

UNC BIOSTATISTICIANS MAKE THE NUMBERS ADD UP IN BIOMEDICAL RESEARCH

Since the department was established in 1949, UNC biostatisticians have been on the cutting edge of applying statistical analysis to health care issues. They laid the groundwork for collecting and analyzing biomedical data and revolutionizing the structure of modern clinical trials. (See page 16.) Φ The momentum of that early work has only increased, as new faculty members have teamed up with veterans, expanding and enhancing the science. Φ In these subsequent pages and throughout this entire issue of *Carolina Public Health*, we illustrate the department's accomplishments by highlighting select examples of work done by both legendary and up-and-coming faculty members. Read on to learn more! \blacktriangleright

When **DR. JAMES E. GRIZZLE** succeeded Bernard Greenberg as chair in 1973, he was set to lead the largest biostatistics department in the world, as measured by the size of the faculty and number of students taught. In the late 1960s and early '70s, more students had received master's and doctoral degrees in the UNC department than at any other institution.

Grizzle had earned a master's degree in animal science from Virginia Polytechnic Institute, where he became curious about genetics and animal breeding. Those interests led him in 1956 to N.C. State University and the doctor of philosophy program in experimental studies. In 1957, he took a job as research assistant in the Department of Biostatistics, then a joint endeavor of N.C. State and UNC-Chapel Hill, with classes being taught on both campuses.

His talents caught the eye of then-chair Greenberg, who invited Grizzle to join the UNC faculty in 1960. Grizzle's research focused on collaborative clinical studies of leukemia and duodenal ulcer and on the development of multivariate statistical methods. In 1971, he was named statistical coordinator for a nine-year study, funded by the National Heart and Lung Institute, to examine abnormalities of blood fats. In March 1984, the results of this first major clinical trial were published, showing that people can reduce their risk of heart disease by lowering their cholesterol levels. (See page 22.)

Grizzle served in an editorial capacity for four journals, including *Journal of the American Statistical Association* (associate



Dr. James E. Grizzle

editor) and *Journal of Chronic Diseases* (advisory board). His tenure as president of the Eastern North American Region of the International Biometric Society makes him one of four UNC faculty who have attained that honor. (Others include Drs. Bernard Greenberg, Gary Koch and Lisa LaVange.)

Now retired, Grizzle lives in Chapel Hill, N.C. The department established the James E. Grizzle Distinguished Alumnus Award in his honor, to recognize UNC biostatistics graduates with outstanding records in the development of new statistical methodologies and the application of statistical methods to important public health challenges.



A native of New York City, **DR. BARRY MARGOLIN** graduated summa cum laude from City College of New York in 1963 and quickly acquired graduate degrees from Harvard University—a master's in 1964 and doctor of philosophy in 1967.

His stellar academic performance was rewarded with a position on the Yale University faculty, where he served from 1967 to 1977 as assistant and associate professor and, for two years, as director of graduate studies in statistics.

From 1977 to 1987, he worked as a mathematical statistician at the National Institute of Environmental Health Sciences in Research Triangle Park, N.C., and was head of the Institute's statistical methodology section. During this time, he also was an adjunct professor of statistics at UNC.

In 1987, Margolin joined the UNC biostatistics faculty as professor and chair. His research specialty was the statistical design and analysis of experiments, particularly studies in genetic toxicology.

He is a fellow of the American Statistical Association and a member of the Environmental Mutagen Society, the Gentoxicity and Environmental Mutagen Society, the Institute of Mathematical Statistics and the International Statistical Institute.

Margolin served as associate editor of the *Journal of the American Statistical Association* and the *Annals of Mathematical Statistics* and as statistical editor for *Environmental Mutagenesis*. Among his many honors were



Dr. Barry Margolin

the American Statistical Association's Snedecor Award and the National Institutes of Health Director's Award.

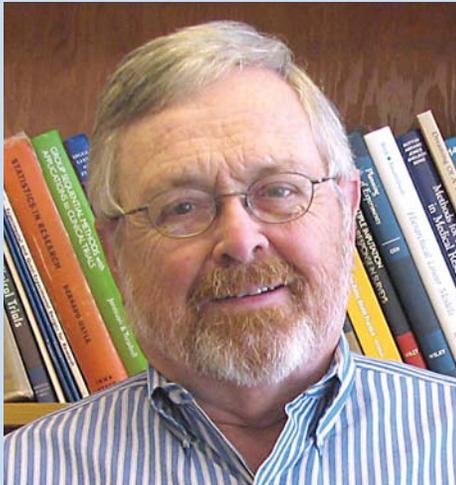
In 1989, Margolin became director of the biostatistics facility at the UNC Lineberger Comprehensive Cancer Center. He retired from UNC-Chapel Hill in 1999 as professor and chair of the Department of Biostatistics and continues to live in Chapel Hill, N.C.



