Original Investigation

Screening and Brief Intervention for Drug Use in Primary Care
The ASPIRE Randomized Clinical Trial

Richard Saitz, MD, MPH; Tibor P. A. Palfai, PhD; Debbie M. Cheng, ScD; Daniel P. Alford, MD, MPH; Judith A. Bernstein, PhD, RN, MSN; Christine A. Lloyd-Travaglini, MPH; Seville M. Meli, MPH; Christine E. Chaisson, MPH; Jeffrey H. Samet, MD, MPH, MA

IMPORTANCE The United States has invested substantially in screening and brief intervention for illicit drug use and prescription drug misuse, based in part on evidence of efficacy for unhealthy alcohol use. However, it is not a recommended universal preventive service in primary care because of lack of evidence of efficacy.

OBJECTIVE To test the efficacy of 2 brief counseling interventions for unhealthy drug use (any illicit drug use or prescription drug misuse)—a brief negotiated interview (BNI) and an adaptation of motivational interviewing (MOTIV)—compared with no brief intervention.

DESIGN, SETTING, AND PARTICIPANTS This 3-group randomized trial took place at an urban hospital-based primary care internal medicine practice; 528 adult primary care patients with drug use (Alcohol, Smoking, and Substance Involvement Screening Test [ASSIST] substance-specific scores of ≥4) were identified by screening between June 2009 and January 2012 in Boston, Massachusetts.

INTERVENTIONS Two interventions were tested: the BNI is a 10- to 15-minute structured interview conducted by health educators; the MOTIV is a 30- to 45-minute intervention based on motivational interviewing with a 20- to 30-minute booster conducted by master's-level counselors. All study participants received a written list of substance use disorder treatment and mutual help resources.

MAIN OUTCOMES AND MEASURES Primary outcome was number of days of use in the past 30 days of the self-identified main drug as determined by a validated calendar method at 6 months. Secondary outcomes included other self-reported measures of drug use, drug use according to hair testing, ASSIST scores (severity), drug use consequences, unsafe sex, mutual help meeting attendance, and health care utilization.

RESULTS At baseline, 63% of participants reported their main drug was marijuana, 19% cocaine, and 17% opioids. At 6 months, 98% completed follow-up. Mean adjusted number of days using the main drug at 6 months was 12 for no brief intervention vs 11 for the BNI group (incidence rate ratio [IRR], 0.97; 95% CI, 0.77-1.22) and 12 for the MOTIV group (IRR, 1.05; 95% CI, 0.84-1.32; P = .81 for both comparisons vs no brief intervention). There were also no significant effects of BNI or MOTIV on any other outcome or in analyses stratified by main drug or drug use severity.

CONCLUSIONS AND RELEVANCE Brief intervention did not have efficacy for decreasing unhealthy drug use in primary care patients identified by screening. These results do not support widespread implementation of illicit drug use and prescription drug misuse screening and brief intervention.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT00876941

Editorial page 488

Author Video Interview at jama.com

Related articles pages 492 and 543

Supplemental content at jama.com

Author Affiliations: Department of Community Health Sciences, Boston University School of Public Health, Boston, Massachusetts (Saitz, Bernstein, Meli, Samet); Clinical Addiction Research and Education (CARE) Unit, Section of General Internal Medicine, Department of Medicine, Boston Medical Center and Boston University School of Medicine, Boston, Massachusetts (Saitz, Cheng, Alford, Samet); Department of Psychology, Boston University, Boston, Massachusetts (Palfai); Department of Biostatistics, Boston University School of Public Health, Boston, Massachusetts (Cheng); Data Coordinating Center, Boston University School of Public Health, Boston, Massachusetts (Lloyd-Travaglini, Chaisson).

Corresponding Author Richard Saitz, MD, MPH, Community Health Sciences, Boston University School of Public Health, 801 Massachusetts Ave, 4th Floor, Boston, MA 02118 (rsaitz@bu.edu).

JAMA. 2014;312(5):502-513. doi:10.1001/jama.2014.7862

Screening and brief intervention (SBI) for unhealthy alcohol use is among the most efficacious and cost-effective of preventive services[1]; systematic reviews support their recommendation by the US Preventive Services Task Force (USPSTF). Based in part on extrapolation from these data, the United States has invested heavily over the past decade to disseminate and implement SBI for alcohol and other drugs.[2,3] Federal health agencies encourage SBI for illicit drug use and prescription drug misuse.[4,5]

A commonly implemented model is a single-session intervention delivered by trained health educators for patients across a range of severity from risky use through severe disorders.[6] Yet the best evidence for efficacy for addressing unhealthy alcohol use is by multicontact intervention by primary care physicians.[7] And the USPSTF concluded that the evidence was insufficient to recommend SBI for unhealthy drug use.[8] That same year, based in part on efficacy for unhealthy alcohol use and on results of preliminary studies for drug use,[9] the National Institute on Drug Abuse (NIDA) called for research on drug SBI efficacy.[10,11]

ASSIST *Alcohol, Smoking, and Substance Involvement Screening Test*

BNI *brief negotiated interview*

MOTIV *adaptation of motivational interviewing*

SBI *screening and brief intervention*

SBIRT *Screening, Brief Intervention, Referral, and Treatment*

TLFB *Timeline Followback*

The objective of our study was to test the efficacy and effectiveness of 2 brief interventions for "unhealthy drug use," defined as illicit drug use or addictive prescription drug misuse (without a prescription or more than prescribed), among primary care patients identified by screening.

Methods

The Assessing Screening Plus Brief Intervention's Resulting Efficacy to Stop Drug Use (ASPIRE) study was a 3-group randomized trial that tested the efficacy of 2 brief interventions for unhealthy drug use—a brief negotiated interview (BNI) and an adaptation of motivational interviewing (MOTIV)—compared with no brief intervention in primary care patients identified by screening as using illicit or misusing prescription drugs. (See trial protocol in Supplement 1.)

Participants

Health educators employed by the hospital in a federally funded Screening, Brief Intervention, Referral, and Treatment (SBIRT) program[12] screened all patients not previously screened in the past year at an urban academic hospital-based primary care clinic (a clinical program in existence prior to ASPIRE study implementation). During the ASPIRE study, health educators and research assistants trained in that same role screened patients for past 3-month unhealthy drug use by asking the second item of the Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST)[13] with minor modifications for local relevance (eg, mention of Klonopin, not Serepax as an example of a sedative and Ritalin as an example of a stimulant). Patients screened positive by the health educators were referred immediately to research assistants. Research assistants completed further screening for study eligibility. Patients were screened at the time of clinic visits in private clinic space.

Eligibility criteria were (1) age 18 years or older; (2) arrived for a visit with a primary care clinician; and (3) substance-specific ASSIST score 4 or greater, which means drug use weekly or more in the past 3 months or less frequent use but with a consequence.[13] Exclusion criteria were (1) inability to provide contact information for 2 persons; (2) inability to interview and consent in English; (3) unwilling or unable to participate in follow-up; (4) pregnancy (self-report); (5) brief intervention by preexisting SBIRT program in past 3 months; or (6) participation in on-site addiction treatment program.

Participants provided written informed consent and received compensation for study assessments. The institutional review board approved the study, including follow-up of incarcerated participants, and we obtained a certificate of confidentiality from the National Institutes of Health.

Assessments

At study entry, we assessed the following by in-person interview: demographics, tobacco use, ASSIST alcohol and drug items,[13] the participant's main drug ("Which substance used in the past month concerns you most?"), Timeline Followback (TLFB) for the main drug (a validated calendar method that determines drug use on each day in the past month),[14] 3 items assessing past-month drinking,[15] the short form Composite International Diagnostic Interview for drug dependence,[16] the 15-item Short Inventory of Problems-Drugs (SIP-D),[17] stage of readiness to change,[18] HIV sex and drug risk behaviors[19,20] using audio-assisted computer self-interview, depression (Patient Health Questionnaire [PHQ-9]),[21] the Overall Anxiety Severity and Impairment Scale (OASIS),[22] health status (EuroQol),[23] and health care utilization and mutual help meeting attendance (Form 90 Alcohol Intake Revised-Economic Development [AIR/ED]).[24] Medical diagnoses were recorded from the electronic record (**Table 1**).[25-28] Hair samples providing a 90-day window of use were tested for drugs by enzyme-linked immunosorbent assay and gas chromatography-mass spectrometry (Psychemedics). Assessments were repeated 6 months later. At 6 weeks, we asked the TLFB for the main drug and SIP-D (30-day time frames) and utilization and mutual help items since study entry by telephone.

