Risk factors for oral cancer: Thematic trends and research agenda

[Factores de riesgo del cáncer oral: Tendencias temáticas y agenda de investigación]

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Abstract

Context: Oral cancer is difficult to define due to several factors. It's known as oral squamous cell carcinoma (OSCC) and is common in the head and neck. Geographic variations in the impact of OSCC highlight the need for research on risk factors and treatment trends.

Aims: To identify the main research trends of studies on oral cancer risk factors in the scientific literature in the Scopus database and Web of Science.

Methods: This was an exploratory study of the risk factors for oral cancer designed considering the eligibility criteria defined by the PRISMA-2020 international statement, that is, inclusion and exclusion.

Results: A total of 215 documents from Scopus and Web of Science were subjected to bibliometric analysis. The years 2020 and 2021 were the most productive, with 18 and 22 articles, respectively. The leading author in productivity and impact was Johnson N, the leading journal was Oral Oncology, followed by the International Journal of Cancer, and the main contributing countries were the United States, the United Kingdom and India. The main thematic cluster was composed of concepts such as Tobacco and Alcohol as the major risk factors; concepts such as Mortality or Head and Neck were positioned as emerging within the scientific literature.

Conclusions: The main risk factors, i.e., alcohol and tobacco consumption, are relevant in terms of mortality in the consumer population, which is why their role should be determined in future studies.

Keywords: malignancy neoplasms; mortality; mouth neoplasms; oral cancer; risk factors; tobacco.

Resumen

Contexto: El cáncer oral es difícil de definir debido a varios factores. Se conoce como carcinoma oral de células escamosas (CCEO) y es frecuente en la cabeza y el cuello. Las variaciones geográficas en el impacto del CCEO ponen de manifiesto la necesidad de investigar los factores de riesgo y las tendencias de tratamiento.

Objetivos: Identificar las principales tendencias de investigación de los estudios sobre los factores de riesgo del cáncer oral en la literatura científica de la base de datos Scopus y Web of Science.

Métodos: Se trató de un estudio exploratorio de los factores de riesgo de cáncer oral diseñado considerando los criterios de elegibilidad definidos por la declaración internacional PRISMA-2020, es decir, inclusión y exclusión.

Resultados: Un total de 215 documentos de Scopus y Web of Science fueron sometidos a análisis bibliométrico. Los años 2020 y 2021 fueron los más productivos, con 18 y 22 artículos, respectivamente. El autor líder en productividad e impacto fue Johnson N, la revista líder fue Oral Oncology, seguida de International Journal of Cancer, y los principales países contribuyentes fueron Estados Unidos, Reino Unido e India. El principal cluster temático estuvo compuesto por conceptos como Tabaco y Alcohol como principales factores de riesgo; conceptos como Mortalidad o Cabeza y Cuello se posicionaron como emergentes dentro de la literatura científica.

Conclusiones: Los principales factores de riesgo, es decir, el consumo de alcohol y tabaco, son relevantes en términos de mortalidad en la población consumidora, por lo que su papel debería determinarse en futuros estudios.

Palabras Clave: neoplasias malignas; mortalidad; neoplasias bucales; cáncer oral; factores de riesgo; tabaco.

INTRODUCTION

Because there is little consensus with regard to a standardised definition or meaning of oral cancer because of the challenges pertaining to the epidemiological, topographic, morphological and behavioural aspects of such tumours (Conway et al., 2018), it is essential to refer to the International Classification of Diseases for Oncology (ICDO), in which this type of cancer is noted as a malignant tumour common in the head and neck, scientifically known as oral squamous cell carcinoma (OSCC).

OSCC is a common malignant neoplasm of the head and neck (Li et al., 2019; Zhu et al., 2022) that has significant geographic diversity in terms of incidence and mortality. It is treated mainly through surgical resection, which can cause intense pain for the patient (Zhu et al., 2022).

The study of cancer has increased in importance, as cancer is positioned as the main cause of death in developed countries and the second leading cause of death in developing countries (Anwar et al., 2020); oral cancer, in particular, accounts for approximately 4% of all cancers in patients in the European context (Capote-Moreno et al., 2020). OSCC is the most common cancer in both men and women in some countries, such as Pakistan (Anwar et al., 2020), and in Peru and other countries, such as India and Bangladesh, OSCC is one of the ten leading causes of death from cancer (Zhu et al., 2022), providing support for the importance of relevant studies.

A good diagnostic modality for OSCC is needed. Computed tomography (CT) and magnetic resonance imaging (MRI) stand out as options. MRI has greater precision in the detection of smaller tumours and those located in soft tissues. CT, as well as new techniques associated with it, such as dual CT, which uses two levels of energy generated from the same emitting tube or from two Xray tubes to analyse tissues with different densities, has greater relevance in the evaluation of cervical lymph nodes (Capote-Moreno et al., 2020). Taking into account that the survival rate for patients with OSCC with cervical lymph node metastases is low and metastasis occurs through the lymphatic vessels (Li et al., 2019), it is necessary to establish its early detection.

As reported by Conway et al. (2018), there is increasing evidence regarding the trend and recognition of the role of risk factors in "oral cancer", for example, tobacco and alcohol, with increasing evidence for HPV as a risk factor (for oropharyngeal cancer).

Risk factor analysis is important in the discussion about the aetiology of this cancer, an aetiology that also includes environmental and genetic factors as well as lifestyle and behavioural factors that are considered modifiable and controllable, with the consumption of tobacco and alcohol (Akinkugbe et al., 2020; Conway et al., 2018) being the two most representative risk factors within this aetiological category. The consumption of both these substances acts synergistically, associated with three out of four cases of cancer in the oral cavity (Akinkugbe et al., 2020).

However, alcohol and tobacco consumption are not the only two risk factors associated with oral cancer. Others include human papillomavirus infection, local chronic trauma, exposure to ultraviolet rays, diets low in antioxidants, immunosuppression, and all potentially malignant oral lesions (Tenore et al., 2020).

In this sense, to understand the complexity and importance of the topic of oral cancer, the current techniques and tools for treatment and diagnosis, and the diversity of risk factors associated with the aetiology of this subtype of cancer, a literature review that allows mapping the scientific activity and identifying the main references and the themes derived from the literary body is necessary so that the information can be unified to guide future studies. Therefore, the aim of this study is to identify the main research trends of studies on oral cancer risk factors in the scientific literature in the Scopus database and Web of Science. This review allows not only an evaluation of the current state of science but also an assessment of the research agenda through the main keywords derived from the literature review process. To achieve the objectives of the research, the following questions are posed:

RQ1: How has the scientific literature on oral cancer risk factors evolved over the years?

RQ2: What are the main research references on risk factors for oral cancer?

RQ3: What is the thematic evolution derived from the scientific production on risk factors for oral cancer?

RQ4: What are the main thematic clusters regarding risk factors for oral cancer?

RQ5: What are the growing and emerging keywords in the field of oral cancer risk factor research?

RQ6: What concepts are positioned as leading issues for designing a research agenda for risk factors for oral cancer?

MATERIAL AND METHODS

To address the research objective outlined in this study, a bibliometric analysis is undertaken in this exploratory study to map the scientific literature around a defined field of research (Mejía et al., 2017), i.e., risk factors for oral cancer. In addition, the literature review process was designed with reference to the PRISMA international statement, 2020 version, in which eligibility criteria are defined, that is, inclusion and exclusion, information sources, search strategy, data management and a flow diagram of the methodological design (Sarkis-Onofre et al., 2021).

