Mortality in HIV Infection: Monitoring Quality Outcomes

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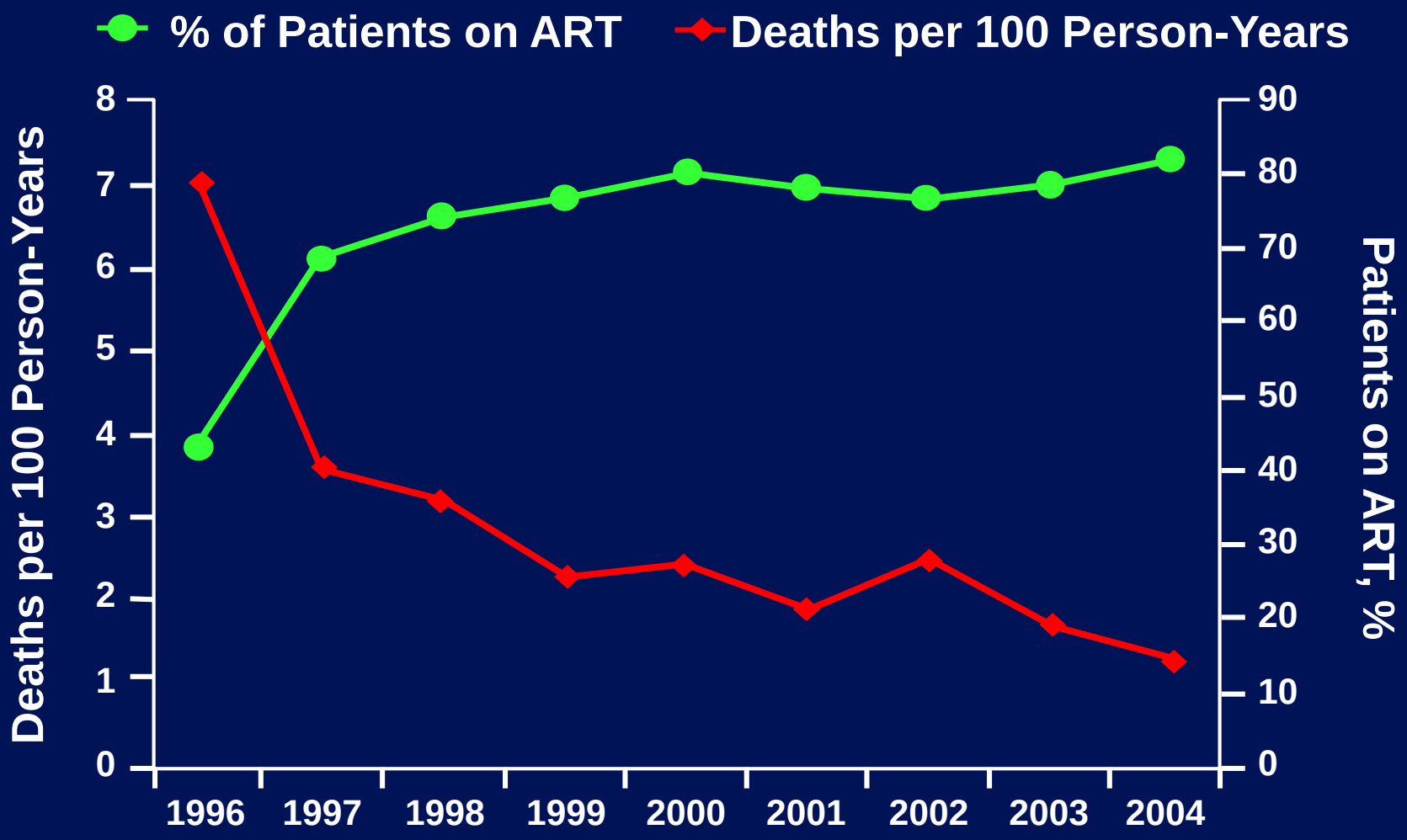
Outline

- Historical Trends in HIV Mortality
- HIV Mortality in the Current Era
- Health Disparities and Mortality
- Measuring Mortality in Clinical Programs

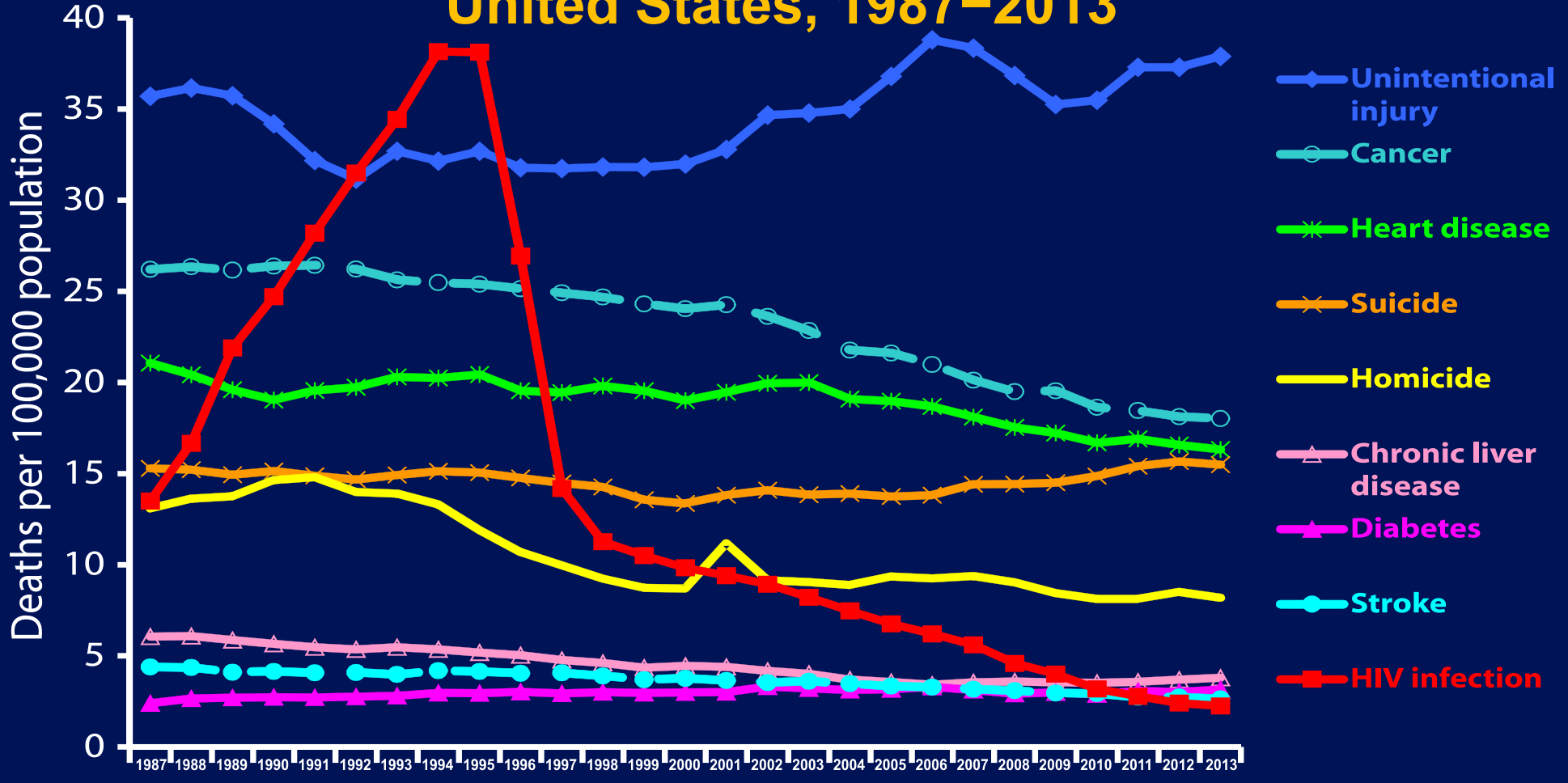
Historical Trends in HIV Mortality

Effect of ART on Mortality Over Time



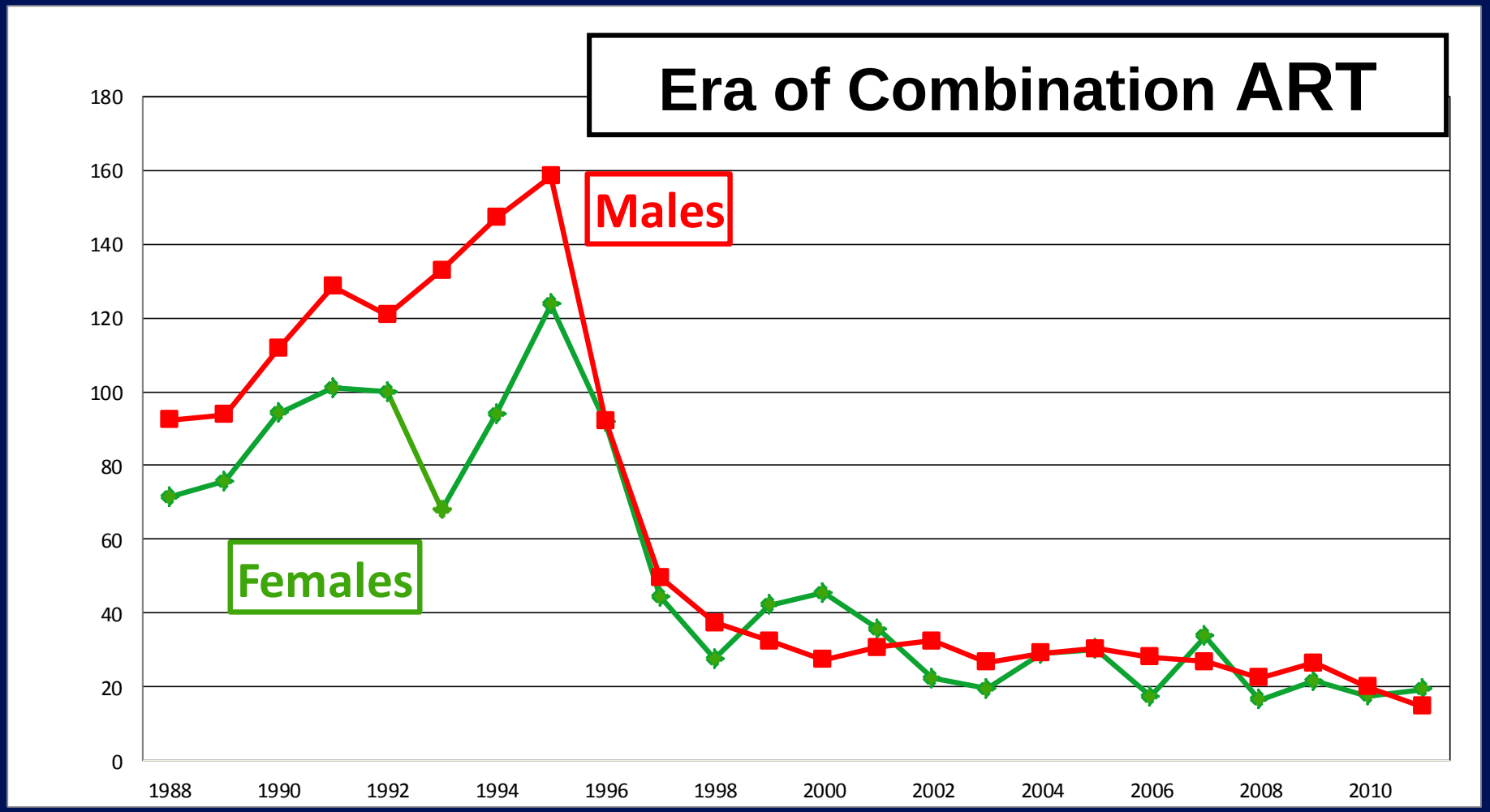
Palella FJ et al. J Acquir Immune Defic Syndr. 2006;43(1):27-34.

