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Behavioral economic demand metrics for abuse deterrent and abuse potential quantification



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ABSTRACT

Introduction: Behavioral economics provides a framework for quantifying drug abuse potential that can inform public health risk, clinical treatment, and research. Hypothetical purchase task (HPT) questionnaires may provide a low-cost and sensitive method by which to measure and predict the appeal of pharmaceutical drugs that differ by formulation. However, the validity of this type of analysis must be empirically established by comparing the “essential value” (EV) of different drugs across subgroups.

Procedures: This pilot study used HPT assessments and the Exponential Model of Demand to quantify the EV of opioid medications—specifically, easily tampered formulations versus (vs.) abuse-deterrent formulations—in patients with a history of opioid abuse.

Main findings: Participants had more inelastic demand for opioid pills than for cigarettes and alcohol. Participants with experience manipulating pills (M group) had more inelastic demand for standard pills vs. participants with no manipulation experience (NM group), and the M group had a more elastic demand for the abuse-deterrent opioid pill than for the standard pill. There was no effect of formulation in the NM group and there was no difference in demand elasticity for abuse-deterrent pills between the two groups. There was a positive correlation between the EVs of different drugs, and between some behavioral economic indices and treatment variables.

Conclusions: Our results suggest that HPTs may provide a sensitive measure of abuse potential that can distinguish between different formulations in at-risk populations.

1. Introduction

Behavioral Economics (BE) provides a framework with which to understand the allocation of resources and consumption of goods and can be applied to the purchasing and consumption of illicit substances. Recent innovations in BE may provide a credible conceptual, methodological, and analytical framework for individual treatment, as well as abuse potential quantification at multiple levels to inform research, development, and marketing. In human research, demand curves are created by using hypothetical purchase task (HPT) questionnaires, in which respondents report the number of units of a commodity they would purchase or the probability of a purchase at various prices (Roma et al., 2016). HPTs provide a complementary low-cost, high-throughput, and sensitive method by which to measure drug demand as

opposed to human self-administration methods (Bruner and Johnson, 2014).

A demand curve plots hypothetical consumption of a good against price, and elasticity describes the degree to which consumption varies with price. The concept of elasticity has been used to index the *essential value* (EV) of commodities like drugs using the Exponential Model of Demand (Hursh and Silberberg, 2008). This modeling procedure allows for the comparison of qualitatively different reinforcers, as the model estimates the rate of change in elasticity of demand independent of dose or potency.

While HPT demand curves are hypothetical, they have been shown to correlate with actual alcohol purchase (Amlung et al., 2012), and to be a reliable and valid measurement of drug reinforcement (Murphy et al., 2009, 2011). These tasks have therefore been used to assess

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demand for a variety of drugs in the laboratory.

One application of hypothetical demand curves is to assess the abuse potential of medications. Examination of the “opioid epidemic” has revealed high rates of misuse, abuse, addiction, and overdose of opioid pain medications, and has emphasized the need to develop therapeutic pain drugs that are resistant to potential abuse (Vowles et al., 2015). The challenges faced by the Food and Drug Administration (FDA) and industry are well illustrated by the OxyContin experience. Its rate of abuse was due, in part, to the ease of tampering with pills by crushing them into a powder, enabling rapid absorption of high doses of oxycodone by swallowing, nasal insufflation, and injection. Development of a new formulation to discourage tampering was complicated by the absence of valid quantitative metrics for predicting ease of tampering. As stated by the FDA in its 2015 guidance for industry, *Abuse Deterrent Opioids – Evaluation and Labeling*, “The goal of laboratory-based Category 1 studies should be to evaluate the ease with which the potentially abuse-deterrent properties of a formulation can be defeated or compromised” (FDA, 2015). One approach is to have laboratory technicians who conduct laboratory studies of new drug formulations rate the level of work required to tamper with the new drug so that it can be used by alternative routes such as injecting, smoking, or by nasal insufflation (Cone et al., 2016, 2017; Henningfield et al., 2016). This has been helpful but is not a substitute for the additional information that can be obtained by studies involving people who abuse drugs and have experience tampering with them (e.g., Vosburg et al., 2013). Together, these approaches suggest that there are discernable differences in work effort across drug formulations. What is missing from this approach is a method to connect the additional effort with reductions in consumption and abuse. We propose that quantitative assessment could be further advanced by the behavioral economics-based approach in which hypothetical purchase tasks are used to measure and predict the attractiveness of pharmaceutical drugs that differ by formulation and tamper resistance (Mackillop et al., 2018; Pickover et al., 2016; Vincent et al., 2017).

In order to use hypothetical demand in abuse potential assessment or substance abuse treatment, the sensitivity of the Exponential Model of Demand must be assessed by comparing demand elasticity across subgroups. The purpose of this pilot study was to use hypothetical demand curves and the Exponential Model of Demand to assess the demand for easily tampered formulations and abuse-deterrent formulations of an opioid like oxycodone. If hypothetical demand is a sensitive measure of drug value, then there may be differential elasticities of demand for different drug formulations, laying the groundwork for using hypothetical demand as a tool for abuse potential assessment. This approach was assessed in people with experience with a broad range of opioid products who were enrolled in an outpatient substance use disorder treatment program.

2. Materials and methods

2.1. Participants and apparatus

The participants were 25 methadone-maintained opioid dependent outpatients from the Institutes for Behavior Resources’ (IBR) Recovery Enhanced by Access to Comprehensive Healthcare (REACH) Health Services clinic. Participants were between 28–57 years of age (56% female), and 64% were African American. All subjects used heroin as their primary opioid drug prior to entering treatment; however, 32% reported having experience crushing, dissolving, or otherwise manipulating prescription opioid pills to inject, snort, or smoke the drug.

