Protocol Title	Onduo Virtual Diabetes Clinic Study
Protocol Number	[redacted]
Version Number	
Date	April 09, 2019
Author(s)	[redacted]
Sponsor	Verily Life Sciences LLC 269 East Grand Avenue South San Francisco, CA 94080

Confidentiality Statement

The information in the following document is provided to you as an investigator, potential investigator, or consultant, for review by you, your staff, and applicable Institutional Review Board, and is considered confidential. It is understood that the information will not be disclosed to others without written authorization from Verily Life Sciences LLC, except to the extent necessary to obtain informed consent from those persons to whom the product may be administered.

Clinical Investigation Plan

Protocol Signature Page

I agree to conduct this study in accordance with all applicable laws and regulations and in compliance with the provisions of this Clinical Investigational Plan.

I am responsible for ensuring that the investigation is conducted according to this plan and for protecting the rights, safety, and welfare of the research subjects.

Principal Investigator Name (Print)	Signature	Date

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1. Protocol Summary

Trial Sponsor	Verily Life Sciences LLC 269 East Grand Avenue South San Francisco, CA 94080
Name of Test Product	Onduo Virtual Diabetes Clinic (VDC)
Regulatory Status	This study uses FDA cleared and approved devices. This trial requires Institutional Review Board (IRB) approval prior to initiation and subject enrollment.
Title of Trial	Onduo Virtual Diabetes Clinic Study
Protocol Number	[redacted]
Sites	Participants will be enrolled in approximately five (5) sites.
Planned Duration of Trial	Recruitment plus study duration of up to one (1) year per subject
Number of Trial Subjects Planned (Sample size)	Up to 60 total evaluable subjects.
Planned Start Date / Date First Subject Enrolled	October 2018
Objective(s)	The primary objective of this study is to evaluate change in hemoglobin A1c (A1c) after 4 months of participation in the Onduo Virtual Diabetes Clinic (VDC) in individuals with Type 2 diabetes (T2D) and suboptimal glycemic control.
Experimental Design	• Prospective • Non-Randomized • Single group
Device Description	The Onduo Virtual Diabetes Clinic (VDC) is the suite of diabetes management services including remote monitoring, diet/lifestyle coaching, medication management accessed via Onduo App and partner apps ([redacted] The Onduo App is a software application which tracks data relevant to diabetes care, such as, but not limited to, medication, meal logs and glucose readings, and activity data. The Onduo App connects wirelessly to a Care Team Console through the Internet. The Onduo App may also connect wirelessly to commercially available FDA-regulated (i.e., cleared and approved) medical devices and non-medical devices through the subject's Smartphone. Subjects will be provided: • Connected Blood Glucose Monitor (BGM) • Continuous Glucose Monitor (CGM) and associated apps • Telemedicine Platform [redacted] Subjects may also be provided: • Hemoglobin A1c (A1c) test kits • Additional smartphone applications (apps) • Insulin pen cap with automated dose logging

	These commercially available devices are used as standalone devices and can be used without being connected to the Onduo App. The Onduo App has been designed as a communication and education tool and allows for messaging between the Care Lead and the study subject. The Care Lead can send messages and educational content from the Care Team Console (Console) directly to the subject and manage their user profiles. The Console is used by the Care Leads and Onduo clinicians such as CDEs, PharmDs and MDs. Subjects will engage with a Care Lead through the App and will have a medical consultation via telemedicine [redacted] with an Onduo Virtual Diabetes Clinic Physician (VDC Physician), an endocrinologist who may initiate and/or change doses of diabetes medications.
Inclusion Criteria	• 18 years of age or older • Legal United States Resident with a Social Security Number and Government Issued ID • Confirmed diagnosis of Type 2 diabetes mellitus • Receive their diabetes care from primary care centers • Able to read and speak English • Able and willing to sign the Informed Consent Form • Have a Google user account (a personal Gmail address or a GAIA account) or be willing to obtain an account and create a free Gmail address • Own a Smartphone with a data plan and be the primary user of that smartphone • Smartphone must use a supported Android OS or iOS • Agree to provide a phone number and email address to enable feedback through communication • A1c result ≥8.0% and ≤12.0% • Willing to use commercially available FDA-regulated (e.g., cleared and approved) blood glucose meter (BGM) and continuous glucose monitor (CGM) • Willing to use commercially available FDA-regulated (e.g., cleared and approved) medical and non-medical device(s), which may include apps, insulin pen cap with automated dose log, or at-home A1c kits. • Willing to have blood lab tests drawn • Willing to have their diabetes medications managed and adjusted by an Onduo VDC physician • Willing to comply with all study requirements
Exclusion Criteria	• Pregnant or breastfeeding • Use of an insulin pump • Employee of Verily Life Sciences, Onduo LLC, or Onduo PC. • Malignant cancer in the previous 12 months (basal and squamous skin cancer will not be considered an exclusion) • Any solid organ transplant(s) • End stage (stage 4 or 5) renal disease, including dialysis • Liver Failure • Cystic Fibrosis • Chronic Heart Failure (Class C, D) • Pancreatic failure related diabetes • Self-reported adhesive allergy

	• Any other condition or situation the Investigator determines as inappropriate for study inclusion

Procedure/Intervention /Study Session	**Screening Visit**
	To be eligible for enrollment, sites will screen potential subjects for eligibility.
	
	Baseline Visit
	After signing the consent form, the study subjects will undergo a baseline visit where the following will be measured:
	• height, weight, waist circumference, blood pressure
	• Non-fasting blood samples including:
	  ○ hemoglobin A1c*
	  ○ lipid panel
	  ○ metabolic panel
	  ○ liver function tests
	  ○ prothrombin time
	  ○ complete blood count (CBC)
	
	*An A1c test will be performed at the Baseline Visit. If the baseline A1c result is less than 8.0% or above 12.0% the subject will be exited from the study as a screen failure and will not be counted towards the subject enrollment total.
	
	Active Period
	
	If all the study requirements are fulfilled and the subject is eligible to participate, the study subject:
	
	• will download and use the Onduo App.
	• will be asked to complete a number of health assessment and survey questions as part of the onboarding process in the Onduo App.
	• will be asked to engage in an initial 30 minute telephone conversation with their Care Lead.
	• will receive a CGM and be asked to use the device for up to 6 wear cycles of 10 days each. A VDC Physician may ask a subject to wear additional CGM sensors during the 4 month period.
	• will receive a connected BGM and may be asked to use this device.
	• will be scheduled for a medical review via a face-to-face telemedicine consultation with a VDC Physician. Subjects will use a commercially available telemedicine app [redacted] on their smartphone or personal computer (PC) for this visit. The scheduled telemedicine visit will occur after approximately two consecutive CGM wear periods (approximately 20 days) after enrollment and participating in study activities.
	• may have their diabetes medications changed by a VDC Physician following their telemedicine visit.
	• when clinically indicated, subjects will receive additional physician consultation and follow up visits by telemedicine with an Onduo VDC physician.
	• may also be asked to use commercially available FDA-regulated (i.e., cleared and approved) medical devices and non-medical devices for the study duration. which may include apps, insulin pen cap with automated dose log, or at-home A1c kits.
	
	All devices will be provided by Verily.

