Behavioral Economics for Abuse Potential Assessment

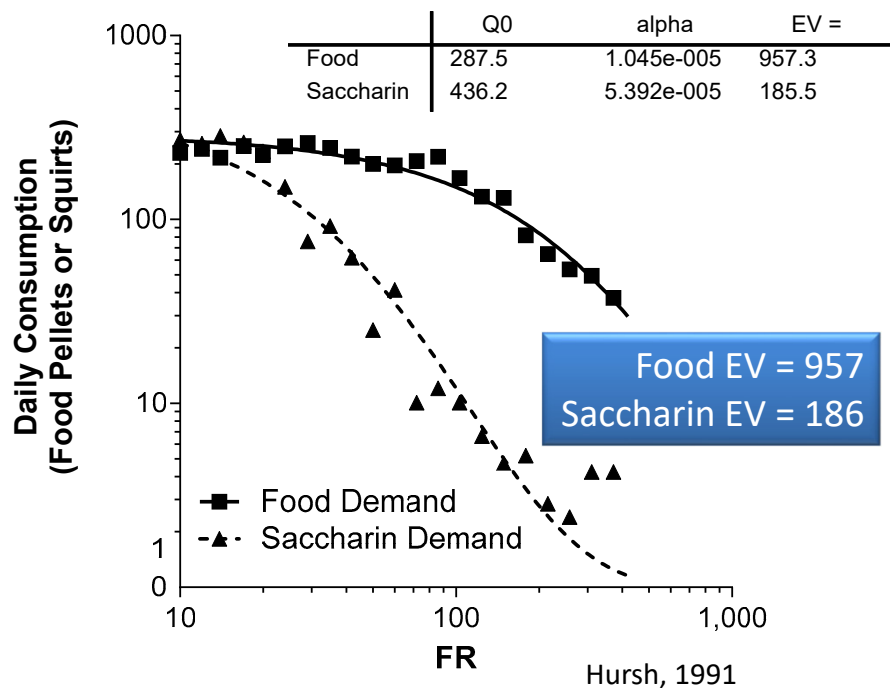Steven R. Hursh, Ph.D.

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Overview

- Benefits of demand curve assessment for scaling abuse potential based on consumption price sensitivity or Essential Value (EV).

- Show dose independence and replicability of findings.

- Summarize EV across pre-clinical studies with primates showing applicability for scaling abuse potential.

- Demand curve examples from rodent work to show that this is a feasible methodology that is stable over time.

- Human hypothetical demand mirrors non-human data for assessing abuse potential.
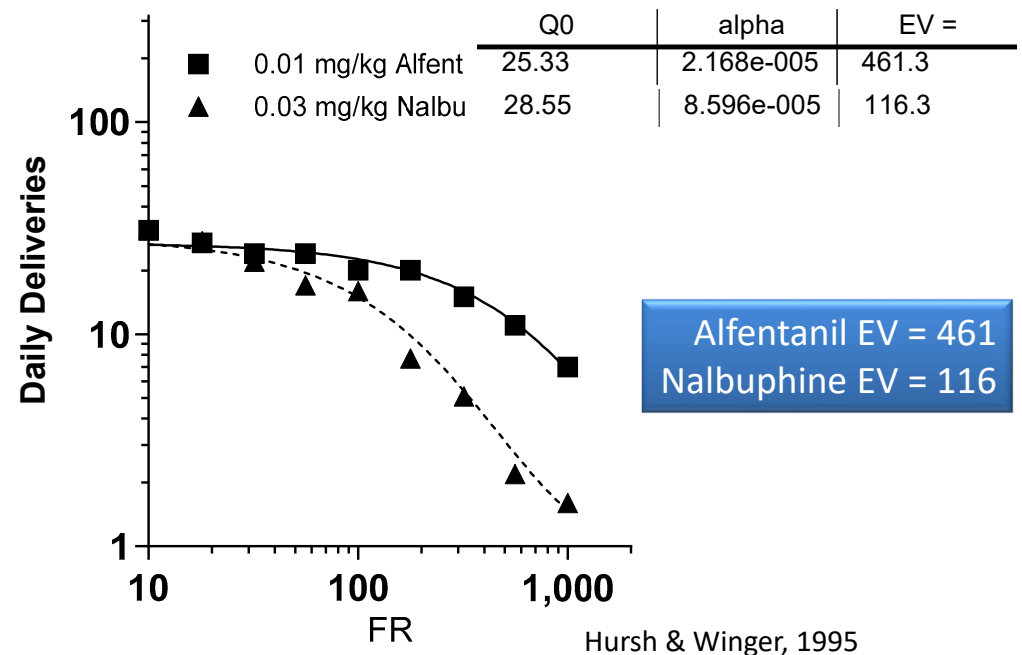
Demand Curves with Varying Price Sensitivity

Consumption at a low price does not necessarily predict consumption at higher prices

Demand for Food and Saccharin

	Q0	alpha	EV =
Food	287.5	1.045e-005	957.3
Saccharin	436.2	5.392e-005	185.5

Food EV = 957
Saccharin EV = 186

- ■ Food Demand
- ▲ Saccharin Demand

Daily Consumption (Food Pellets or Squirts)

FR

Hursh, 1991

Demand for Alfentanil and Nalbuphine

	Q0	alpha	EV =
■ 0.01 mg/kg Alfent	25.33	2.168e-005	461.3
▲ 0.03 mg/kg Nalbu	28.55	8.596e-005	116.3

