Mindfulness training app effect on a cigarette smoking quit attempt: Investigator-blinded 58-county RCT

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Abstract

Background: Cigarette smoking is the leading cause of preventable cancers. A majority of the 34 million people who currently smoke report wanting to quit. Mindfulness training (MT) apps offer a guided telehealth intervention to foster individual's behavioral practice of meditation. We present the main outcomes of a parallel-group RCT that tested app-MT versus attention control on smoking behavior. Methods: We enrolled adult residents from across California who smoked daily and were willing to make a quit attempt (N=213). Participants completed daily sessions in 10-minute segments for 14 consecutive days. Participants then started a quit attempt and reported daily smoking for 28 days following the quit date using the timeline follow back measure. Results: Seven-day point prevalence abstinence (PPA) for each week during the 4-week quit period ranged from 21.8-27.7% for App-MT and 17.9-19.6% for controls. The intention-to-treat sample revealed app-MT outperformed controls on proportion of abstinence days during the quit period (OR=2.00, CI 1.03-3.87, p=.041). While 7-day PPA for week 4 favored App-MT, significance was not reached (OR=1.65, CI 0.84-3.23, p=.148). The mean number of cigarettes smoked per day among smokers was 4.95 for app-MT versus 5.69 for controls (OR=0.81, CI 0.71-0.92, p=.002) suggesting harm reduction in continued smokers. Conclusion: A MT app prescribed for two weeks leading up to a quit date showed advantage over controls for total abstinence days and fewer cigarettes smoked in a diverse sample encompassing urban and rural residents. These findings yield implications for the utilization of apps to reduce exposure to the carcinogenic properties of cigarette smoke.

Keywords: mindfulness; telehealth, smoking; cancer prevention; addiction; NCT05440903

Introduction

Cigarette smoking is connected to a multitude of diseases and is the foremost contributor to preventable cancers. It exacts a toll of nearly 500,000 lives each year and imposes an annual healthcare expenditure exceeding $300 billion dollars. (1, 2) Despite these alarming statistics alongside ubiquitous public health messaging about the harms of smoking, there are still an estimated 34 million cigarette smokers in the United States, with the majority expressing a desire to quit smoking for health reasons. (3) This high rate of failure in quit attempts may be attributed to the fact that many of these attempts are self-initiated and unassisted, lacking the support of a program, medication, or counselor. (4) Given this reality—where most quit attempts are unassisted and result in relapse(5)—it becomes imperative to develop low-cost, easily accessible behavior interventions to support individuals striving for complete cessation and/or harm reduction. Smartphone apps are a promising telehealth option to address this issue. To effectively reach a broad range of smokers, both in rural and urban areas, with varying levels of access to support programs and resources, we propose that current smokers who wish to quit may benefit most from easily accessible remote behavior interventions delivered via a smartphone app.

Mindfulness Training (MT) encompass intervention packages that provide individuals with meditation training and encourage them to incorporate mindfulness into their daily lives. The instructional content of MT guides individuals to simply observe sensory and mental states as they arise and fade away (e.g., discomfort, itchiness, pain, urges, thinking, worrying) during meditation sessions, all without making associated responses (e.g., moving, scratching, thinking about thinking, mental problem solving, etc.). (6) As individuals engage in the practice of experiencing fluctuating sensory and mental states in their meditation sessions without generating corresponding responses, any response previously associated with that state is weakened (i.e., itchiness is less likely to elicit scratching; a smoking urge less likely to elicit

smoking). (7) This general behaviorist principle has been previously explained in terms of “urge surfing” in the arena of smoking cessation. (8) In terms of observable behavior, meditators are instructed to adopt a comfortable posture during meditation, which may include options such as lying down, sitting, standing, slow walking, yoga, and engaging in light stretching. (6)

To apply the principle of non-response during MT sessions as a process of weakening behavior to the aim of enhancing smoking cessation success in the population of smokers willing to make a quit attempt, we proposed here introducing an app-based MT to individuals before their voluntary quit attempt. This pre-quit period offer a time to practice MT and cultivate non-response during meditation to weaken the probability of a smoking response when in a state of smoking abstinence and associated nicotine/tobacco deprivation (see Skinner’s *Science and Human Behavior* (9)). Aversive states experienced by smokers when making a quit attempt commonly include cravings to smoke, restlessness, increased appetite, anxiety, constipation, negative affect, and difficulty concentrating. MT is one approach that allows individuals who are making a quit attempt to experience abstinence and its associated discomforts without responding by smoking, and thus MT potentially supports a greater likelihood of complete abstinence, more abstinence days, and/or fewer number of cigarettes smoked.

The research literature, in general, supports a net benefit to human health associated with participation in various MT programs, such as Mindfulness-Based Stress Reduction and Mindfulness-Based Cognitive Therapy, in both normative and clinical samples. (10, 11) Empirical tests of MBIs are growing in the field of treatment for substance use disorders. (12-14) However, relatively less is known about the effect of MT on smoking cessation among people who smoke and are willing to make a voluntary quit attempt while being assisted by a smartphone app. A meta-analysis of randomized controlled trials suggests that MT intervention assignment is associated with an increased likelihood of remaining abstinent after a smoking quit attempt (15) yet a more recent review from the Cochrane Library concluded with low

confidence that the effect of MT is robust for smoking cessation. (16) Experimental studies show that abstinent individuals display less craving response to an anxiety-provoking task, a common trigger for smoking lapse, after a single seven-minute mindfulness meditation bout. (17, 18)

In an efficacy trial that compared treatment packages, adults with nicotine dependence were randomly assigned to receive four weeks of in-person, group-based MT adapted specifically for smoking cessation, or the American Lung Association's cognitive-behavioral program. (19) The MT group demonstrated significantly greater 7-day point-prevalence abstinence (PPA) at the four-month follow-up (31% vs. 6%). In a separate RCT comparing remote delivery of MT via a mobile app, again specifically adapted for smoking cessation, to mobile app monitoring only (i.e., experiential sampling of smoking behavior and related symptoms), both study groups showed a significant reduction in the number of cigarettes smoked per day; however, there was no significant difference in proportion between groups in terms of 7-day PPA at the six-month follow-up (MT group=10% vs. control=12%). (20) When we consider the evidence in the field to date, available literature indicates a positive effect for MT to support harm reduction defined as fewer cigarettes smoked but mixed effects for 7-day PPA. It is unknown whether generalized MT apps, not adapted for smoking, have a similar effect on smoking outcomes and in a more diverse sample. The rationale for conducting a test of a generalized MT herein is based on the absence of studies that have compared this type of program to a standard care control group among smokers. Consequently, it remains uncertain whether additional smoker-specific adaptations are necessary beyond the typical language associated with mindfulness practices applied in daily life on a broader scale. This reasoning holds significance for smokers keen to quit but would rather not highlight smoking as a central part of their journey toward a healthier lifestyle.