Trends in Annual Rates of Death due to the 9 Leading Causes among Persons 25–44 Years Old, United States, 1987–2013



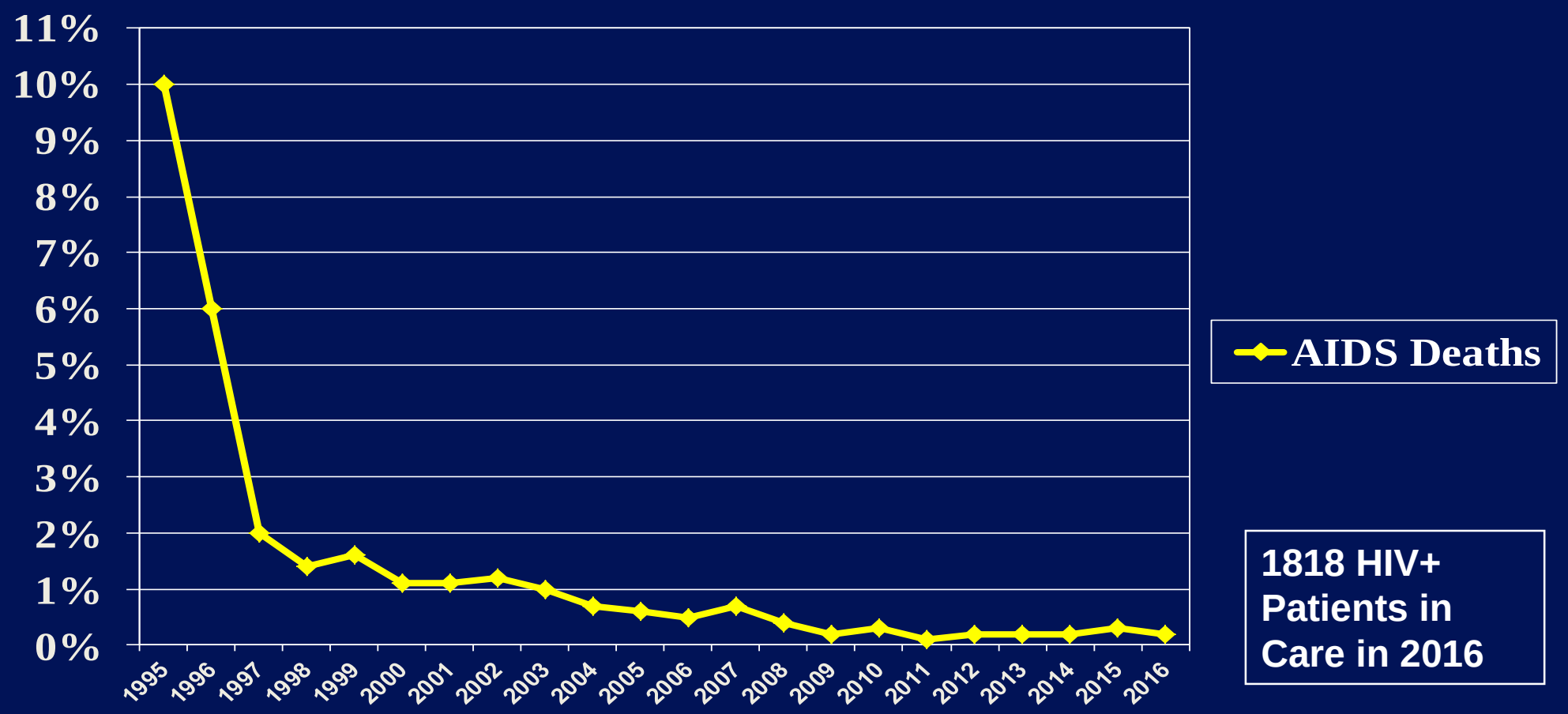
www.cdc.gov

Deaths per 1000 Persons Living with HIV in Colorado, 1988-2011



Source: CDPHE

University of Colorado HIV Clinical Program: AIDS Deaths, 1995-2016

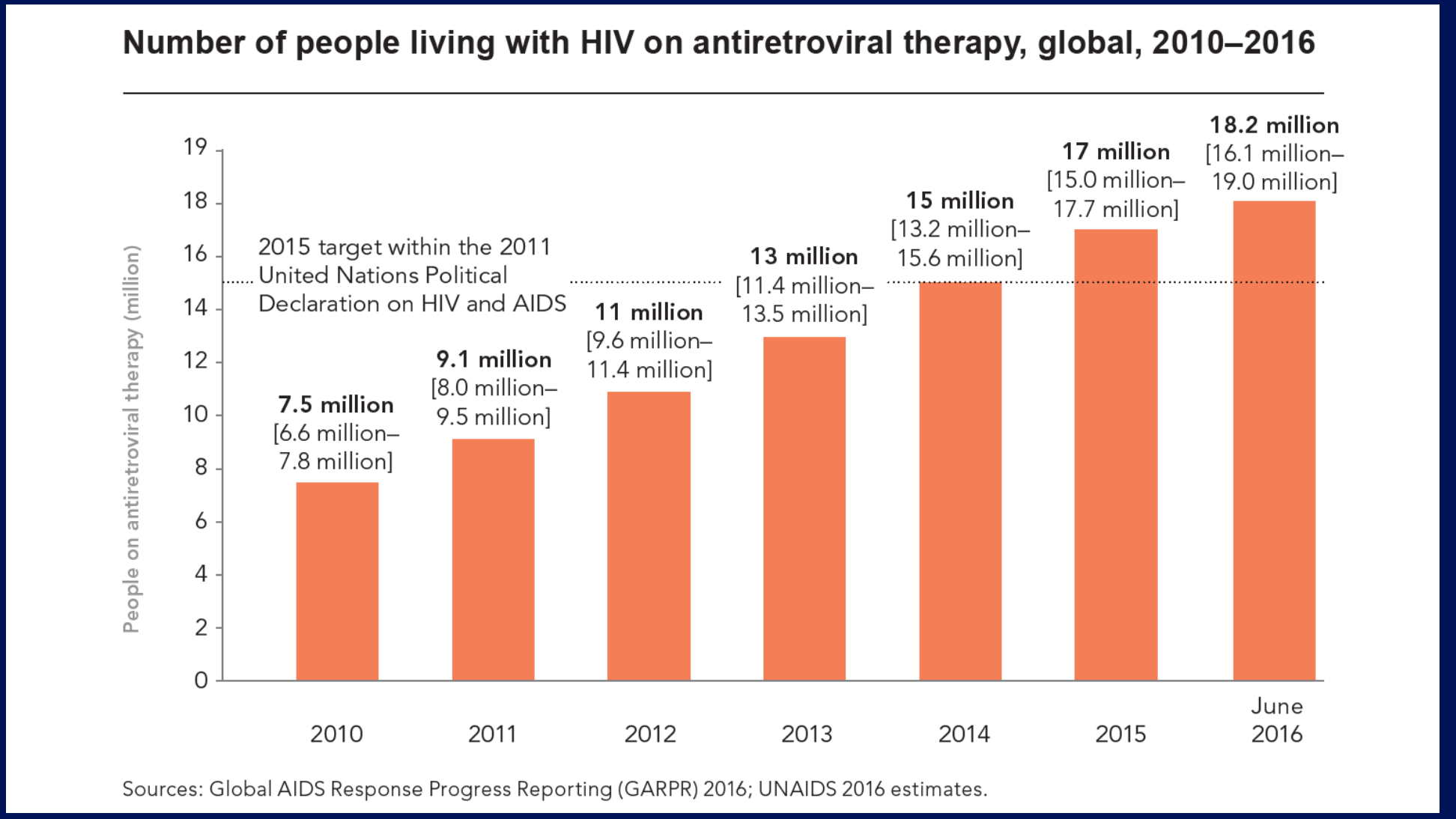


3 Million Years of Life Saved

- Attempt to quantify mortality impact of ART and OI prophylaxis from 1989-2003
- Defined eras of treatment relative to OI prophylaxis, ART, and prevention of mother-to-child transmission
- The model estimated the survival benefit of treatment in each era
- As of 2003 in the U.S., the cumulative survival benefit of HIV treatment estimated at 2,951,371 years of life

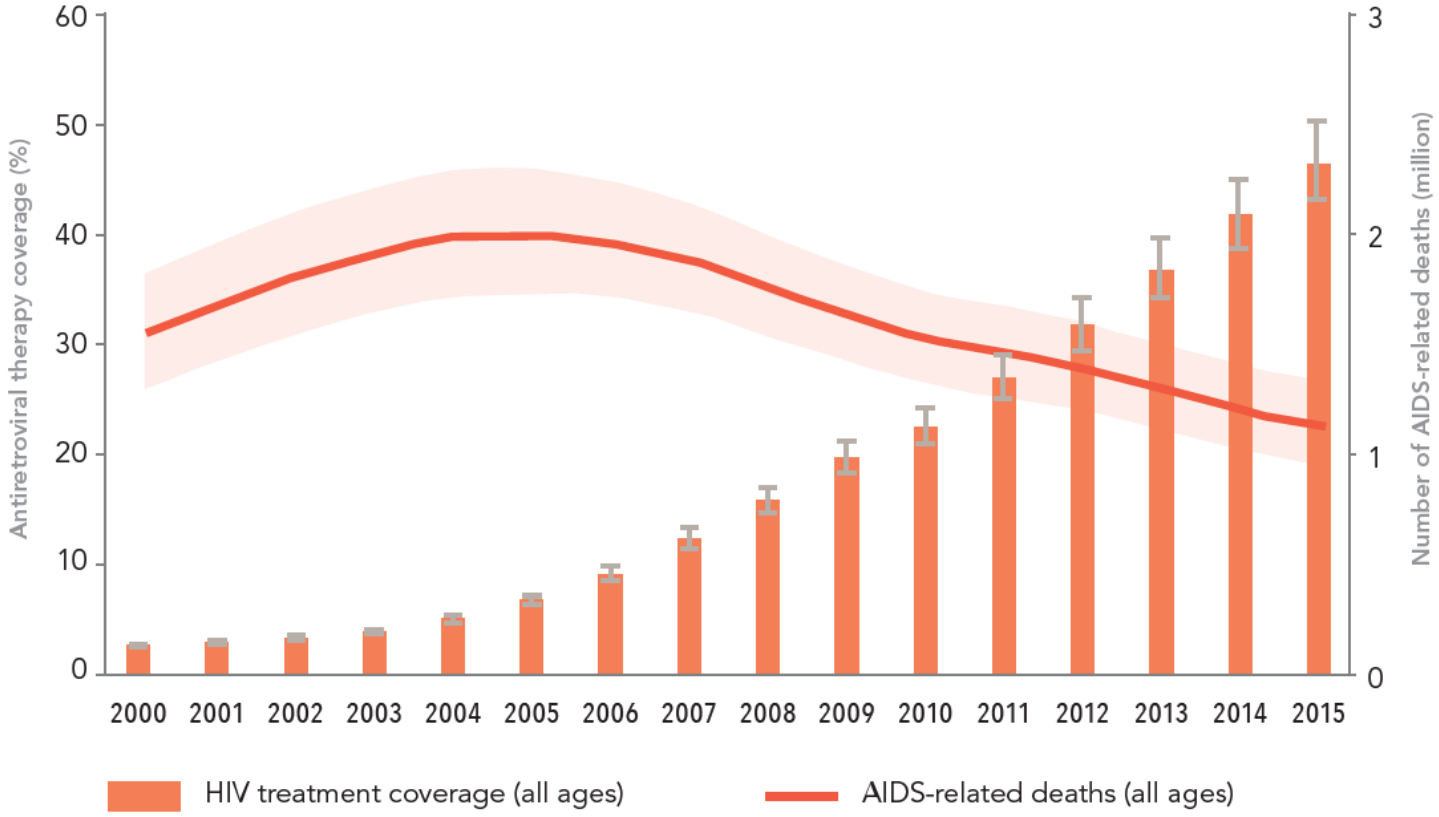
Walensky R, et al. JID 2006;194:11-19

Global ART Coverage



Global ART Coverage and Mortality

Antiretroviral therapy coverage and number of AIDS-related deaths, global, 2000–2015



Sources: GARPR 2016; UNAIDS 2016 estimates.

HIV Mortality in the Current Era

D:A:D Study

- Data Collection of Adverse Events of Anti-HIV Drug Study
- Collaboration of 11 cohorts following HIV+ individuals in 212 clinics in 21 countries in Europe, U.S., and Australia
- Data collection at enrollment and at least every 8 months after

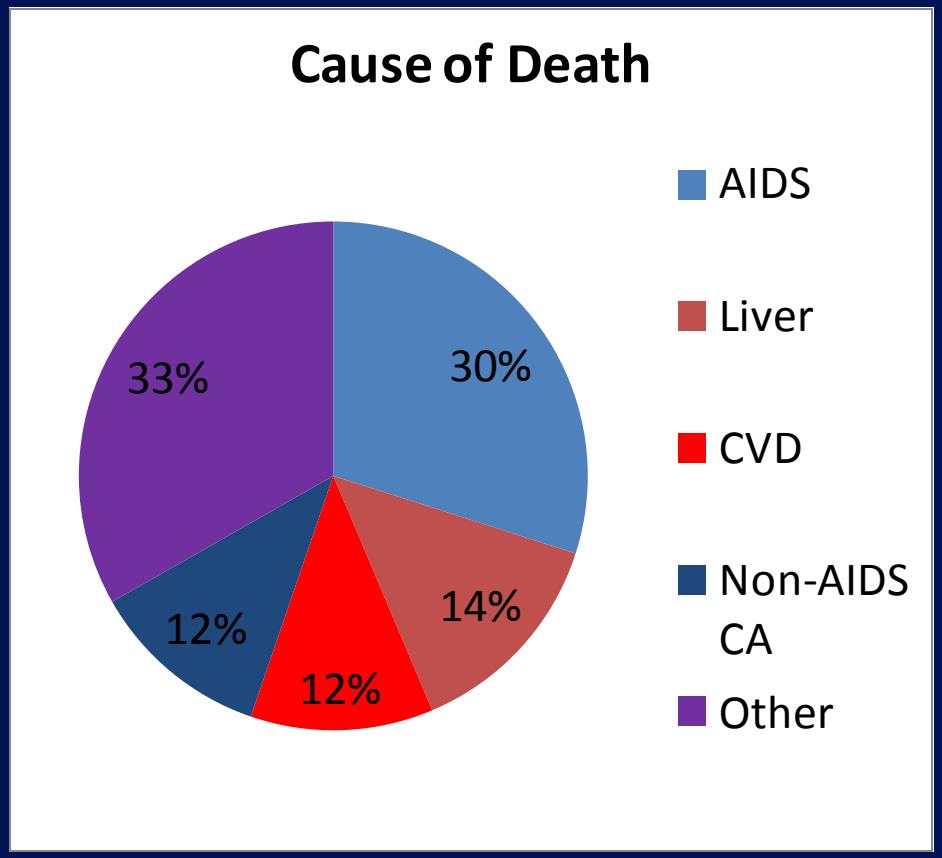
AIDS 2010;24:1537-1548

CoDe Classification System

- Uniform coding system for cause of death
- Detailed data collection form at local site on cause of death and contributing factors
- Centralized review process with at least 2 independent reviewers
- Established process for managing differences of opinion
- Codes used for cause of death are adapted from ICD-10

