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SIMULATING DEMAND FOR CIGARETTES AMONG PREGNANT WOMEN: A LOW-RISK METHOD FOR STUDYING VULNERABLE POPULATIONS

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Abstract

A substantive obstacle to experimentally studying cigarette smoking and use of other tobacco products in pregnant women is the risk of adverse effects on mother and fetus from experimenter administration of the product of interest. The purpose of this study is to investigate bypassing that obstacle by using behavioral economic simulation tasks. In the present study we used the Cigarette Purchase Task (CPT) to simulate changes in demand for hypothetical cigarettes as a function of varying cigarette prices. Participants were 95 pregnant women who completed the CPT prior to participation in a smoking-cessation trial. Aggregate and individual participant demand varied as an orderly function of price and those changes were well fitted by an exponential equation. Demand also varied in correspondence to two well-validated predictors of individual differences in smoking cessation among pregnant women (cigarettes smoked per day, pre-pregnancy quit attempts). Moreover, CPT indices were more effective than these two conventional variables in predicting individual differences in whether women made a quit attempt during the current pregnancy. Overall, these results represent a promising step in demonstrating the validity and utility of the CPT for experimentally examining demand for cigarettes, and potentially other tobacco and nicotine delivery products, among pregnant women.

Keywords

behavioral economics; Cigarette Purchase Task; pregnant women; cigarette smoking; smoking rate; quit attempts; translational science

The overarching aim of the present study is to examine and validate among pregnant women a behavioral economic simulation model known as the Cigarette Purchase Task (CPT) wherein participants estimate their likely cigarette consumption levels under varying hypothetical monetary prices. Simulated purchase tasks were developed as an efficient, ethical, and medically safe strategy for experimentally examining demand curves for abused substances in humans (Jacobs & Bickel, 1999). The task is an adaptation of the more time- and labor-intensive experimental procedures used in generating demand curves in drug self-administration studies conducted with nonhuman (e.g., Hursh & Silberberg, 2008; Hursh & Winger, 1995) and human (e.g., Bickel & Madden, 1999a, 1999b) participants under rigorously controlled laboratory conditions. Demand curves generated in controlled laboratory settings are highly effective in comparing and contrasting the abuse potential of different drugs (e.g., Hursh & Winger, 1995) and the effects of different environmental and biological manipulations of potential utility in reducing drug consumption (e.g., Bickel & Madden, 1999a; Hursh, Galuska, Winger, & Woods, 2005). Likewise, accumulating evidence from studies using simulated purchase tasks in humans are demonstrating them to be a valid experimental method for studying consumption of cigarettes (e.g., Madden & Kalman, 2010; O'Connor et al., 2016; Schlienz, Hawk, Tiffany, O'Connor, & Mahoney, 2014), other abused substances (Collins, Vincent, Yu, Liu, & Epstein, 2014; Murphy et al., 2016), as well as nondrug commodities with addiction potential (Reed, Kaplan, Becirevic, Roma, & Hursh, 2016). Importantly, there is close correspondence between demand curves generated under controlled laboratory conditions involving actual drug consumption and simulation tasks (Amlung, Acker, Stojek, Murphy, & MacKillop, 2012; Wilson, Franck, Koffarnus, & Bickel, 2016).

Because the CPT permits experimental examination of changes in demand without directly having study participants smoke, the task can be used ethically and safely in vulnerable populations such as adolescents (Murphy, MacKillop, Tidey, Brazil, & Colby, 2011), and in the present study pregnant women. To our knowledge, the present study is the first to extend the CPT to pregnant women, a population with whom there are numerous ethical and safety constraints on experimentally studying factors underpinning consumption of cigarettes or other tobacco and nicotine delivery products. Valid simulation models for studying these products among pregnant women have the potential to be highly useful to tobacco regulatory science efforts by allowing investigators to experimentally study factors that influence demand without having to administer the product of interest to participants. The 2009 U.S. Tobacco Control Act granted regulatory authority over the manufacturing and marketing of cigarettes and other tobacco products to the Food and Drug Administration (FDA) (Family Smoking Prevention and Tobacco Control Act, 2009). That legislation charges the FDA with protecting the public health from the adverse health impacts of cigarette smoking and use of other tobacco and nicotine delivery products (Ashley & Backinger, 2012; Ashley, Backinger, van Bommel, & Neveleff, 2014).

