Study Protocol

Title: Study to Understand Gaining Access to blood glucose Records (SUGAR), A Randomized Controlled Trial of the Effect of the Livongo Health Diabetes Management Program vs. Standard Care on Glycemic Control

Brief Title: Study to Understand Gaining Access to Blood Glucose Records (SUGAR)

NCT02956642

Protocol revision approved 5/12/2022

Study Application (Version 1.19)

1.0 General Information

***Enter the full title of your study:**

Eureka #001: Study to Understand Gaining Access to blood glucose Records (SUGAR), A Randomized Controlled Trial of the Effect of the Livongo Health Diabetes Management Program vs. Standard Care on Glycemic Control

***Enter the study alias:**

Eureka #001: SUGAR
* This field allows you to enter an abbreviated version of the Study Title to quickly identify this study.

2.0 Add departments

2.1 and Specify Research Location:

Is Primary?	Department Name
◉	**UCSF** - *138310* - M_MED-CORE-CARD
○	**UCSF** - *136219* - M_PEDS-ENDOCRINOLOGY

3.0 List the key study personnel: (Note: external and affiliated collaborators who are not in the UCSF directory can be identified later in the Qualifications of Key Study Personnel section at the end of the form)

3.1 *Please add a Principal Investigator for the study:

Wong, Jenise MD, PhD

Select if applicable

☐ Department Chair ☐ Resident

☐ Fellow

If the Principal Investigator is a Fellow, the name of the Faculty Advisor must be supplied below.

3.2 If applicable, please select the Research Staff personnel

A) Additional Investigators

Olgin, Jeffrey E MD, MD
Other Investigator

B) Research Support Staff

Maguire, Carol A

Study Coordinator
Peyser, Noah, PhD
UCSF Core Personnel
Rohdin-Bibby, Linnea
Study Coordinator

3.3 *Please add a Study Contact

Maguire, Carol A
Olgin, Jeffrey E MD, MD
Peyser, Noah, PhD
Rohdin-Bibby, Linnea
Wong, Jenise MD, PhD

The Study Contact(s) will receive all important system notifications along with the Principal Investigator. (e.g. The project contact(s) are typically either the Study Coordinator or the Principal Investigator themselves).

3.4 If applicable, please add a Faculty Advisor/Mentor:

3.5 If applicable, please select the Designated Department Approval(s)

Add the name of the individual authorized to approve and sign off on this protocol from your Department (e.g. the Department Chair or Dean).

4.0 Initial Screening Questions

Updated June 2017

4.1 * PROJECT SUMMARY: (REQUIRED) Give a brief overview of this project (250 words or less). Tell us what this study is about, who is being studied, and what it aims to achieve. If you have an NIH Abstract, paste it here: Click on the orange question mark to the right for more detailed instructions.

This is a randomized controlled trial (RCT) exploring the effect of using the Livongo Health Diabetes Management Program versus standard blood glucose (BG) monitoring on glycemic control, as measured by change in hemoglobin A1c (A1c), in adults with diabetes over the course of 6 months. Secondary outcomes include frequency of BG monitoring, frequency of BG measurements outside of the target range, change in diabetes distress, and number of self-reported emergency room visits or hospitalizations.

4.2 * HUD DEVICE: (REQUIRED) Does this application involve a Humanitarian Use Device (HUD):

- (●) No
- ( ) Yes, and it includes a research component
- ( ) Yes, and it involves clinical care ONLY

4.3 * TYPE OF RESEARCH: (Click the Help link for definitions and guidance): (REQUIRED)

- ( ) Biomedical research

- ○ Social, behavioral, educational, and/or public policy research
- ◉ Hybrid - includes aspects of BOTH types of research (check this option if your research is mainly social/behavioral but also involves specimen collection or blood draws to look at biological measures)

4.4 * SUBJECT CONTACT: (REQUIRED) Does this study involve ANY contact or interactions with participants:

- ◉ Yes (including phone, email or web contact)
- ○ No (limited to medical records review, biological specimen analysis, and/or data analysis)

4.5 * RADIATION EXPOSURE: Does your protocol involve any radiation exposure to patients/subjects EITHER from standard care OR for research purposes (e.g., x-rays, CT-scans, DEXA, CT-guided biopsy, radiation therapy, or nuclear medicine including PET, MUGA or bone scans): (REQUIRED)

- ○ Yes ◉ No

4.6 * RISK LEVEL: (REQUIRED) What is your estimation of the risk level, including all screening procedures and study activities (Help Text updated 9/13):

- ◉ Minimal risk
- ○ Greater than minimal risk

4.7 * REVIEW LEVEL: (REQUIRED) Requested review level (Click on the orange question mark to the right for definitions and guidance):

- ○ Full Committee
- ◉ Expedited
- ○ Exempt

4.8 * EXPEDITED REVIEW CATEGORIES: (REQUIRED) If you think this study qualifies for expedited review, select the regulatory categories that the research falls under: (check all that apply)

- ☐ Category 1: A very limited number of studies of approved drugs and devices
- ☑ Category 2: Blood sampling
- ☐ Category 3: Noninvasive specimen collection (e.g. buccal swabs, urine, hair and nail clippings, etc.)
- ☑ Category 4: Noninvasive clinical procedures (e.g. physical sensors such as pulse oximeters, MRI, EKG, EEG, ultrasound, moderate exercise testing, etc.)
- ☐ Category 5: Research involving materials (data, documents, records, or specimens) that were previously collected for either nonresearch or research purposes
- ☐ Category 6: Use of recordings (voice, video, digital or image)
- ☑ Category 7: Low risk behavioral research or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies

4.11 * CLINICAL TRIAL: (REQUIRED) Is this a clinical trial? According to The World Health Organization (WHO) and the International Committee of Medical Journal Editors (ICMJE) a clinical trial is:

- **Any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes.**

ICMJE requires registration of a clinical trial in a public database (such as ClinicalTrials.gov) prior to enrollment, for eventual publication of results in member biomedical journals. Guidance: Public Law 110-85 requires that all investigators who perform an *applicable clinical trial* must ensure that the trial is registered on a government web site called ClinicalTrials.gov. The FDA requires registration for "applicable clinical trials," defined as follows:

- **For any trials of drugs and biologics: controlled clinical investigations, other than Phase 1 investigations, of a product subject to FDA regulation.**
- **For trials of biomedical devices: controlled trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies, and pediatric post-market surveillance.**

For additional information on the ClinicalTrials.gov registration process at UCSF and the definition of a clinical trial for purposes of registration, visit the ClinicalTrials.gov section of the UCSF Clinical Research Resource HUB.

(•) Yes ( ) No

Clinical Trial Registration

"NCT" number for this trial:

NCT02956642

If you don't yet have the NCT#, type 'Pending.'

4.12 * CLINICAL TRIAL PHASE (REQUIRED) Check the applicable phase(s) (Help Text updated 9/13):

- [ ] Phase I
- [ ] Phase II
- [x] Phase III
- [ ] Phase IV

4.13 * INVESTIGATOR-INITIATED: (REQUIRED) Is this an investigator-initiated study:

(•) Yes ( ) No

4.14 SCIENTIFIC REVIEW: If this study has undergone scientific or scholarly review, please indicate which entity performed the review (check all that apply):

- [ ] Cancer Center Protocol Review Committee (PRC) (Full approval is required prior to final CHR approval for cancer-related protocols.)
- [ ] CTSI Clinical Research Services (CRS) Advisory Committee
- [ ] CTSI Consultation Services
- [ ] Departmental scientific review
- [ ] Other:

4.15 * STEM CELLS: (REQUIRED) Does this study involve human stem cells (including iPS cells and adult stem cells), gametes or embryos:

(•) No
( ) Yes, and requires CHR and GESCR review
( ) Yes, and requires GESCR review, but NOT CHR review

4.16 * FINANCIAL INTERESTS: (REQUIRED) Do you or any other responsible personnel (or the spouse, registered domestic partner and/or dependent children thereof) have financial interests related to this study:

( ) Yes (•) No

5.0 Funding

5.1 * FEDERAL FUNDING: (REQUIRED) Is this study currently supported in whole or in part by Federal funding, *even by a subcontract*, OR has it received ANY Federal funding in the past:

○ Yes ◉ No

5.2 * DoD INVOLVEMENT: Is this project linked in any way to the Department of Defense (DoD): (REQUIRED)

○ Yes ◉ No

5.3 SPONSORS: Identify all sponsors and provide the funding details. If funding comes from a Subcontract, please list only the Prime Sponsor:

External Sponsors:

