Aging and HIV: Medical Consequences of Alcohol & Multisubstance Use

Amy C. Justice, MD, PhD
Professor, Yale University Schools of Medicine and Public Health
Chief General Internal Medicine, Veterans Administrative Connecticut Healthcare System
More People Are Living With HIV in the United States than Ever Before

Living Patients

Deaths

New patients

Number of patients (1000)

Mortality per 100 patient-years

www.aids2012.org
Life Expectancy Not “Normal” in cART Era

<table>
<thead>
<tr>
<th>Reference</th>
<th>Cohort/study name</th>
<th>Country of study</th>
<th>LE in HIV-positive population</th>
<th>LE in general population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nakagawa et al. [8]</td>
<td>Computer simulation (HIV Synthesis)</td>
<td>UK</td>
<td>LE at birth: 75.0 years if diagnosed with HIV with high CD4 count; 71.5 years if diagnosed with HIV with low CD4 count</td>
<td>LE at birth: estimated from model to be 82.0 years if not infected with HIV</td>
</tr>
<tr>
<td>The Antiretroviral Therapy Cohort Collaboration [9]</td>
<td>ART-CC</td>
<td>Multi-country study (Europe and North America)</td>
<td>LE at age 20: 43.1 years. LE at age 35: 31.7 years</td>
<td>Not stated</td>
</tr>
<tr>
<td>Johnson et al. [10]</td>
<td>LeDEA-SA</td>
<td>South Africa</td>
<td>LE at age 20: 276 years in men; 368 years in women. LE at age 60: 10.1 years in men; 144 years in women</td>
<td>Not stated</td>
</tr>
<tr>
<td>Mills et al. [11]</td>
<td>The AIDS Support Organization (TASO) cohort</td>
<td>Uganda</td>
<td>LE at age 20: 26.7 years. LE at age 35: 27.9 years</td>
<td>LE at age 20: 41 years</td>
</tr>
<tr>
<td>Losina et al. [12]</td>
<td>Computer simulation (CEPAC)</td>
<td>USA</td>
<td>LE at age 33: 2266 years if optimally diagnosed and treated; 19.36 years if treated with cART and adherence follows normal patterns</td>
<td>LE at age 33: 42.91 years for general population; 3458 years if risk profile similar to those with HIV</td>
</tr>
<tr>
<td>Bor et al. [17]</td>
<td>KwaZulu-Natal, South Africa</td>
<td></td>
<td>No specific estimates</td>
<td>LE at birth: 523 years in 2000; 49.2 years in 2003; 60.5 years in 2011</td>
</tr>
<tr>
<td>Lohse et al. [21]</td>
<td>Danish HIV Cohort Study</td>
<td>Denmark</td>
<td>LE at age 25: 8 years in 1995 to 1996; 23 years in 1997 to 1999; 33 years in 2000 to 2005</td>
<td>LE at age 25: 51 years</td>
</tr>
<tr>
<td>May et al. [23]</td>
<td>UK Collaborative HIV Cohort Study</td>
<td>UK</td>
<td>LE at age 20: 39.5 years in men; 502 years in women. LE at age 35: 30.1 years in women; 37.7 years in women</td>
<td>LE at age 20: 57.8 years in men; 61.6 years in women; LE at age 35: 43.5 years in men; 46.9 years in women</td>
</tr>
<tr>
<td>van Sighem et al. [41]</td>
<td>ATHENA Cohort</td>
<td>The Netherlands</td>
<td>LE at age 25: 527 years in men; 57.8 years in women</td>
<td>LE at age 25: 53.1 years in men; 58.1 years in women</td>
</tr>
</tbody>
</table>

Abbreviations: cART, combination antiretroviral therapy; LE, life expectancy.
Aging with HIV is not just like aging without HIV (at least not as commonly conceived).

