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## Efficacy and implementation of exercise-based smoking cessation treatment for adults with high anxiety sensitivity (STEP): Study protocol for a randomized controlled trial

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### Abstract

Anxiety sensitivity (AS), reflecting the fear of bodily sensations, is a transdiagnostic vulnerability factor that underpins both affective psychopathology and smoking. Phase II research supports the efficacy of a 15-week community-based intervention (STEP) that combines high-intensity exercise

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offered by the YMCA with standard smoking cessation treatment (tobacco quitline and nicotine replacement therapy) for sedentary smokers with elevated AS. This Phase III study aims to enroll 360 adults to evaluate whether STEP efficacy for achieving smoking abstinence generalizes to Black and Hispanic smokers with elevated AS.

## Keywords

Exercise; Anxiety sensitivity; Smoking cessation; Health behavior

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## 1. Introduction

Cigarette use contributes to over 480,000 deaths each year [1]. Anxiety and depression syndromes are the most prevalent psychiatric conditions in the general population and are also exceptionally comorbid with smoking [2]. In particular, affective-vulnerable smokers are at-risk for problematic smoking and relapse [3,2]. Affective-vulnerable smokers smoke greater quantities to manage heightened negative mood states [3] and experience greater distress during the early stages of quitting [2].

Anxiety sensitivity (AS), the fear of anxiety and related bodily sensations [4], is a transdiagnostic factor which contributes to the etiology and perpetuation of several emotional disorders, especially anxiety disorders [5-7]. AS also plays a role in several aspects of smoking (i.e., maintenance, cessation failure, cravings, and withdrawal symptoms) [8,9]. Thus, an integrative effective approach to address negative affect symptoms and disorders associated with smoking may require targeting high AS [10-12].

Our treatment development work (i.e., Phases I and II) supports high-intensity exercise as an intervention strategy for smokers with high AS [10,13,14]. High-intensity exercise reduces AS as well as tobacco withdrawal and craving, depression, and anxiety, all of which predict cessation failure [10]. Our Phase II research showed that a 15-week intervention that combines high-intensity exercise with standard smoking cessation treatment (**Smoking Treatment Enhancement Program [STEP]**) yields significantly higher abstinence rates relative to an intervention that combines wellness education with standard smoking cessation treatment [10]. We also showed that STEP can be adapted for delivery in a community-based setting involving the YMCA and the Texas Tobacco Quitline (TTQ); abstinence rates among participants receiving STEP were double those among participants assigned to the control intervention that was identical to STEP with the exception that it involved low-intensity instead of high-intensity exercise [13].

The current study aims to build upon this research by conducting a Phase III study evaluating the efficacy, mechanisms and moderators, and implementation of STEP in a more diverse sample. Keeping in mind implementation – i.e., what factors may impact STEP “living in the YMCA?” – such Phase III work may be most productive when it complements RCT methodology with an implementation process evaluation design [15]. Specifically, the RE-AIM implementation framework collects data on STEP Reach, Effectiveness, Adoption, Implementation, and Maintenance while continuing to assess the effectiveness of the clinical intervention in diverse populations [16]. We propose to apply the

REAIM framework by using participant and instructor demographic information, conducting participant assessments and interviews, completing intervention fidelity reviews, conducting key informant interviews with YMCA administration, as well as a contextual assessment to assess factors that would promote sustainability within the organization and scalability within YMCA-USA.

## 2. Methods

### 2.1. Study design

Adult smokers with elevated AS will be enrolled in 15 weeks of an integrated exercise and smoking cessation intervention at one of several participating YMCA branches in Texas selected because of the diverse service area and their ability to provide services in English and Spanish. Participants will be randomly assigned to one of two interventions: (1) STEP (programmed high-intensity exercise) or (2) CTRL (programmed low-intensity exercise). Both interventions include a standard smoking cessation program that combines counseling through the Texas Tobacco Quitline (TTQ) with nicotine replacement therapy (NRT). At week 6 of the intervention, all participants will be asked to make a quit attempt. Smoking status will be assessed weekly and up to 12 months after the quit attempt. This trial is registered at [http://www.ClinicalTrials.gov\(NCT06053567\)](http://www.ClinicalTrials.gov(NCT06053567)).

### 2.2. Specific aims

1. **Efficacy:** Compare the effect of STEP to CTRL. Hypothesis 1a: Those assigned to STEP will evidence greater 7-day point-prevalence abstinence (PPA) at 6 months after the quit attempt (primary outcome) relative to the control group. Hypothesis 1b: Those assigned to STEP will evidence greater 7-day point-prevalence abstinence (PPA) at 12 months after the quit attempt (secondary outcome) relative to the control group. Hypothesis 1c: The efficacy of STEP at the 6-month and 12-month follow-up will be evident within each racial/ethnic group.
2. **Mechanisms and Moderators:** Identify mechanisms underlying intervention effects. Hypothesis 2a: Reductions in AS and dysphoria, and increases in distress tolerance and smoking abstinence self-efficacy will mediate efficacy. Hypothesis 2b: Higher perceived discrimination, lower social support, and lower socioeconomic status (SES) will be associated with greater STEP efficacy. Exploratory 2c: Identify predictors and moderators of abstinence outcomes for STEP. Exploratory 2d: Differentiate between moderators of short-term vs. long-term abstinence.
3. **Implementation:** Use the RE-AIM framework to examine the reach, effectiveness, adoption, implementation, and sustainability of STEP in the YMCA across a diverse sample of smokers through interviews, integrated assessments, fidelity reviews, quality assurance reviews, and participant and instructor demographics.

