BIOGRAPHICAL SKETCH

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NAME: Douglas P. Kiel

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

POSITION TITLE: Professor of Medicine, Department of Medicine Beth Israel Deaconess Medical Center and Harvard Medical School, Director Musculoskeletal Research Center, Hinda and Arthur Marcus Institute for Aging Research, Hebrew SeniorLife

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	COMPLETION DATE	FIELD OF STUDY
Duke University, Durham, NC	BS	06/1975	Science Education
University of North Carolina School of Medicine, Chapel Hill, N.C.	MD	06/1981	Medicine
Boston University School of Medicine, Boston, MA	MPH	06/1986	Epidemiol/Biostatistics

A. Personal Statement

The theme of the Boston OAIC is function promoting therapies. As a geriatrician, senior investigator with continuous NIH funding since 1991, co-leader of our current PESC, and as a mentor of junior investigators for many years, I am able to provide the leadership and experience in overseeing the PESC with Dr. Montano, with whom I have worked over the past five years. My own research interests and broad collaborative network at Harvard, Tufts and even Boston University also provide a rich source for research support and mentoring for our PESC candidates. My own research interests harmonize with our OAIC theme, as I have a considerable research focus on sarcopenia and osteoporosis, which are two important elements related to physical function. I have led many randomized trials in older adults, and have extensive experience with study design, analysis and participant recruitment. Over the past decade I have had a productive collaboration with other members of the OAIC leadership. My institution, the Marcus Institute for Aging Research, is the largest geriatrics research institute within Harvard's affiliates, and the resources have also been an important element for previous PESC recipients. In summary, my role as PESC Co-Director is a significant asset to the Core and to the overall leadership of our Boston OAIC.

1. **Kiel DP**, Hannan MT, Barton BA, Bouxsein ML, Sisson E, Lang T, Allaire B, Dewkett D, Carroll D, Magaziner J, Shane E, Leary ET, Zimmerman S, Rubin CT. Low-Magnitude Mechanical Stimulation to Improve Bone Density in Persons of Advanced Age: A Randomized, Placebo-Controlled Trial. J Bone Miner Res. 2015 Jul;30(7):1319-28. doi: 10.1002/jbmr.2448. PMID: 25581217 PMCID: PMC4834704
2. Johannesdottir F, Allaire B, Anderson DE, Samelson EJ, **Kiel DP**, Bouxsein ML. Population-based study of age- and sex-related differences in muscle density and size in thoracic and lumbar spine: the Framingham Study. Osteoporos Int. 2018 Jul;29(7):1569-1580. doi: 10.1007/s00198-018-4490-0. PMID: 29564476. PMCID: PMC6035769
3. Manini TM, Patel SM, Newman AB, Travison TG, **Kiel DP**, Shardell MD, Pencina KM, Wilson KE, Kelly TL, Massaro JM, Fielding RA, Magaziner J, Correa-de-Araujo R, Kwok TCY, Hirani V, Karlsson MK, D'Agostino RB Sr, Mellström D, Ohlsson C, Ribom E, Jordan JM, Bhasin S, Cawthon PM. Identification of Sarcopenia Components That Discriminate Slow Walking Speed: A Pooled Data Analysis. J Am Geriatr Soc. 2020 Jul;68(7):1419-1428. doi: 10.1111/jgs.16524. Epub 2020 Jul 7. PMID: 32633834.
4. Cawthon PM, Manini T, Patel SM, Newman A, Travison T, **Kiel DP**, Santanasto AJ, Ensrud KE, Xue QL, Shardell M, Duchowny K, Erlandson KM, Pencina KM, Fielding RA, Magaziner J, Kwok T, Karlsson M, Ohlsson C, Mellström D, Hirani V, Ribom E, Correa-de-Araujo R, Bhasin S. Putative Cut-Points in Sarcopenia Components and Incident Adverse Health Outcomes: An SDOC Analysis. J Am Geriatr Soc. 2020 Jul;68(7):1429-1437. doi: 10.1111/jgs.16517. Epub 2020 Jul 7. PMID: 32633824.

