Estimating the Daily Milligrams of Oral Amphetamine Equivalent of Illicit Methamphetamine Use

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Abstract

Introduction

The purity, accessibility, and affordability of illicit methamphetamine has increased in recent decades, which has been linked to rising rates of methamphetamine-involved overdoses, psychosis, cardiovascular events, and other health consequences. Nevertheless, information about the quantity of methamphetamine used by regular consumers has been limited, despite the potential clinical utility of exposure quantification.

Methods

From August 2024-April 2025, self-reported daily methamphetamine consumption was assessed among n=68 individuals. Methamphetamine samples (n=112) were analyzed for purity using liquid chromatography-mass spectrometry. Percent bioavailability by route of administration and stimulant equivalency were obtained from literature. A simulation model leveraging bootstrapping was used to estimate MOAE.

Results

The average reported daily methamphetamine consumption was 0.96g (median 0.36g; range 0.1g-4.0g). Average purity was 71.6% (median 75.5%; range 0.1%-95.0%). Given estimated average bioavailability of 52.0% when smoked, 79.3% when insufflated, 67.2% orally or inserted rectally, and a 2:1 amphetamine-methamphetamine equivalency, the average consumer used 1,549.0 MOAE daily (median 516.6; range 1.3-10,112.0).

Discussion

We estimate that consumers of methamphetamine in Los Angeles use a median daily stimulant dose (>500 MOAE) that is nearly tenfold higher than the maximum typical recommended clinical dose of mixed amphetamine salts (60mg). This may help explain the limited efficacy of prescription stimulant treatment for methamphetamine use disorder, which typically employs considerably lower quantities. Given this high dose, these findings shed light on the rising incidence of methamphetamine-related sequalae, such as psychosis, cardiovascular complications, and sudden death. Although exposure quantification is commonplace for alcohol and tobacco use disorders, uncertainties in illicit drug markets has complicated this practice for most illicit drugs. This study supports leveraging emerging information from drug checking programs so that clinicians can approximate exposure quantification.

Introduction

The purity, accessibility, and affordability of illicit methamphetamine has increased in recent decades, which has been linked to rising rates of methamphetamine-involved overdoses, psychosis, cardiovascular events, and other health consequences[1–3]. Nevertheless, information about the quantity of methamphetamine used by regular consumers has been limited, despite the potential clinical utility of exposure quantification. Using recent advancements in community-based drug checking, we estimate the daily Milligrams of Oral Amphetamine Equivalent (MOAE) used among drug checking participants who consume methamphetamine in Los Angeles. This quantity is likely to be more easily interpretable by clinicians, who may be familiar with dosing of mixed amphetamine salts, rather than the quantity of illicit methamphetamine, for which dosing depends on drug concentration, route of administration, and bioavailability.

Methods

Daily MOAE was estimated according to Equation 1, where *Consumption* is the daily milligrams of illicit methamphetamine used, *Purity* is the proportion of active compound in substances sold as illicit "methamphetamine", *Bioavailability* is the route-of-administration-specific proportion of total drug used that is absorbed systemically, $Methamphetamine: Amphetamine\ Equivalence$ is the ratio of physiological potency between methamphetamine and mixed amphetamine salts, and $Bioavailability\ Oral\ Amphetamine\ Salts$ is the fraction of mixed amphetamine salts that is absorbed systemically when taken orally.

$$Milligrams\ of\ Oral\ Amphetamine\ Equivalence\ (MOAE) = Consumption \cdot Purity \cdot Bioavailability \cdot Methamphetamine{:}\ Amphetamine\ Equivalence \cdot \frac{1}{Bioavailability\ Oral\ Amphetamine\ Salts}$$

Equation 1. Calculation of estimated mg of oral amphetamine equivalent (MOAE) self-administered among regular consumers in Los Angeles

