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Short communication

Estimating the daily milligrams of morphine equivalent of illicit fentanyl use in Los Angeles: Clinical and epidemiological implications

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ABSTRACT

Introduction: The market shift from heroin to illicitly-manufactured-fentanyl in North America led to surging opioid mortality. However, limited information exists about the doses of illicit fentanyl regularly consumed. We examined purity of fentanyl samples and estimate the typical daily oral milligrams of morphine equivalent (MME).

Methods: Leveraging community-based drug checking data from Los Angeles, we ascertained the purity of 509 samples of fentanyl collected between September 2023 and January 2026 using liquid chromatography mass spectrometry. We assessed typical consumption quantity and routes of administration among 47 respondents who reported regularly using fentanyl. We estimate bioavailability and MME conversion factors from literature. To estimate daily MME, incorporating all parameter uncertainty, we used a bootstrapping approach with 1,000,000 draws, with sensitivity analyses to assess the impact of factors including the correlation between purity and quantity.

Results: Among participants, the mean daily consumption of fentanyl was 1.07 g (95% prediction interval: 0.03g-4.00 g). Illicit fentanyl products had a mean fentanyl purity of 12.47% (0.23%-38.80%), and the mean estimated bioavailability based on routes of administration was 50.82% (30.64%-76.75%). The mean estimated IV fentanyl to PO morphine MME conversion factor was 1 to 183.15 (71.85–294.21). The mean estimated daily consumption in our sample was 8887.55 MME (156.56 MME-41,761.30 MME).

Conclusions: Under all plausible estimation scenarios, individuals consuming illicit fentanyl in Los Angeles on average use a quantity of MME several orders of magnitude higher than clinical guidelines or typical methadone doses. This likely contributes to high overdose mortality, high opioid tolerance, and more difficult methadone and buprenorphine induction.

1. Introduction

Since the early 2010s, the North American overdose crisis has been driven primarily by illicit fentanyl and its analogues (Friedman and Shover, 2023; Shover et al., 2020). As a synthetic opioid easily produced in large quantities, illicit fentanyl has become a drug of choice for many consumers because it is inexpensive and readily available (Morales et al., 2019). Fentanyl is far more potent than opioids derived from the opium poppy such as heroin and oxycodone, with a milligram of morphine equivalence (MME) conversion factor between intravenous (IV) fentanyl and oral (PO) morphine estimated to range between 1:66 and 1:300 (Fortnightly Review: Morphine in cancer pain: modes of administration 1996; Mercadante et al., 2002; Starlander et al., 2011). It is generally understood that fentanyl's high potency makes it easy for individuals to inadvertently consume more than intended, leading to greatly elevated overdose death rates(Althoff et al., 2020; Friedman and Shover, 2023). However, detailed information about the actual doses of illicit fentanyl consumed in real-world settings by individuals with opioid use disorder (OUD) is extremely limited. For the use of clinically prescribed pharmaceutical opioids, a daily recommended limit of 90 PO MME is often

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recommended, although patient specific factors must be considered (Dowell et al., 2016). For substance use disorders involving legal substances like alcohol and tobacco, exposure quantification is part of the standard approach to treatment, with metrics such as drinks per day and pack-years codified in clinical guidelines. In the illicit market, however, exposure quantification is more difficult, given lack of quality control and the shifting composition of illicit drug products (Krotulski et al., 2022). Patients are often unaware of the actual drugs and amounts in their supply, and reliable dosing guidance can be difficult to ascertain. Consequently, there are important potential clinical and epidemiological benefits of quantifying illicit fentanyl consumption among individuals with OUD. These include improved withdrawal management (Thakrar and Kleinman, 2022), improvements in dosing guidance with medications for opioid use disorder (MOUD) (Shearer et al., 2022), and better characterization of the risk environment for this population (Ciccarone, 2017).

Leveraging advancements in community-based drug checking approaches (Delaney et al., 2023; Friedman et al., 2025; Shover et al., 2025a, 2025b) and analytical technologies (Appley et al., 2023; Sisco et al., 2017), we quantified the purity of illicit fentanyl samples in Los Angeles and combined this with self-reported consumption quantities to estimate the daily MME consumed by participants in a drug checking program who reported recent fentanyl use.

2. Methods

We analyzed 509 drug samples collected between September 2023 and January 2026 at *Drug Checking Los Angeles*, a community-based drug checking program with multiple sites across Los Angeles County. These samples were drawn from a larger pool of n = 2522 collected during 2023–2026; the subset of 509 represents those for which a) quantitative fentanyl results were available and b) samples were expected by participants to contain fentanyl. Drug samples were provided anonymously and voluntarily by drug checking participants. Services occur in harm reduction settings, and participants provide small quantities of sample for testing. Most samples are expected to reflect the retail drug market, i.e. drugs sold in small quantities to end-users. However, for privacy purposes, we do not inquire if participants participate in drug sales, and may have access to 'wholesale' product. For each sample, a few milligrams of drug product were transferred into a vial containing 0.5 mL acetonitrile. Samples were analyzed at the National Institute of Standards and Technology (NIST) using liquid chromatography mass spectrometry (LC-MS) [see previously published methods (Appley et al., 2023; Shover et al., 2025b; Sisco et al., 2017). Similar to previous analyses, fentanyl purity was defined as the combined percentage by weight of each sample represented by either fentanyl or fluorofentanyl; these compounds are of comparable potency and impart comparable biologic effects (Canfield et al., 2025).

