The Veterans Aging Cohort Study

Progress and Future Directions

Amy Justice, PI

October 2011
What is the Veterans Aging Cohort Study (VACS)?
Virtual Cohort (VC)

• SUBJECTS: 41,753 HIV infected; 83,506 uninfected
  – All individuals with HIV diagnoses
  – Age, race/ethnicity, region 2:1 matched controls
  – Last update: September 2010

• SITES: All VA sites

• BASELINE:
  – HIV infected veterans at initiation of HIV care
  – Controls selected and followed in same calendar year
VACS 8

- CURRENT DATA SOURCES (all VC sources plus)
  - All VA Electronic medical records including text fields
  - Sentinel event records (MI) requested outside VA
  - DNA and tissue bank
  - Annual self completed surveys (health behaviors, quality of life, symptoms, outside utilization, etc.)

- SUBJECTS: 3,600 HIV infected; 3,600 uninfected
  - Group matched: age, race/ethnicity, and site

- SITES: Manhattan, Bronx, Washington DC, Baltimore, Pittsburgh, Atlanta, Houston, Los Angeles
Current VACS Cohorts

- **Virtual Cohort (VC)** comprised of national data. Elements include demographics, diagnostic and procedure codes, labs, pharmacy, vital signs ...

- **Virtual Cohort**
  - pos 44000 neg 88000

- **VACS8**
  - pos 3600 neg 3600

- **VC/Queri**
  - pos 31000 neg 70000

- **Exhale**
  - pos 170 neg 150

- **DNA**
  - pos 1600 neg 900

- **Biomarkers**
  - pos 1500 neg 800

- **CVD**
  - pos 150 neg 80

- **VACS8** is the 8 site consented patient study with richer data. Includes surveys, adjudicated outcomes for cancer, mi, liver disease, site downloaded data.

- **Includes**
  - D-dimer, IL 6, sCD14

- **VC limited to patients in 2003 or later. Includes adjudicated MI from IHD Queri**

- **Exhale**
  - pos 170 neg 150

- **DNA**
  - pos 1600 neg 900

- **CVD**
  - pos 150 neg 80

- **4 VACS sites only. Includes pulmonary function tests**

- **3 VACS sites only. Includes GXT, CT and echo data**
Three Guiding Assumptions

• Aging, substance use, comorbidity, and treatment toxicity interact with HIV infection

• Many of these interactions are modifiable

• Strategies of care which individually tailor and prioritize treatment will be most effective
Long Term Goals

1. Understand roles of aging, comorbidity, toxicity, and multisubstance use (alcohol, tobacco, and drugs) in morbidity and mortality among HIV+/-

   and

2. To apply these insights to the development and implementation of interventions to improve outcomes
Veterans Aging Cohort Studies Timeline

Now have support through August 2016 for a total of 20 years of follow up in Virtual Cohort and 16 years for VACS 8
Acknowledgements

- **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 Shahrrir, 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)
- **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
Why is aging with HIV important?
In US: More People Living with HIV Infection Every Year (+38K/yr*)

CDC surveillance data

Each year: 56K new infections - 18K deaths = 38K*
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

Projected

17% 19% 21% 22% 25% 27% 27% 29% 33% 35% 37% 39% 41% 44% 45% 47% 50%

Aging with a Twist

• Common aging issues include
  – “Chronic inflammation”
  – Multimorbidity (medical and psychiatric)
  – Polypharmacy and treatment toxicity

• But (like many veterans in care), HIV+ aging individuals also
  – Continue substance into older ages
  – Among drinkers, 64% smoke or use opioids/cocaine
  – Among drinkers 50+ years, 63% smoke or use opioids/cocaine
Aging with HIV: a Template?