Study objective

Our study objective was to test the effect of a commercially established mobile app MT telehealth intervention, focused on guided mindfulness meditation yet not specific to smoking cessation, relative to a time-matched mobile attention control on smoking among people who currently smoke and are willing to make a quit attempt. In this remotely administered study, we recruited people who were current smokers from all 58 counties in the state of California. Our daily delivery of the interventions for two weeks leading up to a planned quit date provided individuals who smoke the opportunity to prepare for their quit date. We used an investigator-blinded parallel between-group randomized controlled trial design to test the hypothesis that the app-based MT group would show a greater proportion of smoking abstinence (complete 7-day point prevalence abstinence and total days abstinent) and show fewer cigarettes smoked per day among those who continue to smoke (secondary harm reduction outcome) during the month 28 days following the quit attempt start date. We anticipated that our findings could uniquely contribute to fields of medicine and public health by determining whether a low-demand MT stand-alone app, not specific to smoking behavior or craving symptoms as proposed in previous studies,(20) could improve smoking cessation and harm reduction and so reduce exposure to the carcinogenic properties of cigarette smoke.(21)

Method

Study design

This was a parallel-group, outcomes assessor-blind, randomized controlled trial (RCT) involving human subjects recruited from both urban and rural regions across all 58 counties of California (n=58). The trial aimed to assess the efficacy of daily, app-based behavior interventions in helping people who smoke daily to quit smoking and/or reduce their smoking. The pre-trial protocol is published for review. (22) Two intervention groups were included: an app-based MT package (app-MT) and an attention control package (App-Ed), with the control

accounting for extraneous factors elicited from research protocol exposure such as the participant's time, attention, and expected benefit. Participants were asked to self-administer their sessions twice a day in 10-minute segments for 14 consecutive days, for a total of 280 minutes (i.e., the adherence denominator). The trial was conducted between July 2021 and December 2022, amidst the COVID-19 global pandemic, and was registered with clinicaltrials.gov (NCT05440903) and approved by the Institutional Review Board (UP-20-00900). Smoking behavior was assessed with the timeline follow back (TLFB) calendar completed by computer at day 28 after the quit date (see Measures), which is the day when the participants completed their participation in the trial.

Participants and procedures

Individual adults were recruited online through Craigslist advertisements, and participants completed all study protocols and interviews remotely from their preferred location using a secure online videoconferencing platform. This method extended our reach of recruitment and addressed the in-person limitations caused by the COVID-19 pandemic and associated state and local social isolation policies that restricted in-person interactions. Individuals who viewed the study advertisement followed a link to complete an online survey to demonstrate interest in the study, after which they made a voluntary request to be contacted by the study team. The study staff contacted those individuals with positive screens by phone to interview each person and confirm their eligibility for the study. A 15-minute phone screening was used to determine initial study eligibility and to schedule a baseline interview for those who passed the screening phase. During the screening call, the staff confirmed the participant's current smoking status (i.e., smoking 5 or more cigarettes per day for the past 2 years). Those who passed screening received electronic informed consent documents to e-sign and return after completing a phone-based verbal informed consent process, which was led by a trained member of the study staff.

After providing consent, individuals were assessed for additional eligibility criteria during a baseline videoconferencing interview led by trained study staff. Those who met the criteria transitioned to participant status and received the baseline survey to complete prior to their remote interview with the study staff. The baseline interview lasted approximately 120 minutes, during which participants completed surveys, participated in a brief 20-minute motivational interview counseling session, and received instruction on study participation and when to start their quit attempt. This motivational interviewing session was conducted by trained staff members who provided all participants with a 20-minute smoking cessation counseling session. The session was structured into five modules, which covered the following areas: 1) tobacco use and past quit attempts; 2) level of dependence and withdrawal symptoms; 3) smoking triggers and strengths and barriers regarding quitting; 4) quit strategies; and 5) anticipating and planning for lapses. Participants also received an electronic copy of the National Cancer Institute's workbook called *Clearing the Air*, which contains additional information for preparing for a cessation attempt.(23) This smoking cessation counselling ensured that all participants have a similar baseline knowledge of self-directed smoking cessation strategies and is based on evidence-based recommendations for tobacco dependence treatment.

At the end of the baseline interview, participants were enrolled in the trial and randomly assigned to a study group. Participants were informed that they could use their assigned app at will throughout the follow-up period. Study staff assisted participants in installing and registering the assigned app on their personal smartphone device. Staff members who were unblinded to a participant's study group did not complete the outcome assessment for that participant.

Participants voluntarily completed their daily app-based intervention for 14 days and then attended a post-intervention interview on their scheduled quit date. The immediate post-intervention interview included a verbal initiation of the voluntary quit attempt and completion of surveys and interview. All app content remained available for use by participants during the

post-intervention follow-up period. Participant compensation reached a possible maximum of $300 U.S. dollars for completing screening baseline intake survey ($30), baseline interview ($40), daily phone prompt reporting of number of cigarettes ($15 possible per week across 28 days for maximum possible $60), daily audio app trainings ($2.50 for each of 28 possible app-based intervention sessions over 14 days weeks for maximum possible $70 paid as a lump sum at the post-intervention videoconferencing interview), post-intervention videoconferencing interview ($40), and 28-day follow-up surveys ($20), and a bonus for completing over 80% of surveys across 28 days of daily diary assessments ($40).

Eligibility requirements

To be eligible for the study, individuals had to be 18 years of age or older, have smoked daily (at least 5 cigarettes per day) for the past 2 years, be willing to make a self-directed and voluntary cigarette smoking quit attempt during the study period, and be a current resident of California (verified by a state-issued ID with a California mailing address). People were ineligible if they were not fluent in English, lacked access to remote video capability (such as a computer, camera, and internet, or a smartphone), had an ongoing mindfulness or meditation practice of more than 5 minutes per day within the past 30 days, or had used any nicotine replacement products (such as nicotine patch, gum, or lozenge) or smoking cessation medications (such as Chantix [varenicline], or Wellbutrin, Zyban [bupropion]) within 30 days of baseline. The exclusion of ongoing mindfulness practice of more than 5 minutes per day was necessary to test the effect of taking on a new study treatment (meditation) as the independent variable. Cessation aids were also excluded from the study to detect singular behavior intervention effects rather than interactions with pharmacological effects.