Alfentanil EV = 461
Nalbuphine EV = 116

Daily Deliveries

FR
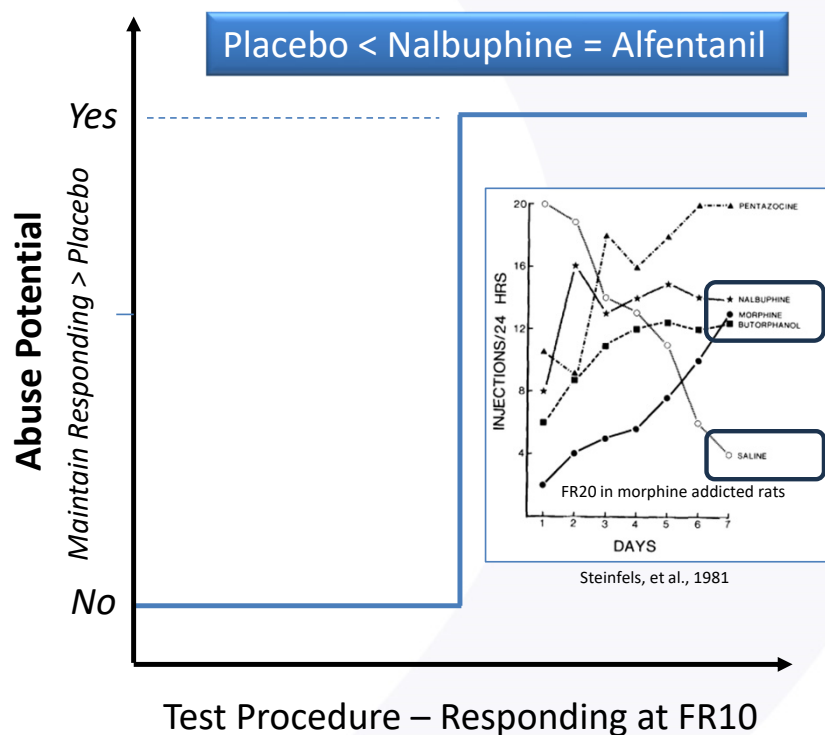
Hursh & Winger, 1995

EV = ƒ (1/α)
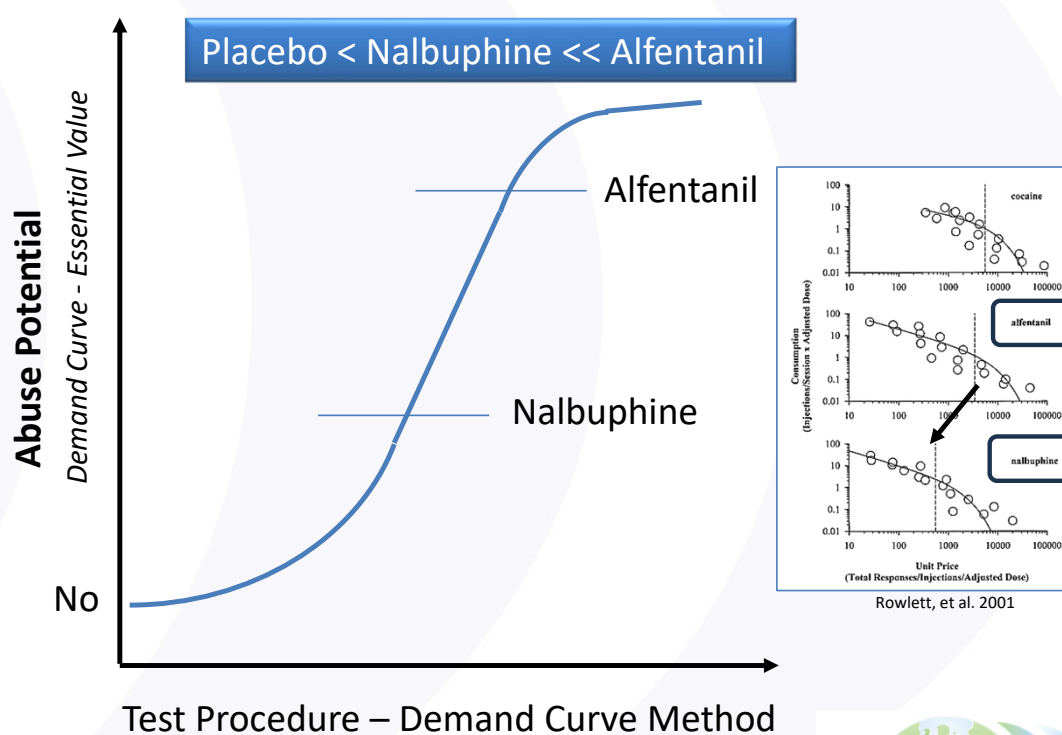Lower price sensitivity is associated with greater Essential Value.

