

Zachary Ryan McCaw

Curriculum Vitae

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Education

Stanford University

01/2021 – 06/2022

GRADUATE CERTIFICATE IN ARTIFICIAL INTELLIGENCE

- COURSEWORK: Computer Vision, Deep Learning, Reinforcement Learning.
- GPA: 4.05 of 4.00.

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.
 - Studied operating characteristics of the rank-based inverse normal transformation for genome-wide association studies of quantitative traits. [25]
 - Developed multivariate regression methodology for leveraging a correlated surrogate outcome to improve inference on a partially missing target outcome. [11, 7]
- ADVISORS: Xihong Lin, Ph.D.
- COMMITTEE: Martin Aryee, Ph.D. and Jeffrey Miller, Ph.D.
- GPA: 3.93 of 4.00.

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; Phi Beta Kappa.

Technical Experience

- **Genetics:** Genome-wide association studies, fine-mapping, Mendelian randomization, polygenic scoring, quantitative trait locus analysis, rare-variant association testing.
- **Machine Learning:** Computer vision, representation learning, survival modeling.
- **Software:** AWS, Git, Python, R, SQL, Tensorflow.
- **Statistics:** Causal inference, longitudinal and multivariate analysis, meta-analysis, regression modeling, survival analysis.

Professional Experience

Insitro

09/2021 – Present

STAFF MACHINE LEARNING SCIENTIST: 04/23 –

- DEPARTMENT: Clinical Machine Learning
- TEAM LEAD: Christopher Probert, Ph.D.
- PROJECTS:
 - Predicted clinical endpoints from histopathology image embeddings.

SENIOR MACHINE LEARNING SCIENTIST: 09/21 – 03/23.

- DEPARTMENT: Statistical Genetics
- TEAM LEAD: Thomas Soare, Ph.D.
- PROJECTS:
 - Developed an allelic series rare-variant test for candidate gene discovery. [1]
 - Identified Parkinson's risk variants using MRI-derived proxy phenotypes.

Google

09/2019 – 09/2021

DATA SCIENTIST

- DEPARTMENT: Health, Genomic Medicine Team.
- SCIENTIFIC AND TEAM LEADS: Babak Alipanahi, Ph.D. and Cory McLean, Ph.D.
- PROJECTS: **Genetic discovery for machine learning derived phenotypes.**
 - Contributed to representation learning for genetic discovery on low-dimensional embeddings (REGLE) [3].
 - Identified genetic variants associated with ML-derived COPD risk ascertained from volumetric flow curves via deep convolutional networks. [5]
 - Developed methodology (DeepNull) to adjust for non-linear covariate effects in GWAS via deep neural networks. [13]
 - Identified genetic variants associated with glaucoma features extracted from retinal fundus images using deep convolutional networks. [18]
 - 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 causal 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 multiple populations allowing for different causal architectures and correlated effect sizes.

Articles

- [1] ZR McCaw et al. “An allelic-series rare-variant association test for candidate-gene discovery”. In: *American Journal of Human Genetics* 110.8 (July 2023), pp. 1330–1342. DOI: [10.1016/j.ajhg.2023.07.001](https://doi.org/10.1016/j.ajhg.2023.07.001).
- [2] X Wang et al. “Using a Clinically Interpretable End Point Composed of Multiple Outcomes to Evaluate Totality of Treatment Effect in Comparative Oncology Studie”. In: *JAMA Network Open* 6.6 (June 2023), e2319055. DOI: [10.1001/jamanetworkopen.2023.19055](https://doi.org/10.1001/jamanetworkopen.2023.19055).
- [3] T Yun et al. “Unsupervised representation learning improves genomic discovery for lung function and respiratory disease prediction”. In: *medRxiv* (Apr. 2023). DOI: [10.1101/2023.04.28.23289285](https://doi.org/10.1101/2023.04.28.23289285).
- [4] PS Jhund et al. “Effect of Dapagliflozin on Total Heart Failure Events in Patients With Heart Failure With Mildly Reduced or Preserved Ejection Fraction: A Prespecified Analysis of the DELIVER Trial”. In: *JAMA Cardiology* (Apr. 2023). DOI: [10.1001/jamacardio.2023.0711](https://doi.org/10.1001/jamacardio.2023.0711).
- [5] J Cosentino et al. “Inference of chronic obstructive pulmonary disease with deep learning on raw spiromograms identifies new genetic loci and improves risk models”. In: *Nature Genetics* (Apr. 2023). DOI: [10.1038/s41588-023-01372-4](https://doi.org/10.1038/s41588-023-01372-4).
- [6] A Das et al. “Assessment of Median and Mean Survival Time in Cancer Clinical Trials”. In: *JAMA Network Open* 6.4 (Apr. 2023), e236498. DOI: [10.1001/jamanetworkopen.2023.6498](https://doi.org/10.1001/jamanetworkopen.2023.6498).
- [7] ZR McCaw et al. “Leveraging a machine learning derived surrogate phenotype to improve power for genome-wide association studies of partially missing phenotypes in population biobanks”. In: *bioRxiv* (Dec. 2022). DOI: [10.1101/2022.12.12.520180](https://doi.org/10.1101/2022.12.12.520180).
- [8] BL Claggett et al. “Quantifying Treatment Effects in Trials with Multiple Event-Time Outcomes”. In: *NEJM Evidence* (June 2022). DOI: [10.1056/EVIDoa2200047](https://doi.org/10.1056/EVIDoa2200047).
- [9] HM Dehbi, A Embleton-Thirsk, and McCaw ZR. “Sample size calculation for randomized selection trials with a time-to-event endpoint and a margin of practical equivalence”. In: *Statistics in Medicine* (June 2022). DOI: [10.1002/sim.9490](https://doi.org/10.1002/sim.9490).
- [10] ZR McCaw, H Julienne, and H Aschard. “Fitting Gaussian mixture models on incomplete data”. In: *BMC Bioinformatics* 23.1 (June 2022), p. 208. DOI: [10.1186/s12859-022-04740-9](https://doi.org/10.1186/s12859-022-04740-9).
- [11] ZR McCaw et al. “Leveraging a surrogate outcome to improve inference on a partially missing target outcome”. In: *Biometrics* (Feb. 2022). DOI: [10.1111/biom.13629](https://doi.org/10.1111/biom.13629).