All procedures described herein conformed to United States (US) and United Nations regulations governing the treatment of human research subjects, and all protocols were approved and monitored by an independent US Department of Health and Human Services-registered and Association for the Accreditation of Human Research Protection Programs (AAHRPP)-accredited Institutional Review Board ([https://](https://www.advarra.com/)

www.advarra.com/, formerly Chesapeake IRB).

2.2. Procedure

All data collection took place during 30-minute sessions conducted by research staff in a private room. Following informed consent review and demographic data collection, a “practice” hypothetical demand curve questionnaire for a familiar food item (chicken nuggets or buffalo wings) was administered to familiarize the subject with the general procedure and to confirm understanding.

Upon completion, two opioid pill purchasing questionnaires (adapted from Jacobs and Bickel, 1999) were administered in counterbalanced sequence across subjects. Both questionnaires asked the subject to imagine that their preferred drug was a prescription opioid pill like oxycodone or oxymorphone, and that they would dissolve or crush the pill to inject, snort, or smoke the drug. The subject was then asked to report how many 10 mg pills they would purchase at various prices on a typical day during the time of their heaviest opioid abuse prior to entering treatment. The only difference between the two opioid questionnaires was that one pill could be crushed, dissolved, or otherwise manipulated for injection, inhalation, or smoking (standard pill), whereas the other pill contained the same drug with the same effect on pain, but could not be crushed or otherwise manipulated, and thus could only be consumed by swallowing (abuse-deterrent pill). The prices per pill ranged from \$0 (free) to \$1120.

After the opioid pill questionnaires, hypothetical purchase tasks for cigarettes and alcohol (adapted from MacKillop et al., 2008 and Murphy and MacKillop, 2006, respectively) were administered in a counterbalanced sequence. These questionnaires were also temporally framed within the time of the respondents’ heaviest opioid abuse prior to entering treatment and documented how many standard drinks or single cigarettes they would purchase at various prices ranging from \$0 (free) to \$1120 per cigarette or \$20 per drink.

2.3. Data analysis

To ensure the quality of the data, individual participant data were analyzed to determine which were non-systematic using algorithms outlined in Stein et al. (2015). Purchasing data were identified as non-systematic if: 1) There was no reduction in consumption from the first to last price (violating trend), 2) more than 10% of price increases contained local increases in consumption (violating bounce), or 3) a participant ceased consumption at one price, and resumed consumption at a higher price (violating reversal). Of the 25 participants, five exhibited non-systematic purchase data. Of these, four participants violated one criteria (trend) on a single purchase task. However, these data may be indicative of high demand (i.e. participant consistently consumes the same large quantity for a commodity across multiple prices) or low demand (i.e. participant consumes 1 unit, then 0 units). Since demand curves were analyzed as group mean consumption and not individually, we did not eliminate those participants’ data. The fifth participant violated both the trend and bounce criteria on multiple purchase tasks. It is more likely that this participant had difficulty understanding or completing the task, and so we eliminated that participant’s data.

Not all participants consumed all of the commodities offered in the purchase tasks; eight participants did not complete tasks for alcohol. Therefore, with the exclusion criteria, the final analysis was based on 24 participants for standard opioid pills, abuse-deterrent opioid pills, and cigarettes, and 17 participants for alcohol.

A custom-programmed template for GraphPad Prism 5.0 was used for Exponential Model of Demand analysis. All other statistics were conducted using SPSS 24. The Exponential Model of Demand (Hursh and Silberberg, 2008) is calculated by:

$$\log Q = \log Q_0 + k(e_0^{-aQC} - 1) \quad (1)$$

In this equation Q is quantity consumed, Q_0 is consumption as price approaches 0, k is a scaling constant defining the consumption range in log units, α determines the rate of decline in consumption, and C is cost. Group consumption data were averaged, and then fit with Eq. (1). Demand elasticity (α) and model fit (R^2) were derived from mean consumption curves. Post-hoc Extra Sum-of-Squares F tests were used on mean consumption data to determine whether the demand elasticity rate parameter (α) differed between drugs. The k parameter was constrained to the best-shared value when comparing reinforcers with F tests. The parameter α describes the rate of change in elasticity of the entire demand curve and is inversely related to a good's EV. The model output α and k were entered in a Microsoft Excel based tool (Kaplan and Reed, 2014) for calculating EV using the equation from Hursh (2014):

$$EV = 1/(100\alpha k^{1.5}) \quad (2)$$

This equation for EV is inversely related to the rate constant α but controls for k when comparing EVs across different reinforcers with different ranges of consumption. This is an important factor in comparing our data as the range in consumption differs between drug types. Individual data were used to calculate maximum demand (units consumed at \$0), and two measures of Breakpoint, BP_0 (highest price in dollars to yield no consumption) and BP_1 (highest price in dollars to yield any consumption).

Prior to conducting correlations, variables were transformed with \log_{10} transformations to obtain normal distributions. Pearson correlations were then conducted between demand curve metrics and treatment variables, as well as among demand curve metrics for each drug. Demographic and treatment variables are reported as the mean (\pm standard error of the mean).

3. Results

3.1. Demographic information

Of the 25 participants that were included in the study, 56% of participants were female, 44% were male, 64% were African-American, and 36% were Caucasian. The average age of participants was 45 years (± 1.81). Participants reported spending an average of \$103 (± 15.8) per day on their primary opioid at their time of heaviest use.

