# PILOT RANDOMIZED CONTROLLED TRIAL OF A SMARTPHONE-BASED SMOKING CESSATION PROGRAM

[redacted]

**PROTOCOL NUMBER: [redacted]**

**NCT04955639**

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**Synopsis**

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| **Device Name(s)** | Pivot Breath Sensor |
| **Protocol Title** | Pilot Randomized Controlled Trial of a Smartphone-based Smoking Cessation Program |
| **Principal Investigator** | [redacted] |
| **Co-Investigators** | [redacted] |
| **Protocol Number** | [redacted] |
| **Protocol Version** | [redacted] |
| **Sponsor** | Pivot Health Technologies Inc. (formerly Carrot Inc.), [redacted] |
| **Study Design** | Two-arm, parallel-group, non-crossover, single-center pilot randomized controlled trial, enrolling up to 180 participants to evaluate the effect of the Pivot smoking cessation program (intervention) compared to usual care (QuitGuide app smoking cessation program plus optional nicotine replacement therapy, control). |
| **Objectives** | Objectives are to collect the following data:<br>• User engagement and retention<br>• Change in attitudes towards quitting smoking<br>• Change in smoking behavior<br>• Participant feedback |
| **Primary Outcome** | Total app opens in Pivot vs QuitGuide at 12 weeks (3 months) |
| **Secondary Outcomes** | • Change in expected difficulty in staying quit (participant self-report, scale 1-10)<br>• Change in confidence levels towards quitting smoking (expected success in quitting, participant self-report, scale 1-10)<br>• Desire to quit (yes/no)<br>• Self-reported abstinence (7-day and 30-day point prevalence abstinence or PPA)<br>• Self-reported abstinence from all tobacco products<br>• Biochemically confirmed abstinence<br>• Self-reported continuous abstinence<br>• Biochemically confirmed continuous abstinence<br>• The proportion of participants who reduced their cigarettes per day (CPD) by ≥ 50% compared to baseline<br>• User satisfaction with the smoking cessation program (set-up and getting started with program, recommend to friend, program design, program was useful for quitting, program helped me quit, program helped me stay quit)<br>• Engagement with program, collected weekly during the first 12 weeks after enrollment: |

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| | ○ Number of times app opened<br>○ Number of days in which app was opened<br>○ Number of weeks in which app was opened<br>• Participant changes in self-efficacy<br>• Participant changes in self-reported health and wellbeing<br>• Self-reported nicotine replacement therapy (NRT) use<br>• Use of other smoking cessation tools (apps, counseling, medications, etc.)<br>• Adverse events |
| **Potential Subjects** | Up to 180 adult participants who are daily cigarette smokers and are planning to quit smoking in the next 30 days. |
| **Inclusion Criteria** | • 21+ years of age<br>• Current daily cigarette smokers (at least 5 cigarettes per day) for the past 12 months<br>• Plans to quit smoking in the next 30 days<br>• Resident of the United States<br>• Able to read and comprehend English<br>• Owns and uses a smartphone compatible with the study app (iPhone 5 and above with operating system iOS 12 and above, or, Android 7.0 and above with operating system Android 7.0 and above)<br>• Has daily internet access on smartphone<br>• Comfortable downloading and using smartphone apps<br>• Willing to sign the Informed Consent Form |
| **Exclusion Criteria** | • Pregnancy (self-reported)<br>• Health contraindications to NRT use (irregular heartbeat, high blood pressure not controlled with medication, heart attack or stroke in last 2 months, pregnant or breast feeding, skin allergies to adhesive tape or serious skin problems, stomach ulcers, history of seizures)<br>• Using other smoking cessation support, including apps and/or actively taking medication to quit smoking<br>• Daily marijuana use<br>• Residence with another person who is a participant in this study<br>• Immediate family member is a participant in this study<br>• Failure to provide contact or collateral information, failure to verify email address, and/or failure to demonstrate videoconference capability<br>• Participation in a previous study sponsored by Pivot Health Technologies Inc. (formerly Carrot Inc.) |
| **Recruitment** | Eligible subjects will be identified via web media (e.g., Facebook, Google ads). |
| **Study Session** | This is an open-label, two-arm, parallel-group, non-crossover, single-center pilot randomized controlled trial conducted with IRB approval enrolling up to |

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| | 180 adult participants (up to 90 in each arm) who report daily smoking of 5 cigarettes or more. The study will be performed remotely on an ambulatory basis. Participants will be asked to setup and use their assigned program (Pivot for intervention or QuitGuide for control). Both study arms include the option for participants to order FDA-approved nicotine replacement therapy (NRT). The study duration is 104 weeks, with the estimated active time using the program of up to 6 months and the time thereafter as follow-up. Participants will receive online questionnaires at intervals throughout the study and may undergo up to 4 videocall biovalidation study visits in which they provide breath samples using a personal carbon monoxide (CO) breath sensor, which measures CO in exhaled breath. |
| **Data Collection** | Data will be collected through participant completion of emailed online questionnaires. |
| **Performance Variables** | Comparison between the two smoking cessation programs on:<br>• User engagement and retention in the program<br>• Attitudes towards quitting: desire to quit, confidence to quit, self-efficacy and difficulty to stay quit<br>• Smoking behavior: quit attempts, change in cigarettes per day (CPD), smoking cessation via 7-and 30-day PPA (self-report and biochemically confirmed), continuous abstinence (self-report and biochemically confirmed), abstinence from all tobacco products (self-report), use of NRT<br>• Participant feedback on the set-up, use experience, design and impact on their assigned smoking cessation program, and use of other (non-study) smoking cessation tools |
| **Performance Endpoint and Analysis** | Change from baseline measurement |

## Contents

## 1. LIST OF ABBREVIATIONS

| | |
|---|---|
| **CO** | Carbon Monoxide |
| **CPD** | Cigarettes Per Day |
| **CRF** | Case Report Form |
| **FDA** | Food and Drug Administration |
| **ITT** | Intention To Treat |
| **USB** | Universal Serial Bus |
| **IRB** | Institutional Review Board |
| **ICF** | Informed Consent Form |
| **HCP** | Health Care Provider |
| **Ppm** | parts per million |
| **NRT** | Nicotine Replacement Therapy |
| **RCT** | Randomized Controlled Trial |

# 2. INTRODUCTION

## 2.1 BACKGROUND

Tobacco use, primarily through cigarette smoking, is the leading cause of preventable disease, disability and mortality in the United States [redacted]

[redacted]

Seeking to expand on these learnings both in intervention design and associated outcomes, the Pivot program is a novel digital health intervention for smoking cessation. Pivot comprises a multiphase mobile app, as well as the first Food and Drug Administration (FDA)-cleared personal carbon monoxide (CO) breath sensor, and dedicated human coaching delivered through in-app text messaging. Pivot users may learn about and order NRT in the Pivot app and participate in the Pivot online community. Pivot is designed for individuals with varying levels of readiness to quit and is based on the USCPG for tobacco cessation.

In 2018, we reported results of a nine-day study of 41 participants using only the first phase of Pivot (which at the time was a six-phase program), that included Pivot's FDA-cleared personal CO breath sensor and dedicated one-on-one human coaching using an asynchronous text messaging interface.[12] The focus of the evaluated program phase was to encourage the participant to explore their smoking behavior. Participants completed activities and had the opportunity to log cigarettes and to interact with a coach via text message. More than 80% of participants (34-39 of 41) took ≥1 CO breath sample each day, and more than 55% (23-27 of 41) took ≥5 samples each day. All 9 in-app activities had completion rates ≥80% (33-40 of 41). Response to coach-initiated outreach was also high, with all contacts receiving ≥73% (30-39 of 41) response. In matched pair analyses, significant positive changes in mean attitudes toward quitting (scale 1-10) were evident from baseline (T1) to study exit (T2), including increased readiness to quit (T1 mean=6.1, T2 mean=7.4, P=.005), lower perceived difficulty of staying quit (T1 mean=3.7, T2 mean=5.6, P=.001), and greater expectations of success (T1 mean=4.5, T2 mean=6.5, P<.001). At exit, 78% (32/41) of participants reported decreasing the number of cigarettes smoked per day during the study. Participants rated program quality and satisfaction very high (mean ≥8 for all items).

