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Original Article

Oral Cavity and Oropharyngeal Cancer in Northern Italy, 1996–2020: Long-Term Incidence Trends, 5-Year Survival Improvements, and No Detectable Impact of the COVID-19 Pandemic

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ABSTRACT

Although new therapeutic strategies have emerged, survival outcomes for oral malignancies have not markedly improved, and the condition often imposes significant functional impairment. This study set out to outline the epidemiological pattern of oral cancers within a northern Italian province. Incident cases from 1996–2020 and EU-standardized rates were presented separately for Oral Cavity (OC) and OroPharyngeal (OP) cancers. Annual percent changes (APC) were quantified via joinpoint regression. Five-year survival was examined across three intervals: 1996–2000, 2001–2010, and 2011–2015. Over the 1996–2020 period, 771 oral cancer cases were identified (442 OC; 329 OP), with an age-standardized incidence of 7.28 overall (10.74 for men; 3.97 for women): 3.82 for OC and 3.47 for OP. Among males, OP incidence rose significantly until 2017 (APC 11; 95% CI 4.9–17.5) and subsequently declined; in females, the pattern remained stable. No reduction in incidence was observed for 2020 compared with 2019, despite the Covid-19 pandemic. Five-year survival for diagnoses made in 2011–2015 reached 55.6% for OC, 56.5% for OP, and 56% when combined, with slightly better outcomes for women and modest temporal variation. As of 1 January 2021, 314 individuals were living with a previous diagnosis (175 OC; 139 OP). Findings indicate an overall decrease in male cancer rates—particularly OP—and gradual long-term survival gains. Covid-19 did not adversely influence diagnosis numbers in 2020.

Keywords: Oral cancer, Incidence, Survival, Prevalence, COVID-19

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Introduction

Malignancies of the oral cavity are relatively uncommon, yet they constitute an overlooked public health concern [1]. When all related anatomical subsites are considered together (oral cavity including lips, pharyngeal area, ICD-O III C00–C14) [2], global incidence approaches 500,000 new cases annually. Though anatomically connected, the oral cavity and oropharynx differ in embryologic development and display distinct carcinogenic pathways [3]. Variations in how investigators classify subsites generate inconsistencies in the literature, making it essential to adopt standardized definitions based on location, histology, and tumor behavior. Current consensus recognizes two separate diseases: Oral Cavity cancer (OC) and OroPharyngeal cancer (OP) [4]. This distinction is fundamental for clarifying the proportion attributable to HPV infection [5], in addition to established risks such as tobacco use and alcohol intake [6].

Risk association patterns have long been documented: OC is strongly related to smoking and alcohol [7-9], whereas OP is predominantly linked to HPV infection [10-12]. Morphology also connects these tumors, as squamous cell carcinoma (SCC) constitutes 90%–95%

of OC cases [13]. SCC may originate de novo or evolve from a potentially malignant disorder (PMD), displaying variable dysplasia and a tendency for local tissue invasion [14]. Over 75% of SCCs occur in the lower lip, oral tongue, floor of mouth, or retromolar area. The tumor's biological aggressiveness directly influences prognosis, and T-stage is defined by size and depth of invasion; nodal involvement significantly worsens survival [15]. Five-year survival plummets from roughly 90% to 25%–40% once lymph nodes are affected [3]. Recognized risk determinants include tobacco, alcohol, and HPV [16-20]. Incidence peaks after age 70 and is considerably higher in males [13].

OP typically originates in the tonsillar region or the tongue base, often presenting as poorly differentiated SCC already locally advanced at diagnosis [14]. Although OC and OP share risk factors, HPV contributes a considerably larger proportion of OP cases. Globally, fewer than 30% of OP cancers are HPV-related, but this percentage is rising [16]. Individuals with HPV-positive OP often exhibit small primary tumors with extensive nodal spread, yet their 5-year survival is superior to HPV-negative cases [17]. These tumors more often occur in younger men, and smoking/alcohol appear to play a reduced etiologic role.

Despite ongoing gaps in public understanding of risk factors, expanding communication and data dissemination remains crucial for raising awareness and improving recognition of oral cancer determinants [21]. Italy currently lacks up-to-date epidemiological figures on oral cancer incidence; available 2018 estimates extrapolate trends from 2003–2014, showing declining incidence and mortality in men and slight increases in women [22].

The purpose of this study is to report incidence, survival, and prevalence figures for oral cancer in a northern Italian province and, with 2020 data available, to assess whether Covid-19 influenced the number of new diagnoses.

Materials and Methods

Data source

This investigation is a population-level cohort analysis based on records from the Reggio Emilia Cancer Registry (RE-CR), authorized by the provincial Ethics Committee of Reggio Emilia (Protocol n. 2014/0019740 dated 04/08/2014). The province, located in northern Italy, has roughly 532,000 residents.

The RE-CR documents every newly identified cancer among individuals living in the province. Its primary data streams consist of pathology laboratory reports, hospital discharge information, and mortality files. The registry has operated since 2000, covering the entire provincial population, and includes all incident cancers from 1996 through 2020, with ongoing updates for deaths and residence status for all known cases up to 01/01/2021. Collected variables include anatomical site, morphological classification, diagnostic basis, survival, and prevalence [23].