- [12] ZR McCaw, DH Kim, and LJ Wei. “Pitfall in the Design and Analysis of Comparative Oncology Trials With a Time-to-Event Endpoint and Recommendations”. In: *JNCI Cancer Spectrum* 6.1 (Feb. 2022), pkac007. DOI: [10.1093/jncics/pkac007](https://doi.org/10.1093/jncics/pkac007).
- [13] ZR McCaw et al. “DeepNull: Modeling non-linear covariate effects improves phenotype prediction and association power”. In: *Nature Communications* 13.1 (Jan. 2022), p. 241. DOI: [10.1038/s41467-021-27930-0](https://doi.org/10.1038/s41467-021-27930-0).
- [14] ZR McCaw et al. “Practical Recommendations on Quantifying and Interpreting Treatment Effects in the Presence of Terminal Competing Risks: A Review”. In: *JAMA Cardiology* (Dec. 2021). DOI: [10.1001/jamacardio.2021.4932](https://doi.org/10.1001/jamacardio.2021.4932).
- [15] 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* 40.28 (Dec. 2021), pp. 6235–6242. DOI: [10.1002/sim.8971](https://doi.org/10.1002/sim.8971).
- [16] R Sun et al. “Moving beyond conventional stratified analysis to assess the treatment effect in a comparative oncology study”. In: *Journal for ImmunoTherapy of Cancer* 9.11 (Nov. 2021), e003323. DOI: [10.1136/jitc-2021-003323](https://doi.org/10.1136/jitc-2021-003323).
- [17] H Julienne et al. “Multitrait GWAS to connect disease variants and biological mechanisms”. In: *PLoS Genetics* 17.8 (Aug. 2021), e1009713. DOI: [10.1371/journal.pgen.1009713](https://doi.org/10.1371/journal.pgen.1009713).
- [18] 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](https://doi.org/10.1016/j.ajhg.2021.05.004).
- [19] 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](https://doi.org/10.1016/j.urolonc.2020.12.012).
- [20] 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](https://doi.org/10.1093/cid/ciaa1563).
- [21] 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](https://doi.org/10.1016/j.jchf.2020.07.005).
- [22] 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](https://doi.org/10.1016/j.cct.2020.106145).
- [23] 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](https://doi.org/10.7326/M20-4044).
- [24] 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](https://doi.org/10.7326/M20-0104).