Inclusion criteria

The inclusion criteria refer to all aspects that the retrieved documents that will be analysed must meet; for this specific study, the main inclusion criterion is that the scientific articles must address the topic of oral cancer and recognised synonyms, such as neoplasia of the mouth, cancer of the mouth, tumour in the mouth, cancer of the tongue, or more technical terms such as squamous cell carcinoma of the mouth, and include the phrase "risk factors" to account for the scope of the investigation. This combination of terms should be presented in the title of each article because the title serves as the main metadata of scientific activity.

Exclusion criteria

According to the PRISMA 2020 statement, the exclusion criteria are defined using three complementary and consecutive screening phases. For the first phase, all records with indexing errors or incomplete indexing are eliminated, thus limiting the bibliometric analysis.

Subsequently, articles for which there is no full text are eliminated. However, this exclusion phase is applicable to systematic literature reviews, which analyse full-text content; in bibliometric analyses, as metadata analysis tools, publications are not excluded for reasons pertaining to full-text articles.

The third phase consists of the elimination of all the documents that, once passing the screening phase, do not have sufficient methodological rigour, as determined using a technical analysis of the metadata derived from the exclusion process; additionally, all conference proceedings are excluded to guarantee the analysis of rigorous documents in terms the evaluation of manuscripts by qualified peer reviewers.

Information sources

To obtain articles on risk factors for oral cancer, the two main databases in terms of metadata registration, thematic coverage and scientific rigor in indexed journals (Pranckutė, 2021) were selected: Scopus and Web of Science.

Search strategy

The search strategy accounts for the inclusion criteria defined at the beginning of the methodological design and for the inherent characteristics of the interface of each database. In this sense, the following search strategy is used in Web of Science:

(TI= ("oral cancer" OR "Mouth Neoplasm" OR "Mouth Cancer" OR "Mouth Tumor" OR "Tongue cancer" OR "Mouth Squamous Cell Carcinoma" OR "Oral Squamous Cell Carcinoma" OR "Mouth Carcinoma") AND TI= ("risk factor*"))

The following search strategy is used in Scopus (technically, it is the same as that for Web of Science, with changes in the form of allusion to the metadata of the titles:

(TITLE ("oral cancer" OR "Mouth Neoplasm" OR "Mouth Cancer" OR "Mouth Tumor" OR "Tongue cancer" OR "Mouth Squamous Cell Carcinoma" OR "Oral Squamous Cell Carcinoma" OR "Mouth Carcinoma") AND TITLE ("risk factor*")).

Data management

The search strategies for both databases yielded a total of 376 documents, of which 246 were retrieved from Scopus, and 130 were retrieved from Web of Science. These documents were extracted, stored and processed using Microsoft Excel®; initially, all duplicate records were eliminated, and later, the two defined exclusion phases were applied. Likewise, Microsoft Excel® was used to develop bibliometric indicators that would allow evaluation of the productivity and impact of the resulting articles; the free access software VOSviewer was also used.

Study risk of bias assessment

A specific approach was followed to adequately address the assessment of the risk of bias in the studies included in this bibliometric review focused on risk factors for oral cancer. To ensure consistency and objectivity in this process, all authors were actively involved in both data collection and risk of bias assessment. The risk of bias was assessed using an automated tool based on Microsoft Excel®, which had been used for data collection. This automated approach allowed for a systematic and consistent assessment of the studies, thus guaranteeing the quality and integrity of the results obtained. It should be noted that this procedure was carried out with the aim of maintaining objectivity and scientific rigour in the assessment of risk of bias in this bibliometric review.

Figure 1. PRISMA flow chart methodological design.
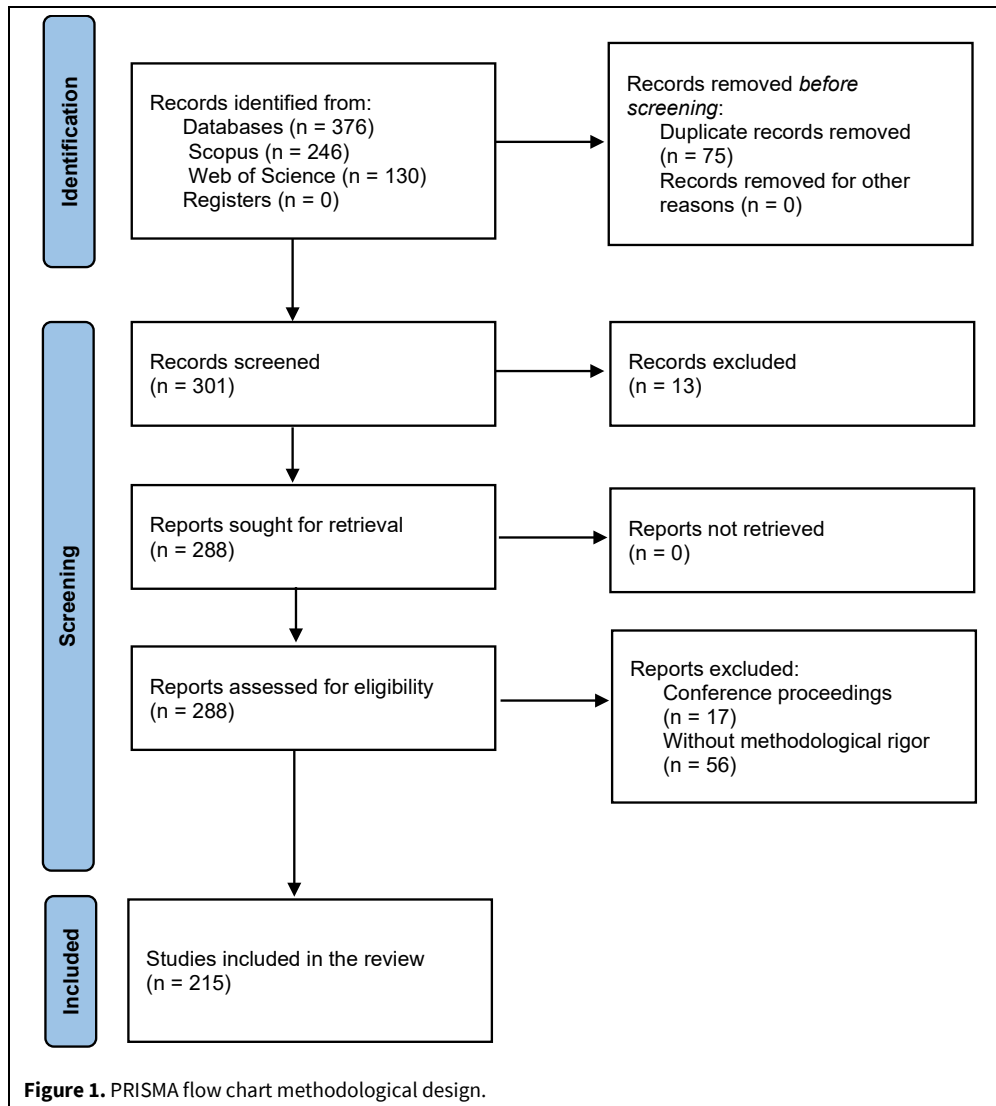
Assessment of reporting bias

In the context of the ongoing bibliometric study focusing on risk factors for oral cancer, the assessment of possible bias due to missing results in the synthesis, which is often due to reporting bias, is a relevant aspect. In this study, it is important to highlight that the methodology used could introduce a certain bias towards certain synonyms, as reflected in the inclusion criteria, search strategy and data collection process. In addition, the nature of conference proceedings and less methodologically rigorous texts, which are among the exclusion criteria, could lead to the omission of valuable information essential for a comprehensive understanding of the topic. This acknowledgement is essential to ensure transparency and rigour in addressing potential sources of bias in this bibliometric analysis.