Definitions of oral cancer

Following the International Classification of Diseases for Oncology, ICD-O (III edition), tumor sites were categorized using predefined coding criteria. Oral cavity malignancies comprise: inner lip (C00.3–C00.9), other and unspecified tongue regions (C02) excluding lingual tonsil (C2.4), gum (C03), floor of mouth (C04), palate (C05), and other or undefined oral locations (C06) [2].

To align data with contemporary literature, oral tumors were grouped according to the scheme introduced by Conway [4]. Oropharyngeal neoplasms include: base of tongue (C01), lingual tonsil (C2.4), tonsil (C09), oropharynx (C10), and nonspecific pharyngeal sites including Waldeyer's ring or overlapping oral–pharyngeal regions (C14).

Beyond categorization by anatomical site, tumors were also described by morphology as defined in ICD-O III; this includes all coded histotypes, such as non-Hodgkin lymphoma arising in Waldeyer's ring.

Data analyses

Analyses were restricted to invasive malignancies in individuals who resided in Reggio Emilia at diagnosis, consistent with national [24] and international standards [25].

Per registry protocols, in situ lesions and tumors classified as benign or of uncertain behavior were excluded, except for bladder and central nervous system cancers. These standardized criteria enable reliable comparison with registries worldwide. Descriptive summaries were produced separately for OP and OC tumors. Age-adjusted incidence (standardized to the 2013 European Standard Population) for 2019–2020 and temporal incidence patterns for 1996–2020 are presented by sex and tumor group. Time-related patterns were evaluated using annual percent change (APC) estimates derived from Joinpoint Regression [26].

For survival, incident cases from 1996–2015 were analyzed across three intervals (1996–2000, 2001–2010, 2011–2015). Five-year survival curves for OP and OC cancers were generated using the Kaplan–Meier method, stratified by sex and period, to determine whether outcomes shifted across intervals.

Graphical displays and tabulated values summarize findings.

Prevalence as of January 1, 2021 was calculated by diagnosis interval (<2, 2–9, ≥9 years), subtype, and sex. All statistical procedures were performed using StataSE v. 16.1 (StataCorp LP, College Station, TX).

Results and Discussion

Across 1996–2020, the registry documented 771 oral cancer cases, comprising 442 OC and 329 OP tumors. The mean age at diagnosis was approximately 65.5 years, with a male predominance (M:F ratio ≈ 2:1). Case numbers rose across the five-year periods examined, increasing from 107 in 1996–2000 to 174 in 2016–2020.

For OC, the most frequent sites were the dorsal tongue (124 cases), the mouth (86 cases), and overlapping tongue lesions (53 cases). For OP, tonsillar cancers accounted for most cases (184). These distributions are presented in **Table 1**.

Table 1. Distribution of 771 oral cancer cases by age, sex, diagnostic interval, tumor site, and morphology.

Characteristic	Oral Cavity Cancer		Oropharyngeal Cancer		Total
	n	%	n	%	n
Overall	442		329		771
Age (mean ± SD)	66.9 ± 14.4		63.5 ± 13.1		65.5 ± 13.9
Sex					
Male	279	63.1	233	70.8	512
Female	163	36.9	96	29.2	259
Diagnosis Year					
1996–2000	66	14.9	41	12.5	107
2001–2005	89	20.1	60	18.2	149
2006–2010	87	19.7	96	29.2	183
2011–2015	97	21.9	61	18.5	158
2016–2020	103	23.3	71	21.6	174
Anatomic Site					
Lip (C00.3–C00.9)	28	6.3	—	—	—
Dorsal surface of tongue, NOS (C02.0–C02.3)	124	28.1	—	—	—
Overlapping lesion of tongue or tongue NOS (C02.8–C02.9)	53	12.0	—	—	—
Gum (C03)	41	9.3	—	—	—
Floor of mouth (C04)	45	10.2	—	—	—
Soft palate (C05.1)	29	6.6	—	—	—
Uvula (C05.2)	2	0.5	—	—	—
Overlapping lesion of palate or palate NOS (C05.8)	0	0.0	—	—	—
Cheek mucosa (C06.0)	34	7.7	—	—	—
Overlapping/unspecified mouth (C06.8–C06.9)	86	19.5	—	—	—
Base of tongue, NOS (C01.0–C01.9)	—	—	101	30.7	—
Lingual tonsil (C02.4)	—	—	4	1.2	—
Tonsil (C09)	—	—	184	55.9	—
Anterior surface of epiglottis (C10.1)	—	—	3	0.9	—
Lateral wall of oropharynx (C10.2)	—	—	11	3.3	—
Pharynx unspecified/overlapping (C14.0)	—	—	24	7.3	—
Waldeyer's ring (C14.2)	—	—	2	0.6	—
Histological Type					
Total	442	100	329	100	771
Carcinoma (non-specified)	41	9.3	20	6.1	61
Squamous cell carcinoma	375	84.8	266	80.9	641
Adenocarcinoma	23	5.2	4	1.2	27
Lymphomas	3	0.7	39	11.9	42