Thereafter, a prospective cohort study evaluated outcomes in 319 adult smokers (intention to treat or ITT cohort) who underwent the full Pivot program; 272 (85.3%) participants completed the end-of-Pivot questionnaire (mean 4.1 months after enrollment) and 288 participants completed the final follow-up questionnaire three months later (mean 7.2 months after enrollment).[13,14] The Pivot program included the Pivot CO breath sensor, smartphone app, and text-based human coaching. The study included individuals along the spectrum of readiness to quit; at study entry most (66.5%, 212/319) were not thinking of quitting smoking in the next 30 days. The study examined participant engagement, changes in attitudes toward quitting smoking, and changes in smoking behavior during, at the end, and three months after active participation in the Pivot program. On average, participants had a mean of 12.4 (SD 7.1) weeks of active program engagement (defined as doing at least 1 of the following per week: completing a breath sample; logging a cigarette; starting or completing a daily activity, challenge or check-in; or messaging one's coach). Repeated measures linear mixed model analyses demonstrated positive changes in attitudes at the end of the pre-quit portion of the program, with increased confidence to quit (4.2 to 7.4, $P$<.001) and decreased expected difficulty maintaining quit (3.1 to 6.8, $P$<.001). The quit attempt rate (i.e., those making ≥1 quit attempt lasting ≥1 day) was 80.6% (232/288, completer) at final follow-up. At the end of Pivot, 7-day point prevalence abstinence (PPA) rates were 32.0% (102/319, ITT) and 37.5% (102/272, completer) which increased to 34.5% (113/319, ITT) and 39.2%

(113/288, completer), respectively, at final follow-up; 30-day PPA rates were 27.6% (88/319, ITT) and 32.4% (88/272, completer) at the end of Pivot, which increased to 31.3% (100/319, ITT) and 34.7% (100/288, completer), respectively, at final follow-up. Moreover, 30-day PPA rates were comparable among those ready and not ready to quit in the next 30 days at baseline. Of those not achieving abstinence, 25.9% (44/170, completer) achieved ≥50% reduction in cigarettes per day (CPD) at the end of the Pivot program.

## 2.2 STUDY RATIONALE

While the aforementioned data is encouraging, there is an ongoing need to assess the performance of Pivot in the context of current standard smoking cessation programs. Accordingly, the present pilot randomized controlled trial compares user engagement and retention, change in attitudes towards quitting smoking, change in smoking behavior and participant feedback in adult smokers randomized either to the Pivot (intervention) or QuitGuide (control) smoking cessation programs.

## 2.3 POTENTIAL RISKS AND BENEFITS

### 2.3.1 Known Potential Risks

There are minimal anticipated risks or harms to the participant. One possible risk is breach of confidentiality should a data breach occur. Regarding the risk of breach of confidentiality, we, the study sponsor (Pivot Health Technologies Inc., formerly Carrot Inc.) comply with HIPAA and state this risk in our privacy and terms of use on our website regarding use of Pivot. As such, we adhere to HIPAA's Breach Notification Rule should a data breach occur. We take careful measures to prevent a data breach including use of encryptions, secure connections, and limited access to data (see section 10.1 "Data Collection and Confidentiality"). The sponsor uses appropriate safeguards and complies, where applicable, with 45 C.F.R. Part 164, Subpart C with respect to Electronic Protected Health Information, to prevent use or disclosure of Protected Health Information. Specifically, Pivot Health Technologies Inc. has implemented the administrative, physical, and technical safeguards set forth in 45 C.F.R. §§ 164.308, 164.310, and 164.312 that reasonably and appropriately protect the confidentiality, integrity, and availability of any Protected Health Information that it creates, receives, maintains, or transmits. The QuitGuide app is maintained by the U.S. Government. It is protected by various provisions of Title 18, U.S. Code. The QuitGuide app notes, "NCI complies with requirements for privacy and security established by the Office of Management and Budget (OMB), Department of Health and Human Services (DHHS), and the National Institutes of Health (NIH)."

Another possible risk is participant anxiety, which could be related to using the Pivot Breath Sensor during the study, or completing biovalidation using the Pivot Breath Sensor on study videocalls. For regular use of the Pivot Breath Sensor during the study, while there are suggested breath sampling patterns provided with the breath sensor packaging, participants will ultimately sample at their discretion. No medical

decisions are made based on study data. For completing biovalidation, participants will be fully informed why the biovalidation is being performed, what it tests for, and they will be asked on each applicable videocall if they feel comfortable proceeding with biovalidation. Participant compensation is not based on breath sampling frequency or results, or on biovalidation results.

Finally, participants will have the option to select, order and use over-the-counter nicotine replacement therapy (NRT). Participants are provided with on-label information about the NRT, and are required to acknowledge their standing relating to contraindications for NRT use before being able to order the NRT. They then select, order and use the NRT as they would when purchasing over-the-counter medications in everyday life. The NRT is provided free of charge to study participants who order it. Risks associated with NRT use are identified in the labeling provided to study participants [redacted].

### 2.3.2 Known Potential Benefits

It is possible some participants will quit or reduce smoking. It is also possible that some participants may experience an increased awareness of their smoking behavior, increased motivation to quit smoking, or learn techniques that help them stay quit, or reduce or quit smoking in the future.

### 2.3.3 Risk Benefit Assessment

Given the non-invasive nature of Pivot and QuitGuide and study data collection, there are minimal anticipated risks. These risks relate to breach of confidentiality in the circumstance of a data breach, possible participant anxiety related to using the Pivot Breath Sensor or related to performing biovalidation with the sensor during videocalls, and possible side effects of the use of over-the-counter NRT if the participant chooses to use it. These risks have been mitigated to the extent possible through data protection measures, through enabling participants to ultimately decide if and when to do breath samples, through fully informing participants why the biovalidation is being done, what it tests for and asking if they would like to proceed with the testing on the applicable videocalls, and through enabling participants to make an informed decision on if they will use NRT and which NRT they will use if they choose to use any at all. Breath samples, biovalidation, NRT selection and NRT use are at the participant's discretion and are not mandated. Indeed, no specific use of Pivot or QuitGuide overall is required. Participants will have the remote support of study staff and customer support as they need over the course of the study. Participants are not required to change their smoking behavior. No medical decisions are made based on study data.

## 3. OBJECTIVES

We aim to assess participants' use of Pivot (which includes the Pivot Breath Sensor, Pivot Health Technologies Inc.; Redwood City, CA, USA; 510(k) number: K171408) and QuitGuide. There will be a focus on assessing use and engagement, changes in attitudes towards quitting smoking and changes in smoking behavior over the course of the 2-year study, as well as participant feedback on the set-up, design, use experience, and impact of each program.

References

- FDA Guidance Document Entitled, "Guidance for Industry and Food and Drug Administration Staff: Applying Human Factors and Usability Engineering to Medical Devices," issued on February 3, 2016
- FDA Guidance Document Entitled, "Design Considerations for Devices Intended for Home Use, Guidance for Industry and Food and Drug Administration Staff" issued on November 24, 2014
- ISO/IEC 62366-1:2015, Medical devices – Application of usability engineering to medical devices. Geneva, International Electro technical Commission.
- AAMI/ANSI HE75:2009, Human Factors Engineering – Design of Medical Devices.
- https://www.bluetooth.com/what-is-bluetooth-technology/bluetooth-technology-basics
- 45 CFR Part 164 – Security and Privacy https://www.ecfr.gov/cgi-bin/text-idx?SID=12bd414e1d9ba63b17bf5b06e19a4d3e&mc=true&node=pt45.2.164&rgn=div5

## 4. DEFINITIONS

Bluetooth Low Energy (BLE): A global wireless communication standard that connects devices together over a certain distance.

Data: Data collected through the Pivot Breath Sensor and participant-completed online email questionnaires.

Pivot Breath Sensor: A personal mobile breath sensor that is capable of measuring the level of carbon monoxide (CO) in exhaled breath. It is portable, battery-powered, and small enough to be carried by the user throughout the day (pocket, purse, backpack). The sensor is intended for single-user use by cigarette smokers to inform the user about how breath CO levels are affected by smoking behavior. The user submits a breath sample by exhaling (blowing) directly into the mouthpiece connected to the sensor with breath sample results displayed on a screen on the sensor. Breath sample results are also displayed in the Pivot app.

Pivot app: A smartphone app that is installed on the user's smartphone. User's smartphone is connected to the Pivot Breath Sensor via BLE. The Pivot app includes educational content, the ability to log cigarettes, set a quit date, create a quit plan, play educational games, watch educational videos, interact with a dedicated human coach via in-app text messaging, view CO breath sample values and trends, learn about and then order NRT and access the moderated online Pivot community discussion forum.

QuitGuide app: A smartphone app that is installed on user's smartphone. The QuitGuide app includes educational content, the ability to log cigarettes and cravings, learn about NRT, set a quit date, create a quit plan, journal, seek social support and receive tips to deal with triggers and cravings.

Nicotine Replacement Therapy (NRT): In the study, participants may order over-the counter NRT [redacted]. They are provided on-label information including information about contraindications. NRT is ordered through the Pivot app in the intervention arm and online in the control arm. NRT options include FDA-approved over-the-counter nicotine patches, nicotine gum and nicotine lozenges. Participants use the over-the-counter NRT labeling to determine if they would like to order NRT and what NRT to order. Participants may order a 2-week supply of NRT every two weeks for up to a 12-week supply of NRT over the first 12

months of the study. Use of any ordered NRT is at the participant's discretion.

