

# BIOE 301/362

## Lecture Three:

### Leading Causes of Mortality, Ages 15-44

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

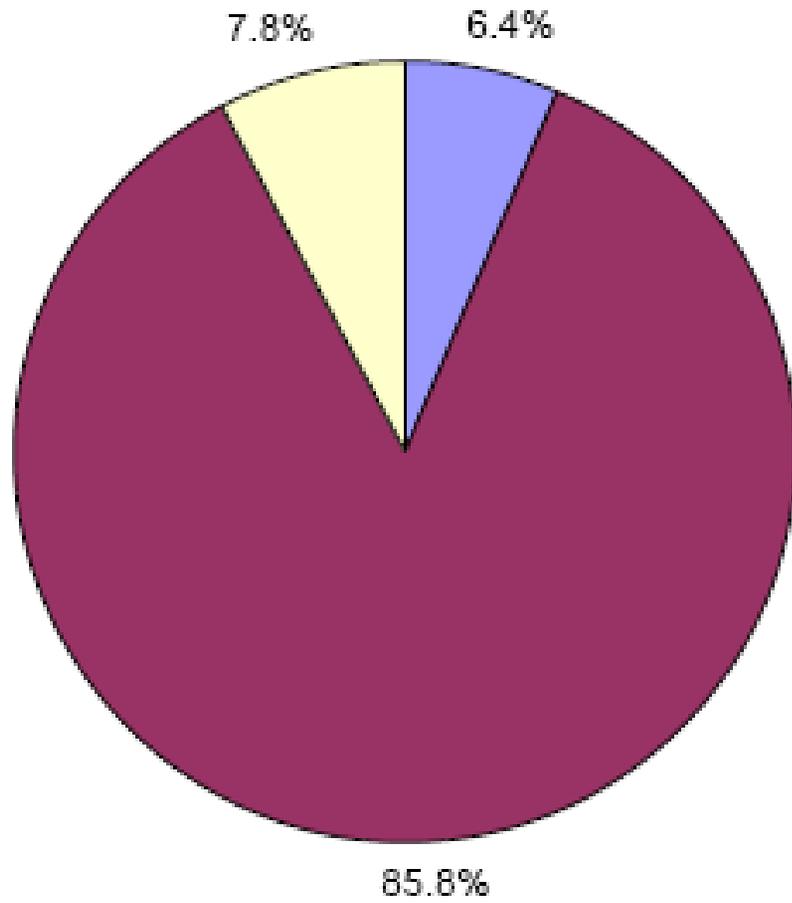
## ■ Developing world

1. Perinatal conditions
2. Lower respiratory infections
3. Diarrheal diseases
4. Malaria

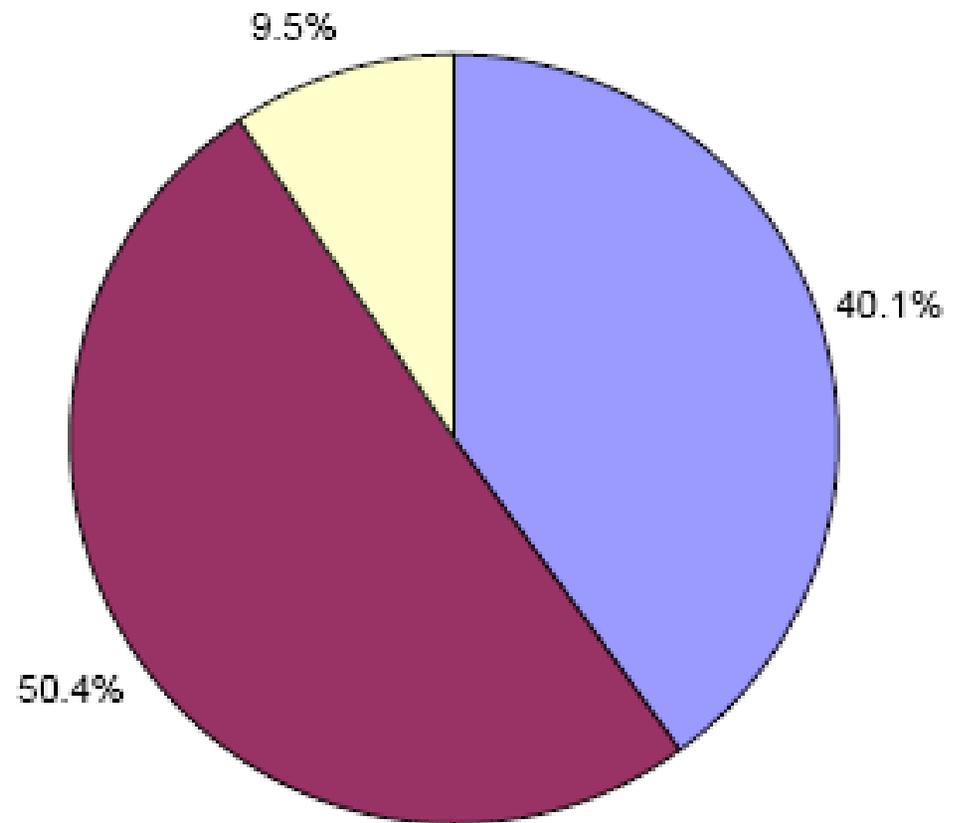
## ■ Developed world

1. Perinatal conditions
2. Congenital anomalies
3. Lower respiratory infections
4. Unintentional injuries

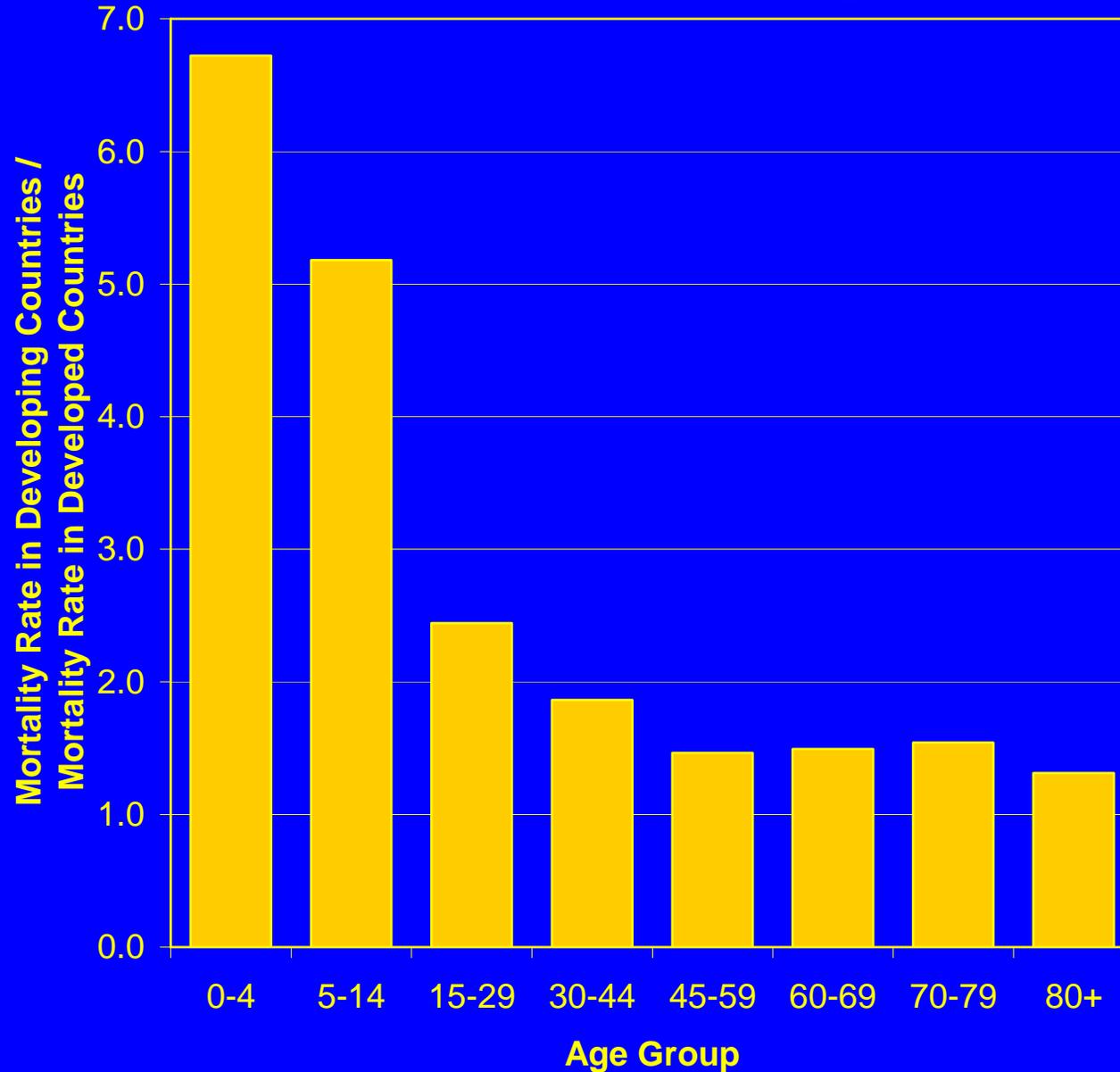
Developed Countries



Developing Countries



# Ratio of Mortality Rate



# 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](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

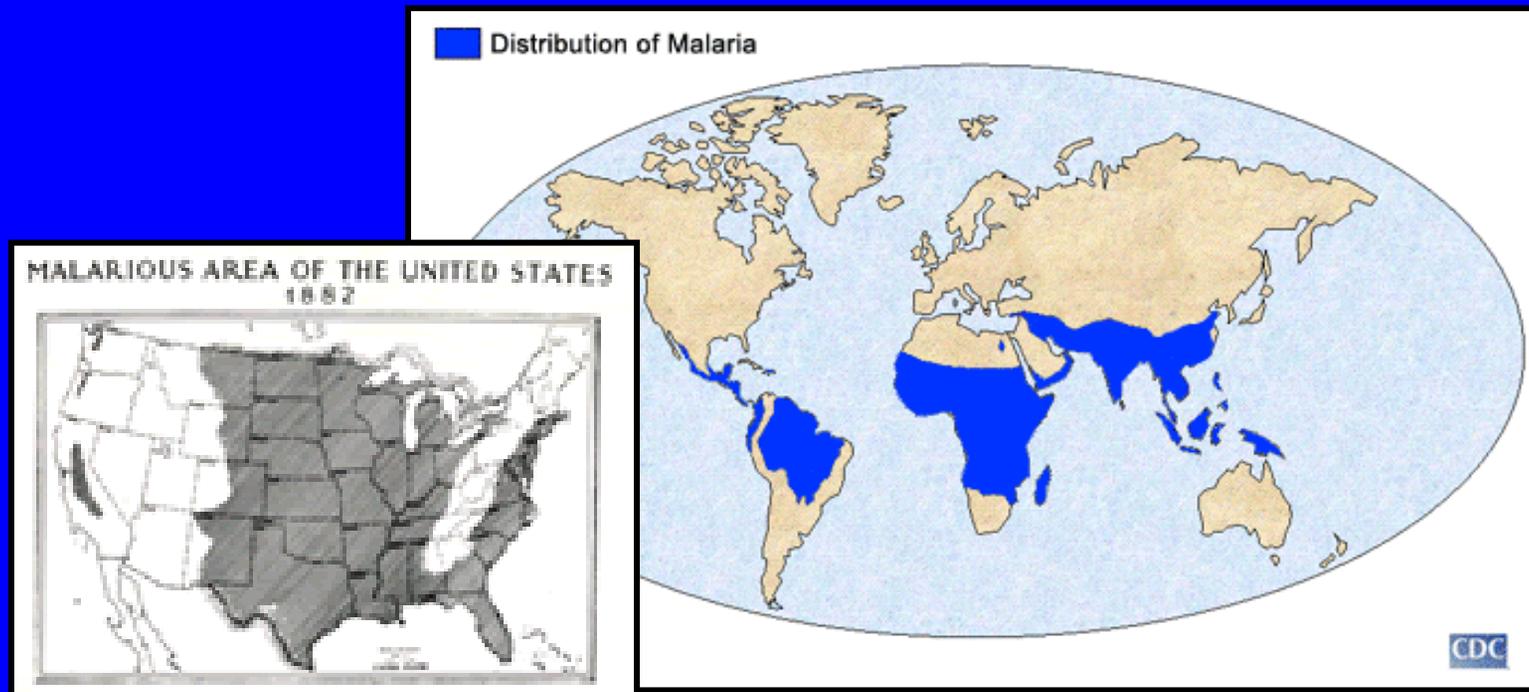


