HIV & AGING: FROM MITOCHONDRIA TO THE METROPOLIS
HIV & Aging:
From Mitochondria to the Metropolis

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Acknowledgements

• **Conference Planner**
  – Association Strategy Group, LLC

• **Conference Planning Committee**
  – Jenny Anderson (Emory CFAR)
  – Cynthia Allen (Community representative)
  – Shelle Bryant (Emory CFAR)
  – Reggie Dunbar (Community representative)
Acknowledgements

HIV & Aging Scientific Working Group, Emory CFAR
A Far-Reaching Audience

- 17 States plus the District of Columbia
- Attendees representing disciplines across basic, clinical, and social sciences
- Why else is this important? ...
HIV Prevalence – 55+
(all races/genders)
HIV & AGING: FROM MITOCHONDRIA TO THE METROPOLIS
Charles A. Emlet, PhD, MSW, ACSW is currently Professor of Social Work at the University of Washington Tacoma and Adjunct Professor at the University of Washington School of Social Work. He is an affiliate faculty with the UW Center for AIDS Research. In 2013, Dr. Emlet was a Fulbright Scholar at McMaster University in Hamilton, Ontario. He has published more than 80 journal articles and book chapters and serves on the editorial boards of The Gerontologist, Journal of HIV/AIDS and Social Services and the Journal of Gerontological Social Work.
The Impact of HIV on Health Disparities Among Older Gay and Bisexual Men: Results From the Aging With Pride - National Health, Aging and Sexuality/Gender Study

Charles A. Emlet, PhD, MSW and Karen Fredriksen Goldsen, PhD (PI)

University of Washington
(Funded in part by NIH/NIA, R01AG026526)

2019 HIV and Aging Conference
April 11, 2019 • Decatur, Georgia
Acknowledgements

R01AG026526 (NHAS)

- R01AG026526-04S1
- R01AG026526-05S1

Research reported in this presentation was supported by the National Institute on Aging of the National Institutes of Health under Award Number R01AG026526 (Fredriksen-Goldsen, PI).

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the National Institute on Aging.
Focus of the Presentation

Special populations aging with HIV
  • Diversity within Older Adults
    • Newly Diagnosed
      • Late Diagnosis/Symptomatic or not
    • Long Term Survivor
      • Diagnosed Pre HAART
      • Diagnosed Post HAART
    • Intersectionality or layering of stigma including ageism
  • Gender
  • Sexual Orientation
  • Gender Identity
  • Race/Ethnicity
Aging with Pride: National Health, Aging, and Sexuality/Gender Study is the first federally-funded, national longitudinal study designed to better understand the aging, health, and well-being of LGBTQ midlife and older adults and their families.

- Better understand the health and well-being of LGBT older adults;
- Investigate explanatory mechanisms of health equity and inequity; and
- Assess subgroup differences by age cohort, gender, race/ethnicity, and identify those at highest risk (including living with HIV).
Health Equity Promotion Model

• 2,450 SGM adults (birth year ≤ 1964)
• Dual sampling frame
  17 organizations across all U.S. census divisions
  Social network clustering of sub groups
• Stratification: sex, gender, age cohort, race/ethnicity, region
• Data collection
  Survey
  In-person interviews
• Two-step post-survey adjustment (Lee & Valliant, 2009)


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Utility of the NHAS in HIV Research

• Sound analysis of the impact of HIV on older adults requires a comparable comparison group

• Wong et al (2014) posits validity of comparison is threatened when demographic, clinical and lifestyle difference are not considered
  • Sample size is of concern

• NHAS (2014) data N = 2,450 with 401 (16.4%) living with HIV

Impact of HIV on Older Gay and Bisexual Men in NHAS

• Older gay and bisexual men are at risk for health disparities compared to their heterosexual counterparts (Fredriksen-Goldsen et al, 2013)

• Are their health disparities between older gay and bisexual men living with and without HIV?

Research Questions to this Analysis

• Are there disparities in poor general health and depressive symptomatology as well as health risk and promoting factors between gay and bisexual older men living with and without HIV?

• Which health risk and promoting factors account for the disparities in poor general health and depressive symptomatology between those with HIV and without HIV?
Methods

Analysis included gay and bisexual men enrolled in NHAS in 2014

• Total N for this analysis was 1,344
  • 973 HIV negative
  • 371 living with HIV infection
Procedures

• We examined distributions of background characteristics, health risk and promoting factors, and health outcomes by HIV status.

• We then examined factors that account for HIV status-related disparities in health outcomes, using background characteristics as well as health-promoting and risk factors that were found to be significantly associated with HIV status.
<table>
<thead>
<tr>
<th></th>
<th>Lesbian, gay, and bisexual adults aged 50 and older</th>
<th>Adults aged 50 and older and living with same-sex partner</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Aging with Pride: NHAS (n = 2450)</td>
<td>NHIS (n = 632)</td>
</tr>
<tr>
<td></td>
<td>unweighted % (n)</td>
<td>weighted % (SE)</td>
</tr>
<tr>
<td>Sexual Identity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lesbian or Gay</td>
<td>85.97 (2,102)</td>
<td>72.26 (1.62)</td>
</tr>
<tr>
<td>Bisexual/Others</td>
<td>14.03 (343)</td>
<td>27.74 (1.62)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age Group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50-64</td>
<td>44.53 (1092)</td>
<td>70.18 (1.35)</td>
</tr>
<tr>
<td>65+</td>
<td>55.47 (1358)</td>
<td>29.82 (1.35)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>81.96 (1,995)</td>
<td>82.30 (1.33)</td>
</tr>
<tr>
<td>Black</td>
<td>9.29 (226)</td>
<td>9.59 (1.03)</td>
</tr>
<tr>
<td>Others</td>
<td>8.75 (213)</td>
<td>8.11 (0.97)</td>
</tr>
<tr>
<td>Ethnicity, Hispanic</td>
<td>6.91 (168)</td>
<td>9.05 (1.04)</td>
</tr>
</tbody>
</table>

Table 2. Background characteristics by HIV status

<table>
<thead>
<tr>
<th></th>
<th>HIV gay/bisexual men (unweighted n = 371)</th>
<th>Non-HIV gay/bisexual men (unweighted n = 973)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>M or % [95% Confidence Interval]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>58.23***</td>
<td>63.38</td>
</tr>
<tr>
<td>Sexual orientation, Gay men</td>
<td>86.47%†</td>
<td>81.15%</td>
</tr>
<tr>
<td>Income, ≤ 200% Poverty</td>
<td>48.44%***</td>
<td>21.65%</td>
</tr>
<tr>
<td>Education, High school or less</td>
<td>45.31%***</td>
<td>21.96%</td>
</tr>
<tr>
<td>Race/ethnicity, Non-Hispanic white</td>
<td>59.64%***</td>
<td>87.31%</td>
</tr>
</tbody>
</table>

Note. Each variable was regressed on HIV status and age as a covariate. Sampling weights were applied.
†p < .10, *p < .05, **p < .01, ***p < .001
# Table 3. Health risk & promoting factors by HIV status

<table>
<thead>
<tr>
<th></th>
<th>HIV gay/bisexual men (unweighted n = 371)</th>
<th>Non-HIV gay/bisexual men (unweighted n = 973)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Historical &amp; Environmental</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LGBT-related lifetime victimization</td>
<td>7.11†</td>
<td>5.19</td>
</tr>
<tr>
<td><strong>Psychological</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LGBT identity stigma</td>
<td>1.80†</td>
<td>1.62</td>
</tr>
<tr>
<td>Resilience</td>
<td>3.94*</td>
<td>4.28</td>
</tr>
<tr>
<td>Spirituality</td>
<td>3.96†</td>
<td>3.61</td>
</tr>
<tr>
<td>Anxiety, ever</td>
<td>42.60%***</td>
<td>21.89%</td>
</tr>
<tr>
<td><strong>Social</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social support</td>
<td>2.42*</td>
<td>2.72</td>
</tr>
<tr>
<td>LGBT community engagement</td>
<td>4.03*</td>
<td>3.80</td>
</tr>
<tr>
<td>Partnered/Married</td>
<td>34.95%***</td>
<td>52.19%</td>
</tr>
<tr>
<td>Death of a partner</td>
<td>43.77%***</td>
<td>29.76%</td>
</tr>
<tr>
<td><strong>Biological</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td># of chronic health conditions</td>
<td>1.98**</td>
<td>1.66</td>
</tr>
<tr>
<td>Drug addiction diagnosed ever</td>
<td>11.38%**</td>
<td>2.20%</td>
</tr>
<tr>
<td><strong>Health outcomes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor general health</td>
<td>3.15***</td>
<td>2.62</td>
</tr>
<tr>
<td>Depressive symptomatology</td>
<td>11.20***</td>
<td>7.19†</td>
</tr>
</tbody>
</table>

*Note. Each variable was regressed on HIV status and age as a covariate with sampling weights. †p < .10, *p < .05, **p < .01, ***p < .001*
Factors explaining health disparities among older HIV-positive gay/bisexual men

<table>
<thead>
<tr>
<th>Poorer general health was associated with:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Higher poverty level</td>
</tr>
<tr>
<td>• Lower education</td>
</tr>
<tr>
<td>• Elevated risks of victimization</td>
</tr>
<tr>
<td>• Lower resilience</td>
</tr>
<tr>
<td>• Lower social support</td>
</tr>
<tr>
<td>• More chronic health conditions</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Higher depressive symptomatology was associated with:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Higher poverty level</td>
</tr>
<tr>
<td>• Elevated risks of victimization</td>
</tr>
<tr>
<td>• Lower resilience</td>
</tr>
<tr>
<td>• Elevated risks of anxiety</td>
</tr>
<tr>
<td>• Lower social support</td>
</tr>
<tr>
<td>• Elevated risks of drug addiction</td>
</tr>
</tbody>
</table>

Higher level of LGBT community engagement among those with HIV contributed to alleviating disparities in both poor general health and depressive symptomatology.
• The NHAS provides a unique opportunity to examine questions related to biopsychosocial issues impacting older sexual minorities throughout the United States.

• The naturally occurring subpopulation of older sexual minorities living with HIV in our study allow for the comparison of risk and protective factors associated with health disparities.

• The Health Equity Promotion Model is useful in identifying unique dimensions that impact health and disparities.
Discussion

• Our most recent analysis of participants living with HIV suggest they face additional disparities

• Demographic characteristics such as age, income, education and race/ethnicity differ between groups and pose risks to good health.

• People in our study living with HIV were negatively impacted by psychosocial, social and biological domains.

• Our findings reinforce the hypothesis that HIV impacts a population already at risk for poorer health outcomes than heterosexual peers.
Future Directions/Opportunities

• The NIH has refunded NHAS for the next five years to continue to explore health disparities and risk and protective factors in study participants.

• We now have three time points of data that will begin to yield longitudinal analysis; We are in the process of collecting 2018 survey data currently.

• NHAS data from 2010 is now publicly available (including participants with and without HIV) and can be obtained by submitting Data Request Application on NHAS webpage (age-pride.org)

• Got questions about data? Contact Project Director, Hyun-Jun Kim, hyunjkim@uw.edu
Publications and information available at

www.Age-Pride.org    AgePride@uw.edu

facebook.com/AgingWithPride    twitter.com/Age_Pride
Thank You For Your Interest

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HIV & AGING: FROM MITOCHONDRIA TO THE METROPOLIS
Deborah Gustafson, MS, PhD is a Professor Neurology at the State University of New York Downstate Medical Center and Director of NeuroEpidemiology. Dr. Gustafson was first to report on a relationship between overweight and obesity and risk of Alzheimer's disease in population-based studies in Sweden. Today, she explores potential mechanisms of adipose tissue, as well as vascular and metabolic factors, in relationship to cognition, neuropsychiatric disorders and brain structure in epidemiologic studies. In Brooklyn, New York, she is the Principal Investigator of the Brooklyn site of the NIH-funded, multicenter MACS WIHS Combined Cohort Study: Brooklyn Clinical Research Site (MWCCS Bklyn CRS), formerly the Women’s Interagency HIV Study (WIHS), for which she chairs the Aging Working Group and leads efforts in assessments of adiposity, frailty, and cognition.
Aging women with HIV: Enquiring minds want to know

Deborah R Gustafson, MS, PhD

Professor, Department of Neurology, Section for NeuroEpidemiology
State University of New York - Downstate Medical Center, Brooklyn, New York, USA

Guest Professor, Department of Health and Education, University of Skövde, Sweden
Docent / Affiliated Researcher, Institute of Neuroscience & Physiology, Sahlgrenska Academy; EPINEP, AGECAP, University of Gothenburg, Sweden
Heart and Mind Study

Gustafson:
A diverse portfolio
Cross-Pollinate Usual Aging Epidemiology to Aging HIV Epidemiology
Fit for Purpose and Fit for Aging HIV Communities
Global 50 year projections: Proportion of adults ≥ 65 years

With the changing age demographic comes changes in distribution and occurrence of disease.
Top 10 global causes of deaths, 2016

- Ischaemic heart disease
- Stroke
- Chronic obstructive pulmonary disease
- Lower respiratory infections
- Alzheimer disease and other dementias
- Trachea, bronchus, lung cancers
- Diabetes mellitus
- Road injury
- Diarrhoeal diseases
- Tuberculosis

Cause Group:
- Communicable, maternal, neonatal and nutritional conditions
- Noncommunicable diseases
- Injuries

## Causes of Death

### Deaths among HIV+ Participants

<table>
<thead>
<tr>
<th>Category</th>
<th>AIDS death</th>
<th>Pneumonia or Infection death</th>
<th>Non-AIDS death</th>
<th>Indeterminate/Missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>SR AIDS at BL</td>
<td>229 (48%)</td>
<td>65 (13%)</td>
<td>158 (33%)</td>
<td>30 (6%)</td>
</tr>
<tr>
<td>SR AIDS during F/U</td>
<td>149 (38%)</td>
<td>65 (17%)</td>
<td>143 (37%)</td>
<td>34 (9%)</td>
</tr>
<tr>
<td>No SR AIDS</td>
<td>101 (30%)</td>
<td>40 (12%)</td>
<td>177 (52%)</td>
<td>20 (7%)</td>
</tr>
</tbody>
</table>

Data based on NDI match through 12/31/16 (LA: 12/31/14) and through 3/31/18 for all sites via other reports

- Includes 7 deaths among 01/02 recruits, 3 11/12 recruits, and 4 Southern recruits
- Includes 58 deaths among 01/02 recruits, 6 11/12 recruits, and 6 HIV seroconverters (HIV SC)
- Includes 58 deaths among 01/02 recruits, 14 11/12 recruits, 14 Southern recruits and 5 HIV SC (3 found at death)
## Non-AIDS Causes of Death

<table>
<thead>
<tr>
<th></th>
<th>Non-AIDS Deaths&lt;sup&gt;d&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>594 (+64)</td>
</tr>
<tr>
<td>HIV+</td>
<td>478 (+44)</td>
</tr>
<tr>
<td>HIV-</td>
<td>116 (+20)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cause</th>
<th>HIV+</th>
<th>HIV-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trauma or OD&lt;sup&gt;a&lt;/sup&gt;</td>
<td>104 (+5) (22%)</td>
<td>28 (+6) (24%)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>117 (+15) (24%)</td>
<td>24 (+5) (21%)</td>
</tr>
<tr>
<td>Liver disease&lt;sup&gt;b&lt;/sup&gt;</td>
<td>68 (+2) (14%)</td>
<td>8 (+1) (7%)</td>
</tr>
<tr>
<td>CVD</td>
<td>73 (+9) (15%)</td>
<td>15 (+3) (13%)</td>
</tr>
<tr>
<td>All other non-AIDS causes&lt;sup&gt;c&lt;/sup&gt;</td>
<td>116 (+13) (24%)</td>
<td>41 (+5) (35%)</td>
</tr>
</tbody>
</table>

