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Electronic cigarette substitution in the experimental tobacco marketplace: A review

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Abstract

The evolution of science derives, in part, from the development and use of new methods and techniques. Here, we discuss one development that may have impact on the understanding of tobacco regulatory science: namely, the application of behavioral economics to the complex tobacco marketplace. The purpose of this paper is to review studies that examine conditions impacting the degree to which electronic nicotine delivery system (ENDS) products substitute for conventional cigarettes in the Experimental Tobacco Marketplace (ETM). Collectively, the following factors constitute the current experimental understanding of conditions that will affect ENDS use and substitution for conventional cigarettes: increasing the base price of conventional cigarettes, increasing taxation of conventional cigarettes, subsidizing the price of ENDS products, increasing ENDS nicotine strength, and providing narratives that illustrate the potential health benefits of ENDS consumption in lieu of conventional cigarettes. Each of these factors are likely moderated by consumer characteristics, which include prior ENDS use, ENDS use risk perception, and gender. Overall, the ETM provides a unique method to explore and identify the conditions by which various nicotine products may interact with one another that mimics the real world. In addition, the ETM permits the efficacy of a broad range of potential nicotine policies and regulations to be measured prior to governmental implementation.

Keywords

Behavioral economics; Demand; Substitution; Experimental tobacco marketplace; Cigarettes; Electronic nicotine delivery system; Electronic cigarettes

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Conflict of interest

W. K. Bickel is a principal of HealthSim, LLC and Notifius, LLC; a scientific advisory board member of Sober Grid, Inc. and DxRx, Inc.; and a consultant for ProPhase, LLC and Teva Branded Pharmaceutical Products R&D, Inc.

1. Introduction

The Food and Drug Administration acquired regulatory control over tobacco projects since the Family Smoking Prevention and Tobacco Control act was passed in 2009. This has led to tobacco regulatory research which focuses on the development of new tools, and practices that permit the assessment of tobacco products in terms of their safety, efficacy, quality, and performance (United States Food and Drug Administration, 2018). Given that the tobacco marketplace features a plethora of tobacco products, this has stimulated the scientific interest in how these products may interact and how that interaction may change under different regulatory policies.

Here, we discuss one development that may have impact on the understanding of tobacco regulatory science: namely, the application of behavioral economics to the complex tobacco marketplace. The behavioral economics of tobacco as a science has developed across 4 epochs, reviewed previously (Bickel et al., 2017; Tidey et al., 2016); that is, laboratory drug self-administration, the hypothetical purchase task, naturalistic demand and finally, the Experimental Tobacco Marketplace (ETM). Most studies to date have examined only pairs of products or, at most, three concurrent commodities. Importantly, when three concurrent commodities have been examined together, complex tobacco product interactions have emerged (Johnson et al., 2004). Specifically, Johnson et al. (2004) gave smokers access to conventional cigarettes, reduced-nicotine cigarettes, and nicotine gum. When the price of conventional cigarettes increased, consumption of both reduced-nicotine cigarettes and nicotine gum increased even though their prices were fixed. Thus, reduced-nicotine cigarettes and nicotine gum functioned as substitutes for conventional cigarettes. Indeed, by concurrently using both products, the smoker could reproduce different aspects of the conventional cigarette experience by consuming the reduced-nicotine cigarette (i.e., sensory effects associated with combustible tobacco smoke inhalation) and nicotine gum (i.e., central effects associated with nicotine ingestion). Importantly, reduced-nicotine cigarettes functioned as a better substitute than gum when each was offered as a substitute alone (the use of reduced-nicotine cigarettes increased the most). This three-way interaction among the products could not have been predicted from the individual demand curves with these commodities. Only when they were measured together did these complex interactions emerge. The ETM provides a method to explore and identify the conditions by which various tobacco or nicotine products may interact with one another that mirrors the real world, thus improving upon previous methods that examine interactions with typically only two products alone (Johnson et al., 2017; O'Connor et al., 2014). This study of product interactions (e.g., substitution) is of particular importance, in part because of the plethora of novel tobacco products as well as the goal of transitioning current smokers to less harmful products. More specifically, given the emerging data suggesting that electronic nicotine delivery systems (ENDS) may be less harmful than combustible tobacco, the ETM may be able to illuminate conditions that may support transitions from conventional cigarettes to ENDS if that were the objective of tobacco policy.

The purpose of this paper is to review studies that examine conditions impacting the degree to which ENDS products substitute for conventional cigarettes in the ETM. Thus, we will first review the general features of the ETM. Next we will review the features of studies that

show this substitution effect. Specifically, we will explore the role of participant demographics, price of conventional cigarettes, nicotine strength of ENDS products, and novel narratives (e.g., testimonials regarding health effects of tobacco products) that can support substitution for ENDS products. Collectively, this review will clarify the current status of the ETM as it pertains to the study of conditions that impact purchasing of ENDS products.

2. Review search criteria and inclusion

The criteria for inclusion for the present review were any 1) peer-reviewed study under-review or published 2) reporting hypothetical or real monetary purchasing among 3) three or more concurrently available nicotine/tobacco products, which are the defining characteristics of the ETM. Operant nicotine/tobacco research studies were excluded (e.g., studies in which participants were rewarded with puffs of cigarette smoke). Using Google Scholar, published studies were screened for inclusion if yielded by the following Boolean search parameters: Demand, Tobacco Marketplace, Substitution, and Cross-price elasticity. The search yielded 511 published results, of which only 6 studies were non-operant, research studies with participants purchasing hypothetical or real nicotine/tobacco products with hypothetical money or real money. Of these 6 studies, only 4 of the studies involved participants purchasing among 3 or more concurrently available hypothetical (Heckman et al., 2017) or real (Pope et al., 2018; Quisenberry et al., 2016; Quisenberry et al., 2017a) nicotine/tobacco products, while the other 2 studies involved only single-product purchasing or comparison-product purchasing (i.e., 2 concurrently available products) scenarios (Johnson et al., 2017; O'Connor et al., 2014). In addition, there are 2 studies that meet all of the above criteria but are under review (DeHart et al., 2018; Pope et al., in press) and, thus, are not available to search via Google Scholar. In total, 6 studies met the inclusion and search criteria mentioned above and will be discussed in the following sections.

3. General features

The ETM contains several unique features that distinguish it from traditional assessments of demand and substitution (Bickel et al., 2017), allowing for even greater approximation to the complex, real-world tobacco marketplace. As mentioned previously, the ETM is ideally suited to examine interproduct relations such as substitutability.

3.1. Product variety and display

One of the defining characteristics of the ETM is its use and display of multiple products and product varieties. Combustible and non-combustible nicotine products can be made available for purchase simultaneously and in any combination, allowing for investigations of specific product relations. Products used in every ETM study thus far include cigarettes, ENDS, nicotine gum, and nicotine lozenges. Specific studies have also used snus, dip, and cigarillos (Quisenberry et al., 2016; Quisenberry et al., 2017a) as well as ENDS liquid, (DeHart et al., 2018; Pope et al., 2018; Pope et al., in press) roll-your-own cigarettes, nicotine patches, and reduced-nicotine containing conventional cigarettes and roll-your-own cigarettes (Heckman et al., 2017).

