BIOGRAPHICAL SKETCH

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NAME: Glynn, Robert J

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

POSITION TITLE: Senior Biostatistician, Brigham and Women's Hospital; Professor of Medicine, Harvard Medical School; Professor in the Department of Biostatistics, Harvard TH Chan School of Public Health

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
Boston College	BA, MA	06/1972	Math and Economics
Brandeis University	MA, PhD	05/1978	Mathematics
Harvard School of Public Health	MS, ScD	05/1985	Biostatistics

A. Personal Statement

I have worked as a statistician on the design and analysis of studies in cardiometabolic diseases for over 40 years. During this time, I have co-authored over 180 papers with faculty in the Division of Pharmacoepidemiology and Pharmacoeconomics at the Brigham and Women's Hospital. I have designed numerous studies that have employed a wide variety of approaches, including retrospective, cross-sectional, and prospective studies, case-control, case-cohort, observational cohort, cluster randomized and individual randomized trial designs. I have been responsible for the design, interim monitoring, analysis and dissemination of results from numerous randomized trials, including large, multi-center trials such as JUPITER, PREVENT, VAL-MARC, CANTOS, CIRT, and HEART, other large trials conducted by mail such as the Physicians' Health Study II, and cluster-randomized trials of interventions such as academic detailing and other strategies to improve the quality of prescribing, or to enhance medication adherence such as the MI-FREEE trial. My role on these trials has included writing the design and analytic components of trial protocols, specification and implementation of interim monitoring of safety and efficacy, development and oversight of approaches to ensure data quality and enhance and monitor adherence during trials, presentation to data and safety monitoring boards, and analysis and dissemination of results. I recently served as principal investigator of the data coordinating center for the NHLBI-funded CIRT trial, a trial of methotrexate for secondary prevention of cardiovascular disease conducted at 371 clinical sites in the US and Canada; and currently serve as the independent academic statistician, responsible for interim monitoring of the international, double-blind PROMINENT trial, testing whether pemafibrate reduces cardiovascular risk by lowering triglycerides in patients with diabetes. Drs. Choudhry, Lauffenburger and I have a long history of collaborating on several projects, including federally-funded pragmatic trials such as the NIA-funded NUDGE-EHR trial for which this supplement is proposed. Given my expertise and interests, I am pleased to be collaborating with Drs. Lauffenburger and Choudhry and their team on this project and am confident that my skills and expertise as a trial methodologist and chair of the data safety monitoring board will be valuable to the project.

1. Choudhry NK, Avorn J, **Glynn RJ**, Antman EM, Schneeweiss S, Toscano M, Reisman L, Fernandes J, Spettell C, Lee JL, Levin R, Brennan T, Shrank WH; Post-Myocardial Infarction Free Rx Event and Economic Evaluation (MI FREEE) Trial. N Engl J Med. 2011; 365:2088-97.

2. Lauffenburger JC, Shrank WH, Bitton A, Franklin JM, **Glynn RJ**, Krumme AA, Matlin OS, Pezalla EJ, Spettell CM, Brill G, Choudhry NK. Association between patient-centered medical homes and adherence to chronic disease medications: a cohort study. Ann Intern Med 2017; 166:81-88.
3. Ridker PM, Danielson E, Fonseca FAH, Genest J, Gotto AM Jr, Kastelein JJP, Koenig W, Libby P, Lorenzatti AJ, MacFadyen JG, Nordestgaard BG, Shepherd J, Willerson JT, **Glynn RJ**. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. N Engl J Med 2008; 359: 2195-2207.
4. Ridker PM, Everett BM, Thuren T, MacFadyen JG, Chang WH, Ballantyne C, Fonseca F, Nicolau J, Koenig W, Anker SD, Kastelein JJP, Cornel JH, Pais P, Pella D, Genest J, Cifkova R, Lorenzatti A, Forster T, Kobalava Z, Vida-Simiti L, Flather M, Shimokawa H, Ogawa H, Dellborg M, Rossi PRF, Troquay RPT, Libby P, **Glynn RJ**; CANTOS Trial Group. Antiinflammatory therapy with Canakinumab for atherosclerotic disease. N Engl J Med. 2017; 377:1119-1131.

