NURS 306

- Epidemiologic Orientation of Health and Disease
  - definition and introduction
  - health and disease
  - natural history of disease
  - levels of prevention
- Epidemiologic Concepts
  - scope
  - epidemic versus endemic disease
  - multiple causation of disease
  - outbreak investigation

NURS 306

- Epidemiology - the study of the distribution and determinants of of diseases and injuries in human populations
  - Frequency and types of illness/injury
    - Health planning
  - What groups of people have illness/injury
    - Factors that affect disease status
  - Quantify the natural history of disease
    - Evaluate new management strategies

NURS 306

  - Evaluation of new preventive and therapeutic measures
    - Impacts on health outcome
  - Foundation for public policy and regulatory decisions
    - Health policy decision making
- Some Historical Context
  - 18th Century
    - Edward Jenner – Small Pox
  - 19th Century
    - John Snow - Cholera

NURS 306

- Knowledge of health and disease
  - anatomy, microbiology, pathology, immunology, clinical medicine, etc.
  - 3 basic groups
    - basic sciences
    - clinical medicine
    - population medicine
      - community medicine
      - preventative medicine
      - public health

NURS 306

- Clinical Medicine
  - care of individuals
  - sick people present themselves for treatment
- Population Medicine
  - community rather than individual patient is the focus
  - need to evaluate the health of a defined community
  - many who may benefit from but do not seek medical care

NURS 306

- An Example:
  - Tuberculosis
    - basis science is concerned with the tubercle bacillus
      - structure, growth, resistance to antibiotics
    - clinical medicine revolves around
      - diagnostic testing, extent/stage of the disease, choice of therapy, adequate patient follow-up

NURS 306

- Population Medicine
  - Tuberculosis approached as a community problem
    - high occurrence in susceptible groups: HIV+, infants, alcoholics
    - need to follow-up with household contacts of cases
    - assurance that chemotherapy is continued for an adequate period
      - costs
      - burden - inpatient vs outpatient
      - family support - cultural attitudes
  - Systematic way of studying the patterns of disease and the patterns of medical care delivery

NURS 306

- Health and Disease
  - usually defined in terms of disease
  - health is a relatively illusive concept
  - WHO (1948)
    - Health is a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity.

NURS 306

- Rates
  - basic epidemiologic measure of health and disease
    - relates cases or events to a defined population
    - Rate=events,cases,deaths/ population for a given time period
      - those in the denominator must be at risk of appearing in the numerator
    - eg.12 deaths/100,000 farm population per year from work related agricultural injuries
    - Looking at just the number of events or cases can be misleading

NURS 306

For example:

	Cars		Private Planes	
Fatalities per year	1000		50	
Number exposed	100,000		1,000	
Rate of fatal injury	$\frac{1,000}{100,000}$	=0.01	$\frac{50}{1,000}$	=0.05
	10/1000		50/1000	

NURS 306

- Natural History of Disease
  - development of disease
    - irregular and/or evolving
    - label of diseased or not diseased may be arbitrary
  - course of disease over time
    - chronic disease may have several stages
    - each disease will have its own distinct course

NURS 306

- Stages of Disease
  - Susceptibility
    - groundwork laid prior to development of disease
  - Pre-symptomatic
    - no signs or symptoms
    - changes to the disease state have started to occur
  - Clinical
    - recognizable signs and symptoms of disease
    - therapeutic classification of the disease

NURS 306

- Stages of Disease
  - Disability
    - post disease
    - disease has run its course
    - or has been successfully treated
    - usually defined by functional activities that can be performed
      - varies between individuals with like impairment

NURS 306

- Levels of Prevention
  - In general this means inhibiting the disease process before is it occurs
  - Primary
    - Health promotion
      - provision of healthy living conditions
      - health education
    - Protective measures
      - immunization
      - sanitation
      - occupational health standards

NURS 306

- Secondary
  - early detection of disease
  - prompt treatment
- Tertiary
  - minimizing disability
  - maximize individual's residual capacity
  - emphasis on remaining ability versus limitations

NURS 306

- Application of prevention and natural history - stroke
  - stroke - neurological deficit lasting at least 24 hours which results from damage to the brain by altered blood supply
    - effects variable
    - impairment of speech and/or paralysis
    - a leading cause of death in Canada

NURS 306

- Epidemiology has contributed to the understanding of the natural history of stroke
  - not a random event
  - risk factors developed early in life linked to future stroke
  - several populations followed over a number of years have provided information on these factors
  - eg. Hypertension, cardiac impairment

NURS 306

- Identification of high blood pressure
  - led to a series of intervention trials
    - reduced BP resulted in lower mortality in intervention groups
    - these interventions as well as health promotion campaigns have resulted in a gradual decline in mortality due to stroke in the past 30 years

NURS 306

- Scope of Epidemiology
  - early epidemiology was largely concerned with infectious disease
  - epidemiologic methods are now applied to all diseases, conditions, and health related events

NURS 306

- Epidemic versus Endemic Disease
- Endemic - the constant presence of a disease or infectious agent within a population - prevalence of disease
- Epidemic - the occurrence in a population of an illness that is clearly in excess of normal expectancy

NURS 306

- Epidemic
  - may include any kind of disease or injury
  - no general rule on the number of cases
  - no specific geographic extent
  - no specific time period eg.food poisoning to drug addiction
  - epidemics that run over a number of years may be considered endemic

NURS 306

- Multiple Causation of Disease
  - humans are considered the host organism
  - humans interact with a variety of organisms and agents in an ecological system
  - many diseases require more than one factor to be present
  - Multi -factorial etiology or multiple causation
  - organism is not exclusively causal
    - necessary but often not sufficient
    - host and environmental conditions also necessary

NURS 306

- Host Factors
  - genetic endowment
    - blood type and ulcers
  - specific immunity
    - measles, chicken pox
  - personality
    - type A versus type B

NURS 306

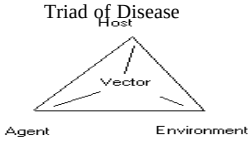
- Extrinsic Factors (environmental)
  - biological environment
    - infectious disease agents
    - reservoirs of infection
    - vectors that transmit disease
    - plants and animals (sources of food and medication)
  - social environment
    - economics
    - politics
    - social integration
    - social customs
    - family

NURS 306

- Physical environment
  - heat
  - light
  - air
  - water
  - radiation
  - chemical agents
  - etc.

