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The impact of opiate cut-off values in urine samples: Evaluation of 8 years of data

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Abstract

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Objective: Opiates are one of the most abused drugs with growing concern.In recent years, it is seen that changes have been made to the cut-off values for opiates.The cut-offs for opiates in screening tests increased from 300 to 2000ng/mL.The aim of this study was to present the opiate results of 8-year study and to evaluate the data according to cut-off values increased from 300 to 2000 ng/mL.
Methods: A total of 11,348 urine samples were analyzed between 2014–2021.Preliminary diagnoses, outpatient admissions, and toxicological test results were compared under two cut-offs. Screening tests were performed using immunoassay method (Randox Evidence and CEDIA), and confirmation analysis was conducted by Gas Chromatography-Mass Spectrometry (GC-MS).
Results: At the 300 ng/mL cut-off value, 3.45% of the cases were opiate-positive. 69.1% of the cases were from addiction clinics, demonstrating the clinical importance of sensitive cut-offs in detecting substance use among patients requiring treatment. In this study, it is shown that 39.8% of cases requiring judicial action were missed when the cut-off value was raised to 2000 ng/mL, highlighting the risk of false negatives in forensic settings.
Conclusion: The findings highlight that opiate cut-off values and analytical sensitivity may influence both medical evaluations and legal interpretations.
Keywords: Cut-off values; GC-MS; Immunoassay; Forensic toxicology; Judicial implications; Retrospective study; Opiates; Urine drug testing

Öz

İdrar örneklerinde opiyat eşik değerlerinin etkisi: 8 yıllık verilerin değerlendirilmesi

Amaç: Opiatlar, en sık kötüye kullanılan maddeler arasında yer almakta ve hem halk sağlığı hem de adli alan açısından artan bir endişe oluşturmaktadır. Son yıllarda opiat taramalarında kullanılan eşik değerlerinde değişikliklere gidilmiş ve tarama testlerindeki cut-off değerleri 300 ng/mL'den 2000 ng/mL'ye yükseltilmiştir. Bu çalışmanın amacı, sekiz yıllık opiat analiz sonuçlarını sunmak ve tarama cut-off değerinin 300 ng/mL'den 2000 ng/mL'ye yükseltilmesinin etkilerini değerlendirmektir.
Yöntem: 2014–2021 yılları arasında toplam 11.348 idrar örneği analiz edilmiştir. Ön tanılar, poliklinik başvuruları ve toksikolojik test sonuçları iki farklı cut-off değeri altında karşılaştırılmıştır. Tarama analizleri immünoassay yöntemleri (Randox Evidence ve CEDIA) ile, doğrulama analizleri ise Gaz Kromatografisi–Kütle Spektrometrisi (GC–MS) ile gerçekleştirilmiştir.
Bulgular: 300 ng/mL cut-off değeri kullanıldığında vakaların %3,45'i opiat pozitif bulunmuştur. Pozitif vakaların %69,1'inin bağımlılık ile ilişkili polikliniklerinden gelmiş olması, tedavi gereksinimi olan kişilerde madde kullanımının saptaması açısından cut-off değerlerinin klinik önemi ortaya konmuştur. Cut-off değeri 2000 ng/mL'ye yükseltildiğinde adli işleme konu olması gereken vakaların %39,8'inin saptanamadığı görülmüş ve bu durum adli bağlamda yanlış negatif sonuç riskinin belirgin şekilde arttığını göstermiştir.
Sonuç: Bulgular opiat cut-off değerlerinin ve analitik duyarlılığın hem klinik değerlendirmeleri hem de hukuki yorumları önemli ölçüde etkileyebileceğini ortaya koymaktadır. Bu nedenle cut-off değerlerinin seçimi, tıbbi ve adli süreçlerde doğru yorumlama yapılabilmesi açısından kritik öneme sahiptir
Anahtar kelimeler: Adli toksikoloji; Eşik değerler; GC-MS; İdrarda madde testi; İmmünoassay; Retrospektif çalışma; Opiatlar; Hukuki sonuçlar

