Integrating Tobacco Cessation Into Mental Health Care for Posttraumatic Stress Disorder

A Randomized Controlled Trial

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Context Most smokers with mental illness do not receive tobacco cessation treatment.

Objective To determine whether integrating smoking cessation treatment into mental health care for veterans with posttraumatic stress disorder (PTSD) improves long-term smoking abstinence rates.

Design, Setting, and Patients A randomized controlled trial of 943 smokers with military-related PTSD who were recruited from outpatient PTSD clinics at 10 Veterans Affairs medical centers and followed up for 18 to 48 months between November 2004 and July 2009.

Intervention Smoking cessation treatment integrated within mental health care for PTSD delivered by mental health clinicians (integrated care [IC]) vs referral to Veterans Affairs smoking cessation clinics (SCC). Patients received smoking cessation treatment within 3 months of study enrollment.

Main Outcome Measures Smoking outcomes included 12-month bioverified prolonged abstinence (primary outcome) and 7- and 30-day point prevalence abstinence assessed at 3-month intervals. Amount of smoking cessation medications and counseling sessions delivered were tested as mediators of outcome. Posttraumatic stress disorder and depression were repeatedly assessed using the PTSD Checklist and Patient Health Questionnaire 9, respectively, to determine if IC participation or quitting smoking worsened psychiatric status.

Results Integrated care was better than SCC on prolonged abstinence (8.9% vs 4.5%; adjusted odds ratio, 2.26; 95% confidence interval [CI], 1.30-3.91; $P=.004$). Differences between IC vs SCC were largest at 6 months for 7-day point prevalence abstinence (78/472 [16.5%] vs 34/471 [7.2%], $P<.001$) and remained significant at 18 months (86/472 [18.2%] vs 51/471 [10.8%], $P<.001$). Number of counseling sessions received and days of cessation medication used explained 39.1% of the treatment effect. Between baseline and 18 months, psychiatric status did not differ between treatment conditions. Posttraumatic stress disorder symptoms for quitters and nonquitters improved. Nonquitters worsened slightly on the Patient Health Questionnaire 9 relative to quitters (differences ranged between 0.4 and 2.1, $P=.03$), whose scores did not change over time.

Conclusion Among smokers with military-related PTSD, integrating smoking cessation treatment into mental health care compared with referral to specialized cessation treatment resulted in greater prolonged abstinence.

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NICOTINE DEPENDENCE INflicts a disproportionate toll on individuals with mental illness, adversely affecting quality and length of life.[1] Posttraumatic stress disorder (PTSD), a prevalent mental disorder,[2] is highly associated with smoking (45%) and unsuccessful quit attempts.[3] Individuals with PTSD smoke more heavily than smokers without PTSD and use tobacco to regulate mood and psychiatric symptoms.[4,5] Tobacco dependence likely contributes to the high mortality,[6] morbidity,[4] and health care costs of persons with PTSD.[7]

Limited access to tobacco cessation treatment is a barrier to quitting smoking in many health care settings. Smokers are infrequently referred to specialized tobacco cessation clinics, and those referred often fail to attend or drop out prematurely.[8,9] Although primary care clinicians screen for tobacco use,[10,11] they usually do not provide treatment to aid quitting.[11] Psychiatrists deliver cessation counseling to patients who smoke at only

See also p 2534 and Patient Page.

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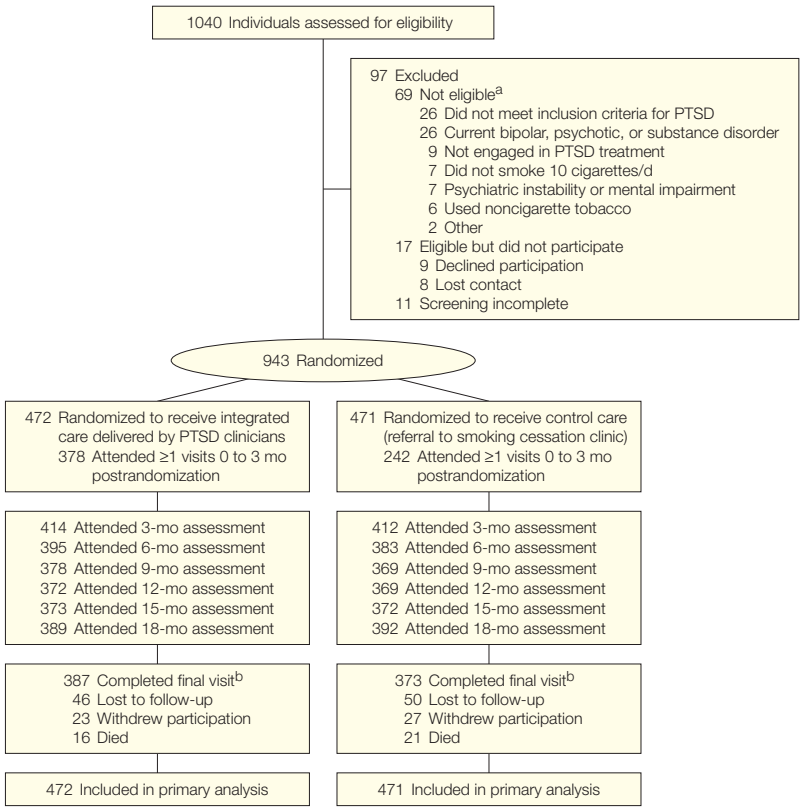
12% of visits.[12] In the US Department of Veterans Affairs (VA), which enrolls more than 1.5 million veterans with mental illness, including more than 400 000 with PTSD, the majority of smokers report not receiving tobacco cessation treatment during the previous year.[10] An effective service delivery approach is needed to improve access to tobacco cessation treatment for patients with PTSD and other psychiatric illnesses.