NURS 306

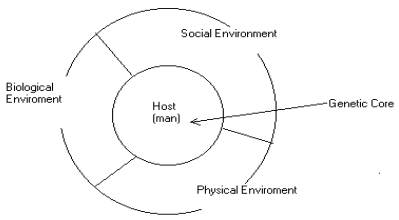
Triad of Disease



- Interrelations of factors
  - balance of forces that determines a person's health state
  - epidemiologic triangle
  - change in any factor can alter the equilibrium
  - not a good model for diseases not linked to a specific agent
    - eg: lifestyle related disease

NURS 306

More Modern View



NURS 306

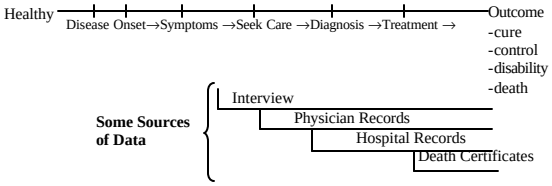
- Who
  - Characteristics of the human host
    - Age
    - Gender
    - Race
- When
  - Periodicity of the disease
    - Seasonal
    - Event related
- Where
  - Not randomly distributed by geography
    - Often related to disease vectors
      - Hanta virus, rabies
    - Related to the environment

NURS 306

- Objectives
  - Describe measures of morbidity
  - Discuss problems of measuring morbidity
  - Describe measures of mortality
  - Discuss problems of measuring mortality
  - Describe methods of comparing mortality in different populations

HSSC 601

- Natural History of Diseases



HSSC 601

- Definition
  - Epidemic
    - any increase in incidence of a particular condition in excess of what is normally expected, also known as epizootic in animals

HSSC 601

- Definition
  - Endemic
    - disease, condition, or health-related behaviours that are constantly present in a human population e.g. common cold, asthma

HSSC 601

- Definition
  - Pandemics
    - widespread epidemics, cover a large geographic area eg.AIDS, malaria, influenza

HSSC 601

- Rate vs. Ration vs. Proportion
  - Rate
    - are those measures of disease occurrence that include time in the denominator (e.g.: incidence)
  - Ratio
    - a fraction in which the numerator is not necessarily a subset of the denominator
  - Proportion
    - a fraction in which the numerator contains a subset of the individuals contained in the denominator

HSSC 601

- Measures of Morbidity
  - Incidence per 1,000=

$$\frac{\text{No. of new cases of a disease occurring in the population during a specified time period}}{\text{No. of persons in the population at that specified time}} \times 1000$$

HSSC 601

- Incidence
  - **NEW** cases of disease
  - Arbitrary choice of per/denominator e.g. cases/1000, cases/10,000 etc.
  - Measure of risk
    - Transition from well to diseased state
  - Can be sub-divided by group
    - Sex, occupational status, age etc.
  - Denominator
    - Persons at risk of developing disease
  - Time is included in the denominator
    - 1 week, 1 month, 1 year for group comprising the denominator
      - Cumulative incidence
      - Incidence density – cumulative observation for different observation periods

HSSC 601

- Measures of Morbidity
  - Prevalence=

$$\frac{\text{No. of cases of a disease present in the population during a specified time period}}{\text{No. of persons in the population at that specified time}} \times 1000$$

HSSC 601

- Prevalence
  - Slice through the population at a point in time to count how many of the disease
  - Does not take into account the duration of the disease
  - Point prevalence
    - Disease present at a point in time
    - Disease present in a certain time period
  - Not a measurement of risk
    - Different durations of disease
      - No clear measurement point as with incidence (new cases)

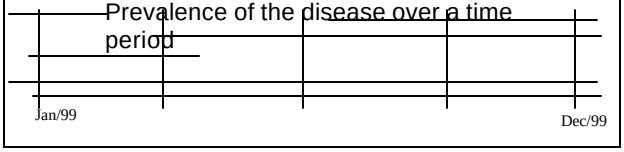
HSSC 601

- Examples of Point and Period Prevalence

Interview Question	**Type of Measure**
Do you currently have asthma?	-Point Prevalence
Have you had asthma during the last (n) years?	-Period Prevalence
Have you ever had asthma?	-Cumulative or lifetime incidence

HSSC 601

- Point Prevalence
  - prevalence of the disease at a point in time.
- Incidence
  - New cases in time period
- Period Prevalence
  - Prevalence of the disease over a time period



HSSC 601
Factors influencing prevalence

- Increased by:
  - longer duration
  - prolongation of life
  - increase in new cases
  - out-migration of healthy persons
- Decreased by:
  - shorter duration
  - high case-fatality
  - decrease in new cases
  - in-migration of healthy persons

