TRACY L. NOLEN

Summary of Professional Experience

Tracy Nolen is a senior research statistician in the Center for Clinical Research Network Coordination (CRNC) at RTI International. In this capacity, she provides statistical support for studies, including those conducted by the TB Alliance and by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Neonatal Research Network (NRN) and Pelvic Floor Disorder Network (PFDN). Dr. Nolen joined RTI in early 2009 after serving for 6 years at Rho Federal Systems Division, Inc., where she was a biostatistical function leader and study statistician for multiple statistical and clinical coordinating centers funded by the National Institute of Allergy and Infectious Diseases (NIAID) that supported research in infectious, autoimmune, and immune system diseases. She specializes in the design, set-up, and operation of clinical trials, as well as the analysis and reporting of clinical trial data. Dr. Nolen has experience in operational aspects of clinical trials, including proposal writing, coordinating center set-up, project management, site auditing and monitoring, clinical study report creation, and Data Safety and Monitoring Board (DSMB) reporting. Her statistical experience includes randomization-based causal inference, exploration of alternative study designs, including Bayesian designs, adaptive dose finding designs and adaptive randomization algorithms. Dr. Nolen's experience also includes the use of various statistical methods (e.g., regression analysis, including generalized linear models; longitudinal data analysis, including generalized estimating equation (GEE) and mixed models; survival analysis; nonparametric analysis; dose-proportionality analysis). Therapeutic areas in which Dr. Nolen has provided statistical support in clinical trials include infectious diseases, focusing on bacteriology and mycology, autoimmune diseases (including lupus, multiple sclerosis, and ulcerative colitis), endocrinology (including diabetes), cardiovascular disease (and stroke), autism, urinary incontinence, and orthopedics. Dr. Nolen received her doctorate of public health in biostatistics at the University of North Carolina at Chapel Hill's Gillings School of Global Public Health in 2012. She earned her master's degree in statistics from North Carolina State University in 2003. Her dissertation work focused on development of randomization-based approaches for assessing causal effects of vaccines on post-infection outcomes.

Education

DrPH, Biostatistics, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, Chapel Hill, NC, 2012.
MStat, Statistics, North Carolina State University, Raleigh, NC, 2003.
BS, Statistics, North Carolina State University, Raleigh, NC, 2002.

Selected Project Experience

TB Alliance (2012 to date)—*Statistical Supervisor*. Provides study development support and oversight of analytic activities for studies conducted by the TB Alliance that are supported by RTI.

Pelvic Floor Disorder Network (PFDN) (2011 to date)—*Statistician*. The NICHD–funded multicenter network conducts studies to improve the condition of women with pelvic floor disorders, including incontinence and pelvic organ prolapse. For this project, provides statistical support for protocol design,

study implementation, and data collection and for data analysis. Assists primary authors with developing presentations and manuscripts.

Neonatal Research Network (NRN) (2009 to date)—*Statistician*. Conducts statistical analysis of data resulting from multiprotocol, multicenter studies of low-birthweight babies and the interventions used to treat them. Statistical methods include longitudinal data analysis and mixed-effects models. Assists primary authors with the analyses required for presentations at professional meetings and publications.

Obstetric-Fetal Pharmacology Research Units Network (2010 to 2013)—*Statistician*. Provided oversight of data monitoring committee tasks, including statistical analyses, report creation, and administrative activities.

Center for HIV-AIDS Vaccine Immunology (2010 to 2012)—*Statistician*. Conducted statistical analysis of data resulting from this multiprotocol, multicenter study of HIV vaccine development and design. Statistical methods included exponential decay modeling, semiparametric Markov modeling, and longitudinal data analysis. Assisted primary authors with preparing abstracts for professional meetings and with conducting analyses for their manuscripts.

Walter Reed Army Institutes of Research (2009 to 2010)—*Statistician*. Participated in protocol development, study design, and statistical analysis of data resulting from observational and randomized controlled studies of infectious diseases. Statistical methods included survival analysis, generalized linear models, and nonparametric regression analysis. Assisted primary authors with preparing abstracts for professional meetings and with conducting analyses for their manuscripts.