But studying aging with HIV might teach us a bit about both.
Veterans Aging Cohort Study (VACS)

• Large, characterized NIAAA cohort
  – >40,000 HIV+ matched to >80,000 HIV-
  – Nested in-depth cohort of >7,000 (half HIV+)
  – ~10 yrs. of longitudinal data on alcohol and MSU
  – Survey sites have new electronic baseline (~2700)
Drank Alcohol Last Year
VACS Subjects (2013-2014)
% Sex in Last Year by Age
VACS Subjects (2013-2014)

- 25-39 yrs.
- 40-49 yrs.
- 50-64 yrs.
- 65+ yrs

- HIV-
- HIV+
% Used a Condom by Age (2013-2014) 
VACS Subjects

HIV-  | HIV+
--- | ---
25-39 yrs. | 40-49 yrs. | 50-64 yrs. | 65+ yrs
30 | 40 | 50 | 20

*Note: The chart shows the percentage of subjects using condoms by age group and HIV status for the VACS subjects between 2013 and 2014.*
% Smoked in Last Year
VACS Subjects (2013-2014)

25-39 yrs. | 40-49 yrs. | 50-64 yrs. | 65+ yrs.
---|---|---|---
HIV-| 50% | 60% | 70% | 40%
HIV+| 30% | 40% | 50% | 30%
Alcohol and Multi Substance Use Among those Aging with and without HIV

- Alcohol
- Opioids
- Benzodiazepines
- Marijuana
- Cocaine/Meth.
- Tobacco

Nearly everyone who smokes, drinks

MSU alters cognitive effects of other drugs

Alcohol, tobacco, other psychoactive drugs and polypharmacy all influence mortality in HIV
### Prescription Opioids/Benzodiazepines, Alcohol, MSU, Mortality

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall (n=64441)</th>
<th>Uninfected (n=47452)</th>
<th>HIV-infected (n=16989)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>P</td>
<td></td>
</tr>
<tr>
<td>Long-term opioid receipt^b</td>
<td>1.39 (1.21, 1.60)</td>
<td>&lt;0.001</td>
<td>1.35 (1.14, 1.61)</td>
</tr>
<tr>
<td>Long-term benzodiazepine receipt</td>
<td>1.33 (1.10, 1.62)</td>
<td>0.004</td>
<td>1.41 (1.12, 1.78)</td>
</tr>
<tr>
<td>Long-term opioid and benzodiazepine receipt</td>
<td>1.51 (1.22, 1.87)</td>
<td>0.0001</td>
<td>1.43 (1.10, 1.86)</td>
</tr>
<tr>
<td>Long-term medication count^c</td>
<td>1.05 (1.04, 1.07)</td>
<td>&lt;0.001</td>
<td>1.04 (1.03, 1.06)</td>
</tr>
<tr>
<td>Alcohol use disorder</td>
<td>1.63 (1.39, 1.90)</td>
<td>&lt;0.001</td>
<td>1.56 (1.30, 1.88)</td>
</tr>
<tr>
<td>Drug use disorder</td>
<td>0.95 (0.81, 1.13)</td>
<td>0.59</td>
<td>0.88 (0.70, 1.11)</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>1.14 (0.92, 1.40)</td>
<td>0.23</td>
<td>1.09 (0.86, 1.38)</td>
</tr>
<tr>
<td>Bipolar</td>
<td>0.92 (0.74, 1.14)</td>
<td>0.44</td>
<td>0.93 (0.71, 1.22)</td>
</tr>
<tr>
<td>Major Depression</td>
<td>0.95 (0.79, 1.15)</td>
<td>0.62</td>
<td>1.07 (0.84, 1.35)</td>
</tr>
<tr>
<td>PTSD</td>
<td>0.79 (0.68, 0.93)</td>
<td>0.004</td>
<td>0.75 (0.63, 0.91)</td>
</tr>
<tr>
<td>Acute pain^d</td>
<td>1.72 (1.43, 2.08)</td>
<td>&lt;0.001</td>
<td>1.76 (1.39, 2.23)</td>
</tr>
<tr>
<td>Chronic pain^e</td>
<td>0.93 (0.83, 1.05)</td>
<td>0.24</td>
<td>0.93 (0.81, 1.07)</td>
</tr>
<tr>
<td>Black vs. white</td>
<td>0.86 (0.77, 0.96)</td>
<td>0.006</td>
<td>0.81 (0.70, 0.92)</td>
</tr>
<tr>
<td>Hispanic vs. white</td>
<td>0.58 (0.45, 0.73)</td>
<td>&lt;0.001</td>
<td>0.56 (0.42, 0.75)</td>
</tr>
<tr>
<td>Other vs white</td>
<td>0.87 (0.63, 1.18)</td>
<td>0.37</td>
<td>0.88 (0.60, 1.29)</td>
</tr>
<tr>
<td>VACS Index score</td>
<td>1.12 (1.11, 1.13)</td>
<td>&lt;0.001</td>
<td>1.23 (1.21, 1.25)</td>
</tr>
<tr>
<td>Current smoking vs. never</td>
<td>1.87 (1.62, 2.15)</td>
<td>&lt;0.001</td>
<td>2.01 (1.69, 2.39)</td>
</tr>
<tr>
<td>Past smoking vs. never</td>
<td>1.43 (1.21, 1.70)</td>
<td>&lt;0.001</td>
<td>1.37 (1.11, 1.68)</td>
</tr>
</tbody>
</table>