DR. CLARENCE E. (ED) DAVIS, research professor of biostatistics at UNC, is well known for his research and teaching in the areas of clinical trials and cardiovascular disease epidemiology.

He has directed studies of heart disease in Russia, Poland, China and Pakistan and was the primary biostatistician for the Lipid Research Clinics clinical trial—one of the first trials to show that lowering blood cholesterol reduces the risk of heart disease. (See page 22.) He teaches a clinical trials course at UNC and has taught similar courses in more than 15 countries. As part of a ten-year collaboration between the UNC Gillings School of Global Public Health and the University of Chile at Santiago, Davis teaches an annual two-week course in Chile about public health research. (Read more at www.sph.unc.edu/school_news/chile2008.)

Davis has been on the UNC Department of Biostatistics faculty since 1972, including his service as director of the Collaborative Studies Coordinating Center (1991–1997) and as interim chair and chair of the department (1997–2005). In addition to his faculty



Dr. Clarence (Ed) Davis

responsibilities, Davis makes himself available for biostatistical consultation with grant writers at the School. Since accurate sampling and analysis are critical to successful proposal development, Davis offers advice about study design, sample size and data analysis.

In 1970, Davis received his doctorate in statistics from North Carolina State University, with a minor in public health from the University of North Carolina. He was on the faculty of the University of Florida for three years prior to coming to UNC.

He has published more than 100 peer-reviewed papers concerning both theoretical and applied methods of conducting clinical trials and epidemiologic studies. A fellow of the American Heart Association and the American Statistical Association, he also has served on the editorial board of the *American Journal of Epidemiology*.



DR. MICHAEL R. KOSOROK, professor and chair of the UNC Department of Biostatistics since 2006, has published more than 80 peer-reviewed papers related to clinical trials, cystic fibrosis epidemiology, and applications of empirical processes and semiparametric methods in biostatistics. Kosorok also holds a joint appointment as professor of statistics and operations research in UNC's College of Arts and Sciences.

His research has included being senior statistician on a large randomized trial which led to a change in national policy favoring nationwide newborn screening for cystic fibrosis.

Kosorok has developed methods for using surrogate and multiple outcomes to increase cost-effectiveness of clinical trials. His work in empirical processes and semiparametric inference has led to foundational theory for improved data analysis in genetics, clinical trials, and epidemiological studies, as well as a book on the subject, published by Springer. He has directed or co-directed 20 doctoral students.

Kosorok has chaired the Data Safety Monitoring Committee for the intramural program of the National Institute of Child Health and Human Development. He is also an associate editor of the prestigious *Annals of Statistics* and an elected fellow of both the American Statistical Association and the Institute of Mathematical Statistics.

Kosorok received his doctorate in biostatistics from the University of Washington in 1991 and was a member of the faculty at the University of Wisconsin-Madison from 1992 through 2006. He holds both bachelor's and master's degrees in music composition, as well as master's degrees in both statistics and biostatistics. He recently composed a new work for full orchestra, "A Singular Continuity," which premiered with the Chapel Hill High School Orchestra on Dec. 4, 2007, in Chapel Hill, N.C. His daughter, Jessica, who graduated from Chapel Hill High School this spring, played violin in the orchestra.

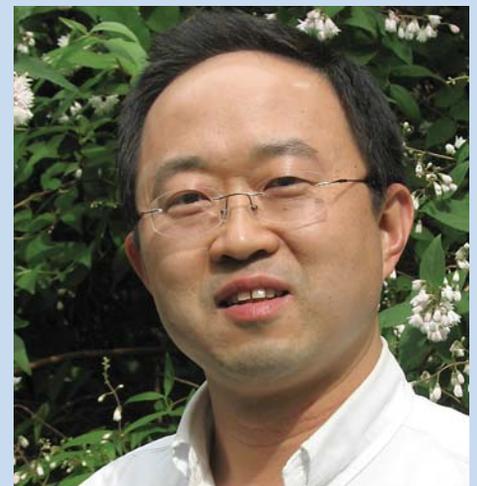
"The piece was composed entirely during weekends and took several months to complete," Kosorok says.



