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The Use of Behavioral Economic Demand in Human Abuse Potential Assessment: A Review and Recommendations for Future Testing

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A key step in the regulatory evaluation of new chemical entities is the assessment of their abuse potential. Human abuse potential (HAP) studies provide insights into the likelihood that new chemical entities have the potential for intentional, nonmedical use and therefore should be considered for greater regulatory control. Behavioral economic demand methods are proposed as a complementary method to improve the resolution of abuse liability testing. These procedures are posited to provide scalar, rank-ordered comparisons of abuse potential that are comparable across drugs and to better model real-world contexts in which constraint and cost influence drug-taking potential. The current review considers the applicability of behavioral economic demand methods to HAP testing frameworks. We review existing studies that have applied procedures broadly consistent with HAP testing and integrated demand procedures to measure abuse potential and/or a drug reinforcement. Procedural details and the demand methods implemented are reviewed toward the goal of informing the methods for applying demand testing in the HAP study framework and the existing gaps in defining those methods. Ultimately, efforts to improve the sensitivity and resolution of assays to detect and differentiate abuse potential stand to improve public health by concentrating efforts on the adequate control of drugs that pose risk while minimizing the restrictions on those with a lower abuse potential to maximize their clinical utility.

Public Health Significance

Demand testing is a procedure proposed to improve the ability to differentiate drugs based on their potential for intentional, nonmedical use. This review summarizes existing applications of demand procedures within human abuse potential frameworks. Improving the measurement of abuse potential can improve public health by allowing for adequate control of drugs that pose risk while reducing restrictions on those with a lower abuse potential to maximize their availability for clinical use.

Keywords: abuse potential, behavioral economics, demand, purchase task

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continued

The U.S. Food and Drug Administration (FDA) is responsible for evaluating the abuse potential of new chemical entities (NCEs) and of novel products that contain already controlled substances.[1] Abuse potential (also referred to as abuse liability) is operationally defined in this context as "the likelihood that abuse [the intentional, non-therapeutic use of a drug product or substance, even once, to achieve a desired psychological or physiological effect] will occur with a particular drug product or substance with CNS activity" (U.S. Food and Drug Administration, 2017, p. 4). The Controlled Substances Act dictates that analysis of abuse potential consider eight factors (i.e., the eight-factor analysis) when evaluating abuse-related data, including the actual or relative potential for abuse, psychic/physiological dependence liability, and history/current patterns of abuse (U.S. Code of Federal Regulations, 2024). Current drug scheduling by the Drug Enforcement Agency based on this guidance then places drugs with "currently accepted medical use in treatment in the United States" into Schedules II through V, with Schedule II representing those with the greatest abuse potential and accompanying control, while drugs without currently accepted medical use but at least some abuse potential are placed into Schedule I. A critical component of a new drug application that guides this eight-factor analysis is abuse-related research in humans (i.e., human abuse potential [HAP] studies). Improving the sensitivity and resolution of these assays to both detect and differentiate abuse potential should improve public health by concentrating efforts on the adequate control of drugs that pose risk while minimizing the restrictions on those with a lower abuse potential to maximize their clinical utility.

Current Method and Challenges in Abuse Potential Assessment

Identifying the most appropriate measure(s) for detecting, scaling, and ranking abuse potential is a near-century-old problem (Hursh & Silberberg, 2008; Miller, 1976; Skinner, 1938). Current FDA guidance recommends that the outcomes of HAP studies include subjective measures, safety measures, abuse-related adverse events, and pharmacokinetic sampling, making subjective-effect data the primary behavioral output for abuse potential. Subjective-effect data are measured using a unipolar or bipolar visual analog scale with "Drug Liking" specified as the primary outcome measure. Test compounds are considered to have abuse potential when they result in the endorsement of drug liking that is greater than placebo and/or similar to positive controls with known abuse potential that are pharmacologically similar to the test drug.

