

Optimizing Contingency Management in Substance Use Disorder Treatment Using Off-Policy Policy Evaluation

Young-geun Kim

Department of Psychiatry and Department of Biostatistics
Columbia University

Younggeun.Kim@nyspi.columbia.edu

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Introduction

- Substance use disorders have taken more than 932,000 lives in the U.S.
- The contingency management (CM) provides motivational incentives for drug abstinence.
- For example, in some trials, subjects who did not use drug from the last visit drew tickets from a fishbowl and got prizes.



The New York Times - *This Addiction Treatment Works. Why Is It So Underused?*

Introduction

- CM has been enhanced treatment effects on various drugs, but clinicians have expressed economic concerns about uncertain cost increments.
- To assist clinical administrators in making decisions, we propose to evaluate costs and treatment effects of various CM regimens.
- We apply off-policy policy evaluation techniques to evaluate potential CM regimens with data collected under existing CM regimens.

Motivating Example: CTN-0007

- The National Drug Abuse Treatment Clinical Trials Network (CTN) collected the CTN-0007 dataset to evaluate the effectiveness of CM.
- Subjects who succeeded in drug abstinence received tickets during the treatment program, and the winning structure is as follows.

Good Job (\$0)	Probability			Winning Rate	Mean (\$)	Std (\$)
	Small (\$1)	Large (\$20)	Jumbo (\$80)			
50.00%	41.80%	8.00%	0.20%	50.00%	2.18	6.36

Motivating Example: CTN-0007

- The treatment period is 12 weeks. Subjects visited clinics twice a week.

Week	Round	Primary Substance				Secondary Substance	Number of Draws			Prize			
		Alcohol	Amphetamine	Cocaine	Methamphetamine		Primary	Secondary	Total	Good Job (\$0)	Small (\$1)	Large (\$20)	Jumbo (\$80)
1	1	Negative	Negative	Negative	Negative	Positive	1	0	1	1	0	0	0
1	2	Negative	Negative	Negative	Negative	Negative	1	2	3	2	0	1	0
2	1	Negative	Negative	Negative	Negative	Negative	2	2	4	4	0	0	0
2	2	Negative	Negative	Negative	Negative	Negative	2	2	4	2	2	0	0
3	1	Negative	Negative	Negative	Negative	Negative	3	2	5	3	2	0	0
3	2	Negative	Negative	Negative	Negative	Negative	3	2	5	4	1	0	0
4	1	Negative	Negative	Negative	Negative	Negative	4	2	6	2	2	2	0
4	2	Negative	Negative	Negative	Negative	Negative	4	2	6	4	1	1	0
5	1	Negative	Negative	Negative	Negative	Negative	5	2	7	4	2	1	0
5	2	Negative	Negative	Negative	Negative	Negative	5	2	7	6	1	0	0

Motivating Example: CTN-0007

- Subjects submitted biological samples for each visit. The primary substance usage is negative if test results for all the alcohol, amphetamine, cocaine, and methamphetamine are negative.

Week	Round	Primary Substance				Secondary Substance	Number of Draws			Prize			
		Alcohol	Amphetamine	Cocaine	Methamphetamine		Primary	Secondary	Total	Good Job (\$0)	Small (\$1)	Large (\$20)	Jumbo (\$80)
1	1	Negative	Negative	Negative	Negative	Positive	1	0	1	1	0	0	0
1	2	Negative	Negative	Negative	Negative	Negative	1	2	3	2	0	1	0
2	1	Negative	Negative	Negative	Negative	Negative	2	2	4	4	0	0	0
2	2	Negative	Negative	Negative	Negative	Negative	2	2	4	2	2	0	0
3	1	Negative	Negative	Negative	Negative	Negative	3	2	5	3	2	0	0
3	2	Negative	Negative	Negative	Negative	Negative	3	2	5	4	1	0	0
4	1	Negative	Negative	Negative	Negative	Negative	4	2	6	2	2	2	0
4	2	Negative	Negative	Negative	Negative	Negative	4	2	6	4	1	1	0
5	1	Negative	Negative	Negative	Negative	Negative	5	2	7	4	2	1	0
5	2	Negative	Negative	Negative	Negative	Negative	5	2	7	6	1	0	0

Motivating Example: CTN-0007

- The secondary substance is opioid.

