STUDY PROTOCOL

STUDY TITLE:
Mindfulness-based Smoking Cessation Enhanced with Mobile Technology

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Tool Revision History

Version Number: 1
Version Date: 2/10/20

Version Number: 2
Version Date: 2/01/21
Changes:

- Additional safety precautions were added for the context of the COVID-19 pandemic.
- Eight weeks of nicotine patches will be provided (vs. the 6 weeks originally proposed).
- Text messages include quotes sharing the experiences of former smokers in our program. These messages are all anonymous and described as being from either “Mike” or “Kim,” depending on the participant’s preference.
- Telephone consent will be documented using REDCap.
- Questionnaires were updated.

Version Number: 3
Version Date: 5/19/21
Changes:

- Mindfulness group sessions will be delivered virtually (via Zoom) rather than in person. This change was made for participant safety during the COVID-19 pandemic and also to increase intervention scalability. In-person study assessments at weeks 8, 12, and 24 will take place in person at GSU, with phone/online surveys as back-up. Surveys at weeks 1, 3, and 5 will be administered online, or by phone depending on participant preference.
- In addition to nicotine patches, participants will be provided nicotine lozenges. Accordingly, the following contraindications for nicotine lozenges have been added to the exclusion criteria: high blood pressure not controlled with medication; stomach ulcers; and diabetes that is not controlled with medication.
- Since participants will not come for as many in-person sessions, they will be given 4 weeks of nicotine replacement therapy (NRT) at baseline and the other 4 weeks of NRT will be mailed when needed.
- The requirement for participants to have adequate health literacy was removed.
- A program evaluation question was added for the usual care condition.
- Trialfacts will assist with the social media recruitment.

Version Number: 4
Version Date: 5/26/21
Change:

- Participants will be excluded if they are currently pregnant, plan to become pregnant in the next 5 months, or breastfeeding. In the unlikely case that a woman becomes pregnant during the study (since we are now excluding those who plan to become pregnant), she will still have access to behavioral treatment depending on her treatment condition, but she will be referred to her healthcare provider to inquire about and potentially obtain nicotine replacement therapy.

Version Number: 5
Version Date: 6/14/21
Change:

- The schedule of questionnaires was updated, and participant compensation was updated.

PRÉCIS

Study Title
iQuit Mindfully: Mindfulness-based Smoking Cessation Enhanced with Mobile Technology

Objectives
Aim I: Test the efficacy of a mindfulness-based text messaging program for smoking cessation ("iQuit Mindfully"), both as a standalone intervention and in combination with in-person counseling.
Aim II: Investigate the mechanisms through which mindfulness training impacts smoking cessation.

Design, Interventions and Outcomes
This study is a 2 X 2 randomized controlled trial to investigate the effects of the iQuit Mindfully text messaging program, both as a standalone intervention and in combination with in-person counseling (Mindfulness-based Addiction Treatment; MBAT), compared to usual care. Participants will be randomized to one of four groups based on assignment to iQuit Mindfully text messages (yes/no) and in-person MBAT (yes/no):

- Usual Care (self-help materials + nicotine patch treatment)
- MBAT (8 weekly virtual MBAT sessions + self-help materials + nicotine patch treatment)
- iQuit Mindfully (iQuit Mindfully text messages + self-help materials + nicotine patch treatment)
- MBAT + iQuit Mindfully (8 weekly virtual MBAT sessions + iQuit Mindfully text messages + self-help materials + nicotine patch treatment)

All study participants will receive self-help smoking cessation materials, including the "Clearing the Air" booklet developed by the National Cancer Institute (NCI) and a referral to the Tobacco Cessation Quitline (1-800-QUIT-NOW). All study participants will also receive nicotine patches. Assessments will occur at baseline and weeks 1, 3, 5, 8, 12, and 24. Primary outcomes are smoking abstinence at 8 weeks after the start of treatment (7-day abstinence, biochemically verified by expired carbon monoxide <6 ppm), 12 weeks after the start of treatment (3 month follow-up; 7-day abstinence, biochemically verified by expired carbon monoxide <6 ppm), and 24 weeks after the start of treatment (6-month follow-up; 7-day abstinence, biochemically verified by saliva cotinine < 20 ng/ml). Secondary outcomes include frequency of home mindfulness practice and self-reported levels of mindfulness, emotions, craving, withdrawal, dependence, self-efficacy, and social support.

Sample Size and Population
Participants will include English-speaking adult smokers (ages 18 and above). Recruitment will target a racially/ethnically diverse sample of individuals with relatively low income levels, with a target sample size of 485 (maximum 500).

1. STUDY OBJECTIVES

Study aims are to test the efficacy of a mindfulness-based text messaging program for smoking cessation ("iQuit Mindfully"), both as a standalone intervention and in combination with in-person counseling, and examine underlying mechanisms of mindfulness treatment. Approximately 485 participants (maximum 500) will be randomized to one of four groups:

- Usual Care (self-help materials + nicotine patch treatment)
- MBAT (8 weekly virtual MBAT sessions + self-help materials + nicotine patch treatment)
- iQuit Mindfully (iQuit Mindfully text messages + self-help materials + nicotine patch treatment)
- MBAT + iQuit Mindfully (8 weekly virtual MBAT sessions + iQuit Mindfully text messages + self-help materials + nicotine patch treatment)

All study participants will receive self-help smoking cessation materials, including the "Clearing the Air" booklet developed by the National Cancer Institute (NCI) and a referral to the Tobacco Cessation Quitline (1-800-QUIT-NOW). All study participants will also receive nicotine patches. Assessments will occur at baseline and weeks 1, 3, 5, 8, 12, and 24. Primary outcomes are smoking abstinence at 8 weeks after the start of treatment (7-day abstinence, biochemically verified by expired carbon monoxide <6 ppm), 12 weeks after the start of treatment (3 month follow-up; 7-day abstinence, biochemically verified by expired carbon monoxide <6 ppm), and 24 weeks after the start of treatment (6-month follow-up; 7-day abstinence, biochemically verified by saliva cotinine < 20 ng/ml). Secondary outcomes include frequency of home mindfulness practice and self-reported levels of mindfulness, emotions, craving, withdrawal, dependence, self-efficacy, and social support. Aims and hypotheses are outlined below:

Aim I. Test the efficacy of a mindfulness-based text messaging program for smoking cessation ("iQuit Mindfully"), both as a standalone intervention and in combination with in-person counseling.

We hypothesize that:

1a) MBAT + iQuit Mindfully will result in higher rates of smoking cessation and lapse recovery than MBAT, which will produce higher cessation and lapse recovery than UC. iQuit Mindfully as a standalone intervention will also produce higher cessation and lapse recovery than UC.

1b) As an exploratory aim, we will examine whether poverty status moderates treatment efficacy (i.e., poverty status will predict worse cessation outcomes in MBAT but not MBAT + iQuit Mindfully).

Aim II. Investigate the mechanisms through which mindfulness training impacts smoking cessation. Participants will complete questionnaires from baseline through 24 weeks after the start of treatment, in addition to intensive diary assessments for 6 contiguous weeks during treatment. We hypothesize that:

2a) Compared to UC, the mindfulness treatment arms (MBAT, iQuit Mindfully, and MBAT + iQuit Mindfully) will increase mindfulness; reduce negative affect (NA) and volatility of NA (i.e., greater affective stability); increase positive affect; reduce craving and withdrawal; and increase self-efficacy and social support, all of which will mediate effects of the mindfulness-based treatment arms vs. UC on abstinence.

2b) Compared to UC, MBAT, iQuit Mindfully, and MBAT + iQuit Mindfully will all attenuate links between NA/craving and smoking. That is, in addition to reducing NA and craving (2a), mindfulness training is hypothesized to weaken the relationships between NA/craving and smoking.