HSSC 601

- The relationship of prevalence to incidence
  - Prevalence= incidence * duration of disease
  - Example
    - Tuberculosis
      - Screen 1000 people in the suburbs and 1000 people in the inner city
        - » Point prevalence in both is 100 cases/1000 pop.
        - » However:
        - » In the suburbs there are 4 new cases per year that live 25 years each
        - » In the inner city there 25 new cases per year that live 4 years
        - » Therefore the prevalence could be the same with dramatically different incidence

HSSC 601

- Problems with measuring morbidity
  - definition of who has the disease
  - case finding
    - available cases or
    - special study
  - hospital data
    - admission policies
    - records are for administrative purposes
    - diagnostic quality/coding
    - denominator - catchment area

HSSC 601

- Other problems
  - undercounting of population
  - classification of various groups
    - Aboriginal status
    - farm worker
  - denominator eligibility

HSSC 601

- Sources of Morbidity Data
  - Disease registries
  - Public/Private insurance plans
    - Provincial hospital data
    - Physician claims
    - Drug plans
    - Life insurance
  - Hospitals and clinics
  - Work records (absenteeism or employee health)
  - Population health surveys
    - Cancer, injury, general health

HSSC 601

- Possible Sources of Error in Health Surveys
  - Persons may be unaware that they have a disease
    - Asymptomatic or non-recognition
  - Misunderstanding of the diagnosis
  - Accuracy of the recall of health events
    - Confusion regarding specific events
    - Time frame covered by the interview
  - Interviewer error
    - Data transcribing
    - Probing
    - Incorrect posing of questions
  - Selection bias
    - e.g. poor response by young single males

HSSC 601

- Limitations of Hospital Data
  - Selectivity of admission
    - Personal characteristics
    - Severity of the disease
    - Associated conditions
    - Admission policies
  - Records not designed for research
    - Incomplete, illegible, missing
    - Variable diagnostic quality
  - Population at risk is generally not well defined

HSSC 601

- Measures of Mortality
  - crude mortality rates
  - specific mortality rates: age, cause, gender, etc.
  - case fatality rates
  - proportionate mortality
  - standardised mortality ratio (SMR)
  - adjusted rates: direct, indirect
  - years of potential life lost (YPLL)

HSSC 601

- Why look at mortality data?
  - Least expensive method of surveillance
  - Provides information on changing health care needs
  - Provides clues for changes in patterns of disease occurrence
    - Mortality data is an appropriate indicator of disease risk only when:
      - the case fatality rate is high (rabies), and
      - the duration of the disease is short (pancreatic cancer)

HSSC 601

- Sources of Mortality Data
  - medical examiners
  - death certificates
  - Immediate cause: rupture of myocardium
    - due to: myocardial infarction
    - due to: ischemic heart disease
    - other significant conditions: COPD, Diabetes
  - Problems
    - changes in disease definition over time
    - actual cause vs. other disease presence
    - case and denominator definitions

HSSC 601

- Reported Causes of Death
  - A mother died in infancy
  - Deceased had never been fatally sick
  - Died suddenly, nothing serious
  - Went to bed feeling well, but woke up dead
  - Died suddenly, without the aid of a physician

HSSC 601

- Annual Mortality Rate

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

Usually expressed at per 1,000

HSSC 601

- Age-specific mortality rate

$$\frac{\text{No. of deaths from all causes in 1 yr. in children under the age of 10}}{\text{No. of children in the population under age 10 yrs. at midyear}}$$

HSSC 601

- Cause specific rate

$$\frac{\text{No. of deaths from lung cancer per year}}{\text{No. of persons in the population at midyear}}$$

HSSC 601

- Case-fatality rates (percent)*

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

*(x100)

HSSC 601

- Proportionate mortality

$$\frac{\text{No. of deaths from cardiovascular disease in '98}}{\text{Total deaths in '98}}$$

HSSC 601

- Years of Potential Life Lost (YPLL)
  - All causes
  - Injuries*
  - Cancers
  - Suicide/Homicide
  - Heart Disease
  - Congenital Anomalies
  - AIDS

HSSC 601

- Adjustment of death rates
  - Direct age adjustments
    - Standard population is applied to two or more different populations to allow comparison

HSSC 601

- Comparison of total death rates in a population at two different time periods

Early Period			Later Period		
Population	**No. of Deaths**	**Death Rate per 100,000**	**Population**	**No. of Deaths**	**Death Rate per 100,000**
900,000	862	96	900,000	1,130	126

HSSC 601

Comparison of age-specific death rates at two different time periods

	Early Period			Later Period		
Age Group	**Population**	**No. of Deaths**	**Death Rate per 100,000**	**Population**	**No. of Deaths**	**Death Rate 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

HSSC 601

Age Group	Standard Population	"Early" Rate per 100,000	Expected No. of Deaths Using "Early" Rate	"Later" Rate per 100,000	Expected No. of Deaths Using "Later" Rate
All	1,800,00				
30-49	800,000	12	96	10	80
50-69	700,000	132	924	100	700
70+	300,000	406	1,238	350	1,050
Total no. of deaths expected			2,238		1,830

Age Adjusted Rates

"Early" = 2,238/1,800,000 = 124.3
"Later" = 1,830/1,800,000 = 101.7

HSSC 601

- Adjustment of death rates
  - Standardized mortality ratios

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

HSSC 601

Age	Est. Pop. of Miners	Death Rate (per 100,000) – Males General Pop.	Expected Deaths	Observed Deaths
	(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	42,494	75.23	31.96	112
Totals			181.09	436

HSSC 601

Standardized Mortality Ratio (SMR)

= Observed Deaths/Expected Deaths

= 436/181.09 * 100 = 241

Over 100 indicates excess in mortality

Less than 100 indicates less death than expected

HSSC 601

- Quality of Life
  - Quality Adjusted Life Years
  - Disability Adjusted Life Years
  - Major challenge here is differences in response on quality of life measures by race, education, culture, religious values etc.

