



A portrait of benzodiazepine use among college students

Inês Jorge Proença Paulo Rato

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Dedicatória

Ao meu avô,
Mestre e Motivo.

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Prefácio

“Não te rendas, ainda estás a tempo
de alcançar e começar de novo,
aceitar as tuas sombras,
enterrar os teus medos,
largar o lastro,
retomar o voo.

Não te rendas que a vida é isso,
continuar a viagem,
perseguir os teus sonhos,
destravar os tempos,
arrumar os escombros,
e destapar o céu.

Não te rendas, por favor, não cedas,
ainda que o frio queime,
ainda que o medo morda,
ainda que o sol se esconda,
e se cale o vento:
ainda há fogo na tua alma
ainda existe vida nos teus sonhos.

(...)

Abrir as portas,
tirar os ferrolhos,
abandonar as muralhas que te protegeram,
viver a vida e acatar o desafio,
recuperar o riso,
ensaiar um canto,
baixar a guarda e estender as mãos,
abrir as asas
e tentar de novo,
celebrar a vida e relançar-se no infinito.

Não te rendas, por favor não cedas:
mesmo que o frio queime,
mesmo que o medo morda,
mesmo que o sol se ponha e se cale o vento,
ainda há fogo na tua alma,
ainda há vida nos teus sonhos.
Porque cada dia é um novo início novo,
porque esta é a hora e o melhor momento.
Porque não estás só, porque eu te amo.

Mario Benedetti

“Omnia vincit amor”.

Resumo

As benzodiazepinas (BZD) são dos fármacos mais prescritos e utilizados em todo o mundo. Portugal é um dos maiores consumidores mundiais de benzodiazepinas. As mudanças biopsicossociais e académicas inerentes ao período do ensino superior contribuem para o aumento do risco de desenvolvimento de psicopatologia nos jovens. De facto, a perturbação de ansiedade, depressão e perturbação do consumo de substâncias estão entre as perturbações mentais mais comuns nos estudantes. Em Portugal não há estudos prévios que se debrucem particularmente sobre o consumo de benzodiazepinas e dos seus fatores preditores em estudantes do ensino superior.

O presente estudo pretende caracterizar o consumo de BZD em estudantes do ensino superior em Portugal, bem como estabelecer (alguns dos seus) potenciais fatores preditores.

Este estudo observacional transversal consistiu na aplicação de um questionário anónimo online, a estudantes matriculados em instituições do ensino superior em Portugal no ano letivo 2019/2020. O questionário, construído para o efeito do estudo, era composto por 9 partes: dados sociodemográficos e académicos, caracterização do consumo de BZD, caracterização do consumo de outras substâncias psicoativas, exercício físico, *Patient Health Questionnaire* (PHQ-9), *WHO Quality of Life Brief Questionnaire* (WHOQOL-Bref), *Zung Self-Rating Anxiety Scale* (SAS), *Five Facet Mindfulness Questionnaire* (FFMQ), *Perceived Stress Scale* (PSS-10). Todas as escalas utilizadas encontram-se validadas para a população portuguesa.

805 questionários de estudantes foram incluídos no estudo. Os resultados evidenciam que 19% dos estudantes consomem ou já consumiram benzodiazepinas, com uma idade média de 19,4 anos no primeiro consumo. Os psiquiatras constituíram o principal meio de acesso a BZD, com proporções relevantes a serem prescritas também por médicos de família e médicos de outras especialidades. No entanto, 20% dos estudantes referiu ter obtido BZD através de familiares ou amigos. As principais razões para o consumo de BZD mencionadas pela maioria dos estudantes foram a ansiedade e problemas de sono. Verificou-se que as variáveis *género*, *idade*, *consumo de tabaco*, *consumo de cocaína*, *sintomas depressivos*, *sintomas de ansiedade*, *stress percecionado*, *acting with awareness*, *nonjudging*, *nonreacting* e *FFMQ total* associam-se significativamente ao consumo de BZD.

Foi encontrado um modelo probabilístico que explicou 29% da variância do consumo atual de BZD entre os estudantes da amostra. Nesse modelo, as variáveis *idade*, *consumo de tabaco*, *consumo de álcool*, *consumo de LSD/outros alucinogénios*, *sintomas depressivos*, *sintomas de ansiedade*, *describing*, *acting with awareness*, *nonjudging* e *nonreacting* desempenharam um papel preditor do consumo atual de BZD.

Parte destes resultados suportam algumas das hipóteses iniciais do estudo. O consumo de BZD é mais comum entre mulheres e sujeitos mais velhos. *Stress percebido*, *sintomas de ansiedade* e *sintomas depressivos* são não só frequentes, como também apresentam associações significativas com o consumo de BZD. Além disso, os *sintomas de ansiedade* e *sintomas depressivos* demonstraram ser preditores positivos do consumo atual de BZD. Em relação a associações entre o consumo individual de substâncias psicoativas e o uso de BZD, o *consumo de tabaco* e de *LSD/outros alucinogénios* assumiram um papel preditor positivo do consumo de BZD, enquanto que o *álcool* demonstrou ser um preditor negativo desse consumo. As facetas do *mindfulness nonjudging* e *nonreacting* aparentam ser fatores protetores do consumo atual de BZD em estudantes, pelo que intervenções baseadas em *mindfulness*, particularmente fundamentadas no desenvolvimento e prática destas facetas poderão ser de interesse em estudos posteriores, já que podem munir os estudantes de estratégias que os auxiliem a lidar com os sintomas *depressivos* e de *ansiedade* preditores do consumo atual de BZD e, conseqüentemente, coadjuvar o seu sucesso académico.

O presente estudo constitui uma contribuição pertinente para o retrato do consumo de BZD em estudantes do ensino superior em Portugal, estabelecendo evidência da influência de variados fatores nesse uso. Os fatores preditores do uso de BZD passíveis de modificação, como os sintomas de ansiedade, os sintomas depressivos e o consumo de substâncias psicoativas, devem constituir o alvo principal no desenvolvimento de estratégias que visem promover a consciencialização e reduzir o consumo de benzodiazepinas.

Palavras-chave

Benzodiazepinas; estudantes ensino superior; psicopatologia; *mindfulness*; qualidade de vida

Resumo Alargado

As benzodiazepinas (BZD) são dos fármacos mais prescritos e utilizados em todo o mundo. Portugal é um dos maiores consumidores de benzodiazepinas a nível mundial. As mudanças biopsicossociais e académicas inerentes ao período do ensino superior contribuem para o aumento do risco de desenvolvimento de psicopatologia nos jovens. De facto, a perturbação de ansiedade, a depressão e perturbação do consumo de substâncias estão entre as perturbações mentais mais comuns nos estudantes. Em Portugal, não há registo de estudos prévios que se debrucem particularmente sobre o consumo de benzodiazepinas e dos seus fatores preditores em estudantes do ensino superior.

O presente estudo pretende caracterizar o consumo de BZD em estudantes do ensino superior em Portugal, bem como estabelecer (alguns dos seus) potenciais fatores preditores.

Este estudo observacional, transversal consistiu na aplicação de um questionário anónimo online, a estudantes matriculados em instituições portuguesas do ensino superior durante o ano letivo 2019/2020. O questionário, construído para o efeito do estudo, era composto por 9 partes: dados sociodemográficos e académicos, caracterização do consumo de substâncias psicoativas, exercício físico, *Patient Health Questionnaire* (PHQ-9), *WHO Quality of Life Brief Questionnaire* (WHOQOL-Bref), *Zung Self-Rating Anxiety Scale* (SAS), *Five Facet Mindfulness Questionnaire* (FFMQ), *Perceived Stress Scale* (PSS-10). Todas as escalas utilizadas encontram-se validadas para a população portuguesa.

805 questionários de estudantes foram incluídos no estudo, dos quais 561 (70%) pertenciam a raparigas, e 244 (30%) a rapazes. A idade média dos estudantes foi 22,6 anos, sendo que 76% dos estudantes se encontravam no intervalo etário entre os 17 e os 23 anos. A maioria dos estudantes estudava Medicina (48%) na Universidade da Beira Interior (54%). Os resultados evidenciam que 19% (n=157) dos estudantes consomem ou já consumiram benzodiazepinas, com uma idade média de 19,4 anos ao primeiro consumo. Dos 157 estudantes que afirmaram já ter tido contacto com BZD, 26,1% referem consumir atualmente, enquanto que 74% referem ter consumido no passado. Dos estudantes que consomem atualmente, um terço dos mesmos consome apenas 1 ou 2 vezes por mês, enquanto que outro terço da amostra consome diariamente. Um terço (33%) dos estudantes foi prescrito BZD por um médico psiquiatra, e outro terço por um médico de medicina geral e familiar (30%). Preocupantemente, 30% dos estudantes referiu ter obtido BZD através de outros meios que não a prescrição médica: 19% obtiveram BZD através de familiares ou amigos, 5%

diretamente através da farmácia e 0.6% através de um psicólogo. Diazepam, alprazolam e loflazepato de etilo foram as três BZD mais consumidas entre os estudantes da amostra. As principais razões para o consumo de BZD reportadas pela maioria dos estudantes foram a ansiedade e os problemas de sono. Mais ainda, 40% dos estudantes considerou que as BZD não são prejudiciais ou são pouco prejudiciais para a saúde, e um terço dos estudantes considerou não ser capaz ou ser pouco capaz de reduzir o consumo atual do fármaco. A maioria dos estudantes referiu que a dependência é um efeito secundário do consumo de BZD, e apenas uma minoria dos jovens referiu acreditar que as mesmas não acarretam efeitos secundários.

Verificou-se que as variáveis *género*, *idade*, *consumo de cocaína*, *sintomas depressivos*, *sintomas de ansiedade*, *stress percecionado*, *acting with awareness*, *nonjudging*, *nonreacting* e *FFMQ total* se associam significativamente ao consumo de BZD. Foi encontrado um modelo probabilístico que explicou 29% da variância do consumo atual de BZD entre os estudantes da amostra. Nesse modelo, as variáveis *idade*, *consumo de tabaco*, *sintomas depressivos*, *sintomas de ansiedade*, *describing* e *acting with awareness* foram preditores positivos do consumo de BZD, enquanto que o *uso de álcool* e as facetas do *mindfulness nonjudging* e *nonreacting* foram preditores negativos desse consumo.

Parte destes resultados confirmam algumas das hipóteses iniciais do estudo. O consumo de BZD é mais comum entre mulheres e sujeitos mais velhos, contudo, tendo em conta o escasso número de estudos que avaliam o consumo de benzodiazepinas em estudantes universitários em Portugal, não é possível fazer comparações quanto à estabilização, ou não, das frequências do consumo de BZD nesta população. Assim, e sobretudo realçando que Portugal é um dos maiores consumidores de BZD a nível mundial, são necessárias investigações futuras que se debrucem sobre a evolução do consumo no país, não só estudando a população geral por faixas etárias e género, mas também por grupos sociais, nomeadamente o dos jovens universitários.

Stress percecionado, *sintomas de ansiedade* e *sintomas depressivos* não só têm frequências importantes na amostra, como também associações significativas com o consumo de BZD. Além disso, os *sintomas de ansiedade* e *sintomas depressivos* demonstraram ser preditores positivos do consumo atual de BZD. De facto, estes resultados são suportados por estudos prévios, que encontraram associações entre a existência de sintomatologia psicopatológica e o consumo de psicotrópicos, nos quais se incluem as benzodiazepinas. Assim, tendo em conta que os estudantes se encontram numa posição particularmente vulnerável ao desenvolvimento de psicopatologia, não só pela sua faixa etária (em que várias perturbações mentais se manifestam), mas também devido à sua posição social e académica que acarreta

diferentes fatores de stress com os quais nem sempre é fácil lidar, é compreensível que os estudantes equacionem farmacologia psicotrópica como uma solução para as suas problemáticas. Contudo, estas soluções, se assentes em benzodiazepinas, podem acarretar complicações a longo prazo, uma vez que estes fármacos estão indicados apenas para períodos de tratamento de 2 a 4 semanas. Assim, embora não se deva deixar de equacionar a prescrição destes fármacos a estudantes que claramente beneficiam e precisam deste tratamento, o mesmo deve ser cautelosamente ponderado quando os riscos podem superar os benefícios, principalmente se o estudante apresentar historial de depressão, abuso de substâncias ou ideação suicida.