### 2.3. Participants

Participants will include 360 adults (age ≥ 18) who have smoked an average of 5 or more cigarettes (including little cigars/cigarillos) per day for at least one year. Eligible individuals must also demonstrate elevated AS, as defined by scoring 5 or higher on the SSASI [11] on two separate screening occasions. In addition, participants must demonstrate a motivation to quit smoking, evidenced by a score of at least 5 on a 10-point Likert scale. Inclusion in the study further requires that participants have a body mass index (BMI) of <40. All eligible persons must obtain medical clearance and provide informed consent to participate.

Individuals will be excluded from the study if they have engaged in moderate-intensity exercise ≥ 3 days per week for ≥ 20 min each bout during the previous 6 months or indicate use of current, psychotherapy, pharmacology, or other interventions for smoking cessation.

### 2.4. Recruitment

Participants are recruited through internet and social media outlets, BuildClinical, and the YMCA. The partner YMCAs have a membership ranging from 1/3 to 2/3 ethnic minority, are located in communities with comparable or higher ethnic diversity and have stated a goal to increase representation. Additional recruitment efforts include outreach to public health and community-based organizations, and professional associations for medical providers.

### 2.5. Screening

Prior to screening, participants select a language preference (English or Spanish); all procedures will be conducted in the participant's preferred language. Interested individuals will be referred to our initial screening battery in REDCap (Research Electronic Data Capture). This online survey assesses eligibility through demographics, smoking history, AS (SSASI; [11]), motivation to quit, height and weight, exercise history, and exercise readiness. Those who pass the initial screener will complete a second AS assessment (SSASI) to confirm high AS levels. At this point, research staff will follow up with eligible participants to facilitate scheduling an appointment to obtain medical clearance. We will offer reimbursement medical clearance expenses should the participant request that.

### 2.6. Enrollment/randomization

Randomization will be overseen by the biostatistician (DR) and employs variable-sized permuted block randomization stratified by race and ethnicity via a sealed envelope system.

After randomization, participants will schedule a 45-min virtual visit with a staff member to complete their enrollment. Prior to the visit, participants will review a 10-min online orientation module providing a rationale for their assigned treatment. Participants will also receive a kit that includes an iCOQuit monitor, cotinine saliva test kits, and a smartwatch (if they do not own one).

During the enrollment visit, staff will review study expectations, provide training on how to use study materials, determine the YMCA branch at which the participant will complete the intervention, and assign the participant to a personal fitness trainer. Participants will also set

a target quit attempt date for week 6 of the intervention and schedule their first intervention session.

## 2.7. Intervention procedures

**2.7.1. STEP**—The intervention consists of 75 min/week of aerobic training at high intensity (60% to 85% of their age-predicted  $HR_{Reserve}$ ) for 15 weeks. Exercise will be completed using equipment that allows participants to achieve a steady heart rate within their assigned training intensity range. As can be seen in Table 1, fitness instructors complete 3 supervised sessions in Week 1 and transition to 1 weekly supervised session in Weeks 2–15.

At the beginning of week 4, a member of the research staff will connect the participant with the TTQ. All participants will receive the standard tobacco cessation package of up to 5 proactive interactions from the TTQ. Interactions are typically phone calls but can be chat or live text if the participant prefers. The intervention protocol aims to provide (1) cognitive-behavioral smoking cessation tools, (2) relapse prevention tools, (3) medication management, and; (4) advice regarding nicotine patch use, with the objective of completing a full course of medication (i.e., 8 weeks of nicotine patch use).

On the target quit date (week 6), participants can begin nicotine replacement therapy (NRT). TTQ staff provides guidance on dosing and tapering schedules. We will provide 8 weeks of NRT per the most recent treatment guidelines [17].

**2.7.2. CTRL**—The intervention procedures for the control (CTRL) condition are identical to STEP with the exception that the exercise prescription will be low-intensity exercise - i.e., training at 20% to 40% of their age-predicted  $HR_{Reserve}$ .

**2.7.3. Training**—YMCA fitness trainers will complete standardized training on the study protocol and procedures through an online module. Trainers can also consult directly with research staff for additional questions, and a Frequently Asked Questions page will be regularly updated on the trainer module.

## 2.8. Assessment

Table 2 describes the assessment protocol for achieving the specific aims. All self-report measures will be collected using the REDCap system.

**2.8.1. Screening**—The screening battery includes questions to assess general demographics (e.g., age, sex, gender, race, ethnicity and employment [SES]), anxiety sensitivity (SSASI) [11], height and weight, as well as exercise history and motivation to quit smoking.

**2.8.2. Efficacy**—The primary outcome will be 7-day point-prevalence abstinence (PPA) at the 6-month follow-up (secondary outcome will be 12-month PPA), defined as self-report of no smoking (not even a puff) during the previous 7 days, verified by expired CO ( < 5 ppm; using iCOquit device) during the intervention period (weeks 1–15) as well as saliva cotinine ( < 30 ng/mL; using Alere Saliva Cotinine test) at the 3-, 6-, 9- and 12- month

follow-up assessments. Participants will be trained in how to collect and submit CO and saliva cotinine sample data (e.g., self-report, photographs and screenshots) to the REDCap system at the end of each protocol week. Verification of smoking status by significant others will be employed when participants do not provide biological verification data. Participants will indicate in the informed consent form two people who they would prefer to list as a significant other (e.g., partner, family member) and provide their contact information to the research team [18].