Nicotine dependence is a chronic, relapsing addiction that responds best to intensive treatment extended over time.[13] Mental health clinicians are well positioned to deliver intensive cessation treatment to smokers undergoing psychiatric care for PTSD owing to frequent visits attended by these patients.[14] Integrating tobacco cessation into psychiatric care allows for monitoring of smoking status and reapplying cessation treatment to relapsers. Integrated cessation interventions also can address exacerbation of smoking by psychiatric symptoms,[15] severe withdrawal symptoms experienced by smokers with mental illness,[16] and possible deterioration in mood following quit attempts.[17,18] Integrating treatment of substance use and other psychiatric disorders in a single clinical setting has been widely advocated[1,19,20] but only preliminarily studied as an effective service delivery approach.[14,21,22]

Our multisite randomized controlled effectiveness trial hypothesized that integrating smoking cessation treatment into mental health care would improve long-term smoking abstinence rates in veterans with PTSD compared with referral for specialized cessation treatment. Smoking cessation treatment sessions and use of tobacco cessation medications were examined as mediators of treatment effects. We also evaluated whether psychiatric symptoms worsened from participating in integrated smoking cessation treatment or stopping smoking.

Figure 1. Flow of Patients



PTSD indicates posttraumatic stress disorder. Numbers of patients determined to be ineligible or declining participation prior to screening were not tracked. Eight patients were screened (n=6) or randomized (n=2) but not included here due to issues with informed consent, Health Insurance Portability and Accountability Act authorization, or both.

[a] Numbers sum to more than the total because multiple categories could be checked.

[b] Final visit ranged between 18 and 48 months. Patients were followed up for a minimum of 18 months and until the end of the study.

METHODS

Study Patients

A total of 943 patients were recruited from outpatient PTSD clinics at 10 VA medical centers and followed up for a minimum of 18 months. Patients enrolled early were followed up to 48 months to obtain long-term outcomes (not presented herein). Patients met inclusion criteria if they (1) were engaged in outpatient PTSD care, (2) had PTSD related to military service, (3) smoked at least 10 cigarettes on at least 15 of 30 days before screening, and (4) consented to receive cessation interventions. Exclusion criteria included (1) use of noncigarette tobacco; (2) current psychotic, bipolar, or substance dependence disorder other than nicotine using *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition) (*DSM-IV*) criteria (substance abuse or dependence in partial remission were allowed; partial remission indicates that full criteria for dependence were no longer met but 1 or 2 current criteria remained); and (3) severe psychiatric symptoms, psychosocial instability, or cognitive impairment assessed by medical record review and discussion with patients' mental health clinicians. Patients who subsequently stabilized could be rescreened for eligibility.

Procedures

This study was approved by the Human Rights Committee of the Palo Alto Cooperative Studies Program Coordinating Center and the institutional review boards at participating sites. Patients gave written informed consent before enrollment. Recruitment occurred between November 2004 and December 2007, with follow-up continuing until July 2009. FIGURE 1 shows study procedures described in detail elsewhere.[23]

Posttraumatic stress disorder and axis I psychiatric disorders were assessed using the Clinician Administered PTSD Scale (CAPS)[24] and Structured Clinical Interview for *DSM-IV*, respectively. At baseline, research staff gathered demographic and smoking data, including the Fagerström Test for Nicotine Dependence.[25] To determine if smoking levels and outcomes varied by race and ethnicity, these characteristics were assessed using patient self-report from preselected options.

Eligible patients were randomized to integrated care (IC) or smoking cessation clinic (SCC) in a 1:1 ratio, stratified within each site by sex, current alcohol abuse or dependence in partial remission, current major depressive disorder, prior smoking abstinence (≥1 year), and heavy smoking (>25 cigarettes/d), using an adaptive randomization procedure[26] to ensure balance of stratifiers between treatment groups within each site. Research staff called a telephone randomization system at the VA Palo Alto Cooperative Studies Program Coordinating Center, Palo Alto, California, for treatment assignments. Neither site investigators nor patients were blinded with respect to treatment assignment.

