ARIC Manuscript Proposal #3792

PC Reviewed: 3/9/21 **Status: _____** **Priority: 2**
SC Reviewed: _____ **Status: _____** **Priority: ____**

1.a. Full Title: Glucose Patterns in Older Adults: A Pilot Study in a Community-based Population

b. Abbreviated Title (Length 26 characters): CGM Pilot

2. Writing Group:
Writing group members: Elizabeth Selvin, Dan Wang, Olive Tang, Justin Echouffo-Tchuegui, Josef Coresh

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. _____ **[please confirm with your initials electronically or in writing]**

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3. Timeline: Pilot data were collected in 2019 and have now been linked to ARIC visit 7 data. Publication <1 year.

4. Rationale: We conducted a pilot study at the Hagerstown (Johns Hopkins) Field Center to evaluate the feasibility and acceptability of conducting continuous glucose monitoring (CGM) in ARIC participants and inform the development of study protocols for visit 9.

Continuous glucose monitoring (CGM) provides nuanced information on glucose patterns, but data in the general population of very old adults are scarce. The latest generation of CGM devices are easy to use and have revolutionized diabetes management for many patients. Nonetheless, CGM is underutilized as a research tool and has rarely been studied in persons without diabetes or in older adults. Indeed, there is no consensus on what constitutes "normal" glucose patterns in older adults as studies of glycemic variability have typically excluded older persons.

We undertook a pilot study to characterize glucose patterns and evaluate the acceptability and feasibility of conducting CGM in a community-based population of very old adults (ages 77 to 91 years) with and without diabetes. We also conducted laboratory measurements of HbA1c, fructosamine, glycated albumin, and 1,5-AG and we will relate them to CGM parameters obtained in the pilot study.

5. Main Hypothesis/Study Questions: High feasibility and acceptability of CGM in very old adults in ARIC.

6. Design and analysis (study design, inclusion/exclusion, outcome and other variables of interest with specific reference to the time of their collection, summary of data analysis, and any anticipated methodologic limitations or challenges if present).

The pilot study and was conducted during the past two months (October and November 2019) of ARIC visit 7 at the Washington County (Johns Hopkins) Field Center. At the time of this visit, all ARIC participants were aged 77 or older. This CGM pilot study involved a separate consent and all participants who attended the last 2 months of visit 7 at the Washington County Field Center were invited to participate. Of these, 61% agreed. All CGM devices were returned but one device did not record any data. We received valid CGM data (ranging from 7 to 14 days) from a total of 27 of participants, 8 with diabetes and 19 without diabetes.

We used the FreeStyle Libre Pro (Abbott Diabetes Care) CGM system to measure glucose in up to 14 days in all participants who consented to participate in the pilot study protocol. The Pro system is factory calibrated (no finger stick), records interstitial glucose every 15 minutes, and stores the 14 days of data. The devices were placed by a technician on the upper arm on participants during the clinic visit. Participants were provided with a pre-paid mailer to return the sensor. They also had the option of returning to the clinic for removal.

All other measurements were obtained using standardized protocols as part of the main ARIC Study. Participants provided fasting blood samples and laboratory measurements of HbA1c, fasting glucose, glycated albumin, fructosamine, and 1,5-anhydroglucitol were obtained. Glucose was measured in serum using the hexokinase method (Roche Diagnostics, Indianapolis, IN). HbA1c was measured in EDTA whole blood on the Tosoh G7 HPLC Glycohemoglobin Analyzer (Tosoh Medics, Inc, San Francisco CA). Fructosamine (Roche Diagnostics), glycated albumin (Asahi Kasei Pharma Corp, Tokyo, Japan), and 1,5-AG (GlycoMark Inc, New York, NY) were measured in serum on the Roche Cobas 6000.

We will evaluate characteristics of the pilot study participants, laboratory biomarkers of hyperglycemia, and CGM parameters according to a diagnosed diabetes status. From the CGM data, we will calculate the mean glucose (average of all available glucose measurements) and the corresponding standard deviation (SD). We will also calculate the coefficient of variation (CV) and the interquartile range (75th percentile minus the 25th percentile). The percent time in the range of 70 to 180 mg/dL and percent time above or below the pre-specified thresholds of 54, 70, 180, and 200 mg/dL are also relevant. We will calculate glycemic excursions (MAGE), the mean of upward and downward glucose excursions exceeding the standard deviation for the individual during the wear-period, and the mean of the differences (MODD).[1, 3, 4] We will evaluate definitions of biochemical hypoglycemia, defined as glucose concentrations <54 mg/dL (level 1) or <70 mg/dL (level 2) for more than 15 minutes (i.e., at least two consecutive readings).[1, 5] We will conduct sensitivity analyses excluding values during the first 24 hours of the CGM sensor wear period.

For each participant, we will a 14-day profile of CGM glucose plotted by time to visualize differences in glucose patterns. We will generate scatterplots with corresponding regression lines (overall and by diabetes status), root mean squared errors (RSME), and Pearson's correlations of CGM mean glucose and HbA1c, fasting glucose, fructosamine, glycated albumin, and 1,5-anhydroglucitol.

7.a. Will the data be used for non-ARIC analysis or by a for-profit organization in this manuscript? ____ Yes __X__ No

b. If Yes, is the author aware that the current derived consent file ICTDER05 must be used to exclude persons with a value RES_OTH and/or RES_DNA = "ARIC only" and/or "Not for Profit" ? ____ Yes ____ No
(The file ICTDER has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript? ____ Yes ___X_ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the current derived consent file ICTDER05 must be used to exclude those with value RES_DNA = "No use/storage DNA"? ____ Yes ____ No

9. The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status.
ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: http://www.cscc.unc.edu/aric/mantrack/maintain/search/dtSearch.html

____X__ Yes _____ No

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? __X__ Yes ____ No

11.b. If yes, is the proposal

_X__ A. primarily the result of an ancillary study (list number* _2019.18_____)

___ B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* _____ _____ _____)

*ancillary studies are listed by number https://sites.cscc.unc.edu/aric/approved-ancillary-studies

12a. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.
CONFIRMED

12b. The NIH instituted a Public Access Policy in April, 2008 which ensures that the public has access to the published results of NIH funded research. It is **your responsibility to upload manuscripts to PubMed Central** whenever the journal does not and be in compliance with this policy. Four files about the public access policy from http://publicaccess.nih.gov/ are posted in http://www.cscc.unc.edu/aric/index.php, under Publications, Policies & Forms. http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed central.
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