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1. INTRODUCTION

The use of psychoactive drugs for various purposes has been increasing worldwide. According to the United Nations Office on Drugs and Crime (UNODC), 275 million people are linked to drug use worldwide in 2020, and this number is expected to increase by 11 percent by 2030 (1,2). Opiates are one of the most commonly abused drugs in recent times and contain some of the most widely prescribed drugs which have high abuse potential (3–5). Opiates, in particular, include both illicit compounds and widely prescribed analgesics with a high potential for misuse, thereby creating significant public health, socio-economic, and legal challenges (6,7).

Opiates have been an integral part of anesthesia and general health care for effective pain management for many years. However, prolonged medical use may increase the risk of dependence and subsequent misuse (8). Over the last two decades, prescription opioid misuse has risen substantially, and these drugs now represent the most frequently abused category of prescription medications (9). The growing prevalence of opioid-related clinical and forensic cases underscores the importance of accurate and reliable toxicological testing. In this context, the determination of appropriate cut-off values is particularly crucial, since they directly affect the interpretation of results in both healthcare and judicial systems. There is a lack of studies evaluating the forensic implications of changes in opiate screening cut-off values, and this study addresses that gap through an eight-year retrospective analysis

Cut-off values in immunoassay-based drug screening serve as critical decision points, balancing sensitivity against specificity. A lower cut-off values (e.g., 300 ng/mL for opiates) increases sensitivity and reduces the likelihood of missing true positive cases, but it also elevates the risk of false positives—for instance, following therapeutic codeine use or ingestion of poppy seed–containing products (10,11). Conversely, higher cut-off values (e.g., 2000 ng/mL, as established by the Substance Abuse and Mental Health Services Administration in 2010) minimize the risk of incidental positives. Inspired by this regulation, Türkiye, as a major producer of legal opium and a high consumer of poppy seed products, introduced national legislation in 2016 revising the cut-off to 2000 ng/mL for both clinical and forensic cases. This adjustment may result in false-negative outcomes in legally sensitive contexts such as probation monitoring, workplace testing, or driving under the influence of drugs (DUID) investigations. Therefore, understanding the effect of the cut-off value on the outcomes remains a critical priority in drug testing applications.

Against this background, the present study provides an eight-year retrospective evaluation of opiate screening results (2014–2021), specifically assessing the impact of raising the opiate screening cut-off from 300 ng/mL to 2000 ng/mL. The study aims to determine how these changes influence diagnostic accuracy, case categorization, and the likelihood of false-negative outcomes, with particular emphasis on its implications for laboratory practice.

2. METHODS

Urine drug testing was performed in 11,348 cases from various services between 2014 and 2021 at the Ege University Institute on Drug Abuse, Toxicology and Pharmaceutical Sciences (BATI), Addiction Toxicology Laboratory in Izmir. Clinical monitoring and treatment are provided in the Emergency Services (Adult Emergency Department, Child Emergency Department), Addiction Services (Adult Addiction Department, Adolescent Addiction Department (EGEBAM), and Mental Health and Diseases Services (inpatient clinics) where cases are brought for urine drug testing. Other services include cases that are performed for workplace drug testing, divorce and custody cases, individual applications, etc. The laboratory information system displays samples from cases that meet the sample acceptance criteria as studied samples. The study included results from cases that met these criteria and were analysed.The study was approved by the Ethics Committee of the Ege University Faculty of Medicine (Decision no: 23-1.1T/32).