Data based on NDI match through 12/31/16 (LA: 12/31/14) and through 3/31/18 via other reports

<sup>a</sup> Includes 2 deaths among HIV seroconverters

<sup>b</sup> Includes 2 deaths among HIV seroconverters (1 found at death); 56 HIV+ and 7 HIV- were HCV Ab+ at baseline

<sup>c</sup> Includes 1 death among HIV seroconverters

<sup>d</sup> Does not include 5 deaths (including 4 new) among HIV- with missing causes
The Women’s Interagency HIV Study
2018 WDMAC Report

### Chronic Disease Indicators

<table>
<thead>
<tr>
<th>Current Cohort (v46 or v47)</th>
<th>HIV+ N=1585</th>
<th>HIV- N=674</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI Median (IQR) % BMI &gt;30 [&gt;40]</td>
<td>30 (26, 37) 32 (27, 38)</td>
<td>51% [18%] 58% [18%]</td>
</tr>
<tr>
<td>Hypertension (SBP≥140, DBP≥90, meds)</td>
<td>52%</td>
<td>50%</td>
</tr>
<tr>
<td>Diabetes (HbA1C≥6.5%, FG≥126, meds)</td>
<td>23%</td>
<td>25%</td>
</tr>
<tr>
<td>Dyslipidemia (LDL&gt;130, HDL&lt;40)</td>
<td>31%</td>
<td>27%</td>
</tr>
<tr>
<td>Chronic Kidney Disease CKD-Epi eGFR &lt;60 [&lt;30]</td>
<td>13% [2%]</td>
<td>6% [1%]</td>
</tr>
<tr>
<td>Baseline Hepatitis C Ab+ (Baseline HCV RNA+)</td>
<td>20% (9%)</td>
<td>15% (7%)</td>
</tr>
<tr>
<td>Baseline Chronic Hepatitis B</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Depressive Symptoms</td>
<td>28%</td>
<td>32%</td>
</tr>
</tbody>
</table>
# Substance Use

<table>
<thead>
<tr>
<th>Current Cohort (v46 or v47)</th>
<th>HIV+ N=1585</th>
<th>HIV- N=674</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Smoking:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current Former</td>
<td>36%</td>
<td>44%</td>
</tr>
<tr>
<td>Former</td>
<td>30%</td>
<td>29%</td>
</tr>
<tr>
<td><strong>Injection Drug Use:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current Ever</td>
<td>&lt;1%</td>
<td>1%</td>
</tr>
<tr>
<td></td>
<td>18%</td>
<td>17%</td>
</tr>
<tr>
<td><strong>Non-Injection Drug Use:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current Ever</td>
<td>25%</td>
<td>32%</td>
</tr>
<tr>
<td></td>
<td>73%</td>
<td>81%</td>
</tr>
<tr>
<td><strong>Recreational Rx Drug Use:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>0.7%</td>
<td>2%</td>
</tr>
<tr>
<td><strong>Alcohol Use:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;12 drinks/week</td>
<td>4%</td>
<td>10%</td>
</tr>
<tr>
<td>7-12 drinks/week</td>
<td>2%</td>
<td>4%</td>
</tr>
</tbody>
</table>
Not only are causes of death with higher ages important....

Top 10 global causes of deaths, 2016

... but ... Geriatric syndromes are more prevalent
Geriatric Syndromes

FORGETFULNESS and CONFUSION
It is important to differentiate the ordinary forgetfulness that comes with aging from dementia or Alzheimer’s disease.

NUTRITIONAL PROBLEMS
Loss of appetite or undernutrition such as a deficiency of protein and vitamin B12.

HEARING LOSS
Difficulty hearing or tinnitus (ringing in the ear).

VISION PROBLEMS
Older adults should have their eyes checked at least once a year for early detection of visual problems such as cataracts or glaucoma.

IMBALANCE AND FALLS
Caused by several factors such as neurological diseases, low blood pressure, osteoarthritis, or as a side effect of medications.

OSTEOPOROSIS
Common in women after menopause or men older than 70, this condition increases the risk of fractures in older adults.

URINARY INCONTINENCE
Greatly affects the quality of life of older adults.

The 9 MOST COMMON HEALTH CONDITIONS IN OLDER ADULTS

Common health conditions in older adults or “GERIATRIC SYNDROMES” are usually caused by several factors. Geriatricians provide comprehensive physical and mental health care for older adults.

Two groups of older adults that require special care

Credit: The New Life Healthy Aging Clinic at Bumrungrad Hospital provides geriatric services delivered by a multidisciplinary team of geriatricians and medical professionals. To make an appointment or inquiry, please contact 02-667-2000.
Geriatric Syndromes

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It is important to differentiate the common forgetfulness that comes with age from dementia or Alzheimer’s disease.

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Oldest adults should have their eyes checked at least once a year for early detection of visual problems such as cataracts or glaucoma.

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Caused by several factors such as neurological diseases, low blood pressure, osteoarthritis, or as a side effect of medications.

NUTRITIONAL PROBLEMS
Loss of appetite or undernutrition such as a deficiency of protein and vitamin B12.

HEARING LOSS
Difficulty hearing or tinnitus (ringing in the ear).

DIZZINESS
Caused by several factors such as low blood pressure or certain medications.

SLEEP DISORDERS
Waking up frequently or difficulty falling asleep.

OSTEOPOROSIS
Common in women after menopause or men older than 70, this condition increases the risk of fractures in older adults.

URINARY INCONTINENCE
Graetly affects the quality of life of older adults.

The 9 MOST COMMON HEALTH CONDITIONS IN OLDER ADULTS

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Life Expectancy is Higher in U.S. Women vs Men
US, 2017, CDC
Life Expectancy is Higher in U.S. Women vs Men
US, 2017, CDC

Will this be observed for people with controlled HIV infection?
Fit for Purpose and
Fit for Aging HIV Communities

HIV Aging Epidemiology - A New Discipline

What are some ‘translational’ challenges across diverse, aging communities?

1. Improve definitions and descriptions of terminology such as low socioeconomic status, diversity & disparities on community, regional, national and global levels

2. Advance identification & characterization of populations at risk and actively recognize & use these characteristics in study design & data interpretation

3. Broaden measurement & detection environments through active & integrated partnerships comprised of industry, healthcare, public health, government & academic entities
What are some ‘translational’ needs across diverse, aging HIV communities?

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2. Advance identification & characterization of populations at risk and actively recognize & use these characteristics in study design & data interpretation

3. Broaden measurement & detection environments through active & integrated partnerships comprised of industry, healthcare, public health, government & academic entities
2. Better identification & characterization of aging HIV populations at risk

Cross-Pollinate Usual Aging Epidemiology to Aging HIV Epidemiology
Adiposity & Obesity

HIV Infection

Rx

Metabolic alterations

Vascular Co-morbidities

Bioenergetics

Cognitive Impairments

2. Better identification & characterization of aging HIV populations at risk to identify intervention windows

Mid-life exposures

Later-life outcomes

| Mid- to late-life longitudinal risk trajectories, e.g., blood pressure, BMI, type 2 diabetes markers, lipids; stratify by type & number of exposures |
| Later-life outcomes by increasing age decade baselines |

<table>
<thead>
<tr>
<th>50-59</th>
<th>60-69</th>
<th>70-79</th>
<th>80-89</th>
<th>90+ years</th>
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</table>

Outcomes assessment

Later life exposures

Later-life outcomes

| Mid- to late-life longitudinal risk trajectories, e.g., blood pressure, BMI, type 2 diabetes markers, lipids; stratify by type & number of exposures |
| Later-life outcomes by increasing age decade baselines |

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Outcomes assessment
BMI by Dementia over 37 years and Presence of the APOE ε4 allele

Prospective Population Study of Women in Gothenburg, Sweden

No dementia, no APOE ε4

Dementia, no APOE ε4

No dementia, APOE ε4

Dementia, APOE ε4

WHR > 0.80
HR 2.22 (1.0, 4.9)

main effect of age
interactions of age by APOE ε4 and age by presence vs absence of dementia

Gustafson, Bäckman et al., JAD 2012
Bäckman..., Gustafson. JAD 2015.
The association between body weight and clinical dementia progression (CDR-Sum of Boxes) varied by baseline (age >65y) body weight and APOEε4 status in clinical AD

- slower clinical progression with high body weight
- slower clinical progression with high body weight and no APOEε4 compared to moderate body weight participants with APOEε4 (p=0.010)

Besser… Gustafson. Alz Disease Assoc Disorders, 2014;28(1):36-43
MIDLIFE ADIPOSITY PREDICTS COGNITIVE DECLINE IN THE MULTICENTER AIDS COHORT STUDY (MACS)

Baseline BMI Status
- normal
- overweight
- obese

HIV-

MWH

Rubin, Gustafson et al., Neurology, in press
• Adipokines measures may provide mechanistic insights of fat-brain or gut-brain associations in middle-aged HIV+ and at risk HIV- women.

• Monitoring adipokines over time in relation to cognitive health may lend insights to the role of adipose and gut in successful brain and body aging.

Gustafson et al., J Neurovirol, 2013; Gustafson et al., J Gerontol Geriatr Res, 2015; McFarlane... Gustafson, Neurology & Neurophysiology, 2017, E-pub Feb;8(1); Dellinger.... Gustafson, in preparation.
A 10 year follow-up of adiposity and dementia in Swedish adults aged 70-years and older
The H70 Study 1930 Birth Cohort in Gothenburg

- Low BMI risky for dementia within 5 years
  - OR 4.2, 95% CI 1.0-17.2, p=0.04

- Intermediate leptin levels protective for dementia within 5 years
  - OR 0.3, 95% CI 0.1-0.9, p=0.04

- No association with HMW adiponectin

Arnoldussen IAC… Gustafson D, J Alzheimers Disease, 2018.
Total Adiponectin Levels, Neuroimaging, & Cognition the Mayo Clinic Study of Aging (MCSA), ≥70 years

- Plasma adiponectin in a population-based sample of adults without dementia, age ≥ 70 years

- Neuroimaging: amyloid PET, FDG PET in Alzheimer signature regions of interest, hippocampal volume, and cortical thickness
- Cognition: MCI, performance on neuropsychological tests

Adiponectin Levels, Neuroimaging, & Cognition
the Mayo Clinic Study of Aging, >70 years

- Adiponectin was higher in women than men ($P < 0.001$)

- Among women, higher adiponectin was associated with
  - smaller hippocampal volume
  - poorer performance on tests of language, global cognition
  - greater odds of Mild Cognitive Impairment diagnosis

  - particularly with evidence of Alzheimer neuropathology (elevated amyloid, PiB-PET>1.4)

RUN DMC – Cerebral small vessel disease cohort

Age 66 years  N=503

71 years  N=287

In men:
Higher BMI, WC and leptin associated with lower gray matter & total brain volumes. Higher BMI & WC associated with lower hippocampal volume.

Obese WC (>102cm) protective for >1 lacune or >1 microbleed

In women:
Increasing BMI and overweight or obesity (BMI ≥25 kg/m² or WC ≥88 cm) associated with ≥1 lacune

Baseline obese WC  9 year decrease in hippocampal volume in men

9 year increase in WMH volume in women and men

Arnoldussen, Gustafson et al. Neurology, in press.
Cross-sectional analyses
- Late-life low BMI \(\rightarrow\) prevalent dementia
- Late-life higher adiponectin \(\rightarrow\) worse cognition and worse AD brain neuroimaging outcomes
- Mid-life higher adiposity \(\rightarrow\) better cognition
- Mid-life higher leptin \(\rightarrow\) worse cognition
- Mid to later-life higher leptin \(\rightarrow\) better cognition
- Mid-life higher gut hormones \(\rightarrow\) better cognition

Longitudinal analyses
- First Report: Late-life more overweight among women born 1901/02 in their 70s \(\rightarrow\) AD at age \(\geq\) 80y
- 37-year natural history of BMI and dementia
- Mid-life higher waist-to-hip ratio (WHR) \(\rightarrow\) higher dementia risk after 32 years
- Late life declining BMI preceding dementia and with usual aging
- Steeper late-life BMI decline with APOE\(\varepsilon\)4 allele among those with and without dementia
- Late-life low BMI \(\rightarrow\) dementia within 5 years
- Late-life intermediate leptin levels \(\rightarrow\) lower odds of dementia within 5 years
- Late-life higher BMI + no APOE\(\varepsilon\)4 \(\rightarrow\) slower dementia progression over 1y based on CDR-Sum of boxes
- Late-life lower BMI + APOE\(\varepsilon\)4 \(\rightarrow\) faster dementia progression over 1y based on CDR-Sum of boxes
- Mid-life higher BMI, WC \(\rightarrow\) greater decline in domain-specific cognitive functioning
2. Better identification & characterization of aging populations at risk to identify intervention windows

Mid-life exposures

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‘Risky’
Mid-life higher BMI, central obesity

‘Protective’
Later-life higher BMI, central obesity, leptin
Lower adiponectin

Later-life exposures

Outcomes assessment

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2. Better identification & characterization of aging HIV populations at risk to identify intervention windows

Mid-life exposures

‘Risky’
Mid-life higher BMI, central obesity in HIV+ & at-risk men

‘Protective’
Mid-life higher BMI, central obesity, leptin in HIV+ & at-risk women

Mid-life outcomes

Outcomes assessment

Metabolic alterations

Vascular Co-morbidities

Bioenergetics

Cognitive Impairments

HIV Infection

Adiposity & Obesity

HIV Infection in Women

Health diversities & disparities
- Socioeconomic status
- Social network
- Built environment
- Food insecurity
- Ethnoracial background
- Access to healthcare
- Control of infection
- ART type
- Control of multi-morbidity
- Polypharmacy
- Medication adherence

Obesity
- Vascula r Alterations
- Obesity Syndromes, T2D
- Metabolic Alterations
- Aging
- Neurodegeneration
- Multimorbidity

Cognitive Impairments and Dementias → Death

McFarlane & Gustafson, 2018.
HIV Infection

HIV Aging Brain

Adiposity & Obesity
Higher blood glucose, HbA1c, lipids
Hypertension, Obesity
Higher Framingham Stroke Risk
Pre-Type 2 Diabetes Mellitus
Genetic vascular risk – APOE, ACE, Clusterin, FTO

Type 2 Diabetes Mellitus
Metabolic syndromes
Hypoglycemic episodes
Cardiovascular Disease

Cognitive decline
Neuropathological changes
Cerebrovascular Disease

Cognitive Impairments & Dementias

Multiple Targets & Interventions

Targets
- Clinical
  - Diagnoses – symptoms, disorders
    - Individual or clusters
  - Change
  - Peripheral & central fluid biomarkers
  - Organ-specific events

Interventions
- Pharmaceutical
  - Fit for purpose
  - Repurposed

- Lifestyle
  - Diet
  - Exercise
  - Intellectual activities
  - Reducing sigma
  - Reducing disparity
Prevention and Treatment Targets

What are we preventing?
What are we treating?
What are we preventing?
What are we treating?

Prevention = Treatment
‘an ounce of prevention is worth a pound of cure’
In conclusion...
HIV Aging Epidemiology - A New Discipline

What are some ‘translational’ challenges across diverse, HIV aging communities?

1. Improve definitions and descriptions of terminology such as low socioeconomic status, diversity & disparities on regional, national and global levels

2. Advance identification & characterization of populations at risk and actively recognize & use these characteristics in study design & data interpretation

3. Broaden measurement & detection environments through active & integrated partnerships comprised of industry, healthcare, public health, government & academic entities
Geriatric Syndromes

**Forgetfulness and Confusion**
It is important to differentiate this ordinary forgetfulness that comes with aging from dementia or Alzheimer’s disease.