There is little question that cigarette smoking among pregnant women has serious adverse public health impacts. Cigarette smoking during pregnancy is the leading cause of poor pregnancy outcomes in the U.S. and other developed countries, and *in utero* tobacco smoke exposure increases risk for a wide range of subsequent adverse infant, child, and adult health outcomes (e.g., Cnattingius, 2004; Dietz et al., 2010; Higgins & Solomon, 2016). Because

cigarette smoking is overrepresented among economically disadvantaged women, it is also a contributor to health disparities (Higgins & Chilcoat, 2009). There is also increasing use of e-cigarettes and other tobacco and nicotine delivery products among women of reproductive age, further underscoring the need for regulatory science addressing the abuse potential of these products as well as factors underpinning vulnerability to using and developing dependence on them (e.g., Chivers, Hand, Priest, & Higgins, 2016). Methods that can support low-risk experimental study of consumption of these products in women of childbearing age, especially pregnant women, could be a boon to this effort. A behavioral simulation procedure for examining the discounting of delayed rewards (Bickel, Odum, & Madden, 1999) has been effective in examining individual differences in risk for cigarette smoking and e-cigarette use in at least one prior study among women of reproductive age (Chivers et al., 2016) and in a study of risk factors for continuing to smoke upon learning of a pregnancy (White, Redner, Skelly, & Higgins, 2014). The current study represents an initial step in evaluating the utility of the CPT in such efforts.

Simulation models for use in pregnant women also have important potential utility for tobacco control efforts. Clinical research has been underway since the mid-1980s to develop effective smoking-cessation interventions for pregnant women (Higgins & Solomon, 2016). There have been some important developments towards meeting this challenge, with the behavioral economic intervention of providing financial incentives generating the best cessation outcomes (Higgins & Solomon, 2016). In meta-analyses on this topic, financial incentives are estimated to increase the odds of achieving late-pregnancy abstinence 3.79 (95% CI: 2.74–5.25) times above control treatments (Cahill, Hartmann-Boyce, Perera, 2015; also see Chamberlain et al., 2013; Lumley et al., 2009). Nevertheless, only approximately 35% of women achieve abstinence even with this relatively effective incentives intervention (Higgins et al., 2012; Higgins & Solomon, 2016). Hence, there is little question about the need for greater scientific understanding of barriers to successfully discontinuing smoking during pregnancy.

Two reliable and independent risk factors for women failing to discontinue smoking during pregnancy, whether trying to quit on their own or in the context of formal treatment, are (1) heavy smoking (i.e., 10 or more cigarettes/day at start of prenatal care); and (2) the absence of prior quit attempts, with the former being the most robust predictor (e.g., Kurti, Davis, Skelly, Redner, & Higgins, 2016; Lopez, Skelly, White, & Higgins, 2015; White et al., 2014). Greater scientific understanding of differences in how cigarettes exert control over consumption among women with these risk factors could be very helpful to efforts to reduce smoking among pregnant women.

This initial study of the CPT with pregnant cigarette smokers has four overarching aims: (1) assess and characterize how well data generated in this simulation task are described by the exponential demand equation (Hursh & Silberberg, 2008) that was developed using data from rigorously controlled experimental studies of drug self-administration (construct validity); (2) examine whether the CPT reveals differences in demand for cigarette smoking among women with versus without the two well-validated independent risk factors for failing to discontinue smoking during pregnancy mentioned above (convergent validity); (3) examine whether the CPT is useful in characterizing cumulative risk for ongoing smoking

associated with the intersection of these two risk factors (i.e., how demand changes across women with neither, only one, or both risk factors) (Higgins et al., 2016); and (4) examine whether CPT indices are effective in predicting individual differences in efforts to discontinue antepartum smoking (predictive validity). Rather than follow women through delivery to assess who discontinues smoking in this initial study on the CPT among pregnant smokers, we used antepartum quit attempts as a proxy measure. A positive history of antepartum quit attempts upon entering prenatal care is a significant predictor of achieving late pregnancy abstinence and can be reasonably conceptualized as an incipient form of eventual quitting (Kurti et al., 2016; Lopez et al., 2015; White et al., 2014). Relationships between CPT performance and late-pregnancy and postpartum smoking status will be detailed in future reports.

Methods

Participants

Study participants were 95 women who were biochemically confirmed to be smoking upon entering prenatal care and enrolled in an ongoing randomized controlled clinical trial on smoking cessation. Participants were recruited from local obstetrical clinics and the Federal Special Supplemental Nutrition Program for Women, Infants, and Children office located in the Burlington, Vermont area. They averaged 25 years of age, had a high school or less education, most were unmarried and without private health insurance, and reported smoking an average of 9.1 ± 5.2 cigarettes/day at study entry and 17.6 ± 8.8 cigarettes/day before learning of the current pregnancy (Table 1).

Trial inclusion criteria were (a) self-reported smoking in past week that was biochemically verified using urine cotinine testing, (b) planning to remain in the geographical area for 3 months following delivering, and (c) English speaking. Exclusion criteria were (a) current incarceration, (b) living with another trial participant, (c) currently enrolled in opioid substitution therapy, (d) current use of psychomotor stimulant or antipsychotic medications, (e) greater than 25 weeks gestation, and (f) living in a group home. The University of Vermont Institutional Review Board approved all study procedures and all participants provided written informed consent.

