

**Drug Early Warning Signals (DEWS):
Operation PAR – North Fort Myers, Florida**



Office of National Drug Control Policy
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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. 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 de-identified 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, 2018a).

This report presents findings from the study of Operation PAR's Medication Assisted Patient Services (MAPS) Program, located in North Fort Myers, Florida. This program provides outpatient methadone treatment to persons seeking treatment for an opioid-related drug addiction. Specimens were collected at intake from 100 consecutive new patients entering the program.

As would be expected of persons seeking methadone treatment, most (80%) of their specimens tested positive for a non-fentanyl opioid, mostly morphine (61%), hydromorphone (40%), codeine (33%), and oxycodone (19%). In addition, a fentanyl compound, mostly fentanyl/norfentanyl (48%), was found in more than half of the specimens, including some fentanyl analogs. Antidepressants were found in 36% of specimens and 31% were positive for a benzodiazepine. Synthetic cannabinoids were found in only 8%, triggered by only one synthetic cannabinoid metabolite, 5F-ADB (metab 7). Drugs detected the most that would have been missed by the program's drug screen were antidepressants, as well as fentanyl and its analogs. The program's routine opiate screen would have likely detected most of the non-fentanyl opioids that the CDEWS expanded testing identified.

Multiple drug use was common in these patients; 57% tested positive for 4 or more of 13 selected drugs/drug classes. A major difference in drugs detected in males and females was that almost one half of females tested positive for amphetamine/methamphetamine, more than twice the percentage for males. Compared with persons testing negative for any fentanyl, persons positive for any fentanyl were significantly more likely to be positive for 4 or more other drugs (59% vs. 33%, $p<.01$), a non-fentanyl opioid, and/or cocaine. This use of opioids and cocaine may be reminiscent of "speedballs", the practice of mixing heroin and cocaine (NDEWS, 2018d). We estimate that about 90% of fentanyl users would have been identified as opioid users by the program's opiate screen

even though their fentanyl use would be missed. It may still be useful, however, for this program to add a test for fentanyl to their panel to help inform clients who might not have known that they had taken fentanyl.

The findings from this study of persons seeking methadone treatment underscore those from our prior CDEWS study of hospital patients (NDEWS, 2018a), our study of fentanyl overdose deaths in New Hampshire (NDEWS, 2018c) and our DOTS series (NDEWS, 2018b) which have all demonstrated that persons who test positive for fentanyl tend to test positive for multiple other drugs, making their drug treatment a much more complex endeavor.

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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 in the CDEWS methodology used in 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, 2018a). This report presents findings from the study of Operation PAR's Medication Assisted Patient Services (MAPS) Program, located in North Fort Myers, Florida. This program provides outpatient methadone treatment to persons seeking treatment for opioid use disorder. A sample of 100 specimens was collected at intake from consecutive new patients entering the program.

Site Specific Methodology

Approximately 1,100 urine specimens are collected monthly from persons enrolled in Operation PAR's Medication Assisted Patient Services (MAPS) programs. Specimens for this study were sampled from adults being assessed at intake for methadone treatment by Operation PAR's MAPS program in North Fort Myers, Florida. An onsite test cup that detects 11 drugs (amphetamine, benzodiazepines, buprenorphine, cocaine, marijuana, MDMA, methadone and its metabolite, EDDP, methamphetamine, opiates, and oxycodone) is the standard screen used by this program. At the time of this study, an onsite laboratory was used for confirmation testing as needed. Following completion of this study, the program transitioned to conducting its confirmation testing at an offsite laboratory. A full description of the CDEWS methodology is contained in a separate report (Billing et al., 2019).

Specimens were collected between February 2018 and April 2018. We targeted for collection a total of 100 specimens obtained from clients being assessed for their methadone treatment program. These specimens were collected from unduplicated, consecutive patients at the time of intake without regard as to whether the specimens were positive or negative by the local urine drug test screen. We received a total of 100 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 local program's test panel.

