

Preliminary Findings: Contingency Management Targeting Psycho-Stimulant Use Results in Secondary Decreases in Smoking for Severely Mentally Ill Adults

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Background: Treatments for drug addiction and smoking in severely mentally ill (SMI) adults are needed.

Objectives: To investigate the effect of a contingency management (CM) intervention targeting psycho-stimulant on cigarette smoking.

Methods: 126 stimulant dependent SMI smokers were assigned to CM or a non-contingent control condition. Rates of smoking-negative (<3 ppm) carbon monoxide breath-samples were compared.

Results: Individuals who received CM targeting psycho-stimulants were 79% more likely to submit a smoking-negative breath-sample relative to controls.

Conclusions and Scientific Significance: This study provides initial evidence that a behavioral treatment for drug use results in reductions in cigarette smoking in SMI adults. (*Am J Addict* 2013; XX:1–4)

cancer^{1–3}. The high rate of cigarette smoking in this population (70–90%)⁴ directly contributes to these chronic medical illness^{1,3,5}, premature mortality¹, and higher health-care costs⁵.

In non-SMI populations there appears to be a relationship between psycho-stimulant (i.e., cocaine, amphetamine, methamphetamine) and nicotine use. An estimated 70–90% of psycho-stimulant users smoke tobacco⁶. Nicotine and cocaine appear to be linked physiologically, as they share a common dopaminergic pathway⁷. Despite high rates of smoking and the negative impact of smoking on health, only 12% of individuals in psycho-stimulant treatment receive smoking cessation⁷. Therefore, adults with SMI who use psycho-stimulants have a great need for smoking cessation treatment, yet are unlikely to receive it⁷.

Contingency management (CM) is a behavioral intervention based on operant conditioning that provides reinforcement contingent on drug abstinence. McDonell and colleagues⁸ observed that adults with SMI who received CM for psycho-stimulant abstinence achieved 2.5 times greater psycho-stimulant abstinence relative to a control group. Those assigned to the CM condition also experienced reductions in alcohol and injection drug use, psychiatric symptoms, and psychiatric hospitalizations, relative to controls. These results suggest that CM provides secondary effects on non-targeted outcomes in this challenging population.

Based on findings demonstrating the secondary effects of CM on non-targeted outcomes in SMI adults and a link between psycho-stimulants and nicotine use/cigarette smoking, we hypothesized that a CM intervention targeting psycho-stimulant abstinence would result in decreased cigarette smoking among adults with SMI and psycho-stimulant dependence.

INTRODUCTION

Adults who suffer from severe mental illnesses (SMI), such as schizophrenia, schizoaffective, bipolar, and re-occurring major depressive disorders experience high rates of chronic respiratory, cardiovascular, and metabolic disorders, as well as

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METHODS

Participants

Participants were recruited from a community mental health center (CMHC) and addiction treatment agency in Seattle, Washington. Inclusion criteria included receiving mental health or addiction treatment, being aged 18–65 years, having a Mini International Neuropsychiatric Interview diagnosis of current methamphetamine, amphetamine, or cocaine dependence, and schizophrenia-spectrum, bipolar, or recurrent major depressive disorders. Exclusion criteria included: dementia, organic brain disorder, or any acute psychiatric, medical or other condition that precluded safe study participation. A total of 176 individuals met these criteria, provided informed consent, and were randomized to treatment conditions.

For the current analysis we selected individuals who submitted carbon monoxide (CO) positive breath samples ($\text{CO} \geq 3$ parts per million [ppm]) during both of the two pre-randomization study visits ($N=126$, 72% of the overall sample). The cutoff of $\text{CO} \geq 3$ ppm has been found to accurately differentiate smokers from non-smokers⁹. Smokers were 38% ($n=48$) female, 41% ($n=52$) non-White, and had a mean age of 41.8 ($SD=9.2$) years and diagnoses of schizophrenia-spectrum ($n=50$, 40%), bipolar ($n=43$, 34%), or major depressive disorders ($n=33$, 26%). Study procedures were approved by the University of Washington's Institutional Review Board.

Study Procedures

Participants were randomized to 12-weeks of treatment-as-usual and either CM or a non-contingent control condition. Treatment-as-usual included case management, psychiatric medications, and outpatient addiction treatment. Participants provided urine and breath samples three times per week throughout the 12-week treatment period. For a full description of study procedures including the treatment and control conditions see McDonell and colleagues⁸. The CM condition provided reinforcers for psycho-stimulant abstinence thrice weekly based on the variable magnitude of reinforcement procedure, which involves making “prize draws” for tokens that say Good Job (no prize), Small Prize (\$1), Large Prize (\$20), and Jumbo Prize (\$80). Small, large, or jumbo tokens could be exchanged for items with the corresponding value. The protocol involved an escalation with a reset condition, which is described extensively in our previous report⁸. Participants earned at least one prize draw for each psycho-stimulant abstinent urine sample they submitted, and an additional prize draw at each visit for every week of continuous psycho-stimulant abstinence. They also received one additional prize draw if they tested negative for opioids, marijuana, and alcohol at that particular visit. Participants were not reinforced for smoking abstinence.

