

**BIOGRAPHICAL SKETCH**

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NAME: Kieburtz, Karl

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

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
Amherst College, Amherst, MA, Magna Cum Laude	BA	05/1980	Neuroscience
Univ of Rochester School of Medicine, Rochester, NY	MD, MPH	05/1985	Medicine, Public Health
Highland Hospital, Rochester, NY	Intern	06/1985-86	Family Medicine
Strong Memorial Hospital, Rochester, NY	Resident	06/1986-89	Neurology

**A. Personal Statement**

As one of the three Directors of the Clinical & Translational Science Institute (CTSI), **I will function as the corresponding Principal Investigator in a multi-PI arrangement.** As such I will have the primary administrative responsibility for the award to the School of Medicine and Dentistry, and will also serve as the Senior Associate Dean for Clinical Research. I have served as one of the mPIs since January 2015 and prior to that served as the sole PI. I fully endorse the mPI approach to leadership and have extensive prior experience in shared scientific and administrative leadership, having conducted many NIH-funded U01s and U10's, largely multi-center clinical trials, in such a leadership format, as evidenced by the cited articles. Jointly the Directors will be responsible for the oversight of the CTSI, including the strategic priorities and major research initiatives. We will also work collaboratively to recruit and mentor key Faculty for the CTSI. We meet weekly with the Operations Committee to insure that the CTSI is functioning in all its missions, and meet alone as Directors weekly to plan strategic directions for the CTSI. We also meet jointly with the individual CTSI Executive Directors, who manage CTSI programs and projects, on a weekly basis. **I will serve as Core Director for Research Methods and Network Capacity. I will also serve as Faculty for the Regulatory Science to Advance Precision Medicine Optional Function; and Mentor for the TL1 Training Program and KL2 Career Development Program.** I have extensive experience with training and mentorship having previous K24 support from NINDS as a career mentor and have been awarded the School of Medicine and Dentistry's 2 highest mentoring awards. I have served on the NINDS Clinical Trials Study section, Chaired the VA's study section for their multi-center trial program 'Cooperative Studies', and Chaired the FDA Advisory Committee on Peripheral and Central Nervous System Drugs, hence have the experience to guide trainees and faculty on the development of proposals for clinical trials, both from the scientific and regulatory perspective. My skills and experience complement and reinforce those of the other 2 current mPIs.

I previously served on the CTSA Consortium Steering Committee (2013-5), and currently serve on the CTSA/PCORI Federal Subcontract working group, and the CTSA Collective Impact of Hub Functions and Activities Metrics Working Group

1. Engel J Jr, McDermott MP, **Kieburtz K**; Early Randomized Surgical Epilepsy Trial (ERSET) Study Group. Early surgical therapy for drug-resistant temporal lobe epilepsy: a randomized trial. JAMA. 2012 Mar 7; 307(9):922-30
2. Rachelle S. Doody, M.D., Ph.D., Rema Raman, Ph.D., Martin Farlow, M.D., Takeshi Iwatsubo, M.D., Ph.D., Bruno Vellas, M.D., Steven Joffe, M.D., M.P.H., **Karl Kieburtz, M.D., M.P.H.**, Feng He, M.S., Xiaoying Sun, M.S., Ronald G. Thomas, Ph.D., and Paul S. Aisen, M.D., for the Alzheimer's Disease Cooperative Study Steering Committee; and Eric Siemers, M.D., Gopalan Sethuraman, Ph.D., and Richard Mohs, Ph.D., for the Semagacestat Study Group. A Phase 3 Trial of Semagacestat for Treatment of Alzheimer's Disease. N Engl J Med, 2013;369(4):341-50

3. Rachele S. Doody, M.D., Ph.D., Ronald G. Thomas, Ph.D., Martin Farlow, M.D., Takeshi Iwatsubo, M.D., Ph.D., Bruno Vellas, M.D., Steven Joffe, M.D., M.P.H., **Karl Kieburtz, M.D., M.P.H.**, et al. for the Alzheimer's Disease Cooperative Study Steering Committee and the Solanezumab Study Group. Phase 3 Trials of Solanezumab for Mild-to-Moderate Alzheimer's Disease *N Engl J Med* 2014; 370:311-321 January 23, 2014 DOI: 10.1056/NEJMoa1312889
4. The NORDIC Idiopathic Intracranial Hypertension Study Group Writing Committee. Effect of Acetazolamide on Visual Function in Patients With Idiopathic Intracranial Hypertension and Mild Visual Loss: The Idiopathic Intracranial Hypertension Treatment Trial. *JAMA*. 2014;311(16):1641-1651. doi:10.1001/jama.2014.3312B. PMID: PMC4362615

