

## BIOGRAPHICAL SKETCH

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NAME: Lewis A. Lipsitz, MD

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eRA COMMONS USER NAME: LIPSITZ

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POSITION TITLE: Chief of Gerontology, Beth Israel Deaconess Med Center; Professor of Medicine, Harvard Medical School; Director, Hinda and Arthur Marcus Institute for Aging Research and Chief Academic Officer, Hebrew SeniorLife

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### EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Franklin & Marshall College, PA	B.A.	06/1973	Chemistry
University of Pennsylvania, School of Medicine, PA	M.D.	06/1977	Medicine
Harvard University, MA	M.A.	05/2000	Medicine
Harvard School of Public Health		02/1999	Program for Chiefs of Clinical Services
Amer. Political Sci. Assoc. and Atlantic Philanthropy		09/2013	Health Care Policy

### A. Personal Statement

Dr. Lipsitz was one of the first geriatricians to be trained in the Harvard Geriatric Fellowship Program. He subsequently became a National Institute on Aging Academic (K23) Awardee, with Hebrew SeniorLife (formerly the Hebrew Rehabilitation Center for Aged) as his primary clinical and research site. As a fellow, he began a systematic series of epidemiologic and physiologic studies evaluating syncope and abnormal blood pressure regulation, discovered postprandial hypotension in the elderly, and subsequently acquired funding for his studies through an NIA-funded Program Project, which he directed for 23 years. This program project supported the prospective, observational MOBILIZE Boston Study, which has elucidated cerebrovascular and other risk factors for falls. During his career, Dr. Lipsitz has received continuous NIA funding for his research, directed a previous Older Americans Independence Center, led a T32 training program for 15 years, directed the Hartford Center of Excellence in Geriatric Medicine at Harvard Medical School (HMS), and acquired two D.W. Reynolds Grants for geriatric education at HMS. He has mentored 45 successful postdoctoral trainees, including 2 Beeson Scholars and 6 T32 trainees, and received the prestigious "William Silen Lifetime Achievement" award for mentoring.

His research is focused on the mechanisms and prevention of cognitive dysfunction, falls, and mobility impairments in older adults. He has identified the "frontal subcortical syndrome of aging," which is the coexistence of executive dysfunction and slow gait, due to cerebral microvascular disease in poorly perfused watershed regions of the brain. Relevant to the theme of the OAIC renewal application, which is focused on function promoting therapies, he was the Principal Investigator of a Falk Foundation Grant that tested transcranial direct current stimulation for its effect on balance, gait, and cognition in older adults with this syndrome. He has also conducted clinical trials of caffeine and L-DOPS to treat postprandial hypotension, ACE inhibitors to improve cerebral blood flow; vibrating insoles to improve gait and balance, and Tai Chi exercises to improve functional ability in frail older adults. He is currently testing a sensory neuroprosthesis to improve gait and balance in older adults with peripheral neuropathy and a TORC-1 inhibitor to prevent COVID-19 symptoms in people who are asymptomatic but test positive or are exposed to a household contact with the infection. His extensive research into the mechanisms and treatment of geriatric syndromes in frail older adults with cognitive and mobility disorders, and his leadership in clinical research and gerontology will all help assure the continued success of the Boston OAIC.

### B. Positions and Honors

#### **Positions:**

1980-82 Research Fellowship, Administration on Aging Gerontology Fellowship, Harvard Medical School

