BIOGRAPHICAL SKETCH

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NAME: Han, Ling

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

POSITION TITLE: Sr. Research Scientist

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
Jining Medical College, Jining, Shandong	OTH	01/1981	Medicine
Jining Medical College Affiliated Neuro-psychiatric Hospital, Jining, Shandong	Resident	08/1985	Psychiatry
Hunan Medical University, Changsha, Hunan	MDOT	08/1988	Psychiatry/Behavioral Medicine
University of Washington, Seattle, WA	Fellow	06/1995	Psychiatry/Anxiety & Depressive Disorders
National Institute of Mental Health, NIH, Bethesda, MD	Fellow	07/1997	Psychiatric epidemiology/ Seasonal affective disorders
McGill University, Montreal, Quebec	MS	05/2000	Epidemiology & Biostatistics
McGill University, Montreal, Quebec	PHD	12/2006	Epidemiology & Biostatistics

A. Personal Statement

With a unique background of an MD psychiatrist and PhD biostatistician, Dr. Han provides vital statistical support for several research projects at the Yale Program on Aging (POA) and the Veterans Administration (VA) Connecticut Healthcare Systems. He has a wealth of experience conducting longitudinal studies using generalized linear models, latent-class modeling and propensity score (PS) based causal analyses. In collaboration with both VA and non-VA investigators, to date he has published more than 70 scientific papers as the primary or a co-author. As a Co-Investigator & Biostatistician in a ongoing RO1 grant, Pain Care Quality and Integrated and Complementary Health Approaches (R01 AT008448, PI: Brandt, Kerns, Luther), Dr. Han plays vital statistical role in the development of PS model and pain care quality (PIQ) indices. Using preliminary EHR data collected for that RO1 grant, he developed a Propensity Score (PS) model of receiving complementary and integrative health approaches (CIH), and alternative PS-based causal approaches to test examine association between CIH exposure and chronic pain, including PS matching, inverse probability of treatment weighting and doubly robust de-confounding methods (Han et al. Pain Med 2019). Dr. Han has worked closely with Dr Fodeh and other team members to apply the tested methodologies to the hypothesis testing, including use of exploratory factor analysis to develop pain care quality indices (Luther et al. Pain 2022 *in press*). In another VHA-based study, he collaborated with Dr. Presley, currently an Assistant Professor in Ohio University Medical Oncology section, using multilevel logistic model to determine the impact of VHA facility-level concurrent care on changes in aggressive care practice at the end of life among veterans in late stage lung cancer (Presley et al, J Palliat Med 2020; 2022 *in press*). Recently in collaboration with Dr Gill and Dr Zang, Assistant Professor of Sociology at Yale University, to examine effects of neighborhood disadvantage on life expectancy beyond individual-level demographic and clinical factors (Gill TM et al 2021). In summary, Dr. Han has demonstrated record of successful and productive research as a senior medical scientist and biostatistician in areas of high relevance to the proposed grant application.

Ongoing projects particularly relevant to this grant application:

R01 AG17560
Role, Senior Biostatistician
09/01/05 □ 08/31/22
Epidemiology of Disability and Recovery in Older Persons
With over 20 years of monthly outcome data, the PEP study has been a platform for testing and expanding complex longitudinal statistical models in geriatrics, critical care, and surgical medicine, with analytic venues being recently extended to measure and assess neighborhood disadvantage as novel social determinant of health beyond individual characteristics and temporal dimension.

VA HSR&D-IIR 19-378 (Zeng, Goulet, PIs)
Role: Senior Biostatistician
06/2021 - 05/2024
Assessing and Reducing Opioid Misuse Among Veterans in VA and Non-VA Systems: Coordination of Fragmented Care This project will assess the impact of dual sources of care on receipt of opioid medications among veterans in VHA care using Natural Language Processing and involves using multi-level model or generalized estimating equation (GEE) model to address clustering among patient, physicians and facilities.

VA HSR&D-VA RIVR (Haskell, Brandt, PIs)
Role: Statistician
07/01/18-10/30/23
RIVR Study of the complexity of women veterans and development of methods to assess and intervene early, with several component projects involving use of multilevel models and GEE (e.g., Bernstein et al, Racial and Rural Disparities In COVID-19 Vaccination Uptake in a National Sample of Veterans, an abstract accepted by ATS 2022).

