Effectiveness of a Smoking Cessation Algorithm Integrated into HIV Primary Care

Study Protocol

NCT Number: NCT03670316

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Purpose and Background

Aim 1: Compare the efficacy of Algorithm Treatment (AT) to Enhanced Treatment as Usual (eTAU) control group for smoking cessation among PLWH smokers engaged in HIV clinical care. We hypothesize that the AT group will have a significantly higher proportion of abstinence (biochemically confirmed primary outcome), 24-hour quit attempts, and greater reduction in mean number of cigarettes smoked per day at 6-months post randomization compared to those in the eTAU group.

Aim 2: Characterize provider-, staff-, patient-, and clinic-level facilitators and barriers to integration of AT treatment and examine intervention cost effectiveness in care. We hypothesize that, compared to the eTAU, written pharmacological prescriptions for smoking cessation and provider knowledge and confidence to treat nicotine dependence will be significantly greater in the AT group. We will also describe clinic characteristics such as size, staffing patterns (e.g., number and type of staff, providers, etc.), average number of annual visits by patients, amount of Ryan White funding, and average appointment time to help inform a future wide-scale implementation project across all CNICS sites.

Aim 3: Estimate the cost effectiveness of the intervention relative to the primary smoking outcomes. This will be done by examining the incremental cost per quit of AT vs. eTAU at 3- and 6-months post intervention.

Site and Staff

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Eligibility Criteria & Approach

Eligibility:

CNICS PRO platform will indicate if the patient is eligible or not for the Algorithm study based on smoking scores.

Inclusion criteria:

1. Age 18 or older
2. Receiving HIV care at UAB, UW or Fenway
3. Smoking 5 or more cigarettes per day for the past month. Black and Milds and other cigars don't count.

Exclusion criteria:

1. Cognitive impairment such that unable to provide informed consent.
2. Non-English speaking
3. Acutely suicidal or intoxicated, manic, or otherwise not stable enough to provide informed consent.
4. Currently receiving smoking cessation treatment

Recruitment Screening and Selection

Participants in the clinic will be identified as eligible through the CNICS PROs (Patient Report Outcomes). Patients enrolled in CNICS complete the PROs at clinic visits roughly 4-6 months apart (90 day minimum). Patients use touch-screen PCs with an easy to navigate interface connected to a network. The following is assessed:

1. Smoking:
    a. The Smoking questions are asked at each visit in which a patient completes the PRO.

Pre Screening

UAB

Research staff will utilize a biweekly data query to identify patients who have previously completed a PRO and qualify based on their smoking score. RA/SC will also review the clinic provider schedule every morning to identify any new patients who haven't completed a PRO.

Screening

Patients taking the PRO on the day of the Primary Care Provider (PCP) visit will be screened for the Algorithm study on the CNICS PRO platform based on the inclusion criteria mentioned above. The CNICS PRO will indicate if the patient is eligible/ineligible for the study.

To check for eligibility: The patient must smoke 5 or more cigarettes daily to be eligible for the study and the suicide risk or IPV page was not initiated.

Pages

The Smoking section will trigger two pages/emails to study staff (page initiated through the University of Washington data system).

1. Page and Email- Sent at the completion of the Smoking section. Includes: patient's ticket number (ticket generated through CNICS, valid only 48 hours), and day/time.

Approach:

Before entering the exam room listen at the door to be sure that the physician is not present and be mindful not to interrupt clinic staff who may be seeing the patient. Once you have confirmed the patient is alone, greet the patient and approach about the study:

If participant responds *'No'*, notify main study coordinator and note one of the refusal or postponement reasons below. If a postponement, mark the patient's next PRO date in the tracking log to reapproach then.

Patients who refuse to participate will be informed that this is not a requirement for their care and that their relationship with the clinic will not be affected in any way. If the patient gives a postponement reason, ask the patient "may we contact you again?". If you receive a definite *"NO",* communicate this to the main study coordinator so study staff will not approach this patient in the future and track the refusal in CNICS. They will note this for entry at the end of the day in the tracking database.

Enrollment

Target Enrollment:

UAB: 250

UW: 200

Fenway: 150

Total: 600

Informed Consent:

For eligible patients, informed consent will be obtained prior to participation in any study-related procedures. Only trained study personnel with appropriate Human Subjects training will detail the requirements of the consent form and study participation with potential enrollees. Study staff will ensure that the participant understands that their consent is voluntary to avoid coercion. Patients will be approached in private rooms or designated study space for informed consent procedures by trained study staff.

