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# ORAL CANCER IN SUB-SAHARAN AFRICA - COMPREHENSIVE LITERATURE REVIEW

[Cancro Oral na Africa Subsaariana – Revisão abrangente da literatura]

Dissertação de Mestrado

(Mestrado Integrado em Medicina Dentária)

Leonilsa Lucrecia Sungo Pitra

Orientador:

Doutor Lúcio Lara Santos

Setembro 2025







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To my dear parents, Estevão and Glória, for their unconditional love, for believing in me even when I doubted myself, for their prayers, support, sacrifice, and for being an example of perseverance that always gave me the strength to keep going.

To my siblings, also an example and guidance in my life, thank you for believing in me and never giving up on me “Family, family, family.”

To my nieces and nephews, for all the affection, strength, and joy you add to my life.

To my friends (Hugo, Tírcia, Lucrecio) for the support, concern, and care during difficult times.

Porque dEle e por Ele, e para Ele, são todas as coisas; glória, pois, a Ele eternamente.

Amém



## RESUMO

África Subsaariana é uma região vasta e culturalmente diversa que enfrenta desafios socioeconômicos, políticos e de saúde significativos. Apesar dos avanços em tecnologia e educação, muitos países da região lutam contra a pobreza e a instabilidade política. A região também é fortemente impactada por doenças como o VIH/SIDA. O cancro, incluindo o cancro oral, é uma preocupação crescente de saúde, com mortes relacionadas com o cancro desproporcionalmente concentradas em países de baixo e médio rendimento socioeconómico. Estima-se que a carga de cancro nestes países duplique até 2040. O cancro oral é uma doença debilitante e desfiguradora, com mais de 175.000 casos diagnosticados globalmente a cada ano. Embora seja o 16º cancro mais comum a nível mundial, prevê-se que a sua incidência duplique até 2040. Na África Subsaariana, o cancro da cabeça e pescoço é o quinto tipo de cancro mais comum. Um desafio significativo na região é a limitada consciência sobre o cancro e o acesso escasso a cuidados oncológicos especializados. Isso leva frequentemente a diagnósticos tardios, quando as opções de tratamento já são reduzidas, contribuindo para uma alta morbidade e baixas taxas de sobrevivência. Enfrentar doenças não transmissíveis como o cancro está a tornar-se uma preocupação médica cada vez mais urgente na região.

O presente trabalho visa fornecer uma visão abrangente sobre o cancro oral na África Subsaariana, destacando a sua epidemiologia, fatores de risco, desafios no diagnóstico e tratamento, bem como estratégias propostas para melhoria, baseando-se na literatura científica mais recente.

**Palavras-chave:** “Cancro Oral”, “África Subsaariana”, “Cancro de Cabeça e Pescoço”, “carcinoma oral espinocelular”, “diagnóstico e tratamento”



## **ABSTRACT**

Sub-Saharan Africa is a vast and culturally diverse region facing significant socioeconomic political and health challenges. Despite advancements in technology and education, many countries in the region struggle with poverty and political instability. The region is also heavily impacted by diseases like HIV/AIDS. Cancer, including oral cancer, is an increasing health concern, with cancer-related deaths disproportionately concentrated in low and medium socioeconomic status countries. The cancer burden in these countries is projected to double by 2040. Oral cancer is a debilitating and disfiguring disease, with over 175,000 cases diagnosed globally each year. While it is the 16<sup>th</sup> most common cancer worldwide its incidence it's expected to double by 2040. In Sub-Saharan Africa head and neck cancer is the fifth most common cancer. A significant challenge in this region is the limited awareness of cancer and scarce access to specialized oncological care, this often leads to late diagnoses when treatment options are limited, contributing to high morbidity and low survival rates. Addressing non-communicable diseases like cancer is becoming an increasingly urgent medical concern in the region.

This present work aims to provide a comprehensive overview of Oral Cancer in Sub-Saharan Africa, highlighting its epidemiology, risk factors, challenges in diagnosis and treatment, and proposed strategies for improvement, drawing upon recent scientific literature.

**Keywords:** “Oral Cancer”, “Sub-Saharan Africa”, “Head and Neck Cancer”, “Oral squamous cell carcinoma”, “diagnosis and treatment”.



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## LIST OF ABBREVIATIONS

<b>5-FU</b>	5-Fluorouracil
<b>AC</b>	Actinic Cheilitis
<b>AIDS</b>	Acquired Immunodeficiency Syndrome
<b>CI</b>	Confidence Index
<b>DNA</b>	Deoxyribonucleic Acid
<b>EBV</b>	Epstein Barr Virus
<b>EP</b>	Erythroplakia
<b>GDP</b>	Gross Domestic Product
<b>HDI</b>	Human Development Index
<b>HIV</b>	Human Immunodeficiency Virus
<b>HNC</b>	Head and Neck Cancer
<b>HNSCC</b>	Head and Neck Squamous Cell Carcinoma
<b>HPV</b>	Human Papilloma Virus
<b>HR-HPV</b>	High-risk Human Papilloma Virus
<b>IARC</b>	International Agency for Cancer Research
<b>LP</b>	Leukoplakia
<b>n</b>	Number
<b>NNK</b>	4-(Methylnitrosamino)-1-(3-Pyridyl)-1- Butanone
<b>NNN</b>	N-Nitrosornicotine
<b>OC</b>	Oral Cancer
<b>OE</b>	Oral Erythroplakia
<b>OLP</b>	Oral Lichen Planus
<b>OPMD</b>	Oral Potentially Malignant Disorders
<b>OR</b>	Odds Ratio

<b>OSCC</b>	Oral Squamous Cell Carcinoma
<b>OSMF</b>	Oral Submucous Fibrosis
<b>PAH</b>	Polycyclic Aromatic Hydrocarbons
<b>PICO</b>	Population, Intervention, Comparison, and Outcome
<b>PRISMA</b>	Preferred Reporting Items for Systematic reviews and Meta-Analyses
<b>PVL</b>	Proliferative Verrucous Leukoplakia
<b>SCC</b>	Squamous Cell Carcinoma
<b>SD</b>	Standard Deviation
<b>UNAIDS</b>	The Joint United Nations Programme on HIV/AIDS
<b>USA</b>	United States of America
<b>UV</b>	Ultraviolet
<b>WHO</b>	World Health Organization
<b>YAG</b>	Yttrium Aluminium Garnet

## 1. INTRODUCTION

Sub-Saharan Africa is a vast region covering most of the African continent, located south of the Sahara Desert. With a rich cultural diversity, it is home to countless ethnicities, languages and traditions. This region is marked by a variety of landscapes, from savannah to lush tropical forests.

Despite its diversity, Sub-Saharan Africa faces significant challenges, including socioeconomic, political and health issues. Many countries in the region struggle with poverty, political instability and development challenges. The HIV/AIDS epidemic has also had a considerable impact on several nations, demanding global efforts to address this health crisis.

Over the years, Sub-Saharan Africa has witnessed remarkable advancements in sectors such as technology, education and entrepreneurship. Development initiatives aim to strengthen local economies, promote education and improve living conditions. The region's dynamic youth play a crucial role in these efforts, contributing to building a brighter future.

Despite its challenges, Sub-Saharan Africa is a vibrant and resilient region whose history and potential continue to inspire hope and positive change.

The approach to oral cancer in dentistry has a solid basis in scientific research and specialized literature. Several studies highlight the importance of early diagnosis and the role of dental professionals in detecting suspicious lesions (Mignogna et al., 2006; Warnakulasuriya, 2009; Epstein et al., 2012; Neville et al., 2015).

Oral squamous cell carcinoma is a potentially disfiguring and debilitating disease that affects patients' physical appearance and devastates their self-esteem. Globally, more than 175,000 cases are diagnosed annually (Parkin et al., 2005).

Many places with low-medium socioeconomic development conditions are in the early stages of optimizing oncological care: awareness about cancer is still limited and access to specialized oncological approaches is scarce (Atun et al., 2015; Brown et al., 2016). As such, many patients present with advanced-stage malignancies with limited treatment options at the time of late diagnosis (Anakwenze et al., 2018; Fidler et al., 2018).

Head and neck cancer is the fifth most common cancer in sub-Saharan Africa. In 2018,

approximately 30% of the 1.5 million newly diagnosed HNC cases worldwide occurred in countries with low-middle socioeconomic status (Bray et al., 2018). Access to many of these diagnostics, specialized oncological and supportive care resources remains limited in countries with low-middle socioeconomic status (McGinnis et al., 2021).

