



Preventive Examinations for Early Detection of Oral Cancer Conducted among Alcohol Addicts

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Key words

Oral, head and neck cancer; preventive examination; alcohol; tobacco; knowledge

Abstract

Aim: This study evaluated oral cancer (OC) awareness, risk factors, preventive measures, and early detection in high-risk populations. **Materials and methods:** Participants included an experimental group (EG) of patients treated for alcohol-related mental disorders at University Hospital Center Sestre milosrdnice (June 2022-March 2023) and a control group (CG) screened during the Oral, Head and Neck Cancer Awareness Week (April 2023) at the University of Zagreb's School of Dental Medicine. Both groups were surveyed to evaluate their understanding of OC, their opinions, smoking and alcohol consumption habits. **Results:** In a study of 282 participants,

68.1 % were in the EG and 31.9 % in the CG, with a gender distribution of 34.4 % female and 65.2 % male, and a median age of 52. Smoking was more prevalent in the EG (72.5 %) than in the CG (24.4 %). The EG also had significantly lower education levels ($p < 0.009$). Awareness of OC was high in both groups (73.2 % EG, 85.4 % CG), but only a small fraction had previously attended screening examinations (SE) (6.9 % EG, 18.7 % CG). A large majority believed that alcohol and smoking together increased OC risk (95.7 % EG, 98.7 % CG), and many expressed interest in learning more about OC (83.2 % EG, 75.3 % CG). Higher education was linked to more frequent SE attendance ($p = 0.041$) and lower smoking rates ($p = 0.042$). **Conclusion:** The study highlights the need for enhanced OC education and screening, especially among high-risk groups, to improve prevention and early detection efforts.

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Introduction

Drinking alcoholic beverages is one of the oldest forms of socially acceptable behavior which may result in alcohol addiction, one of the leading public health issues [1,2]. Alcohol addiction is characterized by alcohol cravings, loss of control over drinking, physical symptoms of withdrawal in case of drinking cessation, rise of alcohol tolerance, increase in the consumed amount, disregard for other interests and continuation of drinking in spite of awareness on harmful consequences. It is often associated with other psychiatric disorders and linked to a change in behavior and also leads to numerous somatic complications and conditions, including consequences on oral health. Research has shown that heavy drinkers have poorer oral hygiene, dental care, periodontal status, fewer teeth, more carious lesions, gingival diseases, interdental papillae bleeding and deep gingival pockets connected with bone loss as well as a higher rate of oropharyngeal cancers [3-6]. It's important to accentuate that around 80 % of alcohol addicts are also heavy smokers. In tobacco smokers, ethanol increases the permeation of tobacco carcinogens by increasing membrane permeability of the oral mucosa epithelial cells [7].

Oral cancer (OC) is the sixth most prevalent malignant tumor in humans and typically the most common tumor found in the head and neck region [8]. Typically, OC predominantly affects males aged 40 and older who engage in smoking and alcohol consumption [9]. However, there has recently been an increase in the incidence of OC among women due to i.e. increased alcohol consumption and smoking habits [10,11]. According to the latest data from the American Cancer Society, approximately 54,000 new cases of OC were reported in the United States in 2021, leading to more than 10,000 fatalities [12]. In the United Kingdom, there was an average of over 12,000 new cases during the period from 2016 to 2018 [13]. Data from the Croatian Institute of Public Health for the year 2018 recorded around 500 new cases of OC, resulting in 377 deaths, with 299 of those being men [14,15]. The most frequently occurring type of OC is squamous cell carcinoma. Squamous cell carcinoma of the oral cavity, as one of the most common malignancies in the world, appears not only in developing countries but also in highly industrialized countries. The junction of the soft and hard palate represents the upper, and the line of large papillae at the base of the tongue represents the lower border of oral and pharyngeal cancer [16]. It often develops from potentially malignant oral disorders such as leukoplakia and erythroleukoplakia, even though clinical presentation of OC is highly variable. In general, mucosal lesion that does not heal for two or three weeks should raise suspicion [17,18].

Despite simple and non-invasive oral cavity examination, many cases are still diagnosed in the advanced

stage [16,19]. Primarily, it's a condition that doesn't show symptoms, and signs typically emerge in the advanced stage, which is the primary cause of delayed diagnosis. Detecting and treating it early remains crucial for enhancing patient survival rates [20]. Individuals diagnosed with OC in its initial stage have an 80% five-year survival rate, whereas those diagnosed OC when regional lymph nodes are involved have a five-year survival rate of 40 % [12]. The duration from the onset of the first symptoms to the patient's initial examination is referred to as the "first lost time." Although multidisciplinary approaches and variety in multimodal therapy have improved, scientific data still shows that many general dentists, as the first step in disease recognition, do not examine oral mucosa during a standard dental appointment [16,21-24].

In separate studies, Rogers and associates and Hollows and associates investigated the causes behind delayed medical appointments. Researchers discovered that half of the patients believed their symptoms would resolve on their own. Additionally, one-third of the patients (36 %) shifted to a soft food diet before seeking medical advice, and a relatively small percentage (13 %) perceived their condition as a severe illness. A majority of OC patients tend to have lower socioeconomic status, engage in alcohol consumption, maintain suboptimal oral hygiene practices, and do not regularly visit both dentists and doctors [25,26]. Poor and late prognosis of patients with oral cavity cancer is attributed to the lack of knowledge about OC in both patients and healthcare professionals [27,28]. Conducted research shows a correlation between a lack of knowledge and inability to perform standardized preventive and diagnostic procedures by doctors and a lack of knowledge in the general population about OC and its risk factors [29,30]. It is of utmost significance that individuals are not only under the care of dentists but also well-informed and educated. This will inspire them to proactively seek more regular oral cavity examinations, leading to the earlier identification of cancer.

OC has a multifactorial etiology. Along with some potential genetic risk factors such as hereditary p53 gene mutation, the dominant role is played by chemical carcinogens such as nitrosamines and hydrocarbonate arising as a result of the metabolic decompensation of tobacco and alcohol [31]. The especially high risk for the disease development lies in the fact that alcohol and tobacco act synergistically, increasing the risk for OC up to 15 times [16,32-36]. Although alcohol and tobacco have a synergistic effect on the etiology of OC, alcohol consumption is linked to an increased risk of cancer even in nonsmokers [16]. Continuous exposure to intense sunlight poses a potential hazard for the onset of lip cancer [10]. Furthermore, human behaviors, socioeconomic position, attitude towards health, and presence of

other comorbidities such as acquired immune deficiency syndrome diagnosis benefit higher incidence of OC diagnosis [37]. Besides genetics, all the risk factors are preventable and can be overcome by proper nutrition, adequate oral hygiene, education, and avoiding smoking and alcohol abuse. An increase in socioeconomic status and lifestyle risk factors change, play an important role in disease prevention as well [32,38-40].

