Drug Early Warning Signals (DEWS): Serenity Lane - Coburg, Oregon

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Abstract

The Drug Early Warning Signals (DEWS) project uses the methodology developed as part of the earlier Community Drug Early Warning System (CDEWS) project. The DEWS provides timely information about emerging drug use in criminal justice and treatment populations in local communities by sampling and re-testing urine specimens already obtained and tested for a limited panel of drugs. The CDEWS methodology samples specimens that are ready to be discarded and sends the de-identified specimens to a collaborating laboratory for testing for an expanded panel of drugs. By using already collected urine specimens, DEWS provides a relatively quick and inexpensive snapshot of the types of drugs recently used by participating populations and can help the local program to identify important drugs that their testing program may be missing. A major innovation of the current study is the expansion of the CDEWS testing panel from 169 to more than 240 licit and illicit substances, including opioids, benzodiazepines, antidepressants, and new psychoactive substances (NPS). The CDEWS methodology has been implemented in nineteen sites and the results are contained in nine reports already released by the Office of National Drug Control Policy (NDEWS, 2018).

This report presents findings from a study of patients admitted to a Medically Supported Withdrawal program at Coburg Inpatient Hospital Unit, part of the Serenity Lane treatment program. This program accepts persons diagnosed with substance use disorder for any substance requiring withdrawal. A sample of 103 specimens was collected from consecutive patients that presented for admission to the detox and residential treatment programs at the Coburg campus or their outlying offices.

Almost two thirds (61%) of the 103 specimens were found to contain methamphetamine, and these specimens came from persons who were, on average, 5 years younger than the persons who tested negative for methamphetamine. Marijuana (47%) was the next most common individual drug detected, followed by amphetamine (39%), diphenhydramine (24%), cocaine (16%) and gabapentin (14%). Fentanyl or its analogues were rare, found only in 3% of the specimens, but a non-fentanyl opioid was detected in 35% of the specimens. Most of these non-fentanyl opioids would have been detected by the program's opiate screen, but without specifying the drug that triggered the positive result. None of the specimens tested positive for any of the 46 synthetic cannabinoid metabolites for which our lab tested. It is also notable that polydrug use was quite common, with 31% of specimens testing positive for 4 or more of 12 drugs/drug classes and 12% for 6+ drugs.

A set of comparisons of methamphetamine positive and negative specimens revealed that in both younger and older persons, non-fentanyl opioids, likely stemming from heroin use, were almost 3 times more common in methamphetamine positive specimens than methamphetamine negative specimens. Future research might examine why and how these persons seeking supervised withdrawal from drugs were using methamphetamine and heroin and how their use may have led them to pursue treatment.

Table of Contents

List of Tables

Introduction

The Drug Early Warning Signals (DEWS) project uses the methodology developed as part of the earlier Community Drug Early Warning System (CDEWS) project. DEWS provides information about emerging drug use in criminal justice and treatment populations in local communities by sampling and re-testing urine specimens already obtained and tested for a limited panel of drugs by local testing programs. CESAR or local staff sample the specimens that are ready to be discarded and send them de-identified to a collaborating laboratory for testing for an expanded panel of drugs. By using already collected urine specimens, DEWS can provide a relatively quick and inexpensive snapshot of the types of drugs recently used by participating populations. The CDEWS methodology is designed to achieve two primary objectives: 1) to identify and describe the use of emerging drugs in populations at high risk for recent drug use; and 2) to specify any important drugs that the current local testing program may be missing. A major innovation of the current study is the expansion of the CDEWS testing panel to include testing for more than 240 licit and illicit substances, including opioids, benzodiazepines, antidepressants, and new psychoactive substances (NPS), using more sensitive testing technology than is typically available to local testing programs. A full description of the CDEWS methodology is contained in a separate report (Billing et al., 2019).