B. Positions and Honors

Positions and Employment

1986 - 1992	Associate Physician, Division of General Internal Medicine, Rhode Island Hospital, Brown University School of Medicine, Providence , RI
1992 -	Director Musculoskeletal Research Center, Marcus Institute for Aging Research, Hebrew SeniorLife, Boston, MA
1992 - 1999	Assistant Professor of Medicine, Harvard Medical School Division on Aging, and Staff Physician , Beth Israel Deaconess Medical Center (BIDMC), Boston, MA
1992 - 2000	Assoc Director Medical Research, Hebrew Rehabilitation Center for Aged (HRCA), Boston, MA
1999 - 2010	Adjunct Associate Professor of Medicine, Brown University School of Medicine, Providence, RI
2010 -	Adjunct Professor of Medicine (Non-voting Faculty), Brown University School of Public Health, Department of Epidemiology, Providence, RI
2010 -	Professor of Medicine, Harvard Medical School, Boston, MA
2013 -	Associate Member, Broad Institute of MIT and Harvard University, Cambridge, MA

Other Experience and Professional Memberships

1994 -	Reviewer Epidemiology and Disease Control-2, Orthopedics, and Geriatrics & Rehabilitation Medicine Study Sections, NIAMS Career Awards, NIAMS SCOR Review, NIAMS K23 Review, HOP-T-02 Special Emphasis Panel, NIH
1998 -	Editorial Board, Clinical Densitometry
2000 -	Scientific Advisory Board/Education Committee, National Osteoporosis Foundation
2000 - 2003	Chair, Research Committee, American Geriatrics Society
2006 -	Technical Advisory Panel, Joint Commission Osteoporosis Initiative
2008 - 2011	Founding Member, NIA Clinical Trials Advisory Panel
2014 - 2015	Senior Associate Editor, Journal of Bone and Mineral Research
2015 - 2016	President, American Society for Bone and Mineral Research

Honors

2004	Nomination for Excellence in Mentoring Award, Harvard Medical School
2005	Outstanding Excellence in Geriatric Research All Categories, American Geriatrics Society
2007	Nomination for Excellence in Mentoring, Harvard Medical School
2008	Elected to Council, American Society for Bone and Mineral Research
2010	A. Clifford Barger Excellence in Mentoring Award, Harvard Medical School
2013	Fellow, American Geriatrics Society and Fellow, Gerontological Society of America
2019	Frederick C Bartter Award American Society for Bone and Mineral Research

C. Contributions to Science

1. My early career focused on the epidemiology of osteoporosis and related fractures. I started the Framingham Osteoporosis Study, an ancillary study of the Framingham Heart Study, in 1991. Multiple lifestyle contributors to osteoporosis and fracture were examined over the subsequent 25 yrs after completing multiple assessments of BMD, hand radiography, quantitative CT, and fracture ascertainment, including estrogen use, thiazide diuretics, visual acuity, smoking, alcohol consumption, fruits and vegetable intake, caffeine use, height loss, and silicon intake. All of these studies added to the growing attention that osteoporosis received in clinical practice. The study also shaped the use of bone densitometry by demonstrating that repeated screening within short intervals may not be useful. In recent years we have performed high resolution peripheral quantitative computed tomography scans on the Framingham cohort which has enabled us to carefully examine the role of obesity on bone microarchitecture. I served as the lead or senior author on most of the publications that have come out of this study.
    a. **Kiel DP**, Felson DT, Anderson JJ, Wilson PW, Moskowitz MA. Hip fracture and the use of estrogens in postmenopausal women: the Framingham study: N Engl J Med. 1987; 317(19):1169-1174. PMID: 3657888 PMCID: N/A
    b. **Kiel DP**, Zhang Y, Hannan MT, Anderson JJ, Baron JA, Felson DT. The effect of smoking at different life stages on bone mineral density in elderly men and women. Osteoporosis Int 1996;6(3):240-8. PMID: 8783299 PMCID: N/A
    c. **Kiel DP**, Hannan MT, Broe KE, Felson DT, Cupples LA. Can metacarpal cortical area predict the occurrence of hip fracture in women and men over 3 decades of follow up? Results from the Framingham Osteoporosis Study. J Bone Miner Res. 2001;16(12):2260-6. PMID: 11760840

PMCID: N/A

d. Liu CT, Broe KE, Zhou Y, Boyd SK, Cupples LA, Hannan MT, Lim E, McLean RR, Samelson EJ, Bouxsein ML, **Kiel DP**. Visceral adipose tissue is associated with bone microarchitecture in the Framingham Osteoporosis Study. J Bone Miner Res. 2016 Aug 3. doi: 10.1002/jbmr.2931. [Epub ahead of print] PMID: 27487454