Cancer prevention means eliminating or minimizing exposure to the most common risk factors: smoking, diet, alcohol, physical inactivity, infections, and exposure to carcinogens. Primary prevention measures are aimed at eliminating known risk factors. The goal of secondary prevention is early and timely diagnosis and treatment, and tertiary prevention aims to reduce or eliminate the complications and consequences of the disease and treatment [41].

According to Sankarharayanah and associates, screening programs represent a great tool to prevent many deaths annually [42]. In 2004, Boundouki and associates conducted a study that revealed distributing pamphlets containing information about OC significantly heightened awareness of the condition, diminished apprehension and anxiety related to screening, and encouraged regular checkups when compared to a control group that did not receive the same informational materials [43]. In case preventive programs are carried out continuously including high-risk individuals, it may improve survival rates, change the stage at which cancer is detected and consequently decrease mortality [44]. The oral cavity can undergo a swift, painless, non-invasive, and cost-effective evaluation, and, if needed, a prompt biopsy can be performed to verify the specific diagnosis.

Screening initiatives should aim for substantial participation rates to ensure effective and efficient testing, diagnosis, and treatment [45]. According to a meta-analysis conducted by Speight and associates for OC screening to transition into a nationally organized program, it must present robust evidence of reducing mortality or morbidity while also demonstrating that its protocol aligns with ethical and societal standards accepted by healthcare professionals and the general public. The advantages of screening should outweigh any psychological or physical harm associated with the procedure. Additionally, there should be a well-defined program management and monitoring strategy in place, supported by facilities staffed with adequately trained healthcare providers [46]. Furthermore, the cost-effectiveness of screening in managing the underlying disease should also be considered.

However, proactive screening programs often target the wrong group of patients. Although smokers and alcohol drinkers are the ones who would benefit the most

from such programs they usually do not visit doctors, let alone respond to preventive check-ups [47-49].

Other important studies confirm that geographical and cultural differences, and level of education, all affect the awareness of OC presence [50,51]. OC and its treatment represent a serious global health challenge affecting our patients' lives in many aspects, including physical, esthetical, speech, psychological, and financial, decreasing the life quality [16]. Therefore, oral health care providers take an important place in managing, as well as preventing OC [17].

This study aimed to examine oral mucosa from the patients who consume alcohol, and the control group during the "Oral head and neck cancer awareness week", and also to compare the awareness of these two groups regarding OC, its risk factors, preventive measures, and early detection during screening. Additionally, the study aimed to investigate whether variables like education level and gender had an impact on the knowledge.

Materials and Methods

The study was conducted from June 2022 to March 2023 and was approved by the Ethics Committee of the School of Dental Medicine University of Zagreb (No. approval: 05-PA-30-VIII-5/2022.) as well as by the Ethics Committee of Sestre milosrdnice University Hospital Center (No. approval 003-06/22-03/011).

There were 282 participants included. The participants were divided into two groups: the experimental group (EG) and the control group (CG). The experimental group consisted of 192 patients who were treated for alcoholism at the Department of Psychiatry, Sestre milosrdnice University Hospital in Zagreb. The control group consisted of 90 patients who attended complimentary screening assessments as part of World Oral, Head, and Neck Cancer Awareness Week at the Department of Oral Medicine at the University of Zagreb School of Dental Medicine. Each participant first underwent a detailed examination of the oral mucosa and then answered the questionnaire. Before filling out the questionnaire all respondents signed an informed consent.

The questionnaire was structured into four sections: The first section covered general and social characteristics of the participants, including age, gender, educational attainment, and employment status. The second section focused on the respondents' smoking and alcohol consumption habits. It consisted of five questions related to smoking, such as whether they smoke, daily cigarette consumption, duration of smoking, attempts to quit, and intentions to quit. Additionally, there were six questions regarding alcohol consumption, including whether they consume alcohol, the frequency of consumption per week, contemplation of drinking less, experiences of criticism from others, feelings of guilt related to alcohol, and instances of

needing to drink in the morning to alleviate a hangover. Alcohol consumption was measured in units, with one unit equivalent to 3 deciliters of beer, 1 deciliter of wine, or 0.03 deciliters of spirits. The third section assessed the respondents' awareness of OC. It included 13 questions about their knowledge of OC, its causes, prevalence, mortality rate, and their own perceived risk of developing OC in the future. The fourth section was exclusively for respondents who identified as smokers and contained two questions related to evaluating their risk of developing OC compared to non-smokers of the same age and gender. The attitudes and awareness of respondents were gauged using the Likert scale, which allowed them to express the extent of their knowledge or agreement with specific statements on a scale from 1 (significantly lower than others) to 5 (significantly higher than others). Additionally, respondents could provide "YES," "NO," or "I DON'T KNOW" responses to certain questions, particularly those concerning smoking and drinking habits. The survey questionnaire was entirely anonymous and did not permit the inclusion of personal information such as names, surnames, dates of birth, or residential addresses of the respondents. The data were arranged into files using Microsoft Excel from Microsoft Inc. (USA) and subjected to statistical analysis utilizing SPSS (IBM Inc, USA). It's worth noting that some participants did not respond to specific questions, resulting in statistics being computed only for those participants who provided answers to those particular questions. To evaluate the normality of the data distribution, the Kolmogorov-Smirnov test was employed. Since the data did not exhibit a normal dis-

tribution, non-parametric tests were applied. Nominal variables were presented as proportions, while ordinal variables were represented by their median values along with their range. Differences between categorical variables were determined using the chi-square test, whereas distinctions between ordinal variables were examined using the Mann-Whitney or Kruskal-Wallis test p - values less than 0.05 were considered statistically significant.

Results

In total, 282 participants attended the screening event, with 94 of them being female (33.3 %) and 178 male (63.1 %). Ten participants did not provide an answer. The median age for female participants was 63 years (ranging from 20 to 85), while for males, it was 48 years (ranging from 20 to 92). The demographic details of the participants are presented in Table 1. There was a significant age difference between males and females ($p < 0.001$, Mann-Whitney test). No significant difference was found in education between the two groups ($p = 0.904$, chi-square test), as majority of the participants had high school education (59.9 %). Table 2 displays smoking and alcohol consumption patterns, and differences between genders, while Table 3 illustrates the variations in these habits across different education levels. There were no significant differences in the proportion of smokers and non-smokers between males and

Table 1. Demographic characteristics of the participants

	Total	Females	Males	Differences among the sexes (p)	Differences in education (p)
Sex N (%) (10 missing)	273 (96.4)	94 (33.3)	178 (63.1)		0.904*
Age (74 missing) (median; min - max)	52 (20 - 92)	63 (20 - 85)	48 (20 - 92)	< 0.001**	0.231***
Education N (%) (6 missing)					
Elementary school	20 (7.3)	6 (6.6)	14 (8.0)		
High school	167 (60.7)	57 (62.6)	103 (58.5)		
College degree	32 (11.6)	11 (12.1)	21 (11.9)	0.904*	
University degree	56 (20.4)	17 (18.7)	38 (21.6)		
Employment N (%) (4 missing)					
Retired	93 (33.6)	52 (55.3)	38 (21.7)		
Employed	139 (50.2)	25 (26.6)	109 (62.3)	< 0.001*	0.016*
Unemployed	45 (16.2)	17 (18.1)	28 (16.0)		

