Fundamentals of Epidemiology I

Measures of Disease Occurrence and Association

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Objectives – Day 1

- Review Fundamentals of Epidemiology
  - Measures of Disease Occurrence and Association
  - Study Designs
  - Epidemiologic Concepts
    - Bias
    - Confounding
    - Random Variation
  - Group Exercise

Measures of Disease Occurrence

PREVALENCE = NUMBER OF EXISTING CASES OF A DISEASE / TOTAL STUDY POPULATION AT THAT TIME

Synonym(s): *Prevalence rate*

Notes: *Prevalence is not a rate, it is a unitless proportion.*
It takes on values from 0 to 1 (e.g. 0.2, 0.7)
Can be thought of as a %

Not a measure of new cases, but all cases
Prevalence a function of incidence rate and disease duration

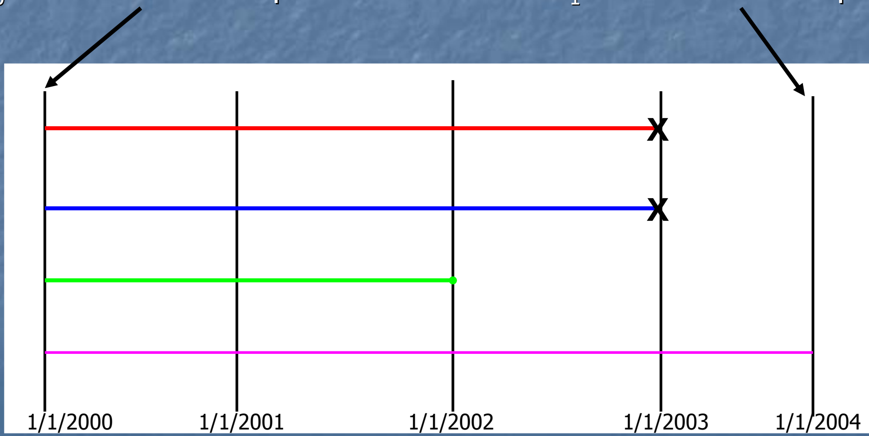
Example: **Among a sample of men aged 50-80 years in Bangkok, 30 of 2400 men examined in 1986 had cancer**

Prevalence = 30/2400 = 0.0125 * 100 = 1.25%

RISK = $\frac{\text{NUMBER OF NEW CASES OF DISEASE FROM } T_0 \text{ TO } T_1}{\text{NUMBER OF SUBJECTS AT RISK AT } T_0}$

$= \frac{2}{4} = 0.50 * 100\% = 50\%$

T_0 = start of follow-up T_1 = end of follow-up



RISK

Synonym(s): *Cumulative incidence, incidence proportion*

Notes: *Individual's probability of developing disease over specified time period*
A unitless proportion, not a rate
It takes on values from 0 to 1 (e.g. 0.2, 0.7)
Can be thought of as a %

Measure of new cases in a population of previously disease free subjects

Example: **Among a sample of men aged 50-80 years in Bangkok, 2370 men of 2400 examined in 1986 were free of cancer.**

From 1986 to 2006, 150 of them developed cancer.

Risk = 150/2370 = 0.021 * 100 = 2.1%

Problems with Risk

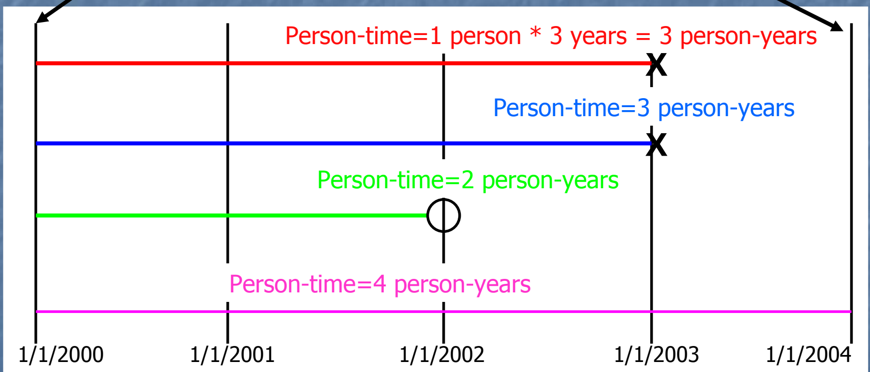
- **Competing risks**
  Subjects may die of other disease early during the study, and thus cannot develop disease of interest. They cannot contribute to numerator. Yet, they contribute to denominator.
- **Loss to follow-up**
  Subjects may move out of study area, or become non-responsive, and thus we do not know if they developed disease or not. Therefore, they cannot contribute to the numerator, but they do contribute to the denominator.

