original reports

Efficacy of a Smoking Cessation Intervention for Survivors of Cervical Intraepithelial Neoplasia or Cervical Cancer: A Randomized Controlled Trial

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abstract

PURPOSE Women who smoke and have a history of cervical intraepithelial neoplasia (CIN) or cervical cancer represent a vulnerable subgroup at elevated risk for recurrence, poorer cancer treatment outcomes, and decreased quality of life. The purpose of this study was to evaluate the long-term efficacy of Motivation And Problem Solving (MAPS), a novel treatment well-suited to meeting the smoking cessation needs of this population.

METHODS Women who were with a history of CIN or cervical cancer, age 18 years and older, spoke English or Spanish, and reported current smoking (≥100 lifetime cigarettes plus any smoking in the past 30 days) were eligible. Participants (N = 202) were recruited in clinic in Oklahoma City and online nationally and randomly assigned to (1) standard treatment (ST) or (2) MAPS. ST consisted of repeated referrals to a tobacco cessation quitline, self-help materials, and combination nicotine replacement therapy (patch plus lozenge). MAPS comprised all ST components plus up to six proactive telephone counseling sessions over 12 months. Logistic regression and generalized estimating equations evaluated the intervention. The primary outcome was self-reported 7-day point prevalence abstinence from tobacco at 18 months, with abstinence at 3, 6, and 12 months and biochemically confirmed abstinence as secondary outcomes.

RESULTS There was no significant effect for MAPS over ST at 18 months (14.2% *v* 12.9%, $P = .79$). However, there was a significant condition × assessment interaction ($P = .015$). Follow-up analyses found that MAPS (*v* ST) abstinence rates were significantly greater at 12 months (26.4% *v* 11.9%, $P = .017$; estimated OR, 2.60; 95% CI, 1.19 to 5.89).

CONCLUSION MAPS led to a greater than two-fold increase in smoking abstinence among survivors of CIN and cervical cancer at 12 months. At 18 months, abstinence in MAPS declined to match the control condition and the treatment effect was no longer significant.

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INTRODUCTION

Smoking is the leading cause of cancer morbidity and mortality. Subpopulations of survivors are at particularly elevated risk for adverse outcomes and warrant special attention. For example, smoking is a primary risk factor for both cervical cancer and cervical intraepithelial neoplasia (CIN), or high-grade cervical dysplasia,[1] the immediate precursor to cervical cancer.[2] Smoking after a CIN or cervical cancer diagnosis is associated with poor treatment response, treatment complications, increased risk of recurrence, second primary cancers,[3] and other diseases.[4-7]

Cervical cancer predominantly affects women who are younger[8] and with low socioeconomic status. Members of racial/ethnic minority groups suffer tremendous disparities with regard to cervical cancer morbidity and mortality and the health consequences of smoking.[9] Cervical cancer incidence is 39% higher among African American women[10] and 80% higher among Hispanic women as compared with non-Hispanic White women,[11] and these women have poorer access to tobacco treatment, have greater difficulty in quitting,[12-14] and suffer disproportionately from the health consequences of smoking.[15-17] Taken together, women who smoke and have a history of CIN or cervical cancer represent a particularly vulnerable subgroup at substantially elevated risk. However, most smoking cessation trials have comprised survivors of multiple cancer types of cancer, and only two of these trials have included patients with gynecologic cancer.[18]

Given that 30%-48% of cervical cancer survivors continue smoking after diagnosis,[19-21] it is critically

ASSOCIATED CONTENT

Appendix

Protocol

Author affiliations and support information (if applicable) appear at the end of this article.

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CONTEXT

Key Objective

What is the efficacy of a novel 12-month smoking cessation intervention approach evaluated in the first randomized clinical trial designed to address the specific smoking cessation treatment needs of women with a history of cervical intraepithelial neoplasia or cervical cancer?

Knowledge Generated

This intervention was associated with more than a two-fold increase in smoking abstinence at 12 months in one of the longest smoking cessation intervention trials among cancer survivors to date. High retention through 18 months signals survivors' motivation for long-term engagement in treatment and highlights the need for sustained interventions. Strategies for extending positive treatment outcomes should be examined in future research.