2.1. Screening Analysis

The laboratory implemented the criteria of the EN ISO/IEC 17025 Quality Management System. Urine integrity parameters (e.g. pH, density and creatinine) were checked using urine adulteration test strips (Intect 7, USA) for all samples before analysis. The screening analysis were performed using two immunoassay devices in different years due to the acquisition process of the laboratory. Samples were analyzed using CEDIA between 2014 and September 2019, and with the Biochip Array Analyzer between September 2019 and December 2021. Both methods are designed for multi-analyte detection and covering a range of drug classes. These methods have a proven high standard of accurate test results with the coefficients of variation (CVs) <10%. For screening tests, a 9-point calibration curve was plotted containing each analyte to be analyzed. Morphine is the primary calibrator for the opiate testing. To ensure the method's validity, two-point quality control samples within the calibration range were analyzed. Once the control results were within the specified range, samples were injected into the device. This study involved analyzing urine samples according to the Drug of Abuse (DOA) panel. The DOA test panel includes substances such as amphetamines, benzodiazepines, cannabinoids, cocaine, and opiates. A full list of analytes and cut-off values

Table 1. Recommended Cut-off Concentrations (ng/mL) for screening analysis in T.C. Ministry of Health, SAMHSA, EWDTS (European Workplace Drug Testing Society), and SCDAT (Swiss Guidelines for Drugs of Abuse Testing) (13–16)

Substance	T.C Ministry of Health	SAMHSA	EWDTS	SCDAT
Amphetamine	500	500	500	500
Benzodiazepine	300	300	200	100
Cannabinoid (THC-COOH)	50	50	50	50
Cocaine	150	150	150	300
Opiate	2000	Codeine/morphine: **2000** Hydrocodone/Hydromorphone: 300 Oxycodone/Oxymorphone: 100	300	300

* SAMHSA regulated guideline at October 12, 2023.

tested is provided in Table 1. The normal creatinine range was defined as 5.6 mg/dL to 22.6 mg/dL, as recommended by the Ministry of Health in Türkiye(12).

2.2. Confirmation Analysis

2.2.1. Extraction of urine samples

In addition to cases being referred to The Adolescent Addiction Department (EGEBAM) for treatment purposes, forensic cases are also admitted from the probation office. Urine samples of forensic cases that were positive according to the cut-off value of 300 ng/ml were subjected to confirmation analysis. The extraction of samples was conducted through the utilization of a liquid-liquid extraction method that was developed within the laboratory. Firstly, the urine samples were subjected to hydrolysis by the addition of 1 ml of 1 mol/L potassium hydroxide (KOH) to 2 ml of the urine sample, followed by incubation at 60°C for 30 minutes. This process facilitates the breakdown of conjugates (e.g. morphine-3-glucuronide) into free morphine, thereby enabling precise quantification. Following a period of cooling, the mixture was extracted using a drug extraction tube (EqC Laboratory Technologies, Türkiye) for cleanup. One milliliter of the upper organic phase was transferred to a clean tube and evaporated to dryness under nitrogen. Derivatization was performed by adding 100 µL of N, O-Bis (trimethylsilyl) trifluoroacetamide (BSTFA) + 1% trimethylsilyl chloride (TMCS) and 50 µL ethyl acetate. After derivatization, the samples were placed in a vial and 1 µL was injected into the GC-MS.

2.2.2. GC-MS Conditions

Confirmation analysis was conducted by Agilent Technologies 5977A GC-MS. Chromatographic separations were carried out with an HP-5MS (30 m × 0.25 mm, 0.25 µm) (Agilent, California, USA) capillary column. The carrier gas utilized in this experiment was helium, with a flow rate of 1.5 mL/min. The temperature programme was initiated at an initial temperature of 150°C for a duration of one minute. Thereafter, the temperature was increased at a rate of 30°C/min until it reached 280°C, where it was maintained for a period of five minutes. The injection temperature was measured at 250°C, while the transfer line registered a temperature of 230°C. Mass spectrometry was performed in selected ion monitoring (SIM) mode. Trimethylsilyl derivatives were produced, and ions were monitored for morphine 196, 236, 414, 429, for morphine-d3 199, 296, 432.