Immune Tolerance Network (ITN) Statistical and Data Coordinating Center (2008 to 2009)—*Biostatistical Functional Leader and Study Statistician*. Rho Inc. functioned as the coordinating center for the ITN, which was a clinical research consortium with the goal of developing new treatments for diseases of the immune system. Specific areas of focus include the prevention of organ transplant rejection, autoimmune diseases, and the prevention and treatment of allergies and asthma. As biostatistical functional leader, was responsible for managing and coordination team of study statisticians, facilitating transition of coordinating center from previous contract research organizations (CRO), and developing guidance and process documents. As study statistician, was responsible for designing and conducting appropriate statistical analyses, creating study status and DSMB reports, and providing data summaries to regulatory staff to complete investigational new drug (IND) annual reports for multiple studies.

Mycology Study Group (MSG) Statistical Support (2007 to 2009)—*Study Statistician.* Rho Inc. provided statistical support for the Mycology Study Group, which conducted clinical trials related to serious fungal infections in high-risk populations. As study statistician for a randomized study of caspofungin prophylaxis followed by preemptive therapy for invasive candidiasis in the ICU, responsible for providing recommendations on appropriate statistical analyses, designing halting rules for safety, and writing DSMB reports.

Bacteriology and Mycology Biostatistics and Operations Unit (BAMBU) (2005 to 2008)—*Study Statistician*. Rho Inc. functioned as the coordinating center for the Bacteriology and Mycology Study Group (BAMSG), which developed clinical interventions designed to address serious fungal and health care–associated resistant bacterial infections in specific high-risk populations. These populations comprise patients with, or at risk of, serious fungal infections as a result of anticancer chemotherapy, HIV infection, or immunosuppression for cellular or solid organ transplantation; non-immunocompromised patients with, or at risk for, serious health care–associated or endemic fungal infections; and patients with, or at risk of, serious health care–associated resistant bacterial infections, including those in intensive care settings. As study statistician, responsible for designing appropriate statistical analyses and participating

in collecting, managing, cleaning, and reporting the data from multiple studies and numerous sites. Performed analyses and authored DSMB, status, and clinical study reports; scientific papers and presentations. Participated in site training, monitoring, and auditing as well as the development of systems for subject registration and randomization, standard operating procedures, tracking systems, and document templates. Collaborated with clinical operations staff to ensure appropriate safety oversight and with regulatory staff to complete IND annual reports.

Statistical and Clinical Coordinating Center for Autoimmune Disease Clinical Trials (SACCC-ADCT) (2007 to 2009)—*Study Statistician*. Rho functioned as the coordinating center for the Autoimmunity Centers of Excellence (ACE) and the Autoimmune Diseases Transplantation Consortium. SACCC provided scientific collaboration and operational support in developing clinical and mechanistic studies in the area of autoimmune disorders. ACE studies ranged from small single-site Phase I studies to larger multicenter Phase II and Phase III studies. As study statistician, participated in protocol development, design of statistical analyses, status report creation, statistical analyses, and preparation of clinical study reports.

Professional Experience

2009 to date — RTI International, Research Triangle Park, NC.

Senior Research Statistician 1 (2012 to date). Supervises and mentors a team of statisticians. Collaborates with investigators to design, conduct, analyze, and interpret results of studies conducted within networks supported by statistical and data coordinating centers located at RTI. Provides oversight of all DSMB activities for the OPRU Network and serves as a DSMB member for the MSG. Coauthors abstracts and manuscripts for presentations at national conferences and publications in peer-reviewed journals.

Research Statistician 3 (2009 to 2012). Was responsible for the design, conduct, and analysis of studies supported by statistical and data coordinating centers located at RTI. Participated in review and selection of electronic data capture system and development of quality assurance standard operating procedures for the conduct of U.S. Food and Drug Administration–regulated clinical trials. Developed training modules and conducted training sessions on topics such as marginal structural models and adaptive study designs.

2003 to 2009 — Rho, Inc., Chapel Hill, NC.

