

Tobacco, heated tobacco products, e-cigarettes, alcohol, cannabis and other psychotropic substances. Polysubstance use during the COVID-19 pandemic in Italy

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Abstract

Objective. Psychoactive substance use is largely found to involve multiple substances. In recent years, the COVID-19 pandemic has changed psychoactive substance use patterns. Aim of this study is to investigate profiles of polysubstance and their pattern during and after the COVID-19 pandemic.

Methods. We collected information on alcohol consumption, use of tobacco, cannabis and other psychotropic substances, and nicotine-containing electronic devices (NCEDs; i.e., heated tobacco products and electronic cigarettes) on representative samples of the Italian adult population in five surveys from 2020 to 2023 (3,000 ≤ n ≤ 6,600). We used a Latent Class Analysis model to identify substance use profiles and their associated variables in each time period.

Results. We initially identified two profiles, “light users”, characterized by a low use of tobacco and NCEDs (3%-20%) and a 40% at-risk alcohol consumption, and “polysubstance users”, characterized by a large use of all psychoactive substances. After the 2020 COVID-19 lockdown, we also found the “dual users” profile, which show a large use of tobacco (90%) and NCEDs (50%), and also alcohol (50%). Being “dual users” and “polysubstance users” were associated with younger age and high economic status, with strengths of association less pronounced during lockdown but more marked immediately thereafter. Moreover, reporting anxiety or depressive symptoms as well as using psychotropic drugs were strongly associated with both profiles, especially in the last two years.

Conclusions. Heterogeneity of polysubstance users and their socio-demographic characteristics need to be considered to design tailored prevention interventions, with special attention to the new “dual users” profile, which confirmed the increasing trend in NCED use.

Key words

- polysubstance use
- COVID-19
- tobacco
- electronic-cigarette
- alcohol
- cannabis

INTRODUCTION

Polysubstance use refers to the consumption of more than one psychoactive substance on separate occasions (sequential use) or at the same time (concurrent/simultaneous) [1]. Although substance use is often centered around individual substances, it is largely found to involve multiple substances [2, 3]. Substance-dependent individuals report using an average of 3.5 substances [4], both simultaneously and sequentially. Psychoactive substances include alcohol, nicotine, cannabis and other psychotropic substances such as opioids and stimulants, and the use of one substance often co-occurs with the use of another. For instance, tobacco smoking is strongly associated with alcohol and marijuana use [1] and cannabis is the most commonly used drug among those who drink, besides tobacco [5].

Polysubstance use leads to poor physical and mental health, including psychotic disorders, and substance use outcomes, such as increased violence and suicidal risk, and increased overdoses and mortality risks [6-8]. Most research on substance use and its consequences (i.e., substance use disorders) addresses use, control and treatment of single substances [2]. Concurrent substance use, which is more often studied in adolescents [9-12], may complicate diagnosis and treatment of substance use disorders, as well as the effectiveness of prevention and control interventions [13].

Many individuals who develop substance use disorders are also diagnosed with mental disorders, and vice versa [14]. In recent years, the COVID-19 pandemic has enhanced mental disorders and changed substance use patterns [15, 16]. Several surveys were carried out in European countries on single substance use during the COVID-19 initial phase [17-24]. In Italy, the COVID-19 pandemic was associated with an increase in anxiety and depressive symptoms and with a worsening in the use of smoking and nicotine-containing electronic devices (NCEDs), i.e., electronic cigarettes (e-cigarettes) and heated tobacco products (HTPs), especially in its initial phase [17-20].

The extent to which polysubstance use has changed during the COVID-19 pandemic was little investigated in Europe only among youths in the initial phase of the COVID-19 pandemic [12], and it needs to be studied more in depth. Moreover, profiles of polysubstance use integrating new consumption patterns, such as the increasing use of NCEDs, are underexplored.

