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**FATORES ASSOCIADOS AO TEMPO PARA O INÍCIO DO
TRATAMENTO DO CÂNCER DE BOCA E OROFARINGE**

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Débora Rosana Alves Braga Silva Montagnoli

FATORES ASSOCIADOS AO TEMPO PARA O INÍCIO DO TRATAMENTO DO CÂNCER DE BOCA E OROFARINGE

Tese apresentada ao Colegiado de Pós-Graduação em Odontologia da Faculdade de Odontologia da Universidade Federal de Minas Gerais, como requisito parcial à obtenção do grau de Doutor em Odontologia- área de concentração em Saúde Coletiva.

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Coorientador: Prof. Dr. Mauro Henrique Nogueira Guimarães de Abreu

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FATORES ASSOCIADOS AO TEMPO PARA O INÍCIO DO TRATAMENTO DO CÂNCER DE BOCA E OROFARINGE

DÉBORA ROSANA ALVES BRAGA SILVA MONTAGNOLI

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“...Bom mesmo é ser um realista esperançoso.”

Ariano Suassuna

RESUMO

Três estudos foram desenvolvidos com intuito de entender os fatores envolvidos no tempo para o tratamento do câncer de boca e orofaringe (CBO), especialmente no Brasil. O primeiro objetivou identificar associação entre fatores socioeconômicos e atraso do tratamento do CBO através de uma revisão sistemática (RS). O segundo propôs investigar os fatores que explicam o tempo para início do tratamento (TIT) do CBO nos municípios brasileiros. O terceiro analisou a tendência temporal dos registros de CBO de 2019 a 2023 e fatores que impactaram o TIT. Para RS, estudos observacionais foram pesquisados em cinco bases de dados e literatura cinzenta, sem restrições de idioma ou ano de publicação. A ferramenta do Instituto *Joanna Briggs* avaliou o risco de viés. O atraso foi definido pelos pontos de corte dos estudos incluídos. A abordagem *Grading of Recommendations Assessment, Development, and Evaluation* (GRADE) avaliou a certeza da evidência. No segundo estudo, dados dos municípios que registraram casos de CBO em 2019 foram coletados do Painel-Oncologia e de outras plataformas públicas. Utilizou-se Árvores de Classificação e Regressão-CART para analisar associações entre TIT e variáveis explicativas, agrupadas nas dimensões: características dos pacientes, acesso aos serviços de saúde, estrutura de apoio diagnóstico do câncer, recursos humanos e características municipais. No terceiro estudo, realizou-se análise de séries temporais dos registros de CBO utilizando os testes *Box-Ljung*, *Sen's Slope* e *Mann-Kendall*. A cointegração entre TIT<30 dias ou TIT>30 dias e as variáveis independentes foi avaliada pelo teste de *Engle-Granger* e a qualidade dos modelos pelo teste de *Breusch-Godfrey*. O Artigo I incluiu 10 estudos de coorte. Tipo de plano de saúde, sexo, pacientes ≥60 anos, não-brancos, baixa escolaridade, tratamento em hospital público ou regional, necessidade de encaminhamentos e residência em áreas regionais/remotas foram fatores associados ao atraso do tratamento do CBO. Todavia, limitações metodológicas quanto ao ajuste para fatores de confusão, heterogeneidades da definição de atraso e das variáveis socioeconômicas e a falta de estudos de diferentes países resultaram em uma certeza muito baixa da evidência com graves problemas de viés, inconsistência e evidência indireta. O Artigo II mostrou que tipo de tratamento (quimioterapia, radioterapia ou ambos), tumores em cavidade oral e orofaringe e número de serviços de tomografia computadorizada por 100 mil habitantes foram preditores do maior TIT nos municípios. O Artigo III revelou tendência crescente do total de registros de CBO de 2019 a 2023, especialmente nas séries de sexo e faixa etária. As regiões Norte e Nordeste apresentaram tendência de aumento do TIT>30 dias. Sexo masculino, idade acima de 60 anos, estágios avançados, radioterapia e região Sudeste contribuíram com TIT>30 dias. A série de tratamentos cirúrgicos contribuiu mais fortemente com registros TIT≤30 dias. A associação entre fatores socioeconômicos e o atraso no tratamento do CBO permanece inconclusiva pelos dados disponíveis. Pesquisas adicionais são recomendadas em diferentes países, principalmente no Brasil. Os achados dos Artigos II e III denotam permanente necessidade de ampliação das ações de diagnóstico e da disponibilidade de serviços oncológicos para que o tratamento do CBO ocorra em tempo oportuno.

Palavras-chave: neoplasias bucais; neoplasias orofaríngeas; tempo para o tratamento; atraso no tratamento.

ABSTRACT

Factors associated with time to start treatment for oral and oropharyngeal cancer.

Three studies were carried out in order to understand the factors involved in time to start treatment of oral and oropharyngeal cancer (OOC), especially in Brazil. The first aimed to identify the association between socioeconomic factors and delay in OOC treatment through a systematic review (SR). The second set out to investigate the factors that explained the time to treatment initiation (TTI) for OOC in Brazilian municipalities. The third aimed to analyze the temporal trend of OOC records from 2019 to 2023 and factors that impacted TTI. For SR, observational studies were searched in five databases and gray literature, with no restrictions on language or year of publication. The Joanna Briggs Institute tool assessed the risk of bias. The delay was defined by the cut-off points of the included studies. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach assessed the certainty of the evidence. In the second study, data from municipalities that registered cases of OOC in 2019 were collected from the Panel-Oncology and other public platforms. Classification and Regression Trees (CART) were used to analyze associations between TTI and explanatory variables, grouped into five dimensions: patient characteristics, access to health services, cancer diagnosis support structure, human resources, and municipal characteristics. In the third study, a time series analysis of OOC records was carried out using the Box-Ljung, Sen's Slope and Mann-Kendall tests. Cointegration between $TTI < 30$ days or $TTI > 30$ days and the independent variables was assessed using the Engle-Granger test, and the quality of the models was assessed using the Breusch-Godfrey test. Article I included 10 cohort studies. Type of health insurance, gender, elderly, non-white patients, low schooling, treatment in a public or regional hospital, need for referrals, and residence in regional/remote areas were factors associated with the treatment delay of OOC. However, methodological limitations in terms of adjusting for confounding factors, heterogeneities in the definition of delay and socioeconomic variables, and the lack of studies from different countries resulted in very low certainty of the evidence with serious problems of bias, inconsistency, and indirect evidence. Article II showed that the type of treatment (chemotherapy, radiotherapy or both), tumors in the oral cavity and oropharynx, and the number of computed tomography services per 100,000 inhabitants were predictors of higher TTI in the municipalities. Article III revealed an upward trend in total OOC records from 2019 to 2023, especially in the sex and age group series. The North and Northeast regions showed an upward trend in $TTI > 30$ days. Male, aged over 60 years, advanced stages, radiotherapy, and the Southeast region contributed to $TTI > 30$ days. Records of surgery contributed most strongly to $TTI \leq 30$ days. The association between socioeconomic factors and delay in treatment of OOC remains inconclusive from the available data. Further research is recommended in different countries, especially in Brazil. The findings of Articles II and III show that there is a permanent need to expand early diagnosis actions and the availability of oncology services so that OOC treatment can take place promptly.

Keywords: mouth neoplasms, oropharyngeal neoplasms, time to treatment, treatment delay.

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LISTA DE ABREVIATURAS E SIGLAS

ARIMA	<i>Auto Regressive Integrated Moving Average</i>
APS	Atenção Primária à Saúde
AS	Acesso aos Serviços de Saúde
BHU	<i>Basic Health Units</i>
CACONS	Centros Oncológicos de Alta Complexidade
CART	<i>Classification and Regression Trees</i>
CBO	Câncer de Boca e Orofaringe
CEC	Carcinoma de Células Escamosas
CEO	Centro de Especialidades Odontológicas
CHAID	<i>Chi-square Automatic Interaction Detection</i>
CID-10	Classificação Internacional de Doenças-10ª Revisão
CM	Características Municipais
CP	Características do Paciente
CS	<i>Cancer Diagnosis Support</i>
DATASUS	Departamento de Informática do SUS
DSC	<i>Dental Specialties Centers</i>
EC	Estrutura de Apoio ao Diagnóstico de Câncer
GLOBOCAN	<i>Global Cancer Observatory</i>
GRADE	<i>Grading of Recommendations Assessment, Development, and Evaluation</i>
HCN	<i>Health Care Network</i>
HPV	Papiloma Vírus Humano
HR	<i>Human resources</i>
IBGE	Instituto Brasileiro de Geografia e Estatística
IDH	Índice de Desenvolvimento Humano
ICD	<i>International Classification of Diseases</i>
JBH	<i>Joanna Briggs Institute</i>
MC	Municipal Characteristics
NCDB	<i>National Cancer Database</i>
OHT	<i>Oral Health Teams</i>
OOC	<i>Oral and Oropharyngeal Cancers</i>

OOSCC	<i>Oral and Oropharyngeal Squamous Cell Carcinoma</i>
OR	<i>Odds Ratios</i>
PC	<i>Patient Characteristics</i>
PHC	<i>Primary Health Care</i>
PNSB	Política Nacional de Saúde Bucal
PRISMA	<i>Preferred Reporting Items for Systematic Reviews and Meta-Analyses</i>
PROSPERO	<i>International Prospective Register of Systematic Reviews</i>
RAS	Rede de Atenção à Saúde
RH	Recursos Humanos
Siscan	Sistema de Informação do Câncer
SPSS	<i>Statistical Package for Social Sciences</i>
SUS	Sistema Único de Saúde
TIT	Tempo até o Início do Tratamento
TTI	<i>Time to Treatment Initiation</i>
UBS	Unidades Básicas de Saúde
UNACONS	Unidades Oncológicas de Alta Complexidade
US	<i>United States</i>

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1 CONSIDERAÇÕES INICIAIS

O câncer de boca e orofaringe (CBO) é uma doença grave e que gera sérias preocupações para os sistemas de saúde em diversos países. Primeiro porque é uma neoplasia com incidência crescente (Wu *et al.*, 2025). Segundo, porque a mortalidade ainda é alta em muitas populações (Wu *et al.*, 2025). Terceiro, porque, ao afetar a face, pode acarretar impactos físicos irremediáveis que levam à baixa qualidade de vida, com prejuízos ao reestabelecimento social dos pacientes, uma vez que as sequelas deixadas por alguns tratamentos interferem em perdas de identidade social, oportunidades, ruptura de laços sociais e deterioração emocional (Schoonbeek *et al.*, 2022, Yuwanati *et al.*, 2021).

O Brasil é o segundo com maior incidência e mortalidade quando comparado aos países da América Latina e Caribe (Serna *et al.*, 2022). A realidade pode parecer mais dramática quando se fala de um tipo de câncer evitável: a maioria dos casos localizados na cavidade oral está relacionada ao consumo de tabaco e álcool (Warnakulasuriya *et al.*, 2009). A vacina contra o papiloma vírus humano (HPV), um dos principais agentes etiológicos do câncer de orofaringe, já existe e é disponibilizada pelo Sistema Único de Saúde (SUS) (Santos; Santos; Fernandes, 2023). Logo, o caminho para o controle dos principais fatores de risco já está posto e aplainado. As estratégias para chegar à redução de novos casos só precisam ser efetivas.

Grande parte dessa alta mortalidade é explicada pela maioria dos estágios avançados na apresentação, ou seja, pelo diagnóstico tardio (Menezes *et al.*, 2020). Mesmo quando o diagnóstico acontece em fases da doença possíveis de serem resolvidas apenas por tratamentos cirúrgicos (Tirelli *et al.*, 2023), esperas por exames complementares, por vagas de internação em hospitais que disponham de equipes especializadas e a necessidade de cuidados multidisciplinares, por exemplo, geram hiatos dentro da rede de cuidados. Enquanto isso, o tumor progride, tornando-se mais invasivo e de difícil manejo (Varghese *et al.*, 2020).

Portanto, a lógica de efeitos deletérios dos atrasos no cuidado à pessoa com CBO se apresenta em cadeia: atrasos do diagnóstico levam a estágios avançados que necessitam de terapias mais complexas, demandando mais tempo para o início do tratamento, ao passo que vai reduzindo significativamente as chances de sobrevida. Sabendo-se da relatividade do tempo e, com isso, do que pode ser

definido como “atraso”, estudos mostram que o início do tratamento 30 dias após o diagnóstico afeta sobremaneira a sobrevida (Murphy *et al.*, 2015, Tsai *et al.*, 2017, Su *et al.*, 2021)

O que foi até aqui exposto já justificaria, por si, a proposta do presente objeto em tese. Ainda assim, consente-se acatar o seguinte questionamento: Por que estudar especificamente o tempo para o início do tratamento do CBO?

Muito tem se falado sobre as causas que levam ao atraso do diagnóstico do câncer bucal. Fatores do paciente, especialmente ligados ao desprezo dos primeiros sinais e sintomas (lesões inicialmente pequenas, pouco percebidas se não há uma investigação cautelosa, indolores e indolentes), o sentimento de negação acerca da gravidade da doença e tentativas de automedicação adiam a decisão por buscar ajuda profissional (Lima *et al.*, 2021). Além disso, existe o atraso relacionado ao profissional que, por debilidade técnica para identificar lesões com potencial malignidade e formalizar os encaminhamentos necessários, alongam o tempo de tomada de decisões pela falta de um diagnóstico acertado e definitivo (Güneri; Epstein, 2014).

Os sentidos que alteram o tempo para o diagnóstico, por mais que incluam certo grau de subjetividade e decisões dos atores envolvidos, conferindo complexidade para contorná-los, perpassa por um ponto em comum: o conhecimento acerca do CBO (Güneri; Epstein, 2014, Lima *et al.*, 2021). Então, quanto mais se falar sobre a existência do CBO e sobre as formas de controle, seja por meio de comunicação científica adequada ao público-alvo como através do aperfeiçoamento dos currículos das graduações de Odontologia, maiores serão as chances de reduzir este lapso. Isso é possível, uma vez que os benefícios do saber sobre a doença foram demonstrados em maior empenho na triagem de pacientes (Warnakulasuriya; Kerr, 2021, Mavedatnia *et al.*, 2023).

Agora, no tocante ao tempo para o tratamento, surge a inevitabilidade de olhares para questões mais amplas. Isso porque o atraso das terapias, além da influência dos aspectos supracitados de atraso do diagnóstico, envolve o contexto social, político e econômico onde o paciente e o sistema de saúde estão inseridos (Weller *et al.*, 2012, Alcaraz *et al.*, 2020). Ou seja, o paciente já foi diagnosticado e, nesse momento da sua trajetória clínica, encontra-se dependente de decisões e regulações do sistema de saúde, especificamente, da disponibilidade de programas,

de serviços e de profissionais qualificados para atuarem no cuidado, bem como da acessibilidade a todos eles (Güneri; Epstein, 2014).

A maioria dos casos de CBO brasileiros encontram-se em condições socioeconômicas desfavoráveis e são dependentes do SUS (da Conceição *et al.*, 2021, Affonso *et al.*, 2022, Pereira *et al.*, 2023). A profunda desigualdade social que o país apresenta reflete a forma heterogênea que as políticas públicas de saúde são implementadas nas diferentes localidades do país (Thomaz *et al.*, 2022, Costa *et al.*, 2023, Pereira *et al.*, 2023). Portanto, pessoas em situação de vulnerabilidade, ao mesmo tempo que estão mais expostas aos fatores que levam ao adoecimento pelo CBO, podem experimentar os impactos mais negativos da doença pela dificuldade de acesso aos serviços de saúde (Lins *et al.*, 2019, Herrera-Serna *et al.*, 2019).

O impacto das disparidades socioeconômicas no atraso do tratamento de vários tipos de câncer foi demonstrado (Emerson *et al.*, 2020, Obrochta *et al.*, 2021, Wagle *et al.*, 2023, Bajwa *et al.*, 2022). Essas evidências são raras para CBO, mas pode-se presumir que esse tipo de câncer não seja exceção. É importante investigar a associação entre os determinantes sociais da saúde relacionados às condições de vida da população e a prestação de serviços de saúde. A possibilidade de entender elementos que implicam nos prazos para tratamento no Brasil cria oportunidades para ajudar a formular estratégias de resolutividade do CBO em tempo hábil, especialmente entre os que mais precisam.

2 REVISÃO DE LITERATURA

2.1 Epidemiologia e determinantes sociais do câncer de boca e orofaringe

O câncer de boca e orofaringe (CBO) representa um desafio contínuo para os sistemas de saúde. O envelhecimento populacional e mudanças comportamentais e ambientais têm influenciado o notável aumento dessa neoplasia maligna em muitos países (Menezes *et al.*, 2020, El-Naggar *et al.*, 2017, Wu *et al.*, 2025). Da mesma forma, tendência ascendente da taxa de mortalidade global tem sido percebida nos últimos anos (Wu *et al.*, 2025).

Segundo as últimas estimativas do Observatório Global do Câncer (GLOBOCAN), foram relatados 389.846 novos casos de câncer de lábio e de cavidade oral em 2022. Também ocorreram 188.438 mortes, fazendo com que este tipo de neoplasia maligna ocupasse a 15ª posição na mortalidade média global. A maioria desses registros se concentram em regiões da Melanésia (Papua Nova Guiné, com a maior taxa de incidência do mundo) e do Sudeste Asiático (Bangladesh, Índia, Paquistão e Sri Lanka) (Sun *et al.*, 2021, Who, 2025). Em relação ao câncer de orofaringe, ocorreram 106.400 e 52.305 mortes no mesmo ano. Maior proporção da incidência e mortalidade foi identificada em países europeus (Who, 2025).

O Brasil se destaca pela alta incidência de CBO em sua população. Estima-se mais de 15.000 novos casos, por ano, para o triênio 2023-2025, sendo o oitavo tipo de câncer mais frequente (Santos *et al.*, 2023). Foram previstos 10,30 casos novos a cada 100 mil homens, perfazendo o sexto tipo de câncer mais comum nesse grupo, e 3,83 a cada 100 mil mulheres (Santos *et al.*, 2023). No cenário global, encontra-se entre os países com maiores taxas de incidência e de mortalidade ajustadas por idade (Who, 2025). Chama mais atenção o fato de ser o décimo sexto no mundo em mortalidade por câncer de orofaringe, especificamente (Who, 2025).

O envolvimento dos cirurgiões-dentistas no diagnóstico e no tratamento do CBO é essencial por se tratar de uma neoplasia maligna que pode se manifestar em lábios, língua, gengiva, assoalho da boca, glândulas parótidas e salivares, mucosa jugal, palato e orofaringe (Peres *et al.*, 2019, Miranda-Filho; Bray, 2020). O carcinoma de células escamosas é o principal tipo histológico, presente em cerca de 90% dos casos, com distintos níveis de diferenciação e propensão para metástases linfonodais (Rivera, 2015, Warnakulasuriya, 2009, Varghese; Rajan, 2020). Os sítios anatômicos

mais comumente afetados abrangem a face lateral da língua, assoalho da boca e mucosa jugal (Das; Sarkar, 2023).

Quanto ao prognóstico, é esperado que quando diagnosticado em estágio I e II as chances de cura sejam de 80% e 65%, respectivamente (Abati *et al.*, 2020, Güneri; Epstein, 2014). Já para a maioria dos casos, que se apresentam em estágios avançados da doença (III ou IV), a sobrevida em cinco anos fica em torno de 50% e a taxa de cura em 30% (Dantas *et al.*, 2016, Bonfante *et al.*, 2014, Güneri; Epstein, 2014). Pacientes com doença metastática, que não são tratados, demonstram sobrevida de cerca de quatro meses (Kowalski; Carvalho, 2000). Um estudo brasileiro mais recente, destacou taxa de sobrevivência de cinco anos em torno de 74% para pacientes diagnosticados em estágio I ou II e apenas 36,2% para pacientes no estágio III ou IV (Tan *et al.*, 2023), denotando que as estimativas de sobrevida podem variar entre países.

A cirurgia é a modalidade terapêutica mais recomendada, quando possível, para tratamento do CBO (Nandini *et al.*, 2020). O principal objetivo é a ressecção completa do tumor com margem adequada, cuja análise pode ser usada como fator prognóstico e predizer a terapia que deverá ser adotada a posteriori (Aaboubout; Hove; Smits, 2021). A radioterapia pós-operatória adjuvante é indicada para pacientes com doença em estágio III ou IV, com margens inadequadas e invasões perineurais, linfovasculares e/ou ósseas (Huang *et al.*, 2020). A radioterapia também pode ser recomendada como tratamento inicial por questões de inoperabilidade médica, quando há tentativa de preservação de estruturas (Hosni *et al.*, 2021) e em situações que se devem levar em conta os fatores do paciente, tais como: comorbidades, idade avançada ou recusa à cirurgia devido ao risco de deformidades faciais pós-operatórias e dificuldades para comer, deglutir e falar (Wang *et al.*, 2020). A quimioterapia também pode estar indicada em diferentes momentos do tratamento de CBO: como terapêutica primária quando a cirurgia não é possível; como quimioterapia de indução antes do tratamento definitivo; como terapia adjuvante pós-operatória; ou concomitante à radioterapia (Pfister *et al.*, 2024).

O CBO é duas a quatro vezes mais prevalente no sexo masculino, na maioria dos grupos étnicos (Akashanand *et al.*, 2024, Zhang *et al.*, 2024), com exceção da África Subsaariana Ocidental e da América Latina Andina, onde a taxa de incidência entre mulheres é maior (Wu *et al.*, 2025). Importante ressaltar que tendência de aumento do câncer de boca entre mulheres já foi encontrada em outras

populações de países europeus e do Japão (Miranda-Filho; Bray, 2020). No Irã também foi demonstrada taxa de incidência mais ascendente desta neoplasia no sexo feminino quando avaliado o período de 1990 a 2019 (Roghanizadeh *et al.*, 2025).

A faixa etária predominantemente acometida está entre a quarta e a sétima décadas de vida (NIH, 2020, Lins *et al.*, 2019, Dhanuthai *et al.*, 2018, Yu *et al.*, 2024, WHO, 2025). Todavia, pesquisadores alertam para estimativas de maior aumento entre os mais jovens (<40 anos) (Gangane *et al.*, 2024).

O uso de tabaco (com ou sem fumaça) (Hecht; Hatsukami, 2022), o consumo de noz de areca/bétel (em comunidades asiáticas) (Yang, 2025), bem como o uso contínuo de bebidas alcoólicas (Guidolin *et al.*, 2021) ainda constituem os principais fatores de risco para o desenvolvimento de lesões malignas ou potencialmente malignas da cavidade oral (Bezerra *et al.*, 2018, Conway; Purkayastha; Chestnutt, 2018, Chatuverdi *et al.*, 2019, Guidolin *et al.*, 2021). A infecção pelo papiloma vírus humano (HPV) é responsável pelo aumento de incidência do câncer de orofaringe (Menezes *et al.*, 2020).

Outros aspectos, tais como, a exposição excessiva à radiação solar (em casos de cânceres localizados em lábio), dieta de baixo valor nutricional, excesso de gordura corporal, fatores genéticos (imunossupressão) e epigenéticos também fazem parte da complexa etiologia do CBO (Conway *et al.*, 2018, Miranda-Filho; Bray, 2020, Tran *et al.*, 2024, Xu *et al.*, 2025). Além disso, riscos ocupacionais, nomeadamente, a exposição excessiva à radiação e a agentes tóxicos (como dióxido de enxofre, amianto, pesticidas, névoas de ácidos inorgânicos e queima de combustíveis fósseis, solventes clorados ou solventes oxigenados) já foram relatados como coadjuvantes em casos de câncer localizados em sítios da cavidade oral, glândulas salivares e orofaringe (Kumar *et al.*, 2016, Awan *et al.*, 2018, Carton *et al.*, 2017, Moirangthem *et al.*, 2024). Ao mesmo tempo, o longo período de desemprego foi relatado como um fator que aumenta o risco de câncer bucal em 2,9 vezes (Greenwood *et al.*, 2003).

Atualmente, esforços ainda estão sendo empenhados para descobertas acerca das causas do câncer bucal em pessoas cada vez mais jovens. Com perfis clínicos singulares, os fatores de risco comumente identificáveis não estão presentes nesse subconjunto de pacientes: não fumam e não bebem, (Hussein *et al.*, 2017), a maioria são mulheres (DeAngelis *et al.*, 2018, Harada *et al.*, 2023) e a língua é o sítio anatômico mais acometido (Tran *et al.*, 2023, Harada *et al.*, 2023).

A infecção por vírus como Epstein-Barr (She *et al.*, 2017) e o próprio HPV (Menezes *et al.*, 2020), anemia de Fanconi (Beddok *et al.*, 2020), composição do microbioma oral (Ganly *et al.*, 2019) e o uso de maconha (Houle; Callahan, 2020) foram levantados como possíveis etiologias. Além disso, pesquisas já destacaram a complexidade dos efeitos dos cigarros eletrônicos com nicotina nas atividades metabólicas das células da mucosa oral que levam ao maior risco ao câncer bucal nessa população. Porém, estudos de longo prazo ainda são necessários para definir tal efeito (Palaia *et al.*, 2025).

Não diferente das demais doenças bucais, as causas que levam ao adoecimento por CBO podem ser evitáveis e fortemente induzidas por fatores socioeconômicos. As desigualdades acentuadas e persistentes refletem na prevalência do CBO de forma consistente e graduada em toda a hierarquia social, representando exemplo clássico de gradiente social na saúde (Peres *et al.*, 2019).

Em nível macrossocial, taxas de incidência e de mortalidade de CBO tendem a ser maiores em países com um Índice de Desenvolvimento Humano (IDH) baixo e médio. Tal efeito surge diante das repercussões socioambientais (como a falta de planejamento urbano) associadas à adoção de estilos de vida e a comportamentos insalubres gerados pelo rápido crescimento socioeconômico ao passo que as iniciativas de saúde pública são insuficientes ou não avançam na mesma proporção (Kijowska *et al.*, 2024).

Nesses cenários, o impacto das desigualdades sociais no adoecimento pelo CBO se torna ainda mais proeminente, uma vez que pessoas em vulnerabilidade social ou pertencentes a grupos minoritários ficam ainda mais expostas a contextos de autonegligência pela dificuldade de acesso a ações preventivas de saúde (Andersen; Davidson, 2001, Akashanand *et al.*, 2024). Não é à toa que o baixo acesso a cuidados odontológicos está significativamente associado à alta taxa de incidência do câncer bucal (Scussiatto *et al.*, 2024). Dessa forma, condições precárias de vida que levam ao abuso de substâncias tóxicas, insegurança alimentar e precarização das formas de trabalho somados à falta de assistência à saúde, além de contribuírem com maior incidência de CBO, repercutem em diagnósticos tardios, piores prognósticos e menor sobrevida nas populações mais pobres (Moi *et al.*, 2018, Herrera-Serna *et al.*, 2019, Hung *et al.*, 2020, Nagao; Warnakulasuriya, 2020).

Johnson *et al.* (2011) conceituou o câncer bucal como uma doença dos “pobres e despossuídos”. Portanto, para o gerenciamento dos fatores de risco e o

cuidado desta doença é necessária a adoção de políticas nacionais coordenadas e direcionadas que incluem maior aquisição de bens materiais, melhorias na segurança alimentar e acesso mais amplo à educação, aos cuidados de saúde, à água potável e ao saneamento básico e redução de violências (Jhonson *et al.*, 2011, Jerjes, 2024). Tendo como exemplo, um estudo ecológico brasileiro mostrou que maior cobertura do Programa Bolsa Família foi associada a menores taxas de mortalidade por câncer bucal, sugerindo que estratégias de transferência de renda, que visam promover redução de desigualdades, também podem reduzir o risco de morte por esta neoplasia (Costa *et al.*, 2022).

Mesmo em países desenvolvidos, as disparidades sociais que abordam, além do aspecto econômico, diferenças raciais, de gênero e regionais foram reveladas em desfechos dessa neoplasia maligna (Ramamurthy *et al.*, 2024, Khanna *et al.*, 2024, Tsai *et al.*, 2017). Nos Estados Unidos, as taxas de sobrevivência de cinco anos do câncer de orofaringe melhoraram significativamente entre homens jovens, mas não entre as mulheres do mesmo grupo etário (Guo *et al.*, 2022). Na Austrália, mulheres apresentaram maior probabilidade de diagnóstico tardio do câncer bucal (Thomas *et al.*, 2021) e, em Taiwan, estiveram mais associadas ao atraso do tratamento (Tsai *et al.*, 2017, Su *et al.*, 2021). Apesar de pessoas brancas serem mais afetadas, pacientes negros exibiram resultados desfavoráveis de sobrevivência para cânceres da cavidade oral e glândulas salivares quando comparados a outros grupos, inclusive no Brasil (Saini; Genden; Megwalu, 2016, Zandberg *et al.*, 2016, Megwalu; Ma, 2017, Affonso *et al.*, 2022).

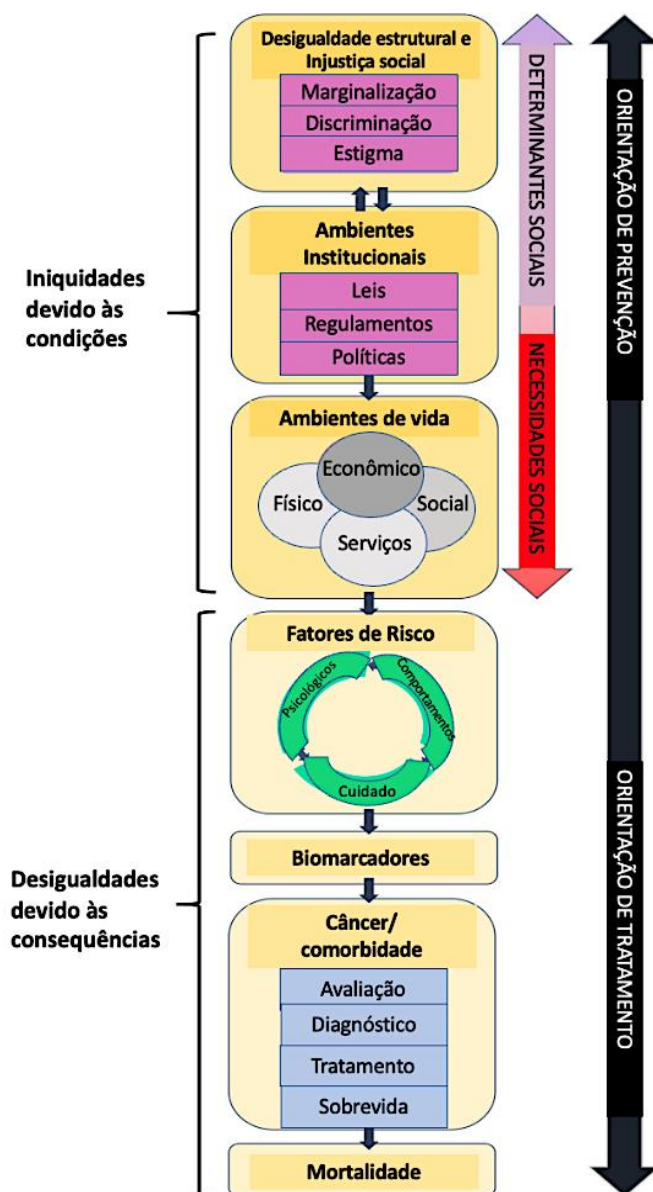
O local de residência também tem influenciado nos desfechos do CBO. Alguns estudos já avaliaram o impacto da ruralidade na incidência e na mortalidade (Ramamurthy *et al.*, 2024, Khanna *et al.*, 2024) bem como no atraso do tratamento, (Venchiariutti *et al.*, 2020) especialmente relacionado à dificuldade de acessibilidade aos serviços, ausência de prevenção e detecção precoce por profissionais de saúde em localidades distantes de grandes centros (Zhang *et al.*, 2024). Semelhantemente, alto risco de desenvolver CBO foi encontrado em moradores de favelas urbanas (Parihar *et al.*, 2024).

No Brasil, regiões mais desenvolvidas (Sudeste e Sul) tiveram redução do risco de morte por câncer bucal, enquanto as regiões menos desenvolvidas apresentaram aumentos em coortes recentes (Perea; Antunes; Peres, 2021). Além disso, foi mostrado que pacientes das regiões Norte e Centro-Oeste precisam

percorrer distâncias médias maiores (entre 170,3 e 188,4 km) para receber tratamento do câncer comparado às demais regiões (Fonseca *et al.*, 2021).

Alcaraz *et al.* (2020) recomendaram um modelo teórico explicativo sobre determinantes sociais para promoção da equidade no tratamento e redução da mortalidade do câncer. Os autores apontaram para a importância de medidas de intervenção estruturais em detrimento de mudanças de atitudes individuais (FIGURA 1).

Figura 1- Estrutura conceitual integrada para compreensão e abordagem dos determinantes sociais para o avanço da equidade em saúde do câncer.



Fonte: Alcaraz *et al.*, 2020, p.33.

(Houve alteração da ilustração para fins didáticos).

Para tanto, foram elencados aspectos que sustentam e perpetuam a iniquidade no cuidado do câncer. O primeiro trata das desigualdades estruturais e iniquidades sociais relativas a questões de discriminação, marginalização e estigmas de gênero, etnia e classe social. Uma revisão sistemática mostrou a relação da interseccionalidade (gênero, raça e classe) e as disparidades ao longo do tratamento do câncer. Mulheres não-brancas com baixo status socioeconômico receberam menos cuidados e apresentaram piores resultados de sobrevivência (Kelly-Brown *et al.*,

2022). Embora os mecanismos biológicos desempenhem papel central na origem e progressão do câncer — como alterações genéticas e epigenéticas, instabilidade genômica, inflamação crônica e falhas nos sistemas de reparo celular, há crescente reconhecimento de que fatores de risco e desfechos oncológicos também decorrem de desigualdades sociais historicamente construídas — em especial, o racismo e o sexismo estruturais — que determinam a distribuição das exposições ambientais, o acesso à prevenção, ao diagnóstico e ao tratamento, e à qualidade do cuidado ao longo da vida (Nelson, 2020, Keenan *et al.*, 2023). Sendo assim, relatórios recentes têm mostrado que vários tipos de racismo contribuem para inúmeras mortes relacionadas a diferentes tipos de câncer entre pacientes de grupos de minorias raciais e étnicas, especialmente devido ao acesso desigual aos serviços de saúde e à falta de interesse em levar em conta aspectos culturais em ações de saúde (Strayhorn-Carter; Batai; Gachupin, 2024). Além disso, preconceitos e estigmas de todas as formas geram sentimentos de marginalização, medos de discriminação e desconforto geral que levam ao isolamento dos pacientes, prejudicando o apoio social essencial que os ajuda a buscar orientações a respeito de seus sintomas para um diagnóstico precoce, bem como a superar os tratamentos médicos (Nelson *et al.*, 2020).

O segundo fala dos ambientes institucionais que reforçam, através de programas e políticas, intencionalmente ou não, a manutenção do *status quo* da desigualdade. Exemplificando, é sabido que a baixa escolaridade influencia no adoecimento por câncer. Frequentemente, essa avaliação é feita a partir de uma perspectiva individual, em que são considerados os anos de estudo do indivíduo. Entretanto, não são avaliadas as políticas, recursos ou qualidade do sistema educacional, muito menos as oportunidades as quais o sujeito foi exposto ao longo da vida (Alcaraz *et al.*, 2020).

O terceiro mostra o quesito ambientes de vida que dizem respeito aos recursos disponíveis nos meios imediatos aos indivíduos. Estes incluem os meios inter-relacionados que dificultam ou facilitam o acesso aos recursos necessários para saúde e bem-estar. Esses ambientes podem estar desprovidos de serviços de saúde, complicando a prevenção, o diagnóstico e tratamento adequados, ao mesmo tempo, podem favorecer comportamentos que induzem a propensão ao câncer pela falta de acesso à alimentação de qualidade e a locais convenientes para prática de atividade física, por exemplo. Assim, alguns hábitos que são entendidos pelo senso comum

como escolhas individuais, na verdade, são concebidos nos meios coletivos, principalmente influenciados pela grande indústria de consumo (como hábito de fumar, uso de álcool, dieta etc.) e pela ausência de políticas de promoção de ambientes saudáveis (Alcaraz *et al.*, 2020).

Diante disso, as consequências dessas iniquidades sociais, que remontam aos efeitos estruturais, interferem em outros domínios de risco individuais (comportamentais, psicológicos e de autocuidado). Esses, por sua vez, modulam a possibilidade de avaliação, diagnóstico, tratamento e sobrevida dos pacientes que resulta em impacto na mortalidade. Embora o tratamento clínico seja primordial para o paciente com câncer, os autores salientam que os esforços precisam estar mais voltados ao planejamento de ações que intentem, ao menos, diminuir disparidades em níveis populacionais (Alcaraz *et al.*, 2020).

Com vistas a reduzir desigualdades em saúde, a Política Nacional de Saúde Bucal (PNSB) tem permitido desenvolver estratégias de diagnóstico do CBO voltadas à população mais vulnerável, dependente do Sistema Único de Saúde (SUS) (Chaves *et al.*, 2017). Os serviços são organizados em redes de atenção a fim de garantir a integralidade do cuidado. Portanto, estabelece a qualificação da atenção primária para ações de promoção da saúde, de prevenção e de controle dos fatores de risco do CBO, bem como para realização de detecção precoce de lesões potencialmente malignas nas unidades básicas de saúde (UBS) (Pucca *et al.*, 2015). Além disso, institui a atenção secundária através dos Centros de Especialidades Odontológicas (CEO), tendo Estomatologia como uma das especialidades mínimas, com ênfase no diagnóstico por meio da realização de biópsias para diagnóstico definitivo do CBO (Brasil, 2004, Chaves *et al.*, 2017).

Tais avanços na oferta e na cobertura da população pelos serviços públicos de saúde bucal foram associados a resultados positivos na redução da hospitalização e da mortalidade por CBO no Brasil (Raymundo *et al.*, 2021). Entretanto, ainda é preciso estabelecer melhorias nos processos de cuidado na rede de atenção à saúde bucal, levando em conta os contextos estruturais (social e econômico) que os serviços de saúde estão inseridos, uma vez que a maioria dos casos ainda são diagnosticados e tratados tardiamente (Soares; Bastos Neto; Santos, 2019, Koawsky *et al.*, 2020).

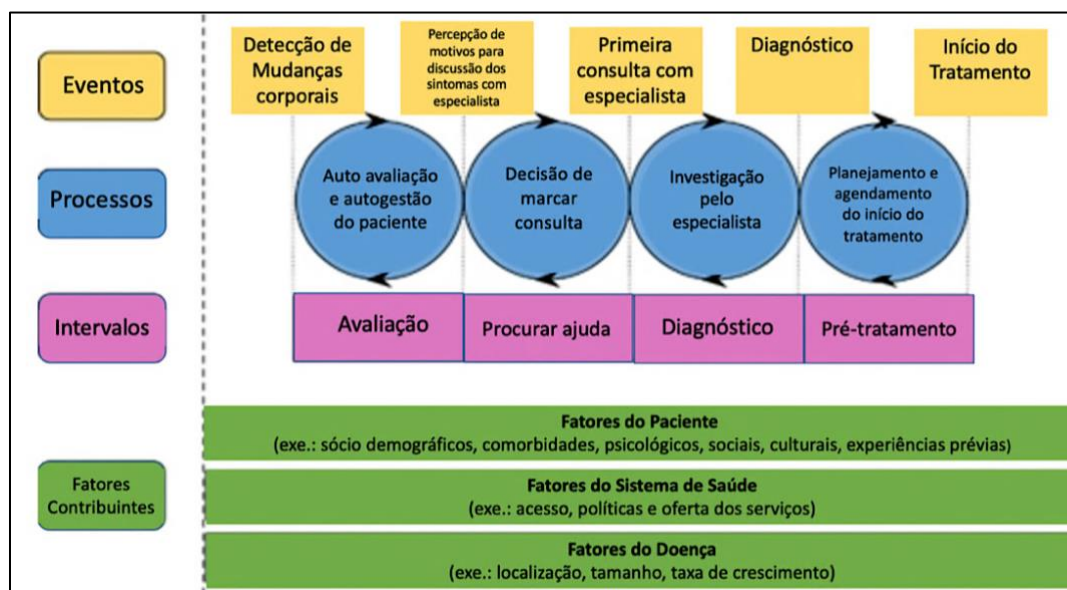
2.2 Atrasos do diagnóstico e do tratamento do câncer de boca e orofaringe

Mesmo com progresso das técnicas de triagem e terapias emergentes, ainda há pouco avanço em melhorias na redução da mortalidade do CBO, uma vez que os casos ainda são diagnosticados em estágios avançados e o atraso no tratamento é uma realidade em muitas populações (Warnakulasuriya *et al.*, 2021, Motlokwa *et al.*, 2022). Em países de baixa renda, os intervalos para o tratamento foram significativamente maiores comparados a países de alta renda (Fernández-Martínez *et al.*, 2023). No Brasil, uma maior frequência de neoplasias bucais diagnosticadas em estágio IV (62,24%) já foi identificada, sendo esse percentual maior que 50% para todas as macrorregiões (Soares; Bastos Neto; Santos, 2019).

Os atrasos no cuidado do CBO ocasionam impactos negativos tanto para os pacientes como para os sistemas de saúde (Ogden, 2020). Diagnósticos tardios levam ao tamanho aumentado do tumor, envolvimento nodal, propensão a metástases à distância e aumento das chances de recorrência, ocasionando prejuízos oncológicos e funcionais com aumento da morbidade, da desfiguração, bem como significativa perda da qualidade de vida e da sobrevida nesse tipo de câncer (Ogden, 2020, Schoonbeek *et al.*, 2022, Yuwanati *et al.*, 2021). Ao mesmo tempo, as terapias curativas e/ou de suporte, indicadas nesses casos, são complexas e demandam maior quantidade de recursos e custos hospitalares (Bonfante *et al.*, 2014, Gomez *et al.*, 2016, Schutte *et al.*, 2020, Su *et al.*, 2021). Portanto, a avaliação dos intervalos do CBO constitui um dos critérios principais para auxiliar a tomada de decisões na gestão dessa doença, pois permite acompanhar trajetórias clínicas e seus efeitos no prognóstico (Weller *et al.*, 2012).

Weller *et al.* (2012) propuseram um modelo teórico identificando os processos envolvidos desde a identificação até o tratamento a fim de proporcionar o melhor prognóstico do câncer (FIGURA 2). Para tanto, são levados em conta três fatores - paciente, doença e sistema de saúde - que modulam, de forma conjunta, os intervalos de tempo entre a detecção e o tratamento.

Figura 2- Modelo de vias de tratamento do câncer.



Fonte: Weller *et al.*, 2012.

(Houve alteração da ilustração para fins didáticos).

Em se tratando dos intervalos para assistência ao CBO, os fatores do psicossociais dos pacientes interferem fortemente na decisão tardia para procurar ajuda profissional, tais como: falta de conhecimento sobre a doença, interpretação indefinida dos sintomas e a cultura de menosprezar problemas bucais, que levam ao auto tratamento ou à expectativa de que a lesão desapareça sem intervenção (Lima *et al.*, 2021). Além disso, fatores sociodemográficos como sexo feminino, idade mais avançada (acima de 60 anos) (Su *et al.*, 2021, Tsai *et al.*, 2017) e baixa escolaridade (Goel *et al.*, 2021) foram associados a atrasos do tratamento.

A taxa de progressão da doença sofre influência, principalmente, da localização anatômica do tumor, do estadiamento e do tipo de intervenção indicada (Zanoni *et al.*, 2019). O CBO pode ter evolução lenta e indolente, mas com agressividade tumoral e proliferativa em muitos casos (Varghese; Rajan, 2020). Dessa forma, tumores localizados em regiões mais posteriores da cavidade oral, como orofaringe, palato duro e trígono retro molar, tendem a ser diagnosticados com estadiamento III e IV (Goel *et al.*, 2019, Su *et al.*, 2021, Tsai *et al.*, 2017). Estágios mais avançados da doença exigem manejo de terapias multimodais, que por sua vez, demandam tempos mais longos para início do tratamento diante da necessidade de maior volume de exames complementares, adequação bucal prévia e ajustes de comorbidades (Goel *et al.*, 2019).

No que tange aos fatores do sistema de saúde, a conjuntura social e econômica em que são implementadas as políticas, bem como os aspectos organizacionais de adequação da acessibilidade, disponibilidade, infraestrutura e recursos humanos dos serviços interferem nos intervalos do câncer. Assim, a dificuldade de acesso da população adulta ao atendimento odontológico preventivo e a falta de ações coordenadas nos diferentes níveis de atenção voltadas ao CBO (primária, secundária e terciária) podem acarretar diagnóstico e tratamento extemporâneos (Conceição *et al.*, 2021, Thomaz *et al.*, 2022). Paradoxalmente, a atenção primária, que tem a resolutividade como premissa, ainda é responsável por longos intervalos de tempo para o diagnóstico de pacientes com câncer bucal (Scalzo *et al.*, 2023).

Günieri e Epstein (2014) definiram três momentos do atraso especificamente para o câncer bucal. “Atraso do paciente”, que se refere ao período entre a primeira detecção de um sinal/sintoma pelo paciente até a procura por atendimento clínico; “atraso profissional” que abrange o intervalo entre o primeiro exame/avaliação por um profissional de saúde até o diagnóstico histológico da condição de malignidade; e “atraso do sistema” que compreende o diagnóstico definitivo até o início da primeira intervenção. Enquanto os dois primeiros são alusivos ao atraso do diagnóstico, o último se refere ao atraso do tratamento.

Os principais motivos que resultam no atraso do paciente foram relacionados ao medo, à negação e à falta de conhecimento sobre a doença (Lima *et al.*, 2021). O atraso profissional inclui o despreparo dos dentistas generalistas para detectar feridas/lesões malignas ou potencialmente malignas, solicitar os exames complementares necessários e realizar o encaminhamento devido para o especialista (Keinänen; Uittamo; Snäll, 2023). Além disso, profissionais de estomatologia, patologia oral, cirurgia bucomaxilofacial e dentistas com experiência clínica e acadêmica de 21 países da América Latina e do Caribe, relataram que a implementação limitada de ações de controle por parte de planos de saúde, a falta de compulsoriedade de notificação de lesões orais em sistemas de informação, caminhos de encaminhamento pouco claros e escassez de profissionais treinados são os principais limitadores para o diagnóstico do CBO em tempo hábil (Martínez-Ramírez *et al.*, 2024).

Embora as etapas de apresentação do paciente e atitudes do profissional influam no atraso global do tratamento (Stefanuto; Doucet; Robertson, 2014), o acesso

às terapias do CBO está estreitamente relacionado à utilização dos serviços de saúde, a qual envolve determinantes individuais e contextuais, conferindo maior complexidade de investigação (Andersen; Davidson, 2001, Günieri; Epstein, 2014). O atraso do tratamento se relaciona, principalmente à dificuldade de acesso a serviços especializados em oncologia, seja por problemas no itinerário terapêutico entre diferentes especialidades médicas e odontológicas, seja pela total ausência desses estabelecimentos (Andrade *et al.*, 2014, Günieri; Epstein, 2014, Barros *et al.*, 2021, Su *et al.*, 2021). Deste modo, pode ser usado como um indicador de qualidade para monitorar o desempenho dos serviços, uma vez que está relacionado ao atraso do sistema de saúde (Günieri; Epstein, 2014).

No Brasil, a população tratada em serviços públicos de saúde apresentou maior atraso para o tratamento do câncer bucal em comparação à do serviço privado (Chiliti *et al.*, 2022). Entraves na disponibilidade de recursos humanos qualificados para o diagnóstico definitivo (Costa *et al.*, 2023), bem como na distribuição de instalações e equipamentos públicos especializadas em oncologia nos municípios também são fatores críticos que tem afetado o tempo para início do tratamento do câncer em pessoas SUS-dependente (Araujo *et al.*, 2018, Ferreira *et al.*, 2020). Semelhantemente, melhorias na triagem de pacientes associaram-se à redução de diagnósticos em estágios avançados, ao mesmo tempo, estiveram relacionadas a atrasos do tratamento pela possível dificuldade de encaminhamento para instalações certificadas para tratar CBO em Taiwan (Tsai; Walker; Wu, 2024).

O intervalo entre o diagnóstico e a terapia do CBO mencionado em estudos de alguns países, variou entre 14 e mais de 120 dias (Goel *et al.*, 2019, Chiou; Lin; Hsieh, 2016, Graboyes *et al.*, 2019, Venchiarutti *et al.*, 2020, Su *et al.*, 2021, Tsai *et al.*, 2017, Fujiwara *et al.*, 2017). Já em pesquisas brasileiras, as quais utilizaram dados de locais e amostras relativamente pequenas, os resultados variaram entre 23 dias e três meses, podendo atingir mais de 200 dias, sendo o atraso mais expressivo na região Norte e menos na região Sul (Costa; Migliorati, 2001, Abdo *et al.*, 2007, Silva *et al.*, 2009, Santos; Batista; Cangussu, 2010, Santos *et al.*, 2012, Le Campion *et al.*, 2016).

Frente a isso, estudos têm buscado demonstrar o impacto do diagnóstico tardio e consequente atraso do tratamento do CBO na sobrevida dos pacientes. Uma revisão sistemática de estudos observacionais identificou que o diagnóstico tardio, com atraso superior a um mês, potencializou a ocorrência de estágios avançados da

doença (Gomez *et al.*, 2016). Além disso, o diagnóstico tardio do câncer bucal pode reduzir as chances de sobrevivência acima de 200% (Seoane *et al.*, 2016).

