A Website & Smart Phone App to Promote Healthy Aging with HIV

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Why Do We Need A Risk Index for HIV?
Projected Proportion of those Living With HIV in United States 50+ Years*
2001-2017

US VA in 2003

As of 2008:
• San Francisco
• NY City

Where Ever ART Available, People with HIV are Ageing

• An estimated 14% of adults with HIV infection in Sub Saharan Africa are >50 years

• AIDS is leading cause of death among >50 yrs. in Nyanza Providence, Western Kenya

• As prevalence increases, incidence will rise
Projected HIV Prevalence by Age in Hlabisa Sub-district of KwaZulu-Natal, South Africa

Hontelez J. Ageing with HIV in South Africa. AIDS
What Drives Patient Outcomes Among those Aging with HIV?
Not AIDS Defining Events
Not Only “Immune Deficiency”
Outcome Disparities Growing
AIDS Events Increasingly Rare

ART-CC, Archives Int Med 2005: 165 416-423
AIDS Events Variably Associated with CD4 and Survival

By Median (IQR) CD4

By Relative Hazard of Death

ART-CC, CID 2009;48:1138-51
>50% of Deaths Attributed to Non-AIDS Events

Death Rate Disparities by HIV, Race/Ethnicity and Age

Death Rates by Age and Race/Ethnicity

- Black Non-HIV-related
- Black HIV-related
- Hispanic Non-HIV-related
- Hispanic HIV-related
- White Non-HIV-related
- White HIV-related
- NYC all-cause

HIV Epidemiology & Field Services Semiannual Report,
# Strategies for Management of ART (SMART)

<table>
<thead>
<tr>
<th>End Point</th>
<th>Drug Conservation Group (N = 2720)</th>
<th>Viral Suppression Group (N = 2752)</th>
<th>Hazard Ratio for Drug Conservation Group vs. Viral Suppression Group (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary end point</td>
<td>120</td>
<td>47</td>
<td>2.6 (1.9–3.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Death from any cause</td>
<td>55</td>
<td>30</td>
<td>1.8 (1.2–2.9)</td>
<td>0.007</td>
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<tr>
<td>Opportunistic disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serious</td>
<td>13</td>
<td>2</td>
<td>6.6 (1.5–29.1)</td>
<td>0.01</td>
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<tr>
<td>Nonserious</td>
<td>63</td>
<td>18</td>
<td>3.6 (2.1–6.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Major cardiovascular, renal, or hepatic disease</td>
<td>65</td>
<td>39</td>
<td>1.7 (1.1–2.5)</td>
<td>0.009</td>
</tr>
<tr>
<td>Fatal or nonfatal cardiovascular disease</td>
<td>48</td>
<td>31</td>
<td>1.6 (1.0–2.5)</td>
<td>0.05</td>
</tr>
<tr>
<td>Fatal or nonfatal renal disease</td>
<td>9</td>
<td>2</td>
<td>4.5 (1.0–20.9)</td>
<td>0.05</td>
</tr>
<tr>
<td>Fatal or nonfatal liver disease</td>
<td>10</td>
<td>7</td>
<td>1.4 (0.6–3.8)</td>
<td>0.46</td>
</tr>
<tr>
<td>Grade 4 event</td>
<td>173</td>
<td>148</td>
<td>1.2 (1.0–1.5)</td>
<td>0.13</td>
</tr>
<tr>
<td>Grade 4 event or death from any cause</td>
<td>205</td>
<td>164</td>
<td>1.3 (1.0–1.6)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

* Numbers of individual events of each type do not sum to the total number because some participants had more than one event. End-point definitions are listed in the Supplementary Appendix. Grade 4 events were determined on the basis of toxicity grades developed by the Division of AIDS of the NIAID. CI denotes confidence interval.

*More AIDS and “Non-AIDS” Events Among Rx. Sparing Arm (HR 1.7 in SMART) NEJM 2006;355:2283-96
General Observations on HANA

• Multiple interacting HIV and non HIV causes
  – HIV typically not the most influential risk factor
  – cART appears to decrease risk (SMART)

• What is common and what has the greatest relative risk for HIV differ

• Relative risk HIV+/- highly variable
  – Association with CD4 variable
  – Competing risk of death is changing and unmasking risk associated with HIV
Case: Routine Follow Up

- 52 yr. old black male HIV+, on stable cART (2 yrs)
- Undetectable HIV-1 RNA since starting cART
- Hepatitis C infected, never treated
HIV Guideline Care