The CDEWS methodology has now been piloted in nineteen sites and the results are provided in nine reports already released by the Office of National Drug Control Policy (NDEWS, 2018). This report presents findings from patients enrolled in a Medically Supported Withdrawal program at the Coburg Inpatient Hospital Unit in Coburg, Oregon (part of the Serenity Lane program). This program accepts persons diagnosed with substance use disorder for any substance. A sample of 103 specimens was collected from consecutive patients that presented for admission to the detox and residential treatment programs at the Coburg campus or their outlying offices.

Site Specific Methodology

Serenity Lane collects about 1,500 urine specimens annually from patients admitted to the Coburg Medically Supported Withdrawal program housed in the Coburg Inpatient Hospital Unit. An onsite test cup that detects 10 drugs (amphetamine, barbiturates, benzodiazepines, buprenorphine, cocaine, marijuana, methadone, methamphetamine, opiates, and oxycodone) is the standard screen used by this program. Other drugs may be tested upon request. At the completion of the instant testing, all specimens (both positive and negative) are sent to an offsite lab, Willamette Valley Toxicology (WVT), for confirmation and additional testing, if needed. DEWS received an aliquot of urine volume from all specimens collected during the study period prior to their shipment to WVT for testing. A full description of the study methodology is contained in a separate report (Billing et al., 2019).

Specimens were collected between December 2017 and February 2018. We targeted for collection a total of 100 specimens. These specimens were collected from unduplicated, consecutive patients reporting for admission to their detox and residential treatment programs without regard as to whether the specimens were positive or negative by the local test screen. We received a total of 103 specimens.

Results

CDEWS test result refers to the expanded drug testing panel used by the CDEWS collaborating laboratory, which includes all of the drugs tested for by the smaller local program's test panel.

A. Demographic Characteristics of Persons Providing Specimens

Table 1 shows that 60% of the specimens came from persons over age 30 and that 67% came from males. Almost all specimens (91%) came from persons who identified as White and were of non-Hispanic descent (97%).

Table 1: Demographic Characteristics of Persons Submitting Specimens

	(N=103) %	
Age		
25 or younger	18%	
26-30	22	
31-39	21	60%
40-51	20	
52+	19	
Total	100%	
Gender		
Male	67%	
Female	33	
Total	100%	
Race		
White	91%	
Asian	2	
American Indian	2	
Alaskan Native	2	
Black/African American	1	
Multi-racial	1	
Other	1	
Total	100%	
Ethnicity		
Non-Hispanic	97%	
Hispanic/Latino	3	
Total	100%	

B. Drugs Detected by the CDEWS Collaborating Laboratory

Table 2 shows the drugs and drug classes detected by the DEWS expanded test panel. We show drug classes because the local screens often detect a class of drugs without indicating the specific drug that triggered the positive result. Drugs or drug classes likely to have been detected by the local panel used by the program are bolded in Table 2. The most commonly detected drug was methamphetamine, found in 61%. Marijuana (47%) was the next most common specific drug detected, followed by amphetamine (39%), diphenhydramine (24%), cocaine (16%) and gabapentin (14%). Diphenhydramine, a drug sometimes mixed with heroin, and/or used in combination with other drugs, and gabapentin, a pharmaceutical neurological medicine that is sometimes misused, would not have been identified by the local test panel. Buprenorphine and methadone, drugs used to treat opioid use disorder and sometimes used illicitly, were rare, and identified in 11% and 3% of the specimens respectively.

A non-fentanyl opioid was detected in 35% of the specimens. Most of these opioids would have been identified by the program's testing as having an opiate positive screen, without specifying the drug that triggered the positive result. Of the drugs that could have led to a positive opiate screen, the most common were morphine (28%), a likely metabolite of heroin or codeine, hydromorphone (22%) codeine (17%) and 6-MAM/heroin (14%). Other non-fentanyl opioids that would not trigger a positive opiate screen were rare and found in 6% or less of the specimens. Fentanyl or its analogues were rare, found in 3% of the specimens.