Em relação a associações entre o consumo individual de substâncias psicoativas e o uso de BZD, o *consumo de tabaco* e de *LSD/outros alucinogénios* assumiram um papel preditor positivo do consumo de BZD, enquanto que o álcool demonstrou ser um fator protetor desse consumo. As facetas do *mindfulness nonjudging* e *nonreacting* aparentam ser fatores protetores do consumo atual de BZD em estudantes, pelo que intervenções baseadas no *mindfulness*, particularmente fundamentadas no desenvolvimento e prática destas facetas poderão ser de interesse em estudos posteriores, já que podem munir os estudantes de estratégias que os auxiliem a lidar com *sintomas depressivos* e de *ansiedade* preditores do consumo atual de BZD e, conseqüentemente, coadjuvar o seu sucesso académico.

O presente estudo constitui uma contribuição pertinente para o retrato do consumo de BZD em estudantes do ensino superior em Portugal, estabelecendo evidência da influência de variados fatores nesse uso. Os fatores preditores do uso de BZD passíveis de modificação, como os sintomas de ansiedade, os sintomas depressivos e o consumo de substâncias psicoativas, devem constituir o alvo principal no desenvolvimento de estratégias que visem promover a consciencialização e reduzir o consumo de benzodiazepinas.

Abstract

Benzodiazepines (BZD) are among the most widely prescribed pharma in the world, and Portugal reports one of the highest BZD consumption rates. Academic and biopsychosocial changes associated with the higher education period contribute to increased risk of psychopathology in youths, being that anxiety, depression and substance abuse disorders are among the most significant mental health problems in this population. In Portugal, there have been no studies examining the correlates of BZD use within a sample of college students, nor has there been an assessment of the frequency of use and characterization of BZD use in this population.

Thus, this study aimed to characterize benzodiazepine use and assess its potential correlates and predictors among Portuguese college students.

This cross-sectional study was conducted using an online anonymous questionnaire, specifically designed for this study, with a final sample of 805 students enrolled in Portuguese universities and polytechnics. The questionnaire was composed by 9 sections: sociodemographic and academic data, characterization of BZD use, characterization of psychoactive substances consumption, physical exercise, *Patient Health Questionnaire* (PHQ-9), *WHO Quality of Life Brief Questionnaire* (WHOQOL-Bref), *Zung Self-Rating Anxiety Scale* (SAS), *Five Facet Mindfulness Questionnaire* (FFMQ) and *Perceived Stress Scale* (PSS-10). All the scales are valid for the Portuguese population.

Results showed a substantial lifetime frequency of BZD use among the sample's students: 19.1% (n=157) and mean age of first use was 19.4 years. BZD were obtained mainly through a psychiatrist or other specialty doctor, nevertheless for 20% BZD's were provided by their relatives. The majority of students reported anxiety and sleeping problems as the main reasons for BZD use. *Gender, age, cigarette smoking, cocaine use, depressive symptoms, anxiety symptoms, perceived stress, acting with awareness, nonjudging, nonreacting and FFMQ total* were all found to be significantly correlated with BZD use on bivariate analysis. A logistic model was found to predict 29% of the variance of current use of BZD, with *age, cigarette smoking, alcohol, LSD/other hallucinogens, depressive symptoms, anxiety symptoms, describing, acting with awareness, nonjudging and nonreacting* as the predictive factors of the outcome.

These results support some of the predicted hypotheses, while others are opposite to the initial ideas. BZD use was more frequent among females and older students, as observed in previous studies. *Perceived stress*, *anxiety symptoms* and *depressive symptoms* were not only highly frequent among the sample's college students but also significantly associated with BZD use. Additionally, *anxiety symptoms* and *depressive symptoms* were found to positively predict current use of BZD. With regard to psychoactive substances consumption, *cigarette smoking* and *LSD/other hallucinogens* were positive predictors of BZD use, while *alcohol* was a negative predictor. Mindfulness facets *nonjudging* and *nonreacting* appear to be independent negative predictors of current BZD use, therefore, mindfulness-based interventions relying fundamentally on the development and practice of these two facets are of interest in further studies, as they might provide students the tools needed to deal with *depressive* and *anxiety symptoms* predictors of current BZD use, and also help with their academic achievements.

A unique contribution of this study is the portrait of benzodiazepine use among college students, and the evidence that several factors influence its use. The modifiable predictors of BZD use, such as anxiety symptoms, depressive symptoms and psychoactive substances consumption, must constitute the main targets on the development of strategies aiming to diminish its use, while advocating a conscious consumption of the drug when needed.

Keywords

Benzodiazepine use; college students; psychopathology; mindfulness; quality of life

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List of Acronyms

ATC	Anatomical Therapeutic Chemical
BZD(s)	Benzodiazepine(s)
CI	Confidence interval
D1/D2/D3/D4	Domain 1/Domain 2/Domain 3/Domain 4
DID	Defined Daily Dose per 1000 inhabitants per day
DSM-5	Diagnostic and Statistical Manual of Mental Disorders
FFMQ	Five Facet Mindfulness Questionnaire
GABA	Gamma-aminobutyric acid
INCB	International Narcotic Control Board
INFARMED	Instituto Nacional da Farmácia e do Medicamento
IQR	Interquartile range
M1	Model 1
M2	Model 2
OECD	Organisation for Economic Co-operation and Development
OR	Odds ratio
PHQ-9	Patient Health Questionnaire-9
PIB	Polytechnic Institute of Bragança
PSS-10	Perceived Stress Scale
QOL	Quality of Life
RR	Risk Ratio
SAS	Self-Rating Anxiety Scale
SD	Standard Deviation
SE	Standard Error
SPSS	Statistical Package for The Social Sciences
USA	United States of America
WHO	World Health Organization
WHOQOL-Bref	World Health Organization, Quality of Life Brief Questionnaire
UBI	University of Beira Interior

1. Introduction

1.1. General overview

Benzodiazepines (BZD) have a sedating effect and ease both physical and psychological effects of anxiety or fear thus relieving the strain and worry arising from stressful circumstances in daily life.

As benzodiazepines can be used in the treatment of anxiety disorders, insomnia, muscle contractures and seizures,¹⁻³ these drugs are among the most widely prescribed pharma in the world.⁴ BZD act as positive allosteric modulators, enhancing the action of gamma-aminobutyric acid (GABA) neurotransmitter, which inhibits anxiety by reducing certain nerve-impulse transmissions within the brain. Benzodiazepines have a safe and effective pharmacological profile for their approved indications, when administered for short to medium periods of two to four weeks.^{3,5}

Nevertheless, BZD also have side effects, mostly cognitive and psychomotor impairment.⁴ BZD administration may result in sedation and drowsiness and affect learning and anterograde memory, which are dose-dependent and potentiated when combined with alcohol.³ BZD are also linked with *delirium* when used with other drugs.⁴ Moreover, some studies suggest BZD increases the risk of dementia, although causality is not completely established.^{6,7} Patients with insomnia chronically treated with BZDs were found to have complex changes in sleep architecture and chronic use may be associated with poor sleep.⁸ BZD are also linked with poor coordination, unsteadiness, increased reaction time and disorientation.⁴ The latter BZD effects on car drivers lead to diminished driving skills and increased risk of collision.^{9,10}

Consequently, BZD use has been discouraged for longer periods of time, as they can induce physical dependence, even in moderate dosages, developing tolerance, promoting the use of progressively larger doses, thus leading to withdrawal syndrome, when treatment is discontinued.¹¹ However, notwithstanding recommendations regarding its use for two to four weeks, evidence shows that prolonged use of BZD is more prevalent than desirable, especially among the elderly.^{4,11}

Portugal is the leading country of anxiolytic (ATC N05B) drug use in Organisation for Economic Co-operation and Development (OECD).¹² Anxiolytics (ATC N05B), sedatives and

hypnotics (ATC N05C) constitute the fourth pharmaceutical group in frequency of use in Portugal,¹³ and are the third most used licit substance, after alcohol and tobacco.¹⁴

By the end of the nineties', the report from the International Narcotics Control Board (INCB) highlighted the concerning use of benzodiazepines in Portugal and advised national authorities to analyze the country's patterns of BZD use and prescription. However, despite public health policies aiming to reduce BZD consumption, Portugal still reported use of 114 Defined Daily Dose per 1000 inhabitants per day (DID) in 2014 (way above the goal of 71 DID by 2010) and nowadays remains among the countries with the highest rates of benzodiazepine use.¹⁵ During 2016, BZD or analogous Z-drugs were dispensed, at least one time, to 1.9 million Portuguese, of which, approximately, 2.4% were 15-24 years (around 45000 youths). Alprazolam, lorazepam and diazepam were the most used benzodiazepines (in descending order), being the first two high-potency anxiolytics, therefore presenting higher risks in terms of side effects and abuse.^{13,15,16}

In contrast, data from the third and fourth Portugal National Inquiry of Consumption of Psychoactive Substances in the General Population, respectively from 2012 and 2016/17, lifetime prevalence of anxiolytics, hypnotics or sedatives use decreased between the two inquiries, regardless of gender and age range considered. Particularly, in young people (15-24 years), lifetime prevalence decreased between the two reports, from 7.8% to 4.1%.^{14,17}

Comparing what is known about harmful drinking and other drug use behaviors among college students with the available data regarding benzodiazepine use, it becomes clear that a big gap of knowledge on this matter still exists.^{18,19} Despite evidence stating Portugal as one of the greatest worldwide BZD consumers, studies on BZD use in Portugal, such as The National Report on Mental Health, survey data by gender and age range but not by social group, therefore students are not particularly addressed.^{15,16}

Concerning frequency of BZD use among college students, it is difficult to understand if consumption is increasing or not, as we are only aware of one study, conducted at Polytechnic Institute of Bragança (PIB) by Correia et al.,²⁰ regarding the frequency of psychotropics (where BZDs were the main used drug) use in college students.

Regarding *perceived stress, anxiety and depressive symptoms*, the following paragraphs will explore briefly what is known on the matter.

An estimate of 20 to 40% of students present clinically significant psychopathological symptoms, and depression, anxiety and stress are accountable for a major part of help-seeking behaviors among students.²¹ In fact, stress, anxiety and depression share such an

undetached symbiotic component of general affective distress, that stimulated the conception of a Tripartite Model exploring the connections between the three concepts.²² In accordance, for example, Eisenberg et al.²³ found co-occurrence of mood and anxiety disorders, with 40% of the students presenting a positive screen for major depression also having a positive screen for generalized anxiety.

Several studies have associated BZD (or psychotropics) use with female gender, older age, lower education, health status and help seeking for emotional or mental health problems.^{15,17,24–27} Demyttenaere et al.²⁴ showed that, in fact, help-seeking behaviors are a more powerful predictor for the use of psychotropic (antidepressants and benzodiazepines) than a formal diagnosis of anxiety or mood disorder, as the *perceived need* of the patient may weigh more on the clinician's judgement to prescribe than the requirement of fulfilling criteria for a structured psychiatric diagnosis.

Moreover, Chau et al.²⁷ showed that lack of family support, being worried, nervous or sad contribute positively to psychotropic use. Hence, this, combined with Demyttenaere's²⁴ findings is the reason why our study focus on psychopathological *symptoms* rather than on clinical psychiatric *entities*.

As referred, students are at high risk of psychotropic use,²⁷ as they report higher levels of anxiety and depressive symptoms when compared with age-matched controls.²⁸ However, this cannot be transduced into the belief that students have more severe mental disorders.^{29,30} College students broadly fall in the 17-25 years interval range which involves the transition between adolescence to adulthood and demarks a specific period of physical, cognitive, psychological and social development of the individual. Coordinating the biopsychosocial changes inherent to this period with the demands of academic and social life is not always easy for students, and the challenges and stressors they face can act as risk factors to the beginning or exacerbation of previous mental health problems.²¹

Kessler et al.³¹ provided evidence that half of all lifetime mental disorders have their onset by age 14 and three fourths occur by age 24, which is compatible with the vast majority of mental disorders occurring prior to college entry.^{31,32} In Portugal, the median age of onset of psychiatric conditions comes slightly in a later age than what Kessler et al.³¹ found in the USA – 21 years in Portugal versus 14 years in the USA.¹⁸

Understanding how stress impacts students' lives may help increase insight on why students are more prone to BZD use. According to Cohen et al., cited by Pais-Ribeiro & Marques,³³ an event is evaluated as threatening or defying based on the subjects' cognitive and coping

resources. Therefore, whether students' coping strategies are adaptive or nonadaptive, stress may, respectively, decrease or increase. In fact, some students start smoking and drinking alcohol as a way of dealing with negative emotions derived from stress.^{34,35} This idea is supported by the fact that different models of addiction over the last decades have proposed stress exposure increases risk of drug abuse.³⁶

Therefore, a question arises: are benzodiazepines a way of college students to escape stress?

