Mortality in HIV Infection: Monitoring Quality Outcomes

March 15, 2017

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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

Trends in Annual Rates of Death due to the 9 Leading Causes among Persons 25–44 Years Old, United States, 1987–2013
Deaths per 1000 Persons Living with HIV in Colorado, 1988-2011

Era of Combination ART

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

AIDS Deaths

1818 HIV+ Patients in Care in 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

Number of people living with HIV on antiretroviral therapy, global, 2010–2016

- **2010**: 7.5 million [6.6 million–7.8 million]
- **2011**: 9.1 million [8.0 million–9.5 million]
- **2012**: 11 million [10.4 million–11.4 million]
- **2013**: 13 million [12.8 million–13.5 million]
- **2014**: 15 million [14.8 million–15.6 million]
- **2015**: 17 million [16.3 million–17.7 million]
- **June 2016**: 18.2 million [16.1 million–19.0 million]

2015 target within the 2011 United Nations Political Declaration on HIV and AIDS.

Sources: Global AIDS Response Progress Reporting (GARPR) 2016; UNAIDS 2016 estimates.
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

Deaths per 100 person-years

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Deaths</td>
<td>1.75</td>
<td>0.91</td>
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</table>


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.

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

Life Expectancy from Age 20 in Patients Starting Antiretroviral Therapy

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

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

Life Expectancy Starting ART after 2006 at age 25

Life expectancy increase in rural South Africa

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

## 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

SBIRT Screening Data, Danielle Osowski, IDGP at UCH
HIV and Hepatitis C in the U.S.

Hepatitis C (3.2 million)

HIV infection (1.2 million)

150,000 – 300,000 Co-infected Patients
## Incidence of Non-AIDS Cancers among HIV+ Persons Compared to General U.S. Population

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

- Lymphoma (EBV, HHV8)
- Lung (smoking)
- Liver (HCV, HBV)
- Tongue (smoking, HPV)
- Anal (HPV)
- Cholangiocarcinoma
- Cervical (HPV)
- Renal (smoking)
- Larynx (smoking, HPV)
- Tonsil (smoking, HPV)
- Gastric (smoking)
- Colon (smoking)
- Prostate
- Bladder (smoking)
- Glioblastoma
- Astrocytoma
Patients Presenting to the University of Colorado Hospital with PCP and a New HIV Diagnosis, 2005-2015

Number of Patients

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<tr>
<td>Value</td>
<td>6</td>
<td>1</td>
<td>2</td>
<td>7</td>
<td>2</td>
<td>3</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>3</td>
</tr>
</tbody>
</table>
Health Disparities and Mortality
Age-Adjusted* Average Annual Rate of Death due to HIV Infection by Sex and Race/Ethnicity, United States, 2009−2013
Disparities Among States in HIV-Related Mortality

- HIV Case-Fatality rates calculated and compared across states

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

- AIDS Conditions: 38%
- Mental Health/OD: 8%
- Liver Disease: 8%
- Non-AIDS Cancers: 9%
- Heart: 19%
- Other*: 8%

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

Cause of Death D:A:D
- AIDS
- Liver
- CVD
- Non-AIDS CA
- Other

2009-2011, N = 627

Cause of Death UCH
- AIDS
- Liver
- CVD
- Non-AIDS CA
- Other

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

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