Week	Round	Primary Substance				Secondary Substance Opioid	Number of Draws			Prize			
		Alcohol	Amphetamine	Cocaine	Methamphetamine		Primary	Secondary	Total	Good Job (\$0)	Small (\$1)	Large (\$20)	Jumbo (\$80)
1	1	Negative	Negative	Negative	Negative	Positive	1	0	1	1	0	0	0
1	2	Negative	Negative	Negative	Negative	Negative	1	2	3	2	0	1	0
2	1	Negative	Negative	Negative	Negative	Negative	2	2	4	4	0	0	0
2	2	Negative	Negative	Negative	Negative	Negative	2	2	4	2	2	0	0
3	1	Negative	Negative	Negative	Negative	Negative	3	2	5	3	2	0	0
3	2	Negative	Negative	Negative	Negative	Negative	3	2	5	4	1	0	0
4	1	Negative	Negative	Negative	Negative	Negative	4	2	6	2	2	2	0
4	2	Negative	Negative	Negative	Negative	Negative	4	2	6	4	1	1	0
5	1	Negative	Negative	Negative	Negative	Negative	5	2	7	4	2	1	0
5	2	Negative	Negative	Negative	Negative	Negative	5	2	7	6	1	0	0

Motivating Example: CTN-0007

- Tickets were provided according to the drug test results.
- The number of draws is increased by one per week as the duration of abstinence for the primary substances increases, and is reset to zero if the test result is positive.
- The bonus two draws were provided if test results for all the primary and secondary substances were negative.

Week	Round	Primary Substance				Secondary Substance Opioid	Number of Draws			Prize			
		Alcohol	Amphetamine	Cocaine	Methamphetamine		Primary	Secondary	Total	Good Job (\$0)	Small (\$1)	Large (\$20)	Jumbo (\$80)
1	1	Negative	Negative	Negative	Negative	Positive	1	0	1	1	0	0	0
1	2	Negative	Negative	Negative	Negative	Negative	1	2	3	2	0	1	0
2	1	Negative	Negative	Negative	Negative	Negative	2	2	4	4	0	0	0
2	2	Negative	Negative	Negative	Negative	Negative	2	2	4	2	2	0	0
3	1	Negative	Negative	Negative	Negative	Negative	3	2	5	3	2	0	0
3	2	Negative	Negative	Negative	Negative	Negative	3	2	5	4	1	0	0
4	1	Negative	Negative	Negative	Negative	Negative	4	2	6	2	2	2	0
4	2	Negative	Negative	Negative	Negative	Negative	4	2	6	4	1	1	0
5	1	Negative	Negative	Negative	Negative	Negative	5	2	7	4	2	1	0
5	2	Negative	Negative	Negative	Negative	Negative	5	2	7	6	1	0	0

Motivating Example: CTN-0007

- Prizes were provided according to draw results.

Week	Round	Primary Substance				Secondary Substance	Number of Draws			Prize				
		Alcohol	Amphetamine	Cocaine	Methamphetamine		Opioid	Primary	Secondary	Total	Good Job (\$0)	Small (\$1)	Large (\$20)	Jumbo (\$80)
1	1	Negative	Negative	Negative	Negative	Positive		1	0	1	1	0	0	0
1	2	Negative	Negative	Negative	Negative	Negative		1	2	3	2	0	1	0
2	1	Negative	Negative	Negative	Negative	Negative		2	2	4	4	0	0	0
2	2	Negative	Negative	Negative	Negative	Negative		2	2	4	2	2	0	0
3	1	Negative	Negative	Negative	Negative	Negative		3	2	5	3	2	0	0
3	2	Negative	Negative	Negative	Negative	Negative		3	2	5	4	1	0	0
4	1	Negative	Negative	Negative	Negative	Negative		4	2	6	2	2	2	0
4	2	Negative	Negative	Negative	Negative	Negative		4	2	6	4	1	1	0
5	1	Negative	Negative	Negative	Negative	Negative		5	2	7	4	2	1	0
5	2	Negative	Negative	Negative	Negative	Negative		5	2	7	6	1	0	0

Important Questions

Important questions include

- ① Do winning rate, prize expectation, and prize variability affect on costs and treatment effects?
- ② Can we find optimal CM regimens maximizing treatment effects under budget constraints?

Method

- Despite the efficacy of CM, clinical administrators have expressed economic concerns about stochastic treatment costs having large ranges.
- It is practically infeasible to collect data whenever a new CM regimen is evaluated.
- We propose to apply off-policy policy evaluation (OPPE), a novel framework in reinforcement learning, that can estimate performances of CM interventions have not been studied with data collected from existing CM.