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Behavioral Economic Advantage for Abuse Potential
Essential Value is a Graded Scale of Abuse Potential

Current Binary Determination

Placebo < Nalbuphine = Alfentanil

FR20 in morphine addicted rats

Steinfels, et al., 1981

Test Procedure – Responding at FR10

Demand-Based Parametric Determination

Placebo < Nalbuphine << Alfentanil

Rowlett, et al. 2001

Test Procedure – Demand Curve Method

Drug Demand Curves with Multiple Doses
Self-administration in Monkeys

Alfentanil Demand

EV = 461.3

- ▲ 0.01 mg/kg Alfent
- ● 0.003 mg/kg Alfen
- ▲ 0.001 mg/kg Alfent
- ■ 0.0003 mg/kg Alfent

Cocaine Demand

EV = 367.8
(higher two doses)

- ● 0.01 mg/kg Cocaine
- ■ 0.03 mg/kg Cocaine
- ▲ 0.1 mg/kg Cocaine

Methohexital Demand

EV = 155.9

- ● 0.1 mg/kg Methohex
- ▲ 1.0 mg/kg Methohexi
- ■ 0.32 mg/kg Methohex

Nalbuphine Demand

EV = 116.3

- ▲ 0.32 mg/kg Nalbu
- ● 0.03 mg/kg Nalbu
- ▲ 0.003 mg/kg Nalbu
- ■ 0.01 mg/kg Nalbu

based on Hursh and Winger, 1995

3-Parameter: $\log Q = \log(Q_0) + k(e^{-\alpha \cdot Q_0 \cdot C} - 1)$

2-Paramter: $\log(Q) = \log(Q_0) \cdot e^{((\alpha/\log(Q_0)) \cdot Q_0 \cdot C)}$

Real Price
$Q_0 \cdot C$

Alfentanil EV = 461
Cocaine EV = 368
Methohexital EV = 156
Nalbuphine EV = 116

Dose independence is not always true, but assessment is simplified by scaling that is relatively insensitive to dose and driven by the essential value of the drug.
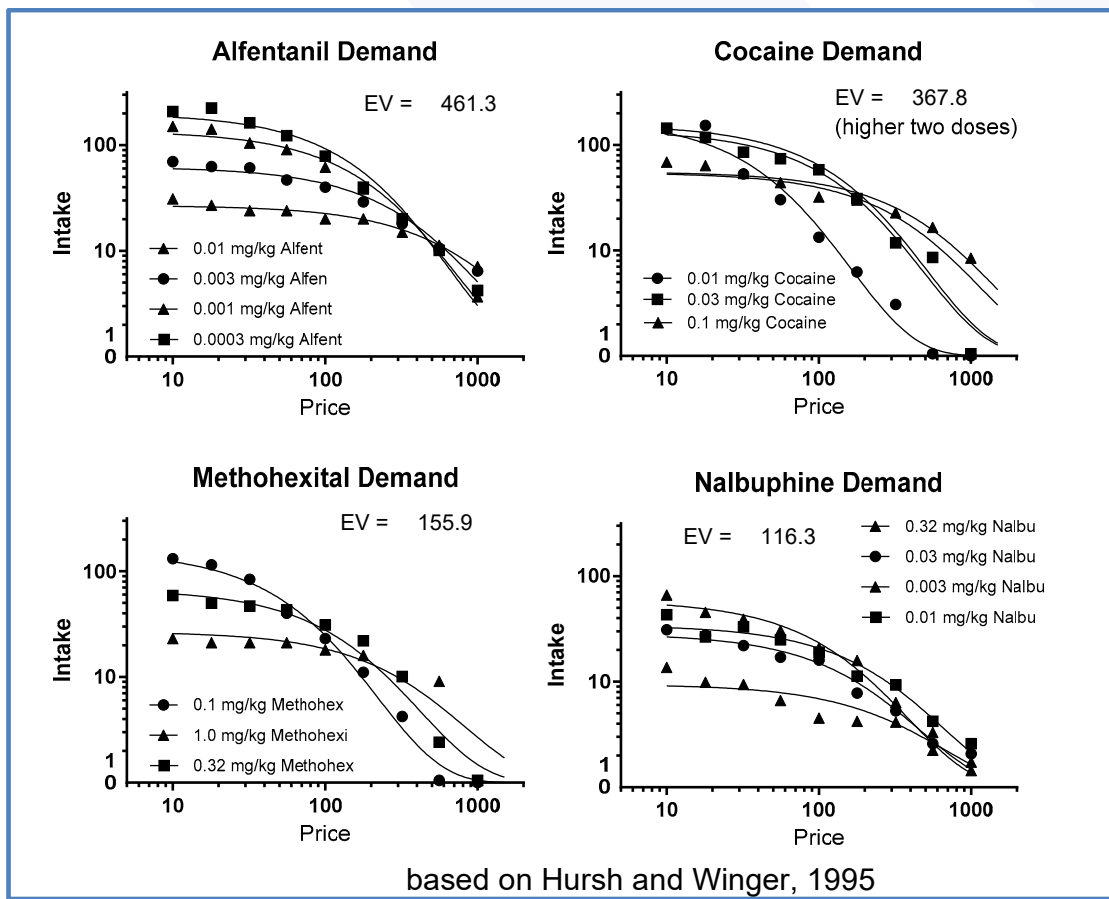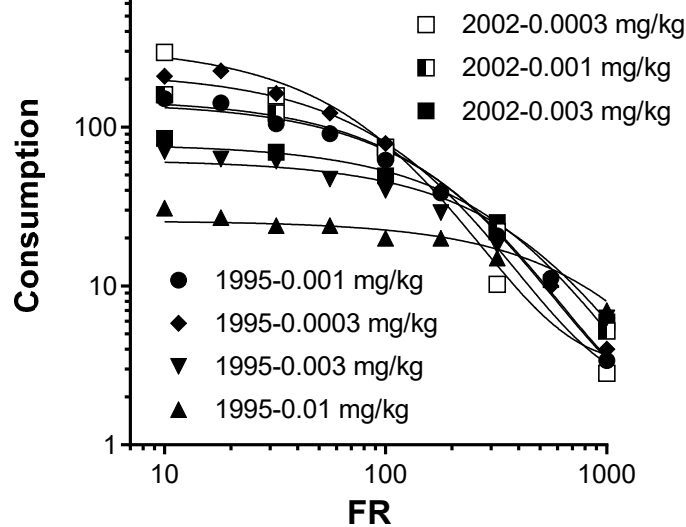
Reliability of Demand Determinations
Two Primate Studies Seven Years Apart
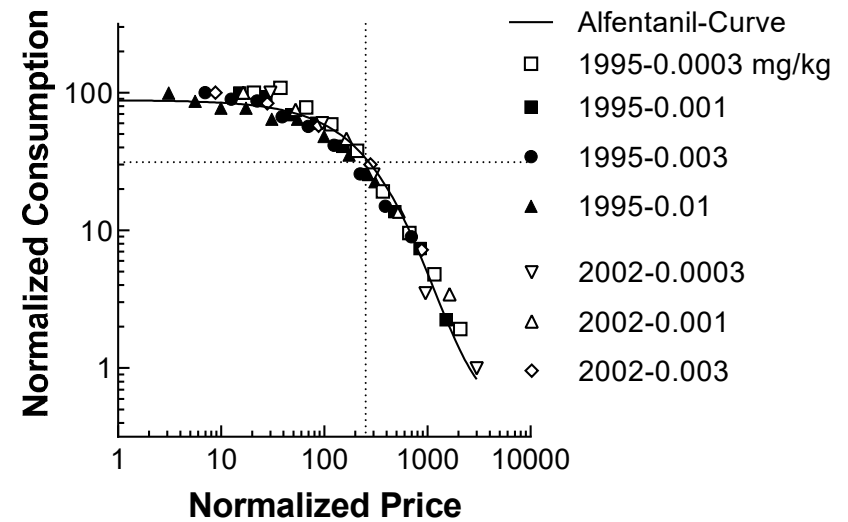