2c) Compared to MBAT, MBAT + iQuit Mindfully will produce stronger effects on the above mechanisms (2a, 2b). Mechanisms outlined in 2a will mediate effects of MBAT + iQuit Mindfully vs. MBAT on abstinence.

2. BACKGROUND AND RATIONALE

Tobacco use, a primary behavioral risk factor for cancer, is the leading cause of preventable morbidity and mortality in the U.S.[1-5] Only 7% of smokers quit each year despite most indicating an interest in quitting.[6] Adults with low socioeconomic status (SES) and members of certain racial/ethnic minority groups (e.g., African Americans) are less likely to quit and consequently experience profound tobacco-related cancer disparities.[6-10] There is an urgent need to improve upon evidence-based smoking cessation interventions to better serve these populations. Mindfulness training substantially increases rates of smoking cessation and lapse recovery.[11,12] There is a dearth of research on mindfulness in low-SES and racial/ethnic minority groups, but these interventions do show promise for smoking cessation in these populations.[12-14] However, additional support may be needed for low-SES smokers, who experience significant day-to-day barriers to quitting and have lower access to smoking cessation resources.

Mobile health technology ("mHealth") could increase treatment engagement and provide vital 24/7 support to improve cessation outcomes for low-SES smokers. Personalized, interactive mHealth messages might encourage participants to use mindfulness and other smoking cessation techniques in the moments when they need them most, thus enhancing treatment effectiveness. Based on iterative feedback from low-SES smokers, we developed a text messaging program ("iQuit Mindfully") as an adjunct to in-person mindfulness-based smoking cessation treatment. In a pilot study (*N*=71), participants were highly engaged and benefited from tailored, in-the-moment strategies and social support from the mHealth messages.[15] Notably, whereas poverty status predicted worse cessation outcomes among participants receiving only in-person treatment, poverty status was unrelated to cessation among those receiving iQuit Mindfully. In fact, 23.1% of participants living in poverty who received iQuit Mindfully achieved biochemically-confirmed abstinence at end of treatment and 1-month follow-up, while none of those living in poverty quit in the in-person-only treatment.[16] Building on this initial work, we incorporated participant feedback to further increase interactivity and personalization so that iQuit Mindfully can more flexibly adapt to participants' changing needs. We have also developed a version of iQuit Mindfully that can be implemented as a standalone program (i.e., without weekly MBAT sessions). Pending clinical trial results, iQuit Mindfully could be highly scalable and cost-effective as a standalone program.

3. STUDY DESIGN

This study is a 2 X 2 randomized controlled trial to investigate the effects of the iQuit Mindfully text messaging program, both as a standalone intervention and in combination with virtual counseling (Mindfulness-based Addiction Treatment; MBAT), compared to usual care. Participants will be randomized to one of 4 groups based on assignment to iQuit Mindfully text messages (yes/no) and virtual MBAT (yes/no) as shown below:

		Mindfulness-Based Addiction Treatment (MBAT; virtual group treatment)	
		No	Yes
iQuit Mindfully (text messages)	No	Usual Care	MBAT
	Yes	iQuit Mindfully	MBAT + iQuit Mindfully

The four conditions are:

- Usual Care (self-help materials + nicotine patch treatment)
- MBAT (8 weekly virtual MBAT sessions + self-help materials + nicotine patch treatment)
- iQuit Mindfully (iQuit Mindfully text messages + self-help materials + nicotine patch treatment)
- MBAT + iQuit Mindfully (8 weekly virtual MBAT sessions + iQuit Mindfully text messages + self-help materials + nicotine patch treatment)

All study participants will receive self-help smoking cessation materials, including the “Clearing the Air” booklet developed by the National Cancer Institute (NCI) and a referral to the Tobacco Cessation Quitline (1-800-QUIT-NOW). All study participants will also receive nicotine patches. Assessments will occur at baseline and weeks 1, 3, 5, 8, 12, and 24. Primary outcomes are smoking abstinence at 8 weeks after the start of treatment (7-day abstinence, biochemically verified by expired carbon monoxide <6 ppm), 12 weeks after the start of treatment (3 month follow-up; 7-day abstinence, biochemically verified by expired carbon monoxide <6 ppm), and 24 weeks after the start of treatment (6-month follow-up; 7-day abstinence, biochemically verified by saliva cotinine < 20 ng/ml). Secondary outcomes include frequency of home mindfulness practice and self-reported levels of mindfulness, emotions, craving, withdrawal, dependence, self-efficacy, and social support.

4. SELECTION AND ENROLLMENT OF PARTICIPANTS

Participants will include English-speaking adult smokers (ages 18 and above). Recruitment will target a racially/ethnically diverse sample of individuals with relatively low income levels.

Inclusion criteria are:

- at least 18 years of age
- current smoker with history of ≥3 cigarettes/day (and expired carbon monoxide [CO] ≥6ppm)
- motivated to quit within next 30 days
- valid home address in the greater Atlanta, GA area
- functioning telephone number
- can speak, read, and write in English

Exclusion criteria are:

- contraindication for nicotine patch or nicotine lozenge
- active substance abuse/dependence or clinically significant depressive symptoms
- current use of tobacco cessation medications
- pregnancy, planning to become pregnant in the next 5 months, or lactation
- household member enrolled in the study
- enrolled in previous smoking cessation study based on mindfulness and/or text messaging at Georgia State University (PI Spears 2017-2020 studies entitled “Mindfulness-based Smoking Cessation Treatment,” “Qualitative Study of Text Messages for Smoking Cessation,” iQuit iText Study: Feasibility Study of Mindfulness and Text Messaging for Quitting Smoking,” or “Evaluation of Mindfulness and Text Messaging for Smoking Cessation”)

Recruitment and Enrollment Procedures

Recruitment will focus on flyers; print, radio, and social media; community outreach; and partnerships with local healthcare systems, with targeted recruitment of low-income and racially/ethnically diverse smokers in Atlanta, GA. Study flyers and example social media recruitment advertisements are attached.

Participants will be recruited through flyers (posted at local clinics/community health centers and other community organizations (e.g., YMCA, libraries, non-profit organizations, organizations serving the LGBTQ community, etc.); on and near GSU campuses; in coffee shops, restaurants, and stores selling tobacco products; near MARTA train/bus stops, shelters, etc.) and media (e.g., radio; print media in local newspapers/magazines (both online and paper versions); through GSU digital signage; and on MARTA buses/trains). Participants may also share flyers or the survey link with other individuals who are interested in participating.

The research team will attend meetings sponsored by county and state health departments to speak with stakeholders and hand out recruitment flyers. We will give presentations, talk with staff, and provide flyers at local clinics and community organizations. For example, we will provide both print and digital flyers to contacts affiliated with Grady Hospital System; Fulton, DeKalb and other County Boards of Health; Atlanta-based universities; community health centers (e.g., HEALing Community Center, Mercy Care, etc.); primary care practices; health fairs; and other healthcare and community organizations. Information about the study will also be provided to the GSU community (e.g., through presentations and print and digital flyers).

Online recruitment strategies will entail targeted ads posted on social media and internet advertising channels including Facebook, Google Adwords, Instagram, Reddit, YouTube, Twitter, Craigslist, Nextdoor, etc. Ads will be tailored according to the platform (e.g., reliance on text vs. images) and the target audience’s digital native lifestyle (e.g., informal vs. formal tone), to encourage high levels of

participation (e.g., clear calls to action). Ads will include content to appeal to a broad range of adult smokers who are interested in quitting. We will monitor ad performance closely and make timely decisions to improve content or change social media channel strategies as appropriate. Example recruitment images and text for social media advertisements are attached. The digital flyer will also be shared through GSU social media and online platforms (e.g., Craigslist, Nextdoor), with a link provided to the Qualtrics online screener. Individuals who are interested in the study will either call our research office to complete telephone screening (with verbal informed consent; see details below) or click on a link to be taken to an online (GSU-hosted Qualtrics) screener survey (with online informed consent; see details below). Individuals will also be able to share the link to the online screener with others who might be interested.

