

BIOE 301

Lecture 3:

Leading Causes of Mortality, Ages 15-44

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Review of Lecture Two: Leading Causes of Mortality, Birth-Age 4

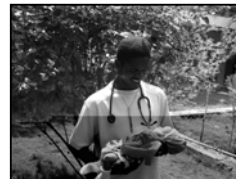
- Developing world
 1. Perinatal conditions
 2. Lower respiratory infections
 3. Diarrheal diseases
 4. Malaria
- Developed world
 1. Perinatal conditions
 2. Congenital anomalies
 3. Lower respiratory infections
 4. Unintentional injuries

1. Perinatal Conditions



- Question: What is the #1 way to prevent septicemia in a newborn in the developing world?

1. Perinatal Conditions



<http://www.path.org/projects/clean-delivery-kit.php>

2. Lower Respiratory Infections



- Question: How can a busy health worker (or a parent) *quickly* screen for pneumonia in a child?

2. Lower Respiratory Infections



3. Diarrheal Diseases

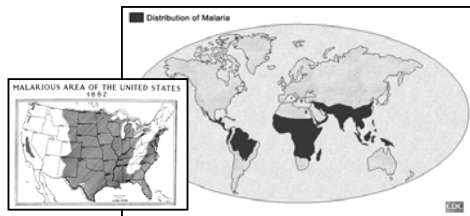


- Question: What is the #1 way to prevent diarrheal illness in a newborn?

3. Diarrheal Diseases



4. Malaria



- Question: How was malaria eradicated from the southern U.S.? What are the challenges with implementing this technology in less developed countries?

4. Malaria

- Challenges for implementing vector control technologies in developing countries
 - Mapping areas that are difficult to access
 - Poor communication
 - Direction – Transfer of vector control efforts from malaria control authorities to local primary health care center
 - Financial support – decreased standard of living from wars, environmental factors, migration
 - Corruption, graft



<http://www.cdc.gov/malaria/history/>

Leading Causes of Mortality Ages 15-44

- Developing World
 1. HIV/AIDS
 2. Unintentional injuries
 3. Cardiovascular diseases
 4. Tuberculosis
- Developed World
 1. Unintentional injuries
 2. Cardiovascular diseases
 3. Cancer
 4. Self-inflicted injuries

1. HIV/AIDS

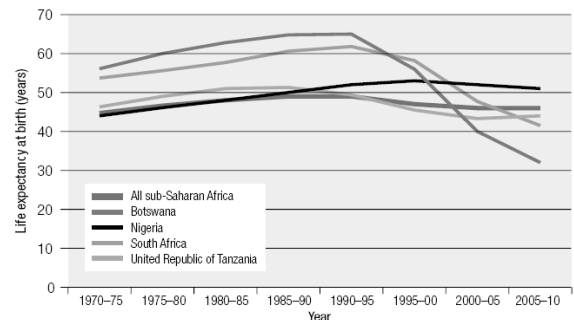
- Burden of HIV/AIDS
- Pathophysiology of HIV
- Clinical course of HIV/AIDS
- Highly Active Antiretroviral Therapy
- Prevention of Mother to Child Transmission (PMTCT)

Burden of HIV/AIDS

- Worldwide
 - 33.2 million people are living with HIV/AIDS
 - 20 million people have been killed by the disease
 - 2007:
 - 2.1 million deaths
 - 2.5 million new HIV infections
 - 17% of new infections occurred in children (<15 yrs)
 - 2/3 of those with AIDS and 3/4 of all AIDS deaths are in sub-Saharan Africa
 - 6800 new infections per day
 - 96% in low- and middle-income countries
 - 1200 children

Source: 2007 AIDS Epidemic Update, UNAIDS/WHO

AIDS has Reduced Life Expectancy



Burden of HIV/AIDS in the U.S.

