

Population Health Research Newsletter

Summer 2021
Newsletter

Welcome to the TPMG **Population Health Research Newsletter!**

This is the inaugural edition of our research newsletter, presenting current or recently completed research projects led by population health clinical leads as well as ongoing studies led by investigators at the Division of Research that involve our clinicians.

DARE is proud to provide our physicians with research collaboration opportunities through the Physician Researcher Program and the DARE research funding mechanisms.

In this issue, we will provide you with updates on the Population Health group's research interests and the impressive recently published research.



A Deeper Look Inside This Update:

- Research Highlight
- Who's doing research
- Funding
- Active and recent research projects
- Recent peer reviewed publications

Research Highlight:

Kudos to our own Rick Dlott and Lisa Gilliam, and their collaborator Andy Karter from the DOR, on their recent JAMA publication evaluating the use of continuous glucose monitoring (CGM) among patients with insulin treated type 2 diabetes mellitus (DM). CGM has been approved for use in type 1 diabetes for several years. In this observational study, CGM initiators had improvements in Hb A1c and a decreased rate of hypoglycemia. This is the kind of study that has the potential to change practice, expanding the use of CGM to type 2 DM. According to Andy Karter, "The improvement in blood sugar control was comparable to what a patient might experience after starting a new diabetes medication."

Association of Real-time Continuous Glucose Monitoring with Glycemic Control and Acute Metabolic Events Among Patients With Insulin-Treated Diabetes

Andrew J. Karter, PhD; Melissa M. Parker, MS; Howard H. Moffet, MPH; Lisa K. Gilliam, MD, PhD; Richard Dlott, MD

IMPORTANCE Continuous glucose monitoring (CGM) is recommended for patients with type 1 diabetes; observational evidence for CGM in patients with insulin-treated type 2 diabetes is lacking.

OBJECTIVE To estimate clinical outcomes of real-time CGM initiation.

DESIGN, SETTING, AND PARTICIPANTS Exploratory retrospective cohort study of changes in outcomes associated with real-time CGM initiation, estimated using a difference-in-differences analysis. A total of 41,753 participants with insulin-treated diabetes (5673 type 1;36,080 type 2) receiving care from a Northern California integrated health care delivery system (2014-2019), being treated with insulin, self-monitoring their blood glucose levels, and having no prior CGM use were included.

EXPOSURES Initiation vs noninitiation of real-time CGM (reference group).

MAIN OUTCOMES AND MEASURES Ten end points measured during the 12 months before and 12 months after baseline: hemoglobin A1c (HbA1c); hypoglycemia (emergency department or hospital utilization); hyperglycemia (emergency department or hospital utilization); HbA1c levels lower than 7%, lower than 8%, and higher than 9%; 1 emergency department encounter or more for any reason; 1 hospitalization or more for any reason; and number of outpatient visits and telephone visits.

RESULTS The real-time CGM initiators included 3806 patients (mean age, 42.4 years [SD, 19.9 years]; 51%female; 91%type 1, 9% type 2); the noninitiators included 37 947 patients (mean age, 63.4 years [SD, 13.4 years]; 49%female; 6%type 1, 94%type 2). **The prebaseline mean HbA1c was lower among real-time CGM initiators than among noninitiators, but real-time CGM initiators had higher prebaseline rates of hypoglycemia and hyperglycemia. Mean HbA1c declined among real-time CGM initiators** from 8.17% to 7.76% and from 8.28% to 8.19% among non-initiators (adjusted difference-in-differences estimate, -0.40% ; 95%CI, -0.48% to -0.32% ; $P < .001$). **Hypoglycemia rates declined among real-time CGM initiators** from 5.1% to 3.0% and increased