The ETM approximates the real-world tobacco marketplace by including product descriptions and pictures (see Fig. 1). General features of the product, such as flavor (e.g., menthol) and nicotine content (e.g., 12mg/mL nicotine) are displayed alongside the typical product pictures. Pictures and products have been branded (Pope et al., 2018; Pope et al., in press; Quisenberry et al., 2017a) as well as unbranded (e.g., "preferred brand"; DeHart et al., 2018), and have been sold as packs and individual units (e.g., per cigarette, per piece of gum). Specific product brands can be personalized to individual preferences.

3.2. Prices

Four cigarette prices have been used most often (e.g., $0.12, $0.25, $0.50, and $1.00; e.g., Heckman et al., 2017; Quisenberry et al., 2016; Quisenberry et al., 2017a). The $0.25 price was determined by obtaining the approximate regional market price of a single cigarette in Southwest Virginia where the initial ETM studies were conducted (e.g., Quisenberry et al., 2016). To provide greater analytical resolution, other variants have added higher prices (e.g., $2.00, $4.00, and $8.00), as well as lower prices ($0.06; e.g., DeHart et al., 2018; Pope et al., 2018; Pope et al., in press). Cigarette prices are shown in either a randomized or ascending order across purchasing trials, while other products (potential substitutes for the target product) are set to fixed prices. The ETM allows investigation of price framing/structuring to further approximate real-world conditions. For example, Pope et al. (in press) integrated various combinations of taxes and subsidies for conventional cigarettes and e-liquid to determine how these variables influence purchasing (described in detail below).

3.3. Budget

The ETM allows specified purchasing over different time frames, with the most common purchasing periods consisting of 5 and 7 days. In an attempt to model real-world purchasing behavior, participants are provided an individualized account balance, typically calculated by multiplying the self-reported number of tobacco products used per day (e.g., Timeline Follow-Back; Sobell and Sobell, 1992) by the market price of those products, and providing an amount that matches the participant's typical tobacco product expenditure for the study's purchasing period. Any money not spent on tobacco products is disbursed to the participant. A previous study found that this method resulted in the greatest correspondence between the number of cigarettes purchased and the number of cigarettes consumed during the previous week, as reported on a Timeline Follow-Back (Koffarnus et al., 2015a).

3.4. Real versus hypothetical

All previous in-lab ETM studies have used a potentially real variant. That is, participants make purchases at several different prices and only one price is actually experienced. Participants randomly draw a price condition and receive the products they purchased, as well as money remaining from the unspent account balance. Importantly, purchasing using this potentially real procedure closely corresponds to purchasing under real (i.e., delivery of purchased items for every price) and hypothetical (i.e., purchased items are not delivered) conditions (Wilson et al., 2016). In a relatively recent application of the ETM, Pope et al. (2018), had participants sample e-liquid containing a range of nicotine strengths, which allowed participants (some of whom were previously naïve ENDS users) to make more informed purchases. Only two studies have investigated the ETM in a hypothetical context

(DeHart et al., 2018; Heckman et al., 2017). General findings of these studies closely aligned to those found from in-lab studies, suggesting the ETM's utility for settings outside of the experiential context.

4. Unit of analysis and quantification

Quantifying purchasing is done in several different ways. Participants purchase units of the product and because products differ in terms of nicotine content, analysis has typically expressed the dependent variable as mg of nicotine purchased. Most studies (Pope et al., 2018; Pope et al., in press; Quisenberry et al., 2016; Quisenberry et al. 2017a) examined purchasing in this way, whereas Heckman et al. (2017) expressed products as the number of conventional cigarette equivalents in mg of nicotine. In a hypothetical variant, DeHart et al. (2018) analyzed demand and substitution using the proportion of dollars spent in each purchasing trial. The rationale for this method, opposed to nicotine purchased, was that because individuals did not necessarily have experience with those products, their purchasing may not have been controlled by the putative reinforcer, nicotine. Another approach would be to use the units actually purchased, especially in situations where products contain little to no nicotine (e.g., 0 mg/mL e-liquid). Although no universally appropriate unit of analysis has been determined and the decision should be driven by the research question, these different methods of analysis have yielded orderly purchasing relations.

Several quantitative models of demand and substitutability have been applied to analyzing ETM data. First, demand for the target product (i.e., the product whose price varies across purchasing blocks) can be analyzed using contemporary equations (Hursh & Silberberg, 2008; Koffarnus et al., 2015b), yielding informative metrics such as demand intensity (i.e., maximum purchasing at near-zero cost) and elasticity (i.e., purchasing price sensitivity) (Bickel et al., 2017; Bickel et al., 2000). Second, degree of substitutability can be obtained using cross-price elasticity functions derived from contemporary demand models (Hursh & Roma, 2013), or more frequently by regressing alternative product purchasing on the price of the target product using simple linear regressions (Pope et al., 2018; Pope et al., in press; Quisenberry et al., 2016; Quisenberry et al., 2017a). Whereas the slope of the linear regression can be used as a proxy for substitutability (i.e., relatively steeper slopes being indicative of greater substitution), the y-intercept of the linear regression can also provide insight into purchasing of the alternative product (DeHart et al., 2018; Pope et al., 2018; Pope et al., in press). Here, we formally introduce the terms "initial intensity" and "terminal intensity" of substitution to refer to the amount of purchasing at the lowest and highest prices of the variable-priced product (i.e., the target product), respectively (see Table 1 for definitions). Fig. 2 (top panel) displays a hypothetical demand curve for cigarettes (i.e., the target product) and hypothetical substitution curves (bottom panel) for three commonly used alternative products.

5. Factors Affecting ENDS Substitution

The flexibility of the ETM allows for modeling of important real-world influences on tobacco purchasing, including product pricing, ENDS nicotine strength, and consumer

characteristics. In the sections that follow, we discuss how these and other variables (e.g., novel narrative devices) have been examined within the context of the ETM and how they affect ENDS product purchasing.

5.1. Price

The most often used manipulation in studies of the behavioral economics of nicotine product purchasing is an alteration of the price of conventional combustible products, most often factory-made cigarettes. In the ETM studies to date, all six have increased the price of combustible products (i.e., factory-made & roll-your-own) to determine the degree of substitutability for flavored disposable ENDS (Heckman et al., 2017; Quisenberry et al., 2016; Quisenberry et al., 2017a), flavored e-liquid for ENDS tanks (DeHart et al., 2018; Heckman et al., 2017; Pope et al., 2018; Pope et al., in press), ENDS cartridges (Heckman et al., 2017), and participants' preferred or usual brand, type, and dose of ENDS (Quisenberry et al., 2017a). Recruiting participants who were current smokers (Heckman et al., 2017; Quisenberry et al., 2016; Quisenberry et al., 2017a), and dual-users (Quisenberry et al., 2017a), every ETM study also investigated the substitutability of one or more of these ENDS products when concurrently available alongside four or five other alternative nicotine products (e.g., snus, dip, nicotine patches, nicotine lozenges, nicotine gum) (DeHart et al., 2018; Pope et al., 2018; Pope et al., in press; Heckman et al., 2017; Quisenberry et al., 2016; Quisenberry et al., 2017a).

