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Abstract – Random drug testing as a program component of professional monitoring programs like Physician Health Programs (PHP) provides a quantifiable measure of abstinence and serves as a deterrent to continued use of alcohol and other drugs. This article summarizes the findings of data analysis of invalid and dilute toxicology as potential predictors for subsequent positive toxicology. Findings have policy implications for future toxicology collection procedures and expectations of donors following invalid and dilute specimens.

Keywords – toxicology, invalid, dilute, predictor, physician health program, alternative to discipline programs, monitoring, addiction, recovery.

Background

Toxicology testing is a key component of substance use disorder recovery and serves as a deterrent to a participant's continued substance use as reported by Pharm, Pronovost, and Skipper (2015) and ASAM (2010). Toxicology testing is required by treatment programs, the Department of Transportation for safety sensitive transportation employees, Physician Health Programs, Alternative to Discipline programs, and other monitoring programs.

Physician health programs have operated in the United States since the late 1970's providing structure for physicians and other health professionals diagnosed with behavioral health conditions so that they may continue to safely practice in their trained field as outlined by McLellan, Skipper, Campbell, and DuPont (2008). In addition to acting as a deterrent, toxicology also serves as a quantifiable record for health professional program participants known to their respective health professional licensing board, demonstrating that they continue to remain abstinent from alcohol and other mind altering substances as shown by DuPont and Skipper (2012). Testing serves a similar function in other programs that seek to monitor for ongoing sobriety following substance use disorder diagnosis.

The potential for specimen adulteration by the participant is always present. Participants who are not in active recovery may look to various options to attempt to modify the outcome of their toxicology tests in an effort to "hide" their continued use of prohibited substances. There is much at stake for participants who continue to use alcohol and other mind altering substances while being monitored such as removal from work and possible termination. They may also face consequences like follow-up substance use disorder evaluation and the addition of further treatment recommendations. For participants in health professional programs, they risk being reported to their professional health licensing board for failure to remain abstinent which may result in the loss of their license to practice.

This potential is best mitigated by collection policies and procedures that mirror the national Department of Transportation (DOT) testing guidelines for urine collection and by validity screening measures employed by laboratories. Strong collection policies and procedures include the observed collection of urine specimens, or monitored collections at a minimum. Further, they include the chain of custody documentation that accompanies toxicology specimens from the collection site to the laboratory. Chain of custody documentation includes positive identification of the toxicology specimen donor and initial specimen validity screening

including temperature readings of the specimen and observation of the specimen's color as outlined by SAMHSA's Medical Review Officer Guidance Manual for Federal Workplace Drug Testing Programs (2017).

These collection policies and procedures are additionally augmented by validity screening measures employed by laboratories to help ensure specimens are actual human urine. One validity screening test performed on the specimen is the measurement of creatinine. When specimen creatinine levels are less than 20 mg/d, the pH levels are also measured and recorded. In addition, the specific gravity of the specimen must be measured and at least one test must be performed on the specimen to determine the presence of oxidizing adulterants (SAMHSA, 2017). These precautionary procedures increase the reliability and validity of the program's toxicology component.

Uprise Health identified an increase in invalid and dilute testing and is always seeking to ensure that best practices are being employed to protect public safety while supporting participants in their recovery. Between July 2, 2010 and September 24, 2021, a combined 1,185 participants produced 66,644 toxicology specimens. The results of these tests are maintained in a data set. Uprise Health Monitoring program staff identified that the data set could be used to determine if invalid and dilute specimens are a predictor for future subsequent positive toxicology. Within the 66,644 tests were 896 confirmed positive toxicology tests among 390 participants.

The combined 1,185 participants are across four monitoring programs operated by Uprise Health. Study participants included 930 participants from Oregon's Health Professionals' Services Program, 170 participants from the Delaware Professionals' Health Monitoring Program, 56 monitoring participants from an east coast health system, and 29 participants from monitoring for other professionals.

Oregon's Health Professionals' Services Program (HPSP) has operated continuously since July 1, 2010 for health professionals licensed by the Oregon Medical Board, Oregon Board of Dentistry, Oregon State Board of Nursing, and the Oregon Board of Pharmacy. HPSP participants sign participation agreements that outline toxicology program requirements that mirror DOT collection procedures and the requirement to follow the HPSP's Guidelines addressing toxicology. In HPSP, urine collections are observed and chain of custody forms follow each urine specimen from collection site to laboratory.

