## BIOGRAPHICAL SKETCH

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NAME: David Schoenfeld

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

POSITION TITLE: Biostatistician, MGH Biostatistics Ctr, MGH; Professor of Medicine, Harvard Medical School

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 |
|---|---|---|---|
| Reed College, Portland, Oregon | BA | 05/1967 | Mathematics |
| Univ. of Oregon, Eugene, Oregon | MA | 06/1968 | Mathematics |
| Univ. of Oregon, Eugene, Oregon | PhD | 05/1974 | Mathematics-Statistics |
| Stanford University Medical School | Post doc. | 05/1975 | Biostatistics |

### A. Personal Statement

I am a Biostatistician at Massachusetts General Hospital and a Professor of Medicine at Harvard Medical School, and a Professor in the Department of Biostatistics at the Harvard School of Public Health. I have provided statistical support for investigators conducting clinical and laboratory research for more than 30 years. I am the principal investigator for the Clinical Coordination Center for the PETAL Network, which represents over 30 hospitals and conducts multi-center clinical trials on Acute Respiratory Distress Syndrome. I am a fellow of the American Statistical Association and have numerous papers in the statistical literature. I developed the first omnibus goodness of fit test for the proportional hazards regression model, a model that is used extensively in clinical trials that have survival or time to progression as an endpoint. I also developed widely used graphical techniques for this model. I have worked closely with different investigators on design and monitoring of biostatistics for preclinical and clinical trials and have provided input into the statistical components of the proposed studies..

1. Nathan DM, Kuenen J, Borg R, Zheng H, Schoenfeld D, Heine RJ, For the A1c-Derived Average Glucose (ADAG) Study Group. Translating the A1C assay into estimated average glucose values. Diabetes Care. 2008 Aug; 31(8):1-6.
2. Zheng H, Nathan DM, Schoenfeld DA. Using A Multi-Level B-Spline Model to Analyze and Compare Patient Glucose Profiles Based on Continuous Monitoring Data. Diabetes Technology and Therapeutics. 2011 Jun; 13(6):675-682.
3. Faustman DL, Wang L, Okubo Y, Burger D, Ban L, Man G, Zheng H, Schoenfeld D, Pompei R, Avruch J, Nathan DM. Proof of concept, randomized, controlled clinical trial of bacillus calmette guerin for treatment of long term Type 1 diabetes. PLoS One. 2012 Aug; 7(8): e41756
4. Paganoni S, Hyman T, Shui A, Allred P, Harms M, Liu J, Maragakis N, Schoenfeld D, Yu H, Atassi N, Cudkowicz M, Miller TM. Pre-morbid type 2 diabetes mellitus is not a prognostic factor in amyotrophic lateral sclerosis. Muscle Nerve. 2015 Sep;52(3):339-43. doi: 10.1002/mus.24688. Epub 2015 Jun 1. PMCID: PMC4536144

### B. Positions and Honors

**Positions and Employment**

1975–1977 Research Assistant Professor, State University of New York at Buffalo

| | |
|---|---|
| 1977–1981 | Assistant Scientist, Dana-Farber Cancer Institute, Boston, MA |
| 1977–1981 | Assistant Professor, Department of Biostatistics, Harvard School of Public Health |
| 1981–1986 | Associate Professor of Biostatistics, Dana-Farber Cancer Institute, Boston, MA |
| 1981–1998 | Associate Professor in the Department of Biostatistics, Harvard School of Public Health |
| 1984–2004 | Associate Biostatistician, Massachusetts General Hospital, Boston, MA |
| 1985–1998 | Associate Professor of Biostatistics in the Department of Medicine, Harvard Medical School |
| 1985– | Director of the Massachusetts General Hospital Biostatistics Center |
| 1998– | Professor of Medicine, Harvard Medical School, Boston MA |
| 1999– | Professor, Department of Biostatistics, Harvard School of Public Health, Boston, MA |

**Honors/Appointments**

| | |
|---|---|
| 1991 | Elected Member of International Statistical Institute |
| 1991 | Fellow of the American Statistical Association |
| 2004–2007 | Member of Food and Drug Administration Pulmonary-Allergy Advisory Committee |