Addressing non-communicable diseases such as cancer is therefore an increasingly important medical concern. Thus, in sub-Saharan Africa, oral cancer is emerging as a significant health concern, with several factors contributing to its prevalence. The consumption of tobacco and alcohol, often rooted in cultural practices, is one of the main drivers of this type of cancer in the region. The lack of access to adequate healthcare is worsened by the scarcity of prevention programs and limited awareness of the risks associated with oral cancer.

More vulnerable communities face additional challenges, exacerbating health disparities. The lack of resources and adequate medical infrastructure makes early detection and effective treatment difficult. Furthermore, the absence of robust educational programs impedes the dissemination of information about healthy practices and warning signs of oral cancer.

To address this public health issue, it is crucial to implement comprehensive strategies. This includes culturally sensitive awareness campaigns, promotion of healthy practices, and easier access to health services, especially in low-income communities. Training local healthcare professionals for early identification and treatment is vital to improving patient outcomes.

This scientific text addresses the risk factors for the development of oral cancer, as well as the circumstances that determine the late diagnosis of oral cancer in sub-Saharan Africa.

## **1.1. Theoretical framework**

Epidemiological data shows that cancer is increasing worldwide. In 2018, there were an estimated 9.6 million cancer-related deaths, an increase of more than 60% since 1990 (Bray et al., 2018). Cancer-related deaths are already disproportionately concentrated in countries of low and medium socioeconomic status; and the cancer burden in these countries is estimated to double by 204. (Bray et al., 2018; Ferlay et al., 2018).

### **1.1.1. Sub-Saharan Africa**

Sub-Saharan Africa is, geographically, the area of the African continent that lies south of the Sahara. According to the United Nations, it consists of all African countries and territories that are fully or partially south of the Sahara and the following regions of Africa, such as Central Africa, Eastern Africa, Western Africa, and Southern Africa can be found under this designation (cf. Table 1). The population in sub-Saharan Africa is estimated at 1 093 988 381 inhabitants, of these 548 020 298 are female. (Sung et al., 2021) Sub-Saharan Africa has the lowest total gross domestic product (GDP) in the world, a measure of everything produced in any country or region. Its average GDP per capita, or the GDP divided by population, is just under 4,000 dollars, a fifth of the world average (World101, 2022).

Africans are susceptible to three big killer diseases in the continent: malaria, tuberculosis, and HIV/AIDS. However, with economic growth, westernization, HIV and increased life expectancy cancer incidence rates have increased. Therefore, the burden of Sub-Saharan Africa cancer related morbidity and mortality is rapidly increasing being expected to increase by 85% between 2008 and 2030, while annual deaths resulting from malaria, HIV and tuberculosis are continuously declining in the region (Faggons et al., 2015).

Alcohol and tobacco consumption have been historically associated with OSCC, although information about alcohol consumption patterns and the contribution of alcohol to health and social problems in African countries still need further studies, specific surveys show that high proportions of Africans do not drink, but those who do drink tend to drink heavily. In fact, some African countries have some of the world highest per capita alcohol consumption rates, especially when we include traditional beverages in the estimates (Obot, 2006).

Regarding to Tobacco consumption, it is known that smoking prevalence varies widely

across Sub-Saharan Africa, even between similar countries remaining uncommon in most of them. Low-and-middle income countries have experienced an increase of nearly 50% of tobacco consumption over the past few decades, as tobacco companies have invested heavily in cigarette marketing across the region aiming youth in particular. Eastern and Southern African regions showed high smoking rates, mainly among men in Ethiopia, Malawi, Rwanda, and Zambia and women in rural Rwanda and Zambia (Brathwaite et al., 2015; Faggons et al., 2015).

**Table 1.**

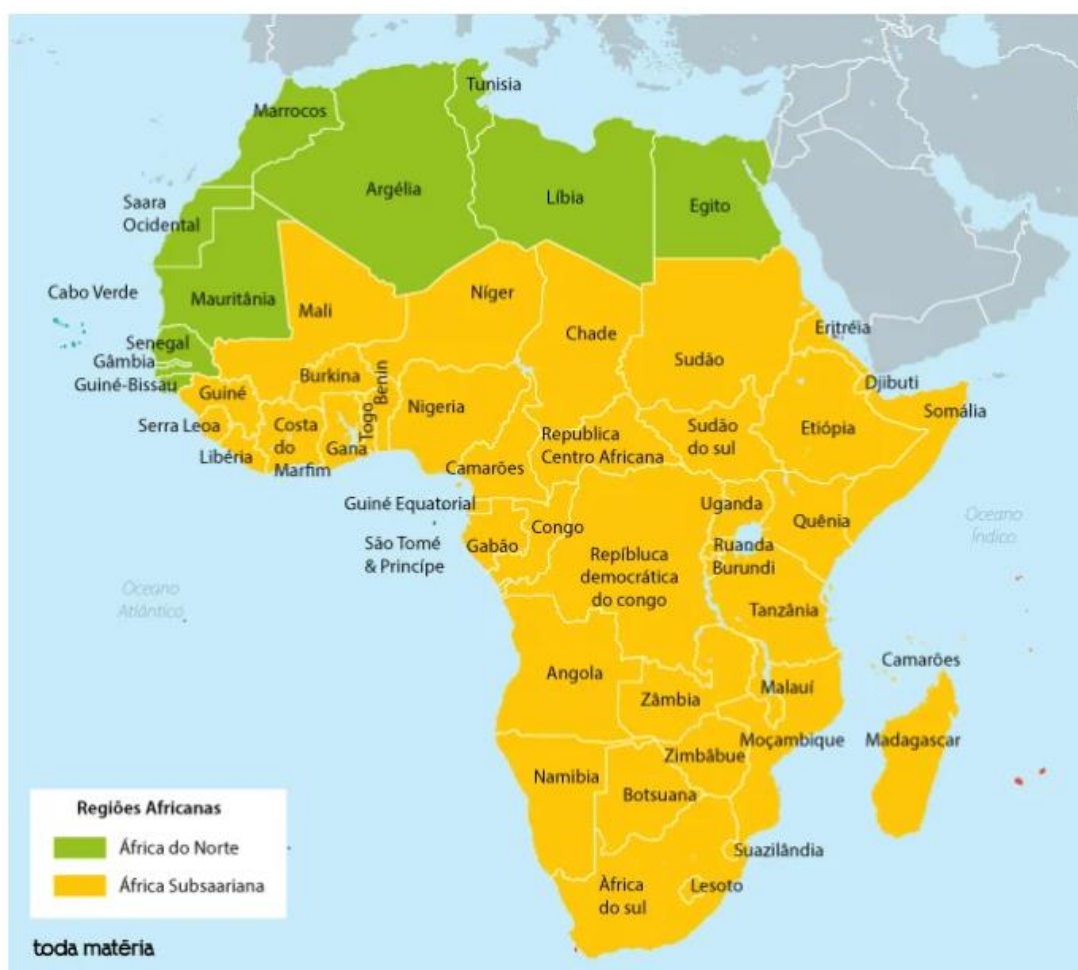
*List of Sub-Saharan African Countries*

<b>Sub-Saharan African countries</b>		
South Africa	Gabon	Nigeria
Angola	Gambia	Kenya
Benin	Ghana	Central African Republic Rwanda
Botswana	Guinea	Democratic Republic of Congo
Burkina Faso	Guinea Bissau	Sao Tome and Principe
Burundi	Comoros Islands	Senegal
Cameroon	Lesotho	Seychelles
Cape Green	Liberia	Sierra Leone
Chad	Madagascar	Somalia
Congo	Malawi	Southern Sudan
Costa do Marfim	Mali	Swaziland
Djibouti	Mauritania	Tanzania
Equatorial	Mauritius	Togo
Guinea	Mozambique	Uganda
Eritrea	Namibia	Zambia
Ethiopia	Niger	Zimbabwe

Although tobacco and alcohol consumption are well established risk factors, in Sub-Saharan Africa one third of cancers are directly associated with infectious agents. Despite the high prevalence of HPV infection in Africa, its impact on oral cancerization it is unknown (Faggons et al., 2017).

**Figure 1**

*Map of Africa: North Africa and Sub-Saharan Africa.*



Adaptado de “África Subsaariana” J. Bezerra, Toda Materia, 2025, 11/09. <https://www.todamateria.com.br/africa-subsaariana>. Copyright 2025 da autora.

Sub-Saharan Africa is the political-geographic term applied to describe the countries on the African continent located in the region south of the Sahara Desert (cf. Figure 1). It is one of the poorest regions in the world with high rates of infant mortality, illiteracy and low life expectancy. Data from the World Bank shows that Sub-Saharan Africa is the poorest region on the planet. At least 41% of the population, of more than 1.2 billion people, live in urban regions. Economic returns are very low and life expectancy at birth is 56 years (Bezerra, 2023).

