R E V I E W

A review of contingency management for the treatment of substance-use disorders: adaptation for underserved populations, use of experimental technologies, and personalized optimization strategies

Sterling M McPherson[1–4]
Ekaterina Burduli[1–5]
Crystal Lederhos Smith[1–4]
Jalene Herron[2,6]
Oladunni Oluwoye[2,6]
Katherine Hirchak[2–4]
Michael F Orr[1–5]
Michael G McDonell[1–5]
John M Roll[1–5]

[1]Department of Medical Education and Clinical Sciences, Elson S Floyd College of Medicine, Washington State University, [2]Programs of Excellence in Addictions Research, Washington State University, [3]Analytics and Psychopharmacology Laboratory (APPL), Washington State University, [4]Translational Addictions Research Center, Washington State University, [5]College of Nursing, Washington State University, [6]Behavioral Health Interventions (BHI), Washington State University, Spokane, WA, USA

Correspondence: Sterling M McPherson
Department of Medical Education and Clinical Sciences, Elson S Floyd College of Medicine, Washington State University, PO Box 1495, Spokane, WA 99210, USA
Email sterling.mcpherson@wsu.edu

Abstract: This review of contingency management (CM; the behavior-modification method of providing reinforcement in exchange for objective evidence of a desired behavior) for the treatment of substance-use disorders (SUDs) begins by describing the origins of CM and how it has come to be most commonly used during the treatment of SUDs. Our core objective is to review, describe, and discuss three ongoing critical advancements in CM. We review key emerging areas wherein CM will likely have an impact. In total, we qualitatively reviewed 31 studies in a systematic fashion after searching PubMed and Google Scholar. We then describe and highlight CM investigations across three broad themes: adapting CM for underserved populations, CM with experimental technologies, and optimizing CM for personalized interventions. Technological innovations that allow for mobile delivery of reinforcers in exchange for objective evidence of a desired behavior will likely expand the possible applications of CM throughout the SUD-treatment domain and into therapeutically related areas (eg, serious mental illness). When this mobile technology is coupled with new, easy-to-utilize biomarkers, the adaptation for individual goal setting and delivery of CM-based SUD treatment in hard-to-reach places (eg, rural locations) can have a sustained impact on communities most affected by these disorders. In conclusion, there is still much to be done, not only technologically but also in convincing policy makers to adopt this well-established, cost-effective, and evidence-based method of behavior modification.

Keywords: contingency management, novel substance-use treatment technologies, drug- and alcohol-use biomarkers, substance-use disorder treatment

Introduction

Contingency management (CM) is an effective behavioral treatment approach commonly applied to substance-use disorders (SUDs). CM has a long history in basic and clinical research and a deep theoretical background for virtually all types of use disorders.[1] Interestingly, while CM was applied first to the field of alcohol-use disorders,[2–5] only now, after a protracted dormancy in that field, is CM being applied in a manner consistent with what has become a largely standardized approach in the field of drug abuse (ie, delivery of reinforcers in exchange for biochemically verified abstinence) to increase abstinence significantly and consistently.[6,7]

Early on, after being utilized for alcohol-use disorders, CM was applied among students with intellectual disabilities.[8] Following that, it was used for smoking[9] and has since then been used primarily for SUD-treatment development.[10] It has also been used to alter a variety of other behaviors, some closely related to substance use, but increasingly among broader, related health behavior, such as HIV-risk behavior.[8] Given the considerable evidence that has accumulated over many decades, CM has been demonstrated clearly to be one of the most effective behavioral interventions for initiating and maintaining abstinence from alcohol and drugs.[11] CM's history in the field of alcohol-use disorder-treatment research is noted herein while discussing innovations in remote technology and biomarker development that may be major antecedents for key developments in the implementation of CM across SUD treatment generally.

We briefly discuss the background of CM and how it has been used. We then spend most of this review discussing innovative developments within the SUD-treatment literature and how CM can play a unique and increasingly significant role in SUD treatment if political and implementation barriers can be overcome. Our core objective is to review, describe, and discuss three critical advancements of CM currently happening (ie, adapting CM for underserved populations, CM with experimental technologies, and optimizing CM for personalized interventions). We close by speculating on possible future directions and methods of maximizing the impact of CM, an area we view as largely underdeveloped.

Conceptual background of CM

CM-based treatments for SUDs originate in basic behavioral science, namely the operant-conditioning literature. Operant conditioning is a type of learning where the operant (ie, behavior) is maintained or modified via behavioral consequences. CM was born out of the early observation that SUDs largely exemplify reinforced operant behavior. As such, these behaviors can be modified effectively through altering the behavioral consequences. In such a framework, consequences are classified as positive reinforcements (ie, delivering tangible consequences to increase desired behavior), negative reinforcements (ie, removing an aversive stimulus to increase desired behavior), positive punishments (ie, delivering a punishing consequence to reduce an undesired behavior), or negative punishments (ie, removing a positive reinforcer to reduce an undesired behavior). Three key principles of CM are the rate of reinforcement (ie, the amount of reinforcement per behavior), immediacy of the reinforcer being delivered (ie, exchange delays), and the

magnitude or size of the reinforcer. These three elements were identified in the behavior-modification literature long before CM was introduced, and they have shaped several lines of work within the CM literature.[12,13] While there has been much work on these three principles in both animal and human laboratories that we will not cover here, this work has often given way to more or less "standard" uses of CM as part of "treatment as usual" packages for various experimental treatments.[14]