Recentemente, Hanna *et al.* (2020) relataram ser o atraso de um mês para o tratamento dos tipos de câncer mais recorrentes (inclusive o de cabeça e pescoço) o motivo do aumento de 6 a 13% do risco de morte. Com o passar das semanas, a depender do tipo de tratamento, a chance de óbito também aumenta. Isso porque o atraso do tratamento também está associado ao aumento do estadiamento clínico e progressão do tumor (Xiao *et al.*, 2018). Idealmente, o tratamento de CBO deveria ser iniciado logo após confirmação do diagnóstico, entretanto, o início do tratamento em até 30 dias é considerado aceitável para um prognóstico satisfatório e maior chance de sobrevivência (Tsai *et al.*, 2017, Goel *et al.*, 2019, Murphy *et al.*, 2016).

Murphy *et al.* (2016) incluíram 51.655 pessoas com câncer de cabeça e pescoço em seu estudo e descobriram que a sobrevida geral para pacientes tratados com intenção curativa era significativamente menor se o atraso do tratamento fosse de 61 dias ou mais, em comparação ao intervalo de 30 dias ou menos. Su *et al.* (2021) encontraram um aumento significativo de 18% no risco de mortalidade se o atraso do tratamento do câncer bucal fosse maior que seis semanas. Além disso, estimou-se que um tempo superior a 60 dias reduz a chance de sobrevida em até 26% (Graboyes *et al.*, 2019).

Com a intenção de estruturar o cuidado a pacientes oncológicos, o Brasil provê amparos legais, como a *Portaria nº 741/2005*, do Ministério da Saúde, que define sobre a gratuidade do diagnóstico e tratamento do câncer no SUS (Brasil, 2005). Ademais, a *Lei Federal nº 12.732/2012*, dispõe sobre o direito de pessoas com neoplasia maligna comprovada se submeterem ao primeiro tratamento no prazo de até 60 dias, contados a partir do dia em que forem diagnosticados, em laudo patológico, ou em prazo menor, conforme a necessidade terapêutica do caso registrada em prontuário único (Brasil, 2012). Quanto ao prazo para o diagnóstico, nos casos em que a principal hipótese diagnóstica seja a de neoplasia maligna, os exames necessários à elucidação devem ser realizados no prazo máximo de 30 dias, mediante solicitação fundamentada do médico responsável. Essa obrigatoriedade passou a vigorar a partir de abril de 2020 (Brasil, 2019).

No sentido de permitir o monitoramento por parte dos gestores da *Lei nº 12.732/2012* em relação ao cumprimento do prazo máximo estabelecido para início do tratamento, foi viabilizado, em 2019, o Painel de Monitoramento de Tratamento

Oncológico (Painel-Oncologia). Este Painel constitui uma base de dados desenvolvida pelo Departamento de Informática do SUS (DATASUS) em parceria com o Instituto Nacional do Câncer (INCA). Até então, a primeira ferramenta de acompanhamento anunciada pelo MS foi o Sistema de Informação do Câncer (Siscan). Entretanto, em decorrência de problemas técnicos no módulo monitoramento e falhas no fornecimento dos dados no sistema, tornou-se inutilizada.

Assim, o Painel-Oncologia apresenta o número de usuários por municípios e estados que realizaram tratamento de câncer no país a partir de 2013, conforme o intervalo de tempo de demora (em dias) entre o diagnóstico confirmado e o início do tratamento, quando a *Lei nº 12.732/2012* passou a vigorar. Segundo o relatório produzido com dados do Painel-Oncologia, notou-se que o percentual de pacientes que iniciou o tratamento no período superior a 60 dias variou de 59% em 2013 para 45% em 2018, validando a importância dessa ferramenta na gestão do tratamento do câncer de boca no país (Atty; Ribeiro, 2020).

Diante do exposto, este estudo avaliou a associação entre fatores socioeconômicos e o atraso do tratamento do CBO por meio de uma revisão sistemática da literatura, analisou os fatores que explicam o tempo de início do tratamento do CBO nos municípios brasileiros, e a tendência dos registros de CBO no Brasil, considerando os fatores que contribuíram com o maior ou menor tempo para início do tratamento.

3 OBJETIVOS

3.1 Objetivo Geral

Verificar a associação entre fatores socioeconômicos e o atraso do tratamento do CBO por meio de uma revisão sistemática da literatura, analisar os fatores que explicam o tempo de início do tratamento do CBO nos municípios brasileiros, bem como analisar a tendência dos registros de CBO no Brasil, considerando os fatores que contribuíram com o maior ou menor tempo para início do tratamento.

3.2 Objetivos Específicos

- Verificar a associação entre os fatores socioeconômicos e o atraso do tratamento do CBO por meio de uma revisão sistemática da literatura.
- Identificar os fatores com maior poder de discriminação da proporção de registros de CBO com tempo até o início do tratamento em até 30 dias após o diagnóstico em municípios brasileiros.
- Analisar as tendências temporais dos registros de CBO no Brasil de 2019 a 2023, bem como identificar os fatores que impactaram o tempo para início do tratamento nesse período.

4 METODOLOGIA EXPANDIDA

4.1 Estudo de revisão sistemática

4.1.1 Protocolo e registro

Foi utilizado o *check-list* de verificação do *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA 2022- <http://www.prisma-statement.org/PRISMAStatement/PRISMAStatement>), que elenca um conjunto mínimo de itens baseado em evidências que devem constar em estudos desse tipo (Page *et al.*, 2021), sob orientação do “*Review Manager/Cochrane*” (COCHRANE COMMUNITY, 2019). O protocolo desta revisão foi registrado no *International Prospective Register of Systematic Reviews* – PROSPERO sob o número #CRD42022361948 com intuito de fornecer transparência e padronização quanto à execução do processo de revisão e de análise dos resultados (Booth *et al.*, 2011).

4.1.2 Pergunta de pesquisa

Utilizou-se o acrônimo PECOS (do inglês “*Population, Exposure, Comparasion, Outcomes*”), desenvolvido para estudos observacionais (Morgan, 2018), para formular a seguinte questão: "Existe associação entre fatores socioeconômicos e o atraso do tratamento do câncer de boca e orofaringe?"

Desse modo, definiu-se como:

- População: Adultos (acima de 18 anos), de ambos os sexos, diagnosticados com câncer de boca/orofaringe.
- Exposição: População submetida a condições socioeconômicas desfavoráveis.
- Comparação: Indivíduos pareados com características socioeconômicas favoráveis.
- Resultados: Atraso para início do tratamento de câncer de boca e orofaringe, que compreende o intervalo entre o diagnóstico definitivo de malignidade e a primeira intervenção (Murphy *et al.*, 2016, Su *et al.*, 2021).

4.1.3 Critérios de inclusão e exclusão

Os critérios de inclusão foram: pacientes com câncer de boca e orofaringe ou tumores em sítios específicos da cavidade oral e orofaringe; adultos (≥ 18 anos); diagnóstico histológico de carcinoma de células escamosas (CEC); estudos que relataram qualquer fator socioeconômico; estudos que avaliaram o tempo desde o diagnóstico até o início do tratamento; e estudos observacionais (estudos transversais, de coorte e de caso-controle). Nenhuma restrição foi imposta em relação ao idioma ou ano de publicação.

Estudos que relataram câncer de cabeça e pescoço sem considerar os cânceres de boca e orofaringe separadamente de outros cânceres (por exemplo, câncer de pele, linfonodos e tireoide) foram excluídos. Da mesma forma, neoplasias malignas de tipos histológicos desconhecidos ou diferentes do CEC também foram desconsideradas, pois apresentam características de progressão e sintomatologia próprios que podem influenciar no atraso do tratamento (Nocini; Lippi; Mattiuzzi, 2020).

4.1.4 Fontes de informação e estratégias de busca

Cinco bases de dados foram pesquisadas desde o início até janeiro de 2023, atualizadas em dezembro de 2023: *MEDLINE (PubMed)*, *Embase (Ovid)*, *Scopus*, *Web of Science* e Biblioteca Virtual em Saúde (Bireme, América Latina). A literatura cinzenta foi pesquisada através do *OpenGrey* e do *Google Scholar* (esta última limitada aos primeiros 100 resultados listados). Estratégias de busca específicas foram desenvolvidas para cada base de dados e revisadas por especialista em revisões sistemáticas com a intenção de resgatar o maior número possível de estudos relacionados ao tema. As listas de referências dos artigos incluídos nessa revisão foram pesquisadas manualmente na tentativa de encontrar artigos adicionais relevantes (Quadro 1).

Quadro 1- Estratégias de busca utilizadas em cada base de dados eletrônica (data: de interceptação até janeiro de 2023, atualizada em dezembro de 2023).

MedLine via Pubmed
((((Head and Neck Neoplasms[MeSH Terms]) OR (Mouth Neoplasms[MeSH Terms]) OR (Oropharyngeal Neoplasms[MeSH Terms]) OR (Squamous Cell Carcinoma of Head and Neck[MeSH Terms]) OR ("Head and Neck Neoplasm"[Title/Abstract]) OR ("Cancer of Head and Neck"[Title/Abstract]) OR ("Head and Neck Cancer"[Title/Abstract]) OR ("Head

Neoplasms"[Title/Abstract]) OR ("Head Neoplasm"[Title/Abstract]) OR ("Cancer of Head"[Title/Abstract]) OR ("Head Cancers"[Title/Abstract]) OR ("Mouth Neoplasm"[Title/Abstract]) OR ("Oral Neoplasm"[Title/Abstract]) OR ("Oral Neoplasms"[Title/Abstract]) OR ("Cancer of Mouth"[Title/Abstract]) OR ("Mouth Cancers"[Title/Abstract]) OR ("Oral Cancer"[Title/Abstract]) OR ("Oral Cancers"[Title/Abstract]) OR ("Cancer of the Mouth"[Title/Abstract]) OR ("Mouth Cancer"[Title/Abstract]) OR ("Oropharyngeal Neoplasm"[Title/Abstract]) OR ("Oropharynx Neoplasms"[Title/Abstract]) OR ("Oropharynx Neoplasm"[Title/Abstract]) OR ("Oropharyngeal Cancer"[Title/Abstract]) OR ("Oropharyngeal Cancers"[Title/Abstract]) OR ("Oropharynx Cancer"[Title/Abstract]) OR ("Oropharynx Cancers"[Title/Abstract]) OR ("Cancer of the Oropharynx"[Title/Abstract]) OR ("Squamous Cell Carcinoma of the Head and Neck"[Title/Abstract]) OR ("Head and Neck Squamous Cell Carcinoma"[Title/Abstract]) OR ("Oral Tongue Squamous Cell Carcinoma"[Title/Abstract]) OR ("Oral Squamous Cell Carcinoma"[Title/Abstract]) OR ("Oral Cavity Squamous Cell Carcinoma"[Title/Abstract]) OR ("Oral Squamous Cell Carcinomas"[Title/Abstract]) OR ("Squamous Cell Carcinoma of the Mouth"[Title/Abstract]) OR ("Oropharyngeal Squamous Cell Carcinoma"[Title/Abstract])) AND ((Socioeconomic Factors[MeSH Terms]) OR (Income[MeSH Terms]) OR (Poverty[MeSH Terms]) OR (Social Class[MeSH Terms]) OR (Educational Status[MeSH Terms]) OR (Demography[MeSH Terms]) OR ("Socioeconomic Factors") OR ("Educational Status") OR ("Socioeconomic Factor") OR ("Standard of Living") OR ("Living Standard") OR ("Living Standards") OR ("Land Tenure") OR ("Social Inequality") OR ("Social Inequalities") OR ("High-Income Population") OR ("High Income Population") OR ("High-Income Populations") OR ("Incomes") OR ("Savings") OR ("Health Insurances") OR ("Income Distribution") OR ("Income Distributions") OR ("Low-Income Population") OR ("Low-Income Populations") OR ("Low Income Population") OR ("Low Income Populations") OR ("Social Classes") OR ("Socioeconomic Status") OR ("Middle Class Population") OR ("Educational Achievement") OR ("Educational Achievements") OR ("Schooling Level") OR ("Educational Levels") OR ("Demographic") OR ("Population Spatial Distributions") OR ("Demographic Factors") OR ("Demographic Factor") OR ("Demographic Impacts") OR ("Demographic Impact") OR ("Patient Profile")) AND ((Time-to-Treatment[MeSH Terms]) OR ("Time-to-Treatment"[Title/Abstract]) OR (Time-to-Treatments[Title/Abstract]) OR ("Door-to-Treatment Time"[Title/Abstract]) OR ("Door to Treatment Time"[Title/Abstract]) OR ("Delayed Treatment"[Title/Abstract]) OR ("Delayed Treatments"[Title/Abstract]) OR ("Treatment Delay"[Title/Abstract]) OR ("Primary Treatment"[Title/Abstract]) OR ("Waiting Time"[Title/Abstract]) OR ("Timeliness"[Title/Abstract]) OR ("Delay in Treatment"[Title/Abstract]) OR ("Time to Start

Treatment"[Title/Abstract]) OR ("Diagnosis-treatment interval"[Title/Abstract]) OR ("Time-to-initiation"[Title/Abstract]) OR ("Treatment initiation"[Title/Abstract]) OR ("Treatment time"[Title/Abstract]) OR ("Treatment times"[Title/Abstract]) OR ("Timely care"[Title/Abstract]) OR ("Diagnosis to treatment"[Title/Abstract]) OR ("Time factors"[Title/Abstract]) OR ("Time to treatment initiation"[Title/Abstract])

Embase via Elsevier

("head and neck tumor"/exp OR "head and neck tumor" OR "mouth tumor"/exp OR "mouth tumor" OR "mouth cancer"/exp OR "oropharynx tumor"/exp OR "oropharynx tumor" OR "oropharynx cancer"/exp OR "squamous cell carcinoma of the head and neck"/exp OR "head and neck squamous cell carcinoma"/exp OR "oral tongue squamous cell carcinoma"/exp OR "mouth squamous cell carcinoma"/exp OR "mouth squamous cell carcinoma" OR "oral cavity squamous cell carcinoma"/exp OR "oropharynx squamous cell carcinoma"/exp OR "oropharynx squamous cell carcinoma" OR "mouth carcinoma"/exp OR "mouth carcinoma" OR "oropharynx carcinoma"/exp OR "oropharynx carcinoma" OR "head and neck neoplasm" OR "cancer of head and neck" OR "head and neck cancer" OR "head neoplasms" OR "head neoplasm" OR "cancer of head" OR "head cancers" OR "mouth neoplasm" OR "oral neoplasm" OR "oral neoplasms" OR "cancer of mouth" OR "mouth cancers" OR "oral cancer" OR "oral cancers" OR "cancer of the mouth" OR "mouth cancer" OR "oropharyngeal neoplasm" OR "oropharynx neoplasms" OR "oropharynx neoplasm" OR "cancer of oropharynx" OR "oropharynx cancer" OR "oropharynx cancers" OR "oropharyngeal cancer" OR "oropharyngeal cancers" OR "oropharynx cancer" OR "oropharynx cancers" OR "cancer of the oropharynx" OR "head and neck squamous cell carcinomas" OR "squamous cell carcinoma of the head and neck" OR "head and neck squamous cell carcinoma" OR "oral tongue squamous cell carcinoma" OR "oral squamous cell carcinoma" OR "oral cavity squamous cell carcinoma" OR "oral squamous cell carcinomas" OR "squamous cell carcinoma of the mouth" OR "oropharyngeal squamous cell carcinoma") AND ("socioeconomics"/exp OR "socioeconomics" OR "economic status"/exp OR "economic status" OR "educational status"/exp OR "educational status" OR "income group"/exp OR "income group" OR "poverty"/exp OR "poverty" OR "socioeconomic distribution"/exp OR "socioeconomic distribution" OR "socioeconomic parameters"/exp OR "socioeconomic parameters" OR "socioeconomic vulnerability"/exp OR "socioeconomic vulnerability" OR "household economic status"/exp OR "household economic status" OR "health insurance"/exp OR "health insurance" OR "income" OR "socioeconomic factors" OR "social class" OR "demography" OR "socioeconomic factor" OR "standard of living" OR "living standard" OR "living standards" OR "land tenure" OR "social inequality" OR "social inequalities" OR "high-income population" OR "high income

population" OR "high-income populations" OR "incomes" OR "savings" OR "income distribution" OR "income distributions" OR "low-income population" OR "low-income populations" OR "low income population" OR "low income populations" OR "social classes" OR "socioeconomic status" OR "middle class population" OR "educational achievement" OR "educational achievements" OR "schooling level" OR "educational levels" OR demographic OR "population spatial distributions" OR "demographic factors" OR "demographic factor" OR "demographic impacts" OR "demographic impact" OR "patient profile") AND ("time to treatment"/exp OR "therapy delay"/exp OR "therapy delay" OR "time to treatment" OR "time-to-treatment" OR "time-to-treatments" OR "door-to-treatment time" OR "door to treatment time" OR "delayed treatment" OR "delayed treatments" OR "treatment delay" OR "primary treatment" OR "waiting time" OR "timeliness" OR "delay in treatment" OR "time to start treatment" OR "diagnosis-treatment interval" OR "time-to-initiation" OR "treatment initiation" OR "treatment time" OR "treatment times" OR "timely care" OR "diagnosis to treatment" OR "time factors" OR "time to treatment initiation")

Scopus

((TITLE-ABS-KEY ("head and neck tumor") OR TITLE-ABS-KEY ("head neoplasms") OR TITLE-ABS-KEY ("mouth tumor") OR TITLE-ABS-KEY ("mouth cancer")) OR TITLE-ABS-KEY ("oropharynx tumor") OR TITLE-ABS-KEY ("oropharynx cancer") OR TITLE-ABS-KEY ("squamous cell carcinoma of the head and neck") OR TITLE-ABS-KEY ("head and neck squamous cell carcinoma") OR TITLE-ABS-KEY ("oral tongue squamous cell carcinoma") OR TITLE-ABS-KEY ("mouth squamous cell carcinoma") OR TITLE-ABS-KEY ("oral cavity squamous cell carcinoma") OR TITLE-ABS-KEY ("oropharynx squamous cell carcinoma") OR TITLE-ABS-KEY ("mouth carcinoma") OR TITLE-ABS-KEY ("oropharynx carcinoma") OR TITLE-ABS-KEY ("Head and Neck Neoplasms") OR TITLE-ABS-KEY ("Mouth Neoplasms") OR TITLE-ABS-KEY ("Oropharyngeal Neoplasms") OR TITLE-ABS-KEY ("Squamous Cell Carcinoma of Head and Neck") OR TITLE-ABS-KEY ("Oral Neoplasm") OR TITLE-ABS-KEY ("Oral Cancer") OR TITLE-ABS-KEY ("Oropharyngeal Cancer") OR TITLE-ABS-KEY ("Oral Squamous Cell Carcinoma") OR TITLE-ABS-KEY ("Oral Cavity Squamous Cell Carcinoma") OR TITLE-ABS-KEY ("Oral Squamous Cell Carcinomas") OR TITLE-ABS-KEY ("Squamous Cell Carcinoma of the Mouth") OR TITLE-ABS-KEY ("Oropharyngeal Squamous Cell Carcinoma")))) AND ((ALL (socioeconomics) OR ALL ("economic status") OR ALL ("educational status") OR ALL ("income group") OR ALL (poverty) OR ALL ("socioeconomic distribution") OR ALL ("socioeconomic parameters") OR ALL ("socioeconomic

vulnerability") OR ALL ("household economic status") OR ALL ("health insurance") OR ALL ("Socioeconomic Factors") OR ALL ("Social Class") OR ALL (demography) OR ALL ("Standard of Living") OR ALL ("Land Tenure") OR ALL ("Social Inequality") OR ALL ("High-Income Population") OR ALL ("Health Insurances") OR ALL ("Income Distribution") OR ALL ("Low-Income Population") OR ALL ("Middle Class Population") OR ALL ("Schooling Level") OR ALL ("Demographic Impacts") OR TITLE-ABS-KEY ("Patient Profile")) AND ((TITLE-ABS-KEY ("time to treatment") OR TITLE-ABS-KEY ("Therapy delay") OR TITLE-ABS-KEY ("Time-to-Treatment") OR TITLE-ABS-KEY ("Door-to-Treatment Time") OR TITLE-ABS-KEY ("Door to Treatment Time") OR TITLE-ABS-KEY ("Delayed Treatment") OR TITLE-ABS-KEY ("Delayed Treatments") OR TITLE-ABS-KEY ("Treatment Delay") OR TITLE-ABS-KEY ("Primary Treatment") OR TITLE-ABS-KEY ("Waiting Time") OR TITLE-ABS-KEY (timeliness) OR TITLE-ABS-KEY ("Delay in Treatment") OR TITLE-ABS-KEY ("Time to Start Treatment") OR TITLE-ABS-KEY ("Diagnosis-treatment interval") OR TITLE-ABS-KEY ("Time-to-initiation") OR TITLE-ABS-KEY ("Treatment initiation") OR TITLE-ABS-KEY ("Treatment time") OR TITLE-ABS-KEY ("Treatment times") OR TITLE-ABS-KEY ("Timely care") OR TITLE-ABS-KEY ("Diagnosis to treatment") OR TITLE-ABS-KEY ("Time factors") OR TITLE-ABS-KEY ("Time to treatment initiation")))

Web of science

TS=((“head and neck tumor” OR “head and neck tumor” OR “mouth tumor” OR “mouth tumor” OR “mouth cancer” OR “oropharynx tumor” OR “oropharynx tumor” OR “oropharynx cancer” OR “squamous cell carcinoma of the head and neck” OR “head and neck squamous cell carcinoma” OR “oral tongue squamous cell carcinoma” OR “mouth squamous cell carcinoma” OR “mouth squamous cell carcinoma” OR “oral cavity squamous cell carcinoma” OR “oropharynx squamous cell carcinoma” OR “oropharynx squamous cell carcinoma” OR “mouth carcinoma” OR “mouth carcinoma” OR “oropharynx carcinoma” OR “oropharynx carcinoma” OR “head and neck neoplasm” OR “cancer of head and neck” OR “head and neck cancer” OR “head neoplasms” OR “head neoplasm” OR “cancer of head” OR “head cancers” OR “mouth neoplasm” OR “oral neoplasm” OR “oral neoplasms” OR “cancer of mouth” OR “mouth cancers” OR “oral cancer” OR “oral cancers” OR “cancer of the mouth” OR “mouth cancer” OR “oropharyngeal neoplasm” OR “oropharynx neoplasms” OR “oropharynx neoplasm” OR “cancer of oropharynx” OR “oropharynx cancer” OR “oropharynx cancers” OR “oropharyngeal cancer” OR “oropharyngeal cancers” OR “oropharynx cancer” OR “oropharynx cancers” OR “cancer of

the oropharynx" OR "head and neck squamous cell carcinomas" OR "squamous cell carcinoma of the head and neck" OR "head and neck squamous cell carcinoma" OR "oral tongue squamous cell carcinoma" OR "oral squamous cell carcinoma" OR "oral cavity squamous cell carcinoma" OR "oral squamous cell carcinomas" OR "squamous cell carcinoma of the mouth" OR "oropharyngeal squamous cell carcinoma") AND ("socioeconomics" OR "socioeconomics" OR "economic status" OR "economic status" OR "educational status" OR "educational status" OR "income group" OR "income group" OR "poverty" OR "poverty" OR "socioeconomic distribution" OR "socioeconomic distribution" OR "socioeconomic parameters" OR "socioeconomic parameters" OR "socioeconomic vulnerability" OR "socioeconomic vulnerability" OR "household economic status" OR "household economic status" OR "health insurance" OR "health insurance" OR "income" OR "socioeconomic factors" OR "social class" OR "demography" OR "socioeconomic factor" OR "standard of living" OR "living standard" OR "living standards" OR "land tenure" OR "social inequality" OR "social inequalities" OR "high-income population" OR "high income population" OR "high-income populations" OR "incomes" OR "savings" OR "income distribution" OR "income distributions" OR "low-income population" OR "low-income populations" OR "low income population" OR "low income populations" OR "social classes" OR "socioeconomic status" OR "middle class population" OR "educational achievement" OR "educational achievements" OR "schooling level" OR "educational levels" OR demographic OR "population spatial distributions" OR "demographic factors" OR "demographic factor" OR "demographic impacts" OR "demographic impact" OR "patient profile") AND ("time to treatment" OR "therapy delay" OR "therapy delay" OR "time to treatment" OR "time-to-treatment" OR "time-to-treatments" OR "door-to-treatment time" OR "door to treatment time" OR "delayed treatment" OR "delayed treatments" OR "treatment delay" OR "primary treatment" OR "waiting time" OR "timeliness" OR "delay in treatment" OR "time to start treatment" OR "diagnosis-treatment interval" OR "time-to-initiation" OR "treatment initiation" OR "treatment time" OR "treatment times" OR "timely care" OR "diagnosis to treatment" OR "time factors" OR "time to treatment initiation"))

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((mh:(head AND neck neoplasms)) OR (mh:(mouth neoplasms)) OR (mh:(oropharyngeal neoplasms)) OR (mh:(squamous cell carcinoma of head AND neck)) OR (cancer of head) OR (cancer of head AND neck) OR (cancer of the head) OR (cancer of the head AND neck) OR (head cancer) OR (head cancers) OR (head neoplasm) OR (head neoplasms) OR (head AND neck cancer) OR (head AND neck neoplasm) OR (cancer of mouth) OR (cancer of the mouth) OR (mouth cancer) OR (mouth cancers) OR (mouth neoplasm) OR (oral cancer) OR (oral cancers) OR (oral neoplasm) OR (oral neoplasms) OR (cancer of oropharynx) OR (cancer of the oropharynx) OR (oropharynx cancer) OR (oropharynx

cancers) OR (oropharyngeal cancer) OR (oropharyngeal cancers) OR (oropharyngeal neoplasm) OR (oropharynx cancer) OR (oropharynx cancers) OR (oropharynx neoplasm) OR (oropharynx neoplasms) OR (head AND neck squamous cell carcinomas) OR (head AND neck squamous cell carcinoma) OR (oral cavity squamous cell carcinoma) OR (oral squamous cell carcinoma) OR (oral squamous cell carcinomas) OR (oral tongue squamous cell carcinoma) OR (oropharyngeal squamous cell carcinoma) OR (squamous cell carcinoma of the mouth)) AND ((mh:(socioeconomic factors)) OR (high income population) OR (high-income population) OR (high-income populations) OR (land tenure) OR (living standard) OR (living standards) OR (social inequalities) OR (social inequality) OR (social inequity) OR (socioeconomic factor) OR (standard of living) OR (educational level) OR (educational status) OR (social class)) AND ((mh:(time-to-treatment)) OR (delayed treatment) OR (delayed treatments) OR (door TO treatment time) OR (time TO treatment) OR (time TO treatments) OR (time-to-treatments) OR (treatment delay) OR (treatment delays) OR (primary treatment) OR (waiting time) OR (timeliness) OR (time TO start treatment) OR (diagnosis-treatment interval) OR (time-to-initiation) OR (treatment initiation) OR (treatment time) OR (treatment times))

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("mouth neoplasms" OR "oropharyngeal neoplasms" OR "oral squamous cell carcinoma") AND ("socioeconomic factors" OR income OR "educational level") AND ("time-to-treatment" OR "treatment delay" OR timeless OR "waiting time")

Open grey

Oral cancer AND treatment delay

Fonte: Elaborado pela autora, 2023.

4.1.5 Seleção dos estudos

Os artigos recuperados das bases de dados foram exportados para o *EndNote Web (Clarivate)* (<http://myendnoteweb.com>) e as duplicatas foram removidas. Dois pares de revisores (D.R.A.B.S.M/ V.F.L. e D.R.A.B.S.M/ Y.S.G.) examinaram independentemente os títulos e resumos. O *software Rayyan (Qatar Computing Research Institute)* (Ouzzani *et al.*, 2016) foi utilizado para o processo de triagem. Os artigos que atenderam aos critérios de inclusão foram selecionados para análise do texto completo, realizada pelos mesmos revisores. As divergências de opinião em todas as etapas foram resolvidas por discussão e consenso. Se a discordância persistisse, um terceiro revisor (R.C.M.) tomava a decisão final. Antes de

cada fase, o investigador principal treinou os revisores com uma amostra de 10% dos artigos.

4.1.6 Extração de dados

Foi criada uma planilha utilizando o programa *Microsoft Excel* para extração de dados. O formulário foi testado com uma amostra de quatro artigos. Dois revisores (D. R. A. B. S. M. e V. F. L.) extraíram os dados de forma independente e um consenso foi alcançado por meio de discussão. O autor sênior avaliou a concordância entre todos os dados.

Foram extraídos os seguintes dados: autores, ano de publicação, país em que o estudo foi realizado, desenho do estudo, tamanho da amostra, distribuição por sexo, faixa etária, definição de atraso no tratamento segundo o autor, distribuição de cada variável socioeconômica relatada nos artigos, medidas de associação, financiamento, conflitos de interesses e conclusão.

4.1.7 Risco de viés dos estudos incluídos

Dois revisores independentes (D.R.A.B.S.M. e C.C.M.P.) avaliaram o risco de viés dos artigos usando a lista de verificação da *Critical Appraisal Tool for Cohort Studies* do *Joanna Briggs Institute* (JBI) (Moola *et al.*, 2020). Essa ferramenta possui 11 domínios que podem ser reconhecidos como “sim”, “não”, “não aplicável” ou “não claro”. Os seguintes critérios para os estudos de coorte foram avaliados: semelhança dos grupos recrutados na mesma população, medidas de exposição, fatores de confusão, estratégias para lidar com fatores de confusão, grupos/ participantes livres do desfecho no início do estudo (ou no momento da avaliação/ exposição), medidas do desfecho, tempo de acompanhamento relatado, *follow-up* concluído, estratégias para lidar com *follow-up* incompleto e análise estatística apropriada.

Sexo e idade foram considerados como fatores de confusão mínimos selecionados para análise ajustada nesta revisão. Os revisores já haviam passado por exercícios de treinamento e calibração coordenados por um pesquisador com experiência em avaliação de qualidade de estudos observacionais (C.C.M.P.). Divergências de opinião foram discutidas até que um consenso fosse alcançado.

4.1.8 Medidas de associação

O desfecho primário de atraso no tratamento foi definido de acordo com os pontos de corte do maior tempo entre diagnóstico e tratamento abordado pelos estudos incluídos: ≥ 30 dias (Tsai *et al.*, 2017, Goel *et al.*, 2019, Sharma *et al.*, 2016) ≥ 38 dias (Morse *et al.*, 2018a), ≥ 45 dias (Fujiwara *et al.*, 2017), ≥ 50 dias (Morse *et al.*, 2018b) > 6 semanas (Su *et al.*, 2021). As variáveis socioeconômicas foram selecionadas de acordo com os fatores relatados pelos artigos. Assim, as definições das variáveis, bem como as categorias apresentadas, foram avaliadas de acordo com a forma como foram relatadas pelos autores, incluindo: sexo (masculino ou feminino), idade (faixa etária ou idade média), seguro (privado, *Medicare*, *Medicaid*, programa governamental ou não segurado), tipo de instalação (acadêmico, comunitário ou programa de rede integrada do câncer), volume de serviços hospitalares (baixo, médio ou alto), nível hospitalar (local/regional e centro médico), propriedade do hospital (público ou privado), localização do diagnóstico inicial (diagnóstico e tratamento em diferentes instalações), nível de urbanização da localização do hospital (variando de 1 [cidades urbanas altamente desenvolvidas] a 7 [distritos remotos]), distância do centro de tratamento (em milhas), local de residência do paciente (regional/remoto, metropolitano ou rural, intermediário e urbano), nível de educação (obtido considerando a porcentagem de indivíduos com ensino médio com base no código postal residencial dos pacientes), raça/cor da pele (branco, não branco/negro/hispânico/outro/desconhecido) e estado civil (casado, solteiro, divorciado ou viúvo).

4.1.9 Síntese dos resultados

Uma tabela foi elaborada com as seguintes características gerais dos estudos: autor, ano de publicação, país, tamanho da amostra, sexo e idade da amostra, definição do desfecho, variáveis socioeconômicas e conclusão.

As estimativas individuais dos estudos que mostraram desfechos com *odds ratios* (OR) e intervalos de confiança de 95% (IC95%) foram analisadas usando o *software STATA*, versão 18 (<https://www.stata.com>). As estimativas finais foram apresentadas em *forest plots* a fim de representar visualmente a direção e magnitude do efeito (McKenzie; Brennan, 2019). A categoria “desconhecido” não foi incluída nos *forest plots*, pois esses dados não permitem interpretação clara.

Estudos que demonstraram associações por meio de coeficientes de regressão ou valores de p foram apresentados apenas em uma tabela descritiva contendo todas as variáveis socioeconômicas relatadas por todos os estudos incluídos nesta revisão sistemática.

A abordagem *Grading of Recommendations Assessment, Development, and Evaluation* (GRADE) foi usada para classificar a certeza da evidência para o resultado relacionado ao tratamento tardio de câncer bucal de acordo com os seguintes critérios: risco de viés, inconsistência, evidência indireta, imprecisão ou viés de publicação. De acordo com os critérios GRADE, um nível de evidência foi reduzido para cada critério avaliado como “grave”. Estudos observacionais começam com baixa certeza da evidência (Zhang; Akl; Schünemann, 2019).

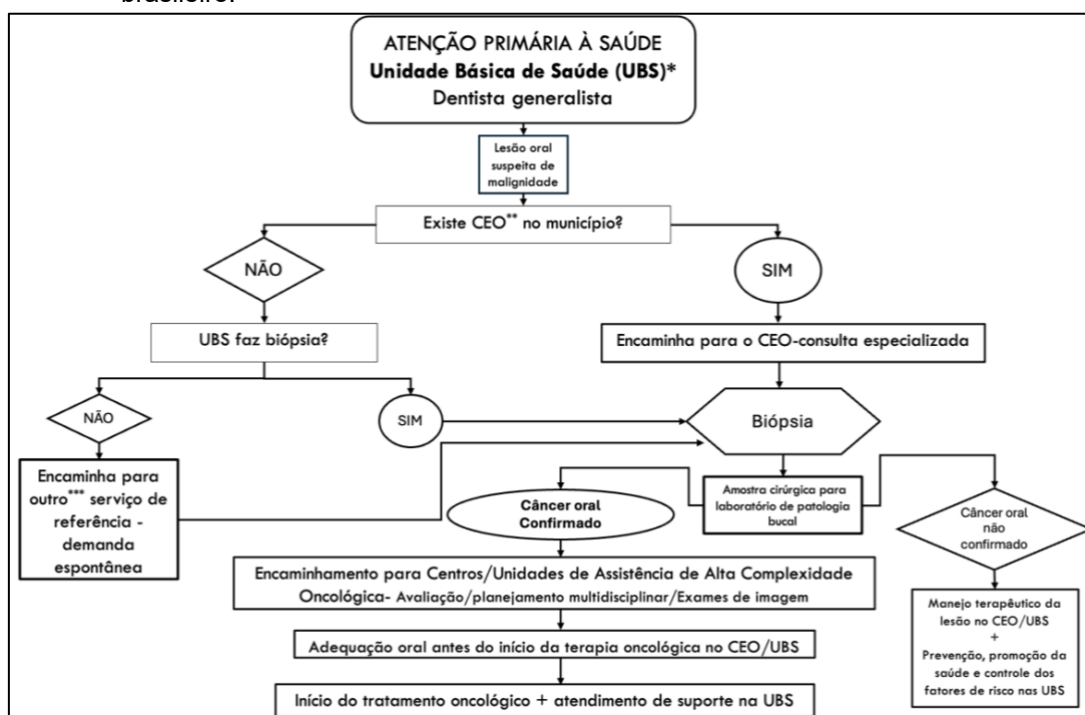
4.2 Estudo Ecológico Transversal Descritivo e Analítico

Foram avaliados 3.218 municípios brasileiros que registraram, pelo menos, um caso de câncer de boca e orofaringe em adultos (20 anos ou mais) em 2019. A esfera municipal organiza, executa e gerencia os serviços e ações que ocorrem na Atenção Primária à Saúde (APS) (Brasil, 2017). A APS é a principal porta de entrada da população para o sistema público de saúde brasileiro e é responsável por coordenar os fluxos entre os diversos pontos da Rede de Atenção à Saúde (RAS) para garantir a integralidade do cuidado (Brasil, 2017). A APS, por meio das Unidades Básicas de Saúde (UBS), atua na promoção da saúde, prevenção e controle dos fatores de risco, triagem e diagnóstico inicial do CBO (Torres-Pereira *et al.*, 2012).

Quando lesões potencialmente malignas são identificadas na APS, os pacientes são encaminhados aos níveis secundários (Centros de Especialidades Odontológicas - CEO) ou terciários para confirmação diagnóstica por meio de biópsia (Thomaz *et al.*, 2022, Leal *et al.*, 2021, Torres-Pereira *et al.*, 2012). Após a confirmação do diagnóstico de malignidade, os pacientes são encaminhados para Centros ou Unidades Oncológicas de Alta Complexidade (CACONS/UNACONS) para serem submetidos à cirurgia oncológica, radioterapia e/ou quimioterapia. A UBS também atua nos procedimentos de adequação do pré-tratamento do câncer, além de apoiar os pacientes durante e após o tratamento oncológico. Nos casos em que a lesão é benigna, o paciente retorna à UBS para manejo terapêutico da lesão, prevenção e controle dos fatores de risco (Torres-Pereira *et al.*, 2012). A Figura 3 mostra os fluxos

entre os diversos pontos da RAS brasileira considerando o caminho para o diagnóstico e tratamento do CBO.

Figura 2- Fluxos de diagnóstico e tratamento de CBO no sistema público de saúde brasileiro.



*Unidade Básica de Saúde; **Centro de Especialidades Odontológicas;

***Hospitais universitários, hospitais gerais, policlínicas.

Fonte: Montagnoli *et al.*, 2024, p. 4.

Todas as informações são de domínio público. Portanto, o Comitê de Ética em Pesquisa com Seres Humanos não precisou aprovar este estudo. Os dados secundários dos registros de CBO foram obtidos no Painel de Monitoramento de Tratamento Oncológico (Painel-Oncologia) do Departamento de Informática do Sistema Único de Saúde (DATASUS) (http://tabnet.datasus.gov.br/cgi/dhdat.exe?PAINEL_ONCO/PAINEL_ONCOLOGIABR.def) em 2 de fevereiro de 2023. Essa plataforma coleta informações dos serviços públicos de saúde (instituições de saúde públicas ou privadas conveniadas ao SUS) que prestam atendimento oncológico no Brasil. É uma ferramenta para gestores e planejadores de saúde acompanharem o tempo desde o diagnóstico até o primeiro tratamento do câncer, utilizando dados dos sistemas de informação consolidados no SUS. Embora não se refira à incidência de câncer no país, abrange alto grau de heterogeneidade na população estudada. Os dados estão

agrupados por local de cadastramento (municípios, estados e macrorregiões) e não é possível identificar diretamente os pacientes.

Este estudo baseia-se no modelo teórico de Weller *et al.* (2012), em que são identificados alvos para facilitar a avaliação dos motivos que interferem no diagnóstico precoce e, conseqüentemente, melhorar o prognóstico dos casos de câncer. Para tanto, são considerados três fatores – paciente, sistema de saúde e doença – que modulam os processos de tomada de decisão que permeiam os intervalos de tempo até o tratamento.

O tempo até o início do tratamento (TIT) foi a variável dependente definida como a proporção de registros municipais de CBO com tratamento iniciado dentro de 30 dias do diagnóstico confirmado pelo total de registros de CBO em 2019. Iniciar o tratamento com mais de 30 dias leva a pior prognóstico e menor sobrevivência em casos de CBO (Tsai *et al.*, 2017, Goel *et al.*, 2019, Fujiwara *et al.*, 2017, Murphy *et al.*, 2015, Graboyes *et al.*, 2019).

De acordo com o teste de normalidade *Kolmogorov-Smirnov*, TIT apresentou distribuição não-normal ($p > 0,05$). Assim, essa variável foi categorizada em três grupos: Atraso (municípios onde todos os tratamentos de CBO iniciaram após 30 dias); $0 < \text{Atraso} < 1$ (municípios com registros de tratamento de CBO dentro de 30 dias e acima de 30 dias); e sem atraso (municípios onde todos os tratamentos CBO começaram dentro de 30 dias).

As variáveis independentes e suas definições, fontes de dados e de acesso estão apresentadas na Tabela 1. As variáveis explicativas foram divididas em cinco dimensões: 1. Características do paciente (CP); 2. Acesso aos serviços de saúde (AS); 3. Estrutura de apoio ao diagnóstico de câncer (EC); 4. Recursos humanos (RH); e 5. Características municipais (CM).

Para construção da dimensão CP, foram coletadas variáveis do Painel-Oncologia de acordo com aspectos mais associados ao atraso no tratamento do CBO relatados na literatura: sexo feminino, faixas etárias mais acometidas pela doença (45-59 e acima 60 anos), estágios mais avançados (III e IV), tratamento com quimioterapia, radioterapia ou ambos (Su *et al.*, 2021, Tsai *et al.*, 2017, Goel *et al.*, 2019). Foram calculadas as proporções de registros de cada variável pelo número total de registros de cada município em 2019. Os dados foram coletados no local de residência dos casos registrados.

Os registros de neoplasias bucais são identificados utilizando a classificação C00-C10 da 10ª revisão da Classificação Internacional de Doenças (CID-10) no Painel-Oncologia. Ao analisar o câncer bucal, alguns autores defendem a exclusão das neoplasias de lábios e glândulas salivares desta categoria por apresentarem comportamento etiológico, histológico e epidemiológico diferentes (Ant *et al.*, 2019, Carlson *et al.*, 2019), o que afeta o momento para o início do tratamento. Por conta disso, a proporção de registros de CBO foi avaliada por grupos de sítios anatômicos separadamente: CP4 (lábio: C00), CP5 (cavidade oral: C02-C04 e C06), CP6 (glândulas salivares: C07 e C08) e CP7 (orofaringe: C05, C09 e C10) (Quadro 2).

Quanto à dimensão EC, foram considerados apenas os serviços públicos ou privados conveniados ao SUS. Para a variável EC1, foram incluídos todos os serviços de oncologia clínica (ambulatorial e hospitalar) disponíveis nos municípios. Hospitais pediátricos foram excluídos tendo em vista que neoplasias malignas orais são raras em crianças (Yuhan *et al.*, 2018). A variável EC3 tratou-se de hospitais gerais, clínicas e laboratórios especializados em diagnóstico patológico disponíveis no município, sendo excluídas unidades básicas de saúde, de atenção primária ou mistas, pois realizam exames citopatológicos voltados ao controle e prevenção do câncer de colo do útero. Hospitais limitados a uma única especialidade médica (por exemplo, nefrologia, oftalmologia, ginecologia, neurologia e urologia) também foram desconsiderados (Quadro 2).

As características socioeconômicas dos municípios foram obtidas no censo de 2010 do Instituto Brasileiro de Geografia e Estatística (IBGE). As estimativas populacionais municipais para 2019 do IBGE foram consideradas para cálculo de percentuais por 100 mil habitantes e obtenção das razões de distribuição dos serviços de saúde prestados pelos municípios.

Quadro 2 -Variáveis explicativas com definições, fonte dos dados e acesso.

VARIÁVEL	DEFINIÇÃO	FONTE DOS DADOS	ACESSO (internet)
Características do paciente (CP)			
CP1 – Percentual de casos de 45 a 59 anos	Total de registros de CBO (C00-C10) com faixa etária de 45 a 59 anos pelo total de registros de CBO do município em 2019.	Painel-Oncologia-DATASUS	http://tabnet.datasus.gov.br/cgi/dhdat.exe?PAINEL_ONCO

			/PAINEL_ONCOLOGIABR.def
CP2 – Percentual de casos de 60 anos ou mais	Total de registros de CBO (C00-C10) do município com faixa etária 60 anos ou mais pelo total de registros de CBO do município em 2019.	Painel-Oncologia DATASUS	http://tabnet.datasus.gov.br/cgi/dhdat.exe?PAINEL_ONCOLOGIABR.def
CP3 – Percentual de casos do sexo feminino	Total de registros de CBO (C00-C10) do sexo feminino pelo total de registros de CBO do município em 2019.	Painel-Oncologia DATASUS	http://tabnet.datasus.gov.br/cgi/dhdat.exe?PAINEL_ONCOLOGIABR.def
CP4 – Percentual de casos de lábio	Total de registros de câncer de lábio (C00) do município pelo total de registros de CBO do município em 2019.	Painel-Oncologia DATASUS	http://tabnet.datasus.gov.br/cgi/dhdat.exe?PAINEL_ONCOLOGIABR.def
CP5 – Percentual de casos de cavidade oral	Total de registros de câncer de cavidade oral (C02-C04, C06) do município pelo total de registros de CBO do município em 2019.	Painel-Oncologia DATASUS	http://tabnet.datasus.gov.br/cgi/dhdat.exe?PAINEL_ONCOLOGIABR.def
CP6 – Percentual de casos de glândulas salivares	Total de registros de câncer de glândulas salivares (C07, C08) do município pelo total de registros de CBO do município em 2019.	Painel-Oncologia DATASUS	http://tabnet.datasus.gov.br/cgi/dhdat.exe?PAINEL_ONCOLOGIABR.def
CP7 – Percentual de casos de orofaringe	Total de registros de câncer de orofaringe (C01, C05, C09, C10) do município pelo	Painel-Oncologia DATASUS	http://tabnet.datasus.gov.br/c

	total de registros de CBO do município em 2019.		gi/dhdat.exe?PAINEL_ONCOLOGIABR.def
CP8 – Percentual de casos de estadiamento (III e IV)	Total de registros de CBO (C00-C10) do município com estadiamentos III e IV pelo total de registros de CBO do município em 2019.	Painel-Oncologia DATASUS	http://tabnet.datasus.gov.br/cgi/dhdat.exe?PAINEL_ONCOLOGIABR.def
CP9 – Percentual de casos de tratamento (quimioterapia, radioterapia ou ambos)	Total de registros de CBO (C00-C10) do município tratados com quimioterapia, radioterapia ou ambos pelo total de registros de CBO do município em 2019.	Painel-Oncologia DATASUS	http://tabnet.datasus.gov.br/cgi/dhdat.exe?PAINEL_ONCOLOGIABR.def
Acesso aos serviços de saúde (AS)			
AS1 – Presença de CEO	Centro de Especialidades Odontológicas (CEO) ativos até dezembro de 2019.	Cadastro Nacional dos Estabelecimentos de Saúde-DATASUS	https://cnes.datasus.gov.br/pages/estabelecimentos/consulta.jsp
AS2 – Cobertura de equipes de saúde da família- saúde bucal (ESF-SB)	Média de cobertura relativa ao ano de 2019.	e-Gestor Atenção Básica	https://egestorab.saude.gov.br/paginas/acessoPublico/relatorios/relHistoricoCoberturaSB.xhtml
AS3-Cobertura de equipes de saúde bucal da atenção básica (ESB-AB)	Média de cobertura relativa ao ano de 2019.	e-Gestor Atenção Básica	https://egestorab.saude.gov.br/paginas/acessoPublico/relatorios/relHistoricoCoberturaSB.xhtml

AS4-Percentual de população com plano odontológico	Total de população do município com plano odontológico em 2019 pela estimativa populacional do município para 2019 x 100 mil habitantes.	Agência Nacional de Saúde- DATASUS	https://www.anstas.gov.br/anstasbnet/cgi-bin/dh?dados/tabnet_tx.def
AS5-Percentual de população com plano de saúde- assistência médica	Total de população do município com plano de saúde em 2019 pela estimativa populacional do município para 2019 x 100 mil habitantes.	Agência Nacional de Saúde- DATASUS	https://www.anstas.gov.br/anstasbnet/cgi-bin/dh?dados/tabnet_tx.def
AS6-Percentual de leitos SUS no município por 100 mil habitantes	Total de leitos cirúrgicos (bucal maxilo facial, cirurgia geral e oncologia); e clínicos (clínica geral e oncologia) disponíveis no município em hospitais públicos e/ou privados conveniados ao SUS em 2019 pela estimativa populacional do município para 2019 x 100 mil habitantes.	Cadastro Nacional dos Estabelecimentos de Saúde – DATASUS	https://cnes2.datasus.gov.br/Mod_Ind_Tipo_Leito.asp?VEstado=11&VMun=110032&VComp=201909
Estrutura de apoio ao diagnóstico do câncer (EC)			
EC1 – Número de serviços de oncologia clínica por 100 mil habitantes	Total de serviços de oncologia cirúrgica (ambulatorio e hospitalar) disponíveis no município pela estimativa populacional do município para 2019 x 100 mil habitantes.	Cadastro Nacional dos Estabelecimentos de Saúde -DATASUS	https://cnes2.datasus.gov.br/Mod_Ind_Especialidades.asp?VEstado=11&VMun=110001&VComp=00&VTerc=00&VServico=132&VClassificacao=004&VAmbu=&VAmbuSUS=1&VHosp=&VHospSUS=1
EC2 – Número de serviços de radioterapia por 100 mil habitantes	Total de serviços de radioterapia (ambulatorio e hospitalar) disponíveis no município pela estimativa populacional do município para 2019 x 100 mil habitantes.	Cadastro Nacional dos Estabelecimentos de Saúde -DATASUS	https://cnes2.datasus.gov.br/Mod_Ind_Especialidades.asp?VEstado=11&VMun=110001&VComp=00

			https://cnes2.d atasus.gov.br/ Mod Ind Esp ecialidades.as p?VEstado=11 &VMun=11000 1&VComp=00 &VTerc=00&V Servico=132& VClassificacao =004&VAmbu =&VAmbuSUS =1&VHosp=& VHospSUS=1
EC3 – Número de serviços de diagnóstico anatomopatológico por 100 mil habitantes	Total de hospitais gerais, clínicas e laboratórios especializados em diagnóstico patológico disponíveis no município, com atendimento SUS, pela estimativa populacional do município para 2019 x 100 mil habitantes.	Cadastro Nacional dos Estabelecimentos de Saúde -DATASUS	https://cnes2.d atasus.gov.br/ Mod Ind Esp ecialidades.as p?VEstado=11 &VMun=11000 1&VComp=00 &VTerc=00&V Servico=132& VClassificacao =004&VAmbu =&VAmbuSUS =1&VHosp=& VHospSUS=1
EC4 – Número de serviços de diagnóstico por imagem -RM-por 100 mil habitantes	Total de hospitais, centros e clínicas especializados em diagnóstico de ressonância magnética (RM) disponíveis no município, com atendimento SUS, pela estimativa populacional do município para 2019 x 100 mil habitantes.	Cadastro Nacional dos Estabelecimentos de Saúde -DATASUS	https://cnes2.d atasus.gov.br/ Mod Ind Esp ecialidades.as p?VEstado=11 &VMun=11000 1&VComp=00 &VTerc=00&V Servico=132& VClassificacao =004&VAmbu =&VAmbuSUS =1&VHosp=& VHospSUS=1
EC5 – Número de serviços de diagnóstico por imagem -TC -por 100 mil habitantes	Total de hospitais, centros e clínicas especializados em diagnóstico de tomografia computadorizada (TC) disponíveis no município, com atendimento SUS, pela estimativa	Cadastro Nacional dos Estabelecimentos de Saúde -DATASUS	https://cnes2.d atasus.gov.br/ Mod Ind Esp ecialidades.as p?VEstado=11 &VMun=11000 1&VComp=00 &VTerc=00&V Servico=132& VClassificacao =004&VAmbu =&VAmbuSUS =1&VHosp=& VHospSUS=1

populacional do município para 2019 x 100 mil habitantes.	&VMun=110001&VComp=00&VTerc=00&VServico=132&VClassificacao=004&VAmbu=&VAmbuSUS=1&VHosp=&VHospSUS=1
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Recursos Humanos (RH)

RH1 – Número de estomatologista e patologista bucal por 100 mil habitantes	Total de estomatologistas e patologistas bucais do município pela estimativa populacional do município para 2019 x 100 mil habitantes.	Cadastro Nacional dos Estabelecimentos de Saúde – DATASUS	https://cnes2.datasus.gov.br/ModIndTipoLeito.asp?VEstado=11&VMun=110032&VComp=201909
RH2 – Número de cirurgião bucomaxilofacial por 100 mil habitantes	Total de cirurgões bucomaxilofacial do município pela estimativa populacional do município para 2019 x 100 mil habitantes.	Cadastro Nacional dos Estabelecimentos de Saúde – DATASUS	https://cnes2.datasus.gov.br/ModIndTipoLeito.asp?VEstado=11&VMun=110032&VComp=201909
RH3 – Número de dentistas especialistas por 100 mil habitantes	Total de estomatologistas, patologistas bucais e cirurgões bucomaxilofacial do município pela estimativa populacional do município para 2019 x 100 mil habitantes.	Cadastro Nacional dos Estabelecimentos de Saúde – DATASUS	https://cnes2.datasus.gov.br/ModIndTipoLeito.asp?VEstado=11&VMun=110032&VComp=201909

Características municipais (CM)

CM1 – IDH Municipal	Índice de Desenvolvimento Humano municipal relativo ao censo 2010.	Atlas Brasil	http://www.atlasbrasil.org.br/ranking
CM2 – Índice de Gini da renda domiciliar <i>per capita</i>	Índice de Gini da renda domiciliar <i>per capita</i> -2010.	IBGE-DATASUS	http://tabnet.datasus.gov.br/cgi/ibge/censo/cnv/ginibr.def

CM3 – PIB	Produto Interno Bruto municipal- 2019.	IBGE	https://www.ibge.gov.br/estatisticas/economicas/contas-nacionais/9088-produto-interno-bruto-dos-municipios.html?t=downloads&c=1100015
CM4 – Taxa de analfabetismo da população de 15 anos ou mais	IBGE Censo 2010.	Atlas Brasil	http://www.atlasbrasil.org.br/consulta/planilha
CM5 – Taxa de desocupação da população de 18 anos ou mais	IBGE Censo 2010.	Atlas Brasil	http://www.atlasbrasil.org.br/consulta/planilha
CM6 – Percentual de pessoas em domicílios urbanos com coleta de lixo	IBGE Censo 2010.	Atlas Brasil	http://www.atlasbrasil.org.br/consulta/planilha
CM7 – Percentual de pessoas em domicílios com abastecimento de água e esgoto inadequado	IBGE Censo 2010.	Atlas Brasil	http://www.atlasbrasil.org.br/consulta/planilha

Fonte: MONTAGNOLI *et al.*, 2024, p. 05.

