

Identifying latent class of risk factors among HIV patients in Iran: results from national HIV/AIDS surveillance data

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Abstract

Introduction: Identifying patterns of human immunodeficiency viruses (HIV) transmission and factors affecting it can help to prevent and control the disease. The present study aimed to identify the latent classes of HIV risk factors in Iran.

Material and methods: This cross-sectional study was conducted among 32,168 HIV patients. We fitted latent class analysis by considering 11 indicators. Models with 2 to 5 classes were fitted, and the best-fitted model was chosen based on Acaik information critical (AIC), Bayesian information criterion (BIC), entropy, and interpretability of the results. Additionally, multinomial logistic regression model was applied to assess relationships between the covariates and latent class membership.

Results: We identified 3 latent classes, including low-risk (41.35%), high-risk (50.28%), and moderate-risk (8.37%) classes. The moderate-risk class was most likely prison history (69.09%) and addiction (67.37%). The high-risk class included addiction (99.68%), injection drugs users (IDUs) (99.06%), prison history (86.27%), and sharing needles (79.64%). Older age and being single increased the odds of membership in high-risk class (OR: 1.021, 95% CI: 1.017-1.024%; OR: 1.34, 95% CI: 1.20-1.50%), respectively, while older age increased the odds of membership in classes of moderate-risk (OR: 1.028, 95% CI: 1.023-1.033%) compared with low-risk group ($p < 0.05$). The odds of membership in classes of high-risk (OR: 0.011, 95% CI: 0.010-0.013%) and moderate-risk (OR: 0.113, 95% CI: 0.098-0.131%) were significantly lower in women than in men compared with low-risk group ($p < 0.05$).

Conclusions: Injection drugs users, drug addiction, sharing needles, and prison history are related to HIV infection in Iran. Moreover, older age, female gender, low education, and being single increase the odds of membership in high-risk classes. These findings highlight the need for preventive interventions and harm reduction programs for people at risk.

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Key words: HIV/AIDS, latent class analysis, people living with HIV, risk factors, Iran.

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Introduction

Despite the global decline in the trend of human immunodeficiency viruses (HIV) infection, in Iran both new cases and deaths related to HIV have shown an increase. Iran is located in the Middle East/North Africa (MENA) of the WHO classification region. According to the Joint United Nations Program on HIV/AIDS (UNAIDS) report, in 2021, 38.4 million people globally were living with HIV, 1.5 million people became newly infected with HIV, 650,000 people died from acquired immunodeficiency syndrome (AIDS)-related illnesses, and 28.7 million people were accessing antiretroviral therapy. Moreover, since the start of the epidemic, 84.2 million people have become infected with HIV and 40.1 million people have died from AIDS-related illnesses [1]. In the 2019 estimation in Iran, 59,000 people were living with HIV (PLWH), and about 4,100 new infections and 2,500 AIDS-related deaths occurred annually in the country. In the general population, HIV prevalence is less than 1%, and the most common route of transmission is injection drugs and sharing needles, with sexual transmission coming next [2]. Along with other countries in the region, Iran pays attention to the 90-90-90 HIV program to reduce the incidence and control the epidemic, especially in mother-to-child transmission and other high-risk populations [3]. According to studies, about one-third of all PLWH in Iran have been diagnosed, while the proportion is somewhat less in children than in adults [4].

Initial evaluations regarding the success of prevention of mother-to-child transmission of HIV (PMTCT) program and the implementation of rapid testing in Iran have been impressive [5]. Although the routes of transmission are well-known, the pattern of risk factors and transmission of infection can be different in regions. Identifying these patterns of transmission and factors affecting them can help to prevent and control the disease through the implementation of appropriate prevention programs using identified patterns [6, 7]. One of the methods that are used in group persons with similar characteristics, and to identify patterns based on probabilities of the model is latent class analysis (LCA) or latent profile analysis, with the first used for categorical variables and the next for quantitative variables [8, 9]. Although studies using this method have been conducted in Iran to investigate the pattern of risk factors related to the incidence or prevalence of HIV in a group of prisoners [6], female sex workers [9], and injection drug users (IDU) [10], no study has been done at the national level with this method in order to determine and classify the pattern of HIV risk factors. Therefore, in the current study, the latent class of high-risk behaviors in HIV patients by using LCA model was investigated.