Patients completed the initial course of cessation treatment within 3 months of randomization. Outcomes were assessed at 3-month intervals through month 18. At each assessment, daily use of cigarettes, other tobacco products, and cessation medications were determined using the timeline follow-back method, which uses a calendar with specific anchor dates to help patients identify the quantity and frequency of tobacco use.[27] Exhaled carbon monoxide was obtained at every in-person assessment. Urine cotinine levels, measured using Accutest NicAlert test strips (JANT Pharmacal, Encino, California),[28] were ascertained at assessments when patients self-reported no use of tobacco or nicotine replacement therapy in the prior 7 days. Laboratory assays of urine cotinine were obtained when self-reported abstinence disagreed with test strip results. Patients missing 1 or more assessments were retained in the study and encouraged to return for future assessments.

Treatments Compared

Integrated Care. Posttraumatic stress disorder clinicians, largely psychologists and social workers, delivered IC in individual sessions using a treatment manual that adhered to evidence-based practices[13] and recommended interventions addressing specific PTSD symptoms dynamically related to smoking relapse.[16,29] Integrated care delivered 5 weekly core tobacco cessation sessions focusing on tobacco use education, behavioral skills for quitting smoking, setting a quit date (following session 5), and relapse prevention. Cessation medications, if desired by the patient, were prescribed before planned quit dates by medical staff managing the patient's pharmacological treatment of PTSD. Prescribers followed an algorithm detailing standard prescribing practices for nicotine replacement therapy, bupropion, and varenicline. Core sessions were followed up by 3 follow-up visits during which clinicians assessed tobacco use, reinforced abstinence and relapse prevention, and reapplied cessation treatment to continued smokers. Assignments from a participant workbook corresponded with treatment session topics. Booster sessions were administered monthly thereafter, providing assessment, relapse prevention, and reinstatement of smoking interventions. Sessions typically were incorporated into regularly scheduled PTSD visits but could be scheduled separately, if necessary.

The study used a "train the trainer" model in which PTSD clinic leaders received IC training at a national meeting and subsequently trained their respective site clinicians. Mayo Clinic experts reviewed audiotapes of 78 PTSD clinicians (92%) and found 66 (85%) were competent in treatment delivery, 8 (10%) were not found competent, and 4 (5%) submitted inaudible tapes.

Smoking Cessation Clinic. The SCC condition consisted of referral to specialized cessation clinics at each site and represented the usual standard of care within the VA. Smoking cessation clinics followed smoking cessation practice guidelines,[30] had clinic directors and patient care staff, provided treatment within 6 weeks of referral, and prescribed cessation medications directly or through patients' primary care clinicians. Participating SCCs reported a typical treatment course of 4 to 16 (median, 7) treatment sessions.

Outcome Measures

The primary outcome measure was 12-month prolonged abstinence from tobacco between 6- and 18-months postrandomization.[31] Prolonged abstinence excluded tobacco use before 6-months postrandomization to allow for initial treatment episode completion and recovery from early relapses. Prolonged abstinence defined nonabstinence as (1) smoking for 7 consecutive days or at least once a week for 2 consecutive weeks or (2) using noncigarette tobacco for 7 consecutive days or at least once a week for 2 consecutive weeks. Self-reported prolonged abstinence was verified by exhaled carbon monoxide of 8 ppm or less and urine cotinine of less than 100 ng/mL cotinine equivalents at the 9- through 18-month visits. Prolonged abstinence was determined for all patients. If carbon monoxide or cotinine was missing (eg, due to current nicotine replacement therapy use or telephone assessment), a single measure was used for verification. If both carbon monoxide and cotinine were missing at any visit between 9 and 15 months, patients reporting prolonged abstinence were considered abstinent if all other available bioverification data confirmed abstinence. Patients who lacked carbon monoxide and cotinine readings at 18 months or failed to attend the 18-month visit were considered nonabstinent.

Predetermined secondary smoking outcomes included 7- and 30-day point prevalence abstinence at each assessment, where abstinence was defined as no tobacco use in the prior 7 or 30 days, respectively. Self-reported point prevalence abstinence was determined for all patients, with patients not completing a visit presumed to be nonabstinent. If bioverification data were missing or did not confirm abstinence, patients were considered nonabstinent at that visit.

For patients who quit smoking for at least 24 hours, time to relapse was de-

fined as time to first tobacco use in which use occurred for 7 consecutive days or at any time during each of 2 consecutive weeks.[31]

Other predetermined secondary outcomes included severity of PTSD, measured by CAPS at 18 months (range, 0-136; scores of 60-79 indicate severe PTSD symptomatology)[24] and PTSD Checklist (range, 17-85; scores of ≥50 indicate a PTSD diagnosis)[32] at every assessment. The Patient Health Questionnaire 9 (PHQ-9; range, 0-27; scores of 10-14, 15-19, and ≥20 indicate mild, moderate, and severe depression, respectively)[33] measured depression at every assessment. Measures of treatment contact included number of cessation treatment sessions delivered (from VA electronic records) and self-reported use of smoking cessation medications.

