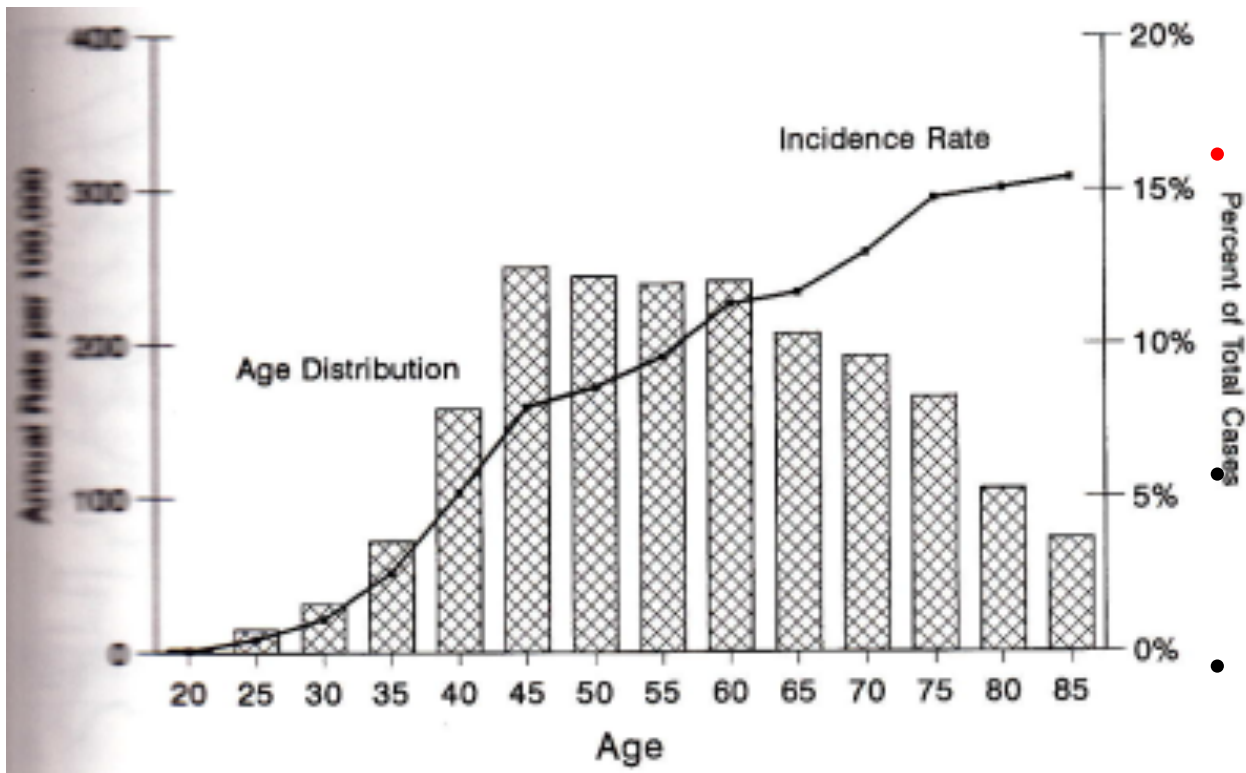


Figure 3-19. Births to married and unmarried women in New Zealand, 1965–1978, based on data from the Department of Statistics. (Adapted from Benfield J, Kjellstrom T: New Zealand ex-nuptial births and domestic purposes benefits in a different perspective. *N Z Nurs J* 74:28–31, 1981.)



- **No increase in the rate of extramarital births.**
- **There had been a decline in total births that was largely accounted for by a decline in births to married women.**
- **A proportion is not a rate**
- **Birth can be viewed as an event, just as the development of disease is an event, and appropriate rates can be computed.**

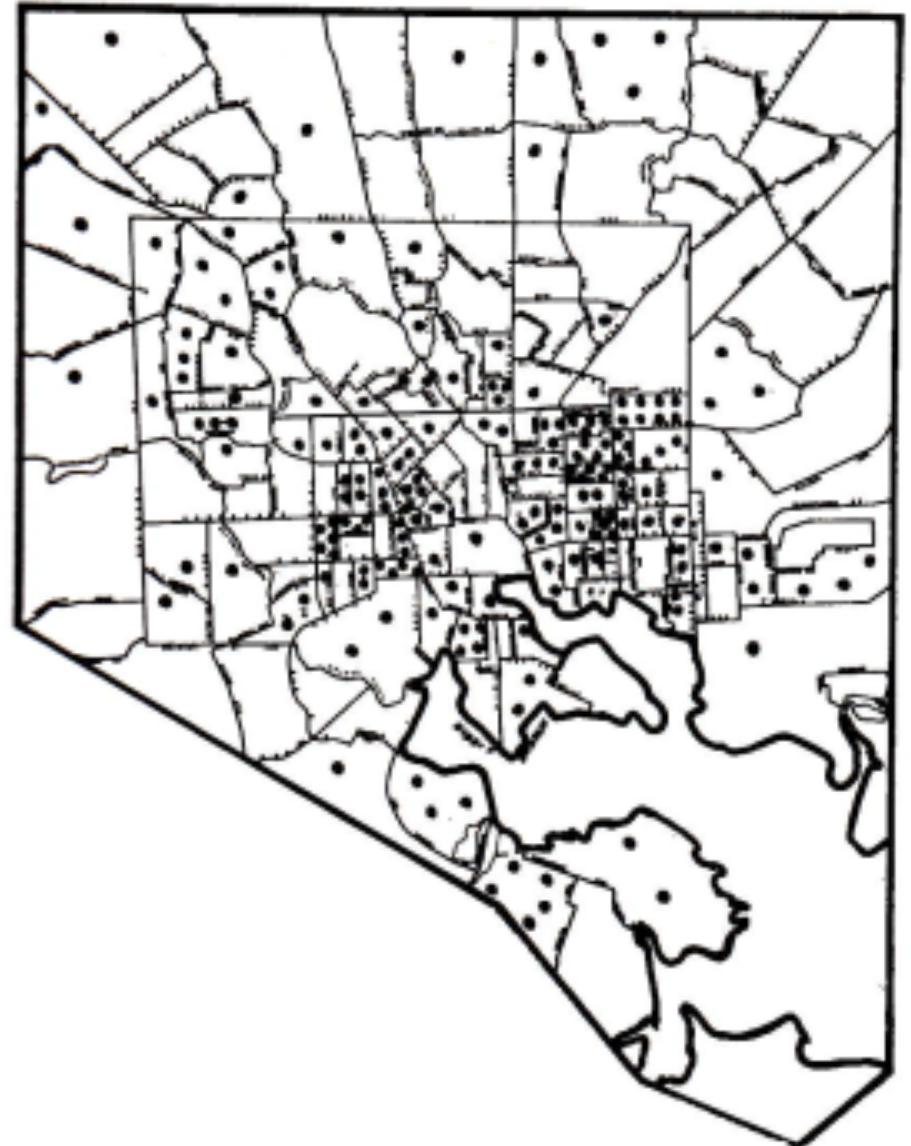
Breast cancer incidence rates in white women and distribution of cases by age



- A change in the slope of the curve between **ages 45 and 50** years.
- **Menopause:** premenopausal and postmenopausal breast cancer may be different disease.
- Even in old age, the incidence rate of BC continues to rise.
- Little proportion of old women.



- **Spot map---clustering**



Spot map of residence distribution of patients with rheumatic fever.

