Latent Class Analysis of DSM-5 Criteria for Opioid Use Disorders: Results from the Iranian National Survey on Mental Health

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Abstract

Background: Assessments of DSM-IV and DSM-5 criteria with sample populations of opioid users are limited. This study aimed to determine the number of latent classes in opioid users and assessment of the proposed revisions to the DSM-5 opioid use disorder (OUD) criteria. ***Methods:*** Data came from the 2011 Iranian National Mental Health Survey (IranMHS) on 7,886 participants aged 15–64 years living in Iran. We used the Composite International Diagnostic Interview (CIDI) version 2.1 in all respondents who indicated using opioids at least 5 times in the previous 12 months (n = 236). ***Results:*** A three-class model provided the best fit of all the models tested. Classes showed a spectrum of severity that was compatible with the DSM-5 classification. 'Legal problems' and 'desire to cut down' showed poor discrimination between classes. The weighted prevalence of OUD using DSM-5 was 20.7% higher than with DSM-IV. ***Conclusions:*** Results support the grouping based on severity of symptoms, combining abuse and dependence into a single diagnosis, omitting legal problems, and addition of craving as a new criterion.

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Introduction

The diagnosis of substance use disorders had been based on the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) criteria which was published in 1994 [1]. These criteria were in two distinct categories: substance abuse and substance depen-

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dence. Diagnosis of abuse was based on meeting one of the four criteria, and confirming dependence required meeting three of the seven criteria. In light of limitations of this method and results of studies conducted in the past two decades, the Substance Use Disorders Workgroup for DSM-5 suggested combining abuse and dependence criteria, removing the old criterion pertaining to 'legal problems', and adding a new 'craving' criterion, which is an ICD-10 criterion. It also classifies substance use disorders in terms of severity as unaffected (0–1 criterion), mild (2–3 criteria), moderate (4–5), and severe (≥6) [2].

In the past two decades, multiple studies have assessed the DSM-IV criteria using factor analysis, item response theory, and latent class analysis (LCA). Results of some older studies demonstrated that abuse and dependence criteria are distinct and show two different aspects [3–6]. However, recent studies on consumers of alcohol [7, 8], cannabis [9–13], opioids [9, 10, 14], nicotine [15, 16], and other addictive substances [9, 17, 18] suggest one aspect for both.

LCA is used for grouping individuals according to their characteristics. Several studies conducted on opioid users in clinical populations [19–21] or the general population [9, 22, 23] have used LCA for determining the number of classes according to the drug use pattern, other drugs used with opioids, or other associated behaviors. There is only one LCA study on DSM-IV criteria for opioid use disorders (OUDs) in 501 clinical cases [21], which categorized cases in two classes. The two classes were close to the classification of abuse and dependence. However, LCA on alcohol, marijuana, and cocaine users showed that the classes are differentiated according to the number of fulfilled criteria and cannot be categorized to abuse and dependence [24].

Recent studies have shown a weaker validity and reliability for DSM-IV abuse criteria than dependence criteria [10, 25], and have concluded that substance abuse should not be considered the beginning or a mild form of dependence for the following reasons. Firstly, some individuals meet at least three of the dependence criteria without any of the abuse criteria [24]. Secondly, the age of onset of substance abuse symptoms in adults and adolescents does not differ, and the age of onset for abuse is not earlier than that for dependence [26, 27]. And thirdly, many individuals who meet the criteria for abuse do not shift to the dependence stage [28]. Thus, the hierarchical approach in DSM-IV is not valid.

On the other hand, some studies have indicated that it seems logical to eliminate the 'legal problems' crite-

rion because it is uncommon among substance users [9, 13, 29], provides little information about the substance use disorder, and has weak factor loading [8, 18, 29–33].

Another weakness of DSM-IV concerns individuals who meet two dependence criteria, but are not diagnosed as dependent; these cases are given diagnostic orphan status [34]. Many adolescents and adults with clinical symptoms may fall in this category [35]. Follow-ups have shown that these individuals may have the same severity as cases with a confirmed diagnosis of dependence [36], or they can be at a higher risk of substance dependence compared to those who meet no criteria [37, 38]. Recent studies suggest that using DSM-5 criteria may reduce the number of subthreshold cases [30, 39].