Incidence rate = Number of events that occur from T_0 to T_1 / Total person-time of observation

Person-time = Sum of total time spent in study for all study subjects

T_0 = start of follow-up

T_1 = end of follow-upT



Total person-time=3 + 3 + 2 + 4 person-years = 12 person-years

INCIDENCE RATE

Synonym(s): *Hazard rate*

Notes: *# new cases occurring in population per unit of person-time*
Has units (i.e. "person-time"), is a rate
Takes on values from 0 to ∞

Example: Among a sample of men aged 50-80 years in Bangkok, 2370 men of 2400 examined in 1986 were free of cancer. From 1986 to 2006, each subject was followed for 20 years, and 150 men developed cancer.

Incidence rate = 150 / (2370 persons * 20 years)
= 0.0032 cases of cancer / 1 person-year
= 3.2 cases of cancer / 1000 person-years

- Prevalence is a function of both incidence rate and duration

$$\frac{\text{Prevalence}}{\text{1-Prevalence}} = \text{Incidence Rate} * \text{Duration}$$

Example:

Prevalence=5%
Incidence rate=10 cases of disease/10 person-years
Duration = ? years

$$\frac{0.05}{(1-0.05)} = \frac{\text{10 cases}}{\text{10 person-years}} * \text{Duration years}$$

Duration = 0.52 years

- If prevalence < 0.10 or 10% then:
Prevalence ~ Incidence Rate * Duration

$$0.05 = \frac{\text{10 cases}}{\text{10 person-years}} * \text{Duration years}$$

Duration = 0.5 years

Measures of Disease Association

Rate Ratio = $IR_{Exposed}$ / $IR_{Unexposed}$

Synonym: ***Relative risk***

Notes: *Ranges from 0 to ∞*
When no association between exposure and disease, RR=1
RR <1 indicates exposure decreases incidence rate
RR >1 indicates exposure increases incidence rate
All ratio measures are unitless

Example:	Radiation	No Radiation
Breast cancer cases	41	15
Person-years	28,010	19,017

RR = (41/28,010 PY) / (15/19,017 PY) = 1.85

Radiation exposure results in an **85% increase in the incidence rate of breast cancer**, compared to no radiation exposure.

Risk Ratio = $\text{Risk}_{\text{Exposed}}$ / $\text{Risk}_{\text{Unexposed}}$

Synonyms: *Cumulative incidence ratio,* ***relative risk***

Notes:
- *Ranges from 0 to ∞*
- *When no association between exposure and disease, RR=1*
- *RR <1 indicates exposure is protective*
- *RR >1 indicates exposure increases risk*
- *All ratio measures are unitless*

Example:	Radiation	No Radiation
Breast cancer cases	41	15
Non-breast cancer	17	27
Subjects at risk	58	42

RR = (41/58) / (15/42) = 1.98

Subjects with radiation exposure have **98% greater risk of developing breast cancer**, than subjects without radiation exposure.

Rate Difference = $IR_{Exposed}$ - $IR_{Unexposed}$

Notes:
- *Ranges from -∞ to +∞*
- *When no association between exposure and disease, RD=0*
- *RD <0 indicates exposure decreases incidence rate*
- *RD >0 indicates exposure increases incidence rate*
- *RD is in units of person-time*

Example:

	Radiation	No Radiation
Breast cancer cases	41	15
Person-years	28,010	19,017

RD = (41/28,010 PY) - (15/19,017 PY) = 0.000675 cases/1 PY
= 6.75 cases/10,000 person-years

Radiation exposure results in an increase of 6.75 breast cancer cases/10,000 person-years, compared to no radiation exposure.

Risk Difference = $Risk_{Exposed}$ - $CI_{Unexposed}$

Synonyms: *Attributable risk, attributable risk among the exposed*

Notes:
- *Ranges from -1 to +1*
- *When no association between exposure and disease, RD=0*
- *RD <0 indicates exposure decreases risk*
- *RD >0 indicates exposure increases risk*
- *unitless*

Example:

	Radiation	No Radiation
Breast cancer cases	41	15
Non-breast cancer	17	27
Subjects at risk	58	42

RD = (41/58) - (15/42) = 0.35 * 100% = 35%

There is a 35% increase in the risk of breast cancer associated with radiation exposure, compared to the risk found in subjects without radiation exposure.

Attributable Risk % = ((RR – 1) / RR) * 100

Synonyms: *Etiologic fraction, relative excess incidence, attributable proportion*

Notes: *Fraction of disease burden among the exposed that can be attributed to exposure.*

Example:

	Radiation	No Radiation
Breast cancer cases	41	15
Non-breast cancer	17	27
Subjects at risk	58	42

RR = (41/58) / (15/42) = 1.98

AR% = (1.98 – 1) / 1.98 * 100 = 49%

Approximately 49% of the breast cancer risk in those exposed to radiation is due to radiation exposure.

