PI: **Rebeiro, Peter F**	Title: The HIV Care Continuum and Health Policy: Changes through Context and Geography	
Received: 01/05/2017	FOA: PA16-190	Council: 05/2017
Competition ID: FORMS-D	FOA Title: MENTORED RESEARCH SCIENTIST DEVELOPMENT AWARD (PARENT K01)	
1 K01 AI131895-01A1	Dual:	Accession Number: 4007925
IPF: 10040927	Organization: VANDERBILT UNIVERSITY MEDICAL CENTER	
Former Number:	Department: Medicine/Infectious Disease	
IRG/SRG: AIDS	AIDS: Y	Expedited: Y
Subtotal Direct Costs (excludes consortium F&A) Year 1: [redacted] Year 2: Year 3: Year 4: Year 5:	Animals: N Humans: N Clinical Trial: N Current HS Code: 10 HESC: N	New Investigator: N Early Stage Investigator: N

Senior/Key Personnel:	*Organization:*	*Role Category:*
Peter Rebeiro	Vanderbilt University Medical Center	PD/PI
Timothy Sterling	Vanderbilt University Medical Center	Other (Specify)-Mentor
John Graves	Vanderbilt University Medical Center	Other (Specify)-Co-Mentor
Richard Moore	Johns Hopkins University	Other (Specify)-Advisor
Stephen Gange	Johns Hopkins	Other (Specify)-Mentoring Committee
Catherine McGowan	Vanderbilt University Medical Center	Other (Specify)-Advisor
David Holtgrave	Johns Hopkins University	Other (Specify)-Mentoring Committee
William Schaffner	Vanderbilt University Medical Center	Other (Specify)-Mentoring Committee
Christopher Fonnesbeck	Vanderbilt University Medical Center	Other (Specify)-Advisor
Bryan Shepherd	Vanderbilt University Medical Center	Other (Specify)-Advisor

APPLICATION FOR FEDERAL ASSISTANCE
SF 424 (R&R)

3. DATE RECEIVED BY STATE	**State Application Identifier** TN: Tennessee

1. TYPE OF SUBMISSION*

❍ Pre-application ❍ Application ● Changed/Corrected Application

4.a. Federal Identifier [redacted]

b. Agency Routing Number

2. DATE SUBMITTED	**Application Identifier**	**c. Previous Grants.gov Tracking Number**
2017-01-05	M0044399	GRANT12314772

5. APPLICANT INFORMATION **Organizational DUNS*:** [redacted]

Legal Name*: Vanderbilt University Medical Center
Department: Medicine/Infectious Disease
Division: [redacted]
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City*: [redacted]
County: [redacted]
State*: [redacted]
Province:
Country*: [redacted]
ZIP / Postal Code*: [redacted]

Person to be contacted on matters involving this application
Prefix: First Name*: Donald Middle Name: Clinton Last Name*: Brown Suffix:
Position/Title: Director, Office of Sponsored Programs
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City*: [redacted]
County: [redacted]
State*: [redacted]
Province:
Country*: [redacted]
ZIP / Postal Code*: [redacted]
Phone Number*: [redacted] Fax Number: [redacted] Email: [redacted]

6. EMPLOYER IDENTIFICATION NUMBER *(EIN) or (TIN)** [redacted]

7. TYPE OF APPLICANT* M: Nonprofit with 501C3 IRS Status (Other than Institution of Higher Education)

Other (Specify):
Small Business Organization Type ❍ Women Owned ❍ Socially and Economically Disadvantaged

8. TYPE OF APPLICATION*

❍ New ● Resubmission
❍ Renewal ❍ Continuation ❍ Revision

If Revision, mark appropriate box(es).
❍ A. Increase Award ❍ B. Decrease Award ❍ C. Increase Duration
❍ D. Decrease Duration ❍ E. Other *(specify)* :

Is this application being submitted to other agencies?* ❍ Yes ● No What other Agencies?

9. NAME OF FEDERAL AGENCY*	**10. CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER**
National Institute of Allergy and Infectious Diseases	TITLE: Mentored Research Scientist Development Award (Parent K01)

11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT*
The HIV Care Continuum and Health Policy: Changes through Context and Geography

12. PROPOSED PROJECT		**13. CONGRESSIONAL DISTRICTS OF APPLICANT**
Start Date*	Ending Date*	TN-005
07/01/2017	06/30/2022	

SF 424 (R&R) APPLICATION FOR FEDERAL ASSISTANCE

14. PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR CONTACT INFORMATION

Prefix: First Name*: Peter Middle Name: F Last Name*: Rebeiro Suffix:
Position/Title: Research Asst Professor
Organization Name*: Vanderbilt University Medical Center
Department: [redacted]
Division: [redacted]
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Street2:
City*: [redacted]
County: [redacted]
State*: [redacted]
Province:
Country*: [redacted]
ZIP / Postal Code*: [redacted]
Phone Number*: [redacted] Fax Number: [redacted] Email*: [redacted]

15. ESTIMATED PROJECT FUNDING

a. Total Federal Funds Requested* [redacted]
b. Total Non-Federal Funds* [redacted]
c. Total Federal & Non-Federal Funds* [redacted]
d. Estimated Program Income* [redacted]

16.IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?*

a. YES ❍ THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON:

DATE:

b. NO ● PROGRAM IS NOT COVERED BY E.O. 12372; OR

❍ PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW

17. By signing this application, I certify (1) to the statements contained in the list of certifications* and (2) that the statements herein are true, complete and accurate to the best of my knowledge. I also provide the required assurances * and agree to comply with any resulting terms if I accept an award. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. (U.S. Code, Title 18, Section 1001)

● I agree*

** The list of certifications and assurances, or an Internet site where you may obtain this list, is contained in the announcement or agency specific instructions.*

18. SFLLL or OTHER EXPLANATORY DOCUMENTATION File Name:

19. AUTHORIZED REPRESENTATIVE

Prefix: First Name*: Donald Middle Name: Clinton Last Name*: Brown Suffix:
Position/Title*: Director, Office of Sponsored Programs
Organization Name*: Vanderbilt University Medical Center
Department: [redacted]
Division:
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*: [redacted]
Province:
Country*: [redacted]
ZIP / Postal Code*: [redacted]
Phone Number*: [redacted] Fax Number: [redacted] Email*: [redacted]

Signature of Authorized Representative* [redacted]

Date Signed* 01/05/2017

20. PRE-APPLICATION File Name:

21. COVER LETTER ATTACHMENT File Name:M-22_RRSF424_Cover_Letter.pdf

OMB Number: 4040-0010
Expiration Date: 06/30/2016

Project/Performance Site Location(s)

Project/Performance Site Primary Location

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: Vanderbilt University Medical Center
Duns Number: [redacted]
Street1*: [redacted]
Street2:
City*: [redacted]
County: [redacted]
State*: [redacted]
Province:
Country*: [redacted]
Zip / Postal Code*: [redacted]
Project/Performance Site Congressional District*: TN-005

Additional Location(s) File Name:

Funding Opportunity Number: PA-16-190. Received Date: 2017-01-05T17:21:11.000-05:00

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* ● **Yes** ○ **No**

1.a. If YES to Human Subjects

Is the Project Exempt from Federal regulations? ○ Yes ● No

If YES, check appropriate exemption number: 1 __ 2 __ 3 __ 4 __ 5 __ 6 If

NO, is the IRB review Pending? ● **Yes** ○ **No**

IRB Approval Date:

Human Subject Assurance Number [redacted]

2. Are Vertebrate Animals Used?* ○ **Yes** ● **No**

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? ○ Yes ○ No

IACUC Approval Date:

Animal Welfare Assurance Number

3. Is proprietary/privileged information included in the application?* ○ **Yes** ● **No**

4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* ○ **Yes** ● **No**

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? ○ Yes ○ No

4.d. If yes, please explain:

5. Is the research performance site designated, or eligible to be designated, as a historic place?* ○ **Yes** ● **No**

5.a. If yes, please explain:

6. Does this project involve activities outside the United States or partnership with international collaborators?* ○ **Yes** ● **No**

6.a. If yes, identify countries:

6.b. Optional Explanation:

	Filename
7. Project Summary/Abstract*	M-5_Project_Summary.pdf
8. Project Narrative*	M-2_Narrative.pdf
9. Bibliography & References Cited	M-4_Bibliography.pdf
10.Facilities & Other Resources	M-1_Facilities.pdf
11.Equipment	M-3_Equipment.pdf

Funding Opportunity Number: PA-16-190. Received Date: 2017-01-05T17:21:11.000-05:00

PROJECT SUMMARY (ABSTRACT).

The HIV Care Continuum is a compelling epidemiologic framework describing the movement of people living with HIV/AIDS through care, including diagnosis, linkage and retention in care, use of antiretroviral therapy (ART), and ultimately, viral suppression. Health policies may profoundly influence outcomes along the Care Continuum, and these effects may be modified across regions and through individual contexts.

In observational cohorts, retention in clinical care, ART use, and viral suppression proportions have varied depending on available data and the population under study. The US National HIV/AIDS Strategy (updated to 2020) and the revised 2013 World Health Organization ART guidelines also reference milestones in the Care Continuum. Because the Patient Protection and Affordable Care Act (ACA) and other national health policies in North and Latin American countries aim to improve healthcare access and reduce health disparities, describing the effect of policy and contextual factors on Care Continuum outcomes in these settings is of great interest to epidemiologists, clinicians, and policy makers.

This research seeks to quantify health policy, sociodemographic, contextual, and geographic patterns and correlates of HIV Care Continuum outcomes among HIV-infected persons in the United States (US), Canada, and Mexico. Contextual factors include psychiatric illness, regional poverty, residential urbanicity, and other individual and environmental characteristics. The North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) and Caribbean, Central and South America network for HIV epidemiology (CCASAnet) provide rich data sources in which to conduct this work.

Aim 1 will quantify disparities in Care Continuum outcomes in North and Latin America, assessing health system, demographic, risk, contextual, and geographic differences. Because research into the influence of contextual factors and health system characteristics on Care Continuum outcomes in longitudinal cohorts with clinical care data have been sparse or geographically limited, this analysis will be novel and of significant importance.

Aims 2 and 3 will provide inferences about the ACA’s effects on improving healthcare among HIV-infected individuals in care in the US. The state-led expansion of Medicaid coverage under the ACA will be used as a quasi-experiment to assess effects on Care Continuum and other HIV disease outcomes, comparing pre-ACA (pre-2014) to ACA implementation periods.

PUBLIC HEALTH RELEVANCE STATEMENT (NARRATIVE).

HIV remains a massive public health challenge both domestically and internationally; the HIV Care Continuum is a widely used and powerful epidemiologic framework applicable to those suffering from HIV, and the influence of public health and health system policies across the Continuum may be profound. By assessing the dynamic process of the HIV Care Continuum in discrete stages, and examining disparities by health policy, geography, and individual context, transitions that demand improvement and specific targets for public health and clinical interventions can more easily be identified. The US National HIV/AIDS Strategy (updated to 2020) and revised 2013 World Health Organization ART guidelines also reference milestones in the Care Continuum; because the Patient Protection and Affordable Care Act (ACA) and other national health policies implemented in North and Latin American countries aim to improve healthcare access and reduce health disparities in accord with these milestones, describing the effect of policy and individual contextual factors on Care Continuum outcomes, as this study aims to do, will be of great interest and utility to epidemiologists, clinicians, and policymakers.

BIBLIOGRAPHY AND WORKS CITED.

References including applicant as author include applicant's name in **bold font**

1. **Rebeiro P**, Althoff K, Buchacz K,. for the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD). Retention Among North American HIV-infected Persons in Clinical Care, 2000-2008. J Acquir Immune Defic Syndr. 2013 Mar 1;62(3):356-62. PMID: 23242158 PMCID: PMC3661708
2. **Rebeiro P**, Horberg MA, Gange SJ,.; for the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD). Strong agreement between nationally recommended retention measures from the Institute of Medicine and the Department of Health and Human Services. PLoS One. 2014 Nov 6;9(11):e111772. PMID: 25375099 PMCID: PMC4222946
3. Althoff KN, **Rebeiro P**, Brooks JT,.; for the North American AIDS Cohort Collaboration on Research Design (NA-ACCORD). Disparities in the quality of HIV care when using US Department of Health and Human Services Indicators. Clin Infect Dis. 2014 Apr;58(8):1185-9. PMID: 24463281 PMCID: PMC3967825
4. Yehia BR, **Rebeiro P**, Althoff KN,.; for the North American AIDS Cohort Collaboration on Research Design (NA-ACCORD). The Impact of Age on Retention in Care and Viral Suppression. J Acquir Immune Defic Syndr. 2015 Apr 1;68(4):413-9. PMID: 25559604 PMCID: PMC4334738
5. Althoff KN, Buchacz K, Hall I, Zhang J, Hanna DB, **Rebeiro P**,. for The North American AIDS Cohort Collaboration on Research and Design. Trends in antiretroviral therapy use, HIV RNA plasma viral loads and CD4 T-lymphocyte counts among human immunodeficiency virus (HIV)-infected persons in care in the United States, 2000-2008. Ann Intern Med. 2012 Sep 4;157(5):325-35. PMID: 22944874 PMCID: PMC3534765
6. **Rebeiro P**, Althoff KN, Lau B,. for the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD). Laboratory measures as proxies of primary care encounters: implications for quantifying clinical retention among HIV-infected adults in North America. Am J Epidemiol. 2015 Nov 17. pii: kwv181. PMID: 26578717 PMCID: PMC4655744
7. **Rebeiro P**, Gange SJ, Sterling TR,. for the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD). Geographic Variations in Retention in Care among HIV-Infected Adults in the United States. PLoS One. 2016 Jan 11;11(1):e0146119. PMID: 26752637 PMCID: PMC4708981
8. **Rebeiro P**, Cesar C, Shepherd BE,. for the Caribbean, Central and South America network for HIV epidemiology (CCASAnet). Assessing the HIV Care Continuum in Latin America: progress in clinical retention, cART use, and viral suppression. J Int AIDS Soc. 2016 Apr 8;19(1):20636. PMID: 27065108 PMCID: PMC4827101
9. Woodward B, Person AK, **Rebeiro P**,. Risk Prediction Tool for Medical Appointment Attendance Among HIV-Infected Persons with Unsuppressed Viremia. AIDS Patient Care STDS. 2015 May;29(5):240-7. PMID: 25746288 PMCID: PMC4410547

[redacted]

11. Ford MA, and Spicer CM. Monitoring HIV care in the United States : indicators and data systems. Washington, D.C.: National Academies Press; 2012. PMID: 25144028
12. Gardner EM, McLees MP, Steiner JF,. The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. Clin Infect Dis. United States; 2011;52(6):793-800. PMID: 21367734
13. Mayer KH. Introduction: Linkage, engagement, and retention in HIV care: essential for optimal individual- and community-level outcomes in the era of highly active antiretroviral therapy. Clin Infect Dis. United States; 2011. p. S205-7. PMID: 21342908

14. Williams CT, Kim S, Meyer J,. Gender differences in baseline health, needs at release, and predictors of care engagement among HIV-positive clients leaving jail. AIDS Behav. United States; 2013;17 Suppl 2:S195-202. PMID: 23314801

15. Thompson MA, Mugavero MJ, Amico KR,. Guidelines for improving entry into and retention in care and antiretroviral adherence for persons with HIV: evidence-based recommendations from an International Association of Physicians in AIDS Care panel. Ann Intern Med. United States; 2012;156(11):817-33. PMID: 22393036

16. Cunningham WE, Sohler NL, Tobias C,. Health services utilization for people with HIV infection: comparison of a population targeted for outreach with the U.S. population in care. Med Care. United States; 2006;44(11):1038-47. PMID: 17063136

17. Stone VE. HIV/AIDS in Women and Racial/Ethnic Minorities in the U.S. Curr Infect Dis Rep. United States; 2012;14(1):53-60. PMID: 22139589

18. Andersen RM. Revisiting the behavioral model and access to medical care: does it matter? J Health Soc Behav. 1995 Mar;36(1):1-10. PMID: 7738325

19. Improving Outcomes: Accelerating Progress Along the HIV Care Continuum. White House Office of National AIDS Policy. Retrieved from: http://www.whitehouse.gov/sites/default/files/onap_nhas_improving_outcomes_dec_2013.pdf

20. Shadish WR, Cook TD, and Campbell DT. Experimental and quasi-experimentaldesigns for generalized causal inference. Wadsworth Cengage learning; 2002.

21. Abara W, and Heiman HJ. The Affordable Care Act and Low-Income People Living With HIV: Looking Forward in 2014 and Beyond. J Assoc Nurses AIDS Care. United States; 2014;25(6):476-82. PMID: 24996850

22. Kates J. Implications of the Affordable Care Act for people with HIV infection and the Ryan White HIV/AIDS Program: what does the future hold? Top Antivir Med. United States; 2013;21(4):138-42. PMID: 24225080

23. Martin EG, and Schackman BR. What does U.S. health reform mean for HIV clinical care? J Acquir Immune Defic Syndr. United States; 2012;60(1):72-6. PMID: 22517415

24. Yehia BR, Fleishman JA, Agwu AL,. HIV Research Network. Health insurance coverage for persons in HIV care, 2006-2012. J Acquir Immune Defic Syndr. 2014 Sep 1;67(1):102-6. PMID: 24977377

25. Hirnschall G, Harries AD, Easterbrook PJ, Doherty MC, and Ball A. The next generation of the World Health Organization's global antiretroviral guidance. J Int AIDS Soc. Switzerland; 2013;16:18757. PMID: 23819908

26. Frenk J, Gómez-Dantés O, and Knaul FM. The democratization of health in Mexico: financial innovations for universal coverage. Bulletin of the World Health Organization. SciELO Public Health; 2009;87(7):542-548. PMID: 19649369

27. Elias PE, and Cohn A. Health reform in Brazil: lessons to consider. Am J Public Health. United States; 2003;93(1):44-8. PMID: 12511382

28. Richards TB, Croner CM, Rushton G, Brown CK, and Fowler L. Information technology: Geographic information systems and public health: Mapping the future. Public Health Reports. Association of Schools of Public Health; 1999;114(4):359. PMID: 10501137

29. Gao S, Mioc D, Anton F, Yi X, and Coleman DJ. Online GIS services for mapping and sharing disease information. Int J Health Geogr. England; 2008;7:8. PMID: 18298859

30. Houle B, Holt J, Gillespie C, Freedman DS, and Reyes M. Use of density-equalizing cartograms to visualize trends and disparities in state-specific prevalence of obesity: 1996-2006. Am J Public Health. United States; 2009;99(2):308-12. PMID: 19059848

31. Koch T, and Denike K. Medical mapping: The revolution in teaching—and using—maps for the analysis of medical issues. Journal of Geography. Taylor & Francis; 2004;103(2):76-85.
32. Klassen AC, Kulldorff M, and Curriero F. Geographical clustering of prostate cancer grade and stage at diagnosis, before and after adjustment for risk factors. Int J Health Geogr. 2005;4(1):1. PMID: 15649329
33. Wallace RG. AIDS in the HAART era: New York's heterogeneous geography. Soc Sci Med. England; 2003;56(6):1155-71. PMID: 12600355
34. Eberhart MG, Yehia BR, Hillier A,. Behind the cascade: analyzing spatial patterns along the HIV care continuum. J Acquir Immune Defic Syndr. United States; 2013;64 Suppl 1:S42-51. PMID: 24126447
35. Centers for Disease Control and Prevention (CDC). Geographic differences in HIV infection among Hispanics or Latinos--46 states and Puerto Rico, 2010. MMWR Morb Mortal Wkly Rep. United States; 2012;61(40):805-10. PMID: 23051610
36. Hanna DB, Selik RM, Tang T, and Gange SJ. Disparities among US states in HIV-related mortality in persons with HIV infection, 2001-2007. AIDS. England; 2012;26(1):95-103. PMID: 22008659
37. Hanna DB, Buchacz K, Gebo KA,. and North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) of the International Epidemiologic Databases to Evaluate AIDS (IeDEA). Association between U.S. state AIDS Drug Assistance Program (ADAP) features and HIV antiretroviral therapy initiation, 2001-2009. PLoS One. United States; 2013;8(11):e78952. PMID: 24260137
38. Reif SS, Whetten K, Wilson ER, McAllaster C, Pence BW, Legrand S, and Gong W. HIV/AIDS in the Southern USA: A disproportionate epidemic. Taylor & Francis. England: Routledge; 2014;26(3):351-9. PMID: 23944833
39. Mugavero MJ, Amico KR, Horn T, and Thompson MA. The state of engagement in HIV care in the United States: from cascade to continuum to control. Clin Infect Dis. United States; 2013;57(8):1164-71. PMID: 23797289
40. Centers for Disease Control and Prevention (CDC). Vital signs: HIV prevention through care and treatment--United States. MMWR Morb Mortal Wkly Rep. United States; 2011;60(47):1618-23. PMID: 22129997
41. Gange SJ, Kitahata MM, Saag MS,. Cohort profile: The North American AIDS cohort collaboration on research and design (NA-ACCORD). Int J Epidemiol. 2007 Apr;36(2):294-301. PMID: 17213214
42. McGowan CC, Cahn P, Gotuzzo E, Padgett D, Pape JW, Wolff M, Schechter M, Masys DR. Cohort Profile: Caribbean, Central and South America Network for HIV research (CCASAnet) collaboration within the International Epidemiologic Databases to Evaluate AIDS (IeDEA) programme. Int J Epidemiol. 2007 Oct;36(5):969-76. PMID: 17846055
43. Stuckler D, Feigl AB, Basu S, and McKee M. The political economy of universal health coverage. In Background paper for the global symposium on health systems research. Geneva: World Health Organization. 2010.
44. Valdiserri RO, Forsyth AD, Yakovchenko V, Koh HK. Measuring What Matters: The Development of Standard HIV Core Indicators across the U.S. Department of Health and Human Services. Public Health Rep 2013; 128(5): 354-359. PMID: 23997280
45. Berry SA, Fleishman JA, Yehia BR, Cheever LW, Hauck H, Korthuis PT, Mathews WC, Keruly J, Nijhawan AE, Agwu AL, Somboonwit C, Moore RD, Gebo KA, and HIV Research Network. Healthcare Coverage for HIV Provider Visits Before and After Implementation of the Affordable Care Act. Clin Infect Dis. United States; 2016;63(3):387-95. PMID: 27143660
46. Eaton EF, and Mugavero MJ. Editorial Commentary: Affordable Care Act, Medicaid Expansion … or Not: Ryan White Care Act Remains Essential for Access and Equity. Clin Infect Dis. United States; 2016. p. 404-6. PMID: 27143674

47. Liang K-Y, and Zeger SL. Regression analysis for correlated data. Annual review of public health. Annual Reviews 4139 El Camino Way, PO Box 10139, Palo Alto, CA 94303-0139, USA; 1993;14(1):43-68. PMID: 8323597
48. Harrell FE. Regression modeling strategies: with applications to linear models, logistic regression, and survival analysis. New York: Springer; 2001.
49. Kulldorff M. A spatial scan statistic. Communications in Statistics-Theory and methods. Taylor & Francis; 1997;26(6):1481-1496.
50. Kulldorff M. SaTScan user guide for version 9.3. SaTScan user guide for version 9.3. 2014.
51. The Kaiser Family Foundation's State Health Facts: Current Status of State Medicaid Expansion Decisions. Accessed Nov. 2014 from: http://kff.org/health-reform/slide/current-status-of-the-medicaid-expansion-decision/
52. Moscoe E, Bor J, and Bärnighausen T. Regression discontinuity designs are underutilized in medicine, epidemiology, and public health: a review of current and best practice. J Clin Epidemiol. United States; 2015;68(2):122-33. PMID: 25579639
53. Sommers BD, Baicker K, and Epstein AM. Mortality and access to care among adults after state Medicaid expansions. N Engl J Med. United States; 2012;367(11):1025-34. PMID: 22830435
54. Martin, Nussey, Wilson and Reale Submitted Measuring between-individual variation in reaction norms in field and experimental studies: a power analysis of random regression models. Methods in Ecology and Evolution. Online early.
55. Hsieh FY, Bloch DA, Larsen MD. A simple method of sample size calculation for linear and logistic regression. Stat Med. 1998 Jul 30;17(14):1623-34. PMID: 9699234
56. Waller LA, Hill EG, Rudd RA. The geography of power: statistical performance of tests of clusters and clustering in heterogeneous populations. Stat Med. 2006 Mar 15;25(5):853-65. PMID: 16453372
57. Tango T. Statistical Methods for Disease Clustering. Springer, New York, 2010. 208-9.
58. Bertrand M, Duflo E, and Mullainathan S. How Much Should We Trust Differences-In-Differences Estimates? The Quarterly Journal of Economics. 2004;119(1):249-275.
59. Greenland S. Basic methods for sensitivity analysis of biases. International Journal of Epidemiology. IEA; 1996;25(6):1107-1116. PMID: 9027513
60. Rubin DB. Multiple imputation after 18+ years. Journal of the American Statistical Association. Taylor & Francis; 1996;91(434):473-489.
61. Marshall BD, and Galea S. Formalizing the role of agent-based modeling in causal inference and epidemiology. Am J Epidemiol. United States; 2015;181(2):92-9. PMID: 25480821
62. Hernán MA. Invited commentary: Agent-based models for causal inference—reweighting data and theory in epidemiology. Am J Epidemiol. United States; 2015;181(2):103-5. PMID: 25480820
63. Lesko CR, Cole SR, Hall HI, Westreich D, Miller WC, Eron JJ, Li J, Mugavero MJ, and CNICS Investigators. The effect of antiretroviral therapy on all-cause mortality, generalized to persons diagnosed with HIV in the USA, 2009-11. Int J Epidemiol. England; 2016;45(1):140-50. PMID: 26772869

FACILITIES AND OTHER RESOURCES.

The following research facilities and resources are available and will facilitate the success of proposed research project and training in epidemiologic research.

Institutional Descriptions:

Vanderbilt University: *(Nicholas S. Zeppos, Chancellor)*
Vanderbilt University is a private, non-sectarian university located in Nashville, Tennessee. It was founded in 1873 as the result of a gift by shipping and rail magnate Cornelius Vanderbilt, who hoped his gift and the work of the new university would "contribute to strengthening the ties that should exist between all sections of our common country" and help to heal the sectional wounds of the Civil War. Today, Vanderbilt is an internationally renowned academic institution offering undergraduate programs in the liberal arts and sciences, engineering, music, education and human development, as well as a full range of graduate and professional degrees. The combination of cutting edge research, liberal arts education, and a distinguished medical center creates an invigorating atmosphere where students tailor their education to meet their goals and researchers collaborate to solve complex problems affecting our health, culture and society.

Vanderbilt University Medical Center: *(Jeffrey R. Balser, M.D., Ph.D., Vice Chancellor for Health Affairs)*
Vanderbilt University Medical Center is a comprehensive health care facility dedicated to patient care, research, and the education of health care professionals. Its reputation for excellence in each of these areas has made Vanderbilt a major patient referral center for the South and Midwest. Vanderbilt University's medical education has been held in high esteem among its peer institutions, and that legacy continues. Translational research into the pathophysiology and treatment of disease, as well as studying fundamental biological properties, is the primary focus of discovery at Vanderbilt. Vanderbilt University Medical Center is ranked among the nation's best hospitals. Vanderbilt has more than 450 research laboratories supported by $385 million in extramural funds and approximately 545 graduate students and 400 postdoctoral fellows involved in research initiatives.

Vanderbilt University School of Medicine: *(Jeffrey R. Balser, M.D., Ph.D., Dean)*
The School of Medicine, originally part of the University of Nashville, was incorporated into Vanderbilt University in 1874 and awarded its first Vanderbilt medical degrees in 1875. Since the inception of the School of Medicine, a Vanderbilt medical education has been held in high esteem among its peer institutions, and that legacy continues today. Biomedical research at the School of Medicine has long been recognized for its contributions to the advancement of medicine. The School of Medicine currently has 2,147 faculty members and has more than 400 students. From 2000-2007, Vanderbilt University School of Medicine (VUSM) had the fastest growth in NIH funding among all academic medical centers (17.8%). Currently it ranks 10th in NIH funding among U.S. Medical Schools, with 586 NIH awards exceeding $240 million annually.

A. Clinical Research Facilities and Resources

1. **Office Space and Logistical Support**
   Infectious Diseases Conference Room, [redacted] The conference room is on [redacted]. It is a fully equipped multifunctional conference room that can be configured for meetings, training, luncheons or other needs for 35-40 people. It is equipped with wired and wireless internet connections, TV/VCR/DVD, dry erase board, projection screen, easels, and an overhead projector. The conference room has state-of-the-art videoconferencing capabilities, which can be utilized for videoconferencing with national and international collaborators (for example, collaborators at the North American AIDS Cohort Collaboration on Research and Design [NA-ACCORD] or external policymakers and policy symposia).

2. **The Vanderbilt AIDS Center**: The Vanderbilt AIDS Center is administratively based in the Division of Infectious Diseases of the Department of Medicine, and will provide research support during award period. The Vanderbilt AIDS Center coordinates all research related to HIV and AIDS at Vanderbilt, and promotes HIV care and education. Faculty is based in the Divisions of Infectious Diseases in the School of Medicine's Departments of Medicine and Pediatrics, as well as the Department of Microbiology and

Immunology, and the Vanderbilt Institute for Global Health (VIGH). However, faculty from the Schools of Nursing, Education, Business, Divinity, Law, and Music also participate. A major goal of the Vanderbilt AIDS center is to foster collaborations between clinicians and investigators, and there is a long history of cutting-edge clinical outcomes research on HIV/AIDS by Vanderbilt faculty. The Vanderbilt AIDS Center will provide an enriched training environment, with broad exposure to an active clinical research and clinical trial program.

a. **The Vanderbilt HIV Clinical Trials Unit** includes clinical research sites for the NIAID AIDS Clinical Trials Group (the Vanderbilt Therapeutics Clinical Research Site) and the NIAID HIV Vaccine Trials Network (the Vanderbilt HIV Vaccine Clinical Research Site), for new medications and vaccines for HIV, respectively. Most of the clinical HIV research programs (including the Vanderbilt HIV Clinical Trials Unit's Therapeutics Clinical Research Site) are integrated at the location of the HIV clinical care site, the Vanderbilt Comprehensive Care Clinic at Vanderbilt Health One Hundred Oaks.

b. **The Epidemiology/Outcomes Unit** conducts observational and translational research studies of HIV outcomes. Dr. Timothy Sterling is director of the unit which meets weekly to discuss ongoing projects and analyses. These meetings are directed by Dr. Sterling and are attended by David Haas, Bryan Shepherd (biostatistician), fellows, residents, and medical students. In addition to publishing work based on patients in the Vanderbilt Comprehensive Care Center, the Epidemiology/Outcomes Unit has collaborated with the Johns Hopkins University Adult HIV Clinic, the Case-Western Reserve University AIDS Clinical Trials Unit, the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD), the Antiretroviral Therapy Cohort, Collaboration (ART-CC), and the Caribbean, Central, and South America Network for HIV research (CCASAnet).

3. **The Vanderbilt Comprehensive Care Center (VCCC)** is the largest HIV/AIDS primary care clinic in the region, and the centralized medical home for almost all HIV-infected patients in Middle Tennessee. The Comprehensive Care Clinic (CCC), a non-profit entity now merged with Vanderbilt, started this clinic in 1994 and has enrolled more than 7000 patients into care. In 2010, Vanderbilt assumed responsibility for the clinical practice and management of the clinic. Using a medical care management approach, the VCCC offers medical treatment, mental health services, nutrition services, medical case management, and laboratory services. Research on HIV care outcomes has always been integral to the VCCC's mission. The VCCC's space has been specially designed for integrating clinical research into patient flow at its new facility at One Hundred Oaks in Nashville. All Vanderbilt medical records are electronic, and developed/maintained/improved by world-class Vanderbilt informatics experts. Outpatient and inpatient records are maintained in an electronic data warehouse that allows for access to data for research, as well as clinical care. An Informatics Working Group consisting of a Biomedical Informatics faculty member, Dr. Sterling, a database analyst based at the electronic data warehouse, and several research data managers and abstracters is supported by the Vanderbilt AIDS Center to meet research needs (as a core resource). This group meets weekly to address data needs in a timely manner.

   The VCCC staff includes four Infectious Diseases Certified HIV primary care physicians, three nurse practitioners providing primary care, and 10 to 15 Vanderbilt Infectious Diseases Fellows at any one time. High risk obstetricians from Vanderbilt Maternal/Fetal Medicine provide obstetric and gynecological care. The VCCC also employs a pharmacist, psychiatrist, psychiatric mental health nurse practitioner, and dietitian. Additional personnel includes four social service medical case managers, two nurse medical case managers, one early intervention services specialist, and a pharmacy assistance program coordinator, ensuring a comprehensive continuum of care for VCCC patients. Approximately 85% of VCCC patients reside in the middle Tennessee region, with the remainder coming from more distant locations in Tennessee and surrounding states. The VCCC has three satellite clinics, located in Springfield, Columbia, and Cookeville, TN.

B. Career Development Facilities and Resources

1. **Clinical and Translational Scientist Development (CTSD):** In 2007, Vanderbilt University was awarded a $40 million Clinical and Translational Science Award (CTSA) from the National Center for Research Resources of the NIH to expedite the translation of laboratory discoveries to patients in the community. The CTSD is the educational component of Vanderbilt's CTSA grant. The program provides an integrated career development program for all physician-scientists, regardless of their scope of research, and for

PhD-scientists engaged in translational or clinical research. The Office for CTSD will use endpoints such as publication rates, grant success (particularly K to R conversion), diversity among the faculty, retention of Newman Society members (see below) in academic medicine on the tenure track, and investment costs per faculty member to evaluate the success of its programs. Several resources available to young investigators are described below. Dr. Katherine Hartmann, M.D., Ph.D. serves as the Assistant Dean for Clinical and Translational Scientist Development.

a. **Vanderbilt Institutional Funding Programs-The Vanderbilt Physician Scientist Development (VPSD) and Vanderbilt Clinical and Translational Research Scholars (VCTRS) Programs:** These programs provide support to junior faculty and fellowship level trainees who are committed to a career in clinical or translational investigation, with a mentored research apprenticeship integrated with the didactic training. The programs provide salary support for trainees in clinical investigation, and additional funds for didactic coursework, research support and travel. The programs require awardees to work within the research space/program of the mentor, to ensure a close supervisory relationship while eliminating the need for the awardees to obtain their own supplies or equipment. The sponsoring clinical department chair must commit to provide 75% research time during the duration of the award. The clinical chair must also 1) provide support to the mentor's laboratory to support the activities of the applicant and 2) identify space and resources for the applicant's eventual emergence from the mentored setting as independent federal funding is secured. Candidates are selected on a competitive basis by a committee of Vanderbilt faculty who emphasize the quality of the mentor and his or her research environment, the training credentials of the applicant, and the quality of the research proposal. These programs are directed by Katherine Hartmann, M.D., Ph.D., Associate Dean for Clinical & Translational Scientist Development, who reports to the Dean of the School of Medicine, monitors the progress of all awardees, and engages departmental leadership if candidates require such support. These programs have been highly successful in bridging junior faculty physician-scientists into extramural career development awards.

b. **The Elliot Newman Society** is a professional organization for all physician-scientists and PhD-scientists supported by the VPSD/VCTRS Programs, by other Vanderbilt K12 programs, or by individual K awards. All members meet every 6 months with the Associate Dean for Clinical and Translational Scientist Development, Dr. Katherine Hartmann, M.D., Ph.D. The purpose of this meeting is to review the candidate’s career plan and mentorship plan. As K awardees, all Newman Society Members are expected to have at least 75% protected time for research. Failure to meet this requirement for protected time will result in withdrawal of institutional salary support or K award. The Newman Society also sponsors an annual retreat for current and former students in the Masters of Public Health (MPH) or Masters of Clinical Science Investigation (MSCI), as well as any current holder of internal Vanderbilt grants to discuss their research projects. Invited speakers include established investigators in various fields of medicine.

c. **Clinical Career Seminars** are monthly one-hour seminars delivered by leading Vanderbilt faculty from diverse backgrounds on career development. Topics for the 2011-2012 academic year include: Mentoring Panel, Clinical and Translational Research Opportunities at Vanderbilt University, Time Management, Getting a Job in Academia: Preparing Yourself, Putting Your Promotion Packet Together, Managing Your Lab Finances, Managing Your Lab Team, Your Professional Portfolio, and Transition to Independence: Getting Your First R01.

d. **Manuscript and Grant Writing Support** is available from the CTSD through the availability of a repository of successfully funded grants, as well as an internal pre-review of grants by senior faculty.

2. Graduate Degree Programs

a. **Master of Public Health (MPH):** The Vanderbilt MPH program was developed in 1996 and provides a basic training program for fellows and junior faculty in an academic career in epidemiologic, behavioral, outcomes, and health services research. This encompasses Phase III clinical trials, cohort, and case-control studies to quantify the effects of patient, environmental, and behavioral factors on risk of disease, health services research, outcomes research, behavioral studies, and policy development. Since the program began in 1996, over 100 students have graduated and 89% of graduates remain in academic medicine or public health fields. Over 600 research articles have been published by program

alumni, including publications in JAMA, New England Journal of Medicine, Cancer Research and other high quality journals and over 150 research grants have been obtained by alumni, including K awards, R awards, and several grants from nongovernment sources.

b. Master of Public Health, Health Policy Track: The Vanderbilt MPH program includes Epidemiology, Global Health, and Health Policy Tracks. The Health Policy track is focused on analyzing how changes to public health policy and financing influence service delivery, health care spending, quality of care, and access to services. The Health Policy track prepares students for health policy leadership positions in the public and private sectors, potentially serving in a wide range of applied roles including as analysts, consultants, and policymakers. Relevant classes offered include: PUBH 5520 Introduction to Health Policy; PUBH 5538 Health Services Administration: Program and Policy Evaluation; PUBH 5525 Health Economics; PUBH 5518 Research Ethics and Health Policy.

Brief course descriptions for select courses follow.

PUBH 5520 *Introduction to Health Policy*: This course addresses health policy from the perspectives of evidence development, analysis and economic impact within a socio-political context. There is a secondary focus on the role of regulation within the U.S. health care system.

PUBH 5538 *Health Services Administration: Program and Policy Evaluation*: The evaluation of changes in the health care delivery system, either through programs specifically implemented to achieve such changes or through changes in health care delivery/financing policies. The primary designs—before/after, concurrent/retrospective control, interrupted time-series—and their strengths and limitations. This course is taught by Wayne Ray, PhD. Dr. Ray is a Professor of Health Policy at Vanderbilt University School of Medicine. He founded the Vanderbilt Master of Public Health program and has been a Fellow of the International Society for Pharmacoepidemiology; he is the winner of Vanderbilt awards for innovative teaching (2004) and translational research (2015). Dr. Ray has research interests in population-based studies of therapeutic interventions and has published 200 studies that use observational methods to assess safety and efficacy or seek to define and improve suboptimal use of therapeutic interventions.

PUBH 5525 *Health Economics:* Conceptual and empirical analysis of demand for health, medical services, and insurance; decisions by physicians and hospitals about price, quantity, and quality of services; technological change; and structure and performance of the pharmaceutical industry. This course is taught by Christopher Carpenter, PhD. Professor Carpenter is a health economist who studies the effects of public policy interventions on health behaviors, particularly in the areas of substance use and cancer screenings. He is also an expert on LGBT economic demography. His current research examines the effects of minimum legal drinking ages in the United States and other countries as well as the effects of federal funding for cancer screenings for low-income populations.

3. The Office of Biomedical Research and Training (BRET) was established in 1999 to support and coordinate graduate education, postdoctoral training, minority affairs, and educational technology initiatives for the Vanderbilt biomedical research community. Under the guidance of Senior Associate Dean Dr. Roger Chalkley, the BRET staff handles applications and admissions to the Interdisciplinary Graduate Program (IGP) as well as Chemical and Physical Biology programs, coordinates the first-year IGP curriculum, provides educational technology support including web-based teaching and online distribution of course materials, organizes the Responsible Conduct of Research training, and maintains databases of research faculty involved in pre- and postdoctoral training. The Office of Career Development and Outcomes Analysis, based in BRET, holds a series of workshops and seminars periodically throughout the year. Topics for the 2011-2012 academic year include: Writing a Budget, Managing a Budget, and Get Clued into VICTR services and support (collaborative space, letters of support)**.**

4. Vanderbilt University Library System

a. Eskind Biomedical Library (EBL): The Annette and Irwin Eskind Biomedical Library (EBL) is the hub of VUMC information services and resources. Opened in 1994, the EBL is prominently located at the center of campus. It is part of the Informatics Center, a federally designated Integrated Advances Information Management System (IAIMS) test site. EBL's philosophy focuses on enabling information use at the point of need, providing extensive digital library of electronic journals, books, databases, and other resources, in addition to over 200,000 print volumes.

b. Jean and Alexander Heard Library, The Geographic Information Systems and Census Information services: The Geographic Information Systems and Census Information services of the Vanderbilt University Library are dedicated to providing the data, tools and training necessary to understand, analyze, and present geographic information. The service is designed to help Vanderbilt Students, Faculty, and staff as well as the community.