- 1.2 million people have HIV/AIDS (prevalence)
- 30,000-40,000 new infections per year (incidence)
- Only 7 countries in the world have more people living with HIV than the U.S.
- Routes of transmission:
 - Unsafe sex between men (53%)
 - Unprotected heterosexual intercourse (32%)
 - Non-sterile drug injection equipment (18%)

Source: 2007 AIDS Epidemic Update, UNAIDS/WHO

Burden of HIV/AIDS in the U.S.

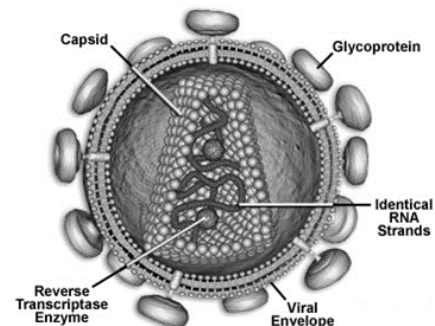
- Racial and ethnic minorities are disproportionately affected:
 - 48% of AIDS diagnoses are African-Americans (15% pop)
 - The rate of new HIV diagnoses was 21x higher in African-American women than in Caucasian women
- Women are increasingly affected:
 - The proportion of women among new HIV/AIDS diagnoses have risen from 15% to 26% in 10 years
- Question: Why is the prevalence of HIV in the U.S. continuing to increase?

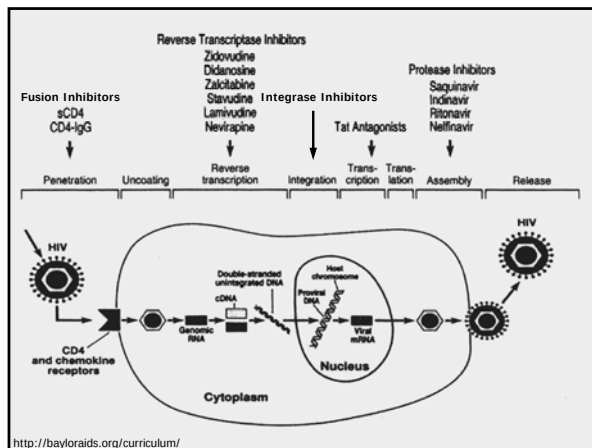
Source: 2007 AIDS Epidemic Update, UNAIDS/WHO

Burden of HIV/AIDS in the U.S.

- Anti-retroviral therapy has accounted for an 80% decrease in AIDS death rates in the last decade
- Annual cost to treat: \$15 billion

Pathophysiology of HIV/AIDS





Pathophysiology of HIV/AIDS

Table 1: Cells Susceptible to HIV Infection

System	Cell
Hematopoietic	- T-cells (CD4+ or CD8+) - Macrophages/monocytes - Dendritic cells - Fetal thymocytes and thymic epithelium - B-cells - NK cells - Megakaryocytic cells - Stem cells
Central Nervous	- Microglia - Capillary endothelial cells - Astrocytes - Oligodendrocytes
Large Intestine	Columnar epithelium
Other	- Kupfer cells (liver) - Synovial cells - Placental trophoblast cells