27 of the 30 countries with the lowest Human Development Index (HDI) are located in Sub-Saharan Africa, meaning poverty is almost endemic (Bezerra, 2023).

### **1.1.2. Oral cancer: the current picture**

Oral cancer (OC), the 16th most common cancer worldwide, is a form of head and neck cancer that is defined, by the International Classification of Diseases as the “set of malignant tumors arising in any localization of the oral cavity, from the lips to throat (including the tonsils and pharynx)”. The most common topographic distribution for oral cancer development is the alveolar ridges, the floor of the mouth, the anterior two-thirds of the tongue and the soft palate (Montero & Patel, 2015).

Oral squamous cell carcinoma (OSCC) is the predominant (90-95%) histological type, developing from the stratified squamous epithelium and it is one of the most common cancer types, accounting for nearly 380.000 new cases diagnosed and 180.000 deaths every year, for both sexes, on a global scale (Elaiwy et al., 2020; World Health Organization, 2021). Moreover, a 58% increase in the diagnosed oral cancer cases was observed in the last decade and, according to data reported by the International Agency for Cancer Research (IARC), it is expected that these numbers will double by 2040 (Hook, 2021; Sung et al., 2021).

OC is more prevalent in developing countries and affects mostly men, with incidence and mortality ratios being 2,7 and 3.8, respectively. The incidence of OSCC is also directly correlated with age. Rates rise after the age of 40-49 years and reach a plateau around the age of 70-79 years (Rivera, 2015; Warnakulariya & Kerr, 2021). Nevertheless, in recent times, a change in trends of incidence and mortality has been observed due to changes in the adopted lifestyle, with an increasing incidence rate in developed countries and in women and younger individuals (Santos, 2011; Gupta et al., 2016).

The major etiological factors of OC are tobacco (either smoking or smokeless forms) and alcohol consumption, being present in 90% of the oral cancer patients and having synergic effects (Carp et al., 2022). However, other factors such as poor oral hygiene, dietary deficiencies, exposition to UV radiation, chronic inflammation and mechanical trauma, betel quid chewing, genetic predisposition, viral infections (mainly by HPV-16 and HPV-18 high-risk subtypes) and socioeconomic factors also play an important role in the development of OC (Santos, 2011). Given that most risk factors can be eliminated or reduced, OC is considered a preventable disease (Hook, 2021).

Usually, OC detection depends on the clinical examination followed by a biopsy for histological analysis. Although the oral cavity is easily accessible for clinical

examination, most cases of OC are not diagnosed until an advanced stage, which is believed to be the major reason for the low survival rate. The five-year survival rate for patients with stage I disease is about 80%, since it is easily curable through surgery, radiation and chemotherapy, whereas patients with advanced stages have little chance of receiving effective treatment, which is believed to contribute to the high morbidity and low survival rates, demonstrating the importance of the early detection of OC (Cheng et al., 2014; Wang et al., 2021).

In this scope, medical and dental professionals have a crucial role in patients' education for OC risk factors, in the early diagnosis of OC, as also in the detection and management of oral lesions that have an increased risk of malignant transformation, to improve the therapeutic interventions and the OC patients' outcome, and consequently, minimizing OC burden (Rivera, 2015; Hadzic et al., 2017).

### **1.1.3. Oral potentially malignant disorders: lesions of increased risk**

Most OC lesions are preceded by oral potentially malignant disorders (OPMD), a group of heterogeneous conditions and lesions of the oral epithelia that increase the risk of malignant transformation, compared to healthy mucosa (Ojeda et al., 2020). The term OPMD was established in 2007, after a consensus of an expert group meeting, coordinated by the World Health Organization Collaborating Centre for Oral Cancer, in which the previously adopted term "pre-malignant" was replaced by "potentially malignant", since these lesions not always lead to cancer development (Warnakulasuriya et al., 2007; Warnakulaasuriya, 2020).

According to a systematic review and meta-analysis performed by (Mello et al., 2018), the estimated incidence of OPMD is 4.50% (95% CI= 2.43 – 7.08), differing between world regions, and likewise OC, they are more commonly identified in male patients (59.99%). OPMD exhibit a wide range of clinical features, including color (white, red or red-white) and topographic changes (plaques, smooth, corrugated, verrucous, granular and atrophic), variable in size, and can cover any anatomical part of the mouth, with mono or multi foci (Speight et al., 2018).

Management of OPMD includes establishing a correct diagnosis (confirmed by a representative tissue biopsy for histological analysis), assessment of patients' risk factors and selection of appropriate therapeutic interventions. In most cases, regular follow-up

with an oral health professional is also required (Warnakulaasuriya, 2020).

The most common OPMD found in clinical practice are oral leukoplakia (LP), erythroplakia (EP), oral lichen planus (OLP), oral submucous fibrosis (OSMF) and actinic cheilitis (AC) (Bugshan & Farooq, 2020).

#### **1.1.3.1. Oral leukoplakia**

Oral leukoplakia is defined by WHO as “*any white lesion (plaque or patch) on the oral mucosa that cannot be rubbed off nor considered clinically or histologically as any other disease*”, and the diagnosis is made by excluding other disorders that are known to not increase the risk for cancer, such as candidiasis infection (Bugshan & Farooq, 2020; Warnakulariya & Kerr, 2021). LP is the most common and also the most studied OPMD. The reported prevalence of LP is 1-3%, with a higher incidence in men, occurring predominantly between the ages of 50-70 years. The most common sites where these lesions usually arise are the alveolar mucosa, followed by buccal mucosa, palate, tongue and floor of the mouth, either in a single or multiple presentations (Abatti et al., 2020; Iocca et al., 2020).

LP is mostly considered an idiopathic condition, however, as for OC, tobacco smoking has been considered the major risk factor for its development (Abatti et al., 2020). Interestingly, the use of areca nut, mostly common in Asia, is also considered a risk factor for the development of LP and OSCC (Hernandez et al., 2017). Histologically, nearly 40% of the LP cases show dysplastic features (from mild to severe) or OSCC, with a malignant transformation rate between 1.50-34%, depending on the homogeneity presentation (Villa & Woo, 2017; Wetzel & Wollenberg, 2020).

Proliferative verrucous leukoplakia (PVL) is a rare type of LP, with a verrucous or exophytic clinical presentation, but with a higher risk of malignant transformation (63.30-100%) and 85% recurrence after surgical excision (Abatti et al., 2020). In contrast to LP, PVL is more prevalent in elderly women, who lack a clinical history of tobacco or alcohol intake (Wetzel & Wollenberg, 2020).

To date, surgical excision and laser therapy are considered the most common treatment modalities for LP, however, further research is needed to determine more effective methodologies. Moreover, tobacco and alcohol cessation has been shown to efficiently reduce LP lesions (Waal, 2009). Since the estimated recurrence rates of LP are 42% (in

which 9% may transform into OSCC), a close follow-up of these patients is of great importance (Sunberg et al., 2019).

### **1.1.3.2. Oral erythroplakia**

Oral erythroplakia is defined by WHO as “a fiery red patch that is not characterized clinically or pathologically as any other definable disorder” and can arise in any site of the oral and oropharyngeal mucosa as a single lesion that as a demarcated flat erythematous area with a smooth or granular surface, being more common in the floor of the mouth, soft palate and ventral tongue (Warnakullasuriya et al., 2007). OE has an estimated prevalence of 0.02-0.83%, affects mainly middle-aged and elderly patients, of both sexes, and is, etiologically, associated with tobacco and alcohol consumption (Waal, 2009; Villa et al., 2011).

OE is considered the OPMD with the greatest potential for malignant development, with a malignant transformation rate of 33.10% (99% CI= 13.6 – 56.2) (Iocca et al., 2020). Histologically, OE commonly shows different grades of dysplasia, ranging from mild to severe. Interestingly, nearly 40% of the histological analyzes of OE lesions already correspond to carcinoma in situ (Ganesh et al., 2018).

Given the high risk of malignant transformation, a biopsy of any suspicious red lesion and prompt resection, particularly of those with severe dysplasia, are recommended, and a close follow-up is crucial, due to the possibility of recurrence of these lesions (Abatti et al., 2020).