The Vanderbilt Library was chosen by the US Census Bureau as a designated Census Information Center (CIC) to assist the federal government in the dissemination of Census data to under-served communities, and to serve in partnerships with the international community, media, and nonprofit service providers in order to accomplish the goals set forth by the Census Bureau.

The Geographic Information Systems (GIS) service exists in conjunction with the CIC as many of our users wish to display their census information in the form of maps. The GIS service now includes, as well as reaches outside of, the use of census data to create maps and accomplish spatial analysis. The service offers practical software instruction, assists in the location, creation, and manipulation of data, and seeks to solve GIS related problems, as well as to produce maps for its users.

Hands-on GIS software, GIS concepts, and census information trainings are available to Vanderbilt students, faculty, and staff. GIS Services staff conduct occasional training for any member of the university community. Training services are listed through the University Calendar or the Scholarly Communication website.

Faculty can utilize the GIS Services staff to help plan and present GIS training and projects. ESRI online training courses are also available to students, faculty, and staff. The GIS office provides keycodes to access most of the training courses at no charge. Courses in GIS are available on campus through the Anthropology and Engineering departments, as are several GIS labs and public workstations.

C. Other Facilities and Resources

1. **Research Funding and Growth:** Vanderbilt University Medical Center (VUMC) has enjoyed a nearly decade-long expansion in NIH funding for biomedical research. For the period 2000-2005, VUMC became the fastest-growing academic medical center (AMC) research program in the nation on a percentage basis, with 17.3% compound annual growth. Since 2000, growth in NIH-sponsored research at VUMC has consistently outpaced the NIH budget annual percentage growth. This pattern has advanced VUMC quickly in the NIH rankings, from 24 in 2000 to 4 in 2011. Support for competitive research grants from all external sources was more than [redacted] in 2011. In 2005, VUMC created a new research enterprise strategic plan that has driven institution growth. Its three major foci are: 1) personalized health and healthcare, 2) therapeutic discovery and translation, and 3) public health and healthcare. A key to VUMC's success has been the ability to optimize research space productivity. Through strategic allocation of resources, VUMC has increased the financial productivity of research space in terms of direct revenue from all sponsors to [redacted] / sq. ft., near the top of the reported range of [redacted] /sq. ft.

2. **Vanderbilt Institute for Clinical and Translational Research (VICTR):** The CTSA helped create a unique resource, the new Vanderbilt Institute for Clinical and Translational Research (VICTR), the purpose of which is to provide next-generation support to faculty working to translate fundamental scientific discoveries into clinical practice, with innovative training programs, and state-of-the-art informatics and biostatistical methods. Examples of programs to support translational investigators are described below:

   a. Synthetic Derivative (SD) is a database containing clinical information derived from Vanderbilt's electronic medical record (EMR), labeled with a unique research identification number derived from the clinical medical record, and stripped of personal identifiers. Thus, the SD is a set of records that is no longer linked to the identified medical record from which it is derived and has been altered to the point it no longer closely resembles the original record. The SD can be used as a stand-alone research resource, or can be used in conjunction with the Vanderbilt DNA Databank (see below) to identify patient sets for genome-phenome analysis. To data there are approximately 1.9 million records which include data from narratives (clinical notes, discharge summaries, history and physicals, problem lists, surgical reports, progress notes, letters), diagnostic codes (including TB and HIV), procedural codes, reports (ECGs, pathology, echocardiograms), laboratory values, vital signs, and medication orders

   b. Vanderbilt DNA Databank (BioVU): In 2007, Vanderbilt investigators began extracting DNA from blood samples of adult patients at Vanderbilt that otherwise would be discarded, to create the

Vanderbilt DNA Databank (BioVU). To date it has acquired DNA samples from nearly 120,000 patients, linked to their matching electronic medical records. Both the samples and the records are “de-identified,” meaning that all personal information has been stripped away to guarantee patients’ anonymity. BioVU has been carefully reviewed to ensure it meets ethical standards for research. The “consent-to-treat” form for Vanderbilt patients includes a box that allows them to “opt out” of the databank. Only Vanderbilt researchers can apply as principal investigators to use BioVU, although their collaborators can be from other centers.

c. **Database Management:** Through resources provided through the CTSA and VICTR, a software application, REDCap (Research Electronic Data Capture), has been developed at Vanderbilt to collect and manage data for diverse clinical, epidemiologic, and translational research studies. The application was designed around the concept of giving research teams an easy method to specify project needs and rapidly develop secure, web based applications for collection, management, and sharing of research data. REDCap Survey was designed for studies where data are collected directly from the research participant. Both products include secure institutional data hosting and include full audit-trails in compliance with HIPAA security requirements. This program is available only to investigators from Vanderbilt and Meharry Medical College, but can be used by investigators at other institutions as long as they are part of a project/group from Vanderbilt that is utilizing REDCap or REDCap Survey. The International Epidemiologic Databases to Evaluate AIDS (IeDEA) network and Caribbean, Central and South America Network for HIV Epidemiology Research (CCASAnet), both funded by the NIH, utilize this distinctive Vanderbilt resource for their data coordination/management. See section C.6 (HIV Cohort Collaborations Associated with Vanderbilt University) below for more detail on CCASAnet.

d. **Studios** are a series of structured, dynamic sessions bringing together relevant Vanderbilt faculty research experts in a particular methodology to focus on a specific stage of research. VICTR offers studios for hypothesis generation, study design, implementation, analysis and interpretation, translation and manuscript development. These sessions are intended to enhance research quality, foster advances in clinical practice and improvements in patient health, increase publications, and generate new hypotheses. A studio consists of 2-6 experienced faculty selected to participate in a guidance session based on specific areas of research and needs identified by the investigator. Translation Studios are also available and are a structured guidance session to help researchers examine the broad community health implications of their research findings and identify opportunities for dissemination of relevant findings into practice.

e. **StarBRITE (Biomedical Research Initiation, Translation, and Education)** is a shared data infrastructure for the initiation and maintenance of human research programs that was developed to establish open channels for feedback and input from VICTR. It is an online central repository storing up-to-date study documents and project characteristics for Vanderbilt investigators. It also serves as a unified system for tracking research education, mentoring, conduct, collaboration, resource utilization, and productivity.

f. **Pilot funding** is available upon a minimal application process via expedited vouchers for up to $2000 for acquiring or analyzing small amounts of data required for a grant submission or funding of final manuscript preparation. The application is reviewed within 48 hours following the request and the funds are immediately accessible upon approval. Request of funding in excess of $2000 requires a more-in-depth application and committee review but the process is efficient and the funds can be made available in as little time as 2-4 weeks.

g. **The Clinical Research Center (CRC):** The purpose of the CRC is to provide the resources needed by clinical and translational investigators to carry out their research in an environment optimized for safety, comfort and convenience of the patient or volunteer, with the facilities and expertise to provide the most advantageous milieu in which to address the investigator's experimental requirements. This includes outpatient space, inpatient beds, laboratories, equipment and supplies for clinical research by the faculty of Vanderbilt University and their collaborating investigators. The CRC also serves as a resource for teaching medical, graduate, and other multidisciplinary students, a site for research on the methodology of patient care systems, and a unique environment for the apprenticeship of young clinical investigators. The CRC offers weekly workshops taught by Carlos Orozco, the Vanderbilt CRC Informatics Manager, and offering basic instruction and practical advice on a variety of issues and skills related to the conduct of clinical research. Sample topics include: how to use Microsoft Excel for

medical research; how to use queries in Microsoft Access; and how to use nQuery Advisor software to compute sample size estimates for common study designs. The class meets once a week and information is presented in an interactive format with computer demonstrations. A schedule of the CRC workshop series can be found at: http://www.mc.vanderbilt.edu/crc/workshop.html?value=archive.

3. **Vanderbilt Institute for Global Health (VIGH)**
The VIGH was inaugurated on July 1, 2005, when director Sten H. Vermund, M.D., Ph.D. came to Vanderbilt to become the first Amos Christie Chair in Global Health. The Institute for Global Health facilitates the expansion and coordination of global health **research, service and training initiatives** at Vanderbilt University, and reflects the university's commitment to improve health services and outcomes in resource limited settings. Under Dr. Vermund's guidance, its "center-without-walls" philosophy nurtures noncompetitive partnerships among and within departments and schools on campus, and with partner institutions around the globe. The Vanderbilt Institute for Global Health is expanding rapidly, having increased to more than 15 faculty members with appointments in Infectious Diseases, Pediatrics, Preventive Medicine, Obstetrics and Gynecology, Epidemiology, Biomedical Informatics, the School of Nursing, which work directly at the Institute, and numerous affiliated faculty members from across the institution. A global vision in health education is a core value of the Institute, and this is reflected in its strong commitment to training and research programs both at home and abroad. The extensive network and contacts that Dr. Vermund and his colleagues brought to Vanderbilt have facilitated the establishment of international training and research programs by Vanderbilt faculty, and broadened the range of opportunities available to students and fellows interested in these areas. Working with their colleagues at Vanderbilt and around the world, VIGH faculty members continually investigate new ways to develop innovative programs for addressing emerging global health challenges.

4. **Vanderbilt Department of Health Policy**
Vanderbilt University's new Department of Health Policy (Department Chair: Melinda Buntin, PhD) brings together a broad group of health policy scholars devoted to developing health policy solutions that can have a profound impact. The Department builds on a history of strong collaborative relationships with the Tennessee Department of Health, the Centers for Disease Control and Prevention, and several frontline policy makers to develop health policy solutions for our nation's most pressing health care challenges. The combination of a major research university and preeminent medical center gives Department faculty incredible opportunities to build relationships with frontline care providers and policymakers which can lead to breakthrough discoveries. The Department fosters a deep belief that research and innovative thinking should guide health policy relationships and help policymakers understand implications. The Department offers weekly seminars in health policy topics and in Fall 2015 began offering a Health Policy Track for the M.P.H. degree program.

   a. **Health Policy Methodology Group**: Dr. John Graves maintains a standing regularly-scheduled meeting of health policy experts, econometricians, clinical researchers, epidemiologists, biostatisticians, and data managers to rigorously interrogate methods which may be applied to epidemiologic cohort data to derive valid inferences for the effects of health policy changes. As selection bias and confounding may be inferential barriers when translating internally valid estimates of effect from a study population to a larger, or more diverse, target population, techniques such as inverse probability of selection weighting, calibration, or propensity score matching may be required to derive unbiased population-appropriate estimates. This group therefore seeks to derive analytic techniques which may be applied to Dr. Graves' ongoing research (e.g., and R01 examining the effects of health insurance coverage expansion on utilization and chronic disease outcomes in the Southern Community Cohort Study) and other, parallel projects, with similar methodologic barriers to overcome.

   b. **Institute for Medicine and Public Health:** The Department of Health Policy is a member of this growing community of researchers, teachers and experts are working collaboratively to address important health care issues, generate innovative hypotheses, and expedite discovery and dissemination of new knowledge. The Institute serves to motivate, educate and support investigators and educators who will translate new evidence into health care practice, thereby improving personal and community health.

5. **Vanderbilt Department of Biostatistics**

The School of Medicine at Vanderbilt University created the Department of Biostatistics in September 2003. The main goal of the Department of Biostatistics is to increase the quality and quantity of research in the School of Medicine with such mechanisms as developing study and experimental designs that maximize efficiency, interpretability, and generalizability of research, refining measurements to increase precision and sensitivity, and analyzing data in a powerful, robust, and reproducible fashion. Vanderbilt biostatisticians are available to assist in grant proposal development, specifically K award development, as well as manuscript writing to improve the chances of funding or publication. In addition to including biostatistician support in a grant budget, vouchers for biostatistics help are available through the VICTR funding mechanism. Relevant classes offered include: BIOS 8398 Special Topics: Spatial Analysis; BIOS 8395: Causal Inference.

Brief course descriptions for select courses follow.

BIOS 8398 *Special Topics: Spatial Analysis*: The Special Topics course on spatial analysis, taught by Dr. Chris Fonnesbeck, will include but not be restricted to the following content: geostatistics, spatial cluster detection, spatial generalized linear models, methods for mapping, and methods for spatial data manipulation. The focus will be on appropriate analytic methods to derive valid inference for spatially and temporally variable exposures and outcomes. Dr. Fonnesbeck currently leads a project on optimal control of disease outbreaks and is particularly interested in the use of spatial statistics and Bayesian hierarchical/multilevel modeling strategies for inference and prediction in epidemiology. Moreover, as a biostatistical software developer, he is the creator and co-developer of PyMC, a popular software package for Bayesian statistical analysis.

BIOS 8395 *Causal Inference*: This course, currently under development, provides an introduction to the framework for causal modeling in observational data. Topics include propensity score adjustment, inverse probability weighting, instrumental variables, and sensitivity analysis. Methods are applied to a variety of biomedical examples. The course will be taught by Dr. Bryan Shepherd. Dr. Shepherd's statistical methods research has a particular emphasis on causal inference and methods for epidemiological data. He has been involved in the development of causal inference methods important to HIV vaccine trials. Since he arrived at Vanderbilt, he has continued to develop and apply causal inference methods, and has branched into other areas including approaches for analyzing ordered categorical data, and measurement error methods.

a. **Daily Biostatistics clinics** are supported by the Vanderbilt CTSA grant and are available free of charge to Vanderbilt Investigators. These walk-in clinics are held in a group setting and cover a different biostatistics theme Monday through Friday (e.g. Monday – General: including Comparative Effectiveness Research, Prognosis, Diagnosis, Observational Research, Study Design, Analysis, Graphics and Thursday – Clinical Research).

b. **The Biostatistics Collaboration Center at Vanderbilt (BCC)** is a university sponsored core resource whose goal is to provide for, enhance, and/or facilitate statistical collaborations involving the design, conduct, analysis or publication of biomedical research at the university. The BCC is comprised of biostatisticians and computer systems analysts from the Department of Biostatistics who are available to work with faculty on a variety of projects. They offer a wide range of highly trained experts with unique expertise for almost any collaboration. The BCC has considerable expertise in the design, conduct, and analysis of large scale clinical trials and research design for basic biomedical research. Varying levels of expertise are available for consultation, from bachelor and master level trained biostatisticians and computer systems analysts to full professors. Services include, but not limited to, salaries, administrative costs, supplies, computing (software, hardware, and shared resources such as the **Advanced Computing Center for Research and Education (ACCRE)**), information technology support, and relevant professional development costs. ACCRE offers computing resources flexible enough to enable high performance computing applications in a wide variety of research and education areas, and also provides access to high performance storage resources.

   The clinics are open to all members of the Vanderbilt and Meharry communities who have methodologic questions about their research projects or about published articles. Mentors should attend with post-docs and students. Attendees should select the appropriate clinic day according to the schedule. Biostatistics clinics are sponsored by the Department of Biostatistics and VICTR.

Investigators should email biostat-clinic@list.vanderbilt.edu by 9am of the day they wish to attend. More information including daily themes and notes may be found at http://biostat.mc.vanderbilt.edu/Clinics.

6. Mentorship

The Department of Medicine and Division of Infectious Diseases place a high importance on mentorship of young investigators. Dr. Rebeiro has a strong relationship with his primary mentor, Dr. Timothy Sterling, as well as with his co-mentor Dr. John Graves. He has maintained standing weekly meetings with Dr. Sterling over the past two years.

Dr. Rebeiro's mentoring committee is composed of experienced and successful investigators who have collectively written numerous funded NIH grants and high-impact publications. The proposed study will benefit from the inclusion of health policy experts (Drs. Graves, Schaffner, and Holtgrave), epidemiologists (Drs. Sterling and Gange), biostatisticians (Drs. Fonnesbeck and Shepherd), and large cohort representatives (Drs. McGowan and Moore) who can provide expertise, mentoring, and advice in study design, health policy research, epidemiology, and biostatistics, specifically as they pertain to HIV quality of care, spatial statistics, and disease outcomes. His mentors' complementary skills will improve his chances for success as his career develops as an independent investigator.

a. Primary mentor: **Timothy R. Sterling, M.D.** (Professor of Medicine, Vanderbilt University) is a skilled clinical investigator with expertise in HIV and TB outcomes research. He has directed the Epidemiology Outcomes Unit in the Vanderbilt AIDS Center as well as TB research at the Nashville Metro-Davidson Health Department since 2003. He also serves as a principal investigator of the Vanderbilt site in the Tuberculosis Trials Consortium of the Centers for Disease Control and Prevention, and the NA-ACCORD. Dr. Sterling has mentored 9 fellows that have gone on to receive K awards and 5 that have received R awards from the NIH. Importantly, Dr. Sterling has a K24 award from the National Institute of Allergy and Infectious Diseases to mentor young investigators in translational HIV and TB research.

b. Co-mentor: **John A. Graves, Ph.D.** (Assistant Professor of Health Policy and Medicine, Vanderbilt University) has an interdisciplinary research focus on the development, implementation and evaluation of health care reforms at the state and federal level. He also leads a Health Policy Methodology group dedicated to exploring methods for obtaining valid inferences for policy impact from epidemiologic cohort data. His research on the dynamics of health insurance has played a particularly important role in recent policy debates: his research was cited in the U.S. Supreme Court's arguments over the Affordable Care Act in 2015 and was a key catalyst for regulatory changes affecting the way patients pay for insurance plans in the state insurance marketplaces created by the Affordable Care Act. His research portfolio includes NIH-funded research on the returns to health care spending and on the appropriate use of hospital quality measures to guide delivery system reforms. He has extensive experience in spatial econometrics. He is Principal Investigator on an R-01 assessing the impact of Medicaid expansion on chronic disease and mortality in the Southeastern United States. In addition, he was PI of a Robert Wood Johnson Foundation-funded national initiative to identify local gaps in primary care capacity under the Affordable Care Act's public and private coverage expansions. He has also mentored and continues to mentor other individuals successfully through T- and K-mechanisms.

c. Mentoring Committee Members:
(1) **William Schaffner, M.D.** (Professor of Health Policy, Professor of Medicine, Vanderbilt University) is an experienced researcher and mentor with more than 30 years of experience directly informing health policy at the state and federal level. Dr. Schaffner has served as the President of the Society for Healthcare Epidemiology of America and as chair of Preventive Medicine at Vanderbilt University. He is a consultant in public health policy for the World Health Organization, the Tennessee Department of Health, and the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention. In those capacities, he has accumulated extensive first-hand experience in translating evidence to policy while working with policy makers. He has mentored dozens of scientists, many of whom have gone on to serve in distinguished capacities directing public health policy, including the current state epidemiologist for Tennessee.

(2) **Christopher J. Fonnesbeck, Ph.D.** (Assistant Professor of Biostatistics, Vanderbilt University) is an established statistical methods expert, with particular expertise in the fields of spatial analysis, Bayesian statistics, and hierarchical/multilevel modeling strategies for inference and prediction in epidemiology. He provides quantitative expertise to the Evidence-based Practice Center (Vanderbilt Institute for Medicine and Public Health), the Department of Pediatrics/Division of Infectious Diseases, and the Department of Orthopedic Surgery and Rehabilitation, as well as leading research on his own grant studying the optimal control of disease outbreaks through decision analysis, collaborating with Penn State University and the University of Warwick. He has taught courses on introductory and advanced statistical computing (BIOS 6301; BIOS 8366) and takes mentoring responsibilities for biostatistics students seriously.

(3) **Bryan E. Shepherd, Ph.D.** (Associate Professor of Biostatistics, Vanderbilt University) is an established biostatistician and causal inference methodologist whose work can be broadly summarized as developing and applying novel statistical methods to medical studies, with an emphasis on studies of HIV/AIDS. For the past 10 years, he has been the lead statistician for the Caribbean, Central and South American network (CCASAnet) of the International epidemiologic Databases to Evaluate AIDS (IeDEA). He is also currently the Director of the Biostatistics and Biomedical Informatics Core of the Tennessee Center for AIDS Research (TN-CFAR). He has published over 130 peer-reviewed publications, and his statistical methods research has had a particular emphasis on causal inference and methods for epidemiological data. He has mentored several successful K-awardees.

(4) **David R. Holtgrave, Ph.D.** (Professor and Chair of Health, Behavior, and Society, Johns Hopkins University) is a researcher and policy maker who pursues the advancement of scientific understanding of the impact on health of behavior and the societal context. Prior to his positions in academia, Dr. Holtgrave oversaw HIV/AIDS services in the United States as director of the Division of HIV/AIDS Prevention: Intervention Research and Support in the National Center for HIV, STD and TB Prevention at the Centers for Disease Control and Prevention (CDC) from 1997 to 2001. Dr. Holtgrave's research has focused on the effectiveness and cost-effectiveness of a variety of HIV prevention interventions, and the relation of the findings of these studies to HIV prevention policy making. He has also investigated the relationship between social capital measures, infectious disease rates, and risk behavior prevalence. He has also examined the cost-effectiveness of mass media approaches to the prevention of tobacco use. He also currently serves as the Vice-Chair of the Presidential Advisory Council on HIV/AIDS.

(5) **Stephen J. Gange, Ph.D.** (Executive Vice Provost for Academic Affairs, Professor of Epidemiology, Johns Hopkins University) is an accomplished biostatistician and epidemiologist, an international leader in the practice of HIV epidemiology who serves on the United States Department of Health and Human Services Antiretroviral Therapy Guidelines Committee. He has an interest in causal inference and application of advanced statistical methods in HIV epidemiology. He has mentored 7 faculty under individual K awards from the NIH, several of whom have advanced to their own R funding. Dr. Gange currently has a U01 award from the NIAID for the "WIHS Data Management and Analysis Center (WDMAC)" (AI-042590) and has previously held a P30 award entitled "Biostatistics and Epidemiology Methodology," (AI-094189) also funded by NIAID. Additionally, he is Director of the Epidemiology/Biostatistics cores of both the NA-ACCORD and the Johns Hopkins University Center For AIDS Research (JHU CFAR).

d. Advisors for cohort utilization:
(1) **Catherine C. McGowan, M.D.** (Associate Professor of Medicine, Vanderbilt University) is a clinical researcher and educator who specializes in the management of adult HIV infection. She participates in the Epidemiology/Outcomes Unit of the Tennessee Center for AIDS Research, which utilizes patient data and specimen repositories from the Vanderbilt Comprehensive Care Clinic to examine HIV treatment outcomes. She is an expert in the international scale-up of HIV care, treatment, and research, and she is principal investigator of the Caribbean, Central, and South America network for HIV epidemiology (CCASAnet) of the NIH-funded International epidemiologic Databases to Evaluate AIDS (IeDEA).

(2) **Richard D. Moore, M.D., M.H.S.** (Professor of Medicine, Professor of Epidemiology, Johns Hopkins University) is recognized for mentorship of medical students, residents, fellows, and junior faculty in

HIV/AIDS Research. Winner of the David M. Levine Mentorship Award in the Johns Hopkins General Internal Medicine Department, he is an expert in pharmacoepidemiology, clinical epidemiology, and health services research, having authored over 450 publications. He is the Director of the Moore Clinic for HIV Care (begun in 1984), Director of the JHU CFAR Clinical Core, and Director of the Johns Hopkins Program for HIV Outcomes Research. He has been principal investigator of multiple NIH and HRSA grants (including both R and U mechanisms), and he is also principal investigator of the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) of IeDEA.

7. HIV Cohort Collaborations Associated with Vanderbilt University

a. North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD): The NA-ACCORD is a regional collaboration of single-site and multi-site cohorts that includes over 125,000 patients from 25 cohorts in the United States and Canada funded by the NIH (U01-AI-069918). The NA-ACCORD is a collaboration of both academic medical centers and community based facilities that deliver HIV primary and specialty care, combines classical epidemiological and clinical HIV cohorts, and is complemented by specimen repositories for conducting translational research. It includes investigators who have a high level of scientific expertise and clinic experience and has an efficient structure for harmonization of data and the conduct of analyses. Their goals are: (1) To establish a collaboration of North American HIV/AIDS cohorts and a data center for compilation of data to address HIV/AIDS research questions that cannot be accomplished through smaller cohorts; (2) To address scientific aims that focus on the failure of HAART; (3) To address additional scientific aims related to events that cannot be as well studied in smaller cohorts (for example, those that require large sample sizes, such as TB disease in a low-incidence setting); (4) To develop and apply novel statistical and epidemiological methodology that is applicable to these scientific research initiatives, and; (5) To collaborate with other regional cohorts to compare results and address questions of inter-regional importance.

The work of NA-ACCORD is organized into three major cores: (1) The Administrative Core (AC) is located at the Johns Hopkins University in Baltimore, MD. The AC staff is responsible for the administrative and operational functions of the NA-ACCORD; (2) The Data Management Core (DMC) is located at the University of Washington in Seattle, WA. The DMC provide expertise and experience in informatics that facilitate the merging of data from multiple heterogeneous sources and the ability to include additional sites over time. The NA-ACCORD does not maintain a centralized data base of all data collected by participating cohorts. For approved concept sheets inclusion criteria, variables, and time-lines are constructed for data collection and these data are abstracted from each cohort and transmitted to the DMC. Monitoring data quality includes systematic review of medical records, event driven audits, and verification of random samples of clinical events. Centralized data mapping was designed to specify how data are integrated into standard NA-ACCORD codes with known meanings; (3) The Epidemiology/Biostatistics Core (EBC) is located at Johns Hopkins and includes a network of leaders of HIV cohort studies who have developed innovative biostatistical and epidemiological methodologies. Databases generated by the DMC are transmitted to the EBC for statistical analyses.

A combination of topic-specific working groups and project-specific writing groups provides forums for communication among study investigators. Working groups have periodic conference calls and meetings to discuss ongoing projects and identify future projects. The following working groups are already established: (1) an antiretroviral therapy effectiveness working group, which oversees initiatives regarding major study outcomes (AIDS, death), therapies, and natural/treated history; (2) a toxicities and comorbidities working group which oversees initiatives regarding ARV toxicities and co-morbidities; (3) a specimen repository working group which advises the steering committee on use of specimens.

b. International Epidemiologic Databases to Evaluate AIDS (IeDEA): The IeDEA network (approximately 250,000 subjects) is an international research consortium established in 2005 and funded by the NIH to address the unique and evolving questions in HIV/AIDS research currently unanswerable by single cohorts. Seven regional centers including North America (NA-ACCORD), the Caribbean, Central, and South America (CCASAnet), Asia Pacific (TREAT Asia),

West Africa, Central Africa, East Africa and Southern Africa, collaborate to collect and define key variables, harmonize data, and implement methodology to effectively pool data-thus providing a cost effective means of generating large datasets to address high priority research questions and streamline HIV/AIDS research. The Vanderbilt Institute for Global Health, utilizing REDCap, serves as the data coordinating/management center for this network. Dr. William Wester, M.D., M.P.H., Assistant Professor of Medicine, and Dr. Mary Lou Lindegren, Associate Professor of Pediatrics, serve as principal investigators of the IeDEA Network Coordinating Center (INCC).

c. **Caribbean, Central and South America Network for HIV Epidemiology (CCASAnet):** CCASAnet is a collaborative network of observational HIV cohorts in Latin America and the Caribbean (approximately 20,000 subjects) and a regional member of IeDEA. The goal of this network is to create a shared repository of HIV data and use the combined data to answer questions about the characteristics of the regional HIV epidemic. Dr. Catherine McGowan at Vanderbilt University is the Principal Investigator for this collaboration and Bryan Shepherd, is a co-investigator. Dr. Timothy Sterling is also a co-investigator in CCASAnet and oversees all TB-related projects conducted in this collaboration. As with IeDEA, Vanderbilt University serves as the data coordinating/management center for this network through utilization of REDCap.

EQUIPMENT.

Please see section “FACILITIES AND OTHER RESOURCES” for additional information regarding support available for this project, including through the Vanderbilt University School of Medicine, within the Health Policy and Biostatistics Departments, and through the NA-ACCORD and CCASAnet Epidemiology/Biostatistics and Data Analysis Cores.

Dr. Rebeiro’s office, [redacted] Dr. Rebeiro has private office space located within the Division of Infectious Diseases [redacted] with a private phone, storage space, and desktop Dell computer. [redacted] He has administrative support for daily needs as well as grants management support from the main administrative office of the Division of Infectious Diseases. He has access to printers, copiers, fax machines, and other office support. He also has access to Adobe Acrobat, Microsoft Office, STATA, STAT Transfer, and Reference Manager software.

Infectious Diseases Conference Room, [redacted] The conference room [redacted] It is a fully equipped multifunctional conference room that can be configured for meetings, training, luncheons or other needs for 35-40 people. It is equipped with wired and wireless internet connections, TV/VCR/DVD, dry erase board, projection screen, easels, and overhead projector. The conference room has state-of-the-art videoconferencing capabilities, which can be utilized for videoconferencing with collaborators within NAACCORD.

North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD): The work of NA-ACCORD is organized into three major cores: (1) The Administrative Core (AC) is located at the Johns Hopkins University in Baltimore, MD; (2) The Data Management Core (DMC) is located at the University of Washington in Seattle, WA; (3) The Epidemiology/Biostatistics Core (EBC) is located at Johns Hopkins and includes a network of leaders of HIV cohort studies who have developed innovative biostatistical and epidemiological methodologies.

The EBC computing system is maintained autonomously by dedicated staff and includes:

- A dedicated Sun Microsystems Sun Fire E2900 server, used primarily for analytical tasks and intensive computational programming. It is an 8 RISC-based multiprocessor server with 1.2 GHZ per CPU and 32 GBs of main memory. A SUN Unified Storage System 7210 is equipped with 2.0 TB of disk space.
- Four PC servers configured to separately serve as user file server support and database management.
- A dual socket Windows 7 64 bit PC with dual Intel Xeon X5680 CPUs (each up to 3.6 GHz) in which each processor has 12 physical cores with 2 logical cores per physical core (i.e. 12 physical cores, 24 logical cores). This PC has 48 GB of RAM so that large data sets can be analyzed in parallel depending on the analysis. Solid-state drives with room for expansion provide fast data transfer from storage to RAM.
- Individual PCs and Mac Book Pro laptops running Windows or Mac OS. The EBC has all major computer packages installed, including current versions of SAS, R/Splus, and STATA. The center biostatisticians maintain an extensive collection of routines, primers, sample code, and validated sample code used for data analysis. The multiplatform configuration will adequately meet future demands for data management and complex statistical analyses and

modeling. PC database software of MS Access, and SQL Server 2005, in conjunction with ASP, XML, Visual Studio, and Java Script are primarily used to develop web-based data management systems. There are various printers, including color LaserJets, LaserJet8000s, LaserJet4100s, LaserJet 2420s, and a LaserJet5MX to support printing needs in TeX, Postscript, word processing and web browsing.

Dr. Richard Moore, M.D., M.H.S. (a collaborator on this project) is the PI for the NA-ACCORD and Professor of Medicine at Johns Hopkins University School of Medicine. Dr. Moore supports Dr. Rebeiro's K award application (see attached letter) and will offer data management and analysis support from the NA-ACCORD Data Management and Epidemiology/Biostatistics Cores.

The Advanced Computing Center for Research and Education (ACCRE): The Vanderbilt University ACCRE High Performance Computing cluster has over 4,000 processor cores. Processor cores each have 3 – 16 GB of memory. Compute nodes all run a 64-bit Linux OS and have a 250 GB – 1 TB hard drive and dual copper gigabit Ethernet ports. Forty-eight computing nodes are each equipped with 4X Nvidia GeForce GTX 480 GPU cards. Nodes are monitored via Nagios. Resource management, scheduling of jobs, and usage tracking are handled by an integrated scheduling system by Moab/Torque.

These utilities include an "advance reservation" system that allows a block of nodes to be reserved for prespecified periods of time (e.g., a class or lab session) for educational or research purposes. IBM's General Parallel File System (GPFS) is used for user home and data directories and scratch space. The ACCRE filesystem provides over 325 TB of usable disk space and can sustain more than 100 Gb/s of I/O bandwidth to the cluster. The home directories of all users are backed up daily to tape. The disk arrays are attached to a SAN fabric along with the storage nodes that then exports the file system to the rest of the cluster using a fully redundant design with no single point of failure. The daily operation and maintenance of ACCRE is provided by ten support personnel, including eight system administrators, programmers and researchers with a combination of more than 60 years of computing experience. Support for system services is provided on a 24/7/365 basis for urgent issues, with on-call pager based support on nights and weekends. Cluster uptime has been better than 95% over the past three years. An online support ticket system is used to track and resolve problems and user questions. ACCRE staff are responsible for maintaining core system hardware, core system software, networking, user support, tape backup services, disk storage, logistical storage development work, education, and management/finance support. Dr. Rebeiro may utilize the ACCRE for data management and analysis as necessary.

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Prefix: First Name*: Peter Middle Name F Last Name*: Rebeiro Suffix:

Position/Title*: Research Asst Professor
Organization Name*: Vanderbilt University Medical Center
Department: [redacted]
Division:
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*:
Province:
Country*:
Zip / Postal Code*:

Phone Number*: [redacted] Fax Number: [redacted]

E-Mail*: [redacted]

Credential, e.g., agency login: [redacted]

Project Role*: PD/PI Other Project Role Category:

Degree Type: Doctor of Philosophy Degree Year: 2014

Attach Biographical Sketch*: File Name: ID-0039416_BN-1_BIOSKETCH.pdf

Attach Current & Pending Support: File Name:

Funding Opportunity Number: PA-16-190 . Received Date: 2017-01-05T17:21:11.000-05:00

PROFILE - Senior/Key Person

Prefix: First Name*: Timothy Middle Name R Last Name*: Sterling Suffix:

Position/Title*: Professor
Organization Name*: Vanderbilt University Medical Center
Department: [redacted]
Division:
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*:
Province:
Country*:
Zip / Postal Code*:

Phone Number*: [redacted] Fax Number: [redacted]

E-Mail*: [redacted]

Credential, e.g., agency login: [redacted]

Project Role*: Other (Specify) Other Project Role Category: Mentor

Degree Type: Medical Doctor Degree Year: 1989

Attach Biographical Sketch*: File Name: ID-0051371_BN-1_BIOSKETCH.pdf

Attach Current & Pending Support: File Name: ID-0051371_BN-2_CURRENTPENDING.pdf

PROFILE - Senior/Key Person

Prefix: First Name*: John Middle Name A Last Name*: Graves Suffix:

Position/Title*: Asst Professor
Organization Name*: Vanderbilt University Medical Center
Department: [redacted]
Division:
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*:
Province:
Country*:
Zip / Postal Code*:

Phone Number*: [redacted] Fax Number: [redacted]

E-Mail*: [redacted]

Credential, e.g., agency login: [redacted]

Project Role*: Other (Specify) Other Project Role Category: Co-Mentor

Degree Type: Doctor of Philosophy Degree Year: 2011

Attach Biographical Sketch*: File Name: ID-0101157_BN-1_BIOSKETCH.pdf

Attach Current & Pending Support: File Name: ID-0101157_BN-2_CURRENTPENDING.pdf

PROFILE - Senior/Key Person

Prefix: First Name*: Richard Middle Name D. Last Name*: Moore Suffix:

Position/Title*: Professor
Organization Name*: Johns Hopkins University
Department:
Division:
Street1*: [redacted]
Street2:
City*:
County:
State*: [redacted]
Province:
Country*:
Zip / Postal Code*:

Phone Number*: [redacted] Fax Number: [redacted]

E-Mail*: [redacted]

Credential, e.g., agency login:

Project Role*: Other (Specify) Other Project Role Category: Advisor

Degree Type: Degree Year:

Attach Biographical Sketch*: File Name: ID-21644_BN-1_BIOSKETCH.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: Stephen Middle Name Last Name*: Gange Suffix:

Position/Title*: Sr. Assoc Dean for Academic Affairs
Organization Name*: Johns Hopkins
Department:
Division:
Street1*: [redacted]
Street2:
City*:
County:
State*: [redacted]
Province:
Country*:
Zip / Postal Code*:

Phone Number*: [redacted] Fax Number: [redacted]

E-Mail*: [redacted]

Credential, e.g., agency login:

Project Role*: Other (Specify) Other Project Role Category: Mentoring Committee

Degree Type: Degree Year:

Attach Biographical Sketch*: File Name: ID-25353_BN-1_BIOSKETCH.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: Catherine Middle Name C Last Name*: McGowan Suffix:

Position/Title*: Assoc Professor
Organization Name*: Vanderbilt University Medical Center
Department: [redacted]
Division:
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*:
Province:
Country*: [redacted]
Zip / Postal Code*:

Phone Number*: [redacted] Fax Number: [redacted]

E-Mail*: [redacted]

Credential, e.g., agency login: [redacted]

Project Role*: Other (Specify) Other Project Role Category: Advisor

Degree Type: Medical Doctor Degree Year: 1987

Attach Biographical Sketch*: File Name: ID-0006287_BN-1_BIOSKETCH.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: David Middle Name Last Name*: Holtgrave Suffix:

Position/Title*: Professor
Organization Name*: Johns Hopkins University
Department:
Division:
Street1*: [redacted]
Street2:
City*:
County:
State*:
Province:
Country*:
Zip / Postal Code*:

Phone Number*: [redacted] Fax Number:

E-Mail*: [redacted]

Credential, e.g., agency login:

Project Role*: Other (Specify) Other Project Role Category: Mentoring Committee

Degree Type: Degree Year:

Attach Biographical Sketch*: File Name: ID-26286_BN-1_BIOSKETCH.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: William Middle Name Last Name*: Schaffner Suffix:

Position/Title*: Professor
Organization Name*: Vanderbilt University Medical Center
Department: [redacted]
Division:
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*:
Province:
Country*:
Zip / Postal Code*:

Phone Number*: [redacted] Fax Number: [redacted]

E-Mail*: [redacted]

Credential, e.g., agency login: [redacted]

Project Role*: Other (Specify) Other Project Role Category: Mentoring Committee

Degree Type: Degree Year:

Attach Biographical Sketch*: File Name: ID-0000414_BN-1_BIOSKETCH.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: Christopher Middle Name J Last Name*: Fonnesbeck Suffix:

Position/Title*: Asst Professor
Organization Name*: Vanderbilt University Medical Center
Department: [redacted]
Division:
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*:
Province:
Country*:
Zip / Postal Code*:

Phone Number*: [redacted] Fax Number: [redacted]

E-Mail*: [redacted]

Credential, e.g., agency login: [redacted]

Project Role*: Other (Specify) Other Project Role Category: Advisor

Degree Type: Doctor of Philosophy Degree Year: 2005

Attach Biographical Sketch*: File Name: ID-0094542_BN-1_BIOSKETCH.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: Bryan Middle Name E Last Name*: Shepherd Suffix:

Position/Title*: Assoc Professor
Organization Name*: Vanderbilt University Medical Center
Department: [redacted]
Division:
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*:
Province:
Country*:
Zip / Postal Code*:

Phone Number*: [redacted] Fax Number: [redacted]

E-Mail*: [redacted]

Credential, e.g., agency login: [redacted]

Project Role*: Other (Specify) Other Project Role Category: Advisor

Degree Type: Doctor of Science Degree Year: 2005

Attach Biographical Sketch*: File Name: ID-0065337_BN-1_BIOSKETCH.pdf

Attach Current & Pending Support: File Name:

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.

Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Rebeiro, Peter F.

eRA COMMONS USER NAME (agency login):

POSITION TITLE: Research Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Yale University, New Haven, CT	BA	12/2005	Biology
Johns Hopkins University, Baltimore, MD	ScM	05/2012	Epidemiology
Johns Hopkins University, Baltimore, MD	MHS	08/2014	Biostatistics
Johns Hopkins University, Baltimore, MD	PHD	08/2014	Epidemiology

A. Personal Statement

The execution of epidemiologic research to inform public health action is an incredibly complex and rewarding task that requires the input, collegial cooperation, and applied knowledge of several dedicated individuals. Beyond my formal education, I have participated in HIV epidemiology and outcomes research in nearly every capacity: as a data abstractor, an IRB liaison, a data manager and quality control officer, a protocol analyst and editor, a statistical analyst, an abstract and manuscript editor and author, and others. I have also received extensive training in epidemiologic methods and biostatistics, making my skillset particularly well suited to the task of analyzing observational data while also providing me a solid foundation on which to build my understanding of policy evaluation and econometrics. Because of this varied experience, both in the development of questions and in the execution of the steps necessary to answer them scientifically and disseminate the results through publication, I believe that I have demonstrated my abilities as a competent researcher and epidemiologist. I believe I have also demonstrated my capacity for productive research collaborations on closely related topics, including through the use of uniquely rich data sources and by availing myself of the expertise of leaders in the field. I am currently working with both the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) and the Caribbean, Central and South American network for HIV epidemiology (CCASAnet) of the NIH-funded International epidemiologic Databases to Evaluate AIDS (IeDEA), and am therefore also experienced in working with longitudinal data from large, geographically diverse HIV-infected populations. I therefore feel that I am well positioned to leverage these opportunities to answer significant questions in the arena of health policy and make a meaningful contribution to improve the lives of those with HIV.