	The active study period is a 4-month period where the subject uses the Onduo App, study devices, and engages with the Care Lead in study-related activities. **4-Month Follow-Up Visit** After 4 months, the subject will come in for an in-person visit where the following will be measured: ● weight, waist circumference, blood pressure ● non-fasting blood samples including: ○ Hemoglobin A1c ○ lipid panel ● subjects will be asked to complete questionnaires and surveys and may be asked to participate in contextual inquiry interviews. Following this visit, subjects will stop using the Onduo App. No other study activities will be conducted until the 12-month follow-up. **12-Month Follow-Up** After 12 months, the subject will be asked to participate in the following study activities: ● have their A1c documented by one of the following methods: ○ a visit to a designated clinic or laboratory ○ an at-home A1c test ○ a copy of the A1c result performed as part of their usual care ● subjects may be asked to complete questionnaires and surveys and may be asked to participate in contextual inquiry interviews. ● subject will be exited from the study
Endpoints	Primary: ● Change in hemoglobin A1c at 4 months Secondary: ● Change in weight from enrollment to 4 months ● Time to first change in diabetes medication or dosage from enrollment ● Change in CGM summary measures from the first wear period versus the final wear period including ○ Glycemic variability ○ Time spent in glycemic range ○ Mean glucose Exploratory: [redacted]
Data Collection	Data will be collected through the Onduo App, Care Team Console, Case Report Forms (CRFs)and Electronic Data Capture system (EDC).
Roles and Responsibilities	Protocol Authors [redacted]

	Monitoring	[redacted]
	Data Management	

2. Background and Rationale

Nearly 30 million Americans have diabetes.[1] This includes almost 10% of the total adult population and over 25% of the population aged 65 years old and older. The incidence of this disease, in both adults and children, continues to increase; worldwide it is estimated that 364 million people have diabetes[2]. This high prevalence of diabetes has created an enormous financial burden on health care programs worldwide and creates significant decrease in quality of life.[3] In 2012, diabetes accounted for approximately $245 billion[3] in direct medical costs and lost productivity in the U.S.[3]

Diabetes management requires a multi-faceted approach including at-home blood glucose monitoring, prescribed medications, alteration of diet and exercise, and coaching support. This approach has placed a high burden on individual patients. For example, at-home monitoring requires painful and tedious finger sticking, and obtaining advice and support requires visiting a clinical site to obtain coaching and dietary education/advice.[4,6] Over the past decade, the ubiquity of smartphones and connected devices has the potential to alleviate much of this burden on individuals with diabetes while improving their care.[7] Specifically, the approval of continuous glucose monitoring (CGM) devices (including the Dexcom G6® CGM System) allow individuals to obtain a week of dense glycemic information with a single application, obviating the need for finger sticks.[4] Mobile app technology on smartphones has progressed to enable remote, on-demand connections with coaching and clinicians.

This study evaluates the Onduo Virtual Diabetes Clinic (VDC), a comprehensive diabetes management system which combines mobile app technology, continuous glucose monitoring (CGM), personalized health coaching and a coordinated team of clinicians which provides subjects personalized diabetes care in real-time without having to go to a doctors office. The lifestyle and clinical guidance follow the best practices of the AADE Diabetes Education Curriculum and the ADA Standards of Care.[5,6] This study focuses on evaluating the outcomes of the Onduo VDC in a T2D sub-population with suboptimal glycemic control.

3. Trial Objectives

The primary objective of this study is to evaluate change in hemoglobin A1c (A1c) after 4 months of participation in the Onduo Virtual Diabetes Clinic (VDC) in individuals with Type 2 diabetes (T2D) and suboptimal glycemic control.

4. Trial Design

This is a prospective, non-randomized, single group study designed to evaluate the real world outcomes of subjects using the Onduo Virtual Diabetes Clinic (VDC). The VDC is the suite of diabetes management services including remote monitoring, diet/lifestyle coaching, medication management accessed via Onduo App and partner apps [redacted]

5. Device Description

Verily has developed the Onduo App which is a software platform to enable Type 2 diabetes management. The Onduo App has been designed as a communication and education tool and allows for messaging between Care Leads/clinicians and the study subject. The Care Lead can send messages and educational materials directly to the subject and manage their profiles in the Care Team Console (Console). The Console is used by the Care Leads and members of the study team.

Subjects will engage with the Care Lead through the App and will have a medical consultation via face-to-face telemedicine using a commercially available telemedicine app [redacted] with a VDC Physician who may initiate and/or change doses of diabetes medications.

The Onduo App contains features including:

- Educational materials about lifestyle and behavior modification based on the American Association of Diabetes Educators (AADE) 7 self-care behaviours for managing diabetes curriculum
- Notifications and reminders
- Display of blood glucose measurements
- Display of continuous glucose measurements
- Medication tracking
- Activity tracking, such as step counting, and logging of activity
- Nutritional support such as meal information/logging, meal photos, and location of meal consumption
- Interface for subjects and Care Lead

A subject may use all or a subset of these features.

The Onduo App connects wirelessly to commercially available FDA-regulated (i.e., cleared and approved) medical devices and non-medical devices through the subject's Smartphone.

Subjects will be provided:

- Continuous Glucose Monitor (CGM) and associated apps
- Blood Glucose Meter (BGM)
- Telemedicine Platform [redacted]

Subjects may also be provided:

- Hemoglobin A1c (A1c) test kits
- Additional smartphone apps
- Insulin pen cap with automated dose logging

Subjects will be asked to use the CGM and associated applications. The subject may be asked to use all, none or a subset of the other commercially available devices and the BGM in accordance with their medical care plan. All commercially available devices can be used as a standalone device without being connected to the Onduo App. Device shipment will be by Verily or any of its approved vendors.

Subjects will be asked to use the Onduo App and commercially available device(s) for up to 4 months. Subjects will be asked to use a BGM when they are not wearing a CGM sensor in accordance with their medical care plan, and at any time a subject's CGM readings do not match their symptoms. The

frequency of use will be in accordance with and customized to the individual and in accordance with the ADA guidelines for self-monitoring blood glucose levels.

The subject will be reminded that the Onduo App is an adjunctive application to their normal diabetes management. Subjects will be instructed that if at any time the Onduo App or Care Lead provides information that differs from the information provided by their primary care physician (PCP) they should always follow the advice of their physician.

6. Sample Size and Number of Participating Sites

6.1. Sample Size

Up to 60 subjects will be enrolled at the study sites.

If the baseline A1c result is less than 8% or more than 12% the subject will be exited from the study as a screen failure and will not be counted towards the subject enrollment total. These subjects will be paid for the first study visit.

6.2. Participating Sites

There will be a total of approximately 5 sites participating in this study. Onduo is an operational site and will not recruit any Subjects into this study. Onduo will conduct telemedicine visits and provide Care Lead support to enrolled subjects.

7. Recruitment, Screening, Enrollment

7.1. Inclusion Criteria

Each volunteer research subject must meet all of the following inclusion criteria to be included in the study:

- 18 years of age or older
- Legal United States Resident with a Social Security Number and Government Issued ID
- Confirmed diagnosis of Type 2 diabetes mellitus
- Receive their diabetes care from Premier Medical Associates or the Palo Alto Medical Foundation
- Able to read and speak English
- Able and willing to sign the Informed Consent Form
- Have a Google user account (a personal Gmail address or a GAIA account) or be willing to obtain an account and create a free Gmail address
- Own a Smartphone with a data plan and be the primary user of that smartphone
- Smartphone must use a supported Android OS or iOS
- Agree to provide a phone number and email address to enable feedback through communication
- A1c result ≥8.0% and ≤12.0%
- Willing to use commercially available FDA-regulated (e.g., cleared and approved) blood glucose meter (BGM) and continuous glucose monitor (CGM)
- Willing to use commercially available FDA-regulated (e.g., cleared and approved) medical and non-medical device(s), which may include apps, Insulin pen cap with automated dose logging, or at-home A1c kits.
- Willing to have blood lab tests drawn

- Willing to have their diabetes medications managed and adjusted by an Onduo VDC physician
- Willing to comply with all study requirements

7.2. Exclusion Criteria

Each volunteer research subject must be excluded from the study if any of the following exclusion criteria are met:

- Pregnant or breastfeeding
- Use of an insulin pump
- Employee of Verily Life Sciences, Onduo LLC, or Onduo PC
- Malignant cancer in the previous 12 months (basal and squamous skin cancer will not be considered an exclusion)
- Any solid organ transplant(s)
- End stage (stage 4 or 5) renal disease, including dialysis
- Liver Failure
- Cystic Fibrosis
- Chronic Heart Failure (Class C, D)
- Pancreatic failure related diabetes
- Self-reported adhesive allergy
- Any other condition or situation the Investigator determines as inappropriate for study inclusion

7.3. Recruitment & Screening

Recruiting sites may identify potential subjects from their populations with T2D. Potential subjects are eligible for screening if they receive care for their T2D from one of the recruiting sites, or receive care from a clinic within the health network of the recruiting site and are willing to attend a recruiting site for study visits.

Potential subjects may be sent or given IRB-approved recruitment materials, learn about the study from clinic staff in-person, learn about the study through IRB-approved advertisements online or posted at participating sites or in public locations. Potential subjects can visit an IRB-approved study recruitment website that provides more information on the study. If a potential subject is interested in participating in the study, they can review a list of inclusion and exclusion criteria.

Potential subjects who are interested in the study are invited to voluntarily register in the study management portal and provide their name, email, phone number, and mailing address. Potential subjects also indicate if they receive their diabetes care from the Allegheny Health Network or the Palo Alto Medical Foundation. Potential subject information is only available to Study Staff at the selected participating study site. Study Staff at sites will contact potential subjects who voluntarily register in the study management portal. Potential subjects may also contact recruiting sites directly.

