AGING AND HIV
CHALLENGES AND OPPORTUNITIES

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HIV Co-morbidities, a Primary Care Update
Provincetown, MA
September 13, 2014
The US Centers for Disease Control & Prevention (CDC) predicts that in one year:

50%

of all people living with HIV will be over age 50.
USA AIDS Cases Over Age 50 - CDC
Concurrent HIV/AIDS among persons diagnosed with HIV in 2006 by age group, United States

Transmission categories

Estimated Diagnoses of HIV Infection among Adults Aged 50 and Older by Gender and Transmission Category 2010, 46 States

- Male-to-male sexual contact/IDU 3%
- Heterosexual contact* 23%
- Male-to-male sexual contact 60%
- IDU† 14%

- Other† <1%

- Males (N=5,726)

- Heterosexual contact* 82%
- IDU† 18%

- Females (N=2,072)

*Injection drug use.
†Other transmission risk factors include hemophilia, blood transfusion, & risk factors not reported or identified.
*Heterosexual contact with a person known to have, or be at high risk for, HIV infection.

Due to rounding, percentages may not add up to 100%.
Affected Sub-Populations

Figure 1: Estimated New HIV Infections in the United States, 2010, for the Most-Affected Sub-Populations

- White MSM: 11,200
- Black MSM: 10,600
- Hispanic MSM: 6,700
- Black Heterosexual Men: 5,300
- White Heterosexual Men: 2,700
- Hispanic Heterosexual Women: 1,300
- Black Male IDUs: 1,200
- Black Female IDUs: 1,100
- Black Female IDUs: 850
Prevalence and Incidence

Figure 7: HIV Prevalence and Incidence, 1980-2010

- People living with HIV
- New HIV infections using back-calculation methodology
- New HIV infections using original incidence surveillance methodology
- New HIV infections using updated incidence surveillance methodology
Impact of HAART


Reported Persons Living with HIV (non-AIDS)

Deaths to Persons with AIDS

New AIDS Diagnoses

Reported Persons Living with AIDS

New HIV Diagnoses

Number of Reported PLWHA

Source: NYC Dept of Health & Mental Hygiene, 2010
Median Age at Death due to HIV Disease
United States, 1987-2007

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.
Number and proportion of older and younger adults at first presentation for HIV clinical care (N=44,491)

Proportion of adults at first presentation for care

- 18-<50 years
- ≥50 years

p-value<0.01

Althoff, AIDS Res Therapy 2010
% of People Living with AIDS Diagnosis Over Age 50 in US

CDC Surveillance Data
Median Life Years at Age 20 With HIV In-Care

- '85-'87: 2 years
- '90 to '92: 4 years
- '95 to '97: 24.3 years
- '00 to '02: 27.1 years
- '03 to '05: 33.2 years
Changes in demographics
## Life Expectancy on HAART

<table>
<thead>
<tr>
<th>CD4 Cell Count (mm$^3$)</th>
<th>At HAART Initiation</th>
<th>A 20 yr old will live to (years)</th>
<th>A 35 yr old will live to (years)</th>
<th>% Remaining Life Lost (all ages)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100</td>
<td>52</td>
<td>62</td>
<td>62</td>
<td>46%</td>
</tr>
<tr>
<td>100-199</td>
<td>62</td>
<td>65</td>
<td>65</td>
<td>27%</td>
</tr>
<tr>
<td>≥200</td>
<td>70</td>
<td>72</td>
<td>72</td>
<td>14%</td>
</tr>
</tbody>
</table>

Trends in the Percentage Distribution of Deaths due to HIV Disease by Age Group, United States, 1987–2007

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.
Mean Increase in CD4 by Age 2 years after HAART

Months since ART initiation

- 18-<30 years
- 30-<40 years
- 40-<50 years
- 50-<60 years
- ≥60 years

Althoff K AIDS 2010
Comorbidity

- Associated with
  - Race, gender, age
  - Socioeconomic status
  - Tobacco, alcohol, drugs
  - Other lifestyle behaviors (obesity, inactivity)

- Caution:
  - May confound association with HIV or ARVs
  - Possibility of synergy—need to study populations at risk
Number of non-HIV meds by age

![Bar chart showing the number of non-HIV medications by age group. The chart indicates that the percentage of participants taking medications decreases with age, with the highest percentage in the <50 years age group and the lowest in the 65+ years age group.](image)

B Haase CROI 2011
Why are older patients getting infected?