*chi-square test; **Mann-Whitney test; ***Kruskal Wallis test

Table 2. Sex-based disparities in smoking and alcohol consumption habits

	Total	Females	Males	Sex differences [p]
Smoking N (%) (1 missing)				
Yes	159 (56.8)	47 (50.0)	109 (61.6)	
No	90 (32.1)	36 (38.3)	50 (28.2)	0.172*
Former	31 (11.1)	11 (11.7)	18 (10.2)	
Years of non smoking (median; min-max)				
	8 (0.3 - 40)	9 (1.5 - 25)	3.5 (0.3 - 40)	0.359**
Cigarettes a day (median min – max)				
	20 (5 - 60)	20 (5 - 60)	20 (5 - 60)	0.009**
Years of smoking (median min – max)				
	24.5 (1 - 56)	21 (2 - 50)	33 (1 - 56)	0.620**
Do you contemplate quitting? N (%) (6 missing)				
No	91 (59.5)	28 (6.9)	63 (58.9)	
I plan to stop in the next 6 months	51 (33.3)	15 (32.6)	36 (33.6)	0.964*
I am currently in the phase of cessation	11 (7.2)	3 (6.5)	8 (7.5)	
Did you ever try quitting? N (%) (1 missing)				
Yes	103 (65.2)	28 (59.6)	72 (66.7)	
No	55 (34.8)	19 (40.4)	36 (33.3)	0.396*
Alcohol drinking? N(%) (8 missing)				
Yes	205 (75.1)	51 (54.3)	147 (86.0)	
No	68 (24.9)	43 (45.7)	24 (14.0)	< 0.001*
How many units a week? N (%)				
< 7 units a week	57 (26.4)	23 (41.8)	32 (20.8)	
7-14 units a week	68 (31.5)	18 (32.7)	47 (30.5)	0.002*
> 14 units a week	91 (42.1)	14 (25.5)	75 (48.7)	
Did you ever think you need to reduce drinking? N(%)				
Yes	195 (87.8)	41 (75.9)	147 (91.3)	
No	27 (12.2)	13 (24.1)	14 (8.7)	0.003*
Did other people ever criticize your drinking? N (%)				
Yes	154 (70.3)	29 (54.7)	121 (76.1)	
No	65 (29.7)	24 (45.3)	38 (23.9)	0.003*
Did you ever feel guilty about your drinking? N (%)				
Yes	190 (84.8)	42 (75.0)	141 (87.6)	
No	34 (15.2)	14 (25.0)	20 (12.4)	0.026*
Did you ever have to drink in the morning to calm down or ease hangover? N (%)				
Yes	130 (57.3)	21 (36.8)	103 (63.2)	
No	97 (42.7)	36 (63.2)	60 (36.8)	<0.001*

*chi-square test; **Mann-Whitney test

Table 3. Disparities in smoking and alcohol consumption habits across various education levels

	Total	Females	Males	Differences among the sexes (<i>p</i>)
Smoking N (%) (1 missing)				
Yes	159 (56.8)	47 (50.0)	109 (61.6)	
No	90 (32.1)	36 (38.3)	50 (28.2)	0.172*
Former	31 (11.1)	11 (11.7)	18 (10.2)	
Years of non smoking (median; min - max)	8 (0.3 - 40)	9 (1.5 - 25)	3.5 (0.3 - 40)	0.359**
Cigarettes a day (median min – max)	20 (5 - 60)	20 (5 - 60)	20 (5 - 60)	0.009**
Years of smoking (median min – max)	24.5 (1 - 56)	21 (2 - 50)	33 (1 - 56)	0.620**
Do you contemplate quitting? N (%) (3 missing)				
No	92 (59.0)	28 (60.9)	63 (58.9)	
I plan to stop in the next 6 months	53 (34.0)	15 (32.6)	36 (33.6)	0.964*
Did you ever try quitting? N (%) (1 missing)				
Yes	103 (65.2)	28 (59.6)	72 (66.7)	
No	55 (34.8)	19 (40.4)	36 (33.3)	0.396*
Alcohol drinking? N (%) (8 missing)				
Yes	205 (75.1)	51 (54.3)	147 (86.0)	
No	68 (24.9)	43 (45.7)	24 (14.0)	< 0.001*
How many units a week? N (%)				
< 7 units a week	57 (26.4)	23 (41.8)	32 (20.8)	
7-14 units a week	68 (31.5)	18 (32.7)	47 (30.5)	0.002*
> 14 units a week	91 (42.1)	14 (25.5)	75 (48.7)	
Did you ever think you need to reduce drinking? N (%)				
Yes	195 (87.8)	41 (75.9)	147 (91.3)	
No	27 (12.2)	13 (24.1)	14 (8.7)	0.003*
Did other people ever criticize your drinking? N (%)				
Yes	154 (70.3)	29 (54.7)	121 (76.1)	
No	65 (29.7)	24 (45.3)	38 (23.9)	0.003*
Did you ever feel guilty about your drinking? N (%)				
Yes	190 (84.8)	42 (75.0)	141 (87.6)	
No	34 (15.2)	14 (25.0)	20 (12.4)	0.026*
Did you ever have to drink in the morning to calm down or ease hangover? N (%)				
Yes	130 (57.3)	21 (36.8)	103 (63.2)	
No	97 (42.7)	36 (63.2)	60 (36.8)	< 0.001*

*chi-square test; **Mann-Whitney test

Table 4. Knowledge about oral cancer and perceived risk

	Yes	No	Don't know / Unsure	Differences among the sexes (p)	Differences in education (p)
Did you ever hear about oral cancer before? N (%)	208 (77.3)	45 (16.7)	16 (5.9)	0.009*	0.620*
Did you ever hear about oral cancer screening before? N (%)	126 (45.3)	127 (45.7)	25 (9.0)	0.025*	0.357*
Did you ever attend oral cancer screening before? N (%)	30 (10.2)	242 (86.7)	7 (2.5)	0.006*	0.047*
Which of the following increases risk of oral cancer? N (%)					
Smoking	251 (90.9)	6 (2.2)	19 (6.9)	0.196*	0.292*
Regular drinking	237 (86.5)	16 (5.8)	21 (7.7)	0.280*	0.401*
Eating spicy foods	121 (44.5)	72 (26.5)	79 (29.0)	0.851*	0.332*
Chronic mechanic trauma	107 (38.9)	60 (21.8)	108 (39.3)	0.006*	0.007*

*chi-square test; **Mann-Whitney test; ***Kruskal Wallis test

females. However, there was a significant difference in the proportion of smokers and non-smokers among different education groups as non-smokers had higher education levels ($p = 0.041$). There was a slight statistical significance indicating a trend where, with an increase in the level of education, participants smoke less ($p = 0.042$). Men smoked more cigarettes daily ($p = 0.002$), and there was a mild difference between genders, indicating that men have smoked more cigarette packs in their lifetime (pack in life; $p = 0.042$). Males reported a significantly higher rate of alcohol consumption than females ($p < 0.001$, chi-square test). Among participants who consumed alcohol, there were no significant differ-

ences in the number of drinks per week among various education groups. However, a significant difference was observed between males and females with males drinking more units per week ($p = 0.002$). Furthermore, men were more frequently irritated by others criticizing their drinking ($p = 0.003$), more often felt guilty about drinking ($p = 0.026$), and more frequently needed to have a drink in the morning to alleviate hangovers ($p < 0.001$).