**Vision Problems**
Older adults should have their eyes checked at least once a year for early detection of visual problems such as cataracts or glaucoma.

**Imbalance and Falls**
Caused by several factors such as neurological diseases, low blood pressure, osteoarthritis, or as a side effect of medications.

**Common health conditions in older adults or “GERIATRIC SYNDROMES”**
are usually caused by several factors. Geriatricians provide comprehensive physical and mental health care for older adults.

**Two groups of older adults that require special care**
- Patients with multiple diseases
- Patients with diseases or symptoms of uncertain or unknown causes

Geriatric Syndromes

**Osteoporosis**
Common in women after menopause or men older than 70, this condition increases the risk of fractures in older adults.

**Urinary Incontinence**
Greatly affects the quality of life of older adults.

**Top 10 global causes of deaths, 2016**

<table>
<thead>
<tr>
<th>Cause Group</th>
<th>Deaths (millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischaemic heart disease</td>
<td></td>
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<tr>
<td>Stroke</td>
<td></td>
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<tr>
<td>Chronic obstructive pulmonary disease</td>
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<tr>
<td>Lower respiratory infections</td>
<td></td>
</tr>
<tr>
<td>Alzheimer disease and other dementias</td>
<td></td>
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<tr>
<td>Diabetes mellitus</td>
<td></td>
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<tr>
<td>Road injury</td>
<td></td>
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<tr>
<td>Diarrhoeal diseases</td>
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<tr>
<td>Tuberculosis</td>
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</tbody>
</table>

HIV Aging
Prevention and Treatment Strategies need to be
Fit for Purpose and Fit for Community

Cross-Pollinate Usual Aging Epidemiology to Aging HIV Epidemiology

Gustafson, Neurology & Neuromed, 2018, in press.
Gustafson DR. Executive Summary: Cost Effective Early Detection of Cognitive Impairment.
While we replicate and expand traditional Aging Epidemiology findings we will better understand:
  • Roles of social determinants of health in aging biology and how these impact pathophysiologic aging mechanisms
  • Subgroups of those with HIV infection who may be more or less at risk for adverse aging events or changes
  • The role and timing of vascular risk and control of that risk
  • ART and the brain
• Change aging paradigms
• Changes aging brain paradigms
Aging Women & Men with HIV: Enquiring Minds (like ours) Want to Know

Deborah.Gustafson@downstate.edu

THANK YOU
HIV & AGING: FROM MITOCHONDRIA TO THE METROPOLIS
Psychosocial Correlates of Successful Aging Among Older HIV-Infected and HIV-Uninfected Women: No Difference by HIV Status

Anna A. Rubtsova, PhD
Psychosocial Correlates of Successful Aging among Older Women with and at Risk of HIV: No difference by HIV Status

Anna Rubtsova, PhD
Emory University
Rollins School of Public Health
102,215 older (50+) women living with HIV (OWLH) in the US in 2015*

OWLH experience multiple challenges**: 
- Multimorbidity and polipharmacy
- Postmenopausal osteoporosis, frailty, falls
- Gender-related stigma and discrimination

Can OWLH experience successful aging (SA)?

* CDC, *HIV Surveillance Supplemental Report*, 2018
** Durvasula *Behav Med* 2014; Rubtsova et al. *Curr HIV/AIDS Rep* 2017
BACKGROUND

SA – capacity of older people to thrive in the presence of age-related declines.

Ernestine Shepherd

Ida Keeling
**BACKGROUND**

- **Self-Rated SA (SRSA)** - positive outcomes of aging from layperson’s point of view; individuals’ own holistic appraisals of how well they are aging

- Prevalence of SRSA>=7 (on a 1-10 scale):  
  - Among PLWH: 67%*
  - Among OWLH: 84%**

- SRSA is achievable among OWLH

- What factors are associated with better SRSA?

* Moore et al. *AIDS Behav.* 2018  
** Rubtsova et al. *GSA* 2019
No research on SRSA correlates among OWLH

SRSA correlates among other populations:

<table>
<thead>
<tr>
<th>SRSA</th>
<th>General population*</th>
<th>PLWH**</th>
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</thead>
<tbody>
<tr>
<td>Associated with</td>
<td>Cognitive functioning</td>
<td>Positive psychosoc. factors</td>
</tr>
<tr>
<td></td>
<td>Mental &amp; physical health</td>
<td>Mental health</td>
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<tr>
<td></td>
<td>Positive psychosoc. factors</td>
<td>Physical health</td>
</tr>
<tr>
<td></td>
<td>Leisure activities</td>
<td></td>
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<tr>
<td>No association or mixed findings</td>
<td>Mixed findings for sociodemographics and negative life events</td>
<td>Age HIV disease characteristics</td>
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<td>HIV disease characteristics</td>
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<td>Negative life events</td>
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OBJECTIVES

- To determine if SRSA correlates differ by HIV status in a sample of older women with and at risk of HIV
- To assess SRSA correlates among OWLH
METHODS
Multicenter prospective cohort study

From Surviving to Thriving (FROST) substudy*

4 WIHS sites: Atlanta, UNC, Brooklyn, Bronx

Sample: 523 WIHS 50+ women (74% HIV+)

Inclusion criteria: a) biol. female, b) 50+, c) HIV+/HIV-, d) consent; e) English speaking

Procedures:
- 10 min FROST survey added to WIHS core interview
- Interviewer-administered
- Collected between October 2, 2017 – March 30, 2018

*This work is supported by the developmental grant from the NIH Center for AIDS Research at Emory (P30AI050409)
**Outcome:**
- Self-rated SA (SRSA)* “Using your own definition, where would you rate yourself in terms of ‘successful aging,’ from “1” (least successful) to “10” (most successful)?”

**Psychosocial exposures:**
- Validated scales: e.g., optimism (LOT-R), resilience (CD-RISC), personal mastery (PMS), anxiety (GAD-7)

**Cross-sectional statistical analyses:**
- Descriptive statistics, t-tests, chi-square
- OLS models: 1) bivariate – full sample, 2) adjusted, interaction terms – full sample; 3) adjusted - OWLH

RESULTS
<table>
<thead>
<tr>
<th></th>
<th>HIV+ (N=386)</th>
<th>HIV- (N=137)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (range: 50-83), mean (SD)</td>
<td>56.5 (5.3)</td>
<td>57.2 (5.2)</td>
<td>0.24</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td>0.83</td>
</tr>
<tr>
<td>White</td>
<td>6.0%</td>
<td>5.1%</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>73.8%</td>
<td>73.7%</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>17.4%</td>
<td>16.8%</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>2.9%</td>
<td>4.4%</td>
<td></td>
</tr>
<tr>
<td>Annual income ≤ $6,000</td>
<td>8.4%</td>
<td>17.5%</td>
<td>0.003</td>
</tr>
<tr>
<td>Education ≤ 11 grade</td>
<td>38.0%</td>
<td>38.3%</td>
<td>0.94</td>
</tr>
<tr>
<td>Employed</td>
<td>30.1%</td>
<td>28.5%</td>
<td>0.73</td>
</tr>
<tr>
<td>Married or partnered</td>
<td>21.8%</td>
<td>19.0%</td>
<td>0.49</td>
</tr>
<tr>
<td>Lives in own home</td>
<td>87.6%</td>
<td>74.5%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Health insurance</td>
<td>98.7%</td>
<td>83.9%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sexual gender minority</td>
<td>10.1%</td>
<td>13.9%</td>
<td>0.23</td>
</tr>
</tbody>
</table>
### HIV Disease Characteristics:

<table>
<thead>
<tr>
<th>HIV Disease Characteristics</th>
<th>HIV+ (N=298)</th>
<th>HIV- (N=110)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>On ART</td>
<td>93.8%</td>
<td>--</td>
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<tr>
<td>ART adherence ≥ 95%</td>
<td>84.5%</td>
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</tr>
<tr>
<td>History of AIDS</td>
<td>35.2%</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Undetectable viral load</td>
<td>73.4%</td>
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</tr>
<tr>
<td>CD4 cells count, median (IQR)</td>
<td>750 (538, 1051)</td>
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</tr>
<tr>
<td>Nadir CD4 cell count, median (IQR)</td>
<td>252 (114, 369)</td>
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### Comorbidities:

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<tr>
<th>Comorbidities</th>
<th>HIV+ (N=298)</th>
<th>HIV- (N=110)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity (BMI≥30)</td>
<td>50.5%</td>
<td>61.3%</td>
<td>0.03</td>
</tr>
<tr>
<td>Diabetes</td>
<td>27.5%</td>
<td>36.5%</td>
<td>0.05</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>86.8%</td>
<td>92.0%</td>
<td>0.11</td>
</tr>
<tr>
<td>Stroke</td>
<td>5.4%</td>
<td>8.0%</td>
<td>0.23</td>
</tr>
<tr>
<td>Cardio-vascular disease</td>
<td>16.3</td>
<td>21.9</td>
<td>0.14</td>
</tr>
<tr>
<td>History of cancer</td>
<td>7.8%</td>
<td>8.8%</td>
<td>0.72</td>
</tr>
</tbody>
</table>
Significantly associated with SRSA:
- **Sociodemographic characteristics:** race, employment status
- **HIV disease characteristics:** nadir CD4 ≤ 200 cells/µL
- **Comorbidities:** history of hypertension

Included as covariates in the adjusted analyses:
- **Full sample:** Black, employed, hypertension, age
- **OWLH subsample:** Black, employed, hypertension, age, nadir CD4 ≤ 200 cells/µL
### Adjusted OLS with Interactions

<table>
<thead>
<tr>
<th>Psychosocial Var</th>
<th>Model</th>
<th>Psych Var - main effect</th>
<th>HIV Status - main effect</th>
<th>Psych Var X HIV Status</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Positive Psychosocial</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Personal mastery</td>
<td>523</td>
<td>0.15***</td>
<td>1.67 (1.05)</td>
<td>-0.07 (0.05)</td>
</tr>
<tr>
<td>Optimism</td>
<td>522</td>
<td>0.09**</td>
<td>0.90 (1.02)</td>
<td>-0.02 (0.03)</td>
</tr>
<tr>
<td>Resilience</td>
<td>521</td>
<td>0.08**</td>
<td>0.37 (0.75)</td>
<td>-0.01 (0.02)</td>
</tr>
<tr>
<td>Spirituality</td>
<td>505</td>
<td>0.07**</td>
<td>1.31 (0.84)</td>
<td>-0.03 (0.02)</td>
</tr>
<tr>
<td>Social support</td>
<td>503</td>
<td>0.03**</td>
<td>1.26 (0.81)</td>
<td>-0.02 (0.01)</td>
</tr>
<tr>
<td>Coping</td>
<td>521</td>
<td>0.02**</td>
<td>0.26 (0.66)</td>
<td>-0.002 (0.01)</td>
</tr>
<tr>
<td>HRQOL (SF-36)</td>
<td>523</td>
<td>0.02*</td>
<td>-0.02 (0.65)</td>
<td>0.002 (0.01)</td>
</tr>
<tr>
<td><strong>Negative Psychosocial</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depressed (CES-D&gt;16)</td>
<td>523</td>
<td>-0.52</td>
<td>0.17 (0.18)</td>
<td>0.05 (0.43)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>504</td>
<td>-0.01</td>
<td>0.29 (0.22)</td>
<td>-0.02 (0.04)</td>
</tr>
</tbody>
</table>
## Adjusted OLS: OWLH Subsample

<table>
<thead>
<tr>
<th></th>
<th>Model N</th>
<th>B</th>
<th>95% CI</th>
<th>P-value</th>
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<tr>
<td><strong>Positive Psychosocial</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Personal mastery</td>
<td>370</td>
<td>0.08</td>
<td>(0.03; 0.13)</td>
<td>0.001</td>
</tr>
<tr>
<td>Optimism</td>
<td>369</td>
<td>0.07</td>
<td>(0.04; 0.09)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Resilience</td>
<td>369</td>
<td>0.07</td>
<td>(0.04; 0.09)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Spirituality</td>
<td>359</td>
<td>0.03</td>
<td>(0.01; 0.06)</td>
<td>0.02</td>
</tr>
<tr>
<td>Social support</td>
<td>360</td>
<td>0.01</td>
<td>(-0.002; 0.03)</td>
<td>0.11</td>
</tr>
<tr>
<td>Coping</td>
<td>369</td>
<td>0.02</td>
<td>(0.01; 0.03)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HRQOL (SF-36)</td>
<td>370</td>
<td>0.02</td>
<td>(0.01; 0.03)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Negative Psychosocial</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depressed (CES-D &gt; 16)</td>
<td>370</td>
<td>-0.54</td>
<td>(-1.01; -0.07)</td>
<td>0.02</td>
</tr>
<tr>
<td>Anxiety</td>
<td>362</td>
<td>-0.04</td>
<td>(-0.10; 0.002)</td>
<td>0.06</td>
</tr>
<tr>
<td>Social isolation</td>
<td>362</td>
<td>-0.10</td>
<td>(-0.20; 0.01)</td>
<td>0.09</td>
</tr>
<tr>
<td>Lifetime discrimination</td>
<td>360</td>
<td>-0.24</td>
<td>(-0.47; -0.004)</td>
<td>0.05</td>
</tr>
</tbody>
</table>
Among disadvantaged older women, SRSA correlates may not differ by HIV status.

Enhancement of positive psychosocial factors and management of depression may increase the likelihood of SRSA among OWLH.

Longitudinal research is needed to examine psychosocial determinants of SRSA.

Further research is needed to compare SRSA correlates by gender and to examine associations with negative psychosocial factors (e.g., stigma).
**Acknowledgements**

- **Co-authors:**

- **WIHS staff and participants:** in Atlanta, UNC, Brooklyn, Bronx, and WDMAC

- **Mentors:**
  - Marcia Holstad, Gina Wingood, David Vance, Maria Marquine, Colin Depp, Molly Perkins, Hannah Cooper

- **Funding:**
  - Primary WIHS funding by NIAID
  - CFAR-03 developmental grant by NIH Center for AIDS Research at Emory (P30AI050409)
  - Sustained Training in HIV and Aging (STAHR) training grant (R25 MH108389)
Menopause Stage Contributes to Sex Differences in Inflammatory Biomarkers in Persons Living with HIV in the US

Rebecca Schnall, PhD
SYMPTOM BURDEN & INFLAMMATORY CYTOKINES IN PLWH IN THE US

An analysis by sex, menopause stage and menstrual cycle phase

Rebecca Schnall, PhD, MPH, RN-BC, FAAN
Haomiao Jia, PhD
Nancy Reame, PhD, MSN, RN, FAAN
Introduction

• With improvements in ART, PLWH are successfully aging into midlife\(^1\)
  
  • More women living with HIV are experiencing menopause and its symptoms\(^2\)
  
  • Among PLWH, higher rates of depression, anxiety, sleep disturbances, and neuropathy have been identified\(^3\)
  
• Between HIV and menopause, the origin of symptoms in midlife women with HIV is unclear\(^4\)

---

Background

• PLWH demonstrate alterations in inflammatory cytokines and coagulation markers, suggesting the persistence of chronic-low grade inflammation\textsuperscript{5}
  
  • Evidenced by significantly higher plasma levels of Interleukin (IL)-6, TNF\textalpha, IL-8, and C-Reactive Protein (CRP)

• In an earlier study, symptom burden scores were significantly higher in women compared to men\textsuperscript{6}
  
  • Post-menopausal women also had significantly higher scores compared to pre-menopausal women
  
  • Findings suggest menopause may be an independent predictor of enhanced burden of HIV symptoms in women


\textsuperscript{6} Schnall R, Jia H, Olender S, Gradilla M, Reame NJM. In people living with HIV (PLWH), menopause (natural or surgical) contributes to the greater symptom burden in women: results from an online US survey2018;25(7):744-52.
Research Gaps

• There has been limited study of whether sex differences and menopause effects on cytokine activity are present in PLWH where chronic inflammation may be present

• A better understanding of how inflammatory cytokines relate to the symptom experience of PLWH is timely and needed
Research Questions

• What is the relationship between menopause status and HIV symptom burden?