Trialfacts will assist with the social media recruitment. Trialfacts creates compliant advertisements used in its social media recruitment strategy. Trialfacts creates a mobile and tablet friendly study Web page, which is the central destination for all interested patients. Trialfacts promotes the study to its database of 60,000+ volunteers interested in participating in clinical trials. Trialfacts accesses highly targeted patients searching online for relevant health information and treatment options through social media i.e. Facebook, Instagram, Youtube, Reddit, Quora, Craigslist, and Google search. Trialfacts creates and manages an automated pre-screening solution (online survey that asks the same eligibility criteria in our IRB-approved online screener). Information about those individuals who pass the pre-screening is sent immediately via email in a password-protected PDF and in a private referral spreadsheet to the study staff. Data is stored in a secure Google Drive folder (more details about Trialfacts privacy policy can be found here: https://trialfacts.com/privacy-policy/). Trialfacts will delete all information at the conclusion of recruitment at Dr. Spears' request. Participants may also request that Trialfacts delete their information at any time. As with all participants who complete screening online, for participants are recruited through Trial Facts, GSU research staff will follow-up with a phone call to confirm eligibility and tell these individuals more about the study.

Enrollment will be ongoing over approximately 3 years. For people who are interested in participating but not able to participate at the time that they initially call (e.g., if the session times do not work for their current schedule), the study team will ask if they would like to be contacted at a later date (within the next year) to see if they may be able to participate.

For our previous smoking cessation study at GSU, the inclusion criteria were slightly more rigid. For example, interested individuals were excluded if they also used tobacco products other than cigarettes. Given that use of other tobacco products (e.g., cigars, little cigars, cigarillos) is common among low-income adult smokers, we believe it is important to include these people and help them quit smoking cigarettes as well as other tobacco products. Accordingly, we will contact individuals who expressed interest in our previous smoking cessation study and did not qualify at that time but might meet the current eligibility criteria. We will describe the current study and if they are interested, they will complete the same screening procedures as other potential participants.

Randomization. Randomization will take place at the end of the baseline session, after baseline assessments have been administered. Stratified permutated block randomization will be implemented. Block randomization can achieve balance in the number of assignments to each treatment group. This form of randomization can be conducted within each stratum (i.e., stratified permutated block design) in efforts to achieve both covariate balance and treatment balance.[17] Given the dangers of over-stratification (e.g., with too many strata, there may be insufficient numbers of participants within each block), researchers have recommended using one or two stratification variables that are expected to be most strongly associated with the outcome.[17] Stratification will be conducted with respect to race/ethnicity and poverty status, both of which are predictors of smoking cessation success.

5. STUDY INTERVENTIONS

Nicotine Replacement Therapy *(all conditions)*. Nicotine patch therapy for participants who smoke >10 cigarettes/day will consist of 4 weeks of 21 mg patches, 2 weeks of 14 mg patches, and 2 weeks of 7 mg patches. Patch therapy for participants who smoke 5-10 cigarettes/day will consist of 4 weeks of 14 mg patches and 4 weeks of 7 mg patches. Nicotine lozenge therapy for participants who smoke their first cigarette within 30 minutes of waking will consist of 8 weeks of 4mg mini lozenges (6-9 4mg mini lozenges per day). Nicotine lozenge therapy for participants who smoke their first cigarette over 30 minutes of waking will consist of 8 weeks of 2mg mini lozenges (6-9 2mg mini lozenges per day).

Participants will receive 4 weeks of nicotine patches and lozenges at baseline, and they will be mailed the additional 4 weeks of nicotine replacement therapy when needed. Research staff will confirm participants' mailing addresses with them over the phone and notify them of the mail date for the nicotine patches and lozenges. Patches will be mailed to participants in padded envelopes via certified mail with 2-day delivery. The package will include the nicotine patch instructions and a cover page indicating: "When you receive this, please call [*Research staff telephone number*] so that we can go over it with you." Participants will also be told to call research staff with any side effects or questions.

In the unlikely case that a woman becomes pregnant during the study (since we are now excluding those who plan to become pregnant), she will still have access to all of the behavioral treatment depending on her treatment condition (MBAT groups, text messages, self-help materials), but she will be referred to her healthcare provider to inquire about and potentially obtain nicotine replacement therapy

Self-Help Materials *(all conditions)*. All participants will be given evidence-based self-help materials for smoking cessation (based on the *Treating Tobacco Use and Dependence Clinical Practice Guideline*).[18] Materials include the "Clearing the Air" booklet developed by the NCI and a referral to the Tobacco Cessation Quitline (1-800-QUIT-NOW). Paper materials will be given at baseline and then reviewed in detail at treatment session 1 (with additional copies provided as needed).

MBAT Treatment *(MBAT and MBAT + iQuit Mindfully conditions).* Participants in the MBAT and MBAT + iQuit Mindfully conditions will receive virtual group counseling based on the Mindfulness-Based Addiction Treatment (MBAT) group protocol.[19] Mr. Dannenfelser (certified mindfulness-based stress reduction teacher and licensed professional counselor), Dr. Swann (certified mindfulness-based stress reduction teacher and licensed clinical social worker) and/or their trained colleagues will lead MBAT sessions. MBAT closely follows Mindfulness-based Cognitive Therapy (MBCT) procedures, but replaces the depression-related material with nicotine dependence-related material. MBAT consists of 8 weekly 2-hour sessions. The core aims are to: 1) become more aware of thoughts, feelings, and sensations from moment to moment, 2) develop a different way of relating to thoughts, feelings, and sensations, and 3) obtain the ability to disengage attention and choose skillful responses to thoughts, feelings, and situations. Participants are encouraged to choose their own quit date between day 7 and day 30 of the program. Sessions 1-4 concentrate on learning how to direct and focus attention. Participants become aware of how little attention is usually paid to activities in their daily life ("automatic pilot"). Next, they learn how to not only notice that the mind is wandering, but to bring it back to focus on the breath. Participants learn how a wandering mind can increase negative thoughts and feelings (e.g., fantasies about smoking can lead to feelings of anger about being deprived). Engaging in these thoughts can escalate to severe craving such that it becomes more difficult to enact purposeful, adaptive responses. By bringing attention back to the present, one can disengage from unhelpful thoughts and deal with the situation more flexibly (e.g., one could note

that craving is a sensation as opposed to an imperative and notice it nonjudgmentally until it passes, choose to engage in a coping behavior, or bring attention back to the breath). MBAT emphasizes daily practice in several forms: sitting meditation, body scan meditation, walking meditation, eating meditation, and gentle yoga. Each of these practices share a focus on awareness of the breath. By offering a menu of practices, differing preferences and learning styles can be accommodated. Sessions 5-8 focus on continued development of awareness of the present, along with expansion of techniques for dealing with thoughts, feelings, and situations.