NURS 306

- Assessing the Validity and Reliability of Diagnostic and Screening Tests
  - Objectives
    - Define Sensitivity and Specificity
    - Define Predictive Value
    - Discuss Reliability of Tests

- Biologic Variation
  - Tests are used to distinguish between individuals
    - diagnosing disease when symptoms present
    - screening of populations for early intervention
  - Distribution of test results
    - bi or poly-modal
    - unimodal
      - no obvious cutoff to delineate well from healthy
      - large gray area between extreme values

- Validity
  - the ability of the test to distinguish between who has the disease and who does not
- Sensitivity
  - the ability of the test to identify correctly those who have the disease
- Specificity
  - the ability of the test to identify correctly those who do not have the disease

- Sensitivity

Test Results	**Population**	
	With Disease	Without Disease
Positive	Have disease and have positive test = true positive (**TP**)	No disease but have positive test = false positive (**FP**)
Negative	Have disease but have negative test = false negative (**FN**)	No disease and have negative test = true negative (**TN**)

$$\text{Sensitivity} = \frac{TP}{TP + FN}$$

- Sensitivity

Test Results	Population: With Disease	Population: Without Disease	
Positive	80	100	180
Negative	20	800	820
	100	900	

$$\text{Sensitivity} = \frac{80}{100} = 80\%$$

- Specificity

Test Results	Population: With Disease	Population: Without Disease
Positive	Have disease and have positive test = true positive (**TP**)	No disease but have positive test = false positive (**FP**)
Negative	Have disease but have negative test = false negative (**FN**)	No disease and have negative test = true negative (**TN**)

$$\text{Specificity} = \frac{TN}{TN + FP}$$

- Specificity

Test Results	Population: With Disease	Population: Without Disease	
Positive	80	100	180
Negative	20	800	820
	100	900	

$$\text{Specificity} = \frac{800}{900} = 89\%$$

- Assessment of Tests
  - must compare results with “gold standard”
    - biopsy results, death etc.
    - often more invasive and/or expensive
  - would like all results to be true positives or true negatives
    - this rarely happens
    - consequences of false positives and false negatives need to be considered

- False positives
  - burden on health system with further work-up
  - labeling of people with disease status
    - assume sick role
    - may be denied insurance
- False negatives
  - may not receive treatment in time
    - depends on nature and severity of disease
    - effectiveness of available treatments
      - » greater effectiveness if early intervention in many cases

- For tests of continuous variables (unimodal distribution)
  - Cut-points must be chosen to determine disease status
    - importance of false positives
      - emotional and financial costs
    - importance of false negatives
      - serious disease may be missed at an early stage

Higher Cut-points $\rightarrow \downarrow$sensitivity $\uparrow$specificity

Lower Cut-points $\rightarrow \uparrow$sensitivity $\downarrow$specificity

- Two stage screening
  - less expensive, less invasive, or less uncomfortable test is carried out first
  - positives are then given a more expensive or invasive test
    - often with better sensitivity and/or specificity
  - ↑ net sensitivity and/or ↑ net specificity

- Predictive Value of a Test
  - Positive Predictive Value
    - what proportion of patients who test positive actually have the disease
  - Negative Predictive Value
    - what proportion of patients who test negative actually do not have the disease

- Positive Predictive Value

Test Results	**Population**	
	With Disease	Without Disease
Positive	Have disease and have positive test = true positive (**TP**)	No disease but have positive test = false positive (**FP**)
Negative	Have disease but have negative test = false negative (**FN**)	No disease and have negative test = true negative (**TN**)

$$\text{Positive Predictive Value} = \frac{TP}{TP + FP}$$

- Positive Predictive Value

Test Results	Population: With Disease	Population: Without Disease	
Positive	80	100	180
Negative	20	800	820
	100	900	

$$\text{Positive Predictive Value} = \frac{80}{180} = 44\%$$

- Negative Predictive Value

Test Results	Population: With Disease	Population: Without Disease
Positive	Have disease and have positive test = true positive (**TP**)	No disease but have positive test = false positive (**FP**)
Negative	Have disease but have negative test = false negative (**FN**)	No disease and have negative test = true negative (**TN**)

$$\text{Negative Predictive Value} = \frac{TN}{FN + TN}$$

- Negative Predictive Value

Test Results	Population: With Disease	Population: Without Disease	
Positive	80	100	180
Negative	20	800	820
	100	900	

$$\text{Negative Predictive Value} = \frac{800}{820} = 98\%$$

- Population Prevalence and Predictive Value
  - higher prevalence of disease generally leads to greater positive predictive value of a test
  - screening the general population for a rare disease can be wasteful
    - high risk subsets can be identified
    - age, genetic background, gender
    - general practice vs. tertiary specialist

- 1% Population Prevalence

Test Results	**Population**		
	With Disease	Without Disease	
Positive	99	495	594
Negative	1	9405	9406
	100	9900	

$$\text{Positive Predictive Value} = \frac{99}{594} = 17\%$$

- 5% Population Prevalence

Test Results	**Population**		
	With Disease	Without Disease	
Positive	495	495	970
Negative	5	9025	9030
	500	9500	

$$\text{Positive Predictive Value} = \frac{495}{970} = 51\%$$

- Specificity and Predictive Value
  - ↑ specificity = ↑ positive predictive value
    - most individuals are not diseased
    - therefore changes to the right side of the 2x2 table will have a greater effect on test diagnostics

- Reliability of Tests
  - Are results the same if the test is repeated?
    - If not, test is pretty useless
  - Factors that effect variation between tests
    - Intra-subject
      - variation within individuals
    - Inter-observer
      - variation between those reading the tests

- Intra-subject Variation
  - time
  - setting
  - fatigue
  - motivation
  - etc.
- Inter-observer Variation
  - training
  - experience
  - time spent doing test
  - etc.