Relevance *(S.B. Wheeler)*

This randomized clinical trial improved smoking cessation among cervical cancer survivors at 12 months; more work is needed to understand how best to sustain quit behaviors over time.*

*Relevance section written by *JCO* Associate Editor Stephanie B. Wheeler, PhD, MPH.

important that these individuals be offered effective cessation treatments. Unfortunately, nearly all randomized clinical trials evaluating interventions for cancer survivors have failed to demonstrate efficacy.[22] One exception is a recent trial comparing the effectiveness of 6 months of telephone counseling and free FDA-approved smoking cessation medication (intensive treatment) versus 4 weeks of telephone counseling and smoking cessation medication advice standard treatment (ST). Biochemically confirmed abstinence rates at 6 months were significantly higher in the intensive treatment condition (ie, 34.5% *v* 21.5%).[23]

The current study evaluated a novel treatment intended to meet the smoking cessation needs of this population. Motivation And Problem Solving (MAPS) is a holistic, dynamic approach to facilitating and maintaining behavior change on the basis of motivational interviewing[24,25] and social cognitive theory.[26,27] MAPS is built around a wellness program that addresses numerous barriers and concerns prevalent among cervical cancer survivors (eg, anxiety, depression, stress, and fear of cancer recurrence).[18] MAPS was adapted for this study through in-depth interviews with cervical cancer survivors who smoked. Participants requested that the treatment include education about the health effects of smoking and benefits of quitting, pharmacotherapy, strategies for planning to quit and coping with cravings, social support, real-time support, a nonjudgmental and understanding counselor, and tailoring. Participants also requested help with stress management, cancer survivorship issues, physical activity, and healthy eating. The adapted MAPS approach incorporated each of these components.[18] This randomized clinical trial compared the efficacy of MAPS in facilitating smoking cessation with that of ST among current smokers with a history of CIN or cervical cancer. It was hypothesized that MAPS participants would have a higher rate of self-reported abstinence at 18 months (6 months post-treatment) and higher rates of abstinence over the length of the study.

METHODS

Eligible and consented participants completed a baseline survey, were randomly assigned, and completed follow-up surveys at 3, 6, 12, and 18 months. Data were entered and stored in a Research Electronic Data Capture (REDCap) database. All assessments were completed by phone or online via a secure REDCap link. Participants received $30 for completing the baseline and $30 for each completed follow-up assessment. Participants received an additional $30 at all assessments to compensate for use of their personal cell phones. All procedures were approved by the institutional review boards of the participating institutions. Additional details have been described elsewhere.[28]

Setting and Participants

Prospective participants were recruited via a gynecologic oncology clinic within an National Cancer Institute (NCI)–designated cancer center, a university-based women's health clinic, a tobacco treatment research program, and nationally via online advertisements. Inclusion criteria were (1) age 18 years and older, (2) self-report of smoking within the past 30 days and history of ≥100 lifetime cigarettes,[29] (3) history of CIN or cervical cancer, (4) working cell phone, (5) valid home address, and (6) English- and/or Spanish-speaking. Exclusion criteria were (1) current use of nicotine replacement therapy (NRT) or other cessation medications, (2) pregnant or breastfeeding, (3) household member enrolled, or (4) contraindication for nicotine patch use. Individuals recruited in clinic were identified through electronic health record reviews and approached by research staff during medical visits or contacted by phone. Individuals referred by the tobacco treatment program were screened by research staff via

TABLE 1. MAPS Session by Session Treatment Content

Counseling Call	Treatment Session Content
Counseling call 1	Introduction of agenda and establishment of rapport Review of confidentiality Review of smoking history, previous quit attempts, and current smoking Importance/confidence/readiness rulers If participant is not ready to quit or set a quit day: Building motivation Decisional balance If participant is ready to quit: Preparing for the quit attempt Introduction of the wellness plan Session wrap-up and scheduling of the next session
Counseling calls 2, 3, 4, and 5	Introduction of agenda and continuous building of rapport Review and possible revision of wellness plan goals Address high-risk smoking situations Completion of values exercise Enhancement of patient's self-efficacy Scheduling of the next session
Counseling call 6	Reconnection with the patient Review of progress Consideration of next steps Goodbye and provision of referrals as necessary

NOTE. Counseling call timing was flexible and determined individually for each patient on the basis of negotiations with the counselor.
Abbreviation: MAPS, Motivation And Problem Solving.

phone. Individuals recruited online completed a brief REDCap screener, and those meeting criteria were screened further by a research coordinator. Eligible individuals who agreed to enroll provided informed consent.

Random Assignment to Treatment Condition

After the baseline survey, participants were randomly assigned to ST or MAPS using minimization.[30,31] Variables for the minimization were race/ethnicity (nonminority and minority), age (35 years and younger and older than 35 years), education (<high school diploma/high school equivalency certificate and ≥high school diploma/high school equivalency certificate), cigarettes per day (≤19 and >19), diagnosis at study enrollment (CIN and stage 1 or 2 or 3 or 4 cervical cancer), treatment status (in active treatment and treatment completed), and time since diagnosis (≤1 year and >1 year).