**2.8.3. Mechanisms**—The battery measuring mediators will be completed at baseline (week 1), during the intervention period (weeks 4, 7, 10, 13, and 16) and at the follow-up assessments. The battery will include validated measures of each of the following constructs of interest: anxiety sensitivity (SSASI; [11]); distress tolerance (Distress Tolerance Scale; [19]), self-efficacy (Smoking Abstinence Self-Efficacy Suivey [SASE]; [20]), and dysphoria (Index of Depression and Anxiety Symptoms - Dysphoria [ISAS; [21]).

**2.8.4. Moderators**—The battery measuring moderators will be completed at baseline assessment, and will include socioeconomic status as determined by self-reported employment status, as well as validated measures of ethnic discrimination and perceived racism (Perceived Ethnic Discrimination Questionnaire-Community Version-Brief [PEDQ-CVB]; [22]), and social support (Social Support Questionnaire (SSQ; [23]).

**2.8.5. Exploratory predictors/moderators**—The battery measuring other potential predictors or moderators includes Social Determinants of Health (ACH HRSN; [24]), Smoking Health Literacy (SHL), Secondhand Smoke (SSMQ; [25]), Nicotine Dependence (FTND; [26]), will be administered at the baseline assessment. Demographic variables (e.g., age, gender, sex assigned at birth) will be collected by self-report during the screening phase.

### **2.8.6. Implementation**

**2.8.6.1. Participant interviews.** Qualitative interviews will be conducted one week after the participant's quit date as well as at the end of treatment. The objective is to collect qualitative data to make recommendations for program improvement and increase participant engagement with the program.

**2.8.6.2. Fidelity checks.** Fitness instructors and participants will complete fidelity checks at week 1, 3, 6, and 12 using a brief REDCap survey. They will indicate what was covered and completed during that week (e. g., supervised exercise session).

**2.8.6.3. Fitness instructor interviews.** At the end of each implementation year, the fitness instructors will participate in interviews to assess program fidelity and acceptability, staff challenges with the program, staff satisfaction with the intervention, and unanticipated outcomes. Fitness instructors will also be asked to review participant process notes to prompt discussion of reasons for dropout or intervention non-adherence and comment on intervention fit with the program site and the interactions of program participants with other YMCA members and fitness instructors.

**2.8.6.4. Key informant interviews.:** At the end of each implementation year, the program supervisors, CEO, other administrative staff, and a member of the Board of Directors will be interviewed to assess intervention fit, integration with other programs, perceptions of mission fit and return on investment, and sustainability of STEP within the YMCA programmatic structure.

### 3. Data analysis

#### 3.1. Quantitative aims

We will assess the equivalence of the treatment groups on key baseline variables; variables on which the groups differ will be used as covariates in the final analyses. A 3-phase piecewise growth curve model will be used to examine PPA over the course of the 54 protocol weeks, using Generalized Linear Mixed Models (GLMM) in SPSS. Phase 1 of the model will be the pre-quit phase (weeks 0–6). Phase 2 of the model will be the post-quit/treatment phase (weeks 7–15). Phase 3 will be the post-treatment phase (weeks 16–54). We will model discontinuity in the growth curve between phase 1 and 2 to reflect the expected increase in abstinence during quit week (week 6). Additionally, analyses will include (and will retain if significant) the following covariates: number of exercise sessions completed (adherence), demographic variables, baseline nicotine dependence, NRT use, and number of TTQ sessions completed.

Treatment Group (STEP vs. CTRL), Ethnicity (Latinx vs. not Latinx), and Race (White, Black, other) will be dummy coded. We will effectively conduct the GLMM version of a Treatment Group x Ethnicity x Race x Time ANOVA (although time will be coded as a 3-phase growth model). Hence, models will include the 3-way interaction between Treatment, Ethnicity, and Race, all the subcomponents of that interaction, and their 4-way interactions with the slopes in all 3 phases of the growth curve. Given the large number of interactions in this full model, we will trim the model by removing non-significant interactions to provide a more parsimonious model [27,28]. P-level will be set to 0.05 for all analyses.

**Hypothesis 1a. and b.—**(STEP will show greater PPA at the 6-month (1a) and 12-month (1b) follow-up, relative to CTRL). The significance of the main effect of the treatment condition at the 6-month and 12-month follow-ups will test our hypotheses.

**Hypothesis 1 c.—**(Treatment group differences will be significant within White participants, within Black participants, within Latinx participants, as well as within non-Latinx White participants). Each of these significance tests can be performed by coding the group of interest as the reference group in the dummy variable coding, while centering the other dummy variables at their means.