Randomization, Interventions, and Control

After the baseline assessment, the data coordinating center randomly assigned participants (1:1:1) to receive BNI, MOTIV, or no brief intervention via a central secure website using random permuted blocks of size 3 and 6 stratified by drug dependence and main drug.

Interventions were audio-recorded. Results of screening (risky use or likely disorder) and any interest in a referral were communicated to the primary care clinician via the electronic medical record. Counselors prepared by reviewing ASSIST results. Those providing the MOTIV also reviewed medical records and additional assessment responses.

Table 1. Demographics, Health Status, and Health Care Utilization of Primary Care Patients With Unhealthy Drug Use Identified by Screening

Characteristic	Study Entry (n = 528)				6 Months (n = 517)			
	Overall	BNI	MOTIV	Control	Overall	BNI	MOTIV	Control
Male sex, No. (%)	369 (69.9)	124 (71.3)	126 (71.2)	119 (67.2)				
Race/ethnicity, No. (%)[a]								
Black	357 (68.8)	116 (68.2)	126 (72.4)	115 (65.7)				
Hispanic	50 (9.6)	18 (10.6)	11 (6.3)	21 (12.0)				
White	105 (20.2)	32 (18.8)	37 (21.3)	36 (20.6)				
Other	7 (1.4)	4 (2.4)	0	3 (1.7)				
Age, mean (SD), y	41.3 (12)	40.0 (12.2)	42.6 (12.2)	41.3 (12.5)				
High school graduate or equivalent, No. (%)	369 (69.9)	119 (68.4)	127 (71.8)	123 (69.5)				
Never married, No. (%)	328 (62.1)	105 (60.3)	108 (61.0)	115 (65.0)				
Health insurance, No. (%)								
Private/commercial[b]	69 (13.1)	24 (13.8)	18 (10.2)	27 (15.3)				
Medicaid/Medicare[c]	429 (81.3)	138 (79.3)	153 (86.4)	138 (78.0)				
None	30 (5.7)	12 (6.9)	6 (3.4)	12 (6.8)				
Any substance use–related health condition, No. (%)[d]	450 (85.2)	145 (83.3)	156 (88.1)	149 (84.2)				
Comorbid illnesses (most common), No. (%)[e]								
Mood disorders	243 (46.0)	74 (42.5)	87 (49.2)	82 (46.3)				
Nontraumatic joint disorders	161 (30.5)	55 (31.6)	53 (29.9)	53 (29.9)				
Spondylosis/disc/back problems	156 (29.6)	50 (28.7)	46 (26.0)	60 (33.9)				
Hypertension	149 (28.2)	46 (26.4)	50 (28.3)	53 (29.9)				
Skin disorders	146 (27.7)	42 (24.1)	53 (29.9)	51 (28.8)				
Health-related quality of life, mean (SD)[f]	70.3 (20.4)	70.8 (18.8)	68.5 (22.4)	71.5 (19.6)	70.7 (20.3)	71.5 (19.4)	68.5 (20.7)	72.1 (20.6)
Depressive symptoms (PHQ-9 ≥10), No. (%)[g]	189 (35.8)	63 (36.2)	66 (37.3)	60 (33.9)	153 (29.7)	43 (25.4)	53 (30.8)	57 (32.6)
Anxiety symptoms (OASIS ≥8), No. (%)[h]	176 (33.3)	59 (33.9)	60 (33.9)	57 (32.2)	163 (31.5)	49 (29.0)	55 (31.8)	59 (33.7)
Hospitalization past 3 mo, No. (%)	75 (14.2)	25 (14.4)	18 (10.2)	32 (18.1)	81 (15.7)	23 (13.6)	34 (19.8)	24 (13.7)
Hospitalization, addiction or mental health related past 3 mo, No. (%)	29 (5.5)	12 (6.9)	10 (5.7)	7 (4.0)	30 (5.8)	10 (5.9)	12 (7.0)	8 (4.6)
ED visit past 3 mo, No. (%)	189 (35.8)	65 (37.4)	59 (33.3)	65 (36.7)	152 (29.4)	49 (29.0)	51 (29.5)	52 (29.7)
ED visit for addiction or mental health past 3 mo, No. (%)	47 (8.9)	12 (6.9)	17 (9.6)	18 (10.2)	41 (7.9)	13 (7.7)	11 (6.4)	17 (9.7)
Mutual help group participation past 3 mo, No. (%)	93 (17.6)	28 (16.1)	36 (20.3)	29 (16.4)	93 (18.0)	34 (20.1)	31 (17.9)	28 (16.0)
Residential stay for addiction or mental health past 3 mo, No. (%)	43 (8.1)	14 (8.1)	15 (8.5)	14 (7.9)	46 (8.9)	15 (8.9)	13 (7.5)	18 (10.3)
Outpatient addiction or mental health treatment or counseling past 3 mo, No. (%)[i]	119 (22.6)	33 (19.1)	56 (31.6)	30 (17.0)	125 (24.2)	45 (26.6)	47 (27.2)	33 (19.0)

Abbreviations: BNI, brief negotiated interview; ED, emergency department; MOTIV, adaptation of motivational interviewing; OASIS, Overall Anxiety Severity and Impairment Scale; PHQ-9, Patient Health Questionnaire.

[a] Race was assessed by patient self-report to describe the sample and because it is required of NIH-funded studies and for reporting to the institutional review board. Classifications were black or African American, white, Asian, Alaska native, Native Hawaiian/other Pacific Islander, American Indian, and none. Hispanic or Latino ethnicity was asked separately. In this table, those reporting Hispanic and black are categorized as black; those categorized as white or other do not include those reporting Hispanic ethnicity.

[b] 22 participants had private insurance plus Medicare, Medicaid, or both.

[c] 317 participants had Medicaid only, 10 Medicare only, and 102 both.

[d] Includes diagnostic codes from electronic medical records at the medical center within 90 days prior to study entry. Diagnoses were selected based on published literature (see Methods). Examples include chronic obstructive pulmonary disease, hypertension, injuries, depression, cirrhosis, HIV, hepatitis C, cellulitis, and drug-induced mental disorders (full listing available on request).

[e] Includes diagnostic codes from electronic medical records at the medical center within 90 days prior to study entry. Codes were grouped using Clinical Classifications Software (http://www.hcup-us.ahrq.gov/toolssoftware/ccs/ccs.jsp) with some reclassified or grouped based on clinical judgment and cell sizes.

[f] EuroQol range, 0-100; higher score indicates better perceived health.

[g] Range, 0-27; higher score means worse depressive symptoms.

[h] Total score ranges from 0-20; higher score means worse anxiety.

[i] Only variable statistically significantly different across groups at baseline.

The BNI was a single 10- to 15-minute structured interview conducted by health educators, all of whom had at least completed high school or the equivalent and had human services experience or a bachelor's degree. The BNI uses some features of motivational interviewing[2] and includes feedback, review of the "pros and cons" of use, and development of a plan for change.

The MOTIV group received 30 to 45 minutes of motivational interviewing with an offered 20- to 30-minute booster follow-up session conducted by counselors who had a master's degree. The MOTIV program was less structured than BNI and included eliciting possible links between drug use and health concerns, heightening discrepancies between negative drug use outcomes and valued goals, enhancing self-efficacy about behavior change, and providing options for change.

Both interventions focused on the participant's main drug but addressed alcohol and other drugs if they emerged as relevant; alcohol was a substance of concern for only 15%. There were 14 BNI and 4 MOTIV counselors. Intervention fidelity was assessed by coding all audible intervention recordings using the Motivational Interviewing Treatment Integrity (MITI) 3.1.1 instrument and an instrument developed for this study.[29] Scores on these rating scales suggested that interventionists used a motivational interviewing style for both interventions (although minimally so for BNI) and adequately delivered the interventions. Ratings on the study-specific measure indicated discriminability between the study interventions. Details about the interventions appear in the eMethods in Supplement 2.

Participants assigned to the control group received no brief intervention. All participants, both intervention and control, were given information on how to contact Alcoholics Anonymous, Narcotics Anonymous, the hospital behavioral health clinic and emergency team, a state hotline, a city triage line, and websites for alcohol and drug screening.

Outcomes

The primary outcome was percentage of days using the main drug determined at study entry, assessed at 6 months using the 30-day TLFB. The distribution of the primary outcome was nonnormal even after attempts at transforming the data (eg, log transformation); thus, we analyzed the number of days of use as count data. At 6 weeks, days using the main drug and using the main drug more than once (in the past 30 days), SIP-D, and self-reported health utilization were secondary outcomes, as were, at 6 months, the following: number of days using the main drug more than once (in past 90 days), any drug use, any drug or heavy alcohol use (>3 standard drinks for women, >4 standard drinks for men in a day), use of ASSIST-specified drugs (marijuana, cocaine, opioids, sedatives, amphetamines, hallucinogens, inhalants), drugs (any, amount, and decreases) by hair testing, any injection drug use,[19,20] ASSIST scores (main substance specific, substance specific, and global), SIP-D, any unsafe sex and number of times (vaginal or anal intercourse without a condom), and self-reported utilization of health services.