Interventions

Consistent with National Comprehensive Cancer Network guidelines,[32] participants were provided with 12 weeks of combination NRT (patch plus lozenge).

ST. The ST group received a mailed packet including a letter referring to their state's tobacco cessation quitline and self-help materials. These components were delivered at baseline and 6 and 12 months.

MAPS. MAPS comprised all ST components plus up to six proactive telephone counseling sessions delivered within 12 months (Tables 1 and 2).[21] A fundamental tenet of MAPS is that the timing of counseling sessions is tailored to meet the needs of each patient. For example, timing can be negotiated to be clustered around a specific quit attempt. Similarly, a patient not motivated to quit might negotiate the next call to occur many months later or sooner if the patient wants to address specific barriers (eg, stress and social support). Similarly, individuals struggling with maintaining abstinence might have several calls over a shorter period to get them through the problematic period, whereas others need less frequent help.

MAPS Treatment Fidelity

All MAPS sessions were conducted by master's level counselors with substantial experience plus 20 hours of MAPS training. To monitor deviation or drift from the manual, counseling calls were recorded. A random 10% were reviewed and coded using the Motivational Interviewing Treatment Integrity 4 (MITI 4) to ensure adequate competence and adherence. MITI 4[33] is empirically validated with ratings on a Likert-type scale from 1 (low) to 5 (high).

Measures and Assessment Procedures

The primary outcome was self-reported 7-day point prevalence abstinence from smoking. Abstinence data were collected following recommendations from the Society for Research on Nicotine and Tobacco.[34] The secondary outcome was biochemically confirmed 7-day point prevalence abstinence. To biochemically confirm self-reported abstinence, participants were mailed a saliva collection kit, detailed instructions, and a prepaid return envelope. Cotinine levels ≤20 ng/mL biochemically verified abstinence. Exceptions were made for participants who exceeded this threshold but reported current use of NRT and/or e-cigarettes.[35,36] Individuals who had higher levels of cotinine or did not return the

TABLE 2. MAPS Treatment Session Engagement Timing by Diagnosis/Stage and Cancer Treatment Status

Diagnosis and Treatment Status	Total Sessions Completed	Months 0-3	Months 4-6	Months 7-9	Months 10-12
All participants	3.9 (2.0)	1.8 (1.3)	0.8 (0.8)	0.5 (0.6)	0.8 (0.9)
Diagnosis/stage					
CIN	4.0 (2.1)	1.7 (1.2)	0.8 (0.8)	0.4 (0.5)	1.0 (1.0)
Cervical cancer, stages I and II	3.8 (2.0)	1.8 (1.5)	0.9 (0.9)	0.5 (0.7)	0.6 (0.6)
Cervical cancer, stages III and IV	3.9 (1.6)	1.8 (0.9)	0.4 (0.5)	0.9 (0.8)	0.9 (0.4)
Treatment status					
Completed treatment	3.9 (2.0)	1.6 (1.2)	0.8 (0.9)	0.5 (0.7)	0.9 (0.9)
Currently in treatment	4.4 (1.6)	1.8 (1.5)	0.6 (0.7)	0.2 (0.4)	0.9 (1.3)
Pending treatment	3.6 (2.4)	2.6 (1.6)	0.9 (1.0)	0.5 (0.5)	0.4 (0.5)

NOTE. Each cell presents mean (SD) for the number of sessions (0-6).
Abbreviations: CIN, cervical intraepithelial neoplasia; SD, standard deviation.

kit were designated as smoking. Participants received $30 compensation for each returned test.[28]

Sociodemographics (ie, age, race, ethnicity, education, income, relationship status, and employment status), financial strain, health literacy, current and past smoking, and cancer status information (ie, cervical cancer *v* CIN, cancer stage at diagnosis, time since diagnosis, current cancer stage, and treatment status) were collected at baseline.

Treatment Engagement and Satisfaction

Engagement in treatment was assessed using the number of MAPS counseling sessions completed, amount of time spent in counseling sessions, self-reported NRT use, and quitline use. Treatment satisfaction was assessed at 12 months using the Client Satisfaction Questionnaire (CSQ).[37]

Analysis Overview

The primary test of MAPS efficacy used logistic regression to evaluate self-reported 7-day point prevalence abstinence at 18 months (6 months postintervention). The model included all sociodemographic and clinical variables that differed by group at baseline ($P < .10$). Generalized estimating equations (GEEs) with a logit link, binomial variance function, and a first-order autoregressive working correlation matrix were used to evaluate the efficacy of MAPS (*v* ST) over the length of the study. Treatment, assessment (with 18 months as reference), and their interaction were the primary predictors. The secondary outcome of biochemically confirmed 7-day point prevalence abstinence was evaluated similarly.