Patient lack of awareness of HIV risk factors

- Many older people are newly single
- Belief that HIV only affects younger people

- Unprotected sexual activity
  - Use of Viagra and other ED drugs may contribute to increased rates of sexual activity
  - Menopause = No risk for pregnancy = No condom
  - No training in safer sexual activities

- Lack of HIV prevention education targeted at older people

- Seniors not considered at risk: don’t ask, don’t tell
Sex is Not Only for the Young

Proportion reporting sex in last 12 months

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>57-64</td>
<td>83.7</td>
<td>61.6</td>
</tr>
<tr>
<td>65-74</td>
<td>67.0</td>
<td>39.5</td>
</tr>
<tr>
<td>75-85</td>
<td>38.5</td>
<td>16.7</td>
</tr>
</tbody>
</table>
Prevention Challenges

- Sexual risk factors
  - Many older adults are sexually active
    - 73% of people age 57-64 had sex in the past year
    - 53% of people aged 65-74
    - 26% of people aged 75-85
  - Viagra, Levitra, Cialis and others
  - Lack of perception of risk
  - More risk in women:
    - Vaginal thinning, dryness
Prevention Challenges 2

- Drug use
  - 16% of HIV+ in older than 50 is related to IV Drug use
  - Older more likely to share needles; avoid stigma of needle exchange programs
  - Just as likely as younger drug users to indulge in high risk sex
  - Older IVDUs tend to be poorer and less likely to have social support than younger cohort
Prevention Challenges 3

- Lack of knowledge about HIV/AIDS is common in all groups but... Older people, when compared to those less than 50 have less AIDS knowledge
- 60% of older women are sexually active without use of condoms
- 50% of older rural African-American women have at least one risk factor of HIV infection
- Many older people have misconceptions about HIV risk and means of transmission, including lack of belief that condoms can be effective
Risk of Minority Race/Ethnicity

- In one study, older black and Latinos MSMs were at greater risk of getting infected because they had greater incidence of multiple partners and/or IVDU
- Older non-white MSMs get diagnosed later in the course of their infection; delaying treatment and increasing the risk of spread to others
- Stigma; particularly for older African Americans; age is a major barrier to seeking medical and social services as well as family support
Risk of Misdiagnosis of HIV/AIDS

- Many HIV symptoms, such as fatigue, weight loss, and confusion can mimic other normal aging processes
- Later diagnosis in the case of an already aging immune system may make treatment less effective and more difficult
- Other age-related chronic health conditions, such as high blood pressure, diabetes, etc., can be affected or worsened by HIV
- HIV may progress more rapidly in the older patient
Underestimation of Risk by Health Professionals

- Many health care providers do not consider discussing HIV with their older patients; and therefore don’t test them for HIV, and don’t discuss prevention
- Believe that older patients don’t have sex and/or don’t use recreational drugs
- Health care providers are often uncomfortable discussing these issues with patients who are older than they are
- In one study, only 38% of men and 22% of women over age 50 said that they had discussed sexual activity with their provider
Stigma

- Stigma of being HIV positive probably more severe amongst older people, leading them to conceal their diagnosis from family and friends.
- This can limit both emotional and practical support.
- Older HIV+ people may not even tell other consultant providers about their status.
Short list of aging conditions associated with HIV

- Lung diseases (COPD, Pulmonary Hypertension, Cancer)
- Liver diseases (Hepatitis, fibrosis, cancer)
- Renal diseases (insufficiency, failure)
- Vascular diseases (Stroke, MI, angina)
- Hematologic diseases (Anemia, thrombocytopenia, lymphoma)
- Neurological diseases (Dementia, peripheral neuropathy)
- Bone diseases (osteoporosis, aseptic [avascular] necrosis)
MI prevalence

**Figure 1.** Rates of myocardial infarction (MI; left) and rates of MI by age (right) in HIV-infected and HIV-uninfected persons. Adapted from Triant et al.³
### Aging changes vs HIV changes