Questionnaires or other tools that assess subjective drug effects are cost-effective and efficient methods to evaluate abuse potential (see historical review in Jaffe & Jaffe, 1989). Nonetheless, decades of human laboratory data also show that subjective-effect measures only moderately predict actual drug taking when evaluated using controlled laboratory self-administration procedures (Haney, 2009). For example, a secondary analysis of three *d*-amphetamine self-administration studies found that subjective measures of "Like Drug" were significantly associated with progressive-ratio self-administration of *d*-amphetamine but only explained 15% of the variance in self-administration (Bolin et al., 2013). Similar results have been observed with cocaine (Strickland et al., 2014) and cannabis (Shellenberg et al., 2025) wherein subjective drug effects significantly but incompletely predict drug-taking behavior. This dissociation is likely attributable to the fact that subjective drug-liking measures query internal states induced by drug administration, while drug use in both laboratory and real-world contexts is determined by many contextual factors, including the availability of alternative reinforcers and aspects of drug cost and benefit not directly related to pharmacological action (Acuff et al., 2024). Procedures that retain the efficiency of subjective-effect measurement while also incorporating these contextual factors would ideally provide complementary information for eight-factor analysis recommendations and ultimately improve prediction and differentiation of future abuse potential.

Behavioral Economic Demand and Abuse Potential Testing

Behavioral economics is a general conceptual framework that integrates behavioral science and economic principles to study choice and decision making (Hursh, 1991; Hursh & Roma, 2013). Within addiction science, behavioral economic approaches such as contextualized reinforcer pathology and related models emphasize that value and the consequent likelihood of drug use are determined by the interaction of a drug's pharmacological properties with the environmental constraints that influence value in specific contexts (Acuff, MacKillop, et al., 2023; Vuchinich et al., 2023). An extension of these models considers that specific drugs may be more

[1] The term abuse is referred to throughout this article. There is a growing recognition that the term abuse carries stigma owing, in part, due to broader drug-related stigma and its use in nonperson first language settings (e.g., abuser). At the same time, the current FDA guidance and other regulatory language refer to abuse potential, abuse liability, and other technical terms in formal guidance documents and policy. We have elected to retain this language for consistency with this current guidance for clarity and consistency while also ensuring the language used separates from the stereotyping, fear-drive avoidance, and othering that underlie stigma-related processes.

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susceptible to future use by specific populations because of lessened sensitivity to these constraints.

Behavioral economic demand (hereafter referred to as "demand") is one approach used to quantify this sensitivity to constraint by evaluating the relationship between consumption of a commodity and its cost (Koffarnus et al., 2022; Mackillop, 2016; Strickland & Lacy, 2020). Various methods used to assess demand in addiction science share the common approach of measuring drug consumption across a series of costs and subsequently generating a demand curve to isolate distinct aspects of reinforcing value. Contemporary quantitative models derive two values from this curve—demand intensity and demand elasticity (Hursh & Silberberg, 2008; Koffarnus et al., 2022). Demand intensity denotes consumption at unconstrained cost and conceptually reflects the desired level of consumption at which an organism behaves to defend in the face of constraint. Demand elasticity, and its inverse transformed metric "essential value," reflects price sensitivity with price normalized to demand intensity to facilitate comparisons across drugs and doses. Other indices may be directly observed (or derived) from the demand curve, including breakpoint (i.e., price at which consumption is suppressed to zero), O_{max} (i.e., maximum expenditure or response output), and P_{max} (i.e., the price at which O_{max} occurs or, quantitatively, the price at which the slope of the demand-curve function in proportional [log-log] space is exactly -1 and consumption shifts from inelastic to elastic; Gilroy et al., 2019).

Demand-curve analysis has been proposed to offer a valuable complementary measure to traditional abuse potential testing for improving the resolution of the empirical data that guide drug scheduling decisions (Banks et al., 2026; Henningfield et al., 2026; Koffarnus, 2023). This behavioral economic approach leverages the essential-value metric derived from demand procedures to generate a scalable, comparable measure for relative abuse potential rankings across drugs that is conceptually unit independent. More broadly, these approaches allow for generation of a metric that could differentiate drugs that share the ability to induce positive or rewarding effects but differ in their relative sensitivity to constraint for consumption and motivation to use. This distinction could inform differences in scheduling level as well as other factors considered when restricting drug access during the NCE approval process (e.g., the requirement for and content of a Risk Evaluation and Mitigation Strategy). These procedures also benefit from the ability to conduct corresponding measures in nonhuman and human experiments with the same output metrics across species (cf. dissociation between drug self-administration in preclinical testing and subjective drug effects in HAP studies; Strickland & Lacy, 2020).