3.2. Adequacy of the demand curve model

Demand curves for standard opioid pills, abuse-deterrent opioid pills, alcohol, and cigarettes were analyzed for all participants; Fig. 1 shows the mean consumption of each reinforcer with the exponential model fit (Eq. 1), as well as EV values. The exponential model fit the data well, with R^2 values ranging from 0.94 – 0.99.

Post-hoc analyses indicated that both opioid pills had significantly more inelastic demand (lower α) than the other reinforcers. Across all participants, elasticity was significantly lower for the standard opioid pill and the abuse-deterrent opioid pill than for cigarettes or alcohol (Standard: $F(1,46) = 33$, $p < .0001$; $F(1,38) = 68$, $p < .0001$; Abuse-Deterrent: $F(1,46) = 35$, $p < .0001$, and $F(1,38) = 81$, $p < .0001$). This indicates participants would defend their baseline consumption of opioids more so than cigarettes and alcohol. Fig. 2 shows the EVs, calculated from the model parameters, for all four drugs.

Subjects were then analyzed in one of two subgroups: Those who had experience manipulating opioid pills for non-oral administration, and those who had no such experience. Fig. 3 shows the mean group consumption of standard and abuse-deterrent opioid pills for participants with and without experience manipulating pills. The exponential model fits were good for both subgroups, with an average R^2 of 0.97 and 0.94, respectively. Subjects with experience manipulating opioid pills had a higher α (higher price sensitivity) for the abuse-deterrent opioid pill formula than for the standard pill ($F(1,44) = 4.4$, $p < .05$).

In contrast, participants with no experience manipulating pills showed no difference in α ($F(1,46) = 0.012$, $p = 0.91$). The group with manipulation experience also had a lower α for standard opioid pills than did the group with no manipulation experience ($F(1,45) = 9.6$, $p < .01$). There was no statistical difference in elasticity between the two groups for the abuse-deterrent opiate pill ($F(1,45) = 2.3$, $p = 0.14$).

Fig. 4 shows the mean group consumption of cigarettes and alcohol for participants with and without experience manipulating pills. The exponential model fits were good for both subgroups, with an average R^2 of 0.99 and 0.94, respectively. The group with manipulation experience had a lower α for cigarettes and alcohol ($F(1,43) = 7.3$, $p < .01$, and $F(1,30) = 116$, $p < .0001$) than did the group with no manipulation experience.

Fig. 5 shows the EV and maximum demand for each commodity and between the two groups. The EV differences shown here are based on the F -test findings on differences in α , as stated above. There were no significant differences in maximum demand for any of the drugs, though the maximum demand for abuse-deterrent pills appears higher for those with experience manipulating pills than those without such experience. While not significantly different ($p = .07$), the effect size was large (Cohen's $d = .82$). This may indicate that those with experience manipulating pills would consume more abuse-deterrent pills to offset the lower efficacy of swallowing tablets.

3.3. Associations among opioid demand metrics

Table 1 presents Pearson correlations among the four demand curve variables (EV, maximum demand, BP_0 , and BP_1) for each substance. EV was significantly correlated with both breakpoints for each drug, and, not surprisingly, the two measures of breakpoint were highly correlated with each other ($p < .0001$). There was no correlation between EV and maximum demand for any drug, indicating that sensitivity to price is independent of the maximum amount of drug that participants are willing to consume.

3.4. Associations between opioid demand metrics and treatment-related measures

Table 2 presents Pearson correlations for the four behavioral economic indices and six treatment-related measures: The number of days in treatment, the percentage of days absent from treatment, current methadone dose, methadone dose at intake, reported money spent per day on drugs, and the percentage of opioid positive urine samples in treatment. Participants had an average of 713 (± 104) days in treatment, an average of 6% (± 1.4) days absent from treatment, an average current methadone dose of 94 mg (± 4.1), average intake dose of 55 mg (± 6.9), average money spent on drugs of \$99.38 ($\pm \15.9), and an average of 18% (± 4.34) opioid-positive urine samples. We found that some measures of EV, maximum demand, and breakpoint, were significantly correlated with treatment variables. Current methadone dose was negatively correlated with EV for standard opioid pills ($r = -.398$, $p < .05$), indicating that higher methadone doses were associated with lower EV for these pills. However, this relationship did not exist with abuse-deterrent opioid pills, cigarettes, or alcohol. Maximum demand for both the standard pills and abuse-deterrent formulation were significantly negatively correlated with the number of days of treatment ($r = -.469$ and $r = -.413$, $p < .05$), indicating that longer time-in-treatment is associated with lower maximum demand for opioid pills in general. Patients' methadone doses at intake were positively correlated with both breakpoints for abuse-deterrent pills and cigarettes, as well as negatively correlated with the maximum demand for alcohol ($r_s > .488$, $p_s < .05$; $r = -.580$, $p < .05$).