Material and methods

Study design and sample

This cross-sectional study was conducted using the national HIV/AIDS surveillance database. HIV/AIDS sur-

veillance information in Iran is completed by counseling centers for behavioral disease under the supervision of universities of medical sciences, and include demographic information, registration of high-risk behaviors (prison history, drug use, injecting drugs, sexual contact, sharing needles, receiving blood, occupational contact, transmission from an infected mother, having a spouse with HIV, or high-risk behaviors), hepatitis B, C, and tuberculosis assessments, routine visits of physicians, CD4+ status and viral load monitoring, and psychological counseling services, which are recorded in the system for each person at each visit. The information is sent electronically to the Center for Infectious Disease Control and Prevention (CDC) in Iran. All HIV patients, who were registered in the Iran national HIV/AIDS surveillance system from October 13, 1985 to May 17, 2016 were included in the study. In total, 32,168 patients were included.

The study was performed according to the ethical guidelines expressed in the Declaration of Helsinki and the Strengthening of the Reporting of Observational Studies in Epidemiology (STORB) guidelines.

Variables used in LCA

To investigate the pattern of high-risk behaviors of HIV infection and identify persons with similar high-risk behaviors based on the possibilities, binary variables, including prison history, drug use, injecting drugs, heterosexual and homosexual contacts, use of shared needles, receiving blood, occupational contact, transmission from an infected mother, having a spouse with HIV, or with high-risk behaviors were used. Table 1 shows the variables used for LCA.

Covariates

In this study, variables, such as age, gender, education levels, and marital status were considered important predictors for the membership possibility of persons in the latent class of high-risk behaviors of HIV in a multinomial logistic regression model.

Latent class analysis

Latent class analysis is a finite mixture model technique that classifies people into separate classes based on their response patterns with the observed variables, which are mentioned in this study as having each of the high-risk behaviors. This classification is done by maximizing the homogeneity within each identified profile so that the individuals grouped are as similar as possible, and by maximizing the heterogeneity between profiles so that each profile shows a distinct grouping [10]. Basic assumption of LCA is that membership in unobserved groups (or classes) can be explained by patterns of answers to questions or indicators. Although cluster analysis and LCA are both similar in grouping homogeneous people, assumptions and statistical methods used

are different. In clustering, it is assumed that people who get the highest score among the variables used for analysis belong to a cluster, while in LCA, it is assumed that there are hidden classes that can be explained through the response patterns to the observations or indicators.

In cluster analysis, the mean of the variable is used to be placed in the cluster, and therefore, the analysis variables should be quantitative. In LCA, because the variables of analysis are categorical, cross-tabulations are applied as input information. In LCA, class membership probabilities are obtained, but in clustering, explicit assignment [11].

Modeling

We fitted the LCA model by using R 4.1.3 software and package (poLCA), considering 11 indicators with high-risk behaviors for HIV (Table 1). In order to select a model with the optimal number of classes, first models with 2 to 5 classes were fitted, and based on the model fit indices including Acaik information critical (AIC) and Bayesian information criterion (BIC), the appropriate model was selected. The lower values of these two indicators indicated a better fit for the model. Because the values of AIC and BIC indexes could decrease by increasing the number of classes, entropy index was also applied. Higher entropy values indicated a more appropriate model. In addition to model fit indices, interpretability of the number of classes in the model was also considered [12]. A probability cut-off value of ≥ 0.5 was estimated to assign a class [13].

Association between covariates with the membership probability in classes

After selecting the final model in LCA, which included a model with 3-class, the prediction was done, and persons were allocated into three classes, including class 1: low-risk, class 2: medium-risk, and class 3: high-risk. To investigate the relationship between the covariates and probability of membership in each class because the classes were ordered, the ordered logistic regression was performed, but due to the proportional odds of assumption being violated in this model, multinomial logistic regression model was applied. in all analyses. A p -value < 0.05 was considered statistically significant.