View Details	Sponsor Name	Sponsor Type	Awardee Institution:	Contract Type:	Project Number	UCSF RAS System Award Number ("A" + 6 digits)
⊟	Livongo Health Inc	04	UCSF	Contract	P0518133	

Sponsor Name:	Livongo Health Inc
Sponsor Type:	04
Sponsor Role:	Funding
CFDA Number:	
Grant/Contract Number:	
Awardee Institution::	UCSF
Is Institution the Primary Grant Holder:	No
if No, then who is the Primary Grantee?	
Contract Type:	Contract
Project Number:	P0518133
UCSF RAS System Award Number ("A" + 6 digits):	
Grant Number for Studies Not Funded thru UCSF:	
Grant Title:	
PI Name: (If PI is not the same as identified on the study.)	
Explain Any Significant Discrepancy:	

If the funding is coming through UCSF and you don't know the A or P number, you can search the eProposal side for the contract or grant (this does NOT replace adding the sponsor by name above AND entering the A or P number):

Project Status	Proposal Number	Project Title	Principal Investigator
No Projects are Linked to this IRB Study			

Other Funding Sources and Unfunded Research - Gift, Program, or Internal Funding (check all that apply):

- [ ] Funded by gift (specify source below)
- [ ] Funded by UCSF or UC-wide program (specify source below)
- [ ] Specific departmental funding (specify source below)
- [ ] Unfunded (miscellaneous departmental funding)
- [ ] Unfunded student project

6.0 Sites, Programs, Resources, and External IRB Review

6.1 UCSF AND AFFILIATED SITES (check all that apply):

- [x] UCSF (including Laurel Heights and all the other sites outside the main hospitals)
- [x] Parnassus
- [x] Mission Bay
- [ ] China Basin
- [ ] Mount Zion
- [ ] Helen Diller Family Comprehensive Cancer Center
- [ ] Langley Porter Psychiatric Institute
- [ ] San Francisco General Hospital (SFGH)
- [ ] SF VA Medical Center (SF VAMC)
- [ ] Blood Centers of the Pacific (BCP)
- [ ] Blood Systems Research Institute (BSRI)
- [ ] Fresno Community Medical Center
- [ ] Gallo
- [ ] Gladstone
- [ ] Jewish Home
- [ ] Institute on Aging (IOA)
- [ ] SF Dept of Public Health (DPH)

6.2 LOCATIONS: At what locations will study visits and activities occur:

This is a remote and mobile-based study. Due to the nature of this study, there is the potential that participants from all over the United States may be recruited.

6.3 OFF-SITE PROCEDURES: Will any study procedures or tests be conducted off-site by non-UCSF personnel:

(•) Yes ( ) No

Please identify which procedures may be done off-site:

Participants will either be directed to a nearby Quest Labs to get their hemoglobin A1c and lipid panel labs done, OR be sent a mail-in lab test kit (Home Access Health Corporations) for them to provide a blood sample at home. If participants choose to use the Home Access mail-in lab kit rather than visit a lab, their sample will be shipped (using the shipping materials provided) to the Home Access centralized lab for testing and determination of hemoglobin A1c and lipid panel levels.

6.4 RESEARCH PROGRAMS: Check any UCSF research programs this study is associated with:

- ☐ Cancer Center
- ☐ Center for AIDS Prevention Sciences (CAPS)
- ☐ Global Health Sciences
- ☐ Immune Tolerance Network (ITN)
- ☐ Neurosciences Clinical Research Unit (NCRU)
- ☐ Osher Center
- ☐ Positive Health Program

6.5 * CTSI CRS SERVICES: (REQUIRED) Will this study be carried out at one of the UCSF Clinical Research Services (CRS) units or utilize CRS services:

○ Yes ◉ No

6.6 * MULTI-CENTER TRIAL: (REQUIRED) Is this a multicenter research trial? By multi-center trial, we mean a study where the protocol is developed by an industry sponsor, consortium, a disease-group, etc., who then selects sites across the nation or in different countries to participate in the trial. The local sites do not have any control over the design of the protocol.

○ Yes ◉ No

6.7 OTHER SITE TYPES: Check all the other types of sites not affiliated with UCSF with which you are cooperating or collaborating on this project: Do NOT check any boxes below if this is a multi-center clinical trial, UCSF is just one of the sites, and neither UCSF nor its affiliates are the coordinating center.

- ☐ Other UC Campus
- ☐ Other institution
- ☐ Other community-based site
- ☐ Foreign Country
- ☐ Sovereign Native American nation (e.g. Navajo Nation, Oglala Sioux Tribe, Havasupai, etc.)

6.10 * RELYING ON AN EXTERNAL IRB: Does this application include a request to rely on an a central IRB (other than the NCI CIRB) or an external IRB (UC, commercial, or institutional): (REQUIRED)

○ Yes ◉ No

7.0 Research Plan and Procedures

7.1 This new consolidated section requests information about:

- **Hypothesis**
- **Aims**
- **Study Design**

- **Background and Significance**
- **Preliminary Studies**
- **Procedures**
- **Statistical Methods**
- **References**

Later sections include:

- **Drugs and Devices**
- **Sample Size, Eligibility, and Subjects**
- **Recruitment and Consent**
- **Risks and Benefits**
- **Data and Safety Monitoring Plan**
- **Confidentiality, Privacy and Security**
- **Financial Considerations**
- **Qualifications of Personnel**
- **Other Approval and Registrations**

7.2 HYPOTHESIS: Describe the hypothesis or what the study hopes to prove (Help Text updated 9/13):

We hypothesize that use of the Livongo Health system results in a greater improvement in hemoglobin A1c (A1c) compared to standard blood glucose (BG) monitoring, measured by the iHealth Bluetooth-enabled glucose meter.

7.3 AIMS: List the specific aims:

To determine the effect of use of the Livongo Health system versus standard BG monitoring in adults with type 2 diabetes on glycemic control as measured by A1c. As a secondary outcome, we will determine the effect of use of the Livongo Health system on fasting lipid panels.

7.4 DESIGN: Briefly describe the study design (e.g., observational, interventional, randomized, placebo-controlled, blinded, cross-over, cross-sectional, longitudinal, pharmacokinetic, etc.):

The study is a two-arm randomized controlled trial (RCT). Participants will either be randomized to receive the Livongo Health system or the iHealth glucose meter for measuring their blood glucose.

7.5 BACKGROUND AND SIGNIFICANCE: Briefly provide the background and significance of this study (e.g. why is this study needed) (space limit: one half page):

The goal of Livongo Health (**http://www.livongo.com/**) is to help people with diabetes and other chronic conditions better manage their health by using a combination of patented technology, smart analytics, and a coaching team. For the purposes of this study, Livongo will provide a comprehensive diabetes care solution that involves unlimited test strips, real-time glucose monitoring with real-time feedback and support of coaches. We will compare this comprehensive system with current standard blood glucose (BG) monitoring with the iHealth Bluetooth glucose meter and standard diabetes care.

The core components of Livongo Diabetes include (1) a cellular connected Livongo glucose meter that measures blood glucose and centrally stores the glucose data in a secure cloud, (2) an unlimited supply of glucose test strips mailed to a member's home, and (3) access to a diabetes coaching team for questions, goal setting and support for extreme glucose excursions.

The Livongo glucose meter captures biometric data including blood glucose data, medication usage and other information. The data is instantly analyzed in Livongo Health's intelligent cloud. Immediate personalized education and support is returned directly through the meter. Livongo Health's Certified Diabetes Educators (CDEs) are on-call to provide further support and education when requested by member or automatically when a member is in their high and low zones. Using the clinically-proven AADE7 Self-Care Behaviors, a member's coaching experience is customized based on the member's health information and biometric data.

Many research studies have shown a positive impact of health coaching, lifestyle interventions, and structured blood glucose monitoring plans on diabetes outcomes. The comprehensive Livongo diabetes program is poised to meet the individual needs of its members with diabetes based on member-reported health information and biometric data. Using data and technology to create a personalized approach, the coaching team receives immediate feedback on whether outreach efforts make a difference in member behavior and blood glucose control. We hypothesize that this novel coaching feedback system will lead to improved blood glucose control compared to the current standard of diabetes care.

This pilot study will utilize the National Institutes of Health-funded Eureka mHealth Research Platform (CHR #16-19397), a platform that enables investigators to conduct mobile and wireless health research in a less costly, more streamlined manner, in order to recruit participants, collect and store study data, and manage study participants. The research platform will accelerate our ability to access a large cohort of volunteers who have agreed to participate in research (over 40,000 participants worldwide), and provide a quick, affordable means for collecting their health data through mobile and wireless technologies. Access to this unique, diverse, real-world study population will allow us to generalize our study results compared to those we might obtain working through a highly specialized diabetes center.

