CURRICULUM VITAE

MICHAEL R. CRAGER, Ph.D.

EDUCATION

Ph.D. (Statistics), Stanford University, 1982.
M.S. (Statistics), Stanford University, 1980.
B.A. (Mathematics/Computer Science), University of Denver, 1978.

EXPERIENCE

Retired **October 2023**

Exact Sciences Corporation
Senior Fellow, Biostatistics **November 2019 – October 2023**
Present

Genomic Health, Inc.
Senior Fellow, Biostatistics **February 2019 – November 2019**
Fellow, Biostatistics **April 2008 – February 2019**

Provide technical guidance and consulting to the Biostatistics Department in particular and the Research and Development organizations in general. Participate on multidisciplinary teams that evaluate new product opportunities and provide technical review and guidance for Research projects. Develop novel statistical methods as necessary for use in company projects. Assist in the technical development of biostatisticians staff. Develop and maintain rapport with external statistical organizations and groups. Coordinate publications and presentations of statistical methodology developed in-house.

CV Therapeutics, Inc.

Executive Director, Biostatistics **March 2005 – March 2008**
Senior Director, Biostatistics **November 2002 – March 2005**

Direct the activities of the Biostatistics Department. Set policy, procedures and standards for the department. Work with clinical scientists, clinical operations specialists, data management experts and regulatory affairs specialists and project managers to set strategy, plan and execute the clinical development of pharmaceutical products. Assume primary statistical role in preparation of regulatory dossiers and interactions with regulatory agencies. Independently develop statistical methodology appropriate for the analysis of clinical studies utilizing knowledge of regulatory agency statistical guidelines and of the statistical literature.

InterMune, Inc.

Senior Director, Biostatistics **August 2001 – November 2002**

Work with clinical scientists, clinical operations specialists, regulatory affairs specialists and project managers to set strategy, plan and execute the clinical development of biopharmaceutical products. Responsible for all statistical and data management aspects of such programs, including the design, analysis and reporting of clinical trials, preparation of regulatory agency submissions and interactions with regulatory agencies. Work with cross functional teams to select contract research organization and

supervise statistical and data management work on sponsored studies. Supervise a small group of in-house statisticians. Develop policy, procedure and standards for statistical work.

Roche Palo Alto

Director and Site Head, Biometrics **June 1996 – August 2001**

Direct the activities of the Biometrics organization at the Palo Alto site of Roche Pharmaceuticals Drug Development. Biometrics Palo Alto has a staff of approximately 110 professionals in the areas of Biostatistics, Data Management, Pharmacovigilance and Informatics and forms an integral part of the global Biometrics organization. Biometrics staff participate in cross-functional teams dedicated to the worldwide clinical development of new medicinal compounds.

Syntex Research

Director and Clinical Program Team Leader **June 1993 – June 1996**

Direct a global cross-functional team dedicated to clinical drug development of a specific compound from phase I through regulatory approval and marketing support. The clinical program team includes experts in the fields of medicine, pharmacokinetics, statistics, data management, clinical trial conduct, analysis/software development and marketing. The clinical program team supervises a worldwide staff of more than 70, covering all of these functional areas, and organized into study management teams.

Director, Biometry **January 1992 – June 1993**

Direct the Biometry Department of 74 statisticians and statistical programmers supporting all U.S.-based clinical, clinical pharmacology/pharmacokinetic and nonclinical areas of Development Research in the design, analysis and reporting of studies and the submission of regulatory dossiers worldwide.

Department Head, Biometry AIE **August 1991– January 1992**
Research Section Leader **October 1989 – August 1991**
Manager **September 1988 – October 1989**

Manage a group of 17 statisticians and statistical programmers supporting the design, analysis and reporting of clinical trials and the submission of regulatory dossiers worldwide in the antiviral, immunology and endocrinology therapeutic areas.

Biostatistician II **August 1987 – September 1988**

Support Medical and Regulatory Affairs departments staff in the design, analysis and reporting clinical trials and registration activities for cardiovascular compounds.