Randomization and blinding

Author M.K. used a computer-generated random selection of block permutations, with a range of 4-20 assignments per block including strata to have sex equivalent, which allowed random assignment of one study intervention to each participant. This block method reduces potential selection bias, as with simple randomization, yet it offers the advantage to increase the likelihood of balanced allocation to groups. (24) The study staff responsible for supplying the app to participants during baseline interview were given the randomization list with only the assigned app. Staff members who trained a participant on app use were not outcomes assessors for that participant in order to eliminate staff expectancies. (25) Participants were unaware of their app assignment until the end of the baseline interview when they were instructed to use the assigned app. The investigators were masked to trial datasets that included the group assignment variable during the active trial and up to the completion of statistical analysis for the trial outcomes. To eliminate investigator expectancies as an extraneous factor, a third-party statistician, guided by a priori decision rules, independently conducted the statistical tests that produced the trial results.

Interventions

App-based mindfulness training (App-MT)

App-MT refers to the commercially-available Headspace software application recordings (https://www.headspace.com; the Foundation Pack; see published trial protocol for more detail(22)), which provided pre-recorded introductory mindfulness meditation audio instructions guided by experienced meditation teachers. The app included both didactive information about mindfulness meditation as well as supplied guided mindfulness meditation practice during each session. We did not make any study alterations to the commercially available sessions. Study participants were instructed to complete 10 minutes of Headspace twice per day for 14 days, which is a total recommended dose of 280 minutes. App-MT practice started on the day after

the baseline interview (i.e., intervention day 1). Participants were instructed to listen to the recordings (including didactics and guided mindfulness meditation) at two separate times each day to maximize daily exposure with low time burden. Study staff tracked adherence to the training regimen by operationalizing it as the number of intervention sessions an individual used out of a total of 28 possible sessions (2 sessions per day for 14 days) calculated as the number of total minutes divided by 28. It is important to note that Headspace, by design, tallies only the number of minutes each participant spent in mindfulness practice during each 10 minute session. This means that all participants in the trial were assigned 10 minutes of app content per session, but in the MT group, the measured meditation time was systematically reduced as an artifact due to how data were recorded for meditation practice time only. As participants had little or no prior experience with mindfulness, all recommended trainings were at the beginner level. Participants had access to all sessions offered by the app and were not restricted to a particular sequence of sessions during the 14 days or during the quit attempt period. Additionally, all participants in this group received a conventional smoking cessation workbook to complete, the National Cancer Institute's *Clearing the Air* publication. This publication provides cessation information and worksheets to support a quit attempt (https://www.cancer.gov/publications/patient-education/clearing-the-air-pdf).

Attention control (App-control)

App-control refers to freely-available audio recordings of TED Talks that provide psychoeducation on field-specific topics by selected experts (https://www.ted.com; see published protocol for more detail(22)). Study participants were instructed to listen to 10 minutes of TED Talks twice per day for 14 days, with a total recommended dose of 280 minutes. The 28 pre-selected sessions delivered by hyperlink to participants were selected by the study team to be of interest to the general public while not including content on meditation, smoking, or other content that might cue behavior change associated with smoking. Like app-MT, app-control

sessions started on the day following the baseline interview (i.e., intervention day 1). Participants were instructed to listen at two separate times each day to maximize daily exposure with low time burden. Additionally, participants were instructed to listen with “full mindful attention and return attention to the audio when attention drifts,” which matches the app-MT instruction and emphasizes the importance of sustaining attention for each 10-minutes period. The instructional statement was planned to ensure all participants paid close attention to the assigned audio content. It was intentionally designed to promote concentration on the material, although it does not constitute a genuine mindfulness strategy. Previous research shows that sham meditation language does not produce the same effects on brain and behavior as does MT. (26) As with the app-MT condition, study staff tracked adherence to sessions. Participants had access to all sessions offered and were not restricted to a particular sequence of sessions during the 14 days or during the quit attempt period. As with the app-MT group, all participants in this group received a conventional smoking cessation workbook to complete, the National Cancer Institute *Clearing the Air* publication that contains cessation information and worksheets to support a quit attempt.

Measures

Cigarette smoking

The primary outcome of the trial was cigarette smoking abstinence, which was the target behavior captured the timeline follow back (TLFB) calendar, collected via REDCap, and completed on day 28 following the quit date (which differs by 2 days, due to a shortened measure to capture increments of 1 week for 7-day PPA scoring, from our original plan for a 30-day follow-up as stated on clinicaltrials.gov: NCT05440903). (27) There was a large amount of missingness of data from the phone-based prompting method for daily cigarettes, making daily analysis based on the daily phone surveys untenable. Therefore, by using the TLFB, we

operationalized smoking cessation at the individual level as 7-day PPA as defined previously (i.e., not smoking a single cigarette in the previous 7 day period) (28) calculated for all weeks and for the final week of follow up. We also quantified total days of abstinence during the overall 28 day follow period given the brief intervention that might function to elicit harm reduction rather than cessation. Finally, we quantified daily cigarette count from each participant, and we calculated mean daily cigarette count for each participant and analyzed this as a secondary outcome again to test for harm reduction among those who continue to smoke during the quit period. (23)

Sample characteristics

We collected descriptive information about each participant on the study baseline survey to understand the characteristics of the sample obtained and to verify that randomization assigned characteristics to study groups in a similar manner. Baseline measures included demographic information, smoking history, the Fagerström Test for Cigarette Dependence (FTCD), (29) and the Five-Facet Mindfulness Questionnaire (FFMQ). (30)

Statistical analysis

Sample size calculation and data analysis

The primary trial outcome in the intent-to-treat sample analysis is the between-group proportional difference in smoking abstinence (7-day PPA and proportion of days abstinent). To guide our original decision on the size of the sample for the trial, we conducted an a priori power analysis using G*Power software. (31) Based on a previous trial findings using this same outcome and comparing a mindfulness training to smoking cessation education in adults who smoke, (32) we estimated the need for a total sample size of N=200 participants (100 per study group) to detect a group-aggregate level proportional difference of medium size (Cohen's

d=0.55) with a calibration of 80% power and a two-tailed test with an alpha cutoff at 5%. We oversampled at baseline to compensate for an anticipated overall 10% attrition rate.