Methodological design

In accordance with the PRISMA 2020 statement, a flow diagram (Fig. 1) is presented that shows the methodological design and expands on the level of detail and replicability of the proposed methodology.

As seen in the figure, there is an identification phase, with the implementation of the search strategy in each database, and all duplicate documents are eliminated. The two defined exclusion phases are applied, resulting in 215 documents eligible for the bibliometric analysis.

Data analysis

In this bibliometric study focused on oral cancer risk factors, several key variables were analysed to gain a comprehensive understanding of the scientific literature. The main variables evaluated were:

V1: Publication Frequency: The number of articles published per year on oral cancer risk factors in the

Scopus and Web of Science databases, which allowed the identification of research patterns over time.

V2: Geographic distribution: The geographic origin of publications will be reduced to map research in different regions and highlight possible regional approaches to risk factor research.

V3: Author productivity and impact: The contribution of authors to the literature was analysed by the number of articles published and their impact, measured by citations received.

V4: Journal productivity and impact: The impact of the journals in which the articles were published was evaluated, considering both the number of articles and the citation impact.

V5: Country productivity and impact: The countries with the highest production and their influence in terms of impact were identified, much in the number of articles and the citations received.

V6: Thematic evolution analysis: It was shown how the keywords associated with risk factors in oral cancer have evolved over time, revealing trends and changes in research.

V7: Keyword Co-Occurrence Network: A keyword co-occurrence network is constructed to visualise relationships between key concepts and themes in the field.

V8: Keyword Frequency and Validity Analysis: The frequency and validity of the most frequently used keywords were analysed, providing information on areas of interest and their evolution.

These variables were operationalised using bibliometric methods and tools such as Microsoft Excel® and VOSviewer. This systematic approach allowed a thorough and rigorous analysis of the literature, providing valuable information for oral cancer risk factor research.

RESULTS AND DISCUSSION

Publications per year

Publications per year are an indicator of the number of published across time in a field of research. Fig. 2 shows the number of studies from 1984 until 2022, with 99% cubic polynomial growth. The most relevant years were 2020 and 2021. In 2021, the year with the most publications on oral cancer (n = 22), a few articles investigated the way in which radiation influences the development of severe mucositis in patients with oral cancer (Soutome et al., 2021).

The year 2020 was the second most productive year, with 18 publications. Some of the articles that year analysed the way in which smokers and alcohol consumers are less likely than abstainers to undergo oral cancer tests because these populations are less likely to visit the dentist and receive an oral cancer examination (Akinkugbe et al., 2020).
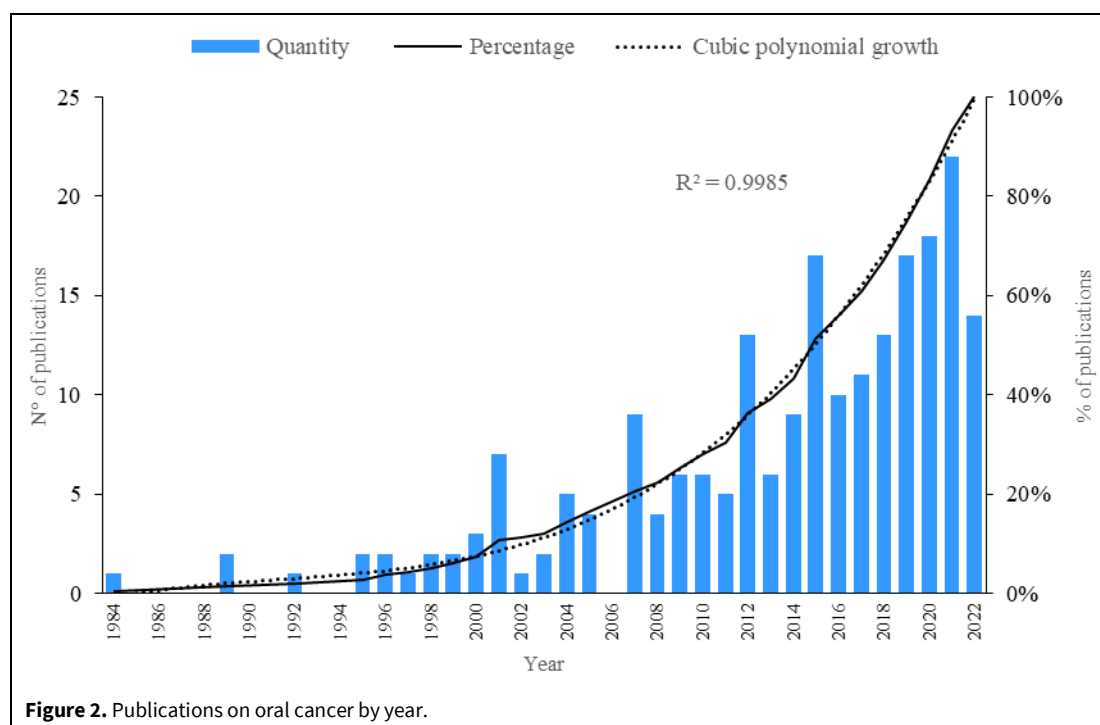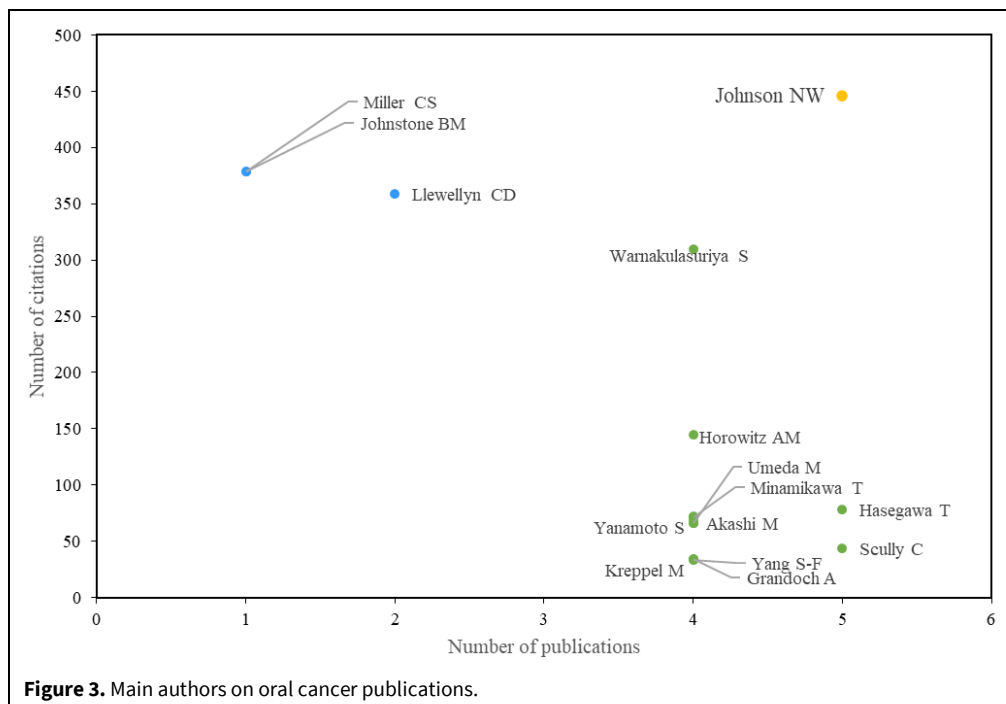

Figure 2. Publications on oral cancer by year.