Team Lead, Biostatistics (2007 to 2009). Supervised and provided statistical guidance to team of two graduate research associates, three biostatisticians, and one senior biostatistician. As functional leader for the ITN coordinating center, managed an additional nine statisticians. Designed and conducted analyses, including adaptive dose-finding designs and conditional power analyses. Prepared clinical study reports, manuscripts, and presentations of study results. Developed training modules and conducted training sessions on topics including the clinical trial process, presentation skills, and a Bayesian study design.

Senior Biostatistics (2005 to 2007). Served as the study or DSMB reporting statistician for Phase II–IV clinical trials and pre-clinical studies. Participated in protocol and case report form development, created monthly DSMB and study status reports, and worked with study management teams and sites to improve

data quality. Trained investigators and study coordinators at meetings in United States and in Thailand on studies and trained graduate research associates and biostatisticians on Rho's processes.

Biostatistics (2003 to 2005). Conducted statistical analyses, including logistic regression, survival analysis, dose proportionality analysis, and non-parametric tests. Wrote analysis plans and associated specifications and developed an analysis plan template. Created programs for statistical analyses, data sets, and displays. Aided in creation of web-based system for expedited data review.

Honors and Awards

RTI President's Award, 2013
Kupper Dissertation Publication Award, University of North Carolina at Chapel Hill, May 2012
Distinguished Student Paper Award, ENAR, May 2011
Rho Inc. Presidential Awards, 2004 and 2007
Phi Kappa Phi, Phi Beta Kappa, Mu Sigma Rho, and Golden Key Honor Societies
National Science Foundation Vertical Integration of Research and Education in the Mathematical Sciences (VIGRE) recipient, January 2002 to May 2003
Recipient of Outstanding Presenter Award at Undergraduate Research Symposium, May 2002
Recipient of NCSU Statistics Research and Leadership Awards, May 2002
NCSU Statistics Honor Program
NCSU Statistics Club, President, August 2001 to May 2002

Professional Associations

Member, Society for Clinical Trials

Special Courses

Society for Clinical Data Management (SCDM) CDISC/CDASH Tutorial, October 2009
University of Pennsylvania Annual Conference on Statistical Issues in Clinical Trials: From Bench to Bedside to Community, April 2008
Society for Clinical Trials (SCT) Biomarker Terminology and Technology and Use of Biomarkers in Clinical Trial Design and Analyses Workshop, May 2008
Bayesian Analysis Workshop, University of North Carolina at Chapel Hill, May 2007
SCT Adaptive Design Workshop, May 2007
SAS Output Delivery System for Data Analysts and Statisticians, March 2005
SCT Recruitment and Retention Strategies Workshop, May 2005
Advanced Topics in the SAS Macro Language, February 2004
SCT Quality of Life Measures and Analyses Workshop, May 2004

Computer Skills

SAS (IML, MACRO, GRAPH), S-Plus/R, StatXact, Stata, C++, and MS Word, Excel, and PowerPoint

Languages

Japanese (basic written and spoken)

Peer-Reviewed Journal Articles

Nolen, T. L., Hudgens, M. G., Sen, P. K., & Koch, G. G. (in press). Analysis of repeated low-dose challenge studies. *Statistics in Medicine*.

Brubaker, L., Nager, C. W., Richter, H. E., Weidner, A. C., Hsu, Y., Wai, C. Y., Paraiso, M. R., Nolen, T. L., et al., & Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Pelvic Floor Disorders Network (PFDN). (2014). Effectiveness of blinding: sham suprapubic incisions in a randomized trial of retropubic midurethral sling in women undergoing vaginal prolapse surgery. *American Journal of Obstetrics and Gynecology, 211*(5), e1–e7.

Jelovsek, E. J., Chagin, K., Brubaker, L., Rogers, R. G., Richter, H. E., Arya, L., Barber, M. D., Shepherd, J. P., Nolen, T. L., et al. (2014). A model for predicting the risk of de novo stress urinary incontinence in women undergoing pelvic organ prolapse surgery. *Obstetrics and Gynecology, 123*(2 Pt. 1), 279–287.

