

BIOGRAPHICAL SKETCH

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NAME: Ian Wray McKeague

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

POSITION TITLE: 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)	Completion Date MM/YYYY	FIELD OF STUDY
Cambridge University, U.K.	B.A. / M.A.	06/1975	Mathematics
Cambridge University, U.K.	M.Math	06/1976	Mathematics
University of North Carolina at Chapel Hill	Ph.D.	12/1980	Statistics

A. Personal Statement

This project is the logical follow-up to my current R01 grant (GM095722, 2011-2019), for which my expertise is ideally suited. My areas of expertise include post-selection inference, functional data analysis, empirical likelihood methods, survival analysis, competing risks models for HIV/AIDS data, inference for stochastic processes, and Markov chain Monte Carlo. I have also done significant work on simultaneous inference, efficient estimation for semi-parametric models, missing data models, Bayesian statistics, wavelet methods and martingale and counting process methods. I have published over 90 peer-reviewed statistical methodology articles as lead author, including 15 articles in the *Annals of Statistics*, and 10 in the *Journal of the American Statistical Association*. I have been the doctoral advisor of 18 students (most of whom have positions in academia). Lab website: <http://www.columbia.edu/~im2131/> Four papers most relevant to the project:

- a. Huang T.-J., **McKeague I.W.** and Qian M. (2019). Marginal screening for high-dimensional predictors of survival outcomes. In press, *Statistica Sinica*. PMID in process.
- b. **McKeague I.W.** and Qian M. (2015). An adaptive resampling test for detecting the presence of significant predictors. *Journal of the American Statistical Association*. 110(512), 1422-1433. PMID: PMC4826762. *T&M Special Invited Paper for 2015 (with discussants)*.
- c. **McKeague I.W.** and Qian M. (2018). Marginal screening of 2 x 2 tables in large-scale case-control studies. *Biometrics*, 75, 163-171. PMID in process.
- d. Wang H.J., **McKeague I.W.** and Qian M. (2018). Testing for Marginal Linear Effects in Quantile Regression. *Journal of the Royal Statistical Society Series B*. 80(2):433-452. PMID:PMC5863930

B. Positions and Honors**Positions and Employment**

1980-1986	Assistant Professor, Department of Statistics, Florida State University, Tallahassee, FL
1986-1991	Associate Professor, Department of Statistics, Florida State University, Tallahassee, FL
1991-2005	Professor, Department of Statistics, Florida State University, Tallahassee, FL
1996-1999	Chair, Department of Statistics, Florida State University, Tallahassee, FL

2000-2004 Ralph A. Bradley Professor, Department of Statistics, Florida State University, Tallahassee, FL
2004- Professor, Department of Biostatistics, Columbia University, New York, NY

Other Experience and Professional Memberships

1989-1995 Annals of Statistics, Associate Editor
1993-1996 Journal of the American Statistical Association, Associate Editor
1998- Statistical Inference for Stochastic Processes, Associate Editor
1998 Served on NSF Knowledge and Distributed Intelligence Program Screening Panel
2000-2005 ESAIM: Probability and Statistics, Associate Editor
2004 NSF Biocomplexity in the Environment Screening Panel member
2005- International Journal of Biostatistics, Associate Editor
2010- Journal of the American Statistical Association, Associate Editor
2016 NIH/NIAID Review Panel (RFA-AI-15-056) "International Centers of Excellence for Malaria Research (U19)"
2017- Statistical Science, Associate Editor
2020-2023 **Editor**, Journal of the American Statistical Association (T&M Editor Elect in 2020)

NSF Statistics Program Screening Panel, 1997, 1999, 2000, 2002, 2003, 2007, 2009, 2010, 2016.