In two experiments in which participants could purchase real nicotine products in the ETM, Quisenberry et al. (2016) changed the price of conventional cigarettes in an ascending manner from $0.12 to $1.00 across 4 conditions to examine the substitutability of alternative tobacco products (e.g., ENDS). In both experiments, ENDS (single counts of Blu disposable electronic cigarettes, $10.00 each) functioned as a significant substitute for conventional cigarettes, but in Experiment 2, when cigarillos were unavailable for purchase in the ETM alongside the other available products, the substitutability of the disposable ENDS was more robust than when cigarillos were available in Experiment 1. Quisenberry et al. (2017a) also changed the price of conventional cigarettes from $0.12 to $1.00, but in randomized order across 4 conditions. When participants' usual brand, type, and dose of ENDS was available in the ETM, increasing cigarette price resulted in significant ENDS substitution, the degree of which was greater than the other 4 available, alternative nicotine products. In each of these studies, increasing the price of conventional cigarettes resulted in decreased cigarette purchasing, approximating the typical demand curves demonstrated in prior behavioral economic (e.g. Johnson & Bickel, 2003; Shahan et al., 2000) and econometric (e.g. Chaloupka, 1999) studies of cigarette purchasing.

Across four hypothetical ETM experiments, Heckman et al. (2017) altered the availability of conventional factory-made (FMC) and roll-your-own (RYO) cigarettes, three different ENDS products (i.e., e-liquid for tanks, cartridges, disposables), and/or very-low nicotine containing cigarettes (VLNCs). Within each experiment, however, the price of conventional cigarettes was randomly changed from $0.12 to $1.00 across 4 conditions. Heckman et al. (2017) then tested the substitutability of ENDS products and VLNCs in the context of an online ETM. The experiments in Heckman et al. (2017) replicated previous research

demonstrating that demand for conventional FMCs was price-sensitive and also found that this pattern of price sensitivity extended to RYO cigarettes. When VLNCs were not available (i.e., experiment 1), ENDS liquid and cartridges had the highest substitutability, with tanks being the only significant substitute for both types of conventional cigarettes. The availability of VLNCs (i.e., experiment 2) dampened conventional cigarette demand and ENDS tank and cartridge substitutability, resulting in only VLNCs and ENDS cartridges functioning as significant substitutes for conventional FMC and RYO cigarettes. When no ENDS products were available (i.e., experiment 3), participants shifted their purchasing to VLNCs, resulting in strong substitution for this product. Interestingly, when conventional cigarettes were unavailable in the ETM (i.e., experiment 4), participants initially shifted use towards VLNCs and ENDS products or quit purchasing nicotine and tobacco products altogether. Overall, tank and cartridge ENDS products and VLNCs had the highest levels of substitutability, but the substitutability of ENDS products was dampened when VLNCs were present concurrently.

Similar to Quisenberry et al. (2016) and Quisenberry et al. (2017a), Pope et al. (2018) increased the price of conventional cigarettes from $0.12 to $2.00 across five conditions to examined the degree of substitutability of four different ENDS liquid nicotine strengths (0, 6, 12, & 24 mg/mL) in a real ETM purchasing context. In contrast to the previous studies, however, participants were provided an ENDS liquid tank device at the start of the study to use throughout the experiment; participants were taught how to use the ENDS tank properly (both vaping & refilling with e-liquid). In addition, participants were asked to sample up to 2 mL of all four e-liquid nicotine strengths (randomized, counterbalanced order) for the 2 days prior to the ETM session in which that same strength was available for purchase. While the effects of nicotine strength on ENDS liquid substitutability will be discussed in the next section, all strengths of ENDS liquid functioned as substitutes. Indeed, potentially due to the ENDS exposure and e-liquid strength sampling throughout the experiment, there was low purchasing of any other alternate products, and this low purchasing was not altered by increases in conventional cigarette price nor the changes in nicotine strength.

DeHart et al. (2018) conducted an examination of how differently framed nicotine and tobacco product narratives, or detailed stories about conventional vs. alternative nicotine product use, might affect the degree of substitutability of ENDS liquid and disposable ENDS in a hypothetical ETM. Across seven conditions, the price of conventional cigarettes increased from $0.06 to $8.00. Participants were randomly assigned to four different narrative conditions, the effects of which will be discussed in detail in a later section, and the substitutability of ENDS liquid and disposable ENDS was assessed. In general, the proportion of account balance spent on ENDS products increased as a function of cigarette price, indicating that ENDS products demonstrated high substitutability relative to the other available alternative products.

While these results offer promising potential avenues for tobacco regulatory policies, increasing conventional cigarette price may not always be feasible for tobacco policy options. Indeed, the development and examination of the effects of other nicotine product pricing policies in the ETM is key to informing policy decisions through forecasting and

estimating how smokers' patterns of purchasing may be influenced by the introduction of different pricing regulations.

Pope et al. (in press) addressed some of these gaps in the ETM and tobacco regulatory control by investigating the effects of taxing conventional cigarettes and subsidizing e-liquid for ENDS tanks in interaction with increasing the price of conventional cigarettes. All procedures were identical to Pope et al. (2018) discussed above, with the exceptions that 1) only one nicotine strength of ENDS liquid was sampled and available for purchase throughout the experiment (24 mg/mL); and 2) across two ETM sessions conventional cigarettes were taxed at rates of 0%, 12.5%, 25%, and 50% or ENDS liquid (price constant at $0.50/mL) was subsidized at those same rates across 4 conditions, respectively, each in combination with increasing cigarette price from $0.12 to $2.00.

The 24 mg/mL ENDS liquid functioned as a significant substitute across all conditions of the tax and subsidy sessions and was the only alternative product to serve as a significant substitute. The purchasing of all other products was low across all conditions, again likely due to the sampling/exposure to the ENDS, but also potentially due to the subsidization of solely ENDS liquid, thus increasing the saliency of the product. Increasing cigarette tax rate resulted in nominal increases in ENDS liquid purchasing, driven by increases in the initial intensity of substitution (y-intercept) without a change in the slope of the functions. Increasing cigarette tax rate also simultaneously decreased cigarette demand through significant declines in demand intensity and nominal increases in elasticity. At the individual subject level, increasing cigarette tax rates increased the number of individual participants for whom 24 mg/mL ENDS liquid functioned as a significant substitute (10, 9, 13, and 16 across the 0%, 12.5%, 25%, and 50% cigarette tax rates). Increasing ENDS liquid subsidy rate from 0% to 50% resulted in significant increases in the initial intensity of substitution (i.e., significant increases in y-intercepts), but non-significant, nominal increases in the slope of the functions. The increases in initial intensity of ENDS liquid substitution were greater when ENDS liquid was subsidized than when conventional cigarettes were taxed. Increasing ENDS-liquid subsidization did not, however, affect conventional cigarette demand. In addition, the number of individual subjects for whom ENDS liquid functioned as a significant substitute increased as a function of subsidy rate (12, 15, 18, and 20 across the 0%, 12.5%, 25%, and 50% e-liquid subsidy rates).

