# Intersection of HIV and CVD
# Improving Outcomes
## HIV-Related CVD Research at NHLBI

**Patrice Desvigne-Nickens, MD**
**National Heart, Lung, and Blood Institute**

**Benefits of HIV Research**

December 1, 2017


# 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


- **AIDS research funding creates opportunity**

# NHLBI Portfolio – HIV Comorbidities

## *Key Programs & Publications*

**REPRIEVE**

Randomized Trial to Prevent Vascular Events in HIV

**JAMA Internal Medicine** HIV Infection and the Risk of Acute Myocardial Infarction

*Frieberg MS, 2013*

**JACC Heart Failure** Novel Biomarkers of Cardiac Stress, Cardiovascular Dysfunction, and Outcomes in HIV-Infected Individuals

*Hsue PY, 2013*

**JAMA** The Journal of the American Medical Association — Arterial Inflammation in Patients With HIV

*Grinspoon S, 2012*

**Annals of Internal Medicine**

Associations Between HIV Infection and Subclinical Coronary Atherosclerosis

*Post WS, 2014*

**inhald** Investigating HIV-Associated Lung Disease

**AIDS** Relationships of pulmonary function, inflammation, and T-cell activation and senescence in an HIV-infected cohort

*Morris A, 2014*

**American Journal of Respiratory and Critical Care Medicine** — Activation-induced Cell Death Drives Profound Lung CD4+ T-Cell Depletion in HIV-associated Chronic Obstructive Pulmonary Disease

*Kirk GS, 2014*

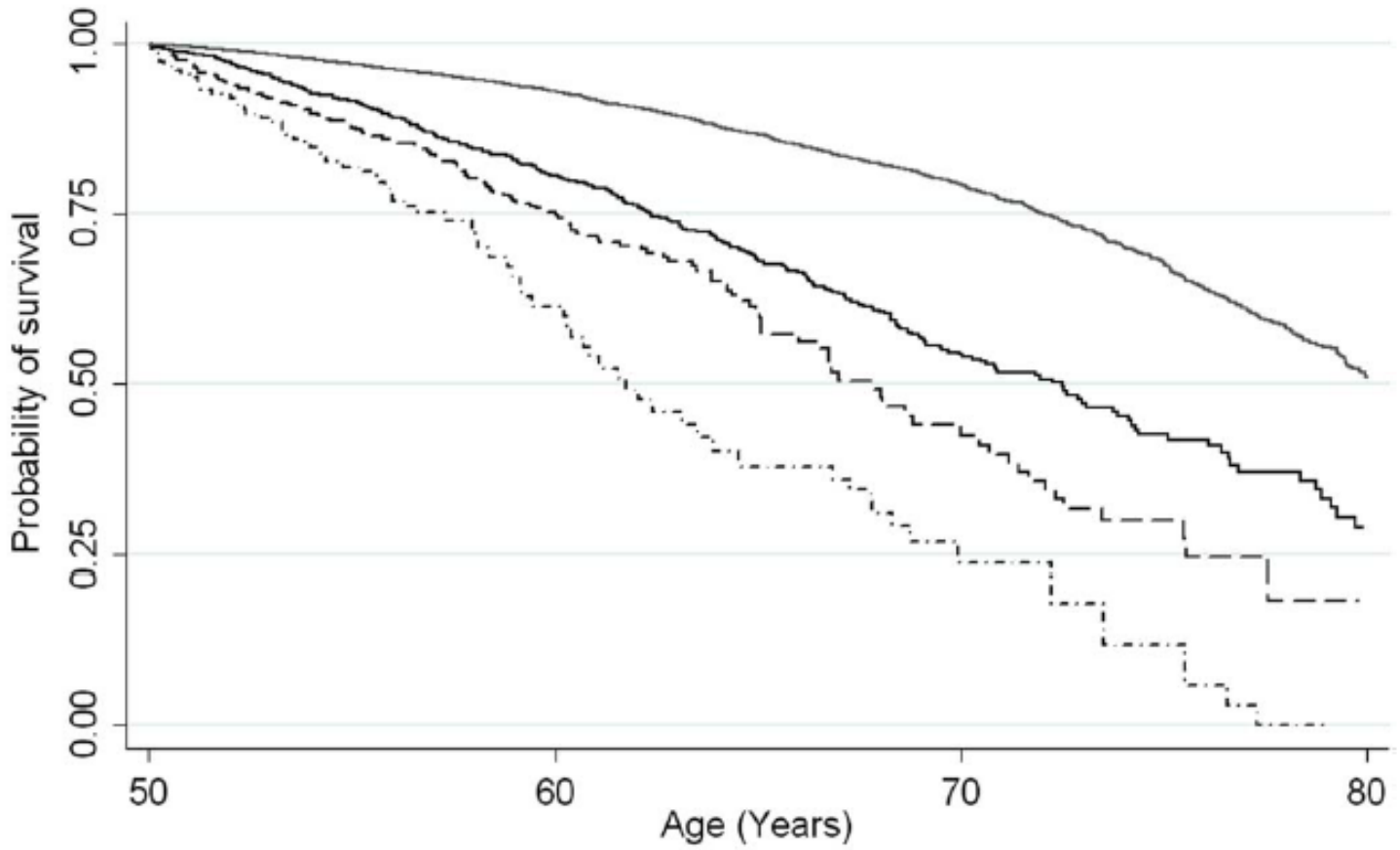
**Basic Research in the Pathogenesis of HIV-Related Heart, Lung, and Blood (HLB) Diseases in Adults and Children**