## C. Contributions to Science

1. **Goodness of Fit to the Proportional Hazards Model**

   I developed statistical and graphical methods for evaluating how well the proportional hazards regression model (Cox model) fits a given set of data. The proportional hazards model is the most common model used for analyzing the effect of covariates and treatment on a possibly censored time to an event. My paper on residuals for the proportional hazards model has received over 1300 citations and is one of the 100 most cited papers in a major biostatistics journal.

   a. Schoenfeld D. Partial residuals for the proportional hazards regression model. Biometrika. 1982; 69:239-241.
   b. Schoenfeld D. Chi-squared goodness of fit tests for the proportional hazard regression model. Biometrika. 1980; 67:145-153.

2. **Power and sample size for clinical trials**

   I have made extensive contributions to the literature on how to calculate sample sizes for clinical trials. These include formulae for the sample size of the proportional hazards model, the log-rank test and of pilot studies. In addition I developed a web-site for sample size calculation that was visited over 52,000 times in 2013.

   a. Schoenfeld D. Sample size formulae for the proportional hazards regression model. Biometrics. 1983; 39:499-503.
   b. Schoenfeld D. The asymptotic properties of non-parametric tests for comparing survival distributions. Biometrika. 1981; 68:316-319.
   c. Schoenfeld DA and Borenstein M. Calculating the power or sample size for the logistic and proportional hazards models. J Stat Computation and Simulation. 2005; 75(10): 771-85. Sample Size Software: http://hedwig.mgh.harvard.edu/biostatistics/tools/software/sample-size

3. **Clinical Trial Design**

   I have been involved in cooperative groups in Cancer, AIDS, ARDS (Acute Respiratory Distress Syndrome), and ALS(Amyotrophic lateral sclerosis). In each of these area's I have made major contributions to how to design and analyze studies for these diseases. In cancer I developed methods for pilot studies in radiation therapy. In AIDS, I was a lead author, along with David Byar, of a position paper on clinical trial design in AIDS, as well as editing a book on the same subject. I was the principal investigator of the clinical and statistical coordinating center for the ARDS network and am currently the principal investigator of the Clinical Coordinator Center for the NHLBI Prevention and Early Treatment of Acute Lung Injury (PETAL) network.

   a. Schoenfeld D. Statistical considerations for pilot studies. Int J Rad Oncol Biol Phys. 1980; 6:371- 374.
   b. Byar DP, Schoenfeld DA, Green SB, Amato DA, Anderson JR, Collins R, Davis R, De Gruttola V, Ellenberg SS, Finkelstein DM, Freedman LS, Gail M, Gatsonis C, Gelber RD, Lagakos S, Lefkopoulou M, Peto J, Peto R, Peto T, Simon R, Tsiatis AA, Zelen M. Design considerations for AIDS trials. N Engl J Med. 1990; 323:1343-1348.

c. Finkelstein DM, Schoenfeld DA. eds. AIDS clinical trials: Guidelines for design and analysis. New York: John Wiley & Sons. 1995
d. Schoenfeld DA, Hayden D, Oldmixon C, Ringwood N, Thompson BT. Statistical design and analysis issues for the ARDS Clinical Trials Network: the Coordinating Center perspective. Clin Invest. 2012 Mar; 2(3): 275-289.

4. **Team Science**

Sometimes one's most important contribution is as a member of a team that accomplishes an important goal. The following four articles were the result of teamwork for four different medical areas. In each case I helped design the study, conduct the study and analyze the data. Highlights of this activity were the introduction of factorial designs to the study of ARDS which broke a deadlock that allowed the study on lower tidal volumes to proceed. The development of a novel method of calculating sample size which helped the study on CT angiography win funding and the development of a new design for ALS studies which was considered to be more ethical and allowed an international group to proceed with a clinical trial.