AIDS 2010;24:1537-1548

Causes of Death in the D:A:D

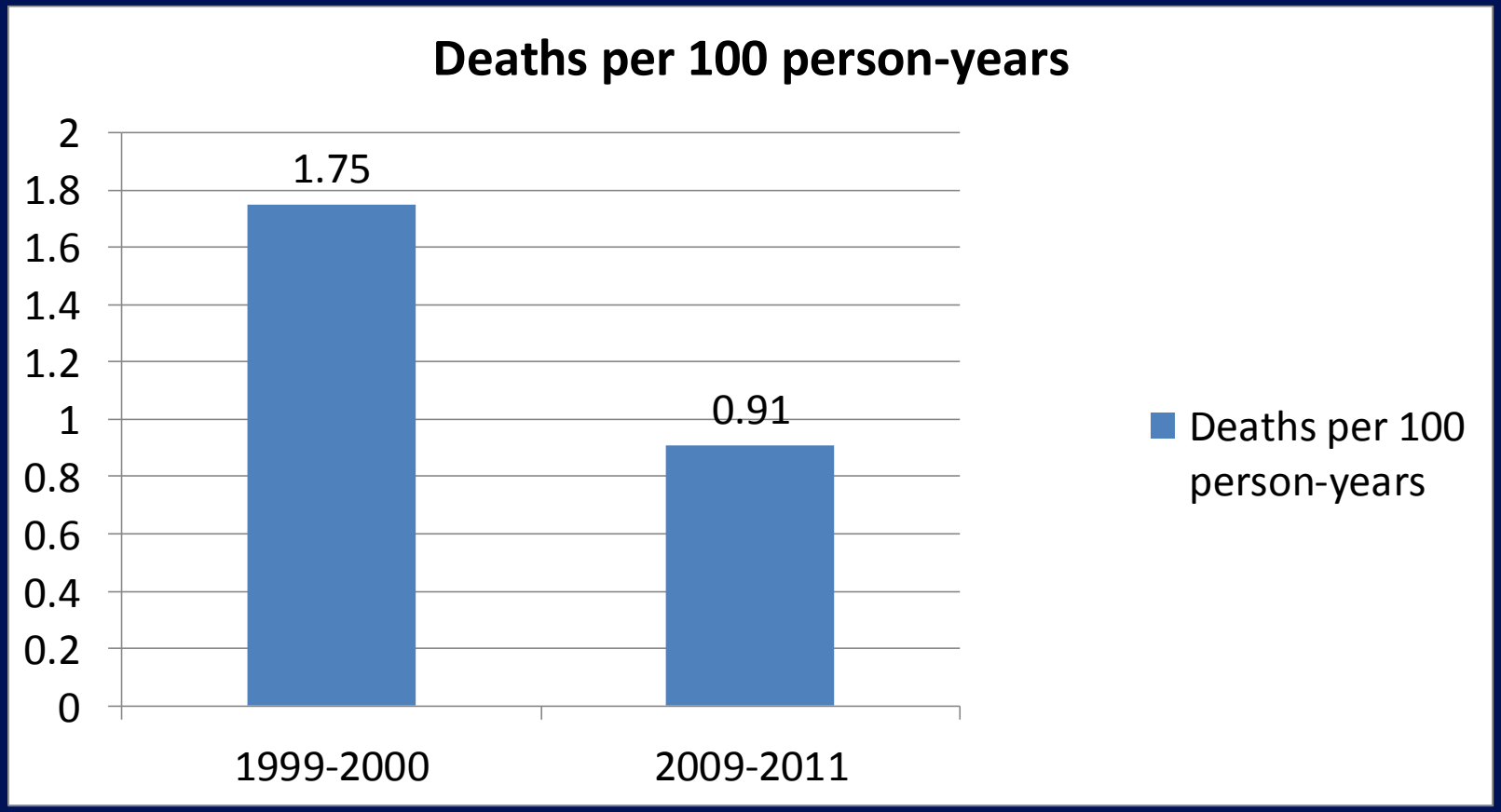


Other

- Suicide (3.9%)
- Drug OD (2.5%)
- Euthanasia (0.2%)
- Homicide (0.6%)
- Accident (1.5%)
- Invasive bacterial infection (6.7%)
- Lactic acidosis (0.6%)
- Pancreatitis (0.7%)
- Renal dysfunction/disease (1.2%)
- Other (10%)
- Unknown (5.3%)

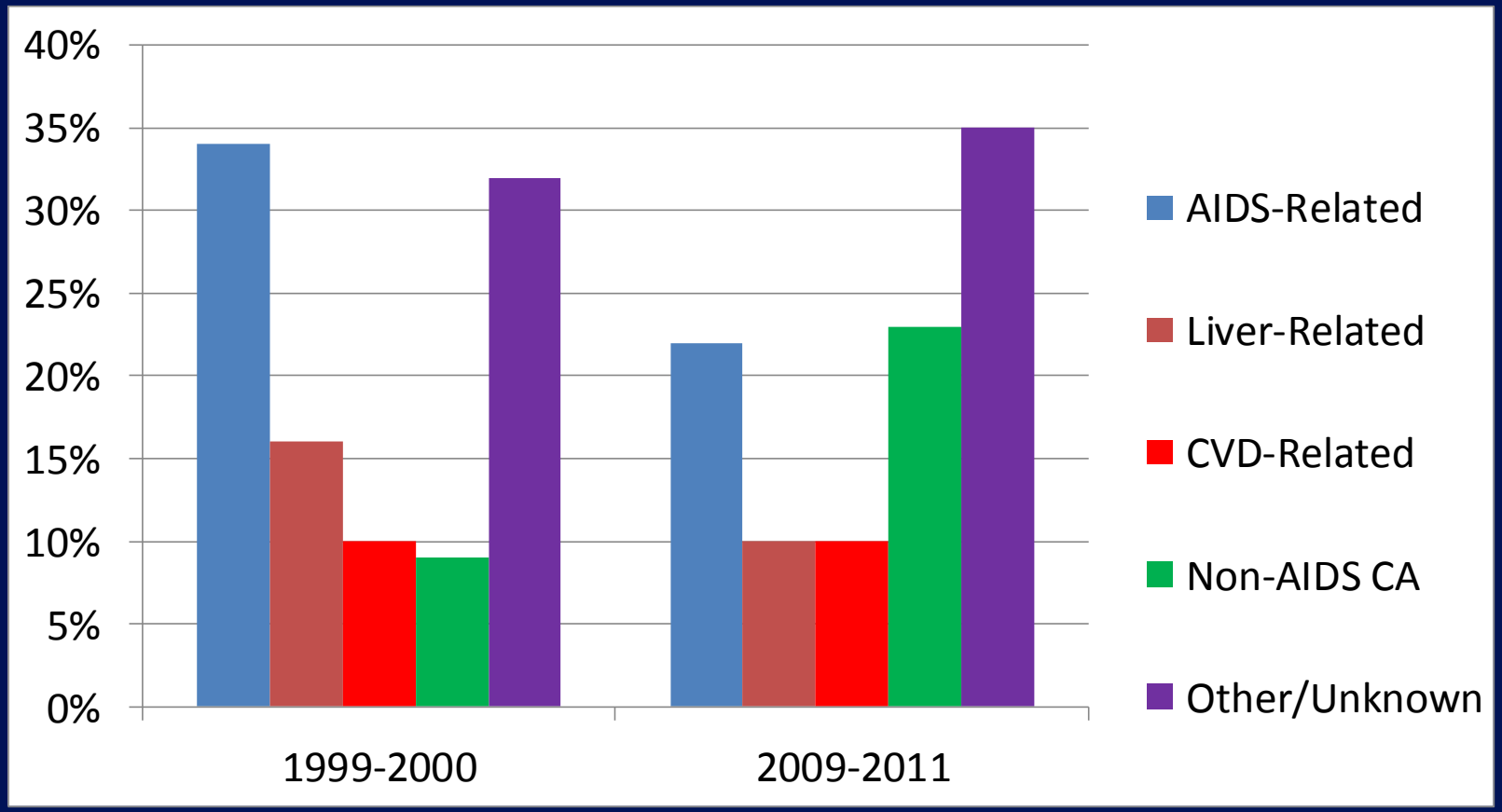
AIDS 2010;24:1537-1548

Trends in Causes of Death in Persons with HIV, 1999-2011 in D:A:D



Smith C, et al. Lancet 2014;384:241-248

Trends in Causes of Death in Persons with HIV, 1999-2011 in D:A:D



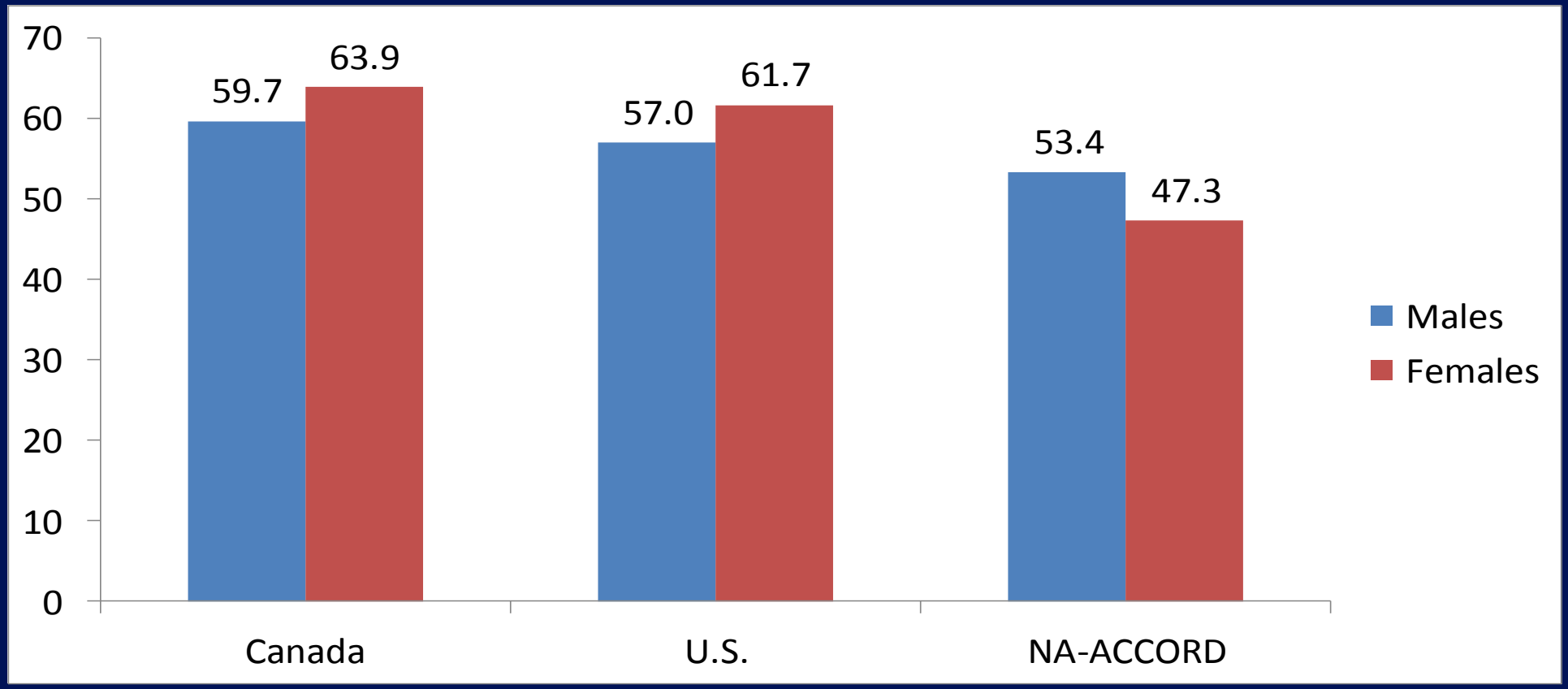
Smith C, et al. Lancet 2014;384:241-248

Life Expectancy from Age 20 in Patients Starting Antiretroviral Therapy

- NA-ACCORD: multicenter study involving cohorts in the U.S. and Canada.
- Current study evaluated a subset of patients ≥ 20 years old, on ART, and evaluated between 2000 and 2007.
- Life expectancy estimated for cohort as well as subsets of patients based on sex, race, transmission category, and baseline CD4 count.
- 1622 deaths occurred during 82,022 person-years of follow up.