2.2.3. Validation of the Method

The confirmation method was validated in terms of selectivity, extraction efficiency, linearity, precision, accuracy, LOD and LOQ, carryover, matrix effect, dilution integrity and stability according to Scientific Working Group for Forensic Toxicology (SWGTOX) Standard Practices for Method Validation in Forensic Toxicology (17,18). Calibration range was between 25-2000 ng/mL. Linearity data was shown in terms of correlation coefficient "r" as 0.9901. Extraction efficiency (R %) was calculated by comparing the standard/morphine-d3 peak areas using four different concentrations of morphine (50, 100, 250, and 500 ng/mL, n=3). To evaluate the accuracy (bias) and precision (repeatability) of the analytical method developed for morphine, same concentration levels were analyzed (n=3). The acceptable performance criteria for the method were defined as CV% ≤15% and bias% within ±20% limits. The LOQ, calculated as 10×signal-to-noise ratio, was determined to be 25 ng/mL for morphine. To evaluate the potential for carryover, blank matrix samples were analyzed right after the highest concentration level (2000 ng/mL) standard. There was no evidence of carryover contamination in the method, as the blank matrix samples produced no detectable relevant peaks. The Matrix Effect (ME%) was calculated using the ratio of the calibration curve slopes: the first derived from matrix samples spiked with the analyte after extraction, and the second derived from pure analyte solutions (absence of matrix). The slope ratio derived from the matrix-present and matrix-absent calibration curves was 0.9. Matrix Effect (ME%) was determined to be 10%, which is acceptable according to SWGTOX guidelines.

Table 2. Demographic information of opiate-positive cases according to admission departments

		Positive cases, n (%)								
		2014	2015	2016	2017	2018	2019	2020	2021	Total
Number of opiate positive cases, n (%)		28 (7.1)	104 (26.5)	95 (24.2)	88 (22.4)	45 (11.5)	4 (1.0)	14 (3.6)	14 (3.6)	392 (100.0)
Age mean		27.3	23.2	24.7	25.7	27.1	21.00	32.9	35.3	25.6
Min, max		(16-60)	(15-67)	(15-79)	(14-62)	(16-60)	(15-31)	(16-71)	(13-60)	(13-79)
<18 years old		7	24	12	10	5	2	3	2	65
Male age mean+ SD		29.9 ± 13.1	23.5 ± 8.9	24.9 ± 10.4	24.2 ± 8.1	29.5 ± 12.3	23.5 ±10.6	35.5 ±20.6	41.2 ±14.1	25.9±11.2
Female age mean + SD		19.9 ± 4.5	19.7 ± 4.5	23.7 ± 10.3	32.4 ± 16.1	16.6 ± 2.4	18.5 ± 4.9	17.5 ± 0.7	24.6±12.4	23.8±11.3
Admitted service, n (%)										
Emergency Services	Adult Emergency Department	3 (10.7)	3 (2.9)	4 (4.2)	4 (4.5)	2 (4.4)	2 (50)	3 (21.4)	6 (42.8)	27 (6.9)
	Child Emergency Department	1 (3.6)	1 (0.9)	-	5 (5.7)	1 (2.2)	2 (50)	-	3 (21.4)	13 (3.3)
Addiction Services	Adult Addiction Department	8 (28.6)	52 (50)	56 (58.9)	47 (53.4)	20 (44.4)	-	-	-	183(46.7)
	Adolescent Addiction Department (EGEBAM)	4 (14.3)	28 (29.6)	20 (21.1)	19 (21.6)	10 (22.2)	-	7 (50)	-	88 (22.4)
Mental Health and Diseases Services (inpatient clinics)*		8 (28.6)	16 (15.4)	12 (12.6)	12 (13.6)	7 (15.6)	-	-	-	55 (14.0)
Other Services**		4 (15.3)	4 (3.8)	3 (3.2)	1 (1.1)	5 (11.1)	-	4 (28.5)	5 (35.7)	26 (6.6)

*In the Mental Health and Diseases Services, inpatients with substance abuse or addiction are subjected to drug testing to follow up the treatment in cases receiving medical services.
* * "Other services" include cases that are performed for workplace drug testing, divorce and custody cases individual applications, etc.