2. Another area of my research focuses on the relation between bone mineralization and the development of vascular calcification. I developed a radiographic index to grade the severity of aortic calcification using either radiographs or images from dual energy x-ray absorptiometry (DXA). Based on work that I have done, one of the manufacturers of DXA equipment received FDA approval to include the grading of vascular calcification to their software. This research focus has also enabled several junior faculty who I have mentored to extend my work as part of their own research. I have also worked with a pharmaceutical company as part of their FDA filing, to review serial radiographs for aortic calcification as part of a randomized controlled trial of denosumab to treat osteoporosis. The methodology has been used around the world to classify vascular calcification and study its etiology.
    a. Kauppila LI, Polak J, Cupples LA, Hannan MT, **Kiel DP**, Wilson PWF. New indices to classify location, severity and progression of calcific lesions in the abdominal aorta: a 25-year follow-up study. Atherosclerosis 1997;132(2):245-50. PMID: 9242971 PMCID: N/A
    b. **Kiel DP**, Kauppila LI, Cupples LA, Hannan MT, O'Donnell CJ, Wilson PW. Bone loss and the progression of abdominal aortic calcification over a 25 year period: The Framingham Heart Study. Calcif Tissue Int. 2001;68(5):271-6. Erratum in: Calcif Tissue Int. 2004;74(2):208. PMID: 11683533 PMCID: N/A
    c. Schousboe JT, Taylor BC, **Kiel DP**, Ensrud KE, Wilson KE, McCloskey EV. Abdominal aortic calcification detected on lateral spine images from a bone densitometer predicts incident myocardial infarction or stroke in older women. J Bone Miner Res. 2008;23(3):409-16. PMID: 17956153 PMCID: N/A
    d. Samelson EJ, Miller PD, Christiansen …Cheung AM, Franchimont N, **Kiel DP**. RANKL inhibition with denosumab does not influence 3-year progression of aortic calcification or incidence of adverse cardiovascular events in postmenopausal women with osteoporosis and high cardiovascular risk. J Bone Miner Res. 2014 Feb;29(2):450-7. doi: 10.1002/jbmr.2043. PMID:23873632 PMCID: PMC3946983.

3. As the PI of the Framingham Osteoporosis Study, I directed the development of a research group that became one of the foremost U.S. genetic epidemiology groups studying musculoskeletal phenotypes. We began with investigations of candidate gene associations with BMD, expanded to describe gene by environment interactions (e.g., interactions between the *MTHFR* C677T and folate, variants in the LRP5 gene and physical activity, and variants in the *PPARG* and dietary fat intake), performed linkage analyses and progressed onto large scale genome wide association studies in large consortia that are now moving into targeted sequencing, whole exome sequencing, and whole genome sequencing.
    a. Ackert-Bicknell CL, Demissie S, Marín de Evsikova C, Hsu YH, DeMambro VE, Karasik D, Cupples LA, Ordovas JM, Tucker KL, Cho K, Canalis E, Paigen B, Churchill GA, Forejt J, Beamer WG, Ferrari S, Bouxsein ML, **Kiel DP**, Rosen CJ. PPARG by dietary fat interaction influences bone mass in mice and humans. J Bone Miner Res. 2008;23(9):1398-408. PMID: 18707223 PMCID: PMC2683155
    b. Estrada K, Styrkarsdottir U,… **Kiel DP**, Rivadeneira F. Genome-wide meta-analysis identifies 56 bone mineral density loci and reveals 14 loci associated with risk of fracture. Nat Genet. 2012;44(5):491-501. PMID: 22504420 PMCID: PMC3338864 NIHMS: 364577
    c. Kwan JS, Hsu YH, Cheung CL, Dupuis J, Saint-Pierre A, Eriksson J, Handelman SK, Aragaki A, Karasik D, Pramstaller PP, Kooperberg C, Lacroix AZ, Larson MG, Lau KS, Lorentzon M, Pichler I, Sham PC, Taliun D, Vandenput L, **Kiel DP**, Hicks AA, Jackson RD, Ohlsson C, Benjamin EJ, Kung AW. Meta-analysis of genome-wide association studies identifies two loci associated with circulating osteoprotegerin levels. Hum Mol Genet. 2014 Jul 30. pii: ddu386. [Epub ahead of print] PMID: 25080503 [PubMed - in process]
    d. Zheng HF, Forgetta V, Hsu YH, Estrada K, …, Soranzo N, Durbin R, Wilson SG, Ntzani EE, Brown MA, Stefansson K, Hinds DA, Spector T, Cupples LA, Ohlsson C, Greenwood CM; UK10K Consortium, Jackson RD, Rowe DW, Loomis CA, Evans DM, Ackert-Bicknell CL, Joyner AL, Duncan EL, **Kiel DP**, Rivadeneira F, Richards JB. Nature. 2015 Oct 1;526(7571):112-7. doi: 10.1038/nature14878. Epub 2015 Sep 14. PMID: 26367794 PMCID: PMC4755714