Foi realizada análise descritiva das variáveis explicativas para avaliar a mediana, P25%, P75% e valores mínimo e máximo. Em seguida, utilizou-se a técnica de “Árvores de Classificação e Regressão” (*Classification and Regression Trees-CART*) para identificar as variáveis explicativas, distribuídas em cinco dimensões, que

apresentaram maior poder de discriminação para a variável resposta do TIT. A lógica desta técnica baseia-se na construção da árvore através da subdivisão sucessiva dos grupos em subgrupos (Breiman *et al.*, 1998). Assim, consiste em uma árvore de decisão na qual os dados são divididos em grupos menores com base em regras específicas, criando uma hierarquia de decisões em que as divisões anteriores afetam as subsequentes. Essas divisões consecutivas do conjunto de dados são realizadas usando o método *Chi-square Automatic Interaction Detection*-CHAID. O procedimento seleciona a variável independente com interação mais significativa com a variável dependente em cada subdivisão. Assim, é possível identificar subgrupos homogêneos, reduzindo os efeitos de multicolinearidade, *outliers* e dados faltantes.

Foi necessário estabelecer previamente alguns critérios na modelação dos dados: 1) cada nó (designação dada a cada subconjunto resultante da aplicação de uma regra de divisão) deveria conter um mínimo de 500 observações; 2) os nós terminais deveriam incluir pelo menos 200 observações; 3) exclusão de subdivisões com valores de probabilidade de significância (p-valor) superiores a 0,05. O algoritmo estabeleceu automaticamente pontos de corte para segmentar os grupos analisados. Esta análise também foi realizada para as cinco regiões brasileiras. Todas as análises foram realizadas utilizando o *Statistical Package for Social Sciences* (SPSS), versão 22.0 (IBM SPSS *Statistics for Windows*, Armonk, NY).

4.3 Estudo Ecológico Longitudinal Descritivo e Analítico

Este estudo ecológico utilizou dados secundários do Painel de Monitoramento do Tratamento Oncológico- Painel Oncologia do Departamento de Tecnologia da Informação do Sistema Único de Saúde (DATASUS) (http://tabnet.datasus.gov.br/cgi/dhdat.exe?PAINEL_ONCO/PAINEL_ONCOLOGIABR.def), de janeiro de 2019 a dezembro de 2023 no Brasil. Este painel monitora o tempo, medido em dias, entre o diagnóstico definitivo do câncer e o início da primeira intervenção terapêutica. Os dados são fornecidos pelos sistemas de informação dos serviços de atendimento oncológico oferecidos pelo Sistema Único de Saúde (SUS) (hospitais públicos ou privados conveniados ao SUS) (Atty *et al.*, 2020). Todas as informações são de domínio público e não identificam os pacientes. Portanto, este estudo não necessitou de aprovação pelo Comitê de Ética em Pesquisa em seres humanos.

Os registros de neoplasias malignas de CBO foram identificados utilizando a 10ª revisão da Classificação Internacional de Doenças - CID-10 (C00-C10), de acordo com a região de residência (Norte, Nordeste, Sudeste, Sul, Centro-Oeste) e foram acessados em 16 de março de 2025. Os seguintes dados foram coletados dos pacientes: sexo (masculino ou feminino) e faixa etária (zero a 44 anos, 45 a 59 anos e acima de 60 anos); estadiamento (estadiamento inicial - 0, I e II; estadiamento avançado - III e IV; e “não aplicável”); modalidade terapêutica (cirurgia, quimioterapia ou radioterapia); e tempo para início do tratamento (TIT) (≤ 30 dias e > 30 dias). Os casos sem informação sobre o tratamento foram excluídos da análise.

No Painel de Oncologia, o estadiamento é registrado quando o tratamento indicado é quimioterapia, radioterapia ou ambos. Os casos tratados cirurgicamente são classificados como estadiamento “não aplicável”.

A variável de desfecho TIT foi classificada da seguinte forma: $TIT \leq 30$ dias foi considerado o momento mais aceitável para iniciar o tratamento, enquanto $TIT > 30$ dias foi classificado como atraso do tratamento, uma vez que a literatura demonstra que tratamentos iniciados após 30 dias estão associados a pior prognóstico e diminuição da sobrevida ou aumento do risco de óbito (Tsai *et al.*, 2017, Graboyes *et al.*, 2019, Tirelli *et al.*, 2023).

As estimativas populacionais foram obtidas a partir da lista populacional por município publicada pelo Instituto Brasileiro de Geografia e Estatística (IBGE). A proporção de registros de TIT por 100.000 habitantes foi calculada para as regiões brasileiras.

Foi realizada uma análise de série temporal dos registros de CBO. O teste de *Box-Ljung* para correlação temporal foi utilizado para verificar se os resíduos da série temporal eram independentes (não autocorrelacionados) ao longo do tempo. Posteriormente, o estimador *Sen's Slope* foi aplicado para determinar a mediana das inclinações de todas as retas que conectam pares de pontos distintos na série ao longo do tempo, a fim de avaliar a taxa mensal de variação dos registros. O teste de *Mann-Kendall* foi utilizado para identificar tendências monotônicas (ou seja, tendências de aumento ou diminuição) nas séries. A tendência monotônica facilita a avaliação do comportamento geral da série ao longo do tempo.

Na etapa seguinte, a presença de cointegração entre as variáveis desfecho ($TIT \leq 30$ dias e $TIT > 30$ dias) e as variáveis independentes (sexo, faixa etária, tipo de tratamento, estadiamento e região de residência) foi avaliada por meio do teste de

Engle-Granger. A cointegração indica se existe uma relação de longo prazo entre as variáveis (Engle; Granger, 1987). Esse teste envolve duas etapas principais: (1) estimar uma regressão linear entre as séries temporais em estudo e (2) avaliar se os resíduos dessa regressão são estacionários. Após a verificação da cointegração, modelos ARIMA (*Auto Regressive Integrated Moving Average*) foram ajustados a todas as séries temporais e a qualidade dos modelos foi avaliada por meio da análise de resíduos, utilizando o teste de *Breusch-Godfrey*. Por fim, regressões lineares simples foram realizadas entre os resíduos das séries para quantificar, por meio do coeficiente de determinação, o impacto das variáveis independentes nas variáveis desfecho. Todos os procedimentos de análise de dados foram conduzidos utilizando o *software R*, versão 4.3.1 (*R Core Team*). Para todos os testes, um valor de $p \leq 0,05$ foi considerado estatisticamente significativo.

5 RESULTADOS E DISCUSSÃO

Os resultados da presente tese de Doutorado foram desenvolvidos no formato de três artigos apresentados a seguir.

5.1 Artigo I - Fatores socioeconômicos que influenciam atrasos no tratamento do carcinoma espinoelular de boca e orofaringe: uma revisão sistemática

Artigo publicado no periódico Cadernos de Saúde Pública em abril de 2025 (Anexo A).

Fator de impacto: 1.9

Qualis Capes: A1

Socioeconomic factors affecting treatment delays in oral and oropharyngeal squamous cell carcinoma: A systematic review

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Abstract

This systematic review investigates associations between socioeconomic factors and treatment delay in adults with oral and oropharyngeal squamous cell carcinoma (OOSCC). Observational studies were searched across five databases (PubMed, Scopus, Web of Science, Embase, and Virtual Health Library) and grey literature. No restrictions were imposed about language or year of publication. Risk of bias was analyzed using the Joanna Briggs Institute tool. The primary outcome was defined as the cut-off points of treatment delays, which was addressed by the studies included. The certainty of evidence was assessed following the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach. In total, 10 retrospective cohort studies were included in the narrative synthesis. Type of insurance plan, sex, older ages, non-white patients, low education level, treatment in public or regional hospital, need for transition care, and living in regional/remote areas were factors associated with treatment delay for OOSCC. However, methodological limitations regarding the adjustment for confounders, the heterogeneity of the definition of delay (different cut-off points), socioeconomic variables, and the lack of eligible articles from different countries resulted in a very low certainty of evidence due to severe issues of bias, inconsistency, and indirectness according to the GRADE guidelines. The association between socioeconomic factors and OOSCC treatment delay is inconclusive by the available data. Given the complexity of the determinants of access to timely OOSCC treatment, further research is recommended in different countries.

Keywords: Oral Cancer; Oropharyngeal Cancer; Squamous Cell Carcinoma; Treatment Delay; Socioeconomic Factors

Introduction

A socioeconomic gradient is found in oral health issues, especially oral and oropharyngeal squamous cell carcinoma (OOSCC) ^{1,2}. Higher incidences of OOSCC are reported in patients with low socioeconomic status in contexts of self-neglect and difficulty accessing preventive healthcare ^{1,2}. Inequalities regarding treatment for OOSCC are related to the difficulty in accessing health services, especially among more vulnerable populations. Poorer individuals often have more advanced stages of the condition and, consequently, a worse prognosis and higher mortality rate ^{3,4}.

Besides socioeconomic factors, the time elapsed between diagnosis and the onset of treatment is an important aspect in cases of OOSCC. The Aarhus Statement was proposed to standardize time points and intervals in screening for early cancer detection ⁵. The declaration suggests four key time points: date of first symptom, date of first presentation, date of referral, and date of diagnosis. Güneri & Epstein ⁶ established three main types of delay in cases of oral cancer: “patient delay”, which refers to the time from the first detection of a sign/symptom to the patient seeking care; “professional delay”, which is the time from the first examination/assessment by a healthcare professional to the final histological diagnosis of the malignancy; and “system delay”, which is the time from the final diagnosis to the onset of the first intervention. While the first two allude to diagnosis delay, the latter is related to treatment delay and involves broader structural issues, including access to healthcare.

Treatment delay has been reported as a consequence of diagnosis delay ⁷. However, the causes of treatment delay or system delay in cases of OOSCC need to be better understood. In addition to the characteristics of the disease, micro- and macro-social factors need to be considered ^{5,8}. Access to treatment is linked to the use of health services, which involves individual and contextual determinants ⁹. Delayed cancer treatment is an issue that impacts health systems worldwide ¹⁰. Ideally, patients should begin treatment as soon as they are diagnosed. As this is often not possible, studies have shown that up to 30 days to the onset of treatment is considered acceptable for a satisfactory prognosis and greater chance of survival in patients with OOSCC ^{11,12,13,14}. The impact of socioeconomic disparities on treatment delay for various types of cancer, such as breast cancer ¹⁵, colorectal cancer ¹⁶, hepatocellular carcinoma ¹⁷, and brain cancer ¹⁸, has been demonstrated. The evidence is rarer for OOSCC, but we can presume that this type of cancer is not the exception. It is

importante to investigate the association between social determinants of health related to the population's living conditions and the provision of health services. Thus, this systematic review aimed to investigate associations between socioeconomic factors and treatment delay in patients with OOSCC.

Material and methods

Eligibility criteria

This review was reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA statement, 2020) ¹⁹. The research question was: "Is there an association between socioeconomic factors and treatment delay in cases of OOSCC?". The question was formed considering the PECO framework for observational studies ⁶:

- Population (P): male and female patients aged 18 years or older with OOSCC;
- Exposure (E): lower/poorer socioeconomic status;
- Comparator (C): higher/better socioeconomic status;
- Outcome (O): treatment delay, defined as the time from the definitive diagnosis of the malignancy to the first intervention.

The inclusion criteria were patients with oral cancer or tumors in specific sites of the oral cavity and oropharynx; adults (≥ 18 years of age); studies with a histological diagnosis of squamous cell carcinoma; any socioeconomic factor; studies that assessed the time from diagnosis to the onset of treatment; and observational studies (cross-sectional, cohort, and case-control studies). No restrictions were imposed regarding language or year of publication.

Studies that reported head and neck cancers without considering oral and oropharyngeal cancers separately from other cancers (e.g., skin, lymph node, and thyroid cancers); and neoplasms of histological types other than squamous cell carcinoma, as they may show different progression rates and symptoms ²⁰, which may exert an influence on treatment delay were excluded.

Search strategy

In total, five databases were searched from inception to January 2023, updated in December 2023: MEDLINE (PubMed), Embase (Ovid), Scopus, Web of Science, and Virtual Health Library (BIREME). Grey literature was searched via OpenGrey and Google Scholar (the latter limited to the first 100 results listed). Specific search strategies were developed for each database and reviewed by an expert in systematic reviews. The reference lists of the articles included in the review were hand searched in an attempt to find additional relevant articles. The Box S1 (Supplementary Material; https://cadernos.ensp.fiocruz.br/static/arquivo/suppl-e00121324_8794.pdf) details the employed search strategies.

Selection process

The articles retrieved from the databases were exported to EndNote Web (<http://myendnoteweb.com>) and duplicates were removed. Titles and abstracts were independently screened by two pairs of reviewers (D.R.A.B.S.M./V.F.L. and D.R.A.B.S.M./Y.S.G.). The Rayyan software (<https://www.rayyan.ai/>) was used for the screening process ²¹. Articles that met the inclusion criteria were selected for full-text analysis, which was performed by the same reviewers. Divergences across stages were resolved by discussion until consensus. If disagreement persisted, a third reviewer (R.C.M.) made the final decision. Prior to each phase, the main investigator trained the reviewers with a sample of 10% of the articles.

Data extraction

A Microsoft Excel spreadsheet (<https://products.office.com/>) was created for data extraction. The form was tested with a sample of four articles. Data were independently extracted by one pair of reviewers (D.R.A.B.S.M./V.F.L.) and a consensus was reached via discussion. The senior author cross-checked all data.

The following data were extracted from each study: authors, year of publication, country, design, sample size, sex distribution, age group, definition of treatment delay, distribution of each socioeconomic variable, association measures, funding, conflicts of interest, and conclusion.

Assessment of risk of bias

The risk of bias was assessed by two independent reviewers (D.R.A.B.S.M. and C.C.M.P.) using the Joanna Briggs Institute (JBI) Critical Checklist for Cohort Studies ²². This tool is composed of 11 domains, each of which is rated as “yes”, “no”, “not applicable”, or “unclear”. Inclusion criteria were recruiting similar groups from the same population, measuring exposures, presenting confounders and strategies for dealing with them, showing groups/participants without the outcome at baseline (or at the time of exposure), measuring outcomes, reporting a complete follow-up time, presenting strategies for dealing with incomplete follow-up, and showing an appropriate statistical analysis. Sex and age were considered required confounders selected for the adjusted analysis. The reviewers had previously undergone training and calibration exercises coordinated by a researcher with expertise in assessing the quality of observational studies (C.C.M.P.). Divergences of opinion were discussed until a consensus was reached.

Data items

The primary outcome of treatment delay was defined according to the cut-off points of the longest time between diagnosis and treatment addressed by the studies included: ≥ 30 days ^{11,13,23}, ≥ 38 days ²⁴, ≥ 45 days ¹², ≥ 50 days ²⁵, and > 6 weeks ²⁶.

The socioeconomic variables were selected according to factors reported in the articles. Thus, definitions of the variables, as well as the categories presented, were evaluated according to the way they were reported by the authors, including: sex (male or female), age (age group or average age), insurance (private, Medicare, Medicaid, government program, or uninsured), facility type (academic, community, or integrated network cancer program), hospital service volume (low, middle, or high), hospital level (local/regional and medical center), hospital ownership (public or private), location of initial diagnosis (diagnosis and treatment at different facilities), urbanization level of the hospital location (ranging from 1 [highly developed urban cities] to 7 [remote districts]), distance from treatment center (in miles), place of patient residence (regional/remote, metropolitan or rural, intermediate, and urban), education level (obtained by considering the percentage of individuals with a high school degree based on the patients' residential zip code), race/skin color (white, non-

white/black/Hispanic/other/unknown), and marital status (married, single, divorced, or widowed).

Synthesis methods

The general characteristics of the articles were reported: author, year of publication, country, sample size, sex and age of the sample, definition of outcome, socioeconomic variables, and conclusion.

The individual estimates of studies that reported outcomes with odds ratios (OR) and 95% confidence intervals (95%CI) were analyzed using the STATA software, version 18 (<https://www.stata.com>). Final estimates were placed in a set of forest plots to visually represent the direction and magnitude of the effect ²⁷. The “unknown” category was not included in the forest plot, as these data cannot be interpreted. Associations that were reported as regression coefficients or p values were presented only in the descriptive table containing all socioeconomic variables reported by all studies included in this systematic review.

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach was used to classify the quality of evidence for the outcome related to the delayed diagnosis of oral cancer, according to the following criteria: risk of bias, inconsistency, indirect evidence, inaccuracy, or publication bias. According to GRADE criteria, a level of evidence was lowered for each severe concern and observational studies started with a low classification ²⁸.

Registration and protocol

The review protocol was registered a priori in the International Prospective Register of Systematic Reviews (PROSPERO) database (registration n. #CRD42022361948).

Results

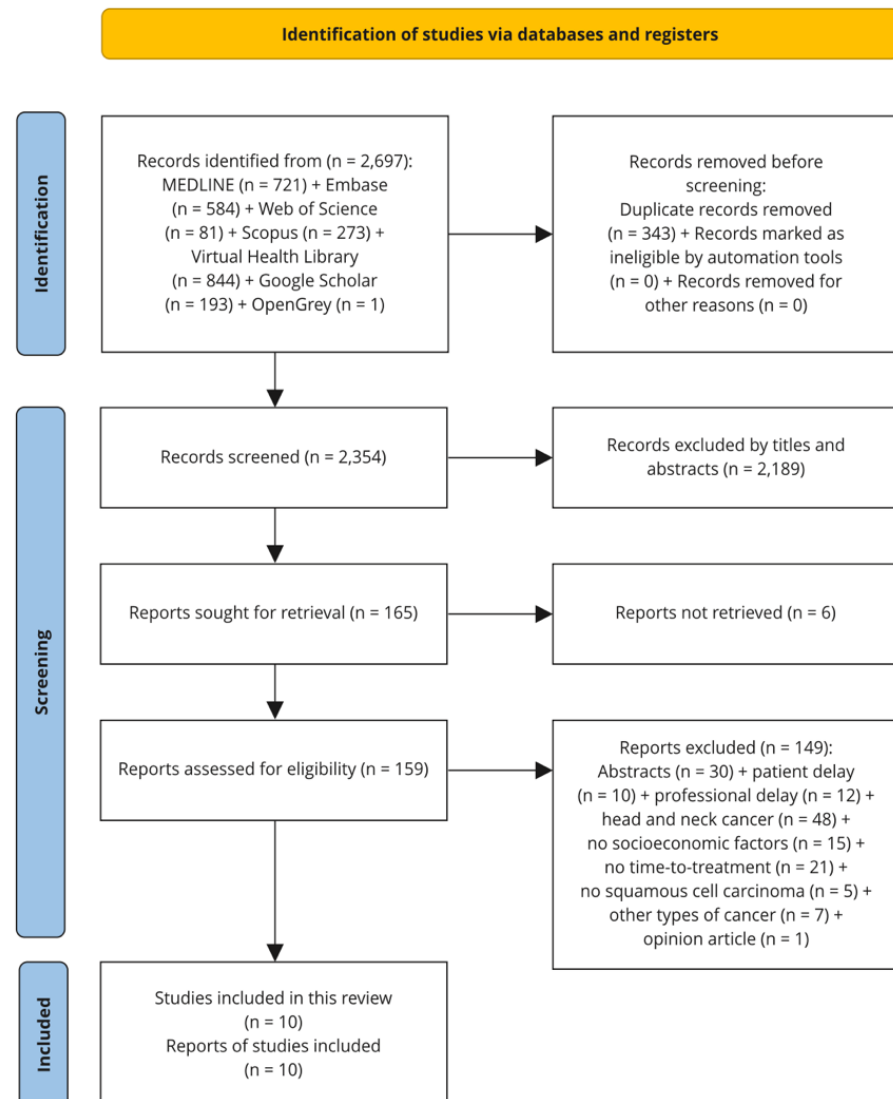
Article selection

Figure 1 shows the screening process for selecting articles based on titles, abstracts, and full texts. In total, 10 retrospective cohort studies were included in this systematic review ^{11,12,13,23,24,25,26,29,30,31}. Box S2 (Supplementary Material;

https://cadernos.ensp.fiocruz.br/static//arquivo/suppl-e00121324_8794.pdf) presents excluded articles and the reasons for exclusion.

Figure 1

Flowchart of the screening process.



Study characteristics

Box 1 shows the characteristics of the studies. All studies were published in English. Only one article was published in 2007²⁹, whereas the others were published from 2015 to 2021. In total, five studies were conducted in the United States^{12,13,23,24,25},

two in Taiwan ^{11,26}, one in Australia ³⁰, one in Canada ³¹, and one in the United Kingdom ²⁹.

A total of six studies included samples from large national health system databases ^{11,12,13,23,24,25}; one study from a national screening program ²⁶; and three studies from hospital records ^{29,30,31}. Sample size ranged from 224 to 21,263 participants. Male participants predominated in all studies (56.13% to 97%). Mean age ranged from 53.5 to 62.2 years in seven studies ^{11,12,13,23,29,30,31}, being ≤ 60 years in the other studies ^{24,25,26}. Tumor site was the oral cavity ^{11,12,31}, only the oropharynx ^{13,23,24,25}, or both ^{26,29,30}. Initial treatment was definitive chemotherapy ²³, radiotherapy or chemotherapy ²⁵, and surgery combined or not with radiotherapy or chemotherapy ^{11,12,13,24}. Type of initial therapy was not reported in four articles ^{26,29,30,31}.

Median time from diagnosis to treatment ranging from 20 to 35 days was reported in seven studies ^{12,13,23,24,25,26,29}. The remaining articles described a mean time ranging from 24.3 to 51.25 days ^{11,30,31}. Treatment delay was heterogeneous among studies. Treatment delay was categorized by four studies as follows: Group 1: < 30 days and Group 2: ≥ 30 days ²³; Group 1: no delay (first and second quartiles) and Group 2: delay (fourth quartile) ²⁵; Group 1: 0 to 3 weeks, Group 2: 4 to 6 weeks, and Group 3: 7 or more weeks ²⁶; Group 1: ≤ 30 days, Group 2: 31 to 120 days, and Group 3: > 120 days ¹¹.

The other studies reported treatment delay as continuous data, using mean or median number of days, quartiles, or specific number of days ^{12,13,24,26,29,30,31}. Among the 10 studies, only two ^{29,31} found no association between any socioeconomic factors and treatment delay for OOSCC.

Box 1

Studies characteristics and data extraction.

STUDY (YEAR) COUNTRY DATABASE	SAMPLE SIZE	SEX	AGE	CANCER SITE/ TREATMENT	TIME TO TREATMENT	DEFINITION OF TREATMENT DELAY	SOCIOECONOMIC FACTORS EVALUATED	CONCLUSION
Sharma et al. ²³ (2016); United States; NCDB	6,606	Male: 5,430 (82.2%); female: 1,176 (17.8%)	< 65 years: 5,053 (76.5%); ≥ 65 years: 1,553 (23.5%)	Oropharynx Definitive chemotherapy	Median: 32 days	Group 1: < 30 days (n = 3,020); Group 2: ≥ 30 days (n = 3,586)	Sex, age, race/skin color, insurance status, treatment facility, facility case-volume, patient distance from treatment center	Non-Hispanic black or Hispanic ethnicity, with Medicare, Medicaid coverage or uninsured status, receiving treatment at academic centers or high case-volume facilities were more likely to experience treatment delay
Morse et al. ²⁵ (2018); United States; NCDB	4,089	Male: 3,387 (83%); female: 702 (17%)	≤ 60 years: 2,518 (62%); > 60 years: 1,571 (38%)	Oropharynx Radiotherapy or concurrent chemotherapy	Median: 35 days	Group 1: no delay (first and second quartiles; n = 2,012); Group 2: delay (fourth quartile; n = 1,032)	Sex, age, race/skin color, primary payor (insurance), facility type, facility volume, care transitions	Non-white skin color, with Medicaid, Medicare, or no insurance, treatment at an academic/ research program, and no care transition between diagnosis and treatment were associated with treatment delay

(continues)

Box 1 (continued)

STUDY (YEAR) COUNTRY DATABASE	SAMPLE SIZE	SEX	AGE	CANCER SITE/ TREATMENT	TIME TO TREATMENT	DEFINITION OF TREATMENT DELAY	SOCIOECONOMIC FACTORS EVALUATED	CONCLUSION
Su et al. ²⁶ (2021); Taiwan; Screening Program of the Ministry of Health and Welfare of Taiwan	5,743	Male: 5,573 (97%); female: 170 (3%)	< 30years: 17 (0.3%); 30-59 years: 4,101 (71.4%); ≥ 60 years: 1,625 (28.3%)	Oral and oropharynx NR	Median: 20 days (IQR: 12-30)	Group 1: < 3 weeks (n = 3,267); Group 2: 3-6 weeks (n = 1,700); Group 3: 6 weeks or more (n = 776)	Sex, age, hospital level for cancer treatment	Female patients, aged 60 years or older and treated at a local/regional hospital experienced a longer delay in starting treatment
Tsai et al. ¹¹ (2017); Taiwan; NHIRD/ TCRD	21,263	Male: 19,505 (91.7%); female: 1,758 (8.3%)	≤ 44 years: 5,001 (23.5%); 45-54 years: 7,376 (34.7%); 55-64 years: 4,988 (23.5%); ≥ 65 years: 3,898 (18.3%)	Oral cavity Surgery, chemotherapy or radiotherapy	Mean: 24.3 days (±76.4)	Group 1: ≤ 30 days (n =18,193); Group 2: 31-120 days (n = 2,498); Group 3: > 120 days (n = 572)	Sex, age, urbanization level, premium-based monthly salary (income), hospital level, hospital ownership, hospital services volume	Female patients, ≥ 65 years, treated in regional hospitals, public hospitals and low services- volume hospitals tended to be treated later
Fujiwara et al. ¹² (2017); United States; NCDB	4,868	Male: 2,915 (59.9%); female: 1,953 (40.1%)	< 60 years: 2,114 (43.4%); ≥ 60 years: 2,754 (56.6%)	Oral cavity Surgery + radiotherapy + chemotherapy	Median: 30 days (range: 1-731; SD = 29.3)	Delayed treatment (fourth quartile of each treatment interval) and compared the first and second quartiles	Sex, age, race/ skin color, insurance, facility type, location of diagnosis	Patients above 60 years old, uninsured, insured, or using Medicaid, treatment at an academic/ research program and diagnosis at an outside facility were significantly associated with prolonged diagnosis- to-surgery intervals

(continues)

Box 1 (continued)

STUDY (YEAR) COUNTRY DATABASE	SAMPLE SIZE	SEX	AGE	CANCER SITE/ TREATMENT	TIME TO TREATMENT	DEFINITION OF TREATMENT DELAY	SOCIOECONOMIC FACTORS EVALUATED	CONCLUSION
Morse et al. ²⁴ (2018); United States; NCDB	3,708	Male: 3,022 (81%); female: 686 (19%)	≤ 60 years: 2,514 (68%); > 60 years: 1,194 (32%)	Oropharynx Primary surgery, with or without radiotherapy and chemotherapy	Median: 27 days	Delayed (fourth quartile) versus not delayed (first and second quartiles) for each interval	Sex, age, race/ skin color, primary payor (insurance), facility type, facility volume, care transition	Medicaid insurance and a care transition were associated with higher chances of treatment delay
Venchiarutti et al. ³⁰ (2020); Australia; Sydney Head and Neck Cancer Institute	224	Male: 162 (72.32%); female: 62 (27.67%)	Mean 60.9 years (SD = 12.1)	Oral and oropharynx NR	Overall mean: 39.5 (SD = 46.79)	Continuous variable (number of days)	Patients' residential geocoding addresses dichotomized into metropolitan or regional/remote	Median time from diagnosis to treatment was longer for regional/ remote patients' oropharyngeal cancer. There was no difference in the median time interval for the treatment of patients with oral cavity cancer from regional/ remote and metropolitan areas
Zhang et al. ³¹ (2015); Canada; ACR	554	Male: 311 (56.13%); female: 243 (43.86%)	Mean 61.3 years	Oral cancer NR	Overall mean: 51.25	Continuous variable (number of days)	Geographical groups: rural, intermediate, and urban	There was no statistically significant difference of mean time to treatment among the rural, intermediate, and urban groups. However, the urban group had the lowest (49.3) days to initiation of treatment

(continues)

Box 1 (continued)

STUDY (YEAR) COUNTRY DATABASE	SAMPLE SIZE	SEX	AGE	CANCER SITE/ TREATMENT	TIME TO TREATMENT	DEFINITION OF TREATMENT DELAY	SOCIOECONOMIC FACTORS EVALUATED	CONCLUSION
Rogers et al. ²⁹ (2007); United Kingdom; Regional Maxillofacial Unit in Liverpool	559	Male: 343 (61%); female: 216 (39%)	Mean 61 years (SD = 13)	Oral and oropharynx NR	Median: 21 days (IQR: 12-30)	Continuous variable (median days)	Sex, age, marital status, IMD 2000	There was no difference in treatment delay time for socioeconomic variables
Goel et al. ¹³ (2019); United States; NCDB	3,550	Male: 2,937 (82.7%); female: 613 (17.3%)	≤ 50 years: 790 (22.3%); 51-60 years: 1,522 (42.9%); 61-70 years: 964 (27.2%); ≥ 71 years: 274 (7.7%)	Oropharynx Surgery resection and adjuvant radiotherapy with or without chemotherapy	Median: 26 days (IQR: 14-39)	Continuous variable (number of days)	Sex, age, race/ skin color, education (percent of people with no high school degree), income (by patient's zip code of residence), insurance, facility type	Residence in an area with low education levels, Medicaid or uninsured status and treatment at an academic facility experienced longer mean treatment delay

ACR: Alberta Cancer Registry; IMD 2000: index of multiple deprivation 2000; IQR: interquartile range; NCDB: National Cancer Database; NHIRD: National Health Insurance Research Database; NR: not reported; SD: standard deviation; TCRD: Taiwan Cancer Registry Database.

Narrative synthesis

Box S3 (Supplementary Material; https://cadernos.ensp.fiocruz.br/static/arquivo/suppl-e00121324_8794.pdf) details the association between treatment delay and socioeconomic factors.

Insurance

In total, five studies conducted in the United States reported associations between treatment delay and type of insurance. Treatment delay was more likely among patients covered by Medicare (OR=1.27, 95%CI: 1.07; 1.51)²³, (OR=1.39, 95%CI: 1.11; 1.73)²⁵, or Medicaid (OR=1.58, 95%CI:1.32; 1.88)²³, (OR=1.97, 95%CI: 1.49; 2.60)²⁵, (OR=2.49, 95%CI: 1.55; 3.99)²⁴, and uninsured patients (OR=1.90, 95%CI: 1.55; 2.33)²³, (OR=2.71, 95%CI: 2.00; 3.68)²⁵, compared to those with private insurance^{13,23,24,25} (Figure 2).

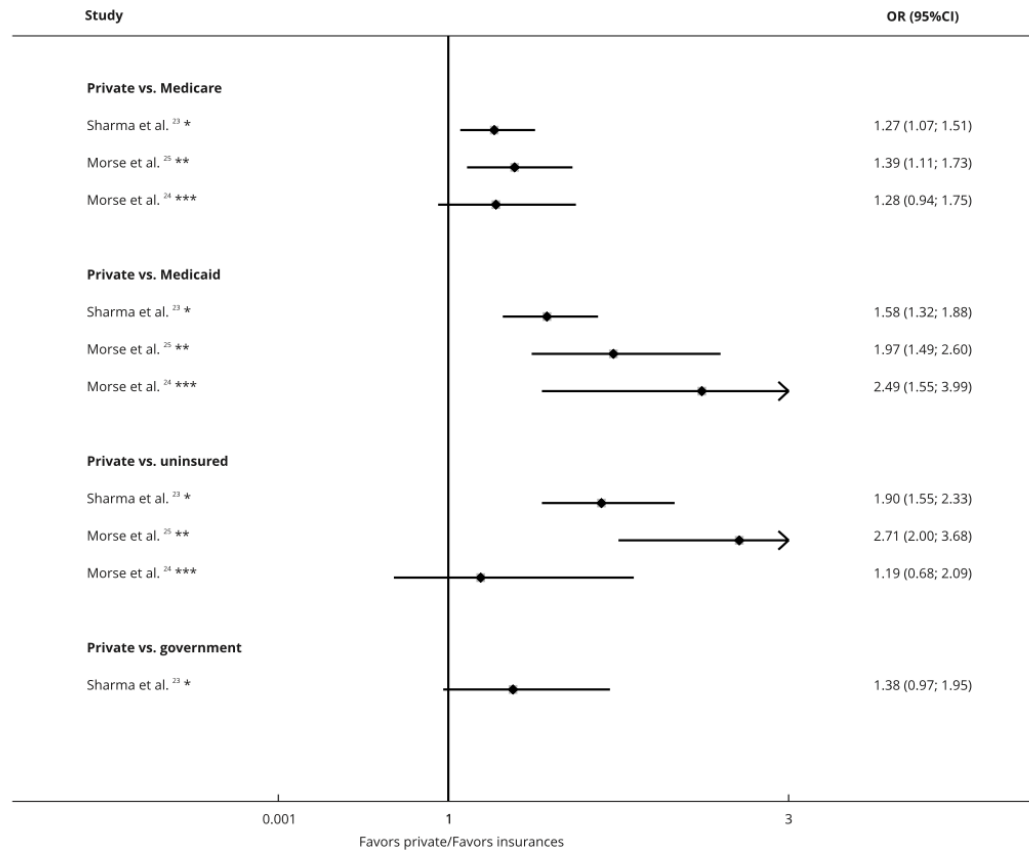
Goel *et al.*¹³ found that Medicaid had more mean days of delay than private insurance (coefficient:3.12, 95%CI: 0.10; 6.14) (Box 2).

The type of insurance reported as “unknown”¹² and associations reported as regression coefficients¹³ are not represented in the forest plot.

The certainty of evidence was very low due to the risk of bias, inconsistency, and indirectness (Box 2).

Figure 2

Forest plot comparing types of insurance and treatment delay organized by subgroups. Right denotes exposure, whereas left denotes the comparison.



95%CI: 95% confidence interval; OR: odds ratio.

* Delay cut-off: ≥ 30 days;

** Delay cut-off: ≥ 50 days;

*** Delay cut-off: ≥ 38 days.

Box 2

Associations between socioeconomic variables and treatment delay along with the certainty of evidence. Imported from GRADEpro Guideline Development Tool (GDT; <https://gdt.gradepro.org/app/#projects>).

OUTCOMES	IMPACT	TYPE OF STUDY	CERTAINTY OF EVIDENCE (GRADE)
Treatment delay Insurance (private versus Medicare)	Medicare showed more treatment delays than private insurance (Sharma et al. ²³ – cut-off 30 days, OR = 1.27, 95%CI: 1.07; 1.51; Morse et al. ²⁵ – cut-off: 50 days, OR = 1.39, 95%CI: 1.11; 1.73). However, Morse et al. ²⁴ (cut-off: 38 days) found that private insurance shows slightly less delay or is similar to Medicare (OR = 1.28, 95%CI: 0.94; 1.75). Goel et al. ¹³ (cut-off 30 days) found no significant differences in mean days of delay for private and Medicare (coefficient: 1.14, -0.98; 3.00)	4 non-randomized	⊕○○○ Very low * * * *
Treatment delay Insurance (private versus Medicaid)	Medicaid showed more treatment delays than private insurance (Sharma et al. ²³ – cut-off 30 days, OR = 1.58, 95%CI: 1.32; 1.88; Morse et al. ²⁵ – cut-off: 50 days, OR = 1.97, 95%CI: 1.49; 2.60; Morse et al. ²⁴ – cut-off: 38 days, OR = 2.49, 95%CI: 1.55; 3.99). Also, Goel et al. ¹³ (cut-off 30 days) showed that Medicaid had more mean days of delay than private insurance (coefficient: 3.12, 0.10; 6.14)	4 non-randomized	⊕○○○ Very low * * * *
Treatment delay Insurance (private versus government program)	Government programs showed more treatment delays than private (Sharma et al. ²³ – cut-off 30 days, OR = 1.38, 95%CI: 0.97; 1.95)	1 non-randomized	⊕○○○ Very low * * *
Treatment delay Insurance (private versus uninsured)	Uninsured showed more treatment delays than private insurance (Sharma et al. ²³ – cut-off 30 days, OR = 1.90, 95%CI: 1.55; 2.33; Morse et al. ²⁵ – cut-off: 50 days, OR = 2.71, 95%CI: 2.00; 3.68; Goel et al. ¹³ – cut-off 30 days, coefficient: 4.95, 0.71; 9.20). However, uninsured showed a similar delay compared to private insurance (Morse et al. ²⁴ – cut-off: 38 days, OR = 1.19, 95%CI: 0.68; 2.09)	4 non-randomized	⊕○○○ Very low * * * *
Treatment delay Facility type (community versus academic)	Academic medical centers showed more treatment delays than community centers (Sharma et al. ²³ – cut-off 30 days, OR = 1.26, 95%CI: 1.13; 1.42; Morse et al. ²⁵ – cut-off: 50 days, OR = 1.52, 95%CI: 1.03; 2.26; Fujiwara et al. ¹² – cut-off: 45 days, OR = 2.17, 95%CI: 1.49; 3.15), being also found to show more or equivalent delay (Morse et al. ²⁴ – cut-off: 38 days, OR = 1.79, 95%CI: 0.92; 3.51). Goel et al. ¹³ (cut-off 30 days) found that community centers show less mean days of delay than academic (coefficient: -5.28, -8.57; -1.99)	5 non-randomized	⊕○○○ Very low * * * *
Treatment delay Facility type (community versus comprehensive)	Comprehensive community cancer programs showed similar delays when compared to community programs (Morse et al. ²⁵ – cut-off: 50 days, OR = 0.98, 95%CI: 0.68; 1.42; Fujiwara et al. ¹² – cut-off: 45 days, OR = 1.16, 95%CI: 0.79; 1.70; Morse et al. ²⁴ – cut-off: 38 days, OR = 1.24, 95%CI: 0.65; 2.35).	4 non-randomized	⊕○○○ Very low * * * *
Treatment delay Facility type (community versus integrated network cancer program)	Integrated network cancer program showed greater or similar delays when compared to community programs (Morse et al. ²⁵ – cut-off: 50 days, OR = 1.33, 95%CI: 0.85; 2.08; Morse et al. ²⁴ – cut-off: 38 days, OR = 1.38, 95%CI: 0.65; 2.93).	2 non-randomized	⊕○○○ Very low * * * *
Treatment delay Facility type (academic versus comprehensive)	Academic facilities showed more mean days of delay than comprehensive programs (Goel et al. ¹³ – cut-off: 30 days, coefficient: -4.95, 95%CI: -6.65; -3.25)	1 non-randomized	⊕○○○ Very low * * * *

(continues)

Box 2 (continued)

OUTCOMES	IMPACT	TYPE OF STUDY	CERTAINTY OF EVIDENCE (GRADE)
Treatment delay Hospital services volume (low versus high)	High-volume hospital services were found to present more delay than low-volume services in a study (Sharma et al. ²³ – cut-off 30 days, OR = 1.38, 95%CI: 1.21; 1.58). However, high-volume services were found to show similar results compared to low-volume services in another study (Morse et al. ²⁵ – cut-off: 50 days, OR: 0.93, 95%CI: 0.67; 1.29; Morse et al. ²⁴ – cut-off: 38 days, OR = 1.09, 95%CI: 0.65; 1.83). Tsai et al. ¹¹ showed that low-volume services was associated with a longer time to treatment (p < 0.001)	4 non-randomized	⊕○○○ Very low * ** #
Treatment delay Hospital services volume (low versus moderate)	Moderate-volume hospitals showed similar treatment delay when compared to low-services (Morse et al. ²⁵ – cut-off: 50 days, OR = 0.81, 95%CI: 0.62; 1.07; Morse et al. ²⁴ – cut-off: 38 days, OR = 1.09, 95%CI: 0.68; 1.76)	2 non-randomized	⊕○○○ Very low * ** ***
Treatment delay Hospital level (medical centers versus local/ regional)	Patients treated at local/regional hospitals showed longer delays compared to those treated at hospital centers (Su et al. ²⁶ – cut-off: > 6 weeks, p < 0.001; Tsai et al. ¹¹ – cut-off: 30 days, p = 0.02)	2 non-randomized	⊕○○○ Very low * ** ***
Treatment delay Hospital ownership (public versus private)	Patients treated at a public hospital showed more treatment delays compared to those treated at a private hospital (Tsai et al. ¹¹ – cut-off: 30 days, p < 0.001)	1 non-randomized	⊕○○○ Very low * ** ***
Treatment delay Care transition (care transition versus no care transition)	Studies reported varying results. Morse et al. ²⁵ (cut-off: 50 days) found that patients who did not need a care transition were more likely to experience treatment delay (OR = 1.73, 95%CI: 1.46; 2.04) and Morse et al. ²⁴ (cut-off: 38 days) found that those who needed a care transition were more than 2-fold more likely to experience treatment delay (OR = 2.70, 95%CI: 2.1; 3.49)	2 non-randomized	⊕○○○ Very low * ** ***
Treatment delay Care transition (at reporting facility versus outside facility)	Location of diagnosis at an outside facility were more than two-fold more likely to experience treatment delay (Fujiwara et al. ¹² – cut-off: 45 days, OR: 2.17, 95%CI: 1.49; 3.15)	1 non-randomized	⊕○○○ Very low * ** ***
Treatment delay Urbanization level hospital (levels 1, 2&3, 4&5, 6&7)	The level of urbanization where the hospital was located was not associated with treatment delay (Tsai et al. ¹¹ – cut-off: 30 days, p = 0.951)	1 non-randomized	⊕○○○ Very low * ** #
Treatment delay Distance from treatment center (< 25 miles versus 25-100 miles)	Sharma et al. ²³ (cut-off: 30 days) showed that distance < 25 miles from the patient's place of residence to the treatment center showed a similar delay compared to 25-100 miles (OR = 1.00, 95%CI: 0.88; 1.14)	1 non-randomized	⊕○○○ Very low * ** ***

(continues)

Box 2 (continued)

OUTCOMES	IMPACT	TYPE OF STUDY	CERTAINTY OF EVIDENCE (GRADE)
Treatment delay Distance from treatment center (< 25 miles versus > 100 miles)	Sharma et al. ²³ (cut-off: 30 days) showed that distance < 25 miles from the patient's place of residence to the treatment center showed a similar delay compared to > 100 miles (OR = 1.08, 95%CI: 0.83; 1.41)	1 non-randomized	⊕○○○ Very low ***
Treatment delay Place of residence (metropolitan versus regional/remote)	Venchiarutti et al. ³⁰ (cut-off: 4 months) showed that patients living in a regional/remote area experienced a higher median treatment delay than those in a metropolitan area for oropharyngeal cancer (p = 0.03), but not for oral cavity cancer (p = 0.19)	1 non-randomized	⊕○○○ Very low * ***
Treatment delay Place of residence (rural, intermediate, urban)	Zhang et al. ³¹ found no significant difference in mean days of treatment delay among patients living in rural, intermediate, and urban areas (p = 0.791)	1 non-randomized	⊕○○○ Very low * ***
Treatment delay Income (low-income, ≤ 17,280 TWD, 17,281 to 22,800 TWD, ≥ 22,801 TWD)	Tsai et al. ¹¹ (cut-off: 30 days) found no significant difference in treatment delay between low- and high-income patients, categorized as ≤ 17,280 TWD, 17,281 to 22,800 TWD, and ≥ 22,801 TWD (p = 0.161)	1 non-randomized	⊕○○○ Very low * ***
Treatment delay Income (< 38,000 USD versus 38,000 to 47,999 USD)	Median household income of < 38,000 USD experienced a delay similar to 38,000-47,999 USD (Goel et al. ¹³ – cut-off: 30 days, coefficient: -0.11, 95%CI: -2.87; 2.64)	1 non-randomized	⊕○○○ Very low * ***
Treatment delay Income (< 38,000 USD versus 48,000 to 62,999 USD)	Median household income of < 38,000 USD experienced a delay similar to 48,000-62,999 USD (Goel et al. ¹³ – cut-off: 30 days, coefficient: 0.78, 95%CI: -1.99; 3.56)	1 non-randomized	⊕○○○ Very low * ***
Treatment delay Income (< 38,000 USD versus ≥ 63,000 USD)	Median household income of < 38,000 USD experienced a mean delay similar to ≥ 63,000 USD (Goel et al. ¹³ – cut-off: 30 days, coefficient: 0.55, 95%CI: -2.45; 3.55)	1 non-randomized	⊕○○○ Very low * ***
Treatment delay Income (IMD 2000 deprivation tertile groups: median rank 149, median rank 1,308, median rank 4,642)	The IMD 2000. There are IMD national ranks attached to each ward of residence. The most deprived rating for each domain was 1 and the least deprived was 8,414. Rogers et al. ²⁹ found no difference in median days of delay across IMD 2000 tertile groups: median rank 149, median rank 1,308, and median rank 4,642 (p = 0.50)	1 non-randomized	⊕○○○ Very low * ***
Treatment delay Education (≥ 21% versus 13% to 20.9%)	Patients living in areas where ≥ 21% of residents had a high school degree experienced a similar mean treatment delay compared to those where 13% to 20.9% of residents had a high school degree (Goel et al. ¹³ – cut-off: 30 days, coefficient: -2.01, 95%CI: -4.77; 0.75)	1 non-randomized	⊕○○○ Very low * ***
Treatment delay Education (≥ 21% versus 7% to 12.9%)	Patients living in areas where ≥ 21% of residents had a high school degree experienced less mean delay compared to those where 7% to 12.9% of residents had a high school degree (Goel et al. ¹³ – cut-off: 30 days, coefficient: -3.11, 95%CI: -6.04; 0.21)	1 non-randomized	⊕○○○ Very low * ***

(continues)

Box 2 (continued)

OUTCOMES	IMPACT	TYPE OF STUDY	CERTAINTY OF EVIDENCE (GRADE)
Treatment delay Education ($\geq 21\%$ versus $< 7\%$)	Patients living in areas where $\geq 21\%$ of residents had a high school degree experienced less mean delay compared to those where $< 7\%$ had a high school degree (Goel et al. ¹³ – cut-off: 30 days, coefficient: -6.42, 95%CI: -9.61; -3.22)	1 non-randomized	⊕○○○ Very low * ***
Treatment delay Race/Skin color (non-Hispanic white versus non-Hispanic black)	Non-Hispanic blacks experienced more treatment delays compared to non-Hispanic whites (Sharma et al. ²³ – cut-off: 30 days, OR = 1.24, 95%CI: 1.04; 1.46)	1 non-randomized	⊕○○○ Very low ***
Treatment delay Race/Skin color (non-Hispanic white versus Hispanic)	Hispanic had more delay than non-Hispanic white (Sharma et al. ²³ – cut-off: 30 days, OR = 1.74, 95%CI: 1.29; 2.34)	1 non-randomized	⊕○○○ Very low ***
Treatment delay Race/Skin color (non-white versus white)	White had less delay than non-white (Morse et al. ²⁵ – cut-off: 50 days, OR = 0.69, 95%CI: 0.54; 0.88). However, white had similar delay to non-white for Morse et al. ²⁴ (cut-off: 38 days, OR = 0.88, 95%CI: 0.59; 1.31) and for Fujiwara et al. ¹² (cut-off: 45 days, OR = 0.96, 95%CI: 0.77; 1.21)	3 non-randomized	⊕○○○ Very low * * * * *
Treatment delay Race/Skin color (white versus black)	No significant difference was found in the mean days of delay between whites and blacks (Goel et al. ¹³ – cut-off 30 days, coefficient: 1.44; 95%CI: -2.27; 5.16)	1 non-randomized	⊕○○○ Very low * * * * *
Treatment delay Marital status (married, single, divorced, and widowed)	No significant difference was found in delay between types of marital status (married, single, divorced, and widowed) (Rogers et al. ²⁹ – $p = 0.62$)	1 non-randomized	⊕○○○ Very low * * * * *
Treatment delay Sex (male versus female)	Females experienced slightly less or similar treatment delay compared to males (Sharma et al. ²³ – cut-off 30 days, OR = 0.99, 95%CI: 0.84; 1.18; Morse et al. ²⁵ – cut-off: 50 days, OR = 1.22, 95%CI: 0.98; 1.51; and Morse et al. ²⁴ – cut-off: 38 days, OR = 1.05, 95%CI: 0.79; 1.41). Moreover, two studies found a tendency for delayed treatment among females (Su et al. ²⁶ – cut-off: > 6 weeks, $p = 0.008$) and Tsai et al. ¹¹ – cut-off: 30 days, $p = 0.010$)	5 non-randomized	⊕○○○ Very low * * *
Treatment delay Age (≤ 60 years versus > 60 years)	Patients aged ≤ 60 years experienced slightly less delay or similar delay compared to those aged > 60 years (Morse et al. ²⁵ – cut-off: 50 days, OR = 0.96, 95%CI: 0.79; 1.17; and Morse et al. ²⁴ – cut-off: 38 days, OR = 0.96, 95%CI: 0.73; 1.27)	2 non-randomized	⊕○○○ Very low * * * * *
Treatment delay Age (< 60 years versus ≥ 60 years)	Patients aged ≥ 60 years experienced more delay compared to those aged < 60 years (Fujiwara et al. ¹² – cut-off: 45 days, OR = 1.22, 95%CI: 1.01; 1.47). Moreover, Su et al. ²⁶ (cut-off: > 6 weeks) showed that patients ≥ 60 years experienced a longer delay ($p = 0.02$)	2 non-randomized	⊕○○○ Very low * * *

95%CI: 95% confidence interval; IMD 2000: index of multiple deprivation 2000; OR: odds ratio.