- Question: What is the #1 way to prevent diarrheal illness in a newborn?

# 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



# 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)

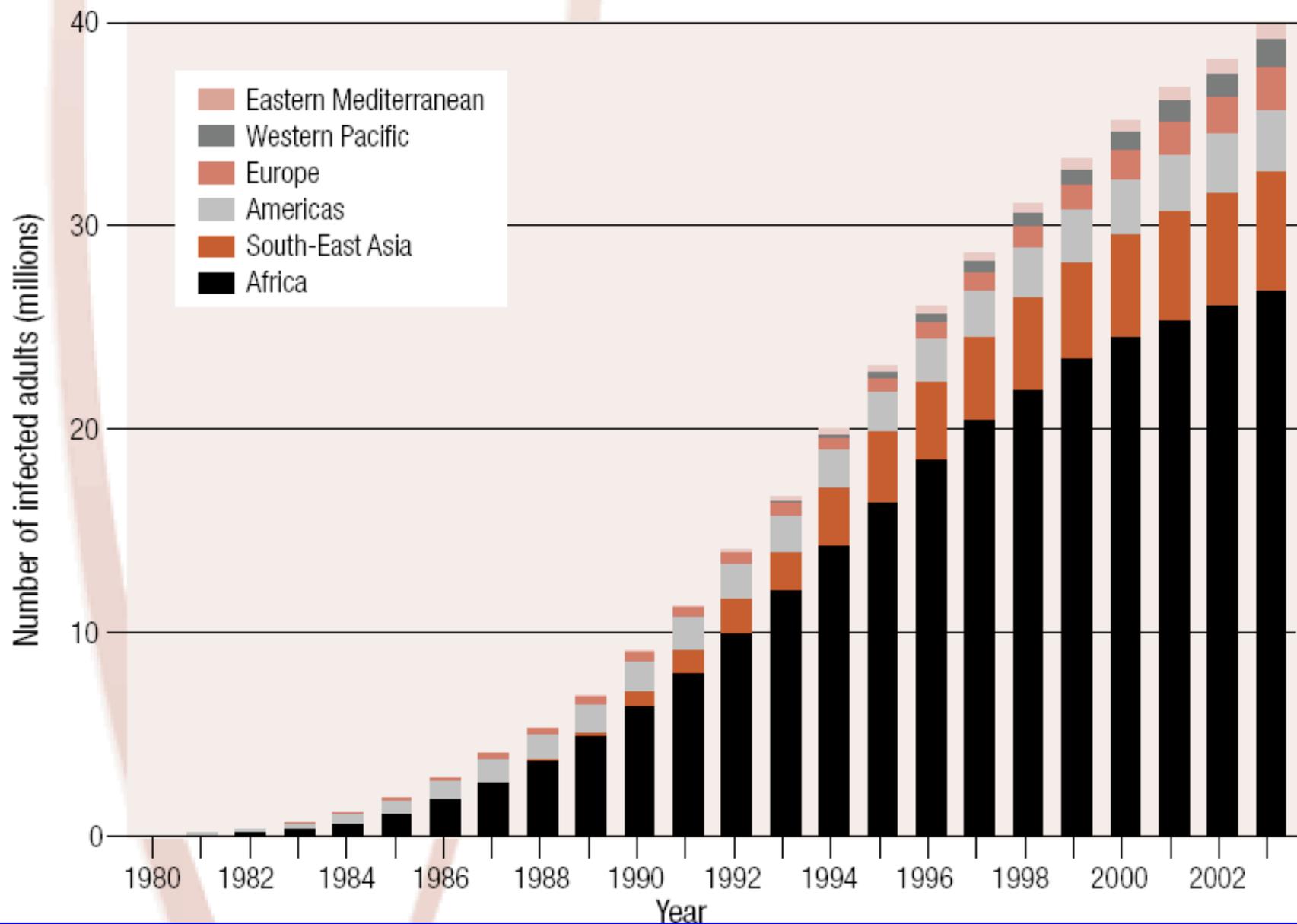
# Burden of HIV/AIDS

## ■ Worldwide

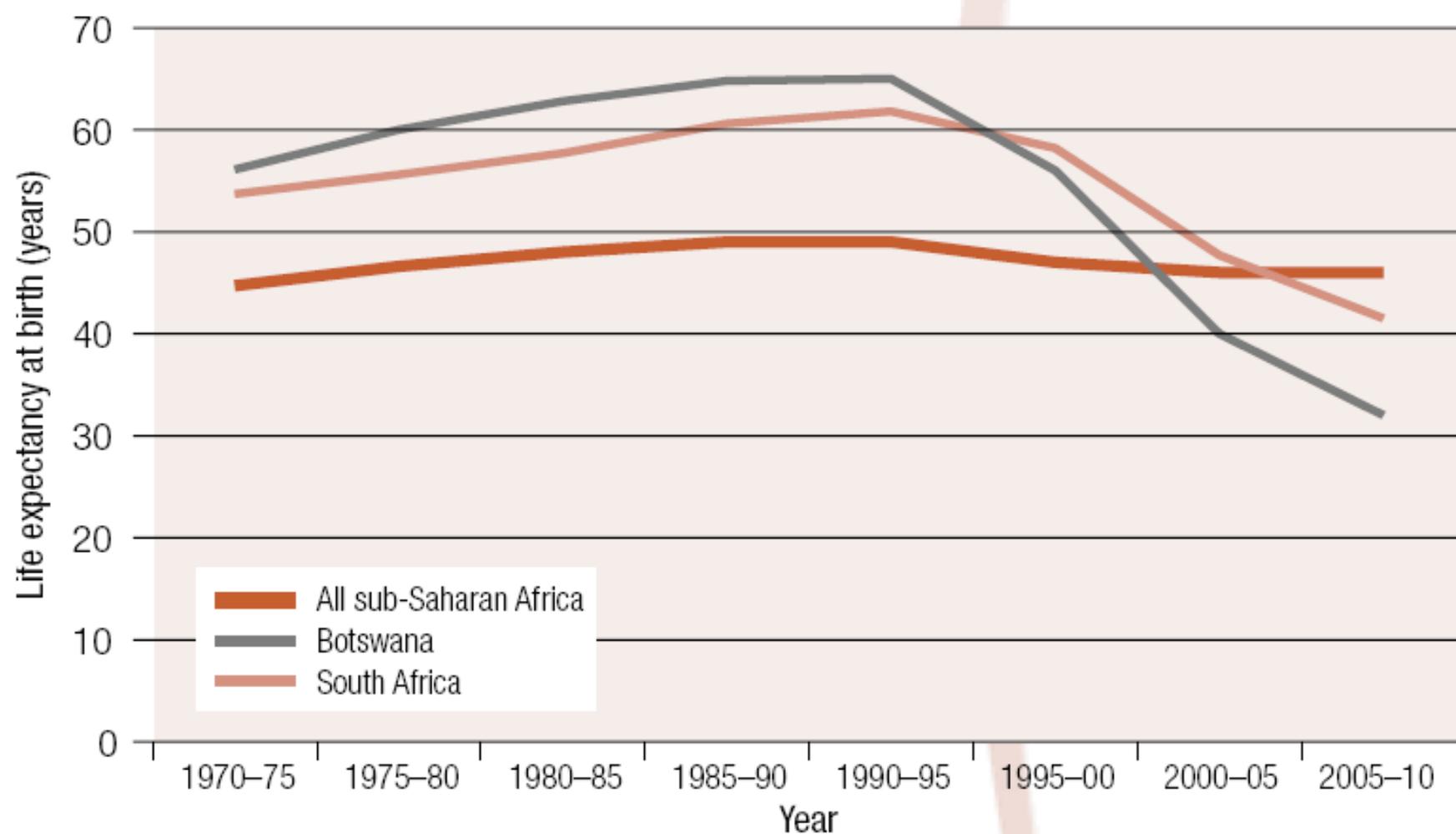
- 33.0 M people living with HIV/AIDS (2 M children)
- 25 M killed, 11.5 M orphans in Africa alone
- 2007:
  - 2.0 M deaths
  - 2.7 M new HIV infections
  - 14% of new infections occurred in children (<15 yrs)
- 2/3 of those with AIDS and 3/4 of all AIDS deaths are in sub-Saharan Africa
- 7400 new infections per day
  - 96% in low- and middle-income countries
  - 1000 children