To estimate the distribution of MOAE combining uncertainty and variation in each of the aforementioned parameter inputs, we employed a bootstrapping approach leveraging 10,000 draws. Methamphetamine purity by weight was assessed using liquid chromatography-mass spectrometry among n=112 samples collected at a community-based drug checking program in Los Angeles County[4]. Samples were limited to those sold as methamphetamine, and for which clients expected only methamphetamine. Daily methamphetamine consumption volume and route of administration was assessed by self-report using a survey among n=68 individuals who regularly consume methamphetamine and brought samples for testing. Bioavailability by route-of-administration and stimulant equivalency factors were drawn from literature review. See supplemental methods. The UCLA IRB approved this project (IRB-22-0760) and additionally determined that aspects of this work constituted public health surveillance and not human subjects research.

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Although exposure quantification is commonplace for alcohol and tobacco use disorders, uncertainties in illicit drug markets has complicated this practice for most illicit drugs. Innovatively, this study supports leveraging emerging information from drug checking programs so that clinicians can approximate exposure quantification—and understand the clinical benefits of treatments that result in dose reductions—by regularly asking their patients about consumption quantities. This can inform risk stratification for cardiac, psychiatric and other outcomes and personalizing care, including withdrawal management. This mirrors efforts to quantify use and employ usage reduction as a clinical endpoint in addiction-related clinical trials[6]. This study also represents an example of how emerging drug checking technologies can provide consumers with information that can empower them to make safer drug use decisions, despite the highly uncertain and rapidly-evolving nature of the illicit drug supply.

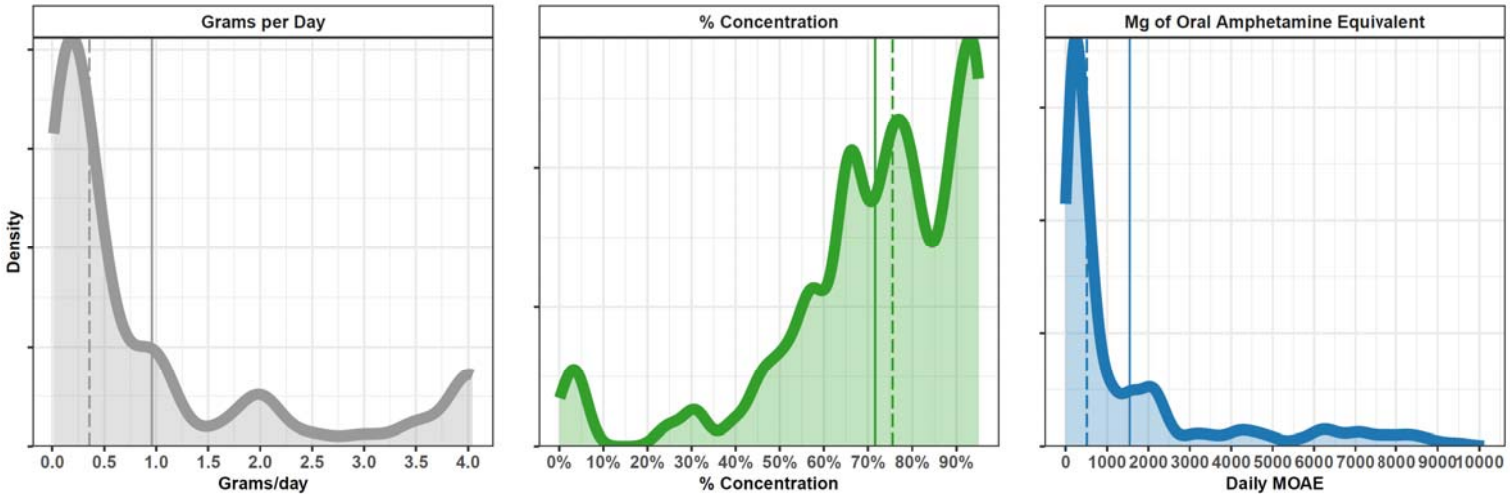

Figure. Distributions, Median, and Mean Grams per Day Consumed, Percent Concentration (Purity) and Estimated mg of Oral Amphetamine Equivalent Self-Administered Among Regular Consumers in LA

For each panel, a dashed vertical line shows the distribution mean, and a dashed solid line shows the distribution mean. Left: The distribution of self-reported grams of methamphetamine ingested per day among regular consumers participating in drug checking services in Los Angeles. Center: Percent concentration (purity) of expected methamphetamine samples provided by clients at drug checking services in Los Angeles. Right: the estimated distribution of milligrams of oral amphetamine equivalent (MOAE) consumed among drug checking clients in Los Angeles.