CM typically modifies behavior by delivering tangible reinforcements (eg, prizes, vouchers, or monetary reinforcement) in exchange for evidence of the desired behavior (eg, abstinence, decreased drug use, consumption of prescribed methadone) or by withholding those reinforcers in instances of undesired behavior (eg, drinking).[15] The reinforcers are dependent on objective evidence of the desired behavior, such as biochemically verified alcohol or drug abstinence, treatment attendance, or medication adherence. Importantly, this underlying rationale does not eliminate other sources of influence on drug-abuse behavior, but it does provide key opportunities for modification in an effort to decrease drug and alcohol abuse or drug self-administration. Although both reinforcing and punishing contingencies can be effective for treatment of SUDs, punishing contingencies can worsen undesirable behaviors without thoughtful development of this contingency.[16] The vast majority of CM treatments for SUDs apply positive reinforcement. The efficacy of CM has been shown repeatedly in the treatment of SUDs; however, two key multisite clinical trials definitively demonstrated the efficacy of CM for stimulant-use disorder, both in a psychosocial treatment setting and in methadone-maintenance settings across several nationally distributed sites.[17,18]

The immediacy of the reinforcer in CM may work as a result of the removal of delay discounting in substance users. Delay discounting, the tendency to devalue positive reinforcement that a subject must wait for, is common in drug-abusing persons.[19] This may be a result of an imbalance in neural systems within the drug abuser.[20,21] Specifically, it is theorized that the planning and forward looking to reinforcement or consequence of the prefrontal cortex is overridden by an overactive amygdala system, which promotes the subject's interest in immediate reinforcement.[22]

Current evidence base and rationale for review

CM has an extraordinarily strong evidence base and is a demonstrably cost-effective technique[23–28] that has been used successfully for decades to promote abstinence from benzo-

diazepines,[29] cocaine,[30] tobacco,[31] opiates,[32,33] alcohol,[6,7] marijuana,[34,35] and methamphetamine.[13,36,37] Several large clinical trials and three meta-analyses support its efficacy.[18,38–40] In fact, one meta-analysis found that CM resulted in successful treatment episodes 61% of the time compared to 39% for other modalities.[38] There have been some clinical trials that have found that CM leads to reductions in drug use that persist for 12–18 months after treatment completion,[41–44] although results have not been consistent across all studies. Longer-term effects of CM are one important area in need of additional research. Notably, relapse is common among people who suffer from SUDs, regardless of the treatment they receive.[45–48] Further, it is important to note that CM's consistent, statistically significant treatment effects across diverse clinical trials may be indicative of CM also being associated with better long-term treatment outcomes compared to other psychosocial interventions. This is in part due to an evidence base indicating that longer abstinence during SUD treatment is associated with better long-term treatment outcomes.[49–51]

We focus on current, novel innovations within the field of SUD treatment with CM that have unique capacities to be leveraged by existing CM behavior-science techniques. We also discuss several populations for which CM may be adapted and/or modified for specific comorbidities or other complications. Moreover, it is also possible that because of these innovations, CM could be exceptionally well positioned to be modified and adapted to create a new generation of CM techniques that could be used to produce behavior change in a scalable fashion for hard-to-reach populations, such as those living in areas where both financial resources and clinical expertise are scarce. This is the rationale that shaped our primary objective of this systematic review: to review, describe, and discuss three critical advancements of CM currently happening: adapting CM for underserved populations, CM with experimental technologies, and optimizing CM for personalized interventions.

Methods
Search strategy
In September 2017, we sought publications in the PubMed database, the search engine of the US National Library of Medicine, and Google Scholar, a free and openly available database for biomedical researchers. The search period was specified for the years 2000–2017. Articles had to be written in English and involve human subjects. The search strategy encompassed three broad a priori themes across CM: CM treatment in underserved populations, novel CM-technology

applications, and personalized CM interventions. Research articles were retrieved using the following search terms for the aforementioned years and databases: CM, CM addiction treatment, CM treatment for underserved populations, CM and SUD treatment, CM and alcohol-use biomarkers, personalized CM interventions, CM medication adherence, mobile CM delivery, novel substance-use treatment technologies, and novel CM technologies. Once unique publications had been identified, we reviewed their reference lists for additional relevant literature.

We culled the initial list extensively for relevance before deciding which articles to include in our review. In addition to the specified search criteria, we included meta-analyses and a couple of noted classic CM works prior to the year 2000. This was done because there were some CM-optimization strategies tested before 2000, but that work has not been picked up to any degree of finality since then. We include those works here in an effort to help shape the review and discussion of how best to optimize CM, especially in light of emerging technology and reaching underserved populations (our other two themes of this review). In addition, we searched reference sections of review papers and CM meta-analyses that have been published. Authors worked in pairs to review articles for inclusion, and discrepancies were resolved through discussion. In the end, all articles were reviewed and approved for inclusion by the authors involved in writing this review prior to paper finalization.