### **1.1.3.3. Oral lichen planus**

Oral lichen planus is described as a chronic inflammatory condition with unknown etiology, associated with cell-mediated immunological dysfunction (Tsushima et al., 2021). This disorder is considered by the literature as an OPMD, however, there is some controversy about the malignant potential of OLP, which is reported to be 0.04-1.74% per year, mostly due to inconsistencies in the diagnostic criteria of the available studies. (Warnakullasuriya et al., 2007; Gonzalez-Moles et al., 2008).

It is estimated to affect from 0.5% to 2.2% of the population, with a higher incidence in middle-aged women (30 to 60 years) (Al-Hashimi et al., 2007). Clinical manifestations

are mostly bilateral and nearly symmetrical asymptomatic white lesions in the oral mucosa (tongue, lip or gingiva), varying between reticular, popular, plaque, ulcerative or bullous lesions. The reticular form is the most common presentation and is characterized by the presence of Wickham striae (McCartan & Healy, 2008; Warnakulariya & Kerr, 2021).

OLPs' treatment is more palliative rather than curative, to reduce inflammation and relieve symptoms. Topical corticosteroids are considered the first-line treatment, with systemic steroids being used in more severe cases (Maymone et al., 2019).

#### **1.1.3.4. Oral submucous fibrosis**

Oral submucous fibrosis is “a chronic, insidious and progressive fibrotic condition, characterized by epithelial immune-cell infiltration, followed by a fibro-elastic change in the lamina propria and submucosa”, that affects the oral cavity and, in moderate to severe cases, the oropharynx and the upper third of the esophagus (Rao et al., 2020; Kumari et al., 2022). Patients with this disorder experience a strong burning sensation, loss of tongue mobility, trismus, dysphagia and oral pain, depending on the severity of the disease (Ganesh et al., 2018).

According to the WHO data, globally, more than 5 million people present OSMF, being more common in the Asian population, particularly in Indians, where the incidence is estimated to be around 4.96% (Gupta & Jawanda, 2021). It is also commonly found in Indian populations living abroad, such as in the United Kingdom and South Africa. Moreover, in Indian populations, this disorder occurs more frequently in women, but it is not observed in other regions, where male individuals are still the most commonly affected, at an average age of 30 years (Shih et al., 2019).

OSMF has a malignant transformation rate of 5.2% (99% CI= 3.8 – 9.6), an annual progression to cancer of 0.98% (Iocca et al., 2020), and the most reported etiological factor is areca nut chewing. However, nutritional deficiencies, high consumption of spicy foods, autoimmunity and genetic/environmental factors are also related to OSMF development (Ganesh et al., 2018).

When OSMF is diagnosed before the development of trismus, cessation of areca nut chewing is often curative. Nevertheless, in more severe presentations of OSMF, it is already irreversible and medical/surgical approaches aim to preserve oral function and

limit disease progression, as also monitoring patients regarding the risk of progression to OSCC (Aziz, 2009).

#### **1.1.3.5. Actinic cheilitis**

AC is defined by the WHO Collaboration Centre 2020 as a “disorder that results from sun damage and affects exposed areas of the lips, most commonly the vermilion border of the lower lip with a variable presentation of atrophic and erosive areas and white plaques” (Warnakulaasuriya, 2020). AC is present predominantly in middle-aged and light skinned men, that are excessively exposed to UV radiation, and has a global prevalence estimated to be between 0.45 and 2.4%, with sun exposure as the main risk factor leading to an increase of 43.2% in AC prevalence rate and that putt those who live in tropical regions at a higher risk of developing lip OSCC (Santana Sarmento et al., 2014; Dancyger et al., 2018).

Due to slow progression of AC lesions, patients often attribute this process to aging and ignore the lesion until it reaches a more advanced stage which can be harmful because AC has a 3.07% chance of malignant transformation, lip OSCC is estimated to account for 12% of all Head and Neck cancers (Dancyger et al., 2018).

Diagnose of this lesion can be made by clinical evaluation but it requires a biopsy to confirm the diagnosis. AC therapy aims at removing or destroying abnormal epithelium these includes excisional biopsy (Vermilionectomy), topical application off of 5-fluorouracil (5-FU), chemical peels with trichloroacetic acid, cryotherapy, electrocauterization, carbon dioxide laser ablation, subsequent enhanced local photoprotection, and more recently, imiquimod Photodynamic therapy and YAG laser (Vieira et al., 2012).

#### **1.1.4. Risk factors**

The use of tobacco, alcohol consumption and nutritional deficiencies together possibly explain about 90% of head and neck cancers (Chaturvedi et al., 2019).

Cigarettes and alcohol are the most common factors, which when combined with viruses in the mouth can lead to a neoplasm. The HPV treatment is aimed at clinical cure because, depending on the immune status of each patient, complete eradication of the virus, with

or without relapse, cannot be achieved. It has been observed in the literature that HPV prevention aims to control the spread of the virus and detect disease early, which requires the implementation of sexually transmitted disease awareness programs and the use of community-based preventive measures (Castro et al., 2004).

The age-adjusted incidence rate and mortality rate for SCC increase with age and are higher in men than in women (Lambert et al., 2011). It is well established that tobacco consumption and alcohol consumption are significant risk factors (Johnsson, 1991). Some studies suggest that, among people with HIV, the risk of oral cancer is high (Shiels et al., 2011).

#### **1.1.4.1. Tobacco**

Defined by Petti (2009) as “any preparation of the leaves of plants of the genus *Nicotiana*, of the nightshade family”, tobacco use remains the main cancer risk factor accounting alone for millions of deaths per year, and responsible for approximately one fourth of total oral cancer cases.

With more than 60 carcinogens present in cigarettes and 16 carcinogens identified in smokeless tobacco (tobacco consumed without combustion), nitrosamines such as 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and N-nitrosornicotine (NNN), and polycyclic aromatic hydrocarbons (PAH) such as benzopyrene and aromatic amines were considered to have a causal relation with oral cancer, leading to DNA damage. (Petti, 2009) Besides those carcinogens, there is also the nicotine factor, although nicotine isn't a carcinogen it is toxic and addictive, and this addiction led people to use tobacco continually (Zhang et al., 2019).

Smoking cigarettes, cigars and loose tobacco are the main form of tobacco consumption in Western countries and is increasing in developing countries, Smokeless tobacco, such as chewed tobacco (betel quid and areca nut) is more present in Asian populations. Tobacco consumption in any form is higher in adults and middle aged (15-65 years) except for Asian countries where people aged 65 and above are the main consumers (Chaturvedi et al., 2019).

When compared with non-smokers, smokers have a three times higher risk of developing oral cancer, and those tobacco related cancers cases are commoner in low and in middle income countries. People who never smoked but are often exposed to cigarette smoke

environment have an 87% higher risk of developing oral cancers (Rivera, 2015; Chaturvedi et al., 2019).

Cessation of tobacco consumption habits (1- 4 years) is proven to reduce the risk of developing head and neck cancers (HNC) and it is also shown that people who quit smoking for at least 20 years present similar risks to those who have never smoked (Marron et al., 2009).

Although data shows that global smoking rates have declined (from 22.7% in 2007 to 19.6% in 2019), the overall number of smokers remains high due to population growth. In 2019, at least 940 million men and 193 million women globally aged 15 and over, were smokers. While per capita consumption has declined in all WHO regions, the number of smokers has significantly increased in Africa region (Tobacco Atlas., 2022).

#### **1.1.4.2. Alcohol**

Alcohol consumption is also one of the major oral cancer risk factors, in fact it has been proved that it has a synergic effect with tobacco being both accountable for more than 80% of oral cancer cases, in fact heavy drinkers and smokers are 38 times more likely to develop OSCC than abstainers from both products (Warnakulasuriya, 2009).

Alcoholic beverages are mainly composed by ethanol, water and glucose. Ethanol itself is not considered to be a carcinogen, but alcohol dehydrogenase oxidizes ethanol to acetaldehyde and aldehyde dehydrogenase, acetaldehyde the first metabolite of ethanol it's known to have carcinogenic and mutagenic effects on DNA, being responsible for ethanol carcinogenic effect (Petti, 2009; Reidy et al., 2011).

Ethanol act both as a local and systemic risk factor, increasing the oral mucosal permeability, dissolving lipid components of the epithelium, causing epithelial atrophy, interfering with DNA synthesis and repair and it is also mutagenic and genotoxic, resulting in decreased salivation flow, compromising the liver ability to process toxic and potentially carcinogenic elements and its chronic use weakens immunity, leading to an increased vulnerability to infections and tumors (Reidy et al., 2011; Rivera, 2015).