Alfentanil Log-log Demand

alpha 1.140e-005

AICc 85% probability that alpha is identical across datasets

- □ 2002-0.0003 mg/kg
- ◧ 2002-0.001 mg/kg
- ■ 2002-0.003 mg/kg

- ● 1995-0.001 mg/kg
- ◆ 1995-0.0003 mg/kg
- ▼ 1995-0.003 mg/kg
- ▲ 1995-0.01 mg/kg

ALFENTANIL

alpha 9.556e-006

AICc 67% probability that alpha is identical across datasets

- —— Alfentanil-Curve
- □ 1995-0.0003 mg/kg
- ■ 1995-0.001
- ● 1995-0.003
- ▲ 1995-0.01
- ▽ 2002-0.0003
- △ 2002-0.001
- ◇ 2002-0.003

Drug Abuse Liability Ranking - Two Parameter Demand Equation

Drug	EV	Relative EV (Fentanyl)
Food (Closed Economy)	957	3.52
Remifentanil (Ko et al.)	543	2.00
Alfentanil (2002)	485	1.78
Alfentanil (1995)	461	1.69
Cocaine (2 higher doses)	368	1.35
Ketamine	358	1.32
PCP	290	1.07
Fentanyl	272	1.00
Saccharin (Open Economy)	186	0.68
Methohexital	156	0.57
Nalbuphine	116	0.43
Dizocilpine	52	0.19

ZBEn Model
$EV = 1/(100 * \alpha)$
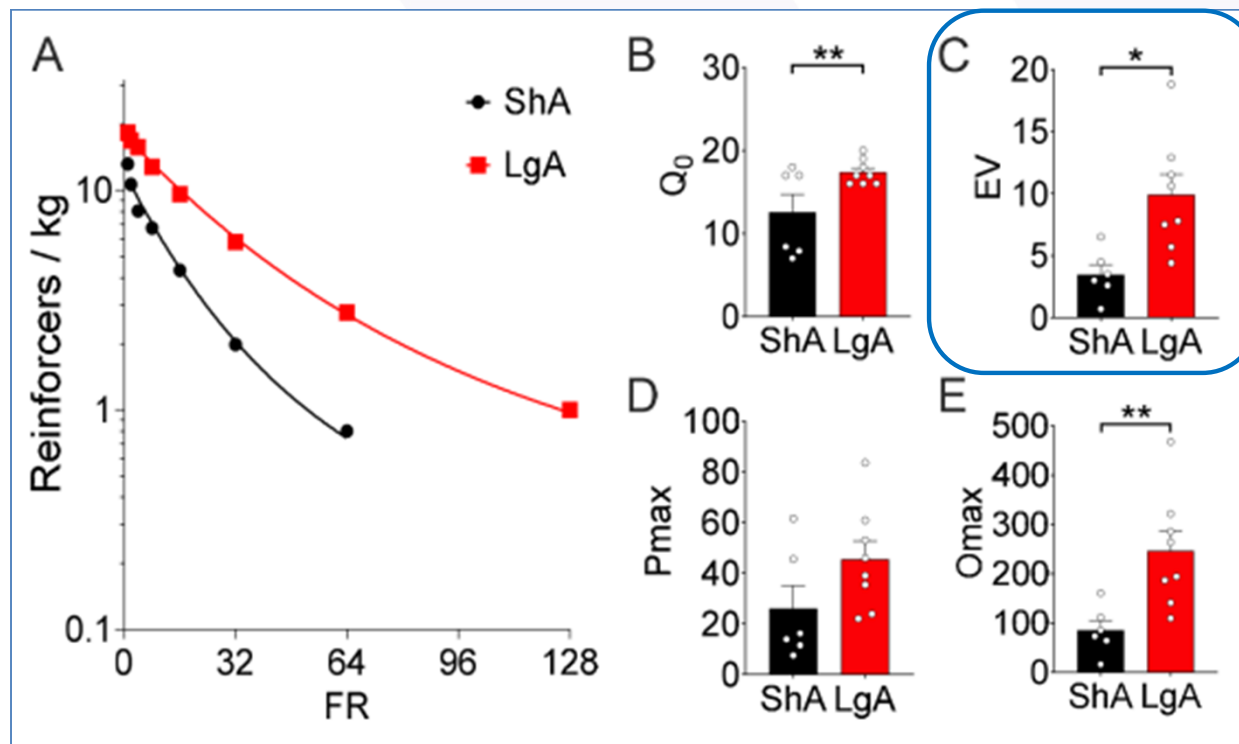ZBEn model, no k