Drug checking participants were invited to answer a brief, confidential survey about their recent drug use. Among 47 unique respondents who reported using fentanyl in the past 30 days, we assessed consumption (grams per day), and routes of administration (see supplement for more details). For each route of administration, we drew bioavailability estimates from a literature review of experimental data [see supplement] (Cook et al., 1993; Darwish et al., 2007; Harris et al., 2003; MacLeod et al., 2012; Mather et al., 1998; Nardi-Hiebl et al., 2021; Streisand et al., 1991; Striebel et al., 1993; Vasisht et al. (n.d.)). IV fentanyl to PO morphine MME conversion factors were also drawn from literature review [see supplement] (Ing et al., 2024; Mercadante et al., 2002; Starlander et al., 2011).

We estimated daily MME consumed by drug checking participants in Los Angeles according to the following formula:

Equation 1. Calculation of estimated daily milligrams of oral morphine equivalent (MME) used among regular consumers of fentanyl, who visited drug checking services in Los Angeles

$$\textit{Estimated Consumption}\ (\textit{in MME}) = \textit{Mass consumed} * \textit{Purity} * \textit{Bioavailability} * \textit{MME Equivalence}$$

In this equation, *Mass Consumed* is the estimated raw quantity of illicit fentanyl product used per day in milligrams, *Purity* is the proportion of active (i.e. either fentanyl or fluorofentanyl) compound in product expected to be fentanyl, *Bioavailability* is the routes of administration-specific proportion of total drug used estimated to reach the systemic circulation, *MME Equivalence* is a metric used to convert doses of different opioids into an approximately equivalent dose of oral morphine to allow for consistent comparisons of potency and risk, which in this case are based on the estimated ratio of physiological potency between IV fentanyl and oral morphine (Fortnightly Review: Morphine in cancer pain: modes of administration 1996; Mercadante et al., 2002; Starlander et al., 2011).

Each of the elements in this equation is associated with a degree of uncertainty. To estimate MME consumed, incorporating uncertainty and individual variation in each parameter, we used a bootstrapping approach. This entailed creating 1,000,000 draws of each parameter—representing the full distribution of uncertainty or variation in each parameter—and calculating MME over these 1,000,000 iterations, yielding a distribution of estimated MME values. At the draw-level, correlation between quantity of fentanyl consumed, and route-of-administration, is preserved from the underlying data, as these quantities are sampled together. When respondents reported employing multiple routes of administration, the fraction of consumption from each route was drawn probabilistically from uniform distributions (which were standardized to sum to 1.0). This assumes that each route of administration was equally likely on average but incorporates uncertainty in the relative proportion of each into the model (see supplement). To generate summary statistics across the draws, we calculate point estimates using means, and 95% prediction intervals (using the 2.5th and 97.5th percentiles) for all estimated quantities. For each, the 95% prediction interval indicates the bounds within which 95% of the estimated parameter for the population fell.

To examine the importance of correlation between purity and quantity of fentanyl consumed, differing estimation scenarios were employed. In a more conservative scenario (sensitivity analysis #1), maximal inverse correlation was induced between quantity of fentanyl consumed and purity of fentanyl consumed, by sorting draws of each quantity in opposite directions (see supplement). This has the effect of assuming that individuals using more potent fentanyl products consume less raw weight than individuals using less potent fentanyl formulation. In a less conservative scenario (sensitivity analysis #2), no correlation was induced, and these two parameters were sampled independently and were virtually uncorrelated. This assumes that individuals using more pure fentanyl were no more, and no less, likely to use a greater quantity of fentanyl. Both scenarios are shown as sensitivity analysis in the supplement. In the primary model—displayed in the main text—these two models were combined, by taking 1,000,000 draws from each approach, and calculating summary statistics across the resulting distribution of 2,000,000 draws.

Additional sensitivity analyses were conducted. Sensitivity analysis #3 assumed that for all individuals who employed various routes of administration that included smoking, their estimated bioavailability reflected only values for smoking, as the other routes were negligible. This was conducted as other research has shown a predominance of smoking among individuals employing various routes (Ciccarone et al., 2024). An additional scenario was employed to emulate a behavioral response where consumers attempt to titrate their usage based on potency but do so imperfectly in the fourth sensitivity analysis. In this model, a "noisy" inverse correlation was induced between the daily quantity consumed and fentanyl purity by applying a uniform noise function to the inversely ranked purity distribution (see supplement).

Finally, a fifth, "maximally conservative" sensitivity analysis was performed by combining the assumptions of both sensitivity analysis #1 and #3. This model assumed a maximal inverse correlation between quantity and purity alongside a smoking-only bioavailability for those reporting smoking, representing the most restrictive estimation approach.

This project received approval by the UCLA IRB (IRB22-0760). All analyses were conducted in R version 4.4.1.

3. Results

Among the 47 participants reporting past 30-day fentanyl use and consumption quantity, the mean daily consumption of raw fentanyl product (not active ingredient) was 1.07 g (95% prediction interval: 0.03g−4.00 g) (Fig. 1). Raw products sold as fentanyl had a mean fentanyl purity (combined concentration of fentanyl and fluorofentanyl, as applicable) of 12.47% (0.23%−38.80%). Almost all participants (n = 46; 97.87%) reported smoking/vaporizing fentanyl. Many (n = 14; 29.79%) also reported injecting, and 7 (14.89%) reported nasal insufflation. One participant reported exclusively oral ingestion, and one reported oral ingestion, insufflation, and smoking. Assuming probabilistically equal consumption via each method when participants reported multiple routes of administration, and accounting for uncertainty in bioavailability associated with each method (see supplemental methods), the average estimated bioavailability was 50.82% (30.64%–76.75%). The average estimated MME conversion factor between IV fentanyl and PO morphine was 1 to 183.15 (71.85–294.20).