2.3. Statistical Analysis

The related data was obtained from the laboratory data information system and analyzed statistically using SPSS 25.0 version from several perspectives. Descriptive statistical analyses were applied to summarize age groups, sex distribution, clinical admission units, the timing of positive cases, and related admission departments. These analyses included measures of central tendency and dispersion for age, as well as frequency and percentage distributions for categorical variables. No comparative or significance tests were performed, as all evaluations focused solely on the positive or negative status of forensic toxicology cases.

3. RESULTS

In the present study, 3.45% of cases (n=392) were found to be opiate positive above the cut-off value of 300 ng/mL. The mean age of these positive cases was 25.64±11.21 years and 83.7% (n=328) of them were male. In order to facilitate a more comprehensive understanding of the purpose of admission and to ascertain whether the request for drug testing was for security, clinical or forensic purposes, cases were methodically classified according to the department in which they were admitted. The majority of opiate positive cases came from drug addiction outpatient clinics, followed by inpatient mental health and diseases services and then the emergency department. Demographic information is given in Table 2.

Positive cases were categorised in accordance with two cut-off values: a) between 300-2000 ng/mL and b) >2000 ng/mL (Figure 1). When the cut-off was raised to 2000 ng/mL, 39.8% of cases that were positive under the 300 ng/mL criterion were reclassified as negative.

Figure 1. Distribution of opiate-positive cases according to 300<x<2000 ng/mL cut-off values and years

The 156 opiate-positive cases (identified using the 300<x<2000 ng/mL cut-off range) were tested for the presence of other controlled or illegal psychoactive drugs. Figure 2 details the yearly distribution of the most common drugs found, including their combinations with opiates. The table indicates a concomitant use rate of 23.8% (n=37) for

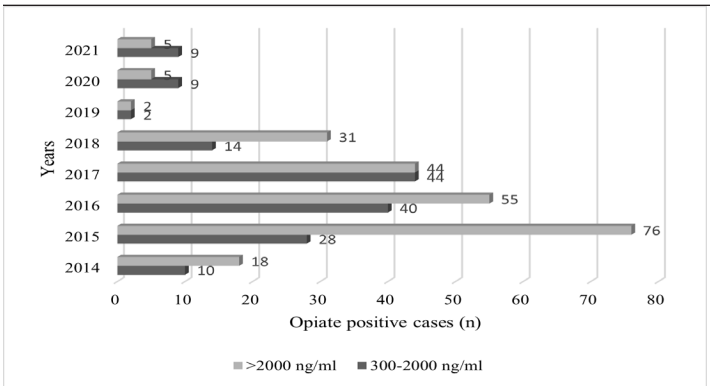


Figure 1. Distribution of opiate-positive cases at 300 and 2000 ng/mL cut-off values according to screening test results

opiates and buprenorphine, a substance frequently misused in opiate addiction treatment. Toxicological analysis also revealed that 18.71% (n=29) of these opiate + buprenorphine combination cases concurrently involved other psychoactive drugs (such as amphetamine-type stimulants (ATS) including amphetamine, methamphetamine, MDMA; benzodiazepine; cocaine; cannabis (THC); and synthetic cannabinoids).

Among opiate positive cases (n=156) in the cut-off range of 300<x<2000 ng/mL, the most frequently detected co-substances were benzodiazepines, ATS, THC and synthetic cannabinoids, respectively. Until 2019 (the pre-COVID-19 period), buprenorphine was commonly used alongside opiates, and it was observed that other psychoactive substances were frequently used in addition to this dual combination. Based on preliminary diagnoses, most cases (67.3%, n=264) were observed to have a diagnosis of "alcohol and substance use disorder," with "psychiatric disorders" representing the next most common finding (20.9%, n=82). Following the diagnoses detailed in Figure 3, the next most