• What associations exist among symptom burden and commonly studied inflammatory biomarkers in a cohort of HIV-infected urban residents?
Methods - Participants

• PLWH were recruited from a CBO and outpatient clinic in NYC serving HIV patients

• Goal of including 25 men matched on age with 75 women stratified accordingly:
  • a) pre-menopausal women
  • b) peri-menopausal women
  • c) post-menopausal women

• Inclusion criteria
  • 18 years or older
  • Black and/or Latino
  • Taking antiretroviral therapy (ART)
  • Females: past history of regular menstrual cycles
Methods - Procedures

• For women who reported a period in the past 3 months, the study visit was synchronized to fall between days 1-6 of the menstrual cycle.

• During the visit, participants completed the following:
  • Blood draw to determine concentrations of sex steroids (estradiol, testosterone) and cytokines (IL-6, IL-8, TNFα, CRP)
  • Survey on demographics, height and weight, reproductive health status (STRAW), HIV symptoms (HIV-SI), health-related quality of life (PROMIS-29) and most recent viral load
Results

- The majority of participants were
  - Black non-Hispanic (n = 74; 74%),
  - middle-aged (mean ± SD = 51.5 ± 7.7 years),
  - with at least some high school education (60%),
  - and reporting less than $20,000 in annual income (67%)
- Viral load was suppressed in the majority of participants (86%)
- Most (57%) were non-smokers
Results

- In both sexes, the most burdensome HIV symptoms were:
  - fatigue
  - neuropathy
  - difficulty falling asleep
  - muscle aches/joint pain

<table>
<thead>
<tr>
<th>Table 2. A Comparison of Symptom Burden Scores (mean +SD) by Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom</td>
</tr>
<tr>
<td>---------------------------------------------------------</td>
</tr>
<tr>
<td>Fatigue or loss of energy</td>
</tr>
<tr>
<td>Fevers, chills or sweats</td>
</tr>
<tr>
<td>Feeling dizzy or lightheaded</td>
</tr>
<tr>
<td>Pain, numbness or tingling in the hands or feet (neuropathy)</td>
</tr>
<tr>
<td>Trouble remembering</td>
</tr>
<tr>
<td>Nausea or vomiting</td>
</tr>
<tr>
<td>Diarrhea or loose bowel movements</td>
</tr>
<tr>
<td>Felt sad, down or depressed</td>
</tr>
<tr>
<td>Felt nervous or anxious</td>
</tr>
<tr>
<td>Difficulty falling or staying asleep</td>
</tr>
<tr>
<td>Skin problems, such as rash, dryness or itching</td>
</tr>
<tr>
<td>Cough or trouble catching your breath</td>
</tr>
<tr>
<td>Headache</td>
</tr>
<tr>
<td>Loss of appetite or a change in the taste of food</td>
</tr>
<tr>
<td>Bloating, pain or gas in your stomach</td>
</tr>
<tr>
<td>Muscle aches or joint pain</td>
</tr>
<tr>
<td>Problems with having sex, such as loss of interest or lack of satisfaction</td>
</tr>
<tr>
<td>Changes in the way your body looks such as fat deposits or weight gain</td>
</tr>
<tr>
<td>Problems with weight loss or wasting</td>
</tr>
<tr>
<td>Hair loss or changes in the way your hair looks</td>
</tr>
</tbody>
</table>
Results

- Three of the five symptoms where burden scores differed by menopause stage related to pain
- Highest burden scores in the pre-menopause group
  - Post-menopausal group demonstrated a similar burden for muscle aches/joint pain
  - Scores for men and peri-menopause women were lowest
Results

- Pain intensity scores on the PROMIS-29 also varied significantly by groups (p=0.03)
Results

- For the total sample, no sex differences were observed in CRP, TNFα, IL-6 or IL-8.
- When the female group was subdivided by menopause stage and compared to males, significant group differences were observed for TNFα (p=0.0045) and IL-8 (p<0.001)
Results

- After controlling for sex/menopause status and BMI, significant differences were noted in CRP, IL-6 and IL-8 for PLWH who reported muscles aches/ joint pain

<table>
<thead>
<tr>
<th>Biomarker (predictor)</th>
<th>Symptom (outcome)</th>
<th>Beta</th>
<th>S.E.</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>hsCRP mg/L</td>
<td>Muscle aches or joint pain</td>
<td>-1.40</td>
<td>0.39</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Lipodystrophy</td>
<td>-1.22</td>
<td>0.43</td>
<td>0.004</td>
</tr>
<tr>
<td></td>
<td>Weight Loss/ Wasting</td>
<td>-0.860</td>
<td>0.363</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>Problems with having sex</td>
<td>-0.91</td>
<td>0.43</td>
<td>0.04</td>
</tr>
<tr>
<td>IL6 pg/ml</td>
<td>Diarrhea</td>
<td>0.81</td>
<td>0.30</td>
<td>0.012</td>
</tr>
<tr>
<td></td>
<td>Loss of appetite</td>
<td>0.72</td>
<td>0.35</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>Muscle aches or joint pain</td>
<td>0.78</td>
<td>0.36</td>
<td>0.04</td>
</tr>
<tr>
<td>IL8 pg/ml</td>
<td>Muscle aches or joint pain</td>
<td>-1.082</td>
<td>0.471</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>Neuropathy</td>
<td>-1.214</td>
<td>0.543</td>
<td>0.03</td>
</tr>
<tr>
<td>TNFa pg/ml</td>
<td>Problems with having sex</td>
<td>-2.37</td>
<td>1.15</td>
<td>0.04</td>
</tr>
</tbody>
</table>
Limitations

- Given the small sample size (n=100):
  - We were unable to control for a number of important covariates, which have been shown to be associated with inflammatory cytokines
    - chronic disease, cognitive impairment, alcohol use, smoking and level of education.
  - We were unable to conduct post-hoc analyses
  - Since we did use convenience sampling, there is also the risk of both sample bias and selection bias
Conclusion

- Evidence suggests enhanced burden for HIV-related pain symptoms in women in the early follicular phase, possibly owing to menstruation
  - This supports the need for more targeted investigations in younger cycling women with HIV at multiple phases across the menstrual cycle
- Further, there is evidence to support that in PLWH, systemic inflammation is heightened even when viral load is undetectable, making them at greater risk for comorbidities such as cardiovascular disease
References


Ecological Study of New HIV diagnoses and PrEP Utilization Among Individuals 55 Years and Older in Southeastern States and DC.

Christina Chandra, BA
Ecological study of new HIV diagnoses and PrEP utilization among individuals 55 years and older in Southeastern states and DC, 2012-2016

Christina Chandra¹, Alejandra Alvarez¹, Robert Lyles¹, Udodirim Onwubiko², Allison Chamberlain¹

¹Rollins School of Public Health, Emory University, Atlanta, USA
²Fulton County Board of Health, Atlanta, USA

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Conflict of Interest Disclosure

The authors have no conflicts of interest due to financial or personal relationships that might be perceived to cause bias.
Background

• People are living longer with HIV. Nearly half of Americans living with diagnosed HIV are age 50 or older, 30% are age 55 or older. (CDC, 2015)

• Older persons are sexually active, and they may underestimate their risk of HIV and engage in risky behavior (e.g., condomless sex). (Pilowsky et al., 2015)

• The South accounts for more than half of new HIV diagnoses in the U.S. (CDC, 2017)

• Only 30% of all pre-exposure prophylaxis (PrEP) users are in the South. (AIDSVu)

• PrEP coverage for older Americans is also lower compared to younger age groups. (AIDSVu)
Objective & Methods

• **Objective:** To examine differences in new HIV diagnoses and PrEP use in individuals 55 years and older in Southeastern states and DC from 2012 to 2016.

• **Methods:**
  - Downloaded publicly available data from AIDSVu on new HIV diagnoses and PrEP utilization in Alabama, Arkansas, DC, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, South Carolina, Tennessee, Virginia, and West Virginia
  - Generated descriptive maps, graphs, and statistics to evaluate trends in HIV diagnoses among persons 55 years and older over the 5-year period
### New HIV diagnoses data

- **Source:** CDC surveillance data, 2012-2016
- **Represents any person newly diagnosed with HIV regardless of disease stage**
- **Rates calculated using** US Census Bureau

### PrEP use data

- **Source:** U.S. Source Healthcare Analytics (SHA) prescription data, 2012-2016
- **Represents “the number of unique persons who had at least one day of prescribed oral TDF/FTC for PrEP**
Among individuals 55 and older from 2012-2016, DC’s average rate of new HIV diagnoses (35.8 ± 9.3) was high compared to that of other states combined (5.3 ± 0.3).
Median Rate of New HIV Diagnoses among Persons Age 55 and Older by Sex in Southeastern States and DC, 2012-2016
Median Rate of New HIV Diagnoses among Persons Age 55 and Older by Race in Southeastern States and DC, 2012-2016
Mean Proportion of New HIV Diagnoses among Persons Age 55 and Older by Transmission Type in Southeastern States and DC, 2012-2016

Year

Percent (%)


Heterosexual contact
Men who have sex with men (MSM)
Injection drug use (IDU)
MSM and IDU
Other
Among individuals 55 and older from 2012-2016, DC’s average rate of PrEP use (31.6 ± 29.0) was high compared to that of other states combined (2.0 ± 1.4).
Median Rate of PrEP use by Age Category in Southeastern States and DC, 2012-2016

Rate (per 100,000)

Year


13-24 years
25-34 years
35-44 years
45-54 years
55 years or older
From 2012-2016, DC’s rate of PrEP use among persons age 55 and older had a 12-fold increase while rates of HIV diagnoses decreased by 38%.
PrEP Use among Persons Age 55 and Older as a Proportion of all PrEP Users in the State, 2016
Implications

• Continued surveillance in the aging population is important
• More research is needed:
  • What are the most effective prevention approaches among the aging population?
  • What are barriers to HIV prevention in the aging population?
• High-resolution geographic data may become less available as cases decrease, so the role of local health departments will be more important than ever.
  • **Ending the Epidemic**: How does this inform national efforts to reduce new HIV infections by 75% in 5 years and by at least 90% in 10 years especially with an aging population in the U.S.?
Limitations

• Denominator doesn’t represent people at risk of infection
• Data resolution (confidentiality concerns):
  • Age categorization stops at 55+
  • ZIP3-level data for new HIV diagnoses
  • PrEP data not stratified by age and sex or race simultaneously
  • Data on disease stage at diagnosis not available geographically (but older persons are more likely to have stage 3 disease at HIV diagnosis compared to younger persons)
• Data underestimates the number of PrEP users (e.g., excludes VA)
• No comparison to rates of HIV testing
• Unknown completeness of new HIV diagnosis reporting
Acknowledgements

• Sponsorship from the Department of Epidemiology, Rollins School of Public Health
• Dr. Ann Do, PRISM, Emory Rollins School of Public Health
• Dr. Ameeta Kalokhe, Emory Rollins School of Public Health
HIV-Tat Induces its Neurotoxic Effects by Downregulation Sonic Hedgehog Signaling in Brain

Vir Singh, PhD
HIV-Tat induces its neurotoxic effects by downregulating Sonic Hedgehog signaling in brain

Vir B Singh, PhD
Research Assistant Professor
University of Rochester Medical Center
People living with HIV/AIDS = 36.9 million (2017)
Total = 70 million
Mortality = 0.94 million (2017)
35 million overall
New infections: 1.8 million (2017)
Comorbidities are more prevalent in people living with HIV

- Cardiovascular disease
- Neurological disease
- Malignancies
- Accelerated Aging (Inflammation)

Figure 1. Distribution of the number of comorbidities stratified by age: comparison between HIV and non-HIV patients.

Maciel et al,
HAND: HIV Associated Neurological Disorder

- Learning, memory and executive function domain are more affected in cART era.

Heaton et al, 2011
HIV-1 induced Neuropathology

Blood-Brain Barrier

Blood → CNS

Macrophage infection and activation

Astrocyte infection and activation

Microglia infection and activation

Uninfected and HIV Infected Monocytes And CD4+ T cells

Chemokines:
CCL2 and CXCL12

Cytokines:
TNF-α, IL-1β, IL-6

Neurotoxic Host Factors:
Nitric oxide, Excitatory amino acids, Free radicals, Quinolinic acid

Neurotoxic Viral Factors:
Tat, gp120, gp41, Nef, Vpr, Rev

Neurons

Demyelination, pruning, neuronal injury and loss

Williams et al 2014
Shh Signaling mediates BBB integrity

- Development of nervous system
- Cell proliferation (mitogen) and differentiation.
- Neuroprotective functions.
  - Spinal cord injury (Heine et al, 2011)
  - Down’s syndrome (Das et al, 2013)
  - Neonatal cerebellar injury (Bambakidis et al, 2010)
  - BBB integrity in MS (Alvarez et al, 2011)
Major Findings:
• Loss of Shh signaling in chronic HIV infection is associated with damaged blood brain barrier integrity, astrocyte/microglial activation and neuronal damage.

• Administration of Smoothened agonist-SAG, reversed BBB damage and reduced astrocyte/microglia activation

Major Findings:
• Administration of SAG during Acute HIV infection, significantly reduced infiltration of HIV infected leukocytes into the brain.

• This reduction was associated with lower brain viral load.

• Pharmacologic intervention with SAG in early infection conferred long term neuroprotection.
Investigating the efficacy of SAG in Tat TG mouse model
Tat Transgenic Mice – Hauser Tat

- Express HIV-Tat under the control of Dox-inducible GFAP promoter

- Thus, allow astrocyte specific expression of Tat.

- HIV-Tat transgenic mouse model mimics key aspects of true pathophysiologic events underlying HAND in post-cART era (Fitting et al., 2013), including Astrogliosis and Neuronal injury.
Brain Infiltrating Leukocytes in Tat Transgenic mice: Effect of SAG

3 weeks of Dox- treatment
Status of Shh signaling molecules in Tat TG mice

Tat Neg       Tat Pos

1 2 3        1 2 3

Gli1

Shh

Tubulin

Smoothened

Tubulin

Relative Claudin 5 expression

Relative Vcam1 expression

*
SAG can rescue the expression of tight junction proteins in BMVECs

Singh et al, Scientific Reports, 2016
*In vitro* treatment with HIV-1 protein Tat resulted in decreased expression of Shh in primary human fetal astrocytes.
In vitro treatment with SAG reversed Tat mediated increase in GFAP expression in primary fetal astrocytes

Singh et al, Scientific Reports, 2016
SAG negatively regulates the expression of inflammatory cytokine/chemokine in Astrocytes
Future Direction

Investigating the potential Shh signaling modulation in challenging HIV induced pathogenesis/accelerated aging.

Neureiter D 2012
Rescuing Shh Signaling (SAG) affects multiple brain conditions:

- BBB protection
- Neuroprotection
- CNS Homeostasis
- rescue developmental defects in Brain
- challenges Aging

Challenges include:
- HAND
- MS
- Neonatal Cerebellar Injury
- Ischemic Injury
- Down Syndrome
- Subarachnoid hemorrhage in Rats
- CNS Tuberculosis

Concern: Mitogenic, might induce tumorigenesis
Concern: Mitogenic, might induce tumorigenesis

Basal Cell Carcinoma, Medulloblastoma, Ovarian fibroma, meningioma, fibrosarcoma, cardiac fibroma etc.

