
BIOGRAPHICAL SKETCH

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NAME: Ngo, Long H

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

POSITION TITLE: Associate Professor of Medicine (Biostatistics), Harvard Medical School

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 |
|---|---------------------------|----------------------------|----------------------------------|
| California State University, Fullerton CA | B.S. | 05/1987 | Computer Science and Mathematics |
| University of California, Berkeley CA | M.A. | 05/1989 | Statistics |
| University of California, Berkeley CA | Ph.D. | 05/2000 | Biostatistics |
| Harvard University, Boston, MA | Fellowship | 09/2004 | Biostatistics |

A. Personal Statement

I have over twenty-five years of experience working as a statistician on numerous collaborative projects with investigators in diverse clinical areas. These include serving as primary biostatistical co-investigator for several of Dr. Edward Marcantonio's projects, including the SAGES Biomarker Discovery project, the Multi-OMICS of delirium, and the newly funded READI: Researching Efficient Approaches to Delirium Identification. I have also been very pleased to serve as biostatistical co-mentor in Dr. Marcantonio's K24-funded Mentoring Program over the past six years. Together, we have co-mentored several fellows and junior faculty trainees who have made high impact contributions to aging research. I look forward to continuing these activities in the renewal period of his K24 program, during which I will continue to devote 5% effort to provide study design and statistical analysis consultation for Dr. Marcantonio's trainees in patient-oriented aging research. Below are several recent representative publications with Dr. Marcantonio's mentees:

- a. Anderson CP, **Ngo L**, Marcantonio ER. Complications in post-acute care are associated with persistent delirium. *J Am Geriatr Soc.* 2012 Jun;60(6):1122-7. PMC3374879.
- b. Herzig SJ, Rothberg MB, Cheung M, **Ngo LH**, Marcantonio ER. Opioid Utilization and Opioid-Related Adverse Events in Non-Surgical Patients in U.S. Hospitals. *J Hosp Med.* 2014; 9: 73-81. PMC3976956
- c. Kuczmaraska A, **Ngo LH**, Guess J, O'Connor MA, Branford-White L, Palihnich K, Gallagher J. Marcantonio ER. Detection of Delirium in Hospitalized Older General Medicine Patients: A comparison of the 3D-CAM and CAM-ICU. *J Gen Int Med.* 2016. Mar; 31(3):297-303. PMC4762827.
- d. Cooper, Z, Rogers SO, **Ngo LH**, Guess J, Schmitt EM, Jones RN, Ayers DK, Walston JD, Gill TM, Inouye SK*, Marcantonio ER* (*co-last). A comparison of frailty measures as predictors of outcomes after orthopedic surgery. *J Am Geriatr Soc.* 2016. Nov 1. doi: 10.1111/jgs.14387. [Epub ahead of print]

B. Positions and Honors

1987-1989 Graduate Student Instructor, Department of Statistics, University of California, Berkeley, CA
1988 Programmer Analyst, IBM Almaden Research Center, San Jose, CA
1989-1992 Statistician, Veterans Administration Medical Center, San Francisco, CA
1990-1999 Director of Biostatistics, Ischemia Research, San Francisco, CA
1999-2001 Senior Data Consultant, Kaiser Permanente, Oakland, CA
1997, 2001 Lecturer, School of Public Health, University of California, Berkeley, CA
2002-2004 Fellow, Harvard University Department of Biostatistics, Boston, MA
2004-2005 Instructor in Medicine, Harvard Medical School, Boston, MA
2005-2013 Assistant Professor in Medicine (Biostatistics), Harvard Medical School, Boston, MA
2013- Associate Professor in Medicine (Biostatistics), Harvard Medical School, Boston, MA