ART Blocks Endogenous RT Activity in Platelets: A Previously-Unrecognized Mechanism of Cellular Control → Thrombosis in HIV Patients

***R01 HL126547; PI: Weyrich PS.***

# An Evolving Epidemic: Survival From 50 Years or Older

Among HIV-infected individuals, median survival time from age 50 years has increased from 11.8 years in the late 1990s to 22.5 years in 2006-2014.




Legarth et al., J Acquir Immune Defic Syndr 2016; 71:213–218

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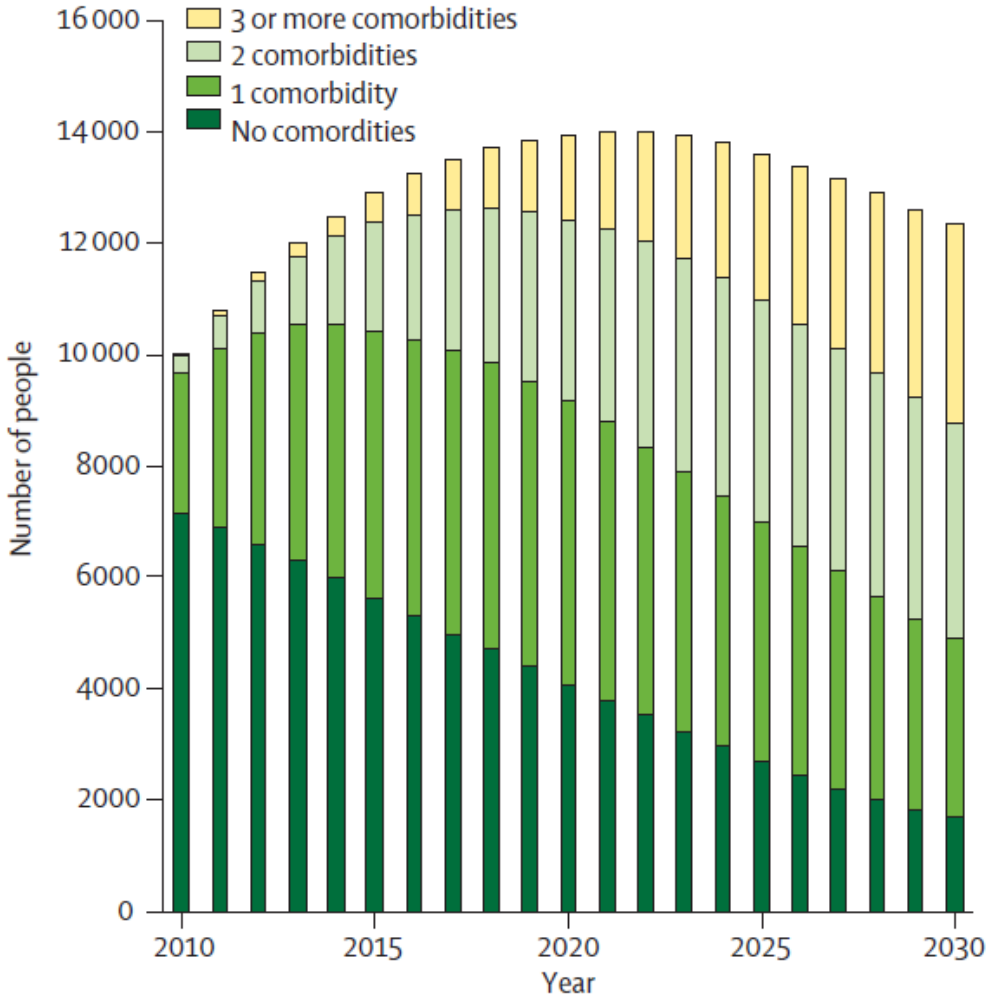
# HIV-related Comorbidities
## *An Impending Public Health Epidemic*




