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**Anxiolytic consumption is associated with tobacco smoking and severe nicotine dependence. Results from the national French medical students (BOURBON) study.**

Running title: anxiolytic consumption and tobacco smoking behavior in medical students

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## Abstract

Tobacco smoking remains common amongst medical students, something which may impact on their ability to promote smoking cessation during their future careers.

*Objectives:* To determine the prevalence of smoking and consumption amongst French medical students and explore the link between both the presence of psychosocial factors and consumption of psychotropic medication and the severity of nicotine dependence and daily smoking behavior.

*Methods.* Medical students were recruited from 35 French universities of medicine through administration mailing lists and social networks, between December 13, 2016 and May 15, 2017. Data was collected via anonymized Internet questionnaire which included questions regarding current daily tobacco smoking behaviors. Severe nicotine dependence was defined by a short Fagerström test equal or greater than 4.

*Results.* 10985 medical students with a mean aged of 21.8 years (+/- 3.3) were included, 31.6% of which were male. 2078 (18.9%) were identified as current daily tobacco smokers and 59 (2.8%) were classed as having severe nicotine dependence. In multivariate analyses, tobacco smoking was independently associated with anxiolytic consumption, alcohol use disorder, cannabis use disorder, financial difficulties, and history of sexual and physical assault. Severe nicotine dependence was independently associated with anxiolytic consumption, cannabis use disorder, domestic violence, physical assault and financial difficulties.

*Conclusion.* Tobacco smoking has been found in almost one on 5 medical students and is associated with anxiolytic consumption as well as professional and personal factors.

Conflicts of interest: none declared.

Keywords: Tobacco smoking, nicotine dependence, medical students, risk factors

## Introduction

According to the World Health Organization, annual smoking related mortality has risen to 7.2 million deaths (World Health Organization, 2017). The Surgeon General's report already estimates that more than 20 million premature deaths can be attributed to cigarette smoking from 1964 to 2014 in the USA (Department of Health and Human Services, 2014), not to mention the tobacco-related morbidity including mental disorders (Mallet et al., 2017). In the general population, tobacco smoking has been associated with increased risk of mental disorders especially major depression (Luger et al., 2014; Rey et al., 2017) and anxiety (Lasser et al., 2000) ; and with other addictions including alcohol (Batel et al., 1995) and cannabis (Agrawal et al., 2012). In 2014, 42% of men and 31% of women aged 18 to 25 years in France were daily tobacco smokers (Beck et al., 2014) but no study has specifically explored tobacco smoking behavior and nicotine dependence in French medical students to date. However, due to increased psychological stress induced by new responsibilities, increased worked hours and shifts, increased burn out risk, length and difficulty of the medical studies and increased smoking behavior in hospital workers, medical students may be at particular risk of tobacco smoking onset (Fond et al., 2016). Tobacco smoking has also been associated with increased risk of anxiodepressive issues (Fond et al., 2013). French medical students are at risk of impaired quality of life specifically in terms of mental health and vitality: 12.2% are followed up by a psychiatrist and/or psychologist (Fond et al., 2018). In a recent meta-analysis, the prevalence of depression or depressive symptoms in medical students across 47 countries was 27.2% (Rotenstein et al., 2016). This increased risk of depression may be due to a particular risk for addictive behaviors including tobacco smoking onset within medical studies. Smoking cessation remains an important aspect of health promotion and prevention of cardiovascular disease, in clinical practice, but a personal history of smoking amongst doctors may hinder their ability to promote behavioral change in a compelling way. The French National Tobacco Control Program has specifically pointed out that healthcare professionals who continue to smoke and thus deviate from clinical advice given to the general population, set a bad example and may have less motivation to broach this topic with their patients and that this rate in healthcare professionals remained high despite decades of public health prevention programs (Ministère des solidarités et de

la santé, 2018). Doctors who smoke are 17% more likely not to promote smoking cessation to their patients, compared with those who have never smoked (Duaso et al., 2014). Early intervention for medical students who do not yet smoke is, therefore, a reasonable approach to consider.

The objectives of the present study were to determine the prevalence of smoking behavior in French medical students and to explore whether daily tobacco smoking, and the severity of nicotine dependence, were associated with a range of psychosocial factors and psychotropic consumption to guide future public health policies.

## **Population and methods**

### *Study design*

The BOURBON study was inspired by previous studies which looked at psychostimulant use in medical students (Fond et al., 2016; Micoulaud-Franchi et al., 2014). This study was a descriptive cross-sectional observational epidemiological study.