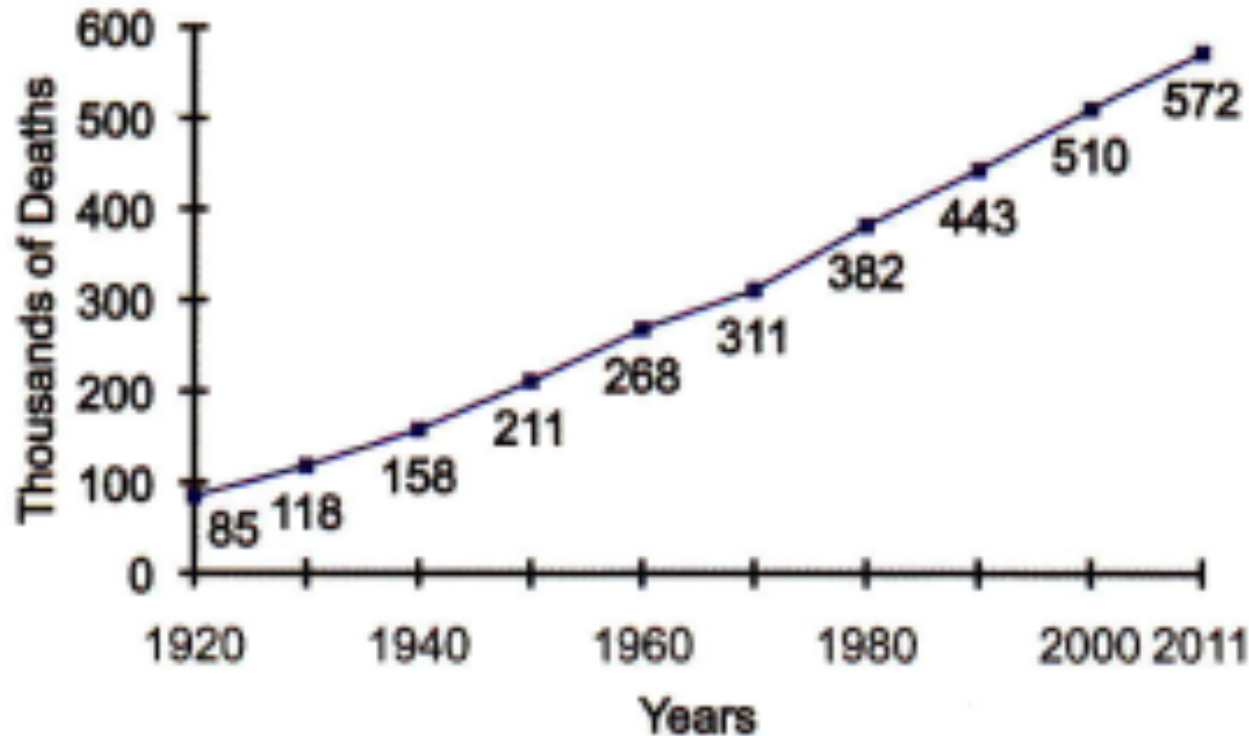


- **Spot map---clustering**



Spot map for patients with rheumatic fever.

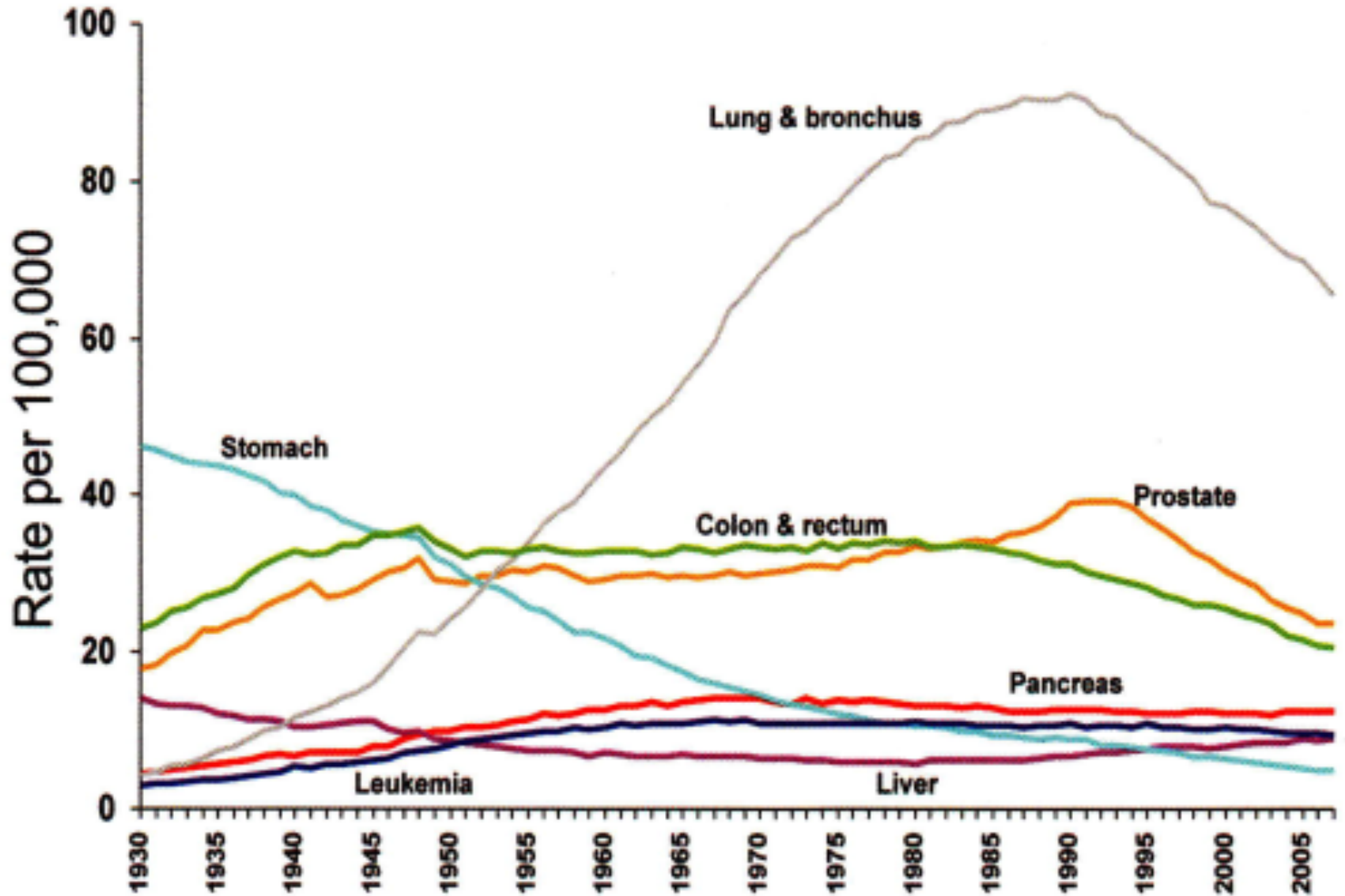
Measures of Mortality



- Trend in number of cancer deaths observed in the USA in the early and mid 20th century
- (have no denominators)