Rat Demand for Fentanyl and Heroin
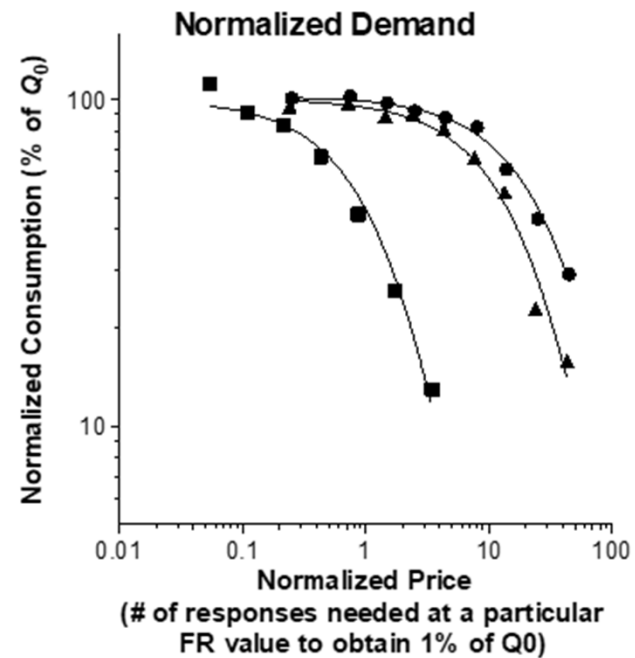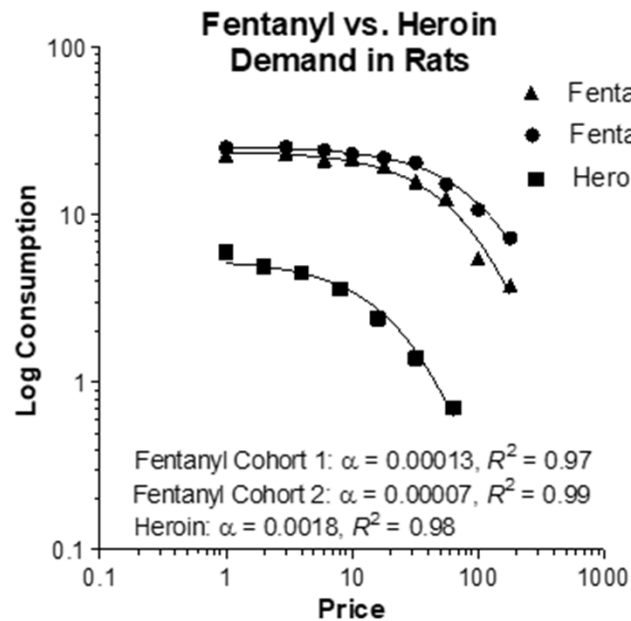
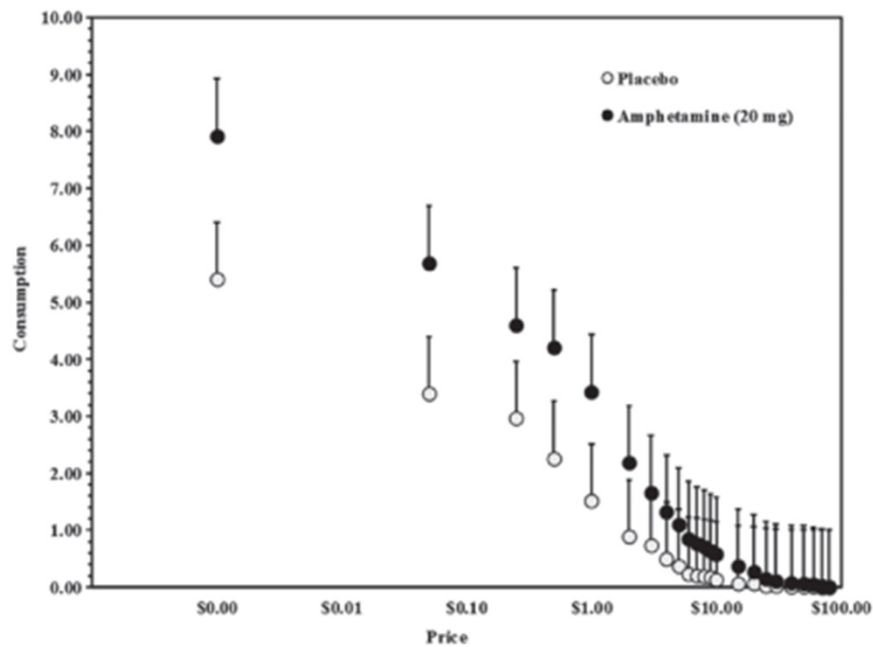# Development of Inelastic Demand for Fentanyl