### *Study population*

The medical students were recruited from 35 medical schools in metropolitan France. In seventeen cases, the survey was sent through faculty administration mailing lists, and for two institutions, social networks were used. 5 universities refused to send the survey to their students. Students from all universities were therefore reached through contact with friends and colleagues, who shared the survey by social networks. We therefore obtain data for all the 35 universities and this is represented in the present study. Given that the questionnaire was only disseminated among French medical students, there was no exclusion criterion.

### *Collected Data*

Data was collected by a self-completed questionnaire between December 13, 2016 and May 15, 2017. All medical students enrolled at a medical faculty in metropolitan France during the year 2016-2017 were included in the present study. The medical students were interviewed through an online, anonymous questionnaire

via the Google Forms software. Completion of the questionnaire took an average of 15 minutes. The questionnaire included:

- At least 23 questions for students who did not consume any substance.
- A maximum of 140 questions for students who, by their answers, opened the entire questionnaire.

#### *Tobacco smoking variables*

**Tobacco smoking group:** Current daily tobacco smoking was self-declared.

**Severe nicotine dependence group:** To increase the response rate, the Heaviness of Smoking Index-validated short form of the Fagerström test (Etter et al., 1999; John et al., 2004; Kozlowski et al., 1994) was used to assess nicotine (NIC) dependence. It combines the two most important questionnaire responses: number of cigarettes per day and the time of the day's first cigarette (Heatherton et al., 1991). **We defined severe nicotine dependence as a score equal or greater than four** (Chabrol et al., 2005).

#### *Other clinical variables*

Sociodemographic data was recorded (age, sex) as well as the number of weekly worked hours and number of shifts per month. Alcohol use disorder was defined by an Alcohol Use Disorder Identification Test (AUDIT) score  $\geq 7$  for men and  $\geq 6$  for women (Gache et al., 2005). Cannabis use disorder was defined by a Cannabis Abuse Screening Test (CAST) score  $\geq 2$  (Legleye et al., 2011). The following psychiatric variables were reported: daily consumption of anxiolytic, antidepressant, hypnotic, mood-stabilizers, antipsychotics. The following psychosocial risk factors were also recorded: mourning, sexual assault, domestic violence, physical assault, parental divorce and financial difficulties during medical school (table 1).

#### *Ethical concerns*

An email inviting participation in the study was sent to medical students using both the database of French medical student associations and professional mailing lists. The same message was also posted on targeted Internet forums. It described and explained the study's rationale, as well as its goals. Participants were invited to

complete a confidential web survey by clicking on a URL link: the study was entirely voluntary and students could withdraw from the survey at anytime before completion and submission. Personal data was anonymized and stored on a secure server. No identifiable data was recorded as part of the survey, to protect anonymity of participants. Care was taken to delete IP addresses from the dataset. Data was stored in an offline database for later analyses. No informed consent form was required. Participants were informed that by submitting their anonymous questionnaires, they gave their informed consent to participate. The study was carried out in accordance with ethical principles for medical research involving humans (WMA, Declaration of Helsinki) and MR003 APHM “Commission Nationale de l’Informatique et des Libertés” (CNIL) methodology.

### *Statistical analysis*

Sociodemographic variables, addictive behaviour, daily psychotropic drug consumption and a history of psychosocial risk factors during medical studies are presented using measures of means and dispersion (standard deviation) for continuous data and frequency distribution for categorical variables (Table 1). The data was examined for normal distribution with the Shapiro-Wilk test and for homogeneity of variance with the Levene test. Comparisons were made between smokers and non-smokers (Table 1), and between smokers with no or moderate nicotine dependence and smokers with severe nicotine dependence (Table 2) regarding sociodemographic variables, addictive behaviour, daily psychotropic drug consumption and history of psychosocial risk factors, using the chi-square test for categorical variables. Continuous variables were analysed with Student t-tests for normally distributed data and in case of normality violation, additional Mann-Whitney tests were performed to confirm the result. A single level of clustering on university was considered. Taylor method of linearization and Jackknife Repeated Replication (JRR) (Rao and Wu, 1985) was applied to calculate standard errors (SEs) of estimates (Armitage, P(Editor), 2005). A sampling weight  $W_i$  was derived for  $i^{\text{th}}$  participant by using the inverse of sampling fraction formula ( $1/SF$ ), where  $SF = (\text{sample proportion}/\text{population proportion})$ . The sample was balanced on the gender characteristic. Census report (“Census Report,” n.d.) found a female proportion equal to 62% versus 68.4% in the sample. Thus weights were equal to:

$$W_{female} = \frac{1}{0.684/0.62} = 0.906 \quad \text{And} \quad W_{male} = \frac{1}{0.316/0.38} = 1.202$$