Participant data were input and stored in the secured Research Electronic Data Capture (REDCap, https://www.project-redcap.org) system. Upon the trial's completion, the data were shared with a third-party statistician consultant from the same university. The purpose was to mask key study personnel and the investigators the knowledge of group assignment during all analyses until the primary outcome tests were completed by an impartial statistician. Group contrast effects on the primary and secondary outcomes of the trial were carried out using the ITT analytic approach. (33) We applied two methods for ITT analysis. The *ITT-randomized* analytic sample includes all 213 participants randomized in the trial and the *ITT-single dose* analytic sample includes the 174 participants that completed at minimum a single app dose during the intervention phase of the study. Both ITT sample types noted offer conservative testing of trial effects relative to analysis of the *per protocol* sample that does not deviate impactfully from the original study protocol. (34) Rather than suffering bias resulting from coding missing data points on the TLFB as smoking, (35) missing data points were addressed by employing the full information maximum likelihood (FIML) estimation procedure, which incorporates all available data from each participant without omitting cases from the analytic sample. (36) As such, fewer assumptions were made about reasons for missing. The results are described in terms of odds ratios (OR) and number needed to treat (NNT) derived from multivariate generalized estimating equations logistic model and incidence rate ratios (IRR) derived from generalized estimating equations Poisson model with associated 95% confidence intervals and p-values. Further, a Kaplan-Meier curve was generated with a statistical contrast test estimate to assess the number of abstinence days prior to return to first cigarette smoked. A significance level of 0.05 was used in relation to a two-sided test for all analyses, and computations were made in Stata/SE 17.0 (StataCorp, College Station, TX). Data used in this

analysis is freely available as online supplemental material for this article, and all analysis codes are available from the first author (DB).

Results

Participant flow through trial and sample characteristics

Figure 1 is a CONSORT diagram depicting the flow of participants in the trial comparing the app-MT group with controls. Of the 545 residents of California who passed the initial online screener for our study, 332 were excluded due to ineligibility reasons, non-response, or loss of interest, 213 were randomized to a study condition and enrolled in the trial, 161 completed their quit date interview assessment conducted via Zoom, and 162 participants completed the one-month follow up assessment that was completed online from the participant's self-selected environment. There were 6/101 (5.9%) active declines in the app-MT group and 3/112 (2.7%) active declines in controls that withdrew themselves from further study but allowed their data to be used for analysis. Passive declines were defined as those participants who ignored multiple contacts from the study team. Final outcomes assessment completion rate was 76% in each respective study group.

Table 1 provides descriptive variable values for the total sample and by group. There was no statistically significant group difference in mean scores for any measured variable shown at baseline. Mean age of the sample was 41.2 years with the majority being White (58%) with income less than $50,000 USD per year, and a quarter having high school education or less (25.4%). Before intervention, the average number of cigarettes smoked per day in the total sample was 12.3 (SD=6.1) cigarettes and the mean FTCD score was 4.7 (SD=2.0), a value indicating moderate dependence on the average.

After the quit date, 7.0% of the sample used a cessation quit aid such as gum or patch even though the study interventions did not actively make this recommendation. Figure 2 provides descriptive statistics for complete 7-day PPA as well as daily count of cigarettes smoked by intervention group across the four weeks of the quit period. Weekly complete 7-day PPA proportions ranged from 21.8% to 27.7% in the app-MT group and 17.9% to 19.6% in controls. Average daily count of cigarettes smoked across the span of one week ranged from 4.9 to 5.2 in the App-MT group and 5.4 to 5.8 in the App-control group.

Study group effect on total abstinence days and complete 7-day PPA

Table 2 displays the results for the model estimated aggregate group-level contrasts comparing the app-MT and control study intervention packages on total abstinence days during the follow period our of 28 in total and 7-day PPA for final week 4. For total abstinence days, the estimated group effect adjusting for sex and cigarette dependence (FTCD) at baseline yielded a significant group effect for the ITT *single dose* sample (OR=2.00, CI 1.03-3.87, p=.041, N=174). The group effect for the ITT *randomized* sample was of similar magnitude and direction but was at the threshold of statistical significance (OR=1.90, CI 0.99-3.63, p=.052, N=213). When modeling the final week of follow up for complete 7-day PPA, the direction of advantage again favored app-MT (OR=1.65, CI 0.84-3.23, p=.148, N=174; model estimated proportion abstinent by group = 36% for App-MT versus 26% for App-controls) yet the threshold for statistical significance was unmet. The estimated number of individuals needed to treat with app-MT produced from this adjusted model was NNT=9.5 to produce one complete 7-day abstinence case. The sex covariate as an a priori randomization strata and level of cigarette dependence at baseline as an a priori nicotine addiction magnitude covariate had a null effect on total abstinence days and 7-day PPA for final week 4.

Study group effect on count of cigarettes smoked per day

Table 3 displays the results for the model estimated contrast comparing the app-MT and control group on mean count of cigarettes smoked per day. The estimated group effect adjusting for sex and cigarette dependence (FTCD) covariate scores at baseline yielded a significant group effect for the ITT *single dose* sample (OR=0.81, CI 0.71-0.92, p=.002, N=174) and the ITT *randomized* sample of similar magnitude and significance (OR=0.87, CI 0.77-0.99, p=.030, N=213). The model estimated mean number of cigarettes per day was 4.95 in app-MT versus 5.69 in controls. The sex covariate as an a priori randomization strata had a null effect whereas the level of cigarette dependence (FTCD) at baseline predicted higher mean count of cigarettes smoked per day. For the ITT *single dose* sample, a 50% reduction in cigarettes smoked was observed in 67.1% of the app-MT group, compared to 57.3% in the control group.

Group effect on time to first cigarette smoked after a quit attempt

In a supplementary descriptive analysis to determine whether smoking abstinence contained a time element that was a function of study group, we produced a Kaplan-Meier curve to assess days from quit date to first cigarette smoked. The overall median abstinence days for the total sample was 24 days. The median abstinence days to first cigarette smoked after the quit day showed advantage in the app-MT group at 24 days compared to controls at 21 days, yet the group contrast did not reach statistical significance (log-rank p = 0.66).

Use of intervention sessions and relation to proportion of days abstinent

The number of app sessions completed in the app-MT group was significantly less than control controls (15.6 versus 19.9 app sessions completed, t=3.30 p=.001, N=213). The app-MT Headspace interface provided the number of minutes each participant completed only meditation practice in opened sessions but omitted the minutes for each session's didactic preamble of instructions, resulting in a method artifact likely responsible for this use discrepancy

by group. For the app-MT group, 26.7% (out of n=86) completed 0-7 sessions, 19.8% completed 8-14 sessions, 17.5% completed 15-21 sessions, and 36.0% completed 22-28 sessions. For controls, 8.3% (out of n=96) completed 0-7 sessions, 15.7% completed 8-14 sessions, 22.9% completed 15-21 sessions, and 53.1% completed 22-28 sessions. Figure 3 plots the descriptive statistics for study app sessions completed in relation to proportion days abstinent by group. The descriptive least squares polynomial fit line suggests an upturn in proportion of abstinence days after the completion of 20 sessions with the positive slope higher for the app-MT group. We used this data-driven analysis to overlay descriptive means (SD) by group for participants completing >20 sessions versus 20 or fewer app sessions. The mean proportion of days abstinent among participants completing >20 sessions was 56% in the app-MT group and 36% in controls, a difference of 20%.