The aim of this study is to investigate profiles of polysubstance use and its pattern in the COVID-19 pandemic and subsequent phases together with the associated risk factors. The study was carried out in the Italian adult population between 2020 and 2023, using representative samples within the study *LOckdown and lifeSTyle IN ITALY (LOST IN ITALY)* and its extension *LOST IN TOSCANA*.

METHODS

Study design and population

The *LOST IN ITALY* study cohort, described in detail elsewhere [25], is based on a cross-sectional survey conducted on 6,003 participants representative of the Italian adult population aged 18-74 years who completed a

web-based interview during the Italian lockdown (April 27-May 3, 2020) which collected information on two time points recording changes before and during the lockdown (Time 1: pre-lockdown, February 2020; Time 2: lockdown, April-May 2020). The fieldwork was conducted by Doxa, the Italian branch of the Worldwide Independent Network/Gallup International Association.

Following surveys, mostly based on the same study participants of the first one, were carried out in correspondence with the main COVID-19 waves. Within the *LOST IN ITALY* study, other two surveys were conducted on about half of the initial sample (Time 3: 3,185 in November 27-December 20, 2020; Time 4: 3,000 in May 7-18, 2021). Finally, two years after the start of the COVID-19 pandemic, 6,600 participants took part to a comparable web-based survey (Time 5: February 24-March 21, 2022) within the *LOST IN TOSCANA* study, and lastly, a follow-up of the *LOST IN TOSCANA* study was conducted between April 4 and May 3, 2023 on 6,600 participants (Time 6). In each follow-up survey, some individuals were lost, therefore, to maintain the sample's representativeness, new individuals were added from the appropriate strata in each survey (*Supplementary Figure S1 available online*). Slight differences in the age distribution between lost and new enrolled respondents were found (*Supplementary Table S1 available online*), but the sample representativeness was maintained.

In all surveys, participants completed an online questionnaire on socio-demographic information, lifestyle habits and symptoms of mental distress. Moreover, in the first survey, changes before and during the lockdown were recorded. Distribution of individuals by socio-demographic and individual features in all time periods considered are reported in *Supplementary Table S2 available online*.

Outcome and independent variables

Current smokers were defined as respondents who reported having smoked ≥ 100 cigarettes during their life and who were current smokers at the time of the interview. Users of NCEDs were defined as respondents using e-cigarettes or HTPs occasionally or regularly. Alcohol drinkers were classified based on the total score obtained on the alcohol use disorders identification test-concise (AUDIT-C). Respondents with a score ≥ 4 for women and ≥ 5 for men were identified as heavy drinkers [26]. Binge drinkers were defined as respondents who drank 6 or more alcoholic beverages at one time at least once in the last month, where 1 alcoholic beverage corresponds to 1 standard unit of alcohol, i.e., 12 g of pure alcohol (approximately a 330 ml beer, a 125 ml glass of wine or a 40 ml of spirits). A dichotomous variable describing respondents with at-risk alcohol consumption was defined as 1 for those who were heavy drinkers according to AUDIT-C or binge drinkers and as 0 for those who were neither heavy drinkers nor binge drinkers. Finally, current users of cannabis and users of other psychotropic substances were defined as respondents who reported using respectively cannabis (or cannabis light) and psychotropic substances (e.g., cocaine, heroin, synthetic psychostimulants, etc.) at least once in the previous month.

Information on sociodemographic characteristics, such as age, sex, level of education and economic status was collected at the baseline. In each survey, information about mental health (anxiety or depressive symptoms, quantity and quality of sleep) and consumption of selected psychotropic drugs was collected [17, 25]. Individuals scoring higher than 3 in the 2-item generalized anxiety disorder (GAD-2) scale [27] or in the 2-item patient health questionnaire (PHQ-2) scale [28] were identified as presenting anxiety or depressive symptoms, respectively. Individuals who reported sleeping less than 7 hours per night or who rated their overall sleep as fairly poor or very poor were identified as having sleep disorders [29]. Individuals reporting the use, in the last month, of at least one drug among antidepressants, hypnotics, anxiolytics/benzodiazepine, antipsychotics and mood stabilizers were considered psychotropic drug users.