Current Review

The current review builds on recent conceptual pieces (Koffarnus, 2023) and reviews of preclinical demand testing (Banks et al., 2026) to evaluate the applicability of behavioral economic demand methods to HAP testing frameworks. Here, we review existing studies that have applied procedures broadly consistent with HAP testing and integrated demand procedures to measure abuse potential and/or a drug's reinforcing effects. Procedural details and the demand methods implemented are reviewed toward the goal of informing the methods for applying demand testing in the HAP study framework and the existing gaps in defining those methods. Recommendations for future research to advance these methods are provided following the review of extant literature.

Method

Search Strategy and Eligibility Criteria

We initially conducted a search to identify peer-reviewed studies using demand analyses in the context of drug use (see Reed et al., 2026 for details on the search). Literature searches were performed in two major electronic databases: PubMed and Web of Science, using the following search terms in July 2024:

> ("stimulant" OR "cocaine" OR "cigarette" OR "marijuana" OR "cannabis" OR "alcohol" OR "opioid" OR "caffeine" OR "drug") AND ("demand" OR "economic*") AND. ("threshold procedure" OR "purchase task" OR "self-administration")

An additional search was conducted on existing review articles evaluating the purchase-task procedure (González-Roz et al., 2019; Kaplan et al., 2018; Martínez-Loredo et al., 2021; Reed et al., 2020; Strickland et al., 2020; Zvorsky et al., 2019) to identify any eligible studies that were not captured in the initial database queries. Finally, we updated our search in February 2026 to include eligible articles published since July 2024.

Articles were eligible for the present review if they (a) reported empirical data, (b) used operant demand methods (e.g., purchase tasks, self-administration paradigms), (c) focused on human drug use, (d) employed demand methods in a study similar to HAP study methods, and (e) reported on a drug other than tobacco. We operationalized HAP study methods broadly to include designs that evaluated either demand for a blinded drug commodity or demand procedures that involved an incentivized consequence. We did not include studies focused exclusively on tobacco because regulatory authority and rulemaking involving tobacco follow a different process than other FDA-regulated NCEs (for review on the regulatory benefit of demand methods in tobacco science, see Bickel et al., 2018; Tidey et al., 2016). These criteria resulted in 14 articles eligible for this review. Two articles reported results from the same study (Amlung & MacKillop, 2015; Mackillop et al., 2014). Details are included for both articles in the overview. However, these two articles are counted as one study for the Table 1 quantitative summary of design.

Data Extraction and Coding

A team of eight trained reviewers evaluated the eligible articles in the parent review search on a prespecified set of variables including drugs studied (open ended with post hoc categorization), demand-curve analysis (e.g., model), demand metrics reported (e.g., observed/derived metrics), and analysis approach (e.g., "2-stage," "pooled curve-fitting"). Each article was independently scored initially by two reviewers. Discrepancies in coding were flagged and resolved through consensus review. The first and second authors adjudicated all disagreements, reviewed open-ended comments, and finalized the data set for analysis. Additional criteria coded among eligible articles by the first and second authors for this review included the drug unit, if drug sampling occurred, if there was blinding, if the demand task was incentivized (i.e., reward delivered), and the systematicity checks employed. We first provide a