## 5. CONTROL – QUITGUIDE PLUS NICOTINE REPLACEMENT THERAPY

### 5.1 QUITGUIDE

QuitGuide is a product of Smokefree.gov—a smoking cessation resource created by the Tobacco Control Research Branch at the National Cancer Institute in collaboration with tobacco control professionals and smoking cessation experts and with input from ex-smokers. A well-established smoking cessation app, QuitGuide has been used in previous randomized controlled trials in which digital smoking cessation programs were compared. [10,11] The app focuses on helping users understand their smoking patterns and build the skills needed to become smoke-free.[15] QuitGuide helps users focus on motivations to quit; prepare to quit through developing a quit plan, identifying and planning how to address triggers for smoking, learning about FDA-approved smoking cessation medications, and identifying social support; quit smoking by teaching skills to address cravings; and stay quit by presenting tips and motivations to stay smoke-free and address slips if they occur. [redacted] QuitGuide is used as the control for the following reasons: the content follows the USCPG, it is an app-based smoking cessation program thus avoiding confounding treatment content with treatment delivery modality, and the app is non-proprietary and is free to the public. The QuitGuide app is compatible with iOS and Android phones. QuitGuide provides technical support to help users download and use the app through smokefreeteam@icf.com.

### 5.2 NICOTINE REPLACEMENT THERAPY

Participants in the QuitGuide control arm may order FDA-cleared over-the-counter NRT online. Participants are provided with on-label information about the NRT, must also acknowledge understanding of contraindications. They will then complete an online order form to order their desired NRT. They will be provided a link through which to order NRT. The NRT is free of charge to the participant. There is no out-of-pocket payment by the participant for the NRT. The types of NRT offered include nicotine patches (7, 14 and/or 21 mg), nicotine gum (2 or 4 mg), and nicotine lozenges (2 or 4 mg) [redacted]. Participants may order patches, gum or lozenges alone as mono-therapy, or they may order patches + gum or patches + lozenges [redacted]. Participants may order NRT every 2 weeks for up to a 12-week course of NRT over the first 12 months of the study. NRT arrives with written instructions/FDA-cleared labeling.

## 6. INTERVENTION - PIVOT

Pivot is a digital smoking cessation program that includes the Pivot Breath Sensor and Pivot app. In the Pivot app, users can order NRT and access text-based one-on-one coaching and the moderated Pivot online community discussion forum. Pivot is based on the USCPG for tobacco cessation and is designed as a 12-month program.

### 6.1 PIVOT BREATH SENSOR

The Pivot Breath Sensor is part of the Pivot program and comprises a personal mobile

breath sensor that measures the level of CO in exhaled breath and displays the exhaled breath CO value to the user directly on the device. When paired to the user's smartphone, the user's exhaled breath CO values also populate the Pivot app, where they can be accessed by the user. The breath sensor range of CO measurement is 0-100 ppm.

The Pivot Breath Sensor (Figure 1) is portable, battery-powered, and small enough to be conveniently carried by the user throughout the day (pocket, purse, backpack). The sensor is rechargeable using a micro-USB cable. The user submits a breath sample by exhaling (blowing) into the sensor mouthpiece.

### 6.1.1 Indications for Use

*The Pivot Breath Sensor is a breath carbon monoxide monitor intended for single-user use by cigarette smokers to inform the user about how breath carbon monoxide levels are affected by smoking behavior. The device is not intended to be used with other inhaled products.*


**Figure 1. Pivot Breath Sensor**

## 6.2 LABELING AND PACKAGING

The Pivot Breath Sensor package includes:

- 1 Pivot Breath Sensor
- 1 USB charging cable
- 1 Replaceable Mouthpiece
- 1 Quick Start Guide [redacted]
- 1 Package Insert [redacted]
- 1 Pivot Breath Sensor Educational Booklet [redacted]

[redacted]

## 6.3 PIVOT BREATH SENSOR SUBMITTING A BREATH SAMPLE (SPECIFIC STEPS)

Submitting a breath sample involves the following steps. Instructions can be accessed in multiple locations including the Pivot Breath Sensor's display screen, in the online User Manual [redacted], Quick Start Guide, and on the packaging.

1. User presses any button to turn on the Pivot Breath Sensor.
2. User presses and holds the center button on the Pivot Breath Sensor until the sensor beeps once.
3. User takes a deep breath in and holds their breath for 10 seconds.
4. After about 10 seconds, the device beeps 3 times, and the user then will exhale slowly until the sensor vibrates at 12 seconds.
5. The user's CO level will display on the sensor's screen.

A properly submitted breath sample is defined as one that initiates after the third beep prompt and is of at least 6 seconds duration. Breath sensor hardware and firmware is capable of detecting when a breath sample submission starts and stops. The suggested breath sampling regimen is 4 breath samples per day, with samples spread over the course of the day.

The CO Log screen on the Pivot Breath Sensor provides the CO (ppm) value for properly submitted breath samples.

The computation of concentration of CO (ppm) is performed within the Pivot Breath Sensor firmware and the data (CO ppm concentration, time and date) are stored in the Pivot Breath Sensor memory. This data is also stored and visible in the Pivot app when the Pivot Breath Sensor and user's smartphone are paired via Bluetooth Low Energy (BLE). Opening the Pivot app syncs the data to its most updated state, which study staff and participants may access in real-time. User's may also sync their breath sensor data by tapping the breath sensor icon in the upper right corner of the Pivot app and then tapping "Sync Now' in the dropdown menu.

## 6.4 CO LOG

The CO Log can be accessed from the Pivot Breath Sensor's display screen and shows the most recent exhaled breath CO value in ppm at the top of the screen. The user can view previous values by scrolling within the log (Figure 2).

Values are color coded and can be interpreted by the user with help from the labeling (Figure 3).

**Figure 2. CO log on Pivot Breath Sensor**

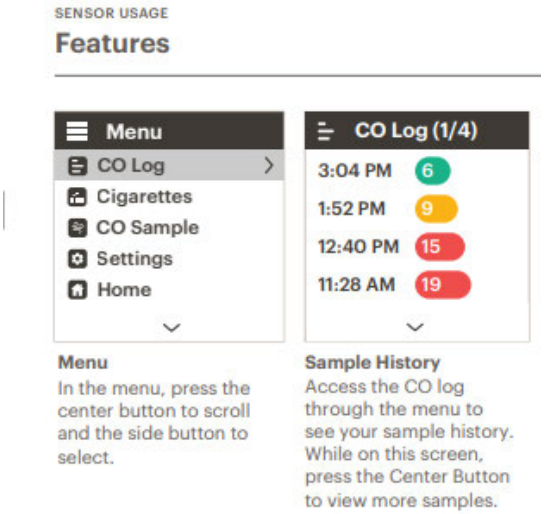
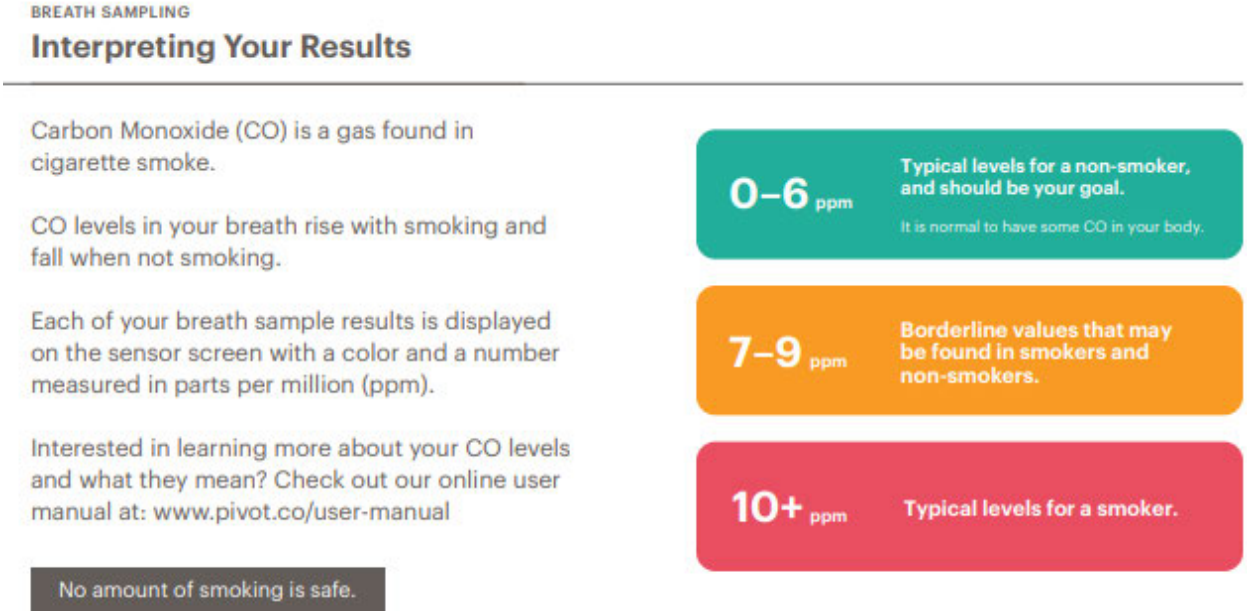



**Figure 3. Labeling to interpret results**




CO values are also stored in the Pivot app on the participant's smartphone. When the Pivot Breath Sensor is paired to a user's phone, his/her CO values and date/time of breath samples populate the Pivot app.