Source: 2008 AIDS Epidemic Update, UNAIDS/WHO

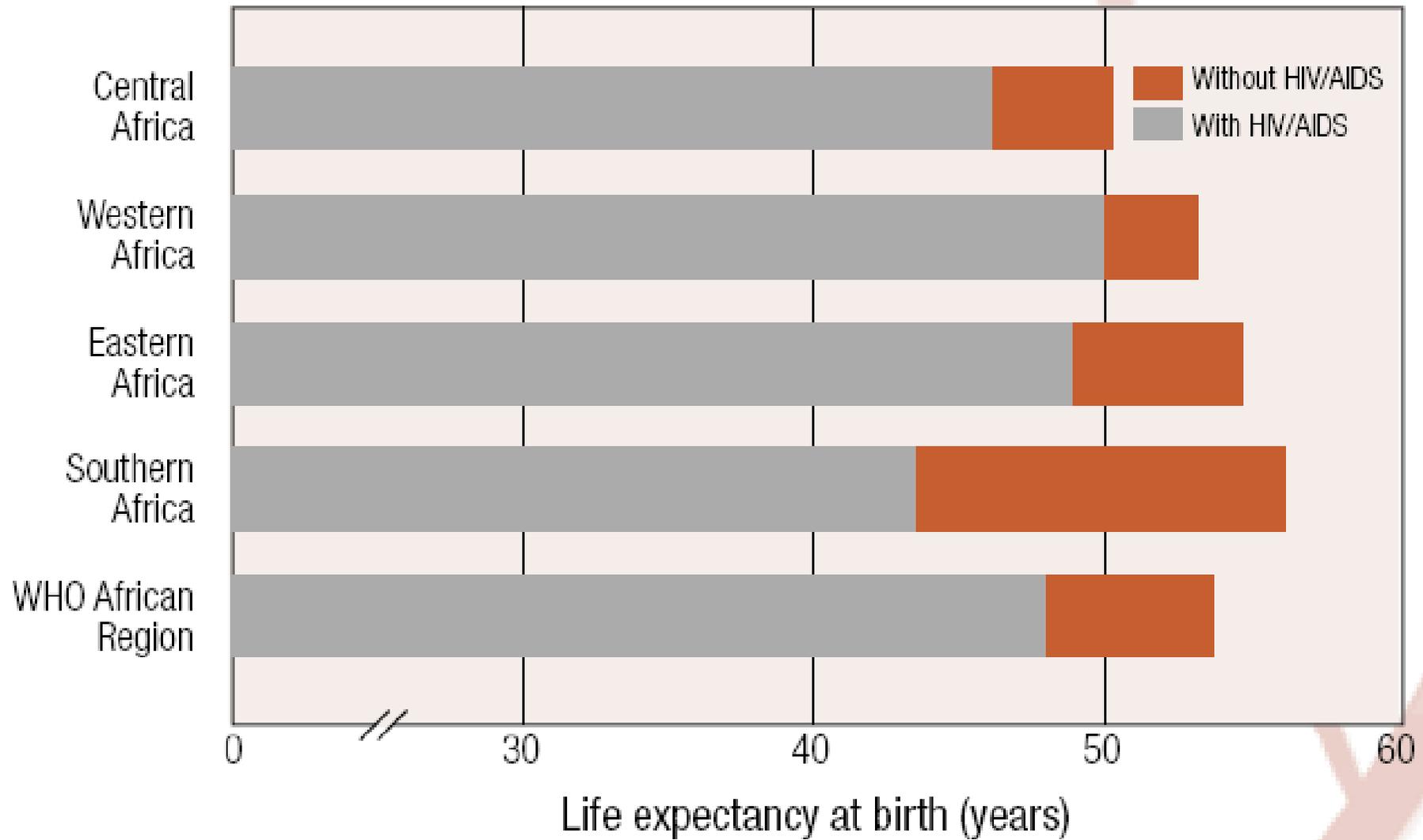
Estimated number of adults infected with HIV,  
by WHO region, 1980–2003



## Trends in life expectancy in sub-Saharan Africa and two selected countries, 1970–2010



## Life expectancy in Africa, with and without HIV/AIDS, 2002



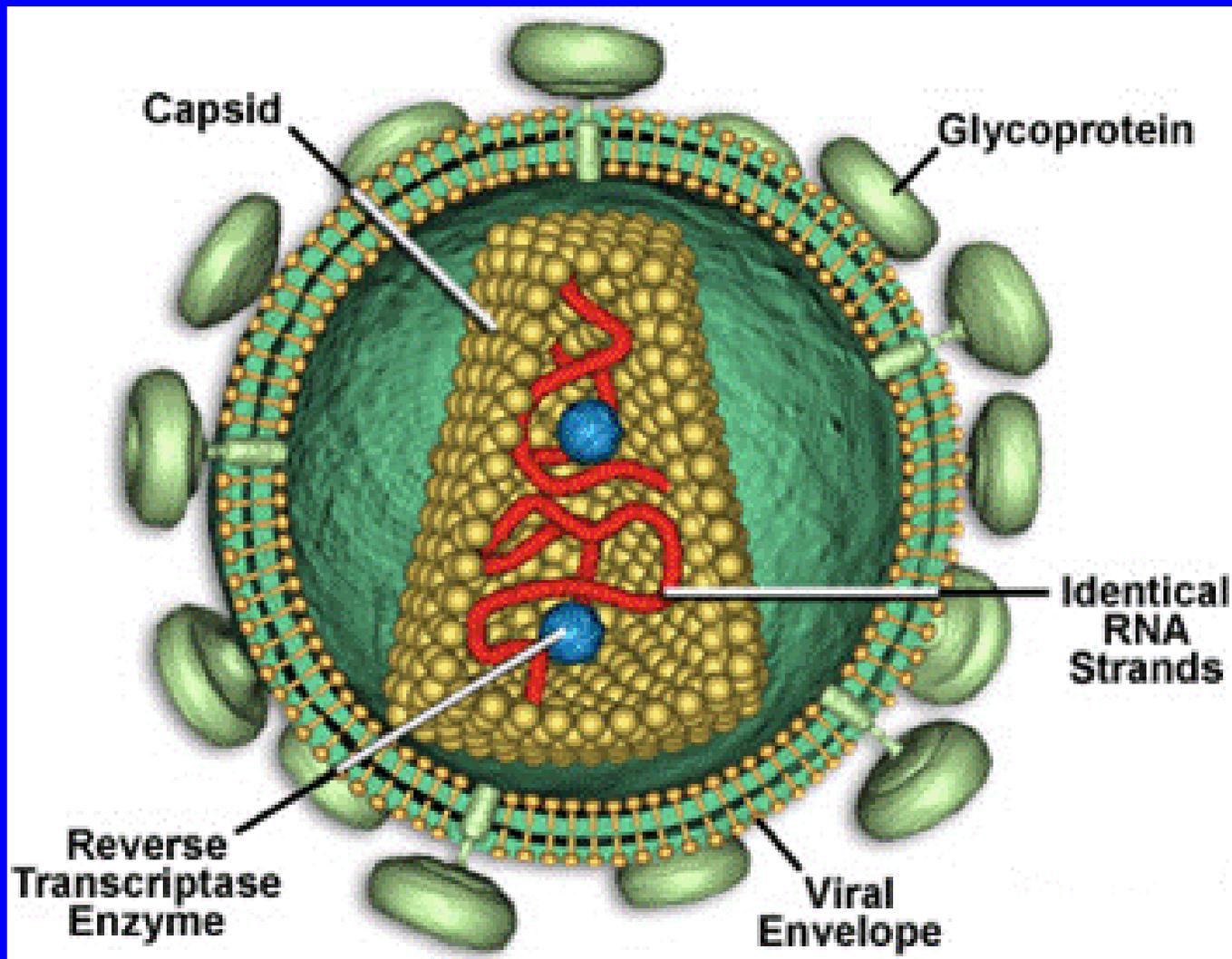
# Burden of HIV/AIDS in the U.S.