A. Demographic Characteristics of Persons Providing Specimens

Table 1 shows that the age of persons submitting specimens was fairly evenly split across the five age groups, with slightly fewer persons being age 50 or older (13%). 52% of the sample were males. Most (92%) of the specimens came from persons who identified as White and were of non-Hispanic descent (90%).

Table 1: Demographic Characteristics of Persons Submitting Specimens

	(N=100) %
Age	
Below 30	20%
30-34	24
35-40	24
41-49	19
50+	13
Total	100%
Gender	
Male	52%
Female	48
Total	100%
Race	
White	92%
American Indian/Alaskan Native	1
Other	7
Total	100%
Ethnicity	
Non-Hispanic	90%
Hispanic/Latino	10
Total	100%

B. Drugs Detected by the CDEWS Collaborating Laboratory

Table 2 shows that the most common specific drugs found in the specimens were marijuana (44%), cocaine (38%), methamphetamine (29%), methadone/EDDP (23%), buprenorphine/norbuprenorphine (21%), and diphenhydramine (12%). All of these drugs, with the exception of diphenhydramine, are included in the local program's drug screen. Most (80%) of the specimens tested positive for a non-fentanyl opioid, mostly morphine (61%), hydromorphone (40%), codeine (33%), and oxymorphone (19%). While the heroin metabolite, 6-MAM, was only detected in 10% of the specimens, 6-MAM is typically metabolized rapidly and shows up as morphine and/or codeine. A fentanyl compound was found in more than half (54%) of the specimens, mostly fentanyl/norfentanyl (48%) and fentanyl analogs were also detected. Antidepressants were found in 36% of specimens and 31% were found to be positive for a benzodiazepine. Fifteen percent of specimens were positive for a psychoactive substance (not already mentioned above), and 8% contained a synthetic cannabinoid compound. The only synthetic cannabinoid detected in the sample was 5F-ADB (metab 7). **Drugs detected the most that would have been missed by the local screen include: fentanyl and its analogs and antidepressants.** The program's routine opiate screen would have likely detected most of the non-fentanyl opioids that CDEWS identified.

Table 2: CDEWS Collaborating Laboratory Test Results

% Positive (drugs likely detected by the local screen are bolded).	(N=100) %
Marijuana	44%
Cocaine	38
Methamphetamine	29
Methadone/EDDP	23
Buprenorphine/Norbuprenorphine	21
Diphenhydramine	12
Amphetamine	6
Gabapentin	1
Any Non-Fentanyl Opioid	80
Opiates	
Morphine	61
Hydromorphone	40
Codeine	33
Oxymorphone	19
Oxycodone	14
6-Monoacetylmorphine (6-MAM)[†]	10
Hydrocodone	2
Any Other Non-Fentanyl Opioid	
Noscapine	9
Tramadol	8
Any Fentanyl	54
Fentanyl/Norfentanyl	48
4-ANPP (Despropionyl Fentanyl)	9
Cyclopropyl Fentanyl	3
Methoxyacetyl Fentanyl	3
Acetyl Norfentanyl	2
Any Antidepressant	36
Amitriptyline	27
Trazodone/mCPP*	5
Citalopram	4
Sertraline	3
Venlafaxine	1
Desvenlafaxine/Desmethylvenlafaxine	1
Paroxetine	1
Nortriptyline	1

Any Benzodiazepine	31
Clonazepam/7-Aminoclonazepam	12
Alprazolam/α-Hydroxyalprazolam	12
Nordiazepam	8
Temazepam	8
Oxazepam	4
Lorazepam	2
Any Synthetic Cannabinoid	8
5F-ADB (metab 7)	8
Any Other Psychoactive Substance	15
3,4,5-trimethoxycocaine	7
Mitragynine/7-Hydroxy-Mitragynine	6
Methcathinone/Ephedrone	1
Butylone	1
Dibutylone	1
Phentermine	1
Other Pharmaceutical Drugs	
Cetirizine	6
Dextromethorphan	6
Loperamide	5
Cyclobenzaprine	3
Hydroxyzine	3
Haloperidol	1
Zolpidem	1
Naloxone	1

[†]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. All 5 of the specimens positive for trazodone were also positive for mCPP.