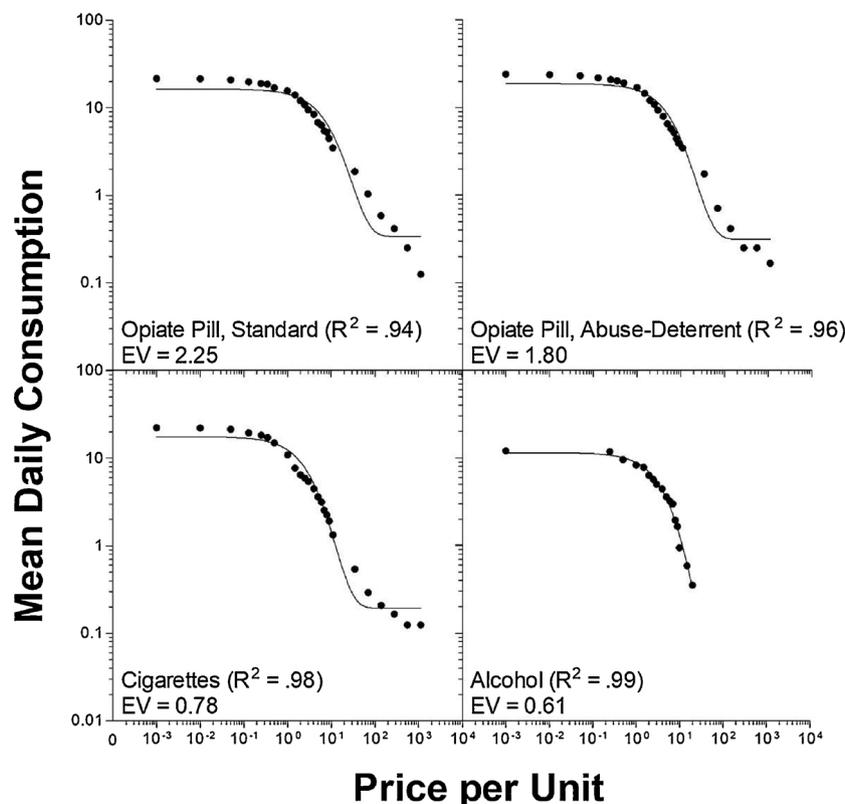


Fig. 1. Group mean demand curves for standard opioid pills, abuse-deterrent opioid pills, cigarettes, and alcohol. Demand curves are fit with Eq. (1).

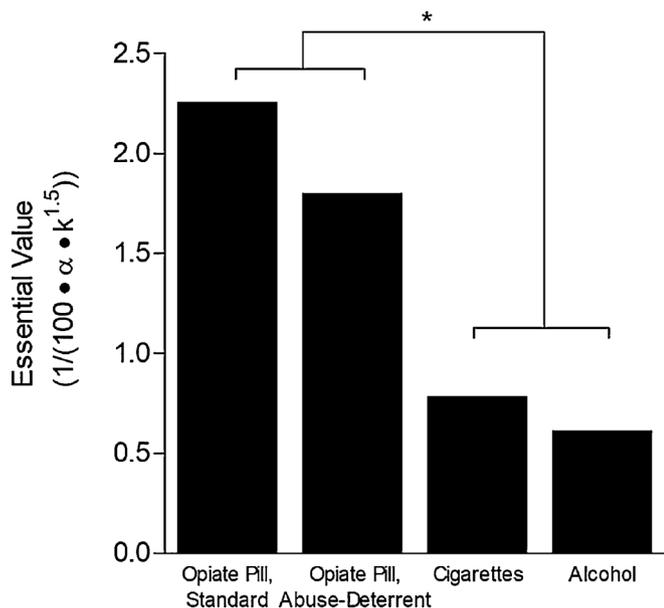


Fig. 2. Group mean EV for standard opioid pills, abuse-deterrent opioid pills, cigarettes, and alcohol. An asterisk indicates a significant difference ($p < .05$).

4. Discussion

The accurate assessment of the abuse potential of different opioid pill formulations, or creation of drug demand “profiles” for individual users, requires a valid metric with which to measure the reinforcing value of a drug. Hypothetical demand curves and the Exponential Model of Demand provide a sensitive measure of drug demand that can distinguish between meaningful sub-populations. In this study, we found that participants who primarily use opioids have significantly

higher demand for opioid pills than for other drugs. This indicates that demand measures are sensitive to a participant’s specific drug of abuse. It is important that BE metrics are specific to certain drugs to ensure that high demand for a drug is not just indicative of a participant with high demand for any commodity. Furthermore, it is important that demand for a drug is somewhat related to the use of, or dependence on, that drug. For example, Strickland and Stoops (2017) showed that demand for alcohol and soda were associated with commodity-similar use variables (i.e. alcohol demand associated with alcohol use), but not commodity-different use variables. Also, Chase et al. (2013) found that nicotine demand was associated with measures of nicotine dependence, but demand for a non-drug commodity, chocolate, was not. This indicates that nicotine dependence is associated with nicotine demand, and not necessarily demand for any other reinforcer or generalized high demand for all reinforcers

Participants with experience manipulating pills for consumption had a higher EV for the standard pills than did the participants without experience manipulating pills. It is possible that experience with manipulating pills can result in a participant having a higher EV for opioid pills, as they experience a more intense high (Bannwarth, 2012), and subjective ratings of heroin increase with drug potency (Comer et al., 1999). However, it is also possible that these participants are generally more likely to abuse opioids for another reason, which leads them to manipulate opioid pills. It is, therefore, difficult to know if participants value opioid pills more because they typically manipulate them, or if they manipulate them because they have a higher value for opioids. There was no difference in maximum demand for the reinforcers as a function of tampering experience, but those who have experience manipulating pills were less sensitive to increases in price for the standard pills than their counterparts without such experience. Thus, participants with manipulation experience may not require a higher dose but will pay higher prices to defend that dose. Since these participants are likely getting more of a high via manipulating the pills, they may consider the pills to be worth more money than do the participants who