## 6.5 PIVOT APP

The Pivot app includes educational content, the ability to log cigarettes, set a quit date, create a quit plan, play educational games, watch educational videos, interact with a dedicated human coach via in-app text messaging, view CO breath sample values and trends, learn about and then order NRT, and access the moderated online Pivot

community discussion forum. The educational journey in the Pivot App comprises 4 tracts: Learn, Reduce, Prepare to Quit, and Maintain My Quit, and is designed to accommodate smokers along the spectrum of readiness to quit. Participants may choose to focus on building self-awareness and learn more about their smoking behavior, create and practice their plan to quit or reduce smoking, make a quit attempt, focus on staying quit, or any combination thereof. Accordingly, participants may navigate between tracts as desired to access content most relevant to their goals and needs. [redacted] The Pivot app is compatible with iOS and Android phones.

### 6.6 PIVOT COACHING

Pivot users are assigned a human coach with whom they will work one-on-one over the duration of their use of Pivot (up to one year). Communication between coach and the Pivot user is via asynchronous in-app text messaging. Pivot coaches are tobacco treatment specialists. Coaching is based on cognitive behavioral therapy and uses evidence-based techniques in tobacco cessation such as motivational interviewing, with the aim to help participants reach their goals related to tobacco use. Participants may reach out to their coach whenever and however often they like. The coach will reach out periodically, approximately once per week, during the participant's active use of Pivot.

### 6.7 PIVOT NICOTINE REPLACEMENT THERAPY (NRT)

Pivot users may order FDA-cleared over-the-counter NRT through the Pivot app. Participants are provided with on-label information about the NRT, must also acknowledge understanding of contraindications. The NRT is free of charge to the participant. There is no out-of-pocket payment by the participant for the NRT. The types of NRT offered in Pivot include nicotine patches (7, 14 and/or 21 mg), nicotine gum (2 or 4 mg), and nicotine lozenges (2 or 4 mg) [redacted]. Participants may order patches, gum or lozenges alone as mono-therapy, or they may order patches + gum or patches + lozenges. Participants may order NRT every 2 weeks for up to a 12-week course of NRT. NRT arrives with written instructions/FDA-cleared labeling.

### 6.8 PIVOT MODERATED ONLINE COMMUNITY

Pivot users may access the moderated online discussion community through the Pivot app. The forum is moderated by a tobacco treatment specialist. The online community forum is a place to give and receive support and advice from others going through the Pivot program.

## 7. STUDY DESIGN AND OVERVIEW

### 7.1 STUDY DESIGN

This is a two-arm, parallel-group, non-crossover, single-center pilot randomized

controlled trial conducted with IRB approval enrolling up to 180 subjects who report daily smoking of 5 cigarettes or more. The study will be performed remotely on an ambulatory basis. Participants will be randomized to use either the Pivot (intervention) or QuitGuide (control) app-based smoking cessation program. They will be asked to setup their assigned app on their smartphone and in the case of being assigned to the intervention arm, also set up their Pivot Breath Sensor. Participants will be able to learn about and order up to a 12-week supply of NRT at their discretion. Participants may participate in up to four videocall biovalidation study visits, depending on the smoking status. During these visits, participants provide a breath sample using the Pivot breath sensor, and share their CO ppm results in real-time. The study lasts for 2 years (104 weeks). It is estimated that up to the first 6 months will be primarily focused on active program use and the remaining time in the study will be devoted to passive periodic follow-up. Participants will receive the online study questionnaires via email, from Survey Monkey, at intervals throughout the study.

### 7.2 STUDY DURATION

The study will run for 2 years (104 weeks).

### 7.3 STUDY OUTCOMES

- User engagement and retention in the program (number of app opens, number of days with at least one app open, number of weeks with at least one app open)
- Attitudes towards quitting: desire to quit, confidence to quit, difficulty to quit and self-efficacy
- Smoking behavior: quit attempts, change in cigarettes per day (CPD), smoking cessation via 7-and 30-day PPA (self-report and biochemically confirmed), continuous abstinence (self-report and biochemically confirmed), abstinence from all tobacco products, use of NRT
- Participant feedback on the set-up, use experience, design and impact of their assigned smoking cessation program

Outcomes include:

Primary:

- Total app opens in Pivot vs QuitGuide at 12 weeks (3 months)

Secondary:

- Change in expected difficulty in staying quit (participant self-report, scale 1-10) at 2, 4, 8, 12 weeks after enrollment
- Change in confidence levels towards quitting smoking (expected success in quitting, participant self-report, scale 1-10) at 2, 4, 8, 12 weeks after enrollment
- Desire to quit (yes/no) at 4 weeks after enrollment
- Self-reported abstinence (7-day and 30-day PPA) at 6, 8, 12, 26, 52 and 104 weeks after enrollment
- Self-reported abstinence (7-day PPA) at 2 and 4 weeks after enrollment
- Self-reported abstinence from all tobacco products at 6, 8, 12, 26, 52, and 104 weeks after

enrollment
- Biochemically confirmed abstinence at 12, 26, 52, and 104 weeks
    - To be considered biochemically abstinent:
        - Breath CO sample should be less than 10 ppm [16]
- Self-reported continuous abstinence at 26, 52 and 104 weeks, defined as a self-report of smoking no more than five cigarettes from 12 weeks after enrollment
    - 12 weeks is chosen because it allows for a full course of NRT, and it has been standard in studies that include pharmacotherapy for smoking cessation [17]
- Biochemically confirmed continuous abstinence at 26, 52, and 104 weeks, defined as a self-report of smoking no more than five cigarettes from 12 weeks after enrollment, and confirmation on all previous and present biovalidation tests:
        - Breath CO sample should be less than 10 ppm for participant to be considered abstinent [16]
- The proportion of participants who reduced their cigarettes per day (CPD) by ≥ 50% compared to baseline at 4, 12, 26, 52 and 104 weeks
- Number of quit attempts at 4, 12, 26, 52, and 104 weeks (defined as answering ≥1 to the following question: “Since you began the study, how many times have you tried to quit smoking where you've gone at least 1 day without smoking a cigarette, even a single puff?”).
- User satisfaction with the smoking cessation program (set-up and getting started with program, recommend to friend, program design, program was useful for quitting, program helped me quit, program helped me stay quit) at 2, 3, 4, 5, 12, 26, 52 and 104 weeks
- Engagement with program, collected weekly during the first 12 weeks after enrollment:
    - Number of times app opened (self-report)
    - Number of days in which app was opened (self-report)
    - Number of weeks in which app was opened (self-report)
- Participant changes in self-efficacy at 6 12, 26 and 52 weeks
- Participant changes in self-reported health and wellbeing at 26 and 104 weeks
- Self-reported NRT use at 4, 8, 12, 26, 52 and 104 weeks
- Use of other smoking cessation tools (apps, counseling, non-study medications, etc.) at 12, 26, 52, and 104 weeks
- Alcohol use behavior at 12, 26 and 52 weeks (Alcohol Use Disorders Identification Test-Concise or AUDIT-C screening questionnaire, 3 items) [18-20]
- Presence of depressive symptoms screening at 12, 26, and 52 weeks (Center for Epidemiological Studies Depression Scale or CES-D screening questionnaire, 10 items) [11,21-23]
- Living and social environment relating to cigarette smoking at 12, 26 and 52 weeks (live with other adults who smoke, live with romantic partner who smokes, number of close friends who smoke)
- Adverse events at 26, 52 weeks

Eligibility Criteria

The study population comprises current smokers, 21 years of age and above, who own and

regularly use a smartphone and are ready to quit smoking in the next 30 days.