---

In Press, Clinical Infectious Diseases, Weisberg DF et al.
Frailty\textsuperscript{1,2}

• Concept: decreased tolerance due to cumulative physiologic injury increasing risk of catastrophic declines

• Biological underpinnings:
  – Dysregulation across systems: Chronic inflammation, anabolic and catabolic hormones, insulin resistance, immune dysfunction/ suppression (telomere length), oxidative stress, and micronutrient deficiencies

• Approaches to measurement vary:
  – Phenotypic (Fried et al.): Weight loss, exhaustion, weakness, slowness, low activity
  – Deficit accumulation (Rockwood et al.): 30 measures of function, symptoms, and diagnoses


Factors Contributing to Frailty in HIV

1. Delayed HIV Diagnosis
   Incomplete Viral Suppression

2. Alcohol and
   Multisubstance Use

3. Multimorbidity &
   Polypharmacy

4. Social Isolation &
   Depression
Pathophysiology of Frailty

Timing of Treatment Matters: Delayed Presentation By Age

Hepatic Fibrosis (FIB-4 >3.25), HIV, HCV, and Level of Alcohol Consumption (n=3,565)

Chi-square test for trend over categories of alcohol use
* HIV/HCV-uninfected, p=0.019
^ HCV-monoinfected, p<0.001
† HIV-monoinfected, p=0.0025
‡ HIV/HCV-coinfected, p=0.060

Figure 2b. Standardized cumulative incidences of hepatic decompensation between antiretroviral-treated HIV/hepatitis C virus-coinfected patients with HIV RNA levels $\geq 1,000$ copies/mL on any result during follow-up (denoted by dashed line), antiretroviral-treated HIV/hepatitis C virus-coinfected patients with HIV RNA $<1,000$ copies/mL on all HIV RNA results during follow-up (denoted by solid line), and hepatitis C virus-monoinfected patients (denoted by dotted line).

Drinks to a Buzz by HIV, Viral Load, and Alcohol

We need to investigate further.

HED= Heavy Episodic Drinking, Revisions invited by AIDS and Behavior
Diagnosis–specific hospitalization rates

Mental Disorder

HIV

Respiratory

GI and Liver

Cardiovascular

Infection

Neurologic

Renal

Endocrine

Non-AIDS Cancer

Other

Rate per 1000 patients


Rate per 1000 patients


Rate per 1000 patients


Rate per 1000 patients


Rate per 1000 patients


Rate per 1000 patients


HIV+/AUD+

HIV+/AUD-

HIV-/AUD+

HIV-/AUD-

Revisions invited by AIDS and Behavior
### Unhealthy Alcohol a Barrier to Quit Attempts

