BIOGRAPHICAL SKETCH

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NAME: Inker, Lesley Ann

eRA COMMONS USER NAME (credential, e.g., agency login): lstevens1

POSITION TITLE: Associate Professor of Medicine

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
McGill University, Montreal QC	B.A.	06/1994	Psychology
McMaster Medical School, Hamilton ON	M.D.	05/1997	Medicine
Tufts University, Boston MA	M.S.	05/2005	Clinical Care Research

A. Personal Statement

Lesley A. Inker, MD, MS is an Associate Professor of Medicine at TUSM and has been affiliated with the Division since 2003. Dr. Inker's primary research interests are in glomerular filtration rate (GFR) measurement and estimation, outcomes for clinical trials of kidney disease progression, and epidemiology and outcomes related to CKD. She is co-Director of Chronic Kidney Disease-Epidemiology (CKD-EPI), a research group funded by NIDDK (UO1DK053869, R01DK097020 and R01DK116790) to address critical issues in CKD epidemiology including development and validation of improved GFR estimating equations using endogenous filtration markers, estimating prevalence of CKD in the US, and evaluating albuminuria and GFR decline as surrogate markers for clinical trials in CKD. The National Kidney Foundation is now supporting CKD-EPI's work to advance the science of evaluation of endpoints. Dr. Inker is the principal investigator or co-investigator in several projects funded by the NIH or industry to measure GFR in multiple clinical sites, and is currently the co-principal investigator of the "Medication Use and Adverse Events in CKD" (R01DK115534), co-investigator in "CKD-Biomarkers Consortium" (U01DK085689), and site-PI for several pharmaceutical sponsored trials. She is the inaugural chair of the first nationwide kidney disease registry, the National Kidney Foundation's Patient Network. She is an active in public health initiatives related to CKD and has worked with both the National Kidney Disease Education Program (NKDEP) of the NIDDK and National Kidney Foundation (NKF) on several issues including implementation of GFR estimates in the United States. She is a member of NKF-American Society of Nephrology (ASN) Task Force on Reassess the Inclusion of Race in Diagnosing Kidney Diseases.

Ongoing projects that I would like to highlight include:

1R01DK116790 12/15/20-11/30/24
NIH/NIDDK
Improving Kidney Function Assessment in Health and Disease
The current project will fill this important gap in knowledge by developing a simple method to estimate kidney function from markers that can be easily measured from a single blood draw and that is more accurate than current estimates for all people across the continuum of health and disease
Role: PI

B. Positions, Scientific Appointments, and Honors

Professional Experience

2012- Director, Kidney and Blood Pressure Center, Division of Nephrology, Tufts Medical Center
2007- Director, Quality Improvement, Division of Nephrology, Tufts Medical Center
2006- Scientist, Human Nutrition Research Center on Aging at Tufts University, Boston, MA

2005-12 Program Director, Implementation, National Kidney Foundation Center for Clinical Practice Guideline Development and Implementation at Tufts Medical Center, Boston, MA
2004- Attending nephrologist, Tufts Medical Center, Boston MA
2003-04 Research Fellowship, Tufts Medical Center, Boston, MA
2002 Research Fellowship, University of British Columbia, Vancouver, BC
2000-02 Nephrology Fellowship, University of British Columbia, Vancouver, BC
1997-00 Medical Residency, Internal Medicine, McMaster University, Hamilton, ON

Other Experience and Professional Memberships

2020-21 ASN-NKF Task Force on reassessment of race in diagnosis of CKD
2019- Chair, Steering Committee NKF CKD Patient Network
2009-13 NIDDK: Vascular Access Consortium External Advisory Committee, member
2008-13 NIDDK: United States Renal Data System (USRDS) External Advisory Committee, member
2009-12 Renal Working Group for development of 11th version of the International Classification of Diseases, World Health Organization, Co-chair.
2008-09 NKDEP Workgroup on Estimation of kidney function for Medication Dosage Prescriptions, Chair
2008-18 National Kidney Disease Education Program, Laboratory Work Group, member
2006-11 Clinical Oversight Committee, Kidney Early Education Program (KEEP), National Kidney Foundation, Chair
2004- National Kidney Foundation, member
2000- American Society of Nephrology, member**.**

Honors and Awards

2020 American Society of Nephrology Midcareer Distinguished Researcher Award
2018 National Kidney Foundation Garabed Eknoyan Award

C. Contributions to Science

1. Assessment of Kidney Function: Clinical assessment of kidney function is part of routine medical care for adults. Most clinical laboratories now report an estimated glomerular filtration rate (eGFR) when serum creatinine is measured. GFR estimates are more accurate and more useful than the serum concentrations of filtration markers alone because they take into account clinical and demographic factors that are associated with their non-GFR determinants. Since 2003, I have been engaged in developing and implementing more accurate GFR estimates that can be used in clinical practice in the United States and worldwide. I am the Director of Data and Clinical Coordination for the Chronic Kidney Disease Epidemiology Collaboration (UO1 DK 053869, R01 DK097020, and R01DK116790). Through this work, we acquired datasets with measured GFR and samples to measure or calibrate creatinine or cystatin C, and novel markers such as beta trace protein and beta-2-microglobulin, newly discovered metabolites, and developed CKD-EPI GFR estimating equations. The creatinine and cystatin C equations are recommended by Kidney Disease International Global Outcomes (KDIGO) guidelines as being the most accurate GFR estimating equations. Our team recognizes that the equations are limited by imprecision and challenges in their use particularly in the chronically ill and racial and ethnic groups. A current focus for analyses use of the coefficient for black race in GFR estimation.