Another suggested change in DSM-5 is adding a 'craving' criterion, which is considered the first criterion in ICD-10 [40] and is expected to increase the comparability and agreement between DSM-5 and ICD-10 [31]. This criterion is considered a core symptom for substance use disorders [31], and addressing it can be a core objective in the treatment of the disorders. Some studies have shown that this criterion appeared to fit well with other criteria and has high discrimination and factor loading [10, 41]. There are also studies that do not recommend adding this criterion. A study indicates that 'craving' is quite similar to 'continued use despite problems' [41], and another study has demonstrated that adding a 'craving' criterion has no effect on the diagnosis of disorders [30]. One LCA study shows that the symptom differentiates substance abuse and substance dependence [21]. This is while most LCA studies agree that classes demonstrate different symptom severity and not symptom type [25, 42].

Assessments of DSM-IV and DSM-5 criteria of OUDs are limited. Globally, Iran has one of the highest rates of opioid consumption [43], and the Iranian National Mental Health Survey (IranMHS), conducted in 2011, has provided an opportunity to examine these criteria in opioid users in the general population. The purpose of this study was to apply LCA on opiate consumers to determine the number of classes they fit in, using the suggested criteria for DSM-5 [2], compare it with DSM-IV, and examine combining the abuse and dependence criteria, examine adding a 'craving' criterion and eliminating the 'legal problems' criterion, look at the relationship between treatment history, number of criteria, and class membership, and compare the DSM-5 cutoffs and the cutoffs that emerged from LCA.

Methods

For this study, we used data from IranMHS, a national cross-sectional household study conducted in the first half of 2011. Sampling for IranMHS was done nationally, targeting the 15- to 64-year-old population residing in households. The study was conducted on 7,886 people selected based on a three-stage random sampling method. The response rate was 86.2%. The main tool, which was also used for data analysis in this research, was the Composite International Diagnostic Interview (CIDI), version 2.1. The reliability of the Persian version regarding alcohol and substance use modules had been examined and approved for psychiatric inpatients and outpatients [44]. The reliability was also reexamined and confirmed during the preliminary stage of the IranMHS in psychiatric inpatients and outpatients, and in outpatients of a primary healthcare center [45]. The modules contained questions for screening, frequency of use, and symptoms of substance use disorders, including abuse and dependence based on the diagnostic criteria of DSM-IV and ICD-10. Considering the three-stage sampling approach, data analyses were performed with weighting based on the national population by 5-year age groups, gender, and urban/rural residence in each province to the number of cases in each of these subgroups. The participants were also asked about their outpatient and inpatient service use in the past 12 months and the main complaints for service use. The design, field procedures, analysis, and ethical considerations of the IranMHS is described in detail elsewhere [46].

Of the 7,886 people who participated in the study, analysis was conducted on the 236 participants who had used opioids at least 5 times in the past 12 months. All 236 participants answered all criteria questions.

We employed LCA, which is a method based on individual characteristics that fits them into distinct classes. For LCA, contingency tables were generated and item response probabilities and latent class prevalence (two parameters in latent class models) were estimated using the maximum likelihood method. According to Collins and Lanza [47], 'The item response probability is the probability of a particular response to a particular task, or item, conditional on membership in a particular latent class.' These probabilities demonstrate the rate of occurrence of a given response (e.g. positive response) in a given class. A high probability in a given class indicates that the response is a characteristic of individuals in that class. Therefore, the output provides the basis for interpreting results and defining labels for the LCA classes. Lack of difference among classes indicates that the respective question lacks the ability to distinguish classes. Latent class prevalence demonstrates how individuals are distributed among different classes and what percentage of individuals each class contains.

To ensure the ability to detect the model, we used an expectation maximization algorithm, and to ensure the reliability of results the model was run with 5,000 iterations 100 times with each analysis. Analyses were done for all DSM-5 criteria with and without 'legal problems' and 'craving' in several stages, and models with 1–7 classes were fit. We used the Bayesian information criterion (BIC) and Akaike information criterion (AIC) to determine the number of latent classes. Lower BIC or AIC indicated a better fitting model. In addition to these criteria, parsimony and model interpretability were noted. All analyses were done using the R software package [48]. We used a Kruskal-Wallis test for comparing median number of criteria in different groups. In order to assess the relationship between treatment history and membership in latent classes, we entered the treatment history as a covariate into the model and calculated the odds ratio. The prevalence of treatment history was determined by posterior probability and was according to membership of each individual in a class.