#### **1.1.4.3. Human Papilloma Virus**

Human Papilloma Virus (HPV) is considered a major risk factor when it comes to

oropharyngeal cancers and over the years it has been shown an association between HPV and oral cancer cases, which has been arising since it was first reported in 1983 (Yete et al., 2018).

HPV is DNA virus that is highly sexually transmissible, its commonly found in genital and anal areas, however because of changes in sexual behavior like the increase of oral sex habit, it also became frequent in the oral mucosa (Castro et al., 2004).

The different HPV types are characterized by changes in the DNA sequence and are classified into high-risk (HPV 16, 18, 31, 32, 33, 35, 39, 45, 51, 52,56, 58,59,66 and 68) and low risk (HPV 6, 11, 42, 43 and 44). High-risk HPV (HR-HPV) types 16 and 18 are the most common pathogens in 70% of cervical cancers worldwide. HPV18 is reported in 66-82% and HPV16 in 26-34% of HPV positive oral cancers (Yete et al., 2018).

Oral manifestations associated with HPV are papilloma, condyloma acuminata, verruca vulgaris, focal epithelial hyperplasia, leukoplasia, oral lichen planus, and oral squamous cell carcinoma. Diagnosis is made by lesion examination and confirmed by biopsy showing HPV genotype revealed by molecular biology techniques (hybrid capture and PCR) (Castro et al., 2004).

The risk factors for positive SCC for the Human Papilloma Virus (HPV) are mainly related to sexual habits and not to the use of tobacco and alcohol in HPV-negative SCC. (Termine et al., 2008) Furthermore, in the last decade, the oncogenic HPV type 16 has been associated with the development of some oropharyngeal tumors, but the association with oral cancer itself has not been evident (Schwartz et al., 2001).

Detection of HPV DNA in some oropharyngeal tumors has been associated with a favorable prognosis, particularly among men (Fakhry et al., 2008).

#### **1.1.4.4. Human Immunodeficiency Virus**

The incidence of head and neck squamous cell carcinoma is also increased two to three times among human immunodeficiency virus (HIV)-positive patients (Grulich et al., 2007; Powles et al., 2009; Deeken et al., 2012): a relevant population in sub-Saharan Africa, where HIV infection remains endemic (Botswana AIDS Impact Survey, 2013).

Botswana, for example, is a middle-income country with a population of 2.3 million people affected by one of the most serious HIV epidemics in the world (22.2% of the

adult population was living with HIV in 2019). Robust efforts, including universal healthcare and access to antiretroviral therapy, have thankfully begun to decrease HIV prevalence and mortality in Botswana (UNAIDS, 2020). However, as HIV-infected patients are living longer, they remain susceptible to late comorbidities, including HIV-related malignancies (Dryden-Peterson et al., 2015).



## 2. METHODOLOGY

The purpose of this literature review is clarified in the following research question (according to the PICO strategy presented in Table 2): what are the determining factors for the development of oral cancer in Sub-Saharan Africa?

**Table 2.**

*Research question according to the PICO strategy*

<b>P (population)</b>	Population life Resident Sub-Saharan Africa
<b>I (intervention)</b>	Oral cancer diagnoses
<b>C (comparaduo)</b>	Not applicable
<b>O (outcome)</b>	Oral cancer prevention, early detection of oral cancer

Bibliographic research was carried out in the Pubmed scientific publications database, without linguistic limits, in the last 10 years (between 2012 and 2023) and available in free full text, with the combination of the following terms (title or abstract): oral cancer and sub-Saharan Africa, and having in consideration the inclusion and exclusion criteria listed in Table 3.

**Table 3.**

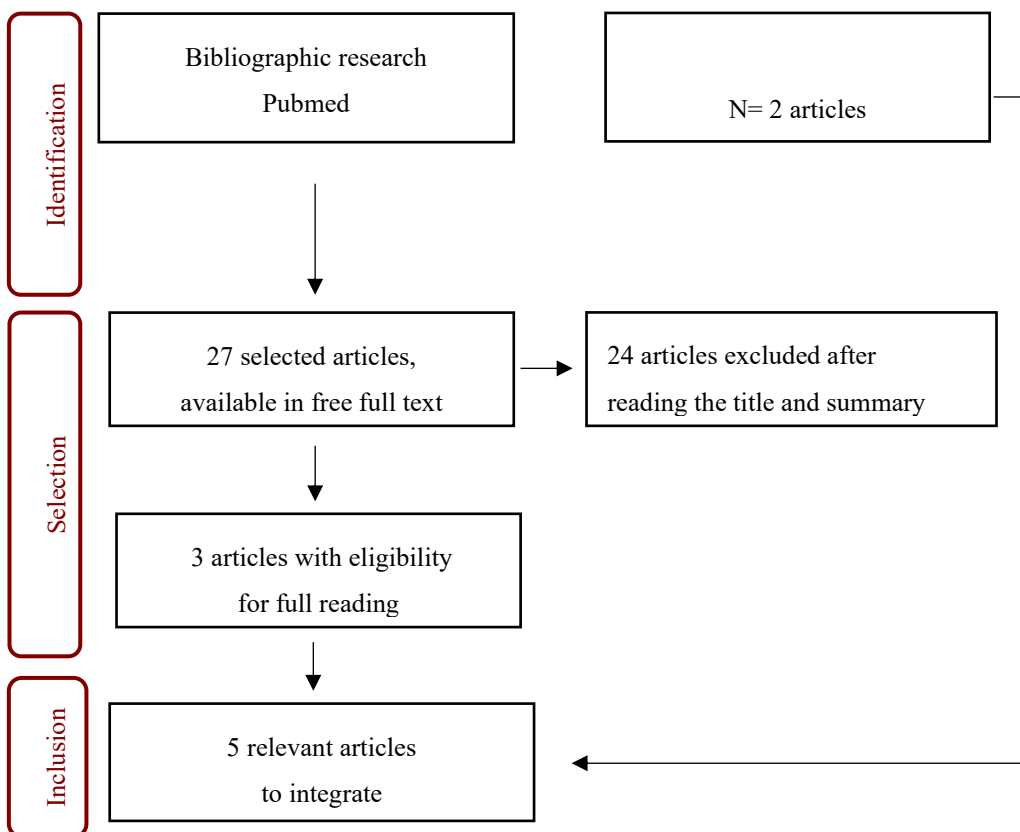
*Inclusion and exclusion criteria*

<b>Inclusion criteria</b>	<b>Exclusion criteria</b>
Studies published in Pubmed	Literature reviews
Quantitative and qualitative studies	Opinion articles
Any language	
Publications in the last 10 years (2013-2023)	
Available in free full text	

The selection of articles was carried out according to the PRISMA methodology (cf. Figure 1). The literature review included articles resulting from bibliographic research in gray literature or from the list of bibliographic references of articles resulting from the main search.

**Figure 2.**

*PRISMA bibliographic search diagram*



After reading the title and summary of the articles, we determined the interest in reading the full text of 4 articles with effective relevance for clarifying the purpose underlying this literature review (cf. Table 4). According to the full reading, 4 articles presented relevant content to clarify the characteristics of oral cancer in sub-Saharan Africa.

The content – main data – of the articles considered relevant for clarifying the purpose of this review is summarized in the results table (cf. Table 5).

**Table 4.***Articles included in the literature review*

	<b>Autor/ano</b>	<b>Título</b>
<b>1</b>	(Motlokwa et al., 2022)	Disparities in Oral Cancer Stage at Presentation in a High HIV Prevalence Setting in Sub-Saharan Africa.
<b>2</b>	(Asio et al., 2018)	Survival and associated factors among patients with oral squamous cell carcinoma (OSCC) in Mulago hospital, Kampala, Uganda.
<b>3</b>	(Anakwenze et al., 2018)	Factors related to advanced stage of cancer presentation in Botswana.
<b>4</b>	(Nabukenya et al., 2018)	Head and neck squamous cell carcinoma in Western Uganda: disease of uncertainty and poor prognosis.