Statistical Analyses

We conducted all analyses on an intention-to-treat basis: participants were analyzed according to randomized assignment regardless of whether they received the intervention. The 2 main comparisons were between each intervention vs control. We corrected for multiple comparisons within each outcome using the Hochberg sequential test procedure.[30] The primary outcome and other count outcomes were analyzed using negative binomial regression models chosen instead of Poisson because of overdispersion in the data (ie, the variance exceeds the mean), adjusting for the randomization stratification variables; baseline value of the outcome; and addiction- or mental health–related outpatient visits (except in the analysis of any outpatient care), the only variable statistically significantly different across groups at baseline.

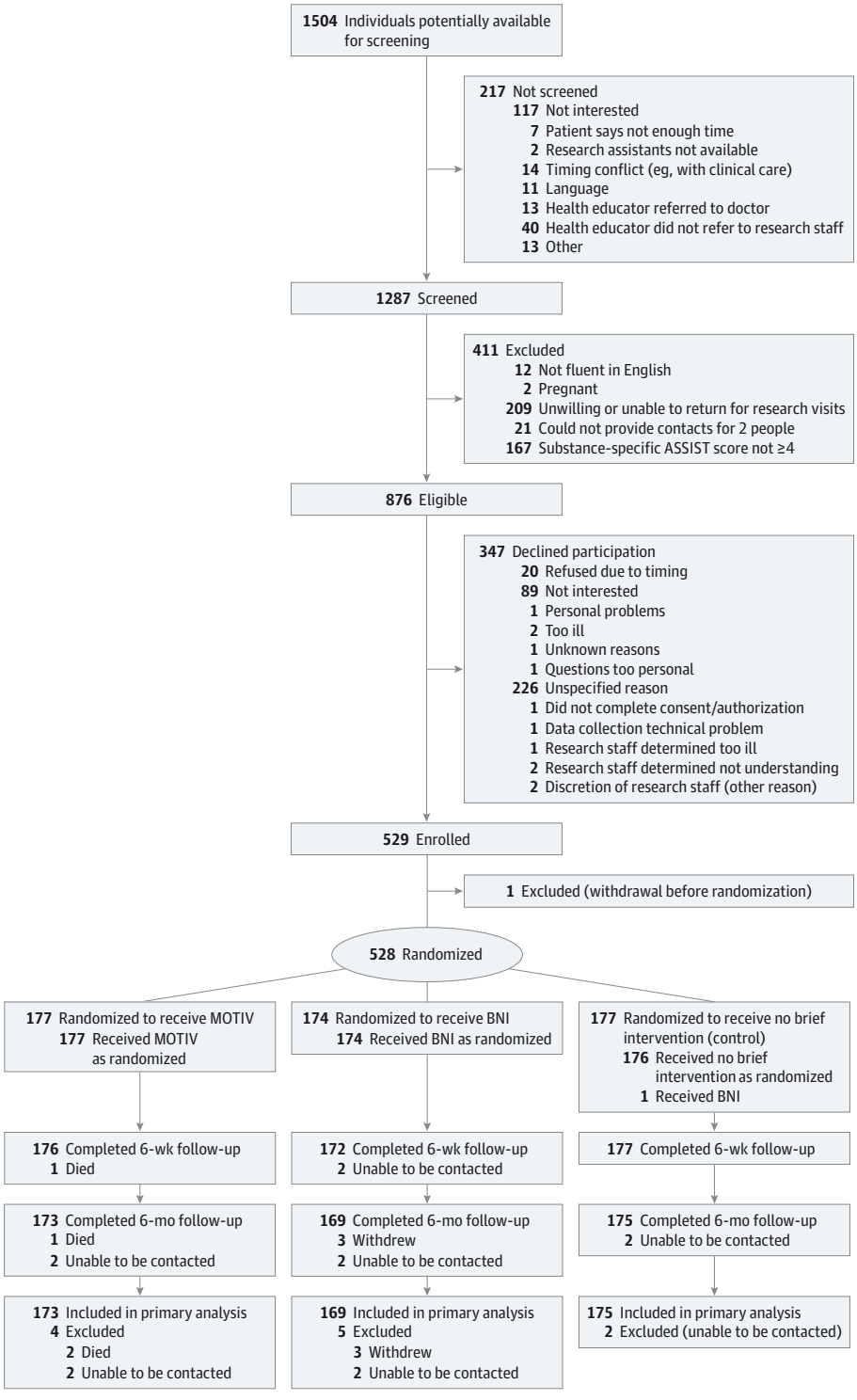
Dichotomous outcomes were analyzed similarly using logistic regression. When events were sparse, we used Fisher exact test. For the ASSIST outcomes and quantitative hair variables, quantile regression[31,32] was used because the distributions were nonnormal. Median regression was used in all cases except substance-specific ASSIST scores where computational difficulties arose due to excess zeros; therefore, the 90th quantile was modeled. To describe the magnitudes of association across prespecified subgroups, we stratified analyses by risk for drug dependence (ie, ASSIST substance-specific score for main drug ≥27) and by main drug. To assess potential effect modification, we tested interactions between randomization group and readiness to change, past month heavy drinking episode and substance use–related health condition (and anxiety, depressive symptoms, and pain, post hoc). In post hoc exploratory analysis, we compared receipt of a booster (MOTIV group) vs control using the same analytic methods as for the primary outcome.

Only observed data were used in the primary analysis; missing data were not imputed. However, results were confirmed using multiple imputation analysis (in 20 generated data sets) to account for missing data for the primary outcome. Variables used for imputation were age, sex, and the variables in the primary analysis. The study was initially designed to have 80% power, but because of feasibility, we enrolled a sample for 90% power to detect an absolute difference of 14.7% in percentage of days with drug use in a sample of 528 participants, assuming 10% loss to follow-up and using 2-sided tests and an overall α of .05 (for power calculations, the primary pairwise comparisons of each intervention vs control was set at $\alpha = .025$). Thus, the study was powered to detect intervention effects among the full sample but not for subgroup analyses, which were conducted for exploratory purposes. All statistical analyses were performed using SAS version 9.2 (SAS Institute).

Results

Study participants were enrolled June 1, 2009, to January 31, 2012, and follow-up continued until October 2012. During study enrollment, 25 302 SBIRT clinical program screenings for drug use were done in primary care, and 2624 patients (10%) were

Figure. Enrollment and Follow-up Flow Diagram for ASPIRE Study of Brief Interventions for Unhealthy Drug Use



ASSIST indicates Alcohol, Smoking, and Substance Involvement Screening Test, BNI, brief negotiated interview; MOTIV, an adaptation of motivational interviewing.

positive for any use in the past 3 months. When research staff were in clinic, 1504 patients were potentially available for study screening, 1287 completed eligibility screening, and 876 were eligible (**Figure**). Of those eligible, 528 (60%) were randomized. Compared with those eligible who did not enroll, patients who enrolled in the study were more likely to be black (68% vs 60%), less likely to report marijuana as their main drug (63% vs 80%), and more likely to use cocaine (26% vs 12%) and opioids (24% vs 16%); they had higher global and main drug ASSIST scores (median, 15 vs 12 and 15 vs 11, respectively); and

they were more likely to have ASSIST scores of 27 or greater (18% vs 7%) and to use more than 1 drug (32% vs 17%).

Of those randomized, 525 of 528 participants (99%) had 6-week follow-up data and 517 of 528 (98%) had 6-month follow-up data; there were no significant differences in follow-up between groups. Baseline characteristics (Table 1, **Table 2**, and **Table 3**) were similar across randomization groups except for past outpatient addiction or mental health treatment. At study entry, the mean (SD) number of days using the main drug was 14.4 (11.5) and the median was 12 (interquartile range [IQR], 3-27); at 6 weeks, the mean (SD) was 12.3 (11.9) days and median, 8 (IQR, 1-26); and at 6 months, the mean (SD) was 14.0 (12.2) days and the median, 11 (IQR, 2-29). Almost all baseline hair samples tested positive for drugs at baseline (Table 3).

All participants received their assigned intervention. One assigned to the control group received a BNI, 158 of 351 participants (45%) received a referral to addiction treatment services, and 54 of 177 participants (31%) received a MOTIV booster session.