Table 1
Study Design and Details for Reviewed Studies

Author (date)	Method	Drug	Unit	Sampling	Incentivized	Subjective effect	Blinding
Amlung et al. (2012)	Purchase task	Alcohol (oral)	Half standard drink (up to eight minidrinks)	No	Yes	No	None
Amlung and MacKillop (2015)[a]	Purchase task	Alcohol (oral)	Half standard drink (up to right minidrinks)	No	Yes	No	None
Aston et al. (2026)	Purchase task	Cannabis (smoked)	Hit of 5.9% THC cannabis cigarette	No	Yes	Yes	Partly
Berry et al. (2023)	Purchase task	Cocaine (oral), methamphetamine (oral), alcohol (oral)	Cocaine: 0, 125, 250 mg/70 kg; methamphetamine: 0, 20, 40 mg; alcohol: 0, 1 g/kg	Yes	No	Yes	Yes
Bickel et al. (1992)	Operant	Coffee (oral), cigarettes (smoked)	Coffee: 2 oz; cigarette: two puffs	Yes	Yes	No	None
Dolan et al. (2020)	Purchase task	Oxytocin (intranasal)	0, 40 IU	Yes	No	Yes	Yes
Mackillop et al. (2014)[a]	Purchase task	Alcohol (oral)	Half standard drink (up to eight minidrinks)	No	Yes	No	None
MacKillop et al. (2019)	Purchase task	d-Amphetamine (oral)	0, 20 mg	Yes	No	Yes	Yes
Mitchell et al. (1995)	Operant	Coffee (oral)	Up to 30 oz (0.18-oz units)	Yes	Yes	No	No
Petry and Bickel (1999)	Other	Buprenorphine (sublingual)	Up to 32 mg (in 1/10th units)	Yes	Yes	Yes	Partly
Rush et al. (2025)	Purchase task	Methamphetamine (oral)	0, 30 mg	Yes	No	Yes	Yes
Spiga et al. (2005)	Operant	Methadone (oral), cigarettes (smoked)	Methadone: up to 54 mg (0.54 mg units); cigarette: 60 cc	Yes	Yes	No	Partly
Strickland et al. (2023)	Purchase task	Cocaine (intravenous)	0, 10, 30 mg/70 kg	Yes	No	No (reported elsewhere)	Yes
Trøstheim et al. (2025)	Purchase task	Morphine (intramuscular)	0.01, 0.15 mg/kg	Yes	No	Yes	Yes

Note. PT = partly blinding refers to designs where participants may be informed of active dosing but unaware of specific dosing.
[a] Data from "Further Evidence of Close Correspondence for Alcohol Demand Decision Making for Hypothetical and Incentivized Rewards," by M. Amlung and J. MacKillop, 2015, *Behavioural Processes*, *113*, pp. 187–191 (https://doi.org/10.1016/j.beproc.2015.02.012), and "The Neuroeconomics of Alcohol Demand: An Initial Investigation of the Neural Correlates of Alcohol Cost-Benefit Decision Making in Heavy Drinking Men," by J. Mackillop, M. T. Amlung, J. Acker, J. C. Gray, C. L. Brown, J. G. Murphy, L. A. Ray, and L. H. Sweet, 2014, *Neuropsychopharmacology*, *39*(8), pp. 1988–1995 (https://doi.org/10.1038/npp.2014.47), were from the same sample.

quantitative summary of design and demand-related features. We then provide a narrative synthesis of these studies.

Quantitative Summary of Extant Literature

Table 1 contains details on the study design and procedures for reviewed studies. The majority of studies used the purchase-task procedure ($n = 10$), in which participants self-report the amount of the drug they would purchase and consume across a standardized series of prices (see details in the Narrative Summary of Extant Literature below). Other studies used operant responding (e.g., fixed-ratio plunger pulls; $n = 3$) or other self-reported measures ($n = 1$; Petry & Bickel, 1999). There was substantial variability in the drugs studied, with alcohol ($n = 3$) being the most common drug evaluated. Most studies ($n = 11$) included a sampling component or session in which participants were provided with experience using the drug. Most studies also used some form of blinding whether it was fully blinded drug administration ($n = 6$) or if aspects of the administration were blinded (e.g., participants knew it was an active dose but were unaware of the exact dose or concentration; $n = 3$). Approximately half of studies ($n = 8$) used incentivized responding such that a reward was delivered contingent on the response, typically using an auction-style method in which one price point was randomly selected to be acted upon. Approximately half of studies reported on subjective-effect data ($n = 7$) such as drug effect visual analog scale or other drug-specific measurement scales.