Member of the American Statistical Association since 1990

Member of the Institute of Mathematical Statistics since 1980

Honors

1995 Fellow of the Institute of Mathematical Statistics
1998 Florida State University Graduate Teaching Award
1999 Florida State University Professorial Excellence Program Award
2000 Florida State University Named Professorship Award
2007 Fellow of the American Statistical Association

C. Contribution to Science

1. **Post-selection inference.** In work funded by my current R01, I published (with Min Qian) a 2015 JASA discussion paper on marginal screening for detecting the presence of significant predictors in high-dimensional regression, which addressed a central problem of post-selection inference. This was the Special Invited JASA paper for the 2015 Joint Statistical Meetings (one paper per year is selected for this honor). Screening large numbers of predictors is a challenging problem due to the non-standard limiting behavior of post-model-selected estimators. We introduced an adaptive resampling test that provides a much more powerful alternative to the popular (yet conservative) Bonferroni method of controlling familywise error rates. Other work in this area has included identifying significant risk factors when screening large numbers of 2×2 tables that cross-classify disease status with each type of exposure (McKeague and Qian, 2018, *Biometrics*), our approach being based on adjusting for complex dependencies between the 2×2 tables and exploiting Monte Carlo simulation from the estimated null distribution of a maximally selected log-odds ratio. Further, in a 2019 *Statistica Sinica* paper with a PhD student (Tzu-Jung Huang) who was jointly advised by Min Qian and myself, we developed a version of the screening test in our JASA paper that applies to right-censored survival outcomes. Also, in a 2018 JRSS-B paper in collaboration with H.J. Wang, we developed a version of that approach for quantile regression.
 - a. **McKeague I.W.** and Qian M. (2018). Marginal screening of 2×2 tables in large-scale case-control studies. *Biometrics*, 75, 163-171. PMID in process.
 - b. Huang T.-J., **McKeague I.W.** and Qian M. (2019). Marginal screening for high-dimensional predictors of survival outcomes. In press, *Statistica Sinica*. PMID in process.
 - c. Wang H.J., **McKeague I.W.** and Qian M. (2018). Testing for Marginal Linear Effects in Quantile Regression. *Journal of the Royal Statistical Society Series B*. 80(2):433-452. PMID:PMC5863930
 - d. **McKeague I.W.** and Qian M. (2015). An adaptive resampling test for detecting the presence of significant predictors. *Journal of the American Statistical Association*. 110(512), 1422-1433. PMID: PMC4826762. *T&M Special Invited Paper for 2015 (with discussants)*.

2. **Survival analysis.** Over the last 30 years I have made many influential contributions to the development of survival analysis, especially in the area of semi-parametric modeling and counting process/martingale methods. Prior to my work on additive risk models, for example, multiplicative hazard models completely dominated research in this area. I introduced efficient methods of estimation for additive risk models of various types, and also for general nonparametric hazard function regression. This has been the starting point for much later research. I have also made contributions to variable selection for survival models, and to cause-specific hazard regression involving continuous marks with applications to data from HIV vaccine efficacy trials. In recent work funded by my current R01, in collaboration with a former PhD student (H.-W. Chang) I have developed empirical likelihood-based tests for stochastic ordering under right censorship, and nonparametric testing for multiple survival functions with applications to non-inferiority testing.
 - a. H.-W.Chang and **I.W. McKeague**. Nonparametric Testing for Multiple Survival Functions with Non-Inferiority Margins. *The Annals of Statistics* 47 205–232 (2019) [with an online supplement of 70 pages.] PMID in process.
 - b. H.-W. Chang and **I. W. McKeague**. Empirical Likelihood Based Tests for Stochastic Ordering under Right Censorship. *Electronic J. Statist.* 10 2511–2536 (2016). PMID in process.
 - c. Sun, Y., Gilbert, P.B., and **McKeague, I.W.** (2009). Proportional hazards models with continuous marks. *The Annals of Statistics*, 37(1): 394-426. PMID: 19838313; PMCID: PMC2762218.
 - d. H.-W. Chang, H. El Barmi and **I.W. McKeague**. Tests for Stochastic Ordering under Biased Sampling. *Journal of Nonparametric Statistics* 28, 659–682 (2016). PMCID: PMC5473665