Search results
The final 31 studies included in this review are categorized by our three overarching themes of CM treatment in underserved populations (Table 1), novel CM-technology applications (Table 2), and personalized CM interventions (Table 3). We discuss these three themes extensively, and each table includes critical study characteristics for our three themes.

Results
Adapting CM for underserved populations
Co-occurring SUDs and serious mental illness (SMI)
CM has been an effective strategy for reducing alcohol and drug use in several clinical trials conducted among individuals with co-occurring SUDs and SMI.[6,18,52–54] In their definitive multisite national clinical trial, Peirce et al demonstrated that CM can significantly increase cocaine (and alcohol) abstinence among patients receiving methadone maintenance compared to those receiving methadone maintenance alone. In this study, the cost of the incentives used to increase

Table 1 Literature reviewed for the "Adapting contingency management for underserved populations" section

Study	Age (years)	n	SUD type	CM type	CM duration (weeks)	Primary outcome
Angelo et al[57]	43.5 (SD 9.31)	96	Stimulant-use disorder	RCT, usual CM	12	Stimulant-negative urine test, psychiatric severity, and rates of outpatient-treatment utilization
Barry et al[66]	Age reported by ethnicity: African-American 42.5 (SD 6.6) Hispanic 37.2 (SD 6.6) White 41.1 (SD 7.3)	191	Stimulant-use disorder	RCT, usual CM	12	CM participants had longer continuous cocaine abstinence and submitted more negative urine samples for cocaine; ethnicity not related to treatment outcomes, and there was no significant interaction between treatment and ethnicity
Bellack et al[53]	42.7 (SD 7.10)	129	Drug (cocaine, heroin, cannabis)-dependence disorder	Usual CM	24	Urinalysis results from biweekly treatment sessions
Helmus et al[60]	43.7 (SD 7.1)	20	Any SUD	A-B-A, usual CM	12	CM participants had higher rates of attendance than UC, but no effect on alcohol use
Kelly et al[55]	40.2 (SD 10.4)	160	Substance abuse and comorbid psychiatric disorders	Usual CM	6	CM participants attended more treatment days compared to UC group
McDonell et al[6]	45.38 (SD 10.20)	79	Alcohol-use disorder	RCT using EtG urine tests, usual CM	12	CM participants 3.1 times more likely to submit EtG-negative urine tests compared to those in the control group
McDonell et al[52]	CM 43.01 (SD 9.27) UC 42.45 (SD 9.97)	176	Stimulant-use disorder	RCT using urine tests, usual CM	12	CM participants significantly less likely to complete treatment period than those assigned to control group (42% vs 65%); CM participants 2.4 times more likely to submit stimulant-negative urine test during treatment
McDonell et al[56]	41.8 (SD 9.2)	126	Stimulant-use disorder	RCT using carbon monoxide breath samples, usual CM	12	CM participants 79% more likely to submit a smoking-negative breath sample compared to UC group
Miguel et al[67]	CM 35.3 (SD 8.7) UC 35.4 (SD 8.5)	65	Stimulant-use disorder	RCT using urine and breath samples, usual CM	12	CM participants more likely to remain in treatment and submit negative crack-cocaine, alcohol, and THC samples compared to UC participants
Oluwoye et al[63]	45.38 (SD 10.2)	79	Alcohol-use disorder	RCT using EtG urine tests, usual CM	12	Heavy drinkers with major depression more likely than those with schizophrenia-spectrum and bipolar disorders to submit EtG-positive urine samples during treatment
Peirce et al[18]	CM 42.5 (SD 8.9) UC 41.6 (SD 8.3)	388	Stimulant-use disorder	RCT using EtG urine tests, usual CM	12	Total number of stimulant- and alcohol-negative samples provided and longest duration of abstinence, retention, and counseling attendance
Ries et al[54]	Not reported	41	Any SUD	RCT, usual CM	27	CM condition used alcohol for few weeks; no significant differences between groups for drug use

Abbreviations: SUD, substance-use disorder; CM, contingency management; RCT, randomized controlled trial; EtG, ethyl glucuronide; EtG, ethyl glucuronide.

Table 2 Literature reviewed for the "Leveraging contingency management with experimental technologies" section