Reinforcement Learning Framework for CM

- To apply OPPE, we view drug test results, incentives, and treatment outcomes as state, action, and reward. The CM regimen can be interpreted as a policy which determines action structure given states.
- We denote state, action, and reward triple at time t by S_t , A_t , and R_t . The $\mathcal{H}_t := (S_1, A_1, R_1, \dots, S_t, A_t, R_t)$ indicates the history at time t . The policy is denoted by $\pi(a|s) := p(A_t = a|S_t = s)$.
- The value of a policy π can be expressed as

$$V(\pi) := \mathbb{E}_{\pi} \left(T^{-1} \sum_{t=1}^T R_t \right).$$

For example, $V(\pi)$ is the proportion of primary substance-free samples when $R_t = I(\text{Primary substance result at time } t \text{ is negative})$.

Importance Sampling OPPE Estimator

- We apply importance sampling OPPE estimator. For a given base policy π^b , the value of a new policy π can be re-expressed as

$$V(\pi) = \mathbb{E}_{\pi^b} \left(T^{-1} \sum_{t=1}^T W_t R_t \right)$$

where $W_t := \prod_{t'=1}^t (\pi(A_{t'}|S_{t'}) / \pi^b(A_{t'}|S_{t'}))$ is the importance weight. The more likely the \mathcal{H}_t is to occur under the target π compared to base π^b , the larger W_t .

- Note that both π and π^b are known, so the weight given states is also known.

Experiments

- We parameterized CM regimens with probabilities for the four prizes: (i) Good job (\$0), (ii) Small (\$1), (iii) Large (\$20), and (iv) Jumbo (\$80). Important characteristics of CM regimens include the winning rate, prize expectation, and prize variance.
- With OPPE, we evaluated various potential CM regimens by adjusting the winning rate, prize expectation, and prize variability with the CTN-0007 dataset.

Marginal Effect of Winning Rate

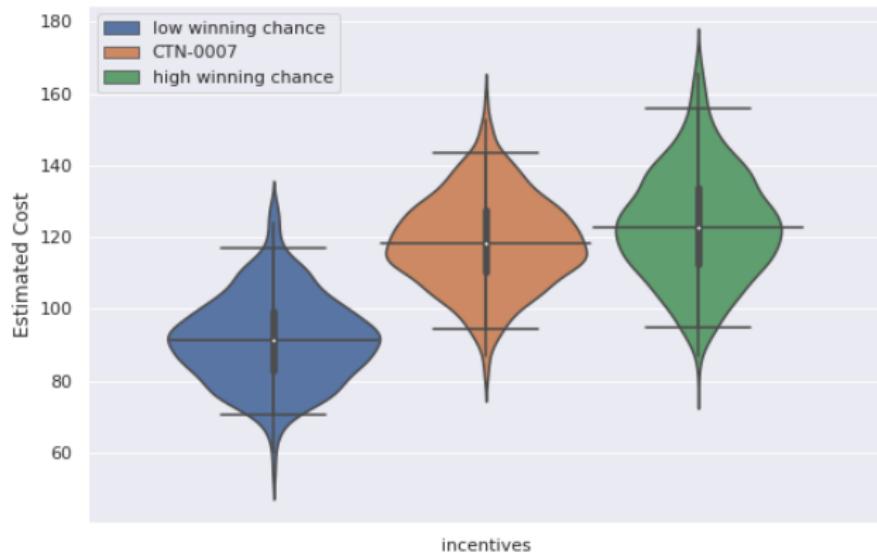
Policy	Probability				Winning Rate	Mean (\$)	Std (\$)
	Good Job (\$0)	Small (\$1)	Large (\$20)	Jumbo (\$80)			
Low winning chance	75.00%	15.15%	9.75%	0.09%	25.00%	2.18	6.36
CTN-0007	50.00%	41.80%	8.00%	0.20%	50.00%	2.18	6.36
High winning chance	25.00%	68.45%	6.25%	0.31%	75.00%	2.18	6.36

Table: Descriptions on policies to evaluate the effect of the winning chance.

- We considered CM regimens having winning chances of 25% and 75% of given prize expectation and variance.
- Note that probabilities are uniquely determined as winning rate, prize expectation, and prize variance are specified once.
- We applied bootstrap with the number of repeats of 1000.