### 3. RESULTS

**Table 5.**

*Evidence of scientific articles*

Ref.	Objective of the study	Type of study	Country	Methodology	Results	Conclusions
(1) (Motlokwa et al., 2022)	Identify risk factors for the (earlier) identification of advanced-stage oral cancer.	Cohort study	Botswana	<p>Retrospective cohort analysis was conducted among individuals with biopsy-confirmed oral cancer at Princess Marina Hospital in Gaborone, Botswana, between 2010 and 2020.</p> <p>The data collected included age at diagnosis, sex, place of residence, serological status, oral cancer stage and location in the oral cavity.</p> <p>Multivariable analyzes were controlled for age, sex, neighborhood of residence and location in the oral cavity.</p>	<p>Of the 218 clinical files analyzed, 79% were male, 58% were HIV positive, the median age was 56 years (interquartile range: 47-63) and 67% had advanced-stage disease.</p> <p>Cancer in hidden locations in the oral cavity is more likely to be identified at an advanced stage, with an adjusted odds ratio (OR) of 2.98 (95% CI, 1.29-6.89; P = .01).</p> <p>Living in neighborhoods whose residents' condition is socioeconomically disadvantaged was associated with a higher probability (OR, 2.36; 95% CI, 1.28-4.39; P = .01) of advanced-stage presentation compared to others districts.</p> <p>HIV infection was not associated with the risk of advanced presentation of the lesion (OR, 1; 95% CI, 0.61-1.61; P = .97).</p>	<p>Difficult to observe locations in the oral cavity and residence in districts with limited access to healthcare were risk factors for advanced oral cancer at the time of diagnosis in Botswana.</p>

Ref.	Objective of the study	Type of study	Country	Methodology	Results	Conclusions
(2) (Asio et al., 2018)	To identify survival and associated factors in patients with oral squamous cell carcinoma.	Retrospective cohort study	Uganda	Retrospective cohort study among patients with histologically confirmed oral squamous cell carcinoma treated at our center from January 1 2002 to December 31, 2011. Total of 384 patients (229 men and 155 women).	The overall age was 55.2 (SD 4.1) years. The 384 patients studied contributed a total of 399.17 person-years of follow-up. 111 deaths were recorded, resulting in an overall mortality rate of 27.81 per 100 person-years (95% CI; 22.97–32.65). The 2- and 5-year survival rates were 43.6% (135/384) and 20.7% (50/384), respectively. Tumors located on the lip had the best 5-year survival rate (100%), while tumors on the floor of the mouth, alveoli and gums had the worst prognosis, with 5-year survival rates of 0%, 0% and 15.9%. respectively. Independent predictors of survival were clinical stage (p = 0.001), poorly differentiated histopathological grade (p < 0.001), male sex (p = 0.001), age > 55 years at diagnosis (p = 0.02) and moderately differentiated histopathological grade (p = 0.027). Tobacco and alcohol consumption, tumor location and treatment group were not associated with survival (p > 0.05).	The 5-year survival rate for oral squamous cell carcinoma was very low (20.7%). Male sex, late clinical stage at presentation, poor histopathological types and advanced age were independent prognostic factors for survival. Early detection through screening and prompt treatment can improve survival.
(3) (Anakwenze et al., 2018)	Explore the factors related to oral cancer identified at an advanced stage.	Analytical study	Botswana	Patients treated at an oncology clinic between December 2015 and January 2017 Questionnaire on sociodemographic and clinical factors, as well as fears related to cancer, attitudes, beliefs and stigma. Odds ratios (ORs) were calculated to identify factors significantly associated with advanced stage (stage III and IV) at diagnosis. 214 patients, 18.7% were men and 81.3% women. The median age at diagnosis was 46 years, with 71.9% of patients over 40 years of age.	Commonly represented tumors included the cervix (42.3%), breast (16%), and head and neck (15.5%). Oncologic stages represented in the study group included 8.4% stage I, 19.2% stage II, 24.1% stage III, 11.9% stage IV, and 36.4% unknown stage. Patients who presented at advanced stages were significantly more likely to not be afraid of having cancer (OR, 3.48; P < .05), believe that their family would not care about them if they needed treatment (OR, 6.35; P = .05), and believed that they did not have the financial means to develop cancer (OR, 2.73; P < .05). The perception that symptoms were less severe was also significantly related to advanced stage (P < .05). Female patients with nonspecific cancers were more likely to present at advanced stages (OR, 5.67; P < .05).	Future cancer mortality reduction efforts should emphasize cancer symptom awareness and early detection through routine cancer screening, as well as increasing the acceptability of seeking care, especially among male patients.

Ref.	Objective of the study	Type of study	Country	Methodology	Results	Conclusions
(4] (Nabukenya et al., 2018)	Describe the clinicopathological features and staging of patients with head and neck squamous cell carcinoma (HNSCC), and document their prognostic outcomes based on clinical experience	Cross-sectional study	Uganda	Cross-sectional study with clinical follow-up. 51 participants were recruited from February to July 2016. A questionnaire was administered to assess patient's characteristics and further investigations included clinical staging, serological assays, biopsy for histopathological examination and immunohistochemistry. Staging was subclassified into two categories: early-stage (stage I and II) and late-stage (stage III and IV).	<p>Of the 51 participants, 44 (86.5%), were male, with a mean age of 57.7 years.</p> <p>41 (80.1%) of the participants presented with late-stage disease. Among the 10 participants with early-stage disease 6 (6%) had laryngeal squamous cell carcinoma.</p> <p>The anatomical distribution of primary tumor sites was as follows: pharynx was the most common (n=19; 37.3%), followed by the oral cavity (n=9; 17.6%), larynx (n=9; 17.6%), unknown primary (n=8; 15.7%) and nasosinusal region (n=6; 11.8%).</p> <p>Tobacco use and alcohol consumption were common characteristics among participants. Moderate differentiation was the most prevalent histological grade (n=23, 45.1%).</p> <p>Among the 51 participants, helicobacter pylori, Epstein Barr virus (EBV), HIV and HPV type 16 were identified. However, none of the patients could afford referral for radiotherapy resulting in a 1-year overall survival rate of (4%).</p>	Most patients with HNSCC present in advanced stages and have poor prognosis. There is a huge need for preventive education through community outreach and targeted screening services aimed at early detection of HNSCC.



## 4. DISCUSSION

In 2020, oral cancer was considered the eighth most common cancer diagnosed among women and men and the fourth most commonly diagnosed among men, in Botswana (Ferlay et al., 2018).

However, few studies describe the distribution of oral cancer stage and the risk factors for the development of oral cancer, which is very often identified at an advanced stage: the study by Motlokwa et al. (2022) filled this gap, by carrying out a retrospective analysis of the stage of presentation of oral cancer (at the time of diagnosis) in the Botswana population. And this analysis was fundamental for identifying risk factors that provide opportunities for improvement in intervention (ideally preventive, as early as possible), and ultimately considering the reduction in morbidity and mortality associated with oral cancer.

Oral cancer is a pressing global public health problem. The lack of improvement in the survival rate of the disease when diagnosed at an advanced stage, despite advances in therapeutic options, the approach to oral cancer represents a continuous challenge, particularly in regions where the majority of patients present with advanced-stage disease (Motlokwa et al., 2022). Despite improvements in patient diagnosis and treatment, survival and prognostic factors of patients with oral squamous cell carcinoma remain largely unknown in most of sub-Saharan Africa (Asio et al., 2018).

The study by Motlokwa et al. (2022) sought to identify the risk factors associated with advanced-stage oral cancer and thereby determine the implementation of facilitating and determining interventions to reduce mortality from oral cancer. This study concluded that difficult to see locations and living in districts with limited access to care were risk factors for oral cancer. In conclusion of this investigation, the authors highlight that hidden locations of the oral cavity and residence in districts with limited access to healthcare were risk factors for advanced oral cancer at the time of diagnosis in Botswana.<sup>1</sup>

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<sup>1</sup> Botswana – where the study by Motlokwa et al. (2022) was carried out – is a country in Sub-Saharan Africa with a high prevalence of HIV and an extensive network of health clinics focused on addressing complications arising from HIV infection (Botswana Demographic Survey Report, 2018). There is a strong regional correlation with poverty, and the North West, Ghanzi, Central and Kweneng districts are the poorest (Botswana Poverty Assessment, 2015). According to the Botswana Ministry of Health, 84% of Botswana's population lives within 5 km of the nearest health facility.

The study by Motlokwa et al. (2022) carried out in Botswana, whose population has a high prevalence of HIV (a very common condition in sub-Saharan African countries), the risk factors for diagnosing the disease at an advanced stage were the anatomical location (primary) oral cancer and living in an area of low socioeconomic status and with difficult access to healthcare (here also considered as determining factors in the late diagnosis of oral cancer, two conditions typically characteristic of sub-Saharan African countries).

The results of the study by Motlokwa et al. (2022) point to the fact that approximately two thirds of patients with oral cancer had advanced stage oral cancer: this was significantly higher than the global estimate of 50% and considered as examples the study of Asio et al. (2018), Ferlay et al. (2018), Iyer et al. (2019), Ketabat et al. (2019) and McGinnis et al. (2021).