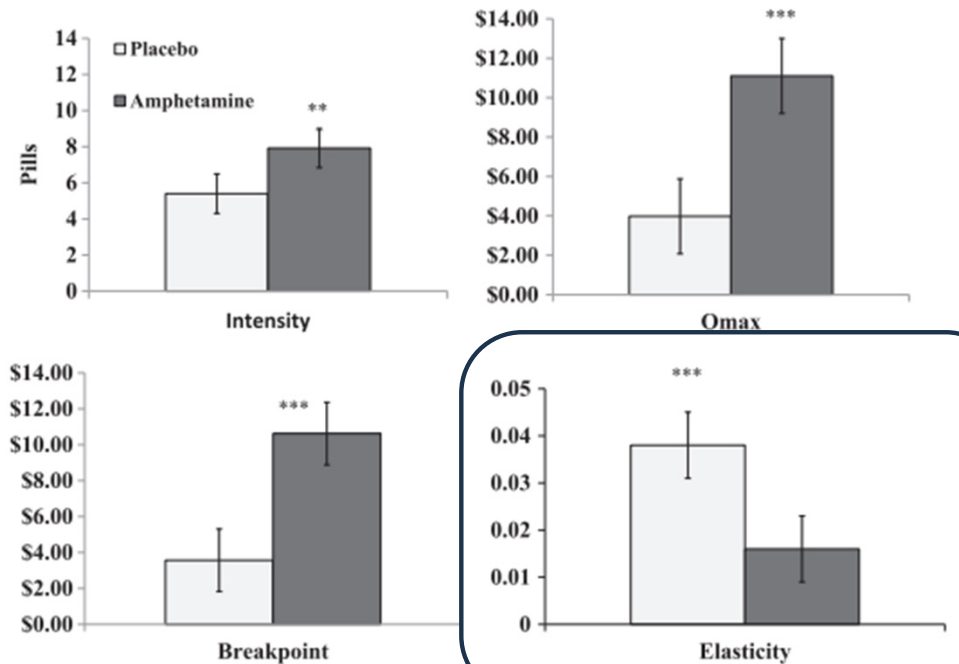Fentanyl Initial EV = 4
Fentanyl Escalation EV = 10

McConnell, et al. 2021: 3 sec of fentanyl vapor.

Human Hypothetical Demand for Abuse Liability

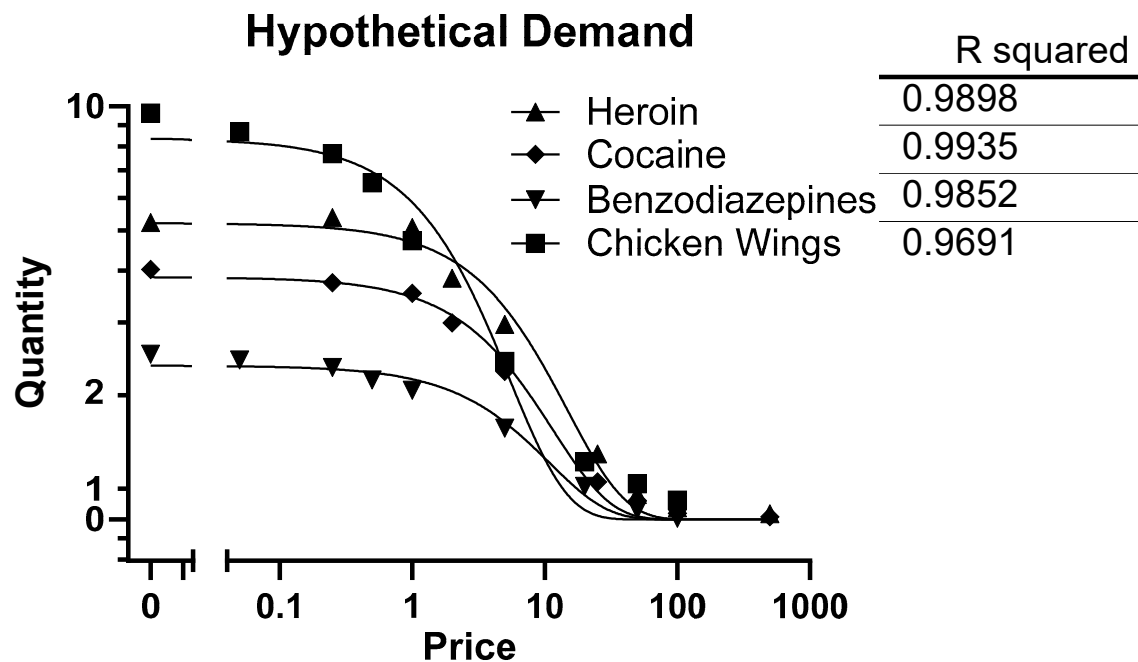Note. Consumption refers to number of pills.