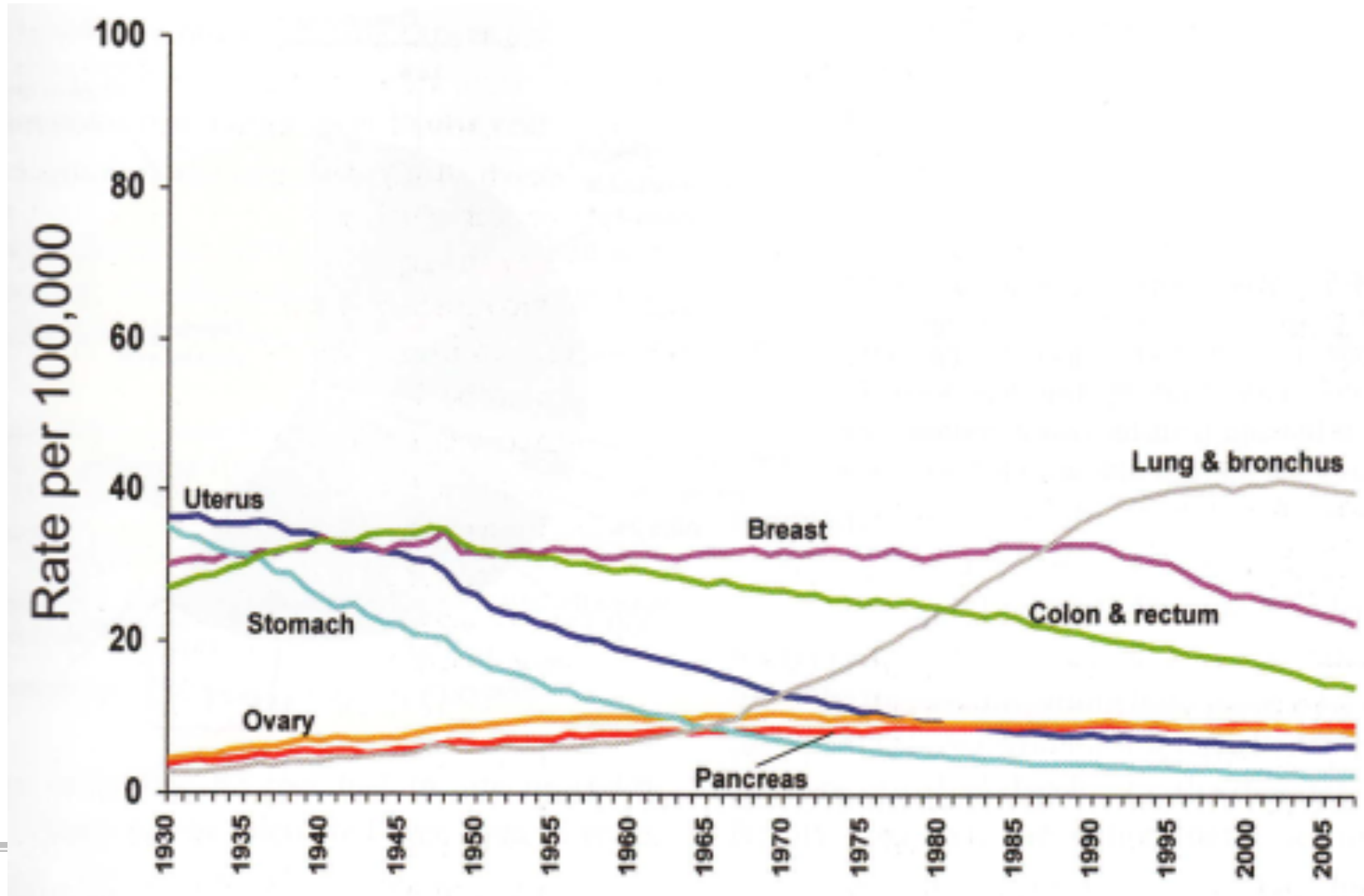


Cancer death rates for males, United States, 1930-2007



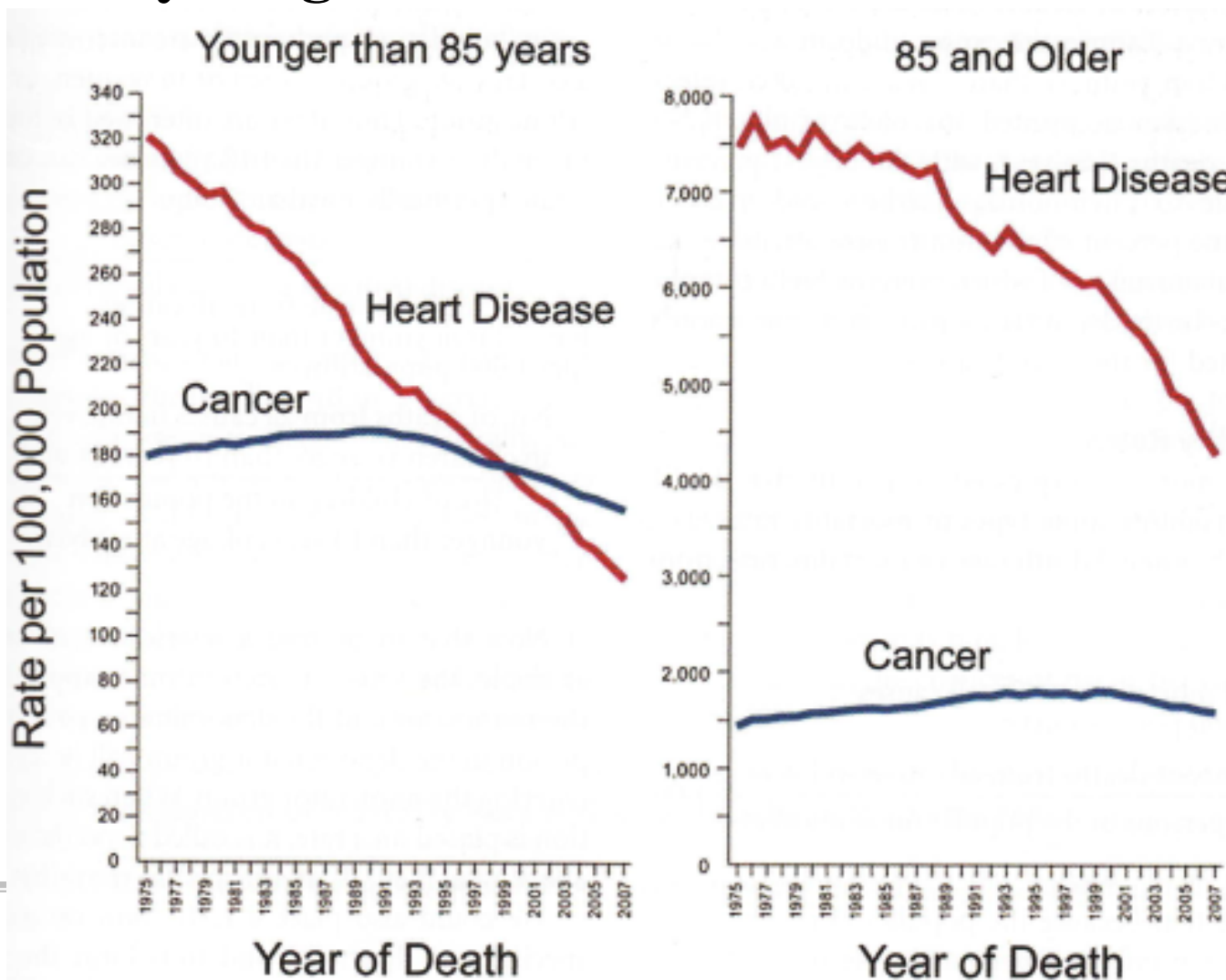


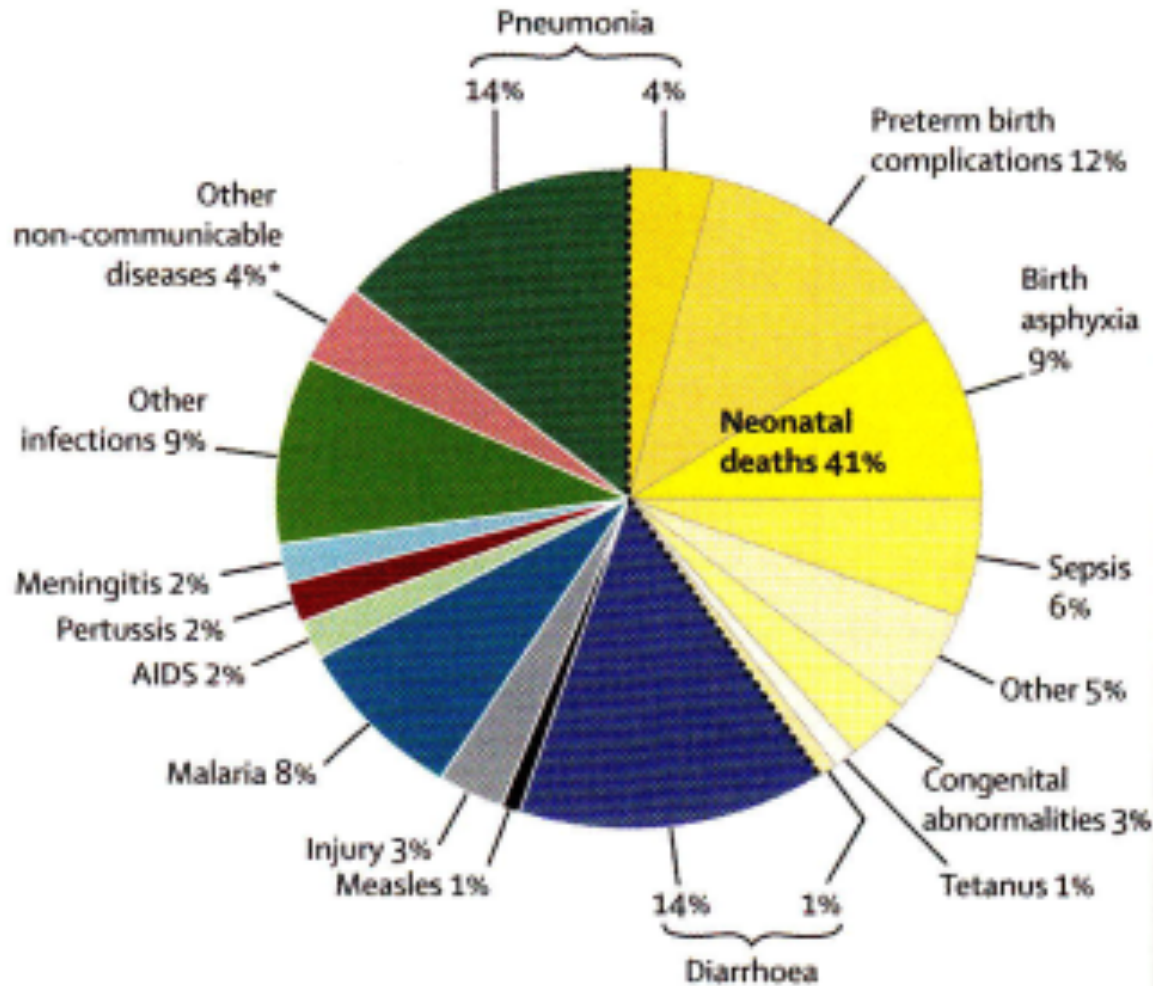
Cancer death rates for females, United States, 1930-2007





Death rates from cancer and heart disease for ages younger than 85 and 85 or older.