Samji H, et al. PLoS ONE 8(12): e81355

Life Expectancy in Years from Age 20 by Sex, General Population vs NA-ACCORD

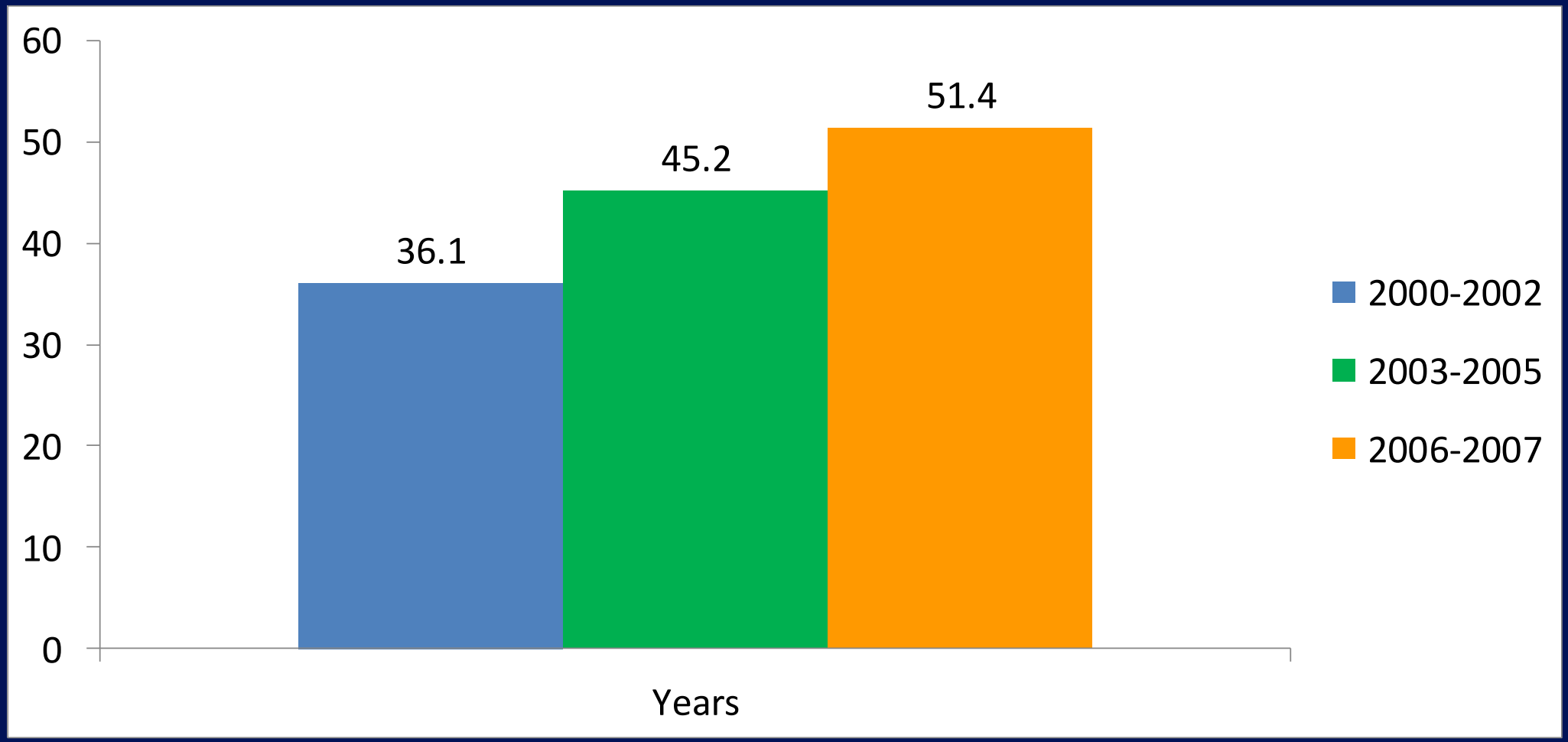


General Population 2009

HIV+ 2006-2007

Samji H, et al. PLoS ONE 8(12): e81355

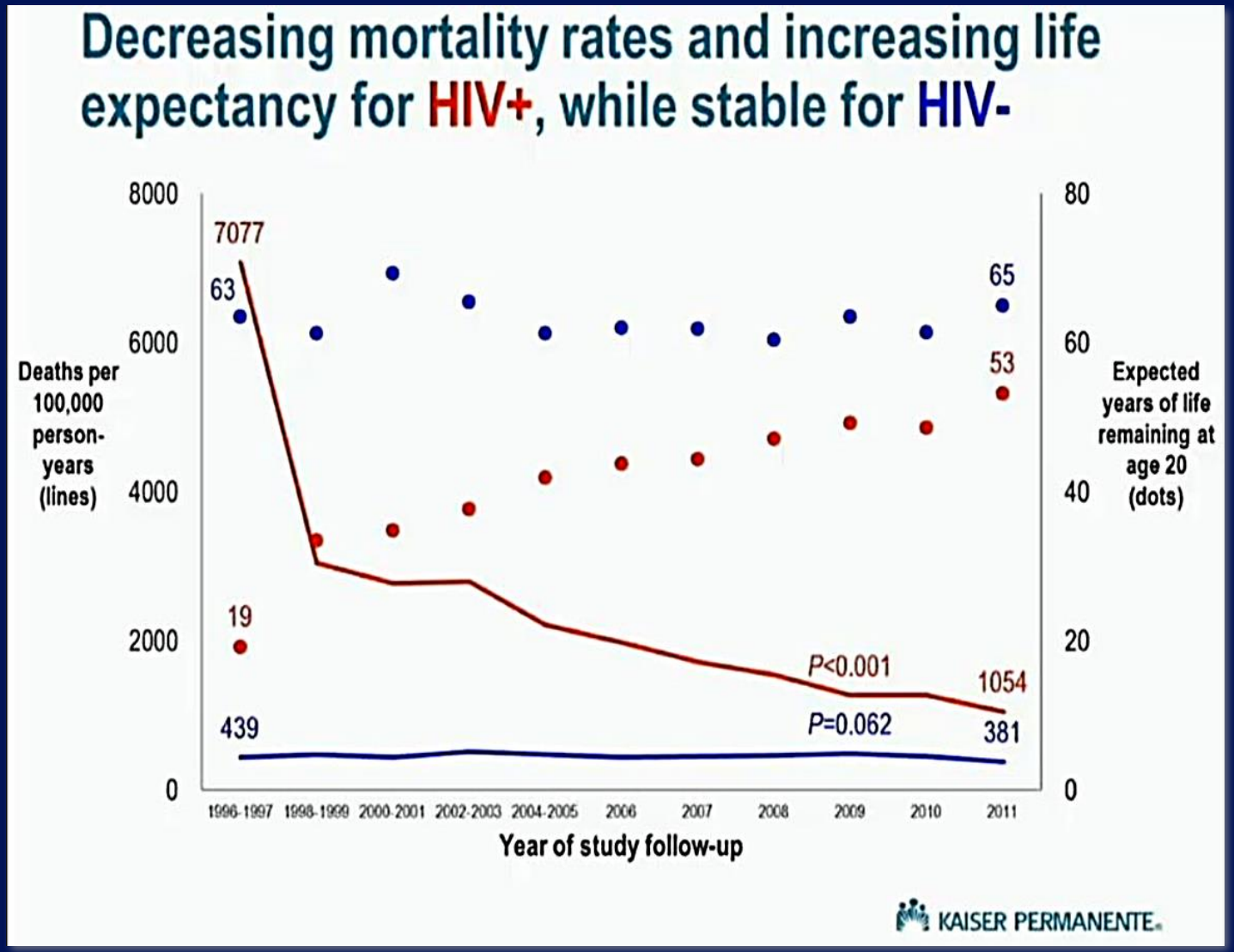
Life Expectancy from Age 20 in Patients Starting Antiretroviral Therapy



Samji H, et al. PLoS ONE 8(12): e81355

HIV+ vs. HIV- Life Expectancy- Kaiser California

- Adults receiving care at Kaiser California, HIV- to HIV+ 10:1 match for those seen between 1996-2011
- 24,768 HIV+, 257,600 HIV-, 91% male, ~25% white, ~35% ever smoked



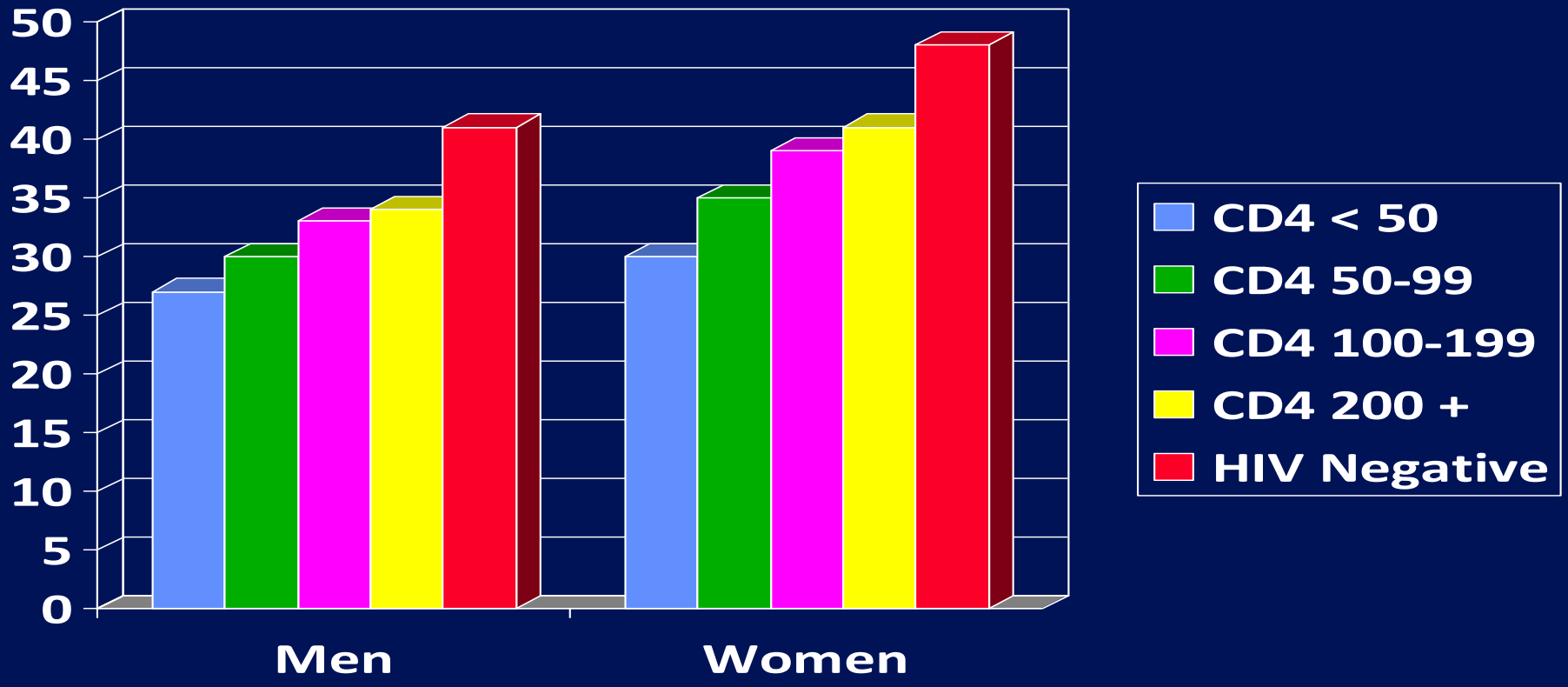
Marcus J, et al. Abstract #54, CROI 2016, Boston, Massachusetts, February 22-25, 2016

Life Expectancies of South African Adults Starting Antiretroviral Treatment: Collaborative Analysis of Cohort Studies

- Analysis of 6 South African Cohorts
- 37,740 persons initiating ART for the first time
- Estimates of mortality by linking patient records to national population register
- Survival models used to estimate excess mortality due to HIV by age, gender, and CD4 at time of initiation
- Higher life expectancies among women and in those starting ART at higher CD4 counts

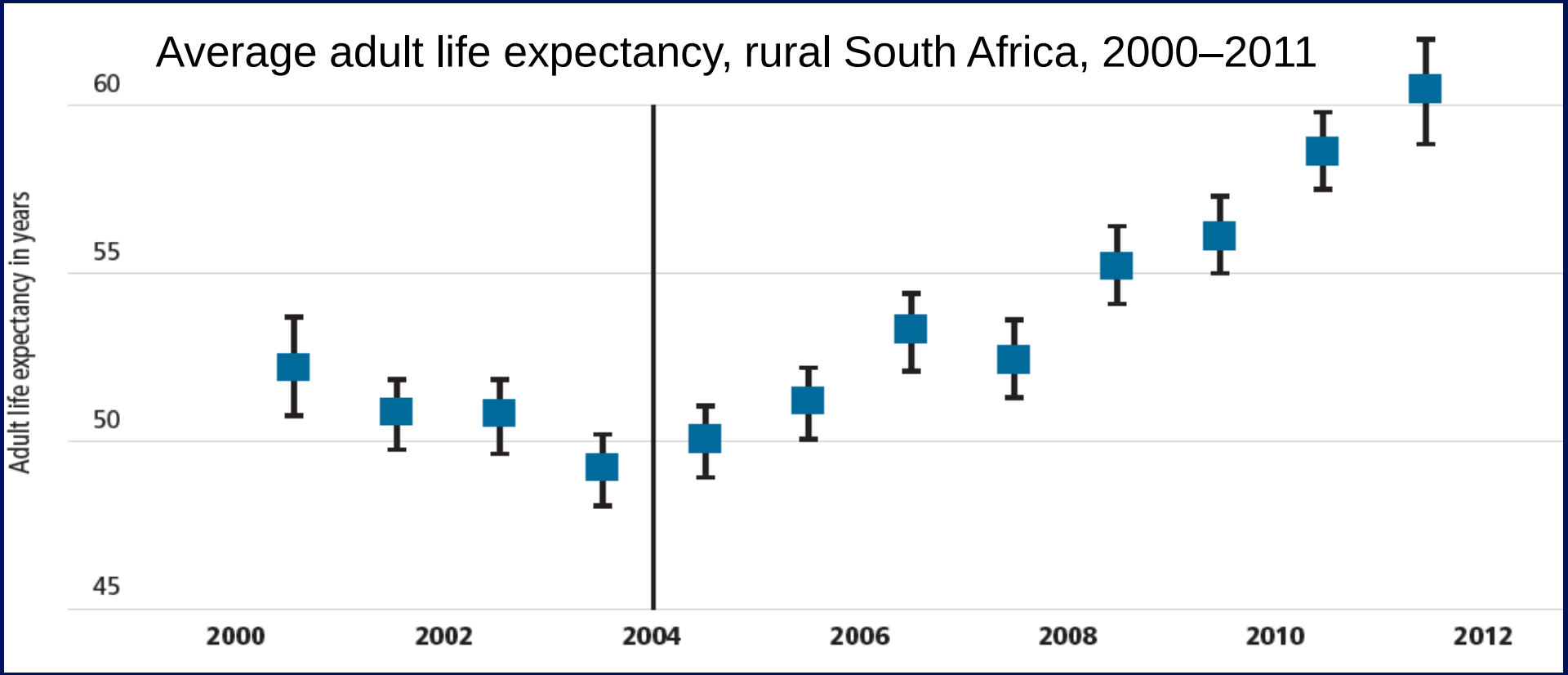
Johnson L, et al, PLOS Medicine 2013;10(4):1-11

Life Expectancy Starting ART after 2006 at age 25



Johnson L, et al, PLOS Medicine 2013;10(4):1-11

Life expectancy increase in rural South Africa



Source: Bor et al. (18). Increases in adult life expectancy in rural South Africa: valuing the scale-up of HIV treatment. Science, 2013, 339:961–965.