**Hypothesis 2a.—**(Treatment differences in PPA are mediated by reductions in AS and dysphoria, and increases in distress tolerance and smoking abstinence self-efficacy). The “a” paths in our mediation model (the effect of treatment group on the mediators) will be calculated using Multilevel Modeling (MLM) since the outcomes for the “a” paths are continuous. The “b” paths in our mediation model (the effect of the mediators on PPA) will be the regression coefficients for the mediators when the mediators are simultaneously

added to the GLMM equation predicting abstinence used in Hypothesis 1. We will use a cross lag mediation analysis, in which the mediators at time “t” predict the outcome at the next assessment (“t + 1”), controlling for the outcome at time “t”. Further, we will disaggregate the between-person and within-person components of the mediators. In exploratory analyses, we will examine whether race/ethnicity moderates the mediation.

**Hypothesis 2b.**—(Higher perceived discrimination, lower social support, and lower socioeconomic status (SES) will lead to lower STEP efficacy). Each of these 3 moderators will be tested in separate analyses. In each analysis, we will add the interaction of the moderator with the growth curve parameters in the model outlined in Hypothesis 1. A significant moderator x treatment group interaction will indicate that the moderator impacts the efficacy of STEP vs. CTRL at the 6- and/or 12-month follow-up. In additional exploratory analyses, we will also explore whether sex moderates STEP efficacy by adding the interactions between sex and all the growth curve parameters in the piecewise growth curve model in Hypothesis 1.

**Exploratory analyses:** 2c and 2d (Use LASSO regression to identify predictors and moderators of short term (1 week post-quit) and long-term (12-months) PPA, separately).

We will use LASSO logistic regression to determine which factors predict/moderate the effects of exercise intensity on PPA. Since LASSO does not provide significance tests, we will use the trimmed pool of factors from the LASSO as IVs in a logistic regression to identify which of the factors are significant. Finally, we will use 10-fold cross-validation (CV), repeated 10 times, to estimate the out of sample prediction ability of our model.

### 3.2. Missing data

We assume complete data from about 50% of the participants. We expect about 26% attrition by post-treatment (2% per week of the remaining participants each week) and then 10% attrition of the remaining subjects at each 3-month assessment after that. Given that GLMM does not require complete data and includes all participants who provide at least one assessment, we will code missing data as missing [29,10,13]. GLMM provides unbiased estimates of regression coefficients in the presence of missing data when data is missing at random (MAR).

As sensitivity analyses for our primary GLMM analyses we will calculate additional “missing not at random” (MNAR) models. We will use pattern mixture modeling (e.g., Hedeker and Gibbons, 2006) as our MNAR model, coding our missing data as either 1) missing during the treatment phase, 2) missing during follow-up, or 3) not missing. The pattern mixture models will determine whether the pattern of missing data moderates the effects of exercise on abstinence, and hence whether our primary GLMM findings replicate for the participants with these patterns of missing data.

### 3.3. Manipulation check

We will verify that %HRR during exercise sessions is greater in STEP than in CTRL.

### 3.4. Statistical power

**Hypothesis 1a. and b.**—In our prior YMCA study with identical STEP and CTRL procedures, we found an effect size of  $\omega=0.02$  for PPA, between a small ( $\omega=0.01$ ) and a medium ( $\omega=0.06$ ) effect size. Assuming a similar effect size in the proposed study, we performed a Monte Carlo simulation with 1000 replications, assuming  $N=360$  with a 50% linear dropout by the 12-month follow-up. The Monte Carlo study indicated a power  $>0.95$  to detect a main effect difference of  $\omega=0.02$  for STEP vs. CTRL.

**Hypothesis 1c.**—We performed Monte Carlo simulations (1000 replications) to determine the power to detect the contrast of STEP vs. CTRL within racial/ethnic groups. Our selection of YMCAs was designed to achieve the following Ns: For race, at least  $N=144$  out of 360 total participants (40%) would be Black, at least 112 out of the 360 (31.1%) would be non-Latinx White, and the balance “other” racial groups. For ethnicity, we expect at least  $N=113$  out of 360 (31.4%) to be Latinx. Again, assuming  $\omega=0.02$  for the STEP vs. Control difference comparison, we had power  $>0.85$  to detect a STEP vs. CTRL difference within each of these racial/ethnic groups.

### 3.5. Aim 2

**Hypothesis 2a.**—Our Monte Carlo study indicated that we would have  $>0.95$  power to detect mediation for a mediated pathway if the “a” path and the “b” path in the mediated pathway were of small-to-medium effect sizes (this result is consistent with the general findings of Fritz and MacKinnon in their Monte Carlo simulations for mediation analysis), and  $>0.85$  power to detect moderated mediation (race/ethnicity moderating the mediation) [30].

**Hypothesis 2b.**—Our Monte Carlo simulation showed that we have  $>0.95$  power to detect a moderator of small to medium effect size ( $d=0.35$ ).

### 3.6. Qualitative aims

Table 3 provides an overview of the integration of the RE-AIM (reach, effectiveness, adoption, implementation, maintenance/sustainability) process evaluation components into the analysis design.

### 3.7. Interviews

The team will review participant, fitness instructor, and partner demographics and interview transcripts as interviews are completed to identify any issues for mid-course correction or negative experiences within the Black and Latinx participants (examining reach, adoption, and reported effectiveness). Full analysis will take place upon completion of the trial. The team will then make final recommendations to improve participant and partner experience with the program and for modifications for specific cultural/ethnic groups. The transcribed interviews will be coded using NVivo v.12. A parallel analysis process will be used for the participant, fitness instructor, and partner/key informant interviews. Following the initial reading of each group of interviews, the study team will create the initial codebook then code 2 interviews from each group together. The codebook will then be revised, and a third

interview coded as a team. If there is high coding agreement between coders, the remainder of the interviews will be coded independently by 2 coders. The inter-coder reliability (ICR) will be calculated, the coding will be checked by the senior qualitative researcher, then the team will then meet to discuss and resolve any coding disagreements. Next, a thematic analysis will be conducted. Themes will be determined first within then across codes and groups of interviewees. An additional team member will then review the coding and analysis for confirming and disconfirming evidence for the themes.