• Complex chronic disease but one in which there is a “dominant” disease (HIV)

• Issues of multimorbidity, polypharmacy, chronic inflammation are accentuated

• Use of alcohol, tobacco, prescription opioids, and illicit drugs into older age increasing

• Much of what we learn may generalize to veterans and others aging without HIV
VA as a Laboratory to Study Aging

- 6 million veterans in care
- National coordination and leadership
- Largely captured, aging population
- National electronic medical record system
- Excellent pharmacy benefits
- *Culture of evidence based medicine*
- Long term time horizon
Limits of Evidence Based Medicine

• Requires evidence that benefit outweighs harm and justifies cost compared to treatment alternatives

• To avoid bias due to indication, RCTs have been the primary evidence for guideline development

• However, RCTs:
  – Often use a single biomarker or short term endpoint that does not capture longer term adverse consequences
  – Exclude patients with competing medical conditions

• 50% of those 65+yrs have 3+ conditions*

*Campbell-Scherer D. Multimorbidity: a challenge for EBM. Evid Based Med 2010: 15:165-166
Multimorbidity HIV+ and Alcohol

• Common co-occurring among HIV+:
  – Medical conditions including hypertension, HCV, diabetes, vascular disease, renal disease, cancer
  – Substance use including alcohol, tobacco, prescription opioids, and cocaine

• Multimorbidity is common among those who drink alcohol and increases with increasing consumption

Justice et al. Medical Disease and Alcohol Use Among Veterans with HIV. Medical Care 2006;44:S52-60
Guideline Overload

- Applied guidelines for 10 common chronic diseases to a closed panel of 2500 primary care patients
  - Age, sex, and disease prevalence matched to US
  - Did not allow for new problems or new patients

- Estimated MD time/workday required assuming
  - All stable (3.5 hours/day)
  - Some active disease (10.6 hours/day)

Multimorbidity is a Game Changer

- Increases treatment benefit if condition interacts with other conditions or behaviors
- Decreased survival time to benefit from screening (e.g. payoff time for screening)
- Increases risk of toxicity
- Introduces competing concerns: how to address active conditions and primary care guidelines and monitor for new problems
Tailor Screening and Treatment to Individual Risk

• Use prediction tools to estimate net benefit
  – Rather than relative benefit
  – Accounting for treatment disutility

• Requires information about risk:
  – Accurate estimation of individual’s risk
  – Likely risk reduction associated with intervention

“Multimorbidity represents the next frontier in the evolution of Evidence Based Medicine”

Campbell-Scherer D. Multimorbidity: a challenge for EBM. Evid Based Med 2010: 15:165-166
Where better to push the frontier of EBM than among aging veterans who drink?
Example: Metabolic Syndrome and CAD

- Individual risk estimated by Framingham index
- Choice of further screening determined by risk (intermediate risk indicates more testing)
- Choice of lipid treatment determined by risk
- Targets for hypertension and lipid treatment determined by presence or absence of multimorbidity (e.g. diabetes)
An Accurate Risk Index is an Essential First Step to Individually Tailoring Care
WHAT IS OUR PROGRESS?
Amy C. Justice, MD, PhD
Consortium PI
Angela Consorte, Director
Administrative Core

Scott Braithwaite, MD, MSc, Director
Operations
Research Core

Cynthia Brandt, MD, MPH, Director
Joseph Erdos, MD, PhD, Co-Director
Medical Informatics Core

Site PIs:
Atlanta: D Rimland, MD
Baltimore: KA Oursler, MD
Bronx: S Brown, MD
Brooklyn/Manhattan: M Simberkoff, MD
Houston: M Rodriguez-Barradas, MD
Los Angeles: M Goetz, MD
Pittsburgh: A Butt, MD
Washington, DC: C Gibert, MD

Proposed New Site
Dallas: R. Bedimo, MD

David Fiellin, MD, Director
Alcohol and Behavioral
Intervention Core

Janet Tate, ScD, MPH, Director
Biostatistics Core

Cores (supported by other grants): Directors
Cancer Disease: R Dubrow, MD, PhD
Cardiovascular Disease: M Freiberg, MD, MSc
Liver Disease: V LoRe, MD & J Lim, MD
Pulmonary Disease: K Crothers, MD