3. **Empirical likelihood.** Over the last 25 years I have contributed extensively to the development of empirical likelihood methodology through the use of empirical process techniques. Empirical likelihood was originally introduced by Art Owen in around 1990 for the purpose of providing more accurate confidence regions for parameters in estimating equations. I have shown that its scope is much wider than first thought. Particular contributions include expanding the method to provide confidence bands for survival functions and Q-Q plots, validating its use in high-dimensional settings and for estimating equations involving nuisance parameters, adapting it to nonparametric hypothesis testing for establishing stochastic ordering and non-inferiority ordering, and in developing a hybrid combination of empirical and parametric likelihoods. Recently, I have been exploring the use of Stein’s method to understand the large sample behavior of certain empirical processes that arise in connection with foundational questions in quantum mechanics.
 - a. N. Hjort, **I.W. McKeague** and I. Van Keilegom. Hybrid Combinations of Parametric and Empirical Likelihoods. *Statistica Sinica* 28 389-2407 (2018). Special issue in honor of Peter Hall. PMID in process.
 - b. H. El Barmi and **I.W. McKeague**. Testing for Uniform Stochastic Ordering via Empirical Likelihood. *Annals of the Institute of Mathematical Statistics* 68 955–976 (2016). PMCID: PMC5473665.
 - c. **I.W. McKeague** and B. Levin. Convergence of Empirical Distributions in an Interpretation of Quantum Mechanics. *The Annals of Applied Probability* 26 2540–2555 (2016). PMCID: PMC5542025
 - d. **I.W. McKeague**, E. Pekoz and Y. Swan. Stein’s Method and Approximating the Quantum Harmonic Oscillator. *Bernoulli* 25 89-111 (2019). PMID in process.

4. **Functional data analysis and trajectory analysis.** In the last 10 years I have been collaborating with epidemiologists on numerous studies of early determinants of adult health, specifically on the impact of health "trajectories" from gestation through childhood on a range of adult health outcomes. For example, one question of interest is whether there are sensitive periods in childhood during which growth rate influences the incidence of neuropsychological disease. This motivated the development of new methodology to address the challenging statistical issues involved, and in particular a flexible new class of “point impact” functional regression models that can provide information about sensitive growth periods. Further, I have developed a novel method of reconstructing growth velocity trajectories based on sparse longitudinal data with such applications in mind. Another recent contribution to this area (joint with Min Qian, the Co-I on my

current R01) has been a method for estimating personalized treatment policies based on functional data (biosignatures such as brain scans, mass spectrometry or gene expression profiles) with applications to precision medicine.

- a. Lopez-Pintado, S. & **McKeague, I.W.** (2013). Recovering gradients from sparsely observed functional data. *Biometrics*, 69(2): 396-404. PMID: 23409753; PMCID: PMC3718453. R software available at: <http://cran.r-project.org/web/packages/growthrate/>
- b. **McKeague, I.W.** & Qian, M. (2014). Estimation of treatment policies based on functional predictors. *Statistica Sinica*, 24(3): 1461-1485. PMID: 25165416; PMCID: PMC4142446.
- c. **I.W. McKeague**, S. Lopez-Pintado, M. Hallin and M. Siman. Analyzing Growth Trajectories. *Journal of Developmental Origins of Health and Disease* 2 322–329 (2011).
- d. **I. W. McKeague** and B. Sen. Fractals with Point Impact in Functional Linear Regression. *The Annals of Statistics* 38 2559–2586 (2010). PMID: 23785219

5. **Collaborative studies in psychiatric epidemiology.** Over the last 10 years I have contributed extensively as lead biostatistician and co-investigator for the Finnish Prenatal Studies (FiPS), which is a collaboration between Columbia University and Turku University in Finland. The study capitalizes on the Finnish Maternity Cohort, which contains maternal serum specimens drawn on over 2 million pregnancies, and several Finnish national registries including the Hospital and Outpatient Discharge Registry, the Medical Birth Registry, and the Finnish military registry including cognitive performance from mandatory tests administered to male conscriptees. We have successfully linked these registries and identified a large sample of patients with schizophrenia, autism spectrum disorders, bipolar disorder, and other psychiatric diagnoses, and matched controls. We have obtained data on several biomarkers of maternal exposures and comprehensive data on other prenatal, perinatal, and childhood antecedents, including cognitive performance and longitudinal measures of growth. We have published important papers on autism and schizophrenia that capitalized on the application of the novel trajectory analysis methods I have developed (funded by my current R01) to these databases. Further, my expertise in survival analytic methods has also led to success in our studies of maternal exposure to SSRIs and psychiatric outcomes in children based on the Finnish data.

