Zachary Ryan McCaw

Curriculum Vitae

GitHub, LinkedIn, ORC ID

October 1st, 2021

Education

Stanford University
01/2021 – Present

Graduate Certificate in Artificial Intelligence

Harvard University
08/2014 – 05/2019

Ph.D. in Biostatistics, A.M. in Biostatistics

- Dissertation: Transformation and multivariate methods for improving power in genome-wide association studies.
- Advisor: Xihong Lin, Ph.D.
- Committee: Martin Aryee, Ph.D. and Jeffrey Miller, Ph.D.

University of North Carolina at Chapel Hill
08/2009 – 05/2013

B.S.P.H. in Biostatistics, B.S. in Quantitative Biology

- Graduate with highest distinction.
- GPA: 4.00 of 4.00; Dean's List: 8 of 8 Semesters.

Professional Experience

Insitro
09/2021 – Present

Senior Data Scientist

- Department: Statistical Genetics
- Team Lead: Francesco Paolo Casale, Ph.D.

Google
09/2019 – 09/2021

Data Scientist

- Department: Health, Genomic Medicine Team.
- Scientific Lead: Babak Alipanahi, Ph.D.
- 20% Project: **Genetic discovery for machine learning derived phenotypes**.
  - Lead author on DeepNull manuscript, a GWAS model that uses a deep neural network to adjust for non-linear covariate effects.
  - Co-first author on manuscript reporting genetic associations for glaucomatous features extracted from retinal fundus images using deep neural networks.

- Developed and implemented tools for GWAS analysis, including fine-mapping, locus formation, replication analysis, and winner's curse correction.

- Department: Core Developer, DevIntel Data Science Team.
- Team Lead: Heng Liu, Ph.D.
- Project: Causal inference to understand factors affecting developer productivity.
  - Developed and implemented methodology for estimating average treatment effects from observational, longitudinal data.

Broad Institute
06/2019 – 09/2019

Visiting Scientist

- Department: Medical and Population Genetics.
- Principal Investigator: Hilary Finucane, Ph.D.
- Project: **Cross-population fine-mapping to identify shared and population specific causal effects.**
  - Developed an extension of sum of single effects regression for the multi-sample setting.

Articles

[1] ZR McCaw et al. "Choosing clinically interpretable summary measures and robust analytic procedures for quantifying the treatment difference in comparative clinical studies". In: *Statistics in Medicine Accepted* (2021).

[2] H Julienne et al. "Multitrait GWAS to connect disease variants and biological mechanisms". In: *PLoS Genet* 17.8 (Aug. 2021), e1009713. DOI: 10.1371/journal.pgen.1009713.

[3] ZR McCaw et al. "DeepNull: Modeling non-linear covariate effects improves phenotype prediction and association power". In: *bioRxiv* (May 2021). DOI: 10.1101/2021.05.26.445783.

[4] B Alipanahi et al. "Large-scale machine learning-based phenotyping significantly improves genomic discovery for optic nerve head morphology". In: *American Journal of Human Genetics* (May 2021). DOI: 10.1016/j.ajhg.2021.05.004.

[5] ZR McCaw et al. "Neoadjuvant chemotherapy in bladder cancer: Clinical benefit observed in prospective trials computed with restricted mean survival times". In: *Urologic Oncology* S1078-1439.20 (Jan. 2021), pp. 30640–30642. DOI: 10.1016/j.urolonc.2020.12.012.

[6] ZR McCaw et al. "Cross-tissue eQTL mapping in the presence of missing data via surrogate outcome analysis". In: *bioRxiv* (Nov. 2020). DOI: 10.1101/2020.11.29.403063.

[7] ZR McCaw et al. "Survival analysis of treatment efficacy in comparative COVID-19 studies." In: *Clinical Infectious Diseases* (Oct. 2020). DOI: 10.1093/cid/ciaa1563.