Benzodiazepines, as a group, were found in 34% of the specimens and probably would have been detected as a group by the local benzodiazepine screen. Our tests identified 6 benzodiazepines that could have triggered a positive screen result. Antidepressants, a class of drugs not tested for by the local program's test panel, were found in 33% of the specimens. Seven antidepressant drugs were identified. Other psychoactive substances were identified in 15% of the specimens. Perhaps most notable was bufotenine (8%), a hallucinogen, and mitragynine, found in 5%. Mitragynine, also known as kratom, was recently considered by the DEA for possible scheduling but was not scheduled due to the public comments received in opposition (DEA, 2016a, 2016b). A number of pharmaceutical drugs were also detected, most commonly cetirizine (15%) and hydroxyzine (11%). None of the specimens tested positive for any of the 46 synthetic cannabinoid metabolites for which our lab tested.

Table 3 summarizes the results for 12 selected drugs/drug classes and shows the number of them that were found in each specimen. Because methamphetamine is metabolized to amphetamine, we combined them in Table 3. In this study, 59% of the methamphetamine positive specimens also contained amphetamine. It is clear that multiple substances were found in the large majority of specimens. In fact, 12% contained 6+ of these 12 substances and 31% contained 4 or more. This finding of multiple drugs in specimens is consistent with the findings from all of the earlier studies using the CDEWS methodology. While some of the drugs detected may have been

inadvertent contaminants of the illegal drug manufacturing and transport processes, or the result of combination drug products (either known or unknown to the user), it is likely that many of these persons seeking supervised withdrawal from drugs were polydrug users.

Table 2: CDEWS Collaborating Laboratory Test Results

% Positive (drugs likely detected by the local screen are bolded).	**(N=103) %**
Methamphetamine	61%
Marijuana	47^
Amphetamine	39
Diphenhydramine	24
Cocaine	16
Gabapentin	14
Buprenorphine/Norbuprenorphine	11
Methadone/EDDP	3
Any Non-Fentanyl Opioid	35%
Opiates	
Morphine	28
Hydromorphone	22
Codeine	17
6-Monoacetylmorphine (6-MAM)†	14
Oxycodone	5
Oxymorphone	5
Hydrocodone	1
Any Other Non-Fentanyl Opioid	
Noscapine	6
Tramadol	5
Any Fentanyl	3%
Fentanyl/Norfentanyl	3
4-ANPP (Despropionyl fentanyl)	1
Cyclopropyl Fentanyl	1
Methoxyacetyl Fentanyl	1
Any Benzodiazepine	34%
Demoxepam	18
Oxazepam	12
Lorazepam	11
Alprazolam/α-Hydroxyalprazolam	10
Nordiazepam	10
Temazepam	6
Any Antidepressant	33%
Citalopram	16
Trazodone/mCPP*	10
Sertraline	6
Bupropion	4
Desvenlafaxine/Desmethylvenlafaxine	1
Venlafaxine	1
Doxepin	1
Any Other Psychoactive Substance	15%
Bufotenine	8
Mitragynine/7-Hydroxy-Mitragynine	5
Methcathinone/Ephedrone	1
3,4,5-trimethoxycocaine	1
Other Pharmaceutical Drugs	
Cetirizine	15
Hydroxyzine	11
Ephedrine/Pseudoephedrine	9
Promethazine	7
Cyclobenzaprine	5
Dextromethorphan	4
Quinine	3
Loperamide	1
Naloxone	1

^N's vary slightly because of missing information.
†The opiate screen does not detect the presence of 6-MAM (heroin metabolite) directly, but can detect morphine, the metabolite of 6-MAM. 100% of the specimens positive for 6-MAM also tested positive for morphine in the sample.
*Trazodone is an antidepressant whose major active metabolite is mCPP. It is not possible to definitively determine whether the presence of mCPP was due to trazodone use or whether mCPP was taken on its own. Nine of the 10 specimens positive for mCPP were also positive for trazodone.
Note: It is not possible to definitively determine whether the presence of these drugs were due to illicit use or whether drugs were administered or prescribed by a physician.