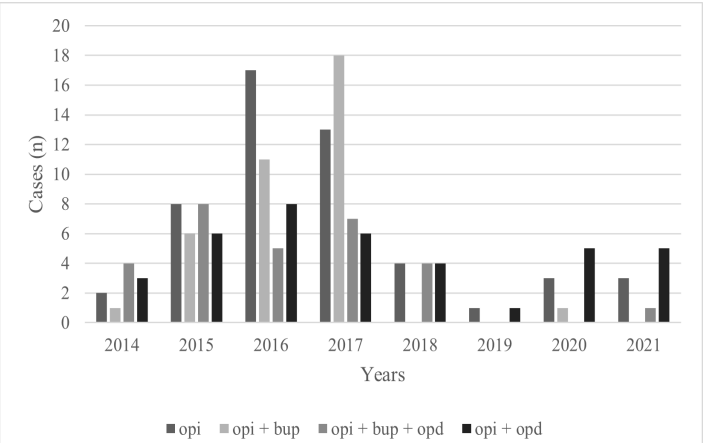
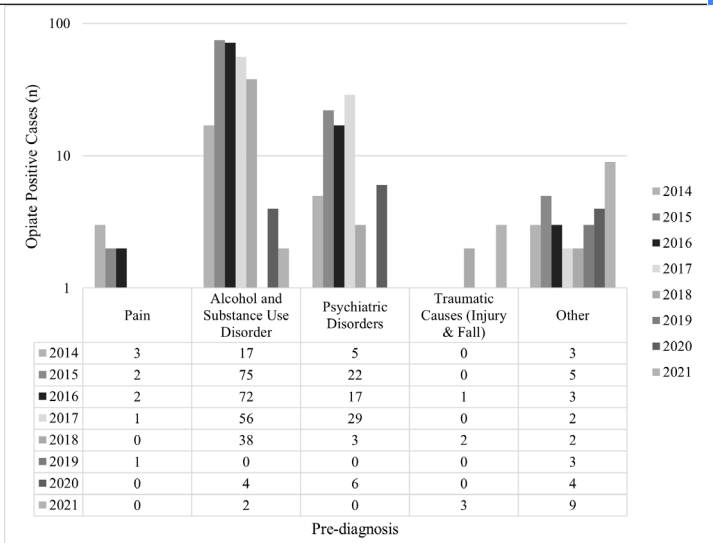


Figure 2. Drug use combination among opiate-positive cases in the cut-off range of 300<x<2000 ng/mL *opi: Opiates, bup: Buprenorphine, opd: Other Psychoactive Drugs ((amphetamine, methamphetamine, MDMA, etc. (amphetamine-type stimulants (ATS)), benzodiazepine, cocaine, cannabis (THC), synthetic cannabinoids)



	Pain	Alcohol and Substance Use Disorder	Psychiatric Disorders	Traumatic Causes (Injury & Fall)	Other
2014	3	17	5	0	3
2015	2	75	22	0	5
2016	2	72	17	1	3
2017	1	56	29	0	2
2018	0	38	3	2	2
2019	1	0	0	0	3
2020	0	4	6	0	4
2021	0	2	0	3	9

Figure 3. Pre-diagnosis of the opiate positive cases between 2014-2021

frequent preliminary diagnoses were related to severe pain and trauma, including falls and injuries. Significantly, 37.5% (n=99) of cases diagnosed preliminarily with alcohol and substance abuse tested opiate positive using the 300<x<2000 ng/mL cut-off range. Despite these cases having a documented history of substance abuse (confirmed by anamnesis and drug test results), they were formally classified as negative according to the higher 2000 ng/mL cut-off value.

4. DISCUSSION

This study presents eight years of opiate analysis data evaluated according to two opiate cut-off values and provides information about opiate use in Türkiye. Using the cut-off value of 300 ng/mL instead of the legal value of 2000 ng/mL used in this study, 39.8% of cases (n=156) could have been considered opiate positive. This study provides concrete findings that cases reported as negative, but should have been considered positive, may have forensic dimensions. These negative cases could have included probation, drive under the influence of drugs (DUID) and cases of workers using or under the influence of drugs in the workplace. A high cut-off value may lead to "false negative" results and underestimation of the possibility of "opiate positivity". This study provides robust laboratory evidence supporting a re-evaluation of the administrative decision to raise opiate screening cut-off value. As can be seen from the data of this study, raising the opiate limit value in legal practice to prevent "false positivity" may increase "false negativity", especially in forensic cases.