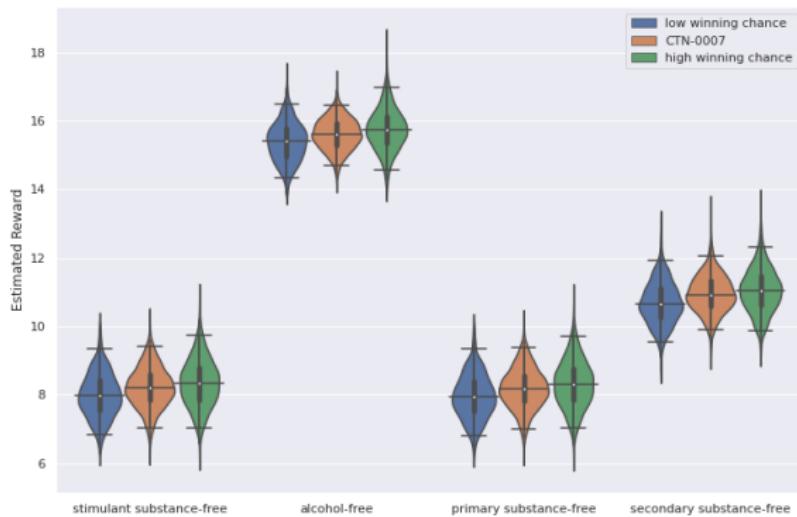
Marginal Effect of Winning Rate

- There was no significant difference in the estimated cost for the three policies.



Marginal Effect of Winning Rate

- There was no significant difference in the estimated treatment effects for the three policies.



Marginal Effect of Prize Expectation

Policy	Probability				Winning Rate	Mean (\$)	Std (\$)
	Good Job (\$0)	Small (\$1)	Large (\$20)	Jumbo (\$80)			
Low prize expectation	50.00%	49.36%	0.00%	0.64%	50.00%	1.01	6.36
CTN-0007	50.00%	41.80%	8.00%	0.20%	50.00%	2.18	6.36
High prize expectation	50.00%	38.07%	11.93%	0.00%	50.00%	2.77	6.36

Table: Descriptions on policies to evaluate the effect of the prize expectation.

- We considered CM regimens maximizing or minimizing prize expectations given chance of winning and prize variance.

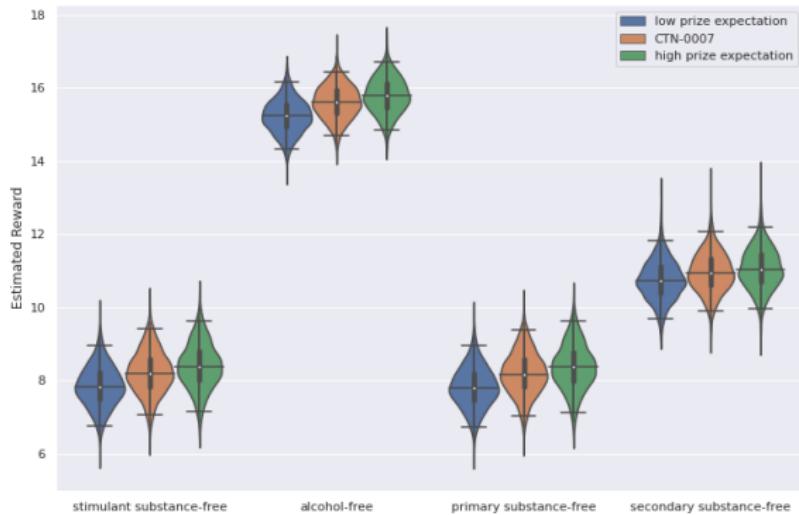
Marginal Effect of Prize Expectation

- Estimated treatment costs for the low prize expectation were significantly low.



Marginal Effect of Prize Expectation

- There was no significant difference in the treatment effects for the three policies.