Participant interview themes will be identified within racial/ethnic groups, then compared across racial/ethnic groups. Finally, responses will be compared between the treatment groups, and branches. Participant responses will be integrated with utilization data and subthemes by utilization will be reviewed by the team. Themes in the *fitness instructor* interviews will be compared with participant themes for program experience, differences by racial/ethnic group, and differences by program site. Fitness instructor themes will also be compared to themes identified in the *partner/key informant* interviews for disconnects between frontline and administrative experiences with the program. *Partner/key informant* interviews will be compared across branches and compared to their organizational priorities and strategic plans.

**3.7.1. Fidelity assessments**—Fitness instructors with fidelity assessments falling below 90% and/ or those with consistent discrepancies from the participant fidelity check will receive additional training and more frequent fidelity assessments. Fidelity differences by instructor and participant sex, site, and race/ethnicity will be examined annually to understand factors impacting implementation and adoption.

**3.7.2. Contextual assessments**—Context will first be assessed by examining the physical environment of each partner site and its correspondence with participants and staff. The joint assessment of the partner/key informant interviews and contextual assessment can provide multiple perspectives on the adoption, implementation, and maintenance/ sustainability of clinical interventions in community-based settings.

## 4. Discussion

High anxiety sensitivity is a risk factor for the maintenance of and relapse to cigarette smoking. This study is designed to investigate whether smoking cessation intervention personalized to high anxiety sensitive smokers and adapted for implementation by the YMCA is effective among racially/ethnically diverse samples. This protocol provides recommended treatment to achieve cessation and randomizes individuals to high-intensity exercise vs. low-intensity exercise as a strategy to engage the mechanisms relevant to high anxiety sensitive smokers to improve smoking cessation outcomes. Future treatment of at-risk smokers may benefit from the successful implementation of a community-based, personalized exercise-based smoking cessation intervention.

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## Data availability

No data was used for the research described in the article.

## References

- [1]. U.S. Department of Health & Human Services, Health Effects of Cigarette Smoking. Centers for Disease Control and Prevention, August 23, [https://www.cdc.gov/tobacco/data\\_statistics/fact\\_sheets/fast\\_facts/diseases-and-death.html](https://www.cdc.gov/tobacco/data_statistics/fact_sheets/fast_facts/diseases-and-death.html), 2023.
- [2]. Leventhal AM, Zvolensky MJ, Anxiety, depression, and cigarette smoking: a Transdiagnostic vulnerability framework to understanding emotion-smoking comorbidity, *Psychol. Bull* 141 (1) (2015) 176–212, 10.1037/bul0000003. [PubMed: 25365764]
- [3]. Brown RA, Kahler CW, Zvolensky MJ, Lejuez CW, Ramsey SE, Anxiety sensitivity: relationship to negative affect smoking and smoking cessation in smokers with past major depressive disorder, *Addict. Behav* 26 (6) (2001) 887–899, 10.1016/s0306-4603(01)00241-6. [PubMed: 11768550]
- [4]. Reiss S, Peterson RA, Gursky DM, McNally RJ, Anxiety sensitivity, anxiety frequency and the prediction of fearfulness, *Behav. Res. Ther* 24 (1) (1986) 1–8, 10.1016/0005-7967(86)90143-9. [PubMed: 3947307]
- [5]. Otto MW, Eastman A, Lo S, Hearon BA, Bickel WK, Zvolensky M, Smits JAJ, Doan SN, Anxiety sensitivity and working memory capacity: risk factors and targets for health behavior promotion, *Clin. Psychol. Rev* 49 (2016) 67–78, 10.1016/j.cpr.2016.07.003. [PubMed: 27611632]
- [6]. Otto MW, Smits JAJ, Anxiety sensitivity, health behaviors, and the prevention and treatment of medical illness, *Clin. Psychol. : A Public. Divi. Clinical Psychol. American Psychol. Assoc* 25 (3) (2018) e12253, 10.1111/cpsp.12253.
- [7]. Smits JAJ, Otto MW, Powers MB, Baird SO, Anxiety sensitivity as a transdiagnostic treatment target, in: *The Clinician’s Guide to Anxiety Sensitivity Treatment and Assessment*, Elsevier Academic Press, 2019, pp. 1–8, 10.1016/B978-0-12-813495-5.00001-2.
- [8]. Farris SG, Langdon KJ, DiBello AM, Zvolensky MJ, Why do anxiety sensitive smokers perceive quitting as difficult? The role of expecting “interoceptive threat” during acute abstinence, *Cogn. Ther. Res* 39 (2) (2015) 236–244, 10.1007/s10608-014-9644-6.
- [9]. Zvolensky MJ, Vujanovic AA, Miller MOB, Bernstein A, Yartz AR, L Gregor K, McLeish AC, Marshall EC, Gibson LE, Incremental validity of anxiety sensitivity in terms of motivation to quit, reasons for quitting, and barriers to quitting among community-recruited daily smokers, *Nicotine & Tobacco Research: Official Journal of the Society for Research on Nicotine and Tobacco* 9 (9) (2007) 965–975, 10.1080/14622200701540812. [PubMed: 17763114]
- [10]. Smits JAJ, Zvolensky MJ, Davis ML, Rosenfield D, Marcus BH, Church TS, Powers MB, Frierson GM, Otto MW, Hopkins LB, Brown RA, Baird SO, The efficacy of vigorous-intensity exercise as an aid to smoking cessation in adults with high anxiety sensitivity: a randomized controlled trial, *Psychosom. Med* 78 (3) (2016) 354–364, 10.1097/PSY.0000000000000264. [PubMed: 26513517]
- [11]. Zvolensky MJ, Garey L, Fergus TA, Gallagher MW, Viana AG, Shepherd JM, Mayorga NA, Kelley LP, Griggs JO, Schmidt NB, Refinement of anxiety sensitivity measurement: the short scale anxiety sensitivity index (SSASI), *Psychiatry Res.* 269 (2018) 549–557, 10.1016/j.psychres.2018.08.115. [PubMed: 30199696]
- [12]. Zvolensky MJ, Rosenfield D, Garey L, Kauffman BY, Langdon KJ, Powers MB, Otto MW, Davis ML, Marcus BH, Church TS, Frierson GM, Hopkins LB, Paulus DJ, Baird SO, Smits JAJ, Does exercise aid smoking cessation through reductions in anxiety sensitivity and dysphoria? *Health Psychology : Official J. Divi. Health Psychol., American Psychol. Assoc* 37 (7) (2018) 647–657, 10.1037/hea0000588.
- [13]. Smits JAJ, Zvolensky MJ, Rosenfield D, Brown RA, Otto MW, Dutcher CD, Papini S, Freeman SZ, DiVita A, Perrone A, Garey L, Community-based smoking cessation treatment for adults