Dr. Michael R. Kosorok



DR. DANYU LIN, Dennis Gillings Distinguished Professor of Biostatistics at UNC, is an internationally recognized leader in survival analysis and statistical genetics. His work has transformed the ways that clinical and epidemiological data are analyzed. Lin's research is focused on developing statistical methods for the design and analysis of medical and public health studies. Several of his methods have been incorporated into commercial software packages (including SAS, S-Plus and STATA) and are widely used in practice.



Dr. Danyu Lin

Lin is on Thomson ISI's list of Highly Cited Researchers in Mathematics—a distinct honor. Thomson ISI (founded as the Institute for Scientific Information) determines inclusion on the list by indexing the world's scholarly literature from a wide range of subjects and collecting citation references from millions of articles over the past 40 years.

Lin's research has been funded continuously for more than 15 years by the National Institutes of Health (NIH). In fact, one of Lin's NIH grants was converted to the prestigious MERIT (Method to Extend Research in Time) Award in 2005. MERIT Awards provide long-term support to investigators with outstanding records of scientific achievement in research areas of special importance or promise.

Lin has been an author on more than 120 peer-reviewed publications, most in premier statistical and genetic journals. Since 1999, he has served as an associate editor of *Biometrika*.

In 1999, Lin received the prestigious Mortimer Spiegelman Gold Medal from the American Public Health Association for outstanding contributions to biostatistics. He was elected a fellow of the Institute of Mathematical Statistics in 1999 and of the American Statistical Association in 2000.

After earning a doctorate from the University of Michigan in 1989, Lin attended a year-long postdoctoral training program at Harvard University before joining the faculty of the University of Washington's Department of Biostatistics. There, he was promoted to tenured associate professor (1994) and professor (1998). He joined the UNC biostatistics faculty in 2001.



DR. JOSEPH IBRAHIM is Alumni Distinguished Professor of biostatistics at UNC's Gillings School of Global Public Health and director of the Biostatistics and Data Management Core at UNC's Lineberger Comprehensive Cancer Center.

Ibrahim is principal investigator for two National Institutes of Health (NIH) grants to develop statistical methodology related to cancer and genomics research. He is biostatistical core leader for an NIH Specialized Program of Research Excellence—or SPORE—grant in gastrointestinal cancers. With funding from NIH's National Institute of Environmental Health Sciences, he also directs the Biostatistics and Data Management Core for a program project to study the systems biology of melanoma. Both projects are housed at the Lineberger Comprehensive Cancer Center.

Ibrahim's areas of research focus are Bayesian inference, missing data problems and genomics. Bayesian methods are gaining popularity in clinical trials because they provide sound mathematical tools for analyzing data about a problem while taking into account information from previous studies. (See page 16.)

With more than 15 years' experience working in cancer clinical trials, Ibrahim directs the UNC Center for Innovative Clinical Trials—one of eight Gillings Innovation Labs funded by a gift to the School from Dr. Dennis and Joan Gillings (see page 29). He is also director of graduate

studies in UNC's Department of Biostatistics and program director of the department's cancer genomics training grant.

Ibrahim has directed or co-directed 15 doctoral students and five postdoctoral fellows. He has served on several national committees and study sections, including as current chair of the American Statistical Association's section on Bayesian statistical science. He is a regular member of NIH's biostatistical methods and research design study section.

Ibrahim received his doctorate in statistics from the University of Minnesota in 1988. He has published more than 160 research papers, most in top statistical journals. He also has published two advanced graduate-level books on Bayesian survival analysis and Monte Carlo methods in Bayesian computation and has served as associate editor for several statistical journals.



Dr. Joseph Ibrahim

Ibrahim is an elected fellow of the American Statistical Association and the Institute of Mathematical Statistics and an elected member of the International Statistical Institute.



DR. JIANWEN CAI, professor and associate chair of the UNC Department of Biostatistics, joined the School's faculty in 1992 after earning a doctorate in biostatistics from the University of Washington. She served as interim chair of the department in 2006.

Cai's research interests include cardiovas-



Dr. Jianwen Cai

cular disease, obesity, dental research and statistical methodologies in clinical trials. She has developed ways to design and analyze biomedical studies to make them more cost-effective. Her collaborative work with Dr. June Stevens, professor and chair of the School's Department of Nutrition, examined the impact of age on optimal body weight and was published in the Jan. 1, 1998, issue of the *New England Journal of Medicine*. Cai has also developed statistical methods for analyzing multivariate failure time and recurrent event data. These methods are important to identify risk factors and interventions for diseases which occur repeatedly, including asthma attacks, diarrheal episodes and recurrent hospitalizations related to certain medical conditions.