Study	Age (years)	n	SUD type	CM type	CM duration (weeks)	Primary outcome
Alessi and Petry[78]	Monitoring-only group 44.5 (SD 14.3) Monitoring and CM group 34.2 (SD 10.4)	30	Frequent alcohol users who were not dependent	Escalating reinforcement with reset contingency	4	Percentage of negative breath-alcohol tests and longest duration of abstinence both significantly greater with CM
Dallery et al[79]	36 (SD not listed)	94	Cigarette smokers	Escalating reinforcement with bonuses	7	Significant differences found in point prevalence between abstinent-contingent and submission-contingent groups at 4 weeks
Reynolds et al[80]	Abstinence-contingent group 16.58 (SD 1.54) Submission-contingent group 16.71 (SD 1.32)	62	Cigarette smokers	Five-phase shaping design, escalating reinforcement with bonuses	5	Active-treatment condition reduced breath-CO levels significantly more than controls
Budney et al[81]	35.9 (SD 10.5)	75	Cannabis-use disorder	Escalating reinforcement with bonuses	10	Both interventions containing CM (therapist and computer) had longer abstinence than non-CM intervention; therapist and computer interventions did not differ from each other in longest abstinence
Barnett et al[85]	32 (SD 9.9)	13	Heavy drinkers	Escalating reinforcement	2	Self-reports of percentage of days abstinent, drinks per week, transdermal measures of average and peak transdermal alcohol concentration, and area under the curve declined significantly in weeks 2–3
Alessi et al[86]	42 (SD 10)	100	Alcohol-use disorder	Not detailed in manuscript	12	84% of participants provided 12 weeks of data, and 96% of SCRAM bracelets returned fully intact; 94 equipment tampers occurred, affecting 2% of monitoring days; 56% (67) of tampers coincided with detected drinking
Raiff et al[88]	45 (SD not reported)	3	Non-SUD (diabetes mellitus)	Escalating reinforcement with bonus and reset contingencies	4–5	Significant increase in precision with which participants took their daily doses in designated time window
Sorensen et al[90]	43.3 (SD 7.55)	66	Methadone maintenance	RCT, escalating reinforcement with reset contingency	12	Significant mean adherence differences between voucher and comparison groups

Abbreviations: SUD, substance-use disorder; CM, contingency management; RCT, randomized controlled trial; SCRAM, secure continuous remote alcohol monitor.

Table 3 Literature reviewed for the "Optimizing contingency management for personalized interventions" section

Study	Age (years)	n	SUD type	CM type	CM duration (weeks)	Primary outcome
Packer et al[12]	30 (SD 9.98)	103	Tobacco-use disorder	Varying durations of CM High vs low magnitude No-delay vs lump sum	1	High-magnitude reinforcement provided immediately, but in incremental amounts was associated with longer intervals to relapse during treatment in comparison with high-magnitude reinforcement provided in a single lump sum after a delay; low rates of responding in the low-magnitude conditions made interpretation of the impact of delay in those conditions difficult
Roll et al[13]	32 (SD 9.53)	118	Methamphetamine-use disorder	Fishbowl CM with 1, 2, or 4 months CM	16	Participants more likely to remain abstinent through the 16-week trial as CM duration increased; longer CM doses more effective at maintaining methamphetamine abstinence
Higgins et al[30]	Voucher group 31.8 (SD 3.9) No-voucher group 30.9 (SD 6.1)	40	Cocaine-use disorder	Voucher exchangeable for retail items	12	Average durations of continuous cocaine abstinence presented via urinalysis during treatment significantly longer for group with vouchers vs group without vouchers (P=0.03); 24 weeks after treatment entry, voucher group showed significantly greater improvement than no-voucher group on the ASI drug and psychiatric scales
Stitzer et al[31]	32.7	34	Tobacco-use disorder	Standard CM With a 5-day reduction period before CM (escalated rewards based on percentage reduction from baseline levels)	4	Participants who earned more during cut-down period had greater levels of absence and length of absence
Higgins et al[32]	Contingent group 32.6 (SD 5.7) Noncontingent group 33.2 (SD 7.0) Control group 31.4 (SD 6.3)	39	Opioid-use disorder	Standard CM with a 3-week methadone-stabilization period	8	Contingent group presented significantly lower opiate-positive urine samples during weeks 8–11 (14% positive) than the noncontingent (38% positive) or control (50% positive) groups
Robles et al[33]	40.73 (SD not reported)	48	Opioid-use disorder	Voucher exchangeable for retail items	22	Participants given CM for attendance or abstinence; participants in CM for abstinence had significantly longer periods of opiate abstinence and lower rates of cocaine use
Budney et al[34]	32 (SD 8.5)	60	Cannabis-use disorder	Voucher exchangeable for retail items	14	Treatment-seeking individuals saw significantly more weeks of continuous cannabis abstinence when given CM in conjunction with MBT
Kadden et al[35]	32.7(SD 9.6)	240	Cannabis-use disorder	Standard CM paired with either CBT and motivational enhancement or CM only	9	Those in the two CM groups provided significantly more urine-negative samples than therapies alone; only CM had higher rates of abstinence at 1 year posttreatment; CM with CBT + MET had higher follow-up rates
Lamb et al[93]	37 (SD not reported)	102	Tobacco-use disorder	Escalating reinforcement reset Treatments delivering incentives for breath COs at or below the 10th, 30th, 50th, or 70th percentile of recent CO values	12	Shaping successful in decreasing CO values across groups; all participants in all groups reached desired CO level at least once