- with high anxiety sensitivity: a randomized clinical trial, *Addiction* 116 (11) (2021) 3188–3197, 10.1111/add.15586. [PubMed: 34033178]
- [14]. Smits JAJ, Zvolensky MJ, Rosenfield D, Marcus BH, Church TS, Frierson GM, Powers MB, Otto MW, Davis ML, DeBoer LB, Briceno NF, The efficacy of vigorous-intensity exercise as an aid to smoking cessation in adults with elevated anxiety sensitivity: study protocol for a randomized controlled trial, *Trials* 13 (2012) 207, 10.1186/1745-6215-13-207. [PubMed: 23148822]
- [15]. Curran Geoffrey M., Bauer Mark, Mittman Brian, Pyne Jeffrey M., Stetler Cheryl, Effectiveness-implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact, *Med. Care* 50 (3) (2012) 217–226, 10.1097/MLR.0b013e3182408812. March. [PubMed: 22310560]
- [16]. Glasgow RE, Vogt TM, Boles SM, Evaluating the public health impact of health promotion interventions: the RE-AIM framework, *Am. J. Public Health* 89 (9) (1999) 1322–1327, 10.2105/ajph.89.9.1322. September. [PubMed: 10474547]
- [17]. Fiore MC, Jaén CR, Baker TB, Bailey WC, Benowitz NL, Curry SJ, Dorfman SF, Froelicher ES, Goldstein MG, Heaton CG, Henderson PN, Heyman RB, Koh HK, Kottke TE, Lando HA, Mecklenburg RE, Mermelstein RJ, Mullen PD, Orleans CT, Leitzke C, *Treating Tobacco Use and Dependence*, 2008.
- [18]. Hecht J, Rigotti NA, Minami H, Kjome KL, Bloom EL, Kahler CW, Price LH, Levy DE, Carpenter KM, Brown RA, Adaptation of a sustained care cessation intervention for smokers hospitalized for psychiatric disorders: study protocol for a randomized controlled trial, *Contemp. Clin. Trials* 83 (2019) 18–26, 10.1016/j.cct.2019.06.001. [PubMed: 31212100]
- [19]. Simons JS, Gaher RM, The distress tolerance scale: development and validation of a self-report measure, *Motiv. Emot* 29 (2) (2005) 83–102, 10.1007/s11031-005-7955-3.
- [20]. Spek V, Lemmens F, Chatrou M, van Kempen S, Pouwer F, Pop V, Development of a smoking abstinence self-efficacy questionnaire, *Int. J. Behav. Med* 20 (3) (2013) 444–449, 10.1007/s12529-012-9229-2. [PubMed: 22350635]
- [21]. Stasik-O'Brien SM, Brock RL, Chmielewski M, Naragon-Gainey K, Koffel E, McDade-Montez E, O'Hara MW, Watson D, Clinical utility of the inventory of depression and anxiety symptoms (IDAS), *Assessment* 26 (5) (2019) 944–960, 10.1177/1073191118790036. [PubMed: 30043620]
- [22]. Brondolo E, Kelly KP, Coakley V, Gordon T, Thompson S, Levy E, Cassells A, Tobin JN, Sweeney M, Contrada RJ, The perceived ethnic discrimination questionnaire: development and preliminary validation of a community Version1, *J. Appl. Soc. Psychol* 35 (2) (2005) 335–365, 10.1111/j.1559-1816.2005.tb02124.x.
- [23]. Sarason IG, Levine HM, Basham RB, Sarason BR, Assessing social support: the social support questionnaire, *J. Pers. Soc. Psychol* 44 (1) (1983) 127–139, 10.1037/0022-3514.44.1.127.
- [24]. Billioux A, Verlander K, Anthony S, Alley D, Standardized Screening For Health-Related Social Needs in Clinical Settings: The Accountable Health Communities Screening Tool, *NAM Perspectives*, 2017, 10.31478/201705b.
- [25]. DeAtley T, Colby SM, Clark MA, Sokolovsky A, Denlinger-Apte RL, Cioe PA, Cassidy R, Donny EC, Tidey JW, Psychometric analysis of a microenvironment secondhand smoke exposure questionnaire, *Int. J. Environ. Res. Public Health* 18 (7) (2021) 3753, 10.3390/ijerph18073753. [PubMed: 33916810]
- [26]. Fagerström K, Determinants of tobacco use and renaming the FTND to the Fagerström test for cigarette dependence, *Nicotine Tob. Res* 14 (1) (2012) 75–78, 10.1093/ntr/ntr137. [PubMed: 22025545]
- [27]. Aiken JC, Cohen Patricia, West Stephen G., Leona S, *Applied Multiple Regression/Correlation Analysis for the Behavioral Sciences*, 3rd ed, 2002, 10.4324/9780203774441. Routledge.
- [28]. Baldwin SA, Imel ZE, Braithwaite SR, Atkins DC, Analyzing multiple outcomes in clinical research using multivariate multilevel models, *J. Consult. Clin. Psychol* 82 (5) (2014) 920–930, 10.1037/a0035628. [PubMed: 24491071]
- [29]. O'Cleirigh Conall, Zvolensky Michael J., Smits Jasper A.J., Labbe Allison K., Coleman Jessica N., Wilner Julianne G., Stanton Amelia M., et al. , Integrated Treatment for Smoking Cessation, Anxiety, and Depressed Mood in People Living With HIV: A Randomized Controlled Trial,