Statistical analysis

To identify substance use profiles in each time, we used latent class analysis (LCA), a statistical model-based approach for clustering individuals in unobserved groups on the basis of substance consumption [30]. In the LCA analysis we included five indicators of substance use (i.e., conventional cigarettes, e-cigarettes or HTPs, at-risk alcohol, cannabis or cannabis light, other psychotropic substances) as binary variables. We ran an iterative process to identify the best profile solutions in each time using the corresponding survey weights. In detail, we tested four different variance-covariance structures for profiles (i.e., invariant diagonal, varying diagonal, invariant non-diagonal, and varying non-diagonal) for each set of models ranging from 1 to 3 profile classes. We used five different sets of random starting points in each model selecting the one with the best log likelihood after the expected-maximization iterations. We used the Akaike information criterion (AIC) and the Bayesian information criterion (BIC) to assess model fit. Once we identified the preferred model, we analyzed whether the profiles of the model were iden-

tified correctly by calculating the average posterior probability (AvePP), the odds of correct classification (OCC) and the entropy which provides a summary for the overall classification precision of the model. AvePP closer to 100% and OCC >5 support adequate profile separation and precision [30, 31], and entropy values <0.8 are considered high [32].

Finally, we assessed factors associated with substance use profiles from the LCA models in logistic regressions with the bias-adjusted three-step approach which consists in first identifying the underlying latent variable, then assigning individuals to latent classes, and finally analyzing class membership and covariates accordingly [33]. We reported adjusted odds ratios (aORs) for sex, age, education, economic status, anxiety or depression symptoms, sleep disorders and use of psychotropic drugs, after adjusting also for geographic area.

All the statistical models were weighted for the corresponding survey weights, applied to guarantee the representativeness of the national sample in terms of sex, age, socio-economic status, and geographic area.

All statistical analyses were performed using Stata Version 17 (StataCorp. 2021. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC).

RESULTS

The weighted prevalence of the use of each substance at all times are displayed in *Table 1*. The use of NCEDs increased throughout the whole period, from 9% before lockdown to 14% in 2023, whereas the use of other psychotropic substances decreased from 4% to 1%. At-risk alcohol use, cannabis use and smoking showed a slight decrease during lockdown, followed by a sharp 61% increase in alcohol use, a maintenance of lockdown prevalence for cannabis use and a return to pre-lockdown levels for smoking.

In the first two times points (i.e., pre-lockdown in February 2020; during lockdown in April-May 2020) only the LCA models with up to two classes converged whereas, in the remaining times, also models with up to three classes reached convergence. The latter was

Table 1
Prevalence of substance use in the time periods (weighted proportions)

	Time 1 ¹ N=6,003 % (95% CI)	Time 2 ¹ N=6,003 % (95% CI)	Time 3 ¹ N=3,185 % (95% CI)	Time 4 ¹ N=3,000 % (95% CI)	Time 5 ¹ N=6,600 % (95% CI)	Time 6 ¹ N=6,600 % (95% CI)
Conventional cigarette smokers	23.3 (22.0, 24.7)	21.9 (20.6, 23.2)	24.5 (22.7, 26.5)	26.3 (24.2, 28.4)	24.4 (23.1, 25.7)	23.3 (22.1, 24.6)
Alcohol at risk ² or binge drinkers	28.1 (26.7, 29.6)	25.2 (23.8, 26.6)	33.2 (31.1, 35.3)	43.7 (41.5, 46.0)	44.9 (43.4, 46.4)	45.4 (43.9, 47.0)
Cannabis or cannabis light users	7.0 (6.2, 7.9)	6.0 (5.2, 6.8)	7.9 (6.8, 9.1)	7.8 (6.6, 9.2)	4.9 (4.3, 5.7)	5.4 (4.7, 6.1)
Psychoactive substances users	4.2 (3.6, 4.9)	4.0 (3.4, 4.7)	2.0 (1.5, 2.7)	1.5 (1.0, 2.2)	0.7 (0.5, 1.0)	1.2 (0.9, 1.6)
NCEDs users	8.9 (8.1, 9.9)	9.8 (8.9, 10.8)	11.8 (10.4, 13.3)	12.1 (10.6, 13.8)	11.7 (10.8, 12.7)	13.8 (12.7, 14.9)

N: number; CI: confidence interval; NCEDs: nicotine-containing electronic devices.