[8] C Perego et al. “Utility of Restricted Mean Survival Time Analysis for Heart Failure Clinical Trial Evaluation and Interpretation”. In: *JACC Heart Failure* (Oct. 2020). DOI: 10.1016/j.jchf.2020.07.005.

[9] ZR McCaw et al. “Selecting Appropriate Endpoints for Assessing Treatment Effects in Comparative Clinical Studies for COVID-19”. In: *Contemporary Clinical Trials* (Sept. 2020). DOI: 10.1016/j.cct.2020.106145..

[10] ZR McCaw et al. “How to Quantify and Interpret Treatment Effects in Comparative Clinical Studies of COVID-19”. In: *Annals of Internal Medicine* (July 2020). DOI: 10.7326/M20-4044.

[11] B Huang et al. “Analysis of Response Data for Assessing Treatment Effects in Comparative Clinical Studies”. In: *Annals of Internal Medicine* (July 2020). DOI: 10.7326/M20-0104.

[12] H Julienne et al. “Multitrait genetic-phenotype associations to connect disease variants and biological mechanisms”. In: *bioRxiv* (June 2020). DOI: 10.1101/2020.06.26.172999.

[13] ZR McCaw, H Julienne, and H Aschard. “MGMM: an R package for fitting Gaussian Mixture Models on Incomplete Data”. In: *bioRxiv* (Dec. 2019). DOI: 10.1101/2019.12.20.884551.

[14] ZR McCaw et al. “Operating Characteristics of the Rank-Based Inverse Normal Transformation for Quantitative Trait Analysis in Genome-Wide Association Studies”. In: *Biometrics* (Dec. 2019). DOI: 10.1111/biom.13214.

[15] J Marzec et al. “Toll-like receptor 4-mediated respiratory syncytial virus disease and lung transcriptomics in differentially susceptible inbred mouse strains”. In: *Physiological Genomics* (Nov. 2019). DOI: 10.1152/physiolgenomics.00101.2019.

[16] ZR McCaw, G Yin, and LJ Wei. “Using the Restricted Mean Survival Time Difference as an Alternative to the Hazard Ratio for Analyzing Clinical Cardiovascular Studies”. In: *Circulation* 140.17 (Oct. 2019), pp. 1366–1368. DOI: 10.1161/CIRCULATIONAHA.119.040680.

[17] ZR McCaw et al. “Applying Evidence-Based Medicine to Shared Decision Making: Value of Restricted Mean Survival Time”. In: *The American Journal of Medicine* 132.1 (Jan. 2019), pp. 13–15. DOI: 10.1016/j.amjmed.2018.07.026.

[18] M High et al. “Determinants of host susceptibility to murine respiratory syncytial virus (RSV) disease identify a role for the innate immunity scavenger receptor MARCO gene in human infants”. In: *EBioMedicine* S2352-3964.16 (2016), pp. 30360–7. DOI: 10.1016/j.ebiom.2016.08.011.

[19] JM Ciencewicki et al. “Effects of mannose-binding lectin on pulmonary gene expression and innate immune inflammatory response to ozone”. In: *American Journal of Physiology-Lung Cellular and Molecular Physiology* 311.2 (2016), pp. 280–91. DOI: 10.1152/ajplung.00205.2015.

[20] BP Kleinstiver et al. "Genome-wide specificities of CRISPR-Cas Cpf1 nucleases in human cells". In: *Nature Biotechnology* 34.8 (2016), pp. 869–74. DOI: 10.1038/nbt.3620.

[21] KC Verhein et al. "Novel Roles for Notch3 and Notch4 Receptors in Gene Expression and Susceptibility to Ozone Induced Lung Inflammation in Mice". In: *Environmental Health Perspectives* 123.8 (2015), pp. 799–805. DOI: 10.1289/ehp.1408852.

[22] J Krishnaswamy et al. "Coincidental loss of DOCK8 function in NLRP10-deficient and C3H/HeJ mice results in defective dendritic cell migration". In: *PNAS* 112.10 (2015), pp. 3056–61. DOI: 10.1073/pnas.1501554112.