Managing Missing Data

Multiple imputation under the Missing at Random assumption was applied to manage missing self-report data using a Markov Chain Monte Carlo method[38] via PROC MI in SAS version 9.4 (SAS Institute, Cary, NC). Twenty data sets were generated for both the primary and secondary outcomes. For smoking status, a post hoc adjustment[39] was implemented for a Missing Not at Random influence (ie, missing is due to smoking). Appendix 1 (online only) provides details.

RESULTS

Recruitment and Retention

Enrollment occurred between February 2017 and January 2020, and the collection of follow-up data ended in August 2021. Figure 1 presents the study CONSORT. Of the 202 participants randomly assigned, eight were known to be deceased before the final assessment and excluded, culminating in n = 194 for data analysis. Retention was high throughout the study, including 166 (82%) of those enrolled providing data at 18 months.

Baseline Characteristics

Table 3 presents sociodemographic, clinical, and smoking-related variables by treatment group. Participants had a mean age of approximately 48 years, were predominantly non-Hispanic White, had generally low socioeconomic status (41.3% had an annual household income <$20,000, and 39.1% had an annual household income between $20,000 and $50,000), and had a mean smoking history of nearly 30 years. Nearly half of the sample reported smoking within 5 minutes of waking, and the mean cigarette per day was approximately 15. Cervical cancer stage varied: 42% had CIN, 33% stage I, 12% stage II, 10% stage III, and 3% stage IV, as did treatment status with 14% preparing to start treatment, 12% in treatment, and 74% post-treatment for CIN or cancer. There were no group differences ($P > .10$).

Missing Data

The primary reason for missing data was failure to complete a follow-up survey. The CONSORT diagram (Fig 1) presents the number of surveys completed by participants. Nearly 70% completed all four surveys, whereas 4% did not return any. The number of missing surveys increased from 17 (9%) at 3 months to 36 (19%) at 18 months. Several nonmonotonic patterns of missing surveys were observed. The multiple