Major cause of death in children younger than age 5 years and in neonates(aged 0-27 days)



□ Mortality rate

- Annual mortality rate for all causes(per 1,000 population):

$$\frac{\text{Total no.of deaths from all causes in 1 year}}{\text{No.of persons in the population at midyear}} \times 1,000$$

- Annual mortality rate for all causes for children younger than 10 years of age (per 1,000 population):

$$\frac{\text{No.of deaths from all causes in 1 year in children younger than 10 years of age}}{\text{No.of children in the population younger than 10 years of age at midyear}} \times 1,000$$



□ Case-fatality

- Case-fatality (percent)=

$$\frac{\text{No. of individuals dying during a specified period of time after disease onset}}{\text{No. of individual with the specified disease}} \times 100$$



- **Difference between mortality and case-fatality**

TABLE 4-1. Comparison of Mortality Rate with Case-Fatality in the Same Year

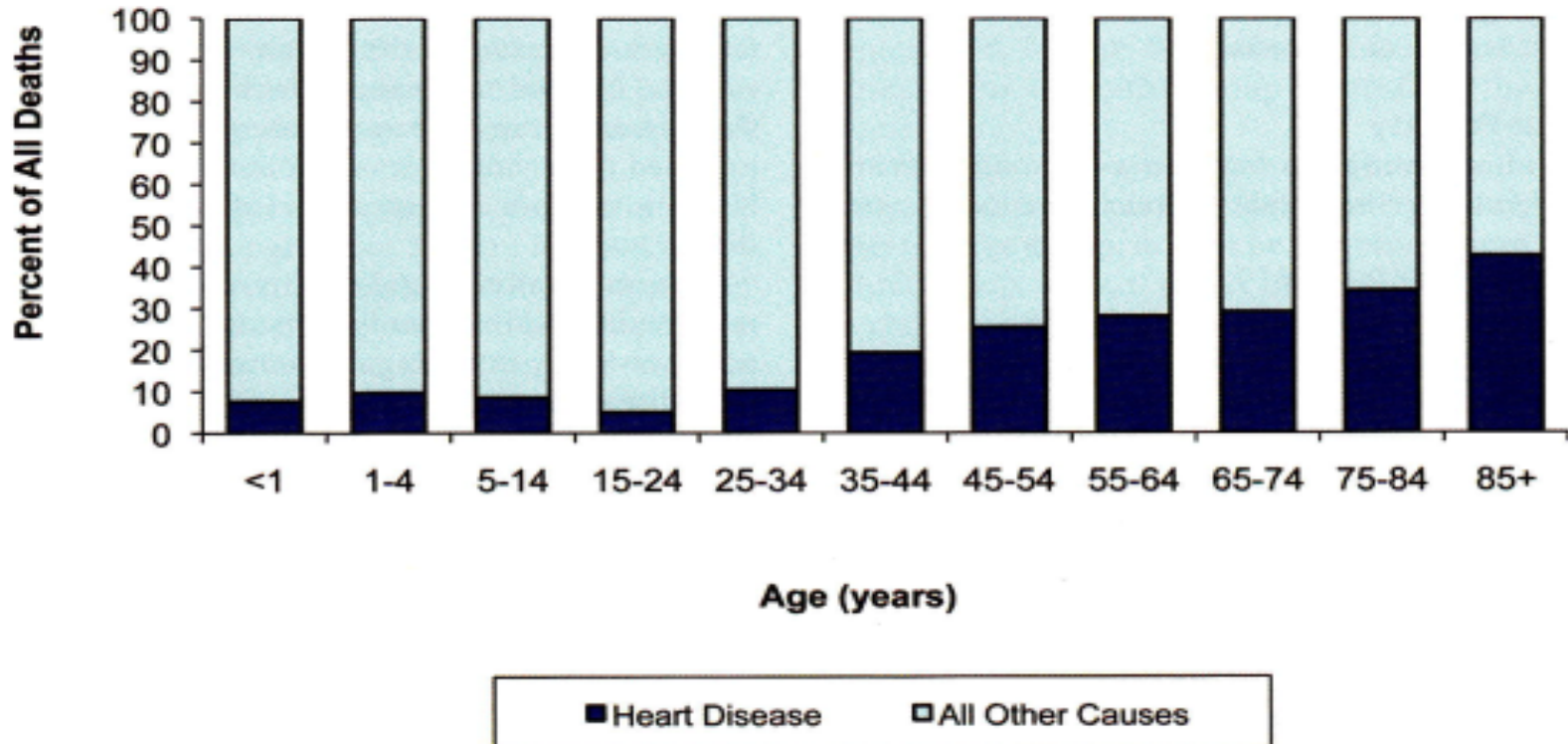
Assume a population of 100,000 people of whom 20 are sick with disease X, and in 1 year, 18 of the 20 die from disease X.

Mortality rate from disease X = $\frac{18}{100,000} = 0.00018$, or 0.018%.

Case-fatality from disease X = $\frac{18}{20} = 0.9$, or 90%.

□ Proportionate Mortality

- Proportionate mortality from cardiovascular diseases in US in 2010(percent)= $\frac{\text{No. of death from cardiovascular disease}}{\text{Total deaths in the U.S. in 2010}} \times 100$





All death and deaths from heart disease in two communities, A and B

TABLE 4-2. Comparison of Mortality Rate and Proportionate Mortality: I. Deaths from Heart Disease in Two Communities

	Community A	Community B
Mortality rate from all causes	30/1,000	15/1,000
Proportionate mortality from heart disease	10%	20%
Mortality rate from heart disease	3/1,000	3/1,000

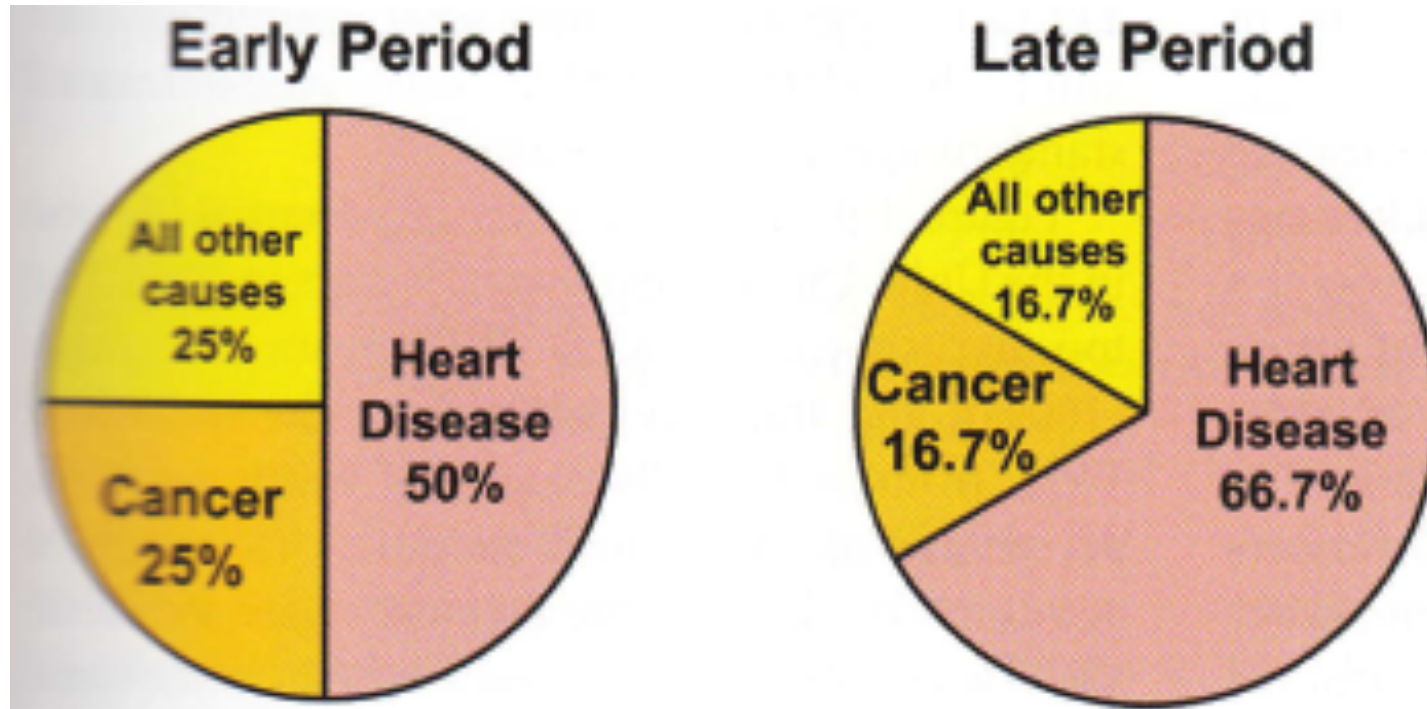


Hypothetical example of mortality rates and proportionate mortality in two periods