Inclusion Criteria

- 21+ years of age
- Current daily cigarette smokers (at least 5 cigarettes per day) for the past 12 months
- Plans to quit smoking in the next 30 days
- Resident of the United States
- Able to read and comprehend English
- Owns and uses a smartphone compatible with the study app (iPhone 5 and above with operating system iOS 12 and above, or, Android 7.0 and above with operating system Android 7.0 and above)
- Has daily internet access on smartphone
- Comfortable downloading and using smartphone apps
- Willing to sign the Informed Consent Form

Exclusion Criteria

- Pregnancy (self-reported)
- Health contraindications to nicotine patch use (irregular heartbeat, high blood pressure not controlled with medication, heart attack or stroke within the last 2 months, pregnant or breast feeding, skin allergies to adhesive tape or serious skin problems, stomach ulcers, history of seizures)
- Using other smoking cessation support, including apps and/or actively taking medication to quit smoking
- Daily marijuana use
- Residence with another person who is a participant in this study
- Immediate family member is a participant in this study
- Failure to provide contact or collateral information, failure to verify email address, and/or failure to demonstrate videoconference capability
- Participation in a previous study sponsored by Pivot Health Technologies Inc. (formerly Carrot Inc.)

### 7.4 PARTICIPANT RECRUITMENT AND INFORMED CONSENT

Participants will be recruited in the United States through web media (e.g. Facebook, Google Ads) [redacted]. Potential participants will be asked to provide contact information (first name, phone number, email address), and answer questions on demographics (gender, age, employment status, location via city and state, race/ethnicity), smartphone ownership, and smoking attitudes and behavior (Stage of Change and CPD) using the Online Screening Form [redacted]. Study staff will review each potential participant's responses to the eligibility questions.

Online screening form responses will be reviewed by study staff. Using non-proportional quota sampling, potential participants will be called on a first-come-first-served basis, as possible, with the aim to enroll 40-60% males, 40-60% females, no more than 50% of participants from any decade-spanning age group (ex. 30-39 years of age, etc.), no more than 70% of participants in the non-Hispanic white race category and up to 20% unemployed. The goals of these non-proportional quota sampling ranges are to ensure

representation among males, racial/ethnic minorities, age groups, and individuals with varying socioeconomic status. Regarding the non-proportional quota sampling for employment, at the time of protocol design (March and April, 2021) the unemployment rate in the U.S. was 6.0%.[24] Acknowledging a higher unemployment rate among people who smoke [25-28], and the desire to include individuals who either do not receive payment for their work or are not pursuing employment (stay-at-home parents, caretakers, students, retired individuals) we will enroll up to 20% of participants who do not currently have employment for which they are compensated.

During the screening phone call, potential participants will be asked questions to confirm study eligibility [redacted]. During this call, study personnel will inform the potential participant of the study details and will answer any questions.

Potential participants will then determine if they would like to proceed. If they would like to proceed, study staff will arrange for a brief (1-2 minute) videocall with the potential participant using the HIPAA-compliant study videoconference platform to confirm capability on the participant's behalf. This call should be completed prior to randomization. Study personnel will email the potential participant an electronic HIPAA Authorization form and an electronic Informed Consent Form (ICF) [redacted]. The potential participant will have ample time to read these forms and the opportunity to ask questions. The participant will sign the electronic HIPAA Authorization and ICF before participating in this study. The ICF will seek documented confirmation of potential study participant's readiness to quit smoking in the next 30 days. Once signing the ICF, the participant will be given a unique identifier [redacted] to protect participant privacy.

### 7.5 PARTICIPANT RANDOMIZATION, STRATIFICATION AND ENROLLMENT

After signing the ICF, the participant will complete an online Baseline Questionnaire. Based on responses to the questionnaire, participants will be randomly assigned in a computer-generated 1:1 manner to either Pivot or QuitGuide using randomly permuted blocks of size 2 and 4, stratified by daily smoking frequency (≤14 vs ≥15 cigarettes per day), employment status (full-time or part-time employment vs unemployed), race/ethnicity (minority race/ethnicity vs non-Hispanic White), and expected difficulty staying quit (scale 1-10; self-reported score of ≤5 vs. ≥6). After randomization, participants will be emailed the link to access their assigned group. In both groups, participants will be able to access their assigned study app from the moment of randomization and beyond (ie, after the end of the 2-year study period).

Participants will be considered enrolled after completing the following 3 tasks: electronically signing the informed consent form, completing the Baseline Questionnaire and reporting the date they first logged in to their assigned app. If participants do not complete all three criteria, they may be removed from the study.

### 7.6 PARTICIPANT STIPEND

Participants are compensated for completing the online questionnaires (up to $365 in total for 16 questionnaires). If participants report 7-day PPA on the 12-, 26-, 52- and/or 104-week questionnaire, they will have the opportunity to do a biovalidation videoconference

study visit. Participants will be compensated $50 for each biovalidation visit they complete (up to 4 biovalidation visits in total) for up to $2000. In total, participants may earn up to $565 over the course of the 2-year study. Compensation will be in the form of Visa or Mastercard gift cards that are mailed or emailed to their provided address. Payments will be bundled as depicted in the Informed Consent Form with participants receiving up to 6 payments over the course of the study. Bundled payments will be processed upon completion of the item(s) for which the participant is receiving payment and will take 2-3 weeks to arrive to the participant after being processed. Participants will be compensated for each questionnaire they complete, even if they do not complete all questionnaires that are included within a payment bundle.

### 7.7 SAMPLE SIZE AND JUSTIFICATION

As this is a pilot RCT and first assessment of Pivot compared to usual care, the study's sample size is powered to show differences in engagement, operationalized as the number of times participants open their assigned app. Previous clinical studies assessing Pivot have reported a mean of 24.2-38.7 app opens (SD range 20.8-25.9) by 90 days (data on file). In addition, Bricker et al. reported app opens comparing ACT-based smoking cessation apps (SmartQuit and iCanQuit) to QuitGuide. In one study, at 2-month follow-up, Bricker et al. reported mean (SD) app opens were 37.2 (46.1) for SmartQuit and 15.2 (13.6) for QuitGuide.[10] In a subsequent study, at 12-month follow-up, mean (SD) app opens were 37.5 (88.4) for iCanQuit and 9.9 (50.0) for QuitGuide.[11]
Based on this data, we estimate mean (SD) 25 (25) app opens in the intervention arm vs. 15 (19) app opens in the control arm at 12 weeks. To detect a difference of 10 app opens or greater between Pivot and QuitGuide with 0.8 power and 0.05 alpha would require 156.7 participants, which we round up to 158. In a previous study, 272/319 (85.3%) participants completed the end-of-Pivot questionnaire at a mean (SD) 4.1 (1.4) months after enrollment. [13,14] Considering that we will assess our primary endpoint at 3 months (12 weeks), we are accordingly including an expected 15% attrition rate, with a plan to enroll up to 180 participants (up to 90 in each arm).

### 7.8 STUDY ARTICLES

Control group:

- QuitGuide App [redacted]
- NRT with associated labeling (optional)

Intervention group:

- Pivot Breath Sensor
- USB charging Cable
- Replaceable Mouthpiece
- Quick Start Guide [redacted]
- Pivot App [redacted]
- Package Insert [redacted]
- Pivot Breath Sensor Educational Booklet [redacted]
- NRT with associated labeling (optional)

### 7.9 USER MANUAL AND TRAINING

Both Pivot and QuitGuide were designed with the intention that users are able to understand how to use these programs independently. For the Pivot Breath Sensor, a Quick Start Guide, Package Insert, Educational Booklet and package labeling are included with the device to aid the user and an online User Manual [redacted] is also available. All of these items will be accessible to study participants in the intervention arm; in addition, a phone number will be included within the labeling material to contact customer support. QuitGuide provides technical support to help users download and use the app through smokefreeteam@icf.com.

### 7.10 STUDY ENVIRONMENT

The study will be performed remotely on an ambulatory basis. Participants will be emailed a link for their respective app to get started. For individuals in the intervention arm, the Pivot Breath Sensor will be mailed to the participant's indicated address and the participant will use the sensor at their discretion, going about life as they normally would.

### 7.11 STUDY PERSONNEL

The study team members will be trained by reading the study protocol. The study team members will have full training on the QuitGuide and Pivot apps, and operation of the Pivot Breath Sensor. Study team members will also have documentation of HIPAA / HITECH Security Awareness training and NIH Protecting Human Research Participants training.

### 7.12 IRB OVERSIGHT

This study will be conducted under IRB oversight.

## 8. STUDY PROCEDURE

### 8.1 SCREENING

See section 7.4 *Participant Recruitment and Informed Consent*

### 8.2 REGISTRATION

After electronically signing the Informed Consent Form, the participant will complete the online Baseline Questionnaire. After completing the Baseline Questionnaire, participants will undergo computer-generated randomization to either the intervention or control study group, as described in section 7.5 *Participant Randomization, Stratification and Enrollment*. Participants are then emailed a link for their assigned app. Upon opening the link, participants will register in their assigned app, providing baseline information on their smoking behavior. While participants are encouraged to select a quit date in their app that occurs within 30 days of enrollment, this is not required for participation.