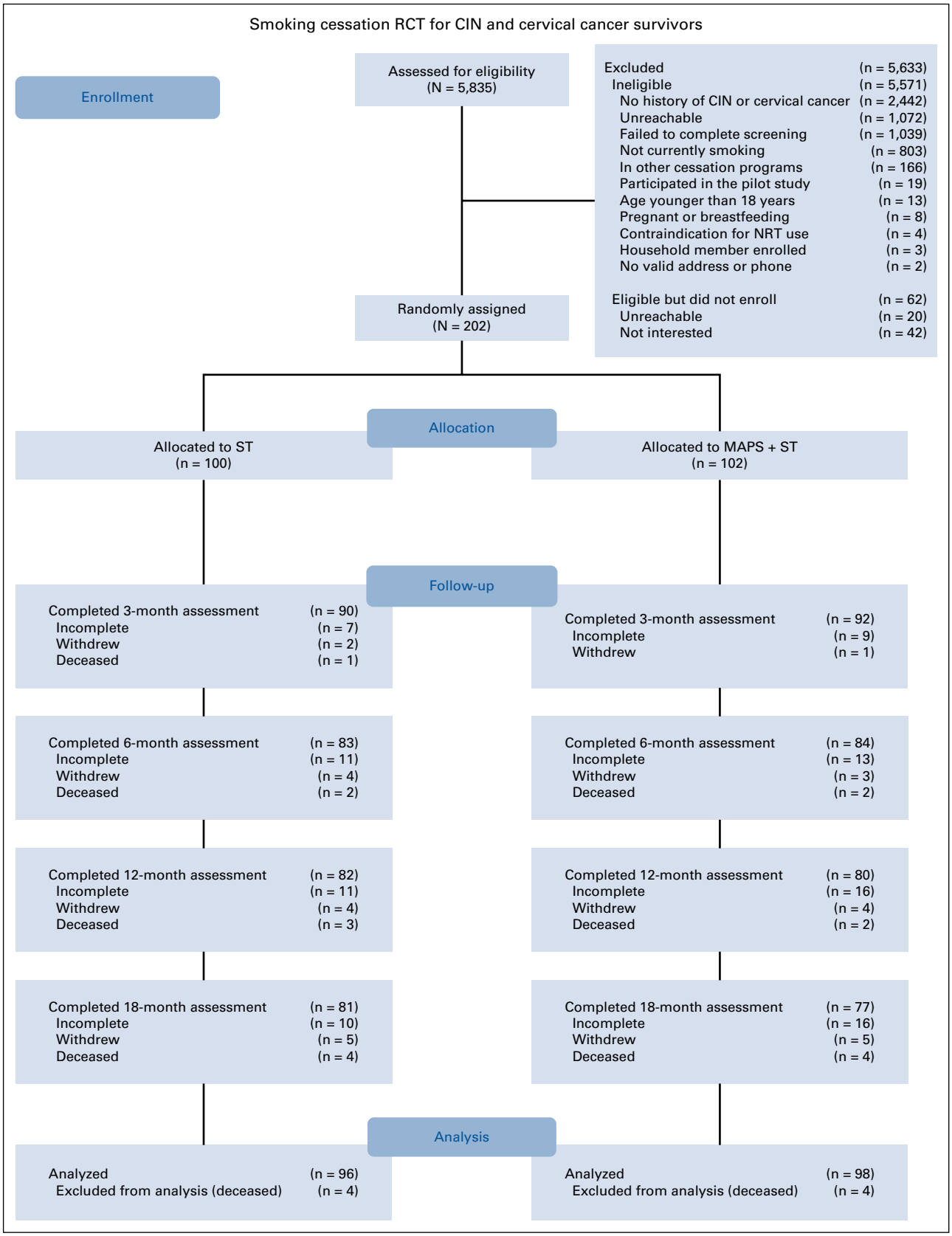

FIG 1. CONSORT diagram. CIN, cervical intraepithelial neoplasia; MAPS, Motivation And Problem Solving; NRT, nicotine replacement therapy; ST, standard treatment.

TABLE 3. Participant Characteristics by Condition

Variable	ST (n = 96)	MAPS (n = 98)
In clinic recruitment, No. (%)	38 (40)	41 (42)
Diagnosis/stage, No. (%)		
CIN	43 (45)	42 (43)
Cervical cancer, stages I and II	37 (39)	48 (49)
Cervical cancer, stages III and IV	16 (17)	8 (8)
Treatment status, No. (%)		
Completed	73 (76)	75 (77)
Currently in treatment	11 (11)	10 (10)
Pending	12 (13)	13 (13)
Age, years, M (SD)	47.8 (10.8)	47.7 (10.9)
Hispanic ethnicity, No. (%)	6 (6)	9 (9)
Race, No. (%)		
White	76 (79)	76 (78)
Black/African American	5 (5)	5 (5)
Native American or Alaska Native	7 (7)	9 (9)
Mixed race	6 (6)	4 (4)
Others	2 (2)	4 (4)
Have spouse or partner, No. (%)	58 (60)	57 (58)
Education, No. (%)		
Less than high school diploma	9 (9)	8 (8)
High school diploma	26 (27)	26 (27)
Beyond high school diploma	61 (64)	64 (65)
Employed: full- or part-time, No. (%)	28 (29)	39 (40)
Annual household income, No. (%)		
Under $20,000	34 (38)	42 (45)
$20,000–$49,999	38 (42)	34 (36)
$50,000 and above	18 (20)	18 (18)
Financial strain scale, M (SD)	11.0 (7.6)	11.5 (7.3)
Adequate health literacy, No. (%)	74 (78)	87 (89)
Cigarettes per day, No. (%)		
1-10	24 (25)	35 (36)
11-20	50 (53)	46 (47)
21-30	14 (15)	12 (12)
More than 30	7 (7)	5 (5)
Age started smoking, M (SD)	16.9 (5.7)	17.2 (7.9)
Time to first cigarette after waking, No. (%)		
<5 minutes	42 (44)	41 (42)
6-30 minutes	30 (31)	34 (35)
31-60 minutes	15 (16)	10 (10)
>60 minutes	9 (9)	13 (13)
Contemplation Ladder (0-10), M (SD)	6.8 (3.0)	6.8 (2.9)
Self-efficacy to abstain from smoking (1-5), M (SD)	2.3 (0.9)	2.5 (1.0)

NOTE. There were no statistically significant group differences, $P > .10$.

Abbreviations: CIN, cervical intraepithelial neoplasia; MAPS, ST plus Motivation And Problem Solving counseling; SD, standard deviation; ST, standard treatment.

imputation model was inclusive with seven sociodemographic and two clinically related variables and three smoking-related variables. Appendix 1 provides details concerning creation of the 20 data sets used for analyses of the primary and secondary outcomes.