Cai has been principal investigator for four National Institutes of Health (NIH) grants, has served as a member of NIH review panels and study sessions and is a member of the NIH Heart Failure Network.

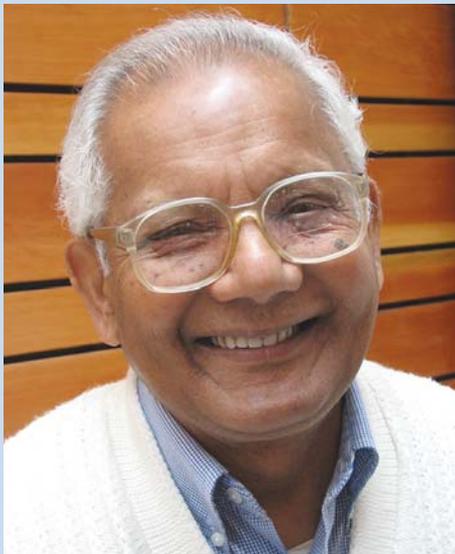
Author of more than 100 peer-reviewed publications in statistical and biomedical journals, Cai currently serves as associate editor for *Biometrics* and *Lifetime Data Analysis*. She is an elected member of the Eastern North American Regional Committee of the International Biometric Society (2007–2009), an elected fellow of the American Statistical Association (ASA), and treasurer/secretary of the ASA biometrics section (2007–2008).

In addition to her research and administrative acumen, Cai is a respected educator. She was the 2004 recipient of the School's Award for Excellence in Teaching.



DR. PRANAB K. SEN, a native of India, first came to UNC in 1965 as a visiting assistant professor of biostatistics at UNC-Chapel Hill. Since 1982, he has served as Cary C. Boshamer Distinguished Professor of biostatistics at the School. He is also professor of statistics and operations research in UNC's College of Arts and Sciences.

Sen has contributed significantly to methodological studies related to diabetes, environmental health and bioinformatics as well as clinical trials. His theoretical research includes a broad spectrum of multivariate, sequential and time-sequential nonparametrics and asymptotic methods. His application-oriented research interests cover nonparametrics in bioassay, multivariate and longitudinal data models and time-sequential analysis.



Dr. Pranab K. Sen

He is one of the most published authors worldwide in the field of (bio-) statistics methodology. Sen has been an author on more than 600 publications in premier journals, co-authored 11 advanced monographs and texts in statistical science, co-edited 11 other volumes, and served on editorial boards of leading journals. He was a founding editor of the statistics journals *Sequential Analysis* and *Statistics and Decisions*. In 2008, the Institute of Mathematical Statistics published a monograph titled *Beyond Parametrics in Interdisciplinary Research: Festschrift in Honor of Professor Pranab K. Sen* to honor

Sen's work. Currently, Sen is editor-in-chief of *Sankhya*, the Indian journal of statistics.

Sen has been recognized with numerous awards throughout his career. He won the Senior Noether Award from the American Statistical Association in 2002, the Commemoration Medal in Mathematics and Physics in 1998, and the UNC School of Public Health's McGavran Award for Excellence in Teaching in 1996, among others.

Sen was Platinum Jubilee lecturer at the Indian Statistical Institute in 2007 and a 1983 lecturer in statistics sponsored by the National Science Foundation's Conference Board of the Mathematical Sciences at the University of Iowa. He is an elected fellow of the Institute of Mathematical Statistics and the American Statistical Association.

Sen earned a Bachelor of Science, Master of Science and doctorate—all in statistics—from Calcutta University. In his leisure, he enjoys reading and writing poetry, in English as well as in his native Bengali.



DR. LAWRENCE L. KUPPER, Alumni Distinguished Professor of biostatistics at UNC, received his PhD in statistics from UNC-Chapel Hill in 1970 and joined the faculty of UNC's Department of Biostatistics that same year.

Kupper's research interests concern the development and application of innovative statistical methods for design and data analysis of public health studies, with specific emphasis on environmental, occupational and women's health. Kupper's work has led to improved statistical methods for quantifying human health risks due to exposure to harmful substances present in the workplace and in the ambient environment.

He has been an author on more than 150 peer-reviewed publications in premier journals and has co-authored three textbooks: *Applied Regression Analysis and Other Multivariable Methods* (four editions), *Epidemiologic Research: Principles and Quantitative Methods* and *Quantitative Exposure Assessment*. His applied regression textbook has been adopted for use by nearly 100 universities nationally and internationally.