a. Collier AC, Bozzette S, Coombs RW, Causey DM, Schoenfeld DA, Spector SA, Pettinelli CB, Davies G, Richman DD, Leedom JM, Kidd P, Corey L. A pilot study of low-dose zidovudine in human immunodeficiency virus infection. N Engl J Med. 1990; 323:1015-1021.
b. The ARDS Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for Acute Lung Injury and the Acute Respiratory Distress Syndrome. NEJM. 2000; 342: 1301-8.
c. Hoffmann U, Truong QA, Schoenfeld DA, Chou ET, Woodard PK, Nagurney JT, Pope JH, Hauser TH, White CS, Weiner SG, Kalanjian S, Mullins ME, Mikati I, Peacock WF, Zakroysky P, Hayden D, Goehler A, Lee H, Gazelle GS, Wiviott SD, Fleg JL, Udelson JE; ROMICAT-II Investigators. Coronary CT angiography versus standard evaluation in acute chest pain. N Engl J Med. 2012 Jul 26;367(4):299-308.
d. Aggarwal SP, Zinman L, Simpson E, McKinley J, Jackson KE, Pinto H, Kaufman P, Conwit RA, Schoenfeld D, Shefner J, Cudkowicz M, Northeast and Canadian Amyotrophic Lateral Sclerosis consortia. Safety and efficacy of lithium in combination with riluzole for treatment of amyotrophic lateral sclerosis: a randomised, double-blind, placebo-controlled trial. Lancet neurol. 2010 May; 9(5):481-8.

5. **Sequential Parallel Comparison Design**

I have had a long a fruitful collaboration with the psychiatry department at the Massachusetts General Hospital. In one notable brainstorming session a group of us tried to determine a way to handle the placebo effect in trials of major depression. We came up with a new way of designing and analyzing trials in major depression and other areas where the placebo response is a problem. The method involves re-randomizing the placebo non-responders to drug or placebo and then pooling these results with the initial randomization. The method has had a large impact and has been used in over 20 clinical trials as of the middle of 2014 and the original paper has been sited over 150 times.

a. Fava M, Evins AE, Dorer DJ, Schoenfeld DA. The problem of the placebo response in clinical trials of psychiatric disorders: culprits, possible remedies, and a novel study design approach. Psychother Psychosom. 2003; 72: 115-127.
b. Ivanova A, Qaqish B, Schoenfeld, DA. Optimality, sample size, and power calculations for the sequential parallel comparison design. Statistics in Medicine. 2011 Jul; 30: 2793-2803.

Complete List of Published Work: http://www.ncbi.nlm.nih.gov/pubmed/?term=david+schoenfeld

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

**Ongoing Research Support**

U01HL123009-03 (D Schoenfeld) 06/17/14–04/30/21

NIH / NHLBI
Clinical Coordination Center for a NHLBI Prevention and Early Treatment of Acute Lung Injury (PETAL) Network
The major goals of this project are the coordination, design, and statistical analysis of clinical trials in Petal.
Role: Principal Investigator

5 R01 MH103402-02 (Misra/Lawson/Eddy) 04/01/14-3/31/19

NIH/NIMH
Homeostatic and Hedonic Food Motivation Underlying Eating Disorder Trajectories
Role: Statistical Consultant

5UL1TR001102-09 (Orf) 10/01/13-09/30/18

NIH/NCRR
Harvard Clinical and Translational Science Center
Provide enriched resources to educate and develop the next generation of researchers trained in the complexities of translating research discoveries into clinical trials and ultimately into practice. Design new and improved clinical research informatics tools for analyzing research data and managing clinical trials. Support outreach to underserved populations, local community and advocacy organizations, and health care providers. Assemble interdisciplinary teams and forge new partnerships with private and public healthcare organizations.
Role: Statistical Consultant

5P50GM02100-35 (Tompkins) 06/01/13-05/31/18

NIH
Burn Trauma Center
The host response to burns and trauma is a collection of biological and pathological processes that depends critically upon the regulation of the human metabolic response. Over the years of P50 funding, our Center has had a tremendous and unique research opportunity to study the physiology of metabolism after injury. Since its inception, the Center has focused on the metabolic aspects of the patient's immuno-inflammatory reaction to injury.
Role: Statistical Consultant