JAIDS J. Acquir. Immune Defic. Syndr 79 (2) (2018) 261, 10.1097/QAI.0000000000001787.  
October 1. [PubMed: 30212438]

- [30]. Fritz MS, MacKinnon DP, Required sample size to detect the mediated effect, Psychol. Sci 18 (3) (2007) 233–239, 10.1111/j.1467-9280.2007.01882.x. [PubMed: 17444920]

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**Table 1**

## Overview of Intervention Activities.

	<ul style="list-style-type: none"> <li>• Program overview</li> <li>• Treatment rationale</li> </ul>
Week 1	<ul style="list-style-type: none"> <li>• Setting target quit date</li> <li>• Develop training progression schedule</li> <li>• 3 supervised exercise sessions</li> </ul>
Week 2–3	<ul style="list-style-type: none"> <li>• 1 supervised exercise session</li> <li>• 2 * non-supervised exercise sessions</li> <li>• Instructor monitors and promotes adherence to training program</li> </ul>
Week 4	<ul style="list-style-type: none"> <li>• Research staff connects participant with quitline</li> <li>• 1 supervised exercise session</li> <li>• 2 * non-supervised exercise sessions</li> <li>• Instructor monitors and promotes adherence to training program</li> </ul>
Week 5	<ul style="list-style-type: none"> <li>• 1 supervised exercise session</li> <li>• 2 * non-supervised exercise sessions</li> <li>• Instructor monitors and promotes adherence to training program</li> </ul>
Week 6	<ul style="list-style-type: none"> <li>• Target quit day</li> <li>• Start of RNT</li> <li>• 1 supervised exercise session</li> <li>• 2 * non-supervised exercise sessions</li> <li>• Instructor monitors and promotes adherence to training program</li> </ul>
Week 7–15	<ul style="list-style-type: none"> <li>• 1 supervised exercise session</li> <li>• 2 * non-supervised exercise sessions</li> <li>• Instructor monitors and promotes adherence to training program</li> </ul>

\* If the trainer assigns an exercise class for non-supervised exercise participation, it is possible that the prescription of 75 min may be met with 1 session. Since classes are 45–60 min in duration, it is possible that the weekly exercise duration will (slightly) exceed the 75-min/week.

Table 2

Intervention and Assessment Schedule.

		Protocol Weeks										
		-3	1	2-6	7	8	9-15	16	18	30	42	54
		Assessment Endpoints										
		Pre-Screen	Baseline	Pre-Quit	WK 0 Quit Week	WK 1 Follow-up	WK 2 Follow-up	EOT	3-M Follow-up	6-M Follow-up	9-M Follow-up	12-M Follow-up
<b>Interventions</b>												
Exercise				X	X	X	X	X				
Quitline				X <sup>1</sup>	X	X	X					
NRT					X	X	X	X <sup>2</sup>				
<b>Assessments</b>												
<b>Screening</b>												
Language Preference		X										
Demographics and SES		X										
Anxiety Sensitivity (SSASI)		X										
Smoking History (SHQ)		X	X									
Motivation to Quit		X										
Exercise History		X										
Medical Clearance		X										
Body Mass Index		X										
<b>Efficacy</b>												
Smoking Status (SRNT)		X	X	X	X	X	X	X	X	X	X	X
Biological Verification		X <sup>7</sup>	X <sup>7</sup>	X <sup>7</sup>	X <sup>7</sup>	X <sup>7</sup>	X <sup>7</sup>	X <sup>7</sup>	X <sup>8</sup>	X <sup>8</sup>	X <sup>8</sup>	X <sup>8</sup>
Other Verification		X	X	X	X	X	X	X	X	X	X	X
<b>Mechanisms</b>												
Anxiety Sensitivity (SSASI)		X	X <sup>5</sup>	X	X	X	X <sup>6</sup>	X	X	X	X	X
Distress Tolerance (DTS)		X	X <sup>5</sup>	X	X	X	X <sup>6</sup>	X	X	X	X	X
Smoking Abstinence Self-Efficacy (SASE)		X	X <sup>5</sup>	X	X	X	X <sup>6</sup>	X	X	X	X	X
Dysphoria (IDAS-Dysphoria)		X	X <sup>5</sup>	X	X	X	X <sup>6</sup>	X	X	X	X	X