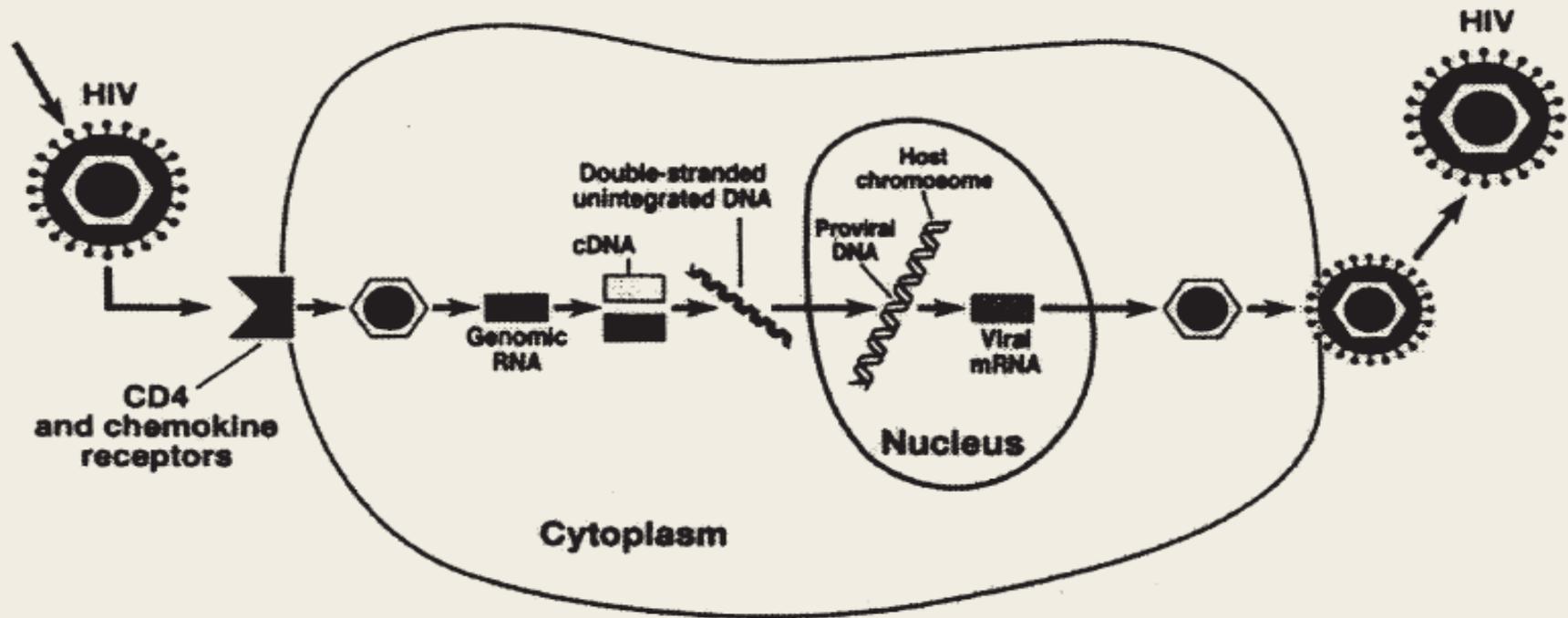
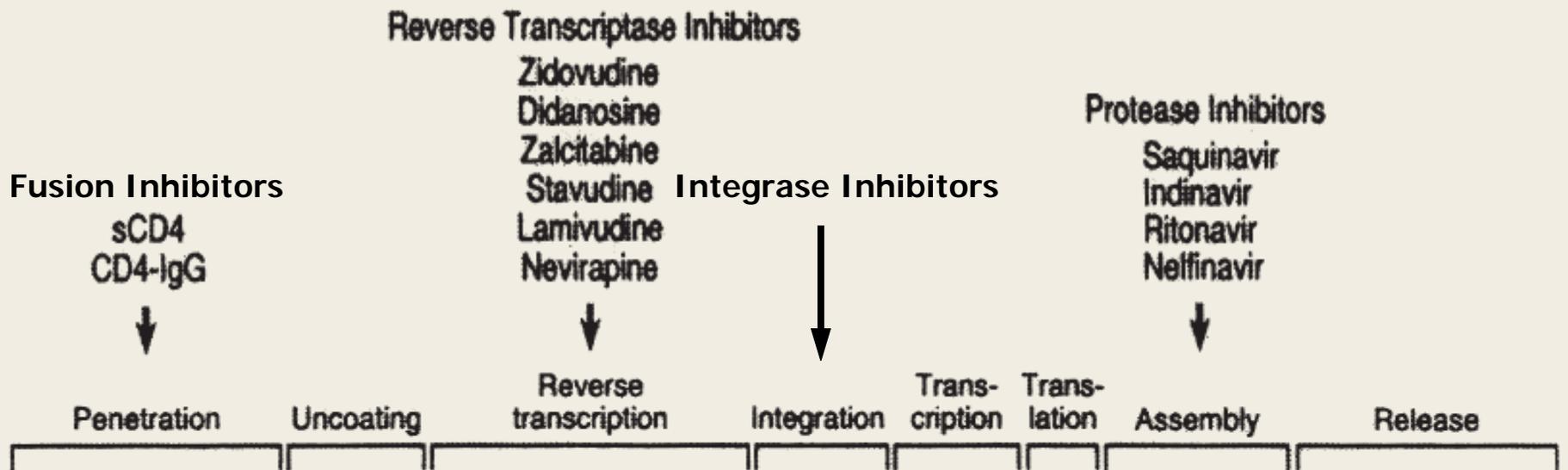
- 1.2 M people have HIV/AIDS (prevalence)
- 56,000 new infections per year (incidence)
- Only 7 countries in the world have more people living with HIV than the U.S.
- Routes of transmission:
  - Unsafe sex between men (53%)
  - High-risk heterosexual intercourse (31%)
  - Non-sterile drug injection equipment (12%)

# Burden of HIV/AIDS in the U.S.

- **Racial and ethnic minorities are disproportionately affected:**
  - 50% of HIV 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?**

# Pathophysiology of HIV/AIDS



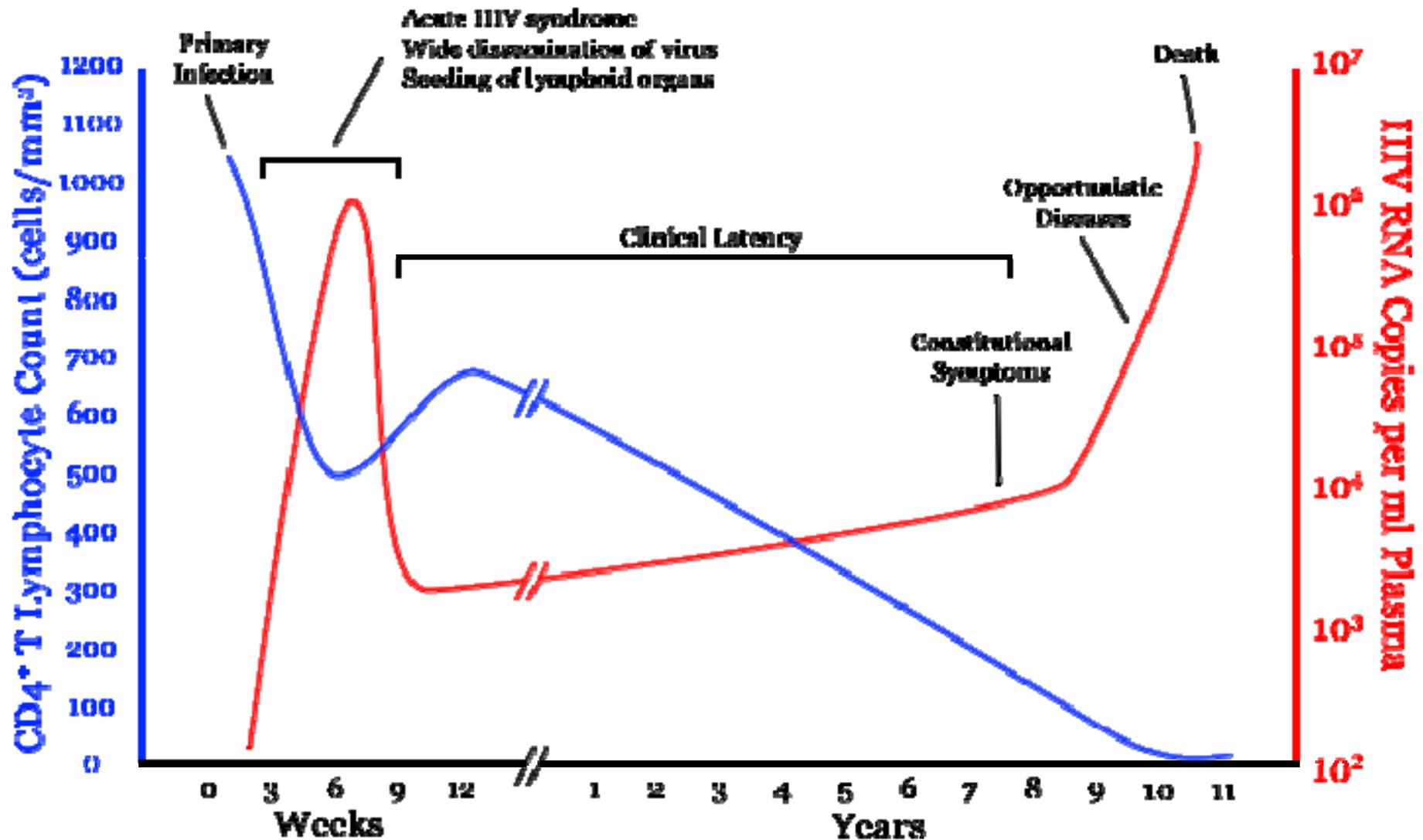


# Pathophysiology of HIV/AIDS

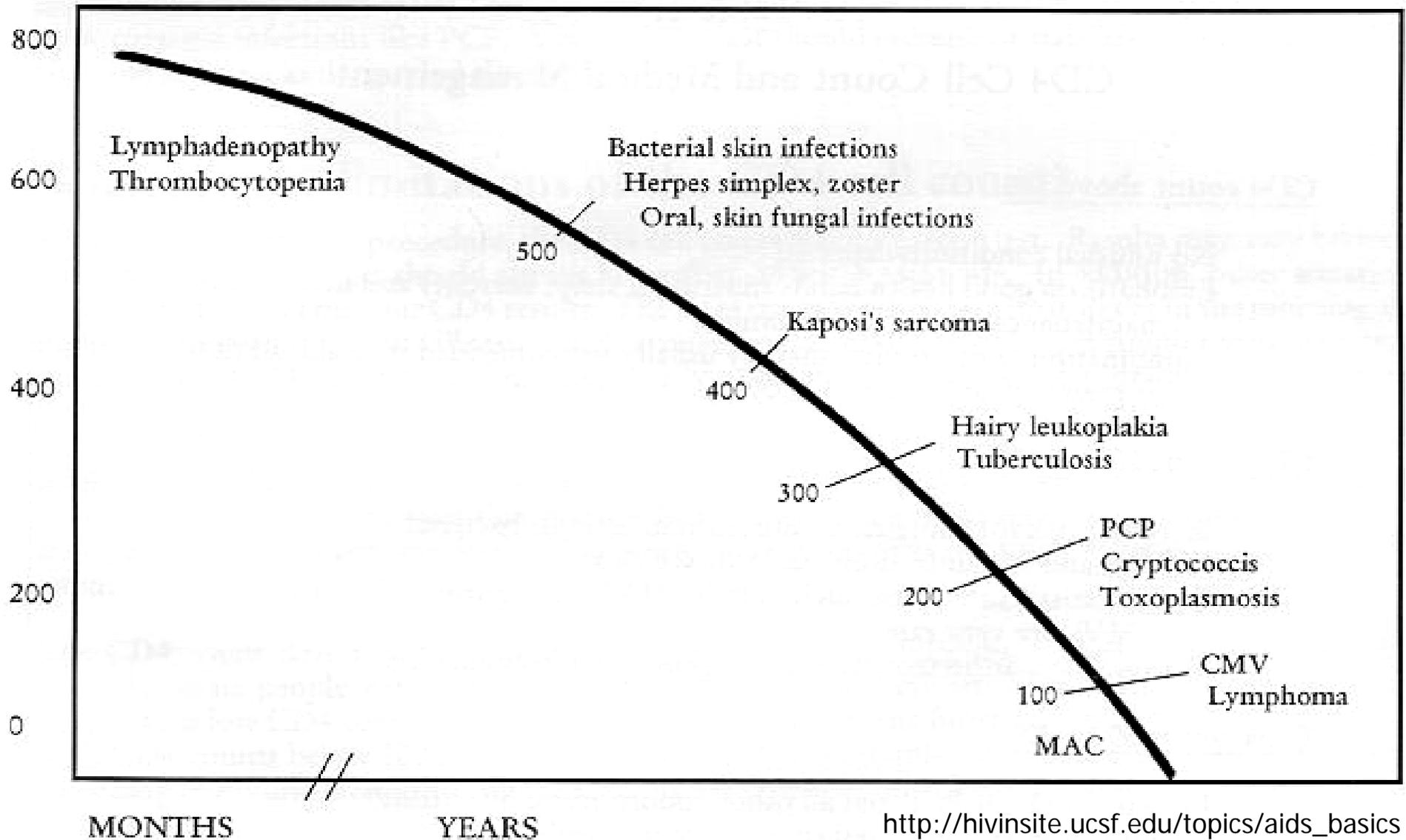
*Table 1: Cells Susceptible to HIV Infection*