Assessments

At the trial intake assessment, all participants completed questionnaires examining socio-demographics, smoking history, smoking environment and motivations, confidence and intentions to quit smoking, and provided breath and urine specimens. They also completed the CPT (detailed below) and other behavioral and psychiatric instruments assessing impulsivity and other states and traits. Abbreviated versions of the intake assessment were administered again at seven subsequent assessments completed antepartum (early- and late-pregnancy) and postpartum (2-, 4-, 8-, 12-, 24-, and 50 weeks). The present study is focused exclusively on information collected at the intake assessment.

Cigarette Purchase Task

The CPT assesses estimated cigarette consumption in a typical day at various escalating prices per cigarette. The version used in the present study was adapted from MacKillop et al. (2008). Participants were provided with the following oral instructions about how to complete the task: “Think about how you are feeling right now. The following questions ask how many cigarettes you would smoke if they cost various amounts of money. Assume that: (1) The available cigarettes are your usual brand. (2) You have the same income/savings that you have now and no access to any cigarettes or nicotine products other than those offered at these prices. (3) You would smoke the cigarettes that you request within 24 hours. You cannot save or stockpile cigarettes for a later date. (4) You can smoke without any restrictions and without factoring in what might occur in the next 24 hours related to your participation in the study.”

The task included the following 19 prices/cigarette: \$0.00 (free), \$0.02, \$0.05, \$0.10, \$0.20, \$0.30, \$0.40, \$0.50, \$0.60, \$0.70, \$0.80, \$0.90, \$1.00, \$2.00, \$3.00, \$4.00, \$5.00, \$10.00, and \$20.00. Associated prices per pack were presented to the right of the individual cigarette prices. Prices were presented in ascending order. Participants completed a computerized version of CPT on a laptop computer when completed in the clinic or an identical paper-and-pencil version of the task when the assessment was completed at the participant’s home.

Data Analysis Methods

Visual inspection of all 95 CPT datasets identified a single outlier with demand intensity (Q_0 ; level of consumption (Q) at no price [free; \$0.00]) of 2000 cigarettes; a subsequent outlier analysis using Grubbs’ procedure in GraphPad Prism[®] version 7.0a for Mac (Graphpad Software, La Jolla California, USA, www.graphpad.com) with alpha set to .05 confirmed this outlier. The associated dataset was excluded from all subsequent analyses. We examined degree of systematic responding for all remaining 94 CPT datasets using the procedure described by Stein, Koffarnus, Snider, Quisenberry, and Bickel (2015) with the following detection limits for trend (Q), bounce (B), and reversals from zero, respectively: 0.025, 0.10, and 0. One dataset did not pass the detection limit for trend (i.e., no elasticity in demand); we excluded this dataset from all subsequent analyses, leaving 93 systematic CPT datasets for inclusion in the analyses described below.

For the 93 systematic CPT datasets, we analyzed both empirical (i.e., observed off demand curve datasets) and derived (i.e., using nonlinear regression) CPT demand metrics at the aggregate, group, and individual levels. Empirical metrics included demand intensity (Empirical- Q_0 ; reported number of cigarettes consumed at free price), $O_{\max}$ (peak expenditure; calculated by multiplying each Q by its associated cost [C] and identifying the largest expenditure value as $O_{\max}$). The financial cost (i.e., price) associated with $O_{\max}$ was coded as $P_{\max}$. We coded the last price with any level of demand as breakpoint, analogous to Roma, Hursh, and Hudja’s (2016) BP_1 metric that circumvents inference of breakpoint in datasets featuring > 0 consumption at highest CPT price; in this dataset, seven participants reported > 0 cigarettes consumed at highest price (\$20.00) rendering their $P_{\max}$ as \$20.00. Derived measures included α (rate of change in elasticity across the demand curve) and Derived Q_0 from Hursh and Silberberg’s (2008) exponential demand equation stating:

$$\log Q = \log Q_0 + k \cdot (e^{-\alpha \cdot (Q_0 \cdot c)} - 1) \quad (1)$$

where k is the range of log units consumption (Q); in all analyses, k was calculated as the log quotient of maximum consumption over minimum nonzero consumption. As per Hursh's recommendations (2016), we altered no zero values in either cost or consumption. Thus, nonlinear regression of Equation 1 began at \$0.02, allowing for separate analyses of empirical and derived Q_0 values. We used the freely available GraphPad Prism[®] template provided by the Institutes for Behavior Resources (<http://www.ibrinc.org/index.php?id=181>) for all Equation 1 fits. Note that this Prism[®] solution uses standard nonlinear regression to minimize the sum of squares via the Marquardt method (Marquardt, 1963). Each Equation 1 analysis featured 1000 as the maximum number of iterations with strict convergence criteria.