Factors Affecting Mortality in HIV Infection

- Immunodeficiency: CD4 nadir, current CD4 count
- HIV viremia
- When ART is started (e.g. the START Study)
- Co-morbidities
  - Hepatitis C
  - Tobacco use
  - Substance use
  - Mental illness
  - Non-AIDS CA
  - Cardiovascular disease

Factors Affecting Mortality in HIV Infection

- Undiagnosed HIV infection
- Late presentations of HIV infection
- Linkage to care
- Retention in care
- Access to care
- Adherence to ART and other therapies
- Health Disparities
- Health insurance and plans for health care reform
- Provider expertise

Viremia Copy-Years Predicts Mortality Among Treatment-Naïve HIV+ Patients

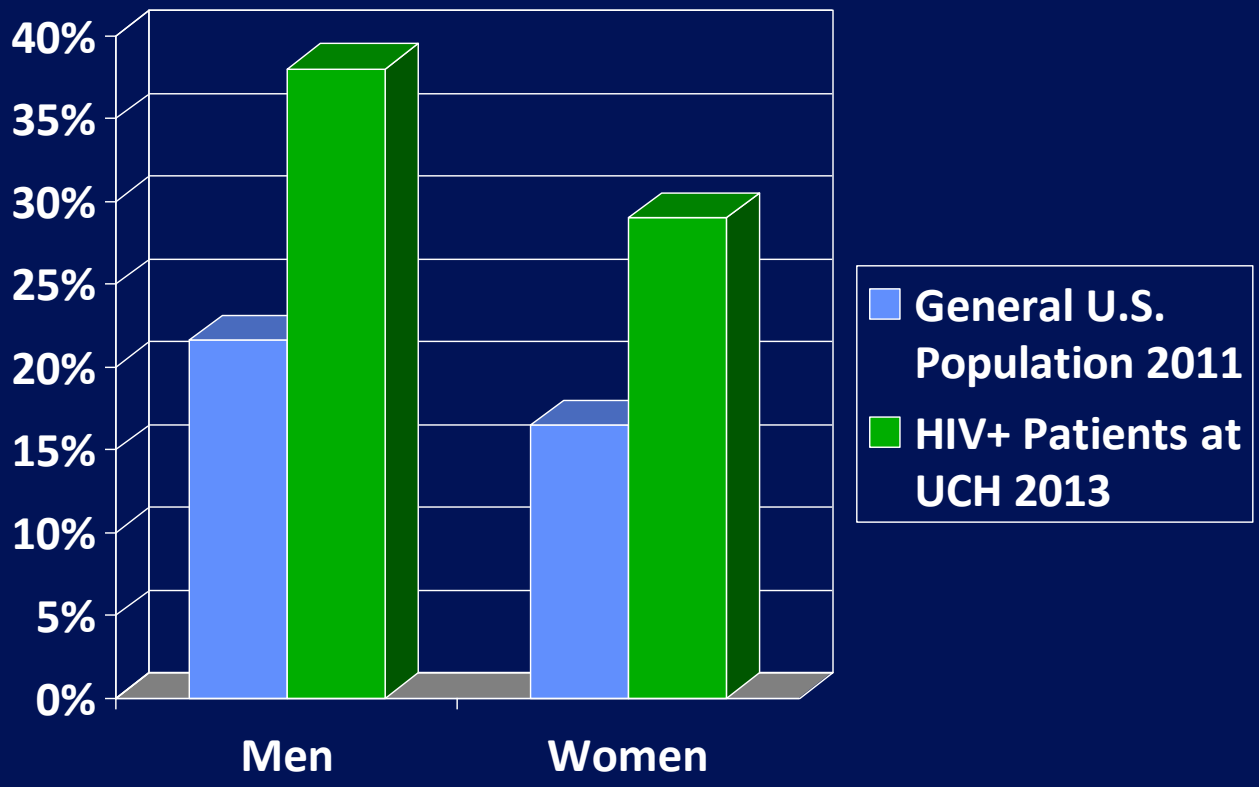
- Treatment naïve patients starting ART from 2000-2008
- Viremia copy-years, a measure of cumulative plasma HIV exposure, determined for each patient
- Viremia copy-years predicted all cause mortality independent of cross-sectional RNA and CD4 count

Mugavero M, et al. CID 2011:53:927-935

Common Co-Morbidities in HIV Infection

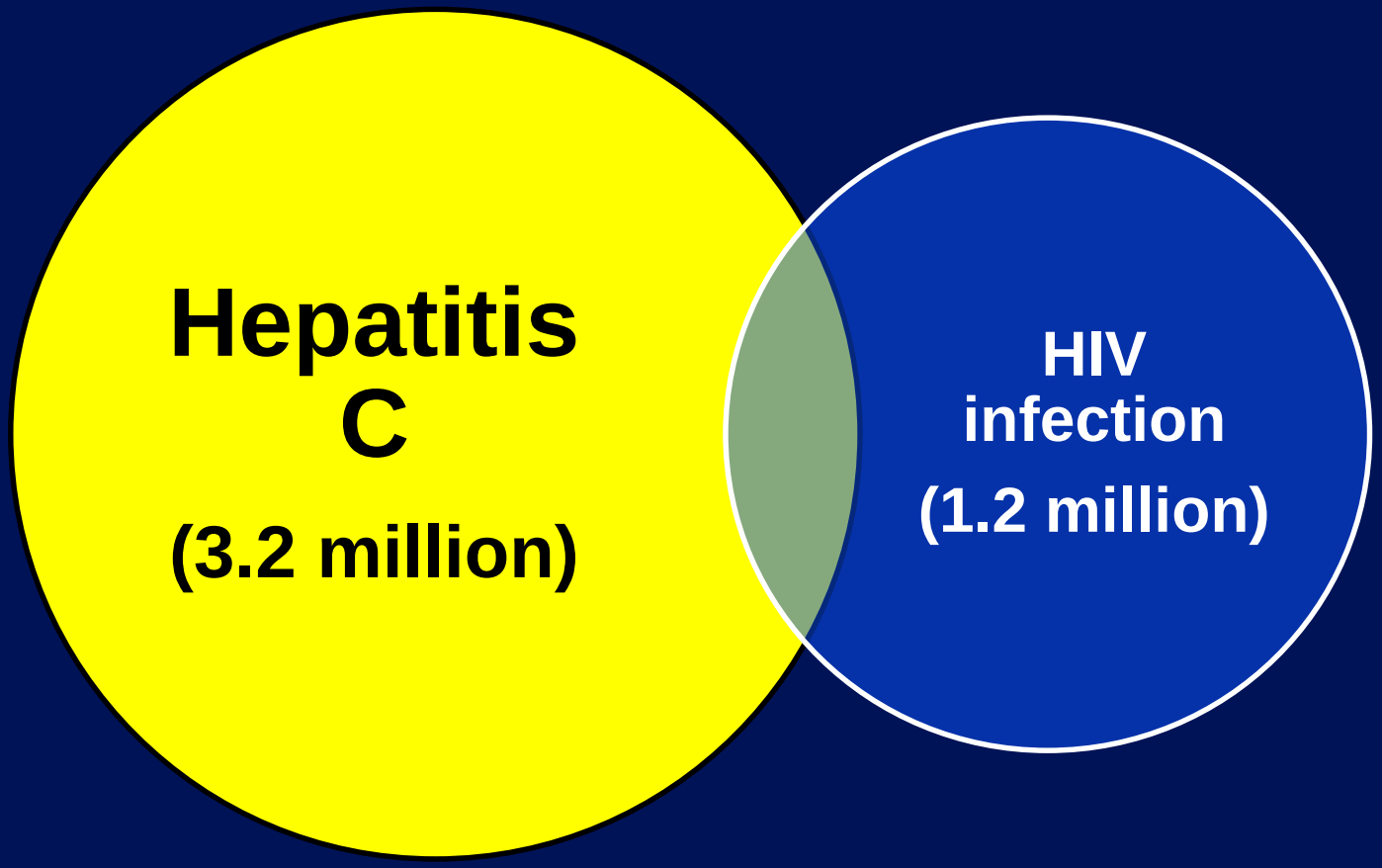
- Depression
- Bipolar Disease
- Alcohol use
- Tobacco use
- Other Drug use
- Human papillomavirus infection
- Hepatitis B
- Hepatitis C
- Syphilis
- Other STIs
- Tuberculosis
- Hyperlipidemia
- Diabetes mellitus
- Hypertension
- Heart disease
- Osteoporosis
- Non-AIDS cancers

HIV+ Patients Smoke More than the General U.S. Population



- Morbidity and Mortality Weekly Report 2012;61(44):889–94
- SBIRT Screening Data, Danielle Osowski, IDGP at UCH

HIV and Hepatitis C in the U.S.



150,000 – 300,000 Co-infected Patients

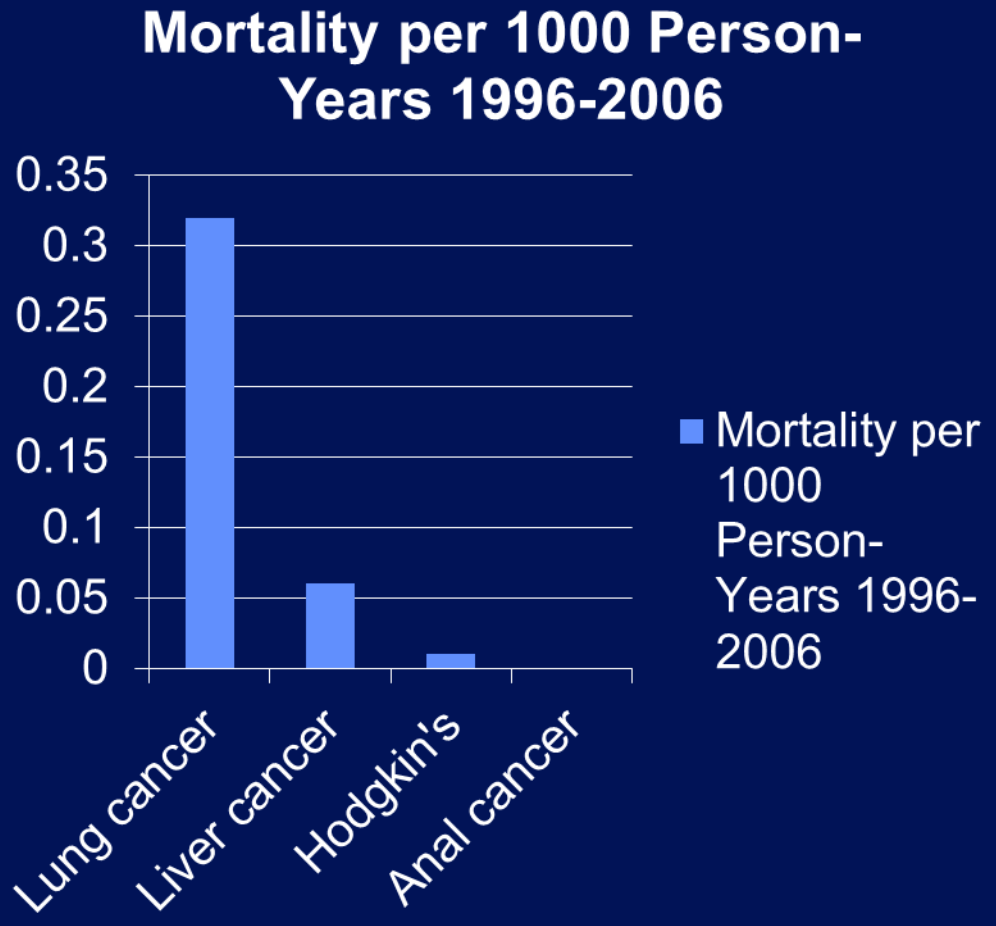
Incidence of Non-AIDS Cancers among HIV + Persons Compared to General U.S. Population

Type of Cancer	Standardized Rate Ratio	95% CI
Anal Cancer	42.9	34.1 - 53.3
Vaginal Cancer	21	11.2 - 35.9
Hodgkin's Lymphoma	14.7	11.6 – 18.2
Liver Cancer	7.7	5.7 – 10.1
Lung Cancer	3.3	2.8 – 3.9
Melanoma	2.6	1.9 – 3.6
Oropharyngeal Cancer	2.6	1.9 - 3.4
Leukemia	2.5	1.6 - 3.8
Colorectal Cancer	2.3	1.8 – 2.9
Renal Cancer	1.8	0.4 – 0.8