<table>
<thead>
<tr>
<th></th>
<th>Adjusted&lt;sup&gt;c&lt;/sup&gt; Odds Ratios (95%CI)</th>
<th>Pooled analysis* (n=1721)</th>
<th>HIV+ (n=975)</th>
<th>HIV- (n=746)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unhealthy alcohol use</td>
<td>0.76 (0.61, 0.94)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.68 (0.51, 0.91)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.86 (0.62, 1.19)</td>
<td></td>
</tr>
<tr>
<td>Cigarettes per day, &lt;10</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>10-20 cig/day</td>
<td>0.73 (0.58, 0.91)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.77 (0.58, 1.04)</td>
<td>0.67 (0.47, 0.97)&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>21+ cig/day</td>
<td>0.68 (0.49, 0.92)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.04 (0.67, 1.62)</td>
<td>0.44 (0.28, 0.71)&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Hard drug use</td>
<td>1.03 (0.79, 1.34)</td>
<td>0.89 (0.63, 1.25)</td>
<td>1.33 (0.87, 2.03)</td>
<td></td>
</tr>
<tr>
<td>Moderate to severe depression</td>
<td>1.64 (1.30, 2.07)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.70 (1.24, 2.34)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.55 (1.10, 2.19)&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Recent pulmonary disease</td>
<td>2.48 (1.27, 4.86)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4.93 (1.41, 17.17)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.62 (0.70, 3.73)</td>
<td></td>
</tr>
</tbody>
</table>

- **a** Significant odds ratio
- **c** Odds ratios adjusted for age, sex, race/ethnicity, alcohol use, cigarettes smoked per day, hard drug use, depression score, recent of shortness of breath/wheezing

*Pooled analysis includes adjustment for HIV in addition to above

Under review
Greater Alcohol Use Associated with Less Interest in Quitting

<table>
<thead>
<tr>
<th>Thinking About Quitting</th>
<th>Pooled analysis* (n=1783)</th>
<th>HIV+ (n=983)</th>
<th>HIV- (n=748)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No alcohol problem</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Unhealthy alcohol use</td>
<td>0.77 (0.57, 1.04)</td>
<td>0.63 (0.43, 0.92)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.12 (0.67, 1.87)</td>
</tr>
<tr>
<td>More extreme alcohol use</td>
<td>0.61 (0.46, 0.80)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.71 (0.48, 1.04)</td>
<td>0.53 (0.36, 0.79)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Attempted to Quit</th>
<th>Pooled analysis* (n=1721)</th>
<th>HIV+ (n=975)</th>
<th>HIV- (n=746)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No alcohol problem</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Unhealthy alcohol use</td>
<td>0.82 (0.62, 1.10)</td>
<td>0.70 (0.48, 1.03)</td>
<td>1.01 (0.65, 1.58)</td>
</tr>
<tr>
<td>More extreme alcohol use</td>
<td>0.72 (0.55, 0.95)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.67 (0.46, 0.98)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.78 (0.52, 1.16)</td>
</tr>
</tbody>
</table>

- No alcohol problem: audit-C≤3 (female), ≤4 (male)
- More extreme alcohol use defined as audit-C≥6
Polypharmacy
Polypharmacy

• Typically defined as >5 chronic drugs

• Associated with diminished marginal benefit from additional medication due to:
  – Non adherence
  – Drug-drug interactions
  – Cumulative toxicity

• Risk of adverse events increases approximately 10% with each additional medication

Gandhi TK. N Engl J Med 2003;348:1556-64
Chronic Medication Count by Age and HIV Status (VACS)

Edelman EJ et al. IDSA [oral], San Francisco, California, October 2-6, 2013.
Medication Count and Mortality (VACS)

Seven or more medications is associated with an increased risk of mortality after adjusting for HIV status and disease severity.

*Note: reference is 3 medications

Edelman EJ et al. IDSA [oral], San Francisco, California, October 2-6, 2013.
Is Frailty Expressed the Same Way Among those Aging with HIV?