7.6 PRELIMINARY STUDIES: Briefly summarize any preliminary studies relevant to your proposed research (space limit: one half page):

Review of data from 4,544 individuals with diabetes who were enrolled in the Livongo program from October 2014 through December 2015 shows that members used the Livongo glucose meter to measure their blood glucose levels an average of 2 times per day. Using an individual fixed-effects logit model to look at the relative change in the odds of having at least one daily high blood glucose reading (defined as BG >180 mg/dL) or one daily low blood glucose reading (defined as < 80 mg/dL) in subsequent months two through twelve compared with month one as the baseline, there was a statistically significant and sustained reduction in the likelihood of having a day with a blood glucose reading >180 mg/dL at all subsequent months compared to baseline. There was a sustained reduction in the likelihood of having a day with a blood glucose reading < 80 mg/dL at all subsequent months compared to baseline. For members enrolled in the Livongo Diabetes program, the likelihood of BG>180 or BG< 80 is decreased in Months 2-12 compared to Month 1 of the program.

In addition, econometric difference-in-difference modeling of lab data provided by a large self-insured employer client suggests that Livongo members experience improvements not only in HbA1c but also in lipid levels. Total cholesterol tests show the strongest effect. Pre-Livongo users and non-users have similar values but towards the end of the one-year intervention period, Livongo users have substantially lower values. The regression results show a 37.2% (p=0.04) reduction which translates into a 64.0-point reduction in cholesterol values. Triglycerides also trended downwards by 8.3% (p=0.80) reduction in test values over one year. This translates to a 10.0-point reduction in cholesterol values.

7.7 * TREATMENT PROTOCOL: Is this a treatment study, i.e. does this study intend to provide treatment to individuals with a medical or psychological condition: (REQUIRED)

- ○ Yes
- ◉ No

7.8 * COMMON RESEARCH ACTIVITIES: Types of research activities that will be carried out. Check all that apply and describe in more detail in the 'Procedures / Methods' section: (REQUIRED)

- ☑ Interviews, questionnaires, surveys
- ☐ Educational or cognitive tests
- ☐ Focus groups
- ☑ Observation
- ☐ Non-invasive imaging or testing (MRI, EEG, pulse oximetry, etc.)
- ☐ Administration of contrast agent
- ☐ Imaging procedures or treatment procedures that involve radiation (x-rays, CT scans, CT-guided biopsies, DEXA scans, MUGA or PET scan)
- ☐ Biopsy conducted solely for research purposes
- ☐ Use of placebo
- ☐ Sham surgical procedure

- [x] Collection of data from wearable tech such as Fitbit, Apple Watch, Garmin, motion actigraphs, etc.)
- [ ] Fitness tests or other exertion activities
- [x] Use of mobile health apps or other apps
- [ ] Social media-based research activities
- [ ] None of the above

7.9 * PROCEDURES / METHODS: (REQUIRED)

Describe the research methods and study activities taking place at each site (e.g. what will participants be asked to do and what will members of the study team do?). If there will be multiple participant groups or study sites, explain what will happen with each group or study sites.

If some of the activities would occur even if the person were not in the study, as in the case of treatment or tests performed for diagnostic purposes, clearly differentiate between those activities that will be done solely for research purposes and those that are happening as part of routine care.

Please call our office at 415-476-1814 and ask to speak to someone on the Expedited Review team if you need help differentiating between what parts are research and what parts aren't.

1. **Surveys and Measurements**

- All study participants may complete surveys via their personal iOS smartphone device on: study qualification (intake survey/eligibility screener discussed further in Section 10.3), diabetes status (initial diabetes survey), physical activity (iPAQ), quality of life (SF-12), vitals (attached), demographics (attached) hospitalizations and interaction with health care provider (attached), and diabetes distress (attached). Most survey data will be collected at 1, 3, and 6 months. There will also be Weekly Engagment surveys (attached) which will be two simple questions each week. At the end of the study, a Feedback survey (attached) will ask participants about their study experiences. Surveys will each have a simple description to introduce participants to the survey they are being asked to take (document attached). These surveys will be administered through the Eureka mHealth Research Platform, the study's main tool for data collection, data storage, and study management. Specific usability assessments that are native to the Livongo or iHealth platform may also be shown through the device to the participants in order to gather user feedback information.
- After qualifying and providing consent to participate in the study, participants will be referred to a convenient lab for establishing hemoglobin A1c (A1c) levels and lipid panel levels. A1c labs will be collected at months 1 (baseline), 3, and 6 (closeout). For each A1c lab, 1mL of blood will be drawn. Lipid panels (total cholesterol, LDL, HDL, and triglycerides) will be collected at months 1 (baseline) and 6 (closeout). For each lipid panel lab, 1mL of blood will be drawn.
- As an alternative to visiting a lab, participants will have the option of using a Home Access Health Co. Mail-in Laboratory Test Kit to collect a sample for establishing A1c and lipid pabel levels. Just as if they were to visit a local lab, these samples will be collected at months 1 (baseline), 3, and 6 (closeout). At months 1 and 6, participants will use a professional use finger prick blood collection kit to collect 75 microliters of blood. The Mail-in Lab Test is coded for A1c and complete lipid panel testing. This professional use kit requires a requisition for the participant, which will be provided by Home Access physicians. At month 3, participants will use an FDA approved direct-to-consumer A1c kit to collect 35 microliters of blood for A1c levels only. No physician authorization is required for this kit. When time for each blood draw at months 1, 3, and 6, participants will be sent the appropriate kit that will include everything

necessary for successful collection, packaging, and mailing of specimen, including a cover letter from the SUGAR Study Team (attached). All samples will be mailed to the Home Access Health laboratory for testing.

- Participants are strongly encouraged to be consistent with whichever method they choose. This means that if their first blood draw occurs at a Quest Labs, we would like them to complete their second and third blood draws at a Quest Labs as well. If they choose to use a home kit for their first blood draw, we would like them to use a home kit for their second and third blood draws if possible.

- If a participant wishes to obtain a copy of the lab results, they may email the study coordinator to request a copy at sugar@eurekaplatform.org. Their results will be sent through the study coordinator's UCSF email securely with "ePHI:" or "Secure:" in the subject field. We have indicated in the consent form how a participant may retrieve their lab results and have also included the statement that we do not provide a clinical interpretation of their data from the study or provide medical advice. Additionally, we have included language indicating participation in this study does not in any way substitute for professional medical advice, diagnosis, or treatment that their doctor or other healthcare provider may give them. If they think they may have a medical emergency, they are recommended to call their doctor or notify emergency services.

2. Randomization

- Once the baseline A1c value is obtained, the patient will be randomized (block randomization by diabetes type).

3. Device Usage

- After randomization, participants will receive either the Livongo Health system or the iHealth glucose meter by mail.
    - If a participant is randomized to the iHealth treatment group, participants will download the iHealth iOS application (iHealth Gluco-Smart) and receive an iHealth blood glucose meter in the mail. Participants will link the iHealth application with a mobile version of the Eureka mHealth Research Platform.
    - If a participant is randomized to the Livongo system treatment group, the participant will receive the Livongo blood glucose meter device in the mail, create a Livongo account, and link their Livongo account with the Eureka mHealth Research Platform.
- Livongo- or iHealth-specific instructions will be provided with each meter and a study coordinator will be available to answer study participant questions about using the BG meters. Participants may be referred to Livongo or iHealth customer service for technical support, if needed.
- Participants will not be given specific instructions on how often to check their BG, or how often they should use the Livongo system or iHealth glucose meter as a part of this study. This is done in order to determine the uptake of the intervention and resulting behavior without outside prompting.
- Participants will either use the Livongo system or the iHealth glucose meter for 6 months from the time of enrollment in the study.

4. Messaging/Reminders

- Participants who have been mailed a BG meter but are not using the device after two weeks will be contacted by in-app push notifications, text messages, email or a phone call for device setup and/or assistance.
- Particpants will also recieve reminders to complete study activities via in-app push notifications, text messages, email or a phone call.
- Two weeks prior to the end of the study period, participants will be contacted by email and/or receive in-app push notifications to remind them to complete their A1c measurement and closeout surveys.