- and Beth Israel Hospital
- 1984- Ad Hoc Study Section Reviewer, National Institute on Aging
  - 1986-96 Director, Harvard Geriatrics Fellowship Program, Harvard Medical School
  - 1988-11 Principal Investigator, HRCA/Harvard Teaching Nursing Home,
  - 1988-15 Director, Hartford Foundation Center of Excellence in Geriatric Medicine at Harvard Medical School
  - 1991-10 Co-Director, Institute for Aging Research, Hebrew SeniorLife
  - 1997-00 Physician-in-Chief, Hebrew Rehabilitation Center for Aged, Boston, MA
  - 2000- Chief of Gerontology Division, Beth Israel Deaconess Medical Center, Boston, MA
  - 2000- Professor of Medicine, Harvard Medical School
  - 2001-02 Chair, Clinical Medicine Section, Gerontological Society of America
  - 2005-12 Advisory Committee and Reviewer, K-Beeson Career Development Awards, NIA and AFAR
  - 2005- Director, Interdisciplinary Center on Aging, Beth Israel Deaconess Med Ctr/Harvard Medical School
  - 2005- Geriatric Research & Education Clinical Center Advisory Committee, Boston Veterans Administration
  - 2010- Director, Hinda and Arthur Marcus Institute for Aging Research, Hebrew SeniorLife
  - 2014-18 Senior Advisor, Center for Medicare and Medicaid Services, Baltimore, MD

**Awards and Honors:**

- 1983-88 Academic Award, National Institute on Aging
- 1991- Irving and Edyth S. Usen Family Chair in Geriatric Medicine, Hebrew SeniorLife, Boston, MA
- 2006-15 NIA Merit Award R37 AG25037
- 2007-09 Hartford Foundation Senior Leadership Scholar, Association of Directors of Geriatric Academic Programs
- 2010 Recipient, William Silen Lifetime Achievement in Mentoring Award, Harvard Medical School
- 2010 Recipient, Joseph T. Freeman Award, Gerontological Society of America
- 2018 Recipient, Donald P. Kent Award, Gerontological Society of America

**C. Contributions to Science**

**Cardiovascular and Cerebrovascular Causes of Falls and Syncope:** Dr. Lipsitz’s research has focused on abnormal blood pressure regulation and its relationship to the development of falls and syncope in elderly people. His initial prospective clinical investigations led to the recognition that nearly one-third of syncopal episodes in frail elderly patients are related to hypotensive responses to common daily stresses such as posture change, meals, and preload-reducing medications. He was the first to identify postprandial hypotension in the elderly, probe its underlying mechanisms, and demonstrate its relationship to syncope. In randomized, double-blind, placebo-controlled trials he found that 3,4-DL-threo-dihydroxy-phenylserine was an effective treatment, but caffeine was not.

In several elderly populations, Dr. Lipsitz observed a relationship between systolic hypertension and the susceptibility to hypotension. He found that both orthostatic and postprandial hypotension are related to supine BP elevation, independent of medication use, due to the additive adverse effects of age and systolic hypertension on baroreflex function and diastolic ventricular filling. In a randomized, double-blind, cross-over trial he showed that treatment of BP elevation with a calcium channel blocker ameliorated postprandial hypotension in older adults. In another trial he showed that the treatment of hypertension can improve cerebral blood flow and carotid distensibility in patients with hypertension.

In addition to cardiac and peripheral vascular mechanisms of falls in elderly people, Dr. Lipsitz has recently shown that abnormalities in cerebrovascular function and network connectivity are associated with slow gait and falls, probably through ischemic injury to frontal subcortical circuits that control gait. He has shown relationships between abnormal cerebral vasoreactivity and falls, and between abnormal neurovascular coupling and motor-cognitive network connectivity and slow gait speed in the MOBILIZE Boston population.

- a. **Lipsitz LA**, Nyquist RP, Wei JY, Rowe JW. Postprandial reduction in blood pressure in the elderly. *N. Engl J Med* 1983; 309: 81-83.
- b. Sorond F, Kiely DK, Galica A, Moscufo N, Serrador JM, Iloputaife I, Egorova S, Dell’Oglio E, Meier D,