[23] H Cho et al. "Association of Nrf2 polymorphism haplotypes with acute lung injury phenotypes in inbred strains of mice". In: *Antioxidants and Redox Signaling* 22.4 (2015), pp. 325–38. DOI: 10.1089/ars.2014.5942.

[24] KC Verhein et al. "Genetic Factors Involved in Susceptibility to Lung Disease". In: *The Lung Second Edition: Development, Aging and the Environment*. Ed. by Plopper CG Harding R Pinkerton KE. London: Academic Press, 2014.

Correspondence

[1] ZR McCaw, L Tian, and LJ Wei. "Quantifying the Effect of Lower vs Higher Positive End-Expiratory Pressure on Ventilator-Free Survival in ICU Patients". In: *JAMA* 325.15 (Apr. 2021), pp. 1566–1567. DOI: doi:10.1001/jama.2021.1700..

[2] ZR McCaw, MA Liu, and LJ Wei. "Olaparib in Metastatic Castration-Resistant Prostate Cancer". In: *New England Journal of Medicine* 384.12 (Mar. 2021), p. 1174. DOI: doi:10.1056/NEJMc2100225.

[3] ZR McCaw, EB Ludmir, and LJ Wei. "Quantifying the Long-term Survival Benefit of Pembrolizumab for Patients With Advanced Gastric Cancer". In: *JAMA Oncology* (Feb. 2021). DOI: 10.1001/jamaoncol.2020.8002.

[4] ZR McCaw, G Fitzmaurice, and LJ Wei. "The COMPASS Trial: Net Clinical Benefit of Low-Dose Rivaroxaban Plus Aspirin as Compared With Aspirin in Patients With Chronic Vascular Disease". In: *Circulation* 143.1 (Jan. 2021), e1–e2. DOI: 10.1161/CIRCULATIONAHA.120.050723.

[5] RR Patel et al. "Transparency in reporting of phase 3 cancer clinical trial results". In: *Acta Oncologica* (Dec. 2020). DOI: 10.1080/0284186X.2020.1856410.

[6] EB Ludmir, ZR McCaw, and LJ Wei. "Interpreting the Effect of Ipilimumab Following Radiotherapy for Patients with Postdocetaxel Metastatic Castration-resistant Prostate Cancer". In: *European Urology* (Oct. 2020). DOI: 10.1016/j.eururo.2020.09.049.

[7] ZR McCaw, L Tian, and LJ Wei. "Appropriate Analysis of Duration of Response Data in Cancer Trials". In: *JAMA Oncology* (Oct. 2020). DOI: 10.1001/jamaoncol.2020.4657.

[8] ZR McCaw, L Tian, and LJ Wei. "What We Learned from Recent COVID-19 Clinical Studies Regarding Statistical Methodology". In: *Biopharmaceutical Report* 27.3 (Oct. 2020).

[9] EB Ludmir et al. "Progression-free survival in the ICON8 trial". In: *Lancet* 396.10253 (Sept. 2020), p. 756. DOI: 10.1016/S0140-6736(20)31175-2.

[10] ZR McCaw et al. "Further clinical interpretation and implications of KEYNOTE-048 findings". In: *Lancet* 396.10248 (Aug. 2020), pp. 378–379. DOI: 10.1016/S0140-6736(20)30904-1.

[11] ZR McCaw, DH Kim, and LJ Wei. "Remdesivir for the Treatment of Covid-19 - Preliminary Report". In: *New England Journal of Medicine* (July 2020). DOI: 10.1056/NEJMc2022236.

[12] ZR McCaw, DH Kim, and LJ Wei. "Risk-Benefit Comparisons Between Shorter and Longer Durations of Adjuvant Chemotherapy in High-Risk Stage II Colorectal Cancer". In: *JAMA Oncology* (June 2020). DOI: 10.1001/jamaoncol.2020.2256.

[13] EB Ludmir et al. "Fulvestrant plus capivasertib for metastatic breast cancer". In: *Lancet Oncology* 21.5 (May 2020), e233. DOI: 10.1016/S1470-2045(20)30228-X.