Workgroups: Directors
ART: N Gandhi, MD, & J Tate, ScD, MPH
Endocrine and Bone Disease: J Womack, APRN, PhD
Health Services Research: Emily Wang & K McGinnis, MS
Kidney Disease: C Parikh, MD
Risk Index: A Justice, MD, PhD & J Tate, ScD, MPH
Translational Research: C Rinaldo, MD & M Freiberg, MD, MSc
Uniform Services: D Rimland, MD

Steering Committee:
Kendall Bryant, PhD, Director
Nancy Day, PhD
David Leaf, MD
Stephen Maisto, PhD
Patrick O'Connor, MD, PhD
David Rimland, MD
Charles Rinaldo, MD
Jeffrey Samet, MD, PhD
Increasing Productivity and Impact

Publications by Year

Citations by Year
2011 Highlights

- Presentation on Aging and HIV at White House Meeting
- VACS Index presented to New York State Department of Public Health for possible inclusion in clinical guidelines
- VACS Index presented at VA National Technical Advisory Group for possible inclusion in decision support
- Chaired, Intervention Subgroup, OAR/NIH Workgroup on Aging and HIV
- Member, Consensus Panel on HIV and Aging, Cosponsored by American Geriatrics Society, American Academy of HIV Medicine, and AIDS Community Research Initiative of America
- Invited as a featured speaker for CROI 2012 Symposium, “The Long and Winding Road of HIV Complications”
Major Papers Under Review

- **VACS Data Only:** HIV is Associated with Clinically Confirmed Acute Myocardial Infarctions. **Revisions requested**, *NEJM*

- **VACS Data Only:** Does an Index Composed of Clinical Data Reflect Effects of Inflammation, Coagulation, and Monocyte Activation on Mortality? **Accepted with revision**, *CID*

- **ART-CC Collaborative Analysis:** An Internationally Validated Risk Index for Mortality After One Year of Antiretroviral Therapy, in HIV-Infected Individuals. **Under review**, *JAMA*

- **NA-ACCORD Collaborative Analysis:** VACS Index Accurately Predicts Mortality among 15,901 HIV Infected Individuals in North America on Antiretroviral Therapy. **Under review**, *NEJM*
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<th>Mentee</th>
<th>Source</th>
<th>VA?</th>
<th>Progress</th>
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<tr>
<td>Courtney Watson</td>
<td>NHLBI Diversity</td>
<td>NA</td>
<td>Oral presentation at Diversity Meeting</td>
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<td>Kathleen Akgun</td>
<td>Pulmonary F.</td>
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<td>Jen Edelman</td>
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<td>William Becker</td>
<td>VA CDA HSR&amp;D</td>
<td>Yes</td>
<td>Excellent score, awaiting decision</td>
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<tr>
<td>Keri Althoff</td>
<td>NIAID CDA</td>
<td></td>
<td>Just awarded</td>
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<tr>
<td>Julie Womack</td>
<td>NINR CDA</td>
<td>Yes</td>
<td>Yale Faculty at VA</td>
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<td>Kris Ann Oursler</td>
<td>NIA CDA</td>
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<td>In process</td>
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<td>Adeel Butt</td>
<td>NIDA CDA</td>
<td>Yes</td>
<td>Submitted RO1 pending</td>
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<td>Vincent LoRe</td>
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<td>Matthew Freiberg</td>
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<td>Kristina Crothers</td>
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<td>Scott Braithwaite</td>
<td>NIAAA/RWJ CDA</td>
<td>Yes</td>
<td>NIAAA grants (R01, U01)</td>
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<tr>
<td>Kristin Mattocks</td>
<td>AMFAR Fellowship</td>
<td>No</td>
<td>New ACOS Research</td>
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<td>Todd Kawecki</td>
<td>VA Informatics F.</td>
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<td>VA Informatics Leadership</td>
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<tr>
<td>Shayan Fatima</td>
<td>VA CDA HSR&amp;D</td>
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<td>VHA leadership: New FDA leadership</td>
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## Active Core Support Grants