<http://bayloraids.org/curriculum/>

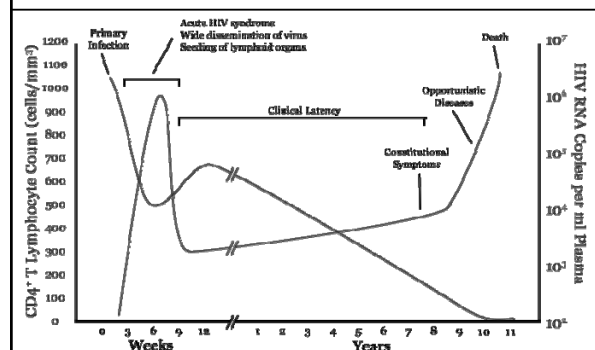
Clinical Course of HIV/AIDS

■ HIV Infection

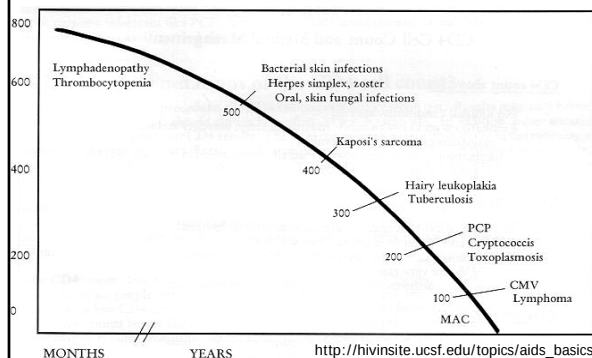
- Spread by sexual contact with infected person or sharing needles with infected person or by transmission from mother to child
- Virus deposited on mucosal surface
- Acute infection (flu like symptoms)
- Viral dissemination
- HIV-specific immune response
- Replication of virus
- Destruction of CD4+ lymphocytes
- Rate of progression is correlated with viral load

■ Latent Period

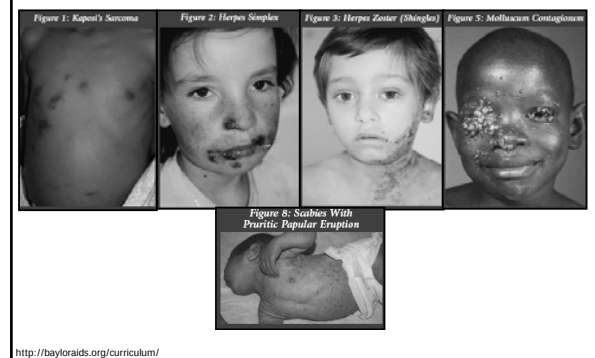
Clinical Course of HIV/AIDS



Clinical Course of HIV/AIDS



Clinical Course of HIV/AIDS



Clinical Course of HIV/AIDS

- AIDS
 - Immunologic dysregulation
 - Opportunistic infections and cancers
 - Risk of infections is correlated with number of CD4⁺ lymphocytes
 - Average patient with AIDS dies in 1-3 years
- Within 10 years of infection (w/o Rx):
 - 50% of patients develop AIDS
 - 40% develop illness associated with HIV
 - 5-10% remain asymptomatic

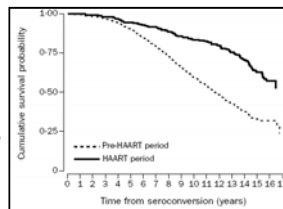
HIV/AIDS Therapy

- Reverse Transcriptase Inhibitor enzymes (1987)
 - Enzyme is specific to HIV
 - Combinations of RTIs appear effective
- HIV Protease Inhibitors (1995)
 - HIV proteases are distinct from mammalian proteases
 - Most significant advance in HIV therapy yet
- Highly Active Antiretroviral Therapy (HAART)
 - Combination of three or more drugs
- Fusion inhibitor (2003)
- Integrase inhibitor (2007)

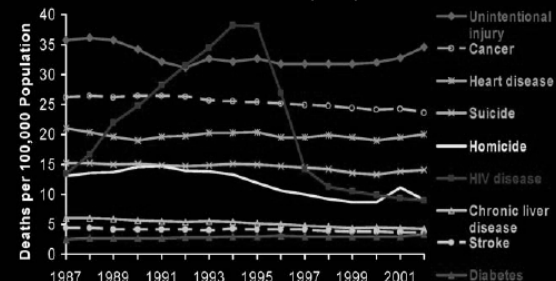


HIV/AIDS Therapy

- HIV can rapidly mutate to quickly develop resistance to a single drug
- Resistance develops much more slowly to drug combinations
- Goal of HAART:
 - Reduce viral levels to undetectable levels
 - Has reduced death rate in US and Europe by 80%



Trends in Annual Rates of Death due to the 9 Leading Causes among Persons 25-44 Years Old, USA, 1987-2002