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Supplemental Methods

Purity

1. Data describing methamphetamine purity and daily quantity ingested among regular consumers were assessed via data generated from anonymous participants accessing a community-based drug checking program, *Drug Checking Los Angeles*. Participants voluntarily provide samples of illicit drug products for testing at four different sites in Los Angeles County, California from August 2024 to April 2025.
2. Samples were analyzed initially in the field with Fourier-transform infrared (FTIR) spectroscopy and immunoassay test strips. Samples were then sent to the National Institute of Standards and Technology (NIST) for secondary laboratory-based qualitative and quantitative testing using direct analysis in real time mass spectrometry (DART-MS) and liquid-chromatography mass spectrometry (LC-MS). Both FTIR and DART-MS assess samples against libraries of over 1,300 substances, including pharmaceutical and illicit drugs, adulterants, cutting and bulking agents, precursor chemicals, and other substances (e.g., adhesives, food products, etc.). The LC-MS quantification panel included twelve substances: fentanyl and fluorofentanyl, fentanyl precursor chemicals (4-ANPP, phenethyl 4-ANPP), heroin, methamphetamine, cocaine, α2-agonists (xylazine and medetomidine), and three common fentanyl adulterants (tetracaine, lidocaine, and Bis(2,2,6,6-tetramethyl-4-piperidyl) sebacate (BTMPS).
3. Of 1,644 total available samples, this study included n=112 that were sold as methamphetamine, expected to contain only methamphetamine, per client self-report, and had quantified results available based on LC-MS.
4. Methamphetamine purity was initially reported as the freebase form which does not account for the additional weight of the hydrochloride salt form. In order to convert this to methamphetamine HCL values (the form that all samples in our dataset were sold as, and the form that medication forms of stimulants typically consist of) concentration values were multiplied by 1.24 to reflect the ratio of the molecular weights between the HCL and freebase forms of methamphetamine.
5. As a result of measurement limitations, concentration at or above 95% was imputed to be 95%. Additionally, samples with methamphetamine concentration below the limit of quantitation were imputed to be 0.1%.
6. The 112 available methamphetamine purity values were resampled to create 10,000 draws representing the distribution of purity using the sample() function in R. A seed was set to ensure the reproducibility of results between code iterations.

Drug Quantity Consumed

1. Information on drug quantity consumed for methamphetamine (and other drugs) were collected through an anonymous, optional survey conducted by trained drug checking staff.
2. Of n=68 participants who regularly consume methamphetamine and brought methamphetamine for testing, n= 46 reported the quantity of methamphetamine they consume in grams and had the option to report the quantity per day, week, or month. Weekly values were converted to days by dividing by 7. Monthly values were converted to daily by dividing by 30. N=22 participants reported quantities in dollars spent on methamphetamine per day or week. Dollar values were converted to grams using a standardized price of $20 per gram, which was known to the drug checking team as a typical 'going rate' for a gram of methamphetamine. This may slightly underestimate the consumption of individuals who spent larger quantities per day and therefore achieve a lower price per gram.
3. The 68 available methamphetamine quantity values (alongside associated route of administration information) were resampled to create 10,000 draws representing the distribution of purity using the sample() function in R.