¹Time 1: pre-lockdown (February 2020); Time 2: lockdown (April-May 2020); Time 3: November-December 2020; Time 4: May 2021; Time 5: February-March 2022; Time 6: April 2023.

²Alcohol at risk: respondents with a total Alcohol Use Disorders Identification Test-Concise score ≥ 4 for women and ≥ 5 for men.

Table 2
Latent Class Analysis models measures of classification and accuracy for all time periods

	Model estimated class proportion % (95% CI)	AvPP	OCC	Entropy
Time 1[†]				
Class 1	90.4 (83.7, 94.6)	95.6	2.3	0.873
Class 2	9.6 (5.4, 16.3)	91.5	102.1	
Time 2[†]				
Class 1	91.7 (88.3, 94.2)	96.9	2.8	0.897
Class 2	8.3 (5.8, 11.7)	92.7	140.1	
Time 3[†]				
Class 1	81.2 (74.5, 86.4)	92.6	2.9	0.824
Class 2	6.5 (5.1, 8.3)	88.6	112.2	
Class 3	12.3 (7.8, 19.1)	85.3	41.2	
Time 4[†]				
Class 1	78.8 (51.6, 92.8)	91.3	2.8	0.812
Class 2	6.5 (4.7, 9.0)	86.7	93.1	
Class 3	14.7 (3.4, 45.8)	91.7	64.2	
Time 5[†]				
Class 1	84.5 (78.2, 89.2)	94.7	3.3	0.845
Class 2	4.6 (3.3, 6.3)	84.5	114.0	
Class 3	11.0 (6.4, 18.2)	90.3	75.7	
Time 6[†]				
Class 1	68.7 (58.4, 77.4)	91.7	5.0	0.708
Class 2	4.3 (3.4, 5.4)	82.7	106.2	
Class 3	27.0 (18.5, 37.6)	77.1	9.1	

CI: confidence interval; AvPP: average posterior probability; OCC: odds of correct classification; Class 1: light users; Class 2: polysubstance users; Class 3: dual users.

[†]Time 1: pre-lockdown (February 2020); Time 2: lockdown (April-May 2020); Time 3: November-December 2020; Time 4: May 2021; Time 5: February-March 2022; Time 6: April 2023.

reached in all times with all the variance-covariance specifications. We then chose the least restrictive variance-covariance structure, i.e., varying non-diagonal, and ran the models at all times. Fit indices suggested a better fit for the two-classes LCA model for times 1 and 2, and the three-class model for the remaining times (*Supplementary Table S3 available online*). At all time points, the selected models returned AvPP above the desired threshold of 70% for all classes, suggesting adequate classification accuracy. The OCC showed a high classification accuracy for Class 2 and Class 3 (in times 3 to 6), for which the OCC was well above the threshold criteria of 5, whereas accuracy classification for Class 1 resulted low. Finally, the entropy was between 0.7 and 0.9 suggesting a borderline overall model classification precision (*Table 2*).