Note: Participation in this research study will not affect individual participants' standard clinical care for diabetes. Participants will remain under the care of their current health care provider and will be able to continute receiving all usual care from that provider. The health care provider will continue to provide recommendations for the number of times the participant shoudl check their blood glucose. Although the participant wil be asked to use a different glucose meter for this study, the number of times they

use it will still be determined by their health care provider. The same information that they received from their existing glucose meter will be available from the study glucose meter. During the study, they will be provided with glucose meter strips at no charge, to ensure that an insufficient number of strips will not interfere with their standard of care.

7.11 INSTRUMENTS: List all questionnaires, surveys, interview, or focus group guides that will be used for this study:

If the instruments are not complete or not available because they will be developed as part of this study, describe the basic content or include an outline and submit the final versions to the IRB with a modification for approval prior to use.

Survey instruments:

- Intake Survey + General Diabetes Status
- Basic Demographics
- Social Demographics
- Internet Use
- Diabetes Distress
- Physical Activity (IPAQ)
- Quality of Life (SF-12)
- Hospital Visit and Health Care Provider
- Diabetes Empowerment

Attach any unpublished instruments in the 'Other Study Documents' section of the Initial Review Submission Packet form after completing the study application. Published instruments should NOT be attached.

7.12 * BIOSPECIMEN COLLECTION: Are you drawing any blood or collecting other biosamples (e.g. tissue, buccal swabs, urine, saliva, hair, etc.): (REQUIRED)

(•) Yes ( ) No

* Could this study generate genetic data that may be broadly shared (e.g., submitted to NIH in compliance with **Genomic Data Sharing (GDS)/Genome-Wide Association Studies (GWAS)** requirements): **(REQUIRED)**

( ) Yes (•) No

Based on current research trends, we strongly recommend including the genomic data sharing language in the consent form to allow future sharing, even if you don't anticipate it now. It's easier than trying to reconsent all the specimen donors!

7.13 * TYPE OF SPECIMENS (check all that apply): (REQUIRED)

- [x] Blood
- [ ] Tissue (describe below):
- [ ] Existing/archival materials (name source below): --
- [ ] Other (describe below):

7.14 * SPECIMENS ARE: (check all that apply): (REQUIRED)

- [ ] Leftover specimens from a clinical diagnostic or therapeutic procedure
- [x] Specimens collected for research purposes only (including extra samples taken during a clinical procedure)
- [ ] Other

7.15 * DESTINATION: Specimens will ultimately be stored (check all that apply): (REQUIRED)

Outside Entity:

- [ ] Cooperative group bank
- [ ] NIH
- [ ] Other university
- [ ] Industry sponsor
- [ ] Other

UCSF:

- [ ] UCSF repository/bank being established under this protocol
- [ ] Existing UCSF specimen repository/bank with CHR approval
- [x] Other location at UCSF (please describe)

Provide the name of the bank and iRIS approval number (if not being banked at UCSF under this protocol). If you checked 'Other,' please provide the location or lab:

The blood samples we draw (through Quest Labs or Home Access mail-in kit) will be used for analysis of the participant's blood sugar levels. The study does not intend to store or bank any of the samples after analysis. The participants will be sent their requisition in a secure email or through a secure download link to bring with them to the lab if they miss their selected date.

7.18 * FUTURE SPECIMEN USE: Will any specimens or portions of specimens be retained after the study is over for possible use in future research studies: (REQUIRED)

- ○ Yes
- ◉ No

7.20 * CLINICAL FOLLOW-UP DATA: Will clinical follow-up data be linked to specimens (i.e., will medical record information continue to be abstracted after the specimen is collected): (REQUIRED)

- ○ Yes
- ◉ No

Provide duration of follow-up or 'indefinitely':

7.25 STATISTICAL METHODS: Briefly summarize the methods and types of analyses that will be performed:

Descriptive statistics (t-tests for continuous variables and chi-squared tests for dichotomous variables) will be used to compare demographic, clinical, and socioeconomic variables. The primary outcome measure is change in A1c. Data will be analyzed as a comparison between experimental and control groups. Data may also be stratified by duration of diabetes and baseline HbA1c (< 7.0% vs 7.0). Methods for analyzing longitudinal data (mixed-effects linear regression models or generalized estimating equations) will be used to look for the effect of using Livongo on change in A1c, adjusting for possible confounding variables. Similar models will be used to examine secondary outcomes.

7.26 REFERENCES: List only the 5-10 most relevant references (a separate bibliography can be attached for reference purposes if this study involves novel approaches, agents, or an emerging technology that the IRB may not be familiar with):

1. Thom DH, Willard-Grace R, Hessler D, et al. The impact of health coaching on medication adherence in patients with poorly controlled diabetes, hypertension, and/or hyperlipidemia: a randomized controlled trial. J Am Board Fam Med 2015;28(1):38–45.

2. Cinar AB, Oktay I, Schou L. “Smile healthy to your diabetes”: health coaching-based intervention for oral health and diabetes management. Clin Oral Investig 2014;18(7):1793–801.

3. Huang X-L, Pan J-H, Chen D, Chen J, Chen F, Hu T-T. Efficacy of lifestyle interventions in patients with type 2 diabetes: A systematic review and meta-analysis. European Journal of Internal Medicine 2016;27(C):37–47.

4. Hesselink A. Effectiveness of a protocol-based lifestyle program to prevent type 2 diabetes.

5. The Look AHEAD Research Group. Eight-year weight losses with an intensive lifestyle intervention: The look AHEAD study. Obesity 2014;22(1):5–13.

6. Allemann S, Houriet C, Diem P, Stettler C. Self-monitoring of blood glucose in non-insulin treated patients with type 2 diabetes: a systematic review and meta-analysis. Curr Med Res Opin 2009;25(12):2903–13.

7. Schnell O, Alawi H, Battelino T, et al. Addressing Schemes of Self-Monitoring of Blood Glucose in Type 2 Diabetes: A European Perspective and Expert Recommendation. Diabetes Technology & Therapeutics 2011;13(9):959–65.

8. Self-Monitoring of Blood Glucose in Type 2 Diabetes: Recent Studies. 2013;:1–11.

9. Robertson E. Barriers and Behaviors in Blood Glucose Monitoring. 2008;:1–3.

10. AADE7TM Self-Care Behaviors. The Diabetes Educator 2008;34(3):445–9.

11. Kollmann A, Riedl M, Kastner P, Schreier G, Ludvik B. Feasibility of a Mobile Phone–Based Data Service for Functional Insulin Treatment of Type 1 Diabetes Mellitus Patients. Journal of Medical Internet Research 2007;9(5):e36.

12. Lanzola G, Capozzi D, D'Annunzio G, Ferrari P, Bellazzi R, Larizza C. Going Mobile with a Multiaccess Service for the Management of Diabetic Patients. J Diabetes Sci Technol 2007;1 (5):730–7.

13. Toscos TR, Ponder SW, Anderson BJ, et al. Integrating an Automated Diabetes Management System into the family management of children with type 1 diabetes: results from a 12-month randomized controlled technology trial. Diabetes Care 2012;35(3):498–502.

8.0 Drugs and Devices

8.1 * DRUGS AND/OR BIOLOGICS: Are you STUDYING any drugs and/or biologics that are either approved or unapproved: (REQUIRED)

○ Yes ◉ No

Note: This question is frequently answered incorrectly. If any drugs or biologics, approved or unapproved, are being administered under this protocol, you should check 'Yes' unless you are *absolutely* sure that NONE of the drugs are part of the research protocol. Tip: Ask the PI or the sponsor if you are not sure how to answer this question.

8.3 * MEDICAL DEVICES: Are you STUDYING any medical devices, in vitro diagnostics, or assays that are either approved or unapproved:(REQUIRED)

(•) Yes ( ) No

8.4 * NSR: Are you requesting a Non-Significant Risk (NSR) determination for an investigational device: (REQUIRED) Note: an NSR determination is different from an Investigational Device Exemption (IDE). Check the Help link for more guidance on what types of devices can qualify for an NSR determination.

( ) Yes (•) No

8.5 LIST THE DEVICES: List the medical devices or in vitro diagnostics to be studied or used. In the device details screen you will be asked questions such as:

- **Whether the device is FDA approved or investigational**
- **Medicare device category**
- **If the device will be provided at no cost**
- **If an IDE is necessary, the IDE number, and who holds the IDE**
- **Risk category of the device**
- **FDA status of the device**

Please see the UCSF IRB website for more details about the use of devices in research, including the Investigator Checklist for Significant Risk, Non-Significant Risk, and/or IDE Exempt Device Studies
Verification of IDE numbers: If the sponsor's protocol does not list the IDE number, you must submit documentation from the sponsor or FDA identifying the IDE number for this study. Attach this documentation in the Other Study Documents section of the Initial Review Submission Packet.