## Positions and Honors

### Positions and Employment

1989-91	Fellow, Experimental Therapeutics, Neurology, University of Rochester School of Medicine (URMC)
1991-92	Sr. Instructor & Fellow, Neurology, URMC
1992-95	Assistant Professor, Neurology, Community & Preventive Med, URMC
1993-08	Director, Clinical Trials Coordination Center, Neurology, URMC
1995-00	Associate Professor, Neurology, Community & Preventive Med, URMC
2000-	Professor, Dept. of Neurology, Public Health Sciences, Environmental Medicine (2006) URMC
2009-2014	Director, Center for Human Experimental Therapeutics
2011-	Robert J Joynt Professor in Neurology
2013-	Director, Clinical & Translational Science Institute
2013-	Senior Associate Dean of Clinical Research

### Other Experience and Professional Memberships

2002 - 2004	NSD-K Study Section Member, NINDS
2003 - 2008	Peripheral & Central Nervous System Advisory Committee (Chair 2005-2008), FDA
2007 - 2013	Chair, Cooperative Studies Scientific Evaluation Committee, Department of Veterans Affairs
2013 -	Fellow, American Association for the Advancement of Science

### Honors

1980	Frank Dow Award in Chemistry, Amherst College
1980	Phi Beta Kappa, Amherst College
1982	Logan Clendenning Fellowship in the History of Medicine, University of Rochester School of Medicine
1984	The Best Doctors in America, Woodward/White, Inc., 2nd edition
1994-7	Dean's Teaching Scholar, University of Rochester School of Medicine
2007	Junior Faculty Mentoring Award, University of Rochester School of Medicine

## C. Contribution to Science

1. **The execution of large, multi-center trials in PD, a common neurodegenerative disease, requires the ability to form and sustain large cooperative groups.** These groups must be able to function over long periods of time, and tolerate internal dissent, yet forge agreement. I worked for decades, within, and led for 5 years, the Parkinson Study Group, as well as forming and leading the NET-PD group, sponsored by NINDS. These cooperative groups were highly successful in conducting complex, novel, and hypothesis testing studies.
  - a. Parkinson Study Group (**K Kieburtz, Medical Director, Steering Com**). Effects of tocopherol and deprenyl on the progression of disability in early Parkinson's disease. *New Engl J Med* 1993; 328:176-183.
  - b. Shults CW, Oakes D, **Kieburtz, K**, Beal F, Hass R, Plumb S, Juncos JL, Nutt J, Shoulson I, Carter J, Kompoliti K, Perlmuter JS, Reich S, Stern N, Watts RL, Kurlan R, Molho E, Harrison M, Lew M, and the Parkinson Study Group. Effects of Coenzyme Q10 in Early Parkinson Disease. Evidence of Slowing of the Functional Decline. *Arch Neurol* 2002;59:1541-1550.
  - c. The Parkinson Study Group (Fahn S, primary author, **Kieburtz K, Steering Com**). Levodopa and the progression of Parkinson's disease. *NEJM* 2004;351:2498-508.

- d. Writing Group for the NINDS Exploratory Trials in Parkinson Disease (NET-PD) Investigators. Effect of Creatine Monohydrate on Clinical Progression in Patients With Parkinson Disease: A Randomized Clinical Trial. *JAMA*. 2015;313(6):584-593. doi:10.1001/jama.2015.120. PMCID: PMC4349346