Between the 300 and 2000 ng/mL cut-off values, the use of psychoactive drugs among opiate positive cases was evaluated and it was observed that the cases used benzodiazepines, THC and ATS with opiate use. Detection of drug use in cases plays an important role in the prosecution of cases in legal proceedings and is also important from a medical point of view in the evaluation of the clinical treatment of cases.

Considering the effects and dangers of polysubstance use and in-depth analysis of the types of substances used by opiate positive cases between 300<x<2000 ng/mL, 23.07% (n=36) were also using benzodiazepines. Taking opiates with central nervous system depressants such as benzodiazepines is known to increase the risk of life-threatening overdose (19,20). 2021 reported that about 14% of opiate-related overdose deaths involved benzodiazepines, a type of prescription tranquilizer often prescribed for anxiety or to help with insomnia. Combining opiates and benzodiazepines increases the risk of overdose as both types of drugs can cause sedation and respiratory suppression as well as impairing cognitive function. Research shows that using opiates and benzodiazepines combination have a higher risk of going to the emergency room, being hospitalized for a drug-related emergency and dying from a drug overdose (21). It should be noted that benzodiazepines are frequently used in addiction treatment processes as well as anxiety treatment in Türkiye. Although 23.07% of the patients also tested positive for benzodiazepines, the study did not distinguish whether their use was therapeutic or illicit, which represents a limitation of the analysis.

The preliminary diagnosis determines the direction of further assessment of a case. The preliminary diagnoses of the cases help to determine whether the case requires a forensic or clinical approach. In this study, when the cases were evaluated according to their preliminary diagnoses, 67.3% of the cases with a preliminary diagnosis of "alcohol and substance use disorder" were found to be opiate-positive according to the cut-off value of 300 ng/mL. However, 37.5% of "alcohol and substance use disorder" cases are considered negative according to the cut-off value of 2000 ng/mL. The possibility of substance use-related harm to the social life, work place or family life of people who are reported as negative due to this situation points should not be ignored. In addition, as can be seen in Figure 3, these individuals had drug-related diagnoses from the relevant outpatient clinics and applied to our laboratory with a request for drug testing. This situation shows that the cases should be evaluated separately with a forensic or clinical approach, considering the polyclinics to which the cases applied and their preliminary diagnoses. It should be noted that if these cases are evaluated within the scope of workplace drug tests, since opiate cut-off values of 300 ng/mL and above affect the individual skills of the person according to the guidelines for workplace drug tests, it will be seen that these cases falling between 300-2000 ng/mL cut-off values are actually possible positives (13,22,23).

The Adolescent Addiction Department (EGEBAM) and addiction polyclinic have large number of clinical cases coming for addiction treatment, as seen in Table 2. The evaluation of drug abuse in children and adolescents under the age of 18 was carried out at the Child and Adolescent Substance Addiction Treatment Center and the same opiate cut-off levels was used. Recommended cut-offs were developed for adult populations and may not be appropriate for children or adolescents who produce less concentrated urine. Under-18 years of age produce less concentrated urine due to the biological and physiological characteristics of this age group. This can have significant implications for the reliability of urine samples, especially those used in tests for illegal drugs (such as immunoassays) (24). Individuals under 18 years produce less concentrated urine due to developmental physiology, which may increase the likelihood of false negatives at fixed cut-off levels (25,26). It can increase the false negative rates of the test and optimizing the cut-off value of the test requires more attention to ensure the accuracy of the test. In this case, it is important to carefully adjust the specificity and sensitivity parameters of the tests and determine appropriate cut-off values for different age groups. According to this retrospective study, 16.5% of opiate-positive cases according to 300 ng/mL belong to people under the age of 18 years, and this data showed that the cut-off value should also differ according to the purpose of the test.