Study	N	Disorder	Intervention	Weeks	Outcome
Lamb et al[94]	71	Tobacco-use disorder	Escalating reinforcement with reset. Participants received incentives for providing breath samples with CO levels that were <4 ppm or that were at or better than the best 60th percentile within a four- or nine-visit window	12	CO levels substantially reduced and readiness-to-quit measure increased in both groups; however, more individuals in four-sample window group achieved CO <4 ppm, indicating recent abstinence; these individuals did so more rapidly and for a greater number of visits
Lamb et al[95]	146	Tobacco-use disorder	Escalating schedule with reset. Standard CM or CM shaping. CM shaped abstinence by providing incentives for CO levels lower than the seven lowest of the participant's last nine samples or <4 ppm	12	Participants were determined to be hard to treat or easier to treat (reached absence during baseline). Participants who were in easier-to-treat and standard CM did significantly better than those who were harder to treat; his difference did not exist in the CM-shaping group

Abbreviations: SUD, substance-use disorder; CM, contingency management; CBT, cognitive behavioral therapy; MET, motivational enhancement therapy.

abstinence was also noteworthy, costing on average US$120 per patient.[18] In another clinical trial, Bellack et al used a cognitive behavioral therapy (CBT) intervention that included CM to treat outpatients with SUDs and SMI. Participants randomized to the treatment condition had higher rates of drug abstinence, improved quality of life, and lower rates of inpatient-treatment episodes compared to those randomized to the control condition.[53]

In a smaller study of just 41 adults with SMI and SUDs, individuals who received access to Social Security benefits contingent on alcohol and drug abstinence achieved higher rates of abstinence than those randomized to the control condition.[54] Among a sample of 160 adults with dual diagnoses that included co-occurring SUDs, participants enrolled in the CM condition received prizes or reinforcement in exchange for treatment attendance. Participants enrolled in the CM condition were approximately twice as likely to remain in treatment longer than those in the control condition.[55] However, this study found no significant differences between participants in the CM and control conditions in levels of depression, anxiety, stress, drug cravings, coping ability, or number of drug-abstinent days. In a larger study reported by McDonell et al in 2013, outpatients with SMI receiving CM for stimulant drug abstinence, participants randomized to the CM condition were 2.4 times more likely than controls to submit a stimulant-negative urine sample during treatment.[52] Reductions were also found in alcohol use, injecting drugs, and cigarette smoking. These findings revealed lower levels of psychiatric symptoms, and participants were five times less likely to experience psychiatric hospitalization.[52,56] Furthermore, participants who submitted a stimulant-positive sample before randomization attained briefer abstinence during CM than participants whose prerandomization samples were negative.[57]

Research investigating CM for alcohol use has been limited, in part due to methodological limitations related to alcohol breath tests being capable of assessing only very recent use (up to 12 hours).[58,59] For example, one team investigated the impact of CM on treatment attendance and alcohol use in 20 patients,[60] and no effect of CM on alcohol use was observed (ie, no breath tests were positive for alcohol use throughout the 5-month study period, despite frequent clinical reports of alcohol use). Recently however, urinary ethyl glucuronide (uEtG; biochemical measure of alcohol use) has been used as the basis for a CM intervention for alcohol abstinence among 79 adults with SMI. With a period of detection of up to 5 days, EtG is an ideal biomarker for a CM intervention focused on initiating abstinence in

conjunction with standard intensive outpatient addiction treatment where individuals attend treatment multiple times a week.[61,62] This study found that participants randomized to the CM condition were 3.1 times more likely to submit uEtG-negative samples across a 12-week treatment period.[6] More specifically, a recent secondary-data analysis assessed the interaction of type of SMI diagnosis and pretreatment drinking severity among adults randomized to a CM condition.[63] Findings revealed that among heavy drinkers randomized to the CM condition, individuals diagnosed with major depression were more likely than individuals diagnosed with bipolar disorder or schizophrenia to submit uEtG-positive samples during treatment.

Lastly, and in line with some of the observations among patients with co-occurring addictions or MI, there is another line of developing inquiry focused on examining the "off-target" effects of CM on co-occurring addiction behavior in an effort to leverage such observed crossover effects. In published examples of this effect, CM exhibited an apparent off-target effect on smoking among smokers who were undergoing methamphetamine-use-disorder treatment[64] and a population of smokers who were also patients with SMI undergoing treatment for psychostimulant use[56] and alcohol-use disorder.[6] It has also been demonstrated that CM indirectly reinforces treatment attendance when attendance is mandatory in order to provide the required urine sample.[65] While these off-target effects are modest and likely insufficient to be considered adequate treatment options on their own, these preliminary findings offer promising pathways for additional development. We discuss this further in our conclusions at the end of this review.

CM in diverse communities

CM is effective among a diverse range of socioeconomic groups, racial and ethnic populations that include African-American adults, and low- and middle-income countries.[66,67] Indeed, there are some existing adaptations that are ongoing and worthy of note in an effort to demonstrate how CM can be easily tailored and personalized for a variety of different communities. Overall, SUD-treatment researchers have struggled to design efficacious treatment options in several diverse communities.

American Indian (AI)/Alaska Native (AN) adults have some of the highest alcohol-abstinence rates compared to the general US population.[68,69] However, many AI/AN communities continue to suffer from alcohol-related health inequities. In the largest clinical trial for alcohol-use disorders among AI/AN adults, three tribal communities partnered with university researchers to adapt and implement CM for alcohol-use disorders. As described by McDonell et al,[7] using components of community-based participatory research and community engagement, 400 AI/AN adults will be randomized in the ongoing trial.