MAPS Fidelity

The mean MITI 4 technical global rating score was 3.5 (SD = 0.5), suggesting good cultivating change talk and softening sustain talk. The mean MITI 4 relational global rating score was 4.1 (SD = 0.5), suggesting very good partnership and empathy. In addition, the ratio of reflections to questions was good (2:1), as was the % of complex reflections (80.0%).

MAPS Efficacy

Figure 2 presents self-reported 7-day point prevalence abstinence rates and *P*-values from statistical tests. Logistic regression evaluating group differences at 18 months found no significant effect for MAPS over ST (14.2% *v* 12.8%; $P = .79$; estimated OR, 1.14; 95% CI, 0.44 to 2.93). GEE for abstinence rates across the four assessments also found no significant main effect ($P = .60$). However, there was a significant condition × assessment interaction ($P = .015$). This interaction was further investigated using logistic regression at 3, 6, and 12 months. MAPS abstinence rates were greater than ST at 12 months (26.4% *v* 11.9%; $P = .017$; estimated OR, 2.60; 95% CI, 1.19 to 5.89).

Parallel analyses were performed for the secondary outcome of biochemically verified abstinence. Participants who failed to return saliva kits were classified as smoking. In addition, 10 participants reported current use of NRT, four reported current vaping, and one reported current use of both NRT and vaping. Although their saliva samples reflected cotinine values inconsistent with abstinence, these participants were classified as abstinent.

Across all assessments, there were 44 instances of self-reported abstinence in ST, with 17 (39%) biochemically verified as abstinent. Similarly, 23 (42%) of 55 instances of self-reported abstinence in MAPS were biochemically verified. Logistic regression evaluating group differences at 18 months found no significant effect for MAPS (8.0%) over ST (7.0%; $P = .78$; estimated OR, 1.14; 95% CI, 0.37 to 3.56). GEE for abstinence rates across the four assessments found no significant effect for condition ($P = .87$) and no significant condition × assessment interaction ($P = .056$).

Treatment Engagement and Satisfaction

The number of MAPS participants completing zero to six sessions was 7, 8, 13, 11, 13, 14, and 32, respectively. MAPS participants completed an average of 3.9 sessions (SD = 2.0), and 60% completed four or more sessions, suggesting high engagement for the majority. The mean length of the MAPS counseling sessions was 32.6 minutes (SD = 13.8). The mean number of minutes spent in counseling was 125.9

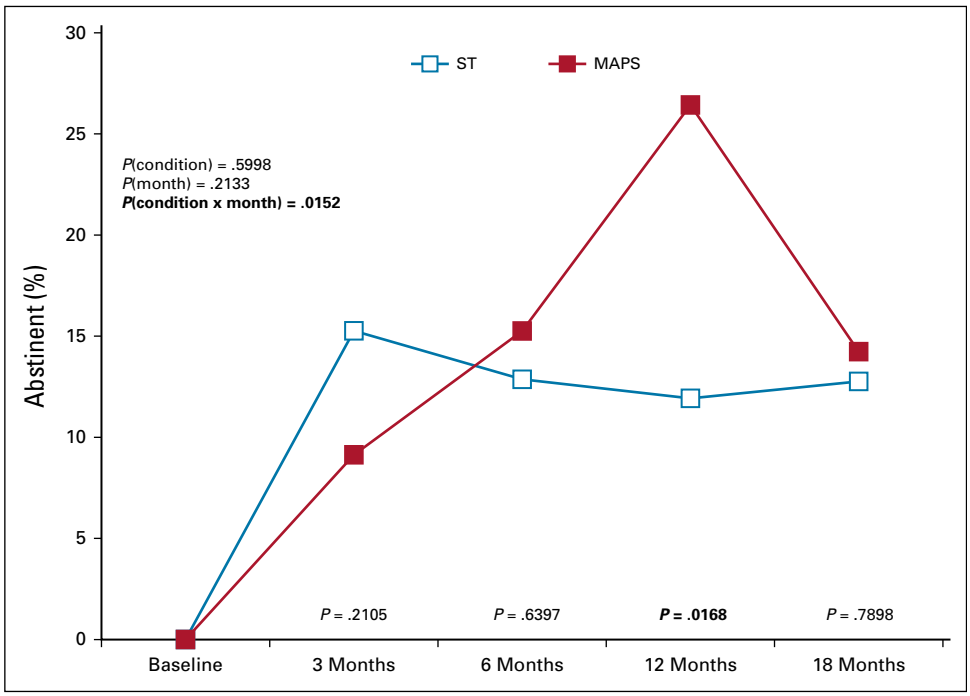

FIG 2. Self-reported 7-day point prevalence abstinent percent averaged across 20 data sets created using multiple imputation to manage missing data. *P* values along the bottom of the figure for logistic regression at each assessment. *P* values in the upper-left box from the generalized estimating equation model of condition and month for the four follow-up assessments (ie, baseline not included). MAPS, ST plus Motivation And Problem Solving counseling; ST, standard treatment.