Tables 4-7 provide information on participants' knowledge about OC (OC) and their perception of its risk. The majority of participants (208 or 77.3 %) had heard of OC but only 126 (45.3 %) heard about OC screening before. The majority of participants had not

Table 5. Attitudes towards oral cancer prevalence and mortality

	Lowest of all cancers	Lower than other cancers	Equal to other cancers	Higher than other cancers	Highest of all cancers	Differences among the sexes (p*)	Differences in education (p*)
Oral cancer prevalence compared to other cancers (lung, breast, colon, prostate) N (%)	30 (10.8)	105 (37.9)	108 (42.6)	22 (7.9)	2 (0.7)	0.835*	0.444*
Oral cancer mortality compared to other cancers (lung, breast, colon, prostate) N (%)	32 (11.6)	109 (39.4)	98 (35.4)	30 (10.8)	8 (2.9)	0.772*	0.524*

Table 6. Attitudes towards oral cancer overall mortality

	< 5%	6-25%	26-50%	51-75%	76-100%	Differences among the sexes (p*)	Differences in education (p*)
Overall oral cancer mortality N (%)	38 (13.8)	96 (34.9)	84 (30.5)	46 (16.7)	11 (4.0)	0.268*	0.468*

previously attended OC screening (242 or 86.7 %). There was a significant difference between males and females, as female participants were more likely to hear about OC ($p = 0.009$), OC screening ($p = 0.025$) or to attend OC screening before ($p = 0.006$). Furthermore, there was a slight difference among participants with different education levels, as participants with higher education levels more frequently attended OC screening ($p = 0.047$).

A significant number of participants (251 or 90.9 %) recognized smoking as a risk factor for OC, but fewer provided correct answers about other risk factors. There was a significant difference found between males and females or among participants with different education levels in terms of this knowledge regarding chronic mechanical trauma, as the majority of women ($p = 0.006$)

and more educated participants ($p = 0.007$) considered it as a risk factor for OC, while most men responded with “don’t know / not sure” (40.6 %). However, there were no statistical differences among education levels of participants about OC prevalence and mortality as most of them considered it equal or lower than other cancers.

Women more frequently visited dentists for regular check-ups ($p = 0.017$), and there was also a trend where, with an increase in the level of education, visits to the dentist were more regular/frequent ($p = 0.015$). Most participants believed that their risk of developing OC was similar to that of others of their age and gender. Smokers were more likely to estimate their OC risk as lower compared to non-smokers of their age and gender. A significant difference was observed between

Table 7. Attitudes towards smoking as a predicting factor

	Significantly smaller than other people	Smaller than other people	Similar to other people	Higher than other people	Significantly higher than other people	Differences among the sexes (p*)	Differences in education (p*)
Compared to people of your age and sex, what is your chance of getting oral cancer? N (%)	30 (10.8)	53 (19.1)	127 (45.7)	55 (19.8)	13 (4.7)	0.680*	0.300*
Smokers only							
Compared to smokers of your age and sex, what is your chance of getting oral cancer? N (%)	4 (2.6)	17 (11.0)	91 (58.7)	34 (21.9)	9 (5.8)	0.215*	0.103*
Compared to non-smokers of your age and sex, what is your chance of getting oral cancer? N (%)	8 (5.2)	16 (10.4)	53 (34.4)	46 (29.9)	31 (20.1)	0.029*	0.661*

*chi-square test

males and females as more women consider that non-smokers of their age and sex have higher OC risk ($p = 0.029$). On the other hand, no statistical difference was present among participants with different education levels in this regard. 80.9% of participants want to learn more about OC.

Statistically significant difference in sex ($p < 0.001$), age ($p < 0.001$), and education ($p = 0.009$) was found between the experimental ($N = 190$; 67.6 %) and control ($N = 91$; 32.4 %) group. The experimental group has more men, the control group had very few participants under 50 years old, and the distribution of education, while not statistically significant in terms of difference, showed a similar trend. More participants in the experimental group have lower education levels (mostly middle and high school education, followed by elementary vocational education). A statistically significant difference was also observed in employment ($p < 0.001$) with more employed and unemployed individuals in the experimental group, while more retired persons were found in the control group. Additionally, higher proportion of smokers was found in the experimental group ($p < 0.001$). Among smokers in the experimental and control groups, there was a significant difference, with those in the experimental group smoking more cigarettes daily ($p = 0.003$) and for a longer time ($p = 0.003$). For all questions related to alcohol (Yes/No, number of units of alcohol per week, thoughts about reducing alcohol consumption, criticism of drinking, guilt feelings, drinking in the morning to reduce/alleviate hangovers), there was a significant difference ($p < 0.001$), which is, in fact, the distinguishing criterion between these two groups (treated alcohol drinkers and the control group). There was no significant difference between the groups in attitudes about the frequency of oral cavity cancer compared to other cancers, but there was a difference in attitudes about the mortality of oral cavity cancer compared to other cancers, with participants in the experimental group generally believing that oral cavity related mortality was similar to other cancers, while the control group considered OC more serious ($p < 0.001$). For questions "Have you ever heard of a screening for early detection of oral cancer?" and "Have you ever been screened for early detection of OC?" there was a significant difference in favor of the control group (both p values are $p = 0.012$). For spicy food, sun exposure, and chronic mechanical irritation as risk factors in the development of OC, there was a significant difference between the groups, with the control group having a higher score for spicy food ($p = 0.029$), and the experimental group having higher scores for sun exposure and chronic mechanical irritation (both p values are $p < 0.001$). There was also a significant difference in the number of dental check-ups in favor of the control group, with as many as

70.4 % of participants in the experimental group visiting the dentist only when something bothered or hurt them ($p = 0.009$).

Discussion

Alcohol dependence is a multifactorial and multidimensional problem, and the association between alcoholism and comprehensive health issues has long been well-documented [52-56]. The oral mucosa and hard dental tissues are directly exposed to the harmful effects of alcohol [57].

