

Original Research

## COVID-19 Impact on Substance Use (Tobacco, Alcohol, Cannabis) and Stress in Medical Students

Mario Muselli <sup>†, \*</sup>, Loreta Tobia <sup>†</sup>, Eleonora Cimino <sup>†</sup>, Carlo Confalone <sup>†</sup>, Martina Mancinelli <sup>†</sup>, Leila Fabiani <sup>†</sup>, Stefano Necozone <sup>†</sup>, Vincenza Cofini <sup>†</sup>

Department of Life, Health and Environmental Sciences, Public Health Section, University of L'Aquila, 67100 L'Aquila, Italy; E-Mails: [mario.muselli@univaq.it](mailto:mario.muselli@univaq.it); [loreta.tobia@univaq.it](mailto:loreta.tobia@univaq.it); [eleonora.cimino@graduate.univaq.it](mailto:eleonora.cimino@graduate.univaq.it); [carlo.confalone@graduate.univaq.it](mailto:carlo.confalone@graduate.univaq.it); [martina.mancinelli@student.univaq.it](mailto:martina.mancinelli@student.univaq.it); [leila.fabiani@univaq.it](mailto:leila.fabiani@univaq.it); [stefano.necozone@univaq.it](mailto:stefano.necozone@univaq.it); [vincenza.cofini@univaq.it](mailto:vincenza.cofini@univaq.it)

<sup>†</sup> These authors contributed equally to this work.

\* **Correspondence:** Mario Muselli; E-Mail: [mario.muselli@univaq.it](mailto:mario.muselli@univaq.it)

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### Abstract

The COVID-19 pandemic has led to unprecedented challenges globally, impacting various aspects of daily life, including education. This study examines the effects of the pandemic on stress levels and substance use among Italian medical students. Two independent surveys were conducted: 388 medical students were interviewed before the epidemic, and 222 medical students a year after the COVID-19 epidemic began. Results revealed significant changes in stress levels, with a reduction in mild stress and an increase in severe stress during the post-pandemic period, rising from 23% (95% CI: 19%-28%) to 46% (95% CI: 39%-52%). While tobacco smoking prevalence remained stable (25% vs 27%), the proportion of students exhibiting high levels of nicotine dependence increased (3.64%) compared to the period



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before the pandemic (1.80%). Alcohol consumption rates remained consistent (66%), with no significant differences in the distribution of risky alcohol consumption between the two periods ( $p = 0.535$ ). Surprisingly, there was a significant decrease in cannabis use post-pandemic (16% vs 6%), though problematic use among users persisted (49% vs 46%). Multivariable analysis confirmed associations between stress and tobacco smoking (AdjOR = 1.98, 95% CI: 1.11-3.53;  $p = 0.020$ ), as well as alcohol consumption (AdjOR = 1.71, 95% CI: 1.01-2.89;  $p = 0.047$ ). Furthermore, male students were more likely to engage in alcohol (AdjOR = 2.16, 95% CI: 1.47-3.19;  $p < 0.001$ ) and cannabis use (AdjOR = 1.79, 95% CI: 1.07-3.00;  $p = 0.027$ ). The study highlighted the complex interplay between stress and substance use among medical students, underscoring the importance of targeted interventions to address stress-related substance use and support the well-being of medical students, particularly in the context of the COVID-19 pandemic. Further research should explore longitudinal trends and the effectiveness of interventions in mitigating stress-related substance use among this vulnerable population.

### Keywords

COVID-19 impact; substance use; stress; medical students; tobacco smoking; alcohol consumption; cannabis use

## 1. Introduction

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has had a devastating global impact. It has represented a large-scale health crisis, imposing restrictions on mobility and social interactions to contain the spread of the virus. These preventive measures have led to significant changes in people's daily lives, health, and work, including lockdowns, social distancing, and widespread adoption of hygiene practices and precautions to reduce the risk of contagion. Such changes have had a significant impact on the mental and physical well-being and social relationships of the population, generating feelings of isolation, anxiety, and stress [1-4].

Universities were forced to rapidly transition to remote working for teaching, administrative, and support staff, with increased work pressures to ensure the continuity of academic and administrative activities [5, 6].

On the other hand, university students were forced to suddenly transition to online learning during the pandemic, requiring them to adapt quickly and navigate the challenges of technology and time management, causing a lack of social interaction in the classroom. In addition, University medical students have had to face a series of unique challenges in pursuing their education goals because the suspension of in-person academic activities has resulted in the loss of practical learning opportunities and collaboration that are fundamental for the training of future professionals in medical fields. The additional pressure resulting from the need to adapt to new study methods and take exams in a virtual environment and the fear of contagion has created in medical students a sense of uncertainty regarding their future with an impact on their well-being [7]. Consequently, while mandatory online learning offered some benefits, such as flexibility, time management, and the availability of recorded lessons [8, 9], it also presented challenges for students. They had limited

access to university resources, lacked in-person interaction with teachers and peers, and faced increased academic autonomy and distractions. Lockdowns lasting nearly a year further exacerbated these challenges, exposing university students to new psychological burdens [8-10].