- Newton E, Milberg WP, Guttmann C, **Lipsitz LA**. Neurovascular Coupling is Impaired in Slow Walkers: The MOBILIZE Boston Study. *Annals of Neurology*. 2011 Aug;70(2):213-20. PMC3152682.
- c. Jor'dan AJ, Manor B, Iloputaife I, Habtemarian D, Bean JF, Sorond FA, **Lipsitz LA**. Diminished Locomotor Control is Associated with Reduced Neurovascular Coupling in Older Adults. *J Gerontol A Biol Sci Med Sci*. 2019 Jan 9. doi: 10.1093/gerona/glz006. [Epub ahead of print] PubMed PMID: 30629129.
- d. Poole VN, Lo OY, Wooten T, Iloputaife I, **Lipsitz LA**, Esterman M. Motor-Cognitive Neural Network Communication Underlies Walking Speed in Community-Dwelling Older Adults. *Front Aging Neurosci*. 2019 Jul 16;11:159. doi:10.3389/fnagi.2019.00159. eCollection 2019. PubMed PMID: 31379552; PubMed Central PMCID: PMC6647911.

**Interventions to Prevent Falls and Mobility Impairments:** Building on the results of the MOBILIZE Boston Study, which identified novel risk factors for falls in a representative population of older adults, Dr. Lipsitz has directed several clinical trials of multisystem interventions to ameliorate the risk of falls. In an initial randomized, controlled pilot trial, he showed that 12 weeks of Tai Chi exercises improved physical function among elderly residents of senior housing facilities. However, a subsequent larger scale cluster randomized trial in a similar population was unable to validate this finding. Dr. Lipsitz has also shown that subsensory vibrations applied to the foot sole or ankle tendons can enhance balance and gait in healthy young and elderly individuals, as well as in patients with diabetic peripheral neuropathy or stroke. He and his colleagues have also shown that transcranial direct current stimulation applied to the dorsolateral prefrontal cortex can improve gait speed, dual task gait, and executive function in older adults with slow gait and executive dysfunction who are at high risk of falls.

- a. **Lipsitz LA**, Macklin EA, Travison TG, Manor B, Gagnon P, Tsai T, Aizpurúa II, Lo OY, Wayne PM. A Cluster Randomized Trial of Tai Chi vs Health Education in Subsidized Housing: The MI-WiSH Study. *J Am Geriatr Soc*. 2019 Sep;67(9):1812-1819. doi: 10.1111/jgs.15986. Epub 2019 May 22. PubMed PMID: 31116883; PubMed Central PMCID: PMC6732029.
- b. Priplata AA, Patriitti BL, Niemi JB, Hughes R, Gravelle DC, **Lipsitz LA**, Veves A, Stein J, Bonato P, Collins J. Noise-enhanced balance control in patients with diabetes and patients with stroke. *Ann Neurol*, 2006, 59:4-12. PMID: 16287079
- c. **Lipsitz LA**, Lough M, Niemi J, Travison T, Howlett H, Manor B. A Shoe Insole Delivering Subsensory Vibratory Noise Improves Balance and Gait in Healthy Elderly People. *Arch Phys Med Rehabil*. 2015 Mar;96(3):432-9. doi: 10.1016/j.apmr.2014.10.004. PMC4339481
- d. Manor B, Zhou J, Harrison R, Lo OY, Travison TG, Hausdorff JM, Pascual-Leone A, **Lipsitz L**. Transcranial Direct Current Stimulation May Improve Cognitive-Motor Function in Functionally Limited Older Adults. *Neurorehabil Neural Repair*. 2018 Sep;32(9):788-798. doi: 10.1177/1545968318792616. PubMed PMID:30132389; PubMed Central PMCID: PMC6143414.

**Loss of Complexity in Aging:** Building upon his observations that physiological measures such as blood pressure and heart rate are highly variable with beat-to-beat fluctuations that resemble nonlinear dynamical processes, Dr. Lipsitz applied the principles of nonlinear dynamics to his work. He proposed that healthy physiologic function is characterized by the nonlinear interaction of multiple control processes and feedback loops that produce highly complex outputs - such as the beat-to-beat irregularity of the normal sinus cardiac rhythm, the moment-to-moment adjustments in center-of-pressure during quiet standing, and the resting state blood oxygen dependent functional activity of the brain. Using a variety of mathematical techniques derived from Fourier analysis and complexity science, he was the first to demonstrate that aging is associated with a loss of complexity in the dynamics of these systems and that this loss of complexity impairs adaptive capacity and predisposes elderly people to frailty, falls, injury, and disease.