<table>
<thead>
<tr>
<th>Immune Risk Profile (IRP)</th>
<th>HIV Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inverted CD4:CD8 ratio</td>
<td>Inverted CD4:CD8 ratio</td>
</tr>
<tr>
<td>Decreased proliferative responses and IL-2 production by T cells</td>
<td>Decreased proliferative responses and IL-2 production by T cells</td>
</tr>
<tr>
<td>Increased levels of CD8+ CD28-negative T cells (senescent cells)</td>
<td>Increased levels of CD8+ CD28-negative T cells (senescent cells)</td>
</tr>
<tr>
<td>Elevated levels of pro-inflammatory cytokines</td>
<td>Elevated levels of pro-inflammatory cytokines</td>
</tr>
<tr>
<td>CMV infection</td>
<td>Narrowing of the T-cell repertoire</td>
</tr>
<tr>
<td><strong>Other Age-Associated Immune System Alterations</strong></td>
<td>Shortened telomeres in T cells</td>
</tr>
<tr>
<td>Narrowing of the T-cell repertoire</td>
<td></td>
</tr>
<tr>
<td>Shortened telomeres in T cells</td>
<td></td>
</tr>
</tbody>
</table>
General guidelines

- HIV+ can increase risk of many “non-AIDS” conditions
- HIV+ risk is low compared to many of the other risk factors, but increases over time
- Care guidelines for treatment of non-HIV conditions may require revision to be adapted for those who need to start HIV treatment
  - Consider earlier start of antiretrovirals
  - Some antiretrovirals may exacerbate some other pre-existing non-AIDS conditions, so must be chosen carefully
Antiretroviral side effects that can mimic the aging process

- Lipoatrophy/lipodystrophy
- Hyperlipidemia leading to cardiovascular disease
- Osteopenia/osteoporosis
- Frailty syndrome
Affect of Aging on Pharmacology

- Blunted reflex responses
- Decreased receptor content/responses (including beta-adrenergic and dopamine receptors)
- Decreased “reserve” of all organs and systems
- Increased bleeding response to anticoagulants
- Take home message: Use as few drugs as possible; and be sure to monitor kidney function (glomerular filtration rate [GFR])
Affect of Age in HIV presentation and response

- CD₄ count at entry into care is lower
- Response of CD₄ response to treatment is blunted
- Older people start with fewer CD₄ cells and gain fewer during treatment; at least in some trials
Age Affects Neurologic Outcome in People with HIV

- Low level viremia can cause amyloid plaques in the brain that are different than Alzheimer’s plaques
- Family history of dementia makes dementia more likely in HIV+
- While frank dementia incidence has decreased in the age of HAART, presence of HIV-associated neurocognitive disorders has NOT decreased, and is more prevalent in older patients
HIV and Bone Disease

- Vitamin D metabolism is affected on HAART, especially with efavirenz.
  - Ongoing trial testing Vitamin D and/or fish oil changes risks
- Age raises fracture risk in olders with HIV+ more than in the general population. This occurs in both men and women
- HIV associated lipoatrophy may play a role in Vitamin D deficiency
Reasons for Hospitalization Differ by age for HIV+
Women with HIV notice aging symptoms more than men.

Figure 5. Compared with men seen at a Barcelona HIV clinic, women gave higher intensity scores to an array of aging-related symptoms on a 1-to-5 scale. (Source: Dr. Eugenia Negredo, Germans Trias i Pujol University Hospital, Spain40)
Co-morbidities
Comorbid Conditions are less likely treated if HIV+

Figure 7. Prevalence of hypertension (Ht) was similar in Italian patients with and without HIV infection in a large case-control comparison. But HIV-positive patients received antihypertensive therapy less often than HIV-negative controls in every age bracket. (Source: Dr. Giovanni Guaraldi, University of Modena, Italy.)
Co-Morbid Conditions

Figure 8. Prevalence of two or more comorbid conditions was higher in HIV-positive cases than in age-, gender-, race-, and region-matched controls in every age group analyzed. (Source: Dr. Giovanni Guaraldi, University of Modena, Italy [59])
Non HIV medications by age

<table>
<thead>
<tr>
<th>Table 4. Non-HIV medication use in older and younger age groups in Toronto</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Gastrointestinal medications*</td>
</tr>
<tr>
<td>Cardiovascular medications</td>
</tr>
<tr>
<td>Anticoagulants/antiplatelets</td>
</tr>
<tr>
<td>Erectile dysfunction agents</td>
</tr>
<tr>
<td>Systemic hormonal agents</td>
</tr>
<tr>
<td>Musculoskeletal agents</td>
</tr>
<tr>
<td>Narcotics/analgesics</td>
</tr>
<tr>
<td>Anticonvulsants</td>
</tr>
<tr>
<td>Psychotropics</td>
</tr>
</tbody>
</table>

*Includes antidiabetics.