Citations: The first two of these original reports are co-authored with Dr. Presley using analytical approaches similar to those proposed in the first aim, a random-intercept multi-level logistic model. The third is a recent paper using VHA HER data in which Dr Fodeh and I worked closely on post-hoc evaluation of pain care quality index. The fourth is an analysis of the PEP study that used intensive, longitudinal cohort data incorporated with multi-state life table approach to derive life expectancy for participants aggregated to neighborhood units, followed by bootstrapping of 95% confidence intervals. The concept of augmenting person-level data to address substantive “bigger” population impact and the use of bootstrapping to determine uncertainty of such impact are akin to the current proposal.

1. Presley CJ, Kaur K, **Han L**, Soulos PR, Zhu W, Corneau E, O'Leary JR, Chao H, Shamas T, Rose M, Lorenz K, Levy CR, Mor V, , Gross CP. Aggressive End-of-Life Care in the Veterans Health Administration vs. Fee-for-Service Medicare among Patients with Advanced Lung Cancer. J Palliat Med 2022 *in press*).
2. Presley CJ, **Han L**, O'Leary JR, Zhu W, Corneau E, Chao H, Shamas T, Rose M, Lorenz K, Levy CR, Mor V, Gross CP. J Palliat Med 2020;1038-1044. http://doi.org/10.1089/jpm.2019.0485
3. Luther S, Finch DK, Bouayad L, McCart J, **Han L**, Dobscha SK, Skanderson M, **Fodeh SJ**, Hahm B, Lee A, Goulet JL, Brandt C, Kerns RD. Measuring Pain Care Quality (PCQ) in the Veterans Health Administration (VHA) Primary Care Setting Pain 2022 *in press*
4. Gill TM, Leo-Summers L, Murphy TE, Gahbauer EA, Festa N, Zang EX, Falvey JR, **Han L**. Neighborhood Disadvantage and Functional Well-being among Community-living Older Persons. JAMA Intern Med 2021;181(10):1297–1304. doi:10.1001/jamainternmed.2021.4260

B. Positions, Scientific Appointments, and Honors

2014 - present	Sr. Research Scientist, Yale School of Medicine Department of Internal Medicine, New Haven, CT
2011 - 2014	Research Scientist, Yale School of Medicine Department of Internal Medicine, New Haven, CT
2008 - 2011	Sr. Epidemiologist & Biostatistician/Manager, Yale School of Medicine Department of Internal Medicine, New Haven, CT

2001 - 2008	Epidemiologist & Biostatistician, Yale School of Medicine Department of Internal Medicine, New Haven, CT
1999 - 2001	Research Associate, McGill University St-Mary's Hospital, Montreal
1997 - 1999	Research Fellow, McGill University Dept. Psychiatry, Montreal
1995 - 1997	Visiting Associate, National Institutes of Health/NIMH Section on Seasonal Affective Disorder and Light Therapy, Bethesda, MD
1993 - 1994	Deputy-chief Psychiatrist , Nanjing Medical University Affiliated Brain Hospital, Nanjing
1990 - 1994	Lecturer, Nanjing Medical University Faculty of Psychiatry& Mental Health, Nanjing
1988 - 1994	Researcher, Nanjing Neuropsychiatric Research Institute, Nanjing
1988 - 1993	Visiting Psychiatrist, Nanjing Medical University Affiliated Brain Hospital, Nanjing
1981 - 1985	Resident Psychiatrist, Jining Medical College Affiliated Psychiatric Hospital, Jining, Shandong, China

Honors

1991	The WHO Awards for Chinese Young Professionals in Neurology and Mental Health, WHO
1992	The SHANGHAI-RHONE-POULENC Award for Outstanding Research Paper , SHANGHAI-RHONE-POULENC Foundation
1993	The WHO Awards for Chinese Young Professionals in Neurology and Mental Health, WHO
1994	International Medical Scholar Program (IMSP) Fellowship, ECFMG
1997	The McGill-Novartis Research Fellowship in Geriatric Psychiatry, Novartis
1999	American Psychiatric Association Colloquium Fellowship, American Psychiatric Association
2009	Alzheimer's Association ICAD Travel Fellowship, Alzheimer's Association

Other Experience and Professional Memberships

1990 - 1994	Member, Chinese Medical Association Psychiatric Society
1990 - 1994	Member, Chinese Psychological Association
1995 - 1997	Corresponding Member, American Psychiatric Association
2010 - present	Member, Gerontological Society of America