System	Cell
Hematopoietic	<ul style="list-style-type: none"><li>• T-cells (CD4+ or CD8+)</li><li>• Macrophages/monocytes</li><li>• Dendritic cells</li><li>• Fetal thymocytes and thymic epithelium</li><li>• B-cells</li><li>• NK cells</li><li>• Megakaryotic cells</li><li>• Stem cells</li></ul>
Central Nervous	<ul style="list-style-type: none"><li>• Microglia</li><li>• Capillary endothelial cells</li><li>• Astrocytes</li><li>• Oligodendrocytes</li></ul>
Large Intestine	<ul style="list-style-type: none"><li>• Columnar epithelium</li></ul>
Other	<ul style="list-style-type: none"><li>• Kupfer cells (liver)</li><li>• Synovial cells</li><li>• Placental trophoblast cells</li></ul>

# Clinical Course of HIV/AIDS



# Clinical Course of HIV/AIDS



# Clinical Course of HIV/AIDS

*Figure 1: Kaposi's Sarcoma*



*Figure 2: Herpes Simplex*



*Figure 3: Herpes Zoster (Shingles)*



*Figure 5: Molluscum Contagiosum*

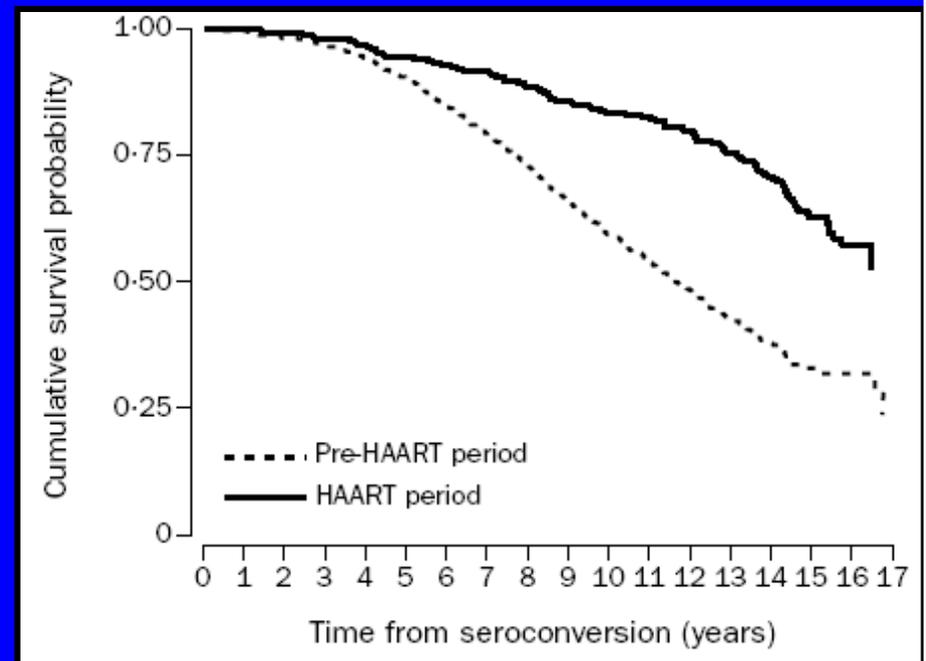


*Figure 8: Scabies With Pruritic Papular Eruption*

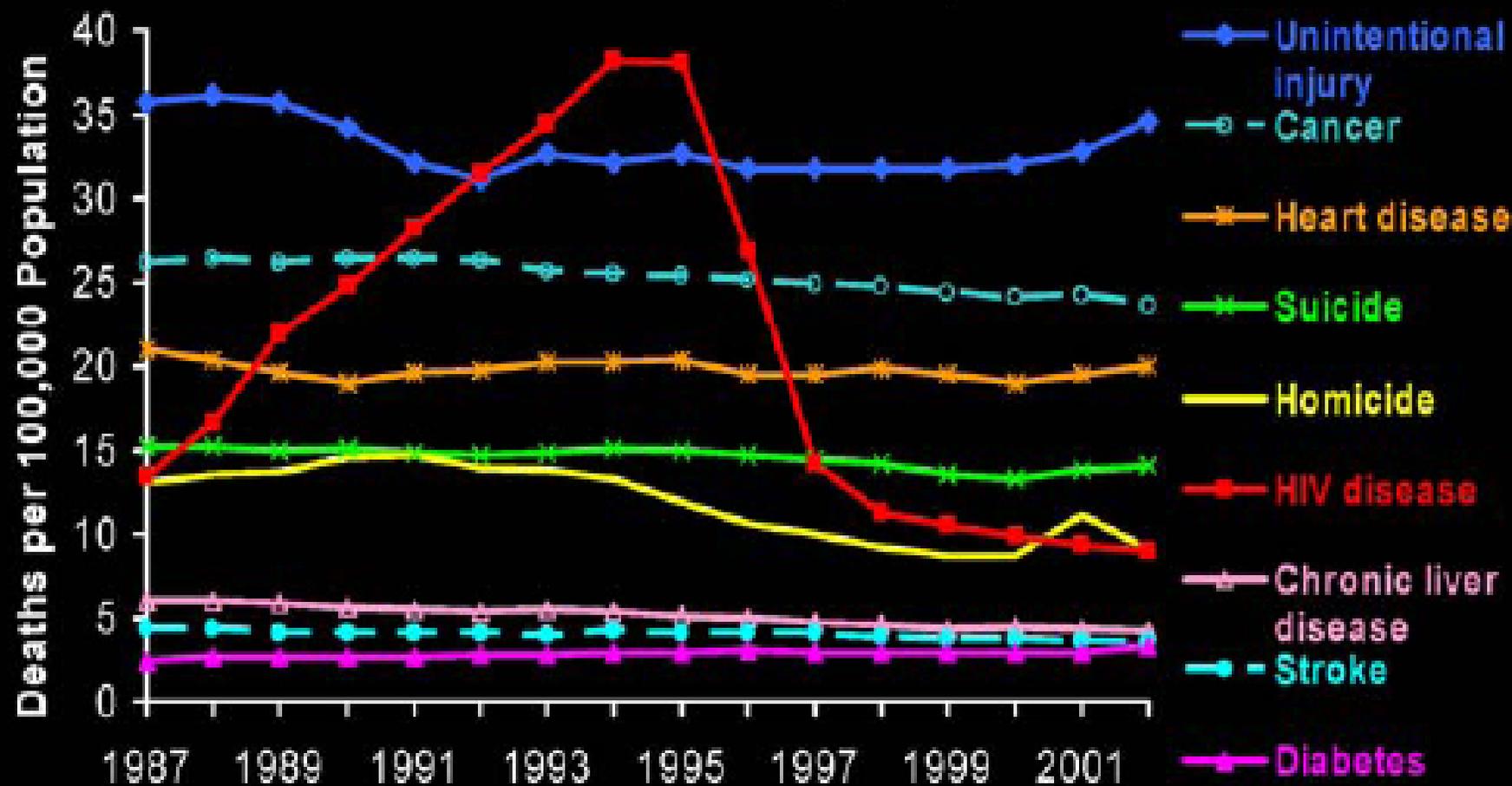


# HIV/AIDS Therapy

- HIV can rapidly mutate to quickly develop resistance to a single drug
- Resistance develops much more slowly to drug combinations
- Goal of ART:
  - 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