When the research coordinator/study staff approaches the patient, they will let him/her know that it is important to understand the information on the consent. After going through the consent, they will allow time to read the consent form and answer any questions patient may have. The research coordinator/study staff will provide a copy of informed consent to the patient. Once patient signs the consent, the research coordinator/study staff will set him/her up for the carbon monoxide test.

Study staff will approach the patient at a future visit if within the 6-month eligibility timeframe and they have not completed another PRO. Once they complete another PRO, eligibility will be based on their next (most recent) PRO. If the patient returns to clinic within 6 months of the last PRO taken or before taking a new PRO, s/he remains eligible and can consent and complete other enrollment activities. If patient comes back after 6 months then s/he will remain eligible based on their next PRO.

In the CNICS PROs, update the drop down menu item for that participant to note they have "Consented" to the study. If time allows, collect patient's phone number in order to contact them for follow-up visits and enrolling them in the texting portion of the study on Qualtrics.

Assign the participant a study ID. UW starts at 100; UAB 500; Fenway 1,000.

Carbon Monoxide Test

RA conducts test with participant immediately following consent. If the provider is waiting to see the participant, the CO test can be done after the visit. RA will instruct participant on how to use CO monitor and will step outside of the room while the participant blows into the monitor. Document the results in the tracking log.

Randomization

Randomization will be programmed into the CNICS PRO platform and will occur after the patient consents to the study. The randomization scheme is a 50/50 ratio between the intervention and control arms. Intervention vs. control status will be tracked in the PRO platform.

Intervention Arm:

Provider Confirmation

1. If the patient is in the intervention arm then:
    a. The patient's provider will be sent a note in the EMR or give a hard copy note describing which medication the algorithm recommends he/she prescribe the patient.
    b. RC will send the physician the pharmacotherapy medication sheet (see Appendix) in the EMR for him/her to review the medication option derived from the algorithm, give him/her a hard copy of the pharmacotherapy medication sheet.

Both Arms:

Questionnaire Completion

Give patient additional questionnaires to complete on tablet in separate research room either before or after the visit with provider, depending on the clinic flow that day. If the participant can't stay to complete the additional questionnaires, you can schedule a time for him to return to complete them, so long as he picks up his prescription at the pharmacy if the provider decides to prescribe him medication. This must be done on the same day as the baseline visit.

Questionnaires:

1. Demographics
2. Smoking Behavior/History
3. Hughes/Hatsukami Withdrawal Scale (HHWS)
4. Fagerstrom Test for Nicotine Addiction (FTND)
5. Questionnaire of Smoking Urges (QSU)
6. Thoughts about Abstinence (TAA)

Texting

Participants will be sent a text-message based survey each week (11 total) between the Initial Visit and the End of Treatment Visit (12 weeks post-Initial Visit). Response options will be listed after every question and participants will respond to the question with the letter or number included in parentheses. The questions below will be administered every week unless otherwise specified.
The Qualtrics platform will be used to send the texts to the participant's cell phone. If the participant doesn't respond one week, call the participant to see if they will complete it over the phone. Otherwise, it will be marked as missing data.
If the participant doesn't have a cell phone that can receive texts, the research coordinator will call the participant weekly to administer the questionnaire over the phone. RAs will call twice over the course of the week (if the participant doesn't answer the first time). After 2 calls, the data will be classified as missing.

1. **How many cigarettes did you smoke yesterday?**
    a. Participant responds with number of cigarettes smoked
2. **Are you taking any medications to help you quit smoking?**
    a. (Y) Yes
    b. (N) No
3. **How good are you at taking your smoking medications as prescribed?**
    a. (0) Poor
    b. (1) Fair
    c. (2) Good
    d. (3) Very Good
4. **How confident do you feel that you can quit smoking?**
    a. (0) Not at all confident
    b. (1) A little confident
    c. (2) Both confident and not confident

d. (3) Somewhat confident
e. (4) Very confident

5. **In the last month, how often have you felt nervous or stressed?**
    a. (0) Never
    b. (1) Almost never
    c. (3) Sometimes
    d. (4) Fairly often
    e. (5) Very often

End of Visit:

1. Give participants $20 and confirm follow-up appointment time in 12 weeks.
2. Confirm the best number to reach the patient at for the weekly text-it surveys.
3. At the end of the visit, give the patient referral to quit line and a hand out containing smoking cessation tips.

Tracking of Study Participants

Study staff will use the CNICS database to capture baseline, 12 week-end of treatment, 1, 3 and 6 month post-treatment assessments, as well as viral loads, and carbon monoxide measurements. Study staff will use excel logs to capture prescreening, enrollment, randomization, timeline/window of outcome assessments, status of assessments, reminder call status for assessments. All study staff will be trained in Human Subjects Protections, and this data will be handled in accordance with UAB, UW, and Fenway electronic storage and data transfer guidelines.