Protocol Weeks											
	-3	1	2-6	7	8	9-15	16	18	30	42	54
Assessment Endpoints											
	Pre-Screen	Baseline	Pre-Quit	WK Quit Week	WK 1 Follow-up	WK 2 Follow-up	EOT	3-M Follow-up	6-M Follow-up	9-M Follow-up	12-M Follow-up
Predictors/Moderators											
Demographics	X										
Socioeconomic Status (SES)	X										
Social Determinants of Health (ACH HRSN)		X									
Smoking Health Literacy (SHL)		X					X				
Nicotine Dependence (FTND)		X									
Discrimination (PEDQ-CVB)		X					X				
Social Support (SSQ)		X									
Implementation											
Participant Interviews					X						
Partner Interviews <sup>3</sup>											
Key Informant Interviews <sup>3</sup>											
QA/QC											
Intervention Adherence			X	X	X	X	X				
Fidelity			X <sup>4</sup>	X		X <sup>9</sup>					
Fitness Instructor Interviews <sup>3</sup>											

Note: 1 = weeks 4-6; 2 = ends on week 15; 3 = occur annually; 4 = weeks 2 and 4 only; 5 = week 4 only; 6 = weeks 10 and 13 only; 7 = Carbon Monoxide only; 8 = Saliva Cotinine only; 9 = week 13 only. (SSASI) = Short Scale Anxiety Sensitivity Index; (SHQ) = Smoking History Questionnaire; (SRNT) = Society for Research on Nicotine and Tobacco Smoking Status Questionnaire; (DTS) = Distress Tolerance Scale; (SASE) = Smoking Abstinence Self-Efficacy Survey; (IDAS-Dysphoria) = Index of Depression and Anxiety Symptoms - Dysphoria; (ERMS) = Emotional Reactivity to Minority Stress Measure; (ESQ) = Exercise Sensitivity Questionnaire; (ACH HRSN) = Accountable Health Communities Health-Related Social Needs Screening Tool; (SHL) = Smoking Health Literacy Construct; (SSMQ) = Secondhand Smoke Microenvironment Questionnaire; (FTND) = Fagerstrom Test for Nicotine Dependence; (PEDQ-CVB) = Perceived Ethnic Discrimination Questionnaire-Community Version-Brief; (SSQ) = Social Support Questionnaire.

**Table 3**

Integration of Intervention and RE-AIM Components.

Assessments	Integration with Intervention	Integration with other Assessments
Participant: <sup>a,b,e</sup> Fidelity Assessment Qualitative Interviews Demographics	<ul style="list-style-type: none"> <li>Fidelity assessments linked to each transition within the STEP program</li> <li>Intervention Experience, perceived cultural relevance, and success in quitting and exercise compliance</li> </ul>	<ul style="list-style-type: none"> <li>Comparison of participant and trainer fidelity assessments</li> <li>Comparison of perceived cultural relevance of intervention and YMCA context</li> <li>Comparison of participant-trainer level of compliance, unanticipated outcomes, reasons for drop out</li> </ul>
Provider/Trainer: <sup>c,d,e</sup> Fidelity Assessment Qualitative Interviews Demographics	<p>Program delivery Unanticipated outcomes</p> <ul style="list-style-type: none"> <li>Compare trainer observations with participant experiences and level of compliance</li> </ul>	<ul style="list-style-type: none"> <li>Comparison of participant intervention experience and key programmatic elements for retention with trainer assessment of program delivery</li> <li>Comparison of trainer programmatic experience with participant compliance</li> </ul>
YMCA (local/national): <sup>c,d,e</sup> Qualitative interviews Contextual assessment	<p>Assessment of mission fit, return on investment (ROI), participant integration with other Y programs, context for program delivery</p> <ul style="list-style-type: none"> <li>Comparisons across sites</li> <li>Reach within the Y and local area</li> </ul>	<ul style="list-style-type: none"> <li>Comparison of participant intervention experience and intention to continue YMCA membership with YMCA assessment of programmatic ROI</li> <li>Comparison of trainer and administration assessment of staff responsibilities/time to implement program</li> <li>Comparison of trainer and administration working relationships with academic partner</li> </ul>

RE-AIM <sup>a</sup>reach, <sup>b</sup>effectiveness, <sup>c</sup>adoption, <sup>d</sup>implementation, <sup>e</sup>maintenance (sustainability)

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