• Fried phenotype uncommon (<7%), doesn’t include cognition, and may be confounded by depression

• Rockwood Index is complex and requires measures not routinely collected in HIV
Components of VACS Index

- Age
- HIV Biomarkers: HIV-1 RNA, CD4 Count
- General Biomarkers: Hemoglobin, HCV, Composite markers for liver and renal injury
- Assessed among those initiating treatment
- Adjusted to predict among those on treatment
Composite Biomarkers

\[ \text{FIB 4} = \frac{\text{AGE} \times \text{AST}}{\text{PLT} \times (\text{ALT}^{1/2})} \]  

\[ \text{eGFR} = 186.3 \times \text{CREAT}^{-1.154} \times \text{AGE}^{-0.203} \times \text{FEM\_VAL} \times \text{BLACK\_VAL} \]  

\text{FEM\_VAL} = 0.742 \text{ if female, } 1 \text{ if male} 

\text{BLACK\_VAL} = 1.21 \text{ if black, } 1 \text{ otherwise} 

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Restricted</th>
<th>VACS</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>50 to 64</td>
<td>23</td>
<td>12</td>
</tr>
<tr>
<td>&gt; 65</td>
<td>44</td>
<td>27</td>
</tr>
<tr>
<td>CD4 cells/mm³</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 500</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>350 to 499</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>200 to 349</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>100 to 199</td>
<td>19</td>
<td>10</td>
</tr>
<tr>
<td>50 to 99</td>
<td>40</td>
<td>28</td>
</tr>
<tr>
<td>&lt; 50</td>
<td>46</td>
<td>29</td>
</tr>
<tr>
<td>HIV-1 RNA copies/ml</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 500</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>500 to 1x10⁵</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>≥ 1x10⁵</td>
<td>25</td>
<td>14</td>
</tr>
<tr>
<td>Hemoglobin g/dL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 14</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>12 to 13.9</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>10 to 11.9</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>&lt; 10</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>FIB-4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 1.45</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>1.45 to 3.25</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>&gt; 3.25</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>eGFR mL/min</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 60</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>45 to 59.9</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>30 to 44.9</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>&lt; 30</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Hepatitis C Infection</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>
A. NA-ACCORD (N = 10835)  
B. VACS (N = 5066)  
C. Men (N = 12785)  
D. Women (N = 3116)  
E. Age < 50 years (N = 11191)  
F. Age > 50 years (N = 4710)  
G. Black (N = 5878)  
H. White (N = 6079)  
I. Undetectable VL (N = 8715)  
J. Detectable VL (N = 7186)  

VACS Index Predicts Fragility Fractures

VACS Index Responsive to Opioid Use

Non overlapping 6 week intervals between 2000-2011 during opioid agonist treatment
VACS Index and Alcohol

• Includes HIV-1 RNA, AST, ALT, platelets and hemoglobin—all of which are known to be altered by alcohol

• Less signal with self reported alcohol than with urine toxicology for opioids!

• WE NEED A BETTER MEASURE OF ALCOHOL EXPOSURE!
VACS Index Correlated with Biomarkers of Inflammation

Table 2. Association of VACS Index and a Restricted Index with Exercise Capacity and Body Composition in HIV-Infected Adults on Antiretroviral Therapy

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean (SD)</th>
<th>VACS Index&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Restricted index&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Endurance</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metabolic equivalents (METS)</td>
<td>6.0 (1.6)</td>
<td>−0.21 (0.1)</td>
<td>−0.25 (0.07)</td>
</tr>
<tr>
<td>Exercise time, median (range), min</td>
<td>12.0 (4-15)</td>
<td>−0.20 (0.2)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>−0.23 (0.09)</td>
</tr>
<tr>
<td>6-min walk distance, m</td>
<td>533 (83)</td>
<td>−0.27 (0.05)</td>
<td>−0.10 (0.5)</td>
</tr>
<tr>
<td><strong>Strength</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quadriceps strength, N</td>
<td>596 (163)</td>
<td>−0.45 (&lt;0.01)</td>
<td>−0.17 (0.2)</td>
</tr>
<tr>
<td>Grip strength, kg</td>
<td>40.5 (7.9)</td>
<td>−0.28 (0.04)</td>
<td>−0.18 (0.2)</td>
</tr>
<tr>
<td><strong>Body composition&lt;sup&gt;c&lt;/sup&gt;</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total percent body fat, %</td>
<td>21.0 (9.0)</td>
<td>−0.04 (0.7)</td>
<td>0.01 (0.9)</td>
</tr>
<tr>
<td>Total lean mass, kg</td>
<td>56.1 (7.4)</td>
<td>−0.51 (&lt;0.001)</td>
<td>−0.22 (0.1)</td>
</tr>
<tr>
<td>Leg lean mass, kg</td>
<td>18.7 (2.8)</td>
<td>−0.49 (&lt;0.001)</td>
<td>−0.19 (0.2)</td>
</tr>
<tr>
<td>Quadriceps cross-sectional area, cm²</td>
<td>68.6 (13.3)</td>
<td>−0.37 (&lt;0.01)</td>
<td>−0.12 (0.4)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Pearson.