- Measures of Reliability between Observers/Raters
  - Overall percent agreement
    - for cells where raters agree
      - may over estimate because there will be much agreement from large numbers of negative tests
    - for only cells where raters agree on positive tests
    - neither of these factor in chance
  - Kappa Statistic
    - factors in chance agreement
    - =(percent observed agreement-percent agreement by chance alone)/(100%-percent agreement by chance alone)

Pathologist B	**Pathologist A** Positive	Negative	
Positive	41	3	44
Negative	4	27	31
	45	30	75

Percent Agreement = [(a+d)/(a+b+c+d)]*100
= [(41+27)/(41+3+4+27)]*100
= (68/75)*100
= 90.7%

Pathologist B	**Pathologist A** Positive	Negative	
Positive	41	3	44
Negative	4	27	31
	45	30	75

Percent Agreement = [a/(a+b+c)]*100
(disregarding negatives) = [41/(41+3+4)]*100
= (41/48)*100
= 85.4%

Pathologist B	Pathologist A: Positive	Pathologist A: Negative	
Positive	41(26.4)	3(17.6)	
Negative	4(18.6)	27(12.4)	44
	45	30	31 / 75

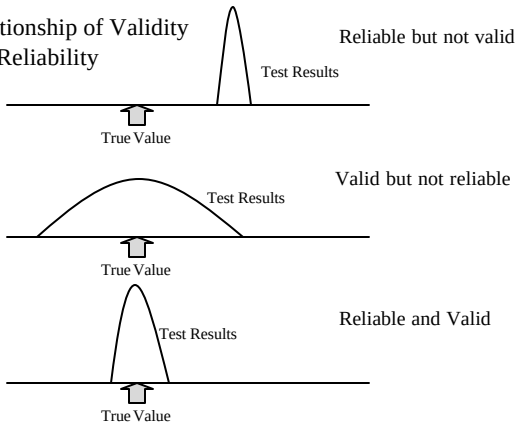
Percent Agreement by Chance
=[(26.4+12.4)/75]*100
=51.7%

Kappa Statistic
=(percent observed agreement-percent agreement by chance alone)/(100%-percent agreement by chance alone)

Kappa Statistic
=(90.1%-51.7%)/(100%-51.7%)
=39%/48.3
=.81

Interpretation
.75 or greater – excellent agreement
.40 to .75 – intermediate to good agreement
less than .40 – poor agreement

Relationship of Validity and Reliability

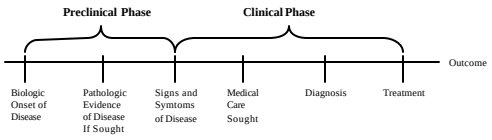


NURS 306

- Prognosis
  - natural history of disease
  - define prognosis
  - lead time bias
  - life tables

- Natural History of Disease
  - needs to be quantified
    - severity needs to be described
      - establish priorities
        - » clinical services
        - » public health programs
    - patients need to know
    - baseline for new treatments
      - expected outcomes vs. new treatment
      - compared effectiveness of different treatments

- Natural History of Disease



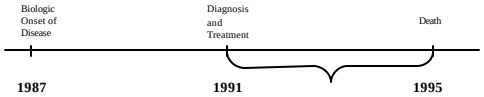
- Questions
  - At what point do we begin to quantify survival time?
    - Biologic onset
      - not usually known or measurable
      - symptoms?
        - » Somewhat subjective
    - Usually use diagnosis as start point
      - can differ as individuals seek care differently
      - people who die prior to diagnosis aren't counted

- Case-fatality Rate
  - Given that a person has the disease, what is the likelihood of death
  - no explicit statement of time
  - used for acute disease of short duration that results in death shortly after diagnosis
  - not good for chronic disease

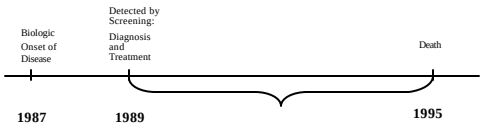
$$\frac{\text{No. of people who die of a disease}}{\text{No. of people who have the disease}}$$

- Five Year Survival
  - frequently employed in clinical medicine
  - percent of patients alive after 5 years of diagnosis or treatment
  - derived from cancer statistics
    - most deaths occur during this period
  - lead time bias as a result of screening

- Lead Time Bias



- Lead Time Bias



- Lead Time Bias
  - extra time in the diseased state
  - no extra life
  - extra medical care, but no better outcome
  - important in the evaluation of screening programs
    - determine if screening is actually beneficial

- Observed Survival
  - 5 year survival rate
  - commonly used in cancer studies
  - measure of successful treatment to survive 5 years
  - calculate the probability of survival at 5 years for a given disease and/or treatment

		No. Alive on Anniversary of Treatment				
Year of Treatment	No. of Patients Treated	1991	1992	1993	1994	1995
1990	84	44	21	13	10	8
1991	62		31	14	10	6
1992	93			50	20	13
1993	60				29	16
1994	76					43

8/84 = .095(9.5%)

		No. Alive at End of Year				
Year of Treatment	No. of Patients Treated	1st Year	2nd Year	3rd Year	4th Year	5th Year
1990	84	44	21	13	10	8
1991	62	31	14	10	6	
1992	93	50	20	13		
1993	60	29	16			
1994	76	43				