Awards and Professional Services and Memberships

| | |
|-----------|---|
| 1983-1987 | Dean's List in Computer Science and Mathematics |
| 1987 | Chairman's 1 st - Rank Scholastic Achievement Award in Mathematics |
| 1987 | Member, Golden Key National Honor Society |
| 2000 | SAS Certified Professional |
| 1998-2001 | Member, SAS Institute's Quality Partner |
| 2002 | Invited panel member, Joint Vietnam-US Scientific Conference on Human Health and Environmental Effects of Agent Orange/Dioxin Hanoi, Vietnam |
| 2003- | Member, American Statistical Association |
| 2004-2007 | Member, Editorial Review Board, Journal of Clinical Endocrinology and Metabolism |
| 2004 | Best Statistical Paper Award, SUGI Conference, Montreal, Canada |
| 2005 | Member Study Review Panel, Health Effects Institute, Boston, MA |
| 2005- | Reviewer, Journal of the American Statistical Association (JASA), Journal of Population Health Metrics, Radiology, Journal of Biopharmaceutical Statistics, Journal of Thoracic Imaging, Atmospheric Environment, International Journal of Cancer, Statistics in Medicine |
| 2007- | Committee member, American Statistical Association (ASA) Ambassador Program with Vietnam |
| 2007-2014 | Member and Chair, American Statistical Association Committee on Statistics and Disability |
| 2010- | Associate Editor, Journal of International Statistics and Management Systems |
| 2010- | Co-Director of Biostatistics, Division of General Medicine and Primary Care, BIDMC |
| 2011- | Associate Director of Biostatistics, Delirium Program Project Core, Hebrew Senior Life |
| 2012 | Member Study Review Panel, Harvard Catalyst Advanced Imaging Pilot Research Grants |
| 2012 | Editors' Recognition Award for Distinction in Reviewing, Journal of Thoracic Imaging |
| 2013 | Department of Medicine Mentorship of Resident Research Award |
| 2013 | Study Review Section and selected to represent review panel for site visit for Disability Statistics and Demographics Grant Review, United States Department of Education, National Institute on Disability and Rehabilitation Research (NIDRR). |
| 2014 | Sherman Award for Excellence in Patient Engagement Contribution to the OpenNotes Collaborative |
| 2014- | Member, Editorial Review Board, E-Health Telecommunication Systems and Networks |
| 2015 | Beth Israel Deaconess Medical Center General Medicine Service Award |
| 2015 | First Prize, Oral Presentation, The 7 th Conference on Public Health of the Mekong Subregional Countries, Hue, Vietnam |

C. Contributions to Science

1. **Statistical Methodology**: Working with Dr. Matthew Wand, I made contributions in the area of semiparametric modeling in the frame work of generalized linear mixed effects models, an area of modeling that has now become indispensable in longitudinal, repeated-measures data analysis. This work, titled *Smoothing with Mixed Model Software* was a 54-page paper provided with software that has been used by many statisticians and epidemiologists worldwide. The paper illustrates the theory and application of a variety of smoothing methods in the context of mixed models. In particular, these smoothing methods can be used to control for confounders without assuming any parametric relationship between the confounders and the outcome. This paper has been cited 239 times (indexed by Google Scholar) and is listed by ISI Web of Knowledge as a highly-cited paper. The paper and software are available at *the Journal of Statistical Software* (<http://www.jstatsoft.org/v09/i01>) and related work was posted from 2004-2012 Harvard Biostatistics website http://www.hsph.harvard.edu/biostats/research/divisions/env_stat/programs_macros.html. Some of this work on the software of these methods was acknowledged and also published in the popular text book *Semiparametric Regression (Cambridge Series in Statistical and Probabilistic Mathematics)*. I have also made methodological contributions in the area of exposure assessment using physiologically-based pharmacokinetic modeling. When a pollutant or a substance enters the body, it is important to understand and estimate the rate it is metabolized, distributed to different organs, and discarded (e.g. via exhalation, or urine). This work on the assessment of the association between demographic factors of age, gender, and ethnicity and pharmacokinetic parameters in workers who were exposed to butadiene, a carcinogenic substance, proposed a novel analytical approach using differential equations and Bayesian statistics. This method could be used as a general approach to exposure assessment in other settings as well. Other statistical methods contributions include work on exponential smoothing which could be used to forecast cases of nosocomial infections in a healthcare setting, and estimation of sample size in machine learning techniques which has important implications in deciding how much data are needed to reach certain target classification performance.

- a. **Ngo L**, Wand MP. (2004), Smoothing with mixed model software, J of Stat Software. 9(1):1-54.
- b. **Ngo L**, Ryan LM, Mezzetti M, Bois FY, Smith TJ. Estimating Metabolic Rate for Butadiene at Steady State Using a Bayesian Physiologically-Based Pharmacokinetic Model. Journal of Environmental and Ecological Statistics. Volume 18, Issue 1 (2011), Page 131-146.
- c. **Ngo L**, Tager IB, Hadley D. Application of exponential smoothing for nosocomial infection surveillance. Am J Epidemiol. 1996 Mar 15;143(6):637-47.
- d. Figuerora RL, Zeng-Treitler Q, Kandula S, **Ngo L**. Predicting sample size required for classification performance. BMC Medical Informatics and Decision Making 2012; 12-8. PMC3307431.