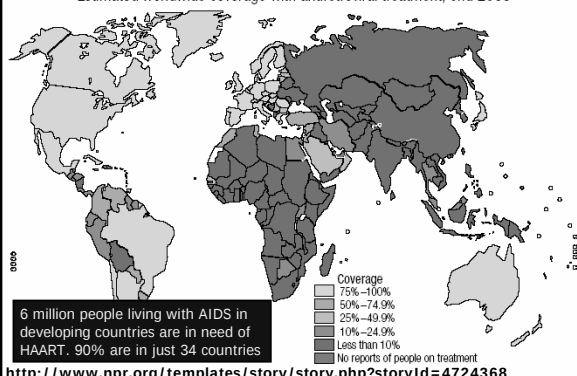


Note: For comparison with data for 1999 and later years, data for 1987-1993 were modified to account for ICD-10 rules instead of ICD-9 rules.



HIV/AIDS: THE TREATMENT GAP

Estimated worldwide coverage with antiretroviral treatment, end 2003



<http://www.npr.org/templates/story/story.php?storyId=4724368>

Prevention of Mother to Child Transmission (PMTCT)

- 3 routes of transmission:
 - Parentally (during pregnancy)
 - Perinatally (during delivery)
 - Breast feeding (through milk)
- 4 Core interventions:
 - HIV testing and counseling
 - ARV prophylaxis (ZDV, NVP)
 - Safer delivery practices
 - Safer infant-feeding practices
- Reduces transmission from 30-40% to 4-6%



2. Unintentional Injuries



2. Unintentional Injuries

- Burden of Unintentional Injuries
- Accident Physics
- Slowed Driver Reaction Time
- Prevention of Road Accidents

Burden of Unintentional Injuries

- More than 1.25 million people ages 15-44 die from unintentional injuries each year
- 1 million deaths in developing countries, 1/4 million in developed countries
- 40x this number are injured
- Major cause of disability
- Leading cause is *road accidents*:
 - 500,000 deaths per year in this age group
 - 90% of these deaths occur in developing countries

Burden of Unintentional Injuries

- Road Accidents in the U.S.
 - Rates declining steadily
 - A leading cause of potential years of life lost
 - 2006:
 - 42,642 Americans killed
 - 2,699,000 Americans injured
 - Fatal accident rates 3X higher for males than for females
 - Motorcycles: 40X higher death rate per mile traveled
 - 39% of fatalities related to alcohol use

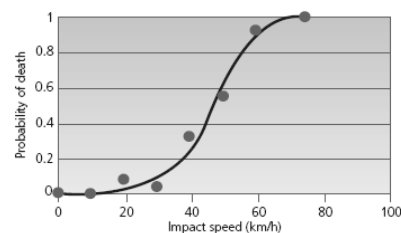
Accident Physics

- Newton's 2nd Law:
 - $F = m a$
 - $a = dv/dt$
 - $a = \text{initial velocity} / \text{time to come to rest}$
- In a crash:
 - Velocity slows to zero in a very short time
 - Generates large forces
- How can we reduce these forces?
 1. Reduce initial velocity of impact
 2. Extend time that it takes passengers to come to rest



Accident Physics

1. Reduce initial velocity of impact
 - Excessive speed contributes to:
 - 30% of deaths in developed countries
 - 50% of deaths in developing countries

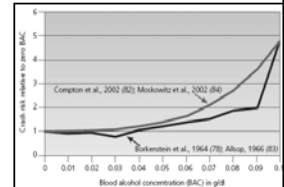


Slowed Driver Reaction Time

- When drivers anticipate a crash, they have time to brake and reduce initial velocity
- Factors which slow driver reaction time:
 - Alcohol use
 - Mobile phone use
 - Poor visibility
 - Driver inexperience

Slowed Driver Reaction Time

- Alcohol impaired drivers have 17X increased risk of being in fatal crash
- Alcohol use increases risk more in younger drivers
- 1 in 5 Americans will be involved in an alcohol-related crash at some time in their lives
- TX BAC limit:
 - 0.08+ g/dl is illegal
 - Approx 3 drinks in a 140 lb individual
 - Significant driving impairment at just 0.04 BAC!