[14] ZR McCaw, LJ Wei, and EB Ludmir. "Interpreting the impact of apalutamide on overall survival among patients with non-metastatic castration-resistant prostate cancer". In: *Annals of Oncology* 31.3 (Mar. 2020), pp. 438–440. DOI: 10.1016/j.annonc.2019.11.020.

[15] D Li, ZR McCaw, and LJ Wei. "Interpreting the Benefit of Simvastatin-Ezetimibe in Patients 75 Years or Older". In: *JAMA Cardiology* (Jan. 2020). DOI: 10.1001/jamacardio.2019.5200.

[16] EB Ludmir et al. "Quantifying the Benefit of Non-small-cell lung Cancer Immunotherapy". In: *Lancet* 394.10212 (Nov. 2019), p. 1904. DOI: 10.1016/S0140-6736(19)32503-6.

[17] ZR McCaw and LJ Wei. "P2Y12 Inhibitor Monotherapy vs Dual Antiplatelet Therapy After Percutaneous Coronary Intervention". In: *JAMA* 322.16 (Oct. 2019), p. 1607. DOI: 0.1001/jama.2019.13159.

[18] ZR McCaw, Z Meng, and LJ Wei. "A Shorter Regimen for Rifampin-Resistant Tuberculosis". In: *New England Journal of Medicine* 381.11 (Sept. 2019), e22. DOI: 10.1056/NEJMc1905782.

[19] G Yin and ZR McCaw. "Design of Noninferiority Trials for Hypofractionated vs Conventional Radiotherapy Among Patients With Cancer". In: *JAMA Oncology* (Aug. 2019). DOI: 10.1001/jamaoncol.2019.2391.

[20] ZR McCaw, DH Kim, and LJ Wei. "Analysis of Long-term Benefits of Intensive Blood Pressure Control". In: *JAMA* 322.2 (July 2019), pp. 169–170. DOI: 10.1001/jama.2019.5840.

[21] Z Yang, ZR McCaw, and G Yin. "Caplacizumab for Acquired Thrombotic Thrombocytopenic Purpura". In: *New England Journal of Medicine* 380.18 (May 2019), e32. DOI: 10.1056/NEJMc1902336.

[22] ZR McCaw, LJ Wei, and DH Kim. "Effects of Aspirin in the Healthy Elderly". In: *New England Journal of Medicine* 380.18 (May 2019), pp. 1775–1776. DOI: 10.1056/NEJMc1901774.

[23] ZR McCaw and LJ Wei. "Interpreting the Survival Benefit From Neoadjuvant Chemoradiotherapy Before Surgery for Locally Advanced Squamous Cell Carcinoma of the Esophagus". In: *Journal of Clinical Oncology* (Mar. 2019). DOI: 10.1200/JCO.18.01164.

[24] ZR McCaw, LJ Wei, and DH Kim. "Interpreting the Prognostic Value of Unrecognized Myocardial Infarction Among Older Adults". In: *JAMA Cardiology* (Mar. 2019). DOI: 10.1001/jamacardio.2019.0184.

[25] Z Yang, ZR McCaw, and G Yin. "Radical Surgery or Watchful Waiting in Prostate Cancer". In: *New England Journal of Medicine* 380.11 (Mar. 2019), pp. 1083–1084. DOI: 10.1056/NEJMc1900410.

[26] ZR McCaw, DH Kim, and LJ Wei. "Evaluating Treatment Effect of Transcatheter Interatrial Shunt Device Using Heart Failure Event Rates". In: *JAMA Cardiology* (Feb. 2019). DOI: 10.1001/jamacardio.2019.0001.

[27] ZR McCaw, JL Vassy, and LJ Wei. "Palbociclib and Fulvestrant in Breast Cancer". In: *New England Journal of Medicine* 380.8 (Feb. 2019), p. 796. DOI: 10.1056/NEJMc1816595.