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<th>Grant</th>
<th>Period</th>
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<td>NIAAA U10, +3 U01s: COMpAAAS</td>
<td>9/11-8/16</td>
<td>11,500</td>
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<tr>
<td>NIAAA U10: Alcohol in HIV+/- Veterans (Justice)</td>
<td>9/06-8/12</td>
<td>13,273</td>
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<td>NIA/NHLBI RO1: Unexplained Anemia (Berliner)</td>
<td>Renewal pending</td>
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<td>VA Fellowship in Medical Informatics (Brandt)</td>
<td>7/06--</td>
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<td>NHLBI R01: HIV-Associated Lung Disease (Crothers)</td>
<td>10/07-9/12</td>
<td>3,965</td>
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<td>VA Merit: Returning OIF/OEF Veterans Cohort (Brandt)</td>
<td>1/08-12/11</td>
<td>900</td>
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<td>NIAAA R01: Computer Simulation Alcohol &amp; HIV Sub-Saharan Africa (Braithwaite)</td>
<td>1/08-12/11</td>
<td>2,210</td>
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<td>VA HSR&amp;D REAP: Pain Research, Informatics, Medical Comorbidities (Kerns)</td>
<td>10/08--</td>
<td>306</td>
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<tr>
<td>NHLBI R01: HIV(HCV) and CVD (Freiberg/Justice)</td>
<td>9/08-8/13</td>
<td>4,558</td>
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COMpAAAS: Consortium to improve Outcomes in hiv/AIDS, Alcohol, Aging, and multi-Substance Use

U24 Coordinating Center PI: Amy Justice, MD, PhD

U01 Observation PI: Amy Justice, MD, PhD
U01 Intervention PI: David Fiellin, MD
U01 OR Model PI: Scott Braithwaite, MD
COMpAAAS Mission

To build and disseminate evidence needed to:

• Optimize health care for HIV+ harmed by alcohol, multisubstance use, HCV infection, and depression

• Through coordinated, integrated, and validated observational, operations research, and intervention studies
Veterans Aging Cohort Study Risk Index (VACS Index)

• Composed of age and laboratory tests currently recommended for clinical management
  – HIV Biomarkers: HIV-1 RNA and CD4 Count
  – “non HIV Biomarkers”: Hemoglobin, hepatitis C, composite markers for liver and renal injury

• Developed in US veterans, validated in Europe and North America
Composite Biomarkers

\[ FIB\ 4 = \frac{\text{AGE} \times \text{AST}}{\text{PLT} \times \sqrt{\text{ALT}}} \]

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

\[ \text{FEM\_VAL} = \begin{cases} 0.742 & \text{if female} \\ 1 & \text{if male} \end{cases} \]

\[ \text{BLACK\_VAL} = \begin{cases} 1.21 & \text{if black} \\ 1 & \text{otherwise} \end{cases} \]
## VACS Index Thresholds and Weights

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<th></th>
<th>Index Score</th>
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<tr>
<td></td>
<td>Restricted</td>
<td>VACS</td>
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<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;50</td>
<td>0</td>
<td>0</td>
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<tr>
<td>50 to 64</td>
<td>23</td>
<td>12</td>
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<tr>
<td>≥ 65</td>
<td>44</td>
<td>27</td>
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<tr>
<td><strong>CD4 cells/mm³</strong></td>
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<td>≥ 500</td>
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<td>0</td>
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<td>350 to 499</td>
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<td>&lt; 50</td>
<td>46</td>
<td>29</td>
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<tr>
<td><strong>HIV-1 RNA copies/ml</strong></td>
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<tr>
<td>500 to 1x10⁵</td>
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<td>7</td>
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<tr>
<td>≥ 1x10⁵</td>
<td>25</td>
<td>14</td>
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<td><strong>Hemoglobin g/dL</strong></td>
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<td>12 to 13.9</td>
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<td>1.45 to 3.25</td>
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<tr>
<td>&gt; 3.25</td>
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<td><strong>eGFR mL/min</strong></td>
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<td>≥ 60</td>
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<td>45 to 59.9</td>
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<td>30 to 44.9</td>
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<tr>
<td>&lt; 30</td>
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**Biomarkers of General Organ System Injury**

- Hepatitis C Infection: 5

*Tate J. et al. Under Review JAMA*
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)
Interactive Web-based Lab: Individualized Risk Portal
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.
How Much More Efficiency from Tailoring Care?