a. **Inker LA**, Schmid CH, Tighiouart H, Eckfeldt JH, Feldman HI, Greene T, Kusek JW, Manzi J, Van Lente F, Zhang YL, Coresh J, Levey AS; CKD-EPI Investigators. Estimating glomerular filtration rate from serum creatinine and cystatin C. N Engl J Med. 2012 Jul 5;367(1):20-9. PubMed PMID: 22762315; PubMed Central PMCID: PMC4398023.
b. Freed TA, Coresh J, **Inker LA,** Toal DR, Perichon R, Chen J, Goodman KD, Zhang Q, Conner JK, Hauser DM, Kate E.T. Vroom, Oyaski ML, Wulff JE, Eiriksdottir G, Gudnason V, Torres VE, Ford LA, and Levey AS. "Validation of a Metabolite Panel for a More Accurate Estimation of Glomerular Filtration Rate Using Quantitative LC-MS/MS." Clinical Chemistry 65, no. 3, 406-418. 2019 Mar. PMID: 30647123
c. **Inker LA,** Couture SJ, Tighiouart H, et al. A New Panel Estimated GFR, Including Beta-Microglobulin and Beta;-Trace Protein and Not Including Race, Developed in a Diverse Population. Am J Kidney Dis. 2020 Dec 07.On line ahead of print. PMID: 33301877
d. **Inker LA** Eneanya, NW; Coresh et al. New Creatinine- and Cystatin C–Based Equations to Estimate GFR without Race . N Engl J Med. 2021. 2021 Sept 23

e. Delgado, C, Baweja, M, Crews, D et al. A Unifying Approach for GFR Estimation: Recommendations of the NKF-ASN Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Disease. J Am Soc Neph 2021. Published on line ahead of print 21 Sept 23

2. Prevalence, complications and prognosis of CKD Chronic Kidney Disease is a public health problem, with an estimated prevalence of 10% in the United States and approximately equivalent numbers reported in other countries. CKD is defined by abnormalities of kidney structure and function that are present for 3 months or longer and its presence is associated with complications of CKD (e.g. anemia, mineral metabolism abnormities), progression to kidney failure, cardiovascular disease and mortality. I have been involved in studies to assess prevalence of CKD and its trends over time using data from the National Health and Nutrition Examination Survey (NHANES). I have also used NHANES as well as other studies to examine the prevalence of complications related to level of eGFR and albuminuria. I was involved in development and validation of the Kidney Failure Risk Equation (KFRE), which is available on smart phone and web based calculators. Finally, I am a member of the CKD-Prognosis Consortium, a research group, composed of investigators who share data for the purpose of a more comprehensive evaluation of the prognosis related to all aspects of CKD, including our publication describing the international validation of the KFRE and most recently adverse events and safety related to medication usage (R01DK115534)

a. Tangri N, Grams ME, Levey AS, et al. Multinational Assessment of Accuracy of Equations for Predicting Risk of Kidney Failure: A Meta-analysis. JAMA. 2016 Jan 12;315(2):164-174. Pubmed PMID: 26757465; PubMed Central PMCID: PMC4752167.
b. Grams ME, Yang W, Rebholz CM, Wang X, Porter AC, **Inker LA**, Horwitz E, Sondheimer JH, Hamm LL, He J, Weir MR, Jaar BG, Shafi T, Appel LJ, Hsu CY; CRIC Study Investigators. Risks of Adverse Events in Advanced CKD: The Chronic Renal Insufficiency Cohort (CRIC) Study. Am J Kidney Dis. 2017 Mar 30; Epub ahead of print. Pubmed PMID: 28366517. PMCID: PMC5572665.
c. Qiao, Y, Shin, J, Chen, TK, **Inker LA,** Coresh, J, Alexander, C, Jackson, J, Chang, A, Grams, ME. Association Between Renin-angiotensin System Blockade Discontinuation And All- cause Mortality Among People With Low Estimated Glomerular Filtration Rate. JAMA Internal Medicine. 2020 Mar 9PMID: 32150237
d. Shin JI, Sang Y, Chang AR, Dunning SC, Coresh J, **Inker LA,** Selvin E, Ballew SH, Grams ME. The FDA Metformin Label Change and Racial and Sex Disparities in Metformin Prescription among Patients with CKD. J Am Soc Nephrol. 2020, 31 (8) 1847-1858..PMID: 32660971

