

BIOGRAPHICAL SKETCH

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NAME: Sean Adam Wasserman

eRA COMMONS USER NAME (credential, e.g., agency login): SEANWASSERMAN

POSITION TITLE: Associate 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)	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
University of Cape Town, Cape Town, South Africa	MBChB	01/1999	12/2004	Medicine
University of Cape Town, Cape Town, South Africa	MMed	07/2008	12/2012	Medicine
Colleges of Medicine of South Africa	FCP (SA)	07/2008	12/2012	Internal Medicine
Colleges of Medicine of South Africa	Cert ID (SA)	01/2013	12/2014	Infectious Diseases
Graduate Summer Institute of Epidemiology and Biostatistics, Johns Hopkins University, Baltimore, MD	N/A	June 2017	June 2017	Biostatistics

A. PERSONAL STATEMENT

I am an adult Infectious Diseases physician, and Senior Lecturer and Consultant in the Division of Infectious Diseases and HIV Medicine at Groote Schuur Hospital and the University of Cape Town, South Africa. I am a Contributing Investigator at the Wellcome Centre for Infectious Diseases Research in Africa, University of Cape Town. My two main research areas are new and repurposed drugs for tuberculosis (TB), with a focus on pharmacokinetics (PK) and resistance, and novel regimens and PK in TB meningitis. I am the national Principal Investigator for the multi-country endTB trial (NCT02754765), investigating shorter all-oral regimens for drug-resistant TB. I am leading a prospective cohort study to evaluate determinants of treatment outcomes amongst HIV-positive patients being treated with a novel injection-free shortened regimen for MDR-TB; pharmacology objectives are exploring PK-PD relationships for clofazimine and use of drug exposures as biomarkers of treatment adherence. I presented the first clofazimine PK data from patients with drug-resistant TB (abstract reference below), which showed markedly different exposures between men and women. I am a pharmacologist on the ACTG IMAGINE-TBM (A5384) protocol. I am site Principal Investigator for LASER-TBM (NCT03927313), a Phase 2A trial investigating the safety of high dose rifampin and linezolid for TB meningitis and was recently awarded a K43 grant to lead the PK sub-studies. I am a co-investigator on the multi-country Phase 3 INTENSE-TBM trial, evaluating efficacy and PK of intensified antitubercular therapy for TB meningitis.

- Wasserman S**, Denti P, Brust JCM, Weisner L, Meintjes G, Maartens G. Clofazimine pharmacokinetics in South African patients with drug-resistant tuberculosis. International Workshop on Pharmacology of Tuberculosis Drugs. The Hague, Netherlands, October 2018.

B. POSITIONS AND HONORSEmployment

2006 Jan – Dec	Medical Intern, GF Jooste Hospital, Cape Town
2007 Jan – Dec	Community Service Medical Officer, Mosvold Hospital, Ingwavuma
2008 Jul – 2009 Jul	Medical Officer, Department of Medicine, University of Cape Town

2009 Aug - 2013 Jan	Medical Registrar/Resident, Department of Medicine, University of Cape Town
2013 Feb – 2014 Jan	Senior Registrar/Fellow, Division of Infectious Diseases and HIV Medicine, Department of Medicine, University of Cape Town
2015 Jan - Dec	Senior Lecturer and Consultant in Internal Medicine, Department of Medicine, New Somerset Hospital and University of Cape Town
2016 Jan – 2017 Dec	PhD Fellowship, Department of Medicine, University of Cape Town
2017 Feb – current	Local Principal Investigator, endTB trial, Medecins Sans Frontieres
2018 Jan – December	Senior Lecturer, Wellcome Centre for Infectious Diseases Research in Africa, Department of Medicine, University of Cape Town
2019 Jan – current	Senior Specialist, Division of Infectious Diseases and HIV Medicine, Department of Medicine, Groote Schuur Hospital and University of Cape Town

Honors

2009	Department of Medicine Jackson Award for best case presentation, University of Cape Town
2012	Distinction for Masters degree dissertation, University of Cape Town
2012	Life Healthcare scholarship for sub-specialist training in Infectious Diseases
2013	Federation of Infectious Diseases Societies of Southern Africa-GlaxoSmithKline (FIDSSA-GSK) research fellowship
2015	European Society of Clinical Microbiology and Infectious Diseases (ESCMID) observer fellowship to the European Centre for Disease Control (ECDC) in Stockholm
2016	International Society for Infectious Diseases (ISID) Research Grant award
2016	ISID Emerging Leader in International Infectious Diseases
2018	Interacademy Partnership (IAP) Young Physician Leader
2019	Stephen Lawn TB-HIV Research Leadership Prize
2019	FIDSSA-Institut Merieux Young Investigator Award