Table 3 presents a summary of 13 drugs/drug classes detected in the specimens, along with a count of the number detected. Because methamphetamine is metabolized to amphetamine, we combined them in our analysis rather than reporting them separately. The majority (57%) of specimens contained 4 or more of these 13 drugs/drug classes and 13% of all specimens contained 6 or more drugs. It is important to note that a single specimen may test positive for two or more drugs as a result of taking a single substance.

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

% Positive (drugs likely detected by the local screen are bolded).	(N=100) %
Marijuana	44%
Cocaine	38
Amphetamine/Methamphetamine	32
Methadone/EDDP	23
Buprenorphine/Norbuprenorphine	21
Diphenhydramine	12
Gabapentin	1
Any Non-Fentanyl Opioid	80
Any Fentanyl	54
Any Antidepressant	36
Any Benzodiazepine	31
Any Synthetic Cannabinoid	8
Any Other Psychoactive Substance	15
Number of Drugs/Drug Classes in Specimens (of 13)[†]	
0	1%
1	8
2	11
3	23
4	16
5	28
6	5
7-10	8
Total:	100%

[†]Select Drugs/Drug Classes (of 13): Amphetamine/Methamphetamine, Buprenorphine/Norbuprenorphine, Cocaine, Diphenhydramine, Gabapentin, Marijuana, Methadone/EDDP, Any Non-Fentanyl Opioid, Any Fentanyl, Any Antidepressant, Any Benzodiazepine, Any Synthetic Cannabinoid and Any Other Psychoactive Substance.

Table 4 shows that there were few significant differences between males and females in the drugs detected, number of drugs/drug classes found in specimens, and demographic information. One exception is that a higher percentage of female patients tested positive for amphetamine/methamphetamine than male patients (46% vs 19%, $p < .01$). The majority of both male (53%) and female (61%) patients tested positive for 4 or more drugs/drug classes. There were no significant differences in the racial/ethnic and age characteristics of males and females.

Table 5 presents a summary of the 12 other drugs/drug classes detected and demographic characteristics of fentanyl positive and fentanyl negative specimens. A higher percentage of fentanyl positive specimens tested positive for cocaine than fentanyl negative specimens (52% vs 22%, $p < .01$). This use of opioids and cocaine may be reminiscent of “speedballs”, the practice of mixing heroin and cocaine (NDEWS, 2018d). Fentanyl positive specimens were also more likely to test positive for a non-fentanyl opioid (91% vs 67%, $p < .01$).

Multiple other drugs were more likely to be found in the fentanyl positive specimens. 59% of the fentanyl positive specimens contained 4 or more other drugs, compared to 33% of the fentanyl negative specimens ($p < .01$). These differences cannot be attributed to variations in the demographic characteristics of the two groups, which were not significantly different.

Table 6 compares fentanyl positive and negative specimens in males and females and specifies the non-fentanyl opioids detected. Benzodiazepines, cocaine, and non-fentanyl opioids were significantly more likely to be detected in fentanyl positive specimens from females as compared to fentanyl negative specimens from females. In addition, in both males and females, the non-fentanyl opioids detected were mostly codeine, morphine, and hydromorphone, drugs that would have likely been detected by the program’s opiate screen. Thus, about 90% of the fentanyl positive specimens would still have tested positive for opiates even though the fentanyl specifically would have gone undetected.