### **1.1 Stress among Students and the COVID-19 Pandemic**

Stress can be caused by physical or psychological factors that disrupt our body's balance (homeostasis) and require us to adapt [11]. Both physical and mental stressors trigger this stress response. In humans, the nervous system (especially the sympathetic nervous system) and hormones (controlled by the hypothalamus-pituitary-adrenal axis) work together to manage stress, as first described by Hans Selye in the 1930s [12].

Medically, stress is the body's reaction to anything that disrupts its balance, while psychologically, it's our response to significant environmental changes [12, 13]. For university students, academic pressure is often the most important stressor. Studies show medical students, in particular, experience higher rates of mental health problems due to academic stress [14].

An Italian study from before the pandemic found that only 27.9% of medical students reported low stress, 55.2% had medium stress, and 16.9% had high stress. Analyzing the factors associated with high-stress levels, females suffered from stress more than males [15]. Academic studies and relationships were the primary sources of stress, with concerns about keeping up with rapid advancements in medicine anticipated to worsen with the pandemic [16].

The COVID-19 pandemic likely made the stress response more complex, with some student groups feeling it more intensely. A study by Barbayannis et al. suggests the link between academic stress and mental well-being is most vital for specific groups. Non-binary students and second-year students experienced a heavier academic burden and lower well-being, while women, non-binary students, and upperclassmen were more impacted by pandemic-related stress [17].

### **1.2 Tobacco Smoking among Students and COVID-19 Pandemic**

Smoking is a leading global health concern, the second leading cause of death globally and the primary preventable cause, responsible for more than 8 million deaths a year [18, 19]. The World Health Organization estimates there are 1.337 billion tobacco smokers worldwide [19].

Chronic tobacco use is linked to severe respiratory and cardiovascular diseases, including lung cancer, asthma, chronic obstructive pulmonary disease (COPD), bronchitis, heart disease, aneurysms, and strokes [20, 21].

In Italy, tobacco use claimed around 93,000 lives in 2019, with over 25% of these deaths occurring between ages 35-65 [22]. The Progressi delle Aziende Sanitarie per la Salute in Italia (PASSI) survey is an Italian National surveillance system that monitors health behaviors and risk factors among the population the National Institute of Health manages. The latest survey conducted indicates a smoking rate of 24%, with a higher prevalence among men, individuals with financial difficulties, and those with lower educational attainment [23].

A recent Milan University study (2020-2021 academic year) found that 19.3% of 6605 students were exclusive cigarette smokers. Another 2.8% used only e-cigarettes or heated tobacco products (HTPs), and 3.7% used both. Overall, 25.8% of students used some form of tobacco product [24]. Studies by Saulle et al. (20 Italian medical schools) and a European study found that medical students smoke more than the general population. Saulle's study showed a 20.4% smoking rate

among third-year students, while the European study found a 29.3% overall rate, with Italy at 31.3% [25, 26]. A more recent study found the smoking rate among Italian medical students had decreased to 29.5%, but it remained significantly higher than the 6.1% rate observed in US medical students [27].

### **1.3 Alcohol Consumption among Medical Students and COVID-19 Pandemic**

Alcohol use is a major public health issue worldwide, particularly for young people like students. In 2018, the World Health Organization (WHO) estimated that over 2.3 billion people consume alcohol globally [28]. This consumption contributes to roughly 3 million deaths annually (5.3% of all deaths) due to various associated health problems [28]. These problems include digestive cancers (throat, esophagus, liver, colon, rectum), liver diseases (infectious and non-infectious), neurological issues, unintentional and intentional injuries (accidents, falls, alcohol poisoning, suicide, violence), and adverse pregnancy outcomes (miscarriage, premature birth, developmental delays) [28].

The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) is an agency established to provide the European Union and its member states with a factual overview of European drug problems and a solid evidence base to support drug policies. A recent report indicates that in Italy, nearly 88% of adults (15-64 years old) regularly consume alcohol, with a similar percentage (87.7%) reported for young adults (15-34) in the past year [29]. Binge drinking, high-intensity drinking, and heavy drinking are all unhealthy consumption patterns [30]. Italy's PASSI surveillance system (2017-2020) found that 2.5% and 9% of Italians aged 18-69 reported heavy and binge drinking, respectively [31].

Studies investigating risky drinking habits among university students using the Alcol Use Disorders Identification (AUDIT) test show that European students tend to have lower-risk patterns, with some variation between northern and southern regions [32]. The average AUDIT score in Italy was 4.00, with a mean of 5.55 and a standard deviation of 5.35 [32]. Interestingly, research suggests medical students are more likely to drink alcohol compared to the general population. This trend holds in Italy, where Lambretti et al. found that 85.5% of medical students at the Second University of Naples reported regular alcohol consumption, with 6.1% exhibiting dangerous drinking patterns [33]. This concerning trend extends beyond Italy. Finland has the highest rate of alcohol misuse among medical students in Europe, with a 2013 survey revealing that 33% were harmful drinkers [34]. Similarly, a Polish study found that 30.9% (167 out of 540) of medical students at the Medical University of Silesia misused alcohol [35]. Studies outside Europe also echo this concern. A Paraguayan study reported that nearly half (49%) of medical students at the National University of Asunción exhibited heavy alcohol dependence [36].