Incorporating each of these parameters, we estimate that participants consumed an average daily estimated MME of 8887.55 MME (156.56 MME−41,761.30 MME) [Fig. 2].

In the first sensitivity analysis, assuming maximal inverse correlation between quantity and purity, the average estimated MME was lower at 6007.91 MME (537.23 MME - 18,483.31 MME) [Supplemental Figure 2]. In the second sensitivity analysis, assuming no correlation between quantity and purity, the average estimated MME was higher (11,767.19 MME), with a significantly more skewed distribution, reflecting a 95% prediction interval of (59.66 MME - 56,137.06 MME).

In the third sensitivity analysis, assuming smoking was the only route of administration for all individuals reporting smoking and other methods, estimated average MME was moderately lower than the main analysis at 7739.18 MME (130.07 MME - 38,105.49 MME) reflecting lower average bioavailability [Supplemental Figure 3].

In a fourth sensitivity analysis incorporating a 'noisy inverse correlation' to simulate imperfect titration behavior (see supplement for methods description and Supplemental Figure 1 for visualization), the estimated average consumption was 7408.10 MME, with a 95% prediction interval of 316.41 MME to 27,814.71 MME [Supplemental Figure 2].

Finally, in a fifth 'maximally conservative' sensitivity analysis combining the assumptions of both Sensitivity Analysis 1 and 3 (see supplement for methods), the estimated average MME was the lowest of our models, yet remained high at 5125.14 MME (465.36 MME - 14,619.50 MME) [Supplemental Figure 2].

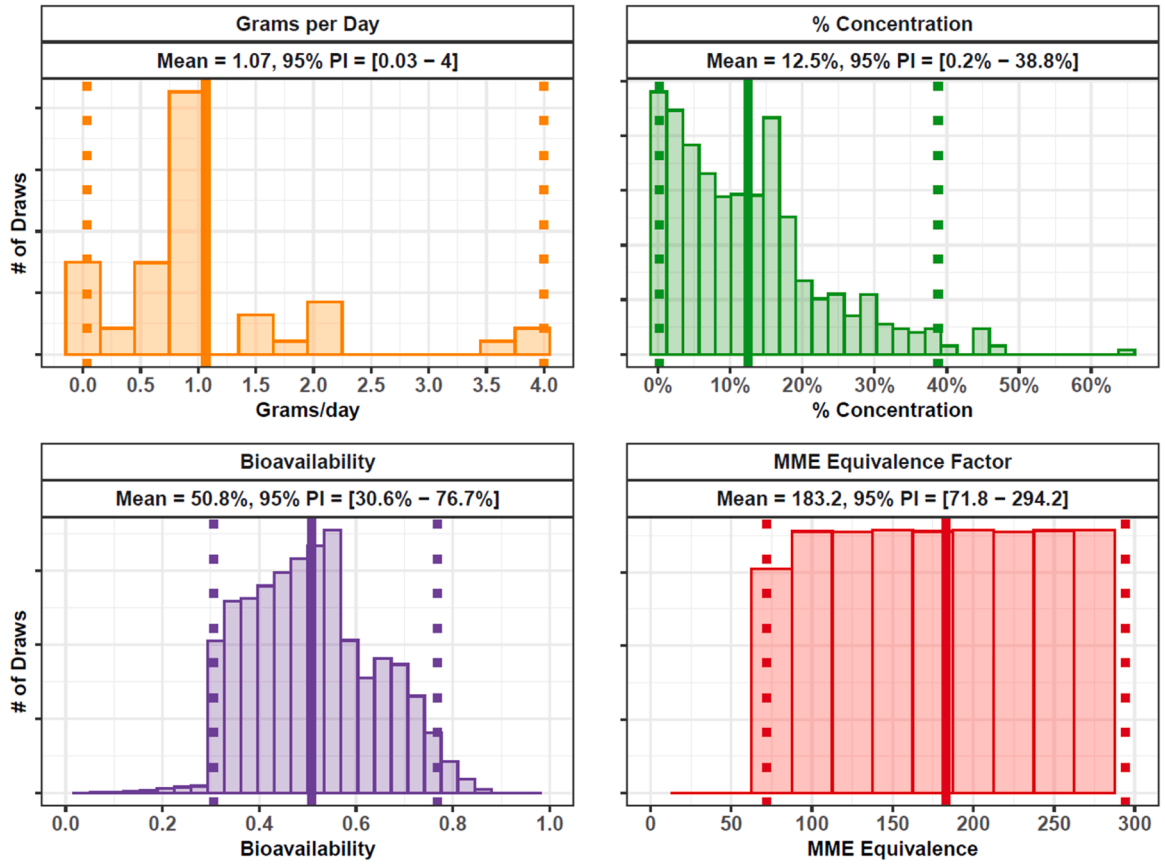


Fig. 1. Model Parameters: Fentanyl Consumption, Percent Concentration (Purity), Bioavailability and MME Equivalence. Model parameters are shown via histograms. Each panel represents all 1,000,000 draws from the underlying model. For each parameter, a solid line shows the distribution mean, and dotted lines show the 95% prediction interval (2.5th and 97.5th percentiles). Top Left: The distribution of self-reported grams of illicit fentanyl consumed per day among regular consumers participating in drug checking services in Los Angeles. Top Right: Percent concentration (purity) of expected fentanyl samples provided by clients at drug checking services in Los Angeles. Bottom Left: The estimated bioavailability of participants corresponding to their reported routes of administration (e.g. oral ingestion, smoking, snorting, injecting). Bottom Right: the distribution of MME equivalence factors estimated from literature.