MEDICATION INFORMATION

If medication is prescribed, the pharmacy will provide a medication fact sheet for the participant and a brief demonstration on how to administer the medication.

Medication List

Name	Method	Dosage	Side Effects

Nicotine Patch	Patch	7 mg/14 mg/21 mg	Mild itching, redness, burning, and stinging at the application site may occur. Nausea, dizziness, flushing, heartburn, headache, trouble sleeping, dizziness, anxiety, depression.
Nicotine Gum	Gum	2 mg/4mg	Mouth/Jaw Pain Hiccups Heartburn Nausea Indigestion
Lozenges	Lozenge	2 mg/4 mg	Nausea Mouth/Jaw Pain Hiccups Sore Throat Heartburn Irregular/fast heartbeat
Nicotrol Nasal Spray	Spray	2 mg/4 mg	Nasal Irritation Watery Eyes Runny Eyes Coughing Sneezing
Nicotrol Inhaler	Inhaler	2 mg/4 mg	Coughing Headache Throat Irritation Nausea Jaw/Neck Pain
Bupropion (Wellbutrin/Zyban)	Tablet	150 mg	Anxiety, dry mouth, hyperventilation,

			irregular heartbeats, irritability, restlessness, shaking, trouble sleeping
Varenicline (Chantix)	Tablet	.5 mg/1 mg	Nausea, sleep problems (trouble sleeping or vivid, unusual, or strange dreams), constipation, gas, vomiting

Refills of Medication
UAB: The same refill system used in the clinic will apply- the patient can come pick up their meds without calling or can call ahead of time to ensure the med is ready; this would be the pharmacy number and not the refill number.

Billing for Medication for Study
UAB: The 1917 Pharmacy will bill the study for any medications (copays or full drug cost) that are not covered by the intervention participant's insurance.

Stocking of Meds in 1917 Pharmacy
UAB: The 1917 Pharmacy stocks nicotine patches, lozenges, bupropion and Varenicline. Nicotine gum, nasal spray and inhalers will be ordered as needed.

Follow-up Visits

12 week End of Treatment:

1. If visit is in person, conduct CO test and document results in tracking log.
2. Patient given QQs (FTND, QSU, HHWS, TAA) and QQ on smoking behavior/medication use after patient has seen providers.
3. Give patient $40 and schedule next study visit.

1 Month Post-Treatment Follow-up:

1. If visit is in person, conduct CO test and document results in tracking log.
2. Patient given QQs (FTND, QSU, HHWS, TAA) and QQ on smoking behavior/medication use. -can be done via text/e-mail if unable to come to clinic. Done after patient has seen providers.
3. Give patient $40 and schedule next study visit.

3 Month Post-Treatment Follow-up:

1. If visit is in person, conduct CO test and document results in tracking log.
2. Patient given QQs (FTND, QSU, HHWS, TAA, Treatment Satisfaction Survey) and QQ on smoking behavior/medication use. -can be done via text/e-mail if unable to come to clinic. Done after patient has seen providers.
3. Give patient $40 and schedule next study visit.

6 Month Post-Treatment Follow-up:

1. If visit is in person, conduct CO test and document results in tracking log.
2. Patient given QQs (FTND, QSU, HHWS, TAA) and QQ on smoking behavior/medication use. -can be done via text/e-mail if unable to come to clinic. Done after patient has seen providers.
3. Give patient $50.

Retention Procedures

Continue to attempt to reach the participant up to six months after the final follow-up visit. After the 6-month mark, the participant can be marked lost to follow-up.

Summary of Compensation

Timepoint	Compensation
Baseline	$20
12 Week End of Treatment	$40
1 mo Post-Treatment	$40
3 mo Post-Treatment	$40
6 mo Post-Treatment	$50

Data Collection and Management

All study documentation will be kept in locked file cabinets in study personnel's offices at UAB, UW, and Fenway. The CNICS database can only be accessed by CNICS personnel using UAB, UW, and Fenway computers of encrypted laptops.