Table 2 contains details on the demand measures and analysis pipelines used. A variety of checks for systematic data were employed including outlier analyses ($n = 4$) and algorithm criteria (e.g., "reversals from zero"; $n = 5$). Most studies reported observed variables ($n = 9$) such as breakpoint and demand intensity. Demand models included the exponential model ($n = 4$), exponentiated model ($n = 2$), and linear demand model ($n = 2$). Analyses primarily ($n = 11$) took a two-stage approach in which summary outputs (e.g., derived demand elasticity, observed breakpoint) were first generated on individual subject data and then compared using inferential statistics by the experimental manipulation of interest.

Narrative Summary of Extant Literature

The following section provides a narrative summary of reviewed articles conceptually grouped by historical context and design. This is followed in the discussion by recommendations to address gaps in the use of demand measures in HAP designs.

Historical Approaches

The first studies to apply demand-curve analyses in HAP-like designs used approaches involving effortful responding (e.g., plunger pulls, lever presses) under set schedules of reinforcement (e.g., fixed ratio [FR] where the number of responses required for a reinforcer delivery is a fixed value; Bickel et al., 1992; Mitchell et al., 1995; Spiga et al., 2005). This experimental arrangement typically requires manipulation of response cost or dose across experimental sessions to generate a demand curve with a single unit price evaluated during each session. Demand analyses can then be applied to the consumption data at each price to derive demand elasticity or other demand outputs.

Spiga et al. (2005), for example, evaluated self-administration of methadone and cigarette puffs among patients in methadone treatment. The FR cost of methadone and cigarette puffs was manipulated across sessions (e.g., FR32, FR64, and FR128) using the operant response of button presses. Demand for methadone and cigarettes was then evaluated under exclusive and concurrent access to the two commodities. This design allowed for determination of both own-price demand for each commodity and the cross-price elasticity (sensitivity of consumption with access to alternatives) of each commodity. While these procedures are rigorous and provide rich experimental data, they are logistically challenging. For instance, the Spiga et al. study required up to 54,180-min sessions across testing and baseline sessions to collect all the reported data.

Purchase-Task Procedure and Incentivized Approaches

The practical challenges of these multisession, operant approaches, in part, led to the development of the purchase-task procedure (Jacobs & Bickel, 1999). The purchase task is a simulation or questionnaire-based method in which participants are asked to report intended purchase and consumption of a drug under a standardized set of escalating prices. This approach yields within-subject consumption data (i.e., quantity purchased) over a dense, continuous unit-price range which allows for the construction of individual demand curves. Verbal behavior manipulations and instructional control stipulate boundary conditions of purchase and consumption such as a closed economy (i.e., this is the only location in which the commodity may be purchased) and exclusive consumption (i.e., you cannot sell or share the item). Numerous meta-analyses have supported the concurrent validity of the procedure for measuring alcohol, cannabis, cocaine, opioid, and other drug demand wherein measures of demand relate to substance use frequency and severity (González-Roz et al., 2019; Martínez-Loredo et al., 2021; Strickland et al., 2020).

The purchase-task procedure normally involves responding to a hypothetical scenario, meaning that no reward is delivered contingent on the responses provided. One HAP-like design includes the actual delivery of drug dependent on the responses provided (i.e., incentivized responding). These procedures typically involve the completion of a purchase task similar to the general format but selection of one price at random that is enacted. Here, a participant is provided a study budget, and at the selected price, the portion of study budget allocated to purchasing is taken, and the amount of drug purchased is provided together with the remaining portion of the budget left unspent. For example, Amlung et al. (2012) evaluated a hypothetical and actual alcohol purchase task for "mini-drinks" that were approximately half the size of a standard drink. Participants in that study had a $15 "bar tab" and were allowed to allocate any or all of their budget at each price on the purchase task to purchase a maximum of eight minidrinks. Correspondence of hypothetical and incentivized task responding was high ($r = 0.87$–0.97 for demand indices). Similar results were observed in a follow-up alcohol study using a similar design for alcohol (Amlung & MacKillop, 2015) and for cannabis use, albeit of a smaller strength of association in the case of cannabis use ($r = 0.46$–0.81; Aston et al., 2026). These studies show both the feasibility of evaluating abuse potential via drug self-administration using purchase-task methods and the good correspondence between fully simulated approaches and ones involving drug delivery.