(SD = 72.7). There was an association between MAPS engagement and abstinence at 12 months. Those completing 4-6 sessions had significantly higher abstinence (38.3%) than those completing 0-3 sessions (8.5%; $P = .009$; estimated OR, 1.95; 95% CI, 1.32 to 2.40). Table 2 presents the timing of sessions using the average number of sessions completed within each of four 3-month periods, with summaries by diagnosis/stage and treatment status. All subgroups completed similar numbers of sessions and showed similar patterns of treatment engagement over time.

NRT use was comparable for the two conditions at the 3-, 6-, and 12-month assessments with self-reported rates of 68%, 58%, and 46% for MAPS and 64%, 53%, and 41% for ST ($\chi^2(1)$'s < 1, all P values $> .49$). Contacting the quitline was comparable for the two conditions, with 9% for MAPS and 14% for ST ($\chi^2[1] < 1$, $P = .34$).

Treatment satisfaction was high in both treatment conditions. The mean CSQ score (1-4 scale) was 3.6 (SD = 0.4) in MAPS and 3.7 (SD = 0.3) in ST There were no group differences (t(94) = 1.01, $P = .32$).

DISCUSSION

In this randomized clinical trial, compared with a control condition comprising repeated quitline referrals, MAPS led to more than a two-fold increase in smoking abstinence at the end of the 12-month treatment period. However, at 18 months, abstinence in MAPS had declined to match the control condition and the treatment effect was no longer significant. To our knowledge, this study represents the first smoking cessation intervention trial specifically designed to address the treatment needs of women with a history of CIN or cervical cancer. Our study is also one of few smoking cessation trials among cancer survivors to evaluate the efficacy of an intervention lasting 12 months and one of only two trials to collect follow-up data through 18 months.[22]

Although our primary hypothesis—that MAPS would be associated with significantly higher abstinence at 18 months compared with ST—was not supported, the significant treatment effect observed at 12 months adds new meaningful knowledge to the existing literature. Very few smoking cessation trials among cancer survivors have demonstrated a significant treatment effect,[22] and efficacious smoking cessation interventions for patients with cancer and survivors are critically needed. There have been numerous calls by professional societies and organizations to prioritize and improve the delivery of smoking cessation treatment to patients with cancer. Furthermore, the NCI has dedicated Cancer Moonshot funding to support clinical implementation of evidence-based tobacco treatment across >60 NCI-Designated Cancer Centers.[40]

As described above, a recent trial by Park et al[23] is notably, to our knowledge, the first to demonstrate a significant treatment effect. The primary outcome was smoking abstinence at 6 months, which represented end of treatment for the intensive counseling condition. Thus, the current study is only the second randomized smoking cessation clinical trial with cancer survivors to date to demonstrate a significant treatment effect. However, our high rate of late relapse highlights the importance of exploring *why* these women relapsed between 12 and 18 months. We attribute this late relapse to (1) treatment ending and (2) high levels of stress, uncertainty, and emotional vulnerability in this population.[18,41] Our findings highlight the potential to promote relapse prevention and enhance continuous quitting through extending and sustaining MAPS in ways that are low-burden and engaging. For example, extending the delivery of personalized, easily accessible, and highly engaging digital MAPS-based treatment content via smartphones might have potential to provide long-term smoking cessation support—and ultimately prevent late relapse—among survivors of CIN or cervical cancer. Previous research has indicated that extended treatment leads to higher long-term abstinence in the general population of smokers.[42] Further research is needed to examine these questions empirically.[43]

This study has several unique strengths. First, to our knowledge, it is the only smoking cessation randomized clinical trial to date to target the specific treatment needs of CIN and cervical cancer survivors. Second, our treatment approach was unique in that participants were not required to set a quit date at the time of study enrollment. Additional strengths include our follow-up of participants through 18 months, excellent retention, and nationwide recruitment and enrollment of participants.

Because of recruitment challenges, eligibility was expanded to include women with a history of CIN rather than cervical cancer. However, MAPS has clear relevance for individuals with CIN and our findings have important clinical implications. Although no differences in abstinence were observed for women with CIN versus cancer, there may be important differences on the basis of disease- or treatment-related variables that warrant further exploration. In addition, all in-clinic recruitment took place in Oklahoma City, whereas online recruitment was nationwide, which may limit the generalizability of our findings. Also, given that only two thirds of the target sample was successfully recruited, the study might have been underpowered. A final limitation is the relatively high proportion of unreturned biochemical confirmation samples.