Randolph, D. A., Nolen, T. L., Ambalavanan, N., Carlo, W. A., Peralta-Carcelen, M., Das, A., et al., & Generic Database and Follow-Up Subcommittees for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. (2014). Outcomes of extremely low birthweight infants with acidosis at birth. *Archives of Disease in Childhood Fetal and Neonatal Edition, 99*(4), F263–F268.

Phelps, D. L., Ward, R., Williams, R. L., Watterberg, K. L., Laptook, A. R., Wrage, L. A., Nolen, T. L., et al. (2013). Pharmacokinetics and safety of a single intravenous dose of myo-inositol in preterm infants of 23–29 wk. *Pediatric Research, 74*(6), 721–729.

Londhe, V. A., Nolen, T. L., Das, A., Higgins, R. D., Tyson, J. E., Oh, W., & Devaskar, S. U. (2013). Vitamin A supplementation in extremely low birth weight infants: Subgroup analysis in SGA infants. *American Journal of Perinatology, 30*(9), 771–780.

Lowe, J., Nolen, T. L., Vohr, B., Adams-Chapman, I., Duncan, A., & Watterberg, K. (2013). Effect of primary language on developmental testing in children born extremely preterm. *Acta Paediatrica, 102*(9), 896–900.

Yates, N. L., Stacey, A. R., Nolen, T. L., Vandergrift, N., Moody, M. A., Montefiori, D. C., et al. (2013). HIV-1 gp41 envelope IgA is frequently elicited after transmission but has an initial short half-life. *Mucosal Immunology, 6*(4), 692–703.

Visco, A. G., Brubaker, L., Richter, H. E., Nygaard, I., Paraiso, M. R., Menefee, S. A., Schaffer, J., Lowder, J., Khandwala, S., Sirls, L., Spino, C., Nolen, T. L., et al. (2012). Anticholinergic therapy vs. Onabotulinumtoxin A for urgency urinary incontinence. *New England Journal of Medicine, 367*, 1803–1813.

Duncan, A., Watterberg, K., Nolen, T. L., Vohr, B. R., Adams-Chapman, I., Das, A., & Lowe, J. (2012). Effect of ethnicity and race on cognitive and language testing at 18–22 months in extremely preterm infants. *The Journal of Pediatrics, 160*(6), 966–971.

Lai, L., Kwa, S., Kozlowski, P. A., Montefiori, D. C., Nolen, T. L., Hudgens, M. G., Johnson, W. E., Ferrari, G., Hirsch, V. M., Felber, B. K., Pavlakis, G. N., Earl, P. L., Moss, B., Amara, R. R., & Robinson, H. L. (2012). SIVmac239 MVA vaccine with and without a DNA prime, similar prevention of infection by a repeated dose SIVsmE660 challenge despite different immune responses. *Vaccine, 30*(9), 1737–1745.

Yates, N. L., Lucas, J., Nolen, T. L., Vandergrift, N., Soderberg, K., Seaton, K., Denny, T., Haynes, B., Cohen, M., & Tomaras, G. D. (2011). Multiple HIV-1 specific IgG3 responses decline during acute HIV-1: Implications for detection of incident HIV infection. *AIDS, 25*(17), 2089–2097.

Anekthananon, T., Manosuthi, W., Chetchotisakd, P., Kiertiburanakul, S., Supparatpinyo, K., Ratanasuwan, W., Pappas, P. G., Filler, S. G., Kopetskie, H., Nolen, T. L., Kendrick, A., & Larsen, R. (2011). Predictors of poor clinical outcome of cryptococcal meningitis in HIV-infected patients. *International Journal of STD and AIDS, 22*(11), 665–670.

Nolen, T. L., & Hudgens, M. G. (2011). Randomization-based inference within principal strata. *Journal of the American Statistical Association, 106*(494), 581–593.

Manosuthi, W., Chetchotisakd, P., Nolen, T. L., Wallace, D., Sungkanuparph, S., Anekthananon, T., et al. (2010). Monitoring and impact of fluconazole serum and cerebrospinal fluid concentration in HIV-associated cryptococcal meningitis infected patients. *HIV Medicine, 11*(4), 276–281.