Group demand curves were generated using average consumption (across group participants) at each cost. We used the extra-sum-of-squares F test in Prism[®] to compare group demand curves with alpha set to .05 to evaluate whether one demand curve best explained the two group aggregate datasets for each of the following: (1) women who smoked < 10 versus ≥ 10 cigarettes per day; (2) women with versus without pre-pregnancy quit attempts; (3) women who smoked < 10 cigarettes per day with pre-pregnancy quit attempts versus those who smoked < 10 cigarettes per day without pre-pregnancy quit; (4) women who smoked ≥ 10 cigarettes per day with pre-pregnancy quit attempts versus those who smoked ≥ 10 cigarettes per day without pre-pregnancy quit attempts. The D'Agostino-Pearson omnibus normality test in Prism[®] suggested deviance from Gaussian distribution for all demand metrics; we thereby used Spearman's ρ correlations and Mann-Whitney U tests for all demand metric analyses.

Logistic regression was used to assess the association between antepartum quit attempts and the two risk factors, smoking rate and pre-pregnancy quit attempts and risk factor groupings. Logistic regression with backward elimination was used to create models predicting antepartum quit attempts with the conventional measures and CPT indices. We investigated the potential for confounders and found that age at which participants began smoking was positively correlated ($r = 0.26$) with antepartum quit attempts and negatively correlated ($r = -0.29$) with smoking rate at study intake. Pre-pregnancy smoking rate was also correlated ($r = 0.32$) with smoking rate at study intake but was not included as a covariate in the modeling to avoid multicollinearity. Age of beginning smoking was forced to remain in the models while all other variables required a p value < .05 to remain in the model. Prior to these regression analyses, each CPT index was examined for outliers and any value that was greater than three standard deviations from the mean was recoded to one unit above the next highest nonoutlier value. All logistic regression analyses were done using SAS version 9.3 (SAS Institute, Cary, NC, USA).

Unless otherwise stated, we set alpha to .05 for all inferential statistics.

Results

Characterizing Demand

Demand in the overall sample—Simulated cigarette consumption among this group of pregnant smokers varied as an orderly function of increasing price per cigarette (Fig. 1). Equation 1 provided an excellent fit to the aggregate data ($R^2 = .99$; RMSE = .08; using $k = 1.96$). For the aggregate demand curve (using a shared $k = 2.10$ for all 93 participants), empirical $Q_0 = 15.96$, derived $Q_0 = 18.00$, empirical $O_{\max} = \$9.94$, empirical $P_{\max} = \$0.50$, and $\alpha = .024$. Correlation analysis between empirical and derived Q_0 indicates significantly strong convergence between these two metrics, $r_s = .93$, $p < .0001$. Finally, for this aggregate analysis only, we also calculated a derived $P_{\max}$ to model potential tax policy impacts (see Hursh & Roma, 2013) using freely available software (Kaplan & Reed, 2014) and the derived $P_{\max}$ equation theorized by Hursh (2014) where:

$$P_{\max} = \frac{(.083 \cdot k + 0.65)}{(Q_0 \cdot \alpha \cdot k^{1.5})} \quad (2)$$

Equation 2 suggests that a price of \$0.75/cigarette yields unit elasticity (i.e., $= P_{\max}$) in this sample.

Equation 1 also provided excellent fits to individual-participant results with R^2 median = .83, (IQR = .66 – .92). Table 2 shows descriptive statistics for each demand metric across the 93 participants analyzed. Distributions of metrics adequately approximate those found in similar CPT studies and demand metrics were significantly correlated in expected directions consistent with past research (e.g., Few, Acker, Murphy, & MacKillop, 2012; MacKillop et al., 2008; Yurasek, Murphy, Clawson, Dennhardt, & MacKillop, 2013; see Table 3).

Demand among heavier versus lighter smokers—Cigarette demand differed significantly ($F(1,36)=123$, $p < .0001$) between women who smoked ≥ 10 versus < 10 cigarettes per day (Fig. 2), with heavier smokers exhibiting significantly greater empirical ($U = 718.5$, $p < .001$) and derived intensity of demand ($U = 680$, $p < .0001$), lower α ($p < .01$), and greater $O_{\max}$ ($U = 493.5$, $p < .0001$). There were no significant differences between heavier and lighter smokers in $P_{\max}$ ($U = 1016$, $p = .13$) or breakpoint ($U = 988$, $p = .09$).

Demand among those with versus without pre-pregnancy quit attempts—Cigarette demand in the group aggregate curves also differed significantly ($F[1, 36] = 8.6$, $p < .01$) between women who did versus did not report making any pre-pregnancy quit attempts (Fig. 3). Those without pre-pregnancy quit attempts exhibited greater median empirical ($U = 737$, $p < .05$) and derived ($U = 708$, $p < .05$) intensity of demand compared to women who reported pre-pregnancy quit attempts, and a slightly greater $O_{\max}$ ($U = 679$, $p < .05$). There were no significant differences in α ($U = 854$, $p = .33$), $P_{\max}$ ($U = 867.5$, $p = .38$), or breakpoint ($U = 786$, $p = .12$).