### 8.3 ACTIVE PROGRAM USE

The participant will initiate use of their assigned program. To be considered enrolled, one must: sign the electronic informed consent form, complete the Baseline Questionnaire, and provide the date they first logged in to their assigned app. Participants may receive up to two text or email messages during the first week of the study reminding them to go into their study app and confirm they have done so. There is no pre-determined time limit on how long a participant can actively engage in their app, although it is expected most participants will complete engagement by 6 months from enrollment. For individuals enrolled in the intervention arm, coaching is available for up to 12 months from enrollment. In both arms, participants may order up to 12 weeks of NRT, in two-week increments over the first 12 months of the study. Pivot is designed to be a 12-month program. There is one possible biovalidation videocall visit at 12 weeks during this portion of the study and weekly online questionnaires at the end of weeks 1 through 12.

### 8.4 FOLLOW-UP

As it is expected that most participants will complete engagement in their respective programs by 6 months, the study will focus on follow-up at that point and beyond. The follow-up period includes three possible biovalidation videocall visits at 26, 52 and 104 weeks, and online questionnaires at 26, 52 and 104 weeks.

### 8.5 BIOVALIDATION

Biovalidation will be sought at 12, 26, 52 and 104 weeks in individuals who reported 7-day (or greater) PPA on the associated questionnaire (from 12, 26, 52 or 104 weeks). A videocall will be scheduled for within 7 days following the participant's response to the associated questionnaire. At the beginning of each biovalidation call, participants will be asked 7-day PPA status. Participants will be asked (yes/no) if they have smoked any other non-cigarette (ex. pipes, cigars, hookah) or combustible materials (ex. cloves, marijuana) over the last 24 hours. They will also be asked how many cigarettes they currently smoke per day. Participants who indicate they are not at least 7 days abstinent (i.e., answer "Yes" to the following question: "In the last 7 days have you smoked any cigarettes, even a single puff?") and/or indicate they currently smoke cigarettes will not be eligible to undergo further biovalidation testing during the visit. Participants who indicate they are at least 7 days abstinent and do not smoke cigarettes will be eligible to proceed with the testing. Participants who indicate they have smoked any other combustible materials over the previous 24 hours will be eligible to undergo biovalidation test, with the option to schedule a follow-up biovalidation test for the following day with instruction to not smoke the previously reported other combustible substance(s) over the intervening 24-hour period. If a participant is eligible for biovalidation and biovalidation is not achieved, the reason will be noted (ex. did not complete a biovalidation study visit, reported relapse so biovalidation visit was not completed, participant's breath CO sample was 10 ppm or more, etc.).
If this is the first study biovalidation visit a participant has participated in, the steps of the visit and the CO breath sample will be described in detail, with questions fielded and verbal confirmation the participant would like to proceed obtained before doing the biovalidation test. If this is not the first study biovalidation visit a participant has participated in, there will be a high-level review of the steps of the visit and the CO

breath sample, with questions fielded and verbal confirmation that the participant would like to proceed obtained.
Biovalidation will be obtained through CO breath sampling. For the 12-, 26- and 52-week biovalidation visits, participants in the intervention arm will use their Pivot Breath Sensor for this test. Participants in the control arm will be mailed a Pivot Breath Sensor prior to the visit that has a limited number (10 or less) of samples it can perform. For the 104-week biovalidation visit, all eligible participants who schedule the biovalidation visit will be mailed a Pivot Breath Sensor. On the call, participants will have the process of giving a breath sample described to them. They will be offered the chance to ask questions, and then study staff will provide an overview of the steps to give a breath sample. When they feel ready, they will give a breath sample and hold the breath sensor up to the screen immediately after completing the sample so that study staff on the videocall can see the CO ppm measurement on the breath sensor screen. A CO ppm value of less than 10 will be considered consistent with abstinence.[16]
After their first biovalidation visit, participants in the control arm will be instructed to not use the breath sensor beyond the visit, and to place the sensor in a safe place (for example, in the original packaging, in a closet) for use at a future biovalidation visit, should there be one. For future biovalidation visits, participants will use their existing breath sensor or will be sent a new one (fully functioning breath sensors for the intervention arm and sensors limited to 10 breath samples for the control arm for 12-, 26- and 52-week visits; and fully functioning sensors for all eligible participants for the 104-week visit) as needed. Participants will keep the breath sensor. While the sponsor will not request the sensors be mailed back, participants may mail their sensor(s) back to the sponsor if they prefer.

### 8.6 REMINDERS

Over the first 12 weeks of the study, participants will receive an email or text reminder to engage with their assigned program every other week (for a total of 6 reminders). These reminders will be sent out during weeks 1, 3, 5, 7, 9 and 11. Two of these communications will remind participants of the availability of NRT. During the first week of the study, participants may receive up to an additional two text or email messages reminding them to log into their study app and confirm they have done so.

Participants will receive periodic reminders from study staff to complete their questionnaires via email, text or phone, as needed. All participants will receive all questionnaires, regardless of completion of previous questionnaires. [redacted]

### 8.7 STUDY COMPLETION

The final study questionnaire will be emailed at 104 weeks (2 years) after enrollment. Completion of this questionnaire, or 110 weeks after enrollment (whichever comes first) will signify study completion. For participants who report 7-day (or greater) abstinence at 104 weeks and agree to participate in a biovalidation visit, completion of this visit, or 110 weeks after enrollment (whichever comes first) will signify study completion.

## 8.8 SCHEDULE OF STUDY ACTIVITIES

[redacted]

## 9. DATA COLLECTION

Study personnel will collect information from the participant over the course of the study including:

- Age
- Gender
- Pregnancy status (self-reported) in women
- Race/ethnicity
- Employment status
- Education
- Type of smartphone participant uses (iPhone or Android)
- Number of years smoking
- Social and living environment relating to smoking
    - Live with other adults who smoke
    - Live with romantic partner who smokes
    - Number of close friends who smoke
- Alcohol use (AUDIT-C, 3 items)
- Screening for depressive symptoms (CES-D, 10 items)
- Quit attempts
    - Past 12 months
    - During the study
- Number of cigarettes currently smoked per day (CPD)
- 7-day point prevalence abstinence (PPA) (self-reported and biovalidated)
- 30-day point prevalence abstinence (PPA) (self-reported and biovalidated)
- Abstinence from all tobacco products (self-reported)
- Continuous abstinence (self-reported and biovalidated)
- Use of other tobacco products other than cigarettes including pipes, cigars, cigarillos, little filtered cigarettes, hookah, water pipe, any electronic cigarette product (e-cigs, vape, vapor), smokeless tobacco, chew, or snuff, and any other inhaled combustible material
- Use of smoking cessation medications past and present
- Use of other smoking cessation methods, past and present (for the present, methods other than those in the study program)
- Attitudes towards smoking
    - Desire to quit (y/n)
    - Confidence to quit (scale 1-10)
    - Perceived difficulty of staying quit (scale 1-10)
    - Self-efficacy
- Engagement
    - App opens (self-reported)
    - Number of days with app opens (self-reported)
    - Number of weeks with app opens (self-reported)
- Feedback on assigned program set-up and use
    - Ease/difficulty getting started
    - Use experience

  - Design
  - Impact on quitting
  - Impact on staying quit
  - How would you improve the experience of your assigned program?
  - How likely are you to recommend your assigned program to a friend/colleague? (scale 1-10)
  - How has using your assigned program affected the number of cigarettes you smoke per day? (increase, no change, decrease)
  - Which of the following best describes your thoughts on your assigned program? ('nothing else can help me with smoking' to 'it will not help me with smoking')
  - Which of the following best describes your assigned program's ability to help someone quit smoking? ('extremely helpful' to 'makes quitting smoking harder')
  - Which of the following best describes what you have learned from using your assigned program ('really unique/key insights' to 'I am more confused after using the program')
  - Which of the following best describes your need for your assigned program? ('I really need this program' to 'I am not interested at all in this program')
  - What has been the most helpful part of your program?
  - What has been the most frustrating part of your program?
  - My study program helped me quit smoking – True or False
  - Skills I learned in my study program have helped me stay quit – True or False
  - My study program helped me with my goals related to smoking– True or False
- NRT
  - Have you ordered nicotine replacement therapy (patches, gum and/or lozenges?) Why or Why not?
  - Over the last 7 days, how many days have you used nicotine replacement therapy (nicotine patches, gum and/or lozenges)?
  - Over the last 7 days, which types of nicotine replacement therapy have you used?
  - For about how many weeks have you used NRT since the study started?
  - Since you began the study, have you purchased or obtained nicotine replacement therapy (patches, gum and/or lozenges) outside of what was provided by the study?

## 10. TECHNICAL APPROACH AND STUDY DESIGN

### 10.1 ACCEPTANCE CRITERIA

Data will be accepted if the participant meets eligibility criteria, and completes the electronic informed consent form, the Baseline Questionnaire and reports a date they first opened their assigned study app.