Results

Of the 236 individuals who had a history of using opioids at least 5 times in the past 12 months, 91% were men. The mean age was 36.4 years, ranging from 17 to 64. The frequency of opioid use in the past 12 months was daily in 58.1%, 3–4 times a week in 4.7%, once or twice a week in 11.4%, 1–3 times a month in 11.9%, and less than once a month (at least 5 times a year) in the remaining 14.0%. The type of opioid used in the past 12 months was opium/opium dross in 85.2% of cases, shireh (a refined opium extract) in 19.9%, methadone (without prescription) in 11.0%, heroin/crack of heroin in 8.5%, and morphine in 0.9%. Crack of heroin is a heroin-based narcotic with a high concentration of acetylcodeine [49].

Of the studied criteria, 'legal problems' (4.7%) and 'desire to cut down' (66.1%) had the lowest and highest counts, respectively. In terms of the number of criteria for each individual, those with one criterion had the highest relative frequency (16.0%), and those with 8 of the 11 DSM-5 criteria showed the lowest relative frequency (3.4%; fig. 1).

Based on DSM-IV criteria, 57.7% of opioid users were diagnosed with OUDs (dependence and abuse), which comes to a weighted prevalence of 1.8% for the total studied sample. Based on the DSM-5 criteria, 71.2% of opioid users had OUDs, which gives a weighted prevalence of 2.2% for the total studied sample. Compared to results with DSM-IV, the rate was 20.7% higher. Table 1 shows distribution of opioid users based on DSM-IV and DSM-5 grouping criteria.

Based on DSM-IV criteria, 49.2% of the 236 individuals were diagnosed with opioid dependence, 8.5% with opioid abuse, and 29.2% were diagnostic orphans, i.e. they only met one or two of the dependence criteria. Among diagnostic orphans, the most frequent criteria were 'desire to cut down' (72.5%), followed by 'withdrawal' (27.5%) and 'tolerance' (14.5%), while only 1.4% had reported the 'give up' criterion. Based on suggested criteria for DSM-5, overall 34.7% were diagnosed with severe OUD, 13.6% were classified as moderate, 22.9% were classified as mild, and the remaining cases were affected but did not reach a diagnostic threshold. Of those who
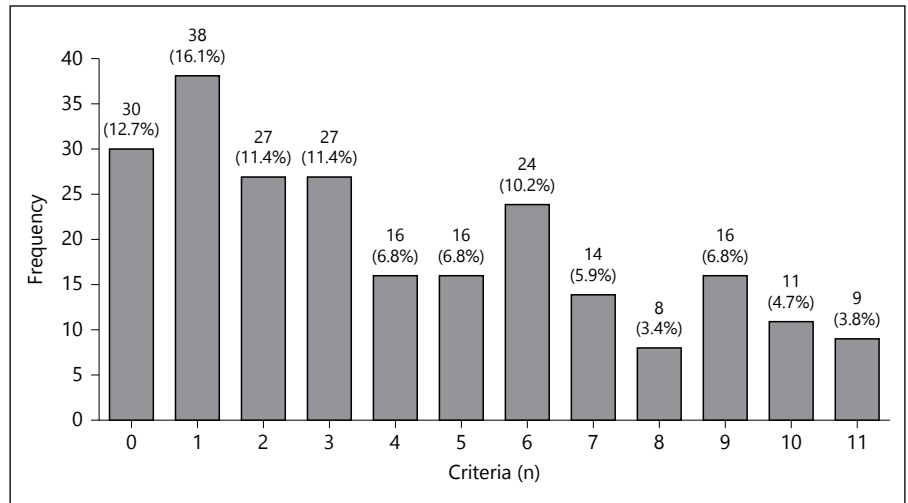
Fig. 1. Distribution of total counts of DSM-5 criteria.

Table 1. Distribution of opium and its derivatives users in the IranMHS based on DSM-IV and DSM-5 grouping criteria

DSM-IV	DSM-5					
	severe	moderate	mild	one criterion	no criteria	total
Dependence	82 (34.7)	24 (10.2)	10 (4.2)	0 (0)	0 (0)	116 (49.1)
Abuse	0 (0)	8 (3.4)	11 (4.7)	1 (0.4)	0 (0)	20 (8.5)
Diagnostic orphan[1]	0 (0)	0 (0)	33 (14.0)	36 (15.3)	0 (0)	69 (29.3)
No criteria	0 (0)	0 (0)	0 (0)	1 (0.4)	30 (12.7)	31 (13.1)
Total	82 (34.7)	32 (13.6)	54 (22.9)	38 (16.1)	30 (12.7)	236 (100)

Values represent n (%). [1] Those with one or two criteria of dependence.