TABLE 4-3. Hypothetical Example of Mortality Rates and Proportionate Mortality in Two Periods

Cause of Death	EARLY PERIOD		LATER PERIOD	
	Mortality Rate	Proportionate Mortality	Mortality Rate	Proportionate Mortality
Heart disease	40/1,000	50%	80/1,000	66.7%
Cancer	20/1,000	25%	20/1,000	16.7%
All other causes	20/1,000	25%	20/1,000	16.7%
All deaths	80/1,000	100%	120/1,000	100.0%

Hypothetical example of proportionate mortality: changes in proportionated mortality from heart disease, cancer and other causes



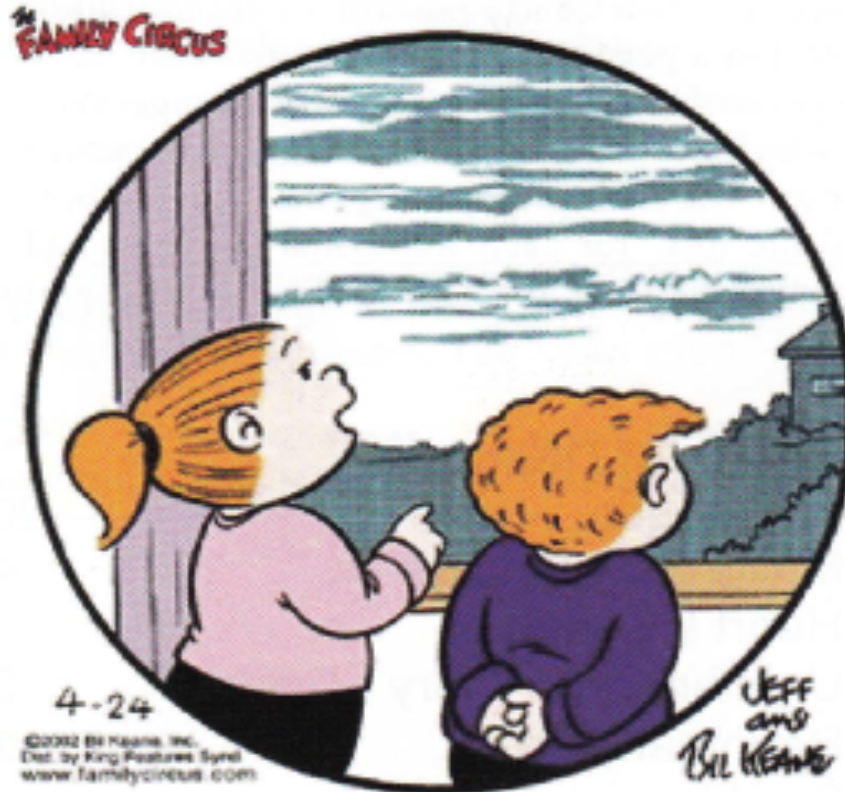


- **If all-cause mortality rates differ, cause-specific mortality rates can differ significantly, even when the proportionate mortality is the same.**

TABLE 4-4. Comparison of Mortality Rate and Proportionate Mortality: II. Deaths from Heart Disease in Two Communities

	Community A	Community B
Mortality rate from all causes	20/1,000	10/1,000
Proportionate mortality from heart disease	30%	30%
Mortality rate from heart disease	6/1,000	3/1,000

Understanding proportionate mortality

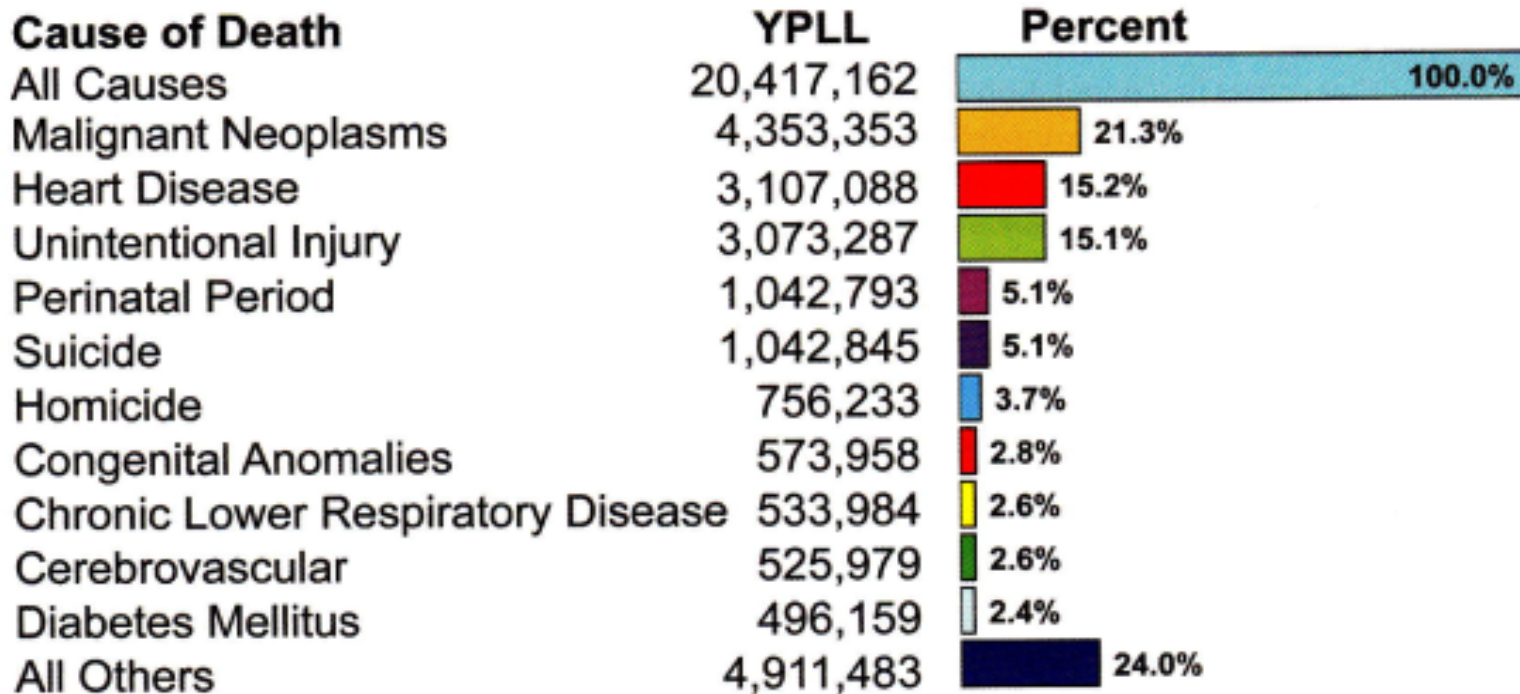


"Know what? The days get longer at the same time the nights get shorter."