Table 3: CDEWS Collaborating Laboratory Test Results for Selected Drugs (of 12) and Number of Drugs Detected

% Positive (drugs likely detected by the local screen are bolded).	(N=103) %	
Amphetamine/Methamphetamine	64%	
Marijuana^	47^	
Diphenhydramine	24	
Cocaine	16	
Gabapentin	14	
Buprenorphine/Norbuprenorphine	11	
Methadone/EDDP	3	
Any Non-Fentanyl Opioid	35	
Any Benzodiazepine	34	
Any Antidepressant	33	
Any Other Psychoactive Substance	15	
Any Fentanyl	3	
Number of Drugs/Drug Classes in Specimens (of 12)*		
0	2%	
1	17	
2	24	
3	26	
4	12	31%
5	7	
6+	12	
Total:	100%	

^N's vary slightly because of missing information.
*Select Drugs/Drug Classes (of 12): Amphetamine/Methamphetamine, Buprenorphine/Norbuprenorphine, Cocaine, Diphenhydramine, Gabapentin, Marijuana, Methadone/EDDP, Any Non-Fentanyl Opioid, Any Benzodiazepine, Any Antidepressant, Any Other Psychoactive Substance and Any Fentanyl.

C. Methamphetamine-Positive Patients

We showed above that 64% of the specimens had tested positive for amphetamine/methamphetamine and had grouped them together because amphetamine is the primary metabolite of methamphetamine. Because methamphetamine may be involved in a possible regional epidemic in the use of the drug (Artigiani, Hsu, McCandlish & Wish, 2018), we examined more closely how testing positive for methamphetamine might be related to testing positive for other drugs and to the demographic characteristics we had measured. This analysis examined specimens on the basis of their methamphetamine result only, regardless of whether it also contained amphetamine. This resulted in our eliminating from our amphetamine/methamphetamine positive group, the 3 specimens that had tested positive for amphetamine only. Table 4 shows that there were some significant differences between the methamphetamine positive and methamphetamine negative specimens.

Gender, race, and ethnicity were similar in the two groups. The majority of persons in both groups were male, White, and of non-Hispanic descent. However, the average age of the persons who provided methamphetamine positive specimens was about five years younger than the age of the persons who provided specimens that contained no methamphetamine (35.3 vs. 40.4, $p<.05$). Almost one half of the methamphetamine positive specimens came from persons 30 or younger compared with 30% of the specimens that tested negative for the drug.

Marijuana was found in almost one half of the specimens from each group. However, a non-fentanyl opioid was about 3 times more common in the specimens that contained methamphetamine than those that did not (48% vs. 15%, $p<.01$). Urinalysis results testing positive for methamphetamine are increasing perhaps because methamphetamine is mixed with other drugs (Artigiani, Hsu, McCandlish & Wish, 2018). Further research as to why people mix methamphetamine with other non-fentanyl opioids needs to be conducted.

In contrast, diphenhydramine and antidepressants were about twice as likely to be detected in the methamphetamine negative specimens. In spite of these differences, multiple drugs were found in both groups of specimens.

Table 4: Selected CDEWS Collaborating Laboratory Test Results and Patient Demographics, by Methamphetamine Test Result