Population Attributable Risk %

$$PAR\% = ((Risk_{TOTAL} - Risk_{Unexposed}) / Risk_{TOTAL}) * 100$$

Notes: *Fraction of disease in the population that is attributable to exposure, and thus could be eliminated if exposure were eliminated*

Example:

	Radiation	No Radiation	Total
Breast cancer cases	41	15	56
Non-breast cancer	17	27	44
Subjects at risk	58	42	100

PAR% = ((56/100) – (15/42)) / (56/100) * 100 = 36%

Approximately 36% of new breast cancer cases would be eliminated in this population if radiation exposure was eliminated

- **Note:** The principles and interpretation of attributable rate percent, and population attributable rate are similar to those given for risks
- They are just calculated with incidence rates rather than risks

Odds Ratio = ad / bc

Used in both case-control and cohort studies

Due to common use of logistic regression

Used to approximate the rate ratio or risk ratio

	Exposed	Unexposed
Disease	a	b
No Disease	c	d

Review/Examples

- If we want to quantify # of existing cases in the population
  - Prevalence = # of existing cases of disease / # of people in the population

- If we want to quantify the # of new cases in a population
  - Risk = # of new cases of disease since T_0 / # of people at risk in the population at T_0

  - Incident Rate = # of new cases of disease since T_0 / # of person-years accrued by population at risk since T_0

Review/Examples

- If you want to compare the burden of disease in an exposed population to that of an unexposed population.

Is exposure associated with a greater/lower risk/rate of disease?

Rate Ratio (RR) = $IR_{Exposed}$ / $IR_{Unexposed}$

Risk Ratio (RR) = $Risk_{Exposed}$ / $Risk_{Unexposed}$

Odds Ratio (OR) = ad/bc

	Exposed	Unexposed
Disease	a	b
No Disease	c	d

Rate Difference = $IR_{Exposed}$ - $IR_{Unexposed}$

Risk Difference = $Risk_{Exposed}$ - $Risk_{Unexposed}$

Harvard Six Cities Mortality Study

Dockery et al, NEJM 1993

- Prospective study of effects of air pollution on respiratory disease
- 8111 subjects randomly selected 1974-77 in six communities
- Questionnaire on risk factors for respiratory disease, PF test
- Mortality follow-up through 1989
- Cities selected to represent range of exposures to air pollution from fossil fuels
- Community air monitors in each city
  - TSP, PM_{10}, $PM_{2.5}$, SO_4
  - SO_2, NO_2, O_3

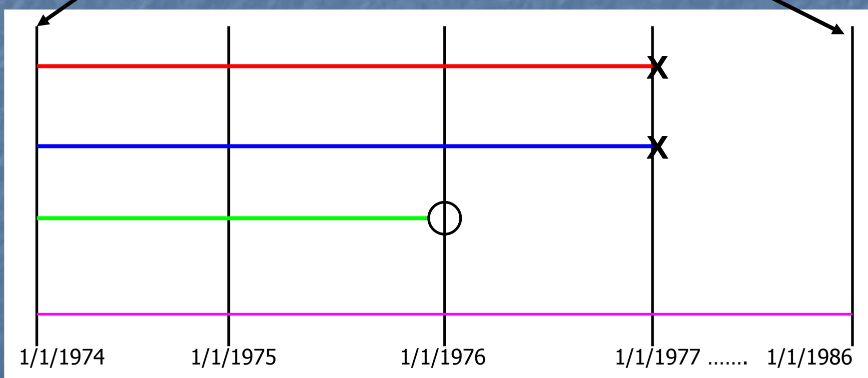
Incidence rate = Number of events that occur from T_0 to T_1 / Total person-time of observation

$$\text{Incidence rate} = \frac{\text{Number of events that occur from } T_0 \text{ to } T_1}{\text{Total person-time of observation}}$$

Person-time = Sum of total time spent in study for all study subjects

T_0 = start of follow-up

T_1 = end of follow-upT



Calculate **incident mortality** with person-years denominator

	Deaths Yes	No	Person-Years	Deaths/1000 p-yrs	Relative Risk (95% CI)
Portage, WI	232	-	21,618	10.73	1.00
Topeka, KS	156	-	16,111	9.68	0.90 (0.74 , 1.11)
Watertown, MA	248	-	19,882	12.47	1.16 (0.97 , 1.39)
Harriman, TN	222	-	17,836	12.45	1.16 (0.96 , 1.39)
St.Louis, MO	281	-	17,715	15.86	1.48 (1.24 , 1.76)
Steubenville,OH	291	-	17,914	16.24	1.51 (1.27 , 1.80)
	1430		111,076		

Next:

Epidemiologic Study Designs