Note. N=98 (Intensity, Omax, Breakpoint); n=41 (Elasticity) *p<0.05; **p<0.01; ***p<0.001.

McKillop, et al., 2018

Hypothetical Demand Sensitivity to Different Drugs - OUD Patients

Hypothetical Demand

	R squared
Heroin	0.9898
Cocaine	0.9935
Benzodiazepines	0.9852
Chicken Wings	0.9691

Heroin EV = 1.09
Cocaine EV = 0.76
Benzo EV = 0.69
Chicken EV = 0.49

Quantity vs *Price*

	Heroin	Cocaine	Benzodiazepines	Chicken Wings
Q0	5.215	3.861	2.358	8.356
alpha	0.009217	0.01308	0.01449	0.02021
EV =	1.085	0.7645	0.6902	0.4947

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Summary

- Drugs that are equal in sustaining consumption at a low price may be very different in sustaining consumption at higher prices – they differ in price sensitivity or essential value.

- Standardized methods for demand curve assessment can provide a parametric scaling of essential value as a forecast of varying degrees of abuse potential.

- BE method increases the precision of abuse potential assessment by exploring a range of "market prices" to better forecast real-world use.

- Methods can be applied to rodents and have been shown to be reliable, but a demonstration of rank ordering of a sample of drugs is needed.

- Similar methods can be used with human volunteers providing hypothetical estimates of consumption across a range of prices.

References

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Madden, G. J., Bickel, W. K., & Jacobs, E. A. (2000). Three predictions of the economic concept of unit price in a choice context. *Journal of the Experimental Analysis of Behavior*, 73, 45–64.

Winger, G., Hursh, S.R., Casey, K.L., and Woods, J.H. (2002). Relative reinforcing strength of three n-methyl-D-Aspartate antagonists with different onsets of action. J. Pharmacol Exp Ther 301: 690-697, 2.

Winger, G., Woods, J.H. and Hursh, S.R. (1996) Behavior maintained by alfentanil or nalbuphine in rhesus monkeys: fixed-ratio and time-out changes to establish demand curves and relative reinforcing effectiveness. *Exp and Clinical Psychopharm*, 4, 2, 131-140.

Sensitivity of Demand to Alternatives

Market Demand with and without Supplement
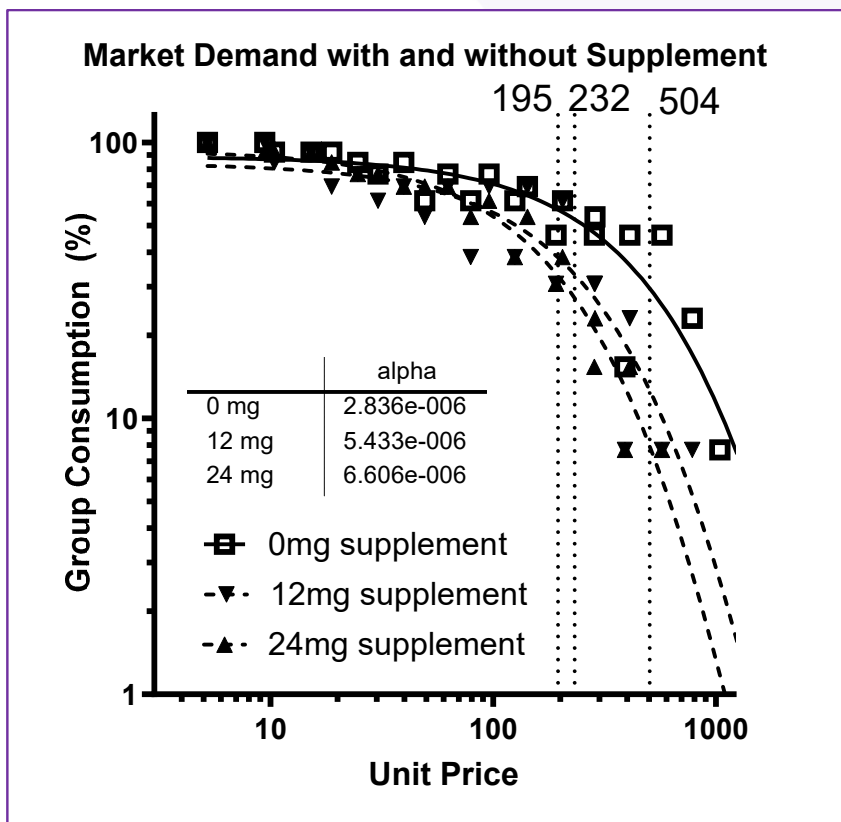
Greenwald and Hursh, 2006

- Demand for an opioid is sensitive to a "free" alternative opioid.

- Model for methadone assisted treatment.

- However, market demand is INSENSITIVE to available alternatives at low market prices (Hursh, 1991; Greenwald & Hursh, 2006).

- Implies that demand for treatment will also be sensitive to market price.

- Foreshadowed current events, 2023.