Regarding *psychoactive substance use*, Sinha's³⁶ systematic review, states

‘Prevalence of anxiety and mood disorders and behavioral conduct problems in adolescents is associated with an increased frequency and regular use of substances such as alcohol, nicotine and marijuana (King et al. 1996; Rohde et al. 1996; Kandel et al. 1997, Riggs et al. 1999; Rao et al. 1999).’ (p.346)

Not surprisingly, Sinha is supported by McCabe,³⁷ who found nonmedical users of prescription BZD anxiolytics were significantly more likely to use other drugs (cocaine, ecstasy, and prescription stimulants) and engage in other risky behaviors such as driving after binge drinking.

Furthermore, investigations have proposed that depressive disorders share the same backbone as substance abuse disorders, due to phenotypic similarities, such as stress vulnerability and rumination, suggesting a common neurobiological and behavioral dysfunction.^{36,38} Indeed, Brewer et al.³⁸ proposes that mindfulness-based therapies might help dually-diagnosed individuals with depression and substance use disorder, and addresses future research: ‘*do the commonalities in regional brain dysfunction (...) [including depressive, anxiety and substance abuse disorders] (...) begin to approximate potential neural correlates of human suffering?*’ (p.7) We join the call by aiming to find the correlates of benzodiazepine use (which ultimately can become a substance abuse disorder) among college students.

With regard to *mindfulness*, it has been defined as the ability to be aware of the present moment, owning the personal experience of living by cultivating the skill to pay attention through a lens of self-inquiry and self-understanding.³⁹ According to Singh et al., and Hayes, & Wilson, quoted by Gregório & Gouveia,⁴⁰ mindfulness concept varies with context and approach, thus it may be understood as a technique, a method or a psychological process.

Mindfulness has also been conceptualized as a five multifaceted construct¹ which can be learned and practiced, contributing to improve individual health and well-being.^{41,42}

In what concerns to *quality of life*, it is defined by World Health Organization (WHO)⁴³ as

‘individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns ... [and incorporates] physical health, psychological state, level of independence, social relationships, personal beliefs and their relationships to salient features of the environment.’ (p.11)

Put together, so far, several factors, associated with a holistic concept of well-being, such as *mindfulness facets* and *quality of life*, may act as protective factors of BZD use, whereas others, like *self-perceived stress*, *anxiety* and *depressive symptoms*, may predict benzodiazepine use among students.

To our knowledge, there have been no studies on the correlates of benzodiazepine use in a sample of Portuguese college students, nor has there been an assessment of the frequency and characteristics of BZD use in this population. Therefore, the purpose of this study was to characterize the use of BZD use among college students, as well to assess how *anxiety* and *depressive symptoms*, *perceived stress*, *consumption of psychoactive substances*, *mindfulness* and *quality of life* correlate with BZD use.

1.2 Objectives

This study aims to characterize benzodiazepine use and assess its potential correlates and predictors in a sample of Portuguese college students.

1.2.1 Research hypotheses

Based on the aims previously defined, and rooted on the conveyed literature review, the following research hypotheses were defined:

- H1: Gender correlates positively with BZD use;
- H2: Age correlates positively with BZD use;
- H3: Consumption of psychoactive substances correlates positively with BZD use;

¹ The five facets include: *Observing*: paying attention to internal and external experiences; *Describing*: labeling internal experiences with words; *Acting with awareness*: to be aware of the now rather than placing attention elsewhere; *Nonjudging*: ability to not categorize thoughts and feelings as good or bad, and *Nonreacting*: tendency to accept experiences without reacting to them.

- H4: Higher levels of perceived stress correlate positively with BZD use;
- H5: Higher levels of anxiety symptoms correlate positively with BZD use;
- H6: Higher levels of depressive symptoms correlate positively with BZD use;
- H7: Higher levels of quality of life correlate negatively with BZD use;
- H8: Higher levels of mindfulness correlate negatively with BZD use.

2. Materials and Methods

This study was approved by the Ethics Committee of University of Beira Interior.

2.1 Study design

The present study is an observational cross-sectional study.

2.2 Sample characterization

A non-probabilistic convenience sample composed of college students was recruited from Portuguese high education institutions (i.e. universities and polytechnics) in the academic year 2019/2020.

2.3 Procedures and participants

Participants were requested to answer an anonymous questionnaire developed with Google forms® platform. This program granted anonymity by not allowing to associate participant's answers with their respective email addresses. In addition, the program constrained students to answer the questionnaire more than once and made the answers inaccessible to people without database access.

An email, appealing to students' participation in answering the research questionnaire, was sent to the public relations/communication's department of several Portuguese high education institutions, which was then forwarded to their students through the university's email. The questionnaire, accessible through a web link, was at students' disposal between September and December of 2019.

The first page of the questionnaire contained a concise descriptive explanation of the study and requested participant's consent.

2.4 Questionnaire and variables

Regarding the aims of this research and in light of the literature review, a questionnaire was developed. The different parts of the questionnaire, variables and instruments used are described below.

1. Sociodemographic and academic data;
2. Characterization of benzodiazepine use;
3. Characterization of psychoactive substances consumption;
4. Physical exercise;
5. *Patient Health Questionnaire* (PHQ-9);
6. *WHO Quality of Life Questionnaire-Bref Version* (WHOQOL-Bref);
7. *Zung Self-Rating Anxiety Scale* (SAS);
8. *Five Facet Mindfulness Questionnaire* (FFMQ);
9. *Perceived Stress Scale* (PSS-10).

Sociodemographic and academic data: gender, age, nationality, high education institution, degree of university studies, course.

Characterization of benzodiazepine use: type(s) of BZD use, reasons for BZD consumption, way of access to BZD, frequency of BZD use, perception of BZD use risk and side effects, self-perceived ability to end BZD use.

Characterization of psychoactive substances consumption: use frequency of the following psychoactive substances: cigarette smoking, alcohol, cannabinoids, ecstasy/MDMA/amphetamines, heroin, cocaine, LSD/other hallucinogens, using a time scale – “never”, “have tried before”, “sporadically” (less than once a month), “sometimes” (more than once a month and less than once a week), “frequently” (more than once a week), “daily”.

Physical exercise: practice of physical exercise and, if affirmative, which type.

Patient Health Questionnaire (PHQ-9) was used to assess the variable *depressive symptoms*. The PHQ-9, developed by Kroenke et al.,⁴⁴ consists of 9 items questionnaire that potentially serves as a dual-purpose instrument by establishing a depressive disorder diagnosis and assessing the severity of depression-related symptomatology, during the past two weeks, on a 4-points Likert-type scale (from 0 "Not at all" to 3 "Nearly every day"). Each of the nine questions addresses the presence of a symptom of major depressive syndrome²

² depressed mood, diminished interest and/or pleasure in almost all activities (anhedonia), sleep disturbances (insomnia or hypersomnia), weight change or appetite disturbance, psychomotor agitation

as established by the DSM-5.⁴⁴ The Portuguese version of the PHQ-9 was made available by Pfizer.⁴⁵ Monteiro et al.⁴⁶ conducted a study evaluating the psychometric properties of the PHQ-9 scale in university students, which revealed good psychometric properties and a satisfactory internal consistency (Cronbach's alpha) $\alpha=0.86$. According to the total score obtained in PHQ-9, depression severity can be interpreted according to the categorical algorithm: minimal depression (PHQ-9 score 1-4), mild depression (PHQ-9 score 5-9), moderate depression (PHQ-9 score 10-14), moderately severe depression (PHQ-9 score 15-19), severe depression (PHQ-9 score 20-27).

WHO Quality of Life Questionnaire-Brief Version (WHOQOL-Bref) was used to assess *quality of life* and its *domains*. The WHOQOL-Bref is an international cross-culturally comparable quality of life assessment instrument that aims to evaluate the individual's perceptions in the context of their culture and value systems, and their personal goals, standards and concerns. The WHOQOL questionnaire is composed of 100 items, and the WHOQOL-Bref is a shorter version of the original instrument, comprising 26 items - one item from each of the 24 facets contained in the WHOQOL-100 and two items from the overall quality of life and general health facet -, measuring the following broad domains: physical health (D1), psychological health (D2), social relationships (D3), and environment (D4). The items are answered on a Likert-type scale, ranging from 1 (Not at all/Very poor/Very dissatisfied) to 5 (completely/Very good/Very satisfied/Extremely). The scores are then reconverted to match the equivalent scores of the longer version (WHOQOL-100), ranging from 0 to 100. Domain scores are scaled in a positive direction, thus higher scores represent higher quality of life.⁴³

Zung Self-Rating Anxiety Scale (SAS) was used to assess the variable *anxiety symptoms*. SAS, created by William W. K. Zung, is a rating instrument for the measurement of anxiety as a clinical entity, rather than a diagnostic entity. The instrument is composed of a self-assessment questionnaire with 20 items about how the patient has felt or behaved during the previous week, on a scale of 1-4, in the following four quantitative terms: "None or a little of the time", "Some of the time", "Good part of the time", "Most or all of the time". Fifteen questions are worded toward increasing anxiety levels and five questions worded toward decreasing anxiety levels. The SAS is constructed so the less anxious the person is the lower the score on the scale.⁴⁷ Afterwards, the total scores obtained in SAS are converted to the correspondent SAS index (ranging between 25 and 100) which is interpreted in four categories of severity of anxiety symptomatology: within normal range (SAS index 45 and

or retardation, fatigue or loss of energy, feelings of worthlessness, diminished ability to think or concentrate, recurrent thoughts of death, suicidal ideation or attempt to commit suicide.

below), minimal to moderate (SAS index 46-59), marked to severe (SAS index 60-74) and most extreme (SAS index 75 and above).

Five-Facet Mindfulness Questionnaire (FFMQ) was used to assess the facets of mindfulness: *observing, describing, acting with awareness, nonjudging* and *nonreacting*. Portuguese translation and validation by Gregório & Gouveia⁴⁰ conceptualizes mindfulness, in its dispositional quality, as a multifaceted construct, evaluated in five facets.^{40,41} The self-report questionnaire is composed by 39 items that evaluate the tendency of an individual to be conscious in daily life. All the items are answered on a Likert-type scale, ranging from 1 (never or very rarely true) to 5 (very frequently or always true). The value of internal consistency (Cronbach's alpha) of the original scale was $\alpha=0.81$. The values of internal consistency of the Portuguese version are: $\alpha_{\text{observe}} = 0.83$; $\alpha_{\text{describe}} = 0.91$; $\alpha_{\text{awareness}} = 0.87$; $\alpha_{\text{nonjudge}} = 0.87$ e $\alpha_{\text{nonreact}} = 0.75$.

Perceived Stress Scale (PSS-10) was used to assess the variable perceived stress. PSS-10 is a unidimensional 14-item scale, which has two reduced versions: a 10-item and a 4-item version. For this research, it was used the 10-item version, which is a result of the analysis of the original scale into main components. A study on the adaptation of the PSS-10 to the Portuguese context was conducted by Pais-Ribeiro & Marques.³³ The value of internal consistency (Cronbach's alpha) of the Portuguese 10-item version was $\alpha=0.87$.³³ All the items are answered on a Likert-type scale, ranging from 1 (never) to 5 (very frequently), based on frequency of occurrence of those thoughts or feelings. Four of the items are worded toward increasing anxiety levels (items 4,5,7 and 8) and six questions worded toward decreasing anxiety levels (items 1,2,3,6,9 and 10). The total scores obtained in PSS-10 are classified in three categories: low perceived stress (PSS-10 score 0-13), moderate perceived stress (PSS-10 score 14- 26) and highly perceived stress (PSS-10 score 27-40).