Numerous socioepidemiological studies have shown the considerable impact of sociobehavioral and environmental factors on oral health and disease [58]. Primary risk factors encompass unhealthy lifestyles, including inadequate diet, nutrition, dental hygiene, and the consumption of tobacco and alcohol. Additionally, limited access to oral healthcare and inadequate living conditions further contribute to these issues [59]. Our findings indicate that a significant portion of patients in the EG had a lower level of education compared to the CG. This underscores the well-established fact that individuals with higher levels of education tend to prioritize their health more and engage in preventive checkups more regularly. Additionally, participants with higher educational attainment were found to be less likely to smoke, with a statistically significant difference in the proportion of smokers between the two groups, with the EG showing a higher prevalence (72.5 % vs. 24.4 %). This observation confirms the established association between alcohol consumption and smoking.

The interplay between alcohol and cigarettes is particularly noteworthy when aiming for abstinence from either substance. Studies suggest that individuals who are smokers and become alcohol-dependent have a higher likelihood of successfully completing alcoholism treatment. However, it is consistently documented that alcohol consumption can trigger a relapse in smoking behavior [60].

Concerning alcohol consumption, our findings reveal significant variations based on gender and educational attainment. To enhance early detection and treatment of OC, future screening initiatives should be more proactive and focused on high-risk populations. Our results demonstrate that men consumed alcohol more frequently than women, and individuals with lower levels of education had higher alcohol consumption rates compared to those with higher educational backgrounds. However, it's worth noting that a study conducted in 2022 by Andabak Roguljand and associates reported contrasting findings regarding education levels [51]. Patients in the EG belong to a high-risk category for OC development,

which may also be indicative of a propensity for riskier health behaviors, including reduced health awareness and less frequent medical visits [61]. Research consistently confirms that poor oral hygiene practices and infrequent dental check-ups increase the risk of developing head and neck cancers, including OC [39,62]. Moreover, it is less probable that individuals in the high-risk category for head and neck cancer development will proactively seek preventive screenings. This, in part, could account for our findings indicating a lower likelihood of early OC detection. Furthermore, our results indicate that general dentists are not routinely conducting preventive screenings for early OC detection in patients undergoing regular dental check-ups, including those in the high-risk group. These findings are not exclusive to the Republic of Croatia and are consistent with research conducted in the United States, Japan, Australia, and Spain [21-24]. In addition, Sankarharayanah and associates conducted research to assess the effectiveness of screening in reducing OC mortality [42]. They studied a total of 29,102 individuals who received annual exams over a period of three years. During these screenings, 5,145 lesions were identified, and 63 % of them were subsequently subjected to further testing. The researchers concluded that cancer screening has the potential to prevent up to 37,000 deaths annually in India, indicating that it could become a widespread practice. Moreover, a dose-response study unveiled a direct relationship between increasing daily alcohol consumption and a heightened risk of death from upper aerodigestive tract cancer. Specifically, when alcohol consumption reached a moderate-to-heavy level, study conducted by Li and associates demonstrated a positive correlation between alcohol intake and mortality from upper aerodigestive tract cancer [49]. It is often observed that individuals grappling with alcoholism tend to deny existing health issues and avoid medical examinations, be they preventive or routine. Cheung and associates demonstrated, in a comprehensive study spanning 9 years of follow-up, that those individuals at the highest risk for OC benefited the most from OC screening [48]. Our research findings reveal that the majority of screening participants neither currently smoke nor have a history of smoking, and they also abstain from alcohol consumption (as shown in Table 2). This places them outside the high-risk groups for OC. Participants in the experimental group also tend to visit the dentist less frequently, typically only when necessary. In contrast to our findings, a study by Akinkugbe and associates indicated that individuals who were current alcohol users in the past year were more likely to have seen a dentist [63]. This same study also suggested a reduced likelihood of OC early detection examinations among current alcohol users compared to former users, which aligns with the results of our research. In our study, it is evident that

the majority of patients in the EG only seek dental care when they have a pressing need. Additionally, patients often prove challenging to treat due to their non-compliance with treatment plans and instructions.

Moreover, a significant portion of patients also experience dental anxiety, and some may fear potential stigmatization by healthcare providers due to their underlying health conditions [64,65]. Alcohol problems are among the most stigmatized of conditions, and this stigma leads to numerous additional harms for individuals with alcohol use disorder. Alcohol stigma encompasses widely accepted negative stereotypes, which in turn result in prejudice and discrimination against people with alcohol use disorder. Moreover, self-stigma exacerbates the harm by inhibiting and undermining the process of recovery for affected individuals [66]. These factors collectively contribute to the observed pattern of infrequent dental visits among the study participants [67]. In terms of opinions regarding the prevalence of oral cavity cancer compared to other malignancies, our data indicate that there was no significant difference between the groups when considering education levels. However, our findings show that patients in the EG, who generally had lower levels of education compared to participants in the CG, expressed the belief of more frequent mortality compared to other cancer patients. This result aligns with the findings reported by Andabak Rogulj and associates, supporting the notion that individuals with lower educational attainment may have a heightened perception of mortality of OC relative to other cancer types [51,68,69]. The majority of participants, as indicated in Tables 4-7, demonstrated awareness that risk factors for OC include regular alcohol consumption and smoking. This suggests that one's perception of the seriousness of OC is significantly influenced by their level of education. A study by Joseph and associates also found a highly significant variation in understanding OC symptoms and indicators based on education levels, which is consistent with our own findings [70]. They observed a noteworthy gender disparity as well, with women exhibiting greater knowledge about OC.

In our present study, more women than men had undergone the same early OC diagnosis examinations and were aware of them ($p = 0.018$ and $p = 0.016$, respectively). Similar findings were noted by Reddy and associates, while study conducted by Andabak Rogulj and associates reported no gender differences in participants' understanding of OC [51,71].

Our findings indicate a relatively lower rate, with 22.8 % of participants from both groups reporting that they had not heard of OC or were unsure about their knowledge of it. In contrast, a recent study from Nepal reported a higher percentage, with 41.80 % of patients indicating that they had not heard of OC [50]. These variations

in awareness levels could be influenced by factors such as geographical location, access to healthcare information, and cultural differences among the study populations. The majority of participants in the CG, who had higher levels of education, had previously undergone oral examinations, whereas none of the EG participants had. This observation supports the notion that individuals with greater levels of education are more inclined to seek out preventive examinations.

