

# Zachary Ryan McCaw

Curriculum Vitae

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## Education

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### 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. [36]
  - Developed multivariate regression methodology for leveraging a correlated surrogate outcome to improve inference on a partially missing target outcome. [22, 3]
- 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

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

# Professional Experience

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## Insitro

09/2021 – Present

STAFF MACHINE LEARNING SCIENTIST: 04/23 –

- DEPARTMENT: Clinical Machine Learning
- TEAM LEAD: Colm O'Dushlaine, Ph.D.
- PROJECTS:
  - **Machine learning enabled prediction of digital biomarkers from whole slide histopathology images** [9]
  - **Pitfalls in performing genome-wide association studies on ratio traits** [11]

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.** [14]
  - 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) [1].
  - Identified genetic variants associated with ML-derived COPD risk ascertained from volumetric flow curves via deep convolutional networks. [17]
  - Developed methodology (DeepNull) to adjust for non-linear covariate effects in GWAS via deep neural networks. [24]
  - Identified genetic variants associated with glaucoma features extracted from retinal fundus images using deep convolutional networks. [29]
  - 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

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- [1] T Yun et al. “Unsupervised representation learning improves genomic discovery for lung function and respiratory disease prediction”. In: *Nature Genetics* (July 2024). DOI: [10.1038/s41588-024-01831-6](https://doi.org/10.1038/s41588-024-01831-6).
- [2] AD Sherry et al. “Bayesian Interim Analysis and Efficiency of Phase III Randomized Trials”. In: *medRxiv* (June 2024). DOI: [10.1101/2024.06.27.24309608](https://doi.org/10.1101/2024.06.27.24309608).
- [3] ZR McCaw et al. “Synthetic surrogates improve power for genome-wide association studies of partially missing phenotypes in population biobanks”. In: *Nature Genetics* (June 2024). DOI: [10.1038/s41588-024-01793-9](https://doi.org/10.1038/s41588-024-01793-9).
- [4] EJ Hsu et al. “Association of differential censoring with survival and suboptimal control arms among oncology clinical trials”. In: *Journal of the National Cancer Institute* 116.6 (June 2024), pp. 990–994. DOI: [10.1093/jnci/djae028](https://doi.org/10.1093/jnci/djae028).
- [5] J Rossen et al. “MultiSuSiE improves multi-ancestry fine-mapping in All of Us whole-genome sequencing data”. In: *medRxiv* (May 2024). DOI: [10.1101/2024.05.13.24307291](https://doi.org/10.1101/2024.05.13.24307291).
- [6] L Siraj et al. “Functional dissection of complex and molecular trait variants at single nucleotide resolution”. In: *bioRxiv* (May 2024). DOI: [10.1101/2024.05.05.592437](https://doi.org/10.1101/2024.05.05.592437).
- [7] Y Zhou et al. “Utilizing multimodal AI to improve genetic analyses of cardiovascular traits”. In: *medRxiv* (Mar. 2024). DOI: [10.1101/2024.03.19.24304547](https://doi.org/10.1101/2024.03.19.24304547).
- [8] AD Sherry, AW Hahn, ZR McCaw, et al. “Differential Treatment Effects of Subgroup Analyses in Phase 3 Oncology Trials From 2004 to 2020”. In: *JAMA Network Open* 7.3 (Mar. 2024), e243379. DOI: [10.1001/jamanetworkopen.2024.3379](https://doi.org/10.1001/jamanetworkopen.2024.3379).
- [9] ZR McCaw et al. “Machine learning enabled prediction of digital biomarkers from whole slide histopathology images”. In: *medRxiv* (Jan. 2024). DOI: [10.1101/2024.01.06.24300926](https://doi.org/10.1101/2024.01.06.24300926).
- [10] C Angermueller, Z Mariet, B Jester, et al. “High-throughput ML-guided design of diverse single-domain antibodies against SARS-CoV-2”. In: *bioRxiv* (Dec. 2023). DOI: [10.1101/2023.12.01.569227](https://doi.org/10.1101/2023.12.01.569227).
- [11] ZR McCaw et al. “Pitfalls in performing genome-wide association studies on ratio traits”. In: *bioRxiv* (Nov. 2023). DOI: [10.1101/2023.10.27.564385](https://doi.org/10.1101/2023.10.27.564385).
- [12] X Li, H Chen, MS Selvaraj, et al. “A statistical framework for powerful multi-trait rare variant analysis in large-scale whole-genome sequencing studies”. In: *bioRxiv* (Nov. 2023). DOI: [10.1101/2023.10.30.564764](https://doi.org/10.1101/2023.10.30.564764).

- [13] AD Sherry, P Msaouel, ZR McCaw, et al. “Prevalence and implications of significance testing for baseline covariate imbalance in randomised cancer clinical trials: The Table 1 Fallacy”. In: *European Journal of Cancer* 194 (Nov. 2023), p. 113357. DOI: [10.1016/j.ejca.2023.113357](https://doi.org/10.1016/j.ejca.2023.113357).
- [14] 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).
- [15] 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).
- [16] 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).
- [17] J Cosentino et al. “Inference of chronic obstructive pulmonary disease with deep learning on raw spirograms 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).
- [18] 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).
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- [21] BL Claggett et al. “Quantifying Treatment Effects in Trials with Multiple Event-Time Outcomes”. In: *NEJM Evidence* 1.10 (June 2022). DOI: [10.1056/EVIDoa2200047](https://doi.org/10.1056/EVIDoa2200047).
- [22] 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).
- [23] 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).
- [24] 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).
- [25] 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).

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- [34] 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).
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## Correspondence

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- [2] ZR McCaw, L Tian, and LJ Wei. “Evaluating the Duration of Response With Mirvetuximab Soravtansine for Treating Platinum-Resistant Ovarian Cancer”. In: *Journal of Clinical Oncology* (Aug. 2023), JCO2300288. DOI: [10.1200/JCO.23.00288](https://doi.org/10.1200/JCO.23.00288).
- [3] 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).
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## Professional Activities

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- **Peer Review** 2024  
Journals: Bioinformatics, ISCB, Statistics in Medicine
- **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

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- **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

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- **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

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### 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.