If you have any correspondence from the FDA or sponsor regarding this device, please attach it to the application.

View Details	Device Name	Is the Device FDA Approved	Is this a new device or a new use of an already approved device	IDE Number
⊟	iHealth Wireless Smart Gluco-Monitoring System	Yes	No	

Manufacturer/Supplier of Device	iHealth Labs
Medicare Category	☐ A ☐ B
Where will the Devices Be Stored	
Will Devices be supplied at no Cost	Yes
Is this a HUD (HDE)	No
HDE Number	
Is the Device FDA Approved	Yes
Is this a new device or a new use of an already approved device	No
Is an IDE necessary	No
IDE Number	
Who holds the IDE	N/A
IDE details	

In the opinion of the sponsor, select the level of risk associated with this device	No Significant Risk			
⊟	Livongo In Touch Blood Glucose Monitoring System	Yes	No	

Manufacturer/Supplier of Device	Livongo
Medicare Category	☐ A ☐ B
Where will the Devices Be Stored	
Will Devices be supplied at no Cost	Yes
Is this a HUD (HDE)	No
HDE Number	
Is the Device FDA Approved	Yes
Is this a new device or a new use of an already approved device	No
Is an IDE necessary	No
IDE Number	
Who holds the IDE	N/A
IDE details	
In the opinion of the sponsor, select the level of risk associated with this device	No Significant Risk

8.6 * Is this an expanded access or compassionate use protocol, meaning the primary purpose is to diagnose, monitor or treat a patient's condition, rather than the collection of safety and efficacy data of the experimental agent: (REQUIRED)

○ Yes ◉ No

9.0 Sample Size and Eligibility Criteria

9.1 ENROLLMENT TARGET: How many people will you enroll:

300

If there are multiple participant groups, indicate how many people will be in each group:

Livongo Health system (experimental group) - 150
iHealth glucose meter (control/standard group) - 150

9.3 SAMPLE SIZE JUSTIFICATION: Explain how and why the number of people was chosen. For multi-site studies, this is referring to the number that will be enrolled across all sites:

- Sample size:
  - *Null Hypothesis:* There is no association between use of Livongo and change in A1c.
  - *Alternative Hypothesis:* (two-sided): The use of Livongo is associated with change in A1c.

- Effect size (t-test) = 0.5%
  - Evidence:
    - A1c decreased from 7.9% to 7.5% in 3 month study of mobile phone-based data service (Kollman, et al., 2007, J Med Internet Res, 9:e36)
    - A1c decreased from 8.4% to 7.85% (adults) and 8.52 to 8.06% (children) in 6 month study using a multi-access diabetes management service (Lanzola, et al., 2007, J Diabetes Sci Technol, 1:730-7)
    - Difference in change in A1c -0.35 (intervention) vs +0.15 (control) after 12 months of using an automated diabetes management system (wireless glucose transfer) (Toscos, et al., 2012, Diabetes Care, 35:498-502)
  - Standard deviation = 1% (based on the above publications)
  - Standardized effect size = E/S = 0.5
- Using a two-sided t-test of 0.05 and power of 80%, n=63 participants per group

We anticipate that we will be able to recruit 300 participants (150 in each arm). Using the above parameters, the study would have 80% power to detect a minimum effect size of 0.33% (and 90% power to detect a minimum effect size of 0.38%).

9.4 * PARTICIPANT AGE RANGE: Eligible age ranges: (REQUIRED)

- [ ] 0-6 years
- [ ] 7-12 years
- [ ] 13-17 years
- [x] 18-64 years
- [x] 65+

9.5 * STUDY POPULATIONS: Data will be collected from or about the following types of people (check all that apply): (REQUIRED)

- [ ] Inpatients
- [ ] Outpatients
- [ ] Family members or caregivers
- [ ] Providers
- [x] People who have a condition but who are not being seen as patients
- [ ] Healthy volunteers
- [ ] Students
- [ ] Staff of UCSF or affiliated institutions
- [ ] None of the above

9.6 * SPECIAL SUBJECT GROUPS: Check the populations that may be enrolled: (REQUIRED)

- [ ] Children / Minors
- [ ] Subjects unable to consent for themselves
- [ ] Subjects unable to consent for themselves (emergency setting)
- [ ] Subjects with diminished capacity to consent
- [ ] Subjects unable to read, speak or understand English
- [ ] Pregnant women
- [ ] Fetuses
- [ ] Neonates
- [ ] Prisoners
- [x] Economically or educationally disadvantaged persons
- [ ] None of the above

If not already addressed in the Background and Significance questions in the Research Plan section or elsewhere, explain why it is appropriate to include the types of subjects checked above in this particular study:

There is a chance that a person who is economically or educationally disadvantaged may have the opportunity to join the study as long as they fulfill all of the inclusion criteria and do not meet any of the exclusion criteria. It is important to allow these participants to join the SUGAR Study because this population, much like others who may participate in the study, may also:

1. Utilizes smartphone and mobile phone technology in daily life, and
2. Suffers from diabetes and can benefit from additional diabetes management.

Describe the additional safeguards that have been included in the study to protect the rights and welfare of these subjects and minimize coercion or undue influence:

Here are some examples:

- evaluating capacity to consent for individuals who may be decisionally impaired (specify how)
- calibrating payment amounts to be non-coercive for the financially disadvantaged
- conducting more in-depth evaluations of subjects' understanding of the study and the voluntary nature of participation
- involving advocates in the consent process

More information and other safeguards are described here: **Vulnerable Subject Populations** and **Recruiting Staff and Students**.

As mentioned in this application, all participants will receive equal treatment, resources (depending on their treatment group), and all active and compliant participants will receive equal payment (see Section 13) during their participation. Additionally, all participants are able to read the consent form before joining the study and are always given the option to opt-out of the study after enrolling. During the enrollment and recruitment phase, participants will sign up for the study on their own volition and will not be forced or coerced to participate. All study activities are completely voluntary.

9.7 INCLUSION CRITERIA: Briefly describe the population(s) that will be involved in this study. Include anyone that data will be collected from or about (e.g. patients, healthy controls, caregivers, providers, administrators, students, parents, family members, etc.):

- People with type 2 DM on any type of medication
- Self-reported A1c level >= 7%
- Adults, age ≥18 years
- Not using continuous glucose monitoring or an insulin pump
- iOS Smartphone with access to data and/or Wi-Fi

9.8 EXCLUSION CRITERIA: List any exclusion criteria (e.g. reasons why someone would not be included in the study):

- Using continuous glucose monitoring during the study period
- People with type 1 DM
- Self-reported A1c level < 7%
- Using an insulin pump during the study period
- Unable or unwilling to switch BG meters to the study meter
- Hospitalization for DKA or hypoglycemia in the past 1 month prior to enrollment
- Pregnant patients, or intention to become pregnant during the study period
- Participants who are currently using, or have every used, the Livongo Health Program

9.9 * RESEARCH CONDUCTED ON PATIENT CARE WARDS: Do any study activities take place on patient care units at UCSF medical facilities: (REQUIRED)

○ Yes ◉ No

10.0 Recruitment and Consent

10.1 * RECRUITMENT METHODS: What kinds of methods will be used to identify potential participants for recruitment (check all that apply): (REQUIRED)

- ☐ Medical records review
- ☐ Recruitment registry
- ☐ Re-contact of participants from the investigators' previous studies
- ☐ Referrals from colleagues (attach the 'Dear Colleague' letter or other recruitment materials you will provide to colleagues)
- ☑ Referrals from the community / word of mouth
- ☑ Advertisements (flyers, brochures, radio or t.v. ads, posting on clinical research sites or social media, presentation of the study at community events/media, etc.)
- ☐ Online recruiting tool such as TrialSpark
- ☐ CTSI Recruitment Services unit
- ☐ Other method (describe below)

Attach your recruitment materials (e.g., flyers, ads, recruitment letter templates, email text, etc.) in the Other Study Documents section of the Initial Review Submission Packet Form.

10.3 DETERMINATION OF ELIGIBILITY: How, when, and by whom will eligibility for recruitment be determined:

Initial eligibility will be determined through a mobile application version of the Eureka mHealth Research Platform.