Patel P, et al. Ann Intern Med 2008;148:728-736

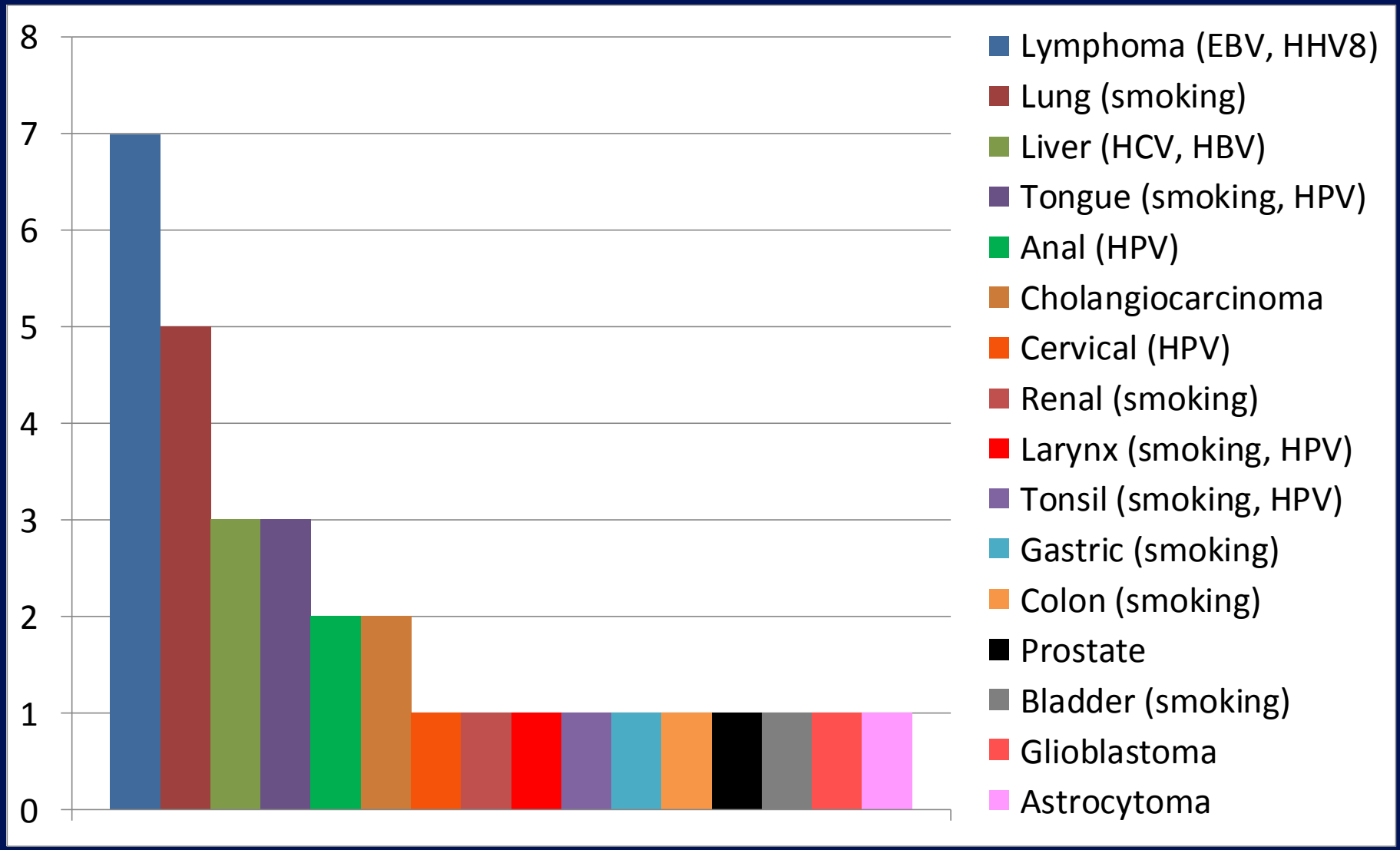
Cancer as a cause of death among people with AIDS in the United States

- Evaluation of cancer deaths in a U.S. cohort of 83,282 persons with AIDS
- NHL was the most common cause of cancer death
- Lung cancer was the most common non-AIDS cancer

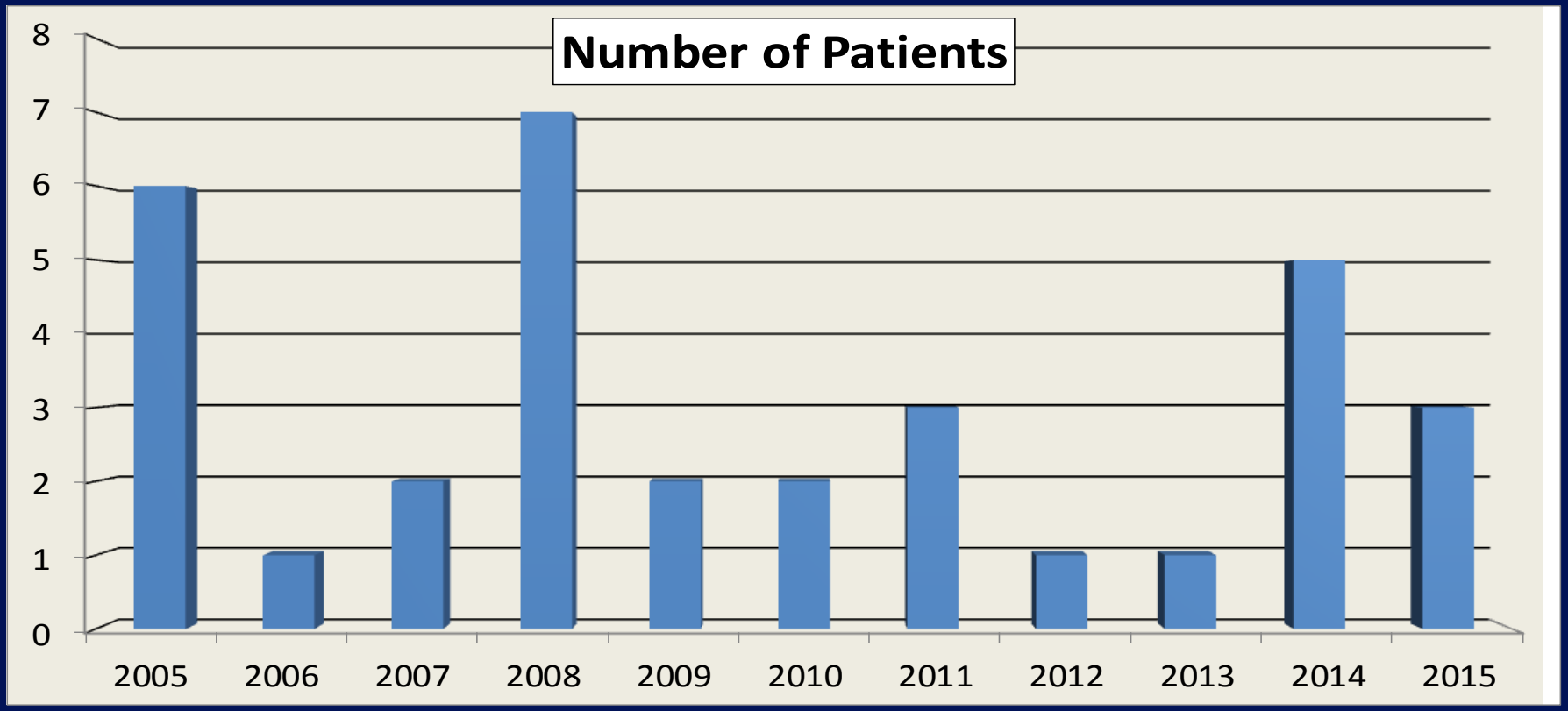


Simard E and Engels E. CID 2010;51:957-962

University of Colorado: Malignancy as a Cause of Death, 2010-2015; 32 cancer deaths out of 100 total deaths

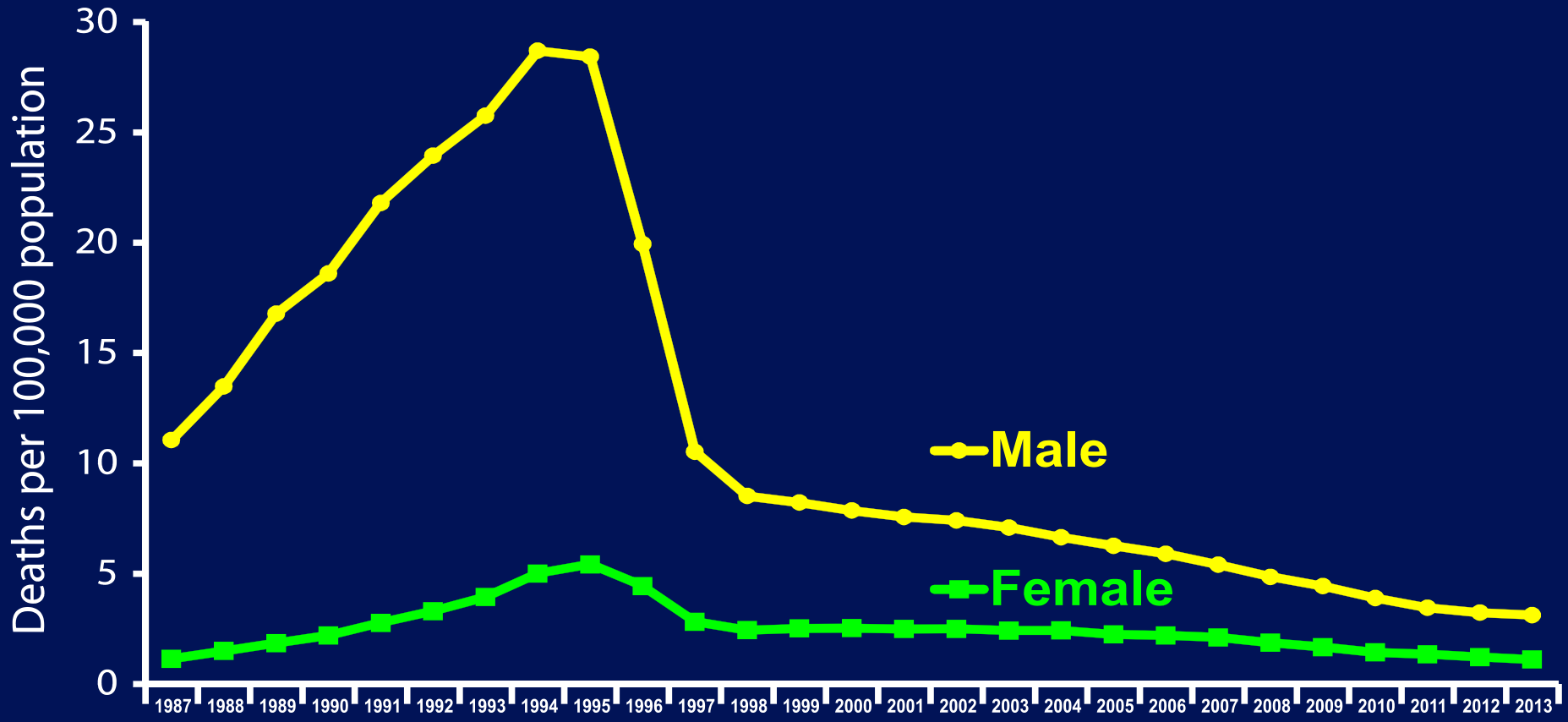


Patients Presenting to the University of Colorado Hospital with PCP and a New HIV Diagnosis, 2005-2015



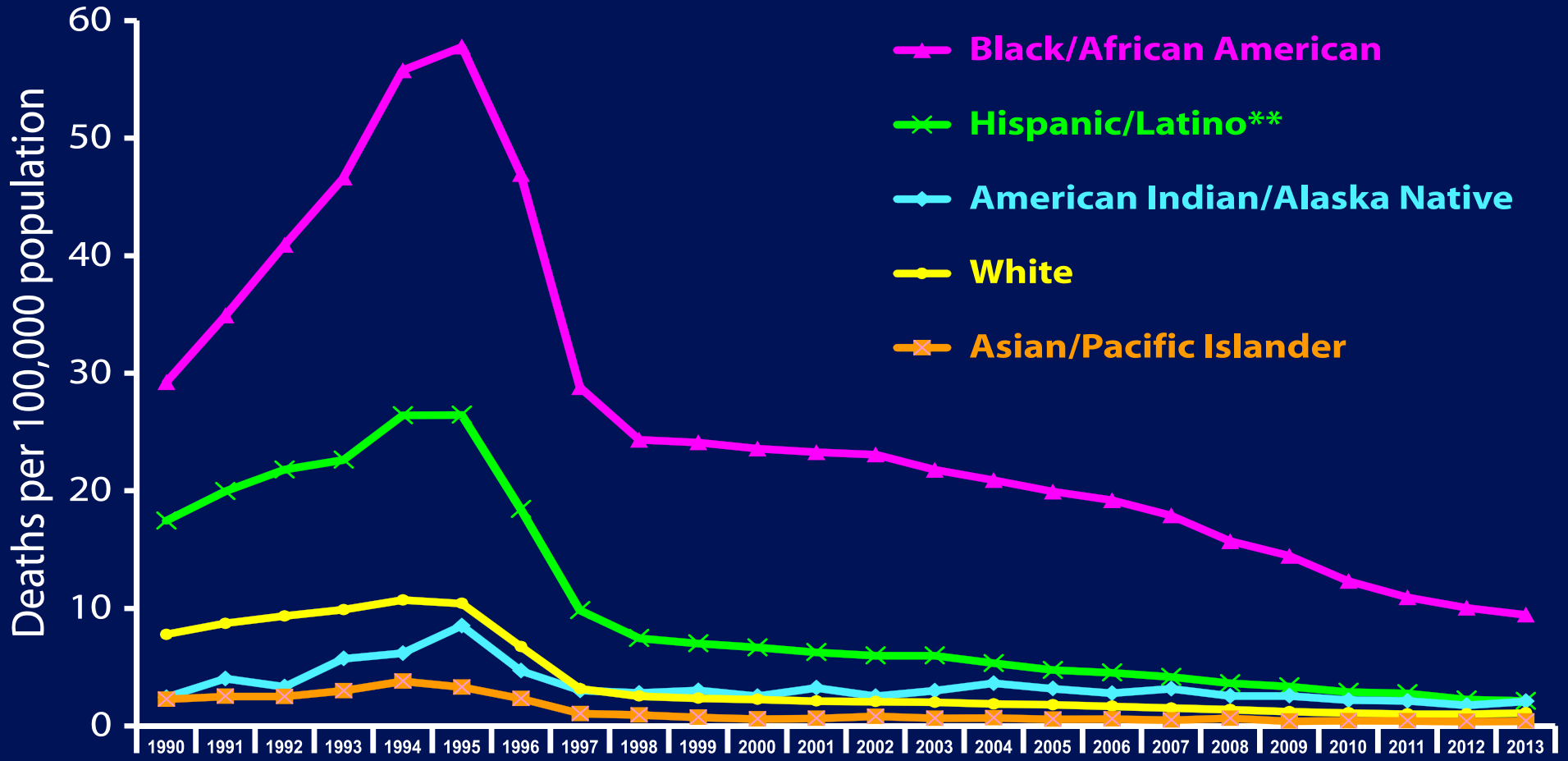
Health Disparities and Mortality

Trends in Annual Age-Adjusted Rate of Death Due to HIV Infection by Sex, United States, 1987–2013