C. Contributions to Science

1. **Expertise and innovation in modeling natural courses of cognitive aging and dementia**. In dementia clinics and anti-dementia drug trials, a common "Annual Cognitive Change" (ARC) has since been hopped for as a gold standard for measuring and distinguishing between normal aging and dementia. In 2000, I collaborated with McGill colleagues and developed a common ARC estimate for Alzheimer's disease (AD) on the most widely used cognitive screening tool, the Mini Mental State Examination (MMSE), using meta-regression and mixed-effect model. That paper was selected among top-cited papers in International Psychogeriatrics in 2009 and cited 222 times by 6/30/2022 (http://www.alzheimersinnovation.com). The synthesized ARC estimate has been used in several clinical trials of Alzheimer's disease. After joining Yale POA, I collaborated with other Yale PEP colleagues and used a group-based trajectory model to "phenotype" cognitive aging among community-dwelling older persons against common functional and institutionalization outcomes defined for AD patients. That study was invited to present as a GSA delegated speech at the 2014 Chinese Congress on Gerontology and Health Industry.

    a. ***Han L**. Top cited papers in International Psychogeriatrics: 6c. Tracking cognitive decline in Alzheimer's disease using the Mini-mental State Examination: a meta-analysis ("mini" is not necessarily trivial!). Int Psychogeriatr. 2009 Dec;21(6):1037-40. PubMed PMID: 19747422.
    b. **Han L**, Gill TM, Jones BL, Allore HG. Cognitive Aging Trajectories and Burdens of Disability, Hospitalization and Nursing Home Admission Among Community-living Older Persons. J Gerontol A Biol Sci Med Sci. 2016 Jun;71(6):766-71. doi:10.1093/gerona/glv159. PubMed PMID: 26511011, PMCID:PMC4888384
    c. Liu Z, **Han L**, Gahbauer EA, Allore HG, Gill TM. Joint trajectories of cognition and frailty and associated burden of patient-reported outcomes. JAMDA 2018;19(4):304-309.

d. MacNeil Vroomen JL, Han L, Monin JK, Lipska KJ, Allore HG. Diabetes, Heart Disease, and Dementia: National Estimates of Functional Disability Trajectories. J Am Geriatr Soc. 2018;66(4):766-772. doi: 10.1111/jgs.15284. PMID: 29521414; PMCID: PMC5906138.

2. **Expertise and innovation in risk assessments associated with anticholinergic medications.** "Central cholinergic deficiency" has long been postulated as a potential neurotransmission mechanism for Alzheimer's Disease (AD). To empirically test this hypothesis using clinical data, I collaborated with McGill colleagues and developed a clinician-rated anticholinergic score (CR-ACHS) to assess the cumulative anticholinergic drug exposure and demonstrated its dose-response relationship with delirium symptoms in medical patients. Since its publication in 2001, the study has inspired research interests to cognitive risk of anticholinergic medications (*538 citations by 6/26/2022*) and proliferation of a variety of subsequent anticholinergic risk scales in the field. In 2008, in collaboration with Yale and VHA colleagues, I updated the CR-ACHS and examined its association with chronic cognitive dysfunction in community-dwelling older Veterans (*244 citations by 6/26/2022*). That study raised awareness of medical and general communities to a broader array of common medications used in elderly and was featured on Yale Bulletin and several mass media websites, including the Tangled Neuron (www.tangledneuron.info), Medicaltribute (www.medicaltribune.com) and Reuters Heath-Doctors' Channel (www.thedoctorschannel.com/video/1227.html?specialty=17).

   a. **Han L**, McCusker J, Cole M, Abrahamowicz M, Primeau F, et al. Use of medications with anticholinergic effect predicts clinical severity of delirium symptoms in older medical inpatients. Arch Intern Med. 2001 Apr 23;161(8):1099-105. PubMed PMID: 11322844. PMCID: N/A
   b. **Han L**, Agostini JV, Allore HG. Cumulative anticholinergic exposure is associated with poor memory and executive function in older men. J Am Geriatr Soc. 2008 Dec;56(12):2203-10. PubMed PMID: 19093918; PubMed Central PMCID: PMC3952110.
   c. **Han L,** McCusker J, Cole MG, Capek R, Abrahamowicz M. Antidepressant use and cognitive functioning in older medical patients with major or minor depression: a prospective cohort study with database linkage. J Clin Psychopharm. 2011;31:429-35. PMCID: PMC3558972
   d. Nishtala PS, Allore H, **Han H**, Jamieson HA, Hilmer SN, Chyou T. Impact of Anticholinergic Burden on Cognitive Performance: A Cohort Study of Community-Dwelling Older Adults. J Am Med Dir Assoc. 2020;21(9):1357–1358.e3. doi:10.1016/j.jamda.2020.03.027.