3. Novel Biomarkers for prognosis: Current biomarkers for CKD primarily consist of creatinine and urine albumin. These provide important information but do not convey all the information about nature, course and prognosis of CKD. I am a co-investigator in the CKD-Biomarker Consortium (CKD-BC, U01 DK085689, as a subcontract to Coresh PI at JHU). Through the first phase of that work, we performed a thorough evaluation of FGF-23, vitamin D, beta trace protein, cystatin C, and beta 2 microglobulin compared to creatinine for prognosis related to ESRD, CVD and mortality. Through CKD-BC, our team also performed proteomic discovery of novel blood based markers for CKD progression. These findings are currently being validated.

a. Sekula P, Goek ON, Quaye L, et al. A Metabolome-Wide Association Study of Kidney Function and Disease in the General Population. J Am Soc Nephrol. 2016 Apr;27(4):1175-1188. Pubmed PMID: 26449609; PubMed Central PMCID: PMC4814172
b. **Inker LA**, Coresh J, Sang Y, Hsu CY, Foster MC, Eckfeldt JH, Karger AB, Nelson RG, Liu X, Sarnak M, Appel LJ, Grams M, Xie D, Kimmel PL, Feldman H, Ramachandran V, Levey AS; CKD Biomarkers Consortium. Filtration Markers as Predictors of ESRD and Mortality: Individual Participant Data Meta-Analysis.Clin J Am Soc Nephrol. 2017 Jan 6;12(1):69-78. PMID: 28062677. PMCID: PMC5220652
c. Luo S, Coresh J, Tin A, Rebholz CM, Chen TK, Hayek SS, Tracy M, Lipkowitz MS, Appel LJ, Levey AS, Inker LA, Reiser J, Grams ME. “Soluble Urokinase-Type Plasminogen Activator Receptor in Black Americans with CKD.” Clinical Journal of the American Society Nephrology. 2018 June 14. [Epub ahead of print]. PMID: 29903900 PMCID: PMC6032570
d. Eriksen BO, Palsson R, Ebert N, Melsom T, van der Giet M, Gudnason V, Indridasson OS, Inker LA, Jenssen TG, Levey AS, Solbu MD, Tighiouart H, Schaeffner E. GFR in Healthy Aging: an Individual Participant Data Meta-Analysis of Iohexol Clearance in European Population-Based Cohorts. J Am Soc Nephrol. 2020 Jul;31(7):1602-1615

4. Surrogate markers for progression of CKD One of the major challenges with development of new therapies for kidney disease progression is the slow nature of the disease process. As such, trials to study drugs that decrease the outcome of kidney failure are long, require many patients or can only study patients in late stages of disease. Surrogate endpoints could facilitate trials of CKD progression if they can be measured prior to development of the hard clinical endpoint, or can be measured more precisely. As part of Chronic Kidney Disease Epidemiology Collaboration (UO1 DK 053869 and R01 DK097020), (CKD-EPI), we undertook an evaluation of early changes in proteinuria as a surrogate endpoint using pooled analysis of 32 trials. The results showed that in some circumstances, it would be possible to use proteinuria. We then went on and demonstrated that time to lesser declines in GFR and GFR slope are valid surrogate endpoint work. Ongoing work examines the association of the treatment effects on the two surrogates and their joint use to predict treatment effects on the clinical endpoint, which are key steps towards use of adaptive clinical trial designs. We are also working on development of novel methods to better define the validity of these results across subgroups of trials.

a. Greene T, Ying J, Vonesh EF, Tighiouart H, Levey AS, Coresh J, Herrick JS, Imai E, Jafar TH, Maes BD, Perrone RD, Del Vecchio L, Wetzels JFM, Heerspink HJL, **Inker LA**. Performance of GFR Slope as a Surrogate Endpoint for Kidney Disease Progression in Clinical Trials: A Statistical Simulation. J Am Soc Nephrol [published online: July 10, 2019]. 10.1681/ASN.2019010009 PMID:31292198
b. Heerspink HJL, Greene T, Tighiouart H, Gansevoort RT, Coresh J, Simon AL, Chan TM, Hou FF, Lewis JB, Locatelli F, Praga M, Schena FP, Levey AS, **Inker LA**; Chronic Kidney Disease Epidemiology Collaboration. “Change in albuminuria as a surrogate endpoint for progression of kidney disease: a meta-analysis of treatment effects in randomised clinical trials.” Lancet Diabetes Endocrinol 7, no. 2 (2019):128-139. PMID: 30635226.
c. **Inker LA**, Heerspink HJL, Tighiouart H, Levey AS, Coresh J, Gansevoort RT, Simon AL, Ying J, Beck GJ, Wanner C, Floege J, Li PK, Perkovic V, Vonesh EF, Greene T. GFR Slope as a Surrogate End Point for Kidney Disease Progression in Clinical Trials: A Meta-Analysis of Treatment Effects of Randomized Controlled Trials. J Am Soc Nephrol 2019 Sep;30(9):1735-1745 PMID:31292197
d. **Inker, LA,** Heerspink HJL, Tighiouart H. Association of Treatment Effects on Early Change in Urine Protein and Treatment Effects on GFR Slope in IgA Nephropathy: An Individual Participant Meta-analysis. Am J Kid Dis 2021Sept; 78 (3). P340-349.E1