B. Positions and Honors

1978–1986	Statistician, Normative Aging Study, Veterans Administration Outpatient Clinic, Boston, MA
1984–1987	Assistant Professor, Epidemiology and Biostatistics, Boston University School of Public Health
1986–1990	Research Associate in Ophthalmology, Massachusetts Eye and Ear Infirmary
1986–1990	Assistant Professor of Ophthalmology (Biostatistics), Harvard Medical School
1990–1994	Assistant Professor of Medicine (Biostatistics), Harvard Medical School
1990–1991	Associate Biostatistician, Department of Medicine, Brigham and Women's Hospital
1992–	Biostatistician, Department of Medicine, Brigham and Women's Hospital
1995–2012	Associate Professor of Medicine (Biostatistics), Harvard Medical School
1995–2012	Associate Professor of Biostatistics, Harvard School of Public Health
2012–	Professor of Medicine, Harvard Medical School
2012–	Professor in the Department of Biostatistics, Harvard School of Public Health
2017–	Member, Arthritis and Musculoskeletal and Skin Diseases Clinical Trials Review Committee, NIH

C. Contributions to Science

1. Building on my work as principal investigator of the coordinating center for the NHLBI funded PREVENT trial, I received two R01 grants for additional studies of the epidemiology of venous thromboembolism. My research in this area has elaborated the links between risk factors for arterial and venous thrombosis, and the potential role for therapies to prevent venous thromboembolism. In particular, I have applied methods for competing risks to make explicit comparisons of strengths of association between risk factors for arterial thrombosis and associations of these risk factors with venous thrombosis. I also published the first large, randomized studies on the relationships of long-term, low-dose aspirin, vitamin E supplementation, and statins with the incidence of venous thromboembolism.
    a. **Glynn RJ**, Ridker PM, Goldhaber SZ, Buring JE. Effects of low-dose aspirin on the occurrence of venous thromboembolism: a randomized trial. Ann Intern Med 2007; 147: 525-533.
    b. **Glynn RJ**, Ridker PM, Goldhaber SZ, Zee RYL, Buring JE. Effects of random allocation to vitamin E supplementation on the occurrence of venous thromboembolism: report from the Women's Health Study. Circulation 2007; 116: 1497-1503.
    c. **Glynn RJ**, Danielson E, Fonseca FAH, Genest J, Gotto AM Jr, Kastelein JJP, Koenig W, Libby P, Lorenzatti AJ, MacFadyen JG, Nordestgaard BG, Shepherd J, Willerson JT, Ridker PM. A randomized trial of rosuvastatin in the prevention of venous thromboembolism. N Engl J Med 2009; 360:1851-61.
    d. Kinsey TL, Stürmer T, Funk MJ, Poole C, Simpson RJ, **Glynn RJ**. Incidence of venous thromboembolism following initiation of non-steroidal anti-inflammatory drugs in U.S. women. Rheumatology (Oxford). 2020; in press.

2. My methodological research has included studies on the use of multiple imputation with missing data, application of methods of competing risks to elucidate risk factors for possibly related outcomes, extension of nonparametric methods to clustered data settings, and evaluation of strategies to improve construction of summary confounder scores, including both disease risk and propensity scores.
    a. **Glynn RJ**, Laird NM, Rubin DB. Multiple imputation in mixture models for nonignorable nonresponse with follow-ups. J Am Statist Assoc 1993; 88:984-993.