### **1.4 Cannabis Use among Medical Students and COVID-19 Pandemic**

Cannabis use is linked to various negative effects, including memory loss, impaired focus, reduced performance, traffic accidents, depression, and dependence [37]. Frequent use can heighten emotional and cognitive risks, with college students particularly vulnerable due to factors like early exposure, high potency strains, pre-existing mental health issues, and genetic predisposition. Potential consequences include psychosis, anxiety, depression, ADHD, sleep problems, and cannabis use disorder [38].

Despite its illegality in many regions, cannabis remains the world's most widely used illicit drug. The United Nations Office on Drug and Crime (UNODC) estimates that roughly 200 million people used cannabis globally in 2021 [39]. In Europe, around 8% of adults (aged 15-64) have used cannabis in the last year, with an estimated 1.3% (3.7 million) using it daily or almost daily [40]. Italy reflects this trend, with a 10.2% prevalence of cannabis use among adults (15-64) and a significantly higher 20.9% prevalence among young adults (15-34) in the past year, according to the 2017 EMCDDA report [29].

Concerningly cannabis appears to be the most common illegal drug used by university students worldwide [41]. Students may use it as a coping mechanism for adverse mental health experiences despite the availability of alternative treatments and therapies [42]. A 2020 study of 4,942 medical students from nine countries found cannabis to be the most prevalent recreational drug, with usage rates as high as 39% reported among Canadian students [16].

In Italy, a pre-pandemic cross-sectional study revealed that 8.45% of medical students used cannabis in the past month, aligning with findings from other studies [43]. This rate is lower than that observed among French medical students in 2020-2021 by Novin et al. (19% lifetime and 13.5% past three months) [44, 45].

### ***1.5 The Relationship between Stress and Substance Use among Students***

Clinicians and researchers have long recognized stress as a major factor contributing to the development, persistence, and relapse of substance use disorders, including alcohol and drugs [46]. Studies in both animals and humans show that exposure to stress increases the likelihood of self-administering medications [47]. For example, smokers often cite stress and anxiety as triggers for smoking and relapse, using tobacco as a way to cope with their emotional state [48]. The link between stress and smoking is so strong that stress is often identified as a leading cause of smoking [49]. Similarly, alcohol consumption, usually associated with social gatherings, can increase during stressful times as some individuals cope with psychological and economic strain by drinking more [50].

The COVID-19 pandemic further highlights this connection. A study by Prowse et al. found that to manage pandemic-related stress, university students turned to substances at concerning rates: 9.3% vaped nicotine products, 23.8% drank alcohol, and 17.5% used cannabis, all at least moderately, as coping mechanisms [51]. Interestingly, another study suggests that college students who experienced more negative consequences from cannabis use (like anxiety and depression) due to COVID-19 were more likely to use cannabis to cope with stress [42, 52].

However, Vasconcelos et al. reported that symptoms such as stress, anxiety, and depression did not help explain changes in drinking behavior during the pandemic among college students [53]. In contrast, recent studies indicate a significant risk of substance use among medical students, with poorer mental health linked to higher use [54]. We hypothesized that the COVID-19 pandemic could exacerbate this population's stress and unhealthy behaviors.

To our knowledge, no research has examined the impact of the pandemic on stress and substance use (e.g., tobacco smoking, alcohol consumption, cannabis use) among Italian medical students. This study aims to address this gap by evaluating the effects of the COVID-19 pandemic on substance use patterns in this population and its association with stress.

## **2. Materials and Methods**

This study was part of a larger online cross-sectional study conducted in 2021 at the University of L'Aquila, which included students enrolled in medical courses, health science courses, and other programs. Partial results from the larger study were reported by Cofini et al. [9].

This study was part of a larger project approved by the Local Ethical Commission of the University of L'Aquila (protocol code: 71684).

### **2.1 Recruitment and Procedure**

During two webinars on the Microsoft team's platform, six teachers from three departments introduced the study and its objectives. The study was open to all students who attended the webinars, and participation was voluntary and anonymous. In June and July 2021, the students could only fill out the questionnaire using a Google Form after giving informed consent using a specific flag. The questionnaire consisted of 4 sections:

- E-learning satisfaction was evaluated with the Satisfaction scale [55];
- Psychological aspects such as stress and coping were assessed with the General Health Questionnaire (GH-12) [56] and Brief Cope Scale [57] respectively;
- Substance use disorder was evaluated with “Fagerström Test for Nicotine and Dependence (FTND)” [58], “Alcohol Use Disorders Identification Test-c (AUDIT-c) [59], and “Cannabis Abuse Screening Test (CAST)” [60];
- Sociodemographic information.

For the present study, we analyzed data on stress and substance use disorder in the specific population of medical students (MMs). To analyze the impact of the COVID-19 pandemic on stress and substance use in MMs, we compare our data with those collected in a previous study involving a different cohort of students [15]. This was an Italian multicenter cross-sectional study in which the Medicine Faculty of L'Aquila participated in 2018. In November 2018, the Local Research team presented the objectives of the National Project and conducted interviews after the students gave their informed consent, adding a module on substance use.

### **2.2 Tools and Measurements**

As reported above, the questionnaire was composed of different scales to investigate the different aspects planned for the large project. All aspects were investigated with validated scales.