Demand corresponding to the intersection of the two risk factors—Comparison of aggregate demand curves related to the intersection of cigarettes per day and pre-

pregnancy quit attempts (Fig. 4) revealed that consumption among women with versus without pre-pregnancy quit attempts differed among lighter smokers (Prism's extra sum-of-squares $F[1, 36] = 9.1, p < .01$), while only approaching significance in heavier smokers (extra sum-of-squares $F[1, 36] = 3.9, p = .05$). Similarly, group comparisons identified significant differences between light smokers who did versus did not report pre-pregnancy quit attempts in empirical Q_0 , derived Q_0 , and empirical $O_{\max}$; there were no significant differences in any demand metrics among heavy smokers who did versus did not report pre-pregnancy quit attempts (see Table 4). In brief, differences in demand corresponding to the intersection of pre-pregnancy quit attempts and smoking rate were largely, although not exclusively, restricted to lighter smokers.

Antepartum Quit Attempts Associated with Different Risk Factor Groupings

There was considerable correspondence between the risk-factor differences in demand outlined above and differences noted in whether women reported making antepartum quit attempts. Differences in smoking rate (< 10 vs. ≥ 10 cigarettes per day) were associated with clear differences in antepartum quit attempts, with 40% (22/55) of lighter smokers reporting attempts compared to only 13% (5/38) of heavier smokers (OR = 4.4, 95% CI = 1.5 – 13.0) (Fig. 5, upper left-most panel). Regarding antepartum quit attempts by pre-pregnancy quit attempts history, 38% (23/61) of women who reported pre-pregnancy quit attempts also reported making antepartum quit attempts compared to only 13% (4/32) of those who reported no pre-pregnancy quit attempts (OR = 4.2, 95% CI = 1.3 – 13.6) (Fig. 5, upper right-most panel).

Examining antepartum quit attempts by the intersection of these two risk factors revealed a high of 50.0% (19/38) of women reporting antepartum quits among those who smoked < 10 cigarettes per day and had a positive history of pre-pregnancy quit attempts, followed by only 17.4% (4/23) among those who smoked < 10 cigarettes per day and had a negative history of pre-pregnancy quit attempts, 13.6% (3/22) among those who smoked ≥ 10 cigarettes per day and had a positive history of quit attempts, and a low of 6.7% (1/15) among those who smoked ≥ 10 cigarettes per day and had a negative history of pre-pregnancy quit attempts (Fig. 5, lower panel). Expressed in terms of odds ratios, the odds (95% CIs) of making an antepartum quit attempt among women who were lighter smokers and had a positive history of pre-pregnancy quit attempts were 4.7 (1.1 – 18.9) times greater than lighter smokers with a negative history of pre-pregnancy quit attempts, 4.7 (1.4 – 16.6) times greater than heavier smokers with a positive history of quit attempts, and 14.0 (1.67 – 117.3) times greater than heavier smokers with a negative history of pre-pregnancy quit attempts. None of the other risk-group comparisons in odds of antepartum quit attempts were significant.

Predicting Antepartum Quit Attempts

In this section we report results of the multiple logistic regression analyses examining the extent to which the conventional risk factors and CTP indices can predict antepartum quit attempts alone and in combination, controlling for potential confounding by other characteristics.

Conventional predictors—When the two conventional risk factors were examined, both were retained as independent predictors at $p < .05$ even after adjusting for the age that the women began smoking. Those who smoked < 10 cigarettes per day had 3.32 greater odds (95% CI: 1.04 – 10.64) of reporting antepartum quit attempts compared to women who smoked ≥ 10 cigarettes per day. Similarly, women who reported having made pre-pregnancy quit attempts had 4.21 greater odds (95% CI: 1.23 – 14.41) of an antepartum quit attempt compared to women who reported no pre-pregnancy quit attempts. Overall model fit based on the C statistic (.76) was in the acceptable range. There was not a significant interaction of the predictors ($p = .69$) in this model, consistent with the evidence described above showing that the association of pre-pregnancy quit attempts and antepartum quit attempts, while discernibly stronger among lighter smokers, was not specific to them.

CPT predictors—When the ability of the five CPT empirical indices (Q_0 , $O_{\max}$, $P_{\max}$, α , breakpoint) to predict antepartum quit attempts were examined in a multiple logistic regression model, two indices ($O_{\max}$, breakpoint) were retained as independent predictors at $p < .05$. After adjusting for age at beginning smoking, the odds of reporting antepartum quit attempts decreased 15% for every one unit increase in $O_{\max}$ (OR = 0.85; 95% CI: 0.75 – 0.96). Similarly, a lower breakpoint predicted 1.35 (95% CI, 1.03 – 1.78) greater odds of antepartum quit attempts. Overall model fit based on the C statistic (.74) was similar to that of the conventional predictors.