Asio et al. (2018), in their study carried out in Uganda, sought to establish the survival rate and factors determining prognosis in patients with oral squamous cell carcinoma (Asio et al., 2018). According to the study by Asio et al. (2018), a very low oral cancer survival rate was concluded: 2- and 5-year survival rates of 43.6% and 20.7%, respectively.<sup>2</sup> Asio et al., (2018) noticed that male gender, late clinical stage at the time of diagnosis due to delay in seeking healthcare, histopathological types with poor prognosis and advanced age were independent predictors of the survival rate (Asio et al., 2018).

The discrepancy observed in the early versus late identification (thus, worse prognosis) of oral cancer may be a reflection of the implementation of better screening programs for early detection of the pathology and better treatment modalities, which, ultimately, improves survival in countries with better resources (Chen et al., 2009).<sup>3</sup>

In the study by Asio et al. (2018), gender had a significant effect on the survival rate: risk

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However, around 39% of people living in Kweneng, Central and Ghanzi districts reside within 5 to 15km of the nearest health facility, compared to 20% in the other remaining districts (Health Statistic Botswana, 2016). HIV treatment in Botswana has been highly successful, and the burden of HIV comorbidities resulting in morbidity and mortality is a major focus of attention for the country's Ministry of Health (Gaolathe et al., 2016; Motlokwa et al., 2022). Cancer, including oral cancer, threatens the increase in life expectancy gained from improved HIV outcomes (Iyer et al., 2019; McGinnis et al., 2021).

<sup>2</sup> The results of the research by Asio et al. (2018) are similar to the low 5-year survival rate observed in studies carried out in Egypt on oral cancer (20.8%), as is the example of the research by Ibrahim et al. (2009). However, better survival, especially for stages III and IV, has been reported in resource-rich countries such as Taiwan 26.6% and 11.8% (Chen et al., 1999), Brazil 32.6% and 24.5% (Leite & Koifman, 1998) and USA (Hoffman et al., 1998).

<sup>3</sup> The defense of standardized treatment and its effect on survival, regardless of ethnic and economic differences, has already been advocated for all head and neck squamous cell carcinomas (Chen et al., 2009).

of death twice as high in males compared to females.<sup>4</sup>

Age was a significant prognostic factor for survival in the study by Asio et al. (2018) (remember, carried out in Uganda): patients with oral squamous cell carcinoma and aged over 55 years had a significantly shorter survival time than younger patients. Age was also considered a prognostic factor in other investigations (note that these were studies carried out outside Sub-Saharan Africa): in Brazil (Leite & Koifman, 1998), USA (Mehta et al., 2010), Taiwan (Chen et al., 1999) and Egypt (Ibrahim et al., 2009).

There appears to be a general consensus that lower survival among older patients may be related to a higher rate of comorbidities associated with aging. It is also possible that these comorbidities make older patients unable to undergo long surgical interventions, which impairs their survival, but radiotherapy alone has been reported as a determinant of a worse prognosis (Leite & Koifman, 1998; Morris & Ganly, 2011).

Furthermore, with the emerging role of HPV in the development of mouth and pharyngeal cancer, it may be that the younger population has a different causal factor, therefore, better outcomes. However, a study carried out in Uganda showed a low prevalence of HPV among patients with head and neck cancer (Nabukenya et al., 2018).

Well, in the study of Nabukenya et al. (2018), the majority of patients with HNSCC had a late stage and poor prognosis: 80.1% had a late stage; the pharynx was classified as the most prevalent anatomical site (37.3%), followed by the oral cavity (17.6%), the larynx (17.6%), a unknown primary (15.7%) and sinonasal area (11.8%). Smoking and alcohol consumption were common characteristics among participants in the study by (Nabukenya et al., 2018). For Asio et al. (2018), education, alcohol consumption and smoking were not significant predictors of survival.

According to research by Asio et al. (2018), tumor site was not an independent predictor of survival – and this was consistent with other studies, like Lo et al. (2003) (Taiwan), but different from others: Ibrahim et al. (2009) (Egypt), Leite & Koifman (1998) and

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<sup>4</sup> The effect of gender on survival still requires clarification. Some studies suggest greater survival for females, such as the study by (Boing et al., 2006), carried out in Brazil, and (Cook et al., 2009), in the United States of America. (Mehta et al., 2010) reported less improvement in survival for women with carcinomas of the oral cavity and pharynx according to their study carried out in the USA. Other studies have reported no significant difference in survival between men and women. (Chen et al., 1999) It is believed that more men than women are affected by oral squamous cell carcinoma and have worse survival due to greater exposure to tobacco and alcohol. (Lambert et al., 2011) Furthermore, men have poor health-seeking behaviors, which can result in delays in diagnosis and, therefore, initiation of treatment. (Massano et al., 2006)

Boing et al. (2006) (Brazil).

The possibility of misclassifying the original site of OSCC is high, given the complex anatomy of the oral cavity combined with the delayed presentation observed in patients (Kakande et al., 2010).

In advanced stages, there may be overlapping oral tumors arising from adjacent structures, leading to misclassification. In Asio et al. (2018) study approximately two-thirds of patients presented with advanced-stage disease, making misclassification of the original OSCC site highly likely.

According to the study by Asio et al. (2018), OSCC arising from the lip had the best 5-year survival rate (100%), compatible with the results of other studies: Ibrahim et al. (2009) and Boing et al. (2006), which may be due to the fact that cancer located on the lip is noticed earlier by patients and, therefore, they tend to seek healthcare earlier. On the other hand, and according to the study by Asio et al. (2018), the floor of the mouth, alveoli and gums had the worst 5-year survival rates (0%, 0% and 15.9%, respectively). Contrary to what was observed in the Asio study, in the investigation conducted by Leite & Koifman (1998) and Hoffman et al. (1998), the tongue presented the lowest survival rate.

Differences in survival by tumor site may be due to the ease of early diagnosis, the accessibility of tumor excision with sufficient surgical margin and the different lymph node involvement presented in each location (Asio et al., 2018).

In the study by Kakande et al. (2010) late presentation of oral cancer was reported. Another important fact in the panorama of research into oral cancer is the fact that carcinomas of the tongue can progress to the floor of the mouth, making it difficult to know the place of origin (Asio et al., 2018). Furthermore, some anatomical sites manifest greater metastatic capacity due to high lymphatic drainage (Massano et al., 2006).

Research by Asio et al. (2018) pointed to an inverse relationship between tumor stage and survival. This relationship was also observed in the study by Ibrahim et al. (2009) Leite & Koifman (1998), Morris & Ganly (2011), Lo et al. (2003) and Kantola et al. (2000).

Consider that in the study by Asio et al. (2018), the 5-year survival rate was 100%, 61.5%, 14.5% and 0% for patients with stages I, II, III and IV, respectively. A study carried out by Ibrahim et al. (2009) in Egypt found similar survival rates of 100%, 65.5%, 42.2% and 0% for stages I, II, III and IV of disease, respectively. However, the survival rate in the

study by Asio et al. (2018) was lower than those reported by studies that investigated the results of OSCC after surgery and/or radiotherapy, such as America (Pulte & Brenner, 2010) and Taiwan (Lo et al., 2003).

The much lower survival rate reported in the study may be due, according to its authors, to the fact that the study population included more patients in clinical stages III and IV than in stages I and II stages more prevalent in the populations studied by Pulte & Brenner (2010) and Lo et al. (2003) For Asio et al. (2018) and according to their investigation, histopathological grading was a significant predictor of survival.

In the study by Asio et al. (2018), it was observed that the risk of death increased in patients with less well-differentiated tumors; Patients with poorly and moderately differentiated tumors had three times and almost twice the risk of death, respectively, compared to those who had well-differentiated tumors. However, it is worth noting that some reports have not shown that tumor grade has an effect on survival (Leite & Koifman, 1998; Kantola, et al., 2000).

The type of treatment <sup>5</sup> received by the patient was not a predictor of survival in the investigation conducted by Asio et al. (2018): of the 384 patients, around two thirds (67.3%) received at least one form of treatment; radiotherapy, alone or associated with surgery, was the most common treatment modality. Patients treated with surgery had the highest two- and five-year survival rates, followed by surgery and radiotherapy.

However, according to the study of Asio et al. (2018), most untreated patients died within 5 years, as did many of the patients treated with radiotherapy or chemotherapy alone. Other studies (carried out in countries where surgery was the main treatment modality found treatment modality as a significant predictor of survival: Chen et al. (1999) and Lo et al. (2003) carried out in Taiwan, Leite & Koifman, (1998) carried out in Brazil, Hoffman et al. (1998), in the USA.