Different cut-off values are used in drug testing depending on the purpose of analysis, laboratory technique, biological matrix, and national regulations(12,27–29). In Europe, cut-off levels for opiate testing vary considerably. For instance, Belgium generally applies lower cut-off values for rapid and sensitive screening, while Germany (30) and Italy (31) tend to use higher cut-off values (commonly 1000–2000 ng/mL in Germany and 300–1000 ng/mL in Italy) to increase specificity and reduce false positives (35,36). Such variability may lead to international inconsistencies, potentially affecting test reliability and producing false-positive or false-negative results. Some countries, such as Portugal, use a 300 ng/mL cut-off for workplace testing. Overall, laboratories may adopt cut-off values independent of SAMHSA guidelines to align with national legal requirements, and several countries publish their own standards, such as AS/NZS 4308, AS 4760, or European Guides for Occupational Drug Testing in Urine (22,32).

On the one hand, there are different practices and regulations among countries for the recommended cut-off value of 2000 ng/mL for opiates (27,33), and on the other hand, as a hot news, SAMHSA Department of Health and Human Services decided to use a cut-off value of 4000 ng/mL for the confirmatory cut-off value of morphine in the guideline published in 2023 (34). However, it is pointed out that this guideline should not apply to the persons in the criminal justice system, such as arrestees, detainees, probationers, incarcerated persons, or parolees. It is thought that this decision may cause undesirable effects such as a further

increase in false-negative results when the cut-off value is increased from 300 ng/mL to 2000 ng/mL and a decrease in the sensitivity of the tests, and may create problems that will be discussed in the coming years. The differences between forensic and clinical laboratories significantly affect the approach to the case and results of drug analysis. Krug and Scott reported in 2020 that this situation makes it imperative for laboratories to remain vigilant (35). While forensic toxicological laboratories require a much more careful and meticulous approach in terms of legal validity and accuracy of results, clinical laboratories produce more health-oriented results and aim to guide treatment. In forensic toxicological laboratories, case details (cause of case, time, and history of the incident, drug use etc.) are evaluated with the cases. These differences directly affect the sensitivity of the tests, cut-off values and interpretation (9,36,37).

5. CONCLUSION

In recent years, opiate cut-off values have undergone several revisions, affecting the interpretation of drug screening results. In this study, raising the cut-off value to 2000 ng/mL would have resulted in missing 39.8% of cases that required judicial action, highlighting the substantial impact of administratively determined thresholds on outcomes in contexts such as probation monitoring, workplace safety assessments, and legally mandated treatment programs. These findings underscore the need for context-specific and population-adjusted screening limits. Overall, the study demonstrates that cut-off values are not merely analytical benchmarks but critical determinants of accuracy, fairness, and safety in both clinical and judicial applications.

Limitations of the Study

6-Monoacetylmorphine (6-MAM) analysis, which was conducted from 2014 to 2018 (6-MAM was positive in 4.2% (n=15) of opiate-positive cases in that period), could not be performed after 2018 due to technical issues with the laboratory equipment, which may have affected the completeness of the data.

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Peer-Review

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Conflict of Interest

The authors declare that they have no conflict of interests regarding content of this article..

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Ethical Declaration

Ethical permission was obtained from the Ege University Faculty of Medicine, Medical Research Ethics Committee (Decision no: 23-1.1T/32) and Helsinki Declaration rules were followed to conduct this study.

Is Previously Presented?

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Authorship Contributions

Idea: DYO, RA, SAA Design: DYO, RA, Supervision: SAA, Funding: -, Instrumentation: DYO, RA, Data collection and processing: DYO, RA Analysis and interpretation: DYO, RA, JR SAA Literature review: DYO, RA,JR, SAA Writing: DYO, RA,JR Critical review: SAA.

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