Year of Treatment	No. of Patients Treated	No. Alive at End of Year				
		1st Year	2nd Year	3rd Year	4th Year	5th Year
1990	84	44	21	13	10	8
1991	62	31	14	10	6	
1992	93	50	20	13		
1993	60	29	16			
1994	76	43				
Total	375	197				

Prob. Surviving the First Year = 197/375 = .65

Year of Treatment	No. of Patients Treated	No. Alive at End of Year				
		1st Year	2nd Year	3rd Year	4th Year	5th Year
1990	84	44	21	13	10	8
1991	62	31	14	10	6	
1992	93	50	20	13		
1993	60	29	16			
1994	76	43				
Total		197	71			

Prob. Surviving the 2nd Year = 71/(197-43) = .46

Year of Treatment	No. of Patients Treated	No. Alive at End of Year				
		1st Year	2nd Year	3rd Year	4th Year	5th Year
1990	84	44	21	13	10	8
1991	62	31	14	10	6	
1992	93	50	20	13		
1993	60	29	16			
1994	76	43				
Total		197	71	36		

Prob. Surviving the 3rd Year = 36/(71-16) = .65

Year of Treatment	No. of Patients Treated	No. Alive at End of Year				
		1st Year	2nd Year	3rd Year	4th Year	5th Year
1990	84	44	21	13	10	8
1991	62	31	14	10	6	
1992	93	50	20	13		
1993	60	29	16			
1994	76	43				
Total				36	16	

Prob. Surviving the 4th Year = 16/(36-13) = .70

Year of Treatment	No. of Patients Treated	No. Alive at End of Year				
		1st Year	2nd Year	3rd Year	4th Year	5th Year
1990	84	44	21	13	10	8
1991	62	31	14	10	6	
1992	93	50	20	13		
1993	60	29	16			
1994	76	43				
Total					16	8

Prob. Surviving the 5th Year = 8/(16-6) = .80

Probability of Survival for Each Year of the Study

- P1 = Probability of surviving the first year = **197/375 = 0.52 = 52%**
- P2 = Probability of surviving the second year given survival to the end of the first year = **71/(197-43) = 0.46 = 46%**
- P3 = Probability of surviving the third year given survival to the end of the second year = **36/(71-16) = 0.65 = 65%**
- P4 = Probability of surviving the fourth year given survival to the end of the third year = **16/(36-13) = 0.70 = 70%**
- P5 = Probability of surviving the fifth year given survival to the end of the fourth year = **8/(16-6) = 0.80 = 80%**

- What is the probability of surviving 5 years after beginning treatment?
- = P1*P2*P3*P4*P5
- =.52*.46*.65*.70*.80
- **=.088 or 8.8%**

- Assumptions
  - no change in the effectiveness of treatment during the study period
    - over many years this is likely not valid
    - treatments improve over time
  - persons who are lost to follow-up have the same experience of those followed
    - die and not traced
    - seek care elsewhere
    - move
    - get better

- Survival Curves
  - illustrate different survival experiences
    - between populations
    - between treatment groups

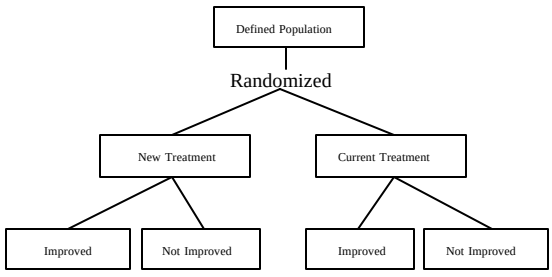
- Other Measures
  - Median survival time
    - length of time half the population survives
      - less affected by extreme values than mean value
      - only have to track the deaths of half the group rather than all survival times
  - Relative Survival Rate
    - comparison of observed rate to relative rate if disease were absent

- Generalizability
  - depends on the population in the study
    - primary vs. tertiary care
    - community vs. hospital population
    - generalist vs. specialist
    - clinic vs. population based
  - examine selection criteria for patients included in the study and compare that to your population

NURS 306 - Randomized Trials

- Objective in public health and clinical practice is to modify the natural history of disease
- selection of best possible treatment or intervention
- randomized trials are the gold standard for establishing the effectiveness of new therapies and interventions

- Basic Design of Randomized Trial



- Ambroise Paré - surgeon
  - 1537 – unplanned trial
    - Treatment of war wounds by cauterization with oil
      - Ran out of oil for numerous injury
      - Used a mix of egg yolks, oil of roses, and turpentine
        - » Improved patient outcome
- James Lind - physician
  - 1747 – planned trial
    - Treatment of scurvy
      - 12 patients
        - » 2 given cider, 2 given elixir vitriol, 2 given vinegar, 2 given sea water, 2 given nutmeg, 2 given lemons and oranges

- Uses of randomized trials
  - evaluation of new drugs
  - new technology
  - community trials (health promotion)
  - evaluation of screening programs
  - delivery of health services

- Selection of Subjects
  - criteria must be pre-determined
  - precise definition of who comprises the study population
  - no subjective decision making by the investigator for who is in or out of the study
  - procedures for subject selection needs to be reproducible by others

- Alternatives to Randomization
  - no comparison group
    - problems with inferring causal relationship
    - patients may get better naturally
    - cannot clearly attribute improvement to the treatment
  - historical controls
    - records of patients treated prior to intervention
      - data may be of poor quality
      - necessary outcomes have not been measured
    - concomitant changes over time
      - healthier lifestyles
      - other therapies may be developed
    - may work well for fatal diseases