- a. **Lipsitz LA**, Goldberger AL. Loss of "complexity" and aging: potential applications of fractals and chaos theory to senescence. *JAMA* 1992;267:1806-1809.
- b. **Lipsitz LA**. The dynamics of stability: the physiologic basis of functional health and frailty. *J Gerontol Biol Sciences* 2002;57A(3):B115-B125.
- c. Manor B, Costa MD, Hu K, Newton E, Starobinets OV, Kang HG, Peng CK, Novak V, **Lipsitz LA**. Physiological complexity and system adaptability: Evidence from postural control dynamics of older adults. *J Appl Physiol*, 2010. Vol 109 (6): 1786 -91. PMC3006415
- d. Zhou J, Poole V, Wooten T, Lo OY, Iloputaife I, Manor B, Esterman M, **Lipsitz LA**. Multi-scale

dynamics of spontaneous brain activity is associated with walking speed in older adults. J Gerontol A Biol Sci Med Sci. 2019 Oct 5. pii: glz231.doi: 10.1093/gerona/glz231. [Epub ahead of print] PubMed PMID: 31585008.

For full list of publications see: <https://www.ncbi.nlm.nih.gov/myncbi/lewis.lipsitz.1/cv/28879/>

#### **D. Research Support**

##### ***Ongoing:***

- 1) R01 AG052282 (Aristidis, Veves) 09/30/16 – 03/31/21  
“Skin Inflammatory Phenotypes as Biomarkers of Myocardial and Vascular Remodeling”  
This study identifies markers of vascular inflammation in the skin and their relationships to myocardial and vascular remodeling.  
Role: Co-investigator
- 2) R01 AG025037 (Lipsitz) 02/01/15-01/31/21  
“Health Outcomes of Tai Chi in Subsidized Senior Housing”  
This study aims to determine the effects of Tai Chi exercises conducted at least twice weekly over a 1-year period on 1) functional performance measured by the Short Physical Performance Battery and 2) health care utilization and costs determined from Medicare claims data in poor, multiethnic, elderly residents of low income housing facilities.  
Role: Principal Investigator
- 3) T32 AG023480 (Lipsitz) 05/01/16-04/30/21  
“National Institute on Aging Translational Research in Aging Training Grant”  
The aims of this training program are: 1) to provide a 2-year training program basic & clinical aging research for 6 postdoctoral trainees each year, 2) To provide an 8-12 week short-term research training experience for 6 pre-doctoral candidates each year in basic & clinical aging research, and 3) to bring together scientists across a broad range of basic & clinical research through seminars, didactic sessions, shared laboratory experiences, and collaborative projects.  
Role: Principal Investigator
- 4) P30 AG048785 (Lachman, Margie) 09/01/19-8/31/24  
“Boston Roybal Center for Active Lifestyle Interventions”  
The Pilot Core will support a group of innovative and scientifically rigorous pilot studies each year that will enable the Boston Roybal Center to develop and test behavior change- strategies that promote healthy aging, especially for persons at high risk for poor health outcomes. The work of the Core will ultimately lead to interventions to achieve health-promoting behavior change in vulnerable, at-risk populations.  
Role: Principal Investigator
- 5) P30 AG031679 (Bhasin, Shalender) 07/01/16-06/30/20  
“Boston Older Americans Independence Center: A Translational Approach to Function Promoting Therapies”  
The Boston OAIC will forge an interdisciplinary research network to foster translational research in function promoting therapies (FPTs) – pharmacologic, physical, nutritional, technological and behavioral interventions that reduce the burden of disabling functional limitations in older adults. The overarching goal is to strengthen and expand our expertise and scientific resources in the areas of vascular biology, physiology, genetics, epidemiology, and biostatistics, in order to enhance our understanding of the vascular role in age-related physical and cognitive functional decline, design new interventions to ameliorate this decline, and train new investigators skilled in related areas of gerontologic research.  
Role: Core Leader/Co-Investigator
- 6) R01 AG059089 (Manor, Brad) 09/01/18-05/31/23  
“Personalized brain activity modulation to improve balance and cognition in elderly fallers”  
This study seeks to determine the effects of transcranial direct current stimulation (tDCS) on the control of standing and walking in older adults with previous falls. By using state-of-the-art technology to 1) target brain regions involved in both motor and mental function, and 2) personalize tDCS to each individual’s head and