G. D. Searle and Co.

Senior Biostatistician/Supervisor **April, 1985 – August, 1987**

Support Medical and Regulatory Affairs departments in the design, analysis and reporting of clinical trials and in registration activities in the cardiovascular, gastrointestinal and rheumatoid arthritis therapeutic areas, as well as bioavailability and pharmacokinetic studies.

Senior Biostatistician **October 1982 – April 1985**

Support Biological Research departments in the design, analysis of reporting of nonclinical studies, and preparation and submission of IND's, in the research areas of cardiovascular, antiplatelet, central nervous system therapy, as well as bioavailability and pharmacokinetic studies.

PROFESSIONAL

Member of Pharmaceutical Research and Manufacturers Association (PhRMA) Biostatistics and Data Management Steering Committee 1997–2000. Phi Beta Kappa, B.A. graduation Magna Cum Laude.

PUBLICATIONS: Statistical Methodology

Crager MR (2022). Accounting for propensity score variability in IPTW weighted Cox proportional hazards regression and risk estimation. *American Journal of Applied Mathematics* **10**(5):176–204. doi: 10.11648/j.ajam.20221005.11

Crager MR, Braun JV (2022). Interval estimation of the absolute risk of an event with competing risks using proportional regression of cause-specific hazards. *American Journal of Applied Mathematics* **10**(2):59–85. doi: 10.11648/j.ajam.20221002.15.

Crager MR (2020). Extensions of the absolute standardized hazard ratio and connections with measures of explained variation and variable importance. *Lifetime Data Analysis* **26**:872–892. DOI: 10.1007/s10985-020-09504-2

Janes H, Brown MD, Crager MR, Miller DP, Barlow WE (2017). Adjusting for covariates in evaluating markers for selecting treatment, with application to guiding chemotherapy for treating estrogen-receptor-positive, node-positive breast cancer. *Contemporary Clinical Trials* **63**:30–39. DOI:10.1016/j.cct.2017.08.004

Crager MR, Ahmed M (2014). Separate class true discovery rate degree of association sets for biomarker identification. *Journal of Biopharmaceutical Statistics* **24**:1022–1034. DOI : 10.1080/10543406.2014.925912.

Crager MR, Tang G (2014). Patient-specific meta-analysis for risk assessment using multivariate proportional hazards regression. *Journal of Applied Statistics* **41**:2676–2695. DOI : 10.1080/02664763.2014.925102.

Crager MR (2012). Prospective calculation of identification power for individual genes in analyses controlling the false discovery rate. *Genetic Epidemiology* **36**:839–847. DOI: 10.1002/gepi.21670.

Crager MR (2012). Generalizing the standardized hazard ratio to multivariate proportional hazards regression, with an application to clinical-genomic studies. *Journal of Applied Statistics* **39**:399–417. DOI:10.1080/02664763.2011.594034.

Crager MR (2010). Gene identification using true discovery rate degree of association sets and estimates corrected for regression to the mean. *Statistics in Medicine* **29**:33–45. DOI: 10.1002/sim.3789

Crager M, Reitman M (1990). Running average analysis of clinical trial ambulatory blood pressure data. *Biometrics* **47**:129–138.

Crager MR. (1987). Analysis of covariance in parallel group clinical trials with pretreatment baselines. *Biometrics* **43**:895–901.

PUBLICATIONS: Studies and Clinical Trials

Crager M, Wijayawardana SR, Gruver AM, Blacklock A, Russell C, Baehner FL, Sapunar F (2022). Population-based estimate for the correlation of the Oncotype Dx Breast Recurrence Score® result and Ki-67 IHC MIB-1 pharmDx in HR+, HER2-, node-positive early breast cancer. *Breast Cancer Research* **24**:74. https://doi.org/10.1186/s13058-022-01571-7.