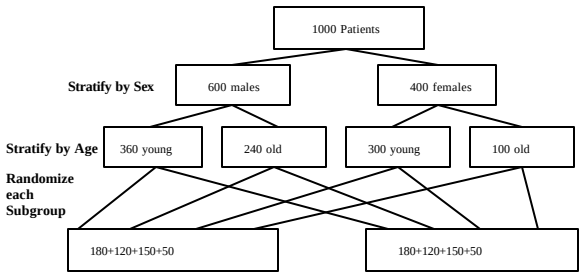
- Non-equivalent Comparison Groups
  - may not be of similar composition as treatment group
  - systematic bias may occur in the selection of controls
  - clinicians may mess with who is getting the treatment
    - Predictability of patient allocation

- Randomization
  - best approach to study design
  - random chance of receiving or not receiving the treatment under investigation
    - random numbers table
    - computer generation
    - coin flipping
    - often patients are group assigned a priori
  - clinicians may have ethical issues with with-holding treatment

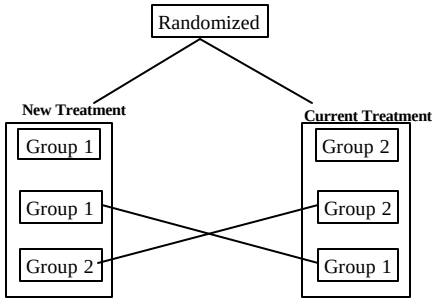
- What Does Randomization Achieve
  - no subjective bias of investigators
    - overt or covert
  - hope that groups will be comparable on various characteristics
    - variables we can measure
    - unknown/non-measurable variables that impact treatment
      - genetics
      - immune status
      - other stuff we simply don't know about

- Stratified Randomization
  - used to ensure that groups are comparable on a few characteristics
    - age
    - gender
    - tumor type
    - etc.

- Stratified Randomization



Planned Crossover Design



- Cross-over trial
  - Patient serves as their own control
  - Smaller sample needed
  - Issues
    - Carryover/washout
    - Order of the therapies may elicit differential response from patients
      - Enthusiasm may diminish over time

- Blinding
  - Subjects do not know the treatment they are getting
    - not always possible
    - use of placebo
  - Double blinding
    - investigators/clinicians do not know treatment group
    - if not possible outcomes should be assessed by someone who does not know treatment status

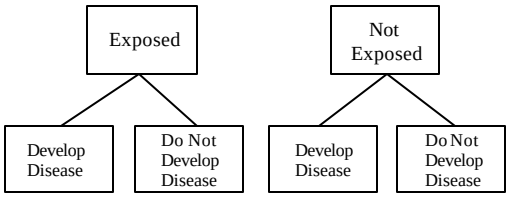
- Non-Compliance
  - refuse to comply with treatment
    - drop-outs
    - poor compliance
  - contamination
    - persons who get the treatment in the control group
    - other medications, desire for better outcomes
  - to measure effectiveness, it is important to test treatment among those who comply and those who do not - different health outcomes
    - efficacy vs. effectiveness

- Generalizability of Results
  - External validity
    - does the study population reflect the reference population
  - Internal validity
    - randomization worked
    - few issues with non-compliance and contamination

- Cohort Studies
- Case-Control Studies
- Cross-Sectional Studies
- Estimating Risk

- Cohort Studies
  - also called prospective studies
  - selection of a group of exposed and unexposed persons
    - persons using and not using a needle exchange program
    - persons exposed and not exposed to exercise at work
    - persons exposed to mine coal dust and workers who are not
  - if there is an association between the exposure and the disease we would expect more disease in the exposed group (higher incidence)

- Basic design of a cohort study



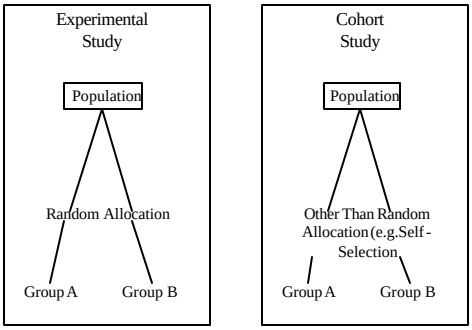
- Design (using a 2 x 2 table)

		Then Follow to See Whether			
		Disease Develops	Disease Does Not Develop	Totals	Incidence Rates of Disease
First Select	Exposed	a	b	a + b	$\frac{a}{a+b}$
	Not Exposed	c	d	c + d	$\frac{c}{c+d}$

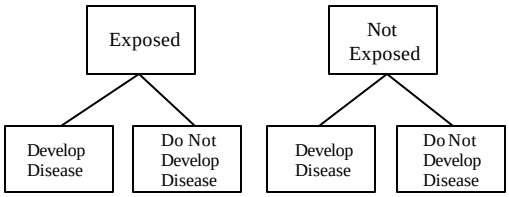
- For Example: Smoking and CHD

		Then Follow to See Whether			
		Disease Develops	Disease Does Not Develop	Totals	Incidence Rates of Disease
First Select	Smokes	84	2,916	3,000	28.0
	Non-Smoker	87	4,913	5,000	17.4

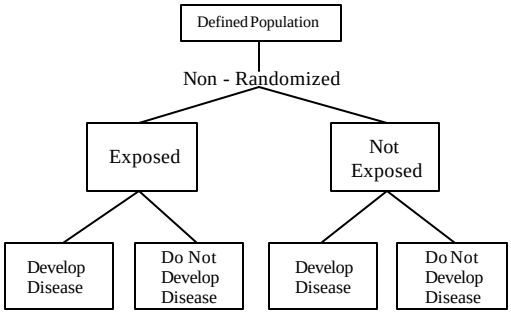
- Comparing Cohort Studies With Randomized Trials
  - both studies compare exposed and unexposed
  - cannot used randomized trials to measure effects of exposure in all situations
    - harmful substances
  - cohort studies are used in many studies of toxic agents
  - unclear in cohort studies whether it is the exposure or what led persons to be exposed that has caused the association with disease