Once a participant expresses interest in participating in the SUGAR Study, they will receive a study-specific link to download the Eureka mHealth Research Platform application, from the Apple App Store, onto their personal iOS device. After downloading the application and creating an account with the mobile version of the Eureka mHealth Research Platform (refer to CHR #16-19397 for more details on registration process), the participant will answer an intake survey that will be used to assess initial eligibility. The answers to this screener will be stored in an anonymous and de-identified fashion. If the participant meets the eligibility criteria, they will be then be presented with the SUGAR Informed Consent (which contains a link to the Eureka mHealth Platform Privacy Policy) via the Eureka mHealth Research Platform application. After the consenting process, the anonymous eligibility data may be matched up to the consented participant.

Eligibility may also be determined in accordance to the pre-set criteria after a participant completes the initial diabetes status intake survey.

10.4 * INITIATION OF CONTACT: Who initiates contact (check all that apply): (REQUIRED)

- ☑ Investigators/study team
- ☐ UCSF recruitment unit (e.g. CTSI Consultation Services)
- ☑ Potential participant
- ☐ Other (explain below)

10.5 * HOW IS CONTACT INITIATED: (check all that apply): (REQUIRED)

- ☐ In person
- ☐ Phone
- ☐ Letter / email

- [x] Website or app
- [ ] Other (explain below)

Provide the URL for any website in Recruitment Plan section, or attach a mock-up of the website or the app screens in the Other Study Documents section of the Initial Review Submission Packet Form.

10.6 RECRUITMENT PLAN: Based on the checkboxes you chose above, please provide a narrative describing your recruitment plan. We want to know:

- **Who is conducting the search for potential participants, and how?**
- **How are potential subjects being approached for recruitment? By whom, and when?**

If there will be more than one participant group (e.g. patients, healthy controls, caregivers, family members, providers, etc.), provide details about the recruitment plans for each group. (Recommended length - 100-250 words)

Participants may be recruited into the mobile-based study through a few methods:

- Targeted ads displayed through social media (Facebook, Twitter, etc)
- Targeted ads displayed on diabetes awareness or education websites (American Diabetes Association, Diabetes Society, etc)

Participants will initiate interaction with the mobile study on their own accord and volition.

10.7 * CONSENT METHODS: How will permission to participate (i.e., informed consent) be obtained from each potential participant. If there will be multiple groups and different plans for consenting each, check all that apply. See the orange Help bubble to the right for more detailed guidance. Participants will (check all that apply): (REQUIRED)

- [ ] Sign a consent form at the end of the consent discussion (signed consent)
- [x] Provide online 'eConsent' using DocuSign or another E-Signature system
- [ ] Click through a link in a survey or email after reading about the study and then complete the study online (electronic consent)
- [ ] Be told about the study and be given a handout/information sheet and be asked if they agree to participate (verbal consent)
- [ ] Complete the study activities and turn in materials, as in the case of a completed survey that is placed in a drop box or mailed to the study team (implied consent)
- [ ] Not be able to provide consent and will have a family member consent for them, as in the case of a critically ill or unconscious patient (surrogate consent)
- [ ] Not be able to provide consent (emergency waiver of consent - allowed for minimal risk research or greater than minimal risk research with an approved community consultation plan)
- [ ] Not know about the study, as in the case of chart reviews or observations of public behavior (waiver of consent)
- [ ] Other method (describe below)

10.8 * CONSENT PROCESS: Describe the process for obtaining informed consent, including details such as who will have the consent discussion and when participants will be asked to sign the consent form in relation to finding out about the study: (REQUIRED) We encourage researchers to review our guidance on obtaining and documenting informed consent.

- **If there are multiple groups being consented differently, provide details about the consent process for each group.**
- **If you are relying on verbal or implied consent, provide details about how that will happen.**
- **For studies using online recruitment and consent or consent via mail, provide details here.**

Informed consent will be obtained electronically through the mobile-based study workflow. In order to ensure that participants are thoroughly informed, we will implement the following series of screens:

1. An eligibility screen with the inclusion and/or exclusion criteria; participants can only proceed if they are deemed eligible.
2. A summary screen with the most important aspects from the complete informed consent form (ICF).
3. The complete SUGAR ICF; participants are only eligible to consent after they scroll through the entire document (buttton won't activate otherwise).
4. At any point in the SUGAR study, participants can contact a SUGAR study coordinator or team member to address any questions.

10.10 * DECEPTION: Does this study rely on some deception or misinformation about what the researchers are observing to get valid data? (REQUIRED)

○ Yes ◉ No

10.13 TIME: What is the estimated time commitment for participants (per visit and in total):

Total duration of participation in the study is 6 months from date of submitting their baseline hemoglobin A1c lab. We estimate the following time commitments:
- Consent process: 5 minutes
- Baseline surveys: 12 minutes
- HbA1c and Lipid Panel test: At local lab: 5-10 minutes (plus travel time to the lab) x 3 (baseline, month 3, and 6 months/closeout). Using Home Kit: 15 - 20 minutes (no travel time to lab) x 3 (baseline, month 3, and 6 months/closeout)
- Use of the Livongo system vs control meter: 5-15 minutes per day
- Follow-up surveys: 15 minutes x 2 (3 months and 6 months)

IMPORTANT TIP: Ensure this information is consistent with the information provided in the consent form.

10.16 OTHER ALTERNATIVES: Describe other alternatives to study participation, if any, that are available to prospective subjects:

Participants can choose to not participate or withdraw at any point in the study.

11.0 Risks and Benefits

11.1 RESEARCH-RELATED RISKS: Check if your study involves any of these specific research-related risks to participants that may need to be disclosed in the consent form:

- ☑ Physical discomforts or pain
- ☐ Risks to employment, or social or legal standing
- ☑ Possible personal discomfort due to sensitive topics (stress, embarassment, trauma)
- ☐ Risk that the study team may observe possible evidence of child abuse, elder abuse, or a threat to self or others that they are required to report

* For any boxes checked above, describe how you will minimize these risks and discomforts, e.g., adding or increasing the frequency of monitoring, additional screening to identify and exclude people with diminished kidney or liver function, or modification of procedures such as changing imaging studies to avoid giving contrast agent to people who are more likely to suffer side effects from it, etc.: **(REQUIRED)**

Included here is a discussion of the possible risks and discomforts associated with participation in the SUGAR Study. With regard to personal discomfort, the study will ask participants to answer survey questions, some of which may ask about the participant's behaviors, medical conditions, or lifestyle that may be uncomfortable to a patient.

With regard to physical discomfort and pain, the study asks participants to take daily glucose meter readings, which includes a finger prick, in addition to hemoglobin A1c and lipid panel measurements, which involves a puncture in order to collect the blood sample.

Overall, the aforementioned could cause discomfort to participants, but these study activities pose relatively minimal risk. The study team ensures each participant is aware of the possible risks before agreeing to take part in the SUGAR Study.

11.2 RISKS: Describe any anticipated risks and discomforts not listed above:

Participants may experience discomfort from the blood draws, or during blood sample collection using a home kit, required for the study. There may also be financial risks such as wanting increased access to the healthcare system or incurring extra data charges due to increased interaction with the smartphone and increased cellular data usage.

Taking part in the SUGAR study requires us to email each participant their own blood draw order document to present to the lab technician. This email will be unencrypted. The emailed blood draw order, or requisition, contains the participant's name, date of birth, and the lab tests ordered for the study. The email will be sent without the "Secure:" function to reduce the burden on participants of creating a secure account with Cisco Web Services. This risk is clearly outlined in the consent form to ensure all participants are aware of the risk of receiving an unsecured email. If the participant does not wish to receive an unsecured email with PHI of name and birth date, then the participant may opt to not participate or withdraw from the study. We have spoken to the UCSF Privacy Office and they have approved of this process and of our consent language.

Additionally, as with any form of online activity, there may be a small risk of loss of privacy. For more information regarding this risk, please refer to UCSF IRB-approved study, Eureka mHealth Research Platform (#16-19397) as well as the Eureka Privacy Policy and Data Security Measures document (uploaded to "Other Study Documents" of this application).

11.3 MINIMIZING RISKS: Describe the steps you have taken to minimize the risks/discomforts to subjects. Examples include:

- **designing the study to make use of procedures involving less risk when appropriate**
- **minimizing study procedures by taking advantage of clinical procedures conducted on the study participants**
- **mitigating risks by planning special monitoring or conducting supportive interventions for the study**
- **having a plan for evaluation and possible referral of subjects who report suicidal ideation**

All data from this study will be stored on the Eureka mHealth Research Platform. Please see their Privacy Policy and Data Security Measures for details on how the platform protects privacy and ensures data security. The SUGAR informed consent form (ICF) will make sure that the participants are aware that the study will not be responsible for medical or data charges outside of what is specified in the study.