***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**

*Smit, M. et al. Lancet Infect Dis 2015; 15: 810–18*

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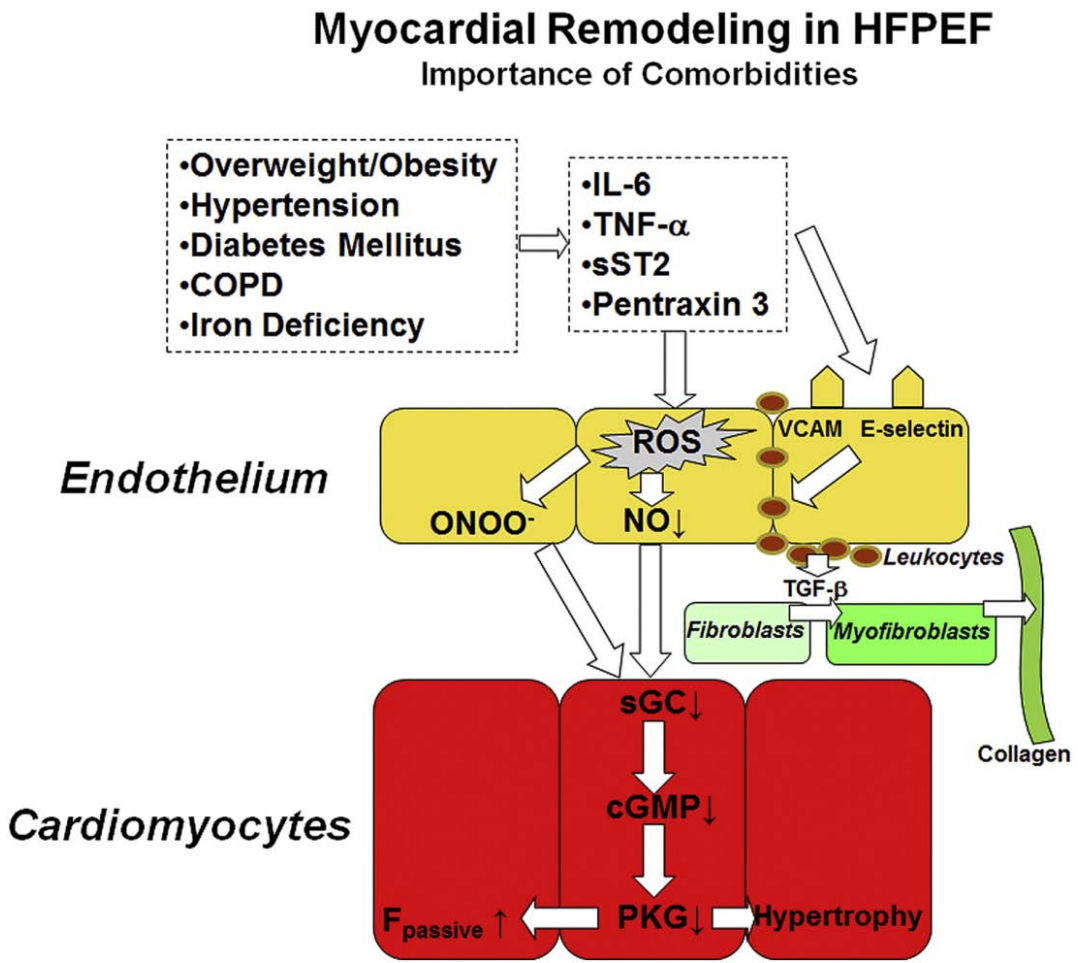
# HIV-related Heart Failure
## *A Proinflammatory State that Drives Dysfunction*

Inflammation and immune activation drive pathobiological mechanisms of comorbid diseases.