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

	Male (N=52) %	Female (N=48) %
% Positive (drugs likely detected by the local screen are bolded).		
Marijuana	48%	40%
Cocaine	33	44
Methadone/EDDP	21	25
Buprenorphine/Norbuprenorphine	19	23
Amphetamine/Methamphetamine	19**	46**
Diphenhydramine	10	15
Gabapentin	0	2
Any Non-Fentanyl Opioid	83	77
Any Fentanyl	56	52
Any Antidepressant	37	35
Any Benzodiazepine	31	31
Any Synthetic Cannabinoid	8	8
Any Other Psychoactive Substance	14	17
Number of Drugs/Drug Classes in Specimens (of 13)[†]		
0	2%	0%
1	10	6
2	12	10
3	23	23
4	15	17
5+	38	44
Total	100%	100%
Percentage White	89	96
Percentage Non-Hispanic	87	94
Mean Age (Years)	40.5	34.5
Median Age (Years)	38.5	33.0

[†]Select Drugs/Drug Classes (of 13): Amphetamine/Methamphetamine, Buprenorphine/Norbuprenorphine, Cocaine, Diphenhydramine, Gabapentin, Marijuana, Methadone/EDDP, Any Non-Fentanyl Opioid, Any Fentanyl, Any Antidepressant, Any Benzodiazepine, Any Synthetic Cannabinoid and Any Other Psychoactive Substance.

**p<.01 by Chi Square.

Table 5: Selected CDEWS Collaborating Laboratory Test Results and Patient Demographics, by Fentanyl Test Result

	Fentanyl Positive (N=54) %	Fentanyl Negative (N=46) %
% Positive (drugs likely detected by the local screen are bolded).		
Cocaine	52%**	22%**
Marijuana	44	44
Amphetamine/Methamphetamine	37	26
Methadone/EDDP	20	26
Buprenorphine/Norbuprenorphine	17	26
Diphenhydramine	17	7
Gabapentin	0	2
Any Non-Fentanyl Opioid	91**	67**
Any Benzodiazepine	35	26
Any Antidepressant	32	41
Any Synthetic Cannabinoid	11	4
Any Other Psychoactive Substance	15	15
Number of Other Drugs/Drug Classes in Specimens (of 12†)		
0	4%	2%
1	9	13
2	9	13
3	19	39
4	35	13
5+	24	20
Total	100%	100%
Percentage Male	54%	50%
Percentage White	91	94
Percentage Non-Hispanic	87	94
Mean Age (Years)	37.5	37.7
Median Age (Years)	35.0	36.5

**p<.01 by Chi Square.

†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 Synthetic Cannabinoid and Any Other Psychoactive Substance.

Table 6: CDEWS Collaborating Laboratory Test Results, By Gender and Fentanyl Test Result

% Positive (drugs likely detected by the local screen are bolded).	Gender			
	Male (N=52)		Female (N=48)	
	Positive for Any Fentanyl† (N=29)	Negative for Any Fentanyl (N=23)	Positive for Any Fentanyl† (N=25)	Negative for Any Fentanyl (N=23)
Any Other Psychoactive Substance	10	17	20	13
Any Benzodiazepine	28	35	44*	17*
Buprenorphine/Norbuprenorphine	17	22	16	30
Any Antidepressant	35	39	28	44
Methadone/EDDP	21	22	20	30
Marijuana	52	44	36	44
Any Synthetic Cannabinoid (SC)	10	4	12	4
Amphetamine/Methamphetamine	24	13	52	39
Diphenhydramine	14	4	20	9
Any Non-Fentanyl Opioid	90	74	92**	61**
Codeine	55*	26*	44***	0***
Morphine	79*	48*	88***	22***
Hydrocodone	7	0	Δ	Δ
Hydromorphone	55	35	40	26
6-Monoacetylmorphine (6-MAM)	14	4	20	0
Oxymorphone	7	22	24	26
Oxycodone	3	13	24	17
Noscapine	10	4	20	0
Tramadol	10	9	8	4
Cocaine	41	22	64**	22**
Gabapentin	Δ	Δ	0	4

†Tested positive for one or more of the following: fentanyl/norfentanyl, 4-ANPP (despropionyl fentanyl), cyclopropyl fentanyl, methoxyacetyl fentanyl, or acetyl norfentanyl.

Δ No cases were positive for both drugs.