11.5 * BENEFITS: (REQUIRED) Note: These are the benefits that the IRB will consider during their review. They are not necessarily appropriate to include in the consent form.

Possible immediate and/or direct benefits to participants and society at large (check all that apply):

- [x] Positive health outcome (e.g. improvement of condition, relief of pain, increased mobility, etc.)
- [x] Closer follow-up than standard care may lead to improved outcomes or patient engagement
- [x] Health and lifestyle changes may occur as a result of participation
- [x] Knowledge may be gained about their health and health conditions
- [x] Feeling of contribution to knowledge in the health or social sciences field
- [ ] The research presents a reasonable opportunity to further the understanding, prevention, or

alleviation of a serious problem affecting the health or welfare of children

☐ Other benefit (describe below)

☐ None

11.6 RISK TO BENEFIT RATIO: Explain why the risks to subjects are reasonable in relation to anticipated benefits, if any, to the participant or society:

The prevalences of mobile health devices and smartphone usage are increasing in our society today. We hope that the research data from this study using these platforms can one day help society towards better understanding, predicting, prevention, and monitoring of diabetes.

11.7 * DATA AND SAFETY MONITORING: Do you have a Data and Safety Monitoring Plan (DSMP) for this study (A DSMP is required for Greater than Minimal Risk research): (Click the Help link for guidance on risk determination) (REQUIRED)

○ Yes ◉ No

This is not required for minimal risk research but the UCSF IRB strongly recommends one to ensure the data collected are adequate to meet the research aims:

12.0 Confidentiality, Privacy, and Data Security

12.1 PROTECTING PRIVACY: Indicate how subject privacy will be protected:

☐ Conduct conversations about the research in a private room

☐ Ask the subject how they wish to be communicated with – what phone numbers can be called, can messages be left, can they receive mail about the study at home, etc.

☐ Take special measures to ensure that data collected about sensitive issues do not get added to their medical records or shared with others without the subject's permission

☑ Other methods (describe below)

Describe the other methods for protecting privacy:

The SUGAR Study will rely on the Eureka mHealth Research Platform Confidentiality, Privacy, and Data Security measures outlined in their CHR application (#16-19397).

This application also includes a copy of the Eureka mHealth Research Platform Privacy Policy and Data Security Measures document which explains, in depth, the ways in which Eureka will protect the privacy and data for the SUGAR Study. Additionally, any personnel involved in this project will have completed UCSF HIPAA Training and will store collected data according to standards. All of the electronic records will be stored under password protection and on a secure network.

12.2 SENSITIVE DATA: Do any of the instruments ask about illegal or stigmatized behavior:

○ Yes ◉ No

12.3 CONSEQUENCES OF A LOSS OF PRIVACY OR CONFIDENTIALITY: Could a breach of privacy or confidentiality result in any significant consequences to participants, such as criminal or civil liability, loss of state or federal benefits, or be damaging to the participant's financial standing, employability, or reputation:

◉ Yes ○ No

Describe the potential consequences:

Health-related data that the participant provides to the SUGAR Study may be sensitive (e.g., obesity or very high blood pressure), and could be embarrassing to participants or lead to insurance coverage problems if there was a breach of privacy of confidentiality.

- [x] Embarrassment
- [ ] Criminal or civil liability
- [ ] Loss of state or federal benefits
- [ ] Damaging to the participant's financial standing, employability, or reputation
- [x] Potential risks to insurability (health, disability, or life insurance)

12.4 EXTRA CONFIDENTIALITY MEASURES: Explain any extra steps that will be taken to assure confidentiality and protect identifiable information from improper use and disclosure, if any:

The Eureka mHealth Research Platform that hosts our mobile study takes confidentiality and privacy very seriously. Please see the Eureka IRB application and the Eureka Privacy Policy and Data Security Measures for details.

12.5 * REPORTABILITY: Do you anticipate that this study may collect information that State or Federal law requires to be reported to other officials, such as elder abuse, child abuse, or threat to self or others: (REQUIRED)

- ( ) Yes
- (•) No

12.6 CERTIFICATE OF CONFIDENTIALITY: Will this study obain a Certificate of Confidentiality:

- ( ) Yes
- (•) No

12.7 SHARING OF RESEARCH RESULTS: Will there be any sharing of EXPERIMENTAL research test results with subjects or their care providers:

- (•) Yes
- ( ) No

Note: This is unusual and not recommended, particularly in cases where the tests are carried out in a non-CLIA certified laboratory, the results are of unproven clinical significance, or where there are not known preventative strategies and/or treatments. If these are the most likely scenarios for your study, you should check 'No.'

If you have an incidental finding of clear clinical significance, call the HRPP QIU at 415-476-1814 for a consult.

Explain under what circumstances research results may be shared:

Participants will go to a nearby Quest Labs, which is an established commercial diagnostic laboratory company or they will use a Home Access mail-in lab kit, a professional use and FDA approved at-home laboratory testing kit, to obtain a baseline and closeout hemoglobin A1c test. We plan to share these results with participants as a courtesy for their participation.

12.8 * IDENTIFIERS: Will any personal identifiers be collected: (REQUIRED)

- (•) Yes
- ( ) No

Check all the identifiers that may be included:

- [x] Names
- [x] Dates
- [x] Postal addresses
- [x] Phone numbers

- [ ] Fax numbers
- [x] Email addresses
- [ ] Social Security Numbers*
- [ ] Medical record numbers
- [ ] Health plan numbers
- [ ] Account numbers
- [ ] License or certificate numbers
- [ ] Vehicle ID numbers
- [x] Device identifiers or serial numbers
- [ ] Web URLs
- [x] IP address numbers
- [ ] Biometric identifiers
- [ ] Facial photos or other identifiable images
- [ ] Any other unique identifier

* Could study records include *ANY* photos or images (even 'unidentifiable' ones): **(REQUIRED)**

○ Yes ◉ No

12.9 DATA DISCLOSURE: Will identifiable information be shared with outside groups:

◉ Yes ○ No

IMPORTANT: The IRB now recommends that all consent forms include a provision for sharing of de-identified/coded data to permit re-use of data for secondary research purposes.

Provide the details of whom the data will be shared with and what types of information and identifiers will be shared:

Data recorded from blood glucose monitoring devices in this study will be shared with the sponsor, Livongo Health.

For study management purposes, personal identifiers will be shared with the sponsor, Livongo Health. These identifiers include:

-Your name
-Your shipping address
-Your phone number
-Your email address

Livongo Health will access secure and encrypted data, and will only use your information for study-related purposes.

The consent form includes the above language to inform particpants of sharing of indentifiable information to the sponsor.

For study purposes, personal identifiers will also be shared with Quest Labs or with Home Access Health Corporations. This is necessary to have lab requisitions faxed to the lab location, and to allow us to requisition out the professional use finger stick test kit to participants. These identifiers include:

- Your name
- Your shipping address
- Your phone number
- Your email address

Quest Labs and Home Access Health Co. will access secure and encrypted data and will only use your information for study-related purposes.

The consent form includes the above language to inform particpants of sharing of indentifiable information to Quest Labs and Home Acccess Health Co.

Participants will be asked to download the iHealth Gluco-Smart app and create an account. The Gluco-Smart app is necessary to connect their iHealth device. We will not be sharing participants' data or identifiers with the iHealth Lab, Inc company. However, any personal identifiers the participants choose to input in the app will be managed by iHealth Lab, Inc such as their name and email address. Participants can choose to not provide information that identifies themselves.

The consent form includes the above language to inform particpants of sharing of indentifiable information to the iHealth Lab, Inc.