* Severe risk of bias issues. Some studies did not adjust for confounding factors;

** Severe issues due to inconsistency: variations in studies occurred due to varying cut-off point for treatment delay;

*** Severe issues of indirectness: the studies represent a single country;

Very severe issues due to inconsistency: varying cut-off points (delay) and methodologies for categorizing the exposure. The authors classified service volume differently: Sharma et al. ²³ divided study patients per facility by quartiles (upper quartile were considered high volume), Morse et al. ²⁵ considered the number of cases treated per year (9: high-volume; 6 to 9: medium-volume; and < 6 : low-volume), Tsai et al. ¹¹ considered the number of services provided (low: lowest quartile; moderate: second and third quartile; and high: highest quartile);

Very severe risk of bias issues: there was no adjustment for confounding factors. There was a lack of clarity in categorizing the variable into urbanization levels from 1 to 7.

Facility type

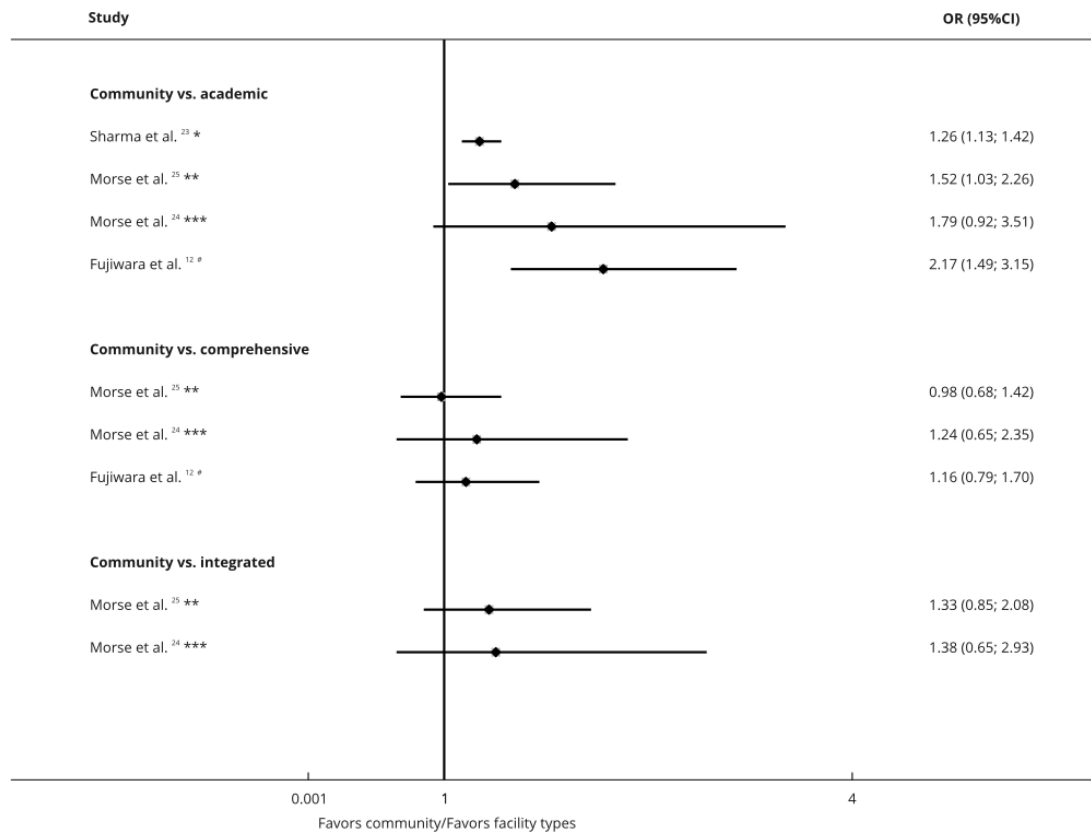
A total of five articles conducted in the United States reported on facility type. From these, three studies found that academic/research programs had a greater chance of treatment delay (OR=1.26, 95%CI: 1.13; 1.42)²³, (OR=1.52, 95%CI: 1.03; 2.26)²⁵, (OR=2.17, 95%CI: 1.49; 3.15)¹² compared to community facilities²³ and comprehensive community cancer programs^{12,25}. Community, comprehensive community^{12,24,25}, and integrated network cancer^{24,25} facilities showed similar delays (Figure 3).

Goel *et al.*¹³ found that comprehensive community facilities (coefficient: -4.95, 95%CI: -6.65; -3.25) and community facilities (coefficient: -5.28, 95%CI: -8.57; -1.99) had shorter treatment delays compared to academic programs (Box 2).

The certainty of evidence was very low due to the risk of bias, inconsistency, and indirectness (Box 2).

Figure 3

Forest plot comparing facility type and treatment delay organized by subgroups.



95%CI: 95% confidence interval; OR: odds ratio.

* Delay cut-off: ≥ 30 days;

** Delay cut-off: ≥ 50 days;

*** Delay cut-off: ≥ 38 days;

Delay cut-off: ≥ 45 days.

Hospital services volume

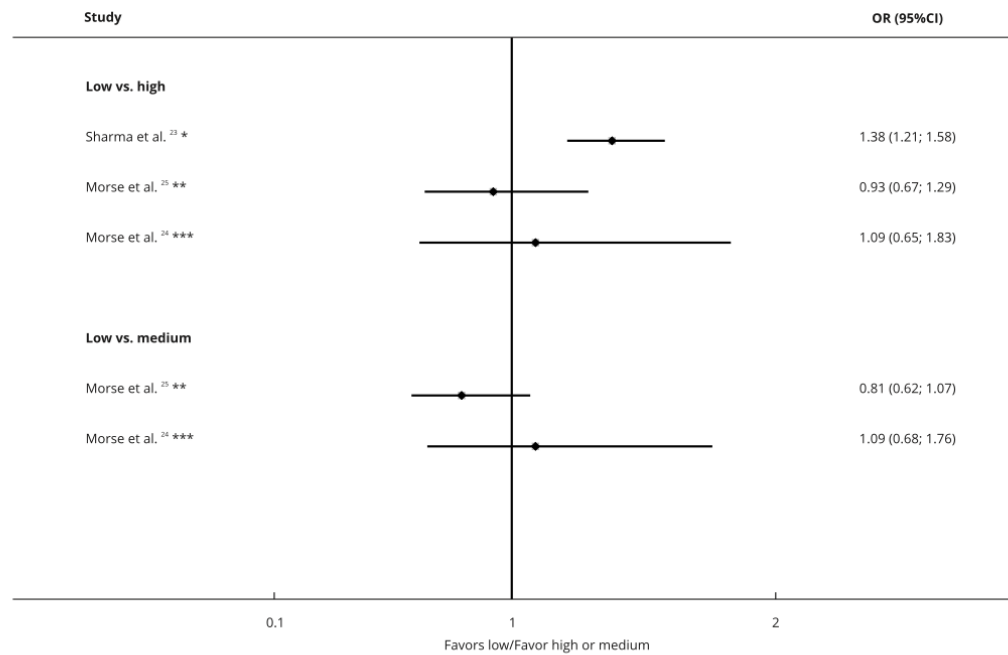
Sharma *et al.* ²³ found that high-volume hospitals were more likely to have treatment delays than low-volume hospitals (OR=1.38, 95%CI: 1.21; 1.58). However, other studies reported no significant difference between high- and low-volume services (OR=0.93, 95%CI: 0.67; 1.29 ²⁵ and OR=1.09, 95%CI: 0.65; 1.83 ²⁴) (Figure 4).

Tsai *et al.* ¹¹ concluded that low-volume hospital service was associated with a longer time prior to the onset of treatment ($p < 0.001$) (Box 2).

The certainty of evidence was very low due to the risk of bias, inconsistency, and indirectness (Box 2).

Figure 4

Forest plot comparing hospital services volume and treatment delay organized by subgroups.



95%CI: 95% confidence interval; OR: odds ratio.

Note: insurance type on the right denotes exposure, whereas left denotes the comparison.

* Delay cut-off: ≥ 30 days;

** Delay cut-off: ≥ 50 days;

*** Delay cut-off: ≥ 38 days.

Hospital level

In total, two studies from Taiwan concluded that patients treated at regional hospitals were more likely to have longer delays than those treated at hospital centers ($p < 0.001$ ¹¹ and $p = 0.02$ ²⁶) (Box 2).

The certainty of evidence was very low due to the risk of bias, inconsistency, and indirectness (Box 2).

Type of hospital facility

A study from Taiwan¹¹ showed that patients treated at a public hospital were more likely to have treatment delay compared to those treated at a private hospital ($p < 0.001$) (Box 2).

The certainty of evidence was very low due to the risk of bias and indirectness (Box 2).

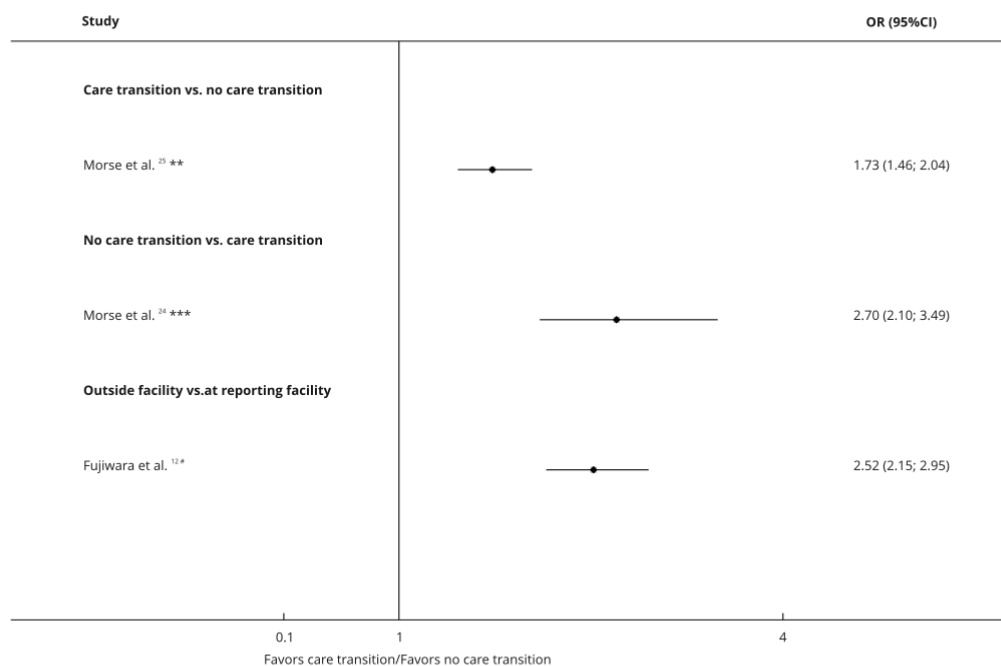
Care transition/location of initial diagnosis

In total, three studies conducted in the United States found an association between treatment delay and the need for referral for treatment at a different facility than that of diagnosis ^{12,24,25}. However, the studies reported different results. From these, one study found that patients who did not need a care transition were more likely to have treatment delay (OR=1.73, 95%CI: 1.46; 2.04) ²⁵, whereas the other studies concluded that those who needed an outside facility were more than 2-fold more likely to have treatment delay (OR=2.52, 95%CI: 2.15; 2.95 ¹² and OR=2.70, 95%CI: 2.10; 3.49 ²⁴) (Figure 5).

The certainty of evidence was very low due to the risk of bias, inconsistency, and indirectness (Box 2).

Figure 5

Forest plot comparing need for care transition and treatment delay organized by subgroups.



95%CI: 95% confidence interval; OR: odds ratio.

Note: insurance type on the right denotes exposure, whereas left denotes the comparison.

* Delay cut-off: ≥ 50 days;

** Delay cut-off: ≥ 38 days;

*** Delay cut-off: ≥ 45 days.

Urbanization level hospital

The level of urbanization seems to show no significant impact on treatment delays. A study conducted in the Taiwan ¹¹ assessed the level of urbanization where the hospital was located and found no association with treatment delay ($p=0.951$).

The certainty of evidence was very low due to the risk of bias and indirectness (Box 2).

Distance from treatment center

The distance (in miles) from the patient's place of residence to the treatment center was not associated with treatment delay in the United States ($p>0.05$) ²³.

The certainty of evidence was very low due to the risk of bias and indirectness (Box 2).

Place of residence

In Australia, patients living in a regional/remote area had a higher median treatment delay than those in a metropolitan area. However, the difference was only for oropharyngeal cancer ($p=0.03$) ³⁰ and not for oral cavity cancer ($p=0.19$) ³⁰ (Box 2).

A study conducted in Canada ³¹ found no difference in mean days of treatment delay among patients who resided in rural, intermediate, and urban areas ($p=0.791$) (Box 2).

The certainty of evidence was very low due to the risk of bias, inconsistency, and indirectness (Box 2).

Income

In total, three studies investigated patient income, and none found an association with treatment delay ($p=0.161$ ¹¹, $p>0.05$ ¹³, and $p=0.50$ ²⁹). Furthermore, these studies categorized this Variable differently according to the economic reality of each country (Taiwan, the United States, and the United Kingdom, respectively).

Thus, the certainty of evidence was very low due to the risk of bias, inconsistency, and indirectness (Box 2).

Education

A study conducted in the United States ¹³ reported that patients living in areas where 7% to 12.9% of residents with a high school degree (coefficient: -3.12,

95%CI: -6.04; -0.21) or < 7% (coefficient: -6.42, 95%CI: -9.61; -3.22) had longer average treatment delays compared to areas where $\geq 21\%$ of residents had a high school degree (Box 2).

The certainty of evidence was very low due to the risk of bias and indirectness (Box 2).

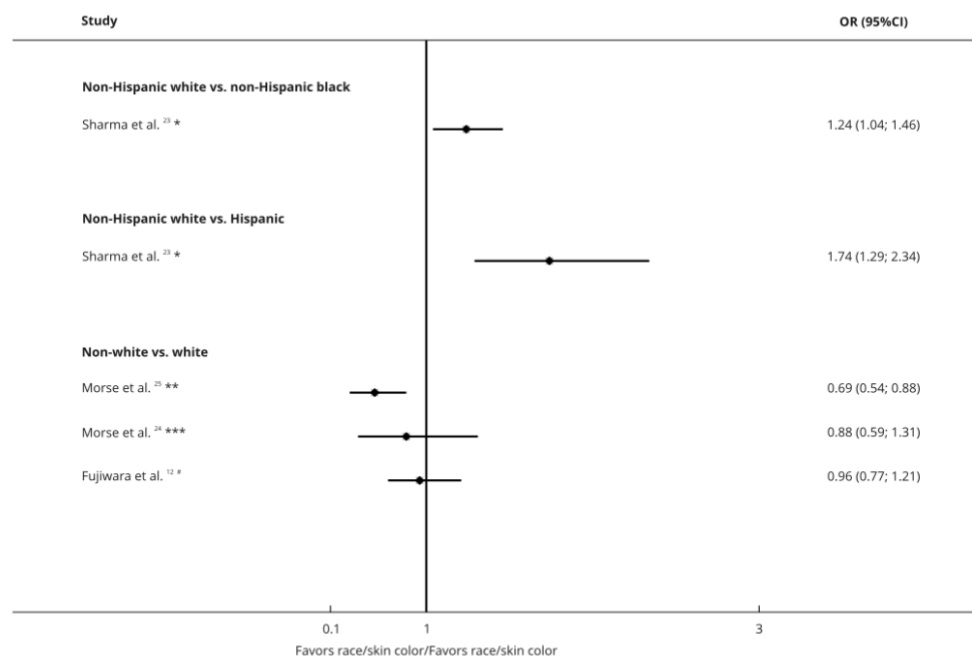
Race/Skin color

Race/skin color was investigated in five U.S. studies. From these, one study²³ showed that non-whites were more likely to have treatment delay (OR = 1.74, 95%CI: 1.29; 2.34 for Hispanics and OR = 1.24, 95%CI: 1.04; 1.46 for non-Hispanic blacks). Another study²⁵ reported a lower likelihood of delay among whites (OR = 0.69, 95%CI: 0.54; 0.88). However, whites and non-whites had similar delay in two studies^{12,24} (Figure 6).

The certainty of evidence was very low due to the risk of bias, inconsistency, and indirectness (Box 2).

Figure 6

Forest plot comparing race/skin color and treatment delay organized by subgroups.



95%CI: 95% confidence interval; OR: odds ratio.

Note: Insurance type on the right denotes exposure, whereas left denotes the comparison.

* Delay cut-off: ≥ 30 days;

** Delay cut-off: ≥ 50 days;

*** Delay cut-off: ≥ 38 days;

Delay cut-off: ≥ 45 days.

Marital status

No association was found between marital status and median days of treatment delay ($p=0.62$)²⁹ (Box 2).

The certainty of evidence was very low due to the risk of bias and indirectness (Box 2).

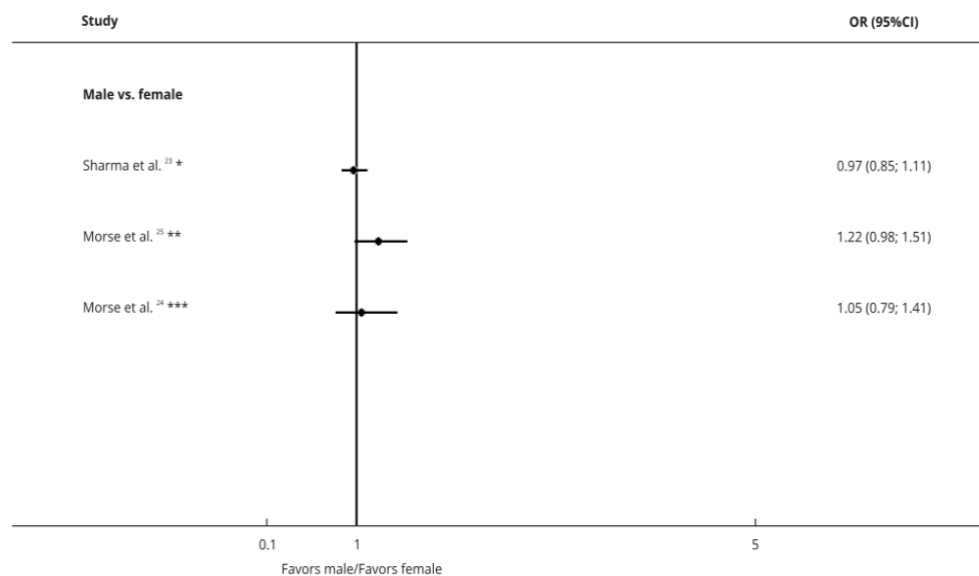
Sex and age

Sex (OR=0.97, 95%CI: 0.85; 1.11²³; OR=1.22, 95%CI: 0.98; 1.51²⁵; OR=1.05, 95%CI: 0.79;1.41²⁴) (Figure 7) and age (OR=0.96, 95%CI: 0.79; 1.17²⁵, OR=0.96, 95%CI: 0.73; 1.27²⁴) (Figure 8) did not impact treatment delay.

The certainty of evidence was very low due to the risk of bias, inconsistency, and indirectness (Box 2).

Figure 7

Forest plot comparing sex and treatment delay organized by subgroups.



95%CI: 95% confidence interval; OR: odds ratio.

Note: insurance type on the right denotes exposure, whereas left denotes the comparison.

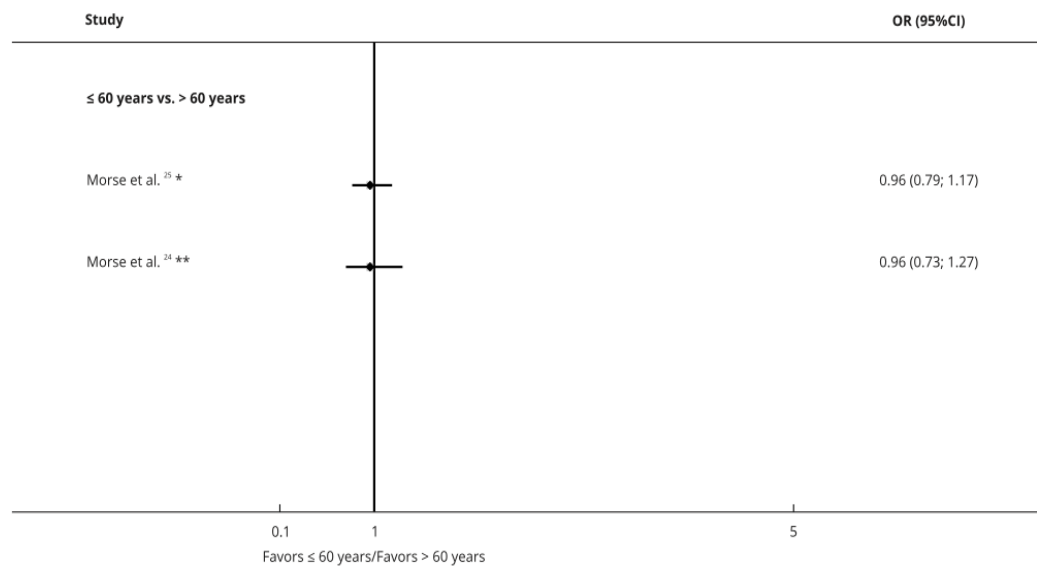
* Delay cut-off: ≥ 30 days;

** Delay cut-off: ≥ 50 days;

*** Delay cut-off: ≥ 38 days.

Figure 8

Forest plot comparing age and treatment delay organized by subgroups.



95%CI: 95% confidence interval; OR: odds ratio.

Note: insurance type on the right denotes exposure, whereas left denotes the comparison.

* Delay cut-off: ≥ 50 days;

** Delay cut-off: ≥ 38 days.

Risk of bias

The most common methodological issues were related to Item 4 (identification of confounders) and Item 5 (strategies for dealing with confounding factors), both rated “no” in nine studies. Domain 10 (strategies for addressing incomplete follow-up) was rated “no” in three studies. Domains 9 (reasons for losses to follow-up described and explored) and 10 (strategies for addressing incomplete follow-up) were considered “not applicable” in six studies that defined missing or incomplete data as exclusion criteria. In total, two studies were rated as “unclear” for Domain 3 (exposure measured in a valid and reliable way), as treatment delay was defined as the fourth quartile, but the precise value of each quartile was unclear (Supplementary Material – Box S4; https://cadernos.ensp.fiocruz.br/static//arquivo/suppl-e00121324_8794.pdf).

Discussion

Most studies found an association between some socioeconomic factors and delayed treatment of OOSCC. However, the certainty of these associations was very low.

The findings regarding the type of insurance were derived exclusively from studies conducted in the United States^{12,13,23,24,25}. Consequently, we suggest caution when interpreting these findings, as they regard the health system of a single country. The U.S. healthcare system is a hybrid of private health insurance and government programs^{32,33}. The U.S. government insurance (Medicaid, Medicare, and other programs) was more frequently associated with treatment delay compared to private insurance.

It seems reasonable to conclude that individuals who rely on government-funded healthcare or are uninsured are socioeconomically disadvantaged and unable to afford the high costs associated with OOSCC treatment. The economic burden may explain the unfeasibility of timely treatment³². However, other factors must be considered. Medicare primarily serves individuals aged 65 and older who have paid taxes on their earnings, thus these patients often present with comorbidities that require treatment before commencing definitive OOSCC therapy^{33,34}. Individuals utilizing Medicaid (main insurance for low-income people), along with those who are uninsured, tend to have more advanced disease stages, potentially due to heightened exposure to health risks and limited access to preventive care^{35,36,37}.

Therefore, depending on the patient's profile and the complexity of cases that require advanced (radiotherapy or chemotherapy) or multimodal (surgery combined with radiotherapy and/or chemo-therapy) therapies, it is likely that additional tests and comorbidity adjustments will be required prior to treatment, leading to longer delays³⁸. Similarly, cases that require care transition also experience longer delays^{12,24}.

At the same time, a study from Taiwan, which has a different healthcare system than the United States³⁹, found that public hospitals were more frequently associated with delayed treatment than private hospitals. However, this study did not control for confounders of disease/treatment. According to the analyses, the group with the longest time to treatment (> 120 days) had a higher percentage of advanced stages (III and IV) and required radiotherapy and chemotherapy treatments. This

suggests that the delay in treatment may not necessarily be due to the service provided by these facilities, but rather to the lack of early detection due to gaps in knowledge about the disease among the population that depends on the public health system ⁴⁰. In other words, people with low socioeconomic status often fail to notice malignant lesions in their early stages and delay seeking healthcare ⁴¹, resulting in advanced stages at presentation. As advanced stages require more pre-treatment care, this impacts treatment delay.

It is crucial to note that tobacco/alcohol use may also be important confounding factors not identified by the studies in this review. In general, patients who are heavy smokers and alcohol users tend to have low socioeconomic status and are often uncooperative with treatment plans or unreliable in keeping appointments ³⁵. Thus, the fact that the utilization of services for OOSCC also depends on the patient's self-perception of the need to cooperate in order to receive timely treatment cannot be overlooked ^{9,41}.

The studies that evaluated type of facilities are also from the United States ^{12,13,23,24,25}. Academic medical centers tend to be located in large urban centers, attending a high number of underprivileged communities and lower socioeconomic status individuals (uninsured and government insured). They also serve as referral centers for other hospitals that lack the equipment and personnel to manage OOSCC ⁴². This suggests that the greater backlog at academic medical centers, as revealed by the studies in this review, may not be due to the facilities themselves, but rather the high demand for OOSCC treatment added to the profile of these patients, which often includes preexisting health conditions and precarious living situations ^{14,42}.

The volume of hospital services showed conflicting results: a high volume of patients seen in the hospital was associated with delayed treatment ²³. However, a low volume of hospital procedures offered was associated with delays in one study ¹¹, whereas another found no association ²⁵. It is possible that the heterogeneity of the authors' definition of the variable and/or the organization of healthcare systems in different countries (United States ^{23,25} and Taiwan ¹¹) may have impacted these results.

Regarding place of residence, a Canadian study ³¹ found no difference in treatment delay for oral cancer patients living in rural, intermediate, or urban areas. According to the authors, the organization of the healthcare system may allow for greater standardization of treatment among patients regardless of where they live, which may explain this finding. On the other hand, an Australian study ³⁰ showed a

greater delay in oropharyngeal cancer treatment for patients living in remote areas compared to those in metropolitan areas, but did not find this difference for oral cancer.

In this case, it is important to note that cancer site must be considered. It is possible that in countries with a high level of socioeconomic development, such as Canada and Australia, both of which have universal healthcare systems, place of residence does not impact delays in treatment for oral cancer, which is often treated with surgery alone ⁴³. However, when more complex therapies are required (such as radiotherapy for oropharyngeal cancer), the greater need for referrals to different services for pre-treatment care creates accessibility barriers for people who live farther away, leading to longer treatment times ⁴⁴.

Studies conducted in the United States have considered two factors related to social class, namely education and race/skin color. Patients living in areas with a higher percentage of individuals with low education ¹³ and non-white individuals ^{23,25} were more likely to have delayed treatment. Although these studies show a high risk of bias, particularly because they did not evaluate the education and income levels of individuals, ethnic and educational disparities in access to cancer care have been reported previously ^{14,45,46}. People with lower levels of education and non-whites were more likely to have inadequate information and lower levels of knowledge about OOSCC, leading to late presentation and more advanced disease stages ⁴⁷, as well as greater refusal or resistance to recommended treatments ⁴⁸.

None of the studies that assessed income found an association with treatment delay ^{11,13,29}. In studies conducted in the United States ¹³ and the United Kingdom ²⁹, the assessment of this variable was limited to the geographic area and rather than the individual's income (e.g., average household income in the patient's zip code of residence) ¹³. Therefore, it cannot be assumed that everyone living in a deprived area is deprived, or vice-versa. Similarly, it is not possible to conclude that an individual's income does not impact time to treatment for OOSCC, even in rich country contexts.

A study conducted in Taiwan assessed patients' monthly income but did not adjust for confounders. The authors concluded that the lack of difference in treatment delay between low-income and high-income patients may be explained by the universal public healthcare system in the country. In that system, cancer patients are exempt from co-payments for treatment, and low-income patients receive subsidies to ensure their right to adequate health care ³⁹.

Only two studies from Taiwan ^{11,26} found female sex to be associated with treatment delay, and three studies ^{11,12,26} found an association between older age and treatment delay. However, these results may have been confounded by the various characteristics of the disease and therapeutic protocols.

Limitations

The overall risk of bias in the studies included in this systematic review was assessed as high. Although the JBI tool holds limitations, as it refers to the potential for bias rather than the actual measurement of bias in the studies, and does not include the assessment of other constructs such as reporting quality, random error, external validity, or ethical considerations, it is still recommended as a valid tool for assessing the risk of bias in line with the GRADE approach classification domains ⁴⁹.

Thus, severe bias issues were found in the studies included, as nine of ten did not identify or address confounding factors ^{11,12,13,24,25,26,29,30,31}, and three did not implement strategies for dealing with incomplete follow-up ^{11,13,25}. The variables were approached by the authors according to the information available in secondary databases, which did not always include key determinants for assessing access to healthcare services, such as education, occupation, place of residence, and income ⁹.

All studies were conducted in countries with high economic and social development, including the United States ^{12,13,23,24,25}, the United Kingdom ²⁹, Taiwan ^{11,26}, Australia ³⁰, and Canada ³¹. However, comparisons were not feasible due to significant heterogeneity in the definition of treatment delay, leading to severe issues of inconsistency. Additionally, socioeconomic variables were defined and categorized differently across studies, often according to the organizational structure of each national healthcare system and geographic classification criteria. This diversity of definitions prevented a grouped analysis.

Similarly, the limited number of studies examining the relationship between socioeconomic factors and delayed OOSCC treatment led to severe issues of indirect evidence. This also limits the generalizability of the findings to diverse healthcare settings, particularly in countries with lower socioeconomic development indicators.

Due to the considerable heterogeneity in the categorization of treatment delay and outcomes across studies, it was not feasible to conduct a meta-analysis or subgroup analysis, such as by sex, race/skin color, age, insurance type, or other

factors. Although language restrictions were not Applied as exclusion criteria, only studies in English were retrieved. Moreover, the impossibility of assessing publication bias and the limitations inherent in the included studies may have impacted the results of our research.

Strengths

Most studies on “delay” address head and neck cancer. This systematic review included OOSCC, including only studies that clearly defined the time to treatment onset following the Aarhus model ⁵.

Although the studies significantly varied in the categorization of treatment delay and outcomes, we synthesized all available results in a narrative format.

Conclusion

An association was found between treatment delay of OOSCC and various socioeconomic factors, such as type of insurance, sex, older age, non-white skin color, low education levels, treatment in public or regional hospital, need for transition care, and living in regional/remote areas. However, the available data do not support a definitive conclusion regarding this association. High methodological discrepancies across studies – particularly in defining treatment delay and categorizing socioeconomic variables – along with limited number of studies, contributed to a very low certainty of evidence.

Implications for practice and future studies

Considering that treatment delay can be used as a quality indicator to monitor service performance, healthcare providers – both public (government) and private – should make efforts to reduce delays in care for patients with OOSCC.

Therefore, future studies are encouraged in different countries with varying healthcare systems and socioeconomic contexts to provide a deeper understanding of the determinants of treatment delay in OOSCC. Studies should focus on OOSCC treatment delay as the primary outcome, defined as the time from definitive diagnosis to the first intervention ^{5,6}. Methodological quality must be improved, with more accurate comparisons of delay and non-delay groups. It is also important to clearly

define the sociodemographic and economic variables of the participants to obtain more consistent and applicable results for clinical decisions.

Contributors

D. R. A. B. S. Montagnoli contributed to the study conception and design, data analysis and interpretation, and writing; and approved the final version. V. F. Leite contributed to the data collection and critical review; and approved the final version. Y. S. Godoy contributed to the data collection, and critical review; and approved the final version. C. C. Martins-Pfeifer contributed to the data analysis and interpretation and critical review; and approved the final version. J. A. Moreno-Drada contributed to the data collection and critical review; and approved the final version. M. C. F. Aguiar contributed to the study conception and design, and critical review; and approved the final version. M. H. N. G. Abreu contributed to the study conception and design, data analysis and interpretation, and critical review; and approved the final version. R. C. Martins contributed to the study conception and design, data analysis and interpretation, and critical review; and approved the final version.

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5.2 Artigo II- Fatores preditivos podem determinar o tempo para o início do tratamento do câncer oral e orofaríngeo? Uma análise de árvore de classificação e regressão

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Can predictive factors determine the time to treatment initiation for oral and oropharyngeal cancer? A classification and regression tree analysis

Factors influencing time to treatment initiation of oral and oropharyngeal cancer

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Abstract

This ecological study aimed to identify the factors with the greatest power to discriminate the proportion of oral and oropharyngeal cancer (OOC) records with time to treatment initiation (TTI) within 30 days of diagnosis in Brazilian municipalities. A descriptive analysis was performed on the variables grouped into five dimensions related to patient characteristics, access to health services, support for cancer diagnosis, human resources, and socioeconomic characteristics of 3,218 Brazilian municipalities that registered at least one case of OOC in 2019. The Classification and Regression Trees (CART) technique was adopted to identify the explanatory variables with greater discriminatory power for the TTI response variable. There was a higher median percentage of records in the age group of 60 years or older. The median percentage of records with stage III and IV of the disease was 46.97%, and of records with chemotherapy, radiation, or both as the first treatment was 50%. The median percentage of people with private dental and health insurance was low. Up to 75% had no cancer diagnostic support services, and up to 50% of the municipalities had no specialist dentists. Most municipalities (49.4%) started treatment after more than 30 days. In the CART analysis, treatment with chemotherapy, radiotherapy, or both explained the highest TTI in all municipalities, and it was the most relevant for predicting TTI. The final model also included anatomical sites in the oral cavity and oropharynx and the number of computed tomography services per 100,000. There is a need to expand the availability of oncology services and human resources specialized in diagnosing and treating OOC in Brazilian municipalities for a timely TTI of OOC.

Keywords: Oral cancer, Oropharyngeal cancer, Squamous cell carcinoma, Treatment delay, Time- to-treatment.

Introduction

Oral and oropharyngeal cancers (OOC) are the sixth most common neoplasm in the world [1]. Brazil stands out for the high incidence of these cancer types. More than 15,000 new cases per year are estimated in the 2023-2025 period, ranking it eighth among the most frequent cancer types [2]. However, cases are still diagnosed at advanced stages, and delayed treatment is a reality in some populations, even with improved screening techniques and emerging therapies [3,4].

Timely treatment of OOC involves access to health services influenced by individual and contextual determinants. Weller et al. [5] listed three contributors influencing the time intervals of pathways to begin cancer treatment: patient, disease, and health system factors.

The delayed onset of the treatment attributed to patients with OOC has been associated with sociodemographic aspects such as female gender and older age (over 60 years) [6,7], low-level education, and low income [8]. Moreover, lack of knowledge about the disease, undefined interpretation of symptoms, cultural beliefs (among them, downplaying oral problems), and self-treatment also modulate the decision time to seek professional help [8].

The location and stage of the tumor and the type of treatment necessary influence the delay in beginning the treatment because of the disease [5]. OOC can have a slow and indolent evolution but with tumor and proliferative aggressiveness [9]. Thus, tumors located in more posterior regions of the mouth, such as the oropharynx, hard palate, and retromolar trigone, can be diagnosed at more advanced stages of the disease (III and IV) [6,7,10], which leads to the need for multimodal therapies (chemotherapy and radiotherapy) and lead to longer times for the start of OOC treatment [7,10].

Concerning the health system, the adult population's difficult access to dental care and the lack of coordinated actions at the different care levels (primary, secondary, and tertiary) [11,12] can influence the late onset of treatment. The coordination of cancer care involves everything from health policies, organizational aspects of services, appropriate infrastructure, and prepared human resources to socioeconomic issues in the health system context [5].

Most of the Brazilian population depends on the public health system (Sistema Único de Saúde – SUS in Portuguese) [13]. The National Oral Health Policy

has allowed the implementation of strategies for the early diagnosis of OOC. However, Brazil is plagued by marked social inequality, and some regions have incomplete access to oral health services [14].

Studies have already reported the influence of unequal population coverage of primary and secondary health services in Brazilian cities on elevated number of hospitalizations and deaths due to OOC, especially when public oral health services are absent [15,16]. Therefore, the SUS-dependent population may have a time interval between diagnosis and treatment almost twice as long as private service patients [17].

The limited number of public facilities specializing in oncology, both diagnostic support and chemotherapy and radiotherapy equipment, is also a critical factor that has affected the increase in time to start cancer treatment in Brazil [18,19]. Similarly, the need for qualified human resources for definitive early diagnosis in some municipalities is a challenge to overcome [20,21]. Contacting an appropriate specialized health provider once the lesion was detected reduced diagnosis and treatment delay in cancer [22].

Furthermore, the unfavorable socioeconomic context of the Brazilian municipalities, such as the low human development Index (HDI), high inequality index, lower sanitation levels, and low education rates, were also associated with worse OOC outcomes [15,23]. These local factors need to be better evaluated during treatment initiation.

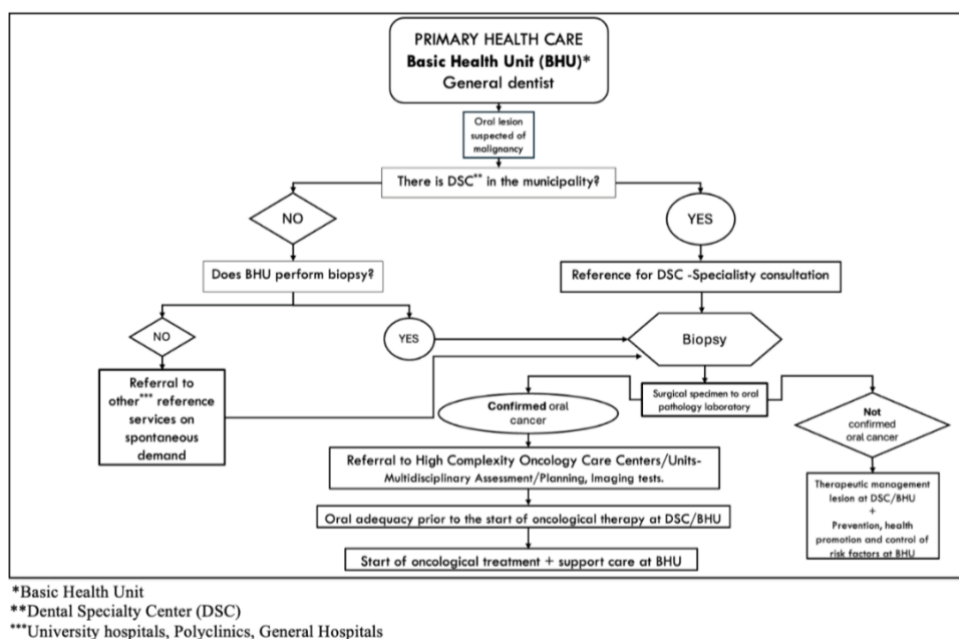
The Brazilian law provides the right of patients with proven malignant neoplasm to undergo their first treatment within 60 days of diagnosis [24]. However, this Federal law is for all types of cancer and is not focused on oral cancer. The literature shows strong evidence that for OOC starting treatment after more than 30 days led to a worse prognosis and lower survival or a higher risk of death [7,10,25-27], stating that the processes involved in the care of these patients require particular attention. In patients with head and neck cancer, including oral cancer, waiting more than 60 days to start treatment affects survival by 26% compared to waiting less than 30 days [27].

Given this, the present study aimed to identify factors with the most significant power to discriminate the proportion of OOC records with time treatment initiation within 30 days after diagnosis in Brazilian municipalities. The alternative hypothesis was that individual and contextual factors are associated with municipalities' records of longer treatment initiation times.

Methods

This ecological study evaluated 3,218 Brazilian municipalities that registered at least one case of oral and oropharynx cancer in adults (20 years and over) in 2019. The municipal level organizes, executes, and manages the services and actions that occur in Primary Health Care (PHC) [28]. The PHC is the population's main gateway to the Brazilian public health system and is responsible for coordinating flows between the many points of the Health Care Network (HCN) to ensure the integrity of care [28]. PHC, through the Basic Health Units (BHU), works on health promotion, prevention and control of risk factors, screening, and initial diagnosis of OOC [29]. When potentially malignant lesions are identified at PHC, patients are referred to secondary (Dental Specialties Centers - DSC) or tertiary levels of care for diagnostic confirmation through biopsy [12,20,29]. After confirming the diagnosis of malignancy, patients are referred to highly complex Oncology Centers or Units to undergo oncological surgery, radiotherapy, and/or chemotherapy. BHU also works on cancer pre-treatment adequacy procedures, as well as supporting patients during and after cancer treatment. In cases where the lesion is benign, the patient returns to the BHU for therapeutic management of the lesion, prevention, and control of risk factors [29]. Fig 1 shows the flows between the various points of the Brazilian HCN considering the path to diagnosis and treatment of OOC.

Fig 1. Flows of diagnosis and treatment of OOC in the Brazilian public health system



All the information is in the public domain. Therefore, the Human Research Ethics Committee did not need to approve this study. Secondary data on OOC registrations were obtained from the Oncology Treatment Monitoring Panel (Panel-Oncology) of the Informatics Department of the Unified Health System (DATASUS) (http://tabnet.datasus.gov.br/cgi/dhdat.exe?PAINEL_ONCO/PAINEL_ONCOLOGIAB_R.def) on February 2, 2023. This platform collects information from public health services (public or private health institutions affiliated with the SUS) that provide cancer care in Brazil. It is a tool for public health managers and health planners to monitor the time from diagnosis to first treatment, using data from the information systems consolidated in the SUS. Although it does not refer to the incidence of cancer in the country, it covers a high degree of heterogeneity in the population studied. The data are grouped by place of registration (municipalities, states, and macro-regions), and it is not possible to identify patients directly.

This study is based on the theoretical model of Weller et al. [5], in which targets are identified to facilitate the evaluation of the reasons interfering with early diagnosis and, consequently, improve the prognosis of cancer cases. To this end, three factors are considered – patient, health system, and disease – and modulate the decision-making processes that permeate the time intervals until treatment.

Time to treatment initiation (TTI) was the dependent variable and was defined as the proportion of municipal OOC records with treatment started within 30

days of confirmed diagnosis/total in 2019. Starting treatment after more than 30 days led to a worse prognosis and lower survival in OOC cases [7,10,25,26,27].

According to the Kolmogorov-Smirnov normality test, this variable showed a non-normal distribution ($p > 0.05$). Thus, TTI was categorized into three groups: Delay: municipalities where all OCC treatments started after 30 days; $0 < \text{Delay} < 1$: municipalities with OOC treatment records within 30 days and over 30 days; and No delay: municipalities where all OOC treatments started within 30 days.

The independent variables and their definitions, data source, and access are shown in Table 1. The explanatory variables were divided into five dimensions: 1. Patient characteristics (PC); 2. Access to health services (AS); 3. Cancer diagnosis support (CS); 4. Human resources (HR); and 5. Municipal characteristics (MC).

Variables were collected from the Panel-Oncology according to aspects most associated with delay in OOC treatment reported in the literature to build the Patient Characteristics (PC) dimension, such as female sex, age groups most affected by the disease (45-59 and above 60 years), more advanced stages (III and IV), treatment with chemotherapy, radiotherapy, or both [6,7,10]. The proportions of records for each variable by the total number of records for each municipality in 2019 were calculated. Data were collected from the place of residence of registered cases.

Oral neoplasm records are identified using the C00-C10 classification of the 10th revision of the International Classification of Diseases (ICD-10) in the Panel-Oncology. When analyzing oral cancer, some authors advocate excluding lip and salivary gland neoplasms from this category because they have different etiologic, histologic, and epidemiologic behavior [30,31], which affects the time to start treatment. Because of this, the proportion of OOC records was evaluated by groups of anatomical sites separately: PC4 (lip cancer: C00), PC5 (oral cavity: C02-C04 and C06), PC6 (salivary glands: C07 and C08), and PC7 (oropharynx: C05, C09, and C10) (Table 1).

As for the dimension of CS, only public or private services affiliated with the SUS were considered. For the CS1 variable, all clinical oncology services (outpatient and inpatient) available in the municipalities were considered. Pediatric hospitals were excluded because of the rare oral malignant neoplasms in children [32]. For the CS3 variable, general hospitals, clinics, and specialized pathology diagnostic laboratories available in the municipality were considered. Essential health or primary care and mixed units were excluded, as these generally perform cytopathology tests related to cervical cancer control and prevention. Hospitals limited to a single medical specialty

(e.g., nephrology, ophthalmology, gynecology, neurology, and urology) were also excluded (Table 1).

Table 1. Explanatory variables and their definitions, data source, and access, Brazil, 2019.