Table 2. Summary of information for selecting number of latent classes among opioid users in IranMHS based on DSM-5 criteria (n = 236)

Model	Number of parameters	log likelihood	BIC	AIC
1 class	11	–1,497.144	3,053.467	3,016.288
2 class	23	–1,211.073	2,545.883	2,468.145
3 class	35	–1,162.779	2,513.855	2,395.558
4 class	47	–1,149.958	2,552.771	2,393.916
5 class	59	–1,137.056	2,591.527	2,392.113
6 class	71	–1,124.279	2,630.531	2,390.559
7 class	83	–1,116.613	2,679.758	2,399.227

were categorized as diagnostic orphans based on DSM-IV criteria, 33 cases (47.8%) were diagnosed with mild OUD using the DSM-5 criteria (table 1).

By LCA, model fitting to the data was done for 1–7 classes using the suggested criteria for DSM-5. Using BIC to compare the fit of the model, the best-fitting model was the 3-class model (table 2). In this model, class 1 with 43.8% of the cases showed the lowest item response probability and class 3, which contained 23.0% of the cases, had the highest item response probability for all criteria.
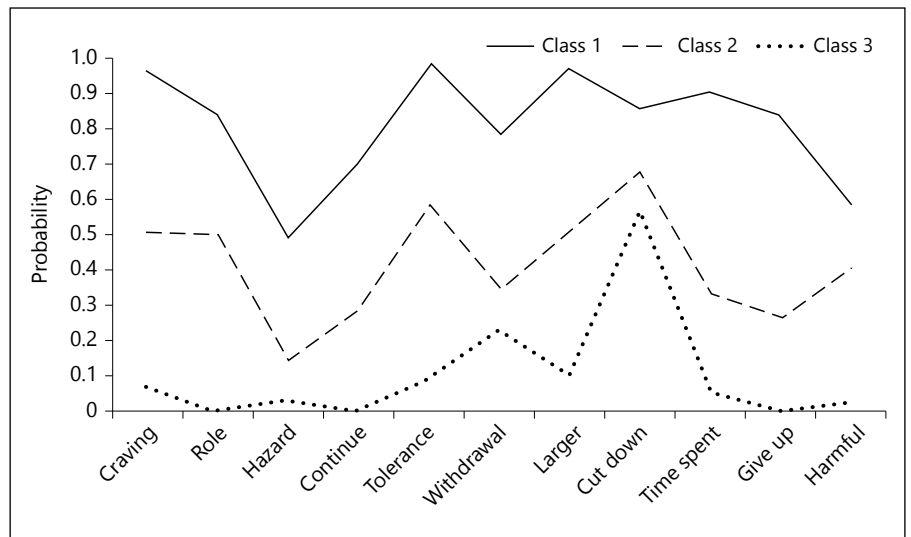
Fig. 2. DSM-5 criteria endorsement probabilities for class 1 (43.8%), class 2 (33.2%), and class 3 (23.0%), n = 236.

Table 3. Item-response probabilities from three latent class models based on DSM-5 OUD criteria among opioid users in IranMHS (n = 236)

	Class 1	Class 2	Class 3	Proportion endorsing
Prevalence	0.438	0.332	0.23	
Craving	0.066	0.514	0.967	0.432
Recurrent use resulting in failure to fulfill major role obligation at work, home or school	0.000	0.505	0.843	0.373
Recurrent use in physically hazardous situations	0.034	0.143	0.490	0.174
Continued use despite persistent or recurrent social or interpersonal problems caused or exacerbated by substance	0.000	0.294	0.714	0.254
Tolerance (marked increase in amount; marked decrease in effect)	0.092	0.601	0.991	0.475
Characteristic withdrawal symptoms; substance taken to relieve withdrawal	0.233	0.355	0.786	0.415
Substance taken in larger amounts and for longer periods than intended	0.107	0.523	0.977	0.432
Desire to cut down	0.573	0.685	0.864	0.661
Much time/activity to obtain, use, recover	0.053	0.339	0.909	0.347
Important social, occupational, or recreational activities given up or reduced	0.000	0.275	0.842	0.292
Use continues despite knowledge of adverse consequences (e.g. failure to fulfill role obligation, use when physically hazardous)	0.024	0.411	0.595	0.280

Class 2, with 33.2% of the cases, had moderate probability (table 3). Response probability for each item is demonstrated in table 3 and figure 2. Model fitting to the data for 1–10 classes was also done using DSM-IV criteria for opioid dependence and abuse. Similarly, BIC indicated that the 3-class model fit best, and class 1, with 48.0% of the cases, showed the lowest item response probability for all criteria. Class 3, which contained 18.9% of the cases, had the highest item response probability for all criteria, and class 2, with 33.2% of the cases, had moderate probability (table 4).