Ethical approval and consent to participate

Ethical issues, including plagiarism, informed consent, misconduct, data fabrication and/ or falsification, double publication and/or submission, redundancy, etc. have been completely observed by the authors. The study was performed according to the ethical guidelines expressed in the Declaration of Helsinki and the Strengthening of the Reporting of Observational Studies in Epidemiology (STORB)

Table 1. Indicators variables used for latent class analysis

Indicators/Sub-group	n (%)
Prison history	
No	16,195 (50.35)
Yes	15,973 (49.65)
Injection drugs users (IDUs)	
No	15,913 (49.47)
Yes	16,255 (50.53)
Sharing needle	
No	19,286 (59.95)
Yes	12,882 (40.05)
Blood transfer	
No	31,902 (99.17)
Yes	266 (0.83)
Having HIV-infected spouse	
No	29,586 (91.97)
Yes	2,582 (8.03)
Addiction	
No	14,132 (43.93)
Yes	18,036 (56.07)
Heterosexual contacts	
No	24,352 (75.70)
Yes	7,816 (24.30)
Males who have sex with male (MSM)	
No	31,283 (97.25)
Yes	885 (2.75)
Mother-to-child transmission	
No	31,649 (98.39)
Yes	519 (1.61)
Having a spouse with high-risk behaviors	
No	31,432 (97.71)
Yes	736 (2.29)
Other routes of transmission	
No	30,565 (95.02)
Yes	1,603 (4.98)

guidelines. The study was approved by the Research Ethics Committee of Shiraz University of Medical Sciences (approval No.: IR.SUMS.SCHEANUT.REC.1400.045). Informed consent was waived by the Research Ethics Committee of Shiraz University of Medical Sciences.

Results

This study was conducted among 32,168 subjects. The mean \pm SD of age of the study participants was 33.25 \pm 9.29 years. Among them, 15,973 (49.65%) had a prison history. The prevalence of different risk factors is shown in

Table 2. Comparison of latent class analysis models with different latent classes based on model selection statistics

Number of latent classes	Number of parameters estimated	G ²	df	AIC	BIC	χ ²	Maximum log-likelihood	Entropy
2	23	8346.239	2024	182710.0	182902.7	8346.239	-91331.98	2.84
3	35	4536.367	2012	178924.1	177852.5	5040.129	-89427.05	2.71
4	47	3801.155	2000	177458.7	178217.3	3046.972	-88682.35	2.73
5	59	2502.19	1988	176471.2	179965.5	2035.441	-88176.58	2.74

AIC – Acaik information criteria, BIC – Bayesian information criterion, df – degree of freedom.

Table 3. Class membership and item response probabilities of three latent classes

Parameter	Latent class		
	Class 1 Low-risk	Class 2 High-risk	Class 3 Moderate-risk
Latent class prevalence	0.4135	0.5028	0.0837
Item-response probabilities	0.4172	0.5066	0.0762
Prison history	0.0120	0.8627	0.6909
Injection drugs users (IDUs)	< 0.001	0.9906	0.0864
Sharing needle	< 0.001	0.7964	0.0002
Blood transfer	0.0191	0.0006	0.0191
Having HIV-infected spouse	0.1808	0.0040	0.0419
Addiction	0.0075	0.9968	0.6737
Heterosexual contacts	0.1478	0.2890	0.4367
Male who have sex with male (MSM)	0.0117	0.0370	0.0486
Mother-to-child transmission	0.0382	0.0006	0.0005
Having a spouse with high risks behaviors	0.0474	0.0015	0.0304
Others	0.0658	0.0210	0.1437

Table 1. This table shows that the prevalence of IDUs was higher than other transmission routes (50.53%). Moreover, it demonstrates that sharing of a needle, blood transfer, heterosexual contacts, and males who have sex with males (MSM) were reported as 40.50%, 0.83%, 24.30%, and 2.75%, respectively.

Table 2 indicates model selection criteria for all latent classes. We attempted to fit LCA models with classes ranging from 2 to 5. For each model, G², AIC, and BIC were computed. Considering these indices and interpretability of the results, the three-class model was chosen for sub-grouping of patients.

The results of LCA model are shown in Table 3, and includes latent class prevalence and item-response probabilities. The probabilities of membership in each latent class appear in the first section of Table 3 and Figure 1. Patients in this study were classified into low-risk class (41.35%), high-risk class (50.28%), and moderate-risk (8.37%). Patients in the low-risk class had very low probabilities of any risk factors. Patients in the moderate-risk class had a high probability of prison history (69.09%). Also, in this class, the probability of addiction was 67.37%. However, other items presented

a low probability in this class. Patients in the high-risk class also showed a higher risk of getting infected through addiction (99.68%) and IDUs (99.06%). Also, In the high-risk class, the odds of prison history (86.27%) and sharing needles (79.64%) were higher among the patients.