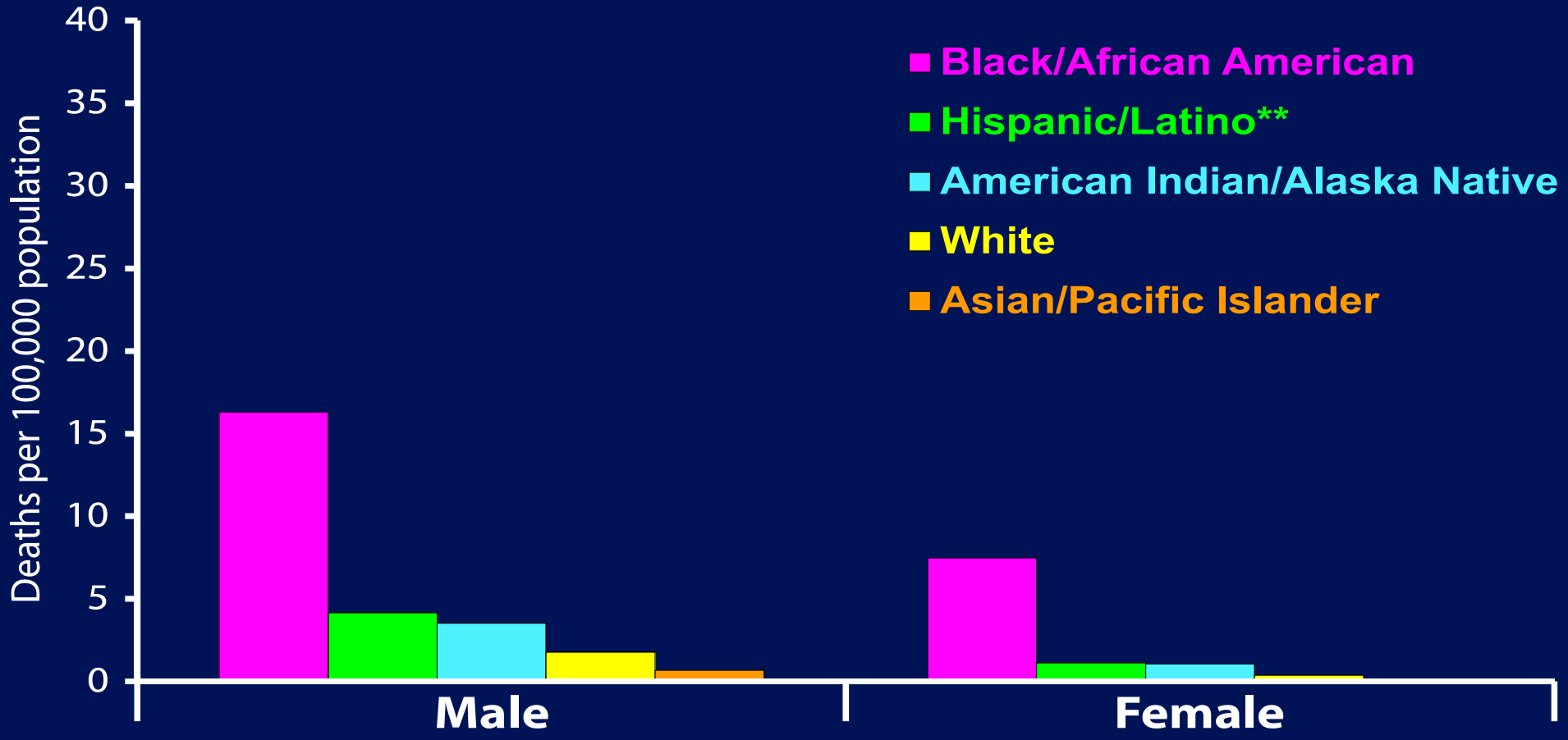
www.cdc.gov

Trends in Age-Adjusted* Annual Rates of Death due to HIV Infection by Race/Ethnicity, United States, 1990–2013



www.cdc.gov

Age-Adjusted* Average Annual Rate of Death due to HIV Infection by Sex and Race/Ethnicity, United States, 2009–2013

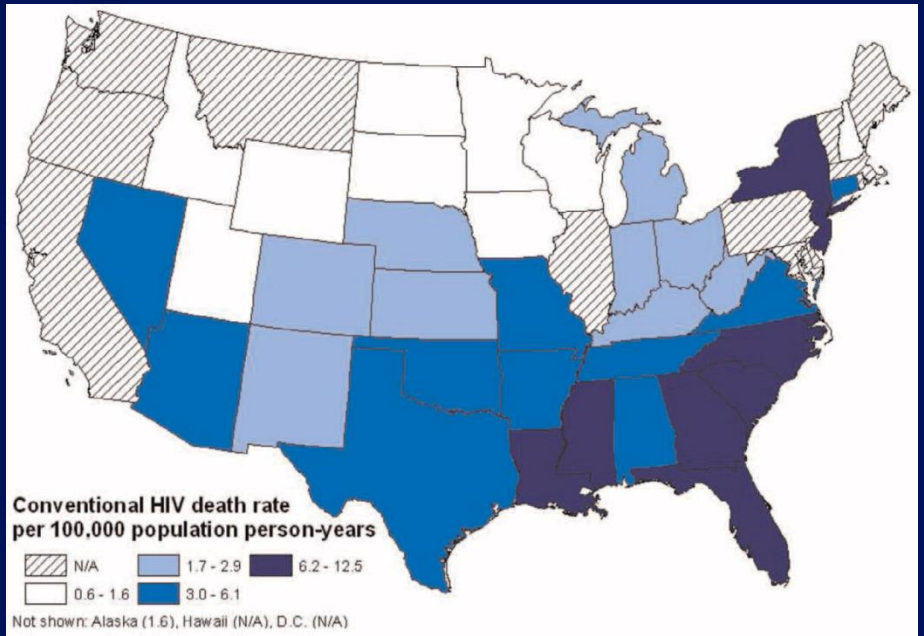


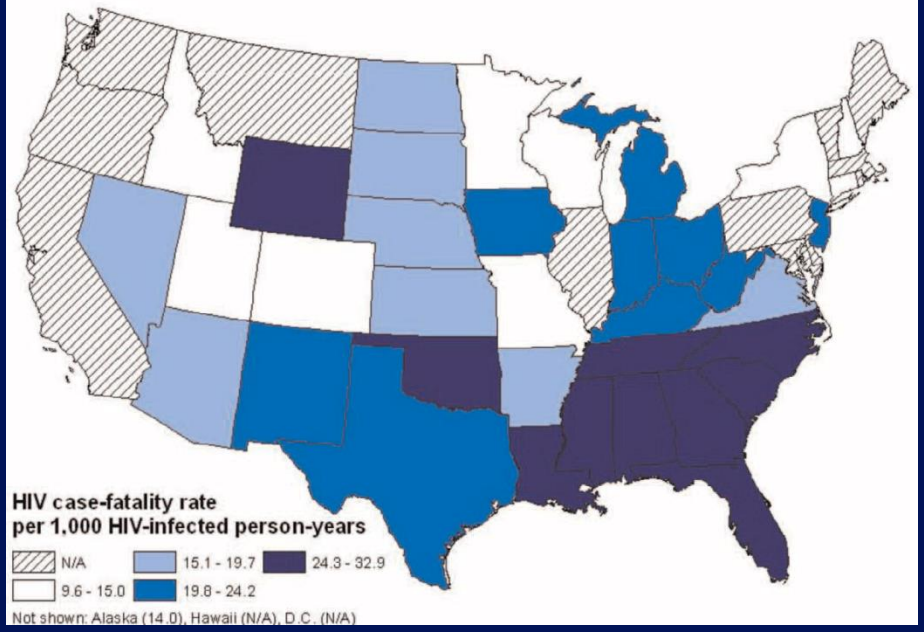
www.cdc.gov

Disparities Among States in HIV-Related Mortality

- Cross-sectional analysis of deaths due to HIV in the National Vital Statistics System in relationship to reported HIV/AIDS cases in 37 states, 2001-2007
- HIV Case-Fatality rates calculated and compared across states

Hanna et al. AIDS 2011; epub ahead of print.





Hanna et al. AIDS 2011;
epub ahead of print.

Measuring Mortality in Clinical Programs

Case Summary

- 49 year old male with HIV/AIDS, prior PML with residual disability, seizure disorder, depression, and chronic pain
- HIV infection under excellent control on TDF/FTC and ritonavir/atazanavir
  - CD4 660 with HIV viral load of 0 in March of 2016
- Management of pain included oxycodone, ibuprofen, and gabapentin
- 3/21/16: presents for routine follow up. Mood stable. Oxycodone 5 mg #30 refilled

Case Summary

- 4/23/16: Refill request for oxycodone 5 mg #30 and dispensed on 4/26/16
- 5/5/16: I was contacted by the Coroner:
  - Patient found dead in his apartment.
  - No evidence of foul play.
  - Found on bed.
  - Burner on stove still going.
  - No suicide note.
  - Coroner unaware of recent oxycodone refill.
  - After my discussion, search of the apartment found an empty bottle of oxycodone.

Case Summary

- 5/5/26: Preliminary cause of death determined to be an overdose, either intentional or unintentional.
- Provider and mother very surprised by this event.
- The patient had been stable regarding mood, looking forward to several upcoming events.
- 11/23/16: Contacted by the Coroner.
  - Toxicology: levels of oxycodone were potentially in toxic range although not dramatically high
  - Autopsy findings: diffuse pneumonia
  - Coroner’s cause of death : Respiratory failure from bacterial pneumonia

HIVQUAL Survey-2011

- Do you currently measure mortality in your HIV program? 11 yes, 7 no
- Methodology
  - Review of Death Records = 3
  - Phone calls to patients who are LTF = 9
  - Check with death registries = 4
  - Medical record audits = 6
  - Autopsies infrequent
- Concerns about accuracy and feasibility

Potential Use of Mortality Data

- Compare performance between HIV programs.
- Provide individual programs with data for internal analysis and development of local quality improvement initiatives.
- Analyze aggregate outcomes data to determine the importance of existing measures and aid in the development of new measures.
- Use aggregate outcomes data as a tool to advocate for ongoing support of RW programs.

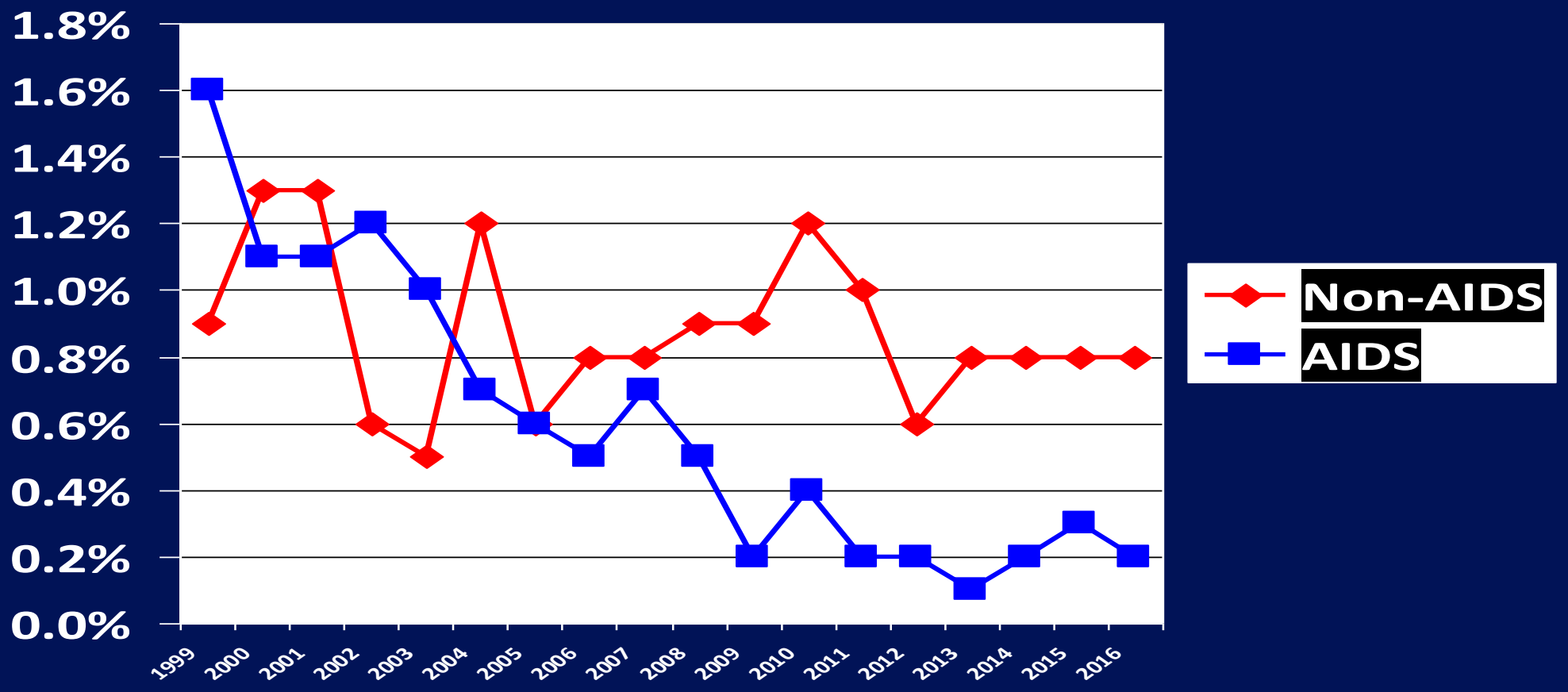
Potential Issues with Using Mortality As A Measure

- Programs will vary based on the patient population and underlying co-morbidities.
- Defining when a patient is in care and a death is attributable to the program can be difficult.
- Ascertaining cause of death can be difficult (autopsies are uncommon).
- Outcomes may be unknown for patients not retained in care (lost to follow up).
- Small programs may have variations in mortality from year to year that may not be related to quality.