Marginal Effect of Prize Variance

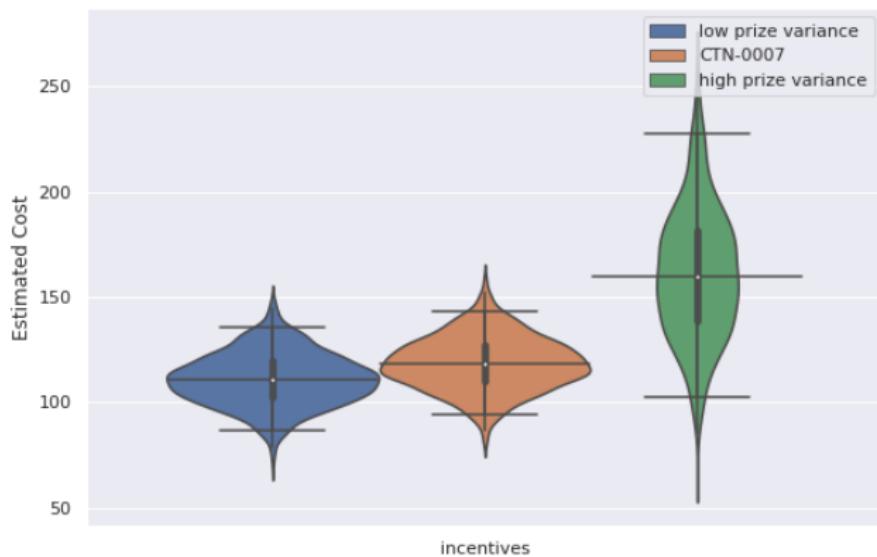
Policy	Probability				Winning Rate	Mean (\$)	Std (\$)
	Good Job (\$0)	Small (\$1)	Large (\$20)	Jumbo (\$80)			
Low prize variance	50.00%	41.17%	8.83%	0.00%	50.00%	2.18	5.57
CTN-0007	50.00%	41.80%	8.00%	0.20%	50.00%	2.18	6.36
High prize variance	50.00%	47.88%	0.00%	2.12%	50.00%	2.18	11.47

Table: Descriptions on policies to evaluate the effect of the prize variance.

- We considered CM regimens maximizing or minimizing prize variances given chance of winning and prize expectation.

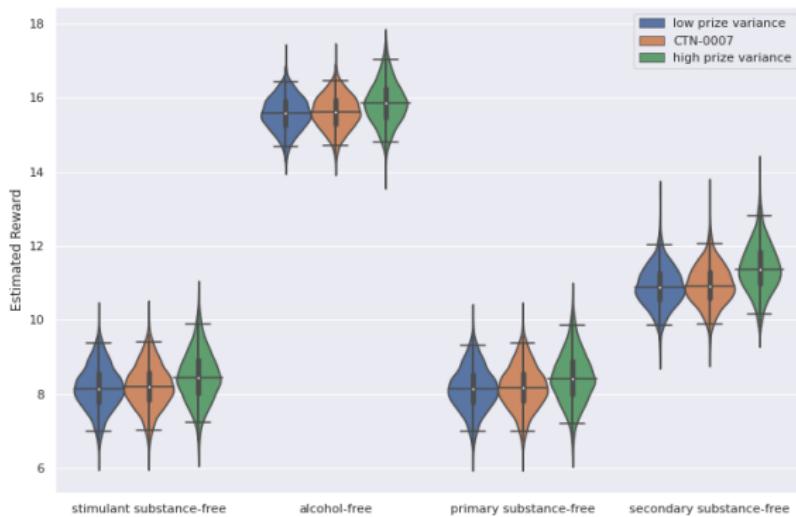
Marginal Effect of Prize Variance

- There was no significant difference in the estimated cost for the three policies.



Marginal Effect of Prize Variance

- There was no significant difference in the treatment effects for the three policies.



Optimal CM under Budget Constraints

- We varied winning rate, prize mean, and prize variance to find optimal CM under budget constraints.
- We selected CM policies having treatment costs smaller than that of CTN-0007 as feasible policies, and found the optimal one having the largest treatment effects.
- For the number of primary substance-free samples, the optimal CM significantly increased them from 8.24 to 8.50 (p-value < 0.001): Winning rate=10%; Prize mean=1.74; Prize std=10.18
- We observed similar patterns in other treatment effect measures.

Conclusion and Future Direction

- We applied OPPE in reinforcement learning to evaluate CM regimens have not been studied with data collected from existing CM regimens.
- There are potential CM regimens having lower costs and comparable treatment effects compared with the one applied to the CTN-0007 trial. We found a significant effect of the prize expectation on costs.
- We plan to evaluate more CM regimens to find optimal one maximizing treatment effects given budget constraints.



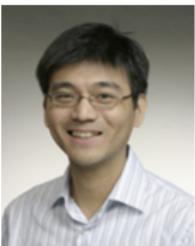
Dr. Young-geun Kim
(Columbia University)



Dr. Ying Liu*
(Columbia University)



Dr. Laura Brandt
(The City University of New York)



Dr. Ken Cheung
(Columbia University)



Dr. Edward V. Nunes
(Columbia University)



Dr. John Roll
(Washington State University)



Dr. Sean X. Luo
(Columbia University)

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