2. **A major focus of research in neurodegenerative disorders is on the identification of interventions that will slow the progression of clinical disability.** Much of this research has been hampered by a less than ideal understanding of disease mechanisms, but clinical trial design has also been sub-optimal. Much of my work has focused on the development of new research methods to speed the identification of effective treatments. These methods include novel trial designs and statistical approaches.
  - a. The NINDS NET-PD Investigators (**Kieburtz K, Corresponding author**). A randomized, double-blind, futility clinical trial of creatine and minocycline in early Parkinson disease. *Neurol* 2006;66:664-671.
  - b. Tilley BC, Palesch YY, **Kieburtz K**, et al. Optimizing the ongoing search for new treatments for Parkinson disease. Using futility designs. *Neurol* 2006;66:628-633.
  - c. Elm JJ; NINDS NET-PD Investigators. Design innovations and baseline findings in a long-term Parkinson's trial: the National Institute of Neurological Disorders and Stroke Exploratory Trials in Parkinson's Disease Long-Term Study-1. *Mov Disord*. 2012 Oct;27(12):1513-21. PMCID: PMC3481179
  - d. Sheng Luo, Junsheng Ma and **Karl D. Kieburtz**. Robust Bayesian inference for multivariate longitudinal data by using normal/independent distributions. *Statistics in Medicine* 2013 Feb 7; DOI: 10.1002/sim.5778 PMCID: PMC3884581
3. Much of my investigative career has focused on the **new development of treatments for Parkinson disease, via well designed, controlled clinical trials.** This research work has brought several new treatments to patients with this disease, primarily to better manage symptoms. The trial designs and outcome measures differ from studies designed to show an impact on the long-term progression of illness.
  - a. Parkinson Study Group (**Kieburtz K, primary author**). Safety and efficacy of pramipexole in early Parkinson disease. A randomized dose-ranging study. *JAMA* 1997;278:125-130.
  - b. Parkinson Study Group (**Kieburtz K, primary author**). Entacapone improves motor fluctuations in levodopa-treated Parkinson's disease patients. *Ann Neurol* 1997;42:747-755.
  - c. Parkinson Study Group (Siderowf A, primary author, **Kieburtz K, Coordination Ctr Dir**). A controlled trial of Rasagiline in early Parkinson disease. The TEMPO study. *Arch Neurol* 2002;59:1937-1943
  - d. **Kieburtz K**; The Parkinson Study Group PramiBID Investigators. Twice-daily, low-dose pramipexole in early Parkinson's disease: A randomized, placebo-controlled trial. *Mov Disord*. 2011 Jan;26(1):37-44
4. I was very active early in the HIV epidemic **identifying the risk factors for and characteristics of HIV related neurologic syndromes.** I also participated in some of the first clinical trials for HIV dementia, and then designed and ran trials for both HIV dementia and neuropathy. I led two consortia dedicated to HIV Neurology clinical trials, funded by the Charles A Dana Foundation and the NINDS.
  - a. Sidtis J, Gatsonis C, Price R, Singer E, Collier A, Richman D, Hirsch M, Schaerf FW, Fischl M, **Kieburtz K**, Simpson D, Koch M, Feinberg J, Danfni O. Zidovudine Treatment of the AIDS dementia complex: results of a placebo controlled trial. *Ann Neurol* 1993; 33:343-349.
  - b. **Kieburtz K**, Simpson D, Yiannoutsos C, Max MB, Hall CD, Ellis RJ, Marra CM, McKendall R, Singer E, Dal Pan GJ, Clifford DB, Tucker T, Cohen B, and the AIDS Clinical Trial Group 242 Protocol Team. A randomized trial of amitriptyline and mexiletine for painful neuropathy in HIV infection. *Neurology* 1998;51:1682-1688.
  - c. Schifitto G, McDermott MP, McArthur JC, Marder K, Sacktor N, Epstein L, **Kieburtz K**, and the Dana Consortium on the Therapy of HIV Dementia and Related Cognitive Disorders. Incidence of and risk factors for HIV-associated distal sensory polyneuropathy. *Neurology* 2002;58:1764-1768.

- d. Sacktor, McDermott MP, Marder K, Schifitto G, Selnes OA, McArthur JC, Stern Y, Albert S, Palumbo D, **Kieburtz K**, DeMarcaida JA, Cohen B, Epstein L. HIV-associated cognitive impairment before and after the advent of combination therapy. J Neurovirol 2002;8(2):136-42.

**5. Applied research ethics are rarely studied empirically and quantitatively.** Along with colleagues at the University of Michigan and the NIH, I have studied the informed consent process especially focusing on research participant comprehension in chronic disorders considering high risk research studies.