In another CM example, African-American adults are three times more likely to use drugs and alcohol relative to whites.[70–72] African-American adults show significantly less improvement during treatment and are less likely to adhere to treatment compared to whites. These findings are not likely to be due to genetic variation, but possibly to a lack of critical preliminary work designed to address important treatment components unique to African-American communities (eg, health-behavior, cultural, and environmental factors).[73–76] To our knowledge, only one study has examined the efficacy of CM for cocaine abstinence among a predominantly Hispanic (n=79) and African-American (n=76) population (whites, n=36).[66] Although CM increased abstinence among African-Americans, Hispanics, and whites compared to those in the control condition, these racial and ethnic minorities still reported a shorter duration of cocaine abstinence than whites (mean 4.1 days vs mean 5.5 days).

There has been limited research focused on determining if CM interventions are differentially effective for racial, ethnic, and other groups for whom CM could benefit from adaptation (eg, patients with co-occurring SMI, rurally dwelling patients, and patients with co-occurring SUDs) to maximize its effectiveness in treating SUDs. More preliminary work is needed to improve the acceptability and efficacy for populations with unique barriers and needs. New research is emerging, but additional research is needed to examine the efficacy and necessary adaptation of CM among several populations.

Leveraging CM with experimental technologies

Technologies to monitor health outcomes

In spite of its effectiveness, one barrier to be overcome for CM has been the common necessity of participants to attend visits for biochemical monitoring of recent substance use and delivery of immediate behavioral consequences (ie, obtain reinforcers). In many applications of CM, staff must be on hand to meet participants frequently, which can be time-intensive and costly, and participants must travel to the site to supply specimens, which can be difficult in rural areas and for participants who do not have access to transport. However, mobile phones are increasingly becoming a part of everyday life,[77] paving the way for new technologies to bridge this gap and allowing for progressively easier remote

monitoring and incentive delivery through the Internet. While most technology-based CM is in the feasibility stage, significant progress has been made in remote monitoring of participants, intervention delivery, and incentive delivery through a variety of technologies.

In 2013, a randomized study assessed the feasibility and efficacy of a technology-based CM intervention to reinforce alcohol abstinence.[78] This study included 30 frequently drinking adults that were given a mobile phone and portable breathalyzer and trained on how to video-record themselves giving their breath samples. Participants were randomized to either a control group that received moderate compensation for submitting timely breath samples regardless of the result or a treatment group that received the same compensation as the control group, but in addition also received CM with escalating vouchers for timely alcohol-negative breath samples. Study staff texted participants daily reminders when their breath samples were due. They found medium–large effect sizes in which CM was associated with increased alcohol abstinence, alcohol-abstinence duration, and decreases in self-reported days of drinking and drinking-problem severity during the intervention.[78]

Another example is a recently published smoking-cessation trial that compared the efficacy of an Internet-based CM intervention to an Internet-based monitoring and goal-setting control intervention that did not include CM. The CM intervention delivered through the Internet improved short-term smoking-abstinence rates compared with the control condition. Distribution of funds happened nearly instantly after submission of negative carbon monoxide (CO; biochemical measure of recent smoking) samples.[79] Another Internet-based "video-observed CO submission" program was developed specifically for Appalachian adolescents, who tend to have smoking rates that are significantly higher than the national average (ie, another population in need of adapted CM interventions). In this trial, 62 participants were asked to submit three daily video recordings showing them submitting their breath samples through a manual CO breathalyzer. For those in the CM condition, provision of a negative sample would earn participants electronic vouchers that could be redeemed for prizes, while those randomized to the control condition received incentives only for submitting video recordings. Although this study was carried out remotely, it still required study staff to review the video for accuracy before reinforcement was delivered.[80]

Another recent example of CM-related experimental technology was a computer-assisted behavioral therapy that incorporated CM for cannabis-use disorder. This trial compared motivational enhancement therapy (MET) to a combination of MET therapy, CBT, and CM that was delivered either by a therapist or by a computer. MET-CBT-CM was superior to MET alone and was just as efficacious in abstinence rates and reduction in days of use over time when delivered by computer as it was when delivered by a therapist.[81] In addition, the computer-based intervention cost an average of $130 per participant, which was significantly less than the cost of administration by a therapist. Though this intervention was not delivered online, it provides support for the continued efficacy of CM with limited human contact and could potentially be delivered remotely, resulting in increased access. Moreover, per patient costs were similar to previously reported "low-cost" CM clinical trials, speaking again to the cost-effectiveness of CM.

Lastly, a systematic review examining 39 CM-based remote-monitoring studies (18 targeting substance use, ten targeting medication adherence or home monitoring, and eleven targeting diet, exercise, or weight loss) reported that 71% of the reviewed studies resulted in significant and substantial treatment effects. These results support the benefits of remote, technology-based CM interventions for SUDs and other health behavior.[82] In fact, the US Food and Drug Administration has cleared a mobile CM app for substance abuse (Pear Therapeutics Reset).[83] Others are currently in development, some of which are through National Institute of Health Small Business Innovation Research and Small Business Technology Transfer programs.