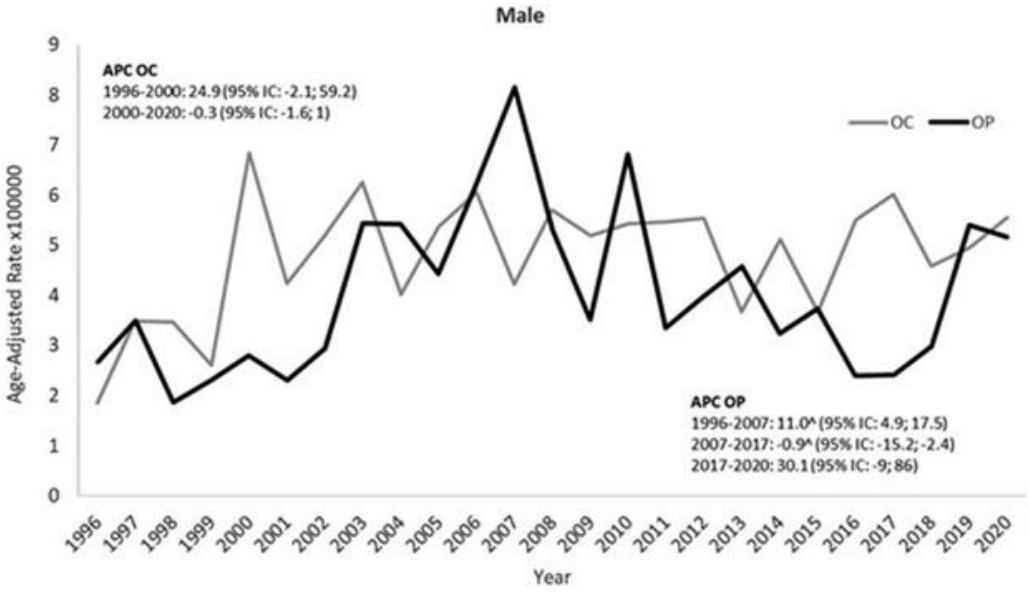
With respect to histology, 84.8% of OC tumors and 80.9% of OP tumors were squamous in nature, while 11.9% of OP lesions were classified as lymphomas. In 2020, the age-standardized incidence reached 7.28 overall (10.74 for men, 3.97 for women), exceeding the 2019 estimate of 5.60 (10.36 in men, 1.33 in women). When examining individual subsites during the most recent period influenced by Covid-19, OC and OP showed values of 3.82 and 3.47 in 2020, higher than the 2.62 and 2.97 recorded in 2019 **(Table 2)**.

Table 2. Age-standardized incidence by subtype and sex, 2020 vs. 2019.

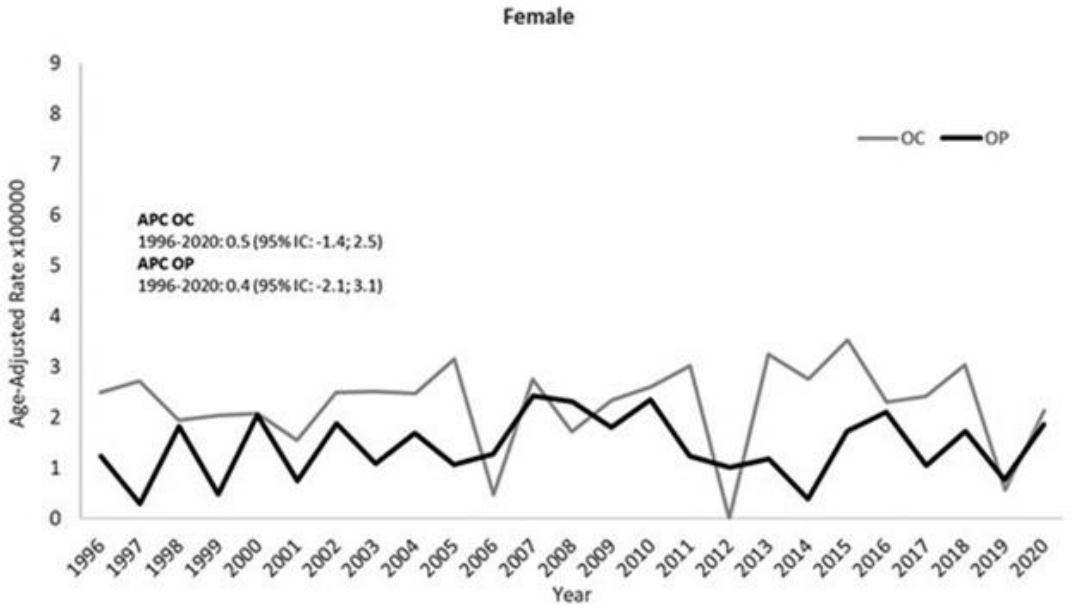
Cancer Site	2019			2020		
	Cases (n)	Crude Incidence Rate*	Age-Standardized Incidence Rate†	Cases (n)	Crude Incidence Rate*	Age-Standardized Incidence Rate†
Oral cavity cancer						
Total	15	2.82	2.62	22	4.15	3.82
Males	13	4.97	4.96	15	5.75	5.56
Females	2	0.74	0.56	7	2.60	2.12
Oropharyngeal cancer						
Total	17	3.20	2.97	20	3.78	3.47
Males	14	5.35	5.40	14	5.37	5.17
Females	3	1.11	0.76	6	2.23	1.85
Oral cavity and oropharyngeal cancer combined						
Total	32	6.02	5.60	42	7.93	7.28
Males	27	10.32	10.36	29	11.12	10.74
Females	5	1.85	1.33	13	4.83	3.97

a EUROPE 2013.