1. **Rebeiro PF**, Cesar C, Shepherd BE, De Boni RB, Cortes CP, Rodriguez F, Belaunzarán-Zamudio P, Pape JW, Padgett D, Hoces D, McGowan CC, Cahn P for the Caribbean, Central and South America network for HIV epidemiology (CCASAnet). Assessing the HIV Care Continuum in Latin America: progress in clinical retention, cART use, and viral suppression. J Int AIDS Soc. 2016 Apr 8;19(1):20636. Pubmed PMID: 27065108 PMCID: PMC4827101
2. **Rebeiro PF**, Althoff KN, Lau B, Gill J, Abraham AG, Horberg MA, Kitahata MM, Yehia BR, Samji H, Brooks JT, Buchacz K, Napravnik S, Silverberg MJ, Rachlis A, Gebo KA, Sterling TR, Moore RD, Gange SJ. Laboratory Measures as Proxies for Primary Care Encounters: Implications for Quantifying Clinical Retention Among HIV-Infected Adults in North America. Am J Epidemiol. 2015 Dec 1;182(11):952-60. PubMed PMID: 26578717. PubMed Central PMCID: PMC4655744.
3. **Rebeiro PF**, Horberg MA, Gange SJ, Gebo KA, Yehia BR, Brooks JT, Buchacz K, Silverberg MJ, Gill J, Moore RD, Althoff KN. Strong agreement of nationally recommended retention measures from the Institute of Medicine and Department of Health and Human Services. PLoS One. 2014;9(11):e111772. PubMed PMID: 25375099; PubMed Central PMCID: PMC4222946.

4. **Rebeiro P**, Althoff KN, Buchacz K, Gill J, Horberg M, Krentz H, Moore R, Sterling TR, Brooks JT, Gebo KA, Hogg R, Klein M, Martin J, Mugavero M, Rourke S, Silverberg MJ, Thorne J, Gange SJ. Retention among North American HIV-infected persons in clinical care, 2000-2008. J Acquir Immune Defic Syndr. 2013 Mar 1;62(3):356-62. PubMed PMID: 23242158; PubMed Central PMCID: PMC3661708.

B. Positions and Honors

Positions and Employment

2001 - 2003	Research Assistant, Vanderbilt University, Medicine/Infectious Diseases, Nashville, TN
2004 - 2007	Research Analyst, Vanderbilt University, Medicine/Infectious Diseases, Nashville, TN
2007 - 2010	Research Coordinator, Vanderbilt University, Medicine/Infectious Diseases, Nashville, TN
2010 - 2014	Research Assistant, Johns Hopkins University, Epidemiology, Baltimore, MD
2011 - 2011	Teaching Assistant, Johns Hopkins University, Epidemiology, Baltimore, MD
2012 - 2012	Teaching Assistant, Johns Hopkins University, Epidemiology, Baltimore, MD
2012 - 2012	Lead Teaching Assistant, Johns Hopkins University, Epidemiology, Baltimore, MD
2014 -	Research Assistant Professor, Vanderbilt University, Medicine/Infectious Diseases, Nashville, TN

Other Experience and Professional Memberships

2012 -	Member, International AIDS Society
2013 -	Member, Society for Epidemiologic Research

Honors

2011	Merit-based 75% tuition scholarship, Johns Hopkins University
2012	Merit-based 100% tuition scholarship (100%, 85%, and 85% in years I, II, and III), Johns Hopkins University
2012	Mary Meyer Scholarship (100% and 50% stipend for years I and II), Johns Hopkins University
2013	Student Dissertation Workshop scholarship (competitive scholarship for conference attendance and participation in the Student Dissertation Workshop), Society for Epidemiologic Research
2014	Gordis Fellowship (Competitive Teaching Award including Salary as an Undergraduate Instructor), Johns Hopkins University
2015	National Institutes of Health (NIH) Loan Repayment Program awardee

C. Contribution to Science

1. My work on HIV Continuum of Care outcomes, particularly the key stage of clinical retention and the "churn" of patient populations through clinical care in North America, has been highly cited among prominent scholars in the field. This work has also been used by Office of National AIDS Policy members to inform public health policy, including the US National HIV/AIDS Strategy. I continue to be engaged in productive collaborations with the NA-ACCORD and CCASAnet groups of IeDEA, examining topics related to the quality of HIV care, health services, and health policy in the United States, Canada, and Latin America.

    a. **Rebeiro PF**, Cesar C, Shepherd BE, De Boni RB, Cortes CP, Rodriguez F, Belaunzarán-Zamudio P, Pape JW, Padgett D, Hoces D, McGowan CC, Cahn P for the Caribbean, Central and South America network for HIV epidemiology (CCASAnet). Assessing the HIV Care Continuum in Latin America: progress in clinical retention, cART use, and viral suppression. J Int AIDS Soc. 2016 Apr 8;19(1):20636. Pubmed PMID: 27065108 PMCID: PMC4827101

    b. **Rebeiro PF**, Althoff KN, Lau B, Gill J, Abraham AG, Horberg MA, Kitahata MM, Yehia BR, Samji H, Brooks JT, Buchacz K, Napravnik S, Silverberg MJ, Rachlis A, Gebo KA, Sterling TR, Moore RD, Gange SJ. Laboratory Measures as Proxies for Primary Care Encounters: Implications for Quantifying Clinical Retention Among HIV-Infected Adults in North America. Am J Epidemiol. 2015 Dec 1;182(11):952-60. PubMed PMID: 26578717. PubMed Central PMCID: PMC4655744.

c. **Rebeiro PF**, Horberg MA, Gange SJ, Gebo KA, Yehia BR, Brooks JT, Buchacz K, Silverberg MJ, Gill J, Moore RD, Althoff KN. Strong agreement of nationally recommended retention measures from the Institute of Medicine and Department of Health and Human Services. PLoS One. 2014;9(11):e111772. PubMed PMID: 25375099; PubMed Central PMCID: PMC4222946.

d. **Rebeiro P**, Althoff KN, Buchacz K, Gill J, Horberg M, Krentz H, Moore R, Sterling TR, Brooks JT, Gebo KA, Hogg R, Klein M, Martin J, Mugavero M, Rourke S, Silverberg MJ, Thorne J, Gange SJ. Retention among North American HIV-infected persons in clinical care, 2000-2008. J Acquir Immune Defic Syndr. 2013 Mar 1;62(3):356-62. PubMed PMID: 23242158; PubMed Central PMCID: PMC3661708.

2. While working as a research assistant with the Vanderbilt Adult AIDS Clinical Trials Group, I was fortunate to be allowed to contribute substantively to work on oxidant stress and pharmacogenomics related to early PI and NNRTI regimens. These studies have added considerably to the body of knowledge on metabolic processes during advanced HIV infection and its treatment with antiretroviral agents. The work on NNRTI hepatotoxicity mediation through CYP2B6, CYP3A4, and MDR1 variants has been particularly highly cited.

a. Hulgan T, Donahue JP, Hawkins C, Unutmaz D, D'Aquila RT, Raffanti S, Nicotera F, **Rebeiro P**, Erdem H, Rueff M, Haas DW. Implications of T-cell P-glycoprotein activity during HIV-1 infection and its therapy. J Acquir Immune Defic Syndr. 2003 Oct 1;34(2):119-26. PubMed PMID: 14526200.

b. Hulgan T, Morrow J, D'Aquila RT, Raffanti S, Morgan M, **Rebeiro P**, Haas DW. Oxidant stress is increased during treatment of human immunodeficiency virus infection. Clin Infect Dis. 2003 Dec 15;37(12):1711-7. PubMed PMID: 14689356.

c. Ritchie MD, Haas DW, Motsinger AA, Donahue JP, Erdem H, Raffanti S, **Rebeiro P**, George AL, Kim RB, Haines JL, Sterling TR. Drug transporter and metabolizing enzyme gene variants and nonnucleoside reverse-transcriptase inhibitor hepatotoxicity. Clin Infect Dis. 2006 Sep 15;43(6):779-82. PubMed PMID: 16912956.

3. This work, performed while I was a research assistant with the Vanderbilt-Meharry Center For AIDS Research, contributed greatly to clinical awareness of the impact of laboratory processing procedures using PPT tubes on the spurious detectability of plasma HIV-1 RNA viral loads. The manuscript was later cited in the recommendations for ART from the International AIDS Society: "Antiretroviral Treatment of Adult HIV Infection: Recommendations of the International AIDS Society–USA Panel" (Thompson, Aberg, et al.; JAMA 2010).

a. **Rebeiro PF**, Kheshti A, Bebawy SS, Stinnette SE, Erdem H, Tang YW, Sterling TR, Raffanti SP, D'Aquila RT. Increased detectability of plasma HIV-1 RNA after introduction of a new assay and altered specimen-processing procedures. Clin Infect Dis. 2008 Nov 15;47(10):1354-7. PubMed PMID: 18922071; PubMed Central PMCID: PMC2605467.

4. As a research assistant with the Epidemiology/Outcomes unit of the Vanderbilt-Meharry Center For AIDS Research, I contributed to work examining the effect of pregnancy on various HIV clinical outcomes, and disparities in antiretroviral therapy use and mortality by sex. These studies enriched the body of literature related to outcome and treatment disparities in a vulnerable population of concern and addressed complications in the understudied population of pregnant HIV-infected women in resource-rich settings.

a. Tai JH, Udoji MA, Barkanic G, Byrne DW, **Rebeiro PF**, Byram BR, Kheshti A, Carter JD, Graves CR, Raffanti SP, Sterling TR. Pregnancy and HIV disease progression during the era of highly active antiretroviral therapy. J Infect Dis. 2007 Oct 1;196(7):1044-52. PubMed PMID: 17763327.

b. Lemly DC, Shepherd BE, Hulgan T, **Rebeiro P**, Stinnette S, Blackwell RB, Bebawy S, Kheshti A, Sterling TR, Raffanti SP. Race and sex differences in antiretroviral therapy use and mortality among HIV-infected persons in care. J Infect Dis. 2009 Apr 1;199(7):991-8. PubMed PMID: 19220139.

c. Melekhin VV, Shepherd BE, Stinnette SE, **Rebeiro PF**, Barkanic G, Raffanti SP, Sterling TR. Antiretroviral therapy initiation before, during, or after pregnancy in HIV-1-infected women: maternal virologic, immunologic, and clinical response. PLoS One. 2009 Sep 9;4(9):e6961. PubMed PMID: 19742315; PubMed Central PMCID: PMC2734183.

d. Melekhin VV, Shepherd BE, Jenkins CA, Stinnette SE, **Rebeiro PF**, Bebawy SS, Rasbach DA, Hulgan T, Sterling TR. Postpartum discontinuation of antiretroviral therapy and risk of maternal AIDS-defining events, non-AIDS-defining events, and mortality among a cohort of HIV-1-infected women in the United States. AIDS Patient Care STDS. 2010 May;24(5):279-86. PubMed PMID: 20438375; PubMed Central PMCID: PMC2875979.

5. This work surrounding substance use and its impact on HIV clinical outcomes in a large Southeastern clinical cohort was completed while I was research coordinator at the Vanderbilt-Meharry Center For AIDS Research. The manuscripts contributed substantively to the literature exploring the relationship between substance use and HIV disease progression in clinical settings.

   a. McGowan CC, Weinstein DD, Samenow CP, Stinnette SE, Barkanic G, **Rebeiro PF**, Sterling TR, Moore RD, Hulgan T. Drug use and receipt of highly active antiretroviral therapy among HIV-infected persons in two U.S. clinic cohorts. PLoS One. 2011 Apr 25;6(4):e18462. PubMed PMID: 21541016; PubMed Central PMCID: PMC3081810.
   b. Qian HZ, Stinnette SE, **Rebeiro PF**, Kipp AM, Shepherd BE, Samenow CP, Jenkins CA, No P, McGowan CC, Hulgan T, Sterling TR. The relationship between injection and noninjection drug use and HIV disease progression. J Subst Abuse Treat. 2011 Jul;41(1):14-20. PubMed PMID: 21349679; PubMed Central PMCID: PMC3110534.

Complete List of Published Work in MyBibliography
http://www.ncbi.nlm.nih.gov/sites/myncbi/1f1ECwwJzoyAs/bibliography/40647706/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

U01-AI069923-12, NIAID/NIH
Catherine C. McGowan (PI)
07/01/16-06/30/21
Caribbean, Central and South American Network for HIV Epidemiology
This project aims to assess the epidemiology of HIV/AIDS as the Caribbean, Central and South American component of the International epidemiologic Databases to Evaluate AIDS (IeDEA) consortium
Role: KP

P30AI110527, NIAID/NIH
Simon A. Mallal (PI)
04/01/15-03/31/20
Tennessee Center for AIDS Research (TN-CFAR)
The Tennessee CFAR (TN-CFAR) is an HIV/AIDS research collaboration between Vanderbilt University, Meharry Medical College, and the Tennessee State Department of Health. The TN- CFAR aims to enhance HIV/AIDS-related research by coordinating institutional and community resources, with the goal of reducing the burden of HIV/AIDS in our state and generalizing these benefits nationally and internationally.
Role: KP

Completed Research Support

F31 DA035713-01
Rebeiro, Peter F (PI)
09/01/13-08/31/14
Epidemiology of Clinical Retention Among HIV-Infected Persons in North America
Role: PI

U01-AI069918, NIAID/NIH
Richard D. Moore (PI)
06/30/14-06/30/15
North American AIDS Cohort Collaboration on Research and Design (Mapping Supplement)
This project aims to assess the epidemiology of HIV/AIDS as the North American component of the International epidemiologic Databases to Evaluate AIDS (IeDEA) consortium. In particular, this supplement is concerned with geographic mapping of common HIV indicators in an informative and timely manner in a publically accessible forum
Role: KP

U01-AI042590, NIAID/NIH
Stephen J. Gange (PI)
01/01/13-01/01/14
WIHS Data Management and Analysis Center (WDMAC)
This project addressed data cleaning and analytic dataset construction for studies conducted within the Women's Interagency HIV Study (WIHS)
Role: GR

U01-AI069918, NIAID/NIH
Richard D. Moore (PI)
01/01/10-01/01/13
North American AIDS Cohort Collaboration on Research and Design
This project addressed data cleaning and analytic dataset construction for studies conducted within the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD)
Role: GR

P30-AI54999, NIAID/NIH
David W. Haas (PI)
01/01/04-01/01/10
Vanderbilt-Meharry Center for AIDS Research (CFAR)
This project addressed HIV basic science and epidemiologic research in a clinical cohort based in Nashville, TN.
Role: KP

BIOGRAPHICAL SKETCH

NAME: Sterling, Timothy R.

eRA COMMONS USER NAME: [redacted]

POSITION TITLE: Professor of Medicine

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Colgate University Hamilton, NY	B.A.	05/1985	Chemistry, German
Columbia University College of Physicians & Surgeons New York, NY	M.D.	05/1989	Medicine
Columbia Presbyterian Medical Center New York, NY		06/1992	Internal Medicine
Johns Hopkins University School of Medicine Baltimore, MD		06/1998	Infectious Diseases

A. Personal Statement

I am an infectious disease physician-scientist with expertise in the epidemiology and treatment of HIV and TB. I am the director of the Epidemiology and Outcomes Working Group of the Vanderbilt Comprehensive Care Clinic HIV Cohort. I established the Epi-Outcomes group in 2003 and have led it since its inception. I have been successful in mentoring young trainees and junior faculty for academic positions and NIH funding. Since 1998 I have mentored 58 investigators, including 10 who have obtained K23 or K08 awards, and 6 who have R01 funding. My trainees have also benefited from three multi-center HIV cohort collaborations that I participate in: the North American ACCORD, the Caribbean Central America South America network (CCASAnet) (both in the International epidemiologic Databases to Evaluate AIDS (IeDEA) network, and the Antiretroviral Therapy Cohort Collaboration (ART-CC). I lead efforts for the Regional Prospective Observational Research for TB **(**RePORT)-Brazil, and I have additional TB research collaborations in Peru and South Africa, as well as through the IeDEA network. I am well-suited to mentor Dr. Rebeiro. Of my 184 publications, the following are of interest for this application, including recent studies performed with Dr. Rebeiro:

1. Rebeiro P, Althoff, KN, Buchacz K, Gill MJ, Horberg M, Krentz H, Moore R, **Sterling TR**, Brooks JT, Gebo KA, Hogg R, Klein M, Martin J, Mugavero M, Rourke S, Thorne J, Gange SJ for the North American AIDS Cohort Collaboration (NA-ACCORD). Retention Among North American HIV–infected Persons in Clinical Care, 2000-2008. J Acquir Immune Defic Syndr. 2013 Mar 1; 62(3): 356-362. PMCID: PMC3661708
2. Althoff KN, Rebeiro P, Brooks JT, Buchacz K, Gebo K, Martin J, Hogg R, Thorne JE, Klein M, Gill MJ, **Sterling TR**, Yehia B, Silverberg MJ, Crane H, Justice AC, Gange SJ, Moore R, Kitahata MM, Horberg MA; for the NA-ACCORD. Disparities in the quality of HIV care when using US Department of Health and Human Services indicators. Clin Infect Dis. 2014 Apr;58(8):1185-9. PMCID: PMC3967825
3. Rebeiro PF, Althoff KN, Lau B, Gill J, Abraham AG, Horberg MA, Kitahata MM, Yehia BR, Samji H, Brooks JT, Buchacz K, Napravnik S, Silverberg MJ, Rachlis A, Gebo KA, **Sterling TR**, Moore RD, Gange SJ for the NA-ACCORD. Laboratory measures are imperfect proxies of primary care encounters: implications for quantifying clinical retention among HIV-infected adults in North America. Am J Epidemiol 2015 Dec 1;182(11)952-60. PMCID: PMC4655744
4. Althoff KN, Rebeiro PF, Hanna DB, et al, **Sterling TR**, et al, Pape JW, Cahn P, McGowan C; NA-ACCORD) and the Caribbean, Central and the South America Network for HIV Epidemiology (CCASAnet). A picture is worth a thousand words: maps of HIV indicators to inform research, programs, and policy from NA-ACCORD and CCASAnet clinical cohorts. J Int AIDS Soc. 2016 Apr 4;19(1):20707. PMCID: PMC4821890

B. Positions and Honors

Positions and Employment

1992-1996 Staff Physician, U.S. Air Force Medical Center Keesler, Keesler AFB, MS.
1998-2002 Assistant Professor of Medicine & Epidemiology, Johns Hopkins University School of Medicine
2002-2003 Associate Professor of Medicine & Epidemiology, Johns Hopkins University School of Medicine
1998-2003 Medical Director, Baltimore City Tuberculosis Clinic
2003-2008 Associate Professor of Medicine, Vanderbilt University School of Medicine
2003-present Director, Epidemiology Research, Division of Infectious Diseases
Director, Epi / Outcomes Working Group, Vanderbilt Comprehensive Care Clinic HIV Cohort
Director, Tuberculosis Research, Metro-Davidson Health Department
2008-2011 Professor of Medicine, Vanderbilt University School of Medicine
2011-present David E. Rogers Professor of Medicine, Vanderbilt University School of Medicine
2012-present Visiting Scientist, KwaZulu Natal Research Institute for Tuberculosis and HIV (K-RITH).Durban
2012-present Director, Vanderbilt Tuberculosis Center

Other Experience and Professional Memberships

- Centers for Disease Control and Prevention (CDC): Guidelines for the Use of Rifamycins for the Treatment of TB Among HIV-infected Patients Taking Protease Inhibitors or Nonnucleoside Reverse Transcriptase Inhibitors. January 2004. Updated September 2007, January 2012, July 2013.
- CDC: Adult/Adolescent HIV/AIDS Surveillance Case Definition and Clinical Staging Consultation. 2005.
- American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA)/Centers for Disease Control (CDC): Diagnostic Standards and Classification of Tuberculosis in Adults and Children. 2007-2011.
- CDC: Expert consultation:3 months of rifapentine+isoniazid for treatment of latent *M. tuberculosis*. 2011.
- Tuberculosis Trials Consortium: Chair, Core Science Group. May 2011-present
- ATS/IDSA/CDC. Guidelines for Treatment of Latent Tuberculosis Infection. Co-chair. 2011-present
- World Health Organization. Guidelines Development Group: Latent Tuberculosis. May 2014
- World Health Organization. Latent Tuberculosis Task Force. April 2015-present
- U.S. Dept of Health and Human Services Adult HIV OI Guidelines, TB section. October 2015-present

Honors (last 5 years)

2011 Robert Koch Award for TB Prevention Research—National TB Controller's Association
2011 Excellence in Public Health Impact Award—Centers for Disease Control and Prevention
2012 Charles C. Shepard Science Award—Centers for Disease Control and Prevention
2014 Fellow, Infectious Diseases Society of America

C. Contributions to Science

1. Outcomes of HIV infection

I have led several observational studies of HIV outcomes that have provided insights into optimal management of HIV, as well as HIV pathogenesis. This has included studies of the sex difference in HIV-1 RNA, the association between pregnancy and improved HIV outcomes, the optimal timing of antiretroviral therapy initiation, and the relationship between body mass index and immune restoration on antiretroviral therapy.

a. **Sterling TR**, Vlahov D, Astemborski J, Hoover DR, Margolick JB, Quinn TC. Initial plasma HIV-1 RNA and progression to AIDS in women and men. N Engl J Med. 2001; 344:720-5. PMID: 11236775
b. Kitahata MM, Gange SJ, Abraham A, et al, **Sterling TR**, et al, Moore RD, for The North American AIDS Cohort Collaboration on Research and Design. Effect of early versus deferred antiretroviral therapy for HIV on survival. N Engl J Med. 2009; 360(18):1815-26. PMCID: PMC2854555
c. Koethe JR, Grome H, Jenkins CA, Kalams SA, **Sterling TR**. The metabolic and cardiovascular consequences of obesity in persons with HIV on long-term antiretroviral therapy. AIDS. 2015 Sep 28. PMID: 26418084.
d. Castilho JL, Shepherd BE, Koethe J, Turner M, Bebawy S, Logan J, Rogers WB, Raffanti S, **Sterling TR**. CD4+/CD8+ ratio, age, and risk of serious non-communicable diseases in HIV-infected adults on antiretroviral therapy. AIDS 2016 Mar 27;30(6):899-908. PMCID: PMC4785819

2. Treatment of HIV-related TB

I have led a series of studies of HIV-related TB that have characterized risk factors for TB relapse, acquired rifamycin resistance, immune reconstitution inflammatory syndrome (IRIS), and mortality. These studies have helped inform the optimal timing of antiretroviral therapy initiation in TB patients, and the optimal duration of TB therapy in HIV-infected persons.

a. Pettit AC, Jenkins CA, Stinnette SE, Rebeiro PF, Blackwell RB, Raffanti SP, Shepherd BE, **Sterling TR**. Tuberculosis risk before and after highly active antiretroviral therapy initiation: does HAART increase the short-term TB risk in a low incidence TB setting? J Acquir Immune Defic Syndr. 2011;57(4):305-10. PMCID: PMC3141096
b. **Sterling TR**, Lau B, Zhang J, et al, for the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD). Risk factors for tuberculosis after highly active antiretroviral therapy initiation in the United States and Canada: implications for tuberculosis screening. J Infect Dis. 2011;204(6):893-901. PMCID: PMC3156918
c. Cortes CP, Wehbe FH, McGowan CC, Shepherd BE, Duda SN, Jenkins CA, Gonzalez E, Carriquiry G, Schechter M, Padgett D, Cesar C, Madero JS, Pape JW, Masys DR, **Sterling TR** and the Caribbean, Central American, South American network for HIV research (CCASA-net) of the International Epidemiologic Databases to Evaluate AIDS (IeDEA). Duration of anti-tuberculosis therapy and timing of antiretroviral therapy initiation: association with mortality in HIV-related tuberculosis. PLoS ONE. 2013; 8(9):e74057. PMCID: PMC3774609
d. Pettit AC, Mendes A, Jenkins C, Napravnik S, Freeman A, Shepherd BE, Dowdy D, Gill J, Rachlis A, Moore R, **Sterling TR**; North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD). Timing of antiretroviral treatment, immunovirologic status and TB risk: implications for test and treat. J Acquir Immune Defic Syndr. 2016 Apr 5. [Epub ahead of print] PMCID: PMC4942351

3. Drug-resistant TB, with a focus on fluoroquinolone resistance

I have studied drug-resistant TB for more than 20 years. Recently, our focus has been on the role that fluoroquinolone exposure prior to TB diagnosis—for indications other than TB—plays on phenotypic and genotypic fluoroquinolone resistance. The identification of novel resistance mutations and mechanisms could improve the sensitivity of diagnostic tests for fluoroquinolone-resistant *M. tuberculosis*.

a. Frieden TR, **Sterling T**, Pablos-Mendez A, Kilburn JO, Cauthen GM, Dooley SW. The emergence of drug-resistant tuberculosis in New York City. N Engl J Med. 1993; 328:521-6. PMID: 8381207
b. Ginsburg AS, Woolwine SC, Hooper N, Benjamin WH, Dorman SE, Bishai WR, **Sterling TR**. The rapid development of fluoroquinolone resistance in *M. tuberculosis*. N Engl J Med. 2003; 349:1977-8. PMID: 14614180
c. Devasia RA, Blackman A, Gebretsadik T, Griffin M, Shintani A, May C, Smith T, Hooper N, Maruri F, Warkentin J, Mitchel E, **Sterling TR**. Fluoroquinolone resistance in *Mycobacterium tuberculosis*: the effect of duration and timing of fluoroquinolone exposure. Am J Respir Crit Care Med. 2009;180(4):365-70. PMCID: PMC2731810
d. Eilertson B, Maruri F, Blackman A, Guo Y, Herrera M, van der Heijden Y, Shyr Y, **Sterling TR**. A novel resistance mutation in eccC5 of the ESX-5 secretion system confers ofloxacin resistance in Mycobaterium tuberculosis. J Antimicrob Chemother 2016 Jun 3. Epub ahead of print. PMID:27261264.

4. Immunogenetic factors associated with TB risk, particularly extrapulmonary disease

In a series of studies we have identified subtle immune defects among HIV-uninfected persons who have completed treatment for extrapulmonary TB. These abnormalities include decreased CD4+ counts, low unstimulated and stimulated cytokine production, increased regulatory T-cell frequency, and increased CD4+ activation. We also identified genetic polymorphisms associated with extrapulmonary TB. This suggests that an underlying host defect could predispose to extrapulmonary TB. This provides insight into TB pathogenesis, in which only a small sub-set of persons infected with *M. tuberculosis* progress to TB.

a. **Sterling TR**, Dorman SE, Chaisson RE, Ding L, Hackman J, Moore K, Holland SM. Human immunodeficiency virus-seronegative adults with extrapulmonary tuberculosis have abnormal innate immune responses. Clin Infect Dis. 2001; 33(7):976-82. PMID: 11528568

b. Antas PR, Ding L, Hackman J, Reeves-Hammock L, Shintani AK, Schiffer J, Holland SM, **SterlingTR**. Decreased CD4+ lymphocytes and innate immune responses in adults with previous extrapulmonary tuberculosis. J Allergy Clin Immunol. 2006;117(4):916-23. PMID: 16630952
c. **Sterling TR**, Martire T, de Almeida AS, Ding L, Greenberg DE, Moreira LA, Elloumi H, Torres AP, Sant'Anna CC, Calazans E, Paraguassu G, Gebretsadik T, Shintani A, Miller K, Kritski A, Lapa e Silva JR, Holland SM. Immune function in young children with previous pulmonary or miliary/meningeal tuberculosis and impact of BCG vaccination. Pediatrics. 2007; 120(4):e912-21. PMID: 17908747
d. Motsinger-Reif AA, Antas PR, Oki NO, Levy S, Holland SM, **Sterling TR**. Polymorphisms in IL-1beta, vitamin D receptor Fok1, and Toll-like receptor 2 are associated with extrapulmonary tuberculosis. BMC Med Genet. 2010;11:37. PMCID: PMC2837863

5. Short-course treatment of latent *M. tuberculosis* infection

I led a large multi-center clinical trial which demonstrated that a 3-month once-weekly regimen of isoniazid + rifapentine given under direct observation was as effective and well-tolerated as the gold-standard 9-month daily self-administered isoniazid regimen. The higher completion rate of the short-course regimen could improve the effectiveness of TB prevention efforts, and contribute to a decrease in the global TB burden.

a. **Sterling TR**, Villarino ME, Borisov AS, Shang N, Gordin F, Bliven-Sizemore E, Hackman J, Hamilton CD, Menzies D, Kerrigan A, Weis SE, Weiner M, Wing D, Conde MB, Bozeman L, Horsburgh CR, Chaisson RE, and the TB Trials Consortium. Three months of once-weekly rifapentine and isoniazid for the treatment of latent *M. tuberculosis* infection (PREVENT TB). N Engl J Med. 2011; 365:2155-66. PMID: 22150035.
b. Villarino ME, Scott NA, Weis SE, Weiner M, Conde MB, Jones B, Nachman S, Oliveira R, Moro RN, Shang N, Goldberg SV, **Sterling TR**; IMPAACT, TB Trials Consortium. Treatment for preventing tuberculosis in children and adolescents: a randomized clinical trial of a 3-month, 12-dose regimen of a combination of rifapentine and isoniazid. JAMA Pediatr. 2015; 169(3):247-55. PMID: 25580725
c. **Sterling TR**, Moro RN, Borisov AS, Phillips E, Shepherd G, Adkinson NF, Weis S, Ho C, Villarino ME; TB Trials Consortium. Flu-like and other systemic drug reactions among persons receiving weekly rifapentine plus isoniazid or daily isoniazid for treatment of latent tuberculosis infection in the PREVENT TB Study. Clin Infect Dis. 2015 Aug 15;61(4):527-35. PMID: 25904367. PMCID: PMC4560029
d. **Sterling TR**, Scott NA, Miro JM, Calvet G, La Rosa A, Infante R, Chen MP, Benator DA, Gordin F, Benson CA, Chaisson RE, Villarino ME, the Tuberculosis Trials Consortium, and the AIDS Clinical Trials Group. Three months of weekly rifapentine and isoniazid for treatment of *M. tuberculosis* infection in HIV co-infected persons. AIDS 2016 June 19;30(10):1607-15. PMCID: PMC4899978

Complete List of Published Work in MyBibliography: http://www.ncbi.nlm.nih.gov/sites/myncbi/timothy.sterling.1/bibliography/40632070/public/?sort=date&direction=descending

D. Research Support

Current

NIAID R56 AI118361 PI: Sterling TR 08/01/16-07/31/17
National Institutes of Health
Fluoroquinolones and efflux-mediated cross-resistance in HIV-related TB
This project studies novel fluoroquinolone resistance mutations and mechanisms in *M. tuberculosis*, their contribution to resistance to other drugs, and the role of HIV infection.

NIH R01 AI120790 PI: Sterling TR 08/12/16-07/31/20
Predictors of treatment toxicity, failure, and relapse in HIV-related tuberculosis
This project seeks to identify pharmacogenomic predictors of TB/HIV treatment toxicity and effectiveness in Brazil.

CDC10FED TB Trials Consortium, PI: Sterling TR; Peru PI: Gotuzzo E 09/30/09-09/29/19
Universidad Cayetano Heredia, Lima, Peru
Centers for Disease Control and Prevention
This consortium conducts programmatically relevant studies of tuberculosis treatment and prevention.

NIAID 5 U01 AI069923 Project PI: Sterling TR 07/01/16-06/30/17
National Institutes of Health
Regional Prospective Observational Research for TB (RePORT)-Brazil
Supplement to Caribbean, Central and South America network for HIV epidemiology (CCASAnet)
With joint funding from the NIH and the Brazilian Ministry of Health, this is a prospective, multi-center cohort of TB cases and close contacts in Rio de Janeiro, Salvador, and Manaus, Brazil. There is a biorepository of *M. tuberculosis* isolates, cells, DNA, and RNA. Studies will be performed of host and pathogen determinants of TB treatment response, recurrence, acquiring *M. tuberculosis* infection, and progressing to TB disease.

TB Epidemiologic Studies Consortium PI: Stout JE -Duke 09/30/11-09/29/21
Centers for Disease Control and Prevention
This consortium conducts studies of the diagnosis and treatment of latent *M. tuberculosis* infection.
Role: Vanderbilt PI

NIAID P30AI110527 PI: Mallal S 04/01/15 – 03/31/20
National Institutes of Health
Tennessee Center for AIDS Research
Vanderbilt-Meharry-Tennessee Department of Health
Role: Associate Director, Developmental Core

NIAID U01AI069918 PI: Moore RD -Johns Hopkins 07/01/16-06/30/21
National Institutes of Health: Interntional Epi Databases to Evaluate AIDS
North America (NA-ACCORD)
Role: Vanderbilt PI

NIAID U01AI069923 PI: McGowan C 07/01/16-06/30/21
National Institutes of Health: International Epi Databases to Evaluate AIDS
South America and the Caribbean (CCASAnet)
Role: Co-investigator

[redacted]

Completed (past 3 years)

Biomarker Discovery for TB Infection and Disease PI: Sterling 04/01/15-06/30/16
NIH / Brazilian Ministry of Health (CNPq)
Role: Vanderbilt PI

NIAID K24 AI65298 PI: Sterling TR 05/01/05-04/30/16
Mentoring In HIV and Tuberculosis Research
National Institutes of Health
Dr. Sterling's research is focused on the following areas: 1) fluoroquinolone resistance in *M. tuberculosis*; 2) outcomes of HIV infection that influence timing of antiretroviral therapy initiation; 3) immunogenetic risk factors for tuberculosis infection and disease; 4) novel strategies to treat *M. tuberculosis* infection and disease; and 5) optimizing effectiveness of treatment of tuberculosis in HIV-infected persons. The K24 award allows Dr. Sterling to mentor young investigators in these areas of HIV and tuberculosis research.

NIAID 5 U01 AI069924 PI: Sterling TR 1/1/2013-06/30/15
National Institutes of Health
Bringing K-RITH into IeDEA and the IeDEA TB Data Collection Form Project
Supplement to the International Epidemiologic Databases to Evaluate AIDS- Southern Africa (IeDEA-SA) study (M Egger- University of Bern, PI), to study TB epidemiology in Durban, South Africa.

[redacted]

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Graves, John Andrew

POSITION TITLE: Assistant Professor of Health Policy and Medicine

eRA COMMONS USER NAME (credential, e.g., agency login): [redacted]

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Sewanee: The University of the South	BS	05/2003	Economics, English Literature
Harvard University	Ph.D.	05/2011	Health Policy

A. Personal Statement

My career in empirical health policy research spans over 13 years in academic and quasi-academic research at universities and think tanks throughout the U.S. The focus of my research is on the use of statistical, econometric and decision analytic methodologies to understand the impact of policy and clinical interventions on health care spending and patient health outcomes. For example, I currently serve as Principal Investigator on an NIH Common Fund Health Economics Program collaborative U01 research project on the economic, behavioral and patient health consequences of integrating genomic information into clinical practice and insurance design. In addition, I also lead an NCI-funded R01 that considers the utilization and health effects of insurance coverage expansions in the Southern United States. My research portfolio in health policy also includes an R01 from the National Institute on Aging to assess the patient health returns to medical spending, technology adoption and hospital quality in the United States. Based on these funded research programs I have published widely on insurance design, quality measurement and reporting, and the design of clinical and policy approaches to improving value in U.S. health care. This background ideally positions me to offer mentoring expertise to Dr. Rebeiro as he looks to become an expert in health policy evaluation, and in particular, to evaluate the impact of the Affordable Care Act on HIV outcomes across the United States.

B. Positions and Honors

Positions

2003-2009 Research Associate II and Research Consultant, The Urban Institute, Health Policy Center, Washington, D.C.

2011-present Assistant Professor, Vanderbilt University School of Medicine; Institute for Medicine and Public Health; Department of Health Policy; Department of Medicine, Nashville, Tennessee.

Honors

2006-2008 Pre-doctoral fellow in Health Services Research, Agency for Health Care Research and Quality, Cambridge, Massachusetts.

2008-2011 Pre-doctoral Fellow in Aging and Health Economics, National Institute on Aging, National Bureau of Economic Research, Cambridge, Massachusetts.

2011 Student Award, American Statistical Association, Section on Health Policy Statistics, Miami, Florida.

2012 Heinz Award (Honorable Mention), National Academy of Social Insurance

C. Contribution to Science

1. The Dynamics of Health Insurance Coverage in the U.S.

Over the last 25 years the number of uninsured in the U.S. has risen considerably, from 31 million in 1988 to nearly 50 million in 2013. Rising numbers of uninsured are symptomatic of growth in health care spending that has outpaced income growth and a fragmented insurance system characterized by frequent disruptions in coverage. Over the last 10 years I have published widely on the implications of these trends and what they portend for the design and future of the U.S. health insurance system. In previous research, for example, I demonstrated that coverage expansions in Massachusetts resulted in insurance gains mostly among adults with longer uninsured spell durations.[1] My methodological contributions to small area estimation techniques, moreover, were critical in research that was able to demonstrate significant geographic variation in how often and for how long U.S. adults were going uninsured.[2] This research, in turn, led to additional work on how these lessons could be used in the design of health policies to reduce the incidence and duration of uninsurance. For example, this research demonstrated that the dynamics affecting whether and how low-income people obtain insurance coverage also play into how programs should be designed to account for fluctuations in income and family circumstances.[3] My research also evaluated how, once programs results in large numbers of newly insured adults, additional policies could be implemented to mitigate the adverse effects of coverage losses due to dynamic changes in job status, income and family composition.[4]

a) “Health Insurance Dynamics: Methodological Considerations and a Comparison of Estimates from Two Surveys,” with Pranita Mishra. *Health Services Research*. 2016 Jan 1.
b) “Health Care Reform and the Dynamics of Insurance Coverage: Lessons from Massachusetts,” with Katherine Swartz. *New England Journal of Medicine* 2012*,* 367: 1181-1184.
c) “Understanding State Variation in Health Insurance Dynamics Can Help Tailor Enrollment Strategies for ACA Expansion,” *Health Affairs (Millwood)* 2013;32(10).
d) "Medicaid and Marketplace Eligibility Changes Will Occur Often In All States; Policy Options Can Ease Impact," with Benjamin Sommers, Katherine Swartz, and Sara Rosenbaum. *Health Affairs* 33.4 (2014): 700-707.

2. The Impact of State and Federal Health Reform

Implementation health care reforms over the last 15 years has given rise to significant interest in understanding how coverage expansions impact insurance premiums and the financing of health care delivery. In this domain, I have conducted significant simulation-based and evaluation research as primary investigator that has helped inform policymakers’ understanding of design and impact of reforms at the state and federal level. This research has shown, for example, how coverage expansion in Massachusetts – which predated and informed the design of the Affordable Care Act – affected insurance premiums in private insurance markets.[5] Moreover, using survey analyses and simulation techniques I was able to demonstrate how the design of open enrollment periods, premium payment mechanisms, and subsidy programs for health insurance could be redesigned to optimize enrollment.[6,7] Finally, my research in this domain has also been influential in identifying the financial implications of coverage expansion – and non-expansion – for U.S. hospital financing of uncompensated care.[8] In terms of impact, my research on the design of open enrollment and premium payment mechanisms under the ACA was instrumental in leading to federal policy shifts (allowing, for example, for alternative ACA health insurance premium payment mechanisms and a special enrollment period to be opened during the Spring of 2015), while my research on hospital uncompensated care financing has been featured in numerous state-level debates over the merits of Medicaid expansion under the ACA.

a) Richards MR, Nikpay SS, Graves JA. The Growing Integration of Physician Practices: With a Medicaid Side Effect. *Medical Care.* 2016 Apr.
b) 14. Graves JA, Mishra P, Dittus RS, Parikh R, Perloff J, Buerhaus PI. Role of Geography and Nurse Practitioner Scope-of-Practice in Efforts to Expand Primary Care System Capacity: Health Reform and the Primary Care Workforce. Medical care. 2016 Jan 1;54(1):81-9.
c) K Swartz and JA Graves, “Shifting the Timing of the Marketplaces’ Open Enrollment Period Could Increase Enrollment and Improve People’s Plan Choices ” *Health Affairs*, July 2014.

d) JA Graves, "Medicaid Expansion Opt-Outs and Uncompensated Care," *New England Journal of Medicine* 2012 367:2365-2367.