among noninitiators from 1.9% to 2.3%(difference-in-differences estimate, -2.7% ; 95%CI, -4.4% to -1.1% ; $P = .001$). There were also statistically significant differences in the adjusted net changes in the proportion of patients with HbA1c lower than 7%(adjusted difference-in-differences estimate, 9.6% ; 95%CI, 7.1% to 12.2% ; $P < .001$), lower than 8%(adjusted difference-in-differences estimate, 13.1% ; 95%CI, 10.2% to 16.1% ; $P < .001$), and higher than 9% (adjusted difference-in-differences estimate, -7.1% ; 95%CI, -9.5% to -4.6% ; $P < .001$) and in the number of outpatient visits (adjusted difference-in-differences estimate, -0.4 ; 95%CI, -0.6 to -0.2 ; $P < .001$) and telephone visits (adjusted difference-in-differences estimate, 1.1 ; 95%CI, 0.8 to 1.4 ; $P < .001$). Initiation of real-time CGM was not associated with

statistically significant changes in rates of hyperglycemia, emergency department visits for any reason, or hospitalizations for any reason.

CONCLUSIONS AND RELEVANCE In this retrospective cohort study, insulin-treated patients with diabetes selected by physicians for real-time continuous glucose monitoring compared with noninitiators had significant improvements in hemoglobin A1c and reductions in emergency department visits and hospitalizations for hypoglycemia, but no significant change in emergency department visits or hospitalizations for hyperglycemia or for any reason. Because of the observational study design, findings may have been susceptible to selection bias.

JAMA. doi:[10.1001/jama.2021.6530](https://doi.org/10.1001/jama.2021.6530)

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KPNC Population Health Physicians are Interested in Research

Thank you to the 12 Population Health Physicians who responded to our recent survey expressing interest in research and how they would like to get involved. Please continue to keep us informed about any research grants, presentations and publications that you receive!

Survey Results



Several research ideas are of highest interest to this group, including:

- **Social determinants of health** and how it affects health outcomes
- **Integrated population management** to improve care quality and experience
- **Treatment guidelines** and decision-making
- **Health disparities** and effective strategies

- **Outreach strategies** for targeted messaging
- **Weight management** in pregnancy
- **Screening and surveillance**

Who's Interested in What?

Opportunities for collaboration:

Descriptive (retrospective) studies of quality interventions (telling our story)

- Catherine Gutfreund
- Lisa Fazzolari
- Suk Seo
- Lisa Gilliam
- Marc G Jaffe
- Marc Ikeda
- Dawn Belardinelli
- Tracy Seo
- Amir Axelrod
- George Minowada
- Nayan Sivamurthy

Implementation studies: non-randomized trials

- Lisa Fazzolari
- Marc G Jaffe
- Tracy Seo
- Amir Axelrod
- George Minowada
- Nayan Sivamurthy
- Renee Fogelberg

Implementation studies: randomized trials–cluster, stepped-wedge, etc.

- Lisa Fazzolari
- Lisa Gilliam
- Marc G Jaffe
- Tracy Seo
- George Minowada
- Nayan Sivamurthy

Etiologic/epidemiologic studies

- Catherine Gutfreund
- Suk Seo
- Dawn Belardinelli
- Nayan Sivamurthy

Patient reported outcomes

- Suk Seo
- Catherine Gutfreund
- Dawn Belardinelli
- Tracy Seo
- Nayan Sivamurthy
- Renee Fogelberg

Evaluation of new diagnostic tests

- Suk Seo
- Tracy Seo
- George Minowada
- Renee Fogelberg

Qualitative/Mixed Methods studies

- Suk Seo
- Tracy Seo

Internal Research Funding Opportunities



General Funding Opportunities



Delivery Science and Applied Research



Division of Research

Active or Recently Completed Research Projects and Collaborations

Lisa Fazzolari, DO

- Delivery science grant pop management for schizophrenia, schizoaffective disorder, and bipolar disorder utilizing trained psychiatric pharmacists
Investigators: Lisa Fazzolari, DO and Esti Iturralde, PhD

Suk Seo

- Delivery Science Grant, understanding state of hep C infection in KPNC and developing region-wide strategy for screening and staging and curing.