The effects of changing conventional cigarette prices in the ETM is clear and consistent across all studies conducted to date: Increasing the price of conventional cigarettes increases purchasing of ENDS products by increasing ENDS product substitutability. The different studies suggest that ENDS substitutability depends on the type of ENDS product available and that changes in ENDS liquid substitutability may be differentially affected by various pricing manipulations (e.g., base price change, taxation, subsidization), procedural manipulations (e.g., narratives, sampling/exposure periods), and product availability. In addition, increasing the base price of conventional cigarettes, increasing cigarette taxation, and the availability of VLNCs and ENDS products each simultaneously decreased conventional cigarette demand. Overall, the results of these studies suggest that harm reduction approaches that explicitly encourage transitions from conventional cigarettes to ENDS purchasing may require increasing cigarette prices (base prices and/or taxation),

increasing the differential taxation of cigarettes and ENDS products, increasing the availability of ENDS products, and/or increasing subsidization of ENDS products in order to maximize success.

5.2. Nicotine strength of ENDS products

Nicotine, as a crucial constituent of tobacco and the relevant reinforcer in behavioral economic analysis of purchasing, is a major factor that drives self-administration, purchasing, and consumption. The nicotine strengths available in ENDS products are critical in determining the extent to which ENDS products are subjectively valued and used, either instead of or alongside conventional cigarettes. Moreover, the degree of substitutability of different nicotine strength ENDS products may depend upon the point of transition, or lack thereof, of the smoker, vaper, or dual-user during the time of purchasing. Indeed, constraining the e-liquid nicotine strength available for consumers is being debated (e-cigarette Politics, 2017; London Economics, 2017), and regulations vary by country. For example, retail sale of nicotine-containing ENDS is prohibited in Australia and Canada. In the United Kingdom, only ENDS products with 20 mg/mL or less are available for retail sale with stronger products available via prescription.

Interestingly, accumulating evidence suggests that higher nicotine strength ENDS products may minimize the number of puffs required to attain sufficient nicotine blood levels compared to lower strengths (Kosmider et al., 2017). By increasing the amount of vaping, lower nicotine strength ENDS products can increase exposure to the harmful constituents of ENDS products, namely the aerosol carbonyls, thus potentially reducing the harm-reduction value of ENDS products relative to higher nicotine strengths (Kosmider et al., 2017). However, increasing nicotine strength could also potentially increase nicotine dependency and other health problems, further complicating nicotine strength regulations that require additional research to understand.

Of the ETM studies conducted to date, only Pope et al. (2018) has examined the effects of different nicotine strengths on the substitutability of ENDS products. In all other ETM studies, the ENDS product(s) available were only offered in a single nicotine strength throughout the experiment. Thus, differential substitutability of ENDS nicotine strengths cannot be directly examined within any of these studies other than Pope et al. (2018).

In Pope et al. (2018), recall that participants were given an ENDS liquid tank device, taught how to use and refill it, and then, across four different Sampling session-ETM session pairs, participants sampled and were able to purchase each of four ENDS liquid nicotine strengths (0, 6, 12, & 24 mg/mL) in randomized order. The authors reported nicotine strength-dependent increases in ENDS liquid purchasing, driven by significant increases in both the slopes (substitutability) and y-intercepts (initial intensity of substitution) of the substitution functions. The 24 mg/mL e-liquid had the highest nominal levels of purchasing and overall substitutability (i.e., y-intercepts and slopes), although initial intensity and substitutability were not statistically different between the 12 and 24 mg/mL ENDS liquid strengths. However, the number of individual subjects for whom ENDS liquid functioned as a significant substitute increased as a function of nicotine strength (6, 8, 11, and 16 participants across the 0, 6, 12, and 24 mg/mL strengths), suggesting that 24 mg/mL

demonstrated the greatest substitutability of all strengths available. Indeed, in the study of the effects of conventional cigarette taxation and ENDS liquid subsidization, Pope et al. (in press) had participants sample and purchase only 24 mg/mL ENDS liquid across different conditions because of that strength's previously demonstrated level of substitutability. Note that although increasing ENDS-liquid nicotine strength increased ENDS-liquid substitutability, nicotine strength did not affect conventional cigarette intensity or elasticity, possibly due to the participants' relative naivety of ENDS use prior to the study (Pope et al., 2018) (see also Rass et al., 2015).

Overall, the ETM is well-suited for assessing the effects of nicotine dose-related effects, or similar interventions, on conventional cigarette demand and purchasing and ENDS product substitutability. Given that nicotine strength may be vital to ENDS substitutability, governmental limits and regulations may be informed by proper experimental data, with the ETM providing an ecologically valid context well-suited for such an investigation. Indeed, understanding the relationship between nicotine strength and ENDS substitutability may help to maximize the substitutability of modified-risk products and decrease the associated harm. Further research is required to inform regulations and recommendations for availability and use of nicotine strength as ENDS substitutability also depends on the relative risks and benefits of different nicotine strengths.

5.3. Consumer characteristics

When considering policy changes that impact tobacco product purchasing, the consequences of such changes can differ by population. Demographic differences play an important role in the type and amount of tobacco product use. Age, gender, ethnicity, and education are only a few characteristics that differentiate conventional cigarette smokers from non-smokers (Jamal et al., 2015; Schoenborn & Gindi, 2015; Siahpush et al., 2006). The ETM provides an effective forum for further understanding the influences of consumer characteristics on tobacco product purchasing. To date, three categories have been investigated: prior tobacco product use, tobacco product risk perception, and gender.

Tobacco product use, as measured through a Timeline Follow-Back (Sobell and Sobell, 1992) or other methods, can predict both conventional cigarette and alternative tobacco product purchasing in the ETM. Heckman et al. (2017) found different patterns of demand elasticity for conventional cigarettes and cross-price elasticity for ENDS between participants who smoked less than 10 conventional cigarettes compared to participants that smoked 10 or more conventional cigarettes per day with fewer ENDS products serving as a substitute for conventional cigarettes in the less than 10 conventional cigarettes a day group. DeHart et al. (2018) found that an intervention that increased ENDS purchasing was less effective in heavy smokers. DeHart et al. also found that previous ENDS use predicted overall purchasing but not changes substitution of ENDS as a result of the intervention. DeHart et al. (2018) also found that ENDS risk perception predicted ENDS purchasing in the ETM. Participants who rated ENDS as having a low risk of disease (e.g., cancer, lung disease, heart disease) purchased more ENDS in the ETM. This suggests that altering consumer expectations of ENDS may serve as an effective intervention.