7.4. Informed Consent

Subjects who meet the initial eligibility requirements for the study and voluntarily wish to enroll in the study will be provided an Institutional Review Board (IRB) approved Informed Consent Form (ICF) and, if applicable, the California Experimental Subject's Bill of Rights. Appropriately trained Study Staff will review and discuss the ICF with the subject. The subject will be given adequate time to review the ICF and other document(s) and discuss any questions with the Principal Investigator or Study Staff. Subjects indicating they cannot conform to the requirements of the study will not sign the ICF documents and will not be enrolled in the study. After the subject agrees to participate in the study, they will sign the ICF documents along with the Principal Investigator or designee. The subject will be given a copy of the ICF. The ICF may be paper or electronic. Final eligibility will be verified in the Baseline Visit.

7.5. Subject Enrollment

Subjects are enrolled in the study when they are confirmed to have met all inclusion criteria, none of the exclusion criteria, signed the IRB approved ICF document(s) and have been notified by Study Staff that they have been enrolled in the study. A unique study subject identification number will be assigned to the subject upon enrollment.

8. Procedure and Follow-ups

8.1. Screening Visit

To be eligible for enrollment, sites will verify potential subjects for eligibility

8.2. Baseline Visit

An A1c test will be performed at the Baseline Visit. If the A1c result from the Baseline Visit is less than 8% or above 12%, the subject will be considered a screen failure and exited from the study. Additionally,The following will be conducted during the Baseline Visit in person at a study site:

- The Investigator (or designee) will verify that the subject still meets eligibility criteria, reviews the study with the subject, and answers any questions the subject may have.
- The Investigator (or designee) and subject sign the ICF documents.
- The Investigator (or designee) will verify the correct spelling of the subject's full name, last name, and date of birth using the subject's government issued photo ID or other appropriate documentation.

8.2.1. Anthropometrics

The following subject anthropometric measurements will be conducted and recorded:

- height
- weight
- waist circumference
- 2 blood pressure measurements performed at least 1 minute apart using the American Heart Association Guidelines for In-Clinic Blood Pressure Measurement

8.2.2. Laboratory

Venipuncture will be performed to obtain blood samples for the below laboratory studies:

- Hemoglobin A1c
- Lipid panel:
  - Total Cholesterol
  - HDL Cholesterol
  - Triglycerides
  - LDL Cholesterol (direct)
  - Cholesterol/HDL Ratio (calculated)
  - Non-HDL Cholesterol (calculated)
- Comprehensive metabolic panel, including:
  - electrolytes: serum sodium, potassium, chloride, and carbon dioxide
  - serum creatinine/eGFR
- Liver function tests (AST, ALT, bilirubin, albumin, PT-INR)
- Complete Blood Count (CBC)

Blood samples will be processed by laboratories that are verified as performing A1c assays by a method or instrument certified by the National Glycohemoglobin Standardization Program (NGSP).

The subject will have between 4 and 6 tubes of blood drawn via standard venipuncture procedure. Each tube will withdraw 4 - 8 mL of blood each (totalling between 24 and 48 mL of blood), which is equivalent to approximately 1.5 and 3.5 tablespoons (Tbsp) of blood. No fasting is required for this bloodwork.

Once the A1c results are received, a member of the Study Staff will contact the study subject with the results and advise them if they are still eligible for the study.

If the baseline A1c result is less than 8% or more than 12% the subject will be exited from the study as a screen failure and will not be counted towards the subject enrollment total. These subjects will be paid for the first study visit.

If the baseline A1c result is 8-12% inclusively (equal to or greater than 8.0% and equal to or less than 12.0%) the subject will continue in the study. A copy of the subject's laboratory results will be transmitted by a secure method to the Onduo VDC Physician for clinical management.

The Baseline Visit may occur on the same day as the Screening Visit.

8.3. Active Period

The active period is a 4 month period where the subject uses the Onduo App, study devices, and engages with the Care Lead in study-related activities.

During the Procedure (Study Session), the following will occur:

- The subject will be instructed how to download and install the Onduo App to their Smartphone.
- The subject will receive instructions for use of the Onduo App.

- The subject will complete the App setup process. The subject enters their name, medication list, general diabetes health history, [redacted]
- The subject will be assigned a Care Lead.
- Once the subject has downloaded and logged into the Onduo App and exchanged at least one message with the Care Lead, commercially available devices (BGM and CGM) will be shipped to the subject. Additional study supplies including test strips, lancets, CGM sensors, transmitters and CGM receiver, will also be included, if applicable. Additional supplies may be sent to subjects during the course of the study, as required.
- The subject will be asked to engage in an initial 30 minute telephone conversation with their Care Lead. During this conversation, subjects will be instructed how to use and connect the commercially available device(s) BGM and CGM to the Onduo App. Instructions will be available in the Onduo App, including any links to videos on device use and manufacturer instructions for use.
- Subjects will be asked to use the Onduo App and commercially available device(s) for up to 4 months.
- Subjects will be asked to engage with their Care Lead, at a minimum, on a weekly basis. Engagement includes text messaging with the Care Lead.
- Subjects will be asked to consult at least once with an Onduo VDC physician via a face-to-face telemedicine visit using a commercially available telemedicine app [redacted] on their smartphone or PC.
- When clinically indicated, subjects will receive additional physician consultation and follow up visits by telemedicine with an Onduo VDC physician.
- Subjects may be asked to complete additional activities within the Onduo App. These may include but are not limited to: logging medications, logging meals/meal photos, logging exercise/activity and viewing/reading educational content that encourages behavior modification.
- Subjects may have their diabetes medications optimized (a new diabetes medication initiated, or an existing diabetes medication dose adjusted, or an existing diabetes medication discontinued) by an Onduo VDC Physician. The site may designate medical staff as points of contact to assist in coordination of the clinical care and information between the PCP and the Onduo VDC physician.
- Any medication changes made by the Onduo VDC physicians will be prescribed for a period of 12 months, unless otherwise indicated. Prescriptions are transmitted to the subject's retail pharmacy to be filled.
- Care leads will assess adherence to medication changes of subjects and communicate their assessments with Onduo VDC physicians.
- Any Adverse Events related to a diabetes medication managed by a VDC physician will be recorded as described in **Section 11.**
- Subjects may be asked to provide feedback on their experience using the Onduo App by completing questionnaires and surveys.

The Investigator and/or Study Staff may contact the subject's PCP) for reasons including: to give notice of enrollment in the study; request recent medical history from the subject's medical record; advise of changes to diabetes medications prescribed by an Onduo study physician; or

alert a physician if the Study Staff notice anything of concern related to the subject's diabetes such as low or high blood sugar. Subjects agree to contact their primary care physician(s) as part of the Informed Consent process.

8.4. Device Use

8.4.1. Onduo App

Subjects will be asked to use the Onduo App and will be asked to use commercially available FDA-regulated (i.e., cleared and approved) medical devices and non-medical devices, for up to 4 months. All devices will be provided by Verily for the length of time the subject is enrolled in the study.

Individualized communication will be sent to the subjects via Onduo App or Care Lead. Device use will be encouraged by the Care Lead in accordance with the subjects' pre-existing care plan and under the supervision of Onduo VDC physicians. This includes CGM use and BGM use.

No treatment recommendations or decisions will be made by the Care Lead or the Onduo App and no information provided to a subject in the course of the study, whether through the Care Lead, the Onduo App or otherwise, is intended as a substitute for the subject's primary care provider's guidance.

Subjects may be contacted periodically throughout the study to provide feedback on their experience with the Onduo App. Subjects may be contacted via email/phone or on-site visits or through the Care Team Console and may be asked to complete surveys and questionnaires (as described in **Section 8.2.**

Subjects may optionally give feedback about the Onduo App by using a feedback function of the Onduo App. Subjects may have the option of providing screenshots from their smartphone, which may include other personal information, through the feedback function of the Onduo App; however, submission of such information is not required to use the feedback function.

8.4.2. Telemedicine Platform

Telemedicine visit(s) will be conducted via a telemedicine app installed on the subject's smartphone. Subjects will download a commercially available telemedicine app [redacted] and create a separate login for their telemedicine visit(s) using the same email address used for logging into the Onduo app. Instructions for downloading and installing the [redacted] will be provided to the subject through the Onduo App.