2.5 Statistical analysis

The program SPSS Statistics 21[®] (Statistical Package for the Social Sciences, Inc., Chicago, IL) from IBM was used for statistical analysis. First, the characterization of the sample was conducted according to a usual descriptive analysis of data (relative and absolute frequencies, means, medians, standard deviations). Second, a bivariate analysis was performed between *use of benzodiazepines* and the variables *age, gender, physical exercise, use of psychoactive substances* (each substance tested individually for its association with the use of BZD), *anxiety symptoms, depressive symptoms, perceived stress, quality of life domains* (each domain tested individually with use of BZD), and *mindfulness facets* (each

of the five facets tested individually). The chi-square test was used to test associations between dichotomous variables and BZD use. Parametric tests, particularly the student t test, were used to compare the mean values of the continuous variables between current/past use of BZD (n=157) and non-BZD use (n=648). Moreover, it is common that for larger samples (n>30), small deviances from a normal distribution takes researchers to reject the null hypothesis of normality when the latter is true (type 1 error).⁴⁸ The null hypothesis of the student t test is that the mean between the two samples are equal, against the alternate hypothesis that they are different. For p-values<0.05, the null hypothesis is rejected, and it is concluded that the means of the two samples differ, thus there is an association between BZD use and the continuous variable. In the statistical analysis, the 95% confidence interval was calculated for the difference of means. A p-value≤0.05 was considered significant in the bivariate analysis.

Third, logistic regression analysis was conducted to find an adjusted logistic model for BZD use and explain the probabilities of BZD use in the population of the present study (binomial distribution). The first logistic model (Model 1) intended to explain the odds of current or past BZD use (n=157) versus non-BZD use (n=648). The second model (Model 2) intended to explain current use of BZD (n=41) versus non-current use (n=764, past use of BZD or never used BZD). Independent variables which were found to have a moderately significant or significant association in bivariate analysis, with confidence intervals of 90% or 95% were tested in the regression model (p-value<0.1 or p-value<0.05, respectively). *Perceived stress*, *anxiety symptoms* and *depressive symptoms* were assessed in their categorical form³. Psychoactive substances use were also included⁴, as well as the five mindfulness facets, regardless of their significance on the bivariate analysis, due to their usual relevance for substance use behaviors in general. The same criteria were applied in the adjustment of both models, Wald's test was used to find the significant variables for both models (p-value>0.1), and the logistic regression analysis was conducted through R Studio software. Backward logistic regression method was used to remove the non-significant variables from Model 1, and forward method was used to select the significant variables to Model 2.

³ explained above in the section of each variable.

⁴ alcohol, cigarette smoking, cannabinoids, ecstasy/MDMA/amphetamines, LSD/other hallucinogens, cocaine and heroin, assessed in their original form as ordinal variables with six categories.

3. Results

3.1 Sample characterization

Table 1 presents a descriptive analysis of the study sample. A total of 805 college students, of which 561 (70%) were females and 244 (30%) were males, took part in this study. Most students were in the age range of 17-23 years and the sample's mean age was 22.6 years (± 5.4 years). 48% studied Medicine at University of Beira Interior (54%). Around sixty percent (62%) were taking a master's degree. Half (50%) of the students were physically active.

Concerning *depressive symptoms*, assessed through the PHQ-9, 42% of the students reported minimal depressive symptoms, 51% reported mild or moderate symptoms and a smaller number of students reported moderately severe (5%) to severe depressive symptomatology (2%).

With respect to *perceived stress*, assessed through the PSS-10, 30% of the students reported low levels of perceived stress, while almost the double (58%) reported moderate levels of perceived stress and 100 (12%) students were classified with high levels of perceived stress.

Only half (44%) of the students reported normal levels of *anxiety symptoms*, and more than half (56%) of the students reported levels of anxiety symptoms above the established SAS normal anxiety threshold. Moreover, 17% of the students had marked (14%) to severe (3%) anxious symptomatology.

Analyzing *quality of life* (QOL), through the WHOQOL-Bref, *physical health* (D1) scored a mean of 48 (± 9), *psychological health* (D2) scored a mean of 59 (± 9), *social relationships* (D3) scored a mean of 66 (± 22) and *environment* (D4) scored a mean of 59 (± 8).

Regarding dispositional *mindfulness*, the mean total of *FFMQ* was 124 (± 18). Concerning the five mindfulness facets, *describing* mean score was 26 (± 6), *observing* mean score was 24 (± 7), *acting with awareness* mean score was 27 (± 8), *nonjudging* mean score was 27 (± 7) and *nonreacting* mean score was 20 (± 5).

Table 1 – Descriptive analysis of the sample (n=805)

Gender, n (%)		
Female		561 (70)
Male		244 (30)
Age,		
mean (SD)		22.6 (5.4)
n (%)		
17-23		614 (76)
24-29		131 (16)
>30		60 (8)
Institution, n (%)		
University of Beira Interior		436 (54)
University of Lisboa		157 (20)
University of Minho		82 (10)
University of Coimbra		47 (6)
University of Algarve		18 (2)
University of Porto		17 (2)
Catholic Portuguese University		9 (1.1)
NOVA University of Lisboa		7 (0.9)
Polytechnic Institute of Coimbra		4 (0.5)
Polytechnic Institute of Viseu		3 (0.4)
University of Trás-os-Montes e Alto Douro		3 (0.4)
University of Aveiro		3 (0.4)
University Institute of Lisboa (ISCTE)		2 (0.2)
Polytechnic Institute of Castelo Branco		2 (0.2)
University of Evora		1 (0.1)
Others/Not specified		14 (1.7)
Degree of university studies, n (%)		
Licentiate's degree		264 (33)
Master's degree/Integrated master		498 (62)
PhD		21 (3)
Other/Not specified		22 (3)
Course, n (%)		
Medicine		390 (48)
Others		415 (52)
Benzodiazepine use, n (%)		
Yes		157 (19)
No		648 (81)
Physical exercise, n (%)		
Yes		402 (50)
No		403 (50)
Depressive symptoms (PHQ-9)		
mean (SD)		1.0 (1.0)
n (%)		
Minimal depression		339 (42)
Mild depression		287 (36)
Moderate depression		121 (15)
Moderately severe depression		39 (5)
Severe depression		19 (2)
Perceived stress (PSS-10)		
mean (SD)		1.8 (0.6)
n (%)		
Low perceived stress		239 (30)
Moderate perceived stress		466 (58)
High perceived stress		100 (12)

Anxiety symptoms (SAS index)	
mean (SD)	11.8 (0.8)
n (%)	
Within normal range	353 (44)
Minimal to moderate anxiety	312 (39)
Marked to severe anxiety	115 (14)
Most extreme anxiety	25 (3)
Mindfulness (FFMQ), mean (SD)	
Describing	26 (6)
Observing	24 (7)
Acting with awareness	27 (8)
Nonjudging	27 (7)
Nonreacting	20 (5)
FFMQ total	124 (18)
Quality of Life (WHOQOL-Bref), mean (SD)	
Physical health (D1)	48 (9)
Psychological health (D2)	59 (9)
Social relationships (D3)	66 (22)
Environment (D4)	59 (8)

SD, Standard deviation; PHQ-9, Patient Health Questionnaire; PSS-10, Perceived Stress Scale; SAS, Self-Rating Anxiety Scale; FFMQ, Five-Facet Mindfulness Questionnaire; WHOQOL-Bref, WHO Quality of Life Brief Questionnaire; D1, Domain 1; D2, Domain 2; D3, Domain 3; D4, Domain 4.

Table 2 presents the frequency of psychoactive substances' consumption in this population, specifically: *cigarette smoking, alcohol, cannabinoids, cocaine, heroin, ecstasy/MDMA/amphetamines and LSD/other hallucinogens.*

	Never, n (%)	Have tried before, n (%)	Sporadically, n (%)	Sometimes, n (%)	Frequently, n (%)	Daily, n (%)
Cigarette smoking	342 (43)	289 (36)	57 (7)	27 (3)	33 (4)	57 (7)
Alcohol	41 (5)	158 (20)	255 (32)	262 (33)	87 (11)	2 (0.2)
Cannabinoids	483 (60)	212 (26)	63 (8)	22 (3)	20 (3)	5 (0.6)
Cocaine	779 (97)	24 (3)	2 (0.2)	0 (0)	0 (0)	0 (0)
Heroin	799 (99)	6 (0.7)	0 (0)	0 (0)	0 (0)	0 (0)
LSD/Other hallucinogens	769 (96)	33 (4)	3 (0.4)	0 (0)	0 (0)	0 (0)
Ecstasy/ MDMA/ Amphetamines	765 (95)	29 (4)	10 (1.2)	0 (0)	0 (0)	1 (0.1)

Sporadically, less than once a month; Sometimes, more than once a month; Frequently, more than once a week.

Table 3 describes patterns of BZD use. Mean age of first BZD use was 19.4 years (SD: ± 4.5 years). Of those reporting current or past BZD use (n=157), 41 (26%) students stated an ongoing BZD use, while 116 (74%) students reported past BZD consumption only.

The main reasons for BZD use were anxiety and sleep problems. Benzodiazepines with higher rates of use were diazepam, alprazolam and ethyl loflazepate.

51 (33%) students had access to BZD through a psychiatrist, while 47 (30%) resorted to a general medicine doctor and 21 (13%) to other specialty doctors. However, around 30% students had access to BZD without a personal pharma prescription: 29 (19%) had access to BZD through their family members or friends, 7 (5%) obtained BZD directly from the pharmacy and 1 (0.6%) through a psychologist. 64 (41%) students considered BZD not harmful or slightly harmful to health and 94 (60%) students considered BZD harmful or very harmful to health. The majority of students (78%) believed dependence is a side effect of BZD. Only a minority (5%) of students were convinced BZD have no side effects.

Table 3 – Characterization of benzodiazepine use (n=157)

Benzodiazepine use, n (%)	
Currently using BZD	41 (5)
Used BZD in the past	116 (14)
Never used BZD	648 (81)
Age of first BZD use, mean (SD)	19.4 (4.5)
Reasons, n (%)	
Anxiety	121 (77)
Sleep problems	79 (50)
Adjuvant treatment for other conditions	17 (11)
Sporadic/others	5 (3)
Recreational effect	4 (3)
Muscle relaxant	1 (0.6)
Benzodiazepine(s) used, n (%)	
Diazepam	61 (39)
Alprazolam	52 (33)
Ethyl loflazepate	24 (15)
Lorazepam	16 (10)
Others	33 (21)
Way of access to benzodiazepines, n (%)	
Psychiatrist	51 (33)
General Medicine doctor	47 (30)
Family members/friends	29 (19)
Other specialty doctor	21 (13)
Pharmacy	7 (5)
Psychologist	1 (0.6)
Dentist	1 (0.6)

Harmful to health, n (%)	
Not harmful	11 (7)
Slightly harmful	52 (33)
Harmful	69 (44)
Very harmful	25 (16)
BZD side effects, n (%)	
Dependence	122 (78)
Cognitive impairment	26 (17)
Drowsiness	21 (13)
Bereavement or mood impairment	11 (7)
Others	27 (17)
Unknown/None	8 (5)

BZD, Benzodiazepine; SD, Standard deviation.

Note 1: Frequency of “reasons”, “benzodiazepine(s) used” and “BZD side effects” do not add to 100%, as individuals were able to select more than one option. Note 2: Individuals selected “drowsiness” or one of the following: sedation, psychomotor retardation/danger on operating machines, increased reaction time.

Note 3: Individuals selected “dependence” or one of the following: habituation, addiction or abstinence syndrome.

Students who reported current BZD use (n=41) answered four additional questions: frequency of BZD use, number of BZD pills taken per week, importance of reducing BZD dose and their perceived ability to reduce BZD dose (table 4).

One third of the students used BZD only once or twice a month (34%), while the other third (37%) used BZD daily. Almost sixty percent of the sample (59%) reported a consumption of four or less BZD pills per week, while only two students (5%) referred a weekly use of twenty or more BZD pills.

Inquiring about the importance of reducing BZD dose currently taken, 58% of the students acknowledged it to be important or very important, while 42% did not consider it important or slightly important.