In conclusion, MAPS was dynamically tailored to the specific treatment needs of women with a history of CIN or cervical cancer and was associated with more than a two-fold increase in abstinence at 12 months compared with a quitline control condition. This effect was no longer significant at 18 months, suggesting that the efficacy of MAPS dissipated as the time from the end of treatment increased. This decline does not appear to have been driven by dropout as retention was high, which signals motivation for long-term treatment engagement and highlights the need for sustained intervention.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Efficacy of a Smoking Cessation Intervention for Survivors of Cervical Intraepithelial Neoplasia or Cervical Cancer: A Randomized Controlled Trial

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APPENDIX 1. MULTIPLE IMPUTATION ADDENDUM

Missing data for the outcome variable were due to unreturned follow-up surveys. Seven (4%) of the 194 participants providing data for analysis did not return any of the four follow-up assessments; with nine (5%) missing three, 17 (9%) missing two, and 26 (13%) missing one. The other 135 (70%) returned all surveys. The number of unreturned surveys at each assessment was 17 (9%) at 3 months, 29 (15%) at 6 months, 33 (17%) at 12 months, and 36 (19%) at 18 months. Patterns of unreturned surveys were varied, with eight of 12 being nonmonotonic patterns. For the follow-up surveys that were returned, there were no missing data for the items used to derive the outcome variable. Baseline variables used in analyses were missing <0.5% of responses, ranging from 0% (eg, sex and age) to 5% (household income).

Missing data were managed using multiple imputation with the multivariate normal approach under the Missing at Random assumption[1,2] as implemented by the PROC MI procedure in SAS v 9.4. The multivariate normal method was applied for the following reasons: first, the primary outcome measures (point prevalence) are binary (abstinent = 0, smoking = 1), predictor variables that are ordinal can be dichotomized, and other categorical variables can be dichotomized to focus on a single level (eg, marital status dichotomized to married versus other); second, there is high likelihood of identifying baseline variables that either predict missing surveys or predict smoking status at follow-ups. Those not already in the imputation model as prospective moderators can be added as auxiliary variables to increase the credibility of the Missing at Random assumption. Third, there are typically numerous patterns of missing data, many of which are not monotonic (eg, one or more later surveys are returned after an earlier follow-up survey that is not returned).

The imputation model was intended to cover all possible analyses involving smoking status at follow-up assessments. This approach provides imputed data sets that would be the same for multiple planned and post hoc analyses using a subset of variables from the more complete data sets created by the imputation models (versus an imputation model that is unique to an analysis). The imputation model included the intervention group (coded ST = 0 and MAPS = 1), the outcome measure (point-prevalent smoking status) for each of the four assessments, seven prospective moderators (ie, age, non-Hispanic White, employment, education, married, income, and recruitment), and the interaction term of the moderator with intervention.

In addition, the model included auxiliary variables that were identified via preliminary univariate and multivariable logistic regression analyses. Candidates were baseline measures that may predict smoking status at multiple follow-up assessments and/or may predict unreturned surveys. These analyses produced the following additions to the imputation model: (1) Contemplation Ladder and health literacy (dichotomized) as predictors of missing surveys and (2) smoking cessation self-efficacy, time to first cigarette after waking, and financial stress as predictors of smoking status as predictors of subsequent smoking status. The interaction of each auxiliary variable with the intervention group was also in the imputation model.

A separate set of these procedures was performed for the primary and second outcome variables given the difference in the observed 7-day point prevalence for self-reported abstinence and biochemically verified abstinence. The only difference for the two imputation models was the observed outcome variable at the four follow-up assessments. For both outcomes, 20 data sets were generated.

After the imputation modeling, a post hoc adjustment was applied to imputed smoking status values to reflect that missing implies smoking with a small to medium effect size (ie, Cohen's d = 0.35).[1] The adjusted imputed values for smoking status were dichotomized using adaptive rounding.

Across all variables in the imputation model, the amount of missing data was 3.0%. There were 22 patterns of missing data on the basis of unreturned surveys and a few missing responses to some baseline measures. Relative efficiency is one index of the quality/sufficiency of the imputation modeling using the multivariate normal method, with greater efficiency represented by higher values (max, 1). It was applied here via a single-sample t-test of the mean against 0 for each variable with imputed values. Relative efficiency values were very high for all variables within each set of imputation models. All relative efficiencies were >0.998 for baseline measures and >0.988 for smoking status across the four assessments (percent missing ranged from 9% to 19%).