3. Measuring Hospital Quality and the Returns to Health Care Spending

A key component of efforts to improve healthcare system delivery is the ability to measure hospital performance. It is often noted that if the payment system rewarded quality rather than volume, patient health could be improved at lower costs. To this end, I have been involved in significant research projects that aim to improve our scientific understanding on the returns to medical spending in the U.S. Using quasi-random assignment of patients to different local hospitals brought about my ambulance care, we demonstrated substantial returns to inpatient spending in the United States.[9] Our estimates imply that a one standard deviation increase in Medicare reimbursement leads to a 4 percentage point (or 10 percent) reduction in mortality; the implied cost per at least one year of life saved is approximately $80,000. In follow-up work, we then demonstrated that positive returns to inpatient spending for acute care episodes are offset by negative returns to post-acute care spending.[10] This significant finding not only reconciles our earlier work with that of the influential Dartmouth Atlas (which finds that areas that spend more do not achieve better outcomes) – but provides policymakers with more precise recommendations on where to find and measure wasteful spending in the U.S. health care system.

a) JJ Doyle, JA Graves, J Gruber and S Kleiner, "Estimating the Returns to Medical Spending: Evidence from *Journal of Political Economy* 123 (1) 2015.
b) JJ Doyle, JA Graves and J Gruber, "Uncovering Waste in U.S. Health Care," *National Bureau of Economic Research Working Paper* 2015.

Google Scholar Page: https://scholar.google.com/citations?hl=en&user=NXMBoRUAAAAJ

D. Research Support

Ongoing Research Support

U01HL122904 09/2013 – 09/2017
Common Fund Health Economics Program
National Heart, Lung and Blood Institute
Role: Principal Investigator (Multi-PI)
Rational Integration of Genomic Healthcare Testing (RIGHT)
A widely-held vision arising from the Human Genome Project is to guide therapeutic decision making with genetic data to improve the safety and efficacy of patient care, a promise that is fueled by extraordinary advances in the discovery of genomic variation that predicts drug response. For the RIGHT project, we are developing a Discrete Event Simulation (DES) to estimate the average clinical efficacy and cost-effectiveness of prospective pharmacogenetic testing across a diverse patient population. The RIGHT project will rigorously test hypotheses on the cost-effectiveness and factors that may affect cost-savings over time using different strategies for pharmacogenomic implementation.

R01 CA189152 07/2015-07/2020
National Cancer Institute
Role: Principal Investigator (Multi-PI)
Effects of Expanded Coverage on Access, Health Care and Health in the South
This project provides timely and rigorous analysis of the effect of health insurance coverage expansions on health care use and outcomes among a large cohort of low-income adults in 12 southeastern states. Using a quasi-experimental research design, we will quantify the effects of coverage expansion through Medicaid and private health insurance exchanges on access to care, cancer screening and use of preventive clinical services; self-reported health outcomes, mortality, cancer care, and use of emergent and inpatient care; and on access to care, utilization, and outcomes for adults with prior coverage whose access might be compromised by the expansions.

R01 AG041794 03/2016 – 02/2019

National Institute on Aging
Role: Co-Investigator
Estimating the Returns to Medical Care Spending
The very high cost of health care in the U.S. relative to other nations, and in high cost areas of the U.S. relative to low cost areas, raises the question of whether health care spending in the U.S. is productive in terms of improving health. This question is difficult to answer because providers generally direct the greatest amount of resources towards individuals for whom the returns may be greatest – those in poor health. This project seeks to overcome the confounding influence of health on spending and outcomes by relying on essentially random variation in the hospital to which patients are admitted based on which ambulance company picked them up and which hospitals are most proximate to them during an emergency. By using multiple approaches and a variety of populations and outcome measures, we both produce a cross-validated set of findings and extend the previous literature on the returns to spending.

Completed Research Support

[redacted]

Center for Medicare and Medicaid Innovation 07/2012 – 07/2015
Role: Co-Investigator
MyHealth Team: Regional Team-based and Closed-Loop Control Innovation Model for Ambulatory Chronic Care Delivery
The MHTAV pilot will focus on a group of patients followed by the Adult Primary Care Center. It is a population of about 11,000 patients all of whom have diabetes, hypertension and/or congestive heart failure. The project will be built in several phases, at first focusing on patients with comorbidities or having more severe single morbidity. Phase one (six months) involves design and proof of concept implementation in a small number of practices. Phase two involves implementation throughout the APCC with analysis that ensures that the system is in control and that outcome measures are improving. Phase three involves adding the single morbidity patients who are less severe and further optimizing the system. Finally, since the model design is not specific to primary care or to a particular set of conditions, we will analyze the feasibility of sustainability and spread of this model.

[redacted]

R01 DC011338 2012 – 2013

Role: Co-Investigator

National Institute on Deafness and Other Communication Disorders
Administrative Supplement for Collaborative Applied Research on Outcomes and Health Services in Deafness and Other Communication Disorders
The aim of this project is to study the feasibility of a cost-effectiveness approach to watchful waiting vs. medical intervention in the study of deafness and other communication disorders.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Moore, Richard D.

eRA COMMONS USER NAME (credential, e.g., agency login): [redacted]

POSITION TITLE: Professor of Medicine, Johns Hopkins University School of Medicine

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Arkansas	BA	05/1974	Chemistry
Vanderbilt University, Nashville, TN	MD	05/1978	Medicine
Vanderbilt University, Nashville, TN		06/1981	Residency Int. Medicine
Johns Hopkins University, Baltimore, MD		06/1984	Postdoctoral Fellow
Johns Hopkins University, Baltimore, MD	MHS	06/1988	Epidemiology

A. Personal Statement

I am an HIV specialist physician and epidemiologist with more than 25 years of experience conducting HIV-associated epidemiologic and clinical outcomes research at Johns Hopkins. I am well versed in the conduct of human subjects research, serving as the chairman of the Johns Hopkins IRB for the past 10 years. I am the Director of the Johns Hopkins Center for AIDS Research Clinical Core, and am the Director of the Johns Hopkins Program for HIV Outcomes Research, based in the School of Medicine, and affiliated with the Department of Epidemiology of the JH Bloomberg School of Public Health. The Program is the home of the NIH-supported Johns Hopkins HIV Clinical Cohort, AHRQ/HRSA-supported HIV Research Network, and most relevant to this proposal, the North American AIDS Cohorts Collaboration on Research and Design (NA-ACCORD), which will provide both data and support to Dr. Rebeiro for this proposal. The NA-ACCORD has been a resource for multiple K- and R- awards from junior investigators and has a well-established process for providing both data and support. Dr. Rebeiro has substantial experience working with the NA-ACCORD and has been highly productive in generating manuscripts and national and international presentations using these NA-ACCORD resources. As the PI of the NA-ACCORD, I am happy to continue to provide him with this access for this important proposal.

B. Positions and Honors

Positions and Employment

1981-1984 Postdoctoral Fellow, Division of General Internal Medicine, Johns Hopkins University School of Medicine
1984-1996 Instructor, Johns Hopkins University School of Medicine
1984-1991 Assistant Professor of Medicine, Johns Hopkins University School of Medicine
1988- Joint appointment in Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health
1990- Director, Program for HIV Outcomes Research, Johns Hopkins University
1991-1998 Associate Professor of Medicine, Johns Hopkins University School of Medicine
1998- Professor of Medicine, Johns Hopkins University School of Medicine
2005- Director, Johns Hopkins HIV Clinic
2012- Director, Clinical Core, Johns Hopkins Center for AIDS Research

Other Experience and Professional Memberships

1991- International AIDS Society, 1991-current
1991- American Society for Microbiology, 1991-current
1997-2001 Executive Committee, National Association of HIV Care, Infectious Diseases Society of America
1998- Fellow, American College of Physicians, 1998-current

1999-	Fellow, Infectious Diseases Society of America, 1999-current
2000-	HIV Medicine Association, 2000-current
2001-	American Academy of HIV Medicine, 2000-current
2010-13	HIV Medicine Association, Board of Directors 2010-2013
1995,1999	National Institutes of Diabetes and Digestive and Kidney Disease, Special Review Committee
2005-07	National Institutes on Drug Abuse, K-Award Review Committee (ad hoc reviewer)
2008-09	National Institutes on Drug Abuse Avant Garde Award Review Committee (ad hoc reviewer)

Honors

1989 American College of Preventive Medicine-Burroughs Wellcome Pharmacoepidemiology Scholar Award
2007 Johns Hopkins Department of Medicine Mentoring Award, 2007

C. Contribution to Science

1. After training in medicine and epidemiology and early publications in antibiotic utilization and efficacy and in substance and alcohol abuse, my career focus coalesced on HIV/AIDS in the late-1990s, not long after the HIV epidemic began its rapid growth. My earliest work in this area specifically focused on the treatment and outcomes of HIV infection in substance users, a behavior associate with a high incidence of HIV infection in Baltimore, Maryland. I created an HIV cohort in 1991, the Johns Hopkins HIV Clinical Cohort, a longitudinal study of HIV-infected patients designed to better describe how HIV disease progression is affected by antiretroviral therapies and the risk factors associated with toxicity and effectiveness of these rapidly evolving therapies. This cohort has been funded by NIDA first as an R01 and now as a U01 for almost 20 years. It has been the source of over 250 publications which have documented how substance abuse interferes with HIV therapy, and results in worse clinical disease progression. However, it has also been used to document how the HIV epidemic has evolved over the past 25 as new antiretroviral and other therapies for HIV have become available that are more potent, have less toxicity and are easier to use. Over 100 investigators have used this resource. Representative publications that trace the evolution of HIV infection treatment and outcomes include.

    a. Chaisson RE, Keruly JC, **Moore RD**. Race, sex, drug use and progression of HIV disease. N Engl J Med 1995;333:751-6.
    b. Lucas GM, Chaisson RE, **Moore RD**. Highly active antiretroviral therapy in a large urban clinic: risk factors for virological failure and adverse drug reactions. Ann Intern Med 1999; 131:81-7.
    c. **Moore RD**, Keruly JC, Gebo KA, Lucas GM. An improvement in virologic response to HAART in clinical practice from 1996-2002. J Acquir Immune Def Syndr 2005; 39:195-198.
    d. Lucas GM, Griswold M, Gebo KA, Keruly JC, Chaisson RE, **Moore RD**. Illicit drug use and HIV-1 disease progression: a longitudinal study in the era of highly active antiretroviral therapy. Am J Epidemiol 2006; 163:412-420.

2. Building upon my earlier work, I established two multisite longitudinal cohorts of HIV-infected persons for purposes of expanding sample size and sociodemographic heterogeneity to address to better study HIV treatment and disease progression in a much broader population. The first and largest of these is the North American AIDS Cohorts Collaboration on Research and Design (NA-ACCORD) supported by NIAID as part of the International epidemiologic Databases to Evaluate AIDS (IeDEA) initiative, and the subject of this current proposal. The NA-ACCORD, encompassing most of the NIH-supported HIV cohorts in North American has been particularly important for addressing questions requiring large sample sizes such as the optimal timing of ARV initiation, impact of aging with HIV, non-AIDS comorbidities affecting HIV progression and the HIV care continuum. In particular, both our size and demographic heterogeneity are allowing us to assess region-wide trends in the natural history of the HIV epidemic. Examples include.

    a. Kitahata MM, Gange SJ, Abraham AG, et al. Initiating rather than deferring antiretroviral therapy at a CD4+ count between 351-500 cells/mm3 and greater than 500 cells/mm3 is associated with improved survival. New Engl J Med 2009; 360:1815-26.
    b. Althoff K, Buchacz K, Hall HI, et al. U.S. trends in antiretroviral therapy use, HIV RNA plasma viral loads, and CD4 T-lymphocyte counts among HIV-infected persons in care, 2000-2008. Ann Intern Med 2012; 157:325-35.

c. Rebeiro PF, Horberg MA, Gange SJ, Gebo KA, Yehia BR, Brooks JT, Buchacz K, Silverberg MJ, Gill MJ, **Moore RD**, Althoff KN for the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD). Strong agreement of nationally recommended retention measures from the Institute of Medicine and the Department of Health and Human Services. PLoS One. 2014 Nov 6; 9(11):e111772.
d. Abraham AG, Althoff KN, Jing Y, Estrella MM, Kitahata M, Wester W, Bosch R, Crane H, Eron J, Gill MJ, Horberg M, Justice A, Klein M, Krishnasami Z, Mayor A, **Moore RD**, Palella F, Parikh CR, Silverberg MJ, Golub ET, Jacobson LP, McKaig R, Napravnik S, Rodriguez B, Lucas GR, for the NA-ACCORD of International Epidemiologic Databases to Evaluate AIDS (IeDEA). End stage renal disease among HIV-infected adults in North America. Clin Infect Dis 2015; 60:941-9.

3. The HIV Research Network has been important in describing how the costs of care have evolved and those factors that have impacted HIV health care utilization and outcomes. This multisite cohort was created with a specific focus on health care utilization and both the delivery and quality of care in HIV disease. The results have directly impacted policy decisions at HRSA (funder for the Ryan White CARE Act). Examples include.

a. Gebo KA, Fleishman JA, Conviser R, Hellinger J, Hellinger FJ, Josephs JX, Keiser P, Gaist P, **Moore RD**, HIV Research Network. Contemporary costs of HIV healthcare in the HAART era. AIDS 2010; 13:2705-15.
b. Fleishman JA, Yehia BR, **Moore RD**, Korthuis PT, Gebo KA, for the HIVRN. Establishment, Retention, and Loss to Follow-Up in Outpatient HIV Care. J Acquir Immune Defic Synd 2012; 60:249-59.
c. Schackman BR, Fleishman JA, Su AE, Berkowitz BK, **Moore RD**, Walensky RP, Becker JE, Voss C, Paltiel AD, Weinstein MC, Freedberg KA, Gebo KA, Losina E. The lifetime medical cost savings from preventing HIV in the United States. Med Care 2015; Feb 21 [Epub ahead of print]
d. Crowell TA, Gebo KA, Blankson JN, Korthuis PT, Yehia BR, Rutstein RM, **Moore RD**, Sharp V, Nijhawan AE, Mathews WC, Hanau LH, Corales RB, Beil R, Somboonwit C, Edelstein H, Allen SL, Berry SA, for the HIV Research Network. Elite controllers are hospitalized more often than persons with medically controlled HIV. J Infect Dis 2015; 211:1692-1702.

4. As HIV infection has evolved into a chronic illness and an aging population in the U.S., I have contributed to a better understanding of the non-AIDS comorbidities that appear to be occurring at a higher rate than might be expected in an HIV-uninfected population and the complex interactions among HIV infection, traditional disease risk factors and aging. This work, representing all of the cohorts for which I am PI, includes:

a. Engels EA, Brock MV, Chen J, Hooker CM, Gillison M, **Moore RD**. Elevated incidence of lung cancer among HIV-infected individuals. J Clin Oncology 2006; 24:1383-1388.
b. Long JL, Engels EA, **Moore RD**, Gebo KA. Incidence and outcomes of malignancy in the HAART era in an urban cohort of HIV-infected individuals. AIDS 2008; 22:489-96.
c. Lucas GM, Jing Y, Sulkowski M, Abraham AG, Estrella MM, Atta MG, Fine DM, Klein MB, Silverberg MJ, Gil MJ, **Moore RD**, Gebo KA, Sterling TR, But AA, for the NA-ACCORD of the IeDEA. Hepatitis C viremia and the risk of chronic kidney disease in HIV-infected individuals. J Infect Dis 2013; 208:1240-9.
d. Silverberg MJ, Lau B, Achenbach CJ, Jing Y, Althoff KN, D'Souza G, Engels EA, Hessol N, Brooks JT, Burchell AN, Gill MJ, Goedert JJ, Hogg R, Horberg MA, Kirk GD Kitahata MM, Korthuis PT, Mathews WC, Mayor A, Modur SP, Napravnik S, Novak RM, Patel P, Rachlis AR, Sterling TR, Willig JH, Justice MC, **Moore RD**, Dubrow R, Cumulative Incidence of Cancer among HIV-infected Individuals in North America. Ann Intern Med 2015; 163: 507-18.

5. Liver disease and hepatitis C are problems of particularly high incidence in North America, and I have teamed with investigators at Johns Hopkins to delineate that effect of HIV and its treatment antiretroviral therapies and on the progression of HIV and HCV infection on the HIV/HCV co-infected patient.

a. Sulkowski MS, Thomas DL, Chaisson RE, **Moore RD**. Hepatoxicity associated with antiretroviral therapy in HIV-infected adults: role of antiretroviral drugs and hepatitis C and B virus infection. JAMA 2000; 283:74-80.
b. Sulkowski MS, Mehta SH, Torbenson M, Afdhal NH, Mirel L, **Moore RD**, Thomas DL. Hepatic steatosis and antiretroviral drug use among adults coinfected with HIV and hepatitis C virus. AIDS 2005 19:585-592.
c. Mehta SH, Thomas DL, Torbenson M, Brinkley S, Mirel L, Chaisson RE, **Moore RD**, Sulkowski MS. The effect of antiretroviral therapy on liver disease among adults with HIV and hepatitis C coinfection. Hepatology 2005; 41:123-131.
d. Limketkai BN, Mehta SH, Sutcliffe CG, Higgins YM, Torbenson MS, Brinkley SC, **Moore RD**, Thomas DL, Sulkowski MS. Relationship of liver disease stage and antiviral therapy with liver-related events and death in HIV/HCV coinfected adults. JAMA 2012; 308:370-8.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/richard.moore.2/bibliography/40858943/public/?sort=date&direction=ascending.

D. Research Support

ACTIVE

NIAID 2UO1AAI069918 (PI: Moore) 7/01/16 – 6/30/21
North American AIDS Cohorts Collaboration on Research and Design: Consortium HIV/AIDS databases from academic medical centers and community based facilities that deliver HIV care in the U.S. and Canada to identify and answer questions of intraregional and interregional importance

NIDA IU01-DA036935 (PI: Moore) 4/01/14 – 3/31/19
HIV Disease Outcomes in Drug Users in Clinical Practice: Project compares illicit drug users with non-drug users in regards to utilization of antiretroviral therapy, long-term effectiveness of antiretroviral therapy.

AHRQ HHSA290201100007C (PI: Moore) 10/01/06 – 9/30/16
HIV Research Network: Network of HIV care providers from across the U.S. who provide timely health services costs and utilization data linked to relevant clinical data on HIV-infected persons.

HRSA IHHSH250201400019C (PI: Moore) 9/27/14 – 9/26/16
Utilizing HIV Research Network Data to Examine HIV Care Continuum: Project to assess retention in HIV care, adherence to ART and costs of HIV care in the setting of insurance coverage change under the Affordable Care Act in states not expanding Medicaid vs. those instituting Medicaid expansion.

NIAID P30AI094189 (PI: Chaisson) 5/02/2012 – 4/30/2017
Center for AIDS Research (CFAR): Coordinate and mobilize the substantial scientific, clinical and public health resources at JHU to generate new knowledge to understand, respond to, and control the HIV pandemic.

NIAID R24AI1077039 University of Alabama (PI: Saag) 5/01/16 –8/31/17
Subcontract
CFAR Network of Integrated Clinical Systems (CNICS): Goals of providing a resource for HIV research for the evolving HIV epidemic in the U.S.
Role: Co-Investigator

NIDA R01DA037601 (PI: Beach) 4/01/14 – 3/31/19
Maximizing respect and improving outcomes in HIV and substance abuse (MaRIPOHSA)
The aim of this project is to create a repository of audio-recorded patient-provider encounters that we will use to measure communication and its impact on patients with HIV and substance use.

COMPLETED

NIAID 2UO1AAI069918 (PI: Moore) 7/01/11 – 6/30/16

North American AIDS Cohorts Collaboration on Research and Design: Consortium HIV/AIDS databases from academic medical centers and community based facilities that deliver HIV care in the U.S. and Canada to identify and answer questions of intraregional and interregional importance

NIAAA 1U24AA020801 (PI: McCaul) 7/01/11 – 6/30/16
Alcohol Research Consortium in HIV – Administrative Core (ARCH-AC): This administrative core provides support to a consortium investigating the intersection of alcohol and HIV epidemiology and treatment.

R24AI1077039 University of Alabama (PI: Saag) 5/01/11 – 4/31/16
Subcontract
CFAR Network of Integrated Clinical Systems (CNICS): Goals of providing a resource for HIV research for the evolving HIV epidemic in the U.S.
Role: Co-Investigator

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Gange, Stephen J.

eRA COMMONS USER NAME (credential, e.g., agency login): [redacted]

POSITION TITLE: Executive Vice Provost for Academic Affairs & Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Cornell University, Ithaca, NY	B.S.	06/1989	Animal Science/ Quantitative Genetics
University of Wisconsin, Madison, WI	Ph.D	06/1994	Statistics

A. PERSONAL STATEMENT

I have substantial experience in mentoring and collaborating with numerous K12/K23/K01 scholars both at Johns Hopkins and other universities and have been a recipient of the School's Advising, Mentoring, and Teaching Recognition Award. I have been working with Dr. Rebeiro since 2009 when he joined the department as a masters' student as my advisee. I continued as a doctoral advisor and continue to work closely with him on a number of different initiatives.

Relevant to this proposal, I have been the Director of the Biostatistics and Epidemiology Core of the NA-ACCORD since its inception and have been involved with directing or advising on the design and analysis of all the major study initiatives. I have also been the Principal Investigator of the Women's Interagency HIV Study (WIHS) Analysis Center since 2001, the largest US natural history study devoted to HIV-infected women. Lastly, I am a member of several editorial boards, and have participated with numerous review and oversight panels, including as a member of the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents and co-chair of the Office of AIDS Research Planning Workshop for Natural History and Epidemiology.

Of my 225+ publications, the following are of interest for this application, including studies performed with Dr. Rebeiro:

1. Rebeiro P, Althoff KN, Buchacz K, Gill J, Horberg M, Krentz H, Moore R, Sterling TR, Brooks JT, Gebo KA, Hogg R, Klein M, Martin J, Mugavero M, Rourke S, Silverberg MJ, Thorne J, **Gange SJ**; North American AIDS Cohort Collaboration on Research and Design. Retention among North American HIV-infected persons in clinical care, 2000-2008. J Acquir Immune Defic Syndr. 2013 Mar 1;62(3):356-62. PubMed PMID: 23242158; PubMed Central PMCID: PMC3661708.

2. Althoff KN, Rebeiro P, Brooks JT, Buchacz K, Gebo K, Martin J, Hogg R, Thorne JE, Klein M, Gill MJ, Sterling TR, Yehia B, Silverberg MJ, Crane H, Justice AC, **Gange SJ**, Moore R, Kitahata MM, Horberg MA; North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD). Disparities in the quality of HIV care when using US Department of Health and Human Services indicators. Clin Infect Dis. 2014 Apr;58(8):1185-9. Epub 2014 Jan 23. PubMed PMID: 24463281; PubMed Central PMCID: PMC3967825.

3. Rebeiro PF, Horberg MA, **Gange SJ**, Gebo KA, Yehia BR, Brooks JT, Buchacz K, Silverberg MJ, Gill J, Moore RD, Althoff KN; North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD). Strong agreement of nationally recommended retention measures from the Institute of

Medicine and Department of Health and Human Services. PLoS One. 2014 Nov 6;9(11):e111772. eCollection 2014. PubMed PMID: 25375099; PubMed Central PMCID: PMC4222946.

4. Rebeiro PF, Althoff KN, Lau B, Gill J, Abraham AG, Horberg MA, Kitahata MM, Yehia BR, Samji H, Brooks JT, Buchacz K, Napravnik S, Silverberg MJ, Rachlis A, Gebo KA, Sterling TR, Moore RD, **Gange SJ**; North American AIDS Cohort Collaboration on Research and Design. Laboratory Measures as Proxies for Primary Care Encounters: Implications for Quantifying Clinical Retention Among HIV-Infected Adults in North America. Am J Epidemiol. 2015 Dec 1;182(11):952-60. Epub 2015 Nov 17. PubMed PMID: 26578717; PubMed Central PMCID: PMC4655744.

5. Rebeiro PF, **Gange SJ**, Horberg MA, Abraham AG, Napravnik S, Samji H, Yehia BR, Althoff KN, Moore RD, Kitahata MM, Sterling TR, Curriero FC; North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD). Geographic Variations in Retention in Care among HIV-Infected Adults in the United States. PLoS One. 2016 Jan 11;11(1):e0146119. doi: 10.1371/journal.pone.0146119. eCollection 2016. PubMed PMID: 26752637; PubMed Central PMCID: PMC4708981.

B. POSITIONS AND HONORS:

Positions and Employment

1988 - 1989 Cornell Theory Center, National Supercomputer Facility, Ithaca, NY. Computer Analyst.
2003 - 2004 Amgen Inc, Epidemiology Department, Thousand Oaks, CA. Associate Director.
1994 - Johns Hopkins Bloomberg School of Public Health, Dept. of Epidemiology, Baltimore, MD.
1994-2007 Faculty positions from Research Associate to Associate Professor
2007-present Professor with Tenure
2009-2012 Deputy Department Chair
2013-2015 Senior Associate Dean for Academic Affairs
2015 - Johns Hopkins University, Office of the Provost. Executive Vice Provost for Academic Affairs.

Selected Honors:

2002 Elected Member, Delta Omega Honorary Public Health Society, Alpha Chapter
2005 Advising, Mentoring, and Teaching Recognition Award from Student Assembly, JHSPH
2007 - 2010 Elected Faculty Senate President & Member of the School's Advisory Board (3 yr term)
2010 Fellow, American College of Epidemiology
2012 Invited Member, American Epidemiological Society
2015 Ernest L. Stebbins Faculty Award Recognizing Excellence and Innovation in Education, JHSPH

Selected Federal Advisory Committees:

2001 - 2006 NIH AIDS Clinical Studies & Epidemiology Study Section
2001 - 2007 Office of AIDS Research, Natural History and Epidemiology Committee, [Co-Chair, 2005-7]
2006 - 2014 Chair, Data Safety & Monitoring Committee, LCA Trials of Gene Therapy (NEI)
2010 - 2012 Invited Member, NIH Center for Scientific Review, College of CSR Reviewers
2011 - 2015 Member, Data Safety & Monitoring Committee, Phase I/II HCV Vaccine Trial (NIAID/DMID)
2011 - 2015 Member, Data Safety & Monitoring Committee, Phase III Antimicrobial Trial (NIAID/DMID)
2011 - Member, DHHS Panel on Antiretroviral Guidelines for Adults & Adolescents

Other Selected Experience:

2005 - 2014 Editorial Board, *AIDS Research and Therapy*
2010 - Editorial Board, *JAIDS: Journal of Acquired Immune Deficiency Syndromes*
2010 - 2014 Chair, Safety Review Committee, Raltegravir post-licensure safety study (Merck)

C. CONTRIBUTION TO SCIENCE

1. Epidemiology of HIV/AIDS in US

Understanding the epidemiology of the HIV epidemic in the US has been, and will continue to be, a cornerstone for domestic public health efforts. For over 20 years, my research interests and experience has spanned basic, clinical, and policy-level domains in HIV/AIDS epidemiology. I believe my efforts have helped to better understand biomarkers for HIV disease progression, measured the use and impact of therapies in

observational settings, and characterize health disparities across the US. Much of my work has been in collaboration with mentored junior faculty (K. Althoff, B. Lau) and doctoral students (D. Hanna, P. Rebeiro, C. Wong). Selected relevant publications include:

a) Kitahata MM, **Gange SJ**, et al. Effect of early versus deferred antiretroviral therapy for HIV on survival. N Eng J Med, 2009:360. [With Editorial Commentary]. PMC2854555
b) Hanna DB, Buchacz K, .., & **Gange SJ**. Trends and disparities in antiretroviral therapy initiation and virologic suppression among newly treatment-eligible HIV-infected individuals in North America, 2001-2009. Clin Infect Dis 2013 Apr;56(8):1174-82. PMC3657490
c) Rebeiro P, Althoff K, Buchacz K, …, **Gange S** for the NA-ACCORD. Retention among North American HIV-infected persons in clinical care, 2000-2008. J Acquir Immune Defic Syndr. 2013 Mar 1;62(3):356-62. PMC3661708.
d) Rebeiro PF, Althoff K, Lau B, …, & **Gange SJ**. Laboratory measures are imperfect proxies of primary-care encounters: Implications for quantifying clinical retention among HIV-infected adults in North America. Am J Epidemiol. 2015 Dec 1;182(11):952-60. Epub 2015 Nov 17. PMC4655744.

2. Leadership of HIV Cohort Studies

The data from NA-ACCORD and other cohort studies, collected using standardized procedures established by professional data centers, provide a basis for describing the full spectrum of the natural and 'treated' history of HIV infection. All successful data centers and cores establish efficient operations to ensure the validity of study findings. Exceptional groups, however, complement operational methods with added scientific value by contributing as scientific partners and simultaneously integrating scientific knowledge with appropriate study designs, data management, and statistical methodology. I believe my leadership of NA-ACCORD Biostatistics & Epidemiology Core, the Women's Interagency HIV Study Data Management and Analysis Center (since 1996), the JHU Center for AIDS Research Biostatistics & Epidemiology Core, and other similar activities has not only increase the breadth of initiatives that have been pursued but also their depth and quality. Selected relevant publications include:

a) Bacon MC, Von Wyl V, Alden C, et al. The Women's Interagency HIV Study (WIHS): An Observational Cohort Brings Clinical Sciences to the Bench. Clinical and Diagnostic Laboratory Immunology. 2005;12(9):1013-1019. PMC-Exempt
b) **Gange SJ**, Kitahata MM, Saag MS, …, & Moore RD. The North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD). Int J Epidemiology 2007:36(2):294-301. PMC-Exempt
c) Lau B, **Gange SJ**, Moore RD. Interval and clinical cohort studies: epidemiologic issues. AIDS Research and Human Retroviruses. 2007;6;769-776.

3. Statistical and Epidemiology Methodology

Appropriate and innovative statistical and epidemiological methodology is essential to high-quality science. I have lead or collaborated on the refinement of novel analytical methods and the adaptation and interpretation of modern methodological approaches in epidemiology. Further, I have worked to integrate these new methods into educational programs here at Johns Hopkins. I am the primary instructor for a spectrum of on-site and online methods courses in Epidemiology, and led the Department's Gateway Sciences Initiative for innovation and modernization of introductory courses. Selected relevant publications include:

a) **Gange SJ**. Teaching Epidemiologic Methods. Epidemiology. 2008;19:353-6. [With Editorial Commentary]. PMC – Exempt
b) Lau B, **Gange SJ**, Kirk GD, and Moore RD. Evaluation of human immunodeficiency virus biomarkers: inferences from interval and clinical cohort studies. Epidemiology 2009 20(5):664-72. PMC2818534
c) Ishwaran H, Gerds TA, Kogalur UB, Moore RD, **Gange SJ**, Lau BM. Random survival forests for competing risks. Biostatistics. 2014 Oct;15(4):757-73. PMC4173102.
d) **Gange SJ** and Golub ET. From smallpox to big data: The next 100 years of epidemiological methods. Am J Epidemiol. 2016 Mar 1;183(5):423-6. PMC-Exempt.

D. SELECTED RESEARCH SUPPORT:

Active Research Support:

U01-AI-42590 (Stephen J. Gange & Elizabeth Golub, dual PI) Role: PI & Member of Executive Committee
WIHS Data Management and Analysis Center (WDMAC)

U01-AI-069918 (Richard D. Moore, PI) Role: Director of Epi/Biostat Core & Member of Exec Committee
North American AIDS Cohorts Collaboration on Research and Design (NA-ACCORD)

Selected Past Research Support:

U01-AI035043 (Lisa Jacobson, PI) Role: Co-Investigator
Center for the Analysis and Management of the Multicenter AIDS Cohort Study (CAMACS)

P30-AI094189 (Richard Chaisson, PI) Role: Inaugural Director and Senior Advisor, Biostatistics & Epidemiologic Methods Core
Johns Hopkins University Center for AIDS Research (JHU-CFAR)

Selected Active & Past Research Mentoring Projects (Mentee, Project Title):

Junior Faculty:
K01 AI-071754 (B. Lau, *Biomarkers, Therapy, and Mortality in the Evolving HIV Epidemic*)
K01 AI-071725 (M. Silverberg*, HIV infection, Antiretroviral therapy, Cancer incidence and progression*)
K01 AI-093197 (K. Althoff, *Challenging and Expanding Paradigms of Aging with HIV*)
K23 DK-081317 (M. Estrella, *Burden of Chronic Kidney Disease in HIV Infection*)
K23 AI-084854 (S. Berry*, Universal Screening of HIV-infected persons for gonorrhea and Chlamydia*)

Doctoral Students:
R36 DA-021104 (A. Terzian, *Physical Functioning in a Cohort of HIV-Infected Women*)
F31 MH-076656 (A. Boore, *Trust, Conspiracy Beliefs, and the Use of HAART*)
F31 DA-030254 (D. Hanna, *Epidemiologic Evaluation of State ADAP Features in the US*)
F31 DA-035713 (P. Rebeiro, *Epidemiology of Clinical Retention Among HIV+ Persons in North America)*
F31 DA-037788 (C. Wong, *Multimorbidity among HIV-Infected Adults in North America from 2000-2010*)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: McGowan, Catherine Carey

eRA COMMONS USER NAME (credential, e.g., agency login): [redacted]

POSITION TITLE: Associate Professor of Medicine, Vanderbilt University Medical Center, Nashville, TN

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Kansas, Lawrence, KS	BA	01/1983	Biochemistry
University of Kansas, Medical School, Kansas City, KS	MD	05/1987	Medicine
University of Arizona, Tucson, AZ	Internship/ Residency	06/1990	Internal Medicine
Vanderbilt University, Nashville, TN	Fellowship	06/1995	Infectious Diseases

A. Personal Statement

My research interests focus on the use of observational cohort data to study clinical outcomes in HIV-infected individuals. I have over two decades' experience in providing primary care for HIV-infected patients in a high-volume practice at the Vanderbilt Comprehensive Care Clinic (VCCC). I am also a member of the HIV Epidemiology and Outcomes Working Group of the Tennessee Center for AIDS Research (CFAR) and direct research activities at the VCCC. I have been closely involved with the NIH-funded Caribbean, Central and South America network (CCASAnet) of the International Epidemiologic Databases to Evaluate AIDS (IeDEA) since its inception in 2006, and participate in the Executive, Pediatric, Cancer, Clinical Outcomes, and Strategic Data Working Groups of IeDEA. In my current role as PI of CCASAnet and its regional Data Coordinating Center based at Vanderbilt, I lead efforts to develop large databases of HIV data from adult and pediatric clinical sites in Argentina, Brazil, Chile, Haiti, Honduras, Mexico, and Peru, direct the scientific program for CCASAnet, and oversee data quality activities.

As a member of the IeDEA Executive Committee and several IeDEA working groups, I have worked with Dr. Richard Moore, PI of the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD), to develop a cross-regional collaboration that spans the Americas.

The scientific aims of CCASAnet are closely aligned with those proposed by Dr. Peter Rebeiro in his K-01 grant application. The collaborative projects he proposes within the Americas and globally will benefit the IeDEA consortium in many ways, including informing public health policy.

1. **McGowan CC**, Cahn P, Gotuzzo E, Padgett D, Pape JW, Wolff M, Schechter M, Masys DR. (2007). Cohort Profile: Caribbean, Central and South America Network for HIV research (CCASAnet) collaboration within the International Epidemiologic Databases to Evaluate AIDS (IeDEA) programme. *Int J Epidemiol,* 35(5), 969-76. PMID: 17846055
2. Duda SN, Shepherd BE, Gadd CS, Masys DR, **McGowan CC**. (2012). Measuring the quality of observational study data in an international HIV research network. *PLOS ONE*, 7: e33908. PMCID: PMC332089.
3. Duda SN, Farr AM, Lindegren ML, Blevins M, Wester CW, Wools-Kaloustian K, Ekouevi DK, Egger M, Hemingway-Foday J, Cooper DA, Moore RD, **McGowan CC**, Nash D, and the International Epidemiologic Databases to Evaluate AIDS (IeDEA) Collaboration. (2014). Characteristics and comprehensiveness of adult HIV care and treatment programmes in Asia-Pacific, sub-Saharan Africa and the Americas: results of a site assessment conducted by the International epidemiologic Databases to Evaluate AIDS (IeDEA). *J Intl AIDS Soc*,17:19045. PMCID: PMC4268491.

4. Althoff K, Rebeiro PF, Hanna DB, Padgett D, Horberg MA, Grinsztejn B, Abraham A, Hogg R, Gill MJ, Wolff MJ, Mayor A, Rachlis A, Williams C, Sterling TR, Kitahata M, Buchacz K, Thorne J, Cesar C, Mejía Cordero F, Rourke SB, Sierra-Madero J, Pape JW, Cahn P, **McGowan CC**, for the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) and the Caribbean, Central and the South America Network for HIV Epidemiology (CCASAnet). (2016). A picture is worth a thousand words: Maps of HIV clinical care indicators are essential tools for informing research, programs, and policy. *J Int AIDS Soc*, 1:20707.doi:10.7448/ias.19.20707. PMCID: PMC4821890.

B. Positions and Honors

Positions and Employment

1987 Medical Volunteer, Hôpital Bon Samaritan, Limbe, Haiti, West Indies
1990 Physician Volunteer, Ministry of Primary Health Care, Belize, Central America
1990-1992 Internist, Locum Tenens, CompHealth, Inc., Salt Lake City, UT
1995-1996 Instructor, Division of Infectious Diseases, Department of Medicine, Vanderbilt University, Nashville, TN
1996-2012 Assistant Professor of Medicine, Division of Infectious Diseases, Department of Medicine, Vanderbilt University, Nashville, TN
2012-present Associate Professor of Medicine, Division of Infectious Diseases, Department of Medicine, Vanderbilt University, Nashville, TN
1996-2000 Physician Volunteer, Siloam Family Health Center, Nashville, TN
1996-2001 Physician Volunteer, Christian Mission of Pignon, Pignon, Haiti, West Indies (intermittent basis)
1996-2010 Assistant Medical Director, Comprehensive Care Center, Nashville, TN
1998-2002 Medical Director, Robertson County Comprehensive Care Center, Springfield, TN
2001-2010 Research Director, Vanderbilt Comprehensive Care Center, Nashville, TN

Other Experience and Professional Memberships

1990-present American College of Physicians
1993-2000 Member, Helicobacter Study Group, Vanderbilt University
1993-present Infectious Diseases Society of America
1993-2007 Infectious Diseases Society of Tennessee
1994-2004 American Society for Microbiology
2002-2004 Member, Microbial:Host Interaction Study Group, Vanderbilt University
2002 Ministry of Public Health and Population, Haiti: Therapeutic antiretroviral strategies. Sharing of experiences and future perspectives for Haiti. Panel participant.
2004-present American Academy of HIV Medicine
2004-present HIV Epidemiology and Outcomes Working Group, Tennessee Center for AIDS Research, Faculty Member
2005 Ministry of Public Health and Population, Haiti: International workshop to develop guidelines for the prevention of mother-to-infant HIV transmission in Haïti. Panel participant.
2006-present International AIDS Society
2007 Ministry of Public Health and Population, Haiti: International workshop to revise national guidelines for management of HIV in adults and adolescents. Panel participant.
2010 Ministry of Public Health and Population, Haiti: International workshop to revise national guidelines for antiretroviral therapy. Panel participant.
2011-present Vanderbilt Institute for Global Health, Faculty Member
2013-present Vanderbilt Tuberculosis Center, Faculty Member

Honors

1978 Presidential Freshman Scholarship, Drake University
1993 National Foundation for Infectious Diseases Grant
1995 Grant Liddle Scholar Award, Vanderbilt University
2010 World AIDS Day Hero, Nashville, Tennessee
2013 Five Star Excellence Award, Vanderbilt Medical Group
2014 Five Star Excellence Award, Vanderbilt Medical Group

C. Contribution to Science

1. **HIV Continuum of Care in the Caribbean, Central and South America.** This work assessed several important stages of the HIV Care Continuum in the context of health care delivery in Latin America and the Caribbean. Late diagnosis and late ART initiation were highly prevalent, and there was considerable heterogeneity across the region in long-term survival and loss to follow up rates. Regional HIV Care Continuum outcomes improved over time, though disparities for vulnerable groups remain.
    a. Carriquiry G, Fink V, Koethe JR, Giganti MJ, Jayathilake K, Blevins M, Cahn P, Grinsztejn B, Wolff M, Pape JW, Padgett D, Madero JS, Gotuzzo E, **McGowan CC**, Shepherd BE. (2015). Mortality and loss to follow-up among HIV-infected persons on long-term antiretroviral therapy in Latin America and the Caribbean. *J Int AIDS Soc*,18:20016. PMCID: PMC4499577.
    b. Crabtree-Ramírez B, Caro-Vega Y, Shepherd B, Cesar C, Wehbe F, Cortés C, Padgett D, Pape J, Gotuzzo E, **McGowan C**, Masys D, Sierra-Madero J. (2011). Cross-sectional analysis of late HAART initiation in Latin America and the Caribbean: late testers and late presenters. *PLoS ONE*, 6: e20272. PMCID: PMC3102699.
    c. Crabtree-Ramírez B, Neried Caro Vega Y, Shepherd BE, Turner M, Carriquiry G, Fink V, PM, Cortes CP, Rouzier V, Padgett D, Jayathilake K, **McGowan CC**, Person AK. (2015). Temporal trends in age at HIV diagnosis in cohorts in the United States, the Caribbean, and Central and South America. *AIDS Behav*, 15;19:1599-608. PMCID: PMC4512939.
    d. Rebeiro P, Cesar C, Shepherd BE, De Boni RB, Cortés CP, Rodriguez F, Belaunzarán-Zamudio P, Pape JW, Padgett D, Hoces D, **McGowan CC**, Cahn P. (2016). Assessing the HIV care continuum in the Caribbean, Central and South American network for HIV epidemiology (CCASAnet): progress in clinical retention, cART use, and viral suppression. *J Int AIDS Soc*,19:20636.doi:10.7448/ias.19.1.20636. PMCID: PMC4827101.