In addition to experimental software technologies, there are also emerging hardware technologies that could help leverage the strengths of CM. For example, BACtrack is a battery-operated breath-alcohol analyzer that can be connected to participants' mobile phones via Bluetooth (KHN Solutions, San Francisco, CA, USA).[84] This technology has not been used in conjunction with CM yet, but could be a valuable tool that would allow alcohol use to be monitored in much the same way as the portable CO analyzer utilized in the aforementioned studies. Another hardware tool for remotely monitoring alcohol use is transdermal alcohol monitoring, which removes the need for a staff member or clinician to collect a patient's samples, as the SCRAM (secure continuous remote alcohol monitoring) bracelet continuously monitors the participant's alcohol levels through an ankle monitor.[85,86] This technology has been used in conjunction with CM, but in the most recent investigations where CM was used to reinforce abstinence or treatment attendance in the two randomized groups, there were no differences in the primary outcomes of alcohol abstinence or attendance

between the two groups.[86] However, there have been promising data recently published about the feasibility and utility of transdermal monitoring of alcohol use.[78,86]

Technologies for attendance and medication adherence

There are also emerging technologies designed to monitor medication adherence remotely, including biosensors and pill-bottle electronic monitors,[87,88] another area where CM has been effectively applied in the treatment of SUDs.[82] These make for encouraging developments, because treatment attendance and medication adherence are major barriers to the delivery of efficacious treatments across therapeutic areas.[89] For example, a recent study assessed the feasibility of a remote medication-adherence-monitoring system with CM to target antidiabetic medication adherence in three adults with type 2 diabetes. Adherence to medication was recorded remotely in real time using the Wisepill,[88] a portable electronically monitored pill dispenser. Monetary incentives were dependent on evidence of timely, daily medication adherence. Results indicated that adherence increased for all participants.[79] CM has also shown promise in improving medication adherence in HIV-positive methadone patients.[90] This trial randomized participants to a comparison group (biweekly medication-adherence coaching sessions) or a voucher group (medication-adherence coaching coupled with CM). The CM voucher group had significantly higher medication adherence compared to the comparison group.[90]

A 2012 systematic review of research on incentive-based interventions targeting medication adherence concluded that although CM shows promise in this field, it had been understudied.[91] While a comparison among studies showed that CM interventions increased medication adherence on average by 20%, effect sizes varied greatly, which may be the result of CM being applied nonuniformly.[91] In addition, adherence to medications tended to diminish significantly after cessation of CM interventions.[91] Importantly, this evidence is not dissimilar from a variety of efficacious pharmacotherapies: they work well when being used, but the effect wears off quickly when not taken. Long-term behavior change with CM and several promising SUD therapies is an area that remains understudied.

Optimizing CM for personalized interventions

Alternative versions or optimizations of CM have been used to adequately address population-specific or tailored interventions for individuals that may need different rates, magnitudes, or schedules of reinforcement to improve SUD-treatment outcomes significantly. For example, initial studies of CM in smokers who used cocaine demonstrated that abstinence from cigarettes or cocaine, respectively, can be better achieved by increasing the magnitude of reinforcement (ie, high-magnitude CM) or by reinforcing progressively closer estimates of abstinence (ie, shaping CM) in comparison to requiring 100% abstinence only.[26–32,68–70] Some studies have utilized these methods of CM in an effort to provide varying doses of reinforcement for uniquely difficult addictions, or for individuals who have uniquely low levels of naturally occurring reinforcement and need a greater level of reinforcement to offset the highly reinforcing effects of substance use. Studies with methamphetamine-use disorder patients have also investigated whether or not altering the duration of CM (eg, CM for 2 months versus 4 months) or the schedule (eg, continuous schedule of reinforcement versus predictable intermittent) of CM can significantly improve long-term abstinence rates.[13,37] While there is evidence that altering the rate, magnitude, and schedule can be beneficial, not all evidence points to such modifications as being different from or more beneficial than one another. We now review these optimization strategies.

Several studies have investigated the efficacy of high-magnitude CM in people with severe addictions. In one, nonresponders to a CM intervention for cocaine were exposed to high-magnitude CM (up to $3,480) and usual CM (up to $382). During high-magnitude CM, 45% attained ≥4 weeks of abstinence, while only 5% achieved this goal during standard-magnitude CM.[32] In another study, high-magnitude CM increased drug abstinence in eleven treatment-resistant cocaine and opioid users.[31] In both studies, participants also submitted more opiate- and benzodiazepine-negative urine samples during high-magnitude CM relative to usual-CM or usual-care conditions. In a third study, participants who submitted a pretreatment cocaine-positive urine samples (ie, a proxy measure indicating greater severity of use disorder) were randomized to usual CM (reinforcer value $240), or high-magnitude CM (reinforcer value $560). For those assigned to high-magnitude CM, the duration of abstinence was more than twice as long than for those in usual care and about a week and a half longer than for those in standard CM. Lastly, a study conducted by Packer et al found that among 103 cigarette smokers, high-magnitude CM and lower preintervention smoking severity (ie, measured via cotinine, a biochemical measure of smoking severity) were both correlated with higher rates of smoking abstinence during CM.[12,92]

