Update on the VACS HIV CVD Study

Matthew S. Freiberg, MD, MSc
University of Pittsburgh
October 13th, 2011
Specific Aims

- To evaluate whether HIV is an independent risk factor for CVD and whether HIV VL, CD4 count, ART, and substance increase CVD risk (Aim 1)
- To Evaluate the cross-sectional association of HIV infection and CART (Aim 2) as well as HCV and substance use (Aim 3) on mechanisms of CVD among HIV+ and uninfected Veterans
Study updates

- **Aim 1 (VACS and VACS-VC cohorts)**
  - Completed survey of VACS cohort for CVD events
  - Acquired and analyzed AMI results from Virtual Cohort—soon to acquire fatal AMI data from the NDI
  - Completing formal CHD adjudication of all VACS cases from 1990s-2006
    - ~2500 events identified in this cohort
Study updates

- Aims 2 and 3 (Mechanistic Cohort)
  - Enrolled 239 participants (~2:1 HIV+:HIV-) for mechanistic studies
  - Completed 207 GXT; 202 Echos; 162 CT scans; 155 blood specimens
  - Analyzed 2368 blood specimens (65% HIV +) for biomarkers (IL-6, D-dimer, sCD14)
K23 and R01 supplemental NIH Funding

- K23AA015914
  - 06S1 Biomarker study $53,996

- 3RO1HL095136
  - 02S1 Minority Scholar $60,400
  - 03S1 CHD adjudication $301,416
  - 03S2 Minority Scholar $61,172
  - 04S1 Fatal AMI data $318,659
Conceptual Model: The role of alcohol, hepatitis C, and HIV and the risk of AMI

Presented at the International Society for Biomedical Research on Alcoholism, Paris, France, 2010 as part of a symposium focusing on alcohol consumption, HIV infection, and cardiovascular disease.
Results

- HIV is independent risk factor for AMI and the magnitude of the risk is similar to that of smoking and diabetes. CROI 2011. *Revise and resubmit to NEJM 2011*

- HIV is associated with an increased risk of heart failure even in the absence of CHD and alcohol abuse or dependence. *Archives of internal medicine 2011*

- HIV and HCV co-infected Veterans have an increased risk of CHD compared to HIV mono-infected or HIV and HCV uninfected Veterans even after adjusting for competing risk of death. *Circulation: Cardiovascular Quality and Outcomes. 2011*
Results

- HIV is associated with an increased risk of ischemic stroke. (Presented at *CROI 2010, to be submitted to Circulation*)

- HIV status and burden of comorbid disease are associated with biomarkers of inflammation, altered coagulation, and microbial translocation. (*submitted to CROI 2012*)

- Elevated systolic blood pressure is associated with substantially greater relative risk of AMI among HIV+ compared to uninfected Veterans. This was true even at prehypertensive levels. (*submitted to CROI 2012*)
New investigators

- **Courtney Watson, MPH**
  - Was the recipient of two NHLBI minority scholars supplements
  - Was accepted to PhD program in Epidemiology at University of South Carolina
  - Abstract entitled, “HIV, race, and the risk of HF accepted as oral presentation at AHA meeting 2012

- **Kaku Armah, BA**
  - Currently PhD graduate student at University of Pittsburgh Graduate School of Public Health
  - His studies are supported by an NHLBI supplement award
  - Research focus on HIV and biomarkers and CVD outcomes
  - Submitted two abstracts to CROI 2012
New Investigators

- **Jason Sico MD**
  - Assistant Professor of Neurology at Yale University
  - Interests include HIV and Stroke
  - Recipient of CROI New investigator award
  - Will be preparing a CDA focusing on HIV and stroke

- **Donna Doebler, DrPH, MS, MPH**
  - Kellogg Health Post Doctoral Fellow
  - Interests include propensity score and structural equation modeling to refine our understanding of the association between race/ethnicity, HIV, and CVD outcomes
  - Her work recently accepted to the International Conference on Health Policy Statistics
New Investigators

- **Kathryn Britton, MD, MPH**
  - KL2 scholar and cardiologist at Harvard’s Brigham and Women’s Hospital
  - Interest is in HIV and peripheral vascular disease
  - Submitting proposal to Creative and Novel Ideas in HIV Research (CNIHR) as part of the International AIDS society and NIH CFAR using the VACS HIV CVD mechanistic cohort

