



Published in final edited form as:

*Addiction*. 2009 November ; 104(11): 1874–1880. doi:10.1111/j.1360-0443.2009.02678.x.

## The spatial epidemiology of cocaine, methamphetamine and MDMA use: A demonstration using a population measure of community drug load derived from municipal wastewater

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### Abstract

**Aims**—To determine the utility of community wide drug testing with wastewater samples as a population measure of community drug use and to test the hypothesis that the association with urbanicity would vary for three different stimulant drugs of abuse.

**Design and participants**—Single day samples were obtained from a convenience sample of 96 municipalities representing 65% of the population of the State of Oregon.

**Measurements**—Chemical analysis of 24 hour composite influent samples for benzoylecgonine (BZE, a cocaine metabolite), methamphetamine, and 3,4-methylenedioxymethamphetamine (MDMA). The distribution of community index drug loads accounting for total wastewater flow (i.e. dilution) and population are reported.

**Findings**—The distribution of wastewater derived drug index loads were found to correspond with expected epidemiological drug patterns. Index loads of BZE were significantly higher in urban areas and below detection in many rural areas. Conversely, methamphetamine was present in all municipalities with no significant differences in index loads by urbanicity. MDMA was at quantifiable levels in less than half of the communities, with a significant trend towards higher index loads in more urban areas.

**Conclusion**—This demonstration provides the first evidence of the utility of wastewater derived community drug loads for spatial analyses. Such data have the potential to dramatically improve measurement of the true level and distribution of a range of drugs. Drug index load data provide information for all people in a community and are potentially applicable to a much larger proportion of the total population than existing measures.

### Keywords

Drug epidemiology; spatial analysis; wastewater analysis; methamphetamine; cocaine; benzoylecgonine; MDMA

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The authors report no conflicts of interest.

## Introduction

Drug abuse, including use of cocaine and MDMA, had been considered primarily an urban problem, until the emergence of methamphetamine in rural areas (1, 2) in the United States. Ongoing epidemiological reporting efforts such as the National Institute on Drug Abuse's Community Epidemiology Work Group have long focused on major metropolitan areas as have most attempts at national surveillance systems such as the Office of Applied Studies' Drug Abuse Warning Network (DAWN) which utilizes mortality and emergency department data. Current population measures of drug use are known to have many limitations including limited population coverage, self-report bias, and substantial time lags that negatively impact the reliability, validity and utility of such data (3,4). Most major surveillance efforts are focused on only a few major metropolitan areas, including DAWN and the recently resurrected Arrestee Drug Abuse Monitoring program in the US, which despite their limitations are more than most countries currently have in place. Additionally, population coverage problems for many drug use indicators are due to the exclusion of certain segments of the population, such as those incarcerated or without access to phones who are missed by many surveys. These population omissions lead not just to under-estimation of rates of drug use, but potentially to biased and invalid estimates because those least likely to be included may be most likely to be drug users.

Results from European (5, 6, 7) and US (8) wastewater treatment plant (WWTP) sampling studies document quantifiable concentrations of illicit and pharmaceutical drugs in raw influent wastewaters. The presence of these drugs and related metabolites in wastewater is assumed to be predominately due to excretion and therefore an indicator of drug consumption. MDMA was detected in raw influents at several locations throughout Europe and the US, though it appears to be a substance of interest in many fewer studies than other drugs such as cocaine (8, 9, 10). Findings indicate that cocaine use peaks on weekends (11, 12) as would be expected given its generally intermittent use (13). Although limited, the existing information on temporal trends provides a basic indication of the validity of the wastewater sampling approach. A Belgian study of cocaine index loads included a map suggesting greater urban use, though no statistical tests of the association between place and drug level were conducted (12). Cocaine has historically been used throughout much of Europe and the US, whereas methamphetamine use levels (14) are currently higher in the US than in Europe. Similarly, methamphetamine index loads (mg person/day) estimated from measurements of raw influent wastewater also indicate higher usage of methamphetamine in the US than in Europe (8). Methamphetamine has emerged as a substantial drug abuse problem in the US in recent years with marked and shifting geographic variability. As recently as the early 2000's, methamphetamine was manufactured throughout much of the Western and Mid-western US primarily in rural areas. As laws to limit access to precursor chemicals (e.g. pseudoephedrine) were implemented, local methamphetamine supplies dwindled while manufacturing increased in Mexico with overall supplies in the Northwestern US, for instance, staying relatively constant as trafficking patterns began to follow along the more traditional routes of cocaine and heroin from Mexico. At the time this article was written, January 2009, drug manufacturing and organized crime in Mexico are in a state of flux, with the impacts on methamphetamine use and distribution unknown, but potentially leading to increases in manufacturing within the US once again (15). The fast moving and geographically influenced trends are difficult to monitor in real time with existing drug use indicators. Thus, the need to explore the potential of spatial data on the occurrence and index loads of drugs of abuse in community wastewater for drug epidemiology.