About half of people living with HIV have systolic (~8%) or diastolic (~43%) dysfunction.

Cerrato, et al. European Heart Journal (2013) 34, 1432–1436

Adapted from Paulus WJ and Tshcöpe C. *JACC* 2013; 62: 263-71.

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# HIV Status and Incidence and Outcomes of Heart Failure

Using the unique resources of Kaiser Permanente (KP) and Cardiovascular Research Network (CVRN), this project will identify 39,000 HIV infected HF plus 390,000 controls to address 3 complimentary aims:

1. Elucidate HIV and HF (and HF type)
2. Identify clinically meaningful treatments
3. Effect of HIV status on HF hospitalization

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**HL132640 -01 Alan Go; Michael Silverberg**

# CHART-Heart Failure Network

Cross sectional study to elucidate the pathogenesis of diastolic dysfunction by comparison of:

1. HIV+/DD
2. HIV+/ DD-
3. Non HIV/ DD+ (MESA)

Participants have deep-phenotype with imaging, biomarkers, functional testing and HIV status. A longitudinal follow-up is planned not yet submitted for funding.

REPRIEVE

# Randomized Trial to Prevent Vascular Events in HIV

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NIH National Institute of Allergy and Infectious Diseases

ACTG AIDS CLINICAL TRIALS GROUP

Kowa

GILEAD



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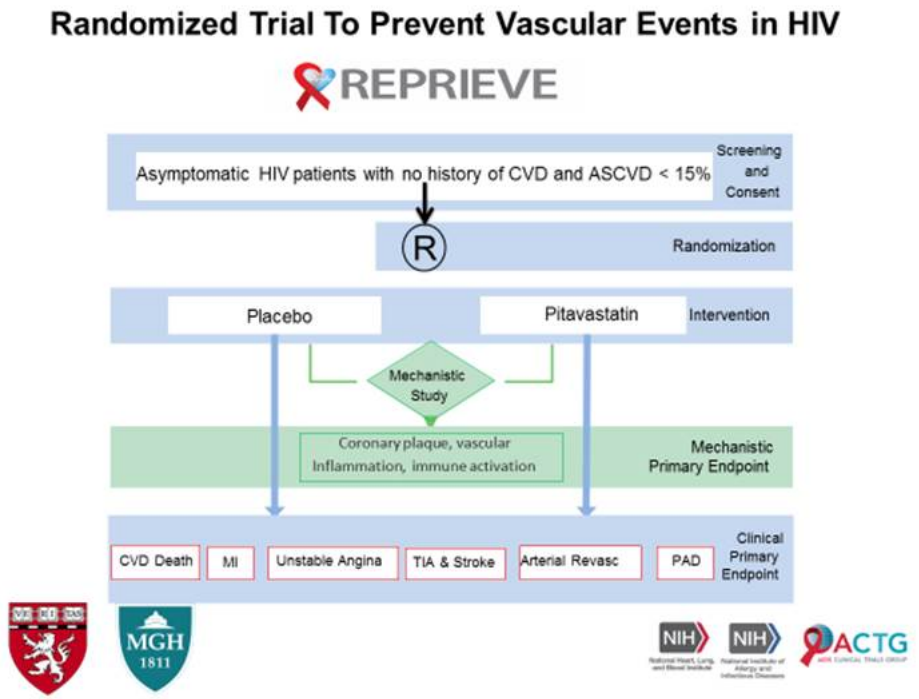
# REPRIEVE
## *Study Design*

- Tests efficacy of Pitavistatin to reduce major adverse cardiovascular events in HIV-infected subjects with ASCVD Risk Score <=15%, LDL less than 130 mg/dL
- Enrollment started 4/2015 & ends 10/2018; n=6500; >100 sites
- Collaboration with NIAID & AIDS Clinical Trials Group (ACTG), Kowa donating study drug & placebo and Gilead contributing unrestricted funds