3. **Expertise and innovation with quasi-experimental design and analyses**. Selection and confounding by indications post huge challenge to observational studies of effectiveness of medical interventions. In this field, I used structural equation modeling to address confounding by indication and applied it to establish potentially "causal" relationships between depression pathology and cognitive impairment, which is often claimed as a side effect of antidepressant treatment. Using data from a delirium trial in ICU units, I proposed and tested a self-matching alternative to remove stable baseline confounding while simultaneously control for time-varying ICU confounding and indications at admissions. More recently, I worked with VA and Yale colleagues under a NIH funded RO1 (PI: Dr Kerns) to develop and validate propensity score-based quasi-experimental methods for evaluating real-world effectiveness of comprehensive and integrative health (CIH) approaches on chronic pain and the Pain Care Quality. In this study, I developed a "hybrid" approach of propensity-score matching IPTW weighting to address both selection and confounding biases.

   a. **Han L**, Kim N, Brandt C, Allore HG. Antidepressant use and cognitive deficits in older men: addressing confounding by indications with different methods. Ann Epidemiol. 2012 Jan;22(1):9-16. PubMed PMID: 22037381; PubMed Central PMCID: PMC4054866.
   b. Tinetti ME, **Han L**, Lee DS, McAvay GJ, Peduzzi P, Gross CP, Zhou B, Lin H. Antihypertensive medications and serious fall injuries in a nationally representative sample of older adults. JAMA Intern Med. 2014 Apr;174(4):588-95. PubMed PMID: 24567036; PubMed Central PMCID: PMC4136657.
   c. **Han L**, Pisani MA, Araujo KL, Allore HG. Use of Self-Matching to Control for Stable Patient Characteristics While Addressing Time-Varying Confounding on Treatment Effect: A Case Study of Older Intensive Care Patients. Int J Stat Med Res. 2016;5:8-16. PubMed PMID: 27123153; PubMed Central PMCID: PMC4844076.
   d. **Han L**, Goulet J, Skanderson M, Bathulapalli H, Luther SL, Kerns RD, Brandt C. Evaluation of

Complementary and Integrative Health Approaches Among US Veterans with Musculoskeletal Pain Using Propensity Score Methods. Pain Med 2019; 20: 90–102. doi: 10.1093/pm/pny027. PubMed PMID: 29584926

4. **Expertise in advanced statistical modeling of functional aging.** Human aging and disablement process is dynamic and heterogenous. In collaborating with fellow biostatisticians and Dr Gill and other clinician researchers, both inside and outside of Yale, I utilized and extended advanced statistical techniques to address clinically important yet methodologically challenging research questions about the course, risk factor, and recovery of functional disability, including general and generalized linear regression models, state transition models, and competing risk models. In the field of latent class modeling, I have gained extensive expertise with applying and adapting the techniques to analyze clinical and EHR data. I have also mentored or provided key statistical guidance for post-doctoral fellows, visiting scholars and junior faculties.

   a. Gill TM, Gahbauer EA, **Han L**, Allore HG. Trajectories of disability in the last year of life. N Engl J Med. 2010;362(13):1173-80. PubMed PMID: 20357280; PubMed Central PMCID: PMC2877372
   b. **Han L**, Allore H, Murphy T, Gill T, Peduzzi P, Lin H. Dynamics of functional aging based on latent-class trajectories of activities of daily living. Ann Epidemiol. 2013;23(2):87-92. PubMed PMID: 23305692; PubMed Central PMCID: PMC3558979c.
   c. Dharmarajan K, **Han L**, Gahbauer EA, Leo-Summers LS, Gill TM. Disability and Recovery After Hospitalization for Medical Illness Among Community-Living Older Persons: A Prospective Cohort Study. J Am Geriatr Soc 2020;68(3):486-495. doi: 10.1111/jgs.16350. Epub 2020 Feb 21. PubMed PMID: 32083319.
   d. Nagurney JM, **Han L**, Leo-Summers L, Allore HG, Gill TM. Risk Factors for Disability After Emergency Department Discharge in Older Adults. Acad Emerg Med. 2020 Dec;27(12):1270-1278. doi: 10.1111/acem.14088. Epub 2020 Aug 8. PMID: 32673434; PMCID: PMC7749835.

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