2. **Competing Risks**: My contribution to another area of research is competing risks. When a time-to-event outcome of interest (such as death due to breast cancer) cannot be observed because another event (competing risk) such as death due to myocardial infarction occurs first, then this problem falls in the area of competing risks. The customary treatment of this type of problem is to treat competing risks as censored events; however, this creates bias in the estimation of the hazard risk of the outcome of interest. In the elderly patient population, this problem is quite prevalent. So in the case of breast cancer death, the risk of death (hazard) is overestimated if competing risks are not properly accounted for. Working with colleagues at the Hebrew Senior Life, I helped implementing the competing risk analysis method to study the risk of repeated hip fracture in the elderly taking into account competing risk of death prior to hip. This work led to the request from the Editor of the Journal of the American Geriatrics Society for the publication of another paper which focused on the methodology of competing risks for a clinical audience, titled *Competing risk of death: an important consideration in studies of older adults*. Together with Dr. Ellen McCarthy in our division, I proposed the use of competing risk methodology in the estimation of breast-cancer mortality in the elderly patients taking into account competing risks of non-breast-cancer death. The American Cancer Society awarded us the grant, and we are in the process of applying this methodology to the National Cancer Institute Medicare-linked SEER (Surveillance Epidemiology and End Results) database. This study will have wide policy implication regarding breast-cancer screening recommendation. We believe that at a certain old age, breast-cancer screening is no longer beneficial since the patient would die of a competing-risk death (e.g. cardiovascular) instead of breast-cancer death. Thus the unbiased estimation of the risk of death is critical in this population. I am currently a PI on an NIH-funded grant to implement competing risk for a class of population-based cancer models published by CISNET (Cancer Intervention and Surveillance Modeling Network). CISNET was one of the models used by the United States Preventive Services Task Force in formulating the breast-cancer screening recommendation in November 2009. CISNET in its current form does not account for competing risks. This work with competing risk implementation, would allow CISNET models to yield better estimates of death due to breast cancer. This work is in collaboration with Dr. McCarthy, and Dr. Sandra Lee of Dana Farber. The application of this methodology is not limited to breast cancer and can be generalized to other cancers and chronic diseases.

- a. Berry SD, **Ngo L**, Samelson EJ, Kiel DP. Competing risk of death: an important consideration in studies of older adults. J Am Geriatr Soc 2010 Apr; 58(4):783-7. PMC2760766.
- b. Liu Y, McCarthy PE, **Ngo L**. Predicting Breast Cancer Mortality in the Presence of Competing Risks using Smartphone Application Development Software. International Journal of Statistics in Medical Research. 2015 Oct.; Vol 4. p322-330.
- d. Schonberg MA, Li VW, Eliassen AH, Davis RB, LaCroix AZ, McCarthy EP, Rosner BA, Chlebowski RT, Rohan TE, Hankinson SE, Marcantonio ER, **Ngo L**. Performance of the Breast Cancer Risk Assessment Tool Among Women Age 75 Years and Older. J Natl Cancer Inst. 2015 Nov 30;108(3). 2016 Mar.
- d. Schonberg MA, Li VW, Eliassen AH, Davis RB, LaCroix AZ, McCarthy EP, Rosner BA, Chlebowski RT, Hankinson SE, Marcantonio ER, **Ngo L**. Accounting for individualized competing mortality risks in estimating postmenopausal breast cancer risk. Breast Cancer Res Treat. 2016 Oct 21.

3. **Mechanisms of Delirium**: I am currently Associate Director of the Statistics Core for the program project grant Successful Aging after Elective Surgery directed by Dr. Sharon Inouye and Dr. Edward Marcantonio. I am responsible for the modeling of inflammatory and proteomic signatures of delirium, and to assess the association between these signatures and cognitive function, and brain imaging parameters. Our goal is to try to understand the pathophysiology of delirium in this aging population. Below are examples of papers from this study. Several (a-c) were first-authored by Dr. Marcantonio's mentees.