VARIABLE	DEFINITION	DATA SOURCE	ACCESS (internet)
Patient Characteristics (PC)			
PC1 – Percentage of OOC records aged 45 to 59	Total municipal OOC records (C00-C10) aged 45-59 by total municipal OOC records in 2019.	Panel-Oncology DATASUS	http://tabnet.datasus.gov.br/cgi/dhdat.exe?PAINEL_ONCO/PAINEL_ONCOLO/GIABR.def
PC2 – Percentage of OOC records aged 60 or over	Total municipal OOC records (C00-C10) aged 60 or over by total municipal OOC records in 2019.	Panel-Oncology DATASUS	http://tabnet.datasus.gov.br/cgi/dhdat.exe?PAINEL_ONCO/PAINEL_ONCOLO/GIABR.def
PC3 – Percentage of female OOC records	Total municipal female OOC records (C00-C10) by total municipal OOC records in 2019.	Panel-Oncology DATASUS	http://tabnet.datasus.gov.br/cgi/dhdat.exe?PAINEL_ONCO/PAINEL_ONCOLO/GIABR.def
PC4 – Percentage of lip cancer	Total municipal lip cancer records (C00) by total municipal OOC records in 2019.	Panel-Oncology DATASUS	http://tabnet.datasus.gov.br/cgi/dhdat.exe?PAINEL_ONCO/PAINEL_ONCOLO/GIABR.def
PC5 – Percentage of oral cavity cancer	Total municipal oral cavity cancer records (C02-C04, C06) by total municipal OOC records in 2019.	Panel-Oncology DATASUS	http://tabnet.datasus.gov.br/cgi/dhdat.exe?PAINEL_ONCO/PAINEL_ONCOLO/GIABR.def
PC6 – Percentage of salivary gland cancer	Total municipal salivary gland cancer records (C07, C08) by total municipal OOC records in 2019.	Panel-Oncology DATASUS	http://tabnet.datasus.gov.br/cgi/dhdat.exe?PAINEL_ONCO/PAINEL_ONCOLO/GIABR.def
PC7 – Percentage of oropharyngeal cancer	Total municipal oropharyngeal cancer records (C01, C05, C09, C10) by total municipal OOC records in 2019.	Panel-Oncology DATASUS	http://tabnet.datasus.gov.br/cgi/dhdat.exe?PAINEL_ONCO/PAINEL_ONCOLO/GIABR.def
PC8 – Percentage of OOC staging III and IV	Total municipal OOC records (C00-C10) with stages III and IV by total municipal OOC records in 2019.	Panel-Oncology DATASUS	http://tabnet.datasus.gov.br/cgi/dhdat.exe?PAINEL_ONCO/PAINEL_ONCOLO/GIABR.def

PC9 – Percentage of OOC treated with chemotherapy, radiotherapy, or both	Total municipal OOC records (C00-C10) treated with chemotherapy, radiotherapy, or both by total municipal OOC records in 2019.	Panel-Oncology DATASUS	http://tabnet.datasus.gov.br/cgi/dhdataxe?PAINEL_ONCO/PAINEL_ONCOLOGIABR.def
Access to Health Services (AS)			
AS1 – Presence of Dental Specialties Centers (DSC)	DSC is active through December 2019	National Health Facilities Census DATASUS	https://cnes.datasus.gov.br/pages/estabelecimentos/consulta.jsp
AS2 – Coverage of Family Health Teams with oral health teams	Average coverage for 2019.	e-Manager Basic Care	https://egestorab.saude.gov.br/paginas/acessoPublico/relatorios/relHistoricoCoberturaSB.xhtml
AS3- Coverage of Primary Care Oral Health Teams	Average coverage for 2019.	e-Manager Basic Care	https://egestorab.saude.gov.br/paginas/acessoPublico/relatorios/relHistoricoCoberturaSB.xhtml
AS4- Percentage of population with private dental insurance	Total population of the municipality with a dental plan in 2019 by the municipality's population estimate for 2019.	National Supplementary Health Agency DATASUS	https://www.ans.gov.br/anstabnet/cgi-bin/dh?dados/tabnet_tx.def
AS5- Percentage of population with health insurance - medical assistance	Total population of the municipality with health insurance in 2019 by the municipality's population estimate for 2019.	National Supplementary Health Agency DATASUS	https://www.ans.gov.br/anstabnet/cgi-bin/dh?dados/tabnet_tx.def
AS6- Percentage of SUS beds in the municipality per 100,000 inhabitants	Total number of surgical beds (oral and maxillofacial surgery, general surgery, and oncology) and clinical beds (general medicine and oncology) available in public and private hospitals affiliated with the SUS in 2019, based on the municipality's 2019 population estimate.	National Health Facilities Census DATASUS	https://cnes2.datasus.gov.br/Mod_Ind_Tipo_Leito.asp?VEstado=11&VMun=110032&VComp=201909
Cancer Diagnosis Support (CS)			
CS1 – Number of clinical oncology services per 100,000 inhabitants	Total surgical oncology services (outpatient and hospital) available in the municipality based on the municipality's population estimate for 2019 x 100,000 inhabitants.	National Health Facilities Census DATASUS	https://cnes2.daasus.gov.br/Mod_Ind_Especialidades.asp?VEstado=11&VMun=110001&VComp=00&VTerc=00&VServico=132&VClassificacao=004&VAmbu=&VAmbuSUS=1&VHosp=&VHospSUS=1
CS2 – Number of radiotherapy services per 100,000 inhabitants	Total radiotherapy services (outpatient and hospital) available in the municipality based on the municipality's population estimate for 2019 x 100,000 inhabitants.	National Health Facilities Census DATASUS	https://cnes2.daasus.gov.br/Mod_Ind_Especialidades.asp?VEstado=11&VMun=110001&VComp=00&VTerc=00&VSe

			rvico=132&VClassifi cacao=004&VAmbu =&VAmbuSUS=1& VHosp=&VHospSU S=1
CS3 – Number of anatomopathological diagnostic services per 100,000 inhabitants	Total number of general hospitals, clinics and laboratories specializing in pathological diagnosis available in the municipality, with SUS service, based on the municipality's population estimate for 2019 x 100,000 inhabitants.	National Health Facilities Census DATASUS	https://cnes2.datasu s.gov.br/Mod_Ind_E specialidades.asp? VEstado=11&VMun =110001&VComp= 00&VTerc=00&VSe rvico=132&VClassifi cacao=004&VAmbu =&VAmbuSUS=1& VHosp=&VHospSU S=1
CS4 – Number of MRI diagnostic services per 100,000 inhabitants	Total number of hospitals, centers and clinics specialized in magnetic resonance imaging (MRI) diagnosis available in the city, with SUS service, based on the municipality's population estimate for 2019 x 100,000 inhabitants.	National Health Facilities Census DATASUS	https://cnes2.datasu s.gov.br/Mod_Ind_E specialidades.asp? VEstado=11&VMun =110001&VComp= 00&VTerc=00&VSe rvico=132&VClassifi cacao=004&VAmbu =&VAmbuSUS=1& VHosp=&VHospSU S=1
CS5 – Number of CT imaging diagnostic services per 100,000 inhabitants	Total hospitals, centers, and clinics specializing in computed tomography (CT) diagnosis available in the city, with SUS service based on the municipality's population estimate for 2019 x 100,000 inhabitants.	National Health Facilities Census DATASUS	https://cnes2.datasu s.gov.br/Mod_Ind_E specialidades.asp? VEstado=11&VMun =110001&VComp= 00&VTerc=00&VSe rvico=132&VClassifi cacao=004&VAmbu =&VAmbuSUS=1& VHosp=&VHospSU S=1
Human Resources (HR)			
HR1 – Number of oral medicine specialists and oral pathologists per 100 thousand inhabitants	Total number of oral medicine specialists and oral pathologists in the municipality according to the municipality's population estimate for 2019 x 100,000 inhabitants.	National Health Facilities Census DATASUS	https://cnes2.datasu s.gov.br/Mod_Ind_T ipo_Leito.asp?VEst ado=11&VMun=110 032&VComp=2019 09
HR2 – Number of maxillofacial surgeons per 100 thousand inhabitants	Total number of maxillofacial surgeons in the municipality based on the municipality's population estimate for 2019 x 100,000 inhabitants.	National Health Facilities Census DATASUS	https://cnes2.datasu s.gov.br/Mod_Ind_T ipo_Leito.asp?VEst ado=11&VMun=110 032&VComp=2019 09

HR3 – Number of specialist dentists per 100,000 inhabitants	Total number of oral medicine specialists, oral pathologists and maxillofacial surgeons in the city based on the municipality's population estimate for 2019 x 100,000 inhabitants.	National Health Facilities Census DATASUS	https://cnes2.datasus.gov.br/Mod_Ind_Tipo_Leito.asp?VEstado=11&VMun=110032&VComp=201909
Municipal Characteristics (MC)			
MC1 – Municipal Human Development Index (M-HDI)	M-HDI Census 2010.	Atlas Brazil	http://www.atlasbrasil.org.br/ranking
MC2 – Gini index of household income per capita	Gini index of household income per capita Census 2010.	IBGE	http://tabnet.datasus.gov.br/cgi/ibge/censo/cnv/ginibr.def
MC3 – Municipal Gross Domestic Product (GDP)	GDP- 2019.	IBGE	https://www.ibge.gov.br/estatisticas/economicas/contas-nacionais/9088-produto-interno-bruto-dos-municipios.html?t=downloads&c=1100015
MC4 – Illiteracy rate among the population aged 15 and over	Municipality Census 2010.	Atlas Brazil	http://www.atlasbrasil.org.br/consulta/pl_anilha
MC5-Unemployment rate for the population aged 18 and over	Municipality Census 2010.	Atlas Brazil	http://www.atlasbrasil.org.br/consulta/pl_anilha
MC6 – Percentage of people in urban households with garbage collection	Municipality Census 2010.	Atlas Brazil	http://www.atlasbrasil.org.br/consulta/pl_anilha
MC7 – Percentage of people in households with inadequate water supply and sewage	Municipality Census 2010.	Atlas Brazil	http://www.atlasbrasil.org.br/consulta/pl_anilha

The socioeconomic characteristics of the municipalities were obtained from the Brazilian Institute of Geography and Statistics (IBGE) census 2010. Municipal population estimates for 2019 were taken from the IBGE to calculate percentages per 100,000 inhabitants to obtain the distribution ratios of health services provided by municipalities.

A descriptive analysis of the explanatory variables was carried out to evaluate the median, P25%, P75% and minimum and maximum values. Next, the “Classification and Regression Trees” (CART) technique was performed to identify the explanatory variables, distributed across five dimensions, which presented greater

discrimination power for the TTI response variable. This technique consists of a decision tree in which data is divided into smaller groups based on specific rules, creating a hierarchy of decisions in which previous divisions affect subsequent ones. The logic of this technique is based on building the tree through the successive subdivision of groups into subgroups [33]. These consecutive dataset splits are performed using the Chi-square Automatic Interaction Detection-CHAID method. The procedure selects the independent variable with the most significant interaction with the dependent variable at each subdivision. Thus, it is possible to identify homogeneous subgroups, reducing the effects of multicollinearity, outliers, and missing data.

It was necessary to establish some criteria in advance when modeling the data: 1) each node (a designation given to each subset resulting from the application of a division rule) should contain a minimum of 500 observations; 2) terminal nodes should include at least 200 observations; 3) exclusion of subdivisions with significance probability values (p-value) greater than 0.05. The algorithm automatically established cutoff points to segment the analyzed groups. This analysis was also carried out for the five Brazilian regions. All analyses were performed using the Statistical Package for Social Sciences (SPSS), version 22.0 (IBM SPSS Statistics for Windows, Armonk, NY).

Results

In 2019, 57.79% of all municipalities in Brazil (n=5,568) recorded at least one case of OOC. Table 2 shows the descriptive analysis of the explanatory variables of the five dimensions.

Table 2. Descriptive analysis of variables related to Patient characteristics (PC), Access to health services (AS), Cancer diagnosis support (CS), Human resources (HR), and Municipal characteristics (MC).

Variable	Median	P25%	P75%	Min.	Max.
Patient characteristics (PC)					
PC1	33.33	0.00	60.00	0.00	100.00
PC2	50.00	0.00	100.00	0.00	100.00
PC3	14.29	0.00	50.00	0.00	100.00

PC4	0.00	0.00	0.00	0.00	100.00
PC5	33.33	0.00	50.00	0.00	100.00
PC6	0.00	0.00	12.50	0.00	100.00
PC7	40.00	0.00	66.67	0.00	100.00
PC8	46.97	0.00	75.00	0.00	100.00
PC9	50.00	20.00	100.00	0.00	100.00
Access to health services (AS)					
AS2	79.14	36.88	100.00	0.00	100.00
AS3	91.66	55.23	100.00	0.00	100.00
AS4	2.49	0.99	6.98	0.00	2,460.33
AS5	6.43	1.89	16.15	0.00	3,775.51
AS6	5.72	0.00	10.99	0.00	245,86
Cancer diagnosis support (CS)					
CS1	0.00	0.00	0.00	0.00	16.72
CS2	0.00	0.00	0.00	0.00	16.72
CS3	0.00	0.00	0.00	0.00	94.56
CS4	0.00	0.00	0.00	0.00	63.45
CS5	0.00	0.00	0.00	0.00	63.45
Human resources (HR)					
HR1	0.00	0.00	0.00	0.00	200.18
HR2	0.00	0.00	1.72	0.00	709.22
HR3	0.00	0.00	2.05	0.00	709.22
Municipal characteristics (MC)					
MC1	0.69	0.62	0.73	0.48	0.86
MC2	0.50	0.46	0.54	0.28	0.78
MC3	20,605.71	11,785.13	32,327.55	4,595	484,883.50
MC4	11.07	6.84	22.20	0.95	44.40
MC5	5.88	3.92	8.10	0.09	25.26
MC6	98.42	95.34	99.54	16.25	100.00
MC7	2.35	0.46	10.67	0.00	72.22

Patient Characteristics (PC)

There was a higher median percentage of records in the age group of 60 years or more (PC2) (50.00;0-100); oropharyngeal cancer (PC7) (40; 0-100) and oral cavity cancer (PC5) (33.33;0-100). The median percentage of records in stages III and

IV (PC8) was 46.97% (0-100), and of records that had chemotherapy, radiotherapy, or both (PC9) as their first treatment was 50% (0-100).

Access to Health Services (AS)

Approximately 73.4% of municipalities did not have active DSC in 2019 (Results not shown).

The median coverage of Family Health Teams was 79.14% (AS2) and 91.66% for Oral Health in Primary Care (AS3), ranging from zero to 100%. However, the median percentage of people with private dental insurance in municipalities (AS4) (2.49; 0 to 2,460.331) and health insurance (AS5) (6.43; 0 to 3,775,508) was low. The median number of SUS beds (AS6) was 5.72, ranging from zero to 245 beds per 100,000 inhabitants.

Cancer Diagnosis Support (CS)

The municipalities had a maximum of 14.98 surgical oncology services; 16.72 clinical oncology (CS1) and radiotherapy (CS2) services; 94.56 anatomopathological diagnoses (CS3) services; and 63.45 MRI (CS4) and CT (CS5) imaging diagnosis services per 100,000 inhabitants.

Human Resources (HR)

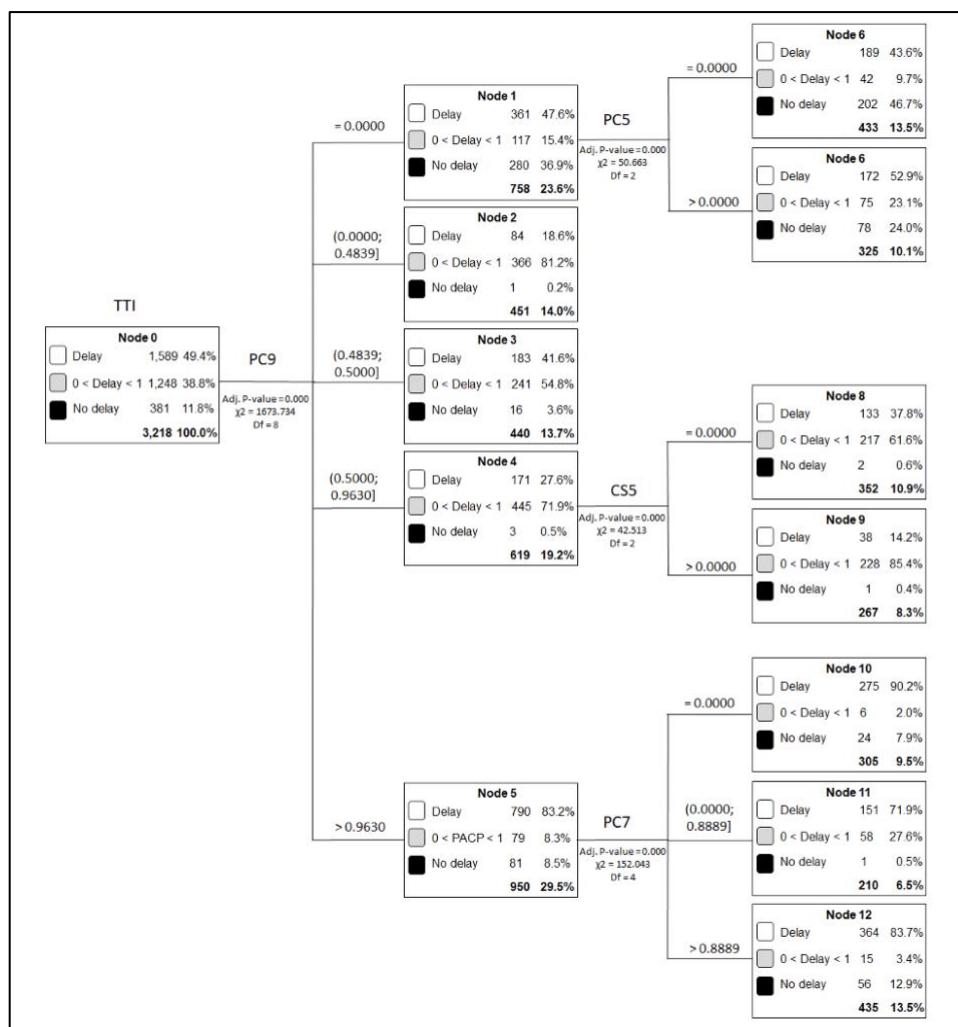
Up to 50% of the municipalities needed a specialist dentist. The maximum value found was 709.22 specialist dentists (HR3) per 100,000 inhabitants.

Municipal Characteristics (MC)

In general, the municipalities had different socioeconomic profiles. The median HDI-M (MC1) revealed medium development, ranging from low to high (0.69; 0.48-0.86). Similarly, the municipalities had a median illiteracy rate for the population aged 15 or over (MC4) of 11.07%, ranging from 0.95% to 44.40%; a median unemployment rate for people aged 18 or over (MC5) of 5.88% (0.09-25.26) and a median percentage of people in households with inadequate water supply and sewage (MC7) of 2.35%, ranging from 0 to 72.22%.

CART models for Brazilian municipalities are shown in Fig 2.

Fig 2. CART analysis for time to treatment initiation of Brazilian municipalities.



Most municipalities (49.4%) started treatment after more than 30 days (Delay group), and 11.8% of municipalities started treatment within 30 days (No delay group).

Treatment with chemotherapy, radiotherapy, or both (PC9) explained the highest TTI in all municipalities; it was the most relevant method for predicting the TTI. When most patients (PC9 > 0.963) were treated by chemotherapy, radiotherapy, or both, a delay of more than 30 days was seen in 83.2% of patients.

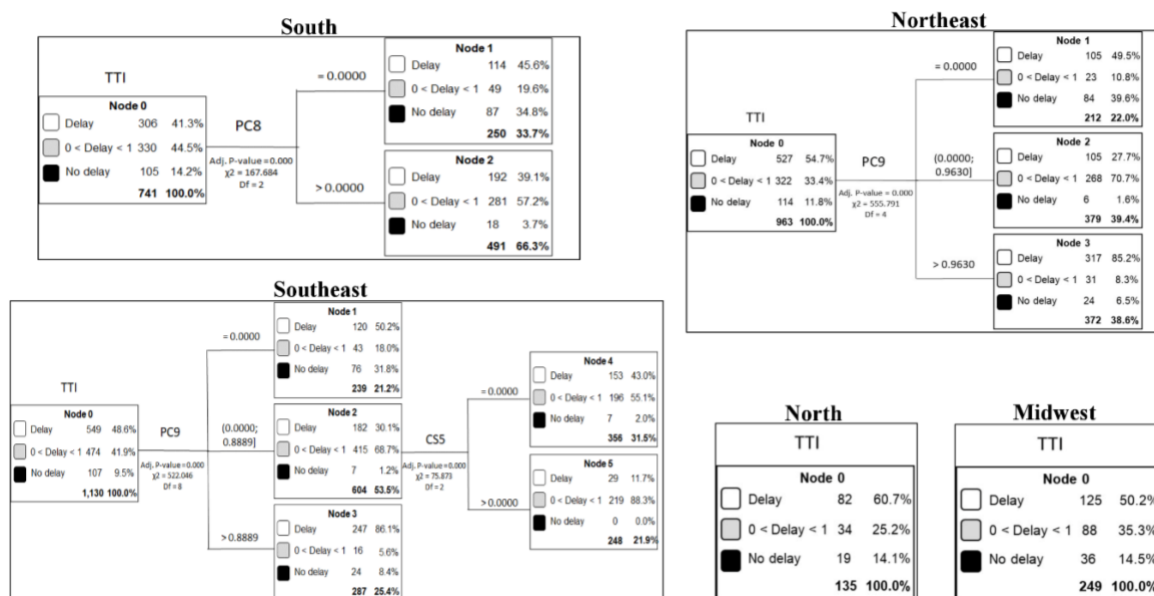
In the decision tree (Fig 2), Node 6 was the only one that showed most municipalities in the "No delay" group of TTI (46.7%). This node shows that when there was no record of first treatment by chemotherapy, radiotherapy, or both (Node 1; PC9 = 0) and, at the same time, there was no record with anatomical location in the oral

cavity (Node 6; PC5=0), most municipalities recorded the start of treatment within 30 days.

Anatomical locations in the oral cavity (PC5) and oropharynx (PC7), and the number of CT imaging services (CS5) available in the municipality per 100,000, were also included in the final model.

Fig 3 shows the CART analyzes for Brazilian regions.

Fig 3. CART analysis for time to treatment initiation for Brazilian regions.



South region had 741 municipalities with OOC records. Most municipalities of South region (41.3%) started treatment after more than 30 days (Delay group), and 14.2% of municipalities started treatment within 30 days (No delay group). In this region the staging III and IV (PC8>0.0001) explained the highest TTI in the most of municipalities (n=491). When the patients (PC8>0.0001) presented staging III and IV a delay of more than 30 days was seen in 39.1% of patients.

In the Southeast, 1,130 municipalities reported cases of OOC. Most municipalities of Southeast region (48.6%) started treatment after more than 30 days (Delay group), and 9.5% of municipalities started treatment within 30 days (No delay group). This region showed two levels of subdivision. The highest TTI was explained by treatment with chemotherapy, radiotherapy, or both (PC9). At Node 2, a subdivision was created where the number of CT imaging services (CS5) available in the municipality per 100,000 explained most municipalities in the 0<Delay<1 group (88.3%).

In the Northeast region, 963 municipalities reported at least one case of OOC. Of these, 54.7% were classified in the 'Delay' group. The highest TTI in Northeast municipalities was explained by treatment with chemotherapy, radiotherapy, or both (PC9).

North (60.7%) and Midwest (50.2%) regions had the majority of municipalities in the "Delay" group. These regions were not subdivided as they did not meet the minimum methodological criteria established for the model once the terminal nodes should include at least 200 observations.

Discussion

Most municipalities delayed the TTI. Chemotherapy or radiotherapy treatment, the number of CT imaging services per 100,000 inhabitants, and anatomical location of cancer classified as oral cavity and oropharynx were associated with the higher OOC TTI in the municipalities.

The higher percentage of records for the 60 or more age group in this study corroborates the literature on this type of cancer in older people [7,8]. The anatomical classification comprising the oropharynx (base of tongue, palate, tonsil, and oropharynx) and oral cavity (unspecified parts of tongue and mouth, floor of mouth, and gums) were the most prevalent and explained a higher TTI among the municipalities in this study in the CART model. OCCs located on the floor of the mouth and of the tongue are the most frequent types of oral cavity cancer already reported [34]. However, oropharyngeal cancer showed the most significant increase in incidence in Brazil [35]. OOC in these sites, coupled with slow and indolent growth, makes it challenging to identify the lesion, which means that patients do not seek professional help in the early stages of the disease and delays the treatment pathway [8]. Also, some OOC types, especially no-HPV, tend to metastasize to the cervical lymph nodes early without noticeable primary lesions, symptoms, or changes in the mucous membranes [36]. Therefore, some professionals may underestimate the assessment of malignancy and incur delays in referral to the specialized service [8].

Given this context, most OOC cases are still diagnosed at stages III and IV in Brazil [37]. The staging III and IV was associated to increases in TTI in South of Brazil. These more advanced stages of the disease require more complex or multimodal therapies involving chemotherapy and radiotherapy [36]. Treatment by

these therapeutic modalities (chemotherapy, radiotherapy, or both) explained the highest TTI for all the municipalities in this study, especially among municipalities in the Southeast and Northeast regions. When this type of treatment is considered, delays can be explained by more time for planning, primarily due to complications associated with tobacco and alcohol use, the need to manage adjacent comorbidities pre-treatment, a more significant number of complementary tests, oral adequacy (such as tooth extractions), referrals to other treatment support professionals and rigorous planning by multidisciplinary teams [38,39].

Considering the situation of Brazilian public health, the delay in OOC explained by chemotherapy and radiotherapy treatment may be related to the low availability of cancer support services denoted in the municipalities of this study. In 2019, Ordinance N° 1.399 was defined as a parameter for enabling Brazilian oncology services, at least one facility per 1,000 new cancer cases per year (except for non-melanoma skin cancer) [40]. However, there is still a need for more machines, especially radiotherapy machines [19], and the geographical distribution seems inadequate for all regions [41]. Other studies on cervical cancer [42], breast cancer [18], and lung cancer [19] showed that place of residence affected TTI, confirming the unequal availability of public oncology services in Brazil. High-complexity services are concentrated in large urban centers, aligning with local economic development [41]. It is no wonder that more developed Brazilian regions have reduced the risk of death from OOC, while less developed regions have shown an increase in recent cohorts [43].

The regions with the highest number of municipalities with OOC records are the Southeast and Northeast, which are also the most populous regions in the country [18]. This suggests that the high demand from patients leads to longer waiting times for chemotherapy/radiotherapy treatment in Brazil [18,41], even in regions such as the Southeast, which, compared to the other, has the greatest technological support for cancer treatment [14,19,41]. The Northeast region, however, has a high concentration of municipalities with low socioeconomic development and barriers to accessing health services are related to poor income distribution and social inequality [15,43].

Therefore, due to the complexity of cancer treatment, it is crucial for municipalities to have well-established care flows to ensure timely OOC treatment in a high-demand patient [12,16,20,42]. Lack of supply or coverage of services, professionals and infrastructure that make it difficult for patients with OOC to access

this care network can lead to delays in treatment [12,15-17]. In addition, the arrangement of chemotherapy and radiotherapy services should consider epidemiological and social factors, the number of qualified professionals, and the capacity of each unit. This is especially important for serving the socioeconomically disadvantaged population that is also the most affected by OOC [34].

In general, the centralization of chemotherapy and radiotherapy facilities in specific reference units subjects patients to long-distance travel, poor road conditions, or unsatisfactory means of transport, and, in the last resort, the imposition of relocating their place of residence, especially in a country as continental as Brazil [41]. The national average distance traveled by cancer patients for treatment varies between 105.8 and 117.1 miles (170.3 and 188.4 km, respectively), with regional disparities, where patients from the North and Midwest travel greater distances than patients in the South, Southeast, and Northeast [14], which can influence limit treatment options and hinder managing side effects [44,45]. In other words, it creates barriers to accessing health services, thus delays treatment [10,39] and leads to worse survival outcomes in OOC cases [45].

The unavailability of radiotherapy services is not exclusive to Brazil. An Italian study showed a higher TTI for patients who needed radiotherapy because the devices were only available in research/academic institutes, generating long waiting lines and patient selection [38]. Infrastructural equipment maintenance failures and lack of radiation oncologists are the main factors in delays in treatment in low and medium-development countries [46]. The difficult access to radiotherapy in low-resource or rural settings may have been associated with higher mortality in these regions [47].

A similar problem occurs in the distribution of CT imaging services, which also explains a higher TTI among municipalities, especially those in the $0 < \text{Delay} < 1$ group. This suggests that the municipality favors lower TTI when it offers CT facilities. On the other hand, the unavailability of these facilities, which is the reality for most municipalities in this study, leads to long waiting lines for appointments and the need for patients to travel to undergo the tests and for returns and appointments. In cases where intensity-modulated radiotherapy (IMRT) is indicated, for example, there is a greater need for CT simulations for case planning and, therefore, greater ITT [48]. One study showed that in Brazil, the degree of use of CT scanners is low in relation to the quantity available in the public health sector, showing that there are public

management and infrastructure problems that need to be overcome, ranging from a lack of qualified professionals to operate the equipment, devices that are out of service for long periods of time, to problems with the electricity supply in the unit or region, for example [49].

The National Policy for Cancer Prevention and Control advocates that cancer care be structured and organized into a line of care that encompasses all care levels in order to guarantee comprehensive care in HCN [50], which incorporates flows and connections for referring patients to different territories. Thus, primary care professionals are responsible for preventing and controlling risk factors and screening for potentially malignant lesions, which should be referred to specialized services to confirm the diagnosis [51]. Although this study's primary care coverage rate is satisfactory, oral health teams hardly conduct OOC-related actions in the country [52,53]. This is because dentists feel unable to identify a potentially malignant lesion and perform biopsies [54], mainly because these are rare lesions to see throughout one's career [55]. However, primary care dentists must be trained to recognize the premalignant lesions early as a clinical routine to reduce delays in OOC diagnosis and treatment [54].

Secondary care facilities and specialized human resources need to be adequately available and distributed to meet the Brazilian OOC demand. In this study, more than 70% of municipalities did not have active DSCs in 2019. DSC is the leading public service for access to OOC diagnosis, where oral medicine is offered as a minimum and mandatory specialty [20,56]. However, DSC support for primary care within the oral healthcare network still needs to be improved since only some carry out all the recommended actions [57]. From 2014 to 2018, there was a reduction in the number of DSCs that performed biopsies [12], meaning that there is a problem with the distribution of DSCs in the country, and only some of them participate in the OOC patient care network. This is very troubling, given that the shortage of DSCs has been linked to a higher risk of hospitalization and death from oral cancer [15]. Furthermore, although Brazil has the most significant number of dental professionals globally, less than 1% are oral medicine specialists [58]. There is also a marked leaving of these professionals from DSC, mainly due to the need for more resources, supplies, and work equipment, for example, to perform biopsies [20].

Studies have already reported that the greater availability of public oral health services has contributed to a lower frequency of stage IV OOC [16], and the

expansion of primary dental care coverage and the number of dental specialty centers are associated with lower mortality rates from OOC in Brazil [51]. Therefore, acting on bottlenecks that influence diagnosis delays is one way to prevent cases from being identified at advanced stages, which can reduce ITT and improve patient survival [59].

Besides the need for more service structures and human resources for OOC care in Brazil, there are areas for improvement in referral and counter-referral flows for OOC prevention, diagnosis, and treatment [60]. The lack of secondary services means that patients with suspected malignant oral lesions are referred to other services through informal and direct contacts [12], such as academic units. However, many of these units are not linked to public health management, leading to gaps in the line of care and the treatment pathway. In addition, many DSCs have difficulties making hospital referrals for confirmed OOC cases [12], and given the high cost of treatment, patients may seek independent access to reference oncology services or face long waiting lists [14].

The coordination of OOC care is complex as it is a type of cancer that requires the involvement of different professionals, from clinical dentists, oral medicine specialists, oral and maxillofacial surgeons, head and neck surgeons, oncologists, among others, who need to be supported by effective government incentive programs. This will require improvements in care integration and the organization and distribution of medium and high-complexity services. Investing in physical infrastructure and human resources is necessary to achieve this. Financial incentives in the human resources of the DSC favor collaborative relationships for articulation between primary and secondary care, improving the quality of dental care [57]. Mortality from OOC has decreased in the more socioeconomically developed Brazilian regions, where there has been more significant government investment in outpatient procedures and hospitalization [61]. Therefore, there is an urgent need to increase public investment in oral health to ensure timely treatment of OOC. This overview will help health managers at different levels of government to plan effective interventions that prioritize the most vulnerable areas.

This study is unique in that it is the first, as far as we know, to use municipalities as the unit of analysis, showing a general overview of the factors that explain the TTI of OOC in Brazil and Brazilian regions. Data are robust as official information systems consolidate them.

At the same time, it has limitations inherent to its ecological design and the use of secondary data sources. The study considered data from population aggregates, and ecological fallacy can occur if its results are interpreted at individual levels. The National Registry of Health Establishments is one of the main repositories of information about the Brazilian health system. Registration and maintenance of registration data in the National Register of Health Establishments is mandatory for all health establishments to operate in the national territory [62]. Unfortunately, there may be inconsistencies or inaccuracies in the information provided by secondary data systems like this one about the real situation of health services. The system records may be completed incorrectly or after the deadline stipulated by the Ministry of Health, resulting in possible underreporting of cases or incomplete/inconsistent information. However, the databases were checked by two senior researchers for possible inconsistencies and nothing was found. Previous articles have confirmed the reliability of this database [41,63,64].

The study of the factors involving the ITT OOC deserves to be more detailed since the delay in treatment is linked to the delay in the system. Brazilian public health management is decentralized and depends on political agreements between managers in each region, which gives it some particularities in the availability of health services that need to be studied more closely to understand the events that lead to an increase in TTI. Moreover, this study showed a pre-pandemic reality in which health services were theoretically functioning correctly. The pandemic is known to have affected delays in cancer diagnosis and treatment in Brazil [65]. Studies evaluating post-pandemic services are also critical.

Conclusion

Most municipalities delayed the TTI. Type of treatment chemotherapy, radiotherapy, tumor location (oral cavity and oropharynx), and factors to cancer diagnostic support (number of services with diagnostic imaging per 100,000 inhabitants) explained the higher TTI. The explanatory variables for the increase in TTI in the municipalities, even if indirectly, are connected to system factors. Therefore, managing the timely treatment of OOC requires expanding actions and services for diagnosis and treatment in Brazilian municipalities.

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5.3 Artigo III- Tendências temporais dos registros de câncer de boca e orofaringe no Brasil de 2019 a 2023 e fatores que impactam o atraso no tratamento

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Temporal trends of oral and oropharyngeal cancer records in Brazil from 2019 to 2023 and factors impacting treatment delay

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Abstract

Objective: Analyze the trend of oral and oropharyngeal cancer (OOC) records in Brazil from 2019 to 2023 and the factors that most impact the time to treatment initiation (TTI) during this period. **Methods:** Time series analysis of the OOC records was performed using the Box-Ljung test, Sen's Slope estimator, and Mann-Kendall test. The cointegration between $TTI \leq 30$ days or $TTI > 30$ days and the independent variables (sex, age, type of treatment, staging, region of residence) was assessed by Engle-Granger test. The quality of the models was assessed by the Breusch-Godfrey test. **Results:** From 2019 to 2023, there was a significant monthly rate of increase and monotonic growth in the total number of OOC records in Brazil. Most OOC records occurred in males over 60 years old in advanced stages who were treated with chemotherapy or radiotherapy and had a TTI of over 30 days. The monthly rate of change and monotonic growth trend increased in both sexes, up to 44 years and over 60 years, although the trend was stronger and more consistent in females and those over 60 years. A significant growth was observed for $TTI > 30$ days in the North. In the Northeast, $TTI \leq 30$ days showed a downward trend, while $TTI > 30$ days showed an upward trend. The variables that most contributed to the total variability of the $TTI > 30$ times series were male sex, age over 60 years, advanced staging, radiotherapy, and the Southeast region. Surgery had the greatest impact on the $TT < 30$ time series. **Conclusion:** There was a growing trend in the total number of OOC registrations from 2019 to 2023, especially by sex and age series. The North and Northeast regions showed an upward trend in delayed treatments. Male sex, age over 60 years, advanced stages, radiotherapy and Southeast region contributed to the greatest variability in $TTI > 30$ days.

Keywords: Oral cancer, Oropharyngeal cancer, Treatment delay, Time-to-treatment

Introduction

Oral and oropharyngeal cancer (OOC) has generated concern for public oral health. The overall incidence and mortality rates have exhibited an upward trend over the past three decades, primarily due to the aging population.¹ The prevalence of well-recognized risk factors associated with OOC, such as tobacco use (with or without smoke), alcohol consumption,² human papillomavirus (HPV) infection,³ and excessive ultraviolet exposure (in cases of lip cancer)⁴ is mediated by socioeconomic factors.² Therefore, a higher incidence is found in low- and middle-income countries.¹ At the same time, late diagnosis is still reported in the majority of cases, resulting in adverse prognoses and significant detrimental impacts on patients' quality of life,⁵ and reduced survival.^{4,6}

Brazil has a high social inequality and stands out for its high incidence of OOC.⁷ More than 15,000 new cases have been estimated for each year of the 2023-2025 triennium, making it the eighth most frequent type of cancer in the population.⁸

Similarly, inequality is reflected in the difficulty of access to OOC treatment in Brazil.⁹ Delayed treatment is still a reality,¹⁰ especially among the population that relies exclusively on public health services.¹¹ In addition, regional disparities are observed in access to oral care¹² and oncology care,¹⁰ since these services are not well distributed and available throughout the country.¹³

It is known that determinants that influence the use of health services need to be addressed to ensure timely access to treatment. Patient, disease, and health system factors are responsible for modulating the intervals between detection, definitive diagnosis, and initiation of cancer treatment.¹⁴ Studies from other countries have already shown that individual factors such as female gender,^{15,16} advanced age,^{15,16} low education, and low income¹⁷ are more associated with delayed OOC treatment. In addition, stages III and IV, more complex treatments require a longer time to start treatment.¹⁸ These issues that lead to delayed treatment still need to be further investigated in Brazilian records.

Thus, given the significant burden on Brazilian health, ongoing evaluation of the epidemiologic situation of OOC is essential. Evaluating records over time can provide basic data to optimize and improve health interventions in the care of OOC.¹⁹ Likewise, the monitoring of treatment initiation intervals allows following clinical trajectories and their

impact on prognosis, as well as indicating the performance of services in terms of care coordination¹⁴ at different levels of care. Therefore, the continuous and updated evaluation of the delay in OOC treatment becomes quite relevant, given that changes in habits and patterns of use of health services may have occurred, especially after the covid-19 pandemic, in which a reduction in the total number of diagnoses was reported,²⁰ an increase in cases in advanced stages²¹ and the possible persistence of dampened demand for new cases in subsequent years. With this in mind, this study aimed to analyze the trend of OOC records in Brazil from 2019 to 2023, as well as the factors that most impact the time to treatment initiation (TTI) during this period.

Methods

This ecological study used secondary data from the Oncology Treatment Monitoring Panel (Panel Oncology) of the Information Technology Department of the Unified Health System (DATASUS) (http://tabnet.datasus.gov.br/cgi/dhdat.exe?PAINEL_ONCO/PAINEL_ONCOLOGIABR.def), from January 2019 to December 2023 in Brazil. This panel monitors the delay, measured in days, between the definitive diagnosis of cancer and the initiation of the first therapeutic intervention. The data are provided by the information systems of the cancer care facilities offered by the Unified Health System - SUS (public or private hospitals affiliated with SUS).²² All the information is in the public domain and does not identify patients. Therefore, this study did not require approval by the Human Research Ethics Committee.

Records of malignant neoplasms of OOC were identified using the 10th revision of the International Classification of Diseases-ICD-10 (C00-C10), according to region of residence (North, Northeast, Southeast, South, Midwest) and accessed on March 16, 2025. The following data were collected on patients: sex (male or female) and age group (zero to 44 years, 45-59 years, and over 60 years); staging (early stage - 0, I and II; advanced stage - III and IV; and “not applicable”); therapeutic modality (surgery, chemotherapy, or radiotherapy); and time to treatment initiation (TTI) (≤ 30 days and > 30 days). Cases without treatment information were excluded from the analysis.

In the Panel Oncology, staging is recorded when the indicated treatment is chemotherapy, radiotherapy, or both. Cases treated surgically are classified as staging “not applicable”.

The outcome variable TTI was classified as follows: $TTI \leq 30$ was considered the most acceptable time to start treatment, while $TTI > 30$ days was classified as treatment delay, considering that the literature has shown that OOC treatments initiated after 30 days are associated with poorer prognosis and decreased survival or increased risk of death.^{16,23,24}

Population estimates were obtained from the list of population per municipality published by the Brazilian Institute of Geography and Statistics (IBGE). The proportion of OOC records per 100,000 inhabitants was then calculated for the Brazilian regions.

Statistical analysis

A time series analysis of the OOC records was performed. The Box-Ljung test for temporal correlation was used to check whether the residuals of the time series were independent (not autocorrelated) over time. Subsequently, the Sen's Slope estimator was applied to determine the median of the slopes of all lines connecting pairs of distinct points in the series over time, to evaluate the monthly rate of change in the records. The Mann-Kendall test was used to identify monotonic trends (i.e., increasing or decreasing trends) in the series. The monotonic trend facilitates the assessment of the overall behavior of the series over time.

In the next step, the presence of cointegration between the outcome variables ($TTI \leq 30$ days and $TTI > 30$ days) and the independent variables was assessed using the Engle–Granger test. Cointegration indicates whether there is a long-term relationship between the variables.²⁵ This test involves two main steps: (1) estimating a linear regression between the time series under study, and (2) evaluating whether the residuals of this regression are stationary. After verifying cointegration, ARIMA (Auto Regressive Integrated Moving Average) models were fitted to all the time series, and the quality of the models was evaluated through residual analysis using the Breusch–Godfrey test. Finally, simple linear regressions were performed between the residuals of the series to quantify, through the coefficient of determination, the impact of the independent variables on the outcome variables. All data analysis procedures were conducted using R software, version 4.3.1 (R Core Team). For all tests, a p-value ≤ 0.05 was considered statistically significant.

Results

Time-series analysis of OOC records in Brazil

Figure 1a shows the series of total OOC records per 100,000 inhabitants in Brazil. There was a sharper increase in registrations during 2019, followed by approximately constant growth in the following years. The series showed an increasing monthly rate of change. Each month, the number of COB registrations increased by 0.0023 cases per 100,000 inhabitants. There is a monotonic trend of growth over time ($p < 0.001$; $\tau = 0.356$) (Table 1).

The number of OOC records was considerably higher in the male population (Figure 1b). However, there was a higher monthly rate of change ($S = 2.0383$) and a stronger and more consistent monotonic growth trend in the female series ($\tau = 0.358$).

The highest occurrence of OOC was seen in the 60 or more-age group (Figure 1c). The series up to 44 years and over 60 years showed a significant monthly rate of change and monotonic growth trend, but the series of 60 years and over showed a higher monthly rate of change ($S = 2.8856$) and stronger and more consistent growth ($\tau = 0.098$) over the years (Table 1).

Chemotherapy and radiotherapy were the most common treatments performed over the years, and surgery was the least used treatment in Brazil (Figure 2a). The series of surgeries showed a significant temporal correlation ($p < 0.001$). All the treatment type series did not show significant changes in variation (growth or reduction) over time (Table 1).

Figure 2b shows that most records were in advanced stages. The advanced staging series showed significant temporal autocorrelation ($p = 0.01$).

Records of $TTI > 30$ days were predominantly higher in Brazil and in all Brazilian regions (Figure 3). In the national scenario, the $TTI \leq 30$ days series showed temporal autocorrelation ($p = 0.02$). Neither series exhibits significant monthly variation rates or monotonic growth trends (Table 1).

In the North, there was a significant monthly rate of change and monotonic growth for $TTI > 30$ days ($p = 0.01$). In the Northeast, the monthly variation rates and monotonic trend were significant for both series. However, $TTI \leq 30$ days showed a downward trend ($\tau = -0.181$) and $TTI > 30$ days showed an upward trend ($\tau = 0.227$). In the Southeast, South, and Midwest TTI series showed no significant changes over time (did not have a significant monthly variation rate or monotonic growth trend) (Table 2).

Analysis of the Impact of sex, age, staging, type of treatment, and region on TTI

The results indicated that male sex ($R^2 = 0.9212$), age over 60 years ($R^2 = 0.7505$), advanced staging ($R^2 = 0.9454$), radiotherapy ($R^2 = 0.8225$), and the Southeast region ($R^2 = 0.7799$) were the variables that most contributed to the total variability of the $TTI > 30$ time series (Table 3). The same variables also showed the greatest impact on the $TTI \leq 30$ time series, except for the type of treatment, in which surgery presented the highest coefficient of determination ($R^2 = 0.8290$). All the coefficients were significant at the 5% significance level (Table 3).

Discussion

The main findings of this study point to an increase in OOC records during 2019, with an upward trend in the remaining years until 2023. Male gender, advanced age (>60 years), advanced stages (III and IV), radiotherapy, and the Southeast region contributed to the greatest variability in delayed treatment records. The surgery series had an impact on the variability of $TTI \leq 30$ days records.

In 2019, Law 13.986/2019 was introduced, guaranteeing that cases whose main diagnostic hypothesis is cancer will have the necessary tests carried out within a maximum of 30 days in the Unified Health System (SUS).²⁶ It could be hypothesized that the determination of a legal deadline for investigating the malignancy of lesions stimulated an increase in biopsies, and OOC records began to rise from this period onwards.

In the same year, the Panel Oncology platform was also made available so that public health managers could monitor and compare the deadlines for starting treatment for all types of cancer in Brazil, considering hospital data from 2013 onwards.²² Thus, it is likely that the availability of mechanisms for improving management, such as the panel, will also partly justify incentives for improvements in hospital cancer registry processes from this year onwards in the country.

At the same time, the growing trend of OOC cases in recent years in Brazil points to two main concerns. The first refers to the urgent and permanent need for more targeted actions to prevent and control risk factors for this disease, which are mediated by precarious living conditions that make access to healthcare unfeasible.² The second concerns the impact of increasing the global burden of OOC in a country with serious socioeconomic disparities.

Adverse events from cancer treatment can negatively affect survivors' ability to work.²⁷ Losses of financial and social capital can be even more evident in cases of OOC due to aesthetic and functional impairments (speech, swallowing) caused by therapies.^{5,28} In addition, with the increase in cases, the country is on the list of leading countries in terms of premature mortality in the population due to a type of cancer that is considered preventable.²⁹

It is worth noting that there were reductions in registrations in the first months of 2020, when the COVID-19 pandemic took hold in Brazil. Dental services began to provide only emergency care or were closed during this period. A 68.8% drop was identified in the country's oral cancer biopsy examination rates between March and May 2020 compared to the same period the previous year.²⁰

In November 2020, the Ministry of Health released guidelines for dental care in the context of covid-19, indicating that oral cancer diagnosis actions should be considered an emergency, regardless of the municipality's epidemiological situation.³⁰ This probably explains the fact that records were not significantly affected, but rather showed an upward trend in the general context of this time series.

The total number of OOC records was higher in the male population in the years studied, which was also seen in series from previous years.^{31,32} Exposure to the main risk factors that favor the development of OOC (smoking, excessive alcohol consumption and excessive exposure to ultraviolet radiation) is closely related to the historical and social construction of male behaviors and persist as the most important causes of illness in men.^{2,31}

However, a greater upward trend in OOC was found in the female series. A similar trend was seen in other populations in European countries, in Japan,³³ and in Iran.³⁴ It should be borne in mind that the habit of smoking was acquired by women more recently,³⁵ while the abandonment of this practice may be later.³⁶ In addition, the Brazilian population has started to consume more alcoholic beverages in recent years, especially women.³⁷ All of this may influence the increase in oral malignancies in this population.

In general, historical series have shown a reduction in smoking in Brazil³¹ as a result of the implementation of a comprehensive national anti-tobacco policy that included measures to ban tobacco advertising, health warnings illustrated on cigarette packages and increases in taxes and prices for these products.³⁸ However, a stabilization of this downward trend has been

noticed, showing that more measures must be taken if the reduction in smoking rates is to continue.³⁵

Notably, some more recent studies^{39,40} have reported an increase in oral cancer cases among people who do not smoke or drink, especially among women. Brazil showed a significant increase in the oral cancer mortality rate among women between 1980 and 2018.⁴¹ Therefore, the importance of OCC control measures that consider gender-related lifestyle factors is highlighted.³⁹

The fact that the majority of records were in the over-60 age group, as well as showing a stronger and more consistent upward trend over the years, is explained by the implications of the cumulative effect of exposure to carcinogenic factors, especially previous chronic smoking, combined with the physiological processes of ageing.²⁸ Smoking is most prevalent among the elderly in Brazil.⁴² In addition, they are less educated⁴³ and have had less opportunity to access dental care and oral health education programs throughout their lives, since we are talking about a SUS-dependent population and the National Oral Health Policy (NOHP), which advocates a model of care based on the prevention of diseases and the promotion of oral health, was only implemented in 2004 in the country.⁴⁴

The increase in incidence with age for tongue and oral cavity cancer has been demonstrated by other age-period-cohort models from 1990 to 2017⁶ and 1990 to 2019.³² The same Brazilian pattern was also confirmed in other international statistics.⁴⁵ Thus, the greater number of records in older people contributed to greater variability in treatment time records, especially TTI>30 days. A trend towards earlier initiation of OOC treatment in younger patients had been identified in a previous series.¹⁰

Unfavorable socio-economic circumstances coupled with the absence of comprehensive dental care policies reflect the construction of a culture of belittling oral problems and lower demand for health services by older individuals.¹⁷ This greatly affects the search for professional help to detect oral lesions promptly and consequently delays the treatment of OOC.¹⁷ In addition, elderly people with low socioeconomic status are more prone to multiple morbidities⁴⁶ that need to be managed before OOC therapy, requiring more time to start treatment.^{15,16}

In the context of this study, it is important to note the growing trend of records in the series in the age group up to 44 years. Researchers have already warned of estimates of a greater increase in oral cancer among younger people (<45 years).⁴⁷ With unique clinical profiles, the commonly identifiable risk factors are not present in this subset of patients: they do not smoke or drink, the majority are women, and the tongue is the most affected anatomical site.⁴⁰ In these cases, the etiology of OOC seems to be unclear because, unlike OOC in the elderly, there was not enough time for the multi-step process of carcinogenesis to take place, suggesting the involvement of other elements.²⁸

Human papillomavirus (HPV) infection is closely related to the increase in OOC cases in younger patients in Brazil, located in the oropharynx.³ Systemic diseases such as Fanconi anemia,⁴⁸ other oral problems (such as periodontal disease), infections, and epigenetic changes that interfere with the composition of the oral microbiome have been pointed out as possible causes in cases reported in other anatomical locations in the younger group.⁴⁹

In addition, the experimentation and daily use of electronic cigarettes has emerged as a new path towards chemical dependency among young Brazilian adults (18-24 years old).⁵⁰ Repercussions of the products originating from these nicotine vapor devices on the metabolic activities of the cells of the oral mucosa have been raised, with an increased risk of developing oral cancer, but long-term studies are still needed to define the degree of such an effect.⁵¹

One issue shown in this recent trend, but which has persisted over the years, is that most records are identified in advanced stages in Brazil.³ Not surprisingly, the series of advanced stages was the one that most strongly influenced TTI>30 days. Stages III and IV require multimodal therapies, when surgery alone is no longer viable given the progression of the disease,⁵² and this is related to the fact that radiotherapy (RT) and chemotherapy (QT) were the most registered therapies.