When asked about their ability to reduce BZD dose, 12 (29%) students recognized not being able or being slightly able to reduce it, while 29 (71%) believed being able or very able to reduce current dose.

Table 4 – Characterization of current benzodiazepine use (n=41)

Frequency of BZD use, n (%)	
1-2 times/month	14 (34)
1-2 times/week	10 (24)
3-4 times/week	2 (5)
Daily	15 (37)
Weekly number of BZD pills, n (%)	
0-4 pills/week	24 (59)
4-8 pills/week	12 (29)
8-12 pills/week	1 (2)
12-16 pills/week	2 (5)
16-20 pills/week	0 (0)
20 or more pills/week	2 (5)
Importance of reducing BZD dose, n (%)	
Not important	7 (17)
Slightly important	10 (24)
Important	12 (29)
Very important	12 (29)
Ability to reduce BZD dose, n (%)	
Not able	1 (2)
Slightly able	11 (27)
Able	20 (49)
Very able	22 (22)

3.2 Bivariate analysis

As shown in Table 5, *gender* (male/female) had a positive and significant association with BZD use (p -value=0.001), and 81% of the users were females (19% of BZD users were males).

In the matter of consumption of psychoactive substances, results show that *cigarette smoking* and *cocaine* correlated positively and significantly with BZD use (risk ratio (RR)=1.46, p -value=0.018; RR=1.96, p -value=0.021, respectively). On the other hand, *alcohol*, *cannabinoids*, *heroin*, *LSD/other hallucinogens* and *ecstasy/MDMA/amphetamines* did not display associations with BZD use among college students. However, regarding *LSD/ other hallucinogens* and *ecstasy/MDMA/amphetamines* one should note a non-significant positive association with BZD use (RR=1.61, p -value=0.072; RR=1.58, p -value=0.070, respectively). Additionally, *physical exercise* did not show association with BZD use (p -value>0.05).

Table 5 - Bivariate analysis comparing dichotomous variables with benzodiazepine use (current + past use)

Variable	BZD use		χ^2	p-value
	Yes (n=157)	No (n=648)		
Gender, n (%)				
Female	127 (23)	434 (77)	11.6	0.001
Male	30 (12)	214 (88)		
Physical exercise, n (%)				
Yes	70 (17)	332 (83)	2.2	0.080
No	87 (22)	316 (78)		
Cigarette smoking, n (%)*				
Yes	45 (26)	129 (74)	5.7	0.018
No	112 (18)	519 (82)		
Alcohol, n (%)*				
Yes	115 (19)	491 (81)	0.4	>0.1
No	42 (21)	157 (79)		
Cannabinoids, n (%)*				
Yes	21 (19)	89 (81)	0.0	>0.1
No	136 (20)	559 (80)		
Cocaine, n (%)**				
Yes	10 (38)	16 (62)	6.2	0.021
No	147 (19)	632 (81)		
Heroin, n (%)**				
Yes	1 (17)	5 (83)	0.0	>0.1
No	156 (20)	643 (80)		
LSD/Other hallucinogens, n (%)**				
Yes	11 (31)	25 (69)	2.9	0.072
No	146 (19)	623 (81)		
Ecstasy/MDMA/Amphetamines, n (%)**				
Yes	12 (30)	28 (70)	3.0	0.070
No	145 (19)	620 (81)		

χ^2 – Statistical test (Chi-square)

*For cigarette smoking, alcohol and cannabinoids: “Yes” represents sporadic (less than once a month), from time to time (more than once a month and less than once a week), frequent (more than once a week) and daily use. “No” represents reporting never used/one experimental use. **For cocaine, heroin, LSD and ecstasy: “Yes” represents all frequencies of use except never tried.

In what concerns the results presented in Table 6, *age* was positively associated with BZD use ($t=-2.205$, $p\text{-value}<0.05$), so as *depressive symptoms* ($t=3.453$, $p\text{-value}=0.001$), *perceived stress* ($t=4.591$, $p\text{-value}=0.000$), and *anxiety symptoms* ($t=7.672$, $p\text{-value}<0.001$). In contrast, mindfulness facets *acting with awareness* ($t=-2.201$, $p\text{-value}<0.05$), *nonjudging* ($t=-3.171$, $p\text{-value}=0.002$), *nonreacting* ($t=-2.222$, $p\text{-value}<0.05$) and *FFMQ total* ($t=-2.319$, $p\text{-value}<0.05$) were negatively associated with BZD use. Additionally, physical exercise did not show association with BZD use ($p\text{-value}>0.05$).

Table 6 – Bivariate analysis comparing continuous variables with benzodiazepine use (current + past use)

Variable	BZD use		95% CI Min; Max	t	p-value
	Yes (n=157)	No (n=648)			
Age, mean	23	22]-2.0; -0.1[-2.205	.028
Depressive symptoms (PHQ-9), mean	2.8	1.8]-0.5; -0.1[3.453	.001
Perceived Stress (PSS-10), mean	2.0	1.8]-0.3; -0.1[4.591	.000
Anxiety symptoms (SAS index), mean	2.2	1.7]-0.7; -0.4[7.672	.000
Quality of Life (WHOQOL-Bref)					
Physical health (D1), mean	47	48]-0.8; 2.2[-0.888	>0.1
Psychological health (D2), mean	60	58]-3.2; 0.1[1.804	.072
Social relationships (D3), mean	64	67]-1.3; 6.3[-1.284	>0.1
Environment (D4), mean	59	59]-0.9; 2.0[-0.764	>0.1
Mindfulness (FFMQ)					
Describing, mean	27	26]-1.6; 0.6[.859	>0.1
Observing, mean	24	24]-1.3; 0.9[.330	>0.1
Acting with Awareness, mean	26	27]0.2; 2.8[-2.201	.028
Nonjudging, mean	25	27]0.8; 3.4[-3.171	.002
Nonreacting, mean	19	20]0.1; 1.7[-2.222	.027
FFMQ total, mean	121	124]0.6; 7.0[-2.319	.021

BZD, Benzodiazepine; CI, confidence interval; t, student t test; PHQ-9, Patient Health Questionnaire; PSS-10, Perceived Stress Scale; SAS, Self-Rating Anxiety Scale; D1, Domain 1; D2, Domain 2; D3, Domain 3; D4, Domain 4; WHOQOL-Bref, WHO Quality of Life Brief Questionnaire; FFMQ, Five Facet Mindfulness Questionnaire.

Note: Benzodiazepine use, n: Yes, 157; No, 648

3.3 Multivariate logistic regression analysis

A multivariate logistic regression analysis was developed in order to assess the predictors of BZD use as the dependent variable.

As previously explained in methods, the logistic preliminary models (model 1 and model 2) included the following variables: *gender, age, cigarette smoking, alcohol, cannabinoids, cocaine, LSD/other hallucinogens, ecstasy/MDMA/amphetamines, heroine, depressive symptoms, perceived stress, anxiety symptoms, physical exercise, psychological health (D2), observing, describing, acting with awareness, nonjudging and nonreacting.*

3.3.1 Model 1: Multivariate logistic regression for current or past BZD use (versus Never used BZD); N=157

Based on the non-significant results of Wald's test, the following variables, with p-value > 0.1 were removed through backward method, one at a time, and successively, by this order: *ecstasy/MDMA/amphetamines, cannabinoids, perceived stress, acting with awareness, heroin, depressive symptoms, nonjudging, gender, cocaine, physical exercise and observing.*

The final Model 1 (M1), which is presented in table 7, was found to have the highest predictive capacity (15%) and better data adjustment to the data (lower AIC), on estimating the probability of a past or present use of BZD. The model included the predictors *age, cigarette smoking, alcohol, LSD/other hallucinogens, anxiety symptoms, psychological health (D2), describing and nonjudging*, with significant coefficients (p-value < 0.1). According to Hosmer and Lemeshow's test, the logistic model with 9 parameters was well-adjusted to the data ($X^2(8)=7.226$ and p-value=0.513), explaining 15% of total variance of BZD use (McFadden's $R^2=0.145$).

Table 7 - Multivariate Logistic Regression for Current or Past BZD Use

Variable [#]	β	SE	OR	95% CI for OR	
Age	0.05	0.02	1.05***	1.01	1.08
Cigarette smoking	0.22	0.07	1.25***	1.09	1.43
Alcohol	-0.28	0.11	0.76***	0.61	0.93
LSD/other hallucinogens	0.77	0.42	2.15*	0.91	4.84
Anxiety symptoms	1.11	0.13	3.02****	2.36	3.91
Psychological health (D2)	0.03	0.01	1.03***	1.01	1.06
Describing	0.06	0.02	1.06****	1.03	1.10
Nonreacting	-0.06	0.02	0.94***	0.90	0.99

Hosmer-Lemeshow's test, $X^2(8) = 7.226$, p -value=0.513; McFadden's $R^2=0.145$; AIC=696.92

[#]Variables excluded: *ecstasy/MDMA/amphetamines, cannabinoids, perceived stress, acting with awareness, heroin, depressive symptoms, nonjudging, gender, cocaine, physical exercise and observing.*

* p -value<0.1; ** p -value<0.05; *** p -value<0.01; **** p -value<0.001

SE, Standard Error; OR, Odds ratio; CI, Confidence interval.

For older subjects, those with *cigarette smoking* and *LSD/other hallucinogens* consumption, the odds of BZD use were significantly increased (OR=1.05, p -value<0.01; OR=1.25, p -value<0.01; OR=2.15, p -value=0.069, respectively), as well for individuals with increased *anxiety symptoms* (OR=3.02, p -value<0.001). Moreover, *psychological health (D2)* and mindfulness facet *describing* also positively predicted the use of BZD (OR=1.03, p -value<0.01; OR=1.06, p -value<0.001, respectively). On the other hand, higher rates of *alcohol* use correlated with lower chances of BZD use and higher scores of the mindfulness facet *nonreacting* predicted lower chances of BZD use (OR=0.76, OR=0.94, respectively, both with p -value<0.01).

3.3.2 Model 2: Multivariate logistic regression for current use of BZD (versus Non-current use of BZD, i.e. past use or never used); N=41

When establishing current use of BZD as the outcome, Model 2 (M2), which is presented in table 8, had different predictors from M1, and was found to adjust to the data. Based on the forward method, the significant variables on Wald's test (p -value<0.1) were added to the model, one at a time, and successively, by this order: *anxiety symptoms, describing, nonreacting, alcohol, cigarette smoking, depressive symptoms, acting with awareness, age* and *nonjudging*.

The binomial logistic model explained 29% of the variance of current BZD use (McFadden's $R^2=0.287$). The model included age, *cigarette smoking, alcohol, depressive symptoms, anxiety symptoms, describing, acting with awareness, nonjudging* and *nonreacting* as the nine variables that play a role on predicting the outcome, here established as current use of

BZD. According to Hosmer and Lemeshow's test, the logistic model with 10 parameters was well-adjusted to the data ($X^2(8) = 7.145$ and $p\text{-value} = 0.521$), explaining 29% of total variance of BZD use (McFadden's $R^2 = 0.287$).

Table 8 - Multivariate Logistic Regression for Current BZD Use

Variable*	β	SE	OR	95% CI for OR	
Age	0.05	0.03	1.05*	0.99	1.11
Cigarette smoking	0.35	0.12	1.42***	1.11	1.81
Alcohol	-0.68	0.20	0.51****	0.34	0.74
Depressive symptoms	0.38	0.23	1.46*	0.94	2.29
Anxiety symptoms	1.32	0.30	3.73****	2.08	6.87
Describing	0.17	0.04	1.19****	1.11	1.28
Acting with awareness	0.05	0.03	1.05**	1.00	1.10
Nonjudging	-0.05	0.03	0.95*	0.90	1.01
Nonreacting	-0.16	0.05	0.85****	0.78	0.93

Hosmer and Lemeshow's test, $X^2(8) = 7.145$, $p\text{-value} = 0.521$; McFadden's $R^2 = 0.287$; AIC=250.9
 #Variables excluded: *gender, physical exercise, cannabinoids, cocaine, heroin, LSD/other hallucinogens, ecstasy/MDMA/amphetamines, perceived stress, psychological health (D2), observing.*
 * $p\text{-value} < 0.1$; ** $p\text{-value} < 0.05$; *** $p\text{-value} < 0.01$; **** $p\text{-value} < 0.001$
 SE, Standard Error; OR, Odds ratio; CI, Confidence interval.