Statistical Analysis

The target sample size (n = 1400) was designed to have 90% power to detect the difference between 6% and 11% prolonged abstinence rates in SCC and IC, respectively, using a 2-sided .05 level χ^2 test. An independent data and safety monitoring board regularly reviewed study data, including formal interim efficacy analyses performed on the primary outcome measure using the Lan-DeMet method with the O'Brien-Fleming–type boundary as a guide for stopping the study early.[34] Final enrollment was 943, because of lower than expected recruitment rate. Due to the data and safety monitoring board's recommendation, the recruitment period was not extended because the achieved sample size provided 78% power to detect the hypothesized prolonged abstinence rates, and the study continued to the end of planned follow-up.

Table 1. Baseline Patient Demographics (N = 943)[a]

Demographics	Integrated Care (n = 472)	Smoking Cessation Clinic (n = 471)
Age, mean (95% CI), y	54.4 (53.6-55.2)	54.7 (54.0-55.5)
Male sex[b]	444 (94.1)	439 (93.2)
Race/ethnicity		
White	272 (57.6)	275 (58.4)
Black	171 (36.2)	174 (36.9)
American Indian/Alaskan Native	7 (1.5)	4 (0.9)
Asian/Pacific Islander/Native Hawaiian	3 (0.6)	3 (0.6)
Other	19 (4.0)	15 (3.2)
Hispanic ethnicity	22 (4.7)	17 (3.6)
Marital status		
Married or remarried	212 (44.9)	217 (46.1)
Divorced or separated	194 (41.1)	187 (39.7)
Never married	48 (10.2)	47 (10.0)
Widowed	18 (3.8)	20 (4.3)
Period of service[c]		
Before Vietnam	10 (2.1)	14 (3.0)
Vietnam	362 (76.7)	369 (78.3)
Between Vietnam and Persian Gulf	68 (14.4)	63 (13.4)
Persian Gulf	57 (12.1)	41 (8.7)
Between Persian Gulf and Iraq/Afghanistan	30 (6.4)	28 (5.9)
Iraq/Afghanistan	66 (14.0)	62 (13.2)
Combat exposure	430 (91.1)	435 (92.4)
Employment status		
Unemployed/retired	363 (76.9)	366 (77.7)
Stable full or part time	94 (19.9)	88 (18.7)
Temporary full or part time	15 (3.2)	17 (3.6)
Education >12th grade	327 (69.6)	307 (65.2)

Abbreviation: CI, confidence interval.
[a] Data are presented as No. (%) unless otherwise specified.
[b] Randomization stratification factor.
[c] Percentages add up to more than 100% because multiple choices could be selected.

Analyses were conducted according to intention-to-treat. Baseline characteristics were compared using χ^2 tests or 2-sample *t* tests. Prolonged abstinence and point prevalence abstinence by visit were compared between treatment groups using logistic regression. Longitudinal point prevalence abstinence, PTSD Checklist, PHQ-9, and CAPS data were compared using generalized estimating equations. Analyses were adjusted for age, race, baseline CAPS, Fagerström Test for Nicotine Dependence, site, and 5 randomization stratification factors. Treatment × subgroup interactions were tested in regression models to assess whether the treatment effect was consistent across subgroups. Time from first 24-hour quit to relapse, censored at the earlier time of last follow-up or 18 months from randomization, was estimated using the Kaplan-Meier method and compared using the log-rank test and Cox proportional hazards regression model, both stratified by quartiles of time to first 24-hour quit. The Baron and Kenny method was used to assess whether differences in prolonged abstinence between IC and SCC were mediated by number of counseling sessions and days of medication use.[35] No adjustment was made for multiple comparisons. All analyses were performed using SAS version 9.2 (SAS Institute Inc, Cary, North Carolina). $P < .05$ was considered statistically significant.

RESULTS

Patient Characteristics

Demographic and baseline smoking characteristics, depression, and psychotropic medication use did not differ between the IC and SCC groups (TABLE 1 and TABLE 2). Both groups reported lengthy smoking histories and had CAPS scores indicative of severe PTSD. A total of 781 patients completed the 18-month assessment within the data collection window (Figure 1) and 70 provided historical 18-month data at a later date, for a total of 851 patients (90% of total sample). Compared with patients providing 18-month data, dropouts were significantly younger, smoked for fewer years, and had higher CAPS scores

(eTable 1, available at http://www.jama.com). Dropouts also were more likely to report Afghanistan or Iraq service and have current alcohol abuse or dependence in partial remission (eTable 1).

Outcome Measures

12-Month Prolonged Abstinence. Seventy-three patients (15.5%) in the IC group and 33 patients (7.0%) in the SCC group self-reported prolonged abstinence between 6 and 18 months (unadjusted odds ratio [OR], 2.43; 95% confidence interval [CI], 1.58-3.74; $P<.001$; and adjusted OR, 2.59; 95% CI, 1.67-4.02; $P<.001$). The IC group had a higher bioverified prolonged abstinence rate than the SSC group did, with 42 patients (8.9%) in IC and 21 patients (4.5%) in SCC achieving bioverified prolonged abstinence (unadjusted OR, 2.09; 95% CI, 1.22-3.59; $P=.007$; and adjusted OR, 2.26; 95% CI, 1.30-3.91; $P=.004$). The treatment effect was consistent across all subgroups (eFigure).