2. **Antiretroviral treatment outcomes in the Caribbean, Central and South America.** This work documented important outcomes after ART initiation in the large multinational CCASAnet cohort including mortality, loss to follow up, rates of regimen change and failure, and need for third-line agents. These data were used by the Pan American Health Organization in its regional report on the HIV epidemic, and to forecast need for expensive third line agents.
    a. Tuboi SH, Schechter M, **McGowan CC**, Cesar C, Krolewiecki A, Cahn P, Wolff M, Pape JW, Padgett D, Madero JS, Gotuzzo E, Masys DR, Shepherd BE. (2009). Mortality during the first year of potent antiretroviral therapy in HIV-1-infected patients in 7 sites throughout Latin America and the Caribbean. *J Acquir Immun Def Syndr*, 51:615-623. PMCID: PMC2780368.
    b. Cesar C, Jenkins CA, Shepherd BE, Padgett D, Mejia F, Ribeiro SR, Cortes C, Pape JW, Madero JS, Fink V, Sued O, **McGowan C**, Cahn P. (2015). Incidence of virological failure and major regimen change of initial combination antiretroviral therapy in the Caribbean, Central, and South America: an observational cohort study. *Lancet HIV,* 2:e492-e500. PMCID: PMC4651009.
    c. Wolff M, Shepherd BE, Cortés C, Rebeiro P, Cesar C, Wagner Cardoso S, Pape JW, Padgett D, Sierra-Madero J, Echevarria J, **McGowan CC**. (2015). Clinical and virologic outcomes after changes in first antiretroviral regimen at 7 sites in CCASAnet. *J Acquir Immun Def Syndr*, 71:102-10. PMCID: PMC4712722.
    d. Cesar C, Shepherd BE, Jenkins CA, Ghidinelli M, Castro JL, Veloso VG, Cortes CP, Padgett D, Crabtree-Ramirez B, Gotuzzo E, Fink V, Duran A, Sued O, **McGowan CC**, Cahn P, Caribbean, Central and South America Network for HIV Epidemiology (CCASAnet). (2014). Use of third line antiretroviral therapy in Latin America. *PLOS ONE*, 15;9(9):e106887. PMCID: PMC4164470.

3. **Evolving epidemiology of clinical outcomes in HIV infection.** These studies demonstrated the changing epidemiology of clinical outcomes in HIV-infected populations receiving combination ART, spanning low- and high-income settings and geographically diverse regions. The findings highlight the shift in the burden of cancer from AIDS-defining cancers to non AIDS-defining cancers, and the increased morbidity related to non-communicable diseases.
    a. Wester CW, Koethe JR, Shepherd BE, Stinnette SE, Rebeiro PF, Kipp AM, Hong H, Bussmann H, Gaolathe T, **McGowan CC**, Sterling TR, Marlink RG. (2011). Non-AIDS defining events among HIV-1 Infected adults receiving combination antiretroviral therapy in urban settings in Sub Saharan Africa and the United States. *AIDS,* 25(12). PMCID: PMC3188442.

b. Fink VI, Shepherd BE, Cesar C, Krolewiecki A, Wehbe F, Cortés CP, Crabtree-Ramírez B, Padgett D, Shafaee M, Schechter M, Gotuzzo E, Bacon M, **McGowan C**, Cahn P, Masys D. (2011). Cancer in HIV-infected persons from the Caribbean, Central and South America. *J Acquir Immune Defic Syndr*, 56:467–473. PMCID: PMC3293455.
c. Castilho JL, Luz PM, Shepherd BE, Turner M, Ribeiro SR, Bebawy SS, Netto JS, **McGowan CC**, Veloso VG, Engels EA, Sterling TR, Grinsztejn B. (2015). HIV and cancer: a comparative retrospective study of Brazilian and U.S. clinical cohorts. *Infect Ag Cancer*, 10:4. PMCID: PMC4477502.
d. Crabtree-Ramirez, B. Caro-Vega, Y. Shepherd, B. E. Grinsztejn, B. Wolff, M. Cortes, C. P. Padgett, **D.** Carriquiry, G. Fink, V. Jayathilake, K. Person, A. K. **McGowan, C**. Sierra-Madero, J. (2016). Time to HAART initiation after diagnosis and treatment of opportunistic infections in patients with AIDS in Latin America. *PLoS One,* Jun 7;11(6):e0153921 doi: 10.1371/journal.pone.0153921. PMCID: PMC4896474.

4. **Impact of non-injection drug use on HIV clinical outcomes.** These studies evaluated non-injection drug use and its impact on clinical outcomes in HIV cohorts in the US and Latin America. The manuscripts contributed to the literature describing the relationship between substance use and HIV disease progression in varied clinical settings. The usefulness of a novel point-of-care rapid screening tool to assess substance use and ART adherence was demonstrated at high-volume HIV clinics in multinational settings.
   a. **McGowan CC**, Weinstein DD, Samenow CP, Stinnette SE, Barkanic G, Rebeiro PF, Sterling TR, Moore RD, Hulgan T. (2011). Drug use and receipt of highly active antiretroviral therapy among HIV-infected persons in two U.S. clinic cohorts. *PLOS ONE*, 6(4):e18462. PMCID: PMC3081810.
   b. Rasbach DA, Desruisseau AJ, Kipp AM, Stinnette S, Kheshti A, Shepherd BE, Sterling TR, Hulgan T, **McGowan CC**, Qian HZ. (2013) Active cocaine use is associated with lack of HIV-1 virologic suppression independent of non-adherence to antiretroviral therapy: use of a rapid screening tool during routine clinic visits. *AIDS Care*, 25(1):109-17. PMCID: PMC3443534.
   c. Qian HZ, Mitchell VJ, Bebawy S, Cassell H, Perez G, **McGowan CC**, Sterling TR, Vermund SH, D'Aquila R, Hulgan T. (2014). Current drug use and lack of HIV virologic suppression: point-of-care urine drug screen versus self-report. *BMC Infect Dis*,14:508. PMCID: PMC4175271.
   d. De Boni R, Shepherd BE, Grinsztejn B, Cesar C, Cortes C, Padgett D, Gotuzzo E, Belaunzaran Zamudio PF, Rebeiro PF, Duda SN, **McGowan CC**. (2016). Substance use and adherence among people living with HIV/AIDS receiving cART in Latin America. *AIDS Behav,* Apr 18. PMID: 27091028. PMCID: pending.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/catherine.mcgowan.1/bibliograpahy/43431356/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

2U01 AI069923-12 (NIH/NIAID) McGowan, Cahn (co-PIs) 07/01/2016 - 06/30/2021
CCASAnet: The Caribbean, Central and South America Network for HIV Epidemiology
This project creates and maintains a shared repository of HIV data from the Caribbean and Central and South America, and uses the combined data to answer questions about the characteristics of the regional HIV epidemic.

2U01 AI069923-12 (NIH/NIAID) McGowan (PI) 08/01/2013 – 06/30/2017
RePORT-Brazil (Administrative Supplement to CCASAnet)
This project creates a multicenter cohort of patients with well-defined tuberculosis infection and their contacts in three different regions in Brazil. Repositories for clinical data and biologic specimens will be established which will allow investigations on relevant epidemiologic, clinical, and pathogenesis questions in the region.

R24 AI124872-02 (NIH/NIAID) Duda, Harris (co-PIs) 04/06/2016 – 03/31/2021
Harmonist: A Scalable Toolkit for Standardizing and Coordinating Data Sharing Across International Research Networks
The goal of the Harmonist project is to develop the “Harmonist toolkit,” a software and standards package that will enable HIV observational research networks to coordinate large-scale research projects and apply data management best practices more effectively and efficiently.
Role: Co-investigator

1R03DA039743 (NIH/NIDA) Kipp (PI) 04/15/2015 - 03/31/2017
Characterizing non-medical prescription opioid use and pain in people living with HIV
The goal of this study is to identify the severity of non-medical opioid use among people with HIV and its association with pain and other substance use, and to inform ways to improve pain management while avoiding risks of non-medical opioid use.
Role: Co-Investigator

Completed Research Support

2U01 AI069923-06 (NIH/NIAID) McGowan, Cahn (co-PIs) 06/01/2011 - 06/30/2016
CCASAnet: The Caribbean, Central and South America Network for HIV Epidemiology
This project creates and maintains a shared repository of HIV data from the Caribbean and Central and South America, and uses the combined data to answer questions about the characteristics of the regional HIV epidemic.

5U01 AI069923-09 (NIH/NIAID) McGowan (PI) 07/01/2014 – 06/30/2016
Coorte Brasil: Validation and epidemiologic study of non-communicable diseases in HIV-infected persons receiving combination antiretroviral therapy in Brazil (Administrative Supplement to CCASAnet)
This project involves the collection, validation and analysis of data related to non-communicable diseases in a multicenter cohort of HIV-positive patients in Brazil.

5U01 AI069923-09/10 (NIH/NIAID) McGowan (PI) 04/01/2015 – 04/30/2016
Biomarker discovery for tuberculosis infection and disease (Administrative Supplement to CCASAnet)
This project seeks to identify relevant biomarkers of key TB outcomes- acquisition of M. tuberculosis infection and progression from M. tuberculosis infection to TB disease in a well-characterized cohort of TB patients and their contacts in Rio de Janeiro.

5U01 AI069923-07 (NIH/NIAID) McGowan (PI) 07/01/2012 – 06/30/2013
Use of a rapid screening tool for substance use and adherence during routine clinic visits (Administrative Supplement to CCASAnet)
This project implemented a rapid clinical screening tool to prospectively collect point-of-care data on active drug use and antiretroviral adherence at CCASAnet sites multicenter cohort of patients with well-defined tuberculosis infection and their contacts in three different regions in Brazil. Repositories for clinical data and biologic specimens will be established which will allow investigations on relevant epidemiologic, clinical, and pathogenesis questions in the region.

OMB No. 0925-0001/0002 (Rev. 08/12 Approved Through 8/31/2015)

BIOGRAPHICAL SKETCH

NAME: HOLTGRAVE, DAVID R

eRA COMMONS USER NAME (agency login): [redacted]

POSITION TITLE: Professor and Department Chair

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Missouri at St. Louis	BA	08/1983	Psychology
University of Illinois at Urbana/Champaign	PHD	01/1988	Quantitative Psychology
Harvard University School of Public Health	OTH	07/1989	Post-doctoral Fellowship in Environmental Health and Public Policy (Interdisciplinary Programs in Health)

A. Personal Statement

Since August of 2005, Dr. Holtgrave has been Professor and Chair of the Department of Health, Behavior and Society at the Johns Hopkins Bloomberg School of Public Health. The Department was established in the summer of 2005 with a mission dedicated to research and training that advances scientific understanding of the impact on health of behavior and the societal context. Dr. Holtgrave's research has focused on the effectiveness and cost-effectiveness of a variety of HIV prevention interventions (defined broadly), and the relation of the findings of these studies to HIV prevention policy making. He has also investigated the relationship between social capital measures, infectious disease rates, and risk behavior prevalence. He has also examined the cost-effectiveness of mass media approaches to the prevention of tobacco use. Dr. Holtgrave teaches "Translating Research into Public Health Programs" (a two-term course in the Department of Health, Behavior and Society with a heavy emphasis on economic evaluation methods and applications) and has guest-lectured in numerous classes at the Johns Hopkins Bloomberg School of Public Health since joining the School in 2005 (primarily on cost-effectiveness and HIV prevention issues). He also recently served as the Vice-Chair of the Presidential Advisory Council on HIV/AIDS. He is therefore ideally suited to serve on Dr. Rebeiro's mentoring committee, offering insight into how evidence informs policy and how health policy effects on HIV Care Continuum outcomes may be best assessed as part of his K01 Career Development Award.

1. Holtgrave DR, Hall HI, Wehrmeyer L, Maulsby C. Costs, consequences and feasibility of strategies for achieving the goals of the National HIV/AIDS strategy in the United States: a closing window for success?. AIDS Behav. 2012 Aug;16(6):1365-72. PubMed PMID: 22610372.
2. Hall HI, Frazier EL, Rhodes P, Holtgrave DR, Furlow-Parmley C, Tang T, Gray KM, Cohen SM, Mermin J, Skarbinski J. Differences in human immunodeficiency virus care and treatment among subpopulations in the United States. JAMA Intern Med. 2013 Jul 22;173(14):1337-44. PubMed PMID: 23780395.
3. Holtgrave DR, Kim JJ, Adkins C, Maulsby C, Lindsey KD, Johnson KM, Montoya DC, Kelley RT. Unmet HIV service needs among Black men who have sex with men in the United States. AIDS Behav. 2014 Jan;18(1):36-40. PubMed PMID: 23892769.
4. Holtgrave DR. Development of year 2020 goals for the National HIV/AIDS Strategy for the United States. AIDS Behav. 2014 Apr;18(4):638-43. PubMed PMID: 23934340.

B. Positions and Honors

Positions and Employment

1989 - 1991 Assistant Professor, UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER (Department of Family Medicine)

1991 - 1995 Behavioral Scientist, CENTERS FOR DISEASE CONTROL AND PREVENTION (National

	Center for Prevention Services, and Office of the Associate Director of HIV/AIDS, CDC)
1995 - 1997	Associate Professor, MEDICAL COLLEGE OF WISCONSIN (Center for AIDS Research)
1997 - 2001	Director, CENTERS FOR DISEASE CONTROL AND PREVENTION (Division of HIV/AIDS Prevention -- Intervention Research and Support)
2001 - 2005	Professor, EMORY UNIVERSITY (Rollins School of Public Health)
2005 -	Professor and Department Chair, JOHNS HOPKINS UNIVERSITY (Bloomberg School of Public Health, Department of Health, Behavior & Society)

Other Experience and Professional Memberships

- Member, American Public Health Association
- Member, Society for Medical Decision Making

Honors

Appointed Member and Vice-Chair, Presidential Advisory Council on HIV/AIDS

The Golden Apple Award and The Johns Hopkins University Alumni Association Excellence in Teaching Award, Johns Hopkins Bloomberg School of Public Health

Positive Leadership Award, National Association of People with AIDS

Partnership Award, National Alliance of State and Territorial AIDS Directors

C. Everett Koop National Health Award, The Health Project

C. Contribution to Science

1. I have conducted cost-effectiveness and cost-utility analyses of a number of public health interventions. This worked has focused most pointedly on HIV prevention and care programs, with a secondary emphasis on smoking-related interventions. The studies help inform program managers and policy makers about the cost and relative cost-effectiveness of a variety of public health services.

   a. Holtgrave DR, Wunderink KA, Vallone DM, Healton CG. Cost-utility analysis of the National truth campaign to prevent youth smoking. Am J Prev Med. 2009 May;36(5):385-8. PubMed PMID: 19211214.

   b. Holtgrave DR, Maulsby C, Kharfen M, Jia Y, Wu C, Opoku J, West T, Pappas G. Cost-utility analysis of a female condom promotion program in Washington, DC. AIDS Behav. 2012 Jul;16(5):1115-20. PubMed PMID: 22434283.

   c. Villanti AC, Curry LE, Richardson A, Vallone DM, Holtgrave DR. Analysis of media campaign promoting smoking cessation suggests it was cost-effective in prompting quit attempts. Health Aff (Millwood). 2012 Dec;31(12):2708-16. PubMed PMID: 23213155.

   d. Holtgrave DR, Wolitski RJ, Pals SL, Aidala A, Kidder DP, Vos D, Royal S, Iruka N, Briddell K, Stall R, Bendixen AV. Cost-utility analysis of the housing and health intervention for homeless and unstably housed persons living with HIV. AIDS Behav. 2013 Jun;17(5):1626-31. PubMed PMID: 22588529.

2. In partnership with key policy makers and program managers, I have conducted a number of resource allocation modeling projects which serve to provide guidance on how best to allocate resources across an array of available program options. These studies have been done on both very high and low HIV prevalence jurisdictions, and have served to directly inform the prioritization of uses of resources in these settings.

   a. Holtgrave DR, Hall HI, Wehrmeyer L, Maulsby C. Costs, consequences and feasibility of strategies for achieving the goals of the National HIV/AIDS strategy in the United States: a closing window for success?. AIDS Behav. 2012 Aug;16(6):1365-72. PubMed PMID: 22610372.

   b. Holtgrave DR, Young PA, Mayer RR, Maulsby C, Kim JJ. Employing resource allocation modeling to inform HIV prevention planning for the state of Iowa. AIDS Educ Prev. 2013 Oct;25(5):423-9. PubMed PMID: 24059879.

c. Holtgrave DR, Kim JJ, Adkins C, Maulsby C, Lindsey KD, Johnson KM, Montoya DC, Kelley RT. Unmet HIV service needs among Black men who have sex with men in the United States. AIDS Behav. 2014 Jan;18(1):36-40. PubMed PMID: 23892769.

d. Holtgrave DR. Development of year 2020 goals for the National HIV/AIDS Strategy for the United States. AIDS Behav. 2014 Apr;18(4):638-43. PubMed PMID: 23934340.

3. Along with key colleagues specializing in HIV surveillance and epidemiology, I have contributed to studies which helped define the concept of HIV transmission rates for the U.S., and to estimate these transmission rates for a number of key populations (such as persons living with HIV who are aware and unaware of HIV seropositivity). Related to this work is research into trends in HIV testing and diagnoses in the U.S.

a. Hall HI, Holtgrave DR, Maulsby C. HIV transmission rates from persons living with HIV who are aware and unaware of their infection. AIDS. 2012 Apr 24;26(7):893-6. PubMed PMID: 22313960.

b. Hall HI, Holtgrave DR, Tang T, Rhodes P. HIV transmission in the United States: considerations of viral load, risk behavior, and health disparities. AIDS Behav. 2013 Jun;17(5):1632-6. PubMed PMID: 23456577.

c. Holtgrave DR, Hall HI, Des Jarlais DC, Mizuno Y, Purcell DW. Estimating number of diagnosed persons living with HIV in the United States engaged in unprotected serodiscordant risk behavior with unsuppressed viral load. J Acquir Immune Defic Syndr. 2014 Mar 1;65(3):e125-8. PubMed PMID: 23978998.

d. Johnson AS, Hall HI, Hu X, Lansky A, Holtgrave DR, Mermin J. Trends in diagnoses of HIV infection in the United States, 2002-2011. JAMA. 2014 Jul 23-30;312(4):432-4. PubMed PMID: 25038362.

D. Research Support

Ongoing Research Support

T28830 DOWDY (PI) 10/01/14-09/30/19

CDC: Emory University

Enhancing Models of HIV, Viral Hepatitis, STI's and Tuberculosis to Inform and Improve Public Health Impact
The goal of this five-year project is to assist the United States Centers for Disease Control and Prevention in their approach to modeling four key infectious diseases for U.S. disease control.

Role: Co-Investigator

[redacted]

2000 G QF123 HOLTGRAVE (PI) 06/07/12-03/31/17

NIMH: UCLA

Implementing Eban II: An Evidence-Based Intervention for Sero-Discordant Couples

The implementation of Eban II is a 5-year study, an evidence-based risk reduction intervention for heterosexual, African American HIV serodiscordant couples, investigating the processes and determinants of implementation in 10 community-based organizations (CBOs) in California, and real-world cost-effectiveness of Eban II as it is delivered to 180 couples
Role: PI

P30AI094189 CHAISSON (PI) 09/01/12-04/30/17
The Johns Hopkins Center for AIDS Research (JHU CFAR)
CFAR will help coordinate, mobilize the substantial scientific, clinical and public health resources at JHU to generate new knowledge to understand, respond to, and control the HIV pandemic.
Role: Co-Investigator

[redacted]

Completed Research Support

[redacted]

[redacted]

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Schaffner, William

eRA COMMONS USER NAME (credential, e.g., agency login): [redacted]

POSITION TITLE: Professor of Preventive Medicine, Department of Health Policy
Professor of Medicine, Division of Infectious Diseases

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Yale University, New Haven, CT	BS	1957	Zoology
Cornell Univ. Med College, New York	MD	1962	Medicine
Vanderbilt University Hospital, Nashville, Tn	Residency	1963-64	Medicine
Vanderbilt University School of Medicine	Fellow	1964-66	Infectious Diseases
Centers for Disease Control, Atlanta, GA	Epidemic Intelligence Service (EIS) Officer Training	1966-68	Public Health Epidemiology

A. PERSONAL STATEMENT

I am Professor of Preventive Medicine in the Department of Health Policy and Professor of Medicine in the Division of Infectious Diseases at the Vanderbilt University School of Medicine. For 31 years (1982-2013) I chaired the Department of Preventive Medicine and for 7 years was Chief of the Division of Infectious Diseases (1982-1989). I am a staunch advocate for collaborative relationships between academic medical centers and governmental public health institutions. Members of my department and I have close working relationships with colleagues at the Tennessee Department of Health and the CDC on research, teaching and service activities. My research has been focused on, but not limited to, communicable diseases, creating new epidemiologic science and translating the science into progressive health policy. My trainees have included infectious disease fellows and CDC EIS officers who have gone on to have successful careers in academia and at CDC in senior policy positions. My primary current research is as Co-PI of the CDC-funded Emerging Infections Program Tennessee site which produces rigorous data that are the basis for national public health policy determinations. This background provides me the experience to mentor Dr. Rebeiro in the design and conduct of his investigations, and I am confident that our excellent mentorship teams will support Dr. Rebeiro fully as he accomplishes his proposed research tasks.

B. POSITIONS AND HONORS

Positions

1969-1973	Assistant Professor of Medicine, Vanderbilt
1969-1979	Director, Clinical Microbiology Laboratory, Vanderbilt
1969-2006	Hospital Epidemiologist, Vanderbilt
1974-1979	Associate Professor of Medicine and Preventive Medicine, Vanderbilt

1979-Present	Professor of Medicine and Preventive Medicine, Vanderbilt
1982-1989	Chief, Division of Infectious Diseases, Department of Medicine, Vanderbilt
1982-2013	Chairman, Department of Preventive Medicine, Vanderbilt

Honors **(**selected**)**

1953-1957	Ford Foundation Scholar, Yale University
1957-1958	Fulbright Scholar, Freiburg, Germany
2009	James D. Bruce Award, American College of Physicians
2010	Ronald Davis Award, American College of Preventive Medicine
2010	Sedgwick Memorial Medal, American Public Health Association
2010	Harvie Branscomb Distinguished University Professor, Vanderbilt University
2010	Distinguished Alumnus Award, Vanderbilt University
2010	Alumni Award of Distinction, Weill Cornell Medical College
2011	Duncan Clark Award, Association for Prevention Teaching and Research
2011	Walter Stamm Mentor Award, Infectious Diseases Society of America
2012	Abraham Lilienfeld Award, American College of Epidemiology
2014	Laureate Award, Tennessee Chapter, American College of Physicians
2015	John Snow Award, Epidemiology Section, American Public Health Association

Federal Government Advisory Committee (selected)

1982-1986	Member, Advisory Committee on Immunization Practices, CDC
1986-Present	Liaison representative, Advisory Committee on Immunization Practices This committee establishes national immunization policy for both children and adults.

C. CONTRIBUTIONS TO SCIENCE

1. Immunization and Vaccine-Preventable Diseases

Several publications have had a specific influence on formulating national immunization policy. Among them are:

(a) The *first* demonstration that vaccine could eliminate measles from a large geographic area and that intensified surveillance could track the disease reliably. This paper gave proof of principle to the national goal of measles elimination.

(b) Research which persuaded the Advisory Committee on Immunization Practices (ACIP) to include asthma as an indication for pneumococcal vaccine.

(c) Demonstration that even the comprehensive deployment of vaccine could not contain an urban outbreak of hepatitis A, convincing the ACIP to change its recommendation and to make a new universal childhood recommendation.

a. **Schaffner W**, Schluederberg AE, Byrne EB. The clinical epidemiology of sporadic measles in a highly immunized population. New Engl J Med 1968;279:783-788.

b. Talbot TR, Hartert TV, Mitchel E, Halasa NB, Arbogast PG, Poehling KA, **Schaffner W**, Craig AS, Griffin MR. Asthma as a risk factor for invasive pneumococcal disease. N Engl J Med 2005;353:2082-2090.

c. Craig AS, Sockwell DC, **Schaffner W**, Moore WL, Skinner JT, Williams IT, Shaw FE, Shapiro CN, Bell BP. Use of hepatitis A vaccine to control a community-wide outbreak of hepatitis A. Clin Infect Dis 1998;27:531-535.

2. Hospital-Associated Infections

(a) This investigation was an early demonstration that hospitals are not islands unto themselves and that healthcare-associated infections can originate in one institution and have transmissible

ramifications throughout an entire community's medical care system. This, along with other studies, has led to the current regional approach to curtail antibiotic resistance.

(b) This was the *first* documentation that legionellosis could be spread from an air conditioning cooling towers. The results stimulated new recommendations specifying the need for regular cooling tower disinfection in order to prevent disease.

(c) Alert investigation of unusual infections in one hospital revealed a manufacturing problem in bronchoscopes that was brought to the attention of the FDA. A world-wide recall was undertaken, preventing perhaps hundreds of life-threatening infections.

a. Schaberg DR, Alford RH, Anderson R, Farmer JJ, Melly MA, **Schaffner W**. An outbreak of nosocomial infection due to multiply resistant Serratia marcescens: evidence of interhospital spread. J Infect Dis 1976;134:181-188.

b. Dondero TJ, Rendtorff RC, Mallison GF, Weeks RM, Levy J, Wong EW, **Schaffner W**. An outbreak of legionnaires' disease associated with a contaminated air conditioning cooling tower. New Engl J Med 1980;302:365-370.

c. Kirschke DL, Jones, TF, Craig AS, Chu PS, Mayernick GG, Patel JA, **Schaffner W**. Pseudomonas aeruginosa and Serratia marcescens contamination associated with a manufacturing defect in bronchoscopes. N Engl J Med 2003;348:214-220.

3. Pharmacoepidemiology

(a) and (b) The results of these two studies prompted the FDA to remove liquid formulations of tetracycline from the market.

(c) and (d) Both of these papers were important in defining these drug-related hazards, now well-known and accepted.

a. Ray WA, Federspiel CF, **Schaffner W**. The malprescribing of liquid tetracycline. Am J Pub Health 1977;67:762-763.

b. Ray WA, Federspiel CF, **Schaffner W**. Prescribing of tetracycline to children less than 8 years old. A two-year old epidemiologic study among ambulatory Tennessee Medicaid recipients. JAMA 1977;237:2069-2074.

c. Ray WA, Griffin MR, **Schaffner W**, Baugh DK, Melton LJ. Psychotropic drug use and the risk of hip fracture. New Engl J Med 1987;316:363-369.

d. Griffin MR, Ray WA, **Schaffner W**. Nonsteroidal anti-inflammatory drug use and death from peptic ulcer disease in elderly persons. Ann Int Med 1988;109:359-363.

(a) Public Health Investigation

The following are indicative of the broad variety of investigations that I have pursued in collaboration with public health colleagues.

(a) This investigation showed that the risk of ehrlichiosis increased in proportion to the golfer's handicap (risk of hitting into the rough and encountering ticks). It is both elegant and fun – so is being used in schools of public health as a teaching exercise

(b) This was the first explicit documentation of the large role that child restraint devices (child car seats) have in preventing child injuries and death in motor vehicle crashes. Tennessee was the first state to require the use of such child restraints and this paper provided the stimulus for the passage of similar laws in the other 49 states.

(c) The first "look-back" investigation of a surgeon with AIDS. Performed during a socially-charged era, the investigation was led by Dr. Schaffner and conducted calmly. It provided the first direct

evidence that HIV-infected surgeons posed a low risk to their patients and had a direct influence on national recommendations by the CDC and the American College of Surgeons.

a. Standaert SM, Dawson JE, **Schaffner W**, Childs JE, Biggie KL, Singleton J, Gerhardt RR, Knight ML, Hutcheson RH. Ehrlichiosis in a golf-oriented retirement community. N ENgl J Med 1995;333:420-425.

b. Decker MD, Dewey MJ, Hutcheson RH, **Schaffner W**. The use and efficacy of child restraint devices: the Tennessee experience, 1982 and 1983. JAMA 1984;252:2571-2575.

c. Mishu B, **Schaffner W**, Horan JM, Wood LH, Hutcheson RH, McNabb PC. A surgeon with AIDS: lack of evidence of transmission to patients. JAMA 1990;264:467-470.

D. RESEARCH SUPPORT

Ongoing Research Support

1U50CK000198-01 (Schaffner) **1/1/12-12/31/16**

Agency: Centers for Disease Control and Prevention

Title: Emerging Infections Program
Description: Emerging Infections Program is an umbrella collaboration of the CDC with 10 state health departments and their academic partners. I am the PI of the Vanderbilt site. The goal of EIP is to conduct a broad portfolio of work of applied research to detect, prevent and control an array of emerging infectious diseases. The data are used directly by CDC to create public policy initiatives.

Completed Research Support

5R01CA092447-12 (Blot) **7/26/13-6/30/14**

Agency: National Cancer Institute

Title: Southern Community Cohort Study
Description: The purpose of the SCCS is (1) to continue passive follow-up of the cohort via linkages with various national and state registries to identify deaths, incident cancers and other health outcomes, (2) to continue active follow-up of the cohort via re-contact with participants to directly update exposure and health information, and (3) to conduct multiple new cohort and nested case-control analyses utilizing the baseline and follow-up data and stored DNA and blood specimens for evaluation of lifestyle, genetic and other risk factors affecting the incidence of and disparities in the major cancers (lung, breast, prostate, and colon/rectum).

U50CCU41623-08 (Schaffner) **1/1/05-12/31/09**

Agency: Centers for Disease Control and Prevention

Title: Emerging Infections Program
Role: Co-Principal Investigator

1U011P000095-01 (Talbot) **9/30/07-9/29/08**

Agency: Centers for Disease Control and Prevention

Title: The Impact of Pertussis Vaccination of Healthcare Workers
Role: Investigator

BIOGRAPHICAL SKETCH

NAME: Fonnesbeck, Christopher J, PhD

eRA COMMONS USER NAME: [redacted]

POSITION TITLE: Assistant Professor of Biostatistics

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
University of British Columbia, Vancouver, BC	BS	08/1996	Biology
University of British Columbia, Vancouver, BC	MS	05/1998	Zoology
University of Georgia, Athens, GA	MS	05/2002	Statistics
University of Georgia, Athens, GA	PhD	07/2003	Quantitative Ecology
University of Georgia, Athens, GA	Postdoc	10/2005	Quantitative Ecology

A. Personal Statement

I am an active collaborator at Vanderbilt University, providing quantitative expertise to the Evidence-based Practice Center (Vanderbilt Institute for Medicine and Public Health), the Department of Pediatrics/Division of Infectious Diseases, and the Department of Orthopedic Surgery and Rehabilitation, as well as leading research on my own grant studying the optimal control of disease outbreaks, collaborating with Penn State University and the University of Warwick. I am particularly interested in the use of spatial statistics and Bayesian hierarchical/multilevel modeling strategies for inference and prediction in epidemiology. Moreover, as a biostatistical software developer, I am able to provide efficient software implementations of state-of-the-art statistical methods, as required by the diverse needs of biomedical data analysis. Notably, I am the creator and co-developer of PyMC, a popular software package for Bayesian statistical analysis. I will provide mentorship to Dr. Peter Rebeiro as part of his K01 mechanism, discussing with and instructing him on topics in spatial analysis such as geostatistics, spatial cluster detection, spatial generalized linear models, and methods for mapping and spatial data manipulation, through an Independent Study course offered in the Vanderbilt Biostatistics Department. I will also consult on study design and data analysis addressing his scientific Aims, which seek to evaluate health policy and quality questions of serious import to improving outcomes in the HIV Care Continuum and informing future public health action.

B. Positions and Honors

Positions and Employment

2005-2008 Adjunct Assistant Professor, University of Georgia, Athens, GA
2005-2008 Associate Research Scientist, Florida Marine Research Institute, St. Petersburg, FL
2008-2010 Lecturer (Assistant Professor), Department of Mathematics and Statistics, University of Otago, Dunedin, New Zealand
2010-2012 Instructor in Biostatistics, Vanderbilt University School of Medicine, Nashville, TN
2012-Pres. Assistant Professor in Biostatistics, Vanderbilt University School of Medicine, Nashville, TN

Other Experience and Professional Memberships

2014-Pres. Associate Editor, Journal of Statistical Software
2009-2012 Associate Editor, Journal of Statistical Computation and Simulation
2012-Pres. Member, International Society for Bayesian Analysis
2008-Pres. Member, American Statistical Association
2008-Pres. Member, International Biometric Society

C. Contribution to Science

1. I employ Bayesian hierarchical modeling, including its integration in analyses with spatial components, as the primary tool for inference and prediction in my research. This is a powerful and flexible approach for model-

based inference in a variety of settings, from clinical trials to large observational epidemiological datasets. Bayesian methods typically require computationally-intensive algorithms to yield results. I implement cutting-edge statistical methods in software so that they may be used by a wider, non-technical audience in biomedical research. This work is critical given the advent of very large electronic databases and modern data collection procedures that collect gigantic quantities of data. My software is used by data scientists and statisticians in a wide variety of scientific fields.

a. Martin J, Edwards HH, Bled F, **Fonnesbeck CJ**, Dupuis JA, Gardner B, Koslovsky SM, Aven AM, Ward-Geiger LI, Carmichael RH, Fagan DE, Ross MA, Reinert TR. Estimating upper bounds for occupancy and number of manatees in areas potentially affected by oil from the Deepwater Horizon oil spill. PLoS One. 2014 Mar 26;9(3):e91683. [PMID: 24670971] [PMCID: PMC3966779]
b. Conroy MJ, Runge JP, Barker RJ, Schofield MR, **Fonnesbeck CJ**. Efficient estimation of abundance for patchily distributed populations via two-phase, adaptive sampling. Ecology. 2008 Dec;89(12):3362-70. [PubMed PMID: 19137943]
c. Salvatier J, Wiecki TV, and **Fonnesbeck C**. Probabilistic programming in Python using PyMC3. PeerJ Computer Science, 2016 Apr; 2:e55
d. Patil A, Huard D and **Fonnesbeck CJ**. PyMC 2.0: Bayesian Stochastic Modeling in Python. Journal of Statistical Software, Journal of Statistical Software, 2010; 35(4), 1-81. [PMID: 21603108] [PMCID: PMC3097064]
e. **Fonnesbeck CJ**, McPheeters ML, Krishnaswami S, Lindegren ML and Reimschisel T. 2012. Estimating the probability of IQ impairment from blood phenylalanine for phenylketonuria patients: A hierarchical meta-analysis. Journal of Inherited Metabolic Disease, 2013 Sep; 36(5): 757-766. [PMID: 23197105]

2. Going back to my own PhD research, my primary research focus is on structured decision analysis, which I currently apply to infectious disease research, specifically related to the optimal control of disease outbreaks through the evaluation of alternative policies/decisions over space and time. More generally, I am interested in the application of adaptive management for optimal control, whereby decisions are made with the best available information in the face of uncertainty, and this uncertainty is reduced over time via information derived from monitoring the outcomes of past decisions, with the aim of improved decision-making. This work can be applied widely in epidemiology wherever sequential decisions are made with the aim of satisfying some explicit objective. My contribution to this work is in the application of stochastic dynamic optimization models to derive optimal policies for making decisions.

a. Shea K, Tildesley M, Runge M, **Fonnesbeck C**, and Ferrari M. Adaptive Management and the Value of Information: Learning via Intervention in Epidemiology. PLoS Biology 2014; 12(10): e1001970.
b. Probert WJM, Shea K, **Fonnesbeck CJ**, Runge MC, Carpenter TE, Du¨rr S, Garner MG, Harvey N, Stevenson MA, Webb CT, Werkman M, Tildesley MJ, Ferrari MJ. Decision-making for foot-and-mouth disease control: objectives matter. Epidemics. 2015; 15: 10-19.
c. **Fonnesbeck CJ**. 2005. Solving Dynamic Wildlife Resource Optimization Problems using Reinforcement Learning. Natural Resource Modeling, 18(1), 1-40.

3. I am a co-investigator for Vanderbilt University's Evidence-based Practice Center (EPC), one of 14 centers contracted by the Agency for Healthcare Research and Quality (AHRQ) to review all relevant scientific literature on a variety of clinical and health services topics to produce evidence reports based on this synthesis. My role is to conduct quantitative meta-analyses to support the conclusions of the review. At Vanderbilt's EPC, we employ sophisticated meta-analytic methods that allow complex medical interventions and multivariate outcomes to be modeled efficiently so that the current evidence and the associated residual uncertainty are adequately quantified. To date, my work has focused on the evaluation of pediatric and obstetric treatments.

a. Chinnadurai S, **Fonnesbeck C**, Snyder K, Sathe N, Morad A, Likis F, McPheeters M. Pharmacologic Interventions for Infantile Hemangioma: A Meta-Analysis. Pediatrics, 2016; 137(2):1-10. [PMID: 26772662]
b. Epstein, RA, **Fonnesbeck CJ**, Potter S, Rizzone KH and McPheeters M. 2015. Psychosocial Interventions for Child Disruptive Behaviors: A Meta-Analysis. Pediatrics. doi:10.1542/peds.2015-2577

c. Likis FE, Velez-Edwards DR, Andrews JC, Woodworth AL, Jerome RN, **Fonnesbeck CJ**, McKoy JN, Hartmann KE. Progestogens for Preterm Birth Prevention: A Systematic Review and Meta-Analysis by Indication. Obstetrics and Gynecology, 2012; 120(4), 1-11. [PMID: 22955308]
d. Krishnaswami S, **Fonnesbeck CJ**, Penson D and McPheeters M. Magnetic Resonance Imaging for Locating Non-palpable Undescended Testicles: A Meta-Analysis. Pediatrics 2013; 131(6):e1908-16. [PMID: 23690512] [PMCID: PMC4074662]

Complete List of Published Work in MyBibliography: http://bit.ly/fonnesbeck_ncbi_bibliography

D. Research Support

5 UL1 TR000445-09 (Bernard)
06/27/2012 – 05/31/2017
NIH/NCATS - "The Vanderbilt Institute for Clinical and Translational Research (VICTR)"
The specific aims of our renewal proposal are to: 1) Systematically remove impediments to research translation; 2) Create and make available novel, research-enabling infrastructure and resources; 3) Train the next generation of investigators; 4) Engage and involve the local community; and 5) Define and continuously measure success in meeting objectives.

R01 GM105247 (Fonnesbeck) 07/01/2012 – 06/30/2016
"Linking models and policy: Using active adaptive management for optimal control of disease outbreaks"
This work develops novel methods and training to combine decision theory and dynamic epidemic modeling to facilitate real-time implementation, evaluation, and adaptation of public health interventions.
Role: Site Principal Investigator

HHSA 290-2015-00003-I (McPheeters) 11/12/2014 – 11/11/2019
AHRQ Agency for Healthcare Research and Quality Evidence-based Practice Centers V The Evidence-based Practice Centers develop evidence reports and technology assessments on topics relevant to the clinical, social science/behavioral, economic, and health care organization and delivery arenas. Role: Co-investigator

[redacted]

Completed Research Support

HHSA 290-2007-10065-I (McPheeters) 11/01/2012 – 09/30/2013
Agency for Healthcare Research and Quality Evidence Based Practice Centers III (TO6)
Systematically reviews scientific literature on clinical, social, science/behavioral, and organization and financing topics to produce evidence reports and technology assessments. Role on the project: Co-Investigator

[redacted]

[redacted]

HHSA 290-2007-10065-I (Hartman) 01/01/2012 – 12/31/2012
"Agency for Healthcare Research and Quality Evidence Based Practice Centers III (TO5)"

Systematically reviews scientific literature on clinical, social, science/behavioral, and organization and financing topics to produce evidence reports and technology assessments
Role on the project: Biostatistican

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Shepherd, Bryan Earl

eRA COMMONS USER NAME (credential, e.g., agency login): [redacted]

POSITION TITLE: Associate Professor of Biostatistics

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Brigham Young University, Provo, UT	B.S.	08/1999	Statistics
University of Washington, Seattle, WA	M.S.	12/2001	Biostatistics
University of Washington, Seattle, WA	Ph.D.	08/2005	Biostatistics

A. Personal Statement

My primary research interests can be broadly summarized as developing and applying novel statistical methods to medical studies, with an emphasis on studies of HIV/AIDS. For the past 10 years, I have been the lead statistician for the Caribbean, Central and South American network (CCASAnet) of the International epidemiologic Databases to Evaluate AIDS (IeDEA). I am currently the Director of the Biostatistics and Biomedical Informatics Core of the Tennessee Center for AIDS Research (TN-CFAR); I served as the head statistician for the former Vanderbilt-Meharry CFAR from 2006-2013. I have also supervised biostatistical support for the Vanderbilt Institute for Global Health (VIGH) since 2006. In these contexts I have collaborated with many researchers on a wide variety of HIV/AIDS research topics, resulting in over 130 peer-reviewed publications, some of which are listed below. My statistical methods research has been motivated by problems I have encountered in my collaborative work, with a particular emphasis on causal inference and methods for epidemiological data. As a graduate student at the University of Washington, I developed causal inference methods important to HIV vaccine trials. Upon coming to Vanderbilt, I have continued to develop and apply causal inference methods, and have branched into other areas including approaches for analyzing ordered categorical data, and measurement error methods pertinent to this proposal. My statistical methods research has led to external funding: I was co-investigator and principal investigator (PI) of the Vanderbilt sub-contract of an R01 to investigate causal inference methods in partially randomized trials. I currently serve as PI of an R01 developing statistical methods applicable to HIV/AIDS that leverage the order information in ordered categorical variables to increase statistical power.