#### **2.2.1 General Health Questionnaire**

The General Health Questionnaire (GH-12) is composed of a 12-item scale to assess perceived psychological distress: each item assesses the severity of a mental problem over the past few weeks [57]. The evaluation is carried out through a 4-point Likert scale with scores from 0 to 3 for each item. The possible answers are “less than usual” (score = 0), “no more than usual” (score = 1), “rather more than usual” (score = 2), or “much more than usual” (score = 3). The 12 items evaluated are: able to concentrate, lost sleep over worry, play a useful part in things, capable of making decisions, constantly under strain, could not overcome difficulties, enjoy day-to-day activities, face up to problems, feeling unhappy and depressed, losing self-confidence, thinking of self as worthless,

and reasonably happy. Literature reported the overall Cronbach's alpha was high (0.84), indicating sufficient internal consistency. In our study, it was computed to be 0.90.

### 2.2.2 Perceived Stress Scale

The Perceived Stress Scale (PSS) is an attitude and self-evaluation test developed by Sheldon Cohen to assess stress levels. It is structured on 10 items, and each response corresponds to a numerical value ranging from 0 (never) to 4 (very often). Therefore, the variety of its total score, given by the sum of the scores obtained from each response, can range from a minimum of 0 to a maximum of 40, and Cronbach's alpha of 0.78 [61]. Our results showed that Cronbach's alpha was high 0.87 [61].

### 2.2.3 Fagerström Test for Nicotine and Dependence

The Fagerström Test for Nicotine and Dependence (FTND) test was used for smoking evaluation. The test evaluates the grade of physical nicotine dependence related to cigarette smoking. It contains 6 items that assess the quantity of cigarette consumption, the compulsion to use, and dependence. In scoring the Fagerström Test for Nicotine Dependence, yes/no items are scored from 0 to 1 and multiple-choice items are scored from 0 to 3 [58, 62]. According to the authors, the coefficient alpha for the FTND was computed to be 0.61 [62]. Our study found a Cronbach's alpha of 0.60 in the first survey and 0.66 in the second survey.

### 2.2.4 Alcohol Use Disorders Identification Test

The Alcohol Use Disorders Identification Test (AUDIT-c) was used to screen students for problem drinking. The AUDIT-C test consists of 3 questions about the longer AUDIT tool, a more comprehensive assessment of problem drinking. Each question has 5 possible answers with a score ranging from 0 to 4 [59]. The reliability of the AUDIT-C score was high (Cronbach's alpha = 0.98) [63]. Our study found a Cronbach's alpha of 0.45 in the first and 0.62 in the second surveys.

### 2.2.5 Cannabis Abuse Screening Test

The Cannabis Abuse Screening Test (CAST) was used to investigate some aspects of cannabis consumption in the past 12 months. All items are answered on a five-point scale ("never" = 0, "rarely" = 1, "from time to time" = 2, "fairly often" = 3, "very often" = 4). The overall score is calculated by summing the scores for every item and it has high internal consistency (Cronbach's alpha = 0.81) [60, 64]. In our study, it was computed to be 0.29 in the first survey and 0.72 in the second.

## **2.3 Variables Selected**

Because of the different tests used to evaluate the stress disorder during the two compared surveys, we computed the categorical variable "Stress level" taking into account the following cutoffs reported in the literature for the GH-12 test and SPP test, respectively: "mild or average" (if the GH-12 score was  $\leq 15$  or if PSS score was  $\leq 13$ ); "Moderate" (if the GH-12 scores were from 16 and 20 or if PSS scores were from 14 to 26); "severe" (if the GH-12 score was  $> 20$  or if PSS score was  $> 27$ ). Smoking habit was investigated with a dichotomous variable "Tobacco smoking: yes/no",

derived from the item “Do you smoke cigarettes?”; then we derived the continuous variable “FTND score” from the total score of the FTND test; we computed the categorical variable “Nicotine dependence”: “minimally dependent” if the FTND score was  $\leq 3$ , “moderately dependent” if the FTND score was from 4 to 6, “highly dependent moderately dependent” if the FTND score was from 4 to 6, “highly dependent” if the wars from 7 to 10. To analyze alcohol consumption, we use the variable “Alcohol consumption: yes/no” from the item “Do you consume alcohol?”; then, from the scoring of the AUDIT-c tool, we defined the dichotomous variable “Alcohol consumption at risk”: “no”, if the score test was  $< 4$  in women and  $< 5$  for men; “yes” if the score test was  $\geq 4$  in women and the score  $\geq 5$  in men respectively. Concerning cannabis consumption, we used the dichotomous variable “Cannabis use: yes/no” from the items “Do you consume cannabis”; we performed the categorical variable “Problematic cannabis use”: “no” if the CAST score was  $\leq 2$ , “yes” if the score was  $> 3$ .

### 2.4 Statistical Analysis

All variables were analyzed and reported with means and standard deviations or absolute frequencies and percentages depending on their nature (continuous or categorical).

The Chi-square test or Fisher's exact test were used to compare categorical variables. T-test or similar nonparametric tests were used to compare continuous variables. Factors associated with substance use were analysed with bivariate and multivariable analysis.

Three multivariable logistic regression models were performed for each unhealthy behavior investigated. The first model was performed with tobacco smoking as the dependent variable, the second model had alcohol consumption as the dependent variable, and the third model reported cannabis use as the dependent variable. The following independent variables: period (pre-COVID-19/post-COVID-19), age (years), sex (males/females), and stress levels (mild/moderate/severe) were entered into each model, reporting the adjusted odds ratios (OR<sub>adj</sub>) and the 95% confidence intervals (95%CI). All analyses were conducted on STATA/MP 14 software, setting alpha equal to 0.05.