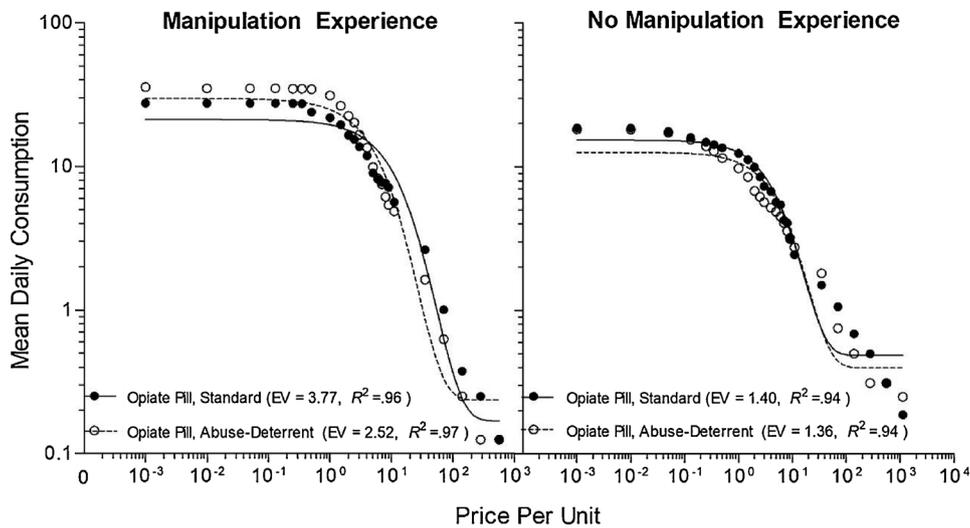


Fig. 3. Group mean demand curves for standard opioid pills and abuse-deterrent opioid pills for subjects with manipulation experience, and without manipulation experience. Demand curves are fit with Eq. (1).

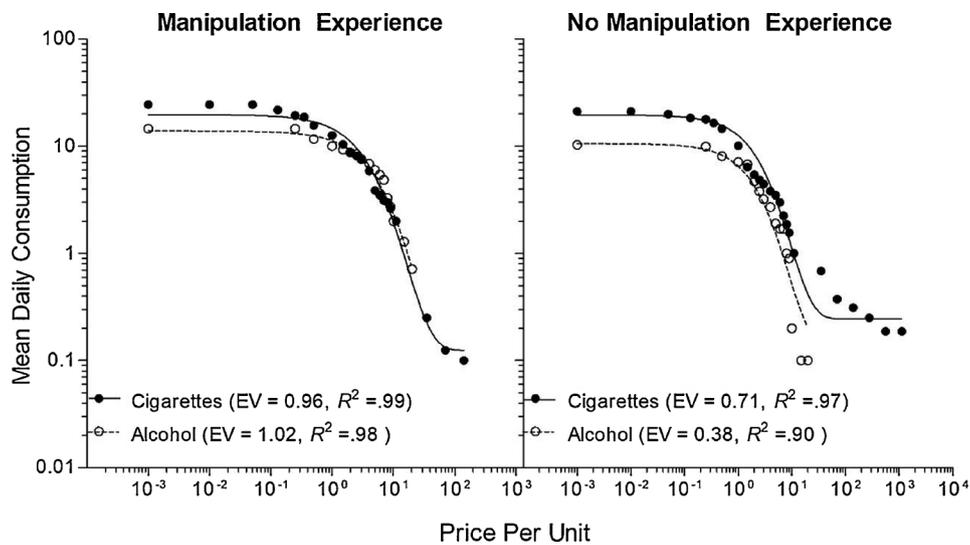


Fig. 4. Group mean demand curves for cigarettes and alcohol for subjects with manipulation experience, and without manipulation experience. Demand curves are fit with Eq. (1).

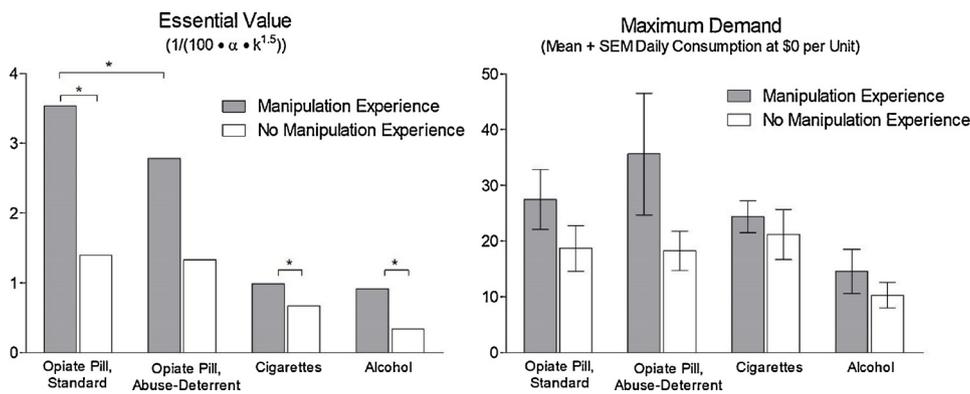


Fig. 5. Essential value and maximum demand for standard opioid pills, abuse-deterrent opioid pills, cigarettes, and alcohol, for both subgroups. An asterisk indicates a significant difference ($p < .05$).

would only consume the pills orally.

Our results also indicate that users who have experience manipulating opioid pills have a lower EV for pills that cannot be manipulated compared to the standard formulation of these pills. Essentially, the

participants who are willing to manipulate pills prefer the pills that can actually be manipulated. Notably, the HPT is sensitive enough to distinguish differences in how this sub-population values these two types of pills. These results suggest that the formulation of a drug can affect

Table 1
Pearson correlations (*r*) among demand curve variables for each substance.

