

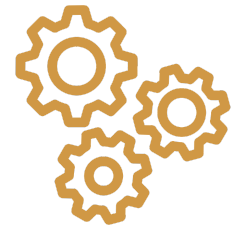
## Analysis Plan

Project Name: Enhancing the Effect of Cash Buyback on Return of Unused Opioids

Project Code: 1804

Date Finalized: 8/27/2021

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### *Project Description*

The White River Junction VA Medical Center is running an opioid buyback program called "Cash for Your Stash" in which patients who are prescribed opioids to manage post-surgery pain are also offered a cash incentive to return any unused pills. OES is testing a behaviorally informed intervention that involves two cards with behaviorally informed messaging — one given to the patient when they receive their opioid pills, and another mailed to the patient approximately one week later, at which time they likely know if they have unused pills. The goal is to enhance the effect of the cash incentive and increase the return of unused opioids. Patients in a treatment condition receive the cards in addition to the standard information about the buyback program. Patients in a control condition receive the standard information only. Patients are randomly assigned to treatment and control conditions by the week of their surgery; within consecutive two-week periods, one week is randomly assigned to treatment, and the other to control. Thus randomization is by cluster within blocks, where clusters are weeks, and blocks are two-week periods.

### *Data and Data Structure*

This section describes variables that will be analyzed, as well as changes that will be made to the raw data with respect to data structure and variables.

#### **Data Source(s):**

Data is recorded by the team that implements the Cash for Your Stash program at the White River Junction VA Medical Center. In addition to recording characteristics and outcomes for every patient who is offered the buyback option, the team is also recording the implementation of the two cards for patients in the treatment condition. After the trial period, OES will receive a dataset that includes:

- Patient age (in years)
- Patient gender
- Date of surgery
- CPT code for surgical procedure
- CCS code for surgical procedure
- Type of opioid medication dispensed

- Number of pills dispensed
- Morphine equivalent of pills dispensed
- Service (general, urology, plastics, ortho, . . . )
- Prescriber (PA, attending, PGY1, . . . )
- Pre-op opioid status (naive or acute)
- Number of pills returned to the White River Junction VA pharmacy
- Payment received for pills returned
- Return time (number of days between surgery and return of pills)
- Whether the patient received card #1 (designed by OES) on the day of surgery
- Whether the patient was mailed card #2 (designed by OES)
- Date when card #2 was mailed

**Outcome Variables to Be Analyzed:**

Primary outcome: whether the patient returns unused pills (binary)

Exploratory outcomes: number of pills returned, length of time from surgery to pill return

**Transformations of Variables:**

Categorical variables such as gender, service, and surgical procedure code will be transformed into factors for regression analysis. No other transformations are anticipated.

**Imported Variables:**

Randomization was blocked by consecutive two-week periods, and this blocking variable will be imported from the random assignment table generated by OES prior to study launch. Treatment assignment itself will also be imported to check for consistency with the intended randomization scheme. No other imported variables will be required.

**Transformations of Data Structure:**

NA

**Data Exclusion:**

Patients will be excluded for two reasons:

- Previous prescription for chronic use of opioids: Patients whose pre-op opioid status is “chronic,” meaning that they have previously received a prescription for chronic use of opioids, were not eligible for the buyback program and will be excluded from analysis.
- Received an elixir rather than pills: A few patients may have received an elixir rather than pills, in which case they would not be eligible for the buyback program and so will be excluded from analysis.

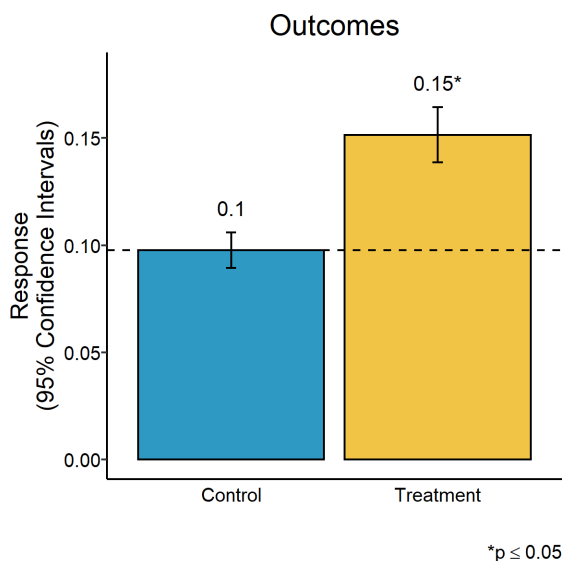
These exclusions from analysis are expected to be very rare.

**Treatment of Missing Data:**

Based on a review of pre-trial data and a subset of trial data (with outcomes redacted), we anticipate little or no missing data on patient characteristics, medical services, and prescriptions.

## Descriptive Statistics, Tables, & Graphs

Our main graph will plot the proportion of individuals returning pills in the control and treatment groups, created using the sample code for OES graphs (an example graph is below):



## Statistical Models & Hypothesis Tests

This section describes the statistical models and hypothesis tests that will make up the analysis – including any follow-ups on effects in the main statistical model and any exploratory analyses that can be anticipated prior to analysis.