Figure 1 displays the three profiles identified with the LCA. The first, defined as “light users”, included most of the total sample at all times (from 68.7% in time 6 to 91.7% in time 2, *Table 2*) and shows proportions close to 0 for cannabis and psychotropic substance use, up to 8.8% and 20.9% for NCEDs and conventional cigarette, respectively, and up to 40.4% for at-risk alcohol use. The second class identifies the “polysubstance users” and it includes between 4.3% (in time 6) and 9.6% (in time 1) of respondents characterized by an average proportion of 23.3% and 23.7% of psychotropic substance and NCEDs users, respectively, around 44.8% of tobacco smokers and over 80% of at-risk alcohol users and cannabis users. Finally, the third class, defined as “dual users”, which arises from December 2020, includes between 11.0% and 14.7% of the total sample in times 3 to 5 and up to 27.0% in time 6. In addition to the at-risk alcohol use (on average 54.2%) that characterizes all the profiles, it is mainly characterized by the dual use of tobacco cigarettes and NCEDs with average proportions of 82.3% and 59.1%, respectively (*Table 2*, *Figure 1*, *Supplementary Table S4 available online*).

The proportion of substance use shows variations in time. At-risk alcohol users increased in the last three

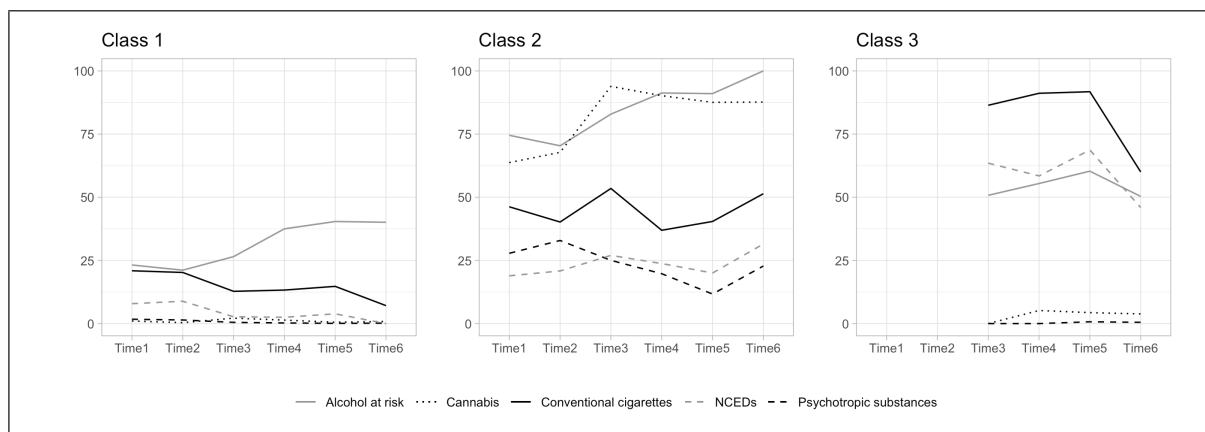


Figure 1

Expected proportions, at each time, of the population by substance use in each class identified by the Latent Class Analysis model. Time 1: pre-lockdown (February 2020); Time 2: lockdown (April-May 2020); Time 3: November-December 2020; Time 4: May 2021; Time 5: February-March 2022; Time 6: April 2023.

NCEDs: nicotine-containing electronic devices (electronic-cigarettes or heated tobacco products).

time points compared to the previous time points in both “light users” (almost doubling) and “polysubstance users”. Cigarette smokers and NCEDs users in “light users” show a reduction from time 3 afterwards presumably captured in the new class of “dual users”.

Tables 3 and 4 report the results of the logistic regression models for the analysis of factors (*Supplementary Table S2 available online*) associated with the substance use profiles identified with the LCA models, respectively the “polysubstance users” or “dual users” in comparison to “light users”. In all the time points, males were more likely to be “polysubstance users” vs “light users” in comparison to females, with a strength of association that decreased from time 4, i.e., May 2021. Increasing age was associ-

ated with a decreasing odds of being “polysubstance users”, with younger respondents that were up to 10 times more likely to be “polysubstance users” than older ones. During lockdown (time 2) such differences appeared slightly less pronounced and became more marked immediately afterwards. Increasing self-reported economic status was associated with an increasing odds of being “polysubstance users” vs “light users”, with people with high economic level that were over 2 times more likely to be “polysubstance users” than people with low economic level before lockdown and immediately afterwards. During lockdown (time 2), such difference reached 3 times and, from time 4, i.e., May 2021, it increased up to 6 times. Finally, reporting anxiety or depressive symptoms