Figure 3. Main authors on oral cancer publications.

Main authors

The following indicator is used to analyse scientific production by author, making a comparison between the number of citations and the number of publications, so that referent authors, high-impact authors and productive authors can be identified (Fig. 3).

As seen in Fig. 3, the main author in research on oral cancer risk factors is Johnson NW, who is among the top authors who disseminate the most knowledge on the topic, with a total of five publications, and who has the greatest total number of citations (n = 446). Some of his articles have investigated the global epidemiology of oral cancer and changes in the disease with the appearance of cancers induced by the human papillomavirus and the increased susceptibility of the poor population (Johnson et al., 2017).

Furthermore, Johnson NW, in different publications, identified that knowledge about oral cancer, potentially malignant oral disorders and their associated risk factors was deficient in rural Sri Lankan populations, indicating the urgent need to implement oral health education strategies (Amarasinghe et al., 2010).

There is a group of authors who, although they do not account for a large number of publications on the topic of risk factors for oral cancer, have had a high number of citations, which is why they are considered authors of high impact in the scientific community. Among this group of authors, Miller CS and Johnstone BM stand out; despite having a single publication, they have a total of 379 citations. They conduct-

ed an important investigation examining the way in which the human papillomavirus is detected more frequently in the oral epithelium than in the normal oral mucosa, providing evidence that oral human papillomavirus infection is a significant risk factor for oral squamous cell carcinoma (Miller and Johnstone, 1982).

There is another group of authors who, although they do not have a large total number of citations pertaining to their scientific production on risk factors for oral cancer, are among the most productive authors and who, therefore, have the greatest interest in the generation of knowledge. Among this group of authors, Hasegawa T. stands out, with a total of five publications, placing him as the most scientifically productive author; he has investigated the way in which cisplatin administration concomitant to radiotherapy improved locoregional control but without positive results regarding decreased metastasis rates (Hasegawa et al., 2017).

Top journals

In this subsection, the main scientific journals that disseminate knowledge about oral cancer risk factors are analysed, i.e., the total number of publications and citations in articles published by each journal (Fig. 4).

The most important journal within the research field is Oral Oncology, with a total of 10 publications, positioning it as the most scientifically productive journal, and a total of 428 citations associated with these publications, placing it also among journals with the greatest academic impact. Among the most recent publications by the journal, one analyses the

Figure 4. Main journals on oral cancer publications.
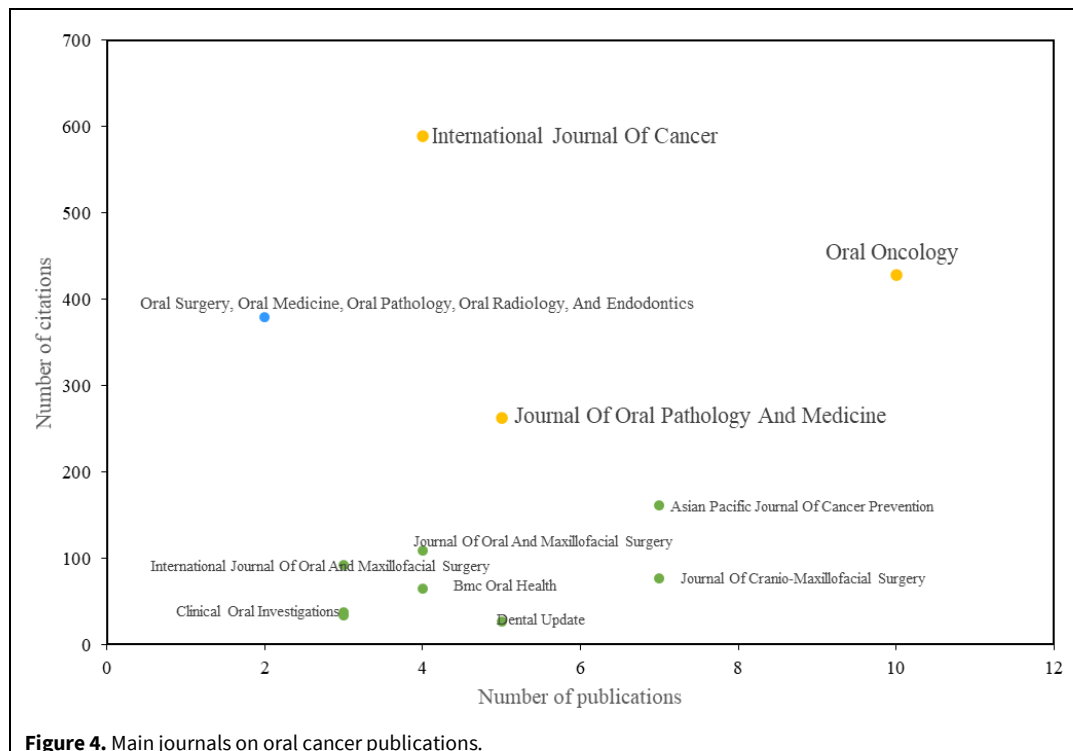
way in which smoking and alcohol, both in men and women, can lead to the development of oral cancer, stating, in addition, that oral cancer is on the rise in younger populations (Zhu et al., 2022). Another of the main investigations derived from the journal Oral Oncology focuses on analysing the way in which prophylactic neck dissection or prophylactic adjuvant radiotherapy in the neck can be a treatment option for early primary oral cancer with a grade >2 (Chuang et al., 2020).

In the same group of leading journals in the research field, the International Journal of Cancer has a total of 589 citations, ranking first for the greatest academic impact, associated with its four scientific publications, positioning it in the group of the most productive journals. Among the main publications in the journal is an article that analyses factors that are directly related to the production of oral cancer cells, for example, the consumption of tobaccoless paan leaves, oral submucosal fibrosis, smoking, alcohol use and chewing tobacco (Merchant et al., 2000).

Another journal that is positioned among the leading journals in terms of productivity and impact is the Journal of Oral Pathology and Medicine, with five publications and 263 citations. In this journal, relevant publications conclude that traditional behavioural risk factors are present in younger people diagnosed with oral cancer and that in women, risk factors differ from tobacco and alcohol consumption because of the relatively short duration of exposure and the number

of cases without identified or known risk factors (Llewellyn et al., 2004).

There are also journals that are positioned among those with the greatest scientific impact, based on the total number of citations, but do not have a high number of publications, for example, Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics, a journal that also published one of the main articles in the field of research (Miller and Johnstone, 1982), in which the relationship between OSCC and human papillomavirus is analysed.