Major Causes

• Ptch mutations- loss of function
• Smoothened- activating mutations
• Shh mutations- extremely rare

Bottomline:

• Transient activation of Shh signaling might prove beneficial in multiple neurodegenerative disorders
• Warrants studies focused at efficacy of Shh signaling inducers (toxicity, off target effects)
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University of Nebraska Medical Center
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Santhi Gorantla, PhD

Department of Microbiology & Immunology, URMC
NIH Grants to Dr. Maggirwar- R01 HL128155,
R01 NS054578, and R01 NS066801
Evans Blue BBB Permeability assay

Plasma S100B ELISA

DAPI, GFAP
Follow-up study....

Sonic Hedgehog mimetic prevents leukocyte infiltration into the CNS during acute HIV infection

Vir B. Singh¹, Meera V. Singh¹, Dorota Piekna-Przybylska¹, Santhi Gorantla², Larisa Y. Poluektova² & Sanjay B. Maggirwar¹

Received: 8 May 2017
Accepted: 7 August 2017
Published online: 29 August 2017
1. Significant reduction in numbers of BILs
2. Long term protection of CNS in terms of
   • lower VL
   • rescue of BBB integrity
   • rescue of Shh signaling- tight junction
   • diminished astrocytosis
   • rescue of neuronal damage
HIV & AGING: FROM MITOCHONDRIA TO THE METROPOLIS
Dr. Justice is a Clinical Epidemiologist who has developed multiple large national cohorts based on data from the Veterans Affairs Healthcare System Electronic Medical Record enhanced with National Death Index and CMS data, patient completed surveys, DNA and tissue repositories, and stored pathology samples. She has two decades of experience in the processes required to clean, validate, and standardize raw EMR data and in its analysis using standard statistical methods, machine learning techniques, and cross cohort validations. The oldest and best known of her projects is the Veterans Aging Cohort Study (VACS). VACS is an ongoing, longitudinal study of >170,000 United States veterans with and without HIV infection continuously funded by National Institutes of Health (NIH) since 1996.
Substance Use and HCV Among “Baby Boomers” * with HIV

Amy C Justice*, MD PhD
Professor, Yale University Schools of Medicine and Public Health
PI, Veterans Aging Cohort Study

* Baby Boomers were born between 1945-1965. They are now 54-74 yrs. old & AC Justice is one.
Substance use is a risk factor for HIV and HCV risk is high. Those with HIV often self-medicate with substances, and health care increases medication use. Baby Boomers with HIV are likely to have used multiple substances in the past and many continue to do so.
<table>
<thead>
<tr>
<th>Substance</th>
<th>Last 12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harmful Alcohol Use</td>
<td>94.5%</td>
</tr>
<tr>
<td>Smoking (current/ever)</td>
<td>46.3/73.7%</td>
</tr>
<tr>
<td>Marijuana</td>
<td>32.6%</td>
</tr>
<tr>
<td>Cocaine</td>
<td>10.5%</td>
</tr>
<tr>
<td>Heroin/ Prescription Opioids</td>
<td>7.4%/ 7.4%</td>
</tr>
<tr>
<td>Methamphetamines</td>
<td>6.3%</td>
</tr>
</tbody>
</table>

April to August 2014 people seeking HIV care at St-Lukes NYC. Had to be: HIV+, 50-69 years of age, and have no prior history of traumatic brain injury.

Ompad DC et al. Drug use among HIV+ adults aged 50 and older: Findings from the GOLD II Study. AIDS Care 2016 Nov:28(11):1373-7
A Hierarchy of Substances Used

- Alcohol
- Tobacco
- Marijuana
- Cocaine
- Opioids
- Amps
What is VACS and What Have We Learned?
Veterans Aging Cohort Study (VACS)

- NIH, NIAAA study continuously funded since 1998
- Built on national VA Electronic Health Record (EHR)
- Updated annually (FU data & additional subjects)
- All people in VA system:
  - With HIV (~60K)
  - Age/race/site matched to uninfected (~120K)
- Largest HIV cohort in North America
National VACS Project Team 2016-2018
Let the Consumers of Substance Use Data Beware

• Self report is subject to social desirability bias
• Direct biomarkers often tell a different story
• Multi-substance use is more common than single use
• Current use is relevant for
  • ART adherence
  • Risk of overdose
  • Drug-drug interactions
• But, past use is often also important
People reporting “no current” alcohol may be saying what they think they should be doing rather than what they are doing.
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>PEth</th>
<th>Deaths</th>
<th>Rate per 100 PY (95% CI)</th>
<th>Deaths</th>
<th>Rate per 100 PY (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>HIV+ (n = 1513)</td>
<td>Uninfected (n = 831)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>AUDIT-C</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>&lt;8</td>
<td>85</td>
<td>3.36 (2.72 to 4.15)</td>
<td>31</td>
<td>2.04 (1.43 to 2.90)</td>
</tr>
<tr>
<td></td>
<td>≥8</td>
<td>23</td>
<td>5.69 (3.78 to 8.56)</td>
<td>8</td>
<td>3.03 (1.52 to 6.07)</td>
</tr>
<tr>
<td>1–3/1–2</td>
<td>&lt;8</td>
<td>30</td>
<td>1.78 (1.25 to 2.54)</td>
<td>12</td>
<td>1.59 (0.90 to 2.79)</td>
</tr>
<tr>
<td></td>
<td>≥8</td>
<td>22</td>
<td>2.59 (1.71 to 3.93)</td>
<td>11</td>
<td>2.62 (1.45 to 4.74)</td>
</tr>
<tr>
<td>4–7/3–7</td>
<td>&lt;8</td>
<td>10</td>
<td>3.79 (2.04 to 7.05)</td>
<td>1</td>
<td>0.66 (0.09 to 4.71)</td>
</tr>
<tr>
<td></td>
<td>≥8</td>
<td>33</td>
<td>3.34 (2.38 to 4.70)</td>
<td>13</td>
<td>2.22 (1.29 to 3.83)</td>
</tr>
<tr>
<td>≥8</td>
<td>&lt;8</td>
<td>0</td>
<td>N/A</td>
<td>0</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>≥8</td>
<td>17</td>
<td>6.12 (3.82 to 9.85)</td>
<td>2</td>
<td>0.87 (0.21 to 3.49)</td>
</tr>
</tbody>
</table>

*The mortality rate in the entire sample was 2.71 (95% CI: 2.42 to 3.03) per 100 person-years.

(J Acquir Immune Defic Syndr 2018;77:135–143)
Past and Current Alcohol Use by Age and HIV Status

Alcohol and Tobacco
Do Alcohol Misuse, Smoking, and Depression Vary Concordantly or Sequentially? A Longitudinal Study of HIV-Infected and Matched Uninfected Veterans in Care

R. Scott Braithwaite¹ · Yixin Fang¹ · Janet Tate² · Sherry M. Mentor¹ · Kendall J. Bryant³ · David A. Fiellin² · Amy C. Justice²

Abstract We analyzed temporal patterns of alcohol misuse, smoking, and depression among veterans in care to determine whether these conditions vary concordantly or sequentially. Using the Veterans Aging Cohort Study, harmful alcohol use (AUDIT-C ≥ 4), current smoking, and depression (PHQ-9 ≥ 8), were measured. In regression analyses, predictors included each outcome condition at baseline, the other two conditions in the same survey, the other two conditions in the immediately preceding survey, number of years since enrollment, and HIV status. We found that current smoking and depression were more common among HIV infected individuals. Harmful alcohol use was more common among uninfected individuals. Temporal analyses suggested a concurrent pattern: each condition was associated with the other two conditions (p < 0.03; OR 1.12–1.66) as well as with the prior presence of the same condition (p < 0.0001; OR 6.38–22.02). Smoking was associated with prior depression after controlling for current depression (OR 1.16; p = 0.003). In conclusion, alcohol misuse, smoking, and depression were temporally concordant and persistent, raising the question of whether they constitute a common syndrome in HIV infected patients and others with chronic diseases.
Table 1 Baseline characteristics of the VACS participants who ever drank and smoked.

<table>
<thead>
<tr>
<th></th>
<th>HIV+</th>
<th></th>
<th>HIV-</th>
<th></th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean or %</td>
<td>N</td>
<td>Mean or %</td>
<td></td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>2892</td>
<td>49.8 (8.2)</td>
<td>2717</td>
<td>51.3 (9.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male, %</td>
<td>2813</td>
<td>97.3 %</td>
<td>2570</td>
<td>94.6 %</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Race White, %</td>
<td>549</td>
<td>19.0 %</td>
<td>624</td>
<td>23.0 %</td>
<td>0.001</td>
</tr>
<tr>
<td>Race Black, %</td>
<td>1953</td>
<td>67.5 %</td>
<td>1733</td>
<td>63.8 %</td>
<td>-</td>
</tr>
<tr>
<td>Race other, %</td>
<td>390</td>
<td>13.5 %</td>
<td>360</td>
<td>13.2 %</td>
<td>-</td>
</tr>
<tr>
<td>HCV+, %</td>
<td>1609</td>
<td>55.6 %</td>
<td>919</td>
<td>33.8 %</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Died, %</td>
<td>857</td>
<td>29.6 %</td>
<td>478</td>
<td>16.6 %</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>AUDIT-C, mean (SD)</td>
<td>2481</td>
<td>4.0 (3.3)</td>
<td>2251</td>
<td>4.5 (3.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Current smoke, %</td>
<td>1852</td>
<td>64.5 %</td>
<td>1484</td>
<td>58.1 %</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PHQ-9, mean (SD)</td>
<td>2866</td>
<td>6.0 (6.3)</td>
<td>2693</td>
<td>5.9 (6.6)</td>
<td>0.53</td>
</tr>
<tr>
<td>AUDIT-C ≥ 4</td>
<td>782</td>
<td>28.1 %</td>
<td>783</td>
<td>31.6 %</td>
<td>0.005</td>
</tr>
<tr>
<td>PHQ-9 ≥ 8</td>
<td>908</td>
<td>31.7 %</td>
<td>798</td>
<td>29.6 %</td>
<td>0.10</td>
</tr>
<tr>
<td>Smoker and AUDIT-C ≥ 4, %</td>
<td>610</td>
<td>21.9 %</td>
<td>537</td>
<td>21.7 %</td>
<td>0.84</td>
</tr>
<tr>
<td>Smoker and PHQ-9 ≥ 8, %</td>
<td>652</td>
<td>22.9 %</td>
<td>506</td>
<td>20.0 %</td>
<td>0.01</td>
</tr>
<tr>
<td>AUDIT-C ≥ 4 and PHQ-9 ≥ 8, %</td>
<td>293</td>
<td>10.6 %</td>
<td>241</td>
<td>9.8 %</td>
<td>0.35</td>
</tr>
<tr>
<td>At least two conditions, %</td>
<td>1058</td>
<td>38.3 %</td>
<td>905</td>
<td>36.9 %</td>
<td>0.29</td>
</tr>
</tbody>
</table>
| All three conditions, %  | 238  | 8.6 %            | 179  | 7.3 %            | 0.08    

VACS Survey Cohort Participants Endorsing Having Ever Drank & Smoked: 2892/ 3632 (80%) HIV+ 2717/3695 (74%) Uninfected
Table 3 Logistic regression analysis of current smoking and the current and prior status of alcohol and depression (c-stat = 0.85)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds ratio&lt;sup&gt;a&lt;/sup&gt;</th>
<th>95% CI of OR</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of years from enrollment</td>
<td>0.91</td>
<td>(0.89, 0.92)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HIV+ status</td>
<td>1.08</td>
<td>(0.96, 1.22)</td>
<td>0.22</td>
</tr>
<tr>
<td>Current smoking status at baseline</td>
<td>22.02</td>
<td>(19.31, 25.10)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Harmful alcohol use</td>
<td>1.64</td>
<td>(1.45, 1.85)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Harmful alcohol use at preceding survey&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.10</td>
<td>(0.97, 1.23)</td>
<td>0.13</td>
</tr>
<tr>
<td>Positive depression status</td>
<td>1.23</td>
<td>(1.11, 1.35)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Positive depression status at preceding survey&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.16</td>
<td>(1.05, 1.28)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

<sup>a</sup> Adjusted for HIV status and number of years from enrollment

<sup>b</sup> Controlling for current alcohol use

<sup>c</sup> Controlling for current depression
Liver Disease Risk HIV, HCV, and Alcohol

Lim JK. et al, Relationship Between Alcohol Use Categories and Noninvasive Markers of Advanced Hepatic Fibrosis in HIV-Infected, Chronic HCV-Infected, and Uninfected Patients, Clin Infect Dis 2014; 58(10):1449-58
Harm from Alcohol is Greater Among HIV+ than Uninfected

Medical and Recreational Marijuana
Growing Use of Marijuana Among HIV+

**Pro**
- Decreased Overdose Deaths
- Symptom Management

**Con**
- Decreased ART Adherence
- Increased Neuro-Cognitive Burden

[In-text citations]
Polypharmacy, NC-PIMS and Prescription Opioids
Polypharmacy: What Matters?

• Absolute number of medications?
• Specific medication?
• Class of medications that matters?
• What other medications are also being taken?
• Co-occurring substance use?
Co Prescribed and Filled VA Medications Among 4.5 Million Veterans Born 1945-65

Node size relative to prevalence of PIM

Edge width relative to frequency of dual-exposure

Birth Cohort
A Chicken & Egg Problem

- With age, health conditions develop, indications for medications
- As conditions accumulate, so does frailty & risk of adverse outcomes
- Polypharmacy associated outcomes may be confounded by indication
VACS Index 2.0

• Categories create “step effects”—convert to a continuous measure

• Consider other variables:
  • CD8
  • Nadir CD4
  • Albumin
  • Absolute neutrophil count
  • White blood count (WBC)
  • Body mass index (BMI)

Tate JP, Sterne JAC, Justice AC, et al. Albumin, white blood cell count, and body mass index improve discrimination of mortality in HIV-positive individuals. AIDS 2019 Apr 1; 33(5): 903-12 PMID 30649058
Discrimination by Subgroup

VACS Index 1.0 (left) vs 2.0 (right)
VACS Index 2.0 Vs. Charlson (Age Adj) in Uninfected

Rentsch C. et al. Accepted Poster at 2019 Society of General Internal Medicine to be held May 8-11
Potentially Inappropriate Medications (PIMs) when Drinking Alcohol

• **Neurocognitive (NC-PIMS):** anticonvulsants, antidepressants (SSRI/SNRI and other), antipsychotics, muscle relaxants, **opioids**, sedative/hypnotics (barbiturates, benzodiazepines, sleeping meds and other anxiolytics), ART (cobicistat, dolutegravir, efavirenz, ritonavir)

• **Cardiovascular and metabolic:** statins, beta-blockers, calcium antagonists, hypoglycemics

• **Anti-coagulants and NSAIDS:** warfarin and antiplatelets, NSAIDS

• **GI:** histamine antagonists, proton pump inhibitors
NC-PIMS, Alcohol and Community Acquired Pneumonia

Leads: Rentsch, Tate, Edelman, Crothers
Community-Acquired Pneumonia: NC-PIMS and Alcohol

<table>
<thead>
<tr>
<th>No. of meds</th>
<th>Alcohol</th>
<th>1 Med</th>
<th>2 Meds</th>
<th>3 Meds</th>
<th>4 Meds</th>
<th>≥5 Meds</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>≥5</td>
<td>4-5</td>
<td>≥6</td>
</tr>
<tr>
<td>1 Med</td>
<td>2 Meds</td>
<td>3 Meds</td>
<td>4 Meds</td>
<td>≥5 Meds</td>
<td>4-5 Meds</td>
<td>≥6 Meds</td>
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<tr>
<td>IM</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