Among males, OP incidence rose up to 2007, then moved downward; the uptick noted in the last two years aligns with normal random variability. OC increased sharply between 1996 and 2000 and afterwards remained stable **(Figure 1)**. In females, both OC and OP maintained nearly unchanged incidence throughout the timeline.



a)



b)

Figure 1. European age-standardized incidence trajectories for OC and OP in males and females (1996–2020).

Five-year survival for OC + OP measured 51.2% (95% CI 41.3–60.2), 50.7% (95% CI 45.2–56.0), and 56.0% (95% CI 47.7–63.4) in the three evaluated eras **(Table 3; Figure 2)**. For OC alone, survival was 52.6% (95% CI 39.9–63.9), then 45.1% (95% CI 37.5–52.3), then 55.6% (95% CI 45.0–65.0). For OP, the corresponding values were 48.8% (95% CI 32.9–62.9), 57.1% (95% CI 48.9–64.4), and 56.5% (95% CI 43.0–68.1).

Table 3. Five-year survival by subtype, sex, and period (1996–2015).

Cancer Site	1996–2000		2001–2010		2011–2015	
	5-year Survival (%)	95% Confidence Interval	5-year Survival (%)	95% Confidence Interval	5-year Survival (%)	95% Confidence Interval
Oral cavity cancer						
Overall	52.6%	39.9% – 63.9%	45.1%	37.5% – 52.3%	55.6%	45.0% – 65.0%
Males	59.5%	42.0% – 73.2%	43.6%	34.2% – 52.5%	56.3%	42.2% – 68.3%
Females	43.6%	25.2% – 60.6%	47.8%	34.9% – 59.6%	54.7%	38.0% – 68.6%
Oropharyngeal cancer						
Overall	48.8%	32.9% – 62.9%	57.1%	48.9% – 64.4%	56.5%	43.0% – 68.1%
Males	44.4%	25.6% – 61.8%	56.3%	46.6% – 64.9%	53.9%	38.4% – 67.1%
Females	57.1%	28.4% – 78.0%	59.1%	43.2% – 71.9%	66.7%	37.5% – 84.6%
Oral cavity and oropharyngeal cancer combined						
Overall	51.2%	41.3% – 60.2%	50.7%	45.2% – 56.0%	56.0%	47.7% – 63.4%
Males	53.1%	40.3% – 64.4%	49.9%	43.2% – 56.3%	55.1%	44.8% – 64.2%
Females	48.1%	32.5% – 62.1%	52.5%	42.6% – 61.5%	57.8%	43.5% – 69.6%