REPRIEVE

Randomized Trial to Prevent Vascular Events in HIV

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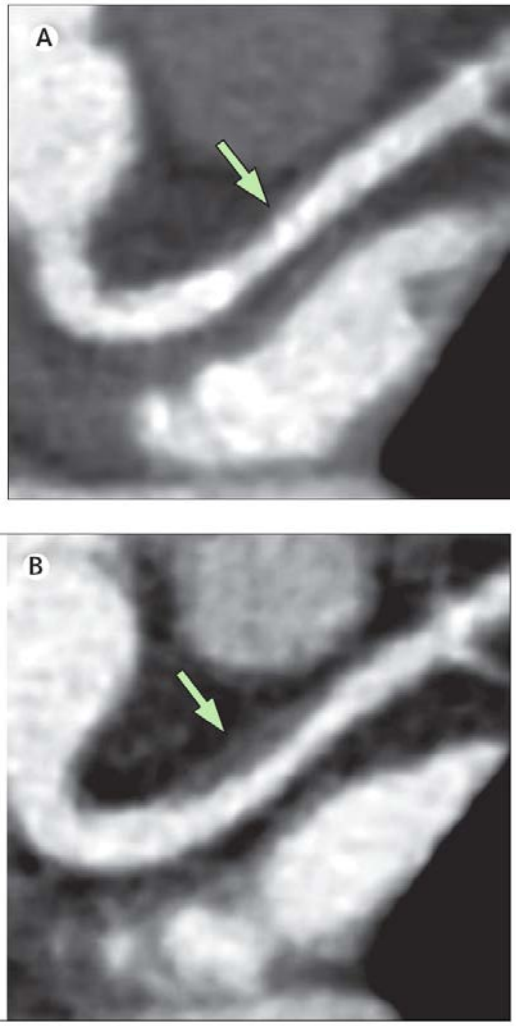
# REPRIEVE CCTA mechanistic substudy

**PRIMARY:** Effect of Pitavistatin on non-calcified coronary plaque volume measured on serial coronary computed tomography angiography (CCTA).

**SECONDARY:**

1. High risk plaque features on CCTA.
2. Serum markers immune activation, inflammation, and CVD risk
3. Relative contributions to coronary plaque progression

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# 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.
  - Chronic immune activation and inflammation.
  - May be a model for accelerated aging.
- Continued support of research on health of people living with HIV, including leveraging extant cohorts (MACS & WIHS) and supporting high impact clinical and implementation science.
- Priorities consistent with NHLBI Strategic Vision.

# NHLBI's Strategic Vision Aligns with NIH Priorities for HIV Related Research

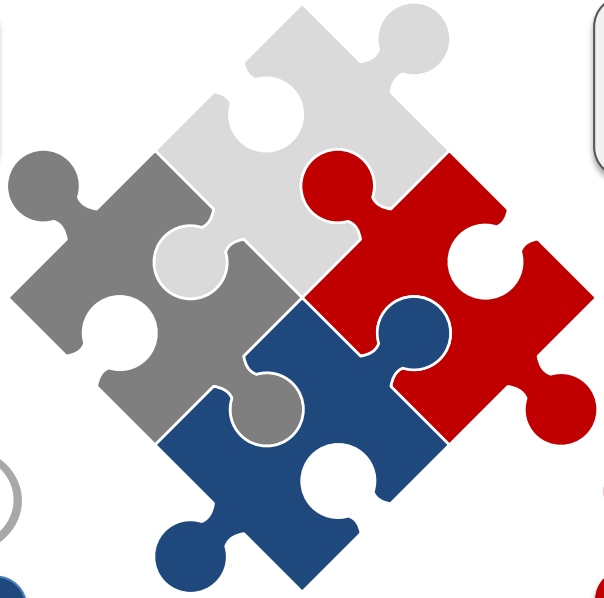
**Understand** **Human Biology**

**Goal 1** –Expand knowledge of the mechanisms governing normal function

Mitigating Comorbidities

**Reduce** **Human Disease**

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



**Advance** **Translational Research**

Goal 3 –Facilitate innovation and accelerate research translation

Accelerating Cures

**Develop** **Workforce and Resources**

**Goal 4** –Develop a diverse workforce with the resources to implement evidence into practice



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