	Methamphetamine Positive (N=63) %		Methamphetamine Negative (N=40) %	
Percentage Male	70%		63%	
Percentage White	92%		90%	
Percentage Non-Hispanic	97%		98%	
Age				
25 or younger	22%	47%	12%	30%
26-30	25		18	
31-39	21		20	
40-51	19	32%	20	50%
52+	13		30	
Total	100%		100%	
Mean Age (Years)	35.3*		40.4*	
Median Age (Years)	33.00		39.50	
% Positive (drugs likely detected by the local screen are bolded).				
Marijuana	48^		46^	
Diphenhydramine	18*		35*	
Gabapentin	16		10	
Cocaine	16		15	
Buprenorphine/Norbuprenorphine	13		8	
Methadone/EDDP	3		3	
Any Non-Fentanyl Opioid	48**		15**	
Any Benzodiazepine	27		45	
Any Antidepressant	22**		50**	
Any Fentanyl	2		5	
Any Other Psychoactive Substance	11		20	
Number of Drugs/Drug Classes in Specimens (of 11)†				
0	15%		5%	
1	22		22	
2	30		30	
3	11	33%	22	43%
4	8		8	
5+	14		13	
Total:	100%		100%	

*p<.05 by Chi Square or T-Test for Independent Samples; **p<.01 by Chi Square.
^N's vary slightly because of missing information.
†Select Drugs/Drug Classes (of 11): Buprenorphine/Norbuprenorphine, Cocaine, Diphenhydramine, Gabapentin, Marijuana, Methadone/EDDP, Any Non-Fentanyl Opioid, Any Benzodiazepine, Any Antidepressant, Any Fentanyl, and Any Other Psychoactive Substance.

It was possible that some of these differences in the drugs found in the two groups was caused by their age differences. Table 5 shows that for persons both older and younger than age 30, non-fentanyl opioids were more than twice as likely to be detected in methamphetamine positive specimens than the negative specimens. Among persons age 30 or younger, the methamphetamine negative specimens were almost four times more likely to contain diphenhydramine. Antidepressants were almost three times more likely to be detected in methamphetamine negative specimens from persons over age 30. It is not possible to know whether diphenhydramine and/or antidepressants were being taken under medical supervision.

Table 5: Other Drugs Detected, By Methamphetamine Result and Age Group

	Age ≤30 (N=42)		Age >30 (N=61)	
% Positive by CDEWS Lab (drugs likely detected by the local screen are bolded).	**Methamphetamine Positive (N=30) %**	**Methamphetamine Negative (N=12) %**	**Methamphetamine Positive (N=33) %**	**Methamphetamine Negative (N=28) %**
Any Non-Fentanyl Opioid	60*	25*	36*	11*
Diphenhydramine	13*	50*	21	29
Any Antidepressant	23	25	21**	61**

*p<.05 by Chi Square or Fisher's Exact Test; **p<.01 by Chi Square

Table 6 shows the specific non-fentanyl opioids that the methamphetamine positive specimens contained. The fact that 6-MAM, along with morphine and codeine were among the drugs most likely detected suggests that these methamphetamine users were also using heroin. Hydromorphone, a pharmaceutical opioid, was also detected in about one quarter or more of these specimens. These four substances can cause a urine drug screen to test positive for opiates. A future study designed to learn more about why persons use methamphetamine and heroin might therefore seek to interview patients in this program who have tested positive for both opiates and methamphetamine.

Table 6: Non-Fentanyl Opioids Detected In Methamphetamine-Positive Specimens, By Age Group

% Positive by CDEWS Lab (drugs likely detected by the local screen are bolded).	Age ≤30 (N=30) %	Age >30 (N=33) %
Morphine	57	30
Hydromorphone	37	27
Codeine	33	15
6-Acetylmorphine (6-MAM)	27	15
Noscapine	13	6
Oxycodone	3	6
Oxymorphone	3	6
Tramadol	7	0

Study Limitations

The CDEWS methodology relies on re-testing a small number of specimens that have already been collected and tested by a local testing program. We do not know whether the patients enrolled in this study are representative of all patients coming to this program during the period of this study. DEWS was designed to learn more about the types of drugs recently used by patients being assessed for inpatient drug treatment and cannot provide precise prevalence estimates.

Every effort was made to include in the CDEWS Laboratory test panel most of the currently available drugs likely to be misused. However, the rapidly changing nature of new psychoactive substances can cause some drugs to have been missed by the CDEWS testing panel. It is extremely difficult to develop urine tests for all of the new drugs as quickly as they are discovered.