### 3. Results

Data analyzed were from 222/731 (27.9%) medical students interviewed a year after the COVID-19 epidemic began and 388/796 (53.1%) medical students interviewed before the epidemic. The first sample was younger than the second sample, and in the second sample, the proportion of males was lower, as shown in Table 1.

**Table 1** Sample characteristics.

	Pre COVID-19	Post COVID-19	<i>p</i> -value
	<i>N</i> = 388	<i>N</i> = 222	
Age	23 (2.4) 22 [21-24]	24 (4.5) 24 [21-26]	0.001
Gender			
• Male	155 (40.4%)	67 (30.2%)	0.012
• Female	229 (59.6%)	155 (69.8%)	



### 3.1 Stress Results

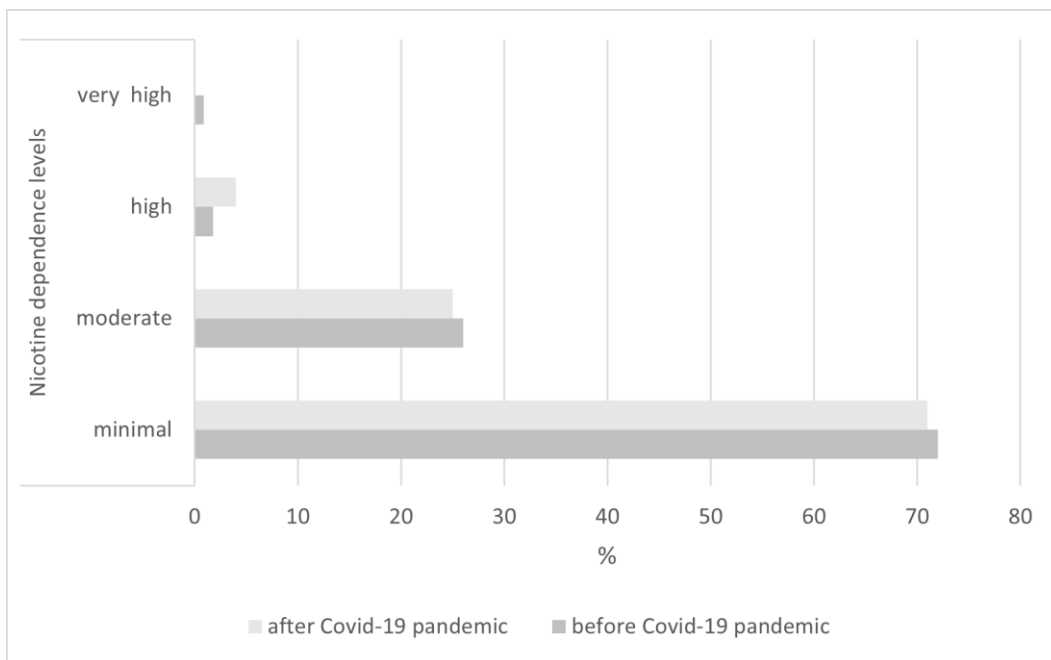
Table 2 presents data from the two surveys. While the mild stress level remained consistent, there were notable shifts in the distribution of students experiencing moderate or severe stress. Before the pandemic, a higher percentage of medical students reported moderate stress than in the post-pandemic period (57%; 95% CI: 57%-62% versus 36%; 95% CI: 30%-42%, respectively). Conversely, there was a marked increase in the proportion of students reporting severe stress over time, rising from 23% (95% CI: 19%-28%) before the pandemic to 46% (95% CI: 39%-52%) afterward.

**Table 2** Pre and Post-COVID-19 stress levels.

Stress level	Pre COVID-19		Post COVID-19		<i>p</i> -value
	n (%)	[95%CI]	n (%)	[95%CI]	
Mild or average	72 (20%)	16%-24%	40 (18%)	14%-24%	
Moderate	209 (57%)	52%-62%	79 (36%)	30%-42%	<0.001
Severe	85 (23%)	19%-28%	101 (46%)	39%-52%	

### 3.2 Tobacco Smoking

In 2021, fifty-five students reported a tobacco smoking habit (25%; 95% CI: 19%-31%), showing no statistically significant difference compared to data collected before the COVID-19 pandemic, when 101 out of 378 medical students reported the same habit (27%; 95% CI: 22%-31%). Regarding the analysis of nicotine dependence, there was no significant change in the FTND scores between the two periods ( $1.56 \pm 1.9$  vs  $1.65 \pm 1.8$ ;  $p > 0.05$ ). Figure 1 displays the categories of nicotine dependence analyzed. The proportions did not differ significantly between the two periods,  $\chi^2 (3, N = 610) = 0.02$ ,  $p = > 0.05$ . However, the analysis revealed that following the COVID-19 pandemic, the proportion of students exhibiting high levels of nicotine dependence increased (3.64%) compared to the period before the pandemic (1.80%). Conversely, no students were exhibiting very high levels of nicotine dependence after the pandemic, whereas approximately 1% did so before the COVID-19 pandemic.