To explore the potential utility of wastewater data as a community drug use measure a study of community drug index loads was conducted. The aims were to describe the spatial

distribution of stimulant drug index loads and to test their association with urbanicity. MDMA and BZE were expected to be more commonly detected and at higher index loads in urban areas whereas methamphetamine detection was expected in rural areas as well with uniformity in index loads across the State of Oregon.

## Methods

A single day study of a convenience sample of WWTP throughout Oregon was conducted in 2008. There are 145 municipal wastewater facilities in the State of Oregon which have National Pollutant Discharge Elimination System permits. Due to resource constraints 128 of these facilities were selected for recruitment, exclusion was based on WWTP similarities with other facilities in terms of geography and populations served. Two additional facilities were included that do not need NPDES permits, since they do not discharge, because they are medium sized cities in an area of the state where geographic coverage was desired. The majority of WWTP approached agreed to participate, with 96 out of 130 municipalities agreeing to provide a wastewater sample. Pre-paid mailers shipped to each WWTP included: 1) a cover letter with the sampling protocol and statements that participation was voluntary and that results could not be kept confidential, 2) a questionnaire requesting total influent flow during the period of sampling and the population served by the facility, and 3) sample collection bottles containing a preservative. Composite samples collected over a single 24 hour period corresponding to raw influent entering the respective WWTPs on Tuesday March 4<sup>th</sup> 2008 were collected and shipped by WWTP operators and received in the laboratory within three days of collection and frozen at  $-20^{\circ}\text{C}$  until analysis. Measured drug indicators included benzoylecgonine (BZE) which is the major metabolite of cocaine (16, 5), methamphetamine, and 3,4-methylenedioxyamphetamine (MDMA), substantial proportions of both methamphetamine and MDMA are excreted unchanged (17 18). The analytical method, quality control procedures, instrumental detection and lower limits of quantification for BZE, methamphetamine, and MDMA were reported previously (8). Index loads (mg/person/day) were computed by multiplying each drug concentration (ng/L) by the total flow of wastewater (L) and dividing by the population served by each WWTP. Index loads were grouped into tertiles. If individual drugs were detected but their concentrations in wastewater were below the reporting limits they were termed “below the level of quantification”. Alternatively, if the responses for individual drugs were below the analytical detection limits they were categorized as a “no detect”.

Rural urban commuting area (RUCA) codes incorporate census definitions of urban and rural as well as census data on work commuting patterns. RUCA codes indicate both the urban status of a location as well as its relationship to other places (19). RUCA codes for 5-digit zip code of each of the WWTP were aggregated into three categories: urban, large rural city/town, or small and isolated small rural town (20). Stata 9.0 (21) was used for descriptive statistics and to determine the Pearson’s chi-square statistic. The “opartchi” command (22) for contingency table analysis of ordered categorical variables in Stata was used to test for differences and trends in drug index loads by RUCA code. The test for trends determined whether differences in row distributions of the contingency table are due to increasing values across the row i.e. RUCA code. Mapping was completed using ArcMap 9.2 (23).