- a. Dillon ST, Vasunilashorn SM (co-first author), **Ngo L**, Otu HH, Inouye SK, Jones RN, Alsop DC, Kuchel GA, Metzger ED, Arnold SE, Marcantonio ER, Libermann TA. Higher C-Reactive Protein Levels Predict

Postoperative Delirium in Older Patients Undergoing Major Elective Surgery: A Longitudinal Nested Case-Control Study. *Biol Psychiatry*. 2016; Mar 25. pii: S0006-3223(16)32231-4. PMC5035711.

b. Vasunilashorn SM, **Ngo L (co-first author)**, Inouye SK, Libermann TA, Jones RN, Alsop DC, Guess J, Jastrzebski S, McElhaney JE, Kuchel GA, Marcantonio ER. Cytokines and Postoperative Delirium in Older Patients Undergoing Major Elective Surgery. *J Gerontol A Biol Sci Med Sci*. 2015 Jul 27. PMC4817082.

c. Vasunilashorn SM, **Ngo L**, Kosar CM, Fong TG, Jones RN, Inouye SK, Marcantonio ER. Does Apolipoprotein E Genotype Increase Risk of Postoperative Delirium? *Am J Geriatr Psychiatry*. 2015 May 21. pii: S1064-7481(15)00168-2. PMC4591079.

d. Cavallari M*, Hshieh TT* (co-first), Guttman CRG, **Ngo LH**, Meier DS, Shmitt EM, Marcantonio ER, Jones RN, Kosar CM, Fong TG, Press D, Inouye SK*, Alsop DC* (co-last). Brain atrophy and white matter hyperintensities are not significantly associated with incidence and severity of postoperative delirium in older persons without dementia. *Neurobiology of Aging*. 2015;36(6):2122-9. PMID: PMC4433616.

4. Delirium Assessment Methods: Delirium can be challenging to assess, both in research and clinical settings. I have collaborated closely with Dr. Edward Marcantonio and his team to develop better measurement tools for delirium. We used item response theory (a) and model selection to derive the 3D-CAM, a diagnostic assessment for delirium that takes less than 3 minutes to complete, and still maintains high sensitivity and specificity (b). We are now pursuing new work to develop strategies for clinical implementation, including development of an ultra-brief 2-item bedside screening test of delirium (c), which effectively rules out delirium in less than 1 minute. Finally, we derived and validated a method using items from the 3D-CAM to measure delirium severity (d).

a. Yang FM, Jones RN, Inouye SK, Tommet D, Crane PK, Rudolph JL, **Ngo L**, Marcantonio ER. Selecting optimal screening items for delirium: an application of item response theory. *BMC Med Res Methodol*. 2013 Jan 22;13:8. PMC3598414.

b. Marcantonio ER, **Ngo L**, O'Connor MA, Jones RN, Crane PK, Metzger ED, Inouye SK. 3D-CAM: Validation of a 3-Minute Diagnostic Interview for CAM-defined Delirium. *Ann Int Med*. 2014;161(8):554-61. PMC4319978.

c. Fick DM, Inouye SK, Guess J, **Ngo L**, Jones RN, Saczynski JS, Marcantonio ER. Preliminary development of an ultra-brief 2-item bedside test for delirium. *Journal of Hospital Medicine*. *J Hosp Med*. 2015 Oct;10(10):645-50. PMC4665114.

d. Vasunilashorn SM, Guess J, **Ngo L**, Fick DM, Jones RN, Schmitt E, Kosar CM, Saczynski JS, Trivison TG, Inouye SK*, Marcantonio ER* (*co-last). Derivation and validation of a severity scoring method for the 3-Minute diagnostic interview for CAM-defined delirium. *J Am Geriatr Soc*. 2016;64(8):1684-9. PMC4988867.

5. Air Pollution: I was a Principal Investigator on an international project in Vietnam which aimed to evaluate the effect of air pollution on the prevalence of acute respiratory infection in the children of Ho Chi Minh City in Vietnam. The grant was funded by the Health Effects Institute, a federally-mandated, EPA-funded institute charged with funding research projects which examine environmental health effects due to pollutants. I was responsible for the overall implementation of the study which includes the analysis plan, the drafting of the detailed standard operating procedures, training of staff, communicating with team members in four different countries, and disseminating research findings which would help public health officials of the Vietnamese government to set appropriate regulatory guideline for air pollution control. The main finding of this study was that the research team found harmful effect of air pollutants (PM10, ozone, sulfur dioxide, and nitrogen dioxide) on the respiratory outcome of ALRI (acute lower respiratory tract infection) in children at the age of five or younger in the dry season months (November to April). During the rainy season months (May to October), however, we unexpectedly found a protective effect. Additional analysis via simulation indicated that the protective effect was potentially due to residual confounding of an unmeasured confounder, which was likely to be RSV (respiratory syncytial virus) which is known to be much more prevalent in the rainy season in Asia.

a. Mehta S, **Ngo L**, Do D, Cohen A, Thach T, Vu D, Nguyen T, Le G. Air pollution and admissions for acute lower respiratory infections in young children of Ho Chi Minh City. *Air Qual Atm Hlth* 6.1 (Mar 2013):167-179.

b. HEI Collaborative Working Group on Air Pollution, Poverty, and Health in Ho Chi Minh City, Le TG, **Ngo L**, Mehta S, Do VD, Thach TQ, Vu XD, Nguyen DT, Cohen A. Effects of short-term exposure to air pollution on hospital admissions of young children for acute lower respiratory infections in Ho Chi Minh City, Vietnam. *Res Rep Health Eff Inst*. 2012 Jun;(169):5-72; discussion 73-83. PMID: 22849236.