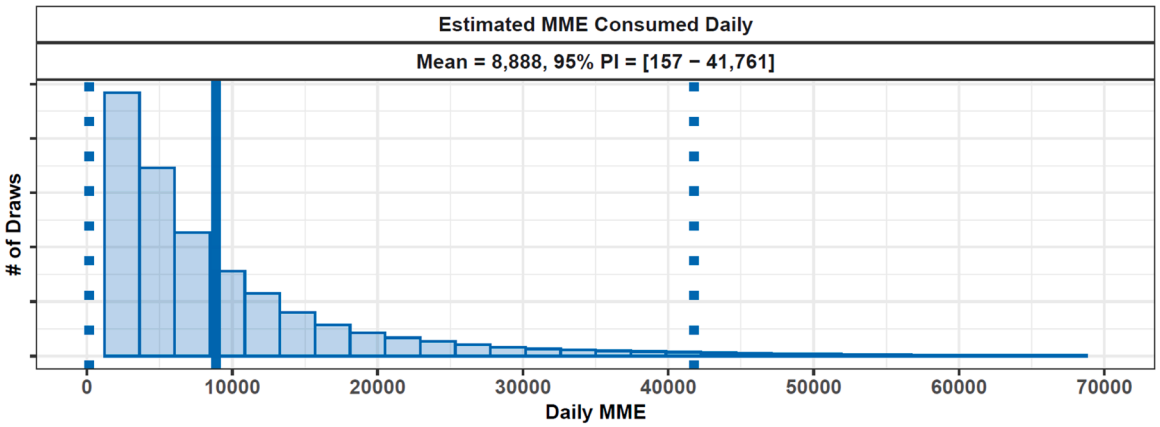


Fig. 2. Estimated Daily Fentanyl Consumption in MME. The distribution of the 2,000,000 draws of the model output (estimated daily fentanyl consumption in MME) is shown as a histogram. A vertical solid line shows the distribution mean while dotted lines show the 95% prediction interval (2.5th and 97.5th percentiles).

4. Discussion

Using drug samples from the real-world illicit drug supply in the Los Angeles area, we found that one gram of a raw product understood to be "fentanyl" in fact contained a range of < 1 mg to almost 650 mg of fentanyl. Survey data from people who report recent, regular fentanyl use, report using about 1 g of raw product use per day on average, consistent with previous estimates (Ciccarone et al., 2024). Combining these parameters, we estimate that a typical consumer of illicit fentanyl uses the equivalent of almost 9000 milligrams of oral morphine daily, an extraordinary amount when considered in light of treatment guidelines that discourage doses in excess of 90 milligrams daily for the treatment of chronic pain (Dowell et al., 2016).

It is generally recognized that as a result of tolerance, opioids have no set upper dose threshold, and that usage quantities can escalate rapidly among individuals with OUD who have ample access to opioids. It has also been previously described that the illicit market shift from heroin to illicit fentanyl drastically increased the potency of illicit opioid products, a key factor in skyrocketing rates of overdose and mortality (Ciccarone, 2017; Friedman and Shover, 2023). To our knowledge, this analysis represents the first effort to quantify these phenomena in estimated MME consumed per day among individuals consuming illicit opioids in the fentanyl era.

The advent of community-based drug checking techniques provides a powerful opportunity to open the 'black box' of illicit drug products, and quantify drug contents with accuracy and precision (Bailey et al., 2023; Delaney et al., 2023). We find that the typical product sold in Los Angeles as fentanyl, and expected to be illicit fentanyl, is about 12.5% pure. One gram of this product, sold for approximately $100 USD in Los Angeles, would contain about 125 mg of active fentanyl, roughly 100-fold higher than a typical daily amount used for IV analgesia in an opioid-naïve adult. However, purity of illicit fentanyl samples in Los Angeles is also highly variable, ranging from 0.1% to almost 65% among quantified samples. A gram of illicit fentanyl could therefore contain from less than 180 MME to almost 120,000 MME. Assumptions about bioavailability, MME conversion factors, and the correlation between parameters, do influence the overall estimated dosage. However, under all plausible scenarios, individuals consuming illicit fentanyl in Los Angeles on average appear to be consuming MME ranges many orders of magnitude above clinical dosing regimens.

This high—and highly variable—potency illustrates the impact of illicit fentanyl on the risk environment for people with OUD. The extraordinarily elevated overdose risk in the fentanyl era can be understood, in part, as a logical consequence of extreme variations in purity, wherein a gram of street product can vary wildly in its overall opioid content.

Our findings illustrate how insights gleaned from drug checking data can have potential implications for clinical practice—in particular, withdrawal management and stabilization of patients initiating MOUD. High average MME content of illicit fentanyl samples is reflected in the extremely elevated tolerance noted among people using illicit opioids. Many individuals report difficulty returning to heroin use after initiating illicit fentanyl use (Friedman et al., 2022a). Similarly, MOUD dosing requirements have also increased sharply in the fentanyl era (Bolshakova et al., 2024; Shearer et al., 2022; Tsui et al., 2025). Of note, these results do not imply that individuals stabilized on methadone require doses that fully equal the MME of the illicit fentanyl that they had been consuming; due to cross-tolerance when switching opioids, as well as differences between the steady-state induced by methadone and the pulsatile plasma concentrations induced by illicit fentanyl use, sufficient methadone doses may only represent a much smaller fraction of MME. Nonetheless, quantifying the MME of illicit fentanyl consumed by patients may be predictive of the ultimate dose of methadone needed.