□ Years of potential life lost

- Years of potential life lost (YPLL) before age 75, all races, both sexes, all death, United States, 2008





- Years of potential life lost (YPLL) before 65 years among children younger than 20 years from injuries and other disease, USA, 1986**

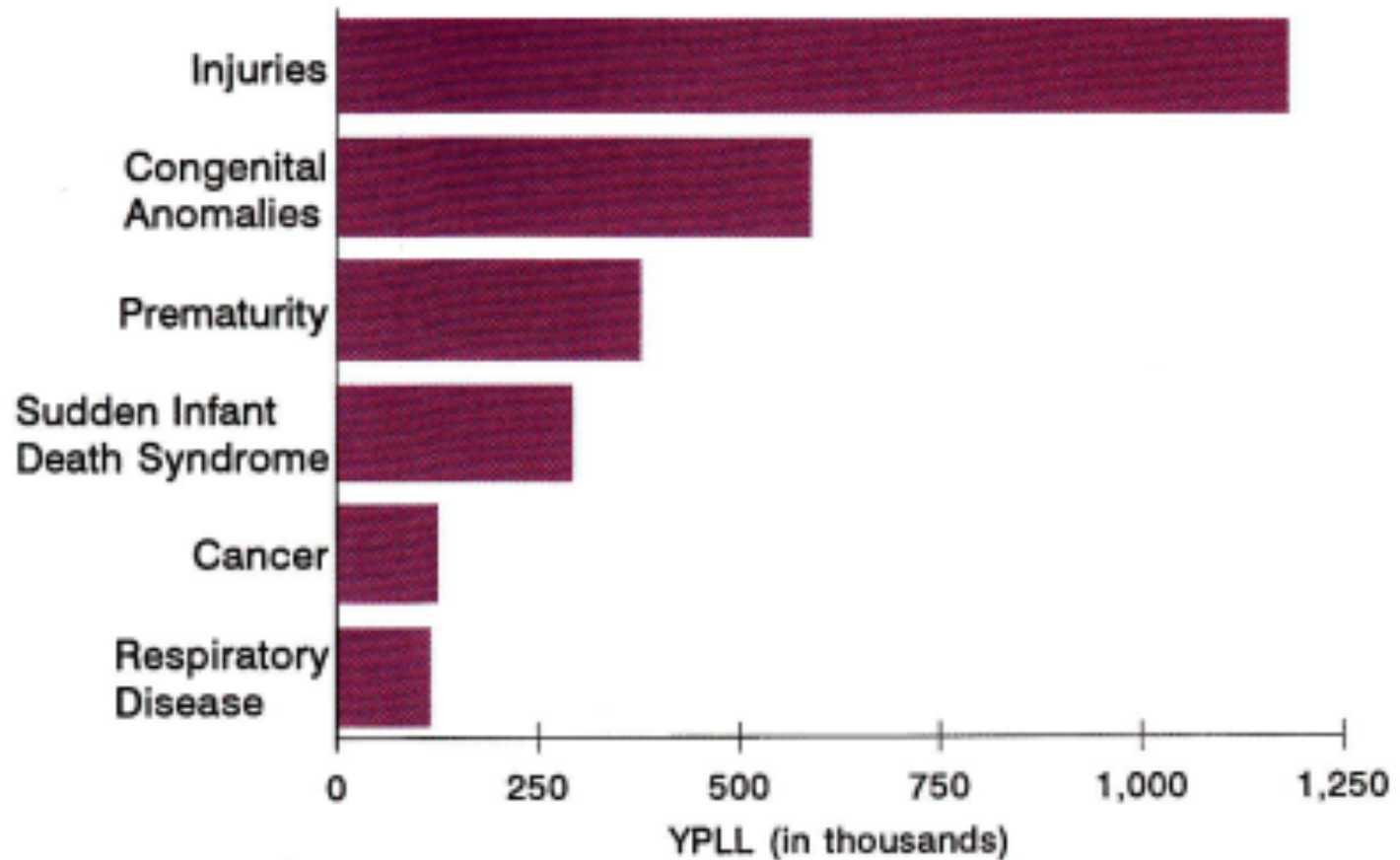




TABLE 4-5. Estimated Years of Potential Life Lost (YPLL) Before Age 65 Years and Mortality Rates per 100,000 Persons, by Cause of Death, United States, 1989 and 1990

Cause of Death (ICD-9 Codes)	YPLL for Persons Dying in 1989	YPLL for Persons Dying in 1990	Cause-Specific Crude Death Rate, 1990
All causes (total)	12,339,045	12,083,228	861.9
Unintentional injuries (E800–E949)	2,235,335	2,147,094	37.3
Malignant neoplasms (140–208)	1,832,039	1,839,900	201.7
Suicide/homicide (E950–E978)	1,402,524	1,520,780	22.5
Diseases of the heart (390–398, 402, 404–429)	1,411,399	1,349,027	289.0
Congenital anomalies (740–759)	660,346	644,651	5.3
Human immunodeficiency virus infection (042–044)	585,992	644,245	9.6
Prematurity (765, 769)	487,749	415,638	2.5
Sudden infant death syndrome (798)	363,393	347,713	2.2
Cerebrovascular disease (430–438)	237,898	244,366	57.9
Chronic liver disease and cirrhosis (571)	233,472	212,707	10.2
Pneumonia/influenza (480–487)	184,832	165,534	31.3
Diabetes mellitus (250)	145,501	143,250	19.5
Chronic obstructive pulmonary disease (490–496)	135,507	127,464	35.5

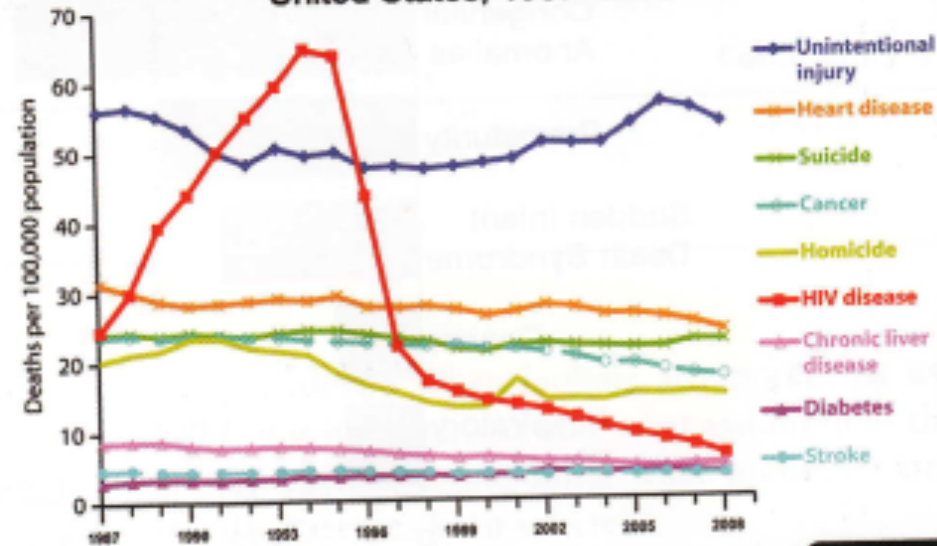
Data from Centers for Disease Control and Prevention: MMWR 41:314, 1992.



- **Why look at mortality?**
 - ✓ **An index of the severity of a disease from both clinical and public health standpoints, and index of the risk of disease.**
 - ✓ **Mortality rate is a good reflection of the incidence rate under two conditions:**
 - 1) when the case-fatality rate is high**
 - 2) when the duration of disease (survival) is short.**

- **Mortality trends in the U.S. from 1987 to 2008 for the leading causes of death in men and women, aged 25-44 years.**

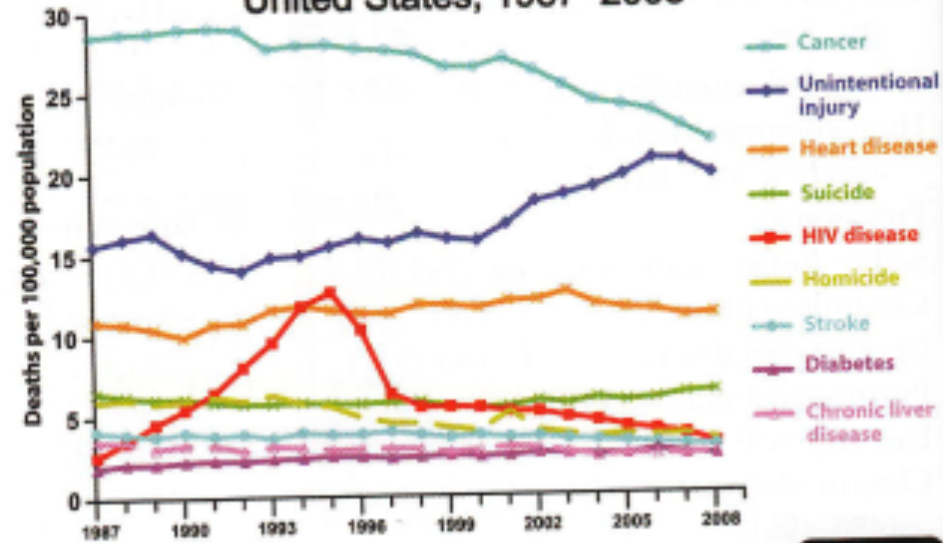
Trends in Annual Rates of Death due to the 9 Leading Causes among Men 25-44 Years Old, United States, 1987-2008



Note: For comparison with data for 1999 and later years, data for 1987-1998 were modified to account for ICD-10 rates instead of ICD-9 rates.