3. Discussion

In this registered RCT, structured by a two-week intervention period preceding a voluntary planned smoking quit date, we tested the effect of an app-based mindfulness training (MT) compared to an attention control on smoking behavior during a 28-day quit attempt period. The trial results suggest that among the sample opening apps at least once (a single dose), the app-MT group showed an advantage on proportion of total days abstinent during a quit attempt period. However, the model estimated advantage of app-MT on 7-day PPA at the last week of assessment (week 4 of the quit period) did not reach statistical significance. In practical terms, our model estimated that it would require about 10 smokers willing to quit in the context of a trial to produce one successful complete 7-day (PPA) abstinence case by week four of a quit attempt period. Further, the app-MT group showed advantage on fewer average count of cigarettes smoked per day across the quit period. This is an initially promising pattern of results, especially given that the Headspace app used in the app-MT is already fully developed and available to the public and can be accessed by people in remote settings. While the evidence

yielded from this trial is limited for interpreting complete 7-day PPA abstinence at week 4 of a quit attempt, our results are more promising for *smoking reduction*, which is considered an important harm reduction strategy to reduce exposure to the carcinogenic properties of cigarette smoke and for the prevention of tobacco-related diseases. (37)

To address a gap in the field, we also used a data-driven approach to assess number of study app sessions completed in relation to proportion of days abstinent to attempt to decipher a target number of app sessions that might be productive for future studies using this mindfulness app or similar app types. This tentative finding suggests that among the sample completed more than 20 app sessions, the average proportion of days abstinent in App-MT was more than double that of controls (56% vs. 36%, respectively). If this descriptive finding maintains generality for other samples, it offers users with a clear goal of 20 app sessions to complete which equates to about 3.5 hours of commitment across 14 days. This finding is helpful to research and practice domains given that concrete recommendations for dosing MT are not well established, especially when delivered by app. (38)

We presume mindfulness meditation is the independent variable to function on smoking behavior as the dependent variable given that our selected attention control mirrors the intervention package on daily time exposure to digital educational content, study protocols, staff contacts, assessments, monitoring, and compensation schedules. All participants also received the self-administered smoking cessation workbook developed by the National Cancer Institute (NCI) to hold constant the existing minimum standard of support offered to the public for free. Thus, there is a basic level of quit smoking education offered to all participants in the trial including the education offered to all participants during our single motivational interview session at baseline conducted by our trained research staff. We suspected that adding an app-MT intervention assigned daily, twice per day, for the two weeks offered preparatory period to practice MT to gain skills in non-response to fluctuating states, including aversive states

associated with not smoking and deprivation of tobacco/nicotine. We specifically selected the Headspace app for the MT group for it focuses on guided meditation content not adapted for smoking cessation to determine if a generalized MT app holds benefit beyond what has been found previously for MT program specifically adapted to smoking. (20) Our findings suggest that MT shows benefit without being specific to smoking behavior. A future study comparing a generalized MT app, such as Headspace, to smoking-specific MT intervention packages appears to be warranted at this time to determine the level of equivalence in their effects on smoking outcomes. Smokers could have the choice to select either the general MT or MT focused on smoking, depending on their preference and tolerance for educational material on smoking.

The design characteristics of this RCT contribute to a general overall strength of our study. For example, our remote research protocols for recruitment, interviewing, and surveying can be replicated at relatively low cost in future studies that could examine longer periods of MT and/or MT combined with pharmacotherapy such as nicotine replacement therapy (NRT). In support of this future aim, previous studies have identified telehealth approaches (e.g., delivery of quit smoking counseling by telephone) combined with NRT to be a cost effective strategy for cessation in clinical settings.(39) There are ways in which our interpretations yielded from the results produced by the trial are limited. First, any findings from the current study cannot generalize to individuals not willing to use app technologies. This limitation is evident in some older adults who are unfamiliar with smartphone technology and those lacking access to a personal smartphone or unwilling to use phone apps. Second, smoking abstinence was not biologically verified with carbon monoxide shipping and testing due to budget constraints. Our previous work indicates that self-report measurement of smoking is reliable, (40) and so we do not expect major group differences in veracity of self-report although this is possible. Third, any detected effect by group in this trial may be due to extraneous factors not uncovered by our

assessment strategy. For example, instructions in the app-MT group may lead participants to initiate other behaviors as part of lifestyle modification such as change yogic physical activity, and/or alter social relationships (e.g., seeking out people who do not smoke to spend time with), which are not directly attributable to our presumed independent variable (i.e., Headspace app guided mindfulness meditation). Fourth, given the nature of the behavior intervention that includes practice and skill development, participants become aware of their study group content immediately following trial enrollment which is a ubiquitous artifact of behavior intervention research. Unmasked study group content in this way can function to differentially reinforce participant adherence to select or preferred study interventions and protocols. Fifth, participants gained compensation after the intervention period for the number of app session they completed possibly increasing motivation to complete sessions. However, the total possible incentive amount was small (2.50 USD per session) and not paid until the end of the intervention period, and compensation schedules were the same in both study groups. Sixth, the post-quit date follow period did not include assessment of additional app use nor sustained abstinence at 3 and 6 months. This limited follow period masks the potential to detect lagged effects on smoking, effects that increase or decrease over time, and null effects that persist over time. Finally, our ITT analysis, which modeled the 7-day PPA outcome, could be underpowered, as the actual missing data at the final 7-day PPA period was 19% (162/200), which was higher than the expected 10% (180/200) we used in our pre-trial power analysis.

In summary, we find that the low-demand daily app-guided mindfulness training called Headspace for the two weeks leading up to a planned quit date shows empirical advantage over attention control that includes basic education for smoking cessation resulting in fewer days smoked and fewer cigarettes smoked in a sample of regionally diverse adults willing to make a quit attempt. These findings have implications for the utilization of commercially available mindfulness training apps that can be widely disseminated by health workers to potentially

reducing exposure to the carcinogenic properties of inhaled cigarette smoke.

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References

1. DHHS U. Smoking Cessation: A Report of the Surgeon General. Washington (DC)2020 2020.

2. Xu X, Bishop EE, Kennedy SM, Simpson SA, Pechacek TF. Annual Healthcare Spending Attributable to Cigarette Smoking: An Update. American Journal of Preventive Medicine. 2015;48(3):326-33.

3. Commerce UDo. National Cancer Institute-sponsored Tobacco Use Supplement to the Current Population Survey (2010-11). 2012 [

4. Soulakova JN, Crockett LJ. Unassisted Quitting and Smoking Cessation Methods Used in the United States: Analyses of 2010–2011 Tobacco Use Supplement to the Current Population Survey Data. Nicotine & Tobacco Research. 2017;20(1):30-9.