b. Krumme AA, **Glynn RJ**, Schneeweiss S, Choudhry NK, Tong AY, Gagne JJ. Defining exposure in observational studies comparing outcomes of treatment discontinuation. Circ Cardiovasc Qual Outcomes. 2018; 11:e004684.
c. Rosner B, **Glynn RJ**. Power and sample size estimation for the clustered Wilcoxon test. Biometrics 2011; 67:646-653. PMCID: PMC3119759.
d. Yoshida K, Solomon DH, Haneuse S, Kim SC, Patorno E, Tedeschi SK, Lyu H, Franklin JM, Stürmer T, Hernandez-Diaz S, **Glynn RJ**. Multinomial extension of propensity score trimming methods: a simulation study. Am J Epidemiol 2019; 188: 609-616. PMCID: PMC6395163.

3. A particular focus of my work has been on study design and analytic methods to improve inferences in observational studies of older people. Non-random nonresponse to questions about sensitive issues including cognitive function and behaviors including alcohol consumption patterns can lead to bias. Further, comorbid conditions can influence biomarkers such as blood pressure and lipid measures and distort their associations with diverse outcomes ranging from cardiovascular disease to cognitive function. My work has evaluated the relevance of modifiable risk factors for cardiovascular disease in older people.
    a. **Glynn RJ**, Bouchard GR, LoCastro JS, Laird NM. Aging and generational effects on drinking behaviors in men: results from the Normative Aging Study. Am J Public Health 1985; 75:1413-1419. PMCID: PMC1646430
    b. **Glynn RJ**, Field TS, Rosner B, Hebert PR, Taylor J, Hennekens CH. Evidence for a positive linear relation between blood pressure and mortality in elderly people. Lancet 1995; 345:825-829.
    c. **Glynn RJ**, Beckett LA, Hebert LE, Morris MC, Scherr PA, Evans DA. Current and remote blood pressure and cognitive decline. JAMA 1999; 281:438-445.
    d. **Glynn RJ**, Koenig W, Nordestgaard BG, Shepherd J, Ridker PM. Rosuvastatin for primary prevention in older individuals with elevated C-reactive protein and low to average low density lipoprotein levels: exploratory analysis of a randomized trial. Ann Intern Med 2010; 152:488-96. PMCID:PMC 2946369.

4. Over the past 25 years, I have published well over 200 papers in pharmacoepidemiology, with particular focus on medication use and in methods to account for the complexity of confounding related to treatment initiation and persistence, including barriers as well as indications for treatment. I have published widely on the development and use of disease risk scores and propensity scores and have contributed to the development of methods including propensity score calibration and strategies to improve study validity by trimming on the propensity score.
    a. **Glynn RJ**, Knight EL, Levin R, Avorn J. Paradoxical relationships of drug treatment with mortality in older persons. Epidemiology 2001; 12:682-689.
    b. Stürmer T, Rothman KJ, Avorn J, **Glynn RJ**. Treatment effects in the presence of unmeasured confounding: dealing with observations in the tails of the propensity score distribution—a simulation study. Am J Epidemiol 2010; 172: 843-854. PMCID 3025652
    c. **Glynn RJ**, Gagne JJ, Schneeweiss S. Role of disease risk scores in comparative effectiveness research with emerging therapies. Pharmacoepidemiol Drug Saf 2012; 21 Suppl 2:138-47. PMCID 390547
    d. **Glynn RJ**, Lunt M, Rothman KJ, Poole C, Schneeweiss S, Stürmer T. Comparison of alternative approaches to trim subjects in the tails of the propensity score. Pharmacoepidemiol Drug Saf 2019; 28:1290-1298. PMCID in process.