Zoom group sessions will be audio and video recorded. These recordings will be used to assess treatment fidelity. Also, if a group member is unable to attend a session they may make it up by watching the video recording. They will only be able to do this by making an appointment with study staff, who will play the recording while on Zoom with the participant.

iQuit Mindfully Text Messages ***(iQuit Mindfully and MBAT + iQuit Mindfully conditions).*** Participants the iQuit Mindfully and MBAT + iQuit Mindfully conditions will receive text messages throughout the 8-week treatment period, as well as less frequent messages during the follow-up period depending on participant preferences. Upland Mobile Commons, a service that supports the development and implementation of automated SMS applications, will be used to build the automated text message system and send and receive the text messages. iQuit Mindfully text messages were designed to encourage participants to practice mindfulness (e.g., reminders for informal practice, such as awareness of the breath throughout the day, and reminders for formal practice such as the body scan and sitting meditation). They also remind participants to use specific strategies to aid in cessation (e.g., removing cues to smoke, reaching out for social support, and trying other coping techniques from the MBAT protocol [19]). The messages are designed to be interactive. That is, participants are asked questions through a series of flow logic (e.g., “Would you like to practice mindfulness right now?”; if participant replies yes, they are then provided a mindfulness technique; later asked about how it went; and provided encouragement for continued practice). Participants can also text CRAVE, STRESS, SLIP, or FACT at any point to receive additional text message support for coping with cravings, stress, smoking lapses, or to receive facts about the effects of smoking, respectively. Participants can also answer “group poll” questions so that they later receive a text with the most common responses (without any identifying information). Text messages include quotes sharing the experiences of former smokers in our program. These messages are all anonymous and described as being from either “Mike” or “Kim,” depending on the participant’s preference. Participants can also text keywords (MIND, BODY, 3MIN) to receive a phone call with a short recording of a mindfulness practice after receiving a prompting text message. Participants will be given small pocket cards with basic information on the text messaging program and reminders about the text keywords.

Messages are personalized based on first names, personal reasons for quitting, and amount of money to be saved based on individual smoking habits and price paid per pack. Texts are also tailored based on responses to text questions (e.g., whether or not they have smoked or practiced mindfulness). Texts include messages timed around major holidays and personalized messages on participants’ birthdays. Picture messages are included based on our initial qualitative work. Our previously developed program sent 2-3 messages per day during Week 1, 3-4/day during Week 2, 4-5/day during Week 3, 5-7/day during Week 4, 6-7/day during Week 5, 4/day during Week 6, and 3-4/day during Week 7 (See Appendix for example text messages and Spears et al. 2019[20] for details on the pilot study). Based on feedback from our previous message testing, message timing and frequency is more flexible and personalized for the current project. This study offers participants the option to be included in the frequency of their choice (e.g.: very low, low, medium, high, very high) as well as a 12-hour time slot of their choice (e.g.: 7am-7pm or 10am-10pm). Text messages will periodically ask participants about their preferred text message frequency and timing so that participants can change their message schedule as needed.

Financial Compensation and Retention Procedures. Participants receive financial compensation for the time and inconvenience associated with participation, as well as parking validation/MARTA vouchers to defray the cost of travel. Participants will be compensated up to $30 for assessments during weeks 1, 3, and 5, for a total of $90. (Specifically, for each of the week 1, 3 and 5 assessments, which take place online, participants will be compensated $25 for doing the survey and a $5 bonus if they do it within 24 hours). Participants will be compensated $40 for the assessment completed at week 8 (this is an in-person visit). Participants will be compensated $60 for the first post-treatment follow-up assessment at week 12 and $70 for the second post-treatment follow-up assessment at week 24 (both follow-up visits are in-person visits). Participants will also be compensated $5 per survey for the every other day surveys, for a total of $120 for all 6 weeks. Maximum compensation per person for completing all aspects of the study is $380.

Other procedures to increase adherence include: 1) reminder phone calls, emails and text messages (including checking in with participants between baseline and start of treatment, during treatment and during follow-up period as well as messages timed on participants' birthdays and major holidays), 2) requiring a phone number and valid home address so that participants can be contacted, and 3) obtaining names, addresses, and phone numbers of up to three collaterals who can provide information on participants' whereabouts if necessary. Written permission to contact the collaterals will be obtained from participants during the baseline session.

Participants who do not complete assessments or attend in-person visits will be contacted via phone, email, text message, and/or mail to reschedule or (if not able to reschedule) provide self-reported smoking status and feedback about the program/reasons for discontinuation. These individuals will also be emailed a link to the REDCap survey assessment.

6. STUDY PROCEDURES

6.1 Schedule of Treatment Procedures and Evaluations

			Weeks									
	Phone/ Online Screen	**Base-line**	**1 Start of Tx**	**2**	**3**	**4**	**5**	**6**	**7**	**8 End of Tx**	**12 (3 Month Follow-Up)**	**24 (6 Month Follow-Up)**
Telephone/Online Screening	X											
Compensation			$30		$30		$30			$40	$60	$70
Electronic Diary Assessments		Every other day surveys from week 2 to week 8; $5 per survey for up to $120 total										
TREATMENT PROCEDURES												
Virtual MBAT groups (*MBAT & MBAT + iQuit Mindfully conditions*)			Tx 1	Tx 2	Tx 3	Tx 4	Tx 5	Tx 6	Tx 7	Tx 8		
iQuit Mindfully text messages *(iQuit Mindfully & MBAT + iQuit Mindfully conditions*)		Text messages based upon participants' choice in frequency and timing of messages										
Self-Help Materials *(all conditions)*		X	X									
Nicotine Replacement Therapy Dispensation *(all)*			Participants receive 4 weeks of patches and lozenges in person at baseline, and then the remaining 4 weeks of patches are mailed.									
IN-PERSON ELIGIBILITY												
Carbon Monoxide		X								X	X	X
Cotinine (Saliva Sample)												X
Screening for Depression and Substance Dependence		X										
SMOKING												
Information for Setting Up Text Messages		X										
Tobacco History	X											
Smoking Status, use of other tobacco products, electronic vapor products, NRT, pharmacotherapy		X	X		X		X			X	X	X

	Phone/ Online Screen	Base-line	1 Start of Tx	2	3	4	5	6	7	8 End of Tx	12 (3 Month Follow-Up)	24 (6 Month Follow-Up)
Additional Resources Used for Smoking Cessation										X	X	X
Wisconsin Inventory of Smoking Dependence Motives (WISDM)		X								X	X	X
Wisconsin Smoking Withdrawal Scale (WSWS)			X		X		X			X	X	X
Self-Efficacy Scale		X	X		X		X			X	X	X
MINDFULNESS												
Mindfulness Attention Awareness Scale (MAAS)		X								X	X	X
Five Facet Mindfulness Questionnaire (FFMQ short form)		X								X	X	X
Mindfulness Practice Frequency					X		X			X	X	X
Self-Compassion Scale (short form)		X								X	X	X
STRESS/ NEGATIVE AFFECT												
Perceived Stress Scale		X								X	X	X
Positive and Negative Affect Scale		X	X		X		X			X	X	X
Experiences with Discrimination		X										
SOCIAL SUPPORT												
Multidimensional Scale of Perceived Social Support			X							X	X	X
Group Climate Questionnaire (*MBAT & MBAT + iQuit Mindfully*)										X		
PROGRAM EVALUATION												
Text Message Feedback					X		X				X	X
Perceived Benefits										X	X	X
Program Evaluation Questionnaire										X		

6.2 Description of Evaluations

Screening Evaluation and Consenting Procedure

Telephone Screening. Interested individuals who prefer to complete initial screening by telephone will be given a detailed description of the study over the phone. The voluntary nature of the study will be emphasized, and it will be made clear that if they decide not to participate, there will be no repercussions. Research staff will read the telephone consent form to potential participants and answer any questions. After provision of verbal informed consent (a Waiver of Documentation of Consent has been included in the GSU IRB protocol), the research staff member will document verbal consent and sign and date the consent form through REDCap. Potential participants will then be screened for inclusion/exclusion and answer questions about demographic information (to be documented through Qualtrics as noted below). Eligible individuals who are interested in participating will be scheduled for an initial in-person session. Participants will receive a reminder telephone call, text, and/or email on the day before their scheduled session.