[28] ZR McCaw et al. "Trifluridine/tipiracil in metastatic gastric cancer". In: *Lancet Oncology* 20.1 (Jan. 2019), e8. DOI: 10.1016/S1470-2045(18)30908-2.

[29] ZR McCaw, F Jiang, and LJ Wei. "Trastuzumab Therapy for 9 Weeks vs 1 Year for Human Epidermal Growth Factor Receptor 2-Positive Breast Cancer". In: *JAMA Oncology* (Dec. 2018). DOI: 10.1001/jamaoncol.2018.5730.

[30] ZR McCaw et al. "Interpreting Clinical Benefits of Neoadjuvant Chemoradiation With Gemcitabine Versus Upfront Surgery in Patients With Borderline Resectable Pancreatic Cancer (BRPC)". In: *Annals of Surgery* (Nov. 2018). DOI: 10.1097/SLA.0000000000003115.

[31] ZR McCaw, S Piantadosi, and LJ Wei. "Quantifying the Added Value of Low-Molecular-Weight Heparin to Intermittent Pneumatic Compression for Preventing Venous Thromboembolic Events Under the Risk-Benefit Perspective". In: *JAMA Surgery* (Nov. 2018). DOI: 10.1001/jamasurg.2018.4294.

[32] ZR McCaw, D Liu, and LJ Wei. "Body Composition and Overall Survival in Patients With Nonmetastatic Breast Cancer". In: *JAMA Oncology* (Nov. 2018). DOI: 10.1001/jamaoncol.2018.5290.

[33] ZR McCaw, LJ Wei, and DH Kim. "Gene Expression-Guided Adjuvant Chemotherapy in Breast Cancer". In: *New England Journal of Medicine* 379.17 (Oct. 2018), p. 1681. DOI: 10.1056/NEJMc1810515.

[34] BL Claggett et al. "Sex as a predictor of response to cancer immunotherapy". In: *Lancet Oncology* 19.8 (Aug. 2018), e377. DOI: 10.1016/S1470-2045(18)30517-5.

Professional Activities

- **Peer Review** 2021
  Journals: Circulation – Cardiovascular Quality and Outcomes, Frontiers in Genetics, International Society of Computational Biology
- **Peer Review** 2020
  Journals: International Society of Computational Biology, Statistics in Medicine
- **JSM Section Chair** 07/2019
  Regression Methods for Longitudinal Data
- **JSM Section Chair** 07/2018
  Gene-Gene and Gene-Environment Interactions

Awards and Distinctions

- **Distinguished Student Paper Award** 07/2019
  Joint Statistical Meeting, Section in Genetics and Genomics.
- **Stellar Abstract Award** 11/2018
  Program in Quantitative Genomics
- **Ruth L. Kirschstein National Research Service Award (F31)** 03/2018
  Title: Innovations in Genome Wide Association Testing Inspired by Obstructive Sleep Apnea Phenotypes.
- **Teaching Fellow** 11/2017
  Global Initiative for Neuropsychiatric Genetic Education in Research
- **NIH Pre-Doctoral Training Grant** 08/2016
  Statistical and Quantitative Training in Big Data Health Science
- **NIH Pre-Doctoral Training Grant** 08/2014
  Interdisciplinary Training Grant in Biostatistics and Computational Biology
- **NIH Post-Baccalaureate Research Fellow** 09/2013
  National Institute of Environmental Health Sciences
- **Undergraduate Academic Achievement Award** 04/2013
  UNC Department of Biostatistics
- **Phi Beta Kappa National Honors Society** 11/2011
- **NIH Summer Internship** 05/2011
  National Institute of Environmental Health Sciences 05/2010

Presentations

- **American Society of Human Genetics** 10/2019
  Cross-population Fine-mapping to Identify Shared and Population-specific Causal Effects.
- **Joint Statistical Meeting** 07/2019
  Cross-tissue eQTL Calling via Surrogate Expression Analysis.
- **Program in Quantitative Genomics** 11/2018
  Leveraging the UKB to Empower Association Testing on Scarce Phenotypes.