### Statistical Models:

We rely on the following reduced form regression specification for our primary analysis, which provides an estimate of the impact of treatment assignment on the outcome of interest:

$$Y_i = \beta_0 + \beta_1 T_i + \delta Z'_i + \varepsilon_i$$

where  $i$  indexes patients and:

- $Y_i$  is our outcome of interest, as defined above (an indicator for whether the patient returned pills; how many pills were returned; and the length of time between surgery and pill return);
- $T_i$  is equal to one if the patient was assigned to the treatment group and zero otherwise;
- $Z'_i$  is a vector of control variables, including:
  - Patient age (in 5-year bins)

- Patient gender
- Block fixed effects
- CCS code for surgical procedure
- Whether opioid medication dispensed is oxycodone 5mg
- Morphine equivalent of pills dispensed (quartiles)
- Service (general, urology, plastics, ortho, other)
- Prescriber (PA, attending, PGY)
- Pre-op opioid status (naive or acute)
- $\varepsilon_i$  is an error term.

We will use heteroskedasticity-robust standard errors.

We will conduct a one-sided test of the null hypothesis that  $\beta_1 \leq 0$ .

#### **Follow-Up Analyses:**

We will look for heterogeneous treatment effects according to (i) the patient's risk of developing an opioid addiction, as proxied by their pre-op opioid status, (ii) the number of pills in the prescription, and (iii) the patient's age.

#### **Inference Criteria, Including Any Adjustments for Multiple Comparisons:**

We will use a cutoff of  $p = .05$  to determine statistical significance (with stars according to  $^+p < .10$ ,  $^*p < .05$ , and  $^{**}p < .01$ ).

We are only analyzing one primary outcome (whether the patient returns unused pills), so multiple hypothesis corrections are not relevant.

Importantly, at the time of posting this analysis plan we will have collected roughly two year's worth of data but have yet not committed to a stopping rule for enrollment. To inform this rule, we are planning to access the data available to date after posting the analysis plan. We will then run power simulations using these data to estimate the power we will be expected to reach for different sample sizes. We will then make a decision about stopping based on whether and when we can achieve a minimum detectable effect (MDE) of 5 percentage points (pp), since this has been determined to be the minimum effect size for which it would be valuable to scale up the treatment in the future. Our decision rules with respect to how long to run the study are as follows:

- We are able to detect an effect greater than or equal to 5pp when we first look at the data → Stop immediately.
- We are estimated to be able to detect an effect of at least 5pp within the next two years → Set the enrollment cutoff equal to the sample size where power to detect a 5pp effect reaches .8.
- We are estimated to *not* be able to detect an effect of at least 5pp within the next two years → Stop immediately.

We commit to looking at the data only once before enrollment is complete, to inform this stopping rule. We will additionally:

1. Publish the results of an interim analysis that includes the results from the primary specification at the time when we stop to look at the data.
2. Include adjustments in the final analysis to account for the fact that we accessed and analyzed the data midway through. These adjustments will be calculated via the following approach:
  - a. At the end of the trial, run simulated hypothesis tests with randomly-assigned treatment and control groups using the existing data and incorporating the stopping rules identified via our power calculations.
  - b. For each iteration, we only "collect" the number of observations in the data when we checked if we've already triggered the stopping rule by then, and continue to the identified enrollment cutoff otherwise.
  - c. We end up with a distribution of test statistics. We compare the distribution to the empirically observed test statistic to identify our adjusted  $p$ -value.

**Limitations:**

Importantly, the implementation of the OES-developed cards overlapped with the COVID-19 pandemic, which affected both the number of surgeries (and therefore participants assigned to treatment and control groups) as well as the accessibility of in-person pill returns.

The field portion of this project launched on June 3, 2019, and was then paused on March 13, 2020, due to the closure of the WRJ VA clinic. By June, 2020, the clinic was in the process of reopening, but it limited scheduling surgeries to 25% of pre-pandemic levels. By June, 2021, scheduling was up to 80% of pre-pandemic levels.

During the pandemic, patients could still return pills at the WRJ VA pharmacy. However, the pharmacy encouraged curbside pick-up of medications for a period of time, which might have reduced pill returns in cases where patients would have returned pills at the same time as picking up new medications.

During the trial period, an option to return pills by mail was introduced. Patients who returned pills by mail could not claim the cash buyback (i.e., they could not participate in the "Cash for Your Stash" program), and they could not be tracked in our data. Only a small number of patients did return pills by mail, but this might have slightly reduced participation in the program.

**Exploratory Analysis:**

Our exploratory outcomes include number of pills returned and length of time from surgery to pill return. We will additionally explore heterogeneities across our remaining control variables. For instance, are there some surgery types with patients that benefit more from the cards, perhaps due to differences in post-surgery cognitive impairment? Or, do women/men benefit more?