brain anatomy, this study is expected to identify tDCS as a viable intervention to enhance standing, walking, and other important physical and mental functions on the causal pathway to falls in older adults.

Role: Co-investigator

- 7) R01 HS025702 (Lipsitz) 09/30/18 –08/31/21  
Agency for Healthcare Research and Quality (AHRQ)  
“Improving Safety of Transitions to Skilled Nursing Care Using Video-conferencing”  
If it can be demonstrated that ECHO-CT can be replicated in a tertiary and community based hospital and leads to safer transitions of care, fewer hospital readmissions, reduced health care costs compared to conventional patient transition practices, the team will disseminate instructional materials and toolkits to hospitals, SNF’s and health care organizations nationwide. This may ultimately reduce the high rates of adverse events, medication errors and re-hospitalizations that are currently associated with transitions in care.  
Role: Principal Investigator
- 8) Rx Function (Lipsitz) 08/1/19-07/31/21  
“Walk2Wellness: Long-term Use Effects of Walkasins® Wearable Sensory Prosthesis on Gait, Balance-Confidence, Social Participation, and Brain Structure and Function”  
The main objective of the study is to show a long-term (10 weeks) sustained improvement in FGA score >4 following Walkasins use as compared to initial baseline assessment and to examine a potential relationship between initial baseline assessment data and long-term outcome.  
Role: Principal Investigator
- 9) 4UH3-AG056925-03 (Colon-Emeric, Kathleen) 09/30/19-08/31/20  
“Physical Resiliencies: Indicators and Mechanisms in the Elderly Collaborative”  
PRIME Collaborative is a consortium that combines expertise from many disciplines and institutions and leverages existing scientific resources to advance the ability to measure and predict resilience in three important areas: musculoskeletal function (after orthopedic surgery); cognitive function (after surgery/anesthesia); and immune function (after infection).  
Role: Co-Chair
- 10) R01 AG062492 (Berry, Sarah) 05/01/19 – 01/31/22  
“Nursing Home Prevention of Injury in Dementia (NH PRIDE)”  
The purpose of this project is to develop and implement an Injury Liaison Service in four nursing home facilities that will promote deprescribing psychoactive and cardiometabolic drugs and encourage osteoporosis treatment.  
Role: Co-Investigator
- 11) resTORbio (Joan B. Mannick) 08/28/20-12/31/20  
“Pilot study of RTB101 as COVID-19 prophylaxis in older adults”  
The overall goal of this project is to test the preventive effect of a TORC-1 inhibitor on the development of severe symptoms in asymptomatic older adults who tested positive for COVID-19 or were exposed to someone who tested positive within their household.  
Role: Co-Investigator
- 13) Brown University IMPACT Supplement (Mor, Vince) 09/03/20-06/30/21  
“Evaluation of a State-wide Effort to Improve COVID-19 Infection Control in Massachusetts NHs”  
The overall goal of this project is to identify infection control processes and procedures that helped reduce the high morbidity and mortality of COVID-19 in Massachusetts Nursing Homes.  
Role: Co-Investigator

## **OVERLAP**

There is no financial or scientific overlap of the above studies. As pending grants are awarded and made active, the effort contributions will be reallocated within federal policy limits to prevent over commitment.