Online Screening. Individuals who click on the study link through an advertisement or digital flyer will be taken to an online (GSU-hosted Qualtrics) screener survey. Before beginning the survey, participants will be given information about the study, including the voluntary nature of the study, through an online informed consent form. After providing consent, participants can complete the survey online. Data collected via this screener survey will be encrypted with access limited to select study personnel. Eligible individuals who are interested in participating will provide their contact information in order for research staff to contact them by phone to confirm eligibility and answer any

questions. Eligible individuals who are interested in participating will then be scheduled for an initial in-person session. Participants will receive a reminder telephone call, text, and/or email on the day before their scheduled session. Qualtrics includes survey protection features to prevent people from taking an online survey more than once. If it appears that an individual has attempted more than one screening method (e.g., telephone and online), research staff will call the person again to confirm eligibility and resolve any inconsistencies if needed.

In-Person Baseline Visit and Consent Procedure. Following the telephone or online screener, interested individuals will attend an in-person session to finalize eligibility, engage in further discussion about the study, and provide written informed consent.

Before in-person assessment of eligibility criteria, participants will review the consent form for in-person screening. Study personnel will offer an opportunity for participants to ask questions and have them answered, the consent form for in-person screening will be signed and dated by the participant and staff member, and a copy of this form will be given to the participants. Then, in order to confirm eligibility, participants will provide a breath sample for assessment of expired carbon monoxide. Health literacy will be assessed with the Rapid Estimate of Adult Literacy in Medicine (REALM[21]), and for the proposed study participants who have at least a sixth-grade level will be eligible. Individuals who decline or are ineligible will be given self-help materials and referral to other cessation programs. In addition, potential participants will complete the Patient Health Questionnaire-2 PHQ-2; [22,23] and Severity of Dependence Scale (SDS[24]) in order to screen for clinically significant depressive symptoms and substance dependence, respectively. Individuals who are not eligible for these reasons will be provided with appropriate mental health referrals in addition to smoking cessation referrals.

Next, the research staff will engage eligible individuals in a discussion of pros and cons of participating, as well as participants' ambivalence about behavior change and research participation (these methods have been suggested to improve retention[25]).

For eligible individuals who are interested in participating, study personnel will initiate the informed consent process which will include: 1) A thorough review of the Informed Consent Form (ICF; see Appendix), particularly study procedures; 2) Study personnel will offer an opportunity for participants to ask questions and have them answered; 3) The ICF will be signed and dated by the participant and staff member; and 4) A copy of the ICF will be given to the participants.

Participants will be given the choice of using their own tablet or laptop computer or one provided by the study. For participants in MBAT and MBAT + iQuit Mindfully conditions, study personnel will explain the requirements for joining the treatment session via the video conferencing program, Zoom. Research staff will conduct separate sessions with participants to ensure they can access Zoom.

Participants who choose to use the basic tablet provided by the study will include those who:

-do not own a tablet or other device with a web camera,
-do not have access to consistent wireless internet needed to join virtual group sessions, or
-prefer to use a study tablet

Participants will be given the choice of using their own mobile phone or one provided by the study. For participants in the iQuit Mindfully and MBAT + iQuit Mindfully conditions, study personnel will explain the text messaging procedures in detail and send a test message to the participant, who will respond and ask any questions.

Participants who choose to use the basic cellphone provided by the study will include those who:

-do not own a wireless cellphone,

-do not own a wireless cellphone that can receive and send phone calls, SMS and MMS messages,
-prefer to use a study phone, or
-do not have consistent phone service with a working number

These participants will have the option of borrowing a study device for the duration of the study. The research team will explain to participants that all wireless devices must be returned. Mobile phones must be returned by the final week 24 assessment, and tablets must be returned at the week 8 assessment. Wireless devices that are borrowed will be wiped upon returning them to the research team. All sim-cards will be wiped clean. New sim-cards will be used for each participant requesting a phone. All data collected via text message will be stored either on the Mobile Commons platform or the REDCap platform. No data will be saved to the device. For text messages and all other data remaining on the study devices when they are turned in from participants, the research team will wipe and reset the device.

Individuals who would like to participate and express informed consent will then be asked to complete questionnaires (see Appendix). Questionnaires will be administered through REDCap, to be taken either in-person at GSU (baseline and weeks 8, 12, and 24) or off site (REDCap links to be emailed/texted when participants do not come to GSU in person). See Table 6.1 for schedule of questionnaire assessments. Descriptions of the assessments are provided below:

- The *Telephone Screening* assesses eligibility criteria and demographic characteristics, including age, race, ethnicity, education, employment, and income.
- The *Patient Health Questionnaire-2* PHQ-2; [22,23] is a 2-item questionnaire designed to screen for symptoms of depression. Participants are asked, “Over the last 2 weeks, how often have you been bothered by the following problems?”: “feeling down, depressed or hopeless” and “little interest or pleasure in doing things.” These items which correspond to the two core diagnostic criteria for Major Depressive Disorder; [26] are rated on a 0-3 scale (0 = not at all, 3 = nearly every day). Individuals with scores of 3 or above which has been identified as the cut-off for obtaining optimal sensitivity and specificity for identifying depressive disorders; [22,23] will not be eligible but will be provided with appropriate mental health referrals.
- The *Severity of Dependence Scale* (SDS) is a 5-item questionnaire that measures the extent of psychological dependence on illicit drugs in the past 12 months.[24] The scale has been validated for several illicit drugs including cannabis, cocaine, amphetamines, benzodiazepines, and heroin. Each of the five items is scored on a 4-point scale ranging from 0 (Never/Almost Never) to 3 (Always/Nearly Always) and summed for a total score. Individuals with scores of 4 or higher[27,28] will not be eligible but will be provided with appropriate mental health referrals.
- The *Information for Setting Up Text Messages* questions assess participants’ amount of money spent on cigarettes, personal reasons for quitting, preferences about timing and frequency of text messages, and quit date. This information is incorporated into iQuit Mindfully to personalize the content, frequency and timing of text messages.
- *Tobacco History* assesses onset of regular smoking, previous quit attempts, abstinence history, smoking rate, and partner smoking status. This includes the *Heaviness of Smoking Index* comprises two items from the *Fagerström Test for Nicotine Dependence* (FTND) [29]: self-reported average number of cigarettes smoked per day and time to first cigarette upon waking (“time to first cigarette”). The HSI is a strong indicator of nicotine dependence [30].
- *Smoking Status (SRNT)* surveys tobacco use, use of other tobacco products, and nicotine replacement medications. Smoking Abstinence will be assessed according to the SRNT guidelines [31], which suggest reporting point prevalence abstinence (i.e., no smoking during

past week), continuous abstinence (i.e., no smoking since quit date), and time to relapse (i.e., any tobacco use over 7 consecutive days or 2 consecutive weeks). All self-reported abstinence will be biochemically confirmed by CO<6ppm. Use of novel tobacco products (e.g., e-cigarettes and heated tobacco products) will also be assessed. Participants will also indicate which forms of nicotine replacement therapy and/or pharmacotherapy (if any) they used in the past week.