Last, there is a group of journals that are positioned among those that highly disseminate knowledge about risk factors for oral cancer but do not, to date, have a high total number of citations. Among these is the Asian Pacific Journal of Cancer Prevention, with a total of seven publications, including some that analyse the way in which surviving polymorphisms are associated with the prevalence of oral squamous cell carcinoma and one that found that the male population in Asia is susceptible to oral cancer, mainly in the mucosa of the mouth (Mehdi et al., 2019).

Main countries

This section reports the main findings pertaining to the main countries that produce knowledge about risk factors for oral cancer, comparing the number of citations and publications on the topic (Fig. 5).

Figure 5. Main countries on oral cancer publications.
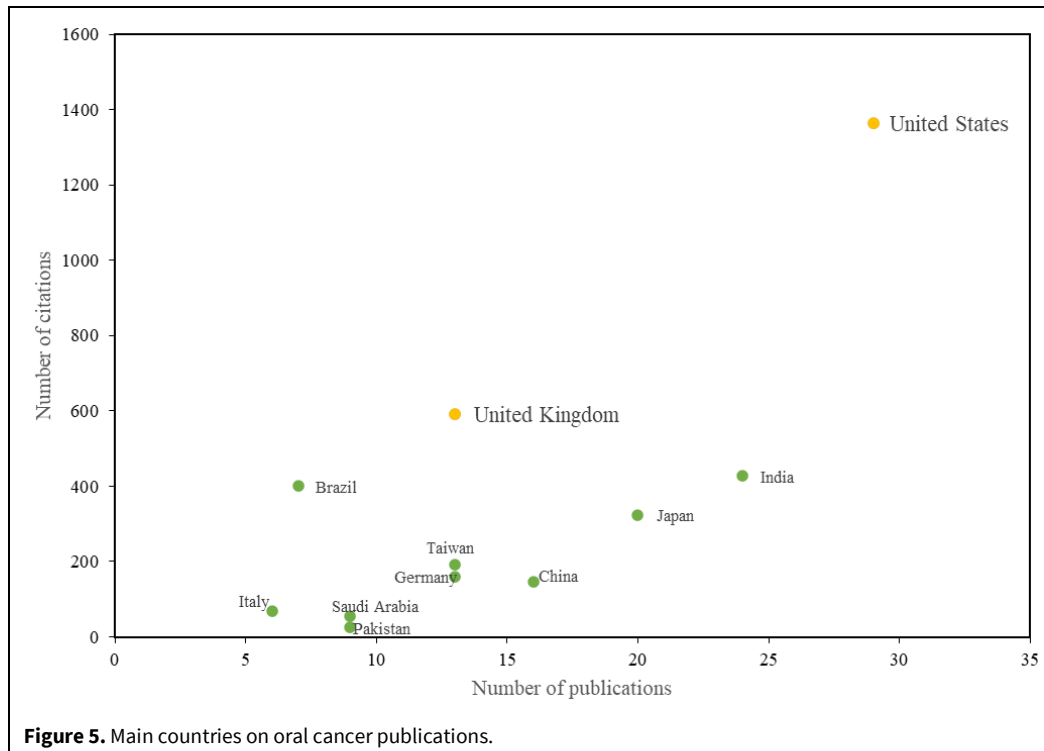
The leading country and reference in scientific production on the topic is the United States, with a total of 29 publications, making it the most productive country or the country with the greatest tendency to publish, and 1,364 citations, making it the country with the greatest impact on the scientific community. Among its most recent publications, there are some that analyse the way in which the high infusion rate of intraoperative colloids and previous radiotherapy may increase the risk of reoperation in patients who underwent oral squamous cell carcinoma surgery and vascularised free flap reconstruction (Fu et al., 2022).

Another of the main publications derived from the United States identified that performing chest CT or positron emission tomography before surgery in patients with two or more risk factors is useful for identifying patients with early distant metastasis (Cariati et al., 2021).

Among the same group of reference countries with regard to scientific production, the United Kingdom is also identified, with a total of 13 publications and 591 citations, positioning it as the country with the second-highest impact or scientific significance. In the context of this country, the most important publication is focused on the way in which specialised psycho-oncology services are important in the management of patients with oral cancer, addressing the mental health needs of the most vulnerable population, for which psychological interventions and medi-

cations were used to treat these patients (Mukherjee et al., 2022).

Another group of countries generated the most knowledge about risk factors for oral cancer despite not accounting for a significant number of citations, for example, India, which is the country with the second-most publications on the topic. Some studies have identified that the age of 45 years is significantly associated with oral cancer in patients with systematic lupus erythematosus and that apparent improvements in survival are obtained for patients with stage II cancers who underwent primary surgery (Thakar et al., 2021).

Thematic evolution

This bibliometric analysis allowed the identification of thematic or conceptual evolution in the scientific literature on oral cancer between 1995, the year in which the topic was consolidated, and the present (Fig. 6). Each highlighted keyword refers to the concept addressed most frequently in each year. In this sense, in 1995, studies focused mainly on sialic acid, with the purpose of analysing the risk factors that, according to Monaharan and Nagini (1995), alter the levels of glycoprotein in patients with oral cancer.