Lisa Gilliam

- Optimization and Personalization of Diabetic Retinopathy Screening in the Eye Care Monitoring Program
Investigators: Dariusz Tarasewicz (PI), Ron Melles, Carol Conell, Lisa Gilliam (sub-investigator)
Funding: KP Community Benefits Program (2019)
Description: Determination of risk factors that impact diabetic retinopathy progression
- Comparative Effectiveness of Real-Time Continuous Glucose Monitoring (CGM) Among Insulin-Treated Diabetes Patients from Kaiser Permanente Northern California
Investigators: Andrew Karter (PI), Howard Moffet, Melissa Parker, Rick Dlott, Lisa Gilliam (Consultant/Co-investigator)
Funding: Dexcom, Inc (Investigator-initiated trial)
Description: Retrospective cohort study evaluating clinical benefit associated with real-time continuous glucose monitoring in insulin-treated diabetes patients.
- Development of a prediction algorithm for deteriorating glycemic control in the NCal KP population with diabetes.
Investigators: Lisa Gilliam (PI), Julie Schmittiel
Funding: Delivery Science Targeted Analysis Program (TAP), 2020

Description: Development of a predictive model based on EMR data that identifies patient factors most predictive of losing glycemic control over a designated follow up period in our KP NCal population

- Reducing Treatment Risk in Older Patients with Diabetes
Principal Investigators: RW Grant (PI), others..., Lisa Gilliam (Senior Clinical Consultant)
Funding: Patient-Centered Outcomes Research Institute (PCORI)
Description: Evaluating different strategies for effecting diabetes medication deprescribing in older patients with type 2 diabetes at high risk for medication SEs.
- Title: Using continuous glucose monitoring data to predict acute metabolic crises in diabetes
Investigators: Lisa Gilliam (PI), Andrew Karter, Howard Moffet, Melissa Parker
Funding: KP Community Benefits Program (2021)
Description: Evaluation of whether continuous glucose monitoring (CGM) data can be used to predict near-term, preventable acute metabolic events that are clinically serious (potentially fatal) or strategically important (expensive to care for).

Marc G Jaffe

- I am involved in ongoing descriptive research publications partnering with WHO/PAHO (see publications)

Recent Peer Reviewed Publications authored by Population Health clinicians (2018-present).

Suk Seo

- **Marcus, J, Seo S**, et al. Life expectancy of insured people with and without hepatitis C virus infection, 2007-2017. *Open Forum Infectious Diseases*, Volume 7, Issue 2, Feb 2020
- Lam J, **Seo S**, et al. Hepatitis C treatment uptake and response among human immunodeficiency virus/hepatitis C virus-coinfected patients in a large integrated healthcare system. *Int J STD AIDS*. 2019 Jun;30(7):689-695
- **Seo S**, Silverberg M, et al. Prevalence of spontaneous clearance of hepatitis C virus infection doubled from 1998 to 2017. *Clin Gastroenterol Hepatol*. 2020 Feb;18(2):511-513

Lisa Gilliam

- Banerjee S, Kim E, Parker MM, **Gilliam LK**, Dlott R, Adams A. Clinical Response to Real-Time Patient-Reported Diabetic Peripheral Neuropathy Symptoms. *Perm J*. 2019;23:18-180. doi: 10.7812/TPP/18-180. PMID: 31050645; PMCID: PMC6499113.
- Corathers SD, Yi-Frazier JP, Kichler JC, **Gilliam LK**, Watts G, Houchen A, Beal S. Development and Implementation of the Readiness Assessment of Emerging Adults With Type 1 Diabetes Diagnosed in Youth (READDY) Tool. *Diabetes Spectr*. 2020 Feb;33(1):99-103. doi: 10.2337/ds18-0075. PMID: 32116461; PMCID: PMC7026752.
- Karter AJ, Parker MM, Moffet HH, **Gilliam LK**, Dlott R. Association of Real-time Continuous Glucose Monitoring With Glycemic Control and Acute Metabolic Events Among Patients With Insulin-Treated Diabetes. *JAMA*. 2021;325(22):2273-2284. doi:10.1001/jama.2021.6530