### 10.2 ADVERSE EVENTS

Participants will be asked to detail any issues with their assigned smoking cessation program and/or NRT on the 26- and 52-week questionnaires. In addition, participants may offer up such issues at any point during the study by reaching out to study staff and/or customer service. The study sponsor follows a department operating procedure (DOP-1748, Clinical Adverse Event Reporting, [redacted]) for adverse event

reporting. In accordance with the sponsor's adverse event policy, Quality Assurance will be made aware of these issues. Additional information will be sought from participants reporting issues, as needed. Upon collection of adequate information on the issue, or an adequate good-faith effort to obtain such information, a determination will be made regarding any associated reporting requirements, in compliance with DOP-1748 and Quality Assurance reporting policies.

### 10.3 DATA SAFETY MANAGEMENT BOARD

As the study interventions of app-based smoking cessation programs and over-the-counter NRT are standard and low-risk, a data safety monitoring board is not used. This is aligned with a recent RCT with similar design, which assessed web- and social-media based quit programs combined with NRT.[29]

## 11. STUDY RESULTS

### 11.1 DATA COLLECTION AND CONFIDENTIALITY

The study sponsor follows a department operating procedure (DOP-1749, [redacted]) for clinical data management. Participants will be assigned a unique participant ID which will be used for data collection. Data collection will take place on electronic case report forms (CRFs) via online questionnaires completed by study participants, through data collected in the Pivot app and on the biovalidation videocalls. The biovalidation videocalls will be conducted on a HIPAA-compliant version of a video call platform (Zoom or Google Meet). CRFs will be reviewed by the study team prior to the end of the study to ensure completeness. Based on this review, additional or complete data will be sought from participants as needed. Access to electronic CRFs will be limited to necessary study personnel. Study data will be kept in a secure database by the investigator. This database will be accessible only by necessary study personnel. The database will not contain personal identifying information; all subject data in the database will be associated with study identification numbers. The data will be kept for a minimum of 5 years. The data shall be retained for a maximum period of time that is equivalent to the design and expected life of the Pivot smoking cessation product or the duration of the study sponsor's (Pivot Health Technologies Inc., formerly Carrot Inc.) existence, whichever is the shortest of the two.

Regarding use of Pivot, associated data will be accessed by study investigators with the Pivot app, including data on the use of the Pivot Breath Sensor. This app is the commercially available Pivot app. With regard to the information we will collect, we, the study sponsor, associate each logged-in user to a user ID that is a unique identifier which is generated randomly on account creation. We will periodically synchronize logs from the sensor and upload them based on this user ID only. The breath samples we collect only contain information regarding: sample ID, type, value, and time. When we upload this breath sample information, the only additional information included would be the Pivot app build information and user's breath sensor ID. Through the Pivot app, we are able to assess user app engagement characteristics such as time and duration of app openings and content accessed. We are also able to assess user inputs into the app such as cigarette logging, responses to questions asked during activities, quit dates, and the ordering of NRT. We comply with HIPAA and state this in our privacy and terms of use on our

website. As such we adhere to HIPAA's Breach Notification Rule should a data breach occur. We take careful measures to prevent a data breach including use of encryptions, secure connections, and limited access to data. We use appropriate safeguards and comply, where applicable, with 45 C.F.R. Part 164, Subpart C with respect to Electronic Protected Health Information, to prevent use or disclosure of Protected Health Information. Specifically, Pivot Health Technologies Inc. (formerly Carrot Inc.) has implemented the administrative, physical, and technical safeguards set forth in 45 C.F.R. §§ 164.308, 164.310, and 164.312 that reasonably and appropriately protect the confidentiality, integrity, and availability of any Protected Health Information that it creates, receives, maintains, or transmits.

Regarding use of QuitGuide, we do not have access to automated data from app use. As such, use and engagement data will be self-reported on electronic CRFs via online questionnaires completed by study participants. The QuitGuide app is maintained by the U.S. Government. It is protected by various provisions of Title 18, U.S. Code. The QuitGuide app notes, "NCI complies with requirements for privacy and security established by the Office of Management and Budget (OMB), Department of Health and Human Services (DHHS), and the National Institutes of Health (NIH)."

### 11.2 ANALYSIS

In this pilot randomized control study, changes in measurements from baseline to intra-study to exit will be assessed. Participants will serve as their own controls and comparisons will be made to no change. One sample t-test will be used for numerical data. Fisher's Exact or Chi square tests will be used for categorical data. Analyses will be conducted to calculate mean (SD) for normally distributed variables for actual data or mean (SE) for modeled data and median (interquartile range) values in instances of non-normally distributed variables. McNemar test will be used for 2-category match-paired data. Cohen kappa statistic will be used for 3-category match-paired data. Statistical significance is set at $P<.05$. All deviations from the study protocol will be identified, recorded and analyzed.

### 11.3 STUDY REPORT

A final study report will be produced at the end of the study; PowerPoint format is acceptable. The report will detail participant characteristics, program usage, the aforementioned outcomes of changes in attitudes towards quitting and smoking behavior as well as participant feedback.

### 11.4 DEVIATIONS FROM PROTOCOL

Deviations will be determined by the study team during the study. Deviations will be assessed through a consensus review by the study team. All deviations will be identified, recorded and analyzed in the final report.

### 11.5 RECORD RETENTION

Record keeping is performed in accordance with the SOP Control of Quality Records, [redacted]

## 12. CONFLICTS OF INTEREST

The following conflicts of interest are noted:

- The study sponsor is Pivot Health Technologies Inc. (formerly Carrot Inc.), [redacted]
- The principal investigator and co-investigator own equity in Pivot Health Technologies Inc. (formerly Carrot Inc.), which is the company that invented and owns the Pivot smoking cessation program (which includes the Pivot Breath Sensor), which is assessed in this study.
- The company ((Pivot Health Technologies Inc. (formerly Carrot Inc.)) holds patent rights to the Pivot Breath Sensor, which is included as part of the Pivot smoking cessation program in this study.

The investigator [redacted] holds a position of senior management officer, as VP, Clinical and Medical Affairs. The co-investigator [redacted] holds a position of Sr. Director of Clinical Affairs. These conflicts of interest are mitigated by the following:

- The risk profile of the study, specifically, that there are minimal anticipated risks or harms to the subject. No medical decisions are made based on study data. The process of setting up and using Pivot is non-invasive, and participants have access to trained study and customer support personnel for assistance as needed. Use of Pivot, including completing breath samples with the Pivot Breath Sensor, ordering and using over-the-counter NRT and otherwise using the Pivot app are done at the discretion of the study participant. No specific use of Pivot is required.
- The role of Pivot Health Technologies Inc. (formerly Carrot Inc.) in the study is outlined in the study Informed Consent Form; participants will be aware of this role prior to providing informed consent.
- The aim of the study is to assess the performance of Pivot compared to QuitGuide, and then use this data to inform future studies and optimize Pivot as needed. This study will inform resultant improvements made to the Pivot Health Technologies Inc. (formerly Carrot Inc.) products. As such, it is imperative, and the goal, that the study sponsor uses this data to ensure its products are as user-friendly and accurate as possible.

[redacted]

[redacted]

## 14. LITERATURE REFERENCES

1. U.S. Department of Health and Human Services. The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General. Atlanta (GA): U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2014.
2. Cornelius ME, Wang TW, Jamal A, Loretan CG, Neff LJ. Tobacco Product Use Among Adults — United States, 2019. MMWR Morb Mortal Wkly Rep 2020;69:1736–1742. DOI: 1
3. Jha P, Ramasundarahettige C, Landsman V, Rostron B, Thun M, Anderson RN, McAfee T, Peto R. 21st-century hazards of smoking and benefits of cessation in the United States. New England Journal of Medicine 2013;368(4):341–50. PMID: 23343063
4. Babb S, Malarcher A, Schauer G, Asman K, Jamal A. Quitting smoking among adults—United States, 2000–2015. Morbidity and Mortality Weekly Report 2017;65(52):1457–64. PMID: 28056007
5. Hartmann-Boyce J, Chepkin SC, Ye Weiyu, Bullen C, Lancaster T. Nicotine replacement therapy versus control for smoking cessation. Cochrane Database Syst Rev. 2018 May 31;5(5):CD000146. Doi: 10.1002/14651858.CD000146.pub5. PMID: 29852054
6. Lancaster T, Stead LF. Individual behavior counselling for smoking cessation. Cochrane Database Syst Rev. 2017 Mar 31;3(3):CD001292. Doi: 10.1002/14651858.CD001292.pub3. PMID: 28361496
7. Stead LF, Carroll AJ, Lancaster T. Group behaviour therapy programmes for smoking cessation. Cochrane Database Syst Rev. 2017 Mar 31;3(3):CD001007. doi: 10.1002/14651858.CD001007.pub3. PMID: 28361497
8. Stead LF, Koilpillai P, Fanshawe TR, Lancaster T. Combined pharmacotherapy and behavioural interventions for smoking cessation. Cochrane Database Syst Rev. 2016 Mar 24;3:CD008286. doi: 10.1002/14651858.CD008286.pub3. PMID: 27009521
9. Whittaker R, McRobbie H, Bullen C, Rodgers A, Gu Y, Dobson R. Mobile phone text messaging and app-based interventions for smoking cessation. Cochrane Database Syst Rev. 2019 Oct 22;10(10):CD006611. doi: 10.1002/14651858.CD006611.pub5. Epub ahead of print. PMID: 31638271.
10. Bricker JB, Mull KE, Kientz JA, Vilardaga R, Mercer LD, Akioka KJ, Heffner JL. Randomized, controlled pilot trial of a smartphone app for smoking cessation using acceptance and commitment therapy. Drug Alcohol Depend. 2014 Oct 1;143:87-94. doi: 10.1016/j.drugalcdep.2014.07.006. Epub 2014 Jul 17. PMID: 25085225.
11. Bricker JB, Watson NL, Mull KE, Sullivan BM, Heffner JL. Efficacy of Smartphone Applications for Smoking Cessation: A Randomized Clinical Trial. JAMA Intern Med.