Zimmer, L., Nolen, T. L., Pramanpol, S., Wallace, D., Walker, M. E., Pappas, P. G., et al. (2010). International collaboration between US and Thailand on a clinical trial of treatment for HIV-associated cryptococcal meningitis. *Contemporary Clinical Trials, 31,* 34–43.

Manosuthi, W., Sungkanuparph, S., Anekthananon, T., Supparatpinyo, K., Nolen, T. L., Zimmer, L. O., et al., for the BAMSG 3-01 Study Team. (2009). Effect of high-dose fluconazole on QT interval in patients with human immunodeficiency virus (HIV)-associated cryptococcal meningitis. *International Journal of Antimicrobial Agents,* 34(5), 494–496.

Sungkanuparph, S., Filler, S. G., Chetchotisakd, P., Pappas, P., Nolen, T. L., Manosuthi, W. et al. (2009). Cryptococcal immune reconstitution inflammatory syndrome after antiretroviral therapy in AIDS patients with cryptococcal meningitis: A prospective multicenter study. *Clinical Infectious Diseases, 49*(6), 931–934.

Pappas, P. G., Chetchotisakd, P., Larsen, R., Manosuthi, W., Morris, M., Anekthananon, T. et al. (2009). A phase II randomized trial of amphotericin b alone or combined with fluconazole in the treatment of HIV-associated cryptococcal meningitis. *Clinical Infectious Diseases, 48*(12), 1775–1783.

Nolen, T., Dimmick, B., Ostrosky-Zeichner, L., Kendrick, A., Sable, C., Ngai, A., et al. (2009). A web-based endpoint adjudication system for interim analyses in clinical trials. *Clinical Trials, 6*, 60–66.

Feng, J., Lurati, L., Ouyang, H., Robinson [Nolen], T., Wang, Y., Yuan, S., et al. (2003). Predictive toxicology: Benchmarking molecular descriptors and statistical methods. *Journal of Chemical Information and Computer Sciences,* ASAP Article.

Presentations and Proceedings

Wilson, K. A., Whitworth, R. E., Hollingsworth, C. R., Pickett, J. W., Nolen, T. L., & Wallace, D. D. (2014, May). *Best practices and lessons learned in transitioning a large data coordinating center*. Presented at Society for Clinical Trials Annual Meeting, Philadelphia, PA.

Wilson, K. A., Whitworth, R. E., Pickett, J. W., Hollingsworth, C. R., Nolen, T., Huitema, C. M., & Wallace, D. (2013, September). *Operational and data quality considerations in the transition of a large data coordinating center*. Poster presented at the annual conference of the Society of Clinical Research Associates , New Orleans, LA.

Phelps, D., Watterberg, K., Nolen, T. L., Ward, R., & Inositol Subcommittee. (2012, April). *Inositol serum concentrations and safety in a daily dose ranging study for extremely preterm infants*. Poster presented at the annual meeting of the Pediatric Academic Societies, Boston, MA.

Londhe, V. A., Nolen, T. L., Higgins, R., Tyson, J. E., Oh, W., & Devaskar, S. U. (2011, May). *Vitamin A supplementation for extremely low birth weight infants: Subgroup analysis in SGA infants*. Poster presented at the joint meeting of the Pediatric Academic Societies and Asian Society for Pediatric Research, Denver, CO.

Zollner, G., Brambilla, D., Nolen, T., & Lim, C. (2010, October). *Effect of insecticide-treated bed nets on the feeding behavior of sand flies in the laboratory.* Accepted for presentation at the annual U.S. Army Conference on Applied Statistics, Cary, NC.

Lowe, J., Duncan, A., Nolen, T. L., Vohr, B. R., Adams-Chapman, I., Watterberg, K., & NICHD Neonatal Research Network. (2010, May). *Effect of ethnicity/race on cognitive and language testing at 18-22 months in extremely low birth weight infants.* Presented at the annual meeting of the Pediatric Academic Societies, Vancouver, BC, Canada.