Hand in hand to what was found on Model 1, the variables *age*, *cigarette smoking* and *anxiety symptoms* were positive predictors of current BZD use (OR=1.05, $p\text{-value} = 0.054$; OR=1.42, $p\text{-value} < 0.01$; OR=3.73, $p\text{-value} < 0.001$, respectively), while *alcohol* and *nonreacting* were negative predictors (OR=0.51, OR=0.85, both with $p\text{-value} < 0.001$). Although not included in Model 1, higher levels of *depressive symptoms* predicted higher chances of current BZD use (OR=1.46, $p\text{-value} = 0.094$). Mindfulness facets also had a part in predicting BZD use. Two of them, *describing* and *acting with awareness* were positive predictors of current BZD use (OR=1.19, $p\text{-value} < 0.001$; OR=1.05, $p\text{-value} < 0.05$, respectively), while other two, *nonjudging* and *nonreacting*, negatively predicted the outcome (OR=0.95, $p\text{-value} = 0.078$; OR=0.85, $p\text{-value} < 0.001$, respectively).

4. Discussion

This study sought to characterize use of benzodiazepines and assess the predictors of its use among Portuguese college students, and, despite not being a prevalence study, high frequencies of BZD use (19%) were found, with approximately one third (28%) of BZD users acknowledging not being able to reduce current dose. *Smokers* (OR=1.25, p-value<0.001) and *LSD/other hallucinogens* users (OR=2.15, p-value=0.069) had increased chances of being past or current BZD users (M1). *Anxiety* (OR=3.73, p-value<0.001) and *depressive symptoms* (OR=1.46, p-value=0.094) predicted current use of BZD (M2), while mindfulness facets *nonjudging* (OR=0.95, p-value=0.078) and *nonreacting* (OR=0.85, p-value<0.001) acted as independent negative predictors of the outcome.

4.1 Characterization of BZD use among college students

About one in five students (19%) reported past or current use of BZD. The Portuguese study conducted at Polytechnic Institute of Bragança (PIB),²⁰ found that, at the time of the study, 11.6% of the inquired students were currently using psychotropics (with special focus on BZD), a lower frequency than the one found in the present research (19%). Notwithstanding, taking into account differences in methodological approaches and in the populations studied, it is not possible to make statements regarding prevalences of BZD use among Portuguese college students without further studies using a probabilistic and random sample.

As studies solely focusing on students reveal higher rates of psychotropic/BZD use than the ones in the general population, one could hypothesize that Portuguese college students have higher rates of medication use than non-college Portuguese youngsters of the same age. However, as different studies have proposed, higher rates of medication use among students may not necessarily be related with increased risk or severity of mental disorders in students^{29,30} but with the stressors they're exposed to (academic demands, moving out of home, etc.)²¹ and increased help-seeking behaviors.^{24,30}

With regard to access to benzodiazepines, 76% of the students recurred to a physician (psychiatry, general medicine or other specialty). Of those students, 30% were prescribed BZD mainly by primary care physicians. Although other studies^{20,49} suggest BZD prescriptions originate mainly from primary care services, the present research shows psychiatrists were the main source of prescribed BZD (33%). Of note, a non-negligible

proportion of students had access to BZD directly from the pharmacy (5%), or through family members or friends (19%), a value sixteen times higher than what Balsa, Vital & Urbano's study¹⁴ found. These results are consistent with data from a previous study which found that the vast majority of students who used BZD without prescription obtain these controlled medications from a relative or friend,²⁶ and should instigate health authorities to develop measures of prevention and awareness of the risk associated with BZD use without prescription and medical control.

For students with current BZD use, 37% used it daily. Almost half (43%) did not consider important to reduce BZD consumption, which sheds some light on the student's risk perception on benzodiazepines. Approximately one third (28%) acknowledged not being able of reducing the dose currently taken, such as what Balsa, Vital & Urbano¹⁴ found, with half of medicaments' users not imagining life without such drugs, evidencing some degree of dependence among students currently taking BZD. Moreover, 41% of the sample's population did not consider BZD consumption harmful to one's health, demonstrating the need for prescriber clinicians to give appropriate explanations at the initial usage period, and the first repeat prescription, about benefits but also the risks of BZD use, especially if long-term.

4.2 Discussion of research hypotheses

4.2.1 Gender correlates positively with BZD use

23% of all women are current or former BZD users, compared to only 12% of men, meaning 84% more women use BZD than men ($p=0.001$), which is compatible with other studies evidencing women as the main users of BZD.^{15,17,24-27} Indeed, women, whether students or not, have more anxiety/depression/stress-related problems^{18,21,23} when compared with men, and, in line with this, after the multivariate analysis (table 7 and 8), gender showed no effect on BZD use after adjusting for confounders. According to Correia et al.,²⁰ several authors mention women are more aware of disease-related symptomatology, more prone to engage in help-seeking behaviors and less resistant to use medication than men, which leads to higher rates of medication use, among which benzodiazepines.

4.2.2 Age correlates positively with BZD use

The present study found benzodiazepine use was significantly more common with increasing age, as the odds of using BZD increased 5% per year (i.e. per each age unit), (M1: OR=1.05, $p\text{-value}<0.01$; M2: OR=1.05, $p\text{-value}=0.054$). This finding is consistent with previous studies.^{14,15,17,25}

4.2.3 Use of psychoactive substances correlates positively with BZD use

Cigarette smoking and *cocaine* significantly correlated with BZD use ($p\text{-value} < 0.05$) in bivariate analysis, while *LSD/ other hallucinogens* and *ecstasy/MDMA/amphetamines* had non-significant positive associations ($p\text{-value} < 0.1$).

Cigarette smoking was found to be a positive predictor of BZD consumption in both multivariate models, with tobacco users having a 1.3 to 1.4 times greater chances of being current or past BZD users (M1: OR=1.25, $p\text{-value} < 0.01$; M2: OR=1.42, $p\text{-value} < 0.01$). A student who smoked daily had 168% (42% times 4) increased chances of currently using BZD when compared to a student who only tried experimental cigarette smoking.

Also worth discussing is that although *alcohol* did not significantly associate with BZD use on the bivariate analysis, it negatively predicted benzodiazepine consumption in both multivariate models. Interestingly, for each increase of frequency of *alcohol* consumption, the chances of BZD use decreased between 24% and 49%. (M1: OR=0.76, $p\text{-value} < 0.01$; M2: OR=0.51, $p\text{-value} < 0.001$). One might consider this inverse relation might be related with advices on the non-recommended use of alcohol drinking whilst on BZD treatment,³ or as Santos¹⁹ found an inverse relation between alcohol consumption and stress, alcohol may mimic BZD anxiety-relief effects and substitute BZD as a stress-coping mechanism.³

LSD/other hallucinogens was found to be a positive predictor of BZD use, with students who report (experimental or occasional) LSD consumption having 2.2 greater chances of being current or past BZD users (M1: OR=2.15, $p\text{-value} = 0.069$). In fact, the present findings, regarding the influence of cigarette smoking and LSD consumption on BZD use, are supported by Baumann et al.⁵⁰ who, although focusing on psychotropics instead of BZD in particular, also found that smoking and illicit drug use were associated with psychotropic drug use.

Noteworthy is that McCabe and West,²⁶ who studied medical and non-medical BZD users, show that individuals who reported medical use of prescription BZD anxiolytics were not at increased risk for substance use behaviors (e.g., cigarette smoking, binge drinking, marijuana and other drug use) when compared to their peers who were non-BZD users. On the other hand, nonmedical use of BZD was a high-risk marker for substance use behaviors.²⁶

4.2.4 Higher levels of perceived stress correlate positively with BZD use

The frequency of *perceived stress* in this study was higher than what Santos¹⁹ found in her study with University of Aveiro's students (5.8% of students with elevated levels of stress),

however these dissimilarities must be considered carefully taking into account methodological differences.

Higher levels of *perceived stress* were reported by BZD users of the study sample. As expected, *perceived stress* correlated significantly and positively with BZD use (p-value<0.001). Stress has been found to be related with drug abuse behaviors.^{20,36}

Furthermore, as stress is an important factor on psychopathology development²² as well as on academic success,²¹ it is understandable how it might impact the decision of college students to use benzodiazepines.

4.2.5 Higher levels of anxiety symptoms correlate positively with BZD use

Anxiolytic. The suffix “-lytic” derives from “*lysis*”, which means to break apart. Benzodiazepines’ main therapeutic target is to break apart (i.e. to reduce) anxiety. In fact, anxiety was the main reason stated by the sample of college students for benzodiazepine use, as in previous studies focusing on young adults⁴⁹ and the general population.^{14,51} Anxiety appears to be one of the best well-established predictors of BZD use, therefore it is not surprising that *anxiety symptoms* were positively correlated with benzodiazepine use. In fact, BZD users reported higher levels of *anxiety symptoms* when compared with non-BZD users and higher anxiety symptomatology correlated positively and significantly with BZD use (p-value<0.001). Multiple logistic regression results reinforced the bivariate findings, as the odds of students using benzodiazepines were considerably higher among individuals with increased levels of *anxiety symptoms* (M1: OR=3.02 p-value<0.001; M2: OR=3.73, p-value<0.001). A college student with moderate *anxiety symptoms* had 38% higher chances of currently using BZD when compared with a student with normal levels of anxious symptomatology.

In accordance, Sidorchuk et al.⁴⁹ evaluated prescribing patterns of benzodiazepines among children, adolescents and young adults (0 to 24 years), and found that 45.3% of the sample had a record of a psychiatric disorder diagnosed within 6 months of BZD dispensation, with anxiety and depression being the most frequent diagnoses (20.3% and 20.1%, respectively). In fact, being older, and suffering from a comorbid anxiety disorder are predictive factors for prescription of a BZD.⁴

4.2.6 Higher levels of depressive symptoms correlate positively with BZD use

The chances of a student to currently use BZD were found to increase 46% per each category of depressive symptomatology in PHQ-9 (M2: OR=1.46, p-value=0.094).

Moreover, sleeping problems were the second commonest reason for BZD use among students of the sample. Insomnia is quite frequent among depressed individuals, hence benzodiazepines might help students as short-term treatment for insomnia.² Even if BZDs are not licensed as antidepressants,⁴ co-prescription of a BZD improves first-month adherence and response to antidepressant treatment.⁵² One large-scale study showed that among patients who received combined treatment, 14.1% subsequently used BZDs for at least 1 year, and of the 0.7% patients who were diagnosed with anxiolytic abuse or dependence, most had a context of other substance abuse disorders (i.e. alcohol or illicit drug abuse).⁵³

Therefore, higher depressive symptomatology might be an additional explanation for BZD use being more common among students. However, when prescribing, clinicians must be aware of benzodiazepine side-effects, particularly related to dosage, and anticipate the duration of treatment needed, as well as the patient's age and lifestyle. Among students, it is particularly important to know if the patient is depressed, has suicidal ideation or if is alcohol or substance abuser, as this might be risk-factors for BZD long-term dependence.^{2-4,52} Indeed, as considered by previous studies,^{36,38} depression, as a mood disorder, might co-occur with substance abuse disorders, in which BZD abuse is included.

4.2.7 Higher levels of quality of life correlate negatively with BZD use

Although physical, psychological, social and environmental compounds of quality of life affect every individual's well-being, facing the present results, one cannot yet postulate quality of life as a predictor of BZD use among students. In fact, opposite to what was expected, quality of life's domain *psychological health (D2)* associated, with past or current benzodiazepine use (but not current use only) among college students. In multivariate analysis, per each unit increase in *psychological health (D2)*, students' odds of using BZD rose 3% (M1: OR=1.03, p-value<0.01).

As psychologic distress, lack of family support and belonging to lower socioeconomic categories were found to predict psychotropic use among youths, one could infer that the same relations could be applied to BZD use in particular.²⁷ One could even speculate this relation may be the product of benzodiazepine use in improving psychological health.