Subjects will be assessed by a VDC Physician to determine if changes to their diabetes medications are indicated. The medication management protocol used by Onduo VDC physicians is based on the ADA Standards of Care.

To ensure that the PCP becomes aware of any medication changes, an After-Visit-Summary report is sent to the subject's PCP after the Telemedicine visit. These may be entered into the subject's record by the PCP's office. To facilitate any necessary communication between the subject's PCP and the Onduo VDC Physician, the contact information of these physicians is made available to each other.

VDC Physicians providing telemedicine assessments and medication changes in the study will be endocrinologists. These VDC Physicians may be described to subjects as doctors who are diabetes specialists. In this Protocol, they are also referred to as telemedicine physicians.

The VDC text notes from the VDC physicians will be entered into the Console. The most important information about medication changes will also be captured on the eCRF, [redacted]

8.4.3. Continuous Glucose Monitor (CGM)

All subjects will be asked to use a CGM six times for 10 days each wear cycle during the 4 month active study period.The first CGM cycle will begin as soon as the subject receives the device after enrollment. The subject will be asked to initially wear the CGM for 2 back-to-back cycles totaling 20 days (two cycles of 10-day sensor wear).

Subsequent sensors will be deployed in a 21 day cycle with a cadence of 10 days on CGM followed by 11 days off. The exact schedule of CGM wear may be adjusted by a VDC physician. If required to evaluate the efficacy of medication changes and to monitor blood sugar impact, a VDC Physician may ask a subject to wear additional CGM sensors during the 4 month period.

The CGM schedule is outlined in **Table 2**.

Subjects will be scheduled for a medical consultation via a face-to-face virtual telemedicine consultation with a VDC Physician to occur after approximately two consecutive CGM wear periods (approximately 20 days) after enrollment.

8.4.4. Blood Glucose Monitor (BGM)

Subjects will be asked to use a BGM in accordance with their pre-existing care plan when they are not wearing a CGM sensor, and at any time a subject's CGM readings do not match their symptoms. The frequency of use will be in accordance with and customized to the individual and in accordance with the ADA guidelines for self-monitoring blood glucose levels.

8.4.5. Other Devices

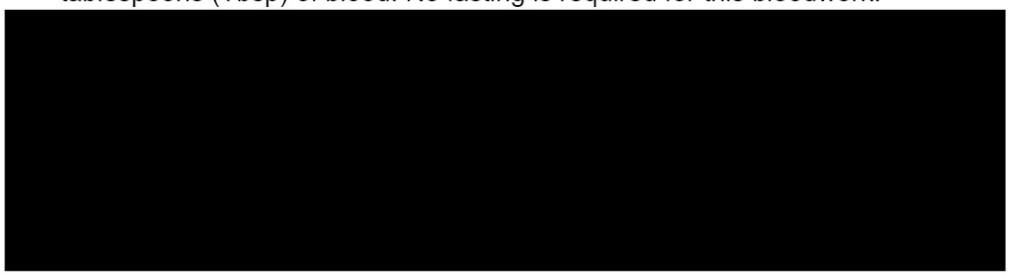
Subjects may also be asked to use commercially available FDA-regulated (i.e., cleared and approved) medical devices and non-medical devices for the study duration which may include, apps, Insulin pen cap with automated dose logging, or at-home A1c kits. All devices will be provided by Verily.

8.5. Follow-up Visits and Schedule

8.5.1. 4-Month Follow-Up Visit

After 4 months (±14 days) from the date of enrollment, a second in-person visit will occur where the following will be measured:

- weight
- waist circumference
- 2 blood pressure measurements performed at least 1 minute apart using the American Heart Association Guidelines for In-Clinic Blood Pressure Measurement
- Venipuncture will be performed to obtain blood samples for the below laboratory studies
    - Hemoglobin A1c
    - Lipid Panel:
        - Total Cholesterol
        - HDL Cholesterol
        - Triglycerides
        - LDL-Cholesterol (direct)
        - Cholesterol/HDL Ratio (calculated)
        - Non-HDL Cholesterol (calculated)
- Blood samples will be processed by laboratories whose A1c assay is performed by a method or instrument certified by the National Glycohemoglobin Standardization Program (NGSP).
- The subject will have between 2 and 3 tubes of blood drawn via standard venipuncture procedure. Each tube will withdraw 4 - 8 mL of blood each (totalling between 8 and 24 mL of blood), which is equivalent to approximately 0.5 and 1.5 tablespoons (Tbsp) of blood. No fasting is required for this bloodwork.



This visit will occur as close as practical to the 4 month mark but may occur up to 2 weeks (±14 days) before or after this date to accommodate subject and Study Staff scheduling.

Following the 4 month in-person visit, the Onduo App will be deactivated and the subject will be asked to remove the App from their smartphone. At the discretion of the Study Staff, subjects may be able to keep any FDA cleared or approved devices and unused supplies.

8.5.2. 12-Month Follow-Up

After 12 months (±21 days), the subject will be asked to participate in the following study activities:

- Have their A1c measured by one of the following methods:
    - an at-home A1c fingerstick test
    - a copy of the A1c result performed as part of their usual care provided to Study Staff, or
    - a visit to a clinic or laboratory for venipuncture
    - If venipuncture is required to obtain a blood sample for Hemoglobin A1c:
        - The subject will have 1 tubes of blood drawn via standard venipuncture procedure. The tube will withdraw 4 - 8 mL of blood

which is equivalent to approximately 1/4 and ½ of a tablespoon (Tbsp) of blood. No fasting is required for this bloodwork.

- Blood samples will be processed by laboratories whose A1c assay is performed by a method or instrument certified by the National Glycohemoglobin Standardization Program (NGSP).

[redacted]

- Subjects will be exited from the study.

The 12-month follow-up will occur as close as practical to the 12 month mark following the original date of study enrollment but may occur up to 3 weeks (±21 days) before or after this date to accommodate subject and Study Staff scheduling.

8.5.3. Optional Follow-up Visits

Additional follow-up visits may be scheduled, if needed.

- If the device(s) is not performing as intended, subjects may also be asked to come in for further assessment of the device(s) and to replace or remove the device(s) if necessary.
- If a commercially available device(s) (such as a BGM or CGM) falls off or malfunctions prior to the required follow-up visits, the subject may be instructed to come in for an optional follow-up visit(s). The subject will be instructed to contact the Care Lead and to stop using the device(s).

If a VDC Physician determines additional assessment of a subject's diabetes medications are required, subjects may have additional virtual telemedicine visits [redacted].

8.6. Schedule of Events

The schedule of events (**Table 1**) outlines the recruitment, on site visit, device use and follow-up visits.

Table 1: Schedule of Events

	Screening	**Baseline Visit/ Study Session**			**Follow-Up Visits**	
	Recruitment	*Baseline Visit*	*Final eligibility confirmed (A1c ≥ 8 and ≤12)*	*Active Period*	*4 month study visit (end of active period)*	*12 month follow-up visit (Study Exit)*

Method	online, phone	on-site	app, phone	app, phone, PC	on-site	phone, online
Recruitment Materials	X					
Informed Consent		X				
Anthropometrics (height, weight, waist circumference, blood pressure)		X			X	
Laboratory studies (blood draw) (including A1c)		X			X	X^^
Background Health Information		X		X		
Onduo App downloaded			X	X		
*Surveys, feedback and assessment of user experience**			X	X	X	X
Commercially available BGM and CGM				X		
*Commercially available device(s) (such as apps)**				X		X^^
Care Lead Communication				X	X	X
Interaction with the Onduo App			X	X	X	
Adverse Event Assessment		X	X	X	X	X
*Telemedicine Consult(s)***				X		
Onduo App de-activation					X^	
Study Exit						X

*Optional
**Additional consults completed, as needed.
^In the event the subject does not return for the Follow-up Visit, the Onduo App will be deactivated remotely.
^^A1c only

Subjects are instructed to not return the commercially available device(s) as they are designed for single-patient use.

8.7. CGM Sensor Use

All subjects will be asked to use a CGM six times for 10 days in each wear cycle during the 4 month active study period.The first CGM cycle will begin after approximately 1 week of enrollment in the study. The subject will be asked to wear the CGM for 2 back-to-back cycles totaling 20 days (two cycles of 10-day sensor wear. Subsequent sensors will be deployed in a 21 day cycle with a cadence of 10 days on CGM followed by 11 days off.