Bioverification failed to confirm prolonged abstinence for 43 of 106 patients (41.0%) who self-reported prolonged abstinence. Of these 43 patients, 13 (30.2%) had cotinine-confirmed abstinence (<100 ng/mL), but a carbon monoxide level of more than 8 ppm at 1 or more visits. Another 11 patients (25.6%) had carbon monoxide levels of more than 8 ppm and missing cotinine levels at 1 or more visits (carbon monoxide ≤10 ppm for 7 patients and >10 ppm for 4 patients). An additional 11 patients (25.6%) had cotinine levels of more than 100 ng/mL and 8 patients (18.6%) were missing 18-month bioverification.

Point Prevalence Abstinence. FIGURE 2 shows 7- and 30-day point prevalence abstinence. Bioverification confirmed 60% of self-reported 7-day abstinence and 63% of self-reported 30-day abstinence. The 7- and 30-day bioverified point prevalence abstinence rates were similar after 6 months. Differences in bioverified point prevalence abstinence between the IC and SCC groups were largest at 6 months for both 7-day (78/472 [16.5%] for IC vs 34/471 [7.2%] for SCC, $P<.001$) and 30-day (65/472 [13.8%] for IC vs 28/471 [5.9%] for SCC, $P=.001$) abstinence, and remained significant at 18 months (7-day abstinence: 86/472 [18.2%] for IC vs 51/471 [10.8%] for SCC, $P<.001$; and 30-day abstinence: 80/472 [16.9%] for IC vs 44/471 [9.3%] for SCC, $P<.001$). Assuming a common treatment effect over time, patients in the IC group were twice as likely as patients in the SCC group to achieve 7-day (OR, 2.09; 95% CI, 1.54-2.84; $P<.001$) and 30-day (OR, 2.17; 95% CI, 1.56-3.03; $P<.001$) abstinence between 3 and 18 months.

Time to Relapse. FIGURE 3 shows time to relapse for patients with a 24-hour quit between randomization and 18 months in the IC (n=361) and SCC (n=321) groups. Median (interquartile range) time to relapse following the initial 24-hour quit was 29 (18-42) days and 8 (7-12) days for the IC and SCC groups, respectively (stratified by quartiles of time to quit: hazard ratio, 0.72; 95% CI, 0.60-0.86; $P<.001$).

Table 2. Baseline Smoking, Depression, and Medication Characteristics (N = 943)[a]

Characteristics	Integrated Care (n = 472)	Smoking Cessation Clinic (n = 471)
Smoking characteristics		
Age when started smoking, mean (95% CI)	17.6 (17.1-18.2)	17.0 (16.6-17.5)
Years smoking cigarettes regularly, mean (95% CI)	34.5 (33.5-35.5)	35.1 (34.1-36.1)
Average cigarettes/d last 30 d, mean (95% CI)	21.9 (21.0-22.9)	21.4 (20.4-22.3)
≥25 cigarettes/d last 30 d	149 (31.6)	134 (28.5)
Daily smoker last 90 d	431 (91.3)	427 (90.7)
Prior quit lasting ≥1 y	143 (30.3)	160 (34.0)
Quit attempt in the past year	202 (42.9)	192 (40.8)
Past treatment in a VA smoking cessation clinic	156 (33.1)	147 (31.2)
Living with smokers past 90 d	176 (37.3)	203 (43.1)
Fagerström Test for Nicotine Dependence		
Minimally dependent (<4 points)	74 (15.7)	80 (17.0)
Moderately dependent (4-6 points)	213 (45.1)	238 (50.5)
Highly dependent (7-10 points)	185 (39.2)	153 (32.5)
DSM-IV diagnoses[b]		
Major depression current[c]	205 (47.2)	193 (45.0)
Major depression past only	121 (27.9)	134 (31.2)
Bipolar disorder past only	27 (6.3)	26 (6.2)
Psychotic disorder past only	11 (2.7)	15 (3.6)
Anxiety disorder current (excludes PTSD)	102 (24.8)	91 (22.2)
Anxiety disorder past only (excludes PTSD)	49 (11.9)	53 (12.9)
Current alcohol abuse/dependence in partial remission[c]	21 (4.8)	24 (5.5)
Alcohol disorder past only	325 (74.7)	331 (76.4)
Stimulant disorder past only	132 (30.1)	135 (31.1)
Cannabis disorder past only	125 (28.5)	126 (29.1)
Opioid disorder past only	63 (14.4)	60 (13.8)
Total score, mean (95% CI)		
CAPS (range, 0-136)	75.5 (73.8-77.2)	74.9 (73.3-76.6)
PTSD Checklist (range, 17-85)	59.6 (58.6-60.7)	58.9 (57.7-60.0)
PHQ-9 (range, 0-27)	13.6 (13.1-14.2)	13.4 (12.8-14.0)
Psychotropic medication use		
Antidepressants	347 (73.5)	356 (75.6)
Mood stabilizers	70 (14.8)	72 (15.3)
Sedative/hypnotics and anxiolytics	159 (33.7)	169 (35.9)
Antipsychotics	111 (23.5)	113 (24.0)

Abbreviations: CAPS, Clinician Administered PTSD Scale; CI, confidence interval; *DSM-IV*, *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition); PHQ-9, Patient Health Questionnaire 9; PTSD, posttraumatic stress disorder; VA, Veterans Affairs.