Yothers G, Venook AP, Oki E, Niedzwiecki D, Lin Y, Crager MR, Chao C, Baehner FL, Wolmark N, Yoshino T (2022). Patient-specific meta-analysis of 12-gene colon cancer recurrence score validation studies for recurrence risk assessment after surgery with or without 5FU and oxaliplatin. *Journal of Gastrointestinal Oncology* **13**:126–137. doi: 10.21037/jgo-21-620

Brooks MC, Thomas L, Magi-Galluzzi C, Li J, Crager MR, Lu R, Baehner FL, Abran J, Aboushwareb T, Klein EA (2022). Validating the association of adverse pathology with distant metastasis and prostate cancer mortality 20-years after radical prostatectomy. *Urologic Oncology* **40**(3):104.e1-104.e7. https://doi.org/10.1016/j.urolonc.2021.10.005

Brooks MC, Thomas L, Magi-Galluzzi C, Li J, Crager MR, Lu R, Abran J, Aboushwareb T, Klein EA (2021). GPS assay association with long-term cancer outcomes: twenty-year risk of distant metastasis and prostate cancer–specific mortality. *JCO Precision Oncology*. https://doi.org/10.1200/PO.20.00325

Sparano JA, Crager MR, Tang G, Gray RJ, Stemmer SM, Shak S (2020). Development and validation of a tool integrating the 21-gene recurrence score and clinical-pathological features to individualize prognosis and prediction of chemotherapy benefit in early breast cancer. *Journal of Clinical Oncology* **39**:557-564. DOI https://doi.org/10.1200/JCO.20.03007.

Geyer CE, Tang G, Mamounas EP, Rastogi P, Paik S, Shak S, Baehner FL, Crager M, Wickerham DL, Costantino JP, Wolmark (2018). *npj Breast Cancer* **4** article 37. DOI 10.1038/s41523-018-0090-6

Rakovitch E, Gray R, Baehner FL, Sutradhar R, Crager M, Gu S, Nofech_Mozes S, Badve SS, Hanna W, Hughes LL, Wood WC, Davidson NE, Paszat L, Shak S, Sparano JA, Solin LJ (2018). Refined estimates of local recurrence risks by DCIS score adjusting for clinicopathological features: a combined analysis of ECOG-ACRIN E5194 and Ontario DCIS cohort studies. *Breast Cancer Research and Treatment* **169**:359-369. DOI 10.1007/s10549-018-4693-2

Brand TC, Zhang N, Crager MR, Maddala T, Dee A, Sesterhenn IA, Simko JP, Cooperberg MR, Srivastava S, Chane JM, Febbo PG, Carroll PR, Cullen J, Lawrence HJ (2016). Patient-specific meta-analysis of 2 clinical validation studies to predict pathologic outcomes in prostate cancer using the 17-gene Genomic Prostate Score. *Urology* **89**:69-75. DOI:10.1016/j.urology.2015.12.008

Sinicropi D, Qu K, Collin F, Crager M, Liu ML, Pelham RJ, Pho M, Dei Rossi A, Jeong J, Scott A, Ambannavar R, Zheng C, Mena R, Esteban J, Stephans J, Morlan J, Baker J (2012). Whole transcriptome RNA-seq analysis of breast cancer recurrence risk using formalin-fixed paraffin-embedded tumor tissue. *PLoS One* **7**(7): e40092. DOI:10.1371/journal.pone.0040092

Tang G, Cuzick J, Costantino JP, Dowsett M, Forbes JF, Crager M, Mamounas RP, Shak S, Wolmark N (2011). Risk of recurrence and chemotherapy benefit for patients with node-negative, estrogen receptor-positive breast cancer: recurrence score alone and integrated with pathologic and clinical factors. *Journal of Clinical Oncology* **29**:4365-4372. DOI: 10.1200/JCO.2011.35.3714.

Koren M, Crager M, Sweeney M (2007). Long-term safety of a novel antianginal agent in patients with severe chronic stable angina: the ranolazine open label experience (ROLE). *Journal of the American College of Cardiology.* **49**:1027–1034.

Rich MR, Crager M, McKay CR (2007). Safety and efficacy of extended-release ranolazine in patients aged 70 years or older with chronic stable angina pectoris. *American Journal of Geriatric Cardiology* **16**:216-221.

Timmis A, Chaitman B, Crager M (2006). Effects of ranolazine on exercise tolerance and HbA1c in patients with chronic angina and diabetes. *European Heart Journal* **27**:24–48.

Spector S, Hsia K, Crager M, Pilcher M, Cabral S, Stempien MJ (1999). Cytomegalovirus (CMV) DNA load is an independent predictor of CMV disease and survival in advanced AIDS. *Journal of Virology* **73**:7027–7030.