Professional Societies and Public Advisory Committees

2012 –	Fellow of the Colleges of Physicians of South Africa
2015 –	South African Antibiotic Stewardship Program (SAASP) - member of the national antibiotic stewardship working group
2016 –	International Society for Infectious Diseases (ISID)
2016 –	Western Cape Department of Health Clinical Advisory Committee for drug-resistant TB
2017 –	National Department of Health working group on 'Guidelines for hospital-level antimicrobial stewardship activities'
2018 –	Federation of Infectious Diseases Societies of Southern Africa (FIDSSA): Chairperson of the Expert Review Committee
2019 –	Assistant editor: International Journal of Infectious Diseases

C. CONTRIBUTIONS TO SCIENCE

I have 34 publications in peer-reviewed scientific journals: 14 as first author and 5 as senior last author. The full list of publications can be found at:

<https://www.ncbi.nlm.nih.gov/myncbi/1FSceD7tnZh51/bibliography/public/>

Drug-resistant TB

My focus has been on understanding mechanisms of resistance and PK/pharmacodynamic relationships of linezolid for drug-resistant TB. This work addresses a knowledge gap in the field by defining PK targets for efficacy and toxicity using data from a large clinical cohort to inform optimal dosing of this important antituberculosis agent. I published a comprehensive review of the use of linezolid in drug-resistant TB, with a focus on PK issues. My research on linezolid PK showed that putative efficacy targets may not be achieved at the standard dose of 600 mg daily for strains with MICs at the critical concentration; these data were presented at the WHO Guideline Development Group meeting in July 2018 and helped to inform policy on linezolid dosing.

1. **Wasserman S**, Meintjes G, Maartens G. Linezolid in the treatment of drug-resistant tuberculosis: the challenge of its narrow therapeutic index. Expert review of anti-infective therapy. Expert Review of Anti-infective Therapy. 2016;14(10):901-15.

2. **Wasserman S**, Denti P, Brust JC, Tareq M, Hlungulu S, Wiesner L, Norman J, Sirgel FA, Warren RM, Esmail A, Dheda K, Gandhi NR, Meintjes G, Maartens G. Linezolid Pharmacokinetics in South African Patients with Drug-Resistant Tuberculosis and a High Prevalence of HIV Coinfection. *Antimicrobial agents and chemotherapy*. 2019; 63(3).

I led a study to describe clinical associations and genotypic correlates of linezolid resistance amongst South African patients with linezolid-based treatment failure for drug-resistant TB. We showed that resistance occurred in a third of patients after a median of 22 months on linezolid therapy. Resistance was predicted by a limited number of mutations.

3. **Wasserman S**, Louw G, Ramangoela L, Barber G, Hayes C, Omar SV, Maartens G, Barry C, Song T, Meintjes G. Linezolid resistance in patients with drug-resistant TB and treatment failure in South Africa. *Journal of Antimicrobial Agents and Chemotherapy*. 2019; **74**(8): 2377-84.

I was the PI of a retrospective cohort study which showed that the use of bedaquiline as a substitute for injectable agents in MDR-TB was safe and resulted in improved outcomes.

4. Zhao Y, Manning K, Stewart A, Fox T, Tiffin N, Boule A, Mudaly V, Kock Y, Meintjes G, **Wasserman S**. Clinical outcomes with bedaquiline when substituted for second-line injectable agents in multidrug resistant tuberculosis: a retrospective cohort study. *Clinical Infectious Diseases*. 2019 Apr; 68(9):1522-1529.