[a] Data are presented as No. (%) unless otherwise specified.

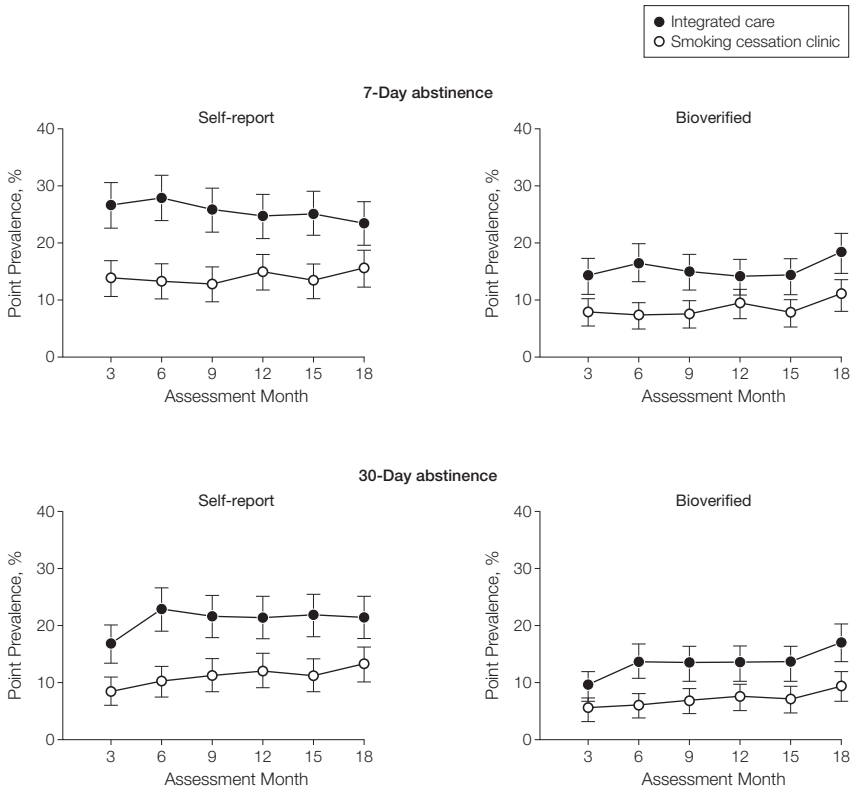
[b] Excludes Structured Clinical Interview for *DSM-IV* data from 1 site due to administration error.

[c] Randomization stratification factor.

Smoking Cessation Treatment Received

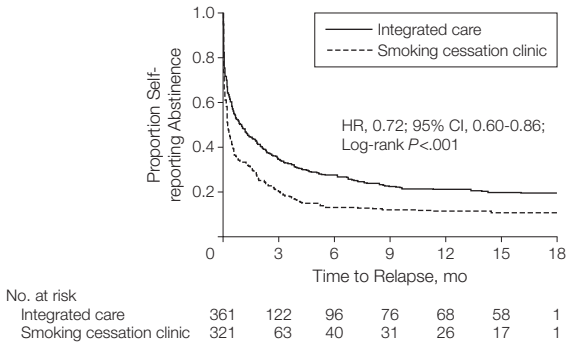
Patients in the IC group attended more cessation sessions than did patients in the SCC group and were more likely to use bupropion, nicotine polacrilex, and bupropion and nicotine replacement therapy in combination; the proportion of patients using any cessation medication was similar in both IC and SCC groups (TABLE 3). Total counseling sessions received and self-reported medication use days mediated 29.5% (95% CI, 26.6%-32.5%) and 9.6% (95% CI, 7.7%-11.5%) of the difference in prolonged abstinence between the IC and SCC groups, respectively.

Figure 2. Seven- and 30-Day Point Prevalence Abstinence by Treatment Condition



Error bars indicate 95% confidence intervals. Data are based on all 943 randomized patients. Patients with missing data were presumed to be nonabstinent. Data at the 3-, 6-, 9-, 12-, 15-, and 18-month assessments were collected an average of 96, 187, 280, 370, 461, and 566 days after randomization, respectively.

Figure 3. Months to Relapse Following Initial 24-Hour Quit Between Randomization and 18-Month Assessment (n=682)



No. at risk

Integrated care	361	122	96	76	68	58	1
Smoking cessation clinic	321	63	40	31	26	17	1

HR indicates hazard ratio; CI, confidence interval. A total of 111 patients from integrated care and 150 patients from smoking cessation clinic did not quit smoking for 24 hours between randomization and 18 months and were not included in the analysis. Time to relapse from first 24-hour quit was longer in integrated care than in smoking cessation clinic (stratified by quartiles of time to quit; log-rank test, $\chi^2_1=14.53$; $P<.001$).