4. Another major focus of my work has been the testing of interventions to prevent falls and fractures in older individuals. As such, I have led single site and multi-center randomized, placebo-controlled clinical trials that recruited seniors from a variety of settings including long term care and community settings. These trials have included the use of vitamin D to prevent falls, which has contributed to the understanding of dosing of vitamin D to prevent falls in the most vulnerable seniors, use of hip protectors to prevent fractures in nursing home residents, and most recently, the efficacy of low magnitude mechanical stimulation to enhance bone density.
    a. Broe, KE, Chen TC, Weinberg J, Bischoff-Ferrari HA, Holick MF, **Kiel DP**. A higher dose of vitamin D reduces the risk of falls in nursing home residents: A randomized, multiple-dose study. J Am Geriatr Soc. 2007;55(2):234-39. PMID: 17302660 PMCID: N/A
    b. **Kiel DP**, Magaziner J, Zimmerman S, Ball L, Barton BA, Brown KM, Stone JP, Dewkett D, Birge SJ. Efficacy of a hip protector to prevent hip fracture in nursing home residents: the HIP PRO randomized controlled trial. JAMA. 2007;298(4):413-22. PMID: 17652295 PMCID: N/A
    c. **Kiel DP**, Hannan MT, Barton BA, Bouxsein ML, Sisson E, Lang T, Allaire B, Dewkett D, Carroll D, Magaziner J, Shane E, Leary ET, Zimmerman S, Rubin CT. Low-Magnitude Mechanical Stimulation to Improve Bone Density in Persons of Advanced Age: A Randomized, Placebo-Controlled Trial. J Bone Miner Res. 2015 Jul;30(7):1319-28. doi: 10.1002/jbmr.2448. PMID: 25581217 PMCID: PMC4834704

5. The last area of research contributions is in the area of accidental falls. Early in my career I performed studies of risk factors and outcomes of falls in older adults. Based on my expertise, I have been writing the "falls" chapters for multiple textbooks, including the Geriatric Review Syllabus, UpToDate, and the major Osteoporosis textbook in the field. Later I went on to study fall prevention (see above vitamin D intervention trial by Broe., et al.) I was a key investigator in the MOBILIZE Boston Study, which assembled a population based cohort from the Greater Boston area, and characterized novel risk factors for falls.
    a. Kiely DK, **Kiel DP**, Burrows AB, Lipsitz LA. Identifying nursing home residents at risk for falling. J Am Geriatr Soc 1998;446(5):551-5. PMID: 9588366 PMCID: N/A
    b. Leveille SG, Jones RN, Kiely DK, Hausdorff JM, Shmerling RH, Guralnik JM, **Kiel DP**, Lipsitz LA, Bean JF. Chronic musculoskeletal pain and the occurrence of falls in an older population. JAMA. 2009;302(20):2214-21. PMID: 19934422 PMCID: PMC2927855 NIHMS: 218458
    c. Kelsey JL, Berry SD, Procter-Gray E, Quach L, Nguyen US, Li W, **Kiel DP**, Lipsitz LA, Hannan MT. Indoor and outdoor falls in older adults are different: the maintenance of balance, independent living, intellect, and zest in the Elderly of Boston Study. J Am Geriatr Soc. 2010;58(11):2135-41. PMID: 20831726 PMCID: PMC2975756 NIHMS: 222890
    d. Berry SD, Placide SG, Mostofsky E, Zhang Y, Lipsitz LA, Mittleman MA, **Kiel DP**. Antipsychotic and Benzodiazepine Drug Changes Affect Acute Falls Risk Differently in the Nursing Home. J Gerontol A Biol Sci Med Sci. 2016 Feb;71(2):273-8. doi: 10.1093/gerona/glv091. Epub 2015 Aug 5. PMID: 26248560 PMCID: PMC4881828 [Available on 2017-02-01]

Complete List of Published Work in MyBibliography: http://www.ncbi.nlm.nih.gov/myncbi/ douglas.kiel.1/ bibliography/40374222/public/?sort=date&direction=ascending

D. Additional Information: Research Support

Ongoing Research Support

NIH/NIAMS R01AR061445 (Kiel) 08/06/18 – 05/31/22

The Gut Microbiome and Bone Microarchitecture

This project will determine the association between 16S rRNA taxonomic profiles and whole metagenomes of the gut microbiome and measures of bone density, architecture and strength measured using HR-pQCT. It will test for associations between bone microarchitecture measures, diet, and microbiome taxonomies, and will interrogate the *microbiome metabolic potential* in relation to bone metabolism using newly developed analytic tools. Measurement markers of inflammation will be used to assess their potential mediation of the association between the microbiome and bone.