Screening:
- Behaviors
  - Adherence
  - Risk of transmission
- Measurements
  - HIV-1 RNA
  - CD4 count
  - Electrolytes, glucose
  - CBC
  - ALT, AST, T. Bilirubin
  - Fasting lipids
  - Urinalysis
  - Anal Ca. screen

Findings:
- No difficulty with cART
- 1 partner, no condoms
- HIV-1 RNA <50 copies/ml
- CD4 count 400 cells/ml
- Creatinine 1.2
- Hgb 13 mg/dL, Platelets 140K
- ALT 35, AST 44
- Fasting LDL 120, HDL 35
- Urine normal
- Normal anal pap smear

DHHS Guidelines for the Use of ART in HIV-1 Infected Adults and Adolescence
Additional US Preventative Task Force A or B Recommendations

• Behaviors
  – Tobacco, alcohol
  – Depression
  – Diet, obesity
  – Aspirin for CVD

• Measurements
  – Colorectal ca. screen
  – Blood pressure
  – Diabetes (if BP>135/80)

Findings:
  – Smokes 1 ppd; drinks (6 pack of beer on weekend)
  – Feels blue, not suicidal
  – BMI 30, up from 27, 2 yrs ago
  – No exercise
  – No ASA
  – Never screened for c. cancer
  – Blood pressure 155/85
  – Fasting blood sugar normal

http://www.uspreventiveservicestaskforce.org/recommendations.htm
Pertinent Positives

Behaviors
• Smoking cessation?
• Lung ca. screening?
• Alcohol reduction?
• Antidepressant?
• Partner notification?
• Exercise prescription?
• Nutrition counseling?

Treatment Issues
• Hepatitis C
  – Treatment? Risk reduction?
  – Liver ca. screening?
• Cardiovascular Risk
  – Aspirin? Statins?
• Colonoscopy?
• Antihypertensives?
• Erectile dysfunction?
• Toxicity?

6 Possible additional medications --before considering HCV treatment
Decision to Screen and Treat a Balancing Act

Polypharmacy

• Typically defined as >5 drugs

• Associated with
  – Nonadherence
  – Cognitive compromise
  – Organ system toxicities

• Risk of adverse events in uninfected subjects approximates 100%
Swiss Cohort

Comedications

- No comedication
- One comedication
- Two comedinations
- Three comedications
- Four or more comedications

Comorbidities

- No comorbidity
- One comorbidity
- Two comorbidities
- Three comorbidities
- Four or more comorbidities

Agegroups

- <50 years: n=5761
- 50-64 years: n=2233
- 65+ years: n=450

Daily Pill Count By Age and Purpose 1990-2010
(Southern Alberta Cohort, Canada)

ARV Pill Count
Decreasing For <45/45+ Years of Age

Non ARV Pill Count
Differentially Increasing For 45+ Years of Age

Krentz HB et al. Pill burden in HIV infection: 20 years of experience. Antiviral Therapy, published online 2/23/2012
## Resource Constraints: ADAP

<table>
<thead>
<tr>
<th>Coverage Limitation</th>
<th>Number of State ADAPs</th>
<th>Top 10 HIV Prevalence States</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waiting lists</td>
<td>9</td>
<td>FL, GA, NC</td>
</tr>
<tr>
<td>Not all ARV’s</td>
<td>24</td>
<td>TX, MD</td>
</tr>
<tr>
<td>Less than half of 31 “A1” opportunistic infection drugs</td>
<td>17</td>
<td>FL, TX</td>
</tr>
<tr>
<td>Less than 100 “other drugs”</td>
<td>37</td>
<td>FL, TX, PA, GA, NC</td>
</tr>
<tr>
<td>Less than 20 “other drugs”</td>
<td>13</td>
<td>TX, GA</td>
</tr>
<tr>
<td>No Interferon / Ribavirin for Hepatitis C</td>
<td>24</td>
<td>FL, TX, GA, IL, NC</td>
</tr>
</tbody>
</table>

* State funding cut by $170 million in 2009, federal support flat

How do we individualize care for those Aging with HIV?