Drug		EV	Max Demand	BP ₀	BP ₁
Opiate Pill, Standard	EV	–	–	–	–
	Max Demand	.164	–	–	–
	BP ₀	.928**	.064	–	–
	BP ₁	.944**	.069	.986**	–
Opiate Pill, Abuse Deterrent	EV	–	–	–	–
	Max Demand	.021	–	–	–
	BP ₀	.936**	.027	–	–
	BP ₁	.946**	.048	.989**	–
Cigarettes	EV	–	–	–	–
	Max Demand	–.184	–	–	–
	BP ₀	.951**	–.348	–	–
	BP ₁	.947**	–.348	.985**	–
Alcohol	EV	–	–	–	–
	Max Demand	.375	–	–	–
	BP ₀	.890**	–.032	–	–
	BP ₁	.890**	–.037	.994*	–

* *p* < .05.

** *p* < .001.

whether patients will use it, even if the drug itself remains the same. Thus, the development of abuse-deterrent formulations of commonly abused pharmaceutical drugs may have the effect of reducing abuse for those drugs. It should be noted that this does not preclude the possibility of users switching to more readily-available opioids such as heroin (Cicero and Ellis, 2015), but nonetheless supports the possibility of HPTs as a potential measure of abuse potential as a function of formulation.

Despite the fact that participants were asked to answer as if they had not yet entered treatment, some of the demand measures were significantly correlated with treatment variables. For example, the EV for standard pills was negatively correlated with participants' current methadone dose. Recall that the participants were instructed to imagine that the standard pill was a dissolvable/crushable opioid pill like oxycodone. This correlation, then, suggests that one effect of methadone is a reduction in hypothetical demand for an opioid pill that is equivalent to oxycodone, a validation of the hypothetical purchase task for detecting the pharmacological properties of methadone. Studies have shown that methadone treatment can reduce the reinforcing effects of heroin (Leri et al., 2004) and results in better treatment outcomes (Greenwald, 2002), but no data yet exist on how methadone directly affects opioid demand. This effect on opioid demand could be due to the methadone dose itself or to a combination of methadone dose and

behavioral treatment (Schwartz et al., 2012). Future research should attempt to isolate the effect of methadone itself on opioid demand.

In addition, maximum demand for both opioid pills was negatively correlated with the number of days spent in treatment, indicating that a longer time spent in treatment may reduce the amount of drug participants wish to consume. Some studies have shown that treatment outcomes improve over the length of treatment. For example, Davstad et al. (2007) found that relapse event lengths decrease with the length of treatment. The longitudinal tracking of drug demand over treatment has yet to be examined, but future research should aim to understand both how demand will change as a function of treatment length, and which aspects of treatment are responsible for any changes.

We found no correlation between the amount of money spent per day on drugs and any BE indices. It is possible that there is no effect of the amount participants were willing to spend on drugs on the demand metrics, but there are also other variables to consider. This study was largely exploratory in nature and is, therefore, limited by its small sample size. The span of time between the study and the framing of the questions (the time of their heaviest opiate use prior to entering treatment) could also have affected the answers; it may have been difficult for participants to remember the exact amount of money they used to spend each day, especially since some participants had been in treatment for over two years.

Another potential application of hypothetical demand curves in clinical populations is the development of quantitative drug demand “profiles” characterizing individuals at different levels of risk. Recent studies have found that measures of demand for alcohol and cigarettes can be predictors of treatment outcomes. These measures have predicted the number of weekly drinks six months after a brief alcohol intervention and were associated with drinking severity (Murphy and Mackillop, 2006; Tucker et al., 2016). Furthermore, alcohol demand may be decreased using psychosocial interventions in college drinkers (Dennhardt et al., 2015; Murphy et al., 2015). Thus, if demand can predict treatment outcomes and is reduced with intervention, then it may provide an easily-obtained measure that can be used to target treatment. Future research should focus on the use of HPTs to track demand over time, and to assess the efficacy of different behavioral or pharmacological treatments.

This study provides evidence that a demand analysis of substance abuse is a sensitive measure that can differentiate between standard and abuse-deterrent drug formulations in relevant subgroups of users. This important feature of the model is necessary to accurately apply these methods to abuse potential and treatment settings. Assessing drug demand using HPTs can aid the pharmaceutical industry and regulatory

Table 2
Pearson correlations (*r*) among behavioral economic indices and treatment outcomes.

Drug	Behavioral Economic Indices	Days in Treatment	% Days Absent	Current Methadone Dose	Intake Methadone Dose	Money per Day	% Opioid Urines
Opiate Pill, Standard	EV	–.256	.004	–.398*	.300	–.092	.350
	Max Demand	–.469*	.163	–.388	.167	.219	.079
	BP ₀	–.292	–.018	–.249	.359	–.081	.321
	BP ₁	–.325	–.047	–.345	.373	–.104	.329
Opiate Pill, Abuse Deterrent	EV	–.227	–.056	–.184	.393	.010	.313
	Max Demand	–.413*	.110	–.359	–.026	–.139	.200
	BP ₀	–.350	.086	–.253	.488*	–.059	.348
	BP ₁	–.363	.075	–.288	.499*	–.072	.323
Cigarettes	EV	–.236	.138	–.246	.468*	.020	.350
	Max Demand	–.263	–.078	–.168	–.157	.034	.116
	BP ₀	–.193	.187	–.288	.521**	–.073	.263
	BP ₁	–.151	.116	–.271	.515*	–.099	.247
Alcohol	EV	–.030	.259	–.072	–.232	.303	.271
	Max Demand	.194	–.202	.171	–.580*	.165	–.391
	BP ₀	–.062	.342	–.090	.028	.275	.377
	BP ₁	–.081	.387	–.111	.003	.329	.370

* *p* < .05.

** *p* < .001.

agencies in quantifying changes in abuse potential of the reformulation of abused drugs, as well as in the assessment of new medications. As the task is hypothetical, experience with a novel drug may be required, but this does not prevent the HPT from being a useful assessment in evaluations of abuse potential. Mackillop et al. (2018) found that after a drug challenge of a novel compound, participants had significantly higher demand for the drug than placebo. This indicates that HPTs can be used to assess the abuse potential of novel compounds.

