MACS & WIHS Combined Cohort Study (MACS/WIHS-CCS)

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NIH Office of AIDS Research Advisory Council
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Navigating the Present and Charting Our Future...

- **HIV: An Evolving Epidemic**
  - Epidemiology of survival
  - Burden of Heart, Lung, Blood and Sleep Comorbidities

- **Seizing Opportunities: NHLBI Priorities in HIV Research**
  - Mitigating Comorbidities
  - Accelerating Cures

- **Stewardship of MACS & WIHS**
Among HIV-infected individuals, median survival time has increased from 11.8 years in the late 1990s to 22.5 years in 2006-2014.
HIV-related Comorbidities
An Impending Public Health Epidemic

By 2030

- 84% of HIV population will have ≥1 co-morbidity
- 28% will have ≥3 co-morbidities
- 78% of pts. will be diagnosed with CVD
- 30% higher than general population

Strategic Priority Setting: Research to Address Public Health Needs

NHLBI AIDS Teamwork

NHLBI AIDS Working Group (2012)

Role of Dysbiosis in Cardiovascular, Pulmonary and Hematological Complications

Integrated Approaches to HIV-Related Heart, Lung, Blood, and Sleep Comorbidities

Implementation Research to Develop interventions

Focused areas of HIV-related HLBS research

Basic and Clinical Research


Organizing for effectiveness

Gathering the intelligence of our community to identify priorities

Scientific Opportunities

Reviewing progress and identifying gaps

Seizing new opportunities
NHLBI’s Strategic Vision Aligns with NIH Priorities for HIV Related Research

Goal 1 – Expand knowledge of the mechanisms governing normal function

Goal 2 – Extend knowledge of pathobiology to advance disease prevention and management

Goal 3 – Facilitate innovation and accelerate research translation

Goal 4 – Develop a diverse workforce with the resources to implement evidence into practice
Charting a Future for HIV-Related HLBS Research

- HIV increasingly a chronic disease.
- People living with HIV at high risk for HLBS and other comorbidities.
  - Dysbiosis
  - Chronic immune activation and inflammation.
  - May be a model for accelerated aging.
- Continued support of research on health of people living with HIV, including stewardship of MACS & WIHS.
- Priorities consistent with NHLBI Strategic Vision.
Multi-center AIDS Cohort Study (MACS)
Women’s Interagency HIV Study (WIHS)

MACS
University of California at Los Angeles
Northwestern University
University of Pittsburgh
Johns Hopkins University

WIHS
University of California at San Francisco
University of North Carolina at Chapel Hill
Hektoen Institute for Medical Research
University of Alabama at Birmingham
University of Mississippi MC Jackson
Montefiore Medical Center
SUNY Downstate Medical Center
Georgetown University
University of Miami
Emory University

Data Analysis & Coordination Centers
Johns Hopkins University
**Multi-center AIDS Cohort Study (MACS)**

Established 1984
2165 Active men
HIV-status:
46% negative
54% positive
24% Black
61% White
14% Hispanic
Median Age:
58 years
Source: CAMACS
June 2017

**Women’s Interagency HIV Study (WIHS)**

Established 1994
2339 Active women
HIV-status:
30% negative
69% positive
75% Black
14% White
14% Hispanic
Median Age:
50 years
Source: WDMACS
June 2017

### MACS Sites

4504 Active Participants
1713 HIV-negative
2791 HIV-positive
2482 prevalent infections
309 serologic converters

### WIHS Sites

75% Black
14% White

### Coordination Center

14% Hispanic
Median Age:
50 years

* Subcontract sites
MACS/WIHS-CCS: Research Focus Transition

- NIAID -- NIH’s steward of MACS and WIHS since inception (1984 & 1994)

- Office of AIDS Research MACS/WIHS-CCS focus moving toward HIV-related comorbidities