To balance the level of reinforcement across groups, participants assigned to the non-contingent (NC) condition received a number of prize draws at each visit equal to the average number of prize draws received by participants in the CM group at each visit of the prior week. However, NC

participants received prize draws each time they submitted a urine sample, regardless of the results of their urine drug test. The number of prizes earned was not statistically different across groups.

Urine samples were analyzed for use of cocaine, methamphetamine, amphetamine, marijuana, and opioids, using onsite immunoassays (Integrated E-Z-Split-Key® Cup, Innovacon-Inc.). Participants provided breath samples for alcohol (Alco-Pro-Alcosensor-III), and carbon monoxide (CO) analysis (Bedfont-Smokerlyzer Micro-IV). Positive CO tests were defined as $\text{CO} \geq 3$ ppm⁹.

Analytic Strategy

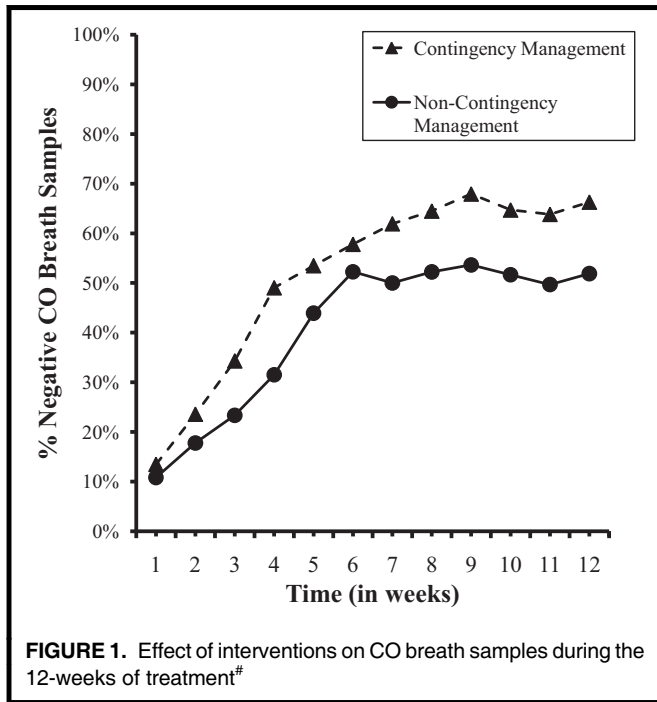
Analyses were conducted on the intent-to-treat sample ($N=126$). *T*-tests for continuous variables and chi-square tests for categorical variables were used to compare baseline characteristics between the CM ($n=66$, 52%) and NC ($n=60$, 48%) conditions.

The analytic model consisted of the likelihood of submitting a smoking-negative breath sample during the 12-week treatment period, with assignment to CM condition as the main predictor. This model adjusted for time, and marijuana smoking (positive urine analysis) at baseline. Generalized estimating equations (GEE) were used to analyze smoking abstinence measured over time in conjunction with the maximum likelihood estimator. GEE is a commonly used method for the analysis of repeated measures where in the outcome is binary. Analyses utilized bi-directional tests to protect against a Type-I error. Odds ratios with 95% confidence intervals are presented for our binary outcome.

Multiple imputation procedures were used to handle missing data, which has significant advantages over single imputation or listwise deletion, and has been used in psychiatric studies with similar levels of missing data. See McDonell et al. for further description of this approach⁸. In the current sub-sample, 41% of those in the CM condition completed treatment, while 62% of the NC group completed treatment, $\text{Chi-square}=(1)5.4$, $P=0.02$. Parameters and standard errors were combined using Rubin's rules¹⁰. Analyses were performed using Stata 12 (StataCorp, College Station, TX).

RESULTS

The CM and NC groups were not statistically different on baseline demographic (i.e., age, sex, and race/ethnicity) and clinical characteristics (i.e., SMI diagnoses, psychiatric hospitalization rates, and drug or alcohol use). When accounting for the effect of baseline marijuana use, and time, participants who received CM for psycho-stimulant abstinence demonstrated a 79% ($\text{OR}=1.79$, $\text{CI}=1.34\text{--}2.39$) increase in the odds of submitting a smoking-negative ($\text{CO} < 3$ ppm) CO breath sample during treatment; relative to those who received the NC control condition (see Figure 1).