Slowed Driver Reaction Time

- Mobile phone use:
 - At any given daylight moment in US:
 - 10% of drivers are using a cell phone
 - Increases driver reaction time by 0.5-1.5 seconds
 - Risk of crash is 4X higher when using a mobile phone
 - Same as driving with a BAC of 0.09 g/ dl
- 4 states and D.C. have banned use of hand held phones while driving (NY, NJ, CT, CA)
 - Partial bans in AR, AZ, FL, GA, IL, ME, MA, MN, NH, NM, OH, PA, TN, VA, WA

Prevention of Road Accidents

2. Extending Time to Come to Rest:

- Crumple zones
 - Allow passengers additional time to decelerate
- Seat belts
 - Keep occupants in the passenger compartment
 - Stretch during impact
 - Reduce risk of death in crash by 40-60%
 - <http://www.regentsprep.org/Regents/physics/phys01/accident/nobelt.htm>
 - <http://www.regentsprep.org/Regents/physics/phys01/accident/withbelt.htm>
- Air bags
 - When combined with seat belts, reduce risk of serious and fatal injuries by 40-65%
 - <http://www.accidentreconstruction.com/movies/5thper.mov>
- Child restraints:
 - Reduce risk of infant death by 71% and toddler death by 54%

Prevention of Road Accidents

- Legislation:
 - Speed
 - Seat belts, Car seats, Air Bags
 - Alcohol use
 - Motorcycle helmets
- Engineering:
 - Restraints
 - Safety standards
- Education:
 - Seat belts, Car seats, Air Bags
 - Alcohol use

Prevention of Road Accidents

- Motorcycle helmets
 - Layer of foam designed to crush upon impact, extending time for head to come to rest
- Laws in Texas
 - Texas exempts riders 21 or older if they either
 - 1) can show proof of successfully completing a motorcycle operator training and safety course
 - Or
 - 2) can show proof of having a medical insurance policy

http://www.iihs.org/laws/state_laws/helmet_current.html#2

3. Cardiovascular Diseases

- 768,000 people ages 15-44 die as a result of cardiovascular disease every year
- Most common causes:
 - Ischemic heart disease (286,000 deaths)
 - Cerebrovascular disease (159,000 deaths)
- Will be covered in depth in *Lecture 4*

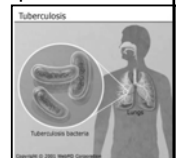


4. Tuberculosis

- Burden of Tuberculosis
- Natural History of TB Infection
- Diagnosis of Tuberculosis
- Drug Resistance
- Directly Observed Therapy
- TB in The Last Century

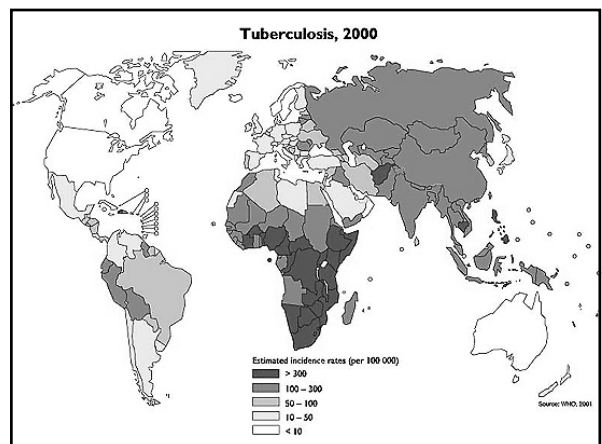
Burden of Tuberculosis

- Bacterial infection of the lungs caused by *Mycobacterium tuberculosis*
- Bacterium infects 1 in 3 people on the planet
- Drugs that cure TB were discovered in 1940s
- Results in death in 5 years in half of cases if untreated
- Kills 600,000 people ages 15-44 each year
- Estimated that TB will kill 35 million people in next 20 years if situation does not change
- 2005:
 - 8.8 million new cases (incidence)
 - Growing 1%/year
 - 1.6 million deaths
 - 98% of deaths occur in developing world