Bioavailability and Equivalence

1. Literature values were used to estimate credible intervals for all other model parameters, including bioavailability and equivalence factors.
2. Bioavailability of orally consumed methamphetamine was estimated using experimental data from: *Cook, C. E., Jeffcoat, A. R., Sadler, B. M., Hill, J. M., Voyksner, R. D., Pugh, D. E., White, W. R., & Perez-Reyes, M. (1992). Pharmacokinetics of oral methamphetamine and effects of repeated daily dosing in humans. Drug metabolism and disposition: the biological fate of chemicals, 20(6), 856–862* and *Cook CE, Jeffcoat AR, Hill JM, et al. Pharmacokinetics of methamphetamine self-administered to human subjects by smoking S-(+)-methamphetamine hydrochloride. Drug Metab Dispos. 1993;21(4):717-723.* The authors estimated the oral bioavailability of methamphetamine to be 67.2% +/- 3.1%. This quantity was used directly as no other studies were found. Draws were estimated using a normal distribution with a mean of 67.2 and a standard deviation of 1.59.
3. Bioavailability of smoked methamphetamine was estimated from three studies:
    a. *Cook CE, Jeffcoat AR, Hill JM, et al. Pharmacokinetics of methamphetamine self-administered to human subjects by smoking S-(+)-methamphetamine hydrochloride. Drug Metab Dispos. 1993;21(4):717-723.* The quantity of interest is the percent of the "total pipe dose" that is ultimately absorbed. This study estimated that a bioavailability of 66% (90% absorption of 73.1% of drug smoked, 26.9% left in pipe).

b. *Harris DS, Boxenbaum H, Everhart ET, Sequeira G, Mendelson JE, Jones RT. The bioavailability of intranasal and smoked methamphetamine. Clin Pharmacol Ther. 2003;74(5):475-486. doi:10.1016/j.clpt.2003.08.002.* This study estimated a bioavailability of 37.4% (67% absorption of 55% of drug smoked, 45% left in pipe). Nevertheless, the authors used a method that was not designed to maximize the methamphetamine extracted from the pipe, as each participant took only 2 inhalations of each dose. The authors of this study estimate, in their discussion section, that true absorption of an effective pipe dose is likely to be 37% to 67% based on user smoking skill.

c. *Perez-Reyes, M., White, R., McDonald, S., Hill, J., Jeffcoat, R., & Cook, C. E. (1990). Pharmacologic effects of methamphetamine vapor inhalation (smoking) in man. NIDA research monograph, 105, 575–577.* This study estimated the bioavailability of "vaporized" (i.e., smoked) methamphetamine to be approximately 50%. This was largely a result of analyzing subjective and cardiovascular effects under experimental conditions between IV and smoked methamphetamine.

Given the above, the bioavailability of smoked methamphetamine was estimated using a uniform distribution with a minimum of 37% and a maximum of 67%.