Variables with P values < 0.20 in univariate analysis were included in the multivariate regression models analyzing factors associated with current tobacco use and severe nicotine dependence. This study was a confirmatory analysis. No correction for multiple testing has therefore been carried out, which is consistent with recommendations (Bender and Lange, 2001). Analyses were conducted using SAS (release 9.3; SAS Statistical Institute, Cary, NC). All statistical tests were two-tailed, with  $\alpha$  level set at 0.05.

## Results

Overall, 10985 medical students were included in the present study. The mean aged was 21.7 years (+/- 3.3), 31.6% were male. No data was missing due to the nature of the online questionnaire: all necessary questions required an answer prior to submission. It was not possible to calculate an accurate response rate, due to the study design. 2078 participants (18.9%) identified themselves as current daily tobacco smokers and, of these, 59 (2.8%) were classed as having severe nicotine dependence. In multivariate analyses, tobacco smoking was independently associated with anxiolytic consumption (aOR = 1.40 [1.14-1.71], p=0.002), alcohol use disorder (aOR = 3.20 [2.92-3.52], p<0.001), cannabis use disorder (aOR = 6.37 [4.78-8.49], p<0.001), with financial difficulties (aOR = 1.43 [1.28-1.59], p<0.001) and a history of sexual (aOR = 0.60 [0.38-0.97], p=0.041) or physical (aOR = 1.56 [1.29-1.89], p<0.0001) assault (table 1).

Severe nicotine dependence was independently associated with anxiolytic consumption (aOR = 2.74 [1.43-5.24], p = 0.003), cannabis use disorder (aOR = 2.31 [1.19-4.50], p = 0.015), domestic violence (aOR = 5.47 [2.30-12.99], p < 0.0001), physical assault (aOR = 1.94 [1.02-3.66], p = 0.041) and financial difficulties (aOR = 2.33 [1.57-3.44], p <0.0001) (table 2).

## Discussion

The major findings of this study may be summarized as follows: in a national sample of 10985 medical students, daily tobacco smoking has been identified in almost 20% of the subjects. Smoking was associated with anxiolytic consumption,



alcohol use disorder, cannabis use disorder, financial difficulties and with a history of sexual or physical assault. Students with severe nicotine dependence (2.8%) were found to have increased rates of anxiolytic consumption and cannabis use disorder. They also reported to have been more frequently exposed to domestic violence, physical assault and financial difficulties.

In France, after 6 years of relatively stable prevalence, daily tobacco smoking has decreased from 34.5% between 2010 and 2016 (Pasquereau A et al., 2017) to 31.9% (Pasquereau A et al., 2018). A strong decrease has been found in young men (44.2% in 2016 to 35.3% in 2017) whilst the prevalence in young women remains stable (29.2% in 2016 against 28.8% in 2017) (Pasquereau A et al., 2018). The prevalence of 18.9% within our study sample, is much lower than national rates but is comparable to the prevalence of 18% found in a recent cross national survey carried out in German and Hungarian medical students (Balogh et al., 2018). It is also similar to the prevalence of 17.2% found in a worldwide literature review on 74001 questionnaires from 1988 to 2013 (Roncero et al., 2015). In contrast, a higher prevalence of 31% has been reported amongst Italian medical students (La Torre et al., 2012), with lower prevalences seen amongst Spanish resident physicians (6.5%, n=634) (Ranchal Sánchez et al., 2018), and Americans medical students (6%, n= 174) (Armstrong et al., 2017) though the small sample sizes here should be taken into consideration in the interpretation of the results.

Due to the paucity of data in other studies, (Armstrong et al., 2017; Balogh et al., 2018; La Torre et al., 2012; Ranchal Sánchez et al., 2018; Roncero et al., 2015) it is difficult to find comparisons for the nicotine dependence presented in our study. Our study is the first study to report nicotine dependence prevalence in such a large sample of medical students. The prevalence of severe nicotine dependence amongst medical students in our study (2.8%) was lower than that of 12% based on 6 questions Fagerström test in a French sample of 255 medical students (Gignon et al., 2015) and that of 6% amongst 433 healthcare students in Nigeria (Aina et al., 2009), and 5% in 392 healthcare students in India (Chopra et al., 2015). The sex ratio of 0.46 in our study (3467 males/ 7518 females) compared to those of 0.79 in Gignon et al. study (Gignon et al., 2015) may provide an explanation for this discrepancy, as males are more likely to smoke than women (35% vs. 6% respectively according to the World Health Organization) (World Health Organization, 2017).