- [25] 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](https://doi.org/10.1111/biom.13214).
- [26] 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](https://doi.org/10.1152/physiolgenomics.00101.2019).
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- [35] 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

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- [2] ZR McCaw, PG Richardson, and LJ Wei. “Assessing the Ability of Long Noncoding RNA Expression to Predict Patient Outcomes in Pediatric AML”. In: *Journal of Clinical Oncology* (June 2023), JCO2300465. DOI: [10.1200/JCO.23.00465](https://doi.org/10.1200/JCO.23.00465).
- [3] TA Lin et al. “Determining the Efficacy of Pembrolizumab in Patients With Previously Treated Advanced Hepatocellular Carcinoma”. In: *Journal of Clinical Oncology* (Apr. 2023). DOI: [10.1200/JCO.23.0007](https://doi.org/10.1200/JCO.23.0007).
- [4] ZR McCaw, EB Ludmir, and LJ Wei. “Assessing the Clinical Utility of Oral Paclitaxel Plus Encequidar Versus Intravenous Paclitaxel in Patients With Metastatic Breast Cancer”. In: *Journal of Clinical Oncology* 41.6 (Feb. 2023), p. 1323. DOI: [10.1200/JCO.22.01759](https://doi.org/10.1200/JCO.22.01759).
- [5] ZR McCaw and LJ Wei. “Clinical Utility Assessment of Gonadotropin-Releasing Hormone Analogs Among Women Younger Than 35 Years”. In: *JAMA Surgery* 8.6 (Apr. 2022), pp. 943–944. DOI: [10.1001/jamaoncol.2022.0488](https://doi.org/10.1001/jamaoncol.2022.0488).
- [6] ZR McCaw and LJ Wei. “Questions About a Risk Prediction Model of Mortality After Esophagectomy for Cancer”. In: *JAMA Surgery* 157.3 (Nov. 2021), pp. 279–280. DOI: [10.1001/jamasurg.2021.5701](https://doi.org/10.1001/jamasurg.2021.5701).
- [7] 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: [10.1001/jama.2021.1700](https://doi.org/10.1001/jama.2021.1700).
- [8] 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: [10.1056/NEJMc2100225](https://doi.org/10.1056/NEJMc2100225).
- [9] ZR McCaw, EB Ludmir, and LJ Wei. “Quantifying the Long-term Survival Benefit of Pembrolizumab for Patients With Advanced Gastric Cancer”. In: *JAMA Oncology* 7.4 (Feb. 2021). DOI: [10.1001/jamaoncol.2020.8002](https://doi.org/10.1001/jamaoncol.2020.8002).
- [10] 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](https://doi.org/10.1161/CIRCULATIONAHA.120.050723).
- [11] RR Patel et al. “Transparency in reporting of phase 3 cancer clinical trial results”. In: *Acta Oncologica* 60.2 (Dec. 2020). DOI: [10.1080/0284186X.2020.1856410](https://doi.org/10.1080/0284186X.2020.1856410).
- [12] 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* 79.1 (Oct. 2020), e10–e11. DOI: [10.1016/j.eururo.2020.09.049](https://doi.org/10.1016/j.eururo.2020.09.049).

- [13] 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).
- [14] ZR McCaw, L Tian, and LJ Wei. “Appropriate Analysis of Duration of Response Data in Cancer Trials”. In: *JAMA Oncology* 6.12 (Oct. 2020), p. 1978. DOI: [10.1001/jamaoncol.2020.4657](https://doi.org/10.1001/jamaoncol.2020.4657).
- [15] 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](https://doi.org/10.1016/S0140-6736(20)31175-2).
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Professional Activities

- **Peer Review** 2023
Journals: Current Cancer Drug Targets, ISCB, RECOMB
- **Peer Review** 2022
Journals: Axioms, ISCB, Life, Statistics in Biopharmaceutical Research, Statistics in Medicine, TEST, Viruses
- **Peer Review** 2021
Journals: Circulation – Cardiovascular Quality and Outcomes, Frontiers in Genetics, ISCB, Statistics in Medicine
- **Peer Review** 2020
Journals: ISCM, Statistics in Medicine
- **JSM Section Chair** 2019
Regression Methods for Longitudinal Data
- **JSM Section Chair** 2018
Gene-Gene and Gene-Environment Interactions

Conference Presentations

- **American Association for Cancer Research** 04/2023
Learned phenotypic embeddings enable scalable imputation of high-content molecular data elucidating prognostic chromatin signatures.
- **American Society of Human Genetics** 10/2022
An allelic series rare variant association test for candidate gene discovery.
- **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.
- **Harvard School of Public Health, 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.
- **National Institute of Environmental Health Sciences** 07/2011
Identifying candidate susceptibility genes for respiratory syncytial virus (RSV) disease severity.
- **National Institute of Environmental Health Sciences** 07/2010
Characterization of transcriptional networks underlying Tlr4-mediated respiratory syncytial virus (RSV) disease in mice.

Awards and Distinctions

- **Distinguished Student Paper Award** 07/2019
Joint Statistical Meeting, Section in Genetics and Genomics.
- **Stellar Abstract Award** 11/2018
Harvard School of Public Health, Program in Quantitative Genomics
- **Ruth L. Kirschstein National Research Service Award (F31)** 03/2018
[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

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, South Africa

- 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.