- **Joint Statistical Meeting** 07/2018
  Leveraging Surrogate Phenotypes to Improve Inference on a Partially Missing Target Phenotype.
- **Joint Statistical Meeting** 07/2017
  Inverse Normal Transformation for Genome Wide Association Testing of Quantitative Traits.
- **American Thoracic Society** 05/2014
  Gene Expression Profiling Predicts Response to Respiratory Syncytial Virus (RSV) in Mice.
- **NIEHS** 07/2011
  Identifying Candidate Susceptibility Genes for Respiratory Syncytial Virus (RSV) Disease Severity.
- **NIEHS** 07/2010
  Characterization of Transcriptional Networks Underlying Tlr4-Mediated Respiratory Syncytial Virus (RSV) Disease in

Predoctoral Experience

Harvard School of Public Health
02/2016 – 05/2019

Graduate Student

- Department: Biostatistics.
- Principal Investigator: Xihong Lin, Ph.D.
- Project 1: Operating characteristics of the rank-based inverse normal transformation for genome-wide association studies of quantitative traits.
- Project 2: Cross-tissue eQTL calling via surrogate expression analysis.
- Project 3: Synthetic surrogate analysis for genetic association testing with a partially missing target outcome.

Broad Institute
07/2016 – 07/2017

Graduate Student

- Department: Computational Methods for Genomics and Epigenomics Lab.
- Principal Investigator: Martin Aryee, Ph.D.
- Project: Identifying differential chromatin boundaries across cell lines.

Dana Farber Cancer Institute
06/2015 – 08/2015

Research Student

- Department: Biostatistics and Computational Biology.
- Principal Investigator: John Quackenbush, Ph.D.
- Project: Network analysis of eQTL.

National Institute of Environmental Health Sciences
Research Student 05/2012 – 08/2014

- Department: Environmental Genetics Group.

- Principal Investigator: Steven Kleeberger, Ph.D.
- Project 1: Identifying genetic signatures of respiratory syncytial virus (RSV) disease susceptibility in mice.
- Project 2: Role of Notch receptors in ozone-induced lung injury.
- Project 3: Mitochondrial determinants of susceptibility to oxidative stress in mice.

UNC Chapel Hill
08/2012 – 12/2012

Undergraduate Research Student

- Department: RNA Folding Bioinformatics Group.
- Principal Investigator: Alain Laederach, Ph.D.
- Project: Quantifying eQTL enrichment of mRNA protein binding sites.

UNC Chapel Hill
08/2010 – 12/2012

Undergraduate Research Student

- Department: Nanoscale Science Research Group.
- Principal Investigator: Michael Falvo, Ph.D.
- Project: Analysis of fibrin clot structure *in vitro*.

Teaching Experience

Harvard University

- Class: Inference II (BST 241) — 02/2019 – 05/2019
  Instructor: Rui Wang, Ph.D.

- Class: Introduction to Biostatistics — 02/2019
  Instructor: Lori Chibnik, Ph.D.
  Location: University of KwaZulu-Natal, Durban, SA

- Class: Multivariate and Longitudinal Analysis (BST 245) — 02/2018 – 05/2018
  Instructor: Sebastien Haneuse, Ph.D.

- Class: Inference I (BST 231) — 02/2017 – 05/2017
  Instructor: Judith Lok, Ph.D.

- Class: Statistical Genetics (BST 227) — 10/2016 – 12/2016
  Instructor: Martin Aryee, Ph.D.

- Class: Computational Biology (STAT 215) — 02/2016 – 05/2016
  Instructor: X. Shirley Liu, Ph.D.

UNC Chapel Hill

- Class: General Chemistry I (CHEM 101) — 08/2012 – 12/2012
  Instructor: Jennifer Krumper, Ph.D.

- Class: Organic Chemistry II (CHEM 262) 08/2011 – 12/2011
  Instructor: Jennifer Krumper, Ph.D.