Sample CGM sensor number start dates (e.g., S1s, S2s...) and end dates (e.g., S2e, S2e…) are shown in **Table 2.**

Table 2: CGM Use (sensor start and end dates*)

Week	Mon	Tue	Wed	Thu	Fri	Sat	Sun
1							
2	S1s						
3			S1e	S2s			
4						S2e	
5							
6	S3s						
7			S3e				
8							
9	S4s						
10			S4e				
11							
12	S5s						
13			S5e				
14							
15	S6s						
16			S6e				

*Actual days (e.g., start date, end date, exact number of days in between wear periods) may vary slightly. The exact schedule of CGM wear may be adjusted by study staff.

If required to evaluate the efficacy of medication changes and to monitor blood sugar impact, a VDC Physician may ask a subject to wear additional CGM sensors during the 4 month period.

8.8. Data Collection

All of the data collected in the study can be found in **Table 3** including data type, frequency and data source.

Table 3: Data Collection			
Data Type	**Data**	**Frequency of Collection**	**Source**
Demographics	Demographics	Periodic throughout the study	Screening, Baseline, Care Team Console
Contact Information	Mailing address	Baseline and throughout the study if any changes	Screening, Baseline, Care Team Console
Contact Information	E-mail Address	Baseline and throughout the study if any changes	Screening, Baseline, Care Team Console
Contact Information	Phone number	Baseline and throughout the study if any changes	Screening, Baseline, Care Team Console
Health insurance information	Health insurance plan name, group number, subscriber number	Baseline and throughout the study if any changes	Subject provided (required to get medication and utilization records)
Health	Alerts (allergies or other serious health alerts)	Periodic throughout the study	Baseline, Care Team Console, Onduo App
Health	Medication list (drug name, dosage, schedule)	Periodic throughout the study	Screening, Baseline, Care Team Console Onduo App
Health	Vital signs (weight, height, waist circumference, blood pressure)	At baseline visit	Baseline in-person visit
Health	Vital signs (weight, waist circumference, blood pressure)	At 4 month visit	4 month in-person visit
Health	Results (A1c, CBC, LFTs, lipid panel, prothrombin)	At baseline visit	Laboratory, collection may occur at baseline site visit.
Health	Results (A1c, lipid panel)	At 4 month visit	Laboratory, collection may occur at 4 month site visit.
Health	Results (A1c)	At 12 month exit visit	Laboratory result or at home A1c fingerstick kit
Health	Subject-logged activities	While interacting with the Onduo App or commercially available devices	Onduo App, commercially available devices (such as BGM, CGM, apps), Care Team Console
Health	Subject activity level	While interacting with the Onduo App or commercially available devices	Onduo App, commercially available devices (such as BGM, CGM), Care Team Console

Physiological	Glucose Level	One or many times per day (BGM); continuous (CGM)	Onduo App and commercially available devices (such as BGM, CGM), Care Team Console
Behavioral	UI Interactions	While interacting with the Onduo App or commercially available devices	Onduo App, commercially available devices (such as BGM, CGM, apps), Care Team Console
Location	Subject location logging by Smartphone	Periodic throughout the study	Screening, Onduo App, Care Team Console
Subject Feedback	Location of meals	While interacting with the Onduo App	Subject logging via Onduo App, Care Team Console
Subject Feedback	Onduo App usability, user interface, Care Lead experience, study experience	Periodic throughout study	Onduo App, Baseline, follow-up visits, Care Team Console
Subject Feedback	Reporting of any Adverse Events	Periodic throughout study	Onduo App, Baseline, Active Period and follow-up visits, Care Team Console

8.9. Subject Surveys and Questionnaires

[redacted]

8.10. Care Team Console

[redacted]

[redacted]

8.11. Study Withdrawal

Participation in this research study is voluntary and subjects may withdraw at any time. In the event the subject chooses to withdraw, he/she will be instructed to contact the Care Lead or Principal Investigator immediately. The subject may also be terminated from the research study at any time if the Principal Investigator considers it to be in his/her best medical interest. The Principal Investigator may withdraw the subject any time due to the subject's non-compliance with provisions of the protocol.

If a subject withdraws prior to study completion, no new health information identifying him/her will be gathered after the date of withdrawal/exit. Information that has already been gathered may still be used and given to others. Subjects will be informed of any new significant information regarding new findings related to the study device that may develop during the course of the study that may be related to his/her willingness to continue participation as a research subject.

Subjects will either satisfactorily complete all requirements set forth in the study protocol and the ICF or their participation in the clinical study will be prematurely terminated. The completion of a subject's participation in the study or early departure from the study will be fully documented on the appropriate case report form. The Onduo App will be deactivated from the subjects Smartphone (in person or remotely) and there will be no further data collection into the Console. Subjects will be instructed to not return the commercially available device(s) as they are designed for single-patient use.

9. Assignment of Treatment Groups

There is no assignment of treatment groups, therefore subjects will not be randomized or masked in this study.

10. Risk Analysis

Verily Life Sciences has conducted an analysis of the benefits and risks of the Onduo App.Verily Life Sciences has determined that this clinical investigation is justified as the overall potential benefit to the population outweighs its risks.

10.1. Benefits

There is no direct benefit for participating in this study, but the information obtained will be used in scientific research and may be helpful to others in the future.

10.2. Risks

All devices used during the study are commercially available FDA-regulated (i.e., cleared and approved) medical device(s) or commercially available non-medical device(s). Therefore, subjects will not be exposed to significant risk through this study or by using these devices or apps.

10.2.1. Risks of using the Onduo App

The Onduo App is a class I, 510(k) exempt medical device. The types of potential risk the subjects will encounter with the Onduo App are related to:

- Medication errors induced by incorrect reminders from the Onduo App. The Onduo App may provide medication reminders based on the medication list provided by the subject. The subject will be required to input all medication information entered in the Onduo App before medication reminders will be provided. If a subject notices a discrepancy between the medication information provided in the Onduo App and the medication information as prescribed by the subject's primary care provider, the subject is instructed to notify the Care Lead. Subjects are trained to follow medication instructions from their primary care provider regardless of the data provided from the Onduo App. The Investigator and/or Study Staff may retrieve the medication list from the subject's medical chart and provide it to the Onduo VDC Physician to ensure that the Onduo App captures the subject's most recent and accurate medication list.
- Risks for releasing subject private health information. The subject profile in the Onduo App will include personal information including name, contact information, and health information including medication lists and glucose levels. Data in the Onduo App and messages sent within the Onduo App with a Care Lead are encrypted. Information collected during interviews from study subjects will be kept confidential throughout the study. A unique subject identification code will be used when collecting data on standardized Case Report Forms (CRFs). Only Study Staff trained on the clinical study protocol will have access to the study records. If a subject agrees to participate in the study, Verily will store the data collected on Google servers and on the platform hosting the Onduo App. This data will be restricted to authorized Study Staff and access is audited to ensure privacy of this data. All data used in the analysis and reporting of this observational study will be used in a manner without identifiable reference to the study subjects.

10.2.2. Risks of Commercially Available CGM

There may be some discomfort from using the commercially available CGM, including:

- Mild redness, rash, itchiness, mild red bumps, and injection site soreness. This risk is the same as that experienced by those who wear commercially available CGMs. If these risks persist for more than 48 hours, the subject is instructed to remove the CGM and notify the Investigator and/or Study Staff. If the symptoms do not dissipate after device removal, it will be reported as an adverse event.
- Potential user error in understanding CGM data. There is a risk that subjects could misinterpret the data provided by their CGM. Subjects will be provided with training on how to use the CGM and explicitly advised not to make treatment decisions or medication adjustments based on real-time or retrospective CGM data unless instructed by a VDC Physician following a telemedicine visit by a VDC Physician.

10.2.3. Risks of Commercially Available BGM

There may also be some discomfort from using the commercially available BGM device including:

- Potential user error in obtaining BGM readings. This risk is the same as that experienced by millions of people with diabetes who must use these devices to monitor their glucose levels. Obtaining a blood sample for the BGM is similar to the process with most other commercially available BGMs.
- Potential user or technical error in transferring the BGM readings to the Onduo App. The risk is the same as the risk experienced with any connected BGM. BGM readings will be displayed on the BGM device.
- Not obtaining BGM readings due to lack of engagement or confusion about the BGM or the Onduo App. The BGM displays the BGM reading on the screen of the device so the subject still has access to this information even if not connected to a Smartphone with the Onduo App.
- Discomfort from skin prick (to obtain blood sample): There may be discomfort or bruising from pricking the skin to obtain a blood sample. These discomforts are no different than a subject would experience with any other BGM.
- Infection from skin prick (to obtain blood sample): There is a possibility of infection from the skin prick procedure to obtain the blood sample. Subjects will be issued their own lancing device, lancets and glucose meter. This risk is the same as that experienced by millions of people with diabetes who must use these devices to monitor their glucose levels. Obtaining a blood sample for the BGM is similar to the process with most other commercially available BGMs.