Delaware's Health Professionals Monitoring Program (DPHMP) has operated continuously since November 2013 for all licensed professionals in the state of Oregon. Like HPSP, DPHMP participants sign participation agreements that outline toxicology program requirements that mirror DOT collection procedures and the requirement to follow the DPHMP's Guidelines addressing toxicology. In DPHMP, urine collections are monitored rather than observed, although if there are any concerns a participant can be required to switch to observed collections. Chain of custody forms accompany each urine specimen from collection site to the laboratory.

The program for the east coast health system has operated since July 2019. The program operates similarly to DPHMP. Monitoring toxicology requirements for other professionals conducted by Uprise Health mirror either HPSP or DPHMP depending on the participant.

Methods

Adulterated Urine Definitions

SAMHSA's Medical Review Officer (MRO) Guidance Manual for Federal Workplace Drug Testing Programs (2017) defines an invalid toxicology specimen as "a urine specimen that contains an unidentified adulterant or interfering substance, has an abnormal physical characteristic, has an endogenous substance at an abnormal concentration that prevents the laboratory from completing testing or obtaining a valid drug test result, or the concentration of a biomarker is not consistent with that established for human urine" (7-20).

The MRO Guidance Manual reports urine specimens as dilute when:

- The creatinine concentration is greater than 2 mg/dL and less than 20 mg/dL; and
- The specific gravity is greater than 1.0010 and less than 1.0030 (D-3).

Data Set

All 66,644 tests were classified by final MRO outcome for all 1,185 participants. The toxicology records were sorted by participant and by toxicology collection date. For the first data analysis looking at invalid toxicology, each participant was coded as 1) not having produced any invalid toxicology and 2) having produced invalid toxicology. Group 1 (not having produced any invalid toxicology) was further classified as a) not having produced any positive toxicology and b) having produced positive toxicology. Group 2 (having produced invalid toxicology) was further classified as a) not having produced positive toxicology following their invalid toxicology test and b) having produced positive toxicology following their invalid toxicology test.

The dichotomous variables, Group 1 and Group 2 counts, were compared using descriptive crosstab statistics with Pearson Chi-Square and Cramer's V values.

The procedure was repeated for the second data analysis replacing lab reported dilutes for the invalid toxicology test records analyzed in the first data analysis. Descriptive crosstab statistics were also performed with Pearson Chi-Square and Cramer's V values.

Findings: Invalid Results

Among the 66,644 toxicology Tests between 7/2/2010 and 9/24/2021 were 408 invalid toxicology specimens across 207 participants. Additionally, there were 896 positive toxicology tests among 390 of the 1,185 participants.

	Count	% with Non-Negative
All Participants	1,185	
All Participants without Invalids	978	37.73%
All Participants without Invalids with non-negative toxicology	369	
Participants with 1 or more invalids	207	28.02%
Participants with 1 or more invalids with subsequent non-negative toxicology	58	

Thirty-eight percent (38%) of all participants without invalids had at least one non-negative toxicology test. Only 28% of the individuals with invalids had a subsequent non-negative toxicology test following their first invalid. Assuming a normal distribution, this is less non-negative tests than the 38% that would be expected. If the invalid was a predictor, we would expect more than 38% of the individuals with invalids to have subsequent non-negative toxicology, not less. Thus, invalid test results are not a predictor of future non-negative toxicology.

Statistical Tests

Test	Value	Degrees of Freedom	Asymptotic Significance (2-sided)	Symmetric Value	Symmetric Approximate Significance
Pearson Chi-Square	6.989	1	.008	-.077	.008
Cramer's V	-	-	-	.077	.008

Crosstabs of the variable counts were used to determine the significance associated with the Pearson Chi-Square value which is a value that represents the probability that the results were random chance. The probability (Asymptotic Significance (2-sided)) values range from 0.000 to 1. The lower the significance value the less likely the values were a result of random chance. In this case the Pearson Chi-Square value is 6.989 with a probability of .008 with one degree of freedom indicating there is no statistically significant relation between positive tests for participants who had previously produced an invalid toxicology sample.

Cramer's V is a measure of association with a value range from 0.00 to 1. A value of 1 represents the strongest possible bivariate relationship. At .077 there is not a relationship between the variables of invalid toxicology and subsequent non-negative (positive) toxicology.

Findings: Dilute Results

Among the 66,644 toxicology tests between 7/2/2010 and 9/24/2021 were 782 dilute toxicology specimens among 336 participants. Of the 782 dilute specimens, 43 were also concurrently positive per the MRO for alcohol or other drugs.