## Results

The total population served by the 96 participating WWTP was 2,478,168, which is approximately 65% of the State of Oregon’s population in 2008 per the US Census. The smallest municipality served had a population of 170 people, the largest 562,690, with a median of 5,595 and an average of 25,814 (standard deviation 69,922). The total number of urban locations was 36, large rural city/towns 26 and small rural towns 34. Figure 1 presents

the distribution of index loads by RUCA for each drug, Table 1 presents the test statistics for these distributions and Figure 2 presents maps of the index drug loads across the State of Oregon.

Comparing the proportions and counts in Figure 1 the variability in distribution of drug loads by RUCA is evident. For instance, methamphetamine index loads appear approximately equal within each RUCA category, while BZE and MDMA are not equivalent across RUCA categories. Statistical tests for the distribution of the count data in the tables below each of the bar charts in Figure 1 indicate that BZE index loads were not equivalent across RUCA types ( $p < 0.001$ , chi-square 26.14,  $df = 8$ ) and that larger loads were more likely to occur in more urban areas ( $p < 0.001$ , trend in location effect chi-square 10.93,  $df = 2$ ) (Table 1). Methamphetamine was present at quantifiable concentrations in raw influent for every WWTP location. The distribution of index loads for methamphetamine were equivalent across RUCA codes ( $p = 0.447$ , Chi-Square 3.51,  $df = 4$ ) and there was no trend in drug index load by RUCA code ( $p = 0.662$ , trend in location effect chi-square 0.191,  $df = 2$ ). MDMA index loads were statistically equivalent across RUCA codes ( $p = 0.353$ , Chi-Square 8.88,  $df = 8$ ); however, there was a significant trend indicating higher loads in more urban areas ( $p = 0.046$ , trend in location effect chi-square 6.16,  $df = 2$ ).

Figure 2 shows the spatial distribution of each substance across the State of Oregon. Visual inspection of the maps reveals clear contrast between the spatial distribution of the three substances. For instance, along the west coast of Oregon, MDMA was quantified in just four municipalities, while methamphetamine was detected in every municipality and BZE occurred in all but three. These data are index drug loads so they are adjusted for population size and total wastewater flow.

## Discussion

BZE was more common and with higher index loads in urban area compared to rural areas across each of 96 WWTPs participating in Oregon. In contrast, methamphetamine was detected in all locations with no significant difference in index loads by urbanicity. MDMA was quantified in less than half the WWTP and was significantly more likely to be detected in more urban areas compared to less urban and rural areas. The observed geographic distributions are consistent with expected urban-rural patterns based on conventional drug use indicators including drug treatment admissions, morbidity and mortality data (24, 1, 2). Wastewater-derived data indicate variability in index loads and geographic distributions within and between drugs. Findings suggest a valid, rich data source that is complementary to other drug surveillance data sources (25, 26). The computed index loads represent a quantifiable measure of community drug use/excretion that is not a threat to individual privacy and that is not impacted by self-report bias. In addition, the approach is less expensive than other conventional approaches, such as surveying, while providing information that is useful for local and regional planning purposes.

Although others have used wastewater-derived data to estimate the number of drug users and doses consumed (5, 12), multiple possible sources of variability (11) make such back-calculations problematic. Research is needed to determine how to account for all potential sources of variability (e.g. drug purity, routes of ingestion, pharmacokinetics, degradation in transit to WWTPs, sampling, flow estimates, analytical error) in order to create reliable, valid, and comparable index loads.

A limitation of these data is that summary population measures of drug load cannot provide insights into drug usage patterns such as dosage or frequency. However, WWTP data have the potential to provide fine geographic detail and substantial population coverage given that

the majority of the US population has sewer coverage (27) as does much of the industrialized world. Computed index loads use stated populations which are estimates. Therefore, more accurate and dynamic measures of actual population need to be explored in order to account for intra-week population variability as well as inter-season variability e.g. commuting, vacationing and migration. The representativeness of a single, mid-week sample is limited compared to samples from multiple days of the week. Given that cocaine, as indicated by BZE, and MDMA use may vary more by day of week due to their generally more intermittent use pattern than other drugs such as methamphetamine, it is important to note that the findings, for BZE and MDMA in particular, apply to a single mid-week testing date. Testing from a weekend day, or data combined from multiple days, might well have yielded different index loads.