The FDA has provided guidance on labeling regarding claims of abuse-deterrent opioids (FDA, 2015). Behavioral economic research may provide the FDA objective support for such claims. We propose that a hypothetical purchase task, such as that described in this study, may be among the useful sorts of supportive information to help FDA determine whether or not a product warrants labeling suggesting that a product results in meaningful reductions of abuse in the community.

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Contributors

JEH, SRH, and PGR conceived the study; PGR, SRH, JEH, EJC, ARB, RVF, and SHS designed the study; PGR collected the data; PGR and LPS processed the data; LPS, PGR, and SRH analyzed the data; LPS, PGR, SRH, JEH, EJC, ARB, RVF, and SHS interpreted the data; LPS, PGR, SRH, and JEH wrote the paper. All authors have approved this article.

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Conflicts of interest

The authors of this report were entirely responsible for the design of the study, the collection, analysis, and interpretation of data, the preparation of the manuscript, and the decision to submit the work for publication. LPS, PGR, and SRH have no interests that may be perceived as conflicting with the research. JEH, EJC, ARB, RVF, and SHS are employees of PinneyAssociates, which provides consulting services including abuse deterrent opioid assessment, drug abuse potential assessment, and regulatory guidance across a broad range of pharmaceutical products.

References

Amlung, M.T., Acker, J., Stojek, M.K., Murphy, J.G., MacKillop, J., 2012. Is talk “cheap”? An initial investigation of the equivalence of alcohol purchase task performance for hypothetical and actual rewards. *Alcohol. Clin. Exp. Res.* 36, 716–724. <https://doi.org/10.1111/j.1530-0277.2011.01656.x>.

Bannwarth, B., 2012. Will abuse-deterrent formulations of opioid analgesics be successful in achieving their purpose? *Drugs* 72, 1713–1723. <https://doi.org/10.2165/11635860-000000000-00000>.

Bruner, N.R., Johnson, M.W., 2014. Demand curves for hypothetical cocaine in cocaine-dependent individuals. *Psychopharmacology (Berl.)* 231, 889–897. <https://doi.org/10.1007/s00213-013-3312-5>.

Chase, H.W., MacKillop, J., Hogarth, L., 2013. Isolating behavioural economic indices of demand in relation to nicotine dependence. *Psychopharmacology (Berl.)* 226, 371–380. <https://doi.org/10.1007/s00213-012-2911-x>.

Cicero, T.J., Ellis, M.S., 2015. Abuse-deterrent formulations and the prescription opioid abuse epidemic in the United States: lessons learned from oxycodone. *JAMA Psychiatry* 72, 424. <https://doi.org/10.1001/jamapsychiatry.2014.3043>.

Comer, S.D., Collins, E.D., MacArthur, R.B., Fischman, M.W., 1999. Comparison of intravenous and intranasal heroin self-administration by morphine-maintained

humans. *Psychopharmacology (Berl.)* 143, 327–338. <https://doi.org/10.1007/s002130050956>.

Cone, E.J., Sokolowska, M., Lindhardt, K., 2016. Striving for consensus on approaches to category 1 testing of abuse-deterrent formulations of opioids: discussions from the first category 1 focus group meeting. *Pain Pract.* 16, 809–813. <https://doi.org/10.1111/papr.12488>.

Cone, E.J., Buchhalter, A.R., Lindhardt, K., Elhaug, T., Dayno, J.M., 2017. The ALERRT[®] instrument: a quantitative measure of the effort required to compromise prescription opioid abuse-deterrent tablets. *Am. J. Drug Alcohol Abuse* 43, 291–298. <https://doi.org/10.1080/00952990.2016.1278006>.

Davstad, I., Stenbacka, M., Leifman, A., Beck, O., Korkmaz, S., Romelsjö, A., 2007. Patterns of illicit drug use and retention in a methadone program: a longitudinal study. *J. Opioid Manage.* 3, 27–34 PMID:17367092.

Dennhardt, A.A., Yurasek, A.M., Murphy, J.G., 2015. Change in delay discounting and substance reward value following a brief alcohol and drug use intervention. *J. Exp. Anal. Behav.* 103, 125–140. <https://doi.org/10.1002/jeab.121>.

Food and Drug Administration, 2015. Abuse-deterrent Opioids – Evaluation and Labeling Guidance for Industry. <https://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm600788.htm>.

Greenwald, M.K., 2002. Heroin craving and drug use in opioid-maintained volunteers: effects of methadone dose variations. *Exp. Clin. Psychopharmacol.* 10, 39–46. <https://doi.org/10.1037/1064-1297.10.1.39>.

Henningsfield, J.E., Buchhalter, A.R., Fant, R.V., 2016. Behavioral pharmacology contributions to regulation of drug and tobacco products by the Food and Drug Administration. *Behav. Anal. Res. Prac.* 16, 179–189. <https://doi.org/10.1037/bar0000047>.

Hursh, S.R., 2014. Behavioral economics and the analysis of consumption and choice. In: McSweeney, F.K., Murphy, E.S. (Eds.), *The Wiley Blackwell Handbook of Operant and Classical Conditioning*. John Wiley and Sons, Ltd., Oxford, UK, pp. 275–305.

Hursh, S.R., Silberberg, A., 2008. Economic demand and essential value. *Psychol. Rev.* 115, 186–198. <https://doi.org/10.1037/0033-295X.115.1.186>.