	Count	% with Non-Negative
All Participants	1,185	
All Participants without dilutes	849	25.32%
All Participants without dilutes with non-negative toxicology	215	
Participants with 1 or more dilutes	336	41.37%
Participants with 1 or more dilutes with subsequent non-negative toxicology*	139	

*45 of the 336 participants with dilute toxicology produced non-negative toxicology prior to producing their first dilute toxicology specimen.

Twenty-five percent (25%) of all participants without dilutes had at least one non-negative toxicology test. In contrast, forty-one percent (41%) of participants with a dilute had a subsequent non-negative toxicology. Assuming a normal distribution, at 41%, there are more participants with non-negative tests than the 25% that would be expected. With 41% of participants with subsequent non-negative toxicology following one or more dilute toxicology tests, dilute toxicology specimens are a predictor for subsequent non-negative (positive) toxicology.

Test	Value	Degrees of Freedom	Asymptotic Significance (2-sided)	Symmetric Value	Symmetric Approximate Significance
Pearson Chi-Square	29.583	1	.000	.158	.000
Cramer's V	-	-	-	.158	.000

A chi-square test of independence showed that there was a significant association between participants with positive toxicology following a dilute sample, $\chi 2$ (1, N = 1185) = 29.583, p < .001. Probability (Asymptotic Significance (2-sided)) values range from 0.000 to 1. The lower the significance value the less likely the values

were a result of random chance. In this case, the Pearson Chi-Square value is 29.583 with a probability of .000 with one degree of freedom indicating that there is a statistically significant relation between positive tests for participants who had previously produced a dilute toxicology sample. Thus, there is an association between the results and they are not random chance.

Cramer's V is a measure of association with a value range from 0.00 to 1. A value of 1 represents the strongest possible bivariate relationship. At .158 there is a relationship between the variables of dilute invalid toxicology and subsequent non-negative (positive) toxicology.

In summary, the finding that participants that produced dilute toxicology specimens are more likely to produce subsequent non-negative (positive) toxicology are statistically significant. Participants that produced dilute toxicology specimens are 60% more likely to produce future positive toxicology specimens (41.37%) when compared against participants who did not produce dilute toxicology specimens (25.32%).

Conclusion

Dilute toxicology specimens are a predictor for subsequent participant positive toxicology specimens. Positive toxicology specimens for participants who have produced a dilute specimen are 60% more likely than for participants who have not produced previous dilute toxicology specimens. Invalid toxicology specimens are not a predictor of future participant positive toxicology specimens.

Uprise Health reviews all dilute toxicology results and historically has followed up immediately with testing to the lowest limit of detection if it was not already employed and with an additional, immediate toxicology test. In addition, historically participants were notified of the dilute and were educated on steps to eliminate the possibility of future dilutes with example recommendations including to test with first morning urine and not "over-hydrate." After subsequent dilutes, participants have been required to use alternative testing methods such as Peth blood testing and hair testing, to take unannounced back-to-back urine tests and, if dilutes continue, to have a medical evaluation.

Just prior to these findings, Uprise Health revised the guideline governing responses to dilute specimens for participants in monitoring programs. Given these findings, the importance of the revisions is further underscored. Changes include a team approach to reviewing second, and subsequent, dilutes within a rolling year. The team includes the operations manager who oversees toxicology testing, the program manager and the participant's case manager. Additional testing will be implemented with a focus on alternative testing. With a pattern of dilutes, Uprise Health's psychiatric consultant and/or medical director may be involved and the participant may be required to have a medical evaluation.

Uprise Health is not surprised by the invalid toxicology findings. Over the summer of 2021, Uprise Health's national, certified toxicology vendor reformulated the reagent component for the ETG assay based on concern that it was causing the invalid results. The new reagent was tested and in most cases specimens that were invalid under the old reagent were negative with the new one. With the adjusted matrix, all of the toxicology vendor's clients, including Uprise Health, are seeing a significant reduction in invalids. This change validates the data finding that invalid results are not a predictor of future positive toxicology. With the new reagent in place, Uprise Health's monitoring program is observing a significant reduction in invalid toxicology specimens.

Although this study took place with data from physician health programs and alternative to discipline programs for professionals, these are just two monitoring program types with study applicability. The study and findings have generalizability to any abstinent-based monitoring program with a toxicology program component including DOT follow-up testing programs overseen by Substance Abuse Professionals (SAPs), employer-based programs, criminal justice-based programs in probation and parole and specialty court programs like drug treatment court.

Toxicology promotes abstinence and recovery. By better understanding predictors for potential positive toxicology, monitoring programs can adapt their responses to help prevent positive toxicology by addressing dilute toxicology early and conveying that dilute toxicology is unacceptable in an abstinent based program.

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