In addition, while we found that some specimens contained multiple drugs/metabolites, this does not necessarily mean that the user sought all of these drugs or was aware of the composition of the substance(s) ingested. Multiple drugs in a specimen may also simply reflect the byproducts produced from formulating, transporting, or taking the drug.

DEWS results can only provide an indication of the recent use of prescription and illicit drugs by the patients who provided the specimens. The results do not indicate why or how often persons used a drug or where they obtained it.

Summary and Conclusions

Almost two thirds (64%) of the sampled specimens were found to contain amphetamine/methamphetamine, which is not surprising since the use of methamphetamine (which metabolizes to amphetamine) remains quite prevalent on the West Coast (Artigiani, Hsu, McCandlish & Wish, 2018). Persons who tested positive for methamphetamine were, on average, 5 years younger than those who tested negative for the drug.

Many of the drugs detected by the DEWS laboratory's expanded screen would have likely been picked up by the local drug screen, including amphetamine/methamphetamine. Drugs identified that would have likely been missed by the local program's screen included antidepressants, diphenhydramine, gabapentin, and other psychoactive substances. Diphenhydramine, an antihistamine, is a drug sometimes mixed with heroin, and/or used in combination with other drugs, and gabapentin is a pharmaceutical neurological medicine that is sometimes misused. Other psychoactive drugs detected included primarily bufotenine, a hallucinogen, and mitragynine (also known as kratom). The local treatment program may want to consider adding some of these substances to their testing panel.

Fentanyl or its analogues were rare, found only in 3% of specimens. The limited presence of fentanyl and its analogs, despite the relatively common detection of other non-fentanyl opioids in the sample (35%), may indicate that fentanyl has not yet spread to this part of the country or to this population. It is also noteworthy that no synthetic cannabinoids were detected in this population. The absence of fentanyl and synthetic cannabinoids may be the result of regional use patterns and/or indicate that the testing panel needs to be expanded to include additional analogs/metabolites. It may also be possible that the decriminalization/legalization of marijuana has reduced use of the synthetic cannabinoids. According to Dr. Eric Geisler, Director of Medical Services at Serenity Lane, high-potent, legal cannabis is widely available in many retail locations in this locality at affordable prices (E. Geisler, personal communication, March 28, 2019).

It is also notable that polydrug use was quite common across the sample, with 31% of persons testing positive for 4 or more of 12 drugs/drug classes and 12% for 6+ drugs. It is important to note that the use of a single drug may result in the presence of multiple drugs/metabolites. Also, while some of the drugs detected may have been inadvertent contaminants of the illegal drug manufacturing and transport processes, or the result of combination drug products (either known or unknown to the user), it is likely that many of these persons seeking supervised withdrawal were polydrug users.

Finally, our special comparisons of methamphetamine positive and negative specimens found that non-fentanyl opioids were detected in methamphetamine positive specimens almost 3 times as

often as in methamphetamine negative specimens in both younger and older persons. It is possible that methamphetamine is being intentionally used in conjunction with opioids to produce a synergistic high or to balance the effects of the two drugs (Ellis, Kasper & Cicero, 2018). Alternatively, methamphetamine is often used to manage heroin withdrawal while heroin may be used to offset the side effects of methamphetamine (E. Geisler, personal communication, March 28, 2019). Interviews with some of these patients might provide an indication of why the drugs are being detected together. Conversely, methamphetamine negative specimens from persons over age 30 were significantly more likely to contain antidepressants compared to those that were positive. Diphenhydramine was significantly more likely to be found among methamphetamine negative specimens from persons aged 30 or younger compared to those that were positive. It is not possible to know whether diphenhydramine and/or antidepressants were being taken by these persons for medical or other reasons. Polydrug use was again very prevalent in both groups, with approximately one-third or more of methamphetamine positive and negative specimens testing positive for 3 or more drugs/drug classes.

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