- *Additional resources used for smoking cessation* will ask participants about various strategies for quitting smoking (e.g., acupuncture, hypnosis, other text messaging programs or mobile apps). This will allow the researchers to capture resources participants might be using to help them quit smoking apart from what they receive in the study.
- The *Brief Wisconsin Dependence Motives Questionnaire*[32] is a 37-item measures that yields an overall dependence score and subscale scores for other dimensions (i.e., cognitive enhancement, affective enhancement, automaticity, affiliative attachment, loss of control, craving, cue exposure/associative processes, social/environmental goals, taste/sensory processes, weight control, tolerance).
- The *Wisconsin Smoking Withdrawal Scale* [33] includes subscales for anger, anxiety, sadness, concentration difficulty, craving, hunger, and sleep. All subscales have excellent internal consistency and validity.[34]
- The *Self-Efficacy Scale* assesses confidence for resisting smoking urges in specific types of situations (e.g., when feeling stressed, when with friends) [35] Subscales include negative affect, pleasure, social image, social influence, and diet. Scores are predictive of relapse.[36]
- The *Mindful Attention Awareness Scale* MAAS; [37] is a 15-item self-report measure of dispositional mindfulness that has shown good reliability and validity.[37]
- The *Five-Facet Mindfulness Questionnaire-Short Form*[38] is a 24-item self-report questionnaire of facets of dispositional mindfulness. The scale yields five factors: 1) Nonreactivity, 2) Observing, 3) Acting with Awareness, 4) Describing/Labeling with Words, and 5) Nonjudging of Experience, with strong psychometric properties.
- The *Self-Compassion Scale Short Form*[45] is a 12-item self-report measure of self-compassion. Subscales include self-kindness, self-judgement, common humanity, isolation, mindfulness, and over-identification.[45]
- Participants will fill out a *Mindfulness Practice Log*[12] to indicate how frequently they practice each of the mindfulness techniques taught in treatment.
- The *Perceived Stress Scale*[39] is a 10-item self-report measure of the extent to which individuals view their lives as stressful. The scale shows good psychometric properties.
- The *Positive and Negative Affect Schedule* (PANAS [40]) is a 20-item self-report measure of affective experience yielding two factors (Positive and Negative Affect) with strong psychometric properties [40].
- The *Multidimensional Scale of Perceived Social Support*[41] is a 12-item scale, with subscales assessing perceived social support from family, friends, and significant others.
- The *Group Climate Questionnaire (GCQ-S)*[48] is a 12-item self-report scale which measures climate and cohesion of the group (only applicable for MBAT participants). Sub-scales include engaged, conflict, and avoiding.[48]
- Participants will be asked to provide feedback about their experiences receiving the text messages (*Text Message Feedback*).

- Participants will complete 4 items to indicate perceived benefits of the quit smoking program. As described by Hoeppner et al. (2017),[42] participants rate the extent to which the program gave them confidence to quit smoking, made them think that it was worthwhile to quit, made them feel that someone cared if they quit, and made them feel that they knew the right steps to take to quit. Items are rated from 1 (completely disagree) to 5 (completely agree).
- Participants will complete *Program Evaluations* to provide for their feedback about and suggestions for improving the intervention (both MBAT and iQuit Mindfully text messages). Usual care participants will answer 1 program evaluation question: "On the scale below, please circle the number that best represents whether you would recommend this quit smoking program (or something similar) for others who are interested in quitting smoking." (rated on 1-10 scale).

The maximum time between telephone screening and enrollment will be 1 month. The maximum time between baseline assessment and start of treatment will be 1 month. However, we will employ a variety of strategies to ensure that these timeframes are as short as possible. For example, in order to reduce the time between telephone screening and baseline we will offer a variety of days and times for baseline assessment. We will also time our recruitment efforts around planned baseline assessments to maximize potential participants' interest (in order to prevent longer wait time to accrue a sufficient number of participants to start a group).

Electronic Diary Assessments. *Electronic Diary Assessments* (also referred to as short-surveys) will be administered in the evening on every other day from Week 2 to Week 8, thus capturing key processes surrounding quitting smoking. Diary assessments will assess smoking behavior ("How many cigarettes did you smoke today?") and each of the hypothesized mechanisms (mindfulness, emotions, craving and withdrawal, self-efficacy, and social support). Participants will also indicate their mindfulness practice that day (See Appendix). Participants will receive an email and/or text with the REDCap link to the electronic diary assessment survey. Both participant-initiated options allow respondents to complete assessments at a time that is convenient to them between that evening and the next morning (by 9am).

Saliva Samples for Cotinine Analysis. At the last study visit (approximately 24 weeks after the start of treatment), participants will provide a saliva sample by placing an oral swab under their tongue for 1-2 minutes (Salimetrics; https://www.salimetrics.com/collection-method/oral-swab-saliva-collection-device/). Per Salimetrics instructions, consumption of alcohol, caffeine, nicotine and prescription/over-the-counter medications within the past 12 hours, as well as presence of oral diseases or injury, will be documented. Participants will rinse their mouth with water to remove any food residue and wait at least 10 minutes after rinsing before collecting saliva. The saliva sample will then be stored in a locked freezer situated in a locked room in the GSU Urban Life Building, only coded with an ID number and no personally identifying information. Swabs will be mailed to the Salimetrics lab for cotinine analysis, and the Salimetrics lab will discard the saliva after 1 year. Self-reported 7-day abstinence will be confirmed by saliva cotinine <20 ng/ml.[12,43] Use of NRT and other nicotine-containing products (e.g., e-cigarettes) will be assessed to ensure that saliva cotinine levels are not affected by non-combusted nicotine products. Participants who do not attend the in-person 24-week assessment visit will be asked to provide a saliva cotinine sample via mail.

***Procedures for Participant and Research Team Safety in the Context of the COVID-19 Pandemic**

The current study design involves in-person sessions at GSU. During the COVID-19 pandemic, in-person procedures will follow the Georgia State Standard Public Health Precautions for On-Campus Visits Related to Human Subjects Research. For example:

- Pre-visit phone screening and arrival phone screening will be conducted to inquire about possible COVID-19 symptoms and exposure.
- Visitors cleared for study visits will be advised that they must wear face mask coverage while on campus. Research staff will also wear masks.
- Signage to encourage hand hygiene, respiratory hygiene, cough etiquette, and social distancing will be posted in and around the Waiting Area and Research Space.
- All visitors will be directed to wash hands or use hand sanitizer upon entry to Waiting Area/Research Space. Hand sanitizer will be provided.
- Researchers will wash hands or use hand sanitizer prior to and after each participant visit.
- Frequently touched surfaces will be cleaned and disinfected before and after study visits.
- Chairs will be placed at least 6 feet apart to maintain social distance.
- The research space will be regularly cleaned by Facilities Management.

It is possible that people who smoke cigarettes may be at higher risk for COVID-19 (https://www.who.int/news-room/commentaries/detail/smoking-and-covid-19). Accordingly, the following additional measures are proposed during the COVID-19 pandemic:

- The research team will provide a new disposable mask and pair of gloves to each participant for each in-person visit. After that, treatment groups will be held virtually using a video conferencing program, Zoom. Since some participants may not have the appropriate space or technology to join virtually, the research team will give them the option to borrow a tablet study device for 8 weeks.
- If participants do not have access to a private or quiet place to join the weekly group session, they can come to campus and join in a separate room at GSU. They will still be able to use a GSU computer with internet and camera to join the live group sessions.
- Participating in a video conference session presents no more than minimal risk of harm to subjects. The purpose of the video conference is to be able to continue providing the quit smoking group to participants while minimizing the risk of exposure to COVID-19 through elimination of in-person group sessions.