5. Leventhal AM, Dai H, Higgins ST. Smoking Cessation Prevalence and Inequalities in the United States: 2014-2019. J Natl Cancer Inst. 2022;114(3):381-90.

6. Kabat-Zinn J. Mindfulness-Based Interventions in Context: Past, Present, and Future. Clinical Psychology: Science and Practice. 2003;10(2):144-56.

7. Black DS. Mindfulness-Based Interventions: An Antidote to Suffering in the Context of Substance Use, Misuse, and Addiction. Substance Use & Misuse. 2014;49(5):487-91.

8. Bowen S, Marlatt A. Surfing the urge: brief mindfulness-based intervention for college student smokers. Psychol Addict Behav. 2009;23(4):666-71.

9. Skinner BF. Science and human behavior. First Free Press Paperback edition. ed. New York, NY: The Free Press
Distributed by Simon & Schuster Inc.; 1965. x, 461 pages p.

10. Eberth J, Sedlmeier P. The Effects of Mindfulness Meditation: A Meta-Analysis. Mindfulness. 2012;3(3):174-89.

11. Abbott RA, Whear R, Rodgers LR, Bethel A, Thompson Coon J, Kuyken W, et al. Effectiveness of mindfulness-based stress reduction and mindfulness based cognitive therapy in vascular disease: A systematic review and meta-analysis of randomised controlled trials. Journal of Psychosomatic Research. 2014;76(5):341-51.

12. Grant S, Colaiaco B, Motala A, Shanman R, Booth M, Sorbero M, et al. Mindfulness-based Relapse Prevention for Substance Use Disorders: A Systematic Review and Meta-analysis. Journal of Addiction Medicine. 2017;11(5):386-96.

13. Black DS, Amaro H. Moment-by-Moment in Women's Recovery (MMWR): Mindfulness-based intervention effects on residential substance use disorder treatment retention in a randomized controlled trial. Behaviour Research and Therapy. 2019;120:103437.

14. Amaro H, Black DS. Mindfulness-Based Intervention Effects on Substance Use and Relapse Among Women in Residential Treatment: A Randomized Controlled Trial With 8.5-Month Follow-Up Period From the Moment-by-Moment in Women's Recovery Project. Psychosomatic Medicine. 2021;83(6):528-38.

15. Oikonomou MT, Arvanitis M, Sokolove RL. Mindfulness training for smoking cessation: A meta-analysis of randomized-controlled trials. Journal of Health Psychology. 2017;22(14):1841-50.

16. Jackson S, Brown J, Norris E, Livingstone-Banks J, Hayes E, Lindson N. Mindfulness for smoking cessation. Cochrane Database Syst Rev. 2022;4(4):CD013696.

17. Paz R, Zvielli A, Goldstein P, Bernstein A. Brief mindfulness training de-couples the anxiogenic effects of distress intolerance on reactivity to and recovery from stress among deprived smokers. Behaviour Research and Therapy. 2017;95:117-27.

18. Siegel A, Korbman M, Erblich J. Direct and Indirect Effects of Psychological Distress on Stress-Induced Smoking. Journal of Studies on Alcohol and Drugs. 2017;78(6):930-7.

19. Brewer JA, Mallik S, Babuscio TA, Nich C, Johnson HE, Deleone CM, et al. Mindfulness training for smoking cessation: results from a randomized controlled trial. Drug Alcohol Depend. 2011;119(1-2):72-80.

20. Garrison KA, Pal P, O'Malley SS, Pittman BP, Gueorguieva R, Rojiani R, et al. Craving to Quit: A Randomized Controlled Trial of Smartphone App-Based Mindfulness Training for Smoking Cessation. Nicotine Tob Res. 2020;22(3):324-31.

21. Fiore MC. US public health service clinical practice guideline: treating tobacco use and dependence. Respir Care. 2000;45(10):1200-62.

22. Black DS, Kirkpatrick M. Test of daily app-based mindfulness meditation preceding a planned smoking quit attempt date on abstinence: Protocol for a randomized controlled trial recruiting across the 58 counties of California. Contemp Clin Trials. 2022;120:106855.

23. Institute NC. Clearing The Air: Quit Smoking Today. US Department of Health and Human Services
National Institutes of Health. 2008.

24. Efird J. Blocked randomization with randomly selected block sizes. Int J Environ Res Public Health. 2011;8(1):15-20.

25. Schulz KF, Grimes DA. Blinding in randomised trials: hiding who got what. Lancet. 2002;359(9307):696-700.

26. Zeidan F, Johnson SK, Gordon NS, Goolkasian P. Effects of brief and sham mindfulness meditation on mood and cardiovascular variables. J Altern Complement Med. 2010;16(8):867-73.

27. Robinson SM, Sobell LC, Sobell MB, Leo GI. Reliability of the Timeline Followback for cocaine, cannabis, and cigarette use. Psychol Addict Behav. 2014;28(1):154-62.

28. Piper ME, Bullen C, Krishnan-Sarin S, Rigotti NA, Steinberg ML, Streck JM, et al. Defining and Measuring Abstinence in Clinical Trials of Smoking Cessation Interventions: An Updated Review. Nicotine Tob Res. 2020;22(7):1098-106.

29. Svicher A, Cosci F, Giannini M, Pistelli F, Fagerstrom K. Item Response Theory analysis of Fagerstrom Test for Cigarette Dependence. Addict Behav. 2018;77:38-46.

30. Bohlmeijer E, ten Klooster PM, Fledderus M, Veehof M, Baer R. Psychometric properties of the five facet mindfulness questionnaire in depressed adults and development of a short form. Assessment. 2011;18(3):308-20.

31. Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods. 2007;39(2):175-91.

32. Davis JM, Mills DM, Stankevitz KA, Manley AR, Majeskie MR, Smith SS. Pilot randomized trial on mindfulness training for smokers in young adult binge drinkers. BMC Complement Altern Med. 2013;13:215.

33. Lachin JM. Statistical considerations in the intent-to-treat principle. Control Clin Trials. 2000;21(3):167-89.

34. Lewis JA, Machin D. Intention to treat--who should use ITT? Br J Cancer. 1993;68(4):647-50.

35. Blankers M, Smit ES, van der Pol P, de Vries H, Hoving C, van Laar M. The Missing=Smoking Assumption: A Fallacy in Internet-Based Smoking Cessation Trials? Nicotine Tob Res. 2016;18(1):25-33.

36. Enders CK. The impact of nonnormality on full information maximum-likelihood estimation for structural equation models with missing data. Psychol Methods. 2001;6(4):352-70.

37. Rodu B, Godshall WT. Tobacco harm reduction: an alternative cessation strategy for inveterate smokers. Harm Reduct J. 2006;3:37.