4.2.8 Higher levels of mindfulness correlate negatively with BZD use

The study's formulated hypothesis of higher levels of mindfulness being inversely correlated with BZD use is only partly confirmed, as mindfulness facets appeared to dynamically behave in opposite ways when predicting BZD use. In bivariate analysis, *acting with awareness*, *nonreacting* and *nonjudging* associated with lower risk of present or past BZD use. In multivariate analysis, of the five mindfulness facets, *describing* and *acting with awareness* were positive predictors of BZD use, while *nonjudging* and *nonreacting* were negative predictors. The facet *observing* was not significantly associated with BZD use.

The facets *describing* (M1: OR=1.06, M2: OR=1.19, both p-value<0.001) and *acting with awareness* (M1: OR=1.05, p-value<0.05) positively predicted BZD use. Although one might think that *acting with awareness* inversely associating with BZD use on the bivariate analysis contradicts its positive prediction of *current* BZD use (M2), it is worth noticing that the sample being studied on M2 (n=41) represents a sub-sample of the bivariate analysis (n=157).

We found both mindfulness facets *nonjudging* (M2: OR=0.95, p-value=0.078) and *nonreacting* (M2: OR=0.85, p-value<0.001) negatively predicted current BZD use, hence, college students with higher levels of the latter mindfulness facets had decreased chances of currently use BZD.

We are not aware of previous studies on mindfulness relations with BZD use, not whatsoever among college students. The five facets of mindfulness have shown to be differentially related to psychopathological disorders. Brown et al.⁵⁴ found that the facets nonjudging and nonreacting associate negatively with anxiety and depressive symptoms. Moreover, in a study with a mixed sample of meditators and non-meditators undergraduate students, Cash & Whittingham⁴² found that higher levels of the mindfulness facet nonjudging predicted lower levels of depression, anxiety and stress-related symptomatology. Indeed, with nonjudging predicting depressive symptomatology,⁴² it is remarkable how, in this study, both were, in fact, predictors of current BZD use (M2).

Mindfulness-based therapies have not only shown promising results in youth⁵⁵ and in individuals with depression and substance use disorders,³⁸ as well as they also predicted better academic performance in students.⁵⁶ By keeping awareness of ongoing daily activities and understanding, without judgement, one's emotional and physical sensations, specific mindfulness facets might work as preventive factors/mediators of detrimental psychopathological symptoms, therefore consequently preventing BZD use as well, by

allowing students to find other ways of coping with stressors without the aid of psychotropic use.

4.3 Study strengths and limitations

The present study has a few strengths. As far as we are aware, not only this research is the first to assess whether quality of life and mindfulness associate with benzodiazepine use, but also, how stress, anxiety and depression individually relate with such behaviors in college students, rather than evaluating them as a unidimensional psychopathology construct. Nevertheless, it should be considered an exploratory study, and the present results must be carefully interpreted. Moreover, the present study gives voice to an important matter somehow understudied throughout the last years of substance use research. Therefore, it is an innovative topic and students are its primary *leitmotiv*, as they form one of the pillars of future generations, and their contemporary health and behavior will influence tomorrow's society.

Notwithstanding the study strengths, the limitations of the research should be acknowledged. First, the study was limited by the cross-sectional study design, not allowing the demonstration of temporal precedence which is required for making causal inferences. Second, despite being a cross-national study and having students from different high education institutions, the sampling method was not probabilistic, hence does not allow to accurately assume it represents college students nationwide, and inference to the universe of all students must be done carefully. Third, the use of a self-report questionnaire and the presence of several questions addressing events related with past-related BZD use is accountable for the possibility of social desirability bias and recall bias. Fourth, with regard to instrument measures, although shown to have good psychometric characteristics, future studies may consider the use of scales specifically developed to study college population. Moreover, it was not possible to directly assess benzodiazepine dependence rates, nor the length of BZD use, but these matters should be considered in future research.

To the best of our knowledge, studies on characterization of benzodiazepine use among college students and its correlates are scarce. Different studies have focused on alcohol and use of psychoactive drugs in students, while others evaluated a broader group of psychotropic medication, however, studies exploring benzodiazepine use among students are sparse. Therefore, a general data paucity on BZD use in college students (particularly in Portugal) and differences in methodological approaches between studies, makes it difficult to find direct comparisons to the present findings.

4.4 Clinical implications and future directions

The findings of the present study have several implications for research, clinical practice and public health policy.

Future research is invited to further clarify the underlying risk and protective factors that outline patterns of BZD medical and non-medical use among students, along with the assessment of rates of abuse and dependence. Audit of beliefs, convictions and concerns of clinicians on prescribing benzodiazepines are also important for developing this subject, as advanced by previous studies.⁴⁹ Research on the effects of mindfulness-based therapies focused on developing nonjudging and nonreactivity skills' in university students are important as well, as these facets negatively predicted BZD use independently of anxiety and depressive symptoms.

In what concerns the clinical implications some points are remarkable. As initiation of benzodiazepine consumption is a two-way relationship, between the benzodiazepine provider and its user, it is important to assess if benzodiazepine prescription guidelines are being responsively followed by clinicians, while future preventative efforts should educate college students regarding the short-term treatment indications for BZD use, as well as their associated side effects. Furthermore, as 1 in 5 students obtained benzodiazepines through their relatives, society must be informed of the risk of supplying BZD pills to subjects without a medical prescription.

One cannot change the effect of age and gender on BZD use among college students. However, collectively considering the significant but *modifiable* associations found between use of psychoactive substances, stress, anxiety, depression, mindfulness facets and BZD use, it becomes clear how reinforcement of colleges' psychological support may help to prevent development of detrimental psychological symptoms in students. One cannot dismiss how an unhealthy mind, which fairly often pairs with a negatively biased view of the self, others and the world, and concordant (destructive) thoughts and behaviors, impacts the much-needed harmonious equation of students' well-being. Targeting the development of detrimental psychopathological symptoms and providing students with mental health resources they need might positively diminish their increased risk of benzodiazepine use.

Therefore, it is necessary to develop public policies addressing the promotion and awareness of mental health, rather than only focusing on treatment of already established conditions. Furthermore, it appears increasingly important to once more reassure the need to reach Portugal's National Mental Health¹⁶ goals on reducing benzodiazepine consumption among the Portuguese population. This seems more achievable if primary care and psychiatry care

work synergistically in order to find coordinated strategies and guidelines for benzodiazepines prescription and follow-up in youths.

5. Conclusion

A unique contribution of this study is the portrait of benzodiazepine use among college students, and the evidence that several factors influence its use, such as it happens with the use of other psychoactive drugs.

Although this was not a prevalence study, the high frequency of benzodiazepine use among college students encountered in this study is a pushforward to aim for more insight on the matter, as well as to incite changes in public health policies regarding the prescription and use of benzodiazepines among youths.

Furthermore, this study provides evidence that not only benzodiazepine use is closely related with psychoactive substances consumption, perceived stress, depressive and anxiety symptoms, but also that higher levels of the mindfulness facets nonjudging and nonreacting protect, in some degree, from BZD use. The modifiable predictors of BZD use: anxiety symptoms, depressive symptoms and psychoactive substances consumption, must constitute the main targets on the development of strategies aiming to diminish its use, while advocating a conscious consumption of the drug when needed. Mindfulness-based interventions, relying fundamentally on the development and practice of nonjudging and nonreacting, are of interest in further studies, as they might protect students from incurring in risky behaviors.

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7. Attachments

7.1 Study's questionnaire

Retrato do consumo de benzodiazepinas em estudantes do ensino superior

O presente questionário tem como objetivo caracterizar o padrão e fatores preditores da toma de benzodiazepinas em estudantes universitários.

Este estudo insere-se no âmbito da minha tese de Mestrado em Medicina, a decorrer na Faculdade de Ciências da Saúde da Universidade da Beira Interior, sob orientação do Dr. Nuno Rodrigues Silva.

Ao avançares para a próxima secção estás a consentir a tua participação neste estudo. Não existem respostas corretas ou erradas, apenas se procura saber acerca da tua opinião e experiência pessoal. Uma vez que comeces a responder peço-te que respondas até ao fim, com o máximo de autenticidade, de forma a que se possa validar a tua participação.

O preenchimento do questionário demora aproximadamente 20 minutos. Toda a informação recebida será sujeita a tratamento estatístico, sendo totalmente confidencial e anónima.

Agradeço imenso a tua colaboração!

Inês Jorge Proença Paulo Rato

Parte 1

1. Sexo

Masculino

Feminino

2. Idade _____

3. Instituição de Ensino Superior _____

4. Curso _____

5. Ano do Curso _____

6. Já alguma vez tomaste benzodiazepinas?

___ Sim, tomei no passado (*seguir para parte 2*)

___ Sim, tomo atualmente (*seguir para parte 2*)

___ Não (*seguir para parte 3*)

Parte 2

Respondida pelos estudantes que responderam “Sim, tomei no passado”/”tomo atualmente”

7. Geralmente, por que razão tomas/tomaste? (selecciona tudo o que for aplicável)

- Problemas de sono Ansiedade Efeito recreativo
 Tratamento adjuvante de outras doenças Outra _____

8. Como tiveste acesso a benzodiazepinas? (selecciona apenas uma)

- Consultei um médico psiquiatra
 Consultei um médico de Medicina Geral e Familiar
 Consultei um médico de outra especialidade
 Não consultei um médico, disponibilizaram-me na farmácia
 Não consultei um médico, familiares/colegas disponibilizaram-me
 Não consultei um médico, encomendei via internet
 Outra _____

9. Com que idade tomaste benzodiazepinas pela primeira vez?

10. Qual/quais das seguintes benzodiazepinas estás a tomar/tomaste?

- Alprazolam Bromazepam Clobazam
 Clonazepam Clordiazepóxido Diazepam
 Estazolam Loflazepato de etilo Lorazepam
 Mexazolam Midazolam Oxazepam Triazolam

11. Com que frequência tomas benzodiazepinas? (selecciona apenas uma)

- 1-2 vezes por mês
 1-2 vezes por semana
 3-4 vezes por semana
 Diariamente

12. Se estás a tomar benzodiazepinas diariamente, qual a dose total diária? (Caso não saibas a dose exata, coloca o número de comprimidos diários)

13. Quantos comprimidos tomas, em média, numa semana? (*seleciona apenas uma*)

0 a 4 4 a 8 8 a 12 12 a 16 16 a 20 20 ou mais

14. Consideras importante reduzir a dose que tomas?

Nada importante Pouco importante Importante Muito importante

15. Consideras que serias capaz de reduzir a dose/frequência com que tomas BZD?

Nada capaz Pouco capaz Capaz Muito capaz

16. Consideras que o consumo de benzodiazepinas é nocivo para a tua saúde?

Muito nocivo Nada nocivo Nocivo Pouco nocivo

17. Quais consideras serem os riscos associados à toma de benzodiazepinas?

Parte 3 – Consumo de substâncias psicoativas

18. *Seleciona apenas uma opção em cada linha.*

	Nunca	Já experimentei	Esporadicamente (<1x/mês)	Com alguma frequência (>1x/mês e <1x/sem.)	Frequentemente	Todos os dias
Tabaco						
Álcool						
Canabinóides						
Cocaína						
LSD/outras alucinogénios						
Ecstasy/MDMA/Anfetaminas						
Heroína						

Parte 4

19. Praticas exercício físico regularmente?

___ Sim

___ Não

20. Se respondeste sim na pergunta anterior, que tipo de exercício praticas?

Parte 5

Instruções: Durante as duas últimas semanas, em quantos dias foste afetado/a por algum dos seguintes problemas?

Usando a escala fornecida como guia, indica o teu grau de concordância com cada uma das seguintes afirmações, selecionando a opção correspondente.

21. *Seleciona apenas uma opção em cada linha.*

	Nunca	Em vários dias	Em mais de metade dos dias	Todos os dias
Tive pouco interesse ou prazer em fazer coisas				
Senti desânimo, desalento ou falta de esperança				
Tive dificuldade em adormecer ou em dormir sem interrupções, ou dormi demais				
Senti cansaço ou falta de energia				
Tive falta ou excesso de apetite				
Senti que não gosto de mim próprio/a, ou que sou um(a) falhado/a ou me desiludia a mim ou à minha família				
Tive dificuldade em concentrar-me nas coisas, como a ler o jornal ou a ver televisão				
Movimentei-me ou falei tão lentamente que outras pessoas poderão ter notado. Ou o oposto: estive agitado/a a ponto de andar de um lado para o outro muito mais que o habitual				
Pensei que seria melhor estar morto/a, ou em magoar-me a mim próprio/a de alguma forma.				