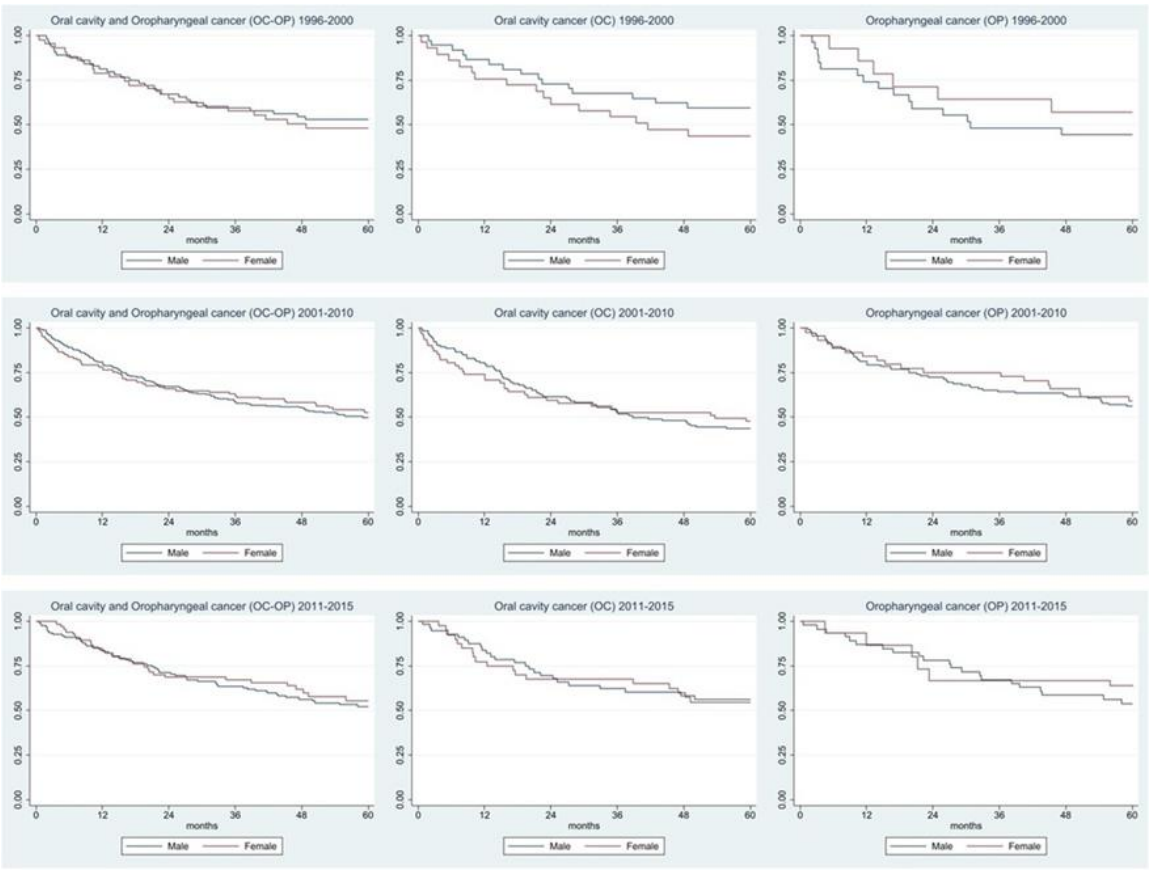


Figure 2. Survival curves across three time periods by subtype and sex.

As of January 1, 2021, 314 people diagnosed in previous years were still alive (175 OC; 139 OP), with men roughly twice as numerous as women. Within OC, most individuals had been diagnosed 2–9 years earlier, whereas within OP, the largest share had diagnoses made ≥9 years earlier **(Table 4)**.

Table 4. Prevalence on January 1, 2021 by subtype, sex, and years since diagnosis.

Cancer Site	Sex	Total (All years)	Survival <2 years	Survival 2–9 years	Survival ≥10 years
Oral cavity cancer					
	Male	23	50	39	112
	Female	6	32	25	63
Oropharyngeal cancer					
	Male	22	25	50	97
	Female	8	16	18	42
Oral cavity and oropharyngeal cancer combined					
	Male	45	75	89	209
	Female	14	48	43	105

This analysis documented incidence levels of 3.8/100,000 (OC) and 3.5/100,000 (OP), with male-to-female ratios of 2.6:1 and 2.8:1, respectively. Global statistics from GLOBOCAN 2012 [27] indicated an overall age-standardized estimate near 4/100,000, comprising 2.7/100,000 for OC and 1.4/100,000 for OP. Internationally, men show higher rates, typically 2:1 for OC and 4.8:1 for OP [28]. OP rates in our setting are among the highest in Europe, whereas OC aligns with figures from other high-income nations [28].

For males, incidence rose in the early years for both cancer types; OC subsequently stabilized, while OP declined until roughly 2017. Among females, no meaningful changes appeared over time. Published work indicates that OP incidence is rising quickly in upper-income countries—especially the U.S. [29, 30]. OC, conversely, tends to be steady or decreasing in

men and mildly rising in women [31]. In England (1995–2011), OC showed yearly increases of 2.8% (men) and 3.0% (women), whereas OP rose 7.3% in men and 6.5% in women [32]. In Scotland (2001–2012), OP increased by 85%, and OC by 10%, with larger shifts among males [32-34] and in deprived communities [33]. These patterns reflect varying contributions from key risk determinants: HPV—much more relevant for OP—expanded in high-income settings [35, 36] and in Italy [37], while alcohol and tobacco exposure, traditionally higher among men, have changed unevenly, with steeper declines in male smoking rates [38].

Several investigations have linked the Covid-19 period to reduced cancer detection. For instance, an Italian study from the Turin metropolitan area [39] observed only 1 OSCC case when 7 were expected, attributing this drop to postponed dental procedures [39]. In contrast, our dataset did not reveal a fall in diagnoses during 2020, consistent with the incidence patterns shown in **Figure 1**.

As for survival, the final period showed a modest rise for both OC and OP, although the magnitude of this change was small enough to fall within what could be expected from normal statistical variation. When examining specific anatomic subsites, OC survival tends to be higher in men, whereas OP survival is better in women. In the report by Montero [40], covering 1960–2012, overall survival improved by 15%, increasing from 48% in 1960–1964 to 63% in 1985–2012. That work also documented 5-year outcomes ranging from 78.5% for stage I to 34.5% for stage IV [41], a pattern echoed by other estimates of 10%–40% [42, 43].

Published evidence indicates that roughly two thirds of OC cases [41-43] are detected at advanced stages (III or IV) [43], where 5-year survival generally falls below 50% [44]. In early disease (stage I or II), oral squamous lesions may produce few or no symptoms, leading many individuals to postpone dental or specialist visits until the condition becomes noticeably worse and substantially harder to manage [45]. In the absence of treatment, patients who already have metastatic spread typically survive only about 4 months [41].