In order to validate the severity criteria with another indicator, the studied sample was categorized into three groups based on their history of presenting to a treatment center in past 12 months. Group 1 did not seek any service (n = 149), group 2 had a history of outpatient care, but not hospitalization (n = 65), and group 3 had received inpatient care (n = 22). The median number of criteria in these three groups was 2, 6, and 9, respectively, and the intergroup difference was significant (p < 0.001). Moreover, history of treatment in class 2 was not significantly higher than in class 1 (odds ratio: 2.2, confidence

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Table 4. Item-response probabilities from three latent class models based on DSM-IV OUD criteria among users of opium and its derivatives in IranMHS (n = 236)

	Class 1	Class 2	Class 3	Proportion endorsing
Prevalence	0.480	0.332	0.189	
Recurrent use resulting in failure to fulfill major role obligation at work, home or school	0.000	0.566	0.889	0.373
Recurrent use in physically hazardous situations	0.038	0.156	0.540	0.174
Recurrent substance-related legal problems	0.000	0.048	0.154	0.047
Continued use despite persistent or recurrent social or interpersonal problems caused or exacerbated by substance	0.014	0.317	0.768	0.260
Tolerance (marked increase in amount; marked decrease in effect)	0.105	0.671	1.000	0.477
Characteristic withdrawal symptoms; substance taken to relieve withdrawal	0.221	0.389	0.857	0.417
Substance taken in larger amounts and for longer periods than intended	0.049	0.387	0.679	0.451
Desire to cut down	0.557	0.716	0.901	0.661
Much time/activity to obtain, use, recover	0.066	0.398	0.934	0.347
Important social, occupational, or recreational activities given up or reduced	0.000	0.356	0.855	0.292
Use continues despite knowledge of adverse consequences (e.g. failure to fulfill role obligation, use when physically hazardous)	0.124	0.596	0.967	0.286

interval: 0.7–6.8), but the difference was significant between class 3 and class 1 (odds ratio: 36.9, confidence interval: 10.4–130.7).

From the 69 cases of diagnostic orphans based on DSM-IV, only 9 had received outpatient care and none had received inpatient care in the past 12 months. Five of the 9 were diagnosed with OUD by DSM-5. Overall, 54 individuals were diagnosed with mild OUD by DSM-5. Thirty-three of these 54 cases were diagnostic orphans by DSM-IV and 15.2% of them had a history of treatment in past 12 months. However, from the remaining 21 who were with OUDs by DSM-IV, 42.9% had been treated for the disorder and the difference was significant (p = 0.02). According to DSM-5, individuals may have 0–11 criteria. All individuals in class 1 had 0–3 of the 11 DSM-5 criteria, the majority of those in class 2 had 3–7 criteria, and the majority of those in class 3 had 7–11 criteria.

Discussion

To the best of our knowledge and according to the published documents, this is the first study examining DSM-IV and DSM-5 criteria for OUD in the general population. Most previous studies carried out on OUD have been conducted in treatment centers and targeted patient populations [10, 14, 19].

Our findings indicated that using DSM-5 criteria for OUD increases the diagnosis in opioid users and the general population by 20.7% compared to DSM-IV. This was due to a reduced cutoff point from three criteria to two criteria and greater diagnosis of DSM-IV orphans by DSM-5 as OUD. With the new classification, only one person changed from affected to unaffected status; this individual only met the hazardous situations criterion. Studying alcohol use disorders in the general population in the United States, using DSM-5 criteria increased the diagnosis by 11.3% [39], while a study in Australia showed an increase of 61.7% [41]. Compared to these results, our observation with opioids was a moderate increase.

The studied opioid users fit in three ordinal classes, which represent a spectrum of severity. In LCA, classes are identified and interpreted based on item response probabilities. As the results demonstrated, the only characteristic that differentiates individuals in class 1 from those in the other two classes is that they had the lowest and those in class 3 had the highest item response probabilities for all criteria. If this probability was higher for some criteria in a class, those criteria would be the prominent symptom that would differentiate the class from the other two classes. These observations confirm the dimensionality model of DSM-5. Other studies using LCA agree that classes represent a continuum of severity [5, 24, 25, 42]. Results of other recent studies on opioids [9, 10, 14], alcohol [7, 8, 10, 29, 31–33, 41], cannabis [9–13], nicotine [16, 38], and other addictive substances [9, 17, 18] are in agreement with this finding. In addition, the association of history of treatment for OUD in the past 12 months

with the resulting classification by LCA showed the validity of the classification.