Use of a convenience sample precludes generalizing the findings to the entire State or creating a single estimate for the entire State. The degree to which the convenience sample is representative of the entire State is unknown as is the nature and direction of any bias due to non-response and the site selection criteria. There were 241 incorporated places in Oregon with a total population of 2,567,087 in 2007, so the 96 participating WWTP and the 2,478,168 residents they serve represent the vast majority of the incorporated places and a majority of the total Oregon population of 3,747,455. The level and nature of substance use in Oregon compared to the rest of the US cannot be assessed with these data. Data were presented in terms of the relative distribution of index drug loads for each substance. This way of presenting data limits comparisons across drugs to whether substances were or were not detectable/quantifiable and precludes direct comparisons of drug index loads. The distribution of the data into tertiles would likely be impacted by non-respondents. Ongoing work of the study team is focused on quantifying the uncertainty around computed index loads and the source of index load variability so as to inform future sampling campaigns and analyses in order to make more refined comparisons between substances and locations.

In conclusion, estimating community drug index loads based on WWTP-sampling is a promising drug use surveillance tool with potentially diverse applications. Data on drug index loads are of value for planning local drug prevention, intervention and treatment efforts at a much smaller geographic level and with better timeliness than previously possible. The sampling and analysis methodologies can be easily adapted for assessing temporal and spatial differences among substances such as nicotine, pharmaceuticals, and other illicit drugs as well as modified for various time and geographic scales.

## Acknowledgments

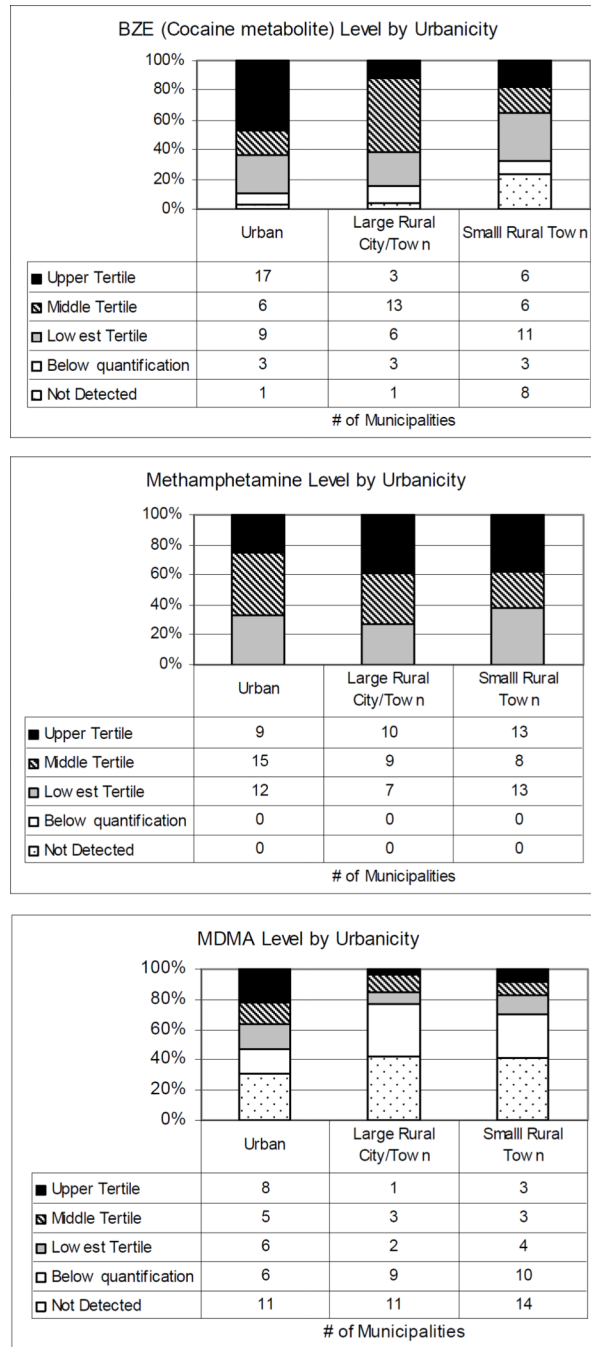
Data collection and analyses were funded by a grant from Oregon Health Sciences University Medical Research Foundation. Data analyses were supported in part by a grant from the National Institute on Drug Abuse (grant 1R21DA024800-01). Thanks to Guy Allen and Pat Friel for their guidance on sampling and methodological issues. Thanks to Janet Gillaspie at the Oregon association of Clean Water Agencies and Pete Schoonover and Meagan Falk at Oregon State University for help with logistics and sample obtainment.