- a. Kim SY, Wilson R, De Vries R, Kim HM, Holloway RG, **Kieburtz K**. It is not guaranteed that you will benefit: True but misleading? Clin Trials. 2015 Aug;12(4):424-31. doi: 10.1177/1740774515585120. Epub 2015 May 11. PMID:25963311
- b. Kim SY, De Vries R, Parnami S, Wilson R, Kim HM, Frank S, Holloway RG, **Kieburtz K**. Are therapeutic motivation and having one's own doctor as researcher sources of therapeutic misconception? J Med Ethics. 2015 May;41(5):391-7. doi: 10.1136/medethics-2013-101987. Epub 2014 May 22. PMID: 24855070
- c. Kim SY, De Vries R, Holloway RG, Wilson R, Parnami S, Kim HM, Frank S, **Kieburtz K**. Sham surgery controls in Parkinson's disease clinical trials: views of participants. Mov Disord. 2012 Sep 15;27(11):1461-5. doi: 10.1002/mds.25155. Epub 2012 Aug 23. PMID: 22927064
- d. Galpern WR, Corrigan-Curay J, Lang AE, Kahn J, Tagle D, Barker RA, Freeman TB, Goetz CG, **Kieburtz K**, Kim SY, Piantadosi S, Comstock Rick A, Federoff HJ. Sham neurosurgical procedures in clinical trials for neurodegenerative diseases: scientific and ethical considerations. Lancet Neurol. 2012 Jul;11(7):643-50. doi: 10.1016/S1474-4422(12)70064-9. PMID: 22710757

**Complete List of Published Work in MyBibliography:**

<http://www.ncbi.nlm.nih.gov/sites/myncbi/karl.kieburtz.1/bibliography/45841668/public/?sort=date&direction=ascending>

**D. Research Support**

**Ongoing Research Support**

5 UL1 TR000042-10 Kieburtz/Bennett/Zand (PI) 7/01/2011 - 6/30/2016

5 KL2 TR000095-10 Kieburtz/Bennett/Zand (PI)

5 TL1 TR000096-10 Kieburtz/Bennett/Zand (PI)

NIH/ National Center for Advancing Translational Sciences

The University of Rochester's Clinical and Translational Science Institute

The major goal of this project is to develop, demonstrate and disseminate methods and approaches to advance translational research, by providing education and training, supporting transdisciplinary teams, improving quality and efficiency, and engaging community stakeholders.

ROLE: Principal Investigator

U01 NS43128 Kieburtz (PI) 12/01/06-11/30/16

NIH, NINDS

Neuroprotection Studies in PD: A Coordinating Center

This project establishes an academically based clinical trials coordination center to handle all aspects of performing trials in experimental treatments in PD.

ROLE: Principal Investigator

Parkinson's Progression Markers Initiative (PPMI) Kieburtz (PI) 05/01/13 – 04/30/16

Michael J. Fox Foundation, Inc.

An observational, multi-center study to assess progression of clinical features and imaging as well as biologic biomarkers in Parkinson Disease patients compared to healthy controls. The primary objective of this study is to collect and examine clinical and biologic measures to track disease progression in early stage PD subjects for use in clinical trials of disease modifying therapies.

ROLE: Principal Investigator

OPEN HART – Kieburtz (PI)

11/1/10-03/31/16

NeuroSearch Sweden AB

A multi-center, North American, open label study of ACR16 versus placebo for the symptomatic treatment of Huntington disease (HART).

ROLE: Principal Investigator

**Completed Research Support**

R21 – NS077460 Kieburtz (PI)

09/30/11 – 01/31/15

NINDS

U.S. India Collaborative Partnership in Parkinson Disease (CPPD)

Project will establish a US-India Collaborative Partnership in Parkinson Disease, establishing the infrastructure to enhance the quality and efficiency of clinical research in PD.

U10 EY017387 Kieburtz (PI)

02/10/09 – 01/31/15

Data Coordination and Biostatistics Center (DCBC)

Lead the Data coordination and biostatistics center that will provide study coordination, data management and biostatistical support for the NORDIC Network in studies of neuro-ophthalmology. This is a new start-up network

ROLE: Principal Investigator

R01 NS 052619 McDermott (PI)

10/1/12-12/30/14

NIH, NINDS

Coordination and Statistics for CoQ10 in HD (2CARE)

To conduct a multicenter randomized, double-blind, placebo-controlled trial of CoQ in ambulatory subjects with HD (Companion grant RO1 NS052592).

ROLE: Co-Investigator

U01 AG010483 Aisen (PI)

7/1/01-12/31/13

NIH, NIA

Alzheimer's Disease Cooperative Study

This project performs multi-center trials in Alzheimer disease

ROLE: Chair, Data Safety Monitoring Board