38. Creswell JD. Mindfulness Interventions. Annu Rev Psychol. 2017;68:491-516.

39. Cao P, Smith L, Mandelblatt JS, Jeon J, Taylor KL, Zhao A, et al. Cost-Effectiveness of a Telephone-Based Smoking Cessation Randomized Trial in the Lung Cancer Screening Setting. JNCI Cancer Spectr. 2022;6(4).

40. Wang SD, Loftus P, Pang RD, Kirkpatrick MG. Impact of self-efficacy on daily intention to not smoke. Addict Behav. 2021;118:106877.

Tables.

Table 1. Baseline descriptive variables for randomized sample and by study group

Variables at baseline	**Total** (N=213)	**App-MT** (n=101)	**Control** (n=112)
Age (years)	41.2 (13.5)	41.9 (12.8)	40.6 (14.1)
Female sex at birth	53.9	55.5	54.5
Education			
< high school	3.3	4.0	2.7
High school diploma	22.1	21.8	22.3
Some college	48.4	48.5	48.2
College degree or higher	26.3	25.7	26.8
Income			
< $15,000	26.7	30.7	23.2
≥ $15,000 - $29,999	28.2	25.7	30.4
≥ $30,000 - $44,999	14.1	15.8	12.5
≥ $45,000 - $74,999	18.3	17.8	18.8
≥ $75,000	12.7	9.9	15.2
Race/ethnicity			
American Indian/Alaskan Native	1.9	1.0	2.7
Asian	2.4	1.0	3.6
Black	6.6	5.0	8.0
White	57.8	58.4	57.1
Other	3.3	4.0	2.7
Multiracial	8.0	7.9	8.0
Hispanic non-White	19.3	22.8	16.1
Missing	1.0	0.0	1.8
Sexual orientation			
Straight	81.2	80.2	82.1
Bisexual	12.7	12.9	12.5
Gay/Lesbian	6.1	6.9	5.4
Five Facet Mindfulness Questionnaire	82.4 (12.6)	81.4 (12.5)	83.4 (12.6)
Smoking-related			
Number of daily cigarettes	12.3 (6.1)	12.4 (6.7)	12.3 (5.5)
Fagerström Test for Cigarette Dependence	4.7 (2.0)	4.9 (2.1)	4.5 (2.0)
Motivation to quit smoking cigarettes	6.9 (2.4)	6.7 (2.5)	7.1 (2.3)

Note. Values are % otherwise M (SD) as noted. There was no statistically significant group difference for any measured variable shown at baseline.

Table 2. Estimated group effect on total abstinence days and 7-day PPA for final week 4 of the 28-day quit period

	ITT randomized (N=213)			ITT single dose or more (N=174)		
Variable	OR	95% CI	*p*	OR	95% CI	*p*
Abstinence days during 28 day quit period						
Study group						
Control	Ref	--	--	Ref	--	--
App-MT	1.90	0.99-3.63	0.052	2.00	1.03 - 3.87	0.041
Sex						
Male	Ref	--	--	Ref	--	--
Female	1.18	0.62 - 2.27	0.614	1.24	0.64 - 2.42	0.527
FTCD	0.91	0.78 - 1.08	0.287	0.93	0.79 - 1.10	0.411
Complete 7-day PPA for final week 4 of quit period						
Study group						
Control	Ref	--	--	Ref	--	--
App-MT	1.65	0.84 - 3.23	0.148	1.60	0.81 - 3.18	0.177
Sex						
Male	Ref	--	--	Ref	--	--
Female	1.24	0.63 - 2.45	0.536	1.25	0.62 - 2.49	0.535
FTCD	1.03	0.87 - 1.23	0.698	1.04	0.87 - 1.24	0.645

Note. OR = Odds ratio with ref denoting the intervention group contrasted against to produce the estimate. Model adjusts for sex as the strata variable used for randomization and for cigarette dependence (Fagerström Test for Cigarette Dependence [FTCD], higher score indicates greater dependence) at study baseline. PPA = complete 7-day point prevalence abstinence.

Table 3. Estimated group effect on mean count of cigarettes smoked per day during the 28-day quit period

Variable	ITT randomized (N=213)			ITT single dose (N=174)		
	IRR	95% CI	*p*	IRR	95% CI	*p*
Study group						
Control	Ref	--	--	Ref	--	--
App-MT	0.87	0.77 - 0.99	.030	0.81	0.71 - 0.92	.002
Quit days	1.00	1.00 - 1.00	.887	1.00	1.00 - 1.00	.588
Sex						
Male	Ref	--	--	Ref	--	--
Female	0.93	0.82 - 1.05	.250	0.92	0.81 - 1.05	.202
FTCD	1.24	1.20 - 1.29	<.001	1.24	1.20 - 1.29	<.001

Note. IRR = Incidence rate ratio with ref denoting the intervention group contrasted against to produce the estimate. Model adjusts for sex as the strata variable used for randomization and for cigarette dependence (Fagerström Test for Cigarette Dependence [FTCD], higher score indicates greater dependence) at study baseline. For the ITT single-dose sample, a 50% reduction in cigarettes smoked was observed in 67.1% of the app-MT group, as opposed to 57.3% in the control group.

Figure legends.

Figure 1. CONSORT diagram showing flow of participants in trial comparing App-MT to controls

Note. A total of 549 individuals completed an online study screener form and completed an e-signature consent form to be contacted by the study staff. Of those assessed by initial survey, 276 people did not finish the e-consent process. The phone-based apps allowed for automated recording of each participant's app use, and records were visually inspected by study staff who transcribed records to the dataset. The Headspace app interface provided the number of minutes each participant completed in opened sessions, so did not include in the total minutes each session's didactic preamble of instructions which were variable in length, resulting in method artifact lower adherence values for App-MT compared to controls.

Figure 2. Descriptive statistics for 7-day point prevalence abstinence and mean count of daily cigarettes by week and study group

Note. Point prevalence abstinence (PPA) refers to complete (not even a single puff) 7-day abstinence quantified by responses made on the timeline follow back (TLFB) for each calendar day during the quit period. 7-day point prevalence abstinence shown on left y axis and shown as bars; mean count of daily cigarettes on right y axis and shown as lines by week and study group.

Figure 3. Relation of number of intervention sessions completed prior to the quit date to abstinence days during the quit period by group

Notes. App-MT = black box; control = triangle; N=154 participants having data for both x and y axis variables. The dashed curved line is App-MT polynomial trend line and solid curved line is the control polynomial trend line. The vertical line indicates the app session linked with data-driven upturn in abstinence proportion occurring after 20 sessions. Diamond shape (black

diamond is app-MT proportion of 56% and gray diamond is control proportion of 36%) indicates sample proportion of days abstinent by group for >20 sessions completed.