<sup>b</sup>Spearman.

<sup>c</sup>By DXA (n=50) and CT (n=48).
FIG. 1. VACS index predicts quadriceps strength adjusted for muscle cross-sectional area (CSA).

Oursler KK et al, AIDS Research and Human Retroviruses 2013; 29(9):1218-1223
The Veterans Aging Cohort Study Index is Associated With Concurrent Risk for Neurocognitive Impairment.


OBJECTIVE: The Veterans Aging Cohort Study (VACS) Index is predictive of mortality and combines age, traditional HIV biomarkers (HIV-1 plasma RNA and current CD4 count), and non-HIV biomarkers (indicators of renal and liver function, anemia, and hepatitis C coinfection). We examined the association between the VACS Index and HIV-associated neurocognitive impairment (NCI).

DESIGN AND METHODS: Participants included 601 HIV-infected adults enrolled in cohort studies at the University of California, San Diego, HIV Neurobehavioral Research Program (ages: 18-76 years; 88% male; 63% white; median current CD4 = 364 cells/mm; 63% on antiretroviral therapy; AIDS = 64%). Biomarkers used in calculating the VACS Index were measured in prospectively collected blood samples using conventional laboratory methods. NCI was defined using prospectively collected blood samples using conventional laboratory methods. NCI was defined using global and seven domain deficit scores.

RESULTS: Higher VACS Index scores were associated with concurrent risk for global NCI [P < 0.001; odds ratio = 1.21, confidence interval (CI): 1.12 to 1.32], even when adjusting for psychiatric comorbidities. This relation was statistically significant for most cognitive domains in adjusted models. Furthermore, the VACS Index predicted concurrent NCI beyond nadir CD4 and estimated duration of infection. Older age, lower hemoglobin, and lower CD4 counts were the VACS components most strongly linked to NCI.

CONCLUSIONS: The findings extend previous research on the potential usefulness of the VACS Index in predicting HIV-associated outcomes to include NCI. Although the effect size was relatively small, our findings suggest that demographic information, HIV-disease factors, and common comorbidities might each play important roles in the clinical manifestation of cognitive impairment among HIV-infected individuals. Additional research is needed to determine if a more sensitive and specific index can be developed.
VACS Index Measures Frailty in HIV

• Is associated with
  – Functional performance
  – Cognitive performance
  – Biomarkers of chronic inflammation

• Predicts
  – All cause and cause specific mortality
  – Hospitalization, MICU admission and 30 day mortality
  – Fragility fractures

• Is responsive to changes in care and behavior
  – ART interruption and intensification
  – Varying levels of ART adherence
VACS Index Also Predictive Among Veterans Aging Without HIV

Randomly selected score and followed for survival. Kaplan-Meier plots by VACS Index score for Hospitalization (top figures) and death (bottom figures) among HIV infected (left side) and uninfected (right side). Poster. 19th International Workshop on HIV Observational Databases (IWHOD), Sitges, Spain
VACS Index Scores Higher in HIV+

**HIV +**

Median 23, IQR 12-39

**Uninfected**

Median 12, IQR 6-27
Sue, age 73

Bill, age 77

Anna, age 64
Social Isolation By HIV Status and Age

Conclusions

• Despite the increased risk for aging associated conditions, these do not occur earlier in HIV