The highest mean age (34.75 years) was in the moderate class. 67.18% of men versus 32.82% of women were in the low-risk group. Men were significantly more likely than females to membership in high-risk and moderate classes. Illiterate or primary school patients were about 44.39% of the low-risk class. In addition, more than 88% of low-risk class people were married (Table 4).

A multinomial logistic regression analysis adjusted for age, gender, educational level, and marital status showed that older age increased the odds of being in the classes of moderate-risk (OR: 1.021, 95% CI: 1.017-1.024%) and high-risk class (OR: 1.028, 95% CI: 1.023-1.033%) compared with the low-risk group. The odds of membership in the classes of high-risk (OR: 0.011, 95% CI: 0.010-0.013%) and moderate-risk (OR: 0.113, 95% CI: 0.098-0.131%) were significantly lower in women than men compared with the low-risk group. In the current study, being single

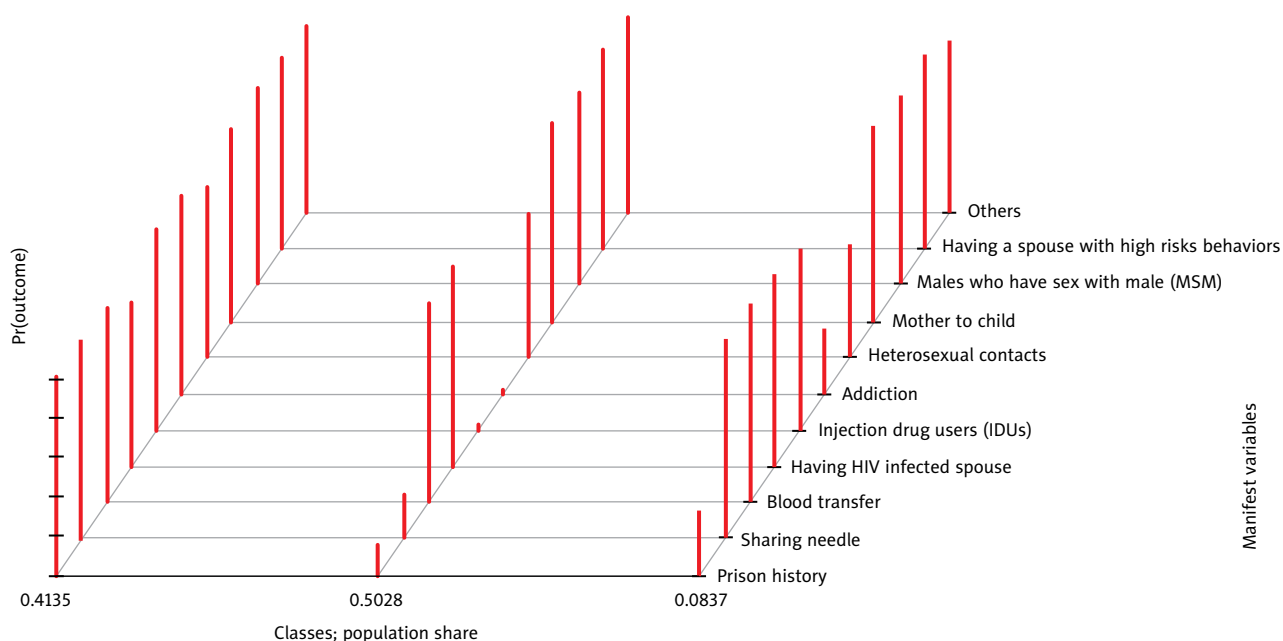


Figure 1. Class membership and item response probabilities of three latent classes