Psychiatric Symptoms

Between baseline and 18 months, CAPS scores improved for patients in both IC and SCC groups by approximately 7 points, a 10% decrease in PTSD severity (eTable 2). Changes in CAPS scores did not differ between quitters and nonquitters (eTable 3). Over 18 months, no significant differences were observed between the IC and SCC groups on PTSD Checklist or PHQ-9 scores (eTable 2). Nonquitters worsened slightly on the PHQ-9 relative to quitters (differences ranged between 0.4 and 2.1, $P=.03$) (eTable 3), whose PHQ-9 scores did not change over time. Differences between quitters and nonquitters were not detected on the PTSD Checklist, with both groups reporting improvement over time (eTable 3).

Serious Adverse Events

The number of patients who experienced serious adverse events during the study did not differ significantly by treatment (218/472 [46%] for IC vs 220/471 [47%] for SCC, $P=.87$) or by prolonged abstinence (26/63 [41%] for abstinent vs 412/880 [47%] for nonabstinent, $P=.39$). The number with serious adverse events possibly related to the study was small (11/472 [2%] for IC vs 8/471 [2%] for SCC, $P=.49$). The serious adverse events that were possibly related to the study included 10 instances in 9 patients of psychiatric hospitalizations, 6 instances in 5 patients of life-threatening or potentially jeopardizing psychiatric conditions that did not result in hospitalization, 3 instances in 3 patients of medical hospitalizations (2 cardiac related and 1 gastrointestinal related), and 4 instances in 3 patients of life-threatening or potentially jeopardizing medical conditions that did not result in hospitalization (1 cardiac related, 2 gastrointestinal related, and 1 nervous system related).

COMMENT

Our study showed that integrating rather than separating treatment for PTSD and nicotine dependence improves smoking quit rates. Integrated care doubled prolonged abstinence compared with the SCC condition, was better on 7- and 30-day point prevalence abstinence at all measurement intervals, and increased time to relapse. The true number of patients in the IC group achieving abstinence may actually fall between the rigorous measure of biologically confirmed prolonged abstinence (8.9%) and less conservative outcomes of self-reported prolonged abstinence (15.5%) and 7-day point prevalence abstinence (range, 14.0%-18.2%). Of the 43 patients who self-reported prolonged abstinence but failed to meet bioverification criteria, nearly half had cotinine-confirmed abstinence with carbon monoxide readings of more than 8 ppm or missing cotinine with carbon monoxide readings of 10 ppm or less, raising the possibility that environmental exposures common in this population may have artificially elevated carbon monoxide readings.

Bioverified point prevalence abstinence for the IC group was comparable with cessation outcomes in studies of other psychiatrically ill smokers, including those with depression (14%-25%),[36,37] alcoholism (7%-19%),[38] and schizophrenia (7%-17%).[39] The IC prolonged abstinence rate cannot be gauged against other treatment trials involving mentally ill smokers because those studies did not report comparable long-term bioverified quit rates. Quit rates from our study were lower than those typically found for non-mentally ill smokers,[13] because smokers with mood and anxiety disorders often are more nicotine dependent and more likely to relapse following treatment.[40,41] Point prevalence abstinence remained steady between 6 and 18 months in both conditions, perhaps because patients could restart cessation treatment as needed during the 18-month study course. Concurrent with the study, the VA launched multiple initiatives to prioritize tobacco cessation, which may have facilitated cessation over time for all study patients.

The superior results of the IC group can be partially attributed to the greater number of cessation counseling sessions received by patients in this condition. The relationship between treatment length and intensity and favorable outcomes has been established in nonpsychiatrically ill smokers[13] and observed to be proportionately greater for smokers with past histories of depression.[40] Although the overall proportions of patients in the IC and SCC groups using cessation medications were similar, days of medication use were significantly higher for the IC group, possibly due to greater treatment contact. Number of counseling sessions received explained more of the treatment effect than total days of cessation medication use. The fact that less than 40% of the treatment effect was mediated by these 2 variables suggests that other factors contributed to effectiveness. These factors may include qualitative aspects of the therapeutic relationship, such as mental health clinicians' ability to motivate patients and skill in managing the dynamic interplay between psychiatric distress and smoking urges.

Worsening psychiatric symptoms have been linked to smoking cessation treatment participation[18] and quitting