Trends in Annual Rates of Death due to the 9 Leading Causes among Women 25-44 Years Old, United States, 1987-2008

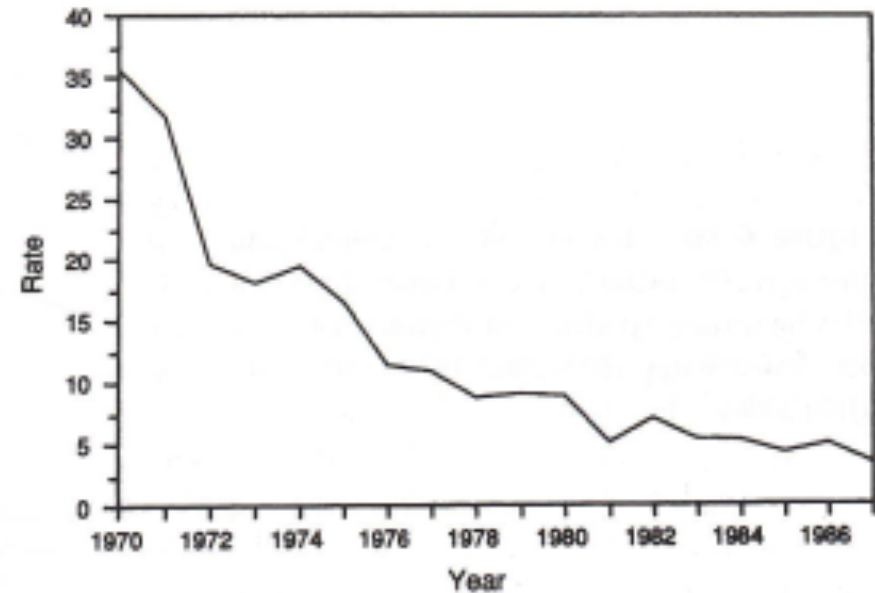
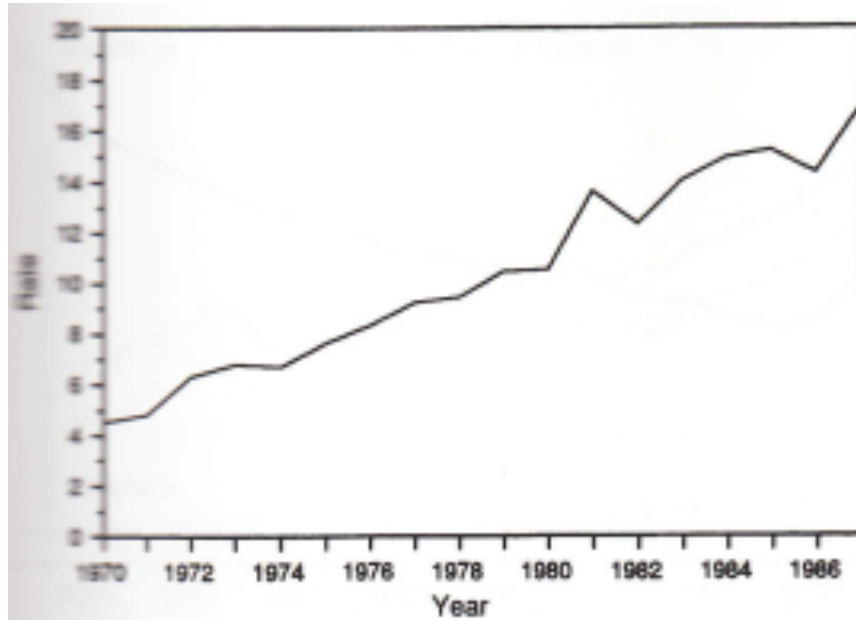


Note: For comparison with data for 1999 and later years, data for 1987-1998 were modified to account for ICD-10 rates instead of ICD-9 rates.

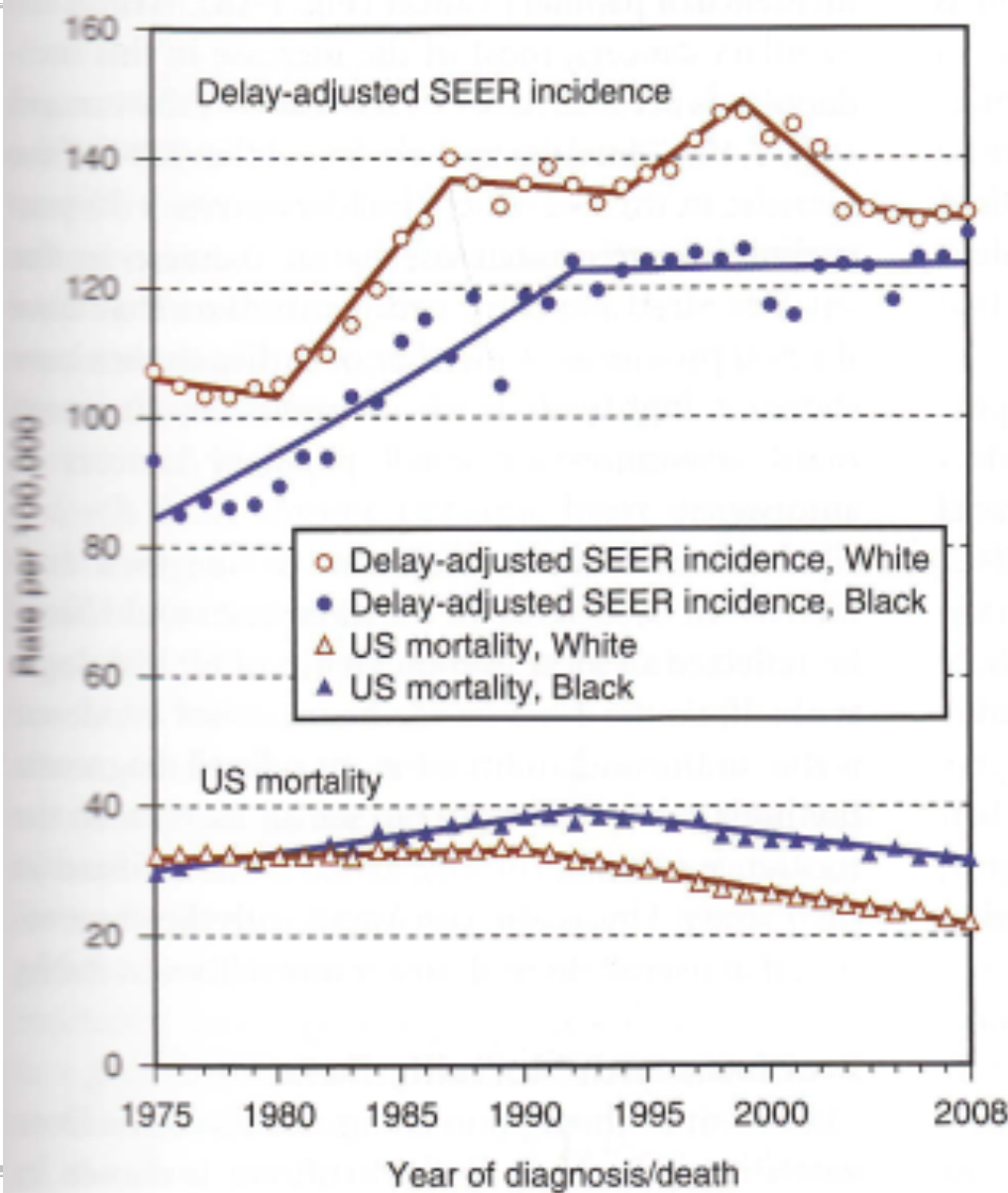


- **HIV mortality increased rapidly in both sexes from 1987 to 1995, but decreased dramatically from 1995 to 1997.**
- **Newly diagnosed, highly active antiretroviral therapy, lifestyle changes, etc.**