For this reason, the RT and QT series also greatly explained the variability of the records with TTI>30 days, since more complex therapies require more preparatory time to start treatment.¹⁸ In another analysis, RT and QT treatments had greater power to explain the majority of OOC treatment delays in Brazilian municipalities.⁵³

Similar to this study, the trend towards shorter treatment times for surgical cases was demonstrated in a Brazilian series from previous years.¹⁰ Surgery is ideally the most suitable

treatment for OOC cases, since it indicates that the diagnosis was early, allows for a greater chance of cure, and generates less expenditure of public resources.²⁴

Although the series of advanced stages, radiotherapy, and TTI>30 days did not show significant monotonic variations, their stability over the years studied denotes the continuous profile of delays in diagnosis and treatment of OOC in Brazil. This scenario is unfavorable for patients affected by this disease and may be associated with the increase in mortality in recent years in the country.⁵⁴

The expansion of oral health teams (OHT) in Primary Care (PC) and the establishment of Dental Specialty Centers (DSC), one of the main focuses of which is the early diagnosis of oral cancer, based on the NOHP, demonstrates the progress of the Brazilian public health system in dental care for the population. However, it has been observed that the OHT teams have difficulty in diagnosing and monitoring OOC cases in all Brazilian regions.¹² The process of implementing the PNSB is quite complex and has taken place in a heterogeneous way as a result of the country's social inequalities, impacting OOC outcomes unequally between regions.^{19,55}

More developed regions, such as the Southeast and South, which have higher levels of education and income and better urban infrastructure conditions, are the same ones that have a greater supply of qualified services, with better organization of the work processes of DSCs concerning OOC.⁵⁶ Meanwhile, regions that face serious social problems, such as the North and Northeast, have a greater number of DSCs that have not performed biopsies,⁵⁷ and are the only ones to show an upward trend in TTI> 30 days in this study, confirming other findings from a previous series.¹⁰ This inverse relationship between oral cancer trends and socioeconomic indicators was also confirmed by the growth in mortality rates in these same regions between 2010 and 2019.⁵⁵

This does not negate the fact that the delay in OOC treatment is a reality that needs to be managed in the country as a whole, especially since there is an unequal distribution of cancer services for treatment,¹³ especially radiotherapy, which is the indicated therapy in most cases.⁵² The Southeast region, being the most populous, had the highest volume of OOC records. Even with all the technological resources available, longer waiting lists for treatment may explain the greater influence of this series on the variability of TTI>30 days. It is therefore necessary to take a careful look at strategies for improving care that take into account the specific demands of each region, to achieve real equity in the care of people with OOC.

Delays in the treatment of OOC persist due to difficulties in implementing a well-defined and efficient network for the timely diagnosis and treatment of OOC in higher-risk groups.^{53,56} At the same time, the increase in cases in groups not considered at risk shown in this study, such as younger people and women, points to the need to increase the installed capacity in services for the diagnosis of OOC for all people. Therefore, the development of technological resources that make it possible to integrate data from different health information systems and connect it to other social information could help improve actions to control risk factors, facilitate screening in target populations and help develop OOC risk prediction models to help identify lesions.⁵⁸

The main limitation of this study is the use of secondary data. The Panel Oncology system is a validated and reliable platform of paramount importance for cancer management in Brazil. Even so, it is not without its flaws, especially regarding missing information, since oral cancer in Brazil is not a compulsorily notifiable disease.¹⁹ Furthermore, the data is aggregated. For this reason, it was not possible to express as clearly how the independent variables (gender, age group, staging, and region) explained the variability in the records of both TTI series at the same time, since stratification of patient data is not feasible. Likewise, it was not possible to identify other information such as income, schooling, work, history of smoking and alcoholism, HPV status, and the presence of comorbidities of the individuals, which can influence therapy decisions and therefore the time to start treatment.⁵⁹

Nevertheless, the approach used has sparked relevant discussions about the alarming situation of OOC in Brazil in recent years. By characterising the behaviour of the disease over time, new control strategies and public health decisions can be indicated, which is especially important in the case of a complex and devastating disease such as OOC, which requires urgent action.

Conclusion

There was an increase in OOC registrations during 2019, with a steady upward trend over the years. The North and Northeast regions showed an upward trend in $TTI > 30$ days. The Northeast also showed a downward trend in $TTI \leq 30$ days. Male sex, older age (over 60), advanced stages (III and IV), radiotherapy treatment, and the Southeast region contributed to the greatest variability in $TT > 30$ days. The surgery series contributed most strongly to the variability of $TT < 30$ days records.

Therefore, improvements in the control of risk factors in target populations and in screening for early diagnosis need to be implemented. In addition, oncology centers need to be made available equitably so that OOC treatment can take place promptly in all regions of Brazil.

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Table 1- Time series analysis of total OOC records according to sex, age group, type of treatment, staging and TTI in Brazil from 2019 to 2023.

Variable	Tests (p-value, S ^a and tau ^b)		
	Box-Ljung	Sen Slope	Mann Kendall
Total OOC	p<0.001	p<0.001; S=0.0023	p<0.001; tau=0.356
Sex			
Male	p=0.303	p=0.046 S=1.5423	p=0.046; tau=0.178
Female	p<0.001	p<0.001; S=2.0383	p<0.001; tau=0.358
Age			
up to 44	p=0.005	p=0.001; S=0.5454	p=0.001; tau=0.293
45-59	p=0.379	p=0.919; S=0.0593	p=0.919; tau=0.0096
60 or more	p<0.001	p<0.001; S=2.8856	p<0.001; tau=0.362
Treatment type			
Surgery	p<0.001	p=0.614; S=0.1428	p=0.614; tau=0.045
Chemotherapy	p=0.745	p=0.055; S= -0.5217	p=0.055; tau= -0.171
Radiotherapy	p=0.106	p=0.24; S=0.3794	p=0.246; tau= 0.075
Staging			
Early	p=0.416	p=0.358; S=0.1589	p=0.358; tau=0.083
Advanced	p=0.01	p=0.216; S=0.5566	p=0.216; tau=0.11

TTI			
≤ 30 days	$p=0.002$	$p=0.511;$ $S= -0.2233$	$p=0.511;$ $\text{tau}= -0.059$
>30 days	$p=0.309$	$p=0.069;$ $S=0.8672$	$p=0.069;$ $\text{tau} = 0.162$

^aS: monthly rate of change by the Sen Slope estimator.

^btau: indicates the strength and consistency of the monotonic trend by Mann Kendall test.

Table 2- Time series analysis of the time to treatment initiation in Brazilian regions from 2019 to 2023.

Region	TTI (days)	Tests (p-value, S* and tau**)		
		Box-Ljung	Sen Slope	Mann Kendall
North	≤30	p=0.519	p=0.361; S=0	p=0.368; tau=-0.085
	>30	p=0.267	p=0.013; S=0.1429	p=0.013; tau=0.226
Northeast	≤30	p=0.267	p=0.044; S = -0.2	p=0.012; tau=0.226
	>30	p=0.016	p=0.011; S = 0.5625	p=0.044; tau=-0.181
Southeast	≤30	p<0.001	p=0.403; S=0.1577	p=0.403; tau=0.075
	>30	p=0.577	p=0.562; S=0.1530	p=0.561; tau=0.052
South	≤30	p=0.08	p=0.487; S= -0.0714	p=0.486; tau=-0.062
	>30	p=0.73	p=0.342; S=0.1111	p=0.342; tau=0.085
Midwest	≤30	p=0.329	p=0.609; S= -0.00862	p=0.609 tau=-0.046
	>30	p=0.07	p=0.195; S=0.1053	p=0.195 tau=0.117

*S: monthly rate of change by the Sen Slope estimator.

**tau: indicates the strength and consistency of the monotonic trend by Mann Kendall test.

Table 3- Analysis of the influence of time-series of OOC records by sex, age, staging, type of treatment, and region of residence on the variability of TTI $\leq$ 30 days and TTI $>$ 30 days in Brazil from 2019 to 2023.

Variable	TTI $\leq$ 30 days			TTI $>$ 30 days		
	Coefficient	R ²	R	Coefficient	R ²	R
Sex						
Male	1.305	0.865	0.930	1.212	0.921	0.959
Female	1.672	0.535	0.731	2.236	0.534	0.731
Age						
≤ 44	1.962	0.219	0.468	3.11	0.194	0.440
45 – 59	1.375	0.373	0.610	1.671	0.667	0.817
60 or more	1.219	0.716	0.846	1.457	0.750	0.866
Staging						
Early stage	1.605	0.237	0.487	2.659	0.509	0.713
Advanced stage	1.046	0.891	0.944	1.184	0.945	0.972
Not applicable	0.214	0.135	0.368	1.226	0.225	0.475
Treatment						
Surgery	1.082	0.687	0.829	3.915	0.069	0.262
Chemotherapy	1.622	0.273	0.523	1.823	0.786	0.887
Radiotherapy	1.840	0.125	0.353	1.494	0.823	0.907
Region						
North	4.575	0.192	0.438	2.684	0.069	0.264
Northeast	1.616	0.385	0.620	1.851	0.503	0.709
Southeast	1.520	0.638	0.798	1.690	0.779	0.883
South	1.629	0.358	0.598	1.648	0.223	0.473
Midwest	2.502	0.221	0.470	2.687	0.182	0.427

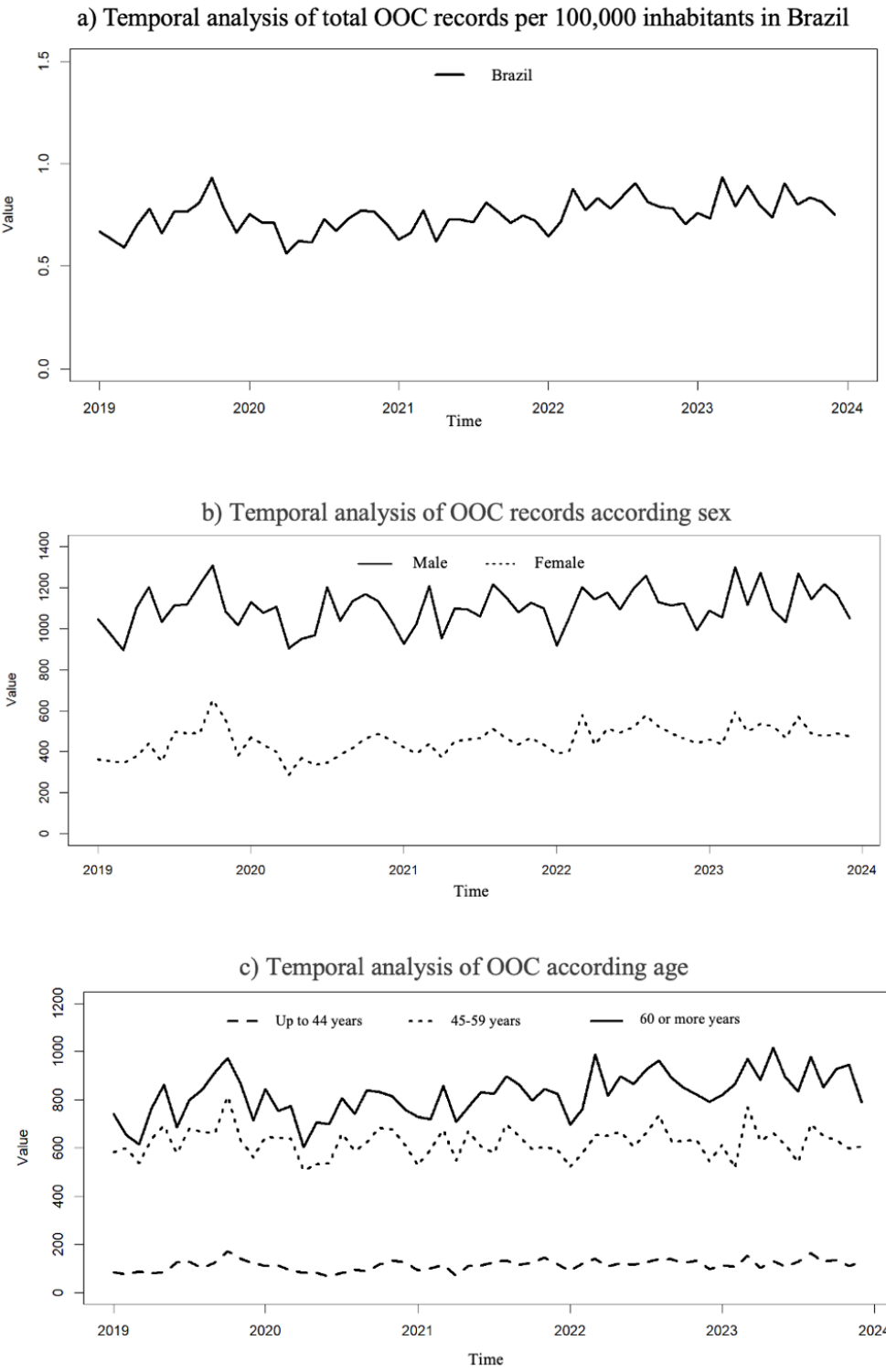


Figure 1- Temporal analysis of records OOC according to sex, age, type of therapy, and staging in Brazil from 2019 to 2023.

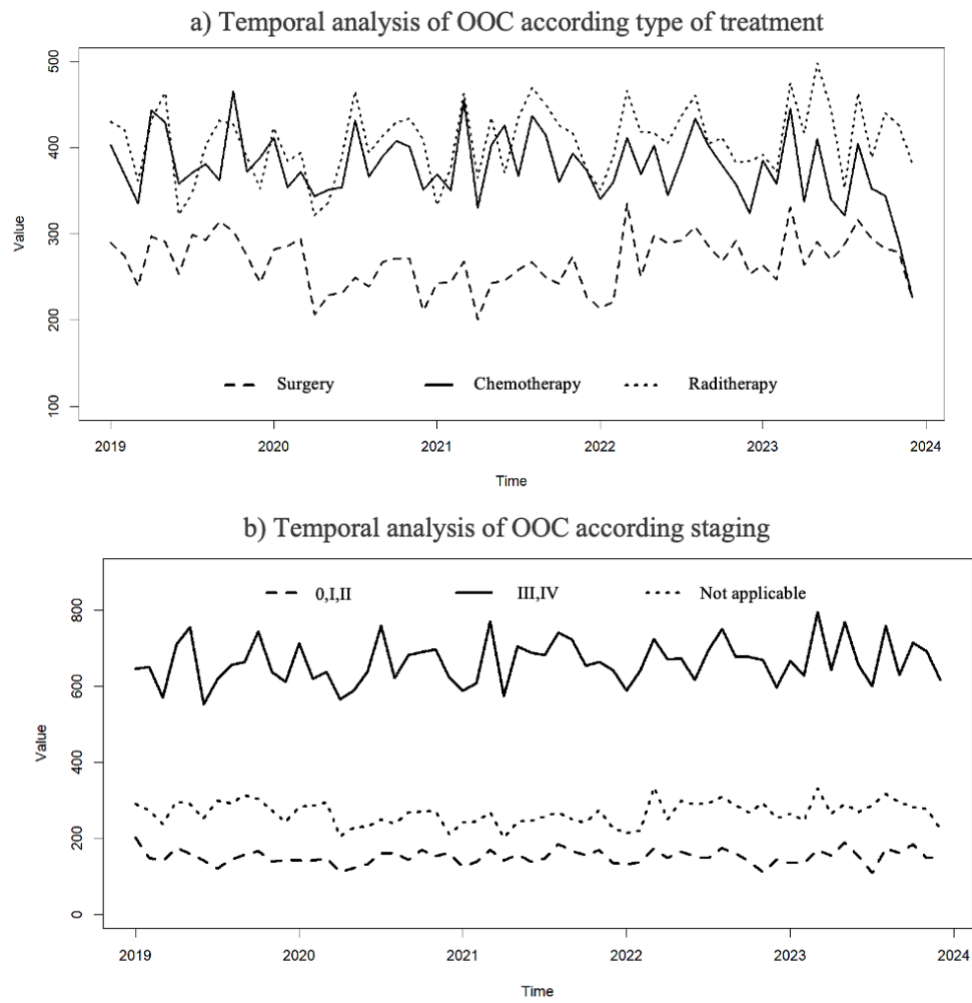


Figure 2- Temporal analysis of records OOC according to type of treatment and staging in Brazil from 2019 to 2023.

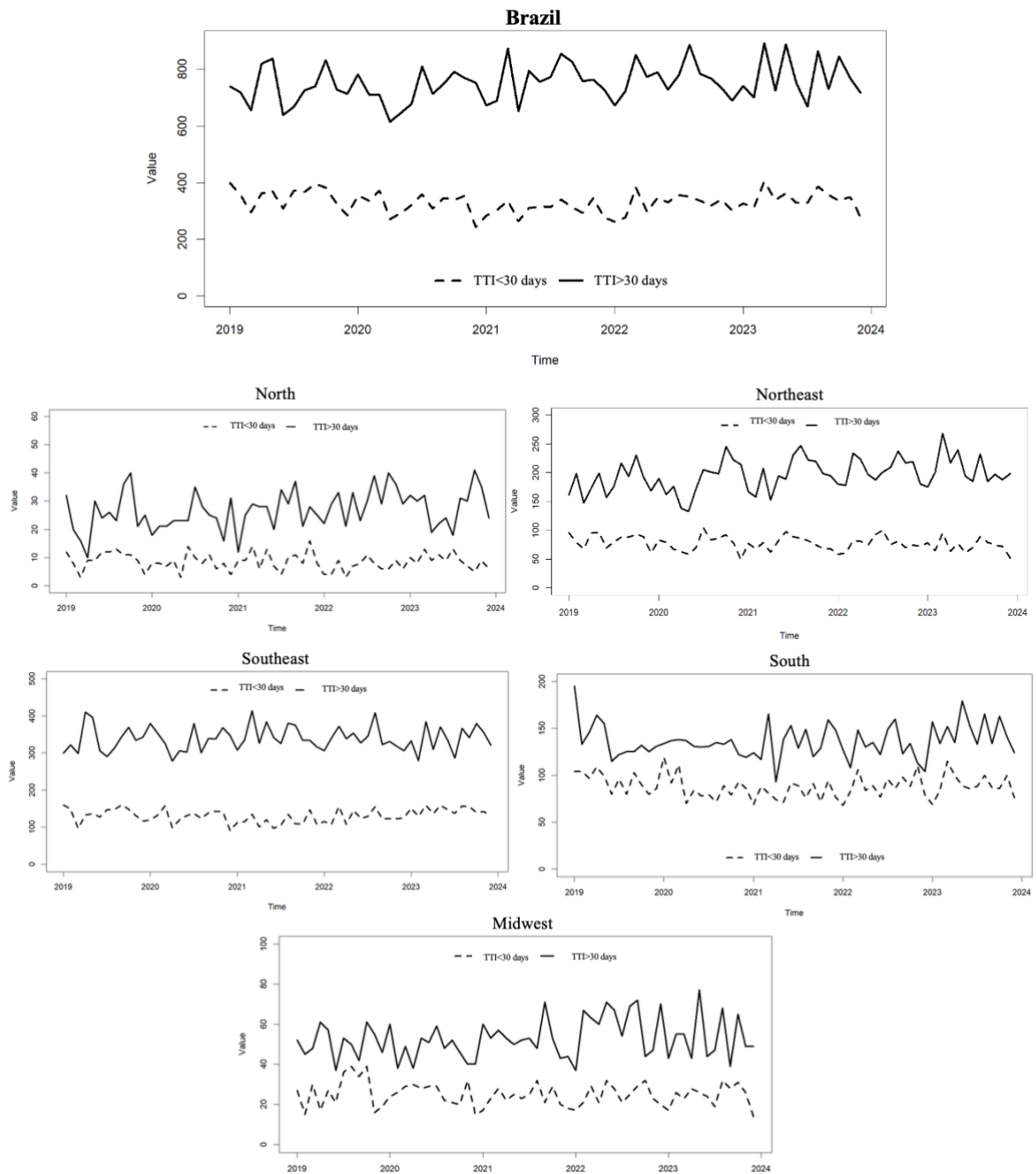


Figure 3- Temporal analysis of time to treatment initiation in Brazil and regions (North, Northeast, Southeast, South, and Midwest) from 2019 to 2023.

6 CONSIDERAÇÕES FINAIS

No Artigo I, foi encontrada uma associação entre o atraso no tratamento do CBO e vários fatores socioeconômicos, tais como: tipo de plano de saúde, sexo feminino, idade avançada, cor da pele não branca, baixa escolaridade, tratamento em hospital público ou regional, necessidade de encaminhamentos e residência em áreas regionais/remotas. No entanto, os dados disponíveis não corroboram uma conclusão definitiva sobre essa associação. Altas discrepâncias metodológicas entre os estudos – particularmente na definição de atraso no tratamento e na categorização de variáveis socioeconômicas – juntamente com um número limitado de estudos, contribuíram para uma certeza muito baixa das evidências.

O Artigo II mostrou que 57,79% dos municípios brasileiros registraram, pelo menos, um caso de CBO em 2019. A maioria dos municípios apresentaram TIT>30 dias. As regiões Norte e Centro-Oeste tiveram maior proporção de casos com atraso do tratamento. O tipo de tratamento (quimioterapia, radioterapia, ambos), localização do tumor (cavidade oral e orofaringe) e fatores de apoio ao diagnóstico do câncer (número de serviços com diagnóstico por imagem por 100.000 habitantes) explicaram o maior TIT nos municípios. As variáveis explicativas para o aumento do TIT nos municípios, ainda que indiretamente, estão conectadas a fatores estruturais e organizacionais de acesso aos serviços de saúde. Portanto, a gestão do tratamento oportuno do CBO requer a expansão das ações e serviços de diagnóstico e tratamento nos municípios brasileiros.

O Artigo III evidenciou que houve um aumento nos registros de CBO em 2019, com uma tendência constante de aumento ao longo dos anos. As regiões Norte e Nordeste apresentaram uma tendência de aumento no TIT>30 dias. O Nordeste também apresentou uma tendência de redução no TIT≤30 dias. Sexo masculino, idade mais avançada (acima de 60 anos), estágios avançados (III e IV), tratamento radioterápico e a região Sudeste contribuíram para a maior variabilidade no TIT>30 dias. A série de cirurgia contribuiu mais fortemente para a variabilidade dos registros de TIT≤30 dias. Assim, melhorias no controle dos fatores de risco nas populações-alvo e na triagem para diagnóstico precoce precisam ser implementadas. Além disso, os centros de oncologia precisam ser disponibilizados de forma equitativa para que o tratamento CBO possa ocorrer prontamente em todas as regiões do Brasil.

Apesar da impossibilidade de extrapolar e comparar os resultados encontrados nos estudos incluídos na RS com a situação do atraso do tratamento do CBO no Brasil, especialmente pela ausência de estudos brasileiros elegíveis, a presente tese permite refletir sobre quem são as pessoas que mais sofrem com dificuldades de acesso ao tratamento a partir de vulnerabilidades comuns: pessoas idosas, não-brancas, com baixa escolaridade, que residem em regiões remotas (ou menos desenvolvidas).

De certa maneira, com os Artigos I e II, tentou-se contribuir com a lacuna encontrada pela RS de estudos que abordasse tal relação no Brasil. No entanto, embora a plataforma utilizada nesses estudos (Painel Oncologia) ser de grande valor para a gestão do tempo para o tratamento do câncer no Brasil, os dados são agregados e informações sociodemográficas (cor da pele, renda, escolaridade) dos pacientes não são disponibilizadas.

Mesmo assim, acredita-se que esses estudos, além de revelar achados importantes, sinalizam a necessidade de aperfeiçoamento da plataforma com a inclusão de mais dados sobre o perfil sociodemográfico e hábitos dos pacientes. Enquanto isso não é possível, incentiva-se o desenvolvimento de mais pesquisas que busquem abordar a relação entre fatores socioeconômicos e o tempo para o início do tratamento do CBO de forma mais clara, seguindo o padrão de intervalos de tempo estabelecidos pela Declaração de *Aarhus* para o tratamento do câncer a partir de dados hospitalares. Além disso, estudos que avaliem o impacto das condições de vida nas possibilidades de realizar determinadas terapias ou que levam à decisão por não tratar também são convidativos.

É importante destacar que os Artigos I e II levantaram dois pontos convergentes importantes: 1) o atraso do tratamento do CBO está bastante relacionado ao tipo de tratamento (especificamente, radioterapia). Ou seja, ambos confirmam possíveis entraves de acesso a esse tipo de terapia, seja por problemas de disponibilidade e/ou de acessibilidade; 2) existência de disparidades regionais no tempo para o início do tratamento, visto que regiões específicas (principalmente a Norte) apresentam maior proporção, bem como maior tendência de crescimento de registros de tratamentos em atraso, atestando, portanto, que o local onde o paciente reside interfere na oportunidade de tratamento, principalmente quando são locais mais remotos como encontrado pela própria RS. Tais resultados jogam luz para a necessidade de avaliação de particularidades organizativas do SUS (repasses

financeiros, descentralização e pactuações políticas) que interferem na disponibilidade equânime de serviços de oncologia em diferentes estados e municípios do Brasil. Assim, pesquisas que visem interpelar gestores de saúde a respeito da oferta dos serviços para o cuidado do paciente com CBO na rede de atenção, são fundamentais.

Por fim, tendo em vista que o diagnóstico do CBO compete, primariamente, aos dentistas dentro da rede de atenção à saúde bucal, esta tese avança na Odontologia corroborando a importância de torná-la cada vez mais integrada nas discussões e decisões sobre regionalização e regulação da assistência aos pacientes com CBO, bem como incluída nos programas de acesso a profissionais especialistas no SUS. Isto posto, permanece a esperança de que os caminhos do cuidado da rede de atenção à pessoa com CBO podem ser mais acessíveis tanto para o diagnóstico quanto para o tratamento o mais cedo possível no Brasil.

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APÊNDICE A- Material suplementar do artigo I

Socioeconomic factors affecting treatment delays in oral and oropharyngeal squamous cell carcinoma: a systematic review and meta-analysis

Supplementary file

Supplementary file 1. Search strategies used in each electronic database (date: from interception to January 2023, updated in December 2023).

MedLine through Pubmed

((((Head and Neck Neoplasms[MeSH Terms]) OR (Mouth Neoplasms[MeSH Terms]) OR (Oropharyngeal Neoplasms[MeSH Terms]) OR (Squamous Cell Carcinoma of Head and Neck[MeSH Terms]) OR ("Head and Neck Neoplasm"[Title/Abstract]) OR ("Cancer of Head and Neck"[Title/Abstract]) OR ("Head and Neck Cancer"[Title/Abstract]) OR ("Head Neoplasms"[Title/Abstract]) OR ("Head Neoplasm"[Title/Abstract]) OR ("Cancer of Head"[Title/Abstract]) OR ("Head Cancers"[Title/Abstract]) OR ("Mouth Neoplasm"[Title/Abstract]) OR ("Oral Neoplasm"[Title/Abstract]) OR ("Oral Neoplasms"[Title/Abstract]) OR ("Cancer of Mouth"[Title/Abstract]) OR ("Mouth Cancers"[Title/Abstract]) OR ("Oral Cancer"[Title/Abstract]) OR ("Oral Cancers"[Title/Abstract]) OR ("Cancer of the Mouth"[Title/Abstract]) OR ("Mouth Cancer"[Title/Abstract]) OR ("Oropharyngeal Neoplasm"[Title/Abstract]) OR ("Oropharynx Neoplasms"[Title/Abstract]) OR ("Oropharynx Neoplasm"[Title/Abstract]) OR ("Oropharyngeal Cancer"[Title/Abstract]) OR ("Oropharyngeal Cancers"[Title/Abstract]) OR ("Oropharynx Cancer"[Title/Abstract]) OR ("Oropharynx Cancers"[Title/Abstract]) OR ("Cancer of the Oropharynx"[Title/Abstract]) OR ("Squamous Cell Carcinoma of the Head and Neck"[Title/Abstract]) OR ("Head and Neck Squamous Cell Carcinoma"[Title/Abstract]) OR ("Oral Tongue Squamous Cell Carcinoma"[Title/Abstract]) OR ("Oral Squamous Cell Carcinoma"[Title/Abstract]) OR ("Oral Cavity Squamous Cell Carcinoma"[Title/Abstract]) OR ("Oral Squamous Cell Carcinomas"[Title/Abstract]) OR ("Squamous Cell Carcinoma of the Mouth"[Title/Abstract]) OR ("Oropharyngeal Squamous Cell Carcinoma"[Title/Abstract])) AND ((Socioeconomic Factors[MeSH Terms]) OR (Income[MeSH Terms]) OR (Poverty[MeSH Terms]) OR (Social Class[MeSH Terms]) OR (Educational Status[MeSH Terms]) OR (Demography[MeSH Terms]) OR ("Socioeconomic Factors") OR ("Educational Status") OR ("Socioeconomic Factor") OR ("Standard of Living") OR ("Living Standard") OR ("Living Standards") OR ("Land Tenure") OR ("Social Inequality") OR ("Social Inequalities") OR ("High-Income Population") OR ("High Income Population") OR ("High-Income Populations") OR ("Incomes") OR ("Savings") OR ("Health Insurances") OR ("Income Distribution") OR ("Income Distributions") OR ("Low-Income Population") OR ("Low-Income Populations") OR ("Low Income Population") OR ("Low Income Populations") OR ("Social Classes") OR ("Socioeconomic Status") OR ("Middle Class Population") OR ("Educational Achievement") OR ("Educational Achievements") OR ("Schooling Level") OR ("Educational Levels") OR ("Demographic") OR ("Population Spatial Distributions") OR ("Demographic

Factors") OR ("Demographic Factor") OR ("Demographic Impacts") OR ("Demographic Impact") OR ("Patient Profile")) AND ((Time-to-Treatment[MeSH Terms]) OR ("Time-to-Treatment"[Title/Abstract]) OR (Time-to-Treatments[Title/Abstract]) OR ("Door-to-Treatment Time"[Title/Abstract]) OR ("Door to Treatment Time"[Title/Abstract]) OR ("Delayed Treatment"[Title/Abstract]) OR ("Delayed Treatments"[Title/Abstract]) OR ("Treatment Delay"[Title/Abstract]) OR ("Primary Treatment"[Title/Abstract]) OR ("Waiting Time"[Title/Abstract]) OR ("Timeliness"[Title/Abstract]) OR ("Delay in Treatment"[Title/Abstract]) OR ("Time to Start Treatment"[Title/Abstract]) OR ("Diagnosis-treatment interval"[Title/Abstract]) OR ("Time-to-initiation"[Title/Abstract]) OR ("Treatment initiation"[Title/Abstract]) OR ("Treatment time"[Title/Abstract]) OR ("Treatment times"[Title/Abstract]) OR ("Timely care"[Title/Abstract]) OR ("Diagnosis to treatment"[Title/Abstract]) OR ("Time factors"[Title/Abstract]) OR ("Time to treatment initiation"[Title/Abstract]))

Embase through Elsevier

("head and neck tumor"/exp OR "head and neck tumor" OR "mouth tumor"/exp OR "mouth tumor" OR "mouth cancer"/exp OR "oropharynx tumor"/exp OR "oropharynx tumor" OR "oropharynx cancer"/exp OR "squamous cell carcinoma of the head and neck"/exp OR "head and neck squamous cell carcinoma"/exp OR "oral tongue squamous cell carcinoma"/exp OR "mouth squamous cell carcinoma"/exp OR "mouth squamous cell carcinoma" OR "oral cavity squamous cell carcinoma"/exp OR "oropharynx squamous cell carcinoma"/exp OR "oropharynx squamous cell carcinoma" OR "mouth carcinoma"/exp OR "mouth carcinoma" OR "oropharynx carcinoma"/exp OR "oropharynx carcinoma" OR "head and neck neoplasm" OR "cancer of head and neck" OR "head and neck cancer" OR "head neoplasms" OR "head neoplasm" OR "cancer of head" OR "head cancers" OR "mouth neoplasm" OR "oral neoplasm" OR "oral neoplasms" OR "cancer of mouth" OR "mouth cancers" OR "oral cancer" OR "oral cancers" OR "cancer of the mouth" OR "mouth cancer" OR "oropharyngeal neoplasm" OR "oropharynx neoplasms" OR "oropharynx neoplasm" OR "cancer of oropharynx" OR "oropharynx cancer" OR "oropharynx cancers" OR "oropharyngeal cancer" OR "oropharyngeal cancers" OR "oropharynx cancer" OR "oropharynx cancers" OR "cancer of the oropharynx" OR "head and neck squamous cell carcinomas" OR "squamous cell carcinoma of the head and neck" OR "head and neck squamous cell carcinoma" OR "oral tongue squamous cell carcinoma" OR "oral squamous cell carcinoma" OR "oral cavity squamous cell carcinoma" OR "oral squamous cell carcinomas" OR "squamous cell carcinoma of the mouth" OR "oropharyngeal squamous cell carcinoma") AND ("socioeconomics"/exp OR "socioeconomics" OR "economic status"/exp OR "economic status" OR "educational status"/exp OR "educational status" OR "income group"/exp OR "income group" OR "poverty"/exp OR "poverty" OR "socioeconomic distribution"/exp OR "socioeconomic distribution" OR "socioeconomic parameters"/exp OR "socioeconomic parameters" OR "socioeconomic vulnerability"/exp OR "socioeconomic vulnerability" OR "household economic status"/exp OR "household economic status" OR "health insurance"/exp OR "health insurance" OR "income" OR "socioeconomic factors" OR "social class" OR "demography" OR "socioeconomic factor" OR "standard of living" OR "living standard" OR "living standards" OR "land tenure" OR "social inequality" OR "social inequalities" OR "high-income population" OR "high income population" OR "high-income populations" OR "incomes" OR "savings" OR "income distribution" OR "income distributions" OR "low-income population" OR "low-income populations")

OR "low income population" OR "low income populations" OR "social classes" OR "socioeconomic status" OR "middle class population" OR "educational achievement" OR "educational achievements" OR "schooling level" OR "educational levels" OR demographic OR "population spatial distributions" OR "demographic factors" OR "demographic factor" OR "demographic impacts" OR "demographic impact" OR "patient profile") AND ("time to treatment"/exp OR "therapy delay"/exp OR "therapy delay" OR "time to treatment" OR "time-to-treatment" OR "time-to-treatments" OR "door-to-treatment time" OR "door to treatment time" OR "delayed treatment" OR "delayed treatments" OR "treatment delay" OR "primary treatment" OR "waiting time" OR "timeliness" OR "delay in treatment" OR "time to start treatment" OR "diagnosis-treatment interval" OR "time-to-initiation" OR "treatment initiation" OR "treatment time" OR "treatment times" OR "timely care" OR "diagnosis to treatment" OR "time factors" OR "time to treatment initiation")

Scopus

((TITLE-ABS-KEY ("head and neck tumor") OR TITLE-ABS-KEY ("head neoplasms") OR TITLE-ABS-KEY ("mouth tumor") OR TITLE-ABS-KEY ("mouth cancer") OR TITLE-ABS-KEY ("oropharynx tumor") OR TITLE-ABS-KEY ("oropharynx cancer") OR TITLE-ABS-KEY ("squamous cell carcinoma of the head and neck") OR TITLE-ABS-KEY ("head and neck squamous cell carcinoma") OR TITLE-ABS-KEY ("oral tongue squamous cell carcinoma") OR TITLE-ABS-KEY ("mouth squamous cell carcinoma") OR TITLE-ABS-KEY ("oral cavity squamous cell carcinoma") OR TITLE-ABS-KEY ("oropharynx squamous cell carcinoma") OR TITLE-ABS-KEY ("mouth carcinoma") OR TITLE-ABS-KEY ("oropharynx carcinoma") OR TITLE-ABS-KEY ("Head and Neck Neoplasms") OR TITLE-ABS-KEY ("Mouth Neoplasms") OR TITLE-ABS-KEY ("Oropharyngeal Neoplasms") OR TITLE-ABS-KEY ("Squamous Cell Carcinoma of Head and Neck") OR TITLE-ABS-KEY ("Oral Neoplasm") OR TITLE-ABS-KEY ("Oral Cancer") OR TITLE-ABS-KEY ("Oropharyngeal Cancer") OR TITLE-ABS-KEY ("Oral Squamous Cell Carcinoma") OR TITLE-ABS-KEY ("Oral Cavity Squamous Cell Carcinoma") OR TITLE-ABS-KEY ("Oral Squamous Cell Carcinomas") OR TITLE-ABS-KEY ("Squamous Cell Carcinoma of the Mouth") OR TITLE-ABS-KEY ("Oropharyngeal Squamous Cell Carcinoma"))) AND ((ALL (socioeconomics) OR ALL ("economic status") OR ALL ("educational status") OR ALL ("income group") OR ALL (poverty) OR ALL ("socioeconomic distribution") OR ALL ("socioeconomic parameters") OR ALL ("socioeconomic vulnerability") OR ALL ("household economic status") OR ALL ("health insurance") OR ALL ("Socioeconomic Factors") OR ALL ("Social Class") OR ALL (demography) OR ALL ("Standard of Living") OR ALL ("Land Tenure") OR ALL ("Social Inequality") OR ALL ("High-Income Population") OR ALL ("Health Insurances") OR ALL ("Income Distribution") OR ALL ("Low-Income Population") OR ALL ("Middle Class Population") OR ALL ("Schooling Level") OR ALL ("Demographic Impacts") OR TITLE-ABS-KEY ("Patient

Profile"))) AND ((TITLE-ABS-KEY ("time to treatment") OR TITLE-ABS-KEY ("Therapy delay") OR TITLE-ABS-KEY ("Time-to-Treatment") OR TITLE-ABS-KEY ("Door-to-Treatment Time") OR TITLE-ABS-KEY ("Door to Treatment Time") OR TITLE-ABS-KEY ("Delayed Treatment") OR TITLE-ABS-KEY ("Delayed Treatments") OR TITLE-ABS-KEY ("Treatment Delay") OR TITLE-ABS-KEY ("Primary Treatment") OR TITLE-ABS-KEY ("Waiting Time") OR TITLE-ABS-KEY ("timeliness") OR TITLE-ABS-KEY ("Delay in Treatment") OR TITLE-ABS-KEY ("Time to Start Treatment") OR TITLE-ABS-KEY ("Diagnosis-treatment interval") OR TITLE-ABS-KEY ("Time-to-initiation") OR TITLE-ABS-KEY ("Treatment initiation") OR TITLE-ABS-KEY ("Treatment time") OR TITLE-ABS-KEY ("Treatment times") OR TITLE-ABS-KEY ("Timely care") OR TITLE-ABS-KEY ("Diagnosis to treatment") OR TITLE-ABS-KEY ("Time factors") OR TITLE-ABS-KEY ("Time to treatment initiation"))))

Web of science

TS=((“head and neck tumor” OR “head and neck tumor” OR “mouth tumor” OR “mouth tumor” OR “mouth cancer” OR “oropharynx tumor” OR “oropharynx tumor” OR “oropharynx cancer” OR “squamous cell carcinoma of the head and neck” OR “head and neck squamous cell carcinoma” OR “oral tongue squamous cell carcinoma” OR “mouth squamous cell carcinoma” OR “oral cavity squamous cell carcinoma” OR “oropharynx squamous cell carcinoma” OR “oropharynx squamous cell carcinoma” OR “mouth carcinoma” OR “mouth carcinoma” OR “oropharynx carcinoma” OR “oropharynx carcinoma” OR “head and neck neoplasm” OR “cancer of head and neck” OR “head and neck cancer” OR “head neoplasms” OR “head neoplasm” OR “cancer of head” OR “head cancers” OR “mouth neoplasm” OR “oral neoplasm” OR “oral neoplasms” OR “cancer of mouth” OR “mouth cancers” OR “oral cancer” OR “oral cancers” OR “cancer of the mouth” OR “mouth cancer” OR “oropharyngeal neoplasm” OR “oropharynx neoplasms” OR “oropharynx neoplasm” OR “cancer of oropharynx” OR “oropharynx cancer” OR “oropharynx cancers” OR “oropharyngeal cancer” OR “oropharyngeal cancers” OR “oropharynx cancer” OR “oropharynx cancers” OR “cancer of the oropharynx” OR “head and neck squamous cell carcinomas” OR “squamous cell carcinoma of the head and neck” OR “head and neck squamous cell carcinoma” OR “oral tongue squamous cell carcinoma” OR “oral squamous cell carcinoma” OR “oral cavity squamous cell carcinoma” OR “oral squamous cell carcinomas” OR “squamous cell carcinoma of the mouth” OR “oropharyngeal squamous cell carcinoma”) AND (“socioeconomics” OR “socioeconomics” OR “economic status” OR “economic status” OR “educational status” OR “educational status” OR “income group” OR “income group” OR “poverty” OR “poverty” OR “socioeconomic distribution” OR “socioeconomic distribution” OR “socioeconomic parameters” OR “socioeconomic parameters” OR “socioeconomic vulnerability” OR “socioeconomic vulnerability” OR “household economic status” OR “household economic status” OR “health insurance” OR “health insurance” OR “income” OR “socioeconomic factors” OR “social class” OR “demography” OR “socioeconomic factor” OR “standard of living” OR “living standard” OR “living standards” OR “land tenure” OR “social inequality” OR “social inequalities” OR “high-income population” OR “high income population” OR “high-income populations” OR “incomes” OR

“savings” OR “income distribution” OR “income distributions” OR “low-income population” OR “low-income populations” OR “low income population” OR “low income populations” OR “social classes” OR “socioeconomic status” OR “middle class population” OR “educational achievement” OR “educational achievements” OR “schooling level” OR “educational levels” OR demographic OR “population spatial distributions” OR “demographic factors” OR “demographic factor” OR “demographic impacts” OR “demographic impact” OR “patient profile”) AND (“time to treatment” OR “therapy delay” OR “therapy delay” OR “time to treatment” OR “time-to-treatment” OR “time-to-treatments” OR “door-to-treatment time” OR “door to treatment time” OR “delayed treatment” OR “delayed treatments” OR “treatment delay” OR “primary treatment” OR “waiting time” OR “timeliness” OR “delay in treatment” OR “time to start treatment” OR “diagnosis-treatment interval” OR “time-to-initiation” OR “treatment initiation” OR “treatment time” OR “treatment times” OR “timely care” OR “diagnosis to treatment” OR “time factors” OR “time to treatment initiation”))

Biblioteca Virtual da Saúde (BVS) through Bireme

((mh:(head AND neck neoplasms)) OR (mh:(mouth neoplasms)) OR (mh:(oropharyngeal neoplasms)) OR (mh:(squamous cell carcinoma of head AND neck)) OR (cancer of head) OR (cancer of head AND neck) OR (cancer of the head) OR (cancer of the head AND neck) OR (head cancer) OR (head cancers) OR (head neoplasm) OR (head neoplasms) OR (head AND neck cancer) OR (head AND neck neoplasm) OR (cancer of mouth) OR (cancer of the mouth) OR (mouth cancer) OR (mouth cancers) OR (mouth neoplasm) OR (oral cancer) OR (oral cancers) OR (oral neoplasm) OR (oral neoplasms) OR (cancer of oropharynx) OR (cancer of the oropharynx) OR (oropharynx cancer) OR (oropharynx cancers) OR (oropharyngeal cancer) OR (oropharyngeal cancers) OR (oropharyngeal neoplasm) OR (oropharynx cancer) OR (oropharynx cancers) OR (oropharynx neoplasm) OR (oropharynx neoplasms) OR (head AND neck squamous cell carcinomas) OR (head AND neck squamous cell carcinoma) OR (oral cavity squamous cell carcinoma) OR (oral squamous cell carcinoma) OR (oral squamous cell carcinomas) OR (oral tongue squamous cell carcinoma) OR (oropharyngeal squamous cell carcinoma) OR (squamous cell carcinoma of the mouth)) AND ((mh:(socioeconomic factors)) OR (high income population) OR (high-income population) OR (high-income populations) OR (land tenure) OR (living standard) OR (living standards) OR (social inequalities) OR (social inequality) OR (social inequity) OR (socioeconomic factor) OR (standard of living) OR (educational level) OR (educational status) OR (social class)) AND ((mh:(time-to-treatment)) OR (delayed treatment) OR (delayed treatments) OR (door TO treatment time) OR (time TO treatment) OR (time TO treatments) OR (time-to-treatments) OR (treatment delay) OR (treatment delays) OR (primary treatment) OR (waiting time) OR (timeliness) OR (time TO start treatment) OR (diagnosis-treatment interval) OR (time-to-initiation) OR (treatment initiation) OR (treatment time) OR (treatment times))

Google Scholar

(“mouth neoplasms” OR “oropharyngeal neoplasms” OR “oral squamous cell carcinoma”) AND (“socioeconomic factors” OR income OR “educational level”) AND (“time-to-treatment” OR “treatment delay” OR timeless OR “waiting time”)

Open grey:

Oral cancer AND treatment delay

Supplementary file 2. References of excluded studies from the systematic review and reason for exclusion.

	Study	Reason for exclusion
1.	Abdo EN, Garrocho Ade A, Barbosa AA, Oliveira EL, Franca-Filho L, Negri SL, Pordeus IA. Time elapsed between the first symptoms, diagnosis and treatment of oral cancer patients in Belo Horizonte, Brazil. <i>Med Oral Patol Oral Cir Bucal</i> . 2007 Nov 1;12(7):E469-73.	Professional delay (interval between symptoms to diagnosis).
2.	Agarwal AK, Sethi A, Sareen D, Dhingra S. Treatment delay in oral and oropharyngeal cancer in our population: the role of socioeconomic factors and health-seeking behaviour. <i>Indian J Otolaryngol Head Neck Surg</i> . 2011 Apr;63(2):145-50. doi: 10.1007/s12070-011-0134-9.	Patient delay (interval between self-perception of symptoms and first consultation).
3.	Agarwal P, Agrawal RR, Jones EA, Devaiah AK. Social Determinants of Health and Oral Cavity Cancer Treatment and Survival: A Competing Risk Analysis. <i>Laryngoscope</i> . 2020 Sep;130(9):2160-2165.	The study compares socioeconomic factors related to survival. It does not report time-to-treatment.
4.	Amsbaugh MJ, Yusuf M, Cash E, Silverman C, Potts K, Dunlap N. Effect of time to simulation and treatment for patients with oropharyngeal cancer receiving definitive radiotherapy in the era of risk stratification using smoking and human papillomavirus status. <i>Head Neck</i> . 2018 Apr;40(4):687-695.	The study is about time-to-treatment. It does not report the socioeconomic factors of the sample.
5.	Andrews GA, Patel VA, Derr J, Zhu J. Timeliness of Treatment for Head and Neck Squamous Cell Carcinoma. <i>Head and Neck Surgery. Otolaryngol Head Neck Surger</i> . 2015;153(1_suppl):P55–P79.	Abstract.
6.	Arbes SJ Jr, Olshan AF, Caplan DJ, Schoenbach VJ, Slade GD, Symons MJ. Factors contributing to the poorer survival of black Americans diagnosed with oral	The study compares socioeconomic factors related to survival. It does

	cancer (United States). <i>Cancer Causes Control</i> . 1999; 10(6):513-23.	not report time-to-treatment.
7.	Baker S, Banerjee R, Debenham B. EP-1056: Treatment delays are associated with disease upstaging in oropharyngeal squamous cell carcinoma. <i>Radiotherapy and Oncology</i> . 2016; 119: S510.	Abstract.
8.	Balchander D. et al. Prognostic Significance of Referral Patterns and Time Trends in Head and Neck Cancer Management. <i>Int J Radiat Oncol Biol Phys</i> . 2022; 112(5):e27.	Abstract.
9.	Balk M, Rupp R, Craveiro AV, Allner M, Grundtner P, Eckstein M, Hecht M, Iro H, Gostian AO. The COVID-19 pandemic and its consequences for the diagnosis and therapy of head and neck malignancies. <i>Eur Rev Med Pharmacol Sci</i> . 2022 Jan;26(1):284-290.	The study is about head and neck cancer patient delay in COVID-19 pandemic.
10.	Barros-Silva PG, Fontes-Borges MM, Costa-Dias C, Mota-Lemos JV, Socorro-Saldanha-Cunha MD, Fernandes-Souza E, Sousa-Dantas T, Bitu-Sousa F. Clinical-pathological and sociodemographic factors associated with the distant metastasis and overall survival of oral cavity and oropharynx squamous cell carcinoma. <i>Med Oral Patol Oral Cir Bucal</i> . 2020 May 1;25(3):e375-e382.	The study compares socioeconomic factors related to survival. It does not report time-to-treatment.
11.	Beaudoin PL, Munden J, Faye M, Ndiaye IC, Sewitch M, Ayad T, Poenaru D. Identifying Barriers in Access to Care for Head and Neck Cancer Patients: A Field Study in Dakar. <i>Laryngoscope</i> . 2022; 132(6):1219-1223.	Professional delay (interval between symptoms to diagnosis).
12.	Bedir A, Abera SF, Efremov L, Hassan L, Vordermark D, Medenwald D. Socioeconomic disparities in head and neck cancer survival in Germany: a causal mediation analysis using population-based cancer registry data. <i>J Cancer Res Clin Oncol</i> . 2021;147(5):1325-1334.	The study compares socioeconomic factors related to survival. It does not report time-to-treatment.
13.	Bhattacharyya N, Abemayor E. Patterns of hospital utilization for head and neck cancer care: changing demographics. <i>JAMA Otolaryngol Head Neck Surg</i> . 2015 Apr;141(4):307-12.	The study compares socioeconomic factors related to survival. It does not report time-to-treatment.
14.	Borrayo EA, Scott KL, Drennen AR, MacDonald T, Nguyen J. Determinants of Treatment Delays Among	Head and neck patient delay

	Underserved Hispanics With Lung and Head and Neck Cancers. <i>Cancer Control</i> . 2016; 23(4):390-400.	without separating oral cancer in the analysis.
15.	Brinkerhoff BT, Choong NW, Massey BL, Gore EM, Firat SY, Wong SJ, Campbell BH, Schapira RM, Visotcky AM, Tripp PM. Diagnosis to Treatment Interval and Outcome in Patients with Locally Advanced Squamous Cell Carcinoma of the Head and Neck in a Veterans Affairs Medical Center. <i>J Cancer Sci Ther</i> . 2012; 4(5):111-15.	Head and neck patient delay without separating oral cancer in the analysis.
16.	Brocklehurst P, Rafiq R, Lowe D, Rogers S. Analysis of the impact of deprivation on urgent suspected head and neck cancer referrals in the Mersey region between January 2004 to December 2006. <i>Br J Oral Maxillofac Surg</i> . 2012; 50(3):215-20.	Professional delay (interval between symptoms and diagnosis).
17.	Carey RM, Fathy R, Shah RR, Rajasekaran K, Cannady SB, Newman JG, Ibrahim SA, Brant JA. Association of Type of Treatment Facility With Overall Survival After a Diagnosis of Head and Neck Cancer. <i>JAMA Netw Open</i> . 2020; 3(1):e1919697.	The study is not about time to treatment. It reports on type of treatment facility and survival.
18.	Carlsen AH, Eriksen JG, Godballe C, Johansen J, Sørensen JA, Bjørndal K. Impact of age, comorbidity, and WHO performance status on delay of treatment in patients undergoing fast-track work-up for head and neck cancer. <i>J Geriatr Oncol</i> . 2019; 10(2):259-264.	Professional delay (interval between symptoms and diagnosis).
19.	Carroll WR, Kohler CL, Carter VL, Hannon L, Skipper JB, Rosenthal EL. 2009. Barriers to early detection and treatment of head and neck squamous cell carcinoma in African American men. <i>Head Neck</i> . 2009; 31(12):1557-62.	Head and neck patient delay without separating oral cancer in the analysis.
20.	Caudell JJ, Locher JL, Bonner JA. Diagnosis-to-treatment interval and control of locoregionally advanced head and neck cancer. <i>Arch Otolaryngol Head Neck Surg</i> . 2011; 137(3):282-5.	Head and neck patient delay without separating oral cancer in the analysis.
21.	Chandarana MN, Pai PS. Demography and treatment pattern of patients with head and neck carcinoma presenting to a tertiary care center in India: Need for urgent decentralization of cancer care. <i>South Asian J Cancer</i> . 2020; 9(1):38-42.	The study is not about time to treatment.
22.	Chapman CH, Ryan WR, Yom SS. Prevalence of Highly Self-Directed Care Among Patients with HPV-	Abstract.