Finally, gender differences in tobacco product purchasing are another important consumer characteristic investigated through the ETM. Quisenberry et al. (2017b) found that while demand for conventional cigarettes did not differ by gender, females purchased fewer ENDS, snus, and dip than males as the price of cigarettes increased. These findings confirm epidemiological data that indicate that men are more likely to use alternative tobacco products (Higgins et al., 2015). Many consumer characteristics influencing tobacco product purchasing (Epidemic, 2011; Gilman et al., 2003) remain to be studied through the ETM.

5.4. Narrative interventions

Finally, the ETM can be employed to investigate the effectiveness of different interventions on conventional cigarette and ENDS product purchasing beyond changes to product price and design. This is especially valuable in exploring different public-health related interventions designed to decrease conventional cigarette purchasing or increase harm-reduction behaviors such as substituting ENDS for conventional cigarettes. To date, one popular public-health intervention, narratives (Kim et al., 2012), have been explored using the ETM.

DeHart et al. (2018) investigated the effectiveness of narratives to increase the substitutability of ENDS in the ETM. Participants read one of four narratives, personalized for gender and age, that depicted a close friend becoming ill. In the Positive narrative, the friend visited a physician and learned they only had the flu. In the Negative narrative, the friend became ill from smoking cigarettes, in the $\text{Negative}_{\text{Regret}}$ narrative, the friend became ill and expressed regret for having started smoking, and in the $\text{Negative}_{\text{Change}}$ narrative, the friend changed to ENDS and recovered from their illness. Participants that read the $\text{Negative}_{\text{Change}}$ narrative purchased fewer conventional cigarettes and more ENDS at the lowest conventional cigarette prices (i.e., initial intensity of substitution). Though ENDS risk perception predicted overall ENDS purchasing across all four groups, it did not moderate the effectiveness of the $\text{Negative}_{\text{Change}}$ in increasing ENDS purchasing. As demonstrated through a narrative intervention, the ETM provides an effective forum for investigating the effects of different public-health interventions on the demand for combustible and noncombustible nicotine products.

6. Considerations of using the ETM

The ETM is still a relatively new framework and as such careful consideration should be taken when constructing it. A strength of the ETM is its flexibility and broad applicability. Consequently, the number and specific sequence of prices (for the target, variable-priced product) used will be dictated by desired resolution (e.g., more prices will provide enhanced resolution of purchasing) and participant characteristics (e.g., if participants are recruited locally, a median price might reflect the approximate market price of a product). A common price sequence would include both a number of higher and lower prices around an approximate market price, with prices high enough to substantially suppress target product purchasing. This type of price sequence achieves twofold aims. First, low prices will reflect near maximum purchasing of the target product and baseline-like relative purchasing preferences of alternative products. Second, high prices will usually result in suppressed

target product purchasing and reveal the degree to which alternative products substitute for the target product. As we have illustrated, such a price sequence reveals changes in demand for the target product, level of initial intensity of substitution, and change in alternative product purchasing (i.e., substitution slope).

The decision to disburse any unspent budget will typically be applicable in experiential contexts and, by definition, not applicable in hypothetical preparations. By endowing participants with a budget and disbursing anything not spent, participants experience real costs (and benefits via products purchased) associated with their spending. One drawback of providing participants with their unspent budget is that it might promote underpurchasing. On the other hand, not distributing the unspent budget may lead to purchasing more than would actually be used. We have found that providing participants an individualized budget based on their previous purchasing, combined with product prices that reflect the local market price, achieves a realistic medium.

Including sampling sessions may be preferred when the research question necessitates experience with the product. Contrast this with a research question focused on initial product perceptions (e.g., estimating adoptability of a novel product not yet on the market) or one that investigates the role of experienced users versus naïve users. When integrated, sampling sessions should be long enough to ensure participants can experience the subjective effects of the product, and the sampling duration may even differ across products.

Additional features of the marketplace may also be customized to fit the research questions. For example, the number and variety of products (e.g., is the focus on specific product interactions or is the focus towards policy as to approximate the diverse, option-rich tobacco marketplace?), experimental preparation (e.g., should the marketplace be customized to include participant-specific usual brand products or will generic brands suffice?), and ETM aesthetics (e.g., a more limited number of products might be preferred if products can only be displayed on one page compared to grouping products based on broader product categories) should all be considered when refining the ETM. As we've noted previously, the ETM is a relatively new framework and the sparse literature does not yet allow for definitive best-practice recommendations. As the research base grows, best practices for the ETM will continue to develop.

7. Conclusion

The purpose of this review was to examine factors affecting substitution of ENDS products for conventional cigarettes within the ETM. To date, the following factors have resulted in increased ENDS purchasing: price manipulations (e.g., increasing the base price of conventional cigarettes, increasing taxation of conventional cigarettes, subsidizing the price of ENDS products), increasing ENDS nicotine strength, and providing narratives that illustrate the health benefits of ENDS consumption in lieu of conventional cigarettes. Additionally, these factors permit understanding which of these manipulations in addition to increasing ENDS purchasing also decreases purchasing of conventional cigarettes. Specifically, increasing the base price of conventional cigarettes, increasing conventional cigarette taxation, providing reduced nicotine cigarettes, providing ENDS products, and

providing narratives that highlight the possible health benefits of switching from conventional cigarettes to ENDS products decreased conventional cigarettes purchases as well. Based on this review we address six points.

First, the ETM allows broad experimental control over tobacco product pricing, including base, taxed, and subsidized prices of combustible tobacco and ENDS, in order to examine complex product interactions. In so doing, the ETM draws on a long history of econometric and laboratory study (Hursh & Silberberg, 2008; Chaloupka, 1999; Chaloupka & Wechsler, 1995; Hursh, 1984; Lewitt & Coate, 1982; Bickel et al., 1991) on the role of price manipulations in cigarette purchasing. Although the FDA does not have control over price policy, governments can and have determined price via taxation with the overall effect of decreasing cigarette consumption (Chaloupka et al., 2011). Here, manipulations of price in the ETM allow identification of substitution between products and, therefore, the likelihood that existing users will transition to these products. Depending on regulatory goals and emerging data on relative harm among products, this information may then be used in policy designed to encourage transition to potentially safer products (e.g., ENDS), discourage consumption of more harmful products (e.g., cigarettes, cigarillos), or facilitate total nicotine cessation.

Second, the FDA has the regulatory authority to restrict certain features of a specific product type. A key product feature the FDA has expressed interest in regulating is the nicotine strength of cigarettes and ENDS. Nicotine has been identified as a determinant of self-administration in a broad set of human studies (Bickel et al., 1991; Henningfield & Goldberg, 1983; Rose & Corrigall, 1997; Corrigall et al., 1994; Higgins et al., 2017). One ETM study demonstrated that ENDS liquid substitutability increased dose-dependently as a function of nicotine strength (Pope et al., 2018). In a hypothetical ETM context, the availability of VLNCs and/or ENDS products decreased conventional cigarette purchasing (Heckman et al., 2017). Whether VLNCs would have similar effects in a potentially real ETM context is being explored in an ongoing experiment.