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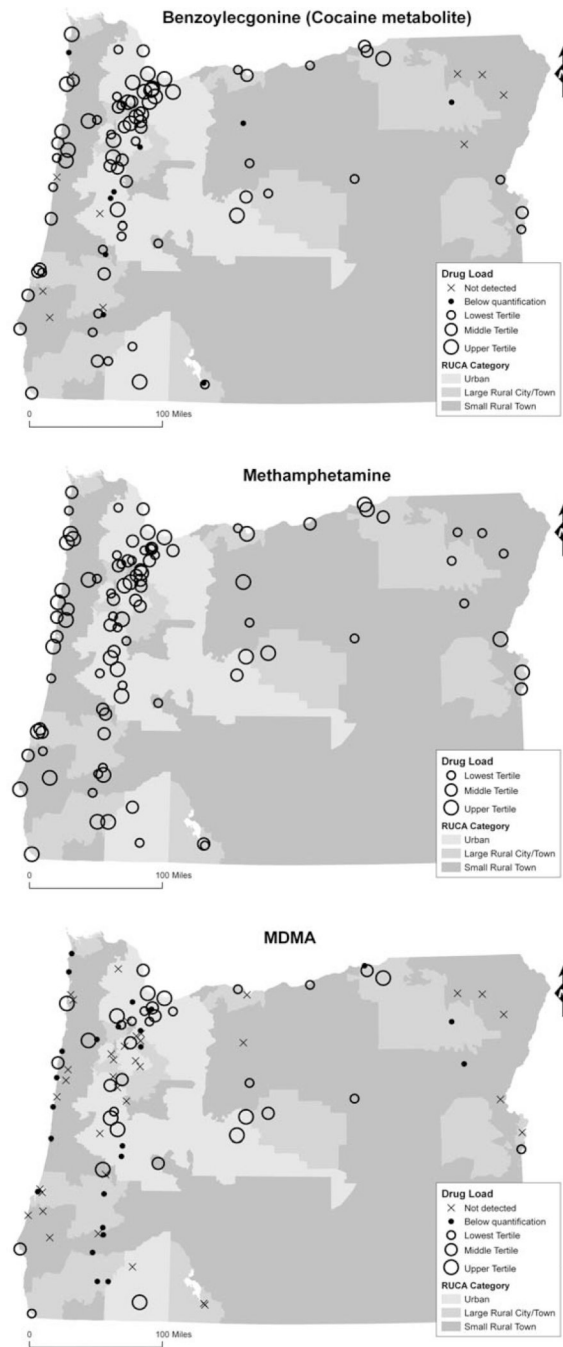
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**Figure 1.** Number and proportion of single-day drug index loads by urbanicity in Oregon for BZE (cocaine metabolite), methamphetamine and MDMA





**Figure 2.** Maps of single-day index loads superimposed on Rural Urban Commuting Area codes in Oregon for BZE (cocaine metabolite), MDMA and methamphetamine

Statistical tests of association between Rural Urban Commuting Area codes and Distribution of Drug Index Loads for 96 Oregon municipal wastewater treatment plants.

**Table 1**

Substance	Equivalency across RUCA*			Trend across RUCA**		
	df	chi-square	p-value	df	chi-square	p-value
Benzoylcegonine (cocaine metabolite)	8	26.1	0.001	2	10.97	0.004
Methamphetamine	4	3.51	0.477	2	0.894	0.640
MDMA	8	8.88	0.353	2	6.16	0.046

\* Pearson's chi-square statistic

\*\* Partition of Pearson's chi-square statistic for ordered categorical variables