Methadone and buprenorphine are the best evidence-based treatments for OUD, and their use is associated with marked reductions in mortality rates (Santo et al., 2021). Nevertheless, a large and growing body of evidence suggests that MOUD initiation has become more difficult in the fentanyl era, with uptake of MOUD and engagement in treatment among people with OUD remaining low in the United States (Jones et al., 2023). Our results suggest that a major reason for this may be the relatively lower MME provided by typical methadone doses compared to typical illicit fentanyl consumption patterns. For instance, typical starting doses of methadone for OUD, ranging from 20 to 40 mg daily, are approximately equivalent to 94–188 MME daily. Even a high-end dose of 180 mg of methadone daily would be equivalent to 846 MME, representing only a small fraction of the estimated almost 9000 MME consumed daily by a typical participant in our sample. Methadone doses in this range are unusual, in part because of concerns about dose-dependent QT prolongation.

Although it is generally not necessary or clinically appropriate to fully replace illicit opioid dosing during MOUD initiation, the provision of higher induction and maintenance doses of methadone, equivalent to a larger fraction of MME consumed via illicit fentanyl ingestion, may be warranted among patients using illicit fentanyl. Alternatively, augmenting methadone with other agents, such as slow-release oral morphine, may have similar benefits without the QT prolongation risk (Klimas et al., 2019). This may also help explain improved outcomes seen by some providers when initiating buprenorphine with higher doses, i.e. 'macrodosing' (Tsui et al., 2025), although the unique pharmacological properties of buprenorphine make a direct MME comparison more difficult. Through a nuanced understanding of their patients' illicit fentanyl consumption patterns, and local drug checking results, physicians prescribing MOUD initiation may be able to better tailor dosing to improve patient comfort and improve retention in treatment.

4.1. Limitations

The illicit fentanyl risk environment in Los Angeles is similar to many other locations on the West Coast—characterized by a later arrival of illicit fentanyl compared to most of the country (Shover et al., 2020), a delayed albeit large-magnitude increase in overdose deaths after the advent of illicit fentanyls (Friedman and Shover, 2023), a more recent arrival of xylazine as a co-adulterant (Friedman et al., 2022b, 2025), and a predominance of smoking over injection use (Ciccarone et al., 2024; Eger et al., 2024). Although the illicit drug market in LA is broadly reflective of trends in the West Coast, the data leveraged here may have certain biases. Information collected from community-based drug checking programs is subject to convenience sampling and may not be representative of the illicit drug supply in Los Angeles as a whole. The purity of fentanyl likely varies by geography. Consumption patterns may be higher among drug checking participants compared to other people who use opioids, as this likely represents a population with high-volume illicit fentanyl intake. Additionally, we only included fentanyl potency from two fentanyl analogs (fentanyl and fluorofentanyl), which composed the vast majority of our sample, and which were assumed to be equipotent. Literature suggests that this is a generally reasonable assumption (Canfield et al., 2025), however it may have had a small effect on the study results. For simplicity we did not include a small number of other fentanyl analogs contained in our samples (e.g. 14 quantified carfentanil samples, mostly at very low concentrations) (Shover et al., 2025b). This may have slightly underestimated the true overall potency of illicit fentanyl samples in our study population.

We used literature sources to describe a range of plausible values for bioavailability and MME conversion factors. These factors considerably affect study results and yet limited high-quality data are available to guide their selection. Where possible, we used conservative estimates for these parameters.

Sensitivity analyses highlight that, like most simulation or bootstrapping exercises, our results do change when parameter assumptions are modified. Nevertheless, under all plausible parameter scenarios, the estimated MME of fentanyl consumed by this population remains extremely high. However, refining parameter assumptions will be an important area of future work.

When comparing these estimates to the clinical guideline of 90 MME daily, it is notable that the lower bounds of the 95% prediction intervals vary significantly depending on model assumptions. In the scenario assuming no correlation between quantity and purity (Sensitivity Analysis 2), the 95% prediction interval encompasses the 90 MME clinical threshold. In contrast, models incorporating an inverse correlation between quantity and purity produce lower bounds that consistently remain above this guideline. This nuance highlights that while the average estimated consumption is staggering, the extreme variability of the illicit supply means that a subset of consumers may be exposed to daily MME totals much closer to clinical maximums, and clinicians should not assume that all individuals that use fentanyl have tolerance levels that are extremely elevated.

One very impactful decision relates to the degree of correlation between fentanyl quantity and purity consumed. In the supplement we present sensitivity analyses, assuming various scenarios. The most extreme include: 1) strong inverse correlation between these parameters (i.e. people using stronger product use less), and 2) no correlation. Given the lack of quality data to differentiate between how correct these scenarios are, we prefer to include both in the final model, combining the distributions to generate final estimates. This approach recognizes that uncertainty from both of these scenarios is worth including in the model, and the true degree of correlation is likely somewhere between these two. Although we suspect the no correlation scenario is likely more accurate, we prefer to present the more conservative hybrid approach in the main text. The lack of a large sample of linked purity and quantity values represents an important limitation of this study. Larger samples may be able to directly measure this correlation in future studies. Additionally, more data about how these quantities vary by participant characteristics, e.g. race/ethnicity, gender, etc. represent important areas of future study. Bioavailability parameters are also consequential for the results. However, given the overall extreme magnitude of estimated MME in our results, these assumptions are unlikely to change the main study conclusions. Further research is needed to better characterize the bioavailability and other pharmacodynamic and pharmacokinetic properties of illicit fentanyl vaporized or smoked via different methods (e.g., pipe, foil, dabbing equipment) via updated laboratory methods. More data is also needed to characterize fentanyl usage patterns throughout the day, e.g. frequency of dosing, and how this affects total MME consumed, tolerance, and MOUD initiation. Additionally, the role of underlying disease processes (e.g., COPD, asthma, pulmonary hypertension) on illicit fentanyl dosing and absorption deserves consideration.