• Tailored vs. JNC 7 guidelines for CAD
  – Treat 24% fewer people to prevent same number of MIs and strokes
  – At 67% of cost

• Aspirin reduces MI/stroke risk ~14-18% but increases risk of ICH and GI bleed
  – Only 28% clearly benefit when disutility considered

Operations Research Model Aims

Aim 1. Synthesize data from VACS and results from literature to compare effectiveness of alternative interventions

Aim 2. Develop OR model to compare effectiveness of alternative intervention sets

Aim 3. Develop web-based laboratory to facilitate design of interventions
UNIVERSE OF POSSIBLE INTERVENTIONS

Alcohol
A1: BMI
A2: CBI
A3: pharm

Drug
D1: BMI
D2: CBI
D3: pharm

Compliance with ARV
C1: Counsel
C2: DOT

Tobacco
D1: BMI
D2: NRT
D3: pharm

Depression
M1: CBI
M2: pharm

INTERVENTIONS APPLICABLE TO PARTICULAR PATIENT

Alcohol
A1: BMI
A2: CBI
A3: pharm

Compliance with ARV
C1: Counsel
C2: DOT

Depression
M1: CBI
M2: pharm

SINGLE INTERVENTION
STANDARD
A1

SINGLE INTERVENTION
TAILORED
M2

STEPPED INTERVENTION
STANDARD
A1 → C2 → M2

STEPPED INTERVENTION
TAILORED
M2 → C2 → A2

SIMULTANEOUS INTERVENTION
STANDARD
A1 + C2 + M2

SIMULTANEOUS INTERVENTION
TAILORED
M2 + C2 + A2
OR Model Output: Tailored to Stakeholder

Now sort by feasibility and require LOE ≥B

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<tr>
<th>RANK</th>
<th>Intervention</th>
<th># New HIV cases prevented</th>
<th>Cost</th>
<th>Feasibility</th>
<th>Level of Evidence</th>
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<td>1</td>
<td>Alcohol: brief motivational</td>
<td>0.43</td>
<td>$100</td>
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<td>B</td>
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<td>2</td>
<td>ARV initiation</td>
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<td>$12000</td>
<td>A</td>
<td>A</td>
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<tr>
<td>3</td>
<td>Behavioral: promote condom use</td>
<td>0.18</td>
<td>$300</td>
<td>A</td>
<td>B</td>
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<tr>
<td>4</td>
<td>Screen drug abuse &amp; treat if +</td>
<td>0.07</td>
<td>$800</td>
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<td>B</td>
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<tr>
<td>5</td>
<td>Circumcision</td>
<td>0.50</td>
<td>$1300</td>
<td>C</td>
<td>A</td>
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<tr>
<td>6</td>
<td>Behavioral: reduce # sexual partners</td>
<td>0.24</td>
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COMpAAAS Impact

- **Comprehensive Observational Data**
- **Finely Grained Risk Assessment and Quantification of Modifiable Risk**
- **Use OR Modeling to Inform a Strategy of Care, Tailored to Each Patient Profile and Implemented Via Decision Support**
- **RCTs of the Strategy of Care Using Change in Risk as Outcome**
- **Link to Evidence Based Treatments through Operations Modeling and Targeted RCTs**
1st COMpAAAS RCT (funded)

- 3 linked clinical trials
- 642 subjects
  - At-risk drinking
  - Alcohol Abuse or Dependence
  - Moderate Alcohol and Liver Disease
- Randomized
- 24 wks of treatment with follow-up at 12 mns
- Integrated Stepped Care vs. Treatment as Usual
Treatment Settings

• HIV Clinics in 4 VA Medical Centers (VACS sites)
  – Manhattan
  – Atlanta
  – Houston
  – Washington DC
Integrated Stepped Care for Unhealthy Alcohol Use in HIV

- At-risk drinking
  - Randomization
  - Integrated Step Care
  - Brief Negotiated Interview
    - No Success
    - Success
  - Psychologist MET counseling
    - Success
  - Monitor / Maintain