Table 4. Characteristics of study participants by latent class membership

Variable	Total	Latent class			p-value
		Low-risk	High-risk	Moderate-risk	
Age	33.25 ± 9.29	32.16 ± 10.63	33.91 ± 7.92	34.75 ± 9.22	< 0.001*
Sex					
Male	27,130 (84.34)	9,016 (67.18)	15,979 (98.06)	2,135 (87.07)	< 0.001**
Female	5,038 (15.66)	4,405 (32.82)	316 (1.94)	317 (12.93)	
Education level					
University	1,747(5.43)	1,406 (10.48)	254 (1.56)	87 (3.55)	< 0.001**
High school	12,059 (37.49)	3,706 (27.61)	7,294 (44.76)	1,059 (43.19)	
Secondary	8,481 (26.36)	2,351 (17.52)	5,398 (33.13)	732 (29.85)	
Illiterate or primary	9,881 (30.72)	5,958 (44.39)	3,349 (20.55)	574 (23.41)	
Marital status					
Married	27,483 (85.44)	11,912 (88.76)	13,451 (82.55)	2,120 (86.46)	< 0.001**
Single	2,777 (8.63)	653 (4.87)	1,930 (11.84)	194 (7.91)	
Temporal	1,908 (5.93)	856 (6.38)	914 (5.61)	138 (5.63)	

*p-value for one-way ANOVA test; **p-value for χ^2 test.

increased the odds of attending high-risk class (OR: 1.34, 95% CI: 1.20-1.50%) compared with the low-risk class. This increase was not significant in the class of moderate-risk. We have shown that a lower education level was a risk factor (OR: 2.23, 95% CI: 1.92-2.59%) for attending the high-risk class. In addition, patients with a high school education level presented higher odds for high-risk class (OR: 18.34, 95% CI: 15.69-21.42%) and moderate-risk class (OR: 6.58, 95% CI: 5.17-8.36%) compared with low-risk class (Table 5).

Discussion

The present study aimed to identify the latent classes of risk factors in HIV patients in Iran. In this study and based on LCA model, 3 latent classes were identified in terms of the pattern of risk factors of the patients. In this analysis, 41.35% of the patients were in the low-risk class, 50.28% in the high-risk class, and 8.37% in the moderate-risk class. In this study, four factors, including prison history, addiction, IDU, and sharing needles caused HIV infection in the population at risk.

Table 5. Adjusted multinomial logistic regression for evaluation relationship between demographic factors and latent class

Variable	Latent class		
	Low-risk (1)	High-risk (2)	Moderate-risk (3)
	Odds ratio (95% CI)		
Age	1	1.021 (1.017-1.024%)	1.028 (1.023-1.033%)
Sex			
Male	1	1	1
Female	1	0.011 (0.010-0.013%)	0.113 (0.098-0.131%)
Education level			
University	1	1	1
High school	1	12.25 (10.57-14.21%)	5.21 (4.14- 6.57%)
Secondary	1	18.34 (15.69-21.42%)	6.58 (5.17-8.36%)
Illiterate or primary	1	2.23 (1.92-2.59%)	1.20 (0.95-1.53%)
Marital status	1		
Married	1	1	1
Single	1	1.34 (1.20-1.50%)	1.03 (0.86-1.23%)
Temporal	1	1.07 (0.93-1.22%)	0.87 (0.72-1.06%)

According to our knowledge, this is the first study in Iran at the national level that investigated the patterns of risk factors in HIV using the LCA method. In a study that was conducted in Iran based on the LCA model to investigate the patterns of drug use and high-risk sexual behaviors in IDUs, 3 latent classes were identified. The probability of membership in the high-risk class was 0.33 compared with 0.26 and 0.40 for the low- and moderate-risk classes, respectively [14]. In a study by Gottert *et al.* investigating multi-factor profiles of HIV acquisition/ transmission risk for men in Africa, four hidden classes, including older high-risk (20%), younger high-risk (24%), younger moderate-risk (36%), and older low-risk class (20%) were identified. In the older high-risk class, the probability of alcohol consumption, substantial age disparity with partners, and multiple sexual partners were high. The authors reported that LCA has the potential to enable more strategic, data-driven programming [15]. The results of our study showed that one of the important risk factors for HIV infection in the population at risk in Iran is drug addiction and sharing injection. In a study in Iran, it was shown that drug use has a significant effect on HIV positivity [16]. Results of a study in Tanzania showed that heroin use and behaviors related to the risk of HIV, such as sharing needles, not using condoms during sex, and using illegal drugs during sex, are HIV risk factors. Tan *et al.* showed that the increase in access to syringe needles with a significant decrease in syringe borrowing and lending would eventually lead to a decrease in the incidence of HIV in IDUs [17]. The results of a study in Afghanistan demonstrated high-risk factors, such as high-risk injecting behaviors among IDU (sharing injecting equipment), unprotected sexual contact with several partners, mass production of drugs, easy access to illegal drugs, high stigma, discrimination against drugs,