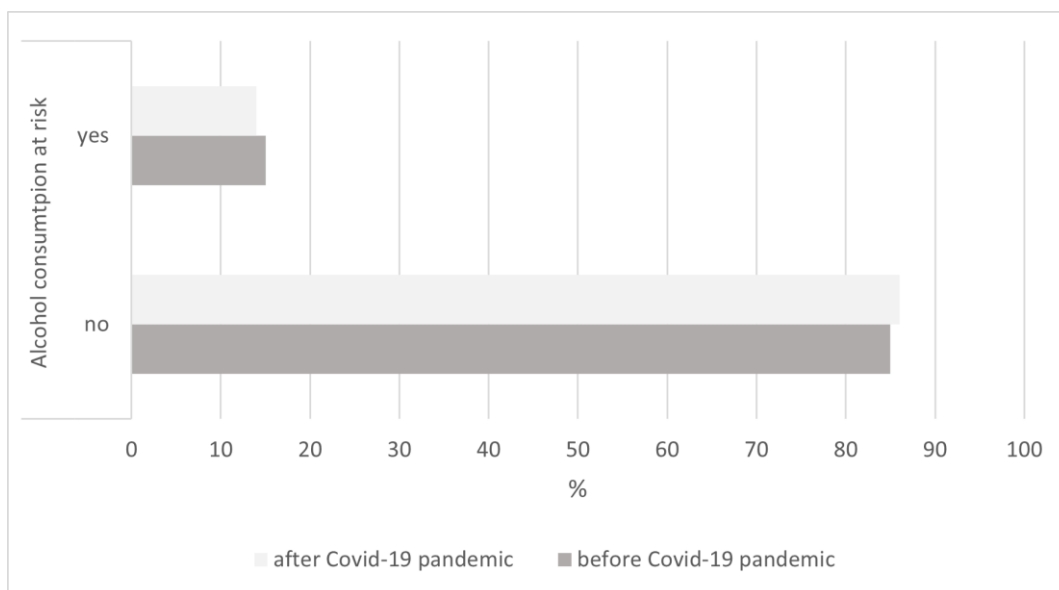


**Figure 1** Nicotine dependence.

### 3.3 Alcohol Consumption

The alcohol consumption among medical students didn't change between the two periods investigated: 66% of the responders reported consuming alcohol in 2019 (249/377) and the proportion was the same during 2021 (147/222).

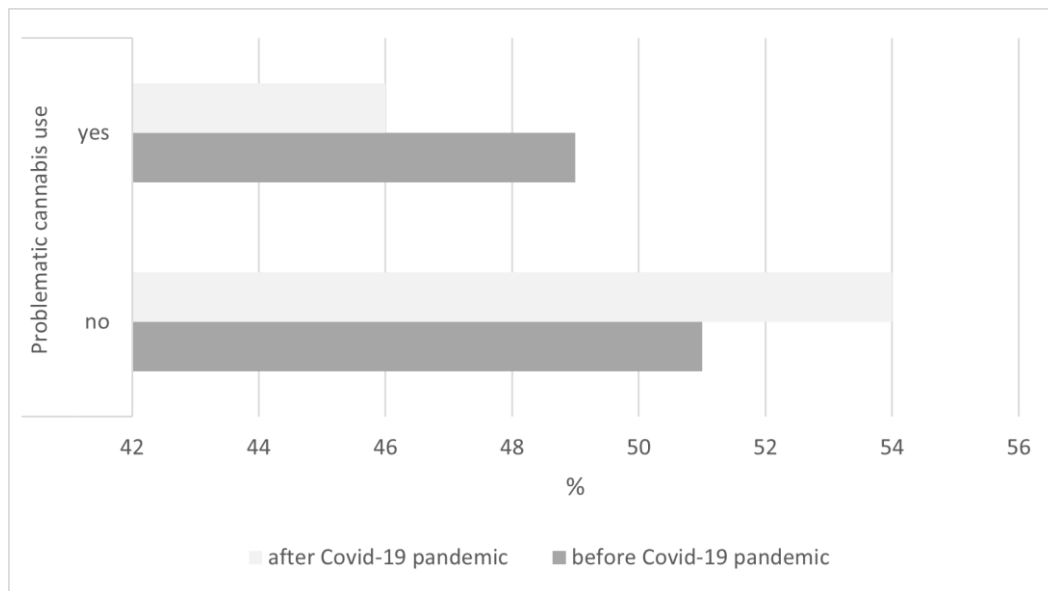
There were no significant differences in the distribution of alcohol consumption at risk between the two periods,  $\chi^2 (1, N = 610) = 0.39, p = > 0.05$ : 59 subjects (15%) were screened as alcohol-at-risk users before the pandemic and 30 (14%) after it (Figure 2).



**Figure 2** Alcohol consumption.

### 3.4 Cannabis Use

We found that only 74 participants answered affirmatively to the item “Do you use cannabis”: 61/377 before the pandemic (16%) with 11 missing answers and 13/222 (6%) reported to be cannabis users after the pandemic,  $\chi^2 (1, N = 599) = 13.76, p < 0.001$ . Using the CAST test score, we found that the proportion of problematic cannabis use among the users was not statistically different in the two periods 30/61 (49%) versus 6/13 (46%),  $\chi^2 (1, N = 74) = 0.04, p > 0.05$  (Figure 3).