5. Since my time working at the Massachusetts Eye & Ear Infirmary, I have maintained a continuing interest in the epidemiology of eye diseases, and in the particular statistical issues associated with paired data, such as arise when interest focuses on the correlated outcomes in a person's two eyes. A focus of this work has been to identify and communicate better ways to analyze and present research on paired outcomes.
    a. **Glynn RJ**, Rosner B. Accounting for the correlation between fellow eyes in regression analysis. Arch Ophthalmol 1992; 110:381-387.
    b. **Glynn RJ**, Rosner B. Multiple imputation to estimate the association between eyes in disease progression with interval-censored data. Stat Med 2004; 23: 3307-3318.
    c. **Glynn RJ**, Rosner B. Regression methods when the eye is the unit of analysis. Ophthalmic Epidemiol 2012; 19:159-65. PMCID: PMC3454458

d. Rosner B, **Glynn RJ**. Estimation of rank correlation for clustered data. Stat Med. 2017; 36: 2163-2186. PMCID: PMC5457370.

Complete List of Published Work in MyBibliography
http://www.ncbi.nlm.nih.gov/sites/myncbi/robert.glynn.1/bibliograpahy/41154000/public/?sort=date&direction=ascending

D. Additional Information: Research Support and/or Scholastic Performance

Research Support (ongoing)

R21/R33 AG057388-01 (Choudhry / Lauffenburger) 09/15/17–09/14/22

NIA

Optimizing electronic health record prompts with behavioral economics to improve prescribing for older adults.

This project involves pragmatic randomized trials to evaluate whether electronic health record (EHR)-based tools that are optimized using behavioral economic principles, such as salience effects, social norming, and default bias, can reduce inappropriate prescribing of potentially harmful drugs and clinically-significant adverse health outcomes among older adults. Dr. Glynn is the trial statistician.

P30AG064199 (Choudhry) 09/15/19–05/31/24

NIH

Roybal Center for Therapeutic Optimization using Behavioral Science - Pilot Core

The overarching goal of the Brigham and Women's Hospital/Harvard Medical School Roybal Center for Therapeutic Optimization using Behavioral Science is to develop principle-driven interventions to enhance the evidence-based use of prescription medications. Dr. Glynn is a study statistician.

U01 AR068043 (Solomon / Bathon) 09/28/15–06/30/20

NIH / NIAMS

Treatments Against RA and Effect on FDG PET CT: The TARGET Trial

This multi-center clinical trial will compare the effects of triple therapy to addition of a TNF antagonist among patients with RA and inadequate disease control on methotrexate. The primary outcome is change in vascular inflammation as measured by the FDG PET-CT from baseline to 6 months. Dr. Glynn is the trial statistician.

P01 CA087969 (Stampfer) 09/12/00–06/30/20

NIH / NCI

Dietary and Hormonal Determinants of Cancer in Women (Project 4)

This competing renewal continues the scientific pursuit of modifiable determinants of breast, colorectal, and ovarian cancers. A primary, cross-cutting theme is the role of metabolites and metabolomic signatures in the etiology and progression of these cancers, including developing novel statistical approaches. Further, gene expression analyses of tumor tissue will enable us to identify pathways linking risk factors to cancer. Dr. Glynn serves as a co-investigator.

N/A (Ridker) 10/01/10–2/28/22

Novartis (Study #CACZ885I2302)

A randomized, double-blind, placebo-controlled, event-driven trial of canakinumab in the prevention of recurrent cardiovascular events and new onset diabetes among stable post-myocardial infarction patients with persistently elevated hsCRP.

This study will utilize a randomized, double-blind, placebo-controlled, event driven trial of Canakinumab in the prevention of recurrent cardiovascular events and new onset diabetes among stable post-myocardial infarction patients with persistent elevations of hsCRP. Dr. Glynn is the independent academic statistician for this trial, responsible for interim monitoring and reports to the trial's Data and Safety Monitoring Board.

R01 HL119718-01A1 (Solomon) 08/15/14–05/31/20

NIH

Towards Evidence-Based Monitoring of Low Dose Methrotrexate: CIRT Ancillary Study

The discovery and clinical use of markers associated with a greater likelihood of AE from LDM would provide an important public health benefit to rheumatic disease patients and potentially to a larger population if the CIRT trial shows reduction on cardiovascular events with LDM. Dr. Glynn is a co-investigator.