Essential Value Differentiates Ketamine, PCP, and Dizocilpine
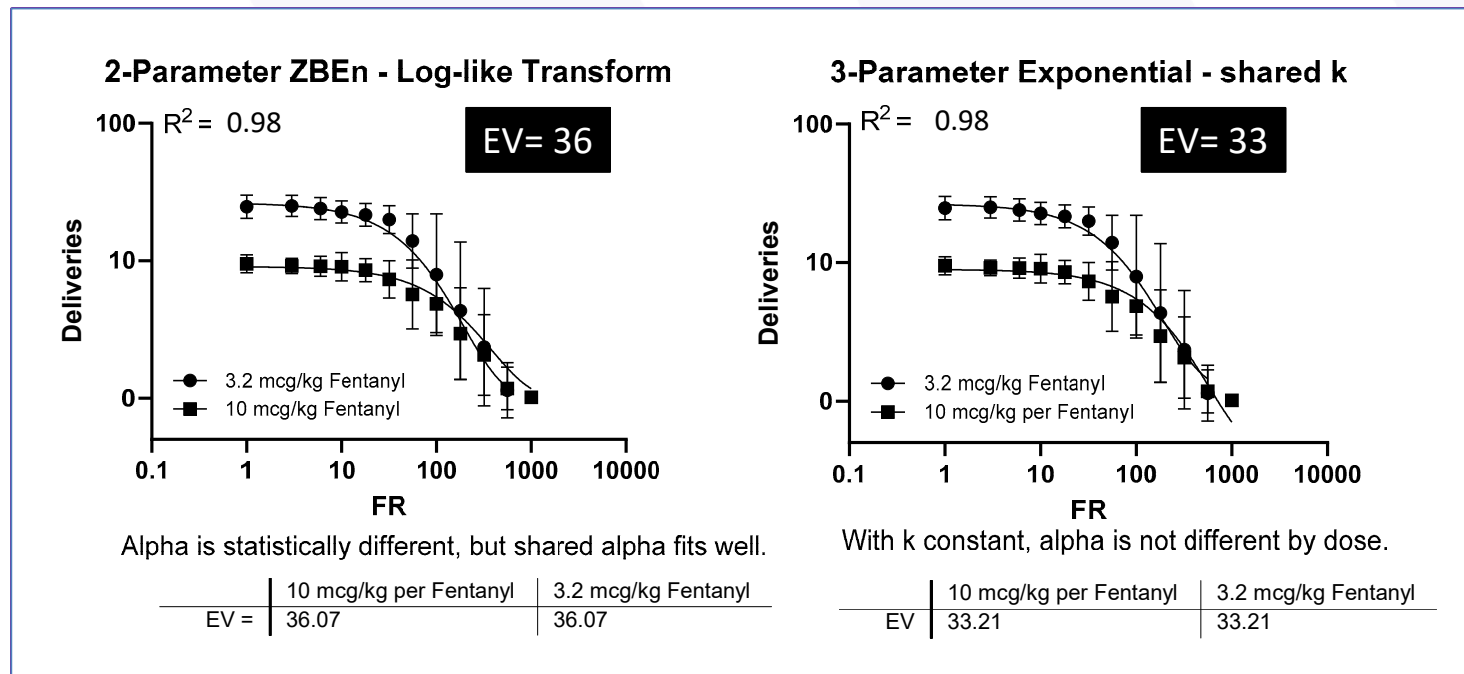## *Time to Peak Effect Relates to EV*
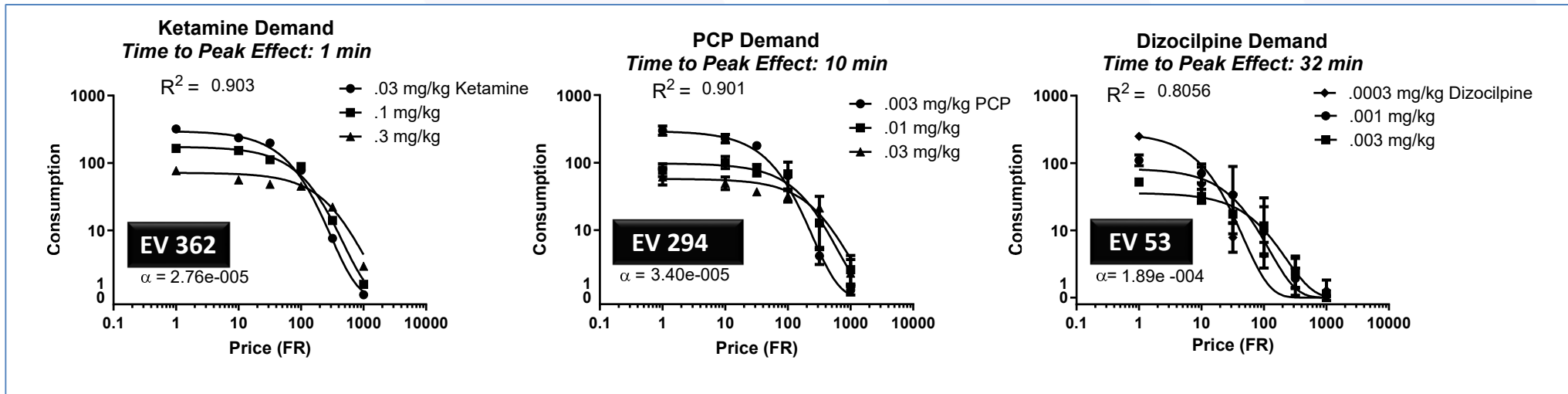
Based on Winger, G., Hursh, S.R., Casey, K.L., and Woods, J.H. (2003)

Rat Demand Curves for Fentanyl
Dose Independence of Essential Value

VCU Data courtesy of S. Negus and M. Banks