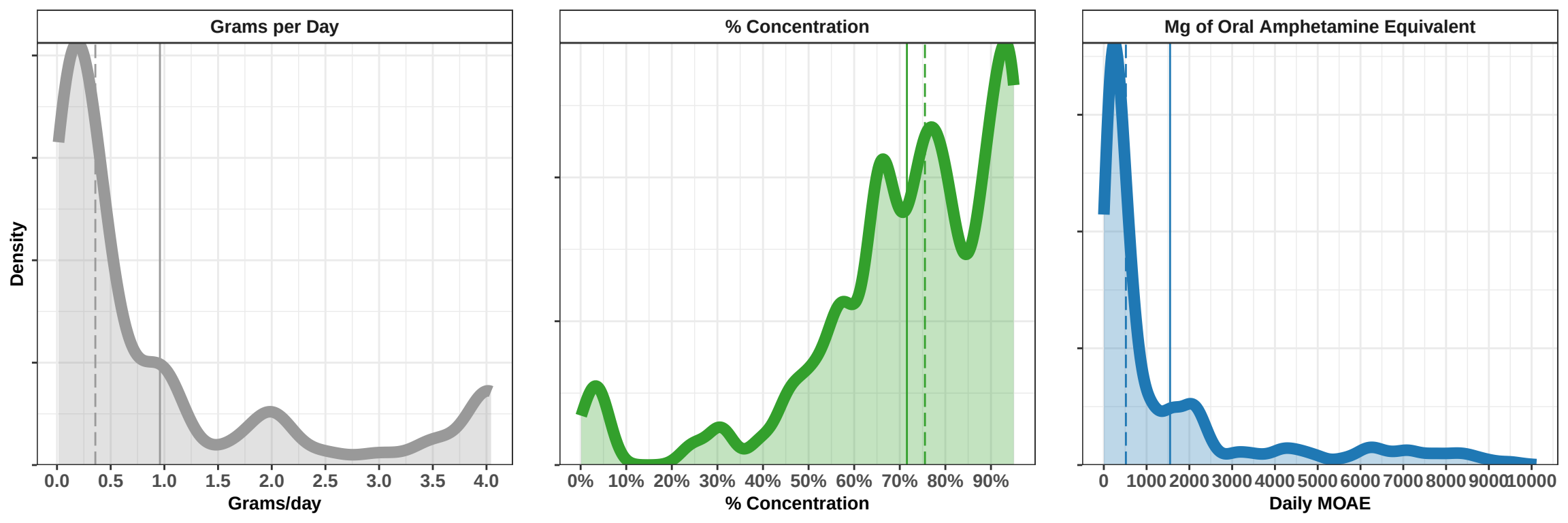
4. The bioavailability of insufflated ("snorted") methamphetamine was estimated using the following study: *Harris DS, Boxenbaum H, Everhart ET, Sequeira G, Mendelson JE, Jones RT. The bioavailability of intranasal and smoked methamphetamine. Clin Pharmacol Ther. 2003;74(5):475-486. doi:10.1016/j.clpt.2003.08.002.* This study estimated a bioavailability of 79% +/- 13.1%. Bioavailability was estimated using a normal distribution with a mean of 79.0 and a standard deviation of 6.72%.
5. No literature sources were found describing the bioavailability of "boofed" or rectally administered methamphetamine. Given that per rectum absorption is often similar or greater than oral absorption, the distribution was estimated using a normal distribution with a mean of 67.2% (the same as for PO bioavailability), yet with a significantly larger standard deviation of 20%, given the lack of data on this topic.
6. The bioavailability of injected methamphetamine was, by definition, set at 100%.
7. Among the n=68 individuals providing route of administration information alongside quantity of consumption information (resampled to create 10,000 draws) bioavailability was calculated for each draw. If an individual reported multiple routes of administration, then the average of the bioavailability coefficients was used for that draw. In effect, this assumes that individuals evenly

split their consumption between the different methods they reported. This could underestimate or overestimate their total absorption depending on their true route of administration habits and the relative frequencies of each method of consumption.

8. The methamphetamine to amphetamine potency ratio was assessed using equivalency tables (https://www.adhdmedcalc.com/), which tend to assign a 2:1 ratio, and based on clinical trials data (https://www.accessdata.fda.gov/cdrh_docs/reviews/K040133.pdf) . This value of 2.0 was used for calculations.
9. The bioavailability of oral mixed amphetamine salts was assessed using literature sources. Although no specific experimental data were identified, review sources generally reported a high-level of absorption, with values ranging from 75%-95%. Bioavailability was therefore estimated using a uniform distribution ranging from 75% to 95%.

Calculations

1. Calculations were performed according to the equation listed in the main text for the 10,000 draws of each parameter, derived as defined above. The distribution of quantity consumed, purity, and MOAE was graphed directly across the draws, and summary statistics were calculated.


Grams per Day
% Concentration
Mg of Oral Amphetamine Equivalent
Density
0.0 0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0
Grams/day
0% 10% 20% 30% 40% 50% 60% 70% 80% 90%
% Concentration
0 1000 2000 3000 4000 5000 6000 7000 8000 9000 10000
Daily MOAE