Complete list of publications:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/long.ngo.1/bibliography/50999732/public/?sort=date&direction=ascending>.

D. Research Support

Current Research Projects:

VEF FS15003M (PI: Ngo)

6/1/2015-12/31/2016

United States Faculty Scholar Grant

This project is to provide biostatistics and research methodology training to faculty members and researchers at Hue University of Medicine and Pharmacy in Vietnam. The additional aim of this grant is to serve as a cultural ambassador representing the United States in our effort to learn from Vietnam and to help foster mutual understanding and professional scientific collaborations between the two countries.

NIH R21 CA180793 (PI: McCarthy, Ngo)

9/1/2014-9/1/2017

Integrating Competing Risks into the CISNET DFCI Breast Cancer Model

Cancer Intervention and Surveillance Modeling Network (CISNET) is a population-based stochastic model developed at the Dana Farber Cancer Institute (DFCI) to assess cancer screening and treatment effect. The current model does not have a mechanism to handle competing risks. This project aims to implement competing risks estimation into the CISNET models. Role: Principal Investigator.

K24 AG035075 (Marcantonio)

9/30/2010-5/31/2017 (NCE)

NIH/National Institute on Aging

Mid-Career Mentoring Award for Patient-Oriented Research (POR) in Aging

The Specific Aims are: 1. To build a research program around improving the quality and outcomes of care for hospitalized older adults with delirium. 2. To build a mentorship program that expands patient oriented research in aging at BIDMC and HMS, with a focus on delirium and related conditions. 3. To expand mentorship to include translational work around biomarker discovery for delirium, and biomarker applications to improve risk stratification, diagnosis, and prognostication of older adults with delirium.

Role: Co-Investigator

R01AG051658 (Marcantonio/Libermann MPI's)

1/15/2016 - 12/31/2019

NIH/National Institute on Aging (NIA)

Advancing the Understanding of Postoperative Delirium Mechanisms via Multi-Omics

This project aims to leverage specimens from two recently completed NIA-funded studies, SAGES (**S**uccessful **A**ging after **E**lective **S**urgery), and an independent orthopedic cohort, HiPOR (**H**ealthier **P**ostoperative **R**ecovery) that collected and stored both plasma and preoperative cerebrospinal fluid (CSF). We will apply cutting edge systems level "Omics" methods to define delirium signatures that integrate proteins, lipids, and metabolites from both plasma and CSF. Ultimately, our goal is to translate our findings to the bedside through improved diagnosis and monitoring of delirium, and through the design of targeted interventions.

Role: Co-Investigator

R01AG03061805 (Marcantonio/Fick MPI's)

4/15/16 - 3/31/20

NIH/National Institute on Aging (NIA)

Researching Efficient Approach to Delirium Identification

This is a competing continuation of our previous 3D-CAM R01, which derived and validated the 3D-CAM, and also identified a highly sensitive two-item screener that can effectively rule out delirium. We now propose to 1) validate this two-item delirium screener in two independent cohorts; 2) combine the screener and 3D-CAM into a two-step delirium identification protocol; 3) measure the effectiveness and cost-efficiency of having clinicians administer this protocol to a new cohort of 400 hospitalized older patients enrolled in two highly diverse hospital settings; 4) employ qualitative methods to determine barriers and facilitators to implementing the protocol. The current Aims will give us the necessary tools and knowledge to implement a practical, effective, and cost-efficient protocol for detection and monitoring of delirium in hospitalized older patients.

Role: Co-Investigator

Institutional Contract Grant (PIs: Delbanco/ Walker)

10/14/15-10/14/18

Robert Wood Johnson Foundation 71082

OpenNotes: Dissemination and Evaluation

The goal of this project is to carry out extensive analyses of the existing large OpenNotes database in order to evaluate the impact of OpenNotes on clinical outcomes and utilization.

Role: Co-Investigator