

## Comparative Effectiveness of Lipid-Lowering and Antihypertensive Medications among Patients Infected with HIV

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### Description

The treatment of cardiovascular disease risk factors among patients with human immunodeficiency virus (HIV) is complicated by the underlying HIV infection, the numerous medications that these patients are often prescribed, and the common occurrence of other comorbidities. Many questions remain unanswered about the effectiveness of medications to treat dyslipidemia (high cholesterol) and hypertension (high blood pressure) among these complex patients. This study evaluated the comparative effectiveness of medications to treat high cholesterol and high blood pressure among HIV-infected individuals. Results can provide clinicians with new information about optimal treatment strategies for cardiovascular disease in people with HIV.

### Specific Aims

1. Develop an estimator (i.e., a new method for calculating an estimate of the effect of treatment) to mitigate the effect of limited and sporadic information on the estimates of heart attack incidence, lipid levels, and blood pressure in causal inference models.
2. Determine which lipid-lowering and blood pressure controlling medications work best to control high cholesterol and manage high blood pressure in patients with HIV.
3. Determine which lipid-lowering and blood pressure controlling medications work best to prevent heart attacks in patients with HIV.

### Findings

- In a cohort of HIV-positive patients starting statin medications, the most commonly prescribed statins were atorvastatin, pravastatin, and rosuvastatin.

### Main Objective

Investigate the best treatment strategies for managing cardiovascular disease risk factors in patients with HIV.

### Chronic Conditions Considered

Human immunodeficiency virus  
Hypertension (high blood pressure)  
Dyslipidemia (high cholesterol)

### Study Design & Methods

Retrospective cohort study

Marginal structural modeling and inverse intensity, rate ratio-weighted generalized estimating equations.

### Data Sources & Sample Size

Longitudinal, clinical data for more than 21,000 HIV-infected individuals from the Centers for AIDS Research Network of Integrated Clinical Systems.

### Strategies Addressed from the HHS Strategic Framework on Multiple Chronic Conditions

- 3.A. Provide best practices and tools
- 4.C. Increase clinical research

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- One year after starting statin therapy, rosuvastatin and atorvastatin were associated with greater improvements in lipid levels than was pravastatin.
  - Patients who received rosuvastatin or atorvastatin had greater declines in total cholesterol, low density lipoprotein cholesterol (LDL-C), non-high density lipoprotein cholesterol (non-HDL-C), and triglyceride values than did patients who received pravastatin. The greatest improvement in dyslipidemia was observed among those receiving rosuvastatin.
- Toxicity associated with statin discontinuation was uncommon and did not differ across statins.

### Implications

Current U.S. recommendations for treating HIV-associated dyslipidemia includes the use of statins and emphasizes the use of pravastatin or atorvastatin. Findings from this study, which advanced the methods available for comparative effectiveness analyses in observational settings, suggest that these recommendations should include rosuvastatin, consistent with recent British guidelines.

### Publications (as of September 2013)

Munoz M, Liu W, Delaney J, Brown E, Mugavero M, Mathews W, Naravnik S, Wilig J, Eron J, Hunt P, Kahn J, Saag M, Kitahata M, and Crane H. Comparative effectiveness of fish oil versus fenofibrate, gemfibrozil, and atorvastatin on lowering triglyceride levels among HIV-infected patients in routine clinical care. *JAIDS*. 2013 Jul 25. [Epub ahead of print].

Schelfhout JE, Stojanovic DA, Houtchens A, Crane HM, Cachay ER, Brown ER, Napravnik SM, Kitahata MM, Saag MS, Hunt PW, Kauf TL, Delaney JAC. Progression of platelet counts in treatment naive HIV/HCV co-infection. *World J AIDS*. 2013 Mar; 3(1); 36-40.

Bird ST, Hartzema AG, Brophy JM, Etminan M, Delaney JA. Risk of venous thromboembolism in women with polycystic ovary syndrome: a population-based matched cohort analysis. *CMAJ*. 2013 Feb 5; 185(2): E115-20.