NIH/NIA R01 AG045441 (Berry) 07/01/19 – 06/30/23

A Clinical Prediction Tool to Guide Treatment of Osteoporosis in the Nursing Home

The purpose of this project is to develop a screening tool for osteoporosis and to use the screening tool to determine a threshold at which osteoporosis medications prevent fractures.

Role: Co-Investigator

NIH/NIA R01 AG041398 (Kiel) 06/01/15 – 05/31/20
Risk Factors for Age Related Bone Loss
Based on the growing epidemic of obesity, and conflicting data regarding the role of visceral adiposity on musculoskeletal health, in this continuation of the Framingham Osteoporosis Study, we will determine the role of visceral adipose tissue on BMD, microarchitecture, and strength, as well as on muscle density, and fracture.
Role: Principal Investigator

1R01AG051647 (Binder) 09/15/17 – 05/31/22
Combining Testosterone Therapy and Exercise to Improve Function Post Hip Fracture
This is a 3-group, multi-center, randomized, placebo-controlled, double-blinded, parallel group clinical trial in frail elderly female hip fracture patients to compare effects of supervised exercise training (ET) alone, ET combined with T therapy (ET+T) and no ET with placebo T treatment to ascertain the incremental impact of adding T to ET
Role: Co-Investigator

NIH/NIA U24 AG051129 (Cummings) 9/15/15 – 5/30/20

The goal of this project is to enable biologically meaningful connections to be drawn between genetic variants associated with longevity and healthy lifespan and molecular factors whose manipulation, potentially via pharmacological agents, could impact sustained health into old age.
Role: Co-investigator

NIH/NIA P30 AG031679 (Bhasin) 07/01/16 – 03/30/21

Boston OAIC: A Translational Approach to Function Promoting Therapies (FPT)
Within the OAIC's, the Pilot and Exploratory Studies Core provides seed funding, core support, and mentorship for innovative pilot research projects that generate data on the mechanisms of FPT action to facilitate more definitive mechanistic studies, feasibility data to guide efficacy trials, hypothesis generating or proof-of-concept exploratory studies and retrospective analysis of existing epidemiologic data that inform FPT interventions
Role: Co-investigator

Radius Health (Samelson) 01/01/19 – 12/31/20
Type 2 Diabetes and Fracture Risk
This grant funds the analysis of data from the Framingham Osteoporosis Study to determine the precise role of T2D on the risk for fragility fractures at various skeletal sites.
Role: Co-investigator

NIH/NIA R33 AG062018 (Kirkland) 01/01/19 – 12/30/23

Translational Geroscience Network
To test the hypothesis that clinical interventions targeting fundamental mechanisms of aging may delay, prevent, or treat age-related diseases and disabilities, this grant will establish an interdisciplinary Translational Geroscience Network to develop infrastructure to: 1) provide regulatory and data management support for new trials; 2) facilitate reverse translation through provision of biobanked samples and data to basic biology and epidemiology labs; and 3) develop materials allowing for the efficient scaling into a larger collaborative network
Role: Co-investigator

NIH/ NIAMS P30 AR072571 (Felson) 09/11/19 – 07/31/24

Boston University CCCR
The Boston University Core Centers for Clinical Research (CCCR) will serve as a central resource for clinical research focused mostly on the most common musculoskeletal disorders, osteoarthritis and gout and will also provide research resources for investigator based research in scleroderma, spondyloarthritis, musculoskeletal pain and osteoporosis.
Role: Co-Investigator

NIH/NIAMS R01 AR072199 (Hsu) 07/01/17 06/30/22
Identifying Osteoporosis Genes by Whole Genome Sequencing and Functional Validation in Zebra Fish
This grant will identify potential causal-variants and their targeted genes via fine-mapping on previously reported GWAS loci of osteoporosis; identifying novel rare variants and structural variations associated with osteoporosis via whole genome sequencing on 10,000 samples; as well as characterizing their biological function by CRISPR/Cas9 gene-editing zebrafish models.