5. Conclusions

We provide the first effort, to our knowledge, to quantify the MME consumed by people who regularly use illicit fentanyl. We find that the average consumption of almost 9000 MME is vastly higher than clinical guidelines (which often recommend limiting opioid use to 90 MME) or typical methadone doses. This may explain highly elevated overdose mortality rates in the fentanyl era, as well as increased difficulty of MOUD initiation. Further research is needed to assess the degree to which these findings generalize beyond this high acuity population in Los Angeles.

CRediT authorship contribution statement

Morgan Godvin: Writing – review & editing, Writing – original draft, Project administration, Methodology, Investigation, Conceptualization. **Joseph R. Friedman:** Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Caitlin A. Molina:** Writing – review & editing, Resources, Project administration, Formal analysis, Data curation. **Adam J. Koncsol:** Writing – review & editing, Validation, Software, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Ruby Romero:** Writing – review & editing, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation. **David N. Juurlink:** Writing – review & editing, Validation, Conceptualization. **Chelsea L Shover:** Writing – review & editing, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Contributors/author contributions

MG: Conceived of the study, data collection, results interpretation, contributed to writing initial draft.

JRF: Study design, statistical analysis, results interpretation, contributed to writing initial draft.

CAM: Data collection, literature review, critically revised.

AJK: Data collection, results interpretation, critically revised.

RR: Data collection, results interpretation, critically revised.

DNJ: Data collection, results interpretation, critically revised.

CLS: Study design, data collection, results interpretation, critically revised, supervision.

Ethical approvals

This project received approval by the UCLA IRB (IRB-22-0760).

Disclaimers

Not applicable.

Declaration of Generative AI and AI-assisted technologies in the writing process

We did not use generative AI in writing this manuscript.

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Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Chelsea L. Shover reports financial support (institutional grant funding) from the Centers for Disease Control and Prevention and the National Institutes of Health. Joseph R. Friedman and Adam J. Koncsol also report financial support from the National Institutes of Health. David Juurlink reports having received payment for lectures and medicolegal opinions regarding the safety and effectiveness of analgesics, including opioids. David Juurlink is a member of the American College of Medical Toxicology and an unpaid membership of PROP; both groups have publicly available positions on opioids and their prescribing.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.drugalcdep.2026.113224.

Data availability

Drug checking data are available in aggregate form at www.drugcheckinglosangeles.com. Additional data requests should be submitted in writing to the corresponding author.

References

Althoff, K.N., Leifheit, K.M., Park, J.N., Chandran, A., Sherman, S.G., 2020. Opioid-related overdose mortality in the era of fentanyl: monitoring a shifting epidemic by person, place, and time. Drug. Alcohol. Depend. 216, 108321. https://doi.org/10.1016/j.drugalcdep.2020.108321.

Appley, M.G., Robinson, E.L., Thomson, A., Russell, E., Sisco, E., 2023. An analytical platform for near real-time drug landscape monitoring using paraphernalia residues. Forensic Chem. 34, 100489. https://doi.org/10.1016/j.forc.2023.100489.

Bailey, K., Abramovitz, D., Artamonova, I., Davidson, P., Stamos-Buesig, T., Vera, C.F., Patterson, T.L., Arredondo, J., Kattan, J., Bergmann, L., Thihalolipavan, S., Strathdee, S.A., Borquez, A., 2023. Drug checking in the fentanyl era: utilization and interest among people who inject drugs in San Diego, California. Int. J. Drug. Policy 118, 104086. https://doi.org/10.1016/j.drugpo.2023.104086.

Bolshakova, M., Simpson, K.A., Ganesh, S.S., Goldshear, J.L., Page, C.J., Bluthenthal, R. N., 2024. The fentanyl made me feel like I needed more methadone: changes in the role and use of medication for opioid use disorder (MOUD) due to fentanyl. Harm. Reduct. J. 21, 156. https://doi.org/10.1186/s12954-024-01075-x.

Canfield, J.R., Fry, K.K., Sprague, J.E., 2025. Enhanced pharmacokinetic and pharmacodynamic effects of combining p-fluorofentanyl and fentanyl. Drug. Alcohol. Depend. 272, 112710. https://doi.org/10.1016/j.drugalcdep.2025.112710.

Ciccarone, D., 2017. Fentanyl in the US heroin supply: a rapidly changing risk environment. Int. J. Drug. Policy 46, 107–111. https://doi.org/10.1016/j.drugpo.2017.06.010.

Ciccarone, D., Holm, N., Ondocsin, J., Schlosser, A., Fessel, J., Cowan, A., Mars, S.G., 2024. Innovation and adaptation: the rise of a fentanyl smoking culture in San Francisco. PLOS ONE 19, e0303403. https://doi.org/10.1371/journal.pone.0303403.