Manosuthi, W., Sungkanuparph, S., Anekthananon, T., Supparatpinyo, K., Nolen, T., Wallace, D., et al., & BAMSG 3-01 Study Team. (2009, February). *Serum and cerebrospinal fluid (CSF) concentration monitoring for high dose fluconazole (FLU) in HIV-associated cryptococcal meningitis (CM) infected patients.* Poster presented at the Conference on Retroviruses and Opportunistic Infections**,** Montreal, Canada.

Manosuthi, W., Sungkanuparph, S., Anekthananon, T., Supparatpinyo, K., Nolen, T. L., Zimmer, L., et al. (2008, October). *Effect of high-dose fluconazole on QT interval in HIV-associated cryptococcal meningitis infected patients*. Poster presented at 46th annual meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy/Infectious Disease Society of America, Washington, DC.

Nolen, T., Eggleston, B., Wallace, D., & Pappas, P. (2008, May). *Combining mortality, mycological and neurological measures for a study in the treatment of acquired immune deficiency syndrome associated cryptococcal meningitis*. Poster presented at the annual meeting of the Society for Clinical Trials, St. Louis, MO.

Pappas, P., Nolen, T., Chetchotisakd, P., Larsen, R., Manosuthi, W., Filler, S., & BAMSG 3-01 Study Team. (2007, September). *Fluconazole plus amphotericin b versus amb alone for primary treatment of AIDS-associated cryptococcal meningitis: Results of a phase II trial*. Presented at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, IL.

Ostrosky-Zeichner, L., Sobel, J., Pappas, P., Shoham, S., Barron, M., Nolen, T., et al. (2007, September). *Pilot study of risk-based caspofungin (CFG) prophylaxis in the ICU: Lessons from a multicenter, randomized, double blind trial and insights into diagnostic performance of surrogate markers*. Poster presented at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, IL.

Nolen, T., Wallace, D., Zimmer, L., & Pappas, P. (2007, May). *A Bayesian approach to a phase III study in the treatment of acquired immune deficiency syndrome associated cryptococcal meningitis*. Poster presented at the annual meeting of the Society for Clinical Trials, Montreal, Canada.

Kendrick, A., Nolen, T., Zimmer, L., & Wallace, D. (2007, May). *Trials and their tribulations: The importance of reality checks when planning a clinical trial*. Poster presented at the annual meeting of the Society for Clinical Trials, Montreal, Canada.

Nolen, T., Dimmick, B., Kendrick, A., Wallace, D., & Ostrosky-Zeichner, L. (2005, May). *Web application for expedited data review*. Poster presented at the annual meeting of the Society for Clinical Trials, Portland, OR.

Robinson [Nolen], T., Zimmer, L., Rosanbalm, S., & Wallace, D. (2004, May). *Design issues of an international study in the treatment of acquired immune deficiency syndrome associated cryptococcal meningitis*. Poster presented at the annual meeting of the Society for Clinical Trials, New Orleans, LA.

Feng, J., Lurati, L., Ouyang, H., Robinson [Nolen], T., Wang, Y., Yuan, S., et al. (2002, August). *Predictive toxicology: An examination of statistical methods and molecular descriptors.* Presented at the Industrial Mathematics Modeling Workshop, North Carolina State University, Raleigh, NC.

Robinson [Nolen], T. (2002, May). *Predicting ground level ozone using Atlanta ozone precursor data.* PowerPoint presentation at Research Triangle Institute Exposure Luncheon Club Meeting, Research Triangle Park, NC.

Robinson [Nolen], T. (2002, May). *Saving the earth by reducing ground level ozone*. (2002, April). Poster presented at the Undergraduate Research Symposium of North Carolina State University; and PowerPoint presentation at the North Carolina Ambient Air Data Analysis Colloquium, 2nd annual informal review of North Carolina air quality data, Raleigh, NC.

Stidham, S., Gallins, P., & Robinson [Nolen], T. (2002, January). *An examination of the Atlanta and Charlotte ozone data*. Briefing for Environment Canada via conference call.