Data Analysis

Using Pearson's chi-square test for 2 independent proportions, we will analyze the difference in the proportion of participants with 7-day point-prevalence cessation at 6 months between the treatment arms. Participants for whom we do not have 6-month follow-up data will be assumed to be smoking. We do not anticipate any difference in baseline variables between arms, but if differences do exist, we will utilize a multivariate logistic regression model with cessation as the outcome, treatment group as the primary independent variable, and imbalanced variables which are known to be correlated with cessation as additional independent variables. The same approach will be taken for 24-hour quit attempt – dichotomized yes/no – at 6 months. For cigarette reduction, we will look at the change in number of cigarettes smoked per day at baseline and 6-month follow-up. Either a 2 independent sample *t*-test or the non-parametric Wilcoxon Rank-sum test as appropriate will be used to test for a difference in the change in cigarettes per day between the 2 groups. If necessary, an ordinary least squares regression model with change in cigarettes per day as the outcome adjusting for baseline

In addition to these primary analyses, we will examine outcomes by sex and racial groups to determine moderator effects. For sensitivity analyses, we will exclude participants without 6-month follow-up data. We will also 1) consider count regressions models that can account for time from enrollment until 6 month visit (such as Poisson regression) if actual timing of planned 6-month follow-up visits differs enough between participants; 2) repeat all analyses using end of treatment and 6-month follow-up outcomes; 3) consider employing models that treat site as a clustering variable (such as Cochran-Mantel-Haenzel [41] and Generalized Estimating Equation); and 4) fit longitudinal models with data from all timepoints. These longitudinal modals will examine the interaction between treatment group and time. Exploratory analyses will be conducted stratified by site, cigarettes per day at enrollment, and quit goal.

Protection of Human Subjects

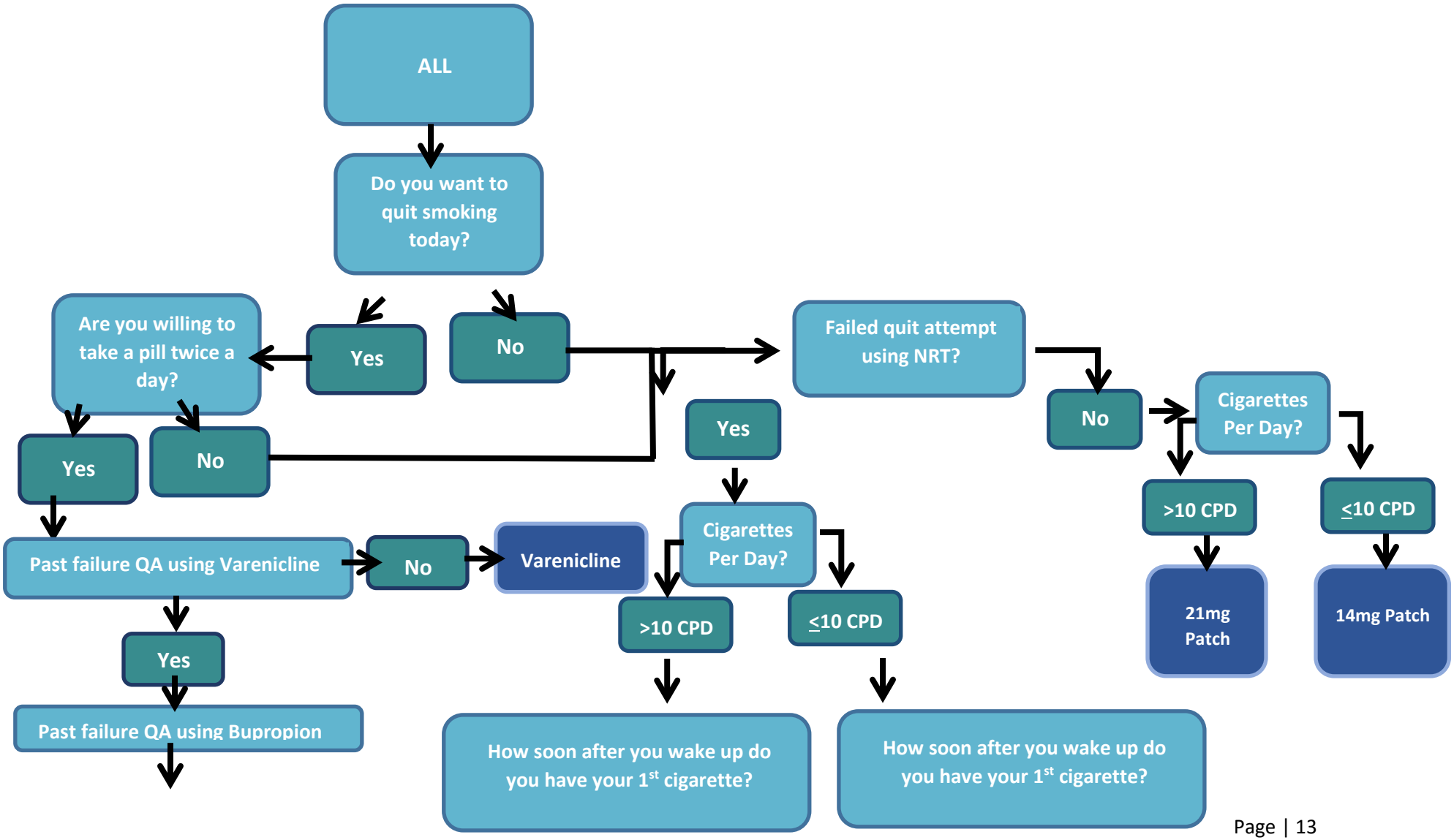
Our team has devised a comprehensive plan for ensuring protection of human subjects throughout the course of the proposed study. We will utilize an English-language consent form with common phrasing that describes that no special privileges or considerations will be conferred because of study participation, and that access to medical care will not be affected by the potential participant's decision to enroll in the study. The procedures listed in the following sections detail procedures that have been approved and utilized during recent years of clinical and behavioral trials at each site for collaborative research that utilizes sensitive information from