In recent years, as evidenced in the years 2019 and 2020, the topic was associated with the analysis of tobacco smokers and their relationship with oral cancer, as evidenced by Herrera-Serna et al. (2019), who analysed the effect of control measures in alcohol
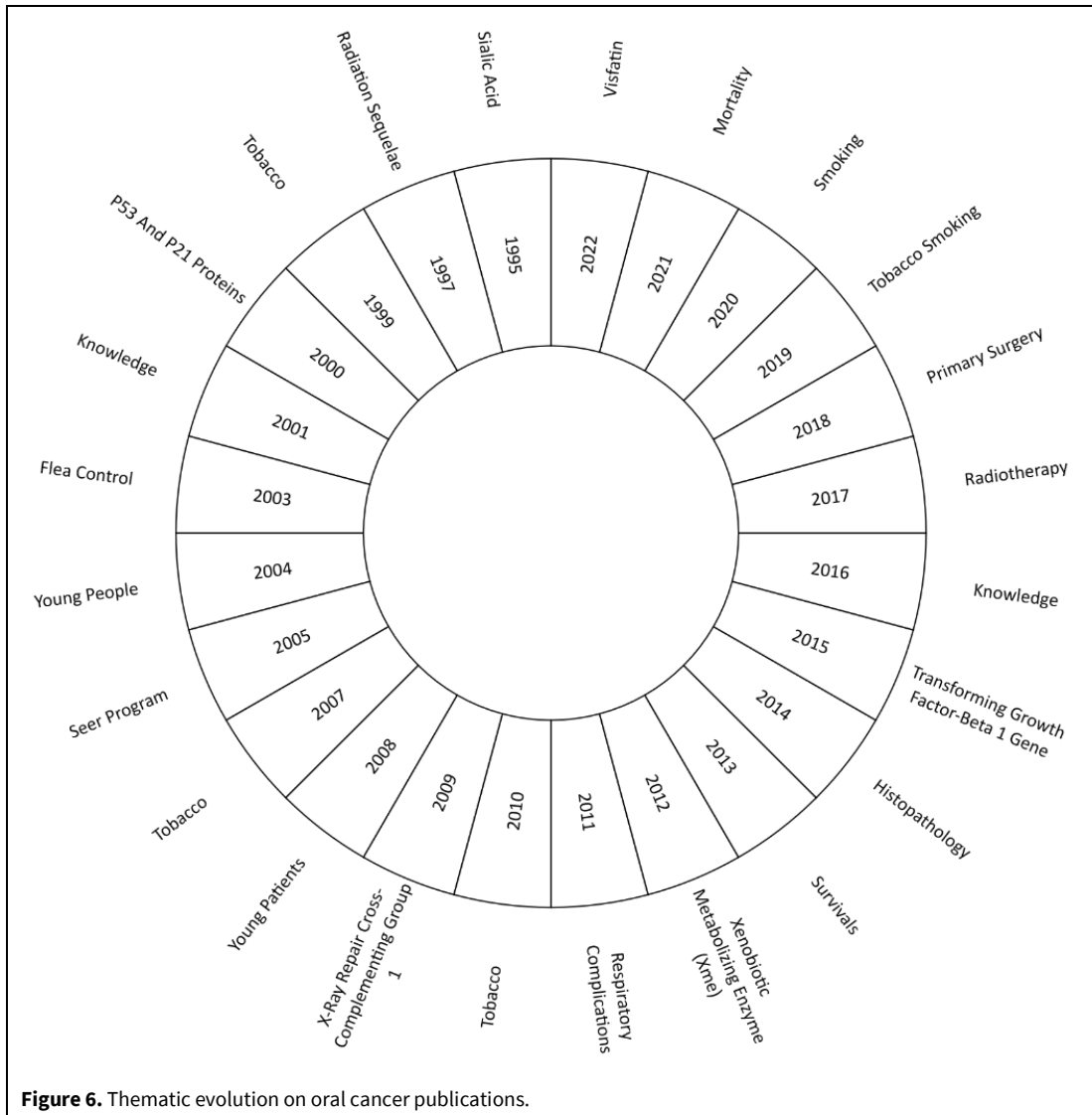
consumers and tobacco smokers on mortality associated with oral cancer in the Latin American context, and in Tenore et al. (2020), who indicate that tobacco is considered one of the main risk factors for developing oral squamous cell carcinoma (COCE) or oral cancer.
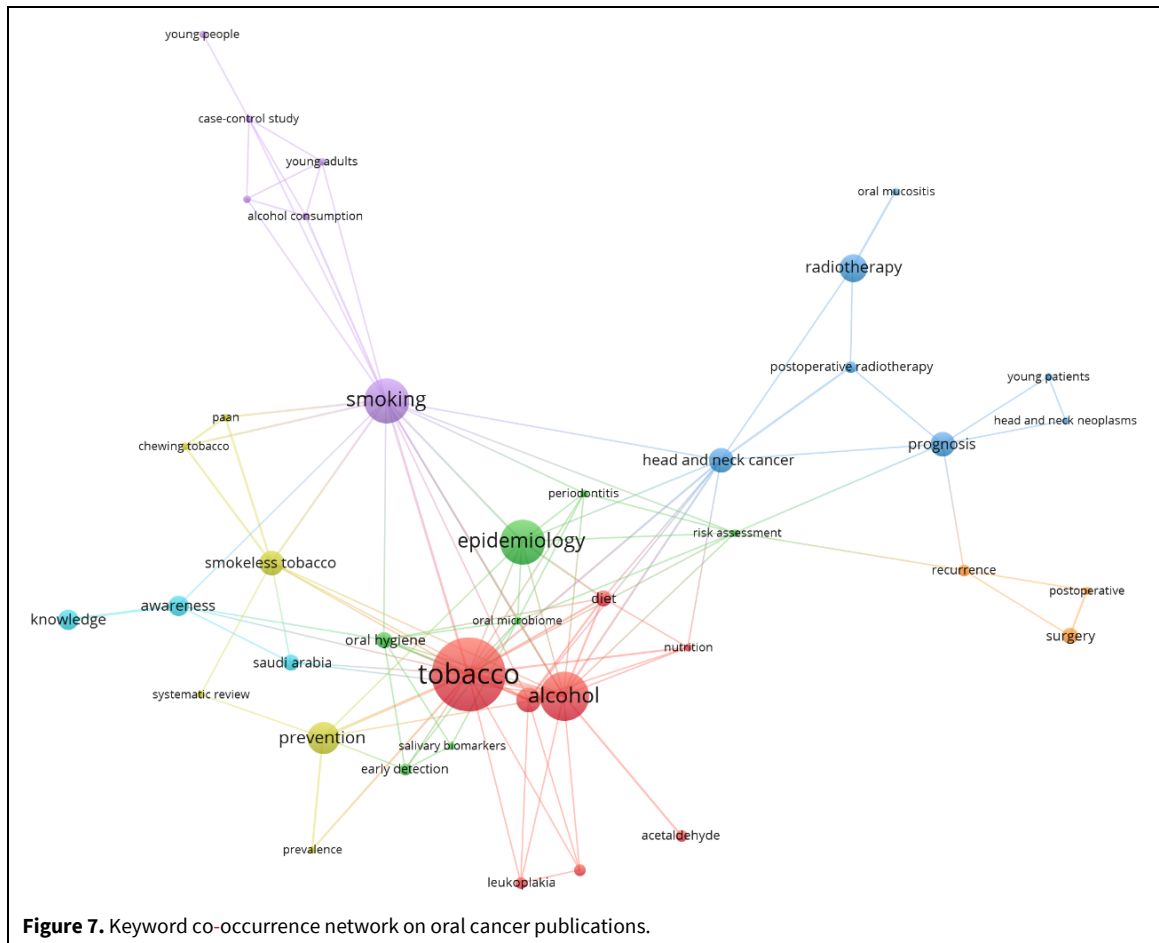
In 2021, one of the central concepts within the analysis of oral cancer, i.e., mortality, is widely addressed by the scientific literature, as evidenced in Yang et al. (2021), who identified an increase in mortality of 196.8% between 1990 and 2017 in the Chinese context. In 2022, the most relevant concept was visfatin (nicotinamide phosphoribosyltransferase), which, according to Chen et al. (2022), promotes accelerated tumour growth. Additionally, an association between high plasma levels of visfatin and OSCC was reported by Tsai et al. (2013).

Fig. 7 shows thematic associations in the main network of keyword co-occurrence, with a total of seven thematic clusters, categorised with a different colour, with the most relevant being the red thematic cluster, composed of concepts such as "tobacco", "alcohol", "acetaldehyde" and "leukoplakia", which have been directly associated with the development of oral leukoplakia from risk habits such as betel quid users, smokers and alcohol users in the context of countries such as Sri Lanka (Ariyawardana et al., 2007).

The second most relevant cluster in the scientific production on oral cancer is the purple cluster, composed of concepts such as "Smoking", "Alcohol consumption", "Young adults", "Case–control study "and" Young people ", associated together with research such as that by Neckel et al. (2020), who profiled young adults with oral cancer, whose risk can be pre-assessed based on symptoms such as secondary organ damage to the liver and lungs.

Figure 6. Thematic evolution on oral cancer publications.

Figure 7. Keyword co-occurrence network on oral cancer publications.

Another relevant thematic cluster in the keyword co-occurrence network is the dark blue cluster, composed of concepts such as "Head and neck cancer", "Prognosis", "Postoperative radiotherapy", and "Radiotherapy", among other concepts that shape a cluster that delves into aspects associated with the results of treatments performed on patients with OSCC who do not have pathological risk factors (Chen et al., 2013).