Opportunistic infections in HIV

There are limited data on the frequency and burden of PCP in sub-Saharan Africa, where the HIV epidemic has been dominated by TB and meningitis. I undertook a systematic review and meta-analysis of the burden of HIV-associated PCP in sub-Saharan Africa, showing that PCP is diagnosed in over a fifth of HIV-infected patients admitted for pneumonia in the region, and that the case fatality was higher than in developed countries. A second paper analyzed the outcomes of HIV-associated PCP amongst South African ICU patients, identifying predictors of mortality in this population. This work informed ICU policy at our hospital

1. **Wasserman S**, Engel ME, Griesel R, Mendelson M. Burden of pneumocystis pneumonia in HIV-infected adults in sub-Saharan Africa: a systematic review and meta-analysis. *BMC Infectious Diseases*. 2016 Sep 9;16(1):482.
2. Chiliza N, Du Toit M, **Wasserman S**. Outcomes of HIV-associated pneumocystis pneumonia at a South African referral hospital. *PLoS ONE*. 2018; 13(8): e0201733.

Management and outcomes of *Staphylococcus aureus* bacteremia is poorly studied in sub-Saharan Africa, particularly in the context of HIV co-infection which may increase risk. I supervised a postgraduate student to conduct a prospective study to describe the management and outcomes of *Staphylococcus aureus* bacteremia at our hospital. The findings led to the implementation of a hospital-wide intervention to improve management of this condition.

3. Steinhaus N, Al-talib M, Ive P, Boyles T, Bamford C, Davies M, Mendelson M, **Wasserman S**. The management and outcomes of *Staphylococcus aureus* bacteraemia at a South African referral hospital: a prospective observational study. *International Journal of Infectious Diseases*. 2018; 73:78-84.

Emergomyces africanus was first reported in a case series of HIV-infected patients from South Africa. I participated in a study showing emergomycosis was the commonest endemic mycosis in South Africa.

4. Schwartz IS, Kenyon C, Lehloenya R, Claasens S, Spengane Z, Prozesky H, Burton R, Parker A, **Wasserman S**, Meintjes G, Mendelson M, Taljaard J, Schneider JW, Beylis N, Maloba B, Govender NP, Colebunders R, Dlamini S.. AIDS-related endemic mycoses in Western Cape, South Africa and clinical mimics: a cross-sectional study of adults with advanced HIV and recent-onset, widespread skin lesions. *Open Forum Infectious Diseases*. 2017 Aug 25;4(4):ofx186.

D. ADDITIONAL INFORMATION: RESEARCH SUPPORT

1. Award: NIH K43 (1K43TW011421)
Period: August 2019 - July 2023
Title: "Characterizing the pharmacokinetics of high dose rifampicin and linezolid in a randomized controlled trial for HIV-associated tuberculous meningitis"
Goals: Describe PK of intensified antibiotic therapy, evaluate drug-drug interactions, and assess bioavailability of rifampin in TB meningitis.
My role: Principal Investigator.

2. Award: European and Developing Countries Clinical Trials Programme (EDCTP) - 109237
Period: January 2019 - December 2023
Title "Intensified tuberculosis treatment to reduce the high mortality of tuberculous meningitis in HIV-infected and uninfected patients (Intense-TBM)"
Goals: Evaluate efficacy of intensified antibiotic and host-directed therapy for TB meningitis.
PI: F Bonnet (University of Bordeaux)
My role: Co-investigator.

3. Award: South African Medical Research Council (SAMRC) Strategic Health Innovation Partnerships grant.
Period: July 2019 – June 2022.
Title: "Determinants of treatment outcomes with an injection-free shorter regimen for MDR/RR-TB."
Goals: prospective cohort study in South Africa to describe outcomes, investigate pyrazinamide resistance, clofazimine toxicity and pharmacokinetics, and treatment adherence in an oral short course regimen for drug-resistant TB.
My role: Co-Principal Investigator.

4. Award: European and Developing Countries Clinical Trials Programme (EDCTP) Career Development Fellowship
Period: April 2017 – March 2020.
Title: "Optimising linezolid for drug-resistant tuberculosis."
Goals: prospective cohort study to investigate the relationship between linezolid exposure and clinical outcomes in drug-resistant TB. This forms the basis of my PhD.
My role: Personal fellowship.

5. Award: NIH R01 (1R01AI114304)
Period: March 2016 – February 2020.
Title: Safety, Pharmacokinetics and Resistance to Bedaquiline in XDR TB and HIV
Goals: prospective cohort study to determine mechanisms of bedaquiline resistance, drug-drug interactions with protease inhibitors, and toxicity in patients with XDR-TB.
PI: JCM Brust (Albert Einstein College of Medicine)
My role: Co-investigator.