Independent effects

Interactive effects
Association of Prescribed Opioids With Increased Risk of Community-Acquired Pneumonia Among Patients With and Without HIV

E. Jennifer Edelman, MD, MHS; Kirsha S. Gordon, PhD; Kristina Crothers, MD; Kathleen Akgün, MD; Kendall J. Bryant, PhD; William C. Becker, MD; Julie R. Gaither, PhD; Cynthia L. Gibert, MD; Adam J. Gordon, MD; Brandon D. L. Marshall, PhD; Maria C. Rodriguez-Barradas, MD; Jeffrey H. Samet, MD; Amy C. Justice, MD; Janet P. Tate, ScD; David A. Fiellin, MD
Immunosuppressive Opioids and CAP

Figure 3. Prescribed Opioid Characteristics and Community-Acquired Pneumonia Risk by HIV Status, Conditional Multivariable Logistic Regression
NC-PIMS, Alcohol, and Delirium

Leads: Akgun, Krishnan
### Any NC PIM, Alcohol and Delirium

**Graph: Independent and Interactive Effects**

- **Y-axis:** Adjusted OR
- **X-axis:** Conditions (Uninf, HIV+, 1 PIM, ≥2 PIMS, AUDIT-C 4-5, ≥6, 1 PIM & AUDIT-C 4-5, ≥6, 1 PIM & AUDIT-C & ≥6)

**Legend:**
- **Cohort:** VACS
- **Outcome:** delirium
NC-PIMS, Substance Use and Medically Significant Falls

Lead: Womack, Murphy
Drug and Hazardous Alcohol Use, Medication Count and Serious Falls

Drug use/abuse HIV+
HIV-
Hazardous alcohol use HIV+
HIV-
Medication count HIV+
HIV-

Odds Ratios

Cohort: VACS  Outcome: falls
NC-PIMs and Serious Falls (1)

Odds Ratios

- Opioids HIV+
  - HIV-

- Benzodiazepin…
  - HIV-

- Muscle…
  - HIV-

- Anticonvulsant…
  - HIV-

- Antihistamines…
  - HIV-

P for interaction = 0.002
NC-PIMs and Serious Falls (2)

Cohort: VACS  Outcome: falls
<table>
<thead>
<tr>
<th>Variables</th>
<th>Combined</th>
<th>Wald Chi-Square</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CNS active medications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opioids</td>
<td>1.35 (1.29, 1.41)</td>
<td>162.40</td>
</tr>
<tr>
<td>Benzodiazepines uninfected</td>
<td>1.01 (0.94, 1.08)</td>
<td>0.06</td>
</tr>
<tr>
<td>Benzodiazepines PLWH</td>
<td>1.24 (1.08, 1.40)</td>
<td>9.95</td>
</tr>
<tr>
<td>Muscle relaxants uninfected</td>
<td>1.02 (0.95, 1.10)</td>
<td>0.36</td>
</tr>
<tr>
<td>Muscle relaxants PLWH</td>
<td>1.29 (1.08, 1.46)</td>
<td>8.94</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>1.31 (1.24, 1.38)</td>
<td>103.79</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>0.98 (0.92, 1.03)</td>
<td>0.75</td>
</tr>
<tr>
<td><strong>Cardiovascular medications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antiarrhythmics</td>
<td>1.29 (1.13, 1.47)</td>
<td>14.85</td>
</tr>
<tr>
<td>Antihypertensives</td>
<td>0.88 (0.84, 0.92)</td>
<td>28.94</td>
</tr>
<tr>
<td>Antithrombotics</td>
<td>1.20 (1.11, 1.30)</td>
<td>21.78</td>
</tr>
<tr>
<td>Nitrates</td>
<td>0.99 (0.90, 1.10)</td>
<td>0.00</td>
</tr>
<tr>
<td><strong>Mental health medications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>0.90 (0.85, 0.96)</td>
<td>10.13</td>
</tr>
<tr>
<td>Atypical antidepressants</td>
<td>1.03 (0.98, 1.09)</td>
<td>1.09</td>
</tr>
<tr>
<td>MAOI</td>
<td>2.29 (1.02, 5.17)</td>
<td>3.81</td>
</tr>
<tr>
<td>SSRI</td>
<td>1.21 (1.15, 1.27)</td>
<td>52.93</td>
</tr>
<tr>
<td>SNRI</td>
<td>1.14 (1.03, 1.27)</td>
<td>6.24</td>
</tr>
<tr>
<td>TCA</td>
<td>0.96 (0.87, 1.05)</td>
<td>0.80</td>
</tr>
<tr>
<td><strong>Hypoglycemics</strong></td>
<td>0.97 (0.91, 1.03)</td>
<td>0.85</td>
</tr>
<tr>
<td><strong>Proton pump inhibitors</strong></td>
<td>1.06 (1.01, 1.11)</td>
<td>5.73</td>
</tr>
<tr>
<td><strong>Non-ART medication count (increments of 5)</strong></td>
<td>1.20 (1.17, 1.24)</td>
<td>213.72</td>
</tr>
<tr>
<td><strong>Hazardous alcohol use (AUDIT-C score ≥3 for women and ≥4 for men)</strong></td>
<td>1.30 (1.23, 1.38)</td>
<td>100.06</td>
</tr>
<tr>
<td><strong>Illicit substance use</strong></td>
<td>1.40 (1.34, 1.47)</td>
<td>203.30</td>
</tr>
<tr>
<td><strong>VACS Index 2.0 (increments of 5)</strong></td>
<td>1.07 (1.06, 1.08)</td>
<td>204.20</td>
</tr>
<tr>
<td><strong>Body Mass Index</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;18.5</td>
<td>0.98 (0.83, 1.15)</td>
<td>0.34</td>
</tr>
<tr>
<td>18.5 – 25</td>
<td>1.01 (0.96, 1.07)</td>
<td>0.07</td>
</tr>
<tr>
<td>25 – 30</td>
<td>1.01 (0.96, 1.07)</td>
<td>0.00</td>
</tr>
<tr>
<td>&gt; 30</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Cohort: VACS
Outcome: falls
Hepatitis C and Injection Drug Use

NB: In VA, nearly all HCV infection is secondary to injection drug use
HCV infection Harms More Than the Liver

Liver
- Inflammation
- Steatosis
- Fibrosis/Cirrhosis
- Hepatocellular carcinoma
- Cholangiocarcinoma

Hematologic & Auto Immune Dz.
- Mixed cryoglobulinemia
- B-cell lymphoma
- Autoimmune thyroiditis
- Membrano-proliferative Glomerulonephritis
- Sicca syndrome

CVD/Metabolic Disease
- Atherosclerosis
- Insulin resistance/diabetes
- Myocardial dysfunction

Neuro-Cognitive Dz.
- Cognitive impairment
- Fibromyalgia

How much of this changes after cure?

HCV Deaths by Age Group & Year

CDC National Surveillance Data: HCV Related Deaths
Injection Drug Use and Hepatitis C as Risk Factors for Mortality in HIV-Infected Individuals: The Antiretroviral Therapy Cohort Collaboration

Margaret T. May, PhD,* Amy C. Justice, MD, PhD,†† Kate Birnie, PhD,* Suzanne M. Ingle, PhD,* Colette Smit, PhD,§ Colette Smith, Ph.D., Didier Neau, MD, PhD,¶ Marguerite Guiguet, PhD,# Carolynne Schwarze-Zander, MD,** Santiago Moreno, MD, PhD,†† Jodie L. Guest, PhD, MPH,‡‡ Antonella d’Arminio Monforte, MD, PhD,§§ Cristina Tural, MD, PhD,¶¶ Michael J. Gill, MB,¶¶ Andrea Bregenzer, MD, Ole Kirk, MD, DMSc,‡‡‡ Michael Saag, MD,‡§‡ Timothy R. Sterling, MD,‡‡‡ Heidi M. Crane, MD, MPH,§§§ and Jonathan A. C. Sterne, Ph.D*

Background: HIV-infected individuals with a history of transmission through injection drug use (IDU) have poorer survival than other risk groups. The extent to which higher rates of hepatitis C (HCV) infection in IDU explain survival differences is unclear.

Methods: Adults who started antiretroviral therapy between 2000 and 2009 in 16 European and North American cohorts with >70% complete data on HCV status were followed for 3 years. We estimated unadjusted and adjusted (for age, sex, baseline CD4 count and HIV-1 RNA, AIDS diagnosis before antiretroviral therapy, and stratified by cohort) mortality hazard ratios for IDU (versus non-IDU) and for HCV-infected (versus HCV uninfected).

Results: Of 32,703 patients, 3374 (10%) were IDU; 4630 (14%) were HCV+. 1,116 (3.4%) died. Mortality was higher in IDU compared with non-IDU [adjusted HR 2.71; 95% confidence interval (CI): 2.32 to 3.16] and in HCV+ compared with HCV− (adjusted HR 2.65; 95% CI: 2.31 to 3.04). The effect of IDU was substantially attenuated (adjusted HR 1.57; 95% CI: 1.27 to 1.94) after adjustment for HCV, while attenuation of the effect of HCV was less substantial (adjusted HR 2.04; 95% CI: 1.68 to 2.47) after adjustment for IDU. Both IDU and HCV were strongly associated with liver-related mortality (adjusted HR 10.89; 95% CI: 6.47 to 18.3 for IDU and adjusted HR 14.0; 95% CI: 8.05 to 24.5 for HCV) with greater attenuation of the effect of IDU (adjusted HR 2.43; 95% CI: 1.24 to 4.78) than for HCV (adjusted HR 7.97; 95% CI: 3.83 to 16.6). Rates of CNS, respiratory and violent deaths remained elevated in IDU after adjustment for HCV.

Conclusions: A substantial proportion of the excess mortality in HIV-infected IDU is explained by HCV coinfection. These findings underscore the potential impact on mortality of new treatments for HCV in HIV-infected people.

Key Words: HIV-1, hepatitis C virus, injection drug use, antiretroviral therapy, cohort study, mortality

(J Acquir Immune Defic Syndr 2015;69:348–354)
**TABLE 1. Patient Demographics and Clinical Characteristics at Start of ART by HCV Status**

<table>
<thead>
<tr>
<th></th>
<th>HCV Uninfected, N (%)</th>
<th>HCV Infected, N (%)</th>
<th>P Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. patients</td>
<td>28,073 (86)</td>
<td>4630 (14)</td>
<td>—</td>
</tr>
<tr>
<td>No. deaths</td>
<td>810 (3)</td>
<td>306 (7)</td>
<td>—</td>
</tr>
<tr>
<td>Male</td>
<td>18,891 (67)</td>
<td>3299 (71)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IDU</td>
<td>506 (2)</td>
<td>2868 (62)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age, median (IQR), yrs</td>
<td>37 (31–45)</td>
<td>39 (34–44)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>16–29</td>
<td>5811 (21)</td>
<td>490 (11)</td>
<td></td>
</tr>
<tr>
<td>30–39</td>
<td>10,833 (39)</td>
<td>1998 (43)</td>
<td></td>
</tr>
<tr>
<td>40–49</td>
<td>7085 (25)</td>
<td>1710 (37)</td>
<td></td>
</tr>
<tr>
<td>50–59</td>
<td>3115 (11)</td>
<td>323 (7)</td>
<td></td>
</tr>
<tr>
<td>≥60</td>
<td>1229 (4)</td>
<td>109 (2)</td>
<td></td>
</tr>
<tr>
<td>AIDS before ART</td>
<td>6607 (24)</td>
<td>998 (22)</td>
<td>0.003</td>
</tr>
<tr>
<td>CD4, median (IQR), cells/mm³</td>
<td>208 (93–312)</td>
<td>206 (101–314)</td>
<td>0.16</td>
</tr>
<tr>
<td>&lt;50</td>
<td>4526 (16)</td>
<td>666 (14)</td>
<td></td>
</tr>
<tr>
<td>50–99</td>
<td>2782 (10)</td>
<td>467 (10)</td>
<td></td>
</tr>
<tr>
<td>100–199</td>
<td>6082 (22)</td>
<td>1081 (23)</td>
<td></td>
</tr>
<tr>
<td>200–349</td>
<td>9299 (33)</td>
<td>1498 (32)</td>
<td></td>
</tr>
<tr>
<td>≥350</td>
<td>5384 (19)</td>
<td>918 (20)</td>
<td></td>
</tr>
<tr>
<td>HIV-RNA, median (IQR), log copies/mL</td>
<td>4.85 (4.12–5.36)</td>
<td>4.76 (3.89–5.27)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**FIGURE 1.** Kaplan–Meier estimate of survival probability by HCV status and IDU transmission group.

Table entries are counts ($) of patients. P values were calculated using the log rank test.

May MT et al, J Acquir Immun Defic Syndr 2015;69:348-54
<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>No. Deaths (%)</th>
<th>IDU Versus Non-IDU</th>
<th>HCV-Infected Versus HCV-Uninfected</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>HR* (95% CI)</td>
<td>Additionally Adjusted for HCV</td>
</tr>
<tr>
<td>All</td>
<td>1116 (100)</td>
<td>2.71 (2.32 to 3.16)</td>
<td>1.57 (1.27 to 1.94)</td>
</tr>
<tr>
<td>AIDS</td>
<td>459 (41.1)</td>
<td>1.40 (1.05 to 1.88)</td>
<td>1.01 (0.69 to 1.48)</td>
</tr>
<tr>
<td>Non-AIDS infection</td>
<td>84 (7.5)</td>
<td>3.18 (1.89 to 5.34)</td>
<td>1.86 (0.88 to 3.93)</td>
</tr>
<tr>
<td>Liver-related</td>
<td>69 (6.2)</td>
<td>10.89 (6.47 to 18.3)</td>
<td>2.43 (1.24 to 4.78)</td>
</tr>
<tr>
<td>Non-AIDS malignancy</td>
<td>103 (9.2)</td>
<td>1.50 (0.78 to 2.88)</td>
<td>0.72 (0.33 to 1.58)</td>
</tr>
<tr>
<td>MI/IHD</td>
<td>22 (2.0)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Stroke</td>
<td>10 (0.9)</td>
<td>1.74 (0.19 to 15.77)</td>
<td>0.71 (0.06 to 8.57)</td>
</tr>
<tr>
<td>Renal failure</td>
<td>12 (1.1)</td>
<td>2.71 (0.56 to 13.12)</td>
<td>1.59 (0.19 to 13.40)</td>
</tr>
<tr>
<td>Violence†</td>
<td>52 (4.7)</td>
<td>7.53 (4.19 to 13.52)</td>
<td>3.65 (1.84 to 7.02)</td>
</tr>
<tr>
<td>CNS (other than stroke)</td>
<td>16 (1.4)</td>
<td>6.02 (2.01 to 18.08)</td>
<td>5.35 (1.00 to 28.60)</td>
</tr>
<tr>
<td>Other heart/vascular disease</td>
<td>34 (3.1)</td>
<td>3.08 (1.33 to 7.13)</td>
<td>1.38 (0.45 to 4.23)</td>
</tr>
<tr>
<td>Respiratory disease†</td>
<td>16 (1.4)</td>
<td>5.55 (1.86 to 16.55)</td>
<td>4.64 (0.84 to 25.69)</td>
</tr>
<tr>
<td>Other</td>
<td>48 (4.3)</td>
<td>2.38 (1.11 to 5.09)</td>
<td>1.27 (0.45 to 3.59)</td>
</tr>
<tr>
<td>Unknown†</td>
<td>191 (17.1)</td>
<td>3.91 (2.76 to 5.54)</td>
<td>2.45 (1.50 to 4.00)</td>
</tr>
</tbody>
</table>

*Adjusted for age, sex, CD4 cell count, HIV-1 RNA, and AIDS at baseline, stratified by cohort.
†Violence includes suicide, substance abuse; respiratory includes chronic obstructive pulmonary disease; unknown includes unclassifiable.
CNS, central nervous system; HCV+, Hepatitis C infected; IDU, injection drug use; IHD, ischemic heart disease; MI, myocardial infarction.