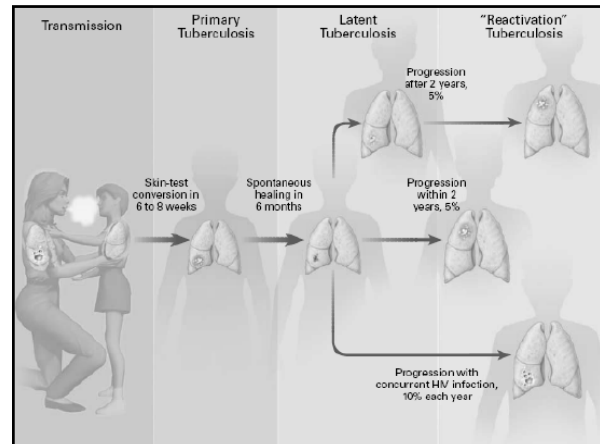
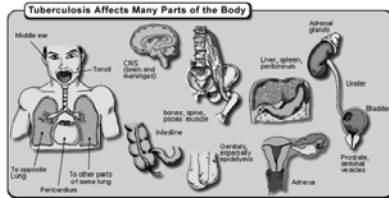
Burden of Tuberculosis

- 1/3 of world's population is infected with TB
 - Not all have active TB
 - Most have latent TB - Immune system has walled off bacilli with waxy coat
- 5-10% of people with normal immune systems will go on to develop active TB
 - Higher in people with compromised immune systems (10X higher in people with AIDS)
 - TB is leading cause of death among people with HIV/AIDS
 - <http://www.npr.org/rundowns/segment.php?wfId=1520699>
- Follows poverty and urban crowding
- Particularly severe in:
 - AIDS patients
 - Those who can't afford medical care
 - Noncompliant patients.



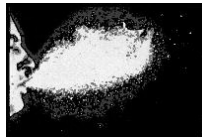
Natural History of TB Infection

- Primary TB
- Latent TB
- Secondary, or reactivation, TB



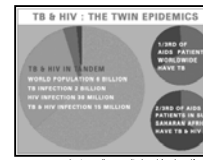
Natural History of TB Infection

- Active TB:
 - Symptoms
 - Fever
 - Night sweats
 - Weight loss
 - Weakness
 - Coughs (productive with bloody sputum)
 - Airborne transmission
 - Left untreated, one person with active TB can cough millions of infectious droplets into the air



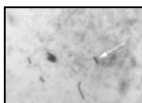
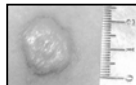
Natural History of TB Infection

- TB and AIDS
 - People with AIDS are 10x more likely to develop active TB once infected
 - TB is the leading cause of death among HIV positive individuals, accounting for 13% of AIDS deaths worldwide



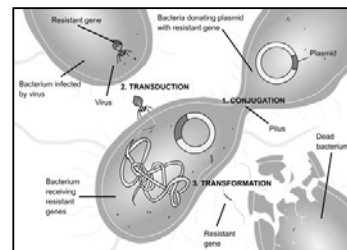
Diagnosis of Tuberculosis

- Skin test (PPD)
- Serum test
- CXR
 - Shows nodules in active TB
- Sputum
 - Acid-fast bacilli



Drug Resistance

- How does an organism acquire drug resistance?
 - Mutation and selection
 - Exchange of genes between strains and species



Source: Essential Biochemistry

Drug Resistance

- Selective pressure –Darwin's theory of survival of the fittest
- Resistance is expected
- Factors can reduce development of resistance
 - Complete the course of antibiotics
 - Only those who need antibiotics
 - Narrow spectrum antibiotics

Drug Resistance

- Multi-Drug Resistant (MDR) TB:
 - Can develop if patients do not take all medicine
 - Growing problem
 - Present in all countries
 - 425,000 new cases per year
 - In Russia and China, 14% of new cases are MDR
 - Must be treated with second-line antibiotics
 - Poorly supervised Rx is worse than no Rx
- Extensive Drug Resistant (XDR) TB:
 - Not only resistant to first-line drugs, but also to 3 or more of the 6 second-line drugs
 - Identified in every region of the world, esp Russia
 - High fatality rate
 - 4% of MDR-TB cases in the US are XDR