Is HIV a template for optimization of care in the context of a “primary” chronic disease?
Need a Summary Measure of Risk

- To determine who might benefit from screening
- To measure net benefit for a wide range of interventions to inform care strategies
  - HCV antiretroviral treatment vs. weight reduction and alcohol cessation
  - Statins and aspirin vs. exercise
### VACS Index Thresholds and Weights

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Restricted</th>
<th>VACS</th>
</tr>
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<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>
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<td>&gt; 65</td>
<td>44</td>
<td>27</td>
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</table>

<table>
<thead>
<tr>
<th>CD4 cells/mm³</th>
<th>Restricted</th>
<th>VACS</th>
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<tr>
<td>≥ 500</td>
<td>0</td>
<td>0</td>
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<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>
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</table>

<table>
<thead>
<tr>
<th>HIV-1 RNA copies/ml</th>
<th>Restricted</th>
<th>VACS</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 500</td>
<td>0</td>
<td>0</td>
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<tr>
<td>500 to 1x10⁵</td>
<td>11</td>
<td>7</td>
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<td>≥ 1x10⁵</td>
<td>25</td>
<td>14</td>
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<table>
<thead>
<tr>
<th>Hemoglobin g/dL</th>
<th>Restricted</th>
<th>VACS</th>
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<tr>
<td>≥ 14</td>
<td>0</td>
<td>0</td>
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<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>
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<tr>
<td>&lt; 10</td>
<td>38</td>
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<table>
<thead>
<tr>
<th>FIB-4</th>
<th>Restricted</th>
<th>VACS</th>
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<tr>
<td>&lt; 1.45</td>
<td>0</td>
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<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>
</tbody>
</table>

<table>
<thead>
<tr>
<th>eGFR mL/min</th>
<th>Restricted</th>
<th>VACS</th>
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<tbody>
<tr>
<td>≥ 60</td>
<td>0</td>
<td>0</td>
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<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>
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<table>
<thead>
<tr>
<th>Hepatitis C Infection</th>
<th>Restricted</th>
<th>VACS</th>
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<tbody>
<tr>
<td></td>
<td>5</td>
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</table>
Accuracy of VACS Index for All Cause Mortality in NA-ACCORD

Discrimination

<table>
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<tr>
<th>Subgroup</th>
<th>VACS Index</th>
<th>Restricted Index</th>
<th>p**</th>
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<tbody>
<tr>
<td>Overall</td>
<td>0.80</td>
<td>0.75</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male</td>
<td>0.81</td>
<td>0.75</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female</td>
<td>0.81</td>
<td>0.77</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>White</td>
<td>0.79</td>
<td>0.74</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Black</td>
<td>0.81</td>
<td>0.76</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0.90</td>
<td>0.78</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age &lt;50</td>
<td>0.81</td>
<td>0.75</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age &gt;=50</td>
<td>0.74</td>
<td>0.69</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HIV-1 RNA &lt;500</td>
<td>0.77</td>
<td>0.68</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HIV-1 RNA &gt;=500</td>
<td>0.78</td>
<td>0.74</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

1-5 Year Mortality Rates

Justice AC. et al. A Prognostic Index for those Aging with HIV. CROI 2011 Poster # 793
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)
Justice AC et al, “Biomarkers of Inflammation, Coagulation, and Monocyte Activation are Strongly Associated with the VACS Index among Veterans on cART” CID published online 1/15/2012
VACS Index Also Predicts

- Hospitalization and MICU admission
- Fragility Fractures
- Functional Status
- Functional Performance
- Mortality among uninfecte
demographically similar veterans
Responsiveness of VACS Index

- cART initiation
  - Differentiated by level of adherence
- Acute illness preceding MICU admission
- MICU treatment
- cART interruption and reinitation
VACS Index Response to 1st Year of cART (+/- 80% adherence)

Solid lines indicate >80% adherence
Response categories

<table>
<thead>
<tr>
<th>Response</th>
<th>HIV RNA</th>
<th>CD4 increase</th>
<th>N</th>
<th>Deaths</th>
<th>% Died</th>
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<tbody>
<tr>
<td>YY</td>
<td>≤500</td>
<td>≥100</td>
<td>5156</td>
<td>207</td>
<td>4%</td>
</tr>
<tr>
<td>NY</td>
<td>&gt;500</td>
<td>≥100</td>
<td>721</td>
<td>65</td>
<td>9%</td>
</tr>
<tr>
<td>YN</td>
<td>≤500</td>
<td>&lt;100</td>
<td>1940</td>
<td>193</td>
<td>10%</td>
</tr>
<tr>
<td>NN</td>
<td>&gt;500</td>
<td>&lt;100</td>
<td>1778</td>
<td>356</td>
<td>20%</td>
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</table>
Added information with VACS Index
OPTIMA: Break vs No Break