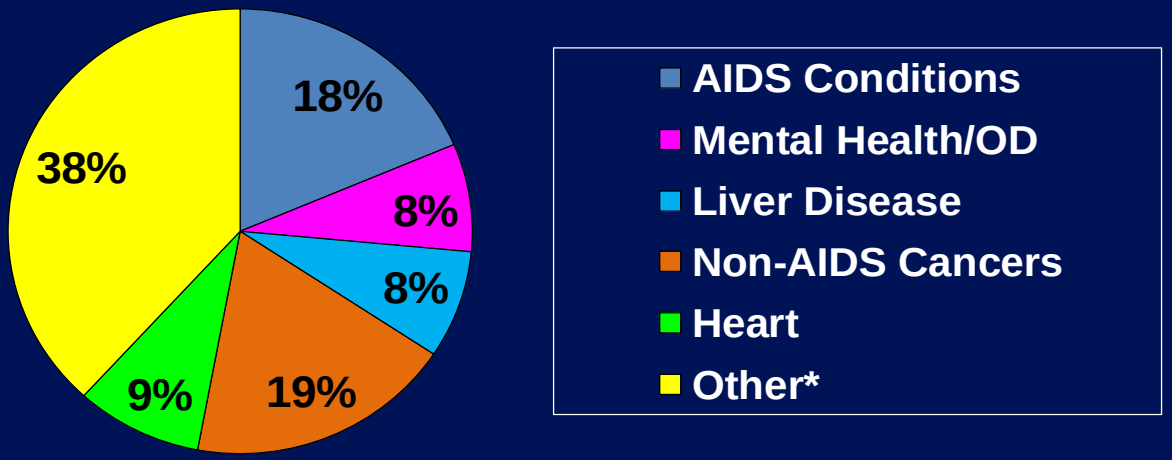
All-Cause and AIDS-Related Mortality

- Mortality is one of the most important outcome measures in an HIV program
- Although a measure of quality, other characteristics of the patient population (e.g. HCV co-infection rate, rate of mental illness, tobacco use, etc.) may independently impact on the mortality rate
- Mortality has been prospectively measured in our program since 1992
- Cause of death is ascertained through medical records review, physician interview, and, rarely, through autopsy and/or toxicology results

University of Colorado HIV/AIDS Clinical Program Mortality, 1999-2016



University of Colorado HIV/AIDS Clinical Program Mortality 2011-2015

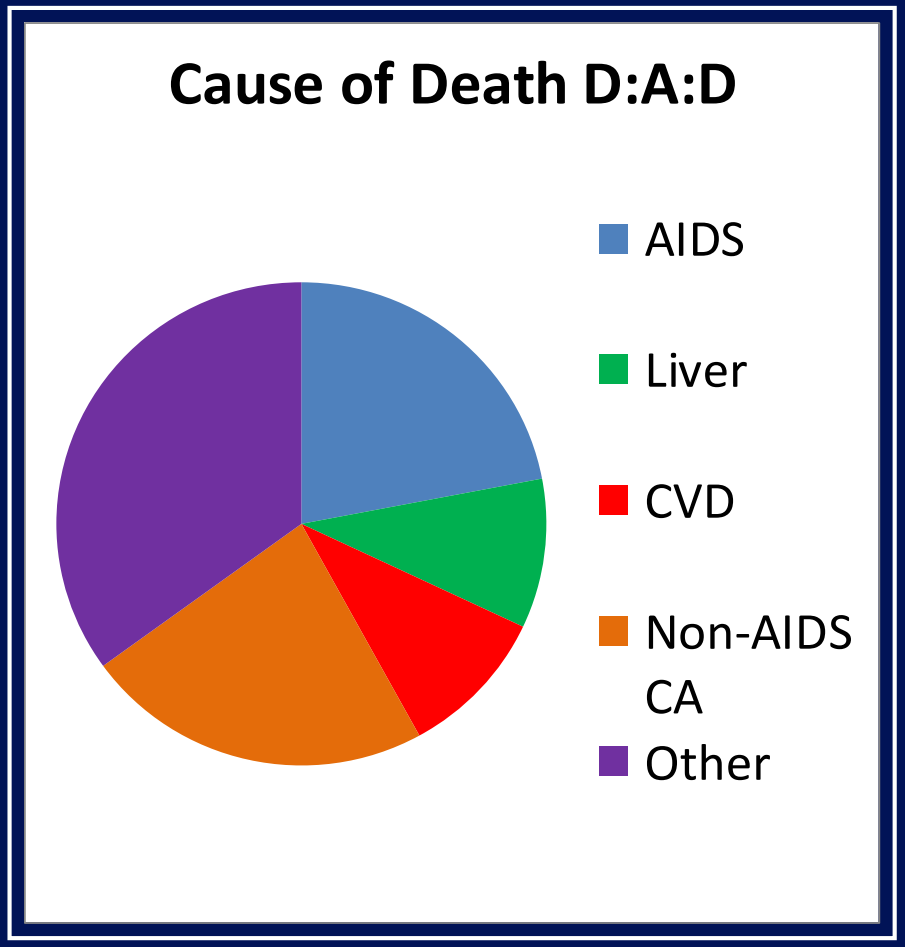


88 deaths over the last 5 years

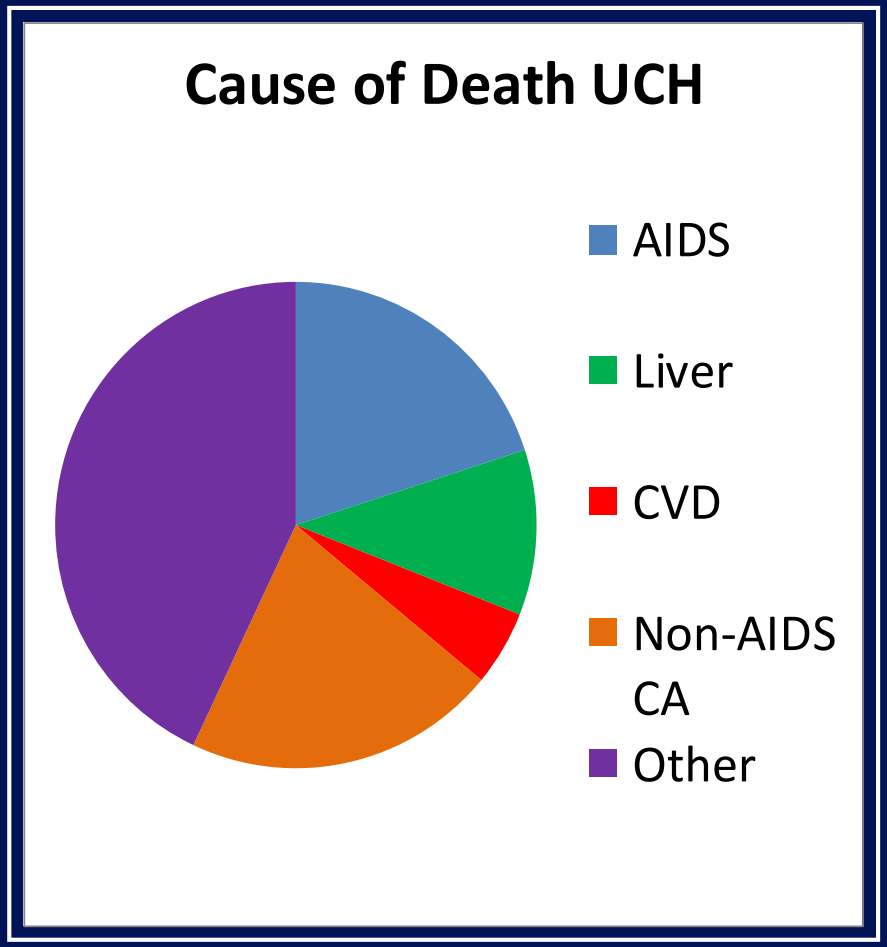
Other*

- Sepsis
- Bee sting
- Murder
- MVA
- COPD
- Brain hemorrhage
- ESRD
- GI bleed
- Unknown

Comparing D:A:D to our Local QI Project



2009-2011, N = 627

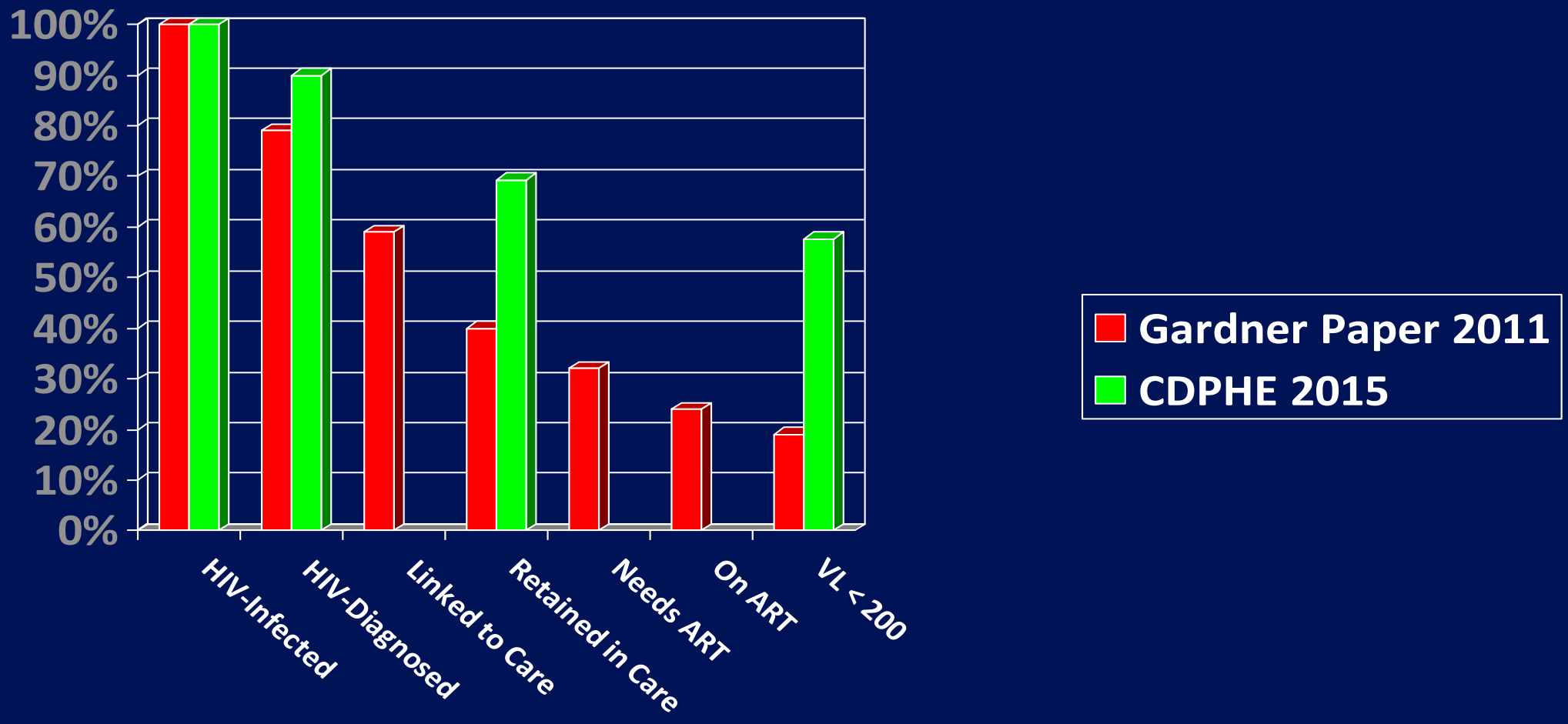


2009-2013, N = 85

Potential Strategies to Reduce Mortality: Community Level

1. Expanded HIV testing efforts
2. Improved linkage to care
3. Retention and reengagement in care
4. Access to expert care (HIV workforce issues)
5. Address health disparities
6. Linkage of electronic health records
7. Health care reform
8. Other funding and resource issues (maintaining the RW CARE Act)

Improvements in the Care Continuum Can be Seen in Colorado



Sources: Gardner E, et al. CID 2011;52:793-800.
Colorado Department of Public Health and the Environment.

Potential Strategies to Reduce Mortality: Clinic Level

1. Earlier use of antiretroviral therapy
2. Integration of HIV and primary care (medical home)
3. Aggressive programs for co-morbidities:
   a) HIV-HCV co-infection programs
   b) Tobacco cessation projects
   c) Cancer screening
   d) Mental health/substance abuse programs
4. Retention in care and engagement in care projects
5. Medication adherence programs
6. Medical case management
7. Use of EHR to track indicators and provide alerts

Clinic Mortality Indicator

- DRAFT Mortality Indicator (1): Percentage of active patients who died during the measurement year.
  - **Denominator:** All active patients.
  - **Numerator:** Number of patients who died during the measurement year.
  - **Exclusion(s):** None.
- DRAFT Mortality Indicator (2): Percentage of active patients who died during the measurement year and for whom **a non-HIV/AIDS-related** cause of death was noted within the clinic's records.
- DRAFT Mortality Indicator (3): Percentage of active patients who died during the measurement year and for whom **an HIV/AIDS-related** cause of death was noted within the clinic's records.

Should We be Measuring Mortality in HIV Clinical Programs?

1. Is the rate of mortality in this era too low to discriminate differences between programs?
2. Do the varying rates of co-morbidities among programs make it too difficult to track and compare mortality rates?
3. Given factors such as lost to follow up and low autopsy rates, can the cause and frequency of death be accurately measured?

Should We be Measuring Mortality in HIV Clinical Programs?

4. Are there local factors external to the program (e.g. late presentations, access to care) that affect mortality independent of program quality?
5. Should individual programs track mortality or can they learn enough from published data?
6. Are aggregate data from multiple programs useful for research, quality improvement, and advocacy? E.g D:A:D, NA-ACCORD, Kaiser

Questions and Discussion