12.11 * DATA COLLECTION AND STORAGE: (check all that apply): (REQUIRED)

Collection methods:

- [ ] Paper-based (surveys, logs, diaries, etc.)
- [ ] Electronic case report forms (CRFs), such as OnCore or another clinical trial management portal
- [x] Web-based online surveys or computer-assisted interview tool
- [x] Mobile applications (mobile or tablet-based)
- [ ] Wearable devices
- [ ] Audio/video recordings
- [x] Other:

* Specify what other methods will you use to collect data: **(REQUIRED)**

Bluetooth-enabled mobile health devices

* What online survey tool will you use: **(REQUIRED)**

- [ ] Qualtrics (Recommended)
- [ ] RedCAP (Recommended)
- [ ] Survey Monkey (NOT recommended and may require UCSF ITS Security review)
- [x] Other

* What's the name of the survey tool and who is it owned by: **(REQUIRED)**

Surveyor, managed by Eureka mHealth Research Platform

* For each app and device, please provide: **(REQUIRED)**

- the name of the mobile application or wearable device
- name of the manufacturer / application owner
- the FDA status (required for mobile health applications and mobile health devices)

Livongo Health System, Livongo, FDA Status: legally marketed device

iHealth Wireless Smart Gluco-Monitoring System, iHealth Labs, FDA Status: legally marketed device

* Data will be collected/stored in systems owned by (check all that apply): **(REQUIRED)**

- [x] UCSF
- [ ] SF VAMC
- [x] Amazon (Amazon Cloud)
- [ ] Other academic institution

- [x] 3rd party vendor (business entity)
- [ ] Other (explain below)

* Do you have a contract or Data Use Agreement with a 3rd party for research data collection, storage, access, and ownership: **(REQUIRED)**

- (•) Yes
- ( ) No

12.12 DATA SECURITY: Indicate how data are kept secure and protected from improper use and disclosure (check all that apply): NOTE: Whenever possible, do not store subject identifiers on laptops, PDAs, or other portable devices. If you collect subject identifiers on portable devices, you MUST encrypt the devices.

- [ ] Data are stored securely in My Research
- [ ] Data are coded; data key is destroyed at end of study
- [x] Data are coded; data key is kept separately and securely
- [ ] Data are kept in a locked file cabinet
- [ ] Data are kept in a locked office or suite
- [x] Electronic data are protected with a password
- [x] Data are stored on a secure network
- [ ] Data are collected/stored using REDCap or REDCap Survey
- [ ] Data are securely stored in OnCore

12.13 * DATA SECURITY: Confirm below that you will keep data confidential: (REQUIRED) I will keep any data sets that include identifiers secure and protected from improper use and disclosure by using methods such as:

- **Physical Security – Keeping data in locked file cabinets, locked offices, locked suites, and physically securing computers and servers.**
- **Electronic Security – Following UCSF minimum security standards for electronic information resources, which includes (but is not limited to): not storing identifiers on portable devices like laptops or flash drives if they are unencrypted, encrypting portable devices, and storing data in password-protected files and on secure networks.**

- (•) Yes

12.15 HIPAA APPLICABILITY: Study data will be:

- [ ] Derived from the Integrated Data Repository (IDR) or The Health Record Data Service (THREDS) at SFGH
- [ ] Derived from a medical record (e.g. APeX, OnCore, etc. Identify source below)
- [ ] Added to the hospital or clinical medical record
- [ ] Created or collected as part of health care
- [x] Obtained from the subject, including interviews, questionnaires
- [ ] Obtained ONLY from a foreign country or countries
- [ ] Obtained ONLY from records open to the public
- [ ] Obtained from existing research records
- [ ] None of the above

13.0 Financial Considerations

13.1 * PAYMENT: Will subjects be paid for participation, reimbursed for time or expenses, or receive any other kind of compensation: (REQUIRED)

◉ Yes ○ No

13.2 PAYMENT METHODS: Subjects payment or compensation method (check all that apply):

Payments will be (check all that apply):

- ☐ Cash
- ☐ Check
- ☑ Gift card
- ☐ Debit card
- ☐ UCSF Research Subject Payment Card
- ☐ Reimbursement for parking and other expenses
- ☐ Other:

13.3 PAYMENT SCHEDULE: Describe the schedule and amounts of payments, including the total subjects can receive for completing the study:

- **If there are multiple visits over time, explain how payments will be prorated for partial completion**
- **If deviating from recommendations in Subject Payment Guidelines, include specific justification below**

As a token of our appreciation, participants will be given a $25 gift card (up to $75) for each completed lab test at baseline, month 3, and closeout. In addition, participants can keep the glucose monitoring device assigned to them after the study ends (up to $190 value).

13.4 COSTS TO SUBJECTS: Will subjects or their insurance be charged for any study activities:

◉ Yes ○ No

Describe the costs that may be incurred by subjects or 3rd party payers as a result of participation:

- Explain why it is appropriate to charge those costs to the subjects
- If this is a therapeutic study, compare subjects' costs to the charges that would typically be associated with receiving care off-study (e.g. is it more expensive to participate in this study than to receive care off-study?)

While the study itself will not charge subjects with any fees for their participation, participants may incur additional data charges from their mobile phone provider while using their smartphone to complete study activities. We do not foresee these additional charges to be very substantial, but understand that this could be a challenge for some participants.

As an alternative, if a participant does not wish to incur data charges or use their data, they may use the Wi-Fi setting on their smartphone.

14.0 Qualifications of Key Study Personnel

14.1 NOTE: This information is required and your application will be considered incomplete without it. If this study involves invasive or risky procedures, or procedures requiring special training or certification, please identify who will be conducting these procedures and provide details

about their qualifications and training. Also identify each person who will be involved in the consent process. Click the orange question mark for more information and examples. **Under qualifications, please include:**

- **Academic Title**
- **Institutional Affiliation (UCSF, SFGH, VAMC, etc.)**
- **Department**
- **Certifications**

November, 2015 - NEW Definition of Key Study Personnel and CITI Training Requirements:

UCSF Key Study Personnel include the Principal Investigator, other investigators and research personnel who are directly involved in conducting research with study participants or who are directly involved in using study participants' identifiable private information during the course of the research. Key Personnel also include faculty mentors/advisors who provide direct oversight to Postdoctoral Fellows, Residents and Clinical Fellows serving as PI on the IRB application. **The IRB requires that all Key Study Personnel complete Human Subjects Protection Training through CITI prior to approval of a new study, or a modification in which KSP are being added. More information on the CITI training requirement can be found on our website.**

KSP Name	Description of Study Responsibilities - Briefly describe what will each person be doing on the study. If there are procedures requiring special expertise or certification, identify who will be carrying these out. Also identify who will be obtaining informed consent.	Qualifications, Licensure, and Training
Wong, Jenise MD, PhD	Study design and oversight, designing study protocols and procedures, data analysis, manuscript preparation, dissemination of research findings.	Jenise Wong, MD, PhD, is an Assistant Adjunct Professor of Pediatrics, Division of Endocrinology. She has clinical research experience in diabetes technology and has completed requirements for Masters in Clinical Research (MAS) at UCSF.
Dr. Olgin, Jeffrey E MD, MD	Other investigator and faculty advisor - will help with study design, interpretation of results, and editing the manuscript.	Professor of Medicine, Chief of Cardiology, holds MD. Dr. Jeffrey Olgin has formal training experience in clinical research. He is experienced in patient-oriented research and in supervising trainees in the same.
Maguire, Carol A	Eureka Project Director - authorized to consent, enroll patients into study,	Carol Maguire manages clinical research in the UCSF's Division of Cardiology. She will oversee the CHR

	manage study documents /databases, etc.	application submission and ongoing regulation only.
Rohdin-Bibby, Linnea	Eureka Project Coordinator - authorized to consent, enroll, and manage patient participation in the study.	Linnea Rohdin-Bibby is currently a clinical research coordinator and experienced in consenting patients. She has been adequately trained to assist patients in clinic on joining the study.
Peyser, Noah, PhD	UCSF CORE Personnel and Data Manager - authorized to analyze data and generate reports on Health eHeart and Eureka Platform data.	Noah Peyser is the Scientific Program Manager for the Health eHeart/ Eureka Platform. He has experience in clinical research and is currently working in reporting and delivering data for Health eHeart and Eureka studies.

15.0 Other Approvals and Registrations

15.4 OTHER APPROVALS: Indicate if this study involves other regulated materials and requires approval and/or authorization from the following regulatory committees:

☐ Institutional Biological Safety Committee (IBC)

Specify BUA #:

☐ Institutional Animal Care and Use Committee (IACUC)

Specify IACUC #:

☐ Controlled Substances

16.0 End of Study Application

16.1

End of Study Application Form

To continue working on the Study Application: Click on the section you need to edit in the left-hand menu. Remember to save through the entire Study Application after making changes. If you are done working on the Study Application: Important: Before proceeding, please go back to Section 4.0 Initial Screening Questions and Save and Continue through the form to make sure all the relevant sections and questions have been included. If you've changed any answers since you started, the branching may have changed. Your application will be incomplete and it will have to be returned for corrections. Once you are sure the form is complete, click Save and Continue. If this is a new study, you will automatically enter the Initial Review Submission Packet form, where you can attach consent forms or other study documents. Review the Initial Review Submission Checklist for a list of required attachments. Answer all questions and attach all required documents to speed up your approval.

The UCSF IRB wants your feedback about this new form. Please click the link to take a brief survey about the new application form.