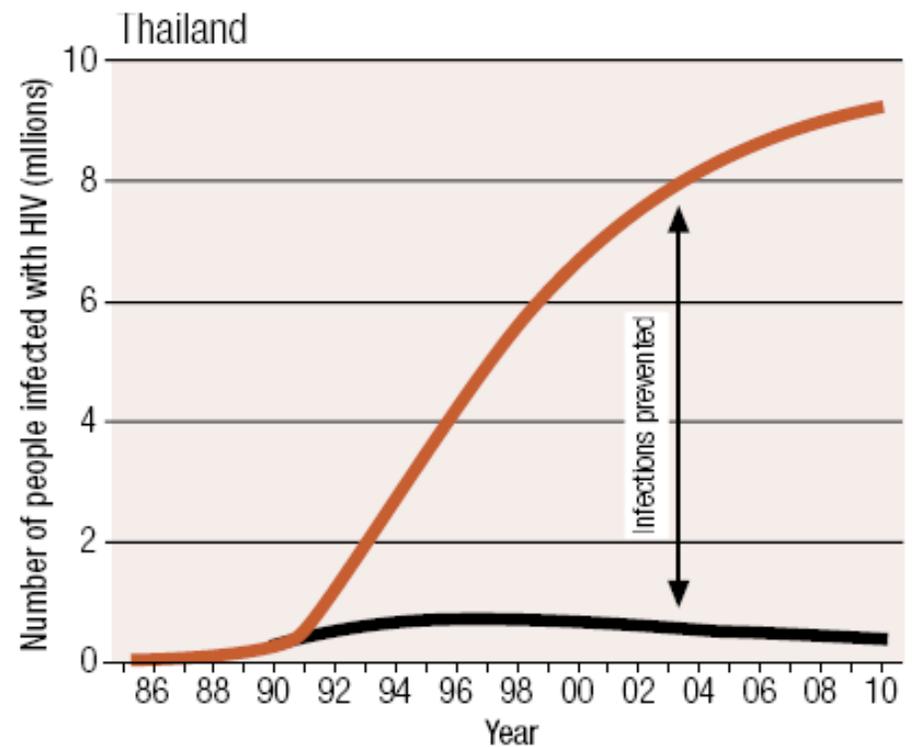
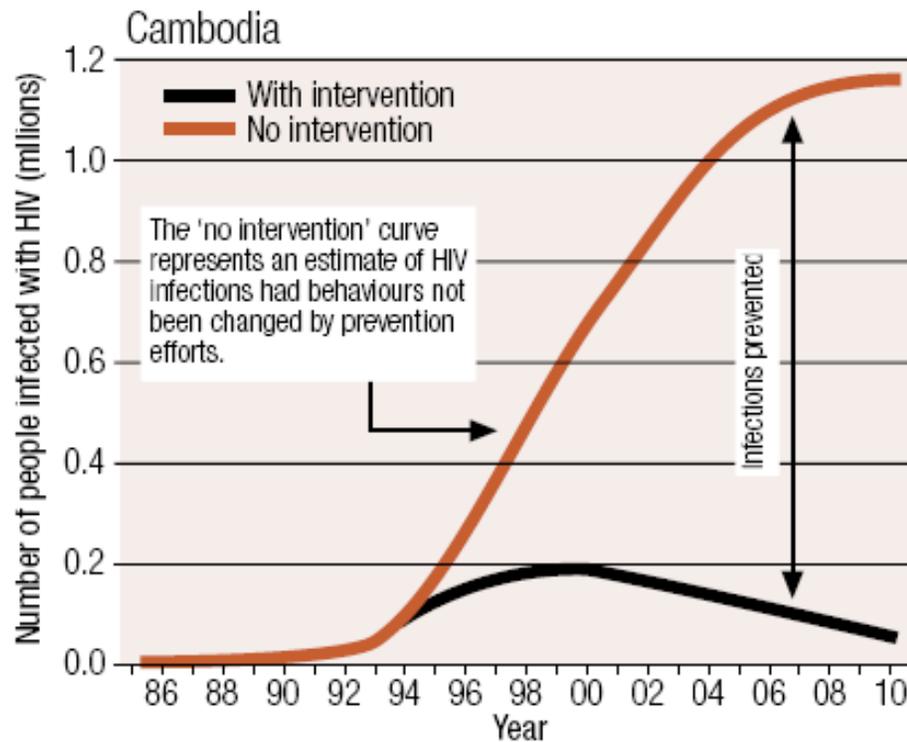


Note: For comparison with data for 1999 and later years, data for 1987–1998 were modified to account for ICD-10 rules instead of ICD-9 rules.



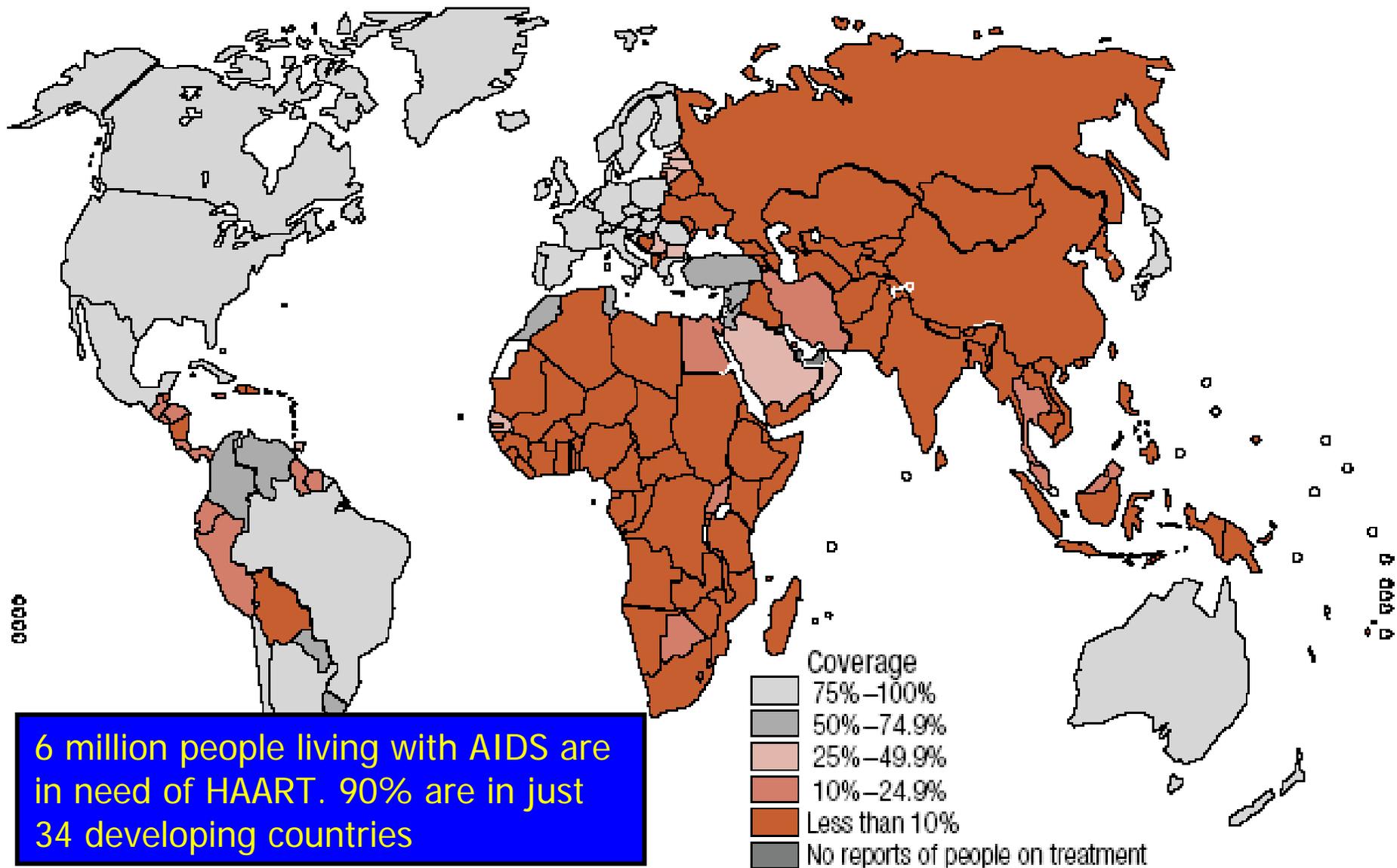
# HIV/AIDS Therapy

## Current and projected impact of HIV prevention efforts



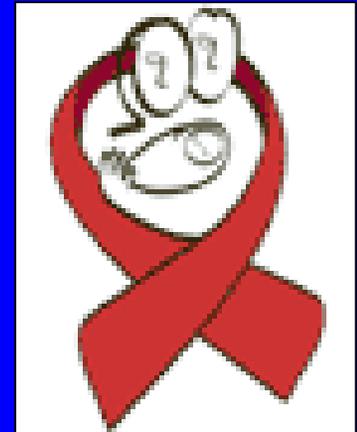
## HIV/AIDS: THE TREATMENT GAP

Estimated worldwide coverage with antiretroviral treatment, end 2003



# 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 M people ages 15-44 die from unintentional injuries each year
- 1 M deaths in developing countries, 1/4 M 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
  - 2008:
    - 37,000 Americans killed
    - 2,500,000 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 2<sup>nd</sup> Law:**

- $F = m a$

- $a = dv/dt$

- $a = \text{initial velocity}/\text{time to come to rest}$

- **In a crash:**

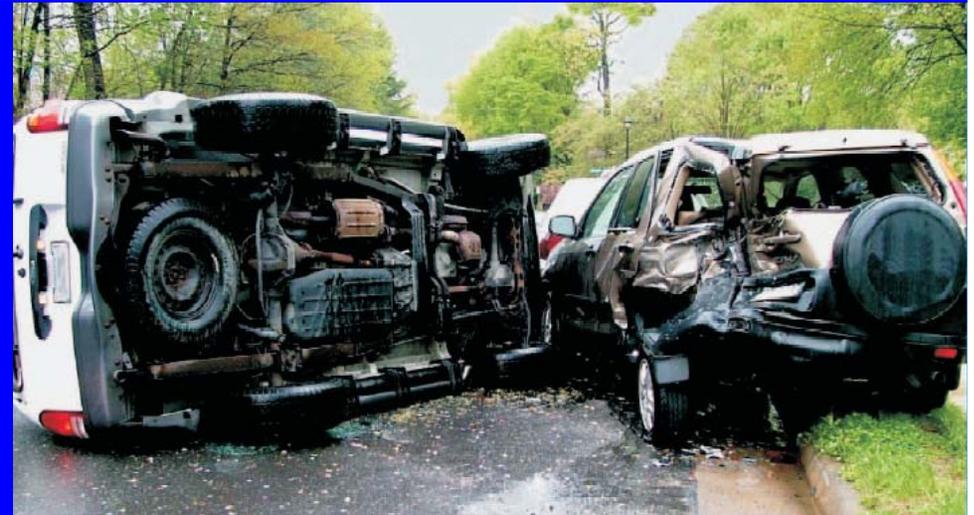
- Velocity slows to zero in a very short time