Table 2
Demand Variables and Details for Reviewed Studies

Author (date)	Systematicity	Model	Observed variable	Analysis type	Demand index
Amlung et al. (2012)	Outliers, inconsistency (no rule set)	Exponential	Yes	Two-stage	Intensity, P_{max}, O_{max}, breakpoint, elasticity
Amlung and MacKillop (2015)[a]	Outliers, reversals	Exponential	Yes	Two-stage	Intensity, P_{max}, O_{max}, breakpoint, elasticity
Aston et al. (2026)	Outliers, stein	Exponentiated	Yes	Two-stage	Intensity, P_{max}, O_{max}, breakpoint, elasticity
Berry et al. (2023)	Outliers, bounce/reversals	Exponentiated	Yes	Two-stage	Intensity, P_{max}, O_{max}, breakpoint, elasticity
Bickel et al. (1992)	None	None	No	Two-stage	Point elasticity
Dolan et al. (2020)	Outliers	Exponential	Yes	Pooled; two-stage	Intensity, elasticity
Mackillop et al. (2014)[a]	None	None	No	Two-stage	Individual consumption values
MacKillop et al. (2019)	None	Exponential	Yes	Two-stage	Intensity, O_{max}, breakpoint, elasticity
Mitchell et al. (1995)	None	Linear	No	Two-stage	Point elasticity
Petry and Bickel (1999)	None	Other	No	Individual subject	Curve elasticity
Rush et al. (2025)	No breakpoint	None	Yes	Two-stage	Breakpoint
Spiga et al. (2005)	None	Linear	No	Pooled; two-stage	P_{max}, O_{max}
Strickland et al. (2023)	Stein	None	Yes	Two-stage	Intensity, P_{max}, O_{max}, breakpoint
Trøstheim et al. (2025)	Stein	None	Yes	Two-stage	Intensity, P_{max}, O_{max}, breakpoint, elasticity[b], area under the curve

Note. Stein refers to 3-point systematicity criteria (Stein et al., 2015).
[a] Data from "Further Evidence of Close Correspondence for Alcohol Demand Decision Making for Hypothetical and Incentivized Rewards," by M. Amlung and J. MacKillop, 2015, *Behavioural Processes*, *113*, pp. 187–191 (https://doi.org/10.1016/j.beproc.2015.02.012), and "The Neuroeconomics of Alcohol Demand: An Initial Investigation of the Neural Correlates of Alcohol Cost–Benefit Decision Making in Heavy Drinking Men," by J. Mackillop, M. T. Amlung, J. Acker, J. C. Gray, C. L. Brown, J. G. Murphy, L. A. Ray, and L. H. Sweet, 2014, *Neuropsychopharmacology*, *39*(8), pp. 1988–1995 (https://doi.org/10.1038/npp.2014.47), were from the same sample. [b] Elasticity was defined in this study using an observed curve average.

Blinded Drug Purchase-Task Approaches

Incentivized purchase-task procedures fulfill one desired criterion of HAP testing by offering a measure of demand combined with self-administration of a drug. However, these approaches are unlikely to be scalable to FDA-guided HAP studies given that they require multiple sessions for drug delivery (i.e., a sampling session and incentivized drug delivery session), thereby increasing costs. An attractive alternative that balances the rigor of demand assessment with the efficiency of existing HAP study designs is the blinded drug purchase-task approach. These designs largely follow traditional HAP structure involving the blinded administration of a test compound and subsequent pharmacodynamic (and sometimes pharmacokinetic) measurements. A purchase task is then completed at the end of an experimental session to query hypothetical consumption for that administered drug. This approach increases rigor by connecting hypothetical responding to the experimentally administered drug under double-blind conditions.