**Figure 3** Problematic cannabis use.

### 3.5 Bivariate and Multivariable Analysis

As shown in Table 3, bivariate analysis revealed that a “severe” stress level was significantly associated with tobacco smoking (OR = 1.91, 95% CI: 1.08-3.37;  $p = 0.026$ ). The association was confirmed by multivariable analysis (AdjOR = 1.98, 95% CI: 1.11-3.53;  $p = 0.020$ ). Male sex was associated with a higher probability of alcohol consumption (OR = 2.16, 95% CI: 1.49-3.13;  $p < 0.001$ ); however, multivariable analysis revealed that alcohol consumption was significantly associated with male sex (OR = 2.16, 95% CI: 1.47-3.19;  $p < 0.001$ ), and “severe” stress level (AdjOR = 1.71, 95% CI: 1.01-2.89;  $p = 0.047$ ). Considering cannabis use, this was associated with the male sex (OR = 2.10, 95% CI: 1.29-3.44;  $p = 0.003$ ) and the COVID-19 period (OR = 0.32, 95% CI: 0.17-0.60;  $p < 0.001$ ). These associations were confirmed by multivariable analysis with, respectively, AdjOR = 1.79 (95% CI: 1.07-3.00;  $p = 0.027$ ) and AdjOR = 0.29 (95% CI: 0.15-0.57;  $p < 0.001$ ).

**Table 3** Bivariate and multivariable analysis.

Variables	OR	95% CI	p-value	Adj. OR	95% CI	p-value
Model 1: Tobacco smoking						
Period						
- Pre COVID-19	Ref			Ref		
- Post COVID-19	0.90	0.62-1.32	0.600	0.84	0.55-1.27	0.403

Age	1.03	0.98-1.09	0.173	1.02	0.97-1.08	0.368
Gender						
- Female	Ref			Ref		
- Male	1.42	0.98-2.06	0.064	1.37	0.92-2.02	0.117
Stress levels						
- Mild or average	Ref			Ref		
- Moderate	1.35	0.78-2.34	0.277	1.37	0.79-2.38	0.265
- Severe	1.91	1.08-3.37	0.026	1.98	1.11-3.53	0.020
<hr/>						
Model 2: Alcohol consumption						
Period						
- Pre COVID-19	Ref			Ref		
- Post COVID-19	1.01	0.71-1.43	0.966	0.98	0.66-1.44	0.918
Age	1.03	0.98-10.8	0.256	1.02	0.96-1.08	0.480
Gender						
- Female	Ref			Ref		
- Male	2.16	1.49-3.13	<0.001	2.16	1.47-3.19	<0.001
Stress levels						
- Mild or average	Ref			Ref		
- Moderate	0.88	0.56-1.39	0.589	0.94	0.58-1.50	0.786
- Severe	1.59	0.95-2.65	0.076	1.71	1.01-2.89	0.047
<hr/>						
Model 3: Cannabis use						
Period						
- Pre COVID-19	Ref			Ref		
- Post COVID-19	0.32	0.17-0.60	<0.001	0.29	0.15-0.57	<0.001
Age	0.99	0.92-1.06	0.746	1.01	0.93-1.10	0.739
Gender						
- Female	Ref			Ref		
- Male	2.10	1.29-3.44	0.003	1.79	1.07-3.00	0.027
Stress levels						
- Mild or average	Ref			Ref		
- Moderate	1.12	0.54-2.31	0.759	1.05	0.50-2.19	0.900
- Severe	1.53	0.72-3.22	0.266	1.87	0.87-4.03	0.109

#### 4. Discussion

This was an observational study to compare stress and substance use among 610 medical students before and after the COVID-19 pandemic.

The COVID-19 pandemic has instigated unprecedented challenges globally, reshaping societal norms and amplifying stressors across various demographics. In particular, the impact of COVID-19

on mental health among the general population, including students, has been reported by several studies [65-67].

Our study showed that the stress levels of the medical students were statistically different between the two periods investigated. These results are in line with the results of a recent meta-analysis that evaluated the prevalence of mental problems among medical students during the COVID-19 pandemic, evidencing the stress pooled prevalence of 34% (95%CI: 27%-42%) [10]. The COVID-19 pandemic brought unprecedented challenges for everyone, and medical students were likely not immune to these. Disruptions to daily life, worries about getting sick, and the overall uncertainty of the situation could all contribute to stress. Moreover, the pandemic may have caused disruptions to medical education, such as shifting to online learning or clinical rotations being cancelled. This could have made it harder for students to keep up with their studies and increased their academic stress.

Notably, the pandemic's impact extended beyond academic stressors, influencing students' substance use patterns. Our study found no significant change in tobacco smoking prevalence and nicotine dependence between the pre-and post-pandemic periods [68]. Our FTND results were lower than those from a study carried out in Turkey among medical students in 2021–2022 ( $3.1 \pm 2.6$ ) [69]. However, there was an increase in the proportion of students exhibiting high levels of nicotine dependence following the pandemic (3.64% vs 1.80%). This underscores the potential role of increased stress levels during the pandemic as a contributing factor to heightened nicotine dependence among medical students. A study in Northern Italy during the COVID-19 pandemic found that among frequent smokers, 38% said their cigarette usage had increased during the quarantine period. [70]. In contrast, some studies showed that lockdown was not associated with a significant change in smoking prevalence but with increases in cessation and quit attempts by smokers [71].