Third, the ETM provides a forum for the investigation of public-health related interventions such as narratives. Importantly, through the ETM, public-health interventions can be piloted and refined under more controlled laboratory conditions and the behavioral outcomes of those interventions can be analyzed. Here, we discussed an experiment that demonstrated that narratives could reduce conventional cigarette purchasing and increase ENDS substitution in the ETM (DeHart et al., 2018). In the future, narratives (and other public-health interventions) can be developed to elicit important behavioral changes regarding conventional cigarettes and the ETM is ideally suited to develop and refine those techniques. Each of the factors investigated in the ETM to date are likely moderated by consumer characteristics, which include prior ENDS use, ENDS use risk perception, and gender. Collectively, this constitutes the experimental understanding of conditions that will affect ENDS use and substitution for conventional cigarettes.

Fourth, as we have detailed throughout this paper, the ETM framework exhibits a number of benefits to examine interproduct purchasing and relations. First and foremost, the ETM is useful in a broad range of conditions. Any number and types of products can be made

available for purchase and as we have described, these products have varied greatly ranging from traditional nicotine replacement therapies (e.g., nicotine lozenge, gum) to products not currently available to consumers (e.g., VLNCs). Second, integrating novel products (e.g., VLNCs) and policies (e.g., subsidizing ENDS products) and subsequently examining how individuals respond differently under these situations allows for a "prospective forecasting" in terms of informing policies prior to large-scale implementation in the real-world. Finally, similarities of the ETM to every-day online marketplaces allow for investigations of factors, such as differential information or "consumer reviews" about a product that may ultimately exert strong influence on purchasing.

Fifth, notwithstanding the benefits of the ETM framework, several considerations should be noted when implementing the ETM. One consideration is the variability in product types and product brands used in the ETM. The plethora of tobacco products in the real world makes having all possible products available in the ETM difficult. Options include stocking the ETM with brands and flavors most popular with consumers (e.g., via market share statistics) or with those in which participants have had experience. Another consideration is using the ETM in hypothetical or experiential contexts. Whereas several studies have examined the correspondence between hypothetical and experiential variants of simulated purchase tasks in general (Wilson et al., 2016; Amlung et al., 2012), to date no direct comparison of purchasing behavior between variants of the ETM has been conducted. The extant ETM studies reviewed here were all short-term. Whether long-term assessments would measure and/or stimulate changes in product preference remains to be determined.

Finally, as the methodology and complexity of the ETM advances, a number of future directions will help improve our understanding of simulating the ever more complex tobacco marketplace. Investigations of product pricing will improve the sensitivity of the task to detect changes in purchasing and product interactions. Integrating different product designs (e.g., cigarette ventilation, heat-not-burn devices), flavor/product availability, and product accessibility will help inform consumer perceptions and allow for a degree of prediction of how these factors will ultimately influence purchasing decisions. Longitudinal or repeated assessments of the ETM will allow for modeling and prediction of how consumer preferences shift over time, potentially as a result of either gradual or abrupt policy changes.

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References

Amlung MT, Acker J, Stojek MK, Murphy JG, 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. [PubMed: 22017303]

Bickel WK, DeGrandpre RJ, Hughes JR, 1991 Behavioral economics of drug self-administration. II. A unit-price analysis of cigarette smoking. J. Exp. Anal. Beh 55, 145–154.

Bickel WK, Marsch LA, Carroll ME, 2000 Deconstructing relative reinforcing efficacy and situating the measures of pharmacological reinforcement with behavioral economics: a theoretical proposal. Psychopharmacology 153, 44–56. [PubMed: 11255928]

Bickel WK, et al., Hanoch Y, Rice T, Barnes A, 2017 The behavioral economics of tobacco products: innovations in laboratory methods to inform regulatory science In: Behavioral Economics and Health Behaviors: Key Concepts and Current Research.

Chaloupka FJ, 1999 Macro-social influences: the effects of prices and tobacco-control policies on the demand for tobacco products. Nicotine Tob. Res 1 (Suppl. 1), S105–9. [PubMed: 11072413]

Chaloupka FJ, Wechsler H, 1995 Price, Tobacco Control Policies and Smoking Among Young Adults. 10.3386/w5012.

Chaloupka FJ, Straif K, Leon ME, Working Group, International Agency for Research on Cancer, 2011 Effectiveness of tax and price policies in tobacco control. Tob. Control 20, 235–238. [PubMed: 21115556]

Corrigall WA, Coen KM, Adamson KL, 1994 Self-administered nicotine activates the mesolimbic dopamine system through the ventral tegmental area. Brain Res. 653, 278–284. [PubMed: 7982062]

DeHart WB, Kaplan BA, Pope DA, Mellis AM, Bickel WK (2018-8). The Experimental Tobacco Marketplace: Narrative influence on electronic cigarette substitution. Experimental and Clinical Psychopharmacology. 2018 Nov 5. doi: 10.1037/pha0000233 [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30394764. doi: 10.1037/pha0000233

Epidemic AH, 2011 Tobacco Use and Mental Illness. American Legacy Foundation, Washington, DC.

Gilman SE, Abrams DB, Buka SL, 2003 Socioeconomic status over the life course and stages of cigarette use: initiation, regular use, and cessation. J. Epidemiol. Community Health 57, 802–808. [PubMed: 14573586]

Heckman BW, et al., 2017 A novel method for evaluating the acceptability of substitutes for cigarettes: the experimental tobacco marketplace. In: Tobacco Regulatory Science. 3 pp. 266–279. [PubMed: 31276024]

Henningfield JE, Goldberg SR, 1983 Nicotine as a reinforcer in human subjects and laboratory animals. Pharmacol. Biochem. Behav 19, 989–992. [PubMed: 6657732]

Higgins ST, et al., 2015 A literature review on prevalence of gender differences and intersections with other vulnerabilities to tobacco use in the United States, 2004–2014. Prev. Med 80, 89–100. [PubMed: 26123717]

Higgins ST, et al., 2017 Addiction potential of cigarettes with reduced nicotine content in populations with psychiatric disorders and other vulnerabilities to tobacco addiction. JAMA Psychiatry 74, 1056–1064. [PubMed: 28832876]

Hursh SR, 1984 Behavioral economics. J. Exp. Anal. Behav 42, 435–452. [PubMed: 16812401]

Hursh SR, Roma PG, 2013 Behavioral economics and empirical public policy. J. Exp. Anal. Behav 99, 98–124. [PubMed: 23344991]

Hursh SR, Silberberg A, 2008 Economic demand and essential value. Psychol. Rev 115, 186–198. [PubMed: 18211190]