Conventional and CPT predictors together—When the conventional and CPT indices were examined together again controlling for age at beginning smoking, only the two CPT indices ($O_{\max}$, breakpoint) were retained as independent predictors at $p < .05$. Odds and model fit were the same as in the model described above examining only CPT predictors.

Discussion

Below we comment on the study results in relation to the four overarching aims of this initial study of the CPT with pregnant women as well their implications for tobacco regulatory science and tobacco control efforts. First, these results provide strong support for the construct validity of simulated cigarette demand in this vulnerable population. At the aggregate and individual participant level simulated demand decreased as a function of increasing price consistent with the economic law of demand and in a manner that was well described by the Hursh and Silberberg (2008) exponential demand equation that is based on experimental analyses of changes in demand for real commodities under direct manipulations of economic constraint. Individual participant demand metrics and the pattern of associations between the different CPT indices (Tables 2 & 3, respectively) also aligned well with observations from prior studies using CPT in other populations (Few et al., 2012; MacKillop et al., 2008; Yurasek et al., 2013). Considered together, these results provide strong and consistent evidence that the CPT generated valid demand curves in this new population that align well with prior evidence from studies examining demand for real and hypothetical cigarettes (Bickel et al., 1999b; Wilson et al., 2016).

Second, the present results provide strong evidence in support of the convergent validity of the CPT by demonstrating its sensitivity to differences in demand related to two well-

established risk factors for continuing to smoke upon learning of a pregnancy. As might be expected considering how the populations are defined, the CPT confirmed that heavier smokers exhibited greater intensity of smoking (consumption at zero cost per cigarette) and $O_{\max}$ (maximal daily expenditure on smoking) than lighter smokers. The results also documented a lower α (i.e., more persistent demand) or greater essential value of smoking among heavier compared to lighter smokers. That difference too may seem intuitive considering the ample evidence of lower cessation rates among heavier smokers, but there is also evidence in the literature supporting the plausibility of an explanation for such differences based exclusively on greater intensity of smoking alone. For example, results from a prior study on the timing and magnitude of changes in smoking rates upon learning of a pregnancy suggested that women who were heavy pre-pregnancy smokers (~20 cigarettes per day) and those who were lighter smokers (~10 cigs day) both decreased smoking rates to a comparable extent (~ 10 cigarettes per day). However, because of the differences in pre-pregnancy smoking rates, the heavier pre-pregnancy smokers continued smoking at a reduced level while the lighter smokers discontinued smoking completely (Heil et al., 2014). The present results suggest that the lower elasticity of demand, or greater essential value of the reinforcing effects of smoking, among heavier compared to lighter smokers is also a likely contributor to those differences in cessation rates.

We know of no prior efforts to consider how pre-pregnancy quit attempts might be associated with differences in demand for smoking, and hypotheses in that regard seem less intuitive than with smoking rate. The evidence from the present study suggests that, like lighter compared to heavier smokers, those who have made prior quit attempts have a lower intensity of demand and a lower $O_{\max}$ compared to those who have not made such attempts.

Third, CPT results in the present study advanced understanding of the intersection of smoking rate and pre-pregnancy quit attempts by showing that the differences in intensity of demand and $O_{\max}$ among those with versus without pre-pregnancy quit attempts were most pronounced among lighter smokers. Put differently, demand among heavier smokers appears to be sufficiently strong to obscure, although in this case not totally eliminate, the influence of other factors. A similar pattern was observed previously with delay discounting wherein the association of steeper discounting of hypothetical monetary reinforcers with a lower likelihood of quitting smoking was more discernible among lighter than heavier smokers (White et al., 2014). A likely explanation for these patterns is that at higher smoking rates choices about whether to continue smoking are more likely to be dominated by more proximal pharmacological and dependence-related factors (e.g., nicotine withdrawal symptoms, salient smoking-related antecedent stimuli) compared to lower smoking rates where more varied and temporally distal factors have a greater opportunity to influence choice. These observations are also consistent with experimental evidence that counseling smokers to reduce their level of smoking increases quit attempts during a 6-month follow-up period (Carpenter, Hughes, Solomon, & Callas, 2004) and that transitioning smokers onto very low nicotine-content cigarettes decreases actual smoking rates (and CPT-measured demand intensity) while also increasing quit attempts (e.g., Donny et al., 2015). Importantly, the pattern of antepartum quit attempts corresponding to the intersection of these two risk factors in the present study was concordant with the evidence from the CPT analyses (see Fig. 5).

