BIOGRAPHICAL SKETCH

NAME: Sterling, Timothy R.

eRA COMMONS USER NAME: SterlingT

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 have been an investigator in the Tuberculosis Trials Consortium (TBTC) of the Centers for Disease Control and Prevention since 1998, Chair of the TBTC Core Science Group 2011-2016, and Chair of the Steering Committee (2016-present). I was the protocol chair for TBTC Study 26, a large international study of 3 months of weekly rifapentine plus isoniazid for the treatment of latent tuberculosis infection; the results changed CDC and WHO guidelines. I have also conducted several large multi-center epidemiologic studies of tuberculosis and HIV. I lead efforts for **Regional Prospective Observational Research for TB (**RePORT)-Brazil, a prospective cohort established to perform translational studies of TB pathogenesis, treatment and prevention. I also participate in RePORT-South Africa, with our partner site in Durban. In addition, I participate in the International Epidemiologic Databases to Evaluate AIDS (IeDEA) network of the National Institutes of Health as a site PI for the North American ACCORD and as a co-investigator in the Caribbean Central America South America network (CCASAnet). For both networks, I contribute to efforts related to TB/HIV studies.

**B. Positions and Honors**

**Positions and Employment**

1992-1996 Staff Physician, U.S. Air Force Medical Center Keesler, Keesler AFB, MS.

* 1. Assistant Professor of Medicine & Epidemiology, Johns Hopkins University School of Medicine

2002-2003 Associate Professor of Medicine & Epidemiology, Johns Hopkins University School of Medicine

* 1. 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, Africa Health Research Institute (formerly 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-March 2016
* ATS/IDSA/CDC. Guidelines for Treatment of Latent Tuberculosis Infection. Co-chair. 2011-2016
* 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
* Tuberculosis Trials Consortium: Chair, Steering Committee. May 2016-present

**Honors** (last 7 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. 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.

1. **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
2. Shepherd BS, 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 JA, **Sterling TR**. Antiretroviral Therapy Cohort Collaboration (ART-CC). Higher rates of AIDS during the first year of antiretroviral therapy among migrants: the importance of tuberculosis. AIDS. 2013;27(8):1321-9. PMCID: PMC3992322
3. 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.
4. 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 Aug 15;72(5):572-8. PMCID: PMC4942351.

2. 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.

1. **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
2. 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
3. Koethe JR, Jenkins CA, Lau B, Shepherd BE, Wester W, Rebeiro PF, Silverberg MJ, Thorne JE, Gill J, Mayor AM, Willig A, Bosch R, Horberg MA, Justice AC, **Sterling TR**, Moore RD. Higher time-updated body mass index: association with improved CD4+ cell recovery on HIV treatment. J Acquir Immune Defic Syndr 2016 Oct 1;73(2):197-204. PMCID: PMC5023455.
4. 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 noncommunicable diseases in HIV-infected adults on antiretroviral therapy. AIDS 2016 Mar 27;30(6):899-908. PMCID: PMC4785819.

3. 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.

1. **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
2. 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
3. **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. PMCID: PMC4560029
4. **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

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

I have studied drug-resistant TB for more than 25 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*.

1. 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
2. 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
3. Eilertson B, Maruri F, Blackman A, Herrera M, Samuels DC, **Sterling TR**. High proportion of heteroresistance in gyrA and gyrB in fluoroquinolone-resistant *Mycobacterium tuberculosis* clinical isolates. Antimicrob Agents Chemother. 2014; 58(6):3270-5. PMCID: PMC4068501
4. 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 Sep;71(9):2419-27. PMCID: PMC4992850

5. 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.

1. **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
2. Antas PR, Ding L, Hackman J, Reeves-Hammock L, Shintani AK, Schiffer J, Holland SM, **Sterling TR**. Decreased CD4+ lymphocytes and innate immune responses in adults with previous extrapulmonary tuberculosis. J Allergy Clin Immunol. 2006;117(4):916-23. PMID: 16630952
3. **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
4. 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

**Complete List of Published Work in MyBibliography:** <https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/40632070/?sort=date&direction=ascending>

D. Research Support

#### Current

NIAID 5 U01 AI069923 Project PI: Sterling TR 07/01/13-06/30/19

### 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.

NIH R01 AI120790 PI: Sterling TR 08/12/16-07/31/20

#### Predictors of treatment toxicity, failure, and relapse in HIV-related tuberculosis in RePORT-Brazil.

This project seeks to identify pharmacogenomic predictors of TB/HIV treatment toxicity and effectiveness in Brazil. Co-PI: Valeria Rolla, Fiocruz, Brazil

NIH R01 AI134430 PIs: Horsburgh (Boston U) and Sterling TR 08/15/17 – 07/31/22

Predictors of Resistance Emergence Evaluation in MDR-TB Patients on Treatment (PREEMPT).

This study assesses the acquisition of resistance to fluoroquinolones and aminoglycosides in Brazil and India

Performed in the RePORT-Brazil and RePORT-India cohorts.

NIAID R56 AI118361 PI: Sterling TR 08/01/16-07/31/19

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. Co-PI: David Sherman; CIDR, Seattle

RePORT South Africa PI: Pym A and Sterling TR 06/01/16-05/31/19

U.S. Civilian Research and Development Foundation. Bacterial, host-mediated biomarkers of TB treatment response; eicosanoid and inflammatory balance in TB-diabetes. Africa Health Research Institute.

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 (CDC).

This consortium conducts programmatically relevant studies of tuberculosis treatment and prevention.

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: Co-investigator

NIAID P30AI110527 PI: Mallal S 04/01/15 – 03/31/20

Tennessee Center for AIDS Research: Vanderbilt-Meharry-Tennessee Department of Health

Role: 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

NIAID R21AI127129-01 PI: Kalams S 08/01/16 - 07/31/19

Molecular analysis of the adaptive immune response to tuberculosis

The purpose of this study is to apply cutting-edge molecular immunology techniques to determine the features of the adaptive immune response likely to protect against tuberculosis.

NIAID AIO68632 PI: Gupta A 12/01/15-11/30/18

Role: Vice-Chair, IMPAACT P1078 Study:

This multi-center study is assessing the safety and effectiveness of peri-partum vs. post-partum isoniazid preventive therapy in HIV-infected pregnant women.

WHIP3TB: 10/01/16 – 09/30/19

Role: Chair, Trial Steering Committee

This multi-center study in Africa is being led by the Aurum Institute, with funding from KNCV and USAID.