U01 HL101422 (Ridker) 07/25/11–10/31/20

NIH / NHLBI

Cardiovascular Inflammation Reduction Trial (CIRT)

The primary aim of this trial is to directly test whether or not low dose methotrexate (LDM) will reduce rates of recurrent myocardial infarction, stroke, and cardiovascular death among patients with stable cardiovascular disease who are at increased risk indicated by metabolic syndrome. Dr. Glynn is the trial statistician.

N/A (Ridker) 08/01/14–07/31/22

KOWA Research Institute

PROMINENT (The Pemafibrate to Reduce cardiovascular OutcoMes by reducing triglycerides IN diabetic patiENTs) DCC

The Triglyceride Reduction and Acute Cardiovascular Events (TRACE) trial is a randomized, double-blind, placebo-controlled, international trial evaluating the ability of the potent PPAR-alpha agonist, K-877, to reduce rates of myocardial infarction, stroke, unstable angina requiring unplanned revascularization, and cardiovascular death among 10,000 men and women with type 2 diabetes (T2D). Dr. Glynn is the trial's independent academic statistician.

R01 EY022445 (Rosner) 04 01/18–03/31/21

NIH/NEI

Nonparametric and Survival Methods in Ophthalmology

This proposal will consider (a) more efficient use of longitudinal data in ophthalmic studies based on ordinal scales, with the eye as the unit of analysis (b) assessment of measures of discrimination for risk prediction rules in ophthalmic studies collected in families where the eye is the unit of analysis (c) assessment of measures of discrimination for risk prediction rules with variable follow-up time using the eye as the unit of analysis (d) innovative approaches for translating work on clustered data methods to the ophthalmic community. Dr. Glynn is a co-investigator.

NOACs-1511-33068 (Gagne) 10/01/16–09/30/21

Patient Centered Outcomes Research

The Dabigatran, Apixaban, Rivaroxaban, Edoxaban, Warfarin Comparative Effectiveness Research Study (The DARE warfarin CER study)

This study will address the important clinical question of how warfarin and the NOACs, dabigatran, apixaban, rivaroxaban, and edoxaban, compare for patients who have completed an initial course of treatment after an initial episode of DVT or PE. This study will compare these options with respect to both effectiveness and safety, as well as their relative impact on all-cause mortality. Dr. Glynn is a co-investigator

HHSF223201710186C (Schneeweiss) 09/22/17–09/21/20

FDA

Effectiveness research with Real World Data to support FDA's regulatory decision making: A Real World Evidence Demonstration Project

This proposal seeks to provide empirically-based recommendations that are guided by theoretical principles on when RWE can substitute RCTs and, if so, how to implement such studies. It will further provide a RWD analytic infrastructure for implementing RWD at scale with high validity, transparency and auditability. Dr. Glynn is a co-investigator.

UL1 TR002541 (Nadler) 05/01/18–04/30/23

NIH

The Harvard Clinical and Translational Science Center

The Harvard Clinical and Translational Science Center, connects, convenes, and catalyzes the faculty, trainees, and teams from across Harvard's 10 Schools and 16 Academic Healthcare Centers to partner with its communities and biomedical ecosystem to address NCATS' five strategic goals to improve health. Dr. Glynn is a project statistician.

R01 AG062713 (Kim, Dae Hyun) 06/01/19–01/31/23

NIH

Prospective monitoring of newly approved cardiovascular drugs in older adults with frailty

The study aims to establish a prospective monitoring program in routine healthcare databases for older adults with frailty and identify predictors of benefit from newly marketed drugs for cardiovascular disease. The evidence generated from this work can enable clinicians to optimize prescribing of new cardiovascular drugs in older adults weighing a patient's frailty level and expected net benefit. Dr. Glynn is a co-investigator.