Main Results

For the primary outcome (**Table 4**), there were no significant differences between the BNI or MOTIV group and the control group (adjusted mean days using the main drug at 6 months, 11 and 12 vs 12, respectively; BNI adjusted incidence rate ratio [aIRR], 0.97; 95% CI, 0.77-1.22; MOTIV aIRR, 1.05; 95% CI, 0.84-1.32). Similarly, in analyses stratified separately by main drug and risk for drug dependence, there were no significant differences between the intervention groups and the control group. There was no significant interaction between randomization group and either readiness to change ($P = .61$), any heavy drinking day in the past month ($P = .94$), or substance-related health condition ($P = .17$) on the primary outcome, number of days (in the past 30 days) using the main drug. Receipt of a MOTIV booster session, compared with no brief intervention, also had no significant effect on the primary outcome (aIRR, 0.96; 95% CI, 0.68-1.34). Results of the multiple imputation analysis were consistent with the main analysis.

Other Drug Use Measures and 6-Week Results

There were no significant differences at 6 months overall (eTable 1 in Supplement 2) or in analyses stratified by main drug or by risk for drug dependence (eTable 2 in Supplement 2) in any drug use, any heavy alcohol or drug use, ASSIST substance-specific score for the main drug, global ASSIST score, 1 or more days using the main drug, and days using the main drug (in the past 90 days). There were no differences overall (eTable 1) or in analyses stratified by main drug or by risk for drug dependence (eTable 2) in use of ASSIST specified drugs. At 6 weeks, there were also no significant differences between groups overall and in analyses stratified by main drug or risk for drug dependence (eTable 3 in Supplement 2).

Hair Testing

There were no significant differences in the proportions of participants testing positive for use of any of the drugs listed in Table 3 (BNI, 95%; MOTIV, 93%; control, 91%) at 6 months (BNI odds ratio [OR], 1.65; 95% CI, 0.64-4.23; MOTIV OR, 1.25; 95% CI, 0.52-3.00) (eTable 4 in Supplement 2). Similarly, there were no significant differences between groups in detection of cocaine or benzoylecgonine, opioids, or carboxy-tetrahydrocannabinol. In sensitivity analyses (missing values assumed positive), there were also no significant differences. There were no significant group differences in concentrations of or decreases in drugs (quantitative hair testing).

Drug Use Consequences and Health Care Utilization (Including Addiction Treatment)

There were no significant between-group differences overall (eTable 1) or in stratified analyses at 6 weeks (eTable 3) or 6 months (eTable 2) in drug use consequences (SIP-D), injection drug use, unsafe sex, health care utilization (hospitalizations and emergency department visits, overall or for addiction or mental health reasons), or mutual help group attendance.

Discussion

This study is among the first to test the efficacy of SBI for illicit drug use and prescription drug misuse in adults in primary care. In patients identified by screening, neither a BNI nor a MOTIV had efficacy for decreasing drug use as assessed by numerous self-report and biological measures, drug use consequences, addiction or mental health care utilization, mutual help meeting attendance, or other health care utilization. In the primary analyses, the point estimate for days using the main drug was generally higher in the MOTIV group compared with the control group, raising the possibility of harm, although not statistically significant and not a hypothesized effect. The lack of effect was consistent regardless of drug used, severity, alcohol use, readiness to change, or presence of a substance-related health condition. More than 90% of participants still had laboratory evidence of drug use at the 6-month follow-up.

Brief intervention trials to address illicit drug use and prescription drug misuse are critical before widespread implementation that assumes efficacy. Although motivational interventions are often effective among people seeking help,[33] efficacy among patients identified by screening (eg, for risky alcohol use) may not translate to reductions in drug use. The approach is the same as that proven efficacious for alcohol. Patients with marijuana use or risky alcohol use who are unaware of any consequences are motivated to make changes when they, as a result of counseling, perceive risks that are inconsistent with their values and behaviors. This change occurs even if before counseling they perceive no obvious risks, which is likely the case for many with low levels of risky alcohol or marijuana use. For those with consequences (eg, recurrent injury related to alcohol intoxication, job loss due to poor performance related to marijuana use), these problems serve as a starting point for discussion.

Table 2. Drug Use Among Primary Care Patients With Unhealthy Drug Use Identified by Screening

Characteristic	Study Entry (n = 528)				6 Months (n = 517)			
	Overall	BNI	MOTIV	Control	Overall	BNI	MOTIV	Control
Substance Use								
Main drug, No, (%)[a]								
Opioid (includes heroin, prescription, and others)	90 (17.1)	31 (17.8)	28 (15.8)	31 (17.5)				
Prescription opioid only	30 (5.7)	8 (5.7)	10 (5.7)	12 (6.8)				
Cocaine	98 (18.6)	32 (18.4)	33 (18.6)	33 (18.6)				
Marijuana	331 (62.7)	109 (62.6)	111 (62.7)	111 (62.7)				
CIDI-SF positive[b]	245 (46.4)	80 (46.0)	83 (46.9)	82 (46.3)				
Tobacco use past year	403 (76.3)	142 (81.6)	130 (73.5)	131 (74.0)				
Days using main drug past 30 d								
Median (IQR)	12.0 (3.0-27.0)	14.0 (3.0-28.0)	10.0 (3.0-27.0)	12.0 (3.0-28.0)	11.0 (2.0-29.0)	11.0 (2.0-29.0)	11.0 (2.0-28.0)	9.0 (2.0-29.0)
Mean (SD)	14.4 (11.5)	15.1 (11.7)	13.8 (11.2)	14.3 (11.4)	14.0 (12.2)	14.2 (12.5)	14.1 (12.1)	13.8 (12.1)
Days >1 time using main drug past 30 d								
Median (IQR)	5.0 (0.0-18.0)	5.5 (0.0-21.0)	4.0 (0.0-16.0)	5.0 (0.0-14.0)	3.0 (0.0-23.0)	4.0 (0.0-24.0)	5.0 (0.0-25.0)	2.0 (0.0-17.0)
Mean (SD)	9.8 (11.1)	10.5 (11.1)	9.4 (11.1)	9.6 (11.1)	10.3 (11.9)	10.8 (12.0)	11.1 (12.2)	9.1 (11.3)
Injection drug use past 3 mo, No. (%)	63 (12.1)	26 (14.9)	19 (11.0)	18 (10.2)	46 (9.0)	18 (10.8)	13 (7.6)	15 (8.7)
Use of >1 drug past 90 d, No. (%)	167 (31.6)	56 (32.2)	56 (31.6)	55 (31.1)	198 (38.3)	61 (36.1)	63 (36.4)	74 (42.3)
Misuse any prescription drug past 90 d, No. (%)	112 (21.2)	37 (21.3)	38 (21.5)	37 (20.9)	125 (24.2)	35 (20.7)	39 (22.5)	51 (29.1)
Heavy alcohol or drug use past 90 d, No. (%)	528 (100.0)	174 (100.0)	177 (100.0)	177 (100.0)	484 (93.6)	158 (93.5)	160 (92.5)	166 (94.9)
Any heavy drinking past month, No. (%)	254 (48.1)	81 (46.6)	82 (46.3)	91 (51.4)	229 (44.3)	78 (46.2)	76 (43.9)	75 (42.9)
No. of heavy drinking days past month								
Median (IQR)	0.0 (0.0-4.0)	0.0 (0.0-4.0)	0.0 (0.0-4.0)	1.0 (0.0-6.0)	0.0 (0.0-5.0)	0.0 (0.0-6.0)	0.0 (0.0-4.0)	0.0 (0.0-8.0)
Mean (SD)	4.5 (8.0)	4.2 (7.9)	4.0 (7.3)	5.3 (8.7)	4.6 (8.0)	4.8 (8.0)	4.2 (8.2)	4.8 (8.0)
ASSIST Scores[c]								
ASSIST score ≥27	97 (18.4)	29 (16.7)	28 (15.8)	40 (22.6)	111 (21.5)	43 (25.4)	34 (19.7)	34 (19.4)
Substance-specific score								
Main drug, median (IQR)	15.0 (9.0-23.0)	14.0 (9.0-23.0)	14.0 (9.0-22.0)	15.0 (9.0-24.0)	18.0 (12.0-25.0)	18.0 (11.0-27.0)	18.0 (12.0-24.0)	18.0 (12.0-24.0)
Mean (SD)	16.8 (9.6)	16.6 (9.9)	16.6 (8.8)	17.3 (10.0)	18.2 (9.4)	18.5 (10.1)	18.1 (9.0)	18.1 (9.2)
Opioid, median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	14.0 (5.0-28.0)	13.5 (5.0-27.0)	19.5 (6.0-28.5)	10.0 (3.0-22.0)
Mean (SD)	4.8 (10.6)	4.8 (10.7)	4.8 (10.4)	4.9 (10.7)	16.1 (12.0)	16.0 (11.8)	18.3 (12.2)	14.7 (12.0)
Cocaine, median (IQR)	0.0 (0.0-2.0)	0.0 (0.0-2.0)	0.0 (0.0-2.0)	0.0 (0.0-2.0)	20.0 (10.0-28.0)	22.0 (8.0-29.0)	19.0 (10.0-27.0)	20.0 (12.0-28.0)
Mean (SD)	5.1 (10.2)	5.2 (10.4)	4.7 (9.4)	5.4 (10.8)	19.1 (10.9)	19.2 (11.4)	18.4 (10.7)	19.7 (10.7)
Marijuana, median (IQR)	10.0 (4.0-15.0)	10.0 (4.0-15.0)	11.0 (5.0-15.0)	10.0 (5.0-15.0)	14.0 (9.0-22.0)	12.0 (7.0-23.0)	15.0 (9.0-22.0)	14.0 (9.0-21.0)
Mean (SD)	11.1 (8.8)	10.5 (8.6)	11.2 (8.4)	11.4 (9.4)	15.5 (8.6)	15.1 (9.1)	16.0 (8.7)	15.3 (8.1)
Global ASSIST score								
Median (IQR)	15.0 (10.0-29.0)	15.0 (10.0-27.0)	16.0 (10.0-27.0)	16.0 (11.0-32.0)	21.0 (12.0-33.0)	23.0 (12.0-34.0)	20.0 (12.0-33.0)	21.0 (12.0-31.0)
Mean (SD)	22.2 (18.8)	21.8 (18.4)	22.0 (18.6)	22.9 (19.5)	25.5 (18.8)	24.8 (17.1)	25.9 (19.9)	25.8 (19.4)