Another challenge stems from the lack of uniform terminology in the literature; the diagnostic labels applied to these tumors have varied, and the broad category of "head and neck cancer" has often obscured distinctions between different anatomical sites. Increasingly, oral cancer is conceptualized as two separate entities: malignancies of the oral cavity and those of the oropharynx. This issue of inconsistent definitions was also highlighted in an English study from 2018 [4]. When the two sites are considered individually, OC accounts for approximately 377,000 new cases and 177,000 deaths annually worldwide, while OP represents around 100,000 new diagnoses and close to 50,000 deaths each year [46, 47].

Because of these definitional complexities, estimating the number of prevalent cases is also problematic [48]. Given the combination of relatively low incidence and modest survival, the number of people living with a prior diagnosis remains small—a little over 300 in our province. This point is relevant because clinical management must address not only newly diagnosed patients and those with precancerous lesions, but also the persistent risk of local recurrence, one of the most difficult aspects of long-term follow-up.

Among the study limitations, we lack information on individual risk factors such as tobacco use, alcohol consumption, and HPV status, and we do not possess stage data.

On the other hand, the study's strengths include a full 25-year incidence series, population-based data free from selection bias, and the inclusion of 2020, a year already influenced by pandemic-related disruptions.

Conclusion

The combination of long-term and recent data provides a clearer picture of how oral cancers are evolving over time. Shifts in terminology and diagnostic criteria, along with changes in exposure to key risk determinants (notably smoking and HPV), help explain the rapid epidemiologic transitions now being observed. In our region, Covid-19 does not appear to have reduced the number of new diagnoses.

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Conflict of Interest: None

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Ethics Statement: This population-based cohort study uses data from the Reggio Emilia Cancer Registry, approved by the Provincial Ethics Committee of Reggio Emilia (ref. no. 2014/0019740 of 4 August 2014). The Ethics Committee authorized, even in the absence of consent, the processing of personal data, including those suitable for revealing the state of health of patients who are deceased or untraceable for the execution of the study.

References

1. The Oral Cancer Foundation. Oral cancer facts. Available from: https://oralcancerfoundation.org/facts/ (Accessed May 3, 2022).
2. Fritz AG. International classification of diseases for oncology: ICD-O. 3rd ed. Geneva, Switzerland: World Health Organization; (2000). [Google Scholar]
3. American Cancer Society. Facts / figures 2021. Atlanta, GA: American Cancer Society; (2021). [Google Scholar]
4. Conway DI, Purkayastha M, Chestnutt IG. The changing epidemiology of oral cancer: definitions, trends, and risk factors. Br Dent J. (2018) 225(9):867–73. 10.1038/sj.bdj.2018.922 [DOI] [PubMed] [Google Scholar]
5. Tulay P, Serakinci N. The role of human papillomaviruses in cancer progression. J Cancer Metastasis Treat. (2016) 2:201–13. 10.20517/2394-4722.2015.67 [DOI] [Google Scholar]
6. Elkashty OA, Ashry R, Tran SD. Head and neck cancer management and cancer stem cells implication. Saudi Dent J. (2019) 31(4):395–416. 10.1016/j.sdentj.2019.05.010 [DOI] [PMC free article] [PubMed] [Google Scholar]
7. Blot WJ, McLaughlin JK, Winn DM, Austin DF, Greenberg RS, Preston-Martin S, et al. Smoking and drinking in relation to oral and pharyngeal cancer. Cancer Res. (1988) 48(11):3282–7. PMID: [PubMed] [Google Scholar]
8. Tuyns AJ, Estève J, Raymond L, Berrino F, Benhamou E, Blanchet F, et al. Cancer of the larynx/hypopharynx, tobacco and alcohol: IARC international case-control study in Turin and Varese (Italy), Zaragoza and Navarra (Spain), Geneva (Switzerland) and Calvados (France). Int J Cancer. (1988) 41(4):483–91. 10.1002/ijc.2910410403 [DOI] [PubMed] [Google Scholar]
9. Hashibe M, Brennan P, Chuang SC, Boccia S, Castellsague X, Chen C, et al. Interaction between tobacco and alcohol use and the risk of head and neck cancer: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. Cancer Epidemiol Biomarkers Prev. (2009) 18(2):541–50. 10.1158/1055-9965.EPI-08-0347 [DOI] [PMC free article] [PubMed] [Google Scholar]
10. Chaturvedi AK, Engels EA, Pfeiffer RM, Hernandez BY, Xiao W, Kim E, et al. Human papillomavirus and rising oropharyngeal cancer incidence in the United States. J Clin Oncol. (2011) 29(32):4294–301. 10.1200/JCO.2011.36.4596 [DOI] [PMC free article] [PubMed] [Google Scholar]
11. Adelstein DJ, Ridge JA, Gillison ML, Chaturvedi AK, D'Souza G, Gravitt PE, et al. Head and neck squamous cell cancer and the human papillomavirus: summary of a National Cancer Institute State of the Science Meeting, November 9–10, 2008, Washington, D.C. Head and Neck. (2009) 31(11):1393–422. 10.1002/hed.21269 [DOI] [PubMed] [Google Scholar]
12. Gillison ML, D'Souza G, Westra W, Sugar E, Xiao W, Begum S, et al. Distinct risk factors profiles for human papillomavirus type 16-positive and human papillomavirus type-16 negative head and neck cancers. J Natl Cancer Inst. (2008) 100(6):407–20. 10.1093/jnci/djn025 [DOI] [PubMed] [Google Scholar]
13. Watters C, Brar S, Pepper T. Oral Mucosa Cancer. [Updated 2021 Apr 13]. In: StatPearls. Treasure Island, FL: StatPearls Publishing (2022).
14. Vogel TWD, Zbaeren P, Thoeny HC. Cancer of the oral cavity and oropharynx. Cancer Imaging. (2010) 10(1):62–72. 10.1102/1470-7330.2010.0008 [DOI] [PMC free article] [PubMed] [Google Scholar]
15. Brierley JD, Gospodarowicz MK, Wittekind C. (eds). TNM Classification of malignant tumours. 8th ed. Chichester: John Wiley and Sons; (2017). [Google Scholar]
16. Rivera C. Essentials of oral cancer. Int J Clin Exp Pathol. (2015) 8(9):11884–94. PMID: ; PMCID: [PMC free article] [PubMed] [Google Scholar]
17. Gandini S, Botteri E, Iodice S, Boniol M, Lowenfels AB, Maisonneuve P, et al. Tobacco smoking and cancer: a meta-analysis. Int J Cancer. (2008) 122(1):155–64. 10.1002/ijc.23033 [DOI] [PubMed] [Google Scholar]
18. Lee YC, Marron M, Benhamou S, Bouchardy C, Ahrens W, Pohlabeln H, et al. Active and involuntary tobacco smoking and upper aerodigestive tract cancer risks in a multicenter case-control study. Cancer Epidemiol Biomarkers Prev. (2009) 18(12):3353–61. 10.1158/1055-9965.EPI-09-0910 [DOI] [PMC free article] [PubMed] [Google Scholar]
19. Kumar M, Nanavati R, Modi TG, Dobariya C. Oral cancer: etiology and risk factors: a review. J Cancer Res Ther. (2016) 12(2):458–63. 10.4103/0973-1482.186696 [DOI] [PubMed] [Google Scholar]