Table 3

Results of the logistic regression models for the factors associated with substance use profiles from the Latent Class Analysis models in all time points: “polysubstance users” vs “light users”

	Time 1 ¹	Time 2 ¹	Time 3 ¹	Time 4 ¹	Time 5 ¹	Time 6 ¹
	aOR (95%CI)	aOR (95%CI)	aOR (95%CI)	aOR (95%CI)	aOR (95%CI)	aOR (95%CI)
Sex						
Female	ref	ref	ref	ref	ref	ref
Male	1.60 (1.22, 2.11)	1.50 (1.15, 1.97)	1.56 (1.07, 2.27)	1.30 (0.84, 2.01)	1.24 (0.87, 1.77)	1.26 (0.89, 1.78)
Age						
55-74	ref	ref	ref	ref	ref	ref
35-54	2.05 (1.38, 3.04)	2.19 (1.51, 3.20)	3.82 (2.16, 6.75)	1.64 (0.77, 3.50)	2.51 (1.38, 4.58)	1.98 (1.18, 3.30)
18-34	4.23 (2.85, 6.27)	3.51 (2.37, 5.19)	7.91 (4.38, 14.31)	4.15 (1.93, 8.95)	10.43 (5.63, 19.32)	7.52 (4.35, 13.01)
<i>p for trend</i>	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Level of education						
High	ref	ref	ref	ref	ref	ref
Medium	1.01 (0.74, 1.36)	1.10 (0.82, 1.48)	0.93 (0.64, 1.35)	0.90 (0.56, 1.44)	0.87 (0.60, 1.28)	0.83 (0.56, 1.22)
Low	1.29 (0.85, 1.97)	1.42 (0.94, 2.15)	1.01 (0.55, 1.88)	0.94 (0.49, 1.81)	1.23 (0.68, 2.23)	1.17 (0.68, 1.99)
Economic status						
Under the national mean	ref	ref	ref	ref	ref	ref
On average	1.10 (0.79, 1.53)	1.13 (0.82, 1.57)	1.34 (0.84, 2.13)	2.09 (1.14, 3.83)	1.77 (1.05, 3.00)	0.98 (0.61, 1.58)
Over the national mean	2.34 (1.54, 3.58)	3.01 (1.99, 4.56)	2.40 (1.33, 4.32)	6.29 (3.43, 11.50)	6.12 (3.40, 11.02)	4.83 (2.89, 8.09)
<i>p for trend</i>	<0.001	<0.001	0.006	<0.001	<0.001	<0.001
Anxiety or depression						
No	ref	ref	ref	ref	ref	ref
Yes	2.61 (1.96, 3.48)	1.35 (1.01, 1.82)	2.48 (1.68, 3.68)	1.89 (1.19, 2.99)	3.26 (2.22, 4.78)	2.12 (1.39, 3.23)
Sleep disorders						
No	ref	ref	ref	ref	ref	ref
Yes	1.13 (0.85, 1.49)	0.99 (0.75, 1.32)	0.98 (0.66, 1.45)	1.13 (0.76, 1.69)	1.13 (0.78, 1.64)	1.19 (0.78, 1.81)
Use of psychotropic drugs						
No	ref	ref	ref	ref	ref	ref
Yes	4.25 (3.07, 5.87)	4.84 (3.57, 6.57)	4.36 (2.82, 6.75)	4.71 (2.92, 7.60)	7.62 (5.23, 11.11)	10.03 (6.79, 14.84)

aOR: adjusted odds ratio; CI: confidence interval.