With regards to the current proposal, I am interested in the application of causal inference methods to many problems in HIV epidemiology, and I will be happy to mentor Dr. Rebeiro as he applies his considerable skill in service of addressing urgent and important questions related to the implementation of Medicaid expansion under the ACA and its impact on HIV Continuum of Care outcomes. He has worked with me on several epidemiologic analyses since 2005 (we have co-authored 17 publications), and we have an excellent working relationship. We have collaborated extensively with the Epi/Outcomes group of the TN Center for AIDS Research (CFAR) at Vanderbilt (Dr. Rebeiro is a member of the TN-CFAR core that I direct), the NA-ACCORD, and CCASAnet. I have also mentored 3 other successful K-awardees regarding causal inference methods and biostatistics. My prior successful methods development and mentorship, and his expertise and prior successful collaborations, demonstrate the feasibility and likely success of his proposed research. Three publications most relevant for this proposal are (candidate's name underlined):

1. **Shepherd BE**, Rebeiro PF; Caribbean, Central, South America network for HIV epidemiology (CCASAnet). Assessing and interpreting the association between continuous covariates and outcomes

in observational studies of HIV using splines. *J Acquir Immune Defic Syndr*. 2016 Oct 27. PMID: 27798430. [PMCID pending]
2. Rebeiro PF, Cesar C, **Shepherd BE**, De Boni RB, Cortés CP, Rodriguez F, Belaunzarán-Zamudio P, Pape JW, Padgett D, Hoces D, McGowan CC, Cahn P. Assessing the HIV Care Continuum in Latin America: progress in clinical retention, cART use and viral suppression. *J Int AIDS Soc*. 2016 Apr 8;19(1):20636. PMCID: PMC4827101.
3. **Shepherd BE**, Jenkins CA, Rebeiro PF, Stinnette SE, Bebawy SS, McGowan CC, Hulgan T, Sterling TR. Estimating the optimal CD4 count for HIV-infected persons to start antiretroviral therapy. *Epidemiology*. 2010 Sep;21(5):698-705. PMCID: PMC3086582.

B. Positions and Honors

Positions and Employment

1998-1998 SAS Programmer, McBride Biostatistical Research, Morristown, NJ.
2000-2000 Research Assistant, Kenya Medical Research Institute and Univ. of Washington, Nairobi, Kenya.
2000-2001 Teaching Assistant, Department of Biostatistics, University of Washington.
2001-2005 Research Assistant, Department of Biostatistics, University of Washington.
2005–2011 Assistant Professor, Department of Biostatistics, School of Medicine, Vanderbilt University
2011–pres. Associate Professor, Department of Biostatistics, School of Medicine, Vanderbilt University

Honors

1993 Trustees Scholarship, full tuition for four years, Brigham Young University (BYU)
1998 Edwin Hinckley Scholarship, BYU
1998 Undergraduate Research Award, Office of Research and Creative Activities, BYU
1999-2000 Graduate Merit Award, Department of Biostatistics, University of Washington
2000-2005 NIH Cardiovascular Training Grant, University of Washington
2005 Senior Student Award, Department of Biostatistics, University of Washington
2016 Shayle Searle Fellow, School of Mathematics and Statistics, Victoria University of Wellington

C. Contribution to Science

1. Causal inference methods and applications. My early methods research was focused on developing statistical methods to compare clinical trial outcomes that only existed in subsets chosen after randomization. These methods were particularly motivated by HIV vaccine trials, where many outcomes (e.g., set point viral load, time from infection diagnosis to AIDS) only exist in participants who become infected; but they have also been applied to other settings (e.g., truncation by death and cancer studies). My work in this area focused on sensitivity analyses within the principal stratification framework – explicitly specifying assumptions to identify causal estimands and then relaxing assumptions through the use of sensitivity parameters elicited by subject-matter experts. More recently, my causal inference research has dealt with time-varying confounding, particularly applications of marginal structural models and dynamic marginal structural models motivated by questions regarding optimal timing of antiretroviral therapy.

a. **Shepherd BE**, Gilbert PB, Jemiai Y, Rotnitzky A. Sensitivity analyses comparing outcomes only existing in a subset selected post-randomization, conditional on covariates, with application to HIV vaccine trials. *Biometrics* 2006; 62:332-342. PMID: 16918897.
b. **Shepherd BE**, Gilbert PB, Lumley T. Sensitivity analyses comparing time-to-event outcomes only existing in a subset selected post-randomization. *Journal of the American Statistical Association* 2007; 102: 573-582. PMCID: PMC2613336.
c. **Shepherd BE**, Jenkins CA, Rebeiro PF, Stinnette SE, Bebawy SS, McGowan CC, Hulgan T, Sterling TR. Estimating the optimal CD4 count for HIV-infected patients to start antiretroviral therapy. *Epidemiology* 2010; 21: 698-705. PMCID: PMC3086582.
d. **Shepherd BE**, Liu Q, Mercaldo N, Jenkins CA, Lau B, Cole SR, Saag MS, Sterling TR. Comparing results from multiple imputation and dynamic marginal structural models for estimating when to start antiretroviral therapy. *Statistics in Medicine* 2016; 35: 4335-4351. PMID:27264354; PMCID: PMC5048599 [Available 10/30/2017].

2. Methods for ordinal data analysis. Motivated by a simple question we encountered in our collaborative research, my colleague, Chun Li and I developed a new statistical method to test for association between two

ordered categorical variables while adjusting for covariates. In the process, we developed a new residual for ordinal outcomes, which we have since discovered to be useful for many other outcome types. This work has opened up new directions for the analysis of ordinal data based on fewer assumptions than traditional approaches and is currently funded by an R01 from the National Institutes of Health.

a. Li C, **Shepherd BE**. Test of association between two ordinal variables while adjusting for covariates. *Journal of the American Statistical Association* 2010; 105: 612-620. PMCID: PMC2946253
b. Li C, **Shepherd BE**. A new residual for ordinal outcomes. *Biometrika* 2012; 99: 473-480. PMCID: PMC3635659

[redacted]

d. Dupont C, Horner J, Li C, Liu Q, **Shepherd BE** (2016) "PResiduals: probability-scale residuals and residual correlation" R package. URL: https://cran.r-project.org/web/packages/PResiduals/index.html

3. Collaborative HIV scientist. I have been involved in many team science studies of HIV/AIDS. In the majority of these studies I have been the head statistician, either performing the analyses myself or supervising the work of others. I have also taken the lead on several of these papers, serving as first or senior author. I take pride in our use of modern statistical methods (e.g., splines for continuous variables, multiple imputation for missing data, and appropriate applications of marginal structural models), the clarity and interpretability of our analyses, and our emphasis on reproducible research (e.g., analysis code is posted at http://biostat.mc.vanderbilt.edu/ArchivedAnalyses). These studies, individually and collectively, have been important contributions to our understanding of HIV/AIDS and its management.

a. Tuboi SH, Schechter M, McGowan CC, Cesar C, Krolewiecki A, Cahn P, Wolff M, Pape JW, Padgett D, Madero JS, Gotuzzo E, Masys DR, **Shepherd BE**. Mortality during the first year of potent antiretroviral therapy in HIV-1-infected patients in 7 sites throughout Latin America and the Caribbean. *Journal of Acquired Immune Deficiency Syndromes* 2009; 51: 615-623. PMCID: PMC2780368.
b. Koethe JR, Jenkins CA, **Shepherd BE**, Stinnette SE, Sterling TR. An optimal body mass index range associated with improved immune reconstitution among HIV-infected adults initiating antiretroviral therapy. *Clinical Infectious Diseases* 2011; 53: 952-960. PMCID: PMC3189168.
c. **Shepherd BE**, Jenkins CA, Parrish DD, Glass TR, Cescon A, Masabeu A, Chene G, de Wolf F, Crane HM, Jarrin I, Gill J, del Amo J, Abgrall S, Khaykin P, Lehmann C, Ingle SM, May MT, Sterne JAC, Sterling TR; the Antiretroviral Therapy Cohort Collaboration. Higher rates of AIDS during the first year of antiretroviral therapy among migrants: the importance of tuberculosis. *AIDS* 2013; 27: 1321-1329. PMCID: PMC3992322.
d. Boulle A, Schomaker M, May MT, **Shepherd BE**, Monge S, Keiser O, Lampe F, Giddy J, Ndirangu J, Garone D, Fox M, Ingle SM, Reiss P, Dabis F, Costagliola D, Castagna A, Ehren K, Campbell C, Gill MJ, Saag M, Justice AC, Guest J, Crane HM, Egger M, Sterne JAC. Mortality in patients with HIV-1 infection starting antiretroviral therapy in South Africa, Europe or North America: a collaborative analysis of prospective studies. *PLoS Medicine* 2014; 11: e1001718. PMCID: PMC4159124.

4. Other statistical/epidemiological research motivated by multi-cohort observational HIV studies. Given my involvement in many multi-cohort observational studies, I often encounter challenges or statistical problems that I feel deserve further study. Many are stand-alone studies – they have resulted in what I believe are interesting publications, but have not led to an extensive research agenda. The first two manuscripts listed below were motivated by a project building a predictive model for the VCCC. I asked (a) Does ignoring model fitting uncertainty caused by checking the proportional hazards assumption impact the validity of confidence intervals and p-values? (Answer: yes.) and (b) Why was our model poor at predicting when applied to a separate cohort? (Answer: substantial between-cohort heterogeneity). With the third paper listed below, we wondered what impact the various different definitions of loss to follow-up (LTFU) could have on study estimates. They had a huge impact: we applied 17 different definitions in the literature to data from the same cohort and found 2-year estimates of LTFU varying from 22% to 84%! The fourth paper listed was an investigation/tutorial into the many different ways one can account for between-cohort heterogeneity in Cox regression models, and their impact on results. Each of these studies increased our understanding and provided guidance for analyses of multi-cohort observational studies.

a. **Shepherd BE**. The cost of checking proportional hazards. *Statistics in Medicine* 2008; 27: 1248-1260.

b. **Shepherd BE**, Sterling TR, Moore RD, Raffanti SP, Hulgan T. Cross-cohort heterogeneity encountered while validating a model for HIV disease progression among antiretroviral initiators. *Journal of Clinical Epidemiology* 2009; 62: 729-737.
c. **Shepherd BE**, Blevins M, Vaz LME, Moon TD, Kipp AM, Jose E, Ferreira FG, Vermund SH. Impact of definitions of loss to follow-up on estimates of retention, disease progression, and mortality: Application to an HIV program in Mozambique. *American Journal of Epidemiology* 2013; 178: 819-828. PMCID: PMC3755641.
d. Giganti MJ, Luz PM, Caro-Vega Y, Cesar C, Padgett D, Koenig S, Echevarria J, McGowan CC, **Shepherd BE**. A comparison of seven Cox regression-based models to account for heterogeneity across multiple HIV treatment cohorts in Latin America and the Caribbean. *AIDS Research and Human Retroviruses* 2015; 31: 496-503.

Complete List of Published Work in MyBibliography: http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/45654384/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

6R01 AI093234-06 (Shepherd) 05/18/2011 - 04/30/2017
Statistical Methods for Ordinal Variables in HIV/AIDS Studies
The major goal of this project is to develop statistical methods that account for the ordered nature of ordinal variables without making linearity assumptions and then applying these methods to HIV studies.

2U01 AI069923-12 (McGowan) 07/25/2011 - 06/30/2021
Caribbean, Central and South America Network for HIV epidemiology (CCASAnet)
The major goals of this project are to create a shared database of HIV epidemiology data from six countries in the Caribbean, Central, and South America perform analyses of data to answer questions that cannot be answered by any single site, and develop novel analytical, informatic, and biostatistical methods for such pooled data.

5K08AI106420-04 (Van der Heijden) 08/01/2014 – 07/31/2019
Fluoroquinolone Resistance in Patients with Multidrug-Resistant Tuberculosis
Drug-resistant tuberculosis and HIV are devastating public health problems in South Africa. Fluoroquinolone antibiotics are critical for the treatment of tuberculosis that is resistant to the most important first-line drugs, but resistance to fluoroquinolones threatens their usefulness. The current study will examine the scope and impact of the problem of fluoroquinolone-resistant tuberculosis in a setting with high rates of HIV and provide new information that will help protect this vital class of medications for the treatment of tuberculosis.

6P30AI110527-02 (Mallal) 04/01/2015 - 03/31/2020
Tennessee Center for AIDS Research (TN-CFAR)
Reducing the overall burden of HIV/AIDS in Tennessee: By forging unique three-way partnership between VU, MMC, and TDH, the Tennessee CFAR (TN-CFAR) is building a research infrastructure toward having impact on the overall burden of HIV diseases in our state.

6R24AI124872-02 (Duda) 04/06/2016-03/31/2021
Harmonist: A Scalable Toolkit for Standardizing and Coordinating Data Sharing Across International Research Networks
The goal of the Harmonist project is to develop the “Harmonist toolkit,” a software and standards package that will enable HIV observational research networks to coordinate large-scale research projects and apply data management best practices more effectively and efficiently.

Completed Research Support (past 3 years)

5U01AI069918-08 (Moore) 1/01/2013 – 07/31/2015
National Institute of Allergy and Infectious Diseases –
North American AIDS Cohorts Collaboration on Research & Design (NA-ACCORD)

Supplement (Vanderbilt PI: Sterling)
This supplement supports a pair of analyses evaluating the effect of being overweight or obese on CD4+ T-cell recovery on antiretroviral therapy, and the role of angiotensin converting enzyme-inhibitors and angiotensin receptor blockers in the prevention of mortality and the development of card inflammation-related non-AIDS defining events among participants in the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD), one of the regional cohort groups supported by the International Epidemiologic Databases to Evaluate AIDS consortium (IeDEA) of the NIH.

5R01AI094562-04 (Vermund) 03/15/2011-03/31/2015
Multi-component HIV Intervention Packages for Chinese MSM
The major goal of this project is to develop and pilot test a multi-component prevention intervention package of Test and Link-to-Care strategy to reduce HIV transmission.
Role: Co-Investigator

3P30 AI054999-08S1 (Kalams) 09/01/2006-08/31/2014
Vanderbilt Meharry Center for AIDS Research
This application proposed a Developmental Center for AIDS Research at Vanderbilt and Meharry, including an administrative core, developmental core, clinical discovery core, molecular virology core, and an immunology core to build infrastructure and collaborations that will enhance HIV/AIDS research at both institutions.
Role: Co-Investigator

1R34AI091446-01A1 (Vermund) 08/01/2011-07/31/2014
Expanded Testing, Linkage, and Treatment for Aids Prevention Among MSM in China
Our goal in this one-year clinical trial planning (R34) grant is to prepare for a community-level randomized clinical trial (RCT) to test the efficacy of our multicomponent TLC intervention package to reduce HIV incidence among MSM in China.

R01HD075075-02 (Aliyu) 09/28/2012-06/30/2014
Optimizing integrated PMTCT services in rural North-Central Nigeria
The goal of this study is to implement and evaluate the impact of a familyfocused integrated PMTCT package comprising task shifting, point-of-care CD4 testing, and a prominent role for influential family members (particularly male partners) in rural primary health centers in Nigeria.

5R01DA26207-02 (Markham, PI) 09/01/2008-05/31/2013
Johns Hopkins University/NIDA/NIH
Effect of Cocaine & AN LTR Polymorphism-ON Campus
The major goal of this study was to evaluate whether the presence of certain variants of HIV-1 which carry genetic alterations might enable them to replicate more rapidly in cells exposed to cocaine therefore altering various parameters of disease progression in cocaine users.
Role on the Project: Co-Investigator

OTHER SUPPORT

STERLING, TIMOTHY

Active Support

R56AI118361-01A1 (Sterling) 08/03/16 – 6/30/2017 2.4 CM
NIH/NIAID $566,475
Fluoroquinolones and Efflux Mediated Cross Resistance in HIV-related TB
This work will identify and characterize the efflux pumps involved in fluoroquinolone resistance in *M. tuberculosis*. It will also characterize the genes that may modify efflux pumps, including transcription factors and phosphate transporters. This work will determine whether HIV infection enables the acquisition of efflux pump-mediated fluoroquinolone resistance, and determine the role of efflux pumps in fluoroquinolone-resistant *M. tuberculosis* in reducing susceptibility to other anti-tuberculosis drugs.

1 R01 AI20790-01A1 (Sterling/Rolla) 08/12/2016 – 06/30/2021 1.8 CM
NIH/NIAID $522,654
Predictors of Treatment Toxicity, Failure, and Relapse in HIV-related Tuberculosis
The over-arching goal of this project is to optimize the treatment of HIV-related tuberculosis in a large, genetically diverse cohort in Brazil. These results will lay the groundwork for drug dosing and regimens that improve outcomes and treatment effectiveness of HIV-related tuberculosis.

2U01AI069923-12 (McGowan) 07/01/2016-06/30/2017 1.8 CM
NIAID $700,874
CCASAnet Supplement—RePORT-Brazil Role: Project PI
The Regional Prospective Observational Research on Tuberculosis (RePORT)-Brazil TB Cohort will harmonize the clinical data and clinical specimens obtained from pulmonary TB cases and their close contacts in three different regions of Brazil: Southeast (Rio de Janeiro), Northeast (Salvador) and North (Manaus), to encompass different types of TB epidemiology in Brazil. The RePORT-Brazil cohort will lay the groundwork for subsequent studies of TB pathogenesis, including risk factors for progression from latent M. tuberculosis infection to active TB disease, and risk factors for TB.

1R21AI127129-01 (Kalams) 08/01/2016 - 07/31/2018 0.60 CM
NIH/NIAID $150,000
Molecular analysis of the adaptive immune response to tuberculosis
The purpose of this R21 is to apply cutting edge molecular immunology techniques to determine the features of the adaptive immune response likely to protect against active tuberculosis infection.

CDC 10FED1007388 (Sterling) 10/01/2009- 9/30/2019 2.4 CM
Centers for Disease Control and Prevention $459,857
TB Trials Consortium-Vanderbilt/Peru
This consortium conducts studies of tuberculosis treatment and prevention.

CDC RFS 200-2011-41276 (Stout, Duke, PI) 09/01/2011-09/29/2021 0.12 CM
Centers for Disease Control and Prevention $150,501
TB Epidemiologic Studies Consortium-TN
This consortium conducts studies of the diagnosis and treatment of latent *M. tuberculosis* infection.

1P30AI110527-01A1 (Mallal) 04/01/15 - 03/31/2020 1.20 CM
NIH/NIAID $1,049,280

Tennessee Center for AIDS Research (TN-CFAR)
Reducing the overall burden of HIV/AIDS in Tennessee: By forging` unique three-way partnership between VU, MMC, and TDH, the Tennessee CFAR (TN-CFAR) is building a research infrastructure toward having impact on the overall burden of HIV diseases in our state.

P30 AI110527 Suppl (Mallal, PI) 07/01/2016 – 03/31/2017 0.24 CM
NIH/CFAR $199,162
Tennessee Center for AIDS Research: Characterizing HIV Phylodynamics in Middle Tennessee
Goal is to address the scientific area of interest tracking HIV transmission Phylodynamics. Using sequences and the patient characteristics in the VCCC database, our team will combine standard phylogeny-based approach as well as innovative statistic modeling to characterize the HIV-1 epidemic in Middle Tennessee.
Role: investigator

5U01AI069918-11 (Moore, JHU, PI) 07/01/2016 - 06/30/2021 0.12 CM
NIH/NIAID $60,000
North American AIDS Cohorts on Collaboration and Design (NA-ACCORD) of the International Epidemiologic Databases to Evaluate AIDS (IeDEA) network. This collaboration conducts observational cohort studies of HIV outcomes.

U01AI069923-12 (McGowan) 07/01/2016 - 06/30/2021 0.6 CM
NIAID $750,000
The Caribbean, Central American, and South American network for HIV epidemiology (CCASAnet) of the IeDEA network brings together the clinical and data expertise and resources of Vanderbilt University and clinical sites in Argentina, Brazil, Chile, Haiti, Honduras, Mexico and Peru. CCASAnet uses state of the art technologies to create a shared data repository and associated methods for data merging that brings together existing HIV-related clinical datasets available at the participating sites.
The project conducts and facilitates research using the shared data repository that enables answers to questions that cannot be answered by any single source, and develops and evaluates new biostatistical methods relevant to HIV epidemiology.

OVERLAP
There is no scientific or budgetary overlap. If all pending grants are funded, Dr. Sterling will reduce his active and pending effort as not to exceed 12 CM of support.

Current & Pending Support

Graves, John

ACTIVE

1U01HL122904-03 (Peterson) 09/30/13 – 05/31/17 7.56 calendar months
NHLBI $367,257
Rational Integration of Genomic Healthcare Testing (RIGHT)
The Rational Integration of Genomic Healthcare Technology (RIGHT) project will evaluate the feasibility and cost-effectiveness of three different pharmacogenomic implementation strategies. Capitalizing on the initial success of one of the largest pharmacogenomic testing programs in place within the Vanderbilt Health System, this project will measure the cost-effectiveness of prospective genotyping and determine factors that support successful genotype-tailored prescribing.

1R01CA189152-01A1 (Graves) 07/01/15-06/30/20 3.0 calendar months
NCI $1,407,632
Effects of Expanded Coverage on Access, Health and Cancer Care in the South
This project will provide timely and rigorous analysis of the effect of health insurance coverage expansions on health care use and outcomes among a large cohort of low-income adults in 12 southeastern states (VA, WV, KY, TN, NC, SC, FL, GA, AL, MS, LA, AR). Using a quasi-experimental research design, we aim to quantify the effects of coverage expansion through Medicaid and private health insurance exchanges on access to care, cancer screening and use of preventive clinical services (**Aim 1**); on self-reported health outcomes, mortality and use of emergent and inpatient care (**Aim 2**); and on cancer stage at diagnosis and quality of cancer care (**Aim 3**).

PENDING

[redacted]

BUDGET JUSTIFICATION.

Personnel

Peter Rebeiro, MHS, PhD (candidate, [redacted] calendar months with salary) will devote [redacted] of his time to this project. He will be the principal investigator and will be responsible for acquiring the advanced skills in health policy analysis and causal inference methods necessary to complete all three aims of this proposal. This will include formal coursework as well as informal instruction and advice on data manipulation, management, and analysis. He will be responsible for overseeing or conducting analyses, interpretation of results, and manuscript preparation.

Timothy R. Sterling, MD (primary mentor, *no salary support*) will oversee the career development of the applicant to ensure that he is meeting his research and academic goals. He will meet with the candidate weekly as well as at semi-annual mentoring committee meetings. He will be available to review submitted meeting abstracts, manuscripts, and future grant applications. He is independently funded and not requesting salary support.

John A. Graves, PhD (co-mentor, *no salary support*) will oversee the methodological components of the proposal and serve as co-mentor for the candidate's career development. He will meet with the candidate bi-weekly as well as at semi-annual mentoring committee meetings. He will guide the applicant in research design and data analysis and will be available to review submitted meeting abstracts, manuscripts, and future grant applications. He is independently funded and not requesting salary support.

William Schaffner, MD (*internal* mentoring committee, *no salary support*) will serve as an internal mentoring committee member advising the applicant on career development. He will meet with the candidate quarterly as well as at semi-annual mentoring committee meetings. He will guide the applicant in communicating evidence for maximal impact with policy makers as part of his career development. He is independently funded and not requesting salary support.

David R. Holtgrave, PhD (*external* mentoring committee, *no salary support*) will serve as an external scientific advisory committee member, advising the applicant on the optimization of his analysis to best inform health policy. He will meet with the candidate at semi-annual mentoring committee meetings. He is independently funded and not requesting salary support.

Stephen J. Gange, PhD (*external* mentoring committee, *no salary support*) will serve as an external scientific advisory committee member, advising the applicant on use of appropriate biostatistical and epidemiologic methods to reach valid inferences regarding policy impact on HIV outcomes. He will meet with the candidate at semi-annual mentoring committee meetings and at monthly NA-ACCORD Epidemiology/Biostatistics Core meetings. He is independently funded and not requesting salary support.

Catherine C. McGowan, MD (*internal* advisor, *no salary support*) will serve as an internal advisor at Vanderbilt, advising the applicant on optimal use of CCASAnet data to meet the objectives of the proposed research. She will meet with the candidate quarterly as well as at weekly CCASAnet data management/analysis core meetings and at semi-annual mentoring committee meetings. She is independently funded and not requesting salary support.

Richard D. Moore, MD, MHS (*external* advisor, *no salary support*) will serve as an external advisor at Johns Hopkins, advising the applicant on appropriate use of NA-ACCORD data to best inform policy makers. He will meet with the candidate at semi-annual mentoring committee meetings and at monthly NA-ACCORD Epidemiology/Biostatistics Core meetings. He is independently funded and not requesting salary support.

Christopher J. Fonnesbeck, PhD (*internal* advisor, *no salary support*) will serve as an internal advisor at Vanderbilt, advising the applicant on appropriate spatial statistical methods to obtain valid inferences for the influence of geographically and temporally variable health policy changes on outcomes. He will also meet quarterly with the candidate as part of his internal advisory committee, in addition to teaching and consulting with the candidate during a "Special Topics" course on spatial analysis, which he will teach, offered with the approval of the Director of Graduate Studies for the Department of Biostatistics (see Letter of Support).

Bryan E. Shepherd, PhD (*internal* advisor, *no salary support*) will serve as an internal advisor at Vanderbilt, advising the applicant on the proper selection and use of causal inference methods germane to his research.

He will meet with the candidate on a weekly basis as part of regular research meetings (e.g., the Epi/Outcomes and CCASAnet research group meetings, see "Candidate Plan for Career Development/Training Activities") and quarterly with the rest of his internal advisory committee.

Educational expenses

The candidate requests funding for tuition to enroll in formal coursework in Vanderbilt School of Medicine's Health Policy track of the Master of Public Health program and in Special Topics coursework in the Department of Biostatistics during the first 1-2 years of the award. The Vanderbilt Graduate School charges $[redacted] per credit hour (2017-2018 rate), but the candidate will receive a 70% discount as a Vanderbilt faculty member ($[redacted] per credit hour after discount). Funds for textbooks and computer software mandated for coursework are also requested. The table below outlines formal coursework planned by semester (see "Candidate Plan for Career Development/Training Activities" and "Facilities and Other Resources" for further course descriptions):

	Year 1	Year 2
1st Semester	PUBH 5520 "Introduction to Health Policy"	PUBH 5538 "Health Services Administration: Program and Policy Evaluation"
2nd Semester	BIOS 8398 "Special Topics: Spatial Analysis"	PUBH 5525 "Health Economics"

The candidate may also require funding for seminars and short courses. For example, seminars on management of big data, simulation analyses for health policy, etc. are offered through membership in Academy Health, a premier Health Services Research organization which supports the production and use of evidence to inform policy and practice and also hosts the annual National Health Policy Conference. Similar Cost Effectiveness Analysis"), American Public Health Association (e.g., "Population Health in the context of the Affordable Care Act: The role and accountability of Hospitals and Health Systems") and the International Conference on Health Policy Statistics (e.g., "Nonparametric Methods for Difference-in-Difference Estimation"). The fees required may include registration as a member with the organization or registration specific to the workshops. Short courses offered over 3-4 days by institutions such as the London School of Economics ("Health Economics", SA4G2, http://tinyurl.com/kfjbl4k) and the University of California San Francisco ("Global Health Policy", GHS 205, http://tinyurl.com/k92youo), may also be essential to the acquisition of new skills in health policy analysis. As an example of the associated fees for short courses, the London School of Economics would charge [redacted] ([redacted], exclusive of VAT) for 1 course; travel expenses would be required, as well.

Data Management, Computing, and Biostatistical Support

The candidate also requests funding for data validation, data management, and computing support through the Vanderbilt Epidemiology/Outcomes Group data validation and management team and through the Biostatistics Collaboration Center (BCC) at Vanderbilt.

The Epidemiology/Outcomes Group has extensive experience in validating, maintaining, and synthesizing demographic, socioeconomic, laboratory, prescription, and other clinical data from the Vanderbilt Comprehensive Care Center Cohort. Rates for the Epidemiology/Outcomes staff are based on a 5-10% percent effort for the data manager (Computer Systems Analyst II), data administrator (Research Coordinator), and data abstractor (Research Analyst I), as necessary for Aims 1-3 of this study.

The BCC is a revenue neutral university resource. Rates for the BCC are based on the complete cost of performing collaborative services including, but not limited to, salaries, administrative costs, supplies, computing (software, hardware, and shared resources such as the Advanced Computing Center for Research and Education (ACCRE)), information technology support, and relevant professional development costs. Rates have been calculated based on 1500 hour work year, explicitly excluding common professional activities not related to this specific project (e.g., seminars, meeting attendance etc.). Vanderbilt University annually reviews the BCC to ensure that it is in compliance with all applicable federal and state regulations, including OMB Circulars A-21, A-110 and A-133. Rates are adjusted annually to ensure that the BCC is operating on a strict non-profit cost recovery basis.

A Computer Systems Analyst will assist the candidate in the management of large datasets at the Advanced Computing Center for Research and Education (ACCRE). The current rate for a Computer Systems Analyst ranges from [redacted], and an estimate of 50 billable hours has been provided for this project (10 hours per year). This yields an estimated cost, excluding estimated inflationary adjustments, of [redacted].

Beginning July 1, 2014 all biostatistics staff and faculty effort is billed directly to each project as a percentage of salary and fringe benefit expenses. In addition, a scientific resource fee of [redacted] per 100% annual FTE (faculty and staff combined) is billed to each project for allowable costs related to providing cutting-edge biostatistics support. The department utilizes robust computing technologies and innovative methodologies to manage complex analyses. This scientific resource fee covers costs necessary to perform the work of biostatisticians and computer systems analysts. These resources are directly related to the many technologies used and types of data generated across multiple disciplines that biostatisticians must competently handle. The scientific resource fee will be billed on a monthly basis via the Core Ordering and Reporting Enterprise System (CORES).

The School of Medicine has created a model described here that allows the costs to be recovered from the sources requesting the assistance. For example, with a faculty biostatistician at 5% annual effort and a staff biostatistician at 10% annual effort, the annual fee is [redacted] will be billed monthly to the project. This scientific resource fee is in addition to the faculty and staff percent-effort salary and fringe benefit charges. These changes have been reviewed and approved by executive leadership of the School of Medicine and the fee schedule is implemented each year on August 1st.

The BCC has worked extensively with Dr. Sterling and others in the Division of Infectious Diseases.

Travel expenses

Funds to travel to 2-3 scientific meetings per year are requested. The candidate plans to submit a minimum of one abstract to at least three meetings per year: the Conference on Retroviruses and Opportunistic Infections (CROI), National Health Policy Conference (NHPC) of Academy Health, and either the Society for Medical Decision Making (SMDM) or the Society for Epidemiologic Research (SER) meetings. Additionally, the annual meeting of the NA-ACCORD Steering Committee is held during CROI and the annual scientific meeting of CCASAnet is typically held in one of the 7 member countries during the fall. Funds to travel to one workshop or short course on marginal structural methodology per year are requested during the first three years of the award. Funds to travel to HRSA/HAB meetings with Dr. Cheever and HRSA partners in Rockville, MD; NIH-sponsored HIV-related health policy symposia in Bethesda, MD; or meetings with the Epidemiology/Biostatistics Core (EBC) of NA-ACCORD in Baltimore, MD for 2-3 days, 1-2 times per year are also requested. Based on searches using Google's ITA Matrix, flights would be [redacted] per round-trip. Hotel accommodations may cost between [redacted] per night.

Additional expenses

The candidate asks for funding to purchase a laptop and printer during the first year of the award and a desktop computer during the fourth year of the award for data analysis and manuscript and grant application preparation. The candidate also asks for funding to purchase updated versions of Adobe Acrobat, ArcGIS, SAS and/or Stata, Microsoft Office, Stat Transfer, and Reference Manager or Sente as necessary for the new hardware.

The natural aging of hardware, accumulation of memory leaks in operating systems, interoperability requirements for updated software packages, and ability of processing power to keep pace with increasingly complex models (potentially including simulation models) using large datasets (millions of observations across dozens of variables, due to the data's longitudinal nature) would require periodic updating/replacement of hardware. This would include a laptop, required for work when away from the office (including time spent in classes, at conferences, during visits to HRSA/Johns Hopkins in MD, and during time at home in the evenings).

This may also include a desktop if much more robust processing power (beyond the standards available in laptops) would be required for complex computational issues in the analysis phase; this may also be required if the computation will be required to run for days or weeks and consume most of the CPUs resources, rendering other critical software such as word processing programs unusable during computation- this would be the case for certain multilevel/mixed effects models, bootstrapping procedures, or simulation models.

A printer is being requested to facilitate the production of reports for collaborators, printing journal articles for consultation with other analysts/colleagues during the course of the project, and printing handouts for conferences.

Publication costs and office supplies are requested for the final three years of the award.

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

Expiration Date: 10/31/2018

1. Human Subjects Section

Clinical Trial? ❍ Yes ● No

*Agency-Defined Phase III Clinical Trial? ❍ Yes ❍ No

2. Vertebrate Animals Section

Are vertebrate animals euthanized? ❍ Yes ● No

If "Yes" to euthanasia

Is the method consistent with American Veterinary Medical Association (AVMA) guidelines?

❍ Yes ❍ No

If "No" to AVMA guidelines, describe method and proved scientific justification

3. *Program Income Section

*Is program income anticipated during the periods for which the grant support is requested?

❍ Yes ● No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

*Budget Period	*Anticipated Amount ($)	*Source(s)

Tracking Number: GRANT12315321 Funding Opportunity Number: PA-16-190 . Received Date: 2017-01-05T17:21:11.000-05:00

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4. Human Embryonic Stem Cells Section

*Does the proposed project involve human embryonic stem cells? ❍ Yes ● No

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Specific stem cell line cannot be referenced at this time. One from the registry will be used.

Cell Line(s) (Example: 0004):

5. Inventions and Patents Section (RENEWAL)

*Inventions and Patents: ❍ Yes ❍ No

If the answer is "Yes" then please answer the following:

*Previously Reported: ❍ Yes ❍ No

6. Change of Investigator / Change of Institution Section

❑ Change of Project Director / Principal Investigator

Name of former Project Director / Principal Investigator

Prefix:

*First Name:

Middle Name:

*Last Name:

Suffix:

❑ Change of Grantee Institution

*Name of former institution:

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OMB Number: 0925-0001
Expiration Date: 10/31/2018

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5. Progress Report Publication List (for RENEWAL applications only)	
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Citizenship*:

U.S. Citizen or Non-Citizen National?* ☑ Yes ❑ No

If no, select most appropriate Non-U.S. Citizen option

- ❑ With a Permanent U.S. Resident Visa
- ❑ With a Temporary U.S. Visa
- ❑ Not Residing in the U.S.

If with a temporary U.S. visa who has applied for permanent resident status and expect to hold a permanent resident visa by the earliest possible start date of the award, also check here: ❑

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INTRODUCTION TO APPLICATION.

I greatly appreciate the Study Section comments on my application. In response, I have made substantive changes in the “Career Development Plan” and “Research Strategy”, which address all major concerns raised. Revisions are denoted by vertical black lines in the left-hand margin of the submitted documents (see this line).

Career Development Plan: The résumé noted that “It is not clear how many of the courses in the budget justification section will be taken.” I have therefore emphasized that there are 4 planned courses in the “Career Development Plan” (following Table 2) and outlined them in the “Budget Justification”: PUBH 5520 “Introduction to Health Policy”, PUBH 5538 “Health Services Administration: Program and Policy Evaluation”, BIOS 8398 “Special Topics: Spatial Analysis”, and PUBH 5525 “Health Economics”. These are most critical, though additional courses available are described in “Facilities and Other Resources”. I will also attend short courses and symposia at health policy conferences (e.g., National Health Policy Conference).

Reviewer 2 specifically noted that “advanced biostatistics courses” in “spatial and temporal data analysis” would be needed, and that more effort for “training or closer interactions with local biostatisticians” would be desirable. Though I studied spatial statistics under Frank Curriero as part of my master’s coursework in biostatistics at Johns Hopkins, I fully recognize the value in further study and continued mentorship during this research. I have therefore revised my proposed effort in the first 2 years to allocate more effort (now 5%, Table 1) to formal coursework, in addition to identifying two biostatistics mentors (with expertise in spatial statistics and causal inference) and formal coursework in spatial analysis in the Vanderbilt Department of Biostatistics (Table 2, and descriptions of mentorship team in the “Career Development Plan” and “Facilities and Other Resources”). The additions to my internal mentoring committee from the Vanderbilt Department of Biostatistics are Drs. Chris Fonnesbeck (Asst. Prof. with an extensive background in spatial statistics, teaching the BIOS 8398 course in spatial analysis) and Bryan Shepherd (Assoc. Prof. with expertise in causal inference, and with whom I have had successful prior collaborations, resulting in 17 co-authored manuscripts). I will meet with both regularly and will take a formal class with Dr. Fonnesbeck.

My co-mentor, Dr. John Graves, also has extensive experience in spatial econometrics, which is germane to this critique and is now mentioned under the “Co-mentor” description of the “Career Development Plan”.

Dr. Sten Vermund, an expert in policy and implementation science, will no longer be a formal member of my internal mentoring committee, as he has accepted a position as Dean of the Yale School of Public Health (effective Feb. 1, 2017). However, he has kindly offered to remain an informal resource for advice in this and other HIV epidemiology research. All new committee-member biosketches are included.

Research Strategy: Reviewer 1 noted the lack of description for including Canadian and Mexican populations in the analysis plan. Though this omission was made merely to save space, I have now described the addition of these populations as a comparator group (a true “universal access” comparator), with which non-expansion, and even expansion, states might be contrasted. This would provide greater depth to our inferences with respect to the merits of Medicaid expansion as either mimicking or still falling short of the promise of universal access and/or coverage.

Reviewer 2 was concerned that the methods may have “limited” novelty. Though the proposed methods are standard for health policy analysis, they have been used in the literature to assess changes in various health outcomes across varying levels of policy implementation (e.g., counties, states, and even countries in a region). However, I have now noted the inclusion of alternate methods which may be explored and used to accomplish the Aims under “Statistical Refinements.” These are not meant to be primary methods for addressing the Aims, but they are intended to demonstrate that I will explore multiple methods (either existing or in development) to execute this research. In particular, I will explore spatial methods with Dr. Fonnesbeck in addition to the proposed agent-based models (exploring future outcome trajectories under proposed policy changes, conditional on data-driven assumptions from observational data), regression discontinuity analyses, and methods to improve generalizability of quasi-experimental evidence from epidemiologic cohorts.

Reviewer 2 wondered about the random error term in the proposed generalized linear mixed model. I have now removed the epsilon notation and clarified that the random error may be decomposed as the random effects for the intercepts and slopes, each normally distributed: $b \sim N(0,\sigma 2)$.

Mentors, Co-Mentors, Collaborators: Reviewer 2 noted it “may be better to have a local biostatistical mentor.” I now have Drs. Fonnesbeck and Shepherd (mentioned above) as part of my internal mentorship team.

Since the prior submission in September 2016, I have published 5 manuscripts, had 2 manuscripts provisionally accepted (under revision), and submitted an additional 4 manuscripts for publication. In addition, I will present work on the HIV Care Continuum related to health literacy as an abstract at the 2017 Conference on Retroviruses and Opportunistic Infections (CROI) in Seattle, WA (Feb. 2017).

CANDIDATE BACKGROUND.