Source: Dr. Alice Tseng, Toronto General Hospital, Canada.
Non-HIV related polypharmacy increases with age

<table>
<thead>
<tr>
<th>Medication Type</th>
<th>&lt;60 years (n = 528)</th>
<th>&gt;60 years (n = 38)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal medications*</td>
<td>38%</td>
<td>63%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Cardiovascular medications</td>
<td>24%</td>
<td>55%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Anticoagulants/antiplatelets</td>
<td>7%</td>
<td>18%</td>
<td>0.01</td>
</tr>
<tr>
<td>Erectile dysfunction agents</td>
<td>1%</td>
<td>5%</td>
<td>0.06</td>
</tr>
<tr>
<td>Systemic hormonal agents</td>
<td>5%</td>
<td>16%</td>
<td>0.01</td>
</tr>
<tr>
<td>Musculoskeletal agents</td>
<td>9%</td>
<td>24%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Narcotics/analgesics</td>
<td>17%</td>
<td>39%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>7%</td>
<td>16%</td>
<td>0.06</td>
</tr>
<tr>
<td>Psychotropics</td>
<td>30%</td>
<td>34%</td>
<td>0.54</td>
</tr>
</tbody>
</table>

*Includes antidiabetics.

Source: Dr. Alice Tseng, Toronto General Hospital, Canada.
What Older People Can Do

- Learn about HIV and other STD prevention
- Talk about HIV and other STD with your partner
- Talk to your provider about HIV, and ask to be tested
  - CDC recommends annual tests for men
  - CDC recommends testing for a woman anytime she has a new sex partner
- Use condoms and lube EVERY time
- Use clean needles and syringes if you must inject drugs
- Try to avoid sex when under the influence of alcohol or drugs
More things older people can do

- Pay attention to screening for age-related non-AIDS diseases
  - Mammograms
  - Prostate (men only)
  - Colon
  - Osteoporosis
  - Cervix and vagina (women only); Anal pap if indicated
  - Diabetes
  - Cardiovascular (blood pressure, heart, etc)
  - Depression
Extra help for older HIV+ people

- Help with adherence. Remembering to take medications on time
- Support groups that are age-friendly to decrease isolation
- Help with access to financial services to insure they are able to pay for their medications and treatment despite gaps in health insurance coverage and access
Insuring Best Care

- Counseling and HIV testing
  - Requires education of patients as well as providers
- Coordination of care
  - Infectious disease experts are uncomfortable and less skilled at providing primary care
  - Most primary care providers are unfamiliar with the complexities of HIV treatments
  - More research in HIV and older adults needs to be done
  - Nationwide shortage of geriatric care providers
Prophylaxis; Prevention

Potential Interventions to Prevent HIV Transmission

- Decrease Source of HIV Infection
  - Barrier protection
  - STI treatment
  - Blood screening
  - ART
    - Maternal-to-child transmission
    - Decrease partner’s viral load
    - Treatment of acute HIV infection

- Decrease Host Susceptibility to HIV Infection
  - Barrier protection
  - STI treatment
  - PEP
  - PrEP
  - Topical microbicides
  - Vaccines
  - Infection control
  - Circumcision

- Alter Risk-Taking Behavior
  - Condom promotion
  - Individual intervention
  - Couples intervention
  - Community-based intervention
  - Structural intervention

Mayer KH, et al.[1]
PrEP IS A NEW HIV PREVENTION METHOD IN WHICH PEOPLE WHO DO NOT HAVE HIV INFECTION TAKE A PILL DAILY TO REDUCE THEIR RISK OF BECOMING INFECTED.
ONLY PEOPLE WHO ARE HIV-NEGATIVE SHOULD USE PrEP. AN HIV TEST IS REQUIRED BEFORE STARTING PrEP AND THEN EVERY 3 MONTHS WHILE TAKING PrEP.
PrEP can only be prescribed by a healthcare provider and must be taken as directed to work.
References

1. http://www.aahivm.org/hivandagingforum
3. http://hivinsite.ucsf.edu/InSite?page=kbr-03-01-16
Pre-Exposure Prophylaxis for HIV Prevention

- Antiretrovirals in HIV patients restores health and may decrease transmission of virus to uninfected partners
- HIV pill taken daily or gel applied to vagina
  - Tenofovir (TDF) and Truvada (FTC-TDF)
- Reduce risk of HIV infection
- Rationale based on:
  - Prevention of mother to child transmission
  - Post exposure prophylaxis
  - Animal Studies
PREP Trials Worldwide