- Selection of Study Populations
  - Select groups based on exposure status
    - e.g. occupational groups



- Selection of Study Populations
  - Defined Population

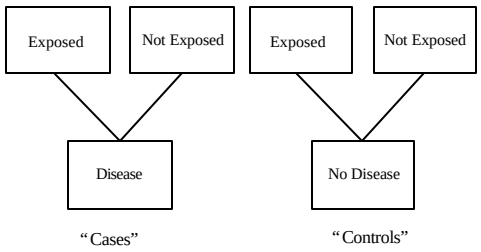


- Types of Cohort Studies
  - prospective or longitudinal
    - groups/population are followed forward through time
      - expensive
      - may take many years until outcome of interest is reached
      - subjects outlive the investigator
  - retrospective or historical
    - use data from the past to shorten length of follow-up
      - outcome is determined as study is started
      - exposure is measured through past records
      - often used with military personnel
      - school populations

- Potential Problems with Cohort Studies
  - assessment of outcome
    - should be blinded if possible
  - quality of information may differ between exposed and unexposed persons
  - losses to follow-up
    - people move, die, withdraw from study
  - non-response
    - systematic bias in who participates in the study
  - analytic bias
    - strong feelings about study hypotheses may introduce bias in the data analysis

- Indications that a Cohort Study is Appropriate
  - prior evidence suggests that the exposure is related to the disease
  - short time between exposure and disease
  - reasonably frequent outcome of interest

- Case Control Study
  - design



- Design (using 2x2 table)

		First, Select:	
		Cases (disease)	Controls (no disease)
Then, Measure Past Exposure:	Were exposed	a	b
	Were not exposed	c	d
	Total	a + c	b + d
	Proportions exposed	$\frac{a}{a+c}$	$\frac{b}{b+d}$

- For Example: Smoking and CHD

	CHD	Controls
Smokes	112	176
Non-Smoker	88	224
Total	200	400
% Smoking	56%	44%

- Case-Control Studies
  - begins with people with disease
  - compares diseased persons (cases) to non-diseased persons (controls)

- Selection of Cases
  - many sources
    - hospital records
      - generalizability is an issue
      - characteristics of the hospital may affect risk factors
    - physician offices
    - disease registries
    - incident cases
      - harder to accumulate but are likely more valid
    - prevalent cases
      - factors may be related more to survival with the disease than the development of the disease
    - cases who have died before diagnosis are not included

- Selection of Cases
  - challenging problem
  - selection of controls can affect the study results
    - may lead to incorrect conclusions
  - reference population for cases may be difficult to define
  - careful study design is necessary to eliminate any systematic selection of controls that will influence study results

- Non-hospitalized controls
  - neighborhood controls
    - many persons no longer will answer their doors
  - random digit dialing
    - can be used only where most people have phones
    - if you are using a specific selection criteria, it may be costly and time consuming
  - best friend controls
    - similar to cases in socio-demographic characteristics and age
    - sibling controls - genetic similarity

- Hospitalized Persons as Controls
  - captive population who can easily be identified
  - are usually not representative of general population
  - referral patterns to a hospital may differ depending on clinical specialties
  - selection of controls by diagnosis can be difficult

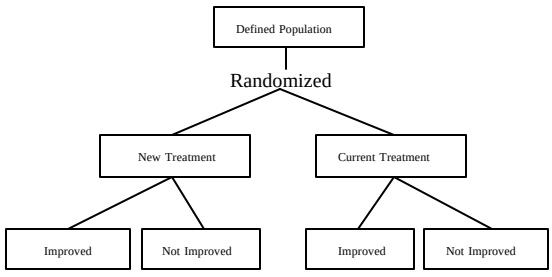
- Matching of Cases and Controls
  - removes the effect of potentially confounding variables
    - eg. Age, gender, race, socioeconomic status, etc.
  - Group Matching
    - same proportion of variable is apparent in the controls as with cases
    - eg. 25% female cases - you would select a control group that had 25% females
  - Individual Matching
    - for each case, a control is selected that is like on one or more characteristics.

- Matching
  - the more characteristics that are chosen to match on the more difficult it will be to find an appropriate control
  - you don't want to match on any factor that you want to study.
    - This eliminates your ability to analyze the data as the proportions of the factor are the same in both the cases and controls
  - control selection can result in unplanned matching - eg. Best friend controls

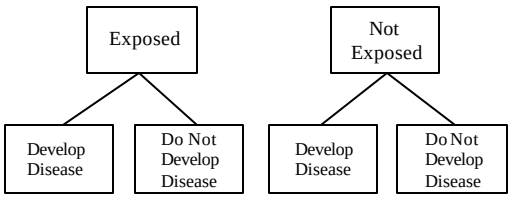
- Problems of Recall
  - Limitations of Recall
    - Individuals may not have the information needed
    - persons vary in their ability to recall information from their past
    - if no systematic difference exists between cases and controls regarding limitation of recall, there is no bias
  - Recall Bias
    - cases and controls may differ on how they remember events - differential recall
    - cases may strive to remember events that controls have totally forgotten about

- Cross-Sectional Studies
  - both disease and exposure are measured simultaneously
  - usually surveys
  - cases are prevalent cases
    - associations may be with survival rather than development of disease
  - temporal relationship is not defined between exposure and disease
  - can provide suggestive information about a factor and disease

- Randomized Trials



- Cohort Studies



- Case-Control Studies