Fourth, the results provide strong support for the predictive validity of the CPT, which was effective in predicting outcomes among pregnant smokers using antepartum quit attempts as a proxy measure of cessation (predictive validity). When examined alone, a multiple logistic regression model based only on the CPT indices provided almost identical fit to the data as a model based on the two conventional risk factors alone. Moreover, when the CPT and conventional risk factors were included together in a backward elimination model, only the CPT indices of $O_{\max}$ and breakpoint were retained suggesting that they provided a stronger independent fit to this important outcome measure than the conventional risk factors. These results are consistent with prior evidence supporting the predictive validity of the CPT (MacKillop et al., 2016; Secades-Villa, Pericot-Valverde, & Weidberg, 2016)

Overall, these results have a number of potentially important implications for tobacco regulatory science and tobacco control efforts. The most substantial and direct implication for regulatory science is the evidence supporting the validity and practical utility of using simulation tasks to experimentally investigate cigarette smoking, and perhaps use of other tobacco and nicotine delivery products, among pregnant women without having to administer the product to participants. These results compliment and extend prior evidence on the utility of the CPT, and other simulation tasks related to the reinforcement process (delay discounting), in prior studies of adolescent smokers (Murphy et al., 2011) and very low nicotine content cigarettes in nonpregnant women of reproductive age, opioid abusers, individuals with affective disorders (Higgins, Heil, et al., 2016) as well as smokers with schizophrenia (MacKillop & Tidey, 2011). Although not directly examined in the present study, these simulation tasks should also allow for low-risk studies comparing differences in the abuse liability of various tobacco and nicotine delivery products (e.g., e-cigarettes) in pregnant women and other highly vulnerable populations (e.g., adolescents).

In terms of tobacco control efforts, the present results provide concrete new information as to how cigarettes may need to be priced in order to achieve unit elasticity (i.e., increases in price would produce proportional reductions in demand) among pregnant smokers. The estimate was that cigarettes would need to be priced at \$0.75 each or \$15.00 per pack in order to achieve unit elasticity. Current cigarette prices vary considerably from state to state in the U.S. ranging from an average low of approximately \$5.00 per pack to a high \$13.50 (e.g., Fair Reporter, 2015; The Awl, 2015), but all appear to be on the inelastic side of the demand curve for the pregnant smoker population based on the present results. This would suggest that a great deal more could be done with excise taxes to reduce smoking among pregnant women. Elasticity estimates from simulated demand curves have been shown to predict changes in consumption among individual smokers following increases in tobacco excise taxes (Grace, Kivell, & Laugesen, 2015). The results also further underscore the importance of encouraging women of reproductive age who smoke to make quit attempts and to reduce their smoking rates as low as possible if they are unable to achieve total abstinence. Indeed, targeted public health messaging that shares this information to women of childbearing age and healthcare providers who care for them would seem to be a prudent public health priority.

In terms of study limitations, there are at least three that merit mention. First, we cannot confirm in the present study that the simulated changes in demand reported above indeed

represent how these study participants or other pregnant smokers would respond to real increases in cigarette price, although the excellent fit of the exponential demand equation, the sensitivity of the CPT to differences related to the two conventional risk factors alone and in combination, and the ability of the CPT to predict antepartum quit attempts, strongly suggests that they do. Second, the study sample was a convenience rather than a nationally representative sample and thus may not be generalizable to pregnant smokers with other sociodemographic or smoking characteristics. We hope that limitation will be addressed through additional studies using this promising simulation method to study consumption of cigarettes and other tobacco and nicotine delivery products among pregnant women specifically and women of reproductive age more generally. Lastly, we cannot confirm that the relationships observed between CTP indices and antepartum quit attempts will extend to actual late pregnancy smoking cessation, although there are studies already underway to address that question. These limitations notwithstanding, we believe that the present study represents an important initial step in demonstrating the construct, convergent, and predictive validity of the CPT for experimentally examining questions related to cigarette smoking, and potentially use of other tobacco and nicotine delivery products, among pregnant women.

Acknowledgments

We are honored to have this opportunity to contribute an article in memory of Alan Baron, PhD, a pioneer in the experimental analysis of human operant behavior and accomplished mentor who will be sorely missed.

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The authors have nothing to declare related to this study and report.

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Fig. 1.

Overall demand curve and associated indices for all participants. Vertical dashed line depicts derived $P_{\max}$; shaded error bands depict 95% CI of the best fitted line. R^2 and RMSE represents the fit of the Exponential Demand Equation (Eq. 1) to the data (see text for details).

Fig. 2.

Demand curves and associated indices among participants smoking <10 versus 10 cigarettes per day at baseline.

Fig. 3.
Demand curves and associated indices among participants who self-reported a positive versus negative history of making one pre-pregnancy quit attempts.

Fig. 4.