- Moderate Alcohol+Liver Disease
  - Randomization
  - Treatment as Usual
  - Health Handout
  - Addiction Physician Management (APM) with Medication Encouraged
    - No Success
    - Success
    - Monitor / Maintain

- Alcohol Abuse / Dependent
  - Randomization
  - Integrated Step Care
    - No Success
  - Psychologist MET counseling
    - Success
  - Detoxification+Aftercare
    - Monitor / Maintain
  - Treatment as Usual
  - Referral to Specialty
Outcomes

• The *primary outcome* is alcohol consumption
  – At-risk drinking and Alcohol Abuse and dependence
    • Drinks per week over the last 28 days at 6 months
  – Moderate alcohol + Liver disease
    • Abstinence over the last 28 days at 6 months

  – Also, adequate power in all 3 groups to detect a clinically meaningful difference in the percent of subjects with no heavy drinking days (PSNHDD)

• **Secondary study outcome:**
  – 1) Change in VACS index
<table>
<thead>
<tr>
<th>Condition</th>
<th>HIV or HCV?</th>
<th>Substance Use?</th>
<th>Toxicity?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial Infarction</td>
<td>Both</td>
<td>Tobacco, Cocaine</td>
<td>Possibly PIs</td>
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<tr>
<td>Diabetes</td>
<td>HCV</td>
<td>Alcohol</td>
<td>PIs</td>
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<tr>
<td>Stroke</td>
<td>Both</td>
<td>Cocaine</td>
<td>Anticoagulants</td>
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<tr>
<td>Fragility Fractures</td>
<td>HIV</td>
<td>Alcohol, Tobacco</td>
<td>Steroids, PPIs</td>
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<td>Liver Cirrhosis</td>
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<td>Alcohol</td>
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<td>Liver-Alcohol</td>
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<td></td>
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<td>Non-Infectious Cancers</td>
<td>Lung-HIV</td>
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<td>Pneumonia</td>
<td>HIV</td>
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<td>Unknown</td>
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<tr>
<td>Obstructive Lung Disease</td>
<td>HIV</td>
<td>Tobacco</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
Future Possible RCTs

• Randomize: targeted behavioral interventions based on individual risk vs. uniform intervention
  – Outcome: behavior change

• Randomize: at point of ART initiation VACS Index guided management vs. usual care
  – Outcomes: hospital admission, change in VACS score, adherence to ART, ART switches
Near Future Work in HIV

- Informatics: Develop information tool that calculates index, counsels on risk, identifies modifiable risk, and suggests patient action
- Observational Analyses: estimate likely effect size for potential interventions: e.g., alcohol cessation, HCV treatment, adherence, etc.
- RCT: strategy trial among those with abnormal FIB 4 who drink alcohol
What Does VACS Have Beyond What is in VINCI and/or CDW

• Ability to validate data using chart review and direct contact with sites
  – Clinical cirrhosis, cancer, MI nearly completed

• Validated clinical endpoints from MI, cancer registry, and Medicare (dialysis)

• Permission to contact patients (follow up, studies)

• Surveys, samples, interviews, non VA data

• Patient consent
What Validation Studies?

- Pharmacy data against chart review and patient report (cART initiation, adherence, changes, proportion getting rx. outside VA)
- Diagnostic codes against chart review (groupings for particular condition, incidence, prevalence, sensitivity and specificity)
- Smoking and alcohol against patient report
- Pain score against patient report
Separate DUA

- Clinical Case Registry (HIV/HCV)
- Cancer Case Registry
- CAD QUERI Database
- Pharmacy Benefits Management
- Medicare/Medicaid
- National Death Index
- Computer Data Warehouse
- VA Informatics and Computing Infrastructure (VINCI)
We Could Use Some Help

• Data Use Agreements
  – Every group has different criteria
  – Not well suited to ongoing cohort study
  – DUAs need to be centralized (VINCI?)
  – De identified data should be treated differently

• Privacy issues
  – Poor coordination between local and national
  – Inconsistent interpretation of rules (e.g. COD)