Jamal A, et al., 2015 Current cigarette smoking among adults - United States, 2005–2014. MMWR Morb. Mortal. Wkly Rep 64, 1233–1240. [PubMed: 26562061]

Johnson MW, Bickel WK, 2003 The behavioral economics of cigarette smoking: the concurrent presence of a substitute and an independent reinforcer. Behav. Pharmacol 14, 137–144. [PubMed: 12658074]

Johnson MW, Bickel WK, Kirshenbaum AP, 2004 Substitutes for tobacco smoking: a behavioral economic analysis of nicotine gum, denicotinized cigarettes, and nicotine-containing cigarettes. Drug Alcohol Depend. 74, 253–264. [PubMed: 15194203]

Johnson MW, Johnson PS, Rass O, Pacek LR, 2017 Behavioral economic substitutability of e-cigarettes, tobacco cigarettes, and nicotine gum. J. Psychopharmacol 31, 851–860. [PubMed: 28612651]

Kim HS, Bigman CA, Leader AE, Lerman C, Cappella JN, 2012 Narrative health communication and behavior change: the influence of exemplars in the news on intention to quit smoking. Aust. J. Commun 62, 473–492.

Koffarnus MN, Wilson AG, Bickel WK, 2015a Effects of experimental income on demand for potentially real cigarettes. Nicotine Tob. Res 17, 292–298. [PubMed: 25168032]

Koffarnus MN, Franck CT, Stein JS, Bickel WK, 2015b A modified exponential behavioral economic demand model to better describe consumption data. Exp. Clin. Psychopharmacol 23, 504–512. [PubMed: 26280591]

Kosmider L, Kimber CF, Kurek J, Corcoran O, Dawkins LE, 2017 Compensatory puffing with lower nicotine concentration E-liquids increases carbonyl exposure in E-cigarette aerosols. Nicotine Tob. Res 10.1093/ntr/ntx162.

Lewitt EM, Coate D, 1982 The potential for using excise taxes to reduce smoking. J. Health Econ 1, 121–145. [PubMed: 10263952]

O'Connor RJ, et al., 2014 Estimating demand for alternatives to cigarettes with online purchase tasks. Am. J. Health Behav. 38, 103–113. [PubMed: 24034685]

Pope DA, Poe L, Stein JS, Kaplan BA, Heckman BH, Epstein LH, Bickel WK, 2018 The experimental tobacco marketplace substitutability as a function of e-liquid nicotine strength. BMJ: Tobacco Control. 10.1136/tobaccocontrol-2017-054024. (4 18), [Epub ahead of print].

Pope DA, Poe L, Stein JS, Kaplan BA, DeHart WB, Mellis AM, Heckman BH, Epstein LH, Chaloupka FJ, Bickel WK (in press). The Experimental Tobacco Marketplace: Demand and substitutability as a function of cigarette taxes and e-liquid subsidies. Nicotine & Tobacco Research.

Quisenberry AJ, Koffarnus MN, Hatz LE, Epstein LH, Bickel WK, 2016 The experimental tobacco marketplace I: substitutability as a function of the price of conventional cigarettes. Nicotine Tob. Res 18, 1642–1648. [PubMed: 26470723]

Quisenberry AJ, Koffarnus MN, Epstein LH, Bickel WK, 2017a The experimental tobacco marketplace II: substitutability and sex effects in dual electronic cigarette and conventional cigarette users. Drug Alcohol Depend. 178, 551–555. [PubMed: 28732318]

Quisenberry AJ, Koffarnus MN, Epstein LH, Bickel WK, 2017b The experimental tobacco marketplace II: substitutability and sex effects in dual electronic cigarette and conventional cigarette users. Drug Alcohol Depend. 178, 551–555. [PubMed: 28732318]

Rass O, Pacek LR, Johnson PS, Johnson MW, 2015 Characterizing use patterns and perceptions of relative harm in dual users of electronic and tobacco cigarettes. Exp. Clin. Psychopharmacol 23, 494–503. [PubMed: 26389638]

Rose JE, Corrigall WA, 1997 Nicotine self-administration in animals and humans: similarities and differences. Psychopharmacology 130, 28–40. [PubMed: 9089846]

Schoenborn CA, Gindi RM, 2015 Electronic cigarette use among adults: United States, 2014. NCHS Data Brief 1–8.

Shahan TA, Odum AL, Bickel WK, 2000 Nicotine gum as a substitute for cigarettes: a behavioral economic analysis. Behav. Pharmacol 11, 71–79. [PubMed: 10821211]

Siahpush M, McNeill A, Hammond D, Fong GT, 2006 Socioeconomic and country variations in knowledge of health risks of tobacco smoking and toxic constituents of smoke: results from the 2002 International Tobacco Control (ITC) Four Country Survey. Tob. Control 15 (Suppl. 3), iii65–70. [PubMed: 16754949]

Sobell LC, Sobell MB, 1992 Timeline Follow-Back In: Measuring Alcohol Consumption Humana Press, Totowa, NJ, pp. 41–72.

Tidey JW, Cassidy RN, Miller ME, Smith TT, 2016 Behavioral economic laboratory research in tobacco regulatory science. Tobacco Regulatory Science 2, 440–451. [PubMed: 28580378]

United States Food and Drug Administration, 2018 Advancing Regulatory Science. US Department of Health and Human Services https://www.fda.gov/ScienceResearch/SpecialTopics/RegulatoryScience/default.htm.

Wilson AG, Franck CT, Koffarnus MN, Bickel WK, 2016 Behavioral economics of cigarette purchase tasks: within-subject comparison of real, potentially real, and hypothetical cigarettes. Nicotine Tob. Res 18, 524–530. [PubMed: 26187389]

