

Zachary Ryan McCaw

Curriculum Vitae

[GitHub](#), [LinkedIn](#), [ORCID](#), [Website](#)

zmccaw@alumni.harvard.edu

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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. [46]
 - Developed multivariate regression methodology for leveraging a correlated surrogate outcome to improve inference on a partially missing target outcome. [32, 13]
- 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, rare-variant association testing.
- **Machine Learning:** Computer vision, representation learning, self-supervised learning, clinical endpoint prediction.
- **Software:** AWS, Git, Python, PyTorch, 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: Statistical Genetics and Clinical Machine Learning
- TEAM LEAD: Colm O'Dushlaine, Ph.D.
- PROJECTS:
 - Extending the coding-variant allelic series test to summary statistics.
 - EmbedGEM: a framework to evaluate the utility of embeddings for genetic discovery. [10]
 - Machine learning enabled prediction of digital biomarkers from whole slide histopathology images. [19]
 - Pitfalls in performing genome-wide association studies on ratio traits. [21]

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

- DEPARTMENT: Statistical Genetics
- TEAM LEAD: Thomas Soare, Ph.D.
- PROJECTS:
 - An allelic series rare-variant test for candidate gene discovery. [24]
 - Identification of Parkinson's risk variants using MRI-derived proxy phenotypes.

Google

09/2019 – 09/2021

DATA SCIENTIST

- DEPARTMENT: Health, Genomic Medicine Team.
- TEAM LEADS: Babak Alipanahi, Ph.D. and Cory McLean, Ph.D.
- PROJECTS:
 - Unsupervised representation learning improves genomic discovery for lung function and respiratory disease prediction [9].
 - Inference of chronic obstructive pulmonary disease with deep learning on raw spiromograms identifies new genetic loci and improves risk models [27].
 - DeepNull: Modeling non-linear covariate effects improves phenotype prediction and association power. [34]
 - Large-scale machine learning-based phenotyping significantly improves genomic discovery for optic nerve head morphology. [39]
 - 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 and longitudinal data.

- DEPARTMENT: Medical and Population Genetics.
- PRINCIPAL INVESTIGATOR: Hilary Finucane, Ph.D.
- PROJECT: Cross-population fine-mapping to identify shared and population specific causal effects.

Articles

- [1] AD Sherry et al. “Evidenced-Based Prior for Estimating the Treatment Effect of Phase III Randomized Trials in Oncology”. In: 8 (Oct. 2024), e2400363. DOI: [10.1200/P0.24.00363](https://doi.org/10.1200/P0.24.00363).
- [2] AD Sherry et al. “Increasing Power in Phase III Oncology Trials With Multivariable Regression: An Empirical Assessment of 535 Primary End Point Analyses”. In: *JCO Clinical Cancer Informatics* 8 (Sept. 2024), e2400102. DOI: [10.1200/CCI.24.00102](https://doi.org/10.1200/CCI.24.00102).
- [3] AD Sherry et al. “Off-Protocol Radiation Therapy in Phase 3 Metastatic Solid Tumor Trials”. In: *Int J Radiat Oncol Biol Phys* (Aug. 2024). DOI: [10.1016/j.ijrobp.2024.05.033](https://doi.org/10.1016/j.ijrobp.2024.05.033).
- [4] V Kanwar et al. “Multi-Artifact Detection and Filtering in Digital Pathology Using Intrinsic Image Properties”. In: *2024 IEEE International Symposium on Biomedical Imaging (ISBI)*. Aug. 2024, pp. 1–5. DOI: [10.1109/ISBI56570.2024.10635902](https://doi.org/10.1109/ISBI56570.2024.10635902).
- [5] A Woicik et al. “In Silico Optimization of Tissue Microarray Design for Machine Learning Analysis”. In: *2024 IEEE International Symposium on Biomedical Imaging (ISBI)*. Aug. 2024, pp. 1–5. DOI: [10.1109/ISBI56570.2024.10635208](https://doi.org/10.1109/ISBI56570.2024.10635208).
- [6] AD Sherry et al. “Improving the clinical meaning of surrogate endpoints: An empirical assessment of clinical progression in phase III oncology trials”. In: *International Journal of Cancer* (Aug. 2024). DOI: [10.1002/ijc.35129](https://doi.org/10.1002/ijc.35129).
- [7] TA Lin et al. “Proportional Hazards Violations in Phase 3 Cancer Clinical Trials: A Potential Source of Trial Misinterpretation”. In: *Clinical Cancer Research* (Aug. 2024). DOI: [10.1158/1078-0432.CCR-24-0566](https://doi.org/10.1158/1078-0432.CCR-24-0566).
- [8] AD Sherry et al. “Towards Treatment Effect Interpretability: A Bayesian Re-analysis of 194,129 Patient Outcomes Across 230 Oncology Trials”. In: *medRxiv* (July 2024). DOI: [10.1101/2024.07.23.24310891](https://doi.org/10.1101/2024.07.23.24310891).
- [9] 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).
- [10] S Mukherjee et al. “EmbedGEM: A framework to evaluate the utility of embeddings for genetic discovery”. In: *Bioinformatics Advances* 4.1 (July 2024), vbae135. DOI: [10.1093/bioadv/vbae135](https://doi.org/10.1093/bioadv/vbae135).
- [11] J Gao et al. “A tutorial on fairness in machine learning in healthcare”. In: *arXiv* (June 2024). DOI: [10.48550/arXiv.2406.09307](https://doi.org/10.48550/arXiv.2406.09307).

- [12] 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).
- [13] 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).
- [14] 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).
- [15] 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).
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- [17] 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).
- [18] 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).
- [19] 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).
- [20] 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).
- [21] 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).
- [22] 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).
- [23] 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).
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Correspondence

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Professional Activities

- **Peer Review** 2024
Journals: Bioinformatics, Briefings in Bioinformatics, BMC Medical Research Methodology, ISCB, ISMB, Statistics in Medicine, Stats
- **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** 04/2024
Machine learning enabled prediction of digital biomarkers from whole slide histopathology images.
- **American Society of Human Genetics** 10/2023
Synthetic slope analysis for progression GWAS.
- **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

The University of North Carolina at Chapel Hill 06/2023 – Present
ADJUNCT INSTRUCTOR: 06/23 –

- DEPARTMENT: MPH@UNC
- PROJECTS: Section instructor for SPHG 711, Data Analysis for Public Health.

UNC Chapel Hill

- CLASS: Data Analysis for Public Health (SPHG 711) 08/2024 - 12/2024
COURSE LEAD: Jane Monaco, Dr.P.H.
- CLASS: Data Analysis for Public Health (SPHG 711) 08/2023 - 12/2023
COURSE LEAD: Jane Monaco, Dr.P.H.

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.