10.2.4. Risks of Commercially Available At-Home A1c Kit

There may also be some discomfort or frustration from using the commercially available at-home A1c kit including:

- Receiving an invalid reading from the A1c kit once it has been processed by the laboratory. Invalid A1c results from the at-home kit is most commonly the result of the subject not obtaining the correct amount of blood in the collection kit. In this case the subject may experience frustration and inconvenience if they are required to repeat the A1c kit or go to a clinic or laboratory for venipuncture to obtain an accurate A1c result.

- Discomfort from skin prick (to obtain blood sample): There may be discomfort or bruising from pricking the skin to obtain a blood sample. These discomforts are no different than a subject would experience with taking a blood sample reading with other devices.
- Infection from skin prick (to obtain blood sample): There is a possibility of infection from the skin prick procedure to obtain the blood sample. The A1c kit contains a single use sterile lancing device. Obtaining a blood sample for the A1c kit is similar to the process with obtaining a blood sample for most commercially available devices.

10.2.5. Risk of Insulin Pen Cap with Automated Dose Logging

There may also be some frustration from using a commercially available Insulin pen cap with automated dose logging, including:

- Potential user error or technical error in using the device. The risk is the same as the risk experience with any other commercial Insulin pen cap with automated dose logging.

10.2.6. Risk of Commercially Available Applications

There may also be some frustration from using the commercially available applications, including:

- Potential user or technical error in transferring the commercially available app data to the Onduo App. The risk is the same as the risk experienced with any connected app.

10.2.7. Risk of Changes to Diabetes Medications Initiated by VDC Physicians

FDA approved diabetes related medications may be prescribed to be added, discontinued, or adjusted for subjects in the study following an assessment by a VDC Physician using via a telemedicine visit and using clinical practice guidelines that follow accepted standards of care for diabetes management. When prescribing any medication changes, the Onduo VDC Physician will consider multiple factors, including the subject's insurance coverage, drug formulary, and subject's medication preference. Also, to ensure continuity of care after the study's 4-month active period, the Onduo VDC physician will issue prescriptions for any medication changes for a period of 12 months. The types of potential risk the subjects will encounter with the Onduo program who receive medication management from a VDC Physician are related to those of any diabetes medication management including:

- The possibility of a subject experiencing a reaction or side effect to a diabetes medication prescribed by a VDC Physician that is listed in the drug's current labeling or is more severe or more specific than indicated in the labeling.
- The possibility of a subject experiencing an unknown reaction or side effect to a diabetes medication prescribed by a VDC Physician that is not listed in the drug's current labeling.
- The possibility of harmful interactions between a new diabetes medication prescribed by a VDC Physician and foods, dietary supplements, or other

medications a subject is currently taking. This includes interactions with medications being taken by a subject not disclosed to the VDC Physician.

10.2.8. Risk from having blood samples drawn

There may be discomfort related to having blood samples drawn.

The risks of the blood draw procedure are similar to those of a standard blood draw or blood donation. The risks of taking blood include local pain, a mild bruise at the point where the blood is taken, redness and swelling of the vein, fainting or lightheadedness, and a small risk of infection.

10.2.9. Other Risks

There may also be other side effects that are not known at this time.

11. Adverse Events and Reporting

11.1. Adverse Events

An Adverse Event (AE) is defined as any untoward medical occurrence, unintended disease or injury in subjects, users or other persons, that is considered a change from baseline or pre-study status, whether or not related to the medical device or study procedure.

Any pre-existing medical condition or symptom present in a subject will not be considered an AE in this study, unless it worsens as a result of this study. Subjects will be routinely questioned about adverse events during study visits and following any change to a diabetes medication by the telemedicine VDC Physician.

Any anticipated risks or AEs related to the Onduo App and commercially available FDA-regulated (i.e., cleared and approved) medical devices (such as BGM, CGM, A1c kits), some of which are outlined in **Section 10.2**, will not be recorded. AEs that are unanticipated or more severe or more specific than indicated in the risks section and or device labeling will be recorded.

All AEs related to changes in diabetes medications by the VDC Physician will be documented on the AE case report form and reported to the Principal Investigator at Onduo within 24 hours of being notified of the event. Subjects will be asked to report any AEs related to diabetes medications changes by the VDC physician to their Care Lead by messaging through the Onduo App. The PI at Onduo will review the AE, determine the relationship to the diabetes medication and follow-up with the subject to initiate appropriate management. Appropriate management may include additional telemedicine or telephone consults or a referral to the subject's primary care physician. Known side effects listed in the diabetes medication (drug) current labeling will be provided to the subject. If a risk or side effect is determined to be a Serious Adverse Event (SAE) it will be handled as described in **Section 11.2.**

Subjects will be instructed that if at any time during the study they experience serious adverse symptoms they should not delay seeking care and contact their primary care physician's office or access emergency medical care immediately.

11.2. Serious Adverse Events

Serious Adverse Event is an Adverse Event that led to: death, (b) serious deterioration in the health of the subject that either resulted in a (i) life-threatening illness or injury or (ii) permanent impairment of a body structure or a body function, or (iii) in-patient or prolonged hospitalization or (iv) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function or (c) fetal distress, fetal death or a congenital abnormality or birth defect. These events are typically reportable to health authorities.

A planned hospitalization for a pre-existing condition or a procedure required by the protocol without serious deterioration in health is not considered a Serious Adverse Event.

Subjects are instructed to contact the Principal Investigator at Onduo if they believe they have experienced a Serious Adverse Event.

The PI at Onduo will report all Serious Adverse Events to the Sponsor within 24 hours of knowledge of event. All SAEs will be reviewed by a Medical Monitor.

All SAEs involving the commercially available FDA-regulated (i.e., cleared and approved) medical devices will be reported to the manufacturer's Customer Care Service Center.

11.3. Unanticipated Adverse Device Effects

An Unanticipated Adverse Device Effect (UADE) is a serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect or problem was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects. Anticipated potential adverse device effects have been identified in the Sponsor Risk Management files.

The Principal Investigator will assure that all unanticipated adverse device effect (UADE) involving risk to subjects or others will be reported to the Sponsor within 24 hours of knowledge of event. All UADE's will be evaluated and the results of such evaluation will be reported to the IRB within ten (10) working days after the event is reported by the study subject. The Sponsor will report all SAE's and UADE's to the appropriate regulatory authority.

Any UADEs involving the commercially available FDA-regulated (i.e., cleared and approved) medical devices will be reported to the manufacturer's Customer Care Service Center.

All Unanticipated Adverse Device Effects will be reviewed by a Medical Monitor.

11.4. Documentation of Adverse Events

AEs and SAEs will be reported on an AE Case Report Form and will include the following: Date of onset, date of resolution, brief description of the event, the severity of the event, assessment of relatedness to the study device and procedure, if the event is anticipated, description of action taken (if any), and the event outcome.

12. Device Deficiencies

Device deficiencies are defined as the device not performing as intended.

If, at any time during the study, the subject's Smartphone (where the Onduo App is installed) physically breaks, or malfunctions, or the Onduo App ceases to function or gives unexpected or erroneous information, subjects will be instructed to stop using the Onduo App and contact their Care Lead or the Customer Service Support team. If the subject has another compatible Smartphone, instructions on installing the Onduo App on a different Smartphone will be provided and the subject will be instructed on how to remove the Onduo App on the first Smartphone (if applicable).

Subjects may have the option of requesting technical assistance related to the Onduo App by reporting a technical issue (a) to the Care Lead, (b) by using a request support function of the Onduo App, or (c) otherwise communicating through the Onduo App. By requesting technical assistance, the subject consents to share contact information with a Customer Service Support team member. If a subject requests assistance, a Customer Service Support team will contact the subject by phone or email.

If, at any time during the study, the commercially available device(s) physically breaks, or malfunctions, or gives unexpected or erroneous information, subjects will be instructed to stop using the device. Replacement device(s) will be provided at Verily's discretion.