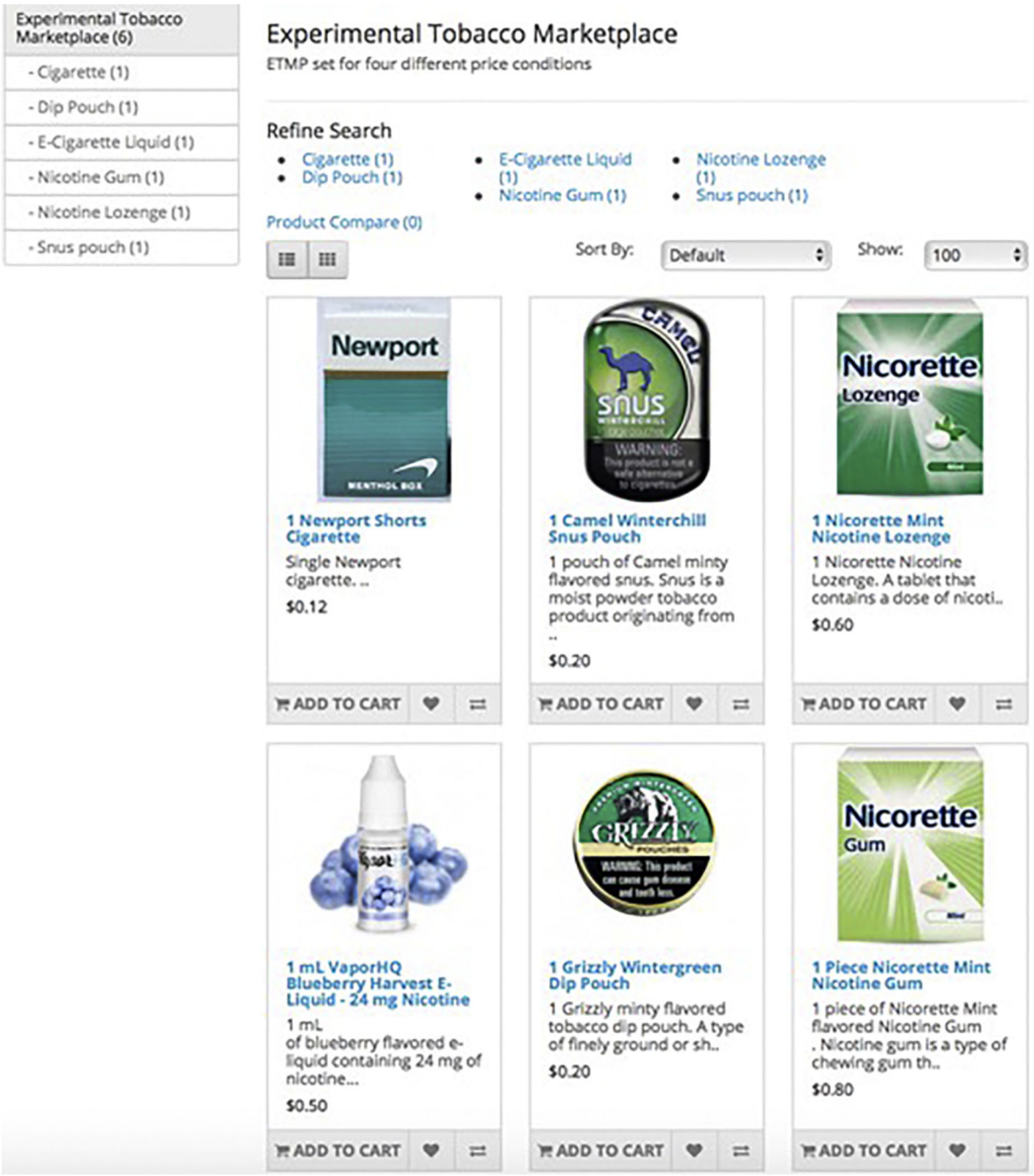

Fig. 1.

The main purchasing screen of the ETM showing all products available, relevant information, and pricing. The type and brand of conventional cigarette and e- liquid is customizable based on participant preferences.

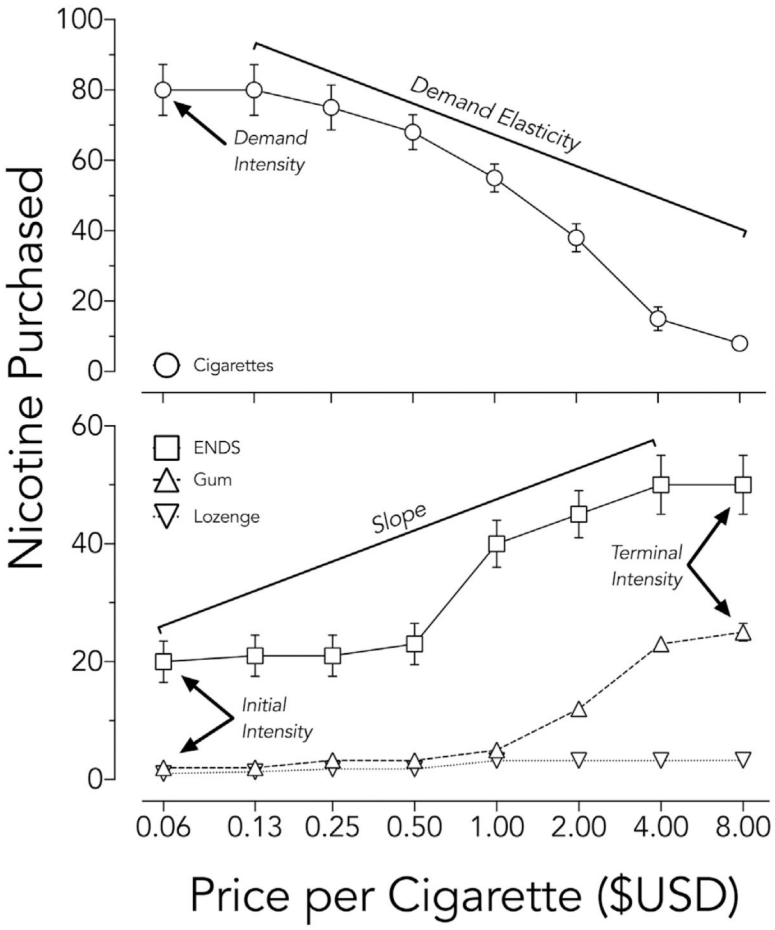

Fig. 2.

Hypothetical demand curve (top panel) and substitution curves (bottom panel) for cigarettes and three common nicotine products, respectively. Note that alternative products are set at a fixed price and their purchasing is examined as a function of the increasing prices of the target product (in this example, cigarettes).

Table 1

Definitions of key behavioral economic terms.

Term	Definition
Demand intensity	Level of purchasing of a commodity when its own price is zero; the elevation of the own-price demand/purchasing function relative to the origin.
Demand elasticity	The sensitivity of purchasing to increases in its own price, specified by the slope of the own-price demand/purchasing function. Inelastic demand specifies that large increases in price result in small decreases in purchasing or consumption. Elastic demand specifies that small increases in price produce large decreases in purchasing or consumption.
Substitution/ substitutability	A form of product switching and an interaction between two products; traditionally defined as an increase in purchasing of a price-constant product as a result of an increase in the price of an alternative commodity. Can be measured by the slope (cross-price elasticity) of the price-constant purchasing function. Can also be measured as an elevation in purchasing of a price-constant commodity at a fixed-price of the price changing, alternative commodity, seen at the y-intercept (initial intensity) or the upper bound (terminal intensity) of the price-constant function.
Cross-price elasticity	The slope of the price-constant purchasing function over the increase in price of the alternative commodity; defines the degree of substitution/substitutability of a product. A steeper slope indicates greater substitutability.
Initial intensity of substitution	The initial elevation or y-intercept of the price-constant purchasing function at the lowest price of the price-manipulated alternative commodity; a higher y-intercept indicates greater initial intensity of substitution.
Terminal intensity of substitution	The terminal elevation or upper-bound of the price-constant purchasing function at the highest price of the price-manipulation alternative commodity; a higher upper-bound indicates a greater terminal intensity of substitution.