Asio et al. (2018) warn that in their study, patients were classified only according to treatment status, without taking into account dose, duration and adherence to treatment. The same authors state that sometimes surgery is not an option due to limited surgical

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<sup>5</sup> The treatment modality depends on the stage of the disease and other parameters such as anatomical location, tumor size, distant metastasis, histological type and lymph node involvement. While surgery alone may be recommended for patients with early-stage disease, adjuvant radiotherapy or chemotherapy is indicated for patients with advanced stages (Hoffman et al., 1998).

space, and that this can lead to significant delays in accessing the service, with consequent progression of the disease and change of stage (Kajja & Sibinga, 2014; Asio et al., 2018).

This condition is no different when it comes to radiotherapy, where machine breakdowns and patient load also lead to delays in treatment, compromising treatment results (Kigula & Wegoye, 2000).

Despite universal access to free healthcare, most Botswana patients<sup>6</sup> with cancer present in advanced stages: motto for the study carried out by Anakwenze et al. (2018) which aimed to explore factors related to the diagnosis of advanced stage cancer in Botswana: sociodemographic and clinical factors, as well as knowledge, attitudes and beliefs.

According to the study by Motlokwa et al. (2022), oral cancer was more common in men than in women, such results were similar to the study by Eskiizmir et al. (2017) and Hille & Johnson, (2017): this may be due to the high rates of smoking and alcohol consumption in men compared to women as concluded by the study by Kruse et al. (2011).

In Botswana, tobacco consumption and alcohol consumption are more prevalent among men than women: consider the results of the study (Ministry of Health Botswana, 2015).

The study by Motlokwa, et al. (2022) observed that men were more likely to have advanced-stage disease, similar to the results of the study by Jafari et al. (2013): this may be due to men being more reluctant to seek healthcare, and women being better informed about oral cancer compared to men (Jafari et al., 2013; Al-Maweri et al., 2015). The place of residence with little access to healthcare was a risk factor for the progression of the disease – this result of the study by Motlokwa et al. (2022) was similar to the results of other studies that sought to identify risk factors for the cancer development.<sup>7</sup> The systematic literature review by Kelly et al. (2016) had pointed to the fact that poor access to healthcare is a risk factor for the diagnosis of advanced-stage oral cancer.

HIV status was not associated with the time of oral cancer diagnosis in both the study by Motlokwa, et al. (2022) carried out in Botswana, and in the study by Zwane et al. (2018),

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<sup>6</sup> Botswana, a country with a high prevalence of HIV, has an increased incidence of cancer-related mortality following antiretroviral therapy. According to the study developed by Anakwenze, et al. (2018), patients who presented at advanced stages were more likely to not be afraid of having cancer and believed that their family would not take care of them if they needed treatment.

<sup>7</sup> Studies whose results discriminate the association between access to healthcare and late diagnosis of cancer: squamous cell carcinoma of the head and neck (Farquhar et al., 2019; Beaudoin et al., 2020), colorectal cancer (Wan et al., 2013), melanoma (Stitzenberg et al., 2007) and breast cancer (Huang et al., 2009).

in South Africa.

HIV infection causes immunosuppression and induces carcinogenesis, which may increase the risk of advanced-stage oral cancer. However, due to robust antiretroviral treatment and HIV treatment in Botswana, the risk of oral cancer may be decreased in immunocompromised individuals (Torres & Mulanovich, 2014). Furthermore, close monitoring of HIV patients by primary healthcare professionals not only ensures virologic control of HIV but also enhances health awareness and promotes early diagnosis (Opio et al., 2019; Motlokwa et al., 2022).

Oral cancer is the sixth most common cancer worldwide. The lack of improvement in oral cancer survival rate, despite the availability of multiple treatment options, may be due to the high prevalence of advanced-stage cancer identification (Motlokwa et al., 2022). It is widely reported that the prognosis is better with early-stage, well-differentiated disease than with other histopathological types (Lo et al., 2003).

The outcome of the study by Motlokwa, et al. (2022) supports the need to increase efforts to improve access to care and increase awareness about oral cancer to decrease the burden of oral cancer diagnosed at an advanced stage – bear in mind that this study was carried out in Botswana, however such results (or rather their interpretation) crosses applies to the entire region of Sub-Saharan Africa, as we ended up verifying in the investigation of Motlokwa et al. (2022)

Late diagnosis of oral cancer is probably multifactorial and related to lack of awareness and limited access to healthcare, in turn associated with precarious socioeconomic conditions more often characteristic of developing countries than developed countries (Kumar et al., 2001; Jafari et al., 2013; Beaudoin et al., 2020). There is a great need for preventive education based on community outreach and screening services focused on early identification (Nabukenya et al., 2018).



## 5. CONCLUSION

GLOBOCAN is the database of the International Agency for Research in Cancer (IARC), the WHO body which is responsible for carcinogens and cancer epidemiology research. It uses data reported from local, regional and national cancer registries to estimate global cancer incidence, mortality and prevalence (Hille & Johnson, 2017). In 2020 there were estimated a total of 377,713 new cases of oral cancer worldwide, 177 757 oral cancer related deaths and 959 248 people living with oral cancer (within 5 years of diagnosis). The Asian continent owns the largest percentage of the total of those new cases (64,2%) followed by Europe (17,4%, Northern America (7,6), Latin America and Caribbean (5,6%), and Africa with the lowest percentage (3,8%). It is important to remember that cancer registries on the African continent, especially in Sub-Saharan Africa, are clearly underdeveloped. Compared with Europe, the proportion of the African population covered by cancer registries is very low (2%) versus (42%).

Early detection through screening and early treatment can improve survival – such measures are seen to have positive implications (Asio et al., 2018). Oral and pharyngeal cancer is one of the deadliest, however its rapid diagnosis and referral is a crucial factor in increasing patient survival. Paying more attention to oral health and existing injuries in this area in women may be the reason why the delay related to men is greater than the delay related to women (Jafari et al., 2013).

Oral cancer represents a significant concern in the field of dentistry, requiring specialized attention for early diagnosis and effective treatment. This type of cancer can affect the lips, tongue, gums, cheeks and palate, and is often associated with tobacco and alcohol consumption, as well as infection with the HPV virus.

Dental professionals play a crucial role in detecting oral cancer early during routine exams. Observation of suspicious lesions, such as persistent ulcers, abnormal white or red patches, allows patients to be referred for further evaluation. Carrying out biopsies and imaging tests contributes to confirming the diagnosis and determining the stage of the disease.

Oral cancer treatment often involves a multidisciplinary approach, where dentists work in collaboration with oncologists and maxillofacial surgeons. Surgeries to remove tumors, radiotherapy and chemotherapy are common options, aiming to eliminate cancer cells and

prevent their spread.

In addition to targeted treatment for oral cancer, dentistry plays a vital role in managing side effects associated with therapies, such as chewing problems, oral mucositis and xerostomia. Dental support helps maintain the patient's oral health, contributing to a better quality of life during and after treatment.

Oral cancer prevention is emphasized through education about healthy habits and promoting regular exams. Quitting tobacco, moderating alcohol consumption and adopting oral hygiene practices are crucial preventive measures that dental professionals highlight to reduce risks.

Oral cancer, a critical manifestation of neoplasia in the oral cavity, emerges as a significant public health challenge in sub-Saharan Africa. While the global incidence of oral cancer has been widely documented, the sub-Saharan region faces unique epidemiological characteristics that demand specific attention (Ferlay et al., 2015).

This scientific text aims to explore the patterns, risk factors and implications of oral cancer in this region, outlining the urgent need for preventive and interventional strategies. The ethnic and cultural diversity of Sub-Saharan Africa, combined with traditional smoking and alcohol consumption practices, contributes to a complex epidemiological scenario (Johnson & Jayasekara, 2011). Recent studies indicate an increasing prevalence of oral cancer cases, often associated with behavioral habits such as chewing tobacco and human papillomavirus infection (Chalya et al., 2015). This specific context emphasizes the importance of localized understanding of risk factors to implement effective preventive measures.

Furthermore, the region's economic and structural challenges significantly impact access to healthcare, including early detection and treatment of oral cancer. The lack of resources, qualified health professionals and adequate infrastructure amplifies the barriers to timely diagnosis, compromising the effectiveness of therapeutic interventions (Fonseca & Zylberberg, 2019).

Efforts aimed at reducing the cancer-related mortality rate should emphasize awareness of cancer symptoms and early detection through routine cancer screening, as well as increasing adherence to health-seeking behaviors through education about the best prognosis when cancer is detected early (Anakwenze et al., 2018).

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