May MT et al, J Acquir Immun Defic Syndr 2015;69:348-54
So What Are We Doing About It?
Medications, Alcohol, and Substance Use in HIV

- VA, Kaiser-Permanente Northern California, Swiss Cohort
- Target enrollment 2,250
- Saliva for DNA to look at genetic susceptibility to drug toxicity
- Biomarker assays for
  - Alcohol (PEth)-Blood spot
  - Tobacco (Cotinine)-Saliva
  - Opioids, Marijuana, Cocaine, & Amphetamines-Finger nails
- Self reported:
  - Substance Use
  - Medications
  - Side Effects
  - Patient preferences
STEP AUD Trial Self-reported drinking outcomes, past 30 days

Figure a. Drinks per week

Adjusted mean difference (95% CI)
- Week 24: -4.2 (-9.4, 0.9)
- Week 52: -6.9 (-15.0, 1.3)

Figure b. Percent with no heavy drinking days*

Adjusted odds ratio (95% CI)
- Week 24: 2.2 (0.8, 6.1)
- Week 52: 4.9 (1.5, 15.8)

Lessons Learned, Response in FIRST

Challenge
- Low patient motivation to address alcohol or enter a study
- Scheduling
  - Alcohol treatment visits more frequent than HIV care
  - Conflict with work, other responsibilities
  - Travel time and expense
- > 50% need “stepping up”

Response
- Expand focus to medical conditions adversely impacted by alcohol
- Financial re-inforcers for abstinence
- Visits every 3 weeks
- Travel vouchers
- Include stepped care
HIV infection + PEth >20ng/mL + unhealthy alcohol use

Randomization

- Continency Management plus Stepped Care

Treatment as Usual

Baseline 24

Week 12

Week 24

Health Handout or Potential Referral

Non-response: Stepped Up

STEP 1
Contingency Management (n=5)

STEP 2
Motivational Enhancement Therapy (n=4) and Addiction Physician Management (n=6)

Response: Monitor and Maintain

Participants are “stepped up” and considered to have non-response to CM if PEth >8ng/mL at week 12 visit.
What Can We Do Right Now?

• Cure HCV infection
• Help patients cut down or stop
  • Motivate change with individual risk of: cognitive decline, fatigue, falls, stroke, MI, GI distress, Immune dysfunction
  • A stepped approach: Cognitive Behavioral Interventions-Stepped up to medication for tobacco, opioids, and alcohol
• Screen for and address
  • ART nonadherence
  • Polypharmacy-substance use interactions
  • Likely complications (cirrhosis, lung and hepatic cancer)

Acknowledgements

- **Consortium PI**: AC Justice*
- **Scientific Collaborator (NIAAA)**: K Bryant
- **Cross Cohort Collaborators**: Richard Moore (NA-ACCORD), Jonathan Sterne (ART-CC), Brian Agan (DoD), Miguel Hernan (HIV-Causal)

**COMpAAAS/Veterans Aging Cohort Study**, a CHAART Cooperative Agreement, supported by the National Institutes of Health: National Institute on Alcohol Abuse and Alcoholism (U24-AA020794, U01-AA020790, U01-AA020795, U01-AA020799; U10 AA013566-completed) and in kind by the US Department of Veterans Affairs. In addition to grant support from NIAAA, we gratefully acknowledge the scientific contributions of Dr. Kendall Bryant, our scientific collaborator.

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HIV & AGING: FROM MITOCHONDRIA TO THE METROPOLIS
Falls in People Living with HIV Infection and Alcohol and Other Drug Use

Susie Kim, MSW, MPH
Falls in People Living with HIV Infection and Alcohol and Other Drug Use

Susie Kim, Kristine M. Erlandson, Christine Lloyd-Travaglini, Seville Meli, Alexander Y. Walley, Timothy C. Heeren, Richard Saitz

Funding: U01AA020784, U24AA020779, U24AA020778, UL1TR001430
Background

- Up to 30% of people living with HIV infection (PLWH) experience falls each year\(^1\)
- Falls are the most common cause of non-fatal injury in the U.S.; costs from ED visits and hospitalizations are high
- Falls can lead to fractures, which are 40-60% more common in PLWH\(^2\)–\(^4\)

---

Background

• Frailty (includes impaired physical function) occurs even among virally suppressed, and is associated with falls, fractures, hospitalizations and death in PLWH

• Alcohol and illicit drug use, and use of many prescribed meds: common in PLWH and associated with falls and fractures

• Risk of falls at earlier age in PLWH – need to understand fall risks and characteristics and distinguish from older adults
To report the prevalence and frequency of falls and characterize falls in PLWH and substance use
Study Design

• Boston ARCH 4F Study* cohort
  • Expansion of an existing cohort
  • Target enrollment = 400
  • Recruited from Center for Infectious Diseases at Boston Medical Center and Boston Healthcare for the Homeless Program

• Cross-sectional analysis of descriptive baseline data

• Data Collection:
  • Falls assessment
  • Substance use assessment
  • Physical function assessment

*Alcohol and HIV associated comorbidity and complications: Falls, Fractures, Frailty, and Functional impairment (the 4F study)
Eligibility Criteria

• Documentation of HIV
• Age 18 years or older
• Ability to speak English (fluency)
• Willing to provide info for >1 contact
• Current drug or alcohol dependence* (past 12-months) or ever injection drug use
  OR
  Any past 12 month use of illicit drugs, marijuana (not recommended by a healthcare provider), or nonmedical use of prescription medications; OR past 12 month alcohol use with positive AUDIT-C score (≥3 for females and ≥4 for males)

*DSM-IV
• NIAID AIDS Clinical Trials Group (ACTG) “Fall” definition:

“An unexpected event, including a slip or trip, in which you lost your balance and landed on the floor, ground or lower level, or hit an object like a table or chair.”

*Falls that result from a major medical event (for example, a stroke, or seizure) or an overwhelming external hazard (for example, hit by a truck or pushed) are not included
Falls Assessment

• NIAID ACTG Fall History Questionnaire

1. “In the past 6 months, have you been concerned with losing your balance and falling while doing your usual daily activities?” (Not at all / A little / Quite a bit / Very much)

2. “In the past 6 months, have you had a fall?” (Yes / No)

3. “How many times have you fallen in the past 6 months?” (1 time / 2 times / 3-5 times / More than 5 times)

4. “Did you seek medical attention after any of these falls (such as calling 911, visiting an on-site nurse, or going to the emergency room or to a doctor’s office)?” (Yes / No)

5. “Did any of these falls result in a broken bone?” (Yes / No)
Falls Assessment

• Additional Falls Questions

  • “Were you using any of the following prior to any fall you just told me about?”

    - Alcohol
    - Cocaine
    - Heroin / Fentanyl
    - Hallucinogens
    - Phencyclidines
    - Cannabis/Marijuana
    - Stimulants/amphetamines
    - Buprenorphine
    - Methadone
    - Other Prescription Opioids
    - Tranquilizers / Sedatives
    - Synthetic marijuana/k2/spice
    - Inhalants
    - Miscellaneous
    - More than one substance (alcohol and/or drugs)

  • “During any of the falls you just told me about in the past 6 months, did you fall because of your alcohol or other drug use?” (Yes / No)
Falls Assessment

• Additional Falls Questions
  • “In the past 6 months, have you...
    • had a fall from an overwhelming external hazard, such as being hit by a car, pushed down the stairs, or falling while biking?
    • had a fall after a medical event like a stroke or a seizure?
    • had a fall after an overdose from alcohol or other drugs?”
Falls Assessment

• Modified Falls Efficacy Scale (MFES)\(^5\)

  • 14 items
  • Confidence in doing daily activities without falling

<table>
<thead>
<tr>
<th>Activity</th>
<th>Not Confident</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Get dressed and undressed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Prepare a simple meal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Take a bath or a shower</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Get in/out of a chair</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Get in/out of bed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Answer the door or telephone</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Walk around the inside of your house</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Substance Use Assessment

• Addiction Severity Index (ASI)\(^6\) – past 30 day use of:

  • Alcohol – heavy drinking days
    (≥ 5 standard drinks on one occasion for men; ≥ 4 drinks for women)

  • Non-prescription drugs (like heroin or cocaine), prescription drugs used without a doctor’s prescription, or used in greater amounts than prescribed

  • All marijuana not recommended by a health care provider

• Short Physical Performance Battery (SPPB)\textsuperscript{7}

(1) Stance
   (a) feet side-by-side
   (b) semitandem stance
   (c) tandem stance

(2) Gait velocity
   (4 m distance)

(3) Sit-to-stand time
   (5x)

\[ \Sigma: 0-12 \text{ points} \]

\textsuperscript{7} Guralnik et al. J Gerontol. 1994; 49(2): M85–M94

Excerpt from figure courtesy of Cambridge University Press
Analyses

• Descriptive
  • Means / standard deviations
  • Frequencies / proportions

• T-tests / Wilcoxon tests
  • Differences between those with vs. without a fall in past 6 months
Baseline Characteristics  
(n = 163)

<table>
<thead>
<tr>
<th></th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD)</td>
<td>54 ± 9 years</td>
</tr>
<tr>
<td>Female</td>
<td>64 (40)</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>96 (59)</td>
</tr>
<tr>
<td>White</td>
<td>33 (20)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>32 (20)</td>
</tr>
<tr>
<td>HIV viral load &lt;200 copies/mL</td>
<td>137 (88)</td>
</tr>
<tr>
<td>CD4 cell count &lt;200 cells/mm³</td>
<td>10 (6)</td>
</tr>
<tr>
<td>Past 30 day substance use</td>
<td></td>
</tr>
<tr>
<td>Alcohol (≥1 heavy drinking day)</td>
<td>56 (34)</td>
</tr>
<tr>
<td>Marijuana</td>
<td>71 (44)</td>
</tr>
<tr>
<td>Cocaine</td>
<td>38 (23)</td>
</tr>
<tr>
<td>Heroin</td>
<td>17 (10)</td>
</tr>
</tbody>
</table>
## Baseline Characteristics

*(n = 163)*

<table>
<thead>
<tr>
<th>Category</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Past 6 month fall</td>
<td>56 (34)</td>
</tr>
<tr>
<td>Other falls</td>
<td></td>
</tr>
<tr>
<td>Overwhelming external hazard</td>
<td>5 (3)</td>
</tr>
<tr>
<td>Medical event</td>
<td>7 (4)</td>
</tr>
<tr>
<td>Overdose</td>
<td>5 (3)</td>
</tr>
</tbody>
</table>
Falls Characteristics  
(n = 56)

<table>
<thead>
<tr>
<th>Number of falls</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>22 (39)</td>
</tr>
<tr>
<td>2</td>
<td>14 (25)</td>
</tr>
<tr>
<td>3-5</td>
<td>15 (27)</td>
</tr>
<tr>
<td>&gt;5</td>
<td>5 (9)</td>
</tr>
</tbody>
</table>

Sought medical attention 21 (38)

- Hospitalized 12 (57)
- Emergency room or urgent care 19 (91)
- Resulted in a broken bone 3 (14)

Used a substance prior to fall 23 (41)

- Fell because of substance use 9 (39)
Falls & Substance Use
(n = 56)

- Alcohol: 21%
- Marijuana: 16%
- Cocaine: 7%
- Heroin/fentanyl: 9%
- Other opioids: 7%
- Stimulants/Amphetamine: 2%
- Tranquilizers/Sedatives: 4%
- Other: 7%
- More than one: 13%
### Fear of Falling & Physical Function

<table>
<thead>
<tr>
<th></th>
<th>Entire Cohort (n = 163)</th>
<th>Past 6 Month Fall (n = 56)</th>
<th>No Past 6 Month Fall (n = 107)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>54 ± 9 years</td>
<td>55 ± 8 years</td>
<td>53 ± 10 years</td>
<td>0.41</td>
</tr>
<tr>
<td>Female (n (%))</td>
<td>64 (40)</td>
<td>28 (50)</td>
<td>36 (34)</td>
<td>0.04</td>
</tr>
<tr>
<td>Fear of falling (MFES score)</td>
<td>9 ± 2</td>
<td>8 ± 2</td>
<td>10 ± 1</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Physical function (SPPB score)</td>
<td>8 ± 3</td>
<td>7 ± 3</td>
<td>8 ± 3</td>
<td>0.03</td>
</tr>
</tbody>
</table>

MFES (Modified Falls Efficacy Scale):
- Score = 0 – 10
- **Lower** score = **more** fear of falling

SPPB (Short Physical Performance Battery):
- Score = 0 – 12
- **Lower** score = **lower** level of physical function
- Score ≤ 9 indicates disability
Limitations

- Preliminary analysis
- Cross-sectional
Conclusions

• Falls appear to be common among PLWH who use substances
• 2/3 reported more than one fall in past 6 months
• Falls are often preceded by substance use
• Those who fell reported greater fear of falling and more limited physical function
Next Steps

• Further study risk factors and mechanisms of falls in this population

• Develop and pilot test a falls prevention intervention that address them
Acknowledgements

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  • Jasmin Choi
  • Alexandra Chretien
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  • Tiana Mason
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• Boston University General Clinical Research Unit
• URBAN ARCH Administrative and Biostatistics and Data Management Cores
Care Coordination for Older Adults Using Medication Assisted Treatment for Opioid Use Disorder

Emma Klein, BS
Care Coordination for Older Adults using Medication-Assisted Treatment for Opioid Use Disorder:
Implications for HIV Management

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Rollins School of Public Health
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Disclosures

No Pertinent Financial Disclosures
Identifying Best Approaches to Assess Support Needs of Older Adults Receiving Medication Assisted Treatment for Opioid Use Disorder

Pilot Project Principal Investigator
Alexis A. Bender, Ph.D.

Funding Agency
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Overview

Background and Significance
- Opioid Use
- Medication Assisted Treatment

Current Study

Methods

Findings
- Training and Awareness
- Care Coordination

Discussion & Implications
From 2010 to 2017, the number of opioid-involved overdose deaths in Georgia increased by 245%, from 426 to 1043 deaths.