This blinded purchase-task approach has been applied to a variety of drug classes including stimulants (Berry et al., 2023; MacKillop et al., 2019; Rush et al., 2025; Strickland et al., 2023), opioids (Trøstheim et al., 2025), and alcohol (Berry et al., 2023). For example, MacKillop et al. (2019) evaluated responding for blinded doses of oral d-amphetamine (20 mg) and placebo. Participants reported significantly greater demand intensity and lower demand elasticity (i.e., less price sensitivity) for d-amphetamine relative to placebo. Similar results have been observed for other drugs tested under blinded conditions (e.g., see the multiple doses and drugs tested in Berry et al., 2023).

These studies have also been applied in contexts relevant to abuse potential testing, such as evaluating abuse potential of a novel drug and the changes in a drug's reinforcing effects after novel pharmacotherapy maintenance. Dolan et al. (2020) evaluated demand for, and the subjective effects of, intranasal oxytocin (4 IU) and placebo among healthy adults. Oxytocin failed to significantly increase drug liking relative to placebo, had highly elastic demand (43% of participants reported no consumption at any price, and median demand reached a breakpoint for oxytocin by $0.30), and did not differ from placebo on measures of demand intensity. The difference in peak drug liking between oxytocin and placebo was significantly related to the difference in demand intensity between oxytocin and placebo ($r = .61$)—measures of demand elasticity were not compared due to the high rates of zero responding for both oxytocin and placebo.

Other studies have evaluated changes in cocaine and methamphetamine demand during maintenance on the candidate pharmacotherapies suvorexant (Strickland et al., 2023) and mirtazapine (Rush et al., 2025). In these studies, blinded intravenous drug or placebo was administered at the start of a drug-challenge session during maintenance on the putative pharmacotherapy, and demand for that blinded drug was measured at the end of the session. For example, Strickland et al. (2023) found that suvorexant maintenance produced dose-related increases in demand for a moderate dose of cocaine (10 mg/70 kg), which was similar to the drug self-administration data from a concurrent progressive-ratio task in that study (Stoops et al., 2022). These findings reinforce the capacity of hypothetical purchase tasks combined with blinded drug demand to capture relevant features of abuse potential and align with more technically and practically complex methods involving drug self-administration.

General Summary

This review highlights the notable heterogeneity in the methods applied and test compounds evaluated when using demand procedures in HAP-relevant clinical designs. Consistent conclusions of existing work include (a) support for the development and evolution of the purchase task as an efficient method for evaluating demand in a single session and at a momentary level, (b) validation of the correspondence in responding between simulated purchase-task approaches and those involving actual drug delivery, and (c) demonstration that drugs with known abuse potential result in significantly greater demand (i.e., lower demand elasticity/higher essential value) than placebo when administered under double-blind laboratory conditions. In the remainder of this review, we describe extant gaps in the integration of demand procedures within HAP testing frameworks and our recommendations for addressing these gaps and uptake.

Our primary recommended use of demand for HAP testing is simple incorporation within existing HAP designs using a hypothetical blinded drug purchase task. Using this approach, a typical HAP design would be employed (e.g., blinded administration of multiple doses of the test compound, a positive control, and a placebo) to include existing pharmacodynamic measures and other design considerations (e.g., population selection). A hypothetical blinded drug purchase task would then be completed at the end of the experimental session that queries a participant's expected purchase of that blinded drug across a standardized price sequence. A demand curve can then be generated, and demand elasticity can be compared to positive controls and placebo. This approach balances the documented rigor of demand measurement and controlled drug administration with the practicality of efficient data collection and cost afforded by simulated purchase-task methods. Specifically, this would require only the completion of a single additional end-of-session measure, which is self-completed by the participant, takes approximately 5–10 min, and requires no added experimental sessions or drug exposure. Demand data could then be used as a complementary measure to subjective drug effects for eight-factor analysis and differentiation of abuse potential.