My passion for research and belief in the power of science to improve the welfare of those suffering the scourge of HIV infection have been evident since, as a high school student, I took my first job in the field: an assistant obtaining informed consents for clinical trials at the Vanderbilt branch of the Adult AIDS Clinical Trials Group (AACTG). As I progressed through my undergraduate studies, I maintained my working life in HIV research under the supervision of Drs. David Haas and Timothy Sterling, next as a research analyst, then as a research coordinator, with the Center For AIDS Research (CFAR) at Vanderbilt University. Throughout, I was immersed in the day-to-day workings of the research enterprise, from data mapping, data abstraction, and validation, to analysis, scientific writing, IRB documentation, and data submissions for intra- and extramural collaborators. After working with a productive group for nearly seven years, I embarked on the next phase of my education at one of the premier institutions of higher learning in my chosen field, Johns Hopkins Bloomberg School of Public Health.

First as a master's student in epidemiology in 2010, then as a doctoral student and Meyer Scholar in epidemiology and master's student in biostatistics in 2012, I progressed in my understanding and practice of modern epidemiologic and biostatistical methods under the mentorship of Dr. Stephen Gange. During my schooling, I pursued my goal of becoming an independent investigator through the execution of a rigorous research program alongside my classroom instruction, collaborating with preeminent scholars in the field as a member of the Epidemiology/Biostatistics core of the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) of the International epidemiologic Databases to Evaluate AIDS (IeDEA). During this period, I also participated in the NA-ACCORD Quality of Care Working Group, collaborating with national leaders in HIV research such as Dr. Richard Moore (PI of the NA-ACCORD), Dr. Kelly Gebo (PI of the HIV Research Network), Dr. Michael Horberg (past member of the Presidential Advisory Council on HIV/AIDS), and Dr. John Gill (originator of the literature on "churn" in HIV epidemiology), among many others. Through work on the clinically important and methodologically challenging topics of "churn" (the movement of patients into and out of care over time) and clinical retention in HIV care, central components of the HIV Care Continuum, I completed my multiple thesis requirements and presented novel research at national and international meetings: the 20th Conference on Retroviruses and Opportunistic Infections (CROI 2013), the 15th, 16th, and 18th International Workshop on HIV Observational Databases (IWHOD 2011, 2012, and 2014), the XIX International AIDS Society Conference (IAS 2012), and the 45th and 46th Society for Epidemiologic Research Meeting (SER 2012, and 2013). My work on these topics during the program also resulted in two first-author publications (*Rebeiro P, et al. J Acquir Immune Defic Syndr. 2013; Rebeiro P, et al., PLoS One. 2014*)[1,2] and two second-authored publications (*Althoff KN, Rebeiro P, et al., Clin Infect Dis. 2014; Yehia BR, Rebeiro P, et al., J Acquir Immune Defic Syndr. 2014*).[3,4] Beyond producing publications in areas of my own interest, I contributed to the ongoing work of colleagues in the Epidemiology/Biostatistics core including Dr. Keri Althoff, resulting in co-authorship on a manuscript concerning temporal trends in HIV disease markers in the North American population (*Althoff KN, et al. Ann Intern Med. 2012*).[5] I also improved my didactic skills by working as teaching assistant for 4 courses and lead teaching assistant for the primary epidemiologic methods course, completing a certificate in the Preparing Future Faculty Teaching Academy program, and competing for and winning a Gordis Teaching Fellowship. As a teaching fellow, I served as primary instructor for a self-designed undergraduate seminar on the epidemiology of HIV.

Upon completion of my degrees in epidemiology and biostatistics in August 2014, I was recruited as a Research Assistant Professor by the working group I had previously been a part of at Vanderbilt University School of Medicine. I continued my working relationship with the Epidemiology/Biostatistics core of NA-ACCORD at Johns Hopkins while forging new connections with another of the IeDEA's regional collaborations: the Caribbean, Central and South America network for HIV epidemiology (CCASAnet), whose data management and analysis cores reside at Vanderbilt. In my capacity as a study epidemiologist for CCASAnet, I have had the good fortune to participate in important HIV outcomes research using advanced epidemiologic and causal inference methods, including the description of HIVCC trends over time, exploration of CD4 recovery after properly accounting for mortality and loss to follow-up during the study period, and the influence of ART regimen transitions and their reasons on subsequent mortality or regimen failure in Latin America and the Caribbean; this work has been executed in collaboration with and under the expert guidance of Drs. Timothy Sterling and Catherine McGowan. My choice of this working environment as an ideal location to pursue my early career development as an epidemiologist was compelled not only by the possibility of joint mentorship by leaders in the field (Drs. Timothy Sterling and John Graves), but by continued involvement in

two remarkably productive research groups with records of outstanding contributions to HIV epidemiology and access to the rich resources of large, long-established HIV research consortia.

Since joining the faculty at Vanderbilt, I have taken full advantage of these opportunities and extended my rigorous research program surrounding the HIV Care Continuum, whether on work completed with the NA-ACCORD (*Rebeiro P, et al., Am. J. Epidemiol. 2015; Rebeiro P, et al., PLoS ONE 2016*), novel work undertaken with CCASAnet (*Rebeiro P, et al., J. Int. AIDS Soc. 2016*), work published in collaboration with the Vanderbilt cohort itself (*Woodward B, Person A, Rebeiro P, et al., AIDS Patient Care STDs 2015*), or work with the Tennessee State Department of Health (TN DOH) Division of HIV/AIDS/STDs [redacted]

Through these experiences as a member of two major international HIV cohort groups, I have gained knowledge and facility in using advanced epidemiologic methods, collaborating with researchers across disciplines and geographic regions, and in using data from large longitudinal cohorts of HIV-infected individuals in North, Central, and South America (the NA-ACCORD and CCASAnet), which I will use in the proposed research. This work will form the bulk of my research proposal, and it is detailed below in the *Research Strategy* section of this application.

If this career development award is successfully funded, I will be able to make great strides toward my goal of becoming a recognized authority in the fields of HIV health policy and HIV epidemiology. The award will cultivate my capacity to be an independent investigator by enabling my research, career development through targeted individual meetings with relevant policy makers, education in the application of epidemiologic methods to health policy questions, and continued mentoring in research, grant writing, and future proposal development. My progress will be facilitated through access to internationally renowned experts in exemplary scholarly environments, and my transition from a junior investigator to a senior scientist making major contributions to the field will be greatly enhanced and accelerated. This award will provide evidence for health policy changes, positively impacting millions of lives.

CAREER GOALS AND OBJECTIVES.

My primary career goal is to become a recognized leader in the fields of HIV health policy and HIV epidemiology, specifically focused on the impact of policy interventions on HIV Care Continuum and other HIV disease outcomes, assessing the influence of contextual factors such as psychiatric health, poverty, and geographic location, alongside health policy implementation factors. This work holds the real potential to positively impact public health on massive scales by informing policy interventions that reach large populations. I hope to pursue this research as an independently funded investigator and tenure-track faculty member in medicine and/or epidemiology at a leading academic research institution. I believe that the education and extension of my research experience gained through my training plan would make me a competitive candidate for future funding and substantially augment my expertise in the practice of health policy evaluation and epidemiology. In tandem, I hope to advance my understanding of the methodology central to policy evaluation and of the workings of healthcare systems in general through additional training.

Over the next five years, I will investigate the confluence of health policy, socioeconomics, psychiatric illness, geography, demography, healthcare, and HIV outcomes through the lens of the HIV Care Continuum, contributing in a meaningful and unique way to the body of knowledge surrounding this topic. In focusing on a well-defined epidemiologic construct (the HIV Care Continuum) and leveraging the resources of established, large HIV consortia to answer questions that require large populations distributed broadly geographically and longitudinally over time, I will enrich the body of scientific knowledge and inform public health policy and clinical practice by highlighting points of possible intervention to improve HIV outcomes. I will also endeavor to create compelling visual displays of the relevant research findings, maximizing the utility and reach of generated evidence for policy makers and other researchers in extending my work to positively influence public health.

Importantly, this award will also give me the opportunity to retain protected time in which to gain a more advanced understanding of statistical and analytic methods pertinent to health policy analyses while attaining proficiency in the application of these methods. This unencumbered time will also be key to my ability to produce high quality research that has the potential to sway policy makers and substantively contribute to the field: namely, by elucidating the influence of contextual factors on HIV Care Continuum outcomes across two continents, and understanding the changes in HIV care in the US wrought by the expansion of Medicaid under the Patient Protection and Affordable Care Act. The Vanderbilt University School of Medicine is an outstanding environment in which I may pursue these goals and this work. The Divisions of Infectious Diseases and Epidemiology, housed within the Department of Medicine, are among the best in the country and offer multiple

resources for junior faculty (these are detailed in the *Facilities and Other Resources* section). Further, the broad array of educational programs and expertise available through the Department of Health Policy, Division of Epidemiology, and the Center for Health Services Research (HSR) at Vanderbilt are noteworthy. These centers house established practitioners of the very disciplines in which I am most interested in honing my skills. Because I intend to continue participating in multiple research groups, indeed across institutions, I will also be able to take advantage of knowledge, programs, and other resources that will afford me fairly rarefied opportunities. I will take advantage of these resources, including collaborative and consultative relationships with others across these divisions through regular meetings and coursework, to advance my understanding and ultimately to improve the quality and impact of my research. Details of these resources are contained in the *Career Development/Training Activities* section below.

Future Directions and Conversion to R: By the conclusion of the award period, I hope to have advanced significantly in my abilities through research and educational activities in a vibrant intellectual environment with mentorship at Vanderbilt and Johns Hopkins Universities. This progress should sufficiently prepare me to successfully compete for R-01 funding to address and intervene on some of the identified contextual factors related to quality of HIV care, access to care, and HIV Care Continuum outcomes. In particular, results from the specific aims of this study may lead directly to applications involving interventions for identified modifiable risks which are mediators of the policy-HIV outcome relationship (e.g., treatment of psychiatric illness). Further, extensions of methods developed to probe the impact of policy using epidemiologic cohort data as part and parcel of this award may contribute to high priority research on the disparate impact of expanded testing or pre-exposure prophylaxis (PrEP) policies/programs in the United States. Because of the difficulties in linking large surveillance data sources with prescription databases, and because of the limitations of ecologic studies to control for confounding, the utilization of longitudinal cohorts with detailed clinical data to assess such policy changes is highly desirable. Multiple R-01 applications addressing these topics both in North and Latin American cohorts, making use of collaborations that will be developed and enriched through this award, would be compelling and highly desirable. These applications would make efficient use of studies that have already garnered millions of dollars of investment and potentially obviate the need for costly investments in other data sources which may be subject to significant inferential barriers.

Critical to my development and success as an independent investigator, this award would also allow me protected time to write and publish high-impact, first-author manuscripts, which would seed and help establish my reputation as a leader within the field. My immediate goals as part of my career plan are to publish at least two first-author peer-reviewed manuscripts per year (related either to the primary outcomes or methodologic details of these analyses). My intermediate goal will be to prepare and submit a compelling R-01 application by the conclusion of the 3rd K-01 award year. My long-term goal is to demonstrate my bona fides as an independent researcher, validated by my promotion to Associate Professor within 7-years of the K-01 award commencing.

CANDIDATE PLAN FOR CAREER DEVELOPMENT / TRAINING ACTIVITIES DURING AWARD PERIOD.
I will optimally utilize the resources and opportunities available to me in service of advancing my research experience and leadership abilities by: **1)** attending and participating in regular mentorship meetings with a team of distinguished researchers; **2)** accessing continuing education opportunities in the form of meetings and symposia; **3)** engaging in formal education through health policy, econometrics, and biostatistics classwork offered at Vanderbilt (4 courses); **4)** attending and participating in national and international policy symposia and scientific conferences. **Table 1** displays the relative effort I will contribute toward these critical training plan components.

Table 1. Distribution of effort: educational, research, & professional activities, by year

Activity	Year 1	Year 2	Year 3	Year 4	Year 5
Mentor/policy meetings, cont. learning, symposia	5%	5%	5%	5%	5%
Formal education (coursework)	5%	5%	2.5%	2.5%	2.5%
Conferences and scientific meetings	2.5%	2.5%	2.5%	2.5%	2.5%
Data collection, analysis, & manuscript submission	71.5%	71.5%	68%	64%	60%
Novel & related project development, grant writing	0%	0%	6%	10%	14%
Total % effort for K-01 award	84%	84%	84%	84%	84%
Education (teaching)	11%	11%	11%	11%	11%
Service (academic committee assignments)	5%	5%	5%	5%	5%
Total % effort for professional responsibilities	16%	16%	16%	16%	16%

The heart of my career development plan may be found in the multidisciplinary mentorship team I will be engaged with. I have collaborated extensively with some members (e.g., Drs. Sterling, Shepherd, Gange, and Moore), enhancing my ability for continued productive research; however, the addition of experts in health policy with whom I have no prior collaborative relationship (e.g., Drs. Graves, Schaffner, Fonnesbeck, and Holtgrave) will add complementary training to my current repertoire for an optimal combination of mentorship. This team will be housed within institutions with myriad resources well suited to extending my epidemiologic research to inform health policy in the context of multi-cohort collaborations. Interacting with investigators in health policy, epidemiology, biostatistics, and health services research will allow me to participate in the conduct of high-quality research in a “big data” setting, gaining an understanding of the flow of information and interaction between researchers and staff that is critical to the success of such endeavors.

Mentor and Co-Mentor: My primary mentor, **Dr. Timothy Sterling**, has decades of experience conducting high-impact clinical infectious disease research using multi-site cohorts around the world. As I am fluent in methodology but not clinical language or practice, his expertise is necessary in translating my analysis into usable science- the evidence which evidence-based policy demands. He has extensive experience leading research collaborations within Vanderbilt University (VU) as well as nationally and internationally. He has been the PI of multiple NIH-funded studies and has a track record of successfully mentoring several young investigators through K mechanisms. He has agreed to continue serving as my faculty mentor and shepherding me through career milestones. Our weekly meetings to discuss research and career progress will continue during the award period. My co-mentor, **Dr. John Graves** is an R-funded Assistant Professor of Health Policy at VU and a nationally renowned expert in spatial econometrics and health policy evaluation. He modeled the Patient Protection and Affordable Care Act’s (ACA) budgetary impact for the White House Office of Health Reform during the ACA’s development; his R01 evaluates the ACA’s impact on utilization and chronic disease outcomes in the Southern U.S. His R01 parallels this proposal, and I will collaborate in addressing its aims as part of my career development: honing newly acquired policy analysis skills in non-HIV cohorts under his guidance. He also leads a methodology development group (described in **Table 2**) that will be a source of alternative analytic approaches for the proposed research. I will meet with him in person on a bi-weekly basis to discuss progress in my proposed research and optimal career development in health policy research.

Mentoring Committees & Advisors: I will engage the expertise of leaders in health policy, program implementation, and methodology at VU through an *internal* career advisory committee and at Johns Hopkins (JHU) through an *external* scientific advisory committee. I will meet quarterly in person with internal committee members, easily assembled due to proximity, and semi-annually with external committee members (via teleconference or in person) to assess: **1)** progress of analyses and how well they mesh with both proposal and career development goals; **2)** educational progress in health policy, econometric, and epidemiologic methods; **3)** quality and continued impact of research products in the fields of HIV health policy and HIV epidemiology. The *internal* committee will include **Drs. William Schaffner, Christopher Fonnesbeck, and Bryan Shepherd**. Dr. Schaffner is a former chair of Preventive Medicine and current professor of Health Policy and of Medicine with decades of experience, including in leadership roles formulating vaccination policy with federal and state policy-making agencies such as the Centers for Disease Control and Prevention (CDC) and the TN DOH. Drs. Fonnesbeck and Shepherd are Assistant and Associate Professors, respectively, in the Department of Biostatistics with expertise and extensive publication records in spatial analysis, Bayesian analysis, and the application of causal inference methods in HIV epidemiology. The *external* committee will include **Drs. David Holtgrave** and **Stephen Gange**. Dr. Holtgrave is Vice-Chair of the US Presidential Advisory Council on HIV/AIDS (PACHA), Chair and Professor in the Department of Health Behavior and Society at JHU, and a recognized leader in HIV health policy, cost effectiveness, and surveillance research. Dr. Gange is Executive Vice Provost of JHU and Professor of Epidemiology, and he is an expert in the use of biostatistical and epidemiologic methods for observational data; he is also Director of the Epidemiology/Biostatistics Core of NA-ACCORD and a member of several federal health policy and guidelines panels. Each member of these committees has received multiple NIH-funded grants and engaged in mentorship activities. The committees also possesses a unique combination of experience and skills in fields directly related to the proposed work, as well as track records of productivity, perfectly suited to my research interests and long-term career goals. Further, **Drs. Catherine McGowan** and **Richard Moore** will act as advisors in the appropriate use of their cohort data. Dr. McGowan is an Associate Professor of Medicine and an HIV epidemiologist who is the principal investigator of the CCASAnet cohort. Dr. Moore is a Professor of Medicine and principal investigator of the NA-ACCORD; he is also Director of the JHU Center for AIDS Research Clinical Core. All meetings will be in-person or via teleconference (e.g., Skype).

In addition, I will leverage the many opportunities for direct contact with policy-makers and continued learning available to me by attending meetings with federal policy-makers and symposia regularly. I will attend quarterly meetings with the Administrator of the Health Resources and Services Administration's (HRSA) HIV/AIDS Bureau (Dr. Laura Cheever) and HRSA partners either in-person in Rockville, MD or via teleconference, and maintain contact with epidemiologists in the CDC's Division of HIV/AIDS Prevention (Drs. John Brooks and Kate Buchacz) through the NA-ACCORD Quality of Care Working Group (see invitation letter in Appendix). As a Scholar in Vanderbilt's Health Services Research group, I will have access to weekly meetings covering current research and advances in diverse fields such as implementation science, clinical economics, health promotion, behavioral health, and health policy (see appointment letter in Appendix). Seminars in methodology and health policy at the Vanderbilt University School of Medicine across the Division of Epidemiology and Departments of Health Policy and Biostatistics, may also serve as fertile ground for advancing my understanding and skills. In addition, I will continue to attend regular meetings of the various research groups I have been involved in, central to the research I will engage in with this award. These groups, their missions, and the regular time commitment I will make to them are outlined in **Table 2.**

Meeting/Group	Frequency (Duration)	Description and Goals
Mentor meeting: Dr. Sterling	**Weekly (60 minutes)**	Individual meetings with mentor, co-mentor, and mentoring committees to guide and assess progress toward career development, educational, and research goals. Includes intensive discussion and feedback from senior faculty and elite researchers in health policy, epidemiology, and biostatistics at both Vanderbilt (*internal* advisory committee) and Johns Hopkins (*external* advisory committee). *Meetings with faculty at JHU will be held via teleconference/videoconference, except for semi-annual visits to Baltimore, MD.*
Co-Mentor meeting: Dr. Graves	**Bi-Weekly (60 minutes)**	
Internal Advisory Committee: Drs. Schaffner, Fonnesbeck, and Shepherd	**Quarterly (90 minutes)**	
External Advisory Committee: Drs. Holtgrave and Gange	**Semi-Annual (90 minutes)**	
Policy meetings: Dr. Cheever, Administrator of HRSA HIV/AIDS Bureau (and HRSA partners)	**Quarterly (90 minutes)**	In-person/teleconference meeting with federal policy makers with implementation of evidence-based policy specific to vulnerable HIV populations in their purview; will focus on practical implications and priorities of research for policy/programmatic changes.
Epidemiology/Outcomes Group (Vanderbilt)	**Weekly (60 minutes)**	Dr. Sterling leads this meeting of data abstractors, data managers, biostatisticians (including Dr. Shepherd), and epidemiologists involving discussion of ongoing research using the Vanderbilt Comprehensive Care Clinic cohort, and collaborations with various outside groups (e.g., NA-ACCORD, CCASAnet, TN DOH, et al.).
Health Policy Methodology (Vanderbilt) (continued)	**Monthly (90 minutes)**	Dr. Graves leads this meeting of health policy analysts, epidemiologists, and biostatisticians to explore solutions to methodologic issues in the use of epidemiologic cohort data to answer policy-oriented questions. As cohort data may not allow inference to the appropriate policy-impacted target population, weighting or calibration techniques may be developed to derive externally valid inferences.
NA-ACCORD Epidemiology/Biostatistics Core (Johns Hopkins)	**Monthly (90 minutes)**	Drs. Moore and Gange lead this meeting of data managers, analysts, investigators, epidemiologists, and coordinators of NA-ACCORD. Epidemiologic/biostatistical challenges are discussed and solutions are proposed. *Meetings at JHU will be held via teleconference/videoconference.*
CCASAnet Data Management/Analysis Core (Vanderbilt)	**Weekly (90 minutes)**	Dr. McGowan leads this meeting of bioinformaticists, biostatisticians (including Dr. Shepherd), epidemiologists, and data coordinators of CCASAnet. It consists of discussion of ongoing CCASAnet projects, data collection, and data management issues.
NA-ACCORD Quality of Care Working Group Teleconferences (Johns Hopkins)	**Semi-Annual (60 minutes)**	Drs. Keri Althoff and Kelly Gebo lead this meeting of NA-ACCORD collaborators including investigators, epidemiologists, and biostatisticians. It addresses research on healthcare access, health policy, and process measures of care for HIV+ individuals.

By working with these mentors, I will be able to expand my understanding of the methods and statistical techniques capable of overcoming impediments to valid inferences in epidemiologic research, while placing these analyses and inferences in a larger public health and policy context. Furthermore, in collaborating with other investigators within and without VU and JHU, I will be working alongside researchers in international

consortia who have provided a foundation for the success of several large ongoing observational studies and have contributed to the body of knowledge on HIV in seminal and significant ways, including through the implementation of novel epidemiologic methods. I will also maintain access to experts in HIV medicine, health disparities, health policy, and health services research that will be vital for ensuring my work's rigor and practical application to the most important and current research questions.

Though I am an experienced epidemiologist, I lack specific training in the advanced methodology required for health policy evaluation, and have therefore identified coursework in the Vanderbilt School of Medicine's Master of Public Health Program, Division of Health Policy, and in the Department of Biostatistics, that will enrich my understanding of health services, health policy, and appropriate methods for analyzing policy impact with spatial data. I have received permission to attend courses of interest and engage in all learning activities, so that I may make full use of these opportunities. Pertinent courses include BIOS 8398 "Special Topics: Spatial Analysis", PUBH 5525 "Health Economics", and PUBH 5538 "Health Services Administration: Program and Policy Evaluation". Course descriptions and faculty are in the *Facilities and Other Resources* section.

Throughout my training, I will continue to develop my scientific writing and presentation skills and will use these to share the results of my research with the broader epidemiology and public health communities. By continuing to present results at scientific conferences I will be able to disseminate my findings to others and learn about new opportunities for collaboration. I will plan to attend two of the following conferences each year: **1)** the Conference on Retroviruses and Opportunistic Infections (CROI); **2)** the National Health Policy Conference (NHPC) of Academy Health; **3)** the Society for Medical Decision Making (SMDM); or **4)** the Society for Epidemiologic Research (SER) meeting. I will attempt to attend CROI and NHPC preferentially, as they align most closely with my interests and would likely offer me the greatest benefit based on the mix of scientific results, methods, and policy issues raised there. Conference preparation and attendance will not consume more than 9 days per year (2.5% effort).

As a faculty member in the Vanderbilt University School of Medicine's Department of Medicine, I will dedicate 16% effort toward Professional/Educational responsibilities, including teaching and service on academic committees (including student thesis and oral examination committees). I currently teach/co-teach two courses in the Epidemiology doctoral program at Vanderbilt: EPID 8310 "Causal Inference" and EPID 8321 "Applied Epi Methods: Logistic Regression". Finally, I will also continue to propose and conduct research related to changes in HIVCC outcomes and HIV epidemiology as influenced by contextual factors and policy through collaborations with NA-ACCORD, CCASAnet, and other groups, insofar as such work aligns with my overall research interests. All of these groups have prioritized research in this domain, providing numerous opportunities for continued productivity regarding these topics in collaboration with the highest caliber of epidemiological researchers. As the primary responsibilities of promotable, independent faculty investigators are education, service, and research, I intend to continue advancing my proficiency in each of these throughout the award period.

My progress will be monitored through multiple mechanisms: **1)** regular meetings with my mentor and co-mentor (≥bi-weekly); **2)** ≥semi-annual reviews with my mentor, co-mentor, and mentoring committees through in-person and teleconference meetings; and **3)** a shared electronic document tracking my educational progress, continued learning activities, scientific meeting/symposium attendance, and progress toward meeting my proposed research aims. At the outset, I will formulate a series of measurable goals for the initial award year through meetings with my mentor and co-mentor. These goals will include **1)** at least one oral presentation at a national or international scientific meeting; **2)** at least three presentations at Divisional (either Infectious Diseases or Epidemiology) or Center for Health Services Research-based meetings annually; and **3)** at least two peer-reviewed primary-author publications per year. My attainment of these goals will be assessed at regular review meetings with my mentor and co-mentor. I will also maintain and share a regularly-updated electronic record of my progress toward my research and educational goals, to be discussed at the review, as well as during my ongoing bi-weekly meetings with my mentor and co-mentor, respectively. Because I will have such regular contact with both my mentor and co-mentor, I expect that I will benefit greatly from heightened scrutiny of my overall progress and ongoing in-depth discussions of solutions to methodologic impediments and approaches to maximize the public health impact of my research. Meetings with my mentoring committees on a ≥semi-annual basis will further guide my application of advanced methods to answering health policy and quality of care questions in the context of HIV care, while providing me valuable feedback on the most meaningful ways to address these questions for consumption even *beyond* the field of HIV epidemiology (i.e., for health policy analysts, policy makers, program funders, and public health officials).

With the implementation of this highly structured mentoring plan, the K-01 award would allow me to advance my career with an optimal combination of education in advanced epidemiologic methods appropriate for health policy assessment and research in a rich and supportive educational environment regarding questions that lend themselves to the application of these advanced methods. This award will facilitate the development of my skills and, with the collaboration of my sponsor; CCASAnet, NA-ACCORD, and VCCC researchers; and the faculty and staff at VU and JHU, will advance my research career in the fields of HIV public health policy and HIV epidemiology.

Training in the Responsible Conduct of Research: As a graduate student at Johns Hopkins Bloomberg School of Public Health, I attended and completed two, face-to-face courses regarding the responsible conduct of research: Responsible Conduct of Research (taught by Dr. Sharon Krag, former Associate Dean for Graduate Education and Research, including eight hours of in-class time over the course of an eight week term, completed in 2010 and again in 2012). In addition, I have completed the following Research Compliance Training courses: Human Subjects Research, Conflict of Interest and Commitment, and HIPAA Compliance. As a junior faculty member, I will enroll in the “Responsible Conduct of Research” training session offered in 2016-2017 through the Vanderbilt University School of Medicine’s Office of Biomedical Research Education and Training (BRET). This course covers the responsible conduct of research, including ethics, data management, research fraud, academic misconduct, and conflict of interest.

In addition to formal training, I will attend symposia and seminars as available on relevant ethical issues in the conduct of health policy research and biomedical research. The Center for Biomedical Ethics and Society at Vanderbilt University School of Medicine’s Institute for Medicine and Public Health conducts “Ethics Grand Rounds” on the first Tuesday of the month every April and November, as well as hosting coursework, research, and symposia related to biomedical research ethics. There is also a formal course offered through the Vanderbilt University School of Medicine’s Master of Public Health program (PUBH 5518 “Research Ethics in Health Policy”) that I may attend as topics of interest arise in the syllabus. Further, my mentorship team members are eminent human subjects researchers involved in observational research with extensive knowledge in these issues related to data collection, management, security, and sharing; responsible authorship and publication; intra- and inter-institutional collaborations; and peer review.

SPECIFIC AIMS & HYPOTHESES.

The HIV Care Continuum has become established as a compelling framework to describe the current clinical goals for managing HIV infection; it tracks the progression of individuals from diagnosis, through linkage, clinical retention, ART use, and ultimately to the goal of viral suppression. Health policy differences over time may profoundly influence Care Continuum outcomes, both domestically and internationally, augmented by differences in patient contexts.

Because improvements in the proportion of patients conforming to each stage of the Care Continuum should lead to improved individual- and population-level disease and transmission outcomes, the work proposed below will harness this lens to provide valuable insight into health policy impact, persistent health disparities in vulnerable populations by geography and context, highlighting possible points of intervention along the Care Continuum.

Not only does the Care Continuum provide a clinical benchmark as reflected in the milestones of the US National HIV/AIDS Strategy (NHAS), the revised World Health Organization ART guidelines, and statements from the Pan American Health Organization (PAHO), it also provides a framework to focus epidemiological investigations on the relevant questions in contemporaneous HIV research. Because the Patient Protection and Affordable Care Act (ACA) and other national health policies implemented in the US, Canada, and Mexico aim to improve healthcare access and reduce health disparities, studies of the effect of policy and contextual factors on the trajectory of Care Continuum outcomes is of great interest and relevance for epidemiologists, clinicians, and policy makers.

Here I will pursue aims relevant to this framework using data from two sources: the Caribbean, Central and South America network for HIV epidemiology (CCASAnet), and the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD), which has been designated by the Institute of Medicine (IOM) as one of 12 data systems ideally suited to assess Care Continuum measures and benchmarks for progress in the NHAS and ACA. The study aims are both descriptive (Aim 1) and inferential (Aims 2 and 3).

The Specific Aims and Hypotheses of this study are as follows:

Aim 1a: To describe disparities in three NHAS-specified HIVCC outcomes across North America: proportion of population clinically retained, using antiretroviral therapy (ART), or virally suppressed. Disparities by demography, geography, patient context (i.e., psychiatric diagnosis and regional poverty level), and health system characteristics (i.e., universal ART access in Canada vs. changing payer structures in the United States and Mexico) will be highlighted.

Aim 1b: To describe temporal trends in these three outcomes, accounting for geographic, contextual, and health policy differences, from 2000 beyond 2014

Hypotheses, Aim 1: The proportion with successful HIVCC outcomes will increase over time, though disparities by demographic, socioeconomic, psychiatric, geographic, and health system characteristics may persist (contrasting the US, Canada, and Mexico).

Aim 2: To measure the effect of ACA implementation on HIVCC outcomes (e.g., clinical retention, ART use, virologic suppression) using data from NA-ACCORD clinical cohorts. Cohorts that provide uniform access to care (e.g., Canadian cohorts) and states opting not to expand Medicaid will be used as comparators.

Aim 3: To measure the effect of ACA implementation on HIV disease status at entry and clinical endpoints (e.g., CD4+ count at enrollment, all-cause mortality incidence, etc.) related to competent HIV care in the NA-ACCORD. Outcomes that are not process measures will be assessed using both interval and clinical cohorts (e.g., all-cause mortality).

Hypotheses, Aims 2, 3: HIVCC and HIV clinical outcomes (e.g., proportion on ART, or incidence of mortality) will improve at a faster rate, comparing the ACA period to the pre-ACA period, among residents of US states fully implementing the law compared to residents of other states.

RESEARCH STRATEGY.

Specific Aims and Hypotheses:

The HIV Care Continuum (HIVCC) is a powerful framework to describe the epidemiology of HIV; it tracks the progression of individuals from diagnosis, through linkage, clinical retention, ART use, and ultimately to the goal of viral suppression. The work proposed below will harness this lens to provide valuable insight into health policy impact, persistent health disparities in vulnerable populations by geography and context, highlighting possible points of intervention along the Care Continuum.

The National HIV/AIDS Strategy (NHAS) formulated in 2010 and the revised 2013 WHO ART guidelines reference milestones in the HIVCC, and because the ACA and other national health policies implemented in various North, Central, and South American countries aim to improve healthcare access and reduce health disparities, describing the effect of policy and contextual factors on the trajectory of HIVCC outcomes is of great interest to epidemiologists, clinicians, and policy makers. This study will use well-characterized data from the Caribbean, Central and South America network for HIV epidemiology (CCASAnet), and the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD), which has been designated by the Institute of Medicine (IOM) as one of 12 data systems ideally suited to assess HIVCC measures and benchmarks for progress in the NHAS and ACA.[11] The study aims are both descriptive (Aim 1) and inferential (Aims 2 and 3).

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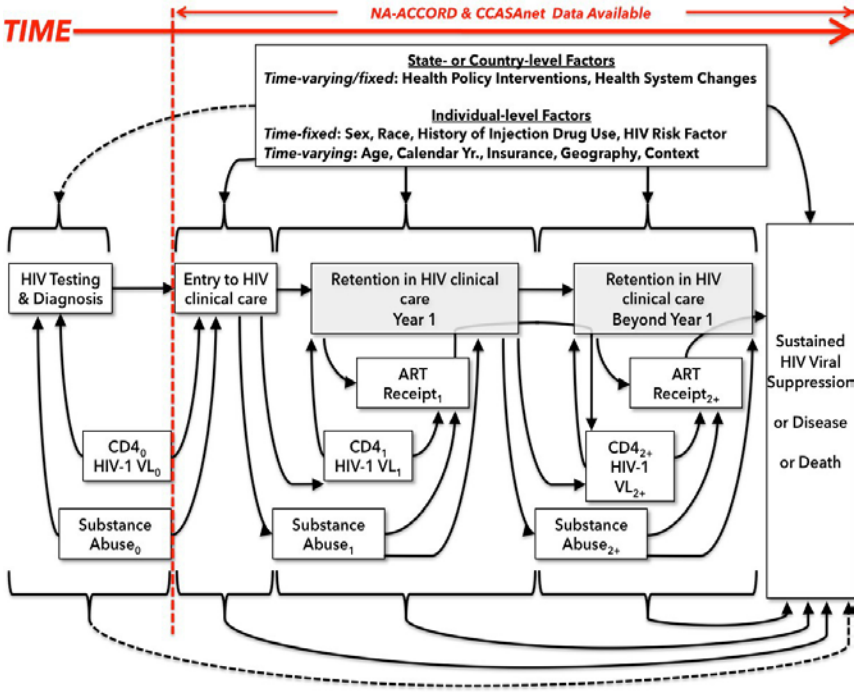
Background and Significance:

The HIVCC describes the path of progress toward improved individual- and population-level HIV outcomes: from testing, to diagnosis, to linkage, retention, ART use, and viral suppression (**Figure 0**). Interventions minimizing disparities and losses at each stage throughout the HIVCC must be sought.[11-14] Disparities in HIVCC and HIV outcomes by demographic, SES, geographic, and structural factors (e.g., health insurance status) have been noted.[15-20] Though improved public health infrastructure, scale-up in ART access programs, and expansion of Medicaid by the ACA holds promise for improved HIV care and diminished disparities (because a plurality of HIV+ patients use Medicaid in the US), careful analysis of high quality data in a large, geographically diverse network is required to render an evidence-based verdict.[21-27] Identifying spatial patterns of disease distribution and health disparities has also provided evidence in health policy decision-making, directing funding and interventions to locales of greatest need, even in HIV epidemiology.[17,28-39] By leveraging high quality longitudinal data on HIVCC and other clinical and process outcomes along with geographic, demographic, and structural data from CCASAnet, the NA-ACCORD, and the VCCC this study is

uniquely positioned to alert policy makers, public health officials, and epidemiologists to persistent disparities in HIVCC outcomes and the real effects of the healthy policies, including the ACA.[15,19,40]

Figure 0. Conceptual framework of HIV Care Continuum, "Testing" to "Viral Suppression"



Evaluation using data from CCASAnet and the NA-ACCORD: We propose to use data from the largest cohort collaborations including HIV-infected individuals in the US and Canada (the NA-ACCORD) and in Latin America (CCASAnet). The NA-ACCORD, an NIH-sponsored collaboration that is one of seven regional members of the International epidemiologic Databases to Evaluate AIDS (IeDEA), began collecting data from multi- and single-site interval and clinical cohorts in 2006.[41] Currently, 25 cohorts comprised of patients residing in all 50 US states, Washington, D.C., Puerto Rico, and 9 of 13 Canadian provinces/territories participate; more than 125,000 patients are currently included. Clinical and demographic data (e.g., laboratory values and collection dates, ART medications and prescription dates, clinic visit information) are transmitted to a centrally-administered Data Management Core semi-annually. CCASAnet, another regional member of IeDEA, consists of multi-site clinical cohorts based in Argentina, Brazil, Chile, Haiti, Honduras, Mexico, and Peru; more than 25,000 patients are currently included.[42] Within NA-ACCORD and CCASAnet, census-derived data for geographic regions within countries, states/provinces, and smaller jurisdictions will be obtained from publically-available sources and used to provide inference for the influence of contextual factors on patient experiences and outcomes of HIV care. In particular, comparisons within the US and between the US and its neighbors Canada and Mexico (where there has been long-standing universal access and progress toward universal access to healthcare, respectively) will lend strength to any inferences drawn.[43]

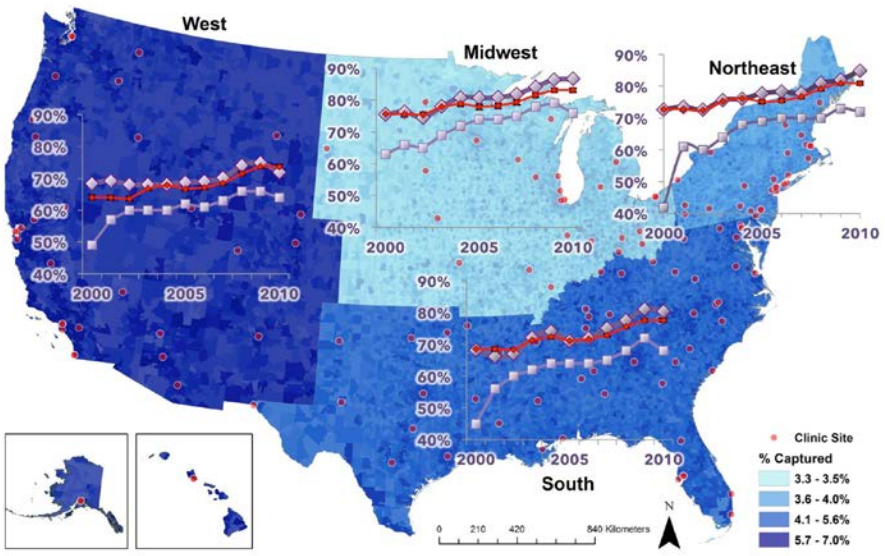
If the data collection capacities of NA-ACCORD and/or CCASAnet are altered after the award period commences, changes in HIVCC outcomes due to state-level policy changes in the years preceding 2014, short-term changes immediately after ACA implementation, and the influence of contextual factors in North, Central, and South America will still be able to be examined using legacy data from these cohorts. Medicaid expansion is still expected to proceed with 100% federal funding for the period of 2014-2017, phasing down to 90% federal funding by 2020. Even so, if the Medicaid expansion provisions of the ACA underwent significant changes, analyses concerning shifts in HIVCC outcomes due to policy changes would still be able to be conducted within the NA-ACCORD, and in fact, might have greater meaning (as negative changes in outcomes following contraction of a program may provide impetus for its restoration).

Innovation: The vast scope (both breadth and depth) of data related to HIV Care Continuum outcomes and the geographic heterogeneity of the clinical populations involved in both the NA-ACCORD and CCASAnet indicate a unique contribution to monitoring clinical care and health services outcomes, particularly in the impact of far-reaching health policy changes, for which few (if any) other cohorts may be well suited to provide evidence.[11,43] Applying a focus on health policy and contextual determinants of health to the realm of HIV Care Continuum research in these settings will involve the synthesis of publically-available data on policy implementation, census-derived characteristics in North and Latin American countries, which should be particularly germane and informative for health policymakers at a time when the healthcare systems in the United States are undergoing dramatic changes. Even the execution of a primarily descriptive Aim 1, in contrast to the more methodologically sophisticated inferential Aims 2 and 3, would provide useful information not otherwise available to policy makers, funders, and epidemiologists on the state of HIVCC outcomes and potential disparities across demographic and intervenable factors (e.g., psychiatric diagnosis) among a wide swath of the HIV-infected population of North America.

Further, the use of a pseudo-experimental design, applicable to the state-determined expansion of Medicaid accompanying implementation of the Affordable Care Act, to assess the influence of policy and context on HIV Care Continuum outcomes has not been executed elsewhere.[20] Taken together, this combination of rich data in a study population covering a geographically expansive area, cultivated in an environment replete with competent expertise in their analysis, and their utility in service of a topic of immediate and great importance to epidemiologists, public health policy makers, and program funders, make the proposed research an obvious candidate for funding and execution in a timely fashion.