To reduce the overall incidence of OC in the future, recommendations from Nagao and Warnakulasuriya suggest that OC screening should focus on high-risk groups and include education about risk habits [47]. Furthermore, we would like to highlight that during oral screening of CG, 5 potentially malignant oral disorders, 2 suspicious lesions indicative of OC, and 1 suspicious lesion suggestive of oral melanoma were identified. In contrast, within the EG, 11 suspicious potentially malignant oral disorders were observed, but the compliance rate among EG patients was 0 %. This lack of compliance could be attributed to the factors mentioned earlier, including lower levels of education compared to CG and possible stigmatization regarding oral health issues. A study conducted in 2011 by O'Sullivan and associates in Southern Ireland among residents of an addiction treatment center identified four red areas that raised suspicion of erythroplakia and two leukoplakic lesions [72]. Despite a relatively low follow-up compliance rate (33 %), two potentially malignant lesions were confirmed within the main study group, resulting in a detection rate of 0.9 %. These findings suggest that implementing an OC screening program targeted at individuals in addiction treatment centers may offer a practical approach to reaching individuals with a history of tobacco and alcohol abuse, both within this specific population and the general population. Additionally, reducing or eliminating risk factors is crucial. For instance, reducing tar concentration in cigarettes, cigars, pipes, and chewing tobacco, as well as eliminating nitrosamines (particularly from smokeless tobacco), could lower risks for individuals who continue to use tobacco. Managing chronic alcoholism is more challenging, but nutritional supplements, especially those containing proteins, minerals, and trace metals, can help mitigate the promotional effects of alcohol.

It's essential for clinicians to have a thorough understanding of all known risk factors for the prevention, early detection, and control of OC. When assessing patients, clinicians should take a detailed history regarding exposure to drugs, alcohol, actinic radiation, and other substances. This should include details such as the age at initial exposure or habit initiation, the duration of exposure or habit (in years), the quantity of tobacco smoked, chewed, or snuffed, and the relationship to the anatomic

site at risk. Similar attention should be given to assessing alcohol exposure. Habits and customs can vary significantly from place to place and from person to person, so dentists and doctors should consider these specific variables when examining patients [73]. Moreover, oral health care providers should receive training in OC prevention services, including tobacco-use cessation and alcohol-abuse counseling and be encouraged to incorporate these services as standard components of oral health care [74]. Based on everything stated, it is crucial to emphasize that OC represents a serious global health challenge, and the role of dentists in its prevention, diagnosis, and treatment is of invaluable importance.

Education of dentists regarding OC plays a key role in ensuring early detection and providing appropriate care to patients. Regardless of their level of experience and skills, regular and comprehensive education is essential to equip dentists with the ability to recognize early signs of OC, make accurate diagnoses, and effectively communicate with patients about risks and treatment needs [75]. The organization of congresses and public health initiatives, such as the Croatian Oral Cancer Week and "Student Congress: The story behind Oral cancer – familiarize and recognize!", plays a significant role in bringing together experts in the field of dentistry and other specialists involved in the treatment of OC. Congresses provide a platform for the exchange of the latest scientific knowledge, sharing of experiences, and establishment of collaboration among experts. For example, "Student Congress: The story behind Oral cancer– familiarize and recognize!" directs medical and dental students' attention to the importance of recognizing and responding correctly to OC. This event allows students to gain a deeper understanding of the disease, its causes, and treatment methods, encouraging them to actively participate in prevention and awareness efforts. It is also important to mention the challenge faced by general practitioners who often have patients who have been treated for alcoholism and smoke, putting them at a particularly high risk of OC. However, due to the fear of stigma or fear of rejection, patients often do not share their history of addiction with dentists [54]. This underscores the importance of sensitizing dentists to this issue and creating an open, supportive environment where patients can freely discuss their addiction history.

Incorporating dentists into multidisciplinary teams for addiction treatment reflects a modern approach to medicine. Dentists are crucial team members as they can provide valuable insights into recognizing physical signs of addiction, such as changes in oral health. Additionally, involving dentists in therapeutic communities for addiction treatment enables them to provide education to patients and their families about the connection between oral health and addiction, thus promoting aware-

ness of the risks. Finally, comprehensive education of dentists about OC, the organization of congresses like “Student Congress: The story behind Oral cancer – familiarize and recognize!”, and the inclusion of dentists in multidisciplinary teams and therapeutic communities for addiction treatment play a pivotal role in prevention, early detection, and a holistic approach to patients. All of these initiatives together contribute to improving healthcare and raising awareness about the importance of oral health and OC prevention.

Conclusion

There is a clear connection between alcohol and development of carcinoma, especially if tobacco products are used together with extensive drinking. The cumulative effect of alcohol drinking and smoking of tobacco

multiplies the risk of oral carcinoma. Enhanced educational approaches regarding OC and its associated risk factors are imperative for bolstering efforts in prevention, early detection, and treatment. Moreover, there is a crucial need to emphasize the significance of regular screening examinations, especially within populations at a heightened risk of developing this disease.

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Conflict of Interest

None to declare.

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References

- Ivoš A, Matošić A, Gradiški IP, Orlović I. The effects of alcohol on oral health, a review. *Arch Psychiatry Res*. 2019;55:61-70.
- Brezovec E. Consumption of alcohol in Croatian social reality alcohol as part of interaction ritual chain. *Alcohol Psychiatry Res*. 2017;53:139-46.
- Araujo MWB, Dermen K, Connors G, Ciancio S. Oral and dental health among inpatients in treatment for alcohol use disorders: a pilot study. *J Int Acad Periodontol* 2004;6:125–30.
- Priyanka K, Sudhir KM, Reddy VCS, Kumar RVSK, Srinivasulu G. Impact of alcohol dependency on oral health - a cross-sectional comparative study. *J Clin Diagn Res*. 2017;11:ZC43–6.
- Franceschi S, Talamini R, Barra S, Barón AE, Negri E, Bidoli E, et al. Smoking and drinking in relation to cancers of the oral cavity, pharynx, larynx, and esophagus in northern Italy. *Cancer Res*. 1990;50:6502–7.
- Maserejian NN, Joshipura KJ, Rosner BA, Giovannucci E, Zavras AI. Prospective study of alcohol consumption and risk of oral premalignant lesions in men. *Cancer Epidemiol Biomark Prev*. 2006;15:774–81.
- Llewellyn CD, Johnson NW, Warnakulasuriya KA. Risk factors for squamous cell carcinoma of the oral cavity in young people-a comprehensive literature review. *Oral Oncol* 2001;37:401–18.
- Kumar M, Nanavati R, Modi TG, Dobarica C. Oral cancer: etiology and risk factors: a review. *J Cancer Res Ther*. 2016;12:458-63.
- Abati S, Bramati C, Bondi S, Lissoni A, Trimarchi M. Oral cancer and precancer: a narrative review on the relevance of early diagnosis. *Int J Environ Res Public Health*. 2020;17:9160.
- Ligier K, Belot A, Launoy G, Velten M, Bossard N, Iwaz J, et al. Descriptive epidemiology of upper aerodigestive tract cancers in France: incidence over 1980-2005 and projection to 2010. *Oral Oncol*. 2011;47:302-7.
- Fu JY, Wu CX, Zhang CP, Gao J, Luo JF, Shen SK, et al. Oral Cancer incidence in Shanghai – a temporal trend analysis from 2003 to 2012. *BMC Cancer*. 2018;18:686.
- American Cancer Society. Key Statistics for Oral Cavity and Oropharyngeal Cancers [Internet]. Atlanta (US): American Cancer Society; 2021 [updated 2021; cited 2023 Oct 20]. Available from: <https://www.cancer.org/cancer/types/oral-cavity-and-oropharyngeal-cancer/about/key-statistics.html>
- Cancer Research UK. Head and neck cancers incidence statistics [Internet]. London (UK): Cancer Research UK; 2022 [updated 2022; cited 2023 Oct 20]. Available from: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/head-and-neck-cancers/> incidence
- Hrvatski zavod za javno zdravstvo (HZJZ). Cancer incidence in Croatia 2018 [Internet]. Zagreb (HR): HZJZ; 2020 [updated 2020;cited 2023 Oct 20]. Available from: https://www.hzjz.hr/wp-content/uploads/2020/12/Bilten_2018_final.pdf
- Hrvatski zavod za javno zdravstvo (HZJZ). Izvješće o smrtnosti prema listi odabranih uzroka smrti u 2018 [Internet]. Zagreb (HR): HZJZ; 2024 [updated 2024; cited 2023 Oct 20]. Available from: https://www.hzjz.hr/wp-content/uploads/2020/01/Bilten_Umrli_2018-2.pdf
- Montero PH, Patel SG. Cancer of the oral cavity. *Surg Oncol Clin N Am*. 2015;24:491-508.
- Wong T, Wiesenfeld D. Oral Cancer. *Aust Dent J*. 2018;63:S91-S99.
- Chi AC, Day TA, Neville BW. Oral cavity and oropharyngeal squamous cell carcinoma - an update. *CA Cancer J Clin*. 2015;65:401-21.
- Rivera C. Essentials of oral cancer. *Int J Clin Exp Pathol*. 2015;8:11884-94.
- Mehrotra R, Gupta DK. Exciting new advances in oral cancer diagnosis: avenues to early detection. *Head Neck Oncol*. 2011;3:33.
- Gajendra S, Cruz GD, Kumar JV. Oral cancer prevention and early detection: knowledge, practices, and opinions of oral health care providers in New York State. *J Cancer Educ*. 2006;21:157-62.
- Haresaku S, Makino M, Sugiyama S, Naito T, Mariño RJ. Comparison of practices, knowledge, confidence, and attitude toward