Kim DJ, Westfall AO, Chamot E, Willig AL, Mugavero MJ, Ritchie C, Burkholder GA, Crane HM, Raper JL, Saag MS, Willig JH. Multimorbidity patterns in HIV-infected patients: the role of obesity in chronic disease clustering. *J Acquir Immune Defic Syndr*. Dec 15 2012; 61(5):600-605.

Buzkova P. Measurement error and outcomes defined by exceeding a threshold: biased findings in comparative effectiveness trials. *Pharm Stat*. Nov-Dec 2012; 11(6):429-441.

Han JH, Crane HM, Bellamy SL, Frank I, Cardillo S, Bisson GP. HIV infection and glycemic response to newly initiated diabetic medical therapy. *AIDS*. Oct 23 2012; 26(16):2087-2095.

Singh S, Willig JH, Mugavero MJ, Crane P, Harrington R, Knopp R, Kosel B, Saag M, Kitahata M, and Crane, H. Comparative effectiveness and toxicity of statins among HIV-infected patients. *Clin Infect Dis*. Feb 2011; 52(3):387-395.

Crane H, Grunfeld C, Willig J, Mugavero M, Rompaey S, Moore R, Rodriguez B, Feldman B, Lederman M, Saag M, and Kitahata M. Impact of NRTIs on lipid levels among a large HIV-infected cohort initiating antiretroviral therapy in clinical care. *AIDS*. 2011 Jan; 25(2):185-95.

(Additional publications currently in preparation).

# Comparative Effectiveness of Lipid-Lowering and Antihypertensive Medications among Patients Infected with HIV (continued)

## Posters and Presentations

Crane H, Heckbert S, and Paramsothy P. Lessons learned from the implementation of myocardial infarction (MI) adjudication in the CFAR Network of Integrated Clinical Systems (CNICS) cohort: update after the first 1000 potential events. Paper presented at: 17th International Workshop on HIV Observational Databases; 2013 Apr 11-13; Cavtat, Croatia.

Crane HM, Paramsothy P, Heckbert S, et al. Secondary myocardial infarctions (MIs) are common among patients with HIV and associated with lower prior predicted 10-year cardiovascular disease risk than primary events. Paper presented at: 16th International Workshop on HIV Observational Databases; 2012 Mar 27-29; Athens, Greece.

Crane H, Paramsothy P, Heckbert S, Budoff M, Willig J, Mugavero M, Matthews C, Grunfeld C, Saag M, Kitahata M. Primary versus Secondary Myocardial Infarction Events among HIV-Infected Individuals: the CNICS cohort. Poster presented at: 19th Conference on Retroviruses and Opportunistic Infections. 2012 Mar 5-8; Seattle, WA.

Teeple E, Delaney J, Brown E, et al. Impact of antiretroviral medications on blood pressure in antiretroviral naïve patients initiating their first regimen in the CNICS Cohort. Poster presented at: Infectious Disease Society of America Annual Meeting. 2011 Oct 20-23; Boston, MA.

Liu W, Munoz M, Delaney J, et al. Comparative effectiveness of fish oil, atorvastatin and fibrates for lowering triglyceride levels among HIV-infected patients. Paper presented at: 27th International Conference on Pharmacoepidemiology and Therapeutic Risk Management 2011; Aug 14-17; Chicago, IL.

Crane H, Heckbert S, Budoff M, Paramsothy P, Delaney J, Barnes G, Stewart M, Webster E, McReynolds J, Lober W, Nevin C, Willig J, Mugavero M, Saag M, and Kitahata M. Design, implementation and implications of the next generation myocardial infarction (MI) adjudication system in the CFAR Network of Integrated Clinical Systems cohort: update after the first 500 potential events. Abstract presented at: 13th International Workshop on Adverse Drug Reactions and Co-morbidities in HIV; 2011 Jul 14 - 16; Rome, Italy.

Crane P, Feldman B, Gibbons L, et al. Comparative effects of initial HMG-co-A-reductase inhibitor ("Statin") choice on depression levels in people living with HIV: an illustration of analytic issues raised by using patient reported outcomes (PROs) in a comparative effectiveness framework. Paper presented at: Methods for Developing and Analyzing Clinically Rich Data for Patient-Centered Outcomes Research, Third Symposium on Comparative Effectiveness Research Methods; 2011 Jun 6-7; Rockville, MD.