	Associated Oropharyngeal Cancer. <i>Int J Radiat Oncol Biol Phys.</i> 2017; 99(2): E327.	
23.	Chen AY, Schrag N, Hao Y, Stewart A, Ward E. Changes in Treatment of Advanced Oropharyngeal Cancer, 1985-2001. <i>Laryngoscope.</i> 2007; 117(1):16–21.	The study is about socioeconomic factors related to treatment facility types. It does not report on time-to-treatment.
24.	Chen AY, Zhu J, Fedewa S. Temporal trends in oropharyngeal cancer treatment and survival: 1998-2009. <i>Laryngoscope.</i> 2013; 124(1): 131–138.	The study is about types of oropharyngeal cancer treatment over the years. It does not report on time-to-treatment.
25.	Chiliti BA, Campos WG, Gallo CB, Lemos CA. Oral cancer analysis in a Brazilian city: interval between diagnosis and treatment. <i>Braz Oral Res.</i> 2022; 36: e073.	The study is not related to Squamous Cell Carcinoma.
26.	Chu KP, Habbous S, Kuang Q, Boyd K, Mirshams M, Liu F-F, ... Liu G. Socioeconomic status, human papillomavirus, and overall survival in head and neck squamous cell carcinomas in Toronto, Canada. <i>Cancer Epidemiol.</i> 2016; 40: 102–112.	The study describes socioeconomic factors related to survival. It does not report time-to-treatment.
27.	Cook L, Woods C, Nicholls T, Ooi EH. Delays in Time to Head and Neck Cancer Treatment: A South Australian Perspective. <i>Medicina (Kaunas).</i> 2022; 58(2):145.	The study includes other types of cancer, not just Squamous Cell Carcinoma.
28.	Costa AASD, Caldeira PC, Sousa AA, Tibúrcio JD, Belligoli LQG, Santos VBD, Bretas PMC, Nunes LL, Prado Neto SCD, Silva GW, Soares JMA. Oral and oropharyngeal cancer: time from first symptoms to treatment initiation and associated factors. <i>Braz Oral Res.</i> 2023 May 29;37:e054.	The study not report time-to-treatment according to the objective of this review.
29.	da Conceição MGD, Emmerick ICM, Figueiró AC, Luiza VL. Oral cancer patient's profile and time to treatment initiation in the public health system in Rio de Janeiro, Brazil. <i>BMC Health Serv Res.</i> 2021; 21(1):145.	Patient delay (interval between first symptom and diagnosis).

30.	Dantas TS, de Barros Silva PG, Sousa EF, da Cunha MDP, de Aguiar ASW, Costa FWG, Mota MRL, Alves APNN, Sousa FB. Influence of Educational Level, Stage, and Histological Type on Survival of Oral Cancer in a Brazilian Population: A Retrospective Study of 10 Years Observation. <i>Medicine (Baltimore)</i> . 2016; 95(3):e2314.	The study describes socioeconomic factors related to survival. It does not report time-to-treatment.
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33.	De Luca P, Bisogno A, Colacurcio V, Marra P, Cassandro C, Camaioni A, Cassandro E, Scarpa A. Diagnosis and treatment delay of head and neck cancers during COVID-19 era in a tertiary care academic hospital: what should we expect? <i>Eur Arch Otorhinolaryngol</i> . 2022; 279(2):961-965.	Head and neck patient delay due to COVID-19 pandemic.
34.	Diz Dios P, Padrón González N, Seoane Lestón J, Tomás Carmona I, Limeres Posse J, Varela-Centelles P. "Scheduling delay" in oral cancer diagnosis: a new protagonist. <i>Oral Oncol</i> . 2005; 41(2):142-6.	The study is about scheduling delay, not treatment delay.
35.	Dooley S, Khakoo NS, Perlow H, Kwon D, Nicolli E, Yechieli R, Samuels MA, Mora M, Friedman LM, Samuels S. Improved Care for Patients Evaluated in a Head and Neck Multidisciplinary Clinic at a Safety Net Hospital. <i>Int J Radiat Oncol Biol Phys</i> . 2020; 108(3): E817-E818.	Abstract.
36.	Dost P, Talanow DD, Kaiser S, Hirche H, Jahnke K. Zum Zeitintervall zwischen Symptom- und Behandlungsbeginn bei Kopf- und Halstumoren [The time span between symptom onset and starting treatment in head and neck tumors]. <i>HNO</i> . 1996; 44(9):492-6. German.	Patient delay (interval between first symptom and diagnosis).
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	burden on time to treatment. <i>Cancer Epidemiol Biomarkers Prev.</i> 2020; 29 (6_Supplement_2): D071.	
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44.	Grønhøj C, Jensen D, Dehlendorff C, Nørregaard C, Andersen E, Specht L, Charabi B, von Buchwald C. Impact of Time to Treatment Initiation in Patients with Human Papillomavirus-positive and -negative Oropharyngeal Squamous Cell Carcinoma. <i>Clin Oncol (R Coll Radiol).</i> 2018; 30(6):375-381.	The study is about time intervals from diagnosis to treatment. It does not report the socioeconomic factors of the sample.

45.	Hemmi T, Yusa K, Kasuya S, Yamanouchi H, Ishikawa S, Kobayashi T, Iino M. Influence of interval between biopsy and surgery on prognosis of patients with early-stage oral squamous cell carcinoma: A preliminary study. <i>J Oral Maxil Sur Med Pathol</i> . 2019; 31(3):159-162.	The study is about time intervals from diagnosis to treatment. It does not report the socioeconomic factors of the sample.
46.	Ho AS, Kim S, Tighiouart M, Mita A, Scher KS, Epstein JB, Laury A, Prasad R, Ali N, Patio C, Clair JM, Zumsteg ZS. Quantitative survival impact of composite treatment delays in head and neck cancer. <i>Cancer</i> . 2018; 124(15):3154-3162.	Head and neck patient delay without separating oral cancer in the analysis.
47.	Hollows P, McAndrew PG, Perini MG. 2000. Delays in the referral and treatment of oral squamous cell carcinoma. <i>Br Dent J</i> . 188(5):262-5.	Professional delay (time to referral to treatment).
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49.	Hsiehchen D, Muquith M, Haque W, Espinoza M, Yopp A, Beg MS. Clinical Efficiency and Safety Outcomes of Virtual Care for Oncology Patients During the COVID-19 Pandemic. <i>JCO Oncol Pract</i> . 2021; 17(9):e1327-e1332.	The study is about different types of cancer.
50.	Itamura K, Kokot N, Sinha U, Swanson M. Association of insurance type with time course of care in head and neck cancer management. <i>Laryngoscope</i> . 2020; 130(11):E587-E592.	Head and neck patient delay without separating oral cancer in the analysis.
51.	Iyer HS, Kohler RE, Ramogola-Masire D, Brown C, Molebatsi K, Grover S, Kablay I, Bvochora-Nsingo M, Efstathiou JA, Lockman S, Tapela N, Dryden-Peterson SL. Explaining disparities in oncology health systems delays and stage at diagnosis between men and women in Botswana: A cohort study. <i>PLoS One</i> . 2019 Jun 6;14(6):e0218094.	The study includes overall types of cancer, including head and neck cancer.
52.	Jafari A, Najafi Sh, Moradi F, Kharazifard M, Khami M. Delay in the diagnosis and treatment of oral cancer. <i>J Dent (Shiraz)</i> . 2013; 14(3):146-50.	Professional delay (delay in diagnosis impacts on delay in treatment).

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54.	Jensen JS, Jakobsen KK, Mirian C, Ghanizada M, Håkansson K, Wessel I, Grønhøj C, Rasmussen JH, von Buchwald C. Impact of time to treatment initiation for patients with oral cavity squamous cell carcinoma: a population-based, retrospective study. <i>Acta Oncol.</i> 2021; 60(4):491-496.	The study is about time intervals from diagnosis to treatment. It does not report the socioeconomic factors of the sample.
55.	Jin MC, Harris JP, Sabolch AN, Gensheimer M, Le QT, Beadle BM, Pollom EL. Proton radiotherapy and treatment delay in head and neck squamous cell carcinoma. <i>Laryngoscope.</i> 2020; 130(11):E598-E604.	Head and neck patient delay without separating oral cancer in the analysis.
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58.	Kompelli A, Cartmell KB, Sterba KR, Alberg AJ, Xiao CC, Sood AJ, Garrett-Mayer E, White-Gilbertson SJ, Rosenzweig SA, Day TA. An assessment of racial differences in epidemiological, clinical and psychosocial factors among head and neck cancer patients at the time of surgery. <i>World J Otorhinolaryngol Head Neck Surg.</i> 2020; 6(1):41-48.	Head and neck patient delay without separating oral cancer in the analysis.
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60.	Krishnatreya M, Kataki AC, Sharma JD, Nandy P, Rahman T, Kumar M, Gogoi G, Hoque N. Educational levels and delays in start of treatment for head and	Head and neck patient delay without separating

	neck cancers in North-East India. Asian Pac J Cancer Prev. 2014; 15(24):10867-9.	oral cancer in the analysis.
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62.	Lai DW, Kim J, Marciscano A, Buckley SA, Schmidt BL, Cohen RF, Nierodzik MNR, Myssiorek D, DeLacure MD, Sanfilippo N, Seetharamu N. <u>The impact of interventions on provider and treatment delays in head and neck cancer patients.</u> J Clinical Oncol. 2012; 30(15): e16052-e16052.	Abstract.
63.	Leachman BK, DeMora L, Churilla TM, Ebersole B, Bauman J, Ridge JA, Lango M, Egleston B, Galloway TJ. Multidisciplinary Care of Head and Neck Cancer in Elderly Patients. Int J Rad Oncol Biol Phys. 2018; 100(5):1329.	Abstract.
64.	Lee SC, Tang IP, Avatar SP, Ahmad N, Selva KS, Tay KK, Vikneswaran T, Tan TY. Head and neck cancer: possible causes for delay in diagnosis and treatment. Med J Malaysia. 2011; 66(2):101-4.	Head and neck patient delay without separating oral cancer in the analysis.
65.	Lee YH. <u>Impact of Delay in Treatment on Survival of 6353 Oral Cancers: Results of a Nationwide Screening Program in Taiwan.</u> J Global Oncol. 2018; 4(Supplement 2): 204s-204s.	Abstract.
66.	Le Tourneau C, Jung GM, Borel C, Bronner G, Flesch H, Velten M. Prognostic factors of survival in head and neck cancer patients treated with surgery and postoperative radiation therapy. Acta Otolaryngol. 2008; 128(6):706-12.	Head and neck patient delay without separating oral cancer in the analysis.
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68.	Liao DZ, Schlecht NF, Rosenblatt G, Kinkhabwala CM, Leonard JA, Ference RS, Prystowsky MB, Ow TJ, Schiff BA, Smith RV, Mehta V. Association of Delayed	The study is about time-to-treatment. It does not report

	Time to Treatment Initiation With Overall Survival and Recurrence Among Patients With Head and Neck Squamous Cell Carcinoma in an Underserved Urban Population. <i>JAMA Otolaryngol Head Neck Surg.</i> 2019; 145(11):1001-1009.	socioeconomic factors of the sample.
69.	Liaquat A, Naseer R, Rashid M, Khan SM, Haq EU, Tayyab TF. The Role of Socioeconomic Status and Literacy in the treatment delay in Oral Cancer patients Visiting Mayo Hospital Lahore, Pakistan – A Tertiary Care Hospital. <i>Pak J Med Health Sci.</i> 2021;15(8): 1785-87.	Patient delay (interval of self-perception of the first symptoms impacts treatment delay).
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71.	Lyhne NM, Christensen A, Alanin MC, Bruun MT, Jung TH, Bruhn MA, Jespersen JB, Kristensen CA, Andersen E, Godballe C, Buchwald C, Bundgaard T, Johansen J, Lambertsen K, Primdahl H, Toustrup K, Sørensen JA, Overgaard J, Grau C. Waiting times for diagnosis and treatment of head and neck cancer in Denmark in 2010 compared to 1992 and 2002. <i>Eur J Cancer.</i> 2013; 49(7):1627-33.	Head and neck patient delay without separating oral cancer in the analysis.
72.	McDermott JD, Eguchi M, Morgan R, Amini A, Goddard JA, Borrayo EA, Karam SD. Elderly Black Non-Hispanic Patients With Head and Neck Squamous Cell Cancer Have the Worst Survival Outcomes. <i>J Natl Compr Canc Netw.</i> 2020; 19(1):57-67.	Head and neck patient delay without separating oral cancer in the analysis.
73.	Metzger K, Moratin J, Horn D, Pilz M, Ristow O, Hoffmann J, Freier K, Engel M, Freudlsperger C. Treatment delay in early-stage oral squamous cell carcinoma and its relation to survival. <i>J Craniomaxillofac Surg.</i> 2021; 49(6):462-467.	Patient delay (treatment delay was defined between the initial presentation of the patient and the date of surgery).
74.	Metzger K, Mrosek J, Zittel S, Pilz M, Held T, Adeberg S, Ristow O, Hoffmann J, Engel M, Freudlsperger C, Moratin J. Treatment delay and tumor size in patients with oral cancer during the first year of the COVID-19 pandemic. <i>Head Neck.</i> 2021; 43(11):3493-3497.	Patient delay (treatment delay was defined between the initial presentation of the patient and the date of surgery).

75.	Molina MA, Cheung MC, Perez EA, Byrne MM, Franceschi D, Moffat FL, Livingstone AS, Goodwin WJ, Gutierrez JC, Koniaris LG. African American and poor patients have a dramatically worse prognosis for head and neck cancer: an examination of 20,915 patients. <i>Cancer</i> . 2008; 113(10):2797-806.	The study is not about time-to-treatment but only about socioeconomic factors.
76.	Morse E, Fujiwara RJT, Judson B, Mehra S. Treatment Times in Salivary Gland Cancer: National Patterns and Association with Survival. <i>Otolaryngol Head Neck Surg</i> . 2018; 159(2):283-292.	The study is not about only Squamous Cell Carcinoma.
77.	Murphy CT, Galloway TJ, Handorf EA, Egleston BL, Wang LS, Mehra R, Flieder DB, Ridge JA. Survival Impact of Increasing Time to Treatment Initiation for Patients With Head and Neck Cancer in the United States. <i>J Clin Oncol</i> . 2016; 34(2):169-78.	Head and neck patient delay without separating oral cancer in the analysis.
78.	Murphy CT, Galloway TJ, Handorf EA, Wang L, Mehra R, Flieder DB, Ridge JA. Increasing time to treatment initiation for head and neck cancer: an analysis of the National Cancer Database. <i>Cancer</i> . 2015; 121(8):1204-13.	Head and neck patient delay without separating oral cancer in the analysis.
79.	Naghavi AO, Demetriou SK, Venkat PS, Abuodeh YA, Ahmed KA, Strom T, Frakes JM, Trotti A, Harrison LB, Caudell JJ. Medicaid Independently Predicts for Poor Outcome in Head and Neck Malignancies. <i>Int J Rad Oncol Biol Phys</i> . 2015; 93(3):E370.	Abstract.
80.	Naghavi AO, Echevarria MI, Grass GD, Strom TJ, Abuodeh YA, Ahmed KA, Kim Y, Trotti AM, Harrison LB, Yamoah K, Caudell JJ. Having Medicaid insurance negatively impacts outcomes in patients with head and neck malignancies. <i>Cancer</i> . 2016; 122(22):3529-3537.	Head and neck patient delay without separating oral cancer in the analysis.
81.	Naghavi AO, Echevarria M, Strom T, Abuodeh YA, Ahmed KA, Venkat PS, Trotti A, Harrison LB, Green BL, Yamoah K, Caudell JJ. Race Is Associated With Poor Outcomes in Head and Neck Cancer. <i>Int J Rad Oncol Biol Phys</i> . 2016; 96(2): E407.	Abstract.
82.	Naghavi AO, Echevarria MI, Strom TJ, Abuodeh YA, Ahmed KA, Venkat PS, Trotti A, Harrison LB, Green BL, Yamoah K, Caudell JJ. Treatment delays, race, and outcomes in head and neck cancer. <i>Cancer Epidemiol</i> . 2016; 45:18-25.	Head and neck patient delay without separating oral cancer in the analysis.
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	neck cancer treatment: case-control study. <i>J Laryngol Otol.</i> 2015; 129(4):383-5.	
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85.	Ning MS, Gomez DR, Shah AK, Kim CR, Palmer MB, Thaker NG, Grosshans DR, Liao Z, Chapman BV, Brooks ED, Tang C, Rosenthal DI, Garden AS, Frank SJ, Gunn GB. The Insurance Approval Process for Proton Radiation Therapy: A Significant Barrier to Patient Care. <i>Int J Radiat Oncol Biol Phys.</i> 2019; 104(4):724-733.	The study is about the time for insurance authorization to treatment of cancer.
86.	Nocon CC, Ajmani GS, Bhayani MK. A contemporary analysis of racial disparities in recommended and received treatment for head and neck cancer. <i>Cancer.</i> 2020; 126(2):381-389.	The study is not about time-to-treatment but only about socioeconomic factors.
87.	Nocon CC, Liederbach E, Sisco M, Yao K, Gerber ME, Lewis CM, Bhayani MK. Factors Affecting Delays to Surgery for Oral Tongue Carcinoma in the National Cancer Data Base. <i>Otolaryngol Head Neck Surg.</i> 2014; 151(1_suppl):P56.	Abstract.
88.	Overgaard J, Jovanovic A, Godballe C, Grau Eriksen J. The Danish Head and Neck Cancer database. <i>Clin Epidemiol.</i> 2016; 8:491-496.	The study is about tumor characteristics and treatment of head and neck cancer.
89.	Pakravan F, Abbasi F, Garshasbi MA, Isfahani MN. Relationship between oral cancer stage and elapsed time from the onset of signs and symptoms to diagnosis and treatment. <i>Cancer Treat Res Commun.</i> 2021; 28:100428.	Professional and patient delay (interval of first symptoms and diagnosis).
90.	Pandrowala S, Ramraj D, Shankar R, Chopra S, Das A, Mishra A, Pandey D. Impact of preoperative COVID infection on the outcomes of planned curative-intent cancer surgeries in the second wave of the pandemic	The study is about treatment delays due to infection by COVID-19 patients with

	from a tertiary care center in India. J Surg Oncol. 2022; 125(2):107-112.	different types of cancer.
91.	Patel PA, Christopher E, Fundakowski MD. Impact of facility and patient demographic on time to treatment initiation in head and neck cancer. Otolaryngol Head Neck Surg. 2018; 159(1_suppl):P206–P250.	Abstract.
92.	Patel UA, Brennan TE. Disparities in head and neck cancer: assessing delay in treatment initiation. Laryngoscope. 2012; 122(8):1756-60.	Head and neck patient delay without separating oral cancer in the analysis.
93.	Patil RD, Meinzen-Derr JK, Hendricks BL, Patil YJ. Improving access and timeliness of care for veterans with head and neck squamous cell carcinoma: A multidisciplinary team's approach. Laryngoscope. 2016; 126(3):627-31.	The study compares two groups before and after multidisciplinary care intervention on the improvement of time-to-treatment in head and neck cancers.
94.	Patni N, Hota A, Patni A, Misra P. Cancer during Corona Pandemic: Plight of cancer patients when two evils join hands. Curr Probl Cancer. 2021; 45(3):100671.	The study is about different types of cancer.
95.	Peacock ZS, Pogrel MA, Schmidt BL. Exploring the reasons for delay in treatment of oral cancer. J Am Dent Assoc. 2008; 139(10):1346-52.	The study describes time intervals from diagnosis to treatment. It does not report the socioeconomic factors of the sample.
96.	Pepin A, Goyal S, Thakkar P, Siegel R, Joshi A, Goodman J, Ojong-Ntui M, Rao YJ. Use of Distress Thermometer to Predict Utilization of Emergency Room Services and Treatment Delays in Head and Neck Cancer Patients Undergoing Radiation Therapy. Int J Rad Oncol Biol Phys. 2020; 108(3):E221.	Abstract.
97.	Perlow H, Ramey S, Jaffe A, Silver B, Kwon D, Chinae F, Samuels S, Yechieli R. Examining head and neck cancer treatment delay in an ethnically diverse population: A look at the impact of hispanic ethnicity,	Abstract.

	spanish language preference, and treatment setting. J Radiat Oncol. 2017; 6(3):225-245.	
98.	Perlow HK, Ramey SJ, Silver B, Kwon D, Chinea FM, Samuels SE, Samuels MA, Elsayyad N, Yechieli R. Assessment of Oropharyngeal and Laryngeal Cancer Treatment Delay in a Private and Safety Net Hospital System. Otolaryngol Head Neck Surg. 2018; 159(3):484-493.	The study is not about squamous cell carcinoma.
99.	Perni S, Busse PM, Chan AW, Connolly RJ, Shih H. A. Time to Insurance Approval and Treatment for Proton Beam Therapy for Head and Neck Cancers. Int J Rad Oncol Biol Phys. 2020; 106(5):1208–1209.	Abstract.
100.	Peters ES, Brashear MM, Ferguson TF. Treatment and survival after head and neck cancer diagnosis by race in Louisiana's public hospital system. <i>Cancer Epidemiol Biomarkers Prev</i> 1. 2015; 24 (10_Supplement): A93.	Abstract.
101.	Pham A, Lai P, Phuong C, Batth S, Chan C, Schechter N, Trakul N, Garsa AA, Jennelle R. Definitive Radiation Treatment Compliance and Outcomes at a Safety Net Hospital. Int J Rad Oncol Biol Phys. 2019; 105(1):E449.	Abstract.
102.	Polesel J, Furlan C, Birri S, Giacomarra V, Vaccher E, Grando G, Gobitti C, Navarria F, Schioppa O, Minatel E, Bidoli E, Barzan L, Franchin G. The impact of time to treatment initiation on survival from head and neck cancer in north-eastern Italy. Oral Oncol. 2017; 67:175-182.	Head and neck patient delay without separating oral cancer in the analysis.
103.	Raman A, Sen N, Ritz E, Fidler MJ, Revenaugh P, Stenson K, Al-Khudari S. Heterogeneity in the clinical presentation, diagnosis, and treatment initiation of p16-positive oropharyngeal cancer. Am J Otolaryngol. 2019; 40(5):626-630.	The study is not about time-to-treatment but only about socioeconomic factors.
104.	Raman S, Shafie AA, Abraham MT, Kiong SC, Maling TH, Rajendran S, Cheong SC. Time-to-Treatment of Oral Cancer and Potentially Malignant Oral Disorders: Findings in Malaysian Public Healthcare. Dent J (Basel). 2022 Oct 24;10(11):199.	The study is about time intervals from diagnosis to treatment. It does not report socioeconomic factors of the sample.
105.	Richardson PA, Kansara S, Chen GG, Sabichi A, Sikora AG, Parke RB, Donovan DT, Chiao E,	The study is about laryngeal and

	Sandulache VC. Treatment Patterns in Veterans with Laryngeal and Oropharyngeal Cancer and Impact on Survival. <i>Laryngoscope Investig Otolaryngol</i> . 2018; 3(4):275-282.	oropharyngeal cancers. It does not separate oral cancer in the analysis.
106.	Rick T, Habtamu B, Tigeneh W, Abreha A, van Norden Y, Grover S, Assefa M, Incrocci L. Patterns of Care of Cancers and Radiotherapy in Ethiopia. <i>J Glob Oncol</i> . 2019; 5:1-8.	The study is about overall types of cancer, including head and neck cancer.
107.	Rosskamp M, Verbeeck J, Sass V, Gadeyne S, Verdoodt F, De Schutter H. Social Inequalities in Cancer Survival in Belgium: A Population-Based Cohort Study. <i>Cancer Epidemiol Biomarkers Prev</i> . 2021; 30(1):45-52.	The study is about overall types of cancer, including head and neck cancer.
108.	Rotsides JM, Oliver JR, Moses LE, Tam M, Li Z, Schreiber D, Jacobson AS, Hu KS, Givi B. Socioeconomic and Racial Disparities and Survival of Human Papillomavirus-Associated Oropharyngeal Squamous Cell Carcinoma. <i>Otolaryngol Head Neck Surg</i> . 2021; 164(1):131-138.	The study is not about time-to-treatment but only about socioeconomic factors.
109.	Rygalski CJ, Zhao S, Eskander A, Zhan KY, Mroz EA, Brock G, Silverman DA, Blakaj D, Bonomi MR, Carrau RL, Old MO, Rocco JW, Seim NB, Puram SV, Kang SY. Time to Surgery and Survival in Head and Neck Cancer. <i>Ann Surg Oncol</i> . 2021; 28(2):877-885.	Head and neck patient delay without separating oral cancer in the analysis.
110.	Sargeran K. Treatment delay among oral cancer patients in Tehran, Iran. <i>J Craniomaxillofac Res</i> . 2015; 1(3-4):37-41.	The study is about the time intervals from diagnosis to treatment. It does not report socioeconomic factors of the sample.
111.	Sargeran K, Murtomaa H, Safavi SMR. The role of socioeconomic factors and dental service utilization in treatment delay among oral cancer patients in Tehran, Iran. <i>Oral Oncology</i> . 2013; 49:S107.	Abstract.
112.	Sharp L, Lewin F, Hellborg H, Lundgren J, Hemmingsson E, Rutqvist LE. When does my treatment start?—The continuum of care for patients with head and neck cancer. <i>Radiother Oncol</i> . 2002; 63(3):293-7.	Professional delay (diagnosis delay).

113.	Schoonbeek RC, Bult FFS, Plaat BEC, Witjes MJH, van der Hoorn A, van Dijk BAC, Halmos GB. Incidental findings during the diagnostic work-up in the head and neck cancer pathway: Effects on treatment delay and survival. <i>Oral Oncol.</i> 2021; 118:105350.	Head and neck patient delay without separating oral cancer in the analysis.
114.	Schoonbeek RC, de Vries J, Bras L, Sidorenkov G, Plaat BEC, Witjes MJH, van der Laan BFAM, van den Hoek JGM, van Dijk BAC, Langendijk JA, Halmos GB. The effect of treatment delay on quality of life and overall survival in head and neck cancer patients. <i>Eur J Cancer Care (Engl).</i> 2022; 31(4):e13589.	Head and neck patient delay without separating oral cancer in the analysis.
115.	Schoonbeek RC, Festen S, Rashid R, van Dijk BAC, Halmos GB, van der Velden LA. Impact of Delay on Hospitalization in Older Patients With Head and Neck Cancer: A Multicenter Study. <i>Otolaryngol Head Neck Surg.</i> 2022; 167(4):678-687.	Head and neck patient delay without separating oral cancer in the analysis.
116.	Schoonbeek RC, de Jel DVC, van Dijk BAC, Willems SM, Bloemena E, Hoebers FJP, van Meerten E, Verbist BM, Smeele LE, Halmos GB, Merkx MAW, Siesling S, De Bree R, Takes RP; Dutch Head, Neck Society, the COVID, Cancer-NL consortium. Fewer head and neck cancer diagnoses and faster treatment initiation during COVID-19 in 2020: A nationwide population-based analysis. <i>Radiother Oncol.</i> 2022; 167:42-48.	Head and neck patient delay without separating oral cancer in the analysis.
117.	Schutte HW, van den Broek GB, Steens SCA, Hermens RPMG, Honings J, Marres HAM, Merkx MAW, Weijs WLJ, Arens AIJ, van Engen-van Grunsven ACH, van Herpen CML, Kaanders JHAM, van den Hoogen FJA, Takes RP. Impact of optimizing diagnostic workup and reducing the time to treatment in head and neck cancer. <i>Cancer.</i> 2020; 126(17):3982-3990.	Head and neck patient delay without separating oral cancer in the analysis.
118.	Sethi HK, Weinsheim T, Brennan M, Walker E, Fundakowski CE. Optimizing head and neck cancer treatment in the community setting. <i>Head Neck Surg.</i> 2021; 165(1).	Abstract.
119.	Sharma A, Madan R, Bharat B, Behera M, Mohanti BK, Rath GK. Multi-modality cancer care- what is planned & what is delivered. <i>Radiot Oncol.</i> 2012; 103: S375.	Abstract.
120.	Sharma S, Bekelman JE, Lin A, Roman B, Mitra N, Swisher-McClure SD. Risk Factors for Prolonged Diagnosis to Treatment Interval (DTI) Among Patients With Head and Neck Squamous Cell Carcinoma	Abstract.

	(HNSCC). <i>Int J Rad Oncol Biol Phys.</i> 2014; 90(1):S558.	
121.	Shin JY, Yoon JK, Shin AK, Diaz AZ. The influence of insurance status on treatment and outcomes in oral cavity cancer: an analysis on 46,373 patients. <i>Int J Oral Maxillofac Surg.</i> 2018; 47(10):1250-1257.	The study is not about time-to-treatment but only about socioeconomic factors.
122.	Simons PA, Ramaekers B, Hoebbers F, Kross KW, Marneffe W, Pijls-Johannesma M, Vandijck D. Cost-Effectiveness of Reduced Waiting Time for Head and Neck Cancer Patients due to a Lean Process Redesign. <i>Value Health.</i> 2015; 18(5):587-96.	Head and neck patient delay without separating oral cancer in the analysis.
123.	Sineshaw HM, Ellis MA, Yabroff KR, Han X, Jemal A, Day TA, Graboyes EM. Association of Medicaid Expansion Under the Affordable Care Act With Stage at Diagnosis and Time to Treatment Initiation for Patients With Head and Neck Squamous Cell Carcinoma. <i>JAMA Otolaryngol Head Neck Surg.</i> 2020; 146(3):247-255.	Head and neck patient delay without separating oral cancer in the analysis.
124.	Souza Cruz AC, Franzolin SOB, Pereira AAC, Hanneman JAC, Beijo LA, Cruz JRS. Oral squamous cell carcinoma: survival, recurrence and death. <i>Acta Scientiarum.</i> 2014; 36(2): 273-279.	The study compares time to treatment with death from oral cancer.
125.	Subramanian S, Chen A. Treatment patterns and survival among low-income medicaid patients with head and neck cancer. <i>JAMA Otolaryngol Head Neck Surg.</i> 2013;139(5):489-95.	Head and neck patient delay without separating oral cancer in the analysis.
126.	Suzuki I, Cullen KJ, Mehra R, Bentzen S, Goloubeva OG. 2019. Racial disparities in outcome among head and neck cancer patients in the United States: An analysis using SEER-Medicare linked database. <i>J Clin Oncol.</i> 37(15):6051	Abstract.
127.	Sawaf T, Virgen CG, Renslo B, Farrokhian N, Yu KM, Somani SN, et al. Association of social-ecological factors with delay in time to initiation of postoperative radiation therapy: a prospective cohort study. <i>JAMA Otolaryngol Head Neck Surg.</i> 2023;149(6):477–84.	Head and neck patient delay without separating oral cancer in the analysis.
128.	Szewczyk M, Pazdrowski J, Golusiński P, Pazdrowski P, Więckowska B, Golusiński W. The impact of the COVID-19 pandemic on the management of head and	Head and neck cancer diagnoses and treatment

	neck cancer patients at a tertiary care institution in Poland. <i>Contemp Oncol (Pozn)</i> . 2021; 25(4):264-269.	initiation during COVID-19.
129.	Tan JY, Otty ZA, Vangaveti VN, Buttner P, Varma SC, Joshi AJ, Kelly J, Collins M, Sabesan SS. A prospective comparison of times to presentation and treatment of regional and remote head and neck patients in North Queensland, Australia. <i>Intern Med J</i> . 2016; 46(8):917-24.	Head and neck patient delay without separating oral cancer in the analysis.
130.	Thaduri A, Dungala D, Panuganti A, Majumdar KS, Sehrawat A. Addressing the challenges of head and neck cancer care in India - A compelling need of the hour. <i>Oral Oncol</i> . 2022; 124:105638.	Opinion Article.
131.	Tham T, Leung E, Khaymovich J, Mitha S, Olson C, Wotman M, Teegala S, Coury J, Costantino P. Evaluation of Time to Surgery and Its Effect on Prognosis in Head and Neck Cancer. <i>Oncol Res Treat</i> 2019; 42:387-395.	Head and neck patient delay without separating oral cancer in the analysis.
132.	Thompson JA, Joy R, Lubek JE, Mehra R, Molitoris JK, Taylor RJ, Wolf JS, Witek ME, Hatten KM. Evaluating the impact of the coronavirus (COVID-19) pandemic on treatment paradigms in head and neck cancer at a tertiary care hospital. <i>Clin Cancer Res</i> . 2020; 26 (18_Supplement): PO-017.	Abstract.
133.	Tirelli G, Boscolo-Rizzo P, Pelloso L, Gardenal N, Giudici F, Marcuzzo AV, Tofanelli M. Impact of time-to-surgery on survival and quality of life in oral cancer. <i>Am J Otolaryngol</i> . 2023 Nov-Dec;44(6):103984.	The study not report the socioeconomic factors of the sample.
134.	Toustrup K, Lambertsen K, Birke-Sørensen H, Uihøi B, Sørensen L, Grau C. Reduction in waiting time for diagnosis and treatment of head and neck cancer - a fast track study. <i>Acta Oncol</i> . 2011; 50(5):636-41.	Head and neck patient delay without separating oral cancer in the analysis.
135.	Tumati V, Hoang L, Sumer BD, Truelson JM, Myers LL, Khan S, Hughes RS, Nedzi L, Sher DJ. Association between treatment delays and oncologic outcome in patients treated with surgery and radiotherapy for head and neck cancer. <i>Head Neck</i> . 2019; 41(2):315-321.	Head and neck patient delay without separating oral cancer in the analysis.
136.	Vaddepally RK, Damarla V, Singal B, Winn J, Winegarden JD, Narayan S, Akervall JA. Impact of single day multidisciplinary clinics on the lead time from diagnosis to initiation of treatment in head and neck cancers. <i>J Clin Oncol</i> . 2015; 33:15: e17523.	Abstract.

137.	van Harten MC, De Haan RR, Hoebbers FJP, Van Dijk BAC, Aaronson N, Van Den Brekel MWM. Treatment waiting times for head and neck cancer in the Netherlands: Their relation to survival and stress. 5th World Congress of the International Academy of Oral Oncology (IAOO). Head Neck. 2015; 37 (Suppl 1):E1-E227.	Abstract.
138.	van Harten MC, Hoebbers FJ, Kross KW, van Werkhoven ED, van den Brekel MW, van Dijk BA. Determinants of treatment waiting times for head and neck cancer in the Netherlands and their relation to survival. Oral Oncol. 2015; 51(3):272-8.	Head and neck patient delay without separating oral cancer in the analysis.
139.	van Harten MC, de Ridder M, Hamming-Vrieze O, Smeele LE, Balm AJ, van den Brekel MW. The association of treatment delay and prognosis in head and neck squamous cell carcinoma (HNSCC) patients in a Dutch comprehensive cancer center. Oral Oncol. 2014; 50(4):282-90.	Head and neck patient delay without separating oral cancer in the analysis.
140.	Venchiariutti, R.; Clark, J. R.; Palme, C. E.; Young, J. M. Patient health literacy correlates with times to diagnosis of head and neck cancer. <i>Asia Pac J Clin Oncol.</i> 2021; 17(S5): 42.	Abstract.
141.	Wadia RJ, Yao X, Deng Y, Li J, Maron S, Connery D, Gunduz-Bruce H, Rose MG. The effect of pre-existing mental health comorbidities on the stage at diagnosis and timeliness of care of solid tumor malignancies in a Veterans Affairs (VA) medical center. Cancer Med. 2015; 4(9):1365-73.	The study is about overall types of cancer, including head and neck cancer.
142.	Wang CP, Liao LJ, Chiang CJ, Hsu WL, Kang CJ, Wang CC, Chen PR, Chen TC, Huang WW, Chien CY. Patients with oral cancer do not undergo surgery as primary treatment: A population-based study in Taiwan. J Formos Med Assoc. 2020; 119(1 Pt 3):392-398.	The study describes time intervals from diagnosis to treatment. It does not report the socioeconomic factors of the sample.
143.	Webb CJ, Benton J, Tandon S, Jones TM, Roland NJ. Head and neck cancer waiting times. Clin Otolaryngol. 2007; 32(4):293-6.	Head and neck patient delay without separating oral cancer in the analysis.
144.	Waaiker A, Terhaard CHJ, Dehnad H, Hordijk G-J, van Leeuwen MS, Raaymakers CPJ, Lagendijk JJW. Waiting times for radiotherapy: consequences of	The study is about time intervals from diagnosis to

	volume increase for the TCP in oropharyngeal carcinoma. <i>Radiat Oncol.</i> 2003; 66(3), 271–276.	treatment. It does not report the socioeconomic factors of the sample.
145.	Worrall SF, Corrigan M. An audit of one surgeon's experience of oral squamous cell carcinoma using computerised malignancy database. <i>Ann R Coll Surg Engl.</i> 1995; 77(5):332-6.	The study is about time intervals from diagnosis to treatment. It does not report the socioeconomic factors of the sample.
146.	Xiao R, Ward MC, Yang K, Adelstein DJ, Koyfman SA, Prendes BL, Burkey BB. Increased pathologic upstaging with rising time to treatment initiation for head and neck cancer: A mechanism for increased mortality. <i>Cancer.</i> 2018; 124(7):1400-1414.	Head and neck patient delay without separating oral cancer in the analysis.
147.	Yarn C, Schwartz DL. Treatment Compliance and Insurance Status in Head and Neck Radiation Therapy Patients. <i>Int J Rad Oncol Biol Phys.</i> 2018; 100(5):P1341.	Abstract.
148.	Zavarez LB, Stramandinoli-Zanicotti RT, Sassi LM, Ramos GH, Schussel JL, Torres-Pereira CC. The interval since first symptoms until diagnosis of squamous cell carcinoma in the head and neck region is still a problem in southern Brazil. <i>Med Oral Patol Oral Cir Bucal.</i> 2020; 25(6):e769-e774.	Patient delay (interval from first symptoms until diagnosis).
149.	Žumer B, Pohar Perme M, Jereb S, Strojman P. Impact of delays in radiotherapy of head and neck cancer on outcome. <i>Radiat Oncol.</i> . 2020; 15(1):202.	Head and neck patient delay without separating oral cancer in the analysis.

Supplementary file 3. Descriptive table of socioeconomic variables found in the included articles, divided by the way the outcome treatment delay was presented (categorical or continuous).

Study	Definition of Treatment Delay (sample)	Sex by group	Age by group	Outcome by category	Available data (ES; 95%CI)	p-value
INSURANCE						
Categorical						
Sharma et al., 2016 [25]	Group 1: DTI < 30 days (n=3,020) Group 2: DTI ≥ 30 days (n=3,586)	Group 1: Male: 2,482 (82.2%) Female: 538 (17.8%) Group 2: Male: 2,951 (82.3%) Female: 635 (17.7%)	Group 1: <65: 2,319 (76.8%) ≥65: 701 (23.2%) Group 2: <65: 2,736 (76.3%) ≥65: 850 (23.7%)	Group 1: Commercial insurance: 1,737 (57.5%) Medicare: 720 (23.8%) Medicaid: 264 (8.7%) Government: 58 (1.9%) Uninsured: 172 (5.7%) Unknown: 69 (2.3%) Group 2: Commercial insurance: 1,772 (49.4%) Medicare: 882 (24.6%) Medicaid: 437 (12.2%) Government: 86 (2.4%) Uninsured: 323 (9.0%) Unknown: 86 (2.4%)	Commercial insurance: Ref. Medicare (OR: 1.27; 1.07 to 1.51) Medicaid (OR: 1.58; 1.32 to 1.88) Uninsured (OR: 1.90; 1.55 to 2.33) Government (OR: 1.38; 0.97 to 1.95) Unknown (OR: 1.25; 0.90 to 1.75)	Commercial insurance: Ref. ^a Medicare: p < 0.05 Medicaid: p < 0.001 Uninsured: p < 0.001 Government: p > 0.05 Unknown: p > 0.05

Morse et al. 2018 (a) [26]	Group 1: No delay (First and second quartiles for each interval of days; n=2,012) Group 2: Delay (Fourth quartile for each interval of days; n=1,032).	Group 1: Male: 1,701 (85%) Female: 311 (15%) Group 2: Male: 829 (80%) Female: 203 (20%)	Group 1: ≤60 years: 1,253 (62%) >60 years: 759 (38%) Group 2: ≤60 years: 634 (61%) >60 years: 398 (39%)	Group 1: Not insured: 115 (6%) Private insurance: 1,187 (59%) Medicaid: 156 (8%) Medicare: 527 (26%) Insurance unknown: 27(1%) Group 2: Not insured: 120 (12%) Private insurance: 456 (44%) Medicaid: 138 (13%) Medicare: 304 (29%) Unknown: 14 (1%)	Private insurance: Ref. Not insured (OR: 2.71; 2.00 to 3.68) Medicaid (OR: 1.97; 1.49 to 2.60) Medicare (OR: 1.39; 1.11 to 1.73) Unknown (OR: 1.30; 0.65 to 2.59)	Private insurance: Ref.^a Not insured: p< 0.001 Medicaid: p< 0.001 Medicare: p= 0.004 Unknown: p=0.458
Continuous						
Fujiwara et al., 2017 [12]	The fourth quartile of each treatment interval was used as an indicator of delayed treatment. Median= 30 days.	NR**	NR**	Not insured: 237 (4.9%) Private insurance: 2,114 (43.4%) Medicaid: 360 (7.4%) Medicare: 2,000 (41.1%) Other/unknown: 157 (3.2%)	Other/unknown: Ref. Not insurance (OR: 2.24; 1.33 to 3.77) Private Insurance (OR: 1.21; 0.79 to 1.85) Medicaid (OR: 2.52; 1.55 to 4.08) Medicare (OR: 1.27; 0.82 to 1.95)	Other/unknown: Ref.^a Not insurance: p=0.002 Private Insurance: p=0.39 Medicaid: p<0.001 Medicare: p=0.28

Sharma et al., 2016 [25]	Group 1: DTI < 30 days (n=3,020) Group 2: DTI ≥ 30 days (n=3,586)	Group 1: Male: 2,482 (82.2%) Female: 538 (17.8%) Group 2: Male: 2,951 (82.3%) Female: 635 (17.7%)	Group 1: <65: 2,319 (76.8%) ≥65: 701 (23.2%) Group 2: <65: 2,736 (76.3%) ≥65: 850 (23.7%)	Group 1: Academic: 1,111 (36.8%) Community: 1,909 (63.2%) Group 2: Academic: 1,632 (45.5%) Community: 1,954 (54.5%)	Community: Ref. Academic (OR: 1.26; 1.13 to 1.42)	Community: Ref. ^a Academic= p<0.001
Morse et al., 2018 (a) [26]	Group 1: No delay (First and second quartiles for each interval of days; n=2,012) Group 2: Delay (Fourth quartile for each interval of days; n=1,032).	Group 1: Male: 1,701 (85%) Female: 311 (15%) Group 2: Male: 829 (80%) Female: 203 (20%)	Group 1: ≤60 years: 1,253 (62%) >60 years: 759 (38%) Group 2: ≤60 years: 634 (61%) >60 years: 398 (39%)	Group 1: Community cancer program: 159 (8%) Comprehensive community cancer program: 751 (37%) Academic/research program: 833 (41%) Integrated network cancer program: 269 (13%) Group 2: Community cancer program: 78 (8%) Comprehensive community cancer program: 297 (29%)	Community cancer program: Ref. Academic/research program (OR: 1.52; 1.03 to 2.26) Comprehensive community cancer program (OR: 0.98; 0.68 to 1.42) Integrated network cancer program (OR: 1.33; 0.85 to 2.08)	Community cancer program: Ref. ^a Academic/research program: p=0.037 Comprehensive community cancer program: p=0.933 Integrated network cancer program: p=0.213

				Academic/research program: 525 (51%) Integrated network cancer program: 132 (13%)		
Continuous						
Fujiwara et al., 2017 [12]	The fourth quartile of each treatment interval was used as an indicator of delayed treatment. Median= 30 days.	NR**	NR**	Community cancer program: 269 (5.5%) Comprehensive community cancer program: 1,819 (37.4%) Academic/research program: 2,718 (55.8) Other: 62 (1.3%)	Community cancer program: Ref. * Comprehensive community cancer program (OR: 1.16; 0.79 to 1.70) Academic/research program (OR: 2.17; 1.49 to 3.15) Other (OR: 1.71; 0.82 to 3.58)	Community cancer program: Ref. ^a Comprehensive community cancer program: p=0.44 Academic/research program: p<0.001 Other: p=0.15
Morse et al., 2018 (b) [27]	Patients were classified as delayed (fourth quartile) vs not delayed (first and second quartiles) for each interval of time to treatment. Median= 27 days.	NR**	NR**	Community cancer program: 252 (7%) Comprehensive community cancer program: 1,101 (30%) Academic/research program: 2,006 (54%) Integrated network cancer program: 349 (9%)	Community cancer program: Ref. Comprehensive community cancer program (OR: 1.24; 0.65 to 2.35) Academic/research program (OR: 1.79; 0.92 to 3.51) Integrated network cancer program (OR: 1.38; 0.65 to 2.93)	Community cancer program: Ref. ^a Comprehensive community cancer program: p= 0.515 Academic/research program: p=0.088 Integrated network cancer program: p= 0.408
Goel et al., 2019 [13]	Time to treatment was presented as	NR**	NR**	Academic: 2,015 (56.8%)	Academic: Ref.	Academic: Ref. ^a

	a continuous variable (number of days). Median= 26 days			Comprehensive community: 965 (27.2%) Community: 177 (5.0%) Other: 393 (11.1%)	Comprehensive community (Coefficient: -4.95; -6.65 to -3.25) Community (Coefficient: -5.28; -8.57 to -1.99) Other (Coefficient: -1.15; -3.69 to 1.38)	Comprehensive community: p<0.001 Community: p=0.002 Other: p=0.37
HOSPITAL SERVICES VOLUME						
Categorical						
Sharma et al., 2016 [25]	Group 1: DTI< 30 days (n=3,020) Group 2: DTI >= 30 days (n=3,586)	Group 1: Male: 2,482 (82.2%) Female: 538 (17.8%) Group 2: Male: 2,951 (82.3%) Female: 635 (17.7%)	Group 1: <65: 2,319 (76.8%) ≥65: 701 (23.2%) Group 2: <65: 2,736 (76.3%) ≥65: 850 (23.7%)	Group 1: Low case-volume: 2,365 (78.3%) High case-volume: 655 (21.7%) Group 2: Low case-volume: 2,539 (70.8%) High case-volume: 1,047 (29.2%)	Low case-volume: Ref. High case-volume (OR: 1.38; 1.21 to 1.58)	Low case-volume: Ref. ^a High case-volume: p<0.001
Morse et al., 2018 (a) [26]	Group 1: No delay (First and second quartiles for each interval of days; n=2,012) Group 2: Delay	Group 1: Male: 1,701 (85%) Female: 311 (15%) Group 2:	Group 1: ≤60 years: 1,253 (62%) >60 years: 759 (38%) Group 2:	Group 1: Low: 345 (17%) Medium: 1,123 (56%) High: 544 (27%) Group 2: Low: 167 (16%) Medium: 529 (51%)	Low: Ref. Medium (OR: 0.81; 0.62 to 1.07) High (OR: 0.93; 0.67 to 1.29)	Low: Ref. ^a Medium: p=0.139 High: p=0.654

	(Fourth quartile for each interval of days; n=1,032).	Male: 829 (80%) Female: 203 (20%)	≤60 years: 634 (61%) >60 years: 398 (39%)	High: 336 (33%)		
Tsai et al., 2017 [11]	Group 1: ≤30 days (n = 18,193) Group 2: 31 to 120 days (n = 2,498) Group 3: >120 days (n = 572)	Group 1: Male: 16,704 (85.6%) Female: 1,489 (84.7%) Group 2: Male: 2,296 (11.8%) Female: 202 (11.5%) Group 3: Male: 505 (2.6%) Female: 67 (3.8%)	Group 1: ≤44: 4,304 (86.1%) 45-54: 6,337 (85.9%) 55-64: 4,296 (86.1%) ≥65: 3,257 (83.6%) Group 2: ≤44: 567 (11.3%) 45-54: 842 (11.4%) 55-64: 554 (11.1%) ≥65: 535 (13.7%) Group 3: ≤44: 131 (2.6%) 45-54: 197 (2.7%) 55-64: 138 (2.8%)	Group 1: Low: 4,665 (85.2%) Middle: 8,901 (85.2%) High: 4,627 (86.7%) Group 2: Low: 603 (11.0%) Middle: 1,286 (12.3%) High: 609 (11.4%) Group 3: Low: 206 (3.8%) Middle: 263 (2.5%) High: 103 (1.9%)	NR**	p<0.001 χ² test

>=65: 106
(2.7%)

Continuous

Morse et al. 2018 (b) [27]	Patients were classified as delayed (fourth quartile) vs not delayed (first and second quartiles) for each interval of time to treatment.	NR**	NR**	Low: 560 (15%) Medium: 1,832 (49%) High: 1,316 (35%)	Low: Ref. Medium (OR: 1.09; 0.68 to 1.76) High (OR: 1.09; 0.65 to 1.83)	Low: Ref. ^a Medium: p=0.714 High: p=0.753
	Median= 27 days.					