- oral cancer among oral health professionals between Japan and Australia. *J Cancer Educ.* 2018;33:429-35.
23. López-Jornet P, Camacho-Alonso F. New barriers in oral cancer. Patient accessibility to dental examination—a pilot study. *Oral Oncol.* 2006;42:1022-5.
 24. Mariño R, Haresaku S, McGrath R, Bailey D, McCullough M, Musolino R, et al. Oral cancer screening practices of oral health professionals in Australia. *BMC Oral Health.* 2017;17:151.
 25. Rogers SN, Vedpathak SV, Lowe D. Reasons for delayed presentation in oral and oropharyngeal cancer: the patients perspective. *Br J Oral Maxillofac Surg.* 2011;49:349-53.
 26. Hollows P, McAndrew PG, Perini MG. Delays in the referral and treatment of oral squamous cell carcinoma. *Br Dent J.* 2000;188:262-5.
 27. Warnakulasuriya KA, Harris CK, Scarrott DM, Watt R, Gelbier S, Peters TJ et al. An alarming lack of public awareness towards oral cancer. *Br Dent J.* 1999;187:319-22.
 28. Hertrampf K, Wenz HJ, Koller M, Wiltfang J. Comparing dentist's and the public's awareness about oral cancer in a community-based study in Northern Germany. *J Craniomaxillofac Surg.* 2012;40:28-32.
 29. Luryi AL, Yarbrough WG, Niccolai LM, Roser S, Reed SG, Nathan CA, et al. Public awareness of head and neck cancers: a cross-sectional survey. *JAMA Otolaryngol Head Neck Surg.* 2014;140:639-46.
 30. Sharp L, McDevitt J, Carsin AE, Brown C, Comber H. Smoking at diagnosis is an independent prognostic factor for cancer-specific survival in head and neck cancer: findings from a large, population-based study. *Cancer Epidemiol Biomarkers Prev.* 2014;23:2579-90.
 31. Benson E, Li R, Eisele D, Fakhry C. The clinical impact of HPV tumor status upon head and neck squamous cell carcinomas. *Oral Oncol.* 2014;50:565-74.
 32. Sankaranarayanan R, Ramadas K, Amarasinghe H, Subramanian S, Johnson N. Oral Cancer: Prevention, Early Detection, and Treatment. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, ed. *Cancer: Disease Control Priorities, 3rd ed.* Washington (US): The International Bank for Reconstruction and Development/The World Bank; 2015.
 33. Mello FW, Melo G, Pasetto JJ, Silva CAB, Warnakulasuriya S, Rivero ERC. The synergistic effect of tobacco and alcohol consumption on oral squamous cell carcinoma: a systematic review and meta-analysis. *Clin Oral Investig.* 2019;23:2849-59.
 34. City of Hope. Double trouble: Tobacco and alcohol combine to elevate cancer risk [Internet]. Duarte (US): City of Hope; 2023 [updated; 2023; cited 2023 Sept 26]. Available from: <https://www.cancercenter.com/community/blog/2023/07/smoking-and-drinking-raise-cancer-risk>
 35. Liu H, Yu Z, Xu Z, Liu T, Liu W. A scientometric study of tobacco and alcohol use as risk factors for oral cavity health. *J Dental Sci.* 2023;18:1883-8.
 36. Paré A, Joly A. Oral cancer: Risk factors and management. *Presse Med.* 2017;46:320-30.
 37. Tranby EP, Heaton LJ, Tomar SL, Kelly AL, Fager GL, Backley M, et al. Oral Cancer Prevalence, Mortality, and Costs in Medicaid and Commercial Insurance Claims Data. *Cancer Epidemiol Biomarkers Prev.* 2022;31:1849-57.
 38. Johnson NW, Warnakulasuriya S, Gupta PC, Dimba E, Chindia M, Otoh EC, et al. Global oral health inequalities in incidence and outcomes for oral cancer: causes and solutions. *Adv Dent Res.* 2011;23:237-46.
 39. Gupta B, Bray F, Kumar N, Johnson NW. Associations between oral hygiene habits, diet, tobacco and alcohol and risk of oral cancer: a case-control study from India. *Cancer Epidemiol.* 2017;51:7-14.
 40. Warnakulasuriya S. Significant oral cancer risk associated with low socioeconomic status. *Evid Based Dent.* 2009;10:4-5.
 41. Saleh A, Kong YH, Haron N, Aripin SF, Vadiveloo M, Hussaini H, et al. Oral cancer screening in private dental practices in a developing country: opportunities and challenges. *Community Dent Oral Epidemiol.* 2017;45:112-9.
 42. Sankaranarayanan R, Ramadas K, Thomas G, Muwonge R, Thara S, Mathew B, et al. Trivandrum Oral Cancer Screening Study Group. Effect of screening on oral cancer mortality in Kerala, India: a cluster-randomised controlled trial. *Lancet.* 2005;365:1927-33.
 43. Boundouki G, Humphris G, Field A. Knowledge of oral cancer, distress and screening intentions: longer term effects of a patient information leaflet. *Patient Educ Couns.* 2004;53:71-7.
 44. Ribeiro MFA, Oliveira MCM, Leite AC, Bruzina FFB, Mendes PA, Grossmann SMC, et al. Assessment of screening programs as a strategy for early detection of oral cancer: a systematic review. *Oral Oncol.* 2022;130:105936.
 45. Sankaranarayanan R. Screening for cancer in low- and middle-income countries. *Ann Glob Health.* 2014;80:412-7.
 46. Speight PM, Palmer S, Morales DR, Downer MC, Smith DH, Henriksson M, et al. The cost of effectiveness of screening for oral cancer in primary care. *Health Technol Assess.* 2006;10:1-144.
 47. Nagao T, Warnakulasuriya S. Screening for oral cancer: future prospects, research and policy development for Asia. *Oral Oncol.* 2020;105:104632.
 48. Cheung LC, Ramadas K, Muwonge R, Kati HA, Thomas G, Graubard BI, et al. Risk-based selection of individuals for oral cancer screening. *J Clin Oncol.* 2021;39:663-74.
 49. Li Y, Mao Y, Zhang Y, Cai S, Chen G, Ding Y, et al. Alcohol drinking and upper aerodigestive tract cancer mortality: a systematic review and meta-analysis. *Oral Oncol.* 2014;50:269-75.
 50. Bajracharya D, Gupta S, Sapkota M, Bhatta S. Oral cancer knowledge and awareness in patients visiting Kantipur Dental College. *J Nepal Health Res Council.* 2018;15:247-251.
 51. Andabak Rogulj A, Škrinjar I, Glazar I, Muhvić Urek M, Alajbeg I, Vidović Juras D, et al. Oral cancer - knowledge and perception of the population in the screening program during world oral, head and neck cancer awareness week. *Med Flum.* 2022;58:132-41.
 52. Rehm J, Guiraud J, Poultnais R, Shield KD. Alcohol dependence and very high risk level of alcohol consumption: a life-threatening and debilitating disease. *Addict Biol.* 2018;23:961-8.
 53. McHugh RK, Weiss RD. Alcohol use disorder and depressive disorders. *Alcohol Res.* 2019;40:arcr.v40.1.01.
 54. Lasserre AM, Imtiaz S, Roerecke M, Heilig M, Probst C, Rehm J. Socioeconomic status, alcohol use disorders, and depression: a population-based study. *J Affect Disord.* 2022;301:331-6.
 55. Gallagher C, Radmall Z, O'Gara C, Burke T. Anxiety and depression among patients with alcohol dependence: co-morbid or substance-related problems? *Ir J Psychol Med.* 2018;35:121-6.
 56. Rudenstine S, Espinosa A, Kumar A. Depression and anxiety subgroups across alcohol use disorder and substance use in a National Epidemiologic Study. *J Dual Diagn.* 2020;16:299-311.
 57. Feng L, Wang L. Effects of alcohol on the morphological and structural changes in oral mucosa. *Pak J Med Sci.* 2013;29:1046-9.
 58. Petersen PE, Bourgeois D, Ogawa H, Estupinan-Day S, Ndiaye C. The global burden of oral diseases and risks to oral health. *Bull World Health Organ.* 2005;83:661-9.
 59. Rehm J, Shield KD. Alcohol use and cancer in the European Union. *Eur Addict Res.* 2021;27:1-8.
 60. Shiffman S, Balabanis M. Do Drinking and smoking go together? *Alcohol Health Res World.* 1996;20:107-10.
 61. Nemoto RP, Victorino AA, Pessoa GB, da Cunha LLG, da Silva JAR, Kanda JL, et al. Oral cancer preventive campaigns: are we reaching the real target? *Braz J Otorhinolaryngol.* 2015;81:44-9.
 62. Divaris K, Olshan AF, Smith J, Bell ME, Weissler MC, Funkhouser WK, et al. Oral health and risk for head and neck squamous