*p<.05 by Chi Square; **p<.01 by Chi Square, ***p<.001 by Chi Square.

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 individuals enrolled in this study are representative of all clients coming to this program during the period of this study. This CDEWS study was designed to learn more about the types of drugs recently used by clients entering drug treatment, and not to 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, given the rapidly changing nature of new psychoactive substances, it is possible that some drugs may have been missed by the CDEWS testing panel. The continuously changing nature of the substances available make it 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.

The CDEWS test results can only provide an indication of the recent use of prescription and illicit drugs by the persons who provided the specimens. A more complete understanding of the results would require additional study. Nor can our test results tell us why or how often persons used a drug or where they obtained it.

Summary and Conclusions

More than three-fourths (80%) of specimens were found to contain non-fentanyl opioids, including most commonly morphine (61%), hydromorphone (40%), and codeine (33%). Fentanyl and its analogues were also detected in more than half (54%) of specimens, mostly fentanyl/norfentanyl (48%). **We expected to find many opioid positive specimens given that they were sampled from a methadone treatment program, however, the high percentage of fentanyl positives was surprising.** Antidepressants were found in 36% of specimens. It is not possible to know whether these antidepressants were the result of prescribed use. Many of the drugs detected by the CDEWS laboratory's expanded screen would have likely been picked up by the local drug screen, including most of the non-fentanyl opioids. Drugs likely to have been missed by the local program's screen included fentanyl and its analogs, other psychoactive substances, antidepressants, and oxycodone. It should be noted that oxycodone is a metabolite of oxycodone, which is currently included on the local program's drug screen. The local program may want to consider adding these substances to their testing panel.

The only synthetic cannabinoid detected was 5F-ADB (metab 7), found in 8% of specimens. The limited detection of synthetic cannabinoids may be the result of regional use patterns and/or indicate that the testing panel missed a metabolite and needs to be expanded to include additional metabolites. 5F-ADB (metab 7) was also the sole synthetic cannabinoid detected in Hillsborough County, Florida at the Central Receiving Facility (Gracepoint), another CDEWS site in 2017-2018 (Wish et al., forthcoming).

Polydrug use was very common across the sample, with 57% of persons testing positive for 4 or more drugs and 13% containing 6 or more drugs. It is important to recognize that the use of a single drug may result in the detection of multiple drugs/metabolites. While some of the drugs detected may have been inadvertent contaminants during the drug manufacturing and transport processes, it is likely that many of these persons were polydrug users.

Few significant differences were detected between males and females with the exception that a higher percentage of female patients tested for amphetamine/methamphetamine than male patients (46% vs 19%, $p < .01$). This affinity of females for methamphetamine is consistent with findings from a review of studies completed over the period of 1966-2007 (Dluzen & Liu, 2008).

More than half (59%) of the fentanyl positive specimens tested positive for 4 or more drugs/drug classes and almost one quarter (24%) tested positive for 5 or more of the 12 selected drugs/drug classes. Persons positive for fentanyl were significantly more likely to be positive for 4 or more drugs (59% vs. 33%, $p < .01$), a non-fentanyl opioid, and/or cocaine, than those negative for

fentanyl. This occurrence may be a result of users attempting to gain an elevated, synergistic high using fentanyl in combination with other substances.

When we reviewed the drugs associated with fentanyl use in males versus females, we found significantly elevated rates of benzodiazepines, cocaine, and non-fentanyl opioids only in fentanyl positive specimens from females. Among males and females, we found that most non-fentanyl opioids detected were codeine, morphine, and hydromorphone, drugs that would likely be detected by the program's opiate screen. We estimate that about 90% of fentanyl users would therefore be identified as opioid users even though their fentanyl use would be missed by the program's current test panel. It may still be useful, however, to add fentanyl to their screen to ensure that clients can be informed that they had taken fentanyl. Given the cost associated with laboratory testing, the development of a CLIA waived instant onsite test would improve the accessibility of fentanyl testing for treatment programs (FDA, 2019).

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