Abbreviations: ASSIST, Alcohol, Smoking, and Substance Involvement Screening Test; BNI, brief negotiated interview; CIDI-SF, Composite International Diagnostic Interview Short Form; IQR, interquartile range; MOTIV, adaptation of motivational interviewing.

[a] Drug of most concern, as determined by the participant.

[b] Based on a memo from Kessler R, the CIDI-SF was only provisionally validated and should not be interpreted as diagnostic without a clinical interview (http://www.hcp.med.harvard.edu/wmhcidi/ftpdir_public/CIDI-SF%20memo.pdf). In this study, it served as a severity marker stratification variable; the ASSIST is a better validated tool to determine actual current severity.

[c] Substance-specific scores range from 0-39; global drug score ranges from 0-273; in both cases, higher score is riskier use/greater severity.

Table 3. Drug Use Consequences, Readiness to Change, and Hair Testing Among Patients With Unhealthy Drug Use Identified by Screening

	Study Entry (n = 528)				6 Months (n = 517)			
	Overall	BNI	MOTIV	Control	Overall	BNI	MOTIV	Control
SIP-D score, median (IQR)[a]	6.0 (1.0-21.0)	6.0 (1.0-19.0)	7.0 (1.0-23.0)	5.0 (1.0-18.5)	3.0 (0.0-16.0)	4.0 (0.0-14.0)	3.0 (0.0-16.0)	3.0 (0.0-16.0)
Mean (SD)	12.0 (13.6)	12.1 (13.8)	12.7 (13.7)	11.3 (13.3)	9.3 (11.7)	9.3 (11.8)	9.2 (11.3)	9.4 (12.1)
Unsafe sex past 3 mo, No. (%)	277 (57.6)	95 (59.0)	94 (58.0)	88 (55.7)	263 (55.8)	88 (55.4)	82 (51.9)	93 (60.4)
No. of unsafe sex encounters past 3 mo, median (IQR)	3.0 (0.0-13.5)	3.0 (0.0-17.0)	2.0 (0.0-10.0)	2.0 (0.0-13.0)	2.0 (0.0-15.0)	2.0 (0.0-10.0)	1.0 (0.0-12.0)	4.0 (0.0-15.5)
Mean (SD)	16.1 (39.7)	13.9 (24.2)	17.6 (46.7)	16.7 (44.5)	13.2 (29.0)	12.7 (26.0)	14.0 (38.0)	12.9 (19.9)
Unsafe sex with nonprimary or transactional partners past 3 mo, No. (%)	50 (10.3)	14 (8.6)	19 (11.7)	17 (10.6)	65 (13.5)	21 (13.1)	19 (11.7)	25 (15.6)
Readiness to Change, No. (%)								
Precontemplation	108 (20.5)	34 (19.5)	35 (19.8)	39 (22.0)				
Contemplation	111 (21.0)	34 (19.5)	42 (23.7)	35 (19.8)				
Determination	45 (8.5)	19 (10.9)	13 (7.3)	13 (7.3)				
Action	264 (50.0)	87 (50.0)	87 (49.2)	90 (50.9)				
Hair Testing, No. (%)[b]								
Any drug use	475 (96.2)	160 (97.0)	158 (95.8)	157 (95.7)	422 (92.8)	142 (94.7)	142 (92.8)	138 (90.8)
Any drug use (missing as positive)	490 (96.3)	164 (97.0)	163 (95.9)	163 (95.9)	452 (93.2)	150 (94.9)	152 (93.2)	150 (91.5)
Any opioids	86 (18.4)	34 (22.2)	19 (12.2)	33 (20.9)	67 (16.3)	28 (20.9)	21 (15.6)	18 (12.6)
Any cocaine or benzoylecgonine	249 (53.4)	81 (52.9)	89 (56.7)	79 (50.6)	199 (49.1)	62 (45.9)	70 (52.2)	67 (49.3)
Any carboxy-tetrahydrocannabinol	366 (75.6)	120 (75.9)	125 (77.2)	121 (73.8)	328 (74.7)	106 (73.1)	117 (79.6)	105 (71.4)
Hair Testing Quantitative Values, ng/mL[c]								
Codeine, median (IQR)	1.8 (0.9-3.6)	1.7 (1.0-2.4)	1.9 (1.4-2.9)	2.1 (0.7-4.0)	2.9 (0.9-6.0)	2.6 (1.4-5.9)	3.7 (0.9-5.9)	4.5 (1.2-7.6)
Mean (SD)	3.3 (5.1)	2.6 (2.6)	5.0 (9.3)	3.0 (3.4)	7.1 (17.3)	4.3 (4.8)	12.1 (30.3)	6.0 (6.91)
Morphine, median (IQR)	6.1 (2.1-11.8)	6.4 (2.3-11.9)	4.6 (2.1-9.4)	6.2 (1.8-10.8)	4.2 (1.9-9.0)	4.2 (1.9-12.1)	2.1 (1.6-5.1)	6.5 (4.7-8.9)
Mean (SD)	11.1 (14.9)	11.9 (13.6)	7.7 (8.6)	12.2 (19.2)	12.5 (20.4)	13.2 (19.1)	7.1 (13.8)	17.9 (29.1)
6-Monoacetylmorphine, median (IQR)	5.3 (2.8-17.8)	5.3 (3.4-19.1)	5.8 (4.5-7.6)	3.6 (1.5-18.6)	5.1 (1.6-14.1)	7.1 (1.9-15.7)	2.4 (0.8-11.5)	4.9 (2.4-47.6)
Mean (SD)	13.4 (19.7)	11.4 (11.4)	12.8 (18.6)	16.4 (28.0)	17.1 (42.8)	11.8 (15.1)	5.8 (6.7)	45.8 (89.7)
Oxycodone, median (IQR)	2.8 (0.9-11.4)	3.4 (0.9-12.3)	2.1 (0.9-3.2)	3.4 (1.1-9.7)	2.7 (1.1-7.3)	3.2 (1.1-7.3)	2.4 (0.5-11.5)	2.7 (1.9-6.2)
Mean (SD)	12.8 (28.5)	7.8 (8.6)	20.1 (44.2)	11.2 (23.4)	11.3 (26.1)	6.4 (8.5)	10.9 (19.6)	19.2 (46.1)
Hydrocodone, median (IQR)	1.7 (1.1-5.9)	1.6 (0.9-17.1)	2.6 (0.8-6.4)	1.4 (1.1-5.1)	2.8 (0.8-7.1)	2.4 (0.6-5.3)	6.6 (2.0-10.3)	2.3 (0.8-5.5)
Mean (SD)	4.9 (6.8)	7.8 (9.3)	6.6 (10.2)	3.0 (2.8)	8.2 (18.8)	3.8 (4.0)	19.7 (34.9)	4.1 (5.1)
Hydromorphone, median (IQR)	0.5 (0.2-0.8)	0.4 (0.2-0.8)	0.4 (0.3-1.2)	0.6 (0.2-0.8)	0.4 (0.2-1.6)	0.3 (0.2-2.7)	1.2 (0.6-1.3)	0.4 (0.2-1.6)
Mean (SD)	0.9 (1.4)	0.8 (0.8)	0.8 (0.8)	1.1 (2.0)	1.1 (1.4)	1.3 (1.8)	1.2 (0.9)	0.7 (0.6)
Cocaine, median (IQR)	46.8 (11.1-197.0)	38.2 (13.5-206.0)	42.1 (10.6-138.0)	64.7 (11.1-200.0)	70.4 (12.5-200.0)	89.6 (15.7-285.0)	42.6 (8.9-145.0)	87.5 (31.4-196.0)
Mean (SD)	116.5 (137.6)	122.4 (147.2)	111.1 (143.2)	116.6 (121.5)	129.6 (138.4)	155.5 (155.1)	105.1 (128.3)	131.2 (129.4)
Benzoylecgonine, median (IQR)	4.8 (1.3-15.7)	4.2 (0.8-13.2)	4.0 (0.9-12.7)	5.9 (1.4-18.8)	6.9 (1.5-16.1)	6.8 (1.9-27.2)	4.7 (1.1-13.0)	9.1 (3.3-16.0)
Mean (SD)	19.3 (49.0)	23.3 (62.9)	18.7 (52.3)	16.0 (22.9)	20.4 (41.7)	33.9 (61.6)	15.8 (33.1)	12.5 (17.4)
Carboxy-tetrahydrocannabinol, median (IQR)	13.4 (4.2-30.3)	14.9 4.2-29.5)	13.9 (5.0-33.7)	11.9 (3.4-26.9)	12.8 (4.6-30.4)	14.0 (4.9-31.6)	12.3 (3.9-33.1)	11.7 (4.3-23.5)
Mean (SD)	22.1 (26.3)	21.9 (28.5)	23.7 (25.3)	20.6 (25.1)	22.5 (27.3)	23.6 (27.4)	22.6 (27.3)	21.2 (27.2)