- cell carcinoma: the Carolina Head and Neck Cancer Study. *Cancer Causes Control*. 2010;21:567-75.
63. Akinkugbe AA, Garcia DT, Brickhouse TH, Mosavel M. Lifestyle risk factor related disparities in oral cancer examination in the U.S: a population-based cross-sectional study. *BMC Public Health*. 2020;20:153.
 64. Shannon CL, Bartels SM, Cepeda M, Castro S, Cubillos L, Suárez-Obando F, et al. Perspectives on the implementation of screening and treatment for depression and alcohol use disorder in primary care in Colombia. *Community Ment Health J*. 2021;57:1579-87.
 65. Rundle SM, Cunningham JA, Hendershot CS. Implications of addiction diagnosis and addiction beliefs for public stigma: a cross-national experimental study. *Drug Alcohol Rev*. 2021;40:842-6.
 66. Morris J, Schomerus G. Why stigma matters in addressing alcohol harm. *Drug Alcohol Rev*. 2023;42:1264-8.
 67. Cuberos M, Chatah EM, Baquerizo HZ, Weinstein G. Dental management of patients with substance use disorder. *Clin Dent Rev*. 2020;4:14.
 68. Scoccianti C, Cecchini M, Anderson AS, Berrino F, Boutron-Ruault MC, Espina C, et al. European code against cancer 4th edition: Alcohol drinking and cancer. *Cancer Epidemiol*. 2016;45:181-8.
 69. Saieva C, Bardazzi G, Masala G, Quartini A, Ceroti M, Iozzi A, et al. General and cancer mortality in a large cohort of Italian alcoholics. *Alcohol Clin Exp Res*. 2012;36:342-50.
 70. Joseph BK, Ali MA, Sundaram DB. Awareness of mouth cancer among adult dental patients attending the Kuwait University Dental School Clinic. *J Cancer Educ*. 2018;33:340-5.
 71. Reddy BS, Doshi D, Reddy MP, Kulkarni S, Gaffar A, Reddy VR. Oral cancer awareness and knowledge among dental patients in South India. *J Craniomaxillofac Surg*. 2012;40:521-4.
 72. O'Sullivan EM. Prevalence of oral mucosal abnormalities in addiction treatment centre residents in Southern Ireland. *Oral Oncol*. 2011;47:395-9.
 73. Baden E. Prevention of cancer of the oral cavity and pharynx. *CA Cancer J Clin*. 1987;37:49-62.
 74. Cruz GD, Ostroff JS, Kumar JV, Gajendra S. Preventing and detecting oral cancer. Oral health care providers' readiness to provide health behavior counseling and oral cancer examinations. *J Am Dent Assoc*. 2005;136:594-601.
 75. Al-Dhahli Z, Al-Sheibani SM, Al-Kalbani F, Hyder J. Outcomes of the National Head and Neck Cancer Awareness and Screening Campaign in Oman. *Sultan Qaboos Univ Med J*. 2020;20:e173-e178.