HOSPITAL LEVEL

Categorical

Tsai et al., 2017 [11]	Group 1: <=30 days (n = 18,193)	Group 1: Male: 16,704 (85.6%) Female: 1,489 (84.7%)	Group 1: <=44: 4,304 (86.1%) 45-54: 6,337 (85.9%) 55-64: 4,296 (86.1%) >=65: 3,257 (83.6%)	Group 1: Medical centers: 14,037 (85.9%) Regional hospitals: 4,065 (84.4%) Others: 91 (81.3%)	NR**	p<0.001 χ ² test
	Group 2: 31 to 120 days (n = 2,498)	Group 2: Male: 2,296 (11.8%) Female: 202 (11.5%)	Group 2: <=44: 567 (11.3%)	Group 2: Medical centers: 1,896 (11.6%) Regional hospitals: 589 (12.2%) Others: 13 (11.6%)		
	Group 3: >120 days (n = 572)	Group 3:				

		Male: 505 (2.6%) Female: 67 (3.8%)	45-54: 842 (11.4%) 55-64: 554 (11.1%) ≥65: 535 (13.7%)	Group 3: Medical centers: 403 (2.5%) Regional hospitals: 161 (3.4%) Others: 8 (7.1%)		
			Group 3: ≤44: 131 (2.6%) 45-54: 197 (2.7%) 55-64: 138 (2.8%) ≥65: 106 (2.7%)			
Su et al., 2021 [29]	Group 1: ≤3 weeks (n= 3,267) Group 2: >3 to 6 weeks (n= 1,700) Group 3: >6 weeks or more (n= 776)	Group 1: Male: 3175 (57.0%) Female: 92 (54.1%) Group 2: Male: 1661 (29.8%) Female: 39 (22.9%) Group 3: Male: 737 (13.2%)	Group 1: <30: 10 (58.8%) 30-59: 2380 (58.0%) ≥60: 877 (54.0%) Group 2: <30: 6 (35.3%) 30-59: 1197 (29.2%) ≥60: 497 (30.6%) Group 3:	Group 1: Medical center: 2380 (56.4%) Local/regional: 877 (58.3%) Unknown: 10 (50.0%) Group 2: Medical center: 1288 (30.5%) Local/regional: 405 (26.9%) Unknown: 7 (35.0%) Group 3:	NR**	p=0.02 χ ² test

		Female: 39 (22.9%)	<30: 1 (5.9%) 30-59: 524 (12.8%) >=60: 251 (15.4%)	Medical center: 551 (13.1%) Local/regional: 222 (14.8%) Unknown: 3 (15.0%)		
HOSPITAL OWNERSHIP						
Categorical						
Tsai et al., 2017 [11]	Group 1: <=30 days (n = 18,193)	Group 1: Male: 16,704 (85.6%) Female: 1,489 (84.7%)	Group 1: <=44: 4,304 (86.1%) 45-54: 6,337 (85.9%) 55-64: 4,296 (86.1%) >=65: 3,257 (83.6%)	Group 1: Public: 4,877 (82.8%) Private: 13,316 (86.6%)	NR**	p<0.001
	Group 2: 31 to 120 days (n = 2,498)	Group 2: Male: 2,296 (11.8%) Female: 202 (11.5%)	Group 2: <=44: 567 (11.3%) 45-54: 842 (11.4%) 55-64: 554 (11.1%) >=65: 535 (13.7%)	Group 2: Public: 850 (14.4%) Private: 1,648 (10.7%)		χ^2 test
	Group 3: >120 days (n = 572)	Group 3: Male: 505 (2.6%) Female: 67 (3.8%)	Group 3: <=44: 131 (2.6%) 45-54: 197 (2.7%)	Group 3: Public: 164 (2.8%) Private: 408 (2.7%)		

55-64:138
(2.8%)
≥65: 106
(2.7%)

CARE TRANSITION/LOCATION OF INITIAL DIAGNOSIS

Categorical

Morse et al., 2018 (a) [26]	Group 1: No delay (First and second quartiles for each interval of days; n=2,012) Group 2: Delay (Fourth quartile for each interval of days; n=1,032).	Group 1: Male: 1,701 (85%) Female: 311 (15%) Group 2: Male: 829 (80%) Female: 203 (20%)	Group 1: ≤60 years:1,253 (62%) >60 years: 759 (38%) Group 2: ≤60 years: 634 (61%) >60 years: 398 (39%)	Group 1: No care transition: 988 (49%) Care transition: 1,024 (51%) Group 2: No care transition: 386 (37%) Care transition: 646 (63%)	Care transition: Ref. No care transition (OR: 1.73; 1.46 to 2.04)	Care transition: Ref. ^a No care transition: p< 0.001
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Continuous

Fujiwara et al., 2017 [12]	The fourth quartile of each treatment interval was used as an indicator of delayed treatment. Median= 30 days	NR**	NR**	At reporting facility: 1,926 (39.6%) Elsewhere: 2,942 (60.4%)	At reporting facility: Ref. Outside facility (OR: 2.52; 2.15 to 2.95)	At reporting facility. Ref. ^a Outside facility: p<0.001
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Morse et al., 2018 (b) [27]	Patients were classified as delayed (fourth quartile) vs not delayed (first and second quartiles) for each interval of time to treatment.	NR**	NR**	No care transition: 1,536 (41%) Care transition: 2,172 (59%)	No care transition: Ref. Care transition (OR: 2.70; 2.1 to 3.49)	No care transition: Ref. ^a Care transition: p<0.001
	Median= 27 days.					

URBANIZATION LEVEL HOSPITAL						
Categorical						
Tsai et al., 2017 [11]	Group 1: <=30 days (n = 18,193) Group 2: 31 to 120 days (n = 2,498) Group 3: >120 days (n = 572)	Group 1: Male: 16,704 (85.6%) Female: 1,489 (84.7%) Group 2: Male: 2,296 (11.8%) Female: 202 (11.5%) Group 3: Male: 505 (2.6%) Female: 67 (3.8%)	Group 1: <=44: 4,304 (86.1%) 45-54: 6,337 (85.9%) 55-64: 4,296 (86.1%) >=65: 3,257 (83.6%) Group 2: <=44: 567 (11.3%) 45-54: 842 (11.4%) 55-64: 554 (11.1%)	Group 1: Level 1: 4,203 (85.5%) Levels 2 & 3: 8,576 (85.5%) Levels 4 & 5: 3,399 (85.6%) Levels 6 & 7: 2,015 (86.1%) Group 2: Level 1: 587 (11.9%) Levels 2 & 3: 1,178 (11.7%) Levels 4 & 5: 469 (11.8%) Levels 6 & 7: 264 (11.3%)	NR**	p=0.951 χ ² test

>=65: 535 (13.7%)	Group 3:
<=44: 131 (2.6%)	Level 1: 128 (2.6%)
45-54: 197 (2.7%)	Levels 2 & 3: 281 (2.8%)
55-64: 138 (2.8%)	Levels 4 & 5: 101 (2.6%)
>=65: 106 (2.7%)	Levels 6 & 7: 62 (2.6%)

DISTANCE FROM TREATMENT CENTER

Categorical

Sharma et al., 2016 [25]	Group 1: DTI < 30 days (n=3,020)	Group 1: Male: 2,482 (82.2%) Female: 538 (17.8%)	Group 1: <65: 2,319 (76.8%) >=65: 701 (23.2%)	Group 1: <25 miles: 2,208 (73.1%) 25-100 miles: 552 (18.3%) >100 miles: 106 (3.5%) Unknown: 154 (5.1%)	<25 miles: Ref. 25-100 miles (OR: 1.00; 0.88 to 1.14) >100 miles (OR: 1.08; 0.83 to 1.41) Unknown (OR: 0.82; 0.65 to 1.04)	<25 miles: Ref. ^a 25-100 miles: p>0.05 >100 miles: p>0.05 Unknown: p>0.05
	Group 2: DTI >= 30 days (n=3,586)	Group 2: Male: 2,951 (82.3%) Female: 635 (17.7%)	Group 2: <65: 2,736 (76.3%) >=65: 850 (23.7%)	Group 2: <25 miles: 2,593 (72.3%) 25-100 miles: 689 (19.2%) >100 miles: 150 (4.2%) Unknown: 154 (4.3%)		

PLACE OF RESIDENCE

Continuous						
Venchiarutti et al., 2020 [30]	NR**	NR**	NR**	Oropharynx: Regional/remote: 47 (42%) Metropolitan: 65 (58%) Oral cavity: Regional/remote: 37 (33%) Metropolitan: 75 (66%)	Oropharynx: Regional/ remote: 47 (IQR 43) median days Metropolitan: 36 (IQR 14) median days Oral cavity: Regional/ remote: 33 (IQR 21) median days Metropolitan: 29 (IQR 21) median days	Oropharynx: p=0.03 Oral cavity: p=0.19 (Mann–Whitney U test)
Zhang et al., 2015 [31]	NR**	NR**	NR**	Rural: 127 (23%) Intermediate: 140 (25,3%) Urban: 287 (51,7%)	Rural: 53.4 (Range 4–159) mean days Intermediate: 53.3 (Range 4–152) mean days Urban: 49.3 (Range 4–155) mean days.	p= 0.791 (ANOVA test).
INCOME						
Categorical						
Tsai et al., 2017 [11]	Group 1: <=30 days (n = 18,193) Group 2: 31 to 120 days (n = 2,498)	Group 1: Male: 16,704 (85.6%) Female: 1,489 (84.7%) Group 2: Male: 2,296 (11.8%)	Group 1: <=44: 4,304 (86.1%) 45-54: 6,337 (85.9%) 55-64: 4,296 (86.1%) >=65: 3,257 (83.6%)	Group 1: Low-income: 383 (85.9%) <= 17,280: 882 (85.6%) 17,281 to 22,800: 9,589 (85.0%) > = 22,801: 7,339 (86.3%)	NR**	p= 0.161 x2 test

Rogers et al., 2007 [28]	The time between diagnosis and treatment was presented as a continuous variable (median days). Median= 21 days (IQR 12-30).	NR**	NR**	IMD 2000 Deprivation tertile groups Median rank 149= 175 (31,3%) Median rank 1308= 175 (31,3%) Median rank 4642= 177 (37,4%)	Median days: Median rank 149= 20 days (IQR 12–29) Median rank 1308= 21 days (IQR 13–30) Median rank 4642= 21 days (IQR 12–32)	p=0.50 (Kruskal–Wallis test).
EDUCATION						
Continuous						
Goel et al., 2019 [13]	Time to treatment was presented as a continuous variable (number of days). Median DTI= 26 days (IQR, 14-39 days).	NR**	NR**	≥21%: 377 (10.6%) 13%-20.9%: 821 (23.1%) 7%-12.9%: 1,257 (35.4%) <7%: 1089 (30.7%)	≥21%: Ref. 13%-20.9% (Coefficient: –2.01; –4.77 to 0.75) 7%-12.9% (Coefficient: –3.12; –6.04 to –0.21) <7% (Coefficient: –6.42; –9.61 to –3.22)	≥21%: Ref. ^a 13%-20.9%: p=0.15 7%-12.9%: p=0.04 <7%: p<0.001
RACE						
Categorical						
Sharma et al., 2016 [25]	Group 1: DTI< 30 days (n=3,020) Group 2: DTI ≥ 30 days	Group 1: Male: 2,482 (82.2%) Female: 538 (17.8%)	Group 1: <65: 2,319 (76.8%) ≥65: 701 (23.2%)	Group1: Non-Hispanic White: 2,594 (85.9%) Non-Hispanic Black: 284 (9.4%)	Non-Hispanic White: Ref Non-Hispanic Black (OR: 1.24; 1.04 to 1.46)	Non-Hispanic White: Ref. ^a Non-Hispanic Black: p< 0.05 Hispanic: p<0.001

	(n=3,586)					
		Group 2: Male: 2,951 (82.3%) Female: 635 (17.7%)	Group 2: <65: 2,736 (76.3%) >=65: 850 (23.7%)	Hispanic: 70 (2.4%) Other/unknown: 70 (2.4%) Group 2: Non-Hispanic White: 2,906 (81.0%) Non-Hispanic Black: 449 (12.5%) Hispanic: 155 (4.3%) Other/unknown: 76 (2.1%)	Hispanic (OR: 1.74; 1.29 to 2.34) Other/unknown (OR: 0.84; 0.60 to 1.17)	Other/unknown: p>0.05
Morse et al. 2018 (a) [26]	Group 1: No delay (First and second quartiles for each interval of days; n=2,012) Group 2: Delay (Fourth quartile for each interval of days; n=1,032)	Group 1: Male: 1,701 (85%) Female: 311 (15%) Group 2: Male: 829 (80%) Female: 203 (20%)	Group 1: ≤60 years: 1,253 (62%) >60 years: 759 (38%) Group 2: ≤60 years: 634 (61%) >60 years: 398 (39%)	Group 1: Non-White: 212 (11%) White: 1,770 (88%) Unknown: 30 (1%) Group 2: Non-White: 179 (17%) White: 836 (81%) Unknown: 17 (2%)	Non-White: Ref White (OR: 0.69; 0.54 to 0.88) Unknown (OR: 0.76; 0.39 to 1.50)	Non-White: Ref. ^a White: p= 0.003 Unknown: p=0.428
Continuous						
Fujiwara et al., 2017 [12]	The fourth quartile of each treatment interval was used as an indicator of	NR**	NR**	White: 4,304 (88.4%) Non-White: 564 (11.6%)	Non-White: Ref. White: (OR: 0.96; 0.77 to 1.21)	Non-White: Ref. ^a White: p=0.75

	delayed treatment.					
	Median= 30 days.					
Morse et al., 2018 (b) [27]	Patients were classified as delayed (fourth quartile) vs not delayed (first and second quartiles) for each interval of time to treatment.	NR**	NR**	Nonwhite: 292 (8%) White: 3,356 (91%) Unknown: 60 (2%)	Non-white: Ref. White (OR: 0.88; 0.59 to 1.31) Unknown (OR: 1.27; 0.53 to 3.03)	Non-white: Ref. ^a White: p= 0.524 Unknown: p=0.595
	Median= 27 days.					
Goel et al., 2019 [13]	Time to treatment was presented as a continuous variable (number of days).	NR**	NR**	White: 3,342 (94.1%) Black: 134 (3.8%) Other: 74 (2.1%)	White: Ref. Black (Coefficient: 1.44; -2.27 to 5.16) Other (Coefficient: -1.21; -6.03 to 3.61)	White: Ref. ^a Black: p=0.45 Other: p=0.62
	Median= 26 days					
MARITAL STATUS						
Continuous						
Rogers et al.,	The time between	NR**	NR	Married= 265 (53,3%) Single= 76 (15,3%)	Median days:	p=0.62

2007 [28]	diagnosis and treatment was presented as a continuous variable (median days). Median= 21 days (IQR 12-30).	Divorced= 66 (13,3%) Widowed= 90 (18,1%)	Married: 20 days (IQR 12-29) Single: 21 days (IQR 14-34) Divorced: 22 days (IQR 13-35) Widowed= 21 (IQR 13-31)	(Kruskal–Wallis test).
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^aRef.: Reference

Study	1	2	3	4	5	6	7	8	9	10	11
Sharma et al., 2016 [25]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Not applicable	Not applicable	Yes
Morse et al., 2018(a) [26]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	Yes
Su et al., 2021 [29]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Not applicable	Not applicable	Yes
Tsai et al., 2017 [11]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	Yes
Fujiwara et al., 2017 [12]	Yes	Yes	Unclear	No	No	Yes	Yes	Yes	Not applicable	Not applicable	Yes
Morse et al., 2018 (b) [27]	Yes	Yes	Unclear	No	No	Yes	Yes	Yes	Not applicable	Not applicable	Yes
Venchiarutti et al., 2020 [30]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Not applicable	Not applicable	Yes
Zhang et al., 2015 [31]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Not applicable	Not applicable	Yes
Rogers et al., 2007 [28]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes
Goel et al., 2019 [13]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	Yes

Supplementary file 4. Methodological quality using Joanna Briggs Appraisal tool for cohort studies. Low methodological quality is represented in red (no); unclear is represented in yellow; high quality is represented in green (yes). “Not applicable” (in blue) was used for articles where data loss was an exclusion criterion.

1. Were the two groups similar and recruited from the same population? 2. Were the exposures measured similarly to assign people to both exposed and unexposed groups? 3. Was the exposure measured in a valid and reliable way? 4. Were confounding factors identified? 5. Were strategies to deal with confounding factors stated? 6. Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)? 7. Were the outcomes measured in a valid and reliable way? 8. Was the follow up time reported and sufficient to be long enough for outcomes to occur? 9. Was follow up complete, and if not, were the reasons to loss to follow up described and explored? 10. Were strategies to address incomplete follow up utilized? 11. Was appropriate statistical analysis used.

ANEXO A- Artigo I publicado na revista Cadernos de Saúde Pública

Acesso: <https://doi.org/10.1590/0102-311XEN121324>

CSP CADERNOS DE SAÚDE PÚBLICA
REPORTS IN PUBLIC HEALTH

REVIEW

Socioeconomic factors impacting treatment delays in oral and oropharyngeal squamous cell carcinoma: a systematic review

Fatores socioeconômicos que influenciam atrasos no tratamento do carcinoma espinocelular de boca e orofaringe: uma revisão sistemática

Factores socioeconómicos que afectan el tratamiento tardío del carcinoma de células escamosas oral y orofaríngeo: una revisión sistemática

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Renata de Castro Martins ¹

doi: 10.1590/0102-311XEN121324

Abstract

This systematic review investigates associations between socioeconomic factors and treatment delay in adults with oral and oropharyngeal squamous cell carcinoma (OOSCC). Observational studies were searched across five databases (PubMed, Scopus, Web of Science, Embase, and Virtual Health Library) and grey literature. No restrictions were imposed about language or year of publication. Risk of bias was analyzed using the Joanna Briggs Institute tool. The primary outcome was defined as the cut-off points of treatment delays, which was addressed by the studies included. The certainty of evidence was assessed following the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach. In total, 10 retrospective cohort studies were included in the narrative synthesis. Type of insurance plan, sex, older ages, non-white patients, low education level, treatment in public or regional hospital, need for transition care, and living in regional/remote areas were factors associated with treatment delay for OOSCC. However, methodological limitations regarding the adjustment for confounders, the heterogeneity of the definition of delay (different cut-off points), socioeconomic variables, and the lack of eligible articles from different countries resulted in a very low certainty of evidence due to severe issues of bias, inconsistency, and indirectness according to the GRADE guidelines. The association between socioeconomic factors and OOSCC treatment delay is inconclusive by the available data. Given the complexity of the determinants of access to timely OOSCC treatment, further research is recommended in different countries.

Oral Cancer; Oropharyngeal Cancer; Squamous Cell Carcinoma; Treatment Delay; Socioeconomic Factors

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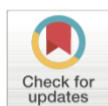
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ANEXO B- Artigo II publicado na revista *Plos One*Acesso: <https://doi.org/10.1371/journal.pone.0302370>

PLOS ONE

RESEARCH ARTICLE

Can predictive factors determine the time to treatment initiation for oral and oropharyngeal cancer? A classification and regression tree analysis

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Competing interests: The authors have declared that no competing interests exist.

Abstract

This ecological study aimed to identify the factors with the greatest power to discriminate the proportion of oral and oropharyngeal cancer (OOC) records with time to treatment initiation (TTI) within 30 days of diagnosis in Brazilian municipalities. A descriptive analysis was performed on the variables grouped into five dimensions related to patient characteristics, access to health services, support for cancer diagnosis, human resources, and socioeconomic characteristics of 3,218 Brazilian municipalities that registered at least one case of OOC in 2019. The Classification and Regression Trees (CART) technique was adopted to identify the explanatory variables with greater discriminatory power for the TTI response variable. There was a higher median percentage of records in the age group of 60 years or older. The median percentage of records with stage III and IV of the disease was 46.97%, and of records with chemotherapy, radiation, or both as the first treatment was 50%. The median percentage of people with private dental and health insurance was low. Up to 75% had no cancer diagnostic support services, and up to 50% of the municipalities had no specialist dentists. Most municipalities (49.4%) started treatment after more than 30 days. In the CART analysis, treatment with chemotherapy, radiotherapy, or both explained the highest TTI in all municipalities, and it was the most relevant for predicting TTI. The final model also included anatomical sites in the oral cavity and oropharynx and the number of computed tomography services per 100,000. There is a need to expand the availability of oncology services and human resources specialized in diagnosing and treating OOC in Brazilian municipalities for a timely TTI of OOC.

ANEXO C- Instrução aos autores da revista *Community Dentistry and Oral Epidemiology*

Author Guidelines

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The aim of *Community Dentistry and Oral Epidemiology* is to serve as a forum for scientifically based information in community dentistry, with the intention of continually expanding the knowledge base in the field. The scope is therefore broad, ranging from original studies in epidemiology, behavioural sciences related to dentistry, and health services research, through to methodological reports in program planning, implementation and evaluation. Reports dealing with people of any age group are welcome.

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It is a requirement that all authors have been credited as appropriate upon submission of the manuscript. Contributors who do not qualify as authors should instead be mentioned under Acknowledgments.

Acknowledgements: Under *acknowledgements*, please specify contributors to the article other than the authors accredited, along with all sources of financial support for the research.

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Manuscripts should be uploaded as Word (.doc or .docx) or Rich Text Format (.rtf) files (not write-protected), along with separate Figure files. For the latter, GIF, JPEG, PICT or Bitmap files are acceptable for submission, but only high-resolution TIF or EPS files are suitable for printing. Tables should be done in Word rather than in Excel. The files will be automatically converted to HTML and a PDF document on upload, and those will be used for the review process. The text file must contain the entire manuscript, including the title page, abstract, text, references, tables, and figure legends, but no embedded figures. Figure tags should be included in the file. Manuscripts should be formatted as described in the Author Guidelines below.

3.3. Suggest Two Reviewers

Community Dentistry and Oral Epidemiology attempts to keep the review process as short as possible to enable rapid publication of new scientific data. In order to facilitate this process, please suggest the names and current email addresses of two potential international reviewers whom you consider capable of reviewing your manuscript. Whether these are used is up to the Editor, but it is helpful to have the suggestions.

3.4. Suspension of Submission Mid-way in the Submission Process

You may suspend a submission at any phase before clicking the 'Submit' button and save it to submit later. The manuscript can then be located under 'Unsubmitted Manuscripts' and you can click on 'Continue Submission' to continue your submission when you choose to.

3.5. E-mail Confirmation of Submission

After submission, you will receive an email to confirm receipt of your manuscript. If you do not receive the confirmation email within 10 days, please check your email address carefully in the system. If the email address is correct, please contact your IT department. The error may be caused by some sort of spam filtering on your email server. Also, the emails should get through to you if your IT department adds our email server (uranus.scholarone.com) to their whitelist.

3.6. Review Procedures

All manuscripts (except some commentaries and conference proceedings) are submitted to an initial review by the Editor or Associate Editors. Manuscripts which are not considered relevant to oral epidemiology or the practice of community dentistry or are not of interest to the readership of *Community Dentistry and Oral Epidemiology* will be rejected without review. Manuscripts presenting innovative, hypothesis-driven research with methodologically detailed scientific findings are favoured to move forward to peer review. All manuscripts accepted for peer review will be submitted to at least 2 reviewers for peer review, and comments from the reviewers and the editor will be returned to the corresponding author.

3.7. Manuscript Status

You can access ScholarOne Manuscripts (formerly known as Manuscript Central) any time to check your 'Author Centre' for the status of your manuscript. The Journal will inform you by e-mail once a decision has been made.

3.8. Submission of Revised Manuscripts

Revised manuscripts must be uploaded within two or three months of authors being notified of a Minor or Major revision decision respectively. Locate your manuscript under 'Manuscripts with Decisions' and click on 'Submit a Revision' to submit your revised manuscript. Please remember to delete any previously-uploaded files when you upload your revised manuscript. Revised manuscripts must show changes to the text in either a coloured font or highlighted text. Do NOT use track changes for this. Prepare and submit a separate "Response to reviewers" document, in which you address EACH of the points raised by the reviewers.

3.9. Conflict of Interest

Community Dentistry & Oral Epidemiology requires that sources of institutional, private and corporate financial support for the work within the manuscript must be fully acknowledged, and any potential grant holders should be listed. Acknowledgements should be brief and should include information concerning conflict of interest and sources of funding. It should not include thanks to anonymous referees and editors.

3.10. Editorial Board Submissions

Manuscripts authored or co-authored by the Editor-in-Chief or by members of the Editorial Board are evaluated using the same criteria determined for all other submitted manuscripts. The process is handled confidentially and measures are taken to avoid real or reasonably perceived conflicts of interest.

4. MANUSCRIPT FORMAT AND STRUCTURE

Community Dentistry & Oral Epidemiology now offers Free Format submission for a simplified and streamlined submission process.

Before you submit, you will need:

- Your manuscript: this should be an editable file including text, figures, and tables, or separate files – whichever you prefer. All required sections should be contained in your manuscript, including abstract, introduction, methods, results, and conclusions. Figures and tables should have legends. Figures should be uploaded in the highest resolution possible. References may be submitted in any style or format, as long as it is consistent throughout the manuscript. Supporting information should be submitted in separate files. If the manuscript, figures or tables are difficult for you to read, they will also be difficult for the editors and reviewers, and the editorial office will send it back to you for revision. Your manuscript may also be sent back to you for revision if the quality of English language is poor.
- An ORCID ID, freely available at <https://orcid.org>. *(Why is this important? Your article, if accepted and published, will be attached to your ORCID profile. Institutions and funders are increasingly requiring authors to have ORCID IDs.)*
- The title page of the manuscript, including:
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 - funding statement
 - conflict of interest disclosure
 - ethics approval statement
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If you are invited to revise your manuscript after peer review, the journal will also request the revised manuscript to be formatted according to journal requirements as described below.

Main Text File

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Your main document file should include:

- A short informative title containing the major key words. The title should not contain abbreviations

- The full names of the authors with institutional affiliations where the work was conducted, with a footnote for the author's present address if different from where the work was conducted
- Acknowledgments
- Abstract
- Up to seven keywords
- Main body
- References
- Tables (each table complete with title and footnotes)
- Figures: Figure legends must be added beneath each individual image during upload AND as a complete list in the text

4.1. Word Limit and Page Charges

Articles should be limited to 3,700 words (including references) and 6 Tables or Figures; alternatively, 4,000 words (including references) and 5 Tables or Figures may be used. This equates to seven published pages, **and authors are strongly encouraged to stay within those limits.** The Methods and Results sections are usually where the word count can “blow out”, and authors are encouraged to consider submitting heavily detailed material for inclusion in a separate online Appendix to their article (at no cost). **Articles exceeding seven published pages are subject to a charge of USD 300 per additional page. One published page amounts approximately to 5,500 characters (including spaces) of text but does not include Figures and Tables.**

If your paper is Open Access, because you have paid an APC, Article Page Charge, then you **do not** pay for the page charges too. For more information on APCs, please [click here](#) to view our resources. If you have further questions please email the journal's editorial office, cdoejournal@wiley.com.

4.2. Format Language

All submissions must be in English; both British and American spelling conventions are acceptable. Authors for whom English is a second language must have their manuscript professionally edited by an English speaking person before submission to make sure the English is of high quality. It is preferred that the manuscript is professionally edited. A list of independent suppliers of editing services can be found at <http://wileyeditingservices.com/en/>. All services must be paid for and arranged by the author, and use of one of these services does not guarantee acceptance or preference for publication.

Font: All submissions must be 1.5 spaced using a standard 12-point font size, and preferably in the Times Roman font.

Abbreviations, Symbols and Nomenclature: Authors can consult the following source: CBE Style Manual Committee. Scientific style and format: the CBE manual for authors, editors, and publishers. 6th ed. Cambridge: Cambridge University Press, 1994

4.3. Structure

All manuscripts submitted to *Community Dentistry and Oral Epidemiology* should follow the structure guidelines below.

Title Page: the names and institutional affiliations of all authors of the manuscript should be included.

Abstract: All manuscripts submitted to *Community Dentistry and Oral Epidemiology* should use a structured abstract under the headings: Objectives – Methods – Results – Conclusions.

Main Text of Original Articles should include Introduction, Methods, Results and Discussion. Subheadings are not encouraged.

Introduction: this should be focused, outlining the historical or logical origins of the study and not summarise the findings; exhaustive literature reviews are not appropriate. It should close with an explicit statement of the specific aims of the investigation.

Methods must contain sufficient detail such that, in combination with the references cited, all studies reported can be fully reproduced. As a condition of publication, authors are required to make materials and methods used freely available to other academic researchers for their own use.

Results should not focus overly on P values – we concur with recent calls for less emphasis on statistical significance (see Amrhein et al, *Nature* 2019; 567: 305-307). In the Results section, have one paragraph of text per Table, and do not repeat Table data in that Results text; instead, draw the reader's attention to the highlights/important parts of the Table. Avoid "compared to" - use 'than' instead.

Discussion: See Docherty and Smith, *BMJ* 1999; 318: 1224-5 for how to structure a Discussion section. That structure is encouraged. The section should end with a brief conclusion and a comment on the potential clinical program or policy relevance of the findings. Statements and interpretation of the data should be appropriately supported by original references. In the Discussion and conclusion, use the term 'findings' rather than 'results'.

4.4. References

Authors are required to cite all necessary references for the research background, methods and issues discussed. Primary sources should be cited. Relevant references published in CDOE are expected to be among the cited literature. The list of references begins on a fresh page in the manuscript. All references should be numbered consecutively in order of appearance and should be as complete as possible. In text citations should cite references in consecutive order using Arabic superscript numerals. Sample references follow:

Journal article:

1. King VM, Armstrong DM, Apps R, Trott JR. Numerical aspects of pontine, lateral reticular, and inferior olivary projections to two paravermal cortical zones of the cat cerebellum. *J Comp Neurol* 1998;390:537-551.

Book:

2. Voet D, Voet JG. *Biochemistry*. New York: John Wiley & Sons; 1990. 1223 p. Please note that journal title abbreviations should conform to the practices of Chemical Abstracts.

For more information about AMA reference style - **AMA Manual of Style**

4.5. Tables, Figures and Figure Legends

Tables are part of the text and should be included, one per page, after the References. Please see our **Guide to Tables and Figures** for guidance on how to lay these out. All graphs, drawings, and photographs are considered figures and should be sequentially numbered with Arabic numerals. Each figure must be on a separate page and each must have a caption. All captions, with necessary

references, should be typed together on a separate page and numbered clearly (Fig.1, Fig. 2, etc.).

Preparation of Electronic Figures for Publication: Although low-quality images are adequate for review purposes, print publication requires high quality images to prevent the final product being blurred or fuzzy. Submit EPS (lineart) or TIFF (halftone/photographs) files only. MS PowerPoint and Word Graphics are unsuitable for printed pictures. Do not use pixel-oriented programmes. Scans (TIFF only) should have a resolution of 300 dpi (halftone) or 600 to 1200 dpi (line drawings) in relation to the reproduction size (see below). EPS files should be saved with fonts embedded (and with a TIFF preview if possible). For scanned images, the scanning resolution (at final image size) should be as follows to ensure good reproduction: line art: >600 dpi; half-tones (including gel photographs): >300 dpi; figures containing both halftone and line images: >600 dpi.

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Check your electronic artwork before submitting it: <http://authorservices.wiley.com/bauthor/eachecklist.asp>

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Figure Legends: All captions, with necessary references, should be typed together on a separate page and numbered clearly (Fig.1, Fig. 2, etc.).

Special issues: Larger papers, monographs, and conference proceedings may be published as special issues of the journal. The full cost of these extra issues must be paid by the authors. Further information can be obtained from the editor or publisher.

5. AFTER ACCEPTANCE

Upon acceptance of a manuscript for publication, the manuscript will be forwarded to the Production Editor, who is responsible for the production of the journal.

5.1. Proof Corrections

The corresponding author will receive an email alert containing a link to a web site. A working email address must therefore be provided for the corresponding author. The proof can be downloaded as a PDF (portable document format) file from this site.

Acrobat Reader will be required in order to read this file. This software can be downloaded (free of charge) from the following Web

site: www.adobe.com/products/acrobat/readstep2.html. This will enable the file to be opened, read on screen, and printed out in order for any corrections to be added. Further instructions will be sent with the proof. Hard copy proofs will be posted if no e-mail address is available; in your absence, please arrange for a colleague to access your e-mail to retrieve the proofs. Proofs must be returned within three days of receipt.

Since changes to proofs are costly, we ask that you only correct typesetting errors. Excessive changes made by the author in the proofs, excluding typesetting errors, will be charged separately. Other than in exceptional circumstances, all illustrations are retained by the publisher. Please note that the author is responsible for all

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ANEXO D- Produção acadêmica durante o doutorado

Prêmios e títulos

- 2023** Prêmio Destaque - XIII Seminário de Iniciação Científica Júnior- Câncer de boca e orofaringe no primeiro ano da pandemia da COVID-19 no Brasil, Pró-reitoria de Pesquisa- Universidade Federal de Minas Gerais (UFMG)
- 2023** Relevância acadêmica na área no XIII Seminário de Iniciação Científica Júnior da Semana do Conhecimento da UFMG de 2023-Câncer de boca e orofaringe no primeiro ano da pandemia da COVID-19 no Brasil, UFMG
- 2023** Relevância acadêmica no XIII Seminário de Iniciação Científica Júnior da Semana do Conhecimento da UFMG de 2023- Câncer de boca e orofaringe no primeiro ano da pandemia da COVID-19 no Brasil, UFMG
- 2023** 1º Lugar Prêmio Myaki Issão- Área Ciências do comportamento / Saúde Coletiva- Registros de Câncer de Glândulas Salivares Antes e no Primeiro Ano da COVID-19 no Brasil, Sociedade Brasileira de Pesquisa Odontológica- 40ª Reunião Anual 2023

Artigos completos publicados em periódicos

- 1.**  LEITE, VITÓRIA FERREIRA; MONTAGNOLI, DÉBORA ROSANA ALVES BRAGA SILVA; GODOY, YASMIM SILVA; CRUZ, ALEX JÚNIO SILVA; AGUIAR, MARIA CÁSSIA FERREIRA; ABREU, MAURO HENRIQUE NOGUEIRA GUIMARÃES; MARTINS, RENATA CASTRO. Analysis of Salivary Gland Cancer before and during the COVID-19 Pandemic in Brazil. REVISTA BRASILEIRA DE CANCEROLOGIA. v.71, p.e-044800, 2025.
- 2.**  MONTAGNOLI, DÉBORA ROSANA ALVES BRAGA SILVA; LEITE, VITÓRIA FERREIRA; GODOY, YASMIM SILVA; MARTINS-PFEIFER, CAROLINA CASTRO; MORENO-DRADA, JOHANA ALEJANDRA; AGUIAR, MARIA CÁSSIA FERREIRA; ABREU, MAURO HENRIQUE NOGUEIRA GUIMARÃES; MARTINS, RENATA DE CASTRO. Socioeconomic factors impacting treatment delays in oral and oropharyngeal squamous cell carcinoma: a systematic review. CADERNOS DE SAÚDE PÚBLICA. JCR, v.41, p.e00121324, 2025.
- 3.**  MONTAGNOLI, DÉBORA ROSANA ALVES BRAGA SILVA; LEITE, VITÓRIA FERREIRA; GODOY, YASMIM SILVA; LAFETÁ, VITÓRIA MARÇOLLA; JUNIOR, EDMILSON ANTÔNIO PEREIRA; CHAURASIA, AKHILANAND; AGUIAR, MARIA CÁSSIA FERREIRA; ABREU, MAURO HENRIQUE NOGUEIRA GUIMARÃES; MARTINS, RENATA CASTRO. Can predictive factors determine the time to treatment initiation for oral and oropharyngeal cancer? A classification and regression tree analysis. PLoS One. JCR, v.19, p.e0302370, 2024. Citações: WEB OF SCIENCE = 2 | SCOPUS 1

Trabalhos publicados em anais de eventos (resumo)

- 1.** AIRES, A. V.; MENDONÇA, M. M.; MONTAGNOLI, D. R. A. B. S.; PALMIER, A. C.; ABREU, MAURO HENRIQUE NOGUEIRA GUIMARÃES; MARTINS, RENATA CASTRO. Análise da taxa de produção odontológica brasileira na atenção primária à saúde In: 41a Reunião Anual da Sociedade Brasileira de Pesquisa Odontológica-SBPQO, 2024, Campinas. *Brazilian Oral Research. Proceedings of the 41st SBPQO Annual Meeting*. Brazilian Oral Research, 2024, v.38,
- 2.** MONTAGNOLI, DÉBORA ROSANA ALVES BRAGA SILVA; LEITE, VITÓRIA FERREIRA; GODOY, YASMIM SILVA; LAFETÁ, VITÓRIA MARÇOLLA; JUNIOR, EDMILSON ANTONIO PEREIRA; AGUIAR, MARIA CÁSSIA FERREIRA; ABREU, MAURO HENRIQUE NOGUEIRA GUIMARÃES; MARTINS, RENATA CASTRO. Análise das variáveis explicativas do tempo para o início do tratamento do câncer de boca e orofaringe nas regiões brasileiras In: 41a Reunião Anual da Sociedade Brasileira de Pesquisa Odontológica-SBPQO, 2024, Campinas. *Brazilian Oral Research. Proceedings of the 41st SBPQO Annual Meeting*. Brazilian Oral Research, 2024, v.38,
- 3.** LEITE, VITÓRIA FERREIRA; MONTAGNOLI, DÉBORA ROSANA ALVES BRAGA SILVA; GODOY, YASMIM SILVA; ABREU, MAURO HENRIQUE NOGUEIRA GUIMARÃES; MARTINS, RENATA CASTRO. CÂNCER ORAL E PAPILOMAVÍRUS HUMANO: CONHECIMENTO DOS ESTUDANTES DE ODONTOLOGIA In: 59a Reunião Anual da Associação Brasileira de Ensino Odontológico- ABENO, 2024, Belo Horizonte. *Revista da ABENO. Anais da 59ª Reunião da ABENO*. Revista da ABENO, 2024, v.24,
- 4.** GODOY, YASMIM SILVA; MONTAGNOLI, D. R. A. B. S.; LEITE, VITÓRIA FERREIRA; AGUIAR, MARIA CÁSSIA FERREIRA; ABREU, MAURO HENRIQUE NOGUEIRA GUIMARÃES; MARTINS, RENATA CASTRO. EVALUATION OF LIP CANCER RECORDS AND ORAL HEALTH SERVICES IN BRAZIL. In: 48º CONGRESSO BRASILEIRO DE ESTOMATOLOGIA E PATOLOGIA ORAL, 2024, Curitiba. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology*. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, 2024, v.137, p.E274
- 5.** LEITE, VITÓRIA FERREIRA; MONTAGNOLI, DÉBORA ROSANA ALVES BRAGA SILVA; ABREU, MAURO HENRIQUE NOGUEIRA GUIMARÃES; MARTINS, RENATA CASTRO. HABILIDADES DESENVOLVIDAS DURANTE A INICIAÇÃO CIENTÍFICA: RELATO DE UMA ESTUDANTE In: 59ª Reunião Anual da Associação Brasileira de Ensino Odontológico-ABENO, 2024, Belo Horizonte. *Revista da ABENO. Anais da 59ª Reunião da ABENO*. Revista da ABENO, 2024, v.24,
- 6.** PINHEIRO, E. L.; MONTAGNOLI, D. R. A. B. S.; MARTINS, RENATA CASTRO; ABREU, MAURO HENRIQUE NOGUEIRA GUIMARÃES; FERREIRA, R. C.; VARGAS, A. M. D.; INTERCÂMBIO COM O AUTOR: ENSINO DA SAÚDE COLETIVA NA POS-GRADUAÇÃO In: 59a Reunião Anual da Associação Brasileira de Ensino Odontológico-ABENO, 2024, Belo Horizonte. *Revista da ABENO. Anais da 59ª Reunião da ABENO*. Revista da ABENO, 2024, v.24,
- 7.** GODOY, YASMIM SILVA; MONTAGNOLI, D. R. A. B. S.; MARTINS, RENATA CASTRO. INTERFACE ENTRE A INICIAÇÃO CIENTÍFICA E O ATENDIMENTO CLÍNICO DIFERENCIADO In: 59ª Reunião Anual da Associação Brasileira de Ensino Odontológico, 2024, Belo Horizonte. *Revista da ABENO. Anais da 59ª Reunião da ABENO*. Revista da ABENO, 2024, v.24,
- 8.** GODOY, YASMIM SILVA; LEITE, VITÓRIA FERREIRA; MONTAGNOLI, DÉBORA ROSANA ALVES BRAGA SILVA; CRUZ, A. J. S.; COSTA, N. C.; OLIVEIRA, A. C. B.; ABREU, MAURO HENRIQUE NOGUEIRA GUIMARÃES; MARTINS, RENATA CASTRO. PROMOVENDO LETRAMENTO CIENTÍFICO ENTRE ESTUDANTES DE ODONTOLOGIA DE INICIAÇÃO CIENTÍFICA In: 59ª Reunião Anual da Associação Brasileira de Ensino Odontológico-ABENO, 2024, Belo Horizonte. *Revista da ABENO. Anais da 59ª Reunião da ABENO*. Revista da ABENO, 2024, v.24,
- 9.** MONTAGNOLI, D. R. A. B. S.; PINHEIRO, E. L.; MARTINS, RENATA CASTRO; ABREU, MAURO HENRIQUE NOGUEIRA GUIMARÃES; VARGAS, A. M. D.; FERREIRA, R. C.; VOZES DA INIQUIDADE: METODOLOGIA ATIVA NO DOUTORADO EM ODONTOLOGIA-SAÚDE COLETIVA In: 59ª Reunião da Associação Brasileira de Ensino Odontológico-ABENO, 2024, *Revista da ABENO. Anais da 59ª Reunião da ABENO*. Revista da ABENO, 2024, v.24,
- 10.** GODOY, Y. S.; MONTAGNOLI, D. R. A. B. S.; LEITE, V. F.; LAFETA, V. M.; AGUIAR, M. C. F.; ABREU, M. H. N. G.; MARTINS, R. C.; ANÁLISE DOS REGISTROS DE CÂNCER DE LÁBIO POR REGIÕES DO BRASIL In: XVI ENCONTRO CIENTÍFICO DA FACULDADE DE ODONTOLOGIA DA UFMG, 2023, Belo Horizonte. *Revista Arquivos em Odontologia*. 2023, v.59, p.64 - 64
- 11.** BRAGA, D. R. A.; LEITE, V. F.; GODOY, Y. S.; LAFETA, V. M.; AGUIAR, M. C. F.; ABREU, M. H. N. G.; MARTINS, R. C.. Câncer de lábio e fatores de risco para doenças crônicas nas capitais do Brasil In: 40ª Reunião Anual da SBPQO, 2023, Campinas. *Brazilian Oral Research*. 2023, v.37, p.382 - 382
- 12.** LEITE, V. F.; BRAGA, D. R. A.; GODOY, Y. S.; LAFETA, V. M.; AGUIAR, M. C. F.; ABREU, M. H. N. G.; MARTINS, R. C.. Registros de câncer de glândulas salivares antes e no primeiro ano da COVID 19 no Brasil In: 40ª Reunião Anual da SBPQO, 2023, Campinas. *Brazilian Oral Research*. 2023, v.37, p.123 - 123
- 13.** LEITE, V. F.; MONTAGNOLI, D. R. A. B. S.; GODOY, Y. S.; LAFETA, V. M.; AGUIAR, M. C. F.; ABREU, M. H. N. G.; MARTINS, R. C.. REGISTROS DE CÂNCER DE GLÂNDULAS SALIVARES NO BRASIL EM 2021 In: XVI ENCONTRO CIENTÍFICO DA FACULDADE DE ODONTOLOGIA DA UFMG, 2023, Belo Horizonte. *Revista Arquivos em Odontologia*. 2023, v.59, p.63 - 63
- 14.** MONTAGNOLI, D. R. A. B. S.; LEITE, V. F.; GODOY, Y. S.; LAFETA, V. M.; AGUIAR, M. C. F.; ABREU, M. H. N. G.; MARTINS, R. C.. TENDÊNCIA DE REGISTROS DE CÂNCER DE BOCA E OROFARINGE NAS REGIÕES DO BRASIL DE 2019 A 2022 In: XVI ENCONTRO CIENTÍFICO DA FACULDADE DE ODONTOLOGIA DA UFMG, 2023, Belo Horizonte. *Revista Arquivos em Odontologia*. 2023, v.59, p.80 - 80
- 15.** PINHEIRO, E. L.; BRAGA, D. R. A.. ANÁLISE DAS REPORTAGENS JORNALÍSTICAS SOBRE A PESQUISA NACIONAL DE SAÚDE BUCAL 2020 In: VII SEMINÁRIO INTERNACIONAL EM PROMOÇÃO DA SAÚDE, 2022, Fortaleza. *Revista Brasileira em Promoção da Saúde*. 2022, v.35, p.72 - 72
- 16.** LEITE, V. F.; BRAGA, D. R. A.; GODOY, Y. S.; LAFETA, V. M.; AGUIAR, M. C. F.; ABREU, M. H. N. G.; MARTINS, R. C.. AVALIAÇÃO DOS REGISTROS DE CÂNCER ORAL E PRESENÇA DE CENTROS DE ESPECIALIDADES ODONTOLÓGICAS In: VII SEMINÁRIO INTERNACIONAL EM PROMOÇÃO DA SAÚDE, 2022, Fortaleza. *Revista Brasileira em Promoção da Saúde*. 2022, v.35, p.164 - 164
- 17.** BRAGA, D. R. A.; LEITE, V. F.; GODOY, Y. S.; LAFETA, V. M.; AGUIAR, M. C. F.; ABREU, M. H. N. G.; MARTINS, R. C.. CÂNCER DE BOCA E OROFARINGE NO PRIMEIRO ANO DA PANDEMIA DA COVID-19 NO BRASIL In: VII SEMINÁRIO INTERNACIONAL EM PROMOÇÃO DA SAÚDE, 2022, Fortaleza. *Revista Brasileira em Promoção da Saúde*. 2022, v.35, p.69 - 69
- 18.** BRAGA, D. R. A.; LEITE, V. F.; GODOY, Y. S.; LAFETA, V. M.; AGUIAR, M. C. F.; ABREU, M. H. N. G.; MARTINS, R. C.. COMPARAÇÃO DOS REGISTROS DE CÂNCER DE BOCA E OROFARINGE: PERÍODO PRÉ E TRANS PANDEMIA In: VII Seminário Internacional de Promoção da Saúde, 2022, Fortaleza. *Revista Brasileira em Promoção da Saúde*. 2022, v.35, p.12 - 12

Apresentação de trabalho e palestra

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2. Pré-avaliação dos trabalhos submetidos na 59ª Reunião Anual da Associação Brasileira de Ensino Odontológico, 2024. Associação Brasileira de Ensino Odontológico.