A major outstanding gap is the prospective evaluation of the relative predictive validity of demand measures as compared to subjective-effect measures for determining abuse potential. The limited work that has evaluated the association between demand measures and subjective effects is mixed with both large effect-size associations ($r = .61$ between demand intensity and Like Drug in Dolan et al., 2020) and smaller effect-size associations (i.e., between demand elasticity and measures of positive mood, $r = -.13$, and drug high, $r = -.30$; MacKillop et al., 2019). It is possible that these differences are attributable to the subjective-effect measure used, demand procedures, or drug studied. Critically, no studies have compared the relative sensitivity of demand and subjective-effect data to provide quantitative comparisons of abuse potential (cf. dichotomous decisions of the absence vs. presence of abuse potential).

Considerable merit would come from the posited benefit of demand procedures in providing quantitative comparisons of abuse potential. It is hypothesized that this benefit comes from the incorporation of constraint that is present in real-world drug-taking scenarios and ultimately could better forecast differences between the abuse potential of different NCEs and provide relative comparisons to positive controls with their known abuse potential.

Experiments to address this question are needed that include testing of multiple compounds varying in Drug Enforcement Agency scheduling and known abuse potential allowing for within-subject comparisons of relative abuse potential.

There is also recognized heterogeneity in the procedures used to measure demand and the pipelines used to analyze them as evidenced in this review and others (Kaplan, Foster, et al., 2018; U.S. Food and Drug Administration, 2017). Purchase tasks can feature several manipulations including the relative closed versus open nature of the economy (i.e., availability of the good or alternatives outside the purchasing scenario), temporal scope of purchase (e.g., single day, week, or month period), and price sequence and density. These manipulations can influence responding and subsequent demand metrics (Acuff, Strickland, et al., 2023; Ferguson et al., 2021; Kaplan & Reed, 2018).

For example, the time window for studying purchasing behavior varies considerably across different task variations with some stipulating purchase for consumption that may occur over a single day, whereas others indicate consumption that may occur over longer periods (e.g., 1 week, 1 month). Few studies have systematically altered purchase/consumption windows to evaluate their impact on demand, although one study showed that alcohol demand became more inelastic as the window of access increased from 1 to 5 to 9 hr (Kaplan & Reed, 2018). Qualitative work has shown that duration is an important variable to consider to ensure participant's appropriate understanding of the purchase task with some participants indicating that shorter durations like a single day may make understanding more difficult for people that use drugs less frequently (Aston et al., 2021). Shorter durations may also create a ceiling effect especially for drugs with a longer half-life that may be used only once in a day. These factors suggest that longer durations like 1 week or 1 month may provide better variability in responding that is necessary to identify differences in abuse liability; however, systematic study is needed to this end.

An example purchase-task design adaptable to current HAP testing formats is included in the Supplemental Materials. Prospective research evaluating the integration of demand methods would benefit from using this version in combination with other task variations to specify the arrangement(s) that provide the most robust and predictive outputs. At the same time, prospective work should also evaluate how adaptations may be needed across space (e.g., different countries in which currencies and economic conditions may influence responding) and time (e.g., adjustments over time due to factors like inflation).

Similarly, analytic methods continue to evolve including the demand models used to derive metrics, the exclusions applied to determine nonsystematic data, and the approaches used to mitigate bias and ensure stable estimates (e.g., mixed-effect modeling; Kaplan et al., 2021). The advent of open-source modeling tools (e.g., *beezdemand* and *shinybeez*; Kaplan et al., 2019; Kaplan & Reed, 2025) both increases the accessibility of these advanced methods and also ensures the rigor of transparent and replicable analysis pipelines. Further refinement and validation efforts to standardize analysis processes stand to benefit demand-curve analysis in HAP settings, specifically, and addiction science, broadly.

Ultimately, cross-species designs could effectively address the prognostic utility of preclinical methods when applying demand as a harmonized and translatable abuse potential measure. As noted in the introduction, current FDA abuse potential testing relies upon disconnected measures of drug self-administration used in preclinical testing and subjective-effect reporting used clinically in HAP studies. A practical benefit of demand testing is that the summary outputs are consistent across species. Demand studies designed to address the relative consistency of abuse potential assessment testing the same compounds in rodent and human laboratory settings would inform the relative strengths of this cross-species approach.

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