- a. **I.W. McKeague**, A. S. Brown, Y. Bao, S. Hinkka-Yli-Salomaki, J. Huttunen, Sourander, A. Autism with Intellectual Disability Related to Dynamics of Head Circumference Growth during Early Infancy. *Biological Psychiatry* 77 833–840 (2015). PMID: 25444163.
- b. A. S. Brown, D. Gyllenberg, S. Hinkka-Yli-Salomaki, A. Sourander and **I.W. McKeague**. Altered growth trajectory of head circumference during infancy and schizophrenia in a National Birth Cohort. *Schizophr. Res.* 182: 115–119 (2017). PMID 5376228.
- c. Brown, A.S., Cheslack-Postava, K., Rantakokko, P., Kiviranta, H., Hinkka-Yli-Salomaki, S., **McKeague, I.W.**, Surcel, H.-M., and Sourander, A. Association of Maternal Insecticide Levels With Autism in Offspring From a National Birth Cohort. *American Journal of Psychiatry*, (2018). PMID: 30111184. *Nature News & Comment* coverage: <https://www.nature.com/articles/d41586-018-05994-1>
- d. A. S. Brown, D. Gyllenberg, H. Malm, **I.W. McKeague**, S. Hinkka-Yli-Salomaki, M. Artama, M. Gissler, K. Cheslack-Postava, M. M. Weissman, J. A. Gingrich, A. Sourander. Association of Selective Serotonin Reuptake Inhibitor Exposure During Pregnancy With Speech, Scholastic, and Motor Disorders in Offspring. *JAMA Psychiatry* 73(11): 1163–1170 (2016). PMID: 27732704.

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

NIH 2R01 GM095722 (PI: McKeague)

9/1/2011 – 7/31/2019

Post-selection inference and trajectory analysis

Goals: To provide new methods of post-selection inference for detecting the presence of significant predictors in high-dimensional screening of scalar outcomes.

Role: PI

NIH 1R01AG062401 (PI: McKeague)

4/15/2019 – 3/31/2024

Inferential methods for functional data from wearable devices

This project will develop statistical methods for the physiological evaluation of patients on the basis of data collected by inexpensive wearable sensors (e.g., accelerometers).

Role: PI

NIEHS 1R01ES028125 (PI: Brown)

9/1/2017 – 7/31/2022

Prenatal factors in autism and other psychiatric outcomes in a national birth cohort

The goal is extend our investigation on the relationship between environmental factors during pregnancy and the likelihood that the offspring will be diagnosed with autism and other psychiatric outcomes in a large birth cohort in Finland.

Role: PI of subcontract and Co-investigator

DOD AR16007 (PI: Brown)

9/1/2017 – 7/31/2022

Developmental pathways and autism spectrum disorders

To investigate relationships between developmental milestones and biomarkers of inflammation, thyroid function, and smoking and autism spectrum disorder.

Role: Co-investigator

CDC/NCCDPHP U01DP006109 (PI: Bell)

12/1/2016 – 9/29/2020

Male teen pregnancy prevention project

Goals: To evaluate the efficacy of the CAMI-TPP compared to CAMI-Fitness in reducing sexual behaviors that increase the risks of fathering an unintended teen pregnancy by increasing condom use and female partner use of moderately and highly effective reversible contraception.

Role: Co-investigator

R01AG054525 (PI: Cosentino)

08/01/2017 – 04/30/2022

NIH/NIA

Task-specific and person-specific factors related to Subjective Cognitive Decline

The goal of this project is to generate guidelines about how to measure and interpret subjective cognitive decline (SCD), and will set the stage for refining diagnoses of pre-clinical AD.

Role: Co-investigator

Completed Research Support

NSF DMS-1307838 (PI: McKeague)

9/1/2013 – 8/31/2017

Optimal treatment policies and adaptive screening for functional predictors

Goals: This project develops new statistical methodology for assessing the effectiveness of individualized treatment policies based on functional biosignatures. The approach involves specifying the interaction between the treatment and patient profile in terms of a functional regression model, so data from randomized clinical trials can be utilized to simultaneously evaluate the effectiveness of the treatment policies, measured in terms of mean outcome when all patients follow the policy, and to identify features of patient profiles that optimize the interaction effect over competing treatments.

Role: PI

NIH/NICHD R01 HD071180 (Aviv, Factor-Litvak, Susser, Multi-PI)

4/12/2012 – 2/28/2018

Determinants of leukocyte telomere length at birth

Goals: To develop applications of spline fitting and generalized additive models to leukocyte telomere length data on parents and their children.

Role: Co-investigator