Abbreviations: BNI, brief negotiated interview; IQR, interquartile range; MOTIV, adaptation of motivational interviewing; SIP-D, Short Inventory of Problems–Modified for Drug Use.

[a] Ranges from 0-45; higher score means more consequences.

[b] Of 528 participants, 509 provided a sample, but 5 were insufficient for any testing, and 10 were insufficient for confirmatory testing. Thus, 494 provided a sufficient sample for complete testing. At 6 mo, 485 provided a sample, but for 19 it was insufficient for any testing, and 11 were insufficient for confirmatory testing. Thus, 455 provided a sufficient sample for complete testing. Sample size for any drug use (with missing coded as positive), baseline was 509; 6 mo, 485; any opioids, baseline, 467; 6 mo, 412; any cocaine/benzoylecgonine, baseline, 466, 6 mo, 405; any carboxy-tetrahydrocannabinol, baseline, 484; 6 mo, 439.

[c] Only completed when substance in question was confirmed and testing possible. For codeine, number tested was 57 at baseline and 39 at follow-up. For remaining drugs, numbers tested were, respectively: morphine, 62 and 45; 6-monoacetylmorphine, 56 and 39; oxycodone, 45 and 35; hydrocodone, 24 and 22; hydromorphone, 38 and 23; cocaine, 249 and 199; benzoylecgonine, 196 and 183; carboxy-tetrahydrocannabinol, 366 and 328.

Table 4. Main Results: Effects on Days Using the Main Drug by Primary Care Patients With Unhealthy Drug Use Identified by Screening of Brief Interventions

		Predicted Mean[a] No. of Days Using Main Drug[b] in Past 30 Days at 6 Months[c]			BNI vs Control		MOTIV vs Control	
	No.	BNI	MOTIV	Control	IRR (95% CI)	*P* Value[d]	IRR (95% CI)	*P* Value[d]
Overall analysis[e]								
Unadjusted	517	14.2	14.1	13.8	1.03 (0.80-1.34)	.85	1.03 (0.79-1.33)	.85
Adjusted[f]	516	11.2	12.1	11.5	0.97 (0.77-1.22)	.81	1.05 (0.84-1.32)	.81
Stratified by Main Drug[b]								
Opioids								
Unadjusted	88	7.0	8.0	8.8	0.80 (0.33-1.92)	.84	0.91 (0.38-2.21)	.84
Adjusted[g]	88	6.4	7.4	7.6	0.85 (0.35-2.07)	.96	0.98 (0.41-2.34)	.96
Cocaine								
Unadjusted	97	8.0	7.4	5.3	1.51 (0.78-2.91)	.31	1.41 (0.73-2.72)	.31
Adjusted[g]	97	5.7	7.2	5.0	1.15 (0.62-2.14)	.66	1.44 (0.78-2.65)	.48
Marijuana								
Unadjusted	323	18.3	18.2	18.0	1.02 (0.80-1.31)	.91	1.01 (0.79-1.30)	.91
Adjusted[g]	322	16.7	17.1	16.7	1.00 (0.80-1.25)	.99	1.02 (0.82-1.28)	.99
Stratified by ASSIST Score[h]								
ASSIST<27								
Unadjusted	424	14.3	14.3	14.2	1.01 (0.76-1.33)	.96	1.01 (0.76-1.33)	.96
Adjusted[f]	423	11.1	11.7	11.5	0.97 (0.76-1.23)	.86	1.02 (0.80-1.30)	.86
ASSIST≥27								
Unadjusted	93	13.5	13.1	12.2	1.11 (0.55-2.23)	.84	1.07 (0.54-2.12)	.84
Adjusted[f]	93	10.7	12.6	10.6	1.01 (0.52-1.98)	.97	1.19 (0.63-2.26)	.97

Abbreviations: ASSIST, Alcohol, Smoking and Substance Involvement Screening Test; BNI, brief negotiated interview; CIDI-SF, Composite International Diagnostic Interview Short Form; MOTIV, adaptation of motivational interviewing; IRR, incidence rate ratio.

[a] Model-based expected counts from negative binomial regression models calculated for population with observed means and proportions of the overall sample.

[b] "Main drug" was drug of most concern, as determined by the participant.

[c] As measured by Timeline Followback method.[14]

[d] Adjusted for multiple comparisons using the Hochberg procedure.

[e] The results of the multiple imputation analysis were similar to the overall main analysis, adjusted IRR, 0.98 (95% CI, 0.79-1.23) for BNI, and adjusted IRR, 1.05 (95% CI, 0.84-1.31) for MOTIV. Variables used for imputation were age, sex, and the variables in the primary analysis.

[f] Model adjusted for the following baseline covariates: drug of most concern (main drug), number of days main drug used in past 30 days, CIDI-SF drug dependence, and outpatient treatment during past 3 months for addiction or mental health. Results were similar in analyses that did not adjust for outpatient visits.

[g] Model adjusted for the following baseline covariates: number of days main drug used in past 30 days, CIDI-SF drug dependence, and outpatient treatment during past 3 months for addiction or mental health.

[h] Ranges from 0-39; higher score means riskier use.

More than half of our participants with marijuana use reported consequences. One might think intervention would have a better chance of efficacy given a "teachable moment" (eg, being aware of a related consequence). On the other hand, such patients are already aware of consequences and have not changed on their own (having missed a "learnable moment"), so it isn't a given that counseling would be more successful for them. As for those with an alcohol use disorder and for those with likely drug dependence (<1 in 5 of our participants), the goal of brief intervention is to link them with further treatment, again building on their recognizing risks and harms that tip the balance toward change.

Despite the potential for benefit with this approach, drug use differs from unhealthy alcohol use in that it is often illegal and socially unacceptable, and is diverse—from occasional marijuana use, which was illegal during this study, to numerous daily heroin injections. Prescription drug misuse is particularly complex, with diagnostic confusion between misuse for symptoms (eg, pain, anxiety), euphoria-seeking, and drug diversion. Brief counseling may simply be inadequate to address these complexities, even as an initial strategy.

Our findings are consistent with the few published efficacy studies of brief intervention for illicit drug use among patients identified opportunistically in other health settings. Observational studies found reductions in drug use after SBI, but these are likely due to regression to the mean and other exposures.[34,35] In one pediatric emergency department randomized trial, brief intervention was associated with less marijuana use.[36] In a general hospital, a brief intervention reduced psychoactive drug use,[37] although it was not clear this was misuse. In 2 small trials in adolescent primary care, one in the United States and one in Brazil, brief intervention reduced drug use.[38,39] In outpatients in women's health, orthopedic, homeless, and urgent care clinics, BNI modestly reduced heroin and cocaine use but did not affect addiction treatment utilization.[9] In an international trial in varied sites (eg, dental, sexually transmitted

disease clinics), brief intervention was associated with a very small difference in a self-report drug use and problem score, with effects for marijuana and stimulants but not opioids and not in US participants.[40] In an emergency department trial, there were no differences in self report of use, addiction severity, or hair test abstinence, although 58% of the sample was lost to follow-up.[41] Four other randomized trials have been registered (NCT01942811, NCT01942876, NCT00877331, NCT01207791).