PrEP Trials Timeline

2004
FHI West Africa
Extended Safety Trial/CDC 4323 US
Bangkok Tenofovir Study/CDC 4370 Thailand
CDC 4940

2005
TDF2/CDC 4940 Botswana

2006
iPrEx multi-country
CAPRISA 004 South Africa

2007
MTN 001 multi-country
Partners PrEP Kenya + Uganda

2008
FEM-PrEP multi-country
VOICE/MTN 003 multi-country
IAVI E001, E002 Kenya + Uganda

2009
PrEP in YMSM/ATN 082 US

2010

2011

2012

2013

AVAC

November 2010

* The trial end-dates listed in this table are estimates. Due to the nature of clinical trials the actual dates may change. AVAC will continue to monitor trial progress and will update the timeline accordingly. To view or download an updated timeline visit www.avac.org/prep.
Study 1: FHI West Africa

- Phase 2, randomized, double-blind, placebo-controlled
- June 2004 to March 2006
- Enrolled in 3 sites: Ghada, Camerron, and Nigeria
- 936 HIV-negative women at high risk of HIV infection
  - 469 received TDF
  - 467 received placebo

- Safety endpoints measured by
  - Serum creatinine >2.0 mg/dl
  - Phosphorus <1.5 mg/dl
  - Alanine aminotransferase elevations >170 U/l

- Efficacy measured by infection of HIV-1 or HIV-2
Study 2: Preexposure Prophylaxis Initiative (iPrEx)

- Phase 3, randomized, double-blind, placebo-controlled
- 11 sites in six countries
- July 2007-December 2009
  - 3,324 person-years
- 2,499 HIV negative men or transgender women who have sex with men
  - 1,251 given FTC-TDF
  - 1,248 given placebo
Study 3: CAPRISA 004

- Phase II, double-blind, randomized, placebo-controlled
- May 2007-March 2010
  - 1,341 women years
- 889 women at high risk of HIV through intercourse
  - 445 tenofovir gel
  - 444 placebo gel
### Efficacy Results

#### Data from FH1 West Africa

<table>
<thead>
<tr>
<th>Person-Years of Follow-Up</th>
<th>TDF</th>
<th>Placebo</th>
<th>Incidence Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV infections/100 person-years</td>
<td>232.6</td>
<td>241.3</td>
<td>0.86</td>
</tr>
</tbody>
</table>

#### Reduction in Risk for HIV Acquisition in iPrEX Trial

<table>
<thead>
<tr>
<th>HIV Infection</th>
<th>FTC-TDF (events)</th>
<th>Placebo (events)</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV Infection</td>
<td>36</td>
<td>64</td>
<td>0.56 (0.37-0.85)</td>
</tr>
<tr>
<td>Pill Use &lt;90%</td>
<td>28</td>
<td>34</td>
<td>0.79 (0.48-1.31)</td>
</tr>
<tr>
<td>Pill Use ≥90%</td>
<td>8</td>
<td>30</td>
<td>0.27 (0.12-0.59)</td>
</tr>
</tbody>
</table>

#### Effectiveness of tenofovir gel in HIV Prevention in CAPRISA 004

<table>
<thead>
<tr>
<th>HIV Incidence/100 Women Years</th>
<th>Tenofovir gel (95% CI)</th>
<th>Placebo gel (95% CI)</th>
<th>Incidence Rate Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV total</td>
<td>5.6</td>
<td>9.1</td>
<td>0.61</td>
</tr>
<tr>
<td>Gel Use &gt;80%</td>
<td>4.2</td>
<td>9.3</td>
<td>0.46</td>
</tr>
<tr>
<td>Gel Use &lt;50%</td>
<td>6.2</td>
<td>8.6</td>
<td>0.72</td>
</tr>
</tbody>
</table>
Results from TDF2 and Partners PrEP

- **TDF2 Study** – Reduced risk by 63%
  - Separate analysis showed 78% risk reduction

- **Partners PrEP**
  - 62% with Tenofovir ($p=0.0003$)
  - 73% with Truvada ($p<0.0001$)
Conclusions

- PrEP effective in HIV prevention
- Adherence is critical
- Used in high risk populations
- PrEP should be used in combination with other prevention methods