- **Ectopic pregnancy rates and Ectopic pregnancy death rates**



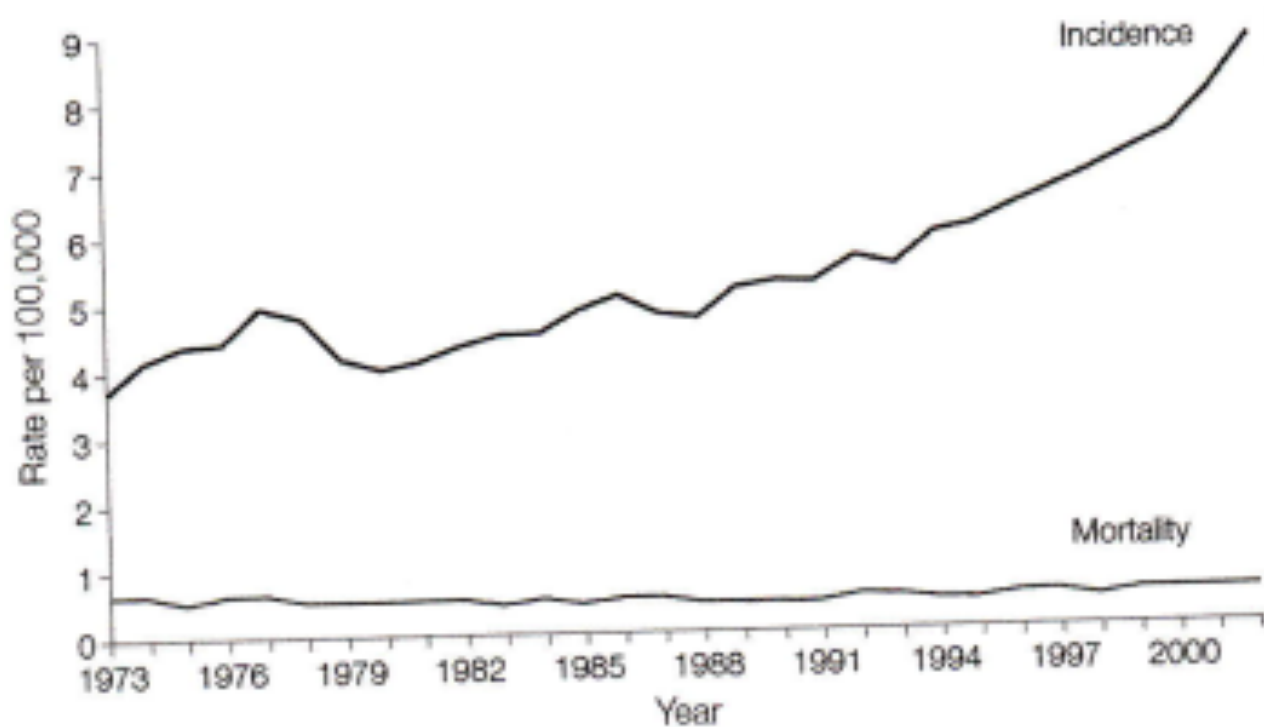
- **The increasing rate: improved diagnosis and increased frequency of pelvic inflammatory disease**
- **The decline rate: earlier of detection and increasingly prompt medical and surgical intervention**



- **Breast cancer incidence and mortality: white women versus black women.**
- **What do these curves tell us about new cases of breast cancer over time and survival from breast cancer?**



- **Thyroid cancer incidence and mortality, 1973-2002**



● Comparing mortality in different population

TABLE 4-7. **Crude Mortality Rates by Race, Baltimore City, 1965**

Race	Mortality per 1,000 Population
White	14.3
Black	10.2

- Although in each age-specific group mortality is higher in blacks than in whites, the overall mortality is higher in whites than in blacks.
- Why is this so?---Old age is the major contributor to mortality.

TABLE 4-8. **Death Rates by Age and Race, Baltimore City, 1965**

DEATH RATES BY AGE PER 1,000 POPULATION

Race	All Ages	DEATH RATES BY AGE PER 1,000 POPULATION					
		<1 yr	1-4 yrs	5-17 yrs	18-44 yrs	45-64 yrs	>65 yrs
White	14.3	23.9	0.7	0.4	2.5	15.2	69.3
Black	10.2	31.3	1.6	0.6	4.8	22.6	75.9

From Department of Biostatistics: Annual Vital Statistics Report for Maryland, 1965. Baltimore, Maryland State Department of Health, 1965.



- **Direct age adjustment**

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From Department of Biostatistics: Annual Vital Statistics Report for Maryland, 1965. Baltimore, Maryland State Department of Health, 1965.



TABLE 4-9. A Hypothetical Example of Direct Age Adjustment: I. Comparison of Total Death Rates in a Population at Two Different Times

EARLY PERIOD			LATER PERIOD		
Population	Number of Deaths	Death Rate per 100,000	Population	Number of Deaths	Death Rate per 100,000
900,000	862	96	900,000	1,130	126

TABLE 4-10. A Hypothetical Example of Direct Age Adjustment: II. Comparison of Age-Specific Death Rates in Two Different Time Periods

Age Group (yr)	EARLY PERIOD			LATER PERIOD		
	Population	Number of Deaths	Death Rates per 100,000	Population	Number of Deaths	Death Rates per 100,000
All ages	900,000	862	96	900,000	1,130	126
30-49	500,000	60	12	300,000	30	10
50-69	300,000	396	132	400,000	400	100
70+	100,000	406	406	200,000	700	350



TABLE 4-11. A Hypothetical Example of Direct Age Adjustment: III. Carrying Out an Age Adjustment Using the Total of the Two Populations as the Standard

Age Group (yr)	Standard Population	"Early" Age-specific Mortality Rates per 100,000	Expected Number of Deaths Using "Early" Rates	"Later" Age-specific Mortality Rates per 100,000	Expected Number of Deaths Using "Later" Rates
All ages	1,800,000				
30-49	800,000	12	96	10	80
50-69	700,000	132	924	100	700
70+	300,000	406	<u>1,218</u>	350	<u>1,050</u>
Total number of deaths expected in the standard population:			2,238		1,830
Age-adjusted rates:		$\text{"Early"} = \frac{2,238}{1,800,000} = 124.3$		$\text{"Later"} = \frac{1,830}{1,800,000} = 101.7$	



TABLE 4-12. An Example of Direct Age Adjustment: Comparison of Age-adjusted Mortality Rates in Mexico and in the United States, 1995–1997

Age Group (yr)	Standard Population	Age-specific Mexico Mortality Rates per 100,000	Expected Numbers of Deaths Using Mexico Rates	Age-specific United States Mortality Rates per 100,000	Expected Numbers of Deaths Using United States Rates
All ages	100,000				
<1	2,400	1,693.2	41	737.8	18
1–4	9,600	112.5	11	38.5	4
5–14	19,000	36.2	7	21.7	4
15–24	17,000	102.9	17	90.3	15
25–44	26,000	209.6	55	176.4	46
45–64	19,000	841.1	160	702.3	133
65+	7,000	4,967.4	<u>348</u>	5,062.6	<u>354</u>
Total numbers of deaths expected in the standard population:			639		574
Age-adjusted rates:					
Mexico = $\frac{639}{100,000} = \frac{6.39}{1,000}$				United States = $\frac{574}{100,000} = \frac{5.74}{1,000}$	

From Analysis Group, Pan American Health Organization Special Program for Health Analysis: Standardization: A classic epidemiological method for the comparison of rates. Epidemiol Bull 232(3):9–12, 2002.



- **Indirect age adjustment (Standardized mortality ratios)**

- ✓ **Standardized mortality ratios(SMR)**

$$\text{SMR} = \frac{\text{Observed no.of deaths per year}}{\text{Expected no.of deaths per year}}$$



TABLE 4-13. Computation of a Standardized Mortality Ratio (SMR) for Tuberculosis, All Forms (TBC), for White Miners Ages 20 to 59 Years, United States, 1950

	Estimated Population for White Miners	Death Rate (per 100,000) for TBC in Males in the General Population	Expected Deaths from TBC in White Miners if They Had the Same Risk as the General Population	Observed Deaths from TBC in White Miners
Age (yr)	(1)	(2)	(3) = (1) × (2)	(4)
20-24	74,598	12.26	9.14	10
25-29	85,077	16.12	13.71	20
30-34	80,845	21.54	17.41	22
35-44	148,870	33.96	50.55	98
45-54	102,649	56.82	58.32	174
55-59	<u>42,494</u>	75.23	<u>31.96</u>	<u>112</u>
Totals	534,533		181.09	436

$$\text{SMR} = \frac{\text{Observed deaths for an occupation - cause - race group}}{\text{Expected deaths for an occupation - cause - race group}} \times 100$$

$$\text{SMR (for 20-59-yr-olds)} = \frac{436}{181.09} \times 100 = 241$$

Adapted from Vital Statistics: Special Reports, Washington, DC, Department of Health, Education, and Welfare, Vol. 53(5), 1963.



Summary

- Quantitatively measuring
- Morbidity
- mortality

Thanks for your attention!