If the commercially available A1c kit, BGM, or CGM physically breaks, malfunctions, or gives unexpected or erroneous information, subjects will be instructed to resume the use of their original BGM device and contact their Care Lead or the Customer Service Support team. Any device malfunctions and/or complaints involving the commercially available FDA-regulated (i.e., cleared and approved) medical devices will be reported to the manufacturer's Customer Care Service Center or in accordance with the requirements prescribed by regulatory requirements or commercial agreements.

Device deficiencies will be documented on the device deficiency case report forms.

All device-related adverse events will be reported on the Adverse Event Form.

13. Statistical Considerations

[redacted]

[redacted] 50 enrolled subjects is the smallest subgroup of interest to ensure an adequate number of analyzable subjects [redacted]

Endpoints include primary, secondary, and exploratory analysis:

Primary

- Change in hemoglobin A1c at 4 months

Secondary

- Change in weight from enrollment to 4 months
- Time to first change in diabetes medication or dosage from enrollment
    - Supplemental summary of type of change (discontinuation, addition, switch, dosage increase, or dosage reduction)
    - Supplemental summary of medications changed, including second, third, and later changes
- Change in CGM summary measures from the first wear period versus the final wear period:
    - Glycemic variability
    - Time spent in glycemic range
    - Mean glucose

Exploratory

[redacted]

13.1. Primary Analysis

The primary analysis will be conducted after the last subject enrolled completes the week 16 visit. A paired t-test will be conducted for the change in A1c for those subjects who contributed A1c values at both enrollment and follow-up. Although the study is powered for limited subgroup analysis, the primary analysis will include all enrolled and followed subjects.

13.2. Secondary Analysis

Change in weight and change in CGM summary measures (variability, mean glucose, and time in range) will all be evaluated using paired t-tests. The mean at enrollment, the mean at follow-up, and the mean change will all be reported.

Time to first medication change (i.e., addition, subtraction, switch, or change in dosage) will be evaluated using a Kaplan-Meier curve. Subjects will be censored at time of lost to follow up. It is unlikely that loss to follow-up represents non-informative censoring, as assumed in Kaplan-Meier estimates, so a sensitivity analysis will be performed assuming no medication changes occurred in subjects lost to follow-up.

The secondary analysis will also include an exploration of the predictors of the primary endpoint. This will include both subset analysis and a linear regression model.

13.3. Exploratory Analysis

[redacted]

[redacted]

14. Ethical and Regulatory Considerations

14.1. Conformity with Regulatory Standards

This clinical study will be performed in accordance with ICH E6 and applicable local regulations, International Conference of Harmonization (ICH) and Good Clinical Practice (GCP) will be used as guidance for the preparation and conduct of the clinical study.

Prior to the first subject enrolled, the Sponsor will ensure that IRB approval is obtained prior to the start of this clinical study.

14.2. Subject Confidentiality

Subject confidentiality will be maintained throughout the study. For this purpose, unique subject identification codes will be used by the Investigational site and Sponsor in place of relevant subject identifiers (e.g., subject name) that allow identification of all data reported for each subject while maintaining subject confidentiality.

The names and identities of the subjects in the study will be treated as confidential information by all authorized Study Staff with access to such information. Information will be disclosed if required by law, but will otherwise remain confidential. An enrollment log will be maintained for each Investigational site to enable tracing of the unique subject identifier to a study subject in the event that such tracing is required. This log, along with all confidential study records that identify the subject, such as the Informed Consent Form, will be kept confidential and will be maintained in a secured file cabinet (if paper) or secure online storage (if digital) with access limited to authorized personnel. Additionally, the Sponsor may maintain its own unique subject identifier and will restrict access to this identifier and subject information to authorized personnel.

During the study, subjects will use the study's software application, which stores data securely in accordance with ISO/IEC 27001:2013 certification requirements. Any identifying information which a subject may enter into the application or that will be collected by the application will be treated as confidential and will be accessible only to the subjects themselves and to authorized personnel.

Data collected via the study's software platform (Onduo App and Console) will be kept confidential by being accessible only to the subject themselves and authorized personnel.

Data collection not collected via the study software, including Case Report Forms, will only use a subject identifier to ensure subject confidentiality.

14.3. Institutional Review Board

The clinical study will begin once documented approval of the study materials (including Protocol, Informed Consent Form, and recruitment materials) has been confirmed by an Institutional Review Board (IRB).

All amendments to the Protocol and Informed Consent must be reviewed and approved by the IRB prior to implementation, except where necessary to eliminate apparent immediate hazards to human subjects.

The Investigator (or designee) will maintain copies of communications from the IRB indicating approval of the clinical protocol and Informed Consent Form and amendments to the Protocol and Informed Consent Form.

The Sponsor will be responsible for obtaining annual IRB renewal for the duration of the study.

The Sponsor will submit a final report to the IRB within six months after completion or termination of the study.

14.4. Compensation

Subjects will be compensated for their participation in the study. The details of the compensation will be provided in the Informed Consent Form.

14.5. Informed Consent

The IRB-approved Informed Consent Form and CA Experimental Subject's Bill of Rights (if applicable) will be signed and dated by each volunteer subject prior to the subject undergoing the Baseline Visit. The Informed Consent Form will conform to 21 CFR 50.20-50.27. The Informed Consent will be obtained from each potential subject after he/she has received a full verbal and written explanation of the purpose, including potential risks and benefits involved, as provided by the Principal Investigator or designee. The original signed and dated Informed Consent Form will be maintained in a secure file at the clinical site, and a copy of the Informed Consent form will be given to the subject.

14.6. Voluntary Nature of Study

Participation in this study is entirely voluntary. It is the Sponsor's responsibility to ensure that subjects do not feel any pressure to be in the study as participation in the study is entirely up to the subject. If a subject decides not to participate, or if they choose to drop out after the study has started, they may withdraw at any time without jeopardy or penalty.

15. Data Quality Assurance

15.1. Confidentiality of Data

Information about study subjects will be kept confidential throughout the study. A unique subject identification code will be used for all data collected on standardized Case Report Forms (CRFs) within EDC. Data collected via the study's software will be kept confidential by being accessible only to the subject themselves and authorized personnel. The privacy and confidentiality of the personal health information will be kept confidential. Only research Study Staff trained on the clinical study will have access to the study records. If a subject agrees to participate in the study, Verily Life Sciences will store the data collected on Google servers and on the platform hosting the mobile app.

All data used in the analysis and reporting of this evaluation will be used in a manner without identifiable reference to the study subject.

15.2. Data Collection and Reporting

Data will be collected on the appropriate Case Report Forms (CRFs) which may be paper or electronic in an Electronic Data Capture system (EDC) as specified in the study data management plan. CRFs will be used to record demographic, procedural and follow-up data, as

well as any unscheduled visits or adverse events which may occur during the study period. The Adverse Events will be reviewed by an Investigator to assess the relationship to the study device.

The Onduo App will be used by the subject and authorized Study Staff to record study-related events. See **Section 8.8** for additional information regarding data collection.

15.3. Data Retention

If a subject at any time chooses to withdraw consent, no new data will be collected. Data collected up to the time of subject withdrawal will be retained and may be used for data analysis for this research study. As a general rule, Verily will store the data for a minimum of five (5) years; however, certain data may be stored for a longer minimum period consistent with **Section 17.2.**

15.4. Monitoring

The progress of the study will be monitored to ensure that it is conducted in accordance with the Protocol and applicable study and regulatory requirements. Study monitoring will include reviewing the integrity of the clinical study data, ensuring that all subjects signed an IRB-approved ICF prior to study participation and obtaining and maintaining all required Investigator and IRB documentation. The Monitor (or Sponsor designee) will be appropriately trained on this clinical research study, and will review the progress of this study in accordance to the Clinical Investigational Plan, GCP/ICH Guidelines and the Sponsors' internal procedures. Monitoring activities may be conducted at the study site or remotely. In all cases, Monitors will have access to all subject data. It is the responsibility of the Investigator to oversee and accommodate regular monitoring visits. Direct access to all subject data and relevant source documentation for this clinical study must be made available to the Monitor during these routine visits.

15.5. Protocol Deviations

A Protocol Deviation is when a procedure, process, or test required by the Protocol is not followed. There are two types of protocol deviations in this study: major deviations and minor deviations.

A major deviation is defined as an event that resulted in an increased risk to a subject or others; affecting the rights, safety, and welfare of the subject; or affect the integrity of the clinical study. Major deviations include (but are not limited to): failure to obtain Informed Consent prior to enrollment, enrolled subject does not meet inclusion/exclusion criteria or unauthorized use of study device on a subject not enrolled in the study.