¹Time 1: pre-lockdown (February 2020); Time 2: lockdown (April-May 2020); Time 3: November-December 2020; Time 4: May 2021; Time 5: February-March 2022; Time 6: April 2023.

as well as using psychotropic drugs was strongly associated with being “polysubstance users”. In the last two time points, i.e., 2022 and 2023, people using psychotropic drugs resulted 8-10 times more likely to be “polysubstance users” compared to non-users (Table 3).

Being “dual users” in comparison to “light users” was associated with a younger age, especially in latest time points, with a high economic status, with anxiety or depressive symptoms and psychotropic drugs use, although the association of the last two factors only reached significance at the last time points (Table 4).

DISCUSSION

In the present study we found that patterns of psychoactive substance use among Italian adults in the COVID-19 pandemic period was initially characterized by two profiles, “polysubstance users” and “light users”, that become three after the lockdown, with the identification of a new profile of “dual users”, e.g., those who mainly smoked tobacco cigarettes and used NCEDs.

At-risk alcohol use characterizes all profiles. “Light users” were characterized by no use of cannabis neither psychotropic substances, a light use of conventional cigarettes and NCEDs, which decreased after lockdown (since November-December 2020), and use of alcohol at risk, which, albeit it showed a little reduction during lockdown, it largely increased afterwards. Polysubstance use was characterized by the use of all substances, especially alcohol at risk and cannabis which showed an increase in use after lockdown. Finally, the “dual users” profile showed a constant use of conventional cigarettes, NCEDs and alcohol at risk, with a decrease, especially in smokers, in the last time point.

Results confirm findings on the use of single substances during the COVID-19 pandemic in Italy, which showed a modest reduction during the phase of first restrictions followed by an increase to values higher than those recorded in the pre-pandemic period [19, 34-36].

The emergence of the new profile of “dual users” confirms the increasing trend in NCEDs use, in particular

Table 4

Results of the logistic regression models for the factors associated with substance use profiles from the Latent Class Analysis models in all time points: “dual users” vs “light users”

	Time 3 ¹	Time 4 ¹	Time 5 ¹	Time 6 ¹
	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)
Sex				
Female	ref	ref	ref	ref
Male	1.06 (0.76, 1.48)	1.20 (0.81, 1.79)	1.10 (0.85, 1.43)	1.15 (1.00, 1.33)
Age				
55-74	ref	ref	ref	ref
35-54	1.41 (0.92, 2.17)	1.32 (0.85, 2.05)	1.33 (1.02, 1.73)	1.13 (0.97, 1.32)
18-34	1.69 (1.00, 2.84)	1.78 (1.03, 3.07)	1.48 (1.01, 2.16)	1.26 (1.02, 1.57)
<i>p for trend</i>	0.042	0.039	0.034	0.028
Level of education				
High	ref	ref	ref	ref
Medium	1.00 (0.70, 1.45)	1.08 (0.72, 1.63)	1.12 (0.87, 1.46)	1.27 (1.08, 1.49)
Low	1.06 (0.57, 1.97)	0.99 (0.53, 1.88)	1.07 (0.74, 1.55)	1.22 (0.98, 1.53)
Economic status				
Under the national mean	ref	ref	ref	ref
On average	1.14 (0.73, 1.79)	1.06 (0.68, 1.67)	1.17 (0.82, 1.68)	0.93 (0.79, 1.09)
Over the national mean	1.90 (1.05, 3.44)	2.68 (1.30, 5.54)	1.67 (1.05, 2.63)	1.01 (0.80, 1.27)
<i>p for trend</i>	0.064	0.028	0.046	0.85
Anxiety or depression				
No	ref	ref	ref	ref
Yes	0.91 (0.63, 1.32)	1.06 (0.70, 1.61)	1.39 (1.07, 1.79)	1.23 (1.06, 1.44)
Sleep disorders				
No	ref	ref	ref	ref
Yes	1.21 (0.87, 1.68)	1.29 (0.88, 1.88)	1.04 (0.82, 1.31)	0.99 (0.86, 1.14)
Use of psychotropic drugs				
No	ref	ref	ref	ref
Yes	1.44 (0.88, 2.35)	1.33 (0.75, 2.35)	1.10 (0.69, 1.73)	1.39 (1.1, 1.77)

aOR: adjusted odds ratio; CI: confidence interval.