The prevalence of anxiolytic consumption within smokers in the present study was lower than those of a previous French study involving 10252 persons (9.8% in men, 14.3% in women) (Chéron-Launay et al., 2011). In the present study, smokers reported higher anxiolytic consumption compared to non-smokers (8.5% vs. 5% respectively). This is consistent with previous studies reporting an association between cigarette smoking and anxiety (for review see (Moylan et al., 2013)) and for a meta-analysis including 15 observational studies see (Jiang et al., 2014)). Tobacco smoking has been extensively described as a strategy to deal with anxiety (King et al., 2018). Findings from Mendelian randomization analyses do not support a causal relationship between smoking history and the development of depression and anxiety (Taylor et al., 2014), which suggests that anxiety may increase the risk of subsequent onset and maintenance of tobacco smoking. Our study has also found an association between severe nicotine dependence and anxiolytic consumption, which is consistent with the results of a recent meta-analysis (Jiang et al., 2014). Dealing with anxiety may therefore be crucial to help students successfully stop smoking. Despite these alarming results, however, no prevention programs are carried out to date in French hospitals and faculties. Some effective strategies have been evaluated in other countries, for example work hour reductions or self-care workshops (Busireddy et al., 2017; Panagioti et al., 2017)). In 2012, smoking cessation training at medical school was only reported by 16.5% of European medical students (La Torre et al., 2012).

Our results also highlighted that medical students reported high rates of personal and professional adversity during their medical studies. In the professional field, smoking was significantly associated with working more than five night shifts per month. This is consistent with previous results (Knutsson and Nilsson, 1998) and may be explained by increased need to deal with anxiety, stress, because of night shift work (Sancini et al., 2012). Tobacco may be used for both its psychostimulant and anxiolytic effects.

Medical students who smoke had almost a 3 times higher incidence of sexual and physical assault compared to non-smokers (9.2% vs. 3.9%). Of the whole sample, almost 5% reported being assaulted to at least once whilst at medical school, a lower rate than that reported globally by the World Health Organization for medical doctors (8-38%) (World Health Organization, 2017). This lower rate is probably explained by the younger age of our population. It is noteworthy that the questions relating to

assault in this study did not determine the precise circumstances surrounding the incident, something which would be valuable to explore further.

Tobacco smoking was significantly associated with increased financial difficulties (29.3% vs. 20.1%). This is not consistent with the results of a recent study of European medical students, which found no association between financial situation and tobacco consumption among the cohort (Balogh et al., 2018). However the rate of financial difficulties reported by our study population was three times higher than presented by Balogh and al (21.8% vs 7.6%). Further studies should explore the impact of financial status of medical students on their health outcomes and the reasons for such high rates in France.

*Limits.* These results should be interpreted with caution. As a cross-sectional study, we cannot confirm causality. This data was self-reported. To avoid any declaration bias, the results were strictly anonymized. Due to the study design, it is not possible to calculate an accurate response rate. Tobacco data presented in this study relate solely to cigarette smoking. Other types of smoking were not considered, for example: water pipes, cigars, or pipes, though we hypothesise that these are rarely used by medical students. We have also not explore the use of e-cigarettes, nicotine replacement therapies and other drugs used in smoking cessation, such as bupropion and varenicline . Finally, it is noteworthy that participants'past medical history was not included in the questionnaire, something which may have impacted on the prevalence of severe nicotine dependence. (Dome et al., 2010).

*Strengths.* Results presented here have been collated from a large multicentric sample, representing medical students from all French medical schools, using standardized questions (for example in the assessment of nicotine dependence).

## **Conclusion**

Despite several decades'worth public health programs aimed at preventing smoking in the French general population, almost one in five medical students still smoke, of which 3% are severely nicotine dependent. Daily tobacco smoking appears to be associated with higher anxiolytic consumption, alcohol and cannabis use disorders,; a high number of night shifts per month, a history of sexual and physical assault and financial difficulties. These results may help to guide future specific health programs aimed at medical students. Combined with other published data, the

present study suggests that effective management of anxiety using psychiatric/psychotherapeutic intervention may be crucial in helping students to stop smoking.

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### **Conflicts of interest**

None declared.

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