Figures

Figure 1. CONSORT diagram showing flow of participants in trial comparing App-MT to controls

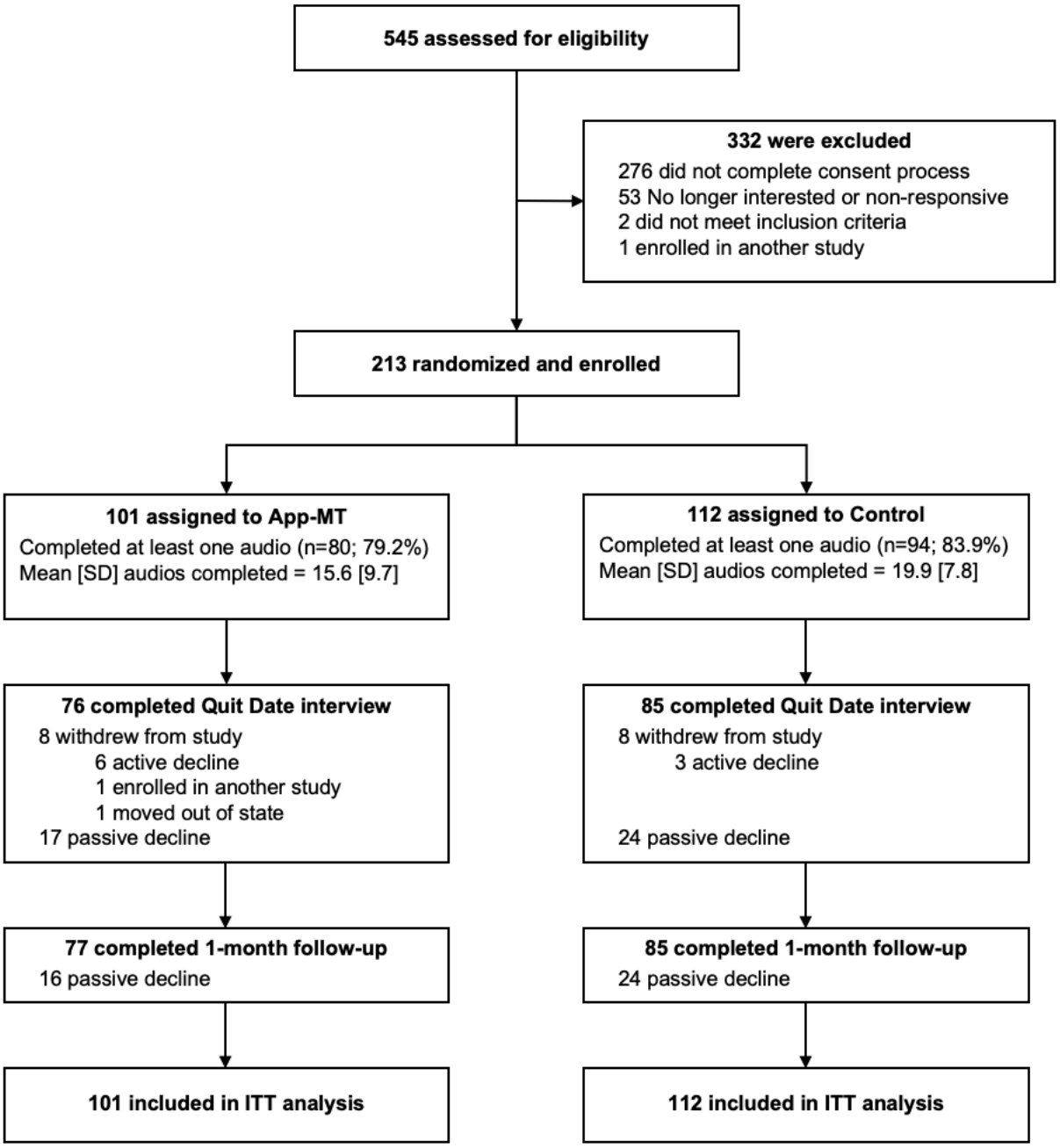
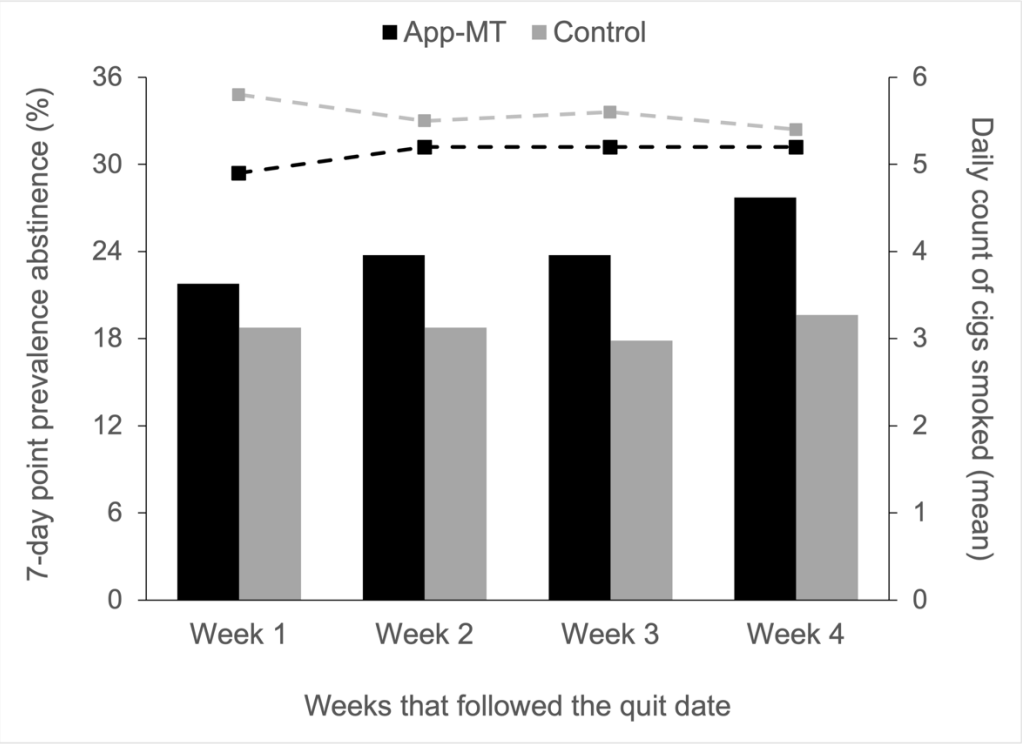


Figure 2. Descriptive statistics for 7-day point prevalence abstinence and mean count of daily cigarettes by week and study group



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