This bibliometric study analysed the frequency and validity of keywords from a Cartesian plane (Fig. 8) to understand the behaviour of the concepts that are positioned as relevant and emerging within the research field. This Cartesian plane measures, from the X-axis, the frequency of use of each concept, that is, the number of times a term is repeated, and the Y-axis evaluates the average year of use of these keywords, allowing the identification of validity or not within the scientific body.

Quadrant 4, where the most frequent and least current are positioned, indicates decreasing concepts, such as "Tobacco", which is the most used keyword within the scientific literature and has been previously identified as relevant in studies that detail the clinicopathological profiles for OSCC (Krishna et al.,

2014), as well as "Epidemiology", which has been evaluated from retrospective observational studies (Capote-Moreno et al., 2020).

Quadrant 3 indicates the least frequent and current keywords in the scientific literature, being relevant for the critical analysis of the omission of concepts in future research agendas, and includes concepts such as "Metastasis", "Betel quid", "Diet", "Surgery", "Polymorphism", "Health education", "Postoperative radiotherapy" and "Prognosis".

Quadrant 2 contains rare concepts but those that are positioned among the most current from their average year of use; therefore, they are considered emerging keywords in the field, including concepts such as "mortality", which was introduced to the field of research in 2021 in studies that analyse the risk factors associated with mortality rates in patients with ICC (Ahmad et al., 2021); "head and neck", referring to patients with head and neck cancer who have undergone prospective evaluations of risk factors for postoperative dysphagia (Hasegawa et al., 2021); and other emerging concepts such as "alcohol consumption", "awareness", "diagnosis" and "prevention", among others.
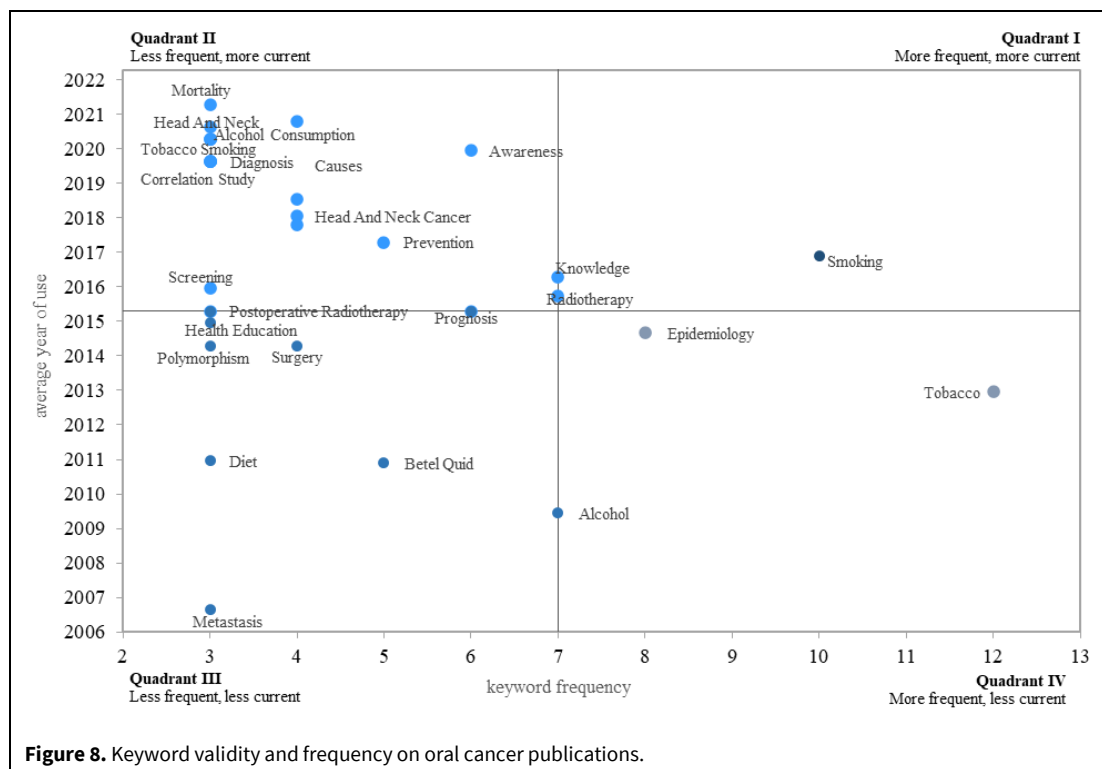
Figure 8. Keyword validity and frequency on oral cancer publications.

Quadrant 1 contains the most frequent and current concepts in the research field, concepts that are considered increasing. This quadrant, for the literature on oral cancer, only contains "smoking", which is positioned among the main studies on the topic, for example in Cheong et al. (2009), who claim that gene expression in OSCC is influenced by exposure to risk factors, i.e. smoking, and in other recent studies, in which it is questioned whether the only way to reduce the burden of the disease is to reduce exposure to avoidable risk factors (Subash et al., 2022).

Finally, this research concludes with an analysis of the research agenda to guide future research (Fig. 9), initially positioning the 30 concepts that have been most used in the scientific literature on oral cancer in the selected databases.

Although concepts such as betel quid, surgery and metastasis are positioned among the most common concepts and among those that have been analysed across a longer time period, they are not academically relevant in terms of recent research because their most relevant years occur much earlier and they have not been specifically addressed at least in the last three years, a finding that is consistent with the previous graph.

Although the concepts of alcohol consumption and mortality are important in terms of frequency, they are considered among two of the main emerging concepts in the field of oral cancer research in recent years; therefore, future research should analyse the topic from new perspectives that can strengthen the current knowledge about oral cancer and allow clinicians and patients to make new and better decisions in terms of health.

Other rare but emerging concepts are evident in the field of research and could expand in future studies on the topic, for example, the causes of oral cancer, the use of correlational studies in different populations, the analysis of the frequency of disease contraction and the processes of disease diagnosis.

It is evident that concepts such as epidemiology, radiotherapy, prevention, health education, diet and tobacco smokers, which, although not highly prominent in the last five years, are well-positioned and, from new findings or new perspectives, may be among the most important concepts in the near future.

To further explore the research agenda, it is essential to consider the role of genetics and molecular biology in oral cancer predisposition. Concepts such as "polymorphism" and "gene expression" have emerged as key areas in the study of risk factors. Investigation of the genetic variants associated with oral cancer susceptibility and how these interact with environmental factors could provide a more complete understanding of aetiology and allow the development of personalised approaches to prevention and treatment.