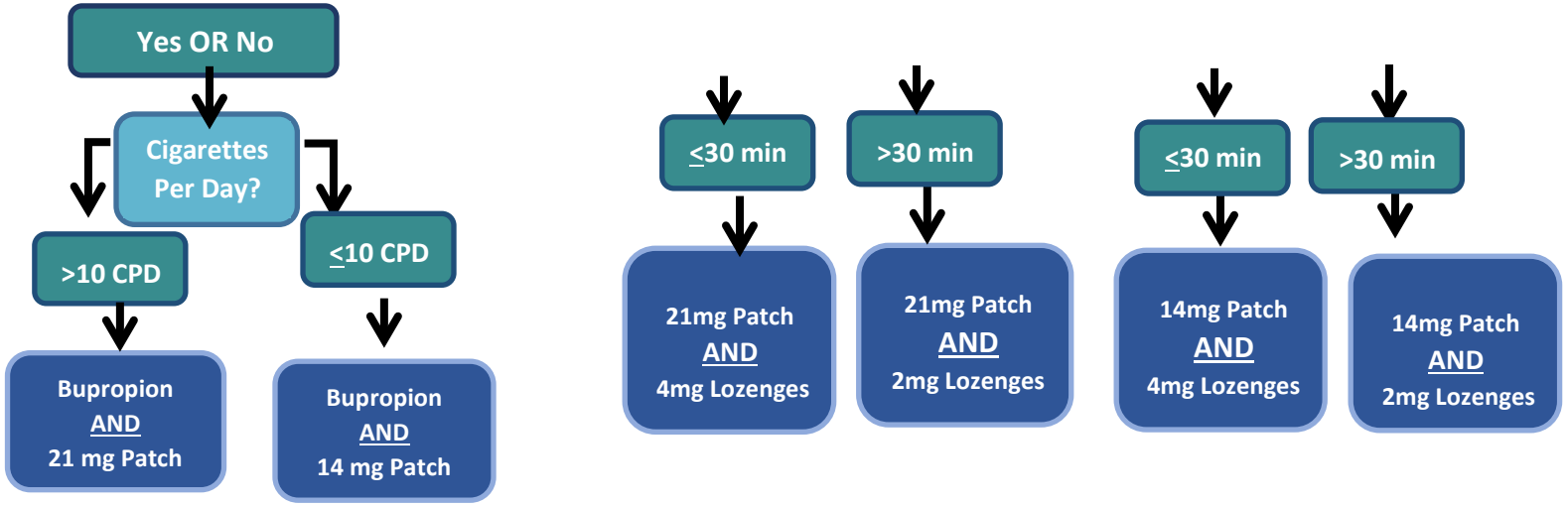
participants. Our team will make every effort to protect all participants' confidential and private information in order to minimize possible study-associated risks.

All findings related to this research will be available and provided to study participants in accordance with standard practices. Clinical and measurement data used for research studies will be released only in de-identified fashion.

In addition, all study personnel are required to renew Human Subjects trainings annually, or in accordance with their site regulatory mandates.

Study Algorithm




Yes OR No
Cigarettes Per Day?
>10 CPD
≤10 CPD
Bupropion AND 21 mg Patch
Bupropion AND 14 mg Patch
≤30 min
>30 min
21mg Patch AND 4mg Lozenges
21mg Patch AND 2mg Lozenges
≤30 min
>30 min
14mg Patch AND 4mg Lozenges
14mg Patch AND 2mg Lozenges