and unsafe injection sites, such as under bridges, put these people at high-risk, being vulnerable to HIV, so a conscious and multi-sectoral response is necessary to control HIV epidemic [18]. Ball *et al.* also showed that sharing needles and syringes is an important risk factor for HIV infection in IDUs. These findings highlight the necessity of adequate and easy access to sterile needles and syringes, and a supportive environment for behavior change to reduce the risks of HIV transmission in the community [19].

We showed that people with a prison history were more likely to belong to the moderate-risk and high-risk classes for HIV infection. Prisoners with different social and cultural backgrounds, including low education and having risk factors before imprisonment, such as drug use, sexual intercourse outside the framework, and also in prison due to overcrowding, poor medical facilities, especially for faster disease diagnosis, and unavailability of harm reduction methods, such as condom use or needle exchange program, they are exposed to HIV infection in prisons [20, 21]. The results of a study in Pakistan revealed that the prevalence of HIV in prisons is 1.6%, which is much higher than the prevalence in the general population in this country. Khan *et al.* showed that the prevalence of HIV infection in Iranian prisons is relatively high [22]. Therefore, maintaining the health of prisoners protects the general health of society. Successful HIV prevention programs in prisons include providing HIV education and information, availability of clean needles and syringes, drug treatment, and condoms. Apart from the many risk factors that cause the spread of infection in prison environments, prisons are also a favorable place for HIV screening and treatment because prisoners in prison are easily available for diagnosis, treatment, and education, and this can help to stop the spread of HIV infection

in the community [22]. Our study showed that compared with men, women had lower odds of belonging to high-risk and medium-risk classes. It seems that there are different results regarding the role of gender in acquiring HIV. Contrary to our findings, Mahathir showed that the risk of acquiring HIV in women is related to gender inequalities. Also, economic pressures and poverty increase the risk of infection in women [23]. In line with our findings, Mbita *et al.* showed that men are more at risk of contracting HIV due to drinking alcohol before sex, not being circumcised, having sex with men, and inconsistent condom use [24]. The results of the present study demonstrated that people with a low level of education significantly increase the odds of membership in high-risk and medium-risk classes compared with low-risk classes. Yousufzai showed that people with a high level of education are less likely to engage in behaviors that increase the likelihood of acquiring HIV [25]. In Uganda, educational attainment is a significant predictor of HIV risk reduction, as health-related outcomes, such as reduced risk behaviors and better health, are improved in educated individuals [26]. Education and low socio-economic level cause unsafe sexual behaviors, injecting addiction, and as a result, the need for drugs. These relationships are probably associated with the risk of HIV in people at risk [26]. Our study showed that unmarried people have higher odds of membership in the high-risk and medium-risk classes than married people. Results of a study in Africa showed that compared with married people, the risk of HIV infection in people who were never married or widowed was nearly double [27]. Results of another study showed that a long period of marriage is associated with a decrease in the risk of HIV infection, so it is necessary to implement interventions that increase stability of married life [27]. Marriage leads to a reduction in risky behaviors, especially alcohol and drug usage [28].

Limitations and strengths

The strength point of this study is the use of national HIV/AIDS surveillance data, which had a suitable sample size for LCA. However, due to the unavailability of socio-economic status of patients in the data, we could not evaluate the relationship between them and the probability of membership in the latent classes.

Conclusions

In the present study, we evaluated the clustering of HIV-related risk factors in Iranian patients. Among Iranian HIV patients, the high-risk class has the highest prevalence. In this study, factors, such as injecting drug use, drug addiction, sharing needles and syringes, and prison history were related to HIV infection in Iran. Also, older age, female gender, low education, and being single increased the odds of membership in high-risk classes for HIV infection. These results highlight the determinants of HIV risk, so that planners and policy-makers can focus on different aspects

of HIV infection. Also, these findings highlight the need for preventive interventions and harm reduction programs for people at risk.

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Conflict of interest

The authors declare no conflict of interest.

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