- **Sunil Agarwal, MD, PhD**
  - Second year internal medicine resident on fast track for GIM fellowship at the University of Pittsburgh
  - Completed his PhD in CVD epidemiology with the Atherosclerosis Risk in Communities Cohort at UNC
  - His interests are in HIV and Atrial fibrillation
  - Will prepare CDA focusing on HIV and atrial fibrillation
Future Grants

- The risk of and survival with heart failure among Veterans with and without HIV
  - PIs Adeel Butt and Matt Freiberg
  - R01 NHLBI to be reviewed 11/2011

- An RCT focusing on the impact of zinc on biomarkers of inflammation and health outcome among participants in the Russia ARCH cohort
  - PIs Matt Freiberg and Jeffrey Samet
  - R01 NIAAA to be submitted 1/2012

- The association between HIV infection, microvascular disease and endothelial dysfunction in the HIV CVD mechanistic study cohort
  - PI Kathryn Britton
  - Creative and Novel Ideas in HIV Research Grant (NIH, CFAR) to be submitted 10/2011
Future Grants

- Examining CVD repair mechanisms and the risk of CVD among HIV infected and uninfected Veterans
  - PIs Mathius Klauss (IU) and Matt Freiberg
  - R01 NHLBI or MERIT review

- Using competing risk modeling to assess CVD risk among HIV infected and uninfected Veterans
  - PI Joyce Chang
  - R01 NHLBI

- Career Development Awards
  - HIV and Stroke—Jason Sico
  - HIV and Atrial Fibrillation—Sunil Agarwal
  - Propensity scores and structural equation modeling to assess race, HIV, and CVD outcomes—Donna Doebler
Future plans

- Complete all CHD adjudication in the VACS through present
- Obtain updated AMI data for VC cohort from QUERI and fatal AMI data from NDI
- Complete analyses examining HIV, alcohol consumption, biomarkers, and CVD outcomes
- **New investigations including**
  - Assessing the Framingham risk score and AMI risk among HIV infected and uninfected Veterans
  - Assessing the association between HIV status and CAC, myocardial function, silent ischemia, and novel biomarkers of inflammation and altered coagulation
  - Assessing the role of new potential risk factors (liver disease, depression, psoriasis)
  - HIV and atrial fibrillation
  - HIV and peripheral vascular disease
Acknowledgements

Project Officers:
Kendal Bryant
Cheryl McDonald

Co-PI Investigator
Amy Justice

Co-Investigators
John Gottdiener
Dan Edmundowicz
Adeel Butt
Sheldon Brown
Joyce Chang
Matthew Budoff
Matthew Goetz
Cynthia Gilbert
David Leaf
Maria Rodriguez-Barrada
KrisAnn Oursler

Programmers and Web construction
Stephen Gottlieb
Lewis Kuller
Russ Tracy

Coordinators
Carol Rogina
Glory Koerbel
Joan McMorris-Marrow
Wendy Lanner Rossen
Elizabeth Sorek
Walter Williams

Adjudication Team
Travis Rabbit
Kaku Armah
Joseph Lawrence
Bridget DeGraaf

All coordinators at all 8 VACS sites

Biostatisticians
Kathy McGinnis
Donna Doebler

Programmers and Web construction
Melissa Skanderson
Farah Kidwai-Khan
Patricia Cunningham
Acknowledgements

- **PI and Co-PI**: AC Justice, DA Fiellin

- **Scientific Officer (NIAAA)**: K Bryant

- **Participating VA Medical Centers**: Atlanta (D. Rimland), 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 Faculty**: K Mattocks (Deputy Director), K Akgun, S Braithwaite, C Brandt, K Bryant, R Cook, K Crothers, J Chang, S Crystal, N Day, R Dubrow, M Duggal, J Erdos, M Freiberg, M Gaziano, M Gerschenson, A Gordon, J Goulet, N Kim, M Kozal, K Kraemer, V LoRe, S Maisto, P Miller, P O’Connor, C Parikh, C Rinaldo, J Samet

- **Staff**: H Bathulapalli, T Bohan, D Cohen, A Consorte, P Cunningham, A Dinh, C Frank, K Gordon, J Huston, F Kidwai, F Levin, K McGinnis, C Rogina, J Rogers, L Sacchetti, M Skanderson, J Tate, E Williams

- **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

- **Major Funding by**: National Institutes of Health: NIAAA (U10-AA13566), NIA (R01-AG029154), NHLBI (R01-HL095136; R01-HL090342; RCI-HL100347), NIAID (U01-A1069918), NIMH (P30-MH062294), and the Veterans Health Administration Office of Research and Development (VA REA 08-266) and Office of Academic Affiliations (Medical Informatics Fellowship).