Although it indicated a continuum of severity among the three classes, the 'legal problems' criterion, is not diagnostically helpful because the response probabilities for this criterion was low in all classes compared to other criteria, and thus including or excluding it would not impact the overall results. In light of the addictive nature of opioids, this observation was quite expected and is in agreement with results of other studies [8, 12, 13, 18, 29–33].

As for the craving criterion, the positive response rate was as high as 97% for class 3 and only 6.6% in class 1 where cases have no or minimal problems. The good fit of this criterion along with other criteria and its association with the continuum of severity among classes, as suggested in previous studies [10, 31, 41], indicate that the criterion can simply be used with all other DSM-5 criteria. In addition, excluding 'legal problems' and including 'craving' in a sample of heroin users under treatment [10] was validated, but only the exclusion of 'legal problems' was recommended in another study on opioid users [30].

Combining abuse and dependence criteria for opioid use disorders has been suggested in some studies of opioid users, alone or with other substances [9, 10, 14]. Also, performing LCA on a sample of individuals under treatment for OUDs indicated that these individuals fall into two separate classes. These two classes, which were in line with the classification suggested in DSM-5, showed moderate or severe symptoms [19].

Applying DSM-IV criteria leaves a number of individuals with no diagnosis (diagnostic orphans). However, results of our study indicated that about half of these cases fit in the mild category when DSM-5 criteria were applied. As suggested by other studies, using DSM-5 criteria can help make a diagnosis in this group [30, 39]. However, due to the lower prevalence of receiving drug treatment in the group of diagnostic orphans in comparison of those diagnosed as OUDs by DSM-IV, it is possible that DSM-5 is overdiagnosing.

Another observation in this study was the high response probability of the 'desire to cut down' in all three classes. This criterion was also the most common one to define diagnostic orphans. This can be examined from two aspects. Firstly, the probabilities are close in the three classes, i.e. it provides weak discrimination in the studied sample and, thus, may not be helpful in the diagnosis of OUDs in Iran. Secondly, the response probabilities are high in all three groups, i.e. most individuals, irrespective of their class, are willing to cut down or pretend to do so during the interview, which can be due to social and cultural issues in Iran. Nonetheless, other studies have reported that this criterion has lower item discrimination compared to other criteria [8, 29, 31] or have not reported high factor loading [29, 33]. The other symptoms reported as diagnostic orphans were withdrawal and tolerance. It seems possible that there might be underreporting of tolerance or possible overendorsement of withdrawal.

Our study has three strengths. First, no similar study had been conducted on the population of Iran before. Second, the study was conducted on a national level, which increases its external validity. The third strength is that our data was new and collected in 2011, and thus reveals the status on current users. Many recent publications in this field are conducted by reanalyzing old data, which has been mentioned as a limitation of these studies as it may differ from the current symptomatology in their populations.

One of the three main limitations of our study was the small number of cases. The second limitation was that the data was collected through self-report and it may have been affected by recall bias; referring to the past 12 months reduced this limitation. The third limitation was that consuming, carrying, buying, and selling opioids is a criminal offense in Iran; although several measures were taken in IranMHS to ensure participants of the confidentiality of their information, it is very likely that this limitation has led to an underestimated number of substance users and has impacted the declared pattern of symptoms.

In conclusion, the present study demonstrated that opioid users fit in three classes whose patterns of response to criteria differ only in terms of number of symptoms to identify cases with no disorder, moderate disorder, and severe disorder. The study confirmed combining abuse and dependence criteria in DSM-5, excluding 'legal problems', and including 'craving'. In the studied sample, 'desire to cut down' lacked the ability to distinguish classes. Due to the similarities in cultural background and the drug scene between Iran and neighboring countries, these findings might be relevant to opioid users of those countries, as well.

Disclosure Statement

Dr. Afarin Rahimi-Movaghar is a member of the 'World Health Organization (WHO) International Advisory Group for the Revision of the ICD-10 Mental and Behavioral Disorders' and a member of 'WHO ICD-11 Working Group on the Classification of Substance-Related and Addictive Disorders'. The other authors have no competing interests.

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