Cook, C.E., Jeffcoat, A.R., Hill, J.M., Pugh, D.E., Patetta, P.K., Sadler, B.M., White, W.R., Perez-Reyes, M., 1993. Pharmacokinetics of methamphetamine self-administered to human subjects by smoking S-(+)-methamphetamine hydrochloride. Drug. Metab. Dispos. Biol. Fate Chem. 21, 717–723.

Darwish, M., Kirby, M., Robertson, P., Tracewell, W., Jiang, J.G., 2007. Absolute and relative bioavailability of fentanyl buccal tablet and oral transmucosal fentanyl citrate. J. Clin. Pharmacol. 47, 343–350. https://doi.org/10.1177/0091270006297749.

Delaney, S.R., Konforte, D., Stefan, C., Palaty, J., Sun, D., McDonald, K., Thompson, H., Werb, D., Beriault, D.R., 2023. Drug checking services as a surveillance tool for clinical laboratories: examining trends in the unregulated fentanyl supply. Clin. Biochem. 111, 11–16. https://doi.org/10.1016/j.clinbiochem.2022.11.003.

Dowell, D., Haegerich, T.M., Chou, R., 2016. CDC guideline for prescribing opioids for chronic pain—United States, 2016. JAMA 315, 1624–1645. https://doi.org/10.1001/jama.2016.1464.

Eger, W.H., Abramovitz, D., Bazzi, A.R., Bórquez, A., Vera, C.F., Harvey-Vera, A., Friedman, J.R., Strathdee, S.A., 2024. Changes in injecting versus smoking heroin, fentanyl, and methamphetamine among people who inject drugs in San Diego, California, 2020–2023. Drug. Alcohol. Depend. 259, 111318. https://doi.org/10.1016/j.drugalcdep.2024.111318.

Fortnightly Review: Morphine in cancer pain: modes of administration, 1996. BMJ 312, 823. https://doi.org/10.1136/bmj.312.7034.823

Friedman, J., Bourgois, P., Godvin, M., Chavez, A., Pacheco, L., Segovia, L.A., Beletsky, L., Arredondo, J., 2022a. The introduction of fentanyl on the US–Mexico border: an ethnographic account triangulated with drug checking data from Tijuana. Int. J. Drug. Policy 104, 103678. https://doi.org/10.1016/j.drugpo.2022.103678.

Friedman, J., Molina, C.A., Koncsol, A.J., Romero, R., Godvin, M.E., Jalayer, E., davila, spider, Arellano, O., Cowan, A., Hurley, B., Shover, C.L., 2025. Xylazine Prevalence and Concentration in the Los Angeles Fentanyl Market, 2023 – 2025. Drug. Alcohol. Depend. Rep., 100364 https://doi.org/10.1016/j.dadr.2025.100364.

Friedman, J., Montero, F., Bourgois, P., Wahbi, R., Dye, D., Goodman-Meza, D., Shover, C., 2022b. Xylazine spreads across the US: a growing component of the increasingly synthetic and polysubstance overdose crisis. Drug. Alcohol. Depend. 233, 109380. https://doi.org/10.1016/j.drugalcdep.2022.109380.

Friedman, J., Shover, C.L., 2023. Charting the fourth wave: geographic, temporal, race/ethnicity and demographic trends in polysubstance fentanyl overdose deaths in the United States, 2010-2021. Addict. Abingdon Engl. 118, 2477–2485. https://doi.org/10.1111/add.16318.

Harris, D.S., Boxenbaum, H., Everhart, E.T., Sequeira, G., Mendelson, J.E., Jones, R.T., 2003. The bioavailability of intranasal and smoked methamphetamine. Clin. Pharmacol. Ther. 74, 475–486. https://doi.org/10.1016/j.clpt.2003.08.002.

Ing, M.C., Keane, O.A., Lakshmanan, A., Kim, E., Lee, H.C., Kelley-Quon, L.I., 2024. Opioid equipotency conversions for hospitalized infants: a systematic review. J. Perinatol. 44, 1709–1718. https://doi.org/10.1038/s41372-024-02121-z.

Jones, C.M., Han, B., Baldwin, G.T., Einstein, E.B., Compton, W.M., 2023. Use of medication for opioid use disorder among adults with past-year opioid use disorder in the US, 2021. JAMA Netw. Open. 6, e2327488. https://doi.org/10.1001/jamanetworkopen.2023.27488.

Klimas, J., Gorfinkel, L., Giacomuzzi, S.M., Ruckes, C., Socías, M.E., Fairbairn, N., Wood, E., 2019. Slow release oral morphine versus methadone for the treatment of opioid use disorder. BMJ Open. 9, e025799. https://doi.org/10.1136/bmjopen-2018-025799.

Krotulski, A.J., Shinefeld, J., DeBord, J., Logan, B.K., 2022. Fentanyl purity, potency, & synthesis: Real-time testing of opioid drug products in the United States. (Report). Center for Forensic Science Research and Education, USA.

MacLeod, D.B., Habib, A.S., Ikeda, K., Spyker, D.A., Cassella, J.V., Ho, K.Y., Gan, T.J., 2012. Inhaled fentanyl aerosol in healthy volunteers: pharmacokinetics and pharmacodynamics. Anesth. Analg. 115, 1071–1077. https://doi.org/10.1213/ANE.0b013e3182691898.

Mather, L.E., Woodhouse, A., Ward, M.E., Farr, S.J., Rubsamen, R.A., Eltherington, L.G., 1998. Pulmonary administration of aerosolised fentanyl: pharmacokinetic analysis of systemic delivery. Br. J. Clin. Pharmacol. 46, 37–43. https://doi.org/10.1046/j.1365-2125.1998.00035.x.