- Generates large forces

- **How can we reduce these forces?**

1. Reduce initial velocity of impact

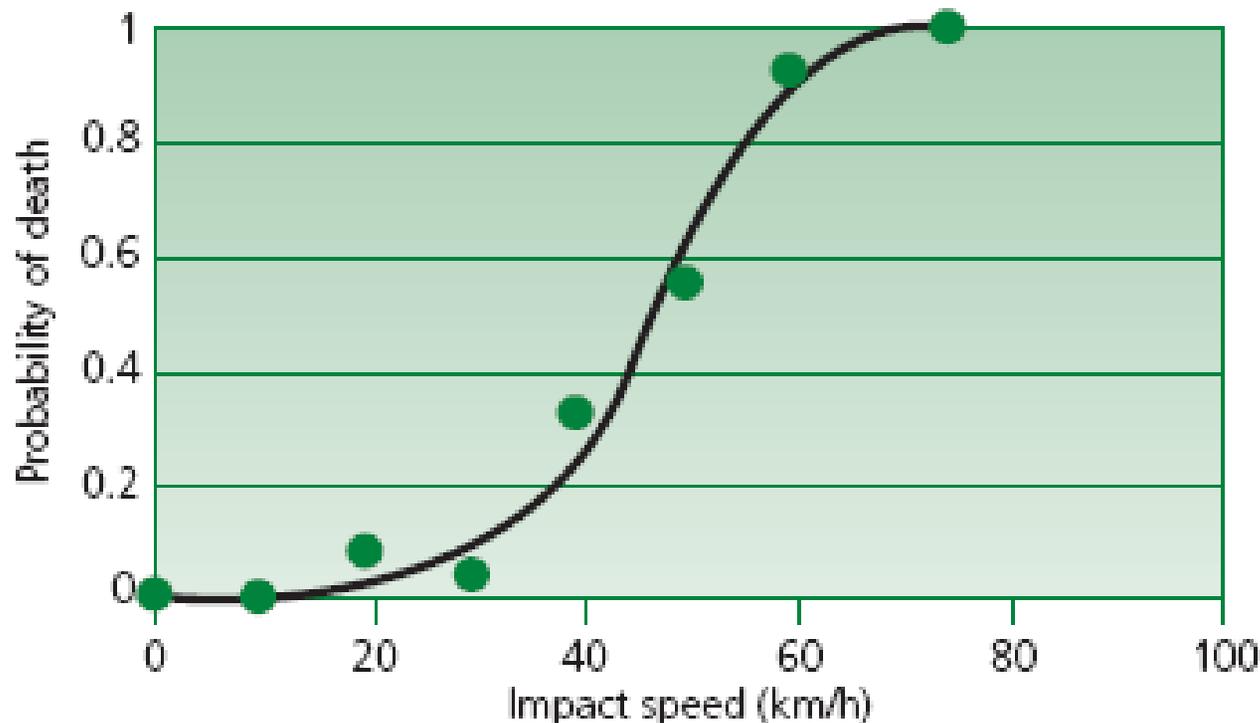
2. Extend time that it takes passengers to come to rest



# Prevention of Road Accidents

## 1. Reduce initial velocity of impact

- Excessive speed contributes to:
  - 30% of deaths in developed countries
  - 50% of deaths in developing countries

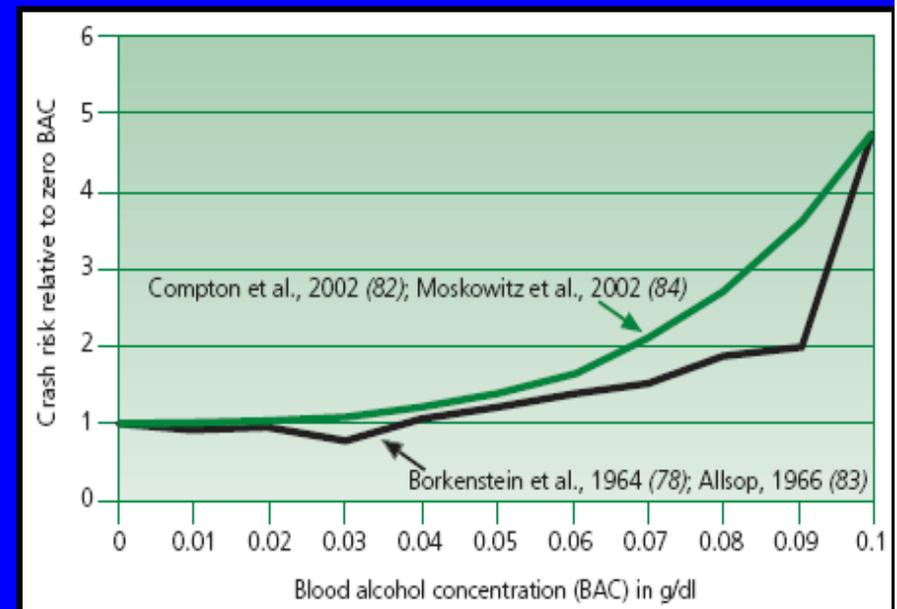


# 1. Reduce Initial Velocity of Impact

- 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

# 1. Reduce Initial Velocity of Impact

- 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!



# 1. Reduce Initial Velocity of Impact

## ■ 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

## ■ 6 states and D.C. have banned use of hand held phones while driving (CA, CT, NJ, NY, OR, WA)

- Partial bans in AR, AZ, CO, DE, GA, IL, IN, KY, LA, ME, MD, MA, MI, MN, NE, NH, NM, NC, OH, PA, RI, TN, TX, UT, VA, WV

- TX: Banned for novices (1<sup>st</sup> 12 mos) and in school crossing zones

# 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%
- Air bags
  - When combined with seat belts, reduce risk of serious and fatal injuries by 40-65%
- Child restraints:
  - Reduce risk of infant death by 71% and toddler death by 54%

# Prevention of Road Accidents

## 3. Legislation:

- Speed
- Seat belts, Car seats, Air Bags
- Alcohol use
- Motorcycle helmets

## 4. Engineering:

- Restraints
- Safety standards

## 5. Education:

- Seat belts, Car seats, Air Bags
- Alcohol use

## 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*

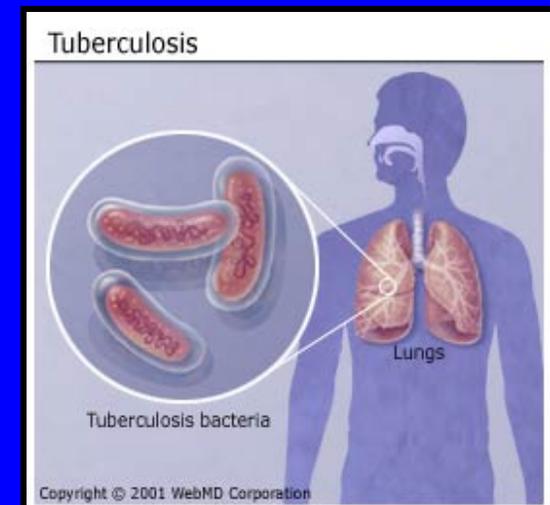


# 4. Tuberculosis

- Burden of Tuberculosis
- TB Pathophysiology
- Diagnosis of Tuberculosis
- Directly Observed Therapy

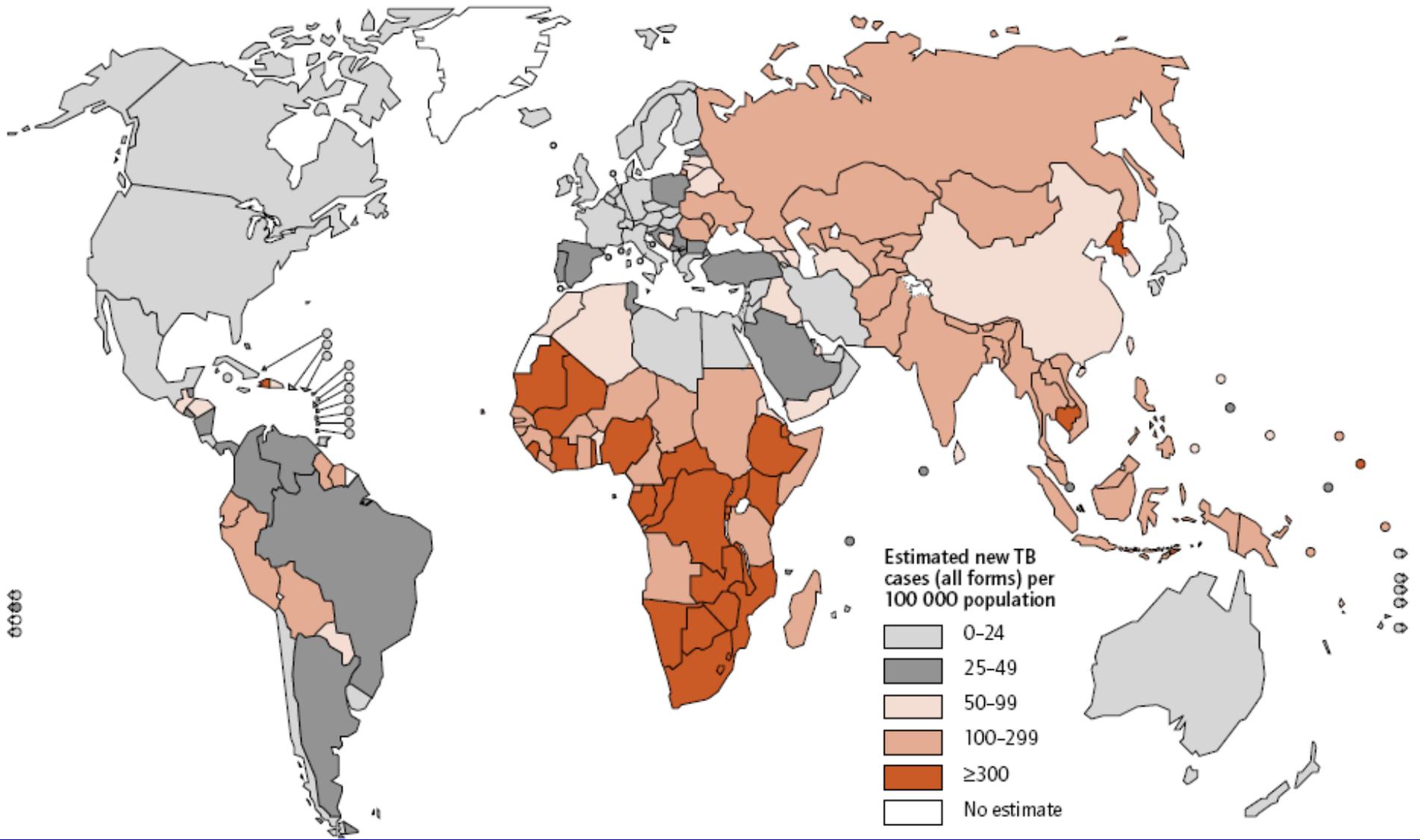
# Burden of Tuberculosis

- 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 M people in next 20 years if situation does not change
- 2007:
  - 9.27 M new cases (incidence)
  - 500,000 cases of MDR-TB
  - 1.7 M deaths
  - 98% of deaths occur in developing world