In 1971, Kupper was instrumental in



Dr. Lawrence L. Kupper

beginning a training grant in environmental biostatistics funded by the National Institute of Environmental Health Sciences (NIEHS). He served as the grant's program director from 1972 through 2006. The grant currently is funded through June 2011. It annually supports 20 predoctoral and eight postdoctoral students—the largest number of pre- and postdoctoral trainees supported by any NIEHS training grant.

Kupper has won numerous teaching and mentoring awards, including two university-wide awards at UNC-Chapel Hill—the 2007 UNC Mentor Award for Lifetime Achievement in Teaching and Mentoring, and the 1996 UNC Distinguished Teaching Award for Post-Baccalaureate Instruction. He also has been recognized with three UNC School of Public Health awards—the 2003 John E. Larsh Jr. Award for Mentorship; the 1990 Bernard G. Greenberg Alumni Endowment Award; and the 1985 McGavran Award for Excellence in Teaching. In 1986, Kupper was elected a fellow of the American Statistical Association (ASA). He received the Distinguished Achievement Medal from the ASA's Section on Statistics and the Environment in 1995.

Kupper also was a member of the UNC Appointments, Promotions and Tenure (APT) Committee from 2003 through 2007 and chaired the committee during the 2006-2007 academic year. The committee reports to the UNC-Chapel Hill provost concerning all tenure-related appointment and promotion decisions on the UNC-Chapel Hill campus. ■

DR. FRED A. WRIGHT has a doctorate in statistics from the University of Chicago. He held faculty positions at the University of California-San Diego and Ohio State University before taking the position of associate professor with UNC's Department of Biostatistics in 2002. He also directs the Carolina Environmental Bioinformatics Center. Wright is currently researching methods to handle gene expression and activity data, map disease genes in high-density genome scans and control errors in multiple testing.



DR. HAIBO ZHOU has a doctorate in statistics from the University of Washington. He worked as a statistician at the National Institute of Environmental Health Sciences before taking the position of professor with UNC's Department of Biostatistics in 1997. He is also the director of the Biostatistics Core at UNC's Center for Environmental Medicine, Asthma and Lung Biology. Zhou's areas of expertise include statistical methods in outcome-dependent sampling, measurement error problems, survival analysis, toxicology risk assessment and translational research.



DR. JASON FINE has a Doctor of Science degree in biostatistics from Harvard University. He worked as a statistician at the Dana Farber Cancer Institute and the University of Massachusetts Medical Center before taking the position of professor at the University of Wisconsin-Madison's (UW-M) Department of Statistics and Department of

Biostatistics and Medical Informatics as well as becoming a member of UW-M's Comprehensive Cancer Center. He joined UNC's Department of Biostatistics in 2007. Fine's areas of expertise include time-to-event data analysis, statistical genetics, diagnostic imaging methodology, and semi-parametric modeling.



DR. DONGLIN ZENG has a doctorate in statistics from the University of Michigan at Ann Arbor. He joined UNC's Department of Biostatistics in 2001 and was promoted to associate professor in 2007. Zeng's research interests include medical diagnostics, statistical methods for medical imaging, and applications of empirical processes and semi-parametric methods in biostatistics.



DR. AMY HERRING has a doctorate in biostatistics from Harvard University. She is an associate professor with UNC's Department of Biostatistics. Herring has served as principal investigator on four projects funded by the National Institutes of Health and the Environmental Protection Agency. Her research in missing data, latent variables and longitudinal analysis has been motivated by her interest in reproductive and environmental epidemiology, maternal and child health and nutrition.



HONGTU ZHU has a doctorate in statistics from the Chinese University of Hong Kong. He was a postdoctoral associate at Yale University from 2001 to 2003 and has been on the faculty at Columbia University. He also worked as a research scientist at the New York State Psychiatric Institute before taking the position of associate professor with UNC's Department of Biostatistics. His research interests include statistics as applicable to psychiatry, psychometrics, and the applications of statistical methods in the analysis of magnetic resonance imaging (MRI) data.



Other accomplished current faculty members of the UNC Biostatistics Department are:

Richard Bilsborrow
Shrikant Bangdiwala
Diane Catellier
Haitao Chu
David Couper
Rosalie Dominik
Lloyd Edwards
Mayetri Gupta
Robert Hamer
Michael Hudgens
Anastasia Ivanova
Ethan Lange
Steve Marron
Jane Monaco
Andrew Nobel
John Preisser
Bahjat Qaqish
Katherine Roggenkamp
Todd Schwartz
Richard Smith
Paul Stewart
Chirayath Suchindran
Wei Sun
Young Truong
Fei Zou