Directly Observed Therapy (DOT)

- A health care worker watches and helps as the patient swallows anti-TB medicines in his/her presence.
- DOTS shifts responsibility for cure from patient to health care system
- Requires political commitment, accurate diagnosis, quality drugs, observation, follow up
- DOTS works well in many developing countries

Directly Observed Therapy (DOT)

- 6 month supply is \$10
- Cure rates of up to 95% even in poorest countries
- 17 million patients worldwide have been treated with DOT since 1995
- 25% of world's population does not have access to DOT.

TB in The Last Century

- TB incidence declined in the 1960's and 1970's. Incidence increased in the 1980's.
 - Why?
- Drug prescription practices followed the previously mentioned guidelines.
 - Why did therapy fail?

TB in the Last Century

- Overlapping Epidemics
 - TB and HIV
 - TB is the leading killer of people with HIV
 - In Africa, half of all TB cases are associated with HIV.
 - Malaria and HIV
 - For people with HIV, especially pregnant women, episodes of acute malaria are complicated and more serious.

Leading Causes of Mortality Ages 15-44

- Developing World
 1. HIV/AIDS
 2. Unintentional injuries
 3. Cardiovascular diseases
 4. Tuberculosis
- Developed World
 1. Unintentional injuries
 2. Cardiovascular diseases
 3. Cancer
 4. Self-inflicted injuries

3. Cancer

- 580,000 people ages 15-44 die as a result of cancer every year
- Most common causes:
 - Liver Cancer (68,000 deaths per year)
 - Leukemias (65,000)
 - Stomach Cancer (58,000)
 - Breast Cancer (57,000)
- Will be covered in depth in *Lecture 4*

4. Self-Inflicted Injuries

- Burden of Self-Inflicted Injuries
- Risk Factors Associated with Suicide
- Methods of Suicide
- Screening and Prevention

Burden of Self-Inflicted Injuries

- 480,000 people ages 15-44 take their own lives each year (4th leading cause of death)
- Unipolar depressive disorder ranks #1 for DALYs in this age group in developed countries
 - Second to HIV/AIDS in developing countries
- Highest rate of completed suicides
 - Men >65 years old
- Highest rate of attempted suicides
 - Men and women ages 20-24

Risk Factors Associated with Suicide

- Psychiatric illness
 - Affective, substance abuse, personality, other mental disorders
- Other risk factors
 - Social adjustment problems
 - Serious medical illness
 - Living alone
 - Recent bereavement
 - Personal history of suicide attempt or completion
 - Divorce or separation
 - Unemployment

Methods of Suicide

- Most common:
 - Firearms are used in 60% of suicides
- 2nd leading cause:
 - Men: Hanging
 - Women: Drug overdose or poison
- Alcohol is involved in 25-40% of suicides
- Women attempt suicide more often; men are more often successful

Screening and Prevention

- 50-66% of all suicide victims visit physician <1 month before event
- 10-40% in the preceding week
- Hard to identify who is at risk
 - Direct questioning has low yield
 - General questions about sleep disturbance, depressed mood, guilt and hopelessness
 - Survey instruments aren't good at predicting what will happen

Screening and Prevention

- How do we quantify the efficacy of such questionnaires?
 - Goal of screening:
 - Catch as many positives as possible, even at the risk of some false positives
 - Sensitivity:
 - Se = probability of testing positive if you will commit suicide
- Sensitivity of best questionnaires: 56% (low)

Screening and Prevention

- How many false positives result?
 - Positive predictive value:
 - PPV=probability of committing suicide if you test positive
- PPV of best questionnaires: 3% (pathetic)

Screening and Prevention

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Summary of Lecture 3

- Developing World
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 3. Cardiovascular diseases
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