- NHLBI -- MACS/WIHS-CCS steward in FY 2019

- Collaboration of OAR, NHLBI, 11 Institutes
National Heart, Lung, and Blood Institute (NHLBI)  
National Cancer Institute (NCI)  
National Human Genome Research Institute (NHGRI)  
National Institute on Aging (NIA)  
National Institute of Allergy and Infectious Diseases (NIAID)  
*Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD)  
National Institute of Dental and Craniofacial Research (NIDCR)  
National Institute on Drug Abuse (NIDA)  
National Institute of Mental Health (NIMH)  
National Institute on Minority Health and Health Disparities (NIMHD)  
National Institute of Neurological Disorders and Stroke (NINDS)  
National Institute of Nursing Research (NINR)
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Leveraging Extant Cohorts Previously Focused on HIV Pathogenesis for Comorbidities Research

### Cardiac Pathobiology
- Assessment of clinical and subclinical CVD
- Echocardiogram
- Cardiac MRI

### Dysrhythmias
- Extent and basis of heightened risk, especially women
- Assessment of differences and progression in ECG

### Biomarkers
- Changes assoc with structural abnormalities on echo and HF symptoms
- Traditional cardiac markers
- Novel markers of stretch/strain, myocardial necrosis/injury, and fibrosis

### Venous Thromboembolism
- Assoc of platelet activation, endothelial injury and hypercoagulability with VTE and CV outcomes
Leveraging Extant Cohorts Previously Focused on HIV Pathogenesis for Comorbidities Research

**Pulmonary Disease**
- Assessment of pulmonary health, lung function abnormalities, and lung disease burden
- CT scan to assess lung fibrosis
- PFTs
- Respiratory questionnaire

**Sleep Disorders**
- Influence of sleep apnea and quality on metabolic, subclinical CV, autonomic, and neurobehavioral function
- Sleep apnea, quality, and duration assessments

**Management of Comorbidities**
- Prevention of CVD and management of COPD, hematological complications, and sleep disturbances
- Implementation research related to guideline-driven strategies
MACS/WIHS-CCS: Program Interests

- Retention, clinical event adjudication
- Potential recruitment criteria:
  - Goal: 2500 new ppts
  - Site size, study efficiency
  - Target underrepresented HIV affected groups
    - MSMs: Black, Hispanic, southern US residents
    - Recent infection with early ART initiation
    - Adults 18 to 50 years of age
MACS/WIHS-CCS: Two FOAs

1. Data Analysis and Coordination Center*

2. Clinical Research Sites**

3. Related Memoranda:
   - Request for 7-Year Project
   - Request for Limited Competition
   - Request for Cooperative Agreement
   - MOU with OAR and funding Institutes

* RFA-HL-19-007, Limited Competition: Data Analysis & Coordination Center for the MACS/WIHS Combined Cohort Study, MACS/WIHS-CCS (U01)*

** RFA-HL-19-008, Limited Competition: Clinical Research Sites for the MACS/WIHS Combined Cohort Study, MACS/WIHS-CCS (U01)
**MACS/ WIHS-CCS: FOA Milestones**

**MACS/ WIHS-CCS Notice of ITP in June 2017**

**Other Major Milestones:**

- Trans-NIH Teamwork: Past 2 Years
- NHLBI Review: Now
- MOU between ICs: Now
- OER Review: November 2017
- FOA Publication: Autumn 2017
- Peer Review: Spring 2018
- NHLBI Council: Autumn 2018
- Awards: Early FY 2019
Other Initiatives to Leverage MACS/WIHS

Some participating ICs have FOAs supporting ancillary studies. MACS/WIHS Team considering whether to develop specific FOA.

- Participant burden
- Current investment
- Incremental ROI

Interested in your thoughts.
Acknowledgment

MACS/WIHS Transition an excellent example of NIH team work:

- OAR: Gina Brown, Susan Plaeger, Donna Adderly
- NIAID: Carolyn Williams, Robin Huebner, Gerald Sharp, Joana D. Roe
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  - NIA: Basil Eldadah
  - NICHD: Denise Russo
  - NIDCR: Gallya Gannot
  - NIDA: Richard Jenkins, Katherine Davenny
  - NIMH: Pim Brouwers, Gregory Greenwood
  - NIMHD: Rick Berzon
  - NINDS: May Wong
  - NINR: Rebecca Henry

Scientific, Review, Financial and Other Officials from each ICO