4 R01 DK095792-04 (Miller & Bredella) 05/08/13-03/31/18

NIH/NIDDK
Skeletal Physiology Dysregulation in Obesity: The Role of Growth Hormone
The major goal of this project is to investigate the role of growth hormone in the pathogenesis of obesity-related bone loss.
Role: Statistical Consultant

2K24DA030443-06 (Evins) 07/01/16–06/30/21

NIH/NIDA
Mentoring in Addiction Treatment Research
This K award supports the mentoring activities of Dr. Eden Evins in addiction treatment research by providing salary support for Dr. Evins and enabling the hiring of statistical support staff.
Role: Statistical consultant

W81XWH-11-1-0835 (D Schoenfeld) 06/12/13-10/29/17

American Burn Association
Data Coordinating Center–Protective Effects of Propranolol in Adults Following Major Burn Injury: A Safety and Efficacy Trial
The major goals of this project are the coordination, design and statistical analysis of clinical trials in Propranolol study
Role: Statistical Consultant

PPRN-1306-04925 (Nierenberg) 01/01/14 - 09/30/18 PCORI

Mood Patient Powered Research Network
The major goals of this project are to provide database and website support for this PCORI PPRN study.
Role: Statistical Consultant

5U19CI000514-06 (Ryan) 09/30/16-09/29/21
CDC
Global TravEpiNet: Global Travelers' Health National Research Center Consortium
This project proposes forming a national consortium of global travelers' health research centers to assess vaccination strategies.
Role: PI Biostatistics Core

**Completed Research Support**

1R01 HL092022-01A1 (D Schoenfeld) 09/15/09–06/30/14
NIH / NHLBI
Rule-Out Myocardial Infarction Using Computed Assisted Tomograpy–ROMICAT II, DCC
The major goals of this project are the coordination, design, and statistical analysis of the multicenter trial in 1000 subjects with acute chest pain. The objective is to determine whether rate of discharge from the Emergency Department is increased by the use of Cardiac Computer Assisted Tomography.
Role: PI

HHSN268200536179C (D Schoenfeld) 09/30/05–06/30/14
NIH / NHLBI
Clinical Coordination Center for a Clinical Research Network for the Treatment of Acute Lung Injury and Acute Respiratory Distress Syndrome
The major goals of this project are the coordination, design, and statistical analysis of clinical trials in ARDS.
Role: PI

5R01 NS049640-04SI (Cudkowicz) 09/30/04-06/30/14
NIH
Clinical Trial of Ceftriaxone in ALS
The major goal of this project is to provide statistical support for clinical studies.
Role: Statistical Consultant

1 R01 HS019371-01 (Nierenberg) 08/16/10-09/29/13
AHRQ
Comparative Effectiveness Study for Bipolar Disorder
The major goal of this project is to determine the clinical implications of treatment with quetiapine in comparison to lithium when used in conjunction with treatment as usual.
Role: Statistical consultant

1R01MH091078-05 (Wilhelm) 10/01/11-9/30/16
National Institute of Mental Health
CBT versus Supportive Psychotherapy for BDD
The purpose of this study is to examine the efficacy of a manualized CBT treatment in comparison to manualized enhanced supportive psychotherapy (SPT) for adult BDD. The major goal of this project is to provide statistical support for clinical studies.
Role: Statistical consultant

5R01DA030992-05 (MPI) (Evins/Fava) 4/01/2011–01/31/2017
NIH/NIDA
Proof-of-Concept Trial of an Alpha-7 Nicotinic Agonist for Nicotine Dependence
The study proposes to evaluate the effects of novel pharmacotherapies aimed at ameliorating baseline or reducing withdrawal-emergent cognitive impairment.

1 R34 MH099315-01A1 (Miller & Fava) 07/15/13-6/30/16 NIH
1/2-Collaborative Study: Testosterone Antidepressant Augmentation in Women
The major goal of this collaborative study is to determine, with a randomized, placebo-controlled study, whether low- dose transdermal testosterone augmentation will improve depression severity in women with treatment-resistant major depressive disorder.
Role: Statistical Consultant