¹Time 3: November-December 2020; Time 4: May 2021; Time 5: February-March 2022; Time 6: April 2023.

HTPs and disposable e-cigarettes. Most use of NCEDs is accompanied by more than replacing the use of conventional cigarettes [37].

We found that men were more likely to be polysubstance users than women, confirming results from several studies [38] although a growing body of research suggests a narrowing of the “gender gap” in overall drug patterns [39]. Moreover, according to the literature, we found that polysubstance use was associated with having younger age [1, 5, 40-41] and being lower educated [41]. Our findings also highlight an association of polysubstance use with high economic status that provides greater access to a wider range of substances, potentially contributing to polysubstance use [42].

Finally, our results confirm the association between the risk of polysubstance use and the increase in symptoms of anxiety and depression, and, above all, with the use of psychotropic drugs (aOR=3.90 for ≥ 2 substances) [14].

Strengths and limitations

Among the strengths of the present study, there are the large samples considered in the various surveys. The selection of the samples from online panels should be considered, since this could invalidate the generalizability of the findings to the whole Italian adult population. However, our results are in line with other national studies (IPSA, ISTAT) [43-44] confirming the good degree of representativeness obtained in the LOST samples. In order to explore the generalizability of our findings, it should be noted that the definitions of at-risk behaviours could be different among studies depending on both the questions and the scales, as well as the age size of the samples, returning in different prevalence estimates. As an example, the prevalence of at-risk alcohol users defined using the AUDIT-C score is higher in comparison to that defined from the National Institute of Health in the Report to the Parliament [45]. In addition, we did not take into account for the longitudinal structure of our data in order not to reduce sample size and to add complexity to the models, but further analyses exploring changes in time in polysubstance use could improve understanding the phenomenon. Although other studies used the same data of this work to study trends in the use of substances during the pandemic period and their associated factors [17-20, 34, 35], here we wanted to investigate a different aspect, i.e. the characteristics and trends in the concomitant use of substances, an aspect that has been little studied, especially in adults. Our analysis employed LCA models which have emerged in recent years as a modern approach to polysubstance research, especially among adolescents, emphasizing a person-centered, rather than variable-centered, approach [46]. Finally, the surveys were carried out during most of the COVID-19 pandemic waves, thus allowing us to capture the possible effect of the pandemic peaks on the population's psychological distress and lifestyle changes. Several surveys were carried out during the COVID-19 pandemic in Europe, however most of them focused on the lockdown period. The added value of this study is also to explore changes in the long term after the emergency period and the pattern of polysubstance use normalization.

CONCLUSIONS

The COVID-19 pandemic has carried changes in psychoactive substance use patterns as highlighted by the emergence of consumption profiles diversified over time. To facilitate the development and design of tailored prevention strategies, it is essential to acknowledge the peculiarities within polysubstance users, including their associated socio-demographic factors and developmental antecedents. Given the harmful health consequences of polysubstance use and since polysubstance use seems to be associated to similar characteristics as heavy users of single substances (e.g., higher psychological distress, male) a special attention of prevention should be focused on this subgroup of users. Targeting specific polysubstance use patterns and corresponding risk profiles may offer significant benefits in both prevention efforts and clinical research.

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Ethics approval

The two study protocols of the LOST IN ITALY and LOST IN TOSCANA studies were approved by the Ethics Committee of the coordinating centres (Istituto Besta, file number: 71-73, April 2020, and Comitato Etico Regionale per la Sperimentazione Clinica della Toscana, Sezione Area Vasta Centro, file number: CEAVC 19834, April 2021, respectively). All the enrolled participants provided informed consent to participate in the study.

Availability of data and materials

Data that support the findings of the present study and materials are available from the corresponding author upon reasonable request.

Conflict of interest statement

None to declare.

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