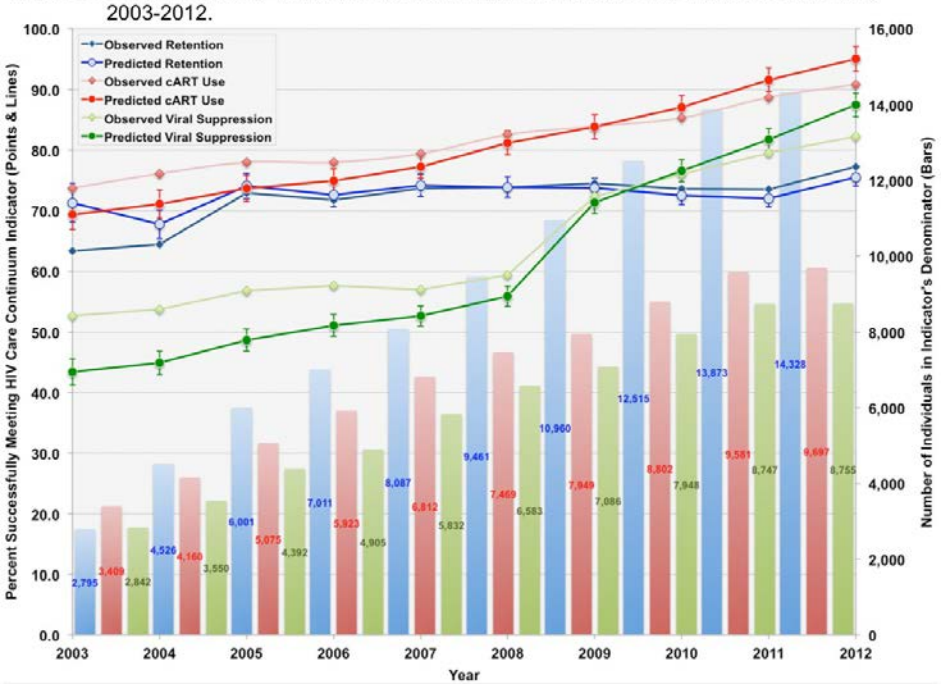
Preliminary Studies: Analyses of NA-ACCORD data from 2000-2012 have shown a steady, significant improvement in the HIVCC outcome of clinical retention (measured using the IOM indicator). Adjusted predicted probabilities of retention tracked closely with observed patterns (stratified by region) (**Figure 1**). Multiple HIVCC outcomes have also been noted to improve over time within the CCASAnet countries (**Figure 2**).[7,8] Publications noting disparities in the quality of HIV care using the NHAS and US Department of Health and Human Services (DHHS) indicators have also been produced in the NA-ACCORD cohort.[1-4,44] *Aims 1, 2, and 3 will seek to capitalize on these data by supplementing current data in the post-2014 period and expanding these analyses to include assessments of intervention effectiveness, influences of psychiatric illness, and geographic clustering for other HIVCC and HIV clinical outcomes. These may serve as baseline, or "placebo", data in 2014 to gauge ACA or other policy effectiveness as a "treatment" in the ACA period (post-implementation) for Aims 2 and 3.*

Figure 1. Clinical retention status of patients by region of the US, NA-ACCORD, 2000-2010.



Purple diamonds with linear segments are clinical retention percents by the IOM definition: ≥2 visits within 12 months, >90 days apart. Red circles with linear segments are predicted retention values from a demographically adjusted regression model, accounting for clustering of outcomes.

Figure 2. Clinical retention, cART use, and viral suppression status of patients in CCASAnet, 2003-2012.



Research Design and Methods:

Data collection: The NA-ACCORD's latest wave of data collection was in 2014 (data updated through December 31, 2013). CCASAnet most recently received updated data from its cohorts in January 2015 (data updated through December 31, 2014). This retrospective study will begin with a baseline assessment and will continue until ≥2 full years of data following 2014 have been collected. The study population for all Aims will be adults contributing geographic data and either laboratory (CD4 count or HIV-1 viral load) or visit data at least once between January 1, 2000 and the study close. Aligning data collected at the individual level with state/region-level data derived from publicly-available sources over time and across countries (i.e., the US, Canada, and Mexico) will require extensive data cleaning and codification. Rigorous interrogation of the data, their linkages, and derivation of an analytic dataset from

the source data will require collaboration with data management personnel and bioinformaticians across cohorts. This process will be time-consuming and iterative; as new data are collected in these cohorts, and data are accumulated in the post-ACA implementation period (from 2014 onward), new challenges in collating and integrating these longitudinal data may arise. Fortunately, resources germane to these obstacles are available within the research groups and mentoring committee described above. However, data preparation for analyses spanning time, multiple comparator groups, and multiple outcomes will consume a significant portion of the award period.

Outcomes: The outcomes will be clinical retention, ART use, viral suppression (Aims 1 and 2), CD4+ count at enrollment (or at ART start), incident AIDS, all-cause mortality, and cause-specific mortality (due to HIV/AIDS) (Aims 1 and 3). Retention will be assigned each year by the IOM/NHAS indicator between entry to the study and the closing year or year of death: ≥2 HIV primary care visits within 12 months, >90 days apart.[11,19] Death during the study period will be treated as a competing event or "absorbent state". ART use and viral suppression will be assigned by the DHHS indicators: ART use during the year, of those with ≥1 visit in that year; HIV-1 viral load <200 copies/mL at last measurement in the year, of those with ≥1 visit and a measurement in that year.[44] CD4+ count at enrollment (or at ART start) will be defined as the first available CD4+ count within 6 months of enrollment date. Missing CD4+ counts may be multiply imputed.

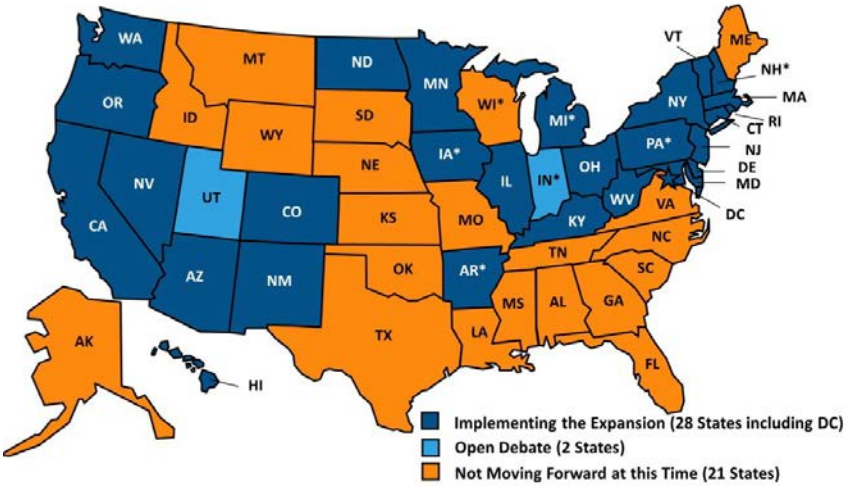
Risk factors of interest: Factors such as age, race, sex, history of injection drug use, state/jurisdiction of residence, laboratory measures (e.g., lipid levels, HbA1C, etc.), diagnoses (e.g., psychiatric diagnoses, hypertension, hyperlipidemia, etc.), and clinic encounters are already regularly collected and may be analyzed as risk factors, mediators, or confounders of the relationship between various exposures and HIVCC or clinical outcomes. ART will be multidrug regimens including ≥3 antiretroviral agents, excluding triple-nucleoside regimens abacavir+tenofovir+lamivudine and didanosine+tenofovir+lamivudine.

These variables are part of standard data already collected by NA-ACCORD and CCASAnet. Additional factors related to geographic location of patient residence may also be collected, either at the site level, or else using publically available data through government or non-profit organizations (e.g., Kaiser Family Foundation) databases (e.g., census-derived poverty levels, jobless rates, urbanicity, Ryan White income eligibility threshold, etc.); these data will be obtained, geocoded, and cleaned during a pre-award timeline. In particular, Ryan White eligibility thresholds will be treated as a potential confounder, as more generous thresholds may be associated with Medicaid expansion decisions and with HIVCC outcomes (i.e., changes in access to care through Ryan White may alter the measured effect of Medicaid expansion at the population level).[45,46]

Statistical Analysis Plan:

Aim 1. Regression methods using Generalized Estimating Equations (GEE) and restricted cubic splines will be used to assess temporal trends in outcomes, accounting for within-individual clustering of outcomes.[47] Categorical indicator variables will be used to denote health system differences, and restricted cubic splines may be used to model continuous factors (e.g., age, CD4+ count, etc.).[48] Spatial analyses using regression or cluster detection techniques, identifying locations as clusters by likelihood ratio testing, will be used.[34,49,50] These analyses will be primarily descriptive, focusing on trends and disparities in HIVCC outcomes by demographic, geographic, psychiatric, and socioeconomic characteristics. For example, the adjusted difference in viral suppression by sex, across states and over time, will be estimated.

Figure 3. Current status of state Medicaid expansion decisions (as of Aug. 2014)



Aims 2 and 3. Currently, 27 states and the District of Columbia are expanding Medicaid under the ACA, 2 are debating expansion, and 21 are not expanding Medicaid (**Figure 3**).[51] The expansion of Medicaid by state enactments of the ACA may be treated as a quasi-experimental, pre-post study design, entailing a difference-in-difference analysis or else a piecewise generalized linear mixed model.[20,51,52] An indicator for states implementing ACA provisions vs. not, an indicator for pre-ACA vs. post-ACA period, and an interaction term for the two to observe effect modification from the pre- to post-ACA periods by state of residence will be used.

Alternatively, a piecewise generalized linear mixed model with random intercepts and slopes by state and separate intercepts in the post-ACA period may be utilized.[52] Due to the distribution of states by expansion status, an analysis of neighboring states with different statuses (minimizing confounding) will be possible.[53] These states have large patient populations in the NA-ACCORD. Mexican and Canadian populations (with universal access) in CCASAnet and NA-ACCORD may be a second comparator group, contrasting outcomes in non-expansion, expansion, and true universal-access "states." Aims 2 and 3 are inferential, involving multiple methodologies to assess ACA implementation impact on HIVCC outcomes. Novel methods, which may be developed with the Health Policy Methodology group and Department of Biostatistics (described below), may be applied to improve external validity of inferences derived using these cohorts. Analyses may be conducted in SaTScan v 9.1.1 or R v 3.0.3 software.

Sample Size Calculations:

Aim 1. With >40,000 patients in each year (using the current NA-ACCORD and CCASAnet samples) clustered by cohort, under variance-covariance structure constraints, the power to detect an odds ratio of 0.95 (or 1.05) for an outcome by an individual factor would be >0.90 at α=0.05.[54] Power for a logistic marginal structural model calculated by simulation allows a similar range of effects at >0.90 power and α=0.05 with the same sample.[55] Power for geographic clustering depends on background population, outcome incidence, and relative spatial location of events.[50,56] Tango's statistic (similar to Kulldorff's statistic) has a power of ~0.95 at α=0.05, with relative risk of 4 and sample size of 200.[57] Because sample size per calendar year is exponentially larger here (~200^2), the risk difference required for power of 0.9 at α=0.05 is factors smaller.

Aims 2 and 3. A difference-in-differences analysis for a quasi-experimental design may use a regression model: $Y_i = \beta_0 + \beta_1 S_i + \beta_2 T_i + \beta_3 S_i T_i$ with β_3 as the estimated effect of Medicaid expansion (S) on the outcome (Y), comparing the pre- to post-ACA time periods (T). Using arbitrary autocorrelation, detection of an effect size of 2% with sufficient power (>0.8) requires observations of >10 states and >1 year in the pre- and post-intervention periods. These sample sizes are available within the NA-ACCORD (patients residing in all 50 states and Washington, D.C. across >2 years).[41,58]. In a piecewise generalized linear mixed model, the model could be specified: $\text{Logit}(\pi_{ij}) = (\beta_0+b_{0i}) + (\beta_{00}+b_{00i})$*post-ACA + $(\beta_1+b_{1i})*t_{ij}$*pre-ACA + $(\beta_2+b_{2i})*t_{ij}$*post-ACA + β_x*X with b_{0i}, b_{00i} as random effects for intercepts, b_{1i}, b_{2i} as random effects for slopes, and each $b \sim N(0,\sigma^2)$. Power would be similar to that for Aim 1.[52]

For all Aims, the number of events in each exposure category should be sufficiently large to accommodate inferences with adequate power, as 71% were retained in care, 82% were prescribed treatment, and 78% had HIV RNA ≤200 copies/mL from 2009 to 2010 in the NA-ACCORD.[3]

Statistical Refinements: Sensitivity analyses will be conducted for inclusion of unmeasured confounding (using methods of Cornfield)[59], due to multiple influences on receipt of HIV care, some of which may be unavailable. Data missingness will also be explored (e.g., for CD4+ counts at entry), and some data cleaning will be conducted, though the source data are already cleaned and validated at multiple stages during and after extraction and collection. If data are missing within sites, multiple imputation techniques will be used.[60]

Additional "cutting-edge" techniques such as agent-based modeling may be employed to explore the range of plausible effects under different policy decisions and individual behaviors, with input parameters derived from our observational research.[61,62] Dr. Fonnesbeck will help Dr. Rebeiro develop this, and apply appropriate spatial statistical techniques to tackle inferential hurdles posed by spatial and temporal variability in both the exposure and outcomes. Dr. Graves' Health Policy Methodology group may also develop alternative methods pertinent to both this research (Aims 2 and 3) and to his funded R01, assessing ACA impact on outcomes. In extracting data from epidemiologic cohorts outside of a quasi-experimental design, the translation of inferences to a target population is not methodologically trivial. Assuming control for confounding, selection bias and other impediments to generalizability or transportability may remain. Inverse probability of selection weighting may be of use, but research on the application of these methods to program/policy-specific questions is required.[63]

Timeline and Milestones: I will serve as the primary investigator, analyst, and author for all analyses involved in this research, though it will be conducted in collaboration. Working closely with my mentor, Dr. Sterling, my co-mentor Dr. Graves, and others in the Epi/Outcomes, CCASAnet, and NA-ACCORD working groups, I will conduct data cleaning and analyses during the first through fifth years of research (see table below), assuming a 1-2 year lag in updated data submissions from NA-ACCORD cohorts. Deliverables for each Aim will include conference presentations and manuscript publication (following protocols for collaboration and authorship within NA-ACCORD and CCASAnet); data visualizations and maps may be hosted online by NA-ACCORD as available. A detailed timeline is depicted in the table below:

Requested start date: July 2017	2017 (Year 1)				2018 (Year 2)				2019 (Year 3)				2020 (Year 4)				2021 (Year 5)			
Preparatory to Research																				
Acquire concept sheet and IRB approvals from all groups																				
Aim 1																				
Clean & aggregate data; perform longitudinal analyses																				
Abstract submission (Fall, 2018)																				
Internal peer-review and manuscript submission/revision																				
Perform spatial analyses and map adjusted outcomes																				
Internal peer-review and manuscript submission/revision																				
Aim 2																				
Clean data; perform difference-in-difference analyses																				
Abstract submission (Fall, 2019)																				
Internal peer-review and manuscript submission/revision																				
Aim 3																				
Clean data; perform difference-in-difference analyses																				
Abstract submission (Fall, 2020)																				
Internal peer-review and manuscript submission/revision																				
Additional analyses, agent-based models, & publications																				
R-01 grant writing/submission																				
Initial submission in Sept. 2019 (allows for resubmission)																				

TRAINING IN THE RESPONSIBLE CONDUCT OF RESEARCH.

Training in the responsible conduct of research is required for all faculty engaged in human subjects research both at Vanderbilt University School of Medicine (VUSM) and at the Johns Hopkins Bloomberg School of Public Health (JHSPH). In 2017, I will enroll in the **"Responsible Conduct of Research"** training session offered through the VUSM Office of Biomedical Research Education and Training (BRET). This course presents issues in the responsible conduct of research, including ethics, data management, research fraud, academic misconduct, and conflict of interest. The course covers federal and institutional guidelines regarding research in human and animal subjects. Topics include vulnerable populations in research, confidentiality, and the Institutional Review Board (IRB). The course is a full-day face-to-face training session, and attendance and completion are tracked and recorded by the BRET office.

The VUSM Master of Public Health program also offers a course (**PUBH 5518 "Research Ethics in Health Policy"**) that I will attend. This face-to-face course will meet weekly during the semester it is offered. Course topics include: conflict of interest – personal, professional, and financial; policies regarding human subjects; mentor/mentee responsibilities and relationships; collaborative research including collaborations with industry; peer review; data acquisition and laboratory tools – management, sharing and ownership; research misconduct and policies for handling misconduct; responsible authorship and publication; the scientist as a responsible member of society, contemporary ethical issues in biomedical research, and the environmental and societal impacts of scientific research.

Further, my mentor, co-mentor, mentoring committee members, and collaborators are eminent human subjects researchers involved in observational research with extensive knowledge in these issues related to data collection, management, security, and sharing; honest and responsible authorship and publication; intra- and inter-institutional collaborations; and peer review.

My mentor and co-mentor, **Drs. Sterling and Graves, serve on multiple data safety monitoring boards and clinical trial endpoint committees**. My external advisor, **Dr. Richard Moore** (Professor of Medicine, Johns Hopkins School of Medicine) also **chairs the Johns Hopkins School of Medicine IRB**. The combination of formal and informal resources to guide me in conducting my own research in a responsible manner will ensure a rigorously ethical environment, which will complement my prior coursework in this topic (the **"Responsible Conduct of Research"** (**550.600**) course taught by Sharon Krag, PhD, professor emeritus and Associate Dean for Graduate Education and Research at JHSPH).

In addition to taking the courses noted above, I have completed and passed the online "Human Research" Collaborative Institutional Training Initiative (CITI) module as a requirement of the VUSM and JHSPH Institutional Review Boards. The basic course contained the following sections: Belmont Report and CITI Course Introduction; History and Ethical Principles; Basic Institutional Review Board (IRB) Regulations and Review Process; Informed Consent; Research with Protected Populations - Vulnerable Subjects: An Overview. Certification for my CITI coursework is included in the Appendix to my application.

In addition to formal training, I will attend symposia and seminars as available on relevant ethical issues in the conduct of health policy research and biomedical research. The Center for Biomedical Ethics and Society at VUSM's Institute for Medicine and Public Health conducts "Ethics Grand Rounds" on the first Tuesday of the month every April and November, as well as hosting coursework, research, and symposia related to biomedical research ethics. The mission of the Center is to provide leadership in education, research, and clinical service at Vanderbilt University Medical Center concerning the ethical, legal, and social dimensions of medicine, health care, and health policy. The Center is committed to multi-disciplinary exploration of the individual and social values, cultural dynamics, and legal and professional standards that characterize and influence clinical practice and biomedical research. The Center aims to be a catalyst for collaboration in teaching, research, and practice at Vanderbilt and to contribute to scholarship and policy making from the local to the international level. The Center for Biomedical Ethics and Society is therefore a rich source for ethics training within Vanderbilt University, and I will make use of the resources they offer. **I will also incorporate discussions of the Responsible Conduct of Research into my presentations and talks,** relating the challenges and rewards of ethical human subjects research, issues of consent and secure data management, and IRB guidance and interactions that I encounter through the proposed work.

The VUSM and JHSPH IRBs will also be a resource. Guidance documents and policies for researchers are easily accessible through their websites: https://www4.vanderbilt.edu/irb/, https://phirst.jhsph.edu. Finally, the VUSM and JHSPH IRB offices have staff available to answer questions on an as-needed basis.

INSTITUTIONAL ENVIRONMENT.

Description of Institutional Environment: Vanderbilt University includes one of the largest academic medical centers in the Southeast with more than 450 research laboratories supported by over $587 million in extramural funds. Vanderbilt is among the top 15 NIH funded institutions and one of the fastest growing research institutions in the US as measured by annual increases in extramural support.

- The Department of Medicine has a diverse research portfolio currently supported by more than $150 million of annual external funding. In 2012, it was ranked 4th in NIH funding for research among all Departments of Medicine in US medical schools.
- The Division of Infectious Diseases is a national leader in academic research and houses the Vanderbilt AIDS Center, which coordinates all research and care related to HIV/AIDS at Vanderbilt. The Epidemiology/Outcomes Unit of the Vanderbilt AIDS Center conducts observational research studies of HIV outcomes and has collaborations with the Johns Hopkins University Adult HIV Clinic, the Case-Western Reserve University AIDS Clinical Trials Unit, the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD), the Antiretroviral Therapy Cohort Collaboration (ART-CC), and the Caribbean, Central, and South America Network for HIV research (CCASAnet). The AIDS Center also oversees the HIV Clinical Trials Unit (including HVTN and ACTG sites), and the TN Center for AIDS Research.
- The Vanderbilt Comprehensive Care Clinic (VCCC) of the Vanderbilt AIDS Center and the Vanderbilt Medical Group, is the largest HIV provider in central Tennessee. VCCC has enrolled over 7,000 patients since 1994 and provides a full spectrum of HIV primary care services. The preliminary data (found in the Research Strategy section of this K application) were generated through data collected from patients enrolled in care in this clinic in which observational research and clinical trials are tightly integrated.

Description of Institutional Scientific Environment:

- Vanderbilt Institute for Clinical and Translational Research (VICTR): VICTR is supported by the NIH via a Clinical and Translational Science Award (CTSA) to support faculty working to translate fundamental scientific discoveries into clinical practice. Examples of programs include: (1) StarBRITE (Biomedical Research Initiation, Translation, and Education) is a shared online data infrastructure storing up-to-date study documents and project characteristics; tracking research education, mentoring, conduct, collaboration, resource utilization, and productivity; and linking investigators to VICTR; (2) Pilot funding is available for up to $100,000 to support promising early-stage research; (3) Research Electronic Data Capture (REDCap) was developed at Vanderbilt with the goal to rapidly collect and manage clinical or translational research data using a secure web-based application; (4) Studios are structured sessions bringing together research experts to focus on a specific stage of research including hypothesis generation, study design, implementation, analysis and interpretation, translation and manuscript development. Dr. Rebeiro may make use of these resources for future grant applications and manuscript development.

Description of Institutional Educational and Career Development Environment:

- The Clinical and Translational Scientist Development (CTSD) is the educational component of Vanderbilt's CTSA grant. Resources available include: (1) The Elliot Newman Society is a professional organization for all investigators supported by individual K awards. Members attend semi-annual meetings with the Associate Dean to review career development and mentorship; a monthly Clinical Career Seminar on research resources, career advancement, and grant writing; and a yearly workshop retreat on successful transitioning to independence; (2) Manuscript and Grant Writing Support is available through a repository of successfully funded grants and an internal grant pre-review by senior faculty.
- Vanderbilt Department of Biostatistics: Resources available include: (1) Daily Biostatistics clinics supported by the Vanderbilt CTSA grant and available free of charge to Vanderbilt investigators; (2) The Biostatistics Collaboration Center at Vanderbilt (BCC), is a university sponsored core resource, whose services include computing software, hardware, and shared resources such as the Advanced Computing Center for Research and Education (ACCRE). Dr. Rebeiro will also enroll in biostatistics coursework under the mentorship of Drs. Chris Fonnesbeck and Bryan Shepherd (approved by DGS Dr. Jeffrey Blume).
- The Vanderbilt Department of Health Policy brings together a broad group of health policy scholars devoted to developing solutions that can have a profound impact. The Department builds on a history of strong collaborative relationships with the Tennessee Department of Health, the CDC, and several frontline policy makers to develop health policy solutions for our nation's most pressing health care challenges. The Department offers weekly seminars, a Health Policy Track for the M.P.H. degree program, and hosts a Health Policy Methodology group. Dr. Rebeiro will enroll in coursework, attend symposia, and attend Health Policy Methodology group meetings under the mentorship of Dr. John Graves.

PROTECTION OF HUMAN SUBJECTS.

Risks to human subjects

Human subjects involvement and characteristics

Existent data currently collected by clinical cohorts participating in the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) and the Caribbean, Central and South America network for HIV epidemiology (CCASAnet) will be used for the proposed research. No additional information is required from individual subjects to complete analyses.

The NA-ACCORD has data on >120,000 individuals and CCASAnet has data on >23,000 individuals. The study population for this research project will be comprised of approximately 140,000 individuals ≥18 years of age who had at least one CD4 count or HIV-1 viral load measured or at least one clinic visit recorded between January 1, 2000 and December 31, 2014 (or beyond, for Aims 2 and 3). For Aims 2 and 3, the additional inclusion criteria of participation in an NA-ACCORD clinical cohort may be applied, bringing the total number for that analysis closer to 80,000. Based on age at study entry in data through December 31, 2012, the age distribution among individuals eligible for Aim 1 of this study is as follows: age 18-24, 5.2%; age 25-34, 21.6%; age 35-44, 35.1%; age 45-54, 26.8%; age 55-64, 8.8%; age 65+, 2.6%. Inclusion criteria of individuals enrolled in clinical cohorts within the NA-ACCORD and CCASAnet, and with at least one laboratory measurement and/or one clinic encounter render this patient population likely healthier than the HIV-infected population at large, since these are individuals who have been successfully diagnosed and linked to care, though some engage in care at later stages of their HIV disease than others.

As stated in the “Research Strategy”, individuals excluded will be pediatric patients, those with no clinic encounter data (records of actual clinic visits and/or appointments) for retention outcomes, and for Aims 2 and 3, those patients not in NA-ACCORD clinical cohorts (unless the outcomes are not health service related in Aim 3). These variables either define the outcome or the exposure group of interest for their respective analyses, and so cannot be missing. Vulnerable populations are not specifically targeted in the proposed research.

Clinical cohorts will contribute patient information for the proposed research, however no direct patient contact will occur as a result. The data that will be used are collected on an ongoing basis as part of standard clinical activities at the cohort-level. Investigators representing these clinical cohorts within the NA-ACCORD and CCASAnet will have the choice of opting in to the proposed research, contributing to the analysis plan, preparation of results, and writing. The clinical cohorts with patients currently meeting inclusion criteria are as follows:

In the NA-ACCORD

- **Case Western Reserve University Immunology Unit Patient Care and Research Database**: Cleveland, OH
- **Fenway Community Health Center**: Boston, MA
- **HIV Research Network**: Baltimore, MD; Boston, MA; Dallas, TX; Detroit, MI; Kansas City, MO; La Jolla, CA; Memphis, TN; New York, NY; Oakland, CA; Philadelphia, PA; Portland, OR; Rochester, NY; San Diego, CA; Tampa, FL
- **HAART Observational Medical Evaluation and Research**: Vancouver, BC, Canada

- **HIV Outpatient Study**: Chicago, IL; Denver, CO; Philadelphia, PA; San Leandro, CA; Stony Brook, NY; Tampa, FL; Vienna, VA; Washington, DC
- **Johns Hopkins HIV Clinical Cohort**: Baltimore, MD
- **Kaiser Permanente, Northern California**: Oakland, CA
- **Kaiser Permanente, Mid-Atlantic States**: Rockville, MD
- **Montreal Chest Institute Immunodeficiency Service Cohort**: Montreal, QC, Canada
- **Ontario HIV Treatment Network Cohort Study**: Toronto, ON, Canada
- **Southern Alberta Clinic Cohort**: Calgary, AB, Canada
- **University of Alabama at Birmingham 1917 Clinic Cohort**: Birmingham, AL
- **University of North Carolina, Chapel Hill HIV Clinic**: Chapel Hill, NC
- **University of Washington HIV Cohort**: Seattle, WA
- **Veterans Aging Cohort Study and Virtual Cohort**: Clinical sites in all 50 US States, Washington, DC, and 2 Territories
- **Vanderbilt-Meharry CFAR Cohort / VCCC**: Nashville, TN

In CCASAnet

- **Hospital Fernandez**: Buenos Aires, Argentina
- **Centro Médico Huésped**: Buenos Aires, Argentina
- **Instituto de Pesquisa Clinica Evandro Chagas**: Rio de Janeiro, Brazil
- **Fundação Oswaldo Cruz**: Rio de Janeiro, Brazil
- **Fundación Arriarán**: Santiago, Chile
- **Le Groupe Haïtien d'Etude du Sarcome de Kaposi et des Infections Opportunistes (GHESKIO)**: Port-au-Prince, Haiti
- **Instituto Hondureño de Seguridad Social**: Tegucigalpa, Honduras
- **Hospital Escuela**: Tegucigalpa, Honduras
- **Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán**: Mexico City, México
- **Instituto de Medicina Tropical Alexander von Humboldt**: Lima, Perú

Sources of materials

Existent “on the shelf” electronic data from participating clinical cohorts will be used for the proposed research. Individual cohorts transmit all data elements, as prescribed in a centrally assembled data submissions document based on approved concept sheets and protocols, to the Data Management Cores of NA-ACCORD (located at the University of Washington) and CCASAnet (located at Vanderbilt University). The Data Management Cores use established methods for data assembly and harmonization to integrate transmitted data and maintain comparability across cohorts. Only those data elements which are required for analyses in Steering-Committee-approved protocols are maintained. These data comprise variables related to basic demographic information (e.g., age, sex, race/ethnicity, HIV-transmission risk factors), clinic encounter information (e.g., types of clinical encounters, status of appointment as kept or missed, etc.), insurance status (e.g., publicly insured vs. privately insured), geographic information (e.g., city of residence, state of residence, 3-digit ZIP code of residence, etc.), clinical diagnoses (e.g., AIDS-defining illnesses, psychiatric illnesses, cardiac/vascular diseases, liver diseases, renal diseases, endocrine/metabolic disorders, substance abuse disorders, etc.), medications (e.g., antiretroviral therapy, opportunistic infection prophylaxis medications, antihypertensive medications, psychotropic medications, etc.), laboratory measurement values (e.g., CD4+ lymphocyte counts, HIV-1 viral load measures, serum cholesterol measures, etc.),

and vital status. Also, elements of dates associated with these variables (e.g., date of medication prescription or laboratory measure collection, etc.) are transmitted and maintained in accordance with the HIPAA guidelines for de-identified datasets. For geographic data, individuals residing in 3-digit ZIP code areas with resident populations <20,000 have their ZIP code entered as “000” before transmission to the Data Management Core (in accordance with HIPAA guidelines). The Data Management Cores are responsible for the integration of data obtained from cohorts’ individual electronic or paper-based data systems. Census-derived contextual data on regions of patient residence (e.g., regional poverty levels, urbanicity, etc.) may be extracted from publically available data sources and merged with individual-level cohort data for analysis.

Because the population of interest for this research is comprised of those patients accessing regular clinical care in North and Latin America, patients enrolled in interval cohorts (or classic cohort studies) will not be included in Aims 1 or 2; they may potentially be included in Aim 3 if the HIV disease outcome is not a health service indicator (e.g., incidence of AIDS). Therefore, the bulk of the data being utilized are largely obtained from medical records (both electronic and paper) that are part of routine clinical HIV care at academic centers and community-based facilities where primary and specialty care are available. Nevertheless, routine data audits to control data quality are conducted within cohorts to verify how data are collected, maintained, and captured from individual sites’ electronic or paper records. Data mapping processes are conducted at the cohort-level and cohort-specific data maps applying standardized labels are generated through an iterative process. Data quality issues associated with specific data elements are documented. The generated databases are transmitted to the NA-ACCORD Epidemiology/Biostatistics Core and the CCASAnet Data Analysis Core for statistical analyses, and these are the databases which will be used in the proposed research.

For this study, additional granular geographic information on individual participants that may be pertinent to the study of contextual factors in Latin American settings will be obtained through a uniform survey at the cohort-level, and there will be no involvement of individual subjects. This information will be transmitted to the Data Management Core of CCASAnet where it will be maintained.

All information maintained within the Data Management Cores and transmitted to the Epidemiology/Biostatistics Core (NA-ACCORD) or Data Analysis Core (CCASAnet) will be de-identified in accordance with HIPAA guidelines and no NA-ACCORD or CCASAnet staff, including myself, will have access to individually identifiable private information about human subjects.

Potential risks

There are no perceived potential risks to human subjects because the data used in these analyses is routinely collected, on-the-shelf data, which are completely de-identified prior to analysis. No individually identifiable information on any subject will be shared with NA-ACCORD or CCASAnet staff, including myself.

Adequacy of protection against risks

Recruitment and informed consent

There is no additional recruitment of subjects for this study, since all participants are already enrolled in their parent cohorts, which then contribute to the NA-ACCORD and CCASAnet. The

NA-ACCORD and CCASAnet maintain their current Institutional Review Board (IRB) approvals from the Johns Hopkins School of Medicine and Vanderbilt University School of Medicine IRBs (respectively), and each contributing cohort must maintain their current approvals from their own institutional IRBs. A waiver of informed consent will be requested from the IRB for the Vanderbilt University School of Medicine for this project prior to the start of the funding period.

Protections against risk

All data used in these analyses will be completely stripped of individually identifiable private information before maintenance in the Data Management Cores (either at the University of Washington or Vanderbilt University) as part of this study, and there are therefore no potential perceived risks to individual subjects. Each subject is given a unique study identifier distinct from any identifiers they may use in their parent cohort. Geographic information on areas of residence will be de-identified in accordance with HIPAA guidelines; 3-digit ZIP codes will be entered as “000” for individuals residing in areas with fewer than 20,000 total residents.

All data are transmitted from the Data Management Cores to the Epidemiology/Biostatistics Core or Data Analysis Core computer systems, which function in line with university-wide systems and network security guidelines and recommendations for both Johns Hopkins and Vanderbilt Universities. The five levels of security monitored are: user access, data access, Network File System (NFS) export access, tape security, and monitoring for damaging software (viruses). Study staff maintain the computer systems and therefore completely control access to the system. All computer equipment used for analyses is located behind the tightly controlled security firewall of Vanderbilt University School of Medicine.

An analytic dataset domain has been configured with a domain controller to manage user IDs, access privileges, computer membership, and file and printer sharing within the domain at both Johns Hopkins and Vanderbilt Universities. Access to Windows servers and workstations, as well as UNIX-shared directories, is restricted to legitimate user IDs and passwords within the domain.

All study administrative webpages, fora, and web-based data management tasks are further restricted by user and group access control settings. Local access to SQL Server and MySQL is limited to domain-wide administrators only. Secure Shell Client (SSL) is used to enable secure transfer of data between external sites and central databases. The UNIX server provides shell access for external users to transfer documents, distribute data, communicate, and program in SAS/S-PLUS using certain summarized data sets. SSL (as opposed to clear text, telnet, or ftp) is required to access the UNIX server’s director and shell operations; access via all other protocols is disabled.

Potential benefits of proposed research to human subjects and others

There will be no direct benefit to subjects included in this study. However, living NA-ACCORD and CCASAnet participants who access clinical HIV care may indirectly benefit from more appropriately targeted policies and funding and implementation of more effective strategies to improve patient retention in clinical care, access to ART, and viral suppression rates, based on the findings of these analyses. Other HIV-infected patients in North and Latin America may benefit from increased emphasis on health policy or healthcare system strengthening to improve HIV outcomes, and HIV-uninfected individuals may benefit from the reduction in disease transmission associated with improved clinical retention, ART use, and HIV virologic control.

Subjects will not be re-contacted for this study. Additional information collected for the purposes of this study (i.e., granular geographic information in Latin American settings) will be obtained from cohort representatives and not from subjects directly. Therefore, the risks to subjects are minimal and are reasonable in relation to the anticipated benefits for research participants and others.

Importance of knowledge to be gained

Because many large, cross-sectional studies assessing HIV Care Continuum outcomes do not have access to high quality, longitudinal clinical care data from a geographically heterogeneous population, a quantification of trends in these outcomes, as well as assessments of disparities and health policy influences from a large, diverse population in which the necessary data are available, would be quite valuable. Such quantification could be used to guide future interventions in different geographic regions and inform health policy.

Because no large, geographically diverse study has yet assessed the influence of ACA reforms on HIV Care Continuum or other HIV disease outcomes among people living with HIV/AIDS in the United States, analyses demonstrating relative effectiveness of implemented interventions at the state-level would be valuable to direct future research, interventions, and ultimately, further health policy reforms.

Finally, because funding may be directed to geographic regions or high-risk demographic groups differentially, comparisons of which groups (regionally, demographically, clinically, and socioeconomically) may be at higher risk for suboptimal HIV Care Continuum outcomes using methodologically appropriate and sophisticated techniques may help redirect funding priorities. Further, the evaluation of these risk factors for suboptimal Care Continuum outcomes could provide future researchers with a template for assessing progress in National HIV/AIDS Strategy goals and ACA benchmarks.

As mentioned above, subjects will not be re-contacted for this study. Additional information collected for this study (i.e., types of cohort-level intervention strategies to improve retention in clinical care, and dates of their implementation) will be obtained from cohort representatives and not from subjects directly. Therefore, the risks to subjects are minimal and reasonable in relation to the importance of knowledge that may reasonably be expected to result from this research.

INCLUSION OF WOMEN AND MINORITIES

There will be no exclusions based on sex or race/ethnicity. Preliminary estimates of potential participants indicate that 19% are women, 34% are black or African-American, 34% are white, 0.01% are Asian or Pacific Islander, 0.01% are American Indian or Alaskan Native, and 0.002% are Multiracial; 24% are of Hispanic ethnicity (of any race), and 0.04% are of unknown or other race/ethnicity.

More detailed descriptions of the racial composition of potential participants for Aims 1, 2, and 3 are presented in the Targeted/Planned Enrollment Tables in the next section (**TARGETED/PLANNED ENROLLMENT**).

PHS Inclusion Enrollment Report

This report format should NOT be used for collecting data from study participants.

OMB Number:0925-0001 and 0925-0002
Expiration Date: 10/31/2018

***Study Title:** The HIV Care Continuum and Health Policy: Changes through Context and Geography (Aim 1)

***Delayed Onset Study?** ❑ Yes ☑ No

If study is not delayed onset, the following selections are required:

Enrollment Type ☑ Planned ❑ Cumulative (Actual)

Using an Existing Dataset or Resource ❑ Yes ☑ No

Enrollment Location ☑ Domestic ❑ Foreign

Clinical Trial ❑ Yes ☑ No

NIH-Defined Phase III Clinical Trial ❑ Yes ☑ No

Comments: By assessing the dynamic process of the HIV Care Continuum in discrete stages, and examining disparities by health policy, geography, and individual context, transitions that demand improvement and specific targets for public health and clinical interventions can more easily be identified.

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/Alaska Native	418	905		0	0					1323
Asian	191	1270		0	0					1461
Native Hawaiian or Other Pacific Islander	7	116		0	0					123
Black or African American	11649	38324		0	0					49973
White	4109	46423		0	0					50532
More than One Race	11376	232		0	0					11608
Unknown or Not Reported										
Total	27750	87270		0	0					115020

PHS Inclusion Enrollment Report

This report format should NOT be used for collecting data from study participants.

OMB Number:0925-0001 and 0925-0002
Expiration Date: 10/31/2018

***Study Title:** The HIV Care Continuum and Health Policy: Changes through Contect and Geography (Aims 2 &3)

***Delayed Onset Study?** ❑ Yes ☑ No

If study is not delayed onset, the following selections are required:

Enrollment Type ☑ Planned ❑ Cumulative (Actual)

Using an Existing Dataset or Resource ❑ Yes ☑ No

Enrollment Location ☑ Domestic ❑ Foreign

Clinical Trial ❑ Yes ☑ No

NIH-Defined Phase III Clinical Trial ❑ Yes ☑ No

Comments: By assessing the dynamic process of the HIV Care Continuum in discrete stages, and examining dispartities by health policy, geography, and individual context, transitions that demand improvement and specific targets for public health and clinical interventions can more easily be identified.

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/Alaska Native	418	905		0	0					1323
Asian	191	1270		0	0					1461
Native Hawaiian or Other Pacific Islander	7	116		0	0					123
Black or African American	11649	38324		0	0					49973
White	4109	46423		0	0					50532
More than One Race	89	232		0	0					321
Unknown or Not Reported										
Total	16463	87270		0	0					103733

INCLUSION OF CHILDREN.

The National Institutes of Health (NIH) defines “children” as those individuals who are under the age of 18 years. Cohorts participating in the NA-ACCORD pre-enroll only individuals at least 18 years of age. There are therefore no children under age 18 included in the NA-ACCORD, per its design. In CCASAnet, there are indeed pediatric cohorts, though these will not be included in this study as they are limited in their geographic extent (i.e., they are not present across areas with great heterogeneity in health system structures or geographic location), and may therefore be insufficient to address Aim 1. This fulfills the exclusionary circumstance noted in the NIH policy on the Inclusion of Children:

- Study designs are aimed at collecting additional data on pre-enrolled adult study subjects (e.g., longitudinal follow-up studies that did not include data on children).

The research questions in this proposal may be relevant to children infected with HIV as to adults. Because the proposed research focuses on HIV Care Continuum outcomes and health policy, demographic, clinical, and geographic characteristics associated with these outcomes, and because the factors associated with these outcomes among children may differ from those among adults due to adult parents, relatives, or caregivers being responsible for maintaining their clinical care or different policies applying specifically to children, the policies or strategies this research may inform may not apply to children.

SELECT AGENT RESEARCH.

NOT APPLICABLE

RESOURCE SHARING PLAN.

All data acquired through NIH funds and the conduct of the proposed research will be shared and made publicly available through publication in the peer-reviewed literature.

However, this application does not request direct costs of $500,000.00 or greater in any single year. Further, it does not involve the development of model organisms, nor is funding being sought for a genome-wide association study.

AUTHENTICATION OF KEY BIOLOGICAL AND/OR CHEMICAL RESOURCES.

Our proposal does not utilize key biological and/or chemical resources; there are therefore no biological and/or chemical resources to be fully authenticated and/or validated prior to embarking upon work within the proposed Aims.