“From 2010 to 2017, the number of opioid-involved overdose deaths in Georgia increased by 245%, from 426 to 1043 deaths”
Hospitalization for opioid overdose more **common among older adults, especially women**

Older adults more likely to use non-heroin, non-fentanyl opioids

---

SUD in Older Adults – Unique Factors

- Multiple Health Issues & Polypharmacy
- Arthritis, Musculoskeletal Issues, Chronic Pain
- Cognitive Impairment And Dementia
- Isolation & Loss Of Social Supports
- Opioid Use History
SUD in Older Adults – Unique Factors

16% - 41%

Of Patients Enrolled in MAT Are >50

(from clinics in our study)
Medication-Assisted Treatment (MAT)

- All-Cause Mortality
- Transmission Of Infectious Diseases
- Social functioning
- Criminal activity

Positive Outcomes
MAT – Opioid Agonists

Methadone (Liquid or Pill)
- Full Agonist at the Opioid Receptor
- Half Life >24 Hours
- Opioid Treatment Program Only

Buprenorphine
- Partial agonist at the opioid receptor
- Prescribers must have a DATA waiver*
- Individual limits (30/100/275)*

Naltrexone
- Completely blocks the effect of opioids
- Must be off all opioids 7-10 days before starting
- Less popular

*For non-OTP providers
Healthcare Support for MAT patients

- 7.3% Of Patients Over 55 Report Having A PCP
- 71.7% Reported Taking Medications For a Chronic Health Condition

Stigma Surrounding SUD Treatment and MAT

- Age
- Incarceration History
- Mental Health
- HIV

MAT Stigma


Current Study

Pilot & feasibility study

Barriers and access to care

Focus groups & pilot survey administration with patients in 4 diverse clinics

Scaled up pilot survey administration with patients in 4 additional clinics

Individual interviews with OTP providers (n=12) in 6 diverse clinics

Thematic Analysis
Participant Characteristics (Providers)

Table 1. Descriptive Statistics for staff (n=12)

<table>
<thead>
<tr>
<th>Variables</th>
<th>n (%)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sociodemographic Characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>10 (83%)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-hispanic</td>
<td>11 (92%)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian/White European</td>
<td>10 (83%)</td>
<td></td>
</tr>
<tr>
<td>Mean Age (SD)</td>
<td>38 (10)</td>
<td>28 - 62</td>
</tr>
<tr>
<td>Mean Tenure at Clinic (SD)</td>
<td>6 (6)</td>
<td>1 - 21</td>
</tr>
<tr>
<td>Mean Tenure in OTP (SD)</td>
<td>9 (7)</td>
<td>2 - 24</td>
</tr>
<tr>
<td>Mean Tenure in Substance Abuse (SD)</td>
<td>11 (9)</td>
<td>2 - 27</td>
</tr>
</tbody>
</table>

**Education**
- 58% had at least a Master’s

**Role**
- 3 Program Directors
- 1 Nurse
- 1 Pharmacist
- 7 Counselors
## Participant Characteristics (Patients)

### HIV
- n=2, 6%

### HCV
- n=15, 48%
  - 40% Fully Treated

### Table 2: Descriptive Statistics for Patients (n=31)

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Prevalence of HCV Infection & Importance of Service Connection

For some of my older patients, one of the things that I actually do at … our particular clinic is assist them with a treatment for Hepatitis C. There's a lot of people that are 50 and over, a lot of baby boomers that need assistance with getting the treatment for Hepatitis C. We work with a company, a non-profit [Imagine] Hope which is cool and they know what … treatment that they need so they won't have to pay for medication.

- Urban Counselor
Limited Training about Aging & Managing Chronic Conditions

I think having an understanding of what the average Joe goes through with aging issues ... and what we can kind of [say], okay, no let’s pay attention to this because that’s not necessarily a normal part of the process.

-Urban Counselor
Limited Awareness of Resources for Older Adults

We have a vast list of resources for people, but I don’t know if any of those include aging .... We really need to have a second or a third list of resources for people 50 and older.

- Urban Counselor

AAAs/ADRCs  Transportation  Benefit Enrollment
Complications in Care Coordination Due to MAT Stigma
It went as far [that she] **felt uncomfortable asking for a copy of her blood work** herself because she's like, "What would be my reason for wanting it? She went over all of it with me. Why would I need a copy? What would I say to her?" **Scared to death about her primary knowing that she's on methadone.** She's prescribed blood pressure medicine, a whole slew of ... She's diabetic ... That's a big problem. We don't really know how to battle that.

-Urban Nurse
No, I don't [tell my PCP about treatment]. He's a very good doctor, but he's a real straight arrow. He knows about my drug history, and based on that he's reluctant to prescribe certain drugs to me ... I don't really want him to know about this. I think it would harm our relationship, I don't think he needs to know. Although when he's prescribing certain things, it might be good for him to know ... I've thought about talking to him about it, but I personally don't think he'd handle it well.

-Suburban patient
I think one of the difficult things to combat, [is] trying to educate [Dr.’s] about medication-assisted treatment, it's not trading a drug for a drug so to speak, because while yes, methadone and Subutex are "drugs," they're not illicit use ... it's being used for stability purposes.... That's where people get a lot of stigma with ... the medical field, how undereducated the medical field is. **Doctors specifically ... you see it all the time, is that doctors don't really understand the purpose of methadone in treatment.**

-Rural Counselor
Discussion

Reducing stigma around the use of MAT for recovery will:

- Increase care coordination between medical and opioid treatment providers
- Decrease reliance on opioid treatment provider who are not trained in aging
- Disclosing MAT allows for open dialogue
- Simplifies medication management
Care Coordination for Aging HIV+ MAT Clients

HIV Treatment Providers
Improved coordination with OTPs (HCV as model)
Explore opportunities to co-locate OUD care (e.g. through OBOT)

PCP
Physician education about addiction & MAT
Decrease stigma by medical providers

OTP
Training about age-related conditions
Improved integration with medical system
Thank You!

Questions

Contact:

emma.margaret.klein@emory.edu
alexis.anne.bender@emory.edu
HIV & AGING: FROM MITOCHONDRIA TO THE METROPOLIS
John Blevins, MDiv, ThD

John Blevins, MDiv, ThD's professional career has, in various ways, kept him at an intersection of religion and health. Upon graduating from seminary, the first job was to work as a chaplain to adults and children with HIV/AIDS in Chicago. In the early 1990s, an era of antiretroviral monotherapy when only 4 drugs were approved to treat the virus, this work made me keenly aware of the power of religion in ways conducive to health and in ways that exacerbated illness. In contexts outside of chaplaincy, John Blevins, MDiv, ThD, worked in the outpatient HIV clinic at Grady Health System in Atlanta, where he coordinated patient education; as coordinator for clinical education on mental illness and substance abuse as co-morbidities in HIV clinical care in the School of Medicine at Emory; as a psychotherapist at Grady's HIV program and in private practice; and as a faculty member at Rollins and in the School of Theology at Emory.
Spirituality

April 11, 2019

John Blevins
Associate Research Professor
Director, Interfaith Health Program
Rollins School of Public Health, Emory University

HIV and Aging: From Mitochondria to the Metropolis
Learning Objectives

1. Define and describe similarities and differences between religion and spirituality in the context of HIV today.

2. Describe common cultural forces that affect the spiritual dimensions of life for older adults living with HIV in the United States today.

3. Identify and describe common spiritual questions or concerns that many older adults living with HIV in the United States commonly face.
Religion and spirituality in the context of HIV today.

What is religion? What is spirituality?

Religion is a social force that represents the organization of spiritual beliefs and practices into institutions that regulate those beliefs and practices.

Spirituality is a practice or experience by which one examines questions of meaning and purpose, often (but not always) in relation to a higher power.
Many people living with or affected by HIV experience religion ambivalently because HIV was (and often still is) socially cast in moral terms at least as much as in medical terms.

Experiences of spirituality vary but because spirituality does not generally exert social influence or social control in the ways that religion does, perceptions of spirituality are generally not so ambivalent.
Religion — a driving force for stigma and rejection.
   -- a driving force for compassionate responses at both individual and social levels.

Spirituality — a resource for understanding HIV for those both infected and affected.

For many older adults in the US, religion and spirituality largely overlap; for many living with HIV, this has not been the case.
Common spiritual questions or concerns today

Ambivalence with religious tradition
-- Theological questions

-- De-prioritize spirituality

-- Religion may be a resource (both personal and social) in some aspects of life but not in relation to HIV.
Common spiritual questions or concerns today

Spiritual questions which may be asked outside of religious context
-- reframing HIV over time

-- many in peer cohort died from HIV

-- common questions of aging (e.g., meaning, purpose, reflection on life).
HIV and Aging: From Mitochondria to the Metropolis
Mark Brennan-Ing, PhD focuses their research on psychosocial issues affecting persons living with HIV and older sexual and gender minority adults. They are Past President of the State Society on Aging of New York (SSANY), a Fellow of the Gerontological Society of America (GSA), a Fellow of Division 44 (Psychology of Sexual Orientation and Gender Diversity) of the American Psychological Association, and past Board Member of the New York Association on HIV over Fifty (NYAHOF). They were the Principal Convener for GSA’s HIV/AIDS and Aging Interest Group, a member of the American Society on Aging’s LGBT Aging Information Network Leadership Council, and 2016 Chair of the American Psychological Association’s Committee on Sexual Orientation and Gender Diversity. They were an invited member of the NIH Office of AIDS Research Working Group on HIV and Aging in 2011.
Social Support Systems and Social Network Characteristics of Older Adults with HIV

Mark Brennan-Ing, PhD
Senior Research Scientist
Brookdale Center for Healthy Aging, Hunter College, CUNY
New York, NY

Breakout Session
HIV & Aging: From Mitochondria to the Metropolis
Decatur, GA
April 11, 2019
Social Supports in Later Life

• Social networks are crucial to both physical and mental well-being for people of all ages, especially as one grows older and encounters the challenges of managing multiple chronic illnesses (Cantor & Brennan, 2000)

• If the informal caregiving provided by family, friends, and neighbors were replaced by formal caregivers (i.e., paid), the cost would exceed $450 billion annually (AARP, 2009)

• Thus, social networks are a critical health-care resource
Social Support Issues among Older PWH

- Older adults people with HIV (PWH) have fragile social networks characterized by a reliance on friends, rather than family. (Shippy & Karpiak 2005a; 2005b)

- Older PWH do not receive adequate support from their social networks (Nichols et al., 2002): Older PLWHA:
  - report feelings of isolation, stigmatization
  - have trouble coping with the demands of illness management (i.e., keeping medical appointments, adhering to treatment)

- When social supports are available for older PWH, they report lower levels of psychological distress and higher levels of well-being (Chesney et al., 2003)
Why Social Supports among PWHA are Important

• Older PWH have high levels of comorbid physical and mental health conditions that require care and assistance now and in the future.

• Government and Community-based services are being stretched due to:
  • The aging of the population in general
  • Decreased funding and program cutbacks due to budget shortfalls
  • AIDS Service Organizations (ASOs) lack experience in serving an older population who’s needs may differ from younger PWH.
Source of Data

• Research on Older Adults with HIV (ROAH) (Brennan et al., 2009; Karpiak et al., 2006)
• Adults 50+ with HIV living in or receiving services in New York City
• N = 914
• Comprehensive survey of health and psychosocial needs, including stigma and psychological well-being
• Approved by Copernicus Group IRB
Multimorbidity Proportions: ROAH HIV + vs USA (NHANES) Age 50+ (2006)
CES-D Symptoms of Depression

- Severe (23+) 39%
- Moderate (16-22) 24%
- Not Depressed (1 to 15) 37%
Currently Need Care 19%

Needed Care in Past 19%

Have Not Needed Care 62%

• Average Age = 55.5 Years

• Average Number Comorbid Conditions = 3.4

• 46% reported difficulty with at least one Instrumental ADL

• 22% reported difficulty with at least one Personal ADL

Living Alone: ROAH vs. NYC Elderly

ROAH: 70%
NYC Elderly 65+: 39%
ROAH:
Informal Network Composition

- **Parent**: 41.2% Living, 27.2% Functional
- **Child**: 54% Living, 37.7% Functional
- **Sibling**: 78.7% Living, 43.8% Functional
- **Other Relative**: 50.4% Living, 31.4% Functional
- **Friend**: 69.4% Living, 66.1% Functional

The bar chart illustrates the composition of informal networks with different types of relationships, comparing the percentage of living and functional relationships.
Typology of Social Networks of Older PWH

• In order to better understand the social networks of older PWH, we conducted a cluster analysis on a variety of social network and demographic characteristics:
  • degree of face-to-face and telephone contact with different social network members (i.e., functionality)
  • living arrangements,
  • religious participation

• The final analysis identified three groups that were significantly different (Chi-square tests with Bonferroni adjustment for multiple comparisons)
Social Network Types

- **Isolated** (32%) the most socially isolated, had intermediate contact with their children, little contact with other family members or friends, and little interaction with religious groups.

- **Friend-Centered** (35%) had contact with friends but not with children, family or religious groups.

- **Integrated** (33%) had the broadest spectrum of relationships, including children, family, friends, and the highest levels of religious participation.
Gender and Social Network Type

- **Integrated**
  - Male: 53%
  - Female: 45%
  - Trans: 2%

- **Friend-Centered**
  - Male: 84%
  - Female: 15%
  - Trans: 1%

- **Isolated**
  - Male: 73%
  - Female: 26%
  - Trans: 1%
Sexual Identity & Network Type

- Integrated: 86% Heterosexual, 6% Homosexual, 9% Bisexual, 10% Other
- Friend...: 36% Heterosexual, 10% Homosexual, 9% Bisexual, 10% Other
- Isolated: 81% Heterosexual, 10% Homosexual, 9% Bisexual, 10% Other
UCLA Loneliness Scale by Type

- Isolated: 47.6
- Friend-Centered: 43.2
- Integrated: 41.1

UCLA Loneliness Scale; Russel, 1996
Depression by Network Type

- Isolated: 21.7
- Friend-Centered: 18.9
- Integrated: 19.1

Center for Epidemiological Studies Depression Scale [CES-D]; Radloff, 1977
HIV Stigma by Network Type

HIV Stigma Scale; Berger, Ferrans, & Lashley, 2001
Instrumental Help Availability

- **Isolated**
  - Always: 26%
  - Sometimes: 24%
  - Occasionally: 17%
  - Not at All: 33%

- **Friend-Centered**
  - Always: 31%
  - Sometimes: 24%
  - Occasionally: 24%
  - Not at All: 21%

- **Integrated**
  - Always: 34%
  - Sometimes: 29%
  - Occasionally: 17%
  - Not at All: 19%
Emotional Support Availability

- **Isolated**
  - Always: 33%
  - Sometimes: 29%
  - Occasionally: 18%
  - Not at All: 20%

- **Friend-Centered**
  - Always: 51%
  - Sometimes: 29%
  - Occasionally: 14%
  - Not at All: 6%

- **Integrated**
  - Always: 55%
  - Sometimes: 23%
  - Occasionally: 13%
  - Not at All: 9%

Legend:
- Always
- Sometimes
- Occasionally
- Not at All
# Support from Family

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<th>Isolated %</th>
<th>Friend-Centered %</th>
<th>Integrated %</th>
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<tr>
<td>Shop/Run Errands***</td>
<td>31.9</td>
<td>20.8</td>
<td>51.6</td>
</tr>
<tr>
<td>Keep House/Prepare Meals***</td>
<td>27.0</td>
<td>17.3</td>
<td>44.1</td>
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<tr>
<td>Take/Drive Places***</td>
<td>21.8</td>
<td>15.7</td>
<td>44.1</td>
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<tr>
<td>Mail/Correspondence***</td>
<td>24.2</td>
<td>16.6</td>
<td>32.0</td>
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<tr>
<td>Manage Money/Pay Bills***</td>
<td>22.8</td>
<td>13.7</td>
<td>28.8</td>
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<tr>
<td>Give Advice***</td>
<td>35.4</td>
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<td>Talk When Feeling Down/Low***</td>
<td>48.4</td>
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<tr>
<td>Talk About Personal/Family Problem***</td>
<td>42.1</td>
<td>48.2</td>
<td>71.6</td>
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* p < .05, ** p < .01, *** p < .001
### Support from Friends

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<td>76.0</td>
<td>74.2</td>
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Aggregate Help from Network

Average Number Types Assistance Received

- **Family**
  - Isolated
  - Friend-Centered
  - Integrated

- **Friend**
  - Isolated
  - Friend-Centered
  - Integrated

*p < .05, ** p < .01, *** p < .001*
Summary

• Those with *Friend-Centered* network types received most of their assistance from friends, but still less than the *Integrated* group who had reported a greater variety of functional family members.

• However, for those with *Friend-Centered* networks, the amount of assistance received from friends did not compensate for the lack of family support.

• The *Isolated* reported significantly lower levels of assistance, lower perceptions of support availability and adequacy, greater stigma and psychological distress, and lower well-being compared to their peers.
Conclusions

• While friends dominate many social networks in this population, a more nuanced interpretation is needed; many have no friends and a substantial proportion receive significant family support.

• Those with *Isolated* network types will likely need to access a high volume of community-based services as they age as they lack informal support resources.
Thank You!

For further information please contact:

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