Shaping CM is an optimization strategy that reinforces reductions in use in a stepwise fashion (eg, 25% reduction

in use during week 1, 50% reduction in use during week 2) toward eventually requiring 100% abstinence. It has been associated with better treatment outcomes in people who do not respond to CM interventions that required 100% abstinence for the entire treatment period.[26–28] One study randomized 95 adults to receive either 8 weeks of CM or 3 weeks of a shaping CM for cocaine use, in which participants were initially required to reduce cocaine metabolite levels by 25% to receive reinforcers, and then received 5 weeks of CM for 100% abstinence.[27] Participants in the shaping condition had significantly higher rates of abstinence compared to the 100%-abstinence group. In a series of studies conducted by Lamb et al,[93–95] they reported consistent, statistically significant support for shaping CM among treatment-resistant smokers. Lamb et al used preintervention CO levels to personalize targets for subsequent shaping-CM schedules. In one of these trials, patients who received shaping CM submitted six times as many smoking-negative samples compared to those in the 100%-abstinence CM group.[95]

Finally, there have been two recent investigations into the duration of CM to compare whether 1, 2, or 4 months of CM produced higher levels of methamphetamine abstinence among methamphetamine-use-disorder patients who were attending psychosocial treatment. As expected, in a stepwise fashion, longer duration of CM consistently produced proportionally better treatment outcomes not only in methamphetamine-negative urine-sample submission but also in treatment attendance.[13] In a similarly designed trial, the schedule of reinforcement was manipulated to be continuous, predictable intermittent, unpredictable intermittent, or the standard CM condition. In this study, over 100 methamphetamine-use-disorder patients who were receiving psychosocial treatment found that the different schedules essentially did not impact treatment outcomes (eg, abstinence rates, attendance rates).[37] This is important to consider when modifying and personalizing future interventions and further illustrates the flexibility of CM in treating SUDs. Many of these optimization strategies have not been examined in depth through additional Phase II or Phase III clinical trials across substances or different populations; however, such studies could help enormously to personalize treatment for SUDs better.

Discussion

We have reviewed in depth three core themes across the use of CM for multiple SUDs: adapting CM for underserved populations, CM with experimental technologies, and optimizing CM for personalized interventions. It is our hope that this will help inform future iterations of CM being utilized in multiple settings. For example, while some of the early work on magnitude, delay, and shaping produced promising results, we still do not know for whom these schedules work best or for which SUDs it may or may not work best. Additionally, there has not been enough work done on mobile-based CM systems to provide a systematic review of those studies, but this is emerging quickly, which will hopefully act as an accelerant to new and promising CM adaptations when combined with the aforementioned optimization strategies that need additional research.

Similar to all reviews, this review has its limitations, with two notable weaknesses. First, this review did not focus on much of the promising work on combining CM with various psychotherapies and medications. This is an important emerging area that will likely leverage further some of the developments discussed herein, as it adds a layer of optimization potential for different patient populations (eg, those with more than one addiction). Another possible limitation of this review is that we chose not to conduct a quantitative meta-analysis. Such reviews can be instrumental when wanting to quantify the effect of a treatment across settings, samples, and other factors. In this review, we deliberately chose to focus our review on three a priori-selected themes in an effort to build on the excellent work already published on the consistent, strong effects of CM across various factors. Our objective with this review was to build on that work and expose readers to novel possibilities in the application of CM across SUDs.

One of the biggest barriers to utilizing CM in real-world treatment situations effectively is not a scientific one, but a political one. Convincing policy makers of why this should be more broadly integrated into drug- and alcohol-use-disorder treatment has proven difficult. However, CM interventions are being applied in clinical practices throughout the US and UK. For example, CM is being increasingly used as the SUD treatment of choice within the US Veterans Administration system.[96] Since 2011, the Veterans Administration has successfully integrated CM into 70 of its intensive outpatient substance-abuse-treatment clinics for veterans.[96] At the same time, the National Health Service in the UK has also implemented CM into its SUD-treatment guidelines.[97] Investigations of CM dissemination are under way, including studies designed to understand systemic and clinician variables that impede or facilitate CM implementation better.[98–104] One of the most important pieces of evidence that has emerged in the CM literature, especially in light of the political challenges, is that it is a cost-effective treatment option.[23–26,28] In theory,

this should lead to greater adoption across the US health care system, in desperate search of economically viable alternatives in the face of scarce and diminishing resources. More economic work on CM is under way that should contribute to this discussion.

Finally, one last important aspect of CM that makes it amenable to several different adaptations and optimizations using the aforementioned emerging utilities is that CM produces virtually no adverse events. In fact, Petry et al[96] examined 260 serious adverse events across two large[105] national multisite CM trials (along with two other psychosocial intervention investigations) and found that none was judged by the Data Safety and Monitoring Board to be related to the CM intervention. This makes CM both effective and amenable to ongoing experimentation and optimization efforts across a diverse array of settings and populations that will only be leveraged further by ongoing technological developments.

Acknowledgments

Disclosure

The authors report no conflicts of interest in this work.

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