2020 Sep 21;180(11):1–9. doi: 10.1001/jamainternmed.2020.4055. Epub ahead of print. PMID: 32955554.

12. Patrick H, Fujii CA, Glaser DB, Utley DS, Marler JD. A Comprehensive Digital Program for Smoking Cessation: Assessing Feasibility in a Single-Group Cohort Study. JMIR Mhealth Uhealth. 2018 Dec 18;6(12):e11708. doi: 10.2196/11708. PMID: 30563807.
13. Marler JD, Fujii CA, Utley DS, Tesfamariam LJ, Galanko JA, Patrick H. Initial Assessment of a Comprehensive Digital Smoking Cessation Program That Incorporates a Mobile App, Breath Sensor, and Coaching: Cohort Study. JMIR Mhealth Uhealth. 2019 Feb 4;7(2):e12609. doi: 10.2196/12609. PMID: 30670372.
14. Marler JD, Fujii CA, Galanko JA, Balbierz DJ, Utley DS. Durability of Abstinence After Completing a Comprehensive Digital Smoking Cessation Program Incorporating a Mobile App, Breath Sensor, and Coaching: Cohort Study. J Med Internet Res. 2021 Feb 15;23(2):e25578. doi: 10.2196/25578. PMID: 33482628.
15. https://smokefree.gov/tools-tips/apps accessed March 9, 2021
16. Benowitz N, Jacob P, Ahijevych K, et al. Biochemical verification of tobacco use and cessation. Nicotine Tob Res. 2002;4:149–159. PubMed: 12028847.
17. Jackson SE, McGowan JA, Ubhi HK, Proudfoot H, Shahab L, Brown J, West R. Modelling continuous abstinence rates over time from clinical trials of pharmacological interventions for smoking cessation. Addiction. 2019 May;114(5):787-797. doi: 10.1111/add.14549. Epub 2019 Jan 29. PMID: 30614586; PMCID: PMC6492005.
18. Bradley KA, DeBenedetti AF, Volk RJ, Williams EC, Frank D, Kivlahan DR. AUDIT-C as a brief screen for alcohol misuse in primary care. Alcohol Clin Exp Res. 2007;31(7):1208-17. Epub 2007/04/25. doi: 10.1111/j.1530-0277.2007.00403.x. PubMed PMID: 17451397.
19. Frank D, DeBenedetti AF, Volk RJ, Williams EC, Kivlahan DR, Bradley KA. Effectiveness of the AUDIT-C as a screening test for alcohol misuse in three race/ethnic groups. J Gen Intern Med. 2008;23(6):781-7. Epub 2008/04/19. doi: 10.1007/s11606-008-0594-0. PubMed PMID: 18421511; PubMed Central PMCID: PMCPMC2517893
20. https://cde.drugabuse.gov/instrument/f229c68a-67ce-9a58-e040-bb89ad432be4 Instrument: AUDIT-C Questionnaire accessed August 23, 2021.
21. Andresen EM, Malmgren JA, Carter WB, Patrick DL. Screening for depression in well older adults: evaluation of a short form of the CES-D (Center for Epidemiologic Studies Depression Scale). Am J Prev Med. 1994 Mar-Apr;10(2):77-84. PMID: 8037935.
22. Zhang J, Sun W, Kong Y, Wang C. Reliability and validity of the Center for Epidemiological Studies Depression Scale in 2 special adult samples from rural China. Compr Psychiatry. 2012;53(8):1243-51. Epub 2012/04/24. doi: 1061 10.1016/j.comppsych.2012.03.015. PubMed PMID: 22520090; PubMed Central PMCID: 1062 PMCPMC3404200
23. Zhang W, O'Brien N, Forrest JI, Salters KA, Patterson TL, Montaner JSG, et al. (2012) Validating a Shortened Depression Scale (10 Item CES-D) among HIV-Positive People in British Columbia, Canada. PLoS ONE 7(7): e40793. https://doi.org/10.1371/journal.pone.0040793
24. https://www.bls.gov/news.release/pdf/empsit.pdf News Release, Bureau of Labor Statistics, U.S. Department of Labor. The Employment Situation – March 2021. USDL-21-0582. Accessed 4-2-2021.
25. Prochaska JJ, et al. Likelihood of Unemployed Smokers vs Nonsmokers Attaining Reemployment in a One-Year Observational Study. JAMA Intern Med. 2016 May

1;176(5):662-70. doi: 10.1001/jamainternmed.2016.0772. PMID: 27065044; PMCID: PMC5111825.
26. Fielding-Singh P, Vogel EA, Prochaska JJ. Occupying multiple stigmatized identities: Smoking and unemployment stigmas among the unemployed. SSM Popul Health. 2020 May 15;11:100598. doi: 10.1016/j.ssmph.2020.100598. PMID: 32490137; PMCID: PMC7262435.
27. Prochaska JJ, Shi Y, Rogers A. Tobacco use among the job-seeking unemployed in California. Preventive Medicine 2013;56(5)329-332. ISSN 0091-7435, https://doi.org/10.1016/j.ypmed.2013.01.021.
28. Substance Abuse and Mental Health Services Administration, Results from the 2012 National Survey on Drug Use and Health: Summary of National Findings, NSDUH Series H-46, HHS Publication No. (SMA) 13-4795. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2013.
29. Pechmann CA, Calder D, Phillips C, Delucchi K, Prochaska JJ. The Use of Web-Based Support Groups Versus Usual Quit-Smoking Care for Men and Women Aged 21-59 Years: Protocol for a Randomized Controlled Trial. JMIR Res Protoc. 2020 Jan 14;9(1):e16417. doi: 10.2196/16417. PMID: 319348

15. **DOCUMENT REVISION HISTORY:**

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| Rev. 1 - Original Protocol |
| Rev. 4 – Added questions to Week 12 Questionnaire:<br>• Alcohol use behavior at 12 weeks (Alcohol Use Disorders Identification Test-Concise or AUDIT-C screening questionnaire, 3 items)<br>• Presence of depressive symptoms screening at 12 weeks (Center for Epidemiological Studies Depression Scale or CES-D screening questionnaire, 10 items)<br>• Living and social environment relating to cigarette smoking at 12 weeks (live with other adults who smoke, live with romantic partner who smokes, number of close friends who smoke) |
| Rev 5:<br>Added questions to Week 26 (6-month) and Week 52 (12-month) Questionnaires:<br>• AUDIT-C<br>• CED-S<br>• SASEQ<br>• Living and social environment relating to cigarette smoking (live with other adults who smoke, live with romantic partner who smokes, number of close friends who smoke)<br>• Recommend program to a friend (net promotor score) for Week 26 only<br>• Time to first cigarette for Week 26 only<br>• "True or False: The program I used during the study helped me quit smoking" for Week 26 only<br>Added clarifying questions regarding possible carbon monoxide exposure sources to biovalidation videoconference visit in instance when participant's breath sample is > 6 PPM and they indicate they have not smoked cigarettes or other combustible substances in the last 24 hours |

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| Rev 6:<br>• Corrected description of nicotine lozenge and gum doses to include 4 mg (previously only mentioned 2 mg)<br>• Removed description of control arm participants mailing the breath sensor (limited to 10 samples) back after completing biovalidation visits<br>• Updated sponsor name from Carrot Inc. to Pivot Health Technologies Inc. |
| Rev 7:<br>• Added the 104-week (2-year) videoconference biovalidation visit, ICF was updated accordingly.<br>• Added 3 participant feedback questions to 104-week (2-year) questionnaire |