Parte 6

Instruções: O próximo questionário procura obter informação acerca da tua qualidade de vida, e saúde em diferentes áreas. Responde a todas as perguntas e, se não tiveres a certeza de que resposta dar uma pergunta, escolhe a opção que te parecer mais apropriada. Esta pode, muitas vezes, ser a primeira resposta que te vier à cabeça. Por favor tem presente os teus padrões, expectativas, alegrias e preocupações, tendo como base a tua vida nas duas últimas semanas.

22. Como avalia a sua qualidade de vida?

Muito má Má Nem boa nem má Boa Muito boa

22. Até que ponto está satisfeito com a sua saúde?

Muito insatisfeito Insatisfeito Nem insatisfeito nem satisfeito
 Satisfeito Muito satisfeito

23. Seleciona apenas uma opção em cada linha.

	Nada	Pouco	Nem muito nem pouco	Muito	Muitíssimo
Em que medida as suas dores físicas o impedem de fazer o que precisa de fazer?					
Em que medida precisa de cuidados médicos para fazer a sua vida diária?					
Até que ponto gosta da sua vida?					
Em que medida sente que a sua vida tem sentido?					
Até que ponto se consegue concentrar?					
Em que medida se sente em segurança no seu dia-a-dia?					
Em que medida é saudável o seu ambiente físico?					

24. Selecciona apenas uma opção em cada linha.

	Nada	Pouco	Moderadamente	Bastante	Completamente
Tem energia suficiente para a sua vida diária?					
É capaz de aceitar a sua aparência física?					
Tem dinheiro suficiente para satisfazer as suas necessidades?					
Até que ponto tem acesso fácil às informações necessárias para organizar a sua vida?					
Em que medida tem oportunidade para realizar atividades de lazer?					

25. Como avaliaria a sua mobilidade? Selecciona apenas uma opção.

Muito má ___1 ___2 ___3 ___4 ___5 Muito boa

26. Selecciona apenas uma opção por cada linha.

	Muito insatisfeito	Insatisfeito	Nem satisfeito nem insatisfeito	Satisfeito	Muito satisfeito
Até que ponto está satisfeito com o seu sono?					
Até que ponto está satisfeito com a sua capacidade para desempenhar atividades do dia-a-dia?					
Até que ponto está satisfeito com a sua capacidade de trabalho?					
Até que ponto está satisfeito consigo próprio?					
Até que ponto esta satisfeito com as suas relações pessoais?					

Até que ponto está satisfeito com a sua vida sexual?					
Até que ponto está satisfeito com o apoio que recebe dos seus amigos?					
Até que ponto está satisfeito com as condições do local onde vive?					
Até que ponto está satisfeito com o acesso que tem aos cuidados de saúde?					
Até que ponto está satisfeito com os transportes que utiliza?					

27. Com que frequência tem sentimentos negativos tais como tristeza, desespero, ansiedade ou depressão?

Seleciona apenas uma opção.

Nunca ___1 ___2 ___3 ___4 ___5 Muito boa

Parte 7

Instruções: Para cada questão, indica com que frequência te sentiste ou pensaste de determinada maneira, durante o último mês. Apesar de algumas perguntas serem parecidas, existem diferenças entre elas e deves responder a cada uma como perguntas separadas. Responde de forma rápida e espontânea. Para cada questão seleciona a alternativa que melhor se ajusta à tua situação.

28. “No ultimo mês, com que frequência...”

Seleciona apenas uma opção por linha.

	Nunca	Quase nunca	Às vezes	Frequentemente	Muito frequentemente
...Esteve preocupado/a com alguma coisa que aconteceu inesperadamente?					
...Se sentiu incapaz de controlar as coisas importantes na sua vida?					
...Se sentiu nervoso/a e em stress?					

...Sentiu confiança na sua capacidade para enfrentar os seus problemas pessoais?					
...Sentiu que as coisas estavam a correr à sua maneira?					
...Sentiu que não aguentava com as coisas todas que tinha para fazer?					
...Foi capaz de controlar as suas irritações?					
...Sentiu ter tudo sob controlo?					
...Se sentiu furioso/a por coisas que ultrapassaram o seu controlo?					
...Sentiu que as dificuldades se estavam a acumular tanto que não as conseguia ultrapassar?					

Parte 8

Instruções: Por favor avalia cada uma das afirmações seguintes de acordo com a escala. Assinala com uma cruz o número que melhor descreve a tua opinião sobre o que consideras ser geralmente verdadeiro para ti. Para cada opção assinala somente um espaço. Não deixes nenhuma pergunta por responder.

29. *Selecciona apenas uma opção por linha*

	Nunca ou muito raramente verdadeiro	Raramente verdadeiro	Algumas vezes verdadeiro	Frequentemente verdadeiro	Muito frequentemente ou sempre verdadeiro
Quando caminho presto deliberadamente atenção às sensações do meu corpo em movimento.					
Encontro facilmente as palavras para descrever os meus sentimentos.					
Critico-me por ter emoções irracionais ou inapropriadas.					
Apercebo-me dos meus sentimentos e emoções sem ter que lhes reagir.					
Quando estou a fazer qualquer coisa a minha mente vagueia e distraio-me facilmente.					
Quando tomo um duche ou banho fico atento(a) às sensações da água no meu corpo					
Consigo traduzir facilmente as minhas crenças, opiniões e expectativas em palavras.					

Não presto atenção ao que estou a fazer porque estou a sonhar acordado(a), preocupado(a) ou distraído(a) com qualquer coisa.					
Observo os meus sentimentos sem me “perder” neles.					
Digo a mim próprio(a) que não devia sentir-me como me sinto					
Noto como a comida e a bebida afetam os meus pensamentos, as minhas sensações corporais e emoções.					
Tenho dificuldade em encontrar palavras para descrever o que penso.					
Distraio-me facilmente					
Acredito que alguns dos meus pensamentos são anormais ou maus e que não devia pensar dessa forma.					
Presto atenção às sensações, tais como o vento no meu cabelo ou o sol no meu rosto.					
Tenho dificuldade em pensar nas palavras certas para exprimir o que sinto acerca das coisas.					
Faço julgamentos sobre se os meus pensamentos são bons ou maus.					
É-me difícil permanecer focado no que está a acontecer no presente.					
Quando tenho pensamentos ou imagens muito perturbadoras distancio-me e torno-me consciente do pensamento ou imagem sem ser “apanhado” por este(a).					
Presto atenção a sons, tais como o bater do relógio, o chilrear dos pássaros ou os carros a passar.					
Em situações difíceis consigo parar e não reagir imediatamente					
Quando tenho uma sensação no meu corpo é-me difícil descrevê-la porque não consigo encontrar as palavras certas.					
Parece que funciono em “piloto automático” sem muita consciência do que estou a fazer.					
Pouco tempo depois de ter pensamentos ou imagens perturbadoras, sinto-me calmo(a).					
Digo a mim próprio(a) que não devia pensar do modo como estou a pensar					
Noto o cheiro e o aroma das coisas.					
Mesmo quando estou profundamente triste ou terrivelmente perturbado consigo encontrar uma forma de colocar isso em palavras					

Faço as atividades sem estar realmente atento(a) às mesmas					
Quando tenho pensamentos ou imagens perturbadoras consigo aperceber-me deles sem reagir					
Penso que algumas das minhas emoções são más e inapropriadas e que não as devia sentir.					
Noto elementos visuais na arte ou na natureza, tais como cores, formas, texturas ou padrões de luz e sombras.					
A minha tendência natural é traduzir as minhas experiências em palavras.					
Quando tenho pensamentos e imagens perturbadores, apenas me apercebo deles e “deixo-os ir”.					
Realizo trabalhos ou tarefas automaticamente sem estar atento ao que estou a fazer.					
Quando tenho pensamentos ou imagens perturbadoras julgo-me como bom (boa) ou mau (má), em função desses pensamentos ou imagens.					
Presto atenção à forma como as minhas emoções influenciam o meu comportamento.					
Normalmente consigo descrever como me sinto no momento, com grande pormenor.					
Dou por mim a fazer coisas sem prestar atenção.					
Desaprovo-me quando tenho ideias irracionais.					

Parte 9

Instruções: Indica o teu grau de concordância com cada uma das seguintes afirmações selecionando a opção mais adequada.

30. *Seleciona apenas uma opção por linha.*

	Nunca ou muito raramente verdadeiro	Raramente verdadeiro	Algumas vezes verdadeiro	Frequentemente verdadeiro
Sinto-me mais nervoso e ansioso do que o costume				
Sinto-me com medo sem nenhuma razão para isso				
Sinto-me facilmente perturbado ou em pânico				

Sinto-me como se estivesse para “rebentar”				
Sinto que tudo corre bem e que nada de mal acontecerá				
Sinto os braços e as pernas a tremer				
Tenho dores de cabeça, no pescoço e nas costas que me incomodam				
Sinto-me fraco e fico facilmente cansado				
Sinto-me calmo e com facilidade me posso sentar e fico sossegado				
Sinto o meu coração a bater depressa demais				
Tenho crises de tonturas que me incomodam				
Tenho crises de desmaio ou a sensação de que vou desmaiar				
Posso inspirar e expirar com facilidade				
Sinto os dedos das minhas mãos e dos meus pés entorpecidos e com picadas				
Costumo ter dores de estômago e más digestões				
Tenho de esvaziar a bexiga com frequência				
As minhas mãos estão habitualmente secas e quentes				
A minha face costuma ficar quente e corada				
Adormeço facilmente e consigo obter um bom descanso durante a noite				
Tenho pesadelos				

7.2 Authorization request for use of FFMQ Portuguese version



Inês Paulo-Rato

Pedido de autorização p/ uso - "Questionário das Cinco Facetas de Mindfulness"

Inês Paulo Rato

26 de março de 2019

Para: Sónia Gregório

Cara Professora Doutora Sónia Gregório,

O meu nome é Inês Paulo Rato, e sou estudante do 5ºano do mestrado integrado em medicina na Faculdade de Ciências da Saúde, na Covilhã, na Universidade da Beira Interior. Estou neste momento a iniciar a minha tese em psiquiatria, debruçando-me mais especificamente sobre os temas da ansiedade e depressão e da sua relação com estratégias adaptativas de Mindfulness, sendo orientada pelo Doutor Nuno Rodrigues Silva, médico psiquiatra. Deste modo, venho por este meio pedir a sua autorização para o uso da escala "Questionário das Cinco Facetas de Mindfulness", de forma a poder usá-la na elaboração dos questionários que farei.

Desde já, obrigada pela atenção. Saudações Académicas,

Inês Paulo Rato

Sónia Gregório

21 de abril de 2019

Para: Inês Paulo Rato

Estimada Dr.ª Inês,

desde já as mais sinceras desculpas pela demora na resposta. De facto não tinha visto os emails. Peço por favor, a ser possível, que actualize o meu endereço electrónico para ***** Em anexo envio a escala que me solicita, bem como o respectivo artigo de adaptação. Se necessitar de algum esclarecimento, não hesite em contactar-me.

Atentamente,

Sonia Martins Gregorio

Ph.D., Clinical psychologist & Mindfulness instructor

7.3 Study's approval by the Ethics Committee of University of Beira Interior



Comissão de Ética
Universidade da Beira Interior

comissaodeetica@ubi.pt
Convento de Santo António
6201-001 Covilhã | Portugal

Parecer relativo ao processo n.º CE-UBI-Pj-2019-036:ID1249

Na sua reunião de 11 de junho de 2019 a Comissão de Ética apreciou a documentação científica submetida referente ao pedido de parecer do projeto “*Fatores preditivos do consumo de benzodiazepinas em estudantes universitários*” da proponente **Inês Jorge Proença Paulo Rato**, a que atribuiu o código n.º CE-UBI-Pj-2019-036.

Na sua análise não identificou matéria que ofenda os princípios éticos e morais sendo de parecer que o estudo em causa pode ser aprovado.

Covilhã e UBI, 25 de junho de 2019

O Presidente da Comissão de Ética

Professor Doutor José António Martinez Souto de Oliveira
Professor Catedrático