Mercadante, S., Villari, P., Ferrera, P., Casuccio, A., Fulfaro, F., 2002. Rapid titration with intravenous morphine for severe cancer pain and immediate oral conversion. Cancer 95, 203–208. https://doi.org/10.1002/cncr.10636.

Morales, K.B., Park, J.N., Glick, J.L., Rouhani, S., Green, T.C., Sherman, S.G., 2019. Preference for drugs containing fentanyl from a cross-sectional survey of people who use illicit opioids in three United States cities. Drug. Alcohol. Depend. 204, 107547. https://doi.org/10.1016/j.drugalcdep.2019.107547.

Nardi-Hiebl, S., Ndieyira, J.W., Al Enzi, Y., Al Akkad, W., Koch, T., Geldner, G., Reyher, C., Eberhart, L.H.J., 2021. Pharmacokinetic characterisation and comparison of bioavailability of intranasal fentanyl, transmucosal, and intravenous administration through a three-way crossover study in 24 healthy volunteers. Pain. Res. Manag. 2021, 1–11. https://doi.org/10.1155/2021/2887773.

Santo, T., Jr, Clark, B., Hickman, M., Grebely, J., Campbell, G., Sordo, L., Chen, A., Tran, L.T., Bharat, C., Padmanathan, P., Cousins, G., Dupouy, J., Kelty, E., Muga, R., Nosyk, B., Min, J., Pavarin, R., Farrell, M., Degenhardt, L., 2021. Association of opioid agonist treatment with all-cause mortality and specific causes of death among people with opioid dependence: a systematic review and meta-analysis. JAMA Psychiatry 78, 979–993. https://doi.org/10.1001/jamapsychiatry.2021.0976.

Shearer, D., Young, S., Fairbairn, N., Brar, R., 2022. Challenges with buprenorphine inductions in the context of the fentanyl overdose crisis: a case series. Drug. Alcohol. Rev. 41, 444–448. https://doi.org/10.1111/dar.13394.

Shover, C.L., Falasinnu, T.O., Dwyer, C.L., Santos, N.B., Cunningham, N.J., Freedman, R. B., Vest, N.A., Humphreys, K., 2020. Steep increases in fentanyl-related mortality west of the Mississippi River: recent evidence from county and state surveillance. Drug. Alcohol. Depend. 216, 108314. https://doi.org/10.1016/j.drugalcdep.2020.108314.

Shover, C.L., Godvin, M.E., Appley, M., Pyfrom, E.M., Castrillo, F.M., Hochstatter, K., Nadel, T., Garg, N., Koncsol, A., Friedman, J.R., Molina, C.A., Romero, R., Harshberger, B., Gonzalez, J.A.M., Spoliansky, J., Laurel, S., Jalayer, E., Ruelas, J., Gonzales, J., Snakeoil, S., Guerra, S., Arellano, O., Winstead, C., Rybak, M., Champney, J., Waninger, B., Torruella, R., Sisco, E., 2025a. UV stabilizer BTMPS in the illicit fentanyl supply in 9 US Locations. JAMA, e2427550. https://doi.org/10.1001/jama.2024.27550.

Shover, C.L., Koncsol, A.J., Godvin, M.E., Goodman-Meza, D., Pardo, B., Poimboeuf, M., Molina, C.A., Romero, R., Feng, J., Friedman, J.R., 2025b. High variation in purity of consumer-level illicit fentanyl samples in Los Angeles, September 2023–April 2025. Int. J. Drug. Policy 145, 104977. https://doi.org/10.1016/j.drugpo.2025.104977.

Sisco, E., Verkouteren, J., Staymates, J., Lawrence, J., 2017. Rapid detection of fentanyl, fentanyl analogues, and opioids for on-site or laboratory based drug seizure screening using thermal desorption DART-MS and ion mobility spectrometry. Forensic Chem. 4, 108–115. https://doi.org/10.1016/j.forc.2017.04.001.

Starlander, J., Melin-Johansson, C., Jonsson, H., Axelsson, B., 2011. Oral-parenteral conversion factor for morphine in palliative cancer care: a prospective randomized crossover pilot study. Pain. Res. Treat. 2011, 1–5. https://doi.org/10.1155/2011/504034.

Streisand, J.B., Varvel, J.R., Stanski, D.R., Maire, L.L., Ashburn, M.A., Hague, B.I., Tarver, S.D., Stanley, T.H., 1991. Absorption and bioavailability of oral transmucosal fentanyl citrate. Anesthesiology 75.

Striebel, H.W., Krämer, J., Luhmann, I., Rohierse-Hohler, I., Rieger, A., 1993. Pharmakokinetische Studie zur intranasalen Gabe von Fentanyl. Schmerz 7, 122–125. https://doi.org/10.1007/BF02527870.

Thakrar, A.P., Kleinman, R.A., 2022. Opioid withdrawal management in the fentanyl era. Addiction 117, 2560–2561. https://doi.org/10.1111/add.15893.

Tsui, J.I., Bhatraju, E.P., Hallgren, K.A., Rhew, I.C., Samet, J.H., 2025. High-dose buprenorphine treatment in the setting of fentanyl. JAMA Netw. Open. 8, e2528119. https://doi.org/10.1001/jamanetworkopen.2025.28119.

Vasisht, N., Gever, L.N., Tagarro, I., Finn, A.L., n.d. Single-Dose Pharmacokinetics of Fentanyl Buccal Soluble Filmpme_8751017.1023.