Spector S, Weingeist T, Pollard R, Dietric D, Samo T, Benson C, Busch D, Freeman W, Montague P, Kaplan N, Kellerman L, Crager M, De Armond B, Buhles W, Feinberg J, the NIAID AIDS Clinical Trials Group and Syntex CMV Cooperative Study Group (1993). A randomized, controlled study of intravenous ganciclovir therapy for peripheral retinitis in patients with AIDS. *Journal of Infectious Diseases* **168**:557–563.

Roth S, Agrawal N, Mahowald M, Montoya H, Robbins D, Miller S, Nutting E, Woods E, Crager M, Nissen C, *et al* (1989). Misoprostol heals gastroduodenal injury in patients with rheumatoid arthritis receiving aspiring. *Archives of Internal Medicine* **149**:775–779.

Haigler H, Cahill L, Crager M, Charles E (1987). Met-enkephalin, age and anatomy: a microiontophoretic study in the hippocampus. *Life Sciences* **40**:203–213.

Haigler H, Cahill L, Crager M, Charles E (1985). Acetylcholine, aging and anatomy: differential effects in the hippocampus. *Brain Research* **362**:157–160.

PRESENTATIONS

Crager MR. Risk stratification and risk assessment using tumor biomarkers. Presented at the FDA/AdvaMed Medical Device Statistics Issues Conference, 12 May 2021.

Jakubowski D, Crager MR. Joint propensity scores for the analysis of real-world data with biomarker driven treatment selection. Presented at the Bay Area Biotech-Pharma Statistics Workshop, 8 November 2019, Foster City, CA.

Crager MR, Zhang N, Maddala T. Patient-specific meta-analysis with application to a genomic prostate cancer diagnostic. Presented at the Joint Statistical Meetings, 13 August 2015, Seattle, WA.

Crager M. Separate class true discovery rate degree of association sets for biomarker identification. Presented at the FDA-Industry Statistics Workshop, 17 September 2013, Washington, DC.

Crager M. Prospective calculation of identification power for individual genes in analyses controlling the false discovery rate. Presented at the ASA San Francisco Bay Area Chapter Biostatistics Symposium, 1 June 2013, Stanford University.

Crager M. Gene identification using true discovery rate degree of association sets and estimates corrected for regression to the mean. Presented at the Joint Statistical Meetings, 2 August 2011, Miami, Florida.

Crager M, Tang G, Shak S. Using the 21-gene recurrence score (RS) and the recently developed recurrence score-pathology-clinical (RSPC) to assess recurrence risk in node-negative, ER-positive early stage breast cancer patients receiving aromatase inhibitor treatment alone. Poster presentation at the Annual Meeting of the American Society of Clinical Oncology, 6 June 2011, Chicago, Illinois.

Crager M. Gene identification using true discovery rate degree of association sets and estimates corrected for regression to the mean. Presented at the ASA San Francisco Bay Area Chapter Statistical Genomics, Genetics, and Proteomics Symposium, 14 May 2011, Hayward, California.

Crager M. Gene identification using true discovery rate degree of association sets and estimates corrected for regression to the mean. Presented at the Stanford Workshop in Biostatistics, 31 March 2011, Stanford University, Palo Alto, California.

Crager M. Statistical, ethical and confidentiality issues in the analysis of genetic data in clinical trials. Presented at the Pharmaceutical Research and Manufacturers Biostatistics and Data Management Workshop, 8–10 November 1999, Washington D.C.

Crager M. An easy to use, low tech, low cost tool for immediate on-screen access to clinical data. Presented at the PMA Clinical Data Managers Group 1992 Annual Meeting, 20–23 September 1992, Kansas City, Missouri.

Crager M. What is clinical trial data quality? Presented at the Pharmaceutical Manufacturers Association Clinical Data Managers Group Quality Assurance Forum, 5 December 1991, Washington, D.C.

Crager M and Barker C. Emerging principles of clinical trial data quality management. Presented at the Pharmaceutical Manufacturers Association Joint Meeting of the Biostatistics and Clinical Data Management Subsections, 7 October 1991, Alexandria, Virginia.