Figure 9. Research agenda on oral cancer publications.
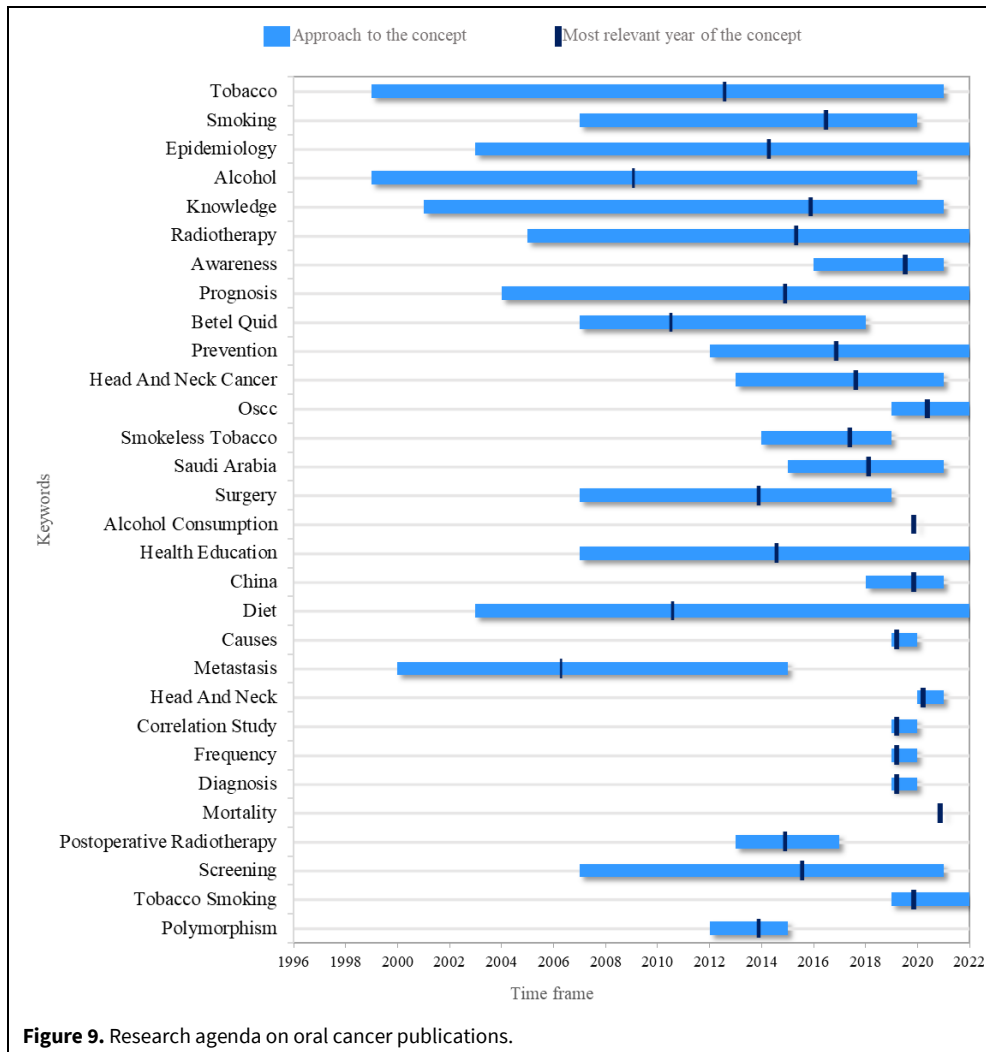
The link between oral cancer and the environment also deserves further attention. For example, the relationship between exposure to ultraviolet radiation and oral disease could be further investigated. "Ultraviolet radiation is an emerging concept that may indicate the need to investigate how solar radiation and other sources of ultraviolet radiation exposure may contribute to the risk of developing oral cancer, particularly in geographic regions with high solar exposure.

The relationship between immunosuppression and oral cancer also merits further analysis. "Immunosuppression" has positioned itself as an emerging concept, suggesting that more extensive research could explore how weakened immunity influences the development and progression of oral cancer. These studies could shed light on the interaction between the immune system and the disease and how boosting the immune response could be an effective strategy in disease management.

Finally, combining the various recommendations and exploring new concepts will allow for a more comprehensive and advanced approach to oral cancer risk factor research. By considering the connections between seemingly disparate concepts and exploring less-studied areas, the scientific community may be better equipped to address the challenges posed by this disease and contribute to the development of more effective prevention, diagnosis, and treatment strategies.

Study limitations

Despite the significant advances made in this bibliometric study of oral cancer risk factors, it is important to highlight certain inherent limitations of the study. First, the data collection was based on the Scopus and Web of Science databases, which may introduce an inclusion bias, as other relevant sources may have been omitted. Although these databases were selected because of their recognised authority in the scientific literature, it is possible that some relevant

contributions are present in other sources that were not considered.

In addition, the bibliometric methodology is based on previously published data, which could introduce a temporal bias. The analysis of keyword frequency and validity reflects the evolution of concepts over time, but does not take into account the possibility that some emerging terms have not yet been widely adopted in the literature. This may lead to an underrepresentation of truly novel concepts that have not yet achieved wide diffusion.

A more specific limitation relates to the automated process of risk of bias assessment and data collection. Although an automated Microsoft Excel®-based tool was used to assess the risk of bias in the studies and to process the data, this automation may have missed subtle or contextual aspects that a manual approach might have captured. The complexity of some bias assessments, particularly in a bibliometric context, may have required additional human review.

Finally, it is important to consider that the terms used in the search and inclusion of studies may introduce a degree of subjectivity. Although efforts were made to be inclusive and precise in the selection of terms and inclusion criteria, the interpretation of terms and the application of criteria may vary between investigators. This may introduce an element of subjectivity into the collection and interpretation of data.

CONCLUSION

Based on the results obtained, the authors with the greatest tendency to publish on risk factors for oral cancer are Hasegawa T, Scully C and Johnson NW, with the latter being the most relevant in terms of the greatest impact in the scientific literature and the main research reference.

Oral Oncology is the main reference in terms of scientific dissemination of risk factors for oral cancer, having published the most scientific articles on the subject. The International Journal of Cancer has the second most citations in the field and is now the seventh most productive journal.

Research on risk factors for oral cancer has materialised mainly in the context of developed countries such as the United States, Japan, China or the United Kingdom, with Brazil being the only Latin American representative among the countries most frequently producing knowledge on the topic, as well as the fourth most cited, indicating the scope of this research field in the Latin American context. Future research should expand the volume of publications regarding risk factors for a context with different demographic,

geographical and cultural characteristics, among others.

The scientific literature on risk factors for oral cancer has been presented in a relatively uniform way, where the most relevant topic in one of the first years was tobacco, which is still widely investigated today, being the most important topic in 1999, 2007, 2010 and 2019. Its continuation as a relevant topic indicates the validity and importance of the analysis of this risk factor in the face of one of the most analysed concepts in recent years, i.e., mortality associated with this subtype of cancer.

Future researchers should expand existing knowledge through detailed analyses of other main risk factors, such as alcohol consumption and its relevance in terms of mortality in the consuming population, and through the use of correlational comparative techniques that measure disease frequencies and that analyse exposure to risk factors and diagnostic processes, so as to understand the complexities and scope of the diagnosis and treatment of oral cancer.

According to the thematic evolution, by 2022, the concept of adipokine visfatin has been introduced; studies based on its four polymorphisms (rs11977021, rs61330082, rs2110385 and rs4730153) should be conducted as some genes of the rs11977021 genetic variant are associated with a greater risk of developing OSCC and other sequence variations such as the GA allele of the rs4730153 polymorphism are associated with lymph node metastases, as in betel nut chewers.

Finally, other leading concepts for the future are epidemiology, radiotherapy, prevention, health education and diet.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ACKNOWLEDGMENTS

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Contribution	Pérez-Delgado O	Millones-Gómez PA	Valencia-Arias A	Rodríguez-Salazar DY
Concepts or ideas	x			
Design			x	
Definition of intellectual content		x		x
Literature search	x		x	
Experimental studies				
Data acquisition	x	x		
Data analysis	x	x	x	
Statistical analysis				x
Manuscript preparation	x	x	x	x
Manuscript editing	x		x	
Manuscript review	x	x	x	x