Moreover, our results reveal concerning trends in alcohol consumption, with a consistent proportion of students reporting alcohol use across both periods. Male students and those experiencing severe stress were more likely to engage in alcohol consumption, highlighting the complex interplay between stress, gender, and substance use among medical students. The analysis on alcohol consumption showed that during the COVID-19 pandemic period, the proportion of alcohol users at risk was higher than the proportion reported in a previous study in Italy by Lamberti et al. (3%) even if the study reported that alcohol consumption was more frequent among medical students than resident physicians or healthcare-professions students [33].

An important finding of our study was that alcohol consumption among medical students didn't change between the two periods investigated. These results are consistent with other literature studies conducted in the same period [72]. A longitudinal study conducted among college students in Portugal before, during, and after the lockdown due to the COVID-19 pandemic highlighted that during the lockdown and post-lockdown, students decreased their consumption compared to the pre-COVID-19 period and maintained a low alcohol intake level during the pandemic, despite an increase in alcohol cravings in post lockdown [53].

Regarding cannabis use, our study identified a significant decrease in the proportion of students reporting cannabis use post-pandemic, according to literature data [73].

This unexpected finding may reflect changes in students' coping mechanisms or lifestyle adjustments during the pandemic. It could be related to the measures taken against COVID-19, which favored it, most likely because younger university students studying in person are more likely

to consume substances for social reasons [74] and preferably at private parties [75] and certain festive events [76]. As reported by Merrill and colleagues, lockdowns and restrictions on social contact drastically reduced the contexts of shared consumption, such as parties and other usual events in the university environment [77]. An extensive study of 18,346 higher education students between the ages of 17 and 24 also revealed that the use of alcohol, tobacco, cannabis, and binge drinking decreased during the pandemic. The authors speculated that it could be due to the absence of social gatherings [78]. However, among cannabis users, the proportion exhibiting problematic cannabis use remained consistent across both periods. This suggests that while overall cannabis use decreased, those who continued to use cannabis may be at heightened risk of experiencing adverse consequences, underscoring the importance of targeted interventions and support services for at-risk students.

Consistent with existing literature [79, 80], the demographic factor “gender” was associated with alcohol and cannabis use: the risk of these unhealthy behaviors was higher in males than females, while tobacco smoking was independent by sex, controlling for all other factors. The association between stress and substance use among medical students is well-documented, with stress serving as a significant predictor of unhealthy behaviors. The multivariable analysis confirmed that stress was a significant factor associated with tobacco smoking and alcohol consumption: the probability for these unhealthy habits was higher in students with severe stress levels than in students with mild stress. These findings are in line with other studies. A study conducted in the USA has shown that college students who participated in the study before the beginning of the COVID-19 pandemic reported higher levels of alcohol consumption and perceived stress [81]. In contrast, stress symptoms were not associated with alcohol consumption in the longitudinal study carried out by Vasconcelos and colleagues [53]. The absence of association between stress levels and cannabis use found in our results is consistent with a cross-sectional study on Italian medical study carried out before the COVID-19 pandemic [43].

Our study's strengths lie in the use of standardized measurements. Gathering data on medical students using standardized measures, we were able to directly compare outcomes between the two distinct periods: before and after the COVID-19 pandemic. However, several limitations must be acknowledged. Firstly, the two surveys were conducted differently: students filled out the questionnaire in person before the pandemic, while the second was online. Secondly, our study relied on self-reported data, which may be subject to recall and social desirability biases. The study's cross-sectional nature also precludes causal inferences regarding the observed associations between stress and substance use. Furthermore, the study's reliance on a single institution may limit the generalizability of our findings to other medical student populations. Finally, no other aspects of the students' mental health and financial situation were investigated, which could be linked to stress and substance use.

## **5. Conclusions**

Consistent with existing literature, our study demonstrates a positive association between severe stress levels and tobacco smoking among medical students. Similarly, male students and those experiencing severe stress were more likely to engage in alcohol consumption, highlighting the need for targeted interventions to address stress-related substance use among university students [82]. In conclusion, our study highlights the complex interplay between stress and substance use among

medical students, particularly in the context of the COVID-19 pandemic. While the pandemic has introduced unprecedented challenges, it has also underscored the importance of proactive interventions to support the mental health and well-being of medical students. Targeted efforts aimed at addressing stressors and promoting healthy coping mechanisms are essential in mitigating the adverse impact of stress on substance use behaviors among this vulnerable population. Future research should explore longitudinal trends in substance use among medical students and investigate the effectiveness of tailored interventions in reducing stress-related substance use.

### **Author Contributions**

Conceptualization: Cofini V, Muselli M, and Necozone S; Formal analysis: Cofini V and Muselli M; Investigation: Cofini V, Cimino E, and Confalone C; Results interpretation: Muselli M, Tobia L, Cimino E, Confalone C, Mancinelli M, Fabiani L, Necozone S, Cofini V; Writing—original draft: Muselli M, Tobia L, Cimino E, Confalone C, Mancinelli M, Fabiani L, Necozone S, Cofini V; Supervision: Cofini V. All authors have read and agreed to the published version of the manuscript.

### **Competing Interests**

The authors have declared that no competing interests exist.

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