***Strategies for Promoting Engagement with Virtual Group Sessions:**
We will use the following strategies to promote engagement:

- Participants in MBAT and MBAT + iQuit will be able to borrow a study tablet for the 8 weeks of the program. This will ensure all participants have equal access to join sessions through the video conferencing software, Zoom.
- Participants will attend an in-person baseline session at GSU, where research staff will help them set up Zoom, practice using Zoom, and troubleshoot any issues. Participants will be given a packet of Zoom instructions/tips to take with them. For those who will be joining virtual sessions from home, study staff will discuss ways to ensure that they have a quiet, private location as best as possible. They will also be encouraged to use a virtual background for privacy, and study staff will help them set this up.
- Participants will be given the option to join virtual groups in an individual room at GSU. In our pilot study virtual sessions, some participants did not have a private place to join. Being able to use a tablet in a private room at GSU would provide a solution.
- MBAT participants will attend a group Zoom orientation within two weeks before the first treatment session. This will give them a chance to meet each other, practice using Zoom together (e.g., muting/unmuting, turning camera on and off), and ask questions of the study staff.

- When participants connect to Zoom, study staff will admit them individually into a separate breakout room to ensure that they are in a private location and troubleshoot any issues.
- We will encourage participants to join Zoom sessions a few minutes early so that they have a chance to get to know their fellow group members better.
- Both mindfulness instructors (certified Mindfulness-Based Stress Reduction teachers through the University of Massachusetts Medical School) have experience leading online mindfulness groups through Zoom and will draw on their past experience. For example, they will encourage participants to stay unmuted during discussion to facilitate natural conversation (unless there is excessive background noise); mute participants during mindfulness practices; and provide brief breaks.

*GSU continues to update guidelines for on-campus research. We will follow updated guidelines as they become available.

7. SAFETY ASSESSMENTS

Reporting of Adverse Events and Serious Adverse Events

An **adverse event (AE)** is defined as any unfavorable and unintended diagnosis, symptom, sign, syndrome or disease which either occurs during the study, having been absent at baseline, or if present at baseline, appears to worsen. Adverse events are to be recorded regardless of their relationship to the study intervention.

A **serious adverse event (SAE)** is defined as any untoward medical occurrence that results in death, is life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly.

Dr. Spears will conduct daily oversight of participant safety, and will meet regularly with staff to review progress and discuss any problems or concerns. Adverse events that are not deemed “serious adverse events” will be included in the final report to the investigators, IRB, and NCI.

SAEs that are unanticipated, serious, and possibly related to the study intervention will be reported to the IRB and NCI in accordance with requirements. Georgia State University defines an unanticipated event as an event that was (1) unforeseen; (2) more likely than not related to the research; and (3) either caused harm to participants or others, or placed them at increased risk of harm. Unanticipated events include any harm or injury (physical, psychological, social or economic) or other unexpected events occurring during the course of participation in a research study. As required by the GSU IRB, Dr. Spears will report a summary of each unanticipated event to the IRB using the IRB Unanticipated Event form within 7 business days.

Unexpected fatal or life-threatening SAEs related to the intervention will also be reported to the NCI Program Officer and investigators within 7 days. Other serious and unexpected AEs related to the intervention will be reported to the NCI Program Official within 15 days. Anticipated or unrelated SAEs will be handled in a less urgent manner but will be reported to the IRB and NCI.

8. INTERVENTION DISCONTINUATION

This study will be stopped prior to its completion if: (1) the intervention is associated with adverse effects that call into question the safety of the intervention; (2) any new information becomes available during the trial that necessitates stopping the trial; or (3) other situations occur that might warrant stopping the trial.

9. STATISTICAL CONSIDERATIONS AND DATA ANALYSES

We will conduct both intent-to-treat (ITT) and per protocol analyses. ITT includes all participants that were randomized, regardless of compliance, withdrawal, and other events after randomization. A strength of ITT is that it is based on original randomization. However, effect estimation using ITT may be conservative and misleading with increasing attrition. Per protocol analysis considers only participants who fully complied and completed the study. Per protocol is less conservative and may reflect true treatment differences for those with full compliance. Including both approaches will provide a more complete understanding of treatment effects.

Analyses will be performed using SAS. Descriptive statistics for all measurements will be reported. Frequency distributions will be created to screen for any coding or entry errors. Frequency distributions summarize categorical data, and measures of central tendency and dispersion will summarize continuous data. All data will be examined for bivariate relationships with the outcomes and with each other. All analyses will control for demographics (age, gender, race/ethnicity, education level, partner status) and baseline nicotine dependence (cigarettes per day and time to first cigarette). The overall study level of significance will be α=.05.

Aim I. Test the efficacy of a mindfulness-based text messaging program for smoking cessation ("iQuit Mindfully"), both as a standalone intervention and in combination with virtual counseling.

The relationship between treatment condition and each dichotomous study outcome (smoking cessation, lapse recovery) will be assessed with a generalized linear mixed model (GzLMM) with a Binomial distribution and logit link function. This is an appropriate statistical model with repeated measures data collected over time.[44] A 2-level multilevel GzLMM will be specified, with time nested within subject. This approach will properly account for the multilevel data structure. Fixed effects considered in each model will include demographics, baseline nicotine dependence, treatment condition and time as main effects, and a treatment condition by time interaction. Testing of covariance structure will be conducted, and information criteria will be used to assess model fit and selection. Linear contrasts will be built into the analysis to estimate specific comparative effects of all treatment conditions. To test treatment effects on primary smoking cessation outcomes, repeated measures outcomes will be biochemically-confirmed 7-day point prevalence abstinence at weeks 8, 12, and 24. To test treatment effects on lapse recovery, this analysis will also be conducted among participants classified as smoking at the last treatment session.[12] In addition, gender and race/ethnicity will be assessed as potential moderators of treatment effects.

The moderating effect of poverty status will be examined with the addition of a poverty status by treatment condition interaction into the models described in 1a). This will be tested using both dichotomous (i.e., below vs. at or above federal poverty threshold) and continuous poverty status variables (i.e., depth of poverty as indicated by income-to-poverty ratio and income deficit/surplus) according to U.S. Census guidelines.[45,46]

Aim II. Investigate the mechanisms through which mindfulness training impacts smoking cessation.

Hypotheses regarding mechanisms will be tested with both traditional questionnaire data (collected from baseline through 24 weeks after the start of treatment) and electronic diary data (collected for 6 continuous weeks during treatment), separately. Mediation testing will be conducted regardless of statistical significance of intervention effects because of statistical, conceptual, and practical reasons for testing mediation in such cases.[47] Volatility will be calculated using the mean square successive

difference (MSSD;[48] average of the squared difference between successive observations at times *i* + 1 and *i*) to capture both within-person variability and temporal instability. Mediation will be examined with multilevel mediation analyses for binary outcomes in the developed GzLMM. Bootstrapping with 5000 replications will be used to estimate standard errors and *p*-values for indirect effects. In addition to mediators of associations between treatment and abstinence outcomes, we will test more fine-grained day-to-day associations using electronic daily diaries.

We will test moderated mediation using a model proposed by Preacher, Rucker, and Hayes[49] that fits the hypothesized model (Figure 3), as the independent variable (mindfulness training) also functions as a moderator. Kline[50] termed this "second-stage moderation," as the second path of the indirect effect of the predictor on the dependent variable depends on the moderator. Conditional mediation and moderation effects will be tested using bootstrapping methods.[49] GzLMM provides an ideal method for assessing the proximal relation between negative affect/craving at a given assessment and smoking at the next assessment (using both questionnaire and daily diary data). For example, using daily diary assessments, we will examine whether the association between negative affect on a given day and next-day smoking is weaker among MBAT vs. UC participants.