The ASPIRE study has a number of strengths. It is among the largest trials. We used biochemical corroboration of drug use and research staff assessed outcomes, minimizing social desirability bias. Follow-up was high. We tested feasible interventions in a real-world setting with few participant exclusion criteria. We did not exclude participants with dependence because in clinical practice they cannot be excluded and some studies suggest efficacy in these groups.[42,43] Counselors referred patients with dependence to treatment, and results suggest no difference in intervention effects between this subgroup and participants with lower severity. Primary care clinicians were given screening results and other information, but they did not perform the study interventions because we wanted to test interventions that might be feasible to adopt broadly (eg, in federal programs,[3-6] under health reform[44]).

The negative results obtained in this study are unlikely to be due to regression to the mean or assessment reactivity because drug use did not decrease. Several randomized trials of assessment vs none have not detected assessment effects.[45-47] Power, at more than 90% for modest effects, is similarly unlikely to be responsible for the findings in the overall sample. Although the study was not adequately powered for subgroup analyses, observed effect sizes were close to null and of clinically unimportant magnitude (for the full sample and the majority of secondary analyses) even if they had been significant.

Methodological features should be considered in interpreting the results. The design had features of effectiveness studies (few exclusions, feasible training). The BNI, delivered by an existing SBIRT program, was characterized by less fidelity to its components than was the MOTIV, yielding a test of efficacy for the MOTIV and of effectiveness for the BNI. However, the BNI was implemented in an ideal practice context: trainers included its original developers and the BNI was grant-funded with more hours of training and supervision than would be likely elsewhere. Counseling sessions were audiotaped, which does not occur in routine practice. Participants were compensated when they completed follow-up interviews. Because patients who did not enroll in the study were more likely to report marijuana as their main drug and appeared to be even less severe than our participants (lower ASSIST scores), we cannot say whether our results would apply to them, although it seems unlikely that brief intervention would be more effective in such a group. Furthermore, our findings may not be generalizable beyond the urban primary care setting.

Given strong prior belief in the efficacy of SBI for drug use, future trials could focus on drug subgroups (eg, marijuana, heroin, prescription drug) for which interventions, to be effective, may need to differ. We performed post hoc additional subgroup analyses among those who reported heavy drinking and marijuana use, heavy drinking and cocaine use, and all 3. In analyses overall and stratified by an ASSIST score of 27 or greater, we found no evidence of effect on total ASSIST score, marijuana- and cocaine-specific scores, or heavy drinking days. We also found no intervention effects among subgroups without dependence risk (ASSIST scores 4-15, 16-26) or subgroups based on frequency of use (≥5 vs <5 days of the main drug). Although it might be reasonable to consider the design and testing of interventions for such subgroups, our findings suggest the ones we tested would not be effective.

There were also no significant interactions between group assignment and anxiety symptoms, depression symptoms, or pain. We also tested whether daily marijuana users benefitted from intervention and found no significant effects. Among a subgroup of 23 participants who also had marijuana consequences and ASSIST scores of 27 or greater, MOTIV was associated with fewer days of marijuana use (mean, 8 vs 20 for BNI, 21 for control; $P = .06$), but given numerous analyses, this should be viewed as hypothesis generating at most. Trials could also test having the primary care clinician as the interventionist, a multicontact (>2) intervention, a multicomponent intervention (eg, several clinicians, electronic), and interventions that address multiple risk behaviors. Combined prespecified outcomes (eg, cocaine and alcohol use) could be used. Trials could also have more exclusion criteria, even greater attention to fidelity than was given for the BNI in our trial, and a focus on suburban populations. But such efficacy designs and reliance on primary care clinicians as counselors are strategies unlikely to yield practices that achieve widespread implementation.

Based on the current literature and our findings, brief intervention for unhealthy drug use in primary care patients identified by screening appears unlikely to be effective for decreasing drug use or consequences. Guideline development groups for primary care preventive services should consider these results. There are other reasons to identify and address drug use in primary care settings (eg, to make appropriate diagnoses, for safer prescribing) but if other trials yield consistent results, widespread implementation of drug SBIRT, the goal of which is reduction of use or consequences, should be reconsidered. Both clinicians and researchers should look beyond screening and brief intervention—and perhaps to lengthier and more complex longitudinal care management strategies—as the main solution to addressing illicit drug use and prescription drug misuse in primary care patients.

Conclusions

Brief intervention did not have efficacy for decreasing unhealthy drug use in primary care patients identified by screening. These results do not support widespread implementation of illicit drug use and prescription drug misuse screening and brief intervention.

ARTICLE INFORMATION

Author Contributions: Dr Saitz had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Saitz, Palfai, Cheng, Alford, Bernstein, Meli, Samet.
Acquisition, analysis, or interpretation of data: Saitz, Palfai, Cheng, Alford, Bernstein, Lloyd-Travaglini, Meli, Chaisson, Samet.
Drafting of the manuscript: Saitz, Palfai.
Critical revision of the manuscript for important intellectual content: Saitz, Palfai, Cheng, Alford, Bernstein, Lloyd-Travaglini, Meli, Chaisson, Samet.
Statistical analysis: Saitz, Cheng, Bernstein, Lloyd-Travaglini.
Obtained funding: Saitz, Bernstein, Meli, Samet.
Administrative, technical, or material support: Saitz, Alford, Bernstein, Meli, Chaisson.
Study supervision: Saitz, Palfai, Alford, Meli, Chaisson.

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Saitz reported having received grants from the National Institutes of Health (NIH), having consulted as editor to *BMJ*, having received speaking fees from academic and governmental institutions and professional societies often concerning the evidence related to addressing substance use in health settings, and having consulted as an expert witness on alcohol and drug topics. Dr Cheng reported having served on data monitoring committees for Johnson & Johnson/Janssen and having received grants from the National Institute on Drug Abuse and the Substance Abuse and Mental Health Services Administration (SAMHSA). Ms Lloyd-Travaglini reported having received grants from NIH. No other disclosures were reported.

Funding/Support: The ASPIRE study was funded by an award from the National Institute on Drug Abuse (R01 DA025068), a portion of which was funded by the Center for Substance Abuse Treatment, SAMHSA. BNI counselors, training, and supervision were supported by a contract from the SAMHSA (TI018311) to the Massachusetts Department of Public Health Bureau of Substance Abuse Services, which contracted with Boston Medical Center to deliver BNI services (INTF233OM04W76112076). The study was also supported in part by the National Center for Research Resources (UL1RR025771).

Role of the Sponsor: The funding sources had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Additional Contributions: We thank both Jacqueline Savetsky German, MPH, Boston Medical Center, and Lucero Leon-Chi, BS, Boston University School of Public Health, for their assistance with project management, manuscript preparation, and editorial support. Their work was supported by the ASPIRE grant.

REFERENCES

1. Solberg LI, Maciosek MV, Edwards NM. Primary care intervention to reduce alcohol misuse ranking its health impact and cost effectiveness. *Am J Prev Med*. 2008;34(2):143-152.

2. Miller WR, Rollnick S. *Motivational Interviewing: Preparing People for Change*. New York, NY: Guilford Press; 2002.

3. SAMHSA grants archives: FY 2001-2013 grant announcements and awards. Substance Abuse and Mental Health Services Administration. http://www.samhsa.gov/Grants/archives.aspx. Accessed February 14, 2014.

4. Screening for drug use in general medical settings: resource guide. National Institute on Drug Abuse. http://www.drugabuse.gov/sites/default/files/resource_guide.pdf. Accessed July 10, 2014.

5. Screening, brief intervention, and referral to treatment (SBIRT). Substance Abuse and Mental Health Services Administration. http://beta.samhsa.gov/sbirt. Accessed May 17, 2014.

6. Systems-level implementation of screening, brief intervention, and referral to treatment: technical assistance publication (TAP) series 33 [HHS publication SMA 13-4741]. Substance Abuse and Mental Health Services Administration. http://www.integration.samhsa.gov/sbirt/tap33.pdf. Accessed July 10, 2014.

7. Jonas DE, Garbutt JC, Amick HR, et al. Behavioral counseling after screening for alcohol misuse in primary care: a systematic review and meta-analysis for the US Preventive Services Task Force. *Ann Intern Med*. 2012;157(9):645-654.