Demand curves across the four risk groups comprised by the cigarettes per day and pre-pregnancy quit risk factors. The demand curves in the left panel represent participants smoking < 10 cigarettes per day who did versus did not attempt to quit smoking pre-pregnancy. The demand curves in the right panel represent participants smoking 10+ cigarettes per day who did versus did not attempt to quit pre-pregnancy.

Fig. 5.

Percentages of participants who reported at least one quit attempt during the current pregnancy (antepartum quit attempts) across different risk-factor groupings. The top left panel depicts the percentage of women with antepartum quit attempts among lighter (< 10 cigarettes per day) versus heavier (≥ 10 cigarettes per day) smokers; the top right panel depicts the same outcome among women who did versus did not make at least one pre-pregnancy quit attempt. The bottom panel depicts the percentage of women who made at

least one antepartum quit attempt across each of the four risk groupings representing the intersection of the cigarettes per day and pre-pregnancy quit attempts risk factors.

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Table 1

Participant demographics, smoking characteristics, beliefs about smoking harm, and psychiatric symptoms.

Demographics:	
Age (years)	25.0 ± 5.0
Education	
% <12 years	21
% 12 years	61
% >12 years	18
% Caucasian	91
% Married	23
% Private insurance	28
% Employed outside of home	56
% 1st pregnancy	47
Weeks pregnant at intake	11.7 ± 6.8
Smoking Characteristics:	
Cigs/day pre-pregnancy	17.6 ± 8.8
Cigs/day at intake	9.14 ± 5.16
Age started smoking (years)	15.3 ± 2.8
% Living with other smoker(s)	81
% With no smoking allowed in home	68
% With none or few friends/family who smoke	28
% Attempted to quit pre-pregnancy	66
% Attempted to quit during pregnancy	29
Number of quit attempts during pregnancy	0.6 ± 1.1
Nicotine withdrawal questionnaire total score	1.5 ± 0.8
Attitude Item:	
% Endorsing that smoking will greatly harm baby	85
Psychiatric Symptoms	
Stress rating	5.5 ± 2.6
BDI-II	10.8 ± 8.3
% Ever having depressive symptoms for 2+ weeks	45

Note: M ± SD or %.

Table 2

Descriptive statistics for demand metrics across all 93 participants analyzed.

Demand Metric	Median	IQR
Empirical Q0	15.00	10.00—20.00
Derived Q0	16.00	8.50—23.00
Elasticity (α)	0.014	.0068—.024
Empirical $O_{\max}$	\$6.00	\$4.00—\$10.00
Empirical $P_{\max}$	\$0.50	\$0.40—\$0.50
Breakpoint	\$0.90	\$0.70—\$2.00

Table 3

Spearman rho correlation matrix of demand metrics (n = 93). Bold values indicate statistical significance; all significant correlations featured $p < .01$.

	Emp. Q_0	Der. Q_0	α	Emp. $P_{\max}$	Emp. $O_{\max}$	Breakpoint
Emp. Q_0	--					
Der. Q_0	.93	--				
α	-.20	-.09	--			
Emp. $P_{\max}$	-.07	-.19	-.31	--		
Emp. $O_{\max}$	.62	.54	-.59	.52	--	
Breakpoint	.06	.02	-.13	.80	.56	--

Table 4

Demand metrics comparisons between risk factor intersection groups.

Demand Metric	Quit Att. PrePreg Median (IQR)	No Quit Att. PrePreg (Median (IQR)	<i>U</i> Value
Light Smokers (<10 CPD)			
Empirical $Q0$	10 (6—15.75)	15 (10—20)	197.5 *
Derived $Q0$	8.5 (6—16)	20 (9—23.5)	192.0 *
Elasticity (α)	.0225 (.0118—.0328)	.015 (.0103—.0245)	251.5
Empirical $P_{\max}$	\$0.55 (\$0.40—\$0.73)	\$0.50 (\$0.40—\$1.50)	306.5
Empirical $O_{\max}$	\$4.00 (\$2.40—\$6.00)	\$6.00 (\$4.75—\$10.00)	159.0 **
Breakpoint	\$0.80 (\$0.60—\$0.93)	\$0.80 (\$0.60—\$1.50)	284
Heavy Smokers (10+ CPD)			
Empirical $Q0$	20 (12.5—20)	20 (11—20)	166.5
Derived $Q0$	20 (15—25)	20 (13—27)	168.0
Elasticity (α)	.011 (.0051—.015)	.013 (.0017—.019)	172.0
Empirical $P_{\max}$	\$0.60 (\$0.50—\$2.03)	\$0.90 (\$0.50—\$1.00)	150.5
Empirical $O_{\max}$	\$10.00 (\$7.00—\$20.00)	\$10.00 (\$6.00—\$20.00)	168.5
Breakpoint	\$1.00 (\$0.70—\$5.00)	\$1.00 (\$1.00—\$3.00)	144.0

*
 $p < .05$,**
 $p < .01$