• In contrast, multimorbidity and polypharmacy do occur earlier in HIV

• Frailty, measured with VACS Index, is more common among HIV infected compared with demographically matched uninfected

• Alcohol and multisubstance use contribute substantially to frailty in those aging with HIV
Veterans Aging Cohort Study (VACS)

The Veterans Aging Cohort Study (VACS) is a prospective, observational cohort study of HIV-positive and an age/race/site matched control group of HIV-negative veterans in care in the United States. The study's aim is to understand the role of comorbid medical and psychiatric disease in determining clinical outcomes in HIV infection. It is funded primarily by the National Institute on Alcoholism and Alcohol Abuse, National Institutes of Health. The study has a special focus on the role of alcohol use and abuse in determining clinical outcomes.

The VACS study is built around the Veterans Health Administration (VA), the largest integrated health-care system in the United States, providing care to 5.6 million patients annually. The VA is also the largest single provider of HIV care in the nation, serving 13,000 HIV-positive veterans in 2003. The VA provides inpatient and outpatient medical care, pharmacy, mental-health services, substance-abuse treatment, long-term care, homeless care, and hospice services. The VA also has a national, fully electronic medical-record system that includes all routine clinical data, administrative data, and comprehensive follow-up data for mortality, as the VA pays some burial expenses for veterans.
National VACS Project Team
Acknowledgements

- **Consortium PI**: AC Justice*
- **Scientific Collaborator (NIAAA)**: K Bryant
- **Affiliated PIs**: S Braithwaite, K Crothers*, R Dubrow *, DA Fiellin*, M Freiberg*, V LoRe*
- **Participating VA Medical Centers**: Atlanta (D. Rimland*, V Marconi), Baltimore (M Sajadi, R Titanji), Bronx (S Brown, Y Ponomarenko), Dallas (R Bedimo), Houston (M Rodriguez-Barradas, N Masozera), Los Angeles (M Goetz, D Leaf), Manhattan-Brooklyn (M Simberkoff, D Blumenthal, H Leaf, J Leung), Pittsburgh (A Butt, K Kraemer, M Freiberg, E Hoffman), and Washington DC (C Gibert, R Peck)
- **Core and Workgroup Chairs**: C Brandt, J Edelman, N Gandhi, J Lim, K McGinnis, KA Oursler, C Parikh, J Tate, E Wang, J Womack
- **Staff**: H Bathulapalli, T Bohan, J Ciarleglio, A Consorte, P Cunningham, L Erickson, C Frank, K Gordon, J Huston, F Kidwai-Khan, G Koeberl, F Levin, L Piscitelli, C Rogina, S Shahrir, M Skanderson
- **Major Collaborators**: VA Public Health Strategic Healthcare Group, VA Pharmacy Benefits Management, Massachusetts Veterans Epidemiology Research and Information Center (MAVERIC), Yale Center for Interdisciplinary Research on AIDS (CIRA), Center for Health Equity Research and Promotion (CHERP), ART-CC, NA-ACCORD, HIV-Causal
- **Cross Cohort Collaborators**: Richard Moore (NA-ACCORD), Jonathan Sterne (ART-CC), Brian Agan (DoD)
- **Major Funding by**: National Institutes of Health: AHRQ (R01-HS018372), NIAAA (U24-AA020794, U01-AA020790, U01-AA020795, U01-AA020799, U24-AA022001, U24 AA022007), NHLBI (R01-HL095136; R01-HL090342), NIAID (U01-A1069918), NIMH (P30-MH062294), NIDA (R01DA035616), NCI (R01 CA173754) and the Veterans Health Administration Office of Research and Development (VA REA 08-266, VA IRR Merit Award) and Office of Academic Affiliations (Medical Informatics Fellowship)

*Indicates individual is also the Chair of a Core or Workgroup
Acknowledgements

Continued

• 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) 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.

QR Codes

QR Code for VACS Homepage
QR Code for VACS INDEX CALCULATOR-
QR Code for VACS INDEX CALCULATOR-MOBILE APP