8. Screening for illicit drug use: US Preventive Services Task Force recommendation statement. US Preventive Services Task Force. http://www.uspreventiveservicestaskforce.org/uspstf08/druguse/drugrs.htm. Accessed February 14, 2014.

9. Bernstein J, Bernstein E, Tassiopoulos K, Heeren T, Levenson S, Hingson R. Brief motivational intervention at a clinic visit reduces cocaine and heroin use. *Drug Alcohol Depend*. 2005;77(1):49-59.

10. Saitz R, Alford DP, Bernstein J, Cheng DM, Samet J, Palfai T. Screening and brief intervention for unhealthy drug use in primary care settings: randomized clinical trials are needed. *J Addict Med*. 2010;4(3):123-130.

11. Screening, brief intervention and referral to treatment (SBIRT) for drug abuse in general medical settings (R01). National Institutes of Health. http://grants.nih.gov/grants/guide/rfa-files/RFA-DA-08-021.html. Accessed February 14, 2014.

12. Kim TW, Saitz R, Kretsch N, et al. Screening for unhealthy alcohol and other drug use by health educators: do primary care clinicians document screening results? *J Addict Med*. 2013;7(3):204-209.

13. Humeniuk R, Ali R, Babor TF, et al. Validation of the alcohol, smoking and substance involvement screening test (ASSIST). *Addiction*. 2008;103(6):1039-1047.

14. Westerberg VS, Tonigan JS, Miller WR. Reliability of form 90D: an instrument for quantifying drug use. *Subst Abus*. 1998;19(4):179-189.

15. Helping patients who drink too much: a clinician's guide, updated 2005 edition. National Institute on Alcohol Abuse and Alcoholism. http://pubs.niaaa.nih.gov/publications/Practitioner/CliniciansGuide2005/guide.pdf. Accessed February 18, 2014.

16. Kessler RC, Andrews G, Mroczek D, Ustun B, Wittchen HU. The World Health Organization Composite International Diagnostic Interview Short Form (CIDI-SF). *Int J Methods Psychiatr Res*. 1998;7(4):171-185.

17. Alterman AI, Cacciola JS, Ivey MA, Habing B, Lynch KG. Reliability and validity of the alcohol short index of problems and a newly constructed drug short index of problems. *J Stud Alcohol Drugs*. 2009;70(2):304-307.

18. Heather N, Smailes D, Cassidy P. Development of a Readiness Ruler for use with alcohol brief interventions. *Drug Alcohol Depend*. 2008;98(3):235-240.

19. Navaline HA, Snider EC, Petro CJ, et al. Preparations for AIDS vaccine trials: an automated version of the Risk Assessment Battery (RAB): enhancing the assessment of risk behaviors. *AIDS Res Hum Retroviruses*. 1994;10(suppl 2):S281-S283.

20. Kamb ML, Fishbein M, Douglas JM Jr, et al; Project RESPECT Study Group. Efficacy of risk-reduction counseling to prevent human immunodeficiency virus and sexually transmitted diseases: a randomized controlled trial. *JAMA*. 1998;280(13):1161-1167.

21. Kroenke K, Spitzer RL, Williams JBW. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med*. 2001;16(9):606-613.

22. Norman SB, Cissell SH, Means-Christensen AJ, Stein MB. Development and validation of an overall anxiety severity and impairment scale (OASIS). *Depress Anxiety*. 2006;23(4):245-249.

23. EuroQol Group. EuroQol: a new facility for the measurement of health-related quality of life. *Health Policy*. 1990;16(3):199-208.

24. Bray JW, Zarkin GA, Miller WR, et al. Measuring economic outcomes of alcohol treatment using the Economic Form 90. *J Stud Alcohol Drugs*. 2007;68(2):248-255.

25. Mertens JR, Lu YW, Parthasarathy S, Moore C, Weisner CM. Medical and psychiatric conditions of alcohol and drug treatment patients in an HMO: comparison with matched controls. *Arch Intern Med*. 2003;163(20):2511-2517.

26. Weisner C, Mertens J, Parthasarathy S, Moore C, Lu Y. Integrating primary medical care with addiction treatment: a randomized controlled trial. *JAMA*. 2001;286(14):1715-1723.

27. Beck CA, Southern DA, Saitz R, Knudtson ML, Ghali WA. Alcohol and drug use disorders among patients with myocardial infarction: associations with disparities in care and mortality. *PLoS One*. 2013;8(9):e66551.

28. De Alba I, Samet JH, Saitz R. Burden of medical illness in drug- and alcohol-dependent persons without primary care. *Am J Addict*. 2004;13(1):33-45.

29. Moyers TB, Martin T, Manuel JK, Hendrickson SM, Miller WR. Assessing competence in the use of motivational interviewing. *J Subst Abuse Treat*. 2005;28(1):19-26.

30. Hochberg Y. A sharper Bonferroni procedure for multiple tests of significance. *Biometrika*. 1988;75(4):800-802.

31. Hao L, Naiman DQ. *Quantile Regression*. Thousand Oaks, CA: Sage Publications; 2007.

32. Koenker R. *Quantile Regression*. New York, NY: Cambridge University Press; 2005.

33. Moyer A, Finney JW, Swearingen CE, Vergun P. Brief interventions for alcohol problems: a meta-analytic review of controlled investigations in treatment-seeking and non-treatment-seeking populations. *Addiction*. 2002;97(3):279-292.

34. Madras BK, Compton WM, Avula D, Stegbauer T, Stein JB, Clark HW. Screening, brief interventions, referral to treatment (SBIRT) for illicit drug and alcohol use at multiple healthcare sites: comparison at intake and 6 months later. *Drug Alcohol Depend*. 2009;99(1-3):280-295.

35. Bernstein E, Bernstein J, Levenson S. Project ASSERT: an ED-based intervention to increase access to primary care, preventive services, and the substance abuse treatment system. *Ann Emerg Med*. 1997;30(2):181-189.

36. Bernstein E, Edwards E, Dorfman D, Heeren T, Bliss C, Bernstein J. Screening and brief intervention to reduce marijuana use among youth and young adults in a pediatric emergency department. *Acad Emerg Med*. 2009;16(11):1174-1185.

37. Zahradnik A, Otto C, Crackau B, et al. Randomized controlled trial of a brief intervention for problematic prescription drug use in non-treatment-seeking patients. *Addiction*. 2009; 104(1):109-117.

38. D'Amico EJ, Miles JN, Stern SA, Meredith LS. Brief motivational interviewing for teens at risk of substance use consequences: a randomized pilot study in a primary care clinic. *J Subst Abuse Treat*. 2008;35(1):53-61.

39. De Micheli D, Fisberg M, Formigoni ML. Study on the effectiveness of brief intervention for alcohol and other drug use directed to adolescents in a primary health care unit [in Portuguese]. *Rev Assoc Med Bras*. 2004;50(3):305-313.

40. Humeniuk R, Ali R, Babor T, et al. A randomized controlled trial of a brief intervention for illicit drugs linked to the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) in clients recruited from primary health-care settings in four countries. *Addiction*. 2012;107(5):957-966.

41. Woodruff SI, Clapp JD, Eisenberg K, et al. Randomized clinical trial of the effects of screening and brief intervention for illicit drug use: the life shift/shift gears study. *Addict Sci Clin Pract*. 2014;9 (1):8.

42. Field CA, Caetano R. The effectiveness of brief intervention among injured patients with alcohol dependence: who benefits from brief interventions? *Drug Alcohol Depend*. 2010;111(1-2): 13-20.

43. Guth S, Lindberg SA, Badger GJ, Thomas CS, Rose GL, Helzer JE. Brief intervention in alcohol-dependent versus nondependent individuals. *J Stud Alcohol Drugs*. 2008;69(2):243-250.

44. Takach M. About half of the states are implementing patient-centered medical homes for their Medicaid populations. *Health Aff (Millwood)*. 2012;31(11):2432-2440.

45. D'Onofrio G, Fiellin DA, Pantalon MV, et al. A brief intervention reduces hazardous and harmful drinking in emergency department patients. *Ann Emerg Med*. 2012;60(2):181-192.

46. D'Onofrio G, Pantalon MV, Degutis LC, et al. Brief intervention for hazardous and harmful drinkers in the emergency department. *Ann Emerg Med*. 2008;51(6):742-750.

47. Daeppen JB, Gaume J, Bady P, et al. Brief alcohol intervention and alcohol assessment do not influence alcohol use in injured patients treated in the emergency department: a randomized controlled clinical trial. *Addiction*. 2007;102(8): 1224-1233.