Participants who had a positive marijuana test at baseline were 60% less likely to submit a smoking-negative CO breath sample (OR = 0.40, CI = 0.26–0.60) during treatment. We examined the time-varying impact of marijuana use on CO sample submissions during the treatment period, but it was non-significant. The main effect of time was significant, with increased smoking abstinence across the study period (OR = 0.95, CI = 0.94–0.96).

DISCUSSION

These pilot data demonstrate an overall reduction in smoking over time, with a larger reduction in the CM condition, relative to controls. Results suggest that smoking behavior can be modified, without a smoking-specific intervention, in adults with SMI, a population in which smoking is nearly ubiquitous and smoking cessation interventions are not widely available.

As Figure 1 displays, we observed overall reductions in smoking over time. This could be due to the effect of self-monitoring on smoking behavior, the relatively brief period of detection of CO breath samples, and other factors. Future research is needed to better understand this effect.

Though we collected up to 40 CO breath-tests for each participant, future studies should gather smoking self-report data to more accurately characterize reductions in smoking, and cotinine to more accurately assess abstinence. While CO breath-tests are sensitive to environmental contaminants, particularly marijuana smoking, rates of marijuana abstinence were high among the CM (91%) and NC (88%) conditions. We

conducted follow-up analyses and found that changes in marijuana use, and smoking of other illicit drugs across time did not predict changes in CO breath-tests. Therefore, illicit drug smoking was unlikely to result in positive CO tests. We observed a higher treatment dropout rate in the CM group, relative to controls. We believe this finding was due primarily to the fact that the NC group received reinforcement for attendance only, while those in the CM group had the additional requirement of abstinence to receive reinforcers. Methodologically, we used modern statistical techniques to address differential rates of missing data, as described in this report, as well as in McDonnell et al⁸. Lastly, we were not able to report on the impact of various SMI prescription medications that participants in this study were taking.

Despite these limitations, the smoking outcomes observed in this study warrant further investigation. Development of treatments that support individuals with SMI in attaining both drug and smoking abstinence is key. This study demonstrates that it may be possible to both increase psycho-stimulant and smoking abstinence, using a relatively low-cost (about \$300 per person) behavioral intervention. CM targeting psycho-stimulant abstinence could also be combined with evidence-based pharmacological or psychosocial smoking cessation interventions to increase both psycho-stimulant abstinence and smoking quit rates in this population.

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Declaration of Interests

Dr. Ries has been on the speaker bureaus of Lilly, Bristol-Myers Squibb, Pfizer, Janssen, Astra-Zeneca, and Suboxone in the past five years. Drs. Roll and McPherson have received research funding in the past twelve months from the Bristol-Myers Squibb Foundation. Dr. Saxon is member of the Advisory Board of Alkermes, Inc. All other authors have no disclosures to report.

REFERENCES

1. Kilbourne A, Morden N, Austin K, et al. Excess heart-disease-related mortality in a national study of patients with mental disorders: identifying modifiable risk factors. *Gen Hosp Psychiatry*. 2009;31:555–563.
2. McGinty E, Zhang Y, Guallar E, et al. Cancer incidence in a sample of Maryland residents with serious mental illness. *Psychiatr Serv*. 2012;63:714–717.
3. Sokal J, Messias E, Dickerson F, et al. Comorbidity of medical illnesses among adults with serious mental illness who are receiving community psychiatric services. *J Nerv Ment Dis*. 2004;192:421–427.
4. McClave A, McKnight-Eily L, Davis S, Dube S. Smoking characteristics of adults with selected lifetime mental illnesses: results from the 2007 National Health Interview Survey. *Am J Public Health*. 2010;100:2464–2472.

5. Hackman A, Goldberg R, Brown C, et al. Use of emergency department services for somatic reasons by people with serious mental illness. *Psychiatr Serv*. 2006;57:563–566.
6. Budney AJ, Higgins ST, Hughes JR, Bickel WK. Nicotine and caffeine use in cocaine-dependent individuals. *J Subst Abuse*. 1993;5:117–130.
7. Weinberger A, Sofuoglu M. The impact of cigarette smoking on stimulant addiction. *Am J Drug Alcohol Ab*. 2009;35:12–17.
8. McDonell MG, Srebnik D, Angelo F, et al. Randomized controlled trial of contingency management for stimulant use in community mental health patients with serious mental illness. *Am J Psychiatry*. 2013;170:94–101.
9. Javors MA, Hatch JP, Lamb RJ. Cut-off levels for breath carbon monoxide as a marker for cigarette smoking. *Addiction*. 2005;100:159–167.
10. Schafer JL, Graham JW. Missing data: our view of the state of the art. *Psychol Methods*. 2002;7:147–177.