![Graph showing the comparison between Break and No Break on VACS Index Score over time. The graph indicates a decrease in VACS Index Score for both groups, with a sharper decline for the Break group initially. Error bars are shown for each data point.](image-url)
Interactive Web-based Lab: Individualized Risk Portal

### Veterans Aging Cohort Study Risk Index (VACS Index)

**VACS Index Calculator (v1.3)**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age:</td>
<td>years</td>
</tr>
<tr>
<td>Sex:</td>
<td>male, female</td>
</tr>
<tr>
<td>Race:</td>
<td>black, other</td>
</tr>
<tr>
<td>CD4:</td>
<td>≥500, 350 to 499, 200 to 349, 100 to 199, 50 to 99, ≤50 cells/mm³</td>
</tr>
<tr>
<td>HIV-1 RNA:</td>
<td>&lt;500, 500 to 10⁵, &gt;10⁵ copies/ml</td>
</tr>
<tr>
<td>Hemoglobin:</td>
<td>≥14, 12 to 13.9, 10 to 11.9, &lt;10 g/dl</td>
</tr>
<tr>
<td>AST:</td>
<td>U/L</td>
</tr>
<tr>
<td>ALT:</td>
<td>U/L</td>
</tr>
<tr>
<td>Platelet count:</td>
<td>10⁹/L</td>
</tr>
<tr>
<td>FIB-4:</td>
<td>&lt;1.45, 1.45 to 3.25, ≥3.25</td>
</tr>
<tr>
<td>Serum Creatinine:</td>
<td></td>
</tr>
<tr>
<td>eGFR:</td>
<td>≥60, 45 to 59.9, 30 to 44.9, &lt;30 ml/min</td>
</tr>
<tr>
<td>Hepatitis C:</td>
<td>No, Yes</td>
</tr>
</tbody>
</table>

**VACS Index:** 0

**5 Year Mortality Risk:** 1%
Your 5 year mortality risk is 4%. Among 100 HIV infected individuals with this score, we would expect that 96 would be alive at five years and 4 would have died. The figures in grey represent those expected to live 5 years and the figures in black represent those expected to have died.
Example

• 52 yr old (12 pts) HCV + (5 pts) man with suppressed HIV-1 RNA (0 pts), CD4 count 400 (6 pts), intermediate FIB-4 (6 pts), mildly anemic (hemoglobin 13-10 pts), drinks alcohol, BMI 30
  – VACS Index: 39; 5 yr. mortality ~18%
  – If FIB-4 normalizes via decreased alcohol and weight, score 33; mortality ~13%
  – If anemia resolves: score 23; mortality ~8%

Note: These changes are more substantial than those for which most RCTs are powered.
Grant Aims: Use a Website and Phone App to Implement the Index

• Patient Care
  – Identify and prioritize modifiable risk
  – Motivate behavior change
  – Monitor response to behavior change
  – Stage care (initiation, maintenance, end of life)

• Research
  – Risk stratification
  – Intermediate outcome

• Direct to Patient
  – Knowledge is power
Veterans Aging Cohort Study

- **Consortium PI:** AC Justice*
- **Scientific Officer (NIAAA):** K Bryant
- **Affiliated PIs:** N Berliner, S Braithwaite, K Crothers*, DA Fiellin*, M Freiberg*, V LoRe*
- **Participating VA Medical Centers:** Atlanta (D. Rimland*, J Guest), Baltimore (KA Oursler*, R Titanji), Bronx (S Brown, S Garrison), 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, E Hoffman), and Washington DC (C Gibert, R Peck)
- **Core and Workgroup Chairs:** C Brandt, R Dubrow, N Gandhi, J Lim, K McGinnis, C Parikh, J Tate, E Wang, J Womack
- **Staff:** H Bathulapalli, T Bohan, J Ciarleglio, D Cohen, A Consorte, P Cunningham, A Dinh, L Erickson, C Frank, K Gordon, J Huston, F Kidwai-Khan, G Koerbel, F Levin, M Mezes, L Piscitelli, C Rogina, S Shahrir, M Skanderson, A Varcas
- **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 Stern (ART-CC), Brian Agan (DoD), Miguel Hernan (HIV-Causal)
- **Major Funding by:** National Institutes of Health: AHRQ (R01-HS018372), NIAAA (U10-AA13566, U24-AA020794, U01-AA020790), NHLBI (R01-HL095136; R01-HL090342; RCI-HL100347), NIA (R01-AG029154), NIAID (U01-A1069918), NIMH (P30-MH062294), 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