20. Jafarey NA, Mahmood Z, Zaidi SH. Habits and dietary pattern of cases of carcinoma of the oral cavity and oropharynx. J Pak Med Assoc. (1977) 27(6):340–3. PMID: [PubMed] [Google Scholar]
21. Amer HW, Wahed AA, Badawi OA, Emara AS. Oral cancer awareness level within the dental community: results from a large scale survey in cairo. J Cancer Educ. (2018) 33(6):1279–84. 10.1007/s13187-017-1243-2 [DOI] [PubMed] [Google Scholar]
22. AIOM, AIRTUM, PASSI. I numeri del cancro in Italia 2018. Intermedia Editore Brescia (2018).
23. Cancer Incidence in Five Continents Volume XI. IARC Scientific Publication No. 166. Edited by Bray F, Colombet M, Mery L, Piñeros M, Znaor A, Zanetti R, Ferlay J. https://ci5.iarc.fr/ci5-xi/Default.aspx
24. AIRTUM - Associazione Italiana Registri Tumori. Manuale di Tecniche di Registrazione dei Tumori. Piccin-Nuova Libraria, gennaio (2021).
25. https://www.encr.eu/ (EUROPEAN NETWORK OF CANCER REGISTRIES)
26. Joinpoint Regression Program, Version 4.9.0.0. Statistical Research and Applications Branch, National Cancer Institute (2021).
27. https://gco.iarc.fr/ (GLOBOCAN).
28. Shield KD, Ferlay J, Jemal A, Sankaranarayanan R, Chaturvedi AK, Bray F, et al. The global incidence of lip, oral cavity, and pharyngeal cancers by subsite in 2012. CA Cancer Clin J. (2017) 67(1):51–64. 10.3322/caac.21384 [DOI] [PubMed] [Google Scholar]
29. Gillison ML, Chaturvedi AK, Anderson WF, Fakhry C. Epidemiology of human papillomavirus-positive head and neck squamous cell carcinoma. J Clin Oncol. (2015) 33(3):235–42. 10.1200/JCO.2014.59.0919 [DOI] [PMC free article] [PubMed] [Google Scholar]
30. Mehanna H, Beech T, Nicholson T, El-Hariry I, McConkey C, Paleri V, et al. The prevalence of human papillomavirus in oropharyngeal and nonoropharyngeal head and neck cancer: systematic review and meta-analysis of trends by time and region. Head Neck. (2013) 35:747–55. 10.1002/hed.22015 [DOI] [PubMed] [Google Scholar]
31. Chaturvedi AK, Anderson WF, Lortet-Tieulent J, Curado MP, Ferlay J, Franceschi S, et al. Worldwide trends in incidence rates for oral cavity and oropharyngeal cancers. J Clin Oncol. (2013) 31(4):550–9. 10.1200/JCO.2013.50.3870 [DOI] [PMC free article] [PubMed] [Google Scholar]
32. Louie KS, Mehanna H, Sasieni P. Trends in head and neck cancers in England from 1995 to 2011 and projections up to 2025. Oral Oncol. (2015) 51:341–8. 10.1016/j.oraloncology.2015.01.002 [DOI] [PubMed] [Google Scholar]
33. Purkayastha M, McMahon AD, Gibson J, Conway DI. Trends of oral cavity, oropharyngeal and laryngeal cancer incidence in Scotland (1975–2012) – A socioeconomic perspective. Oral Oncol. (2016) 61:70–5. 10.1016/j.oraloncology.2016.08.015 [DOI] [PubMed] [Google Scholar]
34. Junor EJ, Kerr GR, Brewster DH. Oropharyngeal cancer. Fastest increasing cancer in Scotland, especially in men. Br Med J. (2010) 340:c2512. 10.1136/bmj.c2512 [DOI] [PubMed] [Google Scholar]
35. Faraji F, Rettig EM, Tsai HL, El Asmar M, Fung N, Eisele DW, et al. The prevalence of human papillomavirus in oropharyngeal cancer is increasing regardless of sex or race, and the influence of sex and race on survival is modified by human papillomavirus tumor status. Cancer. (2019) 125(5):761–9. 10.1002/cncr.31841 [DOI] [PubMed] [Google Scholar]
36. Ellington TD, Henley SJ, Senkomago V, O'Neil ME, Wilson RJ, Singh S, et al. Trends in incidence of cancers of the oral cavity and pharynx - United States 2007-2016. MMWR Morb Mortal Wkly Rep. (2020) 69(15):433–8. 10.15585/mmwr.mm6915a1 [DOI] [PMC free article] [PubMed] [Google Scholar]
37. Del Mistro A, Frayle H, Menegaldo A, Favaretto N, Gori S, Nicolai P, et al. Age-independent increasing prevalence of Human Papillomavirus-driven oropharyngeal carcinomas in North-East Italy. Sci Rep. (2020) 10(1):9320. 10.1038/s41598-020-66323-z [DOI] [PMC free article] [PubMed] [Google Scholar]
38. Institute for Health Metrics and Evaluation (IHME). GBD Compare data visualization. Seattle, WA: IHME, University of Washington; (2020). Available from: http://vizhub.healthdata.org/gbd-compare (Accessed March 16, 2022). [Google Scholar]
39. Arduino PG, Conrotto D, Broccoletti R. The outbreak of Novel Coronavirus disease (COVID-19) caused a worrying delay in the diagnosis of oral cancer in north-west Italy: The Turin Metropolitan Area experience. Oral Dis. (2021) Suppl 3(Suppl 3):742–3. 10.1111/odi.13362 [DOI] [PMC free article] [PubMed] [Google Scholar]