Marc G Jaffe

- Frieden TR, Varghese CV, Kishore SP, Campbell NR, Moran AE, Padwal R, **Jaffe MG**. Scaling up effective treatment of hypertension—A pathfinder for universal health coverage. *J Clin Hypertens*. 2019;21:1442-1449. <https://doi.org/10.1111/jch.13655>
- Salam A, Kanukula R, Atkins E, Wang X, Islam S, Kishore SP, **Jaffe MG**, Patel A, Rodgers A. Efficacy and safety of dual combination therapy of blood pressure-lowering drugs as initial treatment for hypertension: a systematic review and meta-analysis of randomized controlled trials *Journal of Hypertension*: September 2019 - Volume 37 - Issue 9 - p 1768-1774. doi: 10.1097/HJH.0000000000002096

- Rana JS., Liu JY, Moffet HH, Karter AJ, Nasir K, Solomon MD, **Jaffe MG**, Ambrosy AP, Go AS, Sidney S (2020). Risk of atherosclerotic cardiovascular disease by cardiovascular health metric categories in approximately 1 million patients. *European Journal of Preventive Cardiology*. <https://doi.org/10.1177/2047487320905025>
- Solomon MD, Leong TK, Levin E, Rana JS, **Jaffe, MG**, Sidney S, Sung SH, Lee C, DeMaria A, Go AS. Cumulative Adherence to Secondary Prevention Guidelines and Mortality After Acute Myocardial Infarction. *Journal of the American Heart Association*. <https://doi.org/10.1161/JAHA.119.014415>. 2020;9:e014415
- WHO technical specifications for automated non-invasive blood pressure measuring devices with cuff. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO. (acknowledged as a technical expert who participated in the consultation, and provided technical review)
- Husain MJ, Biplap KD, Joseph KT, Asma S, Richter P, **Jaffe MG**, Kishore SP. Access to Cardiovascular Disease and Hypertension Medicines in Developing Countries: An Analysis of Essential Medicine Lists, Price, Availability, and Affordability. April 2020 <https://doi.org/10.1161/JAHA.119.015302> *Journal of the American Heart Association*. ;0:e015302
- Brady TM, Padwal R, Blakeman DE, Farrell M, Frieden TR, Kaur PD, Moran AE, **Jaffe MG**. Blood pressure measurement device selection in low-resource settings: Challenges, compromises, and routes to progress. *J Clin Hypertens*. 2020;00:1-10. <http s://d oi .org/10.1111/jch.13867>
- Salam A, Huffman MD, Kanukula R, Prasad EH, Sharma A, Heller DJ, Vedanthan R, Agarwal A, MD, Rodgers A, Jaffe MG, Frieden TR, Kishore SP. Two-drug fixed-dose combinations of blood pressure lowering drugs as WHO essential medicines: An overview of efficacy, safety, and cost. *J Clin Hypertens*. 2020;00:1-11. <https://doi.org/10.1111/jch.14009>
- DiPette DJ, Goughnour K, Zuniga E, Skeete J, Ridley E, Angell, Brettler J, Campbell NR, Coca A, Connell K, Doon R, Jaffe M, Lopez-Jaramillo P, Moran A, Orias M, Pineiro DJ, Rosende A, Valdés González Ordunez P Standardized treatment to improve hypertension control in primary health care: The HEARTS in the Americas Initiative. *J Clin Hypertens*. 2020;00:1-11.
- An J, Luong T, Qian L, Wei R, Liu R, Muntner P, Brettler J, **Jaffe MG**, Moran AE, Reynolds K. Treatment Patterns and Blood Pressure Control With Initiation of Combination Versus Monotherapy Antihypertensive Regimens. *Hypertension*.2020:1201543 <https://doi.org/10.1161/HYPERTENSIONAHA.120.15462>

- John O, Campbell NR, Nradly TM, Farrell M, Varghese CV, Velazquez Berumen A, Ruis Gaitan LA, Toffelmire N, Ameel M, **Jaffe, MG**, Schutte AE, Khan T, Lopez Meneses LP. The 2020 “WHO Technical Specifications for Automated Non-Invasive Blood Pressure Measuring Devices With Cuff. Hypertension published 1 Feb 2021 <https://doi.org/10.1161/HYPERTENSIONAHA.120.16625>