Jacobs, E.A., Bickel, W.K., 1999. Modeling drug consumption in the clinic using simulation procedures: demand for heroin and cigarettes in opioid-dependent outpatients. *Exp. Clin. Psychopharmacol.* 7, 412–426. <https://doi.org/10.1037/1064-1297.7.4.412>.

Kaplan, B., Reed, D., 2014. University of Kansas Essential Value, Pmax, and Omax Calculator. <https://kuscholarworks.ku.edu/handle/1808/14934>.

Leri, F., Tremblay, A., Sorge, R.E., Stewart, J., 2004. Methadone maintenance reduces heroin- and cocaine-induced relapse without affecting stress-induced relapse in a rodent model of poly-drug use. *Neuropsychopharmacology* 29, 1312–1320. <https://doi.org/10.1038/sj.npp.1300435>.

MacKillop, J., Murphy, J.G., Ray, L.A., Eisenberg, D.T.A., Lisman, S.A., Lum, J.K., Wilson, D.S., 2008. Further validation of a cigarette purchase task for assessing the relative reinforcing efficacy of nicotine in college smokers. *Exp. Clin. Psychopharmacol.* 16, 57–65. <https://doi.org/10.1037/1064-1297.16.1.57>.

MacKillop, J., Goldenson, N.I., Kirkpatrick, M.G., Leventhal, A.M., 2018. Validation of a behavioral economic purchase task for assessing drug abuse liability. *Addict. Biol.* <https://doi.org/10.1111/adb.12592>.

Murphy, J.G., MacKillop, J., 2006. Relative reinforcing efficacy of alcohol among college student drinkers. *Exp. Clin. Psychopharmacol.* 14, 219–227. <https://doi.org/10.1037/1064-1297.14.2.219>.

Murphy, J.G., MacKillop, J., Skidmore, J.R., Pederson, A.A., 2009. Reliability and validity of a demand curve measure of alcohol reinforcement. *Exp. Clin. Psychopharmacol.* 17, 396–404. <https://doi.org/10.1037/a0017684>.

Murphy, J.G., MacKillop, J., Tidey, J.W., Brazil, L.A., Colby, S.M., 2011. Validity of a demand curve measure of nicotine reinforcement with adolescent smokers. *Drug Alcohol Depend.* 113, 207–214. <https://doi.org/10.1016/j.drugalcdep.2010.08.004>.

Murphy, J.G., Dennhardt, A.A., Yurasek, A.M., Skidmore, J.R., Martens, M.P., MacKillop, J., McDevitt-Murphy, M.E., 2015. Behavioral economic predictors of brief alcohol intervention outcomes. *J. Consult. Clin. Psychol.* 83, 1033–1043. <https://doi.org/10.1037/ccp0000032>.

Pickover, A.M., Messina, B.G., Correia, C.J., Garza, K.B., Murphy, J.G., 2016. A behavioral economic analysis of the nonmedical use of prescription drugs among young adults. *Exp. Clin. Psychopharmacol.* 24, 38–47. <https://doi.org/10.1037/pha0000052>.

Roma, P.G., Hursh, S.R., Hudja, S., 2016. Hypothetical purchase task questionnaires for behavioral economic assessments of value and motivation. *MDE* 37, 306–323. <https://doi.org/10.1002/mde.2718>.

Schwartz, R.P., Kelly, S.M., O’Grady, K.E., Gandhi, D., Jaffe, J.H., 2012. Randomized trial of standard methadone treatment compared to initiating methadone without counseling: 12-month findings. *Addiction* 107, 943–952. <https://doi.org/10.1111/j.1360-0443.2011.03700.x>.

Stein, J.S., Koffarnus, M.N., Snider, S.E., Quisenberry, A.J., Bickel, W.K., 2015. Identification and management of nonsystematic purchase task data: toward best practice. *Exp. Clin. Psychopharmacol.* 23, 377–386. <https://doi.org/10.1037/pha0000020>.

Strickland, J.C., Stoops, W.W., 2017. Stimulus selectivity of drug purchase tasks: a preliminary study evaluating alcohol and cigarette demand. *Exp. Clin. Psychopharmacol.* 25, 198–207. <https://doi.org/10.1037/pha0000123>.

Tucker, J.A., Cheong, J., Chandler, S.D., Lambert, B.H., Kwok, H., Pietrzak, B., 2016. Behavioral economic indicators of drinking problem severity and initial outcomes among problem drinkers attempting natural recovery: a cross-sectional naturalistic study. *Addiction* 111, 1956–1965. <https://doi.org/10.1111/add.13492>.

Vincent, P.C., Collins, R.L., Liu, L., Yu, J., De Leo, J.A., Earleywine, M., 2017. The effects of perceived quality on behavioral economic demand for marijuana: a web-based experiment. *Drug Alcohol Depend.* 170, 174–180. <https://doi.org/10.1016/j.drugalcdep.2017.04.004>.

- [drugalcdp.2016.11.013](#).
- Vosburg, S.K., Jones, J.D., Manubay, J.M., Ashworth, J.B., Shapiro, D.Y., Comer, S.D., 2013. A comparison among tapentadol tamper-resistant formulations (TRF) and oxycontin[®] (non-TRF) in prescription opioid abusers: assessment of Tapentadol TRF. *Addiction* 108, 1095–1106. <https://doi.org/10.1111/add.12114/>.
- Vowles, K.E., McEentee, M.L., Julnes, P.S., Frohe, T., Ney, J.P., van der Goes, D.N., 2015. Rates of opioid misuse, abuse, and addiction in chronic pain: A systematic review and data synthesis. *Pain* 156, 569–576. <https://doi.org/10.1097/01.j.pain.0000460357.01998.fl>.