A minor protocol deviation is defined as deviating from the protocol and include (but are not limited to) missing a protocol-required test, missing a protocol-required visit; adverse events were not reported by the Investigator during the protocol-specified timeframe.

All deviations will be reported on the appropriate case report form.

16. Investigator and Sponsor Responsibilities

The Investigator will be responsible for the preparation, review, signature and retention of the records:

- Device receipt, use, storage, and disposition, as applicable
- Records of each subject's case history including completion of Case Report Forms
- Ensure that all subjects signed an IRB-approved Informed Consent Form prior to study participation
- All relevant observations relating to the device(s)
- Signed Investigator's Agreement and Curriculum Vitae

The Sponsor will be responsible for maintaining the following:

- Obtaining Institutional Review Board (IRB) approval prior to enrolling study subjects
- Selecting qualified Investigators
- Ensuring proper Investigator training, support and monitoring
- Ensuring that IRB is informed of any significant new information about the study
- Maintaining accurate and complete study records and submitting required progress and final reports
- Obtaining signed Investigator Agreements
- Providing case report forms and ensuring that forms are completed correctly
- Ensuring Protocol and Investigator Agreement compliance
- Ensuring proper reporting of all Adverse Events, Protocol Deviations, and Device Deficiencies

The Sponsor will provide training for the Investigator and research Study Staff and will conduct this training in accordance with appropriate procedures. All training will be documented and filed accordingly.

17. Records and Reporting

17.1. Investigator Records and Reports

Records may be audited by regulatory authorities and must be retained for the appropriate period (according to the local country regulations). The Investigator is responsible for the following:

- Records of all persons authorized to conduct the clinical study
- Records of receipt, use, or disposition of the study device(s), as applicable.
- Subject completed Case Report Forms (surveys, questionnaires) and any supporting documentation
- Informed Consent documentation (including a copy of an approved, blank consent form)
- Records of all Adverse Events, Serious Adverse Events and Unanticipated Adverse Device Effects
- Any malfunctions, complaints, SAEs, UADE involving the commercially available FDA-regulated (i.e., cleared and approved) medical devices will be reported to the manufacturer's Customer Care Service Center and documented on the appropriate form.
- Clinical Investigational Plan (including certification of approval) and reasons for deviations from the CIP
- Signed Investigator Agreement and CVs for all Investigators participating in the study
- All correspondence which pertains to the clinical study

The Investigator is responsible for preparation, review, signature and submission of reports (**Table 4**).

Table 4: Reporting Requirements

Report	Description	Report to
Unanticipated Adverse Device Effect (UADE)	The Investigator must submit a report of a UADE as soon as possible to the Sponsor and IRB, but not more than 10 (ten) working days after the Investigator first learns of the event.	Sponsor and IRB
Withdrawal of IRB	A withdrawal of the IRB's approval of the Investigator's part of the study must be submitted to the Sponsor within 5 (five) working days.	Sponsor
Failure to obtain informed consent	If a study device was used without obtaining informed consent, the Investigator must notify the Sponsor and IRB within 5 (five) working days of use of the device.	Sponsor and IRB
Other	Upon request from the IRB or FDA, the Investigator must provide accurate, complete and current information about any aspect of the study.	IRB or FDA

17.2. Record Retention

Without limiting the generality of **Section 15.3**, the Investigator will ensure that the following records are maintained for a period of at least two (2) years after the clinical study is completed or discontinued or a notice of completion of a product development protocol, whichever is longer. The records include (21 CFR §812.140(d)):

- Study subject files containing support documentation, case report forms and a copy of the signed and dated Informed Consent Form
- Investigator files containing originals and copies of the regulatory documents required for the study.

All records and documents pertaining to the study will be available for inspection by authorized representatives of the Food and Drug Administration (FDA) or other regulatory agencies during normal business hours.

18. Device Labeling & Accountability

The Investigator should take adequate precautions, including access to the study devices to prevent diversion of the study devices into unauthorized channels of distribution.

Study devices include commercially available FDA-regulated (i.e., cleared and approved) medical devices and non-medical devices and will be provided with the manufacturers packaging and labeling.

Only Institutions/Investigators participating in the clinical study will be eligible to receive the study devices and can be used only when the following has been received:

- Curriculum Vitae of the Investigator
- A signed Investigator Agreement
- Institutional Review Board (IRB) approval
- IRB-approved Informed Consent Form

19. Sponsor Data Confidentiality

All information and data, including the terms of this protocol, clinical results, and research conducted hereafter concerning products and operations, including patent applications, formulas, manufacturing processes, basic scientific data, and formulation information that has been supplied but not previously published are considered confidential.

20. References

1. Centers for Disease Control and Prevention, Department of Health and Human Services Atlanta, GA, U.S. 2017 National Diabetes Statistics Report, 2017 (https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf)
2. World Health Organization. Fact sheet N°312. (http://www.who.int/mediacentre/factsheets/fs312/en/)
3. American Diabetes Association. Economic Cost of Diabetes in the US 2012. Diabetes Care 2013;36:1033-1046. Centers for Disease Control and Prevention (CDC).
4. Self- monitoring of blood glucose among adults with diabetes--United States, 1997-2006. MMWR Morb Mortal Wkly Rep. 2007; 56: 1133-1137.
5. American Association of Diabetes Educators (2015) Diabetes Education Curriculum: A Guide to Successful Self-Management, second edition. Chicago, Illinois: AADE
6. Haas, L., Maryniuk, M., Beck, J., Cox, C. E., Duker, P., Edwards, L., … on behalf of the 2012 Standards Revision Task Force. (2012). National Standards for Diabetes Self-Management Education and Support. Diabetes Care, 35(11), 2393–2401. http://doi.org/10.2337/dc12-1707
7. Leventhal, H., Singer, R., & Jones, S. (1965). Effects Of Fear And Specificity Of Recommendation Upon Attitudes And Behavior. Journal of Personality and Social Psychology, 2, 20–29. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/14313839

21. Definitions

Adverse Event (AE)

An Adverse Event (AE) is defined as any untoward medical occurrence, unintended disease or injury in subjects, users or other persons, that is considered a change from baseline or pre-study status, whether or not related to the investigational medical device.

Case Report Form (CRF)

A set of documents, designed for complete recording of all relevant subject and device related data, as required by the clinical investigation plan. These may be paper or in an electronic data capture (EDC) system.

Clinical Investigation (Clinical Study, Clinical Trial)

Any controlled systematic study in human subjects, undertaken to verify the safety and performance of a specific medical device, under normal conditions of use.

Clinical Research Associate (CRA, Monitor)

A person appointed by the sponsor and responsible to him for monitoring and reporting on the progress of the clinical investigation.

Contract Research Organization (CRO)

Contract research organizations are independent contractors who assume, by contract, some or all of the regulatory responsibilities of a sponsor and/or monitor.

Electronic Data Capture System (EDC)

An electronic data capture (EDC) system is a 21 CFR Part 11 compliant, closed computerized system to collect and store subject data in electronic format. Data may first be recorded on paper case report forms and then transcribed into the system.

Informed Consent/Consent (ICF)

A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects that are relevant to the subject's decision, including potential risks and benefits to participate. Informed consent is documented by means of a written, signed, and dated informed consent form. Informed consent continues throughout the trial.

Investigator (Principal Investigator, Sub-Investigator)

The investigator responsible for the conduct of a clinical investigation and who takes the clinical responsibility for the well being of the subjects involved.

Protocol (Clinical Investigation Plan)

A document that includes detailed information on the rationale, aims and objectives, design and proposed analyses, methodology, and conduct of the clinical investigation.

Serious Adverse Event (SAE)

A Serious Adverse Event is an Adverse Event that led to: (a) death, (b) serious deterioration in the health of the subject that either resulted in a (i) life-threatening illness or injury or (ii) permanent impairment of a body structure or a body function, or (iii) in-patient or prolonged hospitalization or (iv) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function or (c) fetal distress, fetal death or a congenital abnormality or birth defect. These events are typically reportable to health authorities.

Sponsor

An individual or an organization which takes responsibility for the initiation and/or implementation of a clinical investigation.

Subject (Research Subject, Subject)

A human being, either a patient or a non-patient volunteer, participating in a clinical investigation.

Unanticipated Adverse Device Effect (UADE)

An Unanticipated Adverse Device Effect (UADE) is a serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect or problem was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.