Missing Data. Although there is no complete, comprehensive method for handling missing data for generalized linear mixed models, there are several different approaches that we can draw upon to address this issue.[44] We will use multiple imputation of missing data whereby missing observations for individuals are estimated based on baseline responses and other study covariates, and perform additional sensitivity analyses regarding various missing data assumptions for smoking outcomes.[51]

Power and Sample Size Determination. Sample size was estimated based on the number of participants needed to detect meaningful treatment effects of the iQuit Mindfully and MBAT interventions. We obtained effect sizes (converted to Cohen's *d* for comparability across measures) from relevant meta-analyses and used the Optimal Design program to estimate sample size for GzLMM models.[52] Smoking abstinence in MBIs vs. UC was quantified as d=0.35 in a meta-analysis,[53] and a Cochrane review of primarily text messaging-based interventions for smoking cessation[54] concluded an effect size of d=0.33. Assuming 80% power, level of significance of .05, two-tailed statistical tests, error variance of 1.0, coefficient variance of 2.0, and oversampling to account for 20% attrition, this results in 145 participants in each treatment group. An unequal allocation ratio was used to allocate fewer participants to usual care (n=50),[55,56] for an overall sample size of 485 participants (145 per treatment group and 50 in usual care). We expect this sample size to adequately allow for mediational testing (Aim 2) at the 80% power level. Fritz and MacKinnon[57] offer a guide regarding sample size required to detect mediated effects and report that 79.9% of studies in their literature review applied mediational testing with less than 400 subjects, suggesting our study plan with 485 subjects will be ample for achieving all study aims.

10. DATA COLLECTION AND QUALITY ASSURANCE

During this study, psychosocial assessments and biochemical confirmation of smoking will be conducted at baseline and at regular intervals. All of the materials collected are for research purposes only, and data will be kept in strict confidence. Confidentiality will be ensured by use of identification codes. All data will be identified with a randomly generated identification code unique to the participant. The master list containing participant numbers and participants' names will be kept in a locked file, accessible to study staff only. Although participants will sign informed consent documents, these forms will be kept in a separate locked file and will never be connected to the study data. No names will ever be recorded on the questionnaires, which will be stored in a locked file cabinet and available only to the research personnel.

The online screener will be conducted using the GSU-hosted Qualtrics platform. The qualtrics^{xm} Security Statement (January 31, 2020) reads: "Qualtrics' most important concern is the protection and reliability of customer data. Our servers are protected by high-end firewall systems and scans are performed regularly to ensure that any vulnerabilities are quickly found and patched. Application penetration tests are performed annually by an independent third-party. All services have quick failover points and redundant hardware, with backups performed daily. Access to systems is restricted to specific individuals who have a need-to-know such information and who are bound by confidentiality obligations. Access is monitored and audited for compliance. Qualtrics uses Transport Layer Security (TLS) encryption (also known as HTTPS) for all transmitted data. Surveys may be protected with passwords. Our services are hosted by trusted data centers that are independently audited using the industry standard SSAE-18 method."

Questionnaire data will be collected using the REDCap (Research Electronic Data Capture) system available at Georgia State University. This will provide a secure way to collect and manage data, while avoiding potential issues with manual data entry. Georgia State University belongs to a consortium of institutional partners that work to maintain a software toolset and workflow methodology for electronic collection and management of research data. REDCap data collection projects rely on a study-specific data dictionary defined by the research team. REDCap also contains a Survey tool for building and managing online surveys. The research team can create and design surveys in a web browser and engage potential respondents using a variety of notification methods. Both REDCap and REDCap Survey systems provide secure, web-based applications that are flexible enough to be used for a variety of types of research, provide an intuitive interface for users to enter data and have real time validation rules (with automated data type and range checks) at the time of entry. These systems offer easy data manipulation with audit trails and reporting for monitoring, reporting, and querying patient records, and an automated export mechanism to common statistical packages (SPSS, SAS, Stata, R/S-Plus). REDCap application is securely housed in Amazon AWS and managed by the Research Solutions department at Georgia State University. All web-based information transmission is encrypted and the data is encrypted at rest. Amazon AWS's data centers are state of the art nondescript and secured facilities. Data will be downloaded from REDCap into a secure server that is managed by Georgia State University, password-protected, and available only to research personnel who have completed training in research with human subjects.

Additional safeguards will include appropriate password protection and physical security for all computer systems and physical data. Personal names will not be stored in electronic data files. Physical data will be stored in a locked file cabinet and available only to the research personnel. The master list containing participant numbers and participants' names will be kept in a separate locked file, also accessible to study staff only.

The Mobile Commons platform maintains a high level of security control for sending and receiving text messages. The Mobile Commons HIPAA and Text Messaging Security White Paper indicates: "All

Mobile Commons systems that transmit or store sensitive client information are housed in a secure data center facility that maintains a high standard of physical security controls…. The Mobile Commons information security program includes comprehensive technical security measures geared towards protecting the confidentiality, integrity, and availability of sensitive client data…. Authentication controls are in place for access to all systems and applications that deal with sensitive client data. All activity regarding access to, and transmission of, this data is logged. Sessions are configured to timeout after a period of inactivity. All sensitive data, including PHI and authentication credentials for system and application access, are transmitted via encrypted protocols (SSL or SSHv2) when traversing public or untrusted networks. Strong encryption is used for sensitive data stored on Mobile Commons systems. Multiple layers of procedures and technical controls are in place to verify the identity of any person or entity seeking access to any sensitive client information" (https://www.mobilecommons.com/wp/wp-content/uploads/2014/07/Mobile-Commons-HIPAA-Text-Messaging-Security-White-Paper1.pdf).

11. PARTICIPANT RIGHTS AND CONFIDENTIALITY

Institutional Review Board (IRB) Review

This protocol and the informed consent documents (see Appendix) and any subsequent modifications will be reviewed and approved by the Georgia State University IRB.

Informed Consent Forms

The consent forms (see Appendix) describe the purpose of the study, the procedures to be followed, and the risks and benefits of participation.

The informed consent process will include:
1) A thorough review of the Informed Consent Forms (ICF), particularly study procedures; 2) Study personnel will offer an opportunity for participants to ask questions and have them answered; 3) The ICF will be signed and dated by the participant and staff member; and 4) A copy of the ICF will be given to the participants. (For the consent process prior to telephone screening, the research staff will document participants' verbal consent after reviewing the ICF).

Participant Confidentiality

Participants will be assured that the information gathered from the study (including responses to questionnaires, diary assessments and text messages) will be kept confidential to the extent of the law, and that the findings of the study may be published, but that participants will not be identified. Upon enrollment, participants will receive an ID number. Assessment data will be linked to this number. Personal/identifying information, including consent forms, will be maintained separately from study assessment data. Although participants will sign informed consent documents, these forms will be kept in a separate locked file and will never be connected to the study data. Data will be stored on a secure server to protect the data and to prevent unauthorized access. Databases will be accessed only by members of the research staff who have met the IRB's requirements for training in Human Subjects' Protection.

Participants' first names will be used in the text messages that participants receive (in efforts to increase the personalization of the text messaging, as suggested by our qualitative research to inform this intervention). However, their full names will never be entered into the Mobile Commons platform. First names will be deleted from the data when downloaded from the Mobile Commons platform.

By virtue of participating in a treatment group with other people, participants' verbal responses during MBAT treatment will be known to others in the group. Thus, we will request (in the consent form and verbally at the start of the group) that participants keep what they hear confidential. Of course, we cannot guarantee that the other members of the treatment group will maintain confidentiality of responses, and this is made clear in the consent form.

Study Discontinuation

The study may be discontinued at any time by the IRB, NCI, or other government agencies as part of their duties to ensure that research participants are protected.

12. PUBLICATION OF RESEARCH FINDINGS

In accordance with NIH public access policy, final peer-reviewed journal manuscripts that arise from this study will be deposited to PubMed Central immediately upon acceptance for publication.

13. REFERENCES

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