40. Montero PH, Patel SG. Cancer of the oral cavity. Surg Oncol Clin N Am. (2015) 24(3):491–508. 10.1016/j.soc.2015.03.006 [DOI] [PMC free article] [PubMed] [Google Scholar]
41. Kowalski LP, Carvalho AL. Natural history of untreated head and neck cancer. Eur J Cancer. (2000) 36:1032–7. 10.1016/S0959-8049(00)00054-X [DOI] [PubMed] [Google Scholar]
42. Yao M, Epstein JB, Modi BJ, Pytynia KB, Mundt AJ, Feldman LE. Current surgical treatment of squamous cell carcinoma of the head and neck. Oral Oncol. (2007) 43:213–23. 10.1016/j.oraloncology.2006.04.013 [DOI] [PubMed] [Google Scholar]
43. Guneri P, Epstein JB. Late stage diagnosis of oral cancer: components and possible solutions. Oral Oncol. (2014) 50:1131–6. 10.1016/j.oraloncology.2014.09.005 [DOI] [PubMed] [Google Scholar]
44. Viet CT, Schmidt BL. Biologic mechanisms of oral cancer pain and implications for clinical therapy. J Dent Res. (2012) 91:447–53. 10.1177/0022034511424156 [DOI] [PMC free article] [PubMed] [Google Scholar]
45. Rodríguez-Archilla A. Diagnostic Delay in Oral Cancer (2017). Available from: https://scientonline.org/abstract/21675/Diagnostic-Delay-in-Oral-Cancer (Accessed July 1, 2022).
46. https://seer.cancer.gov/statfacts/html/oralcav.html The National Cancer Institute, Surveillance, Epidemiology, and End Results Program. Cancer stat facts: oral cavity and pharynx cancer.Available from: (Accessed August 20, 2020.)
47. Ferlay J, Colombet M, Soerjomataram I, Parkin MD, Piñeros M, Znaor A, et al. Cancer statistics for the year 2020: an overview. Int J Cancer. (2021) 149:778–89. 10.1002/ijc.33588 [DOI] [PubMed] [Google Scholar]
48. Inchingolo F, Santacroce L, Ballini A, Topi S, Dipalma G, Haxhirexha K, et al. Oral cancer: a historical review. Int J Environ Res Public Health. (2020) 17(9):3168. 10.3390/ijerph17093168 [DOI] [PMC free article] [PubMed] [Google Scholar]