Table 3. Smoking Cessation Treatment Received From Randomization to Month 18

Intervention	Integrated Care (n = 472)	Smoking Cessation Clinic (n = 471)	*P* Value
Behavioral Treatment Received[a]			
Total smoking cessation sessions received in assigned condition, median (IQR)	8 (4-12)	1 (0-4)	<.001
Smoking cessation sessions received in assigned condition, No. (%)			
0	47 (10.1)	152 (32.6)	<.001
1-2	33 (7.1)	150 (32.2)	
3-5	69 (14.8)	113 (24.2)	
6-8	97 (20.9)	27 (5.8)	
>8	219 (47.1)	24 (5.2)	
Attended ≥1 smoking cessation sessions in unassigned condition, No. (%)	10 (2.2)	1 (0.2)	.006
Pharmacotherapy Received[b]			
Any cessation medication used			
Patients reporting use, No. (%)	383 (84.0)	364 (79.3)	.07
Total days of use, median (IQR)[c]	104.0 (33.0-239.0)	68.5 (17.5-178.5)	<.001
Bupropion for smoking cessation			
Patients reporting use, No. (%)	188 (41.2)	134 (29.2)	<.001
Total days of use, median (IQR)[c]	132.0 (49.0-298.0)	122.0 (37.0-312.0)	.92
Any nicotine replacement therapy			
Patients reporting use, No. (%)	317 (69.5)	301 (65.6)	.20
Total days of use, median (IQR)[c]	44.0 (13.0-113.0)	33.0 (12.0-90.0)	.07
Nicotine patch			
Patients reporting use, No. (%)	234 (51.3)	224 (48.8)	.45
Total days of use, median (IQR)[c]	29.0 (10.0-64.0)	28.0 (8.0-63.5)	.31
Nicotine polacrilex, gum, and/or lozenge			
Patients reporting use, No. (%)	171 (37.5)	140 (30.5)	.03
Total days of use, median (IQR)[c]	43.0 (8.0-126.0)	24.5 (7.5-86.0)	.06
Bupropion plus any nicotine replacement therapy			
Patients reporting use, No. (%)	100 (21.9)	60 (13.1)	<.001
Total days of use, median (IQR)[c]	29.5 (11.0-61.5)	27.0 (14.0-60.0)	.73
Varenicline[d]			
Patients reporting use, No. (%)	56 (12.3)	54 (11.8)	.81
Total days of use, median (IQR)[c]	65.0 (30.0-110.5)	40.5 (24.0-89.0)	.11

Abbreviation: IQR, interquartile range.
[a] Data not available for 7 patients in integrated care and 5 patients in smoking cessation clinic.
[b] Data not available for 16 patients in integrated care and 12 patients in smoking cessation clinic.
[c] Days of use calculated for patients self-reporting any use only.
[d] Varenicline did not become available within the Veterans Health Administration until year 3 of the study and was used as a second-line agent; therefore, it was not available to all patients.

smoking[17] in persons with positive depression histories. In our study, patients showed no overall deterioration in psychiatric status regardless of treatment assignment. In fact, 18-month follow-up CAPS scores improved equally for patients in the IC and SCC groups, and the 10% reduction in PTSD symptoms is comparable with that observed in some PTSD clinical trials enrolling highly selected VA patients.[42] Thus, IC did not detract from effectiveness of PTSD treatment. Quitters showed slight improvement on PTSD symptoms and little change in depression, substantiating other reports of no adverse effects of smoking cessation in patients with current PTSD,[14] depression,[43] or past histories of depression.[44,45] Unlike patients in investigations showing deteriorating psychiatric status from smoking cessation,[17,18] patients in our study were engaged in ongoing psychiatric care, which may have attenuated potential adverse effects on mental status of nicotine withdrawal. Such findings counter beliefs that addressing cessation during mental health care detracts from effective treatment of primary mental health concerns and leads to increased instability in smokers with active mental health symptoms.

Our findings are limited by the selected sample, predominantly older male Vietnam-era veterans with chronic PTSD and co-occurring depression, but without current bipolar, psychotic, and substance dependence disorders. Results may not generalize to nonveterans or persons with other psychiatric disorders. Given the relative ease of implementation (manualized treatment with minimal training requirements) and demonstrated effectiveness of IC for smokers with PTSD, future research should translate IC into other practice settings with different populations of psychiatrically ill smokers. Efforts should also be focused on younger Iraq and Afghanistan veterans, who exhibited higher rates of attrition than other veterans. Testable methods for improving outcomes could include increasing the duration of treatment, enhancing pharmacotherapy, adding contingencies for cessation, and telephone or Internet supplements. Although the majority of IC clinicians delivered the treatment as designed, a small minority failed to do so, which may have produced less favorable IC outcomes. Staff obtaining outcome data were not blinded with respect to treatment condition; however, the use of objective outcome measures such as bioverified abstinence lessens the likelihood that outcomes were biased.

This investigation was designed as a practical clinical trial applicable to real world settings, using a clinically relevant comparison group, broad inclusion criteria, and practitioners from diverse health care settings who were not tobacco cessation experts.[46] Delivering cessation assistance as part of primary mental health treatment was both more effective than referral and led to greater intensity of treatment utilization, a major factor in treatment effectiveness. Integrated care could be applied to the sizable proportion of smokers among the approximately 400 000 veterans enrolled in VA care for PTSD. Study findings have further potential to extend to the 10 million individuals in the United States who receive mental health treatment annually,[47] of whom an estimated 41% are smokers.[3] Initiatives to disseminate IC as an evidence-based practice within the VA are under way to meet the challenge of making tobacco cessation treatments available to veterans who need them. These efforts take on particular salience with the cohort of younger Iraq and Afghanistan veterans with PTSD for whom stopping smoking now could prevent long-term adverse health sequelae.

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