**FIGURE 1.2**

Estimated TB incidence rates, by country, 2007



**Transmission**

**Primary Tuberculosis**

**Latent Tuberculosis**

**"Reactivation" Tuberculosis**



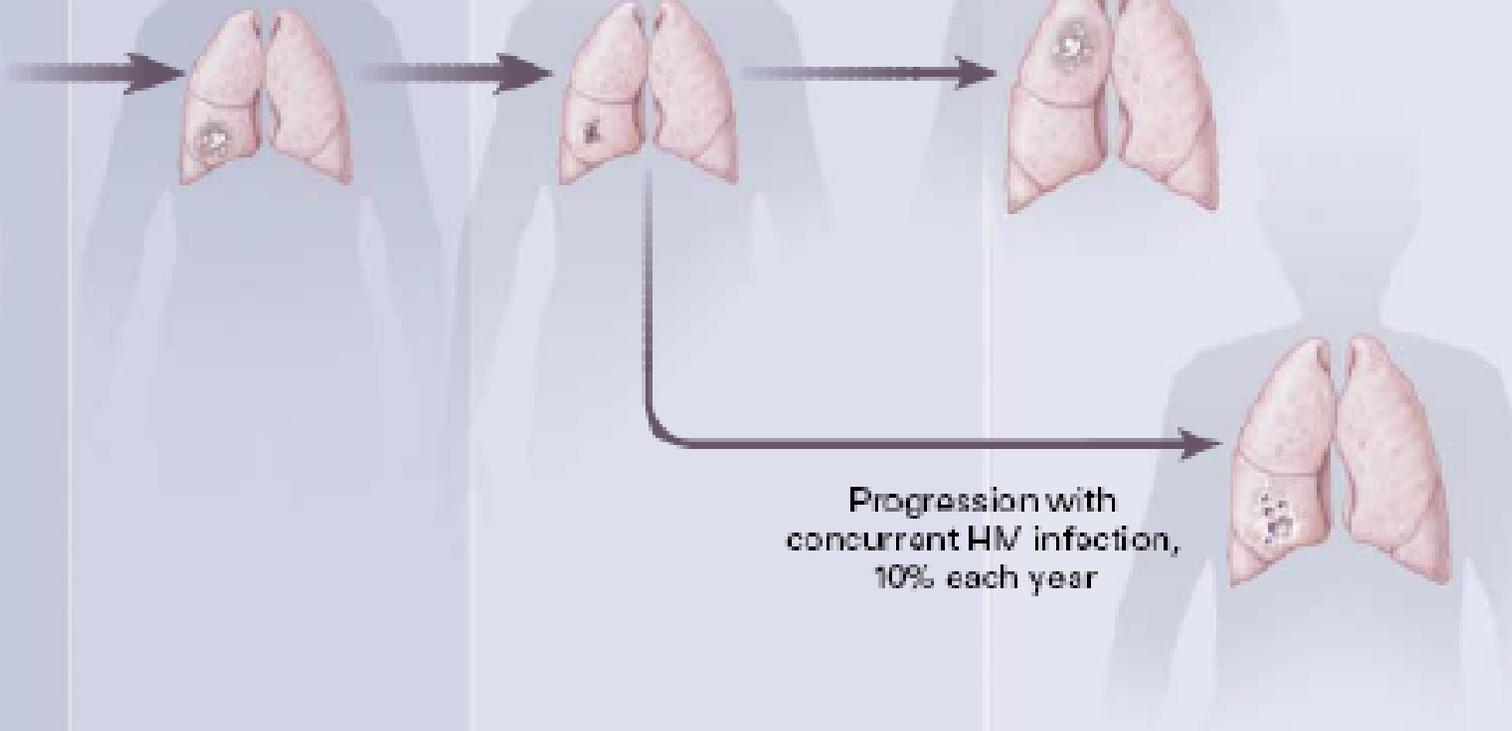
Skin-test conversion in 6 to 8 weeks

Spontaneous healing in 6 months

Progression after 2 years, 5%

Progression within 2 years, 5%

Progression with concurrent HIV infection, 10% each year



# TB Pathophysiology

## ■ Active TB:

### ■ Symptoms

- Fever
- Night sweats
- Weight loss
- Weakness
- Coughs (productive with bloody sputum)

### ■ Airborne transmission

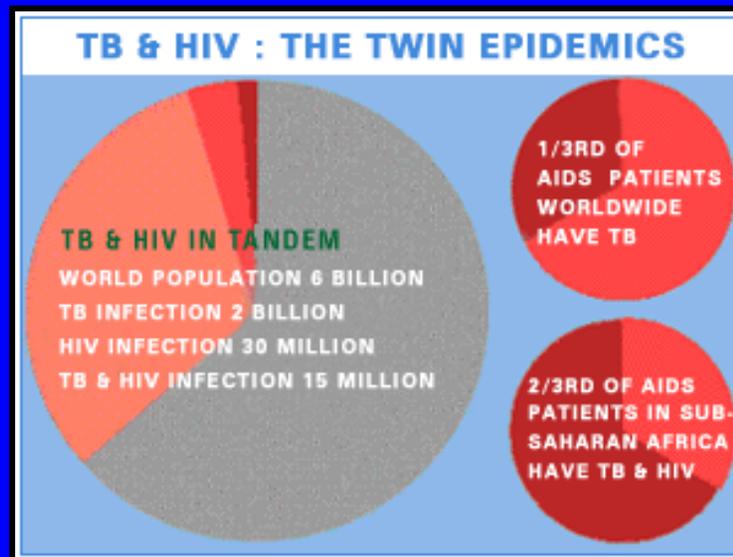
- Left untreated, one person with active TB can cough millions of infectious droplets into the air



# TB Pathophysiology

## ■ 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
- Chest X-ray
  - Shows nodules in active TB
- Sputum
  - Acid-fast bacilli



# Directly Observed Therapy (DOT)

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

# 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*

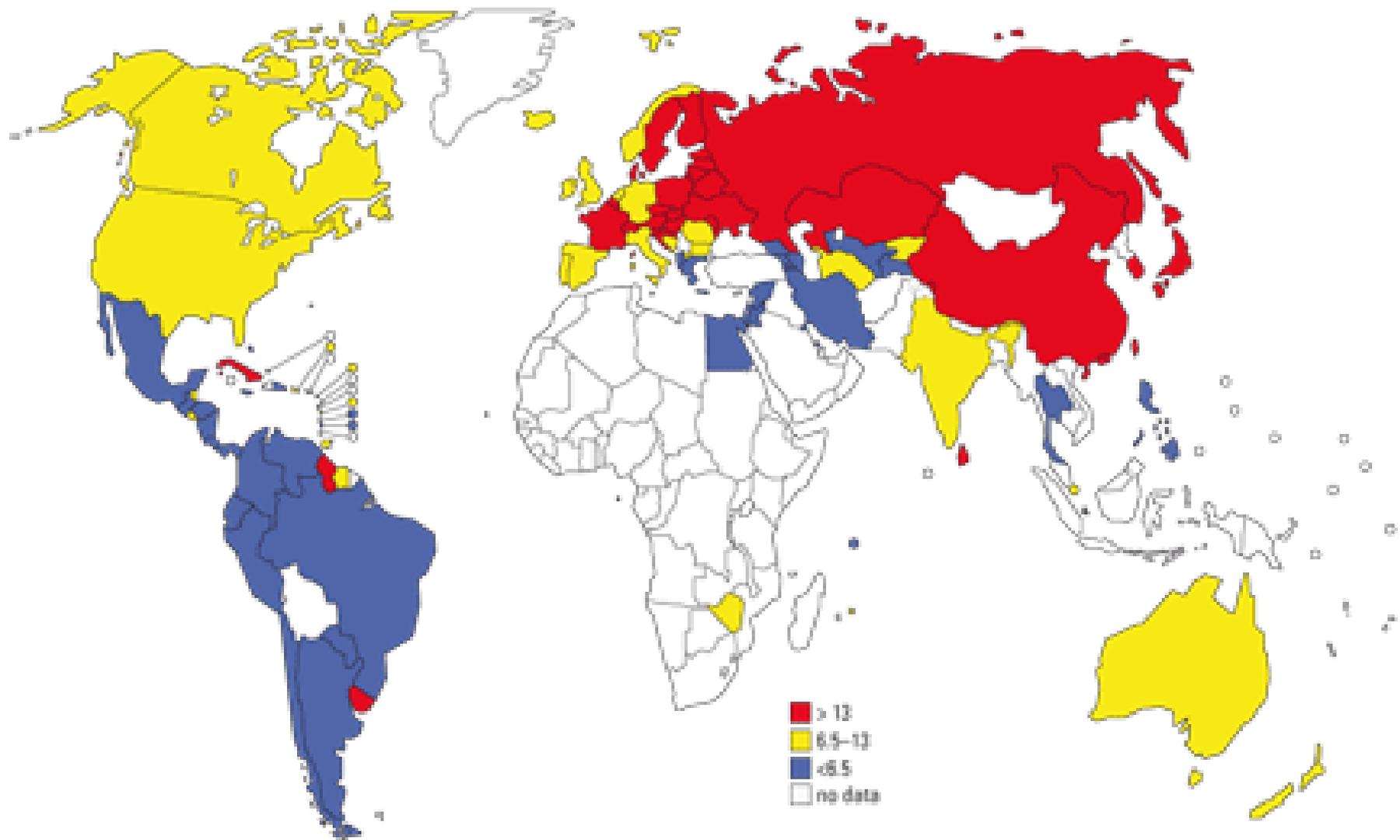
# 4. Self-Inflicted Injuries

- 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 (4<sup>th</sup> leading cause of death)
- Unsuccessful attempts are 20x as frequent
- 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
- Global suicide rates have increased 60% in the last 45 years

### Map of suicide rates (per 100 000; most recent year available as of 2007)



The designations employed and the presentation of material on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dashed lines represent approximate border lines for which there may not yet be full agreement.

WHO/06.100

# 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
- 2<sup>nd</sup> 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

$$Se = \frac{\text{\# who test positive}}{\text{\# who commit suicide}}$$

- 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

$$PPV = \frac{\# \text{ who test positive and commit suicide}}{\# \text{ who test positive}}$$

